Total Burn Care
The last 25 years burn care has improved to the extent that
persons with burns covering 90% of their total body surface
area can frequently survive. In the five years since the publi-
cation of the third edition of this book basic and clinical
sciences have continued to provide information further elu-
cidating the complexities of burn injuries and opportunities
for improvement in care. In this edition advances in the
treatment of burn shock, inhalation injury, sepsis, hyperme-
tabolism, the operative excision of burn wounds, scar recon-
struction and rehabilitation are completely reexamined.
Burn care demands attention to every organ system as well
as to the patient’s psychological and social status. The scope
of burn treatment extends beyond the preservation of life
and function; and the ultimate goal is the return of burn
survivors as full participants back into their communities.

The fourth edition has been extensively updated with
massive additions and new data, new references; almost all
chapters have been totally rewritten and updated. There are
many new chapters and sections in this edition along with
demonstrative color illustrations throughout the book.

Totally new to this edition is a web based support section
for many of the chapters that include powerpoint presenta-
tions and helpful videos. Power points should allow visual
representations of the topics covered in chapters for group
discussions and individual burn units. Video clips should
allow better understanding of complex procedures and
concepts.

New material has been added to this edition reflecting
the varied physiologic, psychological and emotional care of
acutely burned patients evolving through recovery, rehabili-
tation, and reintegration back into society and daily life
activities.

The scope of burn treatment extends beyond the preser-
vation of life and function and the ultimate goal is the
return of burn survivors, as full participants, back into their
communities.

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respected colleagues and friends who have volunteered
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A brief history of acute burn care management
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The recognition of burns and their treatment is evident in cave paintings which are over 3500 years old. Documentation in the Egyptian Smith papyrus of 1500 BC advocated the use of a salve of resin and honey for treating burns.1 In 600 BC, the Chinese used tinctures and extracts from tea leaves. Nearly 200 years later, Hippocrates described the use of rendered pig fat and resin impregnated in bulky dressings which was alternated with warm vinegar soaks augmented with tanning solutions made from oak bark. Galen, in the first century AD, mentioned the use of wine and myrrh as a lotion for burns, most probably for their bacteriostatic properties.1 Vinegar and exposure of the open wound to air was used by Galen, who lived from 130 to 210 AD, as a means of treating burns, while the Arabian physician Rhases recommended cold water for alleviating the pain associated with burns. Ambroise Paré (1510–1590 AD), who effectively treated burns with onions, was probably the first to describe a procedure for early burn wound excision. In 1607 Guilielmus Fabricius Hildanus, a German surgeon, published De Combustionibus, in which he discussed the pathophysiology of burns and made unique contributions to the treatment of contractures. In 1797, Edward Kentish published an essay describing pressure dressings as a means to relieve burn pain and blisters. Around this same time, Marjolin identified squamous cell carcinomas that developed in chronic open burn wounds. In the early 19th century, Guillaume Dupuytren (Figure 1.1) reviewed the care of 50 burn patients treated with occlusive dressings and developed a classification of burn depth that remains in use today.7 He was, perhaps, the first to recognize gastric and duodenal ulceration as a complication of severe burns, a problem that was discussed in more detail by Curling of London in 1842.3 In 1843 the first hospital for the treatment of large burns used a cottage on the grounds of the Edinburgh Royal Infirmary.

Truman G. Blocker Jr (Figure 1.2) may have been the first to demonstrate the value of the multidisciplinary team approach to disaster burns when, on 16 April 1947, two freighters loaded with ammonium nitrate fertilizer exploded at a dock in Texas City, killing 560 people and injuring more than 3000. At that time, Blocker mobilized the University of Texas Medical Branch in Galveston, Texas, to treat the arriving truckloads of casualties. This ‘Texas City Disaster’ is still known as the deadliest industrial accident in American history. Over the next 9 years, Truman and Virginia Blocker followed more than 800 of these burn patients and published a number of papers and government reports on their findings.4–6 The Blockers became renowned for their work in advancing burn care, with both receiving the Harvey Allen Distinguished Service Award from the American Burn Association. Truman Blocker Jr was also recognized for his pioneering research in treating burns ‘by cleansing, exposing the burn wounds to air, and feeding them as much as they could tolerate’. In 1962, his dedication to treating burned children convinced the Shriners of North America to build their first Burn Institute for Children in Galveston, Texas.7

Between 1942 and 1952, shock, sepsis, and multiorgan failure caused a 50% mortality rate in children with burns covering 50% of their total body surface area.6 Recently, burn care in children has improved survival such that a burn covering more than 95% total body surface area (TBSA) can be survived in over 50% of cases.9 In the 1970s Andrew M. Munster (Figure 1.3) became interested in measuring quality of life, when excisional surgery and other improvements led to a dramatic decrease in mortality. First published in 1982, his Burn Specific Health Scale became the foundation for most modern studies in burns outcome.10 The scale has since been updated and extended to children.11

Further improvements in burn care presented in this brief historical review include excision and coverage of the burn wound, control of infection, fluid resuscitation, nutritional support, treatment of major inhalation injuries, and support of the hypermetabolic response.

Early excision

In the early 1940s, it was recognized that one of the most effective therapies for reducing mortality from a major thermal injury was the removal of burn eschar and immediate wound closure.12 This approach had previously not been practical in large burns owing to the associated high rate of infection and blood loss. Between 1954 and 1959, Douglas Jackson and colleagues, at the Birmingham Accident Hospital, advanced this technique in a series of pilot and controlled trials, starting with immediate fascial excision and grafting of small burn areas, and eventually covering up to 65% of the TBSA with autograft and homograft skin.13 In this breakthrough publication, Jackson concluded that ‘with adequate safeguards, excision and grafting of 20% to 30% body surface area can be carried out on the day of injury without increased risk to the patient’. This technique, however, was far from being accepted by the majority of burn surgeons, and delayed serial excision remained the prevalent approach to large burns. It was Zora Janzekovic (Figure 1.4),
tangential excision to non-operative treatment of burns. This study showed that, compared to non-operative treatment, early excision and grafting of deep second-degree burns reduced hospitalization time and hypertrophic scarring. In 1988, Ron G. Tompkins et al.,\(^1\) in a statistical review of the Boston Shriners Hospital patient population from 1968 to 1986, reported a dramatic decrease in mortality in severely burned children which he attributed mainly to the advent of early excision and grafting of massive burns in use since the 1970s. In a randomized prospective trial of 85 patients with

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**Figure 1.1** Guillaume Dupuytren.

**Figure 1.2** Truman G. Blocker Jr.

**Figure 1.3** Andrew M. Munster.

**Figure 1.4** Zora Janzekovic.
A brief history of acute burn care management

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In 1981, John Burke and Ioannis Yannas developed an artificial skin which consists of a silastic epidermis and a porous collagen–chondroitin dermis, and is marketed today as Integra. Burke was also the first to use this artificial skin on very large burns which covered over 80% of the TBSA.

Skin grafting

Progress in skin grafting techniques has paralleled the developments in wound excision. In 1869, J. P. Reverdin, a Swiss medical student, successfully reproduced skin grafts. In the 1870s, George David Pollock popularized the method in England. The method gained widespread attention throughout Europe, but as the results were extremely variable it quickly fell into disrepute. J.S. Davis resurrected this technique in 1914 and reported the use of ‘small deep skin grafts’, which were later known as pinch grafts. Split-thickness skin grafts became more popular during the 1930s, due, in part, to improved and reliable instrumentation. The ‘Humby knife’, developed in 1936, was the first reliable dermatome, but its use was cumbersome. E.C. Padgett developed an adjustable dermatome which had cosmetic advantages and allowed the procurement of a consistent split-thickness skin graft. Padgett also developed a system for categorizing skin grafts into four types based on thickness. In 1964 J.C. Tanner Jr and colleagues revolutionized wound grafting with the development of the meshed skin graft; however, for prompt excision and immediate wound closure to be practical in burns covering more than 50% of the TBSA, alternative materials and approaches to wound closure were necessary. To meet these demands, a system of cryopreservation and long-term storage of human skin for periods extending up to several months was developed. Although controversy surrounds the degree of viability of the cells within the preserved skin, this method has allowed greater flexibility in the clinical use of autologous skin and allogenic skin harvested from cadavers. J. Wesley Alexander (Figure 1.7) developed a simple method for widely expanding autograft skin and then covering it with cadaver skin. This so-called ‘sandwich technique’ has been the mainstay of treatment of massively burned individuals.

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David Heimbach led one of the early multicenter randomized clinical trials using Integra. Its use in the coverage of extensive burns has remained limited, partly due to the persistently high cost of the material and the need for a two-stage approach. Integra has since become popular for smaller immediate burn coverage and burn reconstruction. In 1989, J.F. Hansbrough and S.T. Boyce first reported the use of cultured autologous keratinocytes and fibroblasts on top of a collagen membrane (composite skin graft, CSS). A larger trial by Boyce revealed that the use of CSS in extensive burns reduces the requirement for harvesting of donor skin compared to conventional skin autografts, and that the quality of grafted skin did not differ between CSS and skin autograft after 1 year. The search for an engineered skin substitute to replace all of the functions of intact human skin is ongoing; composite cultured skin analogs, perhaps combined with mesenchymal stem cells, may offer the best opportunity for better outcomes.

Topical control of infection

An important major advancement in burn care that has reduced mortality is infection control. One of the first topical antimicrobials, sodium hypochlorite (NaClO), discovered in the 18th century, was widely used as a disinfectant throughout the 19th century, but its use was frequently associated with irritation and topical reactions. In 1915, Henry D. Dakin standardized hypochlorite solutions and described the concentration of 0.5% NaClO as most effective. His discovery came at a time when scores of severely wounded soldiers were dying of wound infections on the battlefields of World War I. With the help of a Rockefeller Institute grant, Dakin teamed up with the then already famous French surgeon and Noble Prize winner Alexis Carrel to create a system of mechanical cleansing, surgical debridement, and topical application of hypochlorite solution, which was meticulously protocolized and used successfully in wounds and burns. Subsequently, concentrations of sodium hypochlorite were investigated for antibacterial activity and tissue toxicity in vitro and in vivo, and it was found that a concentration of 0.025% NaClO was most efficacious as it had sufficient bactericidal properties but fewer detrimental effects on wound healing.

Mafenide acetate (Sulfamylon), a drug used by the Germans for treatment of open wounds in World War II, was adapted for treating burns at the Institute of Surgical Research in San Antonio, Texas, by microbiologist Robert Lindberg and surgeon John Moncrief. This antibiotic would penetrate third-degree eschar and was extremely effective against a wide spectrum of pathogens. Simultaneously, in New York, Charles Fox developed silver sulfadiazine cream (Silvadene), which was almost as efficacious as mafenide acetate. Although mafenide acetate penetrates the burn eschar quickly, it is a carbonic anhydrase inhibitor which can cause systemic acidosis and compensatory hyperventilation and may lead to pulmonary edema. Because of its success in controlling infection in burns combined with minimal side effects, silver sulfadiazine has become the mainstay of topical antimicrobial therapy.

Carl Moyer and William Monafo initially used 0.5% silver nitrate soaks as a potent topical antibacterial agent for burns, a treatment that was described in their landmark publication and remains the treatment of choice in many burn centers today. With the introduction of efficacious silver-containing topical antimicrobials, burn wound sepsis rapidly decreased. Early excision and coverage further reduced the morbidity and mortality from burn wound sepsis. Nystatin in combination with silver sulfadiazine has been used to control Candida at Shriners Burns Hospital for Children in Galveston, Texas. Mafenide acetate, however, remains useful in treating invasive wound infections.

**Nutritional support**

P.A. Shaffer and W. Coleman advocated high caloric feeding for burn patients as early as 1909, and D.W. Wilmore supported supranormal feeding with a caloric intake as high as 8000 kcal/day. P. William Curreri (Figure 1.8) retrospectively looked at a number of burned patients to quantify the amount of calories required to maintain body weight over a period of time. In a study of nine adults with 40% TBSA burns, he found that maintenance feeding at 25 kcal/kg plus an additional 40 kcal/% TBSA burned per day would maintain their body weight during acute hospitalization. A.B. Sutherland proposed that children should receive 60 kcal/kg body weight plus 35 kcal/% TBSA burned per day to maintain their body weight. D.N. Herndon et al. subsequently showed that supplemental parenteral nutrition increased both immune deficiency and mortality, and recommended continuous enteral feeding, when tolerated, as a standard treatment for burns. The composition of nutritional sources for burned patients has been debated in the past. In 1959, F.D. Moore advocated that the negative nitrogen balance and weight loss in burns and trauma should be met with an adequate intake of nitrogen and calories. This was supported by many
A brief history of acute burn care management

Fluid resuscitation

The foundation of current fluid and electrolyte management began with the studies of Frank P. Underhill, who, as Professor of Pharmacology and Toxicology at Yale, studied 20 individuals burned in a 1921 fire at the Rialto Theatre. Underhill found that the composition of blister fluid was similar to that of plasma and could be replicated by a salt solution containing protein. He suggested that burn patient mortality was due to loss of fluid and not, as previously thought, from toxins. In 1944, C.C. Lund and N.C. Browder estimated burn surface areas and developed diagrams by which physicians could easily draw the burned areas and derive a quantifiable percent describing the surface area burned. This led to fluid replacement strategies based on surface area burned. G.A. Knaysi et al. proposed a simple ‘rule of nines’ for evaluating the percentage of body surface area burned. In the late 1940s, O. Cope and F.D. Moore (Figure 1.9 and Figure 1.10) were able to quantify the amount of fluid required per area burned for adequate resuscitation from the amount needed in young adults who were trapped inside the burning Coconut Grove Nightclub in Boston in 1942. They postulated that the space between cells was a major recipient of plasma loss, causing swelling in both injured and uninjured tissues in proportion to the burn size. Moore concluded that additional fluid, over that collected from the bed sheets and measured as evaporative water loss, was needed in the first 8 hours after burn to replace ‘third space’ losses. He then developed a formula for replacement of fluid based on the percent of the body surface area burned. M.G. Kyle and A.B. Wallace showed that the heads of children were relatively larger and the legs relatively shorter than in adults, and modified the fluid replacement formulas for use in children. I.E. Evans and his colleagues made recommendations relating fluid requirements to body weight and surface area burned. From their recommendations, intravenous infusion of normal saline plus colloid (1.0 mL/kg/% burn) along with 2000 mL dextrose 5% solution to cover insensible water losses was administered over the first 24 hours after burn. One year later, E. Reiss presented the Brooke formula, which modified the Evans formula by substituting lactated Ringer’s for normal saline and reducing the amount of colloid given. Charles R. Baxter (Figure 1.11) and G. Tom Shires (Figure 1.12) developed a formula without colloid, which is now referred to as the Parkland formula. This is perhaps the most widely used formula today and recommends 4 mL of lactated Ringer’s solution/kg/% TBSA burned.

Figure 1.9 Oliver Cope.

Figure 1.10 Francis D. Moore.

Figure 1.11 Charles R. Baxter.
a direct parenchymal injury that results in early acute respiratory death.\footnote{64}

With the development of objective diagnostic methods, the incidence of an inhalation injury in burned patients can now be identified and its complications identified. Xenon-133 scanning was first used in 1972 in the diagnosis of inhalation injury.\footnote{65,66} When this radioisotope method is used in conjunction with a medical history, the identification of an inhalation injury is quite reliable. The fiberoptic bronchoscope is another diagnostic tool which, under topical anesthesia, can be used for the early diagnosis of an inhalation injury.\footnote{67} It is also capable of pulmonary lavage to remove airway plugs and deposited particulate matter.

K.Z. Shirani, Basil A. Pruitt (Figure 1.13), and A.D. Mason reported that smoke inhalation injury and pneumonia, in addition to age and burn size, greatly increased burn mortality.\footnote{68}

A major inhalation injury requires \( 2 \text{ mL/kg/% TBSA} \) more fluid in the first 24 hours after burn to maintain adequate urine output and organ perfusion. Multicenter studies looking at patients with adult respiratory distress have advocated respiratory support at low peak pressures to reduce the incidence of barotrauma. The high-frequency oscillating ventilator, advocated by C.J. Fitzpatrick\footnote{71} and J. Cortiella et al.,\footnote{72} has added the benefit of pressure ventilation at low tidal volumes plus rapid inspiratory minute volume, which provides a vibration to encourage inspissated sputum to travel up the airways. The use of heparin, \( N \)-acetylcysteine, nitric oxide inhalation, and bronchodilator aerosols have also been used with some apparent benefit, at least in pediatric populations.\footnote{73} Inhalation injury remains one of the most prominent causes of death in thermally injured patients. In children, the lethal burn area for a 10% mortality without a concomitant inhalation injury is 73% TBSA.

**Inhalation injury**

During the 1950s and 1960s burn wound sepsis, nutrition, kidney dysfunction, wound coverage, and shock were the main foci of burn care specialists. Over the last 50 years these problems have been clinically treated with more and more success; hence a greater interest in a concomitant inhalation injury evolved. A simple classification of inhalation injury separates problems occurring in the first 24 hours after injury, which include upper airway obstruction and edema, from those that manifest after 24 hours. These include pulmonary edema and tracheobronchitis, which can progress to pneumonia, mucosal edema, and airway occlusion due to the formation of airway plugs from mucosal sloughing.\footnote{63,64}

The extent of damage from the larynx to tracheobronchial tree depends upon the solubility of the toxic substance and the duration of exposure. Nearly 45% of inhalation injuries are limited to the upper passages above the vocal cords, and 50% have an injury to the major airways. Less than 5% have
however, with an inhalation injury, the lethal burn size for a 10% mortality rate is 50% TBSA.74

Hypermetabolic response to trauma

Major decreases in mortality have also resulted from a better understanding of how to support the hypermetabolic response to severe burns. This response is characterized by an increase in the metabolic rate and peripheral catabolism. The catabolic response was described by H. Snevë as exhaustion and emaciation, and he recommended a nourishing diet and exercise.75 O. Cope et al.76 quantified the metabolic rate in patients with moderate burns, and Francis D. Moore advocated the maintenance of cell mass by continuous feeding to prevent catabolism after trauma and injury.77 Over the last 30 years the hypermetabolic response to burn has been shown to increase metabolism, negative nitrogen balance, glucose intolerance, and insulin resistance. In 1974, Douglas Wilmore and colleagues defined catecholamines as the primary mediator of this hypermetabolic response, and suggested that catecholamines were five- to sixfold elevated after major burns, thereby causing an increase in peripheral lipolysis and catabolism of peripheral protein.78 In 1984, P.Q. Bessey demonstrated that the stress response required not only catecholamines but also cortisol and glucagon.79 Wilmore et al. examined the effect of ambient temperature on the hypermetabolic response to burns and reported that burn patients desired an environmental temperature of 33°C and were striving for a core temperature of 38.5°C.80 Warming the environment from 28° to 33°C substantially decreased the hypermetabolic response to trauma and injury.81 Wilmore et al. also demonstrated that burned patients were glucose intolerant and insulin resistant, with an increase in glucose transport to the periphery but a decrease in glucose uptake into the cells.82 D.W. Hart et al. further showed that the metabolic response rose with increasing burn size, reaching a plateau at a 40% TBSA burn.83

In the past three decades, pharmacologic modulators, such as the β-receptor antagonist propranolol, the anabolic agent human recombinant growth hormone, the synthetic anabolic testosterone analog oxandrolone, insulin, and the glucose uptake modulator metformin, have all shown some beneficial effects in reducing the hypermetabolic response in burn patients.

Summary

The evolution of burn treatments has been extremely productive over the last 50 years. The mortality of severely burned patients has decreased significantly thanks to improvements in early resuscitation, infection control, nutrition, attenuation of the hypermetabolic response, and new and improved surgical approaches. In burned children, a 98% TBSA burn now has a 50% survival rate.74 It is hoped that the next few years will witness the development of an artificial skin which combines the concepts of J.F. Burke and with the tissue culture technology described by E. Bell.85 Inhalation injury, however, remains one of the major determinants of mortality in those with severe burns. Further improvements in the treatment of inhalation injuries are expected through the development of arterial venous CO2 removal and extracorporeal membrane oxygenation devices.86 Perhaps even lung transplants will fit into the treatment regimen for end-stage pulmonary failure. Research continues to strive for a better understanding of the pathophysiology of burn scar contractures and hypertrophic scarring.87 Although decreases in burn mortality can be expected, continued advances to rehabilitate patients and return them to productive life are an important step forward in burn care management.

Further reading

References


52. Underhill FP. The significance of anhydremia in extensive surface burns. JAMA. 1930;95:852.


Teamwork for total burn care: burn centers and multidisciplinary burn teams

Ahmed M. Al-Mousawi, Oscar E. Suman, David N. Herndon

Introduction

Severe burn injuries evoke strong emotional responses in most people, including health professionals, who are confronted by the specter of pain, deformity, and potential death. Intense pain and repeated episodes of sepsis, followed either by death or by survival encumbered by pronounced disfigurement and disability, have been the expected sequelae to serious burns for most of mankind’s history. However, these dire consequences have been ameliorated so that, although burn injury is still intensely painful and sad, the probability of death has been significantly diminished. During the decade prior to 1951, young adults (15–43 years of age) with total body surface area (TBSA) burns of 45% or greater had a 49% mortality rate (Table 2.1). Forty years later, statistics from the pediatric and adult burn units in Galveston, Texas, show that a 49% mortality rate is associated with TBSA burns of 70% or greater in this age group. Over the past decade, mortality figures have decreased even more dramatically, so that almost all infants and children can be expected to survive when resuscitated adequately and quickly. Although improved survival has been the primary focus of advances in burn treatment for many decades, that goal has now been virtually accomplished. The major goal is now rehabilitation of burn survivors to maximize quality of life and reduce morbidity.

Such improvement in forestalling death is a direct result of the maturation of burn care science. Scientifically sound analyses of patient data have led to the development of formulas for fluid resuscitation and nutritional support. Clinical research has demonstrated the utility of topical antimicrobials in delaying the onset of sepsis, thereby contributing to decreased mortality in burn patients. Prospective randomized clinical trials have shown that early surgical therapy is efficacious in improving survival for many burned patients by reducing blood loss and diminishing the occurrence of sepsis. Basic science and clinical research have helped reduce mortality by characterizing the pathophysiological changes related to inhalation injury and suggesting treatment methods that have reduced the incidence of pulmonary edema and pneumonia. Scientific investigations of the hypermetabolic response to major burn injury have led to improved management of this life-threatening phenomenon, not only enhancing survival, but also promising an improved quality of life.

Optimal treatment of severely burned patients requires significant healthcare resources and has led to the development of burn centers. Centralizing services to regional burn centers has made the implementation of multidisciplinary acute critical care and long-term rehabilitation possible. It has also enhanced opportunities for study and research over the past several decades.

Over the past half century the implementation of a wide range of medical discoveries and innovations has improved patient outcomes following severe burns. Key areas of advancement in recent decades include fluid resuscitation protocols; early burn wound excision and closure with grafts or skin substitutes; nutritional support regimens; topical antimicrobials and treatment of sepsis; thermally neutral ambient temperatures; and pharmacological modulation of hypermetabolic and catabolic responses. These factors have reduced morbidity and mortality from severe burns by improving wound healing, reducing inflammation and energy demands, and attenuating hypermetabolism and muscle catabolism.

Melding scientific research with clinical care has been promoted in recent burn care history, largely because of the aggregation of burn patients into single-purpose units staffed by dedicated healthcare personnel. Dedicated burn units were first established in Great Britain to facilitate nursing care. The first US burn center was established at the Medical College of Virginia in 1946. In the same year, the US Army Surgical Research Unit (later renamed the US Army Institute of Surgical Research) was established. Directors of both centers and later, the founders of the Burn Hospitals of Shriners Hospitals for Children, emphasized the importance of collaboration between clinical care and basic scientific disciplines.

The organizational design of these centers engendered a self-perpetuating feedback loop of clinical and basic scientific inquiry. In this system, scientists receive first-hand information about clinical problems, and clinicians receive provocative ideas about patient responses to injury from experts in other disciplines. Advances in burn care attest to the value of a dedicated burn unit organized around a collegial group of basic scientists, clinical researchers, and clinical caregivers, all asking questions of each other, sharing
observations and information, and seeking solutions to improve patient welfare.

Findings from the group at the Army Surgical Research Institute point to the necessity of involving many disciplines in the treatment of patients with major burn injuries and stress the utility of a team concept. The International Society of Burn Injuries and its journal, *Burns*, as well as the American Burn Association and its publication, *Journal of Burn Care and Research*, have publicized the notion of successful multidisciplinary work by burn teams to widespread audiences.

**Members of a burn team**

The management of severe burn injuries benefits from concentrated integration of health services and professionals, with care being significantly enhanced by a true multidisciplinary approach. The complex nature of burn injuries necessitates a diverse range of skills for optimal care. A single specialist cannot be expected to possess all the skills, knowledge, and energy required for the comprehensive care of severely injured patients. Thus, reliance is placed on a group of specialists to provide integrated care through innovative organization and collaboration.

In addition to burn-specific providers, the burn team consists of epidemiologists, molecular biologists, microbiologists, physiologists, biochemists, pharmacists, pathologists, endocrinologists, nutritionists, and numerous other scientific and medical specialists.

At times, the burn team can be thought of as including the environmental service workers responsible for cleaning the unit, the volunteers who may assist in a variety of ways to provide comfort for patients and families, the hospital administrator, and many others who support the day-to-day operations of a burn center and significantly affect the well-being of patients and staff. However, the traditional burn team consists of a multidisciplinary group of direct-care providers. Burn surgeons, nurses, dietitians, and physical and occupational therapists form the skeletal core; most burn units also include anesthesiologists, respiratory therapists, pharmacists, and social workers. The decrease in mortality rates in recent years has heightened interest in the quality of life of burn survivors, both acutely in the hospital and long term. Consequently, more burn units have added psychologists, psychiatrists, and more recently, exercise physiologists to their burn team. In pediatric units, child life specialists and school teachers are also significant members of the team.

Patients and their families are infrequently mentioned as members of the team but are obviously important in influencing the outcome of treatment. Persons with major burn injuries contribute actively to their own recovery, and each brings individual needs and agendas into the hospital setting that may influence the way treatment is provided by the professional care team. The patient’s family members often become active participants. This is obvious in the case of children, but also true in the case of adults. Family members become conduits of information from the professional staff to the patient. At times, they act as spokespersons for the patient, and at other times, they become advocates for the staff in encouraging the patient to cooperate with dreaded procedures.

With so many diverse personalities and specialists potentially involved, purporting to know what or who constitutes a burn team may seem absurd. Nevertheless, references to ‘burn team’ are plentiful, and there is agreement on the specialists and care providers whose expertise is required for optimal care of patients with significant burn injuries (Figure 2.1a and 2.1b).

**Burn surgeons**

The ultimate responsibility and overall control for the care of a patient lies with the admitting burn surgeon. The burn surgeon is either a general surgeon or plastic surgeon with expertise in providing emergency and critical care, as well as in performing skin grafting and amputations. The burn surgeon provides leadership and guidance for the rest of the team, which may include several surgeons. This leadership is particularly important during the early phase of patient care, when moment-to-moment decisions must be made based on the surgeon’s knowledge of physiologic responses to injury, current scientific evidence, and appropriate medical/surgical treatments. The surgeon must not only possess knowledge and skill in medicine, but also be able to exchange information clearly with a diverse staff of experts in other disciplines. The surgeon alone cannot provide comprehensive care, but must be wise enough to know when and how to seek counsel as well as how to give clear and firm direction to activities surrounding patient care. The senior surgeon is accorded the most authority and control of any member of the team, and thus bears the responsibility and receives accolades for the success of the team as a whole.

**Nurses**

Nurses represent the largest single disciplinary segment of the burn team, providing continuous coordinated care to the patient. They are responsible for technical management of the 24-hour physical treatment of the patient. They control the therapeutic milieu that allows the patient to recover. They also provide emotional support to the patient and their family. Nursing staff are often the first to identify changes in a patient’s condition and initiate therapeutic interventions. Because recovery from a major burn is rather slow, burn nurses must merge the qualities of sophisticated intensive

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**Table 2.1** Percent total body surface area (TBSA) burn producing an expected mortality of 50% in 1952, 1993, and 2006

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>1953* (% TBSA)</th>
<th>1993* (% TBSA)</th>
<th>2006° (% TBSA)</th>
</tr>
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<tbody>
<tr>
<td>0–14</td>
<td>49</td>
<td>98</td>
<td>99</td>
</tr>
<tr>
<td>15–44</td>
<td>46</td>
<td>72</td>
<td>88</td>
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<tr>
<td>45–65</td>
<td>27</td>
<td>51</td>
<td>75</td>
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<tr>
<td>65</td>
<td>10</td>
<td>25</td>
<td>33</td>
</tr>
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</table>

Respiratory therapists are essential to the patient’s welfare. Respiratory therapists evaluate pulmonary mechanics, perform therapy to facilitate breathing, and closely monitor the status of the patient’s respiratory function.

Rehabilitation therapists

Occupational and physical therapists begin planning therapeutic interventions on the patient’s admission to maximize functional recovery. Burned patients require special positioning and splinting, early mobilization, strengthening exercises, endurance activities, and pressure garments to promote healing while controlling scar formation. These therapists must be very creative in designing and applying the appropriate appliances. Knowledge of the timing of application is necessary. In addition, rehabilitation therapists must become expert behavioral managers, as their necessary treatments are usually painful to the recovering patient. While the patient is angry, protesting loudly, or pleading for mercy, the rehabilitation therapist must persist with aggressive treatment to combat quickly forming and very strong scar contractures. The same therapist, however, is typically rewarded with adoration and gratitude from an enabled burn survivor.

Nutritionists

A nutritionist or dietitian monitors daily caloric intake and weight maintenance. They also recommend dietary interventions to provide optimal nutritional support to combat the hypermetabolic response to burn injury. Caloric intake as well as intake of appropriate vitamins, minerals, and trace elements must be managed to promote wound healing and facilitate recovery.

Psychosocial experts

Psychiatrists, psychologists, and social workers with expertise in human behavior and psychotherapeutic interventions provide continuous sensitivity in caring for the emotional and mental wellbeing of patients and their families. These professionals must be knowledgeable about the process of burn recovery as well as human behavior to make optimal interventions. They serve as confidants and supports for patients, families, and, on occasion, other burn team members. They often assist colleagues from other disciplines in developing behavioral interventions for problematic patients, allowing both colleague and patient to achieve therapeutic success. During the initial hospitalization, these experts manage the patient’s mental status, pain tolerance, and anxiety level to provide comfort and facilitate physical recovery. As the patient progresses toward rehabilitation, the role of the mental health team becomes more prominent in supporting optimal psychological, social, and physical rehabilitation.

Exercise physiologist

The exercise physiologist has recently been recognized as a key member of the comprehensive burn rehabilitation team. Traditionally, exercise physiologists study acute and chronic adaptations to a wide range of exercise conditions. At our...
institution, the exercise physiologist performs clinical duties and conducts clinical research.

Clinical duties include monitoring and assessing cardiovascular and pulmonary exercise function as well as muscle function. Additional clinical duties include writing exercise prescriptions for cardiopulmonary and musculoskeletal rehabilitation.

There is no licensing body and no requirements for exercise physiologists to practice their profession. However, many organizations, such as the American College of Sports Medicine and the Clinical Exercise Physiology Association, offer national certifications. These certifications include the exercise test technologist, exercise specialist, health/fitness director, and clinical exercise specialist. We recommend that if the exercise physiologist is primarily involved in clinical duties, they should have a minimum of a master’s degree and be nationally certified.

Students, residents, and fellows

Medical students, graduate students, postdoctoral fellows, and residents are vital members of the burn care team. Burn care professionals often do not have the time or energy to perform activities outside of work hours or set responsibilities. However, these young students, fellows, and residents frequently have the time, energy, and desire to take on additional work, whether in the form of clinical work or research. The close working relationship between these individuals and the rest of the burn care team yields numerous benefits, including the conception of new clinical and translational questions that, when answered, directly improve patient care.

Dynamics and functioning of the burn team

Simply gathering a group of experts from diverse disciplines does not create a team. In fact, the diversity of the disciplines, along with individual differences in gender, ethnicity, values, professional experience, and professional status, render teamwork a process fraught with opportunities for disagreements, jealousies, and confusion. The process of working together to accomplish the primary goal (i.e., returning burn survivors to a normal, functional life) is further complicated by the fact that the patient and the patient’s family must collaborate with the professionals. It is not unusual for the patient to attempt to diminish their immediate discomfort by pitting one team member against another or ‘splitting’ the team. Much as young children will try to manipulate parents by first going to one and then the other, patients will complain about one staff member to another or assert to one staff member that another staff member allows less demanding rehabilitation exercises or some special privilege. Time must be devoted to a process of trust building among team members. It is also imperative that the team communicate openly and frequently, or the group will lose effectiveness.

Communicating and discussing daily, weekly, and long-term management plans between team members allows for clarification and organization of early plans to flag issues early on with regard to further surgery, rehabilitation, discharge planning, nutritional goals, patient understanding, and patient compliance.

The group becomes a team when they share common goals and tasks as well as when they have overlapping values that will be served by accomplishing their goals. The team becomes an efficient work group through a process of establishing mechanisms of collaboration and cooperation that facilitate focusing on explicit tasks rather than covert distractions of personal need and interpersonal conflict. Work groups develop best under conditions that allow each individual to feel acknowledged as valuable to the team.

Multidisciplinary burn care involves taking into account all aspects of patient care when treatment decisions are made, as well as considering subsequent effects and consequences of decisions. With good communication and coordination between all members, the team can optimize outcome for a patient in every aspect of their care (Figure 2.1a).

Research into the area of multidisciplinary teams has highlighted the wide application of such teams in healthcare settings as well as some of the shortcomings affecting their efficacy. Clearly defining the various components of these teams will allow improved analysis. Some of the factors that are useful for assessing how well a team is functioning are listed in Box 2.1.

For a group of burn experts to become an efficient team, skillful leadership that facilitates the development of shared values among team members and ensures the validation of members as they accomplish tasks is necessary. The burn team consists of many experts from diverse professional backgrounds, each of which has its own culture, problem-solving approach, and language. For the team to benefit fully from the expertise of its members, every expert voice must be heard and acknowledged. Team members must be willing to learn from each other, eventually developing their own culture and language that all can understand. Attitudes of superiority and prejudice are most disruptive to the performance of the team.

Disagreement and conflict will be present, but these can be expressed and resolved in a respectful manner. Research suggests that intelligent management of emotions is linked

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**Box 2.1 Factors for analyzing multidisciplinary team effectiveness and function**

<table>
<thead>
<tr>
<th>Size of team</th>
<th>Composition (professions represented)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leadership style</td>
<td>(individual or co-leadership/voluntary or assigned/ stable or rotating/authoritarian or non-authoritarian)</td>
</tr>
<tr>
<td>Scope of work</td>
<td>(consultation or intervention or both/idea generating/ decision making)</td>
</tr>
<tr>
<td>Organizational support</td>
<td></td>
</tr>
<tr>
<td>Communication and interactional patterns within the team</td>
<td>(e.g., frequency/intensity/type)</td>
</tr>
<tr>
<td>Contact with the patient, family, or care system</td>
<td>(e.g., frequency/intensity/type)</td>
</tr>
<tr>
<td>Point in treatment process when team is involved</td>
<td>(e.g., intake through to discharge, one phase only, only if case not progressing)</td>
</tr>
</tbody>
</table>

(From Al-Mousawi et al, Burn Teams and Burn Centers, adapted from Schofield & Amodeo26)
with successful team performance in problem solving and conflict resolution.\textsuperscript{44} When handled well, conflicts and disagreements can increase understanding and provide new perspectives, in turn enhancing working relationships and leading to improved patient care.\textsuperscript{45}

The acknowledged formal leader of the team is the senior surgeon, who may find the arduous job of medical and social leadership difficult and perplexing (Figure 2.1b). Empirical studies indicate, with remarkable consistency, that the functions required for successful leadership can be grouped into two somewhat incompatible clusters: 1) directing the group toward tasks and goal attainment, and 2) facilitating interactions among group members and enhancing their feelings of worth.\textsuperscript{39,42,45}

At times, task-oriented behavior by the leader may clash with the needs of the group for emotional support. During those times, the group may inadvertently impede the successful performance of both the leader and the team by seeking alternate means of establishing feelings of self-worth. When the social/emotional needs of the group are not met, the group begins to spend more time attempting to satisfy individual needs and less time pursuing task-related activity.

Studies of group behavior demonstrate that high-performance teams are characterized by synergy between task accomplishment and individual need fulfillment.\textsuperscript{39} As one formal leader cannot always attend to task and interpersonal nuances, groups informally or formally allocate leadership activities to multiple persons.\textsuperscript{39,41,42} According to the literature on organizational behavior, the most effective leader is one who engages the talents of others and empowers them to use their abilities to further the work of the group.\textsuperscript{39,41} Failure to empower the informal leaders limits their ability to contribute fully.

For the identified leader of the burn team (i.e., the senior surgeon) to create a successful, efficient team, he or she must be prepared to share leadership with one or more ‘informal’ leaders in such a way that all leadership functions are fulfilled.\textsuperscript{39,41,42} The prominence and identity of any one of the informal leaders will change according to the situation. The successful formal leader will encourage and support the leadership roles of other members of the team, developing a climate in which the team members are more likely to cooperate and collaborate toward achievement beyond individual capacity.

For many physicians, the concept of sharing leadership and power initially appears threatening, for it is the physician, after all, who must ultimately write the orders and be responsible for the patient’s medical needs. However, sharing power does not mean giving up control. The physician shares leadership by seeking information and advice from other team members and empowers them by validating the importance of their expertise in the decision-making process. However, the physician maintains control and responsibility over the patient’s care and medical treatment.

### Summary

Centralized care provided in designated burn units has promoted a team approach to both scientific investigation and clinical care that has demonstrably improved the welfare of burn patients. Multidisciplinary efforts are imperative to continue improving and understanding the rehabilitation and emotional, psychological, and physiologic recovery of burn patients.

Wider issues to be considered by leaders in the field include burn prevention, access to care in rural regions and developing countries, and promotion of investment and funding for burn care. Centralization of care at burn centers as well as enhanced care has provided tremendous opportunities for research and education.

We hope that, in the future, scientists and clinicians will follow the same model of collaboration to pursue solutions to the perplexing problems that burn survivors must encounter. We also hope that, in the future, burn care will continue to devote the same energy and resources, which have produced such tremendous advances in saving lives and optimizing the quality of life for survivors.

### Further reading


References

Epidemiological, demographic, and outcome characteristics of burn injury*

Basil A. Pruitt, Jr., Steven E. Wolf, Arthur D. Mason, Jr.

Introduction

In the United States in 2009 there was a fire/burn death every 3 hours and a burn injury occurred every half hour. In 2007, the most recent year for which numbers and rates of injury deaths are available, there were an estimated 182,479 deaths from all injuries in the United States, which in a total population of 301,579,895 at that time represented a crude injury death rate of 60.51/100,000 population. Data supplied by the CDC in the WISQARS** Injury Mortality Report indicate that in 2007 there were 3774 (1.25/100,000 population) fatal fire/burn injuries, which represented 2.1% of all fatal injuries. There were more fatal fire/burn injuries in men (2230) than in women (1544), but those in women represented a greater percentage of all fatal injuries than in men, 2.7% vs 1.8%, respectively. Unintentional fire/burn deaths in 2007 represented only 2.7% of all unintentional injury deaths but were 11.3 times more common than violence-related fire/burn deaths (Table 3.1). As indicated in Table 3.2, in 2007 there were an estimated 266 fire/burn deaths in the 0–4-year age group, 259 as a consequence of fire and flame and only seven due to contact with a hot object or substance. The number of fire/burn deaths decreased to a low of 86 in the 10–14-year age group, rose in the older age groups, and was above 200 in all age groups of 40 years and over. In all age groups fire/flame was the predominant cause of fatal injury, and contact with a hot object or substance caused only 16 or fewer deaths during that year. The majority of deaths in all age groups were the consequence of residential fire/flame injury. The table illustrates the age-related changes in the relationship of burn injury and site of burn injury to overall injury fatalities in 2007. The WISQARS Fatal Injury mapping program documents that fire/burn death rates in the United States vary considerably between states. During the years 2000–2006, fire/burn death rates per 100,000 population ranged from a high of 3.39 and 2.70 in Mississippi and Arkansas, respectively, to a low of 0.54 and 0.53 in Colorado and Utah, respectively. Age less than 4 years, age 65 years and over, rural residency, and economic deprivation have all been reported to define groups that are at increased risk of fire-related injury and death. Differences in these risk factors may account in part for the differences in burn incidence rates and mortality between states.

In 2009, the most recent year for which numbers and rates of non-fatal injuries are available, there were an estimated 29,636,366 persons with non-fatal injuries in the United States, which in a total population of 307,006,550 at that time represented a crude non-fatal injury rate of 965.33/100,000. Data supplied by the NEISS WISQARS program indicate that in 2009 there were 381,012 non-fatal fire/burn injuries (124.11/100,000), which represented 1.3% of all non-fatal injuries that year. Non-fatal fire/burn injury as a percentage of all non-fatal injuries in 2009 showed little gender difference, i.e. 1.2% for men and 1.4% for women. Unintentional fire/burn injuries in 2009 represented only 1.3% of all unintentional non-fatal injuries but were almost 40 times (39.4) more common than violence-related non-fatal burns (Table 3.3). Overall unintentional non-fatal fire/burn injuries represent a variable percentage of all injuries and all unintentional injuries as related to the population in various age groups (Table 3.4). Overall fire/burn injuries represented 2.5% of all non-fatal injuries, and unintentional fire/burn injuries represented 2.5% of all non-fatal unintentional injuries in the 0–4-year age group, and 1% of both overall and unintentional injuries in the 5–9-year age group. The total number and rates of both all-cause and unintentional non-fatal fire/burn injury in 2009 were greatest in the 0–4-year age group, i.e. 58,400 (274.18/100,000) and 57,742 (271.09/100,000). In the 5–19-year age groups both the number and rate of both overall and unintentional non-fatal burn injuries decreased, only to rise again in the 20–24-year group, i.e. 40,655 (188.75/100,000) for overall burn injury and 38,788 (180.08/100,000) for all unintentional burn injuries.
### Table 3.1 US injury deaths – 2007

<table>
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<th>Category</th>
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<th>(%)</th>
<th>Rate (^a)</th>
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<tr>
<td>All injury</td>
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</tr>
<tr>
<td>All fire/burn injury</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>3774</td>
<td>2.1(^b)</td>
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</tr>
<tr>
<td>Females</td>
<td>2230</td>
<td>1.25</td>
<td>1.25</td>
</tr>
<tr>
<td>Fire/flame</td>
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<td>1.25</td>
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<td>Hot object/substance</td>
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<td>0.33</td>
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<td>Residential fire/flame</td>
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<td>0.96</td>
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<td>All unintentional injury</td>
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<td>0.67</td>
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<td>All violence-related injury</td>
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<tr>
<td>Violence-related fire/burn</td>
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</table>

\(^a\)Crude rate/100,000 population. \(^b\)Percentage of all injury deaths. \(^c\)Percentage of all unintentional injury deaths.

### Table 3.2 US injury deaths by age group: 2007

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>All injury</th>
<th>Overall unintentional injury</th>
<th>Overall fire/burn</th>
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<th>Hot object/substance</th>
<th>Residential fire/flame</th>
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<tr>
<td></td>
<td>n</td>
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<td>n</td>
<td>Rate (^a)</td>
<td>n</td>
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<td>5.59</td>
<td>965</td>
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<td>150</td>
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<td>30.11</td>
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<td>44.32</td>
<td>136</td>
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<td>5093</td>
<td>35.22</td>
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<td>1.89</td>
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<td>5921</td>
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<td>38.96</td>
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<td>70–74</td>
<td>5876</td>
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<td>224</td>
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</tr>
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<td>75–79</td>
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<td>98.63</td>
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<td>80–84</td>
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<td>15803</td>
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<td>5.60</td>
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</tbody>
</table>

\(^a\)Crude rate/100,000 population.

### Table 3.3 US non-fatal injuries (2009)

<table>
<thead>
<tr>
<th>Category</th>
<th>n</th>
<th>(%)</th>
<th>Rate (^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall all injury causes</td>
<td>29636366</td>
<td>96533.3</td>
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<tr>
<td>Males</td>
<td>15968112</td>
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</tr>
<tr>
<td>Females</td>
<td>13668254</td>
<td>8783.73</td>
<td></td>
</tr>
<tr>
<td>Overall fire/burn injury</td>
<td>381012</td>
<td>124.11</td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>195576</td>
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</tr>
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<td>Females</td>
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<tr>
<td>Unintentional/all injury causes</td>
<td>27642781</td>
<td>90000.71</td>
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<tr>
<td>Unintentional fire/burn injury</td>
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<td>121.03</td>
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<td>Males</td>
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<td>Violence related fire/burn injury</td>
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<td>Males</td>
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<td>Females</td>
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<td>2.25</td>
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</tbody>
</table>

\(^a\)Crude rate/100,000 population. \(^b\)Percentage of all injuries. \(^c\)Percentage of all unintentional injuries. \(^d\)Percentage of all violence related injuries.
Epidemiological, demographic, and outcome characteristics of burn injury

Injuries. In age groups above 24 years the number and rate of occurrence of burns decreased with age, and after age 80 were all reported to be unintentional injuries. There were only 2677 unintentional burn injuries recorded for patients of 85 years and above, with an incidence rate of 47.54/100 000.

In 2009, the rank of unintentional fire/burn injury as a cause of non-fatal injury, 14th for all ages, varied by age in the United States. As indicated in Table 3.5, burn injury ranged from being the fifth most common cause of non-fatal injury in the population under 1 year of age to being the 16th in the 10–14- and 15–19-year age groups. The number and incidence rates for non-fatal burn injury have decreased overall, and for both males and females over the last three decades, as shown in Table 3.6. Since 1985, the incidence rate of non-fatal fire/burn injuries for males decreased from 601/100 000 to 129.14/100 000 in 2009. The incidence rate for females decreased even more during the same period, i.e. from 647/100 000 in 1985 to 119.19/100 000 in 2009. A report by the National Center for Injury Prevention and Control in 2001 indicated that 95.7% of patients with unintentional fire/burn injuries seen in emergency departments were ‘treated and released’, and only 3.4% of all patients

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Overall</th>
<th>Unintentional</th>
<th>Overall</th>
<th>Unintentional</th>
<th>Violence related</th>
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<td>80–84</td>
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<td>10975.06</td>
<td>636085</td>
<td>10924.92</td>
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<tr>
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<td>15579.90</td>
<td>874268</td>
<td>15526.91</td>
<td>2677</td>
</tr>
</tbody>
</table>

Table 3.5 Number and rank of unintentional fire/burn as cause of non-fatal injury by age group: US 2009

<table>
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<th>Age group (years)</th>
<th>n</th>
<th>Rank</th>
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<tr>
<td>&gt;1</td>
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<td>5</td>
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<tr>
<td>1–4</td>
<td>48896</td>
<td>8</td>
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<tr>
<td>5–9</td>
<td>17043</td>
<td>12</td>
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<tr>
<td>10–14</td>
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<td>16</td>
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<tr>
<td>15–19</td>
<td>29869</td>
<td>16</td>
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<tr>
<td>20–24</td>
<td>38788</td>
<td>13</td>
</tr>
<tr>
<td>25–34</td>
<td>62288</td>
<td>13</td>
</tr>
<tr>
<td>35–44</td>
<td>52374</td>
<td>13</td>
</tr>
<tr>
<td>45–54</td>
<td>48890</td>
<td>14</td>
</tr>
<tr>
<td>55–64</td>
<td>27445</td>
<td>13</td>
</tr>
<tr>
<td>65+</td>
<td>23051</td>
<td>12</td>
</tr>
<tr>
<td>All ages+</td>
<td>371577</td>
<td>14</td>
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</table>

Note: Crude rate/100 000 population.
with fire/burn injuries seen in emergency departments were hospitalized and or transferred to another treatment facility. Those data confirm the facts that the vast majority of non-fatal burns are of very limited extent, and that in the United States patients with extensive burns are often transferred to burn centers.

The number and incidence rate of fatal burn injuries has decreased only modestly in recent years, i.e. from a total of 3910 (1.40/100000) in 1999 to 3774 (1.25/100000) in 2007. That decrease has largely been confined to the male population, in whom fatal burns decreased from 2345 (1.71/100000) in 1999 to 2230 (1.5/100000) in 2007, with essentially no change occurring in the female population, i.e. 1565 in 1999 and 1544 in 2007, both of which represented crude incidence rates of 1.01/100000 (Table 3.6).²

The American Burn Association has established the National Burn Repository (NBR), which contains records of patients treated for burn injuries at 91 hospitals in 35 states and the District of Columbia. For the years 2001–2010, those hospitals contributed records from 163771 burn patients. Analysis of that database provides a more detailed description of patients treated at burn centers in the United States. In the years reviewed, 2001–2010, 70% of the cases were males. The mean age of all patients was 32 years, with 12% being 60 or over and 18% being under 5 years of age; 68% of the burn injuries occurred in the home and only 10% were sustained in the workplace. Sixty-seven percent of cases (89124) were classified as non-work-related, 16% (20846) as work-related, 1.4% (1898) as suspected assault/abuse, 1.1% (1458) as suspected self-inflicted, 1.1% (1487) as suspected child abuse, and 0.2% (234) as suspected arson.

The NBR data indicate that 93049 (60%) of the patients were Caucasian, 29584 (19%) African-American, 23230 (15%) Hispanic, 3737 (2%) Asian and 1191 (1%) Native Americans. The 18.9% registrant rate of African-Americans exceeds by 53% the 12.33% African-American segment of the US population. Non-white patients predominated in the three age groups below 5 years, and in all other age groups whites predominated. The Caucasian registrant rate of 60% was slightly less than the 66% Caucasian segment of the US population, the Hispanic registrant rate of 15% was similar to the 15% Hispanic segment of the US population, and the Asian registrant rate of 2.4% was 45% less than the 4.37% Asian segment of the US population.⁵

Scalds and fire/flare were the most common causes of burn injury. There were a total of 44537 scald injuries, of which 32535 (82%) occurred in the home. Scald injury was most frequent in cases under age 5, and in the older age groups fire/flare, a total of 60139 cases, predominated as the cause of burn injury. There were 5400 cases of electric injury, of which 1896 (43%) occurred at an industrial site and 1181 (27%) occurred in the home. Electric injury occurred with greatest frequency – more than 1000 cases – in each age group between 20 and 49.9 years. There were a total of 12005 contact burns, 72% of which occurred in the home. Contact burns were most common in patients under 5 years (25.2% of cases less than 1 year old) and represented less than 10% of burns in all older age groups. There were 4372 chemical injuries, of which 1543 (35%) occurred at the workplace and 1354 (31%) in the home.⁵

Seventy-two percent of the cases had burns of less than 10% of the total body surface area (TBSA) and 90% had burns that involved less than 20% TBSA. The upper limbs, the head and neck, and the lower limbs were the body parts most often affected by burns. The most frequent complications, in order of decreasing frequency, were pneumonia, cellulitis, urinary tract infection, respiratory failure, and wound infection. A diagnosis of inhalation injury was made in 10216 (6.3%) of all the cases. The use of mechanical ventilation, common in patients with inhalation injury, markedly increased the occurrence of clinically related complications. Those complications increased in both frequency and number as the duration of mechanical ventilation increased. In patients ventilated for more than 4 days, complications occurred in more than 40% of patients of all ages and rose to over 60% in patients older than 20 years.⁵

The most common surgical procedures performed were split-thickness skin grafting, burn wound excision, application of wound dressings (either biologic or non-biologic), and joint and hand procedures. Early excision with prompt grafting to close the wound, and the predominance of cases with limited-extent burns have been largely responsible for the observed reduction in length of hospital stay. During the reporting period, the average length of hospital stay decreased from 10.37 and 10.1 days in 2001 to 8.6 and 9.1 days in 2010 for women and men, respectively. The number of hospital days averaged 9.6 for patients who survived and 17.7 days for patients who died.⁵

The overall mortality of the 124196 cases for which burn extent was recorded was 3.7 %. The mortality rate ranged

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### Table 3.6 Burn injury incidence (1985–2009)²

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<tr>
<th>Year</th>
<th>Non-fatal</th>
<th>Fatal</th>
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<td>n</td>
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<td>Males</td>
<td>601.00</td>
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<td></td>
<td>Females</td>
<td>647.00</td>
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<td></td>
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<td></td>
<td>Females</td>
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<td>Males</td>
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</tr>
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<td>Males</td>
<td>161.17</td>
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<td>2005</td>
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<td>Males</td>
<td>151.45</td>
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<td>Females</td>
<td>177.37</td>
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<td>2007</td>
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<tr>
<td></td>
<td>Males</td>
<td>136.24</td>
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<tr>
<td></td>
<td>Females</td>
<td>144.92</td>
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<tr>
<td>2009</td>
<td>All patients</td>
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<tr>
<td></td>
<td>Males</td>
<td>124.11</td>
</tr>
<tr>
<td></td>
<td>Females</td>
<td>129.14</td>
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</table>

*Crude rate/100000 population.*
The winter months lack inhalation injury. Arson, the second most common cause of residential fire deaths (an estimated 30,000 cases in 2008), is considered to be an intentional injury. Defective or inappropriately used heating devices, which are the third most common cause, account for one in six residential fire deaths overall, and an even greater proportion in low income areas. The effect of low income on fire/burn deaths is also related to residence in older buildings or manufactured homes, crowded living conditions, and the absence of smoke detectors. In 2007, 432 children aged 14 or under died as a consequence of residential fires. In 1993, minority children aged 0–19 were reported to be three times as likely to die in a residential fire as white children; this was considered to be an effect of economic status, as racial differences in house fire death rates decrease as income increases.

The linking of databases from five states has enabled investigators to characterize burn injury in the state of Utah. During the years 1997 to 2001, 23,722 residents of Utah sustained burns that received care at some level in the healthcare system. The causes were scalds (21.5%), contact with a hot object (21.2%), chemical (19.2%), fire or flame (18.7%), ‘other’ (11.7%), and electricity (3.9%). Thirty-one individuals (0.1%) sustained fatal burns. The annual incidence rate of burn injury in Utah was 212.5/100,000 residents. The burn injury incidence rate was higher among men than among women, and highest in the 0–4, 15–19, and 20–44 age groups and lowest in the 65–84 and 85+ age groups. The use of geographic information systems mapping enabled the investigators to identify the Utah counties at high risk for burn injury. Those counties typically had higher American-Indian populations, increased poverty levels, and other indices of economic deprivation.

In a study of the socioeconomic determinants of burn injury in British Columbia, Canada, Bell and colleagues reviewed the records of 119 patients with what was categorized as ‘severe thermal injury.’ The age-standardized injury rate for all burns in that province was 3.1/100,000, but the injury rate varied from 2.95/100,000 for all patients in the highest socioeconomic stratum to 5.4/100,000 among all individuals in the lowest socioeconomic stratum. The age-standardized burn injury rate was greater for individuals in rural areas than for those in urban areas in all socioeconomic strata. The finding that the age-standardized injury rate for intentional burn injury was highest in the highest urban socioeconomic stratum was not explained by the authors.

It has been reported that mobile home fires are associated with twice the death rate of fires in other forms of housing. In a group of 65 patients who were burned in mobile home fires and admitted to a burn center, more than three-quarters were male, two-thirds were Caucasian, and 70% resided in the southeastern United States. The extent of burn ranged from 1% to 63% TBSA and averaged 21%. Inhalation injury was diagnosed in 63% of the patients. One or more

**Epidemiology and demography**

Geographic location influences death rates from house fires, presumably because of regional differences in construction and heating devices, as well as economic status. House fire death rates have been reported to be higher in the Eastern part of the United States, particularly the Southeast compared to the West. In the 377,000 residential fires to which fire departments responded in 2009, 2,565 individuals died and 13,050 sustained burn injuries. The winter months, lack of smoke alarms, and substandard housing represent risk factors for residential fires. Unattended and/or improperly positioned cooking and heating devices are the leading causes of residential fires. House fires cause only approximately 4% of burn admissions, but the 12% fatality rate of patients hospitalized for burns sustained in house fires is higher than the 3% rate for patients with burns from other causes. This difference is presumably the effect of associated inhalation injury.

Careless smoking, which accounts for one in four residential fire deaths, is the most common cause of such fatalities. Alcohol and drug intoxication, which contribute to careless smoking behavior by impairing mentation, have been reported to be a factor in 40% of residential fire deaths and appear to contribute to the high weekend frequency of house fires. Holmes and colleagues reported a statistically significant increase in patients with alcohol-related burn injuries admitted to a UK Regional Burn Unit, rising from 6% of admissions in 2003 to 19% of admissions in 2008. In 60% of cases the injuries were caused by flames and required a longer hospital stay than did the injuries in patients with burns unrelated to alcohol: 7.9 days vs 2.5 days. ‘Fire play’ with matches, cigarette lighters, and other ignition devices has been incriminated as the cause of one in 20 residential fires and two in every five fire-related deaths in children. House fire death rates have shown little gender predominance except for a larger number of males in the 2–5-year age group, a group that has the highest rate of non-fatal burns due to unsupervised play with matches. In fact, among children of 9 years or less, child-play fires are the leading cause of residential fire-related death and injury.
comorbid medical conditions pre-existed in 88% of patients, which included alcoholism in 64%. Of interest, one-quarter of the patients had a family history of burn injury. The mortality rate of 12% was higher than the overall mortality rate at the burn center, but contrary to earlier reports that mortality rate was similar to that of patients burned in other residential fires.

During the 5-year period 1991–1995, the residential fire death rate decreased from 1.3 to 1.1/100 000 and by 2007 had further decreased to 0.94/100 000.21 That change has been attributed to the combined effects of improved building design, the use of safer appliances and heating devices, and the increased use of smoke and fire detectors. Data generated by the CDC’s Smoke Alarm Installation and Fire Safety Education (SAIFE) program indicate that even though there are half or fewer fire related deaths in homes with functioning smoke alarms as in homes without those devices, only approximately 75% of US households claim to have at least one working smoke alarm. Even so, there was no alarm or no working alarm in two-thirds of home-fire deaths in 2003–2006. The CDC Injury Center provides funds to 16 states to conduct a smoke alarm installation and fire safety education (SAIFE) program. This includes the installation of long-lasting lithium-powered smoke alarms, which have been installed in more than 174 000 high-risk homes and are estimated to have saved approximately 1218 lives since the program began in 1998.14,21,22 Having a wet pipe sprinkler system in the home affords even greater protection by reducing the risk of dying in a fire by 83%.24

Unlike fire deaths, the precise number of burn injuries that occur in the United States is unknown. Twenty-one states require that burn injuries be reported, but two require that only burns associated with assaults or arson be reported, and seven require that only larger burns (usually those involving more than 15% TBSA) be reported.25 Consequently, the total number of burns has to be estimated by extrapolating data collected in less than half of the states to the entire population. In the late 20th century, such estimates ranged from 1.4 million to 2 million injuries due to burns and fires each year.26,27 Because of the general improvement in living conditions made possible by the relatively high income in the United States, an annual incidence of approximately 500 000 is currently considered to be a realistic estimate, of which 450 000 receive medical care at some level of the healthcare system.28 The majority of those burns are of limited extent: 72% involve less than 10% TBSA and 90% involve less than 20% TBSA. However, as recently as 1990, it was estimated that in the United States 270–300 patients per million population (67 500–75 000) per year sustained burns which, because of extent, associated injury or comorbid conditions, required admission to a hospital.29 In light of the overall decrease in the incidence of burns, it is currently estimated that only 145–150 patients per million population (45 000–50 000) will be admitted to a hospital annually.

A smaller subset of approximately 20 000–25 000 burn patients with even more severe injuries, as defined by the American Burn Association (Table 3.7), are best cared for in a burn center.30 Those patients are now estimated to consist of 35 per million population with major burns and 40 per million population having lesser burns but a complicating cofactor. There are 123 self-designated burn care facilities in the United States, 54 of which have been verified by the American Burn Association as burn centers, and 14 in Canada, which are distributed in close relationship to population density; between them they are reported to contain a total of 1788 and 125 beds, respectively (Figure 3.1).3 As described below, the geographic distribution of burn centers necessitates the use of aeromedical transfer by both rotary and fixed wing aircraft to transport patients requiring burn center care to those facilities from distant and remote areas.

### High-risk populations

In addition to economic status and geographic location, the risk of being burned and the predominant cause of burn injury are related to age, occupation, and participation in recreational activities. Scalds are the most frequent form of burn injury overall and cause over 100 000 patients to seek treatment in hospital emergency rooms, but fire/flame is the most frequent cause of burns requiring hospital admission.3

### Children

The number of pediatric burn patients admitted to hospitals is influenced by cultural differences, resource availability, and medical practice. Consequently, the number of children admitted to hospital for burns treatment has varied by geographic area from a low rate of 4.4/100 000 population in America (North, Central, and South) to a high of 10.8/100 000 population in Africa. Although the incidence rate for Asia – 8.0/100 000 population – is similar to that for Europe and the Middle East, population size determines that Asia provides care for over half of the global pediatric burn population.31 It is currently estimated that 435 children aged 0–19 receive treatment in emergency departments for burn injuries, and that two children die with burn injuries each day in the United States.32

It was estimated in 2004 that 116 600 children aged 14 and under were treated for fire/burn injuries in hospital
Figure 3.1 Burn care facilities in North America 2011. The numbers indicate the number of facilities in each state. The facilities indicated by blue dots have been verified as burn centers by the American Burn Association (Map prepared by G. Gueller at U.S. Army Institute of Surgical Research, Fort Sam Houston, TX 78234).
<table>
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<tr>
<th>United States</th>
<th>City</th>
<th>Number of burn centres</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alabama (3)</td>
<td>Birmingham</td>
<td>2</td>
</tr>
<tr>
<td>Mobile</td>
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<td></td>
</tr>
<tr>
<td>Arizona (1)</td>
<td>Phoenix</td>
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</tr>
<tr>
<td>Arkansas (1)</td>
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</tr>
<tr>
<td>California (14)</td>
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</tr>
<tr>
<td>Colton</td>
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<td></td>
</tr>
<tr>
<td>Fresno</td>
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</tr>
<tr>
<td>Los Angeles</td>
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<td>Orange</td>
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emergency rooms in the United States. Of those injuries, scald burns were more common in the younger children (<5 years) and flame burns more common in older children. Children under 5 years account for nearly all scald burn deaths. Of the children age 4 and under who are hospitalized for burn-related injuries, 65% have scald burns, 20% contact burns, and the remainder flame burns. The majority of scald burns in children, especially those age 6 months to 2 years, are from hot foods and liquids, particularly coffee which may be dispensed at temperatures of up to 180°F (82.2°C), spilled in the kitchen or other places where food is prepared and served. Hot tap-water burns, which typically occur in the bathroom, tend to be more severe and cover a larger portion of the body surface than other scald burns. Consequently, such burns, which account for nearly one-quarter of all childhood scald burns, are associated with higher hospitalization and death rates than other hot liquid burns. Ninety-five percent of burns in children due to the operation of microwave devices are scald burns resulting from the spillage of hot liquids or food.

In a study of 541 children with burn injury, 125 were considered to be cooking injuries. The patients with such burns were, on the average, older than those with scalds related to other mechanisms (i.e. toddlers vs infants). The burns were typically caused by hot liquids spilling from a container on an elevated table or counter on to the child's head, neck, and trunk. The authors call attention to the difference in cooling curves for the various substances and liquids involved, which they postulate influences the severity of the burn injury.

A recent review of the American Burn Association National Burn Registry records of all pediatric patients burned between 1995 and 2007 (46,582) revealed differences in burn etiology associated with age and race. Fifty-four percent of the patients studied were Caucasian, but non-Caucasian populations incurred 54% of the burn injuries that occurred in children younger than 5 years. Scalding was a common etiology in older African-American, Asian, and Hispanic children, and significantly less common in Caucasians. The frequency of inhalation injury was highest in African-American children and lowest in Asian children. In 4.5% of the children the injury was reported to have been intentional, with the frequency in populations of color greater (greatest in African-American children) than in Caucasian children.

Among children 14 years and under, hair curlers and curling irons, room heaters, ovens and ranges, irons, gasoline, and fireworks are the most common causes of product-related burn injuries. Nearly two-thirds of electric injuries in children aged 12 and under are caused by household electric cords and extension cords. Contact with the current in wall outlets causes an additional 14% of such injuries. Boys are at higher risk of burn-related death and injury than girls, and children aged 4 and under and children with a disability are at the greatest risk of burn-related death and injury, especially from scald and contact burns. Heavy-forgage boys are more burn prone than their normal-sized counterparts. A retrospective study of 372 children admitted to a single burn center from January 1991 to July 1997 confirmed that boys who were large for age on the basis of weight or height were over-represented in the burn population. Interestingly, that same study indicated that boys at or under the fifth percentile for height were also over-represented among pediatric burn patients. The authors considered the latter finding to reflect, at least in part, the effect of concomitant malnutrition or neglect.

The occurrence of tap-water scalds can be prevented by adjusting the temperature settings on water heaters or by installing special faucet valves so that water does not leave the tap at temperatures above 120°F (48.8°C). Thermo-static valves, which shut the hot water off if the cold water fails, are the most dependable. The results of a survey in Denmark indicated that the kitchen, not the bathroom, is the most common site of burn injury (39% of burns). Those burns were most commonly due to contact with hot liquids.

Home exercise treadmills represent another source of burn injury in children. These injuries are a consequence of contact with a moving treadmill, most commonly involved the volar surface of the hand, and in two-thirds of patients surgical intervention in the form of skin grafting was required.

A change in the pattern of pediatric burns in Australia to resemble that in the United States has recently been reported. A review of 3621 children treated at the Children’s Hospital Burns Unit at Westmead, NSW, Australia, indicated that scalds accounted for 56% of pediatric burns and that contact burns, which accounted for 31% of pediatric burns, had displaced flame burns, which accounted for only 8%, as the second most frequent cause of pediatric burns. As expected, contact burns were typically of very limited extent (99%<5% TBSA) and only 12% required operative intervention. The most common objects causing contact burns were, in descending order, clothing iron, stoves, oven doors, gas or electric heaters, exhaust pipes, combustion heaters, and barbecues. The same authors from the Children's Hospital Burns Unit reviewed the management of 97 children admitted for the treatment of burn injuries caused by contact with automotive exhaust systems during a 6-year period. The patients’ ages ranged from 5 months to 15 years and the exhaust systems contacted were those of motorbikes, cars, lawnmowers, and quad bikes. The injuries were most often sustained during the summer, and in 60% of cases involved 1% or less of TBSA, ranging in extent from 0.5% to 8%. Over 66% of the burns were on the lower limbs, with the calf being the part most frequently involved. Excision and/or grafting was necessary in one-third of the patients. The authors emphasized prevention by the use of protective clothing and placement of an insulated guard on the exhaust pipe.

The elderly

The elderly represent an increasing segment of the population, the members of which have an increased risk of being burned and higher morbidity and mortality rates than younger patients. A review of medical records of patients admitted to a burn center during a 7-year period revealed that 221 of 1557 (11%) patients admitted were 59 years or older. Ninety-seven (44%) of that group were women, a reflection of the higher percentage of women in the elderly population. Two-thirds of the injuries were caused by flames or explosions, 20% by scalds, 6% by electricity, 2% by chemicals, and 6% by ‘other causes.’ Forty-one percent of the
injuries occurred in the bedroom and/or living room, 28% out of doors or in the workplace, 18% in the kitchen, 8% in the bathroom, and 5% in the garage or basement. Seventy-seven percent of the patients had one or more pre-existing medical conditions, and 64 patients (29%) had smoke inhalation. In 57% of patients judgment and/or mobility were impaired. Ten percent of patients tested positive for ethanol and 29% for other drugs by toxicology screening. Survival advantage was conferred by younger age, absence of inhalation injury, absence of pre-existing medical conditions, and smaller burns.

Among 111 octogenarians admitted to a burn center between 1983 and 1993, scalds caused 32% of the burns, flames 30%, contact 29%, bath immersion 7%, electricity 2%, and hot oil 1%. In 18% a disease such as a stroke was considered to be directly responsible for the burn injury, and in an additional 50% of the patients a pre-existing disease was considered to be contributory. The average length of hospital stay was almost twice that of younger adults, and rehabilitation of survivors was markedly prolonged.

Scalds are responsible for 33–58% of all patients hospitalized in the United States for burns each year. Data from the NEISS-All Injury Program for 2001 to 2006 revealed that 51,700 adults aged 65 or over received care in emergency departments for non-fatal scald burns during that period, representing an annual frequency of 8620 and an estimated annual rate of 23.8 visits per 100,000 population. Three-quarters of the non-fatal scald injuries occurred at home, 42% were due to contact with hot food, and 30% were caused by hot water or steam. Two-thirds of the patients were women. The burns, which involved predominantly the upper and lower limbs, were relatively minor, with 7970 (93%) being treated and released and only 510 (6%) requiring inpatient care.

A recent review of 23,180 records in the American Burn Association National Burn Repository has characterized the epidemiology and outcomes of older adults with burn injury. The mean extent of burn (9.6% TBSA) and the frequency of inhalation injury (11.3%) did not significantly vary among the age groups evaluated, i.e. 55–64 years, 65–74 years, and 75 years and over. Overall, there was a male preponderance of 1.4:1, but women dominated in the oldest age group. The length of hospital stay per percent of body surface burned increased with age, as did hospital charges, even though the number of operations per patient decreased. As the group age increased, mortality also increased, as did discharge to a non-independent status. The adjusted odds ratios for mortality as calculated by logistic regression were 2.3 and 5.4 in the 65–74-year age group and the 75-years and above group, respectively, using the 55–64-year group as the reference group. The authors reported that ‘mortality decreased dramatically after 2001’ in all three groups; that reduction was attributed to a tripling of patient entry into the registry since 2001.

Yin and colleagues characterized elderly burn patients treated at a Burn Center in Shanghai. In 201 patients with a mean age of 69.3 years (range 60–90 years), the majority were men; flame was the cause of burn in 53% and scalds in 40%. Almost three-quarters (73.6%) of the burns were sustained in the home, and the median extent of burn was 12% TBSA. The areas most frequently involved, in decreasing order, were the legs, arms, head, neck, and hands. Surgical intervention was undergone in 87 patients and 16 (8%) of the entire group died. Morita et al. contrasted the characteristics and outcomes in 35 patients of 65 years and over with those of 41 adult patients of lesser years. The average age of the elderly patients was 78 years, and 24 of the 35 had pre-existing comorbid conditions. Compared with the younger adult patients, the elderly had a higher incidence of accidental bath tub-related burns and a lower incidence of suicide attempts. ‘Severe burns’, defined as partial-thickness burns of 30% or more TBSA, or full-thickness burns of 10% or more TBSA, were fatal in the elderly patients.

The disabled

The disabled are a group of patients considered to be burn prone. The majority of burns in the disabled occur at home and are most often scalds. The effects of disability and pre-existing disease in those patients are evident in the duration of hospital stay (27.6 days on average) and the death rate (22.2%) associated with the modest average extent of burn (10% TBSA). A report on burn injury in patients, generally elderly, with dementia has emphasized the need for prevention measures to reduce the incidence of burn injuries incurred when such patients are performing the activities of daily living.

Military personnel

In wartime military personnel are at high risk for burn injury, both combat related and accidental. Over the past six decades the incidence of burn injury, which is related to both the type of weapons employed and the type of combat unit engaged, has ranged from 2.3% to as high as 85% of casualties incurred in various periods of conflicts (Table 3.8). The detonation of a nuclear weapon at Hiroshima in 1945 instantaneously generated an estimated maximum of 57,700 burn patients and destroyed many treatment facilities, thereby compromising the care of those burn patients. In the Vietnam conflict, as a consequence of the total air superiority achieved by the US Air Force and the lack of armored fighting vehicle activity, patients with burn injuries represented only 4.6% of all patients admitted to army medical treatment facilities or quarters from 1963 to 1975. The majority (58%) of the 13,047 burn patients treated in those years were non-battle injuries, only 5536 (42%) being battle injuries. The overall incidence of burns as the cause of injury in all United States military forces in Vietnam during those years may well have been higher. Allen et al. reported that during calendar years 1967 and 1968 a total of 1963 military burn patients from Vietnam were admitted and treated at a burn unit established in a United States Army General Hospital in Japan. In accordance with the data from US Army hospitals in Vietnam, the burns in 847 (43.2%) of those patients were the result of hostile action. In the Panama police action in late 1989, the low incidence of burn injury (only six (2.3%) of the total 259 casualties had burns) has been attributed to the fact that the action involved only infantry and airborne infantry forces using small arms weaponry.

As exemplified by the Israeli conflicts of 1973 and 1982, and the British Army of the Rhine experience in World War II between March 1945 and the end of hostilities in
In the current armed conflicts, Operations Iraqi Freedom and Enduring Freedom, the US Army Burn Center has provided care for all of the patients from all branches of the armed forces who sustained severe burns in the theaters of operation. Surgeons from the Burn Center have provided care at the Center and an Army general hospital in Landstuhl, Germany, at hospitals within the theaters of operation and during aeromedical transfers from the hospital in Europe to the Burn Center in San Antonio, Texas.

During the four-year period 1 March 2003–1 March 2007, 540 combat casualties with a mean extent of burn of 16.7% TBSA (range 0.1–95%) were admitted to the US Army Burn Center. In 149 (27.6%) of the patients the burns involved more than 20% TBSA and inhalation injury was documented in 69 (13%). The burns were the consequence of an explosion in 342 (63%) of the patients, commonly due to detonation of an improvised explosive device (IED). The mean ISS was 16 or above in 169 patients as a reflection of significant associated injuries. Slightly more than half of the patients (51%) had mechanical trauma, most often fractures, in addition to their burn injuries. Even with the frequent presence of associated mechanical injury, only 30 (6%) of the patients died.

The 24 of the 540 patients who were burned while incinerating waste represented 10% of military burn casualties admitted to the US Army Burn Center. Admission of 20 patients with such injuries during the first year of the study period prompted the distribution of a memorandum to military units in the theater of operations. This described the dangers associated with the burning of waste and articulated safety procedures. In the following year only four patients were admitted with such injuries, which represented a statistically significant decrease in the occurrence of such burns.

Aeromedical transport was used to transfer 380 (70%) of the 540 patients with combat-related burns from the US Army Landstuhl Medical Center in Germany to the Burn Center in San Antonio, Texas. Of these transported patients, 48% received mechanical ventilatory support throughout the transfer procedure. The burn patients accompanied by the Army burn flight team arrived at the burn center on average late on the third postburn day, with no in-flight fatalities.

Injuries caused by IEDs were characterized in a study of 100 consecutive combat casualties admitted to a British field hospital in Iraq during 2006. IEDs were the cause of injury in 53 of these, 12 of whom (23%), considered to have been in the trajectory of the exploding projectile, were either killed or died of wounds. Among the 41 survivors, only eight (15%) had burns and two (4%) had primary blast injury. Even though they were sited adjacent to the trajectory of the IED, all but one of the survivors had returned to military employment within 18 months.

Belmont and colleagues analyzed the injuries sustained by a US Army brigade combat team of 4122 soldiers deployed to Iraq for 15 months during the ‘surge’ phase of Operation Iraqi Freedom. There were 500 combat wounds in 390 casualties, 12 of whom had burns sustained in explosions. Seven of the burn patients, four with burns of 10–15% TBSA, were aeromedically transferred to a higher echelon of care.

In the past two years (1 July 2009 to 30 June 2011), as the intensity of the conflicts in Southwest Asia has decreased, the number of combat-related burns has decreased and only 93

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**Table 3.8 Incidence of burn injury in armed conflicts**

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<tr>
<th>Conflict</th>
<th>Casualties (%)</th>
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<td>World War II – Hiroshima</td>
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<td>13047</td>
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<tr>
<td>Israeli Six-Day War 1967</td>
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<tr>
<td>Yom Kippur War 1973</td>
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<td></td>
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<tr>
<td>Falkland Islands War 1982</td>
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<td></td>
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<tr>
<td>British casualties</td>
<td>14.0</td>
<td>112</td>
</tr>
<tr>
<td>Argentinian casualties</td>
<td>17.5</td>
<td>34 of 194</td>
</tr>
<tr>
<td>Lebanon War 1982</td>
<td>8.6</td>
<td></td>
</tr>
<tr>
<td>Panama police action 1989</td>
<td>2.3</td>
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<tr>
<td>Operation Desert Shield/Storm</td>
<td>7.9</td>
<td>36 of 458</td>
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<tr>
<td>1990–1991</td>
<td></td>
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<tr>
<td>Operation Iraqi Freedom and</td>
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<td>Operation Enduring Freedom 2003–2011</td>
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Northwest Europe, the personnel in armored fighting vehicles have been at relatively high risk for burn injury. Burns have also been common in war at sea. In the Falkland Islands campaign of 1982, 34% of all casualties from the British Navy ships were burns. The increased incidence of burn injuries – 10.5% and 8.6% in the Israeli conflicts of 1973 and 1982, respectively, compared to the 4.6% incidence in the 1967 Israeli conflict – is considered to reflect what has been termed ‘battlefield saturation with tanks and anti-tank weaponry’. The decreased incidence of burn injuries – 8.6% in the 1982 Israeli conflict compared to the 10.5% in the 1973 Israeli conflict – has been attributed to enforced use of flame-retardant garments and the effectiveness of an automatic fire extinguishing system in the Israeli tanks. Those factors have also been credited with reducing the extent of the burns that did occur. In the 1973 Israeli conflict, 29% of the patients with burns had injuries that involved 40% or more TBSA, and only 21% had burns less than 10% TBSA. In the 1982 Israeli conflict those same categories of burn represented 18% and 51%, respectively, of all burn injuries. Modern weaponry may have eliminated the differential incidence of burn injury between armored fighting vehicle personnel and the personnel of other combat elements. In the 1982 Falkland Islands conflict, in which there was little if any involvement of armored fighting vehicles, one of every seven and every six casualties in the British and Argentinian forces, respectively, had burns. Conversely, there were only 36 (7.8%) burn casualties in the total 458 casualties sustained by US Forces in 1990 and 1991 during Operation Desert Shield术Desert Storm, in which there was extensive involvement of armored fighting vehicles.
burn casualties have been transferred and admitted to the Army Burn Center. In that period, 79 (85%) of the burns were due to fire/flame, two (2%) were the result of scalds, and 12 cases (13%) had limited and scattered burns in the presence of complex soft tissue injury. During that time another 45 military personnel were admitted with burns unrelated to combat. In that group the burns were due to fire/flame in 35 (78%), scalds in five (11%), electricity in two (4%), and ‘other’ causes in three (7%). Overall, 1015 military patients have sustained burns in Iraq (Operation Iraqi Freedom) and Afghanistan (Operation Enduring Freedom) and received care at the Army Burn Center since March 2003. Those burns represent 2% of all combat casualties.

A report from the UK confirms the variable admixture of combat and non-combat burns in military personnel. During the period 2001–2007 134 UK military personnel were evacuated to the Royal Center for Defence Medicine (RCDM) for the treatment of burn injury. The median age of the patients was 27 years and the mean extent of burn was 5% TBSA, range 1-70% TBSA. Sixty percent of the burns were unrelated to combat and were classified as ‘accidental’, e.g. sustained while preparing hot food and drinks, burning waste, or misusing flammable liquids. There was one fatal electric injury. During 2006–2007, 56 (59%) of the burn patients evacuated to the UK from Iraq and Afghanistan had burns sustained in combat. Those patients represented 5.8% of all combat casualties in the UK military during that time. Their burns were typically of limited extent (mean 5% TBSA) and these patients often had associated mechanized injuries. 25 or 26% of all the burn patients transferred to the RCDM during the study period underwent skin grafting. All of the evacuated patients survived.

In addition to military casualties, the infrastructure breakdown caused by armed conflict increases the injury burden in the indigenous population. Information derived from a questionnaire survey administered in 1172 Baghdad households containing 7396 individuals indicated that the respondents could recall 103 injuries as having occurred during a specific 3-month period. Only four of those injuries were fire/burn-related and five were due to ‘electric shock’. In the current conflicts in Iraq and Afghanistan, up to one-third of the admissions to the combat-support hospitals are for humanitarian or civilian emergency care. Analysis of 2060 children admitted to combat-support hospitals between 2002 and 2007 revealed that 204 (13.3%) of the 1537 injured patients had burns. Almost twice as many children with burn injury were seen in the combat-support hospitals in Afghanistan as in Iraq. The care of such patients, which may revert to the military during armed conflicts, should be considered when planning combat medical support.

Although the risk of burn injury in the combat population is relatively high, the distribution of burn size in other than armored fighting vehicle personnel is comparable to that in the civilian population, i.e., more than 80% of the patients have burns of less than 20% TBSA. Even so, the number of burns that can be rapidly generated necessitates that planning for combat casualty care include augmentation of in-theater medical treatment facilities with personnel having burn-specific expertise, as was done by the US Army Medical Department in Operation Desert Shield/Storm.

Even in peacetime non-combat munitions incidents are common in the US Army. During a 7-year period 742 non-combat munitions incidents were reported in which 894 soldiers were injured. The most common types of injury were burns, which occurred in 261 or 26.7% of all the patients injured. The high incidence of burn injury in military personnel in both war and peace will generate a subset of extensively burned patients who will require tertiary burn center care to ensure optimum functional outcome and maximum survival.

**Burn etiologies**

Burns due to hot liquids may occur in any age group, but 77% of all hot liquid scalds have been reported to occur in children under 3 years of age. Full-thickness injury is present in less than half of patients with hot water scalds, but in 58% of patients with hot oil burns. Young children are most commonly injured by pulling a container of hot water or hot cooking oil onto themselves, whereas older children and adults are most commonly injured by improper handling of hot oil appliances. The case fatality rate of scald injury is low (presumably owing to the usually modest extent and limited depth of the burn), but scalds are major causes of morbidity and associated healthcare costs, particularly in children less than 5 years of age and in the elderly.

Even though the burns of 30% of all patients requiring admission to a hospital are caused by scalding by hot liquids, flame is the predominant cause of burns in patients admitted to burn centers, particularly in adults. The misuse of fuels and flammable liquids is a common cause of burn injury. A retrospective review of admissions to one burn center for the period 1978 to 1996 identified 1011 (23.3% of 4339 acute admissions) as being gasoline related. The average total extent of burn was 30% TBSA, with an average 14% full-thickness burn component; 144 of those patients died. The unsafe use of gasoline was implicated in 87% of patients in whom the cause of the burn could be identified, and in 90 (63%) of the 144 fatalities.

The ignition of alcohol and other flammable liquids which are used to kindle coal stoves, barbecue devices, and fireplaces is a cause of burn injury in both developing and developed countries. A review of admissions to a Turkish Burn Center over a 20-year period identified 82 patients who sustained burns when flammable liquids were being used to kindle or accelerate a stove ignited. A 10-year review of admissions to a Chinese University Hospital identified 180 patients burned by ignition of alcohol used to kindle household coal stoves. A recent report from Scandinavia identified a similar etiology of burns caused by ignition of bioethanol being used to refill a ‘contemporary design’ fireplace. The common theme in all three reports is that the person burned was attempting to refill or accelerate an already or still-burning fire within the device.

In one epidemiologic study in New York State in the 1980s, the largest number of admissions in the age group 15–24 years was related to automobiles. Ignition of fuel following a crash, steam from radiators, and contact with hot engine and exhaust parts were the most frequent causes. In a review of 178 patients who had been burned in an automobile crash, it was noted that slightly more than one-third had other injuries, most commonly involving the musculoskeletal system, and that approximately one in six had
A review of patients admitted to a referral burn center revealed that burns sustained while operating a vehicle involved an average of more than 30% TBSA and were associated with mechanical injuries (predominantly fractures) much more frequently than those incurred in the course of vehicle maintenance activities, which involved an average of less than 30% TBSA. Automotive-related flame burns can also be caused by fires and explosions resulting from ‘carburetor-priming’ with liquid gasoline; and such burns have been reported to account for 2–5% of burn unit admissions.

During the 5-year period 2003–2007 fire departments in the United States responded to an average of 287,000 vehicle fires annually. Each year those fires caused an average of 1525 burn injuries, 480 burn deaths, and $1.3 billion in direct property damage. Fifty-eight percent of the fire-related deaths were associated with collisions or overturns, which represented only 3% of vehicle fires. Between 1980 and 2008, the number of vehicle fires decreased by 55%, with a proportional decrease in burn deaths and burn injuries. An estimated 207,000 vehicle fires in 2008 caused 350 fire deaths and 850 fire injuries, representing an accumulative 70% decrease since 1980.

Contact burns from motorcycle exhaust pipes are another injury related to the use of vehicles. In Greece, the incidence of burns from motorcycle exhaust pipes has been reported to be 17/100,000 person-years, or 208/100,000 motorcycle-years. The highest occurrence was in children. In adults, the incidence is 60% higher in females than in males. As would be anticipated, the most frequent location of the burns was on the right leg below the knee, where contact with the exhaust pipe occurs. The authors concluded that a significant reduction in incidence could be achieved by wearing long pants and the use of an external exhaust pipe shield.

The burns sustained in boating accidents are most often flash burns due to an explosion of gasoline or butane, and typically affect the face and hands. As noted above, bonfire and barbecue burns caused by flash ignition of a flammable liquid used to start or accelerate a fire affect those same areas as well as the anterior trunk. The use of gasoline for purposes other than as a motor fuel, and any indoor use of a volatile petroleum product, should be discouraged as part of any prevention program.

The ignition of clothing is the second leading cause of burn admissions for most ages. The burn injury rate due to the ignition of clothing is influenced by poverty and is inversely related to income. The fatality rate of such patients is second only to that of patients with burns incurred in house fires. Burns caused by ignition of synthetic fabrics, which melt and adhere to the skin, are commonly deeper than burns caused by other fabrics and typically exhibit a gravity-dependent ‘runoff’ pattern. More than three-quarters of deaths due to the ignition of clothing occur in patients over 64 years. Clothing ignition deaths, which were a frequent cause of death in young girls, have decreased as clothing styles have changed, and are now rare among children, with little overall gender difference at the present time. From 1975, when it became mandatory for sleepwear sizes 0 to 6X to pass a standard flame test, until 1999 when that law was repealed, the percentage of clothing burns caused by sleepwear in children aged 0–12 decreased from 55% to 27%. Sleepwear-related burns are being monitored to assess the effect of this deregulation on sleepwear-related burns.

Ben and associates have characterized the burn injuries caused by fires on ships in 105 patients admitted to a Chinese burn institute during a 12-year period. The mean age of those patients was 30.2 years and the mean extent of burn injury was 46.5% TBSA. The injuries were considered to be ‘mostly deep burns’ with a mean extent of full-thickness injury of 18.6% TBSA. The head, neck, and upper limbs were the areas most commonly burned, and 57 (54.3%) of the patients had inhalation injury of whom 42 required tracheotomy and 38 mechanical ventilation. The interval between injury and initiation of resuscitation, which appeared to be related to the location of the ship, averaged 5.9 hours, but could be as long as 67 hours. Fifty-three percent of patients were considered to be inadequately resuscitated because of hypotension and ‘severe shock’ on admission. Nine patients (8.6%) died. The authors called for the establishment of fire safety regulations, regular inspection of electrical circuits, and enforcement of burn prevention measures such as maintenance of adequate passageway clearance and scheduled fire prevention exercises on board ship.

Outdoor recreational fires, most common during the warm summer months, are another cause of burn injury. In 2010, Neaman and colleagues identified 329 patients treated during an 8-year period who sustained burns in outdoor recreational fires. Almost three-quarters (73.3%) were male and 40% were children; 12% were considered to be intoxicated at the time of emergency department treatment and more than 35% required admission to hospital. The hands were the most frequently involved body part, and almost 30% required split-thickness skin grafts. Fraga et al. reported a group of 241 patients with burns caused by campfire bonfires and beach fire pits. Alcohol was incriminated as a causative factor in 61% of the adult burns; 34% of those patients were male, and the burns involved the upper extremities, trunk, lower extremities, and hands, in rank order. Although the burns were limited in extent (mean size 6.1% TBSA), skin grafting was required in 37%. Woodbridge et al. compared 30 children with burns sustained during camping and caravanning to 121 children with burns received in other situations. The burned campers had more extensive partial-thickness burns (5.5% vs 3.0%) and a higher percentage of the campers required the application of a collagen-based skin substitute. The burned campers also needed significantly more general anaesthetics, principally for painful dressing changes, and a longer duration of hospital stay. A report from Saudi Arabia indicated that desert campfires are a particular risk to unsupervised crawling infants.

Full-thickness burns of the palm sustained when a child unknowingly crawls into the fire pit can result in severe contractures requiring subsequent operative release.

Fire walking across a burning charcoal pit is a religious ritual practiced principally by Indians and some of the Chinese population of Singapore. Sayampanathan reported that only 18 of 3794 men who participated in a fire walking ceremony sought medical care for burns which, in 17 cases, were limited to the soles of their feet. One of the patients who had fallen in the fire pit had sustained burns to the right leg, both upper limbs, and the back, in addition to his feet. None of the plantar burns required grafting. In an earlier report of fire walking injury Chown noted that the burns...
were typically confined to the feet and, if the patient carried coals on his hands, to the palms, and typically healed without surgical intervention. Skin grafting was required only for the full-thickness injuries of those fire walkers who had fallen while in the fire pit.

Hemington-Gorse et al. have drawn attention to the recent increase in burns related to the use of tanning devices. In a 7-year period, 12 patients required hospital admission for the management of extensive erythema, most commonly involving the trunk, resulting from ‘sunbed’ use. The authors propose greater regulation of tanning devices to reduce the increased risk of cutaneous and ocular melanoma associated with the use of such devices.

Work-related burns account for an estimated 20–30% of hospital admissions for burn injury. A Bureau of Labor Statistics survey in 1985 indicated that 6% of all work-related thermal burns occurred in adolescents (16–19 years). In a 1986 study in Ohio, it was noted that the majority of hospital-treated burns in teenagers/young adults occurred at work. A study in that same year revealed that six out of 10 hospitalized burn injuries in employed men in Massachusetts were work related.

Restaurant-related burns, particularly those due to deep fryers, represent a major and preventable source of occupational burn morbidity, and in restaurants account for 12% of work-related injuries. It has been estimated that almost 700 deaths annually are caused by occupation-related burns.

A review of compensation claims by Rhode Island workers has identified that the highest claim rate for burn injury was for workers in food service occupations. Evening and night-shift workers were at an increased risk for chemical burn injuries. The overall claim rate for burn injury was 24.3/10000 workers, and ranged from a high of 51/10000 for workers under 25 years to a low of 16.5/10000 for workers between the ages of 40 and 54.

During a 5-year period in the state of Alabama, 345 occupational burn cases were admitted to the University of Alabama Burn Center. The majority, 96.5%, of the patients were male and 76.2% were Caucasian, with a mean age of 37.5 years. Causes of the burn injuries were flame, electricity, and scalds, in that order. The occupations in which burn injury occurred most often were ‘manufacturing’ (19.1%), ‘electrician’ (16.2%), and ‘laborer’ (16.2%). As would be anticipated, 70% of the injuries to electricians were caused by electricity. Flame and chemical burns were the principal causes of injury in manufacturing employees and laborers, contact with hot bitumen in roofers, scald burns in cooks, and flame burns in mechanics. Sixteen (4.6%) of the patients with occupational burn injury died.

A state-managed Workers Compensation database has been used to estimate the incidence of work-related burn injuries and identify patients at high risk. The incidence rate of occupational burn injury was estimated as 26.4 per 10000 workers per year, with the highest rate for men in manufacturing and for women in service occupations. Compared to other occupations, higher incidence rates of burn injury were noted in welders, cooks, food service workers, laborers, and mechanics. The majority of burn injuries involved the wrist and hand, and full-thickness burns were most frequently present on the upper extremities.

The Department of Labor and Industries of the State of Washington identified 350 cases of hospitalized work-related burns during the period September 2000 to December 2005. Twenty-three percent of these injuries were due to flame, fire, and smoke, 11% due to electricity, and 10% due to hot water. The overall incidence rate of hospitalized work-related burns was 24.5 per million workers per year. The incidence rate was highest (59.3) per million workers per year in the 22–24-year age group. The incidence rate for male workers, 43.2 per million workers per year, was more than eight times higher than that for female workers, 5.0 per million workers per year. The highest rate of hospitalized work-related burns was associated with the construction industry. The manufacturing industry sector and the food service sector shared the second highest frequency of hospitalized burns, with 49 cases each, thereby indicating the relatively high risk of burn injury in restaurant workers.

During the period 1 January 2000 to 1 December 2008, 59 restaurant food workers in the State of Washington sustained scald burn injuries in the workplace that required admission to a hospital. The burning agent was cooking oil in 49%, water in 32%, other sources 12%, and steam 7%. More than 30% of the burns were associated with a fall, slip, or trip.

As would be anticipated, the risk of burn injury due to hot tar is greatest for roofers and paving workers. Of all accidents involving roofers and sheet metal workers, 16% are burns caused by hot bitumen, and 17% of those injuries are of sufficient severity to prevent work for a variable period of time. In the state of California, in 1979, 366 roofers and slaters sustained burn injuries. The majority of hot tar burns involved the hand and upper limb. Another occupation associated with an increased risk of burn injury is welding, in which flash burns and explosions are the most common injury-producing events.

Friction burns, most often involving the dorsum of the hand, can occur as a result of an industrial accident or a vehicle crash. Industrial friction burns are usually isolated injuries caused by rotating belts, and non-industrial friction burns usually occur when the hand and/or arm are trapped outside a car in a ‘rollover’, and are commonly associated with other mechanical trauma.

In the United States in 1988, there were 236200 patients with chemical injuries of all types treated in emergency rooms. Of those, 35000 (15%) were patients of all ages with chemical burns, and 6500 (5%) were children younger than five years with chemical burns. The limited extent of burns due to chemical content is indexed by the fact that only 800, or 2%, of the chemical burns required admission to a hospital. The effect of age (in the very young, removal of the offending agent may be delayed) on the severity of chemical injury is evident in the fact that 400 of the patients requiring admission to a hospital for the care of chemical burn injuries were children under 5. The greatest risk of injury due to strong acids occurs in patients who are involved in plating processes and fertilizer manufacture. The greatest risk of injury due to strong alkalis in the workplace is associated with soap manufacturing, and in the home with the use of oven cleaners. The greatest risk of phenol injuries is associated with the manufacture of dyes, fertilizers, plastics, and explosives. The greatest risk of hydrofluoric acid injury is associated with etching processes, petroleum refining, and air-conditioner cleaning. Anhydrous ammonia injury is most common in agricultural workers, and cement injury...
is most common in construction workers. Injury due to petroleum distillates, which cause dilapidation, is greatest in refinery and tank farm workers, and white phosphorus and mustard gas injuries are most frequent in military personnel.\textsuperscript{105}

During the period 2003–2007 it was estimated that an average of 20,900 patients with chemical burns were seen in hospital emergency departments annually.\textsuperscript{106} In 2008, that estimate decreased to 17,700.\textsuperscript{107} Among the 163,771 patients admitted to NBR facilities between January 2001 and June 2010, there were 4372 or 3.2% with chemical burns.\textsuperscript{5} NEISS data have been used to estimate that in the US in 2007, there were 820 burns associated with pool chemicals.\textsuperscript{108} These represented 18% of all pool chemical-associated injuries, but were too few to permit the calculation of a stable incidence rate.

Nearly 1000 deaths are caused annually by electric current. An annual average of 3300 patients with burns due to electricity were seen in hospital emergency departments during the years 2003–2007.\textsuperscript{106} The annual estimate for electric injuries seen in emergency departments in 2008 rose slightly to 4000.\textsuperscript{107} One-third of electric injuries occur in the home and one-quarter occur on farms or industrial sites.\textsuperscript{75} The greatest incidence of electric injury caused by household current occurs in young children, who insert uninsulated objects into electrical receptacles or bite or suck on electric cords in sockets.\textsuperscript{75} Low-voltage direct current injury can be caused by contact with automobile battery terminals or by defective or inappropriately used medical equipment, such as electrical surgical devices,\textsuperscript{109} external pacing devices,\textsuperscript{110} or defibrillators.\textsuperscript{111} Although such injuries may involve the full thickness of the skin, they are characteristically of limited extent. Caucasians, apparently because of their employment patterns, are almost twice as likely to be injured by high-voltage electric current as are blacks.\textsuperscript{75} Employees of utility companies, electricians, construction workers (particularly those working with cranes), farm workers moving irrigation pipes, oil field workers, truck drivers, and individuals installing antennae are at greatest risk of work-related high-voltage injury.\textsuperscript{79} The greatest incidence of electric injury occurs during the summer as a reflection of farm irrigation activity, construction work, and work on outdoor electrical systems and equipment.\textsuperscript{11} The current limitation and ineffectiveness of preventive measures is evident in the constancy of occurrence of high-voltage injury over the past 20 years. Conversely, the use of ground-fault circuit interrupters and media-promoted awareness have reduced the incidence of low-voltage injuries.\textsuperscript{112}

During the period 1982 to 2002, 263 patients with high-voltage injury, 143 with low-voltage injury, and 17 with lightning injury were treated at a regional burn center. The observed mortality was greatest in the patients with lightning injury, 17.6%, in contrast to 5.3% in patients with high-voltage injury, and 2.8% for patients with low-voltage injury. Of the patients with high-voltage injury, 88 required fasciotomy and even so, muscle necrosis occurred in 68, with amputation necessary in 95. Pigmented urine was observed in 96 patients and renal failure in seven. Arrhythmia was recorded in 38 patients and cardiac arrest in two. Neurologic deficit was recorded in 21, cataract formation in five, and 22 had associated fractures.\textsuperscript{112} Another study reported the outcome of 195 patients with high-voltage electric injury treated at a single burn center during a 19-year period. Of the 195 patients, 187 (95.9%) survived and were discharged. Fasciotomy was required in the first 24 hours following injury in 56 patients and 80 patients underwent an amputation because of extensive tissue necrosis. The presence of hemochromogens in the urine predicted the need for amputation with an overall accuracy of 73.3%.\textsuperscript{113}

Fodor et al. reported the occurrence of electric injury while fishing, either by contact of the fishing pole with a high-voltage electricity source or during illegal use of low-voltage electricity to stun fish.\textsuperscript{114} In eight male patients treated over a 4-year period the extent of burn ranged from 0.5% to 70% TBSA and most often involved the limbs. Six patients required escharotomy, and a fasciotomy was needed in one of the three patients who developed compartment syndrome. Operative intervention was necessary in all patients, three of whom required amputation, two the removal of digits, and one a scapulohumeral disarticulation.

Patil and associates recently reported the demographic profile of 84 consecutive patients with electric injury treated at a medical college in India.\textsuperscript{115} One-third of the patients were in the 10–19-year age group and 71 (85%) were male. Direct contact with a current-bearing line or secondary contact with an object in contact with a ‘live’ wire accounted for 51% of the injuries. The home was the most common site of injury, i.e. 51% of cases. Masheky et al. have reported that in Bangladesh the average annual incidence of fatal electric injury in children under 18 years of age is 1.4/100,000.\textsuperscript{116} The overall average annual incidence rate of non-fatal electric injury in children was 53.2/100,000, with the rates significantly higher in males than in females, 66.7 vs 39.2/100,000, respectively. The incidence was highest in the 5–9-year age group and lowest in the 1–4-year age group, with electric injury being more common in rural children than urban children. Sixty-nine percent of the injuries occurred in the home and were caused by ‘house current’.

Curinga has recently called attention to the role of economics in high-voltage electric injury.\textsuperscript{117} During a recent 16-year period, 48 of the 560 electric injury patients treated at the Palermo Burn Center, Italy, were injured while stealing copper. The patients were typically young males and the injuries were commonly of limited extent (mean TBSA 11.5%) but very deep, with muscle necrosis, and destruction of joints and upper and/or lower limb tissues necessitating amputation in 29 cases. The authors noted a ‘linear correlation’ between the annual number of cases admitted and the price of copper.

In 2004 Marcucci and associates conducted a survey which identified failure of multimeters (devices used to measure electrical resistance, current, and voltage) as a cause of severe electric injury in 49 (0.5%) of the 900 responding electricians in Canada.\textsuperscript{118} Subsequent modification and use of fused lead multimeters resulted in no recorded critical injuries caused by multimeters in the province of Ontario in the years 2006–2008, illustrating the effectiveness of prevention focused on risk modification of specifically identified hazards.

There are 30 million cloud-to-ground lightning strikes each year in the United States, and each one represents a risk of severe injury and even death. From 1980 to 1995 a total of 1318 deaths were caused by lightning in the United States.
Arizona, Arkansas, and Mississippi had the highest crude and Texas, respectively 145 and 91. However, New Mexico, number of deaths caused by lightning occurred in Florida is seven times greater in males than in females. The greatest per 10 million population; crude rate 3 per 10 million) and lightning was greatest among patients aged 15–19 (six deaths in injuries, 62%, involved males and 58% occurred in individu-

Lightning injuries and deaths can be prevented by taking appropriate precautions. The decrease in lightning-related deaths over the past 20 years appears to be related to a decrease in the farm population, better understanding of the pathophysiology of lightning injury, and improved resuscitation techniques. Analysis of data from the Defense Medical Surveillance System by the US Army and the CDC reveals that the highest lightning-related injury rate occurred in male members of the US military stationed near the East Coast or the Gulf of Mexico, where lightning occurs frequently, who were subjected to outdoor exposure to thunderstorms. During 1998–2001, 350 service members were injured and one was killed by 142 lightning strikes. One-half of the lightning strikes occurred during July and August and three-quarters occurred between May and September. Two hundred and forty-six (70.1%) of the lightning injuries involved active duty personnel, with men being 3.3 times more likely to be struck than women. The overall lightning casualty rate for military personnel was 5.8/100,000 person-years. Louisiana, Georgia, and Oklahoma had the highest rates of lightning injury, i.e., 39.6, 25.2, and 23.5/100,000 person-years, respectively. Fireworks are another seasonal cause of burn injury. In the 2008 Fireworks Annual Report published by the US Consumer Product Safety Commission, Greene et al. reported that seven people died and 7000 patients were estimated to have received treatment in emergency departments for fireworks-related injuries. Seventy percent of the fireworks-related injuries occurred between 20 June and 20 July, which encompassed the 4th of July holidays. A majority of the injuries, 62%, involved males and 58% occurred in individu-

injurious fireworks were, in descending order, firecrackers, sparklers, and rockets. Sparklers, which burn at more than 1000°F, can ignite clothing and cause typical flame burns in addition to contact burns. Children aged 4 and under are at the highest risk for sparkler-related injuries. A report of seven patients with burns due to snap-cap pyrotechnic devices noted that six required hospital admission, with four undergoing split-thickness skin grafting for closure of burns to the leg caused by the explosion of multiple devices in one trouser pocket. Proposed prevention measures include reducing the explosive units per package, package warnings, and limiting the sale of the devices to children. At the US Army Institute of Surgical Research Burn Center, only four (0.1%) of 3628 burn patients admitted during a 15-year period had been burned by fireworks. In 2008, an estimated 22,500 fires were started by fireworks, which caused $42 million of property damage.

Burn injury can also be intentional, either self-inflicted or caused by assault. Data from 16 states evaluated by the National Violent Death Reporting System revealed that in those states in the United States in 2007, 15,882 individuals were fatally injured as a consequence of violence. Within that group fire/burns were the cause of 77 (0.5%) of all violent deaths, representing an incidence rate of 0.1/100,000 population. The violent deaths included 30 suicides (21 males and nine females), of which four were current or former members of the US Military. Only nine of the total 77 violent deaths due to burn injury were in patients aged 50 or over. There were 28 homicides caused by fire/burns, which occurred in 17 males and 11 females and represented 0.6% of all homicides. Burn injury was considered the cause of death in 21 patients or 2.7% of patients killed in multiple violent death incidents. In another 19 deaths in which a specific cause of death could not be determined, burn injury was considered to be the probable cause.

It is estimated that 4% of burns (published range 0.37–14%) are self-inflicted. A retrospective review of 5758 burn patients treated at a regional burn center during a 12-year period identified 51 patients (26 males and 25 females) with a diagnosis of self-inflicted burns. In 42 patients, in whom the injury was an attempt at suicide, the burn involved from 1% to 84% TBSA, with an average extent of 22%. Twelve (28%) of those patients died. There were nine patients in whom the injury was considered a form of self-mutilation. Those injuries typically caused by flames involved 1% to 5% TBSA, with an average extent of 1.4%. Forty-three percent of all the injuries occurred at home, and 14 (33%) occurred while the patient was in a psychiatric institution. Seventy-three percent of the patients had a history of psychiatric disease: in the suicides these were predominantly affective disorders or schizophrenia, and in the self-mutilators personality disorders. Fifty-five percent of the suicides had previously attempted suicide; 66% of the self-mutilators had made at least one previous attempt at self-mutilation. The authors concluded that the very act of self-burning warranted psychiatric assessment.

The extent of such injuries has been reported to be greater than that of accidental burns, with the head and torso more frequently involved than in patients with accidental burns. Consequently, the hospital stay was typically longer than that of patients with accidental burns. Buddhist ritual burning using contact with smoldering incense is a
The vast majority, 84, had only partial-thickness injuries. Fifty-one of the 94 male patients and 12 of the 33 females had been assaulted by their spouses. In cases of spouse abuse the face or genitalia are characteristically splashed with chemicals or hot liquids, whereas cases due to abuse or neglect in elderly, disabled, and handicapped adults resemble those in child abuse cases. In India, a common form of spouse abuse is burning by intentional ignition of clothing. When such burns are fatal they have been called 'dowry deaths', because they have been used to establish the widower's eligibility for a new bride and dowry.

In 41, or 3.3%, of all patients with significant burns admitted to a German Burn Intensive Care Unit over a 15-year period assault was the cause of the burn. The injuries were caused by hot liquids, chemicals, or fire, and 33% of the patients were less than 26 years old. Evaluation by logistic regression identified younger age, ethnic minority, and unemployment as independent variables associated with assault burns.

Assault by paint thinner ignition has been reported as an infrequent form of burn injury among Turkish street children addicted to paint thinner. The nine patients with such injuries who were admitted to a burn center in Turkey during a 10-year period (0.76% of 1170 major burn admissions) had burns involving from 35% to 90% TBSA. The face and neck were most often involved (89% of cases), followed by the trunk and upper limbs. Six patients, of whom three died, had inhalation injury.

The Burn Unit of The National Hospital of Sri Lanka admitted 46 patients with acid burns due to assault during an 18-month period. Those patients represented 4% of all burned admissions and ranged in age from 12 to 60 years, with a male to female ratio of 2.8:1. Formic acid was the most common injuring agent, but in more than half the cases the type of acid was unknown. The average extent of burn was only 14.6% TBSA, but involved the face in 93% of cases, the chest in 65% and the upper limbs in 64%. In 43% of the patients excision and grafting were necessary. A mortality rate of 4.34% reflected the limited nature of the burns.

Disfigurement and blindness caused by chemical assault with acid have been emphasized by Milton et al., who noted that the Acid Survivors Foundation reported 180 incidents of chemical assault in 2006 in which 221 patients in Banani, Dhaka, and Bangladesh were injured. The eye has been reported as injured in 26% of cases, and visual impairment, including blindness, may result, as well as severe disfigurement and long-term psychosocial morbidity.

Child abuse represents a special form of burn injury, most commonly inflicted by parents but also perpetrated by siblings and child-care personnel. Child abuse has been associated with teenage parents, mental deficits in either the child or the abuser, illegitimacy, a single parent household, and low socioeconomic status (although it can occur in all economic groups). Abuse is usually inflicted upon children younger than 2 years of age who, in addition to burns, may exhibit signs of poor hygiene, psychological deprivation, and nutritional impairment. The most common form (approximately one-third of cases) of child abuse thermal injury is caused by cigarettes; because of their limited extent, such injuries frequently do not require admission to a hospital.

Child abuse by burning has also been inflicted by placing a small child in a microwave oven. The burn injuries produced...
in that manner are typically present on the body parts nearest the microwave-generating element, full-thickness in depth, and sharply demarcated. Child neglect, if not child abuse, is considered to be a factor in burns to the hand, particularly those on the dorsum of the hand, due to contact with a hot clothing iron. Most often scalding causes the burns in abused children who require inpatient care. Such injuries are often associated with soft tissue trauma, fractures, and head injury. A distribution typical of child abuse immersion scald burns, i.e. feet, posterior legs, buttocks, and the hands, should heighten suspicion of child abuse.

The presence of such burns mandates a complete evaluation of the circumstances surrounding the injury and the home situation. The importance of identifying child abuse in the case of a burn injury resides in the fact that if such abuse goes undetected and the child is returned to the abusive environment, there is a high risk of fatality due to repeated abuse. Chester et al. recently reported that parental neglect is far more prevalent than abuse as a causative factor for burn injury in children. Children with burns that occurred as a consequence of neglect had deeper burns than children with accidental burns, and were more apt to require skin grafting for wound closure; 83% of the children with burns due to neglect had previously been referred to a child protection agency.

A review of the records of 457 children with burns treated at a burn center identified 100 whose injuries were deemed to be a likely result of abuse or neglect. Multivariate analysis revealed that younger age, female gender, burns on the lower extremities or trunk, longer hospital stay, and death were factors associated with burning due to abuse. Six of the children whose injuries were suspected to be a result of abuse died. The authors note that the prosecution rate of 26% and conviction rate of 11% in their locale are discouragingly low.

Elder abuse can also take the form of burn injury. A congressional report published in 1991 indicated that 2 million older Americans are abused each year, and some estimates claim a 4% to 10% incidence of neglect or abuse of the elderly. A recent retrospective review of 28 patients aged 60 and over admitted to a single burn center during a calendar year identified self-neglect in seven, neglect by others in three, and abuse by others in one. Adult protective services were required in two cases. The authors of that study concluded that abuse was likely to be under-reported because of poor understanding of risk factors and a low index of suspicion on the part of the entire spectrum of healthcare personnel.

Patients may also sustain burns while in hospital for diagnosis and treatment of other disease. In addition to the electric injuries noted above, chemical burns have been produced by inadvertent application of glacial acetic acid, concentrated silver nitrate, iodine, or phenol solutions, and potassium permanganate crystals. Application of excessively hot soaks or towels or inappropriate use of heat lamps or a heating blanket are other causes of burn injury to patients. Infrared heat lamps are often used in conjunction with acupuncture, but inappropriate intensity or excessive duration of exposure may cause full-thickness skin injury. Much more serious are the burns and inhalation injuries caused by electrocautery or laser devices, explosion of gases (including ignition of flammable material in oxygen), or ignition of the instruments used for endotracheal and endobronchial procedures or anesthetic management. Localized high-energy ultrasound may also produce coagulative necrosis, as exemplified by full-thickness cutaneous injury and localized subcutaneous fat necrosis of the abdominal wall in a patient who had received focused-beam high-intensity ultrasound treatment for uterine fibroids. A common cause of burn injury, particularly in disoriented hospital or nursing home patients, is the ignition of bedding and clothing by a burning cigarette. Smoking should be banned in healthcare facilities, or at least restricted to adequately monitored situations.

A retrospective review of 4510 consecutive patients admitted to a burn center between January 1978 and July 1997 identified 54 who had sustained burns while undergoing medical treatment. Twenty-two patients sustained their injuries in a hospital or nursing home, most commonly (12 patients) as a consequence of a fire started by smoking activities. Fifty-eight percent of those patients died. Another two patients were scalded while being bathed in nursing homes, and one of those patients died. Thirty-two patients were burned as a consequence of home medical therapy, including nine vaporizer scald burns, eight burns caused by ignition in therapeutic oxygen, and 11 caused by inappropriate application of heat. In contrast to other studies, no patients in this series sustained burns from medical lasers.

### Burn patient transport and transfer

As noted above, the concordance of burn treatment facility location and population density necessitates that many patients requiring burn center care be transferred from other locations. For transfer across short distances and in congested urban areas, ground transportation is frequently more expeditious than aeromedical transfer. Aeromedical transfer is indicated when the patient requires movement from a remote area, or when such transfer will materially shorten the time during which the patient is in transit compared to ground transportation. Helicopters are frequently employed for the aeromedical transfer of patients over distances of less than 200 miles. Vibration, poor lighting, restricted space, and noise make in-flight monitoring and therapeutic interventions difficult, a fact which emphasizes the importance of carefully evaluating the patient and modifying treatment as necessary to establish hemodynamic and pulmonary stability prior to undertaking the transfer. When transfer requires movement over greater distances, fixed-wing aircraft are used, ideally those in which an oxygen supply is available to support mechanical ventilation. The patient compartment of such an aircraft should be well lit, permit movement of attending personnel, and have some measure of temperature control.

In general, burn patients travel best in the immediate postburn period as soon as hemodynamic and pulmonary stability have been achieved by resuscitation. This avoids the instability caused by infection, secondary hemorrhage, sepsis, or cardiac insufficiency, all of which may occur later in the hospital course. The importance of having an experienced burn physician accompany a patient during aeromedical transfer is indicated by the findings of a study that reviewed the management problems encountered during 124 flights to transfer 148 burn patients. More than half the
patients underwent therapeutic interventions by the surgeon of the burn team prior to aeromedical transfer. Such interventions most commonly involved placement or adjustment of a cannula or catheter, modification of fluid therapy, or endotracheal intubation and modification of ventilatory management. In slightly more than one-third of the patients such interventions were considered necessary to correct physiologic instabilities that would have compromised their safety during the transfer procedure. Six of the 124 patients underwent an escharotomy to relieve compression of the chest or a limb caused by a constricting eschar. The therapeutic alterations most commonly used during the aeromedical transfer procedure itself were changes in fluid therapy, adjustment of a ventilator, and administration of parenteral medications exclusive of analgesics. The medical personnel effecting the transfer must bring with them all the equipment and supplies needed for pre-flight preparation and in-flight management of the patient.

Physician-to-physician case review to assess the patient’s need for and ability to tolerate aeromedical transfer, prompt initiation of the aeromedical transfer mission, examination of the patient in the hospital of origin by a burn surgeon from the receiving hospital, and correction of organ dysfunction prior to transfer, and in-flight monitoring by burn-experienced personnel, ensure both continuity and quality of care during the transport procedure. During the 10-year period 1991–2000, US Army Institute of Surgical Research Burn Care flight teams using such a regimen completed 266 helicopter and fixed-wing transfer missions to transport 310 burn patients within the continental United States without any in-flight deaths. During the same period, the Institute carried out 12 intercontinental aeromedical transfer missions in which 17 burn patients were transported, with only one in-flight death.

Mass casualties

Mass casualty incidents may be caused by forces of nature or by accidental or intentional explosions and conflagrations. Interest in manmade mass casualties has been heightened by recent terrorist activities and the threat of future incidents. The incidence of burn injury in a mass casualty incident varies according to the cause of the incident, the magnitude of the inciting agent, and the site of occurrence (indoors vs outdoors).

Burn injuries can be sustained during an earthquake and as a consequence of post-earthquake living conditions. Data collected by the CDC indicate that in the 3 months following the Haitian earthquake of January 2010, 111 patients required treatment for burn injury, 37 of whom were less than 5 years of age. Overall burn injury represented only 0.4% of the conditions receiving medical treatment during the 3-month study period.

Terrorist attacks may cause a greater number of burns but there are typically no post-incident injuries. The terrorist attacks in which airplanes laden with aviation fuel crashed into the Pentagon and the World Trade Center on 11 September 2001 produced respectively 10 and 39 patients with burns requiring treatment at burn centers. The terrorist attack on a nightclub in Bali in 2002 caused an explosion and fire that killed over 200 people and generated 60 burn patients who, after triage and emergency care, were transported by aircraft to Australia and treated at various hospitals. The casualties produced in terrorist attacks often have associated blast injury and mechanical trauma in addition to burns.

Recent non-terrorist mass casualty incidents have been of greater magnitude in terms of numbers of burn casualties. In 1994 an airplane collision caused nearby military personnel to be sprayed with burning aviation fuel. Of the 130 soldiers injured, 43 required transfer to the US Army Burn Center for treatment. In The Station nightclub fire in Warwick, Rhode Island, in February 2003, 96 people died at the scene and 215 were injured; 47 of the 64 burn patients evaluated at one academic medical center were admitted for definitive care. Lastly, an explosion at a pharmaceutical plant in North Carolina in January 2003 killed three and injured more than 30 to an extent that necessitated admission to a hospital. Ten of the injured patients, all with inhalation injury and six with associated mechanical trauma, were admitted to the regional burn center. To deal effectively and efficiently with a mass casualty situation, burn treatment facilities must have an operational and tested mass casualty disaster plan and be prepared to provide burn care to a highly variable number of patients injured in either natural or manmade disasters.

The international burn burden

Worldwide, an estimated 322,000 patients (5.2/100,000) died as a result of exposure to smoke, fire, and flames in 2002. A majority of those were residents of developing countries, as reflected in the higher incidence rates of fatal burn injury in the low-/middle-income countries of WHO regions, i.e. Africa 5.8/100,000, Eastern Mediterranean 6.4/100,000, Europe 7.4/100,000, and Southeast Asia 11.6/100,000. Fifty-seven percent of fatal burns were sustained in Southeast Asia and two-thirds of those occurred in females. In the Southeast Asia region, fatal burns in 15–45-year-old women represented slightly more than one in every four fatal burns worldwide, and the incidence of fatal burns in the 15–29-year age group of females in that region was 2.6/100,000. During the 3-year period 2003–2005, the standardized mortality rate from fires for persons under 20 years of age in the WHO European region ranged from a high of 3.7/100,000 in Azerbaijan to a low of 0.1/100,000 in Switzerland.

In the 2004 WHO Global Burden of Disease update, it was estimated that worldwide there were 10,900,000 injuries due to fire, with the greatest number in Southeast Asia (3,900,000) and Africa (1,700,000) and the fewest in Europe (800,000), Western Pacific (700,000), and the Americas (300,000). At that time, the worldwide incidence rate of fatal burn injury for all patients younger than 20 was 3.9/100,000. In the low- and middle-income countries of the African region the incidence rate of fatal burn injury for that age group was 8.7/100,000, whereas in the WHO Americas region it was only 0.7/100,000 for high-income countries and 0.6/100,000 for low- and middle-income countries. That 2004 update further reported that the incidence rate of fatal burn injury in patients under 20 years in the low-/middle-income countries of Southeast Asia, the Eastern Mediterranean,
and the Western Pacific regions was 6.1, 4.7, and 0.6/100,000, respectively. In 2007 in the US there were 597 fatal burn injuries in children under the age of 20 years, which represented 3.5% of all fatal injuries and an incidence rate of 0.72/100,000.2

Developed countries

The epidemiology of burn injury in the Australian state of Victoria for the years 2000–2006 has been characterized by Wasiak and associates.164 During the study period there were 178 fatal burns and 36,430 patients who received treatment for non-fatal burns, of whom 21% were admitted to hospitals. Children below age 5 and the elderly of 65 or over had the highest incidence rates for burn injury. Sixty-four percent of hospital admissions were for treatment of burns caused by contact with hot objects and fluids. In contrast to the decreases observed in the United States, the authors reported no change in the incidence rate or number of hospital admissions during the study period.

Analysis of state-wide health administrative data has been used to characterize the 23,450 patients admitted to hospitals in Western Australia during a 26-year period for the treatment of burn injury.165 There were twice as many males as females in the study. During the study period, the overall hospital admission rates for burn injury and the burn-related mortality each decreased an average of 2% per year. Although the hospital admission rates were higher for Aboriginal people, the decrease in hospitalization rate was greater in that population. Children below 5 years of age, males between age 20 and 24, and adults were noted to remain at high risk for burn injury requiring hospital admission.

A retrospective review of the medical records of 14,708 patients admitted for the initial care of burn injury in New Zealand between 1996 and 2006 indicated that the number of admissions was greatest in the 0–4 year age group and highest in the Maori ethnic group.166 Men outnumbered women by almost 2:1. The number of patients admitted to hospitals for the care of burn injury increased as the New Zealand index of deprivation of residence increased, rising from 19/100,000 per year with a deprivation score of residence of 1 to a high of 70/100,000 per year with a deprivation score of residence of 10.

Information from the Norwegian Patient Registry reveals that in 2007 there were a total of 726 patients admitted to hospitals for acute burn care, representing an incidence rate of 15.5/100,000 population.167 The incidence rate of burns requiring admission to a hospital in children of less than 5 years was 5.3 times greater, i.e. 82.5/100,000 per year. The mean age of all burn patients was 26.9 years, two-thirds of them were male, and the mean duration of hospital stay was 11.3 days. The total cost for acute burn care in Norway in 2007 was calculated to be €0.5 million. Fifteen of the patients (2.1%) died of burns in Norwegian hospitals in that year.

A retrospective review of 71 patients burned in civil gas explosions and treated at a German Burn Center revealed that such injuries occurred predominantly in males, with the principal place of injury being a private household.168 Fifty percent of work-related explosions were associated with welding and 22% with professional cooking. The mean extent of burn in those patients was 22% TBSA, and 73% required excision and grafting. Inhalation injury occurred in 13 (18%) of the total group and was fatal in eight. Lung contusion was sustained by nine (13%) of the patients, five of whom died. Overall mortality was 21%, which was significantly higher than that of all burn patients treated at that unit, even though the acute burn severity index scores were comparable.

A study of the epidemiology of ‘minor and moderate’ burns in rural Iran using a pretested questionnaire has documented that 59% of the patients were female, and that patients age 6 and under sustained 36.4% of burn injuries. Spillage of hot water and other liquids was the cause of the majority of the burn injuries.169 In only 43% of patients was there a partial-thickness injury with a mean extent of 1.3% TBSA. A study of 4813 patients treated for burn injury on an outpatient basis in Iran found that the majority of the burns were non-intentional, and that 70.5% occurred at home; scalding was the most common etiology.170 Ninety-six percent of the burns were partial thickness and, as expected, of limited extent (mean=3.16% TBSA).

Torabian and Saba171 illuminated the epidemiology of pediatric burn injury in an Iranian province. They reviewed the records of 371 children under 14 years of age admitted to a provincial referral burn hospital. The incidence rate of pediatric burns requiring hospital care was 33.4/100,000 annually. Patients less than 4 years constituted 69% of the pediatric burn population. Overall, males predominated in the pediatric burn population, and the incidence rate of burn injury was highest in children below the age of 2. The incidence rate for rural areas was more than twice that for urban areas. Scalding was the major cause of burn injury overall. The mean extent of burn injury was 16.36% TBSA, but slightly more than three-quarters of the patients had burns of 20% or less TBSA. Thirteen patients (3.5%) died, with a mortality rate several times higher in patients with flame burns than in patients with scald injuries.

Developing countries

The demographics of pediatric burns in Vellore, India, have been compared to those in the United States.172 A review of 119 pediatric burn patients admitted to the Pediatric Burn Center in Vellore indicated that their average age was 3.8 years and the average extent of burn was 24% TBSA. The cause of the burn injury was scald 64%, flame 30%, and electricity 6%. In Vellore, delayed presentation occurred in 45% of patients and averaged 2 days. Compared with the pediatric patients entered in the American Burn Association National Burn Registry, the average extent of burn was greater in the patients in Vellore and the extent of burn in those children who died was less. Electric injury was more common in Vellore than in the United States, and contact burns were almost non-existent in Vellore.

Trauma deaths in patients under 20 years in Southern India have been analyzed by review of medicolegal autopsy reports.173 ‘Traffic accidents’ and burns were considered to be the cause of death in 38% and 25% of cases, respectively. In the cases of burn death, the male to female ratio was 1:1.5. The 46 burn deaths in the 10–19-year age group were more than triple the 15 burn deaths that occurred in children under 10 years of age. The authors reported a ‘substantial decline’ in burn-related deaths in children and adolescents between 1994 and 2005.
Among 532 patients admitted to a regional referral hospital in Kabul, Afghanistan, for the treatment of burn injury during a recent 15-month period, the overall median age was 19 years and, contrary to the case in Western nations, 60% of the patients were female. The frequency of burn injury was greatest in both males and females in the 16–25-year age group, but that of females was almost twice that of males. The mean extent of burn was 36.5% TBSA, with 41% of patients having burns of less than 20% TBSA and 10% having burns of 80% TBSA or more. The most common causes of burn injury were flames and explosion of a gas cylinder. There were 21 patients who set themselves on fire, of whom 76% expired. Overall, there were 151 deaths for a mortality rate of 28%. Burns involving more than 60% TBSA were invariably fatal.

A recent report from Nigeria has called attention to the burn and fire disasters caused by the explosion of petroleum products leaking from pipelines that have either been deliberately damaged (56% of cases) or have ruptured spontaneously (44% of cases). In nine incidents of pipeline fire disasters, 646 patients were incinerated and died at the site. Forty-eight patients with burns involving from 32% to 100% TBSA survived to be admitted and treated at a university teaching hospital in Lagos. The authors considered poverty, irregular supply, and the high cost of fuel to be responsible for the deliberate pipeline damage, and implicated inadequate maintenance and surveillance in the cases of spontaneous rupture.

To provide more detailed information on nation-specific epidemiologic and demographic characteristics of burn injury the International Society for Burn Injury (ISBI) national representatives were sent a questionnaire and requested to supply current information about the incidence of burn injury and burn fatalities in their country, and to describe any aspects of the burn injuries that were unique and/or of concern. The information supplied by the representatives listed is displayed in Tables 3.9, 3.10, and 3.11. In aggregate, the data document the importance and universality of burn injury as a societal problem and illustrate the inverse relationship between burn injury incidence and economic development.

### Outcome analysis in burn injury

The importance of extent of injury in determining burn outcome was recognized by Holmes in 1860, and discussions expressing that extent as either a measured area or as anatomical parts of the body surface appeared in the later nineteenth and early twentieth centuries. Formal expression of burn size as a percentage of TBSA, however, awaited the work of Berkow in 1924. Despite being accorded little recognition as such, this single advance in the description of thermal injury, along with the corollary understanding that burn size is a crucial determinant of pathophysiological response, made burns the first form of trauma whose impact could be measured and easily communicated. Techniques based on this understanding produced what were in effect the first trauma indices, making assessment of the relationship between burn size and mortality, direct comparison of populations of burned patients, and rational assessment of therapy, possible long before rigorous outcome analysis became feasible for any other form of injury.

The earliest comprehensive statistical technique used for such assessment was univariate probit analysis. This approach, laborious in the days of paper files and rotary calculators, required that the population studied be arbitrarily partitioned into groups which were relatively similar in burn size and age. Such analyses yield equations describing the effect of burn size on mortality which are valid for only the particular age group studied. An early attempt to develop a multivariate evaluation was made by Schwartz, who used probit plane analysis to estimate the relative contributions of partial- and full-thickness burns to mortality. This approach also required arbitrary partitioning of the population.

The advent of computers of suitable power and the further development of statistical techniques have reduced the difficulty of analyzing burn mortality, removed the necessity for arbitrary partitioning, and made these techniques much more accessible. Their use to assess outcome demands an understanding of both the techniques themselves and the population being analyzed. The analysis of a population of 8448 patients admitted for burn care to the US Army Institute of Surgical Research Unit, between 1 January 1950 and 31 December 1991 illustrates the concepts underlying such outcome analysis, and depicts the trends in mortality that have been characteristic of most major burn centers in this country.

For validity, an important first step in studies of outcome is to achieve as much uniformity as possible in the population to be analyzed. These patients reached the Institute between the day of injury and postburn day 531 (mean 5.86d, median 1d), with burns averaging 31% TBSA (range 1–100%, median 26%). Their age distribution was bimodal, with one peak at 1 year of age and another at age 20; the mean age of the entire population was 26.5 years (range 0–97, median 23 years). From this group, 7893 (93.4%) who had flame or scald burns were selected; those with electric or chemical injuries were excluded.

This group included patients who had sustained thermal injuries in Vietnam and were first transferred to Japan and then selectively transferred to the Institute. Arriving at the Institute relatively late in their courses, these survivors of temporal cohorts in which some deaths had already occurred exhibited inordinately low mortality. Outcome is inevitably biased towards survival as the delay between burn and admission increases. To avoid this bias, the analysis focused on the 4870 patients with flame or scald injuries who reached the Institute on or before the second postburn day, excluding later arrivals. Burn size in these patients averaged 34% TBSA (range 1–100%, median 29%), and age was again bimodal, with peaks at 1 and 21 years and a mean of 27.1 years (range 0–93, median 24 years).

One object of this analysis was to evaluate changes in burn mortality during the four decades of experience included in the study. For reliable results, some of the techniques used required more subjects than were available in single years; a moving 5-year interval, advancing 1 year at a time, was used to group the data. The number of patients in each of the overlapping 5-year intervals is shown in Figure 3.2. In this and subsequent plots, the data for a 5-year interval are

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of Patients</th>
<th>Percentage of Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1950</td>
<td>1000</td>
<td>13%</td>
</tr>
<tr>
<td>1955</td>
<td>1200</td>
<td>15%</td>
</tr>
<tr>
<td>1960</td>
<td>1400</td>
<td>18%</td>
</tr>
<tr>
<td>1965</td>
<td>1600</td>
<td>21%</td>
</tr>
<tr>
<td>1970</td>
<td>1800</td>
<td>24%</td>
</tr>
<tr>
<td>1975</td>
<td>2000</td>
<td>26%</td>
</tr>
<tr>
<td>1980</td>
<td>2200</td>
<td>28%</td>
</tr>
<tr>
<td>1985</td>
<td>2400</td>
<td>30%</td>
</tr>
<tr>
<td>1990</td>
<td>2600</td>
<td>32%</td>
</tr>
<tr>
<td>1995</td>
<td>2800</td>
<td>34%</td>
</tr>
<tr>
<td>2000</td>
<td>3000</td>
<td>36%</td>
</tr>
<tr>
<td>2005</td>
<td>3200</td>
<td>38%</td>
</tr>
</tbody>
</table>

This table shows the number of patients admitted each year and their percentage of the total population. The analysis was performed over a 50-year period, with results indicated for each 5-year interval.
### Table 3.9  Burn Injury in Europe

<table>
<thead>
<tr>
<th>Country (Population)</th>
<th>Annual incidence</th>
<th>Fatal burns</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Country (Population)</strong></td>
<td><strong>Annual incidence</strong></td>
<td><strong>Leading cause</strong></td>
<td><strong>Fatal burns</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Overall burn injury</strong></td>
<td><strong>n</strong></td>
<td><strong>Rate</strong></td>
<td><strong>n</strong></td>
</tr>
<tr>
<td><strong>Azerbaijan</strong> (8,238,672)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Children (0–15 years)</strong></td>
<td>2,055 (36% of all burns)</td>
<td>23</td>
<td>Electric injury: 5%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&lt;6 years. 55% scalds</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&gt;6 years. 40% flames</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Flames</td>
</tr>
<tr>
<td><strong>Young adults (16–40 years)</strong></td>
<td>2,723 (47% of all burns)</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td><strong>Older adult (41+ years)</strong></td>
<td>952 (17% of all burns)</td>
<td>10.5</td>
<td></td>
</tr>
<tr>
<td><strong>Czech Republic</strong> (10,211,904)</td>
<td>3,362</td>
<td>32</td>
<td>Scalds: 78%</td>
</tr>
<tr>
<td><strong>Hospital admissions for burn injury – 2009</strong></td>
<td></td>
<td></td>
<td>Scalds: 55%. Flame: 34%</td>
</tr>
<tr>
<td></td>
<td>Children</td>
<td>1,606</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Young adults</td>
<td>738</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Older adults</td>
<td>1,018</td>
<td></td>
</tr>
<tr>
<td><strong>Estonia</strong> (1,299,371)</td>
<td>3,697</td>
<td>288</td>
<td></td>
</tr>
<tr>
<td><strong>Overall burn injury (2007–2009 average per year)</strong></td>
<td></td>
<td></td>
<td>Beven chemical burns admitted to nation’s adult unit 2007–2009</td>
</tr>
<tr>
<td></td>
<td>Children</td>
<td>1,062</td>
<td>(29% of all burns)</td>
</tr>
<tr>
<td></td>
<td>Young adults (16–40 years)</td>
<td>1,352</td>
<td>(36% of all burns)</td>
</tr>
<tr>
<td></td>
<td>Older adults (41+)</td>
<td>1,283</td>
<td>(35% of all burns)</td>
</tr>
<tr>
<td><strong>Germany</strong> (81,471,854)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Fire injury – All ages</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Children (1991)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>All injuries</td>
<td>8.32</td>
<td></td>
</tr>
<tr>
<td></td>
<td>All burns</td>
<td>0.25</td>
<td></td>
</tr>
<tr>
<td><strong>Greece</strong> (11,299,183)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Overall burn injury</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Children (0–19 years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Country</td>
<td>Population</td>
<td>Annual incidence</td>
<td>Leading cause</td>
</tr>
<tr>
<td>--------------</td>
<td>------------</td>
<td>------------------</td>
<td>---------------</td>
</tr>
<tr>
<td><strong>Poland</strong></td>
<td>(38482 919)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All ages</td>
<td>309 000</td>
<td>811</td>
<td>Hot liquids</td>
</tr>
<tr>
<td>Admitted to hospital</td>
<td>9500 (3.1%)</td>
<td></td>
<td>Open flame</td>
</tr>
<tr>
<td>Children</td>
<td>138</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Young adults</td>
<td>255</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Older adults</td>
<td>418</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Romania</strong></td>
<td>(22 215 421)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All burn injury</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Children (0–15 years)</td>
<td>50</td>
<td></td>
<td>Scalds</td>
</tr>
<tr>
<td>Adults</td>
<td>40</td>
<td></td>
<td>Scalds</td>
</tr>
<tr>
<td><strong>Russian Federation</strong></td>
<td>(140 041 247)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall burn injury</td>
<td>400 000</td>
<td>275.8</td>
<td>Boiling water and flame</td>
</tr>
<tr>
<td>Children</td>
<td>114 000</td>
<td></td>
<td>Boiling water and flame</td>
</tr>
<tr>
<td>Young adults</td>
<td>152 000</td>
<td></td>
<td>Boiling water and flame</td>
</tr>
<tr>
<td>Older adults</td>
<td>134 000</td>
<td></td>
<td>Boiling water and flame</td>
</tr>
<tr>
<td><strong>Sweden</strong></td>
<td>(9 059 654)</td>
<td></td>
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<tr>
<td>Burns admitted to hospital: 1987–2004</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Annual mean</td>
<td>1363</td>
<td>15.5</td>
<td></td>
</tr>
<tr>
<td>Children</td>
<td></td>
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</tr>
</tbody>
</table>

Causes as percentage of total burns: open flame 37%, hot liquids 26%, contact 10%, chemical 6%, electric 6%, and structural fires 12%.

Burns = 6% of all ‘external’ causes of death. Scalds in one-half of all cases age 0–4 years. Considerable number of high voltage electric injuries in teenagers. More flame, electric, and chemical burns in adults than in children. Home fires common in elderly patients.

Specific causes: bath house burns, steam, contact with ‘red hot’ stove, smoking while intoxicated.

Males: 69%
M/F = 2.23:1
Reduction in number with time, decrease > in males
0–4 years – 27% of all burns
20–24 years – 7% of all burns.

*Per 100 000. Data sources: 1Elmira Panahova PhD MD; 2Leo Klein MD; 3Ain Seimar MD; 4Professor Norbert Pallua MD PhD; 5Sophia Papadopoulos MD; 6Stanislaw Sakiel MD; 7Dan Enescu MD PhD; Mikhail Gordon MD and Professor Andrey A. Aleeseev MD; 8Folke Sjöberg MD. Fatal burn incidence rates, see http://www.who.int/healthinfo/global_burden_disease/estimates_country/en/index.html and reference 161.
<table>
<thead>
<tr>
<th>Country (Population)</th>
<th>Annual incidence</th>
<th>Fatal burns</th>
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</thead>
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<tr>
<td></td>
<td></td>
<td>Leading cause</td>
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<td></td>
<td></td>
<td>n     Ratea</td>
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<td></td>
<td></td>
<td>n     Ratea</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Comments</td>
</tr>
<tr>
<td>Malaysia (25,715,819)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall burn injury (2009)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Children (0–14 years)</td>
<td>62% of all burns</td>
<td>12</td>
</tr>
<tr>
<td>Young adults (15–40 years)</td>
<td>30% of all burns</td>
<td>2</td>
</tr>
<tr>
<td>Older adult (41+ years)</td>
<td>8% of all burns</td>
<td>8</td>
</tr>
<tr>
<td>Malaysia (25,715,819)</td>
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<tr>
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<td>30% of all burns</td>
<td>2</td>
</tr>
<tr>
<td>Older adult (41+ years)</td>
<td>8% of all burns</td>
<td>8</td>
</tr>
<tr>
<td>New Zealand (4,213,418)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall burn injury (July 2009–June 2010)</td>
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<td></td>
</tr>
<tr>
<td>Children (0–14 years)</td>
<td>62% of all burns</td>
<td>12</td>
</tr>
<tr>
<td>Young adults (15–39 years)</td>
<td>30% of all burns</td>
<td>2</td>
</tr>
<tr>
<td>Older adult (41+ years)</td>
<td>8% of all burns</td>
<td>8</td>
</tr>
<tr>
<td>South Korea (48,508,972)</td>
<td></td>
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</tr>
<tr>
<td>Overall burn injury (2008)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Children (0–15 years)</td>
<td>62% of all burns</td>
<td>12</td>
</tr>
<tr>
<td>Young adults (16–40 years)</td>
<td>30% of all burns</td>
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<tr>
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<td>8% of all burns</td>
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<tr>
<td>Overall burn injury (2009)</td>
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<td>62% of all burns</td>
<td>12</td>
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<tr>
<td>Young adults (16–40 years)</td>
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</tr>
<tr>
<td>Taiwan (29,974,347)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1989–2008</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Children (0–10 years)</td>
<td>62% of all burns</td>
<td>12</td>
</tr>
<tr>
<td>Adults (31–40 years)</td>
<td>30% of all burns</td>
<td>2</td>
</tr>
<tr>
<td>Older adult (81+ years)</td>
<td>8% of all burns</td>
<td>8</td>
</tr>
<tr>
<td>2009</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Children (0–15 years)</td>
<td>62% of all burns</td>
<td>12</td>
</tr>
<tr>
<td>Adults (16–40 years)</td>
<td>30% of all burns</td>
<td>2</td>
</tr>
<tr>
<td>Older adult (41+ years)</td>
<td>8% of all burns</td>
<td>8</td>
</tr>
</tbody>
</table>

*Per 100,000 population. Data sources: "Dr Shah Jumaat Mohd Yussof MB BSh BAO MRCSI MS; "Ms Kendra Sanders at Accident Compensation Corporation; "Dong-Chul Kim MD PhD; "Jui-Yung Yang, MD. 'Includes chemical. Fatal burn incidence rates; http://www.who.int/healthinfo/global_burden_disease/estimates_country/en/index.html
Epidemiological, demographic, and outcome characteristics of burn injury

Figure 3.4 shows the variation in mean burn size during the study interval, and Figure 3.5 shows the roughly parallel mortality. Mean burn size peaked in the two intervals spanning 1969 to 1974 and decreased steadily after that time. Mortality, principally due to burn wound sepsis, peaked at 46% during those years. The two data sets are shown together in Figure 3.6 and suggest a crude index of the results of burn care in this population. There were two intervals in which percent mortality exceeded mean percent burn. The first occurred in the late 1950s and early 1960s, a time when burn wound sepsis due to *Pseudomonas aeruginosa* was uncontrolled. This was succeeded by a 6-year interval of good control of wound infection following the introduction of

<table>
<thead>
<tr>
<th>Country (Population)</th>
<th>Annual incidence</th>
<th>Leading cause</th>
<th>Fatal burns</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Argentina</strong> (40913584)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Burn patients admitted to hospital: 2005–2009</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>19</td>
<td></td>
<td>0.5</td>
</tr>
<tr>
<td>Children (0–15 years)</td>
<td>7.6</td>
<td>Scald</td>
<td></td>
</tr>
<tr>
<td>Young adults (16–40 years)</td>
<td>8</td>
<td>Flame</td>
<td></td>
</tr>
<tr>
<td>Older adult (41+ years)</td>
<td>3.4</td>
<td>Flame</td>
<td></td>
</tr>
</tbody>
</table>

| **Uruguay** (3344938) | | | |
| Burns treated at National Burn Center: July 10, 1995–April 30, 2010 | | | |
| Overall burn admissions | 1850 | | |
| Children (<15 years) | 23 | | |
| Young adults (15–45 years) | 1027 | | |
| Older adult (46+ years) | 800 | | |
| Outcomes by type of burn | n | Mortality (%) | |
| Scald | 169 | 9.5 | |
| Fire/flame | 1357 | 24.6 | |
| Electric injury | 115 | 4.5 | |
| Chemical | 7 | 28.6 | |
| Gas explosion | 126 | 20 | |


*Figure 3.2* Number of patients meeting study criteria. Values are plotted at the first year of each moving 5-year interval.

*Figure 3.3* Mean age of study patients.

*Figure 3.4* shows the variation in mean burn size during the study interval, and *Figure 3.5* shows the roughly parallel mortality. Mean burn size peaked in the two intervals spanning 1969 to 1974 and decreased steadily after that time. Mortality, principally due to burn wound sepsis, peaked at 46% during those years. The two data sets are shown together in *Figure 3.6* and suggest a crude index of the results of burn care in this population. There were two intervals in which percent mortality exceeded mean percent burn. The first occurred in the late 1950s and early 1960s, a time when burn wound sepsis due to *Pseudomonas aeruginosa* was uncontrolled. This was succeeded by a 6-year interval of good control of wound infection following the introduction of

Mean patient age is shown in *Figure 3.3*. Between 1950 and 1965 most of the admissions were young soldiers; their mean age approximated 22.5 years and was relatively stable. During the succeeding decade this value rose to an irregular plateau centering on 30 years of age, a change reflecting a greater number of civilian emergency admissions and increasing age in the military population.
topical wound treatment with mafenide. In turn, this was followed by a second interval of poor control in the late 1960s and early 1970s, during which both *Pseudomonas* and a mafenide-resistant *Providencia stuartii* were major causes of sepsis; by the mid-1970s this endemic had been controlled following changes in topical treatment and wound management.

Raw percent mortality, even in conjunction with burn size, is never an adequate index of the effectiveness of treatment, as the frequency of death after burn injury is also determined by prior patient condition, age, inhalation injury, and the occurrence of pneumonia and burn wound sepsis. Each of these elements, except for prior condition, can be addressed in analysis, but only burn size, age, and the presence or absence of inhalation injury are known at the time of admission. In the studied group, burn size and age were available for every patient, but data on inhalation injury were missing for patients admitted in the earlier years; we elected to use burn size and age for analysis. This choice does not exclude the impact of complications, but does confound that impact with those of burn size and age.

For a uniform population of specific age, a plot of the relationship between burn size and percent mortality is S-shaped, or sigmoid – small burns produce relatively few deaths, but as burn size increases mortality rises steeply and then plateaus as it approaches its maximum of 100%. Figure 3.7 illustrates this dose–response relationship for 50-year-old patients admitted to the Institute between 1987 and 1991. Such curves are mathematically intractable and are usually transformed to more easily managed straight lines for analysis. Several mathematical transformations have been used to accomplish this. As previously noted, the one used in early analyses was probit transformation; in the present study, a logistic transformation, illustrated in Figure 3.8, was used. The choice between these is one of convenience, as either yields essentially the same information.\textsuperscript{184,185}

The locations of a sequence of such curves for groups of patients of increasing age move first to the right (toward larger burn size) as age increases from infancy to young adulthood, and then to the left, passing through the infant location at around age 45 and continuing inexorably leftward with increasing age. These differing locations reflect the greater risk of burn mortality at the extremes of age. The cubic curve in Figure 3.9 describes this curvilinear effect of age on mortality; the effect was least at age 21. In this population, the age function was relatively stable over the entire period of study.\textsuperscript{186} As noted, earlier analyses began by
Epidemiological, demographic, and outcome characteristics of burn injury

The advantage of this approach, as opposed to previously used age- and burn size-partitioned analyses, is that it permits analysis of an entire population without artificial segmentation, and allows an explicit estimation of expected mortality for each member of the population. Serial applications of dividing the studied population into arbitrary age and burn size groups; probit analysis of the relationship between burn size and percent mortality in each age group then permitted estimation of the LD_{50}, the burn size lethal to half the selected age group. To accommodate both age and burn size simultaneously, without arbitrary partitioning of the population, multiple logistic regression was used in this study, with each member of the population entering the analysis as an individual data point.

The result of this three-dimensional form of analysis is most readily visualized as a plane lying within a cube. Figure 3.10 shows the sigmoid response of mortality to burn size for three discrete ages, and Figure 3.11 shows the curvilinear variation of mortality with age in patients entering this study between 1987 and 1991. A best-fitting plane which covers the tips of spikes representing all of the burn sizes and ages of interest is generated by the multiple logistic technique, and it is illustrated for these particular patients in Figure 3.12. The equation representing this plane is of the form shown below, in which $L$ is the natural logarithm of the odds of mortality and $P$ the expected fractional mortality rate.

$$L = a_1 + a_2(\% \text{ burn}) - a_3(\text{age}) + a_4\left(\frac{\text{age}^2}{100}\right) - a_5\left(\frac{\text{age}^3}{10,000}\right)$$

$$P = \frac{\exp L}{1 + \exp L}$$

The advantage of this approach, as opposed to previously used age- and burn size-partitioned analyses, is that it permits analysis of an entire population without artificial segmentation, and allows an explicit estimation of expected mortality for each member of the population. Serial applications of
the technique were used to assess mortality in each of the moving 5-year intervals of the study.

Moreau et al.\textsuperscript{186} have developed an age risk function ($F_{\text{age}}$) based on the Institute’s experience. Expressed as a single value, this function eases exploration of statistical interactions with other independent explanatory variables and simplifies mortality analysis:

$$F_{\text{age}} = -5(\text{age}) + 14(\text{age}^2/100) - 7(\text{age}^3/10000)$$

$$L = a_1 + a_2(\%\text{burn}) + a_3(F_{\text{age}})$$

$$P = \exp^L / (1 + \exp^L)$$

Following the initial study, 4008 additional patients meeting the study criteria were admitted between 1992 and 2010. Mortality in these patients did not differ significantly from that observed between 1987 and 1991. Figure 3.13 reflects the changes in LD$_{50}$ between 1950 and 2010. This value began to increase in the mid-1970s and has been relatively stable since 1986. Many aspects of care changed and improved during these six decades:

- early resuscitation became more widely understood and better practiced;
- the clinical facility was remodeled to permit single bed isolation;

![Figure 3.12](image1.png) **Figure 3.12** Plane of percent mortality with age and burn size coordinates (1987–1991).

![Figure 3.13](image2.png) **Figure 3.13** LD$_{50}$ in moving 5-year intervals in patients 21 years of age. Increasing values indicate improving prognosis.
• topical chemotherapy with alternating applications of mafenide acetate and silver sulfadiazine, coupled with the use of a chlorhexidine-based wash solution (hibiclens), permitted better control of wound infection;
• early wound excision came to be more generally practiced;
• better infection control techniques limited cross-contamination of wounds;
• new antibiotics, more effective against Gram-negative organisms, became available;
• inhalation injury and other pulmonary problems became better understood and are now managed with better equipment;
• improved grafting techniques and the use of biological dressings facilitated earlier coverage of large wounds.

In essence, through integrated clinical and laboratory research, we learned how to apply ordinary principles of trauma and wound care to an extraordinary injury. No single innovation produced a ‘step’ improvement in mortality, but the aggregate effect has been improved survival.

This improvement is reflected in Figures 3.14 and 3.15, which depict early (1950–1963) and more recent (1987–1991) mortality planes, respectively. The improvement was not uniform for all burn sizes or ages, nor would one expect this. Small burns have never been lethal, except at the extremes of age; little improvement in survival could occur with such injuries. At the other extreme, very large burns in older patients have always been lethal and remain so. To define the age and burn size coordinates of the improvement in survival, one subtracts one mortality plane from the other; the result is itself a plane depicting the difference in mortality in age and burn size coordinates (Figure 3.16). The greatest differences occurred in the area of the LD_{50} of the 1950–1963 mortality plane.

Logistic regression permits simple assessment of the odds ratio for mortality between the individual years and the last year of this span, with appropriate adjustment for age and burn size (Figure 3.17). This ratio indexes the effect on mortality of everything beyond burn size and age. Peaks occurred when sepsis was uncontrolled. The lower ratios beyond 1975 reflect the additive effects of the changes in treatment, environment, and infection control. No significant differences in the ratio occurred during the 25 years between 1986 and 2010.

Of 4104 patients meeting the present study criteria between 1950 and 1985, 1320 (32%) died. Of 4895 such patients admitted between 1986 and 2010, 421 (9%) died. This reflects, in part, a diminution in mean burn size, but had the adjusted mortality experienced since 1986 prevailed through

Figure 3.14  Mortality plane for patients admitted between 1950 and 1963. Note location of contour lines in base of cube.

Figure 3.15  Mortality plane for patients admitted between 1987 and 1991. Note contour locations.

Figure 3.16  Plane of differences in percent mortality between 1950–1963 and 1987–1991. Note location of peak.
the earlier interval, only slightly more than half the earlier number would have succumbed. Although this experience corresponds with that of most burn centers in the United States, it should be noted that there are still many areas of the world where the survival of patients with burns of more than 40% TBSA is rare.

As previously noted, estimates of the annual total number of burns in the United States, for which there is little reliable information, range as high as 2,000,000. A more reliable but still imperfect estimate is that between 50,000 and 70,000 acutely burned patients are admitted to hospitals in the United States each year. Figure 3.18 is based on composite data from several sources and depicts an estimate of the age and burn size distribution of these patients. Using the Institute’s mortality experience between 1986 and 2010 as a basis for projecting expected mortality yields the data shown in Figure 3.19, which depicts the age and burn size distribution of expected deaths. According to this model, patients over 50 with burns of 50% or less TBSA account for 19% of admissions and 50% of deaths; at the other age extreme, children under 5 account for 19% of admissions but only 12.5% of deaths.
Much has been accomplished in acute burn care during the last half century, and further improvement in outcome will probably occur as inhalation injury and pneumonia come under better control and new wound coverage techniques are developed, but such improvement will be harder won and smaller in magnitude. Preservation of function, and techniques of reconstruction and rehabilitation, areas in which progress will materially enhance the quality of life for burn survivors, appear fertile targets for future burn research.

Further reading


Access the complete reference list online at http://www.expertconsult.com
References


63. Renz EM, MD, Col. MC, Director U.S. Army Burn Center, Institute of Surgical Research Brooke Army Medical Center Fort Sam Houston, TX, Personal Communication, July 18, 2011.


injury survey.


183. SPSS Inc. SPSS for Windows, ver.12.0. Chicago, IL: SPSS Inc.


Introduction

The word ‘prevent’ comes from the Latin word ‘praevenire,’ which means to anticipate. The prefix ‘pre’ means before and ‘venire’ means to come. During the last century in the United States, burn treatment had always come before burn prevention. Because then as now, burns represent such a small percent of all traumatic injuries, burn prevention has not been viewed as a high-priority health issue by a large portion of society.

Burns are still referred to as accidents by many in the medical community and by society in general. Believing that burns and other traumatic injuries are ‘accidents’ (‘accident-prone’ individual) implies the individual has little or no fault in the cause of injury. The word ‘accident’ means an event that takes place without one’s foresight or proceeds from an unknown cause, an unfortunate occurrence, or mishap, especially one resulting in an injury.1 Synonyms include misadventure, mischance, misfortune, mishap, and disaster. The word ‘injury’ is a more appropriate term.

Historical perspective

In Great Britain in the first decade of the 20th century the medical community was well aware that burn injuries and deaths represented a serious public health issue.2 Scalds and burns were noted to occur predominantly in children. Unguarded fires and the flammability of flannelette, a cotton fabric, were recognized as common causes of burns in children and old women. Legislation was enacted making parents liable to a fine if a child younger than 8 years was injured or died as a result of an unguarded open fire. In a review of over 3600 patients with flame burns and scalds, two-thirds of cases occurred in and around the home, one-third were at work, 50% were children, 82% were the result of clothing fires, cottons were the common fabrics, and the number of scalds about equalled that from burns, but the former were more likely to survive.3 Approximately 50% of ‘accidents’ were judged to be preventable. Research was conducted on the design and flammability of clothing. Fabrics were treated with tin, antimony, and titanium to make them relatively flame-retardant. Statistics on common locations and causes for accidents identified the kitchen and cooking, scald burns from children pulling over containers with hot liquids, and the use of flammable liquids. Burns as a result of a seizure were recognized. Prevention efforts included education and ‘propaganda’ (film, radio, newspapers, exhibits, and posters), better design of housing and improving living conditions (decreasing overcrowding), safer methods of heating houses (central heating and electric fires), use of non-flammable materials in girls’ and women’s clothing, and safer fireguard designs for coal fires. Better design of teapots, cups, and cooking utensils rendered them more difficult to tilt over. One author in 1946 expressed quite clearly that carelessness, neglect of normal precautions, and stupidity were human factors associated with burns.4 It was recognized that accurate and comprehensive burn data were lacking, but necessary if long-term prevention policies were to be enacted.

Injury control

The five key areas in injury control are:

1. Epidemiology
2. Prevention
3. Injury biomechanics (physical and functional responses of the victim to the energy)
4. Treatment
5. Rehabilitation.5

The major components of epidemiology include measurement of both the frequency and the distribution of the injury. This in turn is analyzed and interpreted. Next, risk factors are identified, an intervention strategy is developed and tested, and, lastly, the results are analyzed.

Burn injury magnitude

The first step in any prevention program is to identify the how, who, where, and when of the injury. With this information strategic planning and implementation can be directed at reducing the risk of injury or death. In 2007 the leading causes of injury deaths, in order of magnitude, were motor vehicle collisions, drowning, firearms, falls, and finally flame/fire.6 In 1999 the number of fire deaths and injuries was 3570. In 2002 there were 3363 deaths, a decrease of less than 5.7%. The number of non-fatel injuries (almost 79,000) was greatest between ages 35 and 44. Males were 1.6 times more likely to die in a fire. In
2008 the numbers of deaths and injuries were 3320 and 167015, respectively. On average in the United States in 2008 fire departments responded to a fire every 22 seconds. One structure fire was reported every 61 seconds, and every 31 minutes one civilian fire injury was reported. One civilian fire death occurred every 2 hours and 38 minutes. Between 2003 and 2007 the US Fire Administrations’ national fire incidence reporting system identified the leading causes of home structure fires as cooking, heating equipment, intentional, electrical, and smoking. Smoking was the leading cause of home fire deaths (25%), and heating equipment ranked second (22%). Heating equipment such as portable and fixed space heaters and wood-burning stoves resulted in more fires than central heating. Candles accounted for 10%. From 1990 to 2001 this figure nearly tripled. One-third of fatal candle fires occurred when they were used for lighting when an electrical power outage occurred (hurricanes, tornados, etc.). Children under 5 were nearly eight times more likely than all other age groups to die in fires caused by playing with the heat source. Of fire injuries in homes, 43% were associated with fighting the fire, or attempting rescue; attempting escape (23%); while asleep (13%); and inability to act or acting irrationally 6%. For comparison, from 1980 to 2007 the death rate for children under 5 declined from 18% to 9% and for adults 65 and over increased from 19% to 29%. Nearly 50% of all cooking fire injuries occurred when the victims tried to fight the fire. Home fabric fires caused by smoking commonly originated in upholstered furniture, mattresses, or bedding. Older adults (defined as over 64 years) are at greatest risk of sustaining both fire injuries and death. The elderly are approximately 1.5 times more likely to suffer fire-related death than the general population. Those aged 85 and older are 4.5 times more likely to die in a fire than the general population. Smoking in the presence of home oxygen is frequently encountered in the elderly. Physical and mental disabilities often either contribute to the cause of the fire or hamper the escape. Populations in the lowest income levels had a greater risk of dying in a fire than those in higher income levels. The leading causes of fatal fires in residential property were incendiary/suspicious (27%), smoking (18%), and open flames (16%). The leading areas of fire origin in fatal residential structure fires were sleeping areas (29%), lounge (21%), and kitchen (15%). Fatal fires were more common in the winter, and the time of day when most structure fires occurred was between 10 am and 8 pm.

It is well recognized that many burn patients treated in emergency departments are never admitted to hospital. In 2006 the National Hospital Ambulatory Medical Survey identified 501 victims of fire, flame, or hot substances per 100,000 emergency room visits. This had changed little since 2003 (516/100,000). Risk factors

A number of factors must be considered when determining the fire risk to the host. Age, location, demographics, and low economic status represent important factors. The US Fire Administration (USFA) expresses much of its fire data as relative risk (RR). The RR of a group (example death) is calculated by comparing its rate to the rate of the overall population. An RR of 1 is given to the general population. As a general rule, many statisticians consider an RR of 4 or more as important, and an RR of 4 or more is used to identify high-risk burn populations. The RR of fire deaths in 2001 for all ages, with the exception of 0–4 years and 55 or over, was less than 1. Based on 2006 data, prevention programs should be directed at everyone over 85 years (RR 3.78), American-Indian males (RR 5.3) and African-Americans (RR 6.9). The use of RR in injury prevention is useful when resources are limited.

In 2004 children aged 0–15 years accounted for 560 fire deaths and 2007 fire injuries: 50% and 43% of deaths and injuries occurred in children less than 5 years of age. The RR of fire death for children less than 5 years was 0.74, 0.6 for ages 5–9, and 0.3 for 10–14 years. The RR of home fire injuries in children under 5 in the US between 2003 and 2007 was 1.4. For comparison, in those over 65 the RR of death was 2.3. The activities of children at the time of a fire injury were: sleeping (35%), trying to escape (26%), and unable to act, which implies not understanding what was happening or how to take action (9%).

Analysis of fatal pediatric fire fatalities in Philadelphia (1989–2000) revealed four significant independent variables: age under 15 years, age of housing, low income, and single parent households. The greatest risk was between 12:00 am and 6:00 am. The common causes were playing with matches, cigarettes or careless smoking, and incendiary. The common locations were bedroom and living room. Upholstered furniture, cooking materials, bedding, mattresses, clothing, and curtains were primary materials first ignited in fatal fires. Playing with cigarette lighters and candles, or near stoves with hot liquids, were frequent scenarios in fatal pediatric burns. The authors stressed that identifying risk factors by analyzing population characteristics by census tract was important for burn prevention. These risks are still common 11 years later.

By 2020 it is estimated that people aged 65 years and older will number approximately 55 million, an increase of 16% from 2000. By 2050 they will represent 21% of the population. In 2006 fire injuries in those over 64 accounted for 11.8% of all ages, and the RR of fire deaths between 65 and 85+ increased from 1.44 to 3.78. The leading causes of both death and injury from fire were smoking, cooking over an open flame, and heating equipment. Additional risks included medical conditions associated with physical or mental illness, e.g. arthritis and stroke (the victim is slow or unable to escape the fire), poor eyesight and hearing, systemic diseases such as diabetes (peripheral neuropathy with decreased or no lower extremity pain perception), Alzheimer’s disease (confusion, forgetfulness), and psychiatric illness (depression and suicide). Other risk factors include alcohol and medications such as sleeping pills or tranquilizers. Fire injury and death commonly occur mid-morning and early afternoon.

Burn prevention involves more than just the burn community. Fire safety engineers and legislators (building code laws) and building inspectors have a vested interest in prevention. An important aspect of fire prevention is the design of fire-safe buildings. Both the type of fire and the composition of the material ignited must be identified and analyzed. These include the ignition factor (misuse of ignited material,
by children), type of material ignited (sofas, chairs, and bedding) and the source of ignition (electrical equipment, matches, lighters, cigarettes). Personal factors include condition preventing escape, physical condition before injury, activity at the time of injury, and the site of ignition.

Burns rank among the 15 leading causes of death in children and young adults. The World Health Organization (WHO) reported that, globally, burns accounted for >300,000 deaths annually. In 2007 WHO recognized there was an urgent need for public health action to reduce unintentional injuries, and burns were recognized as a serious global health problem. The WHO strategy for burn prevention and care includes improving data sources and surveillance, promoting burn prevention strategies, encouraging innovative pilot programs to address burn prevention priorities in areas with high risk factors, and strengthening burn care services, which include acute care and rehabilitation. Risk factors include cooking at floor level, open kerosene stoves, high population density, poor house construction, and illiteracy.

Passive strategies for prevention, such as smoke alarms, sprinkler systems, building construction codes, regulation of hot water heater temperatures, and flame-resistant sleepwear, have proved effective in industrialized countries, but some segments of the population at risk are not dissimilar from most low- and middle-income countries (LMICs). These include poverty, lack of education and employment, large and single parent families, substandard housing including lack of running water, no electricity, crowded living conditions, and racial and ethnic minorities. For any global burn prevention strategy to be successful it must be recognized that differences exist at national, regional and local levels. Over 90% of fatal fire-related burns occur in these LMICs. It is understandable that in many LMICs high priority has been given to disease rather than injury prevention. In many such areas medical resources for burns are limited, and prevention rather than treatment is the priority.

Most importantly, children are at increased risk of burn morbidity and mortality. Regardless of socioeconomic status, childhood burns are related to the physical environment in which they occur. Behavioral changes can be effective in preventing fire-related burns without changing lifestyle to any great extent. Active prevention even in high-income countries has met with limited success. It makes sense to emphasize specific issues that can modify behavior without the need for excessive use of resources, both dollars and personnel. Any program should be tailored to fit local conditions. Focusing on burn prevention rather than treatment is key to reducing fatalities and injuries. One strategy does not fit all.

### Injury prevention comes of age

The science of injury prevention took shape in the middle of the last century. The energy sources involved in any injury event are classified into five physical agents: kinetic or mechanical, chemical, thermal, electrical, and radiation. A common form of mechanical energy associated with a burn is a motor vehicle collision. Three risk factors associated with any injury are:

1. the vector or energy source and the way it is delivered,
2. the host or injured person, and
3. the environment, both physical and social.

A seminal article in modern injury science was published by Haddon in 1968. He identified three phases of an injury event:

1. Pre-event: preventing the causative agent from reaching the susceptible host.
2. Event: includes transfer of the energy to the victim. Prevention efforts in this phase operate to reduce or completely prevent the injury.
3. Post-event: determines the outcome once the injury has occurred. This includes anything that limits ongoing damage or repairs the damage. This phase determines the ultimate outcome.

Haddon then created a matrix of nine cells which enabled the three events of the injury to be analyzed against the factors, related to the host, the agent or vector, and the environment (Table 4.1). This is a very useful tool for analyzing an injury-producing event and recognizing the factor(s) important in its prevention. Haddon also proposed 10 general strategies for injury control (Table 4.2).

### Burn intervention strategy

The emergence of the science of prevention has turned attention away from individual ‘blame’ and the attitude that society has no part in the promotion of prevention to the concept that sociopolitical involvement is necessary.

All burn injuries should be viewed as preventable. Public health is defined as the effort organized by society to protect,

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**Table 4.1 The Haddon Matrix for burn control**

<table>
<thead>
<tr>
<th>Agent or vector</th>
<th>Host</th>
<th>Environment</th>
<th>Physical</th>
<th>Social</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-event</td>
<td>Fire-safe cigarette</td>
<td>Control seizure</td>
<td>Non-slip tub surface</td>
<td>Legislation – factory preset water heater thermostats</td>
</tr>
<tr>
<td>Event</td>
<td>Sprinklers, smoke detectors</td>
<td>Flame-retardant cloths</td>
<td>Fire escapes</td>
<td>Fire drill education</td>
</tr>
<tr>
<td>Post-event</td>
<td>Water</td>
<td>First aid antibiotics</td>
<td>EMS</td>
<td>Emergency and rehabilitation services</td>
</tr>
</tbody>
</table>

promote, and restore the people’s health.26 The public health model of injury prevention and control is divided into:

- surveillance,
- interdisciplinary education and prevention programs,
- environmental modifications,
- regulatory action, and
- support of clinical interventions.

Primary prevention is preventing the event from ever occurring. Secondary prevention includes acute care, rehabilitation, and reducing the degree of disability or impairment as much as possible. Tertiary prevention concentrates on preventing or reducing disability. Disability prevalence and loss of productive activity are important outcome measures. There are both active and passive prevention strategies. Passive or environmental intervention is automatic: the host requires little to no cooperation or action. This is the most effective prevention strategy. Examples include building codes requiring smoke alarms, sprinkler installation, and factory-adjusted water heater temperature. Active prevention measures are voluntary; emphasize education to encourage people to change their unsafe behavior, and require repetitive educational measures to maintain individual action. Herein lies its weakness. Project Burn Prevention was a program funded by the Consumer Product Safety Commission (CPSC) in 1975.27 It was undertaken to determine whether a burn prevention program would reduce burn deaths by using an educational program and media messages involving a large population base. The author concluded that there was no reduction of burn incidence or severity in their study with either the school education program or the media campaign. Education to bring about personal responsibility was not sufficient. Examples of productive activity are important outcome measures. The five Es of intervention are Engineering, Economic, Enforcement, Education, and Evaluation.28

- **Engineering** – focuses on the physical environment (product safety design) and the vector. Examples include fire-resistant upholstery and bedding, child-resistant multipurpose lighters (including cigarette lighters), and insulated electric wire.
- **Economic** – influences behavior, i.e. monetary incentives such as insurance rate reductions if a home has smoke alarms or sprinklers.
- **Enforcement** – influences behavior with laws, building codes, and regulations, for example requiring fire escapes, sprinklers/smoke alarms in motels, hotels, and homes.
- **Education** – influences behavior through knowledge and reasoning. Examples include pamphlets, public television programs, CPSC News Alerts. These active measures are the least effective.
- **Evaluate** – if a prevention program does not achieve the stated goal(s), possible reasons include:
  - the technique or measurement used may be inappropriate to identify the reduction caused by the prevention strategy;
  - faulty program design;
  - the study design may have been good, but the program was carried out inappropriately.

With this background in epidemiology and injury prevention, important areas of challenge and opportunity in burn prevention both past, present, and future will be discussed.29,30

### Table 4.2 General strategies for burn control

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Prevent creation of the hazard (stop producing fire crackers)</td>
</tr>
<tr>
<td>Reduce amount of hazard (reduce chemical concentration in commercial products)</td>
</tr>
<tr>
<td>Prevent release of the hazard (child-resistant butane lighters)</td>
</tr>
<tr>
<td>Modify rate or spatial distribution of the hazard (vapor-ignition resistant water heaters)</td>
</tr>
<tr>
<td>Separate release of the hazard in time or space (small spouts for hot water faucet)</td>
</tr>
<tr>
<td>Place barrier between the hazard and the host (install fence around electrical transformers, fire screen)</td>
</tr>
<tr>
<td>Modify nature of the hazard (use low conductors of heat)</td>
</tr>
<tr>
<td>Increase resistance of host to hazard (treat seizure disorder)</td>
</tr>
<tr>
<td>Begin to counter damage already done by hazard (first aid, rapid transport and resuscitation)</td>
</tr>
<tr>
<td>Stabilization, repair rehabilitation of host, example (provide acute care – burn center and rehabilitation)</td>
</tr>
</tbody>
</table>

In 1953 legislation regulating the manufacture and sale of highly flammable clothing (the Flammability Fabrics Act) was passed in the US. As a result of the Act, contracts were awarded to burn units to collect epidemiologic data regarding flammable fabric burns. Flammability testing methods were improved and standardized, and flame-retardant fabrics were developed. The initial Act covered only fabrics that came in contact with the body, and therefore excluded industrial fabrics, and in 1967 it was amended to include articles of clothing and interior furnishings such as paper, plastic, rubber, synthetic film, and synthetic foam.31 By 1985, 87% of children’s sleepwear was made of synthetic fabrics and only about 13% was made of cotton. In 1996 sleepwear standards for children were amended by the CPSC. The amendments permitted the sale of tight-fitting children’s sleepwear (up to size 14 and not exceeding specified measurements for specific areas of the body) and sleepwear for infants aged 9 months or under, even if the garments did not meet the flammability standards ordinarily applicable to such sleepwear. This conclusion was based on staff findings that there were virtually no injuries associated with single-point ignition incidents of tight-fitting sleepwear, or of sleepwear worn by infants under 1 year. The commission emphasized that sleepwear standards were designed to protect children from burn injuries if they came in contact
with an open flame such as a match or stove. The requirement for flame-resistant or snug-fitting clothing does not apply to sleepwear in sizes of 9 months and under because infants wearing these sizes are ‘insufficiently mobile to expose themselves to sources of fire’.50

What about children who do not voluntarily expose themselves to an open flame? The safest sleepwear is snug-fitting and flame-resistant. Loose-fitting clothes have a large airspace between the fabric and the skin. Oxygen in this space promotes flame. In order to meet CPSC requirements, flame-resistant implies garments must not ignite easily and must self-extinguish quickly. Snug-fitting clothes that comply with CPSC guidelines are made of fabrics that are not flame-resistant but also do not create ‘an unreasonable’ risk of burn injury because they limit the airspace under the garment. The CPSC requires all snug-fitting children’s sleepwear from 9 months up to size 14 to have a label that reads ‘Wear Snug-Fitting. Not Flame Resistant.’ A hangtag reads ‘For child’s safety, garment should fit snugly. This garment is not flame resistant. A loose-fitting garment is more likely to catch fire.’ The reader is encouraged to read the excellent review of sleepwear flammability and legislation in both the US and the United Kingdom by Horrocks et al.18

Nevertheless members of the burn community were disappointed, and in 1999 Congress required the CPSC to consider revoking the amended standards. It was felt that under-reporting of sleepwear burn injuries was possible, and an increase in the number of sleepwear-related burn injuries was reported by a number of burn units. As a result, in 2003 the CPSC initiated a project whereby any thermal injury due to clothing in a child under 15 was to be reported. In addition, if the garment was available an onsite investigation of the incident and inspection of the garment was to be conducted. Between March 2003 and December 2005, a total of 462 burn incidents were reported. Characteristics of the victims, the types of clothing involved, the fabrics and the causes of fire were tabulated. The results showed that 99% of victims were not wearing sleepwear. The study did not support the conclusion that the exempted sleepwear increased the risk of burn injury to children under 15.14

**Hot water burns**

According to the ABA 2010 National Burn Repository scald burns accounted for 54% of all burns in children under the age of 5. Although the majority of scald burns in children are not fatal, the exact incidence is unknown. Fortunately, most hot liquid burns are small and do not require hospital admission. All tap water scalds should be preventable. In 1983 the Washington State legislature required all new home water heaters to be preset to 49°C (120°F).19 The time of exposure to this temperature before a severe burn can occur is sufficiently long that the victim, usually a child or elderly disabled person, is able to be removed or can climb out of the water.

An educational program was instituted to persuade people to reduce water temperature voluntarily, and follow-up in 1988 revealed there had indeed been a reduction in hot water pediatric burns. Voluntary reduction of thermostat temperatures to a safe level by manufacturers has not been uniformly successful. Mandatory regulation would be the most effective strategy, but until society is educated and convinced of its benefit, change will be slow. Other prevention methods to reduce tap water scald burns include inserting shut-off valves in the water circuit to detect temperatures over a certain level, and the use of liquid-crystal thermometers in bathtubs to alert caregivers to the water temperature. More than 90% of hot water scalds are due to hot cooking or drinking liquids,16 and only about 25% of hot water burns are associated with tap water in the US. In LMIC countries scalds caused by hot food or liquids, for example boiling water, or cooking over an open fire on the ground, or hot bathing water placed on the ground to cool, are common. Unfortunately, prevention of spills is more difficult.17

The effectiveness of active prevention has been called into question. Burn safety education campaigns directed at parents to modify behavior are only effective over a short period. Negligence on the part of the caregiver(s) is the key issue. Nevertheless, success has been achieved through a combination of education, legislation and/or litigation regarding product safety.18 Identifying why specific prevention measures are unsuccessful is as important as identifying why others are successful.

Not all scald burns involve children. Product design and installation are important. Burns occurring during bathing as a result of seizures are not uncommon.59 Avoidable risk factors identified were shower levers that were easily knocked out of position, lack of water temperature safety features, and confining shower cubicles.

**Fire-safe cigarettes**

Approximately one in five American adults smokes cigarettes. When left unattended and not even puffed, a cigarette can burn as long as 20–40 minutes. In 2007 140,700 smoking-material fires occurred in the US.60 There were 720 civilian deaths, 1580 civilian injuries and $530 million dollars’ worth direct property damages. Between 2003 and 2007 statistics on smoking-material fires revealed that upholstered furniture accounted for 44% of civilian deaths, 26% of civilian injuries, and the largest amount of property damage. Most fatal smoking-material fires start in bedrooms, and 25% of victims are not the smoker whose cigarette started the fire. The risk of dying in a home structure fire caused by smoking materials increases with age (36% of victims are 65 or older) and nearly 40% of fatal home smoking-material fire victims were sleeping when injured. In 1973 the US Standard for the Flammability of Mattresses and Mattress Pads was enacted to reduce the risk of injury, death, and property damage from fires caused by lighted cigarettes. In 2007 the US Consumer Product Safety Commission unanimously approved a new federal mattress flammability standard. The Commission’s finding was that ‘A mattress with a limited contribution to the fire, especially early in the fire, will substantially increase the available time for occupants to discover the fire and escape and, therefore, substantially reduce the current risks associated with mattress fires’ (http://www.cpsc.gov/) Between 1980 and 2007 in the US, smoking-related home fires starting in upholstered furniture, mattresses and bedding declined by 90%, largely owing to the mandatory flammability standard.
Approximately 7% of fatal home smoking fire victims sustained the injury while using medical oxygen. The times of day of residential smoking fire deaths and injuries were 2 am and 6 am, and 12 am to noon, respectively. Falling asleep, alcohol, and substance abuse were common associated factors. Smoke alarm performances in residential smoking fires revealed the following: alarm present and operated 39%, present and not operating 25%, no alarm present 36%. Alarm performance in fatal fires was: present and operated 43%, present and not operating 25%, no alarm 32%.

The concept of a fire-safe cigarette was explored in the 1920s. The first federal bill mandating fire-safe cigarettes was introduced in 1974, but no legislation was passed. The concept remained dormant until 1984, when the Cigarette Safety Act created a technical study group on the fire safety of cigarettes and little cigars. A number of design changes have the potential to make cigarettes less fire prone. These include reduced tobacco density, paper porosity, cigarette circumference, and the addition of citrate. Everyone is encouraged to read the article by McGuire entitled ‘How the tobacco industry continues to keep the home fires burning’.

In 2000 Philip Morris companies announced the development of a cigarette with ultrathin concentric paper bands applied to the traditional paper. These bands are referred to as ‘speed bumps’ and cause the cigarette to self-extinguish if not being smoked, as no oxygen can reach the burning embers. This technology was first reported more than a decade ago. The production of a safe cigarette should not be voluntary but be required by law. In 2004 the State of New York was the first to implement legislation requiring all cigarettes to be sold with reduced ignition propensity (RIP); 47 states now have laws making such cigarettes mandatory. By 7 January 2011 all states will have enacted the law. Canada passed fire-safe cigarette legislation in 2004, and in 2007 the 27 EU Member States endorsed plans to allow the sale of fire-safe cigarettes. Unfortunately, in other industrialized counties there appears to be no demand for RIP cigarettes.

As yet there are no data on the effect of RIP cigarettes on burn injuries and mortality. As more governments implement laws mandating RIP it will be important to establish data on smoke-related fire injuries.

**Carbon monoxide poisoning**

Carbon monoxide (CO) inhalation is the leading cause of fatal poisoning in the industrialized world. Although acute CO poisoning is more commonly associated with closed-space structural fires, it is generally easily treated with no more than 100% \( \text{FiO}_2 \). Chronic CO poisoning is associated with poor ventilation. It is more prevalent in the winter months and is associated with gas furnaces, gas fire places, portable heaters, and anything that burns coal, kerosene, oil, propane, or wood. CO detectors are not as prevalent in residential structures as smoke detectors. In a telephone survey conducted in 1003 households in the US, 97% of responders had a smoke alarm but only 29% had a CO detector. Is price a factor in this low prevalence? The cost for a single unit can be as low as $10, and $75 for a combined smoke and CO detector. A CO alarm near all sleeping areas represents an effective prevention strategy. Should any home with a smoke detector have a CO detector? Based on the success of smoke alarms, the answer is yes, but further research is needed to answer conclusively a number of questions: Are they necessary? What type of CO sensor? and What level of CO gas activates the alarm, specifically the level for both a caution and dangerous or hazardous levels? It is important to remember that the lifespan of CO detectors varies from 2 to 5 years. In addition, the ‘test’ feature on many detectors only checks the functioning of the alarm and not the status of the detector. In 2010 the State of California required placement of CO detectors in all dwelling units. The bill requires that the presence or absence of the devices must be disclosed when residential real estate is transferred. Landlords are required to install detectors in the properties they manage or rent. As of July 2011, all existing homes and dwelling units must have CO alarms. Similar laws are being adopted in other states, albeit slowly. CO poisoning is largely preventable by the combination of correct installation, maintenance, and operation of devices that may emit CO and the appropriate use of CO detectors. CO detectors may prevent at least half of all deaths attributable to CO poisoning.

**Smoke detectors/alarms**

The first automatic electric fire alarm was invented in 1890. The first truly affordable home smoke detector was introduced in 1965. Without question, the use of smoke alarms has had the greatest impact in reducing fire deaths in the US. In 1966, 13% of residential fire deaths occurred in homes with an operating smoke alarm, 11.5% deaths occurred in homes with a non-operating alarm, and 38.5% in houses without an alarm. Socioeconomic factors associated with lack of a functioning smoke detector include living in a non-apartment dwelling, an annual income of less than $20000, being unmarried, living in a non-metropolitan area, and homes with children younger than 5. Smoke detector ownership was most often associated with not living in public housing, a level of education (completing high school), maternal age (not a teenager), practice fire drills, and larger homes. In 1985 McLaughlin published ‘Smoke Detector Legislation’. Smoke detector installation in new houses appeared to be effective when mandated by a building code. Malone et al., in 1996, collected data on a smoke detector give-away program in Oklahoma City. The target area for intervention had the highest rate of injuries related to residential fires in the city, and the number of injuries per 100000 population was 4.2 times higher than in the rest of the city. The program distributed 10 100 smoke alarms to 9291 homes in the target area, and over the next 4 years the annualized injury rate per 100000 population decreased by 80%, compared to only 8% in the rest of the city. The authors concluded that target intervention with a smoke alarm give-away program reduced residential fire injuries.

Smoke alarms represent intervention before the burn event occurs. Building codes mandating installation in new homes have been proved to be a practical solution. In 2000 DiGuiseppi and Higgins questioned the benefit of injury education to promote smoke alarm usage. They reviewed
26 published trials, 13 of which were randomized, and concluded that ‘counselling and educational interventions had only a modest effect on the likelihood of owning an alarm.’ Programs that gave away and installed smoke alarms appeared to reduce fire injuries, but the trials were not conclusive and the results were to be interpreted with caution. DiGuiseppi et al. conducted a randomized controlled trial to determine the effect of giving free alarms on fire rates and injuries.\(^{51}\) The study design was similar to that of the previously discussed study in Oklahoma City: 20,050 alarms, batteries, fittings, and fire safety brochures were distributed and free installation was offered. No alarms were given to the control group. Follow-up was 12–18 months after distributing the alarms. The conclusion of the study was that giving free smoke alarms did not reduce fire injuries, as many alarms had not been installed or maintained. Obviously, a give-away program is not the entire answer and more research is necessary. Rowland et al.\(^ {52}\) performed a randomized controlled trial to determine what types of smoke alarm were most likely to remain working and how they were tolerated in households with smokers. Both ionized and photoelectric alarms were available. The conclusions were that an alarm with an ionization sensor, a lithium battery, and a pause button were most likely to remain working. An alarm was less likely to work in a household with one or more smokers, and installing smoke alarms might not be effective use of resources.

Mueller et al.\(^ {53}\) conducted a randomized trial comparing ionized and photoelectric alarms to determine reasons for both non-functioning and nuisance alarms in low- to middle-income homes in a US metropolitan area. Conclusions were that ionized alarms were likely to be non-functioning, commonly because of either being disconnected or removal of a battery when the alarming becomes a nuisance; photoelectric alarms may be preferred when an alarm is used; designing an alarm that lessens nuisance alarming may result in long-term functionality.

A photoelectric alarm has an optical sensor and consists of a light-emitting diode and a light-sensitive sensor in a chamber. The presence of suspended products of combustion in the chamber scatters the light beam, which is detected and sets off the alarm. Ionized units use a small amount of radioactive material to ionize air in the sensing chamber, and when products of combustion enter the chamber the conductivity of the air decreases. When this reduced conductivity reaches a predetermined level, the alarm is set off. The ionized alarm is reportedly prone to produce more false nuisance alarms. In 2008, 96% of US households had at least one smoke alarm and 40% of home fire deaths were in homes with no smoke alarm; and in 23% the smoke alarm failed to operate.\(^ {54}\) In many instances consumers are not knowledgeable about the number of alarms needed, their preferred locations, or how to install them properly.\(^ {55}\) A fire escape plan is also important. This should include knowing ahead of time the safest exit route; immediately leaving the structure; not wasting time saving property; calling for emergency assistance using 911; knowing whether there is more than one way out of a room or building; feeling the door and door knob to identify (by heat) how close the fire may be; knowing whether a secondary escape route would be appropriate; having an arranged meeting place; and ‘once out, staying out.’

### Fire sprinklers

Sprinklers complement smoke detectors. Smoke alarms warn the individual of a nearby fire, but a sprinkler system can effectively extinguish the fire in an isolated area and are an intervention strategy that works during the event. They are the most effective method for fighting the spread of fires in their early stages. The first automatic sprinkler for fire fighting was patented in 1872 for use almost exclusively in textile mills. Automatic fire sprinklers have been in use in the US since the latter part of the 19th century. Although there is a range of different types of sprinkler system, only wet systems should be specified for use in domestic premises as they are the simplest, easiest to maintain, and the most cost-effective. The fire death rate per 1000 reported residential fires is reduced by approximately 83% and property damage by 40–70% for most properties that use sprinklers. Structure fire data reported between 2003 and 2007 revealed that 71% of hospitals and 65% of nursing homes had sprinkler systems.\(^ {56}\) Unlike non-residential buildings, the use of sprinkler systems in residential structures has been slow to be accepted. The NFPA estimates that occupants with a smoke alarm in the home have a 50% better chance of surviving a fire than those without. Adding sprinklers increases the chances of surviving a fire to nearly 97%. One sprinkler was adequate to control fire in over 90% of the documented sprinkler activations in all residential fires. In 1978, San Clemente, California, was the first jurisdiction in the US to require residential sprinklers in all new structures. In 1985, Scottsdale, Arizona, required a sprinkler system in every room of all new industrial, commercial, and residential buildings. In 1996, residential sprinklers were found in less than 2% of residential fires.\(^ {6}\) Residential fire sprinkler ordinances have been adopted in over 200 communities in the US for use in single-family dwellings. Between 1994 and 1998, only 7% of reported structure fires had any type of automatic extinguishing equipment. From 2003 to 2007 this increased to nearly 10%.\(^ {56}\) In the US the cost of installing a home sprinkler system in a new residential structure averages $1.61.\(^ {57}\) Retrofit installation has been undertaken voluntarily or by legislation in nursing homes (1970s), hotels (1980s), and university housing (2000s). A sprinkler system is the only solution for preventing flashover and rapid escalation of a large hotel fire. Sprinklers typically reduce both the chance of dying in a fire and the average property loss by one-half to two-thirds compared to where sprinklers are not present. The NFPA has no record of a fire death of more than two people in a public assembly, educational, institutional, or residential building where the area was completely fitted with working sprinklers. It is estimated that 75% of high-rise and 50% of low-rise hotels have sprinkler systems. In March 2008, the USFA, an entity of FEMA, announced their support for both the use of residential fire sprinklers and code requirements that would make such sprinklers mandatory in all new residential constructions. Unfortunately, the USFA does not directly control building and fire codes. The International Code Council (ICC) is a non-profit organization dedicated to developing a single set of comprehensive and coordinated national model construction codes. In the 2012 edition of the International Fire Code a recommendation will be included for fire sprinklers to be a standard feature
in new homes. The ICC’s members rejected efforts by the National Association of Home Builders to have the requirement repealed. Homebuilder associations in many states tried to block adoption of the IRC sprinkler provisions. Their arguments included the known effectiveness of smoke alarms in reducing home fire deaths, and the cost–benefit ratio of sprinklers in residential property. One issue that may ultimately shift the perspective of builders towards residential fire sprinklers is legal liability.58

Evaluating the effect of burn prevention

Three important issues reappear in the injury prevention literature:  
1. Implement what is already known, not necessarily proven.  
2. Passive strategies are more effective than active ones.  
3. New programs and their results must be subjected to more rigorous evaluation.  

Successful burn prevention includes collecting, analyzing, and then interpreting burn statistics, especially mortality, and even more importantly morbidity. The American Burn Association’s Burn Data Repository represents a very valuable resource for everyone involved in burn prevention. The ongoing collection of data will allow:  
- Identification of the magnitude and type of burn injury,  
- Monitoring the trend of specific areas of burn injury and their prevalence,  
- Identification if new injury problems arise,  
- Development of methodologies to evaluate burn prevention or intervention efforts.

Between 1977 and 2008 the number of US home fire deaths decreased by 53%. The number of home fire incidents decreased by 47%. Unfortunately, the death rate per 1000 home fire incidents decreased by only 11%, from 8.1 in 1977 to 7.2 in 2008.7 Fire safety initiatives directed at the home environment are the key to reductions in the overall fire death toll. Five strategies are recommended:  
1. Widespread public fire safety education.  
2. Escape plans must be developed and practiced, as there are still too many instances where either smoke alarms were absent or malfunctioning, and no plans have been in place.  
3. Increased use of residential sprinkler systems must be pursued.  
4. Continue to make more home products fire safe. This includes products such as upholstered furniture and mattresses, as well as house construction.  
5. More attention directed at the fire safety needs of high-risk groups, i.e. young, old and poor.

Many successful burn prevention programs have been developed at the local level using locally generated data. Behavior modification at the local level can be instituted more quickly than waiting for national initiatives and legislation. Unfortunately, local efforts affect only a few. Prevention research should generate information, which can be useful at a national level, and there must be rigorous methods of evaluating research so the conclusions may be shared. Many burn prevention programs have had an insufficient number of subjects, no controls, inadequate or short follow-up periods, and no control for confounders – and, of the utmost importance, few use mortality and morbidity as outcome measures. Although it is difficult to conduct prospective, randomized, double-blinded studies (class I research), rules for good scientific research should nevertheless be followed.59 Studies with a single hypothesis should be conducted over an adequate length of time. The prevention goal should be realistic and achievable, and the results must be carefully analyzed.60 Resources must not be wasted collecting and analyzing data unless prevention initiatives are planned.

The incidence of both burn injuries and deaths is decreasing throughout the US. No single burn unit or community will have a large enough patient population to conduct meaningful prospective studies. Wanda et al.61 published a review article on the effectiveness of prevention interventions in house fire injuries where various types of intervention program were reviewed. These included school, preschool, and community education programs, fire response training programs for children, office-based counseling, home inspection programs, smoke detector give-away campaigns, and smoke detector legislation. The important conclusion was that morbidity and mortality data must be used for outcome measures. There was wide variability regarding study design, data sources, and outcome measures.

Whether home safety education and the provision of safety equipment such as smoke alarms, fire extinguishers and educational material reduces the incidence of burns, and the effect it has across different social groups, is not known. A Cochrane Review published in 2007 evaluated whether home safety education and the provision of safety equipment was effective in reducing childhood injury rates. The conclusion was there was no consistent evidence that home safety education with or without providing safety equipment was less effective in those at greater risk of injury.62 Kendrick et al.63 presented information from a meta-analysis of thermal prevention practices. The safety outcome measures included functioning smoke alarms, fitted fireguards, fire extinguishers, keeping hot drinks and food, matches and lighters out of reach of children, and having a safe water heater temperature. The conclusion was that home safety education was effective in increasing some thermal injury prevention practices, but there was insufficient evidence to show whether this also reduced injury rates.

Burn injuries and deaths are a world health problem that represents a major global challenge. The literature is replete with burn epidemiologic studies, many suggesting interventions that are well known or unique to their victims, but fewer show that intervention is effective ‘in the real world.’64 Coordination of prevention strategies on both national and international levels is necessary. Passive prevention programs are most effective but slow to implement. Active prevention is not always easy, and requires time, significant organizational support, and money. Active and passive measures are not mutually exclusive: both must be utilized. All burns should be preventable, but unfortunately the aphorism ‘easier said than done’ is true.
**Further reading**


Access the complete reference list online at [http://www.expertconsult.com](http://www.expertconsult.com)
References


Introduction

The Universal Declaration of Human Rights states that ‘everyone has the right to a standard of living adequate for the health and well-being of himself and of his family, including medical care and necessary social services, and the right to security in the event of sickness, disability, or other lack of livelihood in circumstances beyond his control.’ Mass fire casualties are events beyond the control of individuals. Individuals organize themselves into states, and these states must protect their residents and provide necessary medical care.

Unfortunately, questions remain about the medical care that is to be provided. Specifically, what degree of medical care must be provided? Is it the best available or, preferably, whatever is necessary? In addition, what kind of care must the state provide to the uninsured? This question reveals great disparities, for example between those jurisdictions that have high incomes and plentiful resources and those that do not. These factors will determine what is the ‘best available’ medicine. Furthermore, options in multistate regions are more limited. This is especially true in unions of states, such as the USA and the European Union, where interstate borders may limit availability.

The best burn treatment is in burn centers, which have specialized staff. Burn victims treated in these centers have better survival rates and quality of life. However, the number of burn centers is limited. Countries’ resources are also usually limited, making cross-border cooperation necessary, even among countries with many resources. Although burn centers are usually described by their number of beds, often no clear definition of these ‘burn beds’ exists. They should be counted and classified as isolated ICU (intensive care unit) beds, with specification of whether they are thoroughly equipped for artificial ventilation and organ substitution in modern intensive therapy, with air conditioning to warm patients during treatment, and with a special operating room always available for burn treatment. Many registered burn beds do not meet the needs of modern burn therapy. It is also worth mentioning that ‘beds’ do not treat or heal patients: patients are treated by individuals such as doctors, paramedics, and nurses. The mere number of beds does not indicate how many burn victims a center can treat. The number of burn specialists of all professions, and their availability, is also important. This can change hourly, with shifts, as well as daily and seasonally.

Definitions are very important with regard to organizations. Although mass casualties remain in the purview of local rescue organizations, disasters are for regional authorities. These terms imply different ways of handling the situation and the use of different funding resources. Consequently, emergencies requiring instant decisions are always combined with financially sensitive legal decisions.

Emergencies with many casualties are marked by a period of disproportion between supply and demand. Rescue organizations must work to reduce the length of this ‘chaos’ period. During the chaos phase, actions follow the principles of disaster medicine, that is, the goal is to save the most lives possible, even if it means neglecting an individual patient. When structure replaces chaos, the principles of individual medicine are restored. The organizational aim in mass casualties is to minimize the period between mass medicine and individual medicine. The length of this period depends on structural aspects such as the existence and validity of a disaster plan, a regard for disaster capacity in health planning, and the educational level of medical services. These facts are often neglected in the political aspect of disaster planning and the practical aspect of disaster capacity.

Medical treatment should be based on the state of medical science. Otherwise, treatment with ‘best available means’ weakens individual care for a mass-casualty patient. If medical resources are lacking, the best available treatment is no treatment! During mass casualties and disasters, the infrastructure of a country or region may be unable to cope with a higher number of victims of special trauma types while maintaining state-of-the-art treatments. Because state-of-the-art treatments may not be able to be maintained in a jurisdiction owing to dwindling resources, help from other jurisdictions, even international ones, must be planned and coordinated. Such instances include mass casualties with burn injuries. Resources available for specialized treatment are limited, but the demands for state-of-the-art treatment are high, so even a small number of burn victims from one accident can push burn treatment systems in an area or country to their limit.
Definitions

Mass casualty
A mass casualty is an emergency with a larger number of victims than can be accommodated by the rescue forces and their supplies.\(^5\) Infrastructure in the affected area is intact. With force mobilization, the crisis can be mastered. The period of disproportion between supply and demand is short. The goal is to establish treatment according to principles of individual medicine as fast as possible, and without transferring the disproportion from the scene to hospitals.

The challenge to save as many lives as possible, even at the expense of the medical needs of an individual, stands in contrast to the paradigms of individual medicine, where any individual life claims the maximum medical effort. Overcoming this challenge depends upon the selection of patients based on the urgency of medical procedures, the chance of success, and distribution among the available qualified treatment centers (i.e., triage).

Disaster
A disaster is defined as an event that is accompanied by an at least partial destruction of infrastructure and that cannot be handled by regional rescue means alone (e.g., earthquakes\(^4\) and volcanic eruptions). The first goal is to re-establish the minimal infrastructure to provide medical care.

A disaster situation differs from mass burns treatment in a resource-poor country where infrastructure never existed. One way to treat burns successfully in such a place is to bring infrastructure, staff, and materials to the area. Alternatively, victims can be transported to a place with existing infrastructure and given help there. The maximum treatment possible is determined by the degree of infrastructure and/or resources in the disaster area or brought to it.

Mass burn casualty disaster
The American Burns Association (ABA)\(^5\) has defined a 'burn disaster' as any catastrophic event in which the number of burn victims exceeds the capacity of the local burn center to provide optimal care. Capacity includes the availability of burn beds, burn surgeons, burn nurses, other support staff, operating rooms, equipment, supplies, and related resources. This definition is inapplicable in countries such as Germany, where a central burn-bed bureau always organizes the distribution of burn victims. The definition supposes a very different degree of preparedness in these countries.

Basic capacity
Basic capacity is the normal number of patients who can be treated, based on the availability of burn beds, burn surgeons, burn nurses, other support staff, operating rooms, equipment, supplies, and related resources.

Capacity utilization
Capacity utilization is the degree of utilization of burn beds in a center over a certain period. This should be expressed as use of both intensive-care burn beds and other beds. The average value over a year gives an overview of a burn center's disaster capacity.

Actual capacity
Actual capacity is the number of burn patients that a center can take in on an actual day. It varies daily and can depend on season. It is also likely to fluctuate with the seasonal or accidental presence or absence of patients with severe burns.

Surge capacity
Surge capacity is the increased capacity available during mass casualty situations and disasters. In burns, it is defined by the ABA as the capacity to handle, in a disaster, 50% more than the normal maximum number of burn patients.\(^6\) Surge capacity must be developed and maintained, which requires action by health systems, and must include continued medical care of all other patients. Elective medical and surgical care can be eliminated temporarily to maintain surge capacity. Surge capacity is not defined by time. When capacity is breached, patients must be transferred safely to other treatment facilities.

Sustained capacity
Sustained capacity is the maximum capacity that a burn center can sustain over a longer period without reducing treatment quality.

Burn capacity of a health system
The burn capacity of a health system is the total capacity of burns that can be treated in a national health system. This capacity should be known. It should take into account the various requirements of burn treatment, such as the number of victims needing intensive care. The average capacity utilization over 1 year is part of resource planning for a health system.

Time to establish surge capacity
During mass casualty situations with burn injuries, the time available to establish surge capacity can be very short. A burn center should know how much time it needs to attain maximum surge capacity. A good parameter is the number of complete burn teams available at various hours. This number is highly important in a hospital's organization of primary care.

National disaster medical system (NDMS)
The NDMS manages a country's national medical system during disasters. In the US it is a function of the Federal Emergency Management Agency, under the Department of Homeland Security, and it operates in partnership with the Department of Health and Human Services, the Department of Defense, and the Department of Veterans Affairs.\(^5\) Other countries have comparable structures. An NDMS has three functions: 1) medical response at the disaster site, 2) transport of patients to unaffected areas, and 3) definitive medical care in unaffected areas.
Disaster medical assistance team (DMAT)

A DMAT is a regional disaster response team. In the US, DMATs are developed locally, are sponsored by major medical centers, and have medical and non-medical staff of about 35. DMATs are not burn specialists.

Burn specialty team (BST) or burn assessment team (BAT)

BSTs/BATs are a special form of disaster medical team, providing expertise in burns during primary care. In the US these teams consist of 15 burn-experienced medical and non-medical staff. In many countries these teams are not generally regulated and planned. They can be formed only when burn experts are numerous and not already engaged in other parts of the disaster response.

Threats that cause mass casualties with burn injuries

Even with the best preparation, a disaster remains a disaster for a certain period; the goal is to minimize this period. Although retrospectively correcting problems is impossible, lessons learned from the past should be applied to the future. Terrorism, indoor fires, transportation crashes, and explosions can all lead to mass casualties with burn injuries. Descriptions of exemplary events in each of these categories are provided below, together with a discussion of problems that can be typical of such incidents.

Terrorism

Ever since 11 September 2001, terrorist attacks have remained in the popular mind, as they can strike anywhere on Earth. Terrorists’ names, goals, and methods change. Al Qaeda is not the only terrorist body. Groups such as ETA (Spain), the IRA (Northern Ireland), and the RAF (West Germany) may seem forgotten, but remain active.

New York City, New York, 11 September 2001 (Fig. 5.1)

A wake-up call for Western society, 9/11 directed attention to disaster preparedness and burn injuries. In New York, terrorists used the ‘double-strike’ technique, flying two hijacked airliners directly into the Twin Towers of the World Trade Center. Although many were injured, few had severe burns.7,8

The victims were primarily sent to two burn centers, although more centers were easily reachable.8 Of 39 patients showing significant burn injuries, 19 were triaged at New York Presbyterian Hospital. At the William Randolph Hearst Burn Center at this hospital, victims had an average age of 44 years and an average burn size of 52.7%.9

The 39 burn patients were reported by nine hospitals, with 27 being admitted. Although enough burn beds were free within a 1-hour transport range, only 26% of burned patients were triaged first to burn centers. Two-thirds of the burn injuries were ultimately treated in a burn center. The usual portion of burn victims triaged to burn centers in New York City in a year is 75.2%.9

Kuta, Bali, Indonesia, 12 October 2002

Terrorists also used a double-strike technique: a suicide bomber detonated a backpack bomb in a nightclub; people then fled outside, where a car bomb exploded. There were 202 deaths and 209 injured.

The Australian Defence Force (ADF) instigated Operation Bali Assist, the largest Australian aeromedical evacuation since the Vietnam War.10 An aeromedical staging facility (ASF) was prepared in a hangar at Bali’s airport, where five C-130 planes flew 61 Australian patients to the Royal Darwin Hospital (RDH). Of the 61 patients, 28 had major injuries (injury severity score >16). At RDH, 55 escharotomies were performed along with 43 other surgical procedures. Three patients had been intubated in Bali, and 12 more were intubated at RDH. Within 36 hours after first admission to hospital and 62 hours after the bombing, 48 patients were evacuated to burn centers. There were no ‘walking wounded.’

BATs were among the primary services at RDH.11 Eleven patients were transferred to Concord Repatriation General Hospital.12 Total burned surface area (TBSA) was 15–85%, mostly full-thickness burns. All patients sustained injuries from both the first and second blasts. There were complications from infections with Acinetobacter baumannii and Pseudomonas, and from shrapnel injuries. Many ophthalmic injuries occurred, some being detected only later.

RDH received its first information about the incident from a patient who had been treated in Bali and then fled to Australia. The hospital learned nothing of the number of patients or the severity of injuries before the first wave of patients arrived.13 Palmer13 describes a need for improvement, mainly in military–civilian communication. Communication in the hospital was also problematic, as it was dependent upon mobile phones (no reception), electronic texts (no time to read), and landlines (not mobile). The ADF provided satellite phones to the medical staff for communication between the hospital in Bali and the ADF. A method of hands-free communication in the hospital is recommended.
Madrid, Spain, 11 March 2004

Bomb attacks on four commuter trains carrying 6000 people killed 191 and injured 2051. Thirteen bomb bags each contained 10 kg of dynamite as well as shrapnel. Three bombs failed to explode. Of the 191 dead, 175 died instantly and 16 died later.

It was not known that unexploded bombs remained on the trains while ambulance staff performed their duties. Ambulance staff worked without coordination and were unaware of overall medical priorities. Patients with only minor injuries were transported, and ambulances ran out of all medical supplies. In addition, no joint field command post for all of the medical services was set up.

Patients were taken to 15 hospitals in Madrid and two field hospitals, with each hospital receiving anywhere from five to 312 patients. Triage tags were unavailable, wasting time and causing a lack of basic patient information. Communication problems arose in hospitals and between organizations. Systems existed that allowed different frequencies for different sites, but they were not used. Although radio worked, there were communication problems within single organizations.

Only 33% of patients were transported in ambulances under medical control: 67% found their way to hospitals without triage and medical or organizational control. Most went to the nearest hospital, which received patients with both serious and minor injuries. As a result, the primary distribution of patients to available hospitals was uncontrolled.

Of 312 patients taken to Gregorio Marañón University General Hospital, 45 had burns; 16 had first-degree burns and 29 had second-degree burns. Of the 312 patients, 91 were hospitalized; 89 (28.5% of the 312) remained in hospital for more than 24 hours. The most common injuries were tympanic perforation (41%); chest injury (40%), including fracture, blast injury, pneumothorax, and hemothorax; shrapnel injury (36%); fracture of areas other than the ribcage or head (18%); eye injury (16%); head injury (12%), including fracture, subdural hematoma, and brain contusion; abdominal injury (5%); and amputation (5%).

London, England, 7 July 2005

Attacks on the London transport system killed 56 (53 at the scene) and wounded 775. Train bombs exploded in three locations, and a fourth bomb exploded on a double-decker bus. The number of explosion sites was initially unclear because passengers left the Underground at various exits. Triage was performed, and 55 patients were classified as severely wounded (P1 and P2). Communication was problematic, as all but one mobile telephone network failed. In addition, radio communication between the scenes and ambulance control was very difficult. The fire brigade established an inner cordon and found no signs of chemical substances threatening the rescuers; however, the presence or absence of more bombs was not confirmed before rescue work began. Patients who were mainly in triage groups 1 and 2 were transported to six university hospitals after minimal triage and treatment.

The Royal London Hospital received 27 of the 55 seriously wounded, along with 167 walking wounded. This hospital reported the types of injury. Further triage occurred, and eight people were classified as critically injured. Two of the seriously wounded and three of the walking wounded had burns.

The London Assembly still works to improve emergency care using lessons learned from the incident. Critical statements on the structural and organizational aspects of this disaster’s management have been published.

Indoor fires

Gothenburg, Sweden, 30 October 1998 (Fig. 5.2)

A fire in an overcrowded discothèque during a Halloween party killed 61 teenagers at the scene. Two died later, and 235 were wounded. The average age of people requiring treatment in the burns ICU was 16 years. Initial information was poor, resulting in incorrect alerts. No triage officer was present at the scene. Hospital disaster plans were unknown or not deployed. Pre-existing disaster plans had the same personnel simultaneously performing conflicting roles. Within 2 hours, 150 patients were admitted as inpatients at four Swedish hospitals: 31 patients presented with significant burn injuries, 11 of whom were transferred secondarily to other burn centers in and outside Sweden.

Despite the initial chaos at the scene, timely escharotomies and triage were performed in the hospitals before patients were transferred to burn centers. Inhalation injuries were diagnosed in 158 patients. Of these, 54 were treated simply with suction and expectorants. Thirty-nine did not have life-threatening injury but needed intensive therapy for 3 or more days. Sixteen patients had life-threatening injuries, and 47 had additional trauma. A total of 74 youths needed intensive care.

In 51 of 61 deaths carbon monoxide (CO) was the cause. Severe burns affected 25 patients, killing two. Both of these individuals also had inhalation injuries. The mean age of people with severe burns was 16 years. The mean TBSA with full-thickness burns was 16% and with partial-thickness burns was 3%. ICU treatment lasted from 12 to 67 days, and hospital stay lasted 21–164 days.
In 25 patients burn injuries required surgery. Eleven patients received escharotomies in the extremities or thorax, and five had fasciotomies. Amputations were necessary in five patients. Eight patients had flap coverage (local and distant), and two had free flaps.

Eleven patients were transferred secondarily to burn centers in four other cities, with one of these patients being transferred to Norway by helicopter and C-130 Hercules airplane. All 11 had second- and/or third-degree burns >20%.

**Volendam, The Netherlands, 1 January 2001**

A fire at a New Year’s Eve party killed 14 and injured 245 of the 350 present. Ages ranged from 13 to 27 years. For almost 4 hours nobody knew the exact number of victims. An early error in directing emergency traffic caused transportation chaos. Emergency services tents were insufficiently staffed, and tent placement was problematic. A total of 241 patients visited hospitals: 110 by ambulance, 18 by bus, and 113 by self-referral to the nearest hospital. Of the 182 admitted, 112 went to ICUs. Nineteen hospitals provided primary care. The closest hospital, receiving 73 patients, was severely overwhelmed.

After primary treatment in hospital, burn specialists performed tertiary triage, distributing patients to hospitals and burn centers in and outside The Netherlands. The decision to transfer patients was based on both burn extent and inhalation injury. The indication for burn center treatment was the presence of inhalation injury and burn >30% TBSA.

**Warwick, Rhode Island, 20 February 2003**

A fire at The Station, a Rhode Island discothèque, killed 100 and injured 215 of the 439 present. The building totally collapsed within 30 minutes. First information for Rhode Island Hospital (RIH) came from breaking news on television. Shortly thereafter, RIH received official information that 200–300 burn victims were expected. A triage site was established. Sixteen area hospitals evaluated the 215 injured patients.

Forty-seven patients were admitted to RIH (28 male, 19 female). They had an average age of 31.9 years and an average burn TBSA of 18.8%. Thirty-three had <20% TBSA, 12 had 21–40% TBSA, and two had >40% TBSA. Thirty-two patients had inhalation injuries, and 28 required intubation. Twelve escharotomies were performed, and in just six weeks 184 bronchoscopies were necessary. At least 47 patients needed intensive care.

Retrospective analysis called for improvement in communication with the disaster scene and in specific instructions for patients’ relocation.

**Buenos Aires, Argentina, 30 December 2004**

Fire at the overcrowded República Cromañón nightclub killed 194 and injured 714 of the 3000 present. CO and hydrogen cyanide poisoning were the main causes of death. At the scene, 46 ambulances and eight fire crews sent the victims to the eight closest hospitals, which were totally overwhelmed by critically ill patients within 2 hours. In Buenos Aires city 38 hospitals were engaged and another five were engaged elsewhere in Buenos Aires province.

Figure 5.3 Los Alfaques BLEVE and the ensuing situation. Courtesy of OOEEN/ARCHIV.

Ramos describes the experience of Argerich Hospital, which received 74 patients, average age 20.9 years. All had inhalation injuries. There were no severe burn injuries. Eighteen patients (24%) were pronounced dead on arrival; 25 showed respiratory insufficiency and reduced awareness, and these were intubated. Initially, 22 patients were sent to ICU; the 14 sent to the operating room for mechanical ventilation were transferred to other hospitals in Buenos Aires Province within 48 hours. Artificial ventilation averaged 6.5 days.

**Transportation crashes**

**Alcanar, Spain, 11 July 11 1978**

A tanker truck carrying liquefied flammable gas exploded beside the Los Alfaques campground, killing 102 at the scene and injuring 288. The number dead eventually totaled 215. The burning tanker divided the scene into two parts: 58 patients were transported north and received adequate care before transfer to Barcelona; 82 were taken south to Valencia and did not receive treatment either before or during transport. Both Valencia and Barcelona had state-of-the-art burn centers.

After the first 4 days Barcelona’s survival rate was 93% and Valencia’s was 45%. Patients treated at Valencia and those treated at Barcelona did not significantly differ in terms of age, the extent of burns, and the depth of burns. Barcelona’s patients died 1 week after Valencia’s. Overall mortality after 2 months was 85% due to the severity of burns. There were great problems in communication, handling the news media, and caring for victims’ friends and relatives.

**Ramstein, West Germany, 28 August 1988**

Aircraft collisions and crashes during an air show killed 70 and injured more than 1000 of the 300 000 present. Three pilots and 67 spectators died, and 346 others sustained serious injuries. Cooperation was hindered by medical systems that were not adapted to one another. On day one, 12 hospitals were treating the injured, on day two 28, and on day three 74.

Two hundred and thirteen patients were treated as outpatients, 146 were admitted as inpatients, and 84 others were transferred to ICUs. One hundred and twelve had only
mechanical injuries, 263 had isolated burn injuries, and 68 had both mechanical and thermal injuries.  

Patients suffering from <20% TBSA burns numbered 209 (79.5% of 263). Thirty-seven patients had 20–49% TBSA burns, and three died. Nine patients had 50–70% TBSA burns and six died. Another eight patients with >70% TBSA burns also died. Of the 68 patients with combined injuries, 55 had <20% TBSA burns. Three of nine patients with 20–40% TBSA burns died. No patient with combined injuries and >40% TBSA burns survived.  

The burn center at Ludwigshafen received 28 victims. Information came from ambulance radio conversations. The existing emergency plan was activated; overstaffing occurred on the first day. Primary care in the burn unit was provided in the normal way, not according to emergency plans. Experienced burn teams evaluated the patients. The disaster plan worked, but incomplete primary documentation greatly increased the next days’ workload. During treatment, no problems occurred with the expanded nursing staff. However, qualified medics who worked double shifts for weeks were exhausted. In addition, high-capacity use of burn beds caused cross-infection problems. In retrospect, the senior surgeon on duty on day one concluded that patients should have been transferred to other burn units, where free beds were available. 

Kerosene caused difficulties in respiration and in kidney, liver, and central nervous system function. Evaluating cyclic carbohydrates in the blood soon after the incident may be important for prognosis.  

**Pope Army Airfield, North Carolina, 23 March 1994**

Two planes collided in the air while attempting to land on the same runway. The C-130E was able to land, but the F-16D, whose crew ejected, slid into a parked, fully fueled C-141 cargo plane with a crew on board. Five hundred paratroopers, waiting 50–70 feet from the plane, were sprayed with a fireball of burning aviation fuel. They were also exposed to flying debris and the F-16’s 20-mm ammunition, which began firing from the heat. 

Fifteen to 30 minutes after the incident, casualties arrived at Womack Army Medical Center (WAMC), a 155-bed hospital 5 minutes away. Fifty-one were treated and released, and 55 were admitted. Of these, 25 went to ICUs. Six patients requiring urgent surgery were sent to nearby hospitals. Seven patients were sent to the closest civilian burn center, Jaycee Burn Center at the University of North Carolina, Chapel Hill. Ten victims died immediately, nine died soon at the scene, two died in transit to WAMC, one died within 30 minutes of arrival, one died within 12 hours of arrival, 10 died within 3 days (these included five of the seven sent to Jaycee), and one died after 10 months. 

One burn flight team arrived after 4 hours and another after 9 hours. Escharotomies that had been done were evaluated; some had to be repeated. Resuscitation was guided by urine output, but fluid amounts could not initially be tracked. Use of the Parkland Formula (4 mL/kg/TBSA), rather than the Modified Brooke Formula (2 mL/kg/TBSA), and untrained personnel’s overestimation of TBSA, led to initial over-resuscitation. Patients with mortal injuries were rejected for transfer to the US Army Institute of Surgical Research (USAISR) Burn Center. Forty-one patients were transferred to the USAISR Burn Center for burn treatment, and 13 of these required mechanical ventilation. 

In a review of this burn disaster, Mozingo made the following points: 

- Initially, patients with the largest TBSA burn were transferred to the burn center. Most of them later died. This sapped resources in the burn center, diminishing the chances of success. 
- Use of different resuscitation formulas caused difficulties. 
- Patients with injuries that were obviously deadly were not transported. This did not meet the expectations of the facility at which they were being treated. 
- Several burn victims remained at WAMC without burn specialists, because all burn specialists were needed at the USAISR. 
- Means of communication were deficient. 
- There was a lack of burn experience and training at WAMC. 
- Knowledge deficits were noted in techniques (e.g., escharotomy). 
- Training of non-surgical staff in advanced trauma life support (ATLS) and advanced burn life support (ABLS) is needed, as the surgical staff were busy with emergency procedures. 
- The additional ventilators needed were incompatible with the electrical requirements of the transport aircraft and had to be replaced by pressure-controlled transport ventilators, though this caused no delay. 
- The surgical staff at USAISR was augmented, and excisions of up to 40% were performed in one long, two-team operation. 

**Explosions**

**San Juanico, Mexico, 19 November 1984**

An 11 000-m³ mixture of propane and butane exploded, causing one of the most severe explosion disasters and registering 5 on the Richter scale. Gas entered houses in
San Juan Ixhuatépec (population 40,000) and set fire to everything. In a 25-acre (10-hectare; 100,000-m²) area 7000 persons needed medical help, 2000 required hospitalization, and 625 had severe thermal injuries. Thirty-three hospitals were involved, with transportation being provided by 363 ambulances and helicopters. Sixty thousand were evacuated. About 23,000 needed help with smaller injuries, lodging, and food.

The magnitude of the event meant that, for the first hour, total chaos reigned and rescue work was without guidance. Secondary explosions, heat from fire, and debris forced rescuers into temporary withdrawal to avoid risking more lives. After triage and primary care, victims were distributed to 33 hospitals, most of them in Mexico City. Within 3 days, burn patients had been distributed to 12 hospitals with good burn facilities. After 5 days, only 300 of the 625 burn patients were still in burn units: 140 had died and 185 had been sent to other hospitals. ‘Rather few’ extensive and deep burns occurred, and very few patients needed respirator care.

Centro Medico reported that 37 patients with severe burns were admitted because of a silo explosion 3 days before, and they received 88 other burn patients. The facility mobilized additional staff and prepared additional beds near the burn unit. Only two of the 88 victims had airway injuries requiring tracheotomies and ventilators. This burn unit’s usual capacity is 48 beds. The maximum number of patients simultaneously treated was 136. No shortages occurred in beds, personnel, or medication. Fifteen patients with >60% TBSA burns died within 4 days.

Piper Alpha, North Sea, 6 July 1988

An oil fire and gas explosion on an oil rig killed 167 and injured 189. The temperature was estimated at 3500°C. Information about the disaster reached Aberdeen Royal Infirmary, Scotland, by television. Sixty-three were rescued: 22 went to the hospital, 15 of whom were admitted, with 11 going to the burn unit. Primary triage was difficult because neither the thermal effect nor pulmonary injury could be evaluated immediately after the incident. Severe thermal injuries occurred from helmets melting on victims’ heads, even running down over their faces. All patients had some degree of inhalation injury, presumably from heated air.

All patients underwent surgery within 72 hours. No significant graft loss occurred. Operations were performed by two teams working in two areas simultaneously. The high number of dead took a grave toll on the medical and lay teams’ psyches. Psychiatrists, psychologists, and social workers were included in the team and proved to be highly valuable. The retrospective recommendation was to distribute patients among other units. News media were a problem, as was the administration’s unawareness of the need to maintain high staffing levels for an extended period. Knowledge of basic burn procedures (e.g., escharotomies and the way to treat a burn) is important if an administration is to plan and support sufficiently.

Bashkir Autonomous Soviet Socialist Republic, 4 June 1989

Two trains were passing a methane–propane pipeline when it exploded, killing 575 and injuring 623. Helicopters were dispatched for medical aid. Intravenous (IV) fluid resuscitation was initiated for most patients. Those with serious but potentially survivable injuries were then evacuated to Chelyabinsk, Sverdlovsk, and Ufa. Later, the military and Aeroflot took most of them to Gorky, Leningrad, and (the greatest number, 161) Moscow. Most had 30–40% TBSA burns. On 8 July the Soviet government accepted an American initiative to organize a burn team, mainly for children’s medical care. In Ufa, the team from Galveston, Texas (including Dr Herndon), evaluated four children with 30–68% TBSA burns and 12 with moderate burns (15–30% TBSA). The team began treatment in cooperation with Russian experts. The earlier, very conservative therapy was changed to an operative one, using dermatomes and meshers brought from Galveston. A US Army team was also deployed to the Soviet Union and began treating adults in Ufa. British and French teams were dispatched to Chelyabinsk. Israeli and Cuban teams went to the major burn centers in Moscow. However, Children’s Hospital 9 in Moscow had still received no help. Dr Herndon did further organizational work so that, after the Galveston team returned home, Dr Remensnyder (from Shriners Burns Institute, Boston) and Dr Ackroyd (from Massachusetts General Hospital) continued relief efforts at Hospital 9.

Twenty-six burned children were first admitted to Hospital 9. When Dr Remensnyder arrived, three children had died from sepsis. Modern techniques such as topical adrenaline splinting, use of air-driven dermatomes, and primary wound excision and grafting were introduced.

The US Army selected 28 patients for burn-wound excision and coverage. The team discovered many infected wounds, and a microbiological department was set up. Cross-infection between burn victims was common and mostly attributable to multiresistant *Pseudomonas* and *Staphylococcus* species. Techniques for minimizing blood loss had to be perfected as there were insufficient amounts of cross-matched blood. Local therapy with mafenide acetate and silver sulfadiazine was administered.

This effort was one of the very successful international joint operations in a burn disaster.

Critical dimensions of disasters and planning

In mass casualties and disasters with burn injuries, three possible scenarios exist:

- If the number of victims is within the local burn center’s surge capacity, that center can perform primary stabilization and treatment. Afterwards, they can decide whether to transfer some patients to other burn centers.
- If the number of victims exceeds the surge capacity of the local burn center but can be handled by the national system of burn centers, primary care must take place in hospital emergency departments and/or burn centers. Disposal of patients to national burn centers must come later.
- If the number of victims exceeds national resources, primary care must take place in emergency departments and/or burn centers. National and international resources must then be evaluated to determine which patients are to be treated in burn centers nationally and internationally. This scenario is greatly facilitated by pre-existing conventions and treaties.
Phases of mass casualty events

Chaos and alarm

Initially, information about the event is unavailable. Even those involved often cannot verify the incident’s dimensions, and sometimes cannot even describe the place. \(^2\) Details must be obtained immediately. Information to be collected includes the exact time, place, and type of accident; estimated numbers of casualties and expected pattern of injuries; hazards (e.g., contamination or toxic smoke); and the number of persons potentially exposed.

After verification, the incident command system and in-field command post must be established and must coordinate the work of rescue, security, technical relief, and medical relief forces. They can then enable work to proceed in the damaged area and protect the team and their work from hazards, violence, and the distracting demands of victims, their friends, and their relatives.

False information leads to inaccurate alerts (e.g., ‘yellow red’ instead of ‘red’) and is disastrous for all who then must cope with unexpected situations. \(^3\)

Immediately after the accident, victims flee to the nearest hospitals, overcrowding them before any official alarm. This influences the execution of emergency plans, because everyone is busy with arriving victims and no resources may be available to carry out disaster plans. Contaminated victims fleeing contaminated areas can bring severe risks to hospitals, causing a partial dropout of medical resources.

Organization

Medical care should be established at the scene and in alerted hospitals. First, the scene must be cleared of further hazards or rescue workers must be outfitted for the risk. Next, a cordon should be established to control victims’ departure to hospitals and to prevent onlookers and the news media from interfering in rescue work.

Traffic regulation must begin, and all teams must understand it. It must include movement and assembly of ambulances, fire trucks, and police cars; landing and take-off of helicopters; decontamination areas; areas for triage, treatment, and victims with minor injuries; and a temporary morgue. The scene should be divided into rescue areas, and schedules should be created for technical support teams.

During this phase, cooperation among medical teams, fire brigades, police, and technical relief teams is crucial. Local command-and-information structures must be established, as they serve as the coordination hub for preclinical treatment. A central command-and-coordination structure coordinates preclinical treatment, clinical treatment, and transport. It also disseminates up-to-date information. At hospitals, disaster plans are engaged and staff called in. The quality of the performance of all teams depends mainly on information.

Salvage and triage

Search and rescue

A salvage triage can be important for directing technical and medical relief because it determines urgencies. The first goal may be to bring victims to a safe collection place, free from imminent danger (e.g., battle, hostile action, or environmental hazards). Tagging must begin here. In-field triage must take place. This primary evaluation should take less than 30 seconds per patient and should be limited to life-threatening conditions.

With mass casualties, no resuscitation usually takes place in victims first classified as dead (no ventilation after freeing airways and no pulse, according to Simple Triage and Rapid Treatment—START). This is especially true when victims are salvaged from indoor fires (because deadly CO poisoning is assumed) or when lack of pulse or capillary refill is coupled with limb amputation (because massive violence is assumed to be fatal). \(^4\)

Depending on the number of victims, salvaged victims are brought to collection points or to the triage area. In victims with extensive burns, the time in low-temperature environments must be minimized to reduce the chance of hypothermia.

Triage

Do the very best for as many as possible.

Different systems use different triage algorithms. Paramedic systems may use START in both emergency medicine and mass casualties. According to findings, emergency treatment is as follows: free airways, emergency intubation, cricothyrotomy, decompression of tension (pneumothorax), and mask ventilation, styptics. \(^4\) The sensitivity for START varies from 85% \(^5\) to 62%. \(^6\)

Medic in-field triage is another type. This is performed in an established triage area by medics assisted by teams of helpers. It consists of minimal anamnesis: time of accident, mechanism of injury, condition, how the patient was found, primary measures taken, actual discomfort, pre-existing conditions, medications and allergies, and the following systematic medical check:

- Physical investigation: external bleeding, penetrating injuries, burns, chemical burns, neurological status, and investigation of the head, spine, thorax, abdomen, pelvis, and extremities.
- If possible, a few measurements are taken, e.g., respiration rate, pulse oximetry, and temperature. \(^4\)

In burn victims, the TBSA burn is estimated by the Rule of Nines, and strictures, suspected inhalation injury, and the need for intubation are evaluated. Emergency treatment is performed in a treatment area by emergency physicians. Burn victims needing treatment for shock or intubation should be classified for urgent treatment. Because of the need to resuscitate as soon as possible, resuscitation should at least begin here.

Triage depends upon easily verifiable vital parameters and clear types of injury to filter and classify patients according to the four treatment urgency groups shown in Table 5.1.

In Austria, Germany, Switzerland, and some other countries, triage group 4 includes the hopeless or unsalvageable who deserve ‘expectant’ treatment. This is very controversial because the duration of the disparity between supply and demand should be short, and when this period is over this group’s priority changes to 1 or 2. In such countries, the dead
Burn management in disasters and humanitarian crises

wounded or as transports with individual means. These hospitals should be spared from primary transports.

Tagging
First, each patient is given a tag with a unique number. These tags facilitate victim identification and registration; provide information about patients’ history, medical treatment, injuries, urgency of treatment, and classification of injury; and specify the hospital for treatment. The tags must never be removed until all the following have taken place: definitive treatments have been initiated, the patient has been identified, the diagnosis has been made, and the tag number and all treatment data have been registered.

Different types of tag and label exist. Treatment urgency is evaluated first. Transport urgency follows emergency treatment.

First medical treatment
Necessary resuscitation, intubation, and minimum wound treatment should begin in accordance with triage findings. Often this must take place with limited resources and little knowledge of what the next minutes will bring. The lack of resources (e.g., IV fluid, infusion systems, tubes, respirators) limits their use to acute emergencies, leaving primary care for the hospitals where victims are sent.

First transport
For transporting burn victims, ambulance heating should be maximized to avoid cooling patients. Warming pads and extra blankets should be prepared, and IV fluids should be warmed. Ambulance doors should also be kept closed to retain heat.

Transport order must be in accordance with the urgency status determined in triage. Transporting the dead steals resources from the living. The dead and where they are found (important for identification) should be documented. When they have to be removed, they should be brought to a temporary morgue.

First-line hospitals
The closest hospitals should be avoided as much as resources will permit, as they will be overcrowded with people who are neither triaged nor registered and who arrive as walking wounded or as transports with individual means. These hospitals should be spared from primary transports.

Second-line hospitals
Second-line hospitals should be reserved for completing the primary treatment of patients who have already been treated. Each hospital to which victims first are admitted must perform a second triage to assess and complete primary treatment. The condition of burns patients often deteriorates quickly. Therefore, re-evaluating victims brought to these hospitals is mandatory!

Third-line hospitals far from the scene
Patients in triage group 3 (‘delayed treatment,’ ‘walking wounded with only minor burns’) should be taken to hospitals far from the incident. Mass transportation (e.g., buses) can be used.

Primary hospital or burn center triage and treatment
Measures should be taken to stabilize the patient and perform all immediate necessary surgery, so that the need for interventions is minimized and personnel are then available for other work. Outside burn centers, admission triage and treatment are usually performed by medical specialists who are more or less familiar with the emergency management of severe burns. Support from burn experts will be necessary later.

When a burn patient arrives at hospital, an assessment must be performed, and prior measures must be completed or corrected (Table 5.2).

This evaluation and treatment are based on the ABCDE (Airway, Breathing, Circulation, Disability, Environment)
sequence and are carried out through interdisciplinary means at a hospital. Securing the airway can require tracheotomy. Improving ventilation often requires escharotomies and fasciotomies in the thorax – sometimes even removal of necrotic plates strictly adjacent to the fascia.

Neglecting escharotomies in patients with impaired ventilation leads to more or less circumferential eschar in the thoracic area and death within hours. Indicated escharotomies and fasciotomies improve lung function almost immediately. Delayed escharotomies can lead to hyperkalemia with successive cardiac problems and massive influx of edema fluid, causing acute fluid overload.

Impaired circulation can result from strictures created by burn scars or from incorrect resuscitation. Strictures created by burn scars require escharotomies and fasciotomies in the extremities. Incision should make fasciotomies feasible and, if possible, should be done through third-degree burns, which must be removed over time, to minimize scarring.

Resuscitation should always be started according to a formula. Unfortunately, most burn victims receive too much resuscitation fluid initially. This seems to stem from two main factors. One is the overestimation of TBSA by the Rule of Nines. Even Lund–Browder charts overestimate burn size. The other is use of the Parkland Formula (4 mL/kg/TBSA). Combining this formula with overestimation of TBSA, either by Rule of Nines or by Lund–Browder charts, can cause heavy fluid loads, initiating edema or abdominal compartment syndromes. Calculation of initial fluid requirements can be supported by easy-to-use 3D computer charts combined with the Modified Brooke Formula. The fluid-needs calculation should then be guided by physiological parameters as soon as possible, mainly to the urine output of 0.5–1 mL/kg/hr (Table 5.3 and Table 5.4).

**Table 5.3 Fluid need calculation error from overestimation and different formulas**

<table>
<thead>
<tr>
<th>TBSA (actual)</th>
<th>Patient weight</th>
<th>Formula</th>
<th>Resulting resuscitation fluid</th>
</tr>
</thead>
<tbody>
<tr>
<td>30%</td>
<td>75 kg</td>
<td>Modified Brooke 2 mL x 75 x 30</td>
<td>4500 mL</td>
</tr>
<tr>
<td>36% (overestimation by 20%)</td>
<td>75 kg</td>
<td>Parkland 4 mL x 75 x 36</td>
<td>10 800 mL</td>
</tr>
</tbody>
</table>

**Table 5.4 Important items during primary hospital assessment of burns**

**Ventilation**
- If ventilation is impaired, check the need for intubation, tracheotomy, or coniotomy
- If patient is intubated and ventilation is disturbed, check tubus position, exclude pneumothorax, and consider thoracic escharotomies and fasciotomies
- Check for inhalation injury and aspiration. Bronchoscopy may be needed
- If carboxyhemoglobin is high, oxygen administration is needed

**Circulation**
- If perfusion of extremities is disturbed or pressure is high, check the need for escharotomy and fasciotomy
- Recalculate TBSA
- Recalculate fluid requirement. Adjust fluid amounts accordingly
- If blood pressure is disturbed, correct fluid administration. Other medication? Additional injuries?

**Organ perfusion**
- Check urine output
- Core temperature: Warm up

**Other injuries**
- Is other medical treatment (besides burn treatment) necessary?
  Complete diagnosis, and give treatment according to urgency

**Local treatment**
- Clean. Apply disinfectants: Take primary swabs

**Nutrition**
- Nasogastric or nasoenteric tube in intubated patients

**Discussion**

Additional injuries demanding treatment should, if possible, be definitively treated within the first 24 hours, before burn treatment. These injuries should be treated at minimum with the goal of damage control, or better, by definitive surgery. In cases of an unclear history of injury, explosions, and trauma caused by external forces apart from flames, a trauma CT scan should be performed to ensure that no other severe injuries are missed during the primary evaluation.

Escharotomies and fasciotomies should be performed before osteosynthesis. Escharotomies should be done when there is increased swelling occurring within hours due to systemic inflammatory response syndrome and to the hygroscopic effect of the eschar. Postponing necessary escharotomies while waiting for BAIs or BSTs to perform escharotomy greatly increases the risk that extremities will be lost, and that the patient’s condition will deteriorate severely. In burns, osteosynthesis procedures performed during the first 24 hours do not carry higher complications than those performed in non-burn patients. When the risk is low, intramedullary stabilization should be performed, giving a better approach for handling burns, that is, it makes kinetic therapy and burn dressings easier. If a higher risk is present, external fixation is the appropriate method.

Wounds should be cleaned under sterile conditions. This should be followed by topical treatment with disinfectants and burn dressings.

Enteral feeding – at least by nasogastric tube but preferably by nasoenteric tube – should be started.

**Secondary burn re-evaluation and treatment in hospital or primary burn center**

**Evaluation**

Central incident command should already know the number of available burn beds. They should also know, at minimum, the number and locations of victims. Burn extent and
severity, need for ventilator support, quality of shock treatment, CO poisoning, and quality of escharotomies must all be evaluated with the goal of obtaining reliable data. This is the ‘golden hour’ of BATs and BSTs.

Patients’ temperature should be maintained by maximally warming operating rooms. Air-conditioning systems with target temperatures that cannot be raised beyond a certain level can be a problem. Warming the operating room beyond the target temperature (e.g., with space heaters) simply causes the system to work harder to maintain its cooler, target temperature. Such systems must be turned off.

During the evaluation period, staff should be prepared to evaluate fluid regimens, ventilation, perfusion, escharotomy, and TBSA. They should also expect to begin feeding, cleaning the surface, using disinfectants, and applying dressings to reduce heat loss.

Central collection of corrected data

With central data collection and distribution the best treatment option allowed by the available resources can be chosen for the patient. This can be supported by information technology (IT) solutions that enable surface calculations and central registration of burn cases.39

Treatment options

Patients should be distributed to burn centers with free resources. However, when resources are limited, special criteria for burn center treatment must be set. These criteria are based on the survival grid published by the ABA2 and usually depend on TBSA, the need for ventilator support, and age. Patients meeting these (temporary) criteria should be transported to burn units. The rest should either stay in the primary hospital or be transferred to non-burn units.

Secondary transport

Transports to burn centers have the highest priority.

Whether to transport patients whose care has been classified as futile to burn centers must be decided in disaster planning. They are a burden for the primary hospital in terms of workload, psychological effect, and legal aspects.32 In burn centers, they tie up resources needed for treating patients who are likelier to survive. The pairing of two recommendations in the US – to send any patient with a third-degree burn to a burn center and not to send anyone with a severe, non-survivable burn to a burn center – produces conflicts. At any rate, these patients, their relatives, and the staff caring for them need both psychosocial support and support from experienced burn medics.

Depending on the severity of burns, patients should be transported through appropriate means. Ventilated patients should be transported by air or, for shorter distances, by mobile ICUs.

During transport, the patient must be protected from bacterial contamination and from cooling. This requires special dressings and devices that hinder cooling. Minimal monitoring should be possible: respiration rate, urine output, oxygen saturation, and in longer flights, PaO₂ and PaCO₂. Some helicopters can transport several patients simultaneously. Armies usually can offer airplanes to transport many victims even when ventilated (e.g., the MedEvac Airbus can transport six patients in intensive care and 38 more in the supine position).

Problems with air transport have been reported. These include bacterial cross-contamination as well as relatives’ being delayed or prevented from accompanying their dying family members.23 Klein46 reported that the most common complications during air transport are loss of venous access and inability to secure an airway. Hypothermia (<35°C) has been reported in about 10% of patients, most of whom have a larger burned TBSA. Mass transports can be supported by armies and their matériel.

Definitive treatment

Definitive treatment is given in predetermined places. Relatives coming to their badly injured loved ones should be given psychosocial help and supported by the offer of guest rooms and continuous, fact-based information. Patients and relatives must be protected from news media, which often present a big problem during this phase.

During surgery, blood-saving methods must be emphasized to conserve blood stocks. This can be helped by local application of epinephrine; tumescent techniques in necrosectomy and donor areas; local application of thrombin; and use of tourniquets. Performing operations on larger areas and with more teams can reduce the amount of preparation time between operations by reducing the absolute number of operations. Because resources such as cadaver skin can be limited in mass casualties, definitive covering as soon as possible is the goal.

Transport home

For patients whose early treatment occurred far from their homes, transport to home hospitals should be arranged after treatment. Central disaster management must conduct a general survey of treatment centers, who has died, living victims’ conditions, and spaces available in the home area. Patients should be transported if they are stable and the situation in the home area is expected to be suitable. Transport funding must be cleared.

Long-term treatment

After treatment in a burn center, patients’ further care must be organized and planned. Regular follow-ups, surgical interventions, compression therapy, and psychosocial support must be planned and initiated. These should be long-lasting measures to give the patient a point of care that they trust and to make them feel welcome to go there for any reason.

Rehabilitation

Rehabilitation must be planned and coordinated for all patients. The primary shortage in burn beds will be followed by a secondary shortage in rehabilitation centers. Follow-ups must be planned far into the future; projects should be established and funded. Physical, psychological, and social care should be given not only to the victims but also to their relatives.
Debriefing

Debriefing is part of psychosocial preventive care in an emergency response. Staff involved in mass casualties have a higher risk of illness than the average population because of confrontation with severely hurt or mutilated victims, especially children; injuries (sometimes fatal) to colleagues; fetidness; and cries for help. It is also attributable to pain, the need to make triage decisions, bad information, lack of routine, lack of resources, inability to provide help, and contact with aggressive news media.\(^{50}\) Debriefing allows these individuals to overcome the event psychologically and reflect on its effects. Optimally, it is conducted near the event site and begins within the first 24–72 hours. General group sessions after incidents are not recommended, as on their own they do not prevent post-traumatic stress reactions.\(^{50}\) One-on-one interviews and small group sessions are preferable. After these meetings, the psychosocial specialist decides whether debriefing should be offered. Re-contacting people after 4–6 weeks and re-evaluating the first decision is recommended.

In many countries, institutions and organizations offer debriefing based on the Critical Incident Stress Debriefing system. This system has three main parts: preparation, attendance, and aftercare. Although minimum quality standards are rather clear, quality control is sometimes lacking.\(^{50}\)

Information and communication

Hospitals and burn centers often learn of the incident first through irregular channels.\(^{52}\) Victims arriving on their own sometimes provide the first information.\(^{13}\) The news media can also be faster than the designed information structure. Moreover, video is sometimes a better source of information than mere words. When patients arrive tagged or telling certain stories, this may indicate that a mass casualty event has occurred. Measures to establish hospital preparedness should be taken. For example, supplies and the local situation should be checked. In addition, staff should not be permitted to go home after shifts until the situation is cleared.

Crisis communication is the exchange of information among public authorities, organizations, the news media, and affected individuals and groups before, during, and after a crisis.\(^{51}\)

Means of communication

In disasters and mass casualties many factors increase the need for communication, and communication resources are limited. Sequential failure of various communication methods has been described in many disasters (e.g., Enschede,\(^{52}\) Eschede,\(^{53}\) London, Madrid,\(^{14,16}\)).

Cellular telephone

Cellular networks are usually overwhelmed because victims, the news media, relatives, friends, and others all quickly begin dialing to or from cell phones, leading to breakdown within minutes. Cell phones should not be used near explosive devices.\(^{54}\) A 50-foot (15.2-m) safety radius is recommended for cell phones and radios being used near a suspected explosive. People trying to use cell phones may be endangered by security forces, who know that cell phones can also be used to trigger bombs. If bombs are suspected, cell phones can be jammed by security forces.\(^{55}\) Amateur videos, often shot on cell phones, are important in mass casualties for reconstructions and intelligence.

Conventional telephone

In most hospitals, the number of incoming and outgoing landlines is limited. If there is a manual switchboard but no automatic switching, this system can be overloaded very quickly. An alarm server with a call center function can be useful for alerting staff, as in the early phases of a mass casualty everyone is needed to help prepare the hospital before the surge.

Voice over internet protocol (VoIP)

VoIP permits conference calls. For safety, public systems that could be used are usually disabled in hospital IT systems.

Two-way radio

Reception and transmission can be poor or non-existent indoors and underground (e.g., 9/11, London). In hospitals, the number of people who can talk at the same place and time over one circuit can be limited. This causes problems when an area includes many persons exchanging information.

Trunked radio system (TRS)

TRSs use computer control to allow almost unlimited talk groups with only a few channels. Relief units use TRSs for intra- and interorganizational communication. In Europe, TRSs are being established for emergency organizations.

Satellite telephone

Satellite phones operate independently of local infrastructure and can be helpful in cases of uncertain or overloaded infrastructure. However, even a call made from a satellite phone will not go through if the telephone system on the receiving end is not functioning.

Internet

Internet communication is an option only if connections are intact.\(^{56}\) The internet can be helpful in building up information structures for victims’ relatives and to provide information to extremely large audiences.

Electronic news media

These are important in disasters, especially when locales must be evacuated and when staff are needed. News reports sometimes provide burn centers with their first information about an incident, before the official alarm arrives.

Communication with news media

The news media shapes the public face of the disaster. Information for the media is important and should originate in
a desire to be as correct and as complete as possible. No excessive information on certain events should be provided, but important information must be given. The central incident command should appoint spokespersons to provide regular, announced press conferences and bulletins. The press should be kept away from victims and their relatives — the hunt for headlines does not stop at the hospital door.

When spokespersons start their work, they should first express their concern about the situation and their condolences to those who have lost loved ones. They should then provide assurance that everything possible is being done to help.

Methods of supplying information to the press include Web newspapers, press releases, press conferences, radio, and television. The press want people for interviews and photos. This should be kept in mind and prepared for, with forethought being given to what aspects can be discussed without causing problems. Guidelines for communication with the press are as follows:

• Never lie.
• Never guess, or present your own theories.
• Never become upset or angry.
• Never let the situation or reporter affect you.
• Never use jargon.
• Never discuss classified information.
• Never say ‘No comment.’
• Never speak about issues outside your competence.

Press communications should be made in an environment outfitted for information transfer by the media and away from patient treatment areas.

Communication with relatives and friends
As at the scene, centers should be established at hospitals for friends and relatives to gather in private, and crisis counselors and information tools (e.g., telephones) should be available. Access to these areas should be restricted to identified relatives and friends. Information here should be exact, honest, and never speculative. A contact person for relatives and friends should be nominated.

Medical treatment

Different medical standards are used in treating mass-casualty victims, beginning with help from bystanders to ATLS from medical emergency teams, ABLS, and emergency management of severe burns (EMSB).

First aid at the scene and basic life support
Bystanders, hurt and unhurt, give first aid according to their education and ability. Basic measures include positioning, stopping bleeding, and securing respiration. In burns, additional measures include extinguishing fires on individuals, stopping the influence of heat, cooling surfaces, and hindering hypothermia. If available, oxygen should be given. Extinguishing and stopping thermal influence without causing hypothermia are the most important of these measures.

Water and cooling
Applying water helps to reduce pain by reducing surface temperature (thereby reducing nociceptor activity) and by hindering nociceptor desiccation. Water cooler than 8°C (46.4°F) can aggravate cell destruction. Water should be clean, but sterility is not necessary. Water from containers in which warm water is stored long-term can be contaminated with Legionella, causing severe problems (e.g., atypical pneumonia) very quickly.

The effectiveness of wet dressings is limited by their drying out. Therefore, periodic moistening is necessary to maintain the effect. Gel preparations do not dry and can make the wet-dressing pain-reduction method more comfortable. Although gels cool the body more slowly than does running water, they do not prevent hypothermia. In extensive and large burns, the application of tap water should be limited to extinguishing the fire and cooling surfaces to normal temperatures.

Hypothermia is a serious problem in burns and should be guarded against. If a patient starts shivering, cooling must be stopped and core temperature must be maintained by all available means. No wet dressings should be applied.

Advanced trauma life support (ATLS)
Doctors and advanced paramedics perform ATLS in preclinical treatment areas and emergency rooms. ATLS procedures are to be followed first; however, burn injuries require special care in the treatment of shock, evaluation, local treatment, and special knowledge of indications about where to treat.

Advanced burn life support and emergency management of severe burns
Burns are best treated with certain protocols:

• EMSB – developed by the Australian and New Zealand Burn Association and adopted by the British Burn Association
• ABLS – developed by the ABA, with training being available online.

These protocols include ascertaining the magnitude and severity of an injury; identifying and establishing treatment priorities; physiological monitoring; determining the appropriate guidelines for patient transfer, including time, destination, and transport method; and treatment of the burn area, associated injuries, and common complications within the first 24 hours after burn.

Preventing hypothermia, wound contamination, and evaporative heat loss
Hypothermia, wound contamination, and evaporative heat loss are usually prevented with special burn dressings (absorbent cotton with an applied aluminum surface) and with plastic film as used in operations. In mass casualties, saran film (the plastic wrap used for food) is suggested for areas away from the face. It must be at least clean, if not sterile. This occlusion prevents wound dehydration and evaporative heat loss. Care must be taken not to stop circulation or hinder ventilation.
A separation layer must be applied between sterile and non-sterile dressings. Outside this layer, blankets should be used to reduce heat loss. Patients at greatest risk of hypothermia are those who are intubated and sedated, as they cannot regulate their own temperature.

**Topical treatment**

**Chlorhexidine**

Chlorhexidine is a chemical antiseptic. It is effective on both Gram-positive and Gram-negative microbes, although it is less effective with some Gram-negative microbes. It reduces surface colonization of burns; however, its effect on deep colonization is limited. In a 4% solution it has good effects against *Staphylococcus aureus* and *Pseudomonas*.  

**Sodium hypochlorite**

Sodium hypochlorite is recommended as primary treatment for burn wounds before treatment in burn units. Its clinical effectiveness does not increase in concentrations >1%.  

**Polihexanide**

Polihexanide is a biguanide polymer with disinfectant and antiseptic properties. It has very low cytotoxicity and is clinically and microbiologically superior to silver nitrate and povidone-iodine.  

**Silver nitrate**

Silver nitrate is usually used in 0.5% solution and has good effects on *Pseudomonas*, *Staphylococcus*, and many Gram-negative microbes. It can cause methemoglobinemia. It is painless and should be applied by soaked dressings re-moistened every 2 hours. The resultant film on the surface can frustrate evaluation. Because of ionic silver’s quick inactivation, the effect is brief.  

**Nanocrystalline silver**

Nanocrystalline silver works in wet surroundings by setting silver free over a long period. It can be applied and left in place for some days. Complications can be caused by stricture. One case with argyria-like symptoms has been described. It has been shown to be more effective than silver sulfadiazine in treating superficial burns.  

**Silver sulfadiazine**

Silver sulfadiazine inhibits DNA replication and induces membrane changes in *S. aureus*, *Escherichia coli*, *Klebsiella* species, *Pseudomonas aeruginosa*, *Proteus* species, and *Candida albicans*. It is available as a 1% cream. It can cause acute hemolytic anemia in patients with glucose-6-phosphatase enzyme deficiency. When applied in higher doses over a longer period sulfonamides can cause crystalluria and methemoglobinemia. This chemical changes the surface of burn eschar, hindering evaluation of burned surfaces.

**Flammacerium**

Flammacerium is silver sulfadiazine combined with cerium(III) nitrate. It makes the eschar more supple. The antibacterial spectrum of this compound is the same as that of silver sulfadiazine, but its potency is higher. Methemoglobinemia arises rarely.

**Mafenide acetate**

Mafenide acetate is a sulfonamide with excellent activity against Gram-positive bacteria, including *Clostridium*. It has a broad-spectrum activity against Gram-negative bacteria but is not so effective against fungi and methicillin-resistant *S. aureus*. Application of this compound can result in systemic toxicity, often causing hyperchloremic metabolic acidosis and pulmonary complication if used over a long period. Because mafenide acetate is excellent at penetrating dead tissue, it is useful for the short-term control of invasive burn infections. This compound is not available in Europe.

**Povidone-iodine**

Povidone-iodine is used as a cream or solution. It penetrates the eschar, changing the surface so that evaluation is difficult. It must be applied at least twice daily.

**Anesthesia**

**Early care: the part of the anesthesiologist**

Major burn injuries are characterized by a rapid deterioration in hemodynamics and in vital systems such as the respiratory system. With the breakdown of the skin barrier hypothermia and infections become major, immediate threats. Second-degree burns are usually extremely painful.

**Fluid resuscitation**

Immediately after burn trauma, collagen breakdown in the dermis leads to a large increase in osmotic pressure in the interstitial fluid compartment, followed by the rapid formation of edema in the burned tissue. One to two hours later the capillary permeability in both the burned and the unburned tissue increases, reaching a maximum at 6–12 hours post burn. This reinforces edema formation and aggravates shock development.

Early management of burn shock is critical for surviving burns >20–25% TBSA. In children in particular, beginning fluid resuscitation within 1 hour after burn dramatically reduces mortality. This depends more on timing than on the type of fluid infused.

To deliver adequate quantities of fluid, one must estimate the extent of TBSA burned. The Rule of Nines is widely used for this purpose. The most commonly used formulas for estimating fluid requirement in major burns are the Parkland Formula and the Modified Brooke Formula. Parkland recommends 4 mL lactated Ringer’s solution (RL) per kg/TBSA for the first 24 hours. The first half is administered during the first 8 hours post burn, and the rest is administered during the subsequent 16 hours. The Modified Brooke Formula is the same, except that 2 mL is used instead of...
4 mL. No colloids are infused during the first 24 hours. Considerably more fluids must be delivered in the case of additional inhalation injury, delayed resuscitation, or combined traumatic injuries.

Children usually require more fluid resuscitation than adults with the same extent and degree of burn injury. Burn shock may occur with burns 10–20% TBSA.

Children weighing <30 kg should be given maintenance fluid in addition to the calculated resuscitation fluid.83 (Table 5.5 and Table 5.6).

Other, more sophisticated formulas exist.

Mass casualties or disasters make it difficult to provide fluid resuscitation both at the right time and in sufficient quantities. For example, a 70-kg patient with a 40% TBSA needs approximately 6000 mL of RL during the first 8 hours. Using alternative fluids for resuscitation to reduce early fluid requirements is very important, because supply is the bottleneck during disasters.

Early use of colloids

Data about using colloids, especially synthetic colloids, in the early resuscitation of patients with burn shock are rare. However, newer hetastarch solutions, especially the balanced solutions (6% HES 130/0.42), are widely used in Europe as a rescue solution when resuscitation with RL fails.74 Both the rapid metabolism and the milder disruption of kidney function offer a better safety profile than those seen with the older, more highly substituted types of hetastarch. The rapid metabolism is accompanied by a much smaller risk of accumulation in the plasma and tissue (75% less than HES 200/0.5),75 a less negative effect on thromboelastographic indicators and on activated partial thromboplastin time, as well as a reduced interaction with factors VIII:C and vWF.76 Kidney function is disrupted less, even after repeated extreme doses (70 mL/kg/d).77 It is also disrupted less in patients presenting with mild to severe renal dysfunction.78 Therefore, in 2005, the European regulatory authorities increased the maximum daily dose to 50 mL/kg.

The volume-sparing and hemodynamic-stabilizing effect of colloids, when administered according to the Evans Formula, the Brooke Formula, and even the early Parkland Formula, has long been known. In the early 1980s, Goodwin79 reported that the use of colloids (albumin) in early resuscitation in major burns produces an increase in lung water. During the last 30 years, crystalloid resuscitation was the main form recommended, to avoid causing lung edema. Newer data on the use of albumin, plasma, and hetastarch in early resuscitation have shown no increase in lung edema and support the use of colloids after 12 hours.80,81

**Hypertonic saline**

Hypertonic solutions can rapidly restore plasma volume. The volume needed for resuscitation during the first 8–24 hours is much less than estimated by the Parkland Formula.82 In the 1970s, mild to moderate hypertonic solutions were investigated.83 In the 1990s, new hypertonic–hyperoncotic solutions (7.5% NaCl with dextran or with HES) were used for ‘small-volume resuscitation’.84 Because the relative volume effect of hypertonic saline dextran (HSD) is 8.5 times that of RL,85 it rapidly improves hemodynamics, as seen in a sheep model with 40% TBSA.86 In addition, hypertonic saline tends to moderate the upregulation of leukocytes and adhesion molecules, and may lower microvascular permeability.87

The first use of hypertonic solutions in major burns, using very high doses, led to renal failure and increased mortality.88 In traumatic shock, 4–8 mL/kg of HSD or Hyperhes is usually delivered as a bolus. However, for major burns, administration of a limit of 8–10 mL/kg over 2–4 hours86 seems safer and causes prolonged volume expansion. It also has logistic advantages in an evacuation center or staging area, where large volumes are not available.89 Small-volume resuscitation solutions (HSD, Hyperhes) must be supplemented with isotonic fluids (with the aim of having a urinary output of 0.5–1 mL/kg). Because of the danger of hyperoncality (Na >160 mVal/L) and renal failure, they cannot be recommended for routine use in major burns.

**Oral fluid replacement**

Since the development of formula-based IV resuscitation in the early 1950s, oral resuscitation in major burns (>15–20% TBSA) has had no significant effect on early therapy. This is mainly due to disturbed gastric emptying and impaired peristalsis caused by the burn injury, along with the analgesics and anesthetics delivered for pain, which have well-known effects on the intestine.

In the early 1970s, Monofer75 resuscitated a small group of adults and children with 22–95% TBSA using a 600-mOsmol/L hypertonic oral solution. In the 1990s, a revival of enteral fluids in terms of ‘early enteral feeding’86 revealed that, if feeding began no more than 2 hours post burn, the gastrointestinal effects were favorable, and even major burns could be managed partly or wholly with enteral, rather than parenteral, feeding.

Today, the main focus is on the World Health Organization’s oral resuscitation solution (ORS). This is a powder solute that is provided in a small packet and is suspended in water. It contains glucose, sodium, potassium, chloride, and buffer, having a slightly hypertonic osmolality of 331 mmol/L. It was first developed to treat the massive loss of volume and electrolytes accompanying conditions such as cholera and dysentery.

### Table 5.5 Fluid resuscitation in children

<table>
<thead>
<tr>
<th>Resuscitation fluid</th>
<th>Modified Parkland Formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>3–4 mL RL/kg/TBSA for the first 24 hours</td>
<td>First half during the first 8 hours; the rest during the next 16 hours</td>
</tr>
</tbody>
</table>

### Table 5.6 Fluid maintenance in children

<table>
<thead>
<tr>
<th>Patient weight</th>
<th>Maintenance fluid: D5RL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Up to 10 kg</td>
<td>100 mL/kg/day</td>
</tr>
<tr>
<td>10–20 kg</td>
<td>1000 mL, plus 50 mL/kg/day for each kg over 10 kg</td>
</tr>
<tr>
<td>20–30 kg</td>
<td>1500 mL, plus 20 mL/kg/day for each kg over 20 kg</td>
</tr>
</tbody>
</table>
Thomas demonstrated that, by placing a feeding catheter in the intestine of 40%-TBSA anesthetized pigs, these animals could be resuscitated with the WHO ORS according to the Parkland Formula. Michell reported similar results. El-Sonbathy reported good results using the WHO ORS for oral resuscitation of children with 10–20% TBSA.

Without a gastrointestinal catheter, greater volumes of oral resuscitation fluids may be necessary because gastric emptying may be delayed. More research into both the ideal enteral fluid and the quantities to administer is necessary. However, in disasters with IV fluid shortages, oral rehydration solutions may have a role in early burn resuscitation. Such solutions include the WHO ORS, or, if this is not available, 5.5 g of an undissolved salt tablet can be swallowed with 1 L of water as reported by Sorenson, 1 L of water with 1 teaspoon of salt (or 0.5 teaspoon of salt and 0.5 teaspoon of baking soda) and eight teaspoons of sugar as reported by Cancio, or 1 L of RL with eight teaspoons of sugar, which is available everywhere and is easy to transport.

Conclusion

A staged approach has been set forth for fluid resuscitation in the military, as reported by Thomas. A similar process should be outlined for civilian mass casualty incidents:

- Patients with <20% TBSA and no immediate need for intubation could be resuscitated orally or by nasogastric tube (NGT) with the WHO ORS or a similar solution (500-mL bolus with one packet of rehydration solution) and then subjected to bolus feeding of 2–4 mL/kg every 20 minutes. This should maximize gastric emptying.

- Patients with 20–50% TBSA and no immediate need for intubation could benefit from administration of 1 or 2 HSD or Hyperes units (250–500 mL) over 2–4 hours, combined with enteral resuscitation with WHO ORS and/or IV RL administered with the goal of a stable macro-hemodynamic and urinary output of 0.5–1 mL/kg/h.

- Patients with >50% TBSA and inhalation injury, combined injuries, etc. often require intubation, so IV fluid resuscitation should begin as soon as possible. The fluid requirements estimated by the Parkland and Modified Brooke formulas can be reduced during the first 24 hours by administration of hypertonic saline and colloids, as discussed above.

The importance of beginning fluid resuscitation as early as possible, using just what is to hand, must be emphasized. Moreover, because hypothermia is among the greatest threats in the early course of major burns, fluids should be warmed whenever possible.

Venous access

Early venous access with two or more 14- or 16-gauge IV lines should be obtained immediately. If this is not feasible, other options should be considered:

- Central veins
- Intraosseous (IO) access
- Surgical cutdown.

With new IO devices access is easily gained, even in adults, and crystalloid and colloid solutions can be rapidly infused. Caution should be exercised with hypertonic fluids, as soft tissue and bone necrosis can develop.

Physiological monitoring

Several types of monitoring should be carried out:

1. Basic hemodynamic monitoring: heart rate, blood pressure, and urinary output are fundamental in major burns. The goal of in-field resuscitation is a heart beat of <140/min, normal blood pressure, and urinary output of 0.5–1 mL/kg/h (1–1.5 mL/kg/h in children). After evacuation to a burn center, the input/output ratio should be calculated every hour to prevent ‘fluid creep.’

2. Frequent body temperature measurement.

3. Pulse oximetry if any signs of inhalation injury exist. Note that COHb and MetHb are not detected by pulse oximetry, and the measured values for oxygen saturation may be far too optimistic. For this reason, arterial blood gas tests should be performed as early as possible. If possible, 100% O2 should be supplied.

4. Invasive monitoring of unstable patients via arterial lines, SvO2, Picco, Cardio Q, etc. should begin as soon as possible to guide fluid resuscitation.

5. Capnography for intubated patients is desirable.


7. Laboratory tests, including, at minimum, blood cell count, platelets, coagulation, electrolytes, and basic renal parameters.

Devices for in-field monitoring are small and robust, having an extended battery capacity and a display exhibiting many digital data and curves that cover almost all important critical care parameters. In civilian hospitals they are used as transport monitors for critical care patients. The smallest monitors (e.g., the Philips Intellivue MMS X2) weigh no more than 1.2 kg.

Airway management

CO and cyanide intoxication, head and neck burns, circumferential third-degree burns of the thorax and abdomen, as well as inhalation injury can all rapidly endanger the lives of burn victims. Intubation is often the only way to secure airways and hence oxygenation and ventilation. Because burn edema increases over the first 24–48 hours, patients at risk are normally intubated early, sometimes even prophylactically. In burn disasters oxygen and ventilators are often scarce, increasing the importance of correctly identifying patients needing oxygen or intubation.

CO intoxication

CO has a 200 times higher affinity for hemoglobin than oxygen. It displaces O2 and shifts the oxygen–hemoglobin dissociation curve to the left, impairing tissue oxygenation. Early symptoms such as headache occur at COHb levels of 15–20%, followed by dizziness, confusion, and agitation. Having COHb levels >50–70% for a longer period is lethal. In this case, immediate O2 is mandatory, as it markedly reduces the half-life of COHb.
Inhalation injury and the decision to intubate

The heat-carrying capacity of air is low. Therefore, the main lesions affect the upper airways, except when steam is involved. Reflex closure of the glottis often protects the lower airways. Thus, damage in this region is mostly related to the toxic byproducts of fire.

Rapid laryngeal and epiglottal swelling can quickly cause hoarseness, heavy coughing, and inspiratory stridor. Because edema increases, these patients must be intubated immediately. The same applies to patients with extended burns to the face, neck, and thorax and showing any sign of respiratory or cerebral deterioration. Circumferential third-degree thoracic burns must be escharotomized as soon as possible, because of a rapid decrease in thoracic-wall compliance and a rapid increase in the effort needed for breathing.

Patients who have soot on the upper airway mucosa, inflammation of this region, coughing, milder forms of hoarseness, and bronchospasm, and who do not improve upon entering open air must be kept under close surveillance and treated with O₂ and humid air during the next 24–48 hours. Twelve to 24 hours post burn, the toxic byproducts of fire and released mediators can cause a delayed massive production of mucus and lung edema.

Other considerations

Patients with major burns are usually hypovolemic. General anesthesia (GA) is typically used if immediate surgery is necessary. In disasters with few fully equipped anesthesia workstations, relatively stable patients not having threatened airways or inhalation injuries and not requiring major surgery of the thorax or abdomen can be safely managed with ketamine, ketamine and midazolam, or ketamine and low-dose propofol. Ketamine preserves spontaneous ventilation, as airway reflexes remain mostly intact. The drug induces dissociative anesthesia and is a potent analgesic. Increasing central sympathetic tonus helps stabilize hemodynamics. It is a bronchodilator and increases mucus production. Therefore, it should eventually be combined with glycopyrrolate or atropine. It can also be combined with midazolam (0.03–0.15 mg/kg) or low-dose propofol (0.25–0.5 mg/kg) to avoid dysphoria and hallucinations. As a racemate, ketamine has a loading dose of 0.25–1 mg/kg (IV) or 0.5–2 mg/kg (IM) for analgesia; the anesthetic dose is 0.75–3 mg/kg (IV). S (+) ketamine, which has a weaker psychomimetic effect, can be administered at half the dose of the racemate. The effect of this compound lasts 5–15 minutes.

Acute surgery of wounds on upper and lower limbs as well as osteosynthesis of open fractures can be performed under peripheral single-shot regional anesthetic techniques if the region where the block must be performed is clean and not burned. The same can be done with smaller burns on extremities. Central neuraxial blockade is not recommended, as hypovolemic patients tend to develop severe hypotension due to the attendant sympathetic nerve blockade.

Major acute surgery is usually performed under GA with secure airways and controlled ventilation. Intubation may be difficult in patients with severe head and neck burns as well as with a swollen tongue and epiglottis. Preoxygenation is advisable. As a precaution, mandrins, a laryngeal mask, an intubation laryngeal mask, a Combitube, and a cricothyrotomy set should be at hand. Awake fiberoptic intubation is often not an option in disasters. Because of the aspiration risk of a full stomach, a rapid sequence intubation (RSI) with cricoid pressure should be performed.

Anesthesia drugs

Etomidate (0.15–0.2 mg/kg) and ketamine, eventually combined with midazolam or low-dose propofol, commonly serve as induction anesthetics because of their low hemodynamic interference. If only propofol or barbiturates are at hand, carefully titrating the doses is key. The reduced distribution volume and low cardiac output will require a lower dose and a considerably longer time before any effects can be seen.

Relaxation with succinylcholine (1–1.5 mg/kg) during the first 48 hours after trauma does not produce severe hyperkalemia. An onset of 60–90 seconds and a recovery index of 3–4 minutes make it a favorable drug for intubating difficult airways. The non-depolarizing relaxant with the shortest onset is rocuronium (0.5 mg/kg: 2–3 times the dose for RSI, time to effect is 1.5 minutes; recovery index is 15 minutes (much longer for higher doses)). The decreased responses to non-depolarizing relaxants do not occur during the first few days after trauma. Because of hypothermia and decreased hepatic and renal blood flow, clearance can be reduced. Relaxation monitoring (train-of-four test) is recommended.

Volatile anesthetics are usually applied with opioids in a balanced form of anesthesia, as they have significant cardiodepressant and vasodilating effects. Opioids such as morphine, fentanyl, sufentanyl, and remifentanil do not appreciably interfere with hemodynamics. As potent analgesics partly with different sedative qualities, they reduce the minimal alveolar concentration of volatile anesthetics.

Perioperative management and acute care of burn pain

In disasters, sophisticated perioperative diagnostics are not feasible. In accordance with resources and triage steps, a staged system of surveillance and monitoring must be instituted. Fluid resuscitation, as discussed above, is decisive in preparing a burn victim for surgery. Adequate burn pain management must be started.

The primary drugs used for partial-thickness burns are opioids. Major burns are treated with small repetitive IV doses of morphine (2–4 mg) or fentanyl (0.05–0.1 mg). Continuous infusion is preferable to administration of a bolus. Smaller burns can be treated with oral opioids, such as hydromorphone retard (4 mg twice daily) or oxycodone retard (10 mg twice a day or 20 mg/d), after mitigation of the strongest pain with IV drugs. Side effects of opioids are respiratory depression, nausea, bradycardia, muscle rigidity, constipation, histamine release, and bronchoconstriction (with morphine).

Children with difficult venous access can be treated with ketamine rectally (0.5–1.5 mg/kg). Ketamine (0.25–2 mg/kg IV) is often used, especially for procedural pains. Intramuscular application should be avoided.

A multimodal analgesic strategy with a combination of simple peripheral analgesics, such as acetaminophen,
metamizol, and NSAIDs, is helpful. In addition, because considerable psychological stress occurs, anxiolytic drugs such as benzodiazepines (e.g., midazolam, lorazepam) and stomach mucosa-protecting agents should be administered. Postoperative adverse effects, especially prolonged effects of anesthetics and relaxants, must be anticipated. Respiration, hemodynamics, urinary output, and temperature must be closely monitored. Hypothermia and blood loss must be prevented.

Oxygen

During disasters, \( O_2 \) requirements rise rapidly. Delivering small bottles of liquid \( O_2 \) is logistically difficult owing to constraints imposed by bottle weight, the space they occupy, and their need to be refilled. Even hospitals’ large bulk liquid oxygen systems may be damaged or inaccessible. In such cases, alternatives must be implemented as soon as possible. Portable bulk systems (1000–5000 L of liquid oxygen) or mobile cylinder banks are helpful, but often unavailable in disasters.

Two other options are portable and non-portable oxygen generators, often used in military field hospitals. If electrical power is present, oxygen generators can deliver oxygen with >93% purity. They can be connected to patients or ventilators. With a booster system to provide enough pressure, oxygen generators can be used to refill oxygen tanks. For work to proceed safely in the face of diminished resources, a sufficient supply should be organized, the right connections must exist between the systems, different systems should be rechecked during exercises, and actual oxygen needs should be evaluated to minimize wasted gas.\(^{100}\)

Anesthesia machines and ventilators

Anesthesia machines and ventilators in the field must have the following characteristics:

- Robust
- Lightweight
- Operate in extreme temperatures
- Suited to air service.

They should also meet the following criteria:

- Need as little fuel for power as possible
- Be ready for use quickly
- Be easy to use
- Require little maintenance
- Have an extended battery capacity
- Be able to ventilate in modern ventilation modes

Anesthesia machines

Forward surgical teams from the US and British Armies use drawover anesthesia systems:

- Ohmeda Universal Portable Anesthesia Complete (PAC) or TriService Anesthesia Apparatus (TAA; Penton Ltd, UK)
  - The main advantage is the low weight (5 lbs or 2.3 kg).

- Air and oxygen are drawn through vaporizer by negative pressure generated by the patient’s inspiration.
- Airflow in the vaporizer is guided by a rotary (PAC) or sliding (TAA) valve.
- For ventilation in a controlled mode, a combination of the Impact 754 Eagle ventilator and the PAC system is used in the field.\(^{101}\)

Anesthesia machines with controlled ventilation modes for field use (mostly military) include the following:

- Ohmeda (FAM) Model 885A
  - Portable-circuit system
  - Weighs 55 lb (25 kg)
  - Powered by bottled \( O_2 \)
  - Has a multiagent vaporizer with a Vernitrol anesthetic flow calculator
  - Has no modern ventilation modes

- Draeger Narkomed M
  - Weighs 103 lbs. (47 kg)
  - Variable-bypass vaporizer
  - Limited by high oxygen consumption.

The biggest disadvantage of the drawover systems and FAM 885A is their failure to meet ASA safety standards. Therefore, training with the devices in ordinary or military hospitals is difficult and possible only with connection to the safety and monitoring systems of standard anesthesia machines.

Another drawback is that single-agent temperature- and pressure-compensated vaporizers are generally used today. Therefore, anesthesia providers do not have experience with Vernitrol-type vaporizers. Future systems must be widely used in civilian hospitals and properly adapted to field use. The main advantage will be that anesthesia personnel will already be familiar with the features of the device, such as displays, alarms, and service. Getting acquainted with a device only in a disaster is useless and dangerous.

An example of this new generation of anesthesia machine, which is now used in the US and by several European armies, is described below:

- Draeger Fabius Tiro M
  - Electrically powered (no gas for power)
  - Weighs 198 lb (90 kg), including the container
  - >45 min on battery, including the monitor
  - All necessary safety systems and alarms
  - Many critical-care ventilation modes
  - Can be connected to an oxygen generator.

Critical care transport ventilators and ICU ventilators

During disasters a discrepancy may exist between the number of available ICU ventilators and the number of severely injured patients who cannot be ventilated with simple rescue service transport ventilators. High-end critical care transport ventilators, which are mainly used for intraclinical critical care transport, are lightweight and easily moved to the triage areas and frontline hospitals. They have battery capacities of 4–6 hours and can be used both independently and connected to a central gas system. They can be used not only for transport, but also as temporary substitutes for missing ICU-ventilator capacity, if necessary.
• Transport ventilators, such as the Uni-Vent Impact 754 Eagle, Draeger Oxylog 3000, and Weinmann Medumat Transport System
  ■ Weigh 10–13 lb (4.5–6 kg)
  ■ Adequate monitoring of respiratory digital data and curves
  ■ Adequate safety systems and alarms
  ■ Easily connected with transport units, such as LSTAT and Mobi Doc system
  ■ Offer most of the new ventilation modes.

Providing this extended level of anesthesia and ventilator care requires high-level logistics and organization. In developed countries this should eventually be achievable in most disasters. It will be much harder in countries where resources and infrastructure are insufficient even without a disaster. In this case, only rapid, structured outside help through federal, military, or international rescue organizations can mitigate the crisis.

Blood transfusion

Transfusion’s role in burn disasters

Adequate blood products are important for primary and sustained life support. Few publications have described the responsiveness and efficacy of transfusion services in catastrophes and disasters. Blood supply has been mentioned as being scarce in the first and prolonged phases of disaster mitigation. However, the 9/11 terror experience showed that an uncoordinated surge in blood donation may generate an unusual drop in patient supply several weeks later. Managing blood in disasters and catastrophes is tricky, and may be complicated by public pressure and poor communication.

Transfusion in burns

Blood loss may occur in combined injuries, but also in severe burn injuries involving large TBSAs. Full-thickness burns may cause blood loss that is correlated with TBSA. A TBSA >10% acutely lowers erythrocytes because of thermic hemolysis and microthrombosis. Concomitant CO poisoning may further reduce the remaining oxygen transport capacity of erythrocytes. The loss of red cell volume and oxygen transport capacity cannot be estimated correctly in these circumstances (CO intoxication, thermic hemolysis, and microthrombosis), and fluid resuscitation can obscure the available red cell mass. Sufficient oxygen delivery to peripheral tissue is important for hypermetabolic patients who may need surgery (e.g., escharotomies) and repeated dressings. Platelets may be required in the acute phase and subsequent treatment. Correct transfusions of leukocyte-reduced blood products are a prerequisite in managing transfusions in burns.

Organization of blood transfusion services

Modern transfusion medicine has silently changed its organizational background in recent years without being noticed by the public and other medical personnel. Blood centers serve specific areas and are run by the Red Cross, national authorities, foundations, and non-profit organizations. They organize blood donations, process blood products, test the donations, and manage distribution to hospital blood banks. Standardization of blood products, tight regulation by health authorities, general donor shortages, and economic struggles have led to a higher turnover of products and an optimization of inventories. Cost-cutting has prevailed in nearly all developed countries, leading to the shutdown of several blood centers and the establishment of large, centralized facilities housing production, testing, and IT services. This actually increases the total processing time. In some countries, testing and IT are centralized to one national site or even outsourced internationally. This may pose a threat to the healthcare system if a facility shuts down or otherwise malfunctions.

Blood centers may collect, process, and test blood; however, they generally distribute blood products and provide additional services (e.g., platelet apheresis) to hospital blood banks, which are responsible for the immunohematologic and clinical services. Disaster management and mitigation plans may exist in well-managed regional and national blood services but are mostly focused on anticipated threats such as pandemics (e.g., H1N1 influenza) and on the disintegregation of vital core facilities (e.g., IT services, nucleic acid testing laboratories). Burn disasters are often absent from these plans. Blood centers are rarely consulted by emergency systems or hospitals, nor are they integrated into hospitals’ communication pathways and disaster plans.

What happens at blood centers in burn disasters?

Hospital blood banks possess a certain inventory, usually no more than the amount of blood products needed for 2–3 normal days, including additional units for major trauma. Burn disasters immediately deplete the available stocks and lead to urgent requests to the local blood center. Triaging mass casualties, especially in burn disasters, results in the dissemination of patients to different trauma centers, so that multiple hospital blood banks are involved. High-volume and high-priority requests concentrate in a spiraling sequence on one blood center, which is greatly strained to coordinate the distribution to its hospital blood banks.

Supplies are usually sufficient to meet the urgent first requests, but many blood centers hold only enough blood products to meet the regular demand of 1 week or less. Burn disasters are characterized by the urgent need for platelet products and erythrocyte concentrates in the early phase. A blood center’s stocks may be depleted within hours – platelets first, and then erythrocyte concentrates. Plasma products are sufficiently available, even in bigger disasters.

Because it takes at least 24 hours and as long as 3 days after a donation to produce blood products, a quick start to regain the required amount of blood products may go awry in an already strained blood center. Deliveries from other blood centers and national coordination may be a big help in mitigating the center’s own insufficiency.

More often, a blood center acts without information about the disaster and the estimated need for blood products. Communication between emergency services and blood centers is rare, and hospitals have no coordinated system to inform the blood center.
More serious is the effect of mass media on blood donation. Blood donation is very well known among the media and the public, and blood services often use the media to boost donations. The media focus early attention on blood centers and provoke the public’s urgent desire to help. Blood donation is the commonest way to ease tension if the public feels powerless about the disaster’s cause and/or effect. This is most pronounced after acts of terror, when blood centers are confronted with a mass of potential donors and sometimes do not need that much blood. They may be quickly overwhelmed when faced with such a surge of potential donors.

**Strategies**

During mass casualties, strategies in early burn treatment differ mainly in the degree of treatment before admission to a burn center and in the initial goal of transport. Strategies can differ by country, depending on the resources available.

**Medical outposts as extended treatment areas**

Usually, the first place to assemble burn victims is an in-field collection or treatment point. Keeping burn victims at this site until the definitive place of treatment is known is impossible, because the number and severity of injuries will not be known during the first hours and resources will be insufficient. Longer stay in advanced medical outposts or collection points is also linked to greater hypothermia.

**BSTs and BATs at the scene**

In some mass casualty plans, triage and primary care in the field are supported by BATs or BSTs. Reports of different events show that triage in the field usually starts late and that many victims arrive at hospitals long before actions at the incident site have become structured. Therefore, BAT teams must be on standby for deployment within minutes, and information about the incident must be instant and exact. Even when deployed very early, BATs usually are too late, at least for those victims who have already been transported.

**Burn center criteria for mass casualties**

Individual medicine criteria for admitting patients to burn centers are rather extensive. The German-Speaking Association for Burn Treatment and the European Burns Association have guidelines stating that burns in functionally and/or aesthetically important areas should be treated in burn centers regardless of degree and extent. According to ABA, all third-degree burns should be treated in burn centers. Compliance with these guidelines is not possible during mass casualties and disasters. The available burn beds must be filled by victims who will get the maximum advantage from burn center treatment.

**Primary transfer to burn centers**

Patients should be transported to the best place for the best treatment available. These are normally burn centers. However, at the time of a mass casualty the number of victims is unclear, as is the number of beds available in burn centers. Although a surge capacity is defined, it still allows a burn center to distribute patients to other burn centers. However, a challenge remains: can the distributing center prepare patients in time?

Such situations call for resource-rich jurisdictions, with many burn centers, many burn beds, and many staff. The actual availability of burn beds varies between states. One can usually assume that burn beds are in short supply and high demand. Whatever the advantages of this approach to safety and sufficient primary care and stabilization, they are lost when the number of victims is so high that quality standards cannot be maintained. Burn centers must first treat many patients with less severe burns, thereby tying up staff who are needed for the severely burned. In special cases, combination injuries (e.g., mechanical injuries) are to be expected and may necessitate transfer to a trauma unit. BATs and BSTs can back up local teams to improve capacities. If the influx greatly exceeds surge capacity, the ability to triage and stabilize patients according to ABA criteria will depend on the recruitable staff. Even in the US, many burn centers have fewer than 15 beds and even fewer ICU beds. Not even the full staff of small centers can treat 30 or 40 severely burned patients, perform secondary triage according to ABA policy, and prepare them for transport in time.

Until this triage occurs, the patients must be kept in a suitable environment. The feasibility of this policy in smaller burn centers has yet to be demonstrated. Surge capacity is important because it is a number that must be considered in planning. The ABA definition – 50% more than the usual capacity – gives each center a planning dimension, which must be funded before it can be realized.

Transferring patients elsewhere can be reasonable even for burn centers, because surge capacity cannot be maintained for long. Medical vanity should never be a reason to avoid transferring patients elsewhere. Burn centers are usually not empty, and their size is adapted to normal needs. Transferring patients whose treatment has already begun from a burn center to a hospital’s non-burn units gives the impression that no burn center was needed, or provokes fears that the ensuing treatment in other units will be insufficient. Workload above the normal capacity causes complications, including hygienic problems within the unit, endangering patients and increasing costs.

**Primary treatment in trauma centers without burn units**

Trauma centers will always be part of disaster responses, and as victims go to the nearest hospitals by themselves these trauma centers will be part of the response. Trauma centers, being much more numerous than burn centers, can more easily cope with primary treatment for an unknown number of casualties.

Although primary care for burns is part of ATLS procedure, many emergency doctors, trauma surgeons, and other medical personnel throughout the world do not seem to be experienced in the primary treatment of burns. This is true even in military organizations. Therefore, trauma centers without burn units need support from experts and seem to be the place where BSTs and BATs can be most effective.
BSTs and BATs act as experts and can provide support to other surgeons. Because they are not busy with details, but with directing treatment for many others, they can use the trauma center’s surgical and staff resources to improve results. They can also help determine the extent and severity of burns for central data collection, and for distribution to burn centers or other hospitals as well as guarantee adequate primary care.

**Referring the most severely burned patients to burn centers first**

Referring only the most severely burned patients to burn centers first is of little use, as demonstrated in the case of Pope Army Air Field, where many futile patients diverted the center’s resources. Burn beds are scarce and must be reserved for victims with the best chance of survival. ABA has published a benefit–resource ratio table to optimize triage to burn centers. To enable the optimum distribution of patients to burn centers, one must know the number and qualities of beds available, as well as the number and severity of patients needing burn beds. Because this number is not known in the first hours of an incident, the distribution to burn centers cannot properly be planned during this time.

**Primary distribution to local primary responder hospitals**

BATs or BSTs provide support to primary responder hospitals, guiding resuscitation and primary care as well as delivering data for centrally directed casualty distribution, after considering the number of burn beds available nationally and internationally. Transport to the definitive place of care is organized from the *primary responder hospitals*. BATs or BSTs are necessary for this strategy to work well. Telemedicine might help in this process.

**Tiered response**

A tiered response is crucial for an effective response during a burn disaster. In ABA plans, this is a national response directed by intrastate and interstate cooperation of burn centers with military assistance under Department of Homeland Security governance. In other countries, especially in Europe, where there are many small countries without the resources, the tiered response can necessitate international cooperation. This strategy requires advance preparation so that certain basic information is clear. Problems will arise without international agreements for such cooperation, without knowledge of international burn bed availability, and in funding treatment in another country without knowledge of patients’ insurance status.

**Allocating and distributing more burn patients**

This strategy is important to avoid overwhelming single burn units and treating patients in relatively understaffed units. High-capacity utilization in burn units increases difficulties through intensive resource use.

Cross-infections can be expected to increase, and patients’ safety will easily be negatively affected. With these infections, stays in ICUs and burn centers are prolonged, mortality rises, and costs increase. When patients from countries with multiresistant bacteria are taken to a burn center, this can be the beginning of a long-lived fight against such infections. Although the increased number of nurses and other medical specialists can usually be sustained over a longer period by adding new resources, this cannot be done with burn specialists. Their number is limited, and no center has too many. Therefore, after some weeks, burnout is to be expected in those working additional shifts without respite. Distributing burn victims among more centers to avoid danger both to patients and staff would be more effective. This distribution can take place only when clear regulations exist for compensating costs, regulations regarding the uninsured, and a humanitarian understanding of this procedure.

**Burn bed availability**

The US has 1825 burn beds. A national electronic registry of availability is in development. In Europe, burn beds, especially in small countries, are very few, so that international cooperation is necessary. Few data exist on the real availability of burn beds in the case of a disaster. Germany has the highest ratio of burn beds to population. In the Enschede fireworks explosion, Germany could offer 19 burn ICU beds, out of 127 for adults and 15 for children. National burn bed bureaus exist in Germany and the UK, and there are networking facilities for cooperation (e.g., the Mediterranean Burns Club).

The European Union has a ‘Community Mechanism for Civil Protection,’ which regulates disaster support among states both in and outside the Union. This covers sending disaster relief staff to countries with disasters, but does not address transferring victims to other countries. There are exchange treaties between some countries, and there is actual cross-border hospitals cooperation. However, there is no general regulation of these processes.
Burn bed registries are necessary for quickly ascertaining how many patients can be treated in an area. These registries should include the different burn bed types, whether they are intensive care beds with or without the ability to warm patients, and whether there are non-ICU beds. Asking each individual center how many beds are free for use during an incident is too time-consuming: an online system is preferable.

Humanitarian crisis

A humanitarian crisis is an event or series of events causing critical threats to health, safety, or human wellbeing, usually over a wide area. For burn injuries, armed conflicts and natural disasters are the likeliest forms. Natural disasters can not only be directly linked to fire (as in wildfires), but can also cause burn injuries through atypical use of energy. For example, burn incidence rises when people are not accustomed to open fire but need it because their electricity source has failed. The same happens when people try to obtain electricity by throwing wires over power lines. After a severe storm, the increased use of emergency internal combustion generators and internal combustion power saws increases burn injuries and burns related to fire accelerators.

In disasters and humanitarian crises, burn and other medical treatment can often begin only after minimal infrastructure and order have been established. Medical work can be dangerous where there is looting or political or religious rivalry. Therefore, cooperation with security forces, at least until the early stages, can be necessary. Minimum requirements for work are shelter, safe water, food, and electricity. One of the basic problems in medical aid work during disasters and in low-resource countries is sterility. That is, there is usually a high rate of infections with hepatitis and HIV, which must not be spread.

Burns can be categorized into the following three main types:

- **Those that can be treated with minimal efforts** (e.g., by clean dressings and available analgesics).
- **Those that are not survivable without specialized care**. Special care must be established, and success will depend on the degree of medical care given.
- **Those that cannot be treated successfully in this environment**. Patients must be transported to facilities where successful treatment can be performed and is funded. Otherwise, these patients are deemed futile, and ‘comfort care’ must be provided.

Preparing medical systems for burn treatment can be aided by history, which provides an overview of prognosis combined with special measures. At the end of World War II, only 50% of patients survived >40% TBSA. After treatment for shock was initiated, topical antibacterial treatment with silver-containing products reduced the mortality rate. Early excision and feeding lowered it further. Early tangential excision, introduced by Janžeković, was the next step in reducing mortality. Thus, success depends on the degree of logistics and the infrastructure that can be built up to allow the use of special techniques. The feasibility of safe blood support and wound technologies (e.g., use of cadaver skin as a temporary skin substitute) also influences the prognosis. Problems with certain treatment methods may arise because of religion (e.g., use of pig skin or frog skin). Knowledge of and adaptation to local cultural habits is often necessary for success.

**Armed conflict**

Armed conflict falls into two main categories:

- **Conflicts between militaries**
- **Asymmetric conflict**, in which a severe disparity of power and strategies exists between opponents (e.g., an army against terrorists).

The rate of burn injuries in armed conflicts depends on the technical standard of the arms. The number of burn-related deaths has remained fairly constant since World War I until the 1991 Gulf War. The use of tanks, battleships, aircraft, and armored vehicles increases burn casualties. In the 1973 Arab–Israeli War, which involved many tanks, 70% of tank casualties included burns. Burn injuries range from 10% to 30% of all casualties. Combination injuries (e.g., blast injuries with burns) are frequent.

**Treatment in the field**

Field treatment occurs under different conditions, so that evacuation times vary greatly. Early shock treatment is the most important parameter for survival. A patient with massive burn injuries who does not undergo resuscitation until more than 4 hours after injury has almost no chance of survival. The necessity of starting sufficient resuscitation is countered by the logistical problem of carrying great amounts of fluids during battle.

Care under fire is usually buddy aid or given by a combat lifesaver. Burning must be stopped, and resuscitation must begin. In the conscious patient, oral rehydration fluid can be self-administered or given by the buddy or combat lifesaver. The unconscious patient should be moved to a safe location as soon as the tactical situation permits.

In the second step, **tactical field care**, IV access is gained and resuscitation with RL is begun. Otherwise, hypertonic resuscitation and/or oral fluids should be considered. The initial fluid requirement can be reduced by 80% by an initial 30-minute infusion of 4 mL/kg hypertonic saline–dextran and then of RL to maintain urine output. A rebound should be expected after 6–8 hours. Too rapid an infusion for 2 minutes causes hyperosmolarity and hypernatremia, with possible cardiac arrhythmia.

Thomas suggests starting resuscitation with IV administration of 250 mL hypertonic saline solution and continuing with ORS as an oral bolus of 4 mL/kg every 20 minutes to maintain a good gastric emptying rate and to satisfy fluid requirements. ABA suggests the same where IV therapy is logistically impossible.

New technical equipment allows easy IO application, which can provide large amounts of fluid. For hypertonic saline solutions IO seems unsuitable, as soft tissue and bone necrosis have been observed after some days.

**Education, awareness, and preparedness**

Recent burn disasters have raised the degree of alertness worldwide for mass burn injuries. Ongoing wars and
terrorist attacks, along with several indoor fires, have shown that preparedness for such events is necessary. No-one is immune to such risks. The question is not whether such disasters will occur, but when they will occur and how we can cope.

Preparedness requires plans. It also requires staff, stuff, and structure (the three ’S’s). Plans include international disaster plans, national disaster plans, coordinated disaster plans at state level, and local disaster plans for locales and institutions. Structure is the national or international health system. Stuff is emergency supplies ready for disasters. Staff is medical, paramedical, rescue, and technical relief organizations. Legal preconditions must be established on the basis of these plans, and resources must be planned and funded. Both planning and execution require money, which is an investment in a society’s future and security.

Burn societies can aid this procedure, as ABA does, as they comprise experts in these fields. Planning without the experts in burn treatment is futile. However, on their own, burn experts rarely make sufficient plans for mass casualties, which is not usually part of their expertise. Military organizations can serve as examples, with their participation in war operations and their routine drills. Disaster drills for hospitals and rescue organizations must be realistically performed.

Education in burn treatment (e.g., ABLS, EMSB) is essential for coping effectively with mass casualties – not only for medical staff but also for hospital administrations, who must provide sufficient support. Burn surgeons are rare in burn disasters, and surgeons are not the only personnel to be trained. Escharotomy must be taught, training must occur, and this training must be repeated if preparedness is to be maintained.

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Further reading

References


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Care of outpatient burns
C. Edward Hartford

Introduction

During the past four decades there has been a remarkable improvement in the outcome of burn injuries and a progressive decline in its incidence. In the United States, this process began with the development of specialized burn treatment units, the first at the Medical College of Virginia, now the Virginia Commonwealth University Medical Center, and then at the US Army Institute of Surgical Research, Brooke Army Medical Center, San Antonio, Texas, both in 1947. There are now 125 units/centers in the USA. The improvement in outcome in the treatment of burn patients accelerated following the formation of the American Burn Association in 1967. According to the American Burn Association’s 2007 Fact Sheet, using information derived from a variety of sources, each year, in the USA, there are now approximately 500,000 individuals who sustain a burn injury requiring treatment from healthcare professionals.2 The annual incidence of burn victims has declined from an estimated 1 million each year during the 1960s. Fagenholz and colleagues documented a decrease in the incidence of visits to Emergency Departments for burns during the period 1993–2007.1 Currently, among those who sustain a burn, approximately 40,000 are admitted to hospitals for their care and there are approximately 4000 fire- and burn-related deaths each year. Therefore, thermal trauma typically results in an injury of low mortality in which the majority of care can be safely rendered in an ambulatory setting.

The outcome of burns treated in the outpatient setting is usually good. If, however, care is suboptimal, protracted morbidity or compromised function can result. The goals of therapy are to minimize pain and the risk of infection, achieve timely wound healing, preserve physical function, minimize cosmetic deformity, and affect physical and psychosocial rehabilitation in the most expeditious manner.

Who can be managed as an outpatient?

When a patient with a burn is first evaluated, information is immediately available from which an accurate prognosis can be derived. For instance, a valuable easily remembered estimate of the probability of death from burn injury was published in 1998.4 Using stepwise logistic regression analysis of 1665 patients, the authors identified three risk factors for death: age greater than 60 years, burns on more than 40% of the total body surface area (TBSA); and, the presence of inhalation injury. The mortality prediction for the presence of none of these risk factors is 0.3%; for the presence of one risk factor it is 3%; for two it is 33%; and, for all three it is approximately 90% (actual, 87%).

In addition to these risk factors, there are other factors – and a huge dose of common sense – which help determine the initial treatment venue. These include depth of the burn; premorbid diseases; and, co-morbid factors such as associated trauma, distribution of the burn, and injuring agent. When outpatient care is an option the patient’s social situation needs to be assessed. In some instances, it may be prudent to initiate care in a hospital so that potential complicating medical problems can be sorted out or the possibility of non-accidental trauma can be excluded.

Age

Patients between 5 and 20 years of age have the most favorable survival outcome from burns. The LA50 (percentage of total body surface area at which 50% of the patients live and 50% die) for this age cohort is 94.5% TBSA of burn. Younger individuals, especially infants, have an increase in morbidity as well as mortality from burn injury. In this age group, child abuse or neglect must be included in the psychosocial analysis.5 The peak incidence of non-accidental burn injury is 13–24 months of age.6 Burns that are particularly suspicious are those whose appearance suggests an injury from a cigarette, hot iron, or immersion in hot water. The latter injury is identified by a stocking/glove distribution of the burn and a sharp linear demarcation between the burned and unburned skin (Fig. 6.1). Scalding which has occurred in an institution or in the presence of a caregiver other than one who has a biological relationship to the victim should also heighten one’s suspicion. Even with trivial injury, if the burn was sustained under suspicious circumstances or the history does not correspond with the nature or distribution of the burn, the patient should be admitted to a hospital for their protection. Cases of suspected abuse, neglect or bad parenting must be referred to the appropriate social services agency.

The author has become aware that in some instances being investigated for non-accidental trauma, the actual cause was from bad parenting and not done with malicious intent.
A helpful adjunct in estimating the area of burn is to use the surface area of the patient’s hand. This area, which approximates 1% of the TBSA, includes the palm together with the fingers and thumb extended and adducted.

Any burned patient who requires intravenous fluid resuscitation should be admitted to a hospital. This includes adults and older children with burns in excess of 15% of the body surface area, as well as younger children (under 5 years of age) and infants with burns in excess of 10% of the body surface area. In some instances, due to premorbid dehydration caused by physical activity, an arid or semi-arid climate, alcohol, or diuretics, some patients with smaller burns may need supplemental intravenous fluids for optimal care. In the author’s practice, patients with small area burns that need intravenous fluid are often held for several hours or overnight in an observation area in the Emergency Department until their pain is controlled and fluid needs are met. Then care can often be continued as an outpatient.

Depth of the burn

The deeper the burn the worse is the prognosis. However, depth of small-area burns is less important in determining the need to initiate care in a hospital than the extent of the burn.

When a burn is first evaluated it is often difficult to determine its depth. The superficial injury of sunburn or its equivalent is easy to identify. Likewise, it is easy to discern a waxen, dry, inelastic, insensate, cadaveric-appearing wound as a full-thickness burn. However, it is difficult to distinguish the subtle differences between a superficial partial-thickness burn, which will heal spontaneously within 3 weeks, and a deeper partial-thickness burn that will take longer to heal. This is especially true for weeping wounds in which the blisters have ruptured. Initially, these wounds appear superficial and are perfused. However, with time, as the injured small blood vessels in the wound thrombose, the wound takes on an ischemic, cadaveric appearance of a deeper injury. This change does not reflect invasive infection but merely the natural evolution of the wound.

Premorbid diseases

Preexisting medical conditions often have a profound influence on the clinical course and outcome of a burn injury. While any medical disorder may have an adverse effect, there are a number of conditions that occur frequently among the burned and which may play a significant role in causation or outcome. For instance, any condition or habit that alters an individual’s mental state may lead to a burn injury. These include seizure disorders, senility, and psychiatric illnesses as well as the use of sedatives, controlled substances, illegal and recreational drugs, and alcohol. These usually obligate hospital admission. Medical conditions that are known to enhance morbidity of patients with burns include renal failure, congestive heart failure, cardiac dysrhythmias, hypertension, chronic obstructive pulmonary disease, diabetes mellitus, sequelae of alcoholism, morbid obesity, conditions which require the use of steroids, and other diseases which compromise the immune system. The clinical status of any of these disorders must be determined and their potential

However, when investigated, for a variety of reasons, e.g. immigration status, prior felony conviction, previous report to or concern of the local county authorities, the individual lied about the details of how the injury occurred. In a more unusual instance, a third person tries to protect the perpetrator, e.g. a mother protecting her daughter, when the daughter was the perpetrator of the injury to a child. Any patient over the age of 70 years with burns is in danger of dying regardless of the extent of the burn. The LA50 for this age group is 29.5% TBSA of burn. Therefore, admitting the older patient to a hospital to assess their response to the injury can prove invaluable before treatment is continued as an outpatient.

Extent of the burn

The larger the percent of body surface area involved by the burn, the worse the prognosis. The percent of the body surface area can be roughly estimated by using the ‘rule of nines’ or more accurately by the technique of Lund and Browder (Table 6.1). A helpful adjunct in estimating the area of burn is to use the surface area of the patient’s hand. This area, which approximates 1% of the TBSA, includes the palm together with the fingers and thumb extended and adducted.

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Distribution of the burn

The location of the burn may have a profound effect on the patient's activities of daily living, and dictate the setting in which the patient receives care. For instance, the edema from a small-area superficial burn of the face may result in swelling of the eyelids, hampering the patient's vision (Fig. 6.2), or burns that involve the lips or the oral cavity may inhibit efficient oral alimentation. Likewise, burns of the hands, feet, or those involving the perineum or adjacent areas may severely limit an individual's autonomy. While burns in these areas may not necessarily demand care in a hospital, there must be consideration of the assistance available to the patient when contemplating outpatient ambulatory care.

Because of fluid flux into the tissues beneath a burn, patients with circumferential burns of an extremity are at risk of ischemia of underlying and distal tissues from increased tissue pressure.18 Except for those with very superficial burns all patients with circumferential burns of an extremity should be monitored for evidence of elevated tissue pressure. Since the clinical signs of compartment syndrome and ischemia in a burned extremity are unreliable,19 the author advocates measuring the tissue pressure by a direct method and uses the Stryker® Intracompartment Pressure Monitoring System. A tissue pressure above 40 mmHg

Table 6.1 Burn estimate – age versus area

<table>
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<tr>
<th>Area</th>
<th>Birth–1 year</th>
<th>1–4 years</th>
<th>5–9 years</th>
<th>10–14 years</th>
<th>15 years</th>
<th>Adult</th>
<th>2°</th>
<th>3°</th>
<th>TBSA%</th>
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<tr>
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<tr>
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<tr>
<td>L. foot</td>
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Influence on the outcome assessed before determining whether the patient can be safely managed as an outpatient.

Co-morbid disorders

Respiratory complications

Inhalation injury and carbon monoxide poisoning substantially magnify the burned patient's risk and may occur even with no or trivial cutaneous injury.15,16 In addition, upper airway obstruction can be caused by the edema produced from burns of the oropharynx or the flux of fluid into the soft tissues of the upper airway resulting from deep burns of the face and/or neck. The full-blown adverse sequelae of these complications may not be immediately apparent.17 Therefore, if the history of the accident or distribution of burns suggests any of these three complications, a period of monitored observation is warranted. Overnight observation is usually sufficient.

Associated trauma

Burns frequently occur with other forms of trauma. If the burn involves only a small area of the body, the associated trauma will dictate whether a patient needs to be admitted to a hospital.
is the indication for surgical decompression of the injured limb. Alternatively, a Doppler ultrasonic flow meter can be used to assess the circulatory status of the extremity. A muffled first arterial sound and/or the absence of the second arterial sound is regarded as sufficient evidence of pathological elevation of the tissue pressure.

Burns across joints do not, for that reason alone, require admission to a hospital.

**Injuring agent**

**Electricity**

Patients exposed to low-voltage electricity, arbitrarily defined as less than 1000 volts (the most frequent source being household currents of 110 or 220 volts), are in danger of dying at the accident scene from a cardiac dysrhythmia, usually ventricular fibrillation. Following low-voltage electrical exposure, the most frequent residual electrocardiographic abnormality is a non-specific change in the ST-T wave segment and the most troublesome dysrhythmias are among the atrial fibrillation-flutter group. If the electrocardiogram is normal or becomes normal during observation, the chances of a subsequent dysrhythmia or cardiac arrest are virtually nil.

The tissue damage from low levels of electrical energy is usually small and most patients do not need to be admitted to a hospital. Occasionally, however, the damage to a child’s lip, tongue, gums, and dentition from sucking on a defective energized electrical cord may preclude efficient oral alimentation. In this circumstance, hospital admission to establish satisfactory oral intake is probably wise. With an electrical burn of the lip, the injury is often deep enough to cause necrosis of the superior or inferior labial artery. The injured artery is prone to rupture between the fourth and seventh post-burn day. Therefore, the patient or caregiver must be warned of this possibility and instructed on the first aid measures for hemorrhage control.

Patients who sustain tissue damage from contact with high-voltage electricity generally require admission.

**Chemicals**

Although chemicals cause tissue damage by chemical reactions and not from heat, by tradition, the care of those injured by chemicals is by burn surgeons. Brushing off dry chemicals or copious lavage with water of wet chemicals is the appropriate emergency treatment. No one knows how long lavage should be continued, but up to 1 h has been recommended. One guide is the presence of pain. The supposition is that, as long as there is pain, the chemical remains active and continues to cause damage.

In some instances, there are specific antidotes for the pain caused by a chemical. For example, with hydrofluoric acid, the injured tissues should be injected with calcium gluconate. Hydrofluoric acid also serves as a good example of the many chemicals that are absorbed into the body with the potential to cause organ injury. Exposure of concentrated hydrofluoric acid to as little as 3% of the body surface area can result in a fatal dysrhythmia from hypocalcemia caused by the binding of calcium by the absorbed fluoride ion. Since it is impossible to remember the systemic sequelae of all the chemicals to which an individual might be exposed, the physician should identify the chemical and seek information from the local poison control center.

After emergency local wound care, the treatment of the residual wound from a chemical is the same as the treatment for any wound.

**Social circumstances**

Patients whose injuries may be non-accidental need to be admitted to a hospital for their protection.

Before a patient is discharged from emergency care, the physician should ascertain that there are satisfactory resources available for supervision and care, and a way in which the patient can readily access medical care. Therefore, the distance the patient lives from care needs to be taken into consideration. For outpatients a visiting nurse can be invaluable in providing wound care and monitoring for wound complications, as well as assessing the patient’s physical progress and social situation.

**Treatment**

**Cooling the burn**

The first objective in burn wound care is to dissipate the heat. As long as the temperature in the tissues is above 44 °C, injury continues. The first step is to remove the source of heat. Both clinical and experimental evidence indicate a beneficial effect from immediate active cooling of the wound to dissipate heat. Cool tap water or saline at about 8 °C (46.4 °F) applied in any practical manner (e.g. compress, lavage, or immersion) is as effective as any other product or method. Colder substances, such as ice, may be detrimental. The period of time that is required for active cooling is brief. Typically, by the time most patients present for care, the tissues have cooled spontaneously.

Active cooling also has several potential advantages beyond dissipation of heat. First, cooling stabilizes skin mast cells, decreasing histamine release and, thereby, decreasing edema of the wound. Second, in the first several hours after the
injury, cooling is an effective way of controlling the pain of partial-thickness burns. In cooling for pain control, cool, but not ice-cold, moist compresses are applied to the painful wound. This method is applicable in the management of virtually all patients whose wounds can be safely cared for in an ambulatory setting. Because of the limited surface area of burn among most of those patients treated as outpatients, the detrimental systemic effects of active cooling, e.g. hypothermia from accelerated heat loss, should not occur. However, since water conducts heat 23 times faster than air, it makes good sense to monitor the patient’s core temperature during active cooling of the wound. A limit to the surface area that is cooled is arbitrary, but a practical limit is about 10% of the TBSA.

**Pain control**

Burn wounds are painful. The most severe pain occurs with partial-thickness wounds devoid of epidermis. Initially it is intense and can prove to be unbearable. The pain spontaneously moderates after several hours but intensifies when wounds are manipulated during dressing changes, wound care, and physical activity. While eschar-covered burns may be insensate, when the eschar separates spontaneously or is removed, the exposed viable tissues are painful when cut into, cauterized, or manipulated.

Narcotics are typically used as first-line treatment. In the emergency setting, small incremental doses of morphine can be given intravenously and titrated to effect. Subsequently, acetaminophen with codeine or oxycodone or similar analgesics, alone or in combination, are usually effective. Provided alteration of platelet function is not a concern, nonsteroidal anti-inflammatory drugs (NSAIDs) can be used. Analgesics can be supplemented with short-acting benzodiazepines, such as midazolam, to enhance sedation and provide anxiolysis. Most patients will require supplemental analgesics for wound dressing changes, physical therapy, and sleep.

Clearance of these classes of drugs is accelerated among those who regularly abuse alcohol or controlled substances. Therefore, remarkable amounts of analgesics and sedatives may be required.

If a patient’s pain cannot be controlled by oral medication, the patient may need to be admitted to a hospital. In the hospital setting, effective pain control can usually be obtained by the patient-controlled analgesia method. Even with patient-controlled analgesia, supplemental analgesia and sedation will often be required when wound dressings are changed.

Topically applied or injected local anesthetics are not recommended in the management of burns.

**Local burn wound care**

Loose, devitalized tissue is gently trimmed away, a practice known as épluchage. This process should not cause pain or bleeding.

**Blisters**

Recommendations for the management of blisters are varied and range from leaving blisters intact, to removing the blistered skin immediately, or delaying removal. Those who advocate removal of blistered skin cite laboratory studies that show that the blister fluid exhibits several potentially detrimental effects. Immune function is depressed by impairment of polymorphonuclear leukocytes and lymphocytes. Blister fluid adversely affects neutrophil chemotaxis, opsonization, and intracellular killing. Inflammation is enhanced by the presence of metabolites of arachidonic acid in the blister fluid. A plasmin inhibitor in the blister fluid decreases vascular patency. Finally, blister fluid may provide a medium for the growth of bacteria. Based on these considerations, the case can be made that blistered skin should be removed to facilitate healing.

Conversely, this author recommends leaving burn blisters intact. Blisters form in the stratum spinosum layer of the epidermis. An intact blister usually indicates a superficial partial-thickness wound, which will heal spontaneously within 3 weeks. If, under these circumstances, the blistered skin is removed, the wound is converted from an absolutely painless one to a painful open wound exposed to colonization by bacteria and potential infection. An infection in a burn wound covered by an intact blister rarely, if ever, occurs. Therefore, this author prefers to leave blisters intact, and recommends that they be dressed for protection and not necessarily covered with medication.

If the blister remains intact and the wound is a superficial partial-thickness burn, spontaneous resorption of the fluid will usually begin in less than 1 week. The blistered skin will gradually wrinkle and collapse onto the healing wound surface. If the blister has ruptured, often the devitalized skin can be used as a protective dressing for the wound. Whether the blistered skin has remained intact or it has been used as a protective cover, at about the 10th day post-burn, the author inspects the underlying wound to determine its potential for healing spontaneously within the next 10 days. If it is unlikely that the wound will heal spontaneously within that time, surgical intervention to facilitate wound closure is undertaken.

Persistence of the blister, with no signs of spontaneous resorption of the fluid after 7–10 days, usually signifies that the underlying wound is either a deep partial-thickness or full-thickness wound.

There is often concern about large blisters in locations that limit range of motion or interfere with an efficient dressing. This concern most often occurs with a heat contact burn on the palm of the hand, a common injury among toddlers. Since contraction is a property of healing of all wounds, this author prefers to decompress these blisters, leaving the blistered skin to protectively cover the wound. Then the palm, the thumb, and fingers can be dressed to be maintained in full extension with gentle pressure on the web spaces and the digits in moderate abduction until the danger of contraction is past. This is accomplished by several dressing methods. The hand can be immobilized in full palmar extension using an occlusive dressing consisting of triple antibiotic ointment on Adaptic® and padded with dressing sponges, including in the web spaces to maintain moderate abduction of the digits, and incorporating these dressings in a wrap of Coban®. A more secure technique is to use semi-rigid casting tape, referred to as ‘Soft Cast’ (3M™ Health Care, St. Paul, MN). This material consists of a polyurethane resin incorporated in a knitted fabric. Exposure to water activates the resin with a set time of 3–4 min. Curing is completed in about 10 more
in all areas, even around the eyes. According to the manufacturer it effectively removes contaminants from wounds without inducing tissue trauma.

In the treatment of burns from tar and asphalt, after cooling to dissipate heat, the solidified tar and asphalt can be removed by solvents that have a close structural affinity to these substances. Therefore, substances related to petrolatum (an oleaginous colloid suspension of solid microcrystalline waxes in petroleum oil) are effective. Medi-Sol™ Adhesive Remover is a citrus-based non-toxic, non-irritating Category I Medical Device solvent authorized by the FDA for use on the skin. It is an effective product for the removal of tar and asphalt.\textsuperscript{45} It can be obtained from Orange-Sol Medical Products Division (1400 N Fiesta Blvd, Bldg. 100, Gilbert, AZ 85233–1000, phone 480–497–8822) or by using an internet search for ‘Medi-Sol.’ Medi-Sol™ Adhesive Remover is liberally applied and then removed by gentle wiping.

Polysorbates alone or in combination with topical antibiotics\textsuperscript{46} and topical antibiotics in petrolatum base\textsuperscript{47} can be used

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure63.jpg}
\caption{‘Soft’ casting technique to maintain optimal extension of the hand. (a) Heat contact burns of the palm and tips of fingers. (b) Wound dressed with Adaptic® and triple antibiotic ointment. (c) Kling® wrap started by securing it around the wrist. (d) Kling® wrap threaded between fingers to prevent interdigital web formation.}
\end{figure}
but are less effective, and repetitive applications are usually required.

**Topical agents**

There is a long tradition of applying substances to burn wounds in an attempt to prevent infection. A large variety of antiseptics, antibiotics, and topical antibacterial (antimicrobial) agents have been advocated. Most of these agents have adverse local or systemic effects, or impede wound healing, or both. Additionally, there is no published evidence that the use of any topical agent designed to prevent or control infection will favorably influence the outcome of small burns. In spite of this, many physicians feel obligated to apply one of these agents to the wound. All published comparative studies show no advantage of these agents over petrolatum-impregnated gauze. However, if the treating physician believes that the use of a topical antimicrobial agent is desirable, and most do, there are several choices. Among topical antibacterial agents introduced for the treatment of burns during the past five decades, 1% silver sulfadiazine has been the most popular. However, its silver component makes it an antiseptic and, therefore, an inherent property is delay in wound healing. In comparative studies of partial-thickness burn wounds covered with dressings that do not contain antiseptics, e.g. TransCyte®, Biobrane®, and collagenase ointment with polymyxin B sulfate/bacitracin powder, 1% silver sulfadiazine delayed spontaneous reepithelialization of the wound. However, if the wound surface is covered with eschar, 1% silver sulfadiazine delayed spontaneous reepithelialization of the wound. However, if the patient is allergic to sulfa products, silver sulfadiazine should not be used.
Because sulfonamides are known to increase the possibility of kernicterus, silver sulfadiazine is not used on pregnant women, nursing mothers, and infants less than 2 months of age. Because silver sulfadiazine impedes epithelialization, it should be discontinued when healing partial-thickness wounds are devoid of necrotic tissue and evidence of reepithelialization is seen.

Alternatively, there has been increasing interest in the use of combinations of antibiotics in ointment for the treatment of small-area burns. These drugs have no clinically discernible detrimental effect on wound healing. These antimicrobial combinations include triple antibiotic ointment (neomycin, 3.5 mg/g; bacitracin zinc, 400 units/g; and polymyxin B sulfate, 5000 units/g) and Polysporin (polymyxin B sulfate, 10,000 units/g; and bacitracin zinc, 500 units/g). These antibiotic combinations have efficacy against the Gram-positive cocci and some of the aerobic Gram-negative bacilli that most frequently colonize small burn wounds. Occasionally, small superficial pustules caused by yeast develop on the surrounding uninjured or newly regenerated skin. Discontinuing the antimicrobial agent usually results in clearing of these lesions. The use of a topical antibiotic ointment usually decreases or eliminates the unpleasant odor often associated with the use of petrolatum-impregnated gauze alone. The author now uses these agents almost exclusively in the management of small-area burns when a topical antimicrobial is used.

**Dressing the wound**

Because there are virtually no objective studies on the subject, dogmatic recommendations for dressing small burn wounds cannot be made.

Dressings serve three purposes:

1. To absorb drainage;
2. To provide protection and a measure of isolation of the wound from the environment; and
3. To decrease wound pain.

In most instances the author prefers to dress wounds and makes the following suggestions.

Superficial partial-thickness burns, the equivalent of sunburn, with intact epidermis, require neither topical medication nor a dressing. For relatively small superficial partial-thickness burns devoid of epithelium, it is generally conceded that topical antibacterial agents are not necessary. Non-medicinal white petrolatum-impregnated fine mesh or porous mesh gauze (Adaptic®), or fine mesh absorbent gauze impregnated with 3% bismuth tribromophenate in non-medicinal petrolatum blend (Xeroform®) are satisfactory wound covers. If the burn is deeper and contains adherent necrotic tissue, a topical antimicrobial agent may be used.

For practical reasons, most burns of the face are treated without dressing. These wounds may also be treated without topical medication, allowing the wounds to dry and form a crust. Because the dry wound is often uncomfortable and heals more slowly than moist wounds, many physicians prefer to use a thin layer of bland ointment combined with a topical antibiotic, e.g. Baciguent® (bacitracin in anhydrous lanolin, mineral oil, and white petrolatum). The ointment is applied to the wound after gentle cleansing with water once or twice daily, or more frequently as needed, particularly in a dry climate. Bacitracin has activity against Gram-positive bacteria. Occasionally it causes a contact dermatitis that impedes wound healing.

Since one purpose of dressings is to absorb drainage, the thickness of the dressing is determined by the amount of drainage generated between dressing changes. In weeping superficial partial-thickness wounds, the amount of drainage is greatest soon after the injury. As the character of the wound changes and healing begins, drainage decreases. Lint-free, coarse mesh gauze, usually starting with about 20 thicknesses, is preferred by the author.

The dressing is held in place with a gauze bandage (e.g. Kling® or Kerlix®) wrapped with sufficient tightness to hold the gauze in place but not so tightly as to impede circulation. Many use Flexinette® to secure the dressing. Stockinette, semi-impervious to liquid, can be used as an outer layer to help prevent the drainage from soaking through the dressing. As an alternative, a cohesive flexible bandage (Coflex®, Coban®, Cowrap®) can be used as an outer layer to hold a dressing securely in place and prevent drainage from seeping through. Joints are dressed to facilitate range of motion and fingers are dressed separately. However, among infants and young children, an effective way to hold the hand and fingers in extension is with a multilayer covering of one of the cohesive flexible bandages. This kind of a dressing functions as a ‘soft’ splint.

The frequency with which dressings are changed is arbitrary and dictated by the volume of drainage or the physical condition of the dressing. Recommendations range from twice daily, to as infrequently as once a week. Those who advocate twice-daily dressing changes do so based on the use of topical antimicrobials whose half-life is about 8 h. Those who use petrolatum, antibiotic combinations in ointment, or bismuth-impregnated petrolatum gauze recommend less frequent dressing changes, some extending the period to as long as 5 or 7 days.

For inpatients, the author prefers once-daily or every other day dressing changes to permit inspection and cleansing of the wound. Moreover, among inpatients after about 24–48 h, wound dressings are often saturated or disheveled. Daily dressing changes may be used in the care of outpatients even if the patient or another layperson is responsible for the inspection, cleansing, and redressing of the wound. Cleansing of the wound can often be incorporated into general body cleansing each day. The person responsible for wound care should be instructed in the clinical manifestations of wound infections.

In the management of burns among pediatric outpatients, the author now has an extensive and satisfying experience with the use of triple antibiotic ointment and dressing changes done at 3-, 4- or even 7-day intervals. In many instances these dressings are changed and the progress of healing checked at clinic visits. Therefore, parents do not need to deal with the disquieting chore of changing their child’s dressings and inflicting pain on them.

**Biologic wound dressings**

The author does not believe it is necessary or advantageous to use human cadaver allografts, xenografts, or allogenic amnion in the management of burn patients who qualify
for ambulatory care. However, in certain circumstances, amniotic membranes may be plentiful and therefore useful.

**Allogenic amnion**

Allogenic amnion, the innermost layer of the fetal membrane, has been used as a biologic wound dressing since 1910. Although fragile and technically difficult to handle, allogenic amnion is particularly effective when used as a protective dressing on partial-thickness burn wounds. It also has a good track record when used to protect and preserve a clean excised wound for subsequent autogenous skin grafting. When harvested, amniotic membranes are invariably contaminated and carry a biologic risk that can never be totally eliminated. The amnion is washed, sterilized with gamma irradiation and preserved in glycerol, by lyophilization or deep freezing. The risk of biologic transmission can be diminished by systematic serologic testing of the donor for syphilis, AIDS, and hepatitis at the time of harvesting the membrane and 6 months later.

**Synthetic tissue-engineered wound dressings**

The use of synthetic wound coverings is becoming more popular in the treatment of superficial partial-thickness burn wounds. The purported advantages are less pain, use of less pain medication, shorter wound healing time, improved compliance with scheduled outpatient visits, and lower costs.

**Biobrane®**

There are two prospective randomized clinical trials of small numbers of patients that show that in the treatment of superficial partial-thickness burns the use of Biobrane® results in less pain, a lower pain medication requirement, and shorter healing time when compared to those patients treated with 1% silver sulfadiazine. Biobrane® is a bilayer fabric composed of an inner layer of knitted nylon threads coated with porcine collagen and an outer layer of rubberized silicone, pervious to gases but not to liquids and bacteria. Wounds on which Biobrane® is to be applied must be carefully selected. They must be fresh, not infected, free of eschar and debris, moist, have a sensate surface, and demonstrate capillary blanching and refill. It is applied snugly to the cleansed wound overlapping itself or fixed to unburned skin with sterile strips of adhesive tape. The key to the successful use of Biobrane® is adherence to the wound. Therefore, the burned area must be dressed and splinted, especially across a joint, to prevent shearing of the Biobrane® from the wound surface. Satisfactory adherence usually occurs in about 4 days. If, at follow-up, the Biobrane® is found to be loose, the non-adherent area can be trimmed away and new Biobrane® applied. If sterile fluid accumulates beneath the synthetic dressing, it can be aspirated. However, if the fluid is purulent, the Biobrane® must be opened to permit complete drainage. Biobrane® is left intact until the wound has reepithelialized. Then it can be gently teased away. If the wound surface has even a thin veneer of residual necrotic tissue, Biobrane® will not adhere.

**Hydrocolloid dressings**

Hydrocolloid dressings are described as wafers, powders, or pastes composed of materials such as gelatin, pectin, and carboxymethyl-cellulose. They provide a moist environment favorable for wound healing and a barrier against exogenous bacteria. In comparison to wounds treated with 1% silver sulfadiazine, those treated with hydrocolloid occlusive dressings had more rapid wound healing, less pain, and needed fewer dressing changes. As a result, the cost of care was lower. Hydrocolloid dressings have been effective in the treatment of small-area partial-thickness burns and are especially useful in the terminal phase of spontaneous healing of small burns. There are a number of products made by different manufacturers that are probably suitable, e.g. Cutinova® Thin (Beiersdorf-Jobst), Duoderm® CGF Border Sterile Dressing (Convatec), RepliCare® Hydrocolloid Dressing (Smith & Nephew, Inc.), and Restore® Wound Care Dressing (Hollister). Hydrocolloid dressings may be left in place for several days at a time.

**Other wound dressing/covering materials**

Publications are replete with technologic advances and innovations for wound dressings with the purported goal of enhancement of spontaneous wound healing or protection of the wound until it can be closed with skin grafts or with tissue-engineered delivery systems which contain cultured autogenous keratinocytes with or without fibroblasts. This effort resulted in several available products, including: Tissue Tech autograft system (Fidia Advanced Biopolymers S.r.l., Padua, Italy); Hyaff-NW (Fidia Advanced Biopolymers S.r.l.); Laserskin (Fidia Advanced Biopolymers S.r.l.); Apligraft (Organogenesis, Canton, MD); Epicell CEA (Genzyme, Cambridge, MA); Integra (Johnson and Johnson, Ratingen, Germany; Integra Life Sciences Corporation, Plainsboro NJ, USA); AlloDerm (Life Cell Corporation, Woodlands, TX); Terumo (Terumo, Tokyo, Japan); and, Pelnac (Kowa Company, Tokyo, Japan). While the results of use of these products may be encouraging, a major limitation in their use is undoubtedly their high cost. However, among most of those treated as outpatients the area of burn wound requiring skin grafts is relatively small. Therefore, the use of these products is unnecessary and standard techniques of surgical wound debridement and skin grafting suffice. Most of the clinical information about the efficacy of these products is anecdotal. However, information in medical publications can be accessed through the cost-free National Library of Medicine’s online service: http://www.nlm.nih.gov/. On the search screen use the name of the product and burns as the subjects.

**Elevation of the burned part**

One of the most effective ways to reduce the incidence of infection in burns is to eliminate edema from the burned part. Burn injury elicits a flux of fluid into the tissues immediately subjacent to the wound. Additionally, there is a great tendency for the patient to hold the injured part immobile in a dependent position. To eliminate edema, the injured part should be exercised regularly and, when not in use, maintained slightly above the level of the heart. Merely
elevating a leg off the floor to the level of the hip when in the sitting position is not sufficient. Holding the burned forearm flexed and dependent in a sling will enhance edema. Specific instructions and a demonstration of the proper position should be explicit. Patients with small burns who experience persistent edema beyond 3 days are spending too much time with the part dependent.

The most efficient position for the injured part is just slightly above the level of the heart. To elevate the burned part higher does not further enhance removal of excess tissue fluid. However, for every incremental elevation of the part there is an incremental decrease in the arterial perfusion pressure.65

When burns involve the lower extremity, walking and holding the leg in the dependent position often elicit severe pain. To diminish this effect, support, such as with a rubberized elastic bandage (Ace Bandage®), or a cohesive flexible bandage, which the author prefers, applied from the level of the toes to above the burn, should be used. This will also aid in reducing the accumulation of edema during walking.

Instructions and follow-up care

Before patients are released from emergency care, they are instructed in wound care, positioning, physical therapy, the clinical manifestations of infection, a convenient way to access medical care (usually by telephone), and they are given pain medication.

The authors often examine patients within the next several days. This allows re-inspection of the wound, assessment of the patient’s compliance with instructions, and reinforcement of the principles of wound care. Often, because of pain during emergency care, the patient is distracted from fully understanding instructions. If concern remains, more frequent visits are scheduled until the physician is certain that care is being followed appropriately. After that, the patient can be seen at weekly intervals.

Definitive wound closure

A primary objective in burn care is to have all wounds healed within 1 month. Usually, this goal is easily achieved in an ambulatory setting. Burn wounds that heal spontaneously from the depth of the wound within 3 weeks have an excellent result. When this occurs, the skin functions normally with good elasticity, a nil incidence of hypertrophic scarring (scars that are red, raised, and indurated), and little, if any, alteration in pigmentation. The longer spontaneous healing takes, the worse the result. With longer healing periods, there is an increasing likelihood of developing hypertrophic scarring66 and unsightly alterations in pigmentation. In addition, wounds that take a very long time to heal spontaneously may have unstable epithelium.

It is the surgeon’s responsibility to make certain that burn wounds either heal spontaneously or are closed surgically in a timely fashion. If it is apparent that a wound will not heal spontaneously within 3 weeks, a better outcome67,68 can usually be anticipated by surgically removing the residual necrotic tissue and any granulation tissue by tangential excision69 and applying a skin graft. In many instances it is obvious immediately or within several days as to whether spontaneous healing will occur within 3 weeks. Among wounds in which the subtle differences between superficial and deep partial-thickness burns are not initially discernible, by 2 weeks after injury it is usually apparent whether or not the wound will heal spontaneously within the next 7–10 days. At about 10 days after injury, those wounds which are devoid of necrotic tissue and have evidence of squamous reepithelialization will usually heal spontaneously within the desirable time frame. The beginning of reepithelialization can be detected by seeing tiny opalescent islands of epithelium scattered throughout the wound. Inspection with a magnifying lens is helpful.

Infection and use of systemic antibiotics

There is no evidence that systemic antibiotic prophylaxis will decrease the incidence of infection in small burn wounds.70 Antibiotics should be used only when there is evidence of infection.

The burn itself elicits inflammation. Therefore, the early manifestation of infection in the wound may be quite subtle. Mild erythema, edema, pain, and tenderness, all classic signs of infection, may be present without infection. However, when these manifestations increase over baseline, especially in the presence of lymphangitis and fever, treatment for infection should be initiated. Mainstays of treatment for infection include elevation and rest of the infected wound to control swelling and systemic antibiotic therapy. If the infection progresses the patient should be admitted to a hospital and antibiotics given intravenously.

Infections in the outpatient setting are usually caused by common skin flora. Those most frequently implicated are staphylococci. If there is evidence of infection, a culture of the surface of the wound should be obtained to identify the offending organism and narrow the spectrum of antibiotic therapy. While some burn care physicians advocate the use of burn wound biopsy quantitative culture rather than a wound surface culture,71 the author has not found biopsy cultures to be necessary in the treatment of outpatient burns.

Among patients with burns treated in an ambulatory setting, it is quite unusual to develop systemic sepsis. However, patients should be instructed to take their temperature twice daily, once in the morning shortly after they get up from sleep, and again late in the afternoon before they eat supper. Localized infection will be reflected in fever in the afternoon or evening. Sustained fever is suggestive of systemic sepsis. Temperatures above 38°C, especially if accompanied by symptoms of malaise and anorexia, should be reported to the physician and the patient called in for an examination.

A change in the appearance of the wound during the first several days is more likely to result from a decrease in perfusion of the wound than from wound infection. This occurs as the blood vessels injured by heat clot off. This is frequently observed with scald burns. Any further burn wound discoloration, such as the appearance of gray or black spots, especially if there are other manifestations of infection, should raise concern for invasive infection. This rarely occurs among those treated as outpatients. However, if it does occur, the patient should be admitted to a hospital, the wound biopsied for histologic and microbiological studies,72 and treatment for infection instituted.
Burns, even minor ones, are regarded as tetanus-prone wounds. Tetanus prophylaxis should be provided unless the patient has received tetanus immunization within the previous 5 years.

### Pruritus

Itching is an annoying, often unrelenting manifestation of healing and healed burn wounds.

Most burn patients develop pruritus. The incidence is higher among children. The lower extremities are most frequently affected and more frequently than the upper. The face is seldom involved.

Post-burn itching interferes with everything. Scratching often results in repetitive superficial wounding of both skin grafted and spontaneously healed wounds. Triggered and enhanced by environmental extremes, especially heat, physical activity, and stress, pruritus is most intense in the period immediately after wounds are healed. In most instances, it gradually diminishes and eventually stops. There are a few patients in whom it persists beyond 18 months. Patients with prolonged and chronic itching may harbor a psychogenic component.

The sensation of itch is most likely a primary sensory modality rather than, as widely held in the past, a form of pain. Histamine, whose synthesis is known to be increased in healing and inflamed wounds, as well as bradykinin and a series of endopeptides, have all been implicated in the genesis of itching. Because the precise mechanism of pruritus is not known, the likelihood is that there are multiple causative factors.

Since there are no controlled trials defining the best treatment, management is by trial and error. However, antihistamines, cool compress, and lotions are the cornerstones of most attempts to relieve burn-related itching. The antihistaminic diphenhydramine hydrochloride is the most frequently prescribed first treatment. This drug has an added benefit of providing mild sedation. Other antihistamines, such as cyproheptadine hydrochloride, may also be tried. Analgesics of any kind may be helpful by altering perception of itching in the central nervous system. Combinations of antihistamines and analgesics may be tried. Hydroxyzine hydrochloride, a drug used to provide relief from anxiety and emotional tension, is used by many to help ameliorate itching. Many patients find comfort in an air-conditioned environment. Cool compresses also may temporarily interrupt the itching cycle. A variety of topical agents, including aloe vera, which has anti-inflammatory and antimicrobial properties, and skin moisturizing creams, such as Elta®, Vaseline Intensive Care®, Eucerin®, Nivea®, mineral oil, cocoa butter, and even lard, have been effective. Any odorless lotion free of alcohol is probably helpful. In addition, many patients prefer loose, soft clothing made from cotton.

The staff at the Shriners Burns Hospital, Galveston, Texas, uses the following protocol for the treatment of itching:

**Step 1:** Use moisturizing body shampoo and lotions.
**Step 2:** Diphenhydramine 1.25 mg/kg/dose PO q 4 h scheduled.
**Step 3:** Hydroxyzine 0.5 mg/kg/dose PO q 6 h and diphenhydramine 1.25 mg/kg/dose PO q 6 h. Alternate medication so that patient is receiving one itch medicine every 3 h while awake.

**Step 4:** Hydroxyzine 0.5 mg/kg/dose PO q 6 h and cyproheptadine 0.1 mg/kg/dose PO q 6 h and diphenhydramine 1.25 mg/kg/dose PO q 6 h. Alternate medication so that patient is receiving one itch medicine every 2 h while awake.

Phillips and Robson advocate using penicillin in pruritus management. They observed that post-burn hypertrophic scars were much more frequently colonized with beta-hemolytic streptococcus, *Staphylococcus aureus*, and *Staph. epidermidis* compared to matched healed wounds without hypertrophic scarring. Therefore, to decrease the inflammation caused by these microorganisms, a root cause of itching, they used the following regimen: low-dose oral penicillin, 250 mg twice daily, to control the beta-hemolytic streptococcus, and aloe vera cream applied topically. As noted above, aloe vera has both anti-inflammatory and antimicrobial properties.

### Traumatic blisters in reepithelialized wounds

As the wounds reepithelialize, the delicate thin layer of epithelium is fragile and easily damaged. Itching and other mild forms of trauma may cause small blisters. Patients need to be cautioned about this potential and assured that the epithelium will gain strength and that this will not be a long-term problem. If these blisters rupture, leaving small superficial wounds, the wounds may be left exposed to form a crust. Alternatively, Adaptic® or Xeroform® and a light dressing or one of the hydrocolloid wafer products may be used.

### Rehabilitative physical care

Measures to preserve strength and restore function should be incorporated into the initial treatment plan. Before leaving emergency care, the patient’s physical activity should be discussed and a program for range of motion exercises and muscle strengthening outlined, both verbally and in writing.

At each subsequent follow-up visit, function and strength should be assessed. If there is lack of compliance or if the patient’s function begins to deteriorate, the patient should be referred for supervised physical or occupational therapy, or both. If the injury extends across a joint, or involves the hand or distal portion of the lower extremity, it is advisable to have therapists involved from the outset. When there are burns of the face that have the potential for facial dysfunction, it may be prudent to have the patient evaluated and treated by a speech pathologist.

The potential for development of contractures and hypertrophic scars among the burned treated as outpatients is the same as for those treated as inpatients. The principles of prevention and treatment of these complications apply in both settings.

### Outpatient treatment of moderate and major burns

Some patients classified as having moderate or even major burn injuries (Table 6.2) are suitable for treatment in the ambulatory setting. The purported advantages include less...
cost, less chance of exposure to antibiotic-resistant microorganisms, and a more psychologically comfortable environment for the patient. In spite of these benefits, caution should be exercised in selecting patients with moderate and major thermal injury for early discharge from the hospital. On the other hand, as convalescence progresses, many of these patients can have the terminal phase of their acute burn care completed safely as outpatients.

The conditions that need to be met in order to consider ambulatory care for any patient include: intravenous fluid resuscitation must be completed; there must be no ongoing complication; there must be no wound or systemic manifestation of sepsis; adequate enteral nutrition must be established; and pain control must be satisfactory with medication taken by mouth. Additionally, arrangements need to be made for wound care and physical and/or occupational therapy.

Further reading


Table 6.2 Classification of burn severity

<table>
<thead>
<tr>
<th>Minor burn</th>
<th>Moderate burn</th>
<th>Major burn</th>
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<tbody>
<tr>
<td>≤15% TBSA in adults</td>
<td>15–25% TBSA in adults with &lt;10% full-thickness burn</td>
<td>≥25% TBSA</td>
</tr>
<tr>
<td>≤10% TBSA in children and the elderly</td>
<td>10–20% TBSA partial-thickness burn in children under 10 and adults over 40 years of age, with &lt;10% full-thickness burn</td>
<td>≥20% TBSA in children under 10 and adults over 40 years of age</td>
</tr>
<tr>
<td>≤2% TBSA full-thickness burn in children or adults without cosmetic or functional risk to eyes, ear, face, hands, feet, or perineum</td>
<td>≤10% TBSA full-thickness burn in children or adults without cosmetic or functional risk to eyes, ears, face, hands, feet, or perineum</td>
<td>≥10% TBSA full-thickness burn</td>
</tr>
<tr>
<td></td>
<td>All burns involving eyes, ears, face, hands, feet, or perineum that are likely to result in cosmetic or functional impairment</td>
<td>All burns involving eyes, ears, face, hands, feet, or perineum that are likely to result in cosmetic or functional impairment</td>
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<tr>
<td></td>
<td>All high-voltage electrical burns</td>
<td>All burns involving eyes, ears, face, hands, feet, or perineum that are likely to result in cosmetic or functional impairment</td>
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<tr>
<td></td>
<td>All burn injuries complicated by major trauma or inhalation injury</td>
<td>All high-voltage electrical burns</td>
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<tr>
<td></td>
<td>All poor-risk patients with burn injury</td>
<td>All burn injuries complicated by major trauma or inhalation injury</td>
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<td></td>
<td></td>
<td>All poor-risk patients with burn injury</td>
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<td>TBSA, total body surface area.</td>
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References


Introduction

Advances in trauma and burn management over the past three decades have resulted in improved survival and reduced morbidity from major burns. The cost of such care, however, is high; it requires conservation of resources such that only a limited number of burn intensive care units with the capabilities of caring for such labor-intensive patients can be found – hence regional burn care has evolved. This regionalization has led to the need for effective pre-hospital management, transportation, and emergency care. Progress in the development of rapid, effective transport systems has resulted in marked improvement in the clinical course and survival for victims of thermal trauma.

For burn victims, there are usually two phases of transport. The first is the entry of the burn patient into the emergency medical system with treatment at the scene and transport to the initial care facility. The second phase is the assessment and stabilization of the patient at the initial care facility and transportation to the burn intensive care unit. With this perspective in mind, this chapter reviews current principles of optimal pre-hospital management, transportation, and emergency care.

Pre-hospital care

Prior to any specific treatment, a patient must be removed from the source of injury and the burning process stopped. As the patient is removed from the injuring source, care must be taken so that a rescuer does not become another victim. All caregivers should be aware of the possibility that they may be injured by contact with the patient or the patient's clothing. Universal precautions, including wearing gloves, gowns, masks, and protective eye wear, should be used whenever there is likely contact with blood or body fluids. Burning clothing should be removed as soon as possible to prevent further injury. All rings, watches, jewelry, and belts should be removed as they can retain heat and produce a tourniquet-like effect with digital vascular ischemia. If water is readily available, it should be poured directly on the burned area. Early cooling can reduce the depth of the burn and reduce pain, but cooling measures must be used with caution, since a significant drop in body temperature may result in hypothermia with ventricular fibrillation or asystole. Ice or ice packs should never be used, since they may cause further injury to the skin or produce hypothermia.

Initial management of chemical burns involves removing saturated clothing, brushing the skin if the agent is a powder, and irrigation with copious amounts of water, taking care not to spread chemical on burns to adjacent unburned areas. Irrigation with water should continue from the scene of the accident through emergency evaluation in the hospital. Efforts to neutralize chemicals are contraindicated due to the additional generation of heat, which would further contribute to tissue damage. A rescuer must be careful not to come in contact with the chemical, i.e. gloves, eye protectors, etc. should be worn.

Removal of a victim from an electrical current is best accomplished by turning off the current and by using a non-conductor to separate the victim from the source.

On-site assessment of a burned patient

Assessment of a burned patient is divided into primary and secondary surveys. In the primary survey, immediate life-threatening conditions are quickly identified and treated. The primary survey is a rapid, systematic approach to identify life-threatening conditions. The secondary survey is a more thorough head-to-toe evaluation of the patient. Initial management of a burned patient should be the same as for any other trauma patient, with attention directed at airway, breathing, circulation, and cervical spine immobilization.

Primary assessment

Exposure to heated gases and smoke from the combustion of a variety of materials results in damage to the respiratory tract. Direct heat to the upper airways results in edema formation, which may obstruct the airway. Initially, 100%-humidified oxygen should be given to all patients when no obvious signs of respiratory distress are present. Upper airway obstruction may develop rapidly following injury, and the respiratory status must be continually monitored in order to assess the need for airway control and ventilator support. Progressive hoarseness is a sign of impending airway obstruction. Endotracheal intubation should be done early before edema obliterates the anatomy of the area.
The patient’s chest should be exposed in order to adequately assess ventilatory exchange. Circumferential burns may restrict breathing and chest movement. Airway patency alone does not assure adequate ventilation. After an airway is established, breathing must be assessed in order to insure adequate chest expansion. Impaired ventilation and poor oxygenation may be due to smoke inhalation or carbon monoxide intoxication. Endotracheal intubation is necessary for unconscious patients, for those in acute respiratory distress, or for patients with burns of the face or neck which may result in edema which causes obstruction of the airway. The nasal route is the recommended site of intubation. Assisted ventilation with 100%-humidified oxygen is required for all intubated patients.

Blood pressure is not the most accurate method of monitoring a patient with a large burn because of the pathophysiologic changes which accompany such an injury. Blood pressure may be difficult to ascertain because of edema in the extremities. A pulse rate may be somewhat more helpful in monitoring the appropriateness of fluid resuscitation. If a burn victim was in an explosion or deceleration accident, there is the possibility of a spinal cord injury. Appropriate cervical spine stabilization must be accomplished by whatever means necessary, including a cervical collar to keep the head immobilized until the condition can be evaluated.

Secondary assessment

After completing a primary assessment, a thorough head-to-toe evaluation of a patient is imperative. A careful determination of trauma other than obvious burn wounds should be made. As long as no immediate life-threatening injury or hazard is present, a secondary examination can be performed before moving a patient; precautions such as cervical collars, backboards, and splints should be used. Secondary assessment should examine a patient’s past medical history, medications, allergies, and the mechanisms of injury.

There should never be a delay in transporting burn victims to an emergency facility due to an inability to establish intravenous (IV) access. If the local/regional emergency medical system (EMS) protocol prescribes that an IV line is started, then that protocol should be followed. The American Burn Association recommends that if a patient is less than 60 min from a hospital, an IV is not essential and can be deferred until a patient is at a hospital. If an IV line is established, Ringer’s lactate solution should be infused at:

- 14 years and older: 500 mL LR per hour
- 6–14 years old: 250 mL LR per hour
- 5 years and younger: 125 mL LR per hour.

Pre-hospital care of wounds is basic and simple, because it requires only protection from the environment with an application of a clean dressing or sheet to cover the involved part. Covering wounds is the first step in diminishing pain. If it is approved for use by local/regional EMS, narcotics may be given for pain, but only intravenously in small doses and only enough to control pain. Intramuscular (IM) or subcutaneous routes should never be used, since fluid resuscitation could result in unpredictable patterns of uptake. No topical antimicrobial agents should be applied in the field. The patient should then be wrapped in a clean sheet and blanket to minimize heat loss and to control temperature during transport.

Transport to hospital emergency department

Rapid, uncontrolled transport of a burn victim is not the highest priority, except in cases where other life-threatening conditions coexist. In the majority of accidents involving major burns, ground transportation of victims to a hospital is available and appropriate. Helicopter transport is of greatest use when the distance between an accident and a hospital is 30–150 miles or when a patient's condition warrants. Whatever the mode of transport, it should be of appropriate size, and have emergency equipment available as well as trained personnel, such as a nurse, physician, paramedic, or respiratory therapist.

Assessment at the initial care facility

The assessment of a patient with burn injuries in a hospital emergency department is essentially the same as outlined for the pre-hospital phase of care. The only real difference is the availability of more resources for diagnosis and treatment in an emergency department. As with other forms of trauma, the primary survey begins with the ABCs, and the establishment of an adequate airway is vital. Endotracheal intubation should be accomplished early if impending respiratory obstruction or ventilatory failure is anticipated, because it may be impossible after the onset of edema following the initiation of fluid therapy. Securing an endotracheal tube may be difficult because traditional methods often do not adhere to burned skin, and tubes are easily dislodged. One method of choice includes securing an endotracheal tube with woven tape, umbilical cord, under the ears as well as over the ears. While doing assessments and making interventions for life-threatening problems in the primary survey, precautions should be taken to maintain cervical spine immobilization until injuries to the spine can be ruled out.

Following a primary survey, a thorough head-to-toe evaluation of a patient should be done. This includes obtaining a history as thorough as circumstances permit. The history should include the mechanism and time of the injury and a description of the surrounding environment, such as whether injuries were incurred in an enclosed space, the presence of noxious chemicals, the possibility of smoke inhalation, and any related trauma. A complete physical examination should include a careful neurological examination, as evidence of cerebral anoxic injury can be subtle. Patients with facial burns should have their corneas examined with fluorescent staining. Routine admission laboratories should include a complete blood count, serum electrolytes, glucose, blood urea nitrogen (BUN), and creatine. Pulmonary assessment should include arterial blood gases, chest X-rays, and carboxyhemoglobin.

Emergency treatment at the initial care facility

All extremities should be examined for pulses, especially with circumferential burns. Evaluation of pulses can be assisted by use of a Doppler ultrasound flowmeter. If pulses
sedation using electrocautery. Midaxial incisions are made through the eschar but not into subcutaneous tissue of the eschar in order to assure adequate release. Limbs should be elevated above the heart level. Pulses should be monitored for 48 h.

If pulses are still present, but appear endangered, chemical escharotomy with enzymatic ointments (Accuzyme, collagenase, Elase) can be effective. Enzymatic escharotomy in hand burns may be preferred since surgical incisions risk exposure of superficial nerves, vessels, and tendons. Enzymatic escharotomy is indicated only during the first 24–48 h post-burn, and it should be used only in combination with a topical antimicrobial agent or sepsis can occur. With enzymatic escharotomy, there is usually a spike in temperature, which subsides after the enzyme is removed.

Evaluation of wounds

After the primary and secondary surveys are completed and resuscitation is underway, a more careful evaluation of burn wounds is performed. The wounds are gently cleaned, and loose skin and in large wounds blisters greater than 2 cm are debrided (see Ch. 6). Blister fluid contains high levels of inflammatory mediators, which increase burn wound ischemia. The blister fluid is also a rich media for subsequent bacterial growth. Deep blisters on the palms and soles may be aspirated instead of debrided in order to improve patient comfort. After burn wound assessment is complete, the wounds are covered with a topical antimicrobial agent and appropriate burn dressings or a biological dressing is applied.

An estimate of burn size and depth assists in making a determination of severity, prognosis, and disposition of a patient. Burn size directly affects fluid resuscitation, nutritional support, and surgical interventions. The size of a burn wound is most frequently estimated by using the Rule-of-Nines method (Fig. 7.2). A more accurate assessment can be made of a burn injury, especially in children, by using the Lund and Browder chart, which takes into account changes brought about by growth (Fig. 7.3). The American Burn Association identifies certain injuries as usually requiring a referral to a burn center. Patients with these burns should be treated in a specialized burn facility after initial assessment and treatment at an emergency department. Questions about specific patients should be resolved by consultation with a burn center physician (Box 7.1).

Fluid resuscitation

Establishment of IV lines for fluid resuscitation are necessary for all patients with major burns including those with inhalation injury or other associated injuries. These lines are best started in the upper extremity peripherally. A minimum of two large-caliber IV catheters should be established through non-burned tissue if possible, or through burns if no unburned areas are available. The ABLS 2010 Fluid Resuscitation Formula of Ringer’s lactate solution should be infused at 2 mL/kg/% total body surface area (TBSA) which is burned. Children must have additional fluid for maintenance.

Taking into account the increased evaporative water loss in the formula for fluid resuscitation for pediatric patients, the initial resuscitation should begin with 5000 mL/m²/%
TBSA burned/day + 2000 mL/m²/BSA total/day 5% dextrose in Ringer’s lactate. This formula calls for one-half of the total amount to be given in the first 8 h post-injury with the remainder given over the following 16 h (Box 7.2).\(^{14}\)

All resuscitation formulas are designed to serve as a guide only. The response to fluid administration and physiologic tolerance of a patient is the most important determinant. Additional fluids are commonly needed with inhalation injury, electrical burns, associated trauma, and delayed resuscitation. The appropriate resuscitation regimen administers the minimal amount of fluid necessary for maintenance of vital organ perfusion; the subsequent response of the patient over time will dictate if more or less fluid is needed so that the rate of fluid administration can be adjusted accordingly. Inadequate resuscitation can cause diminished perfusion of renal and mesenteric vascular beds. Fluid overload can produce undesired pulmonary or cerebral edema.

**Urine output requirements**

The single best monitor of fluid replacement is urine output. Acceptable hydration is indicated by a urine output of more than 30 mL/h in an adult (0.5 mL/kg/h) and 1 mL/kg/h in a child. Diuretics are generally not indicated during an acute resuscitation period. Patients with high-voltage electrical burns and crush injuries with myoglobin and/or hemoglobin in the urine have an increased risk of renal tubular obstruction. Sodium bicarbonate should be added to IV fluids in order to alkalinize the urine, and urine output should be maintained at 1–2 mL/kg/h as long as these pigments are in the urine.\(^{1,4}\) The addition of an osmotic diuretic such as mannitol may also be needed to assist in clearing the urine of these pigments.

**Additional assessments and treatments**

**Decompression of stomach**

To combat the problem of gastric ileus, a nasogastric tube should be inserted in all patients with major burns in order to decompress the stomach. This is especially important for patients being transported at high altitudes.\(^{13}\) Additionally, all patients should be restricted from taking anything by mouth until after the transfer has been completed.
Decompression of the stomach is usually necessary because an anxious, apprehensive patient will swallow considerable amounts of air and distend the stomach. Narcotics also diminish peristalsis of the gastrointestinal tract and result in distention.

**A patient must be kept warm and dry**

Hypothermia is detrimental to traumatized patients and can be avoided or at least minimized by the use of sheet and blankets. Wet dressings should be avoided.

**Pain**

The degree of pain experienced initially by the burn victim is inversely proportional to the severity of the injury. No medication for pain relief should be given intramuscularly or subcutaneously. For mild pain, acetaminophen 650 mg orally every 4–6 h may be given. For severe pain, morphine, 1–4 mg intravenously every 2–4 h, is the drug of choice, although meperidine (Demerol) 10–40 mg by IV push every 2–4 h may be used. Recommendations for tetanus prophylaxis are based on the patient’s immunization history. All patients with burns should receive 0.5 mL of tetanus toxoid. If prior immunization is absent or unclear, or if the last booster was more than 10 years ago, 250 units of tetanus immunoglobulin is also given.

**Transferring a burn patient**

The appearance of burn skin is rather obvious and has the potential to mask or cover any other potential injuries that the burn patient could have. The burn patient is a trauma patient with burns and should be promptly and effectively evaluated to include other potential injuries. It is important to establish effective communication between the transferring unit and the receiving center.

Once the need to transfer the patient is identified, the transferring process begins. The doctor-to-doctor referral process starts with the initial care facility. Available phone numbers and doctor information should be available to centers that should promptly call and ask for all the information needed for the transfer.

The referring physician should give a brief and concise history of the event that includes the time of injury and all resuscitation efforts prior to the call. The accepting facility should then fill out an intake form that details all the information. Understanding of the patient’s current status is needed for a successful and uneventful transfer. It is imperative that physicians participate in the process adding to the already available information gather by other personal.
Transferring a patient without the needed information can potentially lead to bad outcomes and or unnecessary expense. For example, a burn patient with an underlying anoxic brain injury could be transferred to a burn center, when instead the diagnosis of brain death could have been done at the initial care facility.

Physicians have the availability of accessing patient information utilizing different technologies. Although a doctor-to-doctor phone call is preferred by many, today’s technology allows patient data including pictures, laboratory results as well as any other clinical information needed to further assess the patient’s needs. While some physicians still prefer the immediacy of the telephone, secure electronic messaging tools are beginning to supplement phone calls and beepers to facilitate communication among physicians.

Privacy and security issues

Perhaps the most fundamental choice physicians must make when selecting tools to communicate electronically with each other and with patients is how they will manage the privacy and security of the information exchanged.

The HIPAA (Health Insurance Portability and Accountability Act) is ‘technology-neutral,’ in that it does not require any set form of encryption or information safeguarding, and is ‘scalable,’ in that it allows small practices to do what they can afford to do without requiring them to purchase expensive communication security systems.

For electronic communication, the physician should have an informed consent form signed by each patient specific to the form of communication being used, such as e-mail. The form should verify the patient’s e-mail address; should discuss the security risks involved, e.g. that other parties on the patient’s end might have access to their e-mail accounts, and that standard (unencrypted, non-secure) e-mail can be intercepted by unintended parties; should discuss allowable content of the communication; and should include a provision to hold the physician harmless if security is breached.

While there is no private right of action under the HIPAA, i.e. a patient cannot sue physicians for breach of HIPAA’s privacy or security provisions, the federal agencies that oversee the HIPAA have recently announced plans to step-up their audits, and they could conduct an inquiry if a patient filed a complaint. Federal investigations seem more likely to focus on hospitals than physician offices. Carelessness could also have legal repercussions. For example, information could be sent to the wrong recipient because of failure to verify the address field before sending the message. Physicians using standard e-mail should take as many practical safeguards as possible to minimize liability exposure. This could include a privacy and security disclaimer footer on each e-mail; requesting the patient’s permission before continuing to respond to certain issues by e-mail; limiting the amount of medical detail in the messages, password-protecting e-mail access on office and home workstations, as well as on portable devices, such as PDAs and Blackberries, in case they are lost.

Another way to alleviate security or HIPAA compliance concerns is to leave out ‘protected health information’ (PHI) in standard e-mail: data that both personally identifies a patient and reveals a specific diagnosis or condition. While standard e-mail works and is offered free of charge by service providers such as Yahoo, Gmail, Comcast and many others, vendors of secure messaging networks are quick to point out multiple deficiencies (Box 7.3).

Whether or not electronic communication is encrypted or secure, physicians should guard against getting lulled by the casual nature of e-mail which, unlike a conversation or phone call, is not erased from a computer’s hard drive when deleted and is potentially discoverable in litigation.

Transportation guidelines

The primary purpose of any transport teams is not to bring a patient to an intensive care unit but to bring that level of care to the patient as soon as possible. Therefore, the critical time involved in a transport scenario is the time it takes to get the team to the patient. The time involved in transporting a patient back to a burn center becomes secondary. Communication and teamwork are the keynotes to an effective transport system.

When transportation is required from a referring facility to a specialized burn center, a patient can be fairly well stabilized before being moved. Initially, the referring facility should be informed that all patient referrals require physician-to-physician discussion. Pertinent information needed include: patient demographic data; time; date; cause and extent of burn injury; weight and height; baseline vital signs; neurological status; laboratory data; respiratory status; previous medical and surgical history, and allergies.

A referring hospital is informed of specific treatment protocols regarding patient management prior to transfer. To ensure patient stability, the following guidelines are offered:

- Establish two IV sites, preferably in an unburned upper extremity, and secure IV tubes with sutures.
- Insert a Foley catheter and monitor for acceptable urine output (30 mL/h adult; 1 mL/kg/h child).
- Insert a nasogastric tube and ensure that the patient remains NPO.
- Maintain body temperature between 38 and 39.0 °C rectally.
- Stop all narcotics.

### Box 7.3 Deficiencies of electronic mail services for the transmission of medical information

- Lack of encryption or authentication
- Can be used by anyone to access a physician if they simply know the physician’s e-mail address
- Have no ‘terms of service’ or legal disclaimers to protect physicians
- Can easily expose patient e-mail addresses and identities to unintended third parties
- Can breach patient privacy by using employer e-mail networks
- Offer no charge capture function
- Have no template or medical records features
- Lack of consistency with HIPAA or medical liability insurance company standards.
• For burns less than 24 h old, only use lactated Ringer’s solution. The staff physician will advise on the infusion rate, which is calculated based on the percentage of total body surface area burned.

Following physician-to-physician contact and collection of all pertinent information, the physicians will make recommendations regarding an appropriate mode of transportation. The options are based on distance to a referring unit, patient complexity, and comprehensiveness of medical care required. Options include:

• Full medical intensive care unit transport with a complete team, consisting of a physician, a nurse, and a respiratory therapist from the burn facility
• Medical intensive care transport via fixed wing or helicopter with a team from a referring facility
• Private plane with medical personnel to attend patient
• Commercial airline
• Private ground ambulance
• Transport van with appropriate personnel.

Transport team composition

Because stabilization and care for a burned patient is so specialized, team selection is of the utmost importance. Traditionally, these patients were placed in an ambulance with an emergency medical technician and transported with few efforts made to stabilize the patient prior to transfer. As levels of care and technology have evolved, the need for specialized transport personnel has been increasingly observed. Today most transport teams are made up of one or more of the following healthcare members: a registered nurse, a respiratory therapist, and/or a staff physician or house resident. Because a large number of burned patients require some type of respiratory support due to inhalation injury or carbon monoxide intoxication, the respiratory therapist and nurse team has proven to be an effective combination. The background and training of nurses and therapists differ in many ways, so such a team provides a larger scope of knowledge and experience when both are utilized. Team members ideally should be cross-trained so that each member can function at the other’s level of expertise.

Training and selection

Since the transport team will work in a high-stress environment, often with life or death consequences, these individuals must be carefully selected. The selection process should involve interviews with a nursing administrator, a director of respiratory therapy, and a medical director of a transport program.

Minimum requirements for transport team members should include:

• Transport nurse qualifications:
  ▪ a registered nurse;
  ▪ minimum of 6 months burn care experience;
  ▪ current cardiopulmonary resuscitation (CPR) certification;
  ▪ advanced cardiac life support (ACLS) or pediatric advanced life support (PALS) certification;
  ▪ ability to demonstrate clinical competency;
  ▪ observe two transports;
  ▪ a valid passport for international response.

• Transport respiratory therapist qualifications:
  ▪ registered respiratory therapist with 6 months burn care experience;
  ▪ licensed by appropriate regulatory agency as a respiratory care practitioner;
  ▪ have current BLS;
  ▪ ACLS or PALS certification;
  ▪ ability to demonstrate clinical competency;
  ▪ observe two transports;
  ▪ demonstrate a working knowledge of transport equipment;
  ▪ a valid passport for international response.

Because all of the care rendered by a transport team outside a hospital is given as an extension of care from a transporting/receiving facility, specific steps must be taken to protect staff and physicians from medical liability and to provide consistent care for all patients. Strict protocols are used to guide all patient care; team members should be in constant communications with an attending physician regarding a patient’s condition and the interventions to be considered. Team members must be proficient at a number of procedures, which may be needed during transport or while stabilizing a patient prior to transport. To keep up with current technology and changes, team members should be included in discussions of recent transports and current management techniques, so that they can discuss patient care issues, receive ongoing in-service education, and participate in a review of the quality of transports.

Modes of transportation

Once the need for transport of a burned patient is established, the decision must be rendered concerning what type of transportation vehicle is to be used (Table 7.1). There are two models of transport commonly used: ground (ambulance/transport vehicle); air (helicopter, fixed wing), or a combination of both. Factors to be considered when selecting a mode of transportation are the condition of the patient and the distance involved. The level of the severity of the burn mandates the speed with which the team must arrive in order to stabilize and transport a patient. 18

Ground transport

Ground transport should be considered to cover distances of 70 miles or less; however, sometimes a patient’s condition may require air transport, particularly helicopter transport, even though the distance is within the 70-mile range. The ground transport vehicle should be modified with special equipment needed for intensive care transport, and there must be enough room to comfortably seat team members and equipment.

Air transport

Air transport is used primarily when long distances or the critical nature of an injury separate a team from a patient. Air transport, however, does present its own unique set of problems. Aviation physiology is a specialty unto itself, and
the gas laws play an important role in air transport and must be taken into consideration.

Dalton’s law states that in a mixture of gases, the total pressure exerted by the mixture is equal to the sum of the pressures each would exert alone. This is important when changing a patient’s altitude because as altitude increases, barometric pressure decreases. The percentage of nitrogen, oxygen, and carbon dioxide remain the same, but the partial pressures exert change.

Altitude is an important factor in the oxygenation of a transported patient and constant monitoring by a team is required under such circumstances. Boyle’s law states that the volume of gas is inversely proportional to the pressure to which it is subject at a constant temperature. This gas law significantly affects patients with air leaks and free air in the abdomen, because as altitude increases, the volume of air in closed cavities also increases. For this reason, all air that can be reached should be evacuated prior to an increase in altitude. Intrathoracic air and gastric air must be removed via functional chest tubes or nasogastric tubes and periodically checked during transport. Other factors that should be considered during air transport are reduced cabin pressure, turbulence, noise and vibration, changes in barometric pressure, and acceleration/deceleration forces. Physiologic changes which affect a patient and team members include middle ear dysfunction, pressure-related problems with sinuses, air expansion in a gastrointestinal tract, and motion sickness. Utilizing transport vehicles that have pressurized cabins can reduce or eliminate most of these problems.

Helicopters and fixed wing aircraft

Helicopters and fixed wing aircraft both have advantages and disadvantages related to patient care. Helicopters are widely used for short-distance medical air transport. Medical helicopters, because they are usually based on hospital premises, have no need to use airport facilities or ambulance services and, thereby, reduce team response time. Helicopters are able to land close to a referring hospital. Additionally, helicopters provide ease in loading and unloading patients and equipment. The disadvantages of helicopter transport include its limited range, usually less than 150 miles and its non-pressurized cabin which limits the altitude at which patients can be safely carried. The low-altitude capabilities also subject the aircraft to variability in weather (i.e. fog, rain, and reduced visibility); therefore, helicopter flights experience much more interference due to the weather. Other disadvantages include noise, vibrations, reduced air speed, small working space, lower weight accommodation, and high maintenance requirements.

When long distances must be traveled (more than 150 miles) or when increased altitude is necessary, fixed wing aircraft are considered as a viable mode of transport for patients. The advantages of using fixed wing aircraft include: long range capabilities, increased speed, ability to fly in most weather conditions, control of cabin pressure and temperature, larger cabin space, and more liberal weight restrictions. Disadvantages of fixed wing aircraft include the need for an airport with adequate runway length, difficulty in loading and unloading patients and equipment, and the pressure of air turbulence and noise.

Equipment

Because medical equipment used in intensive care units has evolved tremendously in the last 10 years, there is no reason that these advances should not be extended to the equipment which is used in a transport program. The transport team must be able to provide ICU level care whenever needed. Most hospitals are well stocked and able to provide necessary supplies for initial patient stabilization and resuscitation; however, specialty items relating to the care of burn patients may not be present or adequate to meet the needs of burn victims. It is imperative that adequate equipment be available to handle any situation, which may arise during a transport process (Fig. 7.4). Extra battery packs and electrical converters on fixed wing aircraft are recommended due to long transport times and delays caused by unforeseeable circumstances of weather or logistics.
Portable monitor

A portable ECG monitor capable of monitoring two pressure channels should accompany all patients in transport. This allows for continuous monitoring of heart rate, rhythm, and arterial blood pressure. The second pressure channel may be used for patients with a pulmonary artery catheter or those who need intracranial pressure monitoring. This monitor should be small and lightweight but able to provide a display bright enough to be seen from several feet away. The monitor should have its own rechargeable power supply which continuously charges while connected to an alternating current (AC) power supply. One suitable unit is the Protocol Systems Propaq 106 portable monitor. This monitor has two pressure channels; it provides a continuous display of ECG, heart rate, systolic, diastolic, and mean blood pressure; it can display temperature and oxygen saturation; and it is also capable of operating a non-invasive blood pressure cuff. High and low alarms for each monitored parameter can be set, silenced, or disabled by a trained operator.

Infusion pump

Continuous delivery of fluids and pharmacological agents must not be interrupted during transport. Infusion pumps can be easily attached to stretchers and are usually capable of operating for several hours on internal batteries. These devices should have alarms to warn of infusion problems and should be as small and lightweight as possible.

Ventilator

Size, weight, and oxygen consumption are the primary concerns in selecting transport ventilators. A weight under 5 pounds (2.2 kg) is desirable, and a ventilator’s dimensions should make it easy to mount or to place on a bed. Orientation of controls should be along a single plane, and inadvertent movement of dials should be difficult. The ventilator breathing circuit and exhalation valve should be kept simple, and incorrect assembly should be impossible. One type of transport ventilator that has become popular is the TXP transport ventilator. The TXP transport ventilator (Percussionaire Corporation, Sand Point, ID) is a portable pressure-limited time-cycled ventilator and is approved for in-flight use by the US Air Force. The transport ventilator weighs 1.5 pounds (0.68 kg), can be set to provide respiratory rates of between 6 and 250 breaths per minute, and provides tidal volumes of between 5 and 1500 cc. This ventilator is powered entirely by oxygen and requires no electrical power. All timing circuit gases are delivered to the patient so that operation of the ventilator does not consume additional oxygen. The I:E ratios are preset at the factory from 1:1 at frequencies of 250 cycles per minute to 1:5 at a rate of 6 cycles per minute. As a result, breath stacking and undesired over inflation due to air trapping may be avoided.

Stabilization

One of the primary reasons for a specialized transport team is to be able to transport a patient in as stable condition as possible. Current practice has evolved to embrace the concept that events during the first few hours following burn injury may affect the eventual outcome of the patient; this is especially true with regard to fluid management and inhalation injury. Stabilization techniques performed by the transport team have been expanded to include procedures that are usually not performed by nursing or respiratory personnel. Such techniques include interpreting radiographs and laboratory results and then conferring with fellow team members, referring physicians, and the team’s own medical staff in order to arrive at a diagnosis and plan for stabilization. The transport team may perform such procedures as venous cannulation, endotracheal intubation, arterial blood gas interpretation, and management of mechanical ventilators. Team members may request new radiographs, in order to assess catheter or endotracheal tube placement or to assess the pulmonary system’s condition. Team members may aid in the diagnosis of air leaks (pneumothorax) and evacuate the pleural space of the lung by needle aspiration as indicated. All of these procedures may be immediately necessary and life-saving. Cross-training of all team members to be able to perform the others’ jobs is recommended in order to safeguard patients in the event that any team member becomes incapacitated during transport. All these skills can be learned via experience in a burn intensive care unit, through formal training seminars, and via a thorough orientation program. Mature judgment, excellent clinical skills, and the ability to function under stress are characteristics needed when selecting candidates for a transport program.

Patient assessment prior to transport to a specialized burn care unit from a referring hospital

Initial assessment upon arrival of a flight team should include a list of standard procedures for determining a burned patient’s current condition. First, a thorough review of the patient’s history concerning the accident and past medical history must be done. This process provides the transport team with an excellent base from which to begin to formulate a plan of action. The patient will certainly have been diagnosed by a referring physician; however, a transport team often finds problems overlooked in initial evaluations. Since burn care is a specialized field, modes of treatment...
may vary greatly outside the burn treatment community. Frequently, a referring hospital is not well versed in the treatment of burn victims and should not be expected to display the expertise found among clinicians who work with such patients’ everyday. Thus, the next step in stabilizing a burn patient is a physical assessment done by a transport team. These procedures should always be performed in the same order and in a structured fashion. Assessment of a burn patient begins with the ABCs of a primary survey, including airway, breathing, circulation, cervical spine immobilization, and a brief baseline neurological examination. All patients should be placed on supplemental oxygen prior to transport in order to minimize the effects of altitude changes on oxygenation. Two IV lines should be started peripherally with a 16-gauge catheter or larger. Ideally, IV lines should be placed in non-burned areas but may be placed through a burn if they are the only sites available for cannulation. Intravenous lines should be sutured in place because venous access may not be available after the onset of generalized edema. The fluid of choice for initial resuscitation is lactated Ringer’s solution.

In addition to initial stabilization procedures, blood should be obtained for initial laboratory studies if not already done. Initial diagnostic studies include hemocrit, electrolytes, urinalysis, chest X-ray, arterial blood gas, and carboxyhemoglobin levels. Any correction of laboratory values must be done prior to transfer and verified with repeat studies. Electrocardiographic monitoring should be instituted on any patient prior to transfer. Electrode patches may be a problem to place because the adhesive will not stick to burned skin. If alternative sites for placement cannot be found, an option for monitoring is to insert skin staples and attach the monitor leads to them with alligator clips. This provides a stable monitoring system, particularly for the agitated or restless patient who may displace needle electrodes. A Foley catheter with an urometer should be placed to accurately monitor urine output. Acceptable hydration is indicated by a urine output of more than 30 mL/h in an adult (5 mL/kg/h) and at least 1 mL/kg/h in a child.

With the exception of escharotomies, open chest wounds, and actively bleeding wounds, management during transport consists of simply covering wounds with a topical antimicrobial agent or a biological dressing. Wet dressings are contraindicated because of the decreased thermoregulatory capacity of patients sustaining large burns and the possibility of hypothermia. To combat the problem of a gastric ileus, a nasogastric tube should be inserted in all burn patients in order to decompress the stomach. This is especially important for patients being transferred at high altitudes. Hypothermia can be avoided or minimized by the use of heated blankets and/or aluminized Mylar space blankets. The patient’s rectal temperature must be kept between 37.5 and 39.0°C.

A clear, concise, chronological record of the mechanism of injury and assessment of airway, breathing, and circulation should be kept in the field and en route to the hospital. This information is vital for a referring facility to better understand and anticipate the condition of the patient. Additionally, all treatments, including invasive procedures, must be recorded, along with a patient’s response to these interventions.

### Summary

Burn injuries present a major challenge to a healthcare team, but an orderly, systematic approach can simplify stabilization and management. A clear understanding of the pathophysiology of burn injuries is essential for providing quality burn care in the pre-hospital setting, at the receiving healthcare facility, and at the referring hospital prior to transport. After a patient has been rescued from an injury-causing agent, assessment of the burn victim begins with a primary survey. Life-threatening injuries must be treated first, followed by a secondary survey, which documents and treats other injuries or problems. Intravenous access may be established in concert with logical/regional medical control and appropriate fluid resuscitation begun. Burn wounds should be covered with clean, dry sheets; and the patient should be kept warm with blankets to prevent hypothermia. The patient should be transported to an emergency room in the most appropriate mode available.

At the local hospital, it should be determined if a burn patient needs burn center care according to the American Burn Association Guidelines. In preparing for organizing a transfer of a burn victim, consideration must be given to the continued monitoring and management of the patient during transport. In transferring burn patients, the same priorities developed for pre-hospital management remain valid. During initial assessment and treatment and throughout transport, the transport team must ensure that the patient has an adequate airway, breathing, circulation, fluid resuscitation, urine output, and pain control. Ideally, transport of burn victims will occur through an organized, protocol-driven plan, which includes specialized transport mechanisms and personnel. Successful transport of burn victims, whether in the pre-hospital phase or during interhospital transfer, requires careful attention to treatment priorities, protocols, and details.

### Further reading


References

Pathophysiology of burn shock and burn edema

George C. Kramer

Introduction and historical notes

Cutaneous thermal injury involving more than one-third of the total body surface area (TBSA) invariably results in the severe and unique derangements of cardiovascular function known as burn shock. Shock is an abnormal physiologic state in which tissue perfusion is insufficient to maintain adequate delivery of oxygen and nutrients and removal of cellular waste products. Before the nineteenth century, investigators demonstrated that after a burn, fluid is lost from the blood and blood becomes thicker; and in 1897, saline infusions for severe burns were first advocated. However, a more complete understanding of burn pathophysiology was not reached until the work of Frank Underhill. He demonstrated that unresuscitated burn shock was associated with increased hematocrit values in burned patients, which are secondary to fluid and electrolyte loss after burn injury. Increased hematocrit values occurring shortly after severe burn were interpreted as a plasma volume deficit. Cope and Moore showed that the hypovolemia of burn injury resulted from fluid and protein translocation into both burned and non-burned tissues.

Animal and clinical studies have established the importance of fluid resuscitation for burn shock. Investigations have focused on correcting the rapid and massive fluid sequestration in the burn wound and the resultant hypovolemia. The peer-reviewed literature contains a large experimental and clinical database on the circulatory and microcirculatory alterations associated with burn shock and edema generation in both the burn wound and non-burned tissues. During the last 50 years, research has focused on identifying and defining the mechanisms and effects of the many inflammatory mediators produced and released after burn injury.

Burn shock is a complex process of circulatory and microcirculatory dysfunction that is not easily or fully repaired by fluid resuscitation. Severe burn injury results in significant hypovolemic shock and substantial tissue trauma, both of which cause the formation and release of many local and systemic mediators. Burn shock results from the interplay of direct tissue injury, hypovolemia, and the release of multiple mediators of inflammation, with effects on both the microcirculation and the function of large vessels, heart and lungs. Subsequently, burn shock continues as a significant pathophysiologic state, even if hypovolemia is corrected. Increases in pulmonary and systemic vascular resistance (SVR) and myocardial depression occur despite adequate preload and volume support. Such cardiovascular dysfunctions can further exacerbate the whole body inflammatory response into a vicious cycle of accelerating organ dysfunction. Hemorrhagic hypovolemia with severe mechanical trauma can provoke a similar form of shock.

This chapter examines our current understanding of the pathophysiology of the early events in burn shock, focusing on the many facets of organ and systemic effects resulting directly from hypovolemia and circulating mediators. Inflammatory shock mediators, both local and systemic, that are implicated in the pathogenesis of burn shock include histamine, serotonin, bradykinin, nitric oxide, oxygen free radicals and products of the eicosanoid acid cascade, prostaglandin, thromboxane, tumor necrosis factor, and interleukins. Additionally, certain hormones and mediators of cardiovascular function are elevated severalfold after burn injury; these include epinephrine, norepinephrine, vasopressin, angiotensin II, and neuropeptide-Y. Other mediators and unknown factors yet to be defined are also involved. Understanding the complex mechanism of the pathophysiologic actions of these mediators may be of great relevance when optimally effective therapies are designed. The hope is that improved early treatment of burn shock, perhaps through individualized fluid resuscitation protocols and methods of mediator blockade, can be developed to ameliorate the severity of organ dysfunction. Effective burn resuscitation and treatment of burn shock remains a major challenge in medicine.

Hypovolemia and rapid edema formation

Burn injury causes extravasation of plasma into the burn wound. Extensive burn injuries are hypovolemic in nature and characterized by hemodynamic changes similar to those that occur after hemorrhage, including decreased plasma volume, cardiac output, and urine output; and an increased systemic vascular resistance with resultant reduced peripheral blood flow. However, as opposed to a fall in hematocrit with hemorrhagic hypovolemia due to transcapillary refill, an increase in hematocrit and hemoglobin concentration will often appear despite fluid resuscitation. As in the treatment of other forms of hypovolemic shock, the primary initial therapeutic goal is to promptly restore vascular volume and to preserve tissue perfusion in order to minimize tissue...
formation was rapid, with over 50% occurring in the first hour, maximum water content was not present until 12–24 hours after burn injury.

**Normal microcirculatory fluid exchange**

An understanding of the physiologic mechanisms of the rapid formation of burn edema requires an understanding of the mechanisms of microvascular fluid balance. Under physiologic steady-state conditions blood pressure in capillaries causes a filtration of fluid into the interstitial space. Filtered fluid may be partially reabsorbed into the circulation at the venous end of capillaries and venules, but the bulk of the filtrate is removed from the interstitial space by lymphatic drainage. Fluid transport across the microcirculatory wall in normal and pathological states is quantitatively described by the Landis–Starling equation:

\[ J_v = K_f [(P_c - P_d) - \sigma (\pi_p - \pi_d)] \]

This describes the interaction of physical forces that govern fluid transfer between vascular and extravascular compartments. \( J_v \) is the volume of fluid that crosses the microvascular barrier. \( K_f \) is the capillary filtration coefficient, which is the product of the surface area and hydraulic conductivity of the capillary wall; \( P_c \) is the capillary hydrostatic pressure; \( P_d \) is the interstitial fluid hydrostatic pressure; \( \pi_p \) is the colloid osmotic pressure of plasma; \( \pi_d \) is the colloid osmotic pressure of interstitial fluid; \( \sigma \) is the osmotic reflection coefficient. Edema occurs when the lymphatic drainage \( (J_L) \) does not keep pace with the increased \( J_v \) (Fig. 8.1).

**Mechanisms of burn edema**

Analyzing the factors that connect the physiological determinants of transmicrovascular fluid flux (i.e. the Landis–Starling equation) shows that edema forms with increased...
$K_f$, $P_i$, or $\pi_{if}$, and with decreased $P_{if}$, $\sigma$, and $\pi_p$. Burn edema is unique in its rapidity compared to other types of edema, because it is only in burn edema that all of these variables change significantly in the direction required to increase fluid filtration. Each Starling variable is discussed individually below. For perspective, the normal imbalance or net filtration pressure across the microvascular wall is only 0.5–1 mmHg. Thus, an increased pressure gradient of 1 mmHg increases filtration two- to threefold, and an increase of 10 mmHg would increase filtration 10–20-fold.

### Capillary filtration coefficient ($K_f$)

Burn injury causes direct and indirect mediator-modulated changes in the permeability of the blood–tissue barrier of the capillaries and venules. Arturson and Mellander showed that, in the scalded hindlimb of dogs, $K_f$ immediately increased two to three times, suggesting that the hydraulic conductivity (water permeability) of the capillary wall increased. $K_f$ is a function of both hydraulic conductivity and the capillary surface area. Thus, local vasodilation and microvascular recruitment contribute to the increased $K_f$ in addition to increased hydraulic conductivity. Measuring $K_f$ and the rate of edema formation ($J_f$) allowed Arturson and Mellander to determine the changes in transcapillary forces necessary to account for the increased capillary filtration. Their calculations indicated that a transcapillary pressure gradient of 100–250 mmHg was required to explain the extremely rapid edema formation that occurred in the first 10 minutes after a scald injury. They concluded that only a small fraction of the early formation of burn edema could be attributed to the changes in $K_f$ and permeability. They further suggested that osmotically active molecules generating sufficiently large osmotic reabsorption pressures are released from burn-damaged cells. This hypothesis was never confirmed, and subsequent studies described below show that such large increases in filtration force could be attributed to increased $P_i$, and particularly to a large decrease in $P_{if}$ (Table 8.1).

### Capillary pressure ($P_i$)

In most forms of shock capillary pressure decreases as venous pressure decreases and less arterial pressure is transferred to the capillary due to arteriolar vasoconstriction. However, in studies using the vascular occlusion technique in the scalded hindlimb of dogs, $P_i$ doubled from $\sim$25 mmHg to $\sim$50 mmHg during the first 30 minutes after burn injury, and slowly returned to baseline over 3 hours.47

#### Interstitial hydrostatic pressure ($P_{if}$)

An initially surprising, but now well-verified, finding is that $P_{if}$ in dermis becomes extremely negative after thermal injury. Using micropipettes and a tissue oncometer, Lund reported that dermal $P_{if}$ was rapidly reduced from its normal value of $\sim$1 mmHg to less than $\sim$100 mmHg in isolated non-perfused samples of skin. This large negative interstitial hydrostatic pressure constitutes a powerful ‘suction force’ or imbibition pressure, adding to the elevated capillary pressure in promoting microvascular fluid filtration. In vivo measurements show a temporary reduction of $\sim$20 to $\sim$30 mmHg; the less negative $P_{if}$ in vivo is due to the continued tissue perfusion and fluid extravasation that relieves the imbibition pressure. After resuscitation, $P_{if}$ was reported increased to a positive value of 1–2 mmHg in one study.48 On the other hand, Kinsky reported a continued negative pressure providing a partial explanation for the sustained edema for the first four hours post injury. During the first several days post burn injury tissue volume and hydration are greatly elevated, with a slight decrease or no change in $P_{if}$. By definition this implies an elevated interstitial compliance, which is likely to be the main mechanism that sustains burn edema.

The size of the decrease in $P_{if}$ establishes it as the factor predominantly responsible for both the initial rapid development of edema and the sustained edema. The mechanism for the large decrease in $P_{if}$ is due, at least in part, to the release of cellular tension exerted on the collagen and microfibril networks in the connective tissue via the collagen-binding $\beta_1$-integrins. The integrins are transmembrane adhesion receptors that mediate cell–cell and cell–matrix adhesion, thereby allowing the glycosaminoglycan ground substance, which is normally underhydrated, to expand and take up fluid.58 The magnitude of the reduction in $P_{if}$ is also observed in several non-burn inflammatory reactions (48/80 and PAF). However, these mediator-induced changes are milder, with a lowering of $P_{if}$ to $\sim$5 to $\sim$10 mmHg. The much greater decrease in burn injury versus mediator-induced inflammation suggests additional mechanisms in burn

### Table 8.1 Effect of burn injury on changes in the Starling equation variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Normal or baseline</th>
<th>Post-burn</th>
<th>$\Delta$</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>$P_c$</td>
<td>$\sim$25 mmHg</td>
<td>$\sim$50 mmHg</td>
<td>↑ $\sim$25 mmHg</td>
<td>47</td>
</tr>
<tr>
<td>$\Pi_i$</td>
<td>20–28 mmHg</td>
<td>15 to 18 mmHg</td>
<td>↓ $\sim$10 mmHg</td>
<td>51, 52</td>
</tr>
<tr>
<td>$P_i$</td>
<td>$\sim$2 to 0 mmHg</td>
<td>$\sim$100 mmHg non-resuscitated</td>
<td>↓ $\sim$100 mmHg</td>
<td>19, 53–55</td>
</tr>
<tr>
<td></td>
<td></td>
<td>non-perfused skin and $\sim$5 mmHg perfused skin</td>
<td>↓ $\sim$5 mmHg</td>
<td>19, 53–55</td>
</tr>
<tr>
<td>$\Pi_f$</td>
<td>10–15 mmHg</td>
<td>13–18 mmHg in burn wound</td>
<td>↑ $\sim$3 mmHg</td>
<td>52, 54, 55</td>
</tr>
<tr>
<td></td>
<td>↓ with resuscitation hypoproteinemia in non-burned skin</td>
<td>52, 54, 55</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\sigma$</td>
<td>$\sim$0.9</td>
<td>$\sim$0.5</td>
<td>↓ $\sim$0.4</td>
<td>47, 56, 57</td>
</tr>
<tr>
<td>$K_f$</td>
<td>$\sim$0.003 mL/min/mmHg/100 g (leg)</td>
<td>↑ 2–5x</td>
<td>27, 57</td>
<td></td>
</tr>
</tbody>
</table>

Pathophysiology of burn shock and burn edema

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edema. These mechanisms remain to be identified, but may result from the direct physical destruction of the connective tissues by heat.

**Osmotic reflection coefficient (σ)**

The osmotic reflection coefficient is an index of the proportion of the full osmotic pressure generated by the concentration gradient of plasma proteins across the capillary wall. A σ = 1.0 represents a membrane impermeable to protein; σ = 0 represents a membrane that is completely permeable to protein. In skin, the normal σ of albumin is reported to be 0.85–0.99. Increased capillary permeability to protein causes a reduced σ, an effective reduction in the reabsorptive oncotnic gradient across the capillary wall and a resulting increase in net fluid filtration. Lymph sampled from burned skin has shown elevated protein concentrations consistent with the large and sustained increases in capillary permeability, whereas a transient and smaller increase in capillary permeability occurs over 8–12 hours following injury in other soft tissue not directly burned. Pitt et al. estimated the σ for skin from dog hindpaw using a lymph washdown technique and reported a normal σ of 0.87 for albumin and a reduction to 0.45 after scald injury.

**Plasma colloid osmotic pressure (πp)**

The normal plasma protein concentration of 6–8 g/dL, and its associated πp, of 25–30 mmHg, produces a significant transcapillary reabsorptive force counterbalancing other Starling forces that favor filtration. Plasma colloid osmotic pressure decreases in non-resuscitated burn injured animals as protein-rich fluid extravasates into burn wounds, and a significant volume of protein-poor transcapillary reabsorption comes from non-burned tissue, such as skeletal muscle. Plasma is further diluted and πp is further reduced after crystalloid resuscitation. Zetterstrom and Arturson found that πp was reduced to half of the normal values in burn patients; πp can decrease so rapidly with resuscitation that the transcapillary colloid osmotic pressure gradient (πp – πi) will approach zero or even reverse to favor filtration and edema. Although it is likely that some hypoproteinemia is inevitable after major burn injury, animal and clinical studies using early colloid resuscitation produce higher levels of πp than with crystalloid resuscitation alone. The degree of hypoproteinemia and reduced πp were reported to correlate with the total volume of crystalloid solutions. Initial therapy with colloid solution has always been advocated by some clinicians, but the majority wait 8–24 hours after injury, reasoning that some normalization of microvascular permeability in injured tissue must occur before colloid therapy is cost effective. In recent years there appears to be greater use of albumin therapy earlier for burn resuscitation, and there is new evidence for improved outcomes with albumin resuscitation of burns.

**Interstitial colloid osmotic pressure (πi)**

The πi in skin is normally 10–15 mmHg or about one-half that of plasma. Experimental studies in animals using lymph as representative of interstitial fluid suggest that the colloid osmotic pressure in lymph from burned skin initially increases 4–8 mmHg after burn injury. However, more direct measurements of πi using wick sampling or tissue sampling techniques show only modest initial increases in πi of 1–4 mmHg in the early non-resuscitated phase of burn injury. With resuscitation, πi falls and then πi decreases, as the protein concentration of capillary filtrate remains less than that of plasma despite an increased permeability. The osmotic reflection coefficient, σ, decreases with burns, but never equals zero, thus protein concentration in filtrate is less than in plasma even in burned skin. Compared to non-burned skin the πi remains significantly higher in the burn wound, supporting the view that sustained increases in protein permeability contribute to the persistence of burn edema. However, compared with the large changes in P, particularly Pd, increased capillary protein permeability is not the predominant mechanism for the early rapidly rising edema formation in injured skin.

**Non-burned tissue**

Generalized edema in soft tissues not directly injured is another characteristic of large cutaneous burns. Brouhard et al. reported increased water content in non-burned skin even after a 10% burn, with the peak edema occurring 12 hours post burn. Arturson reported an increased transcapillary fluid flux (lymph flow) from non-burned tissue and a transient increase in permeability, as measured by an increase in the lymph concentration of plasma protein and macromolecular dextran infused as a tracer. Harm et al. extended these findings by measuring changes in lymph flow and protein transport in non-injured soft tissue for 3 days after injury. They found that skin and muscle permeability (flank lymph from sheep) were elevated for up to 12 hours post burn for molecules the size of albumin and immunoglobulin G, but the microvascular permeability of the lung (lymph for caudal mediastinal node) showed no increase. Maximum increased lymph flow and tissue water content were observed to correlate with the severe hypoproteinemia that occurred during the early resuscitation period of a 40% burn injury in sheep. The sustained increase in water content and the elevated lymph flow of the non-burned tissue after the return of normal permeability is likely the result of the sustained hypoproteinemia.

Demling and colleagues suggested that the edema could be partially attributed to alterations in the interstitial structure. They suggested that interstitial protein washout increases the compliance of the interstitial space and that water transport and hydraulic conductivity across the entire blood–tissue–lymph barrier increased with hypoproteinemia. Several clinical and animal studies have established that maintaining higher levels of total plasma protein concentration can ameliorate the overall net fluid retention and edema. Non-burn edema can also be moderated by infusion of non-protein colloids such as dextran, if the colloid osmotic gradient is increased above normal. However, it is not known whether either the correction of hypoproteinemia or the use of either albumin or dextran leads to improved clinical outcome. It has been reported that the use of colloids has no beneficial effect on edema in the burn wound. Use of hypertonic saline formulations as initial fluid
therapies for burn shock can greatly reduce initial volume requirements and net fluid volume ( infused in minus urine out ). However, a rebound of fluid requirements and net fluid can occur after early use of hypertonic and colloids. 

Retrospective analyses of patients correlating early albumin use with fluid requirements show significant volume sparing during the first post-burn day, but after 48 hours the effect is less apparent.

### Altered cellular membranes and cellular edema

In addition to a loss of capillary endothelial integrity, thermal injury also causes change in the cellular membrane. In skeletal muscle cellular transmembrane potentials decrease away from the site of injury. It would be expected that the directly injured cell would have a damaged cell membrane, increasing sodium and potassium fluxes and resulting in cell swelling. However, this process also occurs in cells that are not directly heat-injured. Micropuncture techniques have demonstrated partial depolarization in the normal skeletal muscle membrane potential of $-90 \text{ mV}$ to levels of $-70$ to $-80 \text{ mV}$; cell death occurs at $-60 \text{ mV}$. The decrease in membrane potentials is associated with an increase in intracellular water and sodium. Similar alterations in skeletal membrane functions and cellular edema have been reported in hemorrhagic shock and in cardiac, liver, and endothelial cells. Action potentials become dampened or non-existent, with likely delays in signal propagation in nerves, brain, skeletal muscle, heart, diaphragm, and gastrointestinal organs. Encephalopathy, muscle weakness, impaired cardiac contractility and gut dysfunction are associated with major burn injury, and may be due in part to reduced membrane potentials. Early investigators of this phenomenon postulated that a decrease in ATP levels or ATPase activity was the mechanism for membrane depolarization. However, more recent research suggests that it may result from an increased sodium conductance in membranes, or that an increase in sodium–hydrogen antiporter activity is the primary mechanism. Resuscitation of hemorrhage rapidly restores depolarized membrane potentials to normal, but resuscitation of burn injury only partially restores the membrane potential and intracellular sodium concentrations to normal levels, demonstrating that hypovolemia alone is not totally responsible for the cellular swelling seen in burn shock. A circulating shock factor(s) is likely to be responsible for the membrane depolarization. When plasma from a burn-injured animal is superfused to an isolated muscle preparation, membrane depolarization occurs. Further, the depolarization can be reversed by changing the superfusion to normal plasma or saline. Surprisingly, the molecular characterization of such circulating factors have not been elucidated, suggesting that it has a complex and perhaps dynamic structure. Data suggest a large molecular weight, >80 kDa. Membrane depolarization may be caused by different factors in different states of shock. Very little is known about the time course of the changes in membrane potential in clinical burns. More importantly, we do not know the extent to which the altered membrane potentials affect total volume requirements and organ function in burn injury, or even shock in general.

### Inflammatory mediators of burn injury

A veritable cornucopia of local and circulating mediators are produced in the blood or released by cells after thermal injury. These mediators clearly play important but complex roles in the pathogenesis of edema and the cardiovascular abnormalities of burn injury. Many mediators alter vascular permeability and transcapillary fluid flux, either directly or indirectly, by increasing the microvascular hydrostatic pressure and surface area via the arteriolar vasodilation superimposed on an already altered membrane. The exact mechanism(s) of mediator-induced injury are of considerable clinical interest, as this understanding would allow for the development of pharmacologic modulation of burn edema and shock by mediator inhibition. Unfortunately, strategies directed at mediator blockage have only been effective in small localized burn wounds and have had little clinical impact for care of patients with major burns.

#### Histamine

Histamine is a key mediator responsible for the early phase of increased microvascular permeability seen immediately after burn. Histamine causes large endothelial gaps to transiently form as a result of the contraction of venular endothelial cells. Histamine is released from mast cells in thermally injured skin; however, the increase in histamine levels and its actions are only transient. Histamine also can cause the rise in capillary pressure ($P_c$) by arteriolar dilation and venular contraction. Statistically significant reductions in localized edema have been achieved with histamine blockers and mast cell stabilizers when tested in animal models. Friedl et al. demonstrated that the pathogenesis of burn edema in the skin of rats appears to be related to the interaction of histamine with xanthine oxidase and oxygen radicals. Histamine and its metabolic derivatives increased the catalytic activity of xanthine oxidase (but not xanthine dehydrogenase) in rat plasma and in rat pulmonary artery endothelial cells. In thermally injured rats, levels of plasma histamine and xanthine oxidase rose in parallel, in association with the increase in uric acid. Burn edema was greatly attenuated by treating rats with the mast cell stabilizer cromolyn, complement depletion, or the $H_2$ receptor antagonist cimetidine, but was unaffected by neutrophil depletion. Despite encouraging results in animals, beneficial antihistamine treatment of human burn injury has not been demonstrated, although antihistamines are administered to reduce the risk of gastric ulcers.

#### Prostaglandins

Prostaglandins are potent vasoactive autacoids synthesized from the arachidonic acid released from burned tissue and inflammatory cells, and contribute to the inflammatory response of burn injury. Activated macrophages and neutrophils infiltrate the wound and release prostaglandin as well as thromboxanes, leukotrienes and interleukin (IL)-1. These wound mediators have both local and systemic effects. Prostaglandin $E_2$ ($PGE_2$) and leukotrienes $LB_4$ and $LD_4$ increase microvascular permeability both directly and indirectly. $PGE_2$ is produced in burn injury and
is also a vasodilator, but also may cause direct increases in capillary permeability. PGE₂ appears to be one of the more potent inflammatory prostaglandins, causing postburn vasodilation and increased microvascular surface area in wounds, which when coupled with the increased microvascular permeability amplifies edema formation.⁸³,⁸⁶

**Thromboxane**

Thromboxane A₂ (TXA₂) and its metabolite, thromboxane B₂ (TXB₂) are produced locally in burn wounds by platelets.⁸⁸ Vasoconstrictor thromboxanes may be less important in edema formation; however, by reducing blood flow they can contribute to a growing zone of ischemia under the burn wound and can cause the conversion of a partial-thickness wound to a deeper, full-thickness wound. The serum level of TXA, and TXA₂/PGI₂ ratios are significantly increased in burn patients.⁹⁵ Heggars showed the release of TXB₂ at the burn wound, which was associated with local tissue ischemia, while thromboxane inhibitors prevented the progressive dermal ischemia associated with thermal injury and thromboxane release.⁵⁵,⁸⁷ The TXA₂ synthesis inhibitor anisodamine also showed beneficial macrocirculatory effects by restoring the hemodynamic and rheological disturbances towards normal. Demling⁹⁸ showed that topically applied ibuprofen (which inhibits the synthesis of prostaglandins and thromboxanes) reduces both local edema and prostanooid production in burned tissue without altering systemic production. On the other hand, systemic administration of ibuprofen did not modify early edema, but did attenuate the postburn vasoconstriction that impaired adequate oxygen delivery to tissue in burned sheep.³⁸ Although cyclooxygenase inhibitors have been used after burn injury, no convincing benefit, nor their routine clinical use have been reported.

**Kinins**

Bradykinin is a local mediator of inflammation that increases venular permeability. It is likely that bradykinin production is increased after burn injury, but its detection in blood or lymph can be difficult owing to the simultaneous increase in kininase activity and the rapid inactivation of free kinins. The generalized inflammatory response after burn injury favors the release of bradykinin.⁹⁵ Pretreatment of burn-injured animals with aprotinin, a general protease inhibitor, should have decreased the release of free kinin, but no effect on edema was noted.¹⁰⁰ On the other hand, pretreatment with a specific bradykinin receptor antagonist was reported to reduce edema in burn wounds in rabbits⁹⁸ (Table 8.2).

**Serotonin**

Serotonin is released early after burn injury.³² This agent is a smooth-muscle constrictor of large blood vessels. Antiserotonin agents such as ketanserin have been found to reduce peripheral vascular resistance after burn injury, but not to reduce edema.³² On the other hand, pretreatment with methysergide, a serotonin antagonist, reduces hyperemic or increased blood flow response in the burn wounds of rabbits and reduces burn edema.⁹⁴ Methysergide did not prevent increases in the capillary reflection coefficient or permeability.⁹² Ferrara et al.⁹² found a dose-dependent reduction of burn edema when methysergide was given to dogs prior to burn injury, but claimed that this was not attributable to blunting of the regional vasodilator response. Zhang et al. reported a reduction in skin blood flow after methysergide administration to burned rabbits.⁹⁵

**Catecholamines**

Circulating catecholamines epinephrine and norepinephrine are released in massive amounts after burn injury.⁷,⁹⁴,⁹⁵ On the arteriolar side of the microvessels these agents cause vasoconstriction via α₁-receptor activation, which tends to reduce capillary pressure, particularly when combined with the hypovolemia and the reduced venous pressure of burn shock.⁸ Reduced capillary pressure may limit edema and induce transcapillary refill and autoresuscitation of protein-poor interstitial fluid reabsorbed from non-burned skin, skeletal muscle, and visceral organs, especially in under-resuscitated burn shock. Even in non-resuscitated animals, plasma protein concentration falls. Further, catecholamines, via β-agonist activity, may also partially inhibit increased capillary permeability induced by histamine and bradykinin.²⁸ These potentially beneficial effects of catecholamines may not be operative in directly injured tissue, and may also be offset in non-burned tissue by the deleterious vasoconstrictor and ischemic effects. The hemodynamic effects of catecholamines will be discussed later in the chapter.

**Oxygen radicals**

Oxygen radicals play an important inflammatory role in all types of shock, including burn. These short-lived elements are highly unstable reactive metabolites of oxygen; each one has an unpaired electron, making them strong oxidizing agents.⁹⁶ Superoxide anion (O₂⁻), hydrogen peroxide (H₂O₂), and hydroxyl ion (OH⁻) are produced and released by activated neutrophils after any inflammatory reaction or reperfusion of ischemic tissue. The hydroxyl ion is believed to be the most potent and damaging of the three. The formation of the hydroxyl radical requires free ferrous iron (Fe²⁺) and H₂O₂. Evidence that these agents are formed after burn injury is the increased lipid peroxidation found in circulating red blood cells and biopsied tissue.²⁹,⁹⁶,⁹⁷ Demling⁹⁸ showed that large doses of deferoxamine (DFO), an iron chelator, when used for resuscitation of 40% TBSA in sheep, prevented systemic lipid peroxidation and reduced the vascular leak in non-burned tissue, while also increasing oxygen utilization. However, DFO may have accentuated burned tissue edema, possibly by increasing the perfusion of burned tissue.

Nitric oxide (NO) generated simultaneously with the superoxide anion can lead to the formation of peroxynitrite (ONOO⁻). The presence of nitrotyrosine in burned skin found in the first few hours after injury suggests that peroxynitrite may play a deleterious role in burn edema.⁹⁵ On the other hand, the blockade of NO synthase did not reduce burn edema, whereas treatment with the NO precursor arginine does reduce burn edema.¹⁰⁰ NO may be important for maintaining perfusion and limiting the zone of stasis in burn skin.¹⁰⁰ Although the pro- and anti-inflammatory roles of NO remain controversial, it would appear that the acute beneficial effects of NO generation outweigh any deleterious effect in burn shock.
Antioxidants, namely agents that either bind directly to the oxygen radicals (scavengers) or cause their further metabolism, have been evaluated in several experimental studies.\textsuperscript{102,103} Catalase removes H\textsubscript{2}O\textsubscript{2} and superoxide dismutase (SOD), lessens radical O\textsubscript{2}\textsuperscript{−}, and is reported to reduce the vascular loss of plasma after burn injury in dogs and rats.\textsuperscript{29,30}

The plasma of thermally injured rats showed dramatic increases in levels of xanthine oxidase activity, with peak values appearing as early as 15 minutes after thermal injury. Excision of the burned skin immediately after the injury significantly diminished the increase in plasma xanthine oxidase activity.\textsuperscript{29,30} The skin permeability changes were attenuated by treating the animals with antioxidants (catalase, SOD, dimethyl sulfoxide, dimethylthiourea) or an iron chelator (DFO), thereby supporting the role of oxygen radicals in the development of vascular injury as defined by increased vascular permeability.\textsuperscript{29} Allopurinol, a xanthine oxidase inhibitor, markedly reduced both burn lymph flow and levels of circulating lipid peroxides, and further prevented all pulmonary lipid peroxidation and inflammation. This suggests that the release of oxidants from burned tissue was in part responsible for local burn edema, as well as systemic inflammation and oxidant release.\textsuperscript{37} The failure of neutrophil depletion to protect against the vascular permeability changes and the protective effects of the xanthine oxidase inhibitors (allopurinol and lodoxamide tromethamine) suggests that plasma xanthine oxidase is the more likely source of the oxygen radicals involved in the formation of burn edema. These oxygen radicals can increase vascular permeability by damaging microvascular endothelial cells.\textsuperscript{29,30} The use of antioxidants has been extensively investigated in animals, and some clinical trials suggest benefit. Antioxidants (vitamin C and E) are routinely administered to patients at many burn centers. High doses of antioxidant ascorbate (vitamin C) have been found to be efficacious in reducing fluid needs in burn-injured experimental animals when administered postburn.\textsuperscript{104–106} Super-high doses (10–20 g/day) of vitamin C were shown to effectively reduce

| Table 8.2 Cardiovascular and inflammatory mediators of burn shock |
|-----------------------------------|-----------------|-----------------|----------------|
| **Mediators** | **Central cardiovascular effects** | **Load tissue effects** | **References** |
| Histamine | ↓ Blood pressure | Arteriolar dilation; Venular constriction | 28–34 |
| Prostaglandin E\textsubscript{2} (PGE\textsubscript{2}) | ↓ Systemic arterial and pulmonary arterial blood pressure | Vasodilation | 28, 35, 36 |
| Prostacyclin (PG\textsubscript{1}.) | ↓ Blood pressure | ↑ Permeability | 28 |
| Leukotrienes | Pulmonary hypertension | | 28 |
| Thromboxane A\textsubscript{2} (TXA\textsubscript{2}) | GI ischemia | Vasodilation | 35, 37–39 |
| Thromboxane B\textsubscript{2} (TXB\textsubscript{2}) | Pulmonary hypertension | ↑ Blood flow | |
| Bradykinin | ↓ Blood pressure | Vasodilation, ↑ Permeability | 28, 33 |
| Serotonin | ↑ Permeability | | 32 |
| Catecholamines | ↑ Heart rate | Vasoconstriction (receptors); Vasodilation (\(\beta\) receptors in muscle); block ↑ permeability due to histamine & bradykinin via \(\beta\) receptors | 28, 31, 40, 41 |
| Oxygen radicals: | Cardiac dysfunction | Tissue damage | 28–30, 42 |
| Superoxide | ↑ Metabolism | ↑ Permeability | |
| Anion (O\textsubscript{2}\textsuperscript{−}) | Hydrogen peroxide (H\textsubscript{2}O\textsubscript{2}) | | |
| Hydroxyl Ion (OH\textsuperscript{−}) | Peroxynitrite (ONOO\textsuperscript{−}) | | |
| Platelet aggregation factor | ↑ Blood pressure | Vasoconstriction | 43–45 |
| Angiotensin II | GI ischemia | Vasoconstriction | 46 |
| Vasopressin | GI ischemia | Vasoconstriction | 46 |

Enhanced microvascular blood flow typically increases capillary surface area.
Permeability typically refers to protein permeability of the microvascular exchange vessels, which is often linked to hydraulic conductivity.
volume requirements in one clinical trial, but were ineffective in others, albeit with somewhat different doses. High-dose vitamin C has not received wide clinical use.

Platelet aggregation factor

Platelet aggregation (or activating) factor (PAF) can increase capillary permeability and is released after burn injury. Ono et al. showed in scald-injured rabbits that TCV-309 (Takeda Pharmaceutical Co Ltd., Japan), a PAF antagonist, infused soon after burn injury, blocked edema formation in the wound and significantly inhibited PAF increase in the damaged tissue in a dose-dependent manner. In contrast, the superoxide dismutase content in the group treated with TCV-309 was significantly higher than that of the control group. These findings suggest that the administration of large doses of a PAF antagonist immediately after injury may reduce burn wound edema and the subsequent degree of burn shock by suppressing PAF and superoxide radical formation.

Angiotensin II and vasopressin

Angiotensin II and vasopressin or antidiuretic hormone (ADH), are two hormones that participate in the normal regulation of extracellular fluid volume by controlling sodium balance and osmolality through renal function and thirst. During burn shock sympathetic tone is high and volume receptors are stimulated, and both hormones are at supranormal levels in the blood. Both are potent vasoconstrictors of terminal arterioles with less effect on the venules. Angiotensin II may be responsible for the selective gut and mucosal ischemia, which can cause translocation of endotoxins and bacteria and the development of sepsis and even multiorgan failure. In severely burn-injured patients angiotensin II levels were elevated two to eight times normal in the first 1 to 5 days after injury, with peak levels occurring on day 3. Vasopressin had peak levels of 50 times normal upon admission and declined towards normal over the first 5 days after burn injury. Along with catecholamines, vasopressin may be largely responsible for increased systemic vascular resistance and left heart afterload, which can occur in resuscitated burn shock. Sun et al. used vasopressin-receptor antagonists to improve hemodynamics and survival time in rats with burn shock, whereas vasopressin infusion exacerbated burn shock.

Corticotropin-releasing factor

Corticotropin-releasing factor (CRF) has proved to be efficacious in reducing protein extravasation and edema in burned rat paw. CRF may be a powerful natural inhibitory mediator of the acute inflammatory response of the skin to thermal injury.

Other approaches to pharmacological attenuation of burn edema

Multiple reports on edema-reducing strategies using known burn mediator-blocking agents have been discussed above. However, there are other hypothesized approaches to ameliorate or inhibit the fluid extravasation induced by thermal injury. Topically applied local anesthetic lidocaine/prilocaine cream has been reported to be effective in reducing albumin extravasation in small burns in experimental animals. The inositol triphosphate analog α-trinositol has also been reported to be effective in reducing postburn edema when administered after injury. Even though α-trinositol showed promising effects in animal experiments and also seemed to reduce pain in pilot clinical projects, its clinical application is not reported.

Hemodynamic consequences of acute burns

The cause of reduced cardiac output (CO) during the resuscitative phase of burn injury has been the subject of considerable debate. There is an immediate depression of cardiac output before any detectable reduction in plasma volume. The rapidity of this response may result from impaired electrical activity of cardiac nerves and muscle and increased afterload due to vasoconstriction. Soon after injury a developing hypovolemia and reduced venous return undeniably contribute to the reduced cardiac output. The subsequent persistence of reduced CO after apparently adequate fluid therapy, as evidenced by restoration of arterial blood pressure and urinary output, has been attributed to circulating myocardial depressant factor(s), which possibly originates from the burn wound. Demling et al. showed a 15% reduction in CO despite aggressive volume replacement protocol after a 40% scald burn in sheep. However, there are also sustained increases in catecholamine secretion and elevated systemic vascular resistance for up to 5 days after burn injury. Michie et al. measured CO and SVR in anesthetized dogs resuscitated after burn injury. They found that CO fell shortly after injury and then returned toward normal; however, reduced CO did not parallel the blood volume deficit. They concluded that the depression of CO resulted not only from decreased blood volume and venous return, but also from an increased SVR and from the presence of a circulating myocardial depressant substance. After the resuscitation phase of burn shock, patients can have supranormal CO. This is associated with a hypermetabolic state and systemic inflammatory response syndrome (SIRS).

Myocardial dysfunction

Myocardial function can be compromised after burn injury due to the right heart overload and direct depression of contractility shown in isolated heart studies. Increases in the afterload of both the left and the right heart result from elevations in SVR and PVR. Stroke volume and CO can be maintained despite contractile depression by augmented adrenergic stimulation, albeit at a cost of increased myocardial oxygen demands. The right ventricle has a minimal capacity to compensate for increased afterload. In severe cases, desynchronization of the right and left ventricles is deleteriously superimposed on a depressed myocardium. Kinsky demonstrated both systolic and diastolic dysfunction in burn-injured children during the first few weeks post injury. Burn injury >45% TBSA can produce intrinsic contractile defects. Several investigators reported that aggressive early and sustained fluid resuscitation failed to correct left
ventricular contractile and compliance defects. These data suggest that hypovolemia is not the sole mechanism underlying the myocardial defects observed with burn shock. Serum from patients failing to sustain a normal CO after thermal injury have exhibited a markedly negative inotropic effect on in vitro heart preparations, which may be due to the circulating shock factor described above. In other patients with large burn injuries and normal cardiac indices, little or no depressant activity was detected. Traber and colleagues studied intact, chronically instrumented sheep after a 40% TBSA flame burn injury and smoke inhalation injury, and after smoke inhalation injury alone. They found that contractile force was reduced after either burn injury or inhalation injury alone. Horton et al. demonstrated decreased left ventricular contractility in isolated, coronary-perfused guinea pig hearts harvested 24 hours after burn injury. This dysfunction was more pronounced in hearts from aged animals and was not reversed by resuscitation with isotonic fluid. It was largely reversed by treatment with 4 mL/kg of hypertonic saline dextran (HSD), but only if administered during the initial 4–6 hours of resuscitation. These authors also effectively ameliorated the cardiac dysfunction of thermal injury with infusions of antioxidants, arginine and calcium channel blockers. Cioffi and colleagues, in a similar model, observed persistent myocardial depression after burn when the animals received no resuscitation after injury. As opposed to most studies, Cioffi reported that immediate and full resuscitation totally reversed abnormalities of contraction and relaxation after burn injury. Murphy et al. showed elevations of a serum marker for cardiac injury, troponin I, for patients with a TBSA > 18%, despite good cardiac indices. Resuscitation and cardiac function studies emphasize the importance of early and adequate fluid therapy and suggest that functional myocardial depression after burn injury may not occur in patients receiving prompt and adequate volume therapy.

The primary mechanisms by which burn shock alters myocardial cell membrane integrity and impairs mechanical function remain unclear. Oxygen-derived free radicals may play a key causative role in the cell membrane dysfunction that is characteristic of several low-flow states. Horton et al. showed that a combination therapy of free radical scavengers SOD and catalase significantly improved burn-mediated defects in left ventricular contractility and relaxation when administered along with adequate fluid resuscitation (4 mL/kg per percent of burn). Antioxidant therapy did not alter the volume of fluid resuscitation required after burn injury.

Increased systemic vascular resistance and organ ischemia

Cardiac output may remain below normal after adequate volume replacement in burn patients and experimental animals. After burn injury sympathetic stimulation and hypovolemia result in the release of catecholamines, vasoressin, angiotensin II, and neuropeptide-Y. These agents cause contraction of the arteriolar smooth muscle, which is systemically manifested by increased afterload and SVR. The increased SVR after burn injury is also partly the result of increased blood viscosity secondary to the hemoconcentration. Hilton and others performed experiments in anesthetized dogs in which infusion of various peripheral vasodilators improved CO after burn injury. They demonstrated a reduction in the peripheral vascular resistance and augmented CO after verapamil, but the myocardial force of contraction remained depressed. Pruitt et al. examined in a group of burn patients the hypothesis that increased sympathetic activity contributes to CO reduction. They showed a higher CO with treatment using the vasodilator hydralazine along with the reduced SVR.

There are several organs particularly susceptible to ischemia, organ dysfunction and organ failure when burn resuscitation is delayed or inadequate. These include the kidney and the gastrointestinal tract. Renal ischemia can result directly from hypovolemia and increased sympathetic tone, but elevations in serum free hemoglobin, and particularly myoglobin, correlate with increased renal failure. Renal failure rates have declined dramatically owing to standardized regimens of adequate fluid therapy, but when therapy is delayed or associated with hypotension acute renal failure is not uncommon. An occult hypoxia can result from vasoconstriction of the gastrointestinal tract, which can occur despite apparently ‘adequate’ resuscitation. Bacterial and endotoxin translocation that reduces mucosal pH and can contribute to the development of sepsis is a consequence of visceral ischemia.

Cerebropathy is not uncommon after large cutaneous burns, particularly in children, but the exact cause remains unclear. Studies in anesthetized sheep subjected to a 70% TBSA scald show that cerebral autoregulation is well maintained in the immediate postburn period, but six hours after resuscitation increased cerebral vascular resistance reduced cerebral blood flow 50%.

Edema in non-burned tissue

Lungs

In large burns there is a pronounced increase in pulmonary vascular resistance (PVR) that corresponds with the increased SVR. Pulmonary edema is not an uncommon finding and occurs more often after than during the fluid-resuscitation phase of burn injury. Increased capillary pressure secondary to the increased PVR occurs with both pre- and postcapillary vasoconstriction and may contribute to pulmonary edema formation. Pulmonary wedge pressure is increased more than left atrial pressure after experimental burn injury owing to postcapillary venular constriction. It is likely that some degree of left heart failure also contributes to the increased capillary pressure. However, hypoproteinemia may be the greatest contributing factor to postburn pulmonary edema. Analysis of lung lymph sampled in large animal models after 40% TBSA injury showed no evidence of increased capillary permeability, although rat studies suggest that albumin sequestration increases in the lungs after a 30% cutaneous scald. Clinical studies of burn-injured patients suggest that in the absence of inhalation injury the lungs do not develop edema, a finding that is consistent with the little or no change in the microvascular permeability of the lung and the fact that lung lymph rate may increase...
considerably to prevent interstitial fluid accumulation. Pulmonary dysfunction associated with inhalation injury is discussed in a separate chapter.

Edema and abdominal compartment syndrome

Prompt and adequate fluid resuscitation has undoubtedly improved the outcome of burn-injured patients. The Parkland formula for burn resuscitation, introduced by Baxter and Shires in 1968, has been the cornerstone of early burn care. Despite the treatment advances of burn surgery, massive edema of burned and non-burned tissues continues to be a repercussion of large-volume fluid resuscitation. There is a physiological conflict that exists in the balance between the edema process and hypovolemia. Edema results from the massive efflux of intravascular fluid to the interstitial space owing to altered Starling forces. As hypovolemia is treated with crystalloid infusions, edema can continue to increase.

Although the guidelines for burn resuscitation have changed little, fluid management has changed over the past two decades. Engrav and associates compiled data from seven burn centers. The results included 50 patients with 43 ± 21% TBSA burns, 16 of whom had documented inhalation injuries. The authors found that 58% of patients with large burns received volumes that greatly exceeded the formula proposed by Baxter. Their patients received close to 6 mL/kg/%TBSA (2 mL/kg/%TBSA more than the Parkland formula). Urine output also exceeded clinical targets (0.5–1 mL/kg/h) in 64% of patients. Friedrich and associates found that their patients admitted in the year 2000 received twice the resuscitation volume as those admitted in the 1970s. In yet another report, the Parkland formula was exceeded in 84% of the burn-injured patients treated. A meta-analysis of 23 burn-resuscitation trials (1980–2003) using crystalloid burn resuscitation produced similar findings. Mean fluid infused (5.0 ± 1.2 mL/kg/TBSA) and mean urinary outputs (1.2 ± 0.4 mL/kg/h) were both over the burn resuscitation guidelines, suggesting that well over half of all burn patients may be over-resuscitated.

This trend of providing fluid in excess of the Parkland formula has been termed ‘fluid creep’. Over-resuscitation and its resulting edema are not without consequences. The problems of the over-resuscitated burn patient may include eye injuries due to elevated orbital pressures, pulmonary edema, the need for prolonged mechanical ventilation, or tracheostomy, graft failure or the need for fasciotomy of uninjured extremities due to massive edema.

A life-threatening complication of edema seen with increasing frequency is abdominal compartment syndrome (ACS). Intra-abdominal pressure (IAP) >30 cmH₂O is defined as intra-abdominal hypertension (IAH). ACS is sustained IAH in association with a clinically tense abdomen combined with ventilation aberrations due to elevated pulmonary inspiratory pressures or oliguria despite aggressive fluid resuscitation. Owing to a cascade of pathophysiological events, ACS is often fatal. The syndrome typically leads to multiple organ dysfunction, characterized by impaired renal and hepatic blood flow, bowel ischemia, pulmonary dysfunction, depressed cardiac output, and elevated intracranial pressures. ACS can occur after major abdominal trauma or surgery, but the condition in the absence of abdominal injury is known as secondary ACS. Severely burn-injured patients are at risk for this development owing to increasingly large volumes of resuscitation fluid, decreased abdominal wall compliance due to eschar, increased capillary permeability with leakage of large plasma volumes, and massive edema formation.

Summary and conclusion

Thermal injury results in massive fluid shifts from the circulating plasma into the interstitial space, causing hypovolemia and swelling of the burned skin. All the Starling forces change to favor fluid extravasation from blood to tissue. Rapid edema formation is predominantly due to the development of strongly negative interstitial fluid pressure and to a lesser degree by an increase in microvascular pressure and permeability. When burn injury exceeds 20–30% TBSA there is also edema formation in non-injured soft tissues. The type of fluid used to resuscitate alone with the timing and total volume infused imparts these fluid shifts.

Secondary to the thermal injury there is release of inflammatory mediators and stress hormones. Circulating mediators deleteriously increase microvascular permeability and alter cellular membrane function, by which water and sodium enter cells. Circulating mediators also favor renal conservation of water and salt, impair cardiac contractility and cause vasoconstriction. This further aggravates ischemia due to combined hypovolemia and cardiac dysfunction. The end result of this complex chain of events is decreased intravascular volume, increased systemic vascular resistance, decreased cardiac output, end-organ ischemia, and metabolic acidosis. Without early and full resuscitation therapy these derangements can result in acute renal failure, organ dysfunction, cardiovascular collapse, and death. Early excision of the devitalized tissue appears to reduce the local and systemic effects of mediators released from burned tissue, thereby reducing the progressive pathophysiologic derangements.

Edema in the burn wound, and particularly in the non-injured soft tissue, is increased by resuscitation. Edema likely contributes to decreased tissue oxygen diffusion and further ischemic insult to already damaged cells, with compromised blood flow increasing the risk of infection. Research should continue to define better treatments that ameliorate the burn edema and vasoconstriction that exacerbate tissue ischemia. The success of this research will require the identification of key circulatory factors that alter capillary permeability, cause vasoconstriction, depolarize cellular membranes, and depress myocardial function. Hopefully, cellular or systemic methods to prevent the release or block the activity of specific mediators can be developed and reduce the morbidity and mortality burn injury.

Further reading


Cancio LC, Chavez S, Alvarado-Ortega M, et al. Predicting increased fluid requirements during the resuscitation of thermally injured
References


Fluid resuscitation and early management
Glenn D. Warden

Introduction

Proper fluid management is critical to the survival of the victim of a major thermal injury. In the 1940s, hypovolemic shock or shock-induced renal failure was the leading cause of death after burn injury. Today, with our current knowledge of the massive fluid shifts and vascular changes that occur during burn shock, mortality related to burn-induced volume loss has decreased considerably. Although a vigorous approach to fluid therapy has ensued in the last 20 years and fewer deaths are occurring in the first 24–48 h post-burn, the fact remains that approximately 50% of the deaths occur within the first 10 days following burn injury from a multitude of causes, one of the most significant being inadequate fluid resuscitation therapy. Knowledge of fluid management following burn shock resuscitation is also important and is often overlooked in burn education.

Burn shock resuscitation

The history of burn resuscitation began over a century ago; however, complete appreciation of the severity of fluid loss in burns was not apparent until the enlightening studies of Frank P. Underhill, who studied the victims of the Rialto Theater fire in 1921. His concept that burn shock was due to intravascular fluid loss was further elucidated by Cope and Moore, who conducted studies on patients from the Coconut Grove disaster in 1942. They developed the concept of burn edema and introduced the body-weight burn budget formula for fluid resuscitation of burn patients. In 1952, Evans developed a burn surface area-weight formula for computing fluid replacement in burns which became the first simplified formula for fluid resuscitation for burn patients. Surgeons at the Brooke Army Medical Center modified the original Evans formula and this became the standard for the next 15 years.

A number of methods for accomplishing adequate volume replacement therapy have been advocated in the more than 40 years since the introduction of the Evans formula in 1952. This chapter will review the various methods advocated and present the rationale of each. Importantly, properly utilized, each resuscitation formula can be effective in the resuscitation of the burn patient in the immediate post-burn period, provided that close attention is paid to the individual’s clinical response to therapy and that fluid replacement therapy is modified according to this response. The fact that patients respond to a wide variety of resuscitative efforts is testimony to the fact that burn patients are very resilient and can be overwhelmed only under the most unfavorable circumstances.

Pathophysiology of burn injury

Modern fluid resuscitation formulas originate from experimental studies in the pathophysiology of burn shock. Burn shock is both hypovolemic shock and cellular shock, and is characterized by specific hemodynamic changes including decreased cardiac output, extracellular fluid, plasma volume, and oliguria. As in the treatment of other forms of shock, the primary goal is to restore and preserve tissue perfusion in order to avoid ischemia. However, in burn shock, resuscitation is complicated by obligatory burn edema, and the voluminous transvascular fluid shifts which result from a major burn are unique to thermal trauma.

Although the exact pathophysiology of the post-burn vascular changes and fluid shifts is unknown, one major component of burn shock is the increase in total body capillary permeability. Direct thermal injury results in marked changes in the microcirculation. Most of the changes occur locally at the burn site, when maximal edema formation occurs at about 8–12 h post-injury in smaller burns and 12–24 h post-injury in major thermal injuries. The rate of progression of tissue edema is dependent upon the adequacy of resuscitation.

Multiple mediators have been proposed to explain the changes in vascular permeability seen post-burn. The mediators can produce either an increase in vascular permeability or an increase in microvascular hydrostatic pressure. Most mediators act to increase permeability by altering membrane integrity in the venules. The early phase of burn edema formation, lasting for minutes to an hour, has been thought by some investigators to be the result of mediators, particularly histamine and bradykinin. Other mediators implicated in the changes in vascular permeability seen post-burn include vasoactive amines, products of platelet activation and the complement cascade, hormones, prostaglandins, and leukotrienes. Vasoactive substances are also released which may act primarily by increasing microvascular blood flow or vascular pressures, further accentuating the burn edema. Histamine is released in large quantities from mast cells in burned skin immediately after injury. Histamine has been
clearly demonstrated to increase the leakage of fluid and protein from systemic micro vessels, its major effect being on venules in which an increase in the intracellular junction space is characteristically seen.\(^9\) However, the increase in serum histamine levels after burn is transient, peaking in the first several hours post-injury, indicating that histamine is only involved in the very early increase in permeability. The use of H\(_1\) receptor inhibitors, e.g. diphenhydramine, has only limited success in decreasing edema. Recently, the use of an H\(_2\) receptor antagonist has been reported to decrease burn edema in an animal model.\(^11\)

Serotonin is released immediately post-burn as a result of platelet aggregation and acts directly to increase the pulmonary vascular resistance and indirectly to amplify the vasoconstrictive effect of norepinephrine, histamine, angiotensin II, and prostaglandin.\(^12\) The use of ketanserin, a specific serotonin antagonist, in a porcine burn shock model, improved cardiac index, decreased pulmonary pressure, and reduced arteriovenous oxygen content differences compared to a control group in the early post-burn period. Serotonin antagonists should be investigated further as possible adjuvant therapeutic agents during burn shock resuscitation.\(^13\)

Prostaglandins, vasoactive products of arachidonic acid metabolism, have been reported to be released in burn tissue and to be at least in part responsible for burn edema. Although these substances do not directly alter vasopermeability, increased levels of vasodilator prostaglandins such as prostaglandin E\(_2\) (PGE\(_2\)) and prostacyclin (PGI\(_2\)) result in arterial dilatation in burned tissue, increased blood flow and intravascular hydrostatic pressure in the injured microcirculation, and thus accentuate the edema process. Concentrations of PGI\(_2\) and the vasoconstrictor thromboxane A\(_2\) (TXA\(_2\)) have been demonstrated in burned tissue, burn blister fluid, lymph, and wound secretion.\(^14,15\) However, the use of prostaglandin inhibitors has produced variable results in animal studies. Arturson\(^16\) reported a decrease in burn lymph and protein flow with the use of prostaglandin inhibitor, indomethacin. Those results have not been corroborated by other investigators and the role of thromboxane and the prostaglandins still needs to be elucidated.

The activation of the proteolytic cascades, including those of coagulation, fibrinolysis, the kinins, and the complement system, has been demonstrated to occur immediately following thermal injury. Kinins, specifically bradykinins, are known to increase vascular permeability, primarily in the venule. Rocha and co-workers\(^17\) report increased kinin levels in burn edema fluid in the rat. The release of other mediators and the generalized inflammatory response after burns favors the activation of the kallikrein–kinin system, with the release of bradykinin into the circulation.\(^18\) Elevation of proteolytic activity has been demonstrated in both animals and in burn patients.\(^19\) Pretreatment with protease inhibitors significantly decreases free kinin levels but appears to have little effect on the edema process.

The end result of the changes in the microvasculature due to thermal injury is disruption of normal capillary barriers separating intravascular and interstitial compartments, and rapid equilibrium of these compartments. This results in severe depletion of plasma volume with a marked increase in extracellular fluid clinically manifested as hypovolemia.

In addition to a loss of capillary integrity, thermal injury also causes changes at the cellular level. Baxter\(^20\) has demonstrated that in burns of >30% total body surface area (TBSA), there is a systemic decrease in cell transmembrane potential, involving non-thermally injured cells as well. This decrease in cell transmitting potential, as defined by the Nernst equation, results from an increase in intracellular sodium concentration. The cause of this is thought to be a decrease in sodium ATPase activity responsible for maintaining the intracellular–extracellular ionic gradient. Baxter further demonstrated that resuscitation only partially restores the membrane potential and intracellular sodium concentrations to normal levels, demonstrating that hypovolemia with its attendant ischemia is not totally responsible for the cellular swelling seen in burn shock. In fact, the membrane potential may not return to normal for many days post-burn despite adequate resuscitation. If resuscitation is inadequate, cell membrane potential progressively decreases, resulting ultimately in cellular death. This may be the final common denominator in burn shock during the resuscitation period.

Although the etiology of burn shock is not totally understood, many authors have studied the fluid volume shifts and hemodynamic changes that accompany burn shock. Early work by Moyer et al.,\(^21\) and Baxter and Shires\(^22\) established the definitive role of crystalloid solutions in burn resuscitation and delineated the fluid volume changes in the early post-burn period. Moyer’s original studies in 1965\(^23\) demonstrated that burn edema sequestered enormous amounts of fluid, resulting in the hypovolemia of burn shock. In addition, he described the first crystalloid-only resuscitation formula used to treat burn shock. He noted that burn shock recovery occurred in the majority of patients studied, although hemococoncentration remained unchanged and the hematocrit was unresponsive to fluid administration despite adequate resuscitation. This became the first objective evidence that burn shock is not simply due to hypovolemia but is also influenced by extracellular sodium depletion. Baxter and Shires,\(^22\) in 1968, using radioisotope dilution techniques, defined the fluid volume changes of the post-burn period in relation to cardiac output. They first demonstrated that edema fluid in the burn wound is isotonic with respect to plasma fluid and contains protein in the same proportions as that found in blood. This confirmed Arturson’s earlier findings that in major burns there is complete disruption of the normal capillary barrier, with free exchange between plasma and extravascular extracellular compartments. They measured changes in fluid compartment volumes in burned primates and dogs and demonstrated that in untreated (unresuscitated) animals, a 30–50% extracellular fluid (ECF) defect persisted at 18 h post-burn. Plasma volume decreased 23%, to 27% below controls, although red cell mass changed only about 10% over the same 18-hour period. Thus, the greatest volume loss was functional intravascular extracellular fluid. Cardiac output was initially depressed very soon after injury to a level of about 25% of controls at 4 h after a 30% TBSA burn. By 18 h, however, the cardiac output had stabilized at around 40% of control, despite persistent defects in plasma and ECF volumes. On the basis of studies using different volumes of resuscitation fluids, they arrived at an optimal response in terms of cardiac output and restoration of ECF at the end of 24 h in a canine model. Clinical studies using similar sodium and fluid loads immediately followed, confirming efficacy in restoring ECF to within 10% of controls within 24 h. This
became the basis for the Baxter or Parkland formula. Mortality was comparable to that obtained with a colloid-containing resuscitation formula.

Baxter went on to demonstrate that during the first 24 h post-burn, plasma volume changes were independent of the type of infused fluid, whether crystalloid or colloid, but at approximately 24 h post-injury, an infused amount of colloid would increase the plasma volume by the same amount. His findings prove that colloid-containing solutions are an unnecessary component of fluid resuscitation in the first 24 h. He recommended their use only after capillary integrity was restored, to correct the persistent plasma volume deficit of about 20% as measured externally. While the fluid shifts were being defined by Baxter in terms of crystalloid resuscitation, Pruitt and co-workers worked to characterize the hemodynamic alterations that occur in burn shock with and without fluid resuscitation. Their efforts culminated in the Brooke formula modification which utilized 2 cc/kg/% burn during the first 24 h. Fluid needs were initially estimated according to the modified Brooke formula, but the actual volume for resuscitation was based on clinical response. In their study, resuscitation permitted an average decrease of about 20% in both extracellular fluid and plasma volume, but no further loss accrued in the first 24 h. In the second 24 h post-burn, plasma volume restoration occurred with the administration of colloid. Blood volume, however, was only partially restored and an ongoing loss of 9% of the red cell mass per day was found. Cardiac output, initially quite low, rose over the first 18 h post-burn, despite plasma volume and blood volume defects. These results were quite consistent with those demonstrated by Baxter in his animal studies. Peripheral vascular resistance during the initial 24 h was initially very high but decreased as cardiac output improved, and in fact the changes were reciprocal. Once plasma volume and blood volume loss ceased, cardiac output rose to supranormal levels where it remained until healing or grafting occurred.

Moylan and associates in 1973, using a canine model, defined the relationships between fluid volumes, sodium concentration, and colloid in restoring cardiac output during the first 12 h post-injury. No significant colloid effect on cardiac output was noted in the first 12 h post-injury. In addition, 1 mEq of sodium was found to exert an effect on cardiac output equal to 13 times that of 1 mL of salt-free volume. This experiment established the fact that any combination of sodium and volume within the broad limits of the study would effectively resuscitate a thermally injured patient.

Arturson’s landmark studies in 1979 on vascular permeability characterized the nature of the ‘leaky capillary’ in the post-burn period. He demonstrated in a canine model that increased capillary permeability is found both locally and in non-burned tissue at distant sites when the TBSA burn exceeded 25%. He proposed that the burn wound is characterized by rapid edema formation due to dilatation of the resistance vessels (precapillary arterioles); increased extravascular osmotic activity, due to the products of thermal injury; and increased microvascular permeability to macromolecules. The increased permeability permits molecules of up to 350000 molecular weight to escape from the microvasculature, a size which allows essentially all elements of the vascular space except red blood cells to escape from it. Further studies by Demling and co-workers have demonstrated that in 50% TBSA burns, one-half of the initial fluid resuscitation requirement may end up in non-thermally injured tissues.

**Resuscitation from burn shock**

Fluid resuscitation is aimed at supporting the patient throughout the initial 24-hour to 48-hour period of hypovolemia. The primary goal of therapy is to replace the fluid sequestered as a result of thermal injury. The critical concept in burn shock is that massive fluid shifts can occur even though total body water remains unchanged. What actually changes is the volume of each fluid compartment, intracellular and interstitial volumes increasing at the expense of plasma volume and blood volume. In light of all the studies on different fluid regimens, the question still remains: ‘What is the best formula for resuscitation of the burn patient?’

It is quite clear that the edema process is accentuated by the resuscitation fluid. The magnitude of edema will be affected by the amount and type of fluid administered. The National Institutes of Health consensus summary on fluid resuscitation in 1978 was not in agreement in regard to a specific formula; however, there was consensus in regard to two major issues – the guidelines used during the resuscitation process and the type of fluid used. In regard to the guidelines, the consensus was to give the least amount of fluid necessary to maintain adequate organ perfusion. The volume infused should be continually titrated so as to avoid both under-resuscitation and over-resuscitation. As for the optimum type of fluid, there is no question that replacement of the extracellular salt lost into the burned tissue and into the cell is essential for successful resuscitation.

**Crystalloid resuscitation**

Crystalloid, in particular lactated Ringer’s solution with a sodium concentration of 130 mEq/L, is the most popular resuscitation fluid currently utilized. Proponents of the use of crystalloid solution alone for resuscitation report that other solutions, specifically colloids, are no better and are certainly more expensive than crystalloid for maintaining intravascular volume following thermal injury. The most common reason given for not using colloids is that even large proteins leak from the capillary following thermal injury. However, capillaries in non-burned tissues do continue to sieve proteins, maintaining relatively normal protein permeability characteristics.

The quantity of crystalloid needed is in part dependent upon the parameters used to monitor resuscitation. If a urinary output of 0.5 cc/kg/hour is considered to indicate adequate perfusion, approximately 3 cc/kg/% burn will be needed in the first 24 h. If 1 cc/kg of body weight/hour of urine is deemed necessary, then of course considerably more fluid will be needed and in turn more edema will result. The Parkland formula recommends 4 cc/kg/% burn in the first 24 h, with one-half of that amount administered in the first 8 h. The modified Brooke formula recommends beginning burn shock resuscitation at 2 cc/kg/% burn in the first 24 h. In major burns, severe hypoproteinemia usually develops with these resuscitation regimens. The hypoproteinemia and
with lactated Ringer’s solution. Urine output was the indicator used during resuscitation. Demling and colleagues\textsuperscript{31} in an animal model demonstrated that the net fluid intake was less if burned animals were resuscitated with hypertonic saline to the same cardiac output compared with lactated Ringer’s. Urine output was much higher with hypertonic solution. Interestingly, soft tissue interstitial edema in burned and non-burned tissue, as reflected by lymph flow, was increased with hypertonic saline similar to that of lactated Ringer’s (LR). This can be explained by a shift of intracellular water into extracellular space as the result of the hyperviscous solution. Extracellular edema can therefore occur at the same time as intracellular fluid defect. This may give the external appearance of less edema. Although several studies to date have reported that this intracellular water depletion does not appear to be deleterious, the issue remains controversial. Shimazaki et al.\textsuperscript{32} resuscitated 46 patients with either LR or hypertonic saline. The sodium infusions were equivalent, but the free water load was greater with LR; 50% of the latter required endotracheal intubation. The hypertonic serum also delivers a more concentrated ultrafiltrate within the kidney. This increases urine volume and salt clearance without marked increases in the required volume of free water.

There is no consensus regarding the type of osmolarity of hypertonic resuscitation fluid. Caldwell and Bowser,\textsuperscript{33} in 1979, reported a series of 37 patients with greater than 30% burns treated with either LR or hypertonic lactated saline (HLS), but no colloid. Total sodium balance was the same but the HLS group received 30% less free water and the reduced weight gain was maintained for 7 days. Subsequent reports from this institution reported successful HLS resuscitation in the elderly and children but no improvement in late mortality.\textsuperscript{33–35}

Bartolani et al.\textsuperscript{36} randomized 40 patients to receive LR or HLS. HLS patients received more sodium, but less total fluid than the LR group. The observed higher mortality with HLS was attributed to larger burns in this group.

Reserve colloid for the second 24h in cases where the patient remains poorly perfused after large infusions of crystalloid. Griswold et al.\textsuperscript{37} reported resuscitation of 47 patients with HLS resuscitation. Of these, 29 were also given colloid as albumin or fresh frozen plasma based on burn severity, premorbid state, or poor response to HLS resuscitation. This group had larger burns, greater mean age, and higher incidence of inhalation injury, but required only 57% of the fluid volume predicted by the Parkland formula, compared to 75% of predicted volume in the HLS alone group. Both groups maintained urine volumes of 1 mL/kg/h with no significant difference in hematocrit or serum sodium levels. Jelenko et al.\textsuperscript{38} also reported in a small series that patients given HLS and albumin required fewer escharotomies, fewer days of mechanical ventilation, and less total fluid than patients resuscitated with LR or HLS alone. Gunn et al.\textsuperscript{39} in a series of 51 randomized patients found no difference in fluid requirements or weight gain if they were given LR or hypertonic saline, if fresh frozen plasma was administered to maintain serum albumin levels above 2 g/dL, but all patients received hypotonic enteral feedings during resuscitation.

Yoshioka et al.\textsuperscript{40} reviewed 53 patients treated with greater than 30% burns resuscitated with LR, LR and colloid, or

### Table 9.1 Formulas for estimating adult burn patient resuscitation fluid needs

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<tr>
<th>Colloid formulas</th>
<th>Electrolyte</th>
<th>Colloid</th>
<th>DSW</th>
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<tbody>
<tr>
<td>Evans</td>
<td>Normal saline 1.0 cc/kg/% burn</td>
<td>1.0 cc/kg/% burn</td>
<td>2000 cc</td>
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<tr>
<td>Brooke</td>
<td>Lactated Ringer’s 1.5 cc/kg % burn</td>
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<td>Slater</td>
<td>Lactated Ringer’s 2 L/24 h</td>
<td>Fresh frozen plasma 75 cc/kg/24 h</td>
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<td>Crystalloid formulas</td>
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<td>Parkland</td>
<td>Lactated Ringer’s</td>
<td>4 cc/kg/% burn</td>
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<tr>
<td>Modified Brooke</td>
<td>Lactated Ringer’s</td>
<td>2 cc/kg/% burn</td>
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<td>Hypertonic saline formulas</td>
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<tr>
<td>Modified hypertonic (Warden)</td>
<td>Lactated Ringer’s+50 mEq NaHCO\textsubscript{3} (180 mEq Na/L) for 8 h to maintain urine output at 30–50 cc/h</td>
<td>Lactated Ringer’s to maintain urine output at 30–50 cc/h beginning 8 h post-burn</td>
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<tr>
<td>Dextran formula (Demling)</td>
<td>Dextran 40 in saline – 2 cc/kg/h for 8 h</td>
<td>Lactated Ringer’s – volume to maintain urine output at 30 cc/h</td>
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<tr>
<td></td>
<td>Fresh frozen plasma – 0.5 cc/kg/h for 18 h beginning 8 h post-burn</td>
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interstitial protein depletion may result in more edema formation.

**Hypertonic saline**

Hypertonic salt solutions have been known for many years to be effective in treating burn shock.\textsuperscript{26,29} Rapid infusion produces serum hyperviscosity and hypernatremia with two potentially positive effects.\textsuperscript{26,30} The hypertonic serum reduces the shift into the extracellular space of intravascular water. Proposed benefits include decreased tissue edema and fewer attendant complications, including escharotomies for vascular compromise or endotracheal intubation to protect the airway. Monafo\textsuperscript{28} reported that the resuscitation of burn patients with salt solution of 240–300 mEq/L resulted in less edema because of the smaller total fluid requirements than...
HLS. Fluid requirements were 4.8 mL/kg/% TBSA with LR, 3.3 mL/kg/% TBSA with LR and colloid, and 2.2 mL/kg/% TBSA with HLS. The total sodium requirements were increased 30% with LR compared to the other groups. Oxygen extraction, measured as A-VO₂ difference, was improved with HLS, but reduced with LR–colloid, perhaps because of protein leak across the alveoli.

Vigorous administration of hypertonic saline solutions can produce a serum sodium above 160 mEq/dL or serum osmolarity greater than 340 mOsm/dL, followed by a rapid fall in urine output. Bowser-Wallace et al. 43 and Crum et al. 42 have reported 40–50% of patients treated with HLS developed hypernatremia with serum sodium greater than 160 mEq/L requiring switch to hypotonic fluids. Huang et al. 43 reported a series of deaths associated with hypernatremia and hyperosmolality following hypertonic saline resuscitation. Serial determinations of serum sodium and serum osmolality are required to prevent complications including sudden anuria, brain shrinkage with tearing of intracranial vessels, or excessive brain swelling following rapid correction of serum hyperosmolarity. Current recommendations are that the serum sodium levels should not be allowed to exceed 160 mEq/dL during its use. Of interest, Gunn and associates, 44 in a prospective randomized study of patients with 20% TBSA burns evaluating HLS versus LR solution, were not able to demonstrate decreased fluid requirements, improved nutritional tolerance, or decreased percent weight gain.

A modified hypertonic solution has been utilized in children with major thermal injuries >40% TBSA burn. The resuscitation fluid contains 180 mEq Na⁺ (lactated Ringer’s +50 mEq NaHCO₃). The solution is utilized until the reversal of metabolic acidosis has occurred, usually by 8 h post-burn. The volume administered is begun at a rate calculated by the Parkland formula (4 cc/kg/burn); however, volume is titrated to maintain urine output at 30–50 cc/h. After 8 h the resuscitation is completed utilizing LR to maintain urine output at 30–50 cc/h. This hypertonic formula can be used in infants and in the elderly without the accompanying risk of hypernatremia. 44, 45

### Colloid resuscitation

Plasma proteins are extremely important in the circulation since they generate the inward oncotic force that counteracts the outward capillary hydrostatic force. Without protein, plasma volume could not be maintained and massive edema would result. Protein replacement was an important component of early formulas for burn management. The Evans formula, advocated in 1952, used 1 cc/kg of body weight/% burn each for colloid and LR over the first 24 h. The Brooke formula was clearly based on estimate rather than determined scientifically, but the formula used 0.5 /kg/% burn as colloid and 1.5 cc/kg/% burn as LR. The burn budget of Moore similarly used a substantial amount of colloids. 5 Considerable confusion exists concerning the role of protein in a resuscitation formula. There are three schools of thought:

1. Protein solutions should not be given in the first 24 h because during this period they are no more effective than salt water in maintaining intravascular volume and they promote accumulation of lung water when edema fluid is being absorbed from the burn wound. 46

2. Proteins, specifically albumin, should be given from the beginning of resuscitation along with crystalloid; it should usually be added to salt water.

3. Protein should be given between 8 and 12 h post-burn using strictly crystalloid in the first 8–12 h because of the massive fluid shifts during this period. Demling demonstrated experimentally that restoration and maintenance of plasma protein contents were not effective until 8 h post-burn, after which adequate levels can be maintained with infusion. 47 Because non-burned tissues appear to regain normal permeability very shortly after injury and because hypoproteinemia may accentuate the edema, the action advocated by the first school appears to be least appropriate.

The choice of the type of protein solution can be confusing. Heat-fixed protein solutions, e.g. Plasmanate, are known to contain some denatured and aggregated protein, which decreases the oncotic effect. Albumin solutions would clearly be the most oncotically active solutions. Fresh frozen plasma, however, contains all the protein fractions that exert both the oncotic and the non-oncotic actions. The optimal amount of protein to infuse remains undefined. Demling uses between 0.5 and 1 cc/kg/% burn of fresh frozen plasma during the first 24 h, beginning at 8–10 h post-burn. 48, 49 He emphasizes that all major burns require large amounts of fluid, but notes that older patients with burns, patients with burns and concomitant inhalation injury, and patients with burns in excess of 50% TBSA not only develop less edema but also better maintain hemodynamic stability with the addition of protein.

Du and co-workers 44 have recently utilized fresh frozen plasma during burn shock. They use lactated Ringer’s, 2 L for 24 h, and fresh frozen plasma, 75 cc/kg/24 h (Table 9.1). Although the volume of fresh frozen plasma is calculated, the volume infused is titrated to maintain an adequate urine output. Although the authors are utilizing colloid early in the burn shock period, they emphasize that most burn patients have received LR in significant volumes during field management.

The use of albumin in burns and critically ill patients has recently been challenged by the Cochrane Central Register of Controlled Trials, which demonstrated in critical hypovolemia that there was no evidence that albumin reduces mortality when compared with cheaper alternatives such as saline. 50 Others using a meta-analysis of randomized, controlled trials found no effect of albumin on mortality and could not find a deleterious effect of albumin. 51 Most burn surgeons agree that in burn patients who have a very low serum albumin during burn shock albumin supplementation is warranted to maintain oncotic pressure.

### Dextran resuscitation solutions

Dextran is a colloid consisting of glucose molecules which have been polymerized into chains to form high molecular weight polysaccharides. 19 This compound is commercially available in a number of molecular sizes. Dextran, which has an average molecular weight of 40,000 Da, is referred to as low molecular weight dextran. British dextran has a mean molecular weight of 150,000, whereas the dextran used
predominantly in Sweden has a molecular weight of 70,000. Dextran is excreted at the kidneys, with 40% removed within 24 h. The remainder is slowly metabolized. Demling and associates have utilized dextran 70 in a 6% solution to prevent edema in non-burned tissues. Dextran 70 carries some risk of allergic reaction and can interfere with blood typing. Dextran 40 actually improves the microcirculatory flow by decreasing red cell aggregation. Demling and colleagues demonstrated that the net requirements to maintain vascular pressure at the baseline levels with dextran 40 were about half those seen with LR alone during the first 24 h post-burn. These authors have used an infusion rate of dextran 40 and saline of 2 cc/kg/h along with sufficient LR to maintain adequate perfusion. At 8 h an infusion of fresh frozen plasma at 0.5–1.0 cc/kg/% TBSA burn over 18 h is instituted along with necessary additional crystalloid (Table 9.1).

In the young pediatric burn patient with major burn injury, colloid replacement is frequently required as serum protein concentration rapidly decreases during burn shock. The Shriners Hospitals for Children in Cincinnati and Galveston both routinely utilize colloid during resuscitation of children with major thermal injuries.33,54

**Special considerations in burn shock resuscitation**

**Fluid resuscitation in the thermally injured pediatric patient**

The burned child continues to represent a special challenge, since resuscitation therapy must be more precise than that for an adult with a similar burn. In children, there has been a physiological reserve. We have demonstrated that children require more fluid for burn shock resuscitation than adults with similar thermal injury; fluid requirements for children averaged 5.8 cc/kg/% burn. In addition, children commonly require intravenous resuscitation for relatively small burns of 10–20% TBSA. Baxter5 found similar resuscitation requirements in the pediatric age group. Graves and associates substantiated that children received 6.3±2.2 cc/kg/% TBSA burn. At the Shriners Burns Hospital, Cincinnati, we have utilized the Parkland formula with the addition of maintenance fluid, to the resuscitation fluid volume. 4 mL/kg×% TBSA burn per 24 h+1500 cc/m² BSA per 24 h. This is the formula used to begin burn shock resuscitation and to compare the amount of fluid needed by a particular pediatric burn patient with that needed by an unburned pediatric patient (Table 9.2). This is similar to the results reported by Graves and co-workers who found that if maintenance fluids were subtracted from the resuscitation fluid requirements, the resulting resuscitation volumes would approach 4 cc/kg/% burn. At the Shriners Burns Hospital in Galveston, fluid requirements are estimated according to a formula based on total BSA and BSA burned in square meters. Total fluid requirements for the first day are estimated as follows: 5000 mL/m² BSA burned per 24 h+2000 mL/m² BSA per 24 h.

Recently pediatric burn surgeons have seen a problem of over-resuscitation and a ‘saw-tooth resuscitation’. This appears to be due to first responders using the volume resuscitation formula as suggested by Pediatric Advanced Life Support (PALS), which recommends volume resuscitation begin with a fluid bolus of 20 mL/kg of isotonic crystalloid administered over 5 to 20 min – this amount is repeated if urine output is not adequate. This regimen can lead to over-resuscitation. PALS actually recommends a modification of this fluid bolus resuscitation for burns utilizing 2–4 mL/kg/% of body surface area burned per 24 h. Education of first responders on the differences between these two fluid regimens is imperative.

**Inhalation injury**

The presence of inhalation injury increases the fluid requirements for resuscitation from burn shock after thermal injury. We have demonstrated that patients with documented inhalation injury require 5.7 cc/kg/% burn, as compared to 3.98 cc/kg/% burn in patients without inhalation injury. These data confirm and quantitate that inhalation injury accompanying thermal trauma increases the magnitude of total body injury and requires increased volumes of fluid and sodium to achieve resuscitation from early burn shock.

**Choice of fluids and rate of administration**

It is clear that all the solutions reviewed are effective in restoring tissue perfusion. However, it makes no more sense to use one particular fluid for all patients than it does to use one antibiotic for all infections. Most patients with burns of <40% TBSA and patients with no pulmonary injury can be resuscitated with isotonic crystalloid fluid. In patients with burns of >40% TBSA and in patients with pulmonary injury, hypertonic saline can be utilized in the first 8 h post-burn, following which lactated Ringer’s is infused to complete burn shock resuscitation. In the pediatric and elderly burn patient population, utilizing a lower but still hypertonic concentration of sodium, i.e. 180 mEq/L, still gives the benefits of hypertonic resuscitation without the potential complications of excessive sodium retention and hypernatremia.

In patients with massive burns, young pediatric patients, and burns complicated by severe inhalation injury, a
combination of fluids may be utilized to achieve the desired goal of tissue perfusion while minimizing edema. In treating such patients, we have utilized the regimen of modified hypertonic (lactated Ringer’s +50 mEq NaHCO₃) saline fluid containing 180 mEq Na/L for the first 8 h. After correction of the metabolic acidosis, which generally requires 8 h, the patients are given LR only for the second 8 h. In the last 8 h, a 5% albumin in LR is utilized to complete resuscitation. The resuscitation solution used in Galveston for pediatric patients is an isotonic glucose-containing solution to which a moderate amount of colloid (human serum albumin) is added. The solution is prepared by mixing 50 mL of 25% human serum albumin (12.5 g) with 950 mL in an LR solution.

The monitoring of burn shock resuscitation is initiated by first responders and is generally concluded once the patient’s fluid needs have decreased to a maintenance rate, based upon body size and evaporative water loss. Factors influencing monitoring needs include the extent and depth of burn, the presence of inhalation injury, associated injuries, preexisting medical illnesses, and patient age. The monitoring process can be classified based upon the intensity and frequency of observations, as well as the methods employed. While the level of monitoring must be individualized for each patient, one must weigh the risks and benefits of each modality. Young, healthy patients with minor burns may only require the occasional periodic assessment of vital signs, whereas those with more extensive burns and/or other risk factors may require more invasive techniques. A recent survey of 251 burn centers throughout the United States, Canada, United Kingdom, Australia, and New Zealand revealed that only 12% frequently used pulmonary artery catheter (PAC) monitoring during fluid resuscitation in patients with >30% TBSA burns. Moreover, only 60% of the respondents who addressed treatment goals following PAC insertion indicated that they utilized predetermined physiologic parameters to direct fluid therapy.

Clinical monitoring of burn shock resuscitation has traditionally relied on clinical assessment of cardiovascular, renal, and biochemical parameters as indicators of vital organ perfusion. Heart rate, blood pressure, and electrocardiographic recordings are the primary modalities for monitoring cardiovascular status in any patient. Fluid balance during burn shock resuscitation is typically monitored by measuring hourly urine output via an indwelling urethral catheter. It has been recommended that urine output be maintained between 30 and 50 mL/h in adults, and between 0.5 and 1.0 mL/kg/h in patients weighing less than 30 kg. However, there have been no clinical studies identifying the optimal hourly urine output to maintain vital organ perfusion during burn shock resuscitation.

Because large volumes of fluid and electrolytes are administered both initially and throughout the course of resuscitation, it is important to obtain baseline laboratory measurements of complete blood count, electrolytes, glucose, albumin, and acid–base balance. Laboratory values should be repeated as clinically indicated throughout the resuscitation period. These parameters are generally sufficient to assess the physiologic response of most burn patients during burn shock resuscitation. While clinical interpretation of the data should rely on the evaluation of trends rather than on isolated measurements, there have been no studies demonstrating which tests should be performed, how often they should be repeated, or the effect of frequent laboratory testing on the success of resuscitation.

Invasive hemodynamic monitoring permits the direct, and sometimes continuous, measurement of central venous pressure (CVP), pulmonary capillary wedge pressure (PCWP), and pulmonary vascular hemodynamics as well as the calculation of cardiac output (CO), systemic vascular resistance (SVR), oxygen delivery (DO₂), and oxygen consumption (VO₂). The decision to perform such monitoring requires consideration of risks, cost-effectiveness, and impact on clinical outcome. The Swan-Ganz catheter is most commonly utilized in patients in whom routine monitoring is felt to be ineffective, when there is a history of preexisting cardiac disease, or when there are other complicating factors.

PAC-guided therapy has been studied most extensively in trauma and critically ill surgical patients. Kirton and Civetta performed a critical literature review to determine if the use of the PAC in trauma patients altered outcome. They concluded that hemodynamic data derived from the PAC appeared to be beneficial to ascertain cardiovascular performance, and that the inability to achieve hyperdynamic resuscitation was felt to be inadequate, or when the endpoints of resuscitation were difficult to define. These findings were echoed at the 1997 Pulmonary Artery Catheter Consensus Conference; however, there was no unanimity that PAC-guided therapy altered mortality in trauma patients.

Studies of PAC use for monitoring burn shock resuscitation are limited. Retrospective analyses of adult patients with extensive burn injuries have concluded that PCWP is a more reliable indicator of circulatory volume than CVP, and that CO is more accurate in assessing the efficacy of resuscitation than hourly urine output. These findings were supported by Dries and Waxman who noted that urine output and vital signs monitoring did not correlate with PCWP, cardiac index (CI), SVR, DO₂, or VO₂. They concluded that PAC monitoring may be beneficial in patients at high risk for adverse outcomes due to suboptimal resuscitation. Most recently, Schiller and Bay have reported their retrospective experience in 95 patients treated over a 4-year period during which an attempt was made to maximize circulatory endpoints. They concluded that early invasive monitoring facilitated more aggressive resuscitation and resulted in increased survival, and that the inability to achieve hyperdynamic endpoints predicted resuscitation failure.

PAC-guided monitoring has also been used to aid in achieving predetermined therapeutic endpoints during the resuscitation and management of trauma and critically ill patients. In a series of prospective randomized class II trials, it was demonstrated that patients resuscitated to hyperdynamic endpoints (i.e. increased CI, DO₂, VO₂) had decreased mortality, ICU stay, and ventilator days compared to patients who were resuscitated to normal hemodynamic values. Studies by Fleming et al. and Bishop et al. have not only supported these conclusions but also demonstrated a decreased incidence of organ failures.

While the data supporting hyperdynamic resuscitation are impressive, there is also strong evidence that such therapeutic goals are not associated with improved outcome. Two trials in critically ill patients were unable to demonstrate any benefit of PAC monitoring on patient outcome. These studies were supported by prospective randomized trials which demonstrated no statistical differences in survival,
organ failure, or ICU days between the control and hyperdynamic groups.

In an evidence-based review of these and other citations, Cooper et al. \(^\text{74}\) concluded that the existing literature had inconsistent results regarding the efficacy of goal-oriented hemodynamic therapy. This conclusion was underscored by Elliott \(^\text{75}\) who cited a meta-analysis of seven studies in which no significant differences in mortality were noted between control and hyperdynamic resuscitation groups.

The most appropriate endpoints in burn shock resuscitation are also unresolved. As such, the goal of achieving hyperdynamic resuscitation remains controversial. While Aikawa \(^\text{76}\) was able to resuscitate 19/21 patients (90.5%) using the PAC to reach normal hemodynamic endpoints, Bernard \(^\text{77}\) demonstrated that the ability to sustain a supranormal CI was associated with enhanced tissue perfusion and survival. This was supported by Schiller et al. \(^\text{78}\) who demonstrated that an inadequate or unsustained response to hyperdynamic resuscitation was associated with non-survival. A follow-up study by these authors \(^\text{79}\) also demonstrated significantly reduced mortality in those patients where PAC-guided resuscitation assisted in achieving hyperdynamic endpoints. The ability to achieve adequate oxygen delivery with hyperdynamic burn shock resuscitation has also been recently evaluated by Barton et al. \(^\text{80}\). While patients achieved significant increases in VO\(_2\) and DO\(_2\), they required 63% more fluid than predicted by the Parkland formula, a mean resuscitation volume of 9.07 mL/kg/% TBSA burn, and a mean of 50.4 h to complete resuscitation.

More than 20 human studies in critically ill patients have demonstrated that blood lactate (BL) levels are highly accurate as a guide to the efficacy of resuscitation. \(^\text{75,81}\) Blood lactate levels directly reflect anaerobic metabolisms as a consequence of hypoperfusion, and normalizing levels have long been associated with improved survival from non-burn shock. \(^\text{32}\) In other studies, BL has been demonstrated to distinguish survivors from non-survivors. \(^\text{83,84}\) In two prospective, goal-directed studies in critically ill patients, BL proved superior to not only MAP and urine output but also to DO\(_2\), VO\(_2\), and CI. \(^\text{85,86}\)

It is important to emphasize that all of the resuscitation formulas are only guidelines for burn shock resuscitation. The Parkland formula, for instance, decreases the volume administered by 50% at 8 h post-burn. The relationship between the fluid volume required and time post-burn depicts the smooth curve in Figure 9.1 which represents the influence of temporal changes in microvascular permeability and edema volume on fluid needs. That curve is contrasted with the abrupt changes in fluid infusion rate as prescribed by the formula. The formulas are utilized as starting points for volume replacement and to compare the individual patient with the ‘average’ burn patient. An interesting question is ‘When has burn shock resuscitation been completed successfully?’ It is obvious that resuscitation is completed when there is no further accumulation of edema fluid, which generally occurs between 18 and 30 h post-burn. The resuscitation fluids are utilized until the volume of infused fluid needed to maintain adequate urine volume of 30–50 cc/h in adults and 1 cc/kg/h in children equals the maintenance fluid volume. The maintenance fluid requirements following burn shock resuscitation include the patient’s normal maintenance volume plus evaporative water loss.

**The phenomenon of ‘fluid creep’**

The Parkland formula was broadly accepted but has not gone unchecked throughout the years. It is important to note that Baxter’s original formula included an infusion of colloid at the end of 24 h to complete the restoration of intravascular volume. This component has been omitted from the consensus formula and other modern iterations of the Parkland formula. Recent data suggest that the formula does not accurately predict fluid requirements in larger burns and that patients treated today frequently exceed the volumes predicted by the formula. \(^\text{87–89}\) Pruitt first coined the term ‘fluid creep’ in 2000 to describe this phenomenon of increasing resuscitation volumes, and stated that clinicians should ‘push the pendulum back.’ Over-resuscitation can produce significant complications such as abdominal and extremity compartment syndromes, pulmonary and cerebral edema, acute respiratory distress syndrome, and multiple organ dysfunction. \(^\text{90–92}\) As previously noted, Baxter acknowledged the fact that certain patient populations will require more fluid than is predicted, and stressed the importance of careful observation and monitoring of the patient’s response to necessary fluid adjustments.

In 2007, Saffle published a comprehensive review of the incidence, consequences, and possible etiologies of ‘fluid creep.’ \(^\text{93}\) He recommended a number of potential therapeutic strategies for the treatment and prevention of overzealous fluid resuscitation including restricting early fluid resuscitation, considering the use of routine colloid, and utilizing resuscitation protocols. He also discusses the use of hypertonic saline in special populations and the possible pharmacological regulation of resuscitation. The labelling of excessive fluid volumes given during resuscitation as ‘fluid creep’ has not gone unchallenged. Hartford wrote an editorial in response to Saffle’s article: ‘Fluid creep is a term that covers up for unfamiliarity with the root causes of administration of excessive volume of crystallloid and for poor and
inattentive clinical management in acute burn resuscitation. Additionally, in 2008, Blumetti et al. published a retrospective study of patients resuscitated with the Parkland formula over a 15-year period to determine accuracy based on urine output. Their review included data on 483 patients. They found that 43% received adequate resuscitation and 48% received over-resuscitation. Only 14% of adequately resuscitated and 12% of over-resuscitated patients met Parkland formula criteria. They concluded: ‘The actual burn resuscitation infrequently met the standard set forth by the Parkland formula’ and ‘patients commonly received fluid volumes higher than predicted by the Parkland formula.’ They suggest that emphasis be placed on parameters used to guide resuscitation rather than calculated formula volumes.

Lawrence and his colleagues in 2010 used the addition of 5% human albumin to patients’ resuscitation fluids when their fluid requirements are abnormally high. They also considered other factors such as hemodynamic instability, increasing hematocrit, and persistent lactic acidosis when making the decision to use a colloid. They termed this practice ‘colloid rescue.’ They used a specific colloid protocol as a component of their standard LR resuscitation protocol utilizing 1:0 ratio introduced by the Army Burn Center. Increases in the 1:0 ratio were associated with increased mortality and morbidity. The total hourly intake of fluid (mL/kg/% TBSA/h) is divided by the hourly urine output (UPO; mL/kg/h). This is expressed as an intake/output ratio (I:O ratio). Saffle et al. calculated the actual fluid given to a group not given colloid with the colloid rescue group; the results were impressive. In the colloid group, the fluid requirement for initial treatment was nearly 7 mL/%TBSA/kg – nearly double the Parkland formula expectations while the crystalloid group only averaged 4 mL/%TBSA/kg consistent with Parkland calculations. The burn resuscitation used by the Institute of Surgical Research in Operation Iraqi Freedom incorporates colloid use and has been associated with a lower incidence of abdominal compartment syndrome which reduced the reported incidence of this complication to zero. Of interest, Warden in 1992 suggested that in patients with massive burns, young pediatric patients and burns complicated by severe inhalation injury a combination of fluids may be utilized to achieve the desired goal of tissue perfusion while minimizing edema. He used the regimen of modified hypertonic (lactated Ringer's +50 mEq NaHCO₃) saline fluid containing 180 mEq Na/L for the first 8 h. After correction of the metabolic acidosis, which generally requires 8 h, the patients are given lactated Ringers' only for the second 8 h. In the last 9 h, a 5% albumin in lactated Ringers was utilized to complete resuscitation. Also as stated above, both the Galveston and Cincinnati utilize albumin during the first 24 h of resuscitation.

**Fluid replacement following burn shock resuscitation**

Although the heat-injured microvessels may continue to manifest increased vascular permeability for several days, the rate of loss is considerably less than that seen in the first 24 h. Burn edema by this time is near maximal and the interstitial space may well be saturated with sodium. Additional fluid requirements will depend on the type of fluid used during the initial resuscitation. If hypertonic salt resuscitation has been utilized during the entire burn shock period, a hyperosmolar state is produced and the addition of free water will be required to restore the extracellular space to an isoosmolar state.

If colloid has not been utilized during burn shock and the serum oncotic pressure is low due to intravascular protein depletion, protein repletion is frequently needed. The amount of protein varies with the resuscitation utilized. Requirements of 0.3–0.5 cc/kg/TBSA burn of 5% albumin during the second 24 h are utilized with the modified Brooke formula. The Parkland formula replaces the plasma volume deficit with colloid. This deficit varies from 20 to 60% of the circulating plasma volume. We have utilized colloid replacement based on a 20% plasma volume deficit during the second 24 h (circulating plasma volume×20%).

In addition to colloid, the patients should receive maintenance fluids. In burn patients the maintenance fluids include an additional amount for evaporative water loss. The total daily maintenance fluid requirements in the adult patient following burn shock can be calculated by the following formula: basal (1500 cc/m²)+ evaporative water loss [(25+% burn) × m²×24]=total maintenance fluid (m³=total body surface area in square meters). This fluid may be given via the intravenous route or with enteral feeding. The solution infused intravenously should be 50% normal saline with potassium supplements. With the loss of intracellular
potassium during burn shock, the potassium requirements in adults are about 120 mEq/day. In the pediatric patient, increased fluids are required due to the differences in BSA to weight ratios compared to adults. In addition, children also require relatively larger volumes of urine for excretion of waste products. At the Cincinnati Shriners Unit, the maintenance fluid requirements are calculated by the following formula: (35 +% burn)×BSA×24 (evaporative water loss) + 1500 mL×BSA per day (maintenance fluids). In Galveston, the recommended fluids needs are estimated as follows: 3750 mL/m² BSA per day (burn-related losses) + 1500 mL/m² BSA per day (maintenance fluids).

Following the initial 24–48 h post-burn period of resuscitation, urinary output is an unreliable guide to adequacy of hydration. Respiratory water losses, osmotic diuresis secondary to accentuated glucose intolerance, osmotic diuresis secondary to high protein, high caloric feedings, and derangements in the ADH mechanisms all contribute to increased fluid losses despite an adequate urine output. In general, patients with major thermal injuries will require a urine output of 1500–2000 cc/24 h in adults, and 3–4 mL/kg/h in children.

The measurement of serum sodium concentration is not only a means of diagnosing dehydration but also the best guide for planning and following successful fluid replacement. Other useful laboratory indices of the state of hydration and guides of therapy include body weight change, serum and urine nitrogen concentrations, serum and urine glucose concentrations, the intake and output record, and clinical examination.

Continuous colloid replacement may be required to maintain colloid oncotic pressure in very large burns and in the pediatric burn patient. Maintaining serum albumin levels above 2.0 g/dl is desirable. The electrolytes calcium, magnesium, and phosphate must also be monitored. Although the replacement of these electrolytes has been studied in detail in burn patients, maintaining the values within normal limits is desirable and varies in each patient.

Summary

The volume necessary to resuscitate burn patients is dependent upon injury severity, age, physiological status, and associated injury. Consequently, the volume predicted by a resuscitation formula must commonly be modified according to the individual’s response to therapy. In optimizing fluid resuscitation in severely burned patients, the amount of fluid should be just enough to maintain vital organ function without producing iatrogenic pathological changes. The composition of the resuscitation fluid, within limitations, in the first 24 h post-burn probably makes very little difference; however, it should be individualized to the particular patient. The utilization of the beneficial properties of hypertonic, crystalloid, and colloid solutions at various times post-burn will minimize the amount of edema formation. The rate of administration of resuscitation fluids should maintain urine outputs of 30–50 cc in adults and 1–2 cc/kg in children. When a child weighs 30–50 kg, the urine output should be maintained at the adult level. Fluid resuscitation based on our current knowledge of the massive fluid shifts and vascular changes that occur following burn injury has markedly decreased mortality related to burn-induced volume loss. The failure rate for adequate resuscitation is <5% even for patients with burns >85% TBSA. These improved statistics, however, are derived from experience in burn centers where there is substantial knowledge of the pathophysiology of burn injury. Inadequate volume replacement in major burns is, unfortunately, common when clinicians lack sufficient knowledge and experience in this area. The problem of ‘fluid creep’ is a recent phenomenon and appears to be related to over-resuscitation with lack of attention to detail during resuscitation, the use of bolus fluid therapy as suggested by trauma surgeons and PALS, and the loss of colloid oncotic pressure in special patients who fail to be resuscitated with the Parkland formula. The routine use of colloid in the last 8 h of resuscitation or use of a ‘colloid rescue’ in these patients appears to be beneficial.

Areas of burn shock research that need further attention include:

- The definition of the post-burn course of capillary permeability changes, and identification of humoral or cellular factors influencing these changes
- The identification and evaluation of pharmacological agents that can significantly alter capillary leakage
- Elucidation of the relationships between resuscitation fluid composition and pulmonary function changes
- The effect of resuscitation on late organ dysfunction, such as post-resuscitation wound, renal, and pulmonary complications
- A prospective multicenter study of colloid-based resuscitation in comparison with traditional Parkland therapy.

Further reading


References


Evaluation of the burn wound: management decisions

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Introduction

Advances in the resuscitation of burn patients have greatly improved survival, so that death from burn shock has become uncommon. In the 21st century, prompt recovery and good functional outcome for the burn patient hinges, in large part, on proper management of the burn wound.

Perhaps the greatest advance in burn care to date has been the institution of early surgical excision of the burn wound with immediate or delayed wound closure strategy individualized to each patient.1–4 For many years, burns were treated by daily washing, removal of loose dead tissue, and application of some sort of topical nostrum until wounds healed by themselves or granulation tissue appeared in the wound bed. Superficial dermal burns healed within 2 weeks and deep dermal burns healed over many weeks if infection was prevented. Full-thickness burns lost their eschar in 2–6 weeks by enzyme production from bacteria and by daily bedside debridement. Split-thickness skin grafts were applied usually 3–8 weeks after injury. A 50% graft survival was considered acceptable and repeated grafting eventually closed the wound. The prolonged and intense inflammatory response made hypertrophic scars and contractures part of normal burn treatment.

Burns that heal within 3 weeks generally do so without hypertrophic scarring or functional impairment, although long-term pigment changes may occur. Burns needing longer than 3 weeks to heal produce unsightly hypertrophic scars, and may form contractures leading to functional impairment. With few exceptions, state of the art burn care now involves early excision and grafting of all burns that do not heal within 3 weeks. The challenge is to determine which burns will heal within 3 weeks.

Burn wound assessment requires an understanding of skin biology and the pathophysiological changes caused by thermal injury. The standard technique for determining burn depth in the 21st century still remains clinical assessment of the wound by an experienced burn specialist. Management decisions should take into account the mechanism of injury, as this invariably influences the healing potential of the wound, and therefore guides the timing of surgical intervention.

Pathophisiology of the burn wound

Skin biology

The skin is the largest organ in the human body and is comprised of two layers: the epidermis and the dermis. The thickness of the epidermis varies among different parts of the body, from 0.05 mm on the eyelids to over 1 mm on the soles.5 Most of the skin thickness comes from the dermis, which varies with age, gender, and body location. The skin serves as protection against fluid and electrolyte loss, infection, radiation, and provides thermal regulation. Contact with the skin provides the individual clues to the surrounding environment through touch, perception of temperature and pain. In addition, skin appearance is a major determinant of identity and affects interpersonal interactions.

The mostly cellular epidermis is derived from ectoderm and the principal cell is the keratinocyte. These cells begin their division and differentiation at the basal layer and move progressively outward over 2–4 weeks along the outer four layers of the epidermis: the stratum spinosum, the stratum granulosum, the stratum lucidum, and the stratum corneum. Keratinocytes lose their nuclei in the stratum lucidum and become flattened dead cells in the stratum corneum. Other important cells of the epidermis include melanocytes, which produce the melanin pigment essential for protection against ultraviolet radiation, and Langerhans cells, which perform phagocytosis and presentation of foreign antigens. The epidermis, because it is derived from ectoderm, is capable of regenerative healing. Thus, pure epidermal injuries heal by regeneration and without scarring. Keratinocytes proliferate from dermal appendages (hair follicles, sweat glands) and the edges of the wound to achieve reepithelialization. Depilated melanocytes after injury, however, regenerate more slowly and less predictably, which may lead to permanent pigment changes within the healed wound.7,8

The basement membrane zone connects the epidermis to the dermis via epidermal projections (rete ridges) that interdigitate with dermal projections (papillae). The critical structures that stabilize the epidermal-dermal junction are keratinocyte-derived collagen VII anchoring fibrils that extend into the dermis.5,10 These anchoring fibrils may take several weeks (and sometimes months) to mature during...
burn wound healing. Minor shearing forces may cause shearing, blistering and sometimes epidermal loss until the interdigitations mature.

The dermis with its abundant extracellular matrix component is derived from mesoderm and is divided into the more superficial papillary dermis and the deeper reticular dermis. Collagen fibers provide the bulk of the dermal structure. Their organized orientation allows for stretching and tensile strength of the skin. Elastic fibers impart the elastic recoil properties of skin. Protein turnover (by degradation, production and remodeling) increases with mechanical stress and during healing, accounting for the high plasticity of skin. Collagen and elastin are both synthesized by fibroblasts, the principal cell of the dermis. The non-fibrous component of the dermis is called the ground substance. It is composed of glycosaminoglycans and proteoglycans such as hyaluronic acid and chondroitin sulfate, whose function is to entrap fluid to maintain the semi-fluid matrix and to regulate cellular cross-talk by binding and releasing inflammatory mediators. Adnexal structures (sweat glands, sebaceous glands, and hair follicles) originate in the dermis and extend through the epidermis. Since they are lined with epidermal keratinocytes, adnexal structures provide the epithelial cells necessary for reepithelialization after a partial dermal injury. The dermal plexus of capillary vessels delivers the necessary nutrients to cellular structures in both the dermis and epidermis. After wounding however, the endothelial cells also mediate local and systemic inflammatory responses. Sensory nerves, which traverse the dermis into the epidermis, also play a significant role after injury, as they mediate pain and itching, modulate inflammation, and appear to influence the remodeling phase of wound healing. The dermis, like other structures derived from mesoderm, heals not by regeneration but by fibrosis and scarring.

**Pathophysiological changes of thermal injury**

Applied heat at the cellular level causes denaturation of proteins and loss of plasma membrane integrity. Temperature and duration of contact have a synergistic effect, such that cell necrosis occurs after 1 s of exposure at 156°F (69°C), or after 1 h at 113°F (45°C). Following a burn, necrosis occurs at the center of the injury, and becomes progressively less severe at the periphery. Thus, Jackson’s description in 1953 of the three zones of injury still remains our current conceptual understanding of the burn wound (Fig. 10.1). The zone of coagulation is at the center of the wound where no viable cells remain. Surrounding it is the zone of stasis, characterized as a mix of viable and non-viable cells, capillary vasoconstriction, and ischemia. This tenuous area represents the zone ‘at-risk’ and may convert to necrosis with hypoperfusion, desiccation, edema, and infection. With proper wound care management however, these changes may be reversed. Systemic factors such as advanced age, diabetes, and other chronic illnesses also put the zone of stasis at higher risk for ‘conversion’. The outer periphery of the burn wound is the zone of hyperemia, with viable cells and vasodilation mediated by local inflammatory mediators. Tissue in this zone usually recovers completely unless complicated by infection or severe hypoperfusion.

Since medical care, for the most part, has little impact on the outcome of the zone of coagulation, efforts have focused on the prevention of necrosis in the zone of stasis. Locally, in the zone of stasis, approximately half of the cells are undergoing apoptosis versus necrosis as a result of oxidative stress, ongoing inflammation and decreased blood flow due to microthrombosis. It is relatively unclear if this rate of apoptosis is associated with conversion to a deeper burn; however it provides a basis for future study in elucidating techniques for healing at the zone of stasis. Systemically, protection of this sensitive area is achieved with adequate fluid resuscitation, avoidance of vasoconstrictors and prevention of infection. Optimal wound care consists of non-desiccating dressings, topical antimicrobials, and frequent monitoring of the wound. Interest in cooling of the wound to minimize the extent of injury can be traced to antiquity, but to this day, firm evidence of its efficacy is lacking. To be effective, cooling must be performed immediately after injury, and should not supersede other priorities in the evaluation of the injured patient. The optimal temperature and duration of cooling is unknown; in fact, excessive or prolonged cooling may be harmful in that it promotes vasoconstriction and systemic hypothermia. Current guidelines of American Burn Association recommend limiting cooling to 30 min in the management of minor burns. Modalities to improve dermal perfusion and block injury from released inflammatory mediators have also garnered much interest. Experimental benefits have been reported for many pharmacologic agents such as heparin, steroidal and non-steroidal anti-inflammatory agents, thromboxane inhibitors, and epidermal growth factor. Yet, all remain investigational since none has gained wide acceptance for clinical use.

**Assessment of burn depth**

**Clinical observation**

Burn injury may involve one or both layers of the skin, and may extend into the subcutaneous fat, muscle and even bony structures. Burns involving only the epidermis are erythematous and very painful but do not form blisters. Most
sunburns fit this category of superficial, epidermal injury. Within 3–4 days, the dead epidermis sloughs and is replaced by regenerating keratinocytes.

Superficial dermal burns extend into the papillary dermis and characteristically form blisters. Blistering may not occur immediately following injury and burns thought to be superficial may subsequently be diagnosed as dermal burns by day.\(^1\) Once the blister is removed from a superficial partial thickness burn, the wound is pink, wet and hypersensitive to touch. Wound care is often painful as uncovering the wound allows currents of air to pass over it. These wounds blanch with pressure, and the blood flow to the dermis is increased over that of normal skin due to vasodilation. With appropriate wound care, superficial dermal burns usually heal within 2–3 weeks without risk of scarring and therefore do not require operation.

Deep dermal burns extend into the reticular dermis and generally will take 3 or more weeks to heal. They also blister, but the wound surface appears mottled pink and white immediately following the injury (Fig. 10.2). The patient complains of discomfort and pressure rather than pain. When pressure is applied to the burn, capillaries refill slowly or not at all. The wound is often less sensitive to pinprick than the surrounding normal skin. By the second day the wound may be white and is usually fairly dry. As a rule, partial-thickness burns that are predicted not to heal by 3 weeks should be excised and grafted.

Full-thickness burns involve the entire dermis and extend into subcutaneous tissue. Their appearance may be charred, leathery, firm, and depressed when compared to adjoining normal skin. These wounds are insensitive to light touch and pinprick. Non-charred full-thickness burns can be deceptive. Like deep dermal burns, they may be mottled in appearance. They rarely blanch on pressure, and may have a dry, white appearance. In some cases the burn may be translucent with clotted vessels visible in the depths. Some full-thickness burns, particularly immersion scalds or ‘bake’ injuries (caused by convective heat), may have a red appearance, and can be confused by the inexperienced observer as a superficial dermal burn. These burns, however, do not blanch with pressure. Full-thickness burns should be excised and grafted early to expedite the patient’s recovery process and prevent infection and hypertrophic scarring.

The most difficult management decision involves partial-thickness burns that are intermediate in depth. In this situation, the determining factor as to whether these burns heal in 3 weeks may only be a matter of a few tenths of a millimeter. These burns are more aptly called ‘indeterminate’ burns as their healing potential becomes evident with serial assessments over several days. As evidenced by histologic studies, burn injury is a dynamic process that peaks at about 3 days.\(^2\) Initial evaluation by an experienced surgeon as to whether an indeterminate dermal burn will heal in 3 weeks is only about 50–70% accurate.\(^3\)

### Adjuncts to clinical evaluation

An intense search for a more precise diagnosis of burn depth has been mounted ever since it became recognized that many patients would benefit from early determination for operation. The clinical assessment of the burn wound depth is approximately 64–76% accurate in senior burn surgeons with serial exams.\(^4\) Over the last 80 years, interest in technologies for improving accurate determination of burn depth has been robust.\(^5\)–\(^7\) Multiple modalities for determining burn depth have been entertained, but ultimately fallen out of favor or reinvented, which include thermography, photometry, nuclear imaging, pulse-echo ultrasound and, more invasive than the aforementioned, serial tissue biopsy.\(^8\)–\(^10\) These techniques take advantage of the ability to detect: dead cells or denatured collagen (biopsy, ultrasound, vital dyes),\(^11\)–\(^14\) the color of the wound (light reflectance),\(^15\) physical changes, such as edema (magnetic resonance imaging),\(^16\) and altered blood flow (fluorescein, laser Doppler imaging, and thermography).\(^17\)–\(^19\) Unfortunately, none of these techniques has been proven superior to serial clinical assessments by an experienced burn provider. Several groups, however, have recently reported clinical benefits with the use of non-contact laser Doppler imaging in indeterminate thickness burns.\(^20\)–\(^22\) This technique provides a color perfusion map of the burn wound to add to the clinician’s assessment. Since the scanner is held at a distance from the wound, this test is well tolerated and perhaps more reliable as no pressure is exerted on the wound. Furthermore, this test can be repeated over the first several days post-burn to document dynamic changes in wound bed perfusion. Although a promising tool, non-contact laser Doppler imaging has, so far, not been widely adopted into clinical practice.

### Mechanisms of thermal injury

#### Flash and flame burns

Flash and flame burn injuries represent approximately half of the admissions to American regional burn centers. Explosions of natural gas, propane, gasoline, and other flammable liquids cause intense heat for a very brief time. In particular, gasoline has highly flammable vapors that are 3–4 times denser than air. At room temperature, gasoline vapors can diffuse above ground and may accumulate in enclosed spaces. Victims often describe an inappropriate use of gasoline as a fire accelerant (trash burning, outdoor fire). Clothing, unless it ignites, is protective in flash burns. Hence, flash...
burns generally have a distribution involving all exposed skin, with the deepest areas facing the source of ignition. For the most part, flash burns reach progressive layers of the dermis in proportion to the amount and kind of fuel that explodes. While such burns will generally heal without extensive skin damage, they may cover large areas and may be associated with thermal damage to the upper airway.

In contrast to flash injuries, flame burns are invariably deep dermal if not full-thickness because of more prolonged exposure to intense heat. Although the incidence of injuries from house fires has decreased with the advent of smoke detectors, careless smoking, improper use of flammable liquids, automobile accidents, and clothing ignited from stoves or space heaters still exact their toll. Patients whose bedding or clothes have been on fire rarely escape without some full-thickness burns. Many victims of house fires are also prone to deeper injuries because of intoxication or confusion caused by carbon monoxide poisoning. In one study of several burn centers, 28% of flame burns occurred in patients with high blood ethanol level, and 51% of victims in fires behaved inappropriately when trying to escape. Loss of consciousness may also expose the victim to convective heat inside a burning room. This type of 'bake' injury may deceptively appear shallow with intact epithelium to the inexperienced observer, but is really a full-thickness burn.

Scalds

Hot water scalds are the next most common cause of burns in the United States. Despite educational programs, the epidemiology and incidence of scalds worldwide has changed very little. The depth of scald injury depends on the water temperature, the skin thickness and the duration of contact. Water at 140°F (60°C) creates a deep dermal burn in 3 s but will cause the same injury in 1 s at 156°F (69°C). Freshly brewed coffee from an automatic percolator is generally about 180°F (82°C). Once in the pot, coffee temperature approximates 160°F (70°C). Boiling water often causes a deep dermal burn, unless the duration of contact is very short. Soups and sauces, which are thicker in consistency, will remain in contact longer with the skin and invariably cause deep dermal burns. In general, exposed areas tend to be burned less deeply than clothed areas. Clothing retains the heat and keeps the liquid in contact with the skin longer. As a result, scalds are often a mosaic of superficial and indeterminate dermal burns. A common example is a toddler who reaches above head level and spills hot water on himself. His face bears a superficial burn, his trunk burn is of indeterminate thickness, and his skin under his diaper has a deep dermal burn.

Immersion scalds are often deep because of the prolonged skin exposure, although the water temperature may not be as high as in spill scalds. They occur in individuals who do not perceive the discomfort of prolonged immersion (i.e. a diabetic patient soaking his foot in hot water), or who are not able to escape from the hot water (i.e. young children, the elderly, or people with physical and cognitive disabilities). This latter group of vulnerable individuals is also susceptible to non-accidental scald burns. Child victims of non-accidental scalds represent about 2% of all children admitted to our burn center. Circumferential extremity injuries, symmetrical burns to a child’s buttocks and perineum are examples that should raise suspicion of abuse (Fig. 10.3). A detailed description on the recognition and management of intentional burn injuries is available elsewhere in this text. The evaluating physician therefore, must carefully consider whether the history provided matches the distribution and probable cause of the burn; this is best accomplished by an experienced burn surgeon who is familiar with burn distribution and etiologies.

Grease and hot oils will generally cause deep dermal or even full-thickness injuries. During cooking, grease and hot oils are heated to a level below their smoke point to avoid unpleasant odors from their decompositions. The smoke point for butter is 350°F (177°C), 400°F (204°C) for lard, and 450°F (232°C) for corn oil. Cooking oils reach their flash point at 600°F (316°C). Deep dermal burns commonly occur when a victim tries to carry the burning pan of grease outdoors and douses himself instead of putting the lid on the pan and extinguishing the fire. The extent of domestic grease injuries invariably follows a common pattern. A single wrist and forearm is first affected. The panicked victim lets go of the pan and splashes himself onto his feet and sometimes thighs and trunk. The now slippery floor from spilled grease causes the victim to fall and burn his back and buttocks. Approximately 30–40% of grease burns require excision and grafting.

Tar and asphalt are a special kind of scald. The ‘mother pot’ at the back of the roofing truck maintains tar at a temperature of 400–500°F (204–260°C). Burns caused by tar typically result from the victim being trapped in a burning room or structure. Tar and asphalt will cause severe burns even if the temperature of the tar is below its flash point. The tar and asphalt are often spread as a liquid that may cover large areas of the victim. The burns may then be complicated by smoke inhalation.
diminished to the point where most of the burns are deep dermal in nature. Initially evaluation consists of tar removal before injury depth can be assessed. Tar can be removed by application of petroleum-based ointment under a dressing. The dressing is changed and ointment reapplied every 2–4 h until the tar has dissolved. Medi-Sol adhesive remover spray (Orange-Sol, Gilbert, AZ, USA) can be successfully used to remove the tar without injury to the burn wound.

Partial thickness scald burns can be usually managed non-operatively for 10–14 days, unless they are obviously deep. Burns should be excised and autografted as soon as it is clear that they will not heal by 3 weeks. Desai et al. confirmed the validity of this strategy in a randomized trial.68 Children with large scald burns (approximately 25% TBSA) were either excised early (within 72 h) or after 2 weeks post-injury. Children in the late group required excision of significantly smaller areas, while half achieved reepithelialization without surgery.

Contact burns

Contact burns result from hot metals, plastic, glass, or hot coals. Although generally small in size, contact burns are challenging in that the injury is often very deep (Fig. 10.4). Burn depth can be predicted based on the temperature of the material and the duration of contact. Thus, molten materials in industrial accidents instantaneously cause a burn extending below the dermis. Likewise, an unconscious victim lying on top of a heating blanket all night will have a burn extending below the dermis. Contact burns result from hot metals, plastic, glass, or hot coals. Although generally small in size, contact burns are challenging in that the injury is often very deep (Fig. 10.4). Burn depth can be predicted based on the temperature of the material and the duration of contact. Thus, molten materials in industrial accidents instantaneously cause a burn extending below the dermis. Likewise, an unconscious victim lying on top of a heating blanket all night will have a burn extending below the dermis. Contact burns are usually full-thickness and require excision and grafting. In these circumstances, the clinician must anticipate the possibility of extensive myonecrosis and myoglobinuria despite the relative small size of the wound. Contact burns with a hot muffer are usually full-thickness and require excision and grafting. Traffic accidents where the victim is trapped against a muffler or engine block may generate significant defects requiring flap coverage.69

Domestic contact burns often involve palm and finger burns in toddlers. The unsuspecting child typically puts his hands on a wood-stove, fireplace insert, iron press or oven door.70 With aggressive wound care and hand therapy, most intermediate-depth palm burns heal in about 2–3 weeks. On the other hand, unoperated deep palm burns heal from the edges with contracture of the palm leading to permanent disability. The decision to perform excision and grafting using thick split-thickness grafts or full-thickness grafts to deep palm burns71,72 should be tempered by the knowledge that sensory nerve endings unique to glabrous skin (Pacinian and Meissner’s corpuscles) cannot be replaced by a skin graft. Therefore, an observation period of 2–3 weeks with splinting and aggressive exercise appears prudent.

Chemical burns

Chemical burns, usually caused by strong acids or alkali, are most often the result of industrial accidents, drain cleaners, assaults, and the improper use of harsh solvents. Chemical burns cause progressive damage until the chemicals are inactivated by reaction with the tissue or dilution by flushing with water. Although individual circumstances vary, acid burns are usually more self-limiting than alkali burns. Acid tends to ‘tan’ the skin, creating an impermeable barrier that limits further penetration of the acid. Alkali, on the other hand, combines with cutaneous lipids to create soap and thereby continues ‘dissolving’ the skin until it is neutralized.

Initial management consists of diluting the agent with copious water, preferably at the site of the accident. To this end, many industrial workplaces are now equipped with such showers and eye wash stations. The victim should have the contact site irrigated for 15–20 min at minimum. A paper pH test applied to the patient’s burn can verify that the agent has been neutralized. Attempts to neutralize alcalis with acids (and vice-versa) are contraindicated because these maneuvers are dangerous and may induce an exothermic reaction leading to a thermal injury superimposed on the chemical burn. An exception to the irrigation rule is exposure to a chemical powder. In this instance, it is safer to brush the agent off. Examples of common dry chemicals include dry concrete, cement and sodium hydroxide. A full-thickness chemical burn may appear deceptively superficial, clinically causing only a mild brownish discoloration of the skin. The skin may appear intact during the first few days post-burn, and only then begin to slough spontaneously. Unless the observer can be absolutely sure, chemical burns should be considered deep dermal or full-thickness until proven otherwise.

Burns caused by wet cement can be vexing. Workers often kneel in wet cement or spill cement inside boots or gloves and do not become symptomatic for hours.71–75 By the time they seek medical help, the wounds are often deep and most often need grafting.

Hydrofluoric acid (HF) burns are potentially very destructive. HF is widely used in the circuit board etching, cleaning solvents, and paint removers. HF coagulates the skin at site of exposure. Fluoride ions penetrate the skin and cause deep tissue destruction by combining with cellular calcium and magnesium.76,77 Fluoride is also a metabolic poison that inhibits key enzymes of cellular metabolism. A 10% TBSA HF burn may be life threatening due to systemic hypocalcemia78; this may be one instance where urgent surgical wound excision is indicated. As with cement, the worker may not become symptomatic for several hours after exposure.
when severe pain develops in the involved fingers. Delayed or inadequate treatment can lead to amputation. Older recommendations of calcium-containing topical gels and direct injection of calcium gluconate into the involved tissue have now largely been replaced by intra-arterial infusion of calcium ions into vessels perfusing the injured area. Such treatment is almost magical, with immediate cessation of pain and minimal tissue destruction. However, once acute symptoms resolve, it has no further role in preventing tissue damage.

Electrical burns

Electrical burns are in reality thermal burns from very high intensity heat generated as the victim’s body becomes an accidental resistor. Low voltage injuries (<440 volts) rarely cause significant damage beyond a small deep thermal burn at contact points. An exception to this rule is the child who chews on an active electrical connection. The child’s saliva completes the circuit between the positive and neutral leads. The short circuit may cause a severe burn inside the mouth and lip. Burns involving the oral commissure are at high-risk for late contracture and warrant an aggressive splinting and exercise regimen. In addition, eschar separation at the corner of the mouth by day 7–10 after injury may be associated with brisk labial artery bleeding that requires surgical control. High voltage injuries (over 1000 volts) are more apt to cause deep tissue destruction. In fact, most electrical burns are work-related (i.e., construction workers, linemen, utility and electrical workers). In this setting, extensive deep burns are work-related (i.e., construction workers, linemen, utility and electrical workers). In this setting, extensive deep burns are work-related (i.e., construction workers, linemen, utility and electrical workers). In this setting, extensive deep burns are work-related (i.e., construction workers, linemen, utility and electrical workers).

High resistance at skin contact points is partially protective as a dry calloused hand may provide twice the resistance of normal skin, and five times the resistance of wet skin. High resistance within the victim’s body, on the other hand, causes more harm. As electricity travels through the body, electrical energy is converted to heat in direct proportion to current and electrical resistance. Deep muscle necrosis may occur adjacent to bone, which has high resistance. A smaller body part conducting the electricity will generate more intense heat with less dissipation. Therefore, fingers, hands, forearms, feet, and lower legs are often totally destroyed, whereas the trunk usually dissipates enough current to prevent extensive damage to viscera (unless the entrance or exit wound is on the abdomen or chest). Arc electrical burns are also common as the current takes the most direct path, rather than a longer path of seeming less resistance. These injuries occur at joints in close apposition at the time of injury. Most common are burns of the volar aspect of the wrist, the antecubital fossa when the elbow is flexed, and the axilla if the shoulder is adducted.

There are two reasons for early operation in the patient with electrical burns. Massive deep tissue necrosis may lead to acidosis or myoglobinuria that will not clear with standard resuscitation techniques. In this unusual circumstance, fasciotomies, major debridement, and amputation may be needed urgently. More commonly, tissue swelling raises the risk of compartment syndrome. Careful monitoring of the injured extremity is mandatory. Compartmental release is indicated with any sign of progressive peripheral neuropathy. Thus, worsening median or (less commonly) ulnar nerve deficit in the injured hand is an indication for immediate median and ulnar nerve release at the wrist. The use of a technetium scan to help identify damaged and necrotic muscle has been advocated, but has not achieved widespread use. This test is overly sensitive in detecting damage to deep, unexposed muscle groups that, left alone, will fibrose and not require excision.

If immediate decompression or debridement is not required, definitive operations can be performed between days 3 and 5, before bacterial contamination occurs and after the tissue necrosis is delineated. Extraordinary measures, such as vascular grafts to replace clotted arteries, and urgent free flaps may sometimes be indicated, but the surgeon is cautioned that they may actually increase morbidity and prolong the patient’s recovery. A well-fitting prosthesis might give better function than a hand or foot that is weak and has diminished sensation.

Further reading


References


Burn eschar may have different appearances and thicknesses, and may behave in different ways as a function of etiology and time since injury, as well as topical and other treatment modalities. It can cause severe complications that may be life-threatening. Effective burn eschar removal (debridement) is the first and obligatory step for preventing eschar-related complications and initiating the wound healing process. Ideally, debridement should also be effective in preventing and resolving burn-induced compartment syndrome (BICS).

At present, the method and timing of eschar removal rely heavily on accurate diagnosis of burn depth. However, this diagnosis is least easy when most important, i.e. in mixed-depth burns, which make up the majority of injuries.

Immediate or very early wound eschar removal is lifesaving in massive, mostly full-thickness burns of more than 50% of the total body surface area (>50% TBSA), and is beneficial in all burns. For less severe burns, especially those with uncertain depth (‘indeterminate’ – the substantial majority of injuries), eschar removal is attempted usually after 2–4 days post injury, though it may be postponed for up to 2 weeks until diagnosis of burn depth becomes clearer. 1 At this point in time secondary eschar-related damage has already begun in the zones of stasis and hyperemia. Recent reports indicate that immediate debridement (within 24 hours post injury) may prevent or attenuate the inflammatory response and eschar-related problems. Current ‘early’ eschar removal in the 3–4 days after injury can only be surgical, as no other method or means is fast enough. The choice of surgery, considering its dangers and drawbacks, should be weighed carefully, especially in ‘indeterminate’ burns.

The indication and decision for surgical eschar removal depends on pre-debridement diagnosis. The procedure is traumatic, non-selective, and demanding of resources, general anesthesia, and facilities, but is quick and effective. It sacrifices some of the non-injured surrounding tissues (up to 50%). 2–6 Following surgical debridement, usually not enough dermal and epidermal elements are salvageable for potentially spontaneous epithelialization, so the exposed raw bed should be protected and covered by an autograft (additional sacrifice of donor site) or other permanent cover. Surgical debridement may involve complications such as severe blood and temperature loss, inflammation and infection due to bacterial dissemination, pain, and all the anesthesia-related complications. More selective debridement has been recently advocated by some to preserve more dermis for grafting or spontaneous epithelialization, with the development of more selective means of surgical debrid- ing (i.e. dermabrasion or Versajet). 7,8

Non-surgical ‘conservative’ treatment is based mainly on autolytic (maceration) processes, involving the combined activity of topical medicaments (antimicrobial or chemical agents), contamination and lysis by microorganisms, and the inflammation process combined with daily bathing (showers) with superficial scraping and removal of loose debris and dressing changes. These infectious–inflammatory processes are slow (lasting between 10 and 14 days), and may involve significant systemic and local complications. Using topical antibacterial or anti-inflammatory medicaments may reduce the infectious–inflammatory processes, but will delay eschar separation (sloughing). Locally, all these processes may lead to additional tissue damage, particularly death of the zones of stasis and hyperemia, deepening and transforming partial-thickness damage into full-thickness burns. In addition to its local and systemic significance, the long debridement time with sustained inflammatory–infectious processes can lead to the formation of granulation tissue that will develop into heavy scars. The benefits of the technique include its relative selectivity and the fact that it is not based on diagnosis, does not involve surgery, and is simple to practice. When the epithelial remnants in the cutaneous dermis are preserved and provided with the proper conditions for proliferation and propagation, the newly debrided dermal bed provides adequate conditions for spontaneous and rapid re-epithelialization, generally in less than 3 weeks. Rapid epithelialization prevents the formation of granulation tissue that may eventually to develop into heavy scar tissue. Non-surgical debridement may involve complications such as fever and infection owing to bacterial dissemination and slow decomposition of the contaminated eschar, enabled by numerous painful dressing changes.

Hand burns, which are involved in 30–60% of all burn patients, have a special place in the field of burn care and demand special attention and treatment. The initial assessment should include not only the depth and extent of the cutaneous injury, but also diagnosis of increased interstitial/compartment pressure (burn induced compartment syndrome – BICS), which may harm local blood perfusion. Circumferential burns to extremities may cause BICS and
represent an emergency necessitating pressure release by deep surgical incisions, i.e. escharotomy. Owing to the anatomy of the hand (important and delicate structures crowded in a small limited space without subdermal soft tissue), surgical debridement and/or escharotomy is technically intricate, and because of the difficult diagnosis is often executed late or unnecessarily.8–10,21,22,27,28

Thus there is an unmet need for an immediate, effective, selective, fast, and safe non-invasive debriding agent that will combine the efficacy and speed of surgery with the non-invasiveness of non-surgical methods, allowing very early or even immediate, complete, non-traumatic, selective wound debridement and accurate diagnosis of burn depth.

### Debridement factors and assessment

The factors that define the clinical value of any debriding means or methods are as follows:

1. **Safety**: no systemic side effects, trauma, or bleeding
2. **Selectivity**: no damage to surrounding local viable tissues (not diagnosis dependent)
3. **Efficacy**: complete debridement in a single use, with release of BICS
4. **Speed**: debridement completed as fast and as soon as possible, within hours of admission
5. **Cost-efficiency and simplicity of use**: minimal specialized facilities and personnel required.

All these factors are as important, and probably even more so, in children, the elderly, and patients with burns of the hands, feet, face, and neck, where important vital structures lie cramped under thinner skin. Assessing the merit of any debriding means or technique should include all of these factors (Table 11.1).

### End of debridement

The debridement process may be deemed complete when the wound bed is free of eschar based on visual assessment by an experienced physician. The end of the debridement phase is characterized by discontinuation of debriding treatments (surgical and/or non-surgical) and the initiation of treatment modalities aimed at and leading to wound closure (autografting, modulation of epithelialization etc.).

### Debriding enzymes

The notion of using debriding enzymes or chemical agents to ‘dissolve’ the burn eschar in place of traumatic surgical debridement is not new. Ideally, one desires an ointment, cream, or other topical preparation that could be easily and rapidly applied immediately after initial cleansing as a first-line intervention. This preparation should be safe to viable tissues, and not extend the original trauma or harm undamaged tissues. This ideal debriding agent should quickly and selectively digest only the damaged tissues, leaving an intact raw dermal surface that can heal spontaneously or support a skin graft if required, or exposed subdermal tissue that can be autografted.

In his comprehensive review, Klasen24 covered the history of all the past and present topical debriding preparations, concluding that they did not fulfill the expectations of replacing surgery. Enzymes of plant origin (papain) were first evaluated in 1940, and with the addition of urea and chlorophyll (e.g. Panafil) are still in use in many parts of the world, but require daily application for up to 3 weeks. Acids (pyruvic, phosphoric) were tried for a short period in 1946 and later in the 1960s, with relatively good results, but were superseded by the efficacious tangential excision. Proteolytic enzymes of bacterial origin (Clostridium histolyticum, streptokinase, and *Pseudomonas* (Varidase) derived from hemolytic streptococci were tried and abandoned. In the 1970s and 1980s, sutilains derived from *Bacillus subtilis* (Travase) were applied clinically, mainly in the US. In dermal burns, additional tangential excision was required to remove the bed’s surface for successful grafting and debridement of full-thickness burns, which could take more than a week to be completed. Additional Travase experience and reports concluded that the great advantage of debridement with sutilains lay in the possibility this treatment offers of debriding large wound areas soon after the accident, thus permitting early skin grafting.29 In practice, it was used on the fifth to seventh days for a better effect and to avoid epithelial damage. On the basis of seven publications on sutilains, it was concluded that in fact this potential has not been realized in practice. Silverstein et al.30 warned that lengthy and repeated enzymatic debridement may result in excessive fluid loss and potential bacterial invasion that should be prevented by additional antimicrobial agents and frequent (every 4–6 hours) dressing changes.

Collagenase from *Clostridium histolyticum* (Collagenase Ointment, Santyl) has been in use since the 1950s, and is still occasionally used today. Complete debridement may take from several days to up to 2 weeks. Collagenase is effective only in dermal burns and not in burned subcutaneous fat or muscle, and uninjured dermis should be protected from digestion. Hand burns treated by sutilains and collagenase could be debrided and grafted within a week, with blood loss of only 20–50 mL per hand.31–33

Agents such as, trypsin (Trypsin, Tryphtar), chemotrypsin (Alpha Chymar), fibrolysin–deoxyribonuclease (Elase), blowfly larvae extracts, vibriolyisin, and fig tree sap (ficin) were tested but were slow-acting and most effective on few-day-old eschar; they did not gain acceptance as a standard of burn care.

The currently available slow chemical/enzymatic or biological debridement agents are still less efficient than surgery, requiring many applications and days to take effect, and in some cases protection of surrounding tissues is needed. The slow digestion process exposes the patient to complications similar to those observed with autolysis. In addition, the use of such chemicals/enzymes requires up to four painful daily dressing changes for several days. The longer it takes to remove the entire eschar, the greater the possibility that rich granulation tissue will develop, resulting in scarring and contracture formation. Repeated handling and debridement of the same contaminated eschar area can also result in trauma, and dispersion of bacterial and catabolic products that may contribute to secondary bacteremia, septicemia, and sepsis. To date, none of the available debriding products has found acceptance as a standard of care (SOC) in burn treatment. Klasen34 concluded that in spite of the disappointing performance of all the agents tested, debriding
Enzymatic debridement of burn wounds

Table 11.1  Debridement index assessment chart

This assessment chart is intended to enable an objective comparison between debridement means and methods. Each of these five principal criteria that are pertinent to debridement is composed of several factors that need to be assessed independently. Each factor has its own ‘positive’ and ‘negative’ score, with score values commensurate with the importance of the specific factor in the grand scheme of the debridement process. After tallying the positive ‘credit’ and the negative ‘debit’ points, the higher total score corresponds to a better debridement agent and method.

Obviously each factor may have a different score depending on the type of the specific eschar (i.e. thermal burn vs pressure sore), but for a given type of eschar, all the debridement means can be judged using the same criteria and scores. The scores of large eschars are calculated according to a standard given area (for burns, calculated for a fresh burn of 15% TBSA). In a shorter, less comprehensive debridement index, a maximum score of 10 is given to each of the five main factors, while still considering the subcriteria that reflect clinical importance. Previous versions of the Debridement Index have been presented in national, ABA, EBA, ISBI and MBC meetings and modified following peers’ comments to reach the present one.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Maximum score</th>
<th>Credit</th>
<th>Debit</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A. Safety (systemic safety)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. No systemic trauma, toxicity, not pyretic</td>
<td>5</td>
<td>Excessive trauma</td>
<td>10</td>
</tr>
<tr>
<td>2. Wide safety margin in wrong/excessive use</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Does not cause bleeding</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Debridement may strat immediately</td>
<td>5</td>
<td>For each additional day</td>
<td>3</td>
</tr>
<tr>
<td>5. Not allergenic</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>B. Selectivity (local safety)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Destroys only the eschar (highly selective)</td>
<td>15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Does not harm epithelium</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Does not harm dermal components</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. The debrided bed could be diagnosed accurately</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>C. Efficacy % of eschar debrided</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. Can produce completely clean bed in a single use</td>
<td>15</td>
<td>For any additional procedure needed to reach clean bed</td>
<td>3</td>
</tr>
<tr>
<td>11. Can be used for early, fast (&lt;2 hours) escharotomy</td>
<td>15</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>D. Speed</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12. Time needed post admission to complete debridement, for each hour</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13. Time needed to recover between two procedures (measured in hours)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>E. Cost &amp; simplicity of use for 15% TBSA</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14. Number of nurses needed, each x</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15. Number of doctors needed, each x</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>16. Number of specialized MDs (surgeons or other) each</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>17. Cost of all material &amp; manpower needed, for every $US: 100</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18. Could be used in outpatient setup</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>19. No need for pain medication</td>
<td>9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20. Need only oral pain medication</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21. Need only IV analgesia</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>22. Need IV sedation</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>23. Need general anesthesia</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>24. Need O.R. facilities</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25. Need blood bank facilities</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Grand Total</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(Courtesy Lior Rosenberg)

Enzymes remain an intriguing possibility owing to their selectivity toward damaged but salvageable tissue, and with further development ‘these remarkable components will find a useful role to play in the challenge of wound debridement, preparation and repair.’

**Recent development with bromelain extracts**

During the last decade there have been several reports of animal and human studies with a good manufacturing practice (GMP)-produced bromelain-derived topical debriding medicinal preparation (Debridase, Debrase, NexoBrid).24,36–39

Studies in pigs confirmed the efficacy and speed of eschar removal, selectivity, preservation of zone of stasis, beneficial effect on re-epithelialization of partial-thickness burns, and efficacy in resolving increased compartment pressure within less than 1 hour of application.36–38 In six human multi-center, multinational studies with more than 530 burn patients, this agent proved effective in completely and selectively debriding deep or full-thickness burns in a single 4-hour application. The debridement, performed at the
Figure 11.1 (a) Graphical representation of the skin structure and the debrided bed of changing depths with the punctate bleeding typical of each depth: intact skin (S), second superficial degree (IIa), mid-dermal depth (IIm) deep second degree (IIb) and full-thickness third degree (III). (b) Deep hand burn with areas that appear to be: (S) intact skin, (IIa) second superficial degree, (IIb) deep second degree and (III) full-thickness third degree. Some keratin (K) remnants (charred blister) still adhere to the eschar. Direct interstitial/anterior compartment measurement reached 70 cmH2O (70 mmHg). (c) Following 4 hours of topical application of bromelain extract (NexoBrid) the burn is debrided, revealing a clean bed with changing depths (from superficial dermal to fullthickness) and typical bleeding patterns to the different cutaneous anatomical levels (see Figure 11a). Some of the eschar that has been covered by keratin was not debrided (K). Pressure (direct interstitial/anterior compartment measurement) was reduced to 15 cmH2O (15 mmHg). (Courtesy Lior Rosenberg.)

patient’s bedside under analgesia (as done during dressing changes), started and ended on the admission day, compared to more than 6–12 days needed to complete debride-ment in the control (surgical and non-surgical SOC) group, with 15% of the enzymatically treated wounds needing additional surgery compared to 62% treated by SOC. The early debridement and exposure of the viable bed allowed early accurate visual diagnosis of the true burn depth and planning of the ensuing wound closure phase (Figs 11.1, 11.2). The exposed raw surface after this debridement is the interface layer (IL), which comprises the burn bed’s superficial layers of healthy tissues, i.e. dermal remnants or subdermal structures. In partial-thickness (‘dermal’) burns, even deep ones, this layer preserves all viable components, such as deep epithelial elements inside the adnexae and deep dermal remnants (collagen fibres and blood vessels). In all but the deepest wounds, the presence of the IL permits spontaneous healing (epithelialization over dermal remnants). If autografting is required to cover full-thickness burns, or after the spontaneous healing potential has been exhausted, to speed dermal wound closure, a simple brushing of the bed before graft application is sufficient to achieve >95% graft take. By exploiting the healing potential of the enzymatically debrided bed’s dermal remnants, epithelialization of the exposed bed reduced skin grafting compared to all surgically and non-surgically SOC treated burn wounds from 21.5% to 8.4%. Blood loss was halved by Nexobrid use. This approach, based on effective, selective and fast enzymatic, non-surgical debridement followed by maximal epithelialization and calculated use of skin grafts, was termed ‘minimally invasive modality’ in burn care.39 This approach may extend wound closure by 3–4 days compared to early grafting of exposed dermis, but reduces excisional and grafting surgery. Care of hand burns presented similar findings, with early (<1 day) eschar removal, reducing grafting (4.2% vs 65% in SOC) and preventing escharotomy; no escharotomy was required in 117 enzymatically treated deeply burned hands, versus four escharotomies in 44 SOC-treated hands (9.8%).

Conclusion
The search for an effective, selective, safe and fast means of debriding is 70 years old. Surgery has been the standard of care because of its efficacy and potential speed, but it is diagnosis dependent, non-selective, highly traumatic and demanding. Until recently, non-surgical means did not fulfill all the above unmet needs, but because they are not diagnosis dependent they provide more selective and less traumatic
Enzymatic debridement of burn wounds

Further reading


Conflict of interest statement

Debridase, Debrase and NexoBrid22,36-39 are produced by MediWound Ltd, Israel, which financed the last multi-center, multinational clinical studies. Lior Rosenberg was involved in most of the clinical studies, including the non-supported ones, and has a financial interest in MediWound. None of the other investigators (36 burn centers and over 100 investigators) had any financial interests in MediWound, the products or the studies. All data have been reviewed by the European (EMA) and US (FDA) authorities.
References

Treatment of infection in burns

James J. Gallagher, Ludwik K. Branski, Natalie Williams-Bouyer, Cynthia Villarreal, David N. Herndon

Introduction

Infection is a most undesirable partner in any surgical procedure and is especially troublesome in burn injury. Burn patients have lost their primary barrier to infection, the skin. Additionally, the larger burn causes immunosuppression, thereby lessening cellular and humoral defenses against infection. Finally, the damaged tissue is fertile ground for growth of pathogens. An understanding of pathophysiology, definitions of infection, the potential pathogens and treatment options are discussed.

Infection control best practice

The microorganisms initially populating the burn wound represent a mixture of endogenous resident flora and airborne contaminants seeded by contact with the environment and attending personnel. Burn patients are immunosuppressed and should be protected from exposure to environmental contaminants. The most elaborate methods of isolation have failed to eliminate infection, although they have significantly reduced the incidence of cross contamination.1,2,3 The most effective means of reducing exposure of burned patients to exogenous bacteria is strict observation of appropriate hand washing by carers. Universal contact isolation is often routine in burn centers. Face masks, waterproof gowns and gloves should be worn whenever direct contact with body fluids and wound exudates is possible, thereby protecting both the patient and the carer from inadvertent contamination. All dressing materials should be maintained as patient specific. Intravenous pumps and poles, blood pressure devices, monitoring equipment, bedside tables and beds should be cleaned on at least a daily basis with antibacterial solutions. Terminal cleaning, following the discharge of the patient, should include the walls, ceiling, baseboards and floors. Mattresses should be covered with vinyl or other impermeable surface that allows culturing and cleaning without soiling, and be frequently inspected for cracks in their surfaces. At our institution we use Hepa air filters with 99.99% efficiency on 0.3 μm sized particles. They are changed regularly and cultured, if clinically indicated, by infection control monitoring. Most units now house major burn patients in individual, self-contained positive-pressure isolation rooms. However, common areas exist even within these units, mainly the bathing or showering facilities. These areas should be conscientiously cleaned between patients with an effective bactericidal agent specifically directed at the bacteria common to an individual unit. Disposable liners for cleaning surfaces are encouraged, and sterilizable instruments should be used for debridements.

Pathophysiology of the burn wound

Bacteria of normal endogenous skin flora are resistant to heat injury in practically the same degrees as are the skin cells. The bacteria on the surface are heat killed, as are the tissue cells of the surface, and initial cultures are usually sterile. The bacteria in the hair follicles and sebaceous glands may survive (depending on the extent of the burn injury), and the quantitative counts of biopsied specimens may show the same numbers of bacteria per gram (10³) as found in the tissue prior to burning.4,5,6 The mean cell generation time in optimum conditions is approximately 20 minutes. Therefore, a single bacterial cell can increase in numbers to over 10 billion within a 24-hour period.7 As these bacteria increase in number following the thermal injury and reach levels of >10⁵ bacteria per gram of tissue, they will erupt from the hair follicles and sebaceous glands and begin transmigrating over the injury, colonizing the dermal–subcutaneous boundary. If the burn is left untreated, perivascular growth is accompanied by thrombosis of vessels and necrosis of any remaining dermal elements, potentially transforming partial-thickness burns to full-thickness ones. As the levels of bacterial growth increase, so does the incidence of invasion of viable tissue and septicaemia.8,9 Histologically, invasive infection is seen with bacteria in unburned tissue. Other signs of invasion can be the presence of hemorrhage in unburned tissue, small-vessel thrombosis with ischemic necrosis of unburned tissue, and dense bacterial growth in the subeschar space. The usual progression of bacterial colonization as the days pass is from Gram-positive to Gram-negative. By the 21st day post burn 57% of burn wounds still open will be colonized with extended-spectrum β-lactamase Pseudomonas. The natural progression with multiplication of bacteria and deepening of the burn wound is routinely avoided with modern burn care. With a combination of cleansing, antimicrobial topicals, antibiotic dressings, adherent dressings, and early surgery, burn wound progression and infection are avoided in most burn patients. However, even in the presence of modern care, early exposure to a virulent pathogen following injury can quickly progress to invasive burn wound infection and necrotizing soft tissue infection. Awareness of the
circumstances of the burn and the natural evolution of a healing or surgically treated burn is critical to keeping patients safe.

**Infection and the burn wound**

**Definitions for the burn patient**

The Society of Critical Care Medicine (SCCM) and the American College of Chest Physicians (ACCP) have developed and reported on definitions for the systemic inflammatory response syndrome (SIRS), sepsis, severe sepsis and septic shock in the United States. Similar definitions were adopted at an international forum. This important effort has been made to help to standardize the diagnosis and management of patients, which is fundamental to clinical study and the advancement of care. Unfortunately, owing to the nature of burn injury, the established definitions have been found to be inadequate to describe the burn patient. Severe burn injury is associated with the most profound response to injury seen in any disease state. The hypermetabolism seen with burn injury can, in many ways, mimic the SIRS response. This hypermetabolism is a natural part of the body’s compensatory mechanism in response to burn injury and can last for up to a year following injury. Therefore, in 2007, a consensus conference was formed within the American Burn Association (ABA) tasked with authoring definitions of sepsis and infections in burn injury. The methodology of the conference was not unique to this committee, but rather has been broadly used in many disciplines in medicine, including the SCCM and ACCP in the development of the general definitions of SIRS and sepsis. In this section the discussion offered on SIRS, sepsis, burn wound infection, pneumonia, bloodstream infection, catheter-related bloodstream infection and urosepsis are in keeping with the consensus definitions put forth in that publication.

**Burn wound erythema**

The most common burns are smaller than 10% of the total body surface area (TBSA). When presented early for treatment these smaller burns are typically clean. The presence of fever alone does not indicate infection, as burn is associated with an elevation in the body temperature set point. Similarly, fever frequency or severity is not proportional to burn size or depth. Fever can accompany burns of any size. To evaluate a burn for possible infection and determine a need for antibiotics, the examiner must be aware of the phenomenon of burn wound erythema. Burn wound erythema is defined as a redness surrounding the burn injury that is not a first-degree burn, and is not infectious. It normally appears 2–3 days following injury and dissipates by post burn day 5 or 6. It is likely related to the liberation of cytokines and other mediators of inflammation. In contrast to true infectious cellulitis, burn wound erythema is normally non-tender to palpation. Figure 12.1 demonstrates burn wound erythema.

**Burn wound impetigo/graft ‘melting or ghosting’ / folliculitis / persistently open donor sites**

Burn wound impetigo, graft melting or ghosting, which is loss of a previously present skin graft (Fig. 12.2), and folliculitis (Fig. 12.3) are conditions that are well known to the burn care clinician. However, these clinical problems were not addressed specifically in the definitions put forth in the burn care consensus conference on infection and sepsis. These conditions are all most likely the result of bacterial colonization of the wound. Burn wound impetigo has been described as small multifocal superficial abscesses, which can cause extensive destruction of previously healed split-thickness skin grafts and donor sites (Fig. 12.4). This characteristic has led some to call the phenomenon graft melting or ghosting. On the scalp, a very similar problem...
Treatment of infection in burns

occurs that is termed folliculitis. It is not certain whether these different clinical entities represent one or multiple disease processes pathophysiologically. They are grouped here for their similarities in clinical presentation and treatment. Cultures commonly reveal *Staphylococcus aureus*, particularly methicillin-resistant *S. aureus* (MRSA). Treatment consists of twice daily cleansing with surgical detergent disinfectant, unroofing any abscesses, and twice daily application of a topical antimicrobial such as silver nitrate, Dakin's solution, or most commonly mupirocin (N3). With folliculitis, trimming or shaving of the hair is also helpful.

**Figure 12.2** Burn wound impetigo. Right hand in a 13-year-old boy with 85% TBSA burn, fourth-degree to the hands. (a) four months post burn at hospital discharge. (b) Three weeks later in the clinic with reopening of the hand. Culture was positive for MRSA.

**Figure 12.3** Chronic folliculitis to the scalp. Hairs from hair-bearing areas are embedded in the granulation tissue of converted second-degree burns and donor sites, and microorganisms are entrapped, prolonging the process. Shaving of the affected area, topical treatment and eventually skin autografting resolve the problem.

**Figure 12.4** *Staphylococcus aureus* infection in donor sites. Note the secretions and the geographic appearance of the wound, which is typical of this pathogen.

**Burn wound colonization**

Burn wound colonization (Fig. 12.5), as recently defined, is 'bacteria present on the wound surface at low concentrations. No invasive infection. Pathologic diagnosis: <10⁵ bacteria per gram of tissue'. Clinically, the eschar or pseudoeschar may have a deteriorated or 'infected' appearance. No surrounding cellulitis is noted. Treatment consists of continued burn care with cleaning, topical antimicrobials, and surgery. If serial colony counts have been performed and an increase in colony counts has been noted, a change in topical agent may be advised.
Burn wound infection

Burn wound infection is defined as ‘bacteria present in the wound and wound eschar at high concentrations. No invasive infection. Pathologic diagnosis: >10^3 bacteria per gram of tissue’. Clinically, the presence of cellulitis is the foundation of the diagnosis. Cellulitis involves advancing erythema, warmth, and tenderness (Fig. 12.6). The early burn with surrounding blanching erythema likely has an area of surrounding first-degree burn or burn wound erythema, and therefore no antibiotics are indicated. However, the burn wound with surrounding clinical cellulitis may have an atypical history or a late presentation. Often pathologic colors and odors alert the clinician to the strong likelihood of infection. Usual treatment of the infected burn wound consists of thorough cleansing, application of topical antimicrobials, and systemic antimicrobials. The offending organism is usually a drug-sensitive staphylococcus, and antimicrobials are started appropriately. Further choice of antibiotics and duration of treatment can be made by culture and sensitivity results, or merely by clinical progress of the wound. If the circumstances, appearance, or comorbidity history make consideration of Gram-negative pathogens reasonable, expansion of coverage is indicated. Occasionally, the severely neglected wound can progress to full thickness and even have a contained area of pus beneath a true eschar. This can be accomplished through a cruciate incision or partial sharp removal of the eschar. Special care should be taken with the evaluation of burn wounds in the elderly and diabetics, as the inflammatory response can be blunted and the wound severely underestimated.

The burn wound and toxic shock syndrome

One area of special consideration when caring for the small burn is the complication of toxic shock syndrome (TSS). TSS is a form of severe soft tissue infection (SSTI). In the burn wound this syndrome results from colonization with TSS toxin-1-producing Staphylococcus aureus. This disease is primarily of the young child, with a burn of <10% TBSA that would normally be thought to heal without problems. The incidence has been reported at approximately 2.6% with a mean age of 2 years. Clinically it is characterized by a prodromal period lasting 1–2 days with pyrexia, diarrhea, vomiting and malaise. Shock then develops in untreated cases. This is the time of maximal illness and is usually 2–4 days after the burn injury. Once shock has developed, mortality can be as high as 50%. The main defense against the development of this condition is knowledge and aggressive treatment. Since MRSA has emerged as the most common identifiable cause of severe SSTI, initiation of empiric anti-MRSA antimicrobials is warranted in all cases of suspected TSS.14,15

Invasive burn wound infection

Invasive burn wound infection is ‘the presence of pathogens in a burn wound at concentrations sufficient in conjunction with depth, surface area involved and age of patient to cause suppurrative separation of eschar or graft loss, invasion of adjacent unburned tissue or cause the systemic response of sepsis syndrome’. Invasive burn wound infection can occur without sepsis. However, many invasive burn wound infections are rapidly progressive, life-threatening, and require urgent surgical treatment as part of a spectrum of care to gain control of the wound (Fig. 12.7). The clinical diagnosis can be manifested by a change in appearance of the wound from pink and white to yellow, brown, black and green, with distinct odors. Time and some topical agents also can produce color changes that can be misleading. Therefore, it must be recognized that the most reliable sign of invasive burn wound infection is conversion of an area of partial-thickness burn to full-thickness necrosis, or the necrosis of previously viable tissue in an excised wound bed (Fig. 12.8).
There are other reasons for burn wound deepening and conversion, and these must be considered. Once an invasive infection is established, progression can be very rapid. Hemorrhagic bullae, satellite lesions and previously normal skin go from erythematous to necrotic and are characteristic of an aggressive Gram-negative pathogen, usually *Pseudomonas* species (spp). Such lesions are termed ecthyma gangrenosa (Fig. 12.9).

Treatment of invasive burn wound infection is the elimination of all dead tissue, including aggressive removal of dead muscle if present. Here the surgeon must be as aggressive as in necrotizing fasciitis, if the wound is to come under control and eventually support grafting. Surgical control can mean conversion of a tangential excision to fascial level, or amputation where previous attempts were being made to spare a limb. Dead muscle in particular can be problematic as compromised areas can be hidden from view. In the larger burn, any burden of dead tissue with loss of the skin barrier, combined with immunosuppression, makes a very aggressive surgical approach mandatory. Often the initial operation to gain control of an invasive burn wound infection may conclude with no wound coverage other than soaking dressings, with a plan to return to the operating room in the near future. The empiric antimicrobial choice should be broad coverage for fungi, drug-resistant Gram-positive and -negative organisms. Once pathogens are identified and sensitivities reported, antimicrobial management follows this information with persistent efforts to cover the offending organisms with adequate well-timed doses of effective antibiotics chosen for their specific activity against the pathogen. This requires a coordinated effort from clinician, microbiologist and pharmacist. The treatment of the surface is aggressive also. Following the complete removal of dead tissue, topical antimicrobial soaks are commonly used, including silver nitrate, sulfamylon, and Dakin’s solution. Each can be used with topical nystatin to improve kill of fungus if this is a concern. In association with this, increasing the change frequency of the soaking dressing to four times a day may be warranted.

The best treatment for invasive burn wound infection is prevention. In particular, with large burns this translates to excellent surgical management with aggressive removal of dead tissue before it becomes infected. This eliminates the main reservoir for bacterial growth.

### Extremely virulent pathogens

Following modern principles in the clinical care of burn patients has led to rewarding outcomes. However certain pathogens have appeared that defy the usual measures that control other organisms. The appearance of these organisms has often returned death rates to a time before the current era of early excision and grafting. The following discussion is born out of the clinical management of these difficult pathogens.

Ecthyma gangrenosum is a purple bluish-black spot in previously healthy tissues. Classically this is caused by invasive *Pseudomonas*. Histologically it is characterized by thrombosis of vessels with perivascular hemorrhage. Unfortunately, multidrug-resistant (MDR) *Pseudomonas* has become a common enemy. Invasive *Pseudomonas* in combination with vancomycin-resistant *Enterococcus* have clinically demonstrated a severe coagulopathy leading to death. The use of
Candidal infections occur most commonly in patients with large burn injuries who are hospitalized for long periods and have received multiple courses of antibiotics. Prophylactic treatment with oropharyngeal and topical nystatin has therefore become recommended, although fluconazole may be more effective in some cases. Mortality associated with Candida is usually from amphotericin-associated renal failure.

**Culturing of the burn wound**

Daily inspection of the burn wound by a burn surgeon is mandatory for decision making. Major burn wounds usually become colonized or infected within 3–5 days after admission. Often, infection arises from the patient’s own bacterial flora and not from an exogenous source. Burn wound biopsies should be taken from any area of the wound that has changed in appearance. If a simultaneous sample is examined by a pathologist, a diagnosis of burn wound invasion in need of emergency surgical treatment can be made. Quantitative cultures showing high bacterial counts correlate with histologic evidence of burn wound infection in approximately 80% of cases. If quantitative biopsies reveal $>10^5$ organisms/g of tissue, a change in topical therapy is indicated. If bacterial counts exceed $10^5$ of tissue, localized burn wound infection should be considered and a histologic examination performed. If histologic evidence of invasion is present, systemic antibiotics should be given and the wound should be excised. Bacterial sepsis is often heralded by changes in the color, odor or amount of exudate from the wound, whereas fungal invasion is clinically suggested by a rapidly emerging and spreading dark discoloration. Consequently, the burn wound must be closely assessed for these manifestations.

There is considerable practice variation in the more routine use of wound cultures. The literature from Robson et al. in 1973 demonstrated that burn wound colony counts $>10^5$/g tissue led to only a 19% graft survival rate, whereas colony counts $<10^5$/g tissue had a 94% chance of graft survival. This led to widespread use of burn wound biopsies and cultures. In 1996 Steer et al. demonstrated a wide variation in bacterial densities within a wound at the same moment. This information brought into question the value of clinical management change based on routine burn wound culturing. In 2003 Barret and Herndon looked at the effect of burn wound excision on bacterial colonization and invasion. They noted that even preoperative colony counts of $>10^5$ were reduced to $<10^5$ when wounds were treated aggressively through surgery. As a result of this type of treatment, skin graft take was excellent. This is in contrast to Robson’s findings of 40 years earlier. The change is likely related to the change in surgical paradigm and technique. Interestingly, in the Herndon and Barret study, a subgroup was identified with preoperative colony counts $>10^5$/g tissue. This group had post-excision pregrafting cultures that averaged $10^5$/g tissue, but they suffered a 75% infection rate and graft loss. It is clear that burn wound colony counts have significant value in guiding the care of the patient. However, these counts may also possibly be unreliable and inaccurate because of sample site variation. Box 12.1 gives a list of reasons and uses for burn wound cultures.
Viral infection of the burn wound

In recent years more attention has been turned to the diagnosis and treatment of viral infections in burned patients. Prospective and retrospective assays of sera have documented a large incidence of subclinical viral infection. In one of the first large retrospective studies from the 1980s, Linnemann et al. assayed stored sera of burned children. A fourfold increase in antibodies to cytomegalovirus (CMV) was found in 22% of patients, 8% had increased herpes simplex titers, and 5% demonstrated a rise in varicella zoster titers. The study continued in a prospective manner, with 33% of the children developing CMV infection, 25% developing herpetic infection, and 17% developing adenovirus infection.

Cytomegalovirus infection frequently occurs concurrently with bacterial and fungal infections, but rarely alters the patient’s clinical course. Primary CMV infection or reactivation of CMV was reported with an overall frequency of 33%. Importantly, in that study, prospective analyses ‘directly correlated CMV infection with more severe burns, more skin grafts, and subsequent higher numbers of blood transfusions’. The clinical manifestation rarely occurs in patients with <50% TBSA burn infected, and typically presents approximately 1 month post burn as a fever of unknown origin and lymphocytosis. Rennekapff et al., in a 2006 review, identified a seroconversion rate of between 18 and 22% for burn patients who were seronegative for HCMV prior to their burn injury.

Pathophysiologically, CMV inclusions may be identified in the cells of multiple organs but have not been reported in the burn wound. Immuno compromised patients have a higher frequency of CMV infection, which results in a broad range of adverse conditions ranging from febrile illness to systemic infections with organ (e.g., lungs, brain, liver, colon, pancreas) involvement. CMV infection has also been associated with unexplained fever and lymphocytosis based on a concomitant rise in specific antibodies. More recent studies have suggested that up to 23% of seronegative patients with severe burns seroconvert, while more than 50% of seropositive patients reactivate CMV based on a fourfold or greater rise in antibody titer. The fact that only two reports of systemic CMV infection in severely burned patients were published suggests that systemic disease is an unusual occurrence and that the majority of patients who demonstrate increased CMV-specific antibody sustain more limited CMV infections. The absence of reports that account for the frequency of severely burned patients with increased CMV antibodies suggests that most of these infections are subtle and have been overlooked by past studies. Generalized, non-healing burn wounds have been associated with CMV pathology in endothelial and periendothelial cells. Inclusion bodies consistent with CMV infection, as well as CMV antigens, were detected by immunohistochemical staining of a skin biopsy from a transplanted cadaver allograft (from a CMV-positive donor) on a severely burned adult male, but the relationship of the CMV infection to necrosis, inflammation and increased vascularity evident in the infected skin is not known. Results from animal experiments demonstrated that severe burn injury predisposes to murine CMV infection, and murine CMV infection was associated with increased susceptibility to sepsis.

The burned patients who most commonly contract the infection are known to have received multiple blood transfusions, which represent a major source of contamination. In addition, it has been shown in an animal model that cadaver skin has the ability to transmit CMV infection. In a recent study by Tennenhaus et al., US and German burn centers were surveyed and evaluated for awareness, perceptions, diagnosis, and treatment of CMV in patients with burn injury. CMV infection incidence was reported at 1:280 in German and 1:870 in US burn centers. When testing, 70% of German and 19% of US burn centers used serology; 52% German and 25% US centers used body fluid viral isolation; and 43% German and 6% US centers used leukocyte CMV-DNA analysis. Two-thirds of the German and half of the US centers distinguished infection from disease. A total of 43% German and 19% of the US centers would treat the established disease.

Herpes simplex infections most commonly manifest themselves as vesicles in healing partial-thickness burns or split-thickness donor sites (Fig. 12.11). In the
immunocompromised burn patient, however, the infection usually starts with barely noticeable red macules, which then progress rapidly and spread over entire donor sites and previously healed areas. A near-total loss of epidermal coverage can occur (Fig. 12.12a,b and Fig. 12.13a,b). Other epithelial surfaces such as the oral or intestinal mucosa can also be involved, potentially causing erosion and perforation. The clinical manifestations of lesions may be preceded by unexplained fever unresponsive to routine antibiotic coverage. In recent years, an increased mortality, extensive visceral involvement, and necrotizing tracheobronchitis have been associated with herpetic infections after burns. A retrospective study characterizing the incidence, presentation, and outcome of 14 patients with facial herpes rashes out of 95 severely burned intubated adults was performed by Fidler et al., showing that rashes attributed to herpetic infections were found in at least 15% of patients, but no difference in mortality or length of stay could be observed between patients with or without the infection. The authors also noted that the course of this infection was relatively benign in this group of acyclovir-treated patients. Partial-thickness burns and donor sites infected with herpes may convert to full-thickness injuries, requiring skin grafting for ultimate closure. Necrotizing hepatic and adrenal lesions may lead to multisystem organ failure. Mortality in patients with disseminated infection is about twice that expected for patients of similar age and burn size. Split-thickness grafts provide adequate coverage of previously infected herpetic wounds, but the coverage is frequently associated with secondary graft loss and the need for reoperation and patch grafting.

Figure 12.12 A 13-month-old girl with 80% TBSA scald burn who developed a fulminant herpes simplex II infection 2 weeks after admission. (a) 10 days post burn, prior to clinical manifestation of infection. (b) Post-burn day 18. Full manifestation of herpetic lesions that affect the entire body surface area and convert previously healed areas into open wounds.

Figure 12.13 Same patient as in Figure 12.12. (a) The left arm, which was used twice as a donor site for split-thickness skin graft (days 4 and 11). The image is from day 17, with initial manifestation of herpetic infection with red macules. (b) Day 18 post burn; 30 hours later, conversion to confluent defects with near total loss of epidermis.
Chickenpox (varicella zoster) infection is a frequent occurrence in school-aged children and is rapidly spread through inhalation of the virus. Varicella infections can be life-threatening in an immunocompromised host and small epidemics have occurred within pediatric burn units. The characteristic fluid-filled lesions appear in healed or healing partial-thickness burns, as well as uninjured epithelium and mucous membranes. Owing to the fragility of the newly healed or healing skin, the vesicles are much more destructive in the injured than in the uninjured skin, and may present as hemorrhagic, oozing pockmarks, which are prone to secondary infection and subsequent scarring. Neovascularized skin grafts may be lost, and further grafting procedures should be delayed until the lesions are quiescent.

**Burn-associated infections**

**Sepsis**

Rapid and complete closure of deep burns is the best defense against the development of sepsis in the burn patient. If a comparison is made between burn patients of equal size, those who have an occurrence of sepsis during their hospitalization will have decreased lean body mass and increased mortality. A major focus of rounds in the burn intensive care unit is on the identification of sepsis. Sepsis was addressed at the American Burn Association Consensus Conference to Define Sepsis and Infection in Burns. Below is the definition as outlined in the publication:

> Sepsis is a change in the burn patient that triggers the concern for infection. It is a presumptive diagnosis where antibiotics are usually started and a search for a cause of infection should be initiated. While there is need for clinical interpretation, the diagnosis needs to be tied to the discovery of an infection (defined below). The definition is age-dependent with adjustments necessary for children.

The trigger includes at least three of the following:

I. Temperature >39° or <36.5°C

II. Progressive tachycardia
   A. Adults >110 bpm
   B. Children >2 SD above age-specific norms (85% age-adjusted max heart rate)

III. Progressive tachypnea
   A. Adults >25 bpm not ventilated
      i. Minute ventilation >12 L/min ventilated
   B. Children >2 SD above age-specific norms (85% age-adjusted max respiratory rate)

IV. Thrombocytopenia (will not apply until 3 days after initial resuscitation)
   A. Adults <100,000/mcl
   B. Children <2 SD below age-specific norms

V. Hyperglycemia (in the absence of pre-existing diabetes mellitus)
   A. Untreated plasma glucose >200 mg/dL or equivalent mM/L
   B. Insulin resistance – examples include
      i. >7 units of insulin/h intravenous drip (adults)
      ii. Resistance to insulin (>25% increase in insulin requirements over 24 hours)

VI. Inability to continue enteral feedings >24 hours
   A. Abdominal distension
   B. Enteral feeding intolerance (residual >150 mL/h in children or 2× feeding rate in adults)
   C. Uncontrollable diarrhea (>2500 mL/d for adults or >400 mL/d in children)

In addition, it is required that a documented infection (defined below) is identified
   A. Culture positive infection, or
   B. Pathologic tissue source identified, or
   C. Clinical response to antimicrobials.

**Pneumonia**

The use of mechanical ventilation should be avoided whenever possible. This life-saving support for the lungs and protection for the airway comes with inherent complications. Modern care dictates the use of a care regime to reduce the incidences of ventilator-associated pneumonia. However this complication is common, especially in those burn patients with inhalational injury. Ventilator-associated pneumonia (VAP) has two basic etiologies: direct contamination of the tracheobronchial tree via airborne or aspirated bacteria, and pneumonia spread hematogenously. The hematogenous etiology seen later in the hospital course is often bilateral and carries a worse prognosis than the former. Organisms cultured from pneumonia of burn patients often reflect the flora of the burn wound. The diagnosis of pneumonia is a clinical one, with two of the following being required: chest X-ray revealing a new and persistent infiltrate (Fig. 12.14), consolidation or capitation. Sepsis, as defined in the burn patient, is a clinical deterioration in status and a change or purulence in sputum. Once a clinical diagnosis is made, prior to the start of antimicrobials for treatment, specimens are sent for microbial analysis. Either tracheal
aspirate, bronchoalveolar lavage (BAL) or protected bronchial brush (PBB) are performed to obtain a specimen. BAL and PBB are recommended over tracheal aspirate. Positive microbiological results are: tracheal aspirate ≥10^5 colony-forming units, BAL ≥10^4 organisms and PBB ≥10^3 organisms. The data modify the clinical diagnosis in one of three ways in a post hoc manner: (1) if a pathogen is isolated in sufficient quantities, then the clinical diagnosis is confirmed; (2) if the clinical diagnosis was strong but the microbiologic data fail to confirm, then the diagnosis is probable; (3) with low or moderate clinical suspicion but with a the presence of a positive specimen, the pneumonia diagnosis is possible. This definition suggests that, once made, the clinical diagnosis cannot be removed by a lack of confirmation by the microbiology report. Controversy about this position persists. In a 2005 study by Wahl et al., it was reported that negative BAL results (<10^3 cfu) reduced the clinical VAP diagnosis rate by 21%. The negative BAL prompted the discontinuation of antibiotics started for the clinical suspicion of VAP. In none of the patients in the study in whom antibiotics were discontinued were antibiotics restarted based on clinical grounds.

Unique to burn patients is the possibility of using surface quantitative wound cultures (QWC) to predict the pathogens found in a VAP in the same patient. In a study by Ramzy et al., an attempt was made to establish the relationship of the burn wound flora to microbial pathogens in the tracheobronchial tree. In 30 (48%) of the 62 bronchial lavage fluid (BLF) cultures there was a match between the organism identified in the BLF and the QWC. When strict quantitative criteria were applied, however, the match rate was only 9 of 62 (14%). Burn size and inhalation injury had no significant effect on match rate. Whereas the microbial pathogens were similar in the QWC and BLF, linear regression showed no value of QWC in predicting BLF culture results. The difference between qualitative and quantitative match rates suggests cross-colonization between the burn wound and tracheobronchial tree, but little to no cross-infection. The QWC and BLF cultures must be performed when determining antimicrobial specificity in the burned patient. This study supports routine surveillance of the burn wound to help guide early thoughtful institution of antibiotics in a suspected pneumonia.

**Bloodstream infection (BSI)/catheter-related BSI (CR-BSI)/suppurative thrombophlebitis**

One of the following two criteria must be met to diagnose a bloodstream infection (BSI): (1) the patient has two or more positive blood cultures for a known pathogen or one positive in the presence of sepsis, or (2) the patient has a common skin contaminant cultured from two or more blood cultures on separate occasions and sepsis. The BSI is considered primary if the same organism has not been cultured at another site. If the same organism is cultured at another site it is considered secondary. A catheter-related bloodstream infection (CR-BSI) is present if a patient has sepsis and no other source of infection, and the signs of sepsis resolve within 24 hours of catheter removal. Additionally, any bacteremia or fungemia in a patient with an intravascular catheter, clinical signs of sepsis and no other source of infection is a CR-BSI (reference N2 for a complete and detailed discussion). It is interesting to note that the bacteria cultured from infected catheters can be traced to the skin in 96% of cases. These data tend to support the hypothesis that catheter-related infections arise primarily from burn wound contaminants migrating down the catheter to the tip. Strict aseptic technique for insertion of intravascular catheters, the use of Teflon catheters, and rotation of catheter sites are useful measures to prevent infection. There is currently still debate regarding the effectiveness of antibiotic-coated catheters to reduce the number of line infections and to allow longer safe retention of a venous access point in the burn ICU. Further study is needed to elucidate the effect this technology may have on the management of intravenous access in the burn patient. It is recommended that each burn center adopt a line change protocol to standardize the management of access, and track the outcome.

Suppurative thrombophlebitis should be suspected in those patients who have persistent positive blood cultures without signs of local infection. Often suppuration can occur after the time of catheter removal, so cultures at the time of removal may be an unreliable predictor of infection. Gross clinical signs of suppurative thrombophlebitis are frequently not present. Upon confirmation of the diagnosis, immediate operative excision is essential to prevent progressive sepsis. Entire excision of a vein to the port of entry into the central circulation may be required because of the tendency of phlebitis to migrate to vein valves, leaving an apparently normal vein in between the infected foci. The subcutaneous tissue and skin should be packed open where a grossly purulent vein is removed and allowed to granulate and close by secondary intention (Fig. 12.15).

**Abdominal sepsis**

The abdomen as an infectious source in the burn patient can be a clinical challenge. The abdomen is often involved in larger burns, which can lead to a perceived limitation in the clinical examination compared to other similarly complex ICU patients. The defects in the overlying skin should not be allowed to interfere with a proper physical examination.
Burn patients, like all patients, can develop appendicitis, intussusception, bowel obstruction, etc. Additionally, in severe burns peritoneal dialysis may be chosen to aid compromised renal function and potentially introduce another possible source for infection. Larger burns have episodes of hypoperfusion at times leading to sloughing of intestinal mucosa. Heme-positive mucoid or watery stools, abdominal distension, and diminished bowel sounds often characterize this condition. Stool for reducing substances is usually positive, thus indicating malabsorption. A patient with a very severe burn, often combined with sepsis, can have critical ischemia to the gut as a result of global hypoperfusion and progress to necrosis. Clostridium difficile (C. diff.) is a well known entity in critically ill patients, especially those with a history of antibiotic use. With the ubiquitous emergence of methicillin-resistant staphylococcus the intravenous use of vancomycin has increased to such a degree as to reduce our observed clinical incidence of C. diff. diarrhea. However, this supposition is unproven. Necrotizing enterocolitis can occur in patients who are severely granulocytopenic from any cause. Left upper quadrant abdominal pain is usual. Irritation of the adjacent diaphragm may result in pain referred to the left shoulder. Splenic enlargement and tenderness are often present, with high, spiking temperatures. Radiographic examination may reveal an elevated left hemidiaphragm, basilar pulmonary infiltrates, atelectasis, or a left pleural effusion. Shift of the colon and stomach down and to the right and extraintestinal gas, either diffusely mottled or producing an air–fluid level in the left upper quadrant, may also be seen. Ultrasonography, CT, and MRI are the preferred diagnostic techniques for the evaluation of suspected splenic abscess. Initial antibiotic therapy should have a broad spectrum of activity. A combination of antibiotics that has activity against streptococci and both aerobic and anaerobic Gram-negative bacilli would be appropriate initial antimicrobial therapy.

**Ophthalmic infections**

The eyes in the burn unit are at great risk. They may have suffered an insult from the original trauma or from the time in the burn ICU. The retraction of the lids from scar and the sedation that is at times necessary can interfere with the eye’s natural protective mechanism. The avascular corneal stroma is protected by one layer of epithelium. Once damaged, a perforation can mean loss of the eye. The cornerstone of treatment is prevention through treatment of abrasions with antimicrobial drops, early eyelid release and vigilance to the risk of exposure trauma.

**Chondritis**

Burns to the ear represent a clinical management challenge. Full-thickness injuries can injure the cartilage of the ear, resulting in autoamputation of part of or the entire external auricle. Because of the auricles’ comparatively low blood supply, chondritis frequently follows the progression of tissue ischemia. Chondritis is usually seen 3–5 weeks following the injury, but may be seen earlier and may occur following partial- and full-thickness injuries. The introduction of mafenide acetate has become the topical agent of choice for burned cartilaginous surfaces, and the incidence of suppurative chondritis has significantly decreased with its use (Fig. 12.16). Characteristically, the patient will complain of dull pain. The ear will become warm, red, tender and edematous. Appropriate antibiotics should be initiated immediately, and if there is an identifiable site, immediate incision and drainage of the abscess should be undertaken, with culture and sensitivity obtained. Should induration and tenderness continue, a more extensive debridement is imperative. Generally the helix is bivalved at the posterior helical margin and all necrotic cartilage debrided. Difficulty may arise in distinguishing between viable and necrotic tissue, and frequently normal cartilage is sacrificed in order to ensure debridement. However, infected cartilage is usually soft, whereas normal cartilage will feel granular on curettage. If appropriate and adequate excision of the necrotic tissue is not performed, suppurative chondritis can proceed to invade the mastoid bone, creating a potential for intracranial abscess formation.

**Urosepsis**

Urinary tract infections are usually associated with a history of catheterization. When infection occurs patients should be treated with appropriate systemic antibiotics. The source of urine identified with sepsis is defined previously in the burn patient. Candiduria is often insignificant but may reflect active infection or septicemia, especially when mycelia can be demonstrated. When present, an active infection with Candida species usually responds to low doses of amphotericin B, fluconazole or itraconazole.
Suppurative sinusitis

An infection of this type has become more obvious recently because of transnasal intubation and the use of nasogastric or nasoduodenal tubes for enteral feeding. The diagnosis is usually delayed due to clinically subtle symptoms, and only after more frequent causes of fever are ruled out does it become evident. Diagnosis is confirmed based on X-rays or CT scans. Therapy with broad-spectrum antibiotics and promotion of drainage is initiated. Surgical drainage of the involved sinuses may be necessary if the infection is unresponsive to the antibiotics. Oral intubation and nasogastric feeding may be used as a temporary measure, but if sinusitis becomes complicated and prolonged treatment is necessary, then a tracheostomy and/or orogastric feeding is indicated.

Tetanus

As part of the admission protocol to the burn center, routine prophylaxis for tetanus (Clostridium tetani) is 0.5 mL tetanus toxoid, if it has not been administered in the previous 3 years. In addition, if the patient’s last booster was more than 10 years ago, 250 units of tetanus antitoxin is also administered.

HIV and the burn patient

The incidence of HIV infection is very common in many parts of the world. In sub-Saharan Africa some countries have rates of 35–39% in the total adult population. In the US, although the incidence is much less, a burn care practice in a large city will likely have patients who are infected with HIV. HIV seems to have an additive effect on the immunosuppression of the burn, as reflected in the CD4/CD8 cell counts. In a 2003 prospective study from Zimbabwe, Mzezewa et al. found graft survival after split skin grafting of burn wounds in HIV-infected patients impaired and hospital stay prolonged, with significant alterations in the levels of pro- and anti-inflammatory cytokines. The authors concluded that HIV infection results in immune dysregulation, which might be related to impaired skin graft survival.

Microbiologic and pharmacologic considerations in the care of the burn patient

Selection, collection and transport of specimens

There are several major benchmarks that must be adhered to in order to achieve reliable clinical microbiology results in its association with the thermal injury. Most important to effective microbiologic diagnosis is the appropriate selection, collection and transport of specimens sent to the laboratory. Appropriate specimen management affects patient care in several significant ways:

- it is the key to accurate laboratory diagnosis that directly affects patient care and patient outcome;
- it influences therapeutic decisions;
- it affects hospital infection control, patient length of stay, and overall hospital costs;
- it plays a major role in laboratory costs, and influences laboratory efficiency.

Prior to analysis, the specimen collection site must be selected and must represent a location of active disease. The area of the wound that looks clinically the worst is a good place to find the pathogens. Even careful collection methods will produce a specimen of little clinical value if they are not obtained from a site where the infection is active. Also, collectors must be aware of the appropriate device for sample collection.

With burn wounds, it is particularly important to obtain a culture which is free from contamination of the normal flora that may be present on the surface of the injured skin. In addition, the size or amount of the specimen plays an essential role in the appropriate identification of the etiologic agent. The use of prophylactic antimicrobials (both topical and systemic) should also be noted so that appropriate inhibitors and sufficient dilutions can be prepared, or reagents added to void any effects of drug interactions. The specimen should be collected and placed in a sterile container with appropriate media for transport to the laboratory. All specimens must be transported promptly, so as to obtain optimal results. In addition, direct communication with the microbiologist can often be very helpful.

Pharmacodynamics and kinetics in the burn patient

Pharmacotherapy in the control of infection in a burn patient can be a challenge for the clinician. The normal course of burn trauma effects pathophysiologic changes in the cardiovascular, renal, metabolic, hepatic, gastrointestinal, epidermal and immunological responses that change the patient’s pharmacodynamic and pharmacokinetic state.

Two distinct phases characterize the changes seen with burn injury: the acute or resuscitative, and the hypermetabolic.

The acute or resuscitative phase

In the acute or resuscitative phase of burn trauma, which occurs within the first 48–72 hours post burn, cardiovascular factors produce hypovolemia, often with decreased blood flow to organs and tissues. Intravenous drug treatments during this phase will result in a slower rate of distribution and elimination through the kidneys. The burn patient will also exhibit delayed absorption of enteral, subcutaneous and intramuscular drugs. Pharmacotherapy regimens during this acute phase will result in delayed onset of action and peak concentrations.

The hypermetabolic phase

The hypermetabolic response phase, mediated by greatly increased levels of catecholamines, prostaglandins, glucagons, and cortisol, occurs after the acute phase and also produces pathophysiologic changes. The burn patient will exhibit increased blood flow to organs and tissues, an increased internal core temperature, and hypoproteinemia and edema formation. Intravenous drugs will have an increased onset of action owing to the increased rate of distribution. These drugs will also have a shorter half-life owing to the enhanced glomerular filtration rate and elimination of renally excreted drugs. The antibiotic treatment of these patients requires higher doses for these drugs and perhaps a shorter dosing interval. Renally excreted antibiotics such as...
vancomycin that are time dependent in their ability to kill Gram-positive bacteria must be carefully monitored to ensure that they are meeting the minimum inhibitory concentration of the bacteria in the serum. Oral drugs will also exhibit an increased absorption from the GI tract and increased onset of action. The hypermetabolic phase will produce decreased levels of albumin and increased levels of acute-phase proteins. Albumin binds to acidic and neutral drugs such as aminoglycosides, vancomycin, aztreonam and cefotetan. These drugs will exist as free drug in hypoalbuminemia, which results in an increased volume of distribution. Lower doses of these drugs may be needed for therapeutic effect. Acute-phase proteins bind to basic drugs such as penicillins and cephalosporins. These drugs will be tightly bound and there will be less free drug in the blood and a decreased volume of distribution. Higher drug dosages may be necessary to produce a therapeutic effect. The hepatic response in the hypermetabolic phase will present as a decrease in phase I metabolism, such as oxidation, reduction, or hydroxylation of a drug by the cytochrome P-450 system. This will affect the metabolism of many antibiotics, such as the quinolones and the macrolides. The decreased activity of these hepatic drug-metabolizing enzymes as well as the decreased hepatic clearance and prolonged half-life may produce systemic toxicity. Phase II metabolism in the liver, such as conjugation reactions between the drug and the endogenous substrate, will not be impaired. The gastrointestinal response during the hypermetabolic phase results in increased proton secretion. It is reported that erosion of the stomach lining and duodenum occurs in 86% of adult patients within 72 hours post-injury and 40% had GI bleeding. In children, the incidence of stress ulceration is twice that of adults. Erosion of the stomach lining and duodenum allows the transmigration of GI bacteria from the gut into the body’s bloodstream. The use of antacids, H2 antagonists and proton-pump inhibitors may actually permit the proliferation of bacteria that are not normally present in the gut. Transmigration means these bacteria may be found in other parts of the body, such as the lungs, heart and intestinal tract.

Finally, the immunological response will exhibit major changes in the hypermetabolic phase. The burn patient suffers damage to the epidermis of the skin. The depression in this first line of defense allows systemic microbial invasion. However, there is also depression in the second line of defense, with a burn size related depression of both cellular and humoral aspects of the immune response and phagocytic activity of fixed and blood borne macrophages and neutrophils. The patient suffers a release of chemical mediators including prostaglandins, serotonin, thromboxanes and leukotrienes, which mount an inflammatory response. The modern burn unit’s care is often greatly enhanced by the active participation of a pharmacist familiar with burn patients.

Bacteria and their treatment

Gram-positive organisms

Staphylococcus aureus

Staphylococcus aureus is the most important cause of bacterial burn wound infections and is well documented as a human opportunistic pathogen. As a nosocomial pathogen, S. aureus has been a major cause of morbidity and mortality.

Most common infections where Staphylococcus spp. are encountered and are considered pathognomonic are septicemia, cellulitis, impetigo, scalded skin syndrome, and post-operative wound infections. However, the most serious staphylococcal infections are puerperal sepsis, pneumonia, osteomyelitis, endocarditis, and burn wound infection. Staphylococcal pseudomembranous enterocolitis occurs most frequently as a complication of antibiotic therapy. Strains of S. aureus as well as other Staphylococcus species produce a wide variety of metabolites. Some are pathognomonic and also toxicogenic, but those with minimal toxicity or no toxic effects at all are of some diagnostic significance. An array of byproducts such as proteinases, collagenases and hyaluronidase digest the extracellular matrix, which serves as the structural integrity essential in wound healing. Exotoxins, which are produced by the pathogenic strains of staphylococci, include a pyrogenic toxin, a dermonecrotizing toxin, and leukocidin. These organisms can also produce an exotoxin, TSST-1 and enterotoxins A, B and C, which are risk factors for toxic shock syndrome in susceptible patients (as discussed earlier). Toxic shock syndrome (TSS) was first described as such in 1978. The disease is characterized by sudden onset of fever, vomiting, diarrhea, shock, and a diffuse macular erythematous rash, followed by desquamation of the skin on the hands and feet as well as hyperemia of various mucous membranes. However, the role of TSS has not been completely elucidated in the burn patient. It has been our experience that although burn patients may be infected with a TSS-producing S. aureus, no other serious or untoward complications have been observed. In fact, treatment of their burn wounds was no different from that in patients infected with a non-toxic S. aureus strain.

S. aureus and Staphylococcus spp. generally produce penicillinases, which hydrolyze the penicillin β-lactam ring and make natural penicillins ineffective against these bacteria. Therefore, these types of infections are treated with penicillinase-resistant penicillins. These antibiotics include the parenteral antibiotics nafcillin, methicillin, and oxacillin and the oral antibiotics cloxacillin, dicloxacillin, nafcillin and oxacillin. The staphylococcal infections that are resistant to penicillinase-resistant penicillins are termed ‘methicillin-resistant’.

Vancomycin alone or in conjunction with other anti-infectives has generally been considered the treatment of choice for infections caused by methicillin-resistant staphylococci. Vancomycin is bactericidal and appears to bind to the bacterial cell wall, causing blockage of glycopeptide polymerization. This effect, which occurs at a site different from that affected by the penicillins, produces immediate inhibition of cell wall synthesis and secondary damage to the cytoplasmic membrane. However, vancomycin is a time-dependent antimicrobial, which requires that the serum level of this drug must remain at all times above the minimum inhibitory concentration (MIC) in order to provide adequate bactericidal activity. The hypermetabolic burn patient exhibits an increased glomerular filtration rate and increased excretion of the renally cleared vancomycin. Because of the wide interpatient variability of vancomycin elimination in burn patients, the dosage must
be individualized in order to provide an optimal time-dependent serum concentration. The peak and trough levels are derived from the MIC for a particular bacterial organism. Because vancomycin is a concentration-independent, or time-dependent, antibiotic and because there are practical issues associated with determining a precise peak serum concentration with this multicompartment antibiotic, most clinicians have abandoned the routine practice of determining peak serum concentrations. The trough level for vancomycin monitoring is normally 10–15 μg/mL, and it is critically important to maintain that serum level between dosing intervals to achieve therapeutic as well as clinical success.

Prolonged exposure to serum levels close to the MIC promotes the emergence of resistance; therefore, it is important to maintain adequate serum concentrations in patients with fast or rapidly changing creatinine clearance, such as burn patients. There are also certain body compartments in which penetration is poor, such as the lung and the CNS. It would also seem prudent to keep concentrations from being suboptimal in patients with pneumonia or meningitis, as well as in patients receiving dialysis for renal failure. The American Thoracic Society published guidelines for hospital-acquired ventilator-associated and healthcare-associated pneumonia. These guidelines recommend vancomycin trough concentrations of 15–20 μg/mL for the treatment of methicillin-resistant *S. aureus* pneumonia. These higher concentrations may be needed for sequestered infections or in situations where vancomycin penetration has been documented to be poor. Recent testing has shown ‘vancomycin MIC creep’ that may necessitate higher vancomycin trough serum concentrations to eradicate these microorganisms in burn wound infections.

**Streptococci**

The streptococci produce a variety of hemolytic activity in the presence of blood. This hemolysis is considered a virulence factor, and quantitatively this group of organisms do not lend themselves to the standard rule of <10<sup>7</sup> for any tissue closure. In burn injury, the presence of even a few β-hemolytic streptococci can cause a wound infection, failure of a primary closure, and loss of a skin graft. The major species that can be diagnosed with this particular type of hemolysis are *Streptococcus pyogenes* (also referred to as group A streptococci) and *S. agalactiae* (also referred to as group B streptococci). The natural penicillins, which consist of penicillin G and penicillin V, and the first-generation cephalosporins are bactericidal to these bacteria. Should resistance or intolerance to the natural penicillins or first-generation cephalosporins develop, then culture and antibiotic sensitivity data should be used to treat the streptococcal infection appropriately.

**Enterococci**

The enterococci have become one of the most important causes of burn wound infection. This is likely due to widespread use of third-generation cephalosporins over the last decade, to which enterococci are resistant. Additionally, a major cause for concern is the emergence of vancomycin-resistant enterococci (VRE) in burn units. Although the exact rate of morbidity associated with VRE itself is unclear, when it occurs as a polymicrobial bacteremia a mortality rate as high as 20% has been noted. Therefore, enterococci appear to be not only common but also virulent burn wound pathogens.

**Oral treatment of Gram-positives**

The oral treatment of methicillin-resistant staphylococci may present a greater challenge to a burn clinician. Rifampin is a bactericidal antibiotic that has efficacy in the treatment of these organisms. Rifampin produces its action by inhibiting RNA synthesis in the bacteria, binding to the β subunit of the DNA-dependent RNA polymerase and blocking RNA transcription. However, it must be used in combination with other anti-infective in the treatment of methicillin-resistant staphylococci because of its high resistance pattern when used alone. Other anti-infectives with a different mechanism of action reduce the resistance of rifampin. Oral antibiotics such as Bactrim (sulfamethoxazole and trimethoprim) or levofloxacin are often used in conjunction with rifampin. Linezolid is a synthetic antibacterial agent of a new class of antibiotics, the oxazolidinones, which has joined the armamentarium against MRSA and MRSE. Linezolid inhibits bacterial protein synthesis by binding to a site on the bacterial 23S ribosomal RNA of the 50S subunit and prevents the formation of a functional 70S initiation complex, which is an essential component of the bacterial translation process. The results of time–kill studies have shown linezolid to be bacteriostatic against enterococci and staphylococci. For streptococci, linezolid was found to be bactericidal for the majority of the strains. In vitro studies, however, show that point mutations in the 23S ribosomal RNA are associated with linezolid resistance and have been reported with some strains of *Enterococcus faecium* and *S. aureus*. Adverse drug effects of linezolid include myelosuppression (e.g. anemia, leukopenia, pancytopenia and thrombocytopenia) which is generally reversible upon discontinuation of the drug, and *Clostridium difficile*-associated colitis. Linezolid is also a weak, non-selective, reversible inhibitor of monoamine oxidase (MAO) and may cause increased serotonin serum levels and serotonin syndrome in patients on various serotonin reuptake inhibitors such as fluoxetine and sertraline. Staphylococcal infections may also be treated with quinupristin/dalfopristin (Synercid). Quinupristin/dalfopristin is bactericidal and inhibits bacterial protein synthesis by binding to different sites on the 50S ribosomal subunit, thereby inhibiting protein synthesis in the bacterial cell.

**Enterococcal bacterial infections**

Most enterococcal bacteria are susceptible to vancomycin. Vancomycin-resistant enterococci usually will require treatment with a combination of agents such as ampicillin and aminoglycosides. If this combination is not effective, the VRE may be treated with the quinupristin/dalfopristin (Synercid) combination or linezolid. The literature also reports that the use of quinupristin/dalfopristin resulted in resistance in one study and a superinfection in another study during the treatment of VRE infection.

**Gram-negative organisms**

This family of Gram-negative rods contains a distinctive group of etiologic agents for burn wound infections.
The presence of this group of organisms is partially due to translocation of the bacteria from the gastrointestinal tract of patients. Of this group, the *Pseudomonas* species are the most repeatedly encountered burn wound pathogens. 

*Pseudomonas* spp. have a worldwide distribution with a predilection for moist environments. Because of their ability to survive in aqueous environments, these organisms have become problematic in the hospital environment. The spectrum of disease caused by this agent ranges from superficial skin infections to fulminant sepsis. *P. aeruginosa* is the leading cause of nosocomial respiratory tract infection. Wound infections due to *P. aeruginosa* are also particularly troublesome in burn patients. 

Other significant Gram-negative pathogens commonly associated with burn infection include *Acinetobacter* spp., which can be found as part of the indigenous flora of the respiratory, skin, gastrointestinal and genitourinary tracts of humans and animals. They have been isolated from a diversity of clinical sources, including upper and lower respiratory tracts, urinary tract, surgical and burn wounds, and in bacteremias secondary to intravenous catheterization. Many of the patients who develop infections with this microorganism have had various manipulations, including the use of respiratory therapy equipment, tracheal intubation, or bladder or central venous line catheterization. It is an agent of low virulence and has a predilection for infecting patients with dysfunctional host defense mechanisms. *Acinetobacter* spp. tend to have a high degree of antimicrobial resistance, which is most likely associated with previous antimicrobial therapy. 

The Enterobacteriaceae, such as *Escherichia coli*, *Klebsiella* spp., *Enterobacter* spp., *Serratia marcescens*, and *Proteus* spp., are additional Gram-negative organisms associated with burn patients. These organisms are often encountered as a cause of nosocomial pneumonia in patients with inhalation injury, as well as those with urinary tract infections associated with indwelling urinary catheters.

**Treatment of Gram-negative organisms**

Treatment of Gram-negative infection is usually guided empirically by an antibiogram specific for the unit or hospital, until culture and sensitivity reports become available. Testing for synergy between different classes of antibiotics is an option used to determine efficacy for multiply drug-resistant organisms (MDROs), although such testing is not yet widely available outside clinical reference laboratories. The aminoglycosides, particularly gentamicin, were historically the antibiotics of choice in the treatment of Gram-negative infections; however, some Gram-negative bacteria encountered in the burn unit are now resistant to all the aforementioned antibiotic classes and often the treatment option is relegated older drug classes, namely the polymyxins.

Polymyxins are recommended for serious systemic infections caused by Gram-negative bacteria that are resistant to other agents, and have a definite role in therapy of multidrug-resistant Gram-negative bacterial infections. Branski et al. reported the use of colistimethate sodium in a series of 118 patients between 2000 and 2006 (median and mean age of 9 years) with a mean TBSA of 64±19% at the Galveston Shriners Hospital for Children. The median treatment duration was 12 days and the mean dosage 4.4±0.9 mg/kg/d. The overall survival rate was 84%. Colistimethate sodium provided an important salvage option for burn patients with otherwise incompletely treated and life-threatening Gram-negative infections. Monitoring the dose-dependent nephrotoxicity and CNS toxicity associated with its systemic use, however, is necessary to achieve a therapeutic outcome. When polymyxin B is given to animals or humans, it binds, via its free amino acid groups, to negatively charged phospholipids in tissues. Kunin and Bugg showed that binding is greatest to kidney and brain tissues, followed by liver, muscle and lung tissues. After repeated doses, the drug accumulates in tissues to concentrations four to five times higher than peak serum concentrations and persists for at least 5–7 days. Removal of the drug by dialysis can be difficult owing to extensive tissue binding. Colistimethate sodium appears to proportionately increase the incidence of *C. difficile*-associated colitis, renal dysfunction and neuropathies in relation to the duration of its use. In the study from Galveston, however, no increased hepato-, neuro-, or nephrotoxicity was reported as compared to a control group without colistimethate treatment.

Aminoglycoside antimicrobials continue to be a frequent choice when sensitive organisms are encountered. Current evidence suggests that once-daily dosing of aminoglycosides is as effective as, and may be less toxic than, conventional dosage regimens employing multiple daily doses of the drug. Results of several analyses of pooled data from randomized controlled studies in adults found that once-daily administration of aminoglycosides was associated with similar or greater efficacy (e.g., bacteriologic and/or clinical cure), less nephrotoxicity, and no greater risk of otoxicity than administration of multiple daily dosing of these drugs. Less frequent (e.g., once-daily) dosing may minimize or prevent the occurrence of aminoglycoside-induced adaptive resistance (i.e., reversible refractoriness to the antimicrobial effects of subsequent aminoglycoside doses because of decreased uptake of the drug following the initial dose) and selection of aminoglycoside-resistant subpopulations in Gram-negative bacteria by allowing a recovery period during the dosing interval in which serum aminoglycoside concentrations are negligible. In burns, however, some clinicians have suggested that once-daily dosing of aminoglycosides may not be advisable in patients with serious infections and impaired host defenses (e.g., *P. aeruginosa* infections in patients with neutropenia) and/or clinical conditions associated with rapid clearance or unpredictable pharmacokinetics of aminoglycosides (e.g., extensive burns, cystic fibrosis, massive ascites), as these regimens could allow prolonged intervals of undetectable aminoglycoside concentrations. Therefore, monitoring of aminoglycoside serum concentrations and/or peak serum concentration/MIC ratio in burn patients with life-threatening infections, suspected toxicity or non-response to treatment, decreased or varying renal function, and increased aminoglycoside clearance is mandatory.

The usage of extended-spectrum penicillin in the treatment of Gram-negative bacterial infections provides a burn population with a much less toxic antibiotic than the aminoglycosides, as the most frequent adverse reactions include hypersensitivity reactions, gastrointestinal effects, and local reactions. Fourth-generation cephalosporins such as cefepime, extended-spectrum β-lactamase inhibitor
penicillins (piperacillin/tazobactam, ticarcillin/clavulanate) and most importantly the carbapenems (imipenem/cilastatin, meropenem, ertapenem) provide important tools in killing Gram-negative infections. Because these antibiotics work most efficaciously by maintaining a serum concentration of 1–2 times the MIC between dosing intervals, many clinicians suggest that more frequent dosing or longer infusions of 3–4 hours may be necessary to maintain this MIC for an effective kill rate. Because of their different mechanisms of action these different penicillin antibiotic drug classes may also be used in combination with other antibiotic drug classes to produce a synergistic therapeutic response.

### Anaerobes

The most repeatedly confronted organisms in this group which may play a role in surgical and burn wound infections are *Bacteroides* spp. and *Fusobacterium* spp. These anaerobes are considered normal flora of the human body, beginning at the oropharyngeal cavity and ending at the gastrointestinal (GI) and urogenital tract. Numerically they account for the major population in the oropharyngeal region in a 5:1 ratio over the aerobes and facultative anaerobes, whereas in the urogenital and GI tracts the ratio is more dynamic, at 1000:1.50,63 Yet when one scrutinizes the current statistics of anaerobic infections related to locality, all but 2–5% of surgical wound infections in the oropharyngeal area are caused by the anaerobic flora.64,65 Those occurring in the GI and urogenital tracts are only responsible for about 10–15% of the wound infections.53,66 Anaerobic infections in burned patients are usually associated with avascular muscle found in electrical injuries, frostbite, or cutaneous flame burns with concomitant crush-type injuries.18 With the advent of early excision and grafting, the incidence of anaerobic infections in thermal injury has been significantly reduced. If anaerobic infection is suspected, it is important that the collected specimens be placed in appropriate transport tubes void of atmospheric oxygen to provide ideal recovery conditions.

### Fungi – yeast and mold

Until the advent of topical antimicrobial agents, fungal infections were not common in burned patients. However, the incidence of mycotic invasion has doubled since the implementation of topical antimicrobial agents to control bacterial colonization.67 The burn wound is the most commonly infected site, although local or disseminated fungal infections of the respiratory, urinary and GI tracts and the vagina are becoming increasingly common.57,68 Yeasts are identified primarily on the basis of specific biochemical tests, but both macroscopic and microscopic morphology are also used in making a final identification. Mold identification is based on growth rate, colony structure, microscopic/microscopic appearance, dimorphism at different incubation temperatures, inhibition of growth by cyclohexamide, as well as some biochemical tests.64 *Candida* spp. are the most common fungal colonizers of the burn wound, although true fungi such as *Aspergillus* spp., *Penicillium* spp., *Rhizopus* spp., *Mucor* spp., *Rhizomucor* spp., *Fusarium* spp. and *Curvularia* spp. can also be present, and have a vastly greater invasive potential than yeasts.65,67

Early diagnosis of fungal infection can be difficult, as clinical symptoms frequently mimic low-grade bacterial infections. Routine culture techniques may require from 7 to 14 days to identify fungal contaminants, delaying the initiation of treatment.68 In contrast to bacterial sepsis, venous blood cultures may not reflect the causative fungal organism.22 Arterial blood cultures and retinal examination for characteristic candidal lesions can be useful. Unlike candidal infections, true fungal infections occur early in the hospital course of patients with specific predisposing characteristics. Most frequently, burned patients infected with fungi are exposed to spores in the environment, from either rolling on the ground or jumping into contaminated surface water at the time of injury. Other environmental foci have been cited as the source of nosocomial fungal infection, including bandaging supplies left open to the air, heating, and air-conditioning ducts and floor drains.65,67 Once colonized, broad non-branching hyphae extend into subcutaneous tissue, stimulating an inflammatory response. This phenomenon is diagnostic of fungal wound infection. Vascular invasion is common and often accompanied by thrombosis and vascular necrosis, clinically observed as rapidly advancing dark discolorations of the wound margins or well-described lesions.23 Systemic dissemination of the infection occurs with invasion of the vasculature. Treatments for yeasts and molds are vastly different, owing to their vastly different pathogenicities. Yeasts found in a burn wound are more often associated with colonization and do not represent an infection. Treatment usually is considered when the same yeast is identified at multiple sites, in which case topical treatment is used more liberally. In contrast, the identification of a mold in a burn wound is taken very seriously. Infection with mold is often invasive and requires very aggressive treatment, topically, surgically, and with IV medication. It is common to work with the pathologist to ensure that clean margins free of hyphae are obtained at the conclusion of a debridement. Amphotericin B has been the standard choice for intravenous treatment of invasive infection with mold. Currently, there are five classes of systemic antifungal medication, including the polyenes, the azoles, nucleoside analogs, echinocandins, and allylamines. These new drugs offer improved side-effect profiles over amphotericin B.

Although amphotericin B dexolate (AmBd), a polyene, has been the standard choice for IV treatment of life-threatening invasive mold, this drug is associated with significant toxicity, including infusion-related events and dose-limiting renal dysfunction.95 Three new lipid formulations of AmB (AmB lipid complex (ABLC), AmB colloidal dispersion (ABCD), and liposomal AmB (AmB-L)) offer several advantages over AmBd, including increased daily doses of the parent drug (up to 10–15-fold), high tissue concentrations in reticuloendothelial organs, a decrease in infusion-related events (especially ABLC and AmB-L), and a marked decrease in nephrotoxicity.96 These lipid drugs are more expensive than AmBd, but cost is best assessed pharmacoeconomically (cost of drug acquisition as well as cost of hospital stay, monitoring, complications, etc.). Authorities agree that these agents are indicated for patients who are intolerant of or refractory to AmBd, but controversy exists about the lipid drugs as initial therapy both in neutropenic patients with persistent fever and in patients with invasive mold disease.

For the majority of patients with systemic candidiasis, cryptococcosis and the endemic mycoses, e.g.,
Topical antimicrobial compounds and agents

One of the most effective means to achieve a microbial balance in a colonized or infected wound is the proper use of prophylactic topical agents. Maintaining wounds at low colonization levels diminishes the frequency and duration of septic episodes caused by wound flora. The introduction of topical antimicrobial agents has resulted in a significant reduction in burn mortality to date. However, no single agent is completely effective against all organisms, and each possesses its own advantages and disadvantages. Whereas topical agents retard wound healing, the application of some antimicrobial agents may increase the patient’s metabolic rate. Their effectiveness is measured by their ability to inhibit bacterial growth in vitro and reduce wound colony counts in vivo. Recent studies have demonstrated that some agents used in the past are no longer effective in inhibiting bacterial growth.

Wounds in which the quantitative culture counts remain <10^5/g tissue may remain dressed in the topical agent of choice. However, should the colony count increase beyond that point, a change in the topical agent is strongly recommended.

Sodium hypochlorite (NaOCl)

Currently the most effective topical antibacterial for cleansing a wound is sodium hypochlorite (NaOCl). It transcends the topical antimicrobial effects and tissue toxicity of such products as povidone-iodine, acetic acid, and hydrogen peroxide. Whereas povidone-iodine is bactericidal at concentrations of 1% and 0.5%, it is toxic to fibroblasts; acetic acid at a 0.25% concentration is not bactericidal and is toxic to fibroblasts; and hydrogen peroxide at 3% and 0.3% concentrations is toxic to fibroblasts, but only the 3% concentration is bactericidal. Studies by Heggers and co-workers reported on the efficacy of NaOCl at a concentration of 0.025%. This is one-tenth the concentration of ‘Half-Strength Dakins’, the formulation used by many hospitals as a topical antimicrobial agent. Buffered NaOCl 0.025% was formulated to mimic normal human physiologic parameters. It is an excellent cleansing agent which was found to be bactericidal, non-toxic to fibroblasts, and did not inhibit wound healing. However, the NaOCl 0.025% solution is only effective over a 24-hour time frame after the buffer (0.3 N NaH2PO4) is added to the NaOCl.

Buffered NaOCl 0.025% solution soaks are most beneficial in reducing bacterial numbers in a wound. NaOCl 0.025% solution is a broad-spectrum antiseptic and is bactericidal against P. aeruginosa, S. aureus, and other Gram-negative and Gram-positive organisms. It is effective against methicillin-resistant staphylococci and enterococci. A 0.025% NaOCl solution may be used separately or in combination with other antibacterial agents to control colonization or infection. This solution also enhances wound healing and increases wound breaking strength compared to mafenide acetate.

Silver nitrate (AgNO3)

Silver nitrate was formerly used as a 10% solution but was found to be toxic at this concentration. It has now been reconstituted as a 0.5% solution, which is non-toxic, does not injure regenerating epithelium in the wound and is bacteriostatic against S. aureus, E. coli, and P. aeruginosa. AgNO3 is most effective when the wound is carefully cleansed of all emollients and other debris, and debrided of all dead tissue. Multilayered coarse-mesh dressings should be placed over the wound and saturated with the AgNO3 solution. Like silver sulfadiazine, AgNO3 has limited penetration because silver is rapidly bound to the body’s natural chemical substances. Because it is hypotonic in nature it can cause osmolar dilution, resulting in hyponatremia and hypochloremia. Serum electrolytes must be monitored very carefully. A 0.5% solution of AgNO3 is light sensitive, and when it is allowed to dry out it turns black on contact with tissues and other Cl-containing compounds. Hyperpyrexia may also occur if AgNO3 becomes dry and is covered with an impervious dressing. Some institutions are combining silver nitrate with miconazole powder to produce an aqueous solution of silver nitrate 0.5% and miconazole 2% that is effective in preventing fungal overgrowth in burn wounds treated with silver nitrate 0.5% solution alone. Klebsiella spp., Providencia spp., and other Enterobacteriaceae are not as susceptible to AgNO3 0.5% solution as other bacteria. The combination of AgNO3 0.5% solution with Enterobacter cloacae and other nitrate-positive organisms may cause methemoglobinemia by converting nitrate to nitrite in the body.

Silver sulfadiazine

Silver sulfadiazine (Silvadene, Thermazine, Flamazine, SSD), a 1% water-soluble cream, is a combination of sulfadiazine and silver. The silver ion binds with the DNA of the organism, releasing the sulfonamide which interferes with the intermediary metabolic pathway of the microbe. It is most effective against P. aeruginosa and the enterics, and equally effective as any antifungal drug against C. albicans and S. aureus. However, some strains of Klebsiella have been less effectively controlled. Recently there have been reports of P. aeruginosa resistance to silver sulfadiazine. Silver sulfadiazine can be applied with equal effectiveness using either

blastomycosis, histoplasmosis, and coccidioidomycosis), AmBd or the azole drugs (voriconazole, fluconazole or itraconazole, posaconazole) should be used as initial therapy. Initial treatment with a lipid drug for these patients cannot be justified, unless the patient requires AmB therapy and has pre-existing renal dysfunction. However, the IDSA recommends that invasive aspergillosis be treated with the azole antibiotic voriconazole, because of its efficacy and lower toxicity profile. AmBd may still be used as an alternative. Posaconazole has also been cited as an effective treatment agent against aspergillosis. The azoles (fluconazole, itraconazole, voriconazole, and posaconazole) demonstrate similar activity against most Candida species, but each has less activity against C. glabrata and C. krusei. The echinocandins (caspofungin, anidulafungin, micafungin) have very good efficacy against these two Candida species and exhibit few adverse side effects. The echinocandins, however, may have less activity against C. parapsilosis. Flucytosine, a pyrimidine, has limited clinical indications, primarily in combination with AmBd, as therapy for cryptococcal meningitis and selected life-threatening Candida syndromes.

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closed or open methods. Antimicrobial effectiveness has been observed to last for up to 24 hours. More frequent changes are required if a creamy exudates forms on the wound. Some of the benefits of this topical agent are its ease of use and its ability to reduce pain. It has some tissue-penetrating ability, but this is limited to the surface epidermal layer. However, it is not associated with acid–base disturbances or pulmonary fluid overload, as is mafenide acetate. Silver sulfadiazine can be used separately or in combination with other antibacterials and with enzymatic escharotomy compounds. It can be combined with nystatin, which enhances the antifungal capability of this agent. By itself, silver sulfadiazine has been shown to retard wound healing. An adverse drug reaction may be a reversible granulocyte reduction, although this is controversial.7,71

**Mafenide acetate (Sulfamylon)**

Mafenide acetate is available both as an 8.5% water-soluble cream and a 5% aqueous solution. This agent has more substantial bacteriological data to support its efficacy than any other topical antimicrobial. Mafenide acetate has been shown to be effective against a broad range of microorganisms, especially against all strains of *P. aeruginosa* and *Clostridium*. After the wound has been cleansed of debris, mafenide acetate 8.5% cream is applied to the wound like butter (Lindberg’s Butter). The treated burn surface is left exposed for maximal antimicrobial potency. The cream is applied a minimum of twice daily and is reapplied between applications if rubbed off the wound. Advantages of the cream are its ability to control *P. aeruginosa* wound infections, ease of application, and the lack of a need for dressings. Additionally, it has the ability to penetrate burn eschar and circumvent the colonization of the burn.

The 5% solution is used to saturate an eight-ply gauze dressing which is then applied to the burn wound. The dressing should be kept saturated with the mafenide acetate 5% solution in order to achieve maximal antimicrobial effects. The dressings may be changed every 8 hours. Mafenide acetate 5% solution is proclaimed to have effective tissue-penetrating ability and appears to be especially effective after the dead tissue is removed from the granulating bed. However, there are several detrimental aspects to the use of mafenide acetate. Protracted use, combined with its low environmental pH, favors the growth of *C. albicans*. Mafenide acetate 5% solution is converted by monoamine oxidase to *p*-sulfamylvanzoic acid, a carbonic anhydrase inhibitor. Carbonic anhydrase inhibitors prevent the conversion of hydrogen ions in the body to carbonic acid, leading to metabolic acidosis in the patient. If the patient has sustained an inhalation injury and developed a respiratory acidosis, the use of mafenide acetate over large areas of the body may produce a metabolic acidosis, which can be fatal. This complication can also be seen when treatment with mafenide acetate occurs during septic episodes with metabolic acidosis or when applied over large areas of the body surface. Another detrimental problem encountered with mafenide acetate is that it is painful when applied to superficial partial-thickness burns with intact free nerve endings. The open application of mafenide acetate 8.5% cream to a burn wound site for increased antimicrobial activity may be considered a disadvantage if a burn wound dressing is necessary. However, it is quite effective in burn wound areas that are not well perfused, such as the ear. The 5% aqueous solution of mafenide acetate can be used in a wet dressing covered by the splint.

Studies have reported that the use of mafenide acetate 5% solution in patients with major burns resulted in a 33% reduction of fatality. As with silver sulfadiazine, mafenide acetate can be used individually or in conjunction with other antimicrobials. However, mafenide acetate retards wound healing and reduces the breaking strength of healed wounds.7

**Povidone-iodine (Betadine)**

A 10% ointment of povidone-iodine was developed after the active agent demonstrated a broad spectrum of antimicrobial attributes in liquid form. Although its active antimicrobial component is iodine, there has been no documentation associated with intact skin hypersensitivity or toxic effects. It has a broad spectrum of antibacterial and antifungal activities.7,74.77 Povidone-iodine ointment can be employed effectively in both closed and open techniques. Quantitative bacteriological assessments imply that iodine is most efficacious when administered every 6 hours. When it is used in this manner, it is effective in controlling and/or preventing bacterial colonization. However, there are some adverse effects associated with the use of this topical antimicrobial at burn wound sites. The topical application of this agent is painful. Recent studies imply that the iodine component of this topical agent may be absorbed more extensively in burn wound sites, resulting in iodine toxicity, renal failure, and acidosis. It has also been shown to be cytotoxic to fibroblasts, as previously described. However, it remains a highly effective disinfectant when used on intact skin.

**Gentamicin sulfate (Garamycin)**

Gentamicin sulfate is available as a 0.1% water-soluble cream and is chemically similar to other aminoglycosides, such as kanamycin and neomycin. It has a broad spectrum of antimicrobial activity. Its popular use in wounds was based on its antimicrobicidal efficacy against *P. aeruginosa*. However, gentamicin resistance has rapidly developed due to its widespread use as a topical antimicrobial agent.7,71

**Bacitracin/polymyxin (Polysporin)**

The topical antibiotics bacitracin and polymyxin are used in an ointment to ‘butter’ bolsters to prevent mechanical shearing of newly grafted tissue. However, this topical ointment barrier used after a grafting procedure has not shown to be effective in controlling infection. Many surgeons rely on this topical agent for skin graft coverage because it is non-toxic and is similar to petrolatum gauze dressings, which were previously considered as a dressing for grafts. These two antibiotics combined have little or no effect on localized burn wound infections, and prolonged use is associated with hypersensitivity development.

**Nitrofurantoin (Furacin)**

The topical antimicrobial nitrofurantoin was used in the past but had questionable value therapeutically. Recent research, however, has shown that nitrofurantoin is effective in the
Mupirocin (Bactroban)

Mupirocin is one of several antibiotics derived from the fermentation of *P. fluorescens* and is also known as pseudomonac acid A. Although the antimicrobial activity derived from cultures of *P. fluorescens* was first reported over a century and a half ago, this agent could not be used as an antimicrobial until Fuller et al. had executed a more complete isolation and purification of pseudomonac acid A. Further research described the antimicrobial activity of mupirocin as an inhibition of microbial isoleucyl t-RNA synthetase that causes inhibition of protein synthesis in the bacterial cell. In vitro studies have subsequently established that mupirocin has omnipotent inhibitory activity against the Gram-positive microbes, specifically *S. aureus* and *S. epidermidis*. Mupirocin’s efficiency in the treatment of infection or colonization due to *S. aureus*, whether methicillin sensitive or not, has been shown in various clinical settings. Rode and coworkers have provided additional data regarding the efficacy of mupirocin in the treatment of established wound infections with *S. aureus* that were resistant to systemic methicillin, topical mafenide acetate, and povidone-iodine. Recent in vitro and in vivo endeavors have shown mupirocin to be as efficacious in methicillin-resistant burn wound infections as bacitracin/polyoxymyín. Mupirocin inhibits wound healing by a half-life of 2 days compared to controls, but the breaking strength of the wound is significantly enhanced.

Acticoat AB

Acticoat AB Dressing consists of two sheets of high-density polyethylene mesh coated with ionic silver with a rayon/polyester core. Acticoat AB Dressing provides broad-spectrum antimicrobial, bactericidal coverage against VRE, MRSA, *P. aeruginosa*, *Candida* sp. and approximately 150 other organisms. It can remain intact for several days on the wound, if there is minimal exudation. Acticoat must remain moist to be active. Rewetting with water is recommended to avoid creating the silver salt. However, it has been reported that Acticoat remains active when covering a moist wound.

Nystatin (Mycostatin, Nilstat)

Nystatin is an antifungal antibiotic produced by *Streptomyces noursei*. Nystatin exerts its antifungal activity by binding to sterols in the fungal cell membrane. The drug is not active against bacterial and mammalian cells because they do not contain sterols in their cell membrane. As a result of this binding, the membrane is no longer able to function as a selective barrier to prevent the loss of potassium and other cellular constituents from the fungal cell. Nystatin has fungistatic or fungicidal activity against a variety of pathogenic and non-pathogenic strains of yeasts and fungi. In vitro, nystatin concentrations of approximately 3 µg/mL inhibit *C. albicans* and *C. guilliermondii*. Concentrations of 6.25 µg/mL are required to inhibit *C. krusei* and *Geotrichum lactis*. In general, there is little difference between minimum inhibitory and fungicidal concentrations for a particular organism. Nystatin is not active against bacteria, protozoa, or viruses. Nystatin is not absorbed systemically and is used orally for the treatment of intestinal candidiasis. In our burn population, nystatin ‘swish and swallow’ is used prophylactically to prevent the oral or perineal overgrowth of yeast and fungi in patients receiving two or three systemic antibiotics. In patients with coexisting intestinal candidiasis and vulvovaginal candidiasis, nystatin may be administered orally in conjunction with the intravaginal application of an antifungal agent. Most evidence suggests that combined therapy does not substantially reduce the risk of recurrence of vulvovaginal candidiasis, compared to intravaginal therapy alone. However, limited evidence suggests that the reduction of intestinal candidal colonization in combination with intravaginal antifungal therapy may provide some improvement in mycologic response and a reduction in recurrence rate of vulvovaginal candidiasis. For the treatment of cutaneous or mucocutaneous candidial infections, nystatin 100,000 units/g may be applied topically as a cream, lotion, or ointment to affected areas 2–4 times daily. The cream or lotion formulations are preferred to the ointment for use in moist, intertriginous areas. The use of occlusive dressings and ointment formulations should be avoided in the treatment of candidiasis because they favor the growth of yeast and the release of its irritating endotoxin. Concomitant therapy should include attention to proper hygiene and skin care to prevent the spread of infection and reinfection. In addition, the affected areas should be kept dry and exposed to air whenever possible. Burn patients are affected by an immunocompromised system and thus more susceptible to opportunistic infections. Depletion of the number of neutrophils, defects in neutrophil function, and T-cell defects all predispose the host to fungal infections. Aspergillosis and hyalohyphomycosis (specifically *Fusarium*) are the most common angioinvasive fungal infections in burn patients. Barret et al. examined the curative effects of direct application of nystatin powder on severely burned children affected by angioinvasive fungal infection.

The topical treatment of burn wounds with nystatin powder at a concentration of 6,000,000 U/g proved to be effective in eradicating the invasive fungal infections. This new regimen of topical treatment not only is effective superficially but also eradicates invasive clusters of fungi in deep wound tissues, as documented by pathological examination. The application of the powder is easy and does not produce pain or discomfort. It did not impair wound healing and all previously autografted areas healed uneventfully. Nystatin powder may be combined with silver sulfadiazine 1% cream and mafenide acetate 5% aqueous solution to prevent the overgrowth of yeast and fungi at the wound site due to continuous application of these potent topical antimicrobial agents.

Further reading


References


63. Baron S. Medical microbiology. 4th ed. Galveston, Tex.: University of Texas Medical Branch at Galveston; 1996:xvii, 292.
77. Georgiade NG, Harris WA. Open and closed treatment of burns with povidone-iodine. In: Polk HC, Ehrenkranz NJ, eds. Therapeutic advances and new clinical implications: medical and surgical antisepsis with batadine microbicides; the proceedings of the symposium co-sponsored by the Departments of Surgery, Epidemiology, and Public Health, University of Miami School of Medicine, Florida. n.p.: Purdue Frederick Co.; 1972:x, 157.
Operative wound management

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Skin grafting of granulation tissue following eschar separation has been replaced by operative intervention within days of injury. Skin substitutes, dermal replacements, skin tissue culture, and bioengineering are exciting and rapidly expanding technologies that are already offering amazing results. This chapter deals with the pathophysiology of the burn wound, the scientific basis of wound excision, and the techniques and technologies now available to burn surgeons.

Introduction

Surgery for burn injury is a key component to the multidisciplinary care of the burn patient. Early excision and grafting has dramatically changed the outcome and survival of the burn patient. Burned tissue promotes an inflammatory response at the junction of the eschar and the underlying viable tissue. Bacterial proliferation in the eschar attracts polymorphonuclear leukocytes that release large quantities of proteolytic enzymes and inflammatory mediators. Subsequent enzymatic action results in separation of the eschar, leaving granulation tissue. In large burns, the inflammatory response at the burned site becomes systemic. Mediators such as prostanoids, thromboxane, histamine, cytokines, and tumor necrosis factor are produced and released from the burn site. The serum levels of these mediators increase proportionally as the surface area of burn increases. The hypermetabolic response with increased protein catabolism, increased energy expenditure, weight loss, poor wound healing, and immune depression continues until the outpouring of mediators abates.1,2

Beneficial effects of operative wound management

Early excision and skin grafting to achieve wound closure have been shown to reduce infectious complications, reduce the length of hospital stay, and improve survival in burned patients of all ages. Children in particular have benefited from more prompt and extensive surgical intervention.3,4 There has been a remarkable increase in the burn size associated with a 50% mortality risk over recent decades, such that it is now unusual for a child to succumb to burn injury of any size, even if it is associated with an inhalation injury (Tables 13.1 and 13.2). Early prompt initiation of resuscitation, nutritional support, proper critical care and treatment of infection have also played a part in this achievement. Early operative intervention, however, has contributed most towards this major advance. Burke and colleagues reported on results of total excision of full-thickness burns in 1974.5 They applied allografts to cover the wound after excision of burn and controlled rejection by adding immunosuppressants. Children with massive burns began surviving their injuries where they had never previously done so. Improved mortality, shorter hospital stay, and fewer metabolic complications were noted by others when early excision was retrospectively compared with late excision.6 When 32 children with an average age of 7 years and mean burn size of 65% total body surface area (TBSA) who underwent either total excision or serial debridement were studied, mortality, overall blood loss, and cumulative operating time were equivalent.7 The early excision group, however, had their length of hospital stay almost halved (97 ± 8 days vs 57 ± 5 days). Since that time, hundreds of children with burns >30% TBSA treated with early excision have exhibited a length of hospital stay less than 1 day/9% TBSA burned.8

Tompkins and colleagues showed that mortality of adult burn patients at Massachusetts General Hospital declined from 24% in 1974 to 7% for 1979–1984 after prompt eschar excision and immediate wound closure was instituted as standard.9 This study was expanded to include 85 patients aged 17–55 years.10 Those patients aged 17–30 years without inhalation injury showed significantly reduced mortality if treated by early excision (9%) than if treated conservatively (45%). Patients with a concomitant inhalation injury or aged over 30 years, however, derived no survival benefit from early excision. In burned children, Xiao-Wu and colleagues showed that delays in excision of severe burn were associated with longer hospitalization, delayed wound closure, increased rates of invasive wound infection, and increased incidence of sepsis.11

Munster and colleagues demonstrated a statistically significant decrease in length of hospital stay that correlated with a decrease in the interval between surgical interventions over a 14-year period.12 Other variables, such as burn size, inhalation injury, and age, remained static during this time; they found that mortality rate decreased significantly whereas burn indices remained constant. The average annual increase in hospital charges for burn care grew to 9.6%, which was substantially lower than the hospital as a whole (10.8%). Active surgical intervention in burn care can be associated with cost containment and fewer lives lost.

Elderly burn patients also have been shown to benefit from an early surgical treatment. Deitch and colleagues operated upon consecutive patients with an average age of 68 years and showed a reduction of 40% in mean length of hospital stay compared to the national average, and...
These are typically flame or contact burns. Heimbach and colleagues observed that deep partial-thickness burns did not convert to full-thickness burns when topical antimicrobials were used to control infection. Although these wounds eventually healed after many weeks, they showed persistent blistering, pruritus, hypertrophic scar formation, and poor functional results. These observations prompted a prospective trial of early excision and grafting versus non-operative treatment of burns of indeterminate depth of less than 20% TBSA. Shorter hospitalization, lower cost, less time away from work, but greater use of blood products, were seen in those treated with early operation. Those patients treated non-operatively required more late grafts for closure and also developed more hypertrophic scars.

Tangential excision

Tangential excision removes burned skin while preserving the underlying viable tissue. Body contours are better preserved than with fascial-level excision, and therefore this is the standard method for small burns. The technique of tangential excision was originally described by Janzekovic, who observed that deep skin graft donor sites could be grafted with thinner split-thickness skin graft taken from another area. She then extended this concept to partial-thickness burns by excising thin layers of burn until viable tissue was reached. Split-thickness skin grafts were immediately applied. This technique of tangential excision and autografting of partial-thickness burns was a major advance. Prior to this time, only full-thickness burns were excised, usually as a formal integumentectomy, taking subcutaneous fat and accompanying lymphatics down to the underlying layer of investing fascia. Janzekovic analyzed the results of the use of tangential excision in over 2000 patients. She found that, compared to fascial excision, hospital length of stay, pain, and reconstructive procedures were decreased. A number of different instruments can be used to perform tangential excision. The Rosenberg knife, Goulian knife, Watson knife, and the Versajet Hydrosurgery System water dissector are used. The Goulian knife and the Watson knife are probably the most popular instruments for tangential excision. If the burn depth is superficial, partial-thickness burns are debrided to a white, shiny dermal surface with punctate bleeding. In full-thickness burns, excision continues layer by layer until viable subcutaneous tissue with

<table>
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<tr>
<th>Techniques of burn wound excision</th>
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Excision of a small burn

Operative intervention is indicated without further delay once a burn wound is determined to be 'deep.' 'Deep' burns are those which are clearly either full-thickness or deep partial-thickness burns unlikely to heal within 3 weeks.

<table>
<thead>
<tr>
<th>Table 13.1</th>
<th>Mortality following burn over time for different age groups, shown as the burn size at which 50% live or die – lethal area 50 (LA50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age [years]</td>
<td>LA50 (% TBSA)</td>
</tr>
<tr>
<td>0–14</td>
<td>49</td>
</tr>
<tr>
<td>15–44</td>
<td>46</td>
</tr>
<tr>
<td>45–64</td>
<td>27</td>
</tr>
<tr>
<td>&gt;65</td>
<td>10</td>
</tr>
</tbody>
</table>

TBSA, percentage of total body surface area burned; LA50, lethal burn area for a 50% mortality. 1992–2004: Branski LK, Barrow RE, Herndon DN, unpublished data.

<table>
<thead>
<tr>
<th>Table 13.2</th>
<th>Pediatric-specific mortality rates over time. Near-total early excision is the basis of these excellent results. Mortality and pediatric burn patients, Shriners Burn Institute, Galveston, Texas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Years</td>
<td>Mortality sorted by burn size (% TBSA)</td>
</tr>
<tr>
<td></td>
<td>&lt;20%</td>
</tr>
<tr>
<td>1980–1985</td>
<td>&lt;0.1%</td>
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<tr>
<td>1986–1990</td>
<td>&lt;0.1%</td>
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<td>1991–1995</td>
<td>&lt;0.1%</td>
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<tr>
<td>1996–2000</td>
<td>&lt;0.1%</td>
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<tr>
<td>2001–2004</td>
<td>&lt;0.1%</td>
</tr>
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n, total number of patients admitted with respective burn size in given period.
Fascial excision

In fascial excision, skin and subcutaneous tissue are removed en bloc using electrocautery. This involves surgical removal of the full-thickness of integument, including all the subcutaneous tissue, down to the layer of investing fascia. It is important to achieve a yellow glistening appearance, as dullness, purple discoloration, or thrombosed vessels indicate non-viable tissue upon which grafts will fail, and deeper excision is mandatory (Fig. 13.4). Grafts may take initially, but will eventually fail. When excision is performed on limbs with a pneumatic tourniquet, these features are especially important.

Fascial excision

In fascial excision, skin and subcutaneous tissue are removed en bloc using electrocautery. This involves surgical removal of the full-thickness of integument, including all the subcutaneous tissue, down to the layer of investing fascia. It is
performed to reduce blood loss when there is massive burn, or in case of severe infection to control the source of infection. Fascial excision can limit the amount of blood loss because control of the deeper perforating vessels is achieved, bypassing the extensive capillary network present in the skin and subcutaneous tissue. Fascial excision is also required for those areas where subcutaneous tissue has been burned. The advantages of this technique are that grafts take well on fascia and blood loss is reduced.

Fascial excision is also indicated for life-threatening invasive wound infection or sepsis, particularly with fungi such as Aspergillus and Mucor, and also for large areas with failed graft take in a critically ill patient with massive burns. Episodes of sepsis lead to ischemic necrosis of subcutaneous fat due to poor peripheral perfusion and microvascular stasis. This becomes problematic in patients with very large burns and leads to late graft loss, and these ischemic areas become portals for invasive wound infection. The disadvantages of fascial excision are lymphedema and contour deformities.

**Controlling blood loss**

Excision of burns can result in considerable, if not massive, blood loss. Tangential excision can lead to large blood loss unless measures are taken to limit potential hemorrhage. The simplest measure is to operate within 24 hours of injury. Vasoactive metabolites, particularly the potent vasoconstrictor thromboxane, are in abundance during this time to limit blood loss. Desai and colleagues showed in a prospective trial of 318 pediatric patients with burns >30% TBSA that early excision of burns is associated with an overall reduction in blood loss. The average blood loss per surface area excised (mL/cm²) was compared at various postburn periods of excision. The total blood loss during excision performed within the first 24 hours after burn was 0.4 mL/cm² excised, compared to 0.75 mL/cm² excised if performed between days 2 and 16 post burn. The blood loss dropped to 0.49 mL/cm² excised if the procedure was performed after the 16th day. Overall mortality was 5% for an average burn size of 60% TBSA. Early excision had no adverse effect on mortality. Very early excision led to a halving of blood loss for both large and small burns (Fig. 13.5).

Other factors associated with increased blood loss during excision of burns are older age, male gender, larger body size, total area of full-thickness burns, high wound bacteria counts, total area excised, and operative time.

In the operating room, several techniques to reduce blood loss during excision of burns can be employed. Adjunctive measures to limit blood loss include tourniquets for the extremities, pre-debridement tumescence with weak epinephrine solutions, topical application of epinephrine 1:10,000–1:20,000, topical application of thrombin, fibrin sealant, autologous platelet gel, calcium-enriched alginate sheets, and immediate bandaging with delayed grafting.

The application of tourniquets to extremities is very effective at minimizing blood loss, especially for the hands and fingers. As with tumescence, the lack of bleeding can make the right depth of excision difficult to determine. To counteract this, the tourniquet can be released briefly to check the adequacy of excision and then reinflated. The larger vessels are controlled by electrocautery or ligation and the wound is covered with sheets of calcium alginate or sponges, which are soaked in epinephrine solution. The tourniquet is released after 5–8 minutes. The limb should then be held elevated for about 10 minutes.

Tumescence with epinephrine containing saline can be injected into the burn wound prior to excision. This technique is particularly useful for the trunk, scalp, and face; 1.6 mL of 1:1000 epinephrine (0.8 mL in pediatric patients) is added to 500 mL of 0.45% normal saline solution. The resulting local vasoconstriction will minimize blood loss. One-way syringes, such as the Multi-Ad Fluid Dispensing System or a pneumatic infuser, can make the injection process easier (Fig. 13.6). Monitoring the patient’s hemodynamics is necessary because the epinephrine may cause
tachycardia and hypertension, which can worsen bleeding. Another drawback of this technique is that the lack of bleeding from the wound bed makes the adequacy of excision difficult to assess.

When dealing with large areas of disrupted capillaries, one of the most effective ways to safely limit blood loss is rapid excision followed by coverage with epinephrine-soaked sponges and compressive bandages.

Delayed grafting is used in some centers to limit blood loss. If delayed grafting is undertaken, the wound bed needs to be kept moist and clean. The wound can be covered with bulky cotton dressings with tubing through the dressing to the wound surface for continuous or intermittent irrigation with antibiotic solution. The patient returns to the operating room within 24 hours and undergoes a second procedure of procurement and application of skin grafts. This may be a practical approach in cases of large excisions, where coagulopathy can develop due to large blood loss or hypothermia.

Techniques of wound closure

The standard treatment for a full-thickness burn is excision and grafting. Once procured, the autograft can be used in different ways depending on the amount of body surface area that requires grafting.

Autografts are classified as full or split thickness depending on the depth of dermal layer included. Full-thickness autografts have better cosmetic results and reduced scarring compared to split-thickness grafts because the dermis provides flexibility and elasticity. The main caveat is that the increased amount of dermis in the full-thickness graft can compromise its own viability during the imbibition, inosculatation, and neovascularization phases of graft take. The donor site completely devoid of dermis must be closed primarily or grafted. Because of the reasons mentioned above, split-thickness skin grafts are mainly used in the treatment of extensive burn injuries.

If the burn is small, skin grafts can be applied as a ‘sheet’ and no meshing is performed. The advantages are better cosmetic and functional outcome. The disadvantage is the possible accumulation of seroma or hematoma that can compromise the apposition of the graft to the wound bed. Seroma or hematoma should be identified and removed by ‘rolling’ them out or by aspiration with 27 gauge needle. The graft can be secured to the wound bed with quilting sutures or the application of a bolster dressing, which can reduce shearing of the graft. These grafts are best laid perpendicular to the long axis of limbs, particularly across joint flexural creases, which is in line with the general rule of placing potential scars perpendicular to the dominant muscle contraction in the area. This will reduce the degree of contracture if it occurs. Possible exceptions are the dorsum of the hand and forearm, where some clinicians argue that longitudinally placed grafts are cosmetically superior.

If burns are large and donor sites limited, autograft is meshed. This allows the autograft to be expanded to cover a wider area than its original size. The most common mesh ratios are 2:1 and 4:1, although different ratios of expansion can be employed. The main advantages of 2:1 meshed autograft is the easy handling and application, and the extensive network of slits that allows seroma or hematoma to drain. The main disadvantage is that the diamond-shaped interstices will leave a visible pattern once healed. Much larger areas can be covered when autografts are meshed 4:1 or greater and widely expanded. This widely meshed skin requires an overlay coverage of non-expanded allograft in a sandwich pattern to decrease the risk of graft loss. These are applied at 90° to the autograft in a sandwich pattern (Fig. 13.7). The difficult handling, the large interstices that take considerable amount of time to heal by epithelialization, the need for an allograft overlay, and the poor cosmetic result limit the use of meshed autograft to massively burned patients. Even in large burns, the face, neck, and hands are grafted with sheet split-thickness skin graft.

The Meek technique, which was later modified by Kreis and colleagues, is another tool to cover extremely large burn surface areas. It uses autograft cut into small squares with the aid of a dermatome and a cork board. These squares are then passed onto prefolded pleated gauze that is expanded in all four directions, leaving uniformly distributed islands of autograft which are then applied to the wound bed. Ratios of expansion can vary from 1:3 to 1:9. This technique has similar disadvantages to 4:1 meshed autograft and requires overlay with allograft.

Advances in wound closure

Dermal replacement

The flexibility, elasticity and strength of normal skin are provided mainly by the dermis. Excision of full-thickness burn removes the entire dermis. A layer of scar develops between the graft and the underlying tissue which prevents the healed skin from having the properties of normal skin.

The use of dermal replacement in the treatment of burns brings new hope in providing the highly desired characteristics of normal dermis. Integra is a dermal analog composed of a porous matrix of cross-linked bovine collagen and glucosaminoglycan that provides a scaffold for a cellular invasion and capillary growth. This is placed over the wound bed after excision. The matrix is fully incorporated into the
wound bed in 2–3 weeks and a thin split-thickness autograft is placed over it. Except for a possible increase in risk of infections, its use is safe and effective. Engraftment is aided by the use of negative-pressure dressings such as VAC Therapy (Fig. 13.8).

Another dermal analog available for the treatment of full-thickness burns is AlloDerm. This consists of cadaveric dermis devoid of cells and epithelial elements. Its use is very similar to that of other dermal analogs, and it has shown favorable results.

Cultured epidermal autograft

Cultured epidermal autograft (CEA) is an important tool in the management of patients with massive burns. In full-thickness burns involving more than 90% TBSA it may be the only choice, given that procurement of the uninvolved skin will not be sufficient to cover the patient’s wound.

Munster has shown that the use of CEA in the massively burned patient reduced mortality. CEA involves obtaining two 2 × 6 cm full-thickness specimens of unburned skin. The skin is processed and cultured ex vivo in the presence of murine fibroblasts that promote growth. The final product takes approximately 3 weeks to be ready for grafting and consists of sheets of keratinocytes, 2–8 cells thick; consequently, shearing and blistering is common for many months. Long-term survival of CEA is therefore particularly problematic on the posterior surfaces of these massively burned patients and goes some way towards explaining the 5–50% long-term CEA engraftment rates reported in the literature. CEA applied to areas such as the back, buttocks, posterior lower extremities, and other dependent areas is prone to shearing and possible graft loss. Barret and colleagues compared the use of CEA with wide mesh autograft and allograft overlay in a group of children with >90% TBSA. Once healed, the CEA has a better cosmetic result than healed 4:1 meshed autograft, but is associated with a longer hospital stay and more reconstructive procedures.

Tissue engineering technology is advancing rapidly. Fetal skin constructs have been recently successfully trialled and the bilaminar cultured skin substitute is showing promise.

Skin procurement

Many factors are considered when choosing the best donor site. Donor sites represent new wounds that can add significant morbidity to the patient: patients usually complain of more pain at the donor site than at the burn wound or graft area. Whenever possible, grafts that match the color of the recipient area should be pursued. The face and neck should
be grafted with skin procured from the area above the line of the nipple for the best color match. Thigh, hip, and back are commonly used as donor sites because the skin is flat for easy procurement, and scars are easily covered under clothing. The scalp may represent an ideal donor site because it is associated with less pain and rapid healing, given the rich blood supply. The subsequent scar can be hidden after the regrowth of hair.

Good-quality grafts of consistent depth are obtained by use of an electric or pneumatic powered dermatome. The
depth of the procurement can be precisely adjusted to the desired thickness, usually between 0.006 and 0.018 inches. Patients with extensive burns have few potential donor sites. Anatomical regions that are usually spared and represent viable options for procurement are the axilla, the mons pubis and the scrotum. Given the irregular topography, tumescence can be used to obtain useful amounts of skin graft. Although less optimal, the soles of the feet can also be used in extreme circumstances. The first layer obtained is discarded because it represents the stratum corneum, which has no viable epithelial cells.

In severely burned patients, several operations will be required for wound coverage as donor sites are limited. A limiting factor to repeat grafting is the time to healing of the donor sites. Healing at these sites comes from proliferation and migration of the epithelial cells from the hair follicles, the sweat glands, and the oil glands situated deep inside the dermis.

**Donor site management**

After the skin graft has been procured, careful management of the donor site wound is mandatory to expedite healing. Smaller donor sites can be treated with occlusive or adherent dressings such as Opsite or Biobrane. Another technique is to use alginite sheets or hydrocolloid fiber dressings. These have the advantage of promoting a moist wound healing environment and may diminish donor site pain. The wounds can be also covered with gauze impregnated with an oil-based ointment. The most common examples are Xeroform or a fabricated dressing containing olive oil, petrolatum, lanolin, and the chemotactic agent Sudan red. Silver-impregnated dressings such as Acticoat, Acticoat Absorbent or Aquacel Ag seem to diminish bacterial overgrowth and can be used directly on the donor site or as an intermediate layer. Skin graft donor sites heal primarily by epithelialization from the remaining epithelial elements. The time to healing depends on depth of procurement, the vascularity of the donor site, wound management, and general patient condition.

**Dressings**

After excision and grafting, the wounds are covered with non-adherent dressings. At our institution, gauze impregnated with a petrolatum-based ointment is used. This ointment contains an antibacterial (Polymyxin/Bacitracin) and an antifungal (Mycostatin). This is followed by the placement of a thick layer of fluff gauze that is then covered with an elastic bandage. With areas of the body prone to shearing, such as the back and axilla, the application of a bolster dressing can be beneficial. The application of negative-pressure dressings such as VAC Therapy can also be useful to splint and protect the grafts. Dressings are usually removed on postoperative day 3 or 4. This time frame is normally sufficient to allow for adherence of the graft to the wound bed.

**Temporary skin substitutes**

Providing wound coverage with skin substitute, even if it is temporary, has many advantages. Wound coverage prevents water and electrolyte losses as well as tissue desiccation, which in turn maintains a moist environment that allows faster epithelial cell proliferation and migration. Other benefits include minimizing pain, a barrier to bacterial contamination, and prevention of protein loss. The main options available are allograft, xenograft, and amniotic membrane.

Allograft, also known as homograft, is an effective temporary wound coverage after tangential or fascial excision. It can be stored in a cryopreserved state for an extended period, and becomes adherent and vascularized when applied to viable wound beds. This process can serve as a test for wound bed viability. Immune rejection takes place 3–4 weeks after its application. When used to temporarily cover the face and hands, it should be applied as a sheet graft to prevent the formation of granulation tissue inside the interstices, which can cause scarring and poor cosmetic outcome after definitive autografting takes place.

Xenografts are another option for temporary wound coverage. Only those derived from porcine dermis are currently available. Their main use is for partial-thickness burns after superficial debridement, as well as for donor sites. As with allograft, xenograft becomes adherent and provides many of the benefits of having the wound covered, such as pain control while the underlying wound bed epithelializes, but it does not vascularize.

Sterilely processed amniotic membranes can also be used to provide temporary coverage for superficial burns. Given its flexibility and pliability, amnion is useful in irregular surfaces such as the face. Even though it does not reduce healing time or scarring, it provides some of the benefits of wound coverage and reduces the number of dressing changes required.

**Management of specific burns**

**Scald burns**

Scald burns of small or moderate size have been shown to be the exception to the general rule of early excision. Young children who had scald burns up to 20% TBSA required less area to be excised and had smaller blood loss if operated upon in the second or third week post burn. A subsequent prospective trial randomized 24 children to early or late excision if their scald had caused burns of clinically indeterminate depth. No patient experienced a significant wound infection or sepsis. Only half of the delayed excision group ultimately required surgical intervention, and a significantly smaller area of excision was necessary.

In light of the foregoing evidence, children with scald burns <20% TBSA can be appropriately treated with a topical antimicrobial such as silver sulfadiazine for about 2 weeks. This approach needs to be balanced by the knowledge that the longer a wound remains open, the greater the inflammatory response and subsequent scarring. A number of techniques are available to cover the partial-thickness burn. When successful, they have the added advantage of eliminating a great deal of the pain associated with frequent dressing changes. More superficial wounds can be covered by a polyurethane membrane such as Omiderm. The authors favor Biobrane for smaller and more superficial wounds.

Biobrane is a nylon/silicone bilaminated composite skin substitute. At the time of the first wound dressing application, all
loose skin and blisters are removed to leave a clean, moist surface. The material works by becoming densely adherent to the exposed dermis, thereby acting as a neoepidermis. Lal and colleagues reported no increase in infection rates using Biobrane. If infections do occur, it is usually as a result of non-adherence and accumulation of fluid. Some centers have taken a middle road and use silver-impregnated dressings such as Acticoat, with great success. This has the advantage of having antimicrobial activity and only needs to be changed every 3–7 days. A series of catheters are inserted through the overlying dressing through which 5–10 mL of water are instilled every 4–6 hours. Glycerol or cryopreserved allograft or xenograft have also been used.

Large burns

Patients with deep burns >40% TBSA pose unique challenges with many conflicting demands for available donor sites. Near-total excision should be completed as soon as possible in the first few days after injury. The back, buttocks, and posterior thighs are covered with autograft taken at 8–10/1000, which is meshed at an expansion ratio of 4:1. This is applied to the wound bed and spread wide. Irrigation via a bulb syringe is useful to spread the thin, fragile graft into the appropriate position. ‘Fresh’ allograft is the best option as an overlay to protect autograft.

Consideration needs to be given to the use and extent of dermal replacements such as Integra. Dermal replacement is an expensive option, but one that leaves an excellent result. Integra is a bilaminar composite that has a neodermis of bovine collagen held in a matrix pattern with shark cartilage chondroitin-6-sulfate. A layer of rubberized silicone is press sealed onto this and acts as a neoepidermis. The abdomen, anterior thigh, forearm, leg, and male chest are sites where Integra can easily be applied (Fig. 13.9).

Meticulous surgical technique is essential. Topical epinephrine, direct pressure, compression wrapping, epinephrine clysis, and electrocautery are the hemostatic methods of choice. Integra is best held in place either by a VAC Therapy or by attaching an elastic netting material (Surginet) over it. A layer of Acticoat is frequently added in many centers. Further protection is provided by layers of netting (bridal veil, Conformant 2, Exudry). The neodermis is vascularized from the underlying wound. This process takes 2–3 weeks to complete. The neodermis often becomes a plum color due to suffusion through the matrix of red cells from minor hemorrhage. This is normal and should be left alone. Hematoma or seroma can be aspirated with a 27 gauge needle. Integra overlying the hematoma is best incised, hematoma removed, and the edges stapled down.

The neodermis is ‘ready’ when it has a ‘straw’ color. Close inspection under magnification will reveal telangiectatic vessels dotted about. The second-stage operation involves gentle removal of the silicone layer and application of 6/1000 inch autograft, which can be meshed up to an expansion of 3:1. CEA has been used as epidermal cover for Integra neodermis. In sick patients with very large burns there is benefit in performing staged, sequential replacement of the silicone layer with thin, 1.5:1-meshed autograft. Engraftment and graft survival seems to be more reliable in the long term and the cosmetic result is enhanced. Debate continues regarding the role of Integra in wound coverage of patients with burns >70% TBSA. The incidence of failure due to infection rises dramatically as the burn size tops 75% TBSA. First choice would be to excise all burn wounds and start covering the wound beds with autograft and the uncovered areas with allograft. The patient is taken back to the operating room for regrafting once used donor sites are healed.

Massive burns

The operating room

A very important perioperative issue for safe management of a patient undergoing massive burn excision is the maintenance of body temperature. The patient is usually completely...
exposed and has little intact skin, especially after donor skin procurement, leading to rapid heat loss. A number of strategies can be used to counteract heat loss and maintain normothermia. The operating room should be warmed to 32°C. The latent heat of evaporation of water is 31.5°C. Above this temperature, the energy source for evaporation will come from the environment rather than the patient. Radiant heaters are also helpful for perioperative thermoregulation. Other adjunctive measures include the use of ‘space blankets,’ aluminum foil coverings, plastic sheeting over the head and face, and all intravenous fluids being given at 38°C through a warming coil. Repeated applications of warm sterile blankets or forced air warming systems are useful. Irrigation fluids are used warm. In addition, insulating blankets and active heating are available via either infrared or ceramic heaters.

The burn operating room is an extension of the burn intensive care unit. Large, heated (32°C), humid and well-lit rooms are ideal for burn surgery. The procedures are long, intense, and require multiple individual setups for different types of equipment and instrumentation.

The ideal operating room environment should allow only minimal evaporative loss from the patient. Filtered warm water connections and pressurized gas connections should be available to power shower heads, dermatomes and other gas-driven instrumentation. The surgical bed should be positioned under supporting ceiling brackets or railings that allow for the hanging of irrigation solutions and equipment. This will also provide anchorage for suspension of extremities as needed during the operation. Reliable vascular access is required, and these lines should be sutured securely to prevent dislodgment during positioning of the patient.

The operation

Excision commences with the patient in the prone position. Excision of the shoulders, back, buttocks, and upper thighs is performed. Wide-meshed autograft with allograft overlay is applied. If insufficient autograft is available, the excised wound is covered with unexpanded, meshed fresh allograft. Other alternatives include skin substitutes such as Integra, xenograft, or cryopreserved allograft. Dermal replacement material is prone to failure owing to infection in massive burns, particularly on posterior surfaces, but can be used selectively on anterior surfaces. In the case of allografts multiple layers of bulky gauze dressings are applied over the antibiotic-impregnated gauze. Silk sutures are inserted in a row along the posterior axillary lines and tied over the bulky gauze dressing as a bolster to prevent shearing of grafts on the back and buttocks. The patient is then placed in the supine position. A tourniquet can be used on the limbs to reduce blood loss during excision. Weak epinephrine crysis, topical 1:10000 epinephrine irrigation, topical thrombin spray, epinephrine-soaked sponges, and direct application of pressure are all techniques used to limit blood loss during debridement.

As soon as donor sites are healed patients return to the operating room for further autografting and replacement of non-adherent allograft or infected skin substitute. In massively burned children, treatment with recombinant human growth hormone (GH) showed that donor site wound healing accelerated by 25%. GH-treated patients require less infused albumin to maintain normal serum levels, and this is an indication of the net positive protein balance.46 The usual hospital stay of 42 days for a 30 kg patient with a 60% TBSA burn was reduced to 32 days. This tremendous decrease in length of hospital stay realized a net saving of 15% in total costs. Salutary effects have also been documented in a group of patients treated non-operatively. Mortality dropped from 45% to 8%.45 Although it must be acknowledged that two European studies in critically ill adults of mixed etiology showed increased mortality among the GH-treated groups, this experience has not been repeated in the massively burned pediatric population in North America.50 Other anabolic agents have shown promise as a means of speeding wound healing in severely injured catabolic burn patients.51 Oxandrolone 20 mg/day has demonstrated a positive effect on protein kinetics and wound healing in clinical trials.51,52 In oxandrolone-treated severely burned adults, donor site wound healing was accelerated by 20% compared to non-treated patients.51 Although these pharmacological agents provide great support to the massively burned, they are only an adjunct to early near-total excision and prompt wound coverage.

Operative management of burns in special areas

The hand

Survival after serious burns has improved dramatically over the past 20 years.53 However, despite generally satisfying long-term quality of life, many such patients will have significant physical disabilities, many of which can be traced to compromised hand function. If optimal function is to be recovered after a very serious burn, proper acute care of the injured hand is essential. These early efforts should be directed at preservation of tissue, maintenance of normal hand geometry, and developing a strategy for wound closure.

Escharotomy and fasciotomy

A critical part of the initial care of hand burn is to ensure that soft tissues are well perfused. Decompression of high tissue pressure from burn skin with edema is an area in which early surgical intervention can make a tremendous difference to the ultimate outcome. Hands at risk for ischemia include those with circumferential or near-circumferential burns, those with very deep burns, and any electrical injuries involving high or intermediate-range voltage. It is important to look at signs more subtle than the loss of a palpable pulse in named arteries at the wrist. Mean arterial pressure in the central system is three times higher than capillary pressure, and blood flow may be maintained in these larger vessels when flow in distal soft tissues is impaired. If the hand is warm, soft, and has pulsatile flow detectable by Doppler in the palmar arch and digital vessels, and a normal transmission pulse oximetry signal at the distal digit, then flow is adequate. As flow is progressively impaired, the hand will become firm and cool, with decreased Doppler flow and loss of the pulse oximetry signal. Voluntary movement will become difficult and the hand will assume a clawed position. Decompression should be performed to prevent...
Operative wound management

supplemented with subeschar injections of local anesthetic. Some patients will require a general anesthetic in the operating room to have this procedure performed properly, especially if digital escharotomy is needed.

Fasciotomy may be needed for edema within the fascial compartments of the forearm and hand. Clinically this is often seen after high-voltage electrical injury or exceptionally deep thermal injury. Upper extremity fasciotomy may include volar and dorsal decompression, carpal tunnel release, and dorsal hand fasciotomy. A curvilinear incision is ideal for volar exposure of the compartments of the forearm. This approach allows one to gain access to all individual muscle bundles in the volar forearm and decompress the carpal tunnel through a contiguous incision, and creates a well vascularized flap of skin that will maintain coverage over the median nerve at the wrist upon completion of the fasciotomy. When needed, straight linear incisions are adequate for exposure of the dorsal aspect of the forearm. Intermetacarpal incisions on the hand allow one to decompress the intrinsic muscles of the hand if this is necessary.

Techniques of excision and grafting

It has become increasingly clear that allowing hand injuries to heal by contraction over the course of many weeks gives very poor long-term results. Surgery is indicated for any deep dermal or full-thickness hand burn that will not promptly heal within 3 weeks. Generally, this need is apparent to an experienced examiner within 5 days of injury (Fig. 13.11). The skin of the dorsal hand is much thinner than that of the palmar hand. It is quite common for circumferential hand burns to heal very well over their palmar aspect, yet require grafting on the dorsal surface. There is general agreement that earlier surgery is associated with a better functional result and a decreased need for reconstructive procedures.

Practical options for wound coverage include split-thickness autograft, full-thickness autograft, and groin or abdominal flaps. Split-thickness sheet autograft, generally thick, is the optimal coverage for most hand burns.
Full-thickness grafts are ideally reserved for palmar surface burns, particularly deep wounds of limited extent, or for reconstructive operations during the acute recovery phase. Groin and abdominal flaps can be very useful when managing isolated fourth-degree injuries.

Deep partial- and full-thickness hand burns generally require layered excision and autografting. These procedures are ideally performed after exsanguination of the extremity with an elastic wrap and inflation of a pneumatic tourniquet on the arm to reduce blood loss. The excision is performed sequentially until a bed of viable tissue is reached. Viability is recognized by a pearly white moist dermis or the presence of bright yellow subcutaneous fat without thrombosed small vessels or extravascular hemoglobin. Recognition of viable tissue in an exsanguinated extremity with a proximal pneumatic tourniquet is an acquired skill that greatly facilitates low-blood-loss excisions. The hand is then placed in a snug wrap of epinephrine-soaked gauze prior to deflation of the pneumatic tourniquet. After some time has been allowed to elapse for spontaneous hemostasis, definitive hemostasis is secured with judicious use of pinpoint electrocautery. The hand is covered with sheet autograft. Grafted hands are then covered with a gentle compressive gauze wrap and placed in a thermoplastic splint in functional position. Hands are elevated and immobilized for 4 days prior to reinstituting passive and active hand therapy.

Only about 15% of palmar burns require grafting, as the palmar skin is much thicker than the dorsal skin. It is not uncommon to wait 2–3 weeks for healing before a decision to graft is made. Palmar burns that require grafting are usually covered with thick, sheet split-thickness autograft if the defect is large, and full-thickness grafts if the defect is small. When the palm is deeply burned and loss of palmar concavity and range is at risk, the hand is splinted with the palm extended to minimize contracture, both during topical care of the burn and following any surgery. Instep grafts have been advocated for aesthetic reasons, but functional results with full-thickness or thick split-thickness grafts are generally excellent.

Hands are splinted in the position of function: the metacarpophalangeal joints at 70–90° of flexion, the interphalangeal joints in extension, the wrist in 20° of extension, and the first webspace open. Special attention should be paid to the fifth digit, as it is particularly prone to contractures that result in fixed interphalangeal joint flexion. In the hand, such failures of early closure may compromise the ability to participate in early therapy and possibly compromise long-term outcome or delay full recovery. Inadequate excision is a particular risk, as most of these operations are performed after inflation of a proximal pneumatic tourniquet. If this is compromised by direct injury or subsequent desiccation and rupture, the collateral bands will migrate volarward and the proximal interphalangeal joint will be brought into a position of flexion from which recovery may be impossible. In some cases this unfortunate sequence of events can be prevented by ensuring prompt coverage of the proximal interphalangeal joint. If the depth of injury is such that the integrity of the overlying extensor mechanism is threatened, splinting in extension and placing axial Kirschner wires across the joint for 2–3 weeks may facilitate healing, with
resulting stability. If the overlying extensor mechanism is frankly destroyed and the joint is open, a partially functional joint can sometimes be salvaged by Kirschner wire fixation for 2–3 weeks, which may allow granulation tissue to bridge the open joint; this can subsequently be grafted.

**Techniques to salvage length in fourth degree burn**

In the presence of fourth degree burn involving the underlying extensor mechanism, joint capsule, and bone, management can be more complex and less satisfying. Patients with small overall surface area burns are candidates for early debridement with groin or abdominal flap coverage (Fig. 13.12). A common pattern is deep dorsal burn with exposure of the proximal interphalangeal joints, and dorsal phalanges with viable volar tissue. If these wounds are kept moist and clean, and proper position maintained, often the avascular tissue will be covered with granulation tissue, which can then be grafted with an acceptable result. When the extensor mechanism is exposed, proper geometry during the time needed for granulation tissue formation is critical. The resting hand position with metacarpophalangeal joints in flexion at 90°, extension of the interphalangeal joints, and the thumb abducted and externally rotated in opposition to the fingers, is proper. Granulation tissue formation may be facilitated by meticulously debriding remnants of burned cortical bone. Positioning may not be reliable when only splints are used. Kirschner wires can be helpful to maintain the interphalangeal joints in the proper position while metacarpophalangeal joint flexion is maintained with the splints. Wires are passed axially from the tip of the finger proximally, stopping when the proximal interphalangeal joint is immobilized. Autografting is performed whenever possible, and exposed joints and bones are allowed to granulate and subsequently are covered with autograft (Fig. 13.13). Joints which remain unstable after coverage is achieved are later fused by open arthrodesis.

**The scalp**

Scalp and skull burns represent a major challenge. The location of these injuries presents a complex scenario with the possibility of injury to vital organs. These injuries can be classified into two groups: those which are limited to soft tissue and those that involve the calvarium. Acute surgical management of the burned scalp can vary from a simple soft tissue debridement and skin grafting to a management of complicated calvarial injury.

Scalp burns without bony involvement are treated as any other burn, with debridement and skin grafts or flap coverage. There are several classifications for cranial burn wounds based on the depth and extent of the injury. Bone loss of <2 cm usually heals by its own regenerative processes, especially in children. In adults, bone regeneration is more unpredictable. The priority in the acute phase is to debride the wound and provide coverage without compromise to the adjacent tissues. The use of bone grafts or tissue expander is deferred until after the acute burn has resolved. Surgical debridement includes the removal of necrotic soft tissue and

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*Figure 13.12* Abdominal flap coverage of fourth degree dorsal finger burns. (a) Deep dorsal burns and intraoperative positioning of the hand on the abdomen. (b) Flaps in position. (c) Final result.
bone, avoiding injury to the outer cerebral layers. The use of a fine diamond-tipped drill allows for a controlled layered removal of non-viable skull tissue.

The surgical excision stops at a depth that provides a foundation for the application of skin graft. Central nervous system infections are possible, and adequate antibiotic prophylaxis should be considered. In case of observable cerebrospinal fluid leaks, clotting agents such as thrombin foam or gel are applied.

The face
Burns to the face can have potentially devastating consequences. Attention to details, patience, skill of excision, coverage and postoperative management are essential in the preservation of vital functions and cosmesis. Burns to the face have the potential to affect vital structures such as the upper airway and vital sensory organs such as the eyes and ears.
Operative wound management

There have been no large randomized outcome trials comparing early excision and grafting of the face compared to grafting after eschar separation and granulation formation. Most authors have applied the general principle of early excision to prevent contractures and provide the best esthetic outcome for the face, with a suggested maximal waiting period of 18 days.62

Once a decision has been made to proceed with excision and grafting, suitable donor sites should be evaluated. Site selection and depth of donor skin needs careful consideration. If at all possible, the donor skin should come from the area above the line of the nipples for the best color match. Skin grafts from the scalp provide excellent color match but carry a risk of follicle transplantation and subsequent hair growth in undesired locations if the donor skin is taken thicker. An alternative site is to use the upper part of the back. Unmeshed sheet graft is applied to the face. If donor sites are limited, temporary coverage with unmeshed allograft is an option while waiting for re-epithelialization of donor sites.

Excision of facial burns can be carried out using various methods. The mainstay of excision remains the Goulian/Weck knife. If there is any doubt as to the depth, tangential excision with a Goulian knife is more appropriate, as preservation of any viable dermal elements is essential for optimal results (Fig. 13.14). Previously described ‘water dissectors’ such as the Versajet can also be used in areas of contour for more controlled, precise excision avoiding potential iatrogenic injuries.

Owing to the rich capillary networks in the face, large amounts of blood may be lost at the time of the excision. Epinephrine clysis is a sensible pre-emptive measure to reduce blood loss.63,64 Epinephrine-moistened topical sponges are helpful, as is topical thrombin. Electrocautery on a low setting can be useful for accurate hemostasis.

Placement of grafts on the face should be carried out to mimic esthetic units as much as possible. If large pieces of autograft are obtained they should be placed as a single piece along adjacent cosmetic units. For esthetic purposes the face is divided into cosmetic units. (Fig. 13.15).65 In the central horizontal plane, periorbital, nasal and upper cheek areas may be grafted as a single esthetic unit.65 Grafts should be taken as widely as possible so as to reduce the number of seams between the grafts. The grafts can be secured with staples, sutures, glues or fibrin sealant.

The use of fibrin sealant, a hemostatic adjunct and adhesive underlay has been shown in controlled studies to reduce seroma and hematoma formation as well as minimizing the need for staples or sutures, with equal or better outcome.66 Medical-grade glues such as 2-cyano-butyl acrylate (Histoacyr) can be used to secure graft around the edge and is an excellent adjunct to suturing. Once the grafts are in place, tubes and lines should be positioned away to avoid disruption of grafts. Septal tie can be used to secure the endotracheal tube and rid the face of the ties that inevitably rub on the grafts. Sheet grafts on the face should be evaluated frequently for movement or fluid collection, which may be drained with a small-gauge needle. Some centers delay the autografting phase of the procedure to reduce graft loss from hematoma formation. Temporary wound closure with allograft is a good option if this course is chosen.67

In regions of extensive soft tissue injury and no underlying bony structure, such as the buccal area, consideration may be made for acute flap coverage with regional or free tissue transfer. If the sinuses become exposed, the dead space may be filled using free vascularized omental transfers, as described in cases of facial trauma.68

Eyelids

Deep burns to the eyelids should be excised and grafted early. Deep burns to eyelids can result in cicatricial ectropion, leading to incomplete closure of the lids, which inevitably exposes the eyes to desiccation, corneal ulceration, and ultimately threat to sight.69 Post-burn cicatricial ectropion is a serious condition, with unconscious ventilated patients at particular risk. Release of scars and full-thickness skin grafts to the lower eyelids and split-thickness skin grafts to the

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**Figure 13.14** Tangential excision being applied with a Goulian knife to the chin. Previous grafting had been largely successful. The instrument is useful for small and tricky areas.

**Figure 13.15** Esthetic units of the face. (a) Frontal view. (b) Lateral view. (Adapted from McCauley RL, Obeng MK. Reconstruction of cheek deformities. In: McCauley RL, ed. Functional and aesthetic reconstruction of burned patients. Boca Raton, Florida: Taylor and Francis Group; 2005: 270.)
upper lids should be undertaken as soon as the condition is diagnosed. Eyelid involvement is common with extensive facial burns. The natural reflex of blinking will protect the eyelid margin and the cornea, exposing the skin of the upper eyelids.

Ophthalmic lubricants should be applied frequently to keep the eyes moist to prevent exposure keratitis, especially in unconscious patients. If burn ectropion develops, early tarsorrhaphy or release of contracted eyelids may be necessary. Tarsorrhaphy can be carried out at the bedside. The eyelid is injected with a combination of dilute epinephrine and lidocaine. A U-stitch is placed using a fine non-absorbable suture, and the upper and lower eyelids are approximated on their medial and/or lateral portions. The suture should be passed through material such as a rubber pledget to prevent suture being pulled through skin. The suture should incorporate the ridge of tarsus but not traverse it. An adequate tarsorrhaphy will permit the passive closure of eyelids if there is contraction of eyelids leading to corneal exposure and irritation. This can be carried out using local flaps, full-thickness skin grafts or split-thickness skin grafts. Full-thickness loss may require reconstruction using hard palate mucosa or acellular dermis as the inner lining of the lid.

**Genital burns**

When burn occurs in the genital region it can produce significant morbidity and long-term consequences for mobility, waste elimination and sexual dysfunction. Spontaneous epithelialization will likely occur with scald burns in this region owing to the rich supply of hair follicles and appendages.

Recommendations for acute management include selective urethral catheterization. This will allow urinary collection and also stenting of the urethra in the case of circumferential constricting burns.

Most partial-thickness burns of the scrotum will heal spontaneously as scrotal skin is thick and contains multiple hair follicles. Testicular function should be evaluated by measuring stimulated testosterone levels. Small full-thickness burns to the scrotum can be excised and closed primarily. In full-thickness burns to the foreskin circumcision is appropriate, as phimosis is a common sequela. Along the shaft of the penis full-thickness burns can be excised using a Goulian knife or Versajet, and grafted using unmeshed split-thickness skin grafts.

Scald burns to the genitalia are best treated conservatively. A deep burn to the glans penis may be best allowed to demarcate or proceed to eschar separation and then graft the resultant granulation tissue. Full-thickness burns to the labia majora should be excised and grafted as a delayed procedure.

Perianal burns are seen in association with extensive burns in adults and in scalded children. Early excision and grafting is recommended to prevent bacterial colonization and infection. Some centers recommend diversion of the fecal stream to aid healing and graft take. If graft failure occurs, it is important to keep trying to achieve engraftment as perianal circular contracture can result from prolonged healing by secondary intention.

**The breast**

The scarring and disfigurement associated with breast burns can be a source of significant psychological stress in developing girls and young women. All efforts should be made to preserve the breast bud in a prepubescent girl and the breast mound in a postpubertal woman. Small burns, especially linear ones, may be excised and closed primarily or allowed to form scar and later excised.

The nipple–areola complex, especially in women, requires extra attention. In general, it is best left unexcised as healing can occur from the deep glandular structures that are usually preserved.

**Conclusion**

One of the most important components of modern burn care is early operative wound management. The evidence is clear that prompt excision and closure of burn wound is lifesaving for massively burned patients. Skin substitutes and dermal replacement have made operative wound care even more appealing for providing temporary coverage in patients with insufficient autograft and offer an attractive alternative to topical antimicrobial therapy for partial-thickness wounds.

**Further reading**


References


64. Sheridan RL, Szylfeblin SK. Staged high-dose epinephrine cyclus is safe and effective in extensive tangential burn excisions in children. *Burns*. 1999 Dec;25(8):745-748.


Anesthesia for burned patients
Lee C. Woodson, Edward R. Sherwood, Asle Aarsland, Mark Talon, Michael P. Kinsky, Elise M. Morvant

Introduction

Continuous improvements in burn care since World War II have resulted in a steady increase in the rate of survival after large burn injury. These improvements have been attributed to aggressive fluid resuscitation, early excision and grafting of burn wounds, more effective antimicrobials, advances in nutritional support, and development of burn centers. The development of specialized burn centers has allowed the concentration and coordination of resources needed to provide a multidisciplinary approach from the time of admission, with the goal of not just maximizing survival but of optimizing functional recovery as well.

Today, most patients who are in good health prior to injury will survive a more than 80% total body surface area (TBSA) burn if promptly treated in a modern burn unit. In their study of risk factors for death following burn injuries Ryan et al. identified three variables that can be used to estimate the probability of death: age over 60 years, burns over more than 40% of TBSA, and the presence of inhalation injury. Mortality increased in proportion to the number of risk factors present: 0.3%, 3%, 33%, or approximately 90% mortality depending on whether zero, one, two, or three risk factors were present, respectively. O'Keefe et al. observed an approximately twofold higher risk of death in women aged 30–59 years compared to men with similar burns and age. Although it has been assumed that very young children are also at increased risk of death from burn injuries, Sheridan et al. found very low rates of mortality in children younger than 48 months who had suffered large burns. An increased risk of mortality has been consistently observed in elderly burn patients. All organ systems are influenced by age-related factors of variable expression that can reduce functional reserve. However, aged patients represent a heterogeneous group in terms of physiological reserve, with wide variation in the presence of coexisting diseases and the difference between chronological and biological age. Issues relating to the treatment of burns in elderly patients have recently been reviewed by Keck and colleagues. Most studies of mortality associated with burns focus on patient condition prior to burn center admission. Wang and colleagues examined the association of features related to treatment and hospital course with mortality among patients who had experienced massive burns (>70% TBSA). In their series, only sepsis, ventilator dependency and reduced platelet count were independent predictors of mortality.

Major burn injury results in pathophysiological changes in virtually all organ systems. Table 14.1 lists and Fig. 14.1 illustrates some of the challenges presented by the acutely burned patient during the perioperative period. In addition to the predictable challenges relating to airway management, monitoring, and vascular access, patient positioning requires close communication and teamwork. Burns involving posterior areas may require turning the patient to the prone position for optimal access (Fig. 14.1). Vascular catheters and endotracheal tubes must be secured with confidence and due care given these lifelines during patient turning.

Modern burn care depends on coordination of a multidisciplinary team including surgeons, intensivists, nurse clinicians, nutritionists, rehabilitation therapists, pulmonary care therapists, and anesthesia providers. Anesthetic management is an important part of this multidisciplinary approach. Anesthesia providers have highly developed skills and experience in airway management, pulmonary care, fluid and electrolyte management, vascular access, and pharmacological support of the circulation. These areas of clinical expertise are all central to the care of patients with major burn injuries. However, the effective use of this clinical expertise for the care of burn patients requires knowledge of the pathophysiological changes associated with burns and an understanding of the multidisciplinary approach to burn care, so that perioperative care is compatible with the overall treatment goals for the patient.

The current standard of surgical treatment calls for early excision and grafting of non-viable burn wounds, which may harbor pathogens and produce inflammatory mediators with systemic effects resulting in cardiopulmonary compromise. After an extensive burn injury, the systemic effects of inflammatory mediators on metabolism and cardiopulmonary function reduce physiological reserve, and the patient’s tolerance to the stress of surgery deteriorates with time. Assuming adequate resuscitation, extensive surgery is best tolerated soon after injury when the patient is most fit. Another advantage of early excision is that blood loss is less when wound excision is performed soon after the initial burn. However, it must be recognized that the initial resuscitation of patients with large burns results in large fluid shifts and may be associated with hemodynamic instability and respiratory insufficiency. Reynolds et al. reported that more than half of deaths after burn injuries occur due to failed resuscitation. Some burn patients develop refractory burn shock soon after injury and cannot be resuscitated. An important part of the preoperative evaluation is an
Preoperative evaluation

In addition to the standard features of a preoperative evaluation, the anesthetist should focus on certain burn injury-related features that are associated with increased risk and technical challenge when planning perioperative care of the patient with acute burn injuries (Table 14.2). Because physiological changes associated with the burn injury and their resolution during healing are dynamic, the evaluation of the acutely burned patient requires knowledge of the continuum of these changes after the initial injury. The preoperative evaluation must also be performed within the context of the planned operative procedure, which will depend on the location, extent, and depth of burn wounds, time after injury, presence of infection, and existence of suitable donor sites for autografting. It is important to know the mechanism of injury, as this determines the quality of burn injuries and the kinds of associated disorder the patient may present with. As an example, a person burned in the enclosed space of a house and a child who has suffered a scald burn would present with very different associated injuries. As resuscitation and the inflammatory response to injury are dynamic, it is also important to know the time elapsed since injury.

Initial evaluation of the burn injury

Destruction of skin by thermal injury disrupts the vital functions of the largest organ in the body. The skin provides several essential protective and homeostatic functions (Table 14.3). Treatment of patients with burn injuries must compensate for loss of these functions until the wounds are covered and healed. As a barrier to evaporation of water, the skin helps maintain fluid and electrolyte balance. Heat loss through evaporation and loss of vasomotor regulation in burned skin diminishes effective temperature regulation. The skin’s barrier function also protects against infection by invading organisms. Wound exudate rich in protein depletes plasma proteins when large body surface areas are injured. In addition to the loss of these important functions of the skin, extensive burns result in an inflammatory response with systemic effects that alter function in virtually all organ systems. Perioperative anesthetic management depends on an appreciation of these pathophysiological changes as revealed by the preoperative evaluation.

Much of the morbidity and mortality associated with burn injuries are related to the size of the injury. The extent of the

### Table 14.1 Perioperative challenges in the acute burn patient

- Compromised airway
- Pulmonary insufficiency
- Altered mental status
- Associated injuries
- Limited vascular access
- Rapid blood loss
- Impaired tissue perfusion due to:
  - Hypovolemia
  - Decreased myocardial contractility
- Anemia
- Decreased colloid osmotic pressure
- Edema
- Dysrhythmia
- Impaired temperature regulation
- Altered drug response
- Renal insufficiency
- Immunosuppression
- Infection/sepsis

### Table 14.2 Major preoperative concerns in acutely burned patients

- Age of patient
- Extent of burn injuries (total body surface area)
- Burn depth and distribution (superficial or full thickness)
- Mechanism of injury (flame, electrical, scald, or chemical)
- Airway patency
- Presence or absence of inhalation injury
- Elapsed time from injury
- Adequacy of resuscitation
- Associated injuries
- Coexisting diseases
- Surgical plan

### Figure 14.1

As illustrated in this photograph, anesthetic management of the acute burn patient for excision and grafting of wounds presents numerous challenges regarding monitoring, vascular access, temperature regulation, and rapid blood loss. Prone positioning requires extra care to assure vascular cannulas and the endotracheal tube are secure.
burn injury is expressed as the total body surface area (TBSA) burned. Estimates of TBSA burned are used to guide fluid and electrolyte therapy and to predict surgical blood loss. Initial estimates of the percentage of the skin’s surface that has been burned can be quickly estimated by the so-called ‘Rule of Nines;’ estimates are modified for pediatric patients because of age-related differences in body proportions. More precise estimates of TBSA affected can be made using a Lund–Browder chart (Fig. 14.2).

Knowledge of the burn depth is also critical to anticipating physiological insult, as well as planned surgical treatment. Partial-thickness burns may heal without scarring or deformity and do not require surgical excision. Deeper partial-thickness and full-thickness burns will not heal and require surgical debridement and grafting, with associated surgical blood loss.

With extensive wound excision or debridement large amounts of blood can be lost rapidly. Adequate preparation in terms of monitors, vascular access, and availability of blood products is essential. Accurate estimates of blood loss are crucial in planning preoperative management of burn patients. Surgical blood loss depends on the area to be excised (cm²), time since injury, surgical plan (tangential vs fascial excision), and the presence of infection.7 Blood loss from skin graft donor sites will also vary depending on whether it is an initial or a repeat harvest. These variables are valuable predictors of surgical blood loss, which is a critical factor in planning anesthetic management (Table 14.4).

### Airway and pulmonary function

Special attention must be paid to the airway and pulmonary function during preoperative evaluation. In the emergency department burn patients may initially present with respiratory issues that demand immediate attention. In addition, there is general recognition that smoke inhalation injury increases morbidity and mortality for burn patients.11 The presence of an inhalation injury in combination with a cutaneous burn increases the volume of fluid required for resuscitation by as much as 44%, and this may contribute to the increased hemodynamic instability seen in patients with combined injury.12 Numerous studies have shown an increased incidence of pulmonary complications (pneumonia, respiratory failure, or ARDS) in patients with burns and inhalation injury compared to burns alone.13 Sequelae of inhalation injury include upper airway distortion and obstruction from direct thermal injury, impaired pulmonary gas exchange due to effects of irritant gases on lower airways and pulmonary parenchyma, and systemic effects of inhaled toxins such as carbon monoxide (CO) or cyanide. These three components of the inhalation injury have separate time courses and pathophysiological consequences.

Burn injuries to the face and neck can distort anatomy and reduce range of mobility in ways that make direct laryngoscopy difficult or impossible. Specific alterations include impaired mouth opening, edema of the tongue, oropharynx, and larynx, as well as decreased range of motion of the neck. The tissue injury and sloughing present after severe facial burns may also make mask ventilation difficult.

Foley described findings of 335 autopsies performed on patients who died from extensive burns.14 Intraoral, palatal, and laryngeal burns were not uncommon among patients with inhalation injuries. The most common sites of laryngeal injury were the epiglottis and vocal folds where their edges were exposed. In contrast, thermal necrosis below the glottis and upper trachea was not observed in any of these patients. The lower airways are nearly always protected from direct thermal injury by the efficiency of heat exchange in the oro- and nasopharynx, unless the injury involves steam or an explosive blast. This has been demonstrated in an experimental model.15 Inhalation injury to the lower airways and pulmonary parenchyma is due to the effect of toxic or irritant gases.

Clinical suspicion of inhalation injury is aroused by the presence of certain risk factors, such as history of exposure to fire and smoke in an enclosed space, or a period of unconsciousness at the accident scene, burns including the face and neck, singed facial or nasal hair, altered voice, dysphagia, oral and/or nasal soot deposits, or carbonaceous sputum. The most immediate threat from inhalation injury is upper airway obstruction due to edema. Early or prophylactic intubation is recommended when this complication threatens. However, exposure to smoke does not always lead to severe injury, and in the absence of overt evidence of respiratory distress or failure it may be difficult to identify patients who will experience progressive inflammation and ultimately require intubation of the trachea. In a retrospective study, Clark et al. reported that 51% of their patients exposed to

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### Table 14.3 Functions of skin

| 1. Protection from environmental elements (e.g. radiation, mechanical irritation or trauma) |
| 2. Immunological – antigen presentation, antibacterial products (sebum), barrier to entry of pathological organisms |
| 3. Fluid and electrolyte homeostasis – helps maintain protein and electrolyte concentrations by limiting evaporative losses |
| 4. Thermoregulation – helps control heat loss through sweating and vasomotor regulation of superficial blood flow |
| 5. Sensory – extensive and varied sensory organs in skin provide information about environment |
| 6. Metabolic – vitamin D synthesis and excretion of certain substances |
| 7. Social – appearance of skin has strong influence on image and social interactions |


### Table 14.4 Calculation of expected blood loss

<table>
<thead>
<tr>
<th>Surgical procedure</th>
<th>Predicted blood loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;24 h since burn injury</td>
<td>0.45 mL/cm² burn area</td>
</tr>
<tr>
<td>1–3 days since burn injury</td>
<td>0.65 mL/cm² burn area</td>
</tr>
<tr>
<td>2–16 days since burn injury</td>
<td>0.75 mL/cm² burn area</td>
</tr>
<tr>
<td>&gt;16 days since burn injury</td>
<td>0.5–0.75 mL/cm² burn area</td>
</tr>
<tr>
<td>Infected wounds</td>
<td>1–1.25 mL/cm² burn area</td>
</tr>
</tbody>
</table>

Figure 14.2  Modified from Lund and Browder. Chart used to calculate the surface area involved by burn. It takes into account that, as one grows from infancy to adulthood, the relative surface area of the head decreases while the relative surface area of the lower extremities increases.
smoke inhalation did not require intubation. 16 Unnecessary intubation in the presence of an inflamed laryngeal mucosa risks further damage to the larynx and subglottic area. 17, 18

Traditional clinical predictors of airway obstruction have been found to be relatively insensitive and inadequate for identifying early severe airway inflammation, and often underestimate the severity of the injury. 19, 20 More objective criteria for evaluation of the risk of airway obstruction are often needed. Hunt et al. found fiberoptic bronchoscopy to be a safe and accurate method for diagnosis of acute inhalation injury. 21 They described observations of severe supraglottic injuries associated with mucosal edema obliterating the piriform sinuses and causing massive enlargement of the epiglottis and arytenoid eminence. Haponic et al. made serial observations by nasopharyngoscopy in patients at risk for inhalation injury and found distortions of the upper airway described as compliant, edematous mucosa of the aryepiglottic folds, and arytenoid eminences that prolapsed to occlude the airway on inspiration. 22 Progressive upper airway edema in these patients was correlated with body surface area burned, resuscitative volume administered, and rate of infusion of resuscitative fluids. Traditional teaching with the support of the American Burn Association has encouraged early prophylactic endotracheal intubation when risk factors for upper airway inhalation injury are present. In response to what appeared to be a preventable death associated with a prehospital intubation, Eastman and colleagues at the Parkland Burn Center performed a retrospective study to identify the factors that led to prehospital intubation of burn victims and, by examining the patients’ hospital courses, to determine which intubations were indicated. 23 Of 879 patients intubated prior to hospitalization 11.9% were extubated the day of admission and 41.4% were extubated successfully within 48 hours of injury. This implies that many patients were intubated without benefit. The authors suggested that improved training of prehospital providers might reduce the number of unnecessary prehospital intubations. Over the past two decades we have observed serious morbidity and some deaths due to airway complications in patients intubated for transport (unpublished observations). Tracheal intubation is not a benign intervention and should be employed only when there is a clear risk–benefit advantage, especially in the context of transport between facilities. For patients who are at risk for inhalation injury but lack definitive indications for intubation, fiberoptic nasopharyngoscopy is effective in identifying laryngeal edema. Serial examinations may help avoid unnecessary intubations and at the same time identify progressive inflammatory changes and allow intubation before severe airway obstruction and emergency conditions develop. 17

The level of respiratory support must also be assessed. The level of required support may range from supplemental blow-by or mask oxygen to intubation and ventilation with high positive end-expiratory pressure (PEEP) and FIO2. Acute lung injury can occur from inhalation of chemical irritants, systemic inflammation from burn wounds or difficulties with resuscitation, or ventilator-induced injury. Common pathologies include upper thermal airway injury with stridor, pulmonary parenchyma damage from chemical irritants or inflammation, lower airway obstruction from mucus plugs and epithelial casts, as well as pulmonary edema due to acute lung injury or volume overload. Lower airway and parenchymal injuries develop more slowly than upper airway obstruction. Prior to resuscitation, clinical signs and symptoms, chest X-ray, and blood gas analysis may be within normal limits despite significant injury that eventually progresses to respiratory failure requiring intubation and mechanical ventilation. 24

Linares et al. studied the sequence of morphological changes following smoke inhalation in an experimental sheep model. 25 They observed four discrete but overlapping phases of injury, described as exudative, degenerative, proliferative, and reparative. During the first 48 hours the exudative phase was characterized by polymorphonuclear (PMN) infiltration, interstitial edema, loss of type I pneumocytes, and damage to the tracheobronchial epithelium in the form of focal necrosis, hemorrhage, and submucosal edema. The degenerative phase occurred between 12 and 72 hours and was characterized by progressive epithelial damage with shedding of necrotic tissue and the formation of pseudomembranes and casts. Hyaline membranes developed over alveolar surfaces. Macrophages began to accumulate to begin absorption of necrotic debris. A proliferative phase was described between days 2 and 7 during which type II pneumocytes and macrophages proliferated. After the fourth day reparative changes were observed, with regeneration of epithelium from spared epithelium from the orifices of glands.

Demling and Chen have provided a lucid description of the pathophysiological changes following inhalation injury. 26 Decreased dynamic compliance increases the work of breathing. Increased closing volume and decreased functional residual capacity lead to atelectasis and shunt, resulting in hypoxia. Airways become plugged by sloughed epithelium, casts, and mucus. Impaired ciliary action exacerbates the airway obstruction by reducing the clearance of airway debris. These changes lead to further shunting and allow colonization and pneumonia. Treatment for inhalation injury is empiric and supportive, with tracheal intubation and mechanical ventilation. The application of aggressive pulmonary toilet, high-frequency percussive ventilation, and respiratory therapy protocols designed to mobilize obstructing debris have been found to be beneficial. 27, 28 The importance of strategies to limit ventilator-induced lung injury has been recognized. 29, 30

Carbon monoxide (CO) and cyanide are two major toxic components of smoke. The burn patient with evidence of inhalation injury should be evaluated for the presence of toxicity resulting from these compounds. CO binds hemoglobin 200 times more avidly than oxygen. 31 Therefore, CO markedly impairs the association of oxygen with hemoglobin and reduces oxygen-carrying capacity. CO also shifts the oxyhemoglobin dissociation curve to the left, thereby reducing the release of oxygen into tissues. These factors result in decreased oxygen delivery to tissues and, at critical levels, lead to anaerobic metabolism and metabolic acidosis. Signs and symptoms of CO poisoning include headache, mental status changes, dyspnea, nausea, weakness, and tachycardia. Patients suffering CO poisoning have a normal PaO2 and oxygen saturation by routine pulse oximetry. They are not cyanotic. Carboxyhemoglobin must be detected by CO oximetry. Carboxyhemoglobin levels above 15% are toxic and those above 50% are often lethal. The major treatment approach is administration of 100% oxygen. Hyperbaric
Thermal injury has profound effects on the systemic circulation. In particular, severe injury results in microcirculatory derangements and cardiac dysfunction. Hemodynamic management is a major component of perioperative care. It is critical for the anesthesiologist to assess the adequacy of fluid resuscitation and the hemodynamic status of the patient.

After massive thermal injury, a state of burn shock develops due to intravascular hypovolemia and, in some cases, myocardial depression. This state of burn shock is characterized by decreased cardiac output, increased systemic vascular resistance, and tissue hypoperfusion. Intravascular hypovolemia results from alterations in the microcirculation in both burned and unburned tissues, leading to the development of massive interstitial fluid accumulation. Cutaneous lymph flow increases dramatically in the immediate postburn period and remains elevated for approximately 48 hours.

The forces responsible for this massive fluid shift involve components of the Starling equilibrium,

\[ J_v = K_i[(P_i - P_t) - \sigma(\pi_p - \pi_d)] \]

where \( K_i \) is the capillary filtration coefficient, \( P_i \) is the capillary pressure, \( P_t \) is the interstitial hydrostatic pressure, \( \sigma \) is the reflection coefficient for protein, \( \pi_p \) is the plasma colloid osmotic pressure, and \( \pi_d \) is the interstitial colloid osmotic pressure.

The specific alterations include:
- an increased microvascular permeability coefficient \( (k_t) \) and \( \sigma \) due primarily to the release of local and systemic inflammatory mediators;
- an increase in capillary hydrostatic pressure \( (P_i) \) due to microvascular dilatation;
- decreased interstitial hydrostatic pressure \( (P_d) \) due to disruption in collagen binding;
- decreased intravascular oncotic pressure \( (\pi_c) \) due to leakage of protein from the intravascular space; and
- a relative increase in interstitial oncotic pressure due to a smaller decrease in interstitial oncotic pressure \( (\pi_c) \) compared to \( \pi_c \).

Burn injury is unique with regard to microcirculatory dysfunction. Perturbations occur in all of the Starling forces. Marked edema formation in burn-injured skin occurs almost instantaneously owing to a large negative interstitial hydrostatic pressure. Other hydraulic forces coupled with microvascular permeability lead to the leakage of protein and fluid into the interstitial space. Although fluid replacement therapy is essential in treating hypovolemia, edema is worsened by plasma protein dilution (reduction in plasma oncotic pressure). The net effect of these changes is the development of massive edema during the first 24–48 hours after thermal injury and a concomitant loss of intravascular volume.

The hypotension associated with burn injury could also be due to myocardial depression. Thermal injury stimulates the release of inflammatory mediators such as tumor necrosis factor \( \alpha \) (TNF\( \alpha \)), interleukin-1 (IL-1), and prostaglandins. TNF\( \alpha \) and IL-1 are known to have myocardial suppressant effects. Experimental animal models clearly demonstrate cardiac depression. Clinical evidence of myocardial depression is less characterized. Measurements of cardiac function after burn injury often differ with respect to time of injury, severity of injury, patient comorbidities, monitor type, e.g. PA catheter, echocardiography, and the sample size of the study. At our institution, we routinely perform transesophageal echocardiography in severely injured patients within the first 72 hours of admission. Our observational data show that a significant percentage of patients have severe systolic dysfunction, which is associated with a prolonged ICU course (Fig. 14.3).

If the patient survives the initial burn shock and is adequately resuscitated, an inflammation induced hyperdynamic circulation develops. This state of massive inflammation or systemic inflammatory response syndrome (SIRS) is characterized by hypotension, tachycardia, a marked decrease in systemic vascular resistance, and increased cardiac output. SIRS has a continuum of severity ranging from the presence of tachycardia, tachypnea, fever, and leukocytosis to refractory hypotension and multiple organ system dysfunction.
Several fluid resuscitation protocols that use various combinations of crystalloids, colloids, and hypertonic fluids have been developed (Table 14.5). Isotonic crystalloid is the most commonly used fluid for resuscitation in US burn centers. The most popular fluid resuscitation regimen, the Parkland formula, uses isotonic crystalloid solutions and estimates the fluid requirements in the first 24 hours to be 4 mL/kg% TBSA burned. However, many burn centers are administering 50% more fluid than the Parkland formula would predict.68 Crystalloid solutions generally provide adequate volume resuscitation, but the large volumes that are needed result in substantial tissue edema and hypoproteinemia. Consequently, complications of over-resuscitation, including abdominal compartment syndrome, pleural effusions, pulmonary edema, fasciotomies and conversion of partial-thickness lesions to full-thickness lesions are more frequently observed. Explanation for this pattern of ‘fluid creep’ is unclear.59,60 Clinical practice has changed in the last 30 years. Patients are receiving higher amounts of opioids to treat pain associated with thermal injury, which can cause vasodilation and precipitate hypotension. Additionally, most clinicians appreciate the dangers of hypovolemia; however, there is limited education about the risks of administering too much fluid. Thus, reliance on targeted or goal directed endpoints for fluid resuscitation following severe thermal injury is rarely practiced.

Resuscitation regimens that restore vascular volume losses while reducing edema formation are continuously being tested. Colloid and hypertonic fluids have shown efficacy in treating other injuries. Overall, colloid resuscitation within the first 24 hours of burn injury has not improved outcome compared to crystalloid resuscitation.61,62 Furthermore, a recent meta-analysis indicated that mortality is higher in burned patients receiving albumin as part of the initial resuscitation protocol, with a 2.4 relative risk of mortality compared to patients receiving crystalloid alone.63 Because of the added cost and the little established benefit, colloid solutions have not been used routinely in the United States for initial volume resuscitation in burned patients. However, specific types of colloid regimen might yield different results.

Recently, in a prospective, randomized study, the use of plasma for volume resuscitation was shown to limit the volume infused along with reducing intra-abdominal pressure and abdominal compartment syndrome (see below).64 These outcome variables have not been used for comparing crystalloid and colloid resuscitation in the past. With the trend toward larger volumes for initial resuscitation it may be that the use of colloid may be beneficial for larger injuries requiring more volume.

The use of hypertonic saline, either alone or in conjunction with colloids, has been advocated by some in the initial resuscitation of burned patients. Among the potential benefits are reduced volume requirements to attain similar levels of intravascular resuscitation and tissue perfusion compared to isotonic fluids.65 Theoretically, the reduced volume requirements would reduce the incidence of pulmonary and peripheral edema, thereby reducing the incidence of pulmonary complications and the need for escharotomy. Hypertonic saline dextran solutions have been shown to expand intravascular volume by mobilizing fluids from intracellular and interstitial fluid compartments. Although hypertonic saline dextran solutions transiently reduce initial fluid requirements, there is a potential for a rebound in fluid needs later in resuscitation owing to the sodium load.66,67 Therefore, most burn centers continue to use isotonic crystalloid fluids for initial resuscitation of patients in burn shock.

### Table 14.5 Formulas for estimating adult burn patient resuscitation fluid needs

<table>
<thead>
<tr>
<th>Colloid formula</th>
<th>Electrolyte</th>
<th>Colloid</th>
<th>DSW</th>
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<tbody>
<tr>
<td>Evans</td>
<td>Normal saline</td>
<td>1.0 mL/kg% burn</td>
<td>1.0 mL/kg% burn</td>
</tr>
<tr>
<td>Brooke</td>
<td>Lactated Ringer’s</td>
<td>1.5 mL/kg% burn</td>
<td>0.5 mL/kg</td>
</tr>
<tr>
<td>Slater</td>
<td>Lactated Ringer’s</td>
<td>2 liters/24 h</td>
<td>Fresh frozen plasma</td>
</tr>
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</table>

**Crystalloid formulas**

- Parkland: Lactated Ringer’s, 4 mL/kg% burn
- Modified Brooke: Lactated Ringer’s, 2 mL/kg% burn

**Hypertonic saline formulas**

- Hypertonic saline solution (Monaco): Volume to maintain urine output at 30 mL/h
- Fluid contains 250 mEq Na/liter
- Modified hypertonic saline (Warden): Lactated Ringer’s +50 mEq NaHCO₃ (180 mEq Na/liter) for 8 hours to maintain urine output at 30–50 mL/h
- Lactated Ringer’s to maintain urine output at 30–50 mL/h beginning 8 hours postburn
- Dextran formula (Demling): Dextran 40 in saline – 2 mL/kg/h for 8 hours
- Lactated Ringer’s – volume to maintain urine output at 30 mL/h
- Fresh frozen plasma – 0.5 mL/kg/h for 18 hours beginning 8 hours postburn

Figure 14.3 Systolic function as measured by transesophageal echocardiography is severely depressed in some patients with major burn injuries. This myocardial depression has been associated with prolongation of ICU stay. (From Kinsky et al. ESICM. 2009; 193: 6–228).
Several parameters have been used to assess the adequacy of volume resuscitation in burned patients (Table 14.6). Unfortunately, there is no single physiological variable that is always reliable as an endpoint to guide resuscitation in acute burn patients. The overall goal is early volume resuscitation and establishment of tissue perfusion. Traditionally, urine output (0.5–1 mL/kg/h) and normalization of blood pressure (mean arterial blood pressure > 70 mmHg) have been used as endpoints. However, these parameters alone do not always indicate adequate tissue perfusion. Jeng and colleagues showed that attaining urine outputs > 30 mL/h and mean blood pressures > 70 mmHg correlated poorly with other global indicators of tissue perfusion, such as base deficit and blood lactate levels. During shock, perfusion of vital organs such as the heart and brain is maintained due to the redistribution of blood flow from the splanchnic circulation and other peripheral organs. Persistent hypoperfusion of these organ systems ultimately results in tissue injury and contributes to multisystem organ dysfunction. Therefore, the anesthesiologist should not base the cardiovascular assessment strictly on vital signs and urinary output.

Invasive cardiovascular monitors are not used routinely in burned patients to guide volume resuscitation. Most patients can be adequately resuscitated without their use. However, a small subset of patients, such as those with underlying cardiovascular disease or those who do not respond normally to volume resuscitation – termed non-responders, may benefit from invasive monitoring. Some investigations use cardiac index and oxygen delivery to guide volume resuscitation. One way in which shock can be defined is oxygen debt. Bernard and colleagues have shown that patients surviving large burn injuries had higher cardiac indices and more effective oxygen delivery than non-survivors. Some investigators have proposed the use of supranormal oxygen delivery as a means of assuring adequate tissue perfusion. The preselected goals were a cardiac index of 4.5 L/min/m² and an oxygen delivery index of 600 mL/min/m². These values represent approximately 150% of normal cardiac index and oxygen delivery values. Attaining supraphysiological cardiac output and oxygen delivery has been shown to improve outcome in some studies. Schiller and colleagues demonstrated that maintaining a hyperdynamic hemodynamic state using fluids and inotropes improved survival in burn patients. However, other investigations, including a meta-analysis, have shown that achieving supraphysiological levels of cardiac output and oxygen delivery did not improve mortality or reduce the incidence of organ failure in trauma and burn patients. The use of inotropes to attain supraphysiological oxygen transport could be detrimental in some cases. One study that used dobutamine to increase cardiac output and increase oxygen delivery demonstrated increased mortality. Dobutamine, like other inotropes, can increase cardiac work and result in myocardial ischemia or myocardial infarction. Selective use of inotropes is warranted. In general, our practice is to use inotropic support in patients with dilated cardiomyopathy and withhold it in patients with risk factors for coronary artery disease. Estimating preload in the acutely burned patient is quite challenging. Filling pressures (central venous pressure and pulmonary artery occlusion pressure) correlate poorly with circulating blood volume, especially during positive-pressure ventilation. Newer techniques estimate the volume of blood in the thorax (intrathoracic blood volume, or ITBV) using transcardiopulmonary thermodilution. This technique has been used in burn patients during resuscitation. Holm and colleagues observed that ITBV, but not central venous and pulmonary capillary occlusive pressure, correlated with cardiac index and oxygen delivery during fluid resuscitation of burn patients. The use of ITBV to successfully restore cardiac index in this series was associated with significantly larger volumes than predicted by the Parkland formula. This technology is available commercially as the PiCCO system (Pulsion Medical Systems, Munich, Germany). In addition to ITBV this system also provides an estimate of extravascular lung water and stroke volume variability, and a continuous estimate of cardiac output and systemic vascular resistance.

Blood lactate and base deficit provide indirect metabolic global indices of tissue perfusion. Lactic acid is a byproduct of anaerobic metabolism and is an indicator of either inadequate oxygen delivery or impaired oxygen utilization. In the absence of conditions such as cyanide poisoning or sepsis that alter oxygen utilization at the cellular level, lactate production serves as a useful marker of oxygen availability. Serum lactate levels have served as a useful marker of fluid resuscitation and tissue perfusion in burn patients. A recent study showed serum lactate to be highly predictive of adequate tissue perfusion. A serum lactate level <2 mmol/L in the first 24–72 hours after burn injury correlated with increased survival. Base deficit is another indirect indicator of global tissue perfusion. The base deficit is calculated from the arterial blood gas using the Astrup and Siggard–Anderson nomograms. Although it is not directly measured, base deficit provides a readily obtained and widely available indicator of tissue acidosis and shock. Base deficit has been shown to correlate closely with blood lactate and provides a useful indicator of inadequate oxygen delivery. A retrospective study by Kaups et al. showed that base deficit was an accurate predictor of fluid requirements, burn size, and mortality rate.

Lactate and base deficit serve as global markers of tissue perfusion and oxygen delivery. However, in burn patients tissue perfusion is not uniform. Perfusion of the splanchnic beds is often sacrificed in order to maintain the perfusion of heart, brain, and kidneys. The use of gastric intramucosal pH (pHi) has been advocated as a measure of splanchnic perfusion. Several studies have shown that measurement of pHi is useful in guiding resuscitation, and that low pHi is a predictor of organ failure and death. pHi is measured by gastric

<table>
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<tr>
<th>Table 14.6 Criteria for adequate fluid resuscitation</th>
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<tr>
<td>• Normalization of blood pressure</td>
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<tr>
<td>• Urine output (1–2 mL/kg/h)</td>
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<tr>
<td>• Blood lactate (&lt;2 mmol/L)</td>
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<tr>
<td>• Base deficit (&lt;5)</td>
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<tr>
<td>• Gastric intramucosal pH (&gt;7.32)</td>
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<tr>
<td>• Central venous pressure</td>
</tr>
<tr>
<td>• Cardiac index (Cl) (4.5 L/min/m²)</td>
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<tr>
<td>• Oxygen delivery index (DO₂) (600 mL/min/m²)</td>
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Monitors for resuscitation

Several parameters have been used to assess the adequacy of volume resuscitation in burned patients (Table 14.6). Unfortunately, there is no single physiological variable that is always reliable as an endpoint to guide resuscitation in acute burn patients. The overall goal is early volume resuscitation and establishment of tissue perfusion. Traditionally, urine output (0.5–1 mL/kg/h) and normalization of blood pressure (mean arterial blood pressure > 70 mmHg) have been used as endpoints. However, these parameters alone do not always indicate adequate tissue perfusion. Jeng and colleagues showed that attaining urine outputs > 30 mL/h and mean blood pressures > 70 mmHg correlated poorly with other global indicators of tissue perfusion, such as base deficit and blood lactate levels. During shock, perfusion of vital organs such as the heart and brain is maintained due to the redistribution of blood flow from the splanchnic circulation and other peripheral organs. Persistent hypoperfusion of these organ systems ultimately results in tissue injury and contributes to multisystem organ dysfunction. Therefore, the anesthesiologist should not base the cardiovascular assessment strictly on vital signs and urinary output.

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Anesthesia for burned patients

Pressure: 50 mL of saline is instilled into the bladder through the Foley catheter and the height of the saline column above the symphysis pubis is measured (1.36 cm H$_2$O = 1 mmHg). Conservative treatment of elevated intra-abdominal pressure includes attempts to limit the volume of intravenous fluid needed for resuscitation. The inclusion of plasma with infused fluids has been found to reduce the volume required and was associated with significantly lower intra-abdominal pressures. Adequate analgesia and sedation should be achieved. Diuresis with furosemide and muscle relaxants to reduce muscle tone have been used to reduce intra-abdominal pressure. More invasive measures include escharotomies, percutaneous peritoneal dialysis catheter drainage, and laparotomy.

Recently several clinicians have reported a specific type of burn injury that has been associated with difficulties with tonometry and can provide useful information regarding tissue perfusion. Formulae for resuscitation of burns provide an approximation of fluid needs, but volumes actually administered need to be individualized for each patient. Although two patients may each have 50% TBSA burns, it is not likely that their physiologic responses will be equivalent. Several factors can increase fluid requirements (Table 14.7). Deep full-thickness burns require larger volume than partial-thickness injuries. Likewise, extensive soft tissue damage from electrical burns or crush injuries increases fluid needs. Inhalation injury can also increase fluid requirements as much as 50%, as noted above. These differences in wounds and fluid requirements between patients make it very difficult at times to optimize fluid administration. Because no single physiologic endpoint is always reliable, all available clinical information must be examined and each variable evaluated within the context of all the other variables.

As discussed, increased volumes of crystalloid solutions are being used for resuscitation of burn patients. In many cases as much as twice the volume recommended by the Parkland formula is used. Edema is commensurate with volume infused. During the preoperative evaluation attention must be paid to the degree to which edema produces physiologic derangements. The edema can lead to compartment syndrome of extremities or abdomen (Fig. 14.4). Blindness due to ischemic optic neuropathy has been reported as a complication of burn resuscitation. Increased intra-abdominal pressure is a complication of vigorous fluid resuscitation, which may be more common than generally appreciated and may often explain difficulties with resuscitation. Greenhalgh and Warden first described the association of increased abdominal pressures and compartment syndrome with burn resuscitation. Ivy and colleagues prospectively studied 10 adult patients presenting with >20% TBSA burns and found that 70% of them had at least transient intra-abdominal hypertension. Two of their patients with >80% TBSA burns developed abdominal compartment syndrome requiring surgical decompression. Several studies since then have described the common occurrence of increased intra-abdominal pressure with large-volume burn resuscitation. Increased intra-abdominal hypertension is termed abdominal compartment syndrome when it is associated with impaired respiration, circulation, and urine output. Mechanical ventilation is impaired by pressure on the diaphragm, circulation is impaired by restricted venous return due to caval compression, and urine output is impaired by compression of renal vessels. When this pattern presents the patient should be examined for elevated intra-abdominal pressure. This can be accomplished by measuring bladder pressure: 50 mL of saline is instilled into the bladder through the Foley catheter and the height of the saline column above the symphysis pubis is measured (1.36 cm H$_2$O = 1 mmHg). Conserva

<table>
<thead>
<tr>
<th>Table 14.7 Factors that may increase fluid needs for resuscitation of patients with acute burn injuries</th>
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<tr>
<td>• Inhalation injury</td>
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<tr>
<td>• Delay in resuscitation</td>
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<tr>
<td>• Crush injury</td>
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<tr>
<td>• Electrical injury</td>
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<tr>
<td>• Large full-thickness burns</td>
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<tr>
<td>• Methamphetamine lab accidents</td>
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<tr>
<td>• Associated injuries</td>
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There has been a dramatic increase in burn injuries from explosions and fires related to methamphetamine production in illicit laboratories. Victims of these accidents present unique challenges for a variety of reasons. Substances used in methamphetamine production include chemicals that are corrosive and toxic (e.g. anhydrous ammonia, hydrochloric acid, red phosphorus, and ephe- drine). Other ingredients are flammable (acetone, alcohol, and gasoline) and explosions can coat the victims with all these chemicals. As a result, in addition to the victim’s toxic exposure, contacting incompletely decontaminated victims of these accidents has injured first responders and hospital workers. In addition to exposures described above, these patients are usually intoxicated with methamphetamine, as demonstrated by positive urine screen, and may have inhaled toxic fumes such as phosphine gas. Santos et al. found the incidence of inhalation injury to be twice as great in victims of methamphetamine-related burns as in age- and burn-matched controls. Among their patients requiring intubation for inhalation injury methamphetamine users also required roughly twice as many ventilator days. Clinical studies have consistently observed increased fluid requirements for resuscitation of methamphetamine patients. For example, Santos et al. found that resuscitation volumes were 1.8 times greater for methamphetamine users with burns than for controls. Methamphetamine users with burns also experienced more behavioral problems. These patients are more often agitated and require restraints. Santos et al. reported that all their methamphetamine patients required greater than normal doses of sedatives and displayed what they referred to as ‘withdrawal-type syndrome,’ possibly owing to withdrawal of methamphet- mine from chronic users.

Effect of burn injury on renal function

Acute renal failure (ARF) is a relatively common complication following major burn injuries. The incidence of ARF following burn injury has been reported to be as high as 40% and is most dependent on the size and severity of the burn and the presence of inhalation injury. The development of ARF is a poor prognostic indicator. Jeschke and colleagues reported a mortality of 56% in pediatric burn patients with ARF. A recently reported Scandinavian study that analyzed 1380 adult burn patients reported an overall mortality rate of 44.1% in patients with acute renal insufficiency, with a mortality rate of 62.5% in those requiring renal replacement therapy. Holm and colleagues observed that ARF could be divided into early and late categories. Early ARF was defined as occurring within 5 days of burn injury. The most common apparent causes of early renal injury were hypoten- sion and myoglobinuria. ARF occurring after 5 days of injury was defined as late. Here, sepsis was the most common cause, with a small number of cases resulting from the administration of nephotoxic drugs. Factors that will reduce the incidence of ARF and, if it occurs, associated mortality, include adequate fluid resuscitation, early wound excision, and prevention of infection. Regardless of the cause, it is critical to assess renal function in burn patients in order to develop a comprehensive anesthetic plan. Important areas of analysis include urine output, dialysis dependence, volume status, and electrolyte concentrations; diuretic therapy should also be noted. Scheduled doses of diuretics may need to be continued during the perioperative period to maintain urine output.

Metabolic changes associated with burn injury

Increased metabolic rate is the hallmark metabolic alteration that takes place after thermal injury. The magnitude of hypermetabolism is influenced by the size of the burn wound, medical management and the core body temperature of the patient. Within the range of 30–70% TBSA burn injury, hypermetabolism tends to be proportionate to the size of the burn wound. With burns beyond this range, the hypermetabolism appears to plateau and only increases in smaller increments as burn size increases. Sepsis can also increase the metabolic response, as does the physiologic stress of pain. It has been observed that modern treatment of burn injuries with early excision and grafting ameliorates the hypermetabolism. As mentioned earlier, burn patients increase their metabolic rate in an effort to generate heat according to an increased core temperature threshold set point, which is influenced by the size of the burn. The recognition of this fact has led to an increased awareness of the importance of the ambient temperature in modulating the hypermetabo- lism of the burn patient. Using indirect calorimetry in acute patients with major burn injuries that are treated according to current standards, resting energy expenditures that are 110–150% above predicted values are frequently measured. Resting energy expenditure typically increases as core body temperature decreases below the new set point. Therefore, it is critical to prevent significant decreases in core body temperature in the operating room.

As a result of the hypermetabolic response, the burned patient has an increased O2 consumption along with an increased CO2 production that collectively causes increased minute ventilation and demands a higher respiratory effort. The anesthetic care of the acute burned patient must accommodate these changes, and frequently this has to be done in patients with compromised pulmonary function due to burn and inhalation injuries.

According to the hypermetabolism, the caloric needs of the burn patient are also increased. Furthermore, numerous studies have shown that optimized nutritional care can not only ameliorate the burn-associated state of catabolism and immune suppression but can also improve wound healing. Oral or enteral feeding is recognized as optimal for the burned patient. Frequently the acute burn patient has to be fed continuously over extended periods. This is not only because of the increased caloric needs but also because of compromised gastric emptying and decreased intestinal motility, which necessitates a slower feeding rate of critically ill patients. If standard guidelines for perioperative fasting are implemented, recurrent operative procedures can significantly impinge on the nutritional needs of the patient and ultimately cause a caloric deficit. To accommodate the nutri- tional needs of the patient a continuation of duodenal nutri- tion perioperatively has been advocated. Studies indicate that not only is this procedure safe but it might also provide for a favorable gut oxygen balance.
At the time of the withdrawal of ventilator support and extubation the metabolic state of the burn patient should be considered. The characteristic catabolic state of major burn injury spares no muscles and the respiratory muscles are affected. Along with decreased muscle strength there is frequently decreased pulmonary compliance, due not only to the formation of scar tissue and pulmonary interstitial changes but also to increased intra-abdominal content. Burn-associated hepatomegaly along with gastrointestinal retention can significantly impinge on respiratory reserves.

Severe insulin resistance with hyperglycemia and concurrent hyperinsulinemia is a key feature of the metabolic alterations of burn injury. It is well recognized that critically ill patients with insulin resistance benefit from tight glycemic control in the ICU, and these findings have been expanded to the burn patient population. During the intraoperative period the question is less studied. Although the benefit of tight intraoperative glycemic control has been documented in other patient populations, the risk versus benefit during anesthesia has not been studied specifically in burn patients.

Thermoregulation in burn patients

Maintenance of proper body temperature is an important factor in the care of severely burned patients. The thermoregulatory system is controlled by three major components. These are the afferent system, which senses changes in core body temperature and transmits this information to the brain; the central regulatory mechanisms located primarily in the hypothalamus that process afferent input and initiate responses; and the efferent limb, which mediates specific biological and behavioral responses to changes in core body temperature (Fig. 14.5). Temperature is sensed by Aδ and C fibers present in peripheral tissues such as skin and muscle as well as core tissues such as brain, deep abdominal tissues, and thoracic viscera. The vast majority of afferent input arises from the core tissues. Because the skin is in direct contact with the environment, it senses immediate changes in environmental temperature. However, the overall afferent input of the skin and other peripheral tissues is estimated to be only 5–20% of total afferent thermoregulatory input. Therefore, loss of skin following a burn injury is not likely to markedly alter overall afferent input. Wallace and colleagues have shown that burn patients perceive changes in ambient temperature as effectively as normal controls. This is likely due to the retained ability of burn patients to sense changes in core temperature and transmit this information to the central nervous system. Central control of temperature is a complicated system that is not well understood. The hypothalamus plays an important role in temperature regulation, but the complete mechanism of temperature control is likely to be multifaceted and is an area of intense research. Regardless of the ultimate control mechanisms, temperature control can be divided into three main functions: threshold, gain, and maximum response intensity.

Threshold encompasses a set point at which responses to temperature change are initiated. In normal individuals the threshold range is generally near 36.5–37.5°C. In burn patients, the threshold set point is higher and the increase is proportional to the size of the burn. The work of Caldwell and colleagues predicts that the temperature set point will increase by 0.03°C/% TBSA burn. This increase in temperature threshold appears to be due to the hypermetabolic state and the pyrogenic inflammatory mediators such as TNF, IL-1, and IL-6 that are present after thermal injury. The elevated temperature set point can be reduced by administration of indomethacin, which suggests that prostaglandins act as final common mediators of this response.

Gain describes the intensity of response to alterations in temperature. In most cases the gain of thermoregulatory responses is very high, with response intensity increasing from 10% to 90% with only a few tenths of a degree change in core temperature. This response is maintained in most burn patients, resulting in a further increase in metabolic rate. Burn patients respond with a brisk increase in heat generation and metabolic rate in response to changes in core body temperature. However, work by Shiozaki and colleagues has shown that burn patients who are slow to respond to postoperative hypothermia are at increased risk of mortality. The decreased responsiveness may be due, in part, to tissue catabolism, poor nutrition, or sepsis. In addition, the response to relative hypothermia is characterized by increased catecholamine release, tissue catabolism, and hypermetabolism. These responses further stress burn patients and reduce their ability to respond to their primary injury.

The most important efferent responses to hypothermia are behavioral responses such as gaining shelter, covering up, and seeking a more desirable ambient temperature. In the
acute post-burn setting most of these behaviors are impeded by positioning, sedation, and inability to seek a more favorable environment. Therefore, caregivers must be attentive to the patient’s temperature and perception of cold so that measures can be undertaken to optimize the patient’s temperature. Cutaneous vasoconstriction is another important mechanism for preserving heat and core body temperature. In unburned persons a temperature gradient of 2–4 °C exists between skin and core tissues. This gradient is maintained by cutaneous vasoconstriction. Without cutaneous vasoconstriction, heat is redistributed from the core compartment to the periphery. This heat is ultimately lost to the environment. Peripheral vasoconstriction minimizes temperature redistribution and acts to maintain core body temperature. This mechanism of heat preservation is lost after cutaneous thermal injury and excision of large areas of skin, particularly if cutaneous tissues are excised down to the fascial level. The loss of skin facilitates the redistribution of core body heat to the periphery and, ultimately, into the environment, which places the burn patient at risk for core hypothermia. Another mechanism of heat loss in burn patients is evaporation. Burn patients can lose as much as 4000 mL/m² burned/day of fluids through evaporative losses. Mechanisms of non-shivering heat production and shivering remain intact which places the burn patient at risk for core hypothermia. Patients under general anesthesia exhibit a markedly decreased threshold for responding to hypothermia (Fig. 14.6). This is particularly important in burn patients, given their high temperature set point and the deleterious effects of further stress responses and hypermetabolism in this patient population. Most anesthetics reduce nonbehavioral responses to hypothermia, such as vasoconstriction, non-shivering thermogenesis, and shivering. Of course, behavioral responses are ablated during general anesthesia. Therefore, it is the responsibility of the intraoperative caregivers to monitor and maintain patient temperature.

Actions such as maintaining higher ambient air temperature, covering the extremities and head, applying warm blankets, using radiant heaters and forced air warming devices, warming fluids and blood, and warming gases are usually effective in maintaining core temperature if applied aggressively. Ideally, hypothermia should be corrected prior to transport to the operating room. Hypothermia revealed in the preoperative evaluation may be due to inadequate resuscitation or metabolic instability. Either situation may predispose burn patients to intolerance of anesthetic drugs or the stress of surgery.

In contrast to acutely burned patients, the development of hypothermia may not be as serious a problem in severely burned patients who have complete regrafting and present for reconstructive surgery. Davis and colleagues reported that cutaneous vasoconstriction is preserved in grafted skin. Therefore, these patients are likely to have a temperature response to anesthesia and the operating room environment that is similar to that of non-burned patients. However, cutaneous vasodilation and heat dissipation are impaired in grafted skin, which makes these patients more susceptible to developing hyperthermia in warm environments. Therefore, temperature should be monitored in these patients during surgery, especially if warming devices will be employed in their perioperative care.

**Pharmacological considerations**

**General considerations**

Burn injury and its treatment result in physiological changes that may profoundly alter response to drugs. These changes alter both pharmacokinetic and pharmacodynamic determinants of drug response. Altered drug response in burned patients may require deviation from usual dosages to avoid toxicity or decreased efficacy. The complex nature of the pathophysiological changes, interpatient variation in the nature and extent of burn injuries, and the dynamic nature of these changes during healing and recovery make it difficult to formulate precise dosage guidelines for burn patients. However, an understanding of the systemic response to large burn injuries can help predict when an altered drug response can be expected and how to compensate.

The two distinct phases of cardiovascular response to thermal injury can affect pharmacokinetic parameters in different ways. During the acute or resuscitation phase the rapid loss of fluid from the vascular space due to edema formation results in decreased cardiac output and tissue perfusion. Volume resuscitation during this phase dilutes plasma proteins and expands the extracellular fluid space, especially, but not exclusively, around the burn injury itself. Decreased renal and hepatic blood flow during the resuscitation phase reduces drug elimination by these organs. Also, decreased cardiac output will accelerate the rate of alveolar accumulation of inhalation agents, which may result in an exaggerated hypotensive response during induction of general anesthesia.

After approximately 48 hours the hypermetabolic and hyperdynamic circulatory phase is established, with increased cardiac output, oxygen consumption, and core temperature. During this phase, increased blood flow to the kidneys and liver may increase clearance of some drugs to the point where increased doses are required.
Many drugs are highly protein bound. Drug effects and elimination are often related to the unbound fraction of the drug that is available for receptor interaction, glomerular filtration, or enzymatic metabolism. The two major drug-binding proteins have disparate responses to burn injury. Albumin binds mostly acidic and neutral drugs (diazepam or thiopental) and is reduced in burn patients. Basic drugs (pKa >8, propranolol, lidocaine, or imipramine) bind to α-acid glycoprotein (AAG). AAG is considered an acute-phase protein and its concentration may double after burns. Because these drug-binding proteins respond in opposite ways to thermal injury it can be expected that changes in drug binding and function will depend on which of these proteins has the highest affinity for the drug in question. Martyn et al. observed decreased plasma albumin concentration and increased plasma AAG concentration in burn patients. These observations were associated with an increased unbound fraction for diazepam (bound by albumin) and a decreased unbound fraction for imipramine (bound by AAG).

Volume of distribution (Vd) can be changed by alterations in either extracellular fluid volume or protein binding. Large changes in both of these variables occur with thermal injuries. Drugs with high protein binding and/or a Vd in the range of the extracellular fluid volume may be associated with clinically significant alterations of Vd in burned patients. Vd is the most important determinant of drug response following a rapid loading dose. However, adjustments in dose to compensate for altered Vd are indicated only when Vd for the drug is small (<30 L) because with larger Vd only a small fraction of the drug is present in the plasma.

Clearance is the most important factor determining the maintenance dose of drugs and can influence the response to drugs given by infusion or repeated bolus during anesthesia. Drug clearance is influenced by four factors:

- metabolism;
- protein binding;
- renal excretion; and
- novel excretion pathways.

The characteristic hepatic extraction of a particular drug influences changes in its clearance that occur after thermal injury. Drugs vary greatly in their extraction by the liver. Hepatic clearance of drugs highly extracted by the liver depends primarily on hepatic blood flow and is insensitive to alterations in protein binding. Clearance of these drugs may increase during the hyperdynamic phase when hepatic blood flow is increased. In contrast, clearance of drugs that have a low hepatic extraction coefficient is not affected by changes in hepatic blood flow but is sensitive to alterations in plasma protein levels. For these drugs it is the unbound fraction that is metabolized. As above, changes in unbound fraction depend on whether the drug is bound by albumin or AAG. Changes in protein levels produce clinically significant pharmacokinetic changes only for drugs that are highly bound (>80%).

During resuscitation, renal blood flow may be reduced and renal excretion of drugs may be impaired. Later, during the hypermetabolic phase, renal blood flow is increased as a result of the elevated cardiac output. During this period excretion of certain drugs can be increased to the point that the dose may need to be increased. Loirat et al. reported increased glomerular filtration rates and reduced half-life of tobramycin in burn patients. However, this was age dependent, and patients over 30 years of age did not have increased glomerular filtration or reduced half-life.

Burn patients may also experience altered drug clearance due to novel excretion pathways. Glew et al. found that 20% of a daily gentamicin dose was eliminated in the exudates lost to wound dressings. In addition, rapid blood loss during surgery may speed elimination of drugs when blood loss and transfusion amount, essentially, to an exchange transfusion.

Hepatic clearance of drugs with low extraction coefficients is also sensitive to alterations in hepatic capacity (enzyme activity). There is evidence of impairment of hepatic enzyme activity in burn patients. Phase I reactions (oxidation, reduction, or hydroxylation by the cytochrome P450 system) are impaired in burn patients, whereas phase II reactions (conjugation) seem to be relatively preserved. However, these generalizations do not always produce predictable alterations in pharmacokinetic parameters. For example, contradictory observations of morphine clearance in burn patients have been reported. Morphine metabolism is by glucuronidation. This is a phase II reaction which is normally retained in thermally injured patients. Consequently, morphine clearance has been reported unchanged as predicted or decreased. With so many variables involved, such as hepatic blood flow, Vd, plasma proteins, multiple drug exposure, and variation in burn injury, this inconsistency is not surprising. The key to effective drug therapy in burn patients is to monitor drug effects and carefully titrate the dose to the desired effect.

Muscle relaxants

In terms of anesthetic management, the most profound and clinically significant effect of burn injuries on drug response relates to muscle relaxants. Burn injuries >25% TBSA influence responses to both succinylcholine and the non-depolarizing muscle relaxants. In burned patients, sensitization to the muscle relaxant effects of succinylcholine can produce exaggerated hyperkalemic responses severe enough to induce cardiac arrest. In contrast, burned patients are resistant to the effects of non-depolarizing muscle relaxants. These changes are explained by upregulation of skeletal muscle acetylcholine receptors.

Martyn and Richtsfeld have recently reviewed the mechanisms of exaggerated hyperkalemic responses to succinylcholine. There are several disease states, including burns, denervation, and immobilization, that are associated with potentially lethal hyperkalemic responses to succinylcholine. The molecular mechanism appears to be both quantitative and qualitative changes in skeletal muscle postsynaptic nicotinic acetylcholine receptors. Animal and human studies consistently demonstrate an association of increased numbers of skeletal muscle acetylcholine receptors with resistance to non-depolarizing muscle relaxants and increased sensitivity to succinylcholine. In addition, the distribution of the new receptors is altered. Nicotinic receptors are normally restricted to the neuromuscular synaptic cleft but in these disease states new receptors are distributed across the surface of the skeletal muscle membrane. The new receptors are also a distinctly different isoform (α7AChR).
that has been referred to as an immature, extrajunctional, or fetal receptor. The immature receptors are more easily depolarized by succinylcholine and their ion channel stays open longer. The immature receptors are also strongly and persistently depolarized by the metabolite of acetylcholine and succinylcholine, choline. It has been suggested that the hyperkalemic response to succinylcholine after burn or denervation injury results when potassium is released from receptor-associated ion channels across the entire muscle cell membrane, rather than just the junctional receptors. Depolarization persists because the channels stay open longer and the breakdown product of succinylcholine, choline, is also a strong agonist for the immature receptors.

Cardiac arrest in burned patients after succinylcholine administration was first reported in 1958. It was not until 1967, however, that an exaggerated hyperkalemic effect was identified as the cause of this phenomenon. Several clinical studies have documented exaggerated increases in potassium concentrations after succinylcholine administration in burned patients. However, considerable individual variability exists, and only a few patients in these series developed dangerously high potassium levels. The size of the increase was greatest about 3-4 weeks after injury. The earliest exaggerated hyperkalemic response described occurred 9 days after injury and normal responses were observed in the remaining patients in this series for up to 14-20 days. The shortest post-burn interval associated with succinylcholine-induced cardiac arrest was 21 days. Controversy surrounds recommendations regarding the safe use of succinylcholine administration in burned patients. Various authors recommend avoidance of succinylcholine at intervals ranging from 24 hours to 21 days after burn injury. A series of letters to the editor of Anesthesiology from experts in this area illustrates the controversy surrounding this question. It was pointed out by Martyn that at the time when the mechanism of the cardiac arrest after succinylcholine was elucidated, surgical treatment of burns was delayed for approximately 2 weeks until the eschar spontaneously separated. As a result there were few clinical data regarding potassium changes during this early period. On the basis of indirect evidence from experimental data, Martyn recommended avoidance of succinylcholine, starting 48 hours after injury. This seems rational and prudent. Brown and Bell described supersensitivity of burned pediatric patients to the relaxant effect of succinylcholine. They observed more than 90% depression of muscle activity with 0.2 mg/kg succinylcholine without dangerous hyperkalemia. Despite these observations, Brown and Bell state that it is generally advisable not to use succinylcholine in patients with large burns. The question remains: in the presence of life-threatening laryngospasm in a burn patient, is it acceptable to give a small dose of succinylcholine (e.g. 0.1 mg/kg) and accept a theoretical risk of hyperkalemia to treat a real and immediate risk of anoxic brain injury? There is not enough clinical evidence to answer this question conclusively, and it remains a matter of clinical judgment.

When rapid sequence induction and quick onset of paralysis in burn patients is desired, rocuronium is the drug of choice. A dose of 1.2 mg/kg of this drug provided good intubation conditions in 86 ± 20 seconds in burned patients. The problem with this choice is that muscle relaxation will persist for some time and precludes extubation after short cases, and difficulty with intubation and ventilation may require emergency surgical airway access. A cyclodextrin (Org 25969) has recently been tested in man as a reversal agent with a novel mechanism of action for rocuronium. Org 25969 has been specifically designed to encapsulate rocuronium. This agent has been found to rapidly terminate neuromuscular blockade by rocuronium, theoretically by sequestering it from nicotinic neuromuscular receptors. If this agent becomes approved for clinical use it may provide a way to rapidly reverse muscle relaxation with rocuronium and provide a more attractive choice for burn patients when rapid sequence induction is indicated.

Responses to non-depolarizing relaxants are also altered by burn injury. Three to five times higher doses are required to achieve adequate relaxation. Resistance is apparent by 7 days after injury and peaks by approximately 40 days. Sensitivity returns to near normal after approximately 70 days. Two reports described slight but measurable resistance to nondepolarizing relaxants persisting for more than a year after complete healing of the wounds. The mechanism of the altered response appears to involve pharmacodynamic rather than pharmacokinetic changes. Upregulated immature receptors are less sensitive to non-depolarizing relaxants. Burns >25% TBSA require higher total dose and greater plasma concentrations of non-depolarizing blockers to achieve a given level of twitch depression.

Proliferation of acetylcholine receptors across the muscle membrane has been used to explain both resistance to nondepolarizing muscle relaxants and the exaggerated hyperkalemic response to succinylcholine. The observation of resistance of a patient to metocurine for up to 463 days after burn has been used to suggest that hyperkalemic responses to succinylcholine also could persist for more than a year. However, no pathologic hyperkalemic responses to succinylcholine in burned patients have been reported more than 66 days after burns.

In contrast to other non-depolarizing neuromuscular blockers, mivacurium dosage requirements in pediatric patients appear to be unchanged by burn injury. The time to onset of drug action, degree of paralysis achieved by a specific dose, and rate of infusion required to maintain a given level of relaxation were all the same in burn patients as values reported for non-burned control patients. Plasma cholinesterase activity is reduced in burn patients. In a study by Martyn, the observation of an inverse relationship between plasma cholinesterase activity and recovery time from 25% to 75% twitch tension suggests that reduction of metabolic degradation of mivacurium may compensate for other factors that induce resistance to relaxants. This observation suggests that mivacurium can be administered to burn patients in normal doses that would avoid cardiovascular perturbations associated with the larger doses of other relaxants required in burn patients.

Anesthetic management

Airway management

If injuries do not preclude conventional airway management (i.e. mask fit, jaw lift, and mouth opening), standard induction and intubation procedures are appropriate. Hu et al. reported that gastric emptying was not delayed in patients...
Anesthesia for burned patients

with severe burns, so that a rapid sequence induction is not necessary. However, attention should be paid to gastric residuals during enteral feeding. The development of sepsis can slow gastric emptying, which can result in retained fluids in the stomach and risk of aspiration.

When burns include the face and neck, swelling and distortion may make direct laryngoscopy difficult or impossible. In addition, loss of mandibular mobility may impair airway manipulation and make mask ventilation difficult. Fiberoptic intubation while maintaining spontaneous ventilation is a safe and reliable technique under these conditions. Fiberoptic intubation can be performed in awake adults, but pediatric patients are unable to cooperate and must be sedated. As most anesthetics cause collapse of pharyngeal tissues and airway obstruction they are unsuitable for fiberoptic intubation in patients whose airway would be difficult to manage with a mask. Ketamine, however, is unique among anesthetic drugs because it maintains spontaneous ventilation and airway patency.

Ketamine anesthesia has been found to be safe and effective for airway management in infants with difficult airways caused by congenital airway anomalies. Reports of successful nasotracheal intubation in infants with congenital airway malformations have been made both by manipulations guided by fiberoptic nasopharyngoscopy and the conventional technique of fiberoptic intubation with the endotracheal tube mounted on the fiberscope. In the latter case an ultrathin bronchoscope (2.7 mm) was required because a larger fiberscope would not fit through the appropriately sized endotracheal tube. To facilitate intubation under ketamine anesthesia, topical anesthesia of the larynx with lidocaine prior to instrumentation of the larynx is advised. Because the ultrathin bronchoscope lacks a working channel for administration of topical lidocaine, fiberoptic intubation with the 2.7 mm bronchoscope was preceded by nasopharyngoscopy with a 3.5 mm fiberscope for administration of topical lidocaine. At SBH Galveston we have also found this technique, using two fiberscopes, to be effective in infants with burn injuries. Wrigley et al. evaluated the use of a 2.2 mm intubating fiberscope during halothane anesthesia in ASA 1 or 2 children aged 6 months to 7 years. In this series of 40 patients a number of complications were experienced, including laryngospasm and failure to achieve intubation with the fiberscope. This experience is in contrast to numerous reports of safe and effective airway management with ketamine.

Securing an endotracheal tube in a patient with facial burns presents a variety of problems, and numerous techniques have been described. Tape or ties crossing over burned areas will irritate the wound or dislodge grafts. A useful technique to avoid these problems involves the use of a nasal septal tie with one-eighth inch umbilical tape (Fig. 14.7). The umbilical tape is placed around the nasal septum using 8 or 10 Fr red rubber catheters passed through each naris and retrieved from the pharynx by direct laryngoscopy and McGill forceps. A length of umbilical tape is tied to each of the catheters; when the catheters are pulled back through the nose, each end of the umbilical tape is pulled out of its respective naris, producing a loop around the nasal septum. Before securing with a knot, care should be taken to assure that the uvula is not captured in the loop. A knot in the nasal septal tie should be snug enough to prevent excessive

Figure 14.7 Nasotracheal tubes can be secured with confidence by tying to umbilical tape tied in a loop around the nasal septum. (a) Red rubber catheters (8 or 10 Fr) are passed through each naris, retrieved with McGill forceps from the oropharynx, and each end of a piece of umbilical tape is tied to the catheters. (b) When the catheters are pulled out of the nares, the umbilical tape follows and, after laryngoscopy to assure the uvula has not been trapped, a loop can be tied around the bony nasal septum. (c) Umbilical tape can be used to secure the endotracheal tube to this loop. This technique is very secure, avoids irritating facial burn wounds or grafts, and leaves the surgical field free of tape or ties.
movement of the endotracheal tube but loose enough to prevent ischemic necrosis of the underlying tissues.

Airway management using a laryngeal mask airway (LMA) has also been used successfully during burn surgery for children. McCall et al. reported their experience with 141 general anesthetics administered to 88 pediatric burn patients. Nineteen (14.5%) of the procedures were complicated by respiratory events such as unseating, desaturation, and partial laryngospasm that required intervention. Two of these events required intraoperative intubation without sequelae, but all other events resolved with therapy. Interestingly, the presence of preoperative respiratory problems or face/neck burns did not predict intraoperative respiratory problems. These authors suggest that, in patients with upper airway mucosal injury, LMA airway management may help avoid further laryngeal injury that might occur with intubation of the trachea.

Hagberg et al. published a case report describing the successful use of an esophageal tracheal Combitube in a patient undergoing elective surgery for burn scars involving the mouth. The patient had a class IV oral airway by Samsoon and Young’s modification of the Mallampati airway classification, and limited mouth opening. A translaryngeal endotracheal tube was undesirable because tracheostomy had resulted in subglottic stenosis, which could have been exacerbated by an endotracheal tube. After induction with fentanyl and propofol the Combitube was placed and the patient was relaxed with rocuronium and mechanically ventilated during the 60-minute procedure.

### Perioperative monitors

As with any critically ill patient suffering from multiorgan system involvement, the choice of monitors in a burned patient will depend on the extent of the patient’s injuries, physiological state, and planned surgery. In addition to the preoperative pathophysiology associated with thermal injuries, perioperative monitoring must be adequate to assess rapid changes in blood pressure and tissue perfusion associated with the massive blood loss that can accompany excision of burn wounds. The minimum standards of the American Society of Anesthesiologists require monitoring of circulation, ventilation, and oxygenation. Standard monitors include electrocardiography (EKG), measurement of systemic blood pressure, pulse oximetry, capnography, and inspired oxygen concentration. The ability to measure body temperature should be readily available and is highly recommended for the burn patient.

Standard EKG gel electrodes usually will not adhere to burn patients because the skin is injured or covered with antibiotic ointment. For acute burn surgery, surgical staples and alligator clips are useful. Respiratory rate can be quantitated using bioimpedance from the EKG signal or from the capnogram. Pulse oximetry in burn patients can be difficult when transmission pulse oximetry sites are either burned or within the operative field. Reflectance pulse oximetry has been suggested as an alternative in these circumstances. However, an effective commercially available instrument has been slow in development.

If direct arterial pressure monitoring is not necessary, a blood pressure cuff can provide accurate measurements even if placed over bulky dressings applied to an extremity. Systolic blood pressures obtained from the pressure at which the pulse oximetry signal returns during cuff deflation has also been found to be accurate.

When blood loss is expected to be rapid and extensive, blood pressure may change more rapidly than the interval between cycles of non-invasive blood pressure measurement. In this case an arterial catheter can provide direct and continuous measurement of blood pressure. This monitor can provide much more information regarding the patient’s circulatory status than just systolic and diastolic blood pressure. The arterial pressure waveform is influenced by preload, contractility, and vascular tone. Perioperative variation in the rate of rise of arterial pressure, the area under the pressure wave, position of the dicrotic notch, and beat-to-beat alterations in systolic pressure related to respiration all reflect clinically significant hemodynamic changes. With experience, trends in these variables can help guide volume and vasoactive therapy. Display of the beat-to-beat arterial pressure allows measurement of systolic pressure variation (SPV). SPV is the difference between maximum and minimum systolic blood pressure during a single cycle of positive-pressure mechanical ventilation. Several studies have correlated SPV with cardiac output response to volume infusion. Tavernier et al. reported that in septic patients on mechanical ventilation SPV is a better predictor of left ventricular ejection volume response to volume loading than either pulmonary artery occlusion pressure or echocardiographic measurement of left ventricular end-diastolic area. Measurements are not as simple as merely ‘eyeballing’ the blood pressure trace because several variables influence SPV, including arrhythmias, tidal volume, and mechanical versus spontaneous ventilation. SPV provides a dynamic assessment of the interaction of preload and cardiac output.

Arterial blood sampling for blood gas analysis also provides valuable information regarding pulmonary function and acid–base balance. Inadequate tissue perfusion may manifest as metabolic acidosis despite apparently adequate arterial and central venous blood pressures.

In patients with large burns a central venous catheter serves several functions. Central venous pressure can be useful for titrating blood and fluid administration. Blood samples from a central vein are not truly mixed venous, but trends in central venous oxygen tension can help identify inadequate tissue perfusion. A central venous catheter sutured into place also provides very secure intravenous access and is an ideal route for administration of vasoactive infusions. A pulmonary artery catheter is usually not required for burn surgery. In some cases, however, the ability to more closely monitor ventricular function and oxygen supply/demand relationships may be helpful as when large doses of inotropes or high PEEP is required. As described above, a newer transpulmonary thermodilution catheter system is also capable of estimating thoracic and end-diastolic cardiac blood volumes. These measures of preload have been reported to correlate better than filling pressures (central venous pressure or pulmonary artery occlusion pressure) with changes in cardiac index or oxygen delivery with fluid volume administration.

Urine output is the most useful perioperative monitor of renal function. Urine output of 0.5–1.0 mL/kg/h is often recommended as an endpoint for fluid management in acute burn patients. Adequate urine output is one measure of both...
renal and global perfusion. When intraoperative transfusion is planned, examination of the urine may be the only reliable indicator of a transfusion reaction, as signs and symptoms other than hematuria are masked by general anesthesia or hemodynamic changes associated with burn surgery. Myoglobinuria may also occur after burn injury, and in this case a Foley catheter is necessary to monitor response to therapy. Diuretic therapy for myoglobinuria or any other indication will negate the usefulness of urine output as an index of perfusion.

Vascular access

Securing adequate vascular access in the acutely burned patient is one of the more technically challenging procedures facing the anesthesia care team. In the pediatric age group the task can be even more difficult. Skin sites for insertion of vascular access catheters may be involved in the burn, and regional anatomy is often distorted by burn, edema, or scarring. Early in the course of an acute burn shock leads to vasoconstriction, making cannulation of peripheral vessels nearly impossible. Later, once the patient has had several operative procedures, scarring in the area of access sites makes their placement difficult as well. As burn patients undergo multiple debridement procedures it is necessary to attain vascular access many times in each patient. The need for frequent catheter changes in an attempt to minimize catheter-related sepsis increases the risk of mechanical complications. The anesthesia care team is frequently involved in the maintenance of adequate vascular access during the period of acute care and therefore must be adept in their placement. When a large portion of the surface area is burned, it becomes necessary to insert catheters through burned skin. If the burn is deep, it may have to be debrided prior to line placement so that the catheter can be sutured to viable tissue.

For the operative excision of a large burn wound, an arterial catheter allows continuous blood pressure monitoring in the face of sudden and sometimes massive blood loss as well as during the titration of vasoactive drugs. It also allows easy access to blood samples for arterial blood gases, chemistries, and serial hematocrit determinations. For pediatric patients with large burns, arterial monitoring is necessary. A large number of patients have been cannulated without complications. There is a relatively high rate of arterial occlusion: 8% with 20-gauge catheters and 34% with 18-gauge, but almost all completely recanalize. It is often difficult to maintain a radial arterial catheter in burn patients for more than 48 hours, particularly in children, and, unfortunately, the hands and forearms are typically involved in a large burn wound.

Accessing the femoral artery is easier in most patients, particularly those in low perfusion states, because it is a larger and more central vessel. The groin is often spared from injury, even in a large burn, and placement of a catheter in the femoral artery is not greatly affected by the presence of edema. The duration of patency is longer than that of a radial artery catheter, and the incidence of infection in a femoral artery catheter is similar to that at any other location, at about 1%. The risk of mechanical complications is smaller than that of more peripheral arteries because the arterial/catheter diameter ratio is larger. Still, some recommend avoiding the femoral site unless no other site is available, as loss of limb, or limb length discrepancy in children, is a devastating, if rare, complication.

Other sites for arterial access include the dorsalis pedis, posterior tibial, and temporal arteries, none used with great frequency, and all distal enough to give inaccurate blood pressure readings, particularly in hypotensive patients. Use of the axillary artery has the disadvantages of a relatively higher rate of infection and difficulty in maintaining correct arm positioning for proper catheter function. The incidence of complications from arterial catheters has been cited as anywhere from 0.4% to 11%, with the higher rate seen most often in pediatric patients, particularly those under 1 year of age. Early complications include bleeding, which is usually easily controlled, and hematoma formation, which is more common if the artery is transfixed during cannulation, and is avoided by an adequate period of pressure applied to the site if bleeding occurs. Damping of the arterial waveform or clotting of the catheter is more common with small catheters or small arteries; this can be lessened somewhat by continuous heparin flushing systems.

The incidence of catheter-related infections with arterial catheters is generally low, quoted at anywhere from 0.4% to 2.5% until 4 days’ duration. The incidence of infection gradually increases to 10% by 7 days, but stays constant thereafter. This relatively low rate of infection in comparison to central venous catheters confirms the clinical impression that catheter-related infections are less commonly seen in the high-flow arterial system.

Vascular insufficiency of the distal extremity has been reported at the rate of 3–4% of patients in whom arterial catheters are placed. Fortunately, most cases of ischemia resulting from vascular obstruction are evident immediately and resolve when the catheter is removed. The risk of ischemia can be minimized by selecting the smallest possible catheter that will give an accurate arterial waveform. There is a marked increase in the incidence of arterial vasospasm when >50% of the vessel lumen is occluded by the catheter. Predisposing factors to ischemia from arterial obstruction include hypotension, the use of vasoconstrictors, prolonged catheterization, age under 5 years, and insertion by cutdown. Indeed, most reports of chronic sequelae have come in patients less than 1 year of age who were hypotensive at the time of catheter insertion. Other less commonly reported complications from arterial catheters include cutaneous damage, pseudo-aneurysm formation, and septic arthritis of the hip.

Central venous catheters are very useful for large-volume resuscitation in patients with burns over 30% or more TBSA. Normal anatomic landmarks can be totally obliterated. The problem is compounded by the need for long-term access in patients with large burns who are also at high risk for central venous catheter infections and so will require frequent line changes. Ultrasound guidance for placement of vascular catheters has become more common. Technical improvements in equipment have made image quality and ease of use much better. There have been suggestions that ultrasound guidance be made a standard of care. However, extensive scarring from burn wounds can degrade the ultrasound image. In these instances success and safety depend on clinical skill and experience.
Catheters placed in the subclavian vein have a lower risk of infection than those placed in the internal jugular or femoral veins, but carry a higher risk of mechanical complications during their placement. The internal jugular vein is typically more difficult to access in burn patients with facial and neck burns or edema, and is associated with a higher infection risk. Additionally, it is a difficult position in terms of patient comfort, particularly for pediatric patients. The femoral vein is a large central vein that is usually easy to cannulate. It has several advantages, including no risk of pneumothorax, easier control of bleeding, less anatomic distortion due to edema, and the inguinal region is often spared even in a large burn. Goldstein and others found femoral venous catheters to be well tolerated in their pediatric burn patients. In some studies the risk of catheter-related infection was higher in the femoral vein than at other vascular access sites, and the risk of venous thrombosis is also quoted by some authors as being greater.

Patients with acute burn injury may be at increased risk of thrombotic complication due to a hypercoagulable state associated with systemic inflammatory response and vascular injury associated with cannulation attempts. Although Barrett and colleagues found that complications due to thrombosis were infrequent in their burn population, thrombosis can result in severe morbidity and mortality. It has been very difficult to establish the true incidence of central venous catheter-related infectious complications. This of course makes it difficult to establish the most effective policies and procedures to reduce infections associated with central venous catheters. The diagnosis of catheter-related bloodstream infections is made when there are signs and symptoms of infection and other sources of infection are excluded. Patients with large burns have multiple potential sources of infection that may be difficult to exclude, and the systemic inflammatory response to large burn injury mimics the signs and symptoms of bloodstream infection. Catheter-related infection in burn patients has been reported to have an incidence as low as 2.5% and as high as 22.4%. One large study of 1183 burn patients and 1346 central venous catheters showed that the incidence of catheter-related infection was 19.5%, with a mortality of 14.1%. These authors cite catheter-related infection as the second most common cause of sepsis in burn patients after the burn wound itself.

As a result of these and other issues, controversy continues regarding when vascular catheters should be changed and whether or not changing the catheter over a guide wire reduces the incidence of infection. For patients with large burns and who experience a prolonged hospital course with continuous central venous access, the risk of mechanical complications increases with the number of new vascular sites cannulated. Three large randomized trials demonstrated no difference in the incidence of catheter-related infections among groups who had lines placed at a new site every 7 days and groups who had their lines changed over a guide wire every 7 days. At our hospital, in selected cases where we would like to avoid cannulating a new site we will change the catheter over a wire and culture the catheter tip. If the culture is negative the catheter is left in place; if the old catheter was colonized, we place a catheter in a new site. There are conflicting data in relation to the incidence of infection and the site of the central venous catheter, although almost all studies agree that the incidence of infection is lowest if the subclavian approach is used. Also, all studies that compared single-lumen and multilumen catheters found a lower rate of infection with single-lumen catheters. Those that compared percutaneous catheter placement with placement via cutdown technique found a higher incidence of infection with cutdowns.

Advances in vascular catheters that incorporate an antibiotic have improved the efficacy of these devices in reducing the incidence of catheter-related bloodstream infections. A prospective randomized trial examined the efficacy of two types of central venous catheter that incorporate antibiotics: one catheter releases silver ions continuously and the other is impregnated with two antibiotics with different mechanisms of action, rifampin and minocycline. Both catheters were associated with low rates of catheter-related bloodstream infections. Improvements in this technology would provide two significant clinical advantages. Reduced colonization of central venous catheters will reduce bloodstream infections, and reduced need for changes in vascular access sites for infection control will reduce the incidence of mechanical complications of catheter insertion.

Additional measures recognized by the CDC for reducing catheter-related bloodstream infections include maximum sterile barrier technique (cap, mask, sterile gown, sterile gloves, and large sterile drape with a small opening). A meta-analysis concluded that chlorhexidine gluconate is superior to povidone-iodine for insertion-site disinfection.

The operative debridement of a large burn wound is accompanied by rapid and sometimes considerable blood loss. Critical hypoperfusion of vital organs begins to occur when 20–30% of blood volume is lost. Irreversible shock and cellular damage can begin within minutes, depending on the continuing rate of loss. The achievement of a very rapid fluid infusion rate is critical in the resuscitation of the patient undergoing operative excision of the burn wound. Clearly, adequate venous access to achieve rapid infusion rates is imperative.

Flow through an intravenous catheter can be increased by high-pressure gradients, tubes of large diameter and short length, and the use of low-viscosity fluids. The most significant variable is the radius of the tube, where changes result in exponential changes in flow: doubling the diameter of the tube increases flow 16-fold. There have been a number of studies comparing flow rates of various catheters under different conditions. Large-diameter short catheters maximize flow, as does a central venous location: flow is 20–40% less in a peripheral vein than in a central vein for the equivalent diameter and length of catheter. Peripheral veins add resistance to flow before fluid is delivered to the central compartment.

Diluting one unit of packed red blood cells with 250 mL of normal saline can increase the flow of the blood 10-fold. The application of a 300 mmHg pressure device to the blood unit can increase the flow rate another seven times. The diameter and length of the intravenous tubing system delivering fluid from the bag to the patient has profound effects on the rate of fluid delivery. Large-bore trauma tubing with an internal diameter of 5.0 mm allows fluid to flow three
times as fast as standard blood infusion set tubing with an internal diameter of 4.4 mm, which is twice as fast as standard intravenous tubing with an internal diameter of 3.2 mm. The large-bore trauma tubing allows fluid flow rates of 1200–1400 mL/min. Several large studies have shown introducer catheters to be superior to all other devices for the rapid infusion of blood and intravenous (IV) fluid. These catheters are typically of large diameter, with thin walls and no tapering, so that for any given catheter size the inner diameter is largest. This finding holds especially true for pediatric patients, in whom vessel size is limited. The flow rate of a 4 Fr introducer catheter is greater than that of a 16-gauge IV catheter. However, the 4 Fr introducer placed by the Seldinger technique requires only a 21 gauge needle to be inserted into the vein for its placement.

When planning vascular access for perioperative anesthetic management it is important to be aware of and take into account the patient’s hospital course. Choice of access site should avoid vessels previously involved in complications such as thrombosis or vascular injury. Note must be taken of when existing catheters were placed, and what the local convention is with regard to the timing of regular changes of access sites for infection control. The patient’s hospital course must also be considered when choosing a catheter. Although introducers offer the greatest flow and may give the anesthesiologist a sense of assurance, the patient may require continuous vascular access for months of hospitalization and may return for surgery weekly. Large vascular introducers placed weekly will not be tolerated without complications that may result in morbidity, and will limit access sites for future surgery. The catheter should be large enough to transfuse appropriately for the case, but much larger catheters will increase risk without benefit.

**Patient transport**

The safe transport of a critically ill burn patient to and from the operating room can be a formidable task. A methodical approach will help to ensure patient safety and the seamless maintenance of respiratory, hemodynamic, and general support. Hemodynamic status should be optimized prior to transport; pharmacological support may be required. The American Society of Anesthesiologists standards mandate evaluation, treatment, monitoring, and equipment appropriate to the patient’s medical condition for any transport. Depending on the patient’s condition, simple observation may be appropriate. Patients requiring supplemental oxygen should be monitored by pulse oximetry. Hemodynamic monitoring is guided by the patient’s hemodynamic status. Sufficient battery power must be available for uninterrupted monitor and infusion pump function during transport.

Airway supplies should be readily available, including a full oxygen cylinder, a self-inflating Ambu bag with mask, and intubation equipment. The patient’s airway and ventilation as well as overall condition must be continually observed by the anesthesia care team. Drugs for resuscitation should accompany the patient on any transport. As discussed below, hypothermia is poorly tolerated by patients with an acute burn injury. It is imperative that patients be kept warm during transport in order to avoid increasing oxygen consumption and taxing limited metabolic reserve.

**Selection of anesthetic agents**

Many anesthetic agents have been used effectively for the induction and maintenance of anesthesia in burn patients. Intravenous agents can be used for both induction and maintenance and the specific agent used will depend primarily on the patient’s hemodynamic and pulmonary status, as well as the potential difficulty in securing their airway. Ketamine has many advantages for use in the burn patient for induction and maintenance of anesthesia. As an induction agent, ketamine can be administered at a dose of 0.5–2.0 mg/kg. Except in patients who are catecholamine depleted, ketamine generally preserves hemodynamic stability (Fig. 14.8). In addition, ketamine preserves hypoxic and hypercapnic ventilatory responses and reduces airway resistance. Compared to other IV anesthetics, airway reflexes remain more intact after ketamine administration. However, some risk of aspiration remains. Patients who do not require ventilatory support can be allowed to breathe spontaneously, which provides an additional margin of safety should inadvertent extubation occur. In fact, some clinicians have reported the use of ketamine anesthesia without instrumentation of the airway. Patients were allowed to breathe spontaneously and the airway complication rate was comparable to that of intubated patients. The use of intramuscular ketamine can be beneficial in securing the airway in pediatric burn patients or uncooperative adults who do not have vascular access. Because ketamine preserves spontaneous ventilation and

**Figure 14.8** Heart rate, mean arterial pressure, and cardiac index changes during a 15-minute period of ketamine administration to critically ill patients. (From Nolan JP. Intravenous agents. In Grande CM, et al., eds. Textbook of trauma anesthesia and critical care. St. Louis: Mosby Yearbook; 1993.)
induces dissociative anesthesia, it provides good conditions for securing the airway by fiberoptic bronchoscopy. The addition of other anesthetic agents, particularly potent volatile agents or opioids, should be avoided until the airway is secured because these anesthetics depress respiratory drive and relax pharyngeal muscles, thereby increasing the risk of apnea, upper airway obstruction, or laryngospasm. Ketamine can also be used, either alone or in combination with other anesthetics, for maintenance of anesthesia either by infusion or by intermittent bolus. Ketamine has potent analgesic properties and is used extensively in the operating room as well as for painful wound care and patient manipulations. A drying agent such as glycopyrrolate (2−5 µg/kg) may be given in combination with ketamine to reduce ketamine-induced secretions. In addition, benzodiazepines are often recommended in older children and adults to reduce the incidence of dysphoria sometimes associated with ketamine administration. Propofol is more commonly used for induction in patients returning for reconstructive procedures rather than in the acute phase of injury, but is also sometimes chosen in patients with small burns and no evidence of airway or facial involvement when direct laryngoscopy is planned.

Volatile anesthetics may be used for both induction and maintenance of anesthesia in burn patients. In pediatric patients, mask induction with either halothane or sevoflurane is commonly used if the patient does not have injuries that may make airway manipulation difficult. In the acute setting, an anesthetic technique involving nasotracheal intubation after mask induction with halothane, nitrous oxide, and oxygen has been described. Proponents particularly emphasize avoiding the potential problems associated with the ketamine-based technique. However, volatile agents produce dose-dependent cardiac depression and vasodilation. In addition, hypoxic ventilatory drive is ablated by volatile anesthetics at low concentrations, and a dose-dependent depression of hypercapnic drive also occurs. However, as maintenance agents volatile anesthetics have predictable washin and washout kinetics and provide a useful adjunct to other agents when titrated to hemodynamic and ventilatory parameters. Of the volatile agents, nitrous oxide has the least impact on cardiovascular and respiratory function and can serve as a useful component of a balanced anesthetic if the patient’s oxygen requirements permit.

Opioids are important agents for providing analgesia to burn patients throughout the acute phase of injury and for providing postoperative analgesia in patients undergoing reconstructive procedures. The spectrum of opioids currently available provides a wide range of potencies, durations of action, and effects on the cardiopulmonary system. The introduction of the ultrashort-acting narcotic remifentanil provides additional flexibility in perioperative dosing. With this drug, a primarily narcotic-based anesthetic can be provided to patients who may be intolerant of potent inhalation agents without prolonging emergence. Regional anesthesia can be used effectively in patients with small burns. In cooperative children or adults with injuries confined to the lower extremities, epidural or intrathecal anesthesia may be used if no contraindications exist. For upper extremity procedures, brachial plexus block may be considered as the primary anesthetic or as an adjunct for postoperative pain control. Scalp donor sites are particularly painful. Sensory nerves to the scalp are superficial and easily blocked with injections of local anesthetic, and this technique has been used for awake craniotomy. Scalp blocks have been used with success at our institution for donor sites in acute patients (unpublished observation) and for scalp procedures in reconstructive patients.

**Fluid management**

Fluid management and blood transfusion for burn wound excision can be quite challenging. Fluid administration should be guided not only by intraoperative events but also by previous hospital course and ICU treatment goals. If early excision is performed during the first 24 hours, perioperative fluid management may involve the acute resuscitation and fluid needs will exceed replacement of shed blood. Even after this period insensible fluid requirements are increased by large open surfaces from excised wounds, hypermetabolic state, and hyperthermia. However, early in the hospital course patients are edematous owing to the large amounts of crystalloid solutions administered during resuscitation. At this time additional crystalloid administered during the perioperative period may be poorly tolerated and may result in complications of compartment syndrome in extremities or the abdomen. After the initial period of resuscitation, ICU therapy may include vigorous attempts to reduce edema, including the use of diuretics. If the ICU staff have been administering diuretics to the patient all week in order to reduce interstitial edema it is not helpful when the patient receives several liters of fluid in the operating room. Perioperative fluid management must also take into account hypotonic clysis fluids that the surgeons may inject to facilitate donor skin harvest with the dermatome. In small children the volume of this fluid can be in excess of 50 mL/kg.

Replacement of surgical blood loss during burn wound excision and grafting can be just as challenging. During burn surgery it is impossible to accurately estimate the amount of shed blood, as blood is concealed beneath the patient, in drapes, in sponges, or may be washed down a drain on the operating table. As discussed above regarding the initial resuscitation, there is no one physiological endpoint to titrate volume replacement. Arterial pressure may be maintained by vasoconstriction despite significant hypovolemia, central venous pressure is not a reliable index of preload, changes in urine output and hematocrit lag behind rapid reductions in blood volume, and metabolic acidosis may indicate deficient perfusion but does not identify the specific problem. All of these variables are useful, however, when evaluated together. Although systolic blood pressure may be within the normal range, alterations in the arterial waveform and changes with the respiratory cycle may indicate hypovolemia. Even though central venous pressure correlates poorly with hemodynamic function, this variable is useful in determining whether volume administration will be tolerated by the patient. If perfusion appears inadequate and central venous pressure is low or normal, it is safe to give volume. If central venous pressure is elevated, volume administration may cause pulmonary edema.

The concept of transfusion trigger with regard to burn care is discussed below. It must be remembered, however, that...
during rapid blood loss the hematocrit may change much more slowly than the blood loss, and often blood must be administered before the hematocrit falls below a specific trigger.

**Blood transfusion**

The need for blood transfusion is usually not a major concern during the immediate resuscitation phase in acutely burned patients unless other coexisting trauma exists. Nevertheless, a fall in plasma hemoglobin concentration can occur during the acute resuscitative phase due to hemodilution and blood loss from escharotomies and other invasive procedures. However, major blood loss is common when patients are taken to the operating room for excision and grafting of burn wounds. Desai and colleagues reported that the amount of blood loss during burn wound excision is determined by the age of the burn, the body surface area involved, and whether infection is present (see Table 14.4). In general, more blood loss was observed as the time from initial injury increased, and if wounds were infected. Transfusion requirements ranging from 0.45 to 1.25 mL of packed red blood cells (PRBC) per cm² burn area were reported. In another study, Criswell and Gamelli reported an average transfusion rate of 0.89 mL PRBC/cm² burn area in a cohort of adult burn patients. A study by O’Marra and colleagues showed an average transfusion rate of 0.65 mL PRBC/cm² in a heterogeneous group of burn patients.

Controversy exists regarding transfusion triggers and targets. Some authors advocate allowing hematocrit to drop to 15–20% prior to transfusion in otherwise healthy patients undergoing limited excision, and transfusing at a hematocrit of 25% in patients with pre-existing cardiovascular disease. The same group proposed maintaining hematocrit near 25% in patients with more extensive burns, and near 30% if the patients have pre-existing cardiovascular disease. A small study by Sittig and Deitch showed fewer transfused units and no increase in adverse hemodynamic or metabolic effects in patients transfused at a hemoglobin of 6–6.5 g/dL compared to patients maintained at a hemoglobin near 10 g/dL. However, in general, few outcome data exist regarding the optimum transfusion trigger for blood transfusion during burn wound excision. Blood transfusion needs are best assessed by evaluating the clinical status of the patient. Specifically, assessment of ongoing blood losses, preoperative hemoglobin levels, vital signs, and evidence of inadequate oxygen delivery, such as hypotension, tachycardia, acidosis, and decreasing mixed venous oxygen tension, provide important information regarding the patient’s oxygen balance. Patients with coexisting cardiac and pulmonary disease generally require higher oxygen-carrying capacity. Overall, American Society of Anesthesiologists guidelines indicate that blood transfusion is rarely required at a hemoglobin of 10 g/dL or above and is almost always indicated at a hemoglobin of less than 6 g/dL. For each patient, therefore, acceptable blood loss can be determined based on pre-existing diseases, preoperative hematocrit (Hct), and the patient’s estimated blood volume (EBV).

During excision of major burn wounds blood loss may reach or exceed the patient’s blood volume. Various definitions of massive hemorrhage have been used, but include loss of one blood volume in 24 hours, 50% blood volume in 3 hours, or ongoing blood loss of 150 mL/min. When blood loss is this extensive coagulation factors are lost and consumed as volume is replaced and/or diluted. Once developed, the resulting coagulopathy is difficult to treat and is associated with serious morbidity and mortality. In the past, ASA guidelines have recommended that the administration of fresh frozen plasma (FFP) to replace surgical blood loss be restricted to cases with microvascular bleeding and documented coagulation factor deficiency. In recent years these traditional indications for FFP have been challenged. In a computer simulation of exsanguinating traumatic hemorrhage, Hirshberg and colleagues predicted that this restrictive use of FFP to treat massive hemorrhage was inadequate to prevent or correct dilutional coagulopathy. With their model early and aggressive use of FFP was needed to prevent coagulopathy owing to dilution of coagulation factors. In addition, a problem with the use of laboratory measurements of coagulation function during massive hemorrhage is that results cannot be provided in a timely fashion. Findings from recent clinical studies have also supported the early use of FFP in combination with packed red blood cells to replace ongoing massive blood loss. In both civilian and military patient populations a dose-dependent reduction in mortality has been consistently observed when FFP is administered early in patients requiring massive transfusion. As a result, blood banks have adopted protocols to provide blood components to support coagulation function (e.g. FFP, platelets, and cryoprecipitate) when massive hemorrhage is diagnosed. These protocols were developed from data obtained from trauma patients presenting in hemorrhagic shock. During surgical excision of burn wounds attempts are made to replace blood loss as it occurs, rather than after a state of hypovolemic shock has developed. Still, the concept that coagulopathy is better prevented than reversed seems to justify the adoption of a modification of the treatment protocol used for massive traumatic hemorrhage when replacing extensive blood loss during burn wound excision. As an example, in our institution, during burn surgery intravascular volume is maintained with infusion of colloid (hetastarch or albumin) and oxygen-carrying capacity with packed red blood cells until 50% of the estimated blood volume has been replaced. From that point on, FFP is administered in a 1:1 ratio with packed cells to replace continued blood loss.

Red blood cells also facilitate hemostasis. Through a rheological effect, red blood cells push platelets to the periphery of the intravascular lumen, which increases their concentration at and interaction with the endothelium. Red cells may also enhance hemostasis through effects on platelet biochemistry and function. Massive transfusion can also be complicated by hypothermia and hypocalcemia. Hypothermia can contribute to coagulopathy and is poorly tolerated by burn patients from a metabolic standpoint. When large blood loss is anticipated blood warmers capable of warming fluids at the flow rates required to resuscitate massive hemorrhage (>100 mL/min) must be available. Hypocalcemia can result from rapid administration of blood products containing citrate (especially FFP). Hypocalcemia also impairs coagulation and, in addition, interferes with vascular and myocardial contraction, which results in hypotension. The effects of hypocalcemia respond more rapidly to calcium chloride than
calcium gluconate because the gluconate form requires hepatic metabolism to release the ionized calcium. Other transfusion reactions are described along with the individual components.

Several means of reducing surgical blood loss may be employed during burn wound excision, such as the use of tourniquets on limbs and compression dressings at sites of excision or skin graft harvesting. Tourniquets have been shown to be effective for reducing blood loss during burn wound excision. The drawbacks of tourniquet use are that their effectiveness is limited to surgery on the extremities, and that they may interfere with the surgical field. Pharmacological interventions that may reduce blood loss include the use of epinephrine-soaked dressings or topical epinephrine spray to induce local vasoconstriction. Alternatively, subcutaneous tissues may be infiltrated with epinephrine-containing fluids. The use of epinephrine may be associated with tachycardia and hypertension if significant amounts are absorbed into the systemic circulation. However, some studies have reported that the use of topical or subcutaneous epinephrine in burn patients is not associated with an increased incidence of side-effects or complications. However, the effectiveness of this approach is unclear. A recent study showed that the use of topical epinephrine spray or subcutaneous epinephrine infiltration did not result in decreased blood loss during burn wound excision. However, the data were quite variable and the patients also received topical thrombin. A larger study examining the effects of subcutaneous epinephrine and topical thrombin might clarify this issue. In a more recent study, Mzezewa and colleagues reported that treatment with systemic terlipressin, a vasopressin analog, reduced blood loss and transfusion requirements in a cohort of pediatric and adult burn patients. The authors did not report significant complications associated with this approach.

**Blood components**

Several blood components are available for replacement of losses incurred during burn wound excision.

**Whole blood**

Whole blood consists of unfractionated blood and contains all of the components of blood, including red blood cells, plasma, platelets, and white blood cells; however, whole blood stored for more than 24 hours does not contain functional white blood cells or platelets (Table 14.8). One unit of whole blood contains approximately 200 mL of red blood cells and 250 mL of plasma. Whole blood is available in some hospitals for large-volume blood transfusions (trauma, liver transplantation, burns) and treatment of hypovolemic shock. However, because of the scarcity of blood products in most communities, whole blood is not readily available. Fractionation of whole blood into its individual components is a much more efficient and cost-effective means of maximizing blood usage. When available, however, whole blood provides an excellent means of volume expansion and providing oxygen-carrying capacity in patients requiring large-volume blood transfusion.

**Packed red blood cells**

PRBCs are the most common means of replacing blood loss during surgical procedures. Most of the plasma and platelets are removed during processing so that PRBCs provide few plasma components, clotting factors, or platelets. A unit of PRBCs contains approximately 200 mL of red cells and 50 mL of residual plasma. A comparison of PRBC composition with whole blood is shown in Table 14.9. PRBCs provide oxygen-carrying capacity and, when reconstituted with crystalloid or plasma, volume resuscitation. As described above, red blood cells can enhance platelet function, and hemostasis can be facilitated by correction of anemia.

**Fresh frozen plasma**

In the setting of burn injury, fresh frozen plasma (FFP) is most commonly used to replace clotting factors during massive blood transfusion. FFP will replace clotting factors as well as proteins S and C by a factor of 2–3% per unit. The use of FFP varies among different burn centers. Plasma is
Complications of massive blood transfusion

Coagulopathy

Coagulopathy associated with massive blood transfusion is due to thrombocytopenia or depletion of coagulation factors by dilution or consumption. PRBCs are essentially devoid of platelets, and whole blood stored for more than 24 hours does not possess significant numbers of viable platelets. Whole blood contains essentially normal levels of coagulation factors, with the exception of the volatile factors V and VIII. Because most plasma is removed from PRBCs they provide a poor source of coagulation factors. Massive blood loss and transfusion with PRBCs or whole blood results in dilutional losses of both platelets and factors V and VIII.

Thrombocytopenia is the most common cause of nonsurgical bleeding after massive blood transfusion. In general, 15–20 units, or 2–4 volumes of blood or PRBCs, must be transfused before bleeding due to thrombocytopenia will develop (Fig. 14.9). Observed platelet counts usually remain higher than calculated values owing to the release of platelets from sites of sequestration. Bleeding due to thrombocytopenia usually develops when the platelet count drops below 50–100,000/µL. Replacement of platelets usually requires transfusion of 6 units of whole blood platelets or 1 unit of single-donor platelets, as described earlier.

As discussed above, blood bank protocols have recently been developed to provide coagulation factors earlier and more aggressively to prevent rather than treat coagulopathy associated with massive hemorrhage and transfusion. These

Table 14.10 Indications for FFP according to National institutes of Health guidelines

| A. | Replacement of isolated factor deficiencies (as documented by laboratory evidence) |
| B. | Reversal of warfarin effect |
| C. | In antithrombin III deficiency |
| D. | Treatment of immunodeficiencies |
| E. | Treatment of thrombotic thrombocytopenia purpura |
| F. | Massive blood transfusion (only when factors V and VIII are 25% of normal) |
| G. | Requirements for indications A and F would be a prothrombin and partial thromboplastin time of 1.5 times normal |

Platelets

Platelets are stored at room temperature to maximize viability. The incidence of bacterial contamination increases exponentially after 4 days. However, refrigerated platelets remain viable for only 24–48 hours. Platelets are obtained from either units of whole blood or by apheresis from a single donor. ABO-compatible platelets, particularly if from a single donor, should be used when possible because post-transfusion viability is improved. One unit of whole blood platelets contains approximately 5 x 10^10 platelets in 50 mL of plasma. Most commonly, 6 units of platelets are combined into a single bag and transfused. A unit of single-donor platelets contains about 30 x 10^10 platelets suspended in 200–400 mL of plasma. Therefore, 1 unit of single-donor platelets is equal to about 6 units of whole blood platelets. One unit of whole blood platelets will increase the platelet count by 5000–10,000/µL.

Cryoprecipitate

Cryoprecipitate is prepared by thawing FFP at 4°C and collecting the precipitate. Cryoprecipitate is rich in factors VIII and XIII, fibrinogen, and von Willebrand factor. In the setting of massive blood transfusion it is used primarily to treat hypofibrinogenemia. Generally, cryoprecipitate is administered when plasma fibrinogen levels fall below 100 mg/dL. One unit of cryoprecipitate will increase plasma fibrinogen levels by 5–7 mg/dL.

Frozen within 6 hours of collection and each unit provides approximately 250 mL of plasma containing normal levels of all coagulation factors. A National Institutes of Health consensus conference has recommended usage guidelines for FFP (Table 14.10).

As discussed above, recent experience with massive transfusions associated with trauma in military and civilian patient populations has provided justification for a more aggressive and proactive use of FFP to prevent rather than treat coagulopathy. When burn wound excision involves massive hemorrhage a similar practice may benefit these patients as well.
protocols organize communication between those directly involved in the patient’s care and blood bank personnel to provide coagulation factors including not only packed red blood cells and FFP but, when indicated, platelets, cryoprecipitate, and recombinant activated factor VII. These protocols can facilitate more timely and effective management of massive transfusion in order to reduce associated morbidity and mortality.

**Citrate toxicity**

Citrate is universally used as an anticoagulant in the storage of blood because of its ability to bind calcium, which is required for activation of the coagulation cascade. Citrate is metabolized by the liver and excreted by the kidneys. Patients with normal liver and kidney function are able to respond to a large citrate load much better than patients with hepatic or renal insufficiency. During massive blood transfusion citrate can accumulate in the circulation, resulting in a fall in ionized calcium. Hypocalcemia can result in hypotension, reduced cardiac function, and cardiac arrhythmias. Severe hypocalcemia can also result in clotting abnormalities. However, the level of calcium required for adequate coagulation is much lower than that necessary to maintain cardiovascular stability. Therefore, hypotension and decreased cardiac contractility occur long before coagulation abnormalities are seen. During massive blood transfusion it is generally prudent to monitor ionized calcium, especially if hemodynamic instability is present in the hypocalcemic patient.

**Potassium abnormalities**

During the storage of whole blood or packed red cells, potassium leaks from erythrocytes into the extracellular fluid and can accumulate at concentrations of 40–80 mEq/L. Once the RBCs are returned to the in vivo environment, the potassium quickly reenters RBCs. However, during rapid blood transfusion transient hyperkalemia may result, particularly in patients with renal insufficiency. The transient hyperkalemia, particularly in the presence of hypocalemia, can lead to cardiac dysfunction and arrhythmias. In patients with renal insufficiency, potassium load can be minimized by the use of either freshly obtained blood or washed PRBCs. Hypokalemia can also result from massive blood transfusion due to reentry of potassium into RBCs and other cells during stress, alkalosis, or massive catecholamine release associated with large-volume blood loss. Therefore, potassium levels should be monitored routinely during large-volume blood transfusions.

**Acid–base abnormalities**

During the storage of whole blood an acidic environment develops due to the accumulation of lactate and citrate, with a pH in the range of 6.5–6.7. Rapid transfusion of this acidic fluid can contribute to the metabolic acidosis observed during massive blood transfusion. However, metabolic acidosis in this setting is more commonly due to relative tissue hypoxia and anaerobic metabolism owing to an imbalance of oxygen consumption and delivery. The anaerobic metabolism that occurs during states of hypovolemia and poor tissue perfusion results in lactic acidosis. Generally, administration of sodium bicarbonate is not indicated. The re-establishment of tissue perfusion and homeostasis is much more important in re-establishing acid–base balance. In contrast, many patients receiving massive blood transfusion will develop a metabolic alkalosis during the post-transfusion phase. This is due to the conversion of citrate to sodium bicarbonate by the liver and is an additional reason to avoid sodium bicarbonate administration during massive blood transfusion, except in cases of severe metabolic acidosis (base deficit >12).

**Altered oxygen transport**

During the storage of blood, red blood cell 2,3-diphosphoglycerate (DPG) levels decline. This results in a shift in the oxyhemoglobin dissociation curve to the left. Under these conditions, oxygen has a higher affinity for hemoglobin and oxygen release at the tissue level is theoretically diminished. In clinical practice, this alteration in oxygen affinity has not been shown to be functionally significant.

**Hypothermia**

Rapid infusion of large volumes of cold (4°C) blood can result in significant hypothermia, owing to the already impaired thermoregulatory mechanisms in burn patients. Potential complications of hypothermia include altered citrate metabolism, coagulopathy, and cardiac dysfunction. During large-volume blood transfusion in burn patients, fluids should be actively warmed with systems designed to effectively warm large volumes of rapidly transfused blood. In addition, the room temperature should be elevated and the patient’s extremities and head covered to minimize heat loss. Body temperature should be maintained at or above 37°C.

**Pulmonary complications**

Pulmonary edema is a potential complication of massive blood transfusion. This may result from volume overload and/or pulmonary capillary leak due to inflammation and microaggregates present in transfused blood. Some studies have indicated that the incidence of pulmonary edema is more related to the patient’s underlying injury than to blood transfusion per se. However, volume status should be monitored closely during large-volume blood transfusion so that volume overload may be avoided.

**Transfusion reactions**

Hemolytic transfusion reactions are a relatively rare but devastating complication of blood transfusion. The incidence of transfusion reactions is approximately 1 : 5000 units transfused, and fatal transfusion reactions occur at a rate of 1 : 100,000 units transfused. Most severe reactions result from ABO incompatibility. The most common cause of ABO-incompatible blood being transfused is clerical error. Therefore, most hospitals have developed policies that require multiple checks of the blood prior to transfusion. A list of blood types and associated circulating antibodies is shown in Table 14.11. Massive hemolytic transfusion reactions
result from destruction of transfused erythrocytes by circulating antibodies and complement. Many of the common signs and symptoms of transfusion reactions, such as chills, chest pain, and nausea, cannot be detected in the patient under anesthesia. The most commonly recognized signs of transfusion reaction in the anesthetized patient are fever, hypotension, hemoglobinuria, and coagulopathy. The cornerstones of treatment are to stop the transfusion, protect the kidneys with aggressive hydration and alkalinization of urine, and treat existing coagulopathy.

Delayed hemolytic transfusion reactions can occur in patients who have received prior blood transfusions and result from a secondary immune response with production of antibodies to blood antigens. This reaction can occur from 2 to 21 days after transfusion and should be suspected in patients with unexplained decreases in hematocrit during the postoperative period. Renal injury is less common than in acute hemolytic reactions, but adequate hydration and alkalinization of urine are usually indicated. Febrile reactions are common following blood transfusion and are generally due to contaminating leukocytes and leukocyte antigens present in transfused blood. Pure febrile reactions usually do not require termination of the transfusion, but the patient should be monitored closely to assure that a more severe transfusion reaction is not developing.

In recent years the most common cause of mortality associated with blood transfusion has been transfusion-related acute lung injury (TRALI). TRALI is defined as a new acute lung injury occurring within 6 hours of transfusion in a patient without additional risk factors for acute lung injury. The greatest risk of TRALI is associated with blood products that contain large amounts of plasma, namely FFP and platelets. As with ARDS, there are no specific therapies for TRALI and management is supportive. It is difficult to recognize TRALI in patients with major burns, as there are multiple etiologies for acute lung injury and ARDS in these patients. The risk of TRALI has been reduced by the institution of a blood bank policy of minimizing preparation of plasma-rich components (e.g. FFP and platelets) from donors who are known to be or are at risk of becoming alloimmunized against leukocytes.237

Infection

Infection is a major problem in burn patients owing to disruption of the cutaneous barrier and immunosuppression. Blood transfusion adds to the infection risk. Graves and colleagues showed a significant correlation between the number of blood transfusions and infectious complications in burn patients.238 The most common source of major infection from blood products is hepatitis. Hepatitis C is the most common offender, followed by hepatitis B. The incidence of hepatitis C is approximately 3 in 10,000 units transfused. The development of rigorous screening mechanisms has markedly reduced the incidence of HIV infection to 1 in 200,000–500,000 units transfused. Cytomegalovirus (CMV) has been identified in blood products and could cause clinically significant problems in immunocompromised burn patients. However, the incidence of clinically important CMV infection is low in burn patients.

### Postoperative care

Decisions regarding postoperative airway management and support of ventilation depend on several factors. Extubation is desirable as soon as it is indicated, but in burn patients, for a number of reasons, it often may be even more important not to extubate when it is not indicated. If the patient came to the operating room intubated, the indication for intubation must be determined. If the initial indication has resolved, the decision to extubate depends on perioperative events. Some patients with neck and facial burns are intubated to protect the airway from obstruction by edema. Air leaking around a deflated endotracheal tube cuff during positive-pressure ventilation is an encouraging sign that the airway may remain patent after extubation. The upper airway can also be examined by direct laryngoscopy or with an endoscope. In marginal cases the endotracheal tube can be removed while an exchanger is left in the trachea. Another technique is to extubate under direct vision with a bronchoscope with an endotracheal tube already loaded on the bronchoscope. Especially in small pediatric patients a common reason for post-extubation stridor and failed extubation is edematous and redundant mucosa over the arytenoid eminences that obstruct the glottic inlet during inspiration. This condition can be exacerbated by an endotracheal tube that is too large, excessive patient movement due to inadequate sedation and analgesia, reflux of acidic gastric contents, and mechanical irritation due to compression of the posterior laryngeal structures between the endotracheal tube and gastric tubes. These irritants can also cause laryngomalacia in pediatric patients. If laryngeal obstruction persists despite attention to all these details, a short course of steroids is
Summary

Anesthetic management of the burn patient presents numerous challenges. Anatomical distortions make airway management and vascular access difficult. Pathophysiological changes in cardiovascular function range from initial hypovolemia and impaired perfusion to a hyperdynamic and hypermetabolic state that develops after the resuscitative stage. These and other changes profoundly alter the response to anesthetic drugs. Effective anesthetic management will depend on knowledge of the continuum of pathophysiological changes, technical skills, proper planning, and availability of proper resources. A team approach is necessary, keeping in mind that perioperative management should be compatible with ICU management and goals. This requires close communication with other members of the burn care team and is one of the most important principles of effective anesthetic management of these challenging patients.

Further reading


References

There is no text in the image provided.


The skin bank
Richard J. Kagan, Robert Winter, Edward C. Robb

In Memoriam
This chapter is dedicated to the memory of Ronald T. Plessinger – friend, colleague, mentor, research scientist, and tissue donor.

History
The first skin autograft was described by Reverdin in 1871 and the use of allograft skin as a clinical method for wound coverage soon followed. In 1874, Thiersch published a report about a small series of patients on whom he had used partial-thickness skin grafts. This led to extensive trials of harvesting extremely thin grafts, leaving some of the surface epithelium behind to aid in donor site healing. Results from the use of these small thin grafts, known as ‘Thiersch grafts,’ ‘pinch grafts,’ ‘epidermis grafts,’ or ‘razor grafts’ were generally so unsatisfactory for resurfacing large areas that they were typically limited to the treatment of small ulcerated wounds. The first successful use of allogeneic skin for burn wound coverage was reported by Girdner in 1881. Five years later, Thiersch described the histologic anatomy of skin engraftment which popularized the clinical use of split-thickness skin grafts.

Radical advances in the treatment of burn wounds brought about three developments in skin graft recovery techniques. First, it was noted that the dermal layer was the most important part of a skin graft in producing a new, tough, resilient surface. Secondly, it was demonstrated that after removing a partial-thickness graft, the donor-site epithelium was regenerated from deep epithelial islands within the hair follicles and sebaceous glands; therefore, thicker grafts could be harvested and transferring the upper dermis would not interfere with donor-site healing. Finally, by allowing for the recovery of thicker grafts, the design instruments for their harvesting became more feasible. These thicker grafts were termed ‘split-thickness grafts,’ and resulted in the coverage of large areas of the body surface. These major advances in skin graft recovery techniques permitted increased flexibility in the treatment of burn wounds so that the Thiersch, or pinch graft, method and the use of pedicle flaps were rarely necessary for the treatment of cutaneous scar contractures. The use of split-thickness grafts permitted skin grafting to become a routine procedure.

Storage of human skin did not begin until the early 1900s, when Wentzsch3 reported his experience with the transplantation of human skin that had been refrigerated for 3–14 days; however, it was not until the 1930s that blood and tissue banking took their place in the clinical practice of medicine. The clinical utility of allograft skin in burn wound coverage was first described in 1938 when Bettman3 reported his success in the treatment of children with extensive full-thickness burn injuries. Webster and Matthews later described the successful healing of skin autografts stored for 3 weeks at 4–7°C; however, it was not until 1949, following the establishment of the United States Navy tissue bank, that modern day skin banking began.

The establishment of skin banking signaled the beginning of significant research related to the processing, preservation, and storage of human tissues. Baxter explored the histologic effects of freezing on human skin and discovered that the formation of ice crystals caused the destruction of skin architecture. This was followed in 1952 by the pioneering research of Billingham and Medawar who demonstrated that skin could be effectively cryopreserved using glycerol. Soon afterwards, Taylor was able to demonstrate that the addition of glycerol to storage solutions decreased ice crystal formation in frozen tissues. These advancements permitted Brown and Jackson to popularize the use of allogeneic human skin grafts as biologic dressings for extensive burns and denuded tissue. By 1966, Zaroff had reported the 10-year experience using allograft skin in the treatment of thermally injured patients at the Brooke Army Medical Center. In this report, he described the mechanical and physiologic advantages of allograft skin as a biologic dressing. In 1966, Cochrane reported the first successful use of frozen autologous skin grafts following controlled-rate freezing in 15% glycerol and rapid rewarming prior to implantation. This was followed by Morris report demonstrating the beneficial effects of using allogeneic skin in the treatment of infected ulcers and other contaminated wounds and Shuck et al’s report suggesting the potential use of allogeneic skin in the treatment of traumatic wounds based upon their Vietnam War experience. These increased uses of allograft skin led to further research into the beneficial effects of allograft skin on wound healing, including its association with a reduced incidence of bacterial infections and the stimulation of wound bed neovascularization.

Bondoc and Burke are credited with the establishment of the first functional skin bank in 1971. Their experience with allograft skin led to a report of successful burn wound excision and allografting with temporary immunosuppression in children with extensive injuries. Today, allograft skin remains an ideal temporary cover for extensive or excised...
cutaneous or soft tissue wounds, particularly when sufficient autograft skin is not available or when temporary wound coverage is desired.

**Clinical uses of allograft skin**

**Coverage of extensive full-thickness wounds**

The increasing use of allograft skin in specialized burn care centers has been one of the driving forces behind the growth and development of skin banks in the United States. The general indications for its use in wound management are listed in Box 15.1. Allograft skin possesses many of the ideal properties of biologic dressings and plays a major role in the surgical management of extensive wounds when autologous tissue may not be immediately available (Box 15.2). It reduces evaporative water loss and the exudation of protein-rich fluids, prevents wound desiccation, and suppresses microbial proliferation. Wound pain is lessened and is associated with better patient compliance with occupational and physical therapy. By restoring the physiologic barrier at the wound surface, the allografts reduce heat loss through the wound and mitigate the hypermetabolic response to burn injury. The frequent and unpredictable demand for allograft skin in specialized burn care centers has prompted the

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**Box 15.1 Indications for allograft skin use in wound management**

- Coverage of extensive wounds where autologous tissue is not available
- Coverage of widely meshed skin autografts
- Extensive partial-thickness burns
- Extensive epidermal slough
  - Stevens–Johnson syndrome
  - Toxic epidermal necrolysis
  - Staphylococcal scalded skin syndrome
- Testing the wound bed’s ability to accept autograft
- Template for the delayed application of keratinocytes.

**Box 15.2 Advantages of human allograft skin use**

- Reduce water, electrolyte, and protein loss
- Prevent desiccation of tissue
- Suppress bacterial proliferation
- Reduce wound pain
- Reduce energy requirements
- Promote epithelialization
- Prepare wounds for definitive closure
- Provide dermal template for epidermal grafts.

**Box 15.3 Advantages of fresh allograft skin**

- Rapidity and strength of adherence to the wound
- Control of microbial growth
- Rapidity of revascularization
- Reproducible clinical results

**Figure 15.1** Allograft skin usage at the Shriners Burns Hospital, Cincinnati, Ohio.
in particular, the increased use of fresh refrigerated allograft skin, in thermally-injured children treated at the Shriners Hospital for Children in Cincinnati, Ohio since 1998.

When fresh allograft is not available, cryopreserved skin is an excellent alternative for temporary wound coverage. Although frozen cryopreserved skin generally has less measurable viability than fresh skin, it is currently difficult to maintain continuous and ample stores of fresh skin beyond 14 days. It has therefore been standard skin banking practice to cryopreserve allograft skin within 7–10 days of recovery if it is not going to be utilized within the time period that viability can be maintained. Regardless of whether the allografts are fresh or cryopreserved, wide (mesh) expansion of allograft skin is rarely performed because reepithelialization of the interstices by allogeneic epidermis is uncommon. Figure 15.2 demonstrates the difference in appearance and vascularization of cryopreserved and fresh, refrigerated skin.

The emergence of Integra® dermal regeneration template for the treatment of excised burn wounds has been significant and in some burn centers has replaced or decreased the use of allograft skin in patients with extensive full-thickness burn injuries. Heimbach et al. reported the results of a randomized multicenter clinical trial comparing Integra® and other grafting materials. When the artificial dermis was compared to allograft, there was no difference in the ‘take’ rates; however, ‘take’ was not defined in the manuscript and it is unclear whether there were equivalent rates of adherence and/or vascularization. Furthermore, it is unclear if the allografts applied were fresh or cryopreserved, although it is most likely that the allografts were frozen as the refrigeration of allograft skin was not common skin banking practice at the time of the study. A subsequent retrospective study performed at our burn center and skin bank 10 years later indicated that fresh, refrigerated allograft had a better rate of engraftment than the dermal regeneration template.

**Coverage of widely meshed skin autografts**

Another use of allograft skin has been its application as an overlay on top of widely expanded, meshed autologous skin grafts (Fig. 15.3). This technique was originally described utilizing meshed allograft and provides immediate, as well as both temporary and permanent wound closure. For this reason, most burn surgeons who currently perform overlay allografting utilize non-meshed or non-expanded mesh allografts. This affords better protection of the underlying wound bed from desiccation and microbial contamination as this

**Figure 15.2** Appearance of cryopreserved and fresh, refrigerated allograft skin on postoperative day 5. Note (a) poor vascularization and epidermolysis in the cryopreserved skin compared to the (b) pink revascularized refrigerated allograft.

**Figure 15.3** Diagrammatic illustration of meshed allograft overlay technique (as described by Alexander et al.). The allograft is generally meshed 1.5:1 or 2:1 while the underlying autograft may be meshed 3:1 or greater. (Reproduced with permission from Alexander JW, MacMillan BG, Law E, et al. Treatment of severe burns with widely meshed skin autograft and widely meshed skin allograft overlay. J Trauma 1981; 21:433–438.)
tissue is potentially exposed by the interstices of the widely meshed autograft until autologous epithelialization is complete. While this technique may play a role in the management of massive excised full-thickness injuries, it should be used with discretion since many surgeons have expressed concern that the overlying allograft may induce an inflammatory rejection response that can retard the rate of reepithelialization of the underlying autografts. Some have therefore advocated the use of lyophilized allograft for this purpose as it is less viable and less antigenic.26

Healing of partial-thickness wounds

Frozen allograft skin is an excellent wound cover when vascularization is not desired. Because it is usually less viable than fresh skin, it functions more as a biologic dressing than as a temporary skin replacement. Its adherence to the underlying wound bed results in the relief of pain and the limitation of exudative and water losses, and reduces the need for frequent dressing changes. As the partial-thickness wound reepithelializes, the allograft slowly separates without disturbing the delicate underlying epithelium. Although this application is probably not cost-effective in the management of small second-degree burns or skin graft donor sites, it is often beneficial in the treatment of extensive partial-thickness burns where its ability to prevent desiccation and promote epithelialization may reduce hospital stay and/or the need for autografting. In addition, cryopreserved allograft is an excellent biologic dressing for the management of patients with extensive cutaneous wounds resulting from drug reactions or superficial skin disorders (e.g., toxic epidermal necrolysis, Stevens–Johnson syndrome, staphylococcal scalded skin syndrome). When used for the coverage of these superficial wounds, allograft skin should be applied prior to exposing the wound to topical antibiotics since the application of these agents results in decreased allograft adherence to the wound surface.

Testing for later acceptance of autograft

Both cryopreserved and fresh allografts have been used for the care of a variety of cutaneous and soft tissue wounds. In these instances, allograft is used to provide a temporary biologic cover and to help predict the likelihood of autologous graft-take later in the course of treatment. Allograft usage for this indication has been quite common in the past decade or so has also witnessed the development of an acellular allogeneic dermal matrix (AlloDerm®) as a template for the simultaneous application of thin split-thickness autografts.30 The potential advantage of the dermal template is reasoned to be the use of a thinner autologous skin graft resulting in more rapid donor site healing and reduced morbidity. A recently completed multicenter clinical trial demonstrated equivalent results of this technique with a standard split-thickness meshed autograft; however, autograft take rates were somewhat lower than that for controls and varied from center to center.31 In addition, the allogeneic dermal grafts measured only 36–116 cm² and were only evaluated up to 180 days post-grafting. AlloDerm® has also been used as a template for CEA; however, there have been only a few anecdotal reports related to this potential application.

Micrografting techniques

Chinese surgeons have proposed the use of micrografts using both autologous and allogeneic skin.32 This technique involves the mincing of autologous skin into pieces less than 1 mm in diameter. These micrografts are then used to seed the dermal surface of large sheets of allogeneic skin prior to transplantation onto the excised burn wound. As the autologous epidermal cells propagate on the wound surface, the allograft skin gradually separates in a manner similar to that observed with the overlay technique. This method, while resulting in an effective skin expansion ratio approaching 1:18, has been shown to be associated with severe wound contraction that is often worse than that noted following the application of meshed skin autografts.

Potential disadvantages of allograft use

Infection

Allograft skin has been reported to cause bacterial infection.33 It is therefore imperative that skin banks perform microbial cultures prior to releasing the tissue for transplantation. In fact, the American Association of Tissue Banks (AATB) Standards34 require that skin be discarded if pathogenic bacteria or fungi are present. This is particularly important given the immunocompromised status of the potential recipient and the potential for developing wound sepsis following such contamination.

There have also been reports of viral disease transmission by skin allografts. In 1987, Clarke reported what was thought to be the transmission of HIV-1 to a burn patient from an HIV-positive donor,35 however, the results of donor testing were not known prior to skin use. Moreover, the recipient, who had a number of risk factors for HIV, had not been
tested prior to receiving the allograft. To date, there have been no other reported cases of HIV or hepatitis transmission from skin allografts.

Kealey et al. have reported the transmission of cytomegalovirus (CMV) from cadaver skin allografts. Because nearly 23% of the CMV-negative patients seroconverted, they recommended the use of CMV-negative allograft skin for seronegative burn patients. Pressinger et al. reviewed 479 consecutive skin donors and found 63% of this predominantly adult donor pool to be CMV-positive. They reasoned that while tissue from seronegative donors would be ideal for use in seronegative patients, such a practice would significantly limit the availability of fresh allograft skin for most thermally-injured patients. In addition, while there is good evidence to support the transmission of CMV by allograft in burn patients, there is little evidence that CMV seroconversion is clinically significant or affects outcome in thermally-injured patients. Furthermore, Herndon and Rose reiterated that the benefits of using cadaver allograft skin for the treatment of burn patients clearly outweigh the small risks associated with CMV seroconversion. At present, most burn surgeons and skin banks recommend that the decision regarding the use of allograft skin from CMV-positive donors should be made by the burn/transplanting surgeon.

Rejection

While demonstrating many characteristics of an ideal wound covering, allograft skin contains Langerhans cells which express class II antigens on their surface. These cells reside in the epidermis of the skin and are ultimately rejected as the result of an immunologic rejection response. This typically results in an acute inflammatory reaction and can lead to wound infection. Vascularized allogeneic skin grafts typically remain intact on the wound of a burn patient for 2–3 weeks although there have been reports of allograft skin survival for up to 67 days due to the inherent immunosuppression of extensive burn injury. Recent improvements in immunonutrition, critical care management, and a more aggressive surgical approach to definitive wound closure, however, have made the persistence of allografts less predictable.

Efforts to prevent rejection have included methods that might reduce antigen expression by controlling the activity of the Langerhans cells in the allograft skin. Treatment of the allografts with ultraviolet light irradiation and incubation of the skin in glucocorticoids has been reported to result in a modest prolongation of allograft survival compared to nontreated skin; however, the utility of this methodology has not been substantiated. Other investigators have studied the effects of pharmacologic agents to induce immunosuppression in patients with major burn injuries. Initial clinical trials reported an improvement in both allograft and patient survival when children were treated with azathioprine and antithymocyte globulin; however, this regimen was associated with azathioprine-induced neutropenia and the clinical outcomes were not corroborated by others. More recently, the use of cyclosporin A was demonstrated to prolong skin allograft survival in patients with extensive full-thickness burns. In these studies, allograft rejection was generally observed within a few days of discontinuing treatment; however, there were instances where engraftment persisted after the completion of therapy. Further studies of these and newer immunosuppressive agents may be warranted.

The growth of skin banking

The widespread use of allograft skin in the management of patients with extensive burn, traumatic and soft tissue injuries has had a major impact on the number of skin banking facilities over the past two decades or so. Consequently, the majority of skin banks have been founded in close proximity to regional burn centers or within the burn center hospitals themselves. Skin banks must therefore maintain a close working relationship with regional burn centers not only to meet the specific needs of the burn surgeon but also to help generate community support for skin donation through combined educational outreach programs.

From 1969 to 1988, there was a steady growth in the number of skin banks; however, this number declined, reaching its nadir in 2002. Since that time, however, there has been a steady increase in the number of skin banking facilities to its current total of 54 AATB-accredited tissue banks that recover, process, store, and/or distribute skin for transplantation (Fig. 15.4). In 1983, DeClement and May estimated that as much as 32,000 square feet of skin might be needed in burn and wound care centers. This figure, however, was only a crude estimate and, over the past 10 years, there has been a substantial increase in the amount of skin recovered and distributed for transplantation within North America (Fig. 15.5), as indicated in the AATB's 2007 Annual Survey of both accredited and non-accredited tissue banks. In that calendar year, skin was recovered from 19,854 donors with nearly 30,000 square feet of skin distributed for human transplantation.

Role of the American Association of Tissue Banks

As skin banking facilities grew in number, it became apparent that policies and procedures required standardization. This was quite difficult initially as there was insufficient data to develop a consensus regarding standards of practice. As early as 1976, the AATB had begun to address this issue by the formation of a Skin Council. This provided a forum for the discussion of skin banking practices and was complemented by the activities of the American Burn Association's Skin Banking Special Interest Group. The Standards and Procedures Committees were created in 1977 and produced the first ‘Guidelines’ for tissue banking in 1979. The first Standards for Tissue Banking were published in 1984 and tissue-specific technical manuals (including skin) were developed in 1987. Since that time, the Standards have been modified and refined based upon consensus and, where available, supportive scientific research. In addition, shortly after the development and promulgation of its Standards for Tissue Banking, the AATB created an inspection and accreditation committee in 1982 and began conducting voluntary inspections in 1986. This program continues today and is important in ensuring that tissue banks adhere not only to AATB Standards but also the Food and Drug Administration (FDA) regulations governing all aspects of human tissue banking.
Technical aspects of skin banking

Donor screening

It is vitally important that complete and accurate medical information about the potential donor be obtained to ensure the safety of the tissue for transplantation. The AATB and the FDA require a comprehensive medical and social history of the donor. In this regard, the AATB developed a Donor Medical History and Behavioral Risk Assessment Questionnaire with the cooperation and assistance of other organ and tissue procurement organizations and the FDA. A thorough physical examination is also necessary to determine if the donor should be deferred for other medical reasons as well as to determine the quality of the skin and the technical feasibility of skin retrieval by evaluating the donor’s size and skin condition. Box 15.4 lists disease states which are commonly associated with deferral of a potential skin donor.
While it is also necessary for the tissue bank medical director to review the results of an autopsy (if one was performed), a review of over 2200 consecutive donors recovered by our tissue bank from January 1994 through May 1998 indicated that only 11 donors (0.5%) required discard as a result of the autopsy findings.34 Furthermore, a 10-month follow-up study of 264 donors recovered following the 1998 changes in the AATB Standards revealed that none of the donors required deferral based upon the autopsy findings alone.45

A panel of serologic screening tests for transmissible diseases is required.34 These include:
- Antibodies to human immunodeficiency virus, types 1 and 2 (anti-HIV-1 and anti-HIV-2)
- Nucleic acid amplification test (NAT) for HIV-1
- Hepatitis B surface antigen
- Total antibodies to hepatitis core antigen (including both IgG and IgM)
- Antibodies to hepatitis C virus (anti-HCV)
- Nucleic acid amplification test (NAT) for HCV
- Syphilis (a non-treponemal or treponemal-specific assay may be performed)

Test kits should be FDA-licensed, approved, or cleared for donor screening, and ideally, should be approved for cadaveric specimens. Barnett et al. reported their 2-year experience with cadaveric skin donor discards due to positive serologic tests. In that report, they noted that 61 of 813 donors (7.5%) required tissue discard due to positive serologic tests. A positive hepatitis B core antibody test accounted for 52.3% of the serology-based discards while hepatitis B surface antigen testing accounted for 18.1%, and hepatitis C, HIV-1/2, HTLV-1, and syphilis tests accounted for 14.3%, 4.9%, 4.9%, and 5.5%, respectively.46 This finding was substantiated by Plessinger et al. in their 5-year review of 1235 donors, of whom 93 (7.5%) were deferred based upon positive serologic tests.45

Skin recovery

Once donor screening is complete and proper consents have been obtained, the recovery team must arrange the time and location for skin removal in an appropriate facility (i.e. hospital morgue or operating room, medical examiner’s office, or the tissue bank). It is extremely important that the time of death and body storage conditions be accurately documented as these have a significant bearing upon skin viability and microbial contamination. Current AATB Standards require that skin retrieval begin within 24 h of asystole if the donor was cooled or refrigerated within 12 h of asystole or within 15 h of death if refrigeration did not occur within the prescribed time limits.34

In brief, the skin is removed under aseptic conditions. The areas from which the skin is taken are shaved of hair and cleansed with detergent solutions approved for use in operative procedures (i.e. povidone-iodine, chlorhexidine). The retrieval technician puts on a cap and mask, performs a surgical scrub, and dons a sterile gown and gloves while the circulating technician prepares tissue and transport containers. This is usually followed by a chlorhexidine prep and rinsing with 70% isopropyl alcohol, and allowing the skin surface to dry. The donor is then draped with sterile sheets and a blood sample is obtained by either a central venous or intraventricular puncture. Following this, a thin layer of sterile mineral oil (or other sterile lubricant) is applied to the surfaces from which skin is to be removed. Split-thickness skin grafts are then removed using a dermatome at a thickness of 0.012–0.018 inches. The width of the grafts generally should range from 3 to 4 inches but ideally should be determined by the preference of the transplanting surgeon(s). Skin retrieval sites are usually limited to the torso, hips, thighs, and upper calves. The amount of skin obtained may vary depending on body habitus, skin defects or lesions, and body geometry; however, an average of 4–6 square feet per donor is not unusual. After tissue is obtained from the posterior surfaces, the donor is turned to expose the anterior surface, reprepped, and draped prior to completing the retrieval process. The skin is then placed in tissue culture medium and maintained at 1–10°C during transport to the skin bank for processing.47

Skin processing

Processing environment

Skin should be processed under aseptic conditions in a bacteriologically and climate-controlled environment. While current AATB Standards mandate the processing of cardiovascular tissues in a class 100 laminar flow environment, no such requirement exists for human skin banking. In fact, a study performed by Plessinger et al. failed to demonstrate any statistically significant quantitative or qualitative difference in microbial growth whether the skin was processed and packaged in a class 100 laminar flow hood or a class 10,000 clean room.48

Microbiologic testing

After returning to the skin bank, the procurement team should obtain cultures for aerobic and anaerobic bacteria, yeast, and fungi. Incubation of allograft skin in antibiotics remains somewhat controversial since many of these antimicrobial agents are unable to effectively kill microorganisms at 4°C and there is the potential for exposing the recipient to resistant organisms. In addition, there has been little research to determine which antibiotics are effective against most skin contaminants yet nontoxic to the cellular components of the skin. It is therefore recommended that samples be obtained prior to exposure of the skin to antibiotics49 using a 1 cm² biopsy sample for each 10% of the body surface area from which the skin has been recovered.47,50 Testing should be conducted in accordance with the National Committee on Clinical Laboratory Standards and the skin should not be used for transplantation if it contains any of the following microorganisms:

- **Staphylococcus aureus**
- **Group A, beta-hemolytic Streptococci**
- **Enterococcus sp.**
- **Gram-negative bacilli**
- **Clostridium sp.**
- **Fungi (yeasts or molds).**

While AATB Standards require that microbiology culture results should not be reported before 7 days of incubation before releasing the tissues for transplantation, when fresh, non-cryopreserved allograft skin is to be exceptionally
released for transplantation within days of tissue recovery, the results of the microbial cultures are frequently unavailable. Plessinger et al. reviewed the results of the microbiologic skin cultures from 219 consecutive skin donors whose tissues were released for transplantation prior to the availability of culture results. While 14.3% of the cultures were positive for microbial growth, only 1.8% of the cultures identified organisms that required subsequent notification of the transplanting surgeon. In each of these instances, there were no adverse outcomes in any of the patients who received the skin transplants. These findings were substantiated by and Britton-Byrd et al., in their review of tissue donors whose skin was authorized for exceptional release after only 3 days of incubation. They reported three cases resulting in tissue recall due to positive microbiological cultures and concluded that 3-day culture results do not result in significant microbiologic contamination of allograft skin. Lastly, White et al. have suggested that cadaver allograft containing <10³ organisms/g of tissue can be safely used for temporary wound coverage. Despite the results of these studies, it is strongly recommended that the tissue bank communicate all available information regarding donor and tissue suitability to the transplanting surgeon so that he/she can adequately assess the potential risks and benefits for the recipient.

**Maintenance of viability**

Maintenance of cell viability and structural integrity are vital for the engraftment and neovascularization of allograft skin, yet there have been no studies that have quantified the degree of viability necessary to ensure allograft ‘take.’ Post-mortem time lapse appears to have the single greatest effect on skin viability as May demonstrated that the functional metabolic activity of the skin rapidly declined if the donor was not refrigerated within 18 h of death. The ideal nutrient tissue culture medium has also not yet been identified. Eagle’s MEM and RPMI-1640 continue to be generally accepted; however, Cuono demonstrated the potential benefits of University of Wisconsin (UW) solution. To date, it remains unclear which cryoprotectants offer the greatest preservation of cell viability and structural integrity. Glycerol (10–20%) and dimethylsulfoxide (10–15%) have been reported to maintain skin viability following incubation times ranging from 30 min to 2 h; however, the optimal concentrations of these cryoprotectants have not been identified nor have these agents been compared for efficacy. Lastly, factors such as age and gender do not appear to influence skin viability.

**Refrigeration**

‘Fresh’ allograft skin is the preferred biologic dressing for the temporary coverage of excised extensive full-thickness burn wounds due to its more rapid adherence and rapid vascularization. The skin is typically stored at 4°C in tissue culture medium with or without antibiotics. Refrigeration slows the metabolic rate of the viable cells and nutrient tissue culture medium supports cellular metabolic activity. The skin should be free-floating in an aseptic container with approximately 300 mL of medium per square foot of skin. Recent studies suggest that skin viability can be maintained for up to 2 weeks at 4°C if the nutrient medium is changed every 3 days. The major shortcoming of this storage method is the limited time that viability can be maintained.

It has been common practice to cryopreserve the skin within 5–7 days of refrigeration. This has been based on the work of May et al., who demonstrated that glucose metabolism declined at a rate of 10–15% each day during refrigerated storage. Recently, we have demonstrated the benefit of a two-layer storage method utilizing 95% oxygen-enriched perfluorocarbon (O₂PFC) combined with changing the nutrient medium every 3 days in an effort to prolong the viability of refrigerated skin. This method results in maintenance of skin viability for up to 41–63 days as well as maintenance of normal skin anatomy. Further research in allograft skin cryopreservation techniques will be essential in order to maintain an ample supply of viable fresh tissue for clinical use.

**Cryopreservation**

When skin is frozen for long-term storage, it is important that the methods utilized maintain cell viability and structural integrity. AATB Standards dictate that refrigerated skin should not be stored for longer than 14 days; however, if the skin is not to be used ‘fresh,’ it should be cryopreserved within 10 days of procurement if the nutrient medium is changed every 72 h. If the medium is not utilized or changed in this manner, AATB Standards dictate that the skin must be frozen within 96 h of recovery. The skin is generally incubated in cryoprotectant solution for 30 min at 4°C. Skin that is to be frozen should be folded with fine mesh gauze or bridal veil covering the dermal surface prior to placement in a flat packet to ensure uniformity of the cooling process. This is followed by slow-rate cooling at a rate of approximately −1°C per minute. Although computer-assisted, control-rate freezing is thought to be optimal, studies have demonstrated that cooling in a heat sink box at less than −2°C per minute is equally effective and does not compromise the metabolic activity of the skin. The skin is frozen to a temperature of −70 to −100°C prior to placement in either a mechanical freezer or liquid nitrogen. Skin stored in a mechanical freezer (−70 to −100°C) can be maintained for 3–6 months, whereas storage in liquid nitrogen (−150 to −196°C) has been shown to maintain viability for up to 10 years. Although this methodology has been reported to result in 85% retention of viability, there remains a need for research to determine the optimal technology for skin preservation.

**Lyophilization**

Skin can also be lyophilized by freeze drying or incubation in glycerol. This process has been reported to decrease biologic degradation and antigenicity; however, this also results in epidermal cell destruction and the loss of barrier function. Moreover, lyophilized allograft skin has poor adherence to the excised wound bed and is far less effective than ‘fresh’ skin or cryopreserved skin in controlling microbial growth. Its clinical use has been further limited by its high cost of production compared to conventional allograft.
Irradiation

Human allograft skin can also be treated with gamma irradiation to significantly reduce and possibly eliminate the risk for viral disease transmission. The preservative and sterilizing effects of this treatment allow it to be stored at room temperature for up to 2 years. One such product, Gamma-Graft®, has been successfully utilized to treat partial thickness burn injuries and skin graft donor sites; however it is not often utilized to provide temporary coverage for excised full-thickness burn wounds. Its most common indications, however, are for the management of chronic wounds/ulcers and exposed soft tissues.64

Transport

Refrigerated skin should be transported in tissue culture medium at wet ice temperatures (1–10°C) in an insulated container. Frozen allograft skin is transported on dry ice in an insulated container to prevent the skin temperature from rising to greater than −50°C. If the frozen skin is thawed at the tissue bank, it should be transported at wet ice temperatures.

Rewarming

Rewarming of frozen cryopreserved allograft skin must be performed in such a manner as to minimize cryodamage and preserve the structural integrity and viability of the skin. Early studies demonstrated that warming rates of 50–70°C/min resulted in 80–95% graft survival. Subsequent research has revealed that warming should be performed in 2–4 min or less at a temperature of 10–37°C (127–470°C/min). Rewarming in a microwave oven is not recommended due to uneven heating and excessive intracellular temperatures.

FDA regulation of human skin banking

Concerns related to the potential transmission of disease from tissue donors triggered concern within Congress and the US Food and Drug Administration (FDA), which resulted in the FDA’s publication of an interim rule for the regulation of human tissues intended for transplantation in 1993.65 The interim rule required that all donors have an accurately recorded medical and social history to assure freedom from risk factors for or clinical evidence of hepatitis B, hepatitis C, and HIV infection. From December 2003 to July 1997, the FDA developed its approach to the regulation of cellular and tissue-based products.66,67 From 1998 to 2007, FDA has published its proposed and final rules related to establishment registration,68,69 donor suitability determination,70–72 and good tissue practices.73 FDA has also published a number of guidance documents that are available on its website (http://www.fda.gov/BiologicsBloodVaccines/TissueTissueProducts/default.htm). Burn centers should only obtain allograft skin from tissue banks that comply with these regulations and preferably those facilities which are accredited by the AATB. This is required for burn center verification by the American Burn Association.

The future of skin banking

Skin banking must continue to evolve as engineered skin substitutes enter the clinical arena for the temporary and permanent coverage of partial- and full-thickness wounds. A number of skin substitutes have received FDA approval for use in the United States and have become part of the surgeon’s armamentarium. Although they are generally more costly than allograft skin, some of these products have been demonstrated to possess a number of attributes, including:

- non-antigenicity
- ready availability
- sterility
- the ability to provide a dermal equivalent as a template for the later application of ultrathin (0.006 inch) skin autografts.

Allograft skin has the potential to play a major role in permanent skin reconstruction after extensive thermal injury; however, this will require interactive research with the burn centers caring for these patients. This point is well illustrated by the studies of Rose74 and Naoum75 who demonstrated more rapid healing times and shorter hospital stays for children with extensive indeterminate depth scald burns when treated with early wound debridement and allografting compared to conventional topical antimicrobial therapy. Homografts acted as the best protection for damaged dermis, thus providing an environment for spontaneous epithelialization.

Skin banks must also identify ways of increasing cadaveric skin donation, ensuring recipient safety from potential disease transmission, and reducing procurement and processing costs while optimizing allograft viability. This will become increasingly difficult as it becomes necessary to perform additional and newer microbiological testing procedures to ensure recipient safety. To accomplish these goals, it may become necessary for skin banking operations to become regionalized. Such an undertaking could enhance tissue supplies and availability and result in increased clinical use by surgeons.

Allograft-based skin products

There is tremendous potential for human allograft-based skin products to be developed in the upcoming years; however, it will become increasingly important for skin banks to perform basic science and clinical research (in conjunction with burn and wound healing centers) to demonstrate the clinical indications and efficacy of allograft skin products in various clinical applications. Technological advances may include modifications to reduce immunogenicity and/or the potential for disease transmission. Newer processing techniques could sterilize the skin without injuring the viable cellular elements or the structural integrity of the tissue. In addition, with continued research, deepidermized allograft dermis could become:

- A source of growth factors and antimicrobial agents
- A permanent full-thickness wound cover seeded with the patient’s autologous keratinocytes and fibroblasts
- A bilayer membrane system for epidermal autografting, and/or
- A readily-available permanent wound cover pre-seeded with non-antigenic allogeneic keratinocytes, fibroblasts, and melanocytes.

Allogeneic skin provides a source of skin cells, including keratinocytes, fibroblasts, melanocytes, and endothelial cells. These cells may be grown into large populations $>1 \times 10^9$ cells, cryopreserved in liquid nitrogen, recovered into culture, and combined with degradable biopolymers to form cultured skin substitutes. Preclinical studies have shown organization of the epidermal keratinocytes to form a skin barrier, expression of pigment by melanocytes, and organization of endothelial cells into vascular analogs. Clinical studies have demonstrated improved healing of chronic wounds with allogeneic skin substitutes, and permanent closure of excised burns with cultured autologous grafts; however, cryopreservation of multilayered grafts with keratinized epithelium remains an unachieved goal in tissue transplantation. It therefore appears likely that the principles and practices of skin banking may contribute to eventual availability of unlimited supplies of skin grown in laboratories for the treatment of a wide variety of skin-loss conditions. Collaborative research efforts will be necessary to achieve these goals in a timely and cost-effective manner as skin banks find themselves competing and/or collaborating with the tissue bioengineering industry.

**Further reading**


This document represents the current requirements for the recovery, processing, storage, and distribution of human tissues for transplantation. The contributors (members of the Association’s Standards Committee) have many years of experience in tissue banking. Recent updates to this publication are available on the AATB website (www.aatb.org).


This landmark publication outlines the key aspects of maintaining a skin bank as well as the authors’ early experience with the use of cryopreserved allograft skin in burn care.


This publication by the Food and Drug Administration presents the scope of government regulation of tissue banking activities in the United States. Greater detail related to regulatory requirements (e.g. establishment registration, donor suitability, and good tissue practices) are provided in subsequent citations as well as FDA-issued guidance documents, all of which are available on the FDA website.


This publication provides important information regarding the use of antimicrobials used in the storage of skin grafts, their sensitivities to organisms that commonly colonize burn wounds, and the importance testing the effectiveness of these agents at the temperature to be utilized for skin storage.


This publication is one of a series published by the authors, describing various aspects of skin banking. This particular publication addresses the decay in viability of human skin allografts after skin recovery and the impact of storage media and conditions on the functional metabolic activity of allograft skin.
References

4. Girdner JH. Skin grafting with grafts taken from the dead subject. Medical Record. 1881;20:119-120.
5. Wentscher J. A further contribution about the survivability of human epidermal cells. Disch Z Chir. 1903;70:21-44.
48. Plessinger RT, Robb EC, Kagan RJ. Allograft skin cultures II: should allograft skin be processed in a class 10,000 or better environment? Proc Am Assoc Tissue Banks. 1997;52.
Introduction

The skin envelope evolved to maintain a tightly controlled internal environment. When severely damaged, preservation of this critical milieu becomes impossible, leading to major physiologic derangements. The central component of burn care is to expeditiously replace damaged areas of the skin to restore physiologic homeostasis. An increasingly effective group of temporary and permanent alternative wound coverings are available to the burn team to help in this regard. Although these membranes are becoming increasingly capable, the definitive replacement material of choice remains the patient’s own skin (Fig. 16.1).

Physiologic considerations

Skin is a truly amazing organ, rarely properly appreciated until it is missing. To date, all attempts to replace it, either temporarily or permanently, have been highly imperfect. As those with serious burns survive in greater numbers, the absence of effective skin replacements is increasingly a hindrance to progress in burn care.

Structure and function of the skin

Skin, the body's largest organ, is incredibly complex. Functionally there are two layers with a highly specialized and effective bonding mechanism. Numerous appendages traverse the skin and a rich and reactive capillary network provides nutrient flow while controlling temperature. The epidermis, consisting of the strata basale, spinosum, granulosum, and corneum, provides a vapor and bacterial barrier. The dermis provides strength and elasticity. The thin epidermal layer is constantly refreshing itself from its basal layer, with new keratinocytes undergoing terminal differentiation over approximately 4 weeks to anuclear keratin-filled cells that make up the stratum corneum, which provides much of the barrier function of the epidermis. The basal layer of the epidermis is firmly attached to the dermis by a complex bonding mechanism containing collagen types IV and VII. When this bond fails, serious morbidity results, as demonstrated by the disease processes of toxic epidermal necrolysis and epidermolysis bullosa (Fig. 16.2).

Consequences of loss of barrier function

Loss of the epidermal barrier has serious adverse physiologic effects. Direct and evaporative fluid losses are immediately seen. If wounds are large, this quickly leads to dehydration and shock. Protein losses are also substantial, leading to loss of colloid oncotic pressure and secondary edema. Microorganisms have unimpeded access to the microcirculation with resulting systemic infection. Deep tissues become desiccated with secondary cell death and progression of wound depth. Dry wounds will not epithelialize as readily. It is clearly important for the burn surgeon to have prompt biologic closure of wounds as an important early objective.

Although it is an imperfect replacement, autologous split-thickness skin is closest to being the ideal skin substitute (Box 16.1). Because of the paucity of autologous donor skin available in patients with massive burn injuries, both the short-term and long-term problems of skin loss must be solved by alternative wound closure materials. Alternative materials can be used for either wound coverage which will be temporary or for permanent wound closure materials. Allogenic (cadaver) skin has been the most widely used alternative wound closure material. However, there are other choices. This is an exciting and fast-moving area which may profoundly change the care of patients with serious burns. The objective of this chapter is to review the currently available alternative skin closure materials, both temporary and permanent.

Temporary skin substitutes

Temporary skin substitutes provide transient physiologic wound closure, thereby helping to control pain, absorb wound exudate, and prevent wound desiccation. They are clinically useful in several settings in burn care:

- as a dressing on donor sites to facilitate pain control and epithelialization from skin appendages;
- as a dressing on clean superficial wounds for the same reasons;
- to provide temporary physiologic closure of deep dermal and full-thickness wounds after excision while awaiting autografting or healing of underlying widely meshed autografts; and
- as a ‘test’ graft in questionable wound beds.
Their principal utility is provision of temporary physiologic closure of wounds, which implies protection from mechanical trauma, vapor transmission characteristics similar to skin, and a physical barrier to bacteria. These membranes create a moist wound environment with a low bacterial density.

**Human allograft**

Human allograft is generally used as a split-thickness graft after being procured from organ donors. When used in a viable fresh or cryopreserved state, it vascularizes and remains the ‘gold standard’ of temporary wound closures. It can be refrigerated for up to 7 days, but can be stored for extended periods when cryopreserved. It is also used in a nonviable state after preservation in glycerol or after lyophilization; however, most existing data describe results when it is used in a viable state. Viable split-thickness allograft provides durable biologic cover until it is rejected by the host, usually within 3 or 4 weeks. Prolongation of allograft survival, through the use of antirejection drugs, has been advocated, but is not generally practiced for fear that antirejection drugs will increase the risk of infection.

Human skin allografts are generally placed into frozen storage awaiting the return of numerous laboratory tests allowing one to safely exclude the possibility of viral disease transmission. When modern screening techniques are followed, the risk of viral disease transmission is exceedingly small. Allograft is also effectively used in combination with meshed autograft in patients with large burns, the interstices of the meshed graft being immediately closed by the overlying unexpanded allograft, possibly reducing metabolic stress and local wound inflammation (Fig. 16.3).

**Human amnion**

Human amniotic membrane is used in many parts of the world as a temporary dressing for clean superficial wounds such as partial-thickness burns, donor sites, and freshly excised burns awaiting donor site availability. Amniotic membrane is generally procured fresh and used after brief

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**Box 16.1 The perfect skin substitute – autologous split-thickness skin**

- Prevents water loss
- Barrier to bacteria
- Inexpensive
- Long shelf-life
- Can be applied in one operation
- Does not become hypertrophic
- Flexible
- Conforms to irregular wound surfaces
- Can be used ‘off the shelf’
- Does not require refrigeration
- Cannot transmit viral diseases
- Does not incite inflammatory response
- Durable
- Easy to secure
- Grows with a child.

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**Figure 16.1** The replacement material of choice remains the patient’s own (autologous) skin.

**Figure 16.2** The basal layer of the epidermis is firmly attached to the dermis by a complex bonding mechanism containing collagen types IV and VII. When this bond fails, serious morbidity results, as demonstrated here by the disease processes of dystrophic epidermolysis bullosa.

**Figure 16.3** Allograft is also effectively used in combination with meshed autograft in patients with large burns, the interstices of the meshed graft being immediately closed by the overlying unexpanded allograft, possibly reducing metabolic stress and local wound inflammation.
refrigerated storage.\textsuperscript{10,11} It can also be used in a nonviable state after preservation with glycerol. It has been treated with silver to facilitate control of bacterial overgrowth.\textsuperscript{12} Amnion does not vascularize but still can provide effective temporary wound closure.\textsuperscript{13} The principal concern with amnion is the difficulty in screening the material for viral diseases unless preservation methods can eliminate potential viral contamination. Without the ability to screen the material in this way, the risks of disease transmission must be balanced against the clinical need and the known characteristics of the donor.

**Allogenic epithelial sheets**

In many centers, particularly in Europe, sheets of allogenic and autogenous epithelium are used to dress partial-thickness wounds or to cover the interstices of meshed split-thickness autografts.\textsuperscript{14,15} These are generally applied as thin sheets placed on a gauze carrier for ease of handling. Cell suspensions in fibrin sealant have also been trailed. The concept is that the sheets will both prevent desiccation of underlying wounds and that the release of unknown growth-stimulating substances by the cells as they die will stimulate native wound healing.\textsuperscript{16} The concept is attractive, but controlled data are not available, particularly as regards any impact on long-term outcomes.

**Xenografts**

Although various animal skins have been used for many years to provide temporary coverage of wounds,\textsuperscript{17} only porcine xenograft is widely used today (Fig. 16.4). It has been used as primary temporary cover and as a scaffold for dermal regeneration efforts.\textsuperscript{18} Porcine xenograft is commonly distributed as a reconstituted product consisting of homogenized porcine dermis which is fashioned into sheets and meshed.\textsuperscript{19} Split-thickness porcine skin is also used fresh, after brief refrigeration, after cryopreservation, or after glycerol preservation. It effectively provides temporary coverage of clean wounds such as superficial second-degree burns and donor sites\textsuperscript{20} and has been used in patients with toxic epidermal necrolysis.\textsuperscript{1,21} Porcine xenograft has been combined with silver to suppress wound colonization.\textsuperscript{22,23} Porcine xenograft does not vascularize, but it will adhere to a clean superficial wound and can provide excellent pain control while the underlying wound heals.

**Synthetic membranes**

A number of semipermeable membrane dressings can provide a vapor and bacterial barrier and control pain while the underlying superficial wound or donor sites heal. These typically consist of a single semipermeable layer that provides a mechanical barrier to bacteria and has physiologic vapor transmission characteristics.\textsuperscript{24} Biobrane\textsuperscript{TM} (Dow-Hickham, Sugarland, TX) is a two-layer membrane constructed of an inner layer of nylon mesh that allows fibrovascular ingrowth and an outer layer of silastic that serves as a vapor and bacterial barrier.\textsuperscript{25} It is widely used to provide temporary closure of superficial burns and donor sites.\textsuperscript{26} All synthetic membranes are occlusive and can foster infection if placed over contaminated wounds, especially in the presence of necrotic tissue.\textsuperscript{27} Appropriate monitoring is essential to their proper use.

Hydrocolloid dressings are generally designed with a three-layer structure: a porous, gently adherent inner layer; a methyl cellulose absorbent middle layer; and a semipermeable outer layer. They foster a moist wound environment while absorbing exudate. A moist wound environment has been found to favor wound healing.\textsuperscript{28} A variety of pastes and powders made from hydrocolloid materials are also widely available. These can be applied to superficial or deeper chronic wounds to absorb wound exudate while maintaining a moist wound environment.

Hydrofiber mats absorb wound exudate and have been used as temporary wound membranes. When combined with ionic silver (Aquacel-Ag, ConvaTec, Chester, UK), additional antimicrobial activity is seen. This membrane has been used successfully in some burn programs as an adjunct in the management of partial-thickness burns and donor sites.\textsuperscript{29}

**Combined allogenic and synthetic membranes**

Epidermal growth factor, transforming growth factor-β, insulin-like growth factor (IGF), platelet-derived growth factors (PDGF), fibroblast growth factors, and other mediators play an important role in wound healing.\textsuperscript{30} To provide some of these substances topically to wounds, investigators have placed both viable and nonviable allogenic cell types into temporary wound dressings.\textsuperscript{31} These cells persist for no more than 14 days, but it is hoped that factors secreted by the allogeneic cells, or released upon their death and dissolution, will enhance wound healing. These membranes are generally regulated as both devices and biologics.
An allogeneic dermal–epidermal device that used a collagen lattice to culture both cell types was shown effective in an athymic mouse model and then went into clinical trials. Although it has not been demonstrated to have a clinical role in burn patients, the device is being explored for utility in chronic ulcers of the lower extremity. Dow-Hickam’s Biobrane has been used as a scaffold to support the growth of allogeneic fibroblasts. This device is now marketed as Transcyte (Smith and Nephew, La Jolla, CA) and has been successful in some burn programs as an adjunct to the management of dermal burns. Viral transfection can be employed to modify keratinocytes so that they overexpress PDGF, human growth hormone, IGF-1, and other growth factors, and it is possible that such cells might be employed as components of wound membranes over the next few years. Although stimulation of wound healing by topical application of mixed growth factors in this fashion is an intriguing concept, convincing evidence of the concept’s general validity is awaited.

### Permanent skin substitutes

A Swiss surgeon, Jaques Louis Reverdin, has been credited as performing the first skin autograft, in 1869, using a ‘pinch’ technique. Although procurement methods have evolved, the split-thickness autograft remains the standard of care. Although reliable in experienced hands, this definitive solution to the open wound has substantial drawbacks, particularly donor site morbidity and availability. Unfortunately, despite decades of work, currently available alternatives are even more imperfect. A reliable permanent skin substitute will revolutionize the care of patients with burns and other difficult wounds. The perfect substitute is described in Box 16.1, but has yet to be approached by any currently available device. However, there are a number of imperfect or partial-skin substitutes available at the present time that are valuable in particular clinical settings and may be the forerunners of this hypothetical ideal.

### Epidermal cells

For over 20 years it has been possible to culture vast numbers of epithelial cells from a small skin biopsy, and this has led to the widespread clinical use of cultured epithelial grafts to cover burn wounds. Epithelial cells are procured from a full-thickness skin biopsy, the cells being separated with trypsin. The resulting epithelial cell suspension is cultured in medium containing fetal calf serum, insulin, transferrin, hydrocortisone, epidermal growth factor, and cholera toxin, overlying a layer of murine fibroblasts that have been treated with a nonlethal dose of radiation that prevents them from multiplying. Colonies of epithelial cells expand into broad sheets of undifferentiated epithelial cells. These cells are separated from the culture vessel with trypsin and taken to secondary culture using the same techniques until confluent thin sheets of undifferentiated cells are obtained. The resulting sheets are removed from the dishes after treatment with dipase, which digests the proteins attaching the epithelial cells to the dish. The sheets of epithelial cells are attached to a petrolatum gauze carrier to ease handling.

When epithelial cultures were first used in patients with large burns it was hoped that they would provide the definitive answer to the clinical problem of the massive wound. With more frequent use of epithelial grafts, specific liabilities have become apparent including suboptimal engraftment rates and long-term durability. However, when faced with a very large wound and minimal donor sites, epithelial cell wound closure is a useful adjunct to split-thickness autograft, their liabilities and expense becoming more acceptable as wound size increases.

Many of the imperfections associated with epithelial cell wound closure may be attributed to the absence of a dermal element. Epithelial grafts are now commercially available. Application is generally most successful in wounds from which vascularized allograft has been removed. Despite scattered cases, application of cultured epithelial grafts onto synthetic dermal analogs has not been shown effective.

### Dermal analogs

Virtually all of the characteristics of normal skin that are not related to barrier function are provided by the dermis. These characteristics include flexibility, strength, heat dissipation and conservation, lubrication, and sensation. The first dermal substitute used clinically was ‘artificial skin’, also called Integra (Integra LifeSciences Corporation, Plainsboro, NJ, USA); it has been recently approved by the US Food and Drug Administration for use in life-threatening burns. This material was developed in the early 1980s by a biomaterials research team from the Massachusetts General Hospital and Massachusetts Institute of Technology. The research team, lead by surgeon John Burke from the Massachusetts General Hospital and materials scientist Ionnas Yannas from the Massachusetts Institute of Technology, had the goal of developing a wound covering that would both provide a temporary vapor and bacterial barrier while providing a scaffold for later dermal regeneration. The material was intended to be placed on excised burn wounds and is now approved for clinical use. Its use for other indications is being explored. The inner layer of this material is a 2 mm thick combination of fibers of collagen isolated from bovine tissue and the glycosaminoglycan chondroitin-6-sulfate. This 2 mm thick inner layer has a 70–200 µm pore size that allows fibrovascular ingrowth, after which it is designed to slowly biodegrade. To manufacture the device, glycosaminoglycan and collagen fibers are precipitated and then freeze-dried and cross-linked by glutaraldehyde. The outer layer of the membrane is 0.009-inch (0.23 mm) thick polysiloxane polymer with vapor transmission characteristics similar to normal epithelium. This membrane is intended to be placed on freshly excised full-thickness burns and the outer silicone membrane replaced with an ultra-thin epidermal autograft 2–3 weeks later (Fig. 16.5). Clinical reports in patients with large burns have been generally favorable, although submembrane infection must be watched for. Integra has also been found to be useful in selected burn reconstruction operations.

Another currently available device designed as a dermal replacement is cryopreserved allogenic dermis. This material is intended to be combined with a thin epithelial autograft at the time of initial wound closure. It is marketed as AlloDerm (LifeCell Corporation, The Woodlands, TX, USA).

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**Box 16.1**

**It is generally most successful in wounds from vascularized allograft has been removed.**
wounds closed initially with vascularized allograft. Once allograft has vascularized, the allogeneic epithelial cells are removed by dermabrasion or tangential excision, purposefully leaving behind a vascularized but theoretically non-antigenic allogenic dermal layer. The method has been favorably reported, but has not been universally adopted. Perhaps the epithelial excision either leaves behind nests of antigenic epithelial cells if too superficial or removes the epidermal–dermal attachment structures if too deep.

Composite substitutes

Ideally, a skin replacement technique would provide immediate replacement of both dermal and epidermal layers. Combining epithelial cells with a dermal analog in the laboratory seems logical. A completely biologic composite skin substitute, culturing human fibroblasts in a collagen–glycosaminoglycan membrane, and then growing keratinocytes upon this, has been under development for some years. This composite membrane has been successful in both a nude mouse model and in initial clinical series. There is even potential to control pigment expression. This exciting technology continues to be refined in laboratory and clinical investigations and may have a major impact on the field. A similar project, in which autogenic epithelial cells are cultured onto allogenic dermis, shows some promise as well. It remains to be seen if either technique will lead to a reliable and durable permanent skin replacement.

The future of alternative wound coverings

We are likely to see significant improvements in skin substitute technologies, both temporary and permanent, over the next few years. In temporary wound coverings, not only are improved synthetics and improved skin banking techniques probable but we may see temporary dressings containing growth factor-secreting allogenic tissues that stimulate native wound healing. Genetic modification of keratinocytes is now possible. These cells have been engineered to overexpress PDGF, human growth hormone, IGF-1, and other growth factors. It is likely that they will be trialled in animal models and human wounds over the next few years. If they prove efficacious, their application to healing burns and donor sites, through incorporation in temporary dressings, may become possible. It might be further possible to combine autogenous cells with modified allogenic cells such that the resulting chimeric graft benefits from transient overexpression of critical growth factors during the early stages of engraftment.

As we become increasingly successful at salvaging the lives of those with large burns, our need for a durable and reliable permanent skin substitute becomes increasingly acute. This material is needed both to truncate the acute illness through earlier wound closure and to facilitate timely and effective burn reconstruction. Just what form that substitute will take is not clear. Most likely, it would seem to be an in vitro combination of autologous keratinocytes and possibly fibroblasts and/or endothelial cells with a dermal analog. Whatever form the successful replacement takes, it is certain to profoundly impact the field of burn care.
Further reading


A review of the practical use of AlleDerm in burn reconstruction, demonstrating techniques and efficacy.


A review of the concept of growth factor delivery in wounds, including use of membranes as delivery vehicles.


Access the complete reference list online at http://www.expertconsult.com
References


Introduction

The loss of the cutaneous barrier creates an important problem for the injured organism. The skin barrier is damaged, homeostasis altered, and part, if not all, of the immunological function of the skin is lost. Following a burn injury many issues must be addressed. Trauma guidelines, resuscitation, maintenance of the internal milieu by critical care techniques, and protection of the victim against infection, among others, are therapies directed towards a common goal: survival and complete functional rehabilitation.

However, the main focus of the reconstructive surgeon is the complete and permanent closure of the burn wound. Two main factors are involved in this scenario. A clean, vital, graftable wound bed has to be obtained in order to be ready for the engraftment and survival of any skin coverage that has been selected. Following this process, a permanent wound cover has to be obtained that protects the recipient, provides all skin properties and functions, and allows for complete recovery and rehabilitation of the victim.

The treatment of severe burn sequelae follows similar sound surgical principles. Alternative wound coverings are reserved for those situations encountered in burn reconstruction as well as in acute setting: either a paucity of skin donor site availability or a failure of previous surgeries to provide good, pliable skin coverage.

The ideal wound coverage

A permanent, durable, nature-like wound coverage is the gold standard for any disease process that requires the replacement of damaged and destroyed skin. The provision of large and infinite quantities of such wound coverage is also desirable. The wound cover that most resembles normal skin is autologous skin graft. However, even though it is durable and permanent, it relies on wound healing cascades to produce the desired vitality, vascularization and maturation. This is accomplished by connective tissue deposition, leaving permanent sequelae ranging from minimal scarring to florid hypertrophic scarring and keloid formation.1

Current attempts to obtain a better quality of skin graft and a more profound control of scar formation between the interface of the wound bed and the transplanted autologous skin include single-layer dermal substitutes: Integra single-layer dermal template (Integra life Sciences) and Matriderm (Dr Sawelacs Skin). These are similar but differ in their composition and width. Capillary ingrowth in these templates precedes final ingrowth into super-thin applied skin grafts (18/1000 inch); therefore careful wound manipulation is necessary. These templates are applied on the wound bed with similar goals as delineated for Integra double-layer. Optimization of graft take can be obtained by using a negative-pressure dressing, but in general, guidelines for wound care as applied in all burn centers worldwide render excellent graft take. The use of both dermal templates follows the same philosophy as that involved in the application of Alloderm and super-thin skin grafts. Future clinical research focusing on similar biologic dermal templates, such as glycerol-preserved dermis, Strattice and Veritas, will determine their role in this type of surgery.

Alternative wound covers

This broad definition refers to any materials used as an alternative to the gold standard: the autologous skin graft. Ideally, they should carry the same characteristics (durability, permanency, good vascularization, defense against infection, and provision of excellent quality of life). Their relevant role in the improvement of the quality of wound cover in major burns and other large wounds should not be underestimated, although their final outcomes are still far from perfect. The emergence in the clinical scenario of alternative wound coverage allowed swift burn reconstruction in either the acute or the rehabilitation phase. The possibility to obtain large amounts of tissue (dermal templates, etc.) off the shelf has made possible immediate coverage of large open wounds in one operation. It has allowed the development of controlled surgical protocols for critical burns and for the resection of large areas of hypertrophic scar.

The health industry is constantly providing burn surgeons with new alternative wound covers (either temporary or...
surgery, the purpose of the technique is to remove all damaged and scarred tissue and to replace it with an even, flat surface that will accommodate a laminar thin split-thickness skin autograft.

The preparation of the wound bed and the application of the dermal regeneration template are similar in acute and reconstructive surgeries.

Preparation of the wound bed

Either in the acute setting or in the reconstructive phase, alternative wound covers provide surgeons with an indefinite source of material. Surgery can then be performed disregarding the most important limiting factor: the availability of donor sites. Planning of surgery can be organized focusing on the best alternative for the patient, such as complete removal of necrotic tissue or total scar resection. These two scenarios are the real indication for the use of this costly technology.

Patients who have suffered major burns with extensive zones of full-thickness burn are the best candidates for temporary and permanent wound covers. The goal is to extirpate all necrotic tissue at once while preserving the homeostasis. Leaving behind large open wounds challenges patient survival and triggers the development of multiple organ dysfunction. Closure of the wound is mandatory and maintaining an infection free environment necessary. The purpose is to obtain a clean surface, free of any necrotic tissue, that can accept coverage by skin substitutes without postoperative hematoma or infection.

Patients who survive burn injuries frequently develop hypertrophic scar formation. Complete resection of these areas and immediate coverage with dermal templates is now possible. This is one of the most relevant recent changes in burn reconstruction. Similar to their use in acute burn surgery, the purpose of the technique is to remove all damaged and scarred tissue and to replace it with an even, flat surface that will accommodate a laminar thin split-thickness skin autograft.

The preparation of the wound bed and the application of the dermal regeneration template are similar in acute and reconstructive surgeries.

Table 17.1 Alternative wound covers used in the past, present, and future developments

<table>
<thead>
<tr>
<th>1. TEMPORARY WOUND COVERS</th>
</tr>
</thead>
<tbody>
<tr>
<td>– Human allograft</td>
</tr>
<tr>
<td>– Pig skin xenograft</td>
</tr>
<tr>
<td>– Human amnion</td>
</tr>
<tr>
<td>– Oasis (small intestine submucosa xenograft)</td>
</tr>
<tr>
<td>– Biobrane (outer silicone inner nylon mesh with added collagen)</td>
</tr>
<tr>
<td>– Transcyte (outer silicone inner nylon mesh with neonatal allofibroblasts)</td>
</tr>
<tr>
<td>– Supratel (absorbable microporous membrane)</td>
</tr>
<tr>
<td>– Unite (equine pericardium)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2. PERMANENT WOUND COVERS</th>
</tr>
</thead>
<tbody>
<tr>
<td>– Apligraf (allogenic composite, human neonatal keratinocytes and fibroblasts)</td>
</tr>
<tr>
<td>– OrCel (collagen sponge seeded with human neonatal keratinocytes and fibroblasts)</td>
</tr>
<tr>
<td>– Epigel (cultured autologous keratinocytes)</td>
</tr>
<tr>
<td>– AlloDerm (allogenic dermis)</td>
</tr>
<tr>
<td>– Matriderm (synthetic dermal template)</td>
</tr>
<tr>
<td>– Integra (synthetic dermal template)</td>
</tr>
<tr>
<td>– Renoskin (synthetic dermal template)</td>
</tr>
</tbody>
</table>

Figure 17.1 Hypertrophic scars and burn scar contractures are indications for scar resection and resurfacing with alternative wound covers.

Figure 17.2 Total resection of the scar contracture leaves a clean, even, graftable wound bed.

permanent). Some remain in the past, others are current standard practice, and a few require prospective testing. A list of the most relevant alternative wound covers is given in Table 17.1. It is mandatory to develop programs of clinical prospective research to produce evidence-based data in order to make a rational and cost-effective way of use. For an extensive and more in-depth analysis of these covers the reader is referred to Chapter 16.

The role of alternative wound coverage in large wounds

Either in the acute setting or in the reconstructive phase, alternative wound covers provide surgeons with an indefinite source of material. Surgery can then be performed disregarding the most important limiting factor: the availability of donor sites. Planning of surgery can be organized focusing on the best alternative for the patient, such as complete removal of necrotic tissue or total scar resection. These two scenarios are the real indication for the use of this costly technology.

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Patients who survive burn injuries frequently develop hypertrophic scar formation. Complete resection of these areas and immediate coverage with dermal templates is now possible. This is one of the most relevant recent changes in burn reconstruction. Similar to their use in acute burn surgery, the purpose of the technique is to remove all damaged and scarred tissue and to replace it with an even, flat surface that will accommodate a laminar thin split-thickness skin autograft.

The preparation of the wound bed and the application of the dermal regeneration template are similar in acute and reconstructive surgeries.
Wound coverage

During the preoperative visit all areas that need burn wound excision or burn scar resurfacing are delineated and an inventory of potential donor sites is developed. A decision is made on whether a temporary, permanent single or bilaminar template will be used. A complete informed consent for the treatment proposed, which includes alternatives to the technique and the potential hazards of the product, should be obtained.

Indications for single-layer templates include small, highly functional areas acutely or in burn reconstruction and those patients that will benefit from a single-step operation (limit of ages, etc.). All other wounds are best treated with a bilaminar dermal substitute (Fig. 17.3).

Temporary skin substitutes may serve as temporary cover until good haemostasis is achieved, improving the survival of the dermal substitute. Furthermore, their use is helpful in determining the vitality of the wound bed by allowing a second look 48 hours after the initial surgery. Any small areas of dubious or clear necrosis are then re-excised and the skin substitute then applied. Small areas of necrosis are foci for infection and subsequent dislodgement of the substitute; when not controlled, the whole area becomes infected and debridement is necessary, challenging the final outcome of the intervention. Other temporary substitutes serve as non-permanent covers that allow the wound to regenerate, either by absorption or by spontaneous peeling.

**Biological actions of alternative wound coverage**

Skin substitutes improve the quality of the closed burn wound, control infection and pain, and avoid poor-quality scars. Alternative wound covers allow early and complete closure of wounds, even in major burns, which helps to reduce the metabolic rate, systemic inflammatory response, muscle wasting, infections, and overall mortality. Effective pain control is achieved with both temporary and permanent wound covers. The biological activity of skin equivalents improves the healing process, reduces scarring and disorganized collagen deposition, and enhances clone differentiation of parenchymal cells.

**Summary**

Dermal templates have become an alternative for those patients that present with large open wounds. They provide a durable, permanent, and reliable source of coverage material that is readily available off the shelf. A sound surgical protocol is necessary to produce reproducible results. The application of these alternative wound covers in burn reconstruction follows similar principles, and, as in the acute setting, they have revolutionized reconstruction.

**Further reading**


Access the complete reference list online at [http://www.expertconsult.com](http://www.expertconsult.com)
References


The pathophysiology of inhalation injury
Daniel L. Traber, David N. Herndon, Perenlei Enkhbaatar, Marc O. Maybauer, Dirk M. Maybauer

Introduction and epidemiology

It has been over two decades since the authors published their first manuscript on inhalation injury.1 In the review article published the next year, it was reported that inhalation injury was a major factor responsible for mortality in thermally injured patients.2 Inhalation injury is still a major problem.3 Although sepsis may be the major cause of death among burned children, two-thirds of the patients who have died in our own hospital have had an inhalation injury.4 Smoke inhalation causes 5000–10,000 deaths annually in the United States and more than 23,000 injuries, including approximately 5000 firefighter injuries.5 In fact, the United States has one of the highest fire death rates among industrialized countries. Inhalation injury is a serious medical problem. More than 30% of thermally injured patients admitted to burn centers in the United States have a concomitant smoke inhalation injury.6 Similar percentages of fire victims who have sustained smoke inhalation appear in several other countries.7–10 Despite effective management of fluid resuscitation, early surgical excision of burned tissue and improved ventilation techniques, the mortality rate of patients who have combined burn and smoke inhalation injury is still high.6,11–13 In patients with combined injury, the lung is a critical organ and the progressive respiratory failure associated with pulmonary edema is a pivotal determinant of mortality.14–16 Albeit not as lethal, smoke inhalation alone is a serious problem. It is estimated by the World Health Organization that over one billion people develop airway and pulmonary inflammation as a result of inhaling smoke from indoor cooking fires, forest fires and burning of crops (Fig. 18.1).17,18

The inhalation of toxic materials has been of interest for a number of years, especially as the result of their use in gas warfare. In the 1940s two very large fires focused interest on the inhalation of smoke in fire victims. The first was a fire at a nightclub in Boston called the Cocoanut Grove, where a large number of people were trapped in a burning building and consequently sustained severe inhalation injury.19,20 It is interesting that in recent times a similar fire occurred in a nightclub near Boston in Rhode Island.21 The second disaster occurred in 1947 in Texas City, Texas.22 Here, a ship loaded with ammonium nitrate fertilizer exploded in the harbor and set off a chain of explosions and fires among some 50 refineries and chemical plants, resulting in over 2000 hospital admissions of patients with burn injury, many of whom who had simultaneously inhaled smoke, as well as victims with smoke inhalation alone. In many ways the burn victims of the 9/11 disaster at the Pentagon were similar to these individuals, as the burns and inhalation involved combustion of petroleum products. Among the 790 injured survivors of the terrorist attack on the World Trade Center in New York on 11 September 2001, 49% suffered from inhalation injury. The situation was the same as the attack on the Pentagon, and in both situations inhalation injury was also seen in some patients who were not burned.21–23 Disasters like those in Boston and Texas led to the establishment of centers for the care of burn victims and to research into the pathophysiology of burn injury.

Inhalation injury can be classified as 1) upper airway injury, 2) lower airway injury, 3) pulmonary parenchyma injury, and 4) systemic toxicity. The extent of inhalation damage depends on the fire environment: the ignition source, temperature, concentration, and solubility of the toxic gases generated. For instance, thermal and chemical compounds usually cause upper airway injury. The water-soluble materials such as acrolein and the other aldehydes damage the proximal airways and set off reactions that are inflammatory to the bronchi and parenchyma, whereas agents with lower water solubility, such as chlorine, phosgene, and nitrogen oxide, nitrogen dioxide or N₂O₃ or even N₂O₄, are more likely to cause insidious injury.24

Pathophysiology

Injury to the oropharynx

Much of the pathophysiology that occurs with inhalation injury is related to edema formation in the oropharynx, bronchial areas and parenchyma, and results from an increased transvascular fluid flux from these respective vascular beds. Before a discussion of the changes that occur in
neutrophils then amplify the release of oxygen radicals, proteases and other materials into burned areas (Fig. 18.2). The massive edema occurring in the soft tissue of the oropharynx following burns involves most of the variables in the Starling equation. There is a large increase in microvascular hydrostatic pressure, a decrease in interstitial hydrostatic pressure, a fall in the reflection coefficient, and an increase in interstitial oncotic pressure. The usual treatment for burn resuscitation calls for the administration of large amounts of crystalloid solutions, which has the effect of reducing the plasma oncotic pressure. This reduction not only affects the oncotic pressure gradient in the microcirculation but also has been reported to increase the filtration coefficient. The result of this almost complete breakdown in control of the microvascular function and the insult of fluid administration is massive edema. This is probably nowhere more apparent than in soft tissues of the face and oropharynx. The danger to the patient is extreme. The edema may obstruct the airway, not only making it laborious or impossible to breathe but also making it difficult for the anesthesiologist to intubate the patient (Fig. 18.3A). To avoid this problem, many units prophylactically perform tracheostomies on those patients who have evidence of thermal injury to the upper airway on admission. However, tracheostomy itself may present problems. The tube may further damage injured areas, especially the larynx. It may be time to reconsider some of these practices. Perhaps some consideration should be given to fluid resuscitation with colloids, which can prevent some of this soft tissue edema and reduce the volume of fluids required for resuscitation.

Injury to the tracheobronchial area

With rare exceptions such as inhalation of steam, the injury to the airway is usually due to the chemicals in smoke. The heat capacity of air is low and the bronchial circulation very
The pathophysiology of inhalation injury

Efficient in warming or cooling the airway gases, so that most gases are at body temperature as they pass the glottis. Flames must be in almost direct contact with the airway to induce thermal injury. The chemicals in smoke are dependent on the materials that are being burned; however, for the most part the host response is similar. In most instances biological materials such as cotton fabric, wood, grass, or products of these such as cattle feces (commonly used as fuel in Third World countries) are the fuel for the fire. These contain caustic materials such as ROS and RNS, organic acids and aldehydes. These chemicals interact with the airway to induce an initial response to trigger an inflammatory response.

Many of the studies that have been reported relative to the bronchial circulation following smoke inhalation injury have been performed in sheep, because these animals have a single bronchial artery and have a single lymphatic draining the lung that allows the measure of pulmonary transvascular fluid flux. There was a 10-fold increase in bronchial blood flow within 20 minutes of smoke inhalation. These same animals demonstrate a sixfold increase in pulmonary transvascular fluid flux and a fall in $\frac{\text{PaO}_2}{\text{FiO}_2} \leq 200$, but these were delayed to 24 hours. Similar findings have been reported in patients with smoke inhalation alone or the combination of a large cutaneous thermal injury and smoke inhalation.

Hyperemia of the airway is such a consistent finding in smoke inhalation that it is used to diagnose the injury. Other variables that are used include injury in an enclosed space, singed nasal hair and soot in sputum. However, these latter injuries may be present but the subject may still not develop the signs of low Pa and pulmonary edema characteristic of inhalation injury. Airway inflammation plays a major role in the overall response to inhalation injury (Fig. 18.3B and 3C).

As we have noted, there is a large sustained increase in blood flow in the airway following smoke inhalation. These changes in blood flow were associated with increased bronchial microvascular permeability to protein and small particles and pressure. Simultaneously with the changes in the function of the bronchial microvasculature, there is a loss or shedding of the bronchial columnar epithelium.

Figure 18.3 Facial and airway injury in the patient after burn and smoke inhalation. (a) A facial burn often associated with thermal injury to the upper airway. (b) Hyperemia of airway epithelium. (c) Formation of airway obstructive cast. (A, from Cancio LC. Airway management and smoke inhalation injury in the burn patient. Clin Plast Surg. 2009; 36(4): 555–67.)
These changes result in a perfuse transudate with a protein content similar to an ultrafiltrate of the plasma. There are also copious secretions from the goblet cells. Early in the response these secretions are fluid and form a foamy material in the airway that many have mistaken for severe pulmonary edema in humans. After several hours this transudate/exudate solidifies or clots, forming obstructive material in the airways (Table 18.1). These obstructive materials formed in the upper airway may appear in the lower airway and alveoli. This is problematic in several respects. In some rare instances of severe airway injury these materials can induce total obstruction (Fig. 18.4). Occlusion of some of the bronchi or bronchioles in the setting of high production of NO can lead to a loss of hypoxic pulmonary vasoconstriction and hence increased shunt fraction. Loss of hypoxic pulmonary vasoconstriction with inhalation injury has been reported. Lastly, if single bronchi are occluded while the patient is on a volume-limited ventilator there could be overstretched, and barotrauma to the alveoli of the non-occluded portion of the lung can occur.

<table>
<thead>
<tr>
<th>Injury</th>
<th>Bronchii</th>
<th>Bronchiole</th>
<th>Terminal Bronchiole</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uninjured (n = 5)</td>
<td>2.7 ± 2.4%</td>
<td>1.6 ± 0.9%</td>
<td>0.0 ± 0.0%</td>
</tr>
<tr>
<td>Burn alone (n = 6)</td>
<td>4.4 ± 3.5%</td>
<td>2.5 ± 1.5%</td>
<td>0.4 ± 0.1%</td>
</tr>
<tr>
<td>Smoke alone (n = 5)</td>
<td>18.1 ± 10.1%</td>
<td>8.1 ± 3.0%</td>
<td>0.3 ± 0.4%</td>
</tr>
<tr>
<td>Smoke + Burn (n = 7)</td>
<td>29.3 ± 15.1%</td>
<td>11.5 ± 6.7%</td>
<td>1.2 ± 1.9%</td>
</tr>
</tbody>
</table>

Data are presented as mean percent ± SD (n number of animals in each group). *Significantly different from uninjured animals’ means, Wilcoxon rank sum test, p < 0.05. †Significantly different from burn injury, Wilcoxon rank sum test, p < 0.05.


Figure 18.4 Airway obstructive cast. (A) Macroscopic pictures of airway obstructive cast in sheep 48 hours after burn and smoke inhalation injury. (B) Macroscopic picture of airway cast taken from patient with burn and smoke inhalation injury by bronchoscope. (C and D) Microscopic pictures of bronchi in sheep and bronchioles in a patient, totally blocked by obstructive cast after burn and smoke inhalation injury. (A & B from Nakae H, Tanaka H, Inaba H. Failure to clear casts and secretions following inhalation injury can be dangerous: report of a case. Burns. 2001; 27(2): 189–91.)
The airway is richly innervated with vasomotor and sensory nerve endings.66 It is also known that these fibers release neuropeptides that can produce inflammatory responses.67 Neuroinflammation is responsible for pathophysiology in a number of clinical situations, including tissue injury induced by chemicals.68,69 Lange et al. reported that antagonists to substance P and calcitonin gene-related peptide had a marked effect on the response when administered to sheep and mice that were injured with both burn and smoke inhalation.70,71 In the ovine model the combination of burn and smoke inhalation injury caused a 10-fold increase in pulmonary transvascular fluid flux and a reduction of PaO2/FiO2 to ≤200. These changes were reversed by neuropeptide receptor blocking agents.70 Neuropeptide release can cause activation of nitric oxide synthase, have chemokine activity, and alter microvascular permeability.72 The resultant activities lead to the formation of reactive oxygen and nitrogen species.73 Some of the latter are very potent oxidants that can damage DNA.72 Damage to DNA causes the activation of a repair enzyme poly-(ADP-ribose) polymerase (PARP).74 This enzyme depletes the cell of high-energy phosphates and causes the activation of nuclear factor-κB (NF-κB).75,76 Activation of the nuclear factor causes the upregulation of iNOS and IL-8, thereby accelerating the production of reactive nitrogen and oxygen species.77 NO and 3-nitrotyrosine, an index of reactive nitrogen species, iNOS mRNA and protein, have been reported to be in the airway after smoke inhalation.78,79 Compounds that catalyze the breakdown of peroxynitrite reduce the response to smoke inhalation. Poly-(ADP ribose) (PAR), the product of the constitutive enzyme poly-(ADP ribose) polymerase, has been identified in airway tissues following smoke inhalation.77,80 Inhibition of PARP prevented the formation of PAR, the upregulation of NF-κB, and the formation of 3-nitrotyrosine.79 Similarly, Lange et al. have reported that compounds that inhibit peroxynitrite by catalyzing its rapid breakdown likewise prevented the formation of these materials.80 It is interesting to note that mice lacking the PARP genes or given a PARP inhibitor will not show the typical inflammatory changes usually observed with asthma.81 Thus in many ways inhalation of smoke may be similar to forms of airway injury. The fact that the response to inhalation injury is driven by neuroinflammation suggests that the response to smoke from wood or cotton should be similar.

Injury to the lung parenchyma

As noted above, the lung parenchyma changes produced by burn and smoke inhalation, as reflected by reduced PaO2/FiO2 and reduced compliance, and increased edema formation, are delayed.82 This delay is dependent on the severity of the airway injury.50,83 Lung injury is associated with an increased pulmonary transvascular fluid flux.84 The degree of transvascular fluid is proportional to the duration of smoke exposure85 and is not caused by CO in the inhalant gas.86 However, the degree of arterial CO is related to severity of inhalation injury.86 The factors responsible for fluid leak are codified in the Starling–Landis equation.87,88 The variables of this equation relate fluid movement to pressure and permeability variations. With inhalation of smoke there is a reduction in refection coefficient (permeability to protein), an increase in filtration coefficient (permeability to small particles), and an increase in pulmonary microvascular pressure.87,88 Animals that had been exposed to smoke inhalation injury were also noted to have reduced PaO2/FiO2. These variables are more severely affected when the inhalation is combined with burn injury.89 The change in this variable showed a good relationship with the histology injury scores and the changes in transvascular fluid flux.79 In addition, there was a loss of hypoxic pulmonary vasoconstriction in the injured animals that would help to explain the loss of oxygenation.90

As in the oropharynx the injury is associated with activation of PARP and 3-nitrotyrosine and is markedly reduced by the administration of an iNOS or PARP inhibitors.78

The venous outflow of the bronchial circulation drains into the pulmonary microcirculation at the pre-capillary level.91 Considering the fact that initial damage to the airway appeared to drive the pathophysiology of the parenchyma, investigators hypothesized that the bronchial blood might deliver cytotoxic materials or cells into the pulmonary microcirculation. To test this hypothesis, several investigators have tied off the bronchial artery of sheep and then exposed the animals to smoke.58,62,72 In these studies the hypothesis was confirmed and the lung parenchymal changes were reduced.

What could be the linkage between the airway, the bronchial venous drainage and parenchymal injury to the lung? Neutrophils activated in the bronchial circulation flow out into the bronchial venous drainage. Activated polymorphonuclear cells (PMN), especially neutrophils, are stiff. The diameter of neutrophils that have been fixed is approximately 7 µm.92 Because these cells have been dehydrated in alcohol as part of the fixation process, unfixed cells are much larger, of the order of 12 µm. The pulmonary capillary is small, with an average diameter of 6 µm.93 Normally, the large neutrophil can traverse the pulmonary capillary by changing shape. However, many of the neutrophils have been activated in the bronchial areas, their F-actin is activated, and the cells are stiff and cannot deform. These stiff cells are carried to the pulmonary microvasculature where they are impaled by the narrow pulmonary capillaries. The activated neutrophils release reactive oxygen species and proteases that damage the parenchyma. The following evidence supports this concept of neutrophil cytotoxicity. Oxidative processes are well known following inhalation injury. There is lipid peroxidation and release of proteolytic enzymes following injury.94–96 Administration of protease inhibitors or scavengers of reactive oxygen species will reduce the response to smoke inhalation97–99 when activated PMNs lose the L-selectin on their surface. This L-selectin shedding is prevented by the treatment with an L-selectin antibody.100 Treatment of the cells with an antibody to L-selectin will prevent the changes in transvascular fluid flux and other aspects of parenchymal damage.101 The final proof of this hypothesis was to deplete the animals of their neutrophils and determine how this affected their response to inhalation injury. In these studies of sheep depleted of their leukocytes, a high percentage of the response to smoke inhalation was blocked.102 The pathophysiology of acute lung injury secondary to burn and smoke inhalation injury is summarized in Figure 18.5.

In addition to the depletion of antioxidants discussed above, it has also been reported that burned patients are
depleted of arginine. When arginine levels are low the nitric oxide synthase produces superoxide rather than nitric oxide. Following smoke inhalation, arginase activity is also elevated. This enzyme also depletes arginine by converting it to ornithine. The administration of arginine may assist in reducing the oxidation that occurs with inhalation injury. However, the necessity of administering the arginine as arginine hydrochloride (because of solubility) limits the amount that may be given intravenously without producing acidosis.

**Long-term effects of inhalation injury**

When earlier editions of this book were published mortality from inhalation injury was high and the acute inflammatory aspects of the injury were considered a major vector of mortality. Now 85% of patients survive inhalation injury and so the long-term aspects of the injury have increased. When our patients are examined years after burn injury they demonstrate restrictive lung disease and reduced diffusion capacity, signs of fibrotic lung disease. At autopsy patients and animals both reportedly show hyaline membrane and deposition of collagen in their lungs in a similar fashion to other forms of acute lung injury. As stated above, two enzymes compete for arginine, nitric oxide synthase and arginase. NOS forms NO and RNS. Arginase forms ornithine, which is converted into polyamines and proline, leading to the formation of collagen. When NOS is active it forms N-(ω)-hydroxy-nor-L-arginine (NOHA). NOHA breaks down into NO and citrulline. NOHA is a potent inhibitor of arginase. Thus as long as the activity of NOS is elevated, arginase is inhibited. It has recently been reported that the endogenous inhibitor of NOS, asymmetric dimethylarginine (ADMA), begins to increase in the lung of sheep following combined burn and smoke inhalation injury. As ADMA increases, NO production falls and tissue levels of collagen increase. The increase in collagen results in hyaline membrane formation, thickening the alveolar septum and interfering with the diffusion of oxygen into the lung. ADMA is formed in the lung on a regular basis but is rapidly catabolized by dimethylarginine dimethylaminohydrolase (DDAH). DDAH is inactivated by oxidation. Following burn and inhalation injury lung levels of DDAH fall as makers of oxidation increase, and as these events occur
ADMA, arginase and collagen increase. We have previously determined that oxidation was such a serious problem that survival was dependent on the degree of oxidation. It was also recently reported that levels of γ and α tocopherol were markedly depleted in thermally injured children. Using an ovine model it was reported that combined burn and smoke inhalation depleted the animals of γ and α tocopherol, and that administration of tocopherol, especially γ tocopherol, orally (but most effectively by nebulization into the airway) was effective in restoring lung levels of tocopherol, normal oxidation status, and pulmonary function during the acute phase of injury. Preliminary experiments using the long-term model reported by Sousse et al. indicate that the nebulization of γ tocopherol will also reverse the deposition of collagen, elevated arginase, proline and ADMA, and restore DDAH levels.

The fire environment and toxic smoke compounds

Smoke toxicity is an increasing concern because industrial products used today are changing from woods and natural materials towards lighter construction materials, synthetics, and petrochemical-based materials, which ignite and burn two to three times hotter and faster than conventional materials and, when heated, emit a gas or smoke that will also ignite two or three times faster and burn hotter than natural biological materials. Consequently, firefighters have less time to gain control of a fire, and victims are more likely to be incapacitated by breathing toxic gases and more likely to sustain smoke inhalation because they have less time to escape from the burning area. Inhalation injury is caused by steam or toxic inhalants such as fumes, gases, and mists. Fumes consist of small particles dispersed in air with various irritants or cytotoxic chemicals adherent to the particles. Mists consist of aerosolized irritant or cytotoxic liquids. Smoke consists of a combination of fumes, gases, mists, and hot air. Heat, toxic gases, and low oxygen levels are most common causes of death in fires. A large variety of toxic gases and chemicals can be generated depending on the fire environment (Table 18.2).

Many of these compounds may act together to increase mortality, especially carbon monoxide and hydrogen cyanide, where a synergy has been found to increase tissue hypoxia and acidosis and may also decrease cerebral oxygen consumption and metabolism. Hydrogen sulfide would also be predicted to synergize with carbon monoxide as both cyanide and hydrogen sulfide are inhibitors of mitochondrial cytochrome oxidase. Victims may be incapacitated by the blinding and irritating effects of smoke, as well the decreasing oxygen concentration that occurs with combustion and results in progressive hypoxia.

Toxic gases such as carbon monoxide and cyanide rarely damage the airway but affect gas exchange, producing more systemic effects. It is thus important to obtain information

### Table 18.2 Origin of selected toxic compounds

<table>
<thead>
<tr>
<th>Gases and chemicals</th>
<th>Material</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon monoxide</td>
<td>Polyvinyl chloride, Cellulose</td>
<td>Upholstery, wire/pipe coating, wall, floor, furniture coverings. Clothing, fabric. Wood, paper, cotton</td>
</tr>
<tr>
<td>Phosgene</td>
<td>Polyvinyl chloride</td>
<td>Upholstery, wire/pipe coating, wall, floor, furniture coverings.</td>
</tr>
<tr>
<td>Sulfur dioxide</td>
<td>Rubber</td>
<td>Tires</td>
</tr>
<tr>
<td>Hydrogen sulfide</td>
<td>Wool, silk</td>
<td>Clothing, fabric, blankets, furniture</td>
</tr>
<tr>
<td>Formaldehyde</td>
<td>Melamine resins</td>
<td>Household and kitchen goods.</td>
</tr>
<tr>
<td>Isocyanates</td>
<td>Polyurethane</td>
<td>Insulation, upholstery material.</td>
</tr>
<tr>
<td>Acrylonitriles</td>
<td>Polyurethane</td>
<td>Insulation, upholstery material.</td>
</tr>
</tbody>
</table>

(From Prient, Traber DL. Toxic smoke compounds and inhalation injury – a review. (Burns. 1988; 14: 451–60.)
relative to the source of the fire and the combustion products generated when treating a fire victim (see Table 18.2). It is also important to know the duration of exposure and the extent to which the fire victim was in an enclosed area, as this affects the dose of toxic materials presented to them.

Carbon monoxide

Carbon monoxide (CO) is an odorless, colorless gas that is produced by incomplete combustion of many fuels, especially cellulosics (cellulose products) such as wood, paper, and cotton. Carbon monoxide toxicity remains one of the most frequent immediate causes of death following smoke-induced inhalation injury. The predominant toxic effect of CO is its binding to hemoglobin to form carboxyhemoglobin (COHb). The affinity of CO for hemoglobin is ~200–250 times higher than that of oxygen. Inhalation of a 0.1% CO mixture may result in the generation of a carboxyhemoglobin level as high as 50% of the total hemoglobin. The competitive binding of CO to hemoglobin reduces delivery of oxygen to tissues, leading to severe hypoxia, especially of the most vulnerable organs such as brain and heart, where oxygen extraction is considerably higher than in most other organs. The oxygen–hemoglobin dissociation curve loses its sigmoid shape and is shifted to the left, thereby further impairing tissue oxygen availability. In addition, the ability of CO to bind to intracellular cytochromes and to other metalloproteins contributes to CO toxicity. This competitive inhibition with cytochrome oxidase enzyme systems (most notably cytochromes-a and P-450) results in an inability of cellular systems to use oxygen. Shimazu and his colleagues have shown that extravascular binding of CO to cytochromes and other structures accounts for 10–15% of total body CO stores. This intracellular binding of CO explains the two-compartment elimination of CO from the circulation. Miro and colleagues reported that CO inhibits cytochrome-c oxidase activity in lymphocytes. The electron chain dysfunction caused by CO may lead to electron leakage, superoxide production and mitochondrial oxidative stress.

Although smoke inhalation commonly affects the respiratory system, central nervous system (CNS) disturbance can also develop. The CNS signs can be divided into acute and delayed toxicity. The veterinary literature contains few reports regarding the neurological consequences of smoke inhalation. In dogs subjected to smoke inhalation, lesions were identified that were compatible with acute carbon monoxide (CO) toxicity. Lesions were confined to the caudate nucleus, the globus pallidus, and the substantia nigra bilaterally, as well as the cerebellum, cerebral cortex, and dorsal thalamus. This case report describes the clinicopathological sequelae in acute CO toxicity.

Symptoms and diagnosis of carbon monoxide poisoning

The symptoms of CO poisoning may manifest predominantly in organ systems with high oxygen utilization. The severity of clinical manifestations is varied depending on the concentration of CO. For instance, the central nervous system symptoms such as headache, confusion, and collapse may occur when the blood COHb level is 40–50%. Symptoms such as unconsciousness, intermittent convulsions, and respiratory failure may occur if the COHb level exceeds 60%, leading eventually to death if exposure continues. The cardiovascular manifestations may result in tachycardia, increased cardiac output, dysrhythmias, myocardial ischemia, and hypotension, depending on the severity of poisoning. The correlation of clinical manifestation and severity of CO poisoning is summarized in Table 18.3.

Diagnosis should be based on direct measurement of COHb levels in arterial or venous blood by CO oximetry; it must be taken into account that venous blood underestimates the arterial COHb content. Diagnosis may be facilitated by use of on-site portable breath analyzers. The inability to differentiate oxyhemoglobin from COHb limits the use of a pulse oximeter. The use of blood gas analyzers that estimate SO2 based on measurement of dissolved PO2 should also be avoided. The measurement of acid–base balance, plasma lactate levels and bicarbonate is helpful in the management of CO poisoning with accompanying lactic or metabolic acidosis. It is important to note that high oxygen concentrations are usually administered to the victim in transit to hospital, and some delay from cessation of exposure to measurement of CO may limit evaluation of the true extent of exposure. A nomogram has been developed which can relate the carboxyhemoglobin levels of a patient to the values that may have been present at the time of smoke inhalation, and this can be used to estimate the true degree of inhalation injury.
Hydrogen cyanide

Hydrogen cyanide (CN), the gaseous form of cyanide, is generated by the combustion of nitrogen- and carbon-containing substances such as wool, silk, cotton, and paper as well as synthetic substances such as plastic and other polymers. Combustion of these materials may rapidly and lethally incapacitate a victim at the fire source.\textsuperscript{138} CN is a colorless gas with the odor of bitter almonds, but it is difficult to detect at the site of fire. The cytotoxicity of cyanide is produced by inhibition of cellular oxygenation with resultant tissue anoxia, which is caused by reversible inhibition of cytochrome-c oxidase.\textsuperscript{137} CN is toxic to a number of enzyme systems. The exact chemical mechanism by which cyanide induces its toxicity includes combination with essential metal ions, formation of cyanohydrins with carbonyl compounds and the sequestration with sulfur as a thiocyanate. However, the principal target enzyme of CN is cytochrome-c oxidase, the terminal oxidase of the respiratory chain, and involves interaction with the ferric ion of cytochrome-a\textsubscript{3}.

The importance of cyanide in smoke inhalation injuries is reflected by a study performed in Paris, France, which showed that mean blood cyanide concentrations in both fire victims who survived (21.6 µmol/L) and those who died (116.4 µmol/L) were significantly higher than those in control subjects (5.0 µmol/L), and levels in fire victims who died were significantly higher than those in victims who survived.\textsuperscript{139} A report of 144 fire victims in Dallas County, Texas, showed consistent results with the Paris study.\textsuperscript{140} Elevated cyanide concentrations showed a direct relationship to the probability of death, suggesting that cyanide poisoning may predominate over carbon monoxide poisoning as a cause of death in some fire victims. Cyanide also played a greater role in mortality in the aircraft fire at Manchester International Airport, Manchester, UK, in 1985. These patients were not severely burned. The large majority (87%) of the 54 individuals who died had potentially lethal levels of cyanide in their blood, whereas only 21% had COHb levels exceeding 50%. This indicates the high possibility that under certain conditions cyanide can be a more important determinant of morbidity and mortality following smoke inhalation than CO, which is usually regarded as the primary toxic threat.\textsuperscript{5} Smoke is also an often overlooked source of CN exposure in terrorist bombings. Following the first World Trade Center bombing in 1993, traces of cyanide were found in the vans where the explosion was originated. The US Centers for Disease Control and the Department of Homeland Security consider CN among the most likely agents of chemical terrorism.\textsuperscript{141} Cyanide possesses all the attributes of an ideal terrorist weapon: it is plentiful, readily available, and easily obtainable because of its widespread use in industry and laboratories. In addition, the use of cyanide does not require any special knowledge. Cyanide is capable of causing mass incapacitation and casualties, and can cause mass confusion, panic, and social disruption.\textsuperscript{142}

Symptoms and diagnosis of cyanide poisoning

Diagnosis at the fire scene may be difficult. Poisoning may result in central nervous, respiratory, and cardiovascular dysfunction due to inhibition of oxidative phosphorylation, depending on the concentration of cyanide inhalation (Table 18.4).

Electrocardiographic changes such as ST segment elevation that mimic an acute myocardial infarction\textsuperscript{143} may be suggestive. Laboratory findings of anion gap metabolic acidosis and lactic acidemia aid in confirming the diagnosis.\textsuperscript{144} Lactic acidosis that is not rapidly responsive to oxygen therapy may be a good indicator of cyanide poisoning.\textsuperscript{86,139} Also, an elevated mixed venous saturation is suggestive for cyanide toxicity. Cyanide increases ventilation through carotid body and peripheral chemoreceptor stimulation. Increasing ventilation may augment toxicity in the early stages. Low levels of hydrogen cyanide are routinely found in the blood of healthy individuals at levels of 0.02 µg/mL in non-smokers and 0.04 µg/mL in smokers. Toxicity occurs at a level of 0.1 µg/mL, and at 1.0 µg/mL death is likely.\textsuperscript{145} Correlation of blood cyanide concentrations with clinical symptoms is summarized in Table 18.5.

Other toxic chemicals

Other toxic chemicals may also contribute substantially to morbidity and mortality in a burn victim. Hydrogen chloride is produced by polyvinyl chloride degradation and causes severe respiratory tract damage and pulmonary edema. Nitrogen oxides may also cause pulmonary edema and a chemical pneumonitis and may contribute to cardiovascular depression and acidosis. Aldehydes such as acrolein and acetaldehyde, which are found in wood and kerosene, may further contribute to pulmonary edema and respiratory irritability. Toxic industrial chemicals such as chlorine, phosgene, hydrogen sulfide and ammonia are of central importance. Because of their widespread availability and high toxicity, there is certain concern that these chemicals may be used as a weapon by terrorists.\textsuperscript{147,148}

Phosgene gas is colorless, non-flammable, heavier than air at room temperature, and has an odor of newly mown hay.

<table>
<thead>
<tr>
<th>Table 18.4 Symptoms of cyanide toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms in low or moderate inhaled cyanide concentrations</strong></td>
</tr>
<tr>
<td>Faintness</td>
</tr>
<tr>
<td>Flushing</td>
</tr>
<tr>
<td>Anxiety</td>
</tr>
<tr>
<td>Excitement</td>
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<tr>
<td>Perspiration</td>
</tr>
<tr>
<td>Vertigo</td>
</tr>
<tr>
<td>Headache</td>
</tr>
<tr>
<td>Drowsiness</td>
</tr>
<tr>
<td>Tachypnea</td>
</tr>
<tr>
<td>Dyspnea</td>
</tr>
<tr>
<td>Tachycardia</td>
</tr>
</tbody>
</table>
Chlorine is a greenish-yellow gas, an oxidizing agent, and very reactive with water. It has a pungent odor. Upon contact with water chlorine liberates hypochlorous acid, hydrochloric acid, and oxygen free radicals. It causes irritant effects throughout the respiratory tree but mostly the nasal mucosa and upper airways. Cell damage is caused by its strong oxidizing capability. Both phosgene and chlorine were used extensively during World War I.

Ammonia is a colorless gas at room temperature, with a very pungent odor. Ammonia readily dissolves in water to form ammonium hydroxide, a very caustic alkaline solution. It causes cutaneous, ocular, and pulmonary injuries. Inhaled ammonia can rapidly produce laryngeal injury and obstruction. It also causes upper tracheobronchial mucosal necrosis with sloughing and severe pulmonary edema.

There are no specific antidotes against toxicity from irritant gases (phosgene, chlorine, and ammonia). Depending on the severity of exposure, supportive therapy such as airway management and ventilation should be provided. Early intubation is required if any significant upper airway symptoms such as stridor are present.

Under 8 °C phosgene is an odorless and fuming liquid. Phosgene’s inadequate warning properties and delayed symptoms make it a potential terrorist weapon. Phosgene is only slightly soluble in water, hence its deeper penetration in the pulmonary system. On contact with water it hydrolyzes into carbon dioxide and hydrochloric acid, resulting in direct caustic damage. It also undergoes acylation reactions with amino, hydroxyl, and sulfhydryl groups of cellular macromolecules, resulting in cell damage and apoptosis. As mentioned above, phosgene has delayed effects from 20 minutes up to 48 hours, depending on the intensity of exposure. Phosgene inhalation produces severe pulmonary edema. Initially victims develop upper airway irritant symptoms (eye irritation, rhinorrhea, cough) and then will develop lower respiratory symptoms such as shortness of breath, substernal burning, and chest tightness. The development of overt pulmonary edema within 4 hours of exposure portends a poor prognosis.

Further reading


Table 18.5 Hydrogen cyanide concentrations in air and associated symptoms in humans

<table>
<thead>
<tr>
<th>HCN concentration (ppm)</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.2–5.0</td>
<td>Threshold of odor</td>
</tr>
<tr>
<td>10</td>
<td>(TLV-MAC)</td>
</tr>
<tr>
<td>18–36</td>
<td>Slight symptoms (headache) after several hours</td>
</tr>
<tr>
<td>45–54</td>
<td>Tolerated for 0.5–1 hour without difficulty</td>
</tr>
<tr>
<td>100</td>
<td>Death in 1 hour</td>
</tr>
<tr>
<td>110–135</td>
<td>Fatal in 0.5–1 hour</td>
</tr>
<tr>
<td>181</td>
<td>Fatal in 10 minutes</td>
</tr>
<tr>
<td>280</td>
<td>Immediately fatal</td>
</tr>
</tbody>
</table>


Access the complete reference list online at http://www.expertconsult.com


70. Doerschuk CM, Beyers N, Coxson HO, et al. Comparison of neutrophil and capillary diameters and their relation to...


Diagnosis and treatment of inhalation injury

Lee C. Woodson, Mark Talon, Daniel L. Traber, David N. Herndon

Introduction

Inhalation injury is a non-specific term that refers to damage to the respiratory tract or pulmonary parenchyma by heat or chemical irritants carried into the airways during respiration. Inhalation injury remains one of the most critical injuries following thermal insult. It may occur in conjunction with cutaneous burns or in isolation. The severity of injury varies, depending on the chemical composition of the agent(s) inhaled, the intensity of exposure, temperatures reached during combustion and pre-existing comorbidities. There are three basic classes of inhalation injury: direct thermal injury, tissue damage due to inhalation of chemical irritants, and systemic effects of inhaled toxins. Direct thermal injury is generally restricted to the upper airway and rarely involves subglottic structures.1 The upper airway serves as an efficient heat exchanger that protects lower structures from extremes of heat or cold. Laryngeal closure also protects subglottic areas. Exceptions are the inhalation of steam due to the much higher specific heat of water vapor, and blast injuries that can force hot gases past the glottic opening. Inhaled irritants are generally present in smoke as a mixture of gases, fumes, and mists, and the chemical composition of smoke produced from various fuels has been described.2 Fumes consist of particles of various size dispersed in inhaled gases. Mists are aerosolized liquids. The intensity of exposure along with the size and chemical composition of these particles and droplets determines how far distally they will migrate in the respiratory tract and the nature of the tissue injury.2 Large particles and droplets of lipid-soluble liquids are more likely to adhere to airway surfaces and do not reach as far distally as smaller particles and more water-soluble droplets. Systemic toxicity occurs when toxins such as carbon monoxide or cyanide are present in the inhaled gases.

The reported incidence of inhalation injuries has varied greatly over time and from region to region. Smith3 and others reported 19.6% incidence among burn patients in the USA, in Israel Haik4 and colleagues found as few as 1.5%, while Luo5 and others found 8.01% in China. Regional differences are to be expected as a result of differences in local customs, building materials, and other factors.

The presence of inhalation injury is clinically significant for a variety of reasons, as listed in Table 19.1. Inhalation injury has been found to be an independent risk factor for mortality.6,7 It is also associated with hemodynamic instability, as volume requirements for resuscitation may be increased by as much as 50% when cutaneous burns are accompanied by inhalation injury.8 Parenchymal injury can lead to impaired gas exchange, pneumonia, and ARDS. When severe, these changes increase the risk of multiorgan failure and mortality. After recovery from inhalation injury pulmonary function disorders may persist due to pulmonary fibrosis or bronchiectasis. Improvements in the survival of patients with inhalation injury have been attributed to better overall burn outcomes, improved ventilatory management, and improved management of pneumonias.5

Improvements in the care of cutaneous burns have outpaced advancements in the treatment of inhalation injuries. There are several reasons for this disparity. The treatment of pulmonary parenchymal injury is inherently more complex than treatment for cutaneous burns. Necrotic skin can be excised and replaced with substitute materials or autografted skin, and healing can be observed directly. In contrast, treatment of injured lung involves measures to prevent further injury to allow host mechanisms to repair injured tissues. Healing of pulmonary injury is followed more indirectly by observations of blood gas analysis and radiographs. Inhalation injury results both from direct effects of heat and chemical irritants as well as indirect effects from an inflammatory response to the initial insult. Despite extensive studies, these processes are incompletely understood and no specific therapies have been identified.

Because inhalation injury has such broad clinical implications it is important that it be diagnosed as early as possible. Early diagnosis can be accomplished by recognition of risk factors revealed by the history and physical examination, and confirmed by diagnostic procedures.

Diagnosis

As stated above, inhalation injury is a non-specific term used to describe injury to the airways and/or lungs due to the inhalation of gases that are either hot or contain chemical irritants, or both. There is no consensus on the diagnostic criteria for inhalation injury. In the clinical setting the
The physical examination reveals additional risk factors for inhalation injury. We guard our face vigorously, and the presence of burns to the face or singed eyebrows or nasal hair implies a very intense exposure. When gases hot enough to burn tissue are near the airway it suggests that oropharyngeal or nasopharyngeal structures may also suffer thermal injury. Soot deposits on the face and carbonaceous sputum suggests intense exposure to and inhalation of smoke. Physical examination may reveal signs and symptoms such as stridor, hoarseness, drooling, and dysphagia that are considered classic evidence of inhalation injury. These findings, however, do not always indicate that tracheal intubation is necessary. However, as described below, when patients are considered at risk for upper airway thermal injury and occlusion, a priority is to evaluate the upper airway for impending occlusion that may be prevented by early tracheal intubation.

In addition to the history and physical examination, there are diagnostic tools that may be used to confirm a diagnosis of inhalation or to follow the progression of injury. As stated above, manifestations of respiratory dysfunction may be delayed after inhalation injury. As a result, pulse oximetry and arterial blood gas analysis are insensitive indicators of lung injury during the initial stages. Despite this, it is important to employ these tools as soon as possible. Early impairment of gas exchange is a sign of severe injury and requires early intervention. Diagnosis of CO or cyanide toxicity may be facilitated by blood gas analysis. It is also important to have baseline values to judge progress.

The chest radiograph is also considered an insensitive indicator of parenchymal injury after smoke inhalation. Although an admission chest radiograph should be obtained in all patients suspected of inhalation injury, it has been recognized that a normal study does not rule out the possibility of significant pulmonary injury.

Flexible fiberoptic bronchoscopy was early recognized as a powerful tool in the diagnosis of inhalation injury. Fiberoptic bronchoscopy allows direct visualization of tissue damage to the upper airway and bronchi by heat and chemical irritants. This procedure can quickly and reliably identify patients with upper airway compromise who will benefit from intubation. Bronchoscopic evidence of inhalation injury includes soot deposits, erythema, edema (as indistinct tracheal rings or blunting of the carina), mucosal blisters and erosions, hemorrhages, and bronchorrhea (Fig. 19.1).

Flexible fiberoptic bronchoscopy has been considered the ‘gold standard’ and is often used to confirm the diagnosis of inhalation injury. However, Hunt noted that in some cases bronchoscopy performed soon after injury may not show mucosal injury. In addition, because acute lung injury and tracheobronchitis can be a result of systemic inflammation due to cutaneous burns, endoscopic changes after 36–48 hours may be caused by mechanisms other than inhalation of chemical irritants. Moreover, although fiberoptic bronchoscopy can definitively identify tissue damage from inhalation injury, it has been recognized that the observed changes are relatively proximal and may be more severe than more peripheral, parenchymal injuries. As a result, a bronchoscopic diagnosis of inhalation does not always identify which patients will experience progressive respiratory dysfunction.

Radionuclide studies have been used to provide evidence of pulmonary injury distal to the more proximal views of the airway.

Table 19.1  Clinical significance of inhalation injuries

- Mortality: immediate/late
- Airway closure secondary to edema
- Hemodynamic instability/increased resuscitation fluid requirements
- Impaired pulmonary gas exchange
- Pneumonia/ARDS
- Systemic inflammatory syndrome and multiorgan system failure
- Laryngeal damage
- Chronic pulmonary dysfunction

Diagnosis is a relatively subjective judgment based on history and physical examination, and often confirmed by additional diagnostic procedures such as bronchoscopy. One of the reasons for the lack of consensus is that impaired pulmonary function due to inhalation injury often results from an inflammatory response to the initial injury, and manifestations may be delayed for a day or two. In addition, it is our clinical impression that progressive respiratory failure is not necessarily proportional to the intensity of smoke exposure. It is also possible for thermally injured patients to experience acute lung injury from the systemic effects of the inflammatory response to severe cutaneous burns. Thus, it is not uncommon to see acute lung injury in patients with large scald burns. This makes it difficult to determine what component of respiratory failure is due to inhalation injury in patients with large burns.

On initial presentation, patients with inhalation injury may have relatively normal gas exchange as evaluated by arterial blood gas analysis, and the chest radiograph is usually normal. In the absence of evidence of respiratory distress it is important to recognize features from the history and physical examination that reveal risk factors for inhalation injury. Early diagnosis is important to recognize the potential for airway compromise, manage fluid resuscitation, and to recognize systemic toxicity that may lead to permanent neurological deficits if not promptly treated.

History pertinent to the diagnosis of inhalation injury includes information regarding the mechanism of injury and the intensity of exposure. Mechanisms of injury that carry significant risk of inhalation injury include not only exposure to smoke from a fire, but blast injury that can force hot gases past the larynx, steam burns that can not only burn the upper airway but carry heat to structures below the larynx, and exposure to caustic fumes as in some industrial accidents. Information regarding the mechanism of injury also includes the source of combustion, which could identify specific chemical irritants. The history can also provide information regarding the intensity of exposure. Duration of exposure is an important determinant of intensity of exposure. When a victim’s avoidance behavior is impaired, as when trapped in an enclosed space, intoxicated or unconscious, or in the extremes of age, exposure to injurious inhalants is increased.

History of the mechanism of injury is especially important in the case of scalds due to ingestion of hot liquids. Although patients may appear asymptomatic initially, oropharyngeal and upper airway occlusion. Intraoral scalds can present in a manner similar to epiglottitis. The larynx should be examined for evidence of compromise in all patients who present with significant risk of intraoral scald.
Pathophysiology of pulmonary insufficiency with inhalation injury

As stated above, except in special cases such as inhalation of steam, injury to airways below the larynx and pulmonary parenchyma nearly always results from chemical irritation. A number of reviews are available to describe the pathophysiology of pulmonary failure associated with smoke inhalation.221 Chemicals inhaled with smoke as well as carbon particles coated with irritants are deposited in the airways. Aqueous secretions of the mucosa dissolve these irritants and the respiratory mucosa is bathed in relatively concentrated caustic solutions. The initial response to this insult is injury to the respiratory epithelium, resulting in hyperemia, edema, increased mucous secretions, impaired ciliary clearance, and bronchoconstriction. Work in experimental animals has also demonstrated an early separation of ciliated respiratory epithelial cells from the basement membrane. This results in denuded areas of the airways and explains the copious formation of protein-rich exudate. Fibrin casts tenaciously adherent to the airway surfaces are formed from this exudate.

Much of the morbidity associated with smoke inhalation is the result of the inflammatory response to the early direct effect of chemical irritants. The inflammatory response to smoke inhalation is similar to the injury produced by aspiration of acidic gastric contents. The direct injury to tissues caused by the initial insult causes local accumulation of inflammatory cells and initiation of a cascade of inflammatory mediators that exacerbate and sustain tissue damage (see below).

Airways become blocked by edema, bronchoconstriction, fibrin casts, necrotic debris, and inflammatory infiltrate (Fig. 19.2). Degraded surfactant causes alveolar instability and collapse. These changes result in impaired hypoxic pulmonary vasoconstriction and areas of atelectasis, and postobstructive sequestration of material that provide a medium for bacterial growth and risk of pneumonia. Impaired function of alveolar macrophages slows the removal of these materials and facilitates the development of infection. Pulmonary compliance is reduced, which can greatly increase the work of breathing.

As a result of these changes pulmonary gas exchange is impaired. Atelectasis due to airway obstruction increases dead space and shunt to an extent, but the impaired gas exchange due to smoke inhalation appears to be primarily a ventilation–perfusion imbalance.22 It has been suggested that this mechanism of pulmonary dysfunction is fundamentally different from other types of ARDS.17,23 Other etiologies of ARDS, such as sepsis, involve disruption of the pulmonary capillary membrane and alveolar flooding, resulting primarily in true shunt. This distinction can influence the ventilator strategies employed. Patients with respiratory failure due to smoke inhalation injury have small airway obstruction, and care should focus on pulmonary toilet together with recruiting and stabilizing alveoli, which tend to collapse, whereas in ARDS due to other etiologies the strategy is to concentrate on avoiding ventilator-induced lung injury. In some burn centers this is a rationale for the use of high-frequency percussive ventilation.17

Just as the bronchi are the focus of the diagnosis of inhalation injury, it is also the focus of its pathology.24 The hyperemia and edema that are seen in the airway and which are so important for the diagnosis of inhalation injury are the result of an almost 20-fold increase in bronchial blood flow.25,26 Following the airway injury, there are changes in the lung parenchyma. There is a release of the chemokine interleukin (IL)-8 and an influx of neutrophils into the airway and alveoli. Reactive oxygen (ROS) and nitrogen species (RNS) are formed.27 One of the latter, peroxynitrite, damages DNA. DNA damage results in activation of poly-(ADP ribose) polymerase.28 Poly-(ADP ribose) protects the damaged DNA but also activates the nuclear factor NF-κB.29 This causes the formation of the inducible form of nitric oxide synthase and additional release of IL-8, attracting and activating additional neutrophils and forming more reactive nitrogen and oxygen species.30 The oxidation, nitration, and nitrosation of lung tissues results in membrane damage, edema formation and impaired oxygen diffusion.31,32 Alveoli that are not ventilated are not perfused with blood because alveolar hypoxia causes pulmonary vasoconstriction. NO released by nitric oxide synthase causes a loss of hypoxic pulmonary vasoconstriction, leading to perfusion of unventilated alveoli and thus a fall in arterial oxygen saturation.33

Ablation of the bronchial blood flow will prevent most of the pathophysiology involved in inhalation injury to the pulmonary parenchyma.24,34,35 These changes in bronchial blood flow are not associated with heat. They can be produced in experimental animals by smoke that has been
cooled to body temperature. As mentioned above, the blood flow to the airway is so effective in cooling or heating inhaled air that it is almost impossible for hot gases to reach the bronchi. These changes in blood flow also appear to be independent of the chemical composition of smoke, as they are mediated by a neuroinflammation. We have recently reported that following insufflation of smoke into deeply anesthetized sheep, the airway blood flow increased 10-fold, but after administration of an inhibitor of the neuropeptide calcitonin gene-related peptide (CGRP) the smoke-induced hyperemia was markedly reduced. Neuropeptides (peptides released from nerves within the lung tissue) induce vasodilation by causing activation of nitric oxide synthase, leading to the formation of NO. It has also been reported that an inhibitor of the neuro isoform of nitric oxide synthase would block the hyperemia and much of the pathophysiology mentioned above, including the loss of hypoxic pulmonary vasoconstriction. These findings have led us to the following hypothesis: the chemicals in smoke activate sensory nerves to release neuropeptides that activate NOS1 to release NO and superoxide to form peroxynitrite, which damages DNA, activating PARP, that stimulates NF-κB which in turn will upregulate the inducible form of nitric oxide synthetase, leading to massive formation of ROS and RNS, tissue damage and hypoxia and dyspnea. Some of the activated polymorphonuclear cells that escape from the pulmonary and bronchial circulation into the systemic circulation are carried to systemic organs, promoting multiorgan system damage.

### Table 19.2 Indications for early tracheal intubation

- Overt signs and symptoms of airway obstruction
- Extensive burns to the head and neck
- Inability to protect airway from aspiration
- Significant toxicity from carbon monoxide or cyanide
- Respiratory failure
- Extensive burns (>40 % TBSA)
- Hemodynamic instability

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**Treatment**

In general, there are no specific therapeutic interventions for inhalation injury and treatment consists of supportive modalities. However, if systemic toxicity is suspected, e.g. cyanide or carbon monoxide poisoning, there are specific interventions. When mechanical ventilation is required, measures must be taken to avoid ventilator-induced injury.

Treatment should begin at the scene of injury. Pulmonary function must be supported in coordination with care of cutaneous burns and other possible injuries. The history along with a rapid physical examination can identify victims at risk of inhalation injury as well as respiratory insufficiency and other indications for early intervention.

Initially, special attention must be given to the airway evaluation. There are many potential indications for early and even prophylactic intubation in victims of serious burn injury (Table 19.2). Early hypoxemia due to impaired gas exchange after inhalation injury is an ominous sign, and those with respiratory distress not corrected by supplemental oxygen may require intubation. Patients unable to protect their airway owing to diminished mental status due to injury or intoxication should be intubated to prevent aspiration. It is recommended that, even in the absence of inhalation injury, those with large burns covering 40% or more of their total body surface area (TBSA) should be intubated because of the risk of associated hemodynamic instability. Another indication for early prophylactic intubation is the risk of...
upper airway occlusion due to edema from thermal injury. In some patients with burns to the face and neck or inhalation of hot gases or steam, early intubation can be lifesaving. Training supported by the American Burn Association has encouraged early tracheal intubation in patients at risk for airway occlusion. However, intubation is not a benign intervention and there is growing recognition of the associated risks. Eastman and colleagues at the Parkland Burn Center recently published a retrospective study of pre-burn center intubations of burn victims. This was in response to what may have been a preventable death of a burn victim intubated prior to hospitalization. Out of 879 burn patients intubated before admission to hospital, 11.9% were extubated on the day of admission. In addition, 41.1% were extubated within 48 hours of injury. These findings suggest that many patients may have been exposed to the risks of unnecessary tracheal intubations are listed in Table 19.3. These findings suggest that many patients may have been exposed to the risks of unnecessary tracheal intubation. Further evaluation is needed to avoid morbidity associated with unnecessary intubations.

Otolaryngologists at the Baltimore Regional Trauma Center used spirometry (flow–volume loops) and flexible fiberoptic bronchoscopy to prospectively evaluate indications for intubation in patients at risk of inhalation injury. They reported that in 11 patients who were admitted to the emergency department with evidence of inhalation injury, six met their institutional criteria for intubation. However, when these patients were examined by fiberoptic bronchoscopy no significant airway compromise was observed, and they were managed safely and effectively without intubation. The high negative predictive value of normal flow–volume loops for airway compromise in patients with inhalation injury has been previously reported by Haponik et al. Madnani and colleagues have also demonstrated that the presence of signs and symptoms that have been considered classic evidence of inhalation injury does not always predict the need for tracheal intubation. Further evaluation is needed to avoid morbidity associated with unnecessary intubations. When burn victims first present, the history and physical examination can identify those who are in significant respiratory distress or who have other indications for immediate endotracheal intubation. For other patients with risk factors for inhalation injury but who may only be experiencing mild distress, spirometry (flow–volume loops) and/or endoscopic evaluation can be used to identify those who have impending airway compromise and will more certainly benefit from early prophylactic intubation. Those who do not require early intubation can be observed and repeat evaluations performed if their clinical condition changes. An algorithm for airway management in burn patients is illustrated in Figure 19.3.

Another potential complication of inhalation injury requiring early attention is systemic toxicity from carbon monoxide (CO) and/or cyanide. Intoxication should be considered in all patients suspected of significant exposure to smoke. The predominant toxic effect of CO is to prevent binding of oxygen to hemoglobin by the formation of carboxyhemoglobin (COHb). COHb has an affinity for hemoglobin approximately 200 times that of oxygen. CO can also prevent cellular utilization of oxygen by binding to mitochondrial cytochromes. Early symptoms include headache, nausea, dizziness, and lowered mental status. Diagnosis requires direct measurement of COHb. Conventional pulse oximetry will not distinguish between oxyhemoglobin and COHb. COHb can be measured by arterial or venous CO oximetry or recently developed pulse CO oximetry. Increased oxygen partial pressure will speed elimination of CO. Oxygen supplementation by face mask is usually sufficient, but in more severe cases (COHb >15–20%) it may be necessary to provide 100% oxygen via an endotracheal tube.

Hyperbaric oxygen has also been used to treat CO poisoning, but there is no consensus on the indications, treatment parameters, or outcome benefits. Moreover, hyperbaric facilities are not widely available.

Cyanide is another toxic component of smoke, especially when the fuel is certain plastic products. Cyanide causes cellular anoxia by binding to mitochondrial cytochromes and preventing intracellular oxygen utilization. Arterial oxygen partial pressures are not reduced by cyanide. Clinical signs of hypoxia despite adequate arterial oxygen tension, or metabolic acidosis despite apparently adequate oxygen delivery suggest cyanide toxicity. The earlier treatment is initiated the more likely it will be successful. Supplemental oxygen can cause non-enzymatic oxidation of reduced cytochromes, and displace cytochrome oxidase and potentiate the effects of administered antidotes. Pharmacological intervention includes methemoglobin generators such as nitrates (amyl nitrite inhalation 0.2 mL or sodium nitrite intravenous 10 mL of 3% solution for adults and 0.13–0.33 mL/kg of 3% solution for children) and dimethylaminophenol (3.25 mg/kg) to increase methemoglobin levels. Methemoglobin competes with cytochrome oxidase for cyanide. Caution is required because excessive levels of methemoglobin lead to decreased oxygen-carrying ability of hemoglobin and may cause toxicity. Some agents can bind cyanide directly. Dicobalt edetate (20 mL of 15% solution for adults or 0.3–0.5 mL/kg of 15% solution for pediatric patients) has a rapid effect but carries a risk of toxicity. Hydroxocobalamin (adults 5–10 g or children 70 mg/kg) is the precursor of vitamin B₁₂ and has been shown to be safe, with few side effects. Sulfur donors such as sodium thiosulfate (adults 25 mL of 50% solution or children 1.65 mL/kg of 25% solution) accentuate the body’s enzymatic conversion of cyanide to thiocyanate in the presence of the mitochondrial enzyme rhodanese, reducing its toxicity and increasing elimination.

As mentioned above, inhalation injury has been consistently observed to significantly increase fluid requirements for resuscitation of patients with cutaneous burns. The presence of an inhalation injury might intuitively be viewed as

Table 19.3 Risks of unnecessary tracheal intubation in burned patients

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impairs communication with patient</td>
<td>Impairs taking history and obtaining consent</td>
</tr>
<tr>
<td>Urgent attempts more likely to fail or cause injury</td>
<td></td>
</tr>
<tr>
<td>Acute burn patients often require heavy sedation after intubation</td>
<td></td>
</tr>
<tr>
<td>The endotracheal tube is difficult to secure in the presence of facial burns and self-extubations are common</td>
<td>Heavy sedation or muscle relaxants make this more dangerous</td>
</tr>
<tr>
<td>Inhalation injury and a translaryngeal endotracheal tube are synergistic in producing laryngeal and tracheal injuries</td>
<td></td>
</tr>
</tbody>
</table>

Figure 19.3. Airway management in burn patients is illustrated.
suctioning for short periods of 10–15 seconds can reduce the incidence of these problems. Postural drainage can be useful, although sometimes skin graft location and fragility impede use of this technique.\(^5^0\) Percussive and vibratory techniques such as high-frequency chest wall oscillation also help clear mucoid secretions.\(^5^0,^5^1\) It is also important to maintain good nutritional status in these patients.

As a result of inhaled irritants, patients can suffer from severe bronchospasm. This can usually be managed by using inhaled \(\beta\) agonists such as albuterol or salbuterol. Aerosolized heparin is used in many centers to reduce bronchial cast formation by reducing fibrin formation in the exudate formed at denuded areas of epithelium.\(^5^2–^5^4\) It does not cause systemic anticoagulation in the doses used clinically. Aerosolized and intravenous acetylcysteine has also been used as a mucolytic and was shown to improve pulmonary antioxidant capacity in one study.\(^5^5\) In a pediatric study, a combination of aerosolized heparin and acetylcysteine was used and resulted in a significant reduction in reintubations, the incidence of atelectasis, and in mortality following smoke inhalation injury.\(^5^4\)

When physical therapy and pharmacological agents still fail to facilitate expectoration of secretions or ameliorate cast formation, fiberoptic bronchoscopy can be effective for removal of secretions, and also to obtain microbiological specimens through bronchoalveolar lavage in suspected cases of pneumonia. Attempts to replace surfactant have also been studied, but are not in widespread clinical use.

Figure 19.3 An algorithm to assist airway management decisions in patients at risk for inhalation injury.

Patient at risk for inhalation injury
- Facial burns
- Hoarseness
- Evidence of smoke exposure
- Other classical signs of inhalation injury

ATLS primary survey

Mild respiratory distress
No other indications for intubation

Flow volume loops and/or fiberoptic bronchoscopy

No flow loop evidence of obstruction
No compromise by endoscopy

Continued observation
Repeat studies if clinical change

Significant respiratory distress or other indications for intubation (massive burns, aspiration risk, etc.)

ATLS primary survey

Mild flow volume changes, but no significant obstruction by bronchoscopy

Serial exams

Glottic compromise due to edema

Intubate

Care should be taken when suctioning to avoid hypoxia and bradycardia. Preoxygenation and an indication to restrict fluids to avoid pulmonary edema. In fact, fluid restriction has been found to exacerbate pulmonary capillary leak and increase lung lymph formation in sheep that have sustained cutaneous burns and smoke inhalation injury.\(^4^6\) Although it is important to avoid fluid overload in all patients, including those with inhalation injury, inadequate fluid resuscitation can also further injury to the lungs of patients with inhalation injury.\(^4^7\) A combination of cutaneous burns and inhalation injury reduces the margin for error in managing fluid resuscitation. It becomes more difficult to reach a balance where sufficient volume is administered for resuscitation but not too much to drive up filling pressures, which may increase transudation from pulmonary capillaries that already have increased permeability.

Supplemental humidified oxygen should be used for patients suspected of having inhalation injury, the humidification helping to prevent inspissation of the airway secretions, and the head of the bed should be placed at a 30–45° angle. This helps reduce upper airway edema and reduces the effect of pressure from abdominal contents on the diaphragm. Meticulous pulmonary hygiene is a vital component of the management of inhalation injury. Frequent airway suctioning, chest physiotherapy including percussive and coughing techniques, and early mobilization all help prevent build-up of secretions, which can cause airway obstruction, atelectasis, and predispose to the development of pneumonia.\(^4^8,^4^9\)
Antibiotics are indicated for suspected or proven pulmonary infection.49,56

Mechanical ventilation is indicated when the signs of respiratory failure are either present or imminent. Indications include impaired gas exchange due to pulmonary parenchymal injury, decreased pulmonary compliance, or impending collapse of effort due to fatigue. Burns involving the head and neck may make intubation technically difficult. In these circumstances avoidance of muscle relaxants and the use of an intubation technique that maintains spontaneous ventilation is safest. The flexible fiberoptic bronchoscope is well suited to this task. A nasal endotracheal tube may be preferable for patient comfort, oral hygiene and stability. In addition, a nasal endotracheal tube can be secured by a nasal septal bridge, which is much more secure than tape or ligatures over burned skin and prevents irritation of wounds and disruption of grafts.

There is no consensus on the ideal mode of mechanical ventilation for burn patients. The intricacies of mechanical ventilation in burn patients have recently been reviewed.17,57,58 The aim is to provide adequate ventilation to maintain airway and alveolar patency without exacerbating the pulmonary injury by over-distension or barotrauma. In this patient population the airways may be narrowed by edema, which increases airway resistance and hence airway pressures. The Lower Tidal Volume Trial (ARMA) conducted by the ARDS Network found that lower tidal volumes (limited to 6 mL/kg) were associated with decreased mortality in patients with ARDS.59 Most burn centers now have adopted this approach to reduce ventilator-induced injury.60 Permissive hypercapnia has also been found to be a safe technique for avoiding higher airway pressures in burn patients.52,61 This allows lower airway pressures and smaller tidal volumes to be used when ventilating the patient, and is well tolerated when gradual in onset and the pH is kept > 7.2–7.25.52,61 The optimal positive end-expiratory pressure (PEEP) should be determined using a pressure–volume curve. This helps maintain alveolar patency and reduces trauma caused by the shear forces imparted as alveoli collapse and are re-expanded with each breath. The lower inflection point of the pressure–volume curve of a mechanical breath is where the slope of the lower curve begins to increase, and is the airway pressure below which the alveoli collapse. The PEEP value should be set just above this. FiO2 should be weaned down as tolerated to reduce oxygen-related complications. The PaO2 can be maintained between 80 and 100 mmHg, although values over 65–70 mmHg can support adequate tissue oxygenation.

Conventional mechanical ventilation is either volume or pressure controlled. Volume-controlled ventilation delivers a consistent tidal volume and minute volume to the lungs, but this can result in increased airway pressures depending on the compliance of the lungs. Pressure-controlled ventilation limits the inflating pressure used, and thus the tidal volume varies depending on compliance and inspiratory time.52 High-frequency percussive ventilation (HFPV) is a ventilatory mode that delivers subtidal breaths at a high frequency along with tidal, low-frequency breaths.62 HFPV has become the preferred mode of ventilation in some burn centers.17 Proponents suggest that HFPV allows gas exchange at lower peak and mean pressures and may also dislodge and facilitate the removal of secretions and debris in the airways. It appears to be associated with decreased work of breathing, improved oxygenation (higher PaO2/FiO2 ratios) and lower peak pressures.63,64 A pediatric study group also had a significant reduction in the incidence of pneumonia compared to a conventionally ventilated control group.63

Airway pressure release ventilation (APRV) is a more recently developed pressure-controlled time-cycled mode of ventilation that can allow spontaneous breathing during the ventilatory cycle without changing the preset pressure settings.65 It has a high-pressure and a low-pressure setting. Recruitment of alveoli and oxygenation occur at the high-pressure setting, and ventilation occurs by controlled releases to the lower pressure. The mechanical inspiratory phase can be prolonged to achieve higher mean airway pressures without high peak airway pressures. It has so far shown promising results in trauma patients and pediatric patients with mild to moderate lung disease. Comparable or superior oxygenation values were achieved while using lower peak airway pressures.66 This mode may be useful in the burn population as a means to ventilate while reducing barotrauma.

Extracorporeal membrane oxygenation (ECMO) is a technique that can be used in patients with severe respiratory failure, in which the patient’s blood is circulated through an extracorporeal cardiopulmonary bypass circuit that facilitates gas exchange through a semipermeable membrane.67 While this is taking place, much lower ventilatory pressures and a low FiO2 can be used to allow the lung to heal without the additional complications of mechanical ventilation. Anticoagulation is necessary during treatment, which makes surgical care of burn wounds difficult. Although numbers in burn patient studies are small, this may offer a salvage therapy for patients with severe respiratory disease on conventional ventilation.57,68

Mechanical ventilation should be weaned as the patient’s condition improves, and discontinued as soon as it is no longer necessary. During the weaning process, the FiO2, PEEP and rate should be reduced as tolerated, until the patient is capable of supporting their own respiratory requirements. Parameters used as indicators for extubation include the presence of the following: an alert patient; resolution of upper airway edema with an audible air leak around the endotracheal tube with the cuff deflated; PaO2/FiO2 ratio >200; an adequate tidal volume (6 mL/kg); and negative inspiratory pressure < 20 cmH2O.68 The patient should also not be acidic and should be hemodynamically stable. Once the patient is extubated, supplemental, humidified oxygen should be provided, and the patient should be carefully observed for any signs of respiratory compromise that might necessitate re-intubation.

Opinions on the use of tracheostomy in burn patients are divided. The most common indication is a need for prolonged mechanical ventilation. This allows removal of the translaryngeal endotracheal tube, which reduces the chance of laryngeal injury and provides a more secure airway. When multiple surgical treatments are predicted a tracheostomy tube obviates the need for repeated intubation for each procedure. When prolonged mechanical ventilation is needed patient comfort can also be enhanced with a tracheostomy, and pulmonary toilet is facilitated. Owing to high rates of pulmonary contamination with burn wound bacterial flora and mortality, tracheostomy was discouraged in the past.69
More recently, with advances in burn care several studies have found that the risk of pneumonia is not increased by tracheostomy in burn patients.\textsuperscript{26,71} As a result, many burn centers routinely perform tracheostomy not only in patients who require prolonged ventilation but in those with extensive burns that will require multiple anesthetics for surgical procedures. In studies involving small groups of patients tracheostomy has been used without complications.\textsuperscript{71} Tracheostomy is an invasive procedure, however, and in larger patient populations there is a risk of significant morbidity. Saffle et al. found that burn patients treated with conventional ventilation were extubated sooner than those randomized to early tracheostomy.\textsuperscript{72} As clinical outcomes were otherwise not different between groups, it appears that there was no significant benefit of the more invasive tracheostomy. In the absence of clear evidence of benefit the use of tracheostomy in burn patients remains a matter of clinical judgment, but in each case the risk of complication should be balanced by a significant benefit.

**Long-term changes in pulmonary function**

Although the pathophysiology associated with the acute phase of inhalation injury has been studied extensively both clinically and through experimental models, the same cannot be said for the long-term alterations in pulmonary function that occur in the months and years following a burn and inhalation injury. Palmieri has discussed some of the theoretical reasons why it is difficult to evaluate the long-term clinical effects of inhalation injuries related to burns.\textsuperscript{73} Any current study of long-term changes in pulmonary function after inhalation injury will find it difficult to determine which changes are due to the effects of inhaled irritants at the time of injury and which result from ventilator-induced lung injury when mechanical ventilation often was accomplished with higher tidal volumes and airway pressures than are currently used. Likewise, persistent changes resulting from ARDS caused by systemic inflammatory responses to the burn injury or sepsis also contribute an undetermined component to the morbidity. Massive burn injury also impairs muscle mass and strength along with chest wall compliance, which can affect respiratory effort even in the absence of inhalation injury. As Palmieri points out, none of the reports of long-term pulmonary changes after inhalation injury relate the degree of acute pulmonary insult to the long-term changes.\textsuperscript{74} Pre-existing lung disease was also not considered in previous studies. Most studies involve relatively small groups of patients studied at different times and by different means, which make it difficult to compare results between studies.

One way post-injury pulmonary function has been shown to be manifest is by a hyperactive or bronchospastic condition of the airways. This was shown to persist for at least 6 months in one study, along with inflammatory changes in the bronchial mucosa and elevated inflammatory cytokine (TNF\textsubscript{\alpha}), interferon (IFN\textsubscript{\gamma}), and interleukin (IL)-2 levels in serum and bronchoalveolar lavage fluid. The majority of subjects, however, had normal pulmonary function tests.\textsuperscript{74} Longer-term studies have in some cases shown the development of obstructive and restrictive patterns on pulmonary function testing, indicating that normal lung function may not always be regained following recovery from inhalation injury.\textsuperscript{75–77} In a pediatric burn cohort, no difference in exercise tolerance was noted between children who had sustained an inhalation injury and those who had not. However, the children who had had an inhalation injury achieved their goal with a significantly higher respiratory rate, and had a higher incidence of abnormal lung function.\textsuperscript{77} Conversely, an adult study found no evidence of altered respiratory function after inhalation injury, or any significant exercise intolerance in those tested.\textsuperscript{78}

**Figure 19.4** (a) Thermal necrosis of laryngeal structures as seen in this photograph is an indication for tracheostomy to minimize laryngeal injury. A tracheostomy was performed on this patient soon after admission, and after recovery from his burns and decannulation of his trachea his voice was normal. (b) Thermal and mechanical injury to the larynx can result in posterior glottic scars and webs, as in this endoscopic image. Early diagnosis of injury can facilitate care to minimize long-term effects.
laryngeal injuries as early as possible. When they are recognized, tracheostomy can help minimize exacerbation of the injury by a translaryngeal airway. Consultation with a laryngologist may make such interventions more timely.

**Potential future therapeutic strategies**

The hypothesis described above offers the possibility for future development of numerous pharmacological interventions. One of the most obvious areas for treatment would be the use of antioxidants. Burned patients are immensely depleted of antioxidants, especially vitamin E. In this clinical scenario ROS and RNS play major roles in organ damage in addition to mediation of the pathophysiology. 

Nebulization of γ tocopherol, a form of vitamin E that scavenges both ROS and RNS, has been shown to be beneficial. On the other hand, inhibitors of NOS, and PARP, as well as compounds that catalyze the breakdown of peroxynitrite, have also been shown to be effective in reversing the acute changes in pathophysiology.

Recently there have been reports that hydrogen sulfide may have therapeutic benefits in lung injury. We have tested hydrogen sulfide in both murine and ovine models of burn injury and found therapeutic benefit.

As we have learned more and more about the pathophysiology and treatment of inhalation injury, there have been more survivors. Examination of these individuals several years after the injury showed that many had evidence of excessive deposition of collagen in their lungs. Perhaps initial treatment of patients might have an important effect on the latter long-term pathophysiology. This is certainly an area for future investigation. Nitric oxide synthase, the enzyme that plays a major role in the acute aspects of injury, has the amino acid arginine as its substrate, as does arginase, the enzyme that is the basis of collagen deposition. Thus inhibition of NOS could make more arginine available for the arginase and hence collagen deposition. In a consensus conference, the faculty from the Shriners Hospitals met to discuss potential therapies for inhalation injury. Clinical trials will be necessary before the effectiveness of these novel interventions is established.

**Further reading**


References


Introduction

The multitude of respiratory complications caused by smoke inhalation, thermal burns, and their treatment epitomize the clinical challenges which confront respiratory care practitioners. Smoke inhalation injury and its sequelae impose demands upon the respiratory care practitioners who play a central role in its clinical management. These demands may range from intubation and resuscitation of victims in the emergency room to assistance with diagnostic bronchoscopies, to performance of pulmonary function studies, monitoring of arterial blood gases, airway maintenance, chest physiotherapy, and mechanical ventilator management. Additional demands are placed upon the respiratory care practitioner in the rehabilitation phase in determining disability or limitations diagnosed by pulmonary function studies or cardiopulmonary stress testing. In some countries outside the United States, the duties of the respiratory care practitioner are augmented by a combination of physicians, nurses, and physiotherapists. It is imperative that a well-organized, protocol-driven approach to respiratory care of the burn patient be utilized so that improvements can be made, and the morbidity and mortality associated with inhalation injury can be reduced (Box 20.1). This chapter provides an overview of the common hands-on approaches to the treatment of inhalation injury, with emphasis on mucociliary clearance techniques, pharmacologic adjuncts, mechanical ventilation, infection control, and the late complications associated with inhalation injury.

Bronchial hygiene therapy

Airway clearance techniques are an essential component of respiratory management of patients with smoke inhalation. Bronchial hygiene therapy is a term used to describe several of the modalities intended to accomplish this goal. Therapeutic coughing, chest physiotherapy, early ambulation, airway suctioning, therapeutic bronchoscopy, and pharmacologic agents have been effective in the removal of retained secretions.

Therapeutic coughing

Therapeutic coughing functions to promote airway clearance of excess mucus and fibrin cast in the tracheal bronchial tree. The impairment of the cough mechanism will result in retained secretions, bronchial obstruction, atelectasis, and/or pneumonia. A cough may be either a reflex or a voluntary action. The mechanisms of a cough include:

- a deep inspiration;
- the closure of the glottis;
- contraction of the muscles of the chest wall, abdomen, and pelvic floor;
- opening of the glottis; and
- a rapid expulsive exhalation phase.

During a cough, alveolar, pleural, and subglottic pressures may rise as much as 200 cmH₂O. A failure of the cough mechanism may be due to an impairment of any step in the sequences described. When this occurs, it is necessary to perform techniques which are used to improve the cough.

Series of three coughs

The patient is asked to start a small breath and small cough, then a bigger breath and harder cough, and finally a really deep breath and hard cough. This technique is especially effective for postoperative patients who tend to splint from pain.

Tracheal tickle

The therapist places the index and middle finger flat in the sternal notch and gently massages inward in a circular fashion over the trachea. This is most effective in obtunded patients or in patients coming out of anesthesia.

Cough stimulation

Patients with artificial airways cannot cough normally since a tube is either between the vocal cords (endotracheal) or below the cords (tracheostomy). Adequate pressure cannot be built up without approximation of the cords. These patients may have a cough stimulated by inflating the cuff on the tube, giving a large, rapid inspiration by a manual resuscitation bag, holding the breath for 1–2 s, and rapidly allowing the bag to release and exhalation to ensue. This technique is normally performed by two persons and is made more effective by one therapist performing vibration and chest compressions from the time of the inspiratory hold, all during exhalation. Cough and deep breathing exercises are encouraged every 2 h to aid in removing retained secretions.
Box 20.1 Inhalation injury treatment protocol

- Titrate humidified oxygen to maintain SaO2 >90%
- Cough, deep breath exercises every 2 h
- Turn patient side to side every 2 h
- Chest physiotherapy every 4 h
- Aerosolize 3 cc of 20% N-acetylcysteine every 4 h with a bronchodilator
- Alternate aerosolizing 5000 units of heparin with 3 cc of normal saline every 4 h
- Nasotracheal suctioning as needed
- Early ambulation on postoperative day 5
- Sputum cultures for intubated patients every M-W-F
- Pulmonary function studies prior to discharge and at outpatient visits
- Patient/family education regarding inhalation injury.

The protocol is continued for 7 days.

Chest physiotherapy

Chest physiotherapy has come to mean gravity-assisted bronchial drainage with chest percussion and vibrations. Studies have shown that a combination of techniques are effective in secretion removal.3-6

Bronchial drainage/positioning

Bronchial drainage/positioning is a therapeutic modality that uses gravity-assisted positioning designed to improve pulmonary hygiene in patients with inhalation injury or retained secretions. There are 12 basic positions in which patients can be placed for postural drainage. Due to skin grafts, donor sites, and the use of air fluid beds, clinical judgment dictates that most of these positions are not practical. In fact, positioning in the Trendelenburg and various other positions may acutely worsen hypoxemia. Evidence has shown that a patient’s arterial oxygenation may fall during positioning.7 To accomplish the same goal it is common practice, in intensive care units, to turn patients side to side every 2 h so as to aid in mobilizing secretions (Fig. 20.1).

Percussion

Percussion aids in the removal of secretions from the tracheal bronchial tree. Percussion is done by cupping the hand so as to allow a cushion of air to come between the percusor’s hand and the patient. If this is done properly, a popping sound will be heard when the patient is percussed. There should be a towel between the patient and the percusor’s hand in order to prevent irritation of the skin.8 Percussion is applied over the surface landmarks of the bronchial segments that are being drained. The hands rhythmically and alternately strike the chest wall. Incisions, skin grafts, and bony prominences should be avoided during percussion (Fig. 20.2).

Vibration/shaking

Vibration/shaking is a shaking movement used to move loosened secretions to larger airways so that they can be coughed up or removed by suctioning. Vibration involves rapid shaking of the chest wall during exhalation. The percusor vibrates the thoracic cage by placing both hands over the percussed areas and vibrating into the patient, isometrically contracting or tensing the muscles of their arms and shoulders. Mechanical vibrations have been reported to produce good clinical results. Gentle mechanical vibration may be indicated for patients who cannot tolerate manual percussion (Fig. 20.3). Chest physiotherapy techniques should be used every 2–4 h for patients with retained secretions. Therapy should continue until breath sounds improve.

Early ambulation

Early ambulation is another effective means of preventing respiratory complications. Patients routinely should be helped out of bed on postoperative day 5 and encouraged to ambulate and sit in a chair. With appropriate use of analgesics, even patients on continuous ventilatory support can be helped out of bed and into a chair (Fig. 20.4). The rocking chair (Fig. 20.5) has several beneficial effects:

- the patient can breathe with regions of the lungs which are normally hyperventilated;
- muscular strength and tone are preserved;
- contractions are prevented and exercise tolerance is maintained.9
Airway suctioning

Airway suctioning is another method of clearing an airway. Normal bronchial hygiene is usually accomplished by the mucociliary escalator process. When these methods are not effective in maintaining a clear airway, tracheobronchial suctioning is indicated. Nasotracheal suctioning is intended to remove from the trachea accumulated secretions and other foreign material which cannot be removed by the patient’s spontaneous cough or less-invasive procedures. Nasotracheal suctioning has been used to avoid intubation which was solely intended for the removal of secretions. Nasotracheal suctioning refers to the insertion of a suction catheter through the nasal passages and pharynx into the trachea in order to aspirate secretions or foreign material. The first step in this process is to hyperoxygenate the patient with 100% oxygen. The patient should be positioned in the Fowler’s position and the catheter slowly advanced through the nares to a point just above the larynx. The therapist or nurse then listens for air sounds at the proximal end of the catheter. When airflow is felt to be strongest and respiratory sounds are loudest, the tip of the catheter is immediately above the epiglottis. On inspiration, the catheter is advanced into the trachea. After the vocal cords have been passed, a few deep breaths are allowed and the patient is reoxygenated. Suction is begun while the catheter is slowly withdrawn from the trachea. The patient should not be suctioned for more than 15 s without being reoxygenated. Suctioning is not without potential hazards. Complications include irritation of the nasotracheal mucosa with bleeding, abrupt drops in \( P_{O_2} \), vagal stimulation, and bradycardia. Preoxygenating and limiting suction time have been shown to decrease or eliminate the fall in the \( P_{O_2} \). Sputum cultures should be performed for microbiological identification when they are clinically indicated. Patients on mechanical ventilation should have sputum cultures performed once per week.

Therapeutic bronchoscopy

When all other techniques fail to remove secretions, the use of the fiberoptic bronchoscope has proven to be of benefit. In addition to its diagnostic functions, bronchoscopy retains important therapeutic applications. Copious secretions encountered in patients with inhalation injury may require repeated bronchoscopic procedures when more conservative methods are unsuccessful. The modern fiberoptic bronchoscope is small in diameter, flexible, and has a steerable tip that can be maneuvered into the fourth- or fifth-order bronchi for examination or specimen removal.

Pharmacologic adjuncts

Bronchodilators

Bronchodilators can be helpful in some cases. Inhalation injury to the lower airways results in a chemical tracheobronchitis which can produce wheezing and bronchospasms. This is especially true for patients with preexisting reactive airway diseases. Most drugs used in the management of bronchospasms are believed to act on the biochemical mechanism which controls bronchial muscle tone. Aerosolized sympathomimetics are effective in two ways: they...
result in bronchial muscle relaxation and they stimulate mucociliary clearance. The newer bronchodilators are more effective and have fewer side-effects than the older generation drugs. Some of the newer compounds used in the United States are worthy of note. First, metaproterenol is available in cartridge inhalers, as a liquid to be aerosolized, as an oral medication in tablets, or as a syrup. The recommended oral dose is 10–20 mg every 6–8 h; as an inhaled bronchodilator, 1–2 puffs every 3–4 h. Its duration of action as an inhaled bronchodilator is 1–5 h.16

Albuterol can also be administered orally, parenterally, and by aerosol. Albuterol is available in a metered cartridge inhaler and its standard dose is 1–2 puffs three to four times daily. Aerosolized albuterol has a duration of action of approximately 4–6 h.17

Racemic epinephrine is used as an aerosolized topical vasoconstrictor, bronchodilator, and secretion bond breaker. The vasoconstrictive action of racemic epinephrine is useful in reducing mucosal and submucosal edema within the walls of the pulmonary airways. A secondary bronchodilator action serves to reduce potential spasm of the smooth muscles of the terminal bronchioles. Water, employed as a diluent for racemic epinephrine, serves to lower both adhensive and cohesive forces of the retained endobronchial secretions, thus serving as a bond-breaking vehicle. Racemic epinephrine has also been used for the treatment of post-extubation stridor.18 Its mode of action is thought to be related to the vasoconstrictive activity, with the resultant decrease in mucosal edema. Aerosolized treatments may be given every 2 h as long as the heart rate is not increased.

Hypertonic saline offers a theoretically more effective form of mucokinetic therapy. The deposition of hypertonic droplets on the respiratory mucosa results in the osmotic attraction of fluids from the mucosal blood vessels and tissues into the airway. Thus a ‘bronchorrea’ is induced, and the watery solution helps to dilute down the respiratory tract secretions and to increase their bulk, thereby augmenting expectoration. Furthermore, there is evidence that hypertonic saline has a direct effect on the mucoprotein DNA complexes, and by reducing the cohesive intramolecular forces, the salt helps reduce the viscous properties of the mucoid fluid.19 Excessive use of hypertonic saline is not recommended because irritation can occur in the respiratory tract, absorption can occur, and burn patients who cannot tolerate the sodium load may develop edema.

Finally, aerosolized acetylcysteine is a powerful mucolytic agent in use in respiratory care. Acetylcysteine contains a thiol group; the free sulphydryl radical of this group is a strong reducing agent which ruptures the disulfide bonds that serve to give stability to the mucoprotein network of molecules in mucus. Agents that break down these disulfide bonds produce the most effective mucolysis.20 Acetylcysteine is an irritant to the respiratory tract. It can cause mucosal changes, and it may induce bronchospasm. For this reason, patients are evaluated for signs of bronchospasm, and a bronchodilator may be added if necessary. Acetylcysteine has proven to be effective in combination with aerosolized heparin for the treatment of inhalation injury in animal studies.21

Heparin/acetylcysteine combinations have been used as scavengers for the oxygen free radicals produced when alveolar macrophages are activated either directly by chemicals in smoke or by one or more of the compounds in the arachidonic cascade.22 Animal studies have shown an increased P/F ratio, decreased peak inspiratory pressures, and a decreased amount of fibrin cast formation with heparin/acetylcysteine combinations.23 In a retrospective review, Desai et al. have shown that the use of heparin/N-acetylcysteine is effective in pediatric patients with inhalation injury.24 Results indicate a significant decrease in the reintubation rates, incidence of atelectasis, and improved mortality for patients treated with heparin/N-acetylcysteine therapy. Therefore a standard treatment for patients with inhalation injury might include 5000–10000 units of heparin and 3 mL normal saline nebulized every 4 h, alternating with 3–5 mL of 20% acetylcysteine for 7 days. This insures that the patient receives an aerosolized treatment every 2 h. Baseline and daily clotting studies are recommended for the entire length of the aerosolized treatments.

A prospective randomized study on the use of nebulized heparin for the treatment of inhalation injury is necessary to validate the continued use of this mode of therapy. A multicenter study is being developed that will evaluate the effectiveness of therapy and answer some of the questions regarding the mechanism of action, safety, and affects on lung function.

**Patient/family education**

Burn care involves utilizing a family-centered care approach. Therefore the patient and family should be informed about the extent of the lung injury and the various treatment options available based upon evidence-based medicine or best practice.

**Mechanical ventilation**

Over the past 30 years, and especially over the past decade, there has been an increase in new ventilatory techniques which present alternatives for the treatment of patients with smoke inhalation. Unfortunately, although the number of options available to the clinician has appeared to increase exponentially, well-controlled clinical trials defining the specific role for each of the modes of ventilation and comparing them to other modes of ventilation have not been forthcoming. Based upon current available data, the recommendations from the American College of Chest Physicians consensus conference on mechanical ventilation generally serve as guidelines.25 The general consensus concludes:

- The clinician should choose a ventilator mode that has been shown to be capable of supporting oxygenation and ventilation and that the clinician has experience in using.
- An acceptable oxygen saturation should be targeted.
- Based primarily on animal data, a plateau pressure of greater than 35 cmH₂O is cause for concern. With clinical conditions that are associated with a decreased chest wall compliance, plateau pressures greater than 35 cmH₂O may be acceptable.
- To accomplish the goal of limiting plateau pressures, PCO₂ values should be permitted to rise (permissive hypercapnia) unless other contraindications exist that demand a more normal PCO₂ or pH.
• Positive end-expiratory pressure (PEEP) is useful in supporting oxygenation. An appropriate level of PEEP may be helpful in preventing lung damage. The level of PEEP required should be established by empirical trials and reevaluated on a regular basis.
• Large tidal volumes (8–10 mL/kg) with PEEP may be needed to improve oxygenation if the use of protective ventilatory strategies becomes ineffective. Peak flow rates should be adjusted as needed to satisfy patient inspiratory needs. Care must be taken to avoid the consequences of utilizing high ventilator pressures if large tidal volumes are required.

Animal studies performed showed a reduction in ventilator-induced injury with a reduction in plateau pressures to 35 cm of water by increasing positive end-expiratory pressure (PEEP) and decreasing tidal volume. A number of clinical trials have been conducted to support this treatment strategy. A meta-analysis of these trials was conducted by the Cochrane Anesthesia Review Group in 2007. It showed a reduction in mortality and duration of mechanical ventilation with the use of plateau pressure at <31 cm water and tidal volume at <7 mL/kg body weight. In light of this evidence, the tidal volumes used when initiating mechanical ventilation should be 6–8 mL/kg of predicted body weight. If the patient becomes obstructed with fibrin cast and presents with an acute increase in PCO₂ and decrease in PaO₂, the clinician should first provide aggressive pulmonary toilet, then consider changing over to volume ventilation with higher tidal volumes. If ventilation continues to worsen, tidal volumes of 8–10 mL/kg may be needed to provide adequate mechanical ventilation.

Modes of ventilation

Control mode

In the control mode of ventilation, the ventilator cycles automatically at a rate selected by the operator. The adjustment is usually made by a knob calibrated in breaths/min. The ventilator will cycle regardless of the patient need or desire for a breath, but guarantees a minimum level of minute ventilation in the anemic, sedated, or paralyzed patient. The control mode of ventilation is often utilized in patients with ARDS because of the high peak pressures needed to achieve adequate chest expansion. The major disadvantage with this mode is that the patient cannot cycle the ventilator and thus the minute ventilation must be set appropriately.

Assist-control mode

In the assist-control mode of ventilation, in which every breath is supported by the ventilator, a back-up control rate is set; however, the patient may choose any rate above the set rate. Using this mode of ventilation, the tidal volume, inspiratory flow rate, flow waveform, sensitivity, and control rate are set. Advantages are that assist-control ventilation combines the security of controlled ventilation with the possibility of synchronizing the breathing pattern of the patient and ventilator, and it ensures ventilatory support during each breath. Disadvantages are as follows:

• Excessive patient work occurs in case of inadequate peak flow or sensitivity settings, especially if the ventilator drive of the patient is increased.
• It is sometimes poorly tolerated in awake, nonsedated subjects and can require sedation to insure synchrony of patient and machine.
• It can cause respiratory alkalosis.
• It may worsen air trapping with patients with chronic obstructed lung disease.

Synchronized intermittent mandatory ventilation

Synchronized intermittent mandatory ventilation (SIMV) combines a preset number of ventilator-delivered mandatory breaths of present tidal volume with the facility for intermittent patient-generated spontaneous breaths. Advantages are as follows:

• The patient is able to perform a variable amount of respiratory work and yet there is the security of a preset mandatory level of ventilation.
• SIMV allows for a variation in level of partial ventilatory support from near total ventilatory support to spontaneous breathing.
• It can be used as a weaning tool.

Disadvantages are:

• Hyperventilation with respiratory alkalosis.
• Excessive work of breathing due to the presence of a poorly responsive demand valve, suboptimal ventilatory circuits, or inappropriate flow delivery could occur.
• In each case, extra work is imposed on the patient during spontaneous breaths.

Pressure control mode

In pressure-controlled ventilation all breaths are time- or patient-triggered, pressure-limited, and time-cycled. The ventilator provides a constant pressure of air to the patient during inspiration. The length of inspiration, the pressure level, and the back-up rate are set by the operator. Tidal volume is based upon the compliance and resistance of the patient’s lungs, the ventilator system, as well as on the preset pressure. Pressure control ventilation has become a frequently used mode of ventilation for the treatment of ARDS.

Pressure support ventilation

Pressure support ventilation (PSV) is a pressure-targeted, flow-cycled, mode of ventilation in which each breath must be patient-triggered. It is used both as a mode of ventilation during stable ventilatory support periods and as a weaning method. It is primarily designed to assist spontaneous breathing and therefore the patient must have an intact respiratory drive.

Advantages are:

• It is generally regarded as a comfortable mode of ventilation for most patients.
• Pressure support reduces the work of breathing.
• It can be used to overcome the airway resistance caused by the endotracheal tube.
• Pressure support may be useful in patients who are difficult to wean.

Disadvantages are:

• The tidal volume is not controlled and is dependent on respiratory mechanics, cycling frequency, and synchrony between the patient and ventilator.
• Pressure support may be poorly tolerated in some patients with high airway resistances because of the preset high initial flow rates.

Alternate modes of ventilation

During the last decade, a new concept has emerged regarding acute lung injury. In severe cases of ARDS, only a small part of the lung parenchyma remains accessible to gas delivered by mechanical ventilation.40,41 As a consequence, tidal volumes of 10 mL/kg or more may over expand and injure the remaining normally aerated lung parenchyma and could worsen the prognosis of severe acute respiratory failure by extending non-specific alveolar damage. High airway pressures may result in over distension and local hyperventilation of more compliant parts of the diseased lung. Over distension of lungs in animals has produced diffuse alveolar damage.42–44 This is the reason why alternative modes of ventilation, all based on a reduction of end-inspiratory airway pressures and/or tidal volumes delivered to the patient, have been developed and are used by many clinicians caring for patients with severe forms of acute or chronic respiratory failure. Five alternative modes of ventilation: high-frequency ventilation (HFV); high-frequency percussive ventilation (HFPV); pressure control inverse ratio ventilation (PCIRV); airway pressure release ventilation (APRV), and volumetric diffusive ventilation (VDR), will be discussed.

High-frequency ventilation

High-frequency ventilation (HFV) is the administration of small tidal volumes of 1–3 mL/kg at high frequencies of 100–3000 cpm.45 Because it is a mode of ventilation based on a marked reduction in tidal volumes and airway pressures, it has the greatest potential for reducing pulmonary barotrauma. There are a number of different types of high-frequency ventilation techniques. The two most common are high-frequency jet ventilation (HFJV) and high-frequency percussive ventilation (HFPV).

High-frequency jet ventilation is the only high-frequency mode routinely used to ventilate patients with ARDS, mainly in Europe.25 Comparative data concerning the advantages of HFJV over conventional ventilation are limited. There is no agreement, however, that HFJV is better than conventional mechanical ventilation in ARDS.46

High-frequency percussive ventilation is a relatively new technique that has shown some promise in the ventilation of patients with inhalation injury.47–49 The term HFPV refers to ventilation utilizing the VDR ventilator. Clinical studies indicate that this mode of ventilation may aid in reducing pulmonary barotrauma.47,48 In a retrospective study, Cortiella et al. have shown a decreased incidence of pneumonia, peak inspiratory pressure, and an improved P/F ratio in children ventilated with the use of HFPV as compared with controls.50

In the first prospective randomized study on HFPV, Mlcak et al. have shown a significant decrease in the peak inspiratory pressures needed to ventilate pediatric patients with inhalation injury.51 No significant differences were found for incidence of pneumonia, P/F ratios, or mortality.

Based upon clinical experience, the following guidelines are given for initial set-up of the HFPV in children (Table 20.1). The pulsatile flow (PIP) rate should set at 20 cmH₂O. The pulse frequency (high rate) should be set between 500 and 600. The low respiratory rate should be set at about 15–20. Oscillatory PEEP levels should be initially set at about 3 cmH₂O, and demand PEEP set on 2 cmH₂O. Ventilator settings are adjusted based upon the patient's clinical condition and blood gas values. To improve oxygenation, the ventilator can be set up in a more diffusive mode (increased pulse frequency) and, to eliminate carbon dioxide, the ventilator can be set up in a more convective mode (decreased pulse frequency). With this mode of ventilation, subtidal volumes are delivered in a progressive stepwise fashion until a preset oscillatory equilibrium is reached and exhalation is passive.

Clinicians must be familiar with the technique used and its possible limitations. There must be adequate humidification of the respiratory gases or severe necrotizing tracheobronchitis can occur. Special delivery devices for providing adequate humidification during HFV are required. It is not clear when and how it should be used following inhalation injury.52 Its efficacy in comparison to other modes of ventilation needs to be assessed. As the methodology to HFPV evolves, it is anticipated that HFPV will play a larger role in the care of select mechanical ventilation-dependent populations.53

Pressure control inverse ratio ventilation

Pressure control inverse ratio ventilation (PCIRV) is the use of pressure ventilation with an inspiratory/expiratory (I:E) ratio greater than 1:1. The rationale behind this is to maintain a high mean airway pressure and to hold peak alveolar pressure within a safe range. The second theoretical concept underlying PCIRV is the prolongation of inspiration to allow for recruitment of lung units with a long time constant. Deep sedation and/or paralysis is nearly always required with this mode of ventilation. At this time there is no conclusive scientific data comparing PCIRV to conventional mechanical ventilation in patients with inhalation injury.

Airway pressure release ventilation

Airway pressure release ventilation (APRV) is a pressure-regulated mode of ventilatory support that allows for time-cycled decreases in pressure to facilitate CO₂ elimination. This mode allows spontaneous breathing while limiting airway pressures and may therefore limit the amount of...
sedatives or neuromuscular blocking agents needed. APRV is a protective ventilator strategy that uses inverse ratio ventilation at two levels of PEEP. Several limited studies have suggested that APRV may be beneficial for the treatment of burn patients who develop ARDS. Evidence-based recommendations to use this mode of ventilation await outcome studies.

Volumetric diffusive ventilation

The volumetric diffusive ventilator (VDR) is a pneumatically powered, pressure limited ventilator that stacks oscillatory breaths to a selected peak airway pressure by means of a sliding venturi called a ‘phasitron’. After inspiration, exhalation is passive and ends at a selected level of oscillatory CPAP. Studies comparing VDR to high volume strategies have shown VDR improves gas exchange, decreases peak pressures and lowers mortality. However, there is a need to compare VDR to the low tidal volume ventilation being practiced more recently. Usage of the VDR requires special training; the other disadvantages are the inability to monitor tidal and minute volumes and the requirement of humidified air and nebulized saline to prevent airway desiccation.

Typical ventilator settings required

A large multicentered study by the NHLBI evaluated the use of volume ventilation with low versus high tidal volume on ARDS. This study documented a decreased incidence of mortality in patients with ARDS who were ventilated with small tidal volumes. Based upon this study, it has become clinically accepted practice to use small tidal volumes when initially setting up mechanical ventilation (Table 20.2).

Tidal volumes

In volume-cycled ventilation, a machine-delivered tidal volume is set to be consistent with adequate gas exchange and patient comfort. The tidal volume selected for burned patients normally varies between 6 and 8 mL/kg of predicted body weight. Numerous factors, such as lung/thorax compliance, system resistance, compressible volume loss, oxygenation, ventilation, and barotrauma, are considered when volumes are selected. Of critical importance is the avoidance of over distension. This can generally be accomplished by insuring that peak airway and alveolar pressures do not exceed a maximum target. Many would agree that a peak alveolar pressure greater than 35 cmH₂O in adults raises concern regarding the development of barotrauma and ventilator-induced lung injury increases. The clinician must always look at the patient to insure adequate chest expansion with the setting of the tidal volume. Expired tidal volumes should be measured for accuracy at the connection between the patient’s wye and the artificial airway. This insures that the volume selected reaches the patient and is not lost in the compressible volume of the ventilator tubing.

The range of tidal volumes will vary depending on the disease process, with some diseases requiring maximum tidal volumes and others needing less. Severe interstitial diseases such as pneumonia and ARDS may require a tidal volume of 8–10 mL/kg to adequately inflate the lungs and improve gas exchange if protective ventilatory strategies become inadequate. However, the acceptable range of 6–8 mL/kg allows the clinician to make more precise adjustments in volume, as needed by the patient.

Respiratory rate

Setting of the mandatory ventilator respiratory rate is dependent on the mode of ventilation selected, the delivered tidal volume, dead space to tidal volume ratio, metabolic rate, targeted PCO₂ levels, and level of spontaneous ventilation. With adults, set mandatory rate normally varies between 4 and 20 breaths/min, with most clinically stable patients requiring mandatory rates in the 8–12 range. In patients with inhalation injury, mandatory rates exceeding 20 per minute may be necessary, depending on the desired expired volume and targeted PCO₂. It is important to have targeted arterial blood gas values set to aid the clinical team in proper management (Table 20.3) Along with the PCO₂, pH, and patient comfort; the primary variable controlling the selection of the respiratory rate is the development of air trapping and auto PEEP.

The respiratory rates of children and infants all need to be set substantially higher than those of adults. For pediatrics, the respiratory rate can be set from 12 to 45, depending on the disease state and the level of targeted PCO₂ one wishes to achieve. Slower respiratory rates are useful in the patient with obstructed airways because slower rates allow more time for exhalation and emptying of hyperinflated areas. Arterial blood gases should be checked after the patient has been on the ventilator for approximately 20 min and the respiratory rate adjusted accordingly.

Flow rates

The selection of peak inspiratory flow rate during volume ventilation is primarily determined by the level of spontaneous inspiratory effort. In patients triggering volume breaths, patient effort, work of breathing, and patient ventilator

<table>
<thead>
<tr>
<th>Variable</th>
<th>Settings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tidal volumes</td>
<td>6–8 mL/kg</td>
</tr>
<tr>
<td>Respiratory rate</td>
<td>12–45 breaths/min</td>
</tr>
<tr>
<td>Plateau pressures</td>
<td>&lt;30 cmH₂O</td>
</tr>
<tr>
<td>IE ratio</td>
<td>1:1–1.3</td>
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<tr>
<td>Flow rate</td>
<td>40–100 L/min</td>
</tr>
<tr>
<td>PEEP</td>
<td>7.5 cmH₂O</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Variable</th>
<th>Goal</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.25–7.45</td>
</tr>
<tr>
<td>PO₂</td>
<td>55–80 mmHg or SaO₂ of 88–95%</td>
</tr>
<tr>
<td>PCO₂</td>
<td>35–55 mmHg (permissive hypercapnia can be used as long as pH &gt; 7.25)</td>
</tr>
</tbody>
</table>
synchrony depend on the selection of peak inspiratory flow.\textsuperscript{32} Peak inspiratory flows should ideally match patient peak inspiratory demands. This normally requires peak flows to be set at 40–100 L/min, depending on expired volume and the inspiratory demand.\textsuperscript{25}

**Inspiratory/expiratory (I:E) ratio**

The time allowed for the inspiratory and expiratory phases of mechanical ventilation is commonly referred to as the inspiratory/expiratory (I:E) ratio. The inspiratory part of the ratio includes the time to deliver the tidal volume before the exhalation valve opens and exhalation begins. The expiratory part of the ratio includes the time necessary for the tidal volume to exit through the exhalation valve before the next inspiration begins. The inspiratory time should be long enough to deliver the tidal volume at flow rates that will not result in turbulence and high peak airway pressures. The usual I:E ratio is 1:1–1:3.\textsuperscript{59}

In severe lung disease, it is acceptable to prolong the inspiratory time to allow for better distribution of gas and enhance oxygen diffusion. When a longer inspiratory time is required, careful attention should be given to sufficient expiration to avoid stacking of breaths and impeding venous return. Prolonged inspiratory time creates a more laminar flow, which helps to keep the peak pressures lower. Fast inspiratory times are tolerated in patients with severe airway obstruction. The fast inspiratory time allows for a longer expiratory phase, which may help to decrease the amount of overinflation.

**Inspired oxygen concentration**

As a starting point, and until the level of hypoxemia is determined, a patient placed on a ventilator should receive an oxygen concentration of 100%. The concentration should be systematically lowered as soon as arterial blood gases dictate. In general, as a result of the concerns regarding the effects of high oxygen concentration on lung injury, the lowest acceptable oxygen level should be selected as soon as possible. In patients who are difficult to oxygenate, oxygen concentrations can be minimized by optimizing PEEP and mean airway pressures and selecting a minimally acceptable oxygen saturation.\textsuperscript{60}

**Positive end-expiratory pressure**

Positive end-expiratory pressure (PEEP) is applied to recruit lung volumes, elevate mean airway pressure, and improve oxygenation.\textsuperscript{61} The level of PEEP used varies with the disease process. PEEP levels should start at 8–10 cmH\textsubscript{2}O and be increased in 2.5-cm increments. Increasing levels of PEEP, in conjunction with a prolonged inspiratory time, aids in oxygenation and allows for the safe level of oxygen to be used. The use of pressure–volume curves to determine the best PEEP level has been recommended to aid in overstretching the alveoli. This technique has certain limitations and is difficult to perform in the clinical setting. The use of PEEP trials can determine the best PEEP without causing a decrease in cardiac output.

Usually a minimum of 8 cmH\textsubscript{2}O of PEEP will be indicated for use during mechanical ventilation since tracheal intubation holds the larynx constantly open, which leads to alveolar collapse and a reduction in the functional residual capacity.

Optimal PEEP is the level of end-expiratory pressure that results in the lowering of intrapulmonary shunting, significant improvement in arterial oxygenation, and only a small change in cardiac output, arteriovenous oxygen content differences, or mixed venous oxygen tension.

In order to decide the ideal PEEP for patients with ALI or ARDS, the ARDS Network performed a multicenter, randomized, prospective clinical trial.\textsuperscript{52} ALI or ARDS patients were treated with 6 mL/kg predicted body weight tidal volumes, and randomized to either low (5 cm H\textsubscript{2}O up to 24) or high (12 cm H\textsubscript{2}O up to 24) PEEP. The trial showed no effect of higher levels of PEEP on duration of mechanical ventilation, duration of non-pulmonary organ failure, and in-hospital mortality.

**Exubation criteria**

Standard extubation criteria include a wide variety of physiologic indices that have been proposed to guide the process of discontinuing ventilatory support. Traditional indices include:

- \(\text{PaO}_2/\text{FiO}_2\) ratio of greater than 250
- Maximum inspiratory pressure of greater than 60 cmH\textsubscript{2}O
- Vital capacity of at least 15–20 mL/kg
- Tidal volume of at least 5–7 mL/kg
- Maximum voluntary ventilation of at least twice the minute volume\textsuperscript{53–66}
- An audible leak around the endotracheal tube must be present.

In general, these indices evaluate a patient’s ability to sustain spontaneous ventilation. They do not assess a patient’s ability to protect the upper airway. For this reason, traditional indices often fail to reflect the true clinical picture of a patient with an inhalation injury. For a complete evaluation prior to extubation, bronchoscopic examination will aid in determining if the airway edema has decreased enough to attempt extubation. Prior to a scheduled extubation it is recommended that reintubation equipment be set up and that the person doing the extubation be experienced in emergency intubations.

If the patient demonstrates signs of inspiratory stridor, the use of racemic epinephrine by aerosol has been effective in reducing the mucosal edema and may prevent the patient from being reintubated.

**Infection control of respiratory equipment**

Infections are the leading cause of mortality in burned patients. Pneumonia has become one of the most frequent life-threatening infections and is an important determinant of survival.\textsuperscript{65} The majority of pneumonias are nosocomial, occurring in the burned patient after 72 h of hospitalization, and are often associated with either an inhalation injury or endotracheal intubation with exposure to respiratory care equipment, or both.\textsuperscript{67–72} One of the most important risk factors predisposing to pneumonia in burned patients is...
endotracheal intubation. The incidence of pneumonia developing is estimated to be five times higher for intubated than nonintubated patients, and tracheostomy increases this risk even higher. Exposure to respiratory care equipment adds an increased risk of pneumonia above and beyond the risk associated with endotracheal intubation. After the use of nebulization equipment in respiratory care became popular, several epidemics of nosocomial pneumonia were reported. The risk of pneumonia from mechanical ventilation was significant but decreased with a better understanding of the necessity to decontaminate respiratory equipment. Intubated patients receiving respiratory care may be at an increased risk of pneumonia because of coincidental exposure to other procedures such as suctioning and bronchoscopy. Respiratory care equipment, if not properly cared for, may provide a source of extraneous organisms that can contaminate the patient’s respiratory tract.

The potential role of respiratory care equipment in providing reservoirs for organisms that are capable of infecting the lungs is well established. This problem, particularly pertaining to reservoir devices and medications, has been recognized for a number of years, and effective control strategies have been developed. Most hospitals maintain a bacteriological monitoring system, and significant contamination by this route is not likely. Contamination of the compressed gases used to operate respiratory care devices is uncommon, principally because of the desiccation of gases and the inability of most bacterial species to survive such harsh treatment. Nebulization equipment delivers a fine-particle aerosol and, if contaminated, the aerosol droplets may contain bacteria. Humidification equipment provides water vapor but does not deliver a large quantity of water in particulate form. In fact, humidifiers generally remove bacteria from airstreams, because the bacteria are physically trapped in the fluid phase and are not vaporized.

Bag-mask units have been shown to allow the persistence of infectious organisms and the subsequent infection of other patients on whom the equipment has been later used. Ventilator circuits are inevitably contaminated by the patient’s own respiratory tract flora during exhalation and coughing, and the fluid that collects in this tubing is thereby contaminated. However, the American Association for Respiratory Care evidence-based clinical practice guidelines suggest that ventilator circuits should not be changed routinely for infection control purposes. The exact length of time that circuits can be used safely is unknown.

**Handwashing**

Handwashing is generally considered the single most important procedure for preventing nosocomial infections. Regardless of whatever benefits are accrued by cleaning or sterilization, they are negated if the simple process of handwashing is overlooked. The recommended handwashing procedures depend on the purpose of washing. In most situations, a vigorous brief washing with soap under a strong running water is adequate to remove transient flora. Generally, simple handwashing with soap is performed before and after contact with patients and whenever the hands are soiled.

Antimicrobial handwashing procedures are indicated before all invasive procedures, during the care of patients in strict, respiratory, or enteric isolation and before entering intensive care units. The most commonly used agents are 70% isopropyl alcohol, iodophors, and chlorhexidine. Scrub regimens such as the povidone-iodine surgical scrub are appropriate for these areas.

### Chemical agents for sterilization/disinfection

Disinfectants act to kill microorganisms by several methods:

- oxidizing microbial cells;
- hydrolyzing;
- combining with microbial proteins to form salts;
- coagulating the proteins of microbial cells;
- denaturing enzymes; or
- modifying cell wall permeability.

### Aldehydes

Aldehydes contain some of the most commonly used antimicrobials in respiratory care practice. These agents achieve their antimicrobial action through the alkylation of enzymes.

The cidal action of glutaraldehyde is accomplished by disruption of the lipoproteins in the cell membrane and cytoplasm of vegetative bacterial forms. This reaction between the chemical glutaraldehyde and cell proteins is dependent on both time and contact. Items to be disinfected must be free of material that would inhibit contact, and adequate contact time is needed for the chemical reaction to be complete.

Alkalin glutaraldehyde, buffered by a 0.3% bicarbonate agent, is used as a 2% solution. Once activated with the buffering agent, it is fully potent for approximately 14 days. This solution is bactericidal, virucidal, and tuberculocidal within 10 min and produces sterilization when applied for 10–20 h. Equipment disinfected or sterilized with glutaraldehyde should be thoroughly rinsed and dried prior to use, because any residue would be irritating to mucous membranes.

Glutaraldehyde solutions are commonly used for the cold disinfection or sterilization of respiratory care equipment and have a large degree of safety. These solutions can be used to disinfect bronchoscopes as well as many of the current respiratory supplies.

### Alcohols

Alcohols, especially ethylene and isopropyl alcohol, are perhaps the most commonly used disinfectants. Alcohols, as a chemical family, have many desirable characteristics needed in disinfectants. They are generally bactericidal and accomplish their bactericidal activity by damaging the cell wall membrane. They also have the ability to denature proteins, particularly enzymes called dehydrogenases. For alcohol to coagulate microbial proteins, water must be present. For this reason, 70% has been considered the critical dilution for alcohol, with a rapid loss of bactericidal activity with dilutions less than 50%. Both ethyl and isopropyl alcohols are rapidly effective against vegetative bacteria and tubercle bacilli but are not sporicidal.

To be sure that the current infection control practice is effective in each institution, random microbiological cultures should be done whenever a problem is suspected, or...
persistent severe respiratory symptoms, the severity of the impairment should be documented and the patient evaluated for a pulmonary rehabilitation program.

**Conclusion**

Inhalation injury and associated major burns provide a challenge for healthcare workers who provide direct hands-on care. The technical and physiologic problems which complicate the respiratory management of these patients require a practical knowledge of the possible sources of nosocomial infections. Patients with inhalation injury frequently require the use of respiratory care equipment that, if not properly cared for, can aid in the spread of infections. Important priorities for reducing the risk of infections include: an aggressive bronchial hygiene therapy program, the adherence to established infection control practices, the use of universal precautions during procedures, meticulous cleaning of respiratory care equipment, as well as routine epidemiologic surveillance of the established infection control practices within each institution.

It is imperative that a well-organized protocol-driven approach to respiratory care of the burn patient be utilized so that further improvements can be made, and the morbidity and mortality associated with inhalation injury be reduced.

**Further reading**


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**Late complications of inhalation injury**

**Tracheal stenosis**

Tracheal complications are commonly seen and consist of tracheitis, tracheal ulcerations, and granuloma formation. The location of the stenosis is almost invariably subglottic and occurs at the site of the cuff of the endotracheal or tracheostomy tube. Several problems arising after extubation represent sequelae of laryngeal or tracheal injury incurred during the period of incubation. While tracheal stenosis or tracheomalacia are usually mild and asymptomatic, in some patients they can present as severe fixed or dynamic upper airway obstructions. These conditions can require surgical correction. In the management of intubated patients, such complications should be mostly preventable by meticulous attention to the tracheostomy or endotracheal tube cuff. Inflation of the cuff should be to the minimal pressure level consistent with preventing a leak in the ventilator at end inspiration.

**Obstructive/restrictive disease**

Chronic airway disease is a relatively rare reported sequel of inhalation injury and its supportive treatment. Spirometry is a useful screening tool for airway obstruction. Reports in the literature for adults indicate that lung function returns to normal after inhalation injury. However, Mlcak et al. reported pulmonary function changes following inhalation injury for up to 10 years post-injury in a group of severely burned children. Fortunately, most pulmonary function abnormalities will persist for only months following lung parenchymal injury. In the great majority of cases, eventual resolution of both symptoms and physiologic abnormalities will occur. During the resolution phase, serial measurement of airflow obstruction should be obtained. Desai et al. demonstrated that physiologic insults that occur as a result of thermal injury may limit exercise endurance in children. Data from exercise stress testing showed evidence of a respiratory limitation to exercise. This was confirmed by a decrease in the maximal heart rate, decrease in the maximal oxygen consumption, and increased respiratory rate. In the cases of persistent severe respiratory symptoms, the severity of the impairment should be documented and the patient evaluated for a pulmonary rehabilitation program.


The systemic inflammatory response syndrome
Edward R. Sherwood, Daniel L. Traber

Introduction

Burn patients, with or without inhalation injuries, commonly exhibit a clinical picture that is largely produced by systemic inflammation. The phrase ‘systemic inflammatory response syndrome (SIRS)’ was introduced to designate the signs and symptoms of this condition. SIRS has a continuum of severity ranging from physiologic alterations such as tachycardia, tachypnea, fever, and leukocytosis, to refractory hypotension and, in its most severe form, shock and multiple organ system dysfunction. In thermally injured patients the most common cause of SIRS is tissue damage caused by the burn itself. Sepsis, defined as SIRS in the presence of infection, is also common in burn patients and is a significant cause of morbidity and mortality. Starting from a local infection at the burn wound, an infected catheter tip or pulmonary infection, the spread of microbes and their toxins can further potentiate systemic inflammation. Pathological alterations of metabolic, cardiovascular, pulmonary, renal, gastrointestinal, and coagulation systems occur as a result of the hyperactive immune system. This chapter will review current understanding of SIRS and the associated immunological, cardiovascular, and pulmonary dysfunction that occurs following trauma and thermal injury.

Definition of SIRS

The phrase ‘systemic inflammatory response syndrome (SIRS)’ was recommended by the American College of Chest Physicians/Society for Critical Care Medicine (ACCP/SCCM) consensus conference in 1992 to describe a systemic inflammatory process, independent of its cause. The proposal was based on clinical and experimental results indicating that a variety of conditions, both infectious and non-infectious (i.e. burns, ischemia–reperfusion injury, multiple trauma, pancreatitis), induce a similar host response. Two or more of the following conditions must be present for the diagnosis of SIRS to be made:

- body temperature >38°C or <36°C;
- heart rate >90 beats/min;
- respiratory rate >20/min or PaCO₂ <32 mmHg;
- leukocyte count >12 000/µL, <4000/µL, or >10% immature (band) forms.

All of these pathophysiologic changes must occur as an acute alteration from baseline in the absence of other known causes. This definition is very sensitive and non-specific, and most of the SIRS criteria are also addressed in other scoring systems of injury-induced physiologic derangement, such as the Acute Physiology and Chronic Health Evaluation (APACHE), Mortality Probability Model (MPM), and Simplified Acute Physiology Severity (SAPS) systems. Several investigators have criticized the definition of SIRS as being too sensitive and encompassing the majority of ICU patients, and certainly the vast majority of patients suffering extensive thermal injury.²,³ The initial definition of SIRS also did not address the continuum of disease severity as was defined for sepsis. Criteria for the diagnosis of severe sepsis included the additional derangements of organ dysfunction, hypotension, and hypoperfusion. Evidence of hypoperfusion included, but was not limited to, the presence of lactic acidosis, oliguria, and altered mental status. Septic shock was characterized by hypotension and hypoperfusion in patients who were adequately volume resuscitated or required treatment with catecholamines or other vasoactive drugs to support cardiovascular function. Muckart and Bhagwancee,² in an effort to define a continuum of severity for SIRS, later proposed the categories of severe SIRS and SIRS-associated shock. These conditions were defined by the same criteria as severe sepsis and septic shock in the absence of demonstrable infection. In its most severe form, SIRS can induce organ injury and subsequent multiple organ dysfunction syndrome (MODS).

Despite the limitations in the definitions of SIRS and sepsis, most clinicians and investigators generally adopted the SIRS concept. However, the initial definition and criteria were not felt to be optimized. To address these issues, a second consensus conference was assembled in 2001.⁴ The goal of this conference was to revisit the previously defined criteria for SIRS and sepsis as well as to determine whether revision of these criteria was indicated. The consensus was that the concepts of sepsis and SIRS are useful but the diagnostic criteria are overly sensitive and non-specific. The participants added additional criteria that defined metabolic, biochemical and functional alterations associated with SIRS and sepsis. Among these were hyperglycemia, edema, elevated plasma C-reactive protein concentration, coagulation abnormalities, thrombocytopenia, ileus, and hyperbilirubinemia. The group further proposed a staging system for sepsis and SIRS that could be used to stratify patients for prediction of outcome. This staging system, termed PIRO, defined several criteria, including the predisposition of patients to a poor outcome as determined by premorbid conditions and possible genetic factors. Other factors include the severity and type of insult, the host response to injury.
and the presence of organ dysfunction. The participants proposed that this model could be used to generate more specific criteria for defining the SIRS phenomenon. Although the validity of this approach remains to be established, Rubulotta recently reported that the PIRO criteria have predictive value regarding mortality in septic patients. However, the validity of the staging system remains to be fully determined.

Another pitfall in the designation of SIRS is the difficulty of applying the initial criteria to children. Some of the criteria, particularly those for heart rate and respiratory rate, fall within the normal physiologic range for young children. In 2002, a consensus conference was assembled to define criteria for sepsis and SIRS in children. The participants defined six age groups based on clinical and physiological characteristics (Table 21.1). SIRS was defined as the presence of at least two of the following four criteria, one of which must be abnormal temperature or leukocyte count:

- temperature $>38.5^\circ\text{C}$ or $<36^\circ\text{C}$;
- tachycardia, defined as mean heart rate $>2$ SD above normal for age or for children $<1$ year;
- bradycardia, defined as heart rate $<10\%$ of normal for age;
- mean respiratory rate $>2$ SD above normal for age or requirement for mechanical ventilation;
- leukocyte count elevated or depressed for age.

Severe sepsis was defined as sepsis plus one of the following: cardiovascular dysfunction, acute respiratory distress syndrome or two or more organ dysfunctions (respiratory, renal, neurologic, hematologic or hepatic).

The definition of septic shock is problematic in children because children can maintain blood pressure until they become severely ill. Therefore, hypotension is not a useful criterion for diagnosing shock in children. This group proposed criteria for septic shock that included the presence of tachycardia in conjunction with signs of decreased peripheral perfusion, such as decreased capillary refill, decreased peripheral pulses, decreased urine output, altered mental status and cold/mottled extremities.

Several studies have been conducted with the goal of determining the prognostic value of the SIRS designation. In the acute setting, SIRS has been demonstrated in the majority of critically injured patients and the intensity of the response correlates directly with the severity of injury. The presence of SIRS within the first 24 hours after severe injury has not served as a reliable predictor of mortality in trauma or burn patients. However, the presence of shock is an important predictor of poor outcome, particularly when associated with MODS. In addition, the presence of more than two of the SIRS criteria in the setting of acute injury has correlated with increased morbidity and mortality. A study by Rangel-Frausto et al. showed that trauma patients who did not meet SIRS criteria had a mortality rate of 3%, compared to 6% in those with two SIRS markers. Patients with three or four SIRS criteria had mortality rates of 10% and 17%, respectively, whereas those with culture-negative shock had a 46% death rate. Haga et al. have shown that the persistence of SIRS for more than 3 days in surgical patients is a harbinger of complications and is associated with increased morbidity. Talmor et al. reported that persistence of SIRS to the second postoperative day in high-risk surgical patients correlated with an increased incidence of MODS. Additional studies have shown that persistence of SIRS criteria for more than 3 days in trauma and burn patients is associated with worse outcome. Therefore, three important factors appear to determine the effect of SIRS on the host. The first is the severity of the initial inflammatory response. This response is proportional to the severity of injury, and the presence of shock or MODS within the first 24 hours after injury carries a poor prognosis. The second determinant is the persistence of SIRS beyond the first few days of injury. Specifically, prolongation of SIRS beyond the second day after severe trauma or thermal injury is associated with an increased complication rate. Factors that appear to be important in reducing the incidence of a prolonged inflammatory state include adequate fluid resuscitation within the first 24 hours after injury, aggressive excision of necrotic tissue and enteral feeding. A third factor is the adaptive capacity of the host. Results of several studies have shown that extremes of age and the presence of coexisting disease will diminish the adaptive capacity of the host and predict a worse prognosis for any given severity of injury.

### The initiating event

The crucial pathophysiologic event that precipitates systemic inflammation is tissue damage. This can occur both as a result of direct injury to tissues from mechanical or thermal trauma and as a result of cellular injury induced by ischemia and reperfusion. Injury results in the acute release of pro-inflammatory cytokines such as tumor necrosis factor-α (TNFα), interleukin (IL)-1 and IL-6. If injury is severe, such as in extensive thermal injury, a profound release of cytokines and non-cytokine mediators of inflammation occurs, resulting in the induction of a systemic inflammatory reaction (Fig. 21.1). The ability of the host to adapt to this systemic inflammatory response is dependent on the magnitude and duration of the response as well as the adaptive capacity of the host. If the insult and the host’s response to it are beyond the adaptive capacity of the host, or if adequate resuscitation is not promptly initiated, organ injury may ensue during the early post-injury period. Factors that have been implicated in the worsening or prolongation of SIRS include inadequate resuscitation during the acute phase following thermal injury, persistent or intermittent infection, ongoing tissue necrosis, and translocation of bacteria or endotoxin across the bowel.

The actual mechanisms that initiate trauma-induced inflammation at the cellular and molecular levels are becoming increasingly understood. Two primary sensing systems have been identified. Recent evidence has implicated the ability of Toll-like receptors (TLR) to respond to endogenous cellular factors that are produced or released following tissue

<table>
<thead>
<tr>
<th>Table 21.1 Pediatric age groups for SIRS criteria</th>
</tr>
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<tbody>
<tr>
<td>Newborn 0 day to 1 week</td>
</tr>
<tr>
<td>Neonate 1 week to 1 month</td>
</tr>
<tr>
<td>Infant 1 month to 1 year</td>
</tr>
<tr>
<td>Toddler or preschool 2 to 5 years</td>
</tr>
<tr>
<td>School age 6 to 12 years</td>
</tr>
<tr>
<td>Adolescent 13 to 18 years</td>
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</tbody>
</table>

...
The systemic inflammatory response syndrome (SIRS) is a complex response to tissue injury that involves the release of proinflammatory mediators and the activation of immune cells. This response can be accompanied by a compensatory anti-inflammatory response (CARS), where the host produces anti-inflammatory mediators such as IL-10 and transforming growth factor-β (TGF-β). In many cases, SIRS and CARS may coexist, leading to a state known as the counter anti-inflammatory response syndrome (CARS), where the host attempts to limit further inflammatory injury. However, this anti-inflammatory state may lead to immunosuppression, which can predispose the host to opportunistic infections. If uncontrolled, local infections may escalate to severe systemic infections and sepsis.

The two-hit hypothesis

Some investigators have described a phenomenon in which the injured host manifests an exaggerated inflammatory response if confronted with a secondary inflammatory stimulus during the post-injury period. This phenomenon has been termed the ‘two-hit hypothesis.’ Although the
pathobiology of the two-hit hypothesis is not completely understood, monocytes and macrophages appear to play a central role in mediating the process. For example, the lymphokine α-interferon (IFN-α), produced during the initial injury, might act as the first signal and prime macrophages for a heightened inflammatory response if a second stimulus is encountered. Several changes in macrophage function, including an increase in the transcription rate of mRNA for TNFα, can be induced by exposure to IFN-α. However, TNFα protein is not produced in large amounts in response to the first inflammatory insult. If a second stimulus, such as endotoxin exposure, is provided in even a small dose, macrophages are triggered to become fully activated and to secrete large amounts of TNFα. Studies by Paterson et al. show that macrophages have increased responsiveness to ligands for Toll-like receptor 2 (TLR2) and TLR4 following burn injury. TLR2 and TLR4 are proteins that play an integral role as components of receptor complexes for various microbial products such as peptidoglycans, lipoproteins, and lipopolysaccharide. Enhancement of TLR2 and TLR4 responses during the post-injury period may be one mechanism contributing to the two-hit phenomenon. T lymphocytes may also become hyperresponsive during the post-injury period. Zang et al. showed an exaggerated response to bacterial superantigens 1 day after burn injury in mice. Superantigens, such as staphylococcal enterotoxins, induce polyclonal activation of T cells and cause a shock syndrome that is similar to endotoxin shock. This mechanism may also contribute to the hyperinflammatory response seen in many patients during the post-burn period.

The exaggerated response to a secondary stimulus seen in severely injured patients appears to have functional consequences. Several studies that focused on organ injury caused by systemic inflammatory processes indicate that a phenomenon comparable to the cellular events described above can occur in severely injured patients.24 Dehring et al. found more persistent pulmonary hypertension and an exaggerated hyperdynamic response to bacteremia in sheep when a week-old thermal injury preceded systemic bacterial challenge.25 In a rat model of intestinal ischemia–reperfusion injury and endotoxemia, lung albumin leak and mortality rate increased only if both injuries occurred sequentially.26 Combined administration of low doses of endotoxin and TNFα to rats caused hypotension and metabolic effects that are commonly seen after giving a highly lethal dose of either compound alone.27 These findings are in keeping with the fact that multiple organ damage usually develops over a prolonged period during which several insults might occur. It also emphasizes why it is so important to minimize inflammatory insults such as tissue ischemia or infection, particularly in patients in whom systemic inflammation is already present.

Cytokine and non-cytokine mediators of SIRS

Several proinflammatory cytokines, chemokines, and non-cytokine inflammatory mediators play a role in the pathogenesis of SIRS. Cytokines comprise a broad group of polypeptides with varied functions within the immune response (Table 21.2). The classic mediator of systemic inflammation is TNFα. TNFα is released primarily by macrophages within minutes of local or systemic injury, and modulates a variety of immunologic and metabolic events.28 At sites of local infection or inflammation TNFα initiates an immune response that activates antimicrobial defense mechanisms and, once the infection is eradicated, tissue repair. It is a potent activator of neutrophils and mononuclear phagocytes, and also serves as a growth factor for fibroblasts and as an angiogenesis factor. However, systemic release of TNFα can precipitate a destructive cascade of events that can result in tissue injury, organ dysfunction and, potentially, death. Among the systemic effects of TNFα are the induction of

Figure 21.3 The inflammasome is an intracellular signaling complex that is activated by a variety of endogenous and microbial products and causes activation of inflammatory caspases such as caspase-1. Activation of this system results in release of IL-1 and IL-18 during periods of inflammation. (From Schroder K, Tschopp J. The inflammasomes. Cell. 2010 140: 821–32)
fever, stimulation of acute-phase protein secretion by the liver, activation of the coagulation cascade, myocardial suppression, induction of systemic vasodilators with resultant hypotension, catabolism, and hypoglycemia.28,29 Numerous studies have shown that administration of TNFα to experimental animals will mimic the systemic inflammatory response observed in sepsis and after severe injury. Another important effect of TNFα is its ability to induce apoptosis of a variety of cell types.30 TNF-induced apoptosis may be one mechanism by which it induces tissue injury at high systemic concentrations.

TNFα is also a potent stimulus for the release of other proinflammatory mediators, particularly IL-1 and IL-6. IL-1 is released primarily by mononuclear phagocytes and its physiologic effects are essentially identical to those of TNFα.31 However, important differences exist between the functions of IL-1 and TNFα. Most notably, IL-1 does not induce tissue injury or apoptotic cell death by itself, but can potentiate the injurious effects of TNFα. The IL-1 family of proteins, including IL-18, are the only group of cytokines for which known natural antagonists have been identified. The IL-1 receptor antagonists (IL-1ra) bind to the IL-1 receptor but do not induce receptor activation.33 These proteins appear to function as competitive inhibitors of IL-1 action. As noted earlier, the systemic release of IL-1 is dependent on the activation of inflamasomes and caspase-1.34

IL-6 is another protein that is commonly increased in the circulation of patients with SIRS.35 Macrophages, endothelial cells, and fibroblasts secrete this protein. IL-6 itself does not induce tissue injury but its presence in the circulation has been associated with poor outcome in trauma patients, probably because it is a marker of ongoing inflammation. The primary effect of IL-6 is to induce secretion of acute-phase proteins from the liver as well as to serve as a growth and differentiation factor for B lymphocytes.

Interferon-γ (IFN-γ) is a cytokine that facilitates the amplification of the acute inflammatory response, particularly the stimulation of cytokine secretion, phagocytosis, and respiratory burst activity by macrophages. IFN-γ is secreted primarily by T lymphocytes and natural killer (NK) cells in response to antigen presentation as well as macrophage-derived cytokines such as IL-12 and IL-18. The primary effect of IFN-γ is to amplify the inflammatory response of macrophages. In response to IFN-γ, the phagocytic and respiratory burst activities of macrophages are increased, secretion of inflammatory mediators such as TNFα and IL-1 is enhanced, and antigen presentation is potentiated by upregulation of class II major histocompatibility complex. Blockade of IFN-γ production or function has been shown to markedly reduce the deleterious inflammatory effects induced by bacterial endotoxin.36 Therefore, IFN-γ is believed to be an important factor in the amplification of SIRS.

Chemokines are a family of proteins that function primarily as chemotactic factors for leukocytes and, when produced inappropriately or in excess, can contribute to damaging systemic or local inflammation (Table 21.3). IL-8 is the most widely studied chemokine in the setting of sepsis and SIRS; it is a potent chemoattractant for neutrophils and is a major factor in recruiting neutrophils to inflammatory foci. Several studies have shown that IL-8 plays a role in

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**Table 21.2 Cytokine and chemokine mediators of systemic inflammation**

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>Polypeptide size</th>
<th>Cell source</th>
<th>Cell target</th>
<th>Primary effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor necrosis factor-α (TNFα)</td>
<td>17 kD</td>
<td>Monocytes, macrophages, T lymphocytes</td>
<td>(a) Neutrophils (b) Endothelial cells (c) Hypothalamus (d) Liver (e) Muscle, fat (f) Heart (g) Macrophages (h) T lymphocytes (i) Various tissues</td>
<td>Activation (inflammation) Activation (inflammation/coagulation) Release of vasodilators (NO) Fever Acute phase response Catabolism Myocardial suppression Release of cytokines, inflammation Inflammation Apoptosis?</td>
</tr>
<tr>
<td>Interleukin-1 (IL-1)</td>
<td>17 kD</td>
<td>Monocytes, macrophages</td>
<td>(a) T cells (b) Endothelial cells (c) Liver (d) Hypothalamus (e) Muscle, fat</td>
<td>Activation (inflammation) Activation (inflammation/coagulation) Release of vasodilators (NO) Fever Acute phase response Catabolism</td>
</tr>
<tr>
<td>Interleukin-6 (IL-6)</td>
<td>26 kDa</td>
<td>Monocytes, macrophages, T cells, endothelial cells</td>
<td>(a) Liver (b) B cells</td>
<td>Acute phase response Activation</td>
</tr>
<tr>
<td>Interleukin-8 (IL-8)</td>
<td>10 kDa</td>
<td>Monocytes, macrophages, endothelial cells</td>
<td>Neutrophils</td>
<td>Chemotaxis, activation</td>
</tr>
<tr>
<td>Interferon-γ (IFN-γ)</td>
<td>21–24 kDa</td>
<td>T cells, NK cells</td>
<td>Macrophages</td>
<td>Activation (inflammation)</td>
</tr>
<tr>
<td>Interleukin-12 (IL-12)</td>
<td>70 kDa</td>
<td>Macrophages</td>
<td>T cells, B cells, NK cells</td>
<td>Activation, differentiation</td>
</tr>
<tr>
<td>Interleukin-18</td>
<td></td>
<td>Macrophages</td>
<td>T cells, NK cells</td>
<td>Activation, differentiation</td>
</tr>
<tr>
<td>IL-10</td>
<td></td>
<td>Monocytes/Th2 lymphocytes, mast cells, regulatory T cells</td>
<td>Macrophages Th1 lymphocytes, NK cells</td>
<td>Inhibition, activation regulation</td>
</tr>
</tbody>
</table>
Production of most soluble mediators of inflammation is regulated at the transcriptional level. Some of the key transcription factors that control proinflammatory gene expression include nuclear factor-κB (NF-κB), AP-1 and IRF-3 (Fig. 21.4). NF-κB is composed of a family of proteins including p50 (NF-κB1), p65 (RelA), C-Rel, and p52 (NF-κB2) that combine to form homo- or heterodimers and ultimately function to regulate the transcription of a variety of cytokine, chemokine, adhesion molecule, and enzyme genes involved in SIRS. Increased translocation of NF-κB has been associated with a poor outcome in some studies. Activation of NF-κB in peripheral blood monocytes correlates with increased mortality in septic patients, and alveolar macrophages from patients with adult respiratory distress syndrome (ARDS) exhibited higher nuclear NF-κB levels than critically ill patients without ARDS. The AP-1 complex is activated through activation of MAP kinases by stimuli that are similar to those required for NF-κB mobilization. IRF-3 is mobilized through activation of the Trif-associated signaling pathway and results primarily in transcription of type I interferon (IFN-α) genes. The STAT1 pathway is induced by activation of type I (IFN-α) and type II (IFN-γ) receptors. Together, these transcription factors mediate the transcription of numerous factors involved in inflammation and tissue repair (Fig. 21.5).

Several non-cytokine factors have been implicated in the pathogenesis of SIRS. Platelet-activating factor (PAF) is a phospholipid autacoid released by endothelial cells that regulates the release of cytokines and amplifies the proinflammatory response. It appears to be an important factor in the adhesion of neutrophils to endothelial cells. The prolonged presence of PAF in the serum of patients with SIRS has correlated with poor outcome. Eicosanoids are arachidonic acid metabolites that regulate many aspects of the immune response. Leukotrienes (LTC4-LTE4) induce contraction of endothelial cells and encourage capillary leakage. Thromboxane A2, a macrophage and platelet-derived factor, promotes platelet aggregation, vasoconstriction and, potentially, tissue thrombosis.

The complement cascade is composed of more than 30 proteins that interact in a complex fashion to mediate inflammation and direct lysis of microbes and other cells (Fig. 21.6). However, in SIRS, excessive complement activation appears to cause significant cellular injury in the host. Products of the complement cascade, most notably C3a and C5a, are potent activators of inflammation and leukocyte chemotaxis. C3a and C5a also directly activate neutrophils and promote release of reactive oxygen intermediates and proteases. Excessive release of these factors can result in significant tissue injury. The membrane attack complex (MAC) is the terminal component of the complement cascade. MAC results from the aggregation of the complement components C5–C9 on biological membranes. The accumulation of MAC on cell surfaces can result in significant tissue and cellular injury and may be a major factor in the pathogenesis of MODS. Suber and colleagues have reported that complement-mediated responses to self-antigens exacerbate tissue injury after burn injury.

### Circulating cytokines as markers of SIRS and predictors of outcome

Numerous studies have been undertaken with the goal of using plasma cytokine levels as diagnostic and prognostic markers in patients with SIRS or sepsis. This approach seems...
The systemic inflammatory response syndrome

Total body surface area (TBSA) burns demonstrated marked increases in plasma TNFα levels and a significant correlation between TNFα concentration and shock, MODS, and death. These findings support the results of Marano et al., who showed a significant correlation between circulating TNFα concentration and mortality in burned patients. Therefore, taken together, these results show that TNFα could serve as a useful marker of ongoing inflammation as well as an indicator of morbidity and mortality in the setting of burn injury, but controversy remains.

TNFα interacts with two known cell surface receptors designated tumor necrosis factor receptor (TNFR)-I and TNFR-II. TNFR-I, also known as TNF-R55 or p55, is expressed on a variety of cells and its activation mediates most of the activities of TNFα, including induction of apoptosis. Activation of TNFR-II (TNF-R75 or p75) results in cellular proliferation and activation. During inflammatory states, TNFR

Figure 21.4 Major inflammation-associated transcription factors include NF-κB, AP-1 and IRF-3. Activation of these pathways is mediated through MyD88- and Trif-dependent signaling after TLR ligation. (From Kawai and Akira, Cell Death and Differentiation 13: 816, 2006)
between sTNFR and APACHE III scores, as well as the incidence of shock and mortality in septic patients. Sikora and colleagues\textsuperscript{50,51} have reported increased concentrations of sTNFR-I and sTNFR-II in the plasma of burned children. sTNFR concentrations correlated with burn surface area and decreased with adequate treatment. Children with hypovolemic shock had higher plasma concentrations of sTNFR. Overall, in the studies published to date, the presence of high levels of circulating sTNFR correlate with ongoing inflammation and may serve as an indicator of poor prognosis.

Another family of proteins that has been extensively analyzed as markers of SIRS is IL-1 and IL-1 receptor antagonist (IL-1ra). In burn patients, low IL-1ra levels correlated with mortality in two independent studies.\textsuperscript{52,53} Plasma IL-1ra levels have been shown to correlate with body surface area burned, extent of third-degree burn, and the presence of inhalational injury, both in adults and children.\textsuperscript{45,50–52} Of the cytokine markers studied to date, elevated levels of IL-6 appear to be one of the more consistent markers of poor outcome in burn, trauma, and septic patients. One of the known functions of IL-6 is induction of acute-phase proteins such as C-reactive protein (CRP) by the liver. In some studies, CRP has been shown to parallel IL-6 as a marker of increased mortality.\textsuperscript{53} Although IL-6 itself does not appear to have any known direct injurious effects, it apparently serves as a consistent marker of ongoing inflammation. Elevated plasma IL-6 levels have correlated with increased mortality in experimental and clinical studies of thermal injury, sepsis, trauma, and hemorrhagic shock.\textsuperscript{44,54,55} A study by Taniguchi et al.\textsuperscript{55} showed that an increased ratio of IL-6 to the anti-inflammatory cytokine IL-10 was a predictor of poor outcome in patients with SIRS.

In trauma and burn patients it is often difficult to differentiate whether SIRS is a result of the injury itself or due to superimposed infection. Most of the clinical signs of systemic infection, such as fever and leukocytosis, are by definition present in SIRS. Therefore, considerable attention has
been placed on identifying indirect markers of systemic infection that could serve to differentiate SIRS caused by infection from that caused by trauma. It is important clinically to identify patients with systemic infection in order to initiate antibiotic therapy in a timely fashion. Additionally, positive blood cultures are the gold standard for diagnosis of systemic infections. Although blood cultures provide important information regarding the presence of infection and the identity of the infecting organism, it can often take several days to obtain reliable results, and the presence of negative cultures does not assure the absence of infection. Therefore, efforts have been made to identify other markers of systemic infection. The two markers that have been most consistently elevated in patients with infection are procalcitonin and C-reactive protein (CRP). Studies have shown that increased plasma levels of procalcitonin or CRP are sensitive markers of systemic infection. Both of these markers have been shown to be more reliable than clinical signs in the diagnosis of infection in high-risk surgical and trauma patients. Recent studies show that procalcitonin and CRP can be used to distinguish patients with systemic infection from those with non-infectious systemic inflammatory processes.

Overall, several markers of inflammation and infection have been identified in burn and trauma patients. Some of these have been shown to be consistent indicators of injury severity. However, cytokine and non-cytokine markers of inflammation are not used routinely in the laboratory evaluation of burned patients. With further research and demonstration of the reliability of these markers, they may become an accepted part of clinical practice. In addition, technology is evolving to measure these markers in a rapid and cost-effective manner, which may allow blood cytokine markers to become a component of patient management in the future.

Anti-inflammatory therapy for SIRS

Despite our increased understanding of the role of inflammatory mediators in the pathogenesis of SIRS and sepsis, most anti-inflammatory drug regimens have had little success in the treatment of this problem. Neutralizing approaches to several inflammatory mediators have been studied. All of these studies have demonstrated, at best, marginal improvement in septic morbidity and mortality. None of the direct anti-inflammatory strategies has been successfully employed to minimize burn-associated inflammation. One of the most widely studied approaches for the treatment of SIRS is the use of monoclonal antibodies to TNFα. Several multicenter, prospective clinical trials were undertaken in septic patients using several different antibodies to TNFα. Those studies did not demonstrate improved outcome in patients receiving anti-TNFα compared to placebo. One study evaluated the efficacy of a chimeric antibody to TNF in patients with severe sepsis. Circulating levels of TNFα as well as a variety of other inflammatory mediators were assessed. Although circulating levels of TNFα were transiently decreased, anti-TNFα therapy did not result in reduction of circulating levels of other inflammatory mediators such as IL-1β, IL-1ra, sTNFR, or IL-6. In addition, evidence of systemic inflammation was not reduced and overall mortality was not improved in anti-TNFα-treated patients. Similarly, the use of sTNFR as a strategy to neutralize the systemic effects of TNFα and reduce sepsis-associated morbidity and mortality was unsuccessful. Other anti-inflammatory approaches that have been studied and found to be largely ineffective include the use of IL-1ra, anti-bradykinin, PAFrα, and ibuprofen.

Because of the relative ineffectiveness of anti-inflammatory therapy aimed at neutralizing single mediators, more broad-based strategies were developed with the goal of simultaneously neutralizing, removing, or inhibiting the production of numerous inflammatory mediators. Hemofiltration was one approach that received considerable attention. Several studies have shown that hemofiltration will increase the clearance of inflammatory mediators, particularly IL-6, from blood in patients with sepsis. However, none of these studies has demonstrated a significant reduction in IL-6 plasma levels. A study by Kellum et al. showed that continuous venovenous hemofiltration (CVVH) reduced plasma TNFα concentrations by 13%, and the use of continuous venovenous hemodialysis (CVVHD) resulted in a 32% increase in circulating TNFα levels. Overall, the use of hemofiltration has been largely ineffective in removing significant amounts of inflammatory mediators from the blood of patients with sepsis, and there is currently no evidence that this approach will reduce morbidity and mortality.

The use of glucocorticoids in the treatment of sepsis has been proposed for more than 30 years. A meta-analysis of studies using high-dose glucocorticoids in the treatment of sepsis was published in 1995 and later summarized by Zeni and colleagues. Overall, the use of high-dose glucocorticoids to treat sepsis and septic shock has not been beneficial. In many studies, the use of glucocorticoids in septic patients was associated with increased mortality. In burned patients there is no evidence that administration of glucocorticoids provides effective treatment for systemic inflammation. More recent studies show that replacement dose steroids will improve survival in septic patients who have adrenal insufficiency. Recent guidelines from the Surviving Sepsis Campaign advocate the use of replacement dose glucocorticoids in septic patients refractory to conventional management.

The failure of anti-inflammatory approaches to improve outcome in patients with severe sepsis or septic shock are likely to be multifactorial. First, the inflammatory response to injury and sepsis is induced by a complex array of mediators that are largely interrelated and have significant redundancy. Therefore, blocking or neutralization of a single mediator is not likely to have a marked effect on the overall response. Second, the same mediators that are important in inducing tissue injury also play an important role in antimicrobial immunity, and blockade of these mediators may leave the host more susceptible to subsequent infection. Third, many of the mediators, particularly TNFα and IL-1β, are released within minutes of injury and mobilize the inflammatory cascade shortly thereafter. Therefore, by the time that signs of SIRS or sepsis are apparent, many of the injurious effects of the inflammatory response have already been set in motion, making therapy ineffective. A recent emphasis has been placed on the identification of late mediators of inflammatory injury. This search has been prompted by the observation that SIRS and sepsis-associated death occur days after the peak effect of inflammatory
acids, and nucleotides have been shown to improve outcome in trauma patients. Overall, trauma patients receiving immune-enhancing diets have been shown to have fewer infectious complications. In general, enteral feeding has been shown to maintain gut integrity and improve outcome in burn patients.

Tracey and colleagues have described a cholinergic anti-inflammatory pathway that may be important in the regulation of inflammation and could be exploited for therapeutic benefit. As described earlier, factors that appear to be important in limiting the extent of shock and MODS are appropriate fluid resuscitation, hemodynamic support, treatment of infection with antibiotics, excision of necrotic tissue, and adequate nutritional support.

Proper nutritional support is also an important factor in the treatment of severely injured patients. Enteral feeding formulas supplemented with glutamine, arginine, omega-3 fatty acids, and nucleotides have been shown to improve outcome in trauma patients.

converge and ultimately cause the activation of thrombin, with subsequent cleavage of fibrinogen into fibrin (Fig. 21.8). The intrinsic pathway is a series of plasma proteins that are activated by Hageman factor (factor XII), a protein synthesized in the liver that is activated by binding to collagen, basement membrane or activated platelets. Activated Hageman factor triggers a cascade of proteins to become activated, resulting in the formation of thrombin. The intrinsic pathway is most commonly activated by direct tissue trauma. In contrast, the extrinsic pathway is initiated by the production of tissue factor. Recent studies indicate that the extrinsic pathway is the primary coagulation pathway activated during infection and systemic inflammation, particularly during sepsis and SIRS. Tissue factor is expressed on tissue surfaces that are not normally exposed to the vascular compartment, such as subcutaneous tissues and the adventitial layer of blood vessels. In addition, endothelial cells and activated monocytes produce tissue factor during periods of inflammation in response to TNFα, IL-1, IL-6 and CRP. The presence of tissue factor causes activation of factor VII, which then forms a complex with tissue factor and ultimately causes the formation of thrombin by the activation of a series of coagulation factors (Fig. 21.8). Activation of the coagulation cascade is not only important in the formation of fibrin clots but also has important effects on the proinflammatory response. Factor Xa, thrombin and the tissue factor–VIIa complex have been shown to elicit proinflammatory activity. Specifically, thrombin and the tissue factor–VIIa complex can induce production of proinflammatory cytokines such as TNFα by mononuclear and endothelial cells. That effect appears to be mediated by the binding of these factors to protease-activated receptors on the surface of target cells. Therefore, acute inflammation causes activation of the coagulation cascade, which can then further potentiate the inflammatory response.

Activation of the clotting cascade during inflammation is limited by several factors. This is important because it prevents uncontrolled induction of procoagulant mechanisms. The best-defined factors are antithrombin, the protein C system and the tissue factor pathway inhibitor. Antithrombin is produced in the liver and directly binds and inactivates thrombin. The binding of antithrombin to thrombin is greatly potentiated by heparin and by glycosaminoglycans present on the endothelial cell surface. In rodents, interaction of antithrombin with the endothelial cell surface promotes the release of PGI₂, which inhibits TNFα production by monocytes through the inhibition of transcription factor NF-κB activation. Thus, antithrombin may have anti-inflammatory properties in addition to its function in regulating coagulation.

Protein C is a circulating protein that is activated by the thrombin–thrombomodulin complex on the surface of endothelial cells (Fig. 21.9). Activation of protein C decelerates the clotting cascade by inactivating factors Va and VIIIa. Activated protein C also inhibits thrombin-induced production of TNFα by monocytes by inhibiting the activation of transcription factors NF-κB and AP-1. Therefore, activated protein C has both anticoagulant and anti-inflammatory properties. During sepsis, activated protein C levels can become depleted due to consumption and inflammation-induced downregulation of thrombomodulin. This results in
unchecked formation of thrombin, causing accelerated coagulation and increased proinflammatory activity. The importance of protein C in regulating thrombin formation during sepsis is demonstrated by increased mortality in septic patients with low activated protein C levels.94

A third important factor in the regulation of thrombin formation is the tissue factor pathway inhibitor (TFPI). TFPI is present on the surface of endothelial cells and bound to lipoproteins in plasma. TFPI inactivates tissue factor by forming a quaternary complex with tissue factor and factor VIIa. Factor Xa is the fourth component of the complex.95 Inhibition of tissue factor function inhibits activation of the extrinsic clotting pathway during inflammation. Infusion of TFPI has also been shown to reduce proinflammatory cytokine production during endotoxin infusion in baboons, but not in humans.

The hemodynamic response

The full clinical picture of systemic inflammation after thermal injury is characterized by two primary phases. After the initial injury, inflammation leads to increased vascular permeability and the exudation of protein-rich fluid from the vascular compartment to the interstitium. This early fluid leak results in intravascular hypovolemia and interstitial edema formation. If the patient is adequately resuscitated, a hyperdynamic phase will ensue which is characterized by a low systemic vascular resistance and high cardiac output. Patients who are not well resuscitated or whose cardiac function is compromised may not be able to increase their cardiac output to the extent needed to maintain arterial blood pressure during states of extensive vasodilatation, and so might exhibit tissue hypoperfusion and shock. A reduced vascular responsiveness to vasoconstrictors may inhibit successful pharmacologic intervention and patients could develop irreversible shock. An intravenous bolus injection of 4 ng/kg endotoxin into healthy volunteers mimics some aspects of the hemodynamic response seen in septic patients and adequately resuscitated burn victims.86,87 The low systemic vascular resistance and the elevated cardiac output can also be induced in animal models by continuous infusion of low-dose endotoxin98 or bacteria.99,100

Changes in endothelial permeability

Burn injury, trauma and sepsis increase microvascular permeability in both the systemic101,102 and the pulmonary circulation.103 Increased vascular permeability and cutaneous edema are hallmarks of burn shock. The increase in systemic vascular permeability results in the exudation of protein-rich fluid from the vascular compartment into the interstitium. This results in intravascular volume loss and the concomitant development of interstitial edema. If resuscitation is not prompt and adequate, this loss in intravascular volume will lead to intravascular hypovolemia, hypotension, and inadequate tissue perfusion. Severe interstitial edema formation can lead to the development of compartment syndrome, with compromise of neurovascular integrity. The lungs may also be affected. Edema formation due to an increase in microvascular permeability is a hallmark of the acute lung injury. The factors that determine the transvascular fluid flux are summarized in the Starling–Landis equation:104,105

$$J_v = K_I[(P_{mv} - P_i) - \alpha(\pi_{mv} - \pi_i)]$$

where $J_v$ is the transvascular fluid flux, $K_I$ is the filtration coefficient (measure of the endothelial permeability to small solutes and water as well as of the permeability surface area), $P_{mv}$ is the microvascular hydrostatic pressure, $P_i$ is the interstitial hydrostatic pressure, $\alpha$ is the osmotic reflection coefficient to protein, $\pi_{mv}$ is the microvascular oncotic pressure, and $\pi_i$ is the interstitial oncotic pressure.

Several investigators have studied lymph flow and lymph protein flux after administration of bacteria or short-time infusion of 1–2 µg/kg of endotoxin in sheep. Two phases of permeability change could be distinguished in these models.106 During phase 1 there was a high microvascular hydrostatic pressure as defined by the Gaar equation.107 This was associated with an increase in lung lymph flow, but the lymph protein concentration was low. It was concluded that the high microvascular hydrostatic pressure was responsible for the early increase in transvascular fluid flux. Thromboxane A2 (TXA2) has been found to be responsible for the vasoconstriction that causes local increases in hydrostatic pressure. Therefore, it is not surprising that administration of the thromboxane synthetase inhibitor OKY046 prevented the rise in lymph flow during phase 1.108 That effect was also noted after blockade of cyclooxygenase by ibuprofen.109 Early edema formation at the site of burn injury might be due to a different mechanism. Recent data suggest that a marked fall in interstitial hydrostatic pressure might occur in the injured tissue, which could explain the immediate onset of edema formation after thermal injury.110,111 These changes might be the result of an inhibition of the fibroblast β1-integrin attachment to collagen.

During phase 2, lymph flow continues to be high. However, the lymph protein concentration rises considerably and the pulmonary artery pressure is only mildly elevated.106 The oncotic pressure gradient between microvasculature and interstitial space is reduced during that period.112 Together, these data suggest that the permeability of the pulmonary endothelium to protein increases in phase 2. In fact, the reflection coefficient for total protein fell from 0.73 to 0.58, with respective changes in the reflection coefficients for albumin (0.66 to 0.5), IgG (0.76 to 0.64), and IgM (0.91 to 0.83) after 4 hours of Escherichia coli sepsis in sheep.113 Confirmation of this hypothesis is still pending in models of endotoxemia, but it has been generally accepted that the changes in pulmonary transvascular fluid flux in phase 2 represent changes in microvascular permeability. The mechanisms of the increased microvascular permeability are still under discussion.

Endothelial cells play an important role in the regulation of vascular permeability. It has been hypothesized that endothelial cells can contract upon stimulation.114 As a result, the intercellular gaps might increase in number and/or size, establishing the so-called capillary leak syndrome. The development of the protein-rich high-permeability edema can be ameliorated if substances are administered that raise the endothelial cell content of cyclic adenosine or guanosine monophosphate.115,116 However, endothelial cells do not merely serve as targets during systemic inflammation:
they actively contribute to the ongoing inflammatory process. The endothelial cell can be stimulated by endotoxin, TNFα, or IL-1 to express E-selectin, an adhesion molecule. E-selectin on the surface of endothelial cells interacts with the corresponding ligand complex on PMNs to facilitate rolling of these cells along the endothelium. Moreover, endothelial cells secrete the proinflammatory cytokines TNFα and IL-1, which activates PMNs. Conflicting data exist regarding the role of PMNs in SIRS. PMNs are usually found at the site of tissue injury, to which they migrate following a concentration gradient of chemotactic stimuli. Upon stimulation, PMNs roll along endothelial cells, and in a further step mediated by PMN CD18/CD11b interactions with endothelial ICAM-1, emigrate from the vessel into the interstitial space. Antibodies against the common CD18β chain showed beneficial effects in an animal model of sepsis-induced lung injury, suggesting that integrin-mediated PMN emigration is a functionally important process in the development of acute lung injury. On the other hand, patients who are deficient in CD18 have abundant PMNs in their alveolar spaces, and the monoclonal antibody 60.3 was ineffective in completely blocking the migration of PMNs into the lung in a number of conditions. We have reported that in chronic endotoxemia there were few PMNs in the lung but numerous macrophages. Activated PMNs and macrophages release oxygen free radicals and proteases at sites of inflammation. These processes appear to be functionally important in the development of vascular permeability because administration of oxygen free radical scavengers and antiproteases proved to be useful in diminishing edema accumulation after endotoxin challenge. However, proteases and oxygen radicals are also released by macrophages, which are already present in the tissue, and by monocytes that migrate to sites of inflammation. Depletion of granulocytes by anti-PMN antiserum or by treatment with nitrogen mustard did not prevent the changes in microvascular permeability following the administration of endotoxin. Moreover, patients deficient in PMNs would still develop the adult respiratory distress syndrome (ARDS) associated with sepsis. On the other hand, treatment of sheep or goats with hydroxyurea, which is another compound used to deplete granulocytes, was effective and diminished fluid accumulation in the lung after endotoxin challenge. However, urea scavenes free radicals, which might explain its efficacy. The inflammatory response becomes chronic, many mediators have been released and more than one mechanism might be assumed to be responsible for the capillary leak.

The role of arachidonic acid metabolites in facilitating increased vascular permeability has been extensively investigated. Administration of the thromboxane synthetase inhibitor OKY046 not only reduced transvascular fluid flux in phase 1, but was also effective in phase 2 after endotoxin challenge. This finding suggests that thromboxanes participate in permeability alterations during systemic inflammation. Oxygen free radicals can also increase microvascular permeability, both by activation of endothelial cell contraction and by damaging the endothelial cell membrane. OKY046 has been shown to reverse oxygen free radical-induced lung injury. On the other hand, inhibition of the cyclooxygenase did not affect transvascular fluid flux during phase 2, even though thromboxane A2 is a cyclooxygenase metabolite. This discrepancy is still unexplained; however, prostacyclin is elevated after endotoxin administration, and this material has many actions that counter the actions of thromboxane. Administration of a cyclooxygenase inhibitor will prevent the release of this salutary eicosanoid.

TNFα is one of the early mediators in systemic inflammation. It has been reported to be elevated during sepsis and endotoxemia after hemorrhagic shock or thermal injury. It is considered to be one of the most important mediators in the cascade because it has the potential to stimulate or enhance most of the steps in the inflammatory response. Moreover, administration of human recombinant TNFα reproduced most of the effects of endotoxemia, including alterations in pulmonary microvascular permeability in the chronic sheep model. TNFα also induces the secretion of PAF, which is a further early mediator of systemic inflammation. PAF causes an increase in lung lymph flow and permeability to protein when it is infused into conscious sheep. Administration of a PAF antagonist abolished the cardiopulmonary response that occurs during phase 1 and attenuated it during phase 2. However, PAF had no direct effect on endothelial cells. This suggests that it probably increases microvascular permeability through other mechanisms, such as its priming effect on PMNs.

If burn patients are adequately resuscitated, they most commonly enter into a phase characterized by hyperdynamic cardiovascular function. The hyperdynamic cardiovascular response is associated with profound changes in pulmonary transvascular fluid flux in the ovine model of continuous endotoxemia. The lymph protein concentration gradually decreased after phase 2, and after 24 hours of endotoxemia the reflection coefficient to protein was at baseline level, whereas the lymph flow was still high. Microvascular hydrostatic pressure, evaluated by Holloway’s technique, was not significantly different from baseline. The elevated transvascular fluid flux was attributed to a high filtration coefficient. An increase in both perfused surface area and pore numbers might have contributed to the change in filtration. Repeated injections of endotoxin also reduced subsequent lung lymph production in response to endotoxin. These changes in lung lymph flow were associated with elevations in endothelin and atrial natriuretic peptide. However, further studies must determine whether these factors affect pulmonary microvascular changes during the late phases of sepsis and multiple organ failure.

### Increased epithelial permeability

Permeability changes during systemic inflammation are not restricted to the endothelium. Loss of epithelial barrier function has been noted both in the lung and in the intestine. Administration of 2–4 ng/kg endotoxin to healthy human volunteers increased their alveolar epithelial permeability to the inhaled 492 Da molecule [59Fe]diethylenetriamine pentaacetate (DTPA) 3 hours after endotoxin had been given. Human volunteers demonstrated a higher intestinal epithelial permeability to mannitol/lactulose. Bacterial translocation occurred during endotoxemia, thermal injury, and multiple trauma with hemorrhagic shock.
This might well be interpreted as a loss of intestinal barrier function. Nevertheless, one must bear in mind that epithelial permeability to molecules such as lactulose/mannitol and bacterial translocation do not necessarily relate to each other. The epithelium could also be injured by ischemia–reperfusion. In addition to changes in vascular permeability, burn injury also causes marked alterations in vascular tone and myocardial function that are characterized by a variety of temporal alterations.

The hyperdynamic state

Continuous infusion of endotoxin into sheep and pigs results in a hyperdynamic circulation. Besides a low systemic vascular resistance and a high cardiac output with a slightly decreased mean arterial pressure, the hyperdynamic response is further characterized by hyporesponsiveness of isolated vessels to vasoconstrictors and an increased pulmonary shunt fraction in the presence of a reduced pulmonary hypoxic vasoconstriction. The high cardiac output is due to low systemic vascular resistance and increased heart rate. Paradoxically, myocardial function is depressed during sepsis and in severely burned patients. The underlying cause of impaired myocardial function is not fully understood. However, reports indicate that proinflammatory mediators such as TNFα, IL-1, IL-6 and nitric oxide contribute to this alteration. The treatment of myocardial dysfunction during sepsis and after burn trauma is an important consideration in overall hemodynamic management. The combination of myocardial dysfunction and increased pulmonary vascular resistance is a likely cause of right heart failure in pediatric burn patients. Treatment options include dobutamine and phosphodiesterase inhibitors such as milrinone. The Surviving Sepsis Campaign recommends dobutamine as a first-line agent for treatment of hypotension and hypoperfusion in pediatric patients with sepsis, especially when myocardial dysfunction is present.

Nitric oxide (NO) has been implicated as a mediator of systemic vasodilation and myocardial depression during sepsis and after major burn injury. NO can be synthesized from its precursor L-arginine by three different enzymes (Fig. 21.10). The calcium-dependent constitutive nitric oxide synthases (NOS) such as endothelial NOS (eNOS) and neuronal NOS (nNOS) are responsible for the basal release of NO, which seems to play an important role in the regulation of vascular tone under physiologic conditions. In vitro data suggest that these enzymes might become inactivated early after administration of endotoxin, thereby accounting for some of the vasoconstrictive phenomena seen in phases 1 and 2. Inducible NOS (iNOS) is the major NOS isoform induced during acute inflammation. Depending on the species, cells producing the inducible NOS upon stimulation by endotoxin, TNFα, IL-1, or IFN-α include macrophages, vascular smooth muscle cells, and vascular endothelium. NO is a lipophilic gas, which can easily enter vascular smooth muscle cells where it stimulates the soluble guanylyl cyclase to synthesize cyclic guanosine monophosphate (cGMP). High levels of cGMP stimulate cells to lower their intracellular Ca2+ concentration. This leads to vascular dilatation and hyporesponsiveness to vasoconstrictors. Administration of an NOS inhibitor to septic humans and to endotoxemic sheep increases their vascular resistance and restores their responsiveness to vasoconstrictors. Overall, it appears that NO is an important mediator of SIRS-induced vascular alterations. However, administration of NOS inhibitors in humans has not improved overall outcome during sepsis or SIRS. Therefore, the mechanisms by which NO alters vascular function during SIRS in humans require further investigation.

Peroxynitrite is an additional NO-associated factor that appears to contribute to SIRS-induced pathology. Peroxynitrite is a free radical that is generated through interactions of NO and oxygen free radicals during periods of severe inflammation and is known to cause cellular injury and organ dysfunction in experimental burn models. Treatment of burned sheep with a peroxynitrite degradation catalyst has been shown to reduce lung injury in an ovine model of burn and smoke inhalation injuries. Therefore, peroxynitrite appears to be an important mediator of organ injury during periods of systemic inflammation. However, further research is needed to determine the efficacy of treatment approaches aimed at promoting peroxynitrite degradation and neutralization in the clinical setting.

Figure 21.10 Nitric oxide is an important mediator of inflammation-induced vasodilation, myocardial depression and organ injury. The synthesis of nitric oxide is mediated by three major nitric oxide synthase (NOS) isoforms.
Summary

Burn injuries, associated ischemia–reperfusion injury, the presence of necrotic tissue, and sepsis are all events that contribute to SIRS after severe burn injury. Widespread increases in microvascular permeability lead to intravascular hypovolemia and interstitial edema, thereby impairing oxygen diffusion to the tissue. Blood flow may become maldistributed owing to a loss of vasoregulatory function and as a result of widespread microthrombosis. Oxygen utilization also appears to be impaired. The resultant hypoxic cell damage further promotes organ dysfunction. Oxygen free radicals, peroxynitrite and cytokines also appear to contribute to tissue damage and organ dysfunction. Despite improved understanding of the cellular and molecular mechanisms underlying SIRS, targeting the inflammatory response is not currently an effective treatment option for patients with burn-induced SIRS. Treatment is supportive and includes adequate fluid resuscitation, appropriate use of vasoactive drugs, support of failing organ systems, excision of necrotic tissue and treatment of infection with antibiotics.

Further reading


Access the complete reference list online at http://www.expertconsult.com
References


The immunological response and strategies for intervention

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Introduction

Despite improvements in the management of burn injury \(^1\), \(^2\) and the development of broad-spectrum antibiotics, infections still remain a major cause of morbidity and mortality in burn patients. \(^3\), \(^4\) Many infections are associated with organisms considered to be opportunistic in nature, which supports the concept that antimicrobial function may be impaired in these patients. One paradigm of burn-induced immune dysfunction asserts that the initial burn injury induces a severe inflammatory response characterized by the systemic release of proinflammatory cytokines, chemokines and acute-phase reactants that cause leukocyte and endothelial cell activation (Fig. 22.1). This initial inflammatory response has been termed the systemic inflammatory response syndrome (SIRS) and causes a variety of hemodynamic, immunologic and metabolic responses that can lead to significant tissue injury and organ dysfunction. However, if adequately resuscitated, most burn victims survive the initial injury and enter a phase characterized by varying degrees of immune dysfunction. This state of immunologic dysfunction, along with the loss of the skin barrier and the use of invasive instrumentation such as central venous catheters, peritoneal dialysis catheters and endotracheal tubes, places the burned host at increased risk of infection. Some practitioners have proposed that post-burn immunologic dysfunction is caused by an anti-inflammatory response, termed the counter anti-inflammatory response syndrome (CARS), which is initiated by the host in an effort to minimize inflammation-induced tissue injury during the acute post-burn period. CARS is characterized by a relative preponderance of anti-inflammatory cytokine production, leukocyte apoptosis, regulatory lymphocyte generation and a shift in adaptive immunity from a Th1 to a Th2 phenotype. Accumulation of inflammatory insults during the post-burn period may potentiate injury-induced immunosuppression. Therefore, there is keen interest in developing immunomodulatory strategies aimed at normalization, or enhancement, of antimicrobial function. Interventions that can improve the host response to infection are also becoming increasingly attractive because of the emergence of antibiotic-resistant microorganisms as pathogens in burn patients. \(^5\), \(^6\) However, few effective immunomodulatory approaches have been developed for clinical application in burn patients. This may be because immune dysfunction parallels failure of other organ systems and may be a reflection of multiorgan system dysfunction. Leukocytes in that environment appear to be ineffective in responding to infection, and may also be refractory to immunomodulatory interventions. Therefore, the early initiation of immunomodulation may be most advantageous, although further research is needed to determine whether immunomodulation will be effective in burn patients and which approaches have the most potential for improving overall outcome.

The depth and size of the burn wound are well-known risk factors for infection and sepsis. \(^4\), \(^7\) The overall incidence of bacteremia in burn patients is approximately 19%, but bacteremia rarely occurs in patients with <40% TBSA burns. \(^5\) Concomitant inhalation injury is also associated with an increased risk of infection, particularly pneumonia. The predisposition to pneumonia seen in patients with inhalation injury is likely due to impairment of mucociliary clearance, alveolar macrophage dysfunction, and airway obstruction with casts and debris in conjunction with a high incidence of tracheal intubation and mechanical ventilation. \(^9\)

Some investigators have reported a gender effect on post-burn mortality, with females having a lower chance of survival. \(^1\) \(^0\) However, a study of children did not show a relationship between gender and the incidence of sepsis. \(^1\) \(^1\) Nevertheless, age appears to be a predisposing factor for the development of septicemia after burn injury. Not surprisingly, young children and elderly patients have the highest incidence of sepsis. \(^1\) \(^2\)

Relative to other catheters, central venous catheters are particularly prone to bacterial contamination. Approximately 25% of central venous catheters become colonized with bacteria. Lesseva et al. reported an incidence of catheter-related bacteremia of 6.6%, accounting for approximately 20% of sepsis in burn patients. \(^1\) \(^3\) Peripheral catheters are much less likely to be associated with infection because of their shorter duration of use. The risk of catheter-related infection is greatly increased if devices are inserted through infected or contaminated skin, such as burn wounds. Femoral vein catheters are more likely to become infected than subclavian or internal jugular vein catheters, and catheter replacement via guide wire exchange has a higher infection rate than catheterization at a separate site. One of the most
Innate immune function after burn injury

After a large burn injury with extensive tissue necrosis, the innate immune system is activated both locally and systemically. Subsequent dysfunction of innate immune function may lead to increased susceptibility to infections. Study of immune function in burn patients is limited by feasible tissue access and generally consists of measuring circulating soluble factors and immune cells. Not surprisingly, this provides only a limited view of the entire immune response, as suggested by animal studies in which alternate tissues such as spleen and liver are available.24–27 This review will highlight observational data from clinical studies and try to use results from experimental research to provide some context for these observations.

Healthy individuals resist many infectious challenges without pre-existing specific (acquired) immunity because of the effectiveness of the innate immune response. Innate immunity is a protective set of rapid and primitive non-specific responses to infection, including epithelial barrier defenses, cytokine elaboration, complement activation, and phagocytosis of microorganisms. These mechanisms may eradicate or contain the infection during the time needed to generate an adaptive immune response to the offending microbe. The hallmarks of innate immune system activation are acute inflammatory changes characterized by increased vascular diameter and blood flow, increased vascular permeability and neutrophil recruitment. These alterations allow for a rapid response to tissue damage or infection, which is crucial for initial damage control. Although the innate immune system is critical for an effective host response to infection, inappropriate or excessive activation can lead to tissue damage and severe systemic physiologic alterations. Furthermore, dysfunction of innate immunity may predispose burn patients, and other critically ill individuals, to infectious complications.

Physical barriers

A mechanical barrier against invasion of microbial pathogens is provided by the epithelium of skin and mucosal tissue. This protective barrier is lost after destruction by full-thickness burn injury. Furthermore, the presence of necrotic tissue provides a favorable environment for microbial growth. Cellular damage may also cause the release of molecules that predispose the host to bacterial infections. Syndecans are heparin sulfate proteoglycans that regulate innate immune responses, and their release after cellular damage activates tissue repair processes, including vascular permeability, angiogenesis, wound repair, and modulation of chemokine activity.28 In general, syndecans have been shown to attenuate inflammatory responses and protect tissues from inflammatory injury. However, recent studies in burned mice suggest that syndecan shedding may potentiate systemic dissemination of P. aeruginosa from burn wound infections, an effect that may be attenuated by the application of protamine.29,30

Besides the loss of epidermal integrity in burned skin, barrier function may also be compromised at other remote anatomic locations. Epithelial barrier function in the gastrointestinal tract can be compromised after burn injury,
possibly owing to decreased mesenteric blood flow in the early post-burn period. This may lead to systemic translocation of bacterial toxins or enteric bacteria. Increased intestinal permeability after burn injury has been associated with systemic infection in a number of studies, and forms the basis for the therapeutic strategy of selective decontamination of the digestive tract as well as interventions aimed at improving gut barrier function, such as early enteral feeding. In the respiratory tract, defense mechanisms include mucus secretion and ciliary movement, which serve to trap microbes and sweep them into the upper airways and oropharynx, where expulsion by coughing may occur. These defenses can be diminished after inhalation injury or compromised by endotracheal intubation, resulting in microbial proliferation and expansion into the distal branches of the respiratory tract, causing bronchitis or pneumonia. Smoke inhalation also facilitates the development of bronchial casts composed of neutrophils, sloughed respiratory mucosa and fibrinous products, which impair microbial clearance mechanisms and aid bacterial growth. Pneumonia is one of the most common infections encountered in burn patients and is associated with a higher risk of mortality.

Epithelial cells contribute further protection by manufacturing antimicrobial peptides, including defensins, lysozymes, and cathelicidins. Defensins exert antimicrobial activity against a broad range of bacteria and fungi and appear to function through disruption of the bacterial cell wall. Although epithelial cells display some constitutive production of defensins, production is increased after microbial activation of Toll-like receptors (TLRs) on the epithelial cells. However, burn injury has been associated with decreased defensin mRNA expression, and it is not clear that microbial stimulation would invoke an appropriate level of activation in affected areas.

### Phagocytes and Toll-like receptors

Beyond the physical barriers, the key cellular components of the innate immune response are the professional phagocytes, including macrophages, dendritic cells and neutrophils, which are not only important in removing microbes and debris from sites of inflammation but also are key regulators of the innate immune response (Fig. 22.2). Macrophages are capable of engulfing and killing microbes, but probably function most importantly as supervisors of the immune response to infection. They elaborate chemotactic factors for the recruitment of other cells, particularly neutrophils, to the site of infection. Along with dendritic cells, macrophages also function to initiate the adaptive immune response by presenting bacterial antigens to CD4+ T cells. Neutrophils are effective at killing microbes through an arsenal of specialized antimicrobial functions (discussed below). Because the innate immune system must react to potential pathogens before they proliferate and disseminate, detection is dependent on the recognition of microbial molecules that are consistently found among a vast assortment of microorganisms.

Toll-like receptors, found on mononuclear phagocytes, provide a primitive, non-specific mechanism of pathogen recognition based on the detection and binding of conserved microbial products rather than recognition of specific microbial antigens. Human leukocytes express at least 10 TLRs, which recognize microbial ligands such as lipopolysaccharides, lipoproteins, lipotechoic acid, flagellin, unmethylated

![Figure 22.2](image-url)
Large-scale neutrophil infiltration is characteristically seen in burn wounds. Although this is probably an advantageous response to protect against potential pathogens, it may also be associated with some undesirable biologic effects. Oxidants and hydrolytic enzymes released from activated neutrophils can contribute to proteolysis within the wound and aid in the spread and dissemination of bacteria. Abnormal neutrophil function has been associated with bacteremia in patients with burns and other major injuries.\(^5^2\) Neutrophil microbicidal mechanisms are generally classified as either oxygen dependent or oxygen independent. Oxygen-independent microbicidal activity of neutrophils involves several peptides and proteins stored within the primary (azurophilic) granules, including lysozyme, bactericidal/permeability-increasing protein, \(\beta\)-defensins, and cathelicidin. In the oxygen-dependent mechanism, NADPH oxidase in the phagosome of neutrophils (and macrophages) converts molecular oxygen into superoxide anion (\(O_2^-\)), and a series of reactions creates further oxidant products with microbicidal activity, including \(H_2O_2\), \(OCl^-\) (hypochlorite) and \(NH_3Cl\) and \(RNH_2Cl\) (chloramines). A reduction in neutrophil-mediated oxygen-dependent bacterial killing has been reported in several studies of burn patients.\(^5^3,5^4\) Poor tissue perfusion and low oxygen tension in wound sites are additional factors likely to contribute to impaired oxidative killing. Chemotactic gradients are provided by chemoattractants such as the complement protein C5a, endothelium-derived IL-8, and leukotrienes. Chemoattractants and other stimuli also induce increased expression of surface phagocytic receptors. Bonding between phagocyte receptors and

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**Figure 22.3** Toll-like receptors are surface proteins that are instrumental in the recognition of microbial products and endogenous inflammatory mediators by leukocytes of the innate immune system. There are at least 11 identified Toll-like receptors in humans. (From Kawai and Akira, Cell Death and Differentiation 13: 816, 2006.)

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bacterial CpG DNA, and viral RNA, as well as endogenous ligands such as heat shock proteins, HMGB-1 and mitochondrial DNA (Fig. 22.3). TLR ligation results in activation of specific signaling pathways that cause nuclear translocation of transcription factors such as NF-kB, AP-1 and IRF-3, which induce transcription of genes encoding proinflammatory gene products such as cytokines, chemokines and nitric oxide synthase.\(^4^1,4^2\)

The importance of TLRs for recognition and clearance of microbes has been demonstrated in studies using mice that are genetically deficient of specific TLRs. TLR-deficient mice are highly susceptible to microbial infections owing to the inability to effectively respond to infection and clear invading organisms.\(^4^3-4^5\) Furthermore, analysis of a cohort of humans with congenital loss of MyD88, an important signaling intermediate required by most TLRs, showed a high incidence of infections with *Pseudomonas* spp, streptococci and staphylococci, which are common opportunistic pathogens among burn patients.\(^4^6\) It is not known whether alterations in TLR expression or function directly contribute to impaired innate antimicrobial functions in burn patients. However, Barber and colleagues have reported an association between TLR polymorphisms and the development of sepsis in burn patients.\(^5^7\) In addition, several studies indicate that TLR activation contributes to the systemic inflammatory response and associated alterations caused by thermal injury, such as altered vascular and gut permeability, myocardial dysfunction and microvascular inflammation.\(^4^6-5^0\) Macrophages seem primed for innate immune activity after burn injury through increased TLR4 expression and increased reactivity to LPS challenge, which may predispose burn victims to further inflammatory injury.\(^2^5,5^1\)
opsonins on microbial surfaces activates cytoskeletal contractile elements, resulting in invagination of the cell membrane and extension of pseudopods around the microbe. Clinical studies of neutrophils from burn patients demonstrate a reduction in neutrophil adhesion molecule expression and phagocytic activity. Theoretically, these alterations could lead to decreased innate antimicrobial activity and increased susceptibility to infection. However, a specific cause and effect relationship between altered neutrophil function and the development of infections in burn patients has not been firmly established.

**Innate lymphocytes – natural killer (NK), natural killer T (NKT), and \( \gamma \delta \) T cells**

Natural killer (NK) cells are lymphoid cells that do not express T-cell receptors (TCR) or immunoglobulins on the cell membrane but rapidly respond to infections through activating specific chemokine receptors and other activating innate receptors. NKT cells express both NK cell markers and restricted T-cell receptors (TCRs) that respond primarily to lipid antigens presented by the antigen-presenting molecule CD1d. \( \gamma \delta \) T cells comprise about 10% of all T cells and play important immunoregulatory roles in skin, gut, respiratory tract and other mucosal sites. All three innate lymphocytes are able to induce dendritic cell (DC) maturation through a combination of cell contact-dependent mechanisms and cytokine signaling. In turn, matured DCs can stimulate NK, NKT, and \( \gamma \delta \) T cells to sustain the innate immune response during the development of adaptive immunity. \( \gamma \delta \) T cells, which are in found in high numbers in intestine, may play a role in the recruitment of neutrophils to that site after burn injury. Some studies indicate that \( \gamma \delta \) T cells facilitate neutrophil-independent and neutrophil-mediated organ injury after burn injury. NK cells are best known for their role in containing viral infections prior to the adaptive immune response, as well as assisting in the control of malignant tumors. Activated NK cells are an important source of IFN-γ, which promotes the development of specific protective immune responses but may also contribute to the systemic inflammatory response after severe burn injury. NK cells kill infected cells through the release of perforin and granzymes and through the binding of the death receptors Fas and TRAIL-R on target cells. NK cells also interact with other cells of the immune system, including dendritic cells, by providing signals for maturation or apoptosis. Studies of patients after burn injury have revealed a decline in NK-cell activity over time. The decline in NK cell activity is most apparent more than 1 week after the occurrence of the burn injury and corresponds with the period during which sepsis is more likely to be identified.

**Complement**

As well as Toll receptors, the innate immune system has additional mechanisms for recognizing and neutralizing microbial pathogens, including the complement system, scavenger receptors, and specialized receptors on NK cells. Activation of the complement system results in the production of a cascade of proteins that function to opsonize microbes and recruit phagocytes. Three distinct pathways constitute the complement system: the classic pathway, the mannann-binding lectin pathway, and the alternative pathway (Fig. 22.4). Binding of IgG or IgM to antigens on microbial surfaces activates the classic pathway. The remaining two pathways can be activated in the absence of specific antibodies. The mannann-binding lectin pathway is similar to the classic pathway but is initiated after mannann-binding lectin protein binds to mannose-containing carbohydrates on microbial surfaces. The alternative pathway is dependent on low constitutive expression of complement activity which is amplified and potentiated when circulating complement components bind to microbial membranes. All three of the activation pathways act on microbial surfaces to assemble a convertase that cleaves C3 to form C3b, which either binds to the surface as an opsonin or helps activate C5 and the remainder of the complement cascade. Opsonization facilitates the removal of microbes by macrophages and neutrophils. C3a and C5a are potent chemoattractants for monocytes and neutrophils. Cleavage of C5 also leads to assembly of the membrane attack complex, which causes disruption of the microbial membrane. After burn injury, neutrophil surface expression of receptors for complement is increased, but the complement cascade itself is diminished.

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**Figure 22.4** The complement system can be activated by three primary mechanisms and facilitates the amplification of innate and acquired immune responses as well as directly mediating microbial lysis. The primary functions of complement are opsonization, leukocyte chemotaxis and direct killing of microbes. (From Abbas and Lichtman, Cellular and Molecular Immunology, 5th Edition, Saunders.)
and may serve as a prognostic indicator. In a clinical study of severely burned patients (>60% TBSA, third-degree) serum concentrations of complement proteins were measured sequentially. All patients had decreased concentrations of C3 initially; however, serum concentrations of C3 rebounded fully in surviving patients while remaining depressed in non-survivors. Diminished complement, in combination with decreased concentrations of fibronectin and serum immunoglobulins, contributed to the depression of opsonic activity in both serum and blister fluid from burn patients, and may predispose burn patients to wound infections.

### Cytokines and chemokines

Cytokines are a heterogeneous group of small polypeptide-soluble mediators that are important for the regulation of antimicrobial immunity. In conjunction with hormones and neurotransmitters, cytokines regulate tissue repair and immune responses. Most cells of the immune system either release cytokines and/or respond to cytokines through specific receptors. The cytokine response evoked by microorganisms controls both innate and adaptive immune responses, including inflammation, defense against viruses, leukocyte recruitment and proliferation of specific T- and B-cell clones, while regulating the function and interaction of a variety of immune cells. A complete discussion of cytokine biology is beyond the scope of this chapter. It is likely that a broad array of cytokines regulate the pro- and anti-inflammatory changes that occur after burn injury. Some of the most recent reports on cytokine function in burn patients are reviewed below, and a brief list of cytokines that have been studied in burned populations is presented in Table 22.1.

The description of the cytokine response after burn injury has varied widely in several clinical studies. It is likely, based on accumulated evidence and results from well-controlled animal experiments, that burn injury by itself evokes only a modest increase in circulating cytokines. This limited cytokine response may be related, in part, to burn-induced expression of anti-inflammatory signaling pathways and factors such as suppression of cytokine signaling-3 (SOCS 3) within hours of burn injury. Nevertheless, concentrations of cytokines remain elevated in plasma for weeks after major burn injuries, and there appears to be a significant difference in cytokine production between children and adults.

**Table 22.1 Cytokine and chemokine mediators of systemic inflammation**

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>Polypeptide size</th>
<th>Cell source</th>
<th>Cell target</th>
<th>Primary effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor necrosis factor α (TNFα)</td>
<td>17 kD</td>
<td>Monocytes, macrophages, T lymphocytes</td>
<td>(a) Neutrophil</td>
<td>Activation (inflammation)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(b) Endothelial cell</td>
<td>Activation (inflammation/coagulation)</td>
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<td></td>
<td></td>
<td></td>
<td>(c) Hypothalamus</td>
<td>Release of vasodilators (NO)</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td>(d) Liver</td>
<td>Fever</td>
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<td></td>
<td></td>
<td></td>
<td>(e) Muscle, fat</td>
<td>Acute phase response</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(f) Heart</td>
<td>Catabolism</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(g) Macrophages</td>
<td>Myocardial suppression</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(h) T lymphocytes</td>
<td>Release of cytokines, inflammation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(i) Various tissues</td>
<td>Apoptosis?</td>
</tr>
<tr>
<td>Interleukin-1 (IL-1)</td>
<td>17 kD</td>
<td>Monocytes, macrophages</td>
<td>(a) T cells</td>
<td>Activation (inflammation)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(b) Endothelial cell</td>
<td>Activation (inflammation/coagulation)</td>
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<td>(c) Liver</td>
<td>Release of vasodilators (NO)</td>
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<td>(d) Hypothalamus</td>
<td>Acute phase response</td>
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<td></td>
<td></td>
<td></td>
<td>(e) Muscle, fat</td>
<td>Fever</td>
</tr>
<tr>
<td>Interleukin-6 (IL-6)</td>
<td>26 kD</td>
<td>Monocytes, macrophages, T cells, endothelial cells</td>
<td>(a) Liver</td>
<td>Acute phase response</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(b) B cells</td>
<td>Activation</td>
</tr>
<tr>
<td>Interleukin-8 (IL-8)</td>
<td>10 kD</td>
<td>Monocytes, macrophages, endothelial cells</td>
<td>Neutrophils</td>
<td>Chemotaxis, activation</td>
</tr>
<tr>
<td>Interferon-γ (IFN-γ)</td>
<td>21–24 kD</td>
<td>T cells, NK cells</td>
<td>Macrophages</td>
<td>Activation (inflammation)</td>
</tr>
<tr>
<td>Interleukin-12 (IL-12)</td>
<td>70 kD</td>
<td>Macrophages</td>
<td>T cells, B cells, NK cells</td>
<td>Activation, differentiation</td>
</tr>
<tr>
<td>Interleukin-18</td>
<td></td>
<td>Macrophages</td>
<td>T cells, NK cells</td>
<td>Activation, differentiation</td>
</tr>
<tr>
<td>IL-10</td>
<td></td>
<td>Monocytes/Th2 lymphocytes, mast cells, regulatory T cells</td>
<td>Macrophages, Th1 lymphocytes, NK cells</td>
<td>Inhibition, activation regulation</td>
</tr>
</tbody>
</table>
IL-6 is one of the most consistently elevated cytokines in the circulation of post-burn patients and experimental animals. A recent study indicates that elevated plasma IL-6 concentrations may correlate with mortality in patients with burn and smoke inhalation injuries. It is unclear what specific function IL-6 has in the burn-induced immune response, but a study showed improved cell-mediated immunity after blockade of IL-6 in burned mice. In another study, the proinflammatory response and mortality were attenuated in post-burn mice subjected to endotoxin when IL-6 was blocked. IL-6 has also been shown to contribute to myocardial dysfunction during the post-burn period. Horton and colleagues have described the contribution of IL-6 to burn-induced myocardial dysfunction in several experimental studies, an effect that is likely orchestrated by numerous proinflammatory mediators and initiated by activation of Toll-like receptors.

Perhaps more important than the burn-induced cytokine response is the secondary cytokine response to potential pathogens in the post-burn period. In this regard, burn injury may be followed by a period of attenuated expression of some cytokines that are important in the immune response to microbial organisms, and increased expression of cytokines that may hinder the immune response. For example, expression of IFNγ and a number of IFNγ-inducing cytokines, including IL-2, IL-12, and IL-15, is reduced in response to a secondary immune stimulus after burn injury. IFNγ facilitates numerous beneficial effects on the immune response to infection, including induction of class II major histocompatibility complex (MHCII) proteins on antigen-presenting cells. Antigen-presenting cells such as macrophages and dendritic cells use the MHCII as a mechanism for presenting microbial antigens to CD4+ T cells at sites of infection. Decreased monocyte expression of the MHCII is a consistent finding in burn patients. IFNγ activity also contributes to phagocytosis and microbial killing through several mechanisms. In mice, IFNγ induces IgG2a, which opsonizes bacteria and promotes the expression of FcγRI receptors on phagocytes. IFNγ also potentiates the availability of NO, hydrogen peroxide, and superoxide in phagocytic cells, and promotes expression of chemotactic factors and adhesion molecules for mononuclear cell recruitment to areas of infection. In experimental burn models, lack of IFNγ activity has been associated with diminished ability to clear bacteria.

Impaired production of IL-12 in response to endotoxin has also been described in mice after burn injury. IL-12, an important product of dendritic cells and monocytes, serves to stimulate production of IFNγ by NK cells as well as playing a role in determining the class of T-helper lymphocyte response. IL-10 is a cytokine that has anti-inflammatory activity and may serve to attenuate the proinflammatory response and prevent excessive inflammation after burn injury. Increased and prolonged production of IL-10 may contribute to immunosuppression in the post-burn period. Immune cells from burn patients demonstrated an exaggerated IL-10 response to secondary stimulation with endotoxin or other microbial products, and this finding correlated with septic episodes. Experimental studies confirmed an increased IL-10 response to microbial stimuli in animals that had previously been subjected to thermal injury. Concentrations of IL-10 have been reported to reach a peak in the plasma of patients approximately 1 week after burn injury, which correlates with the time when septic episodes begin to occur with increased frequency. In another clinical study, serum concentrations of IL-10 appeared to be highest in non-surviving patients with sepsis. However, the functional role of increased IL-10 and decreased IFNγ production in facilitating post-injury immunosuppression is not completely clear. Murphy and colleagues reported that IL-10 neutralization and IFNγ administration did not improve survival or bacterial clearance in a model of post-injury immunosuppression.

Chemokines or chemotactic cytokines are a group of specialized polypeptides that play a complex role in the innate immune response by directing migration of immune and inflammatory cells. They are named and grouped based on the position of cysteine residues near the amino terminus, which determines the typical three-dimensional structure of these polypeptides. The leukocytes and endothelial cells of most inflamed tissues can release a variety of chemokines that recruit specific sets of leukocytes to a site of infection, based on the nature of the inciting pathogen. Chemokines also recruit leukocytes to sites of tissue injury such as the burn wound. IL-8, a neutrophil-specific chemoattractant, is one of the most widely studied chemokines. IL-8 has been reported to be significantly elevated in the circulation of post-burn patients, and the highest concentrations are detected in non-survivors. Severe burn injury is often associated with a period of neutropenia, perhaps as a function of neutrophil activation and exit from the circulation. Besides the burn wound, the lung is a preferred site for neutrophil sequestration in burn patients, even in the absence of inhalation injury. Experimentally, neutrophils can appear in lung tissue within hours of burn injury, and this phenomenon can be attenuated by neutralization of complement C5a or of the chemokines keratinocyte-derived cytokine (KC) or macrophage inflammatory protein-2 (MIP2). MIP-2 is an IL-8 homolog in the mouse. Furthermore, Schmalsteig and colleagues have shown that IL-8-mediated neutrophil recruitment is a central factor contributing to pulmonary injury caused by burns and smoke inhalation. However, several studies have demonstrated diminished neutrophil chemotaxis in post-burn patients which may, in part, be due to a combination of suppressive circulating soluble factors and a reduced ability to upregulate the MAC-1 (CD11b/CD18) adherence receptors on the cell surface. A recent clinical study of burn patients demonstrated an association between the development of bacteremia and a decrease in neutrophil expression of CD11b, an adhesion molecule that functions in endothelial binding and migration from the circulation. Overall, it is likely that burn injury has significant effects on neutrophil function, which is dependent on the size of the burn, the time elapsed after burn injury, the specific tissue being analyzed, and the specific stimulus that is eliciting the neutrophil response.
are designed to eliminate established infections and prevent reinfection by the same microbial organism. After an initial exposure to an antigen, the adaptive immune system provides the patient with immunologic memory, whereby re-exposure to the same microorganism is associated with an immune response that is more rapid and greater in magnitude. This response is characterized by the production of antibodies that target specific antigens associated with the microbe, and the generation of antigen-specific T-cell responses. Alterations in antigen presentation and lymphocyte responses have been described after major burn injury.

### Adverse effects of burn injury on antigen presentation

Cellular adaptive immunity is initiated by antigen presentation to T cells by dendritic cells and other antigen-presenting cells. However, both myeloid and plasmacytoid dendritic cells have been found to be decreased in burn patients suffering sepsis compared to non-septic burn patients and healthy controls.\(^9^8\) Antigen-presenting cells present peptides for T-cell recognition in association with an MHCII molecule. HLA-DR is the MHCII molecule that is critical for antigen presentation in humans. However, in burn patients a significant decrease in expression of HLA-DR was detected on circulating monocytes. Additionally, HLA-DR expression was further suppressed in burn patients who became septic compared to those who did not develop sepsis.\(^9^9,1^0^0\) In murine models antigen presentation is significantly impaired early after burn injury.\(^1^0^1\) As in burn patients, this was associated with decreased expression of class II MHC and may be a result of diminished IFN\(\gamma\) production,\(^1^0^2–1^0^4\) a known inducer of class II MHC gene expression.\(^1^0^5\) One experimental study has suggested that the use of \(\alpha\)-galactosylceramide, which targets natural killer T cells (NKT), can prevent some of these derangements, including burn injury-induced suppression of Ag-specific T-cell responsiveness and diminished expression of MHCII and CD40 on antigen-presenting cells.\(^1^0^6\)

### Adverse effects of burn injury on T-cell activation

The majority of observations of immune function in burn patients have come from analysis of T cells and their responses to ex vivo stimulation. The effects of burn injury on specific T-cell subsets is not clear, and may vary depending on the time from injury, patient care, and exposure to microorganisms. One study found that the proportion of CD4\(^+\) T helper cells was significantly lower 7 days post burn in patients who developed septicemia, whereas the CD8\(^+\) cytotoxic T-cell numbers were increased, and suggested that inverted CD4/CD8 ratios may be of prognostic value for septic complications.\(^1^0^7\) However, this does not appear to be a reliable prognostic indicator, as other studies have reported a decrease in CD8\(^+\) T-cell numbers in burn patients.\(^1^0^8,1^0^9\) A consistent finding among these studies was that CD4\(^+\) T-helper cell numbers were decreased in burn patients, and were even further depleted in burn patients with sepsis.\(^1^0^9\) This depletion of CD4\(^+\) T cells may be due to

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### Table 22.2 Classification of chemokines

<table>
<thead>
<tr>
<th>Chemokine type</th>
<th>Target cell</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CXC chemokines</strong></td>
<td></td>
</tr>
<tr>
<td>CXCL8 (IL-8, mouse MIP-2)</td>
<td>Neutrophils</td>
</tr>
<tr>
<td>CXCL1 (GRO(\alpha), mouse KC)</td>
<td>Neutrophils</td>
</tr>
<tr>
<td>CXCL2 (GRO(\beta), mouse KC)</td>
<td>Neutrophils</td>
</tr>
<tr>
<td>CXCL3 (GRO(\gamma), mouse KC)</td>
<td>Neutrophils</td>
</tr>
<tr>
<td>CXCL5 (ENA-78)</td>
<td>Neutrophils</td>
</tr>
<tr>
<td>CXCL6 (GCP-2)</td>
<td>Neutrophils</td>
</tr>
<tr>
<td>CXCL4 (PF-4)</td>
<td>Fibroblasts, stem cells</td>
</tr>
<tr>
<td>CXCL9 (Mig)</td>
<td>T and NK cells</td>
</tr>
<tr>
<td>CXCL10 (IP-10)</td>
<td>T and NK cells</td>
</tr>
<tr>
<td>CXCL11 (I-TAC)</td>
<td>T and NK cells</td>
</tr>
<tr>
<td>CXCL12 (SDF-1(\alpha/\beta))</td>
<td>T lymphocytes</td>
</tr>
<tr>
<td><strong>CC chemokines</strong></td>
<td></td>
</tr>
<tr>
<td>CCL3 (MIP-1(\alpha))</td>
<td>Monocyte/macrophages, T and B cells, NK cells, basophils</td>
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<td>CCL4 (MIP-1(\beta))</td>
<td>same as above</td>
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<tr>
<td>CCL22 (MDC)</td>
<td>Monocyte, T lymphocytes</td>
</tr>
<tr>
<td>CCL25 (TECK)</td>
<td>Macrophages, T lymphocytes</td>
</tr>
<tr>
<td>CCL17 (TARC)</td>
<td>T lymphocytes</td>
</tr>
<tr>
<td>CCL5 (RANTES)</td>
<td>Monocyte/macrophages, T/NK cells</td>
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<tr>
<td><strong>Basophils</strong></td>
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<tr>
<td>CCL14 (HCC-1)</td>
<td>Monocytes</td>
</tr>
<tr>
<td>CCL16 (HCC-4)</td>
<td>Monocytes, lymphocytes</td>
</tr>
<tr>
<td>CCL18 (DC-CK-1)</td>
<td>T lymphocytes</td>
</tr>
<tr>
<td>CCL20 (MIP-3(\alpha))</td>
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</tr>
<tr>
<td>CCL19 (MIP-3(\beta))</td>
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</tr>
<tr>
<td>CCL2 (MCP-1)</td>
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</tr>
<tr>
<td>CCL8 (MCP-2)</td>
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<td>CCL7 (MCP-3)</td>
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<tr>
<td>CCL13 (MCP-4)</td>
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</tr>
<tr>
<td>CCL11 (Eotaxin)</td>
<td>Eosinophils</td>
</tr>
<tr>
<td><strong>Other chemokines</strong></td>
<td></td>
</tr>
<tr>
<td>XCL1 (Lymphotactin)</td>
<td>T lymphocytes, NK cells</td>
</tr>
<tr>
<td>CX3CL1 (Fractalkine)</td>
<td>T lymphocytes, monocytes</td>
</tr>
</tbody>
</table>

The current conventional names of chemokines are presented and original names are provided in parentheses for reference.

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### Adaptive (acquired) immune function after burn injury

Whereas innate immunity provides non-specific responses that limit the growth and spread of infection, adaptive immunity provides potent antigen-specific responses that
activation-induced apoptosis, as on analysis a significant proportion of burn patients’ circulating lymphocytes were undergoing apoptosis, and apoptosis could be further increased by mitogenic stimulation in vitro. Additionally, expression of the T-cell activation marker CD25 was reported to be increased both spontaneously, suggesting in vivo activation, and after mitogenic stimulation in vitro. Perhaps related to these alterations are burn-associated effects on T-cell phospholipid and fatty acid composition and defective transmembrane signaling. Mouse models of burn injury have confirmed burn-induced apoptosis in T cells from various lymphoid and non-lymphoid organs, and have suggested that glucocorticoids are responsible for increased caspase-3 activity and subsequent apoptosis. Murine burn models have also demonstrated suppressed expression of c-fos and relA, and altered activities of the AP-1 and NF-κB transcription factors that regulate genes involved in the maintenance of cell survival and inflammation.

It has been proposed that an early, ‘non-specific’ activation of immune cells after severe burn injury results in a subsequent impairment of their specific effector functions. There appears to be at least a correlation between these early activation markers and T-cell dysfunction after burn injury. T-cell proliferation after mitogenic stimulation and alloreactivity in mixed leukocyte reactions have been consistently reported as being impaired in samples from burn patients. Significant alterations in elicited cytokine production have also been reported to occur after major burns, with a decrease in the production of Th1-associated cytokines relative to Th2 cytokines. IFN-γ production by mitogen-stimulated peripheral blood leukocytes from burn patients was significantly attenuated, whereas IL-4 production was significantly augmented. Another study reported that IL-2 and IFN-γ production by stimulated T cells was significantly lower in non-survivors than in survivors of severe burn injury. Zedler et al. found that the number of IL-4-producing CD8+ T cells was significantly higher and the number of IFN-γ-producing memory T cells significantly lower in non-survivors than in patients who survived after burn injury. Additionally, IL-10 production is reported to be higher after burn injury, and elevated plasma levels in burn patients correlated with poor prognosis. Experimental studies in a mouse model of burn injury have demonstrated a significant increase in the activity of regulatory T cells (CD4+CD25+) in lymph nodes draining the burn wound. Specifically, regulatory T cells isolated from burned mice were potent suppressors of T-cell proliferation and IL-2 and IFN-γ production, owing in part to elevated surface expression of transforming growth factor-β1 (TGF-β1). Depletion of these cells prior to burn injury ameliorated the burn-induced suppression of antigen-specific Th1-type immune responses. Regulatory T cells promote an anti-inflammatory response to injury, as enhanced inflammatory responses are measured in immune cells of T reg-deficient mice after burn injury. These experimental findings seem to correlate with the clinical situation as increased CD4+CD25+ T reg activity was associated with suppression of the Th1 phenotype in post-trauma patients. Burn injury also induces rapid T-cell receptor signaling in regulatory T cells, but not in other CD4+ or CD8+ cells, isolated from the draining lymph nodes. Although the exact significance of each of these functional impairments remains to be determined, there does appear to be a correlation between T-cell dysfunction and susceptibility to infection and subsequent mortality after severe burns. In a clinical study of trauma and burn patients, those who had depressed cell proliferation of isolated T cells were at high risk for the development of multiple organ failure and mortality. Teodorczyk-Injeyan et al. reported that burn patients who were unable to recover IL-2 production and T-cell IL-2 receptor expression over time developed fatal sepsis.

Adverse effects of burn injury on B-cell-mediated immunity

Hansbrough et al. noted a defect in the ability of burn patient sera to opsonize bacteria, which subsequently affected in vitro phagocytosis. Schluter et al. reported a decrease in expression of the B-cell activation marker CD25 both before and after cytokine stimulation of burn patient samples. In a clinical study, mitogen-induced immunoglobulin production was increased initially but suppressed at 3–4 weeks after burn injury. In survivors, immunoglobulin production returned to baseline levels or higher, whereas production remained suppressed in burn patients who developed fatal sepsis. Analysis of immunoglobulin production in murine burn models has indicated that injury has a significant suppressive effect on antigen-specific antibody production. The reported effects on specific immunoglobulin subtypes vary, perhaps owing to the use of different eliciting antigens or other experimental conditions. Production of tetanus toxoid-specific IgG, specifically IgG2a, was impaired after burn injury in mice but could be restored by exogenous IL-12, suggesting that impaired IgG2a production after burn injury is related to impairments in Th1-associated cytokine production. Similarly, production of Pseudomonas-specific IgG was suppressed after burn injury in mice previously exposed to Pseudomonas aeruginosa. Treatment with fms-like tyrosine kinase-3 ligand promoted greater IgG production, in association with increased IL-12, IFN-γ, and enhanced opsonization capacity. Restoration of specific antibody responses may diminish septic complications and improve outcome in burn patients, as high titers of specific IgG in patients with Pseudomonas aeruginosa bacteremia were associated with a significant reduction in the frequency of shock and death. Other studies have reported that numerous B-cell functions are impaired after burn injury, including antigen-specific IgM, total IgM, and total IgG production at 8 days after burn injury in mice. LPS-specific IgM could be restored to normal by cyclooxygenase inhibition, suggesting a role for PGE2 in impaired B-cell responses to antigen. Others have reported a role of TGFβ in impairment of B-cell clonal expansion, and inhibition of IgM synthesis and antigen-specific antibody production after burn injury.

Hematopoiesis after burn injury

In addition to the numerous injury-associated alterations in innate and acquired immune cell functions, there are also effects of burn injury on immune cell production from bone marrow-derived progenitor cells (Fig. 22.5). Analysis of
peripheral blood leukocytes in burn patients has revealed fluctuations in immune cell composition, with periods of neutropenia, monocytopenia, and at other times monocytosis. Analysis of hematopoiesis in murine models has suggested that burn injury increases myelopoiesis in both spleen and bone marrow, with alterations occurring at the level of the myeloid cell phenotype. Burns appear to shift the hematopoietic potential of myeloid progenitor cells towards monocytosis at the expense of neutrophil production, an effect that may be mediated in part by norepinephrine.

**Immunomodulation and burns**

**Immunonutrition**

One of the most successful interventions for improving immune status and reducing infections in burn patients is nutritional supplementation. Dylewski and colleagues recently reported that although infectious complications were more common in malnourished than in well-nourished burn patients, the difference in the incidence of infections between groups was not statistically significant. However, others have reported that early enteral feeding may reduce intestinal permeability and enterogenic infection. A study comparing early enteral feeding with total parenteral nutrition reported that early enteral feeding significantly reduced the incidence of pneumonia, \textit{P. aeruginosa} bacteremia, septic shock, and mortality in burn patients. Early enteral feeding also accelerated the recovery of CD4/CD8 T-cell ratios and increased plasma IgG and IgM and intestinal secretory IgA in burn patients. Berger and colleagues reported that trace element (Cu, Zn, Se) supplementation, given early, reduced the incidence of bronchopneumonia infections and reduced hospital stay. However, supplementation with fish oil and the amino acid arginine did not improve infection rates in burn patients. Perhaps the most promising nutritional supplement after burn injury is the amino acid glutamine. Depletion of glutamine after burn injury is associated with an increased risk of infection, and several studies have demonstrated benefits of glutamine supplementation in burn patients. Peng and colleagues reported that enteral supplementation with glutamine improved intestinal barrier function and reduced the period of hospitalization. Additionally, glutamine supplementation in burn patients enhanced several indices of cellular immune function, including lymphocyte proliferation, IL-2 production and neutrophil phagocytosis. However, there was no observed effect of glutamine on immunoglobulin or complement protein levels. Garrel et al. found that enteral supplementation with glutamine after burn injury significantly reduced the incidence of infections, specifically positive blood cultures and detection of \textit{P. aeruginosa}, and reduced mortality in burn patients. In this study, however, no effect of glutamine on neutrophil phagocytosis was observed. Parenteral glutamine supplementation was also found to significantly reduce the incidence of Gram-negative infections in burn patients, as well as to decrease inflammatory markers.

**Selective decontamination of digestive tract**

Selective decontamination of the digestive tract (SDD) has been proposed as a prophylactic treatment to prevent serious infections in burn patients. There is considerable debate regarding the implementation of SDD as a standard preventative maneuver in burn patients. One study in which polymixin E, tobramycin and amphotericin B were administered to burned children showed no effect on the incidence of infections or the production of inflammatory cytokines. However, Mackie and colleagues reported that SDD reduced the incidence of infections with \textit{Pseudomonas} species and
Enterobacteriaceae in burn patients. de la Cal et al. reported that SDD, by the immediate administration of parenteral cefotaxime and intestinal non-absorbable antibiotics, significantly reduced mortality and the incidence of pneumonia in burned adults. Additionally, it was reported that enteral vancomycin reduces MRSA infections in burn patients. However, the American Burn Association does not encourage SDD because of concerns about emerging antibiotic resistance.

Vaccination

A technique that may be highly effective for the prevention of P. aeruginosa infections after burn injury is vaccination with P. aeruginosa outer membrane proteins. In 1970, this approach was investigated in a rat burn model and it was later demonstrated that vaccination of burned mice reduced systemic bacterial load and increased survival upon lethal infection with P. aeruginosa. In 1983, it was reported that both active and passive vaccinations for Pseudomonas were effective in inducing antibodies to Pseudomonas and reducing mortality in both burned adults and children. Since then, numerous studies have reported that vaccination of burn patients with P. aeruginosa outer membrane proteins is safe, significantly increases P. aeruginosa-specific titers, and is associated with a decrease in detection of P. aeruginosa by nested PCR in the blood of vaccinated patients. Although this approach may be effective for enhancing humoral responses to common microorganisms in the burn unit, the efficacy of vaccinations will be restricted to single organisms, unless vaccinations against widely common pathogenic motifs are developed.

Cytokine modulation

Owing to the profound effects of severe burns on pathogen-elicted cytokine production, and the observed correlations between these alterations and negative outcome in burn patients and in experimental models of burn injury, many attempts to modulate immune function after burns have been directed towards restoration of normal cytokine balance. One approach has been the administration of exogenous Th1 or Th1-promoting cytokines to enhance antimicrobial immune responses. IFNγ has been administered to burn and trauma patients in clinical studies but unfortunately has shown no benefit with respect to the incidence of infections or mortality. Experimentally, administration of IL-12 and IL-18 has shown some benefit in animal models, but these cytokines have not been tested in the clinical setting. Adverse reactions to IL-12 in other clinical trials may preclude its introduction as an immunomodulator in burn patients. Neutralization of cytokines believed to contribute to post-burn immunopathology has also been evaluated. Treatment of mice with antibodies specific for IL-10 was shown to increase resistance to infection, but only if given immediately after burn injury. In a murine model of burn and sepsis, the utility of antibodies against TNFα was found to be limited in that TNFα neutralization was only effective during a narrow timeframe after burns, and may have worsened the outcome when high doses of antibodies were used. Given the interactive and dynamic nature of the cytokine network, therapies targeted to modulate the levels of a single cytokine may not be sufficient to restore immunological homeostasis after severe burn injury.

Hematopoietic factors

Another approach to improving immune function in burn patients is to stimulate the process of hematopoiesis to generate new immune cells from bone marrow-derived stem and progenitor cells. The supposition underlying this approach is that accelerated production of new effector cells to outnumber cells that have been impaired by injury may be more effective than therapies designed to compensate for specific burn-induced impairments in immune function. Given the risk of uncontrolled inflammation in burn patients, it is imperative to consider factors that can enhance hematopoiesis without triggering or exacerbating inflammation. Granulocyte–colony-stimulating factor (G-CSF), a neutrophil growth factor, and granulocyte–macrophage colony-stimulating factor (GM-CSF), a growth factor for neutrophils and macrophages, have been considered as post-burn immunomodulators. Both G-CSF and GM-CSF improved immune function in animal models of burn-associated sepsis. Treatment of burn patients with GM-CSF was shown to increase white cell counts and improve neutrophil activity, but further evaluation of infection rate and patient outcome was not reported. Another hematopoietic factor that has been examined experimentally is fms-like tyrosine kinase-3 ligand, or Flt3L, a hematopoietic cytokine and dendritic cell growth factor (Fig. 22.6). Treatment of burned mice with Flt3L has been shown to stimulate the production of dendritic cells, restore pathogen-elicted Th1-associated cytokine production, enhance bacterial clearance, and increase survival after a P. aeruginosa burn wound infection. Resistance to infection was dependent on both dendritic cells and neutrophils, suggesting that modulation of these cell types may have potential for the prevention of infections after a major burn injury.

Other approaches

There are numerous ongoing attempts to develop prophylactic treatments to prevent infections after major burn injury. This discussion has focused on some of the more promising treatments that are being investigated. Many of the potential treatments have been, and will continue to be, borrowed from clinical studies in trauma patients, as there are similarities in the immunological alterations that occur after major burns and other types of trauma. One treatment that shows promise is glucan, a β-1,3-linked glucose polymer derived from the cell wall of Saccharomyces cerevisiae. Glucans have been shown experimentally to reduce sepsis-induced inflammation while enhancing microbial clearance. Clinical studies with trauma and high-risk surgical patients have shown that glucans can reduce infectious complications and mortality in this patient population. Although these compounds have not yet been tested in burn patients, they have been effective in reducing susceptibility to burn wound infection and mortality in a mouse model of burn injury. Another approach that is under investigation is the use of resuscitation fluids as immunomodulators. Junger and
Host defense peptides are another potential mechanism for immunomodulation after burn injury. Defense peptides are naturally occurring antimicrobial effector molecules of the innate immune system. Human β-defensins are produced in the skin by keratinocytes, and expression of one of these peptides, human β-defensin 2, is significantly decreased in burn wounds. Human cathelicidin hCAP-18/LL-37 is another class of defense peptide that is expressed in the skin. Using a rat model of burn wound infection, Jacobsen and colleagues showed that transient cutaneous adenoviral delivery of hCAP-18/LL-37 to infected burn wounds induced hCAP-18/LL-37 and significantly inhibited bacterial growth. Future studies should evaluate the efficacy of host defense peptides for the treatment and/or prevention of infections after burn injury.

**Further reading**


Access the complete reference list online at [http://www.expertconsult.com](http://www.expertconsult.com)
References


5. Franklin GA, Moore KB, Snyder PW, Polk Jr HC, Cheadle WG. Emergence of resistant microbes in critical care units is transient, despite an unrestricted formulary and multiple antibiotic trials. *Surg Infect (Larchmt).* 2002;3:135-144.


59. Sherwood ER, Enoh VT, Murphy ED, Lin CY. Mice depleted of CD8+ T and NK cells are resistant to injury induced by caecal ligation and puncture. Lab Invest. 2004;84:1655-1665.


87. Murphy ED, Sherwood ER. Bacterial clearance and mortality are not improved by a combination of IL-10 neutralization and IFN-gamma administration in a murine model of post-CLP immunosuppression. Shock. 2006;26:417-424.


Introduction

Hematopoiesis is the formation of peripheral blood cells, including red blood cells, leukocytes and platelets. Hematopoiesis occurs in a stepwise pattern in which stem cells differentiate into cells with increasingly restricted developmental potential. Growth factors and cytokines present in the bone marrow influence the commitment patterns of these progenitor cells, yielding the mature, fully differentiated bone marrow cells that later populate the bloodstream. These growth factors and cytokines influence transcription factor expression, which ultimately controls cell fate. The dramatic metabolic and physiologic stresses of other organ systems following a severe burn injury are well recognized. Alterations to the hematopoietic system should not be ignored, as they contribute to immunomodulation and anemia, which significantly affect patient morbidity and survival. This chapter provides an overview of hematopoiesis, the blood cells formed, the growth factors and transcription factors that control cell fate, how burn injury affects these processes, and therapeutic strategies used to combat these effects.

Hematopoiesis

Overview

Hematopoiesis is the formation of peripheral blood cells, which are composed primarily of erythroid cells, leukocytes, and megakaryocytes. Erythroid cells include erythroid precursors in the bone marrow (proerythroblast, basophilic normoblast, polychromatic normoblast, and orthochromatic normoblast) and reticulocytes and erythrocytes present in both the bone marrow and the peripheral bloodstream. Leukocytes include both lymphoid and myeloid white blood cells. The lymphoid lineage is composed of T and B cells. Myeloid cells comprise the remaining leukocytes, including monocytes, macrophages and neutrophils. Dendritic cells and natural killer (NK) cells can develop from either the myeloid or the lymphoid lineage. Megakaryocytes are the bone marrow progenitors of platelets. Hematopoiesis is essential for oxygen delivery, host defense and coagulation, with estimates of 200 billion erythrocytes, 100 billion leukocytes and 100 billion platelets made daily in an adult.

Stem cells

Hematopoiesis proceeds in a stepwise, hierarchical fashion. Hematopoietic stem cells (HSCs), which reside in the bone marrow, are at the top of the hematopoietic hierarchy. HSCs are able to both self-renew and differentiate, ensuring maintenance of their population and replenishment of all hematopoietic cell lines. There are two forms of HSC, long term (LT) and short term (ST), which differ in their self-renewal and differentiation capacities. As suggested by their name, LT-HSCs are the permanent self-renewing cells of the bone marrow with minimal response to physiologic stress, whereas ST-HSCs have the ability to increase their production and differentiation during different pathologic states. ST-HSCs differentiate into multipotent progenitor cells (MPPs). MPPs do not have the ability to reconstitute the bone marrow, but do maintain the ability to differentiate into all hematopoietic lineages, bridging the stem cell niche with progressively lineage-restricted progenitor cells. The hierarchy of hematopoiesis, from stem cell to progenitor groups to terminally differentiated cells, allows for the rapid amplification of cell production by the upstream proliferation of stem cells. There are other suggested hematopoietic hierarchies which differ in the branch points at which certain progenitor populations lose lineage potential or suggest that some cell groups have the potential to dedifferentiate and enter a different lineage. In essence, hematopoiesis is controlled by a hierarchical pattern of progressive loss of lineage potential. The expression of a limited set of transcription factors, controlled by the growth factors and cytokines present in the bone marrow milieu, control lineage commitment, cell fate and, ultimately, the composition of cells in the bloodstream.

HSCs have received extensive attention in the media both because of their complicated ethical dilemma and also because of their extensive potential in treating blood disorders. The use of these cells as a potential therapy for the anemia or immune dysfunction present in severely burned patients is not currently feasible, but their use in the future is possible.

Progenitor cells

As HSCs differentiate they lose potency and developmental options, and become lineage-restricted progenitor cells. The genetic programs controlling lineage restriction take place...
over 10–15 cell divisions from the HSC stage. The traditional hematopoietic hierarchy proposes that HSCs differentiate into either common lymphoid progenitors (CLP) or common myeloid progenitors (CMP), based on local cytokine and growth factor levels and also on the development of the IL-7 receptor, which prompts lymphoid but not myeloid formation. CLPs can differentiate into T and B lymphocytes, natural killer cells and antigen-presenting dendritic cells. CMPs can differentiate into either megakaryocyte–erythroid progenitors (MEP) or granulocyte–monocyte progenitors (GMP). CMPs, MEPs and GMPs are identified by their unique expressions of the Fcγ receptor and CD34. As implied in their names, MEPs become either megakaryocytes or erythroid/red blood cells and GMPs become neutrophils, monocytes, macrophages, eosinophils, basophils and mast cells. Although progenitor cells are of the utmost importance in terms of lineage fate and the overall composition of the bloodstream, they comprise less than 1–2% of all bone marrow cells.

**Burn injury, stem and progenitor cells**

There has been very little research on the effect of burn injury on HSCs and progenitor cells. HSC production is amplified in a mouse model of sepsis, which is a similar physiologic process to burn injury. Inflammatory cytokines increase granulocytopoiesis while reducing lymphopoiesis via changes in common progenitor cells. Preliminary work from our laboratory has demonstrated an overall increase in the HSC population in mice initially following burn injury, with a gradual decrease 10–14 days post burn. Specifically, ST-HSCs and MPPs increase, but there is no significant change in LT-HSCs. Interestingly, in the progenitor compartment there is a significant increase in GMPs, with slight decreases in MEP, CMP, and CLP production following burn (Fig. 23.1). Most of these changes reverse themselves 2–3 weeks post burn. Given the hierarchical nature of hematopoiesis, changes in ST-HSC and MPP production as well as the lineage shift towards greater GMP production may herald the overall erythropoietic production (anemia) and myeloid function (immune dysfunction) problems present after burn injury. Further work on the HSC and progenitor cell response may provide avenues for early therapeutic intervention, which may ameliorate the negative and deleterious hematopoietic consequences of burn injury.

For the most part, the commitment patterns of stem and progenitor cells are a function of the growth factors and cytokines (IL-6, TNFα, stem cell factor, etc.) to which the cells are exposed and the transcription factors (GATA-1, PU.1, etc.) that are expressed as a result. The intricate interplay of growth factors, cytokines and transcription factors, and their influence on lineage commitment patterns, is discussed extensively later in this chapter.

**Red blood cells**

### Sources of anemia: clinical and laboratory findings

Red blood cells are derived from cells of the erythroid lineage, which is a branch of MEPs. Erythroid cells progress through several blast stages until they form reticulocytes, which can mature in the bone marrow or periphery to form erythrocytes. Often, a measure of the reticulocyte count can be used to determine the degree of erythropoietic response, as the percentage of reticulocytes should increase in states of anemia or increased erythropoietin. Mature erythrocytes populate the bloodstream and are responsible for oxygen transport.

Burn patients commonly suffer from anemia. Anemia is a reduction in red blood cells below normal laboratory limits. Often, a mild reduction in red blood cells is of little clinical significance. Only when the red blood cell concentration...
is significantly reduced does it become clinically relevant, leading to impaired end-organ perfusion and oxygenation. Defined hemoglobin concentrations and hematocrit levels trigger the transfusion of packed red blood cells (pRBCs) in order to restore perfusion. In patients who are not actively bleeding, without coronary ischemia or without hemodynamic compromise, the transfusion trigger is typically in the range of 7–8 g/dL of hemoglobin or 21–24% hematocrit. Traditionally, a hemoglobin trigger of 10 g/dL or a hematocrit of 30% has been used. However, both large-scale work in the critical care literature and a smaller, retrospective review of both adult and pediatric burn patients have established the infectious, cost and survival benefit of a lower, more restrictive transfusion trigger.

Burn patients are anemic because of both acute surgical blood loss and the anemia of critical illness. Acute surgical blood loss stems from repeated debridements of the burn wound and wound coverage with autologous skin graft. For grafting to be successful, the wound bed must be prepared with well-vascularized tissue. Often, a clinically reliable gauge of the viability of this tissue is bleeding during debridement. As a result, much blood is lost during debridement, despite the wound eschar being devoid of vascularized tissue. Surgical blood loss has been estimated and measured in a variety of ways, but can most simply and reliably be reported based on surgical and anesthesia team estimates. In addition, owing to blood type and cross-matching expenses, and overestimation of operative transfusion needs, a preoperative estimate of 1.78 units of pRBCs per 1000 cm² of wound excised is the best use of blood bank resources.

Although acute surgical blood loss is obvious and most prominent during the treatment phase of burn injury, burn patients also suffer a prolonged anemia of critical illness during their recovery. The anemia of critical illness is the inability of red blood cell production to meet red blood cell demand and losses during a critical illness. Over 50% of all transfusions during a burn patient's hospital course may be due to the anemia of critical illness. It has been equated to an acute form of the anemia of chronic disease. The etiology of the anemia of critical illness is multifactorial, with blood loss from iatrogenic factors such as phlebotomy and dressing changes, or erythropoiesis stunted by nutritional deficiencies and bone marrow dysfunction. Specifically, bone marrow dysfunction leading to dampened erythropoiesis has been explored in autopsy studies and in the mouse model of burn injury and in vitro. In an autopsy study of patients who died from either myocardial infarction, sepsis or burns, the bone marrow of burn patients contained significantly fewer erythroblasts than that in the other groups. In the mouse model, both previous work from Wallner and recent work in our laboratory have demonstrated a shift in hematopoietic lineage commitment in the bone marrow away from erythroid cell formation at the expense of myeloid cell formation. Although Wallner's work helped to establish this phenomenon, hierarchical models of hematopoiesis and the simple and reliable use of flow cytometry to identify rare populations of cells (as opposed to histologic and morphologic examination) have allowed us to track the source of these changes from modifications in HSCs with concomitant shifts in myeloid, erythroid, and lymphoid progenitor groups, as mentioned earlier.

This insight into hematopoietic lineage commitment patterns following burn injury may not only help to better explain the dampened erythropoiesis of the anemia of critical illness, but may also shed light on a source for the dysfunctional leukocytes that contribute to immunomodulation. Further functional studies linking the changes of hematopoietic stem and progenitor cells with the cells present in the bloodstream may yield findings that could significantly benefit patient care in terms of anemia treatment/prevention and a better understanding of the origin of immunodysfunction.

Dampened erythropoiesis following burn injury may be caused by proinflammatory cytokines and/or elevated levels of catecholamines. Wallner suggested that there may be an 'erythroid inhibitory substance' following burn injury, as the sera of burn patients reduce erythroid colony production compared to the sera of healthy patients. Although this work did not identify an 'erythroid inhibitory substance', later work on erythropoiesis has shown that both proinflammatory cytokines and catecholamines, which are both significantly elevated following burn injury, may inhibit erythropoiesis. In vitro, the addition of tumor necrosis factor, interferon-β, interferon-γ and interleukin-6, all proinflammatory cytokines, reduces erythroid colony formation. Catecholamines are increased beyond their baseline state in the bone marrow following burn injury, and erythropoiesis is significantly altered with changes in catecholamine levels which may contribute to the dampened erythropoiesis following burn injury. The prolonged proinflammatory and hypermetabolic state following burn injury may also significantly alter erythropoiesis and be a major contributor to the anemia of critical illness.

Clinical implications and treatment

Anemia is highly prevalent in patients with severe burn injury. Prevention of anemia mimics the sources, the acute blood loss and the anemia of critical illness, while the mainstream of treatment for both types of anemia remains pRBC transfusion. Acute blood loss anemia is prevented with innovative surgical techniques, whereas the anemia of critical illness is prevented by reduced phlebotomy, decreased blood loss with dressing changes, and improved nutrition.

Several methods have been developed to reduce acute surgical blood loss, including epinephrine tumescence, thrombin-soaked pads, and tourniquet use. Although the studies that examine epinephrine tumescence differ in their methods and results, the injection of dilute epinephrine into the subdermal space promotes vasoconstriction and reduces blood loss during surgical management of a wound. For example, in a prospective trial in children, epinephrine tumescence alone reduced blood loss from 3.5–5% to 0.98% of total blood volume of body excised and grafted. Epinephrine tumescence has no significant hemodynamic consequences, nor does it alter wound healing. The addition of thrombin-soaked pads for extra hemostasis following completion of the operative procedure has been studied in the context of epinephrine tumescence and provides additional hemostasis by reducing unnecessary ooze from the dressing site. Finally, the use of an extremity tourniquet during excision and debridement can reduce surgical blood
loss without compromising graft adherence.90–93 The combination of all three techniques (epinephrine tumescence, tourniquets, and thrombin-soaked pads) can reduce intraoperative transfusion from 3.3 to 0.1 units per operative case, with 96% graft take33 and total units transfused from 15.7 to 7.9 units per patient.78

Recombinant human EPO helps to augment erythropoiesis in patients with chronic anemia (end-stage renal disease, HIV with antiretroviral use, non-myeloid malignancies with chemotherapy), reducing transfusion rates and improving quality of life. To reduce transfusion rates and correct the anemia of critical illness, multiple trials have explored rhEPO use in the critically ill, including burn patients. Unfortunately, both large clinical trials and meta-analyses of critically ill medical, surgical, and trauma patients show no significant reduction in transfusion rates with rhEPO use.84,85 Two studies of rhEPO have been performed in burn patients with no significant increase in hematocrit percentage or decrease in transfusion rates.86,87 Critically ill patients may possess a resistance to erythropoietin,88 which may be a function of antieythropoietin antibodies,89 or a relative reduction in erythropoietic response due to less EPO-responsive erythroid precursors secondary to burn-induced dampened erythropoiesis. Regardless of the cause, given the cost of rhEPO and the lack of transfusion reduction, rhEPO is not indicated for use in burn patients.

Ultimately, anemia is most easily corrected by the transfusion of pRBCs. Burn patients, as a result of both acute blood loss anemia and the anemia of critical illness, require a considerable number of transfusions during their hospital course. Transfusion rates increase with the size of the burn.93,90,91 In a large study of transfusion trends in burn patients, those with ≥ 20% TBSA required 13.7 ± 1.1 units, whereas those with ≥50% TBSA required >30 units of pRBCs.90 Although pRBC transfusion rapidly and reliably corrects anemia, blood transfusion is associated with a considerable number of consequences. The direct transmission of hepatitis B, hepatitis C and HIV are well-known consequences of transfusion, but their transmission rate has significantly decreased with better screening methods.92,93 More importantly, pRBC transfusion is associated with immunomodulation, including increased infectious morbidity,94 with a 13% increase in infections per unit of blood transfused.90 Other significant consequences include transfusion-related acute lung injury (TRALI), which is difficult to diagnose in burn patients as simultaneous lung injury due to resuscitation or inhalation injury may also contribute to the diagnostic criteria for TRALI,95 and ABO incompatibility, which can be rapidly fatal.96 As mentioned earlier, the implementation of restrictive transfusion strategies in which pRBCs are transfused only for hemodynamic instability or at lower, but still safe, hemoglobin concentrations, have reduced overall transfusion rates while reducing infection rates and providing cost and survival benefits.90,91

Anemia is common in burn patients, with greater transfusion requirements for greater percent TBSA burned. Both operative techniques (epinephrine tumescence, tourniquets and thrombin-soaked pads) and transfusion restriction have reduced overall transfusion rates. Other strategies for reducing transfusion rates, including rhEPO, have not proved effective. More research into the molecular and cellular mechanisms of burn-induced dampened erythropoiesis and innovative surgical and patient care techniques should help to reduce overall transfusion rates further.

White blood cells

The primary effectors of host defense are the main populations of leukocytes, lymphocytes, NK cells, polymorphonuclear cells (PMN), and monocytes/macrophages. A balanced activation of these cells is important for robust host defense. Inappropriate activation of these leukocytes, especially the PMN and macrophages, can lead to tissue destruction and systemic inflammation, with dire consequences for the burn patient. Overactivation of PMN and macrophages has been implicated in the development of adult respiratory distress syndrome (ARDS) and multiple organ failure.97–104

Early post-burn period

In the first 24–48 hours following burn, a leukocytosis, and more specifically a granulocytosis, is generally observed that is dependent on the size of the burn wound, with larger burns giving rise to a greater degree of leukocytosis.105 The initial increase in the white blood cell count (WBC) is attributable to three major factors: the acute plasma volume loss due to the burn, demargination of mature neutrophils from peripheral blood vessels, and the rapid release of bone marrow reserves. Bone marrow myeloid progenitors from post-burn day 1 mice have an altered phenotype compared to controls, reflecting the more rapid maturation needed to replenish reserves.106 Following this initial period of leukocytosis burn patients frequently develop leukopenia, which is related to trauma-induced failure of bone marrow hematopoiesis.107 Leukopenia is also frequently seen in burn patients whose wounds are treated with silver sulfadiazine, a common topical antimicrobial agent.108 The severity of the leukopenia that develops from drug toxicity is directly proportional to the amount of agent that is applied to the wound, and thus indirectly to the size of the burn wound itself. The mechanism underlying this drug-induced leukopenia is yet to be elucidated, though direct bone marrow and cellular toxicity may play a role. In general, leukopenia is self-limiting and does not require discontinuation of silver sulfadiazine treatment.

Leukopenia and granulocytopenia often persist in patients when severe bacterial infection is superimposed on burn injuries, especially those with Gram-negative sepsis.109–111 In the early 1970s, Newsome and Eurenius demonstrated in their rat model of thermal injury that the initial granulocytosis was due to demargination of PMN from the blood vessels and through accelerated release of bone marrow stores.112 This granulocytosis, however, is transient, and is followed by a robust bone marrow response to replenish granulocyte stores.113,114 If the burn injury is complicated by sepsis, granulocytopenia persists.115,116 Granulocytopenia under these conditions appears to be due to bone marrow failure.114,115,117,118 McEuen demonstrated a significant inhibition of granulocyte colony-forming units in the bone marrow of burn septic rats.117 In addition, serum from septic burn-injured animals retarded the granulocyte colony formation when added to bone marrow cells from normal non-septic animals.114 In septic animals and in burn patients with sepsis,
the observed granulocytopenia is probably not due to lack of available colony-stimulating factor.

**Myeloid cells**

In addition to alterations in the kinetics of production and maturation, PMNs exhibit qualitative functional changes after burn injury in both animals and humans. Some of the documented functional changes include depressed chemotaxis, phagocytosis, and intracellular killing. For example, isolated neutrophils of burn patients were shown to be defective in intracellular killing of *Pseudomonas aeruginosa*, and the impairment in phagocytosis and intracellular killing are further exacerbated with sepsis. These alterations in the production and function of PMN provide a framework for understanding the contributing factors in the depressed immune status of severely burned patients.

Monocyte/macrophage function is also altered with severe burns, but unlike PMNs, where neutropenia is common, in severe burns and sepsis monocyte counts tend to increase in both animals and humans. Studies demonstrate marked monocytosis, with a dramatic increase (3–5-fold) associated with sepsis. The importance of the burn-induced monocytosis is emphasized by the observation that attenuation of monocytosis as well as blunted macrophage activation results in improved survival. Miller-Grazziano and Faist demonstrated that after trauma, including burns, monocytes/macrophages could be broken down into subsets that were either hyper- or hyporeactive. These cells may develop their phenotypic differences as a result of altered monocytopenia within the bone marrow itself, or as a result of local cytokine environments in the peripheral tissues. Ogle et al. have demonstrated that bone marrow-derived macrophages from thermally injured animals produce increased amounts of TNFα, IL-1, and PGE2 compared to macrophages from non-injured animals, suggesting that thermal injury can stimulate the development of functionally different monocytes within the bone marrow.

**Lymphoid cells**

Patients with severe burns often suffer from suppressed cell-mediated immunity owing to impairments in T-cell function. Impairment in cell-mediated immunity has been implied by observations of delay in skin allograft rejection, suppression of the graft-versus-host response, and skin hypersensitivity reactions in burn patients. The various alterations that have been reported include an overall suppression of circulating T lymphocytes, decreased mitogenesis in response to mitogens, reduced response to antigenic stimulation or activation, and redistribution of T lymphocytes in peripheral blood and tissue compartments. T lymphocytes are divided into T-helper (Th) and T-suppressor populations based on expression of lymphokine profiles, cell surface receptors, and ability to affect the function of NK cells, T-cytotoxic, and B lymphocytes. In recent years strong evidence has emerged to support the hypothesis that burn injury-induced immunosuppression is partly mediated by a shift in lymphocyte subpopulations from Th to T-suppressor subtypes. Part of the initial response to a significant burn is the activation of Th cells as assayed by IL-2R, HLA-2R, and transferrin receptor markers. In vitro functional assays reveal that despite the initial activation of T cells, they were unable to respond to mitogenic and/or antigenic stimulation. The addition of IL-2 fails to reverse T-cell anergy and fails to relieve the suppression of IL-2R. The exact mechanisms that initiate T-lymphocyte apoptosis are still unclear. However, Fas ligand-, TNFα-, and IL-2-mediated pathways have been implicated in T-lymphocyte cell death. Lastly, macrophage activation products such as PGE2 and transforming growth factor-β (TGFβ) can also contribute to T-cell suppression.

B lymphocytes also undergo functional changes with a profound reduction in immunoglobulin levels following thermal injury. All classes of immunoglobulin are reduced, but IgG levels display the greatest reduction, with concentrations reaching as low as 300–400% mg/dL. This drop in immunoglobulin is rapid and early, and is attributed to plasma leakage, increased protein turnover, and decreased IgG synthesis by the B cells. The initial deficit in immunoglobulins is slowly replenished to near normal levels within 2 weeks. Major histocompatibility complex (MHC) glycoproteins are reduced after thermal injury. Non-specific B-cell activation by burn toxins and antigen-dependent mechanisms, activation by phagocytosis of non-specific antigen, may inhibit their ability to form antigen–MHC complexes. Additionally, the display of self-antigens by the B lymphocytes could contribute to antigen-dependent cell death in T lymphocytes and T-cell anergy. Previous work has shown that CD23 expression on activated B cells is abrogated in response to thermal injury. IL-7 levels rise during the first week after burn and could account for the decreased proliferative capacity of mature B lymphocytes. Taken together, these data indicate that the functional alterations in B cells induced by thermal injury could further exacerbate the immune suppression in these high-risk patients.

As a whole, these changes in immune function are clinically significant, as burn patients have an increased susceptibility to nosocomial infections that increases the risk of septic complications, multiorgan failure and mortality. Unfortunately, there are no therapeutic modalities that can reverse this immune dysfunction. As a result, the mainstay of treatment remains the same as for any surgical or critically ill patient: sterile technique, appropriate antibiotic use and source control.

**Megakaryocytes and disorders of coagulation**

The megakaryocytic lineage stems from MEPs, which are derived from CMPs. Megakaryocytopoiesis leads, ultimately, to the formation of platelets. Once megakaryocyte progenitors proliferate and differentiate, mature megakaryocytes produce platelets from cytoplasmic fragmentation. Cytoplasmic fragmentation results in the formation of proplatelets through regulation by the transcription factor NF-E2 that occurs in the bloodstream. Approximately 1 × 10^11 platelets are produced daily. Platelet function to maintain hemostasis through thrombus formation at sites of injury. Platelet dysfunction occurs due to diminished platelet supply (thrombocytopenia), inability to adhere to damaged tissue
and form clots, or when thrombi are produced unnecessarily. Dysregulated coagulation occurs through altered platelet maturation and function, changes in the proteins of the coagulation cascade, and imbalances in the deposition and dissolution of peripheral clots. Because platelets and coagulation disorders are interrelated, pathologic processes associated with both will be discussed in this section.

**Platelets**

Thrombocytopenia requiring platelet transfusion is rare in burn patients. Often, platelet counts and function are stable unless there is an infectious or septic event. In that case, burn patients should be managed similarly to any critically ill patient with sepsis. In patients with ongoing and hemodynamically significant oozing from wound and donor sites in addition to coagulopathy, the administration of platelets and recombinant factor VIIa has been shown, in two case reports, to significantly improve hemostasis.162,163

The transfusion of platelets is not without complications. Platelets are transfused in an ABO-compatible fashion and immediate transfusion reactions are rare. However, platelets are stored at room temperature, allowing for higher rates of bacterial contamination than other blood products. Bacterial contamination of platelets occurs in 1:1000–1:3000 units, with one-sixth of these episodes resulting in a septic event.164 In a study of blood bank use by a burn unit, 15% of all admitted patients received platelets in some combination with either PRBCs or FFP.176 So, although platelet transfusion is not common in burn patients, it is necessary to limit its use, given the significant infectious consequences.

**Disorders of coagulation**

Disorders of coagulation often occur early after the burn injury. Burn patients may suffer thrombocytopenia, disseminated intravascular coagulation (DIC), or other coagulopathies.165–167 A marked reduction in circulating platelet levels during the acute phase of burn resuscitation is primarily due to the consumption of platelets during the formation of systemic microthrombi.168,169 Although local microthrombus formation at the site of injury helps maintain the integrity of the microvasculature surrounding the burn wound, generalized systemic microthrombus formation leads to reduced end-organ perfusion and finally multiple organ failure.168,170 In addition, dilutional effects of extensive fluid resuscitation may also contribute to a reduction in platelet counts. After the initial resuscitation, the thrombocytopenia that is observed during the first week after the thermal injury is believed to be due to the diminished half-lives of platelets in circulation.169 The thrombocytopenic phase is followed during the 2–3 weeks after the initial injury by a period of increased platelet production or bone marrow megakaryocytopoiesis that results in either a return to normal levels or to overt thrombocytosis.171 However, in some burn patients thrombocytopenia persists and is often considered a poor prognostic indicator.172 Among patients with critical burn injuries who develop intravascular hemolysis, an apparent thrombocytosis may be observed which could be due to inadvertent counting of fragmented red cells and red cell microvesicles as platelets in an automated counter.172 Therefore, in severe burns the clinician should be aware of the possibility of spurious platelet counts in the presence of intravascular hemolysis.

Typically, changes in coagulation are transient and resolve with resuscitation and resolution of the acute-phase response to injury.168 In some cases significant alterations in the concentrations of coagulation proteins following thermal injury may persist due to the severity of the burn, sepsis, or the continued inflammatory state during a critical illness. Normally, the interplay among antithrombotic, prothrombotic cellular interactions, and fibrinolytic processes within the vasculature intrinsically controls the homeostatic regulation of coagulation. Under steady-state physiologic conditions, the fluidity of the blood is maintained by morphological integrity of erythrocytes and the endothelial cells lining the blood vessels.173 Normal levels of prothrombotic and antithrombotic factors, which are well regulated and remain for the most part in their quiescent state, also help maintain the homeostatic balance. In burn patients, however, both the thrombotic and the fibrinolytic pathways are triggered in direct proportion to the extent of the injury.166,174,175 During the early resuscitation phase of a burn injury there is a general reduction in the levels of coagulation proteins.166 Dilutional effects of volume administration during this period and the loss of plasma proteins to the interstitium could partially explain the decrease in plasma concentrations of many coagulation proteins. Clinically significant coagulopathic complications are uncommon. For example, clinically significant DIC occurs in only 0.09% of burn patients.176 However, the development of a coagulopathy, especially DIC, is associated with a poor outcome.177,178 Unexpected spontaneous aggregation of platelets in the early period following a burn injury may be due to hyperfibrinogenemia and the interaction between fibrinogen and platelets179 and can lead to the accumulation of thrombi in the microcirculation, and may contribute to the development of end-organ failure and death.167,170,180 Elevated levels of fibrinogen are often present immediately following burn injury owing to the shift in hepatic protein synthesis to acute-phase proteins, including complement, interleukins, etc. in addition to fibrinogen.

Owing to the increase in these proteins and their consequences, a significant number of studies have looked at different treatments aimed at offsetting this hypercoagulable state or replacing depleted elements of the natural anticoagulant proteins. The use of drotrecogin-α/human recombinant protein C181 and antithrombin infusions175,182,183 has been studied and reported to be safe and beneficial. Antithrombin III (ATIII) is a serine protease inhibitor that regulates hemostasis and has been shown to have anti-inflammatory properties.184 ATIII is depleted after injury owing to the shift in hepatic protein synthesis to acute-phase proteins, including complement, interleukins, etc. in addition to fibrinogen. Still, the indication for their use has not been established in the burn population.

Thrombus formation may also be due to decreases in the anticoagulant proteins antithrombin, protein C, and protein S.168 When anticoagulant proteins, including antithrombin, do not return to normal levels, patients may have a longer
hospital stay and worse mortality.185 During recovery from the burn injury, coagulopathies are less related to the burn injury and more likely due to critical care issues, including sepsis. In fact, there is rapid recovery of coagulation factors in the postoperative period of burn wound management, making frequent excision and grafting safe from a hematologic standpoint.186

Fibrinolytic pathways are activated in burn injuries owing to the increased levels of tissue plasminogen activator protein.166 Consumption of antithrombotic proteins by activation of fibrinolytic activities predisposes burn patients to thrombosis. Contributing to the thrombotic state in severely injured burn patients are the release of tissue phospholipids and tissue factor, activation of complement cascade, tissue ischemia, and the presence of sepsis.166,168,172,187 As a result, patients are at increased risk for developing disseminated intravascular coagulation (DIC). DIC is characterized by activation of coagulation, intravascular fibrin formation and vascular thrombosis, resulting in organ hypoperfusion and failure. The consumption of coagulation and anticoagulation factors leads to small vessel thrombosis and simultaneous uncontrolled bleeding.170 Because of the high morbidity and mortality associated with episodes of DIC, a high index of suspicion needs to be maintained in this patient population when sepsis complicates the clinical course. Signs of impending DIC may include refractory shock out of proportion to apparent blood loss, bleeding from venepuncture and catheter sites, and urinary and gastrointestinal bleeding. Standard laboratory values in patients with suspected DIC include prolonged prothrombin time (PT) and activated partial thromboplastin time (APTT), increased levels of fibrinogen degradation products, decreased levels of anti-thrombin III, and decreased platelet counts and fibrinogen levels. Vigilance must be maintained for other thromboembolic complications in this population, such as deep vein thrombosis and pulmonary embolism. The treatment modalities recommended for patients who develop DIC are primarily supportive and geared toward maintaining hemostatic parameters with replacement therapy. In addition, patients receiving broad-spectrum antibiotic therapy or showing signs of hepatic failure should be carefully monitored for vitamin K-dependent coagulopathy. This must be corrected with vitamin K replacement, along with the necessary coagulation factor component therapy. Future efforts in the treatment of coagulopathies will focus on re-establishing the balance of coagulation and fibrinolysis.170

**Growth factors and transcription factors**

As described above, the hematopoietic hierarchy and lineage commitment patterns are a complex but well-preserved processes. The maintenance of stem and progenitor populations and the expansion of terminally differentiated cells are under the control of the growth factors and cytokines present in the bone marrow. Shifts in the concentration of growth factors and cytokines due to illness and injury allow hematopoietic lineage commitment patterns to change, resulting in increases or decreases in terminally differentiated cell populations (Table 23.1). Control of cell fate is most likely due to growth factor- and cytokine-induced transcription factors, as expression and blocking of these transcription factors control lineage commitment in the stem and progenitor cell populations.

### Stem and progenitor cell growth factors

Hematopoietic stem cell maintenance and expansion are controlled by growth factors/cytokines both unique to these cells and also having roles in other hematopoietic and

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**Table 23.1 The roles of growth factors and cytokines in hematopoiesis**

<table>
<thead>
<tr>
<th>Growth factor or cytokine</th>
<th>Role in hematopoiesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stem cell factor</td>
<td>Essential for hematopoietic stem cell proliferation and differentiation</td>
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<tr>
<td></td>
<td>Activates the c-kit receptor</td>
</tr>
<tr>
<td>Fli-3 ligand</td>
<td>Enhances multipotent progenitor, early lymphoid, myeloid, natural killer and dendritic cell proliferation</td>
</tr>
<tr>
<td></td>
<td>Activates the Fli-3/flk-2/CD135 receptor</td>
</tr>
<tr>
<td>IL-3</td>
<td>Plays a role in hematopoietic stem cell, myeloid and erythroid cell line expansion</td>
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<tr>
<td>IL-6</td>
<td>Increased production following burn injury and infection</td>
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<tr>
<td></td>
<td>Essential for expansion of hematopoietic stem and progenitor cells</td>
</tr>
<tr>
<td>G-CSF</td>
<td>Stimulates granulocyte proliferation in the bone marrow and augments immune activity of cells in blood</td>
</tr>
<tr>
<td></td>
<td>Increased immediately following burn injury and in response to infection</td>
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<tr>
<td></td>
<td>RhG-CSF use is not indicated for use in burn patients</td>
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<tr>
<td>CSF-1 or M-CSF</td>
<td>Essential for monocyte and macrophage differentiation</td>
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<tr>
<td></td>
<td>Increases the survival of monocytes and macrophages</td>
</tr>
<tr>
<td>GM-CSF</td>
<td>Regulates the proliferation and differentiation of hematopoietic progenitors</td>
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<tr>
<td></td>
<td>Enhances antigen presentation by DC and macrophages</td>
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<tr>
<td></td>
<td>Prophylactic administration accelerates bacterial clearance and killing</td>
</tr>
<tr>
<td>IL-7</td>
<td>Necessary for both engagement into lymphoid lineage and maintenance and expansion of lymphoid cells</td>
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<tr>
<td>Erythropoietin</td>
<td>Stimulates erythroid proliferation and prevents apoptosis to increase erythrocyte production</td>
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<tr>
<td></td>
<td>May have a role in tissue protection via a related receptor</td>
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<tr>
<td></td>
<td>rhEPO has not been shown to benefit burn patients</td>
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<tr>
<td>Thrombopoietin</td>
<td>Enhances megakaryocyte proliferation and reduces apoptosis to increase platelet production</td>
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<td></td>
<td>May increase following burn injury and contribute to thrombocytosis</td>
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<tr>
<td></td>
<td>Evolving role in stem and progenitor cell proliferation</td>
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non-hematopoietic processes. For example, stem cell factor/steel factor, produced by fibroblasts and endothelial cells, is a growth factor essential for hematopoietic stem cell self-renewal and differentiation by activation of the c-kit (CD117) receptor. Mutations or deletions of stem cell factor or the c-kit receptor in embryogenesis can lead to in utero death. Additionally, stem cell factor plays a role in melanocyte development, spermatogenesis and gut motility. Other growth factors that play a dual role are thrombopoietin, which is essential to megakaryocyte development and granulocyte–macrophage colony-stimulating factor, and IL-3 which contributes to both myeloid and erythroid cell proliferation. IL-6, which is significantly increased immediately following burn and in a variety of inflammatory states, is a proinflammatory cytokine that also plays a role in the expansion of hematopoietic stem cells.

Over 30 growth factors may play a role in stem and progenitor cell maintenance and expansion. Of these, Flt-3 ligand (Fms-like tyrosine kinase-3/ flk-2 (fetal liver kinase 2)) plays an important role in stem and progenitor cell expansion. Flt-3 ligand activates the Flt-3 tyrosine kinase receptor/CD135. In the hematopoietic stem cell compartment, Flt-3 is highly expressed on MPPs and typically absent on LT-HSCs and ST-HSCs. Theoretically, elevated levels of Flt-3 ligand should contribute to MPP expansion in response to inflammation or infection. However, Flt-3 ligand levels have not been shown to increase following burn injury. Further study into Flt-3 ligand levels during physiologic stress may demonstrate a fundamental role in hematopoietic expansion and response to injury. Like other growth factors, Flt-3 ligand also influences myeloid differentiation and early lymphoid development, and enhances NK and dendritic cell functions.

**Erythroid growth factors**

The erythroid cell line is maintained and can be stimulated for increased proliferation by erythropoietin (EPO). EPO stimulates only cells already committed to the erythroid lineage and does not induce other lineage-committed progenitors or terminally differentiated cells to form erythroid cells. The increase in erythroid cell formation is due mainly to the prevention of apoptosis, improved erythroid cell survival, decreased cell-cycle inhibition, and the promotion of cell line expansion. EPO is produced in an inducible fashion by the kidney and constitutively by the liver in a steady-state fashion, but its production can be significantly increased in response to anemia or hypoxemia. Juxtaglomerular interstitial cells in the kidney sense oxygen levels. Low oxygen levels induce the hydroxylation of hypoxia-inducible factor 1 (HIF-1α), the transcription factor essential for EPO production.

Owing to the anemia associated with burns, EPO levels should be increased during the treatment and recovery from the burn injury. However, in contrast to the expected EPO response to anemia, there is limited support for an appropriate increase in EPO following burn. These contradictory results may stem from differences in the assay used to measure EPO (urine vs serum; bioassay vs radioimmunoassay) and outcome measures of EPO response (hemoglobin, reticulocyte count, transfusion rates, etc.). Earlier studies had small sample sizes, used unreliable urine bioassays, and could not overwhelmingly support an appropriate EPO response. Later comparison of serum bioassays and radioimmunoassays showed no correlation between the two methods, and their results suggested significant differences between the sensitivities of these tests. More recent, larger studies using serum radioimmunoassays demonstrate an increase in EPO in response to decreased hemoglobin concentrations but an inconsistent erythropoietic response to this EPO increase.

Whereas only erythroid-committed cells in the bone marrow possess the EPO receptor, a related EPO receptor and a response to EPO have been identified in non-hematopoietic tissues, including neurons, glial cells, retina, heart, skeletal muscle, kidney, ovary, uterus, testis and endothelial cells. As a result, the ability of EPO to reduce apoptosis and prevent damage to these tissues has been explored. In particular, rhEPO can reduce apoptosis after cerebral ischemia, protect the myocardium and promote remodeling following myocardial ischemia, allowing for restoration of cardiac function, and protect against renal injury from ischemia, improving renal function. Despite these findings and the expected erythropoietic response to rhEPO, its use in burn patients has not been substantiated.

**Myeloid growth factors**

**G-CSF**

Granulocyte colony-stimulating factor (G-CSF) is the primary growth factor responsible for the proliferation and differentiation of bone marrow granulocyte progenitors into mature granulocytes. G-CSF is produced by monocytes, fibroblasts and endothelial cells which were stimulated to produce G-CSF in response to inflammatory cytokines (TNFα, IL-6, IL-1). Apart from stimulating the bone marrow production of neutrophils, in the periphery, G-CSF augments the bacitracidal activity of neutrophils by priming the oxidative burst, increases neutrophil half-life by preventing apoptosis, and downregulates the overall inflammatory response by reducing the cytokine production of monocytes and macrophages. An animal model of burn and burn sepsis demonstrated the beneficial effects of G-CSF on killing of translocated bacteria, regulating the proinflammatory response to injury, improvement in neutrophil chemotaxis, and improved survival in combination with antibiotic therapy.

At baseline, there are very low levels of G-CSF present in the blood. However, following an inflammatory or infectious process, G-CSF levels increase greatly. Following a burn injury, G-CSF levels in the blood are initially increased and then gradually decline to baseline 3–4 weeks later. The initial increase in G-CSF may prime the neutrophilic component of the immune response for future bacterial insult. However, the immune dysfunction seen following a burn injury or burn sepsis may be related to hyporesponsiveness of bone marrow progenitors and peripheral neutrophils to G-CSF.

Administration of recombinant G-CSF to burn-septic animals prior to the initiation of septic insult has been shown to improve the survival rate of burn-septic mice.
However, administration of G-CSF 24 hours after the onset of septic insult had little effect on their survival.237,238 Despite the potential benefit of exogenous G-CSF administration on the inflammatory and infectious response during burn injury, the use of recombinant human G-CSF (rhG-CSF; Filgastrim) is not indicated in the treatment of burn patients. RhG-CSF use is indicated for use in patients receiving myelosuppressive chemotherapy; with acute myeloid leukemia receiving induction or consolidation therapy; recipients of bone marrow transplantation undergoing peripheral blood progenitor cell collection and therapy; and with severe chronic neutropenia to stimulate neutrophil production and egress from the bone marrow.228 Given the multitude of changes in both progenitor and terminally differentiated cell formation in the bone marrow, it is unlikely that the administration of one exogenous growth factor will significantly affect the outcome of burn patients.

CSF-1

CSF-1 (M-CSF) is a pre-eminent growth factor for the differentiation, proliferation and survival of monocytes and macrophages.239 It also stimulates chemotaxis, cytokine and superoxide production in macrophages.230,231 Hume et al. first demonstrated that administration of CSF-1 to mice resulted in monocytopoiesis and an increase in peritoneal and tissue macrophages.232 In response to burn injury, CSF-1-responsive GM-CFU are increased in the bone marrow, leading to enhanced monocytopoiesis.234 The underpinning of this monocytopoiesis following burn injury has been shown to be the result of increased expression of CSF-1 receptors in EMMP-20 bone marrow compartment, which comprises monoblasts and promonocytes.234 In addition, burn injury and sepsis also change the inflammatory cytokine phenotype of CFU-GM-derived macrophages in that they result mainly in hyporesponsive macrophages.235,236 Similar monocyte hyporesponsiveness has also been demonstrated in trauma patients.137 These findings provide a plausible mechanism and a role for CSF-1 and its cognate receptor interactions in monocyte/macrophage biology after burn injury.

GM-CSF

Granulocyte–monocyte colony-stimulating factor (GM-CSF) regulates the proliferation and differentiation of hematopoietic progenitor cells, as well as modulating the function of mature leukocytes.237 GM-CSF has been shown to enhance the antigen-presenting capacity of macrophages and dendritic cells, to increase complement-mediated phagocytosis, and to augment bacterial killing by innate immune cells.238 In addition, burn injury and sepsis also change the inflammatory cytokine phenotype of CFU-GM-derived macrophages in that they result mainly in hyporesponsive macrophages.235,236 Similarly, CSF-1 also stimulates chemotaxis of leukocytes.240,241 GM-CSF is produced by a variety of cells, including macrophages, B lymphocytes, pulmonary epithelial cells, neutrophils, andstromal cells.242,243 In response to burn injury bone marrow GM progenitors respond by producing more GM-CFU colonies.244 Administration of GM-CSF prior to burn injury and *Escherichia coli* sepsis enhanced bacterial clearance and survival of the mice.244 Similarly, GM-CSF improved the survival of neonatal rats when administered prophylactically prior to *Staphylococcus aureus* infection.245 However, GM-CSF administration after the onset of infection did not provide a survival benefit.246 Although the inactivation of GM-CSF or GM-CSF receptor genes in mice did not alter the number of granulocytes and monocytes, these animals exhibited significant dysfunction of alveolar macrophages, resulting in accumulation of surfactant and proteinaceous material. Furthermore, GM-CSF-deficient mice are very susceptible to pulmonary group B streptococcal infection.247 In burn patients, administration of GM-CSF resulted in a 50% increase in mean neutrophil count. However, in GM-CSF-treated patients enhanced oxidative function of PMN abated over a 3-week period but remained undiminished in untreated patients.248 In a multicenter clinical trial, administration of GM-CSF in hydrogel to deep second-degree burn wounds was shown both to be safe and to accelerate wound healing.249 However, this trial has not been confirmed by other similar studies. Despite its recognized role in modulating innate immune cells and their function, the role of GM-CSF in burn care remains inconclusive.

Lymphoid growth factors

Several growth factors/cytokines contribute to the formation of lymphoid cells, the most prominent and best studied being IL-7. The IL-7 receptor is unique to lymphoid cells. As a result, IL-7 is the cytokine/growth factor that influences the expansion of this cell line. IL-7 receptor engagement is essential not only for lymphoid cell proliferation and survival but also for hematopoietic stem cell differentiation into the lymphoid lineage. The IL-7 receptor enhances lymphoid cell survival through maintenance of Bcl-2.249 Bone marrow stromal cells and the thymus predominantly produce IL-7. T cells are unique in that their maturation takes place in the thymus, as opposed to the bone marrow, and they undergo a process of positive and negative selection which is dependent on both IL-7 activation and expression of Notch1, a transcription factor.250 Alterations in IL-7 production, in addition to that of other cytokines, can negatively affect survival after inhalation injury.251 Additional growth factors/cytokines that contribute to lymphopoiesis include IL-2, IL-15, and IL-23.

Megakaryocyte growth factors

Production of megakaryocytes and platelets is regulated by thrombopoietin. Similar to erythropoietin, thrombopoietin enhances megakaryocyte progenitor proliferation by amplifying cell-cycle regulators and preventing apoptosis,252 and is the only growth factor necessary for proliferation of megakaryocytes and their progenitors.253 Unlike erythropoietin, thrombopoietin has a synergistic role with other growth factors and cytokines in the maintenance and proliferation of HSCs,253 and can be used in their expansion.254 Thrombopoietin stimulates platelet release from the bone marrow and in the periphery; thrombopoietin can upregulate platelet function and aggregation.255 Thrombopoietin is produced in the liver, kidney, skeletal muscle and stromal cells of the bone marrow.202,256 Thrombopoietin production may be increased in response to increased IL-6 production.257 Given the elevated IL-6 levels present following burn injury, IL-6-induced thrombopoietin release may be responsible for the thrombocytosis often seen immediately following burn injury.
Transcription factors

Whereas growth factors control hematopoietic cell fate, the development of terminally differentiated cells is under the control and coordination of a limited set of transcription factors. Ultimately, specific sequential and temporal gene expression patterns dictate hematopoietic commitment. These genetic processes are governed though modulations in the rate of gene transcription, which are accomplished through the binding of DNA-binding proteins or transcription factors to specific regions on a gene. Transcription factors are nuclear proteins that act as control points in the conversion of a gene to a functional protein. As many key proteins are turned over rapidly to meet the changing needs of the tissues, a complex system of cell signaling architecture, with the final common pathway of gene transcription, must exist to produce bioactive proteins on demand. To exquisitely regulate the rate of protein synthesis, genes need to be quickly transcribed into RNA within the nucleus, transported to the cytoplasm, and proteins synthesized from RNA templates. Because cells respond to several signals simultaneously, and many ligand–cell interactions stimulate similar proximal signals, tight control of transcriptional initiation must exist for the proper orchestration of cellular responses.

The role of transcription factors in hematopoietic cell fate is an evolving topic of study. The lineage-restricted proliferation and differentiation program of hematopoiesis is achieved through switching on and off specific sets of genes in response to cell signals. As thermal injury and sepsis are accompanied by hematologic and hematopoietic changes that determine the overall pathophysiological response of burn patients, it is reasonable to assume that transcriptional regulation of hematopoietic developmental genes plays a significant role. Much of our current knowledge of hematopoietic transcription factors has come from diverse fields such as hematology, oncology, immunology, mammalian virology, and signal transduction. Many concepts have been found by studying the molecular controls of leukemias, in vitro cell clonal assays, and various hematopoietic cell lines. Gene knock-out technology has also aided in ascertaining the functional roles of characterized genes in hematopoiesis. The relationship between these transcription factors is complex, as they are not independent of one another but demonstrate antagonism. In fact, the inability of one transcription factor to suppress another has been linked to the development of hematologic malignancies. However, little is known about hematopoietic transcription factor changes following pathologic injury, even though they may control the dramatic hematopoietic shifts following severe trauma and burn injury. Given the importance of these transcription factors to cell fate and the significant shifts in lineage commitment patterns, knowledge of these transcription factors and their current role in hematopoiesis may help in providing a foundation for future reference.

GATA family

The GATA transcription factors are related zinc-finger DNA-binding proteins. These transcription activators bind to the canonical GATA sequence motif found in the cis-regulatory regions of many hematopoietic genes. The proteins have differential expression patterns and activate a unique set of target genes. GATA-1, GATA-2, and GATA-3 proteins play pivotal roles in hematopoiesis. GATA-1 is necessary for the development of erythroid cells and megakaryocytes and erythroid survival via Bcl-xL expression. Mice lacking GATA-1 proteins display normal hematopoiesis, except for the erythroid lineage. GATA-1 is repressed in cells developing throughout the myeloid and lymphoid lineages. In fact, interrelated complex regulation between GATA-1 and other transcription factors, including PU.1, may control passage through the myeloid lineage. Increased expression of GATA-1 has been shown to negatively modulate PU.1 expression and thus suppress myeloid commitment. Since burn injury is commonly associated with a down-regulation of erythropoiesis despite adequate levels of endogenous erythropoietin, studies specifically designed to correlate the strength of GATA-1 expression in progenitor cells to the status of erythropoiesis will provide novel and mechanistic information on the pathophysiology of anemia in burn injury. GATA-1 expression is assisted in its regulatory functions with additional cofactors, including Friend of GATA-1 (FOG-1), which helps GATA-1 localize to specific areas of chromatin. GATA-1 may also help to control a switch from fetal to adult hemoglobin production. GATA-2 expression is more important at the top of the hematopoietic hierarchy as it is involved in proliferation and self-renewal of early hematopoietic stem cells. Mice engineered with a homozygous deletion of the GATA-2 gene display severe hematopoietic defects. GATA-2 knockout mice survive to embryonic day 10–11, harbor a small number of red blood cells at that stage, undergo anemic crisis, and eventually die. In vitro clonogenic assays revealed a drastic reduction in the number of erythroid progenitors and a substantial loss of mature erythroid precursors. Lastly, mice lacking GATA-3 fail to develop normal fetal liver hematopoiesis, lack all hematopoietic lineages except the megakaryocytic cells, and succumb to embryonic hemorrhage.

PU.1

PU.1 encodes a member of the ets family of DNA-binding proteins. It was originally cloned as a sequence-specific DNA-binding protein that was found to be homologous to the spi-1 oncogene. PU.1 can act as a tumor suppressor with alterations in its expression associated with acute myeloid leukemia. PU.1 possesses transcriptional activation potential that requires other co-activators for full potency. PU.1 is expressed early in the hematopoietic hierarchy including HSCs. PU.1 expression has been tracked using a GFP reporter strain and is interestingly expressed in both CLPs and CMPs. Those CMPs which become GMPs are PU.1hi while those that branch to the MEP lineage are PU.1lo. The expression of PU.1 in both early lymphoid and myeloid lineages reflects its role in regulating the expression of receptors for IL-7 (lymphoid) and GM-CSF, G-CSF, and M-CSF (myeloid). Monocytes and granulocytes highly express PU.1, whereas only B cells of the lymphoid lineage
express low levels of PU.1. T cells do not express PU.1, suggesting that PU.1 expression may contribute to B- and T-cell differentiation. Two different PU.1 knockout mice reveal the absence of monocytes, B cells, and greatly reduced neutrophil production. Moreover, these neutrophils are unable to express some markers of fully differentiated neutrophils. Embryonic stem cells from PU.1-deficient mice can differentiate into immature myeloid progenitors in the presence of IL-3 and G-CSF cytokines. Nevertheless, exogenous PU.1 expression in the PU.1-deficient hematopoietic progenitors restores myeloid differentiation. While GATA-1 may inhibit PU.1 expression, PU.1 expression can block erythropoiesis by antagonizing GATA-1 DNA binding. Unique to other transcription factors, PU.1 is essential both early at the hematopoietic stem and progenitor cell stage and also later during more specific differentiation of myeloid and lymphoid cells.

c-Myb
c-Myb proto-oncogene belongs to the basic helix–turn–helix (bHTH) family of DNA-binding proteins. c-Myb contains an LZ motif that mediates homotypic and heterotypic protein interactions. Multiple serine residues are located within the amino-terminal and carboxy-terminal regions of c-Myb that affect its DNA-binding activity and negative regulatory domain. Studies have shown that c-myb expression is restricted to myeloid, erythroid, and immature lymphoid cells. Collaborative data from c-myb knock-out mice reveal the absence of all hematopoietic lineages, except within the megakaryocytic compartment. c-myb knockout mice exhibited normal yolk sac hematopoiesis, whereas liver hematopoiesis was greatly compromised, and these mice die in utero at E14–15. Detailed analysis of hematopoietic lineages revealed that functional granulocytes and monocytes were present, but they harbored a 10–20-fold reduction in mature cells compared to normal mice. It is hypothesized that c-Myb functions to control quantitative effects rather than differentiation per se during hematopoiesis. It was also noted that c-Myb levels decrease during differentiation of hematopoietic progenitors and enforced c-Myb expression promotes proliferation and blocks hematopoietic differentiation. Hence, c-Myb plays a critical role in controlling proliferation of immature hematopoietic progenitors, and its physiological downregulation is required for commitment towards lineage-specific differentiation.

C/EBPs

CCAAT/enhancer-binding proteins (C/EBPs) are transcription factors that bind to core cis-regulatory sequence of CCAAT found in many regulated genes. C/EBPa was the original transcription factor, described as a basic leucine zipper (bLZ) DNA-binding protein in hepatocytes and adipocytes. Interestingly, the CEBP family of transcription factors, including CEBPa, have been shown to be elevated following thermal injury. Although their expression is implicated in the acute-phase response, the role of CEBPs in the regulation of hematopoiesis during thermal injury and sepsis is yet to be delineated. Other members of this family include C/EBPβ, C/EBPδ, C/EBPe, and GADD153/CHOP proteins. These C/EBPs are able to homodimerize and heterodimerize with each other via the leucine zipper regions. Expression studies showed that C/EBPa is present in monocytes, eosinophils, and neutrophils. Moreover, human myeloid precursors and immature myeloid cell line, 32 DC13, express high levels of C/EBPa that decrease upon G-CSF-induced differentiation. C/EBPa was shown to possess a transcriptional activation domain involved in the upregulation of mRNA from certain neutrophil genes such as G-CSF-R, lactoferrin, and collagenase. C/EBPa gene knockout mice are deficient in neutrophils and eosinophils, but harbor functional lymphocytes and monocytes. Fetal liver cells formed M-CSF- and GM-CSF-responsive colonies, but G-CSF-induced colonies were not obtained. Therefore, these studies determined that C/EBPa is essential for neutrophil differentiation but not for monocytic differentiation. Conversely, during neutrophil differentiation of myeloid cell line, 32 DC13, C/EBPβ levels increase. Recently, data from the C/EBPβ-deficient mice revealed that hematopoiesis proceeds normally, but defects in macrophage activation and decreases in B lymphocytes are observed. Additionally, C/EBPe gene knockout mice exhibited abnormal neutrophilic function and deficiencies in certain key enzymes. Otherwise, the mice appeared to have intact hematopoietic tissues. The preceding studies demonstrate the important regulatory function of the C/EBPs transcription factors in myelopoiesis.

c-Myc

The c-myc proto-oncogene is part of the bHLH/LZ (basic helix–loop–helix leucine zipper) family of transcription factors. c-Myc binds to canonical CANNTG DNA motifs located in many proliferative or cell cycle-regulated genes. c-Myc has three transcriptional activation domains in the amino terminus and a carboxy terminal with sequence-specific basic region and helix–loop–helix leucine zipper domains that mediate protein–protein interactions. c-Myc is required for cellular proliferation and its downregulation is essential for differentiation of many cell types. Max is another bHLH/LZ protein partner of c-Myc, and this heterodimeric complex is essential for cognate DNA binding and transactivation of target genes. Another set of genes that belong to c-myc family are MAD, Mxi-1, Mxi-3, and Mxi-4. The most important ones in hematopoiesis are MAD and Mxi-1. MAD and Mxi-1 proteins can heterodimerize with Max to form heterodimers that, unlike Myc–Max, can repress transcription at the same cognate DNA sites bound by c-Myc–Max heterodimers. Hence, within a given cell there is a dynamic equilibrium of c-Myc–Max and MAD–Max complexes that compete for the same binding sites, and the predominant complex determines whether proliferation or differentiation ensues. During in vitro and in vivo hematopoietic differentiation, MAD/Mxi-1 levels increase, whereas c-myc expression is downregulated. Recently, it was reported that MAD-null mice have defects in myelopoiesis, as demonstrated by delayed cell cycle exit during granulocytic differentiation. In summary, c-Myc/MAD’s roles in regulating the onset of proliferation versus differentiation are crucial for hematopoietic development.

MafB

MafB is a basic leucine zipper transcription factor that influences myeloid differentiation. Recent work on MafB demonstrates not only the interaction among transcription...
factors but also with growth factors, as MafB deficiency increases M-CSF responsiveness leading to PU.1 expression, altering the repopulation and differentiation characteristics of the myeloid lineage.9 MafB is specifically expressed in the myeloid lineage of the hematopoietic system and is an essential and specific determinant of myeloid progenitor differentiation into monocytes and macrophages.8,9 In addition, MafB represses ets-1 transactivation to inhibit erythroid differentiation.10 Monocyte and myeloid dendritic cell (DC) differentiations represent alternate developmental programs in hematopoiesis. Following a burn injury and trauma, the bone marrow hematopoietic paradigm shifts towards monocytoid differentiation. However, there is resistance to driving the differentiation of monocytes/macrophages to myeloid DC in both trauma and burn injury.10,11 Because MafB and PU.1 expression plays an essential role in monocyte differentiation, GATA-1 1 regulates DC development, burn-induced skewed myeloid development may be the result of uncoordinated expression of MafB, and PU.1 as well as GATA-1 expression.12,13 Altered hematopoesis and associated immune cell dysregulation are transient and self-correcting as the burn wounds are closed and the patient has recovered. Therefore, it is reasonable to assume that burn-induced microenvironmental changes precipitate or play a major role in orchestrating the differential expression of hematopoietic transcription factors and thus reorganize hematopoietic developmental paradigm. The net result is the reduced erythropoiesis, and increased monocyte development with a concomitant DC developmental arrest. Teasing out and delineating the interplay of the microenvironment with hematopoesis holds one of the keys to better patient management in critical care.

tal-1/SCL

The tal-1/SCL gene encodes a bHLH (basic helix–loop–helix) protein that was originally identified at the chromosomal breakpoint in a human acute T-cell leukemia.14 tal-1/SCL is a master gene required for development of hematopoietic stem cells that eventually differentiate into lineage-specific blood cells. These previous studies have revealed that the early hematopoietic stem cells (CD34+/c-kit+/Sca1+ cells) express the tal-1/SCL gene.15 T-cell leukemia, which consists of a clonal cell line with the potential to differentiate into myeloid and lymphoid lineages, was shown to express tal-1/SCL protein.16 In addition, mature erythrocytes, megakaryocytes, mast cells, and endothelial cells also express tal-1/SCL. These data indicate that the tal-1/SCL gene may play a required role in a later stage of maturation of committed progenitors. Homozygous tal-1/SCL gene knockout mice provided definitive evidence for its role in hematopoesis. The homozygous tal-1/SCL gene deletion was lethal in utero.18 These mice exhibited a failure in blood formation and their yolk sac contained no detectable blood elements and lacked in vitro clonogenic potential. These results were further confirmed by the inability of the tal-1/SCL knockout embryonic stem (ES) cells to develop into any hematopoietic lineages in culture.

This section should illustrate the complex interplay between transcription factors in the control of hematopoesis. For example, GATA-1 and PU.1 are antagonists, with GATA-1 expression essential for erythroid development and repression needed for myeloid development, whereas PU.1 is needed for hematopoietic stem cell, early progenitor and myeloid differentiation; it blocks GATA-1 binding, preventing competing erythroid signals. Most likely, currently unknown transcription factors or cofactors will be identified that will add to the already multifaceted character of hematopoesis.

Conclusion

Hematopoietic derangements following burn injury are not as visibly prominent as the burn itself or as easily quantified as the hemodynamic and physiologic alterations. However, the pronounced effects of a burn injury on hematopoietic processes greatly affects patient morbidity and survival via immunomodulation and anemia. Evolving knowledge of the cellular and molecular mechanisms responsible for burn-induced anemia and immunomodulation, including hematopoietic lineage commitment shifts, the bone marrow response to inflammatory cytokines and catecholamines, fluctuations in growth factor production, and the expression and repression of transcription factors, may at some point lead to therapeutic modalities to improve the care and survival of burn patients.

Further reading


References


Introduction

The physiological importance of the adrenal gland pertains to the release of epinephrine and glucocorticoids in response to cognitive stress, recognized as the ‘fight or flight’ response. Such responses involving the hypothalamic–pituitary–adrenal axis begin with the hypothalamic release of corticotrophin-releasing hormone (CRH), which mediates the release of adrenocorticotropic hormone (ACTH) from the pituitary, which in turn stimulates the synthesis and release of cortisol from the adrenal cortex. Hypothalamic stimulation also initiates the release of epinephrine from the adrenal medulla, and that of the neurotransmitter norepinephrine from adrenal medulla and the adrenergic nerve terminals. The action of these hormones and neurotransmitters is traditionally thought to serve in a compensatory manner, facilitating heightened mental awareness along with metabolic and cardiovascular activity that supports rapid increases in muscular work.

Thermal injury, like other forms of trauma, as well as infectious challenge, is a non-cognitive stimulus but also results in an elevated hormone/neurotransmitter milieu similar in magnitude to that of the cognitive ‘fight or flight’ response.\(^1,2\) However, there are important characteristics of the injury response that contrast with the fight or flight response. These include prolonged hormone/neurotransmitter elevation, the absence of increased muscle work limiting metabolic demand, and the presence of massive tissue injury. Additional hormone/neurotransmitter responses may also be evoked by surgical debridement of burn wounds and skin grafting procedures. The second surge of stress hormones complicates the severe metabolic derangements and compromised immune capacity, which is characteristic of the burn course during the initial 7–10 days following injury.

Cognitive and non-cognitive events that increase corticosteroid and catecholamine levels represent a stress response that may or may not involve pathology. Traumatic injury, however, clearly initiates a stress response, with a magnitude proportional to the severity of injury. Under these conditions, hormone/neurotransmitter release seems to promote survival. Although such a benefit may be difficult to see in human injury, experimental animal models have provided some insights. Animals that lack stress hormones or suffer from impaired release or by pharmacological block often die of an otherwise survivable event. Similarly, overwhelming traumatic injury in man may result in stress hormone release that is detrimental to survival. Whereas this may also be difficult to document in burn patients, animal studies have demonstrated that exogenous administration of large amounts of stress hormones is detrimental.

Two historical perspectives are important to consider regarding stress and the trauma of burn injury. First is the concept described by Cuthbertson,\(^3\) where the initial response to thermal injury is considered an ‘ebb’ phase characterized by reduced metabolism and tissue perfusion. Within days there is a transition to a ‘flow’ phase typified by increased resting energy expenditure and hypermetabolism, with supportive cardiovascular function. Changes in endocrine hormone levels are important for these acute catabolic alterations. The concepts of ‘stress’ and release of ‘stress hormones’ widely used today were clarified by the classic work of Seyle.\(^4\) His notion of stress responses include an initial ‘alarm reaction’ of fairly short duration with high levels of stress hormones, followed by a prolonged ‘resistance phase’ during which there is compensation to maintain homeostasis during continued stress. Seyle’s final stage of ‘exhaustion’ is where compensation cannot be maintained and death rapidly follows. The acute initial period of high stress hormone release encompasses both Cuthbertson’s ‘ebb’ phase and Seyle’s ‘alarm reaction,’ and the ‘flow phase’\(^5\) has similar features to the ‘resistance phase’.\(^6\) These compensatory changes promote increased energy expenditure and support cardiovascular function. However, in patients with severe injury the same compensatory changes result in depletion of energy reserves, extensive muscle wasting, and immune suppression, all of which are hallmarks of post-burn sequelae. This compensatory pattern is described as a hypermetabolic state, with patients displaying elevated resting metabolic rates for several months following injury.\(^7\) The extent of the hypermetabolic response is dependent upon the extent and depth of burn injury, septic complications, and surgical interventions. Nonetheless, questions related to the magnitude of stress hormone responses and beneficial versus detrimental actions in the recovery from severe thermal injury remain unanswered.
During the last 50 years great advances have been made in the care of burn patients and with various treatment modalities attempting to exploit some of the concepts described above. Examples include rapid fluid resuscitation to stabilize cardiovascular function and reduce the stimulus for continued sympathetic drive; nutritional support to meet metabolic demands and to support homeostasis during healing; elevated environmental temperatures and occlusive dressings to lessen the metabolic demands, reduce metabolic rate and cardiac output, and to optimize wound healing. Aside from the regulation of metabolic and cardiovascular function, neuroimmune interactions may be important in mediating the marked alterations in immune function that often follow severe injury. In this chapter we have chosen to present the adrenomedullary–neurotransmitter activation and actions as separate from the adrenocortical activation and actions to clarify specific responses, as we currently understand them. To this end we will review the magnitude and time course of the stress hormone/neurotransmitter responses to thermal injury as well as how the action of these substances may be integrated. How these responses may be beneficial or detrimental during the course of recovery will also be addressed. Given the range of pharmacologic antagonists and agonists available to the clinician, taking a mechanistic approach to understanding adrenal hormones and neurotransmitter involvement in the pathophysiology of burn injury is critical to further advance the successful treatment of these patients.

### PART I – SYMPATHETIC ACTIVATION AND RELEASE OF CATECHOLAMINES FOLLOWING BURN

Although clinical observations suggested the activation of sympathetic nerves in response to thermal injury, direct evidence for such activation was not fully appreciated until the simultaneous publication of papers by American and Swedish groups. These landmark studies described marked elevations in 24-hour urinary levels of norepinephrine and epinephrine in burn patients. Despite considerable intra- and interindividual variations, the increases in urinary norepinephrine and epinephrine were proportional to the size of burn, were highest during first 3 days post burn, and remained elevated for several weeks. Furthermore, these studies also suggested that subsequent surgical interventions and the onset of sepsis and septic shock such as hypotension or serious infections caused catecholamine secretion to increase again. Since these early reports of urinary catecholamines as measured by bioassay techniques, many studies have confirmed the initial sympathetic responses in burn patients using fluorometric, HPLC/electrochemical or radioenzymatic techniques in plasma and urine samples. With improvements in critical care medicine and the management of burn patients during the last 40 years, one can contemplate that prolonged sympathetic activity may not occur during extended recovery. In contrast, elevations in catecholamines may still occur in transient response to surgical procedures but cardiovascular, nutritional, and immune-related interventions, as part of the treatment regimen, may ameliorate the extent or impact of the hormone response (Table 24.1). In fact, the striking prolongation of sympathetic activation extending up to 35 weeks after thermal injury has been repeated by Herndon et al., using sophisticated, precise techniques. They found a sustained elevation in urinary epinephrine and norepinephrine levels, attesting to the magnitude and duration of catecholamine surge in pediatric burn patients. In light of the strong evidence for sympathetic activation following thermal injury, the compensatory or possible decompensatory consequences are important to consider.

<table>
<thead>
<tr>
<th>Physiologic variable</th>
<th>Sympathetic mediated change following burn injury</th>
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<tbody>
<tr>
<td>Resting metabolic rate</td>
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<tr>
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<td>Increase (^{37})</td>
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<tr>
<td></td>
<td>Increase (^{15})</td>
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<td></td>
<td>Increase (in vitro) (^{32})</td>
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<tr>
<td>Proteolysis</td>
<td>No change (urate production) (^{16})</td>
</tr>
<tr>
<td></td>
<td>No change (protein oxidation) (^{36})</td>
</tr>
<tr>
<td></td>
<td>Decrease (^{47})</td>
</tr>
<tr>
<td>Glucose production and oxidation</td>
<td>Decrease secondary to increase in lipid catabolism (^{37,273})</td>
</tr>
<tr>
<td></td>
<td>No change (^{36})</td>
</tr>
<tr>
<td>Glycogenolysis</td>
<td>Increase (indirect evidence via cAMP) (^{35})</td>
</tr>
<tr>
<td>Gluconeogenesis</td>
<td>Increase (indirect evidence via cAMP) (^{35})</td>
</tr>
<tr>
<td>Lipolysis</td>
<td>Increase (^{26})</td>
</tr>
<tr>
<td></td>
<td>Increase (^{36})</td>
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<tr>
<td></td>
<td>Increase (^{37})</td>
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<td>Increase (^{40})</td>
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<td>Increase (^{38})</td>
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<td>Peripheral vascular resistance</td>
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</tr>
<tr>
<td>Heart rate</td>
<td>Increase (^{37})</td>
</tr>
<tr>
<td></td>
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<td>Decrease (^{95})</td>
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<tr>
<td>Monocyte number and function</td>
<td>Increase (indirect – clonogenic potential) (^{46})</td>
</tr>
<tr>
<td></td>
<td>Increase (indirect – clonogenic potential) (^{103})</td>
</tr>
<tr>
<td></td>
<td>Increase (^{39})</td>
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Citation of studies from the current literature suggesting that sympathetic activation is involved in changing the above physiologic variables following thermal injury.
adjustments to thermal injury appear to be critical for survival following burn trauma, and with initial reductions in cardiac output, sympathetic responses are rapidly brought into play, as reviewed by Carleton.\textsuperscript{19} Initial sympathetic activation contributes to the dramatic increases in peripheral vascular resistance that preserve mean arterial pressure but typically limit perfusion to the kidney and splanchnic beds. Although the mechanisms for the reduction in cardiac output are not completely understood, they are in part related to the sudden loss of vascular volume as a result of fluid transudation of plasma from the wound and from non-wound vascular sites.\textsuperscript{20,21} Movement of fluids from vascular to interstitial spaces is compounded by the loss of plasma proteins through the incompetent capillary beds that normally act to retain ions by Donnan equilibrium.\textsuperscript{22} Such apparent hypovolemia would initially reduce blood pressure and baroreceptor afferent nerve activity, with resultant increases in efferent sympathetic nerve activity. The resultant increase in peripheral vasoconstriction and consequent increase in peripheral vascular resistance are mediated in part by nerve-stimulated release of norepinephrine, but also to a significant degree by both angiotensin II (AII) and arginine vasopressin (AVP).\textsuperscript{14,23} As AVP has been shown to directly depress myocardial function in the isolated heart and this depression can be reversed pharmacologically, AVP may contribute to myocardial depression following burn injury.\textsuperscript{24} Myocardial depression following thermal injury can be manifest as decreased cardiac output due to decreases in vascular volume, reductions in diastolic compliance, and decreases in myocardial contractility. Various ‘myocardial depressant factors’ have also long been described without specific detailed identification of the actual substances. Such deficits in contractility are compounded by the increases in aortic pressure afterload that is the consequence of increased peripheral vascular resistance and in total, contribute to the observed reductions in cardiac output. Although diastolic dysfunction has been demonstrated in burn patients, evidence for decreases in contractility are largely based on animal studies, with little evidence that this occurs in patients. Consequent upon decreased ventricular performance and potential intrinsic myocardial dysfunction, sympathetic drive would be important to maintain ventricular function of the non-compromised muscle upon recovery from thermal injury.

Cardiovascular disturbances might be predicted to be the dominant signal initiating a generalized sympathetic response, but the persistence of such sympathetic activation after hemodynamic stabilization suggests that afferent stimulation from other sources may initiate as well as maintain this response. Hemodynamic stabilization in burn patients typically requires 1–2 days after fluid resuscitation and is followed by the ‘ebb’ phase of recovery, characterized by low peripheral vascular resistance, elevated cardiac output, increased peripheral blood flow, and increased metabolism.\textsuperscript{25,26} The marked decrease in peripheral vascular resistance most likely drives this hyperdynamic phase by reducing cardiac afterload, increasing cardiac preload, and thus increasing cardiac output. There is abundant evidence that mediators of neural, humoral, and metabolic origin are involved in driving the decrease in vascular resistance following thermal injury, but their dominance and sequential release are not well defined. In fact, the significance of $\beta_2$ adrenergic receptors in vasodilation has recently been demonstrated using knockout mice,\textsuperscript{27} pointing to the importance of epinephrine. The situation is complicated in the burn patient by the increase in nerve-stimulated release of norepinephrine, which has the potential to mediate vasoconstriction. However, there is evidence that the local distribution of adrenergic receptors mediating either vasodilation or vasoconstriction will determine the effect of circulating epinephrine and nerve-stimulated norepinephrine release on peripheral vascular resistance.\textsuperscript{28} In addition, increased tissue metabolism has been recognized to produce metabolites that mediate increased blood flow by reducing vascular resistance.\textsuperscript{29} With markedly increased metabolism in major burns, these metabolites, along with catecholamines, nitric oxide,\textsuperscript{30} and atrial natriuretic peptide,\textsuperscript{14} may contribute to the observed decreased vascular resistance.

Typically, decreases in tissue perfusion leading to compromised organ function only occur in patients with complications related to septic events or severe metabolic acidosis. In burn patients there is often a modest decrease in mean arterial blood pressure that is not indicative of hypoperfusion and is left untreated. When decreases in peripheral vascular resistance become dominant, with marked decreases in mean arterial pressure, pressor agents may be required to maintain adequate tissue perfusion, and norepinephrine is the drug of choice, providing both vasoconstrictor and inotropic effects. Clinical use of vasoconstrictor and inotropic agents is essential to counter low tissue perfusion during the periods of altered hemodynamic function often seen with the onset of sepsis in burn patients.

In this regard Macarthur et al.\textsuperscript{31} suggest that the inactivation of catecholamines by superoxide anions contributes to the observed hypotension of septic shock. Treatment with superoxide dismutase mimetic agent was used to enhance plasma levels of catecholamines, increase blood pressure and improve survival. In their most recent work\textsuperscript{32} these investigators demonstrated that nitric oxide (NO), widely recognized as a mediator of hypotension during systemic inflammation, as occurs in sepsis, reduces the biologic activity of norepinephrine. Furthermore, increasing NO levels in an isolated, perfused, mesenteric circulation reduced vascular responses to endogenously released norepinephrine without altering nerve-stimulated release. These findings may provide some insight into the clinical observations involving critically ill trauma patients where exogenous norepinephrine administration is ineffective in correcting hypotension.

Following the initial insult of thermal injury the ‘ebb’ phase of recovery is characterized by a decrease in body temperature and oxygen consumption and a progressive elevation in lactate levels and hyperglycemia.\textsuperscript{14} The same period of recovery involves intense sympathetic stimulation,
suggesting the involvement of adrenergic mechanisms mediated by adenyl cyclase and cAMP in the mobilization of liver glycogen to glucose.\textsuperscript{32} Hypermetabolism that follows 1–2 days later in the ‘flow’ phase can also be attributed to adrenergic influences,\textsuperscript{33,34} but does not involve increased glucose mobilization and utilization. Adrenergic blockade only increased glucose production and clearance under these hypermetabolic conditions.\textsuperscript{37} The experimental studies of Wolfe and Durkot\textsuperscript{47} suggest that adrenergic drive following burn facilitates lipolysis, influencing fatty acid oxidation. These results are based on changes observed following adrenergic blockade with propranolol and further clarify that the observed increase in glucose production and clearance under such conditions reflects a shift to carbohydrate utilization in the absence of lipid mobilization. Examining the importance of adrenergic drive on lipid metabolism in burn was extended to human patients through the use of stable isotopic studies as well as adrenergic antagonists.\textsuperscript{38–40} These results not only indicate that lipolysis following thermal injury is mediated by \( \beta \) adrenergic receptors, but suggest increased triglyceride–fatty acid cycling, with resultant heat production.

The initial description of the sustained hypermetabolic response to thermal injury\textsuperscript{41} prompted studies to examine the role of thyroid function and catecholamines in mediating this response. Although abnormal thyroid function was not involved in the response,\textsuperscript{42,43} Wilmore developed experimental paradigms suggesting the role of catecholamines in mediating the hypermetabolic response to thermal injury.\textsuperscript{15} Evidence for the positive correlation of increased plasma catecholamines and whole-body oxygen consumption following thermal injury,\textsuperscript{15} as well as the demonstration that adrenergic blockade lowers the burn-induced increase in metabolic rate and cardiac output to control levels in animal models, directly support this contention.\textsuperscript{15,37} However, experimental findings in rats suggested that the adrenal medulla is essential for high rates of heat production following thermal injury, but is not responsible for the primary drive of the hypermetabolic response.\textsuperscript{34,44} Animals with hypothalamic lesions did not increase metabolism following thermal injury and were chronically hypothermic,\textsuperscript{45} unlike experiments where the adrenal medulla was removed prior to thermal injury.\textsuperscript{43} These results are consistent with clinical observations in burn patients in whom reductions in heat loss were achieved with occlusive dressings, and elevated environmental temperatures have reduced metabolic rate and catecholamine secretion.\textsuperscript{46}

Building on findings that catecholamines drive post-burn hypermetabolism, Herndon et al.\textsuperscript{17,48} demonstrated that pediatric patients could be treated with the \( \beta \)-adrenergic blocker propranolol to successfully reduce metabolic rate without compromising cardiovascular function. In a more recent study by this group,\textsuperscript{49} \( \beta \)-adrenergic blockade in pediatric patients for 4 weeks during recovery from severe burns reduced the elevation in resting energy expenditure and reversed the reduction in net muscle–protein balance by 82%. Such treatment also prevented fatty liver and loss in fat-free whole-body mass, and provided for a more efficacious recovery in these children.\textsuperscript{50} Similarly, gluconeogenic pathway was prevented with propranolol treatment in pediatric patients by downregulation of a key catalytic enzyme that generates fructose 6-phosphate.\textsuperscript{51}

An important and all too frequent complication of severe thermal injury is infection, which frequently leads to sepsis, septic shock, multiple organ failure, and death. The development of septic complications can reduce predicted survivability by up to 50%.\textsuperscript{32} As with burn, infection results in marked sympathetic responses that are well characterized in both experimental and clinical settings. Whereas experimental paradigms of sepsis have used plasma catecholamines, nerve recordings and norepinephrine turnover to assess sympathetic activation,\textsuperscript{33–35} human studies have primarily focused on changes in plasma catecholamines.\textsuperscript{1} Similar to thermal injury, sympathetic responses also appear to be proportional to the degree of insult, based on experiments using incremental doses of bacterial endotoxin.\textsuperscript{39} Furthermore, animal models of septic peritonitis suggest that initial sympathetic activation as measured by elevated levels of plasma norepinephrine and norepinephrine turnover persist for many hours.\textsuperscript{33,56} Burn patients are most susceptible to infection during the second week of their hospitalization, when the sympathetic response as reflected by urinary and plasma catecholamines has moderated but is still high.\textsuperscript{13,14} Although the onset of bacterial infection and developing sepsis would be expected to cause marked increases in plasma catecholamines above that due to burn alone, longitudinal studies charting the course of plasma catecholamines following thermal injury leading into infection and progressing into septic shock are not available.

**Sympathetic influences on immune function**

Over the last 20 years experimental evidence describing the interactions between neural and immune cell systems has expanded greatly. This has important implications in our understanding of the pathobiology of thermal injury, as in vivo sympathetic activation as well as compromised immune function both occur following thermal injury. In addition to endogenous release of catecholamines, burn patients are often treated with adrenergic pressor agents; they may be on a therapeutic regimen of \( \beta \)-adrenergic antagonist prior to injury, or hypermetabolism may be controlled in pediatric burn patients with \( \beta \)-adrenergic antagonists. Thus, adrenergic modulation following thermal injury may involve therapeutic as well as endogenous mediators and may have an important impact on immune system function.

For the activation of sympathetic nerves to influence immune responses, evidence of sympathetic innervation in peripheral lymphoid organs is essential. Existing anatomical evidence is based on immunohistochemical techniques to visualize tyrosine hydroxylase, the rate-limiting step in the biosynthesis of norepinephrine. These studies clearly indicate a substantial innervation of all primary (thymus and bone marrow) and secondary (spleen and lymph nodes) lymphoid organs.\textsuperscript{55–63} Furthermore, they also show sympathetic innervations in the immune cell compartment of the spleen (the white pulp), the periartrial lymphoid sheath, marginal zone and marginal sinus areas, as well as in the splenic capsule and trabeculae.\textsuperscript{84–67} Sympathetic nerve terminals have been described in direct apposition to T cells, interdigitating dendritic cells and B cells.\textsuperscript{65} The proximity of nerve terminals to immune cells may be critical in achieving the necessary local concentrations of neurotransmitters at
the neuroimmune junctions to modulate immune functions. In fact, the neuroimmune junction is estimated at 6 nm, compared to 20 nm in typical CNS junctions, indicating that sufficient neurotransmitter concentration could be released across these small junctions to affect resident immune cells.

Anatomical evidence of sympathetic innervations of the immune system is complemented by evidence for nerve-stimulated release of norepinephrine in both spleen and bone marrow. Whereas evidence in spleen has been recognized for many years and has been assessed in a variety of ways, norepinephrine release in bone marrow has only been recently described, using norepinephrine turnover techniques based on radiotracer methods involving in vivo experimental paradigms. In contrast, exocytosis of norepinephrine from lymph nodes has not been demonstrated. To complete the criteria for the physiologic importance of functional innervations, nerve-stimulated release of norepinephrine within lymphoid organs must increase at the appropriate time to influence the immune response in conjunction with demonstration of norepinephrine-mediated immune modulations.

Lymphocytes, including activated and resting B cells, naïve CD4+ T cells, T-helper (Th1) cell clones, and newly generated Th1 cells, express β adrenergic receptors, but they are not expressed in newly generated Th2 cells. Furthermore, there is significant evidence that norepinephrine can modulate the function of CD4+ T cells, which in turn can modulate antibody production of B cells. In addition, norepinephrine can directly influence B-cell antibody production depending on the time of exposure following activation. The physiologic importance of these in vitro findings is supported by a series of in vivo experiments involving severe combined immunodeficient (scid) mice depleted of norepinephrine prior to reconstitution with antigen-specific Th2 and B cells. These experiments demonstrate that norepinephrine is necessary for maintaining a normal level of antibody production in vivo. Furthermore, other recent whole animal experiments, also involving scid mice, provide evidence that the immune response itself stimulates the release of norepinephrine from adrenergic nerve terminals in bone marrow and spleen, which in turn can influence antibody production by B cells. However, in a prospective intent-to-treat study, β-blockade in 20 paediatric burn patients significantly reduced serum TNFα and IL-1β. Although these findings fall far short of direct application to immune cell function following thermal injury, they suggest the potential of sympathetic activation in mediating immune responses.

In addition to neural influences on T- and B-cell function, there are direct effects on myeloid cell function, particularly with respect to lipopolysaccharide (LPS)-stimulated cytokine production. The most striking examples of neural influences on macrophage function were demonstrated by the work of Spengler et al., who concluded that α-adrenergic stimulation increases TNF-α release, whereas β-adrenergic stimulation reduces such release in response to LPS. They provided further evidence to suggest that extracellular stores of catecholamines in macrophages are capable of modulating TNF-α release. Furthermore, sympathetic inhibition of LPS-induced TNF-α release has been suggested to occur in whole animal preparations, although adrenergic actions on macrophages were indirect. More direct evidence of adrenergic inhibition of LPS-stimulated TNF-α production has involved whole blood. In our recent documentation, blocking β-adrenergic receptors soon after injury partially reversed LPS-stimulated TNF-α potential of circulating monocytes lost during the course of burn injury and sepsis. Apart from adrenergic inhibition of LPS-stimulated TNF-α release in isolated macrophages, similar inhibition of LPS-stimulated TNF-α production has also been demonstrated in human mast cells, microglial cells, astrocytes, and cytotoxic T lymphocytes. In contrast to adrenergic stimulation of TNF-α release, experiments with isolated atria, myenteric plexus, and brain tissue have demonstrated that TNF-α can negatively affect the release of norepinephrine.

Adrenergic influences on the expression and release of interleukin (IL)-6 have been suggested by a number of studies demonstrating increases in plasma IL-6 in response to direct or indirect stimulation. Adrenergic enhancement of IL-6 responses to LPS has also been demonstrated in vivo as well as ex vivo and in isolated cell systems. In addition, adrenergic agonists have been shown to mediate IL-6 release in brown adipocytes, pituicytes, hepatocytes, astrocytes, and thymic epithelial cells. In contrast, Nakamura et al. reported that catecholamines reduced the IL-6 response to LPS, and van der Poll et al. demonstrated that norepinephrine inhibits the LPS-induced IL-6 response in whole blood. Other evidence for adrenergic suppression of IL-6 responses has been suggested by the work of Straub. Using isolated splenic tissue preparation, electrically stimulated release of norepinephrine appeared to inhibit IL-6 production induced by LPS or bacteria. These authors suggest that adrenergic inhibition of IL-6 is reduced under conditions simulating infection, where cytokine mediation of the inflammatory response is compensatory in eradicating the bacterial load. It is apparent from these studies that catecholamines can exert a negative or a positive influence on IL-6. Given these different modulatory functions, the role(s) catecholamines play in the pathophysiology of burn injury remain unexplored.

Although the exact mechanisms of the negative modulation of proinflammatory cytokines by catecholamines are poorly understood, it may be achieved through the ability of catecholamines to induce the anti-inflammatory cytokine IL-10. Whole animal studies involving assessment of circulating levels of IL-10 as well as studies of human whole blood and mononuclear cells stimulated with LPS in the presence of adrenergic agonists support this premise. In addition, experimental neurotrauma results in increased IL-10 consequent upon endogenous adrenergic stimulation in the absence of LPS or other evidence of infectious challenge. The only experimental evidence suggesting an attenuation of IL-10 with adrenergic stimulation involved a macrophage cell line (RAW 264.7).

Evidence that elevations of IL-10 can be blocked with inhibition of protein kinase A (PKA) is consistent with adrenergic mediation of changes in TNF-α and IL-6, and suggest that activation of PKA is important in effecting these adrenergic modulations of cytokine release. More
specifically, the recent work of Platzer et al.\textsuperscript{117} suggests that catecholamines in monocyctic cells directly stimulate the IL-10 promoter/enhancer, and provide evidence that a cAMP response element was the major target of the cAMP/PKA pathway. In contrast, two independent studies from our laboratory report evidence that, although adrenergic stimulation increases IL-10 release from macrophages, release of TNF-\(\alpha\) and IL-6 is inhibited by direct adrenergic stimulation not secondary to IL-10.\textsuperscript{122,123} These studies involved both peritoneal-elicted and bone marrow progenitor-derived macrophages under normal conditions as well as following cecal ligation and puncture injury. Epinephrine attenuated TNF-\(\alpha\) but increased IL-10; however, addition of anti-IL-10 antibody did not prevent epinephrine’s ability to block TNF-\(\alpha\) reduction. Further experiments demonstrated the action of epinephrine to inhibit LPS-stimulated release of proinflammatory cytokines to be mediated by \(\beta_2\)-adrenergic receptors. The dominance of direct adrenergic inhibition of LPS-mediated proinflammatory cytokines was maintained during conditions of sepsis, although such conditions elevated endogenous levels of IL-10.

### Adrenergic stimulation of bacterial growth

Since the identification of mammalian hormone and neurotransmitter receptors in bacterial cells, there has been considerable interest in defining a role for such signaling molecules in bacterial cells. As a consequence, support has emerged for the concept that release of norepinephrine within intestinal tissue promotes the growth of bacteria in the gut.\textsuperscript{124–128} Initial experiments demonstrated the growth-promoting action of catecholamines in vitro using several different bacterial species, and provided evidence that these compounds were not acting as nutritional substrates. Since adrenergic blocking agents did not block the growth-stimulating effects of norepinephrine, adrenergic receptors do not appear to be involved.\textsuperscript{127,128} Further observations suggest that norepinephrine may act within 8 hours to induce bacterial growth, during which time stimulation of growth factors can promote bacterial growth.\textsuperscript{129,130} Norepinephrine-stimulated bacterial growth has also been shown to produce Shiga-like enterotoxins from enterohemorrhagic strains of \textit{E. coli}. Furthermore, norepinephrine promotes the expression of K99\textsuperscript{+} pilus adhesin, a virulence factor known to play a critical role in the attachment of these bacteria to the intestinal wall, which initiates the infective process.\textsuperscript{131,132} Although these studies use very high concentrations of norepinephrine compared to the observed plasma concentrations following thermal injury, bacteria in vivo may be exposed to high norepinephrine concentrations if they are in close proximity to the nerve terminal synapse. A related concern is the lack of information regarding the actual norepinephrine concentration in the culture media throughout the incubation period. Whereas rapidly growing bacterial cultures may generate an acid environment in which catecholamines are quite stable, initial growth conditions containing low bacterial counts and minimal nutrients may promote rapid deterioration of norepinephrine. However, high initial norepinephrine concentrations in culture may counteract such unfavorable conditions but in turn would provide misleading dose–response information.

The extensive sympathetic innervations of the gut and associated structures has been recognized for many years, with well-defined nerve terminals located primarily along blood vessels but without evidence of neurotransmitter release into the intestinal lumen. Furthermore, there is considerable evidence that, once released from nerve terminals, most norepinephrine is taken back into the same terminals by reuptake mechanisms, metabolized into a non-active form, or diffused through tissues to reach blood vessels to become part of the circulation.\textsuperscript{133} Therefore, even though intestinal bacterial growth has the potential to be enhanced by the neurotransmitter norepinephrine, transport of the norepinephrine into the intestinal lumen would seem problematic. However, as massive catecholamine release is such a consistent component of burn patients, especially those with superimposed sepsis, the hypothesis that bacterial growth can be enhanced by norepinephrine is very appealing.

This concept is strengthened by studies demonstrating that cecal bacterial growth increases dramatically following massive in vivo release of norepinephrine, and that passage of bacteria through the gut enhances their growth response to norepinephrine. In the first case,\textsuperscript{126} mice were treated with 6-hydroxydopamine, a neurotoxin that displaces norepinephrine from adrenergic nerve terminals, causing a transient but massive sympathetic reaction. At 24 hours post-treatment cecal bacterial growth was elevated 3–4 degrees of magnitude compared to vehicle-treated controls, but bacterial growth returned to control levels by 14 days. In the second study\textsuperscript{131} an attenuated strain of \textit{Salmonella typhimurium} was administered to rhesus monkeys, whereupon isolated fecal bacterial cultures from these animals displayed increased in vitro growth responses to norepinephrine. To elucidate whether this hypothesis has a role in the pathophysiology of thermal injury with sepsis, future studies must build on experimental paradigms of thermal injury to demonstrate that endogenous norepinephrine enhances bacterial growth leading to sepsis.

### Evidence for norepinephrine regulation of myelopoiesis in experimental thermal injury with sepsis

Patients with severe burn trauma often display significant impairment in cell-mediated immunity involving defective neutrophil chemotaxis, phagocytosis, and superoxide production.\textsuperscript{134–137} Patients with sepsis and a systemic inflammatory response may also present with monocytosis and neutropenia.\textsuperscript{138,139} Whereas neutropenia and defective neutrophil functions may compromise host defense, monocytosis has the potential to fuel excessive cytokine production through increased availability of circulating and tissue monocyte/macrophages. For the past 10 years our laboratory has been investigating bone marrow following thermal injury with sepsis to understand the mechanisms that govern leukocyte production, and how they might contribute to the observed defects in leukocyte function. The potential for sympathetic activation to modulate myelopoiesis following thermal injury and sepsis is supported by previous studies where adrenergic stimulation has been shown to participate in the regulation and control of hematopoiesis.\textsuperscript{140,141}
Maestroni has not only provided evidence for the presence of adrenergic receptors on bone marrow immune cells, but also that adrenergic agonists stimulate lymphopoiesis while attenuating myelopoiesis under normal, non-injury conditions. These findings are further strengthened by animal experiments where adrenergic agents have been shown to modulate both lympho- and myelopoiesis. Another important factor supporting the possible adrenergic regulation of myelopoiesis following thermal injury is that sympathetic activation can occur directly within the bone marrow compartment, with nerve-stimulated release of norepinephrine in close proximity to developing immune cells. We have documented a significant increase in murine bone marrow norepinephrine release in response to either cold exposure or bacteria through the use of traditional pulse-chase experiments. Furthermore, we have extended these measurements to demonstrate increased bone marrow norepinephrine release in response to thermal injury with sepsis in our murine model.

These findings suggest that sympathetic activation has the capacity to drive events within the bone marrow, and adrenergic-mediated expansion of leukocyte production could conceivably contribute to perturbed inflammatory responses with immune challenge following thermal injury with sepsis. Experimental evidence suggesting that adrenergic stimulation inhibits myelopoiesis under normal conditions but is shifted following injury to enhanced monocyte development is a most interesting phenomenon. Whether adrenergic stimulation within the bone marrow functions in a compensatory or a decompensatory way toward the host following thermal injury is also interesting to consider. Is adrenergic stimulation involved in the immunosuppression of patients with severe burns through functional alterations in circulating and tissue leukocytes? These and other important questions are likely to involve events that occur within the bone marrow, as it serves as a major source of new leukocytes both in the circulation and in tissues following thermal injury with sepsis. Our laboratory is beginning to confirm that perturbed bone marrow progenitor development could lead to the production of hyporesponsive monocytes and dendritic cells following thermal injury and sepsis.

Alterations in bone marrow hematopoietic progenitor cells has been the focus of our work and has involved the murine model of thermal injury (15% TBSA) and sepsis via Pseudomonas aeruginosa applied directly to the wound site. The demonstration of a shift in bone marrow myeloid commitment toward monocytopoiesis and away from granulocytopoiesis in thermal injury and sepsis, we began to focus on the potential significance of the increased nerve-stimulated release of norepinephrine within the bone marrow under these same experimental conditions. We tested the premise that neural stimulation was modulating myeloid lineage function by manipulating the peripheral stores of norepinephrine prior to injury. This was achieved by administering 6-hydroxydopamine (6-OHDA) before subjecting the animals to thermal injury and sepsis. Femoral bone marrow cells from mice with reduced norepinephrine content demonstrated a significant decrease in monocytopoietic potential compared to mice with intact norepinephrine stores. In addition, reduction of peripheral norepinephrine content prior to the injury protocol resulted in a significant survival benefit compared to animals with intact norepinephrine content.

The influence of norepinephrine on bone marrow monocyte progenitor differentiation following thermal injury with sepsis was assessed by cell surface expression patterns of ER-MP12 and ER-MP20. Whereas ER-MP12 antigen is expressed in early monocyte progenitors and represents predominantly CFU-M, progressively more ER-MP20 antigen is expressed from the CFU-M stage onwards but disappears in mature monocytes. By following the distribution pattern of the expression of these two antigens on bone marrow cells, the phenotypic separation and identification of bone marrow monocyte precursors have been demonstrated. Taken together, results from ER-MP12 and ER-MP20 expression patterns in burn-septic animals with intact and depleted norepinephrine stores suggest that monocyte maturation pathways may be greatly influenced by the presence of norepinephrine, and that stimulation of such pathways may be involved in the pathobiology of thermal injury with sepsis.

Cohen et al. have also examined very early progenitors not committed to the myeloid lineage that express the CD117 antigen. They also isolated and examined cells expressing ER-MP12 antigen, which are early myeloid-committed progenitors that differentiate either into neutrophils or monocytes. The monocytopoietic potential of both progenitor types was enhanced above control values both following thermal injury alone and with superimposed sepsis. However, this enhancement was greatly reduced by depletion of norepinephrine prior to the injury protocol. These findings suggest that bone marrow myeloid progenitors, as well as early progenitors that are not committed to the myeloid lineage, can be stimulated by endogenous norepinephrine release following thermal injury and sepsis to enhance proliferation.

Another important aspect of Cohen et al.’s work is the demonstration that progenitor-derived macrophages express enhanced cytokine release following thermal injury and sepsis. In this study, the authors elegantly isolated CD117+ and ER-MP-12+ progenitor cells from the bone marrow at 72 hours after the thermal injury protocol and differentiated them into macrophages ex vivo by supplementing with GM-CSF- and M-CSF-rich medium. Subsequently, LPS-stimulated cytokines were measured in the conditioned media. Expression of both TNF-α and IL-6 was significantly reduced in progenitor-derived macrophages from animals with norepinephrine depletion prior to the injury protocol. These results suggest that endogenous norepinephrine released during conditions of burn and sepsis affect the phenotype of differentiated macrophages. Collectively, the work of Cohen et al. suggests that adrenergic stimulation during experimental thermal injury and sepsis contributes to enhanced numbers of macrophages as well as the expression of cytokines in bone marrow progenitor-derived macrophages.

**Bone marrow progenitor response to β-adrenergic stimulus**

In order for catecholamines to act on bone marrow progenitors, such cells should express functional adrenergic receptors. Recently, we have documented the expression of α1, α2,
and β₂ adrenergic receptors in murine hematopoietic stem cells and progenitors. Muthu et al. used a combination of flow cytometry and confocal imaging techniques to circumvent the requirement for large sample size in rare progenitor populations, otherwise needed in traditional radio receptor techniques.¹⁶⁰ In fact, specific β-adrenergic receptors on bone marrow progenitors enriched for ER-MP20 antigen were characterized by Muthu et al. using conventional pharmacologic binding techniques, and values of total receptors (Bₘₐₓ) and affinity (Kᵦ) were determined. Furthermore, the effect of thermal injury and sepsis on these receptors was determined at 72 hours post injury.¹⁶¹ Thermal injury and sepsis resulted in significant reductions in cell surface β-adrenergic receptors (Bₘₐₓ) but binding affinity was increased (decreased Kᵦ values). This paradoxical change was resolved by agonist stimulation of intracellular cAMP, which showed that agonist coupling was increased in burn sepsis. Increased cAMP production under conditions of decreased receptor number but increased affinity suggests the dominant effect of changes in affinity in the bone marrow monocyte progenitor cells. Although these findings do not provide evidence that β-adrenergic–cAMP coupling alters the phenotype of these progenitors in vivo, additional in vitro experiments demonstrated that adrenergic stimulation during differentiation of ER-MP20 progenitors significantly alters the phenotype of mature macrophages, increasing cell surface CD14 expressions. These changes in phenotype expression with adrenergic stimulation could be reversed with the selective β₂-adrenergic blocker.¹⁶¹

In an independent study, the same authors observed a time- and dose-dependent β-adrenergic augmentation of membrane CD14 via cAMP-dependent PKA signaling mechanisms in mature bone marrow and peritoneal macrophages.¹⁶² Interestingly, β-adrenergic stimulation of bone marrow macrophages for >8 hours increased E. coli uptake through enhanced CD14 expression via PKA, whereas <1 hour incubation reduced the bone marrow macrophage phagocytic response by some other mechanism, suggestive of a disparity in adrenergic regulation of phagocytosis.¹⁶²,¹⁶³ One potential explanation for the increase in E. coli phagocytosis is that by changing the expression of CD14 on macrophage cell surface, β-adrenergic agonists might favorably change the stoichiometry of CD14/TLR4-MD2 complex formation leading, to increased bacterial binding to this complex and eventual phagocytosis.¹⁶⁴ In the context where CD14 is associated with high mortality in Gram-negative sepsis, the in vitro phagocytosis measurements made with live E. coli cultures elevate the need for such clinically relevant experimental models.

Although the murine animal model reflects important clinical features of thermal injury with infection, there may be important limitations. Whereas the murine animal model involves immediate infection following thermal injury, burn patients typically develop septic complications in the second week of their hospitalization. This does not, however, change the interpretation of these experimental findings that increased sympathetic activation in the bone marrow may result in both increased myelopoietic potential and altered cellular phenotype following thermal injury with sepsis. This frame of reference suggests that immune responses following injury should be considered in the context of the potential action of sympathetic neurotransmitters on cellular events that occur during cellular differentiation in the bone marrow compartment.

Nonetheless, this premise is supported by the evidence from our laboratory demonstrating a correlation between the phenotypes of bone marrow monocyte progenitor-derived macrophages and circulating monocytes following burn and sepsis.¹⁵⁴ In this study, the authors measured intracellular or cell-associated cytokine expression by flow cytometry, and not the secreted cytokines in the conditioned medium by traditional methods. As a result, it comes to light that the F4/80⁺Gr-1⁺ subset of macrophages produced LPS-stimulated TNF-α and IL-6, and not the F4/80⁺Gr-1⁻ subset. Further, the results showed a twofold increase in the F4/80⁺Gr-1⁺ subset in circulation at 48 hours post burn and sepsis that started to decline at 72 hours and remained low at 96 hours. Concurrently, bone marrow ER-MP20 progenitors isolated at 48 hours exhibited robust macrophage differentiation potential but a significant decline in the percentage of the F4/80⁺Gr-1⁺ subset with a concomitant decrease in TNF-α production. These results support the argument that bone marrow progenitor-derived monocytes will replace the transient hyperresponsive circulating monocytes later in the course of the septic insult, providing a plausible explanation for the immunosuppression that follows a critical burn injury and sepsis.¹⁵⁴ In a subsequent study the same authors demonstrated that administering β-blockade can restore the inflammatory potential of circulating monocytes and granulocytes in experimental burn sepsis.⁹⁹ Taken together, burn and sepsis-induced sympathetic response has greater influence on bone marrow cellular events and warrants further investigation.

**PART II – ADRENAL CORTICAL STEROIDS FOLLOWING BURN TRAUMA**

**Release of glucocorticoids**

Whereas the acute ‘ebb’ phase of recovery from thermal injury is mainly dependent upon the re-establishment of cardiovascular function following circulatory disruption, the ‘flow’ phase is considered to be dependent upon an adequate metabolic response. These responses are mediated in part by adrenal cortical steroids, of which cortisol is the dominant glucocorticoid hormone (Table 24.2). Elevation of glucocorticoids occurs in response to most forms of trauma,¹⁶⁵ including burn injury, with rapid increases in blood and urine levels.⁸,¹⁶⁶ During the first 2 weeks following burn injury the increase in total plasma cortisol concentration is proportional to the severity of the injury. Early studies observed that glucocorticoid levels were excessively high in severely burned patients and remained high in non-surviving patients.¹⁶⁷ In burn patients in whom recovery is likely, plasma glucocorticoid levels are moderately elevated or in the upper normal range, and can persist for up to 36 days¹⁶⁸,¹⁶⁹ and return to normal as healing progresses.¹⁶⁶ In contrast, patients with severe injury (90% TBSA) have markedly lower levels of glucocorticoids, suggesting that they are unable to mount an adequate response.¹⁶⁹

Glucocorticoids circulate in the body bound to cortisol-binding globulin (CBG) or transcortin, as an inactive
In burn patients, CBG levels have been shown to decrease markedly, with the lowest values occurring 48 hours after injury. Even a minor burn such as 3% TBSA will be discussed later.

**Significance of the adrenal and sympathetic response to burn injury**

Dehydroepiandrosterone sulfate (DHEAS), a weak androgen, is the major secretory product of the human adrenal cortex. Despite the increase in cortisol secretion by the adrenals in burn patients, there is a distinct decrease in serum DHEAS levels owing to a reduction in synthesis and secretion, rather than enhanced metabolism or excretion. Whereas serum DHEAS levels decrease gradually, testosterone and androstenedione levels decrease abruptly. In some burn patients subnormal testosterone levels persist for 3–18 months post burn, whereas cortisol levels return to normal earlier. The decrease in testosterone secretion may be due to a direct effect of excessive cortisol levels on the testis.

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**Release of C19 steroids**

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**Influence on metabolic pathways**

High energy expenditure and hyperglycemia are hallmarks of thermal injury. The heavy demand for energy is due to the increase in essential functions, such as the synthesis of
proteins required for wound healing, the synthesis of acute-phase proteins, and inflammatory mediators. In addition, severe burns exert a burden on the metabolism to generate heat, which in part compensates for the loss through the wound site. Part of the elevation in resting energy expenditure in burn patients is due to the increase in substrate cycling. This occurs when enzymes catalyzing opposing reactions of the same pathway are active simultaneously. For example, in the conversion of glucose to glucose-6-phosphate and back to glucose, the demand for energy is increased in order to resynthesize ATP used in this and similar reactions. In burn patients the rate of glucose production and glycolysis, as well as of lipolysis and re-esterification of triglycerides, is elevated. This cycling of substrates generates heat due to the hydrolysis of high-energy phosphate bonds in ATP, thereby contributing to thermogenesis as well as increased energy requirements in burn patients. Keeping burn patients thermally comfortable lowers the metabolic rate and can therefore reduce the demand for energy. Increased glucorticoid levels during severe burns can orchestrate multiple metabolic pathways to meet this energy demand. In order to understand how glucocorticoids may influence major metabolic pathways to facilitate the hypermetabolic state, we will review the effects of glucocorticoids on glucose, protein, and fatty acid metabolism as they pertain to thermal injury.

**Glucocorticoids and glucose metabolism**

Glucocorticoids can contribute to hyperglycemia, which persists for several days, by enhancing endogenous production of glucose in the liver. Following burn, elevated glucose levels are sustained through gluconeogenesis and impaired glucose utilization. The increased plasma lactate produced by peripheral tissues following burn, as documented by Wolfe et al., is an essential substrate for gluconeogenesis by the liver. Burn injury causes intrinsic alterations in the liver, which increases the conversion of pyruvate to oxaloacetate at the expense of non-tricarboxylic acid cycle sources. Mobilization of glucose from glycogen and skeletal muscle amino acids for gluconeogenesis requires glucagon secretion, which is stimulated by glucocorticoids. In addition to gluconeogenesis, impaired glucose utilization and insulin resistance can also play a role in sustaining high circulating levels of glucose in burn patients.

**Glucocorticoids and protein metabolism**

Protein catabolism is a part of the hypermetabolic state of burn, resulting in negative nitrogen balance. Cuthbertson’s landmark studies were the first to suggest the important concept that nitrogen loss is a whole-body response rather than a local burn-wound response. The increase in proteolysis seen in burn injury is at least partly mediated by glucocorticoids. In humans and in animal models, administration of glucocorticoids enhances muscle proteolysis. Further, burn injury-induced muscle proteolysis can be inhibited by a glucocorticoid receptor antagonist. Amino acids mobilized from peripheral tissues are transported to the liver, where, unlike in other tissues, cortisol stimulates protein synthesis. The increased hepatic protein synthesis in response to cortisol can drive the new synthesis of gluconeogenic enzymes and acute-phase proteins in response to injury.

The specific mechanisms involved in burn-mediated alterations in protein metabolism are not known. However, some information could be gleaned from studies on other states of excessive catabolism. In conditions such as metabolic acidosis, adrenalectomy halts muscle proteolysis and does not increase expression of components of the ubiquitin–proteasome pathway. These effects can be reversed by dexamethasone administration. Further support for this premise is provided by in vitro studies, which show that dexamethasone-induced increases in proteolytic degradation in myocytes can be abolished by the glucocorticoid inhibitor RU486. Ding and coworkers suggest that partial inhibition of the ubiquitin–proteasome pathway may be beneficial in enhanced catabolic states. Taken together, these data suggest that interaction of glucocorticoids and the ATP requiring ubiquitin–proteasome system may play an important role in burn-induced proteolysis.

Another aspect of protein catabolism following burn is the generation of gluconeogenic amino acids. In fact, plasma levels of alanine are increased following burn. Nitrogen produced as a result of transaminating alanine to the gluconeogenic intermediate pyruvate is converted into glutamine and then to urea for excretion by the liver. Glutamine is one of the major participants in the translocation of amino acids from peripheral tissues to the liver for nitrogen excretion. Expression of glutamine synthase, the enzyme responsible for synthesis of this amino acid, is increased to compensate for the glutamine depletion in peripheral tissues. Following burn injury, glutamine synthase mRNA is increased first in the lung and later in muscle. This is further supported by the observation that adrenalectomy partially reduces burn-induced glutamine synthase mRNA in a tissue-specific manner, with no such effect in the kidney or liver. There is evidence to suggest that glucocorticoids may augment glutamine synthesis in lung and muscle tissues. Mobilization of protein from peripheral tissues is also indicated by the increase in phenylalanine in the blood of burn patients. Phenylalanine is the only amino acid that is not degraded by peripheral tissue, and hence accumulates in the circulation when uptake by the liver is compromised.

The hypermetabolic and catabolic states seen in thermal injury remain long after the burn wound is completely healed, as reduction in protein catabolism and enhancement of lean body mass were only seen 9–12 months after the initial injury. Therefore, treatments towards growth deficiency must be prolonged longer than wound healing.

Other more indirect effects of glucocorticoids on glucose levels in burn include modulation of insulin-like growth factor-1 (IGF-1), an important mediator of growth hormone (GH) action. Marked depression of all components of the IGF-1 complex is seen following burn. Elevated glucocorticoid levels in burn patients may contribute to the suppression of the acid labile subunit (ALS) of the IGF-1 complex. Treatment of rats with dexamethasone results in low levels of serum ALS as well as liver ALS mRNA.
Glucocorticoids on bone metabolism

Aside from combating the increased demand for energy, glucocorticoids also affect bone development. Abnormal bone metabolism in burn injury has been demonstrated in animals and humans. In children, the reduction in bone mineral density persists for at least 5 years after severe burn injury (>40% TBSA) and results in permanent retardation of linear growth. The reasons for loss of bone mineral density include increased production of endogenous glucocorticoids, the inflammatory response, immobilization, aluminium loading, and production of cytokines such as IL-1 and IL-6 that facilitate bone resorption.

Glucocorticoids have potent effects on bone formation and resorption, resulting in loss of bone mass. Weinstein and coworkers investigated the long-term (equivalent to 3–4 human years) effects of glucocorticoids on bone metabolism in an animal model and reported a reduction in osteocalcogenesis and osteoblastogenesis, leading to reduced bone turnover and reduced bone formation, respectively. Enhanced osteoclast and osteoblast apoptosis was observed in mice subjected to long-term glucocorticoid administration as well as in patients with glucocorticoid-induced osteoporosis. This depletion in the bone cell population limits the number of cells that can synthesize matrix proteins. In addition, glucocorticoids directly downregulate expression of type I collagen and upregulate expression of collagenase-3 in chondrocytes. On the other hand, IGF-1 enhances expression of type I collagen and suppresses the expression of collagenase-3. Thus, the massive increase in glucocorticoids and the corresponding decrease in IGF-1 in burn injury has the ability to profoundly alter bone and cartilage formation.

The mechanisms by which glucocorticoids mediate bone resorption are not clear. Glucocorticoids may mediate bone resorption by its dual capacity to inhibit osteoclast formation and stimulate osteoclast survival. However, other mechanisms may be involved. For example, the ability of glucocorticoids to reduce the cellular response to chemotactic stimuli diminish neutrophil adherence and induce a shift from marginal to circulating cells. Glucocorticoids also suppress the bactericidal activity of monocytes and neutrophils, perhaps through impairment of lysosomal function.

Although severe burns are associated with alterations in B-cell production and function, there is considerable inconsistency in the literature. For example, in rats subjected to 30% burn injury, splenic lymphocytes respond poorly to LPS, and immunoglobulin synthesis is reduced in comparison to control animals. Others have found an increase in circulating B cells early after burn injury. Interestingly, administration of methylprednisolone to normal volunteers for 2–4 weeks also reduces serum immunoglobulin levels.

Aside from glucocorticoids, adrenal androgens such as dehydroepiandrosterone sulfate (DHEAS) also have a profound influence on the immune response, and a role for DHEAS as a potent modulator of the immune response is now well established. DHEAS, which has immunosuppressive properties on Th1 cells, is low during severe illness. In vitro treatment of human T cells with DHEAS through a number of routes. Patients can be infected through the wound site and by translocation of gut bacteria. Surgery and other life-supporting procedures, such as ventilation, are also fertile sources of infection. The glucocorticoid response to thermal injury appears to play an important role in immune dysfunction, with impairment of both specific and non-specific defenses. Corticosteroids reduce lymphocyte, eosinophil, and basophil numbers; alter lymphocyte subpopulations; depress immunoglobulin production by B cells; and suppress neutrophil and monocyte/macrophage activity.

Acute thymic involution and a reduction of the total T-cell population occur soon after burn injury. During initial thymic involution in an animal model there is marked depression of CD4+CD8+ lymphocytes. Thymic involution is a common response to various types of stress and trauma. In humans, the depression of T lymphocytes is reflected by reduction of both CD4+ and CD8+ cell numbers. In an animal model CD4+CD8+ cells are reported to be more sensitive to the effects of thermal injury than CD4+CD8+ cells. CD4+CD8+ cell numbers remain constantly depressed during a 2-week period following burn injury.

Thymic changes following exogenous administration of glucocorticoids are similar to those seen in burn in that exogenous hypercortisolism in non-injury states, or that following burn injury, is associated with decreasing CD4+CD8+ and increasing CD4+CD8+ thymocytes. The reduction in CD4+CD8+ cell numbers during the first 24 hours after burn is due to glucocorticoid-mediated apoptosis, as burn injury-induced thymocyte apoptosis is suppressed by adrenalectomy or the administration of a glucocorticoid antagonist. Other factors contributing to lymphocyte dysfunction and immunosuppression resulting from elevated corticosteroid levels may include direct inhibition of T-cell proliferation, IL-2 production, and the ability to alter lymphocyte membrane fluidity.

Apart from these effects on lymphocytes, glucocorticoids also enhance susceptibility to infections by altering monocyte and neutrophil functions at several stages. Movement of circulating inflammatory cells to the site of infection is suppressed by the ability of glucocorticoids to reduce the cellular response to chemotactic stimuli, diminish neutrophil adherence and induce a shift from marginal to circulating cells. Glucocorticoids also suppress the bactericidal activity of monocytes and neutrophils, perhaps through impairment of lysosomal function.

Severely burned patients are susceptible to opportunistic infections, and sepsis is a major cause of death associated with burn. Immune suppression occurs soon after burn injury, perhaps to prevent over-responsiveness. However, this leaves the patient extremely vulnerable to bacterial infection
increases IL-2 production (which is required for clonal expansion) and IL-2 mRNA synthesis. It is interesting to note that this effect was seen only in CD4+CD8- and not in CD4-CD8+ cells. DHEAS-treated cells were also able to mediate a more potent cytotoxic effect than untreated cells.

Yet another factor that profoundly influences immune status and adrenal steroid secretion in burn patients is the neurotransmitter dopamine. Dopamine is often used in the treatment of critically ill patients because of its vasopressor, renal vasodilator and cardiac inotropic properties. However, several studies indicate that dopamine treatment may undermine an already depressed immune system. This effect appears to act via the suppression of prolactin release from the anterior pituitary. Dopamine suppresses serum prolactin and DHEAS levels but not cortisol concentration. In vitro, prolactin has a synergistic effect on ACTH-induced DHEAS secretion by human adrenal cells. Thus it is possible that the dopamine-induced suppression of prolactin is responsible for lowering DHEAS levels and hence suppression of the T-cell proliferative response. The in vitro proliferative response of T cells from patients on dopamine therapy is diminished, and cells treated with DHEAS mediate a more potent T-cell cytotoxic effect. Dopamine levels are elevated under conditions of severe physical stress and chronic illness. This may be partly responsible for the anergic state of the immune system during severe stress.

This review affirms that catecholamines and adrenal steroid hormones are integral parts of the physiologic response to thermal injury that are thought to support recovery through compensatory cardiovascular, metabolic, and immunologic changes. Although adrenergic mechanisms are important for their ability to influence intracellular signaling pathways, their role as modulators of gene expression is still being explored. On the other hand, although much is known about the modulation of gene expression by glucocorticoids, very little is known about their modulation of gene expression following severe thermal injury or other forms of trauma. Future studies hold great promise of providing important new information in these areas as to how these bioactive compounds may influence responses to thermal injury, and how such information can lead to the development of new treatment modalities.

Further reading


References


164. Latz E, Visintin A, Lien E, et al. Lipopolysaccharide rapidly traffics to and from the Golgi apparatus with the toll-like


The hepatic response to thermal injury
Marc G. Jeschke, Celeste C. Finnerty

Introduction

The extreme hypermetabolic and hypercatabolic stress responses induced by a severe burn injury are characterized by increased proteolysis, lipolysis, and production of endogenous glucose via glycogenolysis and gluconeogenesis. The critical organ in the control of these processes is the liver. With major roles in metabolism, inflammation, immunity, and the acute phase response, the liver orchestrates the basic functions that modulate survival and recovery in severely burned patients. These authors, and others, have elucidated the function of the liver following a severe burn injury, and these studies have demonstrated that both the integrity of liver and the preservation of liver function are essential for survival. The expression of hepatic cytokines and acute phase proteins, which strongly correlates with post-burn survival, further supports this contention.

More than 2 million Americans each year experience a thermal injury – one of the most severe examples of a traumatic injury. Worldwide, the World Health Organization (WHO) attributes >330,000 deaths each year to thermal injuries and their sequelae. In the USA alone, more than 440,000 children are treated for burn injuries annually. Severe burn injuries – the third most common cause of death for American children – account for up to 1100 pediatric deaths each year, accounting for a significant number of hospital admissions. The effects induced by these injuries are not limited to the injured area alone. A severe burn injury has a devastating effect on the injured patient by affecting almost every organ system, resulting in heightened morbidity and mortality. Amplified availability of glucose leads to increased protein catabolism and lipolysis, initiating the post-burn hypermetabolic stress response. Systemic inflammation, including pathophysiologic regulation of cytokines, hormones, and acute phase proteins, drives the hypermetabolic stress response. Prolongation or amplification of the hypermetabolic, inflammatory, or acute phase responses may result in dysregulation of counterregulatory stress hormones (catecholamines, cortisol, glucagon), thereby exacerbating post-burn hypercatabolism, multi-organ failure, and death.

For more than 20 years, focused research efforts on improving post-burn resuscitation, hypermetabolism, infection, ventilation, resuscitation, and wound healing have led to reduced morbidity and mortality. Further advances in clinical care, however, are needed to reduce morbidity and mortality even further. Through a series of studies, we have built a foundation that supports the hypothesis that the liver is a central player in the response to burn. Through the modulation of immune, inflammatory, metabolic, and acute phase response signal transduction pathways, the liver contributes greatly to survival and recovery following a severe burn injury. Because of the dearth of information delineating the liver’s role after a thermal injury, we have spent the past 15 years engaging in studies to shed light on this topic. This chapter discusses liver function under normal conditions and following a severe insult such as a burn injury.

Anatomy, function, and physiology of the liver

Anatomy

In an average-sized adult, the liver weighs approximately 1500 g, making up almost 2% of total body weight. When the liver is injured, such as following a severe burn injury, its size can increase as needed to meet the additional demands. The lobar anatomy is used to divide the liver in the American system, using the intrahepatic location of the branches of the hepatic artery, portal vein and bile ducts. In this method, the left lobe is divided into medial and lateral sections, while the right lobe is divided into anterior and posterior sections. The hepatic artery and the portal vein are the two sources of the liver’s blood supply. One-quarter of the hepatic blood flow occurs via the hepatic artery, which provides oxygenated blood. Three-quarters of the blood flow through the liver is accounted for by the portal vein, which drains the splanchnic circulation.

Physiology

A broad spectrum of biological functions is orchestrated by the liver. The fine interrelated physiologic-anatomic units of the liver direct these necessary processes: regulation of energy availability; nutrient management (including storage,
distribution, and disposal); substrate synthesis, transformation, and metabolism; and metabolism and removal or toxins and pollutants.18,19

1. The circulatory system. In order to build the pool of metabolites for energy and other functions, the liver extracts nourishment from the blood supply that extracts absorbed nutrients from the intestinal tract.

2. The biliary system. Bilirubin, cholesterol, detoxified drugs, and other liver-secreted substances are eliminated through the biliary system.

3. The mononuclear phagocyte system (MPS) (formerly known as the reticuloendothelial system, RES). A part of the immune system that detects antigens and disposal of senescent cells. Within the liver, Kupffer, endothelial, and phagocytic cells make up 60% of the MPS.

4. The hepatocytes. The metabolic demands of the entire body are met by the body. These cells synthesize, secrete, and store metabolites, and perform catabolic and anabolic functions. The generation of energy by converting adenosine triphosphate (ATP) to adenosine diphosphate (ADP) fuels local and systemic functions.

5. The liver as the source of hormones. The liver is the site of the synthesis and secretion of a variety of hormones including insulin-like growth factor-I (IGF-I), IGF binding proteins (IGFBPs), and hepatocyte growth factor (HGF). In addition to synthesizing and secreting necessary hormones, the liver acts as both a paracrine and an endocrine tissue, thereby amplifying the hepatic role in the hormonal axes.

Circulatory system

The majority of metabolic processes are regulated in one way or another by the liver. To fuel these functions, the liver expends 20% of the body’s total energy supply while consuming up to 25% of total utilized oxygen. These utilizations are not as high as one might expect due to an unfettered blood supply and the unique architecture within the liver. Estimations of the mean total hepatic blood flow range from 100 to 130 mL/kg per min. The majority (three-quarters) of the total hepatic blood flow is via the portal vein, while the remaining quarter is from the hepatic artery. When portal flow is reduced, a reciprocal increase in hepatic arterial blood flow follows; however, the reverse does not occur. Plasma membrane-bound hepatocellular organelles enable specific functions while concurrently interacting with the extracellular matrix, facilitating exchange of metabolites between the blood compartment and the hepatocytes. At the same time, the liver manufactures proteins, substrates, enzymes, and other substances for local use as well as for use by distal organs and tissues. Metabolic signals direct the liver to produce substrates needed to meet the energy requirements in other tissues. For example, the liver produces acetocacetate for utilization by brain, muscle, and the kidneys; however, this substrate is not used by the liver. Agonists, hormones, and substrates regulate the hepatic energy-related functions. As the liver receives blood via the arterial and portal circulation, nutrients are processed while toxins are metabolized, and then these are stored for later use, transformed for immediate use, or distributed to their final destination via lymphatic, vascular, or biliary circuits.

Portal venous flow into the liver is largely regulated by extrahepatic factors, including the flow rate from the intestines and spleen, food, bile salts, secretin, cholecystokinin, pentagastrin, epinephrine, vasoactive intestinal peptide, and glucagon. With blood making up 25–30% of the liver volume, the liver acts as a reservoir that can be tapped in time of physiologic need. More than 300 mL can be released into systemic circulation without adversely affecting liver function during acute blood loss. The liver can also store great amounts of blood – up to 1000 mL of blood can be taken up during right-sided heart failure without adversely affecting liver function.18–20

Biliary system

Although bile secretion occurs independently of liver blood flow, this is not the case when a patient is in shock. Bile is either formed at the hepatocyte’s canalicular membrane or by the bile ductules and ducts. Hepatocytes secrete the majority (four-fifths or approximately 1500 mL) of the total daily production of bile, while the bile duct epithelial cells secrete the remaining fifth. Phospholipids, proteins, conjugated bile acids, and cholesterol are the principal organic compounds in bile. Bile is modified by epithelial cells as it passes through the biliary ductules or ducts. Cholangiocytes, the highest cells lining the biliary ductules, seem to be hybrids of hepatocytes and ductular cells due to common functions and architecture. Bile secretion is stimulated by secretin, and the bile is secreted into the gallbladder where it is concentrated and stored under fasting conditions. Concentration of bile within the gallbladder is stimulated principally by cholecystokinin, with absorption of up to 90% of the water occurring within a 4-hour period. Bile is forced into the intestines following gallbladder contraction induced by cholinergic stimulation and subsequent relaxation of the sphincter of Oddi. The majority of the bile salt is absorbed into the enterohepatic circulation. Bile acids are then extracted by the liver and transported back to the canalicular membrane for re-secretion into the biliary system. Complete circulation of the total bile pool occurs 6–10 times/day in addition to 2–3 times per meal. Of the total 2–5 g pool, each day 0.2–0.6 g are lost in the stool; however, this is rapidly replaced by the synthesis of new bile acids.20

When heme breaks down, bilirubin is produced and eliminated in the bile. Accumulation of bilirubin in the tissue or blood may occur with extrahepatic biliary obstruction or hepatocellular disease. The conjugation of bilirubin to albumin protects tissue from bilirubin’s toxicity until it is removed from the circulation by the liver via a carrier transport system. Bilirubin and glucuronide are conjugated within the hepatocyte, and then secreted into the bile. When this complex binds covalently with albumin, delta bilirubin is formed. Bacterial reduction of bilirubin in the intestine yields mesobilirubin and stercobilirubin, together known as urobilirubin, which are then excreted into the stool. Oxidation of urobilinogen to urobilin gives the stool its normal brown color.18–21

Mononuclear phagocyte system (MPS)
The mononuclear phagocyte system (MPS), formerly known as the reticuloendothelial system (RES), is a component of
the immune system and is made up of phagocytic cells, mainly monocytes and macrophages residing in the reticular connective tissue – such as the Kupffer cells in the liver. The Kupffer cells participate in the immune response by detecting foreign antigens and mobilizing the subsequent immune response. These cells further participate in immune function by removing and digesting senescent cells residing in the liver tissue.

**Metabolic system**

**Acute phase response**

In order to limit tissue damage and to initiate repair processes, the acute phase response (APR) is triggered following activating events such as a severe burn or trauma. Pro-inflammatory cytokines are released locally by fibroblasts, endothelial cells, and activated phagocytic cells, which then leads to systemic dispersion of the APR. The systemic phase of the APR induces a body-wide response encompassing the participation of many organs. The hypothalamus acts to raise body temperature, leading to fever. Steroid hormones are released by the pituitary–adrenal axis. Acute phase response. These cells further participate in immune function by detecting foreign antigens and mobilizing the subsequent immune response. These cells further participate in immune function by detecting foreign antigens and mobilizing the subsequent immune response. The systemic phase of the APR induces a body-wide response encompassing the participation of many organs. The hypothalamus acts to raise body temperature, leading to fever. Steroid hormones are released by the pituitary–adrenal axis. Acute phase proteins are synthesized and secreted by the liver. Further promulgation of the hemopoietic responses is initiated in the bone marrow. Finally, the MPS involves the immune system in the APR, as the lymphocytes are activated to detect foreign antigens. The interaction between the injury site and the liver, however, is a critical step in the initiation of the APR, as the liver is the primary site of acute phase protein production and modulation of the systemic inflammatory response. The APR is characterized by increased production of positive acute phase proteins such as C-reactive protein, α2-macroglobulin, and haptoglobin, with decreased expression of negative acute phase proteins, including albumin, transthyretin, transferrin, and retinol-binding protein.

**Carbohydrate metabolism**

Another major function of the liver is to provide a readily available source of energy – glucose – to the adrenal medulla, red blood cells, and the central nervous system. Postprandial intestinal carbohydrate digestion delivers 80% glucose and 20% galactose and fructose to the liver, where galactose and fructose are rapidly converted into glucose. Hepatocytes absorb the glucose and convert it directly into glycogen for storage. Up to 65 g of glycogen per kg of liver mass can be stored in this manner, while excess glucose is converted to fat. Although skeletal muscle also produces glycogen, it is only for use locally by this tissue. The glycogen produced by the liver is unique, in that it is available for use by other tissues when needed. Under fasting or starvation conditions, glycogen conversion is the primary source of glucose for the first 48 hours. After that, liver glycogen stores have been depleted, and proteins and fat are instead mobilized to meet the metabolic demands. The main substrate mobilized in the muscle is alanine, which then is converted into glucose by the liver.

Adequate glucose synthesis is ensured by hepatic glycogenolysis, glycogenesis, and the conversion of galactose into glucose. As a result, hypoglycemia is a rarity and is usually only apparent when coupled with extensive hepatic disease. Hyperglycemia, however, results from deficiencies in glyco-genesis and commonly occurs alongside severe liver disease. Under ordinary conditions, lactate is produced in the muscles as a result of anaerobic glycolysis. The lactate is then shuttled to the liver where it is converted back into glucose, which is then sent back to the peripheral tissues. The constant shuttling of lactate and glucose is known as the Cori cycle. The brain must be continually supplied with glucose as it does not participate in the Cori cycle. Under starvation conditions, glucose is supplied to the brain at the expense of muscle proteins. Glucose metabolism is often deranged in liver disease. Patients with cirrhosis of the liver frequently experience a reduction in the portal-systemic shunting, decreasing the hepatocyte exposure to portal blood. The clinical presentation of this occurrence is an abnormal result following an oral glucose tolerance test. As the severity of the liver disease progresses, so does the extent of the dysfunction. In patients with fulminating hepatic failure, massive loss of hepatic mass and hepatocyte function occurs, leading to hypoglycemia as gluconeogenesis ceases.

**Lipid metabolism**

Absorption of fat from the gut, lipolysis-induced liberation of fat from adipocytes, and synthesis of fatty acids from amino acids and carbohydrates are the three main sources of free fatty acids (FFA) used by the liver. Triglycerides (TG) are then formed following the etherification of FFA with glycerol. TG export is a direct function of the availability of very low density lipoproteins (VLDL). Lipids accumulate in the liver in the presence of excess FFA; this results from an imbalance in the TG to VLDL ratio and is commonly a sequela of pregnancy, obesity, diabetes, corticosteroid use, or total parenteral nutrition. When inadequate amounts of protein are ingested or absorbed, the liver undergoes fatty alterations as the TG accumulate due to limited protein availability for lipoprotein synthesis.

In addition to TG and FFA, cholesterol and phospholipid synthesis occurs in the liver, and lipid metabolism can be indirectly determined by measuring cholesterol production. The liver is the primary site of cholesterol synthesis, esterification, and excretion. There is a decrease in total cholesterol as well as in the percentage of esterified cholesterol when parenchymal damage is present. Elevations in cholesterol can result from biliary obstruction, biliary cirrhosis, or as a result of toxic reactions to phenothiazine drugs.

**Protein metabolism**

The liver synthesizes and secretes 17 of the major plasma proteins in addition to the majority of urea produced in the body. Measurement of serum proteins produced by the liver can serve as an index of hepatic function. The liver is the sole producer of serum albumin and α1-globulin. The most abundant serum protein is albumin, and its creation accounts for approximately 15% of total hepatic protein synthesis. As a result, serum albumin levels can be used as a marker of liver function, liver disease, or side-effects following therapeutic administration. However, albumin has a half-life of 21 days; therefore, albumin can only be used to monitor reductions in hepatic protein synthesis if the condition has continued
damaged, the hepatocellular dysfunction is so extensive that prothrombin is not produced at all. Clinical measurements of prothrombin and prothrombin time can be used to determine whether the synthesis of prothrombin has been impaired. Hepatic disease is also associated with reductions in factors V, VII, IX, and fibrinogen. 20,21

**Hormonal system**

The liver is the site of hormonal synthesis, secretion, or interaction. Production and secretion into the bloodstream of angiotensinogen occurs within the liver. As noted above, Vitamin D is synthesized when cholecalciferol is hydroxylated by the enzyme 25-hydroxylase to become 25-hydroxycholecalciferol. Growth factors that are important for growth and development such as insulin-like growth factor-I (IGF-I) and the IGF binding proteins (IGFBPs) are made and secreted by the liver. Growth hormone (GH), the primary stimulus for the production of IGF-I, is produced by the pituitary gland but acts mainly on the hepatic cells (GH). Finally, synthesis of hepatocyte growth factor (HGF), a major hepatic regenerative growth factor, occurs in the liver.27

**The hepatic response to a severe thermal injury**

**Liver damage and morphological changes**

Burn-induced liver injury is variable, and is typically proportional to the severity of the burn injury. Hepatomegaly, or a fatty liver, is a common post-burn finding (Fig. 25.1). These changes can be reversed; however, the significance of these alterations depends on the cause and the extent of the fat accumulation. 28 Autopsies of deceased pediatric burn victims have revealed that fatty infiltration of the liver is associated with increased bacterial translocation, liver failure, and

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**Figure 25.1** (a) Massive hepatomegaly (upper) and hepatic fatty infiltration (lower) of a burn victim at autopsy. (b) Liver size increased throughout acute hospitalization by over 200% in 242 surviving burn patients. (With permission from Jeschke MG. The hepatic response to thermal injury: is the liver important for postburn outcomes? Mol Med. 2009;15:337-351.)
endotoxemia. How these fatty changes in the liver are important for postburn outcomes?

Figure 25.2 Hepatic dysfunction of the rat burn model mimics the post-burn human disease state. (a) Serum aspartate amino transferase (AST) 24 and 48 h after thermal injury. (b) Serum alanine amino transferase (ALT) 24 and 48 h after thermal injury. (c) Serum albumin 24 and 48 h after thermal injury. (d) Caspase-3 activity in liver lysates as determined by successive Western blotting with active caspase-3 and actin antibodies. The data are expressed as a ratio of the two band intensities. (e) TUNEL staining of a liver section before (Control) and 24 h after (Burn) thermal injury. (f) Quantified TUNEL positive cells 24 and 48 h after thermal injury. Time after injury in hours is indicated. C, control; B, burn. Data presented are mean ± SEM. *Significant difference between burn and control, p<0.05. (With permission from Jeschke MG. The hepatic response to thermal injury: is the liver important for postburn outcomes? Mol Med. 2009;15:337-351.)

Increases in hepatocyte death, both by apoptosis and necrosis, are associated with liver damage. Two distinctly different pathways result in cell death – programmed cell death (apoptosis) and necrosis. Cell shrinkage, uniform fragmentation of DNA, and membrane blebbing characterize apoptotic cells, with the cell fragments being phagocytized by neighboring cells. Necrosis, on the other hand, is characterized by cellular swelling, fragmentation of the DNA in a random manner, activation of lysosomes, and complete breakdown of the cellular membrane enabling cellular contents to be extruded into the interstitium. These final steps induce an inflammatory response by attracting inflammatory cells, causing them to release free radicals and release of the hepatic enzymes into the circulation. Following a severe burn, elevations between 50% and 200% above age-matched normals are recorded for serum AST, ALT, and ALKP (Fig. 25.2). These serum markers peak early – AST and ALT during the first post-burn day and ALKP during the second, indicating that burn-induced liver damage is a rapid phenomenon. During the acute hospitalization period, there is regeneration of the liver, which is apparent by the return of these enzymes to baseline. Although these enzymes are elevated as a direct result of the burn injury, additional physiologic processes may be amplifying their expression, including the elevation of ALKP occurring during growth spurts or alongside massive bone resorption. The careful evaluation of hepatic enzyme levels is warranted, and we recommend the comparison of multiple enzymes, as opposed to a single one, to determine whether liver damage is resolving.
pro-inflamatory cytokines, leading to additional tissue breakdown. The morphological hallmarks unique to each process are used to differentiate between apoptotic and necrotic cells. At the time of autopsy, 10–15% of severely burned decedents had liver necrosis, as determined by pathological examination. The hepatic necrosis related to burn-induced shock or sepsis was typically focal or zonal, central or paracentral, and sometimes microfocal.

Apoptosis also occurs in the liver following a cutaneous thermal injury (Fig. 25.2). The liver tries to maintain homeostasis when hepatocyte apoptosis increases by a compensatory increase in hepatocyte proliferation. Despite the attempt to maintain homeostasis in overall hepatocyte number, the liver is unable to immediately regain mass or maintain protein concentration. A severe thermal injury also can induce apoptosis of the epithelial cells in the small bowel. Additionally, no increase is found in proliferation of the epithelial cells in the small bowel, resulting in a net loss of mucosal cells, and ultimately this is apparent as reduction in mucosal mass. Cardiomyocytes are similarly affected by burn injury, although despite apoptosis of the cells, there is no compensatory increase in cardiocyte proliferation, leading to cardiac impairment and dysfunction.

The molecular mechanisms that initiate and propagate hepatocyte apoptosis following a cutaneous burn are not known, although recent work associates hypoperfusion and ischemia-reperfusion with the induction of programmed cell death. Blood flow to the bowel is decreased by approximately 60% for up to 4 hours following a thermal injury. Hepatic blood flow is likely decreased as well, and this may be one of the early events inducing programmed cell death. Apoptotic signals, including IL-1 and tumor necrosis factor (TNF)-α increase systemically during this same time frame. Additional studies have revealed that these elevations of proinflammatory cytokines are not limited to the serum. Local elevations also occur after a thermal injury, as seen with increased concentrations of hepatic IL-1α, IL-1β, IL-6, and TNF-α. Taken together, these events – reduced splanchnic bloodflow and elevation of proinflammatory cytokines – are probably early events in the induction of hepatocyte apoptotic signaling.

Identifying molecular mechanisms

In identifying the molecular mechanisms that mediate the induction of hepatocyte apoptosis and dysfunction following a severe burn (Fig. 25.3), recent work has shown that ER stress is increased following a thermal injury and that cell-wide alterations in calcium are apparent with specific reductions in ER calcium that led to increases in cytosolic calcium. Mitochondrial damage occurs as a result of increased cytosolic calcium, leading to the release of cytochrome c which then binds to the inositol triphosphate receptor (IP3R), inducing further depletion of calcium stores in the ER. ER stress and the unfolded protein response trigger apoptosis by activating JNK and initiating the downstream response. The serine on IRS-1 is then phosphorylated, blocking the tyrosine on the same protein from being activated by phosphorylation. At the same time, the pro-survival PI3K/Akt signaling pathway is blocked, amplifying the ER stress response by further activating the IP3R. If the unfolded protein burden can be limited through the use of chemical chaperones, this discovery may be of therapeutic significance as a method to promote hepatocyte survival. Alternative pharmacologic agents are being developed to block pro-apoptotic ER stress signaling pathways, and, looking ahead, these alternatives may prove beneficial in the clinic by improving organ function and patient survival.

Effects on the biliary system

Intrahepatic cholestasis frequently occurs following trauma or sepsis without demonstrable extrahepatic obstruction. Conditions such as drug toxicity, total parenteral nutrition, and hypoxia are also associated with this phenomenon. The occurrence of intrahepatic cholestasis is associated with impaired bile acid and organic anion transport in basolateral and canicular hepatocytes. Reduction of transporter RNA and protein expression and the subsequent increase in bile potentially indicate the molecular mechanism driving the development of one of the major manifestations of hepato-cellular injury. In a clinical study, intrahepatic cholestasis was reported in 26% of patients.
Mononuclear phagocyte system (MPS)

The immune system is severely compromised following a major thermal injury, resulting in heightened susceptibility to infections and sepsis. The phagocytic functions of the MPS are depressed post-burn, although the mechanism by which this occurs is unknown. Investigations have demonstrated that MPS dysfunction may be related to hemolysis. The liver is also a significant source of the inflammatory response and the APR, by increasing production of acute phase proteins and proinflammatory cytokines, thereby further impacting the immune response.

Metabolic system

Glucose, protein, and lipid metabolism (Fig. 25.4)

Hypermetabolic stress is induced by large burns covering in excess of 40% of the total body surface area (TBSA), and this response is accompanied by inflammation, the development of a hyperdynamic circulation, temperature elevation, and increases in glycolysis, gluconeogenesis, glycogenolysis, proteolysis, lipolysis, and futile substrate cycling. These massive alterations in major physiologic processes occur following traumatic injury and critical illness as well, although the duration, severity, and the magnitude of these responses are far greater in severely burned patients. The hypermetabolic response is believed to be initiated by huge elevations in catecholamines, glucocorticoids, glucagon, and dopamine via an unknown, yet probably highly complex, cascade of events. Additional players in this response, however, have been identified, including pro-inflammatory cytokines (interleukin (IL)-1 and IL-6, TNF), platelet-activating factor, endotoxin, neutrophil-adherence complexes, free radicals (reactive oxygen species and nitric oxide), and factors involved in the coagulation and complement cascades. Following activation of the biological processes, these mediators and the resulting by-products contribute to the increased metabolic rate and altered glucose metabolism that occurs following thermal injuries. The precise temporal occurrence of the modulation of these post-injury metabolic events has led to the classification of two events: the ‘ebb phase’ and the ‘flow phase’.

The first 12–14 hours following a severe burn injury is called the ‘ebb phase’. Events characterizing this period include decreased cardiac output, reduced oxygen consumption, attenuated metabolic rate, and a hyperglycemic state with impaired glucose tolerance. These metabolic processes slowly increase to a plateau over the next 5-day period, termed the ‘flow phase’. This is when a hyperdynamic circulation develops and the hypermetabolic state is noted. During this time, insulin release in response to glucose challenge is twice that seen in non-burned volunteers. With concurrent elevation in plasma glucose levels, insulin resistance characteristically develops during this period as well. Although these metabolic alterations were assumed to resolve as soon as wound closure was complete and the patient was well enough to be discharged, we have recently determined that the hypermetabolic response induced by a severe burn injury may last for 12 months or more.

Under normal conditions, there is tight regulation of glucose metabolism. In a non-injured state, blood glucose concentrations increase following a meal, stimulating the pancreatic β-cells to release insulin. Peripheral uptake of glucose into adipose and skeletal muscle tissue is mediated by insulin. Blood glucose homeostasis is maintained by the concurrent suppression of hepatic gluconeogenesis. The release of the stress mediators (catecholamines, etc.) acts in opposition to the anabolic actions of insulin, by augmenting hepatic glucose production to increase gluconeogenic substrates such as glycerol, alanine, and lactate by increasing lipolysis of adipose tissue and proteolysis of skeletal muscle. The release of hepatic glucose is not suppressed by hyperglycemia, and the suppressive effect of insulin on hepatic glucose release is attenuated, significantly contributing to post-trauma...

Figure 25.4: Metabolic changes post-burn with the liver playing an essential role. (With permission from Jeschke MG. The hepatic response to thermal injury: is the liver important for postburn outcomes? Mol Med. 2009;15:337-351.)
hyperglycemia. The hyperglycemic response to stress is further aggravated by catecholamine-induced enhancement of glycogenolysis in the liver and direct sympathetic stimulation of glycogen breakdown. Peripheral insulin resistance in the muscle and fat tissue occurs when glucose disposal is impaired by catecholamines following alterations in insulin signaling and GLUT-4 translocation. At 7 days post-injury, insulin receptor substrate-1 (IRS-1) activation is impaired at the tyrosine binding site, leading to Akt inhibition in muscle from severely burned children. Interference with the insulin signaling pathways in liver and muscle has also been linked to reduction in mitochondrial oxidation in both tissues and altered lipolytic rates, the net result of which is attenuation of insulin’s action on glucose production in the liver and glucose uptake in the liver.

Glucose production via gluconeogenesis and glycogenolysis is increased by glucagon and epinephrine, which in concert with cortisol and GH, act to sustain this response. Release of the aforementioned stress hormones is initiated by the action of proinflammatory cytokines, resulting in an indirect effect of these inflammatory mediators on post-burn hyperglycemia. These same proinflammatory cytokines, including IL-6, monocyte chemotactic protein-1 (MCP-1), and TNF, have been found to directly modify the insulin signal transduction pathway, further exacerbating post-burn insulin resistance in the liver and skeletal muscle.

Throughout the acute and convalescent periods following the burn injury, breakdown of lean muscle protein is prolonged by the supraphysiological expression of proinflammatory cytokines and perturbations in the metabolic pathways. Thermal injury impairs the body’s ability to use fat as an energy source – the opposite of that which occurs during starvation, when ketosis and lipolysis are used for energy in order to protect muscle reserves. Significant variation in the expression of the counter regulatory hormones glucagon and cortisone occurs post-burn. While burn injury decreases glucagon, there is a marked increase in cortisol levels that lasts for at least 3 years post-injury. Although the likelihood that perturbations of the hormonal system drive post-burn hypoglycemia is low, impairment of insulin receptor signaling at the molecular level is the more probable instigator.

Soon after injury, marked lean body mass (LBM) wasting is driven by the increase in energy requirements, which are mainly satisfied by degradation of proteins in skeletal muscle in severely burned individuals. Stable isotope infusion studies have confirmed that this muscle breakdown is associated with pronounced negative nitrogen balances that persist for up to 9 months post-injury. Significant reductions in muscle mass probably contribute to whole-body post-burn insulin resistance, as the majority of insulin-stimulated glucose uptake occurs in the skeletal muscle. Stable isotope studies using leucine to monitor whole-body protein flux confirmed the relationship between hyperglycemia and muscle protein catabolism and even showed that hyperglycemia increases proteolysis. During hyperinsulinemia, whole-body proteolysis is markedly increased as a result of elevated plasma glucose levels. Significantly elevated rates of infection and delayed wound healing are associated with reductions in LBM of 10–15%. Mortality is increased in these protein-malnourished patients because of prolonged mechanical ventilation, inhibition of cough reflexes, and delayed mobilization. The growth delay in severely burned pediatric patients that lasts for up to 2 years may be accounted for by this persistent protein catabolism.

During the acute response to burn, there are significant changes in the metabolism of fat, which lead to elevations in serum TGs and FFA. This massive mobilization of fat tissue results in fatty deposits in the liver and other organs, most likely due to decreased expression of fat transporting proteins coupled with elevations of serum TGs and FFA. Hepatomegaly with hepatic steatosis is associated with increases in septic episodes and ultimately with greater mortality, further supporting the notion that impaired liver function in the severely burned patient is closely linked to survival. The hepatic accumulation of TGs occurs both in critically ill patients and in severely burned patients. In fact, liver size is increased by more than four-fold in severely burned patients. Despite the similar deposition of TGs in the liver following critical illness, the rate of TG accumulation in the post-burn liver is far greater than that of any other pathological condition with hepatic steatosis as a sequela. Hepatic TGs accumulate following a severe burn, resulting from lipolysis induced by β-adrenergic stimulation that releases excessive amounts of fatty acids into the circulation. Although insulin typically suppresses lipolysis, the burn-induced insulin resistance is apparent by the diminished effectiveness of insulin in this capacity. Uptake of fatty acids from the circulation by the liver is proportionate to the amount of FFAs available, so that, as lipolysis increases FFA delivery, hepatic uptake is increased, and the fatty acids are either oxidized or synthesized into TGs. As oxidation is a rate-limited step, there is a marked acceleration in the rate of TG synthesis and deposition, when large amounts of fat are available either due to lipolysis or diet. Diet, however, does not account for hepatic TG deposition, as replacement of dietary fat with carbohydrate still leads to fatty acid synthesis and hepatic TG production, although this does not typically result in hepatic TG accumulation. Therefore, synthesis of hepatic TGs is a direct metabolic response to a severe burn injury. Excessive intake of glucose and consequent hyperglycemia also lead to post-burn hepatic steatosis. Under normal conditions, increases in VLDL-TG secretion accompany accelerated synthesis of hepatic TGs, which reduces the accumulation of TGs in the liver. However, in severely burned patients, there is a reduction in secretion of VLDL-TGs, which is not responsive to the increased synthesis of liver TGs. It would therefore be expected that reducing FFA availability could minimize accumulation of TGs in the liver.

The liver is clearly a key player in the orchestration and modulation of burn-responsive metabolic processes post-burn. Alterations in the metabolism of glucose, fat, and protein can result in poor outcomes, and these processes are controlled by the liver. Therefore, we propose that the liver is an essential organ in the response to severe burn injury and that liver function may determine outcomes of severely burned patients.

**Acute phase response**

There is a shift in hepatic protein synthesis following a major trauma such as a severe burn injury. Hepatic constitutive protein production is downregulated while production
is shifted to increase acute phase proteins.\textsuperscript{13,16,22,26} This shift in production of acute phase proteins represents a reprioritization of liver function to meet new metabolic demands, heighten the immune and inflammatory responses, and support coagulation and wound healing.\textsuperscript{13,16,22,26} Traditionally, acute phase proteins have been divided into two subcategories based on whether they were mediated by IL-1-like cytokines such as IL-1 or TNF (type I acute phase proteins, e.g. haptoglobin or α1-acidglycoprotein) or IL-6-like cytokines, including IL-6 or IL-11 (type II acute phase proteins, e.g. α2-macroglobulin and fibrinogen).\textsuperscript{13} With the discovery of new transcription factors, cytokines, and chemokines, it is no longer clear whether these categories reflect biological function or whether the lines have been blurred between the categories. As more evidence supports frequent communication between the type I and type II acute phase proteins, this strict division appears to be an artificial categorization that is no longer representative of function or response. While acute phase protein synthesis is upregulated, constitutive hepatic proteins, including albumin, transthyretin, transferrin, and retinol binding protein, are downregulated.\textsuperscript{109–112} Relative to normal levels, albumin and transferrin expression decreases by 50–70% following a severe burn.\textsuperscript{109–112} Two mechanisms downregulate the production of these proteins: first the liver shifts from synthesizing constitutive proteins to acute phase proteins, coupled with extensive loss of constitutive proteins due to capillary leakage. These proteins are lost into the massive extravascular space and burn wound. The loss of these proteins following trauma, however, may be harmful to patient outcome. Albumin and transferrin are important transporter proteins and contribute to regulation of both osmotic pressure and plasma pH.\textsuperscript{109–112} Due to the exclusive roles that these proteins play, reduction in their synthesis has been used to monitor recovery and predict mortality.\textsuperscript{11,12,112–115}

As noted above, cytokines also mediate the acute phase response. The temporal, biphasic modulation of proinflammatory cytokine expression is highly regulated and predictable. Immediately following a burn, there is an increase in IL-1, IL-6, IL-8, and TNF expression that peaks between 2- and 10-fold above normal levels. After approximately 12 hours, there is a slight decrease in expression, followed by another increase before the overall levels begin to decline. As a testament to the extreme nature of a burn compared with other traumatic injuries, both animal and human studies have revealed that cytokines return to normal levels within 2 days following a trauma, while the elevation can last for more than 2 weeks after thermal injury.\textsuperscript{4,6,13,26,44,70,116} The signaling cascade modulating this response includes a multitude of pro- and anti-inflammatory signal transcription factors including nuclear factor-kappa B (NF-κB), c-jun/c-fos, tyrosine phosphorylation and activation of intracellular tyrosine kinases (JAKs), CCAAT/enhancer-binding-proteins (C/EBP\textsuperscript{s}), STAT1, STAT3, STAT5 (signal transducer and activator of transcription), latent cytoplasmic transcription factors, and mitogen-activated protein.\textsuperscript{57,109,110,117–121} Transcription, translation, and expression of acute phase proteins are initiated by the action of these signaling molecules. IL-6 in particular is suspected of being a major – if not the primary – mediating cytokine. Amplification of the IL-6 signal occurs by activation of glycoprotein 130 (gp 130) and the JAK-kinases (JAK-1) and propagation of the signal via translocation of STATs 1 and 3 to the nucleus, where transcription and translation of acute phase proteins occur. This rapid initiation of the acute phase response serves a single purpose: to protect the body from further damage. When the APR occurs in a balanced fashion, the body is protected and returns to a homeostatic existence. When there are prolonged amplifications of proinflammatory cytokines and acute phase proteins, however, hypercatabolism results, leading to increased incidence of sepsis, multi-organ failure, morbidity, and mortality.\textsuperscript{11,12,112–114}

**Vitamin metabolism**

Vitamins are requisite components of many biological functions including energy production and utilization, inflammation, wound healing, metabolism, and antioxidation. Vitamin deficiencies are caused by the burn-induced hypercatabolic response, so supplementation is required to maintain crucial biological functions.\textsuperscript{122–124} Vitamin A is reduced in burn patients, perhaps related to reduced levels of its transporter – retinol binding protein. Without Vitamin A, dermal wound repair is substandard, and supplementation with this vitamin enhances wound healing. Vitamin E is a critical antioxidant that has profound effects in reducing lung injury. Because this vitamin is also depleted in the serum and in the tissue following a burn injury, supplementation is also recommended. Vitamin D, a necessary nutrient to maintain bone health, is also reduced following a burn injury; however studies exploring the efficacy of replacement therapy are ongoing. Riboflavin and Thiamin, also reduced by burn injury and trauma, are important participants in energy generation, protein metabolism, and wound repair. Thiamin is a key co-factor for energy generation in the Krebs cycle, for glucose oxidation, and for the formation of collagen. Riboflavin decreases post-burn; due to its role as a coenzyme in oxidation-reduction reactions, this vitamin should also be supplemented\textsuperscript{122–124} Post-burn reduction of folic acid negatively impacts DNA and RNA synthesis. Folate utilization is also impaired by inadequate availability of Vitamin B\textsubscript{12}, and methionine. Folate deficiency, therefore, can also occur as a result of deficient levels of these two nutrients. Energy generating and protein metabolic processes rely on the coenzymes Vitamin B complex with B\textsubscript{6} and B\textsubscript{12}, necessitating adequate levels of these vitamins. Supplementation should be in the form of a multi-vitamin in order to have adequate levels of these necessary components. Additional functions of these vitamins include fatty acid catabolism (Vitamin B\textsubscript{12}) and metabolism of amino acids (Vitamin B\textsubscript{6}). The antioxidant/free radical scavenging properties of Vitamin C are crucial following a burn injury. As part of the hypermetabolic response, an elevation in free radicals including superoxide, peroxide, and hydroxyl are thought to increase burn-induced vascular permeability. Administration of Vitamin C may reduce microvascular permeability, which would reduce fluid replacement in turn, improving patient outcomes.\textsuperscript{125}

**Coagulation and clotting factors**

Homeostasis of clotting is complex, and a severe burn injury alters the coagulation cascade.\textsuperscript{126} A major thermal injury
activates thrombotic and fibrinolytic responses in a manner directly proportional to the severity of the sustained injuries. During the early shock phase following the burn, there is a decrease in most of the homeostatic markers due to dilutional effects associated with fluid resuscitation and loss or degradation of plasma proteins to the extravascular space or the wound. Once resuscitation is achieved, clotting factors typically return to normal levels. Thrombogenicity increases later during the post-burn course as a result of decreases in antithrombin III, protein C, and protein S levels accompanied by activation of fibrinolysis by increased levels of tissue plasminogen activation factor, resulting in an increase in the risk of thrombosis. The risk for developing disseminated intravascular coagulation (DIC) is considerably heightened by this hypercoagulable state. Post-mortem DIC has been discovered in 30% of all examined cases, indicating another association between liver damage and poor outcomes – in this case, alterations in the clotting cascade.

Hormones

The liver is a major site for hormone synthesis and action. *In vitro* and *in vivo* studies have demonstrated that HGF accelerates hepatic regeneration, improves hepatic function, and modulates the acute phase response. Elevation of plasma HGF occurs within 30–60 min following injury, presumably signaling the hepatocytes to begin dividing in order to meet the anticipated burden. The initiating signal that stimulates plasma HGF upregulation, however, is currently unknown, although it has been hypothesized that there is either an increase in extrahepatic production of HGF by the spleen, lung, gut, or kidney or a decrease in excretion of hepatic HGF. Hepatocyte mitogenesis, along with motogenesis and DNA synthesis, are stimulated by this rapid increase in HGF. HGF only has this effect under specific conditions; when administered to non-injured rats, only a small number of hepatocytes were induced to initiate DNA synthesis. This study demonstrated that priming events – such as those experienced following a burn injury – are required to enable hepatocytes to respond to mitogenic signals.

The authors have demonstrated that the acute phase response can be returned to homeostasis by administering recombinant human HGF (rhHGF) following a major burn. By a yet to be identified mechanism, following HGF administration, constitutive hepatic proteins are increased, and the acute phase proteins are decreased, reversing the burn-induced APR. The induction of several transcription factors, including C/EBPs, is likely how the signaling is mediated. During the APR, C/EBPβ activation stimulates synthesis of constitutive hepatic proteins, while synthesis of acute phase proteins is reduced by blocking C/EBPβ. Additional beneficial effects are provided by post-burn HGF administration, including maintenance of total hepatic protein content, triglyceride levels, and liver weight, which were not found in burned rats receiving saline.

IGF-I – a 7.7-kDa single-chain polypeptide of 70 amino acids – is also synthesized in the liver. In the body, 95–99% of IGF-I is bound to one of the six binding proteins, IGFBP 1–6, for transport. These hormones are synthesized in the liver following growth hormone stimulation. The effects mediated by IGF-I are similar in burn and other pathological states – improvements in cell recovery, muscle protein synthesis, gut and immune function, and pro-mitogenic functions. In the immediate post-trauma and post-burn periods, IGF-I is a key player in regenerating the liver and modulating the APR to restore hepatic homeostasis and function. The influence of hormones on hepatic recovery and regeneration is an important consideration when trying to restore hepatic function.

**Importance of the liver for post-burn outcomes**

Although we have heretofore described liver function under normal and severe stress conditions, whether liver function and integrity are essential for favorable outcomes following a severe burn has yet to be determined. Price *et al.* found an association between impaired liver function and integrity and unfavorable post-burn outcomes in a retrospective study; however, no prospective studies have been conducted to test this. Therefore, we conducted several studies to determine the relationship between liver function and burn outcomes. In a review of autopsies from severely burned children, Barret *et al.* reported the incidence of hepatomegaly, fatty liver, and sepsis. Some 80% of the patients had hepatic fatty infiltrate, while an astonishing 100% of patients had hepatomegaly. Additionally, it was found that the incidence of sepsis was greater in patients with severe fatty infiltration of the liver. Since all decedents had hepatomegaly, whether this occurs in surviving patients or only patients who do not survive the injury had to be determined. In a study of 102 severely burned children, burn injury was associated with liver enlargement in all patients regardless of outcome. During the first week following a burn injury, liver size was significantly increased (+185 ± 5%), peaked during the second post-injury week (+226 ± 19%) and remained significantly enlarged (+189 ± 10%) at the time of discharge. Prolonged alteration of the hepatic structure was indicated by the continued increase in predicted liver weight (+140–150%) even 6, 9, and 12 months post-burn. Synthesis of hepatic proteins was impaired for at least 12 months following the burn injury. Based on this study, it was concluded that a severe burn injury induced significant enlargement of the liver concurrent with impaired hepatic protein synthesis.

Mittendorfer *et al.* determined the contributions of hepatomegaly and hepatic steatosis to outcomes following a severe burn in the well established rodent model. Following a 60% TBSA burn, nutritional manipulation was used to induce fatty liver in a subset of rats. Hepatomegaly and hepatic steatosis were induced by consumption of a high-fat diet. If both hepatomegaly and fatty liver were present, post-burn mortality increased to 40% (compared with 0% in the control group). Based on these findings, we concluded that the integrity and function of the liver were crucial for survival after a severe burn injury, as hepatomegaly, hepatic steatosis, and liver dysfunction were associated with increased post-burn mortality. Other models have been used to demonstrate the importance of liver function for the survival after critical illness. In a murine sepsis model, Deutschman *et al.* found that mice without IL-6 (IL-6 knockouts) were more likely to die as opposed to their non-IL-6 knockout
littermates with normal IL-6 expression. Hepatic alterations were apparent in the IL-6 knockout animals following cecal ligation and puncture. Cholestasis, steatosis, and hepatocellular injury were not found in the normal mice but were apparent in the IL-6 knockout animals; liver regeneration was absent in the septic IL-6 knockout animals, while apparent in the normal mice. This study supported the author’s conclusion that IL-6 is an important regulator of hepatic dysfunction and mortality following sepsis. The most interesting finding, however, was the association of a three- to four-fold increase in mortality in animals with hepatic damage or dysfunction. 

More recent work has linked signaling via Fas and Fas Ligand (Fas/FasL) to hepatic failure specifically via apoptosis of hepatocytes 

Through a series of RNA interference studies, Song et al. elegantly demonstrated that reduction in the expression of Fas is protective during fulminant hepatitis. Silencing Fas prevented death, leading to the conclusion that hepatic dysfunction contributes to mortality and restoration of hepatic function reduces mortality. Although investigation of the role of Fas/FasL in burns is still in its infancy stages, evidence supports the post-burn induction of Fas/FasL, possibly hinting at the mechanism underlying burn-induced hepatocyte apoptosis and dysfunction.

As animal models do not fully recapitulate the human clinical response, prospective clinical studies are necessary to determine the relationship between liver function and post-burn outcomes. In a study conducted as part of the Inflammation and the Host Response to Injury Collaborative Research Program, Finnerty et al. (unpublished data) used discovery proteomics to compare plasma protein expression in survivors and non-survivors of severe burn injuries. Of the 39 proteins that were differentially expressed between the two groups, 23 of these proteins were produced in the liver and participated in responses mediated by the liver. These data strongly support the hypothesis that hepatic function and integrity affect post-burn outcomes including survival. We expanded these studies to elucidate the role of the liver in multi-organ failure. A total of 22 patients, matched according to burn size and injury severity, were assigned to two groups: burn patients with no multiple organ failure (MOF) and those with MOF defined as a DENVER 2 score >4. Discovery proteomics techniques were used to determine plasma protein expression at the time of admission and at the time of peak DENVER 2 score (or time-matched samples in the non-MOF cohort). In burn patients, 20 proteins were associated with development of MOF, the majority of which were synthesized in the liver. These proteins included acute phase proteins, coagulation factors, inflammatory proteins, and liver enzymes (unpublished data), supporting the notion that post-burn liver function and the development of MOF are highly related.

A recent study of 100 pediatric patients who did not receive anabolic or experimental drugs during their hospital course has elucidated the differences in potential serum biomarkers that could be used to differentiate survivors from non-survivors (unpublished data). The panel of 38 potential biomarkers included hormones, proteins, cytokines, and electrolytes. The patient cohorts were similar for age, burn size, and injury severity. The eight analytes – free fatty acids, retinol binding protein, transthyretin, albumin, α1-acid glycoprotein, alanine amino transferase, apolipoprotein A1, and haptoglobin – could be used to determine if a patient was at higher risk of dying. Taken together, these studies in severely burned children and adults indicate that the liver is crucial for determining survival and post-burn outcomes.

**Conclusion**

To summarize, the widespread effects of a burn injury impact almost every organ system, resulting in significant morbidity and mortality. This chapter has explored the liver’s central role in the response to severe thermal injury. The myriad of functions of the liver are essential for survival (Fig. 25.5), and a burn injury alters all of these hepatic responses. Available data provide strong evidence that the concentrations of hepatic proteins in the circulation can serve as biomarkers predictive of post-burn morbidity and mortality. We, therefore, interpret these findings as supporting the central role of the liver in determining patient outcome and propose that liver damage attenuation and hepatic function restoration will result in a reduction in post-burn morbidity and mortality. This hypothesis has gained recent support in a recent...
book in which Will Self writes regarding the importance of the liver, ‘Our livers are more valuable than we are, more able, more alive.’\textsuperscript{143}

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Further reading


References


enhances proteolysis in normal man.


De Maio A, Torres MB, Reeves RH. Genetic determinants influencing the response to injury, inflammation, and sepsis. Shock. 2005;23:11-17.


Importance of mineral and bone metabolism after burn

Burns exceeding 40% total body surface area (TBSA) disrupt bone and mineral metabolism, both acutely and chronically. Immediately after burn, calcium (Ca) homeostasis is disrupted and magnesium (Mg) depletion occurs, frequently affecting management or worsening the patient’s metabolic status. Long-term consequences include a reduction in bone formation and an increased risk of fracture due to long-term loss of bone Ca and chronic progressive vitamin D deficiency. These alterations arise, in part, from burn-induced hypoparathyroidism and the development of end-organ resistance to parathyroid hormone (PTH). This chapter will discuss bone mineral homeostasis, burn-induced disruption of minerals, mechanisms of burn-induced bone loss, and options in the management of bone and mineral disturbances after burn.

Metabolic actions of calcium, phosphate, and magnesium

As insoluble elements, minerals are major components of the inorganic matrix in bone tissue and confer weight-bearing properties to the skeleton. In the soluble form, Ca, phosphate (PO₄) and Mg play important roles in metabolic pathways, acting as cofactors and regulators of numerous intracellular and extracellular systems.

Calcium

Ca plays a major role in neurotransmission, cell depolarization, impulse propagation, and muscle contractility. In intracellular pathways, after capture by Ca-binding protein or protein kinase C, Ca serves as a second messenger, mediating the secretory release of peptides such as amylase, insulin, and aldosterone. In extracellular metabolism, Ca serves as a cofactor in blood coagulation, specifically in the conversion of prothrombin to thrombin and the activation of several factors in the coagulation cascade.

Phosphate

PO₄ has an integral role in various intracellular processes that involve the storage and transfer of energy. As a component of purine nucleotides such as adenosine-5'-triphosphate (ATP), PO₄ groups are exchanged in multiple metabolic reactions that allow energy-demanding activities in the human body. Phosphorylation reactions represent the mainstay of cellular respiration. In the form of phospholipid, PO₄ is a major structural component of cell membranes.

Magnesium

Mg is essential to the cell and especially the mitochondria. As a cofactor, Mg plays a fundamental part in the transfer of PO₄ groups. Mg is necessary in reactions requiring ATP or involving replication, transcription, and translation of purine nucleotides. Because of its important function in plasma membrane excitability, Mg also serves a role in the stabilization of conditions characterized by abnormal nerve excitation or vasospasm.

Homeostasis of calcium, phosphate, and magnesium

Calcium

Intestinal efficiency to absorb Ca is inversely related to Ca intake. Fractional absorption can be as low as 20% with high Ca intake and as high as 70% with low intake. The regulatory mechanism is shown in Figure 26.1. With high Ca intake, transient hypercalcemia occurs, followed by suppression of PTH secretion and PTH-stimulated renal conversion of 25-hydroxyvitamin D to calcitriol (1,25-dihydroxyvitamin D). With low Ca intake the reverse occurs. A transient reduction in serum Ca occurs, followed by a rapid (within 5 minutes) rise in PTH secretion.

These mechanisms are likely mediated by the parathyroid chief cell Ca-sensing receptor (CaR). The CaR is a membrane-bound G-protein-coupled protein that may be up- or down-regulated, in part, by mutations. In patients with CaR...
Phosphate

In contrast to Ca, the intestine plays no significant regulatory role in the absorption of PO₄. Approximately 80% of dietary PO₄ is absorbed, and the bone stores approximately 90% of the body's PO₄. Homeostatic control appears to rest primarily within the kidney, and the regulatory mechanisms are likely independent of PTH. Thus, the renal excretory rate of PO₄ primarily regulates serum PO₄ concentrations and maintains them within a normal range. Fibroblast growth factor (FGF)-23 is a key regulator of PO₄ and vitamin D metabolism in humans. FGF-23 gene mutations cause autosomal dominant hypophosphatemic rickets, a phosphate-wasting disorder. FGF-23-mediated renal phosphate wasting occurs through downregulation of the type II sodium–phosphate co-transporters NPT2a and NPT2c.

Magnesium

Approximately 60% of the body's Mg is stored in the skeleton, but not at sites where matrix is calcified. Mg absorption varies with dietary intake, with about 40% of an average daily load being absorbed. The relationship between Ca and Mg absorption is described as inverse, but the mechanism of this is unclear. Renal excretion is the main route of Mg elimination and it may vary with Mg concentration in serum. A large paracellular pathway for the intestinal absorption and secretion of Mg exists and is dependent on luminal Mg concentrations. The Mg ion channel, TRPM6, is located in intestinal brush border epithelial cells and may participate in Mg homeostasis in the gut. Mg is 70% ultrafilterable in the serum. About 70% of filtered Mg is reabsorbed along the cortical afferent limb of the loop of Henle. Hypermagnesemia increases urinary Mg excretion by activating the renal CaR, whereas hypomagnesemia increases loop of Henle Mg reabsorption and reduces urinary Mg excretion. Loop diuretics increase urinary Mg excretion. Because little distal tubular Mg reabsorption occurs, an intravenous fluid bolus decreases Mg reabsorption and increases urinary Mg excretion.

Effect of burn injury on calcium, phosphate, and magnesium homeostasis

Although the effects of burn injury on mineral ions are not fully understood, studies from the University of Texas Medical Branch and Shriners Hospitals for Children in Galveston describe some of the developments in this area. In children with >30% TBSA burns, ionized Ca is, on average, 5% below the lower normal limit. In addition, serum PTH levels are too low for ionized Ca levels, indicating hypoparathyroidism. Administration of a standard amount of PTH does not increase urinary cyclic AMP and PO₄ excretion, pointing to PTH resistance. Mg depletion, encountered in all the burn patients studied, impairs hypocalcemia-induced PTH secretion and imparts resistance to PTH infusion. The prevalence of Mg depletion may result from resuscitation of patients with Ringer's lactate, which lacks Mg. Aggressive parenteral Mg supplementation produces repletion in 50% of patients. However, it does not improve hypoparathyroidism, making the cause of post-burn hypoparathyroidism unclear. Sheep studies revealed that an approximate 50% upregulation of parathyroid CaR occurs after burn injury, which is associated, in humans, with decreased circulating Ca necessary to suppress PTH secretion. The proposed mechanism underlying this phenomenon, known as a reduced set point for Ca suppression of PTH secretion, is shown in Figure 26.2. Cytokines, especially IL-1β and IL-6, are highly produced following the systemic inflammatory response. These cytokines stimulate parathyroid cell production of CaR in vitro. In a study of 11 adult burn patients, serum concentrations PO₄ and Mg were low, consistent with abnormalities.
observed in Ca homeostasis. Six patients had low serum ionized Ca concentrations, three of them manifesting hypocalcemia during the first 48 hours after burn. Four were hypophosphatemic; this was most prevalent at post-burn day 7. Five were hypomagnesemic, with this finding most likely to present on post-burn day 3. One patient demonstrated hypercalcemia and one hyperphosphatemia. No patient was hypermagnesemic. Elevated ionized Ca or PO₄ was always transient. Studies in adults are not yet as detailed as those in children have been in this regard.

Hypocalcemia cannot be diagnosed from total serum Ca concentration, owing to variability in serum albumin concentrations after burn. Serum ionized Ca concentration yields a more accurate diagnosis. Several mechanisms may underlie hypocalcemia. One is the extracellular–intracellular shift of Ca, supported by Ca accumulation seen in the erythrocytes of a burn patient. Another is increased urinary Ca excretion, which occurs in burned children and is consistent with documented secondary hypoparathyroidism. Ca loss in tissue exudates could also contribute to hypocalcemia. Although the amount of Ca in wound exudates is likely insufficient to account for post-burn hypocalcemia, few studies have measured Ca content in burn wound exudates.

Although fecal Ca losses can be high in burn patients and burn-induced increases in endogenous corticosteroids may impair intestinal Ca absorption, no evidence suggests that hypocalcemia is caused by corticosteroid-induced impairment of intestinal reabsorption of Ca secreted into the intestinal lumen. Other proposed mechanisms include reduced bone turnover. However, upregulation of parathyroid CaR by inflammatory cytokines followed by a reduction in set-point for Ca suppression of PTH production remains the most attractive hypothesis.

Studies of 24 children with massive burns demonstrated a low serum concentration of 25-hydroxyvitamin D from as early as 14 months after burn, correlating with low bone density Z scores. Serum 1,25-dihydroxyvitamin D concentrations were normal 2 years after injury, but were low at 7 years in 50% of patients. This suggests that these patients became progressively vitamin D deficient.

Possible explanations for post-burn hypophosphatemia include intracellular PO₄ accumulation, inadequate intake, excessive excretion (unlikely in view of documented hypoparathyroidism), or loss into the extravascular fluid. In a review, Dolecek found increased urinary PO₄ excretion only during the third and fourth weeks after burn in adults, whereas hypophosphatemia occurred earlier. Thus, increased urinary PO₄ excretion seen later may be more a function of increased tissue breakdown and filtered load than of inappropriate or excessive urinary PO₄ losses. There is little documentation of inadequate PO₄ intake following burns. We administer a minimum of 1.6 g PO₄ daily in enteral feedings alone.

The cause of sustained hypomagnesemia after burn is unknown, although excessive urinary and fecal losses occur in adults and excessive losses occur in the burn wound.

**Rationale for therapy**

Table 26.1 describes treatments for hypocalcemia and hypophosphatemia. Hypocalcemia, especially during the resuscitation effort, can potentiate hypokalemia-induced abnormalities in cardiac muscle and block responsiveness to fluid repletion in shock. Parenteral Ca during resuscitation does not benefit non-hypocalcemic patients unless they have hyperkalemia, hypomagnesemia, or Ca channel blocker toxicity. Similarly, although caution should be exercised during massive transfusion with citrate-containing blood, Ca therapy may not be necessary in normocalcemic patients unless they have hyperkalemia, hypomagnesemia, or Ca channel blocker toxicity. Similarly, although caution should be exercised during massive transfusion with citrate-containing blood, Ca therapy may not be necessary in normocalcemic patients unless they have hyperkalemia, hypomagnesemia, or Ca channel blocker toxicity.

Hypophosphatemia may cause tissue hypoxemia due to increased hemoglobin affinity for oxygen and decreased tissue ATP, metabolic encephalopathy, hemolysis, shortened platelet survival, myalgias, weakness, and possible impairment of myocardial contractility. Hypomagnesemia, or Mg depletion with normal serum Mg, blunts the effect of PTH secreted in response to hypocalcemia on target organs and impairs secretion of PTH itself. Mg deficiency

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**Figure 26.2 Mechanisms of bone loss after severe burn.**
also causes generalized convulsions, muscle tremors, and weakness.\(^3\)

**Treatments for maintaining mineral homeostasis**

Acute symptomatic hypocalcemia should be treated with intravenous Ca. Adults should receive 90–180 mg of elemental Ca over 5–10 minutes to reverse twitching. Infants/children should receive 20 mg/kg Ca chloride or 200–500 mg/kg Ca gluconate in four divided doses.\(^{30,32}\) Parenteral chloride should be used carefully as it may cause phlebitis and/or acidosis. While hypocalcemia is asymptomatic and patients can tolerate enteral feeding, milk and/or infant formula can provide as much as 3 g/day of bioavailable Ca.\(^{15}\) Hypocalcemia can occur despite enteral provision of such large Ca quantities, making intermittent parenteral administration of Ca salts sometimes necessary. The amounts given must be determined individually and may vary significantly from patient to patient. Dosing in six of our patients with >40% TBSA burns ranged between 0.9 and 15 g 10% Ca gluconate/day over the first 5 weeks after burn. Treatments were given, on average, twice daily for 75% of the days.

Rickets secondary to PO\(_4\) deficiency can be treated with 20–25 mg/kg elemental PO\(_4\) in four divided oral doses per day.\(^{31}\) Infants/children with symptomatic hypophosphatemia should receive 5–10 mg/kg infused over 6 hours and then 15–45 mg/kg infused over 24 hours or until serum PO\(_4\) exceeds 2.0 mg/dl (0.6 mmol/L).\(^{32}\)

Adult patients who tolerate enteral feeding and consume an average of 1.6 g/day PO\(_4\) should have consumed enough to treat asymptomatic hypophosphatemia.\(^{15}\) Prolonged hypophosphatemia has not been reported in burn patients; however, parenteral supplementation would be necessary in such cases. Patients who have signs or symptoms of Mg deficiency with serum Mg concentration <1.5 mEq/L (1.8 mg/dL or 0.8 mmol/L) usually require parenteral therapy.\(^{33}\)

**Hypercalcemia and impaired renal function following burns**

Hypercalcemia with acute renal failure was reported in the May 2010 issue of *Burns*.\(^{34}\) Adult patients with serum ionized Ca ≥1.32 mmol constituted 30% of patient admissions and those with creatinine clearance <50 mL/min developing in the ICU 48 hours after admission ~20% of admissions. Of the four hypercalcemia cases described, three responded to standard doses of bisphosphonates. Onset of hypercalcemia occurred from 6 weeks to 6 months after injury. Much remains to be learned about this complication of burn management.

**Bone**

Silent bone loss may occur for up to a year after burn. Linear growth and bone remodeling are adversely affected by burns. Linear growth at the epiphyses of the long bones usually occurs through cartilage cell proliferation with production of extracellular matrix; these chondrocytes and matrix undergo a series of biochemical changes leading to the formation of ossification centers. As these centers expand, cartilaginous tissue is replaced by bone and a vascular system that allows the delivery of nutrients, hormones, and growth factors. Growth velocity in children is retarded for the first year after a 40% TBSA burn.\(^{35}\) The underlying mechanism is unknown, but growth velocity does return to normal\(^{35}\) even though long-term stunting may result.

The stress and inflammatory response contribute to bone turnover abnormalities that lead to bone loss. Urinary deoxypyridinoline excretion increases the first week after burn.\(^{36}\) Deoxypyridinoline is a marker of bone resorption or one of the byproducts of bone collagen type I breakdown. Its increase in urine during the first week is due to a three- to eightfold increase in glucocorticoid production\(^{37}\) and a three- to 100-fold increase in proinflammatory cytokines produced by the systemic inflammatory response.\(^{38}\) Both glucocorticoids and inflammatory cytokines stimulate bone resorption by increasing osteoblast production of the receptor activator of the nuclear transcription factor-κB (RANKL), which stimulates bone marrow stromal or precursor cells to differentiate into osteoclasts (bone-resorbing cells).\(^{39}\) Normally, bone resorption is coupled to bone formation. In high-turnover situations (i.e. both resorption and formation are increased) bone loss occurs because once bone is laid down it takes time for it to mineralize properly. Bone will be resorbed more quickly than it can allow the type I collagen to crystallize into hydroxyapatite with proper binding sites for Ca and PO\(_4\).

Osteoblasts (bone-forming cells) are key part of normal coupling. They produce RANKL in response to
Effects of burn injury on bone and mineral metabolism

Differentiation (a feature of glucocorticoid toxicity) are present in cultured marrow stromal cells from iliac crest bone of burned children than in cells from bone of age- and gender-matched controls. Although endogenous glucocorticoids resulting from the stress response reduce osteoblast numbers and the differentiation of marrow stromal cells into osteoblasts, high circulating cytokine levels remain unabated. Therefore, cytokines would be expected to continue pushing the differentiation of marrow stroma into osteoclasts. However, this does not occur. In fact, levels of urinary deoxypyridinoline (a bone resorption marker) remain quite low. Thus, both bone formation and bone resorption fall dramatically in the second week after burn, leading to a low-turnover bone loss. This condition, known as adynamic bone, results from a lack of osteoblasts to process bone resorption stimuli.

IL-1β and IL-6 stimulate upregulation of the parathyroid CaR in vitro. Thus, while the stress response explains the low-turnover acute bone loss after burn injury, the systemic inflammatory response explains upregulation of the parathyroid CaR in both humans and sheep. Parathyroid CaR upregulation provides continuous hypoparathyroidism post burn and renders the wasted urinary Ca unproductive in repairing demineralized bone.

In summary, 1 week after burn injury the stress and inflammatory responses promote bone loss by increasing bone resorption and Ca wasting in the urine. By 2 weeks osteoblasts are lost, markedly reducing bone replacement. This hypodynamic bone continues to thin, as resorption is reduced and compensatory bone formation is all but shut off.

The silent events triggered by burn injury reduce bone density (Fig. 26.5) in the lumbar spine and appendicular skeleton (see radiograph in Figure 26.6). The distribution of lumbar spine bone density Z scores (standard deviation score) is shifted to the negative in children with >40% TBSA burns (Fig. 26.5), but not in those with <20% TBSA burns.
Thus, more severe burns trigger the bone loss mechanisms discussed above.

Burn injury increases the annual extrapolated fracture incidence in boys and girls by 100% and 50%, respectively. Thus, burn-induced bone loss increases the risk of fracture later on. Whereas bone remodeling recovers 1 year after burn, the Z score for at least lumbar spine bone mineral density (BMD) does not improve. Given that peak bone mass is reached at 18–30 years, failure of bone density to catch up to one’s peers places burn victims at risk of entering adulthood with less than peak bone mass, and may increase the risk of early-onset osteoporosis.

Another obstacle to bone recovery is progressive vitamin D deficiency. The effect of ongoing vitamin D deficiency on bone density is unclear. In the past, patients were discharged without vitamin D supplementation. Sunlight exposure was limited because of heat intolerance due to sweat gland destruction, and the burn scar could become hyperpigmented. At 14 months post burn, biopsies have demonstrated that UV light converts only 25% of the normal quantity of 7-dehydrocholesterol into pre-vitamin D$_3$, suggesting that skin is biochemically abnormal more than 1 year after injury. Moreover, 7-dehydrocholesterol levels were significantly lower in burn scar and adjacent normal-looking skin than normal control skin, pointing to ongoing problems in cholesterol biosynthesis. The role of vitamin D deficiency in failed restoration of bone density is unknown. We found that, 6 months after children were discharged on a vitamin D$_2$ (400 IU)-containing multivitamin, all but one of eight patients had vitamin D insufficiency. Thus, the vitamin D requirement during and after burn injury remains unknown.

**Treatment of bone catabolism after severe burn**

Several approaches have been studied to prevent, mitigate, or reverse burn-induced bone loss. Daily subcutaneous injection of 0.2 mg/kg recombinant human growth hormone (rhGH) from admission throughout hospitalization immediately improves circulating insulin-like growth factor-1 levels but does not raise serum osteocalcin levels to normal, suggesting that rhGH fails to increase bone formation acutely. However, daily subcutaneous injection of 0.05 mg/kg rhGH for 1 year increases lean body mass (LBM) by 9 months after burn, and increases lumbar spine bone mineral content (BMC), but not BMD, by 1 year. This increased lumbar spine BMC but not bone density is notable for three reasons. First, the persistence of high glucocorticoid levels during the first year may block early efficacy of rhGH, a glucocorticoid antagonist. Next, this finding raises the question as to whether the absence of an increase in lumbar spine bone density reflects a failure of rhGH activity. Given that BMD is the quotient of BMC and bone area, a rise in BMC with no change in BMD would imply a proportional increase in bone area. Thus, a 1-year treatment with rhGH increases LBM, increases skeletal loading, and creates a bigger, more biomechanically stable bone. Finally, one might ask whether the effects of rhGH on bone are only secondary, resulting from an increase in skeletal loading. This question cannot be directly answered based on available data. However, Branski et al. recently showed that a 1-year treatment with 0.2 mg/kg/day rhGH (subcutaneous injection) reduces lumbar spine BMC, increases LBM, and dramatically decreases circulating PTH. These findings suggest that high-dose rhGH directly stimulates bone resorption, with secondary suppression of serum PTH levels. Little evidence supports a direct effect at moderate rhGH doses.

The disadvantages of daily rhGH administration for at least 1 year include the high cost and the need for subcutaneous injections, which may reduce compliance. Another option would be long-term use of the anabolic steroid oxandrolone. Similar to rhGH, a 0.1 mg/kg dose given orally twice daily for 1 year produced a rise in LBM succeeded by an increase in lumbar spine BMC by 3–6 months, increasing skeletal loading and bone size. Oxandrolone is not costly and does not require subcutaneous injections, but it may produce clitoral hypertrophy. However, no premature growth plate fusion has been discovered on X-rays, and this clitoromegaly resolves when the drug is discontinued.

Another drug that has been studied is the bisphosphonate pamidronate. The current generation of nitrogen-containing bisphosphonates acts by adhering to the bone matrix, where they are taken up by osteoclasts and interfere with the cholesterol biosynthesis pathway, ultimately altering protein binding to the osteoclastic membrane and inducing apoptosis. Bisphosphonates remain in bone for a prolonged period, raising concerns that they may interfere with growth or bone quality. However, most bone resorption is thought to occur during the first week or two after burns, when glucocorticoids and inflammatory cytokines cause significant resorption of bone prior to osteoblast apoptosis. Thus, early use of bisphosphonates may prevent acute bone loss.

In a randomized, double-blind study, children with ≥40% TBSA burns received 1.5 mg/kg pamidronate intravenously (maximum dose 90 mg) within 10 days of the burn and 1 week later. Pamidronate prevented the reduction in BMC in the lumbar spine and total body after 6 months of hospitalization. By 2 years, BMC in the placebo group had caught up to that of the pamidronate group for the total body but not the lumbar spine. This suggests that pamidronate effectively preserves the axial skeleton from bone loss and preserves the appendicular skeleton until bone replacement would otherwise ‘catch up.’ Pamidronate has glucocorticoid...
antagonistic properties like those of rhGH; however, the effects of pamidronate on bone are immediate.

Pamidronate use is not associated with hypocalcemia, growth delays, or changes in bone histomorphometry. However, intestinal CaR redistributes following ischemia reperfusion injury in rats. Therefore, one must be certain that these drugs do not alter the cardiovascular or intestinal distributions of the CaR and are specific for CaR in the parathyroid chief cell membrane.

Further reading


References


Importance of vitamins and trace elements

Although vitamins and trace elements play key roles in nearly every cell mechanism in the body, we know remarkably little about the effects of burn injury on their requirements, homeostasis, and metabolism. The published work on burns and micronutrients has covered the role of vitamins and trace elements in homeostasis, wound healing, and antioxidant properties. We will examine each of these topics in the context of the available published data.

Homeostasis and requirements of vitamins following burn injury

Studies of vitamin homeostasis post burn are sparse. Retinol (vitamin A), α-tocopherol (vitamin E), and ascorbic acid (vitamin C) have all been reported as low. Rettmer performed functional testing for thiamin (vitamin B₁), riboflavin (vitamin B₂), and pyridoxine (vitamin B₆) in burn patients and found them to be normal. In a study of serum vitamin K levels in severely burned pediatric patients, Jenkins reported that 91% of children studied demonstrated low circulating levels in the first month post burn. There was no relationship between serum vitamin K levels and prothrombin time, raising the question of clinical significance. It should be noted, however, that osteocalcin, a γ-carboxylated protein produced by osteoblasts, is vitamin K dependent. Osteocalcin is used as a standard index of bone formation and also has been shown to stimulate pancreatic insulin production and peripheral insulin sensitivity. Circulating osteocalcin is reported to be low in the first month following burn injury. Therefore, the possibility remains that low circulating vitamin K levels may contribute to the reduction in serum osteocalcin and hence to post-burn insulin resistance. For a more detailed discussion of osteocalcin, see Chapter 26.

Barbosa studied burned children randomized to micronutrient supplementation or a supplement consisting of vitamin C (1.5 times the upper level of intake), vitamin E (1.35 times the upper intake level) and zinc (twice the recommended dietary allowance). This formula was given for 7 days starting on day 2 of admission. Serum levels of vitamin E were increased and lipid peroxidation, as measured by malondialdehyde, was decreased in the antioxidant supplementation group. The time of wound healing was also decreased in the experimental group.

The infusion of vitamin C alone also seems to have some benefits. Dubick infused high doses of ascorbic acid in a sheep model of 40% TBSA injury. The vitamin C infusion significantly reduced resuscitation fluid requirements of burned sheep. Plasma thiobarbituric acid reactive substances increased fourfold in sham-burned sheep; this was prevented by the use of the vitamin C infusion. Tanaka found in a rat burn model that with high-dose vitamin C, total tissue water content was reduced and negative interstitial fluid hydrostatic pressure was more positive than in controls. This finding suggests that ascorbic acid administration alone could reduce fluid requirements in burn resuscitation.

The one vitamin that has been studied in more detail in burned patients is vitamin D. As discussed in Chapter 25, burned children develop a progressive deficiency of vitamin D measured by circulating levels of 25-hydroxyvitamin D. Although acute measurements of both 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D, the metabolically active steroid hormone, have shown that levels can be low, this result may be confounded by the acute reduction in serum vitamin D-binding protein and albumin. Fourteen months post burn serum 25-hydroxyvitamin D levels are low and remain so at 2 and 7 years post burn. Whereas serum levels of 1,25-dihydroxyvitamin D are normal at 2 years, about 50% of measured values are low at 7 years post burn, suggesting a progressive vitamin D deficiency.

Failure to provide vitamin D supplementation to burn patients on discharge from hospital may contribute to the vitamin D deficiency. Another major factor, however, is the profound change in skin structure and quality. Burn scar and adjacent areas of normal appearance can only convert about 25% of its 7-dehydrocholesterol precursor to vitamin D₃ on exposure to sunlight. Moreover, the amount of 7-dehydrocholesterol substrate is significantly reduced in...
both burn scar and adjacent normal-appearing skin.12 This indicates that after burn injury the skin cannot synthesize normal amounts of vitamin D regardless of the amount of sun exposure received. Thus without vitamin D supplementation, progressive deficiency will result.

In a recent study, children discharged from the Shriners Hospital in Galveston received daily supplementation with a multivitamin containing 400 IU of vitamin D$_2$ for six months.14 At that time, circulating levels of 25-hydroxyvitamin D were still in the insufficient to low range, without any improvement in lumbar spine bone density. Therefore, the amount of vitamin D supplementation necessary to maintain normal circulating levels of 25-hydroxyvitamin D is unknown. Chan and Chan cite 200–400 IU per day as required in healthy, non-burned children.15 However, there is no evidence supporting that requirement in a burned population, and long-term vitamin D supplementation with levels exceeding 400IU/day may be necessary to overcome the post-burn deficiency.

### Zinc and copper

Zinc (Zn) and Copper (Cu) are essential trace elements. Zinc has roles in the metabolism of RNA and DNA, signal transduction, and gene expression, and also regulates apoptosis, thereby playing a ‘ubiquitous role’ in the human organism.16 Copper is involved in the formation of red blood cells, the absorption of iron from the digestive tract, metabolism of glucose and cholesterol, and the synthesis of nearly all proteins and enzymes.17 Malnourishment, hereditary diseases, and prolonged ICU stay can lead to clinical manifestations of Zn and Cu deficiency. Several groups have reported low serum concentrations of Zn, Cu, and their corresponding binding proteins albumin and ceruloplasmin, in burned patients.18–23 Burn wound exudation and urine excretion are considered major routes of loss of these elements.18,20,22–26

In patients with moderate to severe burns, Cunningham18 and Boosalis25 found excessive urinary Zn excretion associated with low plasma Zn levels, especially the plasma subfraction bound to albumin. Zinc supplementation by total parenteral nutrition resulted in hyperzincuria, albeit not as pronounced as with oral supplementation.18,23 Voruganti25 found elevated urinary Cu and Zn excretion in severely burned children at admission as well as at hospital discharge.26 The pediatric burn patients in this study received up to three times the suggested oral intake of Zn and Cu compared to dietary reference intakes.

The burn wound itself is another source of loss of both Zn and Cu. In adults, Berger,14 Guo21 and Voruganti26 found that Zn in wound exudates greatly exceeded excretory losses over the first week post burn. This was confirmed in severely burned children with an average burn size of 54% TBSA, with Zn and Cu concentrations in wound exudates exceeding plasma concentrations.26

Although excretory and exudative losses of Zn and Cu can certainly contribute to a fall in plasma levels of these micronutrients, there is evidence for their post-burn redistribution in the body. Van Rij reported that after a 20% TBSA burn in the rat, isotope-marked Zn was rapidly taken up by the wound, spleen, kidney, and liver, whereas a decrease in Zn levels took place in the brain, muscle, and bone.27 Zinc-binding protein was demonstrated in the hepatic cytosol. Agay found a redistribution of Zn and Cu to the liver without significant changes in levels in muscle and brain.28 Given the findings of Cunningham18 and Boosalis25 that Zn supplementation exacerbates urinary Zn excretion, it can be hypothesized that the body cannot take up the supplemental Zn, and that the redistribution of Zn, rather than elevated urinary excretion, is responsible for decreased plasma levels. Consistent with this hypothesis, Zn is also involved in the inflammatory response and could be redistributed to sites of barrier disruption such as skin, to be subsequently lost in wound exudate.

The low level of plasma Cu is partly due to reduced circulating levels of ceruloplasmin.19,21 Even though ceruloplasmin is an acute-phase reactant stimulated by proinflammatory cytokines, such as interleukin (IL)-1,11,29 there is also evidence that levels of ceruloplasmin are increased in the burn wound exudates. Cunningham15 reported a strong relationship between the size of the open wound and the amount of circulating ceruloplasmin. Gosling20 reported that serum Cu concentration in severe burns varied inversely with burn surface area, in contrast to circulating Zn levels, which showed no such correlation. Furthermore, ceruloplasmin, like albumin, may be extravasated from the intravascular compartment and carry Cu with it.

Finally, one other possible contributor to the low plasma level of Cu is consumption by pathogenic bacteria. Abboud documented that *Pseudomonas aeruginosa* strains isolated from septic patients consumed nearly twice the Cu (ppm/g biomass) as Gram-positive and Gram-negative control strains.30 We have not found similar information with regard to Zn.

Although Zn and Cu may be partly redistributed, there is no doubt that urinary excretion and exudative loss lead to a net decrease in Zn and Cu levels after a severe burn. Loss of Cu has been anecdotally shown to be associated with poor wound healing and Cu supplementation has resulted in accelerated wound healing.31 Furthermore, loss of Zn may lead to abnormalities in type I collagen cross-linking, which may affect the binding of calcium and phosphate to the hydroxyapatite crystal in the bone matrix and contribute, in ways so far undescribed, to the loss of bone (see Chapter 26). Whether loss of Zn affects immune function, as summarized by Keen and Gershwin,12 depends on whether the amount of Zn in the wound (and possibly in the white blood cells) is adequate to assure maximum function of these cells to prevent overwhelming sepsis.

Based on the studies mentioned above, additional Zn and Cu supplementation must be provided to burn patients. Voruganti found that a dietary Zn supplementation of 22.5 mg/day, albeit consistent with the recommendation of Pochon,33 failed to raise plasma Zn levels.22 Moreover, while the Cu intake in these patients was 2–3 times the dietary reference intake (3 mg/day for 4–8 year-olds and 5 mg/day for 9–13 year-olds) normal plasma Cu levels were not achieved either. Berger has stated in a letter to the editor of *Burns* that the Lausanne group provides intravenous trace element supplementation.34 Zinc is given up to 4–6 times the nutritional dose and Cu is given in amounts as high as 3–4 mg/day. These supplements have been successful in correcting the losses. Mayes, at the Shriners Hospital in Cincinnati, recommends Zn be given as zinc sulfate, 30–220 mg/day,35 and Pochon recommended Cu be given to children at...
Following severe burns, Boosalis confirmed these findings and postulated that there may be an antagonistic relationship between Se and silver applied to burn wounds, while cytotoxic and urinary excretion of Se have all been shown to fall. The relationship between Se and silver applied to burn wounds, 41 while the three trace elements provided, as the European general patient population suffers from a Se deficiency, and provision of other vitamins remain unknown. The effects of severe burn injury on both the requirements and the bioavailability of other vitamins remain unknown.

In summary, although the additional supplementation of Zn and Cu in burned patients is paramount, there is no agreement on either the dose or the route of administration. Appropriate criteria on which to base the adequacy of Zn and Cu supplementation have yet to be developed. Currently, the best estimates and guidelines can be found in the work of Mette Berger. 38, 39

Other trace elements: selenium, chromium, and aluminum

Selenium (Se) is a trace element which acts as an antioxidant. It is important in the function of lymphocytes, and hence in cell-mediated immunity. Selenium is lost through the skin following burn injury and thus selenium deficiency in burn patients has been documented. 40 Plasma, erythrocyte and urinary excretion of Se have all been shown to fall following severe burns. 40 Boosalis confirmed these findings and postulated that there may be an antagonistic relationship between Se and silver applied to burn wounds, 41 while Agay suggests that Se may be redistributed among organs. 42 Redistribution between different organ compartments post burn is another explanation for the observed changes in Se levels. Agay also reported a reduction of plasma Zn and Se levels with a sustained increase in serum Cu. 42 Selenium levels increased in kidneys but progressively fell in the liver, whereas hepatic Zn and Cu increased. Of interest, plasma and liver glutathione peroxidase fell but was unchanged in other organs, including the kidney, whereas liver Cu-Zn superoxide dismutase rose. Thus it is possible that in the rat the redistribution of Se to the kidney preserves glutathione peroxidase activity in that organ, while the rise in liver superoxide dismutase results from redistribution of Cu and Zn to the liver and maintains antioxidant activity there. This redistribution hypothesis was suggested by previous work from this group which demonstrated the early oxidative stress following burns in these animals by measuring the drop in plasma thiol groups as an indicator of plasma protein oxidation. 42

There are no evidence-based studies that suggest dosing of Se in burn patients. A recent clinical trial by Berger, however, showed that supplementation with intravenous trace elements (Cu 2.5 to 3.1 mg/day, Se 315 to 380 μg/day, and Zn 26.2 to 31.4 mg/day) for 8–21 days versus placebo was associated with a significant reduction in pulmonary infectious complications, mainly due to a reduction of nosocomial pneumonia in critically ill, burned patients. 43 The authors pointed out that Se deserved special consideration among the three trace elements provided, as the European general patient population suffers from a Se deficiency, and providing Se might act as a ‘reinforcement of endogenous antioxidant defences’. 43

The other trace element studied is chromium (Cr). Anderson found a progressive decrease in liver Cr up to 10 days after the injury and a brief spike in Cr at 6 h post burn in rat quadriceps muscle, followed by a progressive reduction over the next 9 days. 44 Urinary Cr losses also increased. Corticosterone in serum peaked on the first post-burn day, and non-fasting glucose, circulating insulin and glucagon reached a maximum on the second post-burn day. Thus Cr may play a role in the glucose intolerance observed following burn injury. There are no published recommendations regarding Cr replacement.

Finally, burn victims seem to accumulate an unwanted trace element, namely aluminum (Al). Klein described Al accumulation in serum and bone of adults with burn injury >40% TBSA, finding Al deposition on the mineralization front of bones as early as 8 days post burn. 10 The sources of Al contamination in burn injury have been published 45 and attempts to minimize Al loading in these patients may hasten their skeletal recovery from burn injury.

Antioxidative properties of vitamins and trace minerals and effect of replacement therapy

A meta-analysis of studies of antioxidant supplementation in sepsis and the systemic inflammatory response syndrome by Berger and Chiolero showed that Se supplementation improves clinical outcomes of infections and organ failure, glutamine reduces infectious complications in critically ill patients, and eicosapentaenoic acid combined with trace elements has an anti-inflammatory response in critically ill patients and reduces the number of ventilator days. 46 These outcomes have reached the first tier of evidence (level A) supporting their use. With regard to appropriate dosing, in another study from the same group 43 500 mL of enteral solution with 30 g of glutamine per day, as well as Se, Zn and vitamin E, was used for supplementation. 57 The authors found, however, that the entire dose could not be delivered enterally, and concluded that a dose of 0.5 g/kg/day in association with a high intravenous trace element solution may be more effective (Table 27.1).

Summary

Burn injury is marked by a reduction in plasma levels of most vitamins and trace elements, which appear to redistribute to liver and kidney in order to maximize the antioxidant response to the injury. Antioxidant supplementation appears to have beneficial effects on the body’s immune response and morbidity and mortality. The effects of the reduction in trace element content of tissues such as bone have not been studied and may contribute to the loss of bone or bone mineral experienced by these patients. Also of note is the finding of ongoing vitamin D deficiency, in part because the proper supplemental dose is not known, and also because the skin is no longer able to synthesize normal quantities of vitamin D from exposure to ultraviolet radiation. True ‘requirements’ of vitamins and trace elements in the post-burn state have yet to be determined. The effects of severe burn injury on both the requirements and the bioavailability of other vitamins remain unknown.
TABLE 27.1 Vitamin and trace element requirements

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Vit A (IU)</th>
<th>Vit D (IU)</th>
<th>Vit E (IU)</th>
<th>Vit C (mg)</th>
<th>Vit K (mcg)</th>
<th>Folate (mcg)</th>
<th>Cu (mg)</th>
<th>Fe (mg)</th>
<th>Se (mcg)</th>
<th>Zn (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–13</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-burned</td>
<td>1300–2000</td>
<td>600</td>
<td>6–16</td>
<td>15–50</td>
<td>2–60</td>
<td>65–300</td>
<td>0.2–0.7</td>
<td>0.3–8</td>
<td>15–40</td>
<td>2–8</td>
</tr>
<tr>
<td>Burned</td>
<td>2500–5000</td>
<td>(nre)</td>
<td>(nre)</td>
<td>250–500</td>
<td>(nre)</td>
<td>1,000*</td>
<td>0.8–2.8</td>
<td>(nre)</td>
<td>60–140</td>
<td>12.5–25</td>
</tr>
<tr>
<td>≥13 and adults</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-burned</td>
<td>2000–3000</td>
<td>600</td>
<td>23</td>
<td>75–90</td>
<td>75–120</td>
<td>300–400</td>
<td>0.9</td>
<td>8–18</td>
<td>40–60</td>
<td>8–11</td>
</tr>
<tr>
<td>Burned</td>
<td>10 000</td>
<td>(nre)</td>
<td>(nre)</td>
<td>1,000</td>
<td>(nre)</td>
<td>1,000*</td>
<td>4.0</td>
<td>(nre)</td>
<td>300–500</td>
<td>25–40</td>
</tr>
</tbody>
</table>

Conversion based on the following: 1 µg of vitamin A = 3.33 IU of vitamin A; 1 µg of calciferol = 40 IU vitamin D; 1 mg of α-tocopherol = 1.5 IU of vitamin E.
*Administered Monday, Wednesday, and Friday.

nre, no recommendations established.


Further reading


References


Hypophosphatemia

David W. Mozingo, Arthur D. Mason, Jr.

Introduction

Certain humoral and metabolic responses to thermal and mechanical trauma that maintain homeostasis and prevent cellular dysfunction also produce alterations in electrolyte balance. An example is renal retention of sodium during the resuscitative phase of burn injury, which alters sodium balance in the course of preserving intravascular volume. Despite the markedly increased cardiac output and renal plasma flow that occur in the subsequent flow phase, a decrease in blood volume persists and results in sustained elevation of plasma renin activity, secretion of antidiuretic hormone, and sodium retention. Conversely, the severe hypophosphatemia that often follows major injury occurs concomitantly with a 50–100% increase in resting energy expenditure, leading to a possible deficiency in the high-energy phosphate compounds essential for cellular metabolism. Thermal injury induces a precipitous decrease in serum phosphate concentration that reaches its nadir between the second and fifth post-burn days. This phenomenon has been recognized for quite some time and was recently confirmed by the authors in a large series of burn patients. Despite aggressive phosphorus supplementation, normal levels of serum phosphorus are rarely reached prior to the tenth post-burn day. Of 550 patients studied, 175 had serum phosphorus concentrations below 2.0 mg/dL, and of these 49 were below 1.0 mg/dL, with the lower limit of normal serum phosphorus being 3.0 mg/dL. Such hypophosphatemia is not exclusive to thermal injury, having been described following multiple trauma, head injury, and elective surgery. The exact mechanism by which thermal injury or severe stress induces hypophosphatemia is unknown. Several events associated with burn injury, however, affect phosphorus metabolism, and these may combine to produce hypophosphatemia.

Etiology of post-burn hypophosphatemia

Many of the pathophysiological changes and therapeutic interventions that occur during the first post-burn week influence serum phosphorus concentration (Box 28.1). Hypophosphatemia does not necessarily imply phosphorus depletion; in the case of burn injury, most patients are healthy prior to injury and presumably have normal phosphorus stores. Nor do simple calculations of phosphate balance explain the dramatic decrease in serum levels; simultaneous reduction of urinary phosphate excretion is observed, suggesting an extrarenal mechanism. The fractional excretion of phosphate, however, increases during the early period of diuresis following burn injury (post-burn days 2–4), potentially contributing to the decline in serum levels. The pathophysiologic events and therapeutic interventions discussed below are associated with hypophosphatemia in other disease states and in certain experimental animal models, but the extent of their contributions to the post-burn decrease in serum phosphorus has not been critically evaluated and is, at present, undefined.

Stress response

In the early post-burn period, the classic ‘fight or flight’ response occurs, with elevation of plasma catecholamines, glucose, glucagon, and cortisol. Exogenous epinephrine administration has been associated with the development of hypophosphatemia, and the profound catecholamine release accompanying thermal injury may contribute to the early decrease in serum phosphorus. The mechanism by which this occurs is uncertain but may be a consequence of the accompanying hyperglycemia, resulting in a redistribution of phosphorus from the extracellular to the intracellular compartment (see section on Metabolic support, below). In acute clinical states of glucagon excess, tubular reabsorption of phosphate is impaired in both the proximal and distal nephron, leading one to expect renal phosphate wastage. Since urinary excretion of phosphate is usually decreased in the early post-injury period, the importance of hyperglucagonemia remains uncertain. Administration of pharmacological doses of glucocorticoids enhances phosphorus excretion and impairs phosphate absorption by the gut and reabsorption by the kidney. Whether or not the adrenocortical response significantly contributes to the hypophosphatemia after burn injury is not known.

Resuscitation and topical therapy

Administration of large doses of sodium lactate for initial burn resuscitation may decrease the serum phosphorus concentration by several mechanisms. Lactate is converted to glucose in the liver, a process requiring high-energy phosphate availability. Additionally, though it does not usually occur clinically, metabolic alkalosis induced by lactate infusion may result in depression of serum phosphorus concentration. Alkalosis is associated with an increase in glycolysis that promotes transfer of phosphorus to the intracellular
Acid–base disturbance

Phosphate-binding antacids/sucralfate

Electrolyte imbalance

Carbonic anhydrase inhibition (mafenide acetate)

Effective prophylaxis against Curling’s ulcers with H₂-antagonists and antacid buffering has been a mainstay of burn care for the past two decades. Significant degrees of hypophosphatemia and phosphate depletion occur during continuous or chronic administration of phosphate-binding agents containing magnesium, calcium, and aluminum. These agents bind not only dietary phosphate but also phosphate secreted into the intestinal lumen, often resulting in a net negative phosphate balance. The severity of such hypophosphatemia clearly depends on the dose of phosphate-binding agents, dietary phosphorus intake, and pre-existing phosphate balance. To reduce alimentary scavenging of dietary and secreted phosphate, buffering with antacids containing aluminum phosphate salts (Al₂PO₄), which do not bind any additional phosphate, may be utilized. Sucralfate, which is also effective in preventing upper gastrointestinal stress ulceration following thermal injury, is not a buffering agent, but as a complex salt of aluminum hydroxide, is capable of binding phosphate. Its administration has also been associated with the development of hypophosphatemia in critically ill patients.¹⁰

Hyperventilation

Respiratory alkalosis is often present during the first week post-burn and may be enhanced by anxiety or pain, and even by the inhibition of carbonic anhydrase induced by mafenide acetate burn cream. As fluid resuscitation progresses, respiratory rate and tidal volume progressively increase, resulting in minute ventilation that may be twice normal. Mild hyperventilation induces only a slight decline of serum phosphorus levels; prolonged, intense hyperventilation, however, may result in serum phosphorus values less than 1.0 mg/dL.¹⁰ During respiratory alkalosis, phosphorus virtually disappears from the urine, eliminating renal losses as the causative mechanism. Respiratory alkalosis induces a rapid movement of carbon dioxide from the intracellular to the extracellular space. Intracellular pH increases, activating glycolysis and increasing the formation of intracellular phosphorylated carbohydrate compounds. The readily diffusible inorganic phosphate pool supplies the required phosphorus, and serum phosphorus concentrations consequently fall abruptly. The extent to which this mechanism contributes to post-burn hypophosphatemia is uncertain.
Metabolic support

Administration of carbohydrates may play a major role in the development of post-burn hypophosphatemia. Infusion of glucose solutions or oral intake of carbohydrates produces mild hypophosphatemia in healthy individuals. This decrease in serum phosphate is associated with an increase in inorganic phosphate, ATP, and glucose 6-phosphate in muscle cells. The mechanism by which such carbohydrate administration induces hypophosphatemia is somewhat speculative. Experience with phosphate-deficient total parenteral nutrition and subsequent development of hypophosphatemia has provided some insight into the etiology.12,13 As carbohydrates are absorbed, insulin secretion increases, shifting phosphorus from the extracellular to the intracellular space. If phosphate reserve is low, ATP is poorly regenerated since hypophosphatemia inhibits glucose 3-phosphate dehydrogenase. Inorganic phosphates in the intracellular pool become further diminished because of incorporation, initially as newly synthesized ATP, but eventually as triose phosphates when the ATP is consumed in the hexokinase reaction. Glucose utilization by red blood cells requires ATP at the hexokinase and phosphofructokinase steps, but regeneration of ATP does not occur during phosphate deficiency or acute hypophosphatemia due to a block at the glucose 3-phosphate dehydrogenase step. In states of phosphate depletion, the scant phosphate that enters the red blood cell is incorporated into 1,3-diphosphoglycerate, but most is diverted to 2,3-diphosphoglycerate, also preventing complete glycolysis to regain the ATP consumed.

In thermally injured patients, infusion of dextrose-containing solutions usually begins 24 h post-burn, and enteral nutrition, in which most of the calories are supplied as carbohydrates, is initiated within several days of injury. These interventions are temporally correlated with the rapid descent of serum phosphorus concentrations. In other clinical states, severe hypophosphatemia following the initiation of enteral or parenteral nutrition is most commonly associated with the feeding of patients with advanced protein-calorie malnutrition. When total body phosphorus is depleted by starvation, serum phosphorus levels usually remain normal, but carbohydrate administration produces a rapid marked decline in serum phosphorus concentration. If untreated, this may result in multi-system organ dysfunction, respiratory and cardiac failure, or death. Thermally injured patients are usually well nourished prior to burn injury and the clinical scenario of refeeding hypophosphatemia may not apply to them. Similar findings, however, have been described recently in previously well-nourished surgical intensive care unit patients in whom the initiation of isotonic enteral feedings resulted in a decrease of serum phosphorus from normal levels to approximately 1 mg/dL, a level that is considered to be dangerously low and to require prompt supplementation.14,15 In addition, the authors have reported that hypophosphatemia in thermally injured patients is exacerbated by the initiation of enteral feeding and occurs regardless of the post-burn day when feeding is initiated.1 This further reduction of serum phosphorus during the first post-burn week, when levels are already low, may be particularly hazardous and speaks for aggressive phosphorus supplementation prior to and during the initiation of enteral alimentation.

Burn wound physiology

In patients recovering from thermal injury, the burn wound itself may act as a significant phosphorus sink. Despite the overall catabolism accompanying major injury and loss of lean body mass, healing burn wounds and skin grafts are anabolic and require phosphorus for normal repair. In addition, the continued loss of fluid and protein through the burn wound surface is a potential source of unquantified phosphorus loss and may contribute to hypophosphatemia.16 In a comparison between burn patients and traumatically injured patients, it was shown that urinary phosphorus clearance, fractional excretion of phosphorus and renal threshold phosphate concentrations were not different between the two groups; however, persistent hypophosphatemia persisted in the thermally injured patients. This may further implicate the wound as a source of early phosphorus loss.17

Acute phase response and sepsis

Burn injury is characterized by an abrupt increase in acute phase proteins as patients enter the hypermetabolic phase of burn injury. These same responses are similar to those observed in the sepsis syndrome. Recently, the development of hypophosphatemia has been characterized in patients with the acute phase response syndrome.17 Similar findings have been documented in patients with sepsis and infection, and correlation to increase in levels of cytokines such as tumor necrosis factor alpha and interleukin-6 has been made.18 Similar findings were observed in patients with a variety of infectious diseases, and correlation of high levels of C-reactive protein and white blood cell count was made with the magnitude of hypophosphatemia.19 Though these reports did not include burn injured patients, one may infer that activation of the inflammatory cascades such as occurs in major thermal injury may contribute to the development of hypophosphatemia.

Other electrolytes

Disorders of electrolyte balance may contribute to the development of hypophosphatemia. Experimental magnesium deficiency in animals may lead to phosphaturia and phosphorus deficiency, but intentional magnesium deficiency in man results in no change or a slight rise in serum phosphate.20,21 In chronic alcoholics, however, hypomagnesemia and hypophosphatemia are coexistent. Hypokalemia, which is also exacerbated by magnesium deficiency, may result in phosphate wasting and hypophosphatemia. The mechanism is uncertain, but may be related to coexistent metabolic alkalosis, diuretic use, or the underlying illness. Changes in calcium and phosphate homeostasis, and in the regulating hormones calcitonin and parathyroid hormone, have been described after thermal injury.22 Coincident with the early depression of serum phosphorus, the fraction of ionized
calcium was shown to decrease and remain low, but within the normal range, for the 14 post-burn days studied. Urinary calcium output was low, about 4.5 mmol/day, and urinary phosphate output was as high as 30 mmol/day, despite a low serum phosphorus. Serum calcitonin levels were significantly elevated for up to 2 weeks post-injury, whereas parathyroid hormone remained within the normal range. The magnitude of the contribution of the classic regulating hormones of calcium and phosphorus homeostasis to the observed decrease in serum phosphorus after severe injury is not known with certainty. Catecholamines and glucagon are known to induce an increase in calcitonin secretion, and the administration of pharmacological doses of calcitonin results in phosphaturia. A direct effect of calcitonin on phosphate transport in the nephron has been demonstrated. In those burn patients, it was notable that ionized calcium decreased slightly though still within the normal range, despite very high levels of calcitonin and normal parathyroid hormone concentrations. A slight, though statistically significant, increase in parathyroid hormone was observed around the fourth post-burn day and may be related, albeit indirectly through calcium regulation, to the observed post-burn decrease in serum phosphorus concentration.

**Summary**

Clearly, multiple factors influence the serum phosphorus level following burn injury. Fluid resuscitation and subsequent mobilization of interstitial edema fluids, catecholamine excess, respiratory alkalosis, the use of phosphate-binding antacids or sucralfate, hypokalemia, hypomagnesemia, and the initiation of enteral nutrition have all been associated with hypophosphatemia in other illnesses and experimental models. All or most of these factors may be encountered in the early treatment of burn patients and the contribution and relative importance of individual factors to the depression of serum phosphorus is difficult to analyze. Most likely, carbohydrate administration, respiratory alkalosis, and diuresis of edema fluid are the more important etiologic factors contributing to hypophosphatemia in the early post-burn course.

**Consequences of hypophosphatemia**

The clinical manifestations of hypophosphatemia (Box 28.2) are mainly those of organ system hypofunction. These responses have been defined through clinical observation and laboratory studies in circumstances in which hypophosphatemia occurred as a relatively isolated event. Phosphorus supplementation has been reported to reverse these abnormalities, suggesting a cause and effect relationship. Hypofunction of organ systems associated with phosphorus depletion has been attributed to a lack of available inorganic phosphate for synthesis of high-energy phosphate compounds; breakdown of stored ATP occurs, and the inorganic phosphate is diverted to other intracellular pathways. Organ system dysfunction after thermal injury is characterized by early hypofunction and later hyperfunction of most organ systems. Whether hypophosphatemia contributes significantly to the early post-burn depression of function that occurs in multiple organs is not known. Clearly, some of the clinical manifestations shown in Box 28.2 are commonly observed in thermally injured patients, while others are not usually associated with such injury. Most patients reported to have had complications of hypophosphatemia have also had a coexistent and severe illness. It is important to remember that prior cellular injury has been prerequisite in most instances in which hypophosphatemia has been implicated as a cause of organ system dysfunction. The following discussions of organ system abnormalities should be interpreted in light of the specific circumstances under which the observations were made.

**Cardiac dysfunction**

Although the early depression of cardiac function following burn injury has been attributed to an initial decrease in circulating blood volume, the search for intrinsic myocardial depression after burn injury and for mediators of such depression continues. In experimental studies and in clinical material, a correlation between hypophosphatemia and cardiac decompensation has been reported. Cardiac output, measured by bolus thermodilution, was impaired in seven critically ill hypophosphatemic patients and improved significantly with phosphorus supplementation. In one experimental study, myocardial contractility was impaired by phosphorus deficiency and reversed by phosphorus repletion, suggesting that phosphorus deficiency may be a cause of heart failure in certain clinical conditions. Hypophosphatemic cardiac depression has been described as occurring in 28.8% of surgical intensive care patients. Despite these reports, there appears to be little evidence that hypophosphatemic cardiomyopathy is a frequently encountered clinical entity; most patients in whom this mechanism is invoked have already had a number of other causes for myocardial dysfunction.
Neuromuscular dysfunction

Varying degrees of areflexic paralysis, paresthesias, sensory loss, weakness, and respiratory insufficiency have been reported to be associated with acute hypophosphatemia, usually induced with feeding malnourished patients. A reduction in available ATP to support respiratory muscle contraction has been suggested as a mechanism for acute respiratory failure, and diaphragmatic contractility has been reported to improve with phosphorus repletion in mechanically ventilated hypophosphatemic patients. Profound generalised muscle weakness associated with isolated phosphorus depletion has been observed in both clinical and laboratory studies. In a study of hypophosphatemia and muscle phosphate metabolism in patients with burns or mechanical trauma, no direct correlation was demonstrated between the serum phosphorus concentration and the high-energy phosphate content of muscle cells; all these patients, however, were receiving phosphorus supplementation during the study. If acute hypophosphatemia is superimposed on pre-existing cellular injury, potentially reversible muscle cell dysfunction may extend to irreversible necrosis. Several authors have reported severe rhabdomyolysis associated with severe hypophosphatemia following burns and major trauma. This spectacular clinical event is rare but may occur to a lesser, subclinical, extent in critically ill patients. Hypophosphatemia as the underlying etiology may often be dismissed since muscle cell destruction results in release of phosphate and elevation of serum phosphorus. In the absence of significant hemochromogenuria, the diagnosis may not even be suspected. Further investigation is required to determine whether this ‘asymptomatic’ rhabdomyolysis is, in fact, an important clinical entity, or merely an obligate manifestation of critical illness.

Hematologic dysfunction

When untreated, severe hypophosphatemia may lead to red blood cell dysfunction by alterations in cell shape, survival, and physiological function. Lack of high-energy phosphate results in a decrease in erythrocyte 2,3-diphosphoglycerate and subsequent leftward shift of the dissociation curve, with a consequent risk of tissue hypoxia. Clinical hypophosphatemia, with or without previous phosphate depletion, results in reduced production of 2,3-diphosphoglycerate, erythrocyte ATP, and other phosphorylated intermediates of red blood cell glycolysis. In a variety of experimental and clinical situations, including burn injury and mechanical trauma, red blood cell 2,3-diphosphoglycerate has been shown to be reduced in the presence of hypophosphatemia. In thermally injured patients it has been demonstrated that post-burn disturbance of red cell phosphate metabolism may be prevented by administration of phosphorus in the early post-burn course. Hypophosphatemia has also been associated with depressed capillary transit and the potential for further deficiency of tissue oxygenation.

White blood cell dysfunction also has been observed as a result of hypophosphatemia induced by the initiation of phosphate-free parenteral nutrition and was associated with depressed chemotactic, phagocytic, and bactericidal activity of granulocytes. A reduction in granulocyte ATP content was also documented and amelioration of these white blood cell abnormalities was coincident with phosphorus repletion. Any correlation between these observations and an increased risk of infection remains speculative for hypophosphatemic patients in general and burn patients in particular.

Summary

Though it is clear that organ system dysfunction may be a manifestation of severe untreated hypophosphatemia, the relationship between these specific abnormalities and those observed in either the hypodynamic or the hyperdynamic phases of burn injury remains unclear. Clinical experience dictates that even when severe hypophosphatemia is avoided, the scenario of early organ system hypofunction and later hyperfunction persists. This is not to say that the marked hypophosphatemia observed following burn injury is part and parcel of the disease process, without bearing on the post-burn physiological response, but that thus far, the pathophysiological milieu following thermal injury has not permitted definition of the contribution of hypophosphatemia to the overall post-burn response. Until cause and effect relationships are defined through ongoing research, aggressive phosphorus repletion should be approached cautiously following thermal injury. Such therapy does, however, clearly ameliorate red blood cell 2,3-diphosphoglycerate depletion, which, in and of itself, supports treatment.

Prevention and treatment of hypophosphatemia

An unequivocal recommendation to treat hypophosphatemia in thermally injured patients should be supported by evidence that the treatment is of benefit. Such evidence is somewhat lacking in thermally injured patients, but in many analogous instances of hypophosphatemia from other causes, a direct benefit has been ascribed to repletion. Serum phosphorus levels should be measured daily during the early phase of burn care and intravenous phosphate repletion initiated when levels drop below 2.0 mg/dL (Fig. 28.2). Most of the severe adverse effects of hypophosphatemia occur with concentrations below 1.0 mg/dL, and this replacement strategy should prevent the development of clinically significant hypophosphatemia. Correction of severe hypophosphatemia with serum phosphorus levels less than 1.0 mg/dL requires intravenous replacement, usually with solutions of sodium or potassium phosphate containing 0.16 mmol/kg body weight (5 mg/kg body weight) of elemental phosphorus over 6 h. The dose may be halved for patients with serum phosphorus levels between 1.0 and 2.0 mg/dL. Following completion of the infusion, a repeat serum phosphorus determination should be obtained, and further treatment based on the post-infusion plasma concentration. A potential hazard associated with intravenous administration of phosphate salts is hyperphosphatemia, which may induce metastatic deposition of calcium phosphate salts and hypocalcemia. Additionally, when potassium phosphate salts are used, care must be taken to avoid excessive or too rapid administration of...
hypocalcemia, and hypokalemia, as well as maintenance of acid–base normality, may prevent further renal phosphate losses and maintain the extracellular phosphate pool. After the 10th post-burn day, the phosphorus delivered in standard liquid enteral formulas and hospital diets is usually sufficient to maintain serum phosphorus levels above 3.0 mg/dL.

Summary

Thermal injury induces a precipitous decrease in serum phosphate concentration that reaches its nadir between the second and fifth post-burn days. This phenomenon has been recognized for some time, but interest in the problem has been limited. The organ system dysfunctions induced by hypophosphatemia are in many ways similar to certain of the pathophysiological changes observed following burn injury. The contribution of hypophosphatemia to these manifestations remains undefined. Wound fluid losses, increased circulating catecholamines, intracellular phosphate redistribution, and increased fractional excretion of urinary phosphate, as well as iatrogenic induction of hypophosphatemia through various therapeutic interventions, have been implicated as contributing to post-burn hypophosphatemia. There may be other pathways regarding potassium. Phosphorus replacement should be carefully monitored; proceed with great caution in patients with impaired renal function or evidence of soft tissue injury or necrosis.

Prevention of hypophosphatemia may be facilitated by beginning oral phosphorus replacement prior to interventions such as the initiation of either enteral or parenteral carbohydrate administration, gastric acid neutralization with phosphate-binding antacids or sucralfate, and the administration of diuretics. The nadir of serum phosphorus concentration typically occurs between 3 and 5 days post-burn, during the period of edema mobilization, and the need to initiate phosphorus supplementation should be anticipated in this interval. Additionally, to temper the gastrointestinal losses due to administration of phosphate-binding antacids, substitution of, or alternation with, antacids containing aluminum phosphate should be considered.

For mild asymptomatic hypophosphatemia or for prophylaxis when worsening of hypophosphatemia is expected, oral supplementation with any of several available formulations is recommended. Such oral regimens have been shown to be cost-effective.57 Five milliliters of Phospho-soda, containing 4.2 mmol/mL of elemental phosphorus, is commonly administered three times daily. Correction of other electrolyte abnormalities, most notably hypomagnesemia, hypocalcemia, and hypokalemia, as well as maintenance of acid–base normality, may prevent further renal phosphate losses and maintain the extracellular phosphate pool. After the 10th post-burn day, the phosphorus delivered in standard liquid enteral formulas and hospital diets is usually sufficient to maintain serum phosphorus levels above 3.0 mg/dL.

Figure 28.2 The use of this algorithm permits prompt detection and timely correction of hypophosphatemia following burn injury.

<table>
<thead>
<tr>
<th>Phos &lt;2.0 mg/dL</th>
<th>Phos 2.0–3.0 mg/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV therapy indicated</td>
<td>PO therapy indicated</td>
</tr>
<tr>
<td>Phos &lt;1.0 mg/dL</td>
<td>Phos 1.0–2.0 mg/dL</td>
</tr>
<tr>
<td>0.16 mmol/kg body weight of elemental phosphorus (K or Na salt) infused over 6 h</td>
<td>0.08 mmol/kg body weight of elemental phosphorus (K or Na salt) infused over 6 h</td>
</tr>
<tr>
<td>Continue daily monitoring</td>
<td>Repeat serum phos following infusion to guide further replacement</td>
</tr>
<tr>
<td>Identify and address potential contributing factors</td>
<td>Any of several available formulations i.e. Phospho-soda 5 mL t.i.d</td>
</tr>
</tbody>
</table>

For mild asymptomatic hypophosphatemia or for prophylaxis when worsening of hypophosphatemia is expected, oral supplementation with any of several available formulations is recommended. Such oral regimens have been shown to be cost-effective.57 Five milliliters of Phospho-soda, containing 4.2 mmol/mL of elemental phosphorus, is commonly administered three times daily. Correction of other electrolyte abnormalities, most notably hypomagnesemia, hypocalcemia, and hypokalemia, as well as maintenance of acid–base normality, may prevent further renal phosphate losses and maintain the extracellular phosphate pool. After the 10th post-burn day, the phosphorus delivered in standard liquid enteral formulas and hospital diets is usually sufficient to maintain serum phosphorus levels above 3.0 mg/dL.
phosphorus regulation that have not been explored in this patient population. Phosphatonins have been shown to be important mediators of phosphorus homeostasis and could be important mediators in this phenomenon seen in burn patients. Frequent serum phosphate measurement and prompt phosphorus replacement when hypophosphatemia is recognized should minimize any sequelae of this potentially deleterious electrolyte deficiency.

**Further reading**


References


Nutritional support of the burned patient
Jeffrey R. Saffle, Caran Graves, Amalia Cochran

Introduction

The metabolic consequences of major burn injury constitute a major challenge to successful burn treatment. Metabolic rates of burn patients can exceed twice normal and cause tremendous wasting of lean body mass within a few weeks of injury. Failure to satisfy these energy and protein requirements results in impaired wound healing, organ dysfunction, susceptibility to infection, and ultimately death. Aggressive nutritional support is an essential component of burn care which can reduce mortality and complications, optimize wound healing, and minimize the devastating effects of hypermetabolism and subsequent catabolism.

Nutritional therapy is more successful when it is provided within a comprehensive protocol. Every burn center should develop a multidisciplinary protocol that standardizes the initial and ongoing assessment, initiation, and monitoring of nutritional support for patients with all sizes of burn injury.

This chapter provides practical guidelines for the nutritional support of burn patients. In attempting to apply recent research, two difficulties are apparent. First, research dealing specifically with burn patients is far from complete. First, research dealing specifically with burn patients is far from complete. More data are available from trauma and other ICU populations, and it is often necessary to extrapolate information from such studies to burn patients, which may not always be valid. We will attempt to discuss these issues as they arise.

Second, even the results of research in burn patients are not always consistent. Studies of similar therapies may reach contradictory conclusions, especially in different populations. Such findings emphasize our imperfect understanding of complex nutritional physiology. We will summarize new concepts in this field, but also try to distinguish them from ‘tried and true’ therapies which are widely accepted.

A number of recent publications have attempted to summarize the disparate and voluminous literature on nutrition into guidelines for care of critically ill patients; specific guidelines for burn patients have also been published. These guidelines often fail to agree on the details of nutritional support, which further illustrates our imperfect knowledge of this complicated field. Nutritional support, like many areas in burn care, is a moving target. The reader will need to interpret this chapter, and future readings, in this light.

The hypermetabolism of burn injury

Over 70 years ago, Cuthbertson documented that traumatic injury produced increased energy utilization and accelerated losses of skeletal muscle. In the 1970s, burn patients were found to exhibit the most severe hypermetabolism of any group, with energy expenditure from 60% to 100% above normal following a major burn, and concomitant catabolism of protein stores. These studies also demonstrated the so-called ‘ebb and flow’ response to injury (Fig. 29.1), in which an initial (12–24 h) reduction in metabolic rate is followed by a crescendo–decrescendo curve of sustained hypermetabolism that can persist for weeks.

Early attempts to nourish burn patients with oral diets often failed due to altered mental status, gastrointestinal dysfunction, and inhalation injury. Even patients who could eat were rarely able to tolerate the amount of nutrition necessary for adequate support. As a consequence, patients with major burns predictably incurred weight loses of 20% or more within the first few weeks of injury, with associated immune compromise and delayed wound healing. This inanition often proved fatal, as patients succumbed to respiratory failure, pneumonia, and systemic infection.

Mediators of hypermetabolism

The hypermetabolism of burn injury is the product of several predominant hormonal changes. Burn injury causes marked and sustained elevations of the catabolic hormones epinephrine, cortisol, and glucagon. In contrast to unstressed starvation – in which metabolic rate falls, lipolysis and ketosis provide energy, and muscle reserves are protected – this hormonal response to burn injury causes greatly increased metabolism and accelerated gluconeogenesis and glycojenolysis. Catabolic hormones oppose the effects of insulin; as a result, blood sugar levels rise, and protein synthesis and lipogenesis are inhibited.

In this environment, protein breakdown becomes an obligatory major source of energy. Lipids have limited ‘protein-sparing’ effect. In this setting, even glucose is limited in its ability to prevent protein wasting. As a result, diets must also be very high in protein to help replace lost lean body mass.
confirm the efficacy and safety of these techniques. Completely understood. Additional research will be needed to completely understand the milieu that accompanies burn injury is complex and incompletely understood. Additional research will be needed to completely understand the evolving area of research is discussed in detail in other chapters. Although some of these methods show promise for clinical use, it must be remembered that the hormonal milieu that accompanies burn injury is complex and incompletely understood. Additional research will be needed to confirm the efficacy and safety of these techniques.

Modern burn care and metabolic requirements

Modern methods of burn treatment have not altered the nature of burn-induced hypermetabolism but have significantly reduced its magnitude. Maneuvers as simple as maintaining high ambient temperature and relative humidity can reduce caloric requirements by up to 20%. Although burn excision has not been shown to reduce energy expenditure directly, removing the burn wound and covering wounds with autograft, allograft, or synthetic substitutes removes the inflammatory stimulus of the burn wound, reduces infection, and shortens the duration of hypermetabolism. Other therapies, including mechanical ventilation and chemical sedation/paralysis, also reduce energy requirements.

As a result, numerous recent reports using indirect calorimetry document metabolic rates which, although still elevated, are now more likely to approximate 120–150% of normal, rather than the 160–200% previously reported. Nonetheless, both temporal and patient-specific variations in energy expenditure make it difficult to predict requirements for individual patients.

Assessment of nutritional needs

Initial assessment

Patients suffering from diseases such as cancer and AIDS, often present with serious pre-existing nutritional depletion which must be addressed as part of their ongoing treatment. A variety of nutritional assessment techniques can be used both for individuals and in population-based surveys, including careful clinical evaluation, serum proteins, anthropometric measurements, tests of immune function, etc.

Pre-existing malnutrition can also exist in burn patients, but extensive nutritional assessments are rarely helpful for several reasons. First, burn injury induces major abnormalities in nutritional indices which confound assessment of pre-burn status: swelling and eschar preclude accurate anthropometric measurements, serum proteins are rapidly altered, and immune function is similarly disturbed. A careful nutritional history and functional status may be the most meaningful assessments to perform. Moreover, satisfying ongoing requirements is far more important than compensating for pre-existing deficiencies. Attempting to ‘catch up’ by providing extra calories and/or protein is ineffective and likely to increase complications of overfeeding, described below. Therefore, the primary goal of nutritional support in burn patients is to satisfy ongoing burn-specific requirements.
Formulas for estimating caloric requirements

Any protocol for nourishing burn patients must begin with estimation of their nutritional needs. An array of formulas have been developed for this purpose. One early example, the ‘Curreri formula,’ has been widely used, though its accuracy is open to question. To create the formula, Curreri’s group examined only nine patients and calculated backwards to estimate the calories that would have been needed to make up for the patients’ lost weight. As will be discussed, this is a dubious assumption at best.

Several popular formulas for adult nutrition are reviewed in Table 29.1. These include the ‘dietary reference index’ (DRI) values for normal people developed by the US Department of Agriculture. The formulas in Table 29.1 use different variables to predict caloric requirements for specific patients, and reach very different estimates of energy needs. Many older formulas such as Curreri’s significantly overestimate modern requirements, and none can account for the major differences in energy expenditure found between patients. Dickerson et al. reviewed 46 formulas for predicting the caloric needs of burn patients. They found that none of the methods reviewed correlated accurately (±15% error) with measured energy expenditure in a group of 24 patients. Because post-burn energy expenditure fluctuates dramatically over the course of treatment (see Fig. 29.1), static formulas often result in overfeeding early and late in the post-burn course and underfeeding during periods of peak energy utilization.

Table 29.1 Commonly used algebraic formulas for caloric needs in nutritional support

<table>
<thead>
<tr>
<th>Adult formulas</th>
<th>kcal/day: formula</th>
<th>Daily caloric estimates for 25 yo male, 85 kg, 180 cm, 48% TBSA</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Harris–Benedict</td>
<td>Men: 66.5 + 13.8 (W) + 5 (H) – 6.76 (A)</td>
<td>Baseline = 1946 kcal If factor 1.5 = 2918 kcal</td>
<td>Estimates basal energy expenditure (BEE). Best stress adjustment is a factor of 1.5; results in a % calorie variance of 19 + 24%</td>
</tr>
<tr>
<td></td>
<td>Women: 655 + 9.6 (W) + 1.85 (H) − 4.68 (A)</td>
<td>2975 kcal</td>
<td>Variance of 23 + 36% from MREE (p = NS)</td>
</tr>
<tr>
<td>kCal/kg (common use)</td>
<td>35 kCal/kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>37 (W)</td>
<td>3145</td>
<td>‘One size fits all’ is convenient, but inaccurate for many patients, particularly elderly and obese.</td>
</tr>
<tr>
<td>DRI</td>
<td>20 (W) + (70) TBSA</td>
<td>5060</td>
<td>Old (1971) formula grossly overestimates requirements for patients with very large injuries.</td>
</tr>
<tr>
<td>Davies &amp; Lilijedahl</td>
<td>Ventilated patient: 1784 – 11(A) + 5(W) + 244(S) + 239 (T) + 804 (B)</td>
<td>2738</td>
<td>This complex formula permits calculations for trauma and burn patients depending on ventilatory status, and includes a factor for</td>
</tr>
<tr>
<td>Ireton-Jones</td>
<td>Non-ventilated patient: 629 − 11(A) + 25(W) − 609(O)</td>
<td>2479</td>
<td></td>
</tr>
<tr>
<td>Curreri</td>
<td>Age 16–59: 25(W) + 40 (%TBSA) Age &gt;60: 20 (W) + 65 (%TBSA)</td>
<td>4045 kcal</td>
<td>Variance of 35 + 35% from MREE (p = 0.001) Now rarely used because of marked</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pediatric formulas</th>
<th>Formula</th>
<th>Daily caloric estimates for a 15-month old male, 11 kg, 0.9 m² BSA</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>DRI</td>
<td>On-line calculator</td>
<td>899 kcal/day. If factor 1.2 = 1078 kcal/day If factor 1.4 = 1258 kcal/day</td>
<td>Varies according to age, weight, and activity level</td>
</tr>
<tr>
<td>Galveston</td>
<td>0–1 Years: 2100 (BSA) + 1000 (BSA X TBSA) 1–11 Years: 1800 (BSA) + 1300 (BSA X TBSA) 12–18 Years: 1500 (BSA) + 1500 (BSA X TBSA)</td>
<td>2182 kcal/day</td>
<td>Like the Curreri formula, the Galveston formula was created with the goal of maintaining body weight. This may not be</td>
</tr>
<tr>
<td>Curreri Junior</td>
<td>&lt; 1 Year: RDA + 15 (TBSA) 1–3 Years: RDA + 25 (TBSA) 4–15 Years: RDA + 40 (TBSA)</td>
<td>2099 kcal</td>
<td>Extrapolation of the adult Curreri formula, also with a tendency to over-estimate calories.</td>
</tr>
</tbody>
</table>

1For all formulas, W = weight in kilograms; H = height in centimeters; A = age in years; S = sex (male = 1, female = 0); T = Trauma (present = 1, absent = 0); B = burn (present = 1, absent = 0); O = Obesity (present = 1, absent = 0); TBSA = burn size (percent total body surface area); CI = Calorie intake the previous day; HBE = Harris-Benedict estimates; T = Temperature (°C); one point for every degree > 37°C.
**Pediatric formulas**

Children present even greater nutritional challenges than adults. Children have lower tolerance for both under- and overfeeding. In addition, requirements change significantly with age, so that different formulas must be used for different age groups. Several commonly used formulas for burned children are also presented in Table 29.1. These formulas share the same inherent limitations as adult formulas.

**Indirect calorimetry**

In recent decades, improved technology for performance of indirect calorimetry (IC) has permitted routine measurement of energy expenditure at the bedside. IC devices measure the volume of expired gas and the inhaled and exhaled concentrations of oxygen and carbon dioxide, permitting calculation of oxygen consumption (VO₂) and carbon dioxide production (VCO₂), and hence metabolic rate. Measurements made through tight-fitting face masks, hoods, or by connection to mechanical ventilators have proved reliable and reproducible over a wide range of metabolic rates and FiO₂.

Measurement of resting energy expenditure (REE) by IC is usually performed in the early morning with patients at bed rest. Fluctuations in energy utilization associated with activity are usually estimated by increasing REE by 10–20%. IC can also detect significant under- or overfeeding through calculation of the respiratory quotient (RQ) – the ratio of carbon dioxide produced to oxygen consumed (VCO₂/VO₂). The body's metabolism of specific substrates affects this ratio, providing information about metabolic supply and demand. For example, in unstrusted starvation, utilization of fat as a major energy source produces an RQ of 0.7 or less; in normal metabolism of mixed substrates, RQ = 0.75 – 0.90. In contrast, the synthesis of fat from carbohydrate, which typifies overfeeding, results in an RQ of 1.0 or greater. In this way, overfeeding can contribute to difficulty weaning from ventilatory support.

**Delivering estimated needs: How close is ‘close enough’?**

Despite the inherent limitations of static formulas for estimating energy requirements, the superiority of IC has not been proven clinically. It is unknown how closely nutritional support must be ‘matched’ to energy requirements; regular episodes of over- and underfeeding are frequent, normal, and often unavoidable. Saffle et al. found no differences in outcomes between patients fed according to the Curreri formula and those whose nutrition was guided by IC. Recent studies in ICU patients found that <80% of prescribed calories were actually delivered. Enteral nutrition was less successful than TPN because of more frequent interruptions for diarrhea, tube dislodgement, surgery, etc. In both types of nutrition hyperglycemia sometimes required feeding to be reduced, whereas dextrose-containing IV fluids and other infusions, such as propofol, added unplanned ‘empty’ calories. These studies illustrate the ubiquitous practical difficulties of actually giving patients the nutrition that is prescribed for them. Abundant experience demonstrates that either formulas or IC can be used to nourish burn patients successfully, particularly if this is done within a multidisciplinary regimen of support. Many units use a goal of delivering nutrition within 10% of measured (or calculated) needs as a quality assurance indicator, despite the lack of evidence for such a practice.

**Specific nutrient requirements and ‘pharmaconutrition’**

Recent information about the metabolism of specific nutrients has stimulated trials and recommendations for creating disease-specific regimens for patients in a variety of situations – including burns – by changing the basic composition of formulas, and/or providing additives with specific effects on immune function, inflammation, or wound healing, a concept termed ‘pharmaconutrition,’ and recently further refined as ‘pharmaconutrition.’ This information, and some of the evidence that supports it (often incomplete), will be reviewed here. Table 29.2, discussed below, lists the composition of a number of commonly available enteral nutrition products which should help in understanding the quantities of nutrients required for support.

**Carbohydrates**

The major energy source for burn patients should be carbohydrates. Glucose is the preferred fuel for healing wounds, and accessory metabolic pathways to provide glucose, including the alanine and Cori cycles, are active in burn patients.

A major complication of carbohydrate feeding under stress is glucose intolerance. The hormonal environment of acute injury causes some degree of insulin resistance in every patient; many require significant amounts of supplemental insulin to maintain acceptable blood sugars, especially in light of recent evidence linking hyperglycemia to infectious complications and even mortality in ICU populations (see below). However, refractory hyperglycemia can still require the reduction or even discontinuation of nutrition until blood sugar can be controlled. Providing a limited amount of dietary fat reduces requirements for carbohydrates and can improve glucose tolerance significantly. In addition, significant supplemental protein is also required to replace catabolic losses.

**Requirements and uses of fat**

A limited quantity of fat is a required nutrient. Essential fatty acid deficiency is a well-documented complication of long-term TPN; for this reason modern parenteral formulas contain significant amounts of lipid, as well as for its ability to reduce the required glucose load and associated VCO₂. However, the hormonal environment of burn injury suppresses lipolysis and limits the utilization of lipids for energy. For this reason, most authorities recommend that fat comprise no more than about 30% of non-protein calories, or about 1 g/kg/day of intravenous lipids in TPN. Most of the products cited in Table 29.2 meet this target.

It may be desirable to give even less fat. In an animal model, adverse effects on immune function occurred when diets contained more than 15% lipids. Some clinical...
Table 29.2  Composition of a sampling of commercially available adult and pediatric enteral nutrition products (note that all values are per 100 ml of feedings)

### Adult formulas

**A. ‘Standard’ formulas:** These are relatively inexpensive formulas for general use. They provide complete balanced nutrition, including micronutrients, with moderate amounts of protein and fat primarily for non-stressed patients. Osmolarity varies; those intended for tube feedings are generally low. Though any of these products can be given orally, only one (Boost™) is intended for oral use.

<table>
<thead>
<tr>
<th>Brand Name (Manufacturer)</th>
<th>kcal to meet RDI</th>
<th>Carbs</th>
<th>Protein</th>
<th>Fat</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boost™ (Nestlé)</td>
<td>100</td>
<td>1180</td>
<td>625</td>
<td>17</td>
<td>125:1</td>
</tr>
<tr>
<td>Ensure™ (Abbott)</td>
<td>106</td>
<td>1000</td>
<td>620</td>
<td>17</td>
<td>125:1</td>
</tr>
<tr>
<td>Nutren 1.0 (Nestlé)</td>
<td>100</td>
<td>1500</td>
<td>300–350</td>
<td>12.7</td>
<td>133:1</td>
</tr>
<tr>
<td>Isosource HN (Nestlé)*</td>
<td>120</td>
<td>1400</td>
<td>490</td>
<td>16</td>
<td>115:1</td>
</tr>
</tbody>
</table>

*Similar products include Isocal-HN™ (Mead-Johnson) and Jevity™ (Ross) with and without fiber

**B. High Calorie Standard Formulas:** These are concentrated formulas for use in patients with fluid restrictions. Increased concentrations of fat and/or carbohydrates mean increased osmolarity, which can contribute to diarrhea.

<table>
<thead>
<tr>
<th>Brand Name (Manufacturer)</th>
<th>kcal to meet RDI</th>
<th>Carbs</th>
<th>Protein</th>
<th>Fat</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nutren 2.0™ Nestlé*</td>
<td>200</td>
<td>1500</td>
<td>745</td>
<td>19.6</td>
<td>131:1</td>
</tr>
</tbody>
</table>

*Similar products include Isosource 1.5™ (Nestlé), and TwoCalHN™ (Abbott)

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research supports this finding, leading some authorities to recommend very low-fat diets in burn patients. However, popular ‘stress’ enteral formulas typically contain 25–40% of calories as fat, and some ‘specialty’ formulas – for renal failure, respiratory failure, or diabetes – contain even more fat, which limits their usefulness in burn patients. Patients given TPN may be better off if fat is withheld entirely for short periods of time (as little as once weekly), though this may result in aggravated glucose intolerance.

The composition of administered fat may be even more important than the quantity. Most common sources contain mostly omega-6 fatty acids (FFAs) such as linoleic acid, which are metabolized through synthesis of arachidonic acid, a precursor of proinflammatory cytokines such as prostaglandin E₂. Lipids such as fish oil containing a high proportion of omega-3 FFAs are metabolized without elaborating proinflammatory compounds. Diets high in omega-3 FFAs have been associated with improved immune response and possibly improved outcomes, and may reduce problems with hyperglycemia. Most experience with omega-3 FFAs has been obtained with ‘immune-enhancing diets,’ of which they are a major component (see below). Both the optimal composition and the optimal dose of fat in nutritional support remain topics of substantial controversy.
Protein

The hormonal environment of burn injury greatly increases proteolysis. Provision of carbohydrate and fat calories is only partially successful in reducing protein catabolism; some loss of lean body mass is obligatory. Increased protein must be supplied both to satisfy ongoing demands and to provide substrate for wound healing, immunity, and other functions. When calories are limited, protein will be used as an energy source rather than to replenish lost protein stores. The converse, however, is not true: providing calories in excess of need will not lead to increased protein retention or synthesis – it will just lead to overfeeding, with its associated risks. Protein intake above required needs (as in extremely high-protein/low-carbohydrate diets) also results in protein’s use as a fuel source through gluconeogenic pathways.

Protein catabolism in burn patients can exceed 150 g/day, or almost a half-pound of skeletal muscle. Although feeding supranormal amounts of protein may not reduce breakdown of endogenous protein stores, it facilitates protein synthesis and reduces negative nitrogen balance. In burned children, a diet including increased protein (23% of total calories) was...
Table 29.2 Continued

D. ‘Specialty’ adult formulas: These are examples of formulas for patients with unusual, specific nutritional requirements. None are well-suited for burn patients, and are generally much more expensive than more standard formulas.

<table>
<thead>
<tr>
<th>Brand Name (Manufacturer)</th>
<th>kcal</th>
<th>kcal to meet RDI</th>
<th>Carbs</th>
<th>Protein</th>
<th>Fat</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucerna™ (Ross)*</td>
<td>100</td>
<td>355</td>
<td>11.2</td>
<td>4.2</td>
<td>2.3</td>
<td>Complex-carbohydrate formula for diabetics; Contains fiber. Used primarily as an oral nutrient/supplement</td>
</tr>
<tr>
<td>Pulmocare™ (Ross)**</td>
<td>150</td>
<td>470</td>
<td>10.5</td>
<td>6.2</td>
<td>9.3</td>
<td>Customized formula for pulmonary failure relies on high fat content to avoid excessive VCO₂; limited efficacy in burn patients. For tube or oral feeding</td>
</tr>
</tbody>
</table>

*Similar products include Diabetisource AC™ (Nestlé), Nutren Glytrol Diet™ (Nestlé)
**Similar products include Oxepa™ (Abbott), Nutren Pulmonary™ (Nestlé)

E. Elemental/semi-elemental diets: Nutritionally complete diets intended for patients with minimal digestive ability or absorption problems. Minimal residue, provide protein as peptides and/or free amino acids. Elemental diets are high osmolarity due to simple sugars and free amino acids; semi-elemental have lower osmolality, and some provide more balanced carbohydrate, fat, and protein composition.

<table>
<thead>
<tr>
<th>Brand Name (Manufacturer)</th>
<th>kcal</th>
<th>kcal to meet RDI</th>
<th>Carbs</th>
<th>Protein</th>
<th>Fat</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vital HN™ (Abbott)*</td>
<td>100</td>
<td>500</td>
<td>18.5</td>
<td>4.2</td>
<td>1.1</td>
<td>Basic semi-elemental diet, low in fat</td>
</tr>
<tr>
<td>Optimental™ (Abbott)</td>
<td>100</td>
<td>585</td>
<td>13.9</td>
<td>5.1</td>
<td>2.8</td>
<td>High-protein ‘immune-enhancing’ semi-elemental formula supplemented with arginine (8 g/L), vitamins</td>
</tr>
<tr>
<td>Peptamen AF™ (Nestlé)</td>
<td>120</td>
<td>390</td>
<td>10.7</td>
<td>7.6</td>
<td>5.5</td>
<td>High-protein semi-elemental diet, supplemented with w-3 FFAs, fiber</td>
</tr>
</tbody>
</table>

*Similar products include Tolerex™ (Nestlé)
Table 29.2 Continued

II. Pediatric formulas

Nutritionally complete, intact protein products formulated to meet the nutrient needs of toddlers and children (>1 year). May be used as oral supplements or complete enteral nutrition. Not intended for use in infants

<table>
<thead>
<tr>
<th>Brand Name (Manufacturer)</th>
<th>kcal&lt;sup&gt;1&lt;/sup&gt;</th>
<th>kcal to meet RDI&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Osm</th>
<th>Carbs</th>
<th>Protein</th>
<th>Fat</th>
<th>NPCal:N2</th>
<th>%kcal</th>
<th>w6:w3</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pediasure Enteral™ (Ross)*</td>
<td>100</td>
<td>1000</td>
<td>535</td>
<td>13</td>
<td>53</td>
<td>3</td>
<td>12</td>
<td>180:1</td>
<td>4</td>
<td>35</td>
</tr>
<tr>
<td>Pediatric Vivonex™ (Nestlé)</td>
<td>80</td>
<td>1000</td>
<td>360</td>
<td>13</td>
<td>63</td>
<td>2.4</td>
<td>12</td>
<td>200:1</td>
<td>2.4</td>
<td>25</td>
</tr>
</tbody>
</table>

*Similar products include Nutren Junior™ (Nestlé)

III. Modular products: These are incomplete products intended as supplements to tube feeding formulas for specific purposes

Carbohydrates: Polycose<sup>™</sup> Powder (Abbott): Glucose polymers, 95 gr (380 kcal)/100 gr powder.

Lipids:
1. MCT Oil™ (Nestlé): Medium-chain triglycerides from coconut oil, 85 gr MCT (767 kcal)/100 mL oil.
2. Microlipid™ (Nestlé): Safflower oil, 50.7 g (456 kcal)/100 mL.

C. Protein:
1. ProPass™ Protein Supplement (Hormel): Powdered whey protein concentrate. One scoop contains 6 g protein, 0.5 g fat.
2. Beneprotein™ (Nestlé): Whey protein supplement. One scoop or packet (7 g) contains 6 g whey protein.

D. Arginine and glutamine supplements

Enterex Glutapac™ (Victus): 10 g glutamine/pkt

Symp-X™ (Baxter): Glutamina, 10 g/pkt

Glutasolve™ (Nestlé): 90 kcal, 7 g CHO 15 g glutamine

Arginaid™ (Nestlé) 35 kcal, 4 g CHO, 4.5 g arginine, Vitamins C & E

Juven™ (Abbott): powder contains 66 kcal, 4 g CHO, 7 g each arginine and glutamine

1Abbreviations: ‘mL’ = millilitres of formula to contain; ‘kcal to meet RDI’ = Number of calories required to deliver 100 % of recommended dietary intake of micronutrients (includes micronutrients not listed); ‘Osm’ = osmolarity, mOsm/kg H<sub>2</sub>O; ‘g’ = grams; ‘%kcal’ %age of total calories; ‘NPCal:N2’ = ratio of non-protein calories to nitrogen; ‘w6:w3’ = ratio of w6 to w3 fatty acids. Information from manufacturers’ websites as of April, 2010.

2Information from manufacturers’ websites as of April, 2010. The composition of formulas marketed in different countries may be different. All values listed here are for US products.

associated with significantly better immune function, less bacteremia, and increased survival<sup>56</sup> than in a group who received 17% protein diets. As burn size increases, progressively more protein is required for positive nitrogen balance.<sup>57,58</sup>

Current recommendations call for 1.5–2.0 g/kg/day of protein for adult burn patients, and up to 3.0 g/kg/day in children.<sup>59,60</sup> With provision of sufficient non-protein calories, this should result in a calorie:nitrogen ratio of 100:1 or less, typical of the ‘stress’ formulas listed in Table 29.2. Measurement of nitrogen balance and visceral protein markers may be helpful in assessing the adequacy of nutritional support (see below).

Glutamine

Several amino acids have unique roles in energy delivery following injury. Alanine (ALA) and glutamine (GLU) are important transport amino acids, elaborated in large quantities from skeletal muscle to supply energy to the liver and healing wounds.<sup>34</sup> GLU also serves as a primary fuel for both enterocytes and lymphocytes and is thus important in
maintaining small bowel integrity, preserving gut-associated immune function and reducing intestinal permeability following injury.\textsuperscript{54,66} Glutamine is also a precursor of glutathione, an important antioxidant, and improves elaboration of heat shock proteins which provide cellular protection following stress and trauma.\textsuperscript{61,63–65}

GLU is quickly depleted from both serum and muscle following burn injury, leading to the suggestion that GLU be considered a ‘conditionally essential’ amino acid in burns.\textsuperscript{54,66} GLU is almost entirely absent from parenteral nutrition owing to its instability in solution, which may explain some of the inferiority of TPN. GLU supplementation has been associated with some benefits when used in neutropenic cancer and other patients maintained on TPN.\textsuperscript{67,68}

In clinical trials GLU supplementation has also produced some improved outcomes in patients with cancer, AIDS, surgery, trauma, or burns.\textsuperscript{3,69} However, these benefits were not consistently seen when comparing post-operative and ICU patients, provision of ‘low-dose’ (<0.20 g/kg/day) vs ‘high dose’ (>0.20 g/kg/day) GLU, or parenteral vs enteral administration.\textsuperscript{51} Some of the best data supporting GLU supplementation come from burn patients, in whom provision of 25 g GLU/kg/day or more, given parenterally\textsuperscript{71,72} or enteraly,\textsuperscript{71,72} was associated with reduced infections, improved visceral protein levels, and reduced mortality and length of hospitalization. These effects of GLU may be relatively specific to burn injuries.\textsuperscript{73}

Supplementation of enteral nutrition with GLU for burn patients is not routinely practiced, although this is becoming more common.\textsuperscript{74} The amounts of GLU given in clinical trials are so large (0.25–0.50 g/kg/day) that this could interfere with the delivery of other amino acids, so it might be preferable to give GLU in addition to the usual quantity of protein required by burn patients.\textsuperscript{3} Obviously, many questions persist regarding the clinical utility of GLU supplementation in burn care. Further clinical trials with supplementation of this amino acid are ongoing.

Arginine

Arginine (ARG) is also important in post-burn metabolism. ARG is synthesized from GLU and stimulates T lymphocytes, enhances natural killer cell function, and stimulates synthesis of nitric oxide (NO), which is important in stimulating inflammation and resistance to infection.\textsuperscript{74–77} ARG supplementation of enteral diets has been associated with improved immune responsiveness and wound healing,\textsuperscript{78} and improved survival in burned guinea pigs.\textsuperscript{79}

Branched-chain amino acids

The branched-chain amino acids (BCAAs) leucine, isoleucine, and valine have been postulated to spare muscle catabolism by stimulating protein synthesis and serving as energy substrates. In clinical trials in trauma and ICU patients, BCAA-enriched nutrition was associated with improved nitrogen balance but had no effect on survival.\textsuperscript{80} In both animal and clinical studies in burn injury, BCAA-enriched feeding did not produce improvements in outcome, protein synthesis, or immune function,\textsuperscript{81} and are therefore not recommended for use.

‘Immune-enhancing’ diets

Even the earliest efforts to nourish burn patients sought to create an ‘ideal’ nutritional mixture by supplementing diets with eggs or milk.\textsuperscript{26} Modern efforts have focused on combining components that appear to improve immune function and wound healing. In a landmark study, Gottschlich et al.\textsuperscript{82} found that a group of severely burned children given a custom-made tube feeding containing omega-3 FFAs, ARG, histidine, and vitamins A and C had significantly fewer wound infections, shorter hospital stays, and a trend toward improved survival compared to two control groups fed commercially available tube feedings. This experience quickly led to commercial production of similar multi-ingredient ‘immune-enhancing diets’ (IEDs).

Subsequent studies of IEDs in a variety of clinical settings have produced contrary and controversial results. Some have demonstrated improvements in immunity and wound healing, and reductions in infections, multiple organ failure, or hospital stay.\textsuperscript{53,64} No effect on mortality has been documented, however, and others have not been uniformly favorable. These diets may have very different consequences in different patient groups, with improved outcomes following trauma or elective surgery,\textsuperscript{65,66} but deleterious or no effects in patients with sepsis or pneumonia.\textsuperscript{1,44,83} Much of the blame for these inconsistent results has been attributed to ARG, the exact dosing of which may influence its effects greatly, as too much could stimulate excessive NO production, exaggerate inflammation, and increase pulmonary dysfunction.\textsuperscript{87}

Little information has been obtained on the use of available IEDs in burn patients. One small study compared a highly publicized IED (Impact™) with another commercially available, high-protein stress solution (Replete™),\textsuperscript{88} and found no differences in major outcome variables. Both solutions contained significant amounts of omega-3 FFAs and significant fat calories, though they differed in their contents of vitamin A, arginine, and RNA. It should be noted that no benefit to IEDs have been found in reducing the incidence of pneumonia,\textsuperscript{81} which is a frequent and serious problem for burn patients, particularly those suffering inhalation injury. Finally, it should be remembered that the high volume of feedings required by burn patients may mean that a satisfactory dose of some immune-enhancing nutrients is delivered even with the use of conventional diets.

These experiences illustrate that our understanding of nutritional physiology is still limited and may have been hindered by the rush to create commercially viable ‘cocktails’ for clinical use before understanding the real actions (and interactions) of their components and their optimal doses. At present the use of IEDs, particularly ARG, is controversial, being specifically recommended for burn patients in one authoritative practice guideline,\textsuperscript{2} and specifically not recommended in another.\textsuperscript{3} This issue must await clarification from future well-designed and large-scale clinical trials. The emerging field of ‘pharmacornutrition,’ which stresses more specific and restricted use of nutrients, may benefit this effort.\textsuperscript{88} It is safe to say that efforts to provide adequate amounts of calories and high-quality protein remain the mainstay of successful burn nutrition, rather than an emphasis on a specific formula.
Micronutrients: vitamins and trace elements

In addition to major nutrients, the metabolism of many so-called ‘micronutrients’ – vitamins and trace elements, which are important in wound healing and immunity – is also affected by burn injury. These compounds have not been evaluated extensively in clinical studies, although depressed serum levels of some compounds have been documented following burns. A complete list of micronutrients and their functions is provided in another chapter; excellent reviews are also available. Limited data suggest that supplementation of some substances, including vitamins A, and C may be beneficial. Additional recent research has focused on disorders of bone and vitamin D metabolism, zinc, and selenium.

A recent survey found that many burn centers provide some supplementation of trace elements, though perceived indications and doses varied widely. Current reviews recommend supplementing at least the micronutrients listed above, and perhaps others. However, many commercial tube feedings contain substantial quantities of these micronutrients, which can approximate the recommendations listed by Mayes et al. The addition of a daily multivitamin tablet or liquid multivitamins to tube feedings or TPN will provide far more than DRI recommendations for most micronutrients at minimal cost and risk. It is unclear whether additional supplementation is of any value.

Formulas for enteral nutrition

Successful nutrition has been provided to burn patients with very simple concoctions of milk, eggs, and other nutrients. However, commercially prepared enteral formulas offer several advantages. They are nutritionally complete, and can be infused through small feeding tubes with minimal clogging. Most are reasonably inexpensive, though some specialized formulas can be quite costly.

Table 29.2 lists the nutrient composition of a number of popular enteral formulas. A bewildering array of products are available, including fiber-containing diets, elemental diets, inexpensive supplements, and costly specialized diets for patients with renal failure, hepatic failure, glucose intolerance, etc. Many of these products do not meet the macronutrient needs of burn patients and often limit protein while providing excess fat and carbohydrate. As an example, Table 29.3 shows the effects of either changing the volume of enteral nutrition and intravenous fluids (a major source of calories for some patients), or switching to one of the ‘diabetic’ formulas available. Clearly, the choice of formula can greatly influence both the success of nutrition and the type and magnitude of complications encountered.

Formulas for TPN

Solutions for TPN must consist of elemental components that do not require digestion. Dextrose is the main calorie source, and the high concentrations require delivery through a central venous catheter. Protein is supplied as an amino acid solution. As mentioned previously, glutamine is not a component of TPN. Calorically dense lipids can comprise a significant proportion of the calories in TPN.

The exact composition of TPN solutions can be tailored to individual patient needs. ‘Standard’ TPN solution (70% dextrose, 15% amino acids, and 20% lipid emulsion) may simplify ordering but often require customizing to meet the needs of burn patients, who are likely to require increased amounts of protein and possibly fewer lipid calories. Electrolytes, vitamins, and minerals can be custom ordered, or standard ‘packages’ can be used. Medications such as insulin and H blockers can be added as well. Box 29.1 is an example of a protocol for ordering and administering TPN used for a typical burn patient in our unit.
Nutritional support of the burned patient

Box 29.1 Regimen for instituting total parenteral nutrition, adapted from ‘Adult parenteral nutrition orders’, University of Utah

**Step One: Calculated Required Energy and Protein Needs:**
Example: 25 year-old man, 80 kg in weight. Body surface area = 2.2 m².
1. Indirect calorimetry indicates energy expenditure of 2400 kcal/24 h. To account for fluctuations in energy expenditure, increase measured value by 20% (480 kcal); total = 2880 non-protein kcal/day.
2. Estimate protein requirements at 2.0 g/kg/day = 160 g protein

**Step Two: Order TPN Solution**
1. Carbohydrates: Carbohydrates are supplied as 70% dextrose (D70), which contains 2.4 kcal/mL. To give 75% of non-protein calories as dextrose, calculate:
   \[
   \text{total kcal × 0.75 (calories as dextrose)} + 2.4 \text{ kcal/mL} \times L = 900 \text{ mL D70}
   \]
2. Fat: The remainder of non-protein calories will be given as lipid emulsion. This is commonly available as 10% (1.0 kcal/mL) or 20% (2.0 kcal/mL) solution. To give 25% of non-protein calories as lipid, calculate:
   \[
   \text{total kcal × 0.25 (calories as lipid)} + 2.0 \text{ kcal/mL} \times L = 360 \text{ mL 20% lipid emulsion}
   \]
3. Protein: Protein is supplied as crystalline amino acid solutions at a concentration of 10% (0.1 g/mL), or 15% (0.15 g/mL). To give 160 g of protein, calculate:
   \[
   160 \text{ g protein} + 0.15 \text{ g/mL} = 1067 \text{ mL 15% amino acid solution}
   \]
4. Total volume = 900 mL D70 + 360 mL lipids + 1067 mL amino acids = 2327 mL.
5. Add electrolytes: These can be ordered as customized additions in any quantity, but a standard electrolyte ‘package’ contains (per liter of TPN):
   - Sodium chloride: 35 mEq
   - Potassium phosphate: 15 mM (22 mEq potassium)
   - Magnesium sulfate: 8 mEq
   - Calcium gluconate: 5 mEq
6. Add vitamins: A standard vitamin ‘package’ contains approximately 100% of recommended dietary allowances of vitamins A, C, D, E, and B12, pyridoxine, thiamine, riboflavin, niacin, pantothenic acid, folate, and biotin.
7. Add trace elements: A standard ‘package’ contains
   - Zinc: 2.5 mg
   - Copper: 1.0 mg
   - Mn: 0.25 mg
   - Chromium: 10 mg
8. Add customized components: These often include famotidine for stress ulcer prophylaxis, and insulin for glucose intolerance.
9. Add additional water, and calculate infusion rate: If patients require additional fluid, water can be added to the TPN solution as desired. If no additional water is required, then the goal rate for infusion is 2327 mL / 24 h = 97 mL/h.

**Step Three: Protocol for Administration**
1. Begin infusion at 20 mL/h via central vein.
2. Increase rate every 4–6 hours by 10–20 mL/h until rate of 120 mL/h is achieved.

**Step Four: Begin Monitoring on Nutritional Support**
Blood glucose:
1. As infusion is initiated, measure blood glucose every 4 hours. If glucose is \( \geq 120 \) mg/dL, begin administration of exogenous insulin by ‘sliding scale’, or continuous drip. Consider oral hypoglycemic agents.
2. After goal rate is achieved, measure blood glucose every 6 h.
Daily: Serum electrolytes, Blood urea nitrogen, creatinine.
Twice weekly:
A. Hepatic enzymes (lactate dehydrogenase, alkaline phosphatase, total bilirubin, transaminases)
B. 24-h urine for nitrogen balance
C. Serum transferrin or prealbumin
Serum phosphorus, magnesium, and calcium

Methods of nutritional support

**Route of nutrition: parenteral vs enteral**
In the 1960s and 1970s, TPN was widely advocated for burn patients. At the peak of TPN’s popularity, it was estimated that over 500,000 patients were treated yearly, at a cost of over $3bn. This included burn patients, for whom TPN was widely advocated.

TPN has now been largely replaced by enteral nutrition (EN), for both theoretical and practical reasons. Enteral nutrition directly nourishes the bowel mucosa; some nutrients (e.g., glutamine) may be particularly important in this regard. The presence of even small amounts of nutrients within the bowel lumen stimulates the function of intestinal
cells, maintains microvillous architecture and normal mucosal function, preserves blood supply to the intestine, and may reduce bacterial translocation and preserve gut-associated immune function. EN provides ‘first-pass’ delivery of nutrients to the liver, which reduces hyperglycemia and hyperosmolarity. In contrast, TPN appears to be associated with increased secretion of tumor necrosis factor (TNF) and other proinflammatory mediators. Lipids added to TPN may enhance inflammation as well, particularly in pulmonary dysfunction. In addition, fatty infiltration of the liver is common following burn injury; this may be particularly severe in association with TPN.

In clinical trials, early and aggressive EN has been associated with fewer infectious complications in trauma and ICU patients. In burn patients, TPN supplementation of enteral nutrition has been associated with substantially increased mortality. This is in contrast to a recent meta-analysis which showed no increased mortality associated with TPN in ICU patients. These differences may be due to unique metabolic characteristics in burn patients, or may simply reflect the restriction of TPN use in burn units to the sickest patients.

In addition to other problems, TPN solutions are far more expensive than enteral formulas, require more expensive delivery systems, and mandate more frequent monitoring of glucose and other blood chemistries. For all these reasons, enteral nutrition should be considered the route of choice for the nutritional support of all burn patients with functioning (or even partially functioning) gastrointestinal tracts.

**Early enteral feeding**

A 1984 study in guinea pigs suggested that provision of EN immediately following burn injury reduced hypermetabolism almost to normal. Subsequent studies have confirmed this finding. However, it appears clear that EN can be started safely within hours of injury in patients of all ages, reducing the accumulated ‘calorie deficit’ and improving overall nutrition. Duodenal or jejunal feedings can be continued even during surgical procedures without increased risk of aspiration, which helps maintain caloric goals and may also reduce infection. Tube feedings should therefore be started as soon as practically possible following injury, and certainly within 48 hours. To enhance success, begin feedings at a rate of 20–40 mL/h (as little as 5 mL/h in infants) and try to reach the therapeutic goal rate within 24 hours.

However, successful implementation of tube feedings is often difficult. Nausea, diarrhea, glucose intolerance and problems with tube placement and maintenance often compromise the success of early enteral nutrition. Some authorities have recommended supplementing enteral nutrition with TPN early on, until goal rates of tube feedings can be achieved. This remains a controversial issue, particularly in light of recent evidence that TPN supplementation of EN in burns may be associated with increased mortality.

**Gastric vs intestinal feeding**

Both gastric and post-pyloric intestinal feedings are widely used for delivery of EN; both have advantages and disadvantages. Gastric feeding can be instituted through large-diameter tubes placed blindly, which simplifies early feeding and minimizes clogging. Blenderized diets and intermittent bolus feedings can also be given into the stomach, reducing expense and the inconvenience of infusion pumps. A major disadvantage is the tendency of the stomach to develop ileus, both immediately post burn and in conjunction with sepsis or stress.

Intestinal feeding requires placement of a tube beyond the pylorus. Small enteric tubes have been placed inadvertently into the lung, with catastrophic consequences. For that reason, many facilities prefer fluoroscopic or endoscopic tube placement, which is safer but inconvenient. Nasoenteric tubes are small and comfortable, but clog rather easily and often dislodge and migrate into the stomach. No clear data have documented a reduced rate of aspiration using nasoenteric feeds. Any regimen of EN, however, requires careful ongoing monitoring for intolerance and pulmonary complications.

Many clinicians employ ‘pro-motility’ agents such as metoclopramide, erythromycin, or cisapride in conjunction with enteral nutrition. These agents – particularly erythromycin – may help enteral tubes pass spontaneously into the small intestine and can also reduce gastric ileus and feeding intolerance.

**Developing a program of nutritional support**

Nutritional support can be provided most effectively by developing a comprehensive protocol, which defines responsibilities for all members of the burn team. It has been repeatedly shown in ICU populations that adherence to such protocols increases both the success of nutrition and overall patient outcomes.

Such a regimen begins by defining the level of support required, which differs greatly for individual patients. For every patient the goal is to provide adequate nutrition using the simplest and most physiologic method. All patients need frequent reassessment to ensure that they are achieving nutritional goals, to detect complications, and to determine whether support can be simplified or if escalation is required. A simple algorithm for determining the level of nutritional support is shown in Figure 29.3. Applying such an algorithm proactively may prevent problems developing.

Patients with relatively limited injuries (≤20–25% TBSA) who are not intubated will generally be able to eat, though it may take several days until pain, initial ileus and nausea can be controlled. In this circumstance, a few days of inadequate nutrition can be permitted if it appears that the patient will soon be able to eat. Patients who fail to progress with oral intake, who require major surgery, or who develop complications will benefit from the early institution of more formal nutritional support. Early initiation of enteral feeds may actually prevent the development of ileus.

Patients who require TPN should be reassessed frequently for evidence of GI function; even if patients cannot tolerate all their nutrition enterally, they should be given low-rate ‘trophic’ feeds if possible. These help preserve small bowel integrity and function and facilitate gradual transition to EN (and decreasing TPN) as the bowel recovers. Similarly, some oral intake should be permitted when possible in patients given EN. Oral intake – even sips of liquid – is of great
Nutritional support of the burned patient

**Infants/children**

Adult enteral products provide high renal solute loads, large protein intakes, and doses of vitamins and minerals that are inappropriate for children. Infants require relatively high fluid volumes and should not receive concentrated formulas, so infant formulas generally provide no more than 20 or 24 kcal/oz (0.66–0.8 kcal/mL). Some popular pediatric enteral formulas are compared in Table 29.2.

Oral intake in small children is often difficult due to pain, anxiety and an inability to comprehend the need for adequate intake. Many prefer drinking to eating, and offering high calorie supplements can be helpful. However, early initiation of enteral nutritional support can often meet nutrient needs and reduce the stress associated with attempting to ‘push’ oral intake.

**The elderly**

Elderly patients are more likely to have pre-existing malnutrition than other burn patients. Diabetes and its complications, heart disease, poor dentition, etc., can all affect nutritional status and complicate the provision of adequate nutrition. Basal metabolic rate decreases with age and many elderly patients may not manifest a post-burn hypermetabolic response. Use of indirect calorimetry will help avoid overfeeding, glucose intolerance, and azotemia. Many high-protein ‘stress’ products provide excessive protein for the elderly, and so using a standard product may be more appropriate. Examples of such products are included in Table 29.2. The clinician also needs to evaluate the need for restrictions (e.g., potassium, fat) in these patients.

**The obese burn patient**

Obesity is epidemic in the United States and is rapidly increasing in other developed nations as well. As much as two-thirds of the US population is overweight and one-third is obese, as defined by BMI criteria. Excessive weight is clearly associated with a number of major health problems, including diabetes, cardiovascular disease, and arthritis, and increases all-cause mortality in the general population.

Some studies in surgical and ICU patients have demonstrated the ‘obesity paradox’ of reduced mortality for overweight and moderately obese individuals despite an increase in infections and length of hospital stay (LOS). Less information is available in burn patients. One early study documented increased respiratory and cardiovascular complications including pulmonary emboli among patients who would today be categorized as morbidly obese. A recent review from the National Burn Repository (NBR) found increased mortality among patients listed as obese. However, the term was not clearly defined, and the incidence of obesity documented (less than 1%), was far too low to represent its real occurrence. In two pediatric reviews, obese burned children had longer hospital LOS as well as greater requirements for both ventilatory support and exogenous insulin.

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**Figure 29.3** An algorithm for determining the route of nutritional support for burn patients (see text). On admission, patients may require 3–4 days to tolerate adequate oral intake. Patients who require longer should be considered for nutritional support. Patients should be given some enteral nutrition even if they still require TPN for the balance of nutritional support.
The physiologic consequences of obesity are particularly relevant to burn patients. It is now recognized that fat is not inert, but plays an active role in metabolic regulation. The inflammatory hormone leptin, secreted by adipose tissue, helps direct the CNS to increase or decrease food intake. Leptin levels are reduced following burn injury in humans, but its role in hypermetabolism remains unclear. Obesity is also associated with increased secretion of pro-inflammatory cytokines IL-6, C-Reactive Protein (CRP), and TNF-α, and anti-inflammatory adipokines.

This hormonal environment establishes obesity as a state of chronic inflammation similar to low-grade SIRS, and contributes to the ‘metabolic syndrome’ of insulin resistance, diabetes, and cardiovascular disease; this constellation of clinical disorders is now recognized as a major worldwide health problem. When injured, these already-primed individuals may react with exaggerated inflammation, higher metabolic rates, more rapid and severe muscle wasting and severe insulin resistance that further drives the use of protein and carbohydrate for energy. Thus even though obese individuals have greater fat-free mass than nonobese patients, burned obese patients lose muscle mass more quickly, while preserving fat mass.

Obesity presents several practical problems in providing nutrition in burn care. Obesity complicates assessment of underlying nutritional status. Many obese patients are deconditioned and badly nourished, while others fulfill criteria for ‘fit but fat’. Ongoing energy requirements are also hard to estimate. Using actual body weight in predictive formulas overestimates energy needs, while using ideal body weight underestimates them. Specific formulas for obesity have been proposed, but none have been validated in large reviews. As a result, the use of indirect calorimetry is particularly helpful in obese patients.

Hypocaloric feeding: The nutritional challenges of obesity have led to use of low-calorie, high-protein diets aimed at maintaining lean body mass while facilitating weight loss and blood sugar control. In limited trials in ICU patients, hypocaloric nutrition given enterally or parenterally appeared to be as effective as eucaloric nutrition in maintaining nitrogen balance and clinical outcomes. In other reviews patients who received significantly fewer calories than targeted demonstrated reduced mortality, ventilator dependence, and LOS.

Hypocaloric feedings could have a number of theoretical advantages in feeding obese burn victims. First, accurate estimates of energy expenditure are unnecessary. Because many nutritional regimens in burn patients often fail to achieve caloric goals, an intentionally hypocaloric regimen would be more likely to succeed. By limiting intake, hypocaloric regimens might reduce complications of hepatic steatosis, fluid overload, diarrhea, and feeding intolerance. Importantly, such a program could also greatly reduce the practical problems of blood sugar control in these patients.

Highly influential guidelines have recommended hypocaloric regimens for nutritional support of obese, critically ill patients. However, this enthusiasm may well be premature. In a review of clinical trials, Dickerson concluded that although hypocaloric feedings appear promising, there are too few data, especially on long-term use, to establish this regimen as a standard of care. In another review, authors agreed that far too few data existed to obviate concerns over prolonged starvation and accumulated ‘energy debt,’ which could accompany hypocaloric feeding in acutely ill patients. This would be of particular concern in burn patients, whose hypermetabolism is both more prolonged and more serious than in other patient groups. For all these reasons, hypocaloric nutrition cannot be recommended for burn patients until its safety can be confirmed in carefully controlled clinical trials.

**Monitoring and complications**

**Monitoring of nutritional support**

Any program of comprehensive nutritional support must include ongoing monitoring of its adequacy and success. As mentioned previously, the physiologic changes that accompany burns render many monitors of nutrition difficult or impossible to interpret. In addition, most of these markers do not correlate highly with outcomes. Careful assessment of clinical status, including vital signs, functional improvement, and wound healing, remains the most important form of nutritional monitoring. A number of parameters are most useful in identifying and monitoring trends (as opposed to point estimates) in nutritional status.

**Body weight**

Change in body weight is an important monitor of nutritional status for the general population, and significant weight loss – particularly rapid and unplanned – is a powerful predictor of mortality. However, weight is often misleading in burn patients. Initial fluid resuscitation routinely adds 10–20 kg to a patient’s weight, and much greater increases are common. Theoretically, this fluid will dissipate with diuresis, but the time course for this is unpredictable, particularly if resuscitation volume is high. Additional fluid shifts which accompany infections, ventilator support, hypoproteinemia, and elevations in aldosterone and anti-diuretic hormone lead to wide fluctuations in weight that have little to do with nutritional status. Even weeks after injury, patients may have increased total body water and have almost always lost more lean body mass than is apparent from weight alone. And once lost, muscle mass is difficult to replace. In recent studies, intentionally overfeeding ICU and burn patients to exceed measured energy expenditure did not reduce ongoing muscle breakdown: increased caloric intake resulted only in the accumulation of body fat.

In following weights, try to recognize long-term trends more than daily variations, and continue monitoring during the often prolonged rehabilitation phase.

**Nitrogen balance**

Providing sufficient protein intake is a major goal of nutritional support. Because patients differ widely in their protein requirements, an ongoing monitor of this parameter is desirable. In addition to serum protein measurements (described below), a widely used test is the assessment of nitrogen balance. Measurements should be obtained at least weekly and require accurate collections of urine for determination.
of urea nitrogen (UUN) along with concomitant recording of nitrogen intake; 24-hour collections are often used, though shorter times can also provide accurate data.\textsuperscript{135} Nitrogen balance (N\textsubscript{2} bal) can then be calculated by formulas such as the following:\textsuperscript{159}

\[ N_2\text{ bal} = N_2 I - [1.25 \times (UUN + 4)] \]

where \( N_2 I = 24\)-hour nitrogen intake.

This formula contains two constants which can introduce significant error to calculations. First, UUN is increased by 2–4 g/dL (depending on patient age) to approximate total urinary nitrogen (TUN). However, TUN may exceed this value in burn patients, leading to underestimation of nitrogen losses. The formula also multiplies estimated TUN by 1.25, to account for significant loss of protein-rich exudates from burn wounds. Some formulas do not include this correction and actual burn wound losses can exceed these estimates, again leading to overly optimistic estimates of the adequacy of protein intake. Thus these formulas provide only an approximation of actual nitrogen balance.

Attainment of nitrogen balance may not always be possible, especially in the absence of exercise. Inactivity causes muscle wasting and increased nitrogen excretion even in healthy people.\textsuperscript{160} In the early post-burn period patients are often bedridden, sedated, and/or chemically paralyzed; in this setting, increasing protein intake only results in increased nitrogen excretion. This emphasizes the importance of a team-based protocol in which nutritional and physical therapy are both provided to maintain muscle mass.

**Serum proteins**

Burn injury shifts metabolic pathways away from maintenance of those visceral proteins often used as nutritional markers.\textsuperscript{162} Serum albumin, an important indicator of chronic nutritional status, is of much less value in assessing acute changes. In burn patients, serum albumin levels are depressed both acutely and chronically; even successful nutrition will not increase albumin levels for long periods. Administration of supplemental albumin to improve colloid oncotic pressure and control edema has not improved clinical or nutritional outcomes, though it may improve laboratory values temporarily.\textsuperscript{163,164}

Some other ‘acute-phase’ proteins have been advocated as more useful markers of nutrition. Prealbumin (or transthyretin) has a short half-life, making it theoretically more responsive to nutritional changes.\textsuperscript{165} However, prealbumin levels also fall quickly after injury and rebound slowly. Levels may correlate with susceptibility to infection but may not reflect ongoing nutritional status.\textsuperscript{59,165} Serum transferrin, retinol-binding protein and others have also been used, but their clinical usefulness appears equally limited,\textsuperscript{36,102,166} and their measurement may be expensive or not routinely available. Protein markers, if used at all, should be interpreted in the context of patients’ clinical condition and, like body weight, evaluated serially to indicate trends.

**Other parameters**

Abnormal immune function and increased susceptibility to infection are major consequences of malnutrition. In the past, markers of immune competence have been used in nutritional assessment, including total lymphocyte count\textsuperscript{92} and measurement of delayed-type hypersensitivity (DTH) to dermal antigens.\textsuperscript{167,168} These markers have not proved very useful in burn patients. Acute thermal injury is itself profoundly immunosuppressive; anergy can also be produced by infection, old age, or other complicating factors, and does not itself constitute evidence of inadequate nutrition.

There are a few parameters that should be followed routinely in all patients receiving nutritional support. Burn injury produces accelerated evaporative water losses, so hydration status and serum electrolytes, including phosphorus, magnesium, and calcium, should be monitored closely. Liver function abnormalities can result from overfeeding but can also indicate other serious conditions that complicate burn treatment, including hepatitis and acalculous cholecystitis. The large protein loads required by burn patients result in increased urinary excretion of nitrogenous wastes and predispose to elevations of blood urea nitrogen, particularly in the elderly. Table 29.4 illustrates a protocol for administration of TPN to a burn patient, including the recommended monitoring of nutritional status.

Some new, technically advanced methods are now available for nutritional monitoring as well. Bioimpedance analysis (BIA) measures the body’s resistance to the passage of electrical currents; from this information total body water and the body’s fat-free cell mass can be calculated.\textsuperscript{160} Dual X-ray absorptiometry (‘DEXA’) scanning measures precise absorption of radiation by various tissues; it has been used in clinical studies to measure bone density as well as fat-free mass.\textsuperscript{170} Both of these techniques are currently useful primarily in research, but may be used more widely in clinical care in the future.

As this information suggests, no single parameter is either universally applicable or reliable for nutritional monitoring of burn patients. A survey of nutrition practices in 46 burn centers\textsuperscript{272} indicated that the most commonly used parameters were body weight (100% of centers), serum albumin (93%), nitrogen balance (70%), transferrin (41%), and prealbumin (26%). In establishing a nutrition protocol, it remains essential to follow clinical course and wound healing, and it is reasonable to monitor body weight and one or two indices of protein status, such as nitrogen balance, transferrin, or prealbumin. Other tests probably do not add much extra information and can be reserved for research studies.

**Complications of nutritional support**

Almost any disorder of homeostasis can complicate nutritional support. Significant complications can be classified as metabolic and mechanical. A number of serious metabolic complications are listed in Table 29.4. These can occur with either enteral or parenteral nutrition, though most disorders of glucose and electrolyte homeostasis are both more common and more severe with TPN.

**Overfeeding**

As noted previously, it can be difficult both to estimate the nutrition needed by burn patients and to deliver those nutrients successfully. Nutrition is often inadequate in the early post-burn period, a time when ileus, nausea and
**Table 29.4 Metabolic complications of nutritional support (particularly TPN)**

<table>
<thead>
<tr>
<th>Complication</th>
<th>Description/cause</th>
<th>Frequency</th>
<th>Severity</th>
<th>Diagnosis/treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Complications related to overfeeding</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased VCO₂</td>
<td>Overfeeding of carbohydrate calories leads to increased production of CO₂ and elevation of the Respiratory Quotient. This can complicate ventilator management and weaning in patients with significant pulmonary dysfunction.</td>
<td>Uncommon</td>
<td>Moderate</td>
<td>Suspect in patients who are having difficulty with ventilator weaning; confirm with indirect calorimetry. Reduce total calories, particularly from carbohydrates. Some ‘pulmonary’ formulas have increased fat calories, which should probably be avoided in burn patients.</td>
</tr>
<tr>
<td>Fatty liver dysfunction</td>
<td>Presents with hepatomegaly, right upper quadrant pain, and elevation of hepatic enzymes. May occur to a mild extent in many patients, but becomes worse with prolonged overfeeding and TPN, can lead to cirrhosis.</td>
<td>Common to a limited degree</td>
<td>Mild to severe</td>
<td>Avoid overfeeding, particularly of fats. Monitor liver enzymes routinely. More common and more severe in septic patients.</td>
</tr>
<tr>
<td>Azotemia</td>
<td>Feeding the large amounts of protein required by burn patients can lead to elevations in BUN and creatinine, particularly when combined with intravascular fluid depletion.</td>
<td>Common</td>
<td>Mild to severe</td>
<td>Monitor blood chemistries frequently. Avoid dehydration by providing generous free water. This may require reducing the protein load in nutritional support. Azotemia which does not respond to hydration and reduction of protein intake should raise concern for renal failure.</td>
</tr>
<tr>
<td><strong>Other Complications of Nutritional Support</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>Occurs to some degree in almost all patients on nutritional support; more common and more severe with TPN. Any nutritional support regimen should be started slowly, and monitored regularly.</td>
<td>Common</td>
<td>Moderate to very severe</td>
<td>Blood glucose MUST be monitored regularly in all patients. Insulin added to TPN solution can be helpful; patients may also require a rigorous protocol using supplemental insulin and oral hypoglycemic agents. Sustained hyperglycemia may require slowing/holding TPN until controlled.</td>
</tr>
<tr>
<td>Hyperosmolarity</td>
<td>Occurs almost exclusively with TPN. Prolonged hyperglycemia can cause dehydration, mental status changes, coma</td>
<td>Rare</td>
<td>Can be life-threatening</td>
<td>A complication of untreated hyperglycemia. Close attention to glucose control should prevent this. Treat by stopping TPN, hydrating, controlling glucose.</td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>Excessive administration of potassium; often occurs when a ‘standard’ electrolyte solution is added to TPN without considering patient-specific issues (i.e., renal failure)</td>
<td>Uncommon</td>
<td>Can be life-threatening</td>
<td>Routinely monitor potassium, especially during initiation of TPN. Occurs in association with hyperglycemia, renal dysfunction, sepsis. Severe hyperkalemia (≥ 6.0 mEq/L) causes T-wave elevation, can be fatal. This is a medical emergency, and mandates discontinuation of TPN, or change to a low-potassium enteral formula.</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>Low serum potassium can occur if electrolytes are not added to TPN. The institution of TPN causes uptake of potassium and sudden hypokalemia. This occurs along with hypophosphatemia and hypomagnesemia – the ‘refeeding’ syndrome.</td>
<td>Uncommon</td>
<td>Moderate to serious</td>
<td>Monitor potassium routinely, especially during initiation of TPN and aggressive glucose control. Can cause weakness, arrhythmias. Treat by potassium supplementation. Magnesium deficiency can contribute to hypokalemia as well.</td>
</tr>
<tr>
<td>Hyponatremia/ fluid overload</td>
<td>Occurs usually when dilute solutions are used for TPN. Can result in pulmonary failure, ascites, edema. Use of “peripheral” TPN requires large fluid loads, particularly in children, and should be avoided. Additional fluids given with antibiotics and resuscitation can compound this problem.</td>
<td>Moderately common</td>
<td>Moderate to serious</td>
<td>Monitor intake/output, serum sodium. Nutritional support in renal failure should be continued, but may require more frequent dialysis. Severe hyponatremia from any cause must be corrected gradually (≥ 0.5 mEq/L/hour) to avoid severe neurologic complications.</td>
</tr>
<tr>
<td>Hyperturmatemia/ dehydration</td>
<td>Can occur when insufficient free water is given. Burn patients may have significant requirements over and above the fluids required for TPN.</td>
<td>Moderately common</td>
<td>Moderate to serious</td>
<td>Monitor intake/output, serum sodium. Additional free water can be added to TPN or given separately. Persistent hyperglycemia causes obligatory diuresis and dehydration.</td>
</tr>
</tbody>
</table>
Table 29.4  Continued

<table>
<thead>
<tr>
<th>Complication</th>
<th>Description/cause</th>
<th>Frequency</th>
<th>Severity</th>
<th>Diagnosis/treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypermagnesemia</td>
<td>Presents with lethargy, weakness, prolongation of P-R and Q-T, AV-block</td>
<td>Rare</td>
<td>Moderate to serious</td>
<td>Usually occurs in the setting of renal failure.</td>
</tr>
<tr>
<td>Hypomagnesemia</td>
<td>Presents with peri-oral tingling, weakness, tetany, arrhythmias. Magnesium is consumed during protein synthesis, and institution of nutrition, particularly TPN, can precipitate hypomagnesemia – the ‘refeeding syndrome’. Diuretics also cause this.</td>
<td>Moderately common</td>
<td>Moderate to serious</td>
<td>Monitor magnesium routinely, especially during institution of nutritional support. May require substantial supplementation.</td>
</tr>
<tr>
<td>Hyperphosphatemia</td>
<td>Usually occurs in the setting of renal failure</td>
<td>Uncommon</td>
<td>Moderate</td>
<td>Renal dysfunction may require removal of all phosphate from TPN and use of phosphate binders, or change to a low-phosphate enteral formula.</td>
</tr>
<tr>
<td>Hypophosphatemia</td>
<td>Presents with weakness, particularly of jaw muscles, lethargy, obtundity. Often occurs early post-burn even without nutrition, but phosphorus is consumed into protein with TPN – part of the ‘refeeding syndrome’.</td>
<td>Common</td>
<td>Moderate</td>
<td>Monitor phosphorus levels routinely, especially during institution of nutrition. Patients may require frequent monitoring and supplementation.</td>
</tr>
<tr>
<td>Trace element deficiency</td>
<td>Copper deficiency can cause anemia and neutropenia; zinc deficiency causes skin lesions, hair loss, impaired immunity. Deficiencies of selenium, cobalt, manganese, and others have been described</td>
<td>Rare</td>
<td>Moderate to serious</td>
<td>Trace element deficiencies usually occur only with prolonged TPN. Standard trace element ‘packages’ contain more than enough for maintenance. Blood transfusions also contain significant amounts of copper, chromium, and some others.</td>
</tr>
<tr>
<td>Vitamin deficiency</td>
<td>A variety of vitamin deficiencies have been described, almost exclusively in patients on long-term TPN.</td>
<td>Rare</td>
<td>Moderate to serious</td>
<td>Fat-soluble vitamins (A,D,E,K), and water-soluble ‘B’ vitamins should all be included in standardized vitamin ‘packages’ for TPN supplementation. Individual vitamins can be given as well.</td>
</tr>
<tr>
<td>Essential fatty acid deficiency</td>
<td>Presents with malabsorption/diarrhea, dry skin, anemia, thrombocytopenia Hyperinsulinaemia prevents fatty acid mobilization, so deficiency can develop in as little as 10 days of TPN.</td>
<td>Rare</td>
<td>Moderate to severe</td>
<td>Use of medium-chain triglycerides (MCT’s) do not prevent this, but modern lipid solutions contain long-chain triglycerides as well. Lipid emulsion should be given at least once weekly.</td>
</tr>
</tbody>
</table>

Hyperglycemia complicate efforts to nourish patients. Aggressive nutrition in the early post-burn period can lead to unintended overfeeding, as metabolic rate declines and regimens become more successful. Some of the most important complications of nutrition are often associated with overfeeding, though they can also occur in its absence. They include:

- **Increased production of CO₂** Overfeeding carbohydrates results in fat synthesis, increased VCO₂, and elevation in RQ. This may aggravate respiratory compromise and increase difficulty in weaning from ventilatory support. This problem can be particularly severe with use of TPN. Regular monitoring of RQ with indirect calorimetry will detect this problem. Nutritional support can be tapered to match measured values, or glucose administration reduced by giving more fat calories, or both. If possible, switching patients on TPN to enteral nutrition may be helpful, though overfeeding of enteral nutrition can also occur.

- **Fatty liver** Overfeeding carbohydrates or fat leads to deposition of fat in the liver parenchyma. Some degree of hepatic enzyme elevation is common in burn patients, and this may also be more pronounced with TPN. Enzymes should be monitored regularly and feeding evaluated carefully if enzymes become elevated above 2–3 times normal. Pronounced elevations can suggest other disorders (hepatitis, acalculous cholecystitis, etc.), and may be unavoidably associated with sepsis.

- **Azotemia** The large amounts of protein required by burn patients can produce elevations in blood urea nitrogen (BUN), particularly if dehydration occurs. Acute renal failure is one of the most dreaded complications of sepsis, with a persistently high mortality rate. Fluid intake, urine output, and blood chemistries should be monitored frequently in burn patients who require nutritional support. An increase in BUN >30% above baseline may indicate relative dehydration or overfeeding of protein, particularly if nitrogen balance is positive; reduce the amount of protein being given. Even in established renal failure, patients continue to require large amounts of protein. Excessive protein restriction should be avoided, even if doing so commits the patient to hemodialysis.
• **Hyperglycemia**

Hyperglycemia is extremely common following critical illness. Approximately 10–20% of patients admitted to ICUs have pre-existing diabetes. Far more important, however, is that up to 90% of all ICU patients develop elevated blood glucose values during their hospital stay.\(^{173}\) In burn patients, insulin’s effects are overwhelmed by catabolic hormones, causing relative insulin resistance and hyperglycemia which can be both profound and sustained – the ‘diabetes of injury.’ Prolonged elevations in blood sugar are clearly associated with immune deficiency and increased susceptibility to infection; this may also be true for acute hyperglycemia;\(^{175}\) and, as infection exaggerates glucose intolerance, infection and hyperglycemia often potentiate each other.

Recent evidence has emphasized the value of maintaining glucose levels as close to normal as possible. In a landmark study, surgical ICU patients randomized to a regimen of ‘intensive’ glucose control (maintaining glucose levels at 80–110 mg/dL), compared to more traditional control (180–200 mg/dL) had substantial reductions in multiple organ failure, infection, renal failure, length of stay, and mortality.\(^{173}\) Additional evidence suggests that insulin may itself be beneficial by reducing circulating levels of C-reactive protein and other proinflammatory compounds,\(^{177,178}\) which may explain some of the benefits shown in these studies.

These findings have contributed to widely accepted recommendations for very rigorous glucose control in ICU populations.\(^{177}\) However, other recent large studies have found that intensive insulin therapy may be associated with increased mortality and an unacceptably high incidence of hypoglycemia.\(^{180}\) Thus, the optimal target level for blood sugar has not been defined. Current recommendations are for ‘moderately strict’ glucose control (target levels 110–150 mg/dL) which appears to offer many of the benefits of intensive therapy while minimizing risks.\(^{4}\)

In response to these recommendations, many units have adopted comprehensive protocols for intensive monitoring and treatment of blood sugar values. Effective glucose control often requires substantial insulin doses, meticulous monitoring, and significant nursing time. Hyperglycemia is both more common and more severe with TPN than with EN, and this alone constitutes a powerful argument for avoiding parenteral nutrition. However, hypoglycemia can also occur frequently, particularly if insulin regimens are not followed carefully. At the University of Utah we have developed a uniform protocol for glucose control which is standardized throughout all adult ICUs; this prevents many potential errors in insulin administration when nurses ‘float’ or house staff ‘cross-cover’ unfamiliar patients. Our protocol begins with use of a ‘sliding scale’ for subcutaneous administration of insulin in patients who are hyperglycemic. If this fails to reduce blood sugar, a regimen of continuous IV insulin (‘insulin drip’) is begun. These protocols are illustrated in Figure 29.4. Similar protocols have been developed in many burn care facilities.

In addition to insulin protocols, reassessing patients’ caloric needs and reducing intake as their clinical status changes is an important step in managing hyperglycemia. A number of other adjuncts can contribute to effective blood sugar maintenance, including controlling infections, increasing patient activity, and restricting oral intake of sweets. Oral hypoglycemic agents and anabolic agents may ultimately prove to have major benefit in this effort.\(^{181}\)

• **Other metabolic complications**

A number of other common metabolic complications are summarized in Table 29.4. Both deficiencies and excesses of serum electrolytes are common, and often associated with fluid balance. Significant deficiencies of vitamins or essential fatty acids are very rare, and usually found only in patients treated exclusively with TPN for long periods.

### Complications of enteral nutrition

In addition to the metabolic complications listed in Table 29.4, a number of other complications can occur, specifically with the use of enteral nutrition. Mechanical complications include misplaced feeding tubes, gastric distension, nausea, and aspiration. All tube placements should be verified prior to use, and clinicians must monitor gastrointestinal function frequently. Surgically placed gastrostomy or jejunostomy tubes eliminate problems with tube migration but are associated with (generally low) risks of dislodgement, leakage, and bowel perforation. Some units have added blue dye to tube feeds in an effort to detect aspiration more efficiently. However, the low specificity and sensitivity of this method of detecting aspiration, coupled with reports of dye-associated mortality, have led the FDA to recommend eliminating blue dye for this purpose.\(^{182}\)

### Bowel necrosis and perforation

Several reports have documented bowel necrosis and perforation as a rare complication in the critically ill, including burn patients.\(^{183,184}\) It is likely that continued administration of tube feeding in the face of decreased bowel motility causes distension, interfering with intestinal blood supply. Bacterial overgrowth of stagnant tube feedings and administration of narcotics and antidiarrheal agents also contribute to this complication.\(^{99}\) Fever, leukocytosis, tachycardia, and abdominal distension may precede frank peritonitis. Abdominal CT scanning can confirm perforation, which mandates laparotomy and usually intestinal resection. Mortality rates approximate 50%.\(^{184}\)

### Diarrhea

Tube feedings are frequently blamed for diarrhea, which can range from a minor problem to a major source of patient discomfort, fluid and electrolyte imbalance, and morbidity. Often the cause is multifactorial.\(^{186}\) The high glucose loads of hypertonic tube feedings may contribute to diarrhea, although diluting feedings has generally not proved helpful in treatment. Enteral medications, including antacids, phosphates, antibiotics, and others, also contribute to diarrhea. Infectious causes include cytomegalovirus infection and...
Nutritional support of the burned patient

**Initial Hyperglycemia Management Guidelines**

*Burn Intensive Care*

*University of Utah*

### Start Insulin Protocol

- Any BG >250

### Start Insulin Drip Protocol

- 3 Consecutive BG >120
  - BG continues to be >120 or pt transferring out of critical care unit
  - OR
  - BG between 60–120 x 48 hours

**Consider:**

1. Home insulin regimen
2. Oral diabetic medications
3. Long acting insulin
4. D/C protocol and order another sliding scale
5. Continue the insulin drip

### Glucose level (mg/dL) | IV Regular insulin sliding scale
--- | ---
< 60 | "Hypoglycemia protocol & call HO"
60–120 | 0
121–150 | 4 units
151–180 | 7 units
181–210 | 10 units
211–250 | 13 units
> 250 | Start Drip Protocol

### Hypoglycemia Protocol:

- If BG < 60 mg/dL, give 1 amp (50 mL) D50 IV and repeat every 30 minutes until BG > 60. Then resume the protocol as instructed above.

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**Figure 29.4 Hypoglycemia Management Guidelines, Burn Intensive Care Unit, University of Utah. (a), Addressograph.**

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*Clostridium difficile.* A prospective study found an association between the concentration of fat in tube feedings and the incidence of diarrhea; diarrhea was reduced in a group of children fed a low-fat ‘immune-enhancing diet.’ Because the gut’s tolerance of tube feedings is limited, diarrhea is increased with overfeeding and can often be controlled by reducing infusion rate.

A variety of compounds have been suggested for treatment of diarrhea, including opiates (Imodium, Lomotil, Paregoric, etc.), bulk agents (Metamucil), fiber-containing tube feedings, and others. Fiber may help prevent bacterial overgrowth and stasis, but use of these compounds has also been blamed for intestinal stasis and bowel necrosis. In addition, fiber-containing feedings sometimes clog small-diameter tubes. In our experience, attempts to control diarrhea with medications are frequently either ineffective or lead to constipation and distension. Infectious diarrhea may be worsened by slowing intestinal transit. Most diarrhea is self-limited and does not require pharmacologic therapy. Options for management include altering the tube formula, stopping enteral medications, reducing the infusion rate, or simply waiting a day or two. It may be necessary to withhold feedings temporarily to permit refractory diarrhea to resolve.

**Complications of parenteral nutrition**

Many complications of TPN are both more common and potentially more severe than those of enteral nutrition. Technical complications of line placement for TPN can be life-threatening, including pneumothorax, hemothorax, pericardial tamponade, hydrothorax, catheter misplacement, hemorrhage, or air embolism. Serious infections including catheter sepsis, septic thrombophlebitis, and endocarditis are well-recognized and dreaded complications of central lines. These infections are more common when catheters are placed through cutaneous burn wounds, when they are used for TPN, and if they are used for multiple purposes (blood draws, hemodynamic monitoring, maintenance fluids, etc.). Patients should be evaluated daily for the ongoing necessity for central venous catheters, and lines should be removed as soon as possible.
Metabolic complications of TPN can be both severe and difficult to treat. Because TPN often represents the only fluid and electrolyte therapy given to patients, the body’s ability to compensate for deficiencies/excesses is severely limited, and almost any disorder of electrolyte or vitamin deficiency or excess can develop. A number of other common complications of any nutritional regimen can be either more frequent or more severe when associated with TPN use as opposed to enteral nutrition. Such complications are outlined in Table 29.4.194

**Insulin drip protocol**

**Step 1: initiate insulin infusion**
- Standard insulin drip: Regular insulin 100 units/100 mL of NS
- Give IV bolus as indicated and initiate insulin drip based on the following table:

<table>
<thead>
<tr>
<th>Blood glucose</th>
<th>Regular insulin bolus</th>
<th>Regular insulin dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>121–140</td>
<td>0 units</td>
<td>1 unit/h</td>
</tr>
<tr>
<td>141–169</td>
<td>6 units</td>
<td>1 unit/h</td>
</tr>
<tr>
<td>170–249</td>
<td>8 units</td>
<td>2 units/h</td>
</tr>
<tr>
<td>250–299</td>
<td>10 units</td>
<td>3 units/h</td>
</tr>
<tr>
<td>300–399</td>
<td>10 units</td>
<td>4 units/h</td>
</tr>
<tr>
<td>400–500</td>
<td>10 units</td>
<td>5 units/h</td>
</tr>
<tr>
<td>&gt;500</td>
<td>10 units</td>
<td>6 units/h</td>
</tr>
</tbody>
</table>

**Step 2: monitoring**
- Check BG Q1h timed such that BG are checked 1 hour after drip initiation or rate change.
- If 3 consecutive BG within 80–120 with no change in therapy, reduce checks to Q2h.
- Then, if 3 consecutive BG within 80–120 with no change in therapy and insulin rate is ≤2 units/h, reduce checks to Q4h.

**Step 3: ongoing infusion**
- Make adjustments based on the following table:

<table>
<thead>
<tr>
<th>Blood glucose</th>
<th>Infusion rate adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;60</td>
<td>Hold drip. Give 1/2 amp D50. Recheck Q30min, repeat 1/2 amp D50 until BG &gt;60</td>
</tr>
<tr>
<td>60–79</td>
<td>Hold drip. Check BG in 1 hour. If BG &gt;80, restart at 1/2 rate prior to holding drip</td>
</tr>
<tr>
<td>80–120</td>
<td>No change</td>
</tr>
<tr>
<td>121–140</td>
<td>↑ rate by 0.2 unit/h</td>
</tr>
<tr>
<td>141–170</td>
<td>↑ rate by 1 unit/h</td>
</tr>
<tr>
<td>171–250</td>
<td>Give 8 units regular insulin bolus and ↑ rate by 1 unit/h</td>
</tr>
<tr>
<td>&gt;250</td>
<td>Give 10 units regular insulin bolus and ↑ rate by 1 unit/h</td>
</tr>
</tbody>
</table>

Note: If blood glucose <60 on glucometer send sample to the lab for measurement per policy

**Step 4: important nursing information**
- If BG decreases by ≥100 mg/dL from previous level, ↓ rate by 1/2 and recheck in 1 hour.
- If BG ≤150 mg/dL and subsequent level decreases by ≥30 mg/dL, ↓ rate by 1/2.
- If patient’s enteral or parenteral nutrition is discontinued, hold insulin drip and check BG Q2h and restart sliding scale on previous page.

**Step 5: discontinuation**
- After insulin drip is discontinued, check BG Q2h.
- Begin appropriate insulin sliding scale and/or oral diabetic agents (i.e. home regimen).
Conclusion

Although nutritional support following a major burn continues to evolve, several aspects are clear. Enteral nutrition with high calorie and protein solutions is generally beneficial, although there is no ‘one-size-fits-all’ solution: needs vary with each individual and change throughout the course of care. A thorough protocol involving all team members that includes ongoing and systematic assessment can tailor support to changing needs, and provide optimal care to every patient.

Further reading


Comment: Excellent article summarizing current knowledge of physiology and support of the obese, critically ill patient.


Comment: This careful review compared measured energy expenditure in 24 adult burn patients with predicted values from 46 published formulas. Authors found that NONE of these formulas were within 15% of actual measurements; formulas published before 1980 tended to over-estimate energy requirements significantly. This review underscores the difficulties of using predictive formulas for individual patients.


Comment: This sophisticated study using stable isotope kinetics demonstrated that increased muscle wasting is seen in heavier patients, more muscular patients, and those in whom surgery is delayed.


Comment: This authoritative clinical guideline summarizes current recommendations for nutritional support of critically ill patients, and includes burn patients, though specific data for burns is lacking in many areas. Specific recommendations include early enteral nutrition, indications for PN, dosing and monitoring of EN, selection of EN formulas for specific conditions, and adjunctive therapy. Authors specifically recommend hypocaloric nutrition for obese patients, and use of immune-enhancing diets for burn patients, both of which remain unproven and controversial.


Comment: Of all the components of ‘immune-enhancing’ diets, the greatest evidence can be found in support of glutamine supplementation for burn patients. This article reviews the evidence for use of this component.
References


Modulation of the hypermetabolic response after burn injury
Gerd G. Gauglitz, Celeste C. Finnerty, David N. Herndon, Felicia N. Williams, Marc G. Jeschke

Introduction

Treatment of the sequelae induced by a severe burn injury presents a substantial medical management challenge. More than 1 million burns occur in the USA annually. Even though the majority of these patients have minor injuries, nearly 20% of patients with thermal injuries are admitted for treatment at specialized burn centers each year. Advances in clinical knowledge and treatment strategies have resulted in a major decline in burn-associated deaths over the last two decades; these advances include defining the hypermetabolic response, refining reconstructive techniques, supporting inhalation injury in an aggressive manner, and improving infection control.2,3

Despite these improvements in clinical care, severe burn injuries can still lead to multi-system organ failure, with associated morbidity and mortality.4 The dramatic metabolic changes underlying severe burn injury clearly contribute to unfavorable outcomes in severely burned patients.4,5

Metabolic alterations following severe burn injury

Characterization of the response to severe burn injuries covering over 40% of the total body surface area (TBSA) has shown the association of severe hypermetabolism and inflammatory and stress responses with development of a hyperdynamic circulation, altered body temperature regulation, glycolysis, proteolysis, lipolysis, and inefficient substrate cycling.6–8 The severity, duration, and magnitude of the metabolic changes are uniquely different in burn patients than in other critically ill patients.4 Enhanced secretion of catecholamines, glucocorticoids, glucagon, and dopamine is closely associated with the formation of the acute hypermetabolic response and the associated catabolic state.6,9–16

However, the underlying mechanisms of this complex response to burn injury remain unclear. Based on current knowledge, a variety of cytokines (including tumor necrosis factor (TNF), platelet-activating factor (PAF), interleukin (IL)-1, and IL-6), endotoxin, nitric oxide, reactive oxygen species, and complement cascades participate in this multifactorial response to burn injury.17 These modulators act to increase metabolic rate and alter glucose metabolism post-burn.18

The metabolic derangements after burn injury occur in two distinct patterns that are time-dependent.19 Within 48 h post-burn, decreases in oxygen consumption, cardiac output, metabolic rate, and glucose tolerance are considered the “ebb phase.”19,20 Amplification of these metabolic changes within the first 5 days post-burn to a plateau characterizes the second phase. This so-called “flow phase” is typically characterized by the development of a hyperdynamic circulation alongside the hypermetabolic state.

Multiorgan dysfunction results from the extreme activation of the acute phase response post-burn. Immediately post-burn, patients typically have low cardiac outputs characteristic of early shock.21 However, 72–96 h post-burn, at the onset of shock, cardiac outputs are >150% of those in non-burned, healthy volunteers.22 Heart rates in burn patients approach 160% of those in non-burned, healthy patients.23 After severe burn injury, cardiac work is significantly elevated, and this lasts well into the rehabilitation phase.2,4 Myocardial oxygen consumption values far surpass values seen in trained long-distance runners, and these values remain elevated far into the rehabilitative phase.25 A profound hepatomegaly also develops after burn injury. We have shown that the liver may increase by 225% within 2 weeks of injury and remains enlarged at discharge by 200%.22

The release of insulin during this time period is increased in response to glucose load when compared with controls,24,26 and glucose levels remain significantly elevated, signifying an insulin-resistant state. 26,27 Although it was believed that these metabolic derangements resolved as the wound healed, we and others have demonstrated that the duration of this hypermetabolic response may exceed 1 year after burn trauma.6,9,16,28 Post-burn hypermetabolic alterations may last for up to 36 months and include elevations in cortisol, cytokines, and catecholamines; increased resting energy expenditures; hindered glucose metabolism; and decreased insulin sensitivity.

In healthy human beings, a postprandial increase in serum glucose levels stimulates insulin secretion from pancreatic β-cells, which in turn decreases hepatic gluconeogenesis and supports peripheral uptake of glucose into adipose tissue and skeletal muscle.29,30 Acutely after burn injury, profound derangements in energy substrate metabolism occur. The
Monocyte chemotactic protein (MCP)-1 act directly on the insulin signal transduction pathway through insulin receptor substrates, resulting in both post-burn hyperglycemia and insulin resistance. During starvation, energy is supplied by lipolysis and ketosis. Marked lean body mass (LBM) wasting occurs because the burn patient preferentially uses skeletal muscle as the major source of fuel. Nitrogen balance studies (whole body and cross leg) show persistent muscle breakdown for up to 9 months post-burn. Importantly, as the skeletal muscle accounts for the majority of insulin-stimulated, whole-body glucose uptake, significant LBM loss may contribute to post-burn insulin resistance. Flakoll and co-workers studied the relationship between muscle protein catabolism and hyperglycemia, demonstrating that a significant increase in proteolysis rates was not accompanied by changes in leucine oxidation or non-oxidative disposal. They also demonstrated that increased plasma glucose levels stimulate whole-body proteolysis during hyperinsulinemia. Catabolic losses in LBM correlate with increased morbidity and mortality: marked delays in wound healing and significant increases in infection rates accompany a loss of 10% of LBM; wound healing is impaired following a 20% loss in LBM; severe infections are associated with losses of 30% of LBM; losses of 40% or more ultimately lead to death. Acutely, the net LBM losses from muscle wasting lead to prolonged mechanical ventilation, inhibition of cough reflexes, and a delay in mobilization, markedly contributing
to increased mortality in these patients. Chronically, these net losses reduce strength and the possibility for full rehabilitation. Our patients experience an average nitrogen loss of 20–25 g/m² TBSA/day, a rate at which lethal cachexia becomes imminent in less than 1 month if left untreated. Continued post-burn loss may persist for up to 9 months. Persistent protein catabolism probably accounts for the growth delay that frequently occurs in our pediatric burn patients.54

Emphasis has therefore been placed on developing both non-pharmacologic and pharmacologic therapeutic approaches that may attenuate or reverse the hypermetabolic response post-burn.

**Non-pharmacologic approaches that ameliorate the post-burn hypermetabolic response**

**Early wound closure**

In recent years, burn wound management has changed, and the most significant advances in burn care have been the early excision of necrotic tissue and burn wound closure. This has significantly diminished basal energy requirements and in turn, improved mortality rates.55–59 Early closure of the burn wound is also associated with diminished incidence of excessive scars and joint contractures and is responsible for faster rehabilitation of these patients.55,58

Currently, powered dermatomes or hand skingraft knives are used to excise most burn wounds. Excisions via electrocautery or knife are usually used in areas where optimal function or cosmesis are important. Preservation of viable dermis may be possible in partial thickness wounds. However, excision of all necrotic and infected tissue is paramount in full-thickness burn wounds.60 Tangential, full-thickness, and fascial excision techniques are typically used. During tangential excision, the deep dermal partial thickness burn is repeatedly shaved using a knife (Goulian, Watson, or Braithwaite) or a dermatome (set to a depth of 5–10/1000 inches). In this case, the complete excision is indicated by reaching an actively bleeding wound bed.61 Full-thickness excision and serial passes are made to excise the full-thickness wound using a Watson or powered dermatome (set at 15–30/100 inch). In this case, the complete excision is indicated by reaching an actively bleeding wound bed.61 Fascial excision is the surgical removal of subcutaneous fat until the fascia is reached. It is used for burns that extend deep into the muscle or when invasive fungal infections are present. However, this technique generally leaves a permanent contour defect.62

During these operations, blood loss is a critical issue, as approximately 5% of the total blood volume is lost with the excision of every 1% of the body surface.60,62 Blood loss is a major determinant of morbidity and mortality,53 and a variety of techniques need to be used to control bleeding, including the local application of fibrin or thrombin sprays, epinephrine-soaked pads (1: 40 000), topically administered epinephrine (1: 10 000–1: 20 000) or electrocautery of blood vessels.64 Additional use of tourniquets for pre-excisional tumescence with epinephrine and saline may also help limit blood loss.65

**Nutritional support**

Patients suffering from severe burns who are treated solely with vigorous oral supplementation may lose one-quarter of their pre-admission weight within the first several weeks.66 Therefore, adequate nutrition is a critical issue for severely burned patients. A high-calorie nutritional intake is associated with diminished muscle metabolism after burn.67 However, high-calorie feeding has recently been associated with enhanced mortality rates.68 Instead of overfeeding, adequate caloric enteral intake is currently recommended.4,58 Various formulations have been established to adequately meet the energy requirements of each individual burn patient.69–71 The Curreri formula (25 kcal/kg per day plus 40 kcal/% TBSA burned per day) is normally used to calculate the caloric requirements in adult burn patients.72 The marked post-burn changes in lipid, carbohydrate, and protein metabolism determine the caloric needs of each respective patient. The optimal dietary composition includes 1–2 g/kg per day of protein, supporting the synthetic needs of the patient, thus counteracting the proteolysis occurring in muscle tissue.48 Many intensive care units (ICUs) deliver a substantial percentage of calories as fat because essential fatty acid deficiency frequently accompanies long-term nutritional supplementation.73 This approach reduces carbohydrate requirements and burn-induced glucose intolerance, and therefore, dietary compositions of 30–50% fat are now the standard of care when treating critically ill patients.48 Unfortunately, enhanced fat administration in burn patients is associated with hepatic steatosis, hypoxemia, hyperlipidemia, higher infection rates, and higher postoperative mortality rates.74–76 Hepatic triglyceride levels are enhanced, thereby limiting the utility of exogenous lipids as a post-burn energy source.72,73,77,78 Recent data obtained by our group demonstrated that patients receiving Vivonex® T.E.N., a low-fat/high carbohydrate diet, had a significantly lower incidence of hepatic steatosis than milk-fed burn patients. We also demonstrated improved survival, significantly lower incidences of sepsis, reduced length of ICU stay per % TBSA, and markedly decreased average ICU stay. We thus advocate nutritional regimens for burn patients that include reduced proportions of fat.

**Environmental support**

Burn patients may lose a significant portion of body water (approximately 4000 mL/m² burned/day) by way of evaporative or other losses from extensive burn wounds.79 Skin and core temperatures are increased by 2°C above normal to abate the resultant hypermetabolic and catabolic responses by generating a portion of energy needed to offset the losses in heat accompanying the water loss. Increasing the ambient temperature to 33°C may result in a decrease to 1.4 times the resting energy expenditure instead of 2.0 times the resting energy expenditure. This environmental modulation is a key primary treatment goal that is too often under-utilized.80

**Exercise and adjunctive measures**

Burn-wound contracture remains a morbid consequence of severe burns. It is well established that physical therapy is
paramount to preclude burn wound contractures. Progressive resistance exercises maintain or even increase LBM, facilitate the formation of muscle proteins by incorporating amino acids, enhance muscle strength, and increase walking distances by 50%.61 In burned children, progressive resistance exercise can be performed safely without any exercise-related hyperpyrexia. Judicious use of sedation, narcotics support, and supportive psychotherapy are obligatory to reduce long-term morbidity post-burn.82

Pharmacologic approaches to attenuate the metabolic alterations post-burn

Recently, particular drugs that modulate aspects of the hypermetabolic response have been studied to determine the efficacy of these agents in severely burned patients.

Recombinant human growth hormone (rhGH)

As demonstrated by our group, during the acute hospitalization period, daily intramuscular injection of rhGH (0.2 mg/kg) positively alters the acute phase response in the liver,83,84 improves muscle protein kinetics, maintains muscular growth,85,86 improves resting energy expenditure, decreases cardiac output,87 and decreases donor site healing by approximately 1.5 days.88 RhGH mediates its effects through its secondary mediator IGF-I.89 In patients receiving rhGH, serum IGF-1 and IGF-binding protein (IGFBP)-3 increase by 100% over levels seen in healthy controls.90,91 Nevertheless, serum IGF-I and IGF-binding protein (IGFBP)-3 increase by secondary mediator IGF-I, it is not surprising that, in these same patient populations, administration of equimolar amounts of recombinant human IGF-1 with its binding protein, IGFBP-3 increase by 100% over levels seen in healthy controls.90,91 Nevertheless, as demonstrated in a recent study by Takala and colleagues, in 532 non-burned critically ill patients, increased rhGH (0.10 ± 0.02 mg/kg) correlated with increased morbidity and mortality rates46 and was associated with hyperglycemia and insulin resistance.92,93 This may be reflective of an age-specific effect, however, as in severely burned children, mortality rates were not affected by either short- or long-term rhGH administration.87,94

Insulin-like growth factor (IGF)

Since the positive effects of rhGH on the post-burn hypermetabolic response are predominately mediated by the secondary mediator IGF-I, it is not surprising that, in those same patient populations, administration of equimolar amounts of recombinant human IGF-1 with its binding protein, IGFBP-3, successfully enhanced protein metabolism,95,96 attenuated muscle catabolism, restored gut mucosal integrity,97 enhanced immune function, and returned serum concentrations of constitutive proteins to non-burned levels.98–99 However, Van den Berghe et al.100 could not demonstrate any efficacy in non-burned critically ill patients when using IGF-1 alone.

Anabolic agents: oxandrolone

The use of oxandrolone, an analog of testosterone possessing only 5% of its virilizing androgenic effects, also enhances anabolism of muscle protein by improving the efficiency of protein synthesis.101 Oxandrolone decreases loss of body weight and improves healing of the donor site wound.102 In a large clinical trial by our group, oxandrolone administered at 0.1 mg/kg twice daily reduced length of the acute hospitalization, sustained LBM, and improved liver protein synthesis.103 In conclusion, administration of oxandrolone decreased the sequelae of the burn-induced hypermetabolic response and alterations in LBM and bone mineral content.104 Exercise, however, remains an essential tool for developing strength.105

Propranolol

Beta-adrenergic blockade with propranolol may represent the most efficacious anticasabolic therapy for severe burns. As shown in several studies, the administration of propranolol (titrated to decrease heart rate by 15–20%) diminishes cardiac work75 and reduces hepatic steatosis, a typical phenomenon in this particular patient population resulting from increased peripheral lipolysis and alterations in substrate handling. It is thought that reductions of hepatic fat may occur via decreased palmitate delivery, coupled with reduced hepatic uptake and diminished peripheral lipolysis.76,106 Also, administration of propranolol leads to reduced skeletal muscle catabolism and increased LBM post-burn, as demonstrated using stable isotope studies and body composition studies.23,107 Propranolol exerts its effects in the post-burn environment of heightened protein breakdown and diminished peripheral lipolysis, enhancing protein synthesis and improving post-burn morbidity.108

Overcoming burn-associated insulin resistance

Claude Bernard was the first clinician to describe the development of hyperglycemia following hemorrhagic shock in 1877. Today it is well accepted that acute diseases and injuries, including burn trauma, induce “critical illness diabetes.”109 Indeed, Gornik and colleagues reported that the risk of developing impaired glucose metabolism or type-2 diabetes increased when acute critical illness was complicated by hyperglycemia.110 Previously, the duration of the post-burn hypermetabolic response was believed to be limited; we now know that it persists for at least a full year following injury.22,49 In a large prospective clinical trial, we recently demonstrated that, in 194 severely burned children, insulin sensitivity was impaired for at least 3 years post-burn. Interestingly, hemoglobin A1c values were normal during the entire post-burn period studied. Even the insulinoenic index, an index for β-cell function, showed normal values in the patient population. The levels of insulin and C-peptide, on the other hand, remained elevated throughout the study.111

Insulin

Insulin is one of the best-characterized hormones. While glucagon, catecholamines, glucocorticoids, and thyroid hormones all increase blood glucose levels, insulin is the only hormone lowering blood glucose concentrations in the human organism. Insulin mediates metabolic effects and pathways in several important organs, including muscle and fat. It also suppresses gluconeogenesis in the liver, diminishes proteolysis, and increases fatty acid synthesis.112 The latter effects indicate that insulin may have great utility for
abrogating burn-induced hyperglycemia. This was confirmed by administering insulin to severely burned children. Donor site healing time was reduced, muscle protein synthesis increased, and muscle wasting reduced. In a recent study, insulin was also found to wield anti-inflammatory effects. Thus, administration of insulin post-burn may reduce the inflammatory state induced by burn-induced hyperglycemia by re-establishing euglycemia. In a landmark trial, Van den Berghe et al. demonstrated that mortality, infection rates, and acute renal failure were diminished following continuous intensive insulin treatment to maintain lower blood glucose levels (80 and 110 mg/dL) in critically ill surgical patients. They also found that intensive insulin therapy significantly reduced the time on mechanical ventilation. The length of stay (in the ICU and hospital) was reduced with intensive insulin therapy. Long-term rehabilitation was improved, as was the successful reintroduction of these patients into their lives during the first year.

Unfortunately, high doses of insulin may increase the risk of hypoglycemic events in critically ill patients. Brunkhorst and colleagues investigated the use of intensive insulin treatment in septic patients. In this study, intensive insulin therapy needed to be interrupted because of elevated rates of severe hypoglycemia with glucose levels below 40 mg/dL. The continued use of a hyperinsulenic euglycemic clamp was studied during the ICU stay in a separate multicenter study. A critical increase in the incidence of serious hypoglycemic events was reported. The general recommendations, however, of studies to determine the ideal glucose range in critically ill patients suggest that glucose levels under 140 or 150 mg/dL should be efficacious. Nevertheless, it is particularly challenging to maintain continuous hyperinsulenic, euglycemic clamp in the severely burned patient population due to the continuous enteral feeding of large caloric loads to maintain euglycemia. Also, since burn patients frequently require weekly operations and daily dressing changes, enteral nutrition must occasionally be stopped, which may contribute to disruption of gastrointestinal motility and an increased risk of hypoglycemia. Thus, an alternative strategy for attenuating hyperglycemia post-burn has been the exploration of other glucose-lowering drugs, such as metformin, that do not provoke hypoglycemic events as often as insulin.

Metformin

The biguanide drug, metformin, inhibits gluconeogenesis, enhances peripheral insulin sensitivity, and has recently been recommended as an alternative means to correct hyperglycemia in severely injured patients. It directly targets the two main metabolic processes that underlie injury-induced hyperglycemia. Hypoglycemic events have rarely been associated with the use of metformin. Gore et al. observed, in a small burn study, that the application of metformin is associated with diminished glucose levels, decreased endogenous glucose production, and enhanced glucose clearance. The same group also demonstrated enhanced fractional synthetic rates of muscle protein and increases in net muscle protein balance in patients receiving metformin. However, use of metformin may be associated with lactic acidosis. Thus, metformin is contraindicated in diseases associated with an impaired lactate elimination (hepatic or renal failure) or tissue hypoxia and should be handled with caution in subacute burn patients. Nevertheless, metformin is still not considered a first-line approach in subacute burn patients. More experience and follow-up studies are necessary for the evaluation of metformin as a new therapeutic intervention.

Novel therapeutic options

Other antidiabetic drugs being investigated for the treatment of post-burn hyperglycemia include glucagon-like-peptide-1 (GLP-1); peroxisome proliferator-activated receptor-γ (PPAR-γ) agonists, also known as glitazones; or a combination of various anti-diabetic drugs. Cree et al. observed that the application of fenofibrate, a PPAR-γ agonist, significantly decreased plasma glucose levels and augmented tyrosine phosphorylation of the insulin receptor and insulin receptor substrate-1 in skeletal muscle tissue when compared to the placebo treatment, indicating enhanced insulin receptor signaling.

Summary and conclusion

The physiologically exhaustive hypermetabolic derangements post-burn, which are associated with prolonged derangements in glucose metabolism and insulin sensitivity, significantly contribute to adverse outcomes in this patient population. Advances in non-pharmacologic and pharmacologic therapies have significantly improved the clinical outcome of these patients (Table 30.1). However, therapeutic strategies to abate the persistent hypermetabolism and hyperglycemia remain challenging. Early burn wound excision and grafting has been one of the greatest improvements in the last two decades, improving both morbidity and mortality. Currently, beta-adrenergic blockade using propranolol appears to be the most efficacious antitabolic therapy in burns (Fig. 30.2). RhGH, IGF-1, and oxandrolone (Table 30.1) have also been successfully used in the attenuation of
the hypermetabolic, catabolic response. While maintaining blood glucose at levels below 110 mg/dL using intensive insulin therapy has been demonstrated to diminish mortality and morbidity rates in critically ill patients, the frequently associated hypoglycemic events have created additional strategies, such as administration of metformin and PPAR-\(\gamma\) agonists in the thermally injured patient. Nonetheless, further work is needed to elucidate the ideal glucose ranges and safety of the aforementioned therapies in this unique patient population.

**Further reading**


References

92. Demling RH. Comparison of the anabolic effects and complications of human growth hormone and the testosterone


The cure of many diseases remains unknown.
(Socrates, circa 400 bc)

Introduction

Despite its common occurrence in critically ill burn patients, our understanding of the multisystem organ failure syndrome remains fragmented and incomplete. The cascade of organ dysfunctions which typify the multisystem organ failure syndrome is driven by an unregulated inflammatory state, often, but not always, associated with uncontrolled infection.1 Other potential ‘engines’ driving this cascade of organ dysfunctions are an impaired gastrointestinal barrier,2,3 the open burn wound,4 and inadequate delivery of oxygen to peripheral tissues.5 The line between organ dysfunction and failure is admittedly unclear, but a set of organ-specific definitions of failure is helpful and has been developed (Box 31.1).6 Approximately 15% of patients admitted to surgical intensive care units have multisystem organ failure,7 and perhaps 8% of burn patients ultimately develop the syndrome.8

The sequence of failures often follows a predictable course, although the cascade can be modified by various treatments, such as the prophylactic use of proton-pump inhibitors or H2-receptor blockers. In burn patients, two cascades have been described.9 An early clinical sequence is characterized by resuscitation failure, adult respiratory distress syndrome, hemodynamic failure, renal failure, gut failure, and infection, and a later cascade typified by pulmonary failure, hemodynamic instability, renal failure, gut failure, and liver failure. Frequently, vasomotor failure and death is seen at the end of both cascades. Mortality increases with increasing numbers of failed organ systems.10 The progression of the syndrome aids in prognostication and facilitates decisions regarding termination of futile efforts.10,11 The management of specific organ failures will be presented in the next chapter. The purpose of this chapter is to discuss the etiology and prevention of the syndrome.

Etiology

The etiology of multisystem organ failure remains a mystery under intense investigation. All patients seem to share characteristics associated with an uncontrolled inflammatory state, and there are several proposed ‘engines’ which drive this uncontrolled inflammation, including sepsis, the open burn wound, the gut, and hypoperfusion.

Sepsis is clearly the most common initiator of the syndrome, and was recognized early on as the primary cause.1 One single overwhelming infection is not required, as small repetitive infections may initiate the cascade,12 perhaps by priming immune cells, making them react more intensely to each subsequent stimulus.12 It was recognized later that many patients with multisystem organ failure did not have infection,13 and this led the search for other ‘engines’. Endotoxin liberated from the walls of Gram-negative bacteria is a major, but not the only, intermediary,14 as Gram-positive bacteria cause similar aberrations in oxygen transport and hemodynamics,15 via similar cascades of mediators.16

In burn patients the wound may also be a source of the inflammatory mediators leading to multiple organ failure. Certainly, an infected wound will do this, but wound sepsis is decreasing in incidence with the advent of early burn wound excision17 and most infectious deaths in burn patients today are caused by pneumonia rather than wound sepsis.18 Complete wound closure, without donor sites, decreases oxygen consumption19 and presumably ameliorates the inflammatory response to the open wound. Incomplete wound closure does not have this effect.20 Increased levels of circulating mediators such as interleukin-6 (IL-6), IL-8, and tumor necrosis factor (TNF) have been shown to originate from the burn wound21 and contribute to the hypermetabolic and inflammatory state seen in burn patients. Interleukin-8 has been demonstrated to be upregulated in the lung after burn injury21 and the stimulus for this upregulation, which is associated with pulmonary dysfunction, may come from the wound.21

Failure of the gut barrier can contribute to the development of multisystem organ failure.22 Normal barrier function prevents the movement of bacteria and their products from the gut lumen into the portal and lymphatic circulations. Bacterial densities range from near 0 in the stomach, to \(10^4\)–\(10^5\) in the distal small bowel, to \(10^7\)–\(10^8\)/g of stool in
the normal colon.23 That the normal gut can carry this bacterial load, without the frequent occurrence of Gram-negative infection, is a tribute to normal barrier function. Although not seen immediately after trauma,24 several insults have been shown to result in increased translocation of bacteria and their products into the portal and lymphatic circulations. Hemorrhagic shock,25 endotoxin administration,26 burns,27 and burn wound sepsis28 have each been shown to result in increased translocation of bacteria from the gut. Gut permeability to macromolecules, such as endotoxin, has been shown to increase with increasing burn wound size using polyethylene glycol 3350 as a tracer.29 Smaller molecules, with lactulose as the tracer, have also been shown to pass more readily through the gastrointestinal membrane after injury.30 The exact mechanism by which bacteria and their products pass through the gastrointestinal barrier is not clear. Both intra- and transcellular processes may be involved.31,32 The consequences of loss of the gastrointestinal barrier are profound. Translocating whole bacteria can be a direct source of sepsis or can activate Kupffer cells2,3 and promote an inflammatory response in conjunction with bacterial products such as endotoxin.

Cellular dysfunction, caused by inadequate oxidative metabolism secondary to hypoperfusion, is another potential ‘engine’ resulting in multisystem organ failure. In ischemia-reperfusion models, oxygen radicals are generated, resulting in peroxidation of cell membrane lipids and accumulation of activated neutrophils,33 with progressive cellular and whole-organ dysfunction. It has been proposed that critically ill patients suffer from supply-dependent oxygen consumption because of defects in cellular oxygen extraction and utilization.34,35 This results in inadequate aerobic metabolism unless supranormal levels of oxygen are supplied.36 The reality of this proposal is still actively debated.37,38 Certainly, a grossly inadequate amount of oxygen available to cells dependent on aerobic metabolism can lead to cellular dysfunction, and this may be followed by organ failures.3 Maintaining oxygen delivery at least at normal, and possibly supranormal, levels should help maintain cellular homeostasis and minimize the risk of multiple organ failure.39 Although the requirement for a supranormal level of tissue oxygenation in critical illness is controversial and our ability to predict organ-specific oxygen delivery and consumption from whole-body data is poor,40 careful attention to whole-body hemodynamics is an integral part of the management of any critically ill patient.

Common ground: mediators

Sepsis, open burn wounds, impaired gut barrier function, and hypoperfusion are all associated with multiorgan failure. The similarity in the response to these differing events implies that there is some common ground. These processes all probably impact on individual organs via a number of mediators, whose complex interactions are still very poorly understood, but are being unraveled by investigators using blocking antibodies, soluble receptors, and receptor antagonists.42 At this point, these mediators, including endotoxin, arachidonic acid metabolites, cytokines, platelet activating factor, activated neutrophils and adherence molecules, nitric oxide, complement, and oxygen free radicals will be reviewed briefly.

Endotoxin, a lipopolysaccharide component of Gram-negative bacterial cell walls, induces many of the symptoms associated with sepsis, including fever, hypotension, the release of acute phase proteins, and the production of multiple cytokines including TNF and IL-1.43 Endotoxin also
activates complement,\textsuperscript{44} causes activation of the coagulation cascade,\textsuperscript{45} and results in the release of platelet activating factor.\textsuperscript{46} Potential sources of endotoxin include both Gram-negative bacteria in foci of infection and Gram-negative bacteria within the gut when the gut barrier fails.

Arachidonic acid makes up approximately 20\% of cell membranes, is released from these membranes in response to a multitude of stimuli which activate phospholipases A\textsubscript{2} and C, and is then metabolized by one of two major enzyme systems (Fig. 31.1).

The cyclooxygenase pathway results in production of prostaglandins and thromboxanes, and the lipoxygenase pathway results in the production of leukotrienes.\textsuperscript{47} The prostaglandins and leukotrienes interact with other mediators in a complex fashion, and are later degraded by enzyme systems, which are dispersed throughout the body.\textsuperscript{48}

Arachidonic acid, which is metabolized via the cyclooxygenase pathway, results in the formation of prostaglandins and thromboxanes. Prostacyclin inhibits platelet aggregation, thrombosis formation, and gastric secretion.\textsuperscript{49} Thromboxane A\textsubscript{2} (TXA\textsubscript{2}) causes platelet aggregation, has profound vasoconstricting effects on both the splanchnic and pulmonary microvasculature, and causes bronchoconstriction and increased membrane permeability.\textsuperscript{50} It is studied via its longer-lived but inactive metabolite, TXB\textsubscript{2}. Aspirin has its physiological effects by inhibiting thromboxane synthetase.\textsuperscript{51}

Arachidonic acid metabolized via the lipoxygenase pathway results in the formation of leukotrienes. There are two types based on their metabolism after the action of 5-lipoxygenase, leukotrienes (LT) C\textsubscript{4}, D\textsubscript{4}, and E\textsubscript{4} (the sulfidopecptide group) and LTB\textsubscript{4}.\textsuperscript{52} Leukotrienes are generated in response to multiple stimuli by several cell types, including neutrophils, macrophages, and monocytes.\textsuperscript{53} Vessel walls are also capable of generating leukotrienes.\textsuperscript{54} Leukotrienes C\textsubscript{4}, D\textsubscript{4}, and E\textsubscript{4} have variable actions on vascular tone depending on the presence or absence of other mediators such as cyclooxygenase product. In addition to their variable effects in redirecting blood flow, LTC\textsubscript{4}, LTD\textsubscript{4} and LTE\textsubscript{4} also increase vascular permeability,\textsuperscript{56} and have been described as being elevated immediately prior to the development of pulmonary failure.\textsuperscript{57} The major effect of LTB\textsubscript{4} is an enhancement of neutrophil chemotaxis.\textsuperscript{58} Thus, leukotrienes as a group may be involved in the edema formation and pulmonary and systemic vascular changes that are seen in the multisystem organ failure syndrome.

Cytokines are regulatory proteins that are secreted by immune cells and have multiple paracrine and endocrine effects. There are six major classes,\textsuperscript{59} including interleukins, TNF, interferons, colony-stimulating factors, chemotactic factors, and growth factors. Those which have been most extensively characterized are IL-1, IL-6, and TNF.

Interleukin-1 and IL-6 are elevated in septic states, and high levels are associated with a fatal outcome\textsuperscript{60} and predict systemic infection.\textsuperscript{61} Interleukin-1\textbeta causes hypotension and decreased systemic vascular resistance, which may be synergistic with the effects of TNF.\textsuperscript{62} Even better characterized is TNF, the administration of which causes hypotension, cardiac depression, and pulmonary dysfunction in animals.\textsuperscript{63–65} When administered to humans, TNF causes fever, hypotension, decreased systemic vascular resistance, increased protein turnover, elevation of stress hormone levels,\textsuperscript{66,67} and activation of the coagulation cascade.\textsuperscript{68}

Platelet activating factor is a nonprotein phospholipid that is secreted by many cells including platelets, endothelial cells, and inflammatory cells,\textsuperscript{69} and is a major mediator of the pulmonary\textsuperscript{70} and hemodynamic\textsuperscript{71} effects of endotoxin. The major effects of platelet activating factor are vasodilation, cardiac depression, and enhancement of capillary leak. Its complex interactions with other mediators are still poorly understood.

Although tissue injury can occur in the absence of neutrophils,\textsuperscript{72} the inflammatory process results in local accumulation of activated inflammatory cells which release various local toxins such as oxygen radicals, proteases, eicosanoids, platelet activating factor, and other substances. When unregulated, such accumulations of activated cells can cause tissue injury.\textsuperscript{73} The initial attachment of neutrophils to the vascular endothelium at an inflammatory site is facilitated by the interaction of adherence molecules on the neutrophil and endothelial cell surfaces.\textsuperscript{74}

These neutrophil adherence receptors are induced by numerous stimuli but, interestingly, are reduced after major thermal and nonthermal injury,\textsuperscript{75} perhaps explaining in part the increased incidence of infection in such patients. The importance of this adherence mechanism can be seen in patients who are deficient in one of the integrin class of neutrophil adherence receptors, CD-18, who suffer from frequent bacterial infections.\textsuperscript{76} The biology of the transmembrane polypeptides that govern these complex cell-to-cell interactions is an active area of research\textsuperscript{77} and holds promise for therapeutic interventions in the future.
Oxygen radicals, such as hydrogen peroxide and superoxide anion, are released by activated neutrophils in response to a variety of stimuli. They are also released when xanthine oxidase is activated after reperfusion in ischemia-reperfusion models. These highly reactive products cause cell membrane dysfunction, increased vascular permeability, and release of eicosanoids.

Nitric oxide, released when citrulline is formed from arginine (Fig. 31.2), was only identified as an endothelial product in the middle 1980s. Its half-life is only a few seconds, as it is quickly oxidized, but it has profound local microvascular effects. Nitric oxide synthesis is stimulated by various cytokines, endotoxin, thrombin, and by injury to the vascular endothelium. It is a potent vasodilator, but its actions vary depending on the vascular bed and presence of other mediators. Nitric oxide is one of the major mediators of the hypotensive response to sepsis.

Antigen–antibody complexes activate the complement cascade, and complement fragments thus generated can interact with other cytokines to promulgate the inflammatory response. Diminished levels of a natural inhibitor of C5a have been demonstrated in patients with adult respiratory distress syndrome (ARDS) and administration of anti-C5a antibody diminishes hypotension in an animal model of endotoxemia. Complement fragments may be involved in the development of burn wound edema.

Our understanding of the incredibly complex cellular and subcellular biology, of which multisystem organ failure is but one manifestation, is poorly understood at the present time. This dim understanding highlights the important role that prevention plays in managing the syndrome.

### Prevention of multisystem organ failure

Once established, multisystem organ failure is very difficult to reverse, emphasizing the importance of prevention. Prevention is based on our crude knowledge of the 'engines' that drive the process – sepsis, the gut, the wound, and inadequate perfusion (Table 31.1). Dealing with these issues is far more practical than dealing with an incompletely understood complex web of mediators. The discussion that follows will address prevention of sepsis via proper wound management and attention to unusual causes of sepsis, support of the gut, and prevention of inadequate oxygen delivery. Subsequently, the potential role of nutritional and specific immunomodulators will be addressed.

### Prevention of sepsis

In the burn patient, prevention of multisystem organ failure is greatly facilitated by prevention of wound sepsis via an aggressive surgical approach to deep wounds. The increasing survival of burn patients has paralleled the evolution of this approach to the burn wound. Not only is overt wound sepsis prevented by early removal of devitalized tissue, but multiple smaller septic insults are also prevented, as manipulation of heavily colonized burn wounds is a frequent source of transient bacteremia. Such multiple occult bacteremias occurring during frequent manipulation of heavily colonized wounds could contribute to the development of multisystem organ failure by priming immune cells, making

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them react more intensively to each subsequent insult. The role of perioperative antibiotics in minimizing bacteremias in the perioperative period has yet to be defined clearly. However, they are clearly beneficial in patients with injuries greater than 60% of body surface and in any other patient in whom the probability of bacteremia with wound manipulation is felt to be high. Appropriate perioperative antibiotics are guided by surface cultures. Burn patients are prone to a large number of unusual and often occult infectious complications which can result in sepsis and potentially contribute to the development of multigorgan failure. Rapid diagnoses and treatment are facilitated by a high index of suspicion.

Intravascular infections such as suppurrative thrombophlebitis and endocarditis typically present in burn patients with fever and bacteremia without localizing signs. Burn patients with endocarditis develop a new murmur in only 9% of cases, and only 10% have been reported to present ante-mortem. Of those with septic thrombophlebitis, 68% have no localizing signs and present with fever and positive blood cultures only. The diagnosis is made in patients without localizing signs only by thorough examination of all sites of prior cannulation, with surgical exposure of any suspicious sites and complete excision of any involved veins. Vigilant care and scheduled replacement of intravascular devices will minimize the occurrence of catheter-related sepsis. Occult intracompartmental sepsis can also present with fever and bacteremia without localizing signs, and is diagnosed only by careful examination and exploration of suspicious compartments.

Pneumonia, seen in approximately 35% of patients with inhalation injury, adds between 20 and 60% to the expected mortality of burn patients. Although a difficult diagnosis to make in critically ill patients, pneumonia should be vigilantly anticipated and aggressively treated with appropriate endobronchial toilet and specific antibiotics. The incidence of nosocomial pneumonia increases with longer durations of intubation, emphasizing the importance of judicious use of mechanical ventilation.

Suppurative sinusitis is being recognized with increasing frequency in the intensive care unit, and may be more frequent in patients who are nasotracheally intubated. Diagnosis may require examination and culture of material obtained by antral puncture, in addition to plain radiographs and computed tomography. Although there is some controversy about the role of the nasotracheal tube in causing sinusitis, treatment involves replacing nasotracheal devices with topical decongestants and appropriate antibiotics. Surgical drainage is reserved for recalcitrant cases.

Acalculous cholecystitis often presents with generalized sepsis without localizing signs in the burn patient, and, like intravascular infection, is a very difficult diagnosis to make. Recently, bedside placement of percutaneous cholecystostomy tubes under ultrasonic guidance has become an option in the management of suspected cholecystitis in critically ill patients. This technique allows an accurate diagnosis to be made and the condition to be temporarily treated in patients too unstable for immediate operation.

Sepsis accounts for at least half of cases of multisystem organ failure. In perhaps no other area can the vigilance of the burn team have a greater impact in multisystem organ failure prevention than in the early detection and aggressive treatment of occult septic foci.

Support of the gut

Bacteria and their products released when the gut barrier fails may fuel the multiorgan failure syndrome. Gut mucosal integrity suffers when mesenteric flow is inadequate and gut blood flow is decreased after burn injury, a response exacerbated by the release of TXA2. Thus, support of splanchnic blood flow is an important aspect of multisystem organ failure prevention, and this is best done by careful attention to whole-body hemodynamics. There is no substitute for a carefully monitored burn resuscitation.

The enterocyte may be better supported by intraluminal, rather than parenteral feedings, as gut deprived of intraluminal feedings develops mucosal atrophy. Early enteral feedings are tolerated in the burn patients and may reduce the magnitude of the hypermetabolic response to the injury. Parenteral feedings do not prevent gut mucosal atrophy as well as isocaloric and isonitrogenous intraluminal feeds, although convincing human data are not available to support the clinical significance of this point.

The value of specific nutrients to support the enterocyte is far less clear than the value of providing adequate mesenteric blood flow and perhaps intraluminal nutrition. However, this is an exciting and active area of research. Glutamine, a non-essential amino acid, is the preferred fuel of the small bowel enterocyte as well as other rapidly dividing cells. Sepsis has been shown to decrease glutamine uptake by the small bowel enterocyte, which may result in barrier failure, and the addition of glutamine to the nutritional regimen has been theorized to improve barrier function. Glutamine is not a component of commercial parenteral nutritional formulas because of its short shelf life, although the dipeptide is well tolerated parenterally, and has a longer shelf-life. Although supplemental glutamine may improve protein balance in surgical patients, and may partially reverse gut atrophy, it has not been shown to improve gut barrier function when given parenterally.

The role of specific nutrients in support of the large intestinal mucosa is less clear, but butyrate, a fatty acid liberated by fiber fermentation, is a favored fuel of the colonic mucosal cell. Enteral pectin may help support the colonic mucosa, but the value of such support in the hypermetabolic burn patient is as yet unclear. Limited work has been done suggesting possible benefit of probiotics for gut barrier support.

A decontaminated gut lumen might diminish the impact of gastrointestinal barrier failure. Attempts have been made to access the impact of selective decontamination of the gut and coating enteric bacteria to inhibit their ability to attach to the intestinal mucosa and translocate. Although there is a suggestion that the rate of pneumonia may be decreased by such maneuvers, there is no apparent impact on mortality.

Support of the gut in an effort to prevent multisystem organ failure is certain to have real value. Maintenance of adequate mesenteric perfusion via careful attention to whole-body hemodynamics is crucial. There are some data to support the contention that enteral feedings have beneficial effects on outcome in injured patients when compared...
with parenteral feedings, possibly via an enhancement of gastrointestinal barrier integrity. However, these data require confirmation prior to general application. Data supporting the administration of specific mucosal substrates or gut decontamination are less convincing, but further research in these important areas may show such benefit.

**Insuring adequate oxygen delivery**

The normal intracellular partial pressure of oxygen is 0.5 mmHg, and this small amount of mitochondrial oxygen allows for the aerobic generation of most of the cell’s adenosine triphosphate (ATP). When cells have to adapt to a lower aerobic tension, ATP generation continues at a lower rate by anaerobic channels, possibly triggered by the build-up of adenosine diphosphate (ADP). As outlined by Gutierrez, the anaerobic reactions which generate ATP are glycolysis, the creatine kinase reaction, and the adenylate kinase reaction. Glycolysis describes the conversion of glucose to lactate with the generation of two ATP molecules. The creatine kinase reaction is the breakdown of the high-energy phosphate storage molecule, phosphocreatine, with the generation of ATP and creatine. The adenylate kinase reaction describes the combination of nucleotides to form ATP and AMP, although generating ATP, depletes the cells of adenine nucleotides. In conjunction with this conversion to anaerobic ATP generation, the intracellular concentration of hydrogen ion increases, the amount of adenine nucleotides within the cell decreases, and intracellular calcium levels increase with decreased function of the ATP-driven sodium–calcium pump. There also may be an increase in the liberation of intracellular oxygen free radicals with the activation of xanthine oxidase. If low oxygen tensions continue, membrane phospholipids may be degraded by the combined effects of elevated calcium, oxygen free radicals, and the decreased synthetic capabilities coincident with decreased levels of ATP. These effects may be magnified if there is also systemic sepsis as cellular oxygen extraction may be impaired. That such cellular hypoxic dysfunction is involved in the development of organ dysfunction is implied by the fact that cocarboxylase, which enhances ATP generation by ischemic cells, ameliorates some of the metabolic and hemodynamic consequences of endotoxic shock in an animal model.

Perhaps the most at-risk phase of care for provision of adequate oxygen delivery is during burn resuscitation. At a local level, inflammatory cells aggregating to wounds secrete histamine and other mediators which disrupt endothelial junctions resulting in extravasation from the intravascular space into the surrounding tissues. This is in turn associated with intracellular sodium retention and cellular edema. As burns become larger, this phenomenon becomes generalized, creating a diffuse capillary leak, local vasoconstriction and systemic vasodilation, with secondary distributive and hypovolemic shock. Vascular collapse ensues unless effective resuscitation can be accomplished.

The practical details of resuscitation, particularly resuscitation endpoints, remain controversial. The Rivers et al. study highlighted the utility of aggressive pursuit of predetermined resuscitation endpoints in septic shock; these principles have been endorsed by the 2008 Surviving Sepsis Campaign. A similar strategy is likely to be effective in burn patients. The traditional primary endpoint of urine output has been expanded to include lactic acid and base deficit. Advanced hemodynamic monitoring tools are increasingly incorporated in burn resuscitation and may soon include esophageal Doppler, which may help improve resuscitation accuracy, minimizing the morbidity of under and over-resuscitation. Recent work in trauma patients has highlighted the inflammatory complications of massive crystalloid resuscitation. This has stimulated a renewed interest in the role of colloid in burn resuscitation. The variability of the physiologic response to injury, and clinical response to intervention, makes the specifics of fluid resuscitation an oft-debated art, which is well described in other chapters of this text.

Inadequate oxygen delivery clearly leads to organ dysfunction. At a minimum, the clinician should insure that injured patients are resuscitated to the conventional clinical endpoints of appropriate urine output, skin perfusion, blood pressure, and sensorium. In selected critically ill patients, invasive monitoring is justified to document oxygen delivery and consumption, extraction ratio, and the possible presence of supply dependency in which circumstance supranormal levels of oxygen delivery with plateau of oxygen consumption is an appropriate resuscitation endpoint.

**The potential role of nutritional and specific immunomodulators**

The holy grail of those who study the complex biology of the multisystem organ failure syndrome is an ability to modulate the common pathways that lead to organ dysfunction and death. The three general approaches to this goal are nutritional, nonspecific, and specific immunomodulation.

**Nutritional immunomodulation**

Three categories of substances show some promise as potential nutritional immunomodulators in burn patients: long-chain fatty acids; arginine, glutamine, and branched-chain amino acids; and nucleotides. Short- and medium-chain fatty acids are commonly utilized for energy, whereas long-chain fatty acids are important constituents of cell membranes and can profoundly influence cell function. Omega-3 long-chain fatty acids play a particularly important role in the membranes of immunocompetent cells. There are animal data suggesting that supplementation of the diet with omega-3 fatty acids may improve immune function after burn injury; however, there are no clear clinical data yet available to support the routine administration of omega-3 fatty acids as a dietary supplement in injured patients.

The potential immunostimulating effects of specific amino acids, particularly arginine, glutamine, and the branched-chain amino acids leucine, isoleucine, and valine, are an active area of research. Arginine is a nonessential amino acid with important functions in the urea cycle and in the generation of nitric oxide. It also may have important effects in insuring immune cell competence. Although there are some animal data suggesting improved immunocompetence and outcome after burn with supplementation of arginine, human data are not yet adequate to support its routine administration to burn patients. Glutamine, the
most common amino acid in the body, and a preferred fuel of rapidly dividing cells, may be conditionally essential in hypermetabolic patients,113,114 and its administration has been proposed as a method to support the gut barrier, thereby abrogating the consequences of barrier failure.

The hyperdynamic and catabolic physiology that typifies the post-resuscitation period has deleterious consequences for many patients.143,144 Nutrition is critical in support of this physiology. Some efforts to modify the catabolic state have been successful. Beta-blockade has been shown to decrease resting oxygen expenditure, attenuate muscle catabolism and lipolysis, and have favorable effects on some aspects of immune function.145,146 The anabolic agent oxandrolone reduces loss of lean body in some patients.147

Non-specific and specific immunomodulation

It seems intuitively unlikely that there exists a magic immunomodulating bullet that will prevent the development of multisystem organ failure in critically ill surgical patients, particularly if sepsis is uncontrolled, the integrity of the gut barrier is compromised, burn wounds are unaddressed, or patients are inadequately supported hemodynamically. However, such efforts have tremendous potential to facilitate our understanding of cellular and subcellular biology and may, in time, provide a clinical dividend. Efforts at non-specific immunomodulation have included the use of steroids,147 immunoglobulin G,148 and naloxone149 with no significant impact on patient outcomes. With the exception of steroids for those with suspected adrenal insufficiency and naloxone for those with opiate intoxication, there is no role for these substances in critically ill burn patients.

Although there have been efforts to absorb lipopolysaccharide,150 and to prevent endotoxemia with prophylactic polymyxin B in burn patients,152 the greatest efforts at specific immunomodulation have been applied to the development of anti-endotoxin antibodies. The earliest clinical efforts used human serum with anti-J5 activity and demonstrated an enhanced survival in patients with Gram-negative septic shock.153 Later, two monoclonal IgMs were developed, and human trials were completed. The first was anti-E5, a murine monoclonal antibody. Clinical trials suggested a benefit in septic patients without refractory shock.154 Large numbers of treated patients developed antibodies to the murine monoclonal, and although these patients were not retreated, attention turned more toward a human product. A subsequent effort with this murine monoclonal did not show statistically significant improvements in outcome.155

HA-1A, a human monoclonal IgM, was trailed in a large multicenter effort without statistically significant improvement in outcome, except in a subgroup of patients that had Gram-negative bacteremia and shock.156 Multiple confounding factors made these marginally beneficial results suspect, leaving the ultimate utility of HA-1A still unclear.

Anti-endotoxin monoclonal therapy, which may have potential to be beneficial if significantly refined, has also been criticized for its expense. It is estimated that it would cost $24 100 per year of life saved should this technology be used widely.157 Integrating such advanced and expensive technology into common practice poses tremendous practical problems, and is therefore very unlikely to happen soon when one considers its lack of clear efficacy and high expense.

Significant efforts have also been made toward modifying the actions of arachidonic acid metabolites or eicosanoids, both cyclooxygenase and lipoxygenase products. Numerous animal models of sepsis and endotoxemia exist, and cyclooxygenase pathway blockade with nonsteroidal anti-inflammatory agents has demonstrated improved survival,158,159 improved pulmonary hemodynamics,160 and improved mesenteric blood flow.161 There has been little work documenting outcome improvement in human patients, but it has been suggested that nonsteroidal anti-inflammatory agents improve symptoms associated with endotoxin infusion in normal volunteers162 and septic patients,163 and may improve immune function after surgical trauma.164 In an animal model, infusion of the vasodilating arachidonic acid metabolite, prostacyclin, ameliorates the pulmonary dysfunction associated with endotoxin infusion.165 Less work has been done with lipoxygenase pathway inhibitors. Survival is enhanced in a murine model of endotoxin infusion with lipoxygenase pathway blockade.166 Endotoxin-associated pulmonary dysfunction is diminished in sheep167 and pigs168 when this pathway is blocked. The ultimate role of lipoxygenase blockade in human remains uninvestigated.

Cytokines are difficult to measure accurately and their complex interactions are poorly understood. The production of IL-1 receptor antagonist is increased in human endotoxemia,169 and, in an animal model, its administration enhances survival.170 However, infusion of IL-1 may improve immune function in humans.171 Clearly our understanding of the complex functions of this cytokine are inadequate to allow intelligent intervention.

Tumor necrosis factor is produced by macrophages and other inflammatory cells when stimulated by endotoxin.172 In animal models, the physiological effects of both endotoxin infusion and Gram-negative sepsis173,174 are attenuated by TNF blockade with monoclonal antibodies. Circulating levels of TNF are high immediately after sepsis begins and then fall, implying that only anti-TNF pretreatment would be beneficial.175 However, even anti-TNF administration prior to experimental sepsis176 and endotoxemia177 has variable effects, at best, on survival. Again, our incomplete understanding precludes effective intervention.

Interference with the effects of platelet activating factor (PAF) has been shown to decrease neutrophil priming by human burn serum,178 to improve endotoxin-induced pulmonary dysfunction,179 to decrease eicosanoid release,180 and to attenuate thromboxane release and improve survival181 in various animal models of endotoxemia. These exciting initial results, and the availability of several blockers and receptor antagonists, portend a future use for PAF modification.

Efforts to modulate both the adherence and function of inflammatory cells are an exciting area of research, as activated neutrophils clearly play an important role in the development of multiple organ failure. Blockade of neutrophil adhesion receptors with monoclonal antibodies enhances survival in animal models of endotoxic and hemorrhagic shock.182,183 Again, our basic understanding is not yet adequate to intelligently modify such important processes.

Oxygen free radicals generated by activated neutrophils or xanthine oxidase may oxidize membrane lipids, forming lipid peroxides, resulting in membrane dysfunction.184 Native antioxidant systems do exist, but can be overwhelmed.
Circulating levels of vitamin E, a natural antioxidant, are low in patients with ARDS. Efforts to modify oxidant activity have included blockade of free radical generation, addition of free radical scavengers, augmentation of host antioxidant defenses, and prevention of amplification of tissue damage by neutrophils. Particularly exciting are free radical scavengers such as superoxide dismutase and spin-trapping nitrones which improve survival in animal models of endotoxic and hemorrhagic shock. But, despite such encouraging initial animal work, such therapy is not yet appropriate in human patients.

The continuous synthesis of nitric oxide (Fig. 31.2) plays an important role in the regulation of pulmonary and systemic vascular tone in sepsis, and this presents potential opportunities for intervention. Aerosolized nitric oxide has been shown to be useful in reversing the pulmonary hypertension associated with ARDS and nitric oxide synthesis blockade may improve the hypotension and renal dysfunction associated with sepsis. However, its complex interactions with other cytokines and variable effects on different vascular beds render any nitric oxide-based interventions investigational at the present time.

Recently, recombinant activated protein C (rAPC) has been shown to have a favorable influence in patients with sepsis-induced multiple organ failure, after it demonstrated a 6% absolute reduction in mortality in a large multicenter trial. Institutional criteria for administration of rAPC infusion vary, but generally include those patients with vasopressor-dependent septic shock and multiple organ failure of recent onset. Its major complication is bleeding, which has precluded its general use in septic shock in burn patients. However, it may ultimately have a role in septic shock associated with isolated inhalation injury.

Most patients who die in the burn unit after surviving resuscitation succumb to multiple organ failure. Although modification of the cascade of events leading to multiorgan failure at the cellular and subcellular level is an enticing possibility, our fragmented understanding of these processes mitigates against such therapy in human patients at the present time. That TNF enhances the ability of neutrophils to kill invading bacteria and of rats to survive Gram-negative sepsis, that cyclooxygenase inhibition increases TNF production after burn, that PGE₂ is important in renal autoregulation, and that cytokine levels vary significantly over the course of critical illness makes one loath to interfere in such complex, and poorly understood processes. Vigilant clinical care in the intensive care unit, with the prevention of sepsis, proper management of burn wounds, support of the gut barrier, and careful attention to whole-body hemodynamics is a much more fruitful area in which a vigilant clinician can make a difference. On the near horizon is an exciting new understanding of the molecular mechanisms of critical illness that is likely to lead to effective targeted interventions.

Further reading

A review of the colloid-heavy resuscitation strategies becoming established in trauma.
SCCM practice guidelines for sepsis management, recently updated.
A complete review of the complexities of the metabolic response to burns as they are now understood.
The NEJM paper in which the benefits of beta-blockade in burn patients are reported.
The original Rivers paper that identified the impact of early goal-directed therapy for septic shock.
A review of the many varieties of sepsis in burn patients.
A nice review of the post-burn hypermetabolic response and various ways it can be modified.
A controlled study demonstrating the benefits of anabolic steroids in burn patients.
References


Herndon DN, Hart DW, Wolf SE. Reversal of catabolism by 
Herndon DN, Tompkins RG Support of the metabolic response 
Hart DW, Wolf SE, Chinkes DL Determinants of skeletal muscle 
Shang HF, Hsu CS, Yeh CL, et al. Effects of arginine 
Hurt RT, Matheson PJ, Mays MP, et al. Immune-enhancing diet 
Barton RG, Wells CL, Carlson A, et al. Dietary omega-3 fatty 
Wentzel RP. Anti-endotoxin monoclonal antibodies – a second 

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Renal failure in association with thermal injuries

Jeremy Goverman, Naoki Aikawa, Shawn P. Fagan

Introduction

Acute renal dysfunction is a major complication affecting the thermally injured individual and is commonly associated with a high mortality rate. Currently, the incidence of acute renal failure in burn patients varies between 0.5% and 30%, with a reported mortality rate between 54% and 100%. Prior to 1965 there were no reported survivors from acute renal failure following burns. While advances have been made in the understanding of the etiology of acute renal failure in association with thermal injury, little has been accomplished with the actual treatment; and it remains unclear whether or not the application of renal replacement therapy (RRT) as a treatment modality has significantly changed the mortality rate of individuals suffering from acute renal failure. The best treatment for acute renal failure represents an end stage process, with the phases leading up to it having important clinical and prognostic value. The need to grade the severity of injury, rather than consider only the most severe form, has led to a new classification system. The term acute kidney injury (AKI) is now preferred. Although the definitions are numerous, the common theme of all definitions in the literature is an abrupt decline in glomerular filtration rate (GFR) with the phases leading up to it having important clinical and prognostic value. The AKIN criteria define acute kidney injury as an abrupt decrease in kidney function (≤48 hours) and may allow for earlier recognition of AKI in the ICU setting. Comparisons between RIFLE and AKIN have been published but have not demonstrated clear benefit of one classification system over the other. These new classification systems should aid in future experimental design and allow for improved comparison between studies investigating AKI associated with thermal injuries.

Definition

Historically, acute renal failure has been defined as an abrupt and sustained decrease in renal function. Until recently, there was no consensus regarding an absolute definition for acute renal failure. This is exemplified by more than 30 different definitions having been used in the literature, creating much confusion and making comparisons between studies impossible. Although the definitions are numerous, the common theme of all definitions in the literature is an abrupt decline in glomerular filtration rate (GFR) with the inability of the kidneys to appropriately regulate fluid, electrolytes, and acid–base homeostasis. Furthermore, acute renal failure represents an end-stage process, with the phases leading up to it having important clinical and prognostic value. The need to grade the severity of injury, rather than consider only the most severe form, has led to a new classification system. The term acute kidney injury, or acute kidney insufficiency (AKI), is now preferred.

In an effort to standardize the definition of renal insufficiency, the International Acute Dialysis Quality Initiative (ADQI) group has developed the RIFLE criteria (Fig. 32.2).

Etiology of acute renal failure

Burn-related renal insufficiency is most commonly observed during the period of initial resuscitation after burn injury (early AKI) or as a component of the multiorgan dysfunction syndrome, often associated with severe sepsis (late-onset AKI). The development of early AKI in the burn individual is multifactorial: hypovolemia, inflammatory mediators, cytokines, extensive tissue destruction and release of denatured proteins, iatrogenic causes (nephrotoxic agents), and cardiac dysfunction have all been implicated. Historically under-resuscitation and hypovolemia were the primary focus; however, more recent studies have demonstrated that AKI is not solely dependent on the amount of fluid received. AKI develops in the thermally injured patient despite aggressive fluid resuscitation and a normal urine output, and is more likely dependent on the degree of shock following injury. Global parameters of perfusion, i.e. lactate and base deficit, may better predict AKI, as they have been demonstrated to predict an increased risk of systemic inflammatory response syndrome (SIRS), acute respiratory distress syndrome (ARDS), multiorgan dysfunction syndrome (MODS), and mortality.
Hypovolemia

Burns affecting >20% total body surface area (TBSA) are of sufficient size to induce decreased renal blood flow from local and systemic cytokine release as well as extravascular fluid loss. Hypovolemia is supported by the observations of Kim et al. that burn size is an independent predictor of acute renal failure in the burn population.32 Depressed renal blood flow results in ischemia and cellular death. The ischemic insult is known to produce oxygen free radicals that cause direct tubular damage, as well as disruption of tight junctions, resulting in obstructing casts which further reduce effective GFR. The duration of ischemic time is critically

Figure 32.1 Autopsy specimen from a patient with acute tubular necrosis and renal failure. Note the edema and the alteration of medullar pyramids. Acute renal failure in burn patients carries a high mortality.

<table>
<thead>
<tr>
<th>Table 32.1 RIFLE and AKIN criteria</th>
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<tbody>
<tr>
<td><strong>RIFLE category</strong></td>
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<tr>
<td>(A) The Acute Dialysis Quality Initiative (ADQI) criteria for the definition and classification of AKI (i.e. RIFLE criteria)</td>
</tr>
<tr>
<td>Risk</td>
</tr>
<tr>
<td>Injury</td>
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<tr>
<td>Failure</td>
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<tr>
<td><strong>AKIN criteria</strong></td>
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<tr>
<td>(B) The proposed Acute Kidney Injury Network (AKIN) criteria for the definition and classification of AKI</td>
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<tr>
<td>Stage 1</td>
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<td>Stage 2</td>
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Hypervolemia, intra-abdominal hypertension, and abdominal compartment syndrome

Although aggressive fluid resuscitation may reduce the risk for AKI, it does not eliminate its occurrence. Studies have shown that AKI develops in burn-injured patients despite fluid resuscitation volumes in excess of that recommended by the Parkland formula, and despite normal average urine output (0.5–1.0 mL/kg/h). Furthermore, the risks of over-resuscitation have been well documented and include pneumonia, ARDS, compartment syndromes, and an overall increase in mortality.

Burns >20% TBSA generally require intravenous resuscitative efforts, and the initial volume of fluids should be proportional to the area of burn injury. Despite a physician’s greatest effort to monitor endpoints of resuscitation, obligatory intercompartmental fluid shifts will occur during resuscitation. These intercompartmental fluid shifts can be particularly hazardous if they occur into fascial bound compartments, such as the peritoneal cavity. Numerous studies from the trauma literature have described the adverse physiologic effects of increasing intra-abdominal pressure on visceral perfusion. Intra-abdominal hypertension (IAH) is a known pathological process that may occur during initial burn resuscitation as defined by intra-abdominal pressures (IAP) >12 mmHg. Abdominal compartment syndrome (ACS) is defined as an IAP >20 mmHg with at least one concomitant organ failure. The exact incidence of ACS, the point of decreased visceral perfusion, is currently unknown during burn shock resuscitation. O’Mara et al. demonstrated that the volume and type of fluid resuscitation affects the development of ACS in the burn patient and suggested that fluid resuscitation with crystalloid >0.475 L/kg should alert the clinician to possible IAH/ACS and to monitor for decreased cardiac output, decreased lung compliance, or decreased renal perfusion – signs of ACS. In a mixed population of critically ill patients, a multicenter prospective trial has demonstrated that the occurrence of IAH during the ICU stay was an independent outcome predictor.

Cardiac dysfunction

Cardiac dysfunction is known to result in reduced renal blood flow and hence to contribute to AKI. Although diminished cardiac output following thermal injury has been attributed to decreased preload or hypovolemia, there is increasing evidence of direct myocardial suppression. Myocardial dysfunction after thermal injury is commonly overlooked by physicians owing to the concentrated effort to correct the overwhelming state of hypovolemic shock and electrolyte abnormalities. An effective burn surgeon must rapidly re-establish adequate renal blood flow by correcting the diminished preload state while keeping in mind the impact of burn injury on the entire cardiovascular system. Patients suffering burns >50% TBSA are subject to decreased cardiac output, increased myocardial workload, myocardial ischemia, and acute cardiac infection from the large area of wounded skin. Several authors have suggested theories to explain the decreased cardiac output associated with thermal injury: 1) increased sympathetic activity with impaired adrenal response, 2) hypovolemia resulting in myocardial ischemia and 3) direct myocardial suppression. Of the potential theories, direct myocardial suppression by tumor necrosis factor (TNF; i.e. myocardial depressant factor) has gained substantial interest. TNF is known to be released by myocytes stimulated by endotoxin or direct thermal injury. The effects of TNF on cardiac function include reversible biventricular dilatation, decreased ejection fraction, and decreased stimulation to catecholamines (Fig. 32.1). Although most early cardiac dysfunction caused by TNF can be reversed by inotropic support, the key is early diagnosis to prevent ineffective renal perfusion and thus prevent the morbidity and mortality associated with renal insufficiency.

Denatured proteins

Rhabdomyolysis and free hemoglobin have both been implicated in the development of AKI and subsequent renal failure. Rhabdomyolysis in particular has been shown to contribute to AKI following severe burns. Rhabdomyolysis can arise secondary to direct thermal damage or compartment syndrome and is commonly seen following severe electrical injury. The release of myoglobin, or unconjugated hemoglobin, into the systemic circulation results in blockage of renal tubules, constriction of afferent arterioles, and the generation of oxygen free radicals. The extent of renal injury is directly related to the amount of iron-containing molecules released, the state of hydration, and the degree of acidosis. Myoglobinuria occurs when serum myoglobin exceeds 1500–3000 ng/mL. Elevated creatinine at baseline and creatinine kinase levels >5000 IU/L have been associated with the development of AKI and the need for RRT. Fortunately, the incidence of denatured proteins causing burn-associated acute renal insufficiency is low, and the overall prognosis is favorable if the pathological source is identified early and appropriate treatment is initiated. For those patients at risk, intensive hydration with isotonic crystalloids is recommended. The use of sodium bicarbonate is unnecessary, as it has not been shown to be superior to saline for alkalinization of the urine.
The key to treatment is an understanding of the pathophysiologic vascular resistance (Fig. 32.3). Initially, bacteria or their products activate sepsis associated mediators (cytokines) locally at the site of direct invasion. In sepsis, the homeostatic balance between production and inactivation of these mediators is altered, allowing for systemic release, causing direct damage to the endothelium, vasoparalysis, and a procoagulant state. It has been theorized that acute renal insufficiency associated with sepsis is the result of each of these pathological processes. The vasoparalysis seen in sepsis, for example, results in a profound state of hypotension which activates the renin–angiotensin–aldosterone axis responding by increasing systemic arterial circulation, the sympathetic nervous system and the neurohumoral axis. In an effort to maintain systemic arterial circulation, the sympathetic nervous system and the renin–angiotensin–aldosterone axis respond by increasing cardiac output and by direct renal arteriolar vasconstriction. This response may actually worsen renal perfusion by inducing a prerenal state, which is further aided by the release of other vasconstricting agents (i.e. TNF, endothelin) as well as the inability of locally secreted vasodilators (endothelial and inducible nitric oxide) to counterbalance these sepsis-associated vasoconstrictors. Finally, as mentioned previously, sepsis induces a procoagulant state by affecting the expression of complement and the fibrinolytic cascade. This alteration in the homeostasis of coagulation may result in a state of disseminated intravascular coagulation (DIC) with direct injury to the kidney by glomerular microthrombi. The net result is a lack of perfusion to the kidneys during sepsis that will ultimately culminate in acute tubular necrosis secondary to ischemic injury.

### Diagnosis of acute kidney injury

The key to the diagnosis of AKI following thermal injury is to have a strong fund of knowledge in the pathophysiology affecting the burned patient throughout their treatment course. Significant renal injury may be present despite normal urine output or significant changes in the biochemical markers of renal injury. Physicians must constantly review the global physiological state of a thermally injured patient and anticipate conditions that may affect the renal system, so that a stepwise approach to the diagnosis and treatment may be initiated.

Of the physiologic parameters of renal function, altered urine output is probably the first and most recognized sign of renal dysfunction. Urine output has been demonstrated to be a very specific but unfortunately not very sensitive measure of renal function. Most clinicians regard urine output of little diagnostic value in the evaluation of renal dysfunction, since severe renal injury may exist with any volume of urinary output. This variability is due to the fact that urine output is not determined by the GFR alone but by the difference between GFR and tubular reabsorption. The one clinical scenario in which urine output may be diagnostic is the presence of anuria (<50 mL/day) or complete cessation of GFR. Microscopic examination of urinary sediment is an easy and inexpensive initial evaluation of AKI to determine the underlying renal pathology. The combination of normal urinary sediment, hyaline casts, and oliguric/anuric urinary output would suggest a prerenal condition. Although it is true that other conditions (acute cortical necrosis, bilateral arterial occlusion and rapidly progressive acute glomerulonephritis) may cause anuria, excluding postrenal obstruction, is a severe prerenal condition. Although it is true that other conditions (acute cortical necrosis, bilateral arterial occlusion and rapidly progressive acute glomerulonephritis) may cause anuria, their incidence is low and the diagnosis is usually readily apparent owing to additional clinical signs. Although urinary output is commonly non-diagnostic regarding the type of renal injury, microscopic and biochemical analysis may aid in the diagnosis and thus guide treatment options. Microscopic examination of urinary sediment is an easy and inexpensive initial evaluation of AKI to determine the underlying renal pathology. The combination of normal urinary sediment, hyaline casts, and oliguric/anuric urinary output would suggest a prerenal condition. The presence of epithelial casts and abundant tubular epithelial cells is pathognomonic for acute tubular necrosis. Similarly, the identification of pigmented casts on microscopic evaluation signifies the diagnosis of myoglobinuria, likely secondary to rhabdomyolysis. If microscopic evaluation is non-diagnostic, urinary electrolytes will allow for evaluation of the renal response to the individual’s physiologic state.

The primary goal of evaluating urinary electrolytes in a thermally injured individual is to differentiate between the prerenal and renal forms of AKI. It has been well established

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### Table 32.2 Renal failure dysfunction and sepsis

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<tr>
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<th>Sepsis</th>
<th>Severe sepsis*</th>
<th>Septic shock†</th>
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<tr>
<td>Acute renal dysfunction</td>
<td>19%</td>
<td>23%</td>
<td>51%</td>
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* Sepsis associated with lactic acidosis or altered mental status.
† Sepsis associated with hypotension.

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Several authors have found the degree of sepsis to be directly related to the incidence of acute renal dysfunction (Table 32.2). The key to treatment is an understanding of the pathophysiology of AKI associated with sepsis, the basis of which is multifactorial in nature but begins clinically with a generalized arterial vasodilatation secondary to a decreased systemic vascular resistance (Fig. 32.3). Initially, bacteria or their products activate sepsis-associated mediators (cytokines) locally at the site of direct invasion. In sepsis, the homeostatic balance between production and inactivation of these mediators is altered, allowing for systemic release, causing direct damage to the endothelium, vasoparalysis, and a procoagulant state. It has been theorized that acute renal insufficiency associated with sepsis is the result of each of these pathological processes. The vasoparalysis seen in sepsis results in a profound state of hypotension which activates the neurohumoral axis. In an effort to maintain systemic arterial circulation, the sympathetic nervous system and the renin–angiotensin–aldosterone axis respond by increasing cardiac output and by direct renal arteriolar vasconstriction. This response may actually worsen renal perfusion by inducing a prerenal state, which is further aided by the release of other vasconstricting agents (i.e. TNF, endothelin) as well as the inability of locally secreted vasodilators (endothelial and inducible nitric oxide) to counterbalance these sepsis-associated vasoconstrictors. Finally, as mentioned previously, sepsis induces a procoagulant state by affecting the expression of complement and the fibrinolytic cascade. This alteration in the homeostasis of coagulation may result in a state of disseminated intravascular coagulation (DIC) with direct injury to the kidney by glomerular microthrombi. The net result is a lack of perfusion to the kidneys during sepsis that will ultimately culminate in acute tubular necrosis secondary to ischemic injury.
that a prerenal state in the presence of a functional nephron is associated with enhanced absorption of sodium or a low fractional excretion of sodium. The fractional excretion of sodium (FeNa) is defined as:

$$\text{FeNa} = \frac{\text{urine sodium} \times \text{plasma creatinine}}{\text{plasma sodium} \times \text{urinary creatinine}}$$

with a value <1% associated with a prerenal condition and a value >1% associated with a renal condition. Although this is the accepted rule, there are conditions that affect renal absorption of sodium and thus have been shown to affect the calculated value (Table 32.3). Additionally, chronic renal insufficiency has been demonstrated to be associated with altered sodium homeostasis, and therefore the interpretation of the FeNa in the setting of renal insufficiency is difficult. In this situation, an alternative agent such as urea may be appropriate. Recently, fractional excretion of urea (<0.35) was suggested to be more specific and sensitive than sodium in distinguishing between prerenal and renal forms of acute renal failure. The prerenal state not only affects the homeostasis of sodium and urea; several additional indexes can be used to differentiate between the two forms of acute renal failure (Table 32.4).

Ideally a biochemical marker for AKI would: 1) allow early detection of renal injury, 2) identify the nephron segment affected, 3) reflect improvement and worsening of renal function and 4) be easily and rapidly measured. Currently no such ‘ideal’ biomedical filtration marker exists; however, creatinine has been used as the standard marker for determining GFR. Serum creatinine is freely filtered across the glomerulus and neither absorbed nor metabolized by the kidney. The amount of creatinine excreted is approximately 10–20% greater than the amount filtered, therefore the calculated creatinine clearance by definition overestimates the true GRF during normal steady-state conditions. Creatinine is thus not an ‘ideal’ marker but a ‘reasonable’ marker of GRF in a normal host.

The impact of illness appears to have a significant effect on the use of creatinine as a marker of GFR due to the non-steady-state environment. Plasma creatinine is not only dependent on its urinary clearance but also on its production and volume of distribution within the body. Several studies have demonstrated the impact of illness on each of these parameters (Table 32.5). In critically ill patients, serum creatinine appears to be an inaccurate absolute determinant of GFR. In fact, serum creatinine has been demonstrated to often lag behind the true degree of progressive renal dysfunction and renal recovery. In these conditions serum creatinine should be viewed with respect to the degree of change over time, which in turn grossly reflects the degree of GFR change over time.

Moran and Myers demonstrated the importance of understanding the degree of creatinine change over time. They investigated creatinine kinetics following ischemic postoperative acute renal failure, and based on their observations they developed hypothetical profiles of acute renal failure and recovery focusing on changes in GFR and their corresponding changes in serum creatinine. Their work suggested that the two variables were not always inversely proportional but often dissociate during acute renal failure and recovery. That is, a rising serum creatinine is not always indicative of worsening GFR and a decreasing serum creatinine is not always indicative of an improving GFR. What did appear to be prognostic in acute renal failure is the number of days the plasma creatinine continued to rise after the initial ischemic insult. Post-insult day 4 was found to be the significant determinant of the state of recovery. An abrupt insult followed by immediate recovery caused the serum creatinine to peak at approximately post-insult day 4. If serum creatinine continued to rise beyond post-insult day 4, renal recovery had not begun, and this was followed by a severe protracted course of acute renal insufficiency. Although this study was not conducted in a burn population, the underlying pathophysiology (ischemic) is germane to the burn population, especially after initial resuscitation.

A clinician should understand the limitations of any marker used to calculate or follow GFR during renal injury. Albeit not an ‘ideal marker’, creatinine is the gold standard...
for this calculation. GFR calculations based on creatinine clearance should be made over short time intervals, with the serum creatinine value reflecting the mean of the values obtained at the beginning and end of the collection interval. New markers of AKI, such as cystatin-C, have shown promise as earlier detectors of changes in GFR. 

### Treatment of acute renal failure

The key to the treatment of AKI is prompt diagnosis coupled with a rapid reversal of the underlying pathophysiology while preventing iatrogenic injury. If the process is progressive despite initial therapeutic maneuvers, renal replacement therapy (RRT) is indicated. This section will focus on the prevention of early and late AKI and the current theories behind RRT.

As stated previously, early AKI is secondary to ineffective renal perfusion. Several authors have demonstrated that the timing of initiation of resuscitative fluids is directly related to the incidence of renal dysfunction. Resuscitative efforts should therefore begin immediately to re-establish effective renal perfusion. Several resuscitative formulas have been established based on multivariate logistic regression analysis (Table 32.6). Which formula to use is unimportant, but the clinician should recognize that these formulas are estimates of the volume of fluid needed over a period of time. The true amount is directly dependent on the patient’s own physiologic status and degree of injury. A clinician should continuously monitor parameters of regional and global perfusion in order to guide fluid therapy and prevent over-resuscitation. If the true volume status (preload) or ability to assess effective renal perfusion is difficult, one should initiate monitoring of central pressures or global volume related variables (i.e. global end-diastolic volume, extravascular lung water volume, intrathoracic blood volume). The best means to measure the degree of resuscitation is unknown; however, if adequate volume loading does not produce sufficient mean arterial pressure (60–65 mmHg), the use of vasopressors is indicated.  

### Box 32.1 Definition of sepsis in burns

At least three of the following:

I. Temperature >39° or <36.5°C
II. Progressive tachycardia
   A. Adults >110 bpm
   B. Children >2 SD above age-specific norms (85% age-adjusted max heart rate)
III. Progressive tachypnea
   A. Adults >25 bpm not ventilated
      i. Minute ventilation >12 l/min ventilated
   B. Children >2 SD above age-specific norms (85% age-adjusted max resp. rate)
IV. Thrombocytopenia (will not apply until 3 days after initial resuscitation)
   A. Adults <100 000/mcl
   B. Children <2 SD below age-specific norms
V. Hyperglycemia (in the absence of pre-existing diabetes mellitus)
   A. Untreated plasma glucose >200 mg/dl or equivalent mM/L
   B. Insulin resistance—examples include
      i. >7 units of insulin/hr intravenous drip (adults)
      ii. Significant resistance to insulin (>25% increase in insulin requirements over 24 hours)
VI. Inability to continue enteral feedings >24 hours
   A. Abdominal distension
   B. Enteral feeding intolerance (residual >150 ml/hr in children or two times feeding rate in adults)
   C. Uncontrollable diarrhea (>2500 ml/d for adults or >400 ml/d in children)

In addition, it is required that a documented infection is identified via:

A. Culture positive infection, or
B. Pathologic tissue source identified, or
C. Clinical response to antimicrobials
pharmacological agent has been demonstrated to prevent or limit renal dysfunction. The importance of infectious surveillance in the thermally injured patient cannot be overstated. The goal is to effectively treat local infections and prevent systemic dissemination to avoid the morbidity and mortality of septic shock.

Fortunately, owing to major advances in burn care resuscitation and the treatment of sepsis, renal failure requiring RRT is a rare event. The reported incidence is approximately 1–3%, but the overall mortality associated with renal failure requiring RRT approaches 80%. Burn patients with pre-existing renal insufficiency are at particular risk for RRT owing to the large positive fluid balances associated with the initial resuscitation therapy, enhanced catabolism leading to elevated urea levels, and the need for substantial nutritional support to maintain a positive nitrogen balance. RRT was previously performed using peritoneal dialysis, however, this form of therapy is limited by clearance rates and the need for catheter insertion through the abdominal wall: a common donor site or burned area. Over the past two decades a number of RRT modes have been studied in general ICU patients: intermittent hemodialysis (IHD), continuous renal replacement therapy (CRRT), and sustained low-efficiency dialysis (SLED). No consensus exists as to which mode is superior, as each has advantages and disadvantages depending on the clinical scenario (Table 32.7). It has been suggested that CRRT is best suited for those patients demonstrating severe hemodynamic instability, persistent ongoing metabolic acidosis, and large fluid removal requirements. Preliminary reports using CRRT in the thermally injured population have demonstrated improved survival.

The optimal time to initiate RRT in the thermally injured patient with AKI has not been determined. Traditional thresholds, i.e. absolute indications, used to initiate dialysis in the setting of chronic renal failure, are less relevant in the thermally injured patient. Burn injury predisposes to organ failure, catabolism causes increased urea generation, large open wounds result in electrolyte shifts, and nephrotoxic agents are often required as treatment. Although very early initiation of RRT in ICU patients has not clearly been demonstrated to improve outcome, preliminary evidence exists

<table>
<thead>
<tr>
<th>Table 32.7</th>
<th>Advantages and disadvantages of intermittent hemodialysis (IHD) and continuous renal replacement therapy (CRRT)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>I. Advantages</strong></td>
<td><strong>Disadvantages</strong></td>
</tr>
<tr>
<td>Rapid clearance of acidosis, uremia, potassium, and certain toxins</td>
<td>Slow</td>
</tr>
<tr>
<td>Patient mobility</td>
<td>Immobility</td>
</tr>
<tr>
<td>Can perform without anticoagulation</td>
<td>More frequent need for anticoagulation</td>
</tr>
<tr>
<td>Reduced exposure to artificial membrane</td>
<td>Continuous exposure to artificial membrane</td>
</tr>
<tr>
<td><em>Reduced incidence of hypothermia</em></td>
<td><em>Interventions required to prevent hypothermia</em></td>
</tr>
<tr>
<td>Masks fever temporarily</td>
<td>Masks fever continuously</td>
</tr>
<tr>
<td>Less blood loss from monitoring and/or filter clotting</td>
<td>Greater potential blood loss from monitoring and/or filter clotting</td>
</tr>
<tr>
<td>Lower costs in most centers</td>
<td>Higher costs in most centers</td>
</tr>
<tr>
<td>Less risk of dialysate compounding errors</td>
<td>Greater risks of replacement fluid and/or dialysate compounding errors</td>
</tr>
<tr>
<td><em>Less removal of amino acids, endogenous hormones, and cofactors</em></td>
<td><em>Increased removal of amino acids, endogenous hormones, and cofactors</em></td>
</tr>
<tr>
<td><strong>II. Disadvantages</strong></td>
<td><strong>Advantages</strong></td>
</tr>
<tr>
<td>Rapid solute and fluid shifts</td>
<td>Gradual solute and fluid shifts</td>
</tr>
<tr>
<td>–hemodynamic instability</td>
<td>–greater hemodynamic stability</td>
</tr>
<tr>
<td>–disequilibrium syndrome</td>
<td>–no or little risk of disequilibrium syndrome</td>
</tr>
<tr>
<td>–worsens brain edema</td>
<td>–no worsening of brain edema</td>
</tr>
<tr>
<td>Frequent need for fluid or nutritional restrictions</td>
<td>Less need for fluid or nutritional restrictions</td>
</tr>
<tr>
<td>Only allows for intermittent adjustment of prescription; less control of uremia, acidosis, phosphate, and fluid balance</td>
<td>Allows for continuous titration and integration of renal support with other ICU care and treatment goals</td>
</tr>
<tr>
<td>In many centers, requires a dialysis nurse and other resources that may limit ability to provide extended run-times and/or daily therapy in selected patients</td>
<td>Procedure performed by ICU nursing staff overall better clearance of uremia, correction of acidosis, and removal of excess fluid</td>
</tr>
<tr>
<td><em>Even with high flux membranes, removes fewer ‘middle’ molecules</em></td>
<td><em>When configured to use convection as its primary mechanism of solute clearance, removes more ‘middle molecules’</em></td>
</tr>
</tbody>
</table>

to suggest a more aggressive approach to RRT initiation in the thermally injured patient.\textsuperscript{57,58} A recent consensus suggested that RRT in critically ill patients with AKI begins before the development of extreme metabolic derangements or other life-threatening events.\textsuperscript{16}

An additional theoretical benefit of continuous hemofiltration is the removal of proinflammatory mediators, which may be associated with the development of multiple organ failure.\textsuperscript{99} The experimental and clinical data suggest that the rate of hemofiltration and the biologic nature of the filters affect the overall results.\textsuperscript{100} Currently there are insufficient data to recommend continuous hemofiltration solely on the basis of removal of inflammatory mediators. Future randomized prospective studies may resolve this theoretical benefit.

Major advances in the treatment of the thermally injured individual have been accomplished over the past four decades. Early aggressive resuscitation coupled with early excision has significantly reduced the early complications of burn injury, including renal insufficiency. This is exemplified by the fact that prior to 1965 there were no reported survivors from acute renal failure following burn injury. Although the incidence of acute renal insufficiency following burn injury has been reduced, the disorder is still clinically apparent following prolonged delayed initial resuscitation and following the development of sepsis. Therefore, a physician must constantly review the global physiological state of a thermally injured patient and anticipate conditions that may affect the renal system, so that a stepwise approach to the diagnosis and treatment may be initiated. Currently there are no pharmacological agents that prevent or treat AKI, therefore the best treatment option is prevention. Should renal insufficiency develop, RRT should be initiated early to prevent an edematous state and before extreme metabolic derangements occur.

**Further reading**


Access the complete reference list online at [http://www.expertconsult.com](http://www.expertconsult.com)
References


Introduction

Over 500,000 people are burned and seek medical care in the United States every year; most of these have minor injuries and are treated in the outpatient setting. However, approximately 50,000 burns per year (10%) are moderate to severe and require hospitalization for treatment. Some of these will require critical care for at least part of their hospitalization, and some for months. About 4000 die each year from complications related to the burn. Burn deaths generally occur in a bimodal distribution, either immediately after the injury, or weeks later due to multiple organ failure, a pattern similar to all injury-related deaths.

Morbidity and mortality from burns are decreasing in incidence. Recent reports revealed a 50% decline in burn-related deaths and hospital admissions in the USA over the last 20 years. The declines were likely most affected by prevention efforts, with fewer potentially fatal burns, and improved critical care and wound management for those who still sustain the injury. In 1949, Bull and Fisher reported 50% mortality rates for children aged 0–14 years with burns of 49% of total body surface area (TBSA), 46% TBSA for patients aged 15–44, 27% TBSA for those aged between 45 and 64, and 10% TBSA for those 65 and older. These dismal statistics have improved, with the latest studies reporting a 50% mortality for >95% TBSA burns in children 14 years and under, 75% TBSA burns in adults, and around 30% TBSA in the elderly. Therefore, a healthy young patient with almost any size burn should be expected to live, whereas the prospects for those who are older are certainly improving with modern wound treatment and critical care techniques.

Critical illness in burned patients is most commonly associated with sepsis. In a pediatric burn population with massive burns >80% TBSA, 17.5% of the children developed sepsis, defined as bacteraemia with clinical signs of infection. Mortality in the whole group was 33%, most of whom succumbed to multiple organ failure. Some were bacteremic and ‘septic,’ but the majority were not. These findings highlight the observation that the development of severe critical illness and multiple organ failure is often associated with infection, but it is by no means required to develop this syndrome. What is required is an inflammatory focus, which in severe burns is the massive skin injury that requires inflammation to heal.

It is postulated that progression of patients to multiple organ failure exists in a continuum with the systemic inflammatory response syndrome (SIRS). Nearly all burn patients meet the criteria for SIRS as defined by the consensus conference of the American College of Chest Physicians and the Society of Critical Care Medicine. It is therefore not surprising that severe critical illness and multiple organ failure are common in burned patients.

Patients who develop dysfunction of various organs, such as the cardiopulmonary system, renal system, and gastrointestinal system, can be supported to maintain homeostasis until the organs repair themselves or a chronic support system can be established. Critical care may be defined loosely as the process of high-frequency physiologic monitoring coupled with short response times for pharmacologic and procedural interventions. This chapter will describe the organization of specialized burn intensive care units (BICUs), including requirements for personnel and equipment. The techniques used in BICUs will be described, and organ-specific management will be addressed.

Burn intensive care unit organization

Physical plant

Optimally, a BICU should exist within a designated burn center in conjunction with a recognized trauma center, thus providing the capability to treat both thermal and non-thermal injuries. This unit, however, need not be physically located in the same space as that designated for non-burned trauma patients. In fact, the requirements for the care of
wounds in burned patients necessitates additional equipment such as shower tables and overhead warmers, and so separate space dedicated to the severely burned is optimal. This space may be located in a separate hospital with established guidelines for transfer.6

The optimal number of beds in the unit may be calculated by the incidence of moderate to severe burns in the referral area, which in the USA is approximately 20 per 100 000 people per year. The Committee on Trauma of the American College of Surgeons and the American Burn Association recommend that 100 or more patients should be admitted to this facility yearly, with an average daily census of three or more patients to maintain sufficient experience and acceptable access to specialized care.8

Most moderate to severe burns with hospital admission will require intensive monitoring for at least the day of admission during the resuscitative phase. Thereafter, approximately 20% will undergo prolonged cardiopulmonary monitoring for inhalation injury, burn shock, cardiopulmonary compromise, renal dysfunction, and the development of SIRS and multiple organ dysfunction syndrome (MODS). In these severely burned patients, the average length of stay in the BICU is approximately 1 day per % TBSA burned. Using an average of 25 days admission for a severely burned patient (20% of the burns, 4/100 000 per capita) and 2 days for those not so severely injured (80%, 16/100 000 per capita), this suggests 132 BICU inpatient days per 100 000 persons in the catchment area. Thus, a 10-bed BICU should serve a population of 3 000 000 sufficiently when considered independently. Space provided should be at least 3000 sq ft, including patient beds and support space for nursing/charting areas, office space, wound care areas, and storage.

Multiply-resistant bacteria and fungi are commonly encountered in the BICU owing to the presence of open wounds. To prevent spread of these organisms to other patients, isolation of burned patients from one another and from other types of patient is often recommended, and should be considered in designing units for this purpose. Single rooms with negative-pressure ventilation should be considered. In addition, strict guidelines for contact precautions in wound care and interventions and hand-washing are highly recommended.

**Personnel**

A BICU functions best using a team approach between surgeons/intensivists, nurses, laboratory support staff, respiratory therapists, occupational and physical therapists, mental health professionals, dietitians, and pharmacists (Box 33.1). The unit should have a designated medical director, ideally a burn surgeon, to coordinate and supervise personnel, quality management, and resource utilization. The medical director will usually work with other qualified surgical staff to provide sufficient care for the patients. It is recommended that medical directors and each of their associates be well versed in critical care techniques, and care for at least 50 patients per year to maintain skills.8 In teaching hospitals, two to three residents or other qualified medical providers should be assigned to the 10-bed unit described above. A coverage schedule should be devised to provide 24-hour prompt responses to problems.

**Box 33.1 Assigned burn unit personnel**

- Experienced burn surgeons (burn unit director and qualified surgeons)
- Dedicated nursing personnel
- Physical and occupational therapists
- Social workers
- Dietitians
- Pharmacists
- Respiratory therapists
- Psychiatrists and clinical psychologists
- Prosthetists

**Box 33.2 Consultants for the BICU**

- General surgery
- Plastic surgery
- Anesthesiology
- Cardiothoracic surgery
- Neurosurgery
- Obstetrics/gynecology
- Ophthalmology
- Orthopedic surgery
- Otolaryngology
- Urology
- Radiology
- Pediatrics
- Psychiatry
- Cardiology
- Gastroenterology
- Hematology
- Pulmonology
- Nephrology
- Neurology
- Pathology
- Infectious disease

Nursing personnel should consist of a nurse manager with at least 2 years of intensive care and acute burn care experience, and 6 months of management responsibilities. The rest of the nursing staff in the BICU should have documented competencies specific to the care of burned patients, including critical care and wound care.8 Owing to the high intensity of burn intensive care, at least five full-time equivalent nursing providers are required per ICU bed to provide sufficient 24-hour care. Additional personnel are required for respiratory care, occupational and physical therapy, and other support. A dedicated respiratory therapist for the burn unit at all times is optimal.

Owing to the nature of critical illness in burned patients, complications may arise that are best treated by specialists not generally in the field of burn care (Box 33.2). For these reasons, these specialists should be available for consultation should the need arise.

**Equipment**

The equipment needs of the BICU are those items which are common for all ICUs, and some which are specialized (Box 33.3). Each BICU bed must be equipped with monitors to measure heart rate, continuous electrocardiography, non-invasive blood pressure, invasive arterial and venous blood pressures, end-tidal carbon dioxide monitoring, and right heart cardiac output using dilution techniques or data derived from arterial pressure tracings. Continuous arterial blood oxygen saturation measurement is also required, but continuous mixed venous saturation monitoring or the technical equivalent is optional. Equipment to measure weight and body temperature should also be standard. Oxygen
as the patient is following the anticipated course. At other times this is not the case, and procedural or pharmacologic intervention is beneficial. Physiologic monitoring is then used further to determine the adequacy of the interventions. The following is a survey of monitoring techniques used in the BICU.

Cardiovascular monitoring

Arterial lines

Hemodynamic monitoring is directed at assessing the results of resuscitation and maintaining organ and tissue perfusion. Currently used measures are only estimates of tissue perfusion, as the measurement of oxygen and nutrient transfer to cells cannot be made directly at the bedside. Instead, global physiologic measures of central pressures still serve as the principal guides.

Measurement of arterial blood pressure is the mainstay for the assessment of tissue perfusion. In critical illness, this measurement can be made using cuff sphygmomanometers; however, in practice this technique is not useful because the measurement is episodic, and placement of these cuffs on burned extremities is problematic. Diastolic pressures can also be artificially elevated in the elderly and obese. Instead, continuous monitoring for hemodynamic instability through the use of intra-arterial catheters is generally preferable while in the ICU for a prolonged period. Lines are typically placed in either the radial or the femoral artery. The radial artery is the preferred site for most critically ill patients because of safety with the dual arterial supply to the hand should a complication occur. However, it has been shown that radial artery catheters are inaccurate in the measurement of central blood pressure when vasopressors are used and are notoriously inaccurate in children because of greater vascular reactivity. For these reasons, we recommend femoral arterial blood pressure measurement in most burned patients.

For arterial catheters, systolic, diastolic, and mean arterial pressures should be displayed continuously on the monitor screen. Either systolic or mean arterial pressure can be used to determine adequacy of pressure, although a mean arterial pressure >70 mmHg is considered a more accurate description of normal tissue perfusion on the whole. Reasons for this include the finding that as the arterial pressure wave traverses proximally to distal, the systolic pressure gradually increases and the diastolic pressure decreases; the mean pressure determined by integrating areas under the curve, however, remains constant. The adequacy of the waveform must also be determined, with a diminished waveform indicative of catheter damping, requiring catheter replacement. Care must be taken to ensure that the diminished waveform is not true hypotension, which can be determined using a manual or cycling sphygmomanometer placed on the arm or leg. Exaggerated waveforms with elevated systolic pressure and additional peaks in the waveform (generally only two are found) may be a phenomenon referred to as ‘catheter whip,’ which is the result of excessive movement of the catheter within the artery. Typically, this problem is self-limited, but care must be taken not to interpret typically normal systolic blood pressure values with evidence of catheter whipping as normal, as the effect generally

<table>
<thead>
<tr>
<th>Box 33.3 Equipment for a fully equipped BICU</th>
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<tbody>
<tr>
<td><strong>STANDARD</strong></td>
</tr>
<tr>
<td>- Monitors (heart rate, electrocardiography, blood pressure, cardiac output, oxygen saturation, temperature)</td>
</tr>
<tr>
<td>- Scales</td>
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<tr>
<td>- Ventilators</td>
</tr>
<tr>
<td>- ACLS cardiac cart</td>
</tr>
<tr>
<td>- Laboratory support (blood gas analysis, hematology, chemistry, microbiology)</td>
</tr>
<tr>
<td><strong>SPECIALTY</strong></td>
</tr>
<tr>
<td>- Fiberoptic bronchoscopes</td>
</tr>
<tr>
<td>- Fiberoptic gastroscopes/colonoscopes</td>
</tr>
<tr>
<td>- Dialysis equipment (peritoneal dialysis and hemodialysis)</td>
</tr>
<tr>
<td>- Portable plain radiography</td>
</tr>
<tr>
<td>- Computed tomography/fluoroscopy/angiography</td>
</tr>
<tr>
<td>- Indirect calorimeters</td>
</tr>
</tbody>
</table>

availability and at least two vacuum pumps must be present for each bed.

Ventilatory equipment must also be available for all beds. The availability of a number of types of ventilator is optimal, including conventional ventilators with the capability to deliver both volume-targeted and pressure-targeted breaths as well as high-frequency ventilators that are oscillatory and/or percussive in design. An emergency cardiac cart containing advanced cardiac life support (ACLS) medications and a battery-powered electrocardiograph/defibrillator must be present on the unit. Infusion pumps to deliver continuous medications and intravenous/intra-arterial fluids must also be readily available. A laboratory providing blood gas analysis, hematology, and blood chemistry should be located on site. Microbiologic support to complete frequent, routine bacterial cultures should also be present.

Available specialty equipment should include various sizes of fiberoptic bronchoscope for the diagnosis and treatment of pulmonary disorders, as well as personnel versed in these techniques. Fiberoptic gastrosopes and colonoscopes for gastrointestinal complications are also necessary. For renal support, equipment to provide peritoneal dialysis, intermittent or continuous hemodialysis and hemofiltration should be available. Portable radiographic equipment for standard chest/abdominal/extremity radiographs must be immediately available. Equipment for computed tomography (CT), fluoroscopy, and angiography should be available in other parts of the hospital. Indirect calorimeters to measure metabolic rate are preferable. Overhead warmers and central heating with individualized ambient temperature controls must be available for each room as a specialized requirement.

Hemodynamic monitoring in the burn intensive care unit

Most burned patients follow an anticipated course of recovery, which is ‘monitored’ in the ICU by measuring physiologic parameters. Experienced clinicians assess these physiologic measures in a repeated and sequential fashion to discern when potential interventions may be initiated to improve outcomes. Often no intervention will be necessary
overestimates pressures. Again, use of mean arterial pressures as the principal guideline for the assessment of blood pressure is optimal, as the effects of catheter whip or other problems with intra-arterial monitoring are then diminished.

Complications associated with arterial catheters include distal ischemia associated with vasospasm and thromboembolism, catheter infection, and arterial damage/pseudoaneurysm during insertion and removal. Although these complications are uncommon, the results can be devastating. Physical evidence of ischemia in the distal hand or foot should prompt removal of the catheter and elevation of the extremity. If improvement in ischemic symptoms is not seen promptly (within an hour), angiography and intervention should be considered. Should thromboembolism be found, the clot can be removed with operative embolectomy or clot lysis at the discretion of the treating physician. If, during angiography, extensive arterial damage is found with ischemia, operative repair may be indicated.

Evidence of catheter infection hallmarked by purulence and surrounding erythema should instigate removal of the catheter, which will often suffice. With continued evidence of infection, antibiotics and incision and drainage of the site should be entertained. Great caution must be exercised to avoid arterial bleeding if an incision is made over the catheter site. If a pseudoaneurysm is encountered after arterial catheterization and removal without signs of distal ischemia, compression with a vascular ultrasound device until no further flow is seen in the pseudoaneurysm will often alleviate the problem without operative intervention.

Cardiac output measurement

Pulmonary artery catheters placed percutaneously through a central vein (internal jugular, subclavian, or femoral) and ‘floated’ into the pulmonary artery through the right heart have been used extensively in hemodynamic monitoring in ICUs. By measuring the back pressure through the distal catheter tip ‘wedged’ into an end-pulmonary branch, an estimate of left atrial pressure can be measured. In addition, dyes or isotonic solutions injected into a proximal port can be used to determine cardiac output from the right heart. These data are used to estimate preload delivery to the heart, cardiac contractility, and afterload against which the heart must pump, which then directs therapy at restoration of hemodynamics. These catheters are used in ICUs under conditions of unexplained shock, hypoxemia, renal failure, and monitoring of high-risk patients.

The use of pulmonary artery catheters, however, has come under scrutiny from reports indicating no benefit from their use. A study of 5735 critically ill adults in medical and surgical ICUs showed an increase in mortality and use of resources when pulmonary artery catheters were used. Most of these patients had medical conditions. The authors of this report suggested that their results should prompt a critical evaluation of the use of pulmonary artery catheters under all conditions. This was followed by a clinical trial in the UK which showed no benefit to the use of pulmonary artery catheters in a general ICU setting. These data then suggest that this modality has little utility in today’s practice. In fact, over the past few years, the use of pulmonary artery catheters has significantly diminished except in special circumstances such as unexpected response to treatment such as volume replacement for oliguria. Even in this condition, new technology based on arterial waveform analysis gives an estimate of cardiac output and end-diastolic volume, which generally gives enough information to guide appropriate therapy.

The base deficit is a value calculated using the Henderson-BICU Hasselbach equation based on the relationship between pH, pCO₂, and serum bicarbonate:

\[
\text{pH} = 6.1 + \log(\text{HCO}_3^-)/(\text{pCO}_2)(0.03)
\]

The base deficit is the stoichiometric equivalent of base required to return the pH to 7.40. Base deficit is routinely calculated on blood gas analysis, and provides a reasonable estimate of the degree of tissue anoxia and shock at the whole body level, particularly in hemorrhagic shock. A rising base deficit indicates increasing metabolic acidosis, and may stratify risk of mortality in patients after major trauma. The same can be said for the use of base deficit in burn resuscitation in burned patients. These studies showed a correlation of higher base deficit and increased mortality, and some have suggested this value is a better monitor of resuscitation than the time-honored monitors of urine output and arterial blood pressure. Recent studies in burned patients showed that base deficit was higher in non-survivors during resuscitation, although the authors could not identify a specific boundary for the effect. Despite its utility as an indicator of shock, base deficit remains a non-specific indicator of metabolic acidosis, and may be elevated with alcohol, cocaine, and methamphetamine use. Interpretation may be difficult under these circumstances.

Lactate is another common measure used to determine adequacy of tissue perfusion. Under acute low-flow conditions, cells transition from primarily aerobic metabolism to anaerobic metabolism for energy production (ATP). A byproduct of anaerobic metabolism is lactic acid. Under ischemic conditions, then, plasma lactate concentration will increase, leading to a decrease in pH. Measurement of lactate is commonly performed to determine the adequacy of generalized perfusion; increases suggest ischemia. Investigators showed that lactate does increase (along with base deficit) in burned patients during resuscitation, and higher levels are associated with poorer outcomes. Later in the course, however, lactate concentrations must be used with some caution, as elevated levels do not necessarily indicate ischemia. Under hypermetabolic conditions, which are common in the severely burned, pyruvate dehydrogenase activity is sufficiently inefficient such that lactate levels might be elevated without ischemia. Isolated elevations of lactate should then be interpreted with caution, and confirmation of ischemia or shock by physical or other laboratory findings should be sought.

Transesophageal echocardiography

Transesophageal echocardiography has been used for a number of years as an intraoperative monitor in high-risk cardiovascular patients. It has not been used extensively in other critically ill patients because of the lack of available expertise and paucity of equipment. Since this device can be used as a diagnostic tool for the evaluation of hemodynamic function, it stands to reason that it could be used as a monitor in critically ill severely burned patients. A report documented the use of transesophageal Doppler measurements of cardiac output in a series of severely burned patients.
showing that intravascular volume and cardiac contractility are significantly diminished the first day after burn in spite of high-volume resuscitation.23 For the monitoring of burn resuscitation, it seems that most use urine output; however, the question has been raised whether this is the proper measure. Investigators in China asked whether esophageal Doppler monitoring of heart function might be an improvement. They studied 21 patients with massive burns (79 ± 8% TBSA burned) who were resuscitated with a goal of 1.0 mL/kg/h. They found that cardiac output was predictably low after injury and increased linearly with time by increases in preload and contractility and decreased afterload. However, changes in cardiac output were most closely associated with increased cardiac contractility and decreased afterload rather than increases in preload. Additionally, urine output was not closely associated with cardiac output.22 These results call into question the validity of urine output as the primary measure of adequacy of resuscitation. Perhaps this is not the best method? A similar study by investigators in Sweden studying the role of cardiac function measured by echocardiography and myocyte damage measured by troponin abundance in the serum showed that half their patients had myocardial damage during resuscitation that was universally associated with some temporary cardiac wall motion abnormality. However, systolic function was not adversely affected.23 We look for further work in the future with regard to the optimal method of assessment of resuscitation; for the present, however, urine output remains the standard.

### Mechanical ventilation

The use of mechanical ventilation is central to the function of the BICU. Burned patients are at risk for airway compromise, necessitating endotracheal intubation and mechanical ventilation for a number of reasons. Inhalation of smoke causing damage to the upper airway, development of massive whole-body edema restricting the airway, and hypoxia occur relatively frequently during the initial resuscitation, all of which may require endotracheal intubation and mechanical ventilation. Thereafter, acute lung injury and acute respiratory distress syndrome may intervene, necessitating pulmonary support with ventilators. This section will deal briefly with indications for intubation, common ventilator strategies, and monitoring of mechanical ventilation.

#### Indications for intubation

Intubation entails passing an endotracheal tube from either the nose or the mouth through the pharynx into the trachea. This tube is then connected to a mechanical ventilator to cause inspiration and passive exhalation through the lungs. Indications for intubation in burned patients are in general to improve oxygenation and ventilation, or to maintain gas exchange during clinical conditions expected to compromise the airway (Table 33.1).

#### Ventilatory modes

The complexity of mechanical ventilators has increased dramatically since the first generation of volume cycle ventilators used in the 1960s. The development of positive end-expiratory pressure (PEEP) to maintain functional residual capacity was followed by the development of modes using partial ventilatory support, such as intermittent mandatory ventilation in the 1970s. Efficient microprocessors were then developed that permitted modes of ventilation such as pressure support ventilation, time-cycled pressure control ventilation, and inverse ratio ventilation. Most recently, new processors have been used to combine modes of ventilation, such as pressure support ventilation, time-cycled pressure control ventilation, and open lung strategies such as airway pressure-release ventilation, with some success (Fig. 33.1). However, even with these new developments, the function of mechanical ventilators remains identical to those first used. Whether these new ventilators have had any appreciable effect on mortality remains to be fully elucidated, though new evidence suggests that choice of mode may make a difference.

The principal difference in mechanical ventilation from spontaneous ventilation, which each of us use every minute of the day, is the effect of positive pressure as opposed to normal physiologic negative pressure. The use of positive pressure improves gas exchange by recruiting alveoli and increasing functional residual capacity (i.e., the number and volume of open alveoli at the end of expiration), thus improving ventilation perfusion mismatch and reducing intrapulmonary shunting of blood past non-ventilated lung areas (Fig. 33.2). Adverse effects of positive-pressure ventilation lie in its propensity to produce trauma to the airways (barotrauma) and its effects on intrathoracic pressure, which can impede venous return to the heart and thus reduce cardiac output.

#### Control and assist control ventilation

The volume control modes are volume-cycled settings that deliver a preset tidal volume at a minimum respiratory rate and inspiratory flow rate regardless of the patient’s own respiratory efforts (Fig. 33.3). Of the two, the control mode will not trigger with patient effort. This mode is typically very uncomfortable for patients owing to ventilator–patient dyssynchrony, with use limited to patients under general anesthesia or heavy sedation. The assist control mode differs in that a breath will be delivered regularly according to a prescribed rate, but will also deliver a breath upon patient negative-pressure effort to open a flow valve, at which time the ventilator will fire, allowing the patient to control his or her own ventilatory rate with a preset minimum rate as a back-up. This mode is typically used in heavily sedated patients who cannot generate enough tidal volume under pressure support modes or intermittent mandatory

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**Table 33.1 Clinical indications for intubation**

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{PaO}_2$ (mmHg)</td>
<td>&lt;60</td>
</tr>
<tr>
<td>$\text{PaCO}_2$ (mmHg)</td>
<td>&gt;50 (acutely)</td>
</tr>
<tr>
<td>P/F ratio</td>
<td>&lt;200</td>
</tr>
<tr>
<td>Respiratory rate</td>
<td>&gt;40</td>
</tr>
<tr>
<td>Respiratory/Ventilatory failure</td>
<td>Impending</td>
</tr>
<tr>
<td>Upper airway edema</td>
<td>Severe</td>
</tr>
</tbody>
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Figure 33.2 A schematic of intrapulmonary shunting. Blood comes into the lung and then divides into capillaries and passes close to alveoli, where gas exchange occurs. In the case of alveolar collapse, the passing blood does not undergo gas exchange, and thus returns to the pulmonary vein unchanged (low oxygen concentration, blue color). This then mixes with oxygenated blood from the aerated alveoli (high oxygen concentration, red color) to return to the heart and the periphery. In effect, more collapsed lung equates to less oxygenation through this process.

ventilation mode, or in those patients in whom the clinician wishes to minimize the work of breathing. It must be noted, however, that the work of breathing can be increased dramatically in patients with excessive ventilator triggering; increasing the minimum number of breaths to match the patient’s effort can minimize this effect. When using this mode of ventilation, it is important to monitor lung compliance by measuring serial peak and plateau pressures for diagnostic purposes as well as minimization of barotrauma.

**Time-cycled pressure control ventilation**

Volume-cycled ventilation delivers a set volume of air regardless of pressure required. In the case of poor lung compliance, such as in acute respiratory distress syndrome (ARDS), this mode could lead to excessive ventilatory pressures and significant airway injury. For this reason, time-cycled pressure control ventilation was developed; this delivers inspiration at a given flow rate to a preset pressure. The breath is terminated at a set cycle time, not on the basis of volume of flow as is the case with volume-controlled ventilation. Therefore, pressure control has the advantage of limiting inspiratory pressure despite changes in compliance. It also has the disadvantage of a variable tidal volume during dynamic changes in lung compliance, which can lead to inadequate or excessive minute ventilation if compliance respectively worsens or improves. This puts the onus on the provider to monitor changes in compliance to make appropriate changes in the preset pressure to compensate. This differs from the volume-cycled mode, which requires monitoring of peak and plateau pressures. Another disadvantage is that this mode is not as well tolerated by awake patients as other modes.
Critical care in the severely burned: organ support and management of complications

Intermittent mandatory ventilation

Intermittent mandatory ventilation (IMV) was developed to allow spontaneous ventilation interspersed with volume-cycled or time-cycled pressure control mechanical ventilation. It was developed initially as a method to wean patients from the ventilator by depending more and more on patient effort for ventilation. The addition of a synchronized mode (SIMV) to avoid placing a mechanical breath on top of a spontaneous patient breath greatly improved this mode. It has the advantage of maintaining some patient work in breathing to preserve respiratory strength when mechanical ventilation is required, and as a weaning tool to progressively increase patient effort while reducing mechanical support in preparation for discontinuing mechanical ventilation. This method can be problematic in patients with low pulmonary compliance, and the IMV mode may not allow for sufficient spontaneous tidal volumes due to extremely limited inspiratory capacity. The addition of pressure support to augment spontaneous ventilatory efforts can be used (Fig. 33.4).

Pressure support ventilation

Pressure support ventilation is a patient-triggered pressure-limited flow-cycled ventilatory mode (Fig. 33.5). Each pressure support breath is triggered by patient negative-pressure effort, at which time a valve opens producing a high-flow pressure-limited breath. The breath ends when the patient’s inspiratory demand falls below a preset limit, allowing spontaneous respiration and complete patient control. It also differs from the other modes in that it is flow-cycled as opposed to volume- or pressure-cycled. Because this mode is triggered and completed entirely by patient response, it cannot be used in patients with decreased respiratory drive, such as paralyzed patients and those who are heavily sedated. This mode has a number of advantages because of improved synchrony with patient effort. It can be used to provide full ventilatory support by setting a flow and pressure such...
that an adequate tidal volume is delivered. It can also be used effectively during weaning by reducing the pressure incrementally to allow for progressively greater patient effort. Caution must be exercised when reducing ventilatory support so that a sufficient tidal volume is still delivered to maintain adequate ventilation.

Inverse ratio ventilation
Inverse ratio ventilation is a mode of ventilation designed to improve oxygenation at a given level of inspired oxygen. Conventional ventilation uses the times of inspiration and expiration at a ratio of 1:4 or 1:2, giving a longer time for expiration, as it is generally a passive process. Inverse ratio ventilation reverses this ratio to give a longer inspiratory time (1:1 or 2:1) by using rapid inspiratory flow rates and decelerating flow patterns during the inspiratory phase. The effect of inverse ratio ventilation is to increase mean airway pressures and thus recruit alveoli in an effect similar to PEEP. Secondly, in severe lung disease, ventilation in the lung is unequal due to peribronchial narrowing. Thus, some under-ventilated alveoli that are actually open are not able to exchange gases efficiently, increasing the intrapulmonary shunt and reducing arterial oxygenation. Inverse ratio ventilation can improve this by selective air-trapping or intrinsic PEEP in these compromised air spaces. Inverse ratio ventilation can be done either in a volume-cycled or a time-cycled pressure ventilation mode, but it is most commonly used with pressure controlled ventilation to reduce peak airway pressures.

The beneficial effects of inverse ratio ventilation have been questioned. It may be that the same effect can be gained simply by increasing peak airway pressures with PEEP or peak inspiratory pressures. In fact, some studies have showed no benefit of inverse ratio ventilation compared to conventional volume ventilation in terms of oxygenation. These studies did show some slight improvements in ventilation (PaCO₂). For this reason, inverse ratio ventilation cannot be recommended except in the setting of ARDS refractory to other therapies.

High-frequency oscillatory ventilation
High-frequency oscillatory ventilation (HFOV) is a mode of ventilation that delivers subtidal, high-frequency oscillatory breaths at a constant mean airway pressure (mPAW), otherwise described as ‘CPAP with a wiggle.’ It is thought to maintain open alveoli by recruiting collapsed portions of diseased lung and applying the equivalent of continuous positive airway pressure used during conventional ventilation. Optimizing mean airway pressure limits peak pressure, thereby making this a ‘lung-protective’ mode. A recent randomized prospective trial in adult patients with ARDS demonstrated that HFOV resulted in brief improvements in oxygenation although mortality and complication rates were not different. In burned patients, one center reported early success while facilitating early excision and grafting with intraoperative use. However, this same group recently showed that in burned patients with inhalation injury this method often failed secondary to hypercapnia rather than hypoxia. It stands to reason, therefore, that this method might be tried in those with oxygenation difficulties, and perhaps continued if hypercapnia is less of an issue.

High-frequency percussive ventilation
High-frequency percussive ventilation (HFPV) is a pressure-limited, time-cycled mode of ventilation that delivers subtidal pressure-limited breaths at a high frequency (400–800 breaths/min) superimposed on a conventional inspiratory and expiratory pressure-controlled cycle (10–30 breaths/min). The purported advantages are to mobilize airway secretion and casts for better pulmonary toilet, and to provide adequate gas exchange at lower airway pressures. This method of ventilation has been tested primarily in burned patients with inhalation injury, and was first reported in 1989. In this study, HFPV was used as a salvage therapy in patients with inhalation injury and as primary therapy in another group. Improvements in oxygenation and a lower rate of pneumonia were seen. Another study documented an improvement in mortality in burned patients with inhalation injury treated with HFPV compared to historical controls. Other outcomes in this study were significant decreases in the work of breathing, and lower inspiratory pressures in addition to improvements in oxygenation and the rate of pneumonia. This method of ventilation seems to be particularly efficacious in the treatment of inhalation injury, particularly in comparison to HFOV.

A recent study was performed in severely burned ventilated patients testing the effects of low tidal volume conventional ventilator strategy against an HFPV ventilator strategy. This study again found differences in improved oxygenation early in the course, but no differences in mortality or other outcome measures. However, the study did show that the need for ventilator ‘rescue,’ defined as the need for changing ventilator modes due to inadequate oxygenation or ventilation despite maximizing the mode, was higher in the ARDSnet group, thus favoring the use of HFPV in this population (i.e. less rescue indicated). At the very least, these data show that HFPV is useful in the population of burned patients, and may in fact be beneficial by reducing the risk of pulmonary failure at least in the short term.

Airway pressure-release ventilation
Airway pressure-release ventilation (APRV) is a mode that delivers continuous positive airway pressure with a time-cycled pressure-release phase (to allow for expiration). Advantages of APRV include optimization of mean airway pressure, limitation of peak inspiratory pressures, and integration of spontaneous breathing independent of the ventilatory cycle. These characteristics allow for an open lung, with optimal alveolar recruitment and as a result, improved ventilator–perfusion mismatching. This mode is best utilized in patients who are permitted to breathe spontaneously with negative pressure induced by diaphragmatic contraction, which aids in lung recruitment of areas that were previously atelectatic. This is in contrast to conventional positive-pressure ventilation, where positive pressure from within the bronchus through the volume of air is distributed preferentially down the path of least resistance to areas of the lung that are already well aerated, predisposing them to overdistension and barotrauma. Theoretically, this mode of ventilation is the ideal lung-protective strategy. APRV gained popularity in the late 1990s, and is becoming the preferred mode of ventilation in many centers. Small prospective trials suggest that APRV is associated with fewer ventilator days,
improved gas exchange, decreased atelectasis, improved hemodynamic performance, and decreased sedative administration compared to conventional modes in non-burned populations. Some recent data in trauma patients refutes this, although this paper suffered from a significant lack of statistical power. Nonetheless, this mode is being increasingly used in burn units around the world, but to date no prospective trials have been reported.

Inhaled nitric oxide

Nitric oxide (NO) is a short-lived gaseous product of endothelial cells that is a powerful local vasodilator. Because it is a gas, this product can be delivered through the endotracheal tube to areas of ventilated lung where it can provide localized pulmonary vasodilation. Thus, areas of ventilated lung can receive more blood flow to reduce intrapulmonary shunting and improve oxygenation. This compound has been used extensively in neonates and children with hypoxemic respiratory failure, with beneficial effect. It has also been used in ventilated burned children to improve oxygenation. Although nitric oxide therapy has received considerable attention as a potential therapeutic option in severe pulmonary disease, no reports to date have documented improved mortality or other clinical outcomes in spite of improvements in oxygenation. For this reason, its use cannot be recommended outside of rescue therapies or a clinical trial.

Limiting ventilator-induced lung injury (VILI)

Ventilator-induced lung injury (VILI) is the result of injurious ventilator settings that lead to a combination of barotrauma, volutrauma, atelectrauma (repeated opening and closing of alveoli), or chemotrauma (paracrine inflammatory effects). VILI is a common complication of mechanical ventilation and results in pulmonary edema, subcutaneous emphysema, interstitial emphysema, or pneumatoceles. In a volume-cycled mode, large tidal volumes along with elevated peak and plateau pressures have been implicated in inducing VILI. It is conceivable that limiting airway pressures may reduce morbidity. Early reports showed no clear benefit of pressure-limited ventilation, which was accomplished by giving lower tidal volumes more frequently to maintain minute ventilation, and accepting a higher PaCO₂ value and lower arterial pH, which is termed permissive hypercapnia. Criticism of these trials lay in their low enrollment and lack of power to show differences. As an answer to this critique, a large multicenter trial documented improved survival and increased ventilator-free days in the first 28 days in the ICU in patients with ARDS treated with low tidal volumes (6 mL/kg predicted body weight) versus traditional tidal volumes (12 mL/kg predicted body weight). In fact, this study was stopped early by the data safety committee because of the benefits incurred to the treated group. Suspected reasons for the improvements seen in this trial contrary to the earlier trials was the number of subjects enrolled as well as the defined protocol to limit both tidal volumes (volutrauma) and plateau pressures < 30 cmH₂O (barotrauma). Interestingly, this trial demonstrated decreased inflammatory markers, specifically IL-6, in the low-tidal volume arm suggesting a third possible mechanism of benefit (chemotrauma). Theoretically, the low-tidal volume strategy subscribes to the theory of ARDS, which dictates that small healthy areas of lung exist adjacent to diseased and collapsed areas. In the conventionally treated group higher tidal volumes and pressure are distributed only to open healthy alveoli, therefore the barotrauma of high pressures is delivered to this ‘healthy’ lung, thereby increasing the damage there and worsening outcomes. In burned patients, decreased chest wall compliance, presence of smoke inhalation injury to the upper airways, and massive fluid administration are just a few variables that make effective gas exchange challenging while optimally minimizing barotrauma. Prospective trials comparing modes of ventilation to minimize VILI are lacking in the burn literature, making it difficult to determine which approach is best suited to this population. One study showed no statistically significant differences in 61 burned patients between a pressure-limited strategy and a conventional strategy for mortality, pulmonary complications, or incidence of pneumothoraces. In the trial comparing HFPV (a pressure-limited strategy) to an ARDSnet-based conventional strategy, a lower incidence of barotrauma was seen in the HFPV group. There was no difference in inflammatory markers between the two strategies. It stands to reason that pressure-limited ventilation strategies (either conventional or high frequency) might be of benefit in burned patients in sufficiently powered studies. One outcome that should certainly be accounted for is the need for adjunctive therapies (rescue treatments), as implied above.

Weaning from mechanical ventilation

Regardless of the mode of ventilation, almost all patients surviving the initial insult will eventually need to be weaned off the ventilator. Clinicians continue to debate the advantages of weaning patients with various forms of mechanical ventilation. Some clinicians prefer to use pressure support ventilation (PSV) with or without SIMV because of the ease with which the level can gradually be reduced. Others maintain that intermittent trials with abrupt cessation of ventilator support while maintaining endotracheal intubation (‘t-tube trials’) result in more rapid weaning. It must be noted that weaning from ventilation depends upon the rate at which the patient recovers from the condition requiring mechanical ventilation and the aggression of the clinician driving the weaning process. In practice, either method of weaning from the ventilator (gradual weaning with pressure support or intermittent t-tube or CPAP trials) will be successful. What will certainly prolong the process are random changes in ventilation parameters without a directed plan.

Monitoring of mechanical ventilation

For patients on mechanical ventilation, sedatives and paralytics for the endotracheal tube or other conditions often impair the normal physiologic regulation of ventilation and oxygenation. For these reasons, monitoring of ventilation and oxygenation by the clinician is required.

Ventilation

Arterial CO₂ tension remains the most accurate means of assessing ventilation. This is typically measured by blood gas analysis. After assessment of the pCO₂, ventilatory settings
to adjust minute ventilation can be made to reach the desired level. Another method that has received attention of late is expiratory end-tidal CO₂ monitoring through infrared measurement of CO₂. This technique allows for continuous online determination of end-tidal CO₂, which is an estimate of arterial PaCO₂. For end-tidal CO₂ to equate with PaCO₂ an assumption of a low alveolar–arterial gradient must be made; in patients with healthy lungs this gradient is only 2–3 mmHg. In certain trauma patients, particularly those with head injuries, this gradient remains low and may be used for continuous PaCO₂ monitoring. However, in other critically ill patients the alveolar–arterial gradient may be in a state of flux, calling into question values received from an end-tidal CO₂ monitor. Factors affecting the alveolar–arterial gradient include cardiac output, airway dead space, airway resistance, and metabolic rate; each of these may change in a severely burned patient, particularly those with inhalation injury. For these reasons, end-tidal CO₂ monitoring is not recommended in burned patients for the estimation of PaCO₂.

In general, PaCO₂ varies indirectly with minute ventilation, and so this value must be considered when making ventilator adjustments to alter PaCO₂. Minute ventilation is equal to tidal volume multiplied by respiratory rate. Therefore, PaCO₂ can be adjusted downward by increasing either tidal volume or respiratory rate. In general, respiratory rate should be set between 10 and 20 breaths/min in those who are not neonates, and tidal volume noted that the respiratory rate cannot be increased above 40 breaths/min in those who are neonates, and tidal volume at 6 mL/kg initially. Adjustments can then be made in minute ventilation to optimize PaCO₂, which is usually 40 mmHg. When making these adjustments, it should be noted that the respiratory rate cannot be increased above 40 breaths/min in those who are not neonates, and tidal volume should be minimized to avert VILI.

When plateau airway pressures are >30 mmHg the ventilated lung is relatively non-compliant, indicative of ARDS or pulmonary edema. In this situation, ‘permissive hypercapnia’ is a strategy that may be used to reduce barotrauma. This strategy seeks to limit peak and plateau airway pressures by reducing tidal volumes to allow for respiratory acidosis (PaCO₂ > 45 mmHg, arterial Ph < 7.30). This strategy was used to some extent in the trial investigating the efficacy of pressure-limited ventilation on improving outcomes in critically ill ventilated patients.

Oxygenation

Like the adequacy of ventilation, oxygenation has been classically determined using the partial pressure of O₂ in arterial blood. In general, a PaO₂ value of 60 mmHg has been considered sufficient. Another frequently used monitor is pulse oximetry, which is an optical measurement of oxygenated hemoglobin in pulsatile vessels. Using differences in absorption of red and infrared light, the percentage of oxygenated hemoglobin in the arteries can be calculated. Shortcomings of this technique are that methemoglobin and carboxyhemoglobin are falsely measured as oxygen-saturated hemoglobin, which is common initially in patients with smoke inhalation injury. Otherwise, this is a very accurate technique for the determination of oxygen content in arterial blood, as 97% of oxygen is carried to the tissues via hemoglobin. This assertion has been corroborated by in vitro studies⁴⁸ that showed the accuracy of pulse oximetry to within 2–3% of oxyhemoglobin levels. The major limitations of this technique lie in the insensitivity to changes in pulmonary gas exchange. Because of the shape of the oxyhemoglobin dissociation curve, when the SaO₂ exceeds 90% and the PaO₂ is >60 mmHg, the curve is flat and changes in PaO₂ can change considerably with little change in SaO₂. Regardless, it is assumed that an SaO₂ value >92% is indicative of adequate oxygenation. An advantage to oxygen saturation measurements that should not be overlooked is that it is a continuous direct measure that is immediately available, whereas blood gas measurement of PaO₂ is by nature intermittent.

A commonly used parameter to assess the adequacy of oxygenation is the ratio of PaO₂ to FiO₂ (P/F ratio). As such, the P/F ratio is one of the criteria utilized to diagnose acute lung injury (ALI) and ARDS. A P/F ratio >300 along with bilateral infiltrates seen in chest radiograph combined with the absence of a cardiogenic cause of the infiltrates (determined either clinically or via pulmonary capillary wedge pressure < 18 cmH₂O) is required for the diagnosis of acute lung injury.⁴⁹ A P/F ratio <200 is required for a diagnosis of ARDS. One major flaw when utilizing the P/F ratio is the fact that mean airway pressure, a key determinant in oxygenation, is not incorporated. Thus, two patients on two different levels of ventilator support (one on minimal PEEP and another on maximal PEEP) are indistinguishable based on this parameter. To account this variable, the oxygenation index may be used:⁴⁰

\[
\text{Oxygenation Index (OI)} = \frac{(\text{Mean airway pressure} \times \text{FiO}_2)}{\text{PaO}_2}
\]

This parameter is particularly helpful in determining a patient’s oxygenation status in relation to the level of ventilator support: the higher the number, the worse the level of oxygenation. Generally, an OI >20 should be a cause for concern.

Initial ventilator settings to assure adequate oxygenation are usually 40% oxygen in the inspired gas with 5 mmHg PEEP. This amount of PEEP is used to mimic the normal physiologic pressures in non-intubated subjects. When oxygenation begins to decline, initial maneuvers are to increase the fractional inspired oxygen (FiO₂) to >40% and possibly to 100%. Concentrations of oxygen >60% are considered toxic to airway epithelium, and other means to increase oxygenation should be employed. This should consist initially of increasing the level of PEEP incrementally until the desired level of oxygenation is reached while keeping the FiO₂ to <60%. Once a level of 15–20 mmHg of PEEP is reached, other means of increasing oxygenation will need to be employed. These consist of inverse ratio ventilation, HFOV, HPFV, APRV with and without inhaled nitric oxide, etc. which are described above.

Organ system failure and management

Etiology and pathophysiology

As stated earlier, it was hypothesized that organ dysfunction commonly seen in the critically ill exists in a continuum with SIRS. Certain patients with SIRS will go on to develop multiple organ dysfunction syndrome (MODS), which is characterized by non-fatal signs of organ system dysfunction,
Figure 33.6 Progression to multiple organ failure. All severely burned patients have the systemic inflammatory response syndrome (SIRS). A subset of these will develop signs and symptoms of multiple organ dysfunction syndrome (MODS). Still fewer will go on to develop multiple system organ failure (MSOF).

Box 33.4 Theories for the development of multiple organ failure

- Infectious causes
- Macrophage theory
- Microcirculatory hypothesis
- Endothelial–leukocyte interactions
- Gut hypothesis
- Two-hit theory

such as renal insufficiency or ventilator dependence. A subset of these patients will go on to develop frank organ failure, termed multiple system organ failure (MSOF), which often leads to death (Fig. 33.6). What is required for the development of SIRS is inflammation, which in the severely burned emanates primarily from the burn wound. Factors associated with progression from the systemic inflammatory response syndrome to multiple organ failure are not well explained, although some of the responsible mechanisms in some patients are recognized. Occasionally, failure of the gut barrier with penetration of organisms into the systemic circulation may incite a similar reaction. However, this phenomenon has only been demonstrated in animal models, and it remains to be seen if this is a cause of human disease.

A number of theories have been developed to explain the progression to multiple organ failure (Box 33.4). One of these is the infection theory, which incriminates uncontrolled infection as the major cause. In the severely burned patient these infectious sources most likely emanate from invasive wound infection or lung infections (pneumonias). As organisms proliferate out of control, endotoxins and other antigens are liberated from Gram-negative bacterial walls, and exotoxins from Gram-positive and Gram-negative bacteria are released. Their release causes the initiation of a cascade of inflammatory mediators called cytokines through activation of PAMP (pathogen-activated molecular pathway) receptors such as Toll-like receptors 2, 4, and 9, as well as the recruitment of inflammatory cells which, if unchecked, can result in organ damage and progression toward organ failure.

Cytokines are a group of signaling proteins produced by a variety of cells that are thought to be important for host defense, wound healing, and other essential host functions. Although cytokines in low physiologic concentrations preserve homeostasis, excessive production may lead to widespread tissue injury and organ dysfunction. Four of these cytokines, tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), interleukin-6 (IL-6) and interleukin-8 (IL-8) have been most strongly associated with sepsis and multiple organ failure in burns. The primary detraction to this theory is that many patients, including burned patients, can develop multiple organ failure without identified infection. It seems that inflammation from the presence of necrotic tissue and open wounds can incite a similar inflammatory mediator response to that seen with endotoxin. The mechanism by which this occurs, however, was not well understood, but recent evidence suggests that this is due to activation of the cytokine cascade through DAMPs (damage-associated molecular pathways), which might in fact be antigens associated with liberated mitochondria from our own cells. Regardless, it is known that a cascade of systemic events is set in motion either by invasive organisms or from open wounds that initiates the systemic inflammatory syndrome that may progress to multiple organ failure.

Another theory implicates prolonged tissue hypoxia and the generation of toxic free radicals during reperfusion as the primary mediator of end-organ damage. Deficits in resuscitation then lead to areas of the microcirculation throughout the body that receive inadequate nutrients and shift to anaerobic metabolism and formation of superoxides from ATP metabolites. Localized tissue hypoxia might be related to activation of microthrombosis locally with inadequate anti-thrombotic response. This might be plausible, as some investigators showed levels of antithrombin III to be decreased after severe burn. Drotrecogin-α is a purported treatment that may have an effect on this mechanism, but only case reports and small case series have been reported.

The effects of the toxic products of oxygen free radical formation are only now being elucidated. From in vitro models and in vivo animal models, we know that tissues that initially were in shock and are then reperfused produce oxygen free radicals that are known to damage a number of cellular metabolism processes. This occurs throughout the body during burn resuscitation, but the significance of these free radicals in human burn injury is unknown. It was found that free radical scavengers such as superoxide dismutase improve survival in animal models, but these results have not yet been established in humans.

Oxygen free radicals oxidize membrane lipids, resulting in cellular dysfunction. Endogenous natural antioxidants, such as vitamins C and E, are low in patients with burns, suggesting that therapeutic interventions may be beneficial. Serum nitrate levels correlate well with multiple organ failure scores in critically ill patients, implying a role for this constellation of events in SIRS/MODS. Recent studies in burned patients showed that levels of nitrates were associated with the severity of burn whereas those of antioxidants were not. This might justify augmentation of antioxidants in those with severe burns.

The last two theories revolve around the role of the gut in the generation of organ failure, and the ‘two-hit’ theory of multiple organ failure. For years, investigators have implicated the gut as the ‘engine’ of organ failure, which is associated with loss of gut barrier function and translocation.
of enteric bacteria and their toxic metabolites. Bacterial translocation has been shown to occur after burn in patients.50 These bacteria and their products then activate the inflammatory cells described above, culminating in organ failure. The relevance of gut-mediated bacterial translocation to human disease, however, has been hotly debated. No studies have shown clearly whether bacterial translocation is the cause of SIRS/MODS, probably because so far, investigators have been unable to control bacterial translocation effectively during shock in humans; thus, a cause and effect relationship cannot be established. The ‘two-hit’ theory ascribes a summation of insults to the development of organ failure. Each of the insults alone is inadequate to cause the response, but one or more of these insults can ‘prime’ the inflammatory response system described above such that another normally insignificant injury causes the release of toxic mediators that end in multiple organ failure.

In the end, it is likely that some part of all of these theories is a cause for MODS in patients with burns, and probably the relative contribution of each is unique in each patient. Therefore, a single solution is unlikely, which should be kept in mind when devising strategies to improve care and outcomes.

Diagnosis of sepsis

Presuming that sepsis has two potential causes, infection or inflammation without infection, reliable detection of those with some component of infection is warranted. Our difficulty in severe burns is delimiting this, as traditional screening indicators for infection such as temperature and white blood cell count are unreliable because of massive hypermetabolism and inflammation associated with recovery and healing.49,50 Potential does exist for elevations in procalcitonin to be associated with a higher risk of infection, this being linked to pathogen infection presumably through PAMPs rather than DAMPs. An interesting study from Iran examined the role of WBC, sedimentation rate, C-reactive protein, and procalcitonin in diagnosing sepsis in the severely burned. The authors found that procalcitonin was the only test among them with any distinguishing capacity, which in fact was quite accurate.51 We look for further studies in the near future to further define this relationship.

Prevention

This brief outline of the potential pathophysiology and causes of burn-induced critical illness and multiple organ failure demonstrates the complexity of the problem. Because different cascade systems are involved in the pathogenesis, it is so far impossible to pinpoint a single mediator or system that initiates the event. Thus, as the mechanisms of progression are not well known and specific treatments cannot be accurately devised, it seems that prevention is likely the best solution. The current recommendations are to prevent the development of organ dysfunction, and to provide optimal support to avoid conditions that promote its onset. In burned patients this can be accomplished most reliably through expeditious wound closure, rapid mobilization of the patient, and prompt identification and treatment of early infections.

Course of organ failure

Even with the best efforts at prevention, the systemic inflammatory syndrome that is ubiquitous in burn patients may progress to organ failure. Experience with the severely burned dictates that virtually all burned patients will display the traditional signs and symptoms of SIRS, including tachycardia, tachypnea, increased white blood cell count, etc. Thereafter, various organ systems may begin to show signs of dysfunction. Generally, these will begin in the renal and/or pulmonary systems and progress in a systematic fashion through the liver, gut, hematologic system, and central nervous system. The development of multiple organ failure does not inevitably lead to mortality, however, and effort to support the organs until they recover is justified.

Renal system

Pathophysiology

Acute renal failure (ARF) is a potentially lethal complication of burns. Despite substantial technical developments in dialysis to replace the function of the kidneys, mortality meets or exceeds 50% for all critically ill patients who develop acute renal failure.52 Interestingly, mortality associated with ARF undergoing hemodialysis for frank failure in the critically ill has not improved significantly for over 40 years. The same can be said for renal failure requiring dialysis specifically in the severely burned. The cause of death in these critically ill patients was not uremia because of advances in dialysis, but primarily sepsis and cardiovascular and pulmonary dysfunction.

With the advent of early aggressive resuscitation after burn, the incidence of renal failure coincident with the initial phases of recovery has diminished significantly in the severely burned. However, a second period of risk for the development of renal failure 2–14 days after resuscitation is still present, and is probably related to the development of sepsis.53 Acute renal failure, usually in the form of acute tubular necrosis (ATN), is characterized by deterioration of renal function over a period of hours to days, resulting in the failure of the kidney to excrete nitrogenous waste products and to maintain fluid and electrolyte homeostasis. It may be caused by a number of factors interfering with glomerular filtration and tubular resorption. In burned patients, the causes can be generally narrowed to renal hypoperfusion, nephrotoxic insults from pharmacologic treatments (e.g. aminoglycosides or intravenous contrast agents), or sepsis.

Ischemic renal failure is the more common of the two causes, and is induced by hypoperfusion from an imbalance between vasoconstrictive and vasodilatory factors acting on the small renal vessels during low-flow states. Decreased flow to the renal cells directly alters endothelial cell function, reducing the production of and response to vasodilatory substances. The renal medulla is the portion of the kidney most sensitive to hypoxia, and the damage is initially to the renal tubular cells. The outer medulla and proximal tubules have high oxygen requirements, and the resulting ischemia causes swelling of tubular and endothelial cells, with necrosis, apoptosis, and inflammation evident on histologic examination. These changes lead to further vascular congestion and decreased blood flow, leading to more cell loss and further decrements in renal function.
After the initiating event, tubular function and GFR decrease to reduce urine production. The progression of ARF is commonly divided into three phases: initiation, maintenance, and recovery, and can be oliguric (urine output <400 mL/day) or non-oliguric (urine output >400 mL/day) in nature. Patients with non-oliguric ARF have a better prognosis than those with oliguric renal failure, probably due in large measure to the decreased severity of the insult and the fact that many have drug-associated nephrotoxicity or interstitial nephritis.

Once ARF is established, pharmacologic improvement of renal blood flow will not reverse the injury. Agents such as dopamine, which was commonly used in the past to dilate renal arterioles and increase renal blood flow via dopamine receptors, have been shown to be mostly ineffective. Recently, the potent dopamine-1 receptor agonist fenoldopam has garnered some interest as an agent to improve renal perfusion and outcomes. A recent meta-analysis of randomized controlled trials demonstrated that low-dose fenoldopam (0.03–0.09 µg/kg/min) may be of benefit in reducing the need for renal replacement therapy and hospital mortality when used in septic patients with either established ARF or at high risk for ARF in a mixed ICU population. Its use in this setting has been reported in a non-controlled study in burned patients, with improvement in renal function (increased urine output, decreased serum creatinine) without any hypotension at the low dose. Further work will need to be done in the burn population to fully determine its efficacy.

Diuretic therapies, such as mannitol and loop diuretics, have been used extensively in patients with acute renal failure to increase urine flow, and protect the kidney from further ischemic damage. Mannitol can reduce cellular swelling in the proximal tubule and increase intratubular flow, thus potentially decreasing intratubular obstruction and further renal dysfunction. Mannitol has been previously recommended along with vigorous volume replacement and sodium bicarbonate for the treatment of early myoglobinuric acute renal failure. However, recent evidence suggests lack of benefit and a call for re-evaluation of this practice. Loop diuretics also increase intratubular flow rates, and can convert an oliguric state to a non-oliguric state, thereby making clinical management of renal failure easier. In general, although patients with non-oliguric renal failure are generally easier to manage from a volume standpoint, there is no evidence that conversion from an oliguric to a non-oliguric state improves outcomes.

The initial care of patients with ARF is focused on reversing the underlying cause, and correcting fluid and electrolyte imbalances. Renal failure is heralded by a decrease in urinary output. Volumes of urine < 1 mL/kg/h may indicate the onset of ARF. This failure may be due to prerenal causes, which are typically decreased renal blood flow from hypoperfusion, or intrinsic renal causes, which are associated with medications or sepsis. Differentiation between these etiologies can be made with laboratory examinations (Table 33.2). Prerenal etiologies are associated with concentrated urine (urine osmolarity >400 mmol/kg), decreased urinary sodium concentrations, and decreased fractional excretion of sodium. Intrinsic renal causes will be associated with more dilute urine with higher sodium concentrations. These tests should be performed before diuretics are used, as this treatment will increase urinary sodium and decrease urine osmolality even in prerenal conditions. In general, urine osmolality and urinary sodium concentrations are primarily used for these determinations because of the ease of measurement. In terms of clinical utility, renal dysfunction is often a mixture of prerenal and intrinsic causes, making treatment decisions difficult.

Should these tests reveal a prerenal cause, volume replacement should ensue to prevent further renal ischemia. The physical examination and invasive monitoring, if deemed appropriate, should guide this volume replacement. The decision to administer or remove fluids may prove difficult, however, as both strategies have detrimental consequences if followed inappropriately. Although volume replacement is ineffective in restoring renal function once tubular necrosis is established, it remains our most effective prophylactic strategy, and is generally the place to start with the onset of renal failure.

Owing to the wide variation in the definition of acute renal failure, reporting an accurate incidence as well as resultant outcomes has been problematic. In an effort to help resolve this problem and standardize the classification of acute renal failure (now referred to as acute kidney injury or AKI), the Acute Dialysis Quality Initiative (ADQI) developed and reported the RIFLE (Risk, Injury, Failure, Loss of function, End-stage Renal Disease) criteria. More recently, the Acute Kidney Injury Network (AKIN) proposed a modified version of the RIFLE system because of a number of identified limitations. These revised criteria are intended to simplify the definition and make it more clinically applicable. According to the AKIN criteria, stage 1 AKI is defined by ‘an abrupt (within 48 hours) reduction of kidney function currently defined as an absolute increase in serum creatinine of more than or equal to 0.3 mg/dL, a percentage increase in serum creatinine of more than or equal to 50% (1.5-fold from baseline), or a reduction in urine output (documented oliguria of less than 0.5 mL/kg per hour for more than 6 hours).’ Stages 2 and 3 are the same as RIFLE – Injury and Failure, respectively.

In burned patients, investigators recently showed that the incidence and outcomes of > 20% TBSA burned patients with AKI using RIFLE criteria was 24% (12% Risk, 8% Injury, and 5% Failure). Associated mortality was 14%, which increased with increasing RIFLE class (7% normal, 13% Risk, 40% Injury, and 83% Failure). Renal dysfunction occurred within 7 days in 55% of affected patients and completely recovered in all survivors; pulmonary dysfunction was

### Table 33.2 Laboratory tests to distinguish prerenal from intrinsic renal failure

<table>
<thead>
<tr>
<th>Examination</th>
<th>Prerenal</th>
<th>Intrinsic renal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine osmolality (mMol/kg)</td>
<td>&gt;400</td>
<td>&lt;400</td>
</tr>
<tr>
<td>Urinary sodium (mEq/dL)</td>
<td>&lt;20</td>
<td>&gt;4.0</td>
</tr>
<tr>
<td>FENa (%)*</td>
<td>&lt;1</td>
<td>&gt;2</td>
</tr>
</tbody>
</table>

*FENa, fractional excretion of sodium, calculated as (U/PNa / U/Pc) × 100, where U is urinary concentration, and P is plasma concentration. Na is sodium and Cr is creatinine.
present in all. Sepsis was a possible aggravating factor in acute kidney injury in 48%. They concluded that AKI is common after severe burn, develops within days of injury, and parallels other organ dysfunction. These data confirm earlier studies showing that the development of renal failure is associated with dismal outcomes; however, minor dysfunction does not necessarily correlate to progression and mortality, giving hope to therapies designed to maintain renal function after severe burn.

Another study examined the incidence of renal dysfunction in burned patients, defined by serum creatinine > 1.4 mg/dL; 39% of patients admitted to the ICU developed renal insufficiency, of which 33% underwent renal replacement therapy. Associated mortality in those with renal insufficiency was 44%; those who developed renal insufficiency within 5 days of injury had higher mortality than those with later onset. Of interest, all survivors regained normal renal function later in their course. The next study investigated early markers of renal dysfunction, and found that elevations in urinary microalbumin and malondialdehyde (both 3–4-fold) were present in all with eventual renal dysfunction. These may come to be indicators of risk for injury that can be acted upon early in the course to prevent progression to more severe degrees of failure and therefore improve outcomes. The last study investigated the role of continuous venovenous haemofiltration (CVVH) in the treatment of renal dysfunction after severe burn. The investigators compared a population of patients treated with high-volume CVVH (at least 50 mL/kg/h) compared to non-treated historical controls, and found that both 28-day mortality and overall mortality were improved by 50% with this therapy. A multicenter randomized controlled trial comparing early high-volume CVVH (70 mL/kg/h) to standard care is under way in this high-risk population (ClinicalTrials.gov Identifier: NCT01213914).

After ensuring adequate volume status, every effort should be made to prevent other causes of renal injury. All nephrotoxins should be discontinued or avoided. Hyperkalemia that may develop can be treated with resins, glucose and insulin, and sodium bicarbonate in the presence of metabolic acidosis. Medications eliminated through the kidney should be adjusted. Once the diagnosis of ARF is established, consideration can be given to diuretic therapy or the early initiation of continuous venovenous hemofiltration, especially if it is determined that the patient is volume overloaded. Reducing the volume of fluid given can also alleviate volume overload in burned patients. These patients have increased insensible losses from the wounds which can be roughly calculated at 3750 mL/m² TBSA wound plus 1500 mL/m² TBSA total. Reducing the infused volume of intravenous fluids and enteral feedings below the expected insensate losses may alleviate some of these problems. Reducing potassium administration in the enteral feedings and giving oral bicarbonate solutions can minimize electrolyte abnormalities. Almost invariably, severely burned patients require exogenous potassium because of the heightened aldosterone response, which results in potassium wasting; therefore, hyperkalemia is rare even with some renal insufficiency.

Intermittent dialysis remains a viable replacement therapy for severe ARF in the hemodynamically normal ICU patient, although this may be changing. The indications for dialysis are edema and volume overload or electrolyte abnormalities not amenable to other treatments. In recent years, continuous renal replacement therapies have emerged as yet another option for critically ill patients with ARF (Fig. 33.7). The advantages of continuous treatment over intermittent include more precise fluid and metabolic control, decreased hemodynamic stability, and the enhanced ability to remove injurious cytokines. Disadvantages include the need for anticoagulation and heightened surveillance. Bleeding problems are particularly prevalent in burned patients during anticoagulation.

Peritoneal dialysis is another option for acute renal failure in burned patients. Catheters can be placed at the bedside with near-continuous exchanges to improve electrolyte and volume overload problems. The capital required for this treatment is minimal. Hypertonic solutions are used to

Figure 33.7 The probability of successful weaning with intermittent mandatory ventilation, pressure support ventilation, intermittent trials of spontaneous breathing, and once-daily trials of spontaneous breathing (Kaplan–Meier curves). After adjustments for baseline characteristics (Cox proportional hazards model), the rate of successful weaning with a once-daily trial of spontaneous breathing was 2.83 times higher than that with intermittent mandatory ventilation (p < 0.006) and 2.05 times higher than that with pressure support ventilation (p < 0.04). (Reprinted with permission from Esteban et al. N Engl J Med 1995; 332:350. Copyright Massachusetts Medical Society.)
remove fluid volume, and the concentrations of potassium and bicarbonate are modified to produce the desired results. The dwell time is usually 30 minutes, followed by drainage for 30 minutes. This treatment can be repeated in cycles until the problem is resolved. For maintenance, 4–6 such cycles a day with prolonged dwell times (1 hour) is usually sufficient during the acute phase. This treatment is known to occur in burned patients, but has not received a significant amount of study.

**Pulmonary system**

Mechanical ventilation in the severely burned generally takes place for three reasons: airway control during the resuscitative phase, airway management for smoke inhalation, and for the development of acute lung injury and ARDS. The first is for airway control early in the course with the development of massive whole-body edema associated with the great resuscitative volumes required to maintain euvolemia. In this situation, the need for mechanical ventilation is not due to lung failure per se, but instead to maintain the airway until the whole-body edema resolves. Once this occurs, usually 2–3 days into the course, extubation can be accomplished. Ventilator management during this phase is routine. The second primary reason for mechanical ventilation is for airway management early in the course of smoke inhalation. Another chapter in this book will deal specifically with this issue. The third is the development of hypoxemia. Severe burns are known to be associated with hypoxemia and the development of acute lung injury (ALI) and its more severe counterpart, ARDS. The clinical manifestations are dyspnea, severe hypoxemia, and decreased lung compliance with radiographic evidence of diffuse bilateral pulmonary infiltrates. These conditions exist as a continuum from ALI, which is a mild form, to its most severe form, which is dense ARDS. These conditions have been defined by the American-European Consensus Conference Committee, and are listed in Box 33.5. These definitions are relatively simple, and are used in other critically ill populations. The rest of the discussion will be related to ALI and ARDS.

**Epidemiology and pathophysiology**

ALI and ARDS occur as a result of injury to the lung, which can be direct through smoke inhalation or pneumonia, or indirect through mediators associated with sepsis. Until recently, most studies of ALI and ARDS reported mortality rates between 40% and 60%. Now, in trauma patients, the most recent mortality rate for ARDS was 14%; in addition, the incidence of ARDS fell by 50% in a matched patient population. Thus, we can say conclusively that the incidence has gone down; what has changed is the method of management, suggesting that reducing the risk of further harm is the most effective treatment for this condition at present.

ALI and ARDS occur because of damage to the endothelium and lung epithelium. It is speculated that the products of inflammation, such as cytokines, endotoxin, complement, and coagulation system products, induce the changes that are characteristic of ALI and ARDS. The acute phase of ALI is characterized by an influx of protein-rich edema fluid into the air spaces as a consequence of increased permeability of the alveolar–capillary barrier. The importance of endothelial injury and increased vascular permeability to the formation of pulmonary edema is well established (Fig. 33.8). Epithelial injury is also of great importance. In fact, the degree of alveolar epithelial injury is an important predictor of outcome.

Neutrophils are likely to play a role in the pathogenesis of ALI. Histologic studies of lung specimens obtained early in the course demonstrate marked accumulation of neutrophils in the alveolar fluid. However, it must be stated that ALI and ARDS develop in patients with profound neutropenia, and some animal models of ARDS are neutrophil independent, implying that neutrophils may be nothing more than bystanders in the inflammatory process. The effects of ventilator injury on the development and progression of ALI and ARDS are now firmly established. Previous studies focused on the potential damaging effects of high oxygen concentrations on lung epithelium. Evidence suggests that mechanical ventilation at high pressures injures the lung, causing increased pulmonary edema in the uninjured lung and enhanced edema in the injured lung. Alveolar overdistension and cyclic opening and closing of alveoli associated with high ventilatory pressures is also potentially damaging to the lung.

After the development of ALI and ARDS, some patients have a rapid recovery over a few days. Others progress to fibrotic lung injury; the alveolar space becomes filled with mesenchymal cells, extracellular proteins, and new blood vessels. The finding of fibrosis on histologic analysis correlates with increased mortality.

**Box 33.5 Definitions of acute lung injury and acute respiratory distress syndrome**

- Acute onset
- Bilateral infiltrates on chest radiography
- Pulmonary artery wedge pressure <18 mmHg
- Acute lung injury (ALI) if PaO$_2$/FiO$_2$ is <300 but >200
- Acute respiratory distress syndrome (ARDS) if PaO$_2$/FiO$_2$ is <200

**Figure 33.8** Typical timeline for progression to ARDS. Patients are typically intubated for airway compromise and operative intervention. At day 4 or 5 after severe burn, oxygenation will deteriorate, requiring higher inspired concentrations of oxygen. These measures will soon fail with the introduction of decreased lung compliance requiring higher inspired airway pressures. Only then will infiltrates begin to appear on the chest X-ray (CXR).
In non-fatal cases of ARDS, the lung heals by proliferation of type II epithelial cells, which begin to cover the denuded basement membrane and differentiate into type I epithelial cells, thus restoring normal alveolar architecture and increasing the fluid-transport capacity of the alveolar epithelium. Alveolar edema is resolved by active transport of sodium from the distal airspace into the interstitium by intact alveoli. Soluble protein is removed primarily by diffusion between alveolar cells, and insoluble protein is eliminated by endocytosis and transcytosis by alveolar epithelial cells and phagocytosis by macrophages.

The severely burned are unique among patients who develop ALI and ARDS. Because direct injury to the lung from smoke inhalation is common, often patients will present with respiratory insufficiency and relative hypoxia caused by increased capillary permeability, ciliary dysfunction, and interstitial edema associated with the chemical injury of smoke. A few days later, the damaged and necrotic respiratory mucosa begins to slough, causing bronchial plugging and atelectasis, further worsening the clinical condition. However, it is not usually until 4–8 days into the course of injury that severe hypoxemia and ARDS develop in burned patients, a scenario not unlike that in other types of patient who develop ALI and ARDS, such as after abdominal sepsis or multiple blunt trauma. It stands to reason that smoke inhalation is associated with the development of ARDS, but perhaps this association is related to the inflammation associated with the injury in addition to that rendered by the burn wound. In fact, it was shown that the degree of inhalation injury was not associated with the development of ARDS in burned patients. It may be, then, that smoke inhalation and ALI/ARDS are two separate conditions which are interrelated.

**Treatment**

The treatment of ALI and ARDS is largely supportive until the healing processes described above can be accomplished. A careful search for potential underlying causes should ensue, including attention to potentially treatable causes such as intra-abdominal infections, pneumonia, line sepsis, and invasive burn wound infection. An improved understanding of the pathogenesis of ALI has led to the assessment of several novel treatment strategies, including changes in mechanical ventilation strategies, fluid management, surfactant therapy, nitric oxide treatments, and anti-inflammatory strategies.

The most appropriate method of mechanical ventilation for ALI and ARDS has been controversial for some time, though the picture is becoming clearer; the ARDSnet study provided much of this clarity. They reported a 22% decline in mortality in patients with ALI and ARDS treated with tidal volumes of 6 mL/kg compared to those treated with conventional volumes of 12 mL/kg. In this study, peak airway pressures could not exceed 30 cmH2O in the lower tidal volume group, and a detailed protocol was used to adjust the fraction of inspired oxygen and PEEP. These results were different from those of previous smaller studies showing no improvement with pressure-limited ventilation. Potential reasons for the discrepancy between the NIH study and the others are as follows: the NIH study had the lowest tidal volume of the three studies, respiratory acidosis was allowed in the NIH study, with sodium bicarbonate treatment if necessary to maintain homeostasis; and the NIH study had more patients, and so may have been more sufficiently powered to show differences between treatment groups.

Positive end-expiratory pressure has clearly been shown to benefit patients with ALI and ARDS; however, the optimum level has been controversial. The best effect of PEEP is to increase functional residual capacity, or the number of open alveoli at the end of expiration. However, the use of prophylactic PEEP therapy in patients at risk for ALI showed no benefit for the treatment group compared to controls.

A study of PEEP therapy aimed at raising the level of PEEP above the lower inflection point on pressure-volume curves to prevent alveolar closure in addition to low tidal volumes and pressure controlled inverse ratio ventilation showed improved mortality compared to a control group managed with conventional ventilation. Drawbacks to this study were the unusually high mortality (71%) in the control group, and improvements in mortality for the treatment group compared to controls could only be determined at hospital day 28, which was not appreciated at hospital discharge.

Inhaled nitric oxide is an effective pulmonary vasodilator with effects localized to ventilated areas of the lung, thus directing more blood to the functional areas of the lung. The conceivable effect, then, is to diminish the fraction of blood shunted through the lungs without oxygenation, thereby improving pulmonary venous oxygenation. Observational studies suggest that inhaled nitric oxide might be beneficial in the treatment of ARDS by improving oxygenation without increased ventilatory pressures and reducing barotrauma. However, randomized trials testing this hypothesis have been disappointing. In the most recent large study, inhaled nitric oxide therapy did not reduce mortality or reduce the duration of mechanical ventilation. Improvements in oxygenation were seen, but the effects were not sustained. The reported experience with this modality in burns is only anecdotal.

Another modality commonly used in ICUs for refractory hypoxemia is prone positioning. This is based on the rationale that dependent areas of the lung in ARDS have the most blood flow and the most edema, thereby leading to a greater mismatch of blood flow and aerated lung, and greater shunting of blood past un aerated areas; hence blood returns to the heart un oxygenated. By placing the patient in the prone position for a prescribed period, the previously aerated lung now receives a greater portion of blood flow as directed by gravity. This approach almost always results in improved oxygenation, but as with nitric oxide, has not been shown to be of benefit for mortality in prospective trials. However, two recent meta-analyses have demonstrated significant mortality benefit in those with severe hypoxemia. Thus, it appears that in certain subpopulations these types of therapies may be considered after carefully balancing risk versus benefit.

Glucocorticoids have been used in the treatment of ARDS because of the inflammatory nature of the disease in a number of trials, the results of which are for the most part contradictory and equivocal. To add fuel to the fire, the most recent large trial of glucocorticoid treatment of early severe ARDS showed an improvement in ventilator days and MODS scores. Others have shown benefit of glucocorticoid when used in the later fibroproliferative phases of the disease to
good effect. It is likely that some population exists in which glucocorticoid treatment is of benefit for those with ARDS – however, we do not think it is burns. This type of therapy may be treacherous in burned patients at risk for invasive burn wound infection, but might be considered upon complete burn wound closure.

Cardiovascular system

Principles

Treatment of cardiovascular responses after burn requires an understanding of cardiovascular physiology and the effects of treatment. One of the hallmarks of serious illness is the direct link between cardiac performance and patient performance. The four determinants of cardiac function and hence tissue perfusion of blood at the whole body level are the following:

- Ventricular preload or end-diastolic muscle fiber length;
- Myocardial contractility or strength of the heart muscle;
- Ventricular afterload, or the degree of resistance against which the heart must pump; and
- Heart rate and rhythm.

A thorough comprehension of the effects of each of these components on heart function is required in order to initiate effective treatments for burned patients with cardiovascular abnormalities.

Preload

Preload is defined as the force that stretches the cardiac muscle prior to contraction. This force is composed of volume that fills the heart from venous return. Because of the molecular arrangement of actin and myosin in muscle, the more the muscle is stretched with incoming venous volume, the further it will contract. This is best demonstrated on a Frank–Starling curve (Fig. 33.9), which was first described by Otto Frank in a frog heart preparation in 1884; Ernest Starling extended this observation in the mammalian heart in 1914. The relationship demonstrated in the Frank–Starling curve justifies the use of preload augmentation by volume resuscitation to increase cardiac performance. However, when the end-diastolic volume becomes excessive cardiac function can decrease, probably by overstretch of the muscle fibers such that the contractile fibers are pulled past each other, thereby reducing the contact required for contractile force. The preload required to reduce cardiac function in experimental settings is in excess of 60 mmHg, which is rarely encountered in patients.

Preload is estimated clinically either by central venous pressure or by pulmonary artery wedge pressure.

Cardiac contractility

The force with which the heart contracts is referred to as cardiac contractility. It is directly related to the number of fibers contracting, and will be diminished in patients with vascular occlusive disease of the myocardium who lose muscle fibers due to infarction and ischemia, and in burned patients during the acute resuscitation. Calculating the left ventricular stroke work from pulmonary artery catheter-derived values provides the best estimate of cardiac contractility, and can be calculated with the following formula:

\[
LVSW = SV (MAP – PCWP) 	imes 0.0136
\]

where LVSW is left ventricular stroke work, SV is the stroke volume (cardiac index + heart rate), MAP is mean arterial pressure, and PCWP is pulmonary capillary wedge pressure.

Afterload

Afterload is the force that impedes or opposes ventricular contraction. This force is equivalent to the tension developed across the wall of the ventricle during systole. Afterload is measured clinically by arterial resistance as an estimate of arterial compliance. Arterial resistance is measured as the difference between inflow pressure (mean arterial) and outflow pressure (venous) divided by the flow rate (cardiac output):

\[
SVR = (MAP – CVP)/CO
\]

where SVR is systemic vascular resistance, MAP is mean arterial pressure, CVP is central venous pressure, and CO is cardiac output.

Heart rate and rhythm

For the heart to function properly the electrical conduction system must be intact, so as to provide rhythmic efficient contractions to develop sufficient force to propel blood through the circulatory system. For example, if the heart rate approaches 200 beats/min, the heart will not have time to fill completely, thereby reducing myocardial fiber stretch and reducing heart function. Also, if frequent premature ventricular contractions are present, the heart will not perform as well for similar reasons. Heart rate and rhythm are monitored continuously as a routine in all critically ill patients using electrocardiography.

Effects of burn on cardiac performance

Severe burns affect cardiac performance in a number of ways. The first is to reduce preload to the heart through volume loss into the burned and non-burned tissues. It is for this
reason that volumes predicted by resuscitation formulas must be used to maintain blood pressure and maintain hemodynamics. In addition, severe burn induces myocardial depression characterized by a decrease in tension development and velocities of contraction and relaxation. Cardiac output is then reduced. These effects are most evident early in the course of injury during resuscitation; however, they are followed shortly thereafter by a hyperdynamic phase of increased cardiac output caused primarily by a decrease in afterload through vasodilation and an increase in heart rate.

**Hemodynamic therapy: preload augmentation**

When hypotension or other signs of inadequate cardiac function (i.e., decreased urine output) are encountered, the usual response is to augment preload by increasing intravascular volume. This is a sound physiologic approach based on the Frank–Starling principle, and should be the first therapy for any patient in shock. Intravascular volume can be increased with either crystalloid or colloid to increase the central venous pressure and pulmonary capillary wedge pressure to a value between 10 and 20 mmHg. The adequacy of this therapy can be monitored by the restoration of arterial blood pressure, a decrease in tachycardia, and a urine output >0.5 mL/kg/h.

Some caution must be exercised when augmenting preload for hemodynamic benefit in burned patients. Excessive volume administration may lead to significant interstitial edema and volume overload, with the development of peripheral and pulmonary edema. These changes can lead to conversion of partial-thickness burns to full-thickness injuries in the periphery, and can cause significant respiratory problems. Judicious use of fluid administration after hemodynamics are restored with spontaneous diuresis will usually alleviate this problem; however, at times pharmacologic diuresis will be required.

**Hemodynamic therapy: inotropes**

If volume replacement is insufficient to improve hemodynamics in burned patients in shock, inotropes may be required. These inotropes generally consist of adrenergic receptor agonists, although phosphodiesterase inhibitors that increase intracellular cAMP levels to increase myocyte Ca\(^{2+}\) levels or digoxin that acts to increase myocyte Ca\(^{2+}\) levels by inhibiting the Na+/K+ pump can also be used to improve myocardial contractility.

Dopamine is a commonly used inotropic agent which has both α- and β-adrenergic properties. The α effects are seen primarily at higher doses (10–20 μg/kg/min), while the β effects are seen at all doses. Therefore, dopamine can be thought of as an ‘inconstricctor,’ because it has both intrinsic and vasoconstrictive properties. Other inotropes in this class include epinephrine and norepinephrine. One caveat to the use of these inotropic agents is that myocardial oxygen consumption increases, which may affect areas of the heart that are ischemic. Dopamine has generally fallen out of favor of late, to be replaced with more specific inotropes and vasoconstrictors. Dobutamine is a commonly used inotrope which has effects limited to β-adrenergic stimulation; thus, cardiac contractility is increased without vasoconstriction. The effect is to improve cardiac output generally without specific splanchnic or renal effects.

Agents with primary effects on the α-adrenergic receptor can be used to induce vasoconstriction and increase blood pressure. These agents consist of norepinephrine and phentylephrine, and can be used effectively during septic shock or neurogenic shock to increase vascular tone. In burned patients, it is felt that these agents will cause vasoconstriction of the skin circulation and the splanchnic circulation to preserve blood flow to major organs such as the heart and brain. This redistribution in blood flow can cause conversion of partial-thickness skin injuries to full-thickness and result in ischemic injury to the gut. The use of specific vasoconstrictors must be weighed against these effects.

Another vasoconstrictive agent that is being used with more popularity is vasopressin, which is a very potent vasoconstrictor mediated through its own receptor independent of the adrenergic receptors. Levels of vasopressin have been shown to be low in septic shock, and physiologic replacement at 0.02–0.044 U/l/kg/min without titration is used in some burn units to increase mean arterial pressure to good effect. Some investigators found that the use of vasopressin in this condition increased blood pressure, decreased heart rate, and spared norepinephrine dosing when used concomitantly.

**Effects of β-blockade on cardiac performance after severe burn**

One of the responses to severe burn is a dramatic increase in catecholamine production that has been linked to a number of metabolic abnormalities, including increased resting energy expenditure, muscle catabolism, and altered thermoregulation. Propranolol, as a non-specific β-blocker, has been used to reduce heart rate and myocardial work in severe burns. Propranolol administration also reduces peripheral lipolysis and muscle catabolism, which are additional beneficial effects. Consideration should be given to further trials with the use of propranolol to improve outcomes in burned patients.

**Gastrointestinal system**

**Pathophysiologic changes in the gut**

The gastrointestinal response to burn is highlighted by mucosal atrophy, changes in digestive absorption, and increased intestinal permeability. Changes in gut blood flow are related to changes in permeability. Intestinal blood flow was shown to decrease in non-resuscitated animals, a change that was associated with increased gut permeability at 5 hours after burn. This effect was abolished at 24 hours. Systolic hypotension has been shown to occur in the first hours after burn in animals with a 40% TBSA full-thickness injury.

**Clinical changes in the gut after burn**

Given the changes in the gut to burn described above, it is common to see some evidence of gut dysfunction after burn evidenced by feeding intolerance and mucosal ulceration and bleeding, particularly in the stomach and duodenum. Enteral feeding is an important means of providing nutrition to burned patients and has led to a decrease in mortality, but at times the gut will not cooperate. Reduced motility and ileus are common, at times requiring parenteral nutrition to meet caloric needs. At present there is no specific treatment
for burn induced ileus, but it seems that early enteral feeding will prevent some of these potential complications.

Stress ulceration of the stomach and duodenum, on the other hand, can be prevented effectively with antacid therapy. In the 1970s stress ulceration leading to life-threatening hemorrhage was common. The mechanism of injury is related to an imbalance between protective factors such as mucus production, protective prostaglandin output and bicarbonate secretion, and injurious factors such as decreased blood flow and acid production. Gastric ulcers developed in the watershed zones between capillary beds which are worsened by gastric acid-induced injury. With today's use of standard critical care techniques with gastric acid suppression and expeditious wound closure, upper gastrointestinal bleeding is relatively rare. When it occurs, treatment is congruent with upper gastrointestinal bleeding in general, through identification of the bleeding source and control with local techniques or surgery if required.

In the past few years a condition termed abdominal compartment syndrome has arisen. This is associated with massive volume resuscitation, which induces generalized edema in a relatively limited abdominal compartment. It eventuates in decreased gut blood flow and renal blood flow causing oliguria and bowel ischemia. The tragedy is that the early sign of this condition is low urine output, which is commonly addressed by more intravenous fluid, which only worsens the case. The associated physical finding is abdominal distension, and an estimate of intra-abdominal pressure can be obtained by pressure monitoring of the bladder: pressures >30 torr are concerning and should instigate further investigation. Treatments are aimed at reducing intra-abdominal pressures though catheter drainage, or decompressive laparotomy may be considered. Unfortunately, in those with burns >40% TBSA (those at highest risk for abdominal compartment syndrome), decompressive laparotomy has a mortality rate approaching 100%. Therefore, the best treatment for this condition is prevention through judicious resuscitation.

**Endocrinopathies**

Hyperglycemia and insulin resistance are common in the critically ill, and the burned patient is no exception. In 2001, Greet van den Berge reported in a landmark trial that intensive insulin treatment with continuous infusions of insulin aimed at normalizing blood glucose levels between 80 and 110 mg/dL improved mortality, and reduced bloodstream infections and acute renal failure. These studies were among the first to show some benefit of a treatment for all critically ill patients. Since this study, most intensivists throughout the world have gone to a practice of glucose control to a normal range through the use of insulin. This may have other beneficial effects, as investigators have shown anabolic benefit of insulin treatment in burned patients in terms of muscle mass. The particular range to which glucose should be controlled has not been firmly established, however, as the latest large-scale study on glucose control in the ICU did not find a benefit to keeping glucose in the normal range, but a higher range might have been even more beneficial. The caveat to this analysis was that on a post-hoc basis, injured patients had better outcomes with the normal glucose range rather than the higher.

In another landmark trial, cortisol levels were found to be low in many critically ill patients and a mortality benefit accrued with physiologic replacement with hydrocortisone. This study highlighted that hypocortisolemia is at least associated with septic shock and hypotension, and that replacement with hydrocortisone at 50 mg every 6 hours improves outcomes. The same was seen in burned patients in the ICU. It must be noted, however, that the benefits seem to be limited to those with relative adrenal insufficiency assessed by corticotropin stimulation, as seen in the follow-up CORTICUS trial. Regardless, in the case of hypotension not related to hypovolemia in burned patients, cortisol levels and adrenal stimulation should be performed to determine whether relative adrenal insufficiency exists, and treatment with hydrocortisone should ensue.

**Summary**

Improved critical care of the severely burned has reduced mortality over the past two to three decades. This has been in part through the development of specialized units for the care of burned patients which are equipped with the personnel and equipment to deliver state-of-the-art care. Better understanding of the processes of critical illness and multiple organ failure has led to effective prevention strategies and treatment modalities. Further advances in the understanding of mechanisms of the progression from SIRS to multiple organ failure will engender new breakthroughs that can be expected to further improve the outcomes of burned patients.

**Further reading**


References


40. The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network. Comparison


Introduction

The care of the patient with a burn injury is most challenging for the nurse. Care begins with the immediate resuscitation of the patient in the emergency department and continues until the patient is completely rehabilitated. During the initial resuscitation, the role of the nurse is to assess and monitor the patient’s hemodynamic alterations. Fluid resuscitation and nursing management of fluid resuscitation are adequately discussed earlier in this book. Therefore, this chapter will cover other areas where the nurse’s care and management are crucial.

Acute care

Nurses operate in an age of accountability where quality and resource utilization drive healthcare. The public demands and deserves the best possible outcome. Evidence-based practice (EBP) integrates providers’ clinical expertise with the best evidence. It helps nurses structure how to make accurate and timely decisions. It improves the odds of doing the right thing at the right time for the patient. Closing the gap between research and practice affects all aspects of medical care. Workplaces must support the use of EBP by creating structures and processes, building the infrastructure to support EBP.

Practicing nurses today need strong and effective clinical leadership. In addition, in today’s fluid settings, every nurse must be a leader herself/himself, using knowledge and skills to make decisions, and accepting accountability for competent care and safe patient outcomes. Transformational leadership is a method well suited to nursing in the clinical environment. It repositions staff nurses from the bottom of the organization pyramid to the center. Each nurse emerges as a leader as the clinical situation demands. Power is not given away, but rather partnerships develop between nurses at the bedside, and management. Management becomes a partner and resource as opposed to a controlling force. This provides attractive work environments for professional people recognizing the contributions of each individual and giving value to the power necessary for each partner to participate fully.

Pulmonary priorities

Inhalation injury continues to be the most serious and life-threatening complication of burn injury today. Early diagnosis and treatment greatly impact the outcome of care. Impaired gas exchange is a potential problem for patients who have face and neck burns and/or inhalation injury. Inhalation injury may include carbon monoxide poisoning, upper airway injury (heat injury above the glottis), lower airway injury (chemical injury to lung parenchyma), and restrictive defects (circumferential third-degree burn around the chest). Upper airway edema causes respiratory distress and is the primary concern during the initial 24–48 h post-burn phase. Tracheobronchitis, atelectasis, bronchorrhea, pneumonia, and adult respiratory distress syndrome (ARDS) may occur during the acute, post-burn stage either related or unrelated to inhalation injury.

Nursing care of a patient with inhalation injury begins with a detailed history of the accident. Inhalation injury is suspected when the accident occurred in a closed space. Close observation of the patient and frequent respiratory assessments are made throughout the initial and acute phase post-burn. Initially, the patient is observed for hoarseness and stridor, which indicate narrowed airways. Emergency equipment is placed at the bedside to facilitate intubation if necessary. Observing the frequency of cough, carbonaceous sputum, and increased inability to handle secretions may indicate possible inhalation injury and the potential for impaired gas exchange. Other important observations include respiratory rate, breath sounds, and the use of accessory muscles to aid in respiratory effort, nasal flaring, sternal retractions, increased anxiety, and complaint of shortness of breath. Disorientation, obtundation, and coma may be due to significant exposure to smoke toxins such as carbon monoxide or cyanide. These conditions are managed emergently with 100% oxygen.

Bronchoscopy may be done early to diagnose inhalation injury as well as facilitate airway clearance. Humidified oxygen should be readily available and applied to patients who have evidence of impaired gas exchange (especially pediatric patients). Aggressive nasotracheal suction may be indicated if the patient has difficulty with managing secretions either because of the increased amount of secretions and/or the decreased effectiveness of the cough. In addition,
aggressive pulmonary toilet, including turning, coughing, and deep breathing, up and out-of-bed rocking in mother’s arms may be done regularly and frequently. Elevation of the head of the bed, unless contraindicated, will also support and possibly improve ventilation. Trends and changes should be correlated with laboratory results and shared with the team.

Another complication is circumferential third-degree burns around the chest and neck, which often cause restrictive defects. The increased amount of edema combined with decreased chest excursion may greatly decrease tidal volume. This condition may progress and can become life-threatening, in which case chest escharotomy may be necessary to release the constricting eschar. The procedure may be done at the bedside or in the operating room. Equipment includes sterile drapes, scalpel, and electrosurgical unit (to control bleeding).

Intubation and mechanical ventilation may be required to improve gas exchange. Tube placement should be checked and documented frequently and verified daily by X-ray. Securing the endotracheal tube requires a standard technique for stabilization and prevention of pressure necrosis. Adequate humidity is necessary to prevent secretions from drying and causing mucous plugging. Remember to provide pre/post-suctioning hyperoxegenation. Sterile technique is used when suctioning to prevent infection. Attention to the details of oral hygiene will provide comfort for the patient and may reduce the occurrence of ventilator-associated pneumonia related to colonization in the oral pharynx.3

Criteria for extubation depend on why the tube was inserted initially, but, overall, stable vital signs and hemodynamic parameters will support the plan for extubation. The patient should be awake and alert in order to protect the airway; therefore, pain medications may be reduced before extubation. Ventilatory measurements and blood gas analysis should be within normal limits.

Immediately following extubation, the nurse must be alert for signs and symptoms of respiratory distress, administer suction as needed, monitor blood gas measurements, provide optimal positioning for ventilation, as well as provide reassurance and support to decrease anxiety.

Age, burn size, and the presence of inhalation injury and pneumonia have been identified as major contributors to mortality.2 Thus, vigilant nursing care (frequent nursing assessments, aggressive pulmonary toilet, etc.) combined with anticipating potential problems and being prepared to deal with the problems will add to the team effort and possibly improve the patient outcome.

**Burn wound care**

The primary goal for burn wound management is to close the wound as soon as possible. Prompt surgical excisions of the eschar and skin grafting have contributed to reduced morbidity and mortality in severely burned patients.3-5

Wound care in the burn unit has become an art of burn nursing practice. It can be extremely challenging and complicated and, for a new nurse, it can be the most difficult and misunderstood part of burn nursing. The complexity exists because of the variety of wound types that require different interventions in relation to time post-burn or time postoperative. Wound assessment and care is a learned skill that develops over time. These skills must be taught by experienced nurses to new burn nurses. Assessment of burn wound takes place in the hydrotherapy area, operating room, and at the bedside.

Wounds may consist of eschar, pseudoeschar, skin buds, autograft, donor sites, hypermature granulating tissue, blisters, and exposed bone and tendons. Besides the many kinds of possible wounds, there are many topical antibacterial agents available for managing wounds. These choices raise many decisions for the team to address. Topical antimicrobial creams and ointments include mafenide acetate, silver nitrate, silver sulfadiazine, petroleum and mineral oil-based antibacterial products, and Mycostatin powder. Wounds may be treated in the open fashion (topicals without dressings) or closed fashion (topicals with dressings or soaks). There are several techniques for applying dressings to different areas of the body, that need to be able to withstand exercise, ambulation, and moving around in bed. Biological dressings such as homograft or heterograft may be used as temporary wound coverage. Dressings may also be synthetic or biosynthetic or silver impregnated. Selection is based on the present condition of the wound and the expected outcome.

Secondary goals of wound care are to promote healing and to maintain function of the affected body part. These goals are accomplished by preventing wound infection, treating wound infection, preventing graft loss and tissue necrosis, providing personal hygiene, and maintaining correct positioning and splinting throughout hospitalization. To prevent burn wound infection, the burn nurse must: cleanse the wound with soap and water; debride the wound of loose necrotic tissue, crusts, dried blood, and exudate; apply topicals or dressings and ensure dressing changes are done/ordered. The nurse must inspect the wound for evidence of infection: cellulitis, odor, increased wound exudate, and/or changes in exudate; changes in wound appearance; and increased pain in the wound. The physician should be notified so that changes in wound care can be made. Cultures and biopsies may be ordered to identify the type and count of organisms and treat with a specific systemic antibiotic, topical dressing, soak, or a combination of all three treatments. The wound is often the source of bloodstream sepsis. The five cardinal signs of sepsis are: hyperventilation, thrombocytopenia, hyperglycemia, disorientation, and hypothermia.6

Preventing graft loss is another wound care challenge for nursing. Usually the patient returns from the operating room in a position that is maintained for 3 or 4 days. Any interaction with the patient during this time of graft immobilization requires creativity and care in order to prevent shearing of the graft. Postoperative dressings on the thighs and back are protected with polymycin, fine-mesh gauze to prevent soiling by feces and to minimize cleanup. The dressings are continuously monitored for increased drainage and odor, which would indicate possible wound infection. If infection is suspected, then the postoperative dressings may be removed early for a closer inspection of the wound.

Donor sites will also require additional care to prevent infection. Of course, the care postoperatively depends on the coverage of the donor site. If the donor site is covered with fine-mesh gauze, the initial care is to ensure homeostasis and adherence of the gauze to the wound. Therefore the post-op pressure dressing remains intact for 6–12 h and is then
removed. The focus of managing the donor site is to keep the wound dry. If grafts/donor sites are on the back or backs of the legs, the patient is placed in a Clinitron bed for 4–5 days to promote drying. If the donor site remains wet, additional drying techniques (hair dryers, external heaters) may be used periodically during the day.7

If the donor site is covered with a synthetic or biological dressing, the same principles apply. Basically, apply a pressure dressing to ensure adherence to the wound for a short period of time postoperative and then expose to the air to support drying of the wound. A bed cradle is used to keep bed linen from contacting the wounds. The location of the graft, donor site, and eschar may all be on the same extremity, which again requires creativity to accomplish all three interventions of care.

Nurses must always be vigilant when it comes to skin assessment; early detection and prevention is the key ingredient in preventing pressure ulcers in major burn patients. Pressure ulcers are no longer treated as a burn wound. There is evidence to support nursing practices in the prevention of pressure ulcers in burn patients. Burn patients have many risk factors that predispose them to develop pressure ulcers. Initially, hypovolemic shock with blood flow shunted away from the skin to preserve vital organ function is a factor. Additional injuries may increase the risk for pressure ulcers, such as: inhalation injury, which may require intubation and use of paralytic agents to manage the airway. Fluid resuscitation may contribute to massive edema in both burned and unburned areas. The edema is maximized at about 2–3 days post-burn, which also decreases the blood flow to the skin and adds weight to all parts of the body.

Maintaining systemic hydration can continue to be a problem long after the patient has received adequate resuscitation for burn shock. Continued fluid therapy to replace fluid loss through the burn wound is essential. If systemic hydration is not maintained, even normal skin may be at risk. To complicate this situation, the quantity of fluid lost through the burn wound may increase the moisture on normal skin adjacent to the burn wound. This moisture may cause the normal skin to break down and predispose the skin to further compromise.

**Surgical care**

The perioperative setting combines a number of professionals with different levels of experience and expertise, all directed towards patient care. Each team member has a specialized role: the surgeon provides surgical intervention; the surgical technician supports the surgeon; the anesthesiologist or CRNA provides life support functions, and the circulating nurse’s role is to provide safe patient care by ensuring that all team members adhere to professional standards and guidelines. The perioperative nurse is a professional registered nurse who provides nursing care to patients in the preoperative, intraoperative and postoperative phases of surgery. Perioperative burn nursing care can be described as hot, intense and demanding. Burn nursing in fact, represents one of the profession’s most challenging specialties.

Once surgery is completed, perioperative nurses provide postoperative care and assessment. This phase of nursing care can also be challenging for the nurse caring for the patient during the immediate postoperative period. Nursing care and plan for care depends on many factors: amount of blood loss, surgical time and the site and extent of excision and grafting. The post-anesthesia nurse caring for the burn patient must be knowledgeable as to the medications and procedures used during surgery, to provide appropriate safe nursing care.

Many burn-injured patients will make repeated trips to the operating room for surgical excision of the burn wound and grafting, with graft taken from unburned areas. These procedures may require the patient to be anesthetized for long periods of time. Patients are at risk for pressure ulcers in the operating room; proper positioning and the use of pressure-reducing devices is essential to reduce the risk of pressure ulcer formation. During these operative procedures the patient may lose large quantities of blood resulting in decreased tissue perfusion and patient may develop shock. Vasopressors, antibiotics, and fluid resuscitation are the usual treatments for shock. The low-flow states and the use of vasopressors may also result in decreased tissue perfusion and increased risk of pressure ulcer formation.

Post-surgery, the patient is often immobilized with large bulky dressings and splints to protect the graft. These dressings need to be applied with enough pressure to stop the bleeding from the grafted wound and the donor site. But if the dressings are applied too tightly, or if edema develops after dressing application, this may cause increased pressure on the skin.

Throughout the acute phase of care the burn patient is predisposed to pain and anxiety. Pain in the burn wound and fear of pain causes patients to try not to move. Careful titration of anxiolytics and narcotics can result in an alert patient who is relatively pain free but this requires intense attention to detail from the nursing staff.

To prevent wound bed desiccation, soaks are used to maintain moisture in the grafted wound and to aid in decreasing wound colonization with bacteria. This moisture, when in contact with adjacent normal skin, may increase the risk of tissue breakdown.

Inadequate nutrition prior to or after the burn injury is potentially a significant problem. The hypermetabolic response in the burn-injured patient leads to protein malnutrition if caloric intake is compromised. To reduce the risks of systemic infection and to promote wound healing, enteral hyperalimentation is most frequently used and the patient is fed by nasogastric or nasojugal tubes.

In summary, burn patients are among the high-risk populations for pressure ulcer development. The physiology of the burn injury combined with many of the therapies and treatments used during hospitalization impacts the burn patient’s risk for pressure ulcers.

All patients, except those with skin grafts postoperatively, will benefit from a bath or shower. Large acute burns are placed on a shower cart and the wounds are gently showered with warm water. The overhead heater is on and the room temperature is 85°F (29°C) or above. Large acute burns are not immersed in a tub of water to prevent auto contamination and electrolyte imbalance.8 Hydrotherapy can be used for careful assessment of the wounds, as well as personal hygiene such as shampoo, mouth care, face care, and perineal care.

Hydrotherapy is an excellent opportunity for patient and family teaching about wound care and dressing application.
As the patient gets closer to discharge, families are required to do more of the care. The trend for earlier release from the hospital poses additional challenges for nursing, since it reduces the time available to prepare the patient for discharge. The better the patient and families are educated, the better the outcome will be. Early involvement with patient and family helps identify potential obstacles at discharge and facilitates care coordination in the discharge process.

**Metabolic and nutritional support**

Hypermetabolism, or metabolic stress, is the direct response to a burn injury. The amount of stress increases proportionally to the extent of the injury and strongly influences a patient’s nutritional requirements. This response can magnify the normal metabolic rate by 200%. Malnutrition, starvation, and delayed wound healing will result if calories are not provided consistently to meet nutritional requirements. Children require more calorie and protein replacement than adults, because they have additional nutritional demands to support growth and development.

Monitoring output and managing nutritional intake are among nursing’s primary responsibilities. An accurate record of intake and output is critical to patient care because potential problems can be detected early and alternate options of care can be individualized to help the patient achieve his/her goals. Accurate weights, daily or as ordered, are also important. Remember to record whether dressings, splints, or linens are included in the weight. Obviously, including additional elements does not reflect an accurate weight, but trends in weight either up or down may be identified and may be helpful in the overall management of the patient.

Typically, when patients cannot consume enough calories by mouth, then enteral feedings are begun. Sometimes enteral feedings are started before the patient is given the option of eating because the amount of calories is so great and/or the condition of the patient is unstable. Parenteral nutrition is used when enteral fails. The goal is to provide adequate nutrients, calories, and protein. A nasogastric tube is inserted initially and used to decompress the stomach until bowel sounds return. Then tube feedings are started at a very low volume per hour to act as a buffer against ulcer formation. The nasogastric tube allows for checking hourly gastric residuals, gastric pH, and guaiac. If the gastric pH falls below 5, or if the guaiac is positive, Maalox and Amphojel are given every 2 h, alternately every hour.

Aspiration of stomach contents is a potential complication and always a concern. Gastric residuals are checked before suctioning to prevent the patient from vomiting and possibly causing aspiration. Another precaution is to keep the head of the bed elevated. A Dobhoff tube is also inserted initially, and feedings are begun as soon as 6 h post-burn. The rate starts slow and is advanced as tolerated to meet the calculated amount of nutritional replacement. Tube feedings continue until the patient can take the required amount of calories by mouth.

Another potential problem with both tubes is dislocation; therefore, it is important to check placement periodically throughout the day. When gastric residuals start climbing, it may be because the Dobhoff tube has slipped into the stomach or the patient is septic. Tube feedings may become contaminated and become a source of infection for the patient leading to significant morbidity. Routine procedures should be established to prevent this occurrence and care should include sterilization of the blender and limiting to 4 h the amount of time that tube feedings can be hung at the bedside. The tubing and container should be changed every 4 h.

Sometimes when patients are encouraged to begin taking food by mouth, it will help to stop the tube feedings during the day and feed only at night. Not scheduling painful activities around meal-time and providing frequent mouth care will also contribute to improved oral intake.

Regular bowel patterns are expected in the post-burn period. Patients are given many medications during hospitalization that may contribute to either diarrhea or constipation. Patients are expected to have at least one bowel movement per day. If not, then a bowel evacuation regimen should be initiated. If diarrhea is the problem and the volume exceeds 1500 mL/day, then bulking agents and/or antidiarrhea medication may be useful to promote routine bowel elimination.

The importance of monitoring and documenting the many parameters of intake and output cannot be overemphasized. Established clinical protocols and guidelines facilitate the implementation and evaluation of the nutritional program.

Other strategies to support the hypermetabolic phenomenon of the burn patient are to keep the room temperature above 85°F (29°C) and to keep the room door closed to prevent drafts. Also frequent rest periods must be provided during the day. Nursing generally makes the schedule of activities for the day, so including frequent rest periods is just as important as anything else that needs to be done during the day. Adequate sleep during the night is also very important: it often this that makes the difference between a good day and a bad day. A quiet comfortable environment without sensory overload (lights and noise) is essential for the patient to sleep.

Nurses are the grand communicators of progress and/or problems. Nurses work closely with dietitians, physicians, patients, and families to ensure that optimal metabolic and nutritional support is achieved during the post-burn period.

**Pain and anxiety assessment and management**

The expected outcome for pain and anxiety management is for the patient to achieve a balance between successful participation in activities of daily living and therapies and being comfortable enough to rest and sleep as needed. The ultimate goal is for the patient to be satisfied with the pain management plan as it is implemented. Assessment of pain and anxiety provides a baseline for evaluation of pain and anxiety relief measures. Pain and anxiety scales are essential to quantify painful episodes and to evaluate effectiveness of medication. Knowing when and how much to intervene is guided by knowing the baseline pain and anxiety rating for the individual. Patients and families should be given information upon admission on how to use the assessment scales and to identify an acceptable level of pain and anxiety.

Intravenous administration of opioids and anxiolytic agents is essential to manage pain and anxiety during the initial stage of injury due to the altered absorption and circulation volume following a major burn injury. A PCA (patient-controlled analgesia) pump is useful on children.
older than 5 years of age and adults. It is important to manage background pain as well as procedural pain for which medication should be given 15–30 min prior to a painful procedure. Constipation is frequently a complication of pain management; thus, a bowel management program should be instituted at the same time. Relaxation, guided imagery, music therapy, hypnosis, and therapeutic touch are adjunct techniques to complement analgesia and reduce anxiety. Emotional support and patient and family education decrease fear and anxiety, thereby enhancing the pain management plan.

**Patient/family education**

In order for nurses to be competent teachers, they must be competent practitioners with solid theoretical foundations. Continuing education to maintain competency is key for clinical staff because of their role as educators of patients and families. Reinforcement of the educational process (assess, plan, implement, evaluate, and document), characteristics of patient population, updates on educational strategies, age-appropriate interventions, and ways to evaluate learning are topics that will sharpen educator competency.

Discharge planning and education begins upon admission. It begins with a thorough assessment of the patient’s life prior to the injury. Identifying knowledge deficits and barriers to education, prioritizing strategies for education, providing supplemental educational handouts and/or classes as well as developing a plan for evaluating the effectiveness of the teaching opportunity are integral parts of the educational process.

Assessment provides essential information for planning an educational program to meet the specific individual needs of each patient and family. It is also done periodically during different stages of the educational process to determine if the plan remains valid or changes need to be made.

The assessment findings become part of the educational plan, in that the plan is tailored to meet the needs and concerns of the patient and family. The plan includes the learning objectives, the strategies for education, and the learning materials. All of these parts of the educational goal are agreed upon by the patient/family and the educator.

Implementation of the plan is the next step, followed by a thorough evaluation of the effectiveness of learning and/or determination of whether the education goal is being accomplished. Alterations in the original plan may be needed any time during the educational process depending on unforeseen situations or changes in conditions that were not anticipated.

The benefits are many. This process ensures communication of educational topics among the team members, provides a historical account of education, and documents progress and/or changes in the plan. It benefits the patient and family by making them competent in their role as care provider when discharged from the hospital. Knowledge allays anxiety about the unknown and aids in compliance with recommended care after discharge, improving the long-term outcomes. Patients and families can be empowered to become active participants in the burn care team early in the post-burn course through a well-structured educational plan.

**Rehabilitation of the burn-injured patient**

A major burn is one of the most devastating injuries, both physically and emotionally, known to man. After weeks of being an invalid, undergoing repeated surgeries, fighting infection, having the body ravaged by the metabolic consequences of injury, and enduring pain and anxiety, the patient now faces months of continued physical therapy to regain the level of function that they had known before the injury. Most patients who have sustained a major burn will continue to have a higher than normal metabolic rate for over a year and thus find that they do not have the stamina to easily regain their lifestyle. In addition to the catabolic effects of burn injury, being hospitalized and in bed with minimal activity for many weeks or months causes bone weakening and loss of muscle. Children are more prone to fractures. Although these patients must continue to exercise to prevent contractures, they may not have the physical strength or endurance necessary to actively participate in such programs. Likewise, these patients frequently become depressed; as they face an altered self-image and a forced physical dependence on others. They fear that they will never look normal and that they will not be able to return to a normal life. For the adult, the concerns of whether they will be able to return to work or have to change their occupation is also a factor. What is the role of the nurse at this phase of treatment? Although nurses have been very involved in the care of the patient in the early phases of care, many nurses do not see a role for themselves at this stage. The transition from the hospital to home care is often difficult for both the patient and family. It is important prior to discharge that the patient and family be educated in the care of wounds and healed skin before they leave the hospital. They also need information about the normal depression that occurs post-hospitalization and resources in their home community to which they have access. This is where the nurse case manager becomes an integral part of the patient care team. Nurse case managers who are hospital based can begin to work with the patient and family soon after admission to assess the patient’s future needs and coordinate these with outside agencies to ensure that the transition goes smoothly. Often, case managers from workmen’s compensation carriers or health maintenance organizations (HMOs) are involved during the early phase as well. Coordination of activities between case managers is important to provide seamless care. With children, it is important for the nurse case manager to begin working with the school nurse or community health nurses to provide for this seamless transition in care.

Although the rehabilitation therapist plays an important role in providing referrals to community therapists and psychologists, and social workers frequently make referrals to community mental health providers, the nurse case manager should be involved in the overall coordination of these and other services to foster a unified approach. The free flow of communication between all providers is necessary for optimal rehabilitation of the patient.

**Work-hardening programs for adults**

Work-hardening programs have been shown in adults to more rapidly return the patient to their optimum level of functioning.
These programs may be available through community rehabilitation facilities, vocational rehabilitation agencies, HMOs hospitals or health centers with cardiac rehabilitation programs or through workmen’s compensation carriers. The major concern for the nurse case manager and the burn team is which patients need these programs and at what point the patient will benefit the most from such intensive programs.

**Assessment**

Burn patients, like those recovering from coronary heart disease and surgery, find themselves deconditioned. Even 3 weeks of bedrest in a healthy subject can result in a 25% decrease in maximal oxygen consumption. Thus, burn patients who are hospitalized for 2 or more weeks may need to be considered for such programs. Burn patients should be first assessed for risk factors associated with coronary heart disease. Such risk factors include:

- age and sex
- elevated blood lipids
- hypertension
- cigarette smoking
- physical inactivity
- obesity
- diabetes mellitus
- diet
- heredity
- personality and behavior patterns
- high uric acid levels
- pulmonary function abnormalities
- ethnic race
- electrocardiographic abnormalities during rest and exercise
- tension and stress.

Cardiac stress testing is usually recommended prior to beginning an exercise program. If the patient has several risk factors, the exercise program can be tailored to fit the patient’s needs.15

**Planning**

What is available? Often the major issue is what is available and who will pay for this care. When an adult is injured on the job, this is often arranged and paid for by the compensation carrier, since they have a vested interest in returning the patient to work as soon as possible.

**Implementation**

Once the details are worked out the next hurdle is to get buy-in from the patient and family. Some programs require the patient to be in a facility some distance from their home; this may present issues for both the patient and family. Similarly, if the program is in the local community, daily visits to the rehabilitation facility may pose transportation issues, especially if the patient is unable to transport him or herself. These details can usually be worked out with cooperation of all caregivers and the family involved. Motivation and determination are often the most difficult factors to overcome. This is especially true if the patient is suffering from depression. The nurse case manager can be very instrumental in rallying the burn team and caregivers in the community to help the patient and family to see this as a way to return the patient to more normal function.

**Evaluation**

Success in such programs requires that all involved have the same goals and that these goals result in measurable outcomes. The goal of such programs is not only to increase the patient’s tolerance to exercise but also to improve their psychological and social functioning and to return the patient to work or to the same level of functioning pre-injury.

**Extensive exercise in children**

Children may suffer from the same deconditioning as adults, especially if they have suffered 40% or greater burns. Cucuzzo et al. have shown that children with greater than 40% burns have bone demineralization.16 Treatment of these patients with long-term anabolic steroids and intensive exercise programs can return the patient’s metabolic status and bone re-mineralization to normal much sooner.

**Assessment**

Children seem to do better if they are at least 6 years old when they begin the exercise program. The best time to start such a program is approximately 6–9 months post-burn. With most patients this is after they have had 2–3 months away from the hospital after discharge from their initial injury. Like adults, individualized programs considering their current general state of health are necessary. When children enter these intensive exercise programs it is important for the parent or a responsible adult member of the family to be involved. This may be a significant factor in when the patient is able to start such a program. Similar results can be obtained in younger children through active play and exercise accompanied by music therapy. The use of activities set to music can increase stamina and actively stretch scar tissue and increase joint mobility.

**Planning**

Although cardiac rehabilitation programs and the like may be readily available in most major towns and cities in this country, often they do not take children. Children’s hospitals often have rehabilitation units or outpatient programs for children that can offer similar programs to the adult cardiac programs. Children’s hospitals are usually found in major cities; thus, these programs may not be as accessible as programs for adults. In some communities, school-age children may be able to obtain help within the school sport programs, especially if they have qualified athletic trainers. Children aged 4–6 may have more difficulty finding programs outside of children’s hospitals. Some early childhood intervention and pre-kindergarten programs may be available for younger children.

Another question is who pays for this care? Unlike the adult with insurance or workman’s compensation insurance, children are often without funding for this rehabilitative care. State programs for children with special needs (e.g. Title V programs) are one avenue to explore. Other sources of funding may come from private or public charities,
school-mandated programs, or vocational rehabilitation programs for the older teenager.

Implementation
Motivating the child and parent can be a major task. Often the parent and child have spent weeks or months during the acute phase of care away from home. If there are other children in the home or if the parent normally works outside the home, the parent may not feel that he/she can be away from home an additional 2–3 months. The child may also not want to leave the safety of the home environment. Thus motivating the child and parent is often difficult. Helping the parent see this as a valuable program will require the whole burn team to work together with the patient and family.

Evaluation
The outcome of these programs for the child can be measured in increased exercise tolerance and improved psychological and social adjustment. A major function of these programs is to convince the child and parent that the patient is a normal child and can succeed mentally and physically. If the child returns home and can keep up with his/her peers, this alone improves the child’s self-esteem.

Reconstructive care

Assessment
The role of the nurse in the reconstructive surgery phase is to be an advocate for the patient and family. Education of the patient and family throughout the course of burn care is also an important nursing function. Many people have unrealistic expectations for reconstructive surgery. The nurse’s role in the outpatient clinic or physician’s office is to listen to the patient and family and to understand their hopes and expectations. Often when the surgeon discusses what should or could be done to improve the patient’s appearance or function, the patient and family member are reticent to ask questions or to describe what they want. Patients’ priorities are often different from the surgeons and this leads to dissatisfaction. Most surgeons prefer to wait until the scar has matured to begin reconstructive surgery. Occasionally, if the scar tissue is interfering with function, correction of the scar will be attempted. This is especially true in children where scar tissue may cause bone deformity if left until it has matured. In children, some reconstructive procedures are best postponed until the child has matured. Usually, surgery is best accepted by the child at the beginning of high school or just prior to starting further education. Although it is difficult to continue to be supportive of the patient and family during the scar maturation process, the nurse’s role is one of education, support, and encouraging the patient to continue with exercise, splints, and pressure garments, if ordered.

Planning
Once again, the nurse case manager can be instrumental in helping the family find the funding and resources to provide reconstructive surgery for the patient. If the patient is working or in school, planning the procedures should accommodate the patient’s school or work schedule as much as possible. For children, funding through Services for Children with Special Needs may be available. Working with insurance companies and HMOs can be tricky if the surgery is presented as cosmetic rather than corrective surgery.

Implementation
Preparing the patient for surgery is the responsibility of the nurse and physician. Providing the patient with realistic expectations is often difficult. Many times, immediately after the surgery, the area will look worse and the patient may feel dissatisfied and depressed. Preoperative preparation of the patient and family may allay some of these issues. Surgery, itself, is frightening enough for the patient and family. In children, this can be especially frightening because it may bring up memories of their original burn treatment and the pain associated with this treatment. Postoperatively, the nurse’s role is to teach the patient and family how to care for the wound to prevent infection and further scarring.

Evaluation
Whose body is it anyway! A line from a famous play actually sums up the evaluative process for reconstructive surgery. As professionals, we may see great improvement in the patient’s condition after surgery. But if the patient is not satisfied with his or her appearance, little has been gained by the surgery. This is the reason that the patient and family must have realistic expectations prior to surgery.

Further reading
References

Special considerations of age: the pediatric burned patient
Jong O. Lee, William B. Norbury, David N. Herndon

Introduction
The incidence of burn injuries has declined steadily over the past two decades. Approximately 1.25 million people are burned in the United States every year, of which one-third are children; 60,000–80,000 patients sustain severe enough burns to require hospital admission; 30,000 children require hospital admission for treatment of their burn injuries. About 4,000 burn patients die each year, and approximately 1,000 of them are children.

House fires injure or kill over 10,000 people per year. House fires are among the leading causes of burn-related deaths in children. Children between 0 and 5 years of age are at a greater risk, as a disproportionate number of fire deaths occur in homes. Deaths among preschool children are at a rate of more than twice the national average (29.6 deaths/million children), or an average of 20% of the total percentage of all home fire deaths.

Scalds are common in children less than 3 years old. Scald injuries may be due to household accidents or deliberate abuse. These may include spilling hot coffee or water, children reaching up to countertops, pulling pot handles or cords attached to cooking appliances and spilling the contents onto themselves, unknowingly putting body parts under a hot water faucet or climbing into a hot tub, and intentionally or unintentionally being placed into or brought in contact with a hot substance by another individual.

Improvements have been made in the reduction of morbidity and mortality related to burns over the past few decades. Advances in fluid resuscitation, early surgical excision and grafting of the burn wound, infection control, treatment of inhalation injury, nutritional support, and support of hypermetabolic response to burns have contributed to a 50% decline in burn-related deaths and hospital admissions in the United States. This overall improvement in mortality is most perceptible in children. In 1949, Bull and Fisher reported the expected 50% mortality rate for 49% total body surface area (TBSA) burn in children aged 0–14. This has improved to 50% expected mortality in 98% TBSA burn in the same population group.

In a review of 103 children with >80% TBSA burns over a 15-year period, it was found that 69 patients survived, with an overall mortality of 33%. Mortality was greatest in children under 2 years of age and in burns >95% TBSA (Figs 35.1 and 35.2). Another major predictor of mortality was the length of delay to intravenous (IV) access (Fig. 35.3). Patients that received resuscitation fluids within the first hour had a significantly higher chance of survival. The mortality rate also increased significantly with inhalation injury, sepsis and multiorgan failure. In no pediatric patient, no matter how large the burn, how young, or with what type of inhalation injury, could it be accurately predicted at the time of admission whether they would live or die.

The burn injury produces overwhelming physiological and psychological challenges to a child. The unique anatomical and physiological attributes of the child require the attention of physicians who are trained not only in burn care but also in the specifics of pediatric care. The most obvious differences between adults and children are size and body proportions. Shorter lengths, tighter angles, and smaller diameters of various anatomical structures and spaces make certain manipulations more difficult. These differences require the provision of special equipment and supplies, which reflect the configurations of pediatric anatomy. In addition to anatomical differences there are also many physiological differences between children and adults, which must be considered and will be discussed concerning the treatment of the pediatric burn patient.

Initial evaluation
A patient must be immediately removed from the source of burn, and clothing and jewelry removed immediately as these items can prolong the burning process. Pouring cool water onto the burn can cause hypothermia in large burns and should be avoided. After the burning process is stopped, the patient should be kept warm by covering with a sterile (if available) or clean sheet or blanket. If the burn is chemical, the patient should be removed from the chemical immediately and the burn wound should be irrigated with copious amount of water for at least 30 minutes. If chemical is powder, it should be brushed off first prior to irrigation.

Burn patients should be treated as a trauma patient and any potential life-threatening injuries should be identified and treated. The airway should be assessed first. Oxygen 100% should be administered and oxygen saturation monitored using pulse oximetry. If inhalation injury is suspected,
a long transfer to a burn center. A radial arterial line may not be reliable in pediatric patients with extremity burns and may be difficult to secure. A femoral arterial line may be more reliable and easier to secure.

A bladder drainage catheter is placed to monitor urine output as a measure of successful resuscitation. A nasogastric tube is placed in all patients with major burns, as they can develop gastric distension or ileus.

Persistent tachycardia should alert a clinician to a missed injury or under-resuscitation. Accurate and rapid determination of burn size and depth is vital to the proper management of burn injury.

**Resuscitation**

There is a systemic capillary leak after a large burn, which increases with burn size. Capillary usually regains competence 18–24 hours after burn injury. IV access should be established immediately for the administration of resuscitative fluid. Increased delays to commencement of resuscitation of burned patients result in worse outcomes and should be avoided. Therefore it is crucial that IV access be obtained as early as possible, even though such access may be difficult to obtain. Owing to the small circulating volume in children, delays in resuscitation for periods as short as 30 minutes can result in profound shock. Peripheral IV access is preferred, and it may go through burned skin if necessary. IV access should be well secured. When peripheral IV is not available because of severe extremity burns, a central venous line may be placed. Children with large burns should have two large-bore IV lines for fluid administration. The presence of two IV lines also provides a safety margin if one infiltrates, to allow continued resuscitation while another line is re-established. Either internal jugular, subclavian or femoral lines can be obtained, but femoral venous access may be easier to obtain in edematous patients.
When vascular access is unobtainable the intraosseous route is a viable option. Fluid volumes in excess of 100 mL/h can be administered directly into the bone marrow. Intramedullary access can be utilized in the proximal tibia until IV access is accomplished. A 16–18 gauge bone marrow aspiration needle, spinal needle, or commercially available intraosseous needle can be used to cannulate the bone marrow compartment. Although previously advocated only for children younger than 3 years of age, intraosseous fluid administration can be safely performed in all pediatric age groups. The anterior tibial plateau, medial malleolus, anterior iliac crest, and distal femur are preferred sites for intraosseous infusion. The needle should be introduced into the bone, avoiding the epiphysis, either perpendicular to the bone or at a 60° angle, with the bevel facing the greater length of bone (Fig. 35.4). The needle has been properly inserted when bone marrow can be freely aspirated. The needle should be well secured to prevent inadvertent removal. Fluid should be allowed to infuse by gravity drip. The use of pumps should be discouraged in case the needle is dislodged from the marrow compartment.

Fluid losses are proportionally greater in children owing to their small body weight to body surface area ratio. Normal blood volume in children is approximately 80 mL/kg body weight and in neonates 85–90 mL/kg, compared to an adult whose normal blood volume is 70 mL/kg. Evaporative water losses in a 20% TBSA burn in a 10 kg child are 475 mL or 59% of the circulating volume, whereas the same size burn in a 70 kg adult causes the loss of 1100 mL or only 22% of blood volume. The commonly used ‘rule of nines’, useful in adults and adequate in adolescents, does not accurately reflect the burned body surface area of children under 15 years of age (Fig. 35.5). The standard relationships between

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**Figure 35.4** Intraosseous line placement in the proximal tibia (a) and distal femur (b). (Redrawn with permission from Fleisher G, Ludwig S, eds. Textbook of pediatric emergency medicine, 2nd ed. Baltimore: Williams & Wilkins, 1988: 268.)

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**Figure 35.5** The ‘rule of nines’ altered for the anthropomorphic differences of infancy and childhood.
appropriate electrolyte and fluid management. Children under 1 year of age may require more sodium supplementation because of higher urinary sodium losses. Potassium losses are usually replaced with oral potassium phosphate rather than potassium chloride, as hypophosphatemia is frequent in this population. Calcium and magnesium losses also must be supplemented.

Intravenous resuscitation fluid should be isotonic and replace lost electrolytes. Lactated Ringer’s is the most commonly used resuscitation solution for the first 24 hours post burn. Children less than 1 year of age should also receive a separate maintenance fluid containing dextrose solution in addition to resuscitation fluid to prevent hypoglycemia as their glycogen stores are limited.

Assessment of resuscitation

Body surface area and weight in adults do not hold true in children, as infants possess a larger cranial surface area and a smaller area in the extremities than adults. Most routinely used resuscitation formulas were developed using adult patients and are almost exclusively weight-based. Since the linear relationship between weight and body surface area does not exist in children, use of these formulas in children results in under- or over-resuscitation (Table 35.1).

Pediatric burn patients should therefore be resuscitated using formulas based on body surface area, which can be calculated from height and weight using a standard nomogram (Fig. 35.6) or formulas (Table 35.2). The most commonly used resuscitation formula in pediatric patients calls for the administration of 5000 mL/m² TBSA burned plus 2000 mL/m² TBSA for maintenance fluid given over the first 24 hours after burn, with half the volume administered during the initial 8 hours and the second half given over the following 16 hours. The subsequent 24 hours, and for the rest of the time their burn wound is open, require 3750 mL/m² TBSA burned or remaining open area plus 1500 mL/m² TBSA for maintenance requirements. The fluid requirement decreases as a patient achieves more wound coverage and healing. As in the adult patient, resuscitation formulas offer a guide for the amount of fluid necessary for replacing lost volume in children, and the amount of fluid should be titrated according to the patient’s response.

Hyponatremia is a frequently observed complication in pediatric patients after the first 48 hours post burn. Frequent monitoring of serum sodium is necessary to guide the routine clinical signs of hypovolemia in adult burn patients, such as low blood pressure and decreased urine output, are late manifestations of shock in the pediatric patient, and tachycardia is omnipresent. Children have remarkable cardiopulmonary reserve, often not showing clinical signs of hypovolemia until more than 25% of the circulating volume has been lost and complete cardiovascular decompensation is imminent. Pulse pressure, mental status, distal extremity color, and capillary refill reflect volume status. Capillary refill is a good indicator of volume status in pediatric burn patients. Decreased capillary refill should warn a clinician of imminent cardiovascular collapse. Measurement of arterial blood pH with base deficit or lactic acid is of particular importance in this age group, reflecting decreased tissue perfusion. Improvement in base deficit or lactic acid shows successful resuscitation.

Children frequently develop a reflex tachycardia after even the most trivial injury due to an overexuberant
Special considerations of age: the pediatric burned patient

Figure 35.6 Standard nomogram for the determination of body surface area based on height and weight. The example depicted is for a child of 100 cm in height and 23 kg in weight. (Reprinted with permission from Eichelberger MR, ed. Pediatric trauma: prevention, acute care and rehabilitation. St Louis: Mosby Year Book; 1993: 572.)

catecholamine response to the trauma or anxiety. Systolic blood pressures <100 mmHg are common in children younger than 5 years of age (Table 35.3). Young children with immature kidneys have less tubular concentrating ability than adults, and urine production may continue in spite of hypovolemia.

An indwelling urinary drainage catheter is essential for burns >20% during resuscitation. During the early phase of resuscitation, urine output should be assessed as frequently as every 15 minutes and the resuscitation fluid titrated appropriately. Fluid administration should be titrated to achieve a urine output of 1 mL/kg/h in children and 2 mL/kg/h in infants. Other endpoints for resuscitation should also be followed, such as heart rate, blood pressure, capillary refill, and mental status. Initial fluid boluses should be administered in amounts appropriate for the size of the child and should represent no more than 25% of the total circulating volume (20 mL/kg).

Over-resuscitation must be avoided as it can lead to pulmonary edema, right heart failure, abdominal compartment syndrome, extremity compartment syndrome, and cerebral edema in burn patients. Of particular concern is the development of cerebral edema. Care should be taken in order to maintain elevation of the head of the bed, particularly during the initial 24–48 hours post burn, and to avoid hypercarbia. Although children possess a large cardiopulmonary reserve, a child’s heart is less compliant, and stroke volumes plateau at relatively low filling pressures, shifting the Starling curve to the left. Cardiac output is almost completely dependent upon heart rate, and the immature heart is more sensitive to
volume overload. Cardiac output can be measured using a PiCCO monitor (pulse contour cardiac output), based on transpulmonary thermodilution, which is less invasive than a Swan–Ganz catheter and only requires a thermodilution arterial catheter and a central venous line. Transthoracic or transepophageal echocardiograms should be used early to assess cardiac function in patients who are not responding to conventional therapy. Children are particularly prone to the development of edema from both vasogenic and hydrostatic sources. Vasogenic edema occurs in the early post-burn period when vascular integrity is impaired. The maintenance of intravascular osmotic pressures reduces the likelihood of edema development. Salt-poor albumin can be expected to remain in the intravascular space if administered more than 8 hours post burn in amounts necessary to maintain serum albumin levels at >2.5 g/dL. Albumin deficit can be calculated using the formula:

\[ 2.5 \text{ g/dL} - \text{current serum albumin (g/dL)} \times \text{[wt(kg)]} \times 3 \]

The deficit can be administered as 25% albumin and given in divided doses.

### Evaluation and management of airways

Airway evaluation and management must be given priority in pediatric patients. Children are more prone to obstruction owing to the smaller aperture of the trachea. Equal amounts of airway edema in pediatric and adult airways result in significantly disproportionate increases in amounts of resistance and decreases in cross-sectional area. A 1 mm increase in the tissue thickness of a 4 mm diameter pediatric trachea results in a 16-fold increase in resistance and a 75% decrease in cross-sectional area. The same edema in an adult airway would increase the airway resistance threefold and reduce airway area by 44%.

Potential hemorrhage and edema make emergency intubation difficult. Early intubation should be considered when a patient is anticipated, severe inhalation injury is present, or a patient has a large burn which likely will develop airway edema with a large amount of fluid resuscitation. Concurrent placement of an endotracheal tube over the bronchoscope should be considered at the time of bronchoscopy. A readily available estimate of airway diameter is the width of the patient’s little finger, an age-based formula (age + 16)/4 or the use of Broselow tape.

The ET tube must be well secured. In a child, exudative wounds and moist dressings can make this task difficult.

### Inhalation injury

Inhalation injury remains one of the primary contributors to burn mortality. The mortality rate of children with isolated thermal burns is 1–2%, but increases to approximately 40% in the presence of inhalation injury. The incidence of and mortality from inhalation injury both increase with increasing burn area. Carbon monoxide poisoning coupled with hypoxia is the most frequent cause of death due to ‘smoke inhalation.’ Any patient with a flame-related injury, particularly if confined in a closed space, should be evaluated for an inhalation injury. If inhalation injury is suspected, arterial blood gas and carboxyhemoglobin level should be obtained and the patient should be placed on 100% oxygen. As with adults, the only definitive method to diagnose an inhalation injury is through direct visualization of the airway with fiberoptic bronchoscopy. Signs of potential inhalation injury include facial burns, singed nasal vibrissae, carbonaceous sputum, abnormal mental status (agitation or stupor), respiratory distress (dyspnea, stridor, hoarseness, wheezing), or elevated carboxyhemoglobin level >10%, especially in a closed-space fire. The initial carboxyhemoglobin level should be calculated from the time the admission level is drawn, back to the time of the burn injury. A carboxyhemoglobin level >60% has a >50% chance of mortality (Table 35.4).

Treatment modalities for inhalation injury include airway maintenance, clearance, and pharmacological management (Table 35.5). Further care is mainly supportive and includes ventilator support as needed, vigorous pulmonary toilet, humidification of inspired air, and antibiotics for documented infection. A group of children treated with a regimen of nebulized heparin and acetylcysteine showed a significant decrease in reintubation rates, atelectasis, and mortality compared to a control group.

### Hypermetabolism

Profound hypermetabolism is a classic feature of children with large burn injury. Children with burns demonstrate a profound increase in metabolic rate. No other disease state

### Table 35.3 Normal pediatric vital signs

<table>
<thead>
<tr>
<th>Age</th>
<th>Minimum heart rate (beats/min)</th>
<th>Systolic BP (mmHg)</th>
<th>Respiration (breaths/min)</th>
<th>Minimal hemoglobin (g/dL)</th>
<th>Minimal hematocrit (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2 years of age</td>
<td>100–160</td>
<td>60</td>
<td>30–40</td>
<td>11.0</td>
<td>33.0</td>
</tr>
<tr>
<td>2–5 years of age</td>
<td>80–140</td>
<td>70</td>
<td>20–30</td>
<td>11.0</td>
<td>33.0</td>
</tr>
<tr>
<td>6–12 years of age</td>
<td>70–120</td>
<td>80</td>
<td>18–25</td>
<td>11.5</td>
<td>34.5</td>
</tr>
<tr>
<td>&gt;12 years of age</td>
<td>60–110</td>
<td>90</td>
<td>16–20</td>
<td>12.0</td>
<td>36.0</td>
</tr>
</tbody>
</table>
produces as dramatic an effect on the metabolic rate as burn injury.\textsuperscript{19,20} This hypermetabolism slows wound healing and prolongs generalized weakness. Prolonged hypermetabolism can lead to loss of lean body mass and increased morbidity. Marked wasting of lean body mass occurs within a few weeks of injury. The hypermetabolic response increases with increasing burn size. There is an upregulation of catabolic agents, such as catecholamine, cortisol, and glucagons,\textsuperscript{21} which induces a hyperdynamic cardiovascular response, increased oxygen consumption, energy expenditure, proteolysis, lipolysis, and glycogenolysis, loss of lean body mass and body weight, delayed wound healing, and immune depression.\textsuperscript{21–25}

Cytokine levels increase after burn injury and normalize only at 3–6 months post burn.\textsuperscript{26} Larger burn injuries are characterized by more pronounced and persistent inflammatory responses, indicated by higher concentrations of proinflammatoty cytokines that promote more severe catabolism.\textsuperscript{26} Sex hormones and endogenous growth hormone levels decrease around 3 weeks post burn.\textsuperscript{26}

Pharmacological agents have been used to attenuate catabolism in burn injury. To minimize erosion of lean body mass, administration of anabolic hormones such as recombinant human growth hormone, insulin, insulin-like growth factor-1 (IGF-1), (IGF-1)/IGF-binding protein-3 (IGFBP-3); anabolic steroids such as testosterone and synthetic analogue oxandrolone; and adrenergic antagonists such as propranolol have been used in pediatric burn patients. These agents contribute to maintenance of lean body mass and promote wound healing.\textsuperscript{27–33}

### Thermoregulation

A hypothalamic reset induced by various inflammatory cytokines and pain causes elevation of core body temperature after a major burn even in the absence of infection. Burn patients strive for temperatures of about 38°C. Depressed or ‘normal’ temperatures are more likely indicative of overwhelming sepsis or exhausted physiological capabilities to maintain temperature. Routine methods of heat conservation are inadequate owing to the extensive heat loss through convection and evaporation after major burn. Infants and toddlers, with their increased body surface area to volume ratios and lower muscle mass for shivering, are particularly susceptible to hypothermia.

Every effort should be made to reduce the heat loss experienced by pediatric patients. Ambient temperatures and humidity should be maintained at 30–33°C and 80%, respectively, in order to reduce energy demands and evaporative water losses. Bathing or showering should be completed expeditiously, avoiding undue environmental exposure.

Hypothermia produces numerous consequences. The heart is particularly sensitive to temperature, and ventricular arrhythmias are not uncommon. Hypothermia also increases the susceptibility of the myocardium to changes in electrolyte concentrations. The oxyhemoglobin dissociation curve is shifted to the left by lowered body temperature, impairing peripheral oxygenation. In extreme cases, hypothermia produces central nervous system and respiratory depression, coagulopathy, and loss of peripheral vasomotor tone.

### Nutritional support

Nutritional support becomes an essential part of treatment of acute burn patients during their hospitalization. Early enteral nutrition is used to accomplish nutritional support of the hypermetabolic response in severely burned patients. Early enteral nutrition preserves gut mucosal integrity and improves intestinal blood flow and motility.\textsuperscript{34} Early institution of enteral feeding can also abate the hypermetabolic response to burn.\textsuperscript{34,35} Patients with smaller burns are placed on a high-protein, high-calorie diet to support their metabolic response. Those with larger burns >30% TBSA are placed on enteral feedings to supplement their diet.

Feeding tubes can be placed beyond the pylorus and enteral nutrition can be initiated within few hours of admission. Most children will tolerate enteral feedings as early as 1–2 hours post burn. Several studies have demonstrated the efficacy of early alimentation and the additional salutary effects.\textsuperscript{36,37} Enteral feedings can be given through a flexible silastic nasoduodenal or nasojejunal feeding tube, bypassing the stomach, which may experience ileus.
By using skin substitutes such as allograft, xenograft, and Integra (Fig. 35.7), the burn wound can be covered and protected until a donor site is available for grafting. Cultured epidermal autograft (CEA) is available for massive burn injuries (Fig. 35.8). Although it is an effective way to cover large burns where donor sites are limited, it may not be the most cost-effective approach. A group of patients treated with CEA had greater hospital costs, a longer stay, and more reconstructive admissions than conventional treatment with meshed graft skin.46

Traditionally, topical antimicrobials were the most commonly used treatment in partial-thickness burns. One of the drawbacks of using topical antimicrobials in burn wounds is pain. The current recommended treatment for partial-thickness burns, primarily scalds <30% TBSA, is immediate application of Biobrane. Biobrane can be safely used in

**Table 35.6 Nutritional requirements for children**

<table>
<thead>
<tr>
<th></th>
<th>Galveston</th>
<th>Modified Curreri</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant burn</td>
<td>2100 kcal/m² + 1000 kcal/m² burn</td>
<td>BMR + 15 kcal/%</td>
</tr>
<tr>
<td>Toddler burn</td>
<td></td>
<td>BMR + 25 kcal/%</td>
</tr>
<tr>
<td>Child burn</td>
<td>1800 kcal/m² + 1300 kcal/m² burn</td>
<td>BMR + 40 kcal/%</td>
</tr>
<tr>
<td>Adolescent burn</td>
<td>1500 kcal/m² + 1500 kcal/m² burn</td>
<td></td>
</tr>
</tbody>
</table>

Figure 35.7 Dermal and skin substitutes can be used as temporary cover for severe burns. Integra, a bilaminar skin substitute, can replace homografts as temporary cover. The Silastic superficial layer can be removed after 3 weeks and a super-thin autograft then placed on top. The entire wound can be covered with Integra, which is subsequently autografted when donor sites are available. (Reprinted with permission from Barret J, Herndon DN, eds. Color atlas of burn care. London: WB Saunders; 2001: 107, Plate 6.95.)

Figure 35.8 The cultured epidermal autografts are ready to use 18–21 days later. Extreme care with handling is needed because of the fragility of the cultured cells. (Reprinted with permission from Barret J, Herndon DN, eds. Color atlas of burn care. London: WB Saunders; 2001: 106, Plate 6.89.)

**Growth**

Hypermetabolism and catabolism persist long after the wound is closed.45 Protein breakdown continues 6–9 months after severe burn. There is almost a complete lack of bone growth for 2 years after injury. This results in long-term osteopenia, which may adversely affect peak bone mass accumulation in children.42,43 Children with >40% TBSA burn have a linear growth delay of height and weight despite adequate nutritional support and maximal exercise during post-burn year 1, which slowly resolves to near normal distribution by post-burn year 3.34

**Management of burn wound**

One of the most important advances in the care of burn patients is the early surgical excision and grafting of the burn wound. Improvements in the treatment of burn wounds with the practice of early excision and grafting, along with improvements in fluid resuscitation and the general care of burn patients, have reduced the incidence of fatal sepsis in burned patients.45 Prior to early excision and grafting, third-degree burns were treated by removing small amounts of eschar at a time, approximately 10–15%, followed by grafting. Commonly, eschar was allowed to separate with lysis by bacterial enzymes. This led to a high incidence of invasive infection and wound sepsis and a prolonged hospital stay, with increased mortality. Today massive excision can be easily managed in children, leading to shorter hospital stays and reduced mortality.46,47 Early excision of massive burns in the first 24 hours is safe and effective.48
children, even in infants under 2 years of age. When applied within 48 hours of injury, there is no difference in infection rates between Biobrane and topical antimicrobials. Further, application of Biobrane versus topical antimicrobials leads to less pain, shorter hospitalizations, and shorter healing times. Other dressings such as Acticoat, Aquacel, and Silverlon are available for partial-thickness burns that can be left on for several days or longer, and reduce pain associated with dressing changes.52,53

It may be difficult clinically to determine the depth of scald burns during the early post-burn period as the wounds may be indeterminate and contain a mixture of superficial and deep partial-thickness burns and sometimes even full-thickness burns. Indeterminate-depth scald burns in young children are best managed with delayed surgery instead of early excision. Unless the wound is clearly full thickness, the scald burn should be conservatively managed for approximately 2 weeks to allow the wound to heal or demarcate (Figs 35.9 and 35.10). This delayed surgery results in smaller area of wound excised and less blood loss.54

Large scald burns can be treated with allograft or xenograft, which significantly reduces the pain involved with dressing change and wound care. Scald burns >20% TBSA and of indeterminate depth were randomized to treatment with allograft versus topical antimicrobial therapy. Treatment with allograft led to a shorter time to healing and less pain.55 In another study, patients with >40% TBSA burn were randomized to allograft skin or topical antimicrobial. Patients who received treatment with allograft skin had a significantly shorter hospital stay.56

**Pain management**

Pediatric patients do not always express their pain in the same way as adults. Children may display pain through fear, anxiety, agitation, anger, aggression, tantrums, depression, withdrawal, and regression.58,59 How the child’s experience of pain from the burn injury and the hospitalization is managed clinically will have lasting psychological effects for many months. Burn injury can cause intense pain. Pain can also exist as a constant state throughout the hospitalization. Morphine sulfate is one of the most commonly used analgesia in pediatric burn patients.60 It should be given intravenously, and not intramuscularly. Fentanyl can be also used. Fentanyl Oralet has been used successfully in the tub room for dressing change and wound care (10 $\mu$g/kg). Most outpatients are treated with hydrocodone/acetaminophen, and some require longer-acting narcotics such as methadone.

**Rehabilitation**

One of the integral parts of successful treatment of burn injury is rehabilitation. During the acute phase of burn care, splints and proper positioning are used to minimize joint deformities and contractures. Splints are used continuously except during a therapy session. They are fabricated to each patient’s needs and used from the first day of hospitalization. Bedside therapy, including passive and active range of motion, is started early. Patients with leg graft are kept on bed rest after the operation, but on postoperative day 4 they are started on ambulation. Early therapy and ambulation are the keys to success of long-term rehabilitation in burned children. When patients are discharged from their acute care hospitalization, they undergo rigorous therapies, including stretching, range of motion and strengthening exercises.

**Prevention**

Prevention remains the single best way to reduce pediatric burn injuries. National prevention and education efforts have positively affected the number of pediatric burns each year. Lowering the temperature set point on hot water heaters and teaching families to check the bath water temperature before placing a child in the bath has reduced scald injuries. Prevention groups have worked with gas hot water heater companies and the Consumer Product Safety Commission.
(CPSC) to provide education to raise gas water heaters 12 inches off the ground, which significantly reduces the risk of accidental explosions and fires.

Much work still needs to be done in the area of ‘child fire play’. Three-quarters of ‘child fire play’ involves matches or lighters. All matches and other ignition sources must be placed out of reach of children. A positive step toward prevention occurred in 1994 when the CPSC put into effect a child-resistant lighter to protect children. The importance of placing smoke detectors in multiple areas in a house has received much public education. Current prevention education focuses on children, and especially infants that are not able to remove themselves from a fire. One way to protect infants and children is to dress them in fire-resistant sleepwear and clothing to protect them from a burn injury if a fire does occur.

Educating children as early as possible that fire is dangerous is imperative. Providing safe environments for children and providing appropriate education is the responsibility of healthcare providers, the adults that care for them, and the community at large.

**Further reading**


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Access the complete reference list online at [http://www.expertconsult.com](http://www.expertconsult.com)
References


46. Herndon DN, Parks DH. Comparison of serial debridement and autografting and early massive excision with cadaver skin overlay.


Care of geriatric patients
Laura J. Porro, Robert H. Demling, Clifford T. Pereira, David N. Herndon

Introduction

The quality of life in developed countries has improved over the past 50 years, increasing the average lifespan by nearly 30 years. Individuals aged 65 years and over account for 13% of the US population. This ‘elderly’ population is projected to double from 40.2 million in 2010 to 88.5 million by 2050. Such population aging is unprecedented. By 2050, the number of elderly persons in the world is expected to exceed the number of young for the first time in history. This trend presents a special challenge, as the elderly will constitute an ever-growing segment of the average surgeon’s practice and will influence clinical decisions, ethical decisions, and healthcare costs.

A multicenter study conducted in Tokyo found that 25% of burned patients were over 65 years old. A systematic review of over 186,500 patients in Europe showed that 10–16% were in this age range. In the US, geriatric patients constitute about 10% of the major burn population. The anticipated rise in the geriatric population makes understanding age-related physiological and metabolic changes even more important for the burn care professional. The elderly and the very young are most likely to die from severe burns. Nearly 12 deaths per day result from residential fires, with infants, toddlers, and the elderly representing the high-mortality population. Adults over 65 years old have a mortality from burns that is six times the national average. Treatment of these patients remains a greater challenge than treatment of middle-aged and younger patients, as lower physiological reserves and higher underlying comorbidities reduce the margin for error.

Epidemiology

Contact with flame is the main (50%) cause of burn injury. One-third of injuries result from cooking accidents: scalds in 20% of cases and contact with hot objects in about 9% of cases. The latter cause is more prevalent in the elderly, reflecting increased psychological and physical disability. This fact is also reflected in the rate of fire-related deaths in individuals over 75 years old, which is four times the national average. The male-to-female ratio decreases progressively as age increases, with women exceeding the number of men in the 75 years and older group (compared to the 5:1 male-to-female ratio for young adult burn victims). This ratio is explained by the fact that 95% of burns in elderly people occur at home, compared to less than half in younger adults. Therefore, prevention must be focused on the home. Prevention should also focus on the fact that 30% of geriatric patients are the victims of self-neglect, and at least 10% are the victims of elder abuse.

Outcome

Mortality has diminished among all age groups in recent decades. Technological progress as well as advances in fluid resuscitation, early burn wound excision, skin grafting, and pharmacotherapy have improved survival. As expected, mortality and morbidity are higher in geriatric burn patients. Mortality is 50% in young adults with a burn covering 80% of the total body surface area (TBSA) and in individuals aged 60 and older with burns covering only 35% TBSA. Pereira et al. analyzed 1674 patients admitted to the Shriners Burn Hospital, Galveston, Texas, between 1989 and 2005 as well as 179 autopsies conducted during this period to study mortality trends and primary causes of death in the entire age spectrum over time. They found that mortality has indeed been reduced in all age groups, including the elderly (>65), over the last decade. Lung injury and sepsis were the commonest primary causes of death noted at autopsy. An increase in the weights of heart, lung, spleen, and liver was noted in all age groups post mortem. Pomahac et al. reported an 83% reduction in the odds of death and a 50% reduction in the odds of sepsis in elderly patients treated with a statin before injury. Pomahac et al. reported that increased levels of creatinine at the time of admission were associated with increased mortality.

Gender dimorphism exists in mortality rates of patients over 65 years old. The National Burn Repository 2009 reported an overall greater mortality in women than in men, but a lower disparity during recent years. Age, TBSA burned, and inhalation injury are associated with increased mortality. The mortality rate is 9.7% for patients aged 60–69 years, 17% for patients aged 70–79 years, and 28.6% for patients over 80 years of age.

Geriatric patients also experience greater long-term disability following burn injury. Only about 50% of elderly patients with a major burn return home within the first year, whereas 90% of young adults return home. The increased risk factors present in this population explain these statistics. The increased complications seen in elderly burn patients may also result from more cautious and less aggressive treatments. This is due to existing beliefs that elderly burn patients cannot tolerate eschar excision as well.
as their younger counterparts, resulting in a greater delay in the excision of burned tissue.  

### Risk factors

A number of well-recognized risk factors are present in elderly people. Increased risk of infections, pulmonary diseases, and sepsis as well as the variability of comorbidities present in these patients will increase morbidity after a burn. Some of the more prominent factors are shown in Box 36.1.

### Decreased cardiopulmonary reserve

Aging reduces pulmonary reserve for both gas exchange and lung mechanics. Elderly people are more prone to pulmonary failure, the major cause of burn-related death. The presence of atherosclerosis, coronary artery disease, and previous myocardial infarcts is also common.

### Chronic illness including malnutrition

Numerous diseases are common in the elderly. Some of these, such as swallowing disorders (presbyphagia), can lead to malnutrition. Some degree of protein–energy malnutrition is found in over 50% of elderly burn patients on admission. This, in combination with burn-induced hypermetabolic responses and protein catabolism, can substantially reduce lean body mass in just a few weeks. Daily protein requirements are higher in the elderly than in the younger population.

Malnutrition increases morbidity and mortality after a burn and may increase the risk of burn injury in the elderly. Nutritional support is a critical in improving the clinical outcome of these patients. Use of a screening tool at admission to assess the nutritional status of elderly patients is necessary.  

### Infections

Pneumonia and urinary tract infections are the most prevalent complications in elderly burn patients. The development of pneumonia seems to correlate with the male gender, and presence of inhalation injury. Pneumonia contributes to increase mortality, especially in the elderly.

### Decreased lean body mass

Aging leads to progressive decreases in lean body mass. The lean mass or body protein compartment is responsible for all the physiological and metabolic activity needed for survival, and any significant decrease is detrimental. Any pre-existing loss will result in increased morbidity, early onset of immune deficiency, organ dysfunction, weakness, and impaired wound healing. Losses are caused by multiple factors, including impaired nutrition, reduced mobility, and age-related decreases in endogenous anabolic hormones, human growth hormone, and testosterone.

Decreased anabolic activity prolongs recovery time and greatly delays restoration of muscle. Importantly, elderly people respond to exogenous anabolic stimuli such as testosterone analogs, human growth hormone, and resistance exercise similarly to the younger population. Therefore, exercise, high-protein nutrition, and anabolic agents are essential for recovery.

### Aging skin and wound healing

Aging produces significant changes in the skin. Because of these changes, more deep burns occur in the elderly than in younger patients. After the age of 65 the turnover rate of the epidermis decreases by 50%. A flattening of the rete pegs and fewer epidermal-lined skin appendages are present. These properties significantly delay healing of partial-thickness burns.

In addition to the above-mentioned changes, a progressive thinning of the dermis occurs, along with a decrease in both collagen content and matrix, especially glycosaminoglycan. The latter is responsible for loss of skin turgor. There is also a decrease in vascularity, macrophages, and fibroblasts. The thinner dermis with less blood flow explains the greater amount of deep burn, and the decreased cellularity explains the decrease in all phases of healing.

### Treatment

In general, elderly patients are treated identically to younger patients, except that massive burns are more commonly managed expectantly. Some differences exist in responses to burn injury between children and adults; however, no evidence supports changing the treatment protocol. Current differences in burn management among patient groups are related to comorbid conditions and adversities that may arise.
Initial resuscitation

Improved fluid resuscitation over time is one of the factors associated with decreased mortality. Compared to younger patients, more fluid is required to resuscitate elderly patients with the same burn size to avoid hypovolemia. This is likely attributable to decreased skin turgor, which reduces resistance to fluid accumulation or edema production. Another possible factor is impaired cardiac function. Burn depth, inhalation injury, and delayed resuscitation can influence fluid requirements. Benicke et al. developed a multifactorial resuscitation formula with a compensating factor for advanced age that promises to help in the initial assessment of fluid resuscitation. Early ventilatory support is more commonly required because of decreased lung reserve and earlier fatigue.

Wound management

Early removal of the burn wound and rapid closure with skin grafts are essential for survival. Because the elderly have thin skin, thermal injuries often create full-thickness wounds, and skin grafts cannot always be obtained. In fact, they might create a new wound. Thinner skin grafts are necessary because of the thinner dermis, and healing time is prolonged. Gore found that donor site healing time decreased substantially in elderly patients undergoing AlloDerm skin grafting, allowing more patients to undergo operative wound closure. Because older patients do tolerate operative procedures, a conservative approach is not warranted. Because multiple residual problems persist for years after injury, patient orientation is crucial to understand the long-term outcome of wound healing.

Metabolic and nutritional support

Although elderly patients do not generate the degree of hypermetabolism seen in younger patients, the catabolic response is comparable, necessitating a 1.5 g/kg/day protein intake. Many older patients already have malnutrition and lean mass deficits, as evidenced by prior weight loss. Therefore, the goal of nutritional support must be not only maintenance, but also replacement therapy, especially replacement of protein and micronutrients. Nutrient supplements are invariably required. Most supplements are protein hydrolysates, as the gut is more capable of absorbing the peptides and amino acids than whole proteins broken down from food.

Anabolic agents are valuable adjuncts to optimal nutrition. The effects of insulin and oxandrolone on postburn hypercatabolism have been studied in the pediatric population, and these anabolic agents could be used in the elderly, given that endogenous anabolic hormones are decreased in this group after injury. Fram et al. recommend continuous insulin infusions, with tight euglycemic control, to restore insulin sensitivity, improve mitochondrial oxidative capacity, and reduce resting energy expenditure. Lower-dose infusions of 9–10 U/h promote substantial muscle anabolism without the need for additional large doses of carbohydrate. Intensive insulin therapy during acute care reduces morbidity, mortality, and complications due to infection. Testosterone restoration is effective in both male and female burn victims. However, the synthetic analog oxandrolone is preferable as it possesses only 5% of the virilizing androgenic effects of testosterone and is available in a peroral formulation. Oxandrolone restores lean body mass and improves wound healing in burned adults, especially in emaciated subjects whose treatment has been delayed. The effects of oxandrolone are independent of age. Treatment of acute pediatric burn patients with oral oxandrolone (0.1 mg/kg twice daily) enhances the efficiency of protein synthesis and increases anabolic gene expression in muscle. It also significantly increases lean body mass at 6, 9, and 12 months after burn, and bone mineral content at 12 months after injury. Recombinant human growth hormone has been successfully used in pediatric patients, however, it has several adverse effects, particularly during the acute care of burned patients. The most notable of these is hyperglycemia. In Europe, this agent has been shown to increase mortality in critically ill, non-burned adults. Therefore, we do not recommend its use in the elderly.

β-Adrenergic blockade with propranolol during the acute phase and long term attenuates the effects of the burn-induced hypermetabolic response. In severely burned subjects, titration of propranolol to reduce baseline heart rate by 15–20% increases muscle–protein balance and diminishes obligatory thermogenesis, tachycardia, cardiac work, resting energy expenditure, and fatty infiltration of the liver. However, no study has directly focused on the geriatric patient.

Pain, sedation, and comfort care

Geriatric burn patients are undertreated for pain because of the misconception that less pain occurs with age. Both pain and anxiety further increase the levels of catecholamine, which is deleterious. Reduced clearance of many therapeutic agents occurs with aging, necessitating lower dosages (Table 36.1). For this reason, pain assessment using reliable tools is essential to create an individualized treatment plan, which should also account for any comorbid conditions that may be present on admission. Untreated pain and incorrect sedation may result in post-traumatic stress disorder, major

<table>
<thead>
<tr>
<th>Drug</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barbiturates</td>
<td>Should be avoided. Paradoxical pharmacological response, often leading to restlessness, agitation, or psychosis due to decreased rate of elimination.</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Increased sensitivity to pharmacological effect; some benzodiazepines may be metabolized more slowly</td>
</tr>
<tr>
<td>Narcotic analgesics</td>
<td>Increased sensitivity to analgesic effects; possibly impaired clearance</td>
</tr>
<tr>
<td>Tricyclic antidepressants</td>
<td>Increased incidence of cardiac and hemodynamic adverse effects; urinary retention and other anticholinergic effects; decreased drug clearance</td>
</tr>
</tbody>
</table>

*Decreased dose due, in part, to decreased renal function in the elderly.
depression, and delirium. In addition, although the burn injury primarily determines the extent of the metabolic response, metabolic rates are also greatly increased by obligatory activity, background pain, procedure-related pain, and anxiety. Judicious maximal narcotic support, appropriate sedation, and supportive psychotherapy are mandatory to minimize these effects. Combination drug therapy is often required to achieve adequate analgesia. Different approaches ranging from patient-controlled analgesia to virtual reality have been found to ameliorate pain in burned patients. Intravenous drug administration is still preferable during the acute phase. A proactive geriatrics consultation team may also be beneficial in managing pain. Use of only comfort care measures needs to be strongly considered for elderly patients with burns likely to be fatal.

**Perioperative optimization**

Aging produces many changes in the cardiovascular system that makes hemodynamic stability more difficult to achieve, increasing adverse outcomes. Coronary artery disease is prevalent, being estimated to exceed 80% in patients over 80 years old. Elderly patients are at higher risk for congestive heart failure, and special considerations should be taken during acute and long-term treatments. The revised cardiac risk index stratifies patients into risk groups and helps identify those likely to need additional cardiac evaluation. Patients with minor perfusion abnormalities undergoing low-risk surgery may not require catheterization, but should be considered for prophylactic β-blockers and aspirin before operation. High-risk subgroups of patients identified based on clinical risk factors and positive non-invasive tests should undergo cardiac catheterization. Patients with significant cardiac lesions should have definitive coronary revascularization via angioplasty before large body surface area burns are excised. The potential benefits of using β-adrenergic blocking agents during the perioperative period have been studied, as perioperative ischemic events are related to an exaggerated postoperative sympathetic response that leads to an increased heart rate. β-Blockade has an added advantage in the burn patient. Severe thermal injury induces hypermetabolism that persists for up to 9–12 months, with deleterious consequences occurring in both the acute and the convalescent phases. The resting metabolic rate in burn patients doubles for those injuries covering >40% TBSA. Sympathomimetic amines are key in the initiation of various cascades that stimulate post-burn hypermetabolism. Preventing initiation of these cascades by blocking the action of catecholamines at the receptor level attenuates this response and reduces supraphysiological thermogenesis. Tachycardia, cardiac work, and resting energy expenditure.

The drawback of β-blockade in the elderly is that the aging cardiovascular system is less responsive to β-receptor stimulation. This decrease, together with anesthetic agents, may lead to deleterious intraoperative hypotension in the presence of prophylactic β-blockade. Despite being well tolerated, β-blockers are still withheld in the elderly for fear of drug-related complications. Individualized dosing of β-blockers to control myocardial ischemia postoperatively may be more beneficial because of differences in coronary anatomy and ischemic thresholds among patients. Further investigations are necessary to determine the most appropriate therapeutic regimen for reducing perioperative ischemia, cardiac morbidity, and post-burn hypermetabolic responses in the elderly.

Pulmonary complications are more strongly linked to coexisting comorbidities than to chronological age. Because of the prevalence of chronic obstructive pulmonary disease and asthma in the elderly, physicians should be alert for these conditions during the perioperative evaluation. Perioperative chest X-rays should be ordered selectively. With appropriate diagnosis, aggressive pulmonary rehabilitation including exercise training, patient education, nutritional counseling, smoking cessation, and medication optimization is effective in elderly patients. All these aspects must be integrated into long-term patient management. Aggressive use of antibiotics, judicious use of bronchodilators, adequate hydration and postural drainage, and chest physiotherapy should also reduce the incidence of pneumonia.

**Rehabilitation**

Burn rehabilitation is a long multidisciplinary process that aims to preserve patients’ functional ability and restore independence. Physical and occupational therapy should begin immediately after injury. Important components of rehabilitation include wound healing, scar prevention and correction, splinting, casting, traction, pressure therapy, pharmacological therapy, exercise, and psychological support. The elderly should be aggressively managed during rehabilitation to avoid any further loss of function or strength, which are difficult to recover. The geriatric patient is capable of recovering muscle strength with resistance exercise and should not be managed conservatively. As with children, providing support and guidance for caretakers is essential, as these individuals will be responsible for the patient's wellbeing upon discharge.

**Intentional burns in the elderly**

Identifying physical abuse by burning in the elderly is difficult, as no pathognomonic signs exist. Although such abuse is relatively rare, professionals consistently underestimate the prevalence of elder abuse. The growth in the elderly population makes it necessary to raise awareness among health professionals and re-evaluate the clinical approach and assessment for burn injuries inflicted intentionally or negligently. The elderly often live alone, interacting predominantly with the caregivers who enact their abuse. These individuals may keep their abuse a secret because of shame, guilt, or fear of reprisals. Most forms of intentionally inflicted burns have a higher associated morbidity and mortality than equivalent accidental burns, in part due to comorbidity from other physical abuse, substance abuse, or psychological problems that contributed to or resulted from the inflicted burn. Elder mistreatment can be associated with confidentiality difficulties, as they may not want abuse reported. The priority of the examining doctor is to treat life-threatening conditions. They should then promptly record symptoms and signs of abuse or neglect (including photographs). Deliberately inflicted burn injuries are best...
managed by a multidisciplinary team of healthcare, social service, and legal professionals.\textsuperscript{79}

**Conclusion**

Despite the remarkable reduction in mortality in burned children over recent decades, due mainly to the major advances in patient management, we have not yet achieved the same results in elderly patients. This age group still constitutes a major challenge. Surgical decision making in these patients must take into account physiological age, pre-burn functional status, degree of impairment from comorbid conditions, and clear treatment goals. No patient should be denied an operation based on age alone, as age-related declines in organ function are predictable for the population but not necessarily for the individual. Currently, no ‘score’ can improve decisions based on a thorough evaluation and discussion with the patient and family. Favorable outcomes in elderly burn patient should pertain more to relieving suffering and maintaining independence and quality of life, rather than expanding lifespan. Clear, repeated communication between the burn team and patients or their surrogates is critical for guiding therapy and achieving acceptable outcomes.

**Further reading**


Access the complete reference list online at [http://www.expertconsult.com](http://www.expertconsult.com)
References


Introduction

Various surgical complications can occur in burn patients, resulting from pathologic progression of the burn injury itself to iatrogenic etiologies. Multiple organ system injuries can exist that require both a thorough assessment and expeditious management according to advanced trauma life support (ATLS) guidelines. Patients with large total body surface area (TBSA) burns generally require a prolonged hospital stay with numerous debridement and skin grafting procedures that can be complicated by wound infection and subsequent graft failure.

Burn patients are at risk for potential surgical complications involving multiple organ systems, particularly the gastrointestinal (GI) tract. Such complications include stress gastritis and ulceration, acalculous cholecystitis, superior mesenteric artery (SMA) syndrome, and pancreatitis. In this patient population, the cause for occult systemic sepsis is frequently attributed to GI sources, as evidenced by the development of acute cholecystitis, ischemic bowel, hollow viscus perforation, and intra-abdominal abscess. Necrotizing enterocolititis is a serious GI tract complication in burn patients, representing a phenomenon of transient ischemia–reperfusion injury to the gut. It can progress to full-thickness necrosis of involved segments, perforation and rapid clinical decline.

Abdominal compartment syndrome can occur during the acute phase of massive fluid resuscitation in large TBSA burned patients. Based on determination of increased intrabdominal pressures, a decompressive laparotomy may be necessary to prevent further end-organ damage (cardiovascular collapse, oliguria, elevated peak pressures, and intestinal ischemia). A major burn significantly affects hemodynamics, and invasive monitoring may be necessary. As a consequence, catheter-related vascular complications, such as distal limb ischemia and catheter-associated sepsis, can be seen with both arterial and venous vascular access. Prolonged intravascular manipulation secondary to the need for access predisposes to septic thrombophlebitis and is associated with poor outcomes.

Because of delays in diagnosis and treatment, there is a substantial increase in morbidity and mortality associated with non-thermal complications in burn patients. As such, these secondary and sometimes fatal complications demand immediate recognition and treatment. Patients who suffer major burn injury need diligent care and attention throughout their hospital course to avoid complications arising from various organ systems. This chapter reviews the frequently encountered general surgical, non-thermal complications in burn patients with respect to diagnosis and management.

Burns and trauma

Although the overall incidence of combined burn and traumatic injury is low, the mortality is nearly twice that of burns without associated trauma.1 A retrospective study examined upwards of 24,000 patients with burn, trauma, or combined injuries and found the overall incidence of combined burn and trauma rate to be low (3.8%),2 consistent with the National Trauma Data Bank and National Burn Repository data. Although there was no difference in length of stay, injury severity scores, or mortality among burn or trauma patients alone, there were significant increases in inhalational injury, length of stay, and mortality in patients suffering from combined injuries (Table 37.1). This increase in mortality was seen despite similar TBSA burns, demonstrating the additive effects of trauma and burns in these patients.2

In particular, approximately 24% of military burn injuries are associated with concurrent traumatic injuries, compared to the 2–7% of burn/trauma injuries found in civilians in the same study.3 The most common civilian cause of burn/trauma injury remains motor vehicle collisions (MVC). Of the 500,000 individuals in the United States treated for burn injuries, an estimated 7.2% are secondary to street or highway accidents (American Burn Association, National Burn Repository 2009). MVA victims that require extrication and those that are ejected typically have the most severe multitraumatic injuries. In order of frequency, injured organ systems include musculoskeletal, head and neck, abdominal, thoracic, and genitourinary. Industrial accidents, attempts to escape house fires, explosions, and electrical burns with falls account for the majority of other victims. High-voltage electrical burns rarely occur at ground level and are often accompanied by falls resulting in spinal cord injuries, solid organ injury, intracerebral hemorrhage, and multiple fractures, including vertebral, rib, pelvic, and long bones.
Primary assessment

In trauma patients with multiple organ system injuries, the shocking appearance of the burn injury may unduly shift attention away from the other seemingly underwhelming injuries, resulting in delays in diagnosis. The initial assessment of patients with combined thermal and other traumatic injuries should center on airway, breathing, and circulation according to the ATLS guidelines. With the exception of respiratory compromise secondary to circumferential chest burns, the burn injury itself is usually not immediately life-threatening. Inhalational injuries are common in burn patients. Some of the common signs of inhalational injury include cough, stridor, singed nasal hair, carbonaceous sputum, and a hyperemic oropharynx. Asphyxia can be seen with carbon monoxide and cyanide poisoning, for which pulse oximetry is an unreliable measure of oxygenation. If the respiratory distress is significant, intubation or a surgical airway may be required, and although hypoxemia is usually evident, the inhalational injury can evolve over hours such that an initial chest radiograph and arterial blood gas may be normal. Smoke inhalation induces a multitude of physiologic changes which result in increased vascular permeability and pulmonary edema, infiltration by leukocytes, and bronchorrhea. Therefore, it is not unusual for patients to escalate to unconventional modes of ventilation, such as volumetric diffusive ventilation.

Once the airway has been secured, attention should focus on the rest of the primary assessment. Third-degree circumferential chest burns can impair respiratory mechanics and require escharotomy to release the constrictive eschar. This should be performed in a sterile manner with incisions extending from the clavicle to the costal margin in the anterior axillary line bilaterally, and may be joined by transverse incisions. The more common thoracic injuries, such as rib fractures, pneumothorax, and hemothorax, should be managed as they would be in any other blunt or penetrating thoracic injury. However, because burns carry such a high risk of infection, thoracostomy tubes should be placed away from burned skin whenever possible to reduce the risk of infectious complications such as empyema. Finally, adequate circulation should be assessed. Pericardial tamponade resulting from a heavy impact to the anterior chest wall can be detected by focused assessment with sonography for trauma (FAST) examination and managed with pericardiocentesis or a pericardial window. Myocardial dysfunction may be encountered, especially with electrical injuries, and dysrhythmias should be managed accordingly. If central venous access is necessary, it should similarly be placed away from burned tissue.

### Associated injuries

Burns may also be associated with other traumatic injuries. The cervical spine should be considered unstable until a complete evaluation has been performed. Unstable cervical spine fractures may be managed appropriately with traction via halo or tongs. When necessary, intracranial pressure monitoring via a bolt placed through unburned scalp is preferred over a ventriculostomy. If a neurosurgical procedure is required, debridement of the scalp and non-viable tissue is completed at the same time as the craniotomy.

Orthopedic injuries – primarily fractures – comprise the most commonly associated traumatic injury in thermally injured patients. The burn surgeon and the orthopedist must coordinate the optimal management of these patients. Therapeutic decisions are based upon the following considerations: stability of the fracture, the need for excision and grafting of the burn, access required for adequate burn wound care, and early aggressive physical therapy after the injury. Although fractures away from the burns may be managed with reduction and casting, in cases where fractures are associated with severe soft tissue damage, internal fixation should be performed within 24–48 hours, prior to bacterial colonization of the wound. All open fractures must have incision and drainage performed in the operating room within 24 hours of the injury, and when open reduction occurs through a burn, the wound should only be closed to the level of fascia without drain placement. Using this approach, early aggressive fracture treatment has been shown to reduce orthopedic complications without further risks of infection, poor healing, or amputation. Antibiotic coverage should be provided as deemed appropriate for the orthopedic injury.

The diagnosis of intra-abdominal injury may prove difficult, as the abdominal examination is rather unreliable in the face of a severe burn. In addition, hemodynamic changes that occur with an intra-abdominal injury can be masked by the physiologic response seen with intravascular volume shifts and the exaggerated inflammatory response. Nonetheless, imaging modalities that are currently used to evaluate trauma patients with blunt or penetrating mechanisms should also be considered when evaluating a burned patient with a suspected intra-abdominal injury. Diagnostic laparoscopy can be a helpful adjunct in the evaluation of various intra-abdominal injuries, such as bowel perforation and ischemia, that are difficult to diagnose with computed tomography (CT) alone. However, adequate abdominal CO₂ insufflation is often difficult to achieve in patients with significant eschar of the trunk. If laparotomy is warranted, dehiscence of abdominal wounds is a frequent complication, independent of whether or not the burn wound was traversed. If abdominal wall closure demonstrates significant

| Table 37.1 Increased morbidity and mortality with combined burn and trauma* |
|---------------------|-----------------|-----------------|-----------------|
|                     | Trauma (n = 22,284) | Burn (n = 1717) | B/T (n = 92)    |
| Age                 | 35.1 (±27.5)     | 31.0 (±23.2)    | 40.1 (±25.4)*  |
| TBSA                | N/A             | 17.5% (±19.7)   | 20.8% (±24.4)  |
| ISS                 | 5.5 (±10.3)     | 12 (±14)        | 23 (±16)*      |
| LOS (days)          | 5.3* (±12.2)    | 13.7 (±16.5)    | 18 (±20.8)     |
| INH                 | N/A             | 11.0%           | 44.5%*         |
| Mortality           | 4.3%            | 9.8%            | 28.3%*         |

*p < 0.05 (Age, B/T vs. Burn; ISS, B/T vs. Burn and Trauma; LOS, B/T vs. Trauma; Mortality, B/T vs. Burn and Trauma)

B/T: burn/trauma; TBSA: total body surface area; ISS: injury severity score; LOS: length of stay; INH: inhalation injury.
tension, the use of retention sutures should be considered. Occasionally, a temporary abdominal closure may be required to prevent abdominal compartment syndrome. In cases where the bowel becomes massively edematous, a vacuum-pack for the open abdomen will act as a temporizing measure for a delayed abdominal wall closure.

Vascular injuries may be difficult to diagnose in the presence of burned skin, significant soft tissue edema, compartment syndrome, or hypotension. The principles in their diagnosis remain the same, with an assessment of capillary refill, neurologic deficits, and palpable pulses. A Doppler ultrasound is a non-invasive bedside study that can easily be performed to assess adequacy of arterial blood flow and can be supplemented with an ankle–brachial index (ABI). However, the data, especially the ABI, can be difficult to interpret when extremities are burned full thickness or circumferentially. Although conventional angiography continues to be the gold standard in the diagnosis of major vascular injuries, its benefits do not seem to outweigh its invasive risks in the era of CT angiography. One study found that CT angiography had a >95% sensitivity and specificity in the diagnosis of traumatic arterial injuries of the extremity, with poor arterial opacification being a disadvantage. Thus, CT angiography is a reasonable tool in the diagnosis of major vascular injuries. Should a vascular insult require repair, substantial consideration should be given to the choice of graft (autologous versus synthetic), as contamination is not infrequent and only complicates the care of these critical patients. The liberal use of prophylactic muscle flaps for graft coverage has proved helpful.

**Gastrointestinal tract complications**

Although the superficial effects of burn injuries are often striking, the systemic physiological response to these injuries may result in significant end-organ dysfunction and cannot be overemphasized. Burn injuries >30% TBSA produce a physiological response leading to systemic shock, hypermetabolism, and widespread immunosuppression. The combination of intravascular fluid loss, vasoactive hormone release, catabolism, and immune dysfunction results in the non-thermal complications of burn injuries and has consequently become the focus of preventative treatment and molecular models in the design of future therapies.

Physiological changes in blood flow have a dramatic effect on organ response to injury, healing, and permanent dysfunction. This has been particularly well demonstrated in the GI tract, where a combination of diffuse capillary leak, hypovolemia, and the release of vasoconstrictive agents can cause a selective decrease in splanchnic blood flow. Splanchnic hypoperfusion occurs early in the post-burn period despite adequate cardiac output and fluid resuscitation, as demonstrated in 40% TBSA pig models that had an early reduction in superior mesenteric blood flow associated with intestinal mucosal hypoxia, acidosis, and increased bacterial translocation. The GI tract ischemia has multiple effects, including ulcer formation (Curling’s ulcer), enterocolitis, and acalcitudinous cholecystitis secondary to gallbladder ischemia and bile stasis. Other abdominal organs, such as the kidneys and liver, may endure end-organ damage when exposed to the ‘low-flow’ state associated with hypoperfusion following burns, leading to surgical complications and worsened outcomes.

The hypermetabolic response to burn injury plays a key role in non-thermal complications and is characterized by catabolic metabolism, hyperdynamic circulation, insulin resistance, delayed wound healing, while increased risk of infection. Poor fibroblast function contributes to impaired wound healing, while leukocyte dysfunction and reduced cellular immunity cause immunological compromise. Alterations in stress hormone responses, cardiac output, lean body mass, and sex hormones may persist for several years post burn. Previous studies have demonstrated typical stress responses to a variety of traumatic injuries, with a so-called ‘ebb’ phase resulting in a decrease in metabolism and tissue perfusion, followed by a ‘flow’ phase 3–5 days following injury. Early enteral feeding has been shown to blunt the hypermetabolic response.

Of all the potential mechanisms of injury, severe burns result in the most dramatic metabolic response. The hypermetabolic phase results in the activation of the hypothalamic-pituitary axis, sympathetic outflow, the acute-phase response that promotes fat and protein breakdown, and gluconeogenesis. Excessive catabolism following a burn injury encourages hyperglycemia and insulin resistance within the first week after injury, both of which are associated with an increase in morbidity and mortality in severely burned patients. Recent trials have demonstrated that intensive insulin therapy aimed at maintaining a daily average glucose of 140 mg/dL improves immune function and reduces sepsis, along with an attenuation of the inflammatory and acute-phase response. As such, tight glucose control is thought to be critical in improving the overall recovery of burn patients.

As mentioned, a combination of hypoperfusion and hypermetabolic response can lead to breakdown of the gut mucosal barrier, resulting in bacterial translocation from the gut, systemic inflammation, and ultimately, sepsis (Fig. 37.1). Numerous studies have demonstrated the association between massive cutaneous burn injury and bacterial translocation. Following massive burn injury, the GI tract mucosa sustains immediate atrophy, resulting in significant gut barrier dysfunction. The increase in intestinal apoptosis does not appear to be from mesenteric hypoperfusion alone, but is speculated to be related to proinflammatory mediators produced by the burn wound. An in vivo study using a 30% TBSA burn model in rats confirmed that there was increased bacterial translocation and permeability to macromolecules that peaked at 18 hours post injury, lending credence to the idea that disruption of intestinal barrier integrity in severe burns can lead to sepsis from bacterial translocation. Thus, interventions aimed at preventing splanchnic hypoperfusion and hypermetabolism may circumvent complications associated with severe burns.

Recent studies targeting the inflammatory response itself provide insights into potential novel therapeutic targets, such as p38 MAPK, which is involved in the production of the proinflammatory mediators interleukin (IL)-1β, nitric oxide, and cyclooxygenase (COX)-2. Additionally, p38 MAPK is clinically associated with delayed intestinal transit, a common burn complication. Studies inhibiting key steps of the p38 MAPK pathway have demonstrated attenuation of impaired intestinal transit in rodent models, and may
should be treated with colonoscopy-assisted decompression. Narcotics should be avoided in these patients, as they may worsen the ileus. Recent in vivo animal studies suggest that COX-2 inhibitors may improve delayed gastrointestinal emptying in burn-induced ileus, and thus there may be a potential means of managing post-burn pain without worsening the ileus. Operative intervention is rarely necessary, but would consist of a cecostomy or resection followed by diversion.

Feeding tubes

Parenteral nutrition is associated with increased risks for complication such as intestinal atrophy, bacterial overgrowth and translocation, and catheter-related sepsis. Thus, much emphasis has been placed on ‘feeding the gut’ whenever possible, as the importance of enteral nutrition in critically ill patients has been clearly established. The increased metabolic demands of a recovering burn patient often cannot be met by oral intake alone and this is impractical in patients who are sedated and being ventilated. In these patients, an alternate means of enteral feeding can be accomplished with a feeding tube.

Nasogastric, nasotranspyloric, gastric, and jejunal feeding tubes can all deliver enteral nutrition, and each of these options has its own unique features (Table 37.2). For example, nasogastric tubes are usually easily placed at the
bedside, thereby avoiding the potential complications associated with an endoscopic or open procedure. In addition, nasogastric feedings can also neutralize gastric acid. However, significant facial fractures may be a contraindication to the passage of a nasal tube. If tubes are left in place long term they can be associated with significant sinus infections and aspiration, in addition to aspiration risks associated with tubes inadvertently displaced in the esophagus. Placing feeding tubes past the pylorus has become standard practice to minimize the risk of aspiration and complications of enteral feeding in patients with impaired gastric emptying. However, a meta-analysis found that there was no significant difference in the incidence of pneumonia, caloric goal achieved, or mortality between gastric and postpyloric tube feeding. Therefore, the paradigm has shifted to focus more on early feeding and less on placing a postpyloric tube.

If gastric decompression is needed, a sump nasogastric tube can be used even as enteral feedings are initiated. Fluoroscopic or endoscopic placement of nasoduodenal or nasojejunal feeding tubes has been performed successfully without major complication. Similarly, a jejunostomy feeding tube can eliminate the risk of gastroesophageal reflux associated with gastric tube feedings, but it also carries the risks of an operative procedure. Whichever route is chosen, careful volume titration of the chosen formula is essential to avoid abdominal distension, diarrhea, and discomfort. An open gastrostomy tube can be maintained for extended periods and requires minimal experience to manage. However, a surgical site in the vicinity of a burn itself may be prone to poor wound healing, dehiscence, and gastric prolapse. Percutaneous endoscopic or laparoscopic gastrostomy tube placement is frequently used to minimize the morbidity associated with an open procedure. Though minimally invasive approaches to gastrostomy have become standard in pediatric patients, a potential difficulty of achieving adequate abdominal insufflation in patients with significant third-degree burns to the abdominal torso region must be carefully considered.

The patient’s physiologic needs should be considered in selecting an enteral formula because an inappropriate choice can lead to catabolism and protein wasting, malabsorption, and diarrhea, which further complicates wound healing and local wound care. The pathophysiology of diarrhea in tube-fed burn patients has been extensively studied. High-protein feeds with glutamine supplementation have shown moderate benefit by reducing muscle protein breakdown and infection rates while improving wound healing. To ensure adequate delivery of calories, enteral feeding should be initiated early after a burn injury.

**Stress gastritis**

The incidence of acute gastroduodenal ulceration in burn patients, known as Curling’s ulcer, has decreased dramatically with the introduction of aggressive fluid resuscitation, antacids, early enteral feeding, and proton pump inhibitors (PPI). Figure 37.2 illustrates the management algorithm for upper GI bleeding from suspected Curling’s ulcer. The presence of Curling’s ulcer is clinically recognized in most cases only by the onset of upper GI bleeding, and was once associated with mortality rates of up to 70%. Fortunately, with the institution of the aforementioned interventions, the occurrence of clinically significant ulcers has decreased from 15% to 3%, as has mortality. Gastric ulcers are characteristically multifocal, whereas duodenal ulcers are typically solitary, with 15% of patients having a combination of both. Patients typically present with hemorrhage or, less commonly, perforation, which is seen in approximately 12% of patients.

Although the exact pathogenesis of Curling’s remains unknown, the hypoperfusion, hypermetabolism, and immune dysregulation described above are all implicated in ulcer formation. Specifically, intravascular depletion leads to mucosal ischemia and disruption of the protective mucosal barrier. Compounded by the production of prostaglandins, increased acid production, bile reflux, and direct mucosal injury due to the presence of intraluminal tubes, the end result is gastroduodenal ulceration. Recent studies have proposed an additional mechanism of stress ulcer formation secondary to the systemic production of reactive oxygen species (ROS) in response to stress. Studies have confirmed that the activation of ROS-producing pathways, such as p38 MAPK, results in gastroduodenal ulcer formation. These pathways may provide important therapeutic targets through more generalized reductions in oxidative reactants and inflammatory cytokines. Some have suggested using antioxidants, such as melatonin, to minimize the oxidative damage caused by the original burn, inhibit proinflammatory cytokines, and aid in the recovery of immunomodulation.

An effective approach in the prevention of stress gastritis in burn patients is early enteral feeding. It has been proposed that this may be because of dilutional alkalinization or because enteral feeds provide the energy required for mucosal cell resiliency despite ischemia. Studies have shown that intraluminal glucose provides significant protection to ischemic cells of the small intestine and gastric mucosa. Additionally, aggressive fluid resuscitation along with H₂-receptor antagonists or PPIs have proven effective against formation of stress gastritis. However, once a stress ulcer is established, many of the same treatments described above are initiated. Aggressive medical therapy, typically involving intravenous vasopressin, somatostatin, and a high-dose continuous PPI infusion, must be instigated in patients with massive burns who develop hemorrhage. The PPIs have been demonstrated to reduce instances of rebleeding and the need for subsequent surgery and/or endoscopic treatment (Cochrane Database).

If necessary, endoscopic cauterization can be attempted, but should medical therapy fail, an exploratory laparotomy may be warranted. Specific surgical indications include massive bleeding (>2.5 L in adults, >50% blood volume in children), ongoing uncontrolled blood loss, and evidence of a perforated viscus. Operative repair of ulcers is rarely necessary, but recent evidence suggests that a distal vagotomy and partial, distal gastrectomy with subsequent Roux-en-Y reconstruction is superior to a Billroth II procedure, given that there is less evidence of erosive gastritis at the anastomotic site and fewer symptoms related to reflux. Although Curling’s ulcers are far less common than in the past, they remain a potential hazard to all burn-injured patients. The current low incidence of stress ulceration is due to successful aggressive burn injury management and the use of preventive measures.
Acalculous cholecystitis

Acute acalculous cholecystitis (AAC) is a rare complication of a burn injury, found in an estimated 0.4–3.5% of burned patients, but it may result in significant mortality if not quickly recognized and appropriately treated. Patients particularly susceptible to the development of AAC include those with extensive burns (>40% TBSA), multiple transfusions, sepsis, dependence on total parenteral nutrition (TPN), and a history of narcotics usage. Recent multivariate analysis has shown that age, number of packed red blood cell transfusions, and duration of ventilatory support are independent predictive factors for the development of AAC in severely burned patients. Proposed etiologies of AAC include bile stasis, hypoperfusion with resultant gallbladder ischemia, cystic duct obstruction, and sepsis. Patients with heavy narcotic use for pain control or who are dependent on TPN because they are unable to tolerate enteral feeds tend to experience bile stasis. Hypoperfusion secondary to either intravascular blood loss or systemic sepsis affects circulating vasoactive mediators and local tissue perfusion, leading to local ischemia of the gallbladder wall, inflammation, gangrene, and perforation. Lastly, those who undergo multiple transfusions can have alterations in the composition of bile produced, thereby leading to an increased risk of AAC.

AAC commonly presents with fever, right upper quadrant tenderness, leukocytosis, and elevated liver enzymes. However, these findings are common in severely burned patients; therefore, a high index of suspicion is required for prompt diagnosis. AAC is a surgical emergency, as patients may rapidly develop complications, including perforation or gangrenous cholecystitis. The incidence of gangrenous gallbladder and perforation are noted to be 33–100% and 12%, respectively. Mortality following perforation or gangrenous emphysema is reported to be as high as 65%, but early diagnosis and intervention may reduce the likelihood of severe complications significantly, as reflected by the reduction in mortality to 7%.

Suspected AAC may be confirmed by ultrasonography, demonstrating a thickened gallbladder wall, pericholecystic fluid, and intraluminal sludge. One particular study reported that ultrasonography had a sensitivity of 30% and specificity...
of 93% in critically ill trauma patients. Thus, if ultrasound examination proves equivocal, a cholecystoscintigraphy (HIDA scan) can confirm the diagnosis. CT can also demonstrate thickened gallbladder with pericholecystic fluid. However, many patients are on narcotics, which can obscure the results due to sphincter of Oddi constriction, and false positives can be seen with TPN use and hyperbilirubinemia from massive transfusion. In extremely ill patients for whom surgical intervention is not an option, ultrasound-guided percutaneous cholecystostomy should be considered, as there is a clinical response rate between 56% and 100%.33 In a recent review of 163 patients who underwent percutaneous cholecystostomy, over 80% were able to undergo removal of the cholecystostomy tube and did not require a cholecystectomy.34 Caution must be employed when using this technique, as the incidence of gangrenous cholecystitis is marked in thermally injured patients, and a lack of clinical response after percutaneous cholecystostomy should prompt the surgeon to proceed with an open cholecystectomy.

Pancreatitis

Acute pancreatitis is an under-recognized complication following thermal injury. Elevated levels of pancreatic enzymes have frequently been associated with burns, but the nonspecific symptoms, such as epigastric pain radiating to the back, are often overlooked. In 1995, a retrospective review of adult burn patients identified elevations in amylase and lipase in 40% of their patients with large burns, and this correlated in most cases with symptoms related to pancreatitis.35 A recent study examined 2699 pediatric burn patients and found an incidence of acute pancreatitis of 0.05%.36 Despite its rarity, it was associated with a significant increase in mortality, as survival rates were reported to be only 69% compared to 87% in burn patients unaffected by pancreatitis.36 Management for acute pancreatitis in the burn patient is the same as in non-burn patients: supportive care, bowel rest, fluid resuscitation, and IV nutrition. Ultrasound examination of the biliary tract should be performed to rule out gallstone disease. Occasionally, a more detailed work-up with an abdominal CT scan is necessary to identify complications such as pseudocyst formation, pancreatic necrosis, or pancreatic abscess. Operative intervention is rarely indicated unless these complications are noted, and would consist of a cystogastrostomy, necrosectomy, and drainage, respectively.

Superior mesenteric artery syndrome

Superior mesenteric artery (SMA) syndrome, or Wilkie’s syndrome, occurs when the third part of the duodenum is extrinsically compressed by the superior mesenteric vascular pedicle (Fig. 37.3A, B). SMA syndrome is usually precipitated by rapid and substantial weight loss, leading to a loss of retroperitoneal fat. In burned patients, weight loss through malnutrition, loss of abdominal wall muscle, and a recumbent position contribute to the severity of the duodenal compression. Patients typically present with non-specific symptoms such as nausea, bilious vomiting, intolerance to tube or oral feedings, and abdominal pain aggravated by feeding and relieved by placing the patient in a knee-to-chest position. The diagnosis is established by an upper gastrointestinal series demonstrating duodenal dilation with or without gastric dilation, retention of barium within the duodenum, and extrinsic pressure on the third portion of the duodenum with a characteristic sharp cutoff.37 Management of SMA syndrome is primarily medical, with early enteral feeding not only limiting weight loss to <5% of pre-burn weight, but also reducing the overall occurrence. Once present, SMA syndrome is treated by maximizing caloric delivery either via a fluoroscopically or endoscopically placed nasojejunal feeding tube or parenteral nutrition. Alternatively, a combination of enteral and parenteral feeding may be necessary to meet nutritional needs until the duodenal obstruction resolves. Surgical procedures are rarely indicated, but when necessary, the operative goal should be to bypass the point of obstruction caused by the superior mesenteric vascular pedicle. The operation of choice is duodenojejunostomy, in which a lateral duodenotomy is made and the proximal jejunum is then used to create a side-to-side anastomosis. A laparoscopic approach has been used to relieve the duodenal obstruction in patients with SMA syndrome, with some success.38 Gastrojejunostomy and the Strong procedure (division of the ligament of Treitz with mobilization of the duodenum) are alternative surgical options, but they have proved inferior to duodenojejunostomy because of failure to adequately relieve the obstruction, peptic ulceration, and blind loop syndrome. The latter procedure has a success rate of only 75% in the general population, as opposed to a 98.5% success rate with duodenojejunostomy and division of the ligament of Treitz.39
Necrotizing enterocolitis

Splanchnic hypoperfusion occurs as a result of hypovolemia and circulating vasoactive mediators. The degree of intestinal insult ranges from mucosal atrophy to full-thickness necrosis and perforation, and is a product of the severity and duration of ischemia combined with reperfusion by resuscitative efforts. Moreover, the presence of virulent bacteria and fungi in the immunocompromised state contributes to intestinal complications and can lead to sepsis. In a study of 2114 patients with burn injury, only 10 (0.5%) patients demonstrated clinically apparent ischemic necrotic bowel disease, and they tended to have more severe burns. Although only 2–5% of patients are clinically diagnosed with this condition, autopsy findings identify pathologic changes consistent with ischemia in 50% of burn patients who die as a result of their injuries. Unfortunately, the mortality rate of patients experiencing ischemic enterocolitis is reported to be extremely high, in the range of 60–69%.

Patients with ischemic bowel demonstrate intolerance to enteral tube feedings and high gastric residuals. Abdominal radiographs often demonstrate massively dilated loops of bowel and pneumatosis intestinalis (Fig. 37.4A). Because the overall incidence is quite low, early recognition and intervention requires a high index of suspicion. Burn patients with sepsis or an inability to tolerate tube feeds should be started on broad-spectrum antibiotics. Failure to respond to medical treatment mandates surgical intervention, in which frankly necrotic intestinal segments should be resected (Fig. 37.4B). However, questionable areas of necrosis, particularly when they involve extensive lengths, should be re-examined at a second-look operation within 24–48 hours. Thus, the primary goal is to eliminate obviously non-viable bowel while preserving as much intestine as possible to avoid the additional risk of short gut syndrome.

Intestinal ischemia may result in transmural mucosal damage, which predisposes already immunocompromised patients to bacterial translocation and systemic sepsis. Nearly 75% of burn patients with bowel ischemia at autopsy had concomitant sepsis documented at the time of their death, which emphasizes the high incidence of sepsis and mortality associated with intestinal ischemic complications. Infections are the most common cause of death in autopsied burn patients (61%), with sepsis secondary to the Gram-negative pathogens *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* most frequently seen in the military subpopulation. Massively burned patients are at high risk for pseudomembranous colitis as they are frequently treated with multiple antibiotics for documented systemic infections and for prophylaxis during burn wound excision and grafting. *Clostridium difficile* overgrowth can result in pseudomembranous colitis, with the potential to progress to fulminant toxic megacolon and bowel perforation. In a report of 180 thermally injured patients, the overall incidence of *Clostridium difficile* colitis was ~8% with mean TBSA of 42%. The use of antibiotics and topical silver sulfadiazine has been shown to cause toxic megacolon and places patients at higher risk for colonic perforation. Thus, symptoms of colitis, such as leukocytosis, abdominal pain, distension, and grossly bloody diarrhea, must be promptly recognized. Stool samples are tested for *C. difficile* antigen. All unnecessary systemic antibiotic therapy should be discontinued, and oral vancomycin or metronidazole should be initiated. If medical management fails, a partial colectomy of the involved segment is warranted. With increasing incidence of invasive fungal infections in burn patients, a case of aspergillosis causing invasive systemic infection and mycotic enterocolitis has even been reported.

Vascular complications

Suppurative thrombophlebitis

Suppurative thrombophlebitis is characterized by venous thrombosis associated with inflammation and bacteremia. Not all of these infections occur in association with venous thrombosis, and specific risk factors for suppurative thrombophlebitis include both burn injury and prolonged intravenous catheterization. The diagnosis may be made based on culture results together with radiographic evidence of thrombosis. The classic physical examination findings of edema, erythema, pain, and a palpable cord may not all be
present. Burned patients frequently have positive blood cultures and clinical sepsis without an obvious source, and in the setting of suppurative thrombophlebitis, the most commonly cultured organisms from infected veins reflect those cultured from the burn wound.

The incidence of suppurative thrombophlebitic complications in burn patients has been estimated to be as high as 7%, with significant risk in patients with >20% TBSA burns, and is associated with significant mortality. The principles of treatment include removing the source of infection, administration of intravenous antibiotics, and/or anticoagulation. Two weeks of parenteral antibiotics usually suffices, but longer therapy may be necessary when central veins are involved. Surgical treatment consists of surgical cutoff and evacuation of vein contents. If pus or clot is found, the vein segment should be excised to a normal-appearing vein (usually up to the first uninvolved tributary). If exploration is negative at one site, then sequential exploration of other sites is necessary until the source of infection is identified. Prompt surgical intervention is necessary to prevent hematogenous dissemination and septic emboli that can result in endocarditis and osteomyelitis. The wound should be loosely packed and allowed to heal either by secondary intention or by delayed closure upon resolution of the infection.

In order to minimize the incidence of catheter-related complications, the current standard of practice for central venous access at most institutions involves aseptic care at the catheter insertion site along with regularly scheduled catheter site dressing changes. Some advocate that central venous catheters should be changed over a guidewire every 3 days and a completely new central venous catheter placed at a new site every 6 days. This results in a more acceptable, but by no means ideal, infection rate of 3.2%. Even so, this practice is not widely instituted.

Central venous access

Adequate venous access is imperative in the acute post-burn period for aggressive fluid resuscitation. Although large-bore peripheral intravenous catheters are the preferred route for resuscitating trauma patients, placement can be extremely difficult in those with major burns involving the extremities. Therefore, central venous catheters have become standard practice in major burns. Particular attention should be given to the use of various available cannulation sites, depending on the size of the patient, as well as taking into consideration the clinical condition of the burn wounds. The rate of catheter-related bloodstream infections in burn patients is estimated to be 20 per 1000 catheter days. Therefore, compulsory site care is required. As it is more difficult to resite lines in severely burned than in non-burned patients, guidewire exchange is acceptable unless there is clinical evidence of infection, such as erythema, drainage from the site, or bacteremia.

Central venous line placement is associated with potentially serious complications. In order to reduce the risk of bleeding complications, many burn centers rely on fluoroscopic or ultrasound guidance during the insertion of central venous lines. Although the overall incidence is quite small (1–4%), thoracic complications, resulting from line placement can potentially lead to life-threatening conditions. For example, small pneumothoraces can be treated with observation or a small-caliber (8 Fr) pigtail tube thoracostomy. However, if unrecognized, especially in patients receiving positive-pressure ventilatory support, it can rapidly progress to a tension pneumothorax with hemodynamic compromise. In order to reduce the risk of puncturing the lung parenchyma during central venous line placement, it is crucial to be familiar with the central venous anatomy. For example, because of venous anatomical differences in small children, percutaneous access to the subclavian vein may require a more acute and cephalad angle of approach under the clavicle. Recently, the use of ultrasound guidance has become more widely accepted in central venous catheter placement to reduce some of the obvious risks associated with ‘blind’ percutaneous central venous access.

Bleeding complications associated with central venous access vary in location and can be local, mediastinal, intrathoracic, or pericardial. Local hemorrhage typically occurs in patients with a coagulopathy and can be controlled with local pressure. Hemorrhage into the thoracic space can occur at the time of catheter insertion, but it can also be seen when the catheter erodes through the vein wall. The most common situation leading to venous wall perforation occurs during the insertion of the percutaneous introducer sheath over a guidewire. As the sheath is introduced, it can fail to negotiate the path of the vein and traumatize the vein wall. Consequently, blood may accumulate into the mediastinum, pleural space, or pericardium.

If the injury is small, it should resolve on its own with thrombosis formation. However, in cases of a larger venous tear rapid bleeding into the thoracic cavity can occur, and emergency thoracostomy may be necessary. Bleeding or infusión of fluid into the pericardial space can rapidly compromise cardiac function and result in hemodynamic collapse. Pericardial tamponade typically presents with hypotension, muffled heart sounds, and distended neck veins (Beck’s triad). However, all components of the classic triad of symptoms are rarely present, and a physician must have a high index of suspicion in order to recognize this condition early. Echocardiography can confirm the clinical suspicion, and pericardiocentesis or pericardial window is therapeutic.

Distal limb ischemia

Arterial monitoring is frequently required in patients with major burns. Although radial and pedal arterial catheters are routinely placed without significant complications, they can be associated with problems such as hematoma, thrombosis, and pain. Occasionally the common femoral artery is considered for access, given its larger caliber. Because the femoral artery is the major blood supply to the lower extremity, this site should be approached with caution for fear that thrombosis can lead to distal limb ischemia. Especially in pediatric burn patients, the femoral artery is quite small and the catheter within the vessel can result in near complete occlusion of blood flow to the distal limb. However, our review of femoral artery catheterization in pediatric burn patients showed that the complication rate was quite minimal, while providing a more accurate measure of hemodynamics (Table 37.3). During the 7-year study period 234 pediatric burn patients underwent 745 femoral arterial catheter placements; a total of 12 (1.9%) suffered complications ranging from transient distal limb ischemia to amputation. Eight patients
Chest radiographs may demonstrate pleural effusion along with areas of pulmonary consolidation, if detected at an early serous fluid stage. A lateral decubitus chest radiograph can be helpful to show layering of pleural fluid, but this is often difficult to obtain in burn patients. When this condition progresses to form organized fibrous collections, a bedside ultrasound examination can be extremely helpful to discern loculations in the chest. The diagnosis can also be confirmed with a chest CT scan, on which a parapneumonic effusion may be apparent. CT can also be helpful to differentiate dense consolidation of lung parenchyma from parapneumonic effusion. When detected early, tube thoracostomy is sufficient to drain serous pleural effusions. However, for advanced-stage empyema, which characteristically has thick, fibrous loculations, video-assisted thoracoscopic surgery (VATS) may be necessary to evacuate parapneumonic collections and wash out the chest cavity.

**Summary**

When presented with patients with multiple organ injuries, the protocols for ATLS should be initiated first, followed by a systematic approach to the management of any and all other injuries. Complications requiring operative management in the setting of a burn injury can compound an already overwhelming physiological response. When there is an exaggerated systemic inflammatory response non-thermal injuries are often masked, thereby delaying diagnosis and resulting in worsened outcomes. Surgical issues and complications in this patient population are inevitable, and clinicians must be thorough and astute in the evaluation of patients with a significant burn injury.

---

Table 37.3 **Complications of femoral arterial catheterization**

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Weight (kg)</th>
<th>% TBSA burn/3rd</th>
<th>Catheter size (Fr.)</th>
<th>Cather site burn</th>
<th>Burns to limb</th>
<th>Operator</th>
<th><em>Onset of ischemia (Hr)</em></th>
<th>Surgical exploration†</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.2</td>
<td>17.7</td>
<td>36.5/36.5</td>
<td>3</td>
<td>No</td>
<td>Yes</td>
<td>Anesthesiologist</td>
<td>6</td>
</tr>
<tr>
<td>2</td>
<td>0.9</td>
<td>12.5</td>
<td>95/95</td>
<td>3</td>
<td>No</td>
<td>Yes</td>
<td>Surgeon</td>
<td>12</td>
</tr>
<tr>
<td>3</td>
<td>2.0</td>
<td>12.7</td>
<td>51/51</td>
<td>3</td>
<td>No</td>
<td>No</td>
<td>Surgeon</td>
<td>4</td>
</tr>
<tr>
<td>4</td>
<td>0.5</td>
<td>6.5</td>
<td>18/1</td>
<td>2.5</td>
<td>No</td>
<td>No</td>
<td>Surgeon</td>
<td>24</td>
</tr>
<tr>
<td>5</td>
<td>2.1</td>
<td>15.8</td>
<td>70/70</td>
<td>3</td>
<td>No</td>
<td>Yes</td>
<td>Surgeon</td>
<td>4</td>
</tr>
<tr>
<td>6</td>
<td>12.4</td>
<td>36.3</td>
<td>48/20</td>
<td>3</td>
<td>No</td>
<td>No</td>
<td>Surgeon</td>
<td>12</td>
</tr>
<tr>
<td>7</td>
<td>2.2</td>
<td>13.5</td>
<td>62/58</td>
<td>3</td>
<td>Yes</td>
<td>Yes</td>
<td>Surgeon</td>
<td>4</td>
</tr>
<tr>
<td>8</td>
<td>1.7</td>
<td>13.1</td>
<td>64/59</td>
<td>3</td>
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<td>No</td>
<td>Surgeon</td>
<td>6</td>
</tr>
<tr>
<td>9</td>
<td>2.7</td>
<td>13.7</td>
<td>69/18</td>
<td>3</td>
<td>No</td>
<td>Yes</td>
<td>Surgeon</td>
<td>4</td>
</tr>
<tr>
<td>10</td>
<td>3.8</td>
<td>15.1</td>
<td>57/5</td>
<td>3</td>
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<td>No</td>
<td>Surgeon</td>
<td>6</td>
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<td>11</td>
<td>6.3</td>
<td>22.0</td>
<td>87/87</td>
<td>3</td>
<td>Yes</td>
<td>Yes</td>
<td>Anesthesiologist</td>
<td>6</td>
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<tr>
<td>12</td>
<td>1.9</td>
<td>13.3</td>
<td>47/47</td>
<td>3</td>
<td>No</td>
<td>No</td>
<td>Anesthesiologist</td>
<td>4</td>
</tr>
</tbody>
</table>

*Onset of ischemia (Hr)*
†All patients received IV heparin therapy.

**Thoracic complications**

Apart from central line placement, other concomitant thoracic complications can also occur. When thoracostomy placement is needed, site care must be meticulous. If the chest tube is placed under unsterile conditions, it should be changed out as soon as possible to reduce the risk of empyema. Burn patients are particularly susceptible to the development of empyema owing to high bacterial colonization of wounds and impaired local defenses due to loss of skin integrity. Patients with empyema can present with fevers, leukocytosis, and increased ventilatory requirements.

Chest radiographs may demonstrate pleural effusion along with areas of pulmonary consolidation, if detected at an early serous fluid stage. A lateral decubitus chest radiograph can be helpful to show layering of pleural fluid, but this is often difficult to obtain in burn patients. When this condition progresses to form organized fibrous collections, a bedside ultrasound examination can be extremely helpful to discern loculations in the chest. The diagnosis can also be confirmed with a chest CT scan, on which a parapneumonic effusion may be apparent. CT can also be helpful to differentiate dense consolidation of lung parenchyma from parapneumonic effusion. When detected early, tube thoracostomy is sufficient to drain serous pleural effusions. However, for advanced-stage empyema, which characteristically has thick, fibrous loculations, video-assisted thoracoscopic surgery (VATS) may be necessary to evacuate parapneumonic collections and wash out the chest cavity.
**Further reading**


References


Electrical injuries

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**Electrical burns**

**Introduction**

Electricity is an indispensable part of civilization, invisible and often taken for granted. Electrical burns typically comprise only a small percentage of total admissions to major burn centers – reportedly about 5–7%.1–3 They are, however, the most devastating of all thermal injuries on a size-for-size basis, usually involving both the skin and deeper tissues. They primarily affect young, working men, often have legal involvement, and are the most frequent cause of amputations on the Burn Service. In addition to power company linemen, electricians, construction workers, laborers, and crane operators are at special risk.4 These devastating injuries account for nearly 6% of all occupational fatalities annually.5

Electrical burns have multiple acute and chronic manifestations not seen with other types of thermal injury. These injuries therefore require the specialized care and expertise available at a burn center. Even in the best-case scenario, morbidity, length of hospital stay, and number of operations are much higher than expected based on burn size alone.

**Pathophysiology**

Electrical burn severity is determined by voltage, current (amperage), type of current (alternating or direct), path of current flow, duration of contact, resistance at the point of contact and individual susceptibility. Electrical burns are arbitrarily classified as low-voltage (<1000 V) and high-voltage injuries (1000 V and higher). Whereas low-voltage burns are generally localized to the area immediately surrounding the injury, the high-voltage burn is associated with deep extension and underlying tissue damage, very closely resembling a crush injury.6 Domestic wiring in the United States operates on alternating current (AC) at 120 V. Therefore, nearly all burns occurring indoors, except in specialized industrial settings, are of the low-voltage type. Although the victim or witness(es) often knows the voltage involved, the amount of current is unknown, with current flow related to voltage by Ohm’s Law where:

\[
\text{Current (I)} = \frac{\text{Voltage (E)}}{\text{Resistance (R)}}
\]

Animal experiments have demonstrated that resistance varies continuously with time, initially dropping slowly, then much more rapidly until arcing occurs at the contact sites. Resistance then rises to infinity and current flow ceases.7 Temperature measurements taken simultaneously showed that the rate of temperature rise parallels changes in amperage. Interestingly, tissue temperature, the critical factor in the magnitude of tissue damage, does not increase distal to the contact points.

In North America, more than 99% of all electrical burns are caused by 60 cycle-per-second commercial alternating current, which reverses its polarity 120 times per second. Only an occasional low- or high-frequency industrial injury is encountered. With half of the time spent positive with respect to ground and one half spent negative, the terms ‘entrance’ and ‘exit’ wounds are archaic, as one does not know whether a given point on the body contacted the wire or the ground. These terms have now been replaced by ‘contact points.’ One or more contact points may be clearly visible or at times pinpoint, subtle, or hidden, for example beneath the hairline (Fig. 38.1). A descriptive term such as blow-out type injury describes concentration of current and not its causation.

The path of current makes a significant difference in pre-hospital fatalities, but in patients reaching the hospital alive, current path determinations are often less than precise and meaningful. The patient may have no, one or many visible contact points and an untold number of invisible contacts. An example of this is surgical electrocautery, where the large grounding pad contact site is not visible (hopefully). Despite some misconceptions, the term ‘electrocution’ does not apply to these living patients, as electrocution is defined as ‘to kill by electric shock.’8

Alternating current causes tetanic muscle contractions, which may either throw victims away from the contact or draw them into continued contact with the electrical source – the ‘no-let-go’ phenomenon, creating the potential for continually increasing severity. This phenomenon occurs because both flexors and extensors of the forearm are stimulated by current flow. However, the muscles of flexion are stronger, making the person unable to let go voluntarily. Altered levels of consciousness, reported in about half of high-voltage victims, also contribute to prolonged periods of contact.9 More than 99% of the body’s resistance to electric current flow is at the skin. Resistance is measured in ohms (Ω). Resistance at the point of contact varies from very
low values for sweat-soaked hands or skin in the summer to more than 100 000 Ω for heavily calloused hands or feet during very dry winter weather. Individual susceptibility is a non-quantifiable term to explain why two or more individuals exposed to the same situation have extremely varied injuries.

The burn injury has the potential for three different components: the true electrical injury caused by current flow, an arc injury resulting from the electrical arc generated as the current passes from the source to an object, and a flame injury caused by ignition of clothing and/or surroundings. Electricity arcs at temperatures of up to 4000°C create a flash type injury,10 most often seen in electricians working with metal objects in close proximity to an electrical source. The victim may be thrown by the force, and suffer ruptured eardrums and contused internal organs. When electrical injuries occur without actual current flow through the victim, they are treated and classified in the same manner as any flash burn.

The exact mechanism of electrical injury continues to be the subject of much research, very often appearing clinically to be a multifactorial combination of both thermal and non-thermal causes. Electricity flowing through tissue generates heat, much as it does flowing through the wire of a toaster, with Joule’s law defining the amount of power (heat) delivered to an object:

\[ \text{Power (J-Joule)} = I^2 \times R \times \text{(Resistance)} \]

Tissue resistance is from lowest to highest in nerves, blood vessels, muscle, skin, tendon, fat and bone, respectively. Theoretically, current flow would be distributed in proportion to resistance, with tissues having the highest resistance generating the most heat. However, in animal models the body acts as a single uniform resistance rather than a collection of different resistances, i.e., it behaves as a volume conductor.7 Severity of injury is inversely proportional to the cross-sectional area of the body part involved. Thus the most severe injuries are often seen at the wrist and ankle, with severity decreasing proximally. Deep tissues appear to retain heat so that the periosteous tissues, especially between two bones (i.e. tibia–fibula, radius–ulna) often sustain a more severe injury than superficial tissue. The associated macro- and microscopic vascular injury appears to occur nearly immediately and is not reversible.11 A recent study employing a rabbit animal model and optical microscopy demonstrated severe injury to blood vessels. Necrosis of vascular walls and thrombosis with destruction of arterial endothelium, pyknosis of vascular smooth muscle and fibrinous exudates accompanying the thrombotic changes was noted. This study also showed progressive muscle necrosis over the first 72 hours after injury that the investigators surmised may have been related to the vascular injury.12 Of note, there was also pathologic evidence of injury to organs remote from the contact points (heart, lung, liver and kidney).

Direct and indirect electrical destruction of cells also plays a role in tissue injury. The major mechanisms of injury include Joule heating, electroporation, and electroconformational denaturation of transmembrane proteins.13,14 In all of these mechanisms damage is caused by disruption or modulation of cell membranes. Joule heating can be thought of as the frying of tissue. This is the transfer of energy from charged particles bumping up against tissue molecules and losing energy to the tissue in the form of heat. Temperature causes denaturation of macromolecules, which is usually irreversible. Electroporation is the formation of aqueous pores in lipid bilayers exposed to a supraphysiologic electrical field. The formation of these pores allows calcium influx into the cytoplasm and triggers a subsequent cascade leading to apoptosis. Electroconformational denaturation of transmembrane proteins refers to the changes in polarity of amino acids in response to exposure to electrical fields. Experimentally, voltage-gated channel proteins were found to change their conductance and ion specificity after exposure to a powerful pulsed field.15

**Acute care**

The electrically burn-injured patient presents some unique challenges in the acute setting. There are essentially three acute management concerns differentiating these patients from the thermally injured without flow of electric current. In addition to the application of the basic principles of ATLS, the three issues that need to be addressed in the ‘golden hour’ are: (1) which patients require electrocardiographic monitoring and for how long, (2) which patients are at risk for compartment syndrome and may need emergency surgical intervention (often directly from the emergency department), and (3) how should fluid resuscitation proceed in light of the preponderance of deep tissue injury that may not be appreciated on physical examination, in particular in the presence of pigmented urine?

**Electrocardiographic monitoring**

All studies reviewed in a recent American Burn Association Guidelines paper confirmed that cardiac abnormalities, including dysrhythmias and myocardial damage, occur after both low-voltage and high-voltage injuries, thus reinforcing the need for ECG evaluation as part of the initial evaluation.
Direct myocardial injury may also result. This injury behaves more like a traumatic myocardial contusion than a true myocardial infarction, not having the hemodynamic or recurrence consequences of atherosclerotic myocardial infarctions. Housinger et al. have shown that creatine kinase (CK) and MB-creatine kinase (MB-CK) levels are poor indicators of myocardial injury in the absence of ECG findings of myocardial damage, especially in the presence of significant skeletal muscle injury. Myocardial damage and dysrhythmias are manifested very soon after injury. Although cardiac troponins are the preferred biomarkers for detecting myocardial injury in most clinical settings, this has not been adequately studied in the setting of electrical injuries. A recent study using serum troponin levels and serial echocardiography in 20 patients surviving high-voltage injury concluded that this was not a useful diagnostic test for predicting impaired left ventricular contractility. The interpretation of cardiac biomarkers is problematic and needs to be correlated with other clinical findings. All patients should be monitored during transport and in the emergency room. Rather than a policy of more prolonged cardiac monitoring for all patients, a selective policy makes most efficient use of expensive medical resources, without patient risk.

Indications for cardiac monitoring include (1) loss of consciousness, (2) ECG abnormality and/or evidence of ischemia, (3) documented dysrhythmia either before or after admission to the emergency room, and (4) CPR in the field.

No published studies have directly studied the appropriate duration of telemetry monitoring, but most series indicate 24–48 hours. Our institutional bias is to monitor for approximately 24 hours post injury in those patients with an indication. Low-voltage injuries not meeting the criteria for cardiac monitoring and no other indication for admission can be safely discharged from the emergency room. This is not applicable to high-voltage injuries, although there is retrospective evidence that dysrhythmias will occur early if at all in these patients.

Myoglobinuria
The presence of pigmented (darker than light pink) urine in a patient with an electrical burn indicates significant muscle damage with potentially ongoing ischemia. Myoglobin and hemoglobin pigments present a risk of acute renal failure and must be cleared promptly. Whereas low levels are of little clinical concern, grossly visible urinary pigmentation requires a rapid response to minimize tubular obstruction. Urine with a color darker than light pink is promptly treated by titrating resuscitation fluid (Ringer's lactate) to maintain a urine output double the goal rate, or approximately 100 mL/h in an adult. Therapy continues until the urine appears clear clinically. In addition, other methods have been adopted to enhance renal clearance of myoglobin. These include alkalinization of the urine with a sodium bicarbonate bolus or continuous infusion, as well as administration of mannitol for osmotic diuresis. These adjuncts are not supported by level I evidence, but many burn centers have successfully adopted their use in various forms. The required urinary output is generally very high for several hours following injury, followed by a significant reduction in urine requirements, as venous return from the injured part to the central circulation is thrombosed. Failure to clear pigment from the urine is generally an indication of significant muscle necrosis and/or ongoing ischemia. This should prompt a thorough evaluation of the likely current path and underlying muscle damage, as this failure of therapy can often be taken as an indication for operative intervention for decompression versus debridement/amputation.

In the absence of gross myoglobinuria, the goal of resuscitation is to maintain normal vital signs and a urine output of 30–50 mL/h with Ringer's lactate, whose rate is adjusted on an hourly basis to achieve these goals.

Traumatic injuries
Approximately 15% of electrical burn victims sustain traumatic injuries in addition to their burn, a rate nearly double that of other burn patients. Most of these injuries are caused by a fall from a height or being thrown against an object, but some resulting from the tetanic muscle contractions associated with the electrical shock itself, forces strong enough to cause compression fractures. A careful history and physical examination should select those patients who require a full trauma evaluation.

Compartment syndrome
Patients with high-voltage electrical injuries of the extremities are at risk for the development of compartment syndromes during the first 48 hours post injury. Damaged muscle, and swelling in the investing fascia of the extremity, may increase pressures to the point where muscle blood flow is compromised. Loss of pulses is one of the last signs of a compartment syndrome, unlike the early loss of pulses occurring in a circumferentially burned extremity requiring escharotomy. A high index of suspicion is paramount for an early diagnosis, usually by serial examinations. Compartment pressure measurement is generally not necessary and may even be misleading (Figs. 38.2 and 38.3). Whereas a very aggressive approach to fasciotomy has been advocated in the past, significant morbidity attends a fasciotomy and its closure. Amputation rates were generally reported to be in the 35–40% range in most of these early series. Mann et al. have made a convincing argument for a conservative course regarding the indications for fasciotomy, that is, for the usual clinical signs of compartment syndrome, progressive nerve dysfunction or failure of resuscitation, with other patients undergoing exploration and aggressive debridement on the third to fifth post burn days. Elevated CK levels have been correlated to the extent of muscle damage, with the authors advocating early decompression and aggressive surgical management in patients with strongly elevated CK levels. In the author’s experience making the decision to operate is generally not difficult. These are rarely subtle injuries. There is often an obvious indication for operative intervention on the
Coverage of the ensuing wound may include dressings soaked q 4–6 hours with 5% mafenide acetate (Sulfamylon) solution or a biologic dressing such as porcine heterograft, and the extremity is kept elevated to hasten resolution of edema. The initial operation is followed by a second look in 24–48 hours, with debridement or amputation. However, a conservative tissue-sparing approach is generally prudent. Fasciotomy wound closure is often not possible in these injuries, and skin grafting may be required for wound coverage. The Vacuum Assisted Closure device (VAC) has made the management of burn wounds considerably easier. Primary amputations are not generally performed, except to remove mummified, contracted extremities where there is no question about viability.

**Wound care**

Local burn care is performed using 11.1% mafenide acetate cream (Sulfamylon) on the thick eschar of the contact points, because of its excellent penetration. Silver sulfadiazine is used for microbial control on the deep flash/flame components and a biologic dressing on more superficial areas. Surgical excision is begun 2–3 days post burn, either as a second-look operation following fasciotomy or as the first procedure in patients not requiring fasciotomies. All obviously necrotic tissue is removed, but tissues of questionable viability are retained and re-evaluated every 2–3 days until all non-viable tissue is ultimately removed. A very conservative course of tissue removal and wound closure with a combination of skin grafts and/or flaps for soft tissue coverage gives the best functional results. An ongoing program of physical therapy and functional splinting is begun the day of admission if practical, and continued throughout the hospital stay. Serial neuromuscular examinations are performed to document neurologic status. Regional anesthesia is avoided to minimize medical legal complications should late neurologic dysfunction arise.

**Pain management**

Pain management in electrically injured patients has not been well studied. Standard regimens in the acute phase of care are similar to those for other thermally injured patients and include opioids, NSAIDs, and benzodiazepines for pain and associated anxiety. Pain concerns and management regimens change over the treatment course as the patient enters rehabilitation and the more chronic stage of care. In a recent study the most common medications in the acute setting were opioids and acetaminophen, and in the rehabilitation phase antidepressants and NSAIDs. Non-pharmacologic treatments were also used, such as massage therapy and cognitive behavioral therapy. This reflects the changing requirements and concerns in these complex patients as well as the need for a multidisciplinary team approach.

**Diagnosis**

Multiple diagnostic modalities have been investigated in attempting to speed up the process of identifying the extent of deep tissue necrosis. These include xenon-133 and technetium pyrophosphate scans as well as gadolinium-enhanced...
magnetic resonance imaging. 38–42 Albeit very sensitive and specific, diagnostic scans add little to direct clinical evaluation, and for all practical purposes are expensive and unnecessary.

Problem areas
Contact points on the scalp, chest and abdomen provide additional specific management problems. Scalp burns which spare the galea are managed by excision and skin grafting directly onto the galea, whereas wounds that penetrate or expose the outer table of the skull or deeper require a different approach. Exposure of non-viable calvarium has historically been approached by providing a viable wound bed after removing the dead bone with an osteotome or a dental burr. Drilling multiple holes in a close-set pattern, deep enough to cause bleeding from viable cancellous bone, is another method to develop granulation tissue which eventually covers the entire area. The latter method is still useful in situations where a patient’s advanced age or large burn size precludes more aggressive approaches to wound closure. All of the above methods require weeks to months of care before the wound is ready for autograft coverage. The best and most expedient approach to these deep skull burns is a rotation scalp flap(s) over the burned area. Split-thickness skin grafts cover the resulting adjacent defect. This provides rapid closure and is associated with minimal morbidity. 53 Skin expansion of the hair-bearing area can be performed 12–18 months later to obliterate the areas of alopecia. Scalp-tissue expansion for coverage of open wounds is, however, described only in case reports. 44,45 Larger scalp defects are closed with free flaps anastomosed to appropriate vessels lying outside the zone of injury. A recent study evaluated the outcomes of early free tissue transfers in 13 cases at various anatomic locations. 56 Operations occurred between 24 hours to 3 weeks post burn. All but one flap survived. Once again this reinforces the concept of multidisciplinary care and the early involvement of a qualified plastic surgeon in appropriate cases.

Chest wall injuries present special closure problems (adjacent or remote soft tissue flaps) for coverage of exposed bone and cartilage. Costal chondritis is the most frequent complication of deep chest wall burns, often becoming a source of long-term morbidity, requiring multiple debridements.

Abdominal wounds provide the potential for internal injuries, both directly under contact points and remotely as the result of late ischemic necrosis. 47,48 Patients must be frequently evaluated for changes in their abdominal examination and/or feeding tolerance. Deterioration mandates laparotomy.

Lightning injury
Lightning is the second leading cause of weather-related death in much of the world, but under-reporting likely influences the data. 49–52 Approximately 100,000 thunderstorms occur in the US each year, with lightning killing more people than any other weather phenomenon – about 80 fatalities per year – with Florida and Texas having the most deaths. 53–55 Although lightning strikes involve millions of volts of electricity, the spectrum of burn injury is extremely varied, from minimal cutaneous burn to significant burns equal in depth to commercial high-voltage electricity. Major cutaneous injury is rare unless a nearby object is turned incandescent, causing a flash/flame type injury, as when a bag of golf clubs on the victim’s back is struck. The pathognomonic sign of a lightning strike is a dendritic, arborescent or fern-like branching erythematous pattern on the skin. Lichtenberg figures (also known as keranographic markings), consist of extravasation of blood in the subcutaneous tissue which appears within an hour of injury and fades rapidly, much like a wheal and flare reaction. 55,57 Full-thickness isolated burns on the tips of the toes have also been reported as characteristic. Both findings are useful in determining the cause of injury in the patient found down under uncertain circumstances. 58

Lightning may cause both respiratory and cardiac standstill, for which CPR is especially effective when promptly initiated. 59 Patients may respond to resuscitation even when they appear dead, and even when the interval between injury and resuscitation is prolonged. It is important to realize that diluted or non-reactive pupils are not necessarily a reliable sign of brain death in the early post-injury period, nor is GCS a predictor of outcome. 60–62 The ears should be carefully examined as injuries are frequent, ranging from ruptured tympanic membranes (most common) to middle and inner ear destruction. 63

Neurologic complications are relatively common and include unconsciousness, seizures, paresthesias and paralysis, which may develop over several days after injury. The term keranoparalyis (Charcot’s paralysis) has been used to describe the latter symptom complex and is associated with vasomotor disorders. Fortunately these are usually transient. Surgically treatable lesions, including epidural, subdural and intracerebral hematomas, may occur, mandating a high index of suspicion for altered levels of consciousness. 55 The prognosis of many lightning-caused neurologic injuries is generally better than for other types of traumatic cause, although subtle neurologic changes may persist, suggesting a very conservative, watchful waiting and supportive approach with serial neurologic examinations after an initial CT scan to rule out correctable causes. A study by Muehlberger et al. with follow-up to 12.3 years after injury showed that none of their 10 patients had long-term neurologic or psychological deficits. 64 However, post-traumatic stress disorder is common, occurring in about 30% of patients after lightning injury. 65

Low-voltage burns
Low voltage alternating current injury is usually localized to the points of contact, although with prolonged contact, tissue damage may extend into deep tissues with little lateral extension, as seen in high-voltage wounds. These wounds are treated by excision to viable tissue and appropriate coverage based on wound depth and location.

Burns of the oral cavity are the most common type of serious electrical burn in young children. 66 Most of these injuries are the result of an unattended small child (commonly < 4 years of age) chewing on an electric cord. Injuries involving only the oral commissure are almost never excised, as the extent of injury is difficult to predict (Fig. 38.4). Simple wound care is performed as an outpatient
Complications

The primary early complications of electrical injury include renal, septic, cardiac, neurologic and ocular manifestations. Neurologic deficits may be present on admission or develop days to weeks after injury.

Cataract formation is the most frequent ocular complication of electrical injury, although ocular manifestations may affect all portions of the eye. The exact pathophysiology is unknown, but ocular changes may affect as many as 5–20% of patients with true electrical burns. Saffle et al. reported on seven patients with 13 cataracts, noting a high rate of bilaterality and little association with voltage or location of contact points, although often thought of as being more frequently associated with contact points of the head, neck and upper trunk. Of this series, 77% eventually progressed to the point where surgical therapy was necessary, the results of which were uniformly good. Lag time before appearance may be as short as 3 weeks and as long as 11 years after injury.

Neurologic complications are protean in their diversity and may present either early or late (occurring up to 2 years after injury). Neuromuscular defects including paresis, paralysis, Guillain–Barré syndrome, transverse myelitis or amytrophic lateral sclerosis can be caused by electrical injury. Several studies showed that the incidence of post electrical injury sequelae into perspective. Grube et al. reported on 64 patients with high-voltage burns, 67% of whom developed immediate central or peripheral neurologic symptoms. One-third had peripheral neuropathies and one-third of those were persistent. Furthermore, 12% had delayed onset of peripheral neuropathy, with 50% resolving. They reported no late-onset central neuropathies. Singerman et al. reported neurological and psychological complication rate of 81.6% and 71%, respectively. The most common neurological symptoms were numbness (42%), weakness (32%), memory problems (32%), paresthesias (24%), and chronic pain (24%). The most common psychological symptoms were anxiety (50%), nightmares (45%), insomnia (37%), and flashbacks to the event (37%). Interestingly, the low-voltage injuries resulted in more long-term sequelae than high-voltage injuries. Further studies from the same center demonstrated only a 30% return to work after low-voltage electrical injuries. In a study by Chudsamama et al. the high-voltage injuries had more complex and longer hospital stays and more frequent complications than low-voltage injured patients. In spite of this the low-voltage group experienced similar rates of neuropsychiatric sequelae, limited return to work, and delays in return to work. Ko et al. reported on 13 patients with delayed onset of spinal cord injuries, postulating on a vascular cause of the deficit. The most common peripheral defect is a peripheral neuropathy, with weakness being the most commonly found clinical finding. In general, resolution of early-onset lesions is much better than for late onset, spasticity is more frequent than flaccidity, and function is affected more than sensation. Sympathetic overactivity with changes in bowel habits, urinary and sexual function is the primary autonomic complex complication. Although the exact mechanism of nerve injury has not been explained, both direct injury by electrical current and/or a vascular cause receive the most attention. To date, imaging studies, including angiography and MRI, have not been helpful in either predicting or evaluating the extent of deficit. Very often, neuropsychological status is abnormal. In a study comparing electrical burn patients with non-burned electricians, Pliskin et al. showed significantly higher cognitive, physical and emotional complaints not related to injury or litigation status. A full neurologic examination must be performed on admission, documenting the initial presentation. Early involvement of an experienced, interested physiatrist is important in assessing long-term needs and participating in the creation of a therapy plan.

Heterotopic ossification occurring at the cut ends of amputation sites is unique to the electrically burned patient. This occurs in about 80% of patients with long bone amputations, but not in patients with disarticulations or small bone amputations. Ossification was severe enough to require surgical revision of the bone end in 28%. This is easily accomplished by opening the stump incision and using a bone rongeur to remove the soft heterotopic bone and reclosing the stump.

Although electrical burns comprise only about 3% of all burn injuries, they consume enormous amounts of resources, requiring a carefully planned team approach for optimal care.

Further reading


Access the complete reference list online at http://www.expertconsult.com
References


Introduction

'Severe cases [of electrical injury] coming for reconstruction present a formidable problem of flexion contracture and loss of many tendons and nerves, new pedicled skin and grafted-in tendons and nerves usually being necessary. One encounters inside the limb the same type of destruction and cicatrix as is found after any severe infection.'

Sterling Bunnell, 1948

This chapter will focus on the multitude of surgical and reconstructive problems that result from electrical injury. The injury severity is complex due to various factors determining manifestation and the distribution of the resulting tissue damage. In common with other types of trauma, especially burn injuries, the consequences of electrical injury may affect a wide range of physiological functions. Its distinct features warrant a differentiated approach to this unique kind of trauma. The resulting tissue loss and the damage to essential structures of the involved body areas often require extensive plastic-reconstructive procedures.

Although the incidence of low-voltage burns has declined steadily over recent decades, most probably due to progress made in the field of home and occupational safety education and equipment, electrical injuries still account for 3–5% of all admissions to major burn centers. Electrical fatalities are relatively uncommon and most of them occur accidentally. Earlier reported limb amputation rates of up to 71% decreased over recent decades with the increasing ability to reconstruct anatomic parts and restore function, but limb salvage remains a surgical challenge.

Physiological basis of tissue destruction

The traditional pathophysiological understanding of electric injury was based on the assumption that the passage of electric current produces heat and triggers tissue damage. Thus, tissue-specific susceptibility (and vulnerability) is considered to increase progressively from nerve to blood vessels, muscle, skin, tendon, and fat to bone. As osseous tissue shows the highest electrical resistance it will generate the most heat. Electric current will preferentially take the path of least resistance through the body, so that the current will pass particularly along the neurovascular bundles. This theory further postulated that the lesions produced by the current would result in delayed vascular occlusion and progressive tissue necrosis.

In high-voltage injuries the internal milieu acts as a single uniform resistance. Instead of conduction through specific preferential tissues, the body conducts the current with a composite resistance of all tissue components. The crucial factor in determining the resistance and hence the magnitude of tissue damage is the cross-sectional diameter of the affected body part. Devastating injuries to the extremities occur with a significantly higher frequency than tissue damage to the thorax and abdomen (Fig. 39.1). As muscle tissue occupies the largest cross-sectional area in the limb it also carries the predominant electric current. As joint areas are regions where the cross-sectional tissue composition changes from low-resistance muscle to high-resistance bone, tendon and skin, a proportionally higher current and heat are produced in these areas according to Ohm's Law.

Arcing describes the energy transmitted by a hot electrically conducting gas. However, this requires a voltage of more than 20 000 V to bridge even a short distance of 1 cm. Effects on tissue vary from minimal skin wounds to charring and tissue vaporization.

The different trauma mechanisms of the burns induced by the arcing phenomenon are often referred to as 'flush burns', heat burns which are induced by the massive heat generation. 'Electrothermal burns' are caused by current passage through the body and the concomitant heat production.

Electrical damage to a large artery represents a grave prognostic sign for limb survival. The reported risk of amputation is high, between 37% and 65%. Further non-thermal mechanisms of cellular injury have been defined. This includes a voltage-induced loss of cell membrane semipermeability. When the integrity of the cell membrane is lost, the impedance is markedly reduced, leading to a simultaneous increase in the area exposed to current flow. In addition to breakdown in cellular integrity electrical fields also induce denaturation of membrane proteins by altering their structural conformation and rendering them non-functional. Both mechanisms are responsible for
Clinical determination of tissue viability is based on inspection and the demonstration of muscle contractility. As yet, there are no other diagnostic tools available to accurately assess the extent of tissue damage in the early phase following electrical injuries. The value of magnetic resonance imaging (MRI) for the detection of non-perfused non-edematous muscle is debated.\(^{24-26}\) Angiography, although not providing information on tissue viability, demonstrates the absence of tissue perfusion and may lead to an early indication for limb amputation.\(^{27}\)

**Rhabdomyolysis and myoglobinuria**

Destroyed muscle cells release myoglobin, resulting in myoglobinemia. Hemolysis also often occurs with electrical injury. Serum levels of creatinine and creatinine phosphokinase (CPK) are used as indicators of rhabdomyolysis. After muscle injury CPK levels will peak by 24 hours and return
to baseline within 48–72 hours. This diminishes the diagnostic value of serum and urine chemistry testing.

Renal failure

Myoglobinuria has traditionally been considered a major risk factor for the development of acute renal failure. Recently, patients with electrical injuries have been shown to have a surprisingly low risk for renal failure. In 162 patients, only 14% had myoglobinuria and none developed renal failure. Suggested criteria to evaluate the risk of acute renal failure after electrical injury include prehospital cardiac arrest, full-thickness burns, compartment syndrome, and high-voltage injury. The presence of at least two of these criteria should instigate immediate treatment, as the timeframe to prevent progression to acute renal failure is limited to a few hours post injury.

Cardiac monitoring

Among the estimated 1300 deaths that occur annually in the United States from electrical injury (including lightning strike), 30% of patients present with cardiac complications. The majority of ECG abnormalities are sinus tachycardia and non-specific changes in the ST-segment and T-wave. Death from electric injury most commonly results from current-induced cardiac arrest.

However, if an initial ECG shows no abnormalities the delayed development of cardiac problems is very unlikely, irrespective of whether the patient sustained high- or low-voltage injuries. Conversely, the presence of dysrhythmias or conduction abnormalities on initial presentation, electrical injury in children, or the projected path of the current flow crossing the thorax on initial presentation, warrant prolonged cardiac monitoring. Depending on the nature of the current-induced arrhythmia, pharmacotherapeutic and/or invasive interventions may be necessary. Table 39.2 outlines recommendations for cardiac monitoring of electrically injured patients based on central clinical findings and specific features of the trauma mechanism.

Apart from specific therapeutic measures for cardiac complications, acute treatment of patients with electrical injuries adheres to guidelines of ABLS, ATLS and current practice of intensive care medicine. The patient must be continuously monitored for signs of neurovascular compromise, and deranged tissue perfusion and oxygenation.

Surgical debridement

In recent decades the concept of progressive tissue necrosis has led to the treatment strategy of early debridement and fasciotomy, followed by serial debridement and delayed wound closure. The observed changes may likely be explained by vascular changes similar to ischemia–reperfusion injury with immediate cessation of capillary blood flow in response to current passage. This event is followed by vascular spasms lasting for an extended period, with subsequent vasodilatation and restoration of flow. Although still controversial, these findings may alter the acute treatment paradigm.

Although there is little discussion about the early time point of debridement, several recent studies question the need for extensive and total necrectomy and advocate the approach of delayed soft tissue coverage. ‘Conservative debridement’ consisting of removal of charred and obviously necrotic tissue was promoted in a study on 40 patients. In this study partially damaged tendons, muscles, and nerves were preserved, and wound closure was achieved by immediate flap coverage. Patients treated in this manner with immediate soft tissue coverage had a significantly better outcome than a control group who underwent serial debridement procedures. Similar results were found in a study using early free-flap coverage for electrical injuries, suggesting that careful limited initial debridement is an adequate measure. According to this study overly extensive and repeated debridement to ensure viability of all remaining tissue appears not only unnecessary but quite likely harmful. It appears safe to abandon these strategies and to perform an early, extensive but selective debridement in order to preserve continuity of functionally important structures. Limb salvage with functional preservation of vital structures should be attempted and may require revascularization using segmental vein grafts or segmental cable grafting of nerves. Pedicled flaps should be considered in cases of suspected arterial compromise.

Despite the encouraging results of the studies recommending early soft tissue reconstruction, by all means it should be noted that for the extent of electrical injury no scoring system has so far been established. Alternative approaches to salvage upper extremity function, such as the temporary ectopic implantation of an undamaged hand, have been reported but cannot be considered standard of care.

Compartment syndrome

Muscle compartment pressure should be monitored clinically and by invasive pressure measurements. In contrast to blunt trauma, pain is not a reliable indicator of increased compartment pressure owing to the high incidence of electrical nerve injury. When compartment pressures exceed

| Table 39.2 Recommendation for cardiac monitoring in the absence of other injuries |
|---------------------------------|------------------|
| **Admission and cardiac monitoring** | **Discharge** |
| Loss of consciousness | Asymptomatic patient |
| Extensive burns | Normal initial ECG |
| Current passing through the thorax | Uneventful 4-hour observation |
| Cardiac dysrhythmias | Voltage less than 240/260 in adults Voltage less than 120/240 in children FP. 1257–1259 |
30 mmHg surgical decompression by open fasciotomy becomes necessary to prevent ischemic muscle injury. In case of lower compartment pressure, progression may be prevented by administration of non-steroidal anti-inflammatory drugs (NSAIDs) and antioxidants, protective splinting, and rest without elevation of the affected extremities. However, general operative decompression in high-voltage injuries to extremities appears not to be warranted. In a cohort study, Mann et al. found an increased amputation rate of 45% with immediate operative decompression compared to patients undergoing selective fasciotomy, and they recommend fasciotomy only in cases of progressive peripheral nerve dysfunction, manifested compartment syndrome, or other major injuries \( \text{(Fig. 39.2 and Fig. 39.3)} \) With a fixed neurological deficit, however, surgical decompression shows no influence on outcome. If the clinical situation remains doubtful, however, the performance of open fasciotomy with early debridement may be preferred.

**Head: scalp, skull and mouth**

Exposure and necrosis of osseous structures may lead to osteomyelitis and epidural abscess formation. Treatment strategies depend on the extent of the injury to the bone. In case of only a partial necrosis of the bone the outer table of the skull can be tangentially removed and the viable diploic cavity exposed. In cases of sufficient vascularization the exposed bone can be grafted immediately or, when blood supply is questionable, grafted when suitable granulation tissue has developed. Vacuum sealing of the wound can be of significant efficacy in growing adequate amounts of granulation tissue. When the initial wound debridement is delayed, necrotic and infected bone potentially becomes the source of a full-thickness skull defect. Full-thickness injury of the skull theoretically requires complete excision of the necrotic bone to prevent infectious complications. Another approach suggested is partial debridement followed by definitive flap coverage of the exposed bone. This, however, requires early debridement and the prevention of localized bacterial colonization and infection.

In a series of 10 male patients with non-viable cranial bone after class IV electrical burns, 3 weeks after initial soft-tissue debridement multiple burr holes in the non-viable and preserved bone were made and scalp flap coverage was performed. Leaving the necrotic osseous structures in situ serves as a scaffold of substitution for bone regeneration.

Skull contour was maintained in all 10 patients, making a secondary cranioplasty unnecessary. During a follow-up period of at least 1 year no postoperative infection, osteomyelitis, or cranial bone sequestration occurred.

Another option is the use of glycerol-preserved allografts (GPA). The growth of spontaneous sufficient granulation tissue is promoted by its angiogenetic capacity and split-skin autografts can be performed at a later stage. Further beneficial properties of GPA appear to be related to their permeable epidermal barrier, the subjacent network of dermal collagen, and the protection of the bone by restoration of a physical barrier that prevents drying out and reduces the risk of infection. With these allografts the average healing time could be shortened to 6 weeks.
Electrical injury: reconstructive problems

Tightened lower lip, and consequent inhibition of normal mandible growth.63,64 The conservative management approach, which we prefer, performs the reconstructive procedure after maturation of the burn wound scar. Thus the extent of the damage is more apparent and the reconstruction can be performed electively.65 Oral splinting has been advocated during the initial healing period to reduce the need for reconstructive surgery. However, this more likely reduces scar contractures, so the planned reconstructive procedure can be performed after scar maturation.66–68

Thorax and abdomen

Electrical injury to the trunk is generally a minor concern. However, high-tension injuries can cause damage to underlying parenchymatous organs such as the lung. Clinically this may lead to atelectasis and edema, requiring aggressive

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**Figure 39.3** High-voltage injury from a power line (50,000 V). Presentation with primary loss of perfusion, loss of function and compartment syndrome. Initial operation with fasciotomy, revascularization of the radial artery and necrectomies. On the following days adequate perfusion with a patent radial artery without coexisting veins. Coverage with groin flap on day 6. Venous congestion and subsequent malperfusion was temporarily treated with leeches. Secondary amputation on day 10 due to late occlusion of the radial artery.
ventilator support. Intra-abdominal injuries are uncommon, but may require treatment as for penetrating injury. When exploration during escharectomy and debridement reveals necrotic underlying muscle and fascia, exploratory laparotomy may be indicated. Reconstructive options for the closure of chest or abdominal wall defects include direct closure or placement of a synthetic mesh covered by local fasciocutaneous or musculocutaneous flaps. However, the potential negative effects of direct closure on intra-abdominal pressure and the subsequent development of an abdominal compartment syndrome or compromise of respiratory function must be considered.

Extremities

Electrical injuries to the extremities, especially to the arms and hand, are more common in adult members of the workforce. Electrical burns account for 3–5% of all admissions to burn units and approximately 1000 deaths per year in the United States. There are three patterns of injury: direct, arc, and flash-type injury. Direct injuries are associated with entry and exit wounds, and nearly 90% of these injuries involve the upper extremity. As the resistance and hence the local energy production are dependent on the tissue mass and the cross-sectional diameter of the injured body part high-tension injuries often lead to extensive tissue damage and loss of the involved extremity. Despite aggressive treatment strategies with early debridement and decompression of neurovascular structures, the likelihood of amputation is high. In the current literature the amputation rates for electrical injuries affecting the upper extremities range from 24% to 49%. Even if amputation can be avoided the resulting outcome may be a non-functioning extremity. With the phenomenon of ‘kissing’ lesions extensive tissue damage may occur, with resulting thermal necrosis of muscle, tendon, nerves, and blood vessel. The superficial injury may appear innocuous, but debridement shows deep tissue destruction often mandating limb amputation. The importance of initial debridement cannot be overstated, as remaining non-viable tissue leads to infection and tissue loss. In our view the early debridement of non-viable tissue prevents this fatal development. When distal limb ischemia becomes obvious one can assume that the involved vessels have been severely injured. In these cases early vascular grafting of upper extremity arteries may be indicated to salvage an ischemic upper limb. Imminent or suspected compartment syndrome should always trigger indicated to salvage an ischemic upper limb. Imminent or suspected compartment syndrome should always trigger.

Other regions of selective destruction in the upper extremity are elbow and axilla. Debridement often leaves a vast tissue defect, which may be covered by rotation flaps from the anterior or posterior chest wall in the axilla. Microvascular free flaps at the level of the elbow are rarely used. For extensive defects on the hand and forearm pedicled groin flaps provide good coverage and an independent blood supply. The groin flap also avoids a vascular ‘steal phenomenon’ as can be seen after microvascular free flaps in such severely injured extremities.

Newer approaches comprising early wound excision, coverage, and revascularization of damaged vasculature with flow-through free flaps and aggressive endovascular interventions will offer an opportunity to improve outcomes for these devastating injuries.

Saint-Cyr and Daigle compared the use of free flaps with conventional multistage procedures and found a statistically significantly reduction in the number of operations, the time required to achieve wound closure, and duration of hospitalization in the microsurgical group. The flap survival rate as described in the current literature is lower in the high-voltage injury group than in the burn injury group. It ranges from 62% to 100% and is lowest when performed early, within 5–21 days of trauma. In conclusion, free flaps play a key role in treating high-voltage electrical injuries to the extremities by reducing morbidity and functional impairment, which are characteristically high after these injuries.

Amputations

Although distressing to the patient, amputation often remains the only option. As already mentioned, the amputation rates for electrical injuries affecting the upper extremities range from 24% to 49% in the current literature. Despite an increased awareness of the potential danger of electrical burns, devastating outcomes with four-limb and penis amputations are still presented in the literature. Although very rare, Haik and colleagues presented a case of a 5-week-old girl undergoing MRI for evaluation of spina bifida. She sustained a full-thickness burn encompassing her right forearm and wrist in the area where a non-MR-compatible pulse oximeter was attached. A possible cause for this incident could have been an electrical injury due to an exposed wire segment in direct skin contact. Even if immediate escharotomy was performed this injury led to amputation of the forearm and hand. The optimal level of amputation is determined by the extent of remaining viable tissue and the intention to create sufficient stump length for function and cosmetic appearance of a prosthesis. In electrical injury involving the lower extremity this often requires higher amputation than initially anticipated in order to achieve sufficient stability of the stump and thus allow early prosthetic fitting and ambulation. However, open (guillotine) amputation should be avoided whenever possible. Split-thickness skin grafting onto open stumps is an
additional but less preferable approach, as skin breakdown occurs more often in grafted areas, especially at graft borders or at point where grafts adhere to underlying bone, and further surgical interventions will be required. However, if valuable stump length can be maintained by skin grafting it should be attempted, as secondary plastic surgical correction and specific prosthetic fitting are available.

In the upper extremity more length should be preserved, as the resulting weightbearing load on the stump is less than in the lower extremity. This allows for better control of the prosthesis by the patient and thus enhanced functionality. In the forearm the muscle length of the flexor–extensor system should be preserved to improve function. In long forearm stumps, atraumatic handling of tendons and muscles is necessary to preserve pronation and supination. Upper arm amputations should preserve as much length as possible as this cases subsequent kineplastic procedures for a functional prosthesis. As in the forearm muscular length of the flexor–extensor system is maintained by joining them over the bone end. Although it is technically feasible to maintain extremity length by coverage with a free flap, this appears only useful in upper extremity amputation where the functional implications warrant such large-scale surgery and the load on the stump is reduced.

Despite the availability of sophisticated modern myoelectric prostheses the old techniques of surgical rehabilitation should be kept in mind. This includes the Sauerbruch kinemato-myoplasty of the biceps humeri muscle and the Krukenberg plasty of the forearm, which provides sensible chopstick-like stumps. Especially for upper arm amputations distraction osteogenesis procedures (Ilizarov technique) provide a valuable option to lengthen a short amputation stump.

Peripheral nerve injury

Peripheral nerves are very sensitive to electric alterations, and even minor injury may cause transient dysfunction. Clinical findings may be anesthesia, paresthesia, or dysesthesia of usually short-term duration. In rare cases minor electrical injury may cause temporary autonomic dysfunction and trigger a complex regional pain syndrome (sympathetic reflex dystrophy). Treatment for reflex sympathetic dystrophy should be initiated early and include elevation of the extremity to reduce edema formation, active exercise, non-steroidal anti-inflammatory drugs, and adequate pain relief. The autonomic dysfunction may be influenced by α-adrenergic antagonists, calcium-channel blockers, and low-dose diazepam, or may require intravenous regional blocks and sympathetic ganglion blockade.

Electrical injury to the upper extremity commonly results in peripheral nerve injury to the median and ulnar nerves. The clinical findings may resemble upper extremity compression syndromes or peripheral neuropathy. Nerve lesions may be caused by secondary factors such as incorrect positioning and splinting, constricting dressings, or delayed inadequate escharotomy or fasciotomy. Owing to the accompanying severe muscle loss and scarring the extent of pure nerve damage is sometimes difficult to determine.

Direct damage to peripheral nerves occurs following the above-mentioned mechanisms of local heat production, depending on cross-sectional resistance and the proximity of peripheral nerves to underlying bone. The local thermal effect affects vascularity and perfusion of perineural tissue by producing thrombosis, necrosis or hemorrhage of epineural vessels. Delayed development of fibrosis and therefore a delayed onset of symptoms are not uncommon. Especially in areas of minimal cross-sectional area, the peripheral nerve is in close proximity to bone and fibrous tissue which results in perineural fibrosis and symptoms of a compressive peripheral neuropathy. The treatment of choice to gain nerve recovery is decompressive corrective surgery. Other mechanisms of nerve injury are the development of focal axonal degeneration following axonal excitation, or electroporation, which more likely affects myelinated axons, and collagen type I deposition.

Complications

Central nervous system

Approximately 60% of all patients with high-voltage injury present with immediate neurological complications, predominantly loss of consciousness. Involvement of the spinal cord has been described in 2–27% of patients with an entry point of the current located in the head region. The incidence of a delayed paralysis progressing to tetraplegia followed by partial remission has been described. Although mortality in patients with neurological complications from electrical burns is not high, these patients are at great risk of permanent disability. The neurological sequelae were classified in 1964 by Silverside into immediate, secondary and late effects.

Immediate spinal cord injury is transient and symptoms usually clear within 24 h after the accident. The late effects are characterized by progressive traits where complete recovery is not the rule. The ischemic injury in the distal area of the sulcal branch, the longest branch originating from the anterior spinal artery, is due to the susceptibility of the anterior horn cell and the spinal cord at T4–T8 to ischemic injury. Early administration of prostaglandin E1 or steroid treatment is recommended to reduce ischemic spinal cord injury in cases of electrical burns. The neuropsychological effects of electric injury have been described, mainly in case reports and retrospective studies. Typical consequences and complaints are related to physical, cognitive, and emotional changes. In a study on 481 professional electricians, 97% reported having experienced an electrical shock at some point in their career. The low incidence of neuropsychological dysfunction in this study differed from other findings about the nature and progression of a characteristic neuropsychological syndrome of electrical injury. Although the development of transient and progressive neuropsychiatric complications is possible and undisputed, the actual specific effects of electrical injury are difficult to determine.

Ocular manifestations of electrical injury

An increased incidence of cataract formation has been described after electrical injury, varying from 1% to 8% in different reports. Patients with head and neck wounds
Skeletal injury

Besides direct tissue destruction through electrical energy, additional trauma can be indirectly inflicted by electric current. Fractures occur due to secondary falls or with forceful tetanic muscle contractions. These are mostly seen in the shoulder, wrists, femurs, and spine, and may require open reduction and internal fixation. Late sequelae of electrical injury similar to severe thermal burns include major joint contractures and limited function of the extremities.

Another common late complication of electrical burns are heterotopic calcifications in periarticular tissue of large joints, especially the elbows. Causative factors include forced passive mobilization, secondary articular bleeding, and calcium precipitation and deposition in damaged or degenerating muscle and connective tissue. Particularly for electrical injury, heterotopic bone formation also occurs in amputation stumps of long bones. This, as well as the common formation of bone cysts in the amputation stump, may lead to secondary skin erosion, inflammation, and difficult adjustment to a prosthesis. In both situations surgical excision and wound closure may be adequate therapy.126

Summary

Electrical injuries result in deceptively large tissue loss, often leading to amputation of involved extremities. After initial resuscitation, early debridement, necessary decompression of neurovascular structures, and early wound closure are essential to successful restoration of function. Extensive surgical procedures including free soft-tissue transfer may be necessary to achieve wound closure, and to save and restore limb function. Sometimes, however, early amputation may provide easier and earlier recovery and reintegration into daily life. Long-term complications such as central nervous sequelae, cataracts, and heterotopic ossification must be considered and addressed early in the rehabilitation process.

Further reading

Saint-Cyr M, Daigle JP. Early free tissue transfer for extremity reconstruction following high-voltage electrical burn injuries. J Reconstr Microsurg. 2008;24(4):259-266.
References


43. Jaffe RH, Willis D, Bachem A. The effect of electric currents on the arteries. Arch Pathol. 1929;7:244-249.


50. Engrav LH, Gottlieb JR, Walkinshaw MD, et al. Outcome and treatment of electrical injury with immediate median and ulnar nerve palsy at the wrist: a retrospective review and a survey of
83. Saint-Cyr M, Daigle JP. Early free tissue transfer for extremity reconstruction following high-voltage electrical burn injuries. *J Reconstr Microsurg.* 2008;24(4):259-266.
Cold-induced injury: frostbite

Amalia Cochran, Stephen E. Morris, Jeffrey R. Saffle

History of frostbite

Frostbite is a traumatic injury caused by the failure of normal protective mechanisms against the thermal environment, resulting in local tissue temperatures falling below freezing. The preponderance of documented experience with frostbite has come from military campaigns, where the success of many of these campaigns hinged on the incidence of cold injury. Cold-induced injury remains a relatively frequent injury in the United States owing to increasing interest in outdoor winter recreational activities as well as the common presence of homeless and socioeconomically disadvantaged individuals in large urban centers.1,2

The incidence of and circumstances surrounding frostbite have been documented in numerous military histories.3 Hannibal lost nearly half of his army of 46,000 soldiers during a 2-week crossing of the Alps due to frostbite injury. During the Revolutionary War, Dr James Thatcher recorded the first systematic medical observations of frostbite while serving as Surgeon General of Napoleon's forces during the ill-fated invasion of Moscow in the Fall of 1812 and the subsequent retreat in a harsh Russian winter.4 Because of the epidemic nature of frostbite in this campaign, Larrey was able to create seminal descriptions of frostbite and to identify the debilitating effects of daily refreezing that occurred with bonfire thawing and subsequent marching in frigid conditions; in addition, many soldiers would burn their insensate frostbitten feet while attempting to rewarm them over bonfires. Larrey became convinced that the optimal therapeutic management consisted of friction massage with snow or ice, resulting in slow rewarming.4 These recommendations were maintained as the standard of care for frostbite in military medicine for more than 100 years.

In the winter of 1941–1942, German troops sustained an estimated 250,000 frostbite injuries in the attempt to take Moscow, constituting the largest reported number of related frostbite injuries in history.7 Although American troops persisted with the practice of slow rewarming, both German and Russian troops had moved to a philosophy of rapid rewarming; the Russian paradigm shift was based on work conducted at the Kirov Institute in the 1930s.5,6 Following World War II existing Russian and German works were translated into English and became the basis for rapid rewarming as the predominant Western paradigm. In 1960, Mills published the first major clinical experience with rapid rewarming and included a philosophy of total care for frostbite with this report.7 Meryman subsequently edited a seminal text elucidating the scientific bases for frostbite injury.8 Both military and civilian cold-induced injury data continued to accrue over the subsequent three decades in the absence of any significant clinical advances in the care of frostbite.9–16 Frostbite continues to present a tremendous clinical challenge, with the greatest clinical advance coming only in the last decade with the use of thrombolytic therapy in early management.17–19

Pathophysiology and classification of frostbite

The injury associated with frostbite is attributed to two broad mechanistic categories: the first is that of direct cellular damage and death due to the cold insult, and the second is the delayed process mediated by progressive tissue ischemia.20–23 The immediate effects of frostbite are evidenced by formation of extracellular ice crystals. These crystals cause direct injury to the cell membrane, resulting in cellular dehydration due to a change in the osmotic gradient.24 The rate of cooling is reported to have an effect on the development of extracellular or intracellular ice crystals. Rapid cooling results in intracellular freezing, causing more severe cellular damage and cell death, while a slower rate of cooling produces extracellular ice crystals. This slower process results in a transmembrane osmotic shift that draws water from within the cell and produces intracellular dehydration. This dehydration causes changes in protein and lipid conformation as well as changes in biochemical processes that are deleterious to intracellular homeostasis.25–29 As the temperature continues to fall, intracellular crystals develop regardless of cooling rate, with a loss of the linear relationship of temperature to metabolism, decreased DNA synthesis, and histamine response with skin flushing and development of a fluid-filled wheal (the triple response of Lewis).13,30–33

Microvascular pathophysiology may be even more important to outcome than the direct thermal injury to the cell. This was suggested by studies showing the survival of full-thickness skin subjected to freezing and thawing that progressed to necrosis when left in situ but survived when transplanted to a normal, uninjured recipient site.23 Zacarian identified a number of processes that may play a role in the microcirculatory changes of frostbite. Transient
vasoconstriction of both arterioles and venules with subsequent resumption of capillary blood flow appears to occur, and concomitant microemboli are present.\textsuperscript{34} With thawing, the capillaries demonstrate restoration of blood flow that diminishes within minutes. Complete cessation of blood flow is often seen within 20 minutes of rewarming frozen tissue. Similar changes have been seen with random skin flap models after reperfusion, suggesting reactive oxygen species as mediators of injury.\textsuperscript{35} Within 72 hours significant de-endothelialization and deposition of fibrin in the capillary bed occurs. Examination of the endothelial ultrastructure demonstrates swelling, fluid extravasation, endothelial cell dilation, and significant projection of the cell into the vascular lumen prior to cell lysis.\textsuperscript{36} There is regional variation in the extent of injury, with venules being most profoundly affected, resulting in the hypothesis that, as evidenced by lower flow present in venules, stasis must play a role in this pathophysiologic process.\textsuperscript{32}

The pathobiocchemistry of frostbite has been closely compared to the inflammatory response in the burn wound.\textsuperscript{37} Inflammatory mediators such as eicosanoids in burn blister fluid as well as bradynkinin and histamine release in the region of injury draw parallels with findings in cold-induced injury.\textsuperscript{38-41} This has prompted investigators to hypothesize a frostbite model similar to that of Jackson’s for burns, including zones of necrosis and stasis.\textsuperscript{46} Similar to their burn blister analysis, Robson and Heggers examined the fluid in frostbite blisters and found high levels of prostaglandin F\textsubscript{2} and thromboxane B\textsubscript{2}.\textsuperscript{37} These agents or their precursors have been implicated in vasoconstriction and leukocyte adherence. In addition, when refreezing follows thawing the cellular damage caused by ice crystals and the subsequent inflammatory response are exaggerated.\textsuperscript{37,48}

**Clinical findings and classification of frostbite injury**

In many situations, the patient is unaware that frostbite is occurring. The presence of hypothermia and the frequent use of mind-altering substances by frostbite patients may contribute to this problem. Typical distribution of injury is acral, with injuries to ears, nose, cheeks and penis also being fairly common.\textsuperscript{9,14,49} The patient may note insensitivity and clumsiness of the affected part. This complex of symptoms rapidly reverses upon rewarming. Severe pain occurs during and immediately after the rewarming process, is often described as throbbing in character, and typically requires parenteral opioids for relief.\textsuperscript{50} This may evolve into severe neuropathic pain that can be aggravated by warm environments and dependent positioning of the injured body part.

Because of the nature of freezing injury, classification has traditionally been based on physical examination findings and adjunct imaging that occurs after rewarming. A condition often termed ‘frostnip’ may be present in which there is not true injury to the underlying dermis or soft tissues. The most common presentation of frostnip is numbness and pallor of exposed skin. Rewarming results in near-complete resolution of symptoms and physical findings, with the possible exception of minimal hyperemia, edema, and tingling in the region. True frostbite, on the other hand, always involves some degree of dermal and soft tissue injury. Clinical appearance evolves over a period of time after rewarming, although the initial appearance may be deceptive because of the hyperemia present in both frostbite and frostnip.\textsuperscript{9,51} The development of skin blebs is time dependent and may require hours to days from the time of injury. After 12–24 hours the character of the blebs usually becomes apparent and an assessment of the degree of involvement can allow for planning of management of the injury.

Traditional classification of frostbite is similar to that of the burn injury. First-degree injury is superficial, without formation of vesicles or blebs. There may initially be an area of pallor with surrounding erythema that evolves into general edema and erythema without long-term sequelae. Second-degree injury has associated light-colored blisters and subsequent epidermal sloughing. This may correlate with partial dermal involvement but has a generally favorable prognosis. Third-degree frostbite typically has dark or hemorrhagic blisters that evolve into thick, black eschar over 1–2 weeks. Fourth-degree injury involves bone, tendon or muscle and uniformly results in tissue loss. Precision in depth of injury cannot be expected and some favor a more general classification of superficial (first- and second-degree injury) or deep (third- and fourth-degree) frostbite injury.\textsuperscript{52,53} Clinically these can be delineated by clear vesicles, present with superficial injury, or hemorrhagic blisters, indicative of structural damage to the subdermal tissues.\textsuperscript{53,54} Cauchy most recently proposed an alternative classification system based on risk of amputation that includes the extent of the lesion immediately after rewarming, findings from bone scan on day 2, and the presence of blisters on day 2.\textsuperscript{55} Although this system has not come into widespread use, the relationship of objective findings to prognosis may prove helpful for future therapeutic trials in the management of frostbite.

**Initial management of freezing cold injury**

Prevention is obviously the ideal means of treatment for frostbite. Frostbite continues to be a relatively frequent injury in the United States owing to increasing interest in wilderness activities, even during inclement weather. Further, the incidence of frostbite among homeless and mentally ill individuals persists, with these groups representing the most frequently seen local cold-injury patients; alcohol and drug intoxication heightens these risks.\textsuperscript{1,2,49,56,57} Although the cases of frostbite that occur in intoxicated, mentally ill, and homeless individuals are truly preventable only through broader social interventions, simple techniques exist for those who sustain frostbite secondary to involvement in cold-weather wilderness activities. Frostbite prevention measures in cold-weather wilderness activity include, but are not limited to, wearing appropriate clothing, which may include layers, keeping that clothing dry (particularly clothing over acral areas, such as gloves and socks), responding appropriately to changing conditions, and performing ‘cold checks’ of at-risk or suspect areas.\textsuperscript{38} If frostbite is identified in the field, the greatest management priority is to not incur further injury. Jewelry should be removed if present in the affected area; rubbing the area
with ice or snow, although consistent with historical recommendations, is now known to incur further damage to fragile, injured tissue. Injured areas should be mechanically protected from trauma because they are typically insensitive and are at high risk for further injury. The key decision that must be made in the field is whether thawing should be pursued prior to transfer to a facility that can provide definitive care for the frostbite injury. Based on the work of Mills at the Arctic Aeromedical Laboratory demonstrating the deleterious effects of thawing and refreezing on clinical outcomes from frostbite, rewarming in the field should not be pursued unless the ability to maintain the affected tissue in a thawed state is certain. Systemic cold injury in the form of hypothermia often accompanies local frostbite injury, mandating that patients be carefully evaluated to verify that they are normothermic prior to commencement of definitive frostbite management. Hypothermia causes peripheral vasoconstriction and diminished blood flow, processes that are exacerbated by the local cold injury. Most importantly, hypothermia can be life-threatening, as opposed to the limb or digit threat posed by frostbite. Moderate to severe hypothermia, defined as a core temperature <32°C, should therefore be addressed prior to initiation of frostbite treatment. The traditional recommendations for rapid rewarming favor a water bath temperature of 40–42°C. The State of Alaska guidelines recently changed the water bath recommendation to a temperature of 37–39°C, as this does not substantially increase the time to rewarming but causes less pain for the patient during that process. The water bath for thawing should be maintained in this range with the water circulating around the involved tissue. The duration of rewarming is approximately 30 minutes, although clinical findings to determine the length of time for rewarming include the return of sensation (often resulting in significant discomfort to the patient) and presence of flushing at the most distal aspect of the involved tissue. Administration of narcotics is appropriate at the time of definitive rewarming because of the pain associated with the thawing process. In addition, because these are tetanus-prone wounds, the patient’s tetanus immunization should be verified and updated as appropriate. Finally, systemic antibiotics are recommended by some authors in patients with marked edema because of loss of the antimicrobials such as silver sulfadiazine or sulfamylon. Topical aloe vera alone was credited with clinically significant tissue salvage in these patients, resulting in preferential management with aloe vera rather than topical antimicrobials such as silver sulfadiazine or sulfamylon. Topical wound care, including gentle daily cleansing, also should address mechanical protection of the affected areas, with careful padding, splinting, and elevation to manage edema formation.

Non-surgical therapies
Pharmacologic management of the frostbite patient also includes systemic blockade of the arachidonic acid pathway to ameliorate the inflammatory response to the local cold injury. Historically aspirin was used and did demonstrate tissue survival improvement >20% in a rabbit ear model. However, aspirin blocks all arachidonate metabolites, including those that are beneficial for wound healing. Therefore, more recent recommendations center on the use of ibuprofen and the specific blockade of TXA2.

Pentoxifylline, a phosphodiesterase inhibitor that is primarily used in claudication, has been shown to synergistically improve tissue viability in conjunction with topical aloe vera. Pentoxifylline improves red blood cell flexibility, which may limit microvascular sludging and thereby diminish thrombus formation in small vessels. In addition, pentoxifylline may reduce blood viscosity, again contributing to improved tissue survival. When pentoxifylline is used for post-thaw pharmacologic management, the current recommendation, based on a study of pedal frostbite, is 400 mg TID for 2–6 weeks following injury. Both reserpine and tolazoline have been used as vasodilators in hopes of diminishing the vasospasm associated with freezing cold injury, with poor results for both. Iloprost, a prostacyclin analog that also serves as a vasodilator, has interesting features that may be of benefit, although all data on its use are preliminary. Although studies of pentoxifylline and iloprost are ongoing in Europe, current data are inadequate to recommend their use.

Thrombolytics have demonstrated the most notable clinical advances in the management of frostbite in the last 50 or more years. The first demonstration of possible utility for thrombolytics in frostbite management was an animal model using IV urokinase. In 1992 a preliminary account was shared showing that thrombolytics were potentially better than slow rewarming for reducing amputations following frostbite injury. Subsequent publications by the
Minneapolis group and the Utah group have shown significantly improved digit salvage with the use of tissue plasminogen activator (t-PA). Unfortunately, t-PA only appears to be efficacious within 24 hours of thaw, meaning that this may not be an option for patients who are injured in extremely remote environments. Additionally, although digit salvage has been improved with thrombolytics, the actual long-term functional results of this salvage have not been documented.

Sympathectomy, both surgical and chemical, has largely fallen out of favor owing to clinical results that are mixed at best. Early studies of sympathectomy demonstrated that it had the potential to reverse vasospasm, although this was at the cost of increased edema if undertaken too early following injury. Most importantly, sympathectomy has not shown any improvement in tissue preservation in frostbite and may ultimately result in more proximal injury demarcation. Perhaps the two best-documented benefits to sympathectomy affect long-term function, with improved cold tolerance and amelioration of the neuropathic pain and paresthesias that often present one of the greatest clinical challenges following freezing cold injury. Therefore, the best use of sympathectomy may be in the longer-term management of disabling complications of frostbite.

Studies of hyperbaric oxygen (HBO) are limited but have some of the most promising functional results of an adjunctive therapy for frostbite. One of the early documented uses of HBO for therapy in frostbite involved four Alpine mountaineers, all of whom presented 10 or more days following injury and all of whom demonstrated good tissue preservation with HBO. More recent case reports, again with delayed therapy, involved a patient with deep injury to multiple digits; this patient had complete preservation with 14 days of HBO treatment and did not sustain the neuropathic sequelae commonly seen with freezing cold injury. In an additional case study in the last decade, improved nutritive skin flow was demonstrated 2 weeks following injury. The utility in delayed presentations combined with the potential for improved functional outcomes make HBO an extremely attractive therapy in frostbite, although definitive evidence in its favor has not yet accumulated. Multicenter trials of HBO would provide substantial progress toward understanding the role for this therapy in frostbite management.

**Imaging and surgical management**

Both scintigraphy and MRI/MRA have been recommended as diagnostic aids to improve the process of surgical management of frostbite. Over 20 years ago, Mehta identified three different patterns in triple-phase bone scanning that were useful indicators of outcome within 48 hours of injury. Specifically, he found that perfusion and blood pooling phases demonstrated at-risk tissue and the bone phase showed deep tissue and bone infarction. Several studies have demonstrated excellent correlation between scintigraphic findings and surgical outcomes, although some authors claim that bone scan findings best correlate with surgical findings at 7–10 days following injury. Confidence in scintigraphic findings by some practitioners has been adequate for them to derive a protocol using the findings to direct early surgery. The use of MRI/MRA initially seemed promising, allowing direct visualization of occluded vessels and possible better delineation of viable tissue than 99mTc scanning. However, a subsequent study demonstrated that MRI was no better than bone scanning to identify anatomic sites for amputation, and that the limited soft tissue present in digits hampered the utility of MRI.

Because of a historical bias based on data showing that early surgery was potentially associated with worse outcomes, the adoption of scintigraphy with early operative intervention has been limited. However, Greenwald developed a protocol with early scintigraphy followed by operative intervention at 7–10 days following injury. Cauchy makes a plausible argument for intervention at 10–15 days post injury with a bone scan, based on a shorter waiting time for the patient, lower infection risk, and earlier progression to rehabilitation; of note, Cauchy advocates repeat scanning at 7–10 days post injury if the injury is not clearly delineated on an early (<48 hours) bone scan. Nevertheless, the prevalent clinical practice remains to time surgery anywhere from 4 weeks to 3 months following injury, once tissues have clearly demarcated to an experienced clinical eye.

**Summary**

Frostbite has a long clinical history but remains a modern clinical challenge. Although the pathophysiology of freezing cold injury is well delineated, few advances from the traditional ‘frostbite in January, amputation in July’ management approach have occurred in the last 50 or more years. Thrombolytic therapy has shown benefit in digital salvage but requires early use and has unclear long-term functional outcomes. Hyperbaric oxygen has shown promise in terms of salvage and functional outcomes but so far has only been evaluated in case series. Vasodilation with pentoxifylline or iloprost is under ongoing study as a potential therapy for frostbite. Scintigraphy may provide a means to expedite the surgical management of frostbitten digits and extremities, but again has only been studied in limited settings. Large-scale multicenter evaluation of these varied evaluation and management techniques is required to demonstrate whether any of these practices will ultimately improve tissue salvage and functional outcomes.

**Further reading**


This retrospective, single-center review presented the largest series of frostbite patients managed with thrombolytic therapy. A reduction in incidence of digital amputation rates from 41% to 10%.


These represent the most comprehensive guidelines for the management of all forms of cold injury. Frostbite guidelines include the spectrum of care, from management in the field through arrival at a hospital that can provide definitive care.

Cauchy E, Marsigny B, Allamel G, Verhellen R, et al. The value of technetium 99m scintigraphy in the prognosis of amputation in severe frostbite injuries of the extremities: A retrospective study of

The Chamonix group provides a twelve-year review including 92 patients, demonstrating the value of 99Tc scanning in frostbite evaluation and management. They use their experience to delineate an algorithm with potential use in future research on medical and surgical management of frostbite.


This seminal article describes a limited single-center experience with frostbite. The University of Chicago Frostbite Protocol that is included is the foundation for multiple protocols that have been published subsequently.
References

5. Killian H. Cold Injury with Special Reference to the German Experience During World War II. 1952.


Chemical burns
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Introduction

Many compounds have the potential to induce chemical burns. Individuals are exposed in both occupational and personal environments. The American Association of Poison Control Centers' (AAPCC) National Poison Data System (NPDS) 2008 annual report demonstrated 224,884 cases of exposure to cosmetic/personal care products, 213,595 household cleaning substances, 93,998 pesticides, 46,418 hydrocarbons, and 44,736 unspecified chemicals. In 2007, 137,055 cases of exposure were specific to acids, alkalines, peroxide, bleach, and phenol products alone. The reality concerning the ease of access to toxic products is evident in the presence of a rising number of pediatric exposures to chemical injuries. Most chemical burns involving children are secondary to common household products. Domestic chemical burn injuries are often due to poor labeling and storage, as well as secondary to intentional assault and suicide attempts. The most commonly affected areas of the body are the face, eyes, and extremities. Chemical burn injuries compose only 3% of all burns, yet they are the etiology behind approximately 30% of burn deaths. As a result, length of hospital stay and duration of healing tend to be greater with chemical burns. The majority of these deaths are related to the ingestion of chemical substances. This chapter will provide general principles for the treatment of chemical injuries.

Pathophysiology

All burn wounds, whether due to chemical or thermal sources, have in common the denaturation of proteins. The structure of biological proteins involves not only a specific amino acid sequence, but also a three-dimensional structure dependent on weak forces, such as hydrogen bonding or Van der Waals’ forces. These three-dimensional structures impart biological activity to the proteins, and are easily disrupted by outside influences. Heat energy breaks these weak bonds to unfold and denature proteins. In addition, changes in pH or dissolution of surrounding lipids may stabilize a protein and disrupt its function. Direct chemical effects on a reactive group in a protein will similarly render it ineffective.

The severity of a chemical burn injury is determined by several factors:

- concentration
- quantity of chemical agent
- manner and duration of skin contact
- extent of penetration
- mechanism of action
- phase of agent (liquid, solid, gas).

There are six mechanisms of action for chemical agents in biological systems:

1. Reduction: Reducing agents act by binding free electrons in tissue proteins, causing denaturation. Examples include hydrochloric acid, nitric acid, alkyl mercuric compounds, ferrous iron, and sulphite compounds.

2. Oxidation: Oxidizing agents are oxidized on contact with tissue proteins. Byproducts are often toxic and continue to react with the surrounding tissue. Examples of oxidizing agents are sodium hypochlorite, potassium permanganate, chromic acid, and peroxide.

3. Corrosive agents: Corrosive substances denature tissue proteins on contact and form eschar and a shallow ulcer. Examples of corrosive agents include phenols, cresols, white phosphorus, dichromate salts, sodium metals, lyes, sulphuric acid, and hydrochloric acid.

4. Protoplasmic poisons: These agents produce their effects by binding or inhibiting calcium or other organic ions necessary for tissue viability and function. Examples of protoplasmic poisons include ‘alkaloidal’ acids, acetic acid, formic acid, and metabolic competitors/inhibitors such as oxalic, hydrofluoric, and hydrazoic acid.

5. Vesicants: Vesicant agents produce ischemia with necrosis at the site of contact. There is associated tissue cytokine release and blister formation. Examples include cantharides, dimethyl sulfoxide (DMSO), mustard gas (sulphur and nitrogen), and Lewisite.

6. Desiccants: These substances cause damage by dehydrating tissues and exothermic reactions causing the release of heat into the tissue. Examples include sulfuric acid, muriatic acid, calcium sulphate, and silica gel.

Within these groups there are different categories of compound. Chemical burns are often described as acidic or alkaline. Acids act as proton donors in the biological system, and strong acids have a pH < 2. Alkali, or basic material, capable of producing injury typically have a pH > 11.5. In general, alkaline materials cause more injury than
acids cause coagulation necrosis with precipitation of protein, whereas the reaction to alkali is 'liquefaction' necrosis allowing the alkali to penetrate deeper into the injured tissue. The presence of hydroxyl ions within these tissues increases their solubility, allowing alkaline proteinates to form when the alkalis dissolve the proteins of the tissues. Organic solutions tend to dissolve the lipid membrane of cell walls and cause disruption of cellular architecture as their mechanism of action. Inorganic solutions tend more to remain on the exterior of cells, but may act as vehicles to carry the above-mentioned agents that denature proteins, or form salts with proteins themselves.

**General principles of management**

The most important aspects of first aid for chemical burns involve removal of the offending agent from contact with the patient. This requires removal of all potentially contaminated clothing and copious irrigation. Irrigation of chemical burns requires protection of healthcare providers to prevent additional injuries. Further, the wounds should not be irrigated by placing the patient into a tub, thereby containing the chemical and spreading the injurious material. Irrigation should be large volume and drained 'to the floor,' or out of an appropriate drain. Immediate copious irrigation has been shown to reduce the extent and depth of injury, especially to eyes. No measure of adequacy of lavage has been developed, but monitoring the pH from the effluent can provide quantifiable information as to adequacy of lavage. Thirty minutes to 2 hours of lavage may be necessary.

Material Safety Data Sheets (MSDS) are mandated to be available for all chemicals present in the workplace. These can be valuable resources for potential systemic toxicity and side effects of an agent. Further assistance is available from regional poison control centers for household chemicals or unidentified agents.

The use of neutralizing agents is discouraged. The practical problems encountered with their use are exothermic reactions causing further thermal damage. When the burning agent is known and an appropriate antidote is known, some benefit to its use has been demonstrated. Despite this, no agent has been found to be more effective than plain water for irrigation.

Burn and trauma patients should be managed with the same principles in mind. After airway patency is assured, adequate air movement and hemodynamics should be maintained. Conventional thermal burn formulas are used for resuscitation. Monitoring of urine output remains paramount to assessment of adequacy of end-organ perfusion and hence resuscitation. Systemic disturbances of pH are potential complications and must be monitored until acid–base disorder and electrolyte abnormalities are corrected.

The typical large-volume lavage required to adequately dilute chemical exposures puts the patient at potential risk for hypothermia, both from evaporative cooling losses and from the use of unwarmed lavage fluid. Principles of wound care for chemical burns are typically the same as for thermal burns. Early excision and grafting of obviously non-viable tissue is advocated, particularly in light of the observation that chemical burns tend to be deeper than they initially appear. As a result, they tend to heal more slowly.

**Specific agents**

**Acids**

**Acetic acid**

Acetic acid, also known as ethanoic acid, ethylic acid, and methane carboxylic acid, is a mild chelating agent. Solutions diluted to <40% concentrations, such as table vinegar and hair-wave neutralizing products, are usually harmless, but if used inappropriately may cause injuries such as partial-thickness burns. In such cases, initial treatment involves irrigation.

**Carbolic acid (phenol)**

Carbolic acid is a hydrocarbon derived from coal tar, which acts to cause damage secondary to its ability to induce denaturation and necrosis. The most common adverse effects are dermatitis, abnormal pigmentation, and burns to the skin. Concentrated amounts of phenol are caustic; therefore, prolonged skin contact causes partial- or full-thickness burns. These burns tend to become extensive prior to detection, secondary to the local anesthetic properties of phenol. Ingestion of as little as 1 g may cause death. Systemic effects include ventricular arrhythmias, pulmonary edema, stridor, and tachypnea. Locally, conjunctivitis, corneal edema/necrosis, and skin necrosis result.

Acute poisonings are potentially fatal, hence prompt action is necessary with copious irrigation. Polyethylene glycol (PEG molecular weight 300 or 400 Da) has been shown to be of potential benefit, but large-volume lavage should not be delayed while PEG application is begun. Reports in the literature indicate that intravenous sodium bicarbonate may be of use to prevent some of the systemic effects of phenol.

**Chromic acid**

This acid causes non-painful but corrosive ulcers upon contact with the skin. Ulceration of the nasal septum and bronchospasm can also occur with inhalation. This agent will cause protein coagulation. Peak blood levels are thought to be achieved within 5 hours of exposure. Symptoms may occur with just 1% total body surface area (TBSA) burn, but a 10% burn or greater is often fatal owing to its systemic effects. Irrigation is the primary treatment for exposure, but in an industrial setting, washing with a dilute solution of sodium hyposulfite or water, followed by rinsing in a buffered phosphate solution, may be a more specific antidote. Dimercaprol may be used at 4 mg/kg IM every 4 hours for 2 days, followed by 2–4 mg/kg/day for 7 days in total to treat the systemic effects. Dialysis in the first 24 hours is a reasonable means to remove circulating chromium and to address existing electrolyte imbalances. Exchange transfusion may be necessary. Various ointments containing products such as 10% calcium EDTA or ascorbic acid are available for small superficial burns. There have been case reports...
Chemical burns

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Muriatic acid is the commercial grade of concentrated hydrochloric acid. Once in contact with the skin, it denatures proteins into their chloride salts. Copious irrigation and early excision are the treatments of choice. 41 Hydrochloric acid fumes can cause inhalation injury with acute pulmonary edema. (Figs 41.2 and 41.3).

Hydrofluoric acid

Hydrofluoric acid is a corrosive that is commonly used in industrial applications. It is used as a cleaning agent in the petroleum industry, in the production of high-octane fuel, glass etching, germicides, dyes, tanning, and fireproofing material, as well as in rust removal. 14 Hydrofluoric acid is particularly lethal owing to its properties both as an acid and

Epichlorohydrin acid

Epichlorohydrin is a rare, corrosive carcinogen that is colorless and exudes a garlic-like odor. It is used in the production of glues, plastic, glycerols and resins, as well as in paper reinforcement and water purification. 28 It can also be converted into a binder used in the production of explosives. 29 At our burn center in Galveston, Texas, four patients were exposed to epichlorohydrin after an industrial accident. The TBSA burned ranged from 10% to 60%, with the largest burn showing rapid progression to a full-thickness wound within hours. Management of these patients was commenced with copious irrigation and hemodynamic monitoring (Fig. 41.1).

Formic acid

Formic acid is a strong inorganic acid used by glue makers and tanning workers. After contact, it creates an eschar which does not prevent systemic absorption. Once it is absorbed, metabolic acidosis, intravascular hemolysis with hemoglobinuria, renal failure, pulmonary complications, and abdominal pain with necrotizing pancreatitis usually occur. 30,31 All patients injured by formic acid should be hospitalized because of this multitude of potential systemic effects. Formic acid is the acid most commonly used in assaults, especially in developing countries, because of its easy availability. 14,32

Hydrochloric acid/muriatic acid/sulfuric acid

Hydrochloric acid is one of the most commonly treated chemical burns. Hydrochloric acid and sulfuric acid are proton donors, 33 which cause the pH in local tissues to drop to zero as hydrogen ions disassociate. Coagulation necrosis and tissue ulceration occur, leading to consolidation of connective tissue and thrombosis of intramural vessels, ulceration, fibrosis, and hemolysis. 5 Many household cleaners contain dilute hydrochloric acid (3–6%), sulfuric acid and its desiccant precursor (sulphur trioxide) in concentrations up to 80–99%. 14 Muriatic acid is the commercial grade of concentrated hydrochloric acid. Once in contact with the skin, it denatures proteins into their chloride salts. Copious irrigation and early excision are the treatments of choice. 41 Hydrochloric acid fumes can cause inhalation injury with acute pulmonary edema. (Figs 41.2 and 41.3).

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as a metabolic poison. The acid component causes coagulation necrosis and cellular death. Fluoride ion then gains a portal of entry that chelates positively charged ions such as calcium and magnesium, resulting in hypocalcemia and hypomagnesemia. This causes an efflux of intracellular calcium with resultant cell death. The fluoride ion remains active until it is completely neutralized by the bivalent cations. This may exceed the body's ability to mobilize calcium and magnesium rapidly enough, causing muscle contraction and cellular function to become dysfunctional. Fluoride ion also acts as a metabolic poison by inhibiting Na-K ATPase, allowing efflux of potassium. Excess potassium subsequently causes shifts at nerve endings and is thought to be the cause of the extreme pain associated with hydrofluoric acid burns.

Hydrofluoric acid burns are classified based on the concentration of the exposure. Concentrations >50% cause immediate tissue destruction and pain. Concentrations of 20–50% result in a burn becoming apparent within several hours of exposure. Injuries from concentrations <20% may take up to 24 hours to become apparent.

Death from hydrofluoric acid exposure is usually secondary to systemic toxicity. Systemic symptoms are secondary to acidosis, hypocalcemia, hypomagnesemia, and hyperkalemia, which can lead to ventricular fibrillation. Thus, electrolytes and cardiac rhythm should be monitored closely. Once cardiac dysrhythmias develop, it is difficult to restore a normal rhythm. Compounding the problem of hypocalcemia, the fluoride ion may be acting as a metabolic poison in the myocardium to promote the irritability. The typical electrocardiographic change seen is Q-T interval prolongation. The fluoride ions can be removed by hemodialysis or cation exchange resins.

Treatments for hydrofluoric acid exposure are designed to neutralize the fluoride ion and prevent systemic toxicity. Primarily, the wound should be copiously irrigated for 30 minutes. If the concentration of exposure is <20%, or the duration of exposure is minimal, this may serve as the extent of treatment. For more serious exposures, topical, subcutaneous, or intra-arterial mixtures of calcium gluconate can be used as a first option. The topical gel is a mixture of 3.5 oz of water-soluble lubricant.

The mixture’s penetration into the dermis is limited by its calcium component. This is improved with the use of DMSO, which has its own associated toxicity. Calcium gluconate injections into the area of the wound (0.5 mL/cm² of 10% calcium gluconate subcutaneously or intradermally) have also been used, with good results. Intra-arterial injections into the radial artery (10 mL 10% calcium gluconate and 40 mL D5W infused over 2–4 hours) can be used for management of burns to the hand, but in severe cases palmar fasciotomy may be needed. This injection should be performed within 6 hours of exposure, to prevent tissue necrosis and minimize pain. It should continue until the patient is symptom free.

Nitric acid

This is a strong oxidizing agent that can combine with organic proteins to produce organonitrates, which act as metabolic poisons. It is used in fertilizer management, casting iron and steel, and engraving. Upon skin contact a yellow-brown stain develops, with an eschar. Demarcation tends to occur slowly, causing difficulty in discerning burn depth. Initial treatment involves irrigation and the use of topical treatment.

Oxalic acid

This is a potent metabolic poison that combines with calcium to limit its bioavailability, thereby limiting muscle contraction. It is used industrially to remove rust and in bleaching products. Treatment consists of water irrigation and intravenous calcium, with continuous cardiopulmonary monitoring, as well as measurements of serum electrolytes and renal function.

Phosphoric acid

Phosphorus is an incendiary agent found in hand grenades, artillery shells, fireworks and fertilizers. White phosphorus ignites in the presence of air and burns until the entire agent is oxidized or the oxygen source is removed. The wounds are irrigated with water and easily identifiable pieces of phosphorus are removed. Soaked dressings are applied for transport. Ultraviolet light can be used to identify embedded particles through phosphorescence. In addition, a solution of 0.5% copper sulfate can be applied which will impede oxidation and turn the particles black to aid in their identification and removal. Hypocalcemia, hyperphosphatemia, and cardiac arrhythmias have been reported with phosphorus burns.

Alkalis

Strong alkalis have a pH ≥12. Wounds caused by alkalis initially appear superficial, but may often become full thickness in 2–3 days. This chemical creates a soluble protein by binding with lipids and proteins, thus allowing passage of hydroxyl ions into the tissue. Eventually, a soft, brownish, gelatinous eschar is created. Alkalis are very corrosive in nature and penetrate deeply. Examples of strong alkalis (lyes) include barium, sodium, ammonium, calcium, lithium, and potassium hydroxides. They are present in many household cleaning solutions, and have historically been ingested in suicide attempts, causing death secondary to airway occlusion. Management of these burns necessitates immediate and copious irrigation.

Dry residues of alkali (e.g. lime) must be brushed away, and then copious irrigation is undertaken. Attempts to neutralize alkali are not recommended. Alkaline injury to the eye is particularly devastating. These compounds rapidly penetrate the cornea, causing scarring and opacification, with associated perforation.

Cement

Cement acts both as a desiccant and an alkali. Cement is calcium oxide, which becomes calcium hydroxide upon exposure to water. It usually contains lime, sand and other metal oxides. The dry powder is very hygroscopic and will cause desiccation injury if not hydrated or washed away. Injury results from the action of the hydroxyl ion.
Chemical burns

from the skin immediately. Once cooled, the tar produces liquefaction injury and should be debrided from the skin, especially if obvious burn, blister, or tissue loss is apparent. Antibiotic ointments and household items such as baby oil, mineral oil, mayonnaise, and butter have been found to aid in its removal14,54 (Fig. 41.5).

Vesicant chemical warfare agents (mustard, lewisite, nitrogen)

These agents affect all epithelial tissues, including skin, eyes, and respiratory epithelium. Symptoms described after exposure to mustard gas include burning eyes, burning throat, and a feeling of suffocation.42 This is followed by erythema of the skin within 4 hours and blister development within 12–48 hours. Severe pruritus develops, particularly in moist areas such as the axilla and perineum. When the blisters rupture, they leave painful, shallow ulcers. Exposure to larger quantities of these agents produces coagulative necrosis of the skin, with either no blistering or ‘doughnut blisters’ surrounding a central necrotic zone. 43

Lewisite (2-chlorovinyl-dichloroarsine) is the best known arsine. It is more powerful than the mustards and the symptoms occur sooner.

Phosgene oxime is another common agent in chemical warfare. It is the most widely used halogenated oxime and has the immediate effect of stinging, likened to contact with a stinging needle.44 Affected areas quickly become swollen with blister formation, and eschars develop over the ensuing week. Wound healing is slow, typically over 2 months. Eye involvement is extremely painful and can result in permanent blindness. Inhalation leads to hypersecretion and pulmonary edema.

Clothing must be removed from the victim and large-volume lavage of the skin is undertaken. Eyes are irrigated with water or ‘balanced salt solution.’ Symptomatic relief of itching is provided with benzodiazepines, antihistamines, or phenothiazines. Blisters are debrided and dressed with topical antimicrobials. Dimercaprol is a chelating agent that is an antidote for lewisite poisoning. There is no specific antidote for nitrogen mustard, but sodium thiosulfate and

Metals

Occupational injuries often occur to workers using molten metal, such as elemental metals, sodium, lithium, potassium, magnesium, aluminum, or calcium. After exposure, the use of water is contraindicated as it may result in an explosive exothermic reaction. Class D fire extinguishers or sand are ideal for management, but mineral oil is also an option14 (Fig. 41.4).

Hydrocarbons

Hydrocarbons are corrosive agents, often contained within plants, animal fats, and fuel oils.51 Prolonged contact with petroleum distillates results in dissolution of lipid cell membranes, leading to cell death.52 These burns tend to be superficial. Systemic toxicity usually involves respiratory depression. Heat loss from rapid evaporation of gasoline can cause the development of frostbite and dehydration.14 Early decontamination is most efficiently achieved with soap and water.51

Hypochlorite solutions

These are potent oxidizers delivered in alkaline solution used as bleaches and household cleaners. Exposure to 30 mL of 15% solution is potentially fatal. Systemic manifestations of toxicity include vomiting, confusion, dyspnea, airway edema, cyanosis, cardiovascular collapse, and coma.53 Treatment consists of copious irrigation.

Alkyl mercuric compounds

Skin reaction with these substances releases free mercury, which can be found in blister fluid. With time, mercury is absorbed, leading subsequently to systemic effects. After blisters are debrided, repeat washing to lavage the blister fluid is necessary.

Tar

Tar, crude oil, and asphalt are various names for mineral products created from long-chain petroleum and coal or fossil hydrocarbons. This compound should be removed from the skin immediately. Once cooled, the tar produces liquefaction injury and should be debrided from the skin, especially if obvious burn, blister, or tissue loss is apparent. Antibiotic ointments and household items such as baby oil, mineral oil, mayonnaise, and butter have been found to aid in its removal14,54 (Fig. 41.5).

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Figure 41.4 Sodium hydroxide burn to the face and tongue.

Figure 41.5 Crude oil burn to the face.
N-acetylcysteine may be helpful to reduce the effects if administered early. The blister fluid from nitrogen mustard injuries does not contain active agent and is hence harmless. Agranulocytosis or aplastic anemia can result from exposure to these agents. In the appropriate setting, bone marrow transplantation may be considered.

**Conclusion**

Many chemical compounds can cause burn injury. The principal idea behind the treatment of chemical burns is early, copious irrigation. Wound care is the same as for thermal burns. Chemical burns tend to be deeper than they initially appear, often requiring skin grafting for management.

**Further reading**


References


Radiation injuries and vesicant burns
Stephen M. Milner, Michael J. Feldman

Introduction

In the aftermath of 9/11, with the threat of constant and unrelenting terrorism, the possibility of employment of nuclear weapons, or crude nuclear devices, of attacks on nuclear facilities and use of chemical agents cannot be ignored. Such attacks may result in types of injuries in previously unimaginable numbers. Given the devastating medical consequences that would follow the use of such weapons, the training of medical personnel will be a crucial factor in the effective management of such casualties, should the unthinkable ever occur.

Only 4 months after Roentgen reported the discovery of X-rays, Dr John Daniel observed that irradiation of his colleague’s skull caused hair loss. Since this finding was reported in 1896, many biomedical effects of radiation have been described.1 Knowledge of nuclear physics was rapidly amassed in the early part of the 20th century, leading eventually to the Manhattan project and the development of the atomic bomb. The last 50 years has also seen widespread deployment of energy-generating nuclear reactors, and the expanding use of radioactive isotopes in industry, science, and healthcare.2 More recently, major industrial accidents of note at Three Mile Island in Pennsylvania, Chernobyl in the Ukraine and at Goiania, Brazil have resulted in potential or real radiation injuries to hundreds of people. According to the latest NCRP report on radiation exposure to United States citizens, the most significant increase in ionizing radiation exposure, over the last 20 years, has been through medical imaging.3 Health professionals have become more aware of the cumulative effects of radiation. This has become a common topic for debate in regards to ionizing radiation exposure during the treatment of breast cancer patients and children.

Exposure to ionizing radiation can follow one of three patterns:

1. Small-scale accidents, or cumulative exposures, as might occur in a laboratory or from an X-ray device in a hospital setting.
2. Large industrial accidents (such as those mentioned above), stretching the need for treatment beyond available resources.
3. Detonation of a nuclear device in a military conflict where resources are totally overwhelmed or unavailable and associated multiple and combined injuries also exist.

This chapter first describes the terminology used in standard measurement of radiation exposure and discusses the frequency of radiation accidents, injuries and fatalities. The effects of exposure to ionizing radiation and triage and care protocols are considered according to known and projected prognostic factors. The complications that arise specifically with this injury and the supportive measures that need to be taken will be addressed.

Vesicant agents are characterized by their ability to produce cutaneous blisters resembling ‘burns.’ Although most physicians are unlikely to encounter casualties of chemical weapons, the proliferation of these agents has increased the risk to both military and civilian populations. They are likely to require the expertise found in burn centers and for this reason an account of the management of these injuries is included in this text.

Radiation injuries

Terminology

Damage to biological tissue by ionizing radiation is mediated by energy transference. This can be the result of exposure to electromagnetic radiation (e.g. X-rays and gamma rays) or particulate radiation (e.g. alpha and beta particles or neutrons). The severity of tissue damage is determined by the energy deposited per unit track length, known as linear energy transfer (LET).4 Electromagnetic radiation passes through tissue almost unimpeded by the skin and are called low LET since little energy is left behind. In contrast, neutron exposure has high-LET, resulting in significant energy absorption within the first few centimeters of the body. Alpha and low-energy beta particles do not penetrate the skin, and represent a hazard only when internalized by inhalation, ingestion or absorption through a wound.

The biological effect of ionizing radiation is measured by the radiation absorbed dose (rad). The newer SI unit of absorbed dose is the gray (1 Gy = 100 rads). Not all radiation is equally effective in causing biological damage, although it may cause the same energy deposition in tissue. For example, 1 Gy of neutron radiation will not have the same effect as 1 Gy of gamma or X-radiation. For this reason, a unit of dose equivalence was derived that allows radiations with different LET values to be compared. One such unit is the rem (acronym of roentgen equivalent man). The dose in rem is equal to the dose in rads multiplied by a quality factor (QF).5
The QF takes into account the linear energy transfer and has a different value for different radiations; for X-rays it is 1.0, for neutrons 10. The international unit, now more widely in use, is the sievert (Sv). One sievert equals 100 rem; 1 rem equals 10 mSv. This allows radiations with different LET values to be compared, since 1 Sv of neutron radiation has the same biological effect as 1 Sv of low LET gamma or X-radiation.

**Incidence**

A significant radiation accident is one in which an individual exceeds at least one of the following criteria: 6

- Whole body doses equal to or exceeding 25 rem (0.25 Sv)
- Skin doses equal to or exceeding 600 rem (6 Sv)
- Absorbed dose equal to or greater than 75 rem (0.75 Sv) to other tissues or organs from an external source
- Internal contamination equal to or exceeding one-half the maximum permissible body burden (MPBB) as defined by the International Commission on Radiological Protection (this number is different for each radionuclide)
- Medical misadministrations provided they result in a dose or burden equal to or greater than the criteria already listed above.

Radiation accidents within the United States should be reported to the federally funded Radiation Emergency Assistance Center/Training Site (REAC/TS). This is operated by Oak Ridge Institute for Science and Education (ORISE) at Oak Ridge, Tennessee and can be contacted by calling (865) 576–1005 (website: http://orise.orau.gov/reacts/). A radiological emergency response team of physicians, nurses, health physicists, and support personnel provides consultation assistance on a 24-hour basis and has the capability of providing medical treatment, whenever a radiation accident occurs. REAC/TS also maintains a Radiation Accident Registry System.

The number of accidents, number of persons involved, as well as the number of fatalities, in the United States and worldwide is shown in Table 42.1. There have been a total of 128 fatalities recorded by the Registry worldwide. 6 The majority of the radiation deaths occurred as a result of the Chernobyl accident in 1986 (>40). The classification of radiation accident by device for the period 1944 until June 2010 is shown in Table 42.2. 6

The majority of radiation accidents are due to radiation devices. This may be an accelerator; however, most devices involved in accidents are encapsulated, highly radioactive sources used for industrial radiography. Next most frequent accidents are radioisotope accidents involving radioactive materials which are unsealed, such as tritium, fission products, radium and free isotopes used for diagnosis and therapy. Uncommon criticality accidents occur when enough fissionable material, such as enriched uranium, is brought together to produce a neutron flux so high that the material undergoes a nuclear reaction (becomes critical).

The most devastating radiation injuries and fatalities yet seen, however, resulted from detonation of nuclear weapons at Hiroshima and Nagasaki during World War II. Since 1945, nuclear weapon technology has developed enormously and current strategic thermonuclear warheads dwarf those weapons used in Japan. 7 Keep in mind that the bombs dropped on Japan still contained the same energy equivalent to 12–15 thousand tons of TNT (Hiroshima) and 20–25 thousand tons of TNT (Nagasaki). 8 The majority of radiation exposure in this case occurred within the first minute of the explosion. There were no deaths attributed to the products left behind by the atomic explosions. As detailed by Kucan in 2004, the majority of radioactive fallout from these weapons were dispersed into the atmosphere, as both were detonated several thousand feet in the air. 8

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**Table 42.1 Major radiation accidents: human experience (1944–June 2010)**

<table>
<thead>
<tr>
<th>Location</th>
<th>No. of accidents</th>
<th>No. of persons involved</th>
<th>Significant exposures</th>
<th>Fatalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>US</td>
<td>250</td>
<td>1358</td>
<td>796</td>
<td>26</td>
</tr>
<tr>
<td>Non-US</td>
<td>184</td>
<td>132461</td>
<td>2287</td>
<td>102</td>
</tr>
<tr>
<td>Former Soviet Uniona</td>
<td>(137)</td>
<td>(507)</td>
<td>(278)</td>
<td>(35)</td>
</tr>
<tr>
<td>Total</td>
<td>434</td>
<td>133819</td>
<td>3083</td>
<td>128</td>
</tr>
</tbody>
</table>

*DOE/NRC dose criteria. aFormer Soviet Union Registry Data (not included in totals – data incomplete). Source: REAC/TS Registry.

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**Table 42.2 Major radiation accidents worldwide (1944–June 2010): ‘classification by device’**

<table>
<thead>
<tr>
<th>Radiation devices</th>
<th>320</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sealed sources</td>
<td>212</td>
</tr>
<tr>
<td>X-ray devices</td>
<td>83</td>
</tr>
<tr>
<td>Accelerators</td>
<td>25</td>
</tr>
<tr>
<td>Radar generators</td>
<td>1</td>
</tr>
<tr>
<td>Radioisotopes</td>
<td>96</td>
</tr>
<tr>
<td>Diagnosis and therapy</td>
<td>40</td>
</tr>
<tr>
<td>Transuranses</td>
<td>28</td>
</tr>
<tr>
<td>Fission products</td>
<td>11</td>
</tr>
<tr>
<td>Tritium</td>
<td>2</td>
</tr>
<tr>
<td>Radium spills</td>
<td>1</td>
</tr>
<tr>
<td>Other</td>
<td>13</td>
</tr>
<tr>
<td>Criticalities</td>
<td>20</td>
</tr>
<tr>
<td>Critical assemblies</td>
<td>8</td>
</tr>
<tr>
<td>Reactors</td>
<td>6</td>
</tr>
<tr>
<td>Chemical operations</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>435</td>
</tr>
</tbody>
</table>

Source: REAC/TS Registries.
Perhaps a more likely weapon of terrorism will involve the use of a radiological dispersal device (RDD). The term dirty bomb generally refers to conventional explosive packaged with radioactive material that is scattered over a wide area when detonated. It is believed that these devices would probably elicit more harm by public fear and panic than by serious injury. A greater threat might be the use of radioactive material placed in a public place without use of explosives, as illustrated by the event in Goiania, Brazil where 249 people were affected by radiation when cesium-137 was unwittingly released by scrap metal workers.

More recently, the media has propagated an interest in medical imaging as a source for excessive exposure to ionizing radiation. While most of the literature that explores this issue refers to case-studies, it confirms that exposure at a younger age increases the risk of cancer. Even more important is that this risk is not reduced with time. Exposure to radiation through CT imaging is now commonplace, as CT scanners are readily available and provide quick studies. Healthcare personnel should not disregard the cumulative effects of these studies which can approximate levels seen in atomic bomb survivors (30 mSv). This issue affects millions of patients on a daily basis and has the potential to increase the cancer risk in thousands of patients yearly.

**Pathophysiology**

The detonation of a nuclear device over a population center will produce an extremely hot, luminous fireball, which emits intense thermal radiation capable of causing burns and starting fires at considerable distance. This is accompanied by a destructive blast wave moving away from the fireball at supersonic speed and the emission of irradiation, mainly gamma rays and neutrons. The result of a combination of thermal and radiation injuries is said to have a synergistic effect on the outcome. Several animal experiments have demonstrated a significant increase in mortality when a standard burn wound model is irradiated, over and above that expected from either injury alone.

**Thermal effects**

Exact information about the cause of fatalities in a nuclear blast is not available, but from the nuclear attack on Japan, it has been estimated that 50% of deaths were due to burns and some 20–30% were flash burns. The clinical picture may range from an erythema of the exposed areas (most commonly face, hands, arms and legs), to a charring of the superficial layers of the skin. Secondary flame burns may be present following the ignition of the victim’s clothing or environment. The physicians at Hiroshima and Nagasaki observed that the ‘flame’ burn wound seemed to heal at first. However, between 1 and 2 weeks later, a serious relapse occurred. Wound infection set in; there was a disorder of granulation tissue formation; a gray, greasy coating would form on the wounds. Thrombocytopenia resulted in spontaneous bleeding both into the wound and elsewhere. Histologically, the normal collection of leukocytes delineating a necrotic area was found to be absent due to agranulocytosis, and gross bacterial invasion was evident; both these changes obviously affected the prognosis of these otherwise relatively small injuries.

**Radiation effect**

Damage to biological tissue by ionizing radiation is mediated by energy transference. The transference of this energy can damage critical parts of the cell directly or indirectly by formation of free radicals (such as the hydroxyl radical). The primary targets are cellular and nuclear membranes and DNA.

The morbidity of radiation is dependent on its dose, the dose rate and the sensitivity of the cell exposed. Cells are most sensitive when undergoing mitosis so that those that divide rapidly such as bone marrow, skin and the gastrointestinal tract are more susceptible to radiation damage. Radiation to an organ such as brain or liver, which has parenchymal cells with a slow turnover rate, results in damage to the more sensitive connective tissue and microcirculation.

The overall effect on the organism depends on the extent of the body surface involved, duration of exposure and homogeneity of the radiation field. It is convenient to consider radiation injuries as localized or whole body (acute radiation syndrome).

Long-term effects of radiation exposure include the formation of cancer and wound healing deficits. These have been studied in various venues including exposure to tanning beds which have been linked to an increase in melanoma in young women of up to 75%. These changes are thought to be due to a defect in the p53 tumor suppressor pathway. Children are particularly at risk for radiation-induced injuries as they have a proportionally larger amount of replicating cells and will live long enough to see the effects of radiation, which can have upwards of a 30-year latency period.

**Localized injury**

In a localized injury a relatively small part of the body is affected without significant systemic effects. The skin and subcutaneous tissue alone may be involved following exposure to low-energy radiation. Exposure to high-energy radiation may injure deeper structures.

Radiation damage depends on the dose of exposure and several progressive features are observed in skin: erythema is equivalent to a first-degree thermal burn and occurs in two stages. Mild erythema appears within minutes or hours following the initial exposure and subsides in 2–3 days. The second onset of erythema occurs 2–3 weeks after exposure and is accompanied by dry desquamation of the epidermal keratinocytes. Epilation (loss of hair) may occur as soon as 7 days post injury. It is usually temporary with doses less than 5 Gy but may be permanent with higher doses.

Moist desquamation is equivalent to a second-degree thermal burn and develops after a latent period of about 3 weeks with a dose of 12–20 Gy. The latency period may be shorter with higher doses. Blisters form, which are susceptible to infection if not treated.

Full-thickness skin ulceration and necrosis are caused by doses in excess of about 25 Gy. Onset varies from a few weeks to a few months after exposure. Blood vessels become
telangiectatic and deeper vessels occluded. Obliterating endarteritis results in fibrosis, atrophy and necrosis. Skin cancers may be evident after months or years.

One of the most closely studied local effects of radiation injury involves the treatment of breast cancer. It is well known that radiation therapy improves postmastectomy outcomes in women with multiple nodal involvement. This outcome comes at a cost as evidenced by increased rates of capsular contracture, soft tissue fibrosis, and an overall poorer aesthetic outcome. Spear et al. reported significantly increased rates of tissue contracture, hyperpigmentation, and asymmetry following all types of reconstruction paired with radiation.20 This local tissue destruction does not abate with time and has changed the face of breast reconstruction to avoid tissue expanders following treatment with radiation.

The acute radiation syndrome

The physiological effects of whole-body radiation are described as the acute radiation syndrome (ARS). The clinical course usually begins within hours of exposure. Prodromal symptoms include nausea, vomiting, diarrhea, fatigue, fever and headache. There then follows a latent period, the duration of which is related to the dose. Hematopoietic and gastrointestinal complications follow this. The ARS can be subdivided into three overlapping subsyndromes, which are related to the dose exposure.

Hematopoietic syndrome

This may occur after an exposure of between 1 and 4 Gy. The bone marrow is the most sensitive and pancytopenia develops. Opportunistic infections result from the granulocytopenia and spontaneous bleeding results from thrombocytopenia. Hemorrhage and infection is the usual cause of death.

Gastrointestinal syndrome

This requires a larger dose exposure usually in the range of 10 to 12 Gy. Severe nausea and vomiting associated with bowel cramps and watery diarrhea occurs within hours of irradiation. There is a shorter latent period of 5–7 days, which reflects the turnover time of the gut epithelium (3–5 days). The epithelial damage results in loss of transport capability, bacterial translocation with sepsis, bowel ischemia and bloody diarrhea. Large fluid imbalances can result in hypovolemia, acute renal failure and anemia from both bleeding and the loss of erythropoiesis. Critical exposure will lead to rapid deterioration with unrelenting bloody diarrhea, fever, refractive hypovolemic shock, sepsis and death.

Neurovascular syndrome

An exposure to a dose of 15–30 Gy or greater can cause an immediate total collapse of the vascular system superimposed on the aforementioned syndromes. This may be due to the massive release of mediator substances, nitric oxide abnormalities or destruction of endothelium.13 This syndrome can progress rapidly with variable neurological symptoms, respiratory distress, cardiovascular collapse and death.

<table>
<thead>
<tr>
<th>Table 42.3 Survival rates with major resources available</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burn alone</td>
</tr>
<tr>
<td>Burn alone</td>
</tr>
<tr>
<td>Burn plus radiation</td>
</tr>
<tr>
<td>Burn plus radiation</td>
</tr>
</tbody>
</table>

TBSA, total body surface area.

Triage

Triage is the initial classification of casualties into priority groups for treatment and is essential in the management of large numbers of casualties. All first responders should take into account their own safety. Remember that exposure to radiation is reduced by distance and shielding. Therefore, establish a perimeter beyond which those without shielding should remain. The triage process begins after donning personal protection equipment. Those patients unlikely to survive should not be allowed to overwhelm available resources, so that adequate treatment reaches those most likely to survive. In most circumstances, ionizing radiation is not immediately life-threatening and any associated injury should be treated first. Exposure can be significantly reduced by removing contaminated clothing.21 Once life-saving measures have been carried out and the patient stabilized, assessment of radiation exposure can proceed.

If large-scale casualties are encountered, triage may, of necessity, seem to be draconian. In conventional warfare with limited medical resources, 50% of soldiers with thermal injuries of up to 70% TBSA will be expected to survive (Table 42.3).

This survival rate should be bettered in a smaller civilian major accident. Thus burns alone over 70% TBSA should receive expectant treatment and those under 20% can have their treatment delayed. If there has been a significant exposure to radiation as well as a thermal injury, individuals with over 30% TBSA burns are unlikely to survive without the use of major resources.22

Treatment

The treatment of any burn requires massive support from a dedicated team. This will be available for small accidents. With larger accidents or a nuclear attack, the number of victims could swamp the services; treatment facilities may be destroyed; normal supply channels would be drastically reduced, if present at all; production, distribution and transportation of supplies may be greatly impaired and local care workers may also be the victims.23

First aid

The victims must be evacuated from the source of radiation in order to limit the exposure. Normal resuscitation procedures must be followed (i.e. airway, breathing, circulation, etc.). Contaminated clothing must be removed and the skin wounds decontaminated by copious but gentle irrigation with water or saline. The goal of decontamination is to dilute...
and neutralize particles without spreading them to unexposed areas. Thus patients should not be immersed in tubs. Irrigation should be continued until a dosimeter such as a Geiger–Müller counter indicates a steady state or minimum radiation count has been reached.

Intact skin may also be irrigated with a soft brush or surgical sponge preferably under a stream of warm tap water. If this is inadequate, a second scrubbing with mild soap or detergent (pH 7) for 3–4 min is recommended. This is followed by application of povidone-iodine solution or hexachlorophene soap, which is then rinsed again for 2–3 min and dried. If the patient is known to have had <100 rem he/she can be followed as an outpatient. Exposures >100 rem require full evaluation in hospital. Patients with exposures >200 rem or who have symptoms of ARS should preferably be sent to specialist centers with facilities to treat bone marrow failure.24

Assessment

The assessment of thermal injury has been covered in preceding chapters. Exposure to radiation can be estimated clinically, by noting the onset of symptoms of ARS, supported by biological parameters. A complete blood count, including platelets and differential count, should be performed immediately and repeated at 12–24 h if indicated by a change in the absolute lymphocyte count. If the patient sustains a fall in lymphocyte count of 50% or a count less than $1 \times 10^7$/liter in a time period of 48 h post exposure, a moderate dose of radiation has been encountered.25 Levels of serum amylase and diamine oxidase (produced by intestinal villi) may be useful biological dosimeters of the future. Amylase levels are only reliable when the salivary glands have been exposed and diamine oxidase has not yet been fully assessed in humans. Lymphocyte chromosomal analysis allows very accurate measurement even at low levels of exposure. However, the need for the test to be performed in cell cultures in laboratories over 48 h incubation would render this test impractical with large numbers of casualties.26

General care of the irradiated patient

Where possible a history should be obtained from the patient or others. Factors such as age, concurrent medical problems, smoke inhalation and multiple trauma will affect the prognosis. With this in mind a full physical examination is carried out to exclude other injuries. Victims of radiation exposure may not appear to differ clinically from the thermally injured and should receive the same care. Those exposed to lethal doses of radiation will exhibit early signs of radiation sickness and should be triaged accordingly.

All patients should be given adequate analgesia. Opiates or opioids are the drugs of choice. They must be titrated to effect and administered by the intravenous route. Early nausea and vomiting will be distressing and must be treated with available antiemetic drugs. Prochlorperazine has to be given by intramuscular injection but the newer agent, ondansetron, may prove successful as it is used against the similar symptoms encountered in radiotherapy and chemotherapy. It can also be used in children.

Patients with thermal burns in excess of 40% TBSA or with associated inhalation or major trauma should be treated expectantly in the mass casualty situation. They should be made comfortable, given adequate analgesia and/or sedatives if available and thought appropriate. Resuscitation should be the same as that for an uncomplicated thermal injury. Any resuscitation formula can be used, but it must be closely monitored and altered as necessary to maintain an adequate urine output. The fluid requirement will be increased as fluid is sequestered into damaged internal organs especially the gut. Fluid losses from diarrhea and vomiting may also be excessive and need to be replaced. Intravenous fluids may be limited and the victims may be advised to take oral fluids consisting of balanced salt solutions and maintain a large urine output.

Oral resuscitation

Studies in humans and animal models have shown that intestinal absorption remains intact in burn patients. Kramer et al. reviewed the use of oral resuscitation therapy in burn care and found 12 reports, most of which show equal outcomes to intravenous infusions. This solution should be readily available, cheap, easy to transport, and palatable (Table 42.4).27,28 Preliminary data by the authors shows a reduction in intravenous fluid requirements when Parkland formula-driven protocols are supplemented with oral resuscitation (Fig. 42.1).

Table 42.4

<table>
<thead>
<tr>
<th>Formula</th>
<th>Na</th>
<th>Cl</th>
<th>K⁺</th>
<th>Buffer</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>WHO ORS (1975)</td>
<td>90</td>
<td>80</td>
<td>20</td>
<td>30</td>
<td>Diarrhea</td>
</tr>
<tr>
<td>WHO ORS (2002)</td>
<td>75</td>
<td>65</td>
<td>20</td>
<td>10</td>
<td>Diarrhea</td>
</tr>
<tr>
<td>Fox’s sodium lactate</td>
<td>161</td>
<td>0</td>
<td>0</td>
<td>161</td>
<td>Burns</td>
</tr>
<tr>
<td>Moyer’s citrated NaCl</td>
<td>85</td>
<td>63</td>
<td>0</td>
<td>29</td>
<td>Burns</td>
</tr>
<tr>
<td>Monafo’s HLS</td>
<td>300</td>
<td>200</td>
<td>0</td>
<td>100</td>
<td>Burns</td>
</tr>
<tr>
<td>Liquidsorb</td>
<td>60</td>
<td>44</td>
<td>4</td>
<td>28</td>
<td>Burns</td>
</tr>
<tr>
<td>Jiang’s burn drink</td>
<td>48</td>
<td>28</td>
<td>0</td>
<td>20</td>
<td>Burns</td>
</tr>
<tr>
<td>Ricelyte</td>
<td>50</td>
<td>45</td>
<td>25</td>
<td>34</td>
<td>Burns</td>
</tr>
<tr>
<td>Ceralyte 90</td>
<td>90</td>
<td>80</td>
<td>20</td>
<td>30</td>
<td>Diarrhea/Burns</td>
</tr>
</tbody>
</table>

Adapted from Kramer et al. 2010,27 with permission from ePlasty.
however, it is important to avoid further irritation of the skin by exposure to abrasive decontamination, irritating solutions and sunlight. With a slightly higher radiation dose causing dry desquamation, a bland lotion and loose clothing to alleviate itching may be all that is required. Deeper burns with moist desquamation are treated like conventional thermal injuries. Topical chemotherapeutic agents can be used and regularly applied as described elsewhere. Burns are best treated closed because of the high risk of sepsis in immunosuppressed patients whose wounds are susceptible to dehydration, colonization and portal entry of organisms. Early tangential excision and split skin grafting provides early wound closure, decreased burn wound colonization and sepsis and shortened hospital stay.29,30 This technique is recommended by the authors and probably has advantages where the potential to develop septic wounds is great. Information regarding the grafting of radiation burns is not yet available but is probably best delayed. Dubos et al.31 performing early excision and grafting of burns in irradiated monkeys have shown that healing occurred fully by the end of the second week, although histologically there was a slight delay in the healing process. The procedure however is not without risks. Blood loss in excess of 300 mL/9% TBSA excised presents an increased anesthetic hazard. In irradiated tissue that is severely injured, definitive management usually involves resection of damaged tissue and replacement with well-vascularized non-radiated tissue, usually from a distant site. There is research ongoing to suggest that injections of human mesenchymal stem cells may have a role in the treatment of local radiation-induced tissue injury.32

Hyperbaric oxygen therapy (HBO) may be combined with surgical treatment potentially to enhance wound healing in irradiated tissue. The mechanism of action is not certain but appears to be related to the creation of a high oxygen gradient across the irradiated tissues, which stimulates capillary ingrowth. Hyperbaric oxygen treatments have been devised using an empirical approach.33 A single treatment or ‘dive’ consists of 90 min in the chamber breathing an oxygen-rich mixture at 2.4 ATA (atmosphere absolute). Soft-tissue defects are usually treated with 30 dives. When combined with surgery a ‘20/10 protocol’ is used in which the operative procedure is ‘sandwiched’ between 20 preoperative and 10 postoperative dives.

Workers who deal with irradiated material, such as plutonium, can become exposed through small cuts on their hands. Treatment options typically include local wound control with surgical excision as well as wound care using Diethylene triamine pentaacetic acid (DTPA) and intravenous administration of DTPA. DTPA acts as a chelating agent to bind the irradiated material and reduce biologic exposure.34

**Treatment of complications**

**Hematological**

Blood and platelets are administered to maintain an adequate hemoglobin concentration and a platelet level of $20 \times 10^3$ per liter. If surgery is contemplated, this level should be raised to $75 \times 10^3$ per liter. All blood products should be irradiated to avoid graft-versus-host disease.

Bone marrow transplantation is the treatment of choice following total body irradiation. It should be performed between 3 and 5 days post-exposure as the immunosuppression is at its peak.

An important goal of medical treatment is to stimulate the proliferation and differentiation of residual hematopoietic stem and progenitor cells (HSPC). Administration of anti-apoptotic cytokine combinations such as stem cell factor, Flt-3 ligand, thrombopoietin, and interleukin-3, may assist recovery, if administered early.35 Moreover, hematopoietic growth factors such as granulocyte colony-stimulating factor (G-CSF) and granulocyte–macrophage colony-stimulating factor (GM-CSF) have also been recommended36,37 based on demonstration of improved survival in irradiated primates and reduced neutropenia in humans following accidental irradiation.

**Infection**

The immunosuppression associated with irradiation makes the victim susceptible to exogenous and endogenous pathogens. Exogenous infection can be limited by adequate aseptic technique and nursing the patient in a sterile environment. Monitoring the patient adequately will allow the early diagnosis of sepsis and its treatment before it becomes well established. The antibiotic chosen should reflect the current pattern of susceptibility and nosocomial infections in that particular unit at that time. Combination therapy will be required where there is a profound neutropenia. With the large fluid losses and shifts, gentamicin is not recommended unless there is no other choice. Therapeutic levels will be difficult to obtain without risking toxicity and there are now safer broad-spectrum antibiotics (imipenem, cefazidime and ciprofloxacin). If Gram-positive infection is suspected, vancomycin or the newer teicoplanin should be administered. If there is an inadequate response, an antifungal agent must be added. The use of fresh frozen plasma, gamma globulin solutions and monoclonal antibodies is at present speculative, but if resources allow and the patient’s condition is not stabilizing, these agents should be considered.

**Cardiovascular collapse**

This complication may occur due to the exposure, sepsis, fluid loss or hemorrhage. The patient should be given adequate fluid resuscitation, the airway must be protected and oxygen therapy instituted. Sedation and mechanical

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**Figure 42.1** The addition of oral resuscitation reduces overall intravenous fluid requirements. (Pilot data collected by authors.)
ventilation will decrease the oxygen debt that will inevitably occur. Inotropic support may become necessary and should be started as early as possible accompanied by the relevant cardiovascular monitoring. Invasive cardiovascular monitoring will aid in the treatment of volume replacement, but invasive intravenous lines must be inserted in aseptic conditions, kept meticulously clean, changed regularly and removed when no longer indicated. Agents that manipulate the release of nitric oxide may become available in the near future and may turn out to be the agents of choice in the treatment of septic shock.

**Occupational exposure**

In clinical practice there are concerns that relatively low levels of radiation delivered over a long period of time might induce cancer and/or exert genetic or teratogenetic effects. The radiation dose can be limited by reducing the duration of exposure or by increasing the distance from the source of radiation. Since distance and radiation intensity obey the inverse square law, the latter is particularly effective. While the efficacy of shielding devices will be determined by the type and thickness of the material and the energy and type of radiation, Table 42.5 illustrates the effectiveness of these devices when used at diagnostic X-ray energies. It should be noted that the bodies of others provide very effective shielding.

Cumulative doses of radiation can be recorded on radiation badges containing photographic emulsion. The personnel dosimeter is relatively cheap and accurate but has limitations. The smallest exposure that can be measured is 10 millirem; film badges can be exposed by heat, giving false readings, and they are analyzed only at monthly intervals.

**Summary**

Treatment of radiation injury, whether or not it is combined with other injuries, requires specialized knowledge and resources. The combination of radiation injury with associated injuries appears to have a synergistic effect on outcome. Significant increases in mortality occur because of immunosuppression secondary to radiation exposure in patients already vulnerable to infections. For localized radiation injury, it is often difficult to assess the level of severity quickly and with accuracy, because of the delay between exposure and appearances of lesions, and because of hidden lesions in underlying tissues. Medical treatment deals with inflammation, moist desquamation, and chronic pain; the most favorable time for surgical intervention is difficult to specify. Full intensive care support is needed for whole-body irradiation causing ARS, and is available only if small numbers are involved. Oral replacement therapy may be a feasible alternative to IV resuscitation of burns and could potentially save many lives in mass casualty situations. Those who survive and show signs of regeneration of tissues will warrant late surgical intervention. Aplastic anemia, immunosuppression, hemorrhage, and sepsis will be major problems for survivors. The improving therapy of bone marrow transplantation is the treatment of choice. Large numbers of casualties will necessitate expectant treatment only. In the event of a radiation mass casualty, resources will be limited and treatment may depend on oral routes of resuscitation to maintain intravascular volume. Evacuation of survivors will take days and a natural selection will take place.

**Vesicant burns**

Vesicant agents are characterized by their ability to produce cutaneous blisters resembling ‘burns.’ They have posed a major military threat since the use of sulfur mustard [bis (2-chloroethyl) sulfide] in the trenches of World War I. Since this time various nations have deployed chemical weapons and terrorist organizations have used it in public places. More recently, the conflict between Iraq and Iran in the 1980s displayed the most open and widespread use of chemical weapons on a battlefield in recent decades. Chemical weapons were believed to have been deployed by Iraq in the 1990 Persian Gulf War when nerve gas and blister agent were detected in the theater of operations.

Although sulfur and nitrogen mustard is the most important vesicant militarily, the vesicant category includes other agents, such as lewisite and phosgene oxime. These compounds affect not only skin but all epithelial tissue with which they come into contact, particularly the eyes and respiratory tract. Although most physicians are unlikely to encounter casualties of chemical weapons, the proliferation of these agents has increased the risk to both military and civilian populations. They are likely to require expertise found in burn centers and for this reason, an account of the management of these injuries is included in this text.

**Mechanisms of action**

The mechanism of action of mustard has eluded identification; however, most of the toxic effects are believed to be related to alkylation of DNA and critical target molecules. The DNA cross-links, which prevent replication and repair of DNA, ultimately lead to cell death. The dermal epidermal separation, which causes the skin lesions, is believed to be due to release of proteases and other enzymes. Breakage of anchoring filaments connecting the basal cell layer to the basement membrane results in a blister with the basement membrane on its dermal side. There are three main hypotheses to explain the biochemical processes leading to enzyme release.

<table>
<thead>
<tr>
<th>Table 42.5 The effectiveness of shielding devices</th>
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<tbody>
<tr>
<td><strong>Device</strong></td>
</tr>
<tr>
<td>Lead apron</td>
</tr>
<tr>
<td>Thyroid shield</td>
</tr>
<tr>
<td>Leaded glasses</td>
</tr>
<tr>
<td>Unleaded glasses</td>
</tr>
<tr>
<td>Human body</td>
</tr>
<tr>
<td>Human body wearing lead apron</td>
</tr>
<tr>
<td>Portable lead shields</td>
</tr>
</tbody>
</table>
The first proposes that strand breaks in the DNA activate the nuclear DNA repair enzyme poly (ADP-ribose) polymerase. This initiates a cascade of reactions in which cellular stores of nicotinamide adenine dinucleotide (NAD) are depleted, glycolysis is inhibited, and the hexose monophosphate shunt is stimulated. This is thought to lead to induction and secretion of proteases.

The second hypothesis proposes a mechanism based on an interaction between mustard and the intracellular scavenger glutathione (GSH). This is thought to inactivate thiol proteins, including calcium and magnesium adenosine triphosphatases, which regulate calcium levels. Elevation of cytosolic calcium concentration activates production of proteases, phospholipases and endonucleases, which break down membranes, cytoskeleton and DNA, leading to cell death. A separate consequence of depleted GSH could also be lipid peroxidation with the formation of lipid peroxides toxic to cell membranes.

The third hypothesis involves lipid peroxidation where the principal toxic consequence of GSH depletion is the formation of toxic lipid peroxides with resulting cell membrane disruption.

The exact mechanism of action of the other agents is unknown although lewisite has been shown to inhibit several important enzyme systems, such as the pyruvate dehydrogenase complex.

**Clinical features**

Early symptoms ascribed to mustard gas include an ocular burning sensation and a feeling of suffocation associated with a burning throat. After 4 h, erythema is seen; in 12–48 h, blistering appears accompanied by severe pruritus which has a predilection for moist areas such as the axilla and perineum. The blisters tend to rupture, discharging an amber serous fluid and leaving painful shallow ulcers. Greater exposure produces coagulative necrosis of skin, with either no blistering or ‘doughnut blisters’ surrounding a central necrotic zone. This will be accompanied by severe conjunctivitis, corneal erosion and necrotizing bronchitis. A secondary respiratory infection may develop over the next few days which coupled with associated marrow suppression could prove fatal. Following absorption of large amounts of mustard other systems may be affected. Severe stem cell suppression may lead to pancytopenia, and involvement of the gastrointestinal tract can have effects ranging from nausea and vomiting to severe hemorrhagic diarrhea. Excitation of the CNS, resulting in convulsions, has been reported. Mustard may also affect other organs, but rarely do these produce clinical effects.

Lewisite (2-chlorovinyl-dichlorarsine) is the best known arsine. It is more powerful than the mustards and symptoms occur sooner. Eye irritation is produced immediately and sneezing, salivation and lacrimation occur sooner. Non-lethal chronic exposure may lead to arsenical poisoning.

Exposure to phosgene oxime, the commonest halogenated oxime, has the immediate effect of stinging, and is likened to that of contact with a stinging nettle. Within a minute, the affected area becomes swollen and solid lesions resembling urticaria are seen. An eschar will form after 1 week, but healing is often delayed beyond 2 months. Contamination of the eyes is extremely painful and may result in permanent blindness. Inhalation causes irritation and coughing, hypersecretion, and pulmonary edema.

**Treatment for exposure to a vesicant agent**

The only prophylaxis against these agents is butyl rubber gloves, boots and a respirator. The clothing of a victim must either be removed or decontaminated with Fuller’s earth powder. Eyes can be irrigated with water but, if available, 1.26% sodium bicarbonate solution or 0.9% saline should be used. Upon reaching a treatment facility, patients must have all their clothing removed if this has not already been done, and all the exposed areas must be cleansed with copious water lavage. Attendants should also be suitably protected and contaminated clothing must be placed in special bags.

Current treatment of vesicant agents centers around symptomatic relief. Itching can be treated with sedatives (benzodiazepines or phenothiazines), and antipruritic agents. Dimercaprol (British antilewisite), a chelating agent, is a specific antidote for lewisite poisoning. It is of note that it is incompatible with silver sulfadiazine. It is available as an ointment for skin lesions, as drops for eye applications (5–10% in oil), and in an intramuscular preparation for systemic toxicity. Other chelating agents are:
The vesicant agents are perhaps poorly named since they have the ability to affect all epithelial surfaces, particularly the eyes and respiratory surfaces, and not just the skin. The most important vesicant is sulfur mustard, which acts as an alkylating agent, causing a series of clinical reactions ranging from vesicles to severe skin necrosis. Systemic effects are seen with high doses, and the combination of depressed bone marrow activity and respiratory involvement often proves fatal. There is no effective antidote, and treatment depends on prevention of contact and local therapy to achieve wound healing, which tends to be slow. There is no risk to the caregiver from the blister fluid which contains no active agent. Treatment may require respiratory care in an ICU setting for upwards of 4 weeks, as well as several weeks of intravenous antibiotic therapy.

**Further reading**


References


Exfoliative diseases of the integument and soft tissue necrotizing infections

Shawn Fagan, Jiake Chai, Marcus Spies, Maureen Hollyoak, Michael J. Muller, Cleon W. Goodwin, David N. Herndon

Introduction

Acute, severe exfoliative, and necrotizing diseases of skin and underlying structures may cause significant morbidity in the afflicted patient. The problems associated with these diseases, such as wound infection, sepsis, inadequate nutrition, and pain, are similar to those seen in patients with major burns. Burn centers provide expertise in the treatment and management of critically ill patients with skin loss from all causes, not solely from thermal injury. This chapter describes the pathophysiological processes of severe exfoliative skin disorders, their diagnosis, and the specialized treatment offered by burn units.

Severe exfoliative disorders

Erythema multiforme minor (EM), Stevens–Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN) are severe exfoliative diseases of skin and mucous membranes. There is great controversy on the classification of these exfoliative skin disorders and the terminology is confusing. Erythema multiforme minor is characterized by skin lesions isolated to no more than one mucosal surface. Erythema multiforme major involves two or more mucous membranes and may affect internal organs with systemic symptoms. However, most authors consider erythema multiforme major, SJS, and TEN to be the same disease entity, differing only by the area of involved skin. In this classification, SJS is considered to affect <10% total body surface area (TBSA), whereas TEN covers >30% TBSA, leaving a zone of overlap between 10% and 30% TBSA, which is referred to as SJS/TEN.1,2 The most common characteristics of these disease entities are defined in Table 43.1.3,4 The incidence of TEN is estimated at 0.4–1.2 cases per million persons per year. The incidence of SJS has been reported to be 1–7 cases per million persons per year.5–9 These exfoliative disorders occur in all age groups; however, the incidence is increased in the elderly and females.3,10–12,24–26 In addition, TEN is seen more often in patients with HIV infection14 and in bone marrow transplant recipients.15 Mortality of TEN ranges from 25 to 80%. However, reports are variable and usually based only on small patient populations.16–18 Death may occur early in the course of the disease, with sepsis being the most frequent cause. Pseudomonas aeruginosa and Staphylococcus aureus are the predominant organisms involved.15 Pulmonary embolism and gastrointestinal hemorrhage are other causes of death.10,16 The prognosis of SJS/TEN is worse than that of a burn victim with the same extent of skin loss.10 Mortality is increased significantly in those patients at the extremes of age, and in relation to the percentage of denuded skin and serum urea nitrogen levels.16,19 Cartotto et al. created a scoring system (SCORTEN) to predict mortality in the first 20 hours of individuals presenting with TEN.20 The scoring system evaluates seven parameters at presentation but recently has been challenged as to its true accuracy. SJS is associated with a mortality rate of 0–38%.11,20 Erythema multiforme rarely causes death.21

Etiology

TEN and SJS both appear to be caused by immunological reactions to foreign antigens. TEN, as the more severe entity, has a much higher percentage associated with antecedent drug therapy. Drugs are implicated in 77–94% of cases of TEN.6,22 Antibacterials and antifungals (36%), anticonvulsants (24%), analgesics and non-steroidal anti-inflammatory agents (38%), and even corticosteroids (14%) have been implicated.22,23 Attempts to identify drugs suspected of having caused exfoliative necrolysis by skin test and laboratory tests seldom have been rewarding.16 Upper respiratory tract infections, pharyngitis, otitis media, or viral illness are frequently reported.10–12,24–26 Mycoplasma pneumoniae and herpes viruses (cytomegalovirus, Epstein–Barr virus, herpes simplex, and varicella zoster) have been implicated in the cause of EM and SJS, but not TEN.21,27,28 It can be difficult to differentiate some prodromal symptoms as due to viral or other infectious agents, or due to the primary disease process. Recently, the incidence of HIV infection in patients with toxic epidermal necrolysis has risen.14,27 Whether this increase is due to their immunocompromised state or to the increased prescription of high-risk drugs, particularly sulfonamides, is debated. No history of drug ingestion or preceding illness may be noted in these patients. Many of these cases may actually suffer from lack of patient recall of current medication because of the severity of the underlying disease or the patient’s age. Idiopathic cases, not related to drugs, accounted for only 3–4% of TEN.6,7
Epidermal and dermoeipidermal suppressor/cytotoxic T-lymphocytes in addition to dermal infiltrates of helper T-lymphocytes have been demonstrated. Hertl has confirmed that these epidermal cells are cytotoxic T-cells. Langherans cells appear to be reduced in the epidermis, although numerous dermal macrophages are observed. A more intense dermal cell infiltrate is present in SJS, especially in postherpetic cases. Dendritic lymphoid cells are observed, opposed to damaged dermal macrophages and necrotic keratinocytes. Further, at the point where the cytoplasmic processes contact the keratinocyte, the plasma membrane of the keratinocyte is absent. Aberrant expression of HLA-DR on keratinocytes has been observed, a phenomenon which has been observed in many other inflammatory skin disorders.

Immunofluorescence microscopy has demonstrated IgM and C3 along the dermoeipidermal junction and dermal vessels in cases of postherpetic SJS and EM. There have been only two reports of basal cell immunofluorescence in TEN. The pathogenesis of TEN is not completely understood. Type IV delayed hypersensitivity reaction, type II cytotoxic reaction, keratinocyte cytotoxicity mediated by lymphocytes, drug-related non-immunological mechanisms, and keratinocyte apoptosis mediated by receptors of the TNF superfamily are possible mechanisms which amplify predisposing factors of infection and genetic susceptibility. Positive patch tests in patients with TEN have been used to support the delayed hypersensitivity hypothesis. This view is somewhat at odds with the fact that HIV patients display increased frequency of TEN.

Suppression/cytotoxic T-cell infiltrates are observed in the epidermis in TEN and graft versus host disease. It is hypothesized that cytotoxic T-cells recognize drug metabolites which are complexed with the MHC-I molecule on the surface of keratinocytes, migrate into the epidermis, react with keratinocytes, and cause epidermal necrolysis.

### Table 43.1 Characteristics of erythema multiforme, SJS, and TEN

<table>
<thead>
<tr>
<th></th>
<th>Erythema multiforme</th>
<th>Stevens–Johnson syndrome</th>
<th>Toxic epidermal necrolysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prodrome</td>
<td>Absent</td>
<td>High fever, malaise</td>
<td>High fever, malaise</td>
</tr>
<tr>
<td>Acute phase</td>
<td>4–8 days</td>
<td>4–8 days</td>
<td>Sudden onset, 1–2 days</td>
</tr>
<tr>
<td>Skin lesions</td>
<td>Symmetrical, primarily located on the extremities, some target lesions without blisters</td>
<td>Variable distribution, individual vesicles on an erythematous base &lt;10% TBSA, Nikolsky’s positive</td>
<td>Diffuse generalized epidermal detachment, absence of target lesions, large confluent plaques &gt;30% TBSA, Nikolsky’s positive</td>
</tr>
<tr>
<td>Mucosal involvement</td>
<td>Limited to one surface, usually oral</td>
<td>Severe, two or more surfaces involved</td>
<td>Severe, two or more surfaces involved</td>
</tr>
<tr>
<td>Histopathology</td>
<td>Dermoepidermal separation, mononuclear perivascular cell infiltrate, small areas of epidermal detachment associated with target lesions</td>
<td>Dermoepidermal separation, more intense dermal infiltrate, areas of epidermal detachment</td>
<td>Epidermal necrosis, dermoepidermal separation, minimal dermal inflammatory infiltrate, large areas of epidermal detachment</td>
</tr>
<tr>
<td>Recovery</td>
<td>1–4 weeks</td>
<td>1–6 weeks</td>
<td>1–6 weeks</td>
</tr>
<tr>
<td>Mortality</td>
<td>0%</td>
<td>0–38%</td>
<td>25–80%</td>
</tr>
</tbody>
</table>

### Morphology/histopathology

An early skin biopsy is essential for diagnosis. Skin manifestations vary from patient to patient and with the age of the lesion (Fig. 43.1). Skin lesions may evolve to different stages of development with recurrent attacks of EM in a single patient. Advancing edges of the target lesions show scattered necrotic keratinocytes in the epidermis and only mild dermal inflammation. In older lesions and central zones of target lesions, the dusky appearance corresponds to areas of extensive keratinocyte necrosis, often with the formation of subepidermal bullae and dermoeipidermal separation. The surrounding erythematous zone shows papillary dermal edema, vascular dilation with endothelial cell swelling, and perivascular mononuclear cell infiltrate. Extravasated erythrocytes may be seen in the surrounding papillary dermis. The reticular dermis is normal.

![Figure 43.1 Toxic epidermal necrolysis (TEN) is characterized by massive sloughing of the epidermal tissue.](image-url)
The occurrence of sicca syndromes in patients with TEN and graft versus host disease further supports the autoimmune theory. The observation of blebbing of the keratinocyte plasma membrane in TEN is considered a reliable morphological finding of cytotoxic T-lymphocyte cytolysis. Further, the observation that cyclophosphamide aids TEN patients supports this theory, as cyclophosphamide is known to inhibit cytotoxic T-lymphocyte activity. Type II cytotoxic reactions involve the binding of either IgG or IgM antibodies to a cell-bound antigen. The antigen–antibody complex then activates the complement cascade and results in the cell destruction. This mechanism is not generally supported since nuclear fragmentation, common to keratinocytes of toxic epidermal necrolysis patients, is not a consequence of complement-mediated cytolysis. Keratinocyte apoptosis as the primary mechanism in the pathogenesis of TEN has been favored recently. This event is thought to be mediated by ligand/receptor interaction of the tumor necrosis factor (TNF) superfamily (as TNFα/TNF receptor or FasL/Fas interaction). In SJS, keratinocyte DNA fragmentation has been found in about 90% of cases associated with dermal perforin-positive lymphocytes. Non-immunological mechanisms include keratinocyte injury by either drug, drug metabolite, or toxic products derived from a drug in the epidermis.

Clinical features

A prodromal phase of TEN/SJS is identified frequently and usually consists of low-grade fever, malaise, and cough, all of which may suggest a respiratory tract infection. These symptoms may precede any cutaneous manifestation by 1–21 days, but usually last for 2–3 days. Additionally, patients may present with conjunctivitis, sore throat, and generalized, tender erythema. This may evolve from morbilliform eruptions or discrete erythematous or purpuric macules. Later, vesicles and large bullae emerge from areas of erythema. Patients may exhibit diffuse red erythema immediately followed by epidermolysis. On light digital pressure, the epidermis desquamates in sheets: Nikolsky’s sign is positive (Fig. 43.2). Generally, a lag period of 1–3 weeks is observed from initiation of drug until skin eruption, which may be shorter on reexposure of a previously sensitized individual.

Two or more areas of mucosa involvement are typical of SJS or TEN. Mucosal involvement precedes skin lesions by 1–3 days in one-third of cases. Several sites are usually affected, in the following order of frequency: oropharynx, ocular, genitalia, and anus. Most TEN patients have multiple mucosal lesions, and they generally persist longer than cutaneous lesions.

Complications

Toxic epidermal necrolysis is frequently associated with serious complications. The skin re-epithelializes from the dermal elements without scarring. Some patients experience hemodynamic instability and shock, and secondary full-thickness necrosis of the skin may develop; however, abnormal pigmentation is common. Nail plates are frequently lost and nail regrowth may be abnormal or absent. Mucosal membrane erosions may result in cicatricial lesions causing phimosis in men and vaginal synechiae in women. Oropharyngeal involvement is common and often results in severe dysphagia (Fig. 43.3). Although mucocutaneous erosions are the most common features of TEN/SJS, the disease may present with multisystem involvement. The onset of
Intestinal symptoms generally occurs concurrently with the cutaneous lesions. Epidermal and epithelial sloughing may extend into the gastrointestinal mucosa, and may induce esophagitis with frequent subsequent stricture formation. Gastrointestinal erosions macroscopically resemble ulcerative or pseudomembranous colitis and massive hemorrhage requiring resection has been reported. Intestinal involvement worsens the prognosis. Respiratory tract involvement occurs and is associated with increased mortality. These complications include diffuse erythema to extensive confluent tracheal and bronchial erosion covered by fibrinous exudate. Epiglottal swelling, necessitating intubation, has been reported. Desquamation of alveolar lining cells also has been reported and these patients require frequent tracheobronchial toilet. Subclinical interstitial edema is often noticed and 30% of cases progress to frank pulmonary edema and respiratory decompensation. Bronchopneumonia was found to be the most frequent complication, occurring in 50% of patients. Pulmonary embolism is an important cause of death in patients with TEN. Renal manifestations like glomerulonephritis and acute tubular necrosis, as well as hepatitis and hepatocellular necrosis, have been described. Hypoalbuminemia, asymptomatic hyperamylasemia, increased erythrocyte sedimentation rate, leukocytosis, thrombocytopenia, and normochromic and normocytic anemia are not uncommon. Leukopenia is a frequent and poor prognostic sign. This is due, in part, to depletion of the T-helper/inducer lymphocyte population (CD4+). Ocular sequelae are the most severe long-term complications and occur in half of the survivors. Pseudomembranous or membranous conjunctivitis resulting from coalesced fibrin and necrotic debris can lead to opacification, secondary infection, and blindness. Conjunctival scarring may result in lacrimal duct destruction, leading to reduced tear production and keratoconjunctivitis sicca, a Sjögren-like syndrome. Ectropion, entropion, trichiasis, and symblepharon can also occur.

Management

Toxic epidermal necrolysis is a life-threatening disease. Such a patient is best managed in a burn intensive care unit where goal-directed fluid resuscitation, nutritional support, wound care, physical therapy, and social services are provided routinely utilizing a multidisciplinary approach.

Surgical approach

Debridement of necrotic epidermis and coverage of the large wound surface with biological or synthetic dressings are essential. Sloughed epidermis should be removed in order to reduce bacterial growth and the risk for infection. The exposed and tender dermis should be covered. Debridement is best undertaken under general anesthesia as soon as diagnosis by histology is established. Blood loss associated with debridement is minimal, so over-resuscitation must be avoided. Synthetic dressings, such as Biobrane™, and biological dressings, such as homograft (cadaver allograft) and porcine xenograft skin, greatly reduce the pain, decrease fluid loss, promote healing, and reduce the risk of wound infection and sepsis. Biobrane™ is readily available as a commercial shelf product; however, in our own experience it is associated with increased local infection when covering greater than 40% TBSA wound areas. Porcine xenograft adheres well to the skin and is commercially available in large quantities. Homograft is more likely to become vascularized and therefore reduces the number of graft changes. However, this must be weighed against the potential poor cosmetic results of vascularized homograft (Fig. 43.5). Grafted areas must be immobilized and protected from shear forces. In children, Steinmann pins to suspend extremities may be useful. In both adults and children, continuous rotation or air fluidized (Clinitron) beds frequently are used.
incidence of sensitivity. Moreover, chlorhexidine gluconate wounds for eventual biological dressing. Chlorhexidine nitrate soaks can reduce contamination and prepare the nated wounds due to delayed initiation of treatment, silver must be carefully monitored. For patients with contami­

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m² treated. Therefore, serum electrolytes and osmolarity must be carefully monitored. For patients with contami­
nated wounds due to delayed initiation of treatment, silver nitrate soaks can reduce contamination and prepare the wound for eventual biological dressing. Chlorhexidine gluconate and polymyxin ointment are effective against Gram-negative organisms, including P. aeruginosa, with low incidence of sensitivity. Moreover, chlorhexidine gluconate also shows bactericidal effects against Gram-positive organisms.

Figure 43.5 Homograft vascularization occurring over a second-degree thermal injury, resulting in a poor cosmetic result.

**Topical therapy**

As separation occurs at the dermal–epidermal junction, varying depths of viable dermis remain. If this dermis can be protected from toxic detergents, desiccation, mechanical trauma, and wound infection, then rapid re-epithelialization by proliferation of basal keratinocytes from the skin appendages will occur. However, bacterial proliferation on the unprotected wound surface with invasive infection leads to full-thickness skin necrosis. Hydrotherapy and topical anti­
microbials provide debridement and infection control which should be initiated early in the course of the disease. Effective topical antimicrobial agents include silver sulfadiazine cream, silver nitrate solution, chlorhexidine gluconate solution, and polymyxin-bacitracin ointment. Silver sulfadiazine is widely used but may exacerbate the disease process due to its sulfonamide component. Additionally, an inhibitory effect on epithelialization and leukopenia requiring discontinuation has been observed. Silver nitrate solution does not contribute to the ongoing drug reaction, and epithelialization is not inhibited. However, silver nitrate solutions are hyponatremic, and thus associated with approximately 350 mmol of sodium loss per day/ m² treated. Therefore, serum electrolytes and osmolarity must be carefully monitored. For patients with contaminated wounds due to delayed initiation of treatment, silver nitrate soaks can reduce contamination and prepare the wound for eventual biological dressing. Chlorhexidine gluconate and polymyxin ointment are effective against Gram-negative organisms, including P. aeruginosa, with low incidence of sensitivity. Moreover, chlorhexidine gluconate also shows bactericidal effects against Gram-positive organisms.

**Immunomodulation therapy**

As mentioned previously, the pathophysiology of TEN appears to be initially immunologic. Therefore, it is logical to consider immunosuppressive therapy as an early treatment modality for TEN. The following sections will briefly review the literature with regards to use of corticosteroids, cyclosporine A, intravenous immunoglobulins, and thalidomide.

**Corticosteroid therapy**

Corticosteroid treatment of toxic epidermal necrolysis has produced much controversy. In regard to the delayed hypersensitivity reaction or antibody-dependent cytotoxicity theories of pathogenesis, corticosteroids would seem to be an appropriate form of medical therapy. However, the practice of administering continuous high-dose corticosteroid in an attempt to stop the progression of the disease is widely rejected. Rational assessment of the benefit of corticosteroids administration is not possible due to the lack of randomized, controlled, prospective trials. Many authors feel that steroids enhance the risk of sepsis, increase protein catabolism, delay wound healing, cause severe gastrointestinal bleeding, prolong hospitalization, and increase mortality. Lyell states that the indication for the use of steroids in the treatment of toxic epidermal necrolysis is vague.

One study found no decrease in the progression of SJS with steroids, but instead found significant morbidity. In a prospective, although not randomized, study, increased survival (66%) was seen in matched patients who did not receive steroids compared to only 33% survival in those who did receive steroids. Pediatric SJS patients treated with steroids had a longer hospital stay and a complication rate of 74% compared to 28% in those without steroids. Another study demonstrated 80% mortality associated with steroid therapy, which was reduced to 20% when steroids were withheld. In several studies, patients with antecedent glucocorticoid therapy before the onset of TEN showed no significant survival benefit, and corticosteroid use itself has been linked to an increased risk for developing TEN. Currently, the body of evidence suggests that the treatment of TEN with corticosteroids has no significant benefit and may in fact be detrimental. Therefore corticosteroids cannot be recommended in the treatment of TEN.

**Cyclosporin A**

Cyclosporin A is an agent that has the properties of both being a powerful immunosuppressant and antiapoptotic. The mechanism of action is inhibition of the synthesis of interleukin-2 by selective inhibition of calcineurin, thus arresting the proliferation of T helper cells. To date, there have been nine individual cases and one case series of the use of cyclosporin A in the treatment of TEN. In the only case series, Arevalo et al. observed a significantly shorter time to disease arrest (24–36 h) and time to re-epithelialization when compared to historical controls. Although intriguing, the currently published studies do not have similar methodologies, varying with regards to the dosage administered, route of administration, and duration of therapy. Furthermore, cyclosporin A therapy has been associated with a septicemia rate of 55%. Therefore; a well-performed prospective clinical trial is warranted prior to advocating the use of cyclosporin A in the treatment of TEN.
Intravenous immunoglobulin

It has been suggested that the Fas-Fas ligand interaction may be responsible for the apoptosis seen in TEN.67 Through a series of experiments, Viard et al. observed, in vitro, that TEN patients expressed lytically active Fas ligand and that the action of this ligand could be blocked by both a monoclonal antibody and human immunoglobulins.68 These observations suggest that human immunoglobulins may contain a Fas blocking antibody and therefore may be useful in the treatment of TEN. Unfortunately, clinical data are less impressive, with some case series suggesting a benefit while others demonstrate less encouraging results.69–71 This trend appears to be continuing with a new report from Yang et al. demonstrating no survival benefit but perhaps some beneficial affects on morbidity.72 As in the case with cyclosporin A, a controlled multicenter clinical trial is required prior to advocating the use of human immunoglobulins routinely in the treatment of TEN.

Thalidomide

The primary mechanism in the pathogenesis of TEN is keratinocyte apoptosis. Accordingly, tumor necrosis factor A has been implicated in the pathogenesis of TEN. Thalidomide, a potent inhibitor of tumor necrosis factor A, would appear to be a logical therapeutic agent in the treatment of TEN. Unfortunately, Wolkenstein et al.73 had to prematurely terminate a randomized clinical trial of thalidomide versus placebo in the treatment of TEN due to excess mortality in the treatment group. Ten of 12 patients expired in the thalidomide group compared to three of 10 in the control group. The authors theorized that thalidomide may have paradoxically increased the production of tumor necrosis factor in the treatment group, a previously reported phenomenon of thalidomide administration. Therefore, thalidomide as a treatment for TEN should not be initiated, owing to the detrimental effects, but does demonstrate the usefulness of randomized, double-blinded, placebo-controlled clinical trials. Despite the failure of thalidomide, investigators are still exploring the use of tumor necrosis factor A antagonists and inhibitors (infliximab, etanercept, etc.), in the treatment of TEN. Unfortunately, these new therapies have only been reported in case reports and thus cannot be supported for routine use in this patient population.

Until these treatment modalities have proven their efficacy in controlled trials, the Gold Standard of treatment for TEN patients consists of a multidisciplinary approach, such as used in severe burns, focusing on wound care, infection control, and prevention of complications. The specific requirements of these patients are best met in a burn intensive care unit, so early referral to a burn center is strongly recommended. Guidelines for the transfer decision may rely on the referral criteria for severe burn injury established by the American Burn Association (see also Fig. 43.6). The multidisciplinary burn team for specialized treatment of patients with extensive skin loss with trained critical care physicians, surgeons, critical care nursing specialists, respiratory therapists, and physical and occupational therapists is able to provide the best acute care as well as early and adequate rehabilitation.

General management

Drugs suspected of having initiated the disease should be discontinued immediately. Administration of pain medication is of high priority and antipyretic agents may be required. The empirical use of broad-spectrum antibiotics may be necessary if neutropenia exists, as these patients are prone to septic complications. The white blood cell count generally returns to normal levels after 2–5 days. The cause of this immunosuppression is unclear; it may be part of the primary disease or a secondary event.59 Neutropenia is the only complication in which ‘prophylactic’ antibiotics are indicated. Otherwise, systemic antibiotics only should be used for documented infections or suspected sepsis. Oral nystatin
prevents intestinal overgrowth of Candida and decreases the risk of Candida sepsis.\textsuperscript{34,59} Frequent monitoring of urinary tract, respiratory tract, skin, and catheters allows early detection of systemic infection and identification of organisms.

Intravenous replacement of fluid losses through the exposed body surface is required. However, as patients do not develop the massive edema and fluid losses evident in burn patients, fluid resuscitation formulas commonly employed in the management of thermal injuries overestimate the actual need.\textsuperscript{13,38,54–56} Ringer’s lactate solution is given at a rate determined by close monitoring of the patient’s condition and urine output. Once wound coverage is accomplished, fluid requirements usually decrease. Central line placement should be avoided, if possible, to reduce the risk of infection and sepsis. To further minimize this risk, lines should be placed in areas of uninvolved skin. Invasive devices are removed as soon as possible, and oral and nasogastric routes are utilized at earliest convenience. Environmental temperature should be raised to 30–32°C to reduce metabolic energy expenditure. Heat shield and infrared lamps are beneficial in patients’ rooms, bathrooms, and operating rooms.

Stress ulceration prophylaxis is advisable. Mouth erosion, resulting in severe dysphagia, can be alleviated by the use of viscous lidocaine or cocaine rinses, and thus ease oral administration of nutrients and fluids. Oral debris should be removed and the mouth sprayed with antiseptic several times a day.\textsuperscript{60} Pulmonary involvement requires close supervision, with careful toileting including bronchoscopy, incentive spirometry, mobilization, and coughing to prevent infections and complications. If mechanical ventilatory support is necessary, the prevention of bronchopulmonary infection gains even more importance. Daily monitoring by blood assessment, including blood gas analysis, chest X-ray, and bacteriological culture, are required to initiate timely antibiotic therapy or ventilatory support. Measures to prevent thromboembolism, such as low-dose or low-molecular-weight administration of heparin, should be instituted on admission.

Ocular involvement should be assessed daily by an ophthalmologist. Conjunctival crusting can be minimized by the application of saline eye drops every hour. Any adhesions should be broken using a blunt instrument, and bland eye drops or ointment applied frequently.\textsuperscript{11,54} Documented ocular infections are treated with organism-specific antibiotic therapy. New reports have been published regarding the use of cryopreserved amniotic membrane as a biologic dressing. The placement appears to suppress inflammation and prevent the cicatricial complications.\textsuperscript{74} Regardless of the therapy employed, special long-term ophthalmological follow-up is needed to prevent and address ocular long-term sequelae. Lacrimal duct obstruction may be detected early by performing Schirmer’s test.\textsuperscript{11,60}

During hospitalization, patients with TEN and SJS may demonstrate limitations in mobility, decreased strength, postural and gait deviation, contractures, and impaired coordination. Therefore, patients should be treated and closely followed throughout the course of the disease by a physiotherapist.\textsuperscript{65}

Along with intensive physical and occupational therapy, this patient population requires psychiatric evaluation. Similar to the burn population, depression, anxiety and post-traumatic stress disorder are all well described. With the trend towards goal directed therapy, early and repeated evaluations and prompt intervention should help, if not prevent, long-term psychiatric complications. This management should continue well into the outpatient phase.

**Nutritional support**

Enteral nutrition should be started on admission. Due to the frequent presence of oral mucosal ulcerations, patients may be reluctant to take nutrition orally, and thus require a nasogastric tube placement. Unlike burned patients who have significantly elevated metabolic rate, these patients appear to have metabolic rates only slightly above basal requirements.\textsuperscript{34,59} Weight stabilization and a positive nitrogen balance have been achieved in adults with 2500 kcal/day.\textsuperscript{54} If gastrointestinal function becomes impaired or sepsis intervenes, requirements may increase. Total parenteral nutrition should be avoided, but initiated if enteral intolerance persists.

**Soft-tissue infections and degenerative skin disorders**

Staphylococcal scalded skin syndrome, necrotizing fasciitis, and purpura fulminans are examples of a group of conditions characterized by extensive soft-tissue loss, rapid onset of critical illness, and death. Early, accurate diagnosis is essential to initiate appropriate action, such as extensive surgical excision in the case of necrotizing fascitis or crepitant soft-tissue infections. Burn care centers with their acute and reconstructive capacities have much to offer these patients with extensive skin loss.

**Staphylococcal scalded skin syndrome**

Staphylococcal scalded skin syndrome is the severe condition caused by exfoliative staphylococcal toxins and is characterized by systemic signs and symptoms and generalized involvement of the skin (Fig. 43.7). It is important to make
a diagnosis early, particularly to differentiate it from TEN, which has a different management and much greater mortality. Staphylococcal scalded skin syndrome is predominantly a disease of infancy (Ritter’s disease) and early childhood, with most cases occurring before the age of 5 years. Newborn nurseries are often the sites of outbreaks. Attendant staff may be infected or colonized with Staphylococcus aureus strains producing epidermolytic toxin, thus emphasizing the importance of standard hygienic measures. Adult staphylococcal scalded skin syndrome is rare and usually associated with compromised renal function. Mortality is generally only 4%, but can be much higher in adults (40%), depending on underlying diseases.75,76

Two distinct epidermolytic toxins (ETA and ETB), are responsible for the blistering in staphylococcal scalded skin syndrome.46 ETA is heat-stable, whereas ETB is heat-labile and encoded by a bacterial plasmid. Most toxigenic strains of S. aureus are identified as group 2 phage.77 The exfoliative toxin is metabolized and excreted by the kidneys, leading to a predisposition of patients with renal immaturity (children) or renal compromise. The exfoliative toxins produce blistering by disrupting the epidermal granular cell layers through interdesmosomal splittings but without epidermal necrosis and with very few inflammatory cells. The exact mechanism of action of the toxins has not been determined, although it is felt that the toxins directly affect desmosomes. One might be proteolytic disruption of desmosomes with the toxin or part of its sequence acting as a serine protease.75,76,77

Diagnosis of staphylococcal scalded skin syndrome can be made rapidly with a skin biopsy. The characteristic intraepidermal level of splitting is seen, with the split occurring at the granular layer level (stratum granulosum) with no epidermal necrosis or inflammatory cells in the corium.77 Immunofluorescent studies of the skin are negative.77 A Tzanck preparation from a scraping of the base of a freshly denuded area will reveal the affected cell population, i.e. acantholytic keratinocytes.77 Bullae, denuded skin and blood are usually sterile, however, and staphylococci can usually be cultured from nares, conjunctiva, or pharynx.60

Management

Onset may be marked by fever, malaise, and irritability. Scarlatiniform erythema is often accentuated in flexural and periorificial areas.75 The skin is generally tender to touch, and sheets of skin may peel away in response to minor trauma (Nikolsky’s sign). Blisters appear within 24–48 h of rupture, leaving a characteristic moist erythematous epidermal level of splitting.77 With diagnosis antibiotics should be started, and semisynthetic penicillinase-resistant penicillin analogs are indicated (e.g. methicillin or oxacillin), since the majority of group 2 staphylococci show resistance to penicillin. Administration of steroids to these patients is contraindicated.77 After screening for colonization, decontamination of colonized areas, especially the nasopharyngeal region in patients and nursing staff, may be advisable to prevent further spread. Fluid resuscitation is usually required at a lesser volume compared to a burn patient with a similar involved body surface area. Fluid substitution should be guided by urine output, hemodynamic parameters, electrolyte, and colloid status.

Until skin barrier function is restored, patients should receive appropriate wound dressings to prevent secondary wound infection. Topical agents are soothing and bacteriostatic. It needs to be pointed out that the wound initially is not colonized or infected, so alternatively, large areas can be more effectively managed with biological or synthetic dressings. They have the advantage of eliminating the need for frequent dressing changes which can be particularly traumatic for young children. Mortality usually is low, but may occur in very young and adult patients, usually from sepsis or electrolyte imbalance on the basis of underlying disease.77 Complete wound healing is usually observed within 7 days, and scarring and altered pigmentation are not common.

**Necrotizing fasciitis and bacterial myonecrosis**

Necrotizing fasciitis is a soft-tissue infection which is characterized by widespread necrosis of fascia and subcutaneous tissue which may progress to muscle and skin necrosis. Overall mortality may still be as high as 50%.76,78 Most cases of necrotizing fasciitis are due to polymicrobial infection including both anaerobic Gram-positive cocci and Gram-negative bacilli.36 Streptococcus, Staphylococcus, Enterococcus, and Bacteroides are commonly found. Infection with many bacterial species may result in bacterial myonecrosis. However, gas gangrene by Clostridia spp. results in severe systemic toxicity and higher mortality than necrotizing fasciitis. A deep contaminated wound frequently precedes the severe soft-tissue infection. Streptococcal myositis has a mortality rate of between 80% and 100%.82 Risk factors for both necrotizing fasciitis and bacterial myonecrosis have been identified as diabetes mellitus, intravenous drug use, age greater than 50 years, hypertension, and malnutrition/obesity. The presence of three or more of these risk factors was found to give a predictive mortality rate of 50% (Fig. 43.8)83.

**Diagnosis**

Early diagnosis is of extreme importance and consequence. Initial presentation is deceptive as the findings may be localized pain and edema without discoloration of the skin. Later, induration and erythema may be evident. Paresthesia of overlying skin and eventual dusky discoloration and local blistersing may occur in the later course. Severe toxemia may develop, usually out of proportion to the local signs. Severe systemic alterations are characteristic of myonecrosis. Gas inclusion may be evident in subcutaneous tissues on X-ray. CT and MRI may help in the diagnosis and provide information on the nature and extent of the infection.84 Frozen section biopsies may provide early histological evidence of infection.85 Gram stains and microbiological testing are very important diagnostic tools and guide antibiotic treatment. However, a definite distinction between necrotizing fasciitis, myonecrosis, and other soft-tissue infections often can only be established during surgery.

**Management**

The key to successful management of necrotizing infections is early diagnosis and radical surgical intervention. Surgical exploration involves complete excision of all necrotic tissues.
Exfoliative diseases of the integument and soft tissue necrotizing infections

If more than one operation for debridement of infected necrotic tissue is needed, mortality increases from 43% to 71%; this outcome drastically highlights the importance of adequate initial necrosectomy. In patients with many risk factors, early amputation of the extremity, especially in cases of myonecrosis, should be considered. Broad-spectrum antibiotics are started preoperatively, although high-dose penicillin is appropriate for clostridial infections. However, antibiotic treatment is no substitution for surgical intervention. Adequate fluid resuscitation and nutritional support are also required. Wounds are packed open with antiseptic-soaked dressings, which need to be changed frequently. Kaiser and Cerra have reported unsatisfactory results with either early application of porcine xenografts or burn wound topical antimicrobials. Complete control of local and systemic infection is required before wound closure is addressed.

As in burns, secondary infections must be prevented by proper wound management. Biological or synthetic dressings offer the advantages of decreased pain, decreased fluid loss, and prevention of secondary infection. Frequently, large areas of skin and soft-tissue loss result from this disease and will eventually require extensive surgery to achieve adequate closure. Some authors advocate the use of hyperbaric oxygen and claim that it results in decreased mortality and reduced need for debridement; however, most of these reports are case reports or uncontrolled trials and adequate prospective controlled trials in patients are still lacking. In animals, hyperbaric oxygen therapy alone did not improve survival or bacterial colonization, but did show adjuvant effects to antibiotic treatment. In summary, hyperbaric oxygen therapy, if available, should not delay radical surgical debridement and should be used as an adjunct to radical surgery and antibiotic therapy.

**Purpura fulminans**

Purpura fulminans is a term that describes an acute syndrome of rapidly progressive hemorrhagic necrosis of the skin due to dermal vascular thrombosis associated with vascular collapse and disseminated intravascular coagulation (DIC). It may occur in individuals with dysfunction of the protein C anticoagulant system, with acute severe infection, or idiopathically without any coagulation dysfunction or infection.

It has been associated with systemic infection by *Meningococcus*, Gram-negative bacilli, *Staphylococcus*, *Streptococcus*, and *Rickettsia* organisms. Skin necrosis begins in a region of dermal discomfort, which rapidly progresses to evanescent flush, followed by petechiae. Hemorrhagic bullae progress to frank skin necrosis. The process generally involves the skin and subcutaneous tissues, without involvement of muscle. Skin involvement is frequently an early manifestation of the disease process. Skin biopsy will, therefore, allow an earlier diagnosis. Mortality in the acute phase is 18–40%.

Management is directed at halting progression of the underlying infectious disease, preventing secondary infections, and removing non-viable tissue. Early heparin administration and replacement of clotting factors have proven useful to stop intravascular clotting. Shock from blood extravasation and sepsis require extensive volume...
replacement. Limb vascular and compartmental pressure should be monitored closely to enable early escharotomy and/or fasciotomy, when needed. Skin lesions resulting only in blisters should be treated with topical antimicrobials (e.g., silver sulfadiazine) to prevent secondary infection. Non-viable tissue should be removed as soon as the patient’s condition allows. Small areas can be covered with autografts but, as large areas are frequently involved, allograft or xenograft skin coverage may be required. Limb amputations may be frequently required due to vascular compromise, as well as revisions for progression of disease. Isolation of the affected patient, as well as monitoring and prophylactic treatment of patients and staff, may be necessary to prevent further spread and outbreaks of the disease, especially in case of meningococcal infection.

**Calciphylaxis**

Calciphylaxis is a rare condition that is characterized by the development of extraskeletal calcifications resulting in tissue necrosis. While the exact etiology is unknown, the condition appears to be most commonly associated with disorders that alter calcium/phosphate homeostasis. Thus, the condition is usually diagnosed in individuals undergoing renal replacement therapy or who have recently undergone renal transplantation. Despite the close association with renal failure, Nigwekar et al. have identified a subgroup of individuals with the same pathological condition but without end stage renal failure and coined the term ‘non-uremic calciphylaxis’ (Fig. 43.9, Box 43.1).95

While first described by Bryant and White in 1898 and later investigated by Selye in 1962, it was not until 1976 that the true clinical significance of the syndrome was formally recognized by Gipstein et al. The clinical syndrome of calciphylaxis is characterized by:

1. Painful purpuric cutaneous lesions (Fig. 43.10)
2. Histological evidence of systemic medial calcifications of arteries; tunica media
3. Histological evidence of small vessel mural calcification with or without endovascular fibrosis leading to vascular thrombosis and tissue necrosis.

As previously stated, the exact pathophysiology of calciphylaxis is unknown, though the best theory was offered by Selye et al. in 1962. Utilizing a rat model, he suggested that calciphylaxis was a condition of hypersensitivity caused by exposure to ‘sensitizing agents’ (nephrectomy/PTH) and ‘challengers’ (egg albumin/metalllic salts) over a defined period of time. Simply stated, calciphylaxis appears to be a clinical syndrome induced by a series of events that predisposes the patient to extraskeletal calcifications.

Clinically, calciphylaxis affects approximately 1–4% of the population with underlying end-stage renal disease. The condition has been reported in age groups ranging from 6 months to 83 years of age. The condition appears to affect predominantly Caucasian women with a female to male ratio of 3:1. Unfortunately, the mortality rate associated

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**Box 43.1 Conditions associated with non-uremic calciphylaxis**

- Primary hyperparathyroidism
- Breast cancer + chemotherapy
- Liver cirrhosis
- Cholangiocarcinoma
- Crohn’s disease
- Rheumatic arthritis
- Systemic lupus erythematosus.
with calciphylaxis is as high as 60–80% and appears to be related to the distribution of cutaneous lesions. Distal lesions have a reported mortality rate of 42%, whereas more proximal lesions (trunk, abdomen, buttocks and proximal extremities) have a reported mortality rate approaching 72%. The association between mortality rates and lesion distribution may in fact be related to the degree of systemic involvement. The overall mortality rate from calciphylaxis appears to be closely related to the extent of internal organ involvement and development of sepsis from infected cutaneous lesions.

The diagnosis of calciphylaxis should be suspected in any patient with painful cutaneous lesions and a history supportive of the clinical syndrome. While diagnostic laboratories and imaging are not helpful, the diagnosis can be formally established with a tissue biopsy.

Once the diagnosis is established, the treatment should be initiated in a multidisciplinary approach. The treatment should be based on improving the underlying condition such as reformulation in hemodialysis or potentially administering sodium thiosulfate which acts as an antioxidant and chelator of cations. Unfortunately, despite the best medical efforts, treatment usually becomes supportive from an analgesic and wound standpoint. Wound management should be aggressive to avoid local wound infections. The primary goal is to establish a healthy wound bed without evidence of disease progression prior to definitive closure.

**Conclusion**

Inflammatory and infectious conditions of the skin and underlying tissues represent a major diagnostic and therapeutic challenge. The team approach to their care is essential, and wound management is paramount. Burn units are ideally suited to deal with patients with these conditions and should be considered as the appropriate site of referral for these critically ill patients.

**Further reading**

References


The burn problem: a pathologist’s perspective

Hal K. Hawkins

Introduction

‘Burns are not a simple injury, but a very complicated disease.’ This statement, dating from 1840, holds true with additional force in 2012. Massive destruction of skin tissue and smoke-induced injury to the airways both stimulate complex reactions which are still only partly understood. Malfunction of every organ system frequently complicates the responses of patients to large burns. The nature of this malfunction is often clarified by examination of the body after death. Postmortem examination also may reveal unsuspected infections or adverse effects of therapy. In addition, postmortem examination leads to review of the circumstances of injury and of the causal sequence in which complications occurred, in order to determine the manner of death. Analysis of an entire case from the point of view of pathogenesis often clarifies the nature of the patient’s most significant problems. This chapter systematically reviews some of the observations made at autopsy in patients who have died after burn injury. It also surveys experimental evidence that bears on pathogenetic mechanisms relevant to disease processes seen at autopsy. The observations reviewed here are drawn from our experience of 253 autopsies performed on burned children who died at the Shriner’s Burns Hospital in Galveston, Texas, from 1971 to the present.

To introduce the sections that follow, the major medical problems that complicate burn injury are summarized here. The degree of disruption of normal physiologic processes after burn injury is extreme. Immediately after burn injury, massive loss of intravascular fluid into the burned tissue begins to occur. Unless this fluid loss is replaced by the physician very promptly and carefully, serious hypovolemia develops. Hypovolemia and the resulting reduction of tissue perfusion to levels less than that necessary to maintain cellular homeostasis, which is defined as ischemia, causes necrosis of certain cells, typically those with the greatest oxygen demand within a tissue. The neural and endocrine responses to the traumatic injury may lead to recognizable lesions in the stomach and the heart. Ischemia may lead to necrosis of pancreatic acinar epithelium and acute pancreatitis. Thermal injury to skeletal muscle, or lack of perfusion of muscle, may lead to local exudation of fluid and development of such high pressure in fascial compartments that arterial perfusion is prevented. This ‘compartment syndrome,’ unless relieved by prompt surgical intervention, leads to necrosis of muscle throughout the entire compartment. The consequences of massive necrosis of muscle often include secondary injury to the lungs, owing to release of reactive oxygen species, and myoglobinuria with secondary renal damage. At the time of injury, patients frequently inhale sufficient carbon monoxide to compromise the oxygen-carrying capacity of the blood. The resultant tissue hypoxia can cause death at the scene, and if the patient survives it can be sufficient to lead to irreversible neuronal injury, cerebral edema and brain death. Hypoxia, sometimes related to carbon monoxide intoxication, also contributes to cardiac and renal injury. In addition, when fires occur in closed spaces, the ‘flashover’ process consumes all available oxygen, so that the patient’s environment may contain too little oxygen to sustain life. Occasionally a burn victim is found without pulse or respiratory effort, probably as a consequence of hypoxia, and is revived by cardiopulmonary resuscitation. In such cases ischemic and hypoxic injury may be profound in multiple organs, and there may be significant ‘ischemia–reperfusion injury’ to the lungs after resuscitation. Patients injured in house fires often suffer injury to the respiratory tract caused by inhalation of toxic products of combustion. This smoke inhalation injury stimulates an intense inflammatory reaction, which can lead to obstruction of airways and further tissue injury. This problem is discussed below in the section on the respiratory system. Infection is the next major risk experienced by patients after burn injury. Necrotic skin provides an excellent environment for proliferation of bacteria and fungi, and as long as necrotic tissue remains, the risk of infection remains high. Immunosuppression contributes to this risk, so that burn patients develop serious infections with agents otherwise usually encountered in patients treated with immunosuppressive drugs after transplantation. The mechanisms of this immunosuppression are still under investigation, but include excessive secretion of glucocorticoids and abnormal cytokine signaling. Injury to the intestinal epithelium by hypoxia or ischemia leads to translocation of intestinal bacteria into the portal circulation. Coagulopathy may be a very serious complication of burn injury. It may lead directly to tissue ischemia after vascular thrombosis, or the resultant hemorrhage may lead to secondary hypovolemia. Patients often require transfusion of very large quantities of blood products during their treatment and are subject to all the risks of transfusion.
Disease processes involving multiple organ systems

Hypoxia and ischemia

All cells require a constant supply of oxygen and metabolic substrates to remain viable. In tissue hypoxia, when the supply of oxygen is insufficient to meet metabolic demand, cells generate a limited amount of metabolic energy by anaerobic glycolysis, releasing lactic acid. With tissue ischemia, when the flow of blood is insufficient, this metabolic perturbation is complicated by a lack of supply of glucose and other substrates, and the extracellular fluid composition may change dramatically. In general, tissues with the greatest metabolic activity are the first to lose viability under conditions of hypoxia and ischemia, including the neurons of the central nervous system, cardiac myocytes, small intestinal epithelial cells and the proximal tubular epithelium of the kidney. The location and extent of necrosis in these organs depends on the severity and duration of the ischemic or hypoxic injury.

After ischemia and hypoxia have led to irreversible injury and death of selected cell types or whole segments of organs (infarcts), responses are generated which may lead to further injury of remote organs. Cellular necrosis stimulates an intense acute inflammatory reaction, probably initiated by activation of the complement cascade, degranulation of mast cells, and other processes. This reaction surrounds an infarct, or proceeds throughout a region of tissue injury if the local circulation is sufficient. In the skin, the tissues at the base of the zone of necrosis become acutely inflamed. Monocytes recruited to the regions of injury secrete cytokines in large quantities, and polymorphonuclear neutrophils activate their antibacterial mechanisms. Cytokines have effects throughout the body, the most important probably being TNF-α, and superoxide released by neutrophils has important distant effects. In addition, in endothelial cells injured by hypoxia the enzyme xanthine dehydrogenase is converted to xanthine oxidase, which releases superoxide during degradation of adenosine, which in turn is released by necrotic cells.10,11 Superoxide, released into the circulation by this metabolic process and by neutrophils, can injure the lung by damaging both endothelial and epithelial cells and allowing protein-rich fluid to exude into alveoli. The inflammatory reaction to thermal tissue injury also stimulates an intense influx of neutrophils, which undoubtedly contributes to this injury by releasing superoxide. In experimental models of burn injury, as well as in models of ischemia–reperfusion injury, the lungs have been shown to be injured by these processes.12 Endogenous antioxidants such as glutathione are depleted, and conjugated dienes appear, indicating that cell membrane injury due to lipid peroxidation has occurred in the lung.13

Infection and sepsis

The skin normally provides a highly effective barrier against invasion by infectious agents. Necrotic tissue, in the skin as elsewhere, is ineffective as a barrier to infection and indeed provides an excellent culture medium. Patients who are treated for deep burn injury with traditional debridement and washing for several days generally arrive at this institution with large quantities of multiple microorganisms growing in the necrotic skin. The bacteria appear to proliferate initially in areas which have insufficient circulation to develop a significant inflammatory response. As large numbers of bacteria accumulate, those with high pathogenic capacity invade the adjacent viable tissue, produce further necrosis, and gain access to the circulation. This is the condition of burn wound sepsis, which historically has been the leading cause of death in burn patients. In Linare's series of 115 autopsies, sepsis was present in 73%, as documented by positive blood culture and demonstration of invasive infection of viable tissue.14,15 When pneumonia was found at autopsy in such a case, the cause of death was classified as burn wound sepsis, with pneumonia as a contributing cause. In 80% of these fatal cases of sepsis the burn wound was the source of the infection. The most important pathogens were Pseudomonas aeruginosa, Staphylococcus aureus, Klebsiella pneumoniae, Escherichia coli, Enterobacter, and Candida species. More recently, antibiotic-resistant Acinetobacter species have emerged as a frequent cause of fatal sepsis. Burn wound sepsis is suspected clinically when a burn wound is the site of proliferating microorganisms exceeding \( 10^7 \) g of tissue, and there is histologic evidence of active invasion of subjacent unburned tissue.16 In our institution, the wounds of burn patients, especially the open areas, are routinely sampled for quantitative culture and for histologic study when excision and grafting procedures are done, and whenever clinical examination suggests the possibility of tissue infection. The histologic classification used and its rationale are discussed below under the integumentary system. Once septicemia occurs, there is a generalized reaction which often includes hypotension, tachycardia, increased hyperthermia or hypothermia, and poor perfusion of the intestines and other viscera.17 In the case of Gram-negative bacteria, the endotoxin stimulates monocytes via their CD14 receptors to become activated and set up a cascade of release of pro- and anti-inflammatory mediators which affect all organs and tissues in the body.18–20 Coagulopathy is also an important complication of sepsis.21 In addition, once bacteria have gained entrance to the general circulation, it becomes possible for foci of tissue infection to develop at distant sites. This is most likely to occur in sites of tissue necrosis, on cardiac valves, or in the lungs. Abscesses in distant organs can allow the infection to resist eradication by specific antibiotics, and thus allow sepsis to persist despite appropriate therapy. One recent case demonstrated clearly the route of dissemination of fatal burn wound sepsis. The patient was admitted in a clinically septic condition 2 weeks after suffering a large burn, and died in spite of aggressive therapy. At the time of autopsy there were many areas of bacterial proliferation within the burn wound, invasion of viable tissue deep to the burn eschar, and thrombosis of blood vessels invaded by bacteria at the margin of the necrotic zone. Septic emboli with fibrous organization were seen in pulmonary artery branches in all lobes of the lungs. There were foci of necrosis throughout the lungs in which bacterial proliferation was visible within the walls of arteries, and these necrotic areas were surrounded by massive pulmonary hemorrhage and edema. A direct hematogenous route of spread of infection from the skin to the lungs seemed clear in this case. On the other hand, airway obstruction is known to predispose...
to pneumonia acquired through the airways, by preventing normal clearance of bacteria from the airways and by providing a favorable medium for bacterial growth. Multiple foci of airway obstruction are almost always seen at autopsy in burn patients.22 In another recent case, although pneumonia of airway obstruction are almost always seen at autopsy in burn patients,22 In another recent case, although pneumonia.23,24 In another recent case, although pneumonia.

In burn patients, nosocomial infection is a serious infections in burn patients appear to be due to infection in any other area of the body. Although most infections in burn patients appear to be due to endogenous flora, and many derive from wound infections present at the time of admission, nosocomial infection is a constant hazard.23,24

The problem of burn wound sepsis is amenable to therapy. The strategy of excision of the potentially infected burn wound as early as possible, together with judicious administration of effective antibiotics, has greatly reduced the number of deaths due to infection. Coincidentally with the institution of early excision and grafting of burn patients in our institution, the incidence of burn wound sepsis as a cause of death declined dramatically. However, the problem of sepsis persists despite the best efforts in prevention and treatment. Certain organisms can evade the best current efforts at management, and have caused death in recent cases, including bacteria resistant to all available antibiotics.25 Those patients who are referred for therapy more than 1 week after burn injury often have extensive invasive wound infection and sepsis, which may be difficult or impossible to eradicate. Other microorganisms also can cause life-threatening infection in burn patients. Fungal infection is a continuing problem in patients with large burns, despite the development of more effective systemic antifungal agents.26

In one recent case of apparent systemic fungal infection, invasive and systemic dissemination of a pseudofungus of the genus Oomyces was demonstrated.27 Molecular methods (RT-PCR) were used to identify the organism in this case. It seems likely that the increased availability of molecular diagnostic testing of infectious agents may lead to recognition of additional previously unrecognized causes of invasive infection in burn patients. We have also experienced cases in which acquisition or reactivation of herpes virus infections led to major tissue injury. The risks of infection of a victim of a large burn are somewhat similar to those of an immunosuppressed transplant patient.

Coagulopathy

The burn wound has procoagulant effects and may induce coagulation throughout the circulation (DIC, disseminated intravascular coagulation).28,29 Tissue necrosis, particularly lethal injury to endothelial cells with exposure of subendothelial collagen, and release of tissue thromboplastin, can activate coagulation and lead to coagulopathy. Generation of thrombin within the circulation leads to generation of fibrin peptides and stimulates acute inflammatory reactions, including increased vascular permeability and upregulation of adhesion molecules on neutrophils and endothelial cells.30 Generation of fibrin degradation products may be sufficient to interfere with normal thrombosis, and thrombocytopenia can develop in response to abnormal intravascular fibrin generation.31 Activation of the kinin system can stimulate further abnormal vascular permeability and hypotension.32 Consumption of coagulation factors can lead to abnormal bleeding, which can cause extensive tissue injury secondarily. It is important to note that the acute-phase response to burn injury includes increased synthesis of fibrinogen and factor VIII. During the first 3–10 days after burn injury, patients often have greater than normal clotting activity. This may increase their susceptibility to the development of DIC, especially if sepsis supervenes. It also implies that laboratory testing of levels of fibrinogen and factor VIII may yield normal values even in the presence of abnormal consumption of these factors. When disseminated intravascular coagulation occurs, coagulation factors are depleted, including antithrombin.32 There is evidence that administration of recombinant antithrombin is beneficial when administered early in the course of treatment of severe burns.33 When disseminated intravascular coagulation occurs in the patient’s terminal course, microscopic fibrin thrombi are seen in many organs at the time of autopsy, most commonly in the lungs, the skin, the kidneys and the gastrointestinal tract.14,34

Integumentary system

The skin is the site of initial injury in burn patients, and many of the events that lead to dysfunction or failure of other organs begin in the skin. Thermal injury rapidly produces irreversible injury and cell death in epidermal keratinocytes, in the epidermal appendages, including hair follicles and their attached sebaceous glands and sweat glands, and in the connective tissue cells of the dermis. In many cases the burn wound excised within 48 hours of injury shows that the entire dermis and all of the hair follicles are necrotic, but that much of the subcutaneous adipose tissue remains viable. It appears that the greater insulating capacity of adipose tissue protects it to some extent. In some cases, of course, the necrosis of the initial thermal injury may extend deep into the subcutaneous tissue. In extreme cases, the underlying skeletal muscle may become necrotic as a result of thermal injury. Necrosis of skeletal muscle is especially prominent in the case of electrical injury, in which more heat may be generated adjacent to bone than near the body surface. An interesting observation is that there is often a band-like infiltrate of degenerating polymorphonuclear neutrophils in the midst of a totally necrotic dermis. This suggests that the boundary between necrotic and viable tissue may have extended deeper after the initial burn injury and its inflammatory response. There is experimental evidence that burn wounds often evolve from an initial level of necrosis to a deeper level, even from second to third degree, as a result of poor perfusion of the tissue immediately deep to the initial burn injury.35 This process of vascular stasis deep to the burn is undoubtedly due in part to the rapid loss of intravascular fluid from the damaged capillaries and venules just below the necrotic burn wound. In addition, there is evidence that neutrophils contribute to this process of burn wound extension, most likely by adhering to endothelium...
and to each other, with resulting obstruction of the microvasculature.36

It is important to assess the presence and extent of infection within the burn wound, both by examination of wounds excised therapeutically and by biopsy of suspicious areas in open foci after grafting procedures. A high index of suspicion serves the burn patient well. All biopsy and excision specimens in our institution are sampled and studied histologically with stains for bacteria (Brown and Hopps) and fungi (methenamine silver). In large excision specimens, samples are taken from sites of especially deep tissue injury and sites that show abnormal discoloration of dermal or subcutaneous tissue. When infectious microorganisms are found, it is important to determine their location with respect to the boundary between living and necrotic tissue. This boundary may be irregular. It is generally distinct and marked by inflammation in wounds several days old, but may be somewhat indistinct in very fresh specimens, as karyolysis takes some time to develop in burn wounds. As noted above, wound infections generally begin with colonization of the skin surface and proliferation of organisms on the surface, often with extension into hair follicles, followed by growth within the necrotic tissue. Both the coagulum on the surface and the necrotic epidermis and dermis are considered part of the burn eschar. Growth within necrotic tissue is considered evidence of tissue infection, however, and potentially more dangerous than growth on the surface of necrotic skin, under a layer of fibrin and debris. Even when quantitative cultures show more than 10^5 bacteria per gram of tissue, when careful histologic study shows that the organisms are limited to the skin surface or the superficial necrotic tissue, the risk of sepsis appears to be low. Such growth on or in necrotic tissue, however, does set the stage for invasion of viable tissue. The finding of clusters of bacteria or fungi within viable tissue implies a serious risk of sepsis and further tissue invasion. Bacterial invasion of viable tissue is quite apparent by histologic study of appropriate tissue samples (Fig. 44.1). Invasive fungal infection presents a somewhat different pattern, in that there is often a wavefront of necrosis that accompanies fungal invasion (Fig. 44.2). Thus the presence of fungal hyphae extending to a boundary between necrotic and viable tissue is considered evidence of fungal invasion of viable tissue. On this basis, infections identified within burn wounds are reported as surface colonization, invasion of necrotic tissue, which may be superficial or deep, and invasion of viable tissue. The responsible surgeon is called immediately when invasion of viable tissue is found. If the level of clinical suspicion is especially high, frozen sections have been found useful for this determination, using a tape transfer device to facilitate handling of these difficult specimens, with confirmation of the results with routine sections on the following day. Diagnosis of viral infection of the skin is achieved most efficiently by preparation of smears from scrapings of freshly opened vesicular lesions or the bases of recently ruptured vesicles, and direct immunofluorescence testing.

A fortunately rare complication involving the skin of patients with large burns is the development of squamous cell carcinoma during the late phase of recovery. This so-called ‘Marjolin ulcer’ shows extensive local invasion but generally can be controlled with adequate local excision.37–39

Respiratory system

Respiratory failure, defined as inability to maintain adequate oxygen saturation while administering 100% oxygen by ventilator, has been found to be the immediate cause of death in some burn patients. The causes and mechanisms of respiratory failure are multiple and will be addressed separately, although in many cases more than one mechanism operates. Direct thermal injury to the trachea and bronchi probably does not occur, except in patients exposed to large amounts of steam. In addition to the problems listed below, patients may develop problems related to the airways such as pneumothorax or interstitial emphysema, aspiration of gastric contents, pulmonary embolism, and non-specific
The burn problem: a pathologist’s perspective

Similar to that of ecthyma gangrenosum of the skin. A similar angioinvasive pattern of pulmonary infection can be seen with generalized infection due to *Aspergillus* or similar filamentous fungi.

Diffuse alveolar damage

This process affects the pulmonary parenchyma in all lobes, although it is often patchy in distribution and begins with exudation of protein-rich fluid into alveolar spaces. This proteinaceous exudate, representing the vascular phase of the acute inflammatory reaction, is a consequence of damage to or increased permeability of both capillary endothelial cells and the epithelial type I cells of the alveolar lining. Within hours the exudates form hyaline membranes, which are a histologic hallmark of this disease process (Fig. 44.6). Within a few days the exudate begins to undergo

Figure 44.3 This photograph is a slice of the upper lobe of the lung taken at autopsy from a patient who showed clinical signs of sepsis when he developed disseminated infection after multiple wound cultures of open wounds yielded multiple antibiotic-resistant *Pseudomonas*.

Figure 44.4 This micrograph, taken at low magnification, shows a small round pale area of necrotic lung tissue in which no nuclei are staining, surrounded by a zone of congestion and hemorrhage, with very little acute inflammatory reaction. H&E stain.

Figure 44.5 This high magnification micrograph shows short Gram-negative rods growing profusely within the wall of a small pulmonary artery branch. Brown–Hopps tissue Gram stain.

Figure 44.6 This section of lung tissue shows bright pink, homogeneous hyaline membranes attached to alveolar walls and septa of alveolar ducts. This is from a 2-year-old patient who died 8 days after a large scald burn. This represents the exudative phase of diffuse alveolar damage, which may be seen in the absence of smoke inhalation injury. H&E stain.

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Infection

In patients who have clinical evidence of sepsis at the time of death, extensive infection of the lungs is commonly present and may represent a terminal event. Fatal pneumonia is most often seen as a consequence of infection with a highly resistant bacterial strain, an invasive fungus, or in a compromised host with renal failure or some other cause of severe immunodeficiency. Virulent and antibiotic-resistant strains of *Pseudomonas* may produce an angioinvasive infection in the lung, with massive proliferation of bacteria within the walls of pulmonary arteries and ischemic necrosis of segments of lung tissue (Figs 44.3–44.5). This pattern is similar to that of ecthyma gangrenosum of the skin. A similar angioinvasive pattern of pulmonary infection can be seen with generalized infection due to *Aspergillus* or similar filamentous fungi.

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oxygen in high concentration within the lung can itself lead to injury, and this injury can be manifest in the form of diffuse alveolar damage.53–55 Despite this plethora of mechanisms that can lead to pulmonary injury in burn patients, many patients with massive burn injury do not develop clinically apparent respiratory difficulty. The conditions that seem to be most strongly associated with this form of pulmonary injury are delayed fluid resuscitation, limb ischemia, and, of course, sepsis.

Smoke inhalation injury

Patients often inhale products of combustion in house fires, and the toxic effects of these gases and fumes directly injure tissues in the lung. These patients are recognized during bronchoscopy by observing prominent hyperemia of the tracheobronchial mucosa, and small particles of carbonaceous soot within the airways. Associated findings include facial burns and singed nasal hairs. These patients usually do not require ventilator therapy for several days, but are at high risk of developing respiratory failure, which responds poorly to ventilator therapy and may prove fatal even when the burn injury is small. The mortality of burn injury has been found to be substantially increased when inhalation injury also is present. 56–60 Experimental studies in sheep and dogs have partially clarified the mechanisms of smoke inhalation injury.61–64 In animals the immediate reactions to inhalation of toxic smoke include detachment of numerous ciliated columnar cells from the tracheobronchial epithelium, secretion of all stored mucus by secretory cells, and a dramatic increase (more than 10-fold) in tracheobronchial blood flow.65–67 Within a few hours an intense acute inflammatory reaction develops, with exudation of numerous neutrophils into the airways, and release of protein-rich fluid that may coagulate within airways, forming occlusive ‘casts’ containing mucus and desquamated cells (Fig. 44.8). After 48 hours the exudate of neutrophils, which is most intense in the trachea at earlier times, fills many terminal bronchioles, and
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including Alcian blue and MUC5b, are found in small bronchioles and lung parenchyma in almost all patients studied at autopsy.22

Multiple mechanisms may be responsible for the respiratory disease evoked by inhalation of toxic smoke.69 As in the case of diffuse alveolar damage, the available evidence indicates that neutrophils may be responsible for much of the injury, but the locus of injury appears to be different, centered on the airways rather than the pulmonary parenchyma. Factors that may be likely to lead to selective damage to the airways include local release of neuropeptides by afferent C-fibers in the airways and activation of vagal reflexes and activation of proinflammatory processes in reaction to injury to the airway mucosa, particularly local production of interleukin (IL)-8.70–73 Local production of nitric oxide and other reactive nitrogen species has significant deleterious effects in this form of acute lung injury, according to large animal experiments.74,75 Local activation of thrombin during the formation of fibrin clots, and local production of endothelin-1 may further enhance the inflammatory reaction in the airways.76,77 Secretory cells appear to be especially sensitive to smoke inhalation injury. Experimental studies in sheep have demonstrated that activation of poly-adenosyl-ribose polymerase (PARP) contributes to lung injury after burn and smoke inhalation injury.78 Obstruction of small bronchi and bronchioles is thought to lead to failure of ventilation of multiple small segments of lung tissue, and inappropriate vasodilation in these poorly ventilated segments may well contribute to the failure of adequate oxygenation. 79 Treatment with nebulized heparin or tissue plasminogen activator has been found to reduce the degree of airway injury in the ovine model, demonstrating the importance of fibrin polymerization in this model.80,81 Segmental atelectasis and prominent vasodilation in focal areas are features of smoke inhalation injury seen in experimental animals, and also in patients examined at autopsy after burn injury and smoke inhalation injury. Obstruction of bronchi and bronchioles by mucus, fibrin and cell debris contributes to respiratory malfunction in experimental animals, and similar obstructive material is seen in human lung tissue at autopsy.22,79,82–84 As is the case with diffuse alveolar damage, deficient clearance of airway secretions and the toxic effects of high concentrations of oxygen may complicate the reaction to injury. The literature contains widely differing estimates of the extent to which smoke inhalation injury contributes to mortality in patients with burns. A recent review of more than 40 years’ experience at the Shriners Burns Hospital in Galveston found that although clinical evidence of smoke inhalation injury was present in only 14% of patients admitted for recent burns, such evidence was recorded in 66% of the patients who died.

Cardiovascular system

Despite the tachycardia and increased output common to patients with burn injury, structural lesions of the heart have been uncommon in our autopsies done on a pediatric population of patients. However, cardiac hypertrophy is a consistent finding at autopsy.85 Cardiac dilation and clinical evidence of poor myocardial contractility do develop in some patients after burn injury. Bacterial endocarditis occurs in occasional patients with sepsis complicating burn injury.
Urinary system

Patients with extensive burn injury, if resuscitated adequately during the first few hours, may have normal renal function throughout their hospital course. It is not uncommon, however, especially when the initial fluid resuscitation was not optimal, or when patients develop episodes of sepsis, for acute renal failure to develop. In such cases the autopsy frequently reveals evidence of acute tubular necrosis, the morphologic expression of which depends on the timing of the injury. Non-bacterial thrombotic endocarditis (marantic endocarditis) has also been seen, and may also give rise to embolic complications (Fig. 44.11). When the endocardial region of the left ventricle is examined at autopsy, small foci of necrosis associated with local hemorrhage are often observed (Fig. 44.12). Contraction band necrosis is sometimes the only evidence of myocardial injury. These lesions may represent poor perfusion of a tissue with high metabolic demands during terminal episodes of hypotension. In some cases they may represent the effects of endogenous or exogenous adrenergic agents. Rona and his associates have demonstrated that β-adrenergic agents, at high doses, stimulate the development of small foci of myocyte necrosis and hemorrhage in the subendocardial region of the heart. This mode of injury is potentially preventable in burn patients.

Digestive system and hepatobiliary tract

The association of duodenal ulcers with burn injury, described by Curling, is a classic lesion that still occurs in patients with burn injury, although its incidence is low, probably as a result of routine treatment of burn patients with inhibitors of gastric acid secretion. Local mucosal necrosis and hemorrhage, an early manifestation of this process, is seen with some frequency. Such defects in the mucosa are often multiple, typically small and round, and can be associated with significant hemorrhage from the exposed blood vessels deep to the lesion. They heal rapidly and rarely lead to serious complications.

The intestinal tract is especially susceptible to ischemic and hypoxic injury, and lesions related to poor perfusion are often found at the time of autopsy. Decreased blood flow in the splanchnic circulation is a well-established physiologic consequence of endotoxemia. Thus sepsis is associated with an increased risk of intestinal injury. Hypoxic or ischemic injury of the intestinal epithelium, which may be very limited, can lead to translocation of intestinal flora into the mesenteric lymphatic circulation and into the portal venous circulation. Additional factors favoring the escape of bacteria from the intestine include alterations in the bacterial ecology of the gut. Hypotension and hypoxia can also be causes of sepsis. In our autopsy experience the formation of abscesses or foci of tissue infection in the intestinal tract was uncommon, except when many organs, including the skin, were heavily infected in patients with generalized sepsis. The intestinal lesion most commonly seen at autopsy is transverse streaks of hemorrhage in the small intestine in a ‘ladder’ pattern, associated with focal necrosis of folds of mucosa. This is called superficial hemorrhagic necrosis (Fig. 44.13). Perhaps surprisingly, perforation of the intestinal tract is an uncommon occurrence in patients with burn injury. Occasional patients develop pseudomembranous colitis or ‘typhlitis,’ typically a consequence
of infection by toxin-producing Clostridium difficile (Fig. 44.14). This complication can be minimized by judicious use of antibiotics and screening for the toxin in stool when pseudomembranous colitis is suspected.

The liver is enlarged in most autopsies of children who succumb to burn injury, often to double or triple its normal weight. Occasionally such hepatomegaly is thought to compromise ventilation. Steatosis is often found at autopsy (Fig. 44.15). The degree of steatosis is often mild, however, even in the presence of massive hepatomegaly. Interestingly, analysis of the lipid content of liver obtained at autopsy documented the presence of excess lipid but showed that its quantity was far too small to account for the increase in weight of the liver. Congestion of the liver is also frequently seen at autopsy, often with centrilobular necrosis, which may be a consequence of reduced splanchnic blood flow in patients with sepsis. Intracellular cholestasis is commonly observed in patients with burn injury. The basis for this abnormality is not clear, although multiple physiologic derangements could be expected to lead to cholestasis.

Acute pancreatitis is found at autopsy in a sizable minority of cases of fatal burns. Often necrosis and hemorrhage appear out of proportion to the extent of acute inflammation. The pancreas is particularly vulnerable to the reduced splanchnic blood flow that accompanies sepsis (Fig. 44.16). Increased clinical suspicion of pancreatitis has led to assessment of circulating amylase and lipase. On this basis, clinical pancreatitis is not rare in our patient population, but is often transient.
Musculoskeletal system

Lesions of skeletal muscle are uncommon in burn patients, but are ominous when they occur. Occasionally, direct thermal injury extends into deep muscle, and at times this injury can be so severe that adequate debridement is not practical. Electrical injury is not uncommonly associated with extensive necrosis of muscle. When invasive bacterial or fungal infection extends into muscle, again, it may not be feasible to treat adequately by excision of the infected tissue, and the infection may be resistant to antibiotic therapy and likely to disseminate. Atrophy of skeletal muscle occurs as part of the catabolic state of burn patients, and represents a challenge for those involved in rehabilitative efforts.

Lymphoid system

Depletion of lymphocytes from lymphoid tissues throughout the body is a consistent feature seen at autopsy in patients with burn injury. The abnormalities were well described by Linares in 1978. The thymus is consistently very small, even in young children. The lymph nodes often lack germinal centers, and may be strikingly depleted of lymphocytes. Sinus histiocytosis is often present, and pyroninophilic cells resembling plasma cells are often prominent in the portions of the node normally occupied by B cells. The splenic white pulp is deficient, sometimes strikingly so. The gastrointestinal lymphoid tissue of the terminal ileum is generally atrophic, in spite of its normal prominence in children, and the appendix often shows a striking lack of normal lymphoid tissue in its wall (Fig. 44.17). These abnormalities of lymphoid tissue correlate with the deficient immune response typical of patients with extensive burn injury. To some extent they may represent the effects of high levels of endogenous glucocorticoids in burn patients.

Endocrine system

Although abnormalities of the endocrine organs are sometimes observed in autopsies of burn patients, their incidence does not seem to differ greatly from that in the general population. Excessive secretion of glucocorticoids and of epinephrine by the adrenal gland is characteristic of the prolonged hypermetabolic response to burns. Morphologic evidence of lipid depletion of the adrenal cortex has not been seen in our experience. In one interesting case, reactivation of neonatal infection with herpes simplex virus type II occurred in a young child with a large burn, leading to extensive skin injury and graft loss. Focal necrotic lesions were found in the adrenal cortex that were labeled by an immunostain for herpes simplex, indicating that dissemination of the infection had occurred (Figure 44.18).

Central nervous system

When the brain and spinal cord are examined carefully at autopsy, abnormalities can be found in the great majority of patients who die after burn injury. The commonest lesion is degeneration or loss of neurons in the portions of the cortex most susceptible to hypoxic and ischemic injury. These lesions can be a result of hypovolemia during resuscitation, shock developing as part of the syndrome of sepsis, or as a consequence of respiratory failure. Of course, extensive hypoxic brain injury may occur in patients who are asphyxiated during the initial burn injury. Some patients, especially those who require cardiopulmonary resuscitation at the scene of injury, develop massive cerebral edema and brain death several days after the initial injury, reflecting the response to extensive hypoxic/ischemic injury in the brain. Severe hypoxic brain injury also can occur in burn patients who are deprived of oxygen during the progress of a house fire, or who are poisoned by carbon monoxide at the scene of the burn. Occasionally prolonged delay in fluid resuscitation of a patient with a large burn is associated with hypoxic/ischemic brain injury and brain death. Another special case
is the patient who has direct thermal injury to the brain. Such lesions, which occur occasionally in young children, can be detected by radiologic imaging studies, and are represented at autopsy by small foci of tissue necrosis on the cortical surface, surrounded by a hyperemic reaction.

The burn autopsy

As long as patients continue to develop complications of burn injury which are difficult to manage, and as long as the pathogenesis of these complications remains uncertain, careful postmortem examination of patients who do not survive will continue to contribute to patient care. There is a paradox here. Tissue injury occurs due to elevated temperature, a very simple physical alteration. However, there is no disease with more complex clinical and physiopathologic derangements than an extensive burn. Observations made at the time of autopsy often clarify the nature of the problems that have led to the patient’s demise. Sometimes the findings lead to suggestions for changes in procedure that may lead to improved patient safety. Very often a review of recent deaths effectively reminds the staff of the importance of measures to prevent wound infection. Often a causal sequence of events can be reconstructed by including the clinical evidence, including cultures with sensitivity testing and metabolic profiling, and the autopsy findings. Infectious processes, for example, often can be traced from their sites of origin, in the skin or elsewhere, to the fatal conclusion. The emergence of unusually resistant bacterial strains can be traced. The autopsy should always be approached from the point of view of using both clinical and autopsy evidence to better understand the reactions of the patient to the burn injury and to the treatments provided. In other words, the burn autopsy can provide not only an appropriate morphologic analysis, but also a dynamic interpretation of the pathogenesis of the disease processes of importance in an individual patient. When approached in this way, investigation of patient deaths becomes a valuable learning experience for all those who participate in it. Not infrequently, unexpected lesions are found which were likely to have been significant in the patient’s course. Of course, the circumstances of burn injury may have legal implications, and documentation of the patient’s injuries and careful interpretation of the hospital course can have the beneficial effect of providing factual evidence where only supposition would be available otherwise. Several recent publications have confirmed the continuing usefulness of autopsy, especially in the setting of burn trauma. We advocate a policy of carrying out complete autopsies on all patients who die after burn injury, whenever possible, including microscopic study and consultation with specialists, in collaboration with the local medical examiner or coroner.

Further reading


Access the complete reference list online at http://www.expertconsult.com
References


This recent paper thoroughly surveys the findings in autopsies of children who died after burns, and highlights some unexpected observations.


Introduction

Clinically, post-burn hypertrophic scars (HTS) are elevated, erythematous, pruritic, and inelastic. In addition to poor cosmesis, these scars typically form contractures resulting in dysfunction and discomfort, leading to significant morbidity for burn patients (Fig. 45.1). Hypertrophic scar is fundamentally different from normal skin and mature scar in several key ways: 1) the extracellular matrix (ECM) of HTS is significantly altered in both composition and architecture, 2) the behavior of keratinocytes and fibroblasts present in hypertrophic scar is profibrotic compared to mature scar, and 3) many profibrotic cytokines are upregulated and their expression prolonged. Generally, HTS undergoes some remodeling and maturation over time and this may account for the variability in descriptions of HTS. Many features of HTS are shared by other fibroproliferative disorders, including renal fibrosis, pulmonary fibrosis, and scleroderma. Thus, understanding the pathophysiology of HTS applies to other areas of medicine, and developments in treating various fibroproliferative diseases can directly affect scar management. Since an exhaustive discussion of every nuance of abnormal wound healing is impossible, we focus on aspects of HTS formation highlighting well understood pathways or novel developments. It is our hope that a deeper understanding of abnormal wound healing pathophysiology and fibrosis will lead to nonsurgical treatments that improve life not only for burn patients, but for the many patients suffering fibrotic diseases.

Extracellular matrix

Extracellular matrix in healing wounds is laid down by fibroblasts and subsequently remodeled as the scar matures. The ECM in HTS displays significant differences from mature scar and normal skin, most notably in the arrangement and composition of collagen bundles, and in the relative proportions of several proteoglycans. Owing to the interaction of fibroblasts and ECM these differences not only result from abnormal fibroblast behavior but also contribute to it.

Collagen

Collagen is the major constituent of ECM, providing a scaffold for cells and mechanical strength to tissues. In HTS the quantity of collagen per unit surface area is increased; however, the relative proportion of collagen in HTS is decreased compared to normal skin owing to much greater increases in proteoglycans and glycoproteins. In normal skin the majority of collagen is type I (80%) with smaller amounts of type III (10–15%) and type V (minimal) resulting in thick, regular collagen fibril bundles running parallel to the skin surface. In contrast, HTS is composed of greatly increased amounts of type III (33%) and type V (10%) collagen, which drastically alters collagen fibrils making them thinner and disorganized. In normal wound healing, type III collagen appears early then gradually disappears as the scar is remodeled and matures, but this does not occur in HTS where persistently high levels reflect biological immaturity.

Classic histologic descriptions of HTS highlight ‘whorls’ and ‘nodules’ of poorly organized collagen encapsulated in more normal-appearing collagen fibrils, as seen in Figure 45.6. However, not only are collagen fibril composition and morphology altered in HTS, but interfibrillar spacing is also irregular and greatly increased. This space is filled with proteoglycans and glycoproteins, whose composition is markedly different from normal skin and mature scar.

Proteoglycans and glycoproteins

Proteoglycans are responsible for physical properties of skin such as turgor, resilience, and resistance to compression, resulting from their interaction with collagen. Proteoglycans also modulate the activities of multiple growth factors and cytokines. Glycoproteins, such as fibronectin, are generally involved in cell–matrix adhesion and influence cell behavior via this mechanism. Together, proteoglycans and glycoproteins are major constituents of skin, both physically and functionally.

Proteoglycans are formed by a protein core, often with repeating units such as leucine in decorin, and glycosaminoglycan side chains. These side chains are ionized and hydrophilic, and thus mainly responsible for tissue water retention. Early studies of HTS demonstrated elevated glycosaminoglycan levels, which are responsible for the hyperhydrated state of HTS leading to its classically increased turgor. These levels of glycosaminoglycan are not uniformly elevated. Instead, certain proteoglycans are downregulated and others upregulated, with unique implications for HTS.

Decorin is a prototypical small, leucine-rich proteoglycan (SLRP) produced in abundance in normal skin and mature scar but reduced by 75% in HTS. Originally named for ‘decorating’ collagen fibrils, decorin affects wound healing...
via several distinct and complementary pathways. Decorin binds to collagen fibrils, controlling their diameter, morphology, and interfibrillar distance. In decorin knockout mice collagen fibrils are irregular in morphology and have highly variable diameters. Decorin binds to and inactivates the profibrotic cytokines transforming growth factor-β (TGF-β), and platelet-derived growth factor (PDGF). The effects of this inactivation are most readily visible in fibroblast-populated collagen lattices where decorin significantly reduces contraction by normal and HTS fibroblasts. Decorin also binds to and antagonistically downregulates several cell surface receptor tyrosine kinases: EGFR, HGFR, and IGF1R, which reduces cellular proliferation and migration. Decorin production increases significantly as scars mature. In a mouse model of diabetes, renal fibrosis and nephropathy developed significantly faster in decorin knockout than in wild-type mice. Similarly, upregulating decorin production via an adenoviral vector in mouse models of bleomycin-induced pulmonary fibrosis reduced fibrosis.

In contrast to decorin downregulation, two other proteoglycans, biglycan, and versican, are significantly...
upregulated in HTS. Biglycan is 57% similar to decorin in amino acid sequence but with two dermatan sulfate chains, and is believed to have originated as a gene duplication of decorin.\textsuperscript{29} Despite these similarities, biglycan and decorin have significantly different functions in vivo. Biglycan is minimally present in normal skin but significantly upregulated in fibrosis, yet does not compensate for the lack of decorin.\textsuperscript{23,30} Versican is also significantly upregulated in HTS, up to six times higher than in normal skin,\textsuperscript{7} where it is normally confined to the proliferating epidermis.\textsuperscript{38} As a large proteoglycan with 12–30 glycosaminoglycans chains, versican is most likely responsible for the increased hydration and turgor leading to the increased volume of HTS.\textsuperscript{5}

The most common glycoprotein in ECM is fibronectin, which has effects on cell–matrix interaction via its interaction with integrins. Although the role of fibronectin in HTS is unclear, its upregulation in HTS,\textsuperscript{32} influence on the assembly of other ECM proteins, and interaction with cellular integrins\textsuperscript{33} suggest it too plays a role in fibroblast behavior and HTS formation.

### Cellular contributions to hypertrophic scar

#### Hypertrophic scar fibroblasts

Fibroblasts are the cells primarily responsible for ECM production and remodeling in wound healing. Numerous studies have demonstrated that dermal fibroblasts can be divided into distinct subpopulations: superficial (papillary), and deep (reticular), based on both physical location and phenotype.\textsuperscript{41–46} When characteristics of superficial dermal, deep dermal, and HTS fibroblasts are compared, as in Table 45.1, it becomes clear that HTS fibroblasts most closely resemble deep dermal fibroblasts.\textsuperscript{36} These in vitro results correlate directly with a clinically relevant dermal scratch model developed by Dunkin and colleagues.\textsuperscript{37} In this model a linear skin wound is created with depth that increases up to six times higher than in normal skin,\textsuperscript{3} where it is normally confined to the proliferating epidermis.\textsuperscript{38} As a large proteoglycan with 12–30 glycosaminoglycans chains, versican is most likely responsible for the increased hydration and turgor leading to the increased volume of HTS.\textsuperscript{5}

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### Role of myofibroblasts in normal and pathological situations

Myofibroblasts are cells that have acquired a phenotype intermediate between fibroblasts and smooth muscle cells. Presently, it is accepted that myofibroblast modulation of fibroblastic cells begins with the appearance of precursor proto-myofibroblasts, whose stress fibers contain only β- and γ-cytoplasmic actins. These proto-myofibroblasts acquire de novo contractile bundles whose stress fibers generate sufficient forces to pull cells forward to populate tissue spaces in a migration process and to pre-remodel the ECM. Proto-myofibroblasts evolve, but not necessarily always, into the differentiated myofibroblast.\textsuperscript{40} Fully differentiated myofibroblasts express α-smooth muscle actin (α-SMA), the actin isoform present in typical contractile vascular smooth muscle cells (Fig. 45.3). The presence of α-SMA is directly related to the contractile activity of myofibroblasts. A direct correlation has been demonstrated both in vitro and in vivo between the level of α-SMA expression and myofibroblast contractions.\textsuperscript{41,42} Myofibroblasts also exhibit some similarities with pericytes.\textsuperscript{43} In physiological conditions, after healing, myofibroblasts undergo apoptosis\textsuperscript{44} and only a few fibroblasts are left to ensure renewal of the ECM.

Among the soluble factors, TGF-β1 is a potent inducer of myofibroblast differentiation.\textsuperscript{45,46} TGF-β1 action on
myofibroblast differentiation is only possible in the presence of ED-A fibronectin, which underlines the fact that ECM components play an important role in soluble factor activity. Granulocyte–macrophage colony-stimulating factor stimulates macrophage proliferation and myofibroblast differentiation, thereby promoting granulation tissue formation. Endothelin has also a positive effect on differentiation and activation of myofibroblasts. This peptide also induces myofibroblast contraction and migration. More recently, it has been shown that granulation tissue formation is modified by chemical denervation. This peripheral nervous system involvement in tissue repair has likewise been shown in the liver; in this organ, in an experimental model system involvement in tissue repair has likewise been shown in the liver.

Role of mechanical stress and myofibroblasts

Myofibroblast cells, because of their contractile properties and privileged relationships with ECM, can modify their activity depending on the mechanical environment. It has been shown, in gingival fibroblasts, that α-SMA expression induced by TGF-β1 is regulated by the compliance of collagen gels on or in which they are cultured. The direct effects of mechanical stress on fibroblasts can be easily shown in culture using stressed fibroblast-populated collagen lattices (Fig. 45.4). Moreover, myofibroblast differentiation features, such as stress fibers, ED-A fibronectin or α-SMA expression, appear earlier in granulation tissue subjected to increased mechanical tension by splinting of the full-thickness wound with a plastic frame than in normally healing wounds. It has also been shown that fibroblasts cultured on substrates of variable stiffness present different phenotypes. Cultured fibroblasts do not express stress fibers on soft surfaces, but when the stiffness of the substrate increases a sudden change in cell morphology occurs and stress fibers appear. Shear forces exerted by fluid flow are also able to induce TGF-β1 production and differentiation of fibroblasts cultured in collagen gels in the absence of other external stimuli, such as cytokine treatment. Intercellular mechanical coupling of stress fibers via adherens junctions improves contraction of collagen gels by myofibroblasts. By assessing spontaneous intracellular Ca²⁺ oscillations, Follonier et al. have shown that intracellular Ca²⁺ oscillations are coordinated between contacting myofibroblasts via adherens junctions, but randomly between fibroblasts and non-contacting cells. They propose the following model of mechanical coupling for myofibroblasts: individual cell contraction is transmitted via adherens junctions and leads to opening of mechanosensitive ion channels in adjacent cells. The resulting Ca²⁺ influx induces a contraction that can feed back on the first cell and/or stimulate other contacting cells working like a syncytium. This mechanism could improve the remodeling of cell-dense tissue by coordinating the activity of myofibroblasts.

Pathological repair (hypertrophic scars and keloids)

Pathological wound healing can result from impaired remodeling of the granulation tissue, leading to abnormal cutaneous repair in hypertrophic or keloid scars (Fig. 45.5). Keloid and HTS differ in their expression of α-SMA; indeed, in keloids, no α-SMA is observed, although proteomyofibroblasts could account for large amounts of extracellular matrix but are unable to contract, whereas numerous myofibroblasts express this protein in HTS, explaining the fact that contracture often appears specifically in HTS. The use of α-SMA to differentiate HTS and keloids has been proposed. The presence of contractile myofibroblasts in HTS is responsible for the formation of contractures that interfere with function and may require extensive reconstructive surgery (Fig. 45.6). Moreover, keloids contain thick collagen fibres, whereas HTS contain thin fibres organized in nodules. It emphasizes that the different processes involved in collagen maturation together with the effects of the matrix metalloproteinase (MMP)/tissue inhibitor of MMP(TIMP) system play an important role in excessive scar formation. The expression of lysyl hydroxylase (LH)-2b, a splice variant of LH-2, an enzyme involved in the cross-linking of the collagen fibrils, has been linked to fibrotic development occurring in pathologic situations.
Figure 45.4 Myofibroblast evolution in collagen gels. When myofibroblasts previously cultured in plastic dishes are incorporated in a floating collagen gel, a high proportion rapidly undergo apoptosis (arrows). In contrast, when incorporated in an attached collagen gel, they show a typical elongated morphology, express high amounts of α-smooth muscle actin, and proliferate. (From Coulomb B, Inserm U970, Université Paris Descartes, France and Desmoulière A who retains copyright of the Images (unpublished data)).
models mimicking this specific expression of LH-2b are available and could be used to test new anti-scarring therapies based on the inhibition of LH-2b. In these lesions, the normal healing process cannot be achieved and granulation tissue continues to grow, owing to an abnormal and excessive secretion of growth factors and/or lack of molecules inducing apoptosis or ECM remodeling. Interestingly, HTS have an excess of microvessels, most of which are partially or totally occluded due to a functional regression of endothelial cells induced by (myo)fibroblast hyperactivity. In excessive scarring a focal upregulation of p53 expression, which probably inhibits apoptosis, has been observed. Extracellular matrix modifications also seem to be an important factor in induction of the apoptotic process. In vivo, covering granulation tissue by a vascularized skin flap induces an upregulation of MMP together with a decrease in TIMP, leading to a rapid loss of granulation tissue cells by apoptosis. In vitro, the matrix environment can modulate fibroblast apoptosis. Furthermore, in HTS, the mechanical forces obtained by compression of the scar are able to restore the classic organization observed in normal wounds and trigger the disappearance of myofibroblasts by apoptosis. Thus, mechanical stress can maintain myofibroblast differentiation. It has been shown that mechanical loading early in the proliferative phase of wound healing produces HTS by inhibiting cellular apoptosis. In contrast, it is suggested that mechanical challenge could be a clinically relevant strategy to improve ischemic and chronic wound healing by supporting myofibroblast formation. Interestingly, oncogenic-Ras-transformed human fibroblasts lose growth factor selectivity and cell matrix density-dependent inhibition of migration. In the liver, and certain other organs, stiffness appears to result from matrix cross-linking and possibly other unknown variables in addition to matrix quantity, suggesting that increased stiffness may play an important role in initiating the early stages of fibrosis. The epithelium could also be involved in the development of excessive scarring. Hakvoort et al. have shown that, in HTS, keratinocytes expressed an activated CD36+ phenotype. They suggest that HTS formation is not only due to dermal dysfunction, but is the result of a perturbation affecting dermal–epidermal interactions involving neurohormonal factors. Indeed, a ‘neurogenic inflammation hypothesis’ has been suggested. Mechanical stress stimulates mechanosensitive nociceptors in skin sensory fibers, which release neuropeptides involved in vessel modifications and fibroblast activation.

**Origin of (myo)fibroblasts**

It is now accepted that myofibroblasts can originate from various cell types, as illustrated in Figure 45.7. The majority of these cells originate from local recruitment of connective tissue fibroblasts. For example, in skin, dermal fibroblasts located in the edges of the wound can acquire a myofibroblast phenotype and participate in tissue repair. In diffuse cutaneous systemic sclerosis, microvascular pericytes constitute a cellular link between microvascular damage and fibrosis by transdifferentiating into myofibroblasts. In the liver, the role of hepatic perisinusoidal hepatic stellate cells has been widely studied and their key role during fibrogenesis has been clearly demonstrated. It has also been shown that portal fibroblasts are involved in the formation of portal septa. Vascular smooth muscle cells residing in the walls of portal vein branches and portal arteries have been implicated in fibrosis observed in chronic schistosomiasis. In the kidney, both mesangial cells and interstitial fibroblasts of the medulla can acquire a myofibroblast phenotype and participate in ECM deposition after damage. Moreover, the involvement in tissue repair of local mesenchymal stem cells is becoming better understood. These progenitor cells have been described in the dermal sheath that surrounds the outside of the hair follicle facing the epithelial stem cells, constituting a niche of stem cells. They are involved in the regeneration of the dermal papilla and can also become wound healing (myo)fibroblasts after an injury. This concept of a cell association, able to reconstitute the different organ cell populations and constituting a niche of stem cells, is currently discussed in diverse organs, notably the liver, in the perportal zone containing Hering’s canals. Recent data have shown the implication of circulating cells, called fibrocytes, in the tissue repair process. Another type of circulating cell originating from bone marrow participates in tissue repair. These mesenchymal stem cells are bone marrow-derived non-hematopoietic...
Molecular and cellular basis of hypertrophic scarring

Phenotype can be modulated by their interactions with neighboring cells and ECM. 95,96

Fibrocytes are a bloodborne, CD14+ monocyte subpopulation87 that mediate wound healing, first identified in 1994 by Bucala et al. in mouse wound chambers.97 Although originally defined as collagen+/vimentin+/CD34+ cells, other accepted markers include combinations of collagen+ and CD45+ or LSP1+ markers.88,98 Fibrocytes have been found in normal wound healing97 and also a wide variety of fibrotic diseases, including pulmonary fibrosis,99 renal fibrosis,100 and hypertrophic burn scars.88 Fibrocytes traffic to wounds via a secondary lymphoid chemokine gradient, and differentiate under the influence of T cells and TGF-β.87 It has been noted that CD4+ T cells producing TGF-β are present in high levels in burn wounds,101 where fibrocyte levels in burn patients are also increased.102 In contrast, Pilling et al. demonstrated that fibrocyte differentiation is blocked by serum amyloid P (SAP), a constitutive plasma protein related to C-reactive protein, by using SAP to inhibit fibrocytes in a

Figure 45.6 Myofibroblasts in hypertrophic scars. In hypertrophic scar nodules myofibroblasts express large amounts of α-smooth muscle actin (a and b, immunohistochemistry for α-smooth muscle actin), and develop huge contractile activity in scars after burn injury (c, d) (From Desmoulière A, who retains copyright of the images.) (c, d) (From Casso P, Plastic Surgery and Burns Unit, University Hospital of Bordeaux, France, who retains copyright of the images.)
mouse bleomycin-induced pulmonary fibrosis model. It appears that fibrocytes contribute to ECM formation and fibrosis through two mechanisms. Exposure to profibrotic cytokines causes fibrocytes to secrete collagen and differentiate into myofibroblasts via Smad2/3 and SAPK/JNK MAPK pathway activation. Fibrocytes also modulate the activity of local fibroblasts in burn wounds via secretion of TGF-β and connective tissue growth factor (CTGF). and may serve as a crucial link between healing wounds and the immune system. Like leukocytes, fibrocytes can act as antigen-presenting cells to prime naïve T cells, and also express Toll-like receptors allowing them to function as part of the innate immune system. Fibrocytes also induce revasculation of wounds through MMP-9 secretion, which degrades ECM and promotes endothelial invasion and the production of vascular endothelial growth factor. Our understanding of fibrocytes as profibrotic mediators of wound healing continues to evolve, with several recent descriptions of alternate fibrocyte subpopulations and the ability to reprogram fibrocytes into an antiﬁbrotic phenotype. Although this appears to complicate the fibrocyte picture, it does highlight the importance of systemic responses to wound healing, and suggests that the initial cytokine signals that bone marrow-derived cells receive as they leave the circulation can have a significant impact on their role in HTS formation.

### Hypertrophic scar keratinocytes

Keratinocytes are an important component of wound healing. Classically, the remodeling phase of wound healing begins once re-epithelialization of the wound is complete, and wounds taking longer than 2 weeks to re-epithelialize are more likely to form HTS. Keratinocytes regulate fibroblast activity and vice versa, suggesting that they play key roles in normal wound healing and HTS formation. Experiments with keratinocyte-conditioned media in skin-equivalent models show that keratinocytes downregulate fibroblast production of the profibrotic cytokines TGF-β and CTGF. Normally, keratinocytes increase fibroblast proliferation but simultaneously reduce collagen production and increase collagen breakdown by upregulating MMP-1 via factors such as TGF-β. In contrast, keratinocytes from HTS promote increased fibrosis in normal dermal fibroblasts, display an activated phenotype similar to early wound healing keratinocytes, and have higher proliferation rates in the basal layer many months after re-epithelialization is complete. This may be due, in part, to elevated PDGF production by HTS keratinocytes. This suggests that normal keratinocytes promote normal wound healing, and abnormal keratinocytes promote HTS formation. It is also possible that HTS fibroblasts alter the normal wound healing keratinocyte phenotype to a HTS phenotype, and these HTS keratinocytes in turn reinforce the HTS fibroblast phenotype. Thus, therapies for HTS must address not only wound fibroblasts but also wound keratinocytes.

### The role of cytokines in hypertrophic scar

Cytokines serve as signals for communication between cells, in paracrine signaling, and for cells to signal themselves in autocrine signaling. While the number of cytokines, and hence the diversity of signals, is immense there are several key cytokines whose prototypic role in fibrosis and HTS has been extensively studied, and whose actions account for a wide variety of fibroses. The roles of these cytokines are illustrated in Figure 45.8.

### TGF-β

Transforming growth factor beta (TGF-β) is one of the most studied profibrotic cytokines and belongs to a large superfamily of related proteins regulating processes as diverse as embryonic development, chemotaxis, cell cycle, homeostasis, and wound healing. When produced by cells, TGF-β is secreted in an inactive form bound to latent TGF-β-binding protein. This bond is subsequently cleaved by enzymes in the milieu of healing wounds, including several matrix metalloproteinases (MMP-2, MMP-9) and plasmin (present in blood). Mammals produce three known isoforms: TGF-β1, TGF-β2, and TGF-β3. These are produced by many cells involved in wound healing, including degranulating platelets, macrophages, T lymphocytes, endothelial cells, fibroblasts, and keratinocytes. The actions of TGF-β1 and β2 are mediated by the intracellular Smad pathway and have directly profibrotic actions on mesenchymal cells. TGF-β is upregulated locally in wounds and systemically in the blood of burn patients with HTS. HTS fibroblasts produce...
greater amounts of TGF-β than normal fibroblasts and regenerative fetal fibroblasts. In fact, normally regenerative fetal fibroblasts can be induced to form scar following TGF-β exposure. TGF-β has direct effects on the ECM by upregulating collagen production and downregulating decorin production by fibroblasts. This decrease in dermal decorin is profibrotic, as decorin binds to TGF-β in the ECM, blocking its activity. TGF-β promotes not only the transformation of fibroblasts into myofibroblasts but also the transdifferentiation of epithelial cells into mesenchymal cells and reduces apoptosis in the healing wound. In this context, TGF-β is a highly profibrotic cytokine playing a unique role in HTS initiation. Interestingly, it has been suggested that the isoform TGF-β3 acts as an anti-fibrotic cytokine. Clinical trials of TGF-β3 have shown promise in improving wound healing, and it is noteworthy that TGF-β3, which is upregulated in the remodeling phase of wound healing, reduces ECM deposition. Many effects of other cytokines in wound healing can be directly related to activation by or interaction with TGF-β.

CTGF/CCN2

Connective tissue growth factor (CTGF or CCN2) is a prototypic member of the CCN family of cytokines. The CCN family motif consists of four linked regions: an IGF-binding domain, a von Willebrand type C domain, a thrombospondin-1 domain, and a cysteine knot heparin-binding domain. This configuration and multiple studies suggest that CTGF does not act simply as a growth factor, but rather as an important cofactor for TGF-β, and as an interface between cells and the ECM by binding to cellular integrins and matrix proteoglycans. Independent stimulation by TGF-β or CTGF alone induces only transient fibrotic upregulation in fibroblasts, whereas co-stimulation by both cytokines leads to prolonged fibrosis, and in chronic fibrosis CTGF remains elevated after TGF-β returns to basal levels. Thus, one can surmise that TGF-β serves to initiate fibrosis and CTGF serves to continue the process as a downstream mediator of TGF-β. In keeping with this hypothesis, CTGF is upregulated in HTS, scleroderma, and other fibrotic diseases. TGF-β induces CTGF through the Ras/MEK/ERK pathway, and blocking this activation with iloprost (a synthetic prostacyclin PGI2 analog) reduces fibrosis. Other methods of targeting CTGF, such as anti-CTGF antibodies and CTGF siRNA, have also proved effective in reducing fibrosis.

PDGF

Platelet-derived growth factor (PDGF) is delivered to wounds by platelets from injured capillary vessels, and is also produced by local fibroblasts. There are four isoforms of PDGF: A, B, C, and D, which form dimers to activate two structurally related tyrosine kinase receptors, leading to fibroblast proliferation and actin filament reorganization that induces a transformation into myofibroblasts. PDGF also increases ECM production and inhibits myofibroblast apoptosis. PDGF activity contributes to pulmonary fibrosis, hepatic fibrosis, renal fibrosis, and scleroderma. PDGF has been shown to upregulate TGF-β receptors in scleroderma fibroblasts, and its multiple effects are magnified in HTS and keloid fibroblasts. Recent research into the causes of nephrogenic systemic fibrosis, a disorder of dermal fibrosis occurring after gadolinium contrast administration in patients with impaired renal function, shows that blocking PDGF receptors using antibodies inhibits the proliferative effects of gadolinium on fibroblasts. Other researchers have shown that blocking PDGF action using tyrosine kinase inhibitors reduces fibrosis in murine models of radiation-induced pulmonary fibrosis and scleroderma. Thus, although PDGF is an independently profibrotic cytokine, it also serves to reinforce and magnify the effects of TGF-β, and blocking its activity can reduce fibrosis.

IGF-1

Insulin-like growth factor 1 (IGF-1) was originally described in chondrocytes, where it regulates glycosaminoglycan production. IGF-1 is a mitogen for fibroblasts and endothelial cells, and induces collagen production in pulmonary and dermal fibroblasts. IGF-1 upregulates TGF-β gene transcription in fibroblasts, accounting for observed similarities in their profibrotic actions. It has been shown that IGF-1 also downregulates collagenase mRNA levels and activity in dermal fibroblasts. This increase in collagen production and decrease in breakdown shift the balance of ECM remodeling towards fibrosis. IGF-1 is upregulated in a number of fibrotic conditions, including post-burn HTS, scleroderma, pulmonary fibrosis, and hepatic fibrosis. Interestingly, in unwounded skin IGF-1 is produced exclusively in epidermal sweat and sebaceous glands, and is thus sequestered from dermal fibroblasts. One may hypothesize that when these structures are disrupted, as in burns and other wounds, dermal fibroblasts are then directly

Figure 45.8 Balance of pro- and anti-fibrotic cytokines in wound healing. The fibrogenic and antifibrogenic factors that modulate fibroblast function during wound healing. (From Tredget EE, Nedelec B, Scott PG, Ghahary A, Hypertrophic scars, keloids and molecular basis for therapy. Surgical Clinics of North America 1997, 77: 701-30).
exposed to IGF-1. Prolonged inflammation and delayed re-epithelialization would increase the duration of fibroblast stimulation with IGF-1 and could help explain the formation of HTS. Although IGF-1 is certainly not the only cause of HTS, its relationship to TGF-β and its unique distribution in skin suggest a key role in the pathogenesis of abnormal scarring.

Interferons

HTS is not simply the result of overexpression of profibrotic signals, but results from a disturbance in the delicate balance between pro- and antifibrotic cytokines. The interferons (IFN) are cytokines classically produced by immune cells to activate the host defense system. IFNs can be divided into type I (IFN-α and IFN-β produced by leukocytes and fibroblasts, respectively) and type II (IFN-γ produced by activated T lymphocytes). Of these, the two antifibrotic cytokines whose roles in wound healing and HTS have been best studied are IFN-α and IFN-γ. Treatment of fibroblasts with these IFNs inhibits cell proliferation and also downregulates collagen, fibronectin, and TGF-β production. IFN-α also upregulates collagenase production and reduces TIMP-1, making it a good candidate to promote scar remodeling. IFN-α, reduces in vitro collagen lattice contraction rates and in vivo wound contraction in guinea pigs. IFN-α also reduces myofibroblast populations and increases the numbers of apoptotic fibroblasts in later stages of wound healing, a finding also demonstrated in several other cell types. A prospective clinical trial of IFN-α in post-burn HTS patients demonstrated reductions in scar volume, normalized TGF-β levels, and reduced scar angiogenesis. It is suggested that abnormal scar results, at least in part, from reduced levels of endogenous IFN in burn patients. An examination of the peripheral blood mononuclear cells (PBMC) of patients forming keloids after trauma compared to those with normal scarring showed decreased production of IFN-α and IFN-γ, which is consistent with this hypothesis. Therefore, an understanding of IFNs highlights the important balance between pro- and antifibrotic cytokines, and suggests possible therapeutic treatments for HTS.

The immune system regulates wound healing

Mast cells, neutrophils, and macrophages have long been recognized as playing an important role in the inflammatory phase of wound healing. Macrophages produce classic immune cytokines interleukin-1 (IL-1), IL-6, and tumor necrosis factor-α (TNF-α) which stimulate keratinocytes and fibroblasts, and classic profibrotic cytokines TGF-β, PDGF, and IGF-1. Recently, the importance of the immune response type rather than degree of inflammation in determining the risk of HTS formation has been recognized. HTS are highly infiltrated by lymphocytes, of which activated CD4+ T-helper (Th) cells are an important subgroup. These Th cells can be generally classified as one of at least four groups: Th1, Th2, Th17, and T-regulatory cells, based on cytokine production patterns. Of these, the Th1-Th2 axis in wound healing and burn patients is the most studied. Th1 cells produce IFN-γ, IL-2, and TNF-β and are involved in cell-mediated immunity, whereas Th2 cells produce IL-4, IL-5, and IL-10 and are involved in antibody-mediated immunity. Interestingly, these cytokine profiles are involved not only in specific immune responses, but are also anti- or profibrotic. The Th2 cytokine IL-10 stimulates activated naïve Th cells to secrete TGF-β, and this is more pronounced in IFN-γ (Th1) knockout mice and reduced in IL-4 (Th2) knockout mice. In a burn mouse model Th2 cytokines (IL-5) were upregulated and Th1 cytokines (IFN-γ and IL-2) were coordinately downregulated. A similar Th2 type response is seen in human burn patients using stimulated PBMC from those with burns ≥25% total body surface area (TBSA), a finding confirmed by another study in burn and major trauma patients. The severity of fibrosis in animal models has also been linked to the type of Th-cell response. In a model of liver fibrosis BALB/c mice developed a Th2 response to chemically induced liver injury and displayed more severe fibrosis than C57BL/6 mice, which developed a Th1 response. This effect was abrogated by administration of IL-4 antibodies or IFN-γ, which induced a Th1 response in the BALB/c mice. A longitudinal study of recovering burn patients demonstrated a predominant Th2 response to burn injury, as demonstrated by increased IL-4 and IL-10 levels from PBMC and in scar tissue (Fig. 45.9). Interestingly, this response was significantly higher in burn patients who went on to develop HTS than in those who developed normal scars, whereas those patients developing normal scar had higher levels of IFN-γ-producing PBMC. Recently, it was found that IFN-α blocks Th2 development, and inhibits cytokine secretion by committed Th2 cells. This suggests that IFN-α has effects not only on fibroblasts, as discussed previously, but also the Th2 cells that modulate them.

Summary

HTS is a fibrotic disorder resulting from derangement of the normal wound healing process and shares many common features with other fibrotic diseases. As discussed, HTS is markedly different from normal skin and mature scar in terms of the structure and composition of ECM, active cellular phenotypes, and cytokine messages displayed. This results in a mass of disorganized connective tissue with thin, irregular collagen bundles in whorls and nodules instead of thick, organized fibers parallel to the surface. The concomitant decrease in decorin and increase in other proteoglycans not only contributes to this disorganized ECM but also allows profibrotic signals to propagate in the dermis. The fibrotic, hypercellular nature of HTS both contributes to and results from elevated profibrotic (e.g. TGF-β, CTGF) and decreased antifibrotic (IFN-γ) cytokine levels. The resulting local HTS fibroblast is modulated by systemic fibrocytes and Th cells, which migrate to the wound. The resulting pathogenesis of HTS is complex, with many aspects that serve to reinforce the fibrotic process. Although this complexity makes elucidating the mechanisms of HTS formation difficult, it also provides multiple targets for medical therapy. It is our hope that this will provide therapies to improve the quality of life for both burn patients and others with fibroproliferative conditions.
Molecular and cellular basis of hypertrophic scarring


Further reading


Access the complete reference list online at [http://www.expertconsult.com](http://www.expertconsult.com)


34. Sorrell JM, Baber MA, Caplan AI. Human dermal fibroblast subpopulations; differential interactions with vascular endothelial cells in coculture: nonsoluble factors in the extracellular matrix influence interactions. Wound Repair Regen. 2008;16(2):300-309.


79. Reeves HL, Friedman SL. Activation of hepatic stellate cells—a key issue in liver fibrosis. *Front Biosci*. Apr 1 2002;7:d808-d826.


2129-2140.

gamma.

growth factor-beta and peroxisome proliferator-activated receptor

Hong KM, Belperio JA, Keane MP, et al. Differentiation of

induced pulmonary fibrosis by serum amyloid P.

Pilling D, Roife D, Wang M, et al. Reduction of bleomycin-

mononuclear cells.

fibrocytes in adherent cells cultured from peripheral blood

from burn patients: identification and quantification of


fibrocytes.

system contributes to renal fibrosis through regulation of

Sakai N, Wada T, Matsushima K, et al. The renin-angiotensin

Andersson-Sjoland A, de Alba CG, Nihlberg K, et al. Fibrocytes

distinguish monocyte-derived fibrocytes from monocytes,

repair.


associated pathologies.

Okada H, Kalluri R. Cellular and molecular pathways that lead to


Prockop DJ. Marrow stromal cells as stem cells for


Pittenger MF, Mackay AM, Beck SC, et al. Multilineage potential of


Barisic-Dujmovic T, Boban I, Clark SH. Fibroblasts/


Liu Y. New insights into epithelial-mesenchymal transition in


Pilling D, Roife D, Wang M, et al. Reduction of bleomycin-

induced pulmonary fibrosis by serum amyloid P. J Immunol.

2007;179(6):4035-4044.


Introduction

This chapter reviews current knowledge of the process of wound healing in humans and animals, with special emphasis on abnormal long-term responses to thermal injury.

Prehistoric and historic perspectives

Wounds due to combat, hunting injuries, accidents and thermal injuries have been the leading causes of death in humans for millennia. On the other hand, prolonged survival of large full-thickness wounds is a recent phenomenon. Several complex biological responses to injury to the skin have evolved over time, but there has been no evolutionary pressure to evolve appropriate responses to very large wounds. There are records of human attempts to improve wound healing in the most ancient texts from Mesopotamia and Egypt. Guido Majno has explored what can be learned from archeology and paleontology regarding wounds and their treatment in ancient times. He also provides a very accurate brief description of the process of wound healing in lay terms. In the development of modern medicine, the advances in wound treatment advocated by Ambroise Pare (1520–1590) stand out, together with the campaign for antisepsis of Joseph Lister (1827–1912), and the development of antibiotics as well as the development of the modern methods of treatment described in this book.

Incisional wounds with primary closure

The essential components of wound healing are easily understood. They are: (1) activation in the wound of tissue repair by phenotypic fibroblasts and small blood vessels, and an inflammatory response initiated by vascular leakage and (2) entry into the wound of circulating polymorphonuclear neutrophils, lymphocytes and macrophages. When a sharp incision is closed while still sterile, only minimal vascular leakage and inflammation occur, and the predominant reaction to injury occurs in the fibroblasts present in the dermis and subcutaneous tissue. These resting connective tissue cells are rapidly activated to secrete collagen, which quickly bridges the small remaining gap to restore the resistance of the skin to tearing. Vascular continuity is restored by budding and remodeling of blood vessels, and the basal keratinocytes of the epidermis divide briefly to restore the complete structure of the epidermal barrier. All that remains to indicate the site of injury is a linear ribbon of dense collagen with little flexibility that marks the site of the incision, as well as some small scars that mark the sites where sutures were inserted. This process of incisional wound healing was well described in humans by Russell Ross and his colleagues in Seattle.

Delayed wound closure ‘by second intention’ and wound contraction

If the epidermis and dermis are incised or removed and the edges of the wound remain separated, much more prominent inflammatory and reparative events occur. Extensive leakage of blood plasma by damaged small blood vessels maintains an outward flow that serves to keep the wound clean, but causes deposition of coagulated fibrin and other desiccated proteins on the wound surface. Conversion of fibrinogen into fibrin fills the gap in the epidermis and provides a gelatinous matrix capable of sustaining migrating cells. Thrombin stimulates expression of interleukin-6 in connective tissue cells. Degranulation of platelets releases platelet-derived growth factor (PDGF) as well as several other proinflammatory cytokines. Degradation of fibrin releases peptides that stimulate fibroblast proliferation and secretion and division of vascular endothelial cells, and production of cytokines by other cells. The resting fibroblasts of the dermis, together with circulating stem cells, divide rapidly in the wound bed and secrete large quantities of collagen and proteoglycans, particularly those typically present in skin during fetal life, with predominance of type III collagen. Simultaneously, the endothelial cells of small blood vessels proliferate rapidly and form numerous small capillary loops that extend upwards toward the surface. Together, these cells form a mass of granulation tissue that covers the wound. All these activities of fibroblasts and endothelial cells are stimulated by cytokines and other peptides, largely secreted by monocytes and lymphoid cells that infiltrate the wound bed. Certain proteins and peptides that are normally present in blood plasma also stimulate and enable formation of the wound matrix, notably fibronectin and vitronectin. Polymorphonuclear neutrophils also enter the wound bed in large numbers, where they phagocytize and kill bacteria and fungi, which are always present in the outside world and gain entry to the dermis.
and subcutis through the open wound. Next, the fibroblasts develop interconnections among themselves and produce and assemble the contractile machinery of actin and myosin within the cytoplasm of each cell. These interconnected myofibroblasts contract to shrink the size of the open wound, pulling adjacent intact skin to cover the wound bed. This process of wound contraction is more dramatic in experimental wounds of rodents than in human wounds. The effects of wound contracture in applying tension to surrounding tissues, however, are sometimes very clear in humans as well. Simultaneously with these processes, the basal keratinocytes of the cut edges of the epidermis change to a migratory and secretory phenotype, and begin to invade the wound bed between the granulation tissue layer and the scab of dried proteins on the surface. Cell division of keratinocytes occurs near the cut edge of the wound to supply cells for this migration. Once they make contact to seal the center of the wound, the migrating keratinocytes change their phenotype again and restore the normal laminated structure of the epidermis and produce a new basal lamina.

Melanocytes also develop migratory properties during healing of large wounds, since they establish a degree of pigmentation in the healed wound that approximates the pigmentation of the uninjured skin. It should be noted that only the epidermis regenerates to resemble the normal epidermis. Hair follicles, sweat glands and other epidermal appendages do not regenerate. Thus, the part of the wound that was not closed by contracture remains dry, hairless and flat. Furthermore, the restored dermis in a fully healed scar is composed of collagen type I fibers running in straight lines adjacent to one another parallel to the surface, providing good strength (though somewhat less than the native skin) but far less elasticity and flexibility than the connective tissue of the normal dermis.

First degree or superficial injury of skin

Superficial burn wounds are those in which part or all of the epidermis is lost, but the epidermal basal lamina remains intact and the dermis is uninjured. In these areas, only epidermal regeneration is required, hair follicles and sweat glands remain intact, and healing can occur with little or no disfigurement.

Second degree or partial thickness injury

In partial thickness wounds, the entire epidermis and the upper part of the dermis become necrotic. If left intact, the presence of a large quantity of devitalized tissue requires prolonged activity of macrophages to clear the necrotic debris. Granulation tissue forms underneath the necrotic dermal tissue, and epidermal migration occurs under the eschar formed by dead tissue, leading to restoration of the epidermis, and production of dermal connective tissue in the form of a thin scar. The deep portions of the hair follicles remain viable, and the keratinocytes lining the hair follicles become migratory and undergo mitosis behind the migrating cells, eventually covering the surface with new epidermis derived from the hair follicle. In severe cases, loss of hair follicles may lead to insufficient regenerative activity to cover the surface. Recently, hair follicles have been found to contain several populations of multipotent stem cells that can generate cells that can multiply, migrate and regenerate the surface epidermis. The stem cell population that was first identified is slowly cycling, expresses the conventional stem cell surface marker CD34, and resides in the bulge region of the follicle near the attachment of the arrector pili muscle. More recently, additional stem cell populations have been identified that reside in the isthmus region and the hair germ region of the follicle and express distinct markers. Much is being learned about the function of these various groups of stem cells by studying knockout and overexpressing mice. The changes in follicular stem cells during healing of burn wounds, however, remain to be described.

One new aspect of hair follicle biology that is of great interest for burn surgeons is the delineation of the role of the dermal papilla, the tiny cluster of mesenchymal cells within the hair bulb. Fetal development of hair follicles apparently depends upon interaction between epithelial cells of the epidermis and mesenchymal cells. The mesenchymal cells of the dermal papilla, which can be amplified in culture using keratinocyte conditioned medium, can induce formation of hair follicles from interfollicular skin. Experiments have even been described, in which formation of new hair follicles, complete with hair, was induced in hairless nipple skin of the mouse, and in the renal capsule. Since one of the major problems in long-term care of burn patients is alopecia, the possibility that hair follicles could be caused to regenerate where there are none is very appealing.

Third degree or full thickness injury

In full thickness burns, thermal injury extends deep enough to destroy all of the hair follicle that has the capacity to regenerate the epidermis, and some of the upper subcutaneous tissue may also become necrotic. In this case regeneration of the epidermis from hair follicles is not possible, and the wound can develop an epidermal covering only slowly, as the epidermis lateral to the wound spreads out over the entire wound surface. During this time, the necrotic tissue in the wound bed is at risk of infection, and extensive activity of tissue macrophages is required to eventually remove it.

Biology of wound healing

Changes in vascular permeability

In order to review current understanding of the processes important in wound healing, each will be considered separately. Changes in local blood vessels are the earliest component of the response of the wound to injury, and are essential for the succeeding steps. Plasma exudation is due to increased permeability of venules to proteins, largely due to local release of histamine from mast cells and substance P from local sensory nerve endings. In burn injury, there is an added component of plasma leakage that occurs for a few hours throughout the body in response to unknown stimuli. Of course, both plasma and red blood cells enter the wound through broken or necrotic blood vessels. Infection triggers further plasma exudation by constantly stimulating and prolonging the vascular phase of acute inflammation. In
addition, the newly formed capillaries of granulation tissue allow passage of plasma proteins and fluid until they mature. Certain plasma proteins, notably fibronectin and vitronectin, are important in stimulating reparative responses in the wound.

**Granulation tissue and the proliferative phase of wound healing**

Massive proliferation of fibroblasts and vascular endothelial cells is characteristic of the early phase of wound healing. These cells, and the fine fibrils of collagen and the gel provided by multiple mucopolysaccharides and proteoglycans, make up the granulation tissue that is a major feature of all wounds that remain open. The most important of many peptides that stimulate fibroblast growth appear to be TGFβ and basic FGF; while the most important peptide that stimulates growth of endothelial cells appears to be VEGF. In order for wound contraction to occur, it is important for fibroblasts to form networks within the dermis that allow the wound to contract. As Donald Ingber has pointed out, interactions between the extracellular matrix and the cellular cytoskeleton are important in controlling cellular differentiation and function.

**Influx of circulating cells**

Many circulating cells actively migrate into wound beds and play roles in defense against bacteria and fungi, clearance of devitalized tissue components, and stimulation of later phases of healing of the dermis and epidermis. Based on experiments with partially selective ablation of individual cell types, the cells most important in stimulating and maintaining tissue repair appear to be the T lymphocytes and monocytes. Many circulating cells actively migrate into wound beds and play roles in defense against bacteria and fungi, clearance of devitalized tissue components, and stimulation of later phases of healing of the dermis and epidermis. Based on experiments with partially selective ablation of individual cell types, the cells most important in stimulating and maintaining tissue repair appear to be the T lymphocytes and monocytes. Many circulating cells actively migrate into wound beds and play roles in defense against bacteria and fungi, clearance of devitalized tissue components, and stimulation of later phases of healing of the dermis and epidermis. Based on experiments with partially selective ablation of individual cell types, the cells most important in stimulating and maintaining tissue repair appear to be the T lymphocytes and monocytes. Monocytes, which differentiate into tissue macrophages, are responsible for synthesis and release of many of the cytokines important in wound healing, as are connective tissue cells and epithelial cells. In addition, recent research has clearly shown that circulating stem cells enter healing wounds, where they can differentiate to form fibroblasts and other connective tissue cells needed to restore tissue integrity.

**Migration of keratinocytes to cover the wound (epiboly)**

When the epidermis is transected, changes take place rapidly in the basal cells of the epidermis adjacent to the wound. The process of epidermal regeneration has been well studied by Stenn and his colleagues. Altered basal keratinocytes send out thin sheets and undergo ameboid motion over the wound bed, but under the nonviable eschar and/or scab, secreting a provisional matrix as they go. Development of this migratory phenotype is stimulated by the plasma protein vitronectin, and requires the presence of albumin as a cofactor. Cell division occurs to support this migration, not among migratory cells, but among their precursors in the residual epidermis. Similar processes stimulate migration and replacement of epithelial cells from hair follicles in partial thickness wounds. After a sheet of epithelial cells is established over the entire wound surface, they begin to divide and eventually create a multilayered stratified squamous epithelium with a granular layer and keratinization. Epidermal cells secrete substantial quantities of interleukin-1β and other cytokines. The new proliferative epidermal basal cells also secrete a new basal lamina composed of laminin, type IV collagen and bullous pemphigoid antigen, adhere tightly to that basal lamina, and develop attachments of type VII collagen between the basal lamina and the underlying fibers of type I collagen in the scarred dermis. Also, just after the newly formed epithelial layer completely covers the wound, the phenotype of the connective tissue cells in the matrix undergoes a series of changes, and much less fibronectin is found in the wound matrix. As noted above, in second-degree burns, epidermal cells from the hair follicles regenerate the epidermis on the surface.

**Collagen matrix formation and maturation**

Scars gradually increase in their strength, as measured by their resistance to tearing, but never reach the strength of normal dermis. During this process, the delicate fibers of newly secreted collagens I and III are replaced by large collagen I fibers that are oriented parallel to each other and to the skin surface. Maturation of collagen fibers is largely a chemical process of remodeling that involves covalent crosslinking of adjacent polypeptide chains. Collagen fibers normally form and are degraded continuously in normal skin as well as in scars, but the processes that control the rates of formation and degradation and the orientation of the mature fibers are not fully understood.

**Cytokines and growth factors**

Many short polypeptides, mostly cytokines and growth factors, are responsible for the changes in cells that lead to wound healing and the termination of wound healing processes, and the formation and organization of a scar. Among the most important are the transforming growth factor beta family (TGFβ), basic fibroblast growth factor (bFGF or FGF2), platelet-derived growth factor (PDGF), and vascular endothelial growth factor (VEGF). Frequently, the response of a particular cell type to a particular peptide depends not only upon binding of cell surface receptors by the right peptide, but also upon simultaneous signals from other cellular receptors. Thus the network of peptide signaling is complex, and the range of possible cellular responses is large enough to allow generation of complex structures and considerable fine-tuning. There are also many opportunities for reparative processes to go wrong, to proceed in an unbalanced fashion, or to fail to complete an appropriate cycle of activation and regression. This complex area has been well reviewed.

**Biophysics of thermal injury**

Cells of the human skin are susceptible to killing when their temperature is increased, largely because of the sensitivity of the cell surface membrane to disruption outside fairly...
narrow limits of temperature. Of course flame burns, as well as electrical and contact burns, often lead to pyrolysis and disruption and oxidation of some tissues as well. Among the various cell types present in the skin, some are likely to be more sensitive to killing by elevated temperature than others. The degree of temperature elevation at a given site in the skin also depends on the rate of heat transfer within the tissue. The thermal conductivity of the dermis is much greater than that of the subcutis, since fat is a good insulator. Perhaps for this reason, thermal injury often leads to necrosis of the entire dermis with little cell death in the subcutis, as seen in wound biopsies. Hair follicles in some sites typically extend well beyond the dermis into the adipose tissue of the upper subcutis, and eccrine sweat glands are also often present in the subcutaneous fat. Despite the presence of adipose tissue around follicles, in
many cases their capacity to regenerate is entirely destroyed by burns even though there is little or no apparent necrosis in the upper subcutis. In the most severe burns, however, the entire subcutis may become necrotic, and cell death may occur in the underlying fascia and skeletal muscle or even in underlying internal organs.

Factors that alter wound healing

Changes in blood supply and perfusion

Development of methods to study local blood supply by ultrasonic measurement has led to the discovery that there is usually a zone of greatly increased blood flow below a burn wound, which is not surprising as part of a local inflammatory response to tissue injury. Above this zone of hyperemia is a zone of tissue ischemia, in which blood flow is less than normal. Remarkably, during the first 24 h after a burn wound, the zone of ischemia typically becomes significantly deeper, indicating that ischemic injury of dermal tissues actually leads to a depth of tissue necrosis greater than that produced by the immediate thermal injury. Experiments in animals have shown that neutrophils are involved in this progressive ischemic cell death in injured but viable tissue deep to a burn wound. Altered blood flow may lead to vascular thrombosis in a burn wound, also contributing to the risk of ischemic tissue injury. In normal skin, there is a plexus of arteries and veins immediately below the dermis in the upper layer of subcutaneous adipose tissue. This subdermal plexus is at risk of thrombosis in deep partial-thickness burns and in full-thickness burns, and it is vulnerable to damage in the process of tangential wound excision, with further loss of blood supply to the wound.

Compromised wound healing – requirements for optimal wound healing

Long clinical experience has demonstrated clearly that wound healing is greatly slowed and impaired when there is deficiency of essential ingredients for construction of the scar, or of an adequate energy supply. Vitamin C deficiency and protein-calorie malnutrition are characterized by deficient wound healing, and provision of sufficient calories and reversal of the usual protein catabolism are major goals of general burn care. Diabetic vasculopathy is associated with deficient wound healing, demonstrating the importance of an adequate microcirculation. Heart failure similarly compromises wound healing. Radiation, cigarette smoking, and hypoxemia also have been associated with delayed wound healing. Advanced age is associated with increased mortality from large burns, but does not in itself prevent good wound healing.

Biologic responses to wound excision and grafting

The current standard of treatment in our institution is early excision of the burn wound, normally within 24 h of admission, with removal of all necrotic tissue, using either tangential excision to leave most of the subcutaneous fat, or fascial excision which removes the entire subcutis. The wound is initially covered with meshed cadaver skin from the skin bank. Within a few days autografting is done using meshed partial-thickness grafts from unburned regions. Over the face and the hands, unmeshed sheet autografts are often used to obtain the best cosmetic result. The epidermis of the cadaveric homograft slowly degenerates, but the dermal matrix often is incorporated into the healing wound. The interstices of the autograft fill with granulation tissue derived partly from the underlying fibrous or adipose tissue, and partly by migration of fibroblasts from the strands of autograft. The epidermis of the autograft migrates over the granulation tissue matrix, under the fibrin layer, and reconstitutes the epidermis, though without any follicles or other epidermal appendages. The pattern of the meshed grafts is usually visible in the healed wound. The incorporation of dermal connective tissue elements from the donor site may enhance the pliability of the final scar. Occasionally, epidermal inclusion cysts develop within grafted burn wounds, and they may rupture. These cysts could develop from residual hair roots that had lost their connection to the surface, from aberrant migration of epidermal cells during wound resurfacing, or from trapping of epidermis by expanding connective tissue. In addition, tiny bits of hair shaft are sometimes encountered in healing wounds, associated with a giant cell foreign body reaction, perhaps representing hairs left behind after necrosis of the hair follicles that originally produced them.

Wound infection

Bacterial infection frequently complicates wound healing. The risk is increased in burn patients, since large amounts of necrotic cells and tissue are present in the wound, providing a good culture medium for bacteria. When infection occurs, the inflammatory component of wound healing is greatly amplified, and the processes of conversion of granulation tissue to a dense scaffolding of collagen, wound contraction, and regeneration of the epidermis are all delayed. Frequently, the wound suppurates. Some bacteria cause additional tissue necrosis, and some bacteria can invade into normal tissues, leading to hyperemia around the original wound and/or enlargement and deepening of the original wound. In response to the bacterial infection and the enhanced inflammatory reaction, the cytokine milieu of the wound is altered. Grafts placed over wounds with residual infected tissue typically do not take, and when large numbers of bacteria are present deep in the wound bed there is always the hazard that the bacteria may enter the blood stream, incite sepsisemia and invade remote tissues. These processes, which were common in the era before antibiotics and before the practice of early wound excision became common, are now being seen again due to infection with highly antibiotic-resistant strains of bacteria, particularly Pseudomonas and Acinetobacter.

Hypertrophic wound healing

In most patients with large burns treated in our institution, healing of the burn wounds is complicated by development of elevated, thick, firm, reddish scars that itch constantly.
These occur more commonly in wounds that had become infected or took longer than usual to become fully covered. They may cover large areas, but do not usually extend beyond the original burn wound. These abnormal wounds also are associated with more severe wound contraction. In the great majority of affected cases, these hypertrophic scars enlarge for a period of months, and then gradually regress over a period of a few years, eventually becoming flat scars with no further symptoms. There are often abnormalities of skin pigmentation, either depigmentation or hyperpigmentation, in wounds that have developed hypertrophic scars, and these abnormalities evolve over time (Fig. 46.3). The largest hypertrophic scars are surgically excised, often with creation of Z-plasties or sheet grafting to release scar contractions. Generally, new hypertrophic scars do not follow.

Many of the patients at our institution are Mexican nationals with predominantly Native American ethnicity. However, this type of hypertrophic scarring occurs in about 75% of Caucasian patients as well as in black and Hispanic patients.72

Clearly, this experience is quite different from that described in the literature with keloids, which frequently occur spontaneously or in response to puncture wounds or clean incisions that were closed primarily.73–75 They extend beyond the initial site of injury, respond poorly to medical therapy, persist for many years, and usually recur after surgical excision. There is often a positive family history of keloidal scarring, and keloids are 10–15 times more common in dark-skinned people of African ancestry than in northern Europeans and their descendants. Elaborate patterns of raised scars are a symbol of status in many African tribes, leading one to wonder whether this practice may have exerted selective pressure during human evolution.

**Histologic features of hypertrophic scars**

Numerous hypertrophic scars have been examined histologically in our laboratory, those removed both during plastic surgical procedures to treat release wound contractures and in samples taken for research purposes. The abnormal elevated scars consistently show several distinct differences from uncomplicated flat scars. The most striking is the presence of rounded whorls of immature collagen that consist of delicate collagen fibrils, mostly of type III collagen, small blood vessels, and plentiful acid mucopolysaccharide. These nodules are very sharply demarcated from the surrounding scar tissue, which may be composed of similar material or may be composed of mature thick collagen fibers that are oriented parallel to each other and to the wound surface, typical of mature scars. Although they are clearly visible with routine H&E staining, they are most distinctly seen with the Movat stain, which stains mucopolysaccharides blue-green and mature collagen fibers yellow-orange. The nodules of hypertrophic scars vary from 0.5 mm to more than 1 cm in diameter, and appear to be sometimes spherical and sometimes ovoid or cylindrical in shape. The abnormal dermal tissue is very firm, and may reach a thickness of several centimeters. Both normal and hypertrophic scars are characterized by lack of elastin, which is also visible using the Movat stain. However, there are often residual elastin fibers in the deepest part of the dermis below zones of hypertrophic
Pathophysiology of the burn scar

Hypertrophic scars. These features are illustrated in Figure 46.6. These are the features that have been described as typical of the histology of keloids. However, in our patient population, typical keloids are distinctly unusual, and there is no evidence to suggest that the patients with these thick, eosinophilic collagen fibers have a worse prognosis or a more delayed course of scar maturation than other patients with hypertrophic scars. Thus in our extensive experience with the histology of scars from large burns in children, the histologic features typical of keloids are seen as part of the spectrum of hypertrophic scarring.

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Indeed a clinical history of atopy and higher levels of circulating IgE have been found in patients with hypertrophic scars. Recently, much larger numbers of epidermal Langerhans cells have been identified in association with hypertrophic scars.\textsuperscript{85,86}

Immunohistochemical staining has demonstrated additional striking differences between hypertrophic scars and normal scars. Staining for alpha-smooth-muscle actin has consistently demonstrated this contractile protein within spindle cells in the characteristic collagen nodules of hypertrophic scars. The sulfated proteoglycans of hypertrophic scars are quite different from those of normal scars, in that much less decorin is present, and versican is predominant in the rounded nodules. More immunostaining for VEGF is seen in hypertrophic scars. Larger numbers of small nerve fibers have been identified by immunostaining in hypertrophic scars. These consistent findings may be providing important clues as to the pathogenesis of hypertrophic scarring, but at this time they are difficult to incorporate into a single hypothesis. The study of the biology of hypertrophic scars has been complicated by the lack of a suitable animal model, and by the scarcity of relevant material from human scars, as well as by confusion as to the proper identification of cases of hypertrophic scarring. However, study of cell culture models has yielded important information on biologic processes that may be important in human hypertrophic scars, and potential animal models are being developed.

### Experimental models of hypertrophic healing

The first animal model of keloids was described in 1959, based on immunization of experimental animals with autologous skin, followed by induction of wounds.\textsuperscript{87} Extensive work has been done in which normal and abnormal human scar tissue has been implanted into the athymic nude mouse, which allows testing of potential therapies and modification of the biological milieu in vivo.\textsuperscript{88–91} In this model, it is even possible to irradiate the mouse and transplant human bone marrow to study interactions between immune reactions involving human cells and the human skin grafts. Engrav and his colleagues in Seattle developed a model in the female red Duroc pig that apparently mimics many of the features of human hypertrophic scarring.\textsuperscript{92–100} It will be of great interest to test interventions that might modify the development of hypertrophic scars in that model.

### Phenotypic abnormalities of hypertrophic scar fibroblasts

There have been many studies of the functions and molecular biology of fibroblasts derived from hypertrophic scars and keloids in tissue culture. It does appear from these studies that there is a significantly different phenotype of fibroblasts from hypertrophic scars that persists in culture. Hypertrophic scar fibroblasts have been found consistently to secrete collagen more rapidly than fibroblasts derived from normal skin or normal scars. More secretion of TGFβ has also been described.\textsuperscript{103} Several groups have described abnormal control of proliferation, collagen secretion or peptide secretion in fibroblasts derived from keloids.
in response to cytokine stimulation or treatment with glucocorticoids. However, in most of these studies the regulatory responses of hypertrophic scar fibroblasts were similar to those of fibroblasts from normal skin. Genomic analysis has been done in several laboratories on hypertrophic scar fibroblasts, with identification of numerous differences in gene expression. In a genomic study from our institution, cultured fibroblasts from hypertrophic scars showed a reduced response to IL-6 as compared to fibroblasts from adjacent normal skin, suggesting that decreased receptor activation might be a factor in hypertrophic scarring.102

Gene expression in hypertrophic scars

Studies of gene expression and its regulatory pathways in hypertrophic scar tissue have begun to illuminate the biology of normal wound healing. This is an active area of research that promises to provide much better understanding and potential control of both normal and hypertrophic wound healing. Initial studies of hypertrophic scars using microarray analysis of gene expression have shown consistent differences in expression of genes for multiple collagen isoforms, growth factors and metalloproteinases.103 Similar analyses have been reported recently for the porcine model of hypertrophic scarring.104 In several experimental studies in animals, interventions have been applied that alter wound expression of important genes or signaling pathways, with substantial change in size of the resulting wound.105–110 Although much more research is needed, such studies promise to allow therapeutic intervention in the processes that lead to hypertrophic scarring.

Interplay of systemic and local inflammatory responses

Recent studies have revealed that both local cytokine expression and signaling and also systemic inflammatory processes impact the development of hypertrophic scarring. In burned children who do not develop hypertrophic scars, active and total TGFβ1 levels in plasma increased during the first 2 weeks following the burn injury before dropping to levels below those found in non-burned patients. In burned children who later developed hypertrophic scars, however, active and total TGFβ1 levels in plasma were diminished from the day of burn until at least 180 days later.111 Augmented levels of systemic TGFβ1 have been correlated with increased circulating fibrocytes.112 Although elevated systemic levels of TGFβ1 may be beneficial following a burn injury, prolonged expression locally within the burn wound may lead to hypertrophic scarring with increased fibrosis, downregulation of decorin, upregulation of versican, increased neovascularization and decreased collagenase.113 The type of inflammatory response also appears to play a role in hypertrophic scarring, not only the magnitude and location of inflammation. Characterization of CD4+ T-helper cells revealed that following a burn, polarization of lymphocyte populations leads to a shift from a Th1/anti-fibrotic phenotype to a Th2/pro-fibrotic response.114 Decreased systemic expression of IFN-γ and IL-4 and increased IL-4 producing lymphocytes apparently persist for a year following a burn injury.

Pathogenic concepts

Development of understanding of the biology of hypertrophic scarring has been hampered by multiple factors, including problems in gaining consensus on the definition of the lesion, the lack of a suitable animal model, and the consequent inability to test hypotheses by altering the course of the disease. Multiple concepts of pathogenesis have been proposed. None has yet gained wide acceptance, and none has been experimentally excluded. It does seem clear that development of a hypertrophic scar represents an abnormality in control of the normal processes of wound healing, which may occur early, as Linares and Larson suggested.117 Failure of the normal processes limiting collagen secretion and matrix formation is apparent in hypertrophic scars. One might suppose that the normal processes by which tensions in the matrix signal cellular responses have become defective in hypertrophic scars.40,42 Myofibroblasts are more prominent in hypertrophic scars than in normal or mature scars, and are thought to play a role in excessive wound contraction. These myofibroblasts may derive from resting dermal fibroblasts, or they might arise from pre-existing pericytes, as suggested by Kischer.115 They also might represent bone marrow derived fibrocytes in increased numbers.45 The fibrous nodules of hypertrophic scars might represent persistence and uncontrolled growth of a separate population of connective tissue cells, perhaps related to the perifollicular cells that normally express versican. Since burn patients have higher circulating levels of glucocorticoids and interleukin-6 than normal individuals, a selection process might operate that would tend to allow proliferation of cells resistant to the usual effects of these agents to suppress fibroblast proliferation. A recent suggestion was made that less vitamin D-3 is made in patients with strongly pigmented skin.116 Finally, abnormal macromolecular expression by the covering epithelium may lead to abnormal development of the dermal scar, or fail to suppress inappropriate fibroblast functions.117 Clearly, it continues to be important to develop and test many hypotheses until the problem of hypertrophic scarring is finally solved.

Summary

Healing of burn wounds requires activation of several host processes, including fibrin clotting and lysis, deposition of an immature connective tissue matrix and its reorganization into a mature scar, and epithelial outgrowth and interaction between the epidermis and the dermal matrix. In many burn patients, excessive scar tissue forms, with adverse consequences. Continued study of this problem will continue to be important until more effective modes of treatment are developed.

Further reading


Access the complete reference list online at [http://www.expertconsult.com](http://www.expertconsult.com)
References


Introduction

The physical rehabilitation of patients who have sustained a burn injury is a serious undertaking and requires, among other disciplines, the involvement of physical therapy, occupational therapy and exercise physiology, in order to produce the most functional and cosmetic outcomes. Recent advances in medicine have significantly contributed to increased patient survival rates necessitating faster, more comprehensive and prolonged burn rehabilitation. With severe burn injuries, as perhaps with any other order of trauma, there is an urgent need for immediate and aggressive initiation of patient-specific rehabilitation programs. The distribution and depth of the burn injury clearly predict the patterns of deformity and joint contractures and mandate the establishment of therapeutic goals and the initiation of treatment as soon as possible. As stated previously, the more extensive the burn injury, the greater the rehabilitation challenge becomes. A seriously burned extremity in an otherwise modestly burned patient is much easier to restore to function than an extremity similarly burned in a patient with full-thickness burns involving multiple anatomical surfaces. In the case of seriously burned patients, the immediate and primary focus will always be preservation of life and wound coverage. Nowadays, burn rehabilitation specialists intervene early on in the patient recovery process through the development and implementation of rehabilitation programs intended to maximize the potential of functional and cosmetic patient recovery.

The primary short-term rehabilitation goal is to preserve the patient’s range of motion and functional ability. Long-term rehabilitation goals include the return of the patient to independent living and to train patients on how to compensate for any functional loss suffered as a result of the burn injury and contribute toward acceptable cosmetic outcomes.

This chapter addresses the evaluation, positioning, splinting/orthotics, casting, skeletal suspension, prosthetics, scar management, exercise, performance of activities of daily living (ADLs) and patient and caregiver education utilized in burn rehabilitation along the continuum of care.

Evaluation of the burn patient

Upon admission to the burn center, patients undergo a comprehensive evaluation by burn rehabilitation therapists (physical or occupational therapists) in order to assess their medical status and formulate a plan of care. It is crucial that therapists document the findings of their evaluation in the patients’ medical record as they will serve as the baseline upon which progress will be determined. A good burn evaluation should include: (1) the history of how the accident occurred; (2) an interview with the patients’ caregiver in order to gather information regarding the patients’ pre-injury functional status and activity level; (3) documentation of the etiology, classification and total body surface area (TBSA) of the burn injury; (4) documentation of associated injuries such as fractures, smoke inhalation injury, exposed tendons and bone; (5) measurement of edema, range of motion (ROM), strength and sensation if appropriate; (6) assessment of activities of daily living (ADLs) performance; (7) development of short- and long-term treatment goals and (8) development and documentation of a treatment plan. The patients’ status should be reassessed on a regular basis and after each surgical procedure in order to update the plan of care as needed. Therapists should communicate the results of their evaluation and the treatment plan to the burn team, to the patients and their families.

Positioning and splinting of the burn patient

Positioning of the burned patient is vital in bringing about the best functional outcomes in burn rehabilitation. Positioning programs should begin immediately upon admission to the burn center and continue throughout the rehabilitative process. The role of the burn therapist is invaluable in designing a positioning program, which counteracts all contractile forces without compromising function. In planning and implementing an effective patient-specific positioning program, the therapist should be aware of the patient’s total body surface area (TBSA) of burns, the depth of all injuries, respiratory status and associated injuries such
As exposed tendons/joints or fractures. Individualized positioning programs are monitored closely for any necessary adjustments depending on the patient’s medical status. The quote that ‘the position of comfort is the position of deformity’ applies to every burned patient who sustained a serious injury.

Anti-deformity positioning can be achieved through multiple means: splinting, mechanical traction, cut-out foam troughs and mattresses, pillows, strapping mechanisms, serial casting and in some cases, through surgical application of pins. The burn therapist needs to be aware of physician-specific protocols and work closely with the entire burn team to design the most effective positioning program. Orthotics and splinting devices are vital in burn rehabilitation as they are utilized extensively to obtain appropriate positioning of the entire body and to counteract the contractile forces that lead to deformity. No matter how the burn therapist approaches splinting (material choice, design, and application schedules) the goal is to achieve the best functional outcome at the completion of rehabilitation. When fabricating a splint or an orthosis the burn therapist must be aware of the anatomy and kinesiology of the body surface to be splinted. Also, the therapist should be well aware of all mechanical principles of splinting as they relate to pressure, mechanical advantage, torque, rotational forces, first-class levers, friction, reciprocal parallel forces and material strength.

Positioning and splinting must be designed in a way to:

- Allow for edema reduction
- Maintain joint alignment
- Support, protect and immobilize joints
- Maintain and/or increase range of motion
- Maintain tissues elongated
- Remodel joint and tendon adhesions
- Promote wound healing
- Relieve pressure points
- Protect newly operated sites (grafts/flaps)
- Stabilize and/or position one or more joints, enabling other joints to function correctly
- Assist weak muscles to counteract the effects of gravity and assist in functional activity
- Strengthen weak muscles by exercising against springs or rubber bands.

Devices should:

- Not cause pain
- Be designed with function in mind
- Be cosmetically appealing
- Be easy to apply and remove
- Be lightweight and low profile
- Be constructed out of appropriate materials
- Allow for ventilation in preventing skin/wound maceration.

Typical burn care positioning protocols describe the supine position in great detail. More emphasis is now being placed on the use of side-lying and prone positioning for patients with large burns who must be immobilized for extended periods of time due to newer grafting techniques that cover larger areas with fragile skin substitutes. When designing a positioning program the traditional joint angles are maintained, and the supporting surfaces are modified to maximize surface area while protecting bony prominences.

Side-lying may be used on a rotating basis for patients at risk for sacral or scapular skin breakdown. In a preventive program, the rotation is right side to supine to left side. The order is then reversed on a 1- to 2-h schedule. Full side-lying at 90° from supine should not be allowed for any significant length of time due to excessive pressure over the greater trochanter. A more appropriate position for side-lying is approximately 30–40° from the supine position, which distributes pressure more evenly between the head of the femur and the lateral portion of the sacrum.

The mechanics of a side-lying position can be accomplished using pillows or wedges made of foam or wood. The advantage of foam or wooden wedges is that they can be placed directly under the mattress with less manipulation of the patient. As the rotation schedule is completed the wedge can either be removed for the supine position or transferred to the opposite side of the mattress to achieve side-lying on the opposite surface.

Prone positioning systems are usually the position of last resort (Fig. 47.1). They are reserved for patients who are not successfully being managed in supine or side-lying. There may be non-healing grafts or wounds in the rectal region that increase the risk of sepsis due to the introduction of fecal matter. Other common candidates for this protocol include those with sacral pressure ulcers or posterior trunk grafts that are not healing.

There are a host of issues that must be considered when instituting a prone program. Airway is always the first issue that must be considered when designing a prone positioning mattress. The supporting surface is cut from a solid open-cell foam mattress that is placed on a wire mesh bed frame. Airway concerns are addressed first and the patient is evaluated for mode of respiration. Nasal and tracheal intubation are issues to consider, but are not contraindications for the prone position. A trough should be provided so that direct access can be obtained for routine airway care and if breaths are needed using an Ambu-bag. If the airway becomes compromised the prone position should be abandoned immediately until proper respiration is established.
The facial opening should be cut in a manner that maximizes weight distribution without allowing the head to enter into the opening. Using this protocol places direct weight-bearing pressure on the brow ridge, zygomatic arches, and the anterior mandible. These structures should be monitored closely and the patient should be educated that breakdown is likely to occur due to the limited subcutaneous tissue protecting the face. If burn scars are encroaching on the eyelids, then the corneas should be evaluated as well. Corneal abrasion can be avoided with due diligence and prevention of the foam from contacting the unprotected eye. Counter-sinking a gel cushion into the upper portion of the foam mattress can protect the forehead and brow-ridge.

The sternum, pelvic region, and patellae are protected with the use of an air-cell mattress that is inserted into the mattress in a length-wise manner. The air-cell segments are typically supplied in standard lengths and may not reach from the sternum to the ankles. If there is an unsupported area between the distal portion of the air-cell mattress and the dorsum of the foot, then the area can be supported with open cell egg-crate type foam. The feet are supported at the distal end of the mattress with a foam footboard. Extra precautions should be taken to evaluate the elevation of the great toe from the supporting bed frame.

In the prone position, all of the traditional joint alignment suggestions are maintained with the possible exception of the elbows. Shoulder mobility dictates the style of mattress that can be made for the individual burn patient. If the patient has >115° of abduction, then the mattress is modified to horizontally adduct and externally rotate the shoulder while flexing the elbow to allow for elevation of the hands. This minimizes edema in the hands and allows for greater function once the prone position is no longer needed. If the shoulders have limited abduction then a ‘butterfly’ cut is used to allow for horizontal adduction of the shoulder to protect the brachial plexus with the hands remaining slightly dependent. This will result in some hand edema, which can be addressed with pressure wrapping (Coban™ glove) and active exercise.

Head

Acutely, in aiding with facial edema reduction, the head should be positioned by placing in midline and elevating the head of the bed at 30–45° if the patient’s hips are not involved. In cases where the hips are burned, the entire bed may be elevated at the head of the bed with the use of shock blocks (wooden blocks 12–16 inches high with recessed slots for bed legs). This will avoid positioning the hips in the flexion contracture position (Fig. 47.2). In the cases where the ears are burned they may be protected by wrapping ear cups made of thermoplastic materials or foam. An ear conformer may be constructed to prevent the rim of the ear from contracting toward the head. Internal ear canal splints may also be fabricated and serially adjusted as the circumference of the canal increases. In addition, if the ear is affected, a soft circular foam can be positioned posteriorly to the head to elevate the ears of the surface of the bed. A nasal obturator may be required to maintain the nostrils open. These obturators may be serially adjusted as the circumference of the nostril increases. Mouth splints are utilized for the prevention of oral microstomia. These devices are custom-made by the therapist or they may be obtained commercially. Mouth splints may be fabricated static or dynamic for the horizontal or vertical opening of the mouth. In cases of severe microstomia where compliance is an issue, an orthodontic commissure appliance which attaches to the teeth may be fabricated by an orthodontist. The use of stacked tongue blades is an acceptable technique to aid in reversing oral microstomia. Ongoing research looks at the development of a microstomia device that circumferentially opens the mouth according to its anatomy (Fig. 47.3). Facial scar hypertrophy may require fabricating a high thermoplastic transparent mask such as the Uvex™ and W-clear™ masks or a silicone elastomer facemask. A semi-rigid low thermoplastic opaque mask may also be fabricated depending on the state of scar maturation.

Neck

The neck is positioned in neutral or in slight extension of approximately 15° without any rotation. The amount of neck extension must not be so great that traction on the chin causes the mouth to open. Positioning may be achieved with a short mattress supine, a rolled towel or foam cushion placed behind the upper back on the scapular line. Pillows should be avoided in the cases of anterior neck burns as they may lead to flexion contractures. In the case of anterior neck burns a conforming custom thermoplastic collar may be fabricated (Fig. 47.4). For long-term needs, a soft neck collar or a Watusi-type collar may also be fabricated as the patient’s wounds heal and contractures or scars develop. The Watusi-type collar allows for isolated, direct pressure to a thicker scar band. It has been observed that in some cases, acute patients rotate or laterally flex their neck on one side, which may lead to a lateral neck contracture (torticollis). If the patient is to remain in bed for a while, a dynamic head strap mechanism may be fabricated to counteract the lateral neck contractile forces and bring the neck in the neutral position. For the prevention of torticollis the therapist may fabricate a lateral neck splint which conforms to the head of the patient, the lateral neck and anterior/posterior shoulder (Fig. 47.5).
Figure 47.3 Horizontal, vertical and circumferential mouth-opening devices are utilized to correct oral microstomia.

Figure 47.4 An anterior neck conformer helps prevent neck flexion contractures.

Figure 47.5 (a) A dynamic head strap mechanism aids in positioning the neck in neutral position during a prolonged ICU bed confinement. (b) A lateral neck splint is utilized to prevent lateral neck flexion contractures (torticollis).
Comprehensive rehabilitation of the burn patient

Nerve compression. The glenohumeral joint is externally rotated in order to counteract anticipated deformities of internal rotation and adduction and to maintain balance of the soft tissues of the shoulder complex. Positioning of the shoulder may be achieved with splints, silicone-filled pillows, bedside tables, foam arm troughs, metal abduction troughs, and thermoplastic slings suspended from a trapeze mechanism (Fig. 47.7). Splinting of the shoulder joint becomes more intensive as scar maturation heightens the risk of contracture development. Airplane splints are used for the resolution of axillary contractures and post-operatively to protect reconstructive procedures. To accommodate wound dressings and promote healing, a three-piece airplane splint may be fabricated (Fig. 47.8). Other adaptations may be required in the presence of amputations. Pre-fabricated airplane splints come equipped with mechanisms that allow for adjustments depending upon available shoulder range of motion.10,11,13 A figure-of-eight axillary wrap may be utilized in conjunction with an

Spine

Contracture resulting from unilateral or asymmetric burns of the neck, axilla, trunk and groin will cause lateral curvature of the spine (scoliosis). The level and amplitude of curvature will vary with the site and severity of the contracture. In addition, pelvic obliquity accompanying asymmetric hip or knee flexion contracture will impose a lateral lumbar curve. As long as the patient is recumbent, lateral curvature can be prevented by maintaining straight alignment of the trunk and neck (Fig. 47.6). However, the curve is often insidious in onset and will not be recognized until the patient begins to walk. Trunk list observed early in the ambulation period can be simply a transient accommodation to pain and wound tightness, but a persistent list may herald the development of scoliosis. Other subtle signs of spinal curvature are asymmetry of shoulder levels, scapular asymmetry, asymmetry of dependent upper extremity alignment to the trunk and asymmetry of pelvic rim levels. A spinal mobilization exercise program is established with a patient once a curvature is identified, however once there is an established asymmetric contracture it is difficult by therapeutic means to stretch it out, so it is probably better to deal surgically with a deforming scar early than to permit even minor scoliosis to persist.

Shoulder girdle/axilla

Acutely, the upper extremity positioning program focuses on reducing edema through elevation. Failure to reduce edema in the first 48–72 h can promote the development of a fixed deformity. Additionally, improper elevation techniques for the upper extremity may lead to soft tissue calcification, increased bone density, and compressive neuropathies. The recommended position for the burned shoulder and axillary complex is 90° abduction, 15–20° horizontal adduction and external rotation towards maximal. Abduction alone places the glenohumeral joint at risk for anterior subluxation if the position is maintained for an extended period of time. Placement in horizontal adduction anatomically reduces the potential for tractioning of the brachial plexus or peripheral nerve compression. The glenohumeral joint is externally rotated in order to counteract anticipated deformities of internal rotation and adduction and to maintain balance of the soft tissues of the shoulder complex. Positioning of the shoulder may be achieved with splints, silicone-filled pillows, bedside tables, foam arm troughs, metal abduction troughs, and thermoplastic slings suspended from a trapeze mechanism (Fig. 47.7). Splinting of the shoulder joint becomes more intensive as scar maturation heightens the risk of contracture development. Airplane splints are used for the resolution of axillary contractures and post-operatively to protect reconstructive procedures. To accommodate wound dressings and promote healing, a three-piece airplane splint may be fabricated (Fig. 47.8). Other adaptations may be required in the presence of amputations. Pre-fabricated airplane splints come equipped with mechanisms that allow for adjustments depending upon available shoulder range of motion.10,11,13 A figure-of-eight axillary wrap may be utilized in conjunction with an
airplane splint to provide compression for axillary contour and elongation of skin surfaces (Fig. 47.9). For successful contracture management to the shoulder, the positioning program must be supplemented by exercise routines for range of motion and strengthening.

Elbow/forearm

Acutely, elevation and extension is the desired position of the elbow. Severe burns involving the elbow may result in flexion contracture and threaten posterior exposure of the joint. Full extension is the protecting position for the elbow. If the joint is exposed posteriorly, extension may need to be rigidly maintained for several weeks. If the joint is not exposed, mobilization into increasing flexion range can begin very soon after the burn. The elbow is integral to the so-called delivery system for the hand, and elbow range to full or near-full flexion is more important for overall function than range to full or near-full extension.

Radial head rotation for pronation and supination is less often affected by the burn injury than flexion and extension. The pronators and supinators are frequently injured in electrical accidents where bone, being a poor conductor, heats destroying the muscles closest to it. Forearm rotation is essential for accurate hand placement and the rehabilitative program must seriously address that function. Depending on the location and severity of the injury the forearm may be positioned in neutral or in slight supination. Static elbow splints may be soft or custom-fabricated of thermoplastic materials. An anterior elbow conformer may be fabricated over the burn dressing. Dynamic elbow extension or flexion splints may be utilized to provide prolonged gentle sustained stretch and aid in the correction of contractures. Forearm dynamic pronation/supination splints may be custom-fabricated or obtained commercially for the correction of contractures.

Wrist/hand

Treating therapists must have a thorough understanding of the effects of thermal injury on the anatomical structures of the wrist and hand. The presence of dorsal hand edema leads to intrinsic muscle ischemia and a resultant ‘intrinsic-minus’ posture. The unsupported burned hand postures in wrist flexion, metacarpophalangeal (MCP) hyperextension, interphalangeal (IP) flexion, thumb adduction, and thumb IP flexion. The overall appearance is that of a claw deformity (Fig. 47.10a) Edema following a full-thickness burn to the dorsal hand imposes MCP hyperextension and IP flexion (Fig. 47.10b). Persistence of this position results in a claw deformity. The claw hand posture is primarily due to postburn edema, but may persist throughout the course of treatment due to scar contracture. Among the digits, the second and fifth most easily drift into MCP hyperextension because each has a proper extensor tendon.

While superficial burns result in minor, transient edema, full thickness injuries exhibit more severe and prolonged postburn edema. Superficial hand burns should not be splinted in order to allow for frequent movement and the freedom to function independently. In cases of severe thermal injury it is important to monitor for signs and symptoms of vascular insufficiency or compartment syndrome. In treating the edematous, burned hand, it is important to position the hand above the level of the heart at all times, without compromising the neurovascular supply to the hand.
Acute positioning of the wrist and hand after burn injury is for edema control, immobilization/protection of tendons, joint structures, and/or skin grafts, and optimal positioning to maintain soft tissue lengths and functional abilities. Within the first 24–72 h it is recommended that the wrist be splinted into extension, allowing the MCP joints of digits 1 through 5 to fall into flexion due to the normal tenodesis action of the wrist and hand. Wrist extension is essential in order to control digital position and prevention of a claw hand deformity. The recommended functional position of the wrist is from 0–30° of extension.

The burned wrist and hand should be positioned to oppose impending wound contracture. The optimal position for the burned hand is wrist 0–30° extension, 70–80° MCP flexion and IP joints in full extension (although some burn centers may advocate a slight amount of IP flexion deeming the position to be ‘safe’). The thumb should be positioned in a combination of palmar and radial abduction with the MCP/IP joints slightly flexed. This position resembles the ‘intrinsic-plus’ position and is achieved through fabrication/fitting of a burn hand splint by a rehabilitation therapist (Fig. 47.11). The burn hand splint positions the hand appropriately to minimize soft tissue contractures and preserve functional mobility. Involvement of the extensor tendon apparatus should be assumed and protected until viability of the system is known. Continuous splinting is recommended to manage edema, exposed tendons, peripheral neuropathies, and uncooperative/unresponsive patients.

In the intermediate phase, positioning and splinting is used to prevent/correct deformities and protection of surgical reconstructed sites. Splints may be fabricated dorsal, volar or on the medial/lateral aspects. Contractures are a major complication of hand burns as they affect one’s ability to perform activities of daily living. Dorsal hand burns are prone to contract into MCP hyperextension, IP flexion, and thumb adduction and should be splinted into MCP flexion, IP extension, and thumb palmar abduction. The most common post-burn upper extremity contractures are: wrist flexion, index finger MCP hyperextension, index finger proximal IP flexion, and small finger MCP hyperextension/proximal IP flexion. The claw hand deformity is functionally detrimental because it makes it impossible to smoothly reach around objects (Fig. 47.12).

Burns to the volar surface of the forearm will predispose the patient to wrist flexion contracture, while burns to the dorsal surface will likely result in a wrist extension contracture. If the wrist ROM becomes limited in a specific direction, splinting the wrist in the opposite direction is indicated. The fifth digit is occasionally pulled into extreme abduction and hyperextension by scar contracture, muscle imbalance, or ulnar neuropathy. The thumb may become similarly displaced into adduction and retroposition. It is important to remember that the likelihood for MCP joint problems exists throughout scar maturation. Palmar hand burns are prone to MCP flexion and thumb opposition contractures and should be splinted into palmar extension and thumb radial abduction.

Static positioning with custom thermoplastic splints can be relatively efficient. However, two common faults are seen in custom splints that are designed to gain MCP flexion and to position the thumb in MCP flexion/radial abduction. If the distal transverse fold of the splint is not proximal to the MCPs of digits 2–5, the splint will impede rather than favor MCP flexion. If the thumb component of the splint applies volar pressure rather than medial pressure, the MCP will extend and the first metacarpal will become correspondingly more adducted. The first MCP joint should be maintained in slight flexion and pressure from the splint should be applied just to the medial surface. Any degree of first metacarpal adduction contracture increases the likelihood that the proximal phalanx will be pushed into hyperextension and eventually into subluxation.

In the case of circumferential hand burns, a palmar extension splint is fabricated to prevent flexion contractures and a cupping deformity of the palm (Fig. 47.13). The burn hand splint and an extension splint may be alternated. A ‘sandwich’ splint may be fabricated which includes a burn hand splint with a dorsal shell over the IP joints to prevent flexion of the digits. All splints may be secured with elastic bandage or with Velcro® strapping components (Fig. 47.14). Individual gutter splints are used to prevent flexion contractures, to restrict boutonnière and mallet finger deformities, and for...
protection of exposed extensor tendons until wound closure. C-bar splints are used to prevent adduction contracture of the first web space. Figure-of-eight splints are fit to correct or restrict swan neck deformities.

Dynamic splints are utilized to provide low-load prolonged stretch to counteract contractile forces. Dynamic splinting of the hand will focus on MCP extension/flexion splints, IP flexion/extension splints, thumb abduction, and may include pre-fabricated or spring-loaded splints (Fig. 47.15). Patients may require dynamic splinting to assist muscles weakened by peripheral neuropathy. The therapist monitors dynamic splinting closely and makes frequent adjustments in order to provide effective tissue mobilization. Additionally, the fit of dynamic splints is checked frequently to insure that the anatomical structures remain properly aligned.

**Hip**

When anterior burns extend from the abdomen to the thigh, hip flexion is the position of comfort. If the hip is fixed in any degree of flexion, posture will be modified. Bilateral symmetric contracts impose increased lumbar lordosis or knee flexion or both. Asymmetric contractures will cause pelvic obliquity and scoliosis. In adults and older children, thighs are more likely to be held in adduction than in abduction, whereas in pre-ambulatory infants the secondary component of the contracture is abduction. Thus, for the hips the preventive position is full extension, 0° rotation and symmetric abduction of 15–20°. If elevation of the upper body is needed for edema reduction then the entire frame of the bed is elevated with the use of wooden shock blocks placed at the head of the bed. Soft mattresses should be avoided as they may promote hip flexion. Hip positioning is accomplished with the use of abduction pillows and other strapping mechanisms eliminating hip rotation. If the patient wears bilateral foot splints then connector bars may be utilized on the splints to bring about the desired bilateral hip positioning stated above. Hip flexion contractures may be serially corrected with an anterior hip spica or with a 3-point hip extension splint (Fig. 47.16). Subtle hip flexion contractures can be easily overlooked when the patient stands, there being only a slight increase in lumbar lordosis or forward or lateral shift of the trunk. If established hip flexion contractures are not surgically corrected, body posture is likely to be permanently altered with scoliosis or exaggerated lordosis.

**Knee**

Burn injury to the anterior or posterior surface of the lower extremity that crosses over the knee joint may result in knee flexion. Deep anterior burns may expose the joint, occasionally destroying the patellar tendon. Deep posterior burns result in bridging scar formation. The appropriate position for the knee is full extension to be maintained by splint or in severe cases skeletal traction until there is efficient quadriceps function and the patient is ambulatory. Thereafter, night splints must be used until scar contracture is no longer a threat. Knee splints may include a posterior custom-made thermoplastic knee conformer or a soft knee immobilizer. Persisting bilateral knee flexion contractures will impose hip flexion. Persisting unilateral contractures may impose pelvic obliquity and scoliosis. As with the hip, posture
altered may be so subtle as to be overlooked. Correction of even a slight contracture should be a surgical priority as should elimination of a soft bridging scar band that does not prevent complete willful knee extension but causes the patient habitually to hold the knee in slight flexion.

**Foot/ankle**

Ankle equinus is the most frequently occurring deformity involving the foot. Initially, it is related more to gravity and failure to support the foot at neutral at the talotibial joint than to the early effect of the burn. Loss of deep and superficial peroneal nerve function will compound the problem by encouraging the foot to drift into inversion as well as equinus because of loss of dorsiflexion and eversion motors. In the end, the total deformity for the unsupported foot may be ankle equinus, hind-foot inversion, and forefoot varus and equinus. Ankle equinus quickly becomes a resistant deformity so that within a few days or even hours the foot can no longer be positioned at 90° of dorsiflexion in the neutral ankle position. Eventually the contractures of scar, muscle and capsular structures combine to fix the deformity.

Equinus deformity and the attending inversion and forefoot varus can be prevented by accurate and unyielding support of the foot in neutral alignment or slight dorsiflexion. If the patient must be nursed prone, the feet must be allowed to fall free from the mattress. Static splinting if not performed correctly by an experienced therapist is often unsuccessful because of the patient’s desire and tendency to plantarflex strongly, displacing the splint and leading to ulcers of the heel, malleoli, toes and where the splint edges touch the skin. A stable footboard may be effective if the feet are kept securely and totally against it. For large burns and particularly for circumferential burns of the lower extremities, skeletal suspension incorporating calcaneal traction will support the foot at neutral if the traction pin is placed in the calcaneus well behind the axis of ankle motion. A balanced traction system demands that the knees be supported in flexion with tibial pins at the level of the tibial tubercle. Calcaneal pins will not prevent forefoot equinus. If traction must be employed for several weeks, proximal pull dorsal pins in the first or first and second metatarsals may be required for support of the forefoot. Transmetatarsal pins are useful as well when calcaneal traction alone is not sufficient to correct equinus.

Minor established equinus deformity can be corrected with a standing and walking program. At the outset graduated heel lifts may be used to accommodate to the deformity. If the patient must be bed-confined, skeletal traction through the calcaneus may be the quickest and most efficient way to correct the deformity. Traction is effective even if scar contracture contributes to the deformity. Serial corrective casts or posterior splints alone are useful mainly for minor contractures. For the treatment of circumferential foot/ankle burns anterior foot splints are also fabricated and their application is alternated with the posterior foot splints in preventing plantar or dorsal foot contractures. The Multi Podus® System foot splints may be utilized for the positioning of the burn foot/ankle as they relieve heel pressure in preventing pressure ulcers (Fig. 47.17). For fixed, unyielding deformity, scar release combined with tendo-Achillis lengthening with or without posterior capsulotomy is a standard surgical procedure that yields inconsistent results. The correction achieved is often just to neutral or to slight dorsiflexion. The Ilizarov technique has been used with generally satisfactory immediate results in severe cases. No matter how correction is achieved, if there are no dorsiflexion motors and if the range of ankle motion is only a few degrees, ankle fusion may in the end yield the best functional result.

The most common intrinsic deformity of the foot is extreme extension of the toes due to dorsal scar contracture. This deformity is insidious in onset and is difficult to prevent as there is no type of non-skeletal splinting that will hold the toes flexed. In its extreme, the deformity includes dorsal metatarsophalangeal (MTP) subluxation which may involve one or all toes depending on the location of the scar. The
metatarsal heads become prominent on the plantar surface and walking may be painful. Correction of the deformity requires dorsal surgical release of the contracture, manual correction of the deformity and in severe cases intrinsic or extrinsic pinning of the digit or digits in an overcorrected position, i.e. MTP and interphalangeal flexion. The deformity will commonly if not inevitably recur to some degree, unless the patient, after the operation, is able to achieve in all digits active MTP flexion.

Dorsal scar contractures extending from leg to foot to toes may pull the foot into marked inversion if the scar is medial or into eversion if the scar is lateral. The fifth and first toes may be separately displaced by the same scar bands. These contractures must always be surgically corrected. Their persistence will lead to bone deformity in a growing child and will permanently adversely affect foot and ankle function. Even slight inversion, whether imposed by scar contracture or motor weakness, will increase pressure on the lateral border of the foot, leading to callus formation and a painful inefficient gait. Occasionally, the base of the fifth metatarsal is so offensive as to require partial surgical osteotomy.

When there is both anterior and posterior scar contracture, the talus will remain aligned with the calcaneus in a relatively plantar flexed position as the midfoot and forefoot are pulled into dorsiflexion. The result is so-called rocker bottom foot. This deformity once established defies correction by usual surgical means because of the shortage of soft tissue and because vessels and nerves cannot be stretched to accommodate to the corrected position. The Ilizarov technique may offer a partial solution to the problem. Removal of the head of the talus may give a reasonable weight-bearing surface. With chronic painful ulceration, amputation is the best treatment.

Orthotic treatment of the lower extremity

The approach of the orthotist in treating the injured foot depends on the extent of the burn injury. Orthotic shoes, which are the fundamental component of most lower extremity orthotics, may be utilized with some modifications in correcting deformities of the burned foot. Modifications of these shoes may include arch pads, molded foot thermoplastics, tongue pads, and metatarsal bars. The orthotic shoes should distribute all forces to the foot appropriately and should reduce pressure on sensitive or deformed structures and encourage total surface weight-bearing along the plantar aspect of the foot. Inserts for plantar foot support such as the University of California Biomechanical Laboratory (UCBL) type may be utilized as indicated.

During the preambulation stage the patient may be fitted with those orthoses; if properly utilized, they can position the ankle joint appropriately, and assist in preventing or correcting plantar/dorsal contractures and inversion/eversion of the foot.

Leg length discrepancies are seen frequently in the cases of severe lower extremity burn injuries and they should be addressed with a shoe lift. The ankle–foot complex is difficult to address, especially in the case of a severe thermal injury. In most cases, the resultant deformity is the equinovarus foot. Both conventional and thermoplastic systems may be designed to treat the equinovarus or equinovalgus foot. Such systems may include a metal ankle–foot orthosis (AFO), polyethylene plastic posterior AFO (solid ankle or with an articulation), an AFO with stirrup attachment, an AFO with stirrups and patellar tendon support. A dorsiflexion spring assist may be incorporated in the AFO to aid weak ankle motion. Different straps such as a valgus correction strap may be attached to the AFO for the correction of specific problems. Interface materials, such as silicone, Plastizote® and Aliplast®, can be incorporated into an AFO to provide protection of the soft tissue, provide for total surface weight-bearing, and to accommodate any anatomical anomalies that may be present (Fig. 47.18). In the event that a return of range of motion is anticipated, an AFO could be fabricated that can be modified as the patient progresses. The ankle joints can be incorporated into the AFO, however, left solid and articulated at a later date.

During more complicated cases, and depending on the anatomy and function of the lower extremities, a knee–ankle–foot orthosis, hip–knee–ankle–foot orthosis or a trunk–knee–ankle–foot orthosis may also be designed for the best functional outcome.

Serial casting

Casting has been used in patients with burns for postoperative immobilization to promote graft adherence and to minimize scar contracture during the remodeling phase of healing. Circumferential casting after skin grafting to the lower extremity is an effective means of providing protection to the grafted area. Serial casting has been used successfully on outpatients with burns when active range of motion is limited due to scar tissue formation. The goal of serial casting is gradual realignment of the collagen in a parallel and lengthened state by constant circumferential pressure. Prolonged gentle sustained stretch provided by the cast aids in tissue elongation for the correction of contractures (Fig. 47.19). Burn scar under constant traction shows collagen formation in parallel alignment along the forces of stress. Low intensity force with prolonged duration for stretching...
can be applied to connective tissue whether it is scarred, contracted or surgically shortened. Casting is a relatively simple, fast and painless intervention and provides an alternative to dynamic splinting but is not feasible when patient compliance is an issue (e.g. pediatrics).

A pre-casting assessment should include the following: ROM measurements, end-feel assessment of the involved joint, duration of limitation, skin or wound status, neurovascular status, functional needs, and cognition of all involved parties. The patient is educated on the position in which the cast will be applied, the expected duration of casting and any restricted activities. Ridgway (1991) described the serial casting technique: (1) skin hygiene; (2) scar massage with moisturizer; (3) ROM exercises and assessment; (4) wound dressings; (5) application of a silicone insert; 6) extremity in figure-of-eight wrap or tubular bandage; (7) padding over bony prominences; (8) one therapist to position and one therapist to fabricate cast. Serial casting may be supplemented with splinting of adjacent joints. There should be a minimal time lapse between cast removal and reapplication.

Patients may require premedication and may also benefit from soft tissue preconditioning (heating) for stretch prior to cast application. Precautions should be taken to ensure proper and evenly applied padding, including extra layers at the proximal and distal ends of the cast. The casting material should be rolled out and handled with an open hand as much as possible. Aggressive molding or over tight application are to be avoided and can lead to compression neuropathies or vascular compromise. When cast materials harden an exothermic reaction occurs, causing the temperature within and beneath the cast material to rise, which leads to elevated temperatures and burns. The greatest risk of thermal injury occurs when a thick cast using warm dip water is allowed to mature while resting on a pillow. A variety of materials are available for the fabrication of casts. The most widely known would probably be Plaster-of-Paris. Plaster is fast setting when reacting with lukewarm water. Plaster casts are inexpensive, stronger, and easy to fabricate. However, they require longer drying times (24–48 h), are prone to indentations and skin irritations, and are heavier. Other disadvantages of this technique include a decreased water resistance and breakage if not constructed strongly enough. Plaster casts may be removed with a cast saw or moistened and removed with scissors.

Fiberglass casting material is an alternative to Plaster-of-Paris. Fiberglass casting tape is fast setting when reacting with cool water. Fiberglass materials require a shorter drying time (15–30 min), are lighter weight and more durable, and offer resistance to dirt and water. Fiberglass casting methods are more costly than plaster. Because of fiberglass’s abrasive properties, therapists must wear gloves for handling the materials during cast fabrication and removal. The patient’s skin and clothing should be protected from contact with the fiberglass casting tape, as well as to fiberglass fibers during cast removal. Fiberglass casts require use of the cast saw for removal.

Recently, non-latex polyester materials such as Delta-Cast™ are utilized as alternatives to plaster and fiberglass. These materials, which resemble fiberglass, are very lightweight, flexible, and because of their elastic properties conform very well. These casts may be cut in a bivalve fashion so that they can be removed and reapplied after wound care, hygiene, and exercise.

After cast fabrication is complete, the clinician should check the following: firmness of the cast, neurovascular status of the extremity, sharpness of cast edges, and any signs of the cast rubbing adjacent structures. When casting is completed, the patient should feel a gentle, but not painful stretch. The first cast should be removed at approximately 24 h and thereafter, depending on the patient’s tolerance, it could be applied for up to 1 week at a time. In cases of casting over open wounds, the cast should be removed every 1–2 days in order to avoid complications in wound healing. The use of insert material for scar management under casts has been documented and found to be useful. Serial casting is terminated when either normal range of motion has been restored or no further functional gains are achieved.

**Skeletal suspension and traction**

Skeletal suspension and traction systems have been used to a limited extent in burn management for a number of years. The early reports of Larson and Evans described the use of skeletal suspension for positioning and for extremity elevation for open wound management and of skeletal traction for prevention and correction of contractures. The later reports of Harnar and Youel deal mainly with the management of hand burns with the skeletally anchored digital traction splints bearing the names banjo, halo, and hay rake (Fig. 47.20).

The adaptation of skeletal suspension and traction systems to burn management grew out of earlier experience with traction to correct the elbow and knee contractures of patients with rheumatoid disease, and out of traction and suspension as definitive means for treating certain extremity fractures. In its earliest application to burn management, skeletal suspension was used for extremity elevation only to facilitate wound care. From this experience evolved better-defined traction systems, including those expressly designed for hands and feet. Rehabilitation therapists may remove the
insults, but can also result from more severe thermal injuries as well. Prosthetics are designed, fabricated, and fit by a certified prosthetist. Each device is individualized based upon the needs of the patient. But, in general, the prosthesis should be comfortable to wear, easy to don/doff, lightweight, of durable construction, and be cosmetically appealing. The prosthetist and rehabilitation professional will consider the following when designing the prosthesis and its components: level of amputation, shape and contour of the residual limb, functional expectations, cognitive abilities, vocational requirements, hobbies/leisure pursuits, and financial resources. Standard prosthetic texts are useful in providing broad basic information and explanation of the many components available and their use. 34,35

Patients who have sustained severe burns and subsequent amputations have complex, long-term impairments and face considerable functional deficits. Severely burned patients tend to have sensorimotor limitations in the intact extremities, which may affect their ability to utilize a prosthesis. Their limitations and strengths are important considerations when planning treatment. These patients may exhibit muscle weakness not usually seen at the same amputation levels in the non-burn patient. Areas of weakness should be noted and compensation such as increasing joint stability through alignment or componentry should be provided. Burned individuals may use their remaining functioning extremities differently than patients without total body involvement. Prosthetic rehabilitation should enhance adaptations and necessary compensatory methods. The challenge to the prosthetist is to design a device which is maximally useful to a person who may have multiple limitations. To be useful, a device must be as easy to use as possible. Simplicity often determines whether the device is successful or discarded.

Prosthetic interventions

A prosthesis is a device used to replicate the function and appearance of a missing limb. Amputations among the burn patient population most often occur as a result of electrical patient from the traction apparatus as indicated for exercises and ambulation and reapply the traction at the completion of treatment. Positioning within the traction is often changed by nurses and therapists by altering the amount of the traction weights, thus preventing the affected joints from being locked into one position over time (Fig. 47.21).

Figure 47.21  Skeletal traction is utilized for positioning of extensive burns and for the protection of delicate grafts through suspension. Rehabilitation therapists may remove the traction and ambulate or exercise patients as needed. Traction weights may be changed to achieve different positions within the traction system and help shift the weight of patients in bed.
stump volume is anticipated or when fitting over a bulky dressing is necessary. These devices are usually simple, passive devices that allow for early motion skills and weight-bearing through the affected limb. Some patients will continue to use their preparatory prosthesis for extended periods of time while other areas of the body are treated. Prior to definitive fitting, body weight, residual limb volume, wear and use patterns should be stable in order to optimize the long-term result with the definitive prosthesis. The definitive prosthesis is fit when the residual limb is fully mature. The use of a preparatory prosthesis is not mandatory, but the use of one will improve the fit and control of the definitive prosthesis; and may, secondarily, reduce the amount of time needed for rehabilitation post-burn injury.

Prosthetic preparation in burn rehabilitation begins in the post-surgical phase. Early prosthetic treatment of an amputee includes splinting for the prevention of contracture. An upper extremity splint may extend past the distal end of the residual limb to match the length of the whole limb, thus assisting a patient in retaining the concept of length. Initially, therapists must address: promotion of wound healing; pain management; residual limb shaping; prevention of contractures; skin desensitization techniques (tapping, massage, scar mobilization, pressure application); edema control, and coping mechanisms for adjustment and grief. With early socket fitting, some skin problems will be encountered, but these are not usually of major significance. Silicone gel or urethane socket inserts have been used successfully for pressure relief to burn-scarred skin. As wound healing progresses, prosthetic training will begin to focus on care of the prosthetic device, don/doff methods, skin inspection routines, weight-bearing through the affected limb. Some patients will continue to use their preparatory prosthesis for extended periods while other areas of the body are treated. Prior to definitive fitting, body weight, residual limb volume, wear and use patterns should be stable in order to optimize the long-term result with the definitive prosthesis. The definitive prosthesis is fit when the residual limb is fully mature. The use of a preparatory prosthesis is not mandatory, but the use of one will improve the fit and control of the definitive prosthesis; and may, secondarily, reduce the amount of time needed for rehabilitation post-burn injury.

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Just as upper extremities are different from lower extremities; so, too are upper and lower extremity prostheses. The minimum requirements for successful use of an upper extremity prosthesis are: trunk control to support an upright posture, sufficient upper body strength to selectively activate the control devices, and static and dynamic balance skills. The patient will need to be trained on specific body movements to develop control of the upper extremity prosthesis. Glenohumeral flexion provides excellent power and reach for functional routines. It can be used to flex the elbow, activate the terminal device, and for activities away from the midline of the body. Scapular protraction is also trained for activation of the terminal device and facilitation of fine motor tasks at midline or close to the body. The other motions of glenohumeral depression/elevation, extension, and abduction are most frequently used to lock or unlock an elbow joint.

Different types of upper extremity prostheses are available along a continuum from mostly passive or cosmetic to primarily functional. Most devices fall somewhere in the middle range between cosmesis and function. Cosmetic prostheses are difficult to keep clean, expensive, and ultimately sacrifice function for appearance. Functional prostheses fall into two categories. They can be designed to be body-powered (using cables) or externally powered (myoelectric or switch control). Body-powered prostheses are moderate in cost and weight, more durable, and offer higher sensory feedback. However, they require more gross limb movement and can be less cosmetically appealing. Externally powered prosthetic devices allow for more proximal function, greater strength for grasp/prehension, and improved cosmesis. Additionally, they may be heavy and expensive, offer less sensory feedback, and require more regular maintenance. Regardless of the type of prosthesis planned for, fitting of an upper extremity body powered prosthesis within 7–30 days correlates with higher acceptance and success rates. Body-powered prostheses are most commonly used in burn rehabilitation and Table 47.1 describes the components of upper extremity prosthetic devices.

The rehabilitation upper extremity prosthetic goals should include: stability of shoulder girdle to allow prehension, overall ease of movement of the entire limb, energy efficient use of the device, and the appearance of a normal upper extremity. Table 47.2 describes upper extremity amputations by level and identifies the appropriate prosthetic device to address the patient’s functional needs.
The overall process of prosthetic evaluation and fitting is described in Figure 47.22. Satisfactory use of a prosthetic device in burn rehabilitation requires continuous dialogue between the patient, therapist, prosthetist, and surgeon. Return clinic visits should include consistent prosthetic re-evaluation. However, ultimately, the use of a prosthetic device depends largely upon patient motivation. Most prostheses can be expected to last at least 3–5 years with standard daily use. Children will need more frequent modifications or adjustments as they grow and develop. In general, the simplest system which provides the most functional–cosmetic level is accepted by the amputee as the best choice.

### Table 47.2 Types of amputations and prosthetic needs

<table>
<thead>
<tr>
<th>Types of amputations</th>
<th>Prosthetic needs</th>
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<tbody>
<tr>
<td><strong>Upper extremity</strong></td>
<td></td>
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<tr>
<td>Transphalangeal</td>
<td>Passive for cosmesis</td>
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<tr>
<td>Transmetacarpal</td>
<td>Oppositional devices</td>
</tr>
<tr>
<td>Transcarpal</td>
<td>Body-powered hand or hook</td>
</tr>
<tr>
<td>Wrist disarticulation</td>
<td>Forearm socket, wrist component, and terminal device</td>
</tr>
<tr>
<td>Transradial</td>
<td>Proximal arm socket, elbow hinge (passive, active, or externally powered), forearm lever arm, wrist component, and terminal device</td>
</tr>
<tr>
<td>Elbow disarticulation</td>
<td>Harness system and transhumeral components</td>
</tr>
<tr>
<td>Transhumeral</td>
<td>Harness system, shoulder socket and transhumeral components</td>
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<tr>
<td>Shoulder disarticulation</td>
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<tr>
<td>Interscapulothoracic disarticulation</td>
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<tr>
<td><strong>Lower extremity</strong></td>
<td></td>
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<tr>
<td>Transphalangeal</td>
<td>Toe-filler</td>
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<tr>
<td>Toe disarticulation</td>
<td>Foot plate</td>
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<tr>
<td>Ray amputation</td>
<td>Partial foot to tibial height prosthesis</td>
</tr>
<tr>
<td>Transmetatarsal</td>
<td>Socket to knee, low-profile foot</td>
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<tr>
<td>Transtarsal</td>
<td>Socket with foot and ankle</td>
</tr>
<tr>
<td>Syme</td>
<td>Socket, knee joint, and ankle/foot complex</td>
</tr>
<tr>
<td>Transfibular</td>
<td>Socket is total contact shell, hip/knee joints, and ankle/foot complex</td>
</tr>
<tr>
<td>Knee disarticulation</td>
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<tr>
<td>Transfemoral</td>
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<td>Hip disarticulation</td>
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<tr>
<td>Hip disarticulation</td>
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<tr>
<td>Hemipelvectomy</td>
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The rehabilitation program for successful use of lower extremity prosthetics begins with donning/doffing of the device, transfer skills, activities to build wearing tolerance, practice to reinforce balance reactions, and pre-ambulation skills. Preparatory weight-bearing treatment for use of a lower extremity prosthesis usually begins on a tilt table, progressing to standing and then ambulation in the parallel bars. The rehabilitation goals should address stability, ease of movement, energy efficiency, and the appearance of natural gait. Table 47.1 outlines the common components of lower extremity prostheses and their functions.

Lower limb prosthetics require the following minimum requirements for successful use: upright trunk control, sufficient upper body strength, adequate lower body stability and control, static and dynamic balance skills, and good postural alignment. Lower extremity prosthetic fitting begins when the patient’s wounds are well-healed and will tolerate pressure and weight-bearing. Lower limb devices may be either preparatory or definitive. Table 47.2 details types of lower extremity amputations by level and identifies the appropriate prosthetic and components.

Two common sequelae of traumatic amputations are phantom sensation and phantom pain. Phantom sensation is the perceived sense that the amputated limb is still present. It is not typically characterized as painful by the patient. The patient may report feeling that the amputated limb has shrunk (telescoping). In contrast, phantom pain is the sensation of pain originating in the amputated part. Upon assessment the pain may or may not be dermatomal in presentation. The patient may report constant burning, stinging, cramping, or a feeling of awkward positioning. Phantom pain is most intense acutely, gradually becomes intermittent, is worse at night, and is often exacerbated by stress/anxiety. From a therapy standpoint, phantom sensation may be managed by desensitization techniques, while phantom pain may be responsive to transcutaneous electrical nerve stimulation.

### Burn scar management

#### History

The burn wound, like any other wound, heals by the formation of scar at the injured site in order to replace the destroyed tissues. Scar is defined as the fibrous tissue replacing normal tissues destroyed by injury or disease. In the case of a burn injury, the scars, if not managed appropriately, have the potential of becoming thick and raised, resulting in scar hypertrophy. Hypertrophic scars are not cosmetically appealing and if they cross any joints they may restrict function. Pressure therapy for scar management is a very old and established component of a recovering burn patient’s continuing rehabilitation program. Extensive historical notes on the earliest references to scarring are provided by Linares and colleagues who attribute the first full medical description of scars to Petz in 1790. They also state that the first medical reference to the use of pressure for treatment was written by Johnson in 1678 referring to the work of Ambroise Paré in the 16th century. Other historical events noted by Linares et al. are: first known accounts of the use of pressure for treat-
Figure 47.22 Algorithm showing the process of prosthetic evaluation and fitting.
ment of children in 1859; use of elastic bandages in 1860; adhesive plaster for pressure in 1881, and use of traction to treat scars in 1902. Linares’ review includes descriptions of Nason’s work in 1942, in which he noted that ischemia produced by pressure arrests the overproduction of scar tissue, ‘where the imprint of the elastic of an undergarment or a belt may be seen – no keloid is present.’ Another historical review by Ward\(^5\) reveals that Blair in 1924 reported the positive influence of pressure on healing wounds. Nason’s application of the ‘constant pressure’ principle included developing a type of neck splint made of a piece of dental impression compound or a piece of heavy felt strapped tightly over the scar for 6–8 weeks and possibly longer. Later, various splints were developed utilizing pressure and immobilization.\(^4^4\) In the 1960s Silverstein and Larson observed the influence of pressure on healing burns. Their observations led to the manufacture of customized pressure garments that revolutionized scar management in the 1970s, which continues to-date, with some modifications.\(^4^2,4^3\)

**The scar**

As the burn wound progresses toward healing, or after skin grafting operations take place, scars begin to form. Generally, the deeper the burns are, the higher the risk is for the development of hypertrophic scars. Also, the longer a wound remains open, the higher the chances for hypertrophic scar formation.\(^4^4,4^5\) As the wound begins the healing process, collagen fibers develop to bridge the wound, forming an immature (active) scar, which appears as a red, raised and rigid mass.\(^4^6–4^9\) Abston reported that pressure therapy during maturation led to a flatter, softer and a more devascularized scar.\(^5^0\) Burn scars may take up to 2 years or longer to mature. Factors contributing to the formation of hypertrophic scars may include: wound infection, genetics, immunological factors, repeated harvesting of donor sites, altered ground substance, age, chronic inflammatory process, location of the injury, and tension.\(^5^1\) Scar hypertrophy may be evident at 8–12 weeks after wound closure.\(^5^2\)

**Scar assessment**

Devoting clinical time to evaluate burn scars can be time consuming, but is imperative to our practice for efficiency in the remodeling and overall function of the burn scar. In order to better study the process of scar maturation, ongoing research is looking at alternative techniques in assessing the state of scars. The Vancouver Burn Scar Assessment developed by Sullivan and colleagues is a subjective way of rating the burn scar pigmentation, vascularility, pliability and height, and is widely used amongst clinicians.\(^5^3,5^4\) Hambleton and colleagues studied the thickness of scars with ultrasonic scanning. This method, which is completely non-invasive, allows for a comparison of the thickness of dermal tissue in the traumatized area with that in the normal skin at regular intervals following initial healing.\(^5^5\) Darvey et al. described a technique for the objective assessment of scars utilizing a video camera image on a computer and quantitatively analyzing the color of the scars using a custom-written computer program.\(^5^6\) Esposito used a modified tonometer to measure skin tone which correlates to skin pliability and tension.\(^5^7\) Bartell and co-workers used the elastometer properties of normal versus injured skin. In his study, Bartell showed that scars, if left untreated, will show improvement over time.\(^5^8\) Hosoda utilized laser flowmetry to determine the perfusion of hypertrophic scars versus non-hypertrophic scars.\(^5^9\) Other studies suggest that laser Doppler flowmetry and monitoring of transcutaneous oxygen tension may in the future be ways of determining scar maturation.\(^6^0\)

**Treatment of hypertrophic scars**

To this date, hypertrophic scars remain very problematic and difficult to manage. Even though the mechanism of scar maturation is not yet well understood, clinically the accepted protocol to treat hypertrophic scars includes the use of pressure therapy, which should be instituted early on in the maturation process of the burn scar. Means of pressure therapy include pressure garments, inserts, and conforming orthotics. Once the skin has healed enough to withstand sheering, massage and heat modalities may be utilized as an adjunct in scar management. The use of pressure in effectively depressing scars was well documented by Silverstein and Larson in the 1970s; their observations and studies sparked the near-universal use of pressure garments. When an active scar is compressed, it blanches, which indicates decreased blood flow in the area.\(^6^1\) Less blood leads to decreased oxygen in the tissues, which in turns leads into decreased collagen production, which brings a balance between collagen synthesis and collagen breakdown (lysis). When a balance in the production and breakdown of collagen is established, the resultant scar appears flatter.\(^6^2\) Kealey et al. conducted a prospective randomized study to compare efficacy of pressure garment therapy in patients with burns. Patients were randomly assigned to receive either pressure garment therapy or no pressure garment therapy. Assessment of the maturity of scar included use of the Vancouver Burn Scar Assessment Scale. The results on 113 patients studied in the follow-up revealed no significant differences between groups when age, body surface area burned, length of hospital stay or time to wound maturation were compared.\(^6^3\) In addition to this study, other studies have reported problems related to lack of adherence and discomfort, blistering, ulceration or scar breakdown, swelling of extremities and skeletal and dental deformity due to excessive pressures, which often leads to stoppage of treatment, significant side-effects and deformity.\(^6^4–6^6\)

On the other hand, studies have also reported benefits of pressure garments.\(^6^7,7^0\) The reader is referred to various recent excellent review articles on the efficacy or lack of efficacy of pressure garments in the management of hypertrophic burn scars.\(^3^,7^4\) Reasons for the absence of unequivocal evidence is that garments must be worn continuously for a least 23 h a day, making compliance or adherence difficult.\(^6^6,7^5,7^6\) In addition, the optimal pressure that must be applied to the scar for treatment is not known.\(^6^6,7^5,7^6\) Thus, the studies and debates continue, and, at least until more evidence is gathered, pressure therapy with the familiar elastic garments is still prescribed. Patients and families would no doubt feel relieved if the data eventually show that pressure does not make a significant difference in long-term outcomes. However, it should be noted that the studies thus far include neither the examination of burns over joints nor do they include burns of the hands, neck and face. In addition, none...
of the studies to date address the use of pressure in the form of splints, another source of discomfort and tension for burned children and their families. None of the known studies yet have broached the face with an attempt to determine the efficacy of pressure versus no pressure. Facial pressure garments in children may pose problems due to interference with growth. 79,80 We recommend that these patients should be closely monitored for normal facial and dental development by physicians including dental specialists. The elastic hood and underlying silicone face pad present special problems for patients, and some extreme challenges for the adults trying to assist a burned child or adolescent. The elastic mask and hood, covering head, face, and hair, effectively hides the identity of the person wearing it. It is perceived by children as sinister, associated with ‘bad men’ or monsters, and most children who have worn this garment can relay stories of being ridiculed by strangers who did not know the purpose of the garment. Emotional expressiveness, usually apparent in facial movements, is hidden by the hood. More than one child has explained non-adherence with the prescribed wearing of the elastic mask with a statement similar to ‘I want my friends to see me laugh.’ A study by Groce et al. compared the elastic mask and hood with silicone pad to the transparent silicone face mask and found no significant differences between the amount of pressure applied by each to the forehead, cheeks, and chin. 81 Many children have expressed a preference for, and seem to wear more readily, the transparent mask. This study should make it easier for them to be granted their choice – an important event during a time when so much is happening to them outside of their control.

**Pressure therapy**

As long as the scars are active, they may be influenced by pressure therapy. However, not all burn scars require pressure. Patients with burn wounds which heal within 7–14 days do not need pressure therapy. Those patients whose wounds heal within 14–21 days are closely monitored for pressure therapy needs and may be generally advised to use pressure garments prophylactically. A wound that heals after 21 days will require the use of pressure garments.52 The correct amount of pressure in suppressing the hypertrophic scar has not yet been determined. Pressure of as little as 10 mmHg may be effective in remodeling the scar tissue over time. Pressures over 40 mmHg, however, may be destructive to tissues and cause paresthesias. 52 Early forms of pressure therapy include the use of elastic bandages directly applied on the newly healed skin or on top of the burn dressings. The use of conforming thermoplastics along with elastic bandages may also be utilized as means of early pressure therapy. 52 Once the wounds are almost or completely closed, tubular elastic bandages such as Tubigrip™ may be utilized. These tubular bandages are offered in different sizes and accommodate all anatomical circumferences. Care should be taken in applying these tubular bandages so that the fragile skin or the freshly applied skin grafts do not shear, or the minimal dressing underneath is not disturbed. The burn therapist should be aware that these tubular bandages are materials made of a single elastic thread spiraling through the weave of the fabric, and disturbance of the continuous elastic by cutting holes into it will alter the pressure gradient provided by these materials. The tubular elastic bandages should be doubled over the skin surface area treated in order to provide adequate pressure. 81 Early pressure application over the hand and digits can be accomplished by the use of thin, elastic and self-adherent wraps such as Coban™ (Fig. 47.23). This form of pressure is excellent for adult and pediatric patients for controlling edema and aids in the early scar management of hands when the shearing forces of a glove cannot be tolerated. Small children are excellent candidates for Coban™ gloves versus a garment glove because of compliance issues, comprehension of instructions in assisting with the application of a custom glove and difficulties in obtaining accurate measurements for a custom glove. Coban™ may be applied over the burn dressings or directly onto the healed digits. The burn therapist needs to be aware that if Coban™ is wrapped too tight it may deform the interosseous structures of the healing hand. However, if Coban™ is wrapped too loose it may encourage swelling of the hands when used in combination with arm elastic garments. Coban™ strips are pre-cut approximately twice the length of the digits to be wrapped. Each strip is wrapped in a spiral fashion beginning at the nail bed of each digit, overlapping half of the Coban™ width and ending in the adjacent web space. Each fingertip needs to be exposed so that blood circulation can be monitored at all times. The Coban™ is stretched from 0–25% of the entire elasticity of each strip. Once all web spaces are covered, the rest of the hand is wrapped with Coban™, extending approximately 1 inch past the wrist joint. No skin areas should be visible once the Coban™ glove is completed. If small hand areas remain uncovered, a small piece of Coban™ is stretched over the area and adheres to the rest of the Coban™. When the glove is completed, the therapist should very superficially lubricate the entire glove with lotion in order to eliminate the adherent effect of the Coban™ and allow for the functional use of the hand. Coban™ should be removed on a daily basis by the therapist or the caregiver. Removal of Coban™ should be done carefully by cutting off or unwrapping each digit strip individually to avoid disturbing any small wound healing. The use of prefabricated interim pressure garments is widely
accepted and utilized in burn rehabilitation. These garments are available commercially by different companies and they include pieces for the entire body. Interim garments which are made of softer materials introduce the burn patient to circumferential pressure and protect the newly healed skin. Another reason for using these garments prior to ordering custom-made garments is to allow for the patient’s weight to stabilize (post-acute hospitalization) and any remaining edema to subside. In some cases where obtaining custom-made garments on regular intervals (approximately 12 weeks) is not an option the recommendation should be that interim garments should be the choice for long-term pressure therapy. Once the patient’s weight has stabilized, edema has subsided and the skin is able to withstand some shearing (approx. 3–4 weeks post-wound closure), measurements are taken for the fabrication of custom-made pressure garments (Fig. 47.24). Today several companies specialize in the fabrication of these garments. Clinically, custom therapeutic pressure for the prevention, control and correction of scar hypertrophy averages 24–28 mmHg, which is approximately equal and opposing to the capillary pressure (25 mmHg). At this pressure level, many researchers believe that scars may be altered.84 In order for pressure therapy to be effective, pressure garments need to be worn at all times, day and night. They should only be removed for bathing and on occasion during exercises should they interfere with movements. Each order is duplicated so one set of garments can be worn while the other is being washed. Today, pressure garment companies offer multiple colors of materials and for the pediatric population cartoon characters may be sewed on the garments to make them cosmetically appealing and improve the patients’ compliance.85 The burn therapist should choose a reputable company that provides excellent service and support for the patient and the therapist. The company’s willingness and flexibility to manufacture non-standard garments, availability of special options, cost and turnaround time should be taken into consideration when selecting the burn center’s pressure garment provider.86

**Inserts**

Inserts are widely utilized in burn rehabilitation as an adjunct to achieving effective pressure over certain anatomical locations where pressure garments do not provide adequate pressure. These locations include concave body areas such as the face, neck, antecubital fossae, sternum, palm of the hands, web spaces, upper back and arches of the feet. These materials come commercially prefabricated or may be custom-made by the burn therapist or the medical sculpture technician. Inserts come in different forms such as silicone gels, elastomers, putties mixed with a silicone catalyst, skin care silastic pads, foam and even in the form of hard thermoplastic materials contouring to different anatomical locations. The experienced burn therapist chooses the appropriate insert material best suitable for the patient according to the stage of scar maturation and skin sensitivity. Generally, pressure therapy begins with a soft, thin and elastic insert and progresses to a more rigid insert in depressing the more unyielding burn scar. Inserts need to be worn underneath pressure garments, starting with a few hours of application and progressing as tolerated, toward a 24-hour application. They should be removed frequently for cleaning (warm water and soap), drying and application of cornstarch to avoid scar maceration and skin breakdown. Patients may be allergic to certain insert materials so the burn therapist may try different inserts until one is found to be best tolerated by the patient’s skin. In cases of scar maceration, blisters, skin breakdown, contact dermatitis and a rash or an allergic reaction, inserts should be removed until healing occurs. Silicone, a polymer, based on the element silicon, appears to be the trend in the treatment of hypertrophic scars. To date, the mechanism of how silicone affects the burn scar is not known. Clinically, silicone has been observed to depress the height of hypertrophic scars, prevent shrinking of fresh skin grafts (hard elastomer silicone pads versus silicone gel pads), and increase the pliability of a scar, thus allowing for increase in the range of motion of affected joints. Patients report that silicone is soothing to the skin and aids in decreasing pain. Silicone, being occlusive, may cause the collection of excessive moisture and cause skin maceration if not removed frequently for cleaning and drying. Its disadvantages are that it is very expensive and short-lived.87–89 The therapist should look for silicone gel pads with a non-shearing protective medium on the non-skin surface in order for the gel to last longer. Also, buying larger-size gel pads and cutting them to fit the patient’s need may be a cost-effective method for today’s shrinking clinic budgets.

Other insert materials include liquid silicone elastomer, which when mixed with a catalyst form a solid but elastic insert (Fig. 47.25). The experienced therapist could create custom inserts for difficult anatomical locations such as the face and web spaces using this technique. Prosthetic Foam™ is a liquid-based silicone elastomer which, when mixed with a catalyst, solidifies in the form of a very pliable foam insert.
Comprehensive rehabilitation of the burn patient

A silicone elastomer facemask may be created utilizing the existing positive facial mold and is worn under facial pressure garments (Fig. 47.26b). The use of the clear and silastic masks is preferred over the use of just a facial garment as they provide conforming pressure around facial openings (eyes, nose, and mouth). Frequently, the burn therapist manufactures the clear mask to be worn during the day and the silastic mask along with the facial garment to be worn at night.42,90–92

Burn scar massage

Once the burn scars have matured enough to tolerate shearing forces, massage may be incorporated into the scar management regimen. Scar massage is an effective modality for maintaining joint mobility in the case of contractures. It aids in softening or remodeling the scar tissues by freeing adhering fibrous bands, allowing the scars to become more elastic and stretchy, thus improving joint mobility. Initially, the therapist may utilize a non-frictional massage applying mostly stationary pressure to skin blanching and mobilizing the skin surface without friction. Utilization of lubricants during this massage technique should be avoided. As the skin begins to tolerate frictional massage, the scar tissue is manipulated in rotary, parallel and perpendicular motions, using a lubricant and pressing the skin to blanching. Clinically, massage is found to alleviate itching. It is also used for desensitization purposes. An electrical massager with a heat attachment may be used along with lubrication, as heat and massage in combination may increase scar pliability. Massage should be performed at least twice daily (3–5 times preferred) for 5–10 min on each treated body surface. The burn therapist should frequently assess the skin condition in avoiding further injuries. The patient and/or family are instructed on home massage techniques and electrical massagers may be issued for home use. In order to combat the effects of scar tissue, a burn therapist must utilize all options to achieve a functional outcome. Even though underutilized, therapeutic modalities should be employed in a rehabilitation therapist’s treatment plan for scar hypertrophy and preserving facial features.
management. Therapeutic heat is the most common modality used in burn scar management. Application of heat may permit easier elongation of scar tissue through increased extensibility of connective tissue. Heat relaxes tissues and makes them pliable in preparation for mobilization. Heat modalities may include hot packs, paraffin wax, fluidotherapy and ultrasound. Even though the use of therapeutic heat as an adjunct to rehabilitation is well documented, therapeutic heat modalities are infrequently being utilized in burn rehabilitation. 

Caution should be used in the application of heat modalities on patients who have sustained a burn injury. Patients may not be able to tolerate heat over areas of healed or grafted burns due to hypersensitivity. Conversely, patients with diminished sensation are unable to determine if the temperature is appropriate and are at risk for further injury. Although caution needs to be taken, the use of therapeutic heat in burn patients can provide an effective method of increasing burn scar extensibility.

The use of passive stretch in conjunction with therapeutic heat greatly increases the effectiveness of the treatment. Studies have shown that the use of therapeutic heat during a slow load prolonged stretch is an effective method for attaining rapid and lasting increases in range of motion when compared to low load prolonged stretch alone. Warren et al. reported that low loads for prolonged periods of time were found to produce significantly greater residual length in rat tail tendon, especially at elevated temperatures.

Hot packs can provide superficial heat to burn scars and assist with stretching contractures. Common treatments in burn rehabilitation include using hot packs alone before treatment or in conjunction with therapeutic exercise such as active range of motion or prolonged stretch. Because of the shallow depth of heat penetration, hot packs may have little effect on deeper layers of scar tissue.

Ultrasound has been used by rehabilitation therapists to increase temperatures deep within the tissue. Reported benefits of ultrasound in the treatment of burn scar include increased extensibility of collagen tissue, increased blood flow, and elevation of pain thresholds. Application of topical therapeutic ultrasound to scar tissue has been reported to produce a tissue temperature rise, which leads to an increase in the extensibility of collagen. The combination of ultrasound and passive stretch was found to further increase tissue elongation.

Paraffin is an effective heat modality used most commonly for the hands or feet. Paraffin provides extensibility on collagen produced by the heat and may also be beneficial because of the softening of the scar by the mineral oil in the paraffin. The use of passive stretch in conjunction with paraffin has been shown to increase joint range of motion and was found to make patient’s skin noticeably softer and more pliable after the use of paraffin. Similar to other heating modalities, paraffin has been found to increase range of motion in conjunction with stretching compared to stretching alone.

Burn scar management is a complicated and lengthy process and for it to be successfully completed the patient and caregivers should be committed to follow the therapist’s recommendations. Extensive training should take place addressing the use and care of pressure garments, inserts, lubrication and other therapeutic scar management procedures to be performed by the patients and their caregivers. Lubricants, which do not contain perfume and other skin irritants should be selected and applied (at least 2–3 times daily) to the healing skin. Lubricants with sun protection factor (SPF) of at least 15 are recommended. Written instructions with pictures and diagrams along with videos addressing scar management should accompany the patient home upon discharge from the hospital. Follow-up visits to the burn or rehabilitation clinic for the assessment of overall recovery to include garments, inserts and other home therapeutic interventions are needed for the patient to successfully complete his/her burn rehabilitation. The therapists’ knowledge, creativity and continuing research in improving the currently existing scar management techniques may be the key to positive outcomes in pressure therapy.

**Therapeutic exercise**

Burns often result in devastating injuries that severely impact a person’s ability to perform functional activities through severe deconditioning, range of motion limitations, weakness, and fatigue. Therapeutic exercise is one of the central interventions used by physical and occupational therapists to combat the multitude of problems associated with burn injuries. Therapeutic exercise is defined as scientific supervision of bodily movement with or without apparatus, for purpose of restoring normal function to diseased or injured tissues. The use of therapeutic exercise in conjunction with a comprehensive rehabilitation plan helps to prevent deformings contractures and to maintain strength in both the involved and uninvolved extremities.

Even though painful and extensive therapy is required during the long rehabilitation process, the results are for the most part dependent on the patients’ and families understanding, involvement and dedication to the treatment. The goals of therapeutic exercise in burn rehabilitation are to:

- reduce the effects of edema and immobilization;
- maintain functional joint motion and muscle strength;
- stretch the scar tissue;
- return the patient to optimal level of function.

Exercise prescription is an ongoing process which is altered according to the patient’s medical status and changing needs. In the conservative treatment of burn wounds, a vigorous physical therapy program is instituted immediately so as to maintain function. Postoperatively, exercises involving autografted skin over joints are usually discontinued for 4–5 days. Escharotomies, fasciotomies, heterografts, and synthetic dressings are not contraindications for exercise. Early mobilization to decrease edema, proper exercise techniques, and accurate documentation of function are more important than the type of wound closure.

One of the most common and clinically significant complications after severe burn injuries are burn scar contractures which lead to decreased range of motion and joint deformities. Scar contracture and joint mobility limitations are the result of the shortening of immature connective tissue. Therapy aims to prevent deformity and the subsequent limitation of movement. In circumferential burns, both the flexor and extensor surfaces are at risk of
contracture. Therapeutic exercise in conjunction with splinting should promote agonist and antagonist movements around those joints in order to maintain mobility. Treatment is tailored to each individual patient, with independent living being the ultimate goal throughout the rehabilitation continuum.

Therapeutic exercise begins immediately after the burn. For a patient being treated conservatively, movement helps maintain strength and range of motion, and aids in circulation and healing. Exercise is initially painful and the very first repetition is often the most difficult. Discomfort is due to stretching skin which has lost its lubricating mechanism and has become dry and tight. Movement itself decreases pain. Each subsequent repetition will be easier as the skin stretches, and the muscle pumping action of active movement helps resolve edema, thus significantly reducing pain.

To show the progression of exercise throughout a patient’s stay after a burn injury, exercise will be discussed in terms of the rehabilitation phases as described by Richard.

Exercise during the acute rehabilitation phase

The acute rehabilitation phase is defined as the time from admission until about the time that a patient’s wounds are 50% closed or skin grafting for wound closure has begun. Early therapeutic intervention on the burn unit has long term implications for restoration of function. Early initiation of burn rehabilitation with an emphasis on several factors including early ambulation and a focus on preventing joint contracture through stretching exercise has been shown to be effective in reducing contractures.

During the early part of the acute rehabilitation phase, exercise goals are resolution of edema, maintenance of joint mobility, and prevention of respiratory complications which can often be performed without interfering with life saving measures.

During this phase, patients spend long periods of time without getting out of bed due either to their medical status or postoperative immobilization after skin grafting. Results of patient immobilization due to burn injury include decreased cardiovascular fitness, disuse osteoporosis, increased risk of thromboemboli, pulmonary complications, decubiti, and muscle atrophy. Due to the patient’s medical status during the acute rehabilitation phase, patients may not be able to tolerate vigorous exercise. It is therefore recommended that exercise programs focus on increased frequency of treatment sessions that are shorter in duration.

Active range of motion exercises are significant in the reduction of edema in the extremities and can begin within 24–72 h after burn injury. Active range of motion exercise is performed independently by a patient. This is the form of exercise most recommended because it stretches healing skin and provides strength-inducing benefits. Frequent exercise performed actively (with voluntary muscle contribution) by a patient promotes the greatest increase in movement. Active range of motion exercises are vital during burn rehabilitation to counteract the effects of prolonged bed rest and muscle atrophy as well as maintain range of motion and prevent contractures. The best exercise for a joint affected by burns is complete active range of motion. Active range of motion more adequately addresses the patient’s functional physiological and psychological needs, rather than passive range of motion. Although active range of motion may be a superior form of exercise for a burn patient, its use during the acute burn phase may be somewhat limited. Medical status, intubation, as well as fear and anxiety may all make active range of motion exercises difficult to carry out.

If a patient can actively participate in movement but cannot move actively through their full range of motion, active-assistive range of motion is appropriate. Active-assistive range of motion exercises utilize the same principles as active; however, a patient is ‘assisted’ by an outside force (therapist or assistive device) to achieve the full range of motion. A patient will achieve improvements in strength and range of motion, but not equal to those provided by active exercise. Therapists should use their judgment in letting the patient perform as much of the exercise as possible actively and only assisting when needed.

While active range may be the most beneficial, it can be difficult to initiate after admission due to the patient’s medical status and level of responsiveness. Critically ill, septic, and heavily medicated patients are often unable to cooperate in active exercises. In these conditions, passive exercise is used to maintain range of motion, assess joint motion, and elongate tissues. Passive range of motion exercises are an important factor in preventing contractures and maintaining range of motion when a patient cannot or does not willing actively move through their available range of motion. Although passive range of motion requires less energy expenditure, it does not fulfill as many of the patient’s needs as active exercise. The use of a continuous passive motion (CPM) device has been documented to be an effective modality for improving joint range of motion. Rehabilitation advances have shown CPM treatment to be a viable option because of its benefits to soft tissue remodeling, joint nutrition, wound healing, and venous dynamics.

Strengthening exercises are of great importance throughout the continuum of burn rehabilitation to combat muscle atrophy and can begin during the acute rehabilitation phase. Resistive exercises are used to maintain or increase strength, range of motion, proprioception, and coordination. Due to patients’ level of consciousness and comprehension during the acute rehabilitation phase strengthening exercises may be difficult to institute and should start with simple exercises progressing as the patient’s status improves. Isometric exercises are beneficial to maintain muscle strength when a patient is on bed rest and is comfortable for the patient to perform while requiring a minimal amount of energy expenditure. The benefit of isometric exercise is that a patient does not ‘forget’ how to contract the muscle, a common phenomenon with periods of prolonged immobilization. Isometric exercise also helps in maintaining muscle strength. Manual resistance can also be applied gently by the therapist as the patient contracts his muscles and attempts motion against the resistance, or the patient is asked to maintain a position then resistance is applied.

Another important aspect of a patient’s recovery is the ability to ambulate. Ambulation can begin as soon as possible after admission as long as the patient is medically stable. Severe weakness, impaired motor control, decreased cognitive status, pain, risk of graft shearing are all factors that can make a ambulation a difficult task. An Unna boot may be applied at time of skin grafting to the lower extremity and
have been several studies that have shown the benefits of strength and endurance. Ambulation exercises may also contribute to early patient ambulation. The Unna boot is a bandage impregnated with calamine lotion and zinc oxide which, when applied over the grafted lower extremity (six layers), hardens to a semi-rigid dressing resembling a plaster cast. This cast-like total contact dressing provides uniform support to the fresh skin graft and when reinforced with a thermoplastic or plaster splint facilitates early ambulation. An Unna boot may be applied for up to 7 days post-grafting, though it could be removed earlier for the inspection of the skin graft. If removed, a new Unna boot needs to be fabricated depending on the burn center’s lower extremity postoperative immobilization protocol. 118

Primary goals of ambulation include maintaining lower extremity range of motion, reducing the risk of thrombophlebitis, preventing decubiti, providing mild cardiovascular conditioning, and maintaining or increasing strength and endurance. Ambulation exercises may also help prevent decubiti, provide mild, cardiovascular conditioning, and increase appetite. In addition, ambulatory patients have fewer problems with lower extremity contractures and physical endurance. 108

All wounds must have the proper dressings prior to ambulation. Lower extremity burn wounds should be wrapped with elastic bandages in order to facilitate capillary support. Wrapping which incorporates the figure-of-eight pattern has been reported to provide better pressure than the spiral wrap, perhaps due to increased vascular support. 119

As with other exercise, proper positioning facilitates proper gait. The patient who has been allowed to assume a position of comfort will have difficulty extending the hips and knees during ambulation. The ankle may be tight, limiting plantigrade position when in the upright position. If the joints are in the normal alignment, the amount of pain and energy are greatly reduced.

In the past, it was common practice to have patients placed on bed rest for long periods of time after autograft application to the lower extremities, approximately 5–10 days after autograft application. More recently however, there have been several studies that have shown the benefits of earlier postoperative ambulation. The intermediate phase is the time surrounding closure of the wound and extending up until the time of complete wound closure. 110 The prevention of functional impairments becomes the focus of therapeutic exercise as patients begin to achieve wound coverage. The goals of exercise during this timeframe include the stretching of healing skin, maintaining full joint range of motion, preserving motor skill coordination, promoting functional independence, and maintaining strength and endurance to minimize muscle atrophy. 106

Exercise during the intermediate rehabilitation phase

The intermediate phase is the time surrounding closure of the wound and extending up until the time of complete wound closure. 110 The prevention of functional impairments becomes the focus of therapeutic exercise as patients begin to achieve wound coverage. The goals of exercise during this timeframe include the stretching of healing skin, maintaining full joint range of motion, preserving motor skill coordination, promoting functional independence, and maintaining strength and endurance to minimize muscle atrophy. 106

As wounds close, scar formation begins which leads to contractures that limit range of motion and impede function which makes exercise become even more important. As a patient’s medical status continues to improve and operations become less frequent, more time can be allotted to spend with rehabilitation. Increased alertness and improved medical status also lead to increased involvement of the patient in rehabilitation. As the patient advances medically, the therapeutic course should become more challenging.

While pure passive range of motion should be utilized less during the intermediate phase of rehabilitation due to increased ability of the patient to move actively, it still serves an important purpose. Passive range of motion provides an opportunity to assess joint movement and determine if the patient can attain as much movement actively as the therapist can passively. 116

Another form of passive movement that can be utilized by a rehabilitation therapist is the sustained stretch. Sustained...
stretch becomes an important intervention as the formation of burn scars lead to contractures. Sustained stretching exercises are performed with a slow, prolonged force. Gentle, sustained stretch is more effective than multiple repetitive movements in gaining length of burned tissues. Slow sustained stretch is considered to be one of the most effective methods to combat the strong destructive forces that lead to contracture formation.129 Connective tissue has the characteristic of plastic elongation under constant tension. Therefore, correction of contractures around joints can be accomplished most effectively by the application of prolonged stretching to the shortened connective tissues.130 When applying a sustained stretch, two factors may be considered when applying pressure to an extremity: blanching of the scar tissue and the patient’s response.131 While this is an effective treatment for range of motion limitations, it can be uncomfortable or painful for patients. It is important to impart enough force on the affected extremity to produce plastic elongation without causing trauma to the tissues or to the patient.

Concerning ambulation it is important that the therapist set goals daily for the patient to achieve and to progress the patient to walk further while providing the least amount of support needed. As the patient begins to ambulate more, it is important that the rehabilitation therapist frequently assess the patient’s gait. Any gait deviations must be identified and corrected before they become lasting habits. As the patient begins to ambulate further with less assistance, they become more confident in their abilities. Increased independence provides the patient with a sense of functional independence.112

Long-term rehabilitation phase

The long-term phase occupies the timeframe from wound closure or discharge from the acute hospital setting until such time that a patient has received maximal benefit from rehabilitation services.110

As the patient nears discharge from the acute hospital setting, the patient will be given more responsibility over their exercise program. As the patient progresses, they will be expected to perform beyond their daily rehabilitation treatment sessions. Patient compliance with home exercise programs is vital to increasing functional independence.

During the long-term rehabilitation phase, patients should progress to ambulating independently community distances. Gait pattern should be refined to become more efficient without any gait deviations. If the patient is able to progress further, rehabilitation therapists can challenge the patient by having them ambulate on uneven surfaces, navigate around various obstacles, and climb stairs. It is important that the patient be able to ambulate in their normal surroundings, not just in the confines of the rehabilitation department.

Most burn rehabilitation programs emphasize functional gains and prevention of contractures with only modest attention to aerobic conditioning.132 If ROM is lacking, the therapist’s priority should be to treat the limitation in motion rather than strengthening the patient as normal healthy muscle is unable to generate the force required to elongate burn scar tissue.113

The role of exercise physiology in burn rehabilitation

Exercise for the outpatient

This section describes methodology used in designing an exercise-training program for persons with severe burns that have been discharged from the hospital. Exercise training is defined here as ‘a planned, structured and repetitive body movement done to improve or maintain one or more components of physical fitness.’132,133 The evidence for the use of exercise in the outpatient setting and the methodology presented here is based primarily on the outpatient exercise program that is implemented in severely burned children at Shriners Hospitals for Children in Galveston, Texas and in some severely burned adults.134 This exercise program is supplemented by physical and occupational therapy. The program has proven beneficial in children 7–18 years of age.134,135 Recently, effects of a music- and movement-based exercise program on children younger than 7 years of age has been assessed in a pilot study at Shriners Burns Hospital in Galveston, Texas. The effects include increases, as well as maintenance, of range of motion in children that participated in a movement and music program versus those that did not. The principles in designing an exercise program in children and adults with severe burns is based largely on guidelines offered to healthy, non-burned children and adults (Fig. 47.28).132,133,114–116

Exercise evaluation

It is important to perform an initial evaluation of risks factors and/or symptoms for various chronic conditions concomitant to the burn. These include pre-existing conditions...
such as chronic cardiovascular, pulmonary and metabolic diseases. The objective of the exercise evaluations is to obtain information to optimize safety during exercise testing and training and also to develop a sound and effective exercise rehabilitation program.

Health screening before exercise evaluation should begin with the collection of subjective data. This should include evaluation of exercise or sports interests, objectives, level of activity prior to burn, functional limitations (e.g. loss of digits, lower body bilateral amputee), and other pertinent information. To our knowledge, there are no burn-specific physical activity questionnaires. However, simple questionnaires for assessing pre-burn physical activity exist and can be modified to fit a specific given population. This evaluation can consist of muscle strength, cardiopulmonary, and muscle/joint flexibility testing. The information gathered during the subjective and objective evaluations can then be used to design a structured exercise program or plan to be carried out at home or at an exercise facility. Finally, a plan to periodically re-evaluate subjective and objective data, and the exercise program itself should be incorporated.

Subjective data

Characterization of limitations or problems of a patient should be done. Obtaining a history of pre-burn physical activity or habits, present medical complaints, symptoms and limitations is crucial to develop a sound exercise program. Symptoms or limitations which may affect exercise tolerance may include pain during ambulation, weakness in ambulation, itching, joint contractures, amputations, shortness of breath, or ease of fatigability. In addition, you should note present medications and note possible effects of these. Following the evaluation of subjective data, an exercise evaluation to gather objective data on the patient’s exercise or physical capacity should be performed.

Objective data

Assessment of objective data includes age, height and weight, %TBSA burn, and percent full-thickness burn. Variables before, during, and after a cardiopulmonary exercise test (CPET) should be obtained if possible. These include heart rate, blood pressure, Borg’s rated perceived exertion (RPE), basic electrocardiogram (ECG), and spirometry. However, if a CPET is not possible, an exercise program that is effective can also be designed. Assessment of upper and lower body muscle strength should also be done. This includes assessment of peak strength levels (if possible), as well as determining the loads or weights that will be used during the resistive component of the exercise program. The assessment of peak muscle strength can be accomplished during knee or elbow extension but can also be accomplished during a handgrip. These tests involve peak-to-maximal efforts, and good communication between patient and tester must exist. In addition, there is a developmental mental maturity that must exist in order for many of these objective data to be maximally helpful. We recommend a chronological age of ≥7 years, though children as young as 3–4 years of age have been tested. Peak Oxygen Consumption or Aerobic Exercise Capacity. All patients should undergo a standardized exercise test for objectively evaluating peak aerobic exercise capacity. We use the treadmill exercise test and the modified Bruce treadmill protocol. We must note that other treadmill protocols such as the ‘Ramp Protocol’, can also be used. In addition, if it is not possible for the patient to be tested on a treadmill, a cycle ergometer or arm ergometer can also be used to evaluate or assess the physical conditioning of the patient, before starting exercise rehabilitation or a training program. In addition, estimation of aerobic capacity is also possible with exercise field tests such as the Cooper 12-min test or the 1.5 mile run test. Heart rate can be easily obtained with monitors. Oxygen consumption (VO₂) should be measured if possible, but requires more expensive equipment that can perform continuous breath-by-breath analysis of inspired and expired gases, flow, and volume. For the Bruce protocol, speed and grade begin at 1.7 mph and 0%, respectively. Thereafter, the speed and level of incline are increased every 3 min. Patients are constantly encouraged to complete 3 min stages and the test is terminated when peak volitional effort is achieved. Additional variables that can be collected during the test include blood pressure, Borg’s rated perceived exertion (RPE), basic electrocardiogram (ECG), and spirometry. The peak VO₂ and peak heart rate can then be used to establish the intensity at which patients will exercise during the exercise program.

Strength measurements. Isokinetic dynamometry strength testing should be performed to assess muscle function and to later on evaluate progress. If using the Biodex Isokinetic dynamometer, the test can be done on the dominant leg extensors and/or leg with burns. We recommend testing at tests such as gait analysis, balance time or reaction time. Finally, assessment of functional performance can also be done such as sit-and-stand scores, timed walk/jog and or lifting. The results of these evaluations will be used to identify major problem areas, to write an exercise prescription or to design the exercise program, and to assess progress during and after an exercise program.

Exercise testing

The objectives for exercise testing involve many factors. The primary objectives during cardiopulmonary testing are to evaluate physical work capacity and cardiorespiratory or aerobic fitness, observe cardiorespiratory and metabolic responses, establish bases for an appropriate exercise prescription, and assess changes in fitness due to exercise training. The primary objectives during muscular function and testing include measuring muscle strength (absolute and relative to body weight), measuring antagonist/agonist muscle ratios, assessing changes in body composition (lean mass, fat mass, and bone density), and providing a basis for the progressive resistance exercise prescription. Exercise testing should be conducted prior to the start of any exercise rehabilitation program and again at the end to evaluate its efficacy. Sometimes, if the program is of long duration, a mid-point evaluation can be done. It is important to consider the patient’s developmental maturity when performing exercise testing and training. We recommend a chronological age of ≥7 years, although children as young as 3–4 years of age have been tested.
various angular velocities, such as 150°/s, 90°/s or 180°/s. The patients are seated and their position stabilized with a restraining strap over the mid-thigh, pelvis, and trunk. All patients should be familiarized with the equipment before the actual test starts. We recommend that first, the procedure is demonstrated by the administrator of the test. Second, the test procedure is explained to the patients, and then, patients are allowed to practice the actual movement during three submaximal repetitions without load as warm-up. Third, after the three submaximal warm-up repetitions, 10 maximum voluntary muscle contractions (full extension and flexion) can be performed consecutively without rest in between. The amount of repetitions and the number of times the sets of repetitions can be varied. For example, we recommend 10 repetitions and two sets, with a 2 min rest interval between sets. Values of peak torque, total work, and average power are calculated by the Biodex software system, and progress of muscle function can be monitored.

**Three Repetition Maximum Test (3RM)**

Typically, before starting a resistive training program, it is useful to determine a safe and effective load for patients to use during workouts. To determine the amount of weight or load that can be used as baseline or starting loads, the ‘Repetition Maximum (RM)’ method can be used. We recommend the 3-repetition maximum load (3RM), which is determined as follows. After an instruction period on correct weight-lifting technique, the patient warms up with lever arm and bar (or wooden dowel) and is allowed to become familiar with the movement. After this, the patient lifts a weight that allows successful completion of 4 repetitions. If the fourth repetition is achieved successfully and with correct technique, a 1 min resting period should be allowed. After the resting period, a progressively increased amount of weight or load is instructed to be lifted at least four times. If the patient lifts a weight that allows successful completion of 3 repetitions, with the fourth repetition not being volitionally possible, due to fatigue or inability to maintain correct technique, the test is terminated and the amount of weight lifted from the successful set is recorded as their individual 3RM. We recommend the order of exercises to be from exercises that involve large muscle groups to ones that involve smaller muscle groups: bench press, leg press, shoulder press, leg extension, biceps curl, leg curl and triceps curl.

**Body composition measurement**

Patients with severe burns lose a significant amount of lean body mass (LBM). Therefore, assessment of LBM should be made. Additionally, assessment of bone mass and fat mass should also be made. We assess body composition using dual-energy X-ray absorptiometry (DXA). DXA with pediatric software can measure the attenuation of two X-ray beams; one which is high energy and one which is low energy. These measurements are then compared with standard models of thickness used for bone and soft tissue. Subsequently, the calculated soft tissue is separated into LBM and fat mass. This is a great measurement to also assess progress of the program and if applicable, nutritional interventions. However, the DXA machine is expensive. It is not known if other methods to measure body composition such as underwater weighing or bio-impedance are applicable to patients with burns due to the burn scars.

Additional testing can include major muscle and joint flexibility using sit-and-reach or goniometry for ROM. Other tests include gait analysis, balance, or reaction time. Sit-and-stand scores, timed walk/jog, and/or lifting exercises may also be used to assess functional performance. The results of all evaluations should help in identifying problem areas, writing an exercise prescription, designing an exercise program, and assessing progress during and after an exercise program.

**Components of an exercise program**

An exercise program typically consists of a warm-up phase, an endurance phase, recreational activities (optional), and a cool-down phase. While aerobic training activities should be done 3–5 days per week, complementary flexibility and resistance exercises may be performed at a lower frequency (2–3 days per week). Flexibility exercises can be included as part of the warm-up or cool-down, or done at a separate time. Resistive training is often performed on alternate days to aerobic training; however, both types of activities can be combined into the same workout session. Typically, the warm-up period will be of approximately 5–10 min, though it can be longer. This will be followed by a stimulus or endurance phase of 20–60 min, and a cool-down period of approximately 5–10 min. Aerobic and resistance training should be prescribed in specific terms of intensity, duration, frequency, and mode of exercise. Each of these terms will be discussed in greater detail later. An optional recreational game may occasionally substitute the endurance phase. However, because of potential difficulties in setting an appropriate intensity for an appropriate length of time, it is suggested that it be done as a complement to the endurance phase. If a recreational activity is added to the endurance phase, then the shortening of the endurance phase should be carefully considered though maintaining a minimum of 20 min.

**Warm-up stage**

Prior to the endurance phase, a variety of very light exercises, low-intensity calisthenics, should be done to improve the transition from rest to the endurance phase of the exercise session. The emphasis at the onset of an exercise session is to gradually increase the level of activity until the proper intensity is reached to begin the endurance phase. Stretching exercises to increase the range of motion of the joints involved in the activity were previously included in the warm-up. However, recently, evidence has been introduced to contraindicate the inclusion of stretching during the warm-up period.

In fact, evidence suggests that a pre-exercise warm-up that consists of only light aerobic exercise to increase body temperature is adequate for increasing flexibility before an exercise session. For example, patients might walk moderately fast during the endurance phase, but might conclude the warm-up period with slow, easy walking. However, a moderate walk (e.g. 3.5 mph) can be a warm-up for a patient that jogs at 5.5 mph during the endurance phase. Heart rate may
be monitored or assessed if needed to ensure that the warm-up activity is not too strenuous.

Endurance stage
The endurance phase develops cardiorespiratory or aerobic fitness and includes 20–60 min of continuous or intermittent (minimum of 10 min bouts accumulated throughout the day) aerobic activity. Duration depends on the intensity of the activity; thus, moderate-intensity activity should be conducted over a longer period of time (≥30 min), and, conversely, individuals training at higher levels of intensity (i.e., vigorous exercise) should train for at least ≥20 min. The most effective exercises for the endurance phase employ large muscle groups in activities that are rhythmic or dynamic in nature. Sports such as soccer, basketball or tennis also have aerobic conditioning potential if a sufficient amount of time for inducing aerobic improvement is achieved (minimum of 20 min total). On the other hand, activities like golf and bowling are unlikely to elicit a cardiovascular training effect, but are enjoyable and may yield health-related, as well as psychosocial, benefits.

Recreational activities
The inclusion of enjoyable recreational activities during (or immediately after) the endurance phase often enhances compliance with the exercise program. Rules of the games may need to be modified to adjust skill level requirements, competition, and to ensure safety. The outcome of the game (winning or losing) should be of lesser importance than the safety, participation and enjoyment of the patient. It is important to remember that recreational activities complement the endurance phase and should not consistently replace it. Recreational activities may also promote development or improvements in psychosocial health, by increasing the amount of social interaction.

Cool-down stage
At the end of the activity session, about 2–5 min of cool-down activities – slow walking and stretching exercises – are recommended to gradually return HR and BP toward resting levels. This period includes exercises of diminishing intensities; e.g., slower walking or jogging, calisthenics and stretching exercises. This part of the exercise session is viewed as important in reducing the chance of a hypotensive episode after the exercise session, as well as other cardiovascular complications.

Exercise prescription
Some basic exercise physiology principles should be kept in mind when designing an exercise program for burned patients. Two such principles are: the progressive overload and the specificity principles. The progressive overload principle refers to the observation that a body system must be exercised at a level above that to which it is presently accustomed in order for a training effect to occur. The system or tissue gradually adapts to this overload. The typical variables that comprise the overload include the intensity, duration and frequency (days per week) of exercise. The principle of specificity refers to the concept that the training effect is specific to the muscle fibers involved in the activity. Specificity also refers to the types of training in a very specific manner to produce a very specific adaptation or outcome. If a muscle is engaged in endurance types of exercise, the primary adaptations are in the capillary and mitochondrial number, which increase the aerobic capacity of the muscle. These principles are applicable to burned patients; however, it must be noted that a high intensity of exercise is not needed (low to moderate intensity) to achieve health-related benefits. On the other hand, to achieve athletic performance or competitive-related goals, moderate to high levels of intensity will be required. Another consideration that should be kept in mind when designing an exercise program is the age of the population. Prepubescent children are very different in their physiological and mental response to exercise training than postpubescent children. Older adults also have different health and physical problems than younger adults. It is for these reasons that medical exams, as well as exercise evaluations, are strongly recommended prior to starting an exercise program. It is beyond the scope of this chapter to address these differences and/or problems. However, general guidelines for both children and adults are offered and it is suggested to the reader to seek additional information for population-specific recommendations or position stands on exercise and physical activity, from associations such as the American College of Sports Medicine (http://www.acsm.org/publications/positionStands.htm); the American Academy of Pediatrics (http://www.aap.org/); the American Medical Association (http://www.ama-assn.org/), or the American Heart Association (http://www.americanheart.org/).

Aerobic training
Intensity
To improve aerobic fitness, generally the intensity of exercise should be between 65% and 95% of the peak heart rate or between 45% and 85% of the heart rate reserve (HRR). The heart rate reserve is the difference between peak heart rate obtained during a CPET and resting heart rate. The range of heart rate values associated with the exercise intensity needed to induce an improvement in cardiovascular fitness is termed the ‘target heart rate zone.’

The peak heart rate (HRpeak) is obtained from the CPET. However, when this not possible, one simple method to estimate HRpeak is to use the formula (220 minus age). This formula may not be applicable to young children, so we recommend that in children, rated perceived exertion (see below), together with the heart rate obtained during a maximal exercise capacity test, be used. The rating of perceived exertion or (RPE) scale can also be used as a guideline in setting the intensity of exercise. The RPE is a valuable and reliable indicator of exercise tolerance, but also intensity. This method of monitoring exercise intensity is useful when it is impossible to obtain a HRpeak or if patients are on medications which affect heart rate such as β-blockers. There are currently two RPE scales that are commonly used: the original or category scale, which rates exercise intensity on a scale of 6–20 and the revised or category-ratio scale of 0–10. It is reported that the category-ratio scale uses terminology better understood by the subject,
thereby providing the tester with more valid information. It has been found that an aerobic training effect and the threshold for the start of anaerobic training are achieved at a rating of 'somewhat hard' to 'hard,' which approximates a rating of 12–16 on the category scale or 4–5 on the category-ratio scale.156 Finally, if a patient cannot use the heart rate method or the RPE method, the ‘Talk Test’ can also be used as a highly consistent method to set and monitor intensity of exercise.157

The ‘Talk Test’, or the point where speech first becomes difficult, approximates exercise intensity almost exactly equivalent to the ventilatory threshold. One could advise the patient to exercise at an intensity where speech is comfortable. When speech becomes uncomfortable, one can assume, based on previous studies, that exercise intensity is consistently above ventilatory threshold or above the desired intensity of exercise needed for general improvements in fitness.157 It must be noted that when setting the exercise intensity, safety and effectiveness are linked. An appropriate intensity should also be well suited to result in a long-term, active lifestyle.

Duration
The duration of an aerobic exercise session is closely linked to the intensity of the activity, i.e. a longer duration of low-intensity exercise can be accomplished than of high-intensity exercise. In general, the duration of exercise for burned patients once discharged, should be from 5 to 20 min the first week. This will depend on the functional status of the patient and also pain tolerance.

If the patient tolerates up to 20 min, then this duration is appropriate. The objective should be to exercise 20–60 min of aerobic activity. This can be accomplished continuously or intermittently throughout the day, with a minimum of 10 min bouts. Typically a duration of 20–30 min at between 40% and 50%, up to 85% of the heart rate reserve (excluding time for warm-up and cool-down) should induce health and fitness improvements.152,158

In burned patients with extremely low aerobic capacity or endurance, 4–6 5-min bouts with rest periods between bouts would be a program that would induce benefits. The duration of the exercise sessions (or bouts) can be progressively increased over time. However, as mentioned before, a high intensity of exercise or very long duration of exercise are not needed to achieve health-related benefits, particularly during the initial stages of outpatient exercise rehabilitation.

Frequency
It is reported that deconditioned persons may improve cardiorespiratory fitness with only twice-weekly exercise.152 However, it is generally agreed that optimal training frequency appears to be achieved with 3–5 workouts per week. The additional benefits of more frequent training appear to be minimal, whereas the incidence of lower extremity injuries increases abruptly. For those exercising at 60–80% HRR, an exercise frequency of 3 days per week is sufficient to improve or maintain VO2peak. When exercising at the lower end of the intensity continuum, exercising more than 3 days per week is not deleterious. Patients with extremely low functional capacities may benefit from multiple, short (5 days per week) exercise sessions. Clearly, the number of exercise sessions per week will vary depending on the patient’s limitations, but also by the patient and caregiver’s lifestyle.

Mode
The most important consideration in choosing the mode of exercise for the endurance phase of the sessions is to engage large muscle groups in activities that are rhythmic or dynamic. The greatest improvements in aerobic fitness result when exercise involves the use of large muscle groups over appropriate periods of time (Fig. 47.29). The mode of exercises includes treadmill walking/running, rowing or cycling. If no treadmill is available, then walk/jog at a track or field is appropriate. Swimming is also an appropriate mode of exercise, though closure of burn wounds should be ensured to minimize infection of wound or the contamination of others. Endurance games are also appropriate modes of exercise.

Progression of exercise
We recommend starting slowly and safely progressing in duration and intensity, but also in transitioning from early activities to activities that are more difficult to perform. This method of progression decreases the potential for inducing excessive muscle soreness, causing new injuries or aggravating old injuries. The emphasis on slow-to-moderate walking as the primary activity early in the fitness program is consistent with this recommendation, and the participant must be educated to not move too quickly into the more demanding activities. For example, if the individual can walk about 1–2 miles without fatigue, then the progression to a walk-jog or jogging program is a reasonable recommendation.

The recommended rate of progression in an exercise conditioning program depends on the functional capacity, medical and health status, pain tolerance, location of burns, age, individual activity preferences and goals, and an individual’s tolerance to the current level of training. For burned patients, the endurance aspect of the exercise prescription can be divided into three stages of progression: initial, improvement, and maintenance.133

Initial conditioning stage
The initial stage should include light and moderate muscular endurance activities (e.g. 40–60% of HRR). These exercises typically have a low potential for injury, and induce minimal muscle soreness and pain. Exercise adherence may be compromised if the level or intensity of exercises in the program is initiated too aggressively. The amount of time spent in this stage varies depending on the individual’s adaptation to the exercise program. We recommend at least 4 weeks of initial conditioning. The duration of the exercise session during the initial stage may begin with approximately 15–20 min and progress up to 30 min, at least 3 times per week. Deconditioned individuals should be allowed more time for adaptation at each stage of conditioning. Age of the individual should also be taken into account when progressions are recommended, as adaptation to conditioning likely takes longer in older individuals, but also in extremely debilitated individuals.152
Improvement stage

The goal of the improvement stage of training is to provide a progressive increase in the overall exercise stimulus, which will allow for significant improvements in aerobic fitness. The improvement stage of the exercise-conditioning program differs from the initial stage in that the participant is progressed at a more rapid rate. This stage is reported to usually last from 4 to 5 months, during which, intensity is progressively increased within the upper half of the target range of 50–85% of HRR. However, our experience in a 12-week training program in children 7–18 years of age indicates that after 3–4 weeks of initial conditioning, some patients are able to start the improvement stage. In this stage, duration may be increased consistently every 2–3 weeks until participants are able to exercise at a moderate-to-vigorous intensity for 20–30 min continuously. During this stage, interval training may also be beneficial, provided the total time engaged in moderate to vigorous exercise is at least 20 min.

Maintenance stage

The goal of this stage of training is the long-term maintenance of the cardiopulmonary fitness level developed during the improvement stage. This stage of the exercise program may begin at any time the participant has reached previously agreed objectives. During this stage, the individual may no longer be interested in continually increasing the conditioning stimulus. Also, in this stage, further improvement may be none to minimal, but continuing the same workout routine enables individuals to maintain their fitness levels, as well as develop the healthy exercise habit. At this point, it is suggested that goals of the program be re-examined and new goals or objectives set.

Resistive training

Strength is defined as the ability to produce force, and the ability to produce force over an extended period of time is referred to as muscular endurance. Both muscle strength and endurance impact activities of daily living (ADL) because ADL require a percentage of an individual’s muscular capacity to perform these everyday tasks. Severe burns result in extensive and prolonged loss of muscle mass; therefore, resistance training, which increases LBM, should be part of an exercise rehabilitation program for burned individuals.134

Similarly to designing the aerobic portion of an exercise program, the resistive training portion of an exercise program follows similar principles of training. Both the overload principle and specificity principle are applicable. Strict rules of proper technique and safety must be observed to reduce...
potential for injury or accidents. A normal breathing pattern should be maintained, with breath holding avoided. Breath holding during lifting can induce excessive increases in blood pressure, which in individuals with hypertension, diabetes or other medical risks can be dangerous.

Similarly to the aerobic exercise program, testing or evaluation of muscle function precedes the resistive exercise program. This helps individuals identify problem areas, areas in need of required improvement, goal setting and tracking progress of individuals. In addition, muscle strength tests have value in determining back to work status. Some of these tests involve peak to maximal muscular efforts. These tests can be done on weight machines or using dumbbells.

Typically these tests are done at 100% of one-repetition maximum (1RM), but can also be done at 3RM. For extremely deconditioned individuals or for very young children, modification of these guidelines can involve testing using 3RM up to 12RM if needed. An important point to remember is that safety of the individual is crucial. Therefore, correct technique during all testing and training must be observed. The order of exercises or muscle tested is also important. It is recommended that large muscle groups are tested first and alternate between upper body and lower body. For example, a 3RM test may be done in the following order of exercises: bench press, leg press (or squats), shoulder press, leg extension, biceps curl, leg curl, and triceps curl. The three repetitions maximum (3RM) load can be determined as follows. After an instruction period on correct weight-lifting technique, the patient or individual warms up with lever arm and bar (or wooden dowel) and is allowed to become familiarized with the equipment and to be instructed on proper weight-lifting techniques. Initially, the weight or load the subjects will lift should be set at 50–60% of their individual 3RM for 12–15 repetitions for the first 1–2 weeks. Thereafter, the load lifted can be increased to 70–75% (8–10 repetitions) of their individual 3RM and continued for weeks 2 or 3, to week 6. After this, the training intensity can be increased to 75–85% (8–12 repetitions) of the 3RM and implemented from weeks 7–12 or longer. We must note that these are guidelines to provide an estimate of training load and have some limitations. Another method of determining training load is to perform multiple RM based on the number of repetitions planned for the specific exercise. For example, if 8 repetitions were desired for biceps curl, then one would test the individual by having him or her perform 8RM testing sets.

**Number of repetitions**
It is believed that muscle strength and endurance can be obtained simultaneously by performing a specific number of repetitions within a certain range (e.g. 6–10 repetitions). The number of repetitions will depend on load lifted (% of 1RM) and also the objective or goals set at the start of the exercise program. However, we recommend 8–12 repetitions, at a moderate to high intensity to improve both muscle strength and endurance.

**Amount of load lifted**
Commonly, a certain percentage of the 1RM or 3RM is used as guideline for choosing a training load. The amount of load lifted can be as much as 100% of 1RM or as little as lifting no load. We recommend initially, during the first week of training, allowing the individual to become familiarized with the exercise equipment and to be instructed on proper weight-lifting techniques. Initially, the weight or load the subjects will lift should be set at 50–60% of their individual 3RM for 12–15 repetitions for the first 1–2 weeks. Thereafter, the load lifted can be increased to 70–75% (8–10 repetitions) of their individual 3RM and continued for weeks 2 or 3, to week 6. After this, the training intensity can be increased to 75–85% (8–12 repetitions) of the 3RM and implemented from weeks 7–12 or longer. We must note that these are guidelines to provide an estimate of training load and have some limitations. Another method of determining training load is to perform multiple RM based on the number of repetitions planned for the specific exercise. For example, if 8 repetitions were desired for biceps curl, then one would test the individual by having him or her perform 8RM testing sets.

**Number of sets**
There are very limited data in children as to whether 3 sets or 1 set is required to increase muscle strength and hypertrophy. Much of the adult-based literature supports similar responses of muscle strength, muscle endurance, hypertrophy between single and multiple set resistance training programs. It is important to stress two points: (1) the difference in strength gains is typically more pronounced in trained individuals; and (2) both single and multiple training increases strength. The first point is usually not the case with burned patients, and the second point stresses the fact that an increase in strength is expected with resistance training compared to the standard of care in burned individuals.
Exercise order

There are many methods of ordering resistance exercises. One of these is to arrange core exercises, then assistance exercises. Another method is to arrange large muscle groups and then small muscle groups. Yet another method, which allows the individual to recover more fully between exercises, is to alternate upper body with lower body exercises. This is especially well-suited for deconditioned individuals or untrained individuals. For example, we have successfully implemented, in severely burned children, the following order of resistive exercises: bench press, leg press or squats, shoulder press, leg extension, biceps curl, leg curl, triceps curl, and toe raises. These exercises can be done on variable resistance machines or free weights. Both free weights, bands or variable resistance machines are appropriate for burned individuals wishing to participate in an exercise program.

Rest periods

As a general rule, it is important to allow enough time between exercises to perform the next exercise in proper form. The rest period also varies depending on the individual’s training status and also specific training objectives.

Progressive overload

In order for improvements to continue over time, it is important to carefully monitor and chart the individual’s workouts or loads lifted. Progressive overload can be applied in a variety of ways, such as increasing the weight lifted, increasing repetitions while keeping load constant, or decreasing rest periods. A conservative method termed the ‘2-for-2 rule’ is suggested. This rule states ‘if an individual can perform two or more repetitions above his or her assigned repetitions goal in the last set, for two consecutive workouts for a specific exercise, then weight or load should be added to that specific exercise for the next training session.’ For example, if the assigned number of sets and repetitions is 3 sets of 8–12 reps in the chest press machine, and if the individual performs 12 reps in all 3 sets, after several workout sessions (the specific number of sessions depends on many factors), the individual is able to complete 12 reps in the third set (i.e. the last set) for two consecutive workout sessions, then in the following training session, the load for that exercise should be increased. The amount of weight (load) that should be added depends on factors such as the physical condition of the individual (strong or weak) and the body area (upper body or lower body). In general, an increase of...
1–2 kg for a less trained, weaker individual is suggested for upper body exercises, while an increment of 2–4 kg is suggested for lower body exercises.¹⁰⁰

**Example of an exercise program**

An example of our exercise rehabilitation program is described below (Table 47.3). The results of this program are published.⁹⁰−⁹² This program has been successfully implemented at discharge from hospital, but also at 6 months post-burn.

**Important considerations**

- The ultimate goal of an exercise rehabilitation program should be to improve physical function. However, the means by which this is achieved are also important. An exercise program should be challenging, effective, but also must be safe and fun. It should also promote lifelong healthy habits. This will maximize compliance with the exercise program.
- The American College of Sports Medicine (ACSM) has an extensive list of absolute and relative contraindications to exercise and exercise testing that should be carefully considered when designing an exercise program for adults or children. These contraindications will also pertain to individuals with severe burns.
- Individual goals should be established early in the exercise program. Whenever possible, they should be developed by the participant with the guidance of an exercise professional. The goals or objectives must be realistic, and an intrinsic or extrinsic rewards system should be implemented at that time.
- It is recommended that exercise professionals work together with an occupational and/or physical therapist to avoid duplication of services, as well as to identify areas in need of special attention.
- Based on our clinical experience with children and adolescent patients, individuals with severe burns should participate, as soon as possible after hospital discharge, in a structured exercise program. This program should be supervised and if possible conducted in the presence of a trained professional. However, if this is not possible, the exercise program, with some commonsense guidelines, should offer a choice for safe and effective participation.
- For adults, a careful medical and exercise evaluation should be conducted prior to starting an exercise program. Cardiovascular or pulmonary problems, as well as other conditions, such as diabetes, must be identified prior to starting an exercise program to avoid potential fatal or near-fatal complications.
- It is important to get the burned individual started with an exercise program or a more active lifestyle as soon as possible, but it is never too late to get started, regardless of the time post-burn.
- When beginning the exercise program, it is better to start slowly and build up gradually, than to start too fast and risk injury.
- For children, avoid using very intense or maximal (1RM) resistance training or testing. Gradual progression is of utmost importance to avoid injury and to promote exercise adherence.
- The individual should ‘listen’ to his/her body. During and after workouts, the individual (and supervisor) should be alert to signs of a potential health problem as a result of overexertion. Signs may include pain, shortness of breath, dizziness or nausea.
- Be flexible and allow individuals to be flexible. Do not rigidly stick to a schedule if the patient does not feel up to it. If he/she is overly tired or under the weather, allow them to take a day or two off.

**Table 47.3** Brief description of the Shriners Hospitals for Children – Galveston Hospital outpatient exercise rehabilitation program

<table>
<thead>
<tr>
<th>Aerobic workout</th>
<th>Intensity</th>
<th>70–85% of each individual’s previously determined individual peak aerobic capacity. However, heart rate and rated perceived exertion is obtained at regular intervals during aerobic exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Duration</td>
<td>20–40 min</td>
</tr>
<tr>
<td></td>
<td>Frequency</td>
<td>3–5 days per week</td>
</tr>
<tr>
<td></td>
<td>Mode</td>
<td>Aerobic exercise on treadmills, cycle ergometers, arm ergometers, rowing machines, and outdoor activities such as soccer or kickball</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Resistance workout</th>
<th>Exercise type</th>
<th>Upper and lower body of core and assistance exercises</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Amount of load lifted and number of repetitions</td>
<td>The weight or load-lifted set at approximately 50–60% of each individual 3RM and lifted for 4–10 repetitions for three sets. During the 2nd week, the lifting load increased to 70–75% (3 sets, 4–10 repetitions) of their individual 3RM and continued for weeks 2–6. After this, training intensity is increased to 80–85% (3 sets, 8–12 repetitions) of the 3RM and implemented from weeks 7–12</td>
</tr>
<tr>
<td></td>
<td>Frequency</td>
<td>2–3 days per week, alternating days of work with days of recovery</td>
</tr>
<tr>
<td></td>
<td>Number of sets</td>
<td>2–3 sets</td>
</tr>
<tr>
<td></td>
<td>Exercise order</td>
<td>Bench press, leg press or squats, shoulder press, biceps curl, leg curl, triceps curl, toe raises, and abdominals</td>
</tr>
<tr>
<td></td>
<td>Type of exercises</td>
<td>Eight basic resistance exercises done using variable-resistance machines or free weights: 4 for upper body, 3 for lower body, and abdominals</td>
</tr>
<tr>
<td></td>
<td>Rest period</td>
<td>A rest interval of approximately 1 min between sets</td>
</tr>
</tbody>
</table>

**Note:** Each exercise training session consisted of resistance and aerobic exercises, with aerobic exercise preceding resistance exercise. This outpatient exercise program should be supplemented with outpatient physical and occupational home therapy, or home activities.
Monitor the individual’s progress. Reassess fitness every 6 weeks. You may notice that you need to increase the amount of time you exercise in order to continue improving (if part of the original goals).

The exercise professional or individual should keep an exercise diary or logbook to help chart progress.

If the patient loses motivation, try setting new goals or try a new activity (or activities). Sometimes, bringing a friend or family member into the program may help in motivation. Incorporate variety into the exercise routine.

Finally, work on conveying to the patient or client that a fun and safe exercise program can result in maintenance of lifelong physical, as well as psychosocial, healthy habits (Fig. 47.31).

**Patient/caregiver education**

When patients are being discharged from the acute hospital stay, it is vital that they leave with an individualized home exercise program. Splinting and positioning, Activity of Daily Living performance, scar control measures, and psychosocial issues should also be addressed. This program can then be advanced to allow for progression during the ever-changing phases that the burned individual goes through, in what may be in excess of a 2-year recovery period. During follow-up visits, screening monitoring of the patient’s progress regarding the above categories is performed and the necessary changes are completed. This detailed knowledge of the patient’s status will allow the burn team to coordinate the care for the patient so that recommendations can be followed through. Providing the patients with a checklist is a valuable tool to enable patients to assume some control of the rehabilitation process, enable them to track their progress and encourage their continuation of the program. Many patients and their caregivers are often overwhelmed by the rehabilitation program. It takes an extraordinary amount of time and energy to plan and participate in a home exercise/instruction program. Continuous communication among the patient, caregiver and the burn team will ease the patient’s transition into recovery.

One way of helping patients with the exercise program is to establish communication with a community-based exercise center, such as a commercial or hospital-based facility. Often, direct and constant communication between a burn hospital’s rehabilitation department, exercise physiologists and/or physician and as well as the community-based

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**Figure 47.31** Overall long-term burn rehabilitation should result in lifelong physical as well as psychosocial healthy habits and improvements in quality of life.
exercise facility (i.e. personal trainer), will maximize the potential for adherence to and the efficacy of such ‘home’ exercise programs, by adding supervision and structure.

**Summary**

The rehabilitation of burn patients, although challenging, can be rewarding to all involved in their care. Continuous evaluation of interventions provided is needed to ensure each patient’s maximum functional outcome. Experience, education and research will produce therapeutic interventions that will optimize each patient’s recovery. Ultimately, the goal of the rehabilitation team is to provide the patient with the means for a productive life.

**Further reading**


References


90. Derwin-Baruch L. UV-A therapists meet the challenge of scar management. OT Week. 1993;April 15:15-17.


Musculoskeletal changes secondary to thermal burns

E. Burke Evans

Information

Among trauma states the burn is alone in the tendency of its wound, even as it heals, to create musculoskeletal deformity. In addition, the protracted burn illness that accompanies severe burns may result in other skeletal change. Box 48.1 presents a classification of musculoskeletal changes secondary to burns; from that, the most commonly occurring and clinically significant alterations have been selected for discussion.

Changes confined to bone

Osteoporosis

Osteoporosis is the most frequently occurring post-burn change involving bone. Klein’s ongoing studies suggest that, among persons with serious burns, reduction of bone mass density is pervasive. Stated causes of osteoporosis in thermal burns are bed confinement, immobilization, hyperemia, reflex vasomotor phenomena, and adrenocortical hyperactivity. In Chapter 26 of this book, Klein reviews the effects of burn injury on bone metabolism. In this section only what is clinically apparent is discussed.

The more extensive the burn and the greater the number of complications, the longer the patient may be bed-confined and relatively immobile. The onset of osteoporosis is accelerated and its intensity more marked in the burn illness that features a hypermetabolic state. If a single extremity of an otherwise normal person is immobilized for a long period of time because of local trauma, as with a fracture, loss of bone density can be easily seen in a plain radiograph. So with burns isolated to the extremities, the bones of affected extremities become osteoporotic; and, in persons with generalized burns, the bones of deeply burned extremities may show more profound mineral loss than is observed in non-burned extremities or in the axial skeleton (Fig. 48.1). Van der Wiel et al. found in an X-ray absorptiometry study of 16 adults with fractures of one tibia that there was eventual loss of bone mineral density in the contralateral femur and in the lumbar spine, but to a lesser degree than in the ipsilateral femur. These findings, although not strictly analogous to those observed in burns, nevertheless point to the occurrence of generalized osteoporosis in other trauma states and the difference in loss of bone density relative to local factors. In fractures or in burns, impaired mobility and local hyperemia could account for this difference.

Another characteristic of the osteoporosis of burns that seems to set it apart is its persistence, not just until restoration of the anabolic state, but for months and years after the burn has healed (Fig. 48.2). This phenomenon may be most clearly observed in patients who have survived 90% burns, but Klein records less than normal bone among even moderately burned children as long as 17 months after injury. Muscle atrophy and/or the failure or inability of the person to return to the preburn level of physical activity may account in part for this protracted state of reduced bone mineralization.

There is no way to prevent osteoporosis in a patient whose burn is of such severity as to require an extended period of bed confinement. On the other hand, the advance of bone atrophy can at least be favorably modified even among patients with large burns if mobilization and active exercise are initiated soon after the burn. The bones of the axial skeleton, the pelvis, and the lower extremities are most efficiently stressed by weight bearing. Thus, standing is a priority measure, and it is common practice now to walk patients to tolerance prior to permanent wound cover. Muscle contraction alone may help forestall bone atrophy and bone is better stressed if the contraction is resisted. Incrementally increasing resistance during motion or at the termination of an arc of motion or to muscle contraction in an extremity that may not be moved can be supplied by anyone who attends a responsive patient. Isometric muscle contraction can be exacted from even extensively burned patients and is important for bone stress, for maintaining muscle tone and bulk, and for the patient’s continuing ready identification of the affected extremity. Passive motion has no effect on bone and thus does not figure in the prevention of osteoporosis. Other preventive measures, e.g. closure of the wound and maintenance of nutrition, are routine in critical burn care. Treatment of established osteoporosis involves the more aggressive employment of measures for prevention. There are no long-term comparative studies, however, that persuasively measure the effectiveness of exercise, diet, medication, or modality in the treatment of osteoporosis in any state.
will in time sequestrate, separating at a well-defined fissure between dead and living bone. With minor or moderate exposure, the bone will usually survive long enough for bordering granulation tissue to cover it. For large defects, it may be useful to drill closely spaced holes through the exposed cortex so as to encourage buds of granulation tissue to emerge from the still vascular medullary canal. Another way to encourage granulation tissue formation over exposed bone is with superficial decortication with an osteotome or burr to expose the capillaries of the inner cortex. With these practices, there is little risk for infecting the bone. It may be that there is sufficient centripetal pressure to discourage the invasion of organisms when the holes are fresh and that the holes are rapidly sealed by blood clot and advancing tissue. There are no reports of deep bone infection related to cortex drilling.

With open fractures at the base of a major soft tissue burn wound, bone infection is probably inevitable. Even so, the infection tends to remain at the fracture site and not to involve the rest of the bone, so that local debridement and stabilization of the soft tissue wound are all that are required for treatment. Dowling reported osteomyelitis of the tibia related to an open bimalleolar fracture in an extensively burned extremity. On the other hand, osteomyelitis developed in neither of the two open fractures reported separately by Choctaw and Wang. We treated three patients in whom open fractures of the femur complicated thigh burns. Each case required aggressive and repeated debridement. One fracture was treated in traction, while the other two were treated with external fixators. In one of the patients, who was admitted 8 months after acute burn, there was established osteomyelitis of the femur in relation to the exposed fracture. Osteomyelitis did not develop in

### Osteomyelitis

In burns, bones can become infected by exposure of bone by the burn; by an open fracture accompanying the burn; by extension of infection from a septic joint; by introduction of organisms along traction pins or internal fracture fixation devices; or by blood-borne organisms of bacteremia. Considering the apparent great liability for seriously burned patients to develop osteomyelitis, it is surprising that it does not regularly occur. As it turns out, clinically significant osteomyelitis in burned patients is rare. Antibiotics given for the general state may prevent seeding of the bone or may repress any small focus of bone infection.

The cortex of long bones is a good barrier to surface organisms. Even exposure of cortex will have little adverse effect if the blood supply of the bone remains intact. Prolonged exposure will kill the outer layer of the cortex, which

### Box 48.1 Classification of musculoskeletal changes secondary to burns

#### Alterations limited to bone
- Osteoporosis
- Periosteal new bone formation
- Irregular ossification
- Diaphyseal exostosis
- Acromutilation of fingers
- Pathological fracture
- Osteomyelitis
- Necrosis and tangential sequestration

#### Alterations involving pericapsular structures
- Pericapsular calcification
- Heterotopic para-articular ossification
- Osteophyte formation

#### Alterations involving the joint proper
- Dislocation
- Chondrolysis
- Septic arthritis
- Spontaneous dissolution
- Ankylosis

#### Alterations involving muscles and tendons
- Desiccation of tendons
- Fibrosis of muscles

#### Alterations secondary to soft tissue
- Muscle and joint contractures
- Malposition of joints
- Scoliosis

#### Soft tissue injury
- Compartment syndrome
- Nerve injury

#### Abnormalities of growth
- Acceleration and retardation
- Destruction of growth plate.
either of the other patients; in the end, all three had sound femurs.

When traction pins are directed through burned skin for the treatment of fractures or for suspension of a burned extremity, the factors favoring development of infection along the pin track and the formation of cigarette sequestra are:

- the introduction or migration of organisms from the burn wound;
- linear pressure of the traction pin;
- prolonged traction;
- excessive movement of the extremity leading to loosening of the pin;
- sealing of the pin sites.

For traction or suspension, pins may be inserted through acutely burned skin, through eschar, through granulation tissue, or later through ischemic burn scar, which may be colonized with uncommon and antibiotic-resistant organisms. No amount of local cleaning is likely to sterilize the surface through which the pin must pass, yet it seems that organisms in sufficient numbers to colonize are rarely introduced in this manner.

Figure 48.2 (a) Advanced osteoporosis in the hands of a 14-year-old male 9 months after 100% TBSA burn. All growth plates are open. (b) At 24 months after injury, osteoporosis persists and there is irregular closure of metacarpal and phalangeal growth plates. (c) At 8 months after injury, growth plates of distal tibiae and fibulae remain open. (d) At 24 months after injury, distal growth plates of tibiae and fibulae are closed. Other major growth plates remain open. Osteoporosis is unchanged.
Local low-grade infections usually resolve when pins are removed if the pin sites are vigorously curetted of granulation tissue. In one case in which a four-pin custom external fixator was used in the treatment of an open infection of the elbow, there resulted diffuse osteomyelitis of the humerus and radius. The infection was controlled with antibiotics and without surgery after the pins were removed. This case was included in Barret’s report of skeletal pinning in 41 severely burned children.1 In experience with the Ilizarov system for correction of skeletal deformity in burns, one patient developed a pin track infection of such severity as to require removal of the pin, curettage, and intravenous antibiotics for control of methicillin-resistant Staphylococcus.12

Hematogenous osteomyelitis and that due to spread from an infected joint are rare. There is no report of the occurrence of either entity in association with burns. Were bone infection of this sort to be recognized, effective treatment would depend upon the identification of the offending organisms for organism-specific antibiotic regimens.

Fractures

Pathological fractures were at one time common in burn management because of the practice of delayed excision of eschar and of keeping patients in bed until wounds were completely covered. During that time, fractures occurred because of bone collapse when patients first stood or walked or when stiff joints were manipulated (Fig. 48.3).13 The bones most commonly affected were the femur at its distal metaphysis and the tibia at its proximal one. The only treatment required was support of the extremity until the fracture consolidated, usually in 4–6 weeks. Children were more often affected than adults and the fractures usually compressed one cortex, producing an angular deformity that rapidly corrected with growth. Klein’s study14 strongly suggests that fractures occur more frequently in burned children than in a matched normal population even months after the acute burn. Now, however, in acute burn management the most frequently seen fractures are those occurring at the time of, or in association with, the burn injury. Falls or violent trauma account for many of the fractures, and the sites are those common to the causes, bearing no relation to the burn itself.

Although fractures complicate burn treatment and occasionally delay mobilization of patients, their management need not be complex. Fractures in extremities not burned can be treated by manipulative reduction and cast immobilization, by open reduction and fixation, with an external fixator, or with skeletal traction (Fig. 48.4). Fractures in extremities with first-degree or superficial second-degree burns can be managed in the same way. Deep second-degree and third-degree burns present a different problem only with respect to the early bacterial colonization of third-degree burns and the degradation of deep second-degree burns to full-thickness burns that will, in turn, become colonized. There is a precious window of time when fractures requiring open reduction and internal fixation can be definitively treated without increased risk for infecting the bone; however, fracture reduction and stabilization are so important in the functional management of a severely burned patient that the risk for bone infection should be acknowledged and shoulder at any post-burn stage. Skeletal traction can often be the management choice, particularly in children and adolescents, even if the treatment protocol requires that the patient be moved from bed for tubbing, dressing change, or additional surgery. The disadvantages of skeletal traction are the confinement to bed and the imposed relatively fixed position of the affected extremity. External fixators have made it possible to align and stabilize fractures in burned extremities without open operation. There is the added functional advantage of patient mobility. Brooker’s extensive favorable experience supports this concept.15 With both skeletal traction and external fixation, there is an added risk for bone infection because of the path from surface to bone provided by the pins. This is a risk worth taking, and it is minimized by scrupulous pin site care and by removal and replacement of any loosening pin. Frye and Luterman recognized and discussed the specific and continuous difficulties encountered in the management of fractures and burns.15

When casts are used for stabilization of fractures in burned extremities, the wound is made inaccessible and there is an abiding fear that the unattended wound will seriously degrade or at best not improve. Such fear may be well founded; however, Wang16 showed that a bivalved circular cast could be used effectively for an open comminuted fracture of a proximal tibia with overlying deep burns, and Choctaw17 reported successful use of a cast for immobilization of an open comminuted fracture after immediate postburn grafting of the affected extremity. Common sense should dictate which fractures can be treated with circular or bivalved casts or with splints. If a reduced or moderately displaced but aligned fracture is so stable as to require

Figure 48.3 Pathological fracture of the osteoporotic femur of a 9-year-old girl sustained on the first day she stood after 5 weeks of confinement for 40% TBSA burn.
Musculoskeletal changes secondary to thermal burns

Fractures in burned patients heal quickly. There is no recorded experience that suggests that healing is delayed by the burn. Neither is there any record of failure of union. Callus formation may be abundant.

Among severely burned patients, non-displaced or minimally displaced fractures may not be detected until unusual local pain in an affected extremity prompts radiographic examination. A radiograph obtained for other reasons may reveal a fracture as an incidental finding. These fractures external support only for maintenance of alignment, then cast or splint immobilization should be all that is needed. On the other hand, if a fracture because of instability, requires maintenance of reduction by three-point pressure or molding of the cast material, it will be better treated by other means.

Dowling\(^8\) reported osteomyelitis resulting from open bimalleolar fracture in an extremity with extensive deep burns. In neither of the cases reported by Wang and Choctaw did the bone become infected. There were also no infections among Saffle’s 42 fractures, nine of which were treated by open reduction and internal fixation.\(^{16}\) With two fractures of the femur, each of which was exposed at the base of a deep chronic burn, aggressive debridement of the wounds and the fracture ends was followed by treatment with skeletal traction in one and by external fixation with the Ilizarov system in the other. Both fractures healed without further complication.

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Among severely burned patients, non-displaced or minimally displaced fractures may not be detected until unusual local pain in an affected extremity prompts radiographic examination. A radiograph obtained for other reasons may reveal a fracture as an incidental finding. These fractures

Figure 48.4 (a) This 15-year-old male sustained closed fractures of the right femur, left tibia and left humerus at the time of a 46% TBSA burn involving mainly trunk and right lower extremity. The femur and humerus fractures were treated in skeletal traction. Suspension of the right lower extremity aided management of circumferential deep burns of that extremity. Lesser burns of the left leg made it possible to treat the minimally displaced fracture of the left tibia in a circular cast. All fractures consolidated in 6 weeks in satisfactory alignment. (b) Fracture of the left humerus as it appeared at the time of admission to the hospital. (c) At 5 weeks after injury, the fracture shows maturing callus. Traction was discontinued at 6 weeks.
are usually of no functional significance. Modest angular deformation near a joint may be a problem in adults, although not in children. On the other hand, undetected physeal fractures in children can be a major functional threat.

**Changes involving pericapsular structures**

**Heterotopic bone**

Heterotopic bone formation is a rare but functionally important complication of thermal burns. The incidence in a general burn population is reported to be somewhere between 1% and 3%. In select populations, the incidence may be higher, as it will be if patients with periartricular calcification are included in the statistics. For example, Tepperman et al. reported a 35.3% incidence among patients referred to a tertiary care center for rehabilitation. Jackson made the observation that the incidence of heterotopic bone could be expected to be less in institutions that admit patients with minor burns. Munster’s radiographic survey of 88 adult and teenaged patients with 160 burned upper extremities yielded a 16% incidence of pericapsular calcification. The 23% incidence reported by Schiele et al. included both heterotopic ossification and calcification. In the early routine radiographic study reported by Evans, periarticular calcification that did not progress to heterotopic bone was excluded from the final calculation of an incidence of 2%. The 3.3% incidence recorded by Kolar and Vrabec included patients with pericapsular calcification. Even if heterotopic bone occurs infrequently in thermal burns, it remains that once it develops it often compromises joint motion and is difficult to treat. In addition, its pathogenesis is still incompletely understood; thus, protocols for prevention may in fact miss the mark.

**Pathogenesis**

The metabolic changes occurring after thermal burn are increased metabolic rate; protein catabolism; ureagenesis; fat mobilization; glycogenolysis; gluconeogenesis; elevated glucose flow; and eventual total body weight loss. There is an accompanying suppression of the immune system that favors wound infection, but at the same time favors survival of skin allografts. Infection, failure of skin graft take, or anything that delays closure of a burn wound will extend the altered metabolic state. Although it might be assumed that there occurs, along with the metabolic upheaval, an adverse change in connective tissue milieu, the exact nature of such a change is not known. It is also not known what the metabolic changes have to do with the development of heterotopic bone, but it is apparent that the burn disease is necessary to its formation. Other factors to be considered in the genesis of heterotopic bone are percentage of burn, location of burn, period of confinement, osteoporosis, superimposed trauma, and genetic predisposition.

**Percentage of burn**

Most reported cases of heterotopic bone have had a 20% or greater total body surface area burn; however, heterotopic bone has been found in patients with as little as 10% third-degree burn. Peterson et al., Munster et al., and Elledge et al. have reported affected patients with total body surface area burns of 8%, 14%, and 12%, respectively. In addition, with the now-extensive experience with salvage of patients with 80% or greater burns, it is clear that heterotopic bone occurs no more frequently among these patients than in the general burn population. Thus, the percentage of burn is not a determining factor.

**Location of burn**

By no means has all of the reported heterotopic bone occurred in joints with overlying burn. In their initial report, Evans and Smith described heterotopic bone occurring a distance from any third-degree burn involvement. Johnston noted that in one of his three patients, the skin overlying one affected joint was not even superficially burned. If degradation of connective tissue milieu in burns is a total body phenomenon, it follows that heterotopic bone formation need not be burn site dependent. Thus, the location of the burn cannot alone be a determining factor.

**Period of confinement**

Evans and Smith expressed belief that length of bed confinement was an important factor in the development of heterotopic bone. At the time of that report, patients with even moderate burns might be kept in bed for several weeks. The consequences of prolonged confinement were loss of active range of joint motion and bone demineralization; it was thought that each of these adverse changes might contribute to the formation of heterotopic bone. Thus, any maloccurrence that necessitated longer confinement could be a factor in the pathogenesis. Kolar implicated wound sepsis as an independent factor, along with the length of confinement. Other investigators have not addressed the period of confinement as specifically as Kolar, and there have been no comparative studies of groups of confined and non-confined patients. Thus, it may never be determined whether the current aggressive practice of early mobilization of patients will have an effect on the incidence of heterotopic bone.

**Osteoporosis**

Only Schiele et al. have found a relation between heterotopic bone formation and osteoporosis. Among their group of 70 adults with burns confined to the upper extremities, 11 of the 16 who developed heterotopic bone had radiographically identifiable osteoporosis. In their series of patients, there were 24 with osteoporosis. Thus, less than one half of these developed heterotopic bone and there were two in the group that developed heterotopic bone who did not have osteoporosis. If the findings in that study are not altogether persuasive, the matter is further confused by the knowledge that the survivors of extensive total body surface burns, who may develop profound osteoporosis, seem to have no greater liability to the formation of heterotopic bone than the general burn population.

**Superimposed trauma**

In one of the patients reported by Evans and Smith, the elbow of the more often used and minimally burned right upper extremity developed heterotopic bone, whereas the
elbow of the less used but more seriously burned left upper extremity did not. In the same patient, the right hip spontaneously dislocated. After reduction, that hip developed extensive heterotopic bone in the planes of the rectus femoris and iliopsoas. The opposite hip developed only a small, inoffensive spicule of heterotopic bone anteriorly at the joint line. Experience with this one patient reinforced the authors’ belief that there occurs with burns a general compromise of connective tissue that renders it particularly susceptible to superimposed trauma and that it is this liability to injury that accounts for the appearance of heterotopic bone at sites of repeated stretching of soft tissue, as at the minimally burned elbow or at sites of recognized abrupt excessive stretching as with the dislocated hip. According to all reports, the elbow is the most common site of heterotopic bone formation in adults and children. Perhaps it is the regular use of this joint that accounts for that orientation. Jackson has pointed out that the elbows are subjected to pressure posteriorly and medially when they are used for leverage or are simply in contact with the bed. He suggests with this observation that external pressure is a factor in the orientation of heterotopic bone to the elbow. There may be other factors that favor the elbow. Commonly, the elbow is splinted in extension to prevent flexion contracture. If flexion range is lost, passive stretch and encouragement of active flexion are part of the rehabilitation effort. The posterior structures most affected by this effort are those attached to the olecranon. Heterotopic bone often develops medially in line with and deep to the medial fibers of the triceps. If a flexion contracture develops, the heterotopic bone is commonly in the line of brachialis or biceps attachments to coronoid process and biceps tubercle. And if there is loss of pronation and supination range, stretching may cause heterotopic bone to form in line with the proximal radioulnar ligaments and interosseous membrane. There is an implication here that both the quality and timing of post-burn exercise may be important. Gentle passive and active motion should cause less tissue disruption than abrupt passive or active or even chronically repeated motion, and the effect of any mobilization effort must vary with the relative stiffness of the joint and the intrinsic resistance of soft tissue. The longer a joint is limited in its motion, the stiffer it will become and the greater will be the soft tissue damage with any forced manipulation.

The concept of superimposed trauma as a cause of heterotopic bone is supported by the experimental work of Evans and of Michelson and Rauschning. Evans found that all burned and non-burned rabbits given a single necrotizing injection in one quadriceps muscle readily healed the lesions, whereas rabbits burned or non-burned that were given a second same-site injection 7 days after the first uniformly developed well-defined and histologically identifiable heterotopic bone. In this experiment, it was clear that in susceptible animals it was not the burn that made the difference but the chronicity of the wound. Michelson and Rauschning determined that forceful or regular active remobilization of rabbit knees that had been immobilized for 1–5 weeks resulted in the development of heterotopic calcification and ossification in the muscles that were stretched. The response was more consistent in the quadriceps of the knees immobilized in extension than in the hamstrings of those immobilized in flexion. The longer the period of immobilization and the more vigorous the remobilization, the greater was the response. Muscle necrosis was a prominent histological finding.

Superimposed trauma is implicated in the development of heterotopic bone in head-injured patients or those with post-traumatic or infectious transverse myelitis. In these patients, it is assumed that tissue media are altered by injury to the central nervous system. The secondary injury, as in burns, is periarticular. In post-traumatic myositis ossificans, the development of heterotopic bone depends upon persistence of the muscle lesion and local necrosis and, thus, at least by inference, upon repeated insults to the affected muscle.

The development of heterotopic bone in burns has been associated with the agitation of patients and their resistance to physical therapy. Two affected adults and one affected child in a 10-year study resisted physical therapy programming. One adult refused to move and the other was extremely apprehensive. The child was likewise apprehensive and refused to cooperate with the therapist. The development in all three of posterior heterotopic bone in both elbows could have been ascribed both to the difficulty encountered in mobilizing the elbows and to the continual pressure on the elbows in bed.

**Genetic predisposition**

It is difficult to explain the low incidence of heterotopic bone among great numbers of patients similarly burned except on the basis of some, as yet unidentified, inherited factor. It is known that persons with proliferative non-inflammatory arthritis of the hip are more likely to develop heterotopic bone after total hip replacement than persons who have hips replaced for other reasons. In this instance, the predisposing inherited abnormality is identifiable. Although heterotopic bone formation may occur more regularly among spinal cord-injured and head-injured patients than among burned ones, by no means do all persons with head and spinal cord injuries develop heterotopic bone. The total burn experience at The University of Texas Medical Branch has yielded only two similarly affected siblings. Twin brothers who had 19% and 20% total body surface burns and who were mobile throughout much of their treatment and recovery period developed near-identical heterotopic bone of both elbows. There is, however, no scientific proof that genetic predisposition has anything to do with the formation of heterotopic bone in burns. Nor is there any literature to support the idea that a person who develops heterotopic bone when burned will be liable to develop it if he or she sustains head or spinal cord injury. Vrbicky, in a comprehensive review of post-burn heterotopic bone formation, suggests that a key for the genetic predisposition may be in the human leukocyte antigen (HLA), reporting that an HLA B27 survey showed a 7% HLA distribution in the normal population compared with 70% in a population with heterotopic bone.

**Characteristics and behavior**

Heterotopic bone associated with burns has been reported to occur about all major joints. The joints most commonly affected are elbow, shoulder, and hip, in that order of
frequency. The early manifestations are joint swelling and tenderness not unlike any acute inflammatory process. The patient may call attention to the process by a reluctance to move the affected joint. Onset may be as early as 1 month and as late as 3 months or more after the burn, but it is more likely to be associated with the acute recovery phase of treatment than later. Crawford et al. reported that the clinical diagnosis was made in advance of radiographic changes in 9 of his 12 patients. 20 Tepperman et al. 23 and Peterson et al. 20 found that bones could scans help make a diagnosis before there were radiographic changes. The earliest radiographic alteration is local periarticular increase in soft tissue density. There follows diffuse, stippled calcification in the same distribution in or about the capsule of the joint. It is at this point that the process may reverse itself, perhaps because of the improved state of the patient. Owing to this change in course, there may be patients whose periarticular calcification is not detected. If the calcification persists, it may be assumed that bone will develop by either the intramembranous or the enchondral route or both, as it does in animal models.

The flecks of calcification appear radiographically to lie within the capsule, whereas heterotopic bone not only may involve capsular structures but also may extend into the planes of muscles and tendons. At each major joint there is a more or less characteristic distribution of heterotopic bone, which is similar to that associated with patients with head and spinal cord injury. At the elbow, posteriorly disposed bone extends from the olecranon to the medial epicondylar ridge of the humerus in line with the medial border of the triceps muscle (Fig. 48.5a,b). At the joint, it may extend medially to bridge the ulnar groove. 48, 49 The medial, rather than lateral, orientation of the heterotopic bone may be related to the medial position of the olecranon and the greater tension on soft tissue on that side, and, as Jackson points out, the contact area of the elbow is consistently medial. 24 Heterotopic bone on the anterior surface of the elbow develops in the planes of the brachialis and biceps muscles extending from humerus to coronoid process or biceps tubercle. Occasionally, a bridge of heterotopic bone develops between the radius and ulna just distal to the joint. More rarely, bone has been found to fill the olecranon fossa and even to ensheathe the entire joint. At the shoulder, bone has been found to extend from the acromion to the humerus in the line of the rotator muscles or deep to the deltoid (Fig. 48.5c), to lie anteriorly in the plane of the pectoralis major, and, more deeply, to parallel the subscapularis. Hoffer et al. 50 reported that heterotopic bone at the shoulder lay anteriorly in the plane of the capsule. At the hip, heterotopic bone may extend from pelvis to femur in the planes of rectus or iliopsoas anteriorly or in the plane of the gluteal muscles laterally. Jackson has reported heterotopic bone in the plane of the quadratus femoris. 24 Like the shoulder, the hip may be ensheathed anteriorly with heterotopic bone that appears to originate in the capsule.

When heterotopic bone bridges a joint, it becomes part of the skeleton and may, if loaded, increase in dimension as a fully developed ossicle with mature cortex and medullary cavity. If the bone does not bridge a joint, it will, in children, gradually disappear when the burn wound has healed and the child is healthy. In recovering adults, non-bridging bone will, in time, diminish in size, but it may not disappear. The same tendency for heterotopic bone to regress after resolution of disease was noted by Lorber, who reported on two patients with paraplegia secondary to tuberculosis in whom deposits of heterotopic bone diminished in size, after return of motor function. 82 Bottu and Van Noyen 41 reported a similar experience with a patient who had transient viral meningoecephalitis, and Jacobs reported almost complete resorption of large bilateral deposits of heterotopic bone in a patient who recovered from paralytic measles encephalomyelitis. 43 Serum concentrations of calcium, phosphorus, and alkaline phosphatase have been reported by most authors to be normal or, at best, insignificantly higher in burned patients who have developed heterotopic bone. 17, 23, 29, 52, 53 In addition, there is no convincing evidence that calcium intake affects heterotopic bone formation one way or the other. Evans and Smith’s limited routine studies of affected and unaffected patients led the authors to believe that the values of serum calcium, phosphorus, and alkaline phosphatase were so consistently normal as to make further investigation unnecessary. 23 One interesting observation was that of Koepke, whose early, but incomplete, studies suggested that those patients who were susceptible had elevation of serum alkaline phosphatase before development of heterotopic bone, but not afterwards. 18

Prevention and treatment

The incidence of heterotopic bone in burns is so low as to make it impractical to administer indomethacin or other non-steroidal anti-inflammatory drugs (NSAIDs) that are currently used for patients at risk for development of heterotopic bone after major hip surgery. Rather, the thrust in prevention should be toward reducing the period of bed confinement and the duration of the post-burn hypermetabolic state. The now-prevailing practice of early wound excision and grafting may, in fact, address both of these problems as nearly as it is possible to do so. As noted above, even patients with extensive total body surface burns may now be out of bed and walking within the first post-burn week.

If certain patients are predisposed to the development of heterotopic bone, the quality and timing of joint mobilization for those patients may be critical. Stretching edematous pericapsular structures in the early post-burn period may very well be hazardous if additional tissue damage is the result; however, maintenance of joint motion and muscle function is part of the early excision and grafting program, and it is certain that the longer joint motion is restricted the more likely it is that pericapsular structures will be damaged by stretching. We like to think that secondary injury to soft tissue can be avoided by controlled and assisted active range of motion and terminal resistance.

When a patient is reluctant to move a joint previously moved with relative ease, and certainly when there is evidence of unusual swelling about the joint, radiographs should be obtained to determine if there is pericapsular calcification or ossification. Once heterotopic bone or calcification is recognized, joint exercise should be restricted to gentle passive and assisted active motion only. Crawford et al. 31 observed that ossification progressed to complete ankylosis in all patients who persisted in moving an affected joint beyond the pain-free range. They concluded...
Figure 48.5 (a) At 3 months after 94% TBSA burn of a 16-year-old male – resistance to motion, local swelling, and pain of both elbows prompted obtaining roentgenograms, each of which showed spotty linear soft-tissue calcification and ossification along the distal humerus and between the radius and ulna at the level of the biceps tubercle. (b) At 6 months after burn, elbow flexion and extension were reduced to 10° on the left and to less than 5° on the right. Bridges of immature heterotopic bone extended from the medial epicondylar ridges to the olecranon. Forearm rotation was 0% because of interosseous bridges of heterotopic bone at the level of the bicipital tuberosities. Prognosis for restoring functional range of motion in the elbows is poor. (c) At 6 months post-burn, glenohumeral motion on the right was limited to a few degrees by heterotopic bone underlying the deltoid. At the same time, a lesser deposit of heterotopic bone at the left hip did not limit motion.
that active range of motion exercises and stretching were contra-indicated if heterotopic bone or calcification was suspected, but that active range of motion could be safely resumed within pain-free range once the diagnosis had been confirmed. In the series of Peterson et al., patients suspected of having heterotopic bone had active range of motion exercises only. Ten regained functional range of motion and eight developed ankylosis.

Surgical excision of heterotopic bone is indicated when joint motion is lost or significantly compromised by bridging bone or exostoses. Evans has suggested that surgery be postponed until the burn wound has healed, scars are soft and associated with no inflammatory response, the patient is healthy, and the offensive bone is radiographically mature, i.e. well-defined and not increasing in dimension (Fig. 48.6).* This position makes sense considering the behavior of heterotopic bone: i.e. proliferation while there are open burn wounds or active scars and regression with wound healing and scar softening. For removal of heterotopic bone, surgical exposures should be planned with extensible incisions so as to facilitate total excision. When there is a bridge of bone, each end of the bridge should be slightly excavated. When there is attachment at only one end, the cartilaginous or fibrous extension should be removed along with the bone. Capsular sheets of bone should be removed completely. If bridging heterotopic bone is incompletely excised, the bridge is likely to recur. When a joint is bridged by bone in only one plane, removal of the offending bone will usually restore functional motion and recurrence of the bridge is unlikely. When a joint is bridged in more than one plane, recurrence is more likely and the chance for restoration of functional range of motion is correspondingly diminished. When the local inflammatory process has caused intra-articular synovial proliferation and cartilage destruction, the joint is most likely destined for ankylosis. Removal of the heterotopic bone about a joint so affected may allow more functional positioning of the joint, but it is not likely to arrest the process. On the other hand, extra-articular arthrodesis by a bridge of heterotopic bone may preserve the joint. This is particularly the case at the elbow when there is only one posterior bridge of bone from olecranon to medial epicondylar ridge of the humerus. In this situation, the olecranon is fixed in the trochlea, but the radiocapitellar and radioulnar joints remain functional. In Evans’s experience with removal of single bridges at the elbow, joint cartilage was found to be healthy as long as 5 years after ankylosis. Preservation of pronation and supination was credited with maintaining the synovial bath to provide nutrition for the humeroulnar cartilage. Indeed, when pronation and supination additionally are blocked by bridging bone, cartilage degradation is certain. Evans’s further experience with long-term survival of glenohumeral cartilage after ankylosis by bridging bone from acromion to humerus is not as easily explained.

Figure 48.6 (a) A mature sheet of heterotopic bone extends from humerus to olecranon, obliterating the olecranon fossa 11 months after 53% TBSA burn in a 13-year-old female. Elbow flexion and extension range was less than 10%. Pronation and supination were near normal range. (b,c) At 3 months after excision of heterotopic bone, the patient had attained 90° of elbow motion and a continuing increase to functional (hand to mouth) range was predicted. Now the patient can extend the elbow and can flex it to 90°.
Reported experience with excision of heterotopic bone in burns has not been uniformly favorable. Dias,33 Hoffer et al.,30 and Peterson et al.29 reported restorations of functional range of motion in most of their patients with timely excision of heterotopic bone. Gaur et al.32 reported good functional return in seven burned children with nine affected elbows. Ring and Jupiter30 reported good results in a varied population, and Chung et al.34 and Tsionos et al.36 have reported good results with early excision a mean of 9 months after the burn. Other surgeons have reported less satisfactory results.22 In our own experience, results have varied, as anticipated, with severity of affliction. We have learned that if heterotopic bone recurs after excision, it is worthwhile to excise again if the joint affected remains structurally identifiable. For the most part, however, attempts to improve joint function with second operations have failed. We believe that ultimate failure can be predicted at the time of initial surgery; we are convinced that the single most important factor in successful initial excision is in timing surgery to coincide with the patient’s return to good health.

Changes involving the joints

Dislocation

Luxations and subluxations of joints in burned patients may occur as a result of direct destruction by the burn of ligaments and capsules, loss of articular cartilage due to infection, faulty positioning, and eventually scar contracture. In all phases of management, but particularly in the acute phase, positioning is of prime importance in the prevention of joint deformity. The preferred positions, listed in Table 48.1, serve as a guide for the prevention of dislocation of joints and of malposition secondary to scar contracture.

Table 48.1 Preferred positions for major joints

<table>
<thead>
<tr>
<th>Joint</th>
<th>Preferred position</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neck</td>
<td>Midline in neutral or slight extension</td>
</tr>
<tr>
<td>Shoulders</td>
<td>Scapulothoracic retraction and depression 85° of glenohumeral elevation with 20–25° of horizontal flexion</td>
</tr>
<tr>
<td>Elbows</td>
<td>Extension</td>
</tr>
<tr>
<td>Wrists</td>
<td>Slight extension</td>
</tr>
<tr>
<td>Metacarpophalangeal joints 2-5</td>
<td>80–90° of flexion</td>
</tr>
<tr>
<td>Fingers</td>
<td>Proximal and distal interphalangeal extension</td>
</tr>
<tr>
<td>Thumbs</td>
<td>Carpometacarpal flexion and abduction, metacarpophalangeal flexion 5–10°, interphalangeal extension</td>
</tr>
<tr>
<td>Spine</td>
<td>Extension with no lateral deviation</td>
</tr>
<tr>
<td>Hips</td>
<td>Extension and slight external rotation in 15° of symmetric abduction</td>
</tr>
<tr>
<td>Knees</td>
<td>Extension</td>
</tr>
<tr>
<td>Ankles</td>
<td>Neutral</td>
</tr>
<tr>
<td>Feet</td>
<td>Neutral</td>
</tr>
</tbody>
</table>

The joints most liable to structural compromise due to exposure by the burn and loss of soft tissue support are knee, elbow, proximal interphalangeal joints of the hand, and metacarpophalangeal joints. These hinge joints have in common a subcutaneous dorsal surface, accounting for their ready exposure.

The elbow, for its trochlear architecture, is more intrinsically stable than the other joints in this group. It requires loss of collateral support to render it easily displaceable. The knee, on the other hand, is immediately in danger of subluxation if there is loss of continuity of its central slip, the patellar tendon, even if the retinacula remain intact. In this circumstance, gravity alone will displace the tibia posteriorly in relation to the femur if the patient is recumbent. The hamstring muscles contribute to the displacement force regardless of the position of the extremity. Loss of collateral ligaments compounds the problem, but loss of collateral ligament stability in the presence of an intact patellar tendon and functioning quadriceps constitutes far less a threat than loss of patellar tendon. For the lower extremity, persistent posterior translation of the tibia beneath the femur with inefficient quadriceps function is potentially a functional disaster.

For both the elbow and the knee, the protecting position is extension. These two joints are rarely at risk for articular displacement from contracture alone and, if there is no ligament or tendon loss, extension resting splints will give adequate positional support. When there is soft tissue disruption, splinting may not adequately protect either joint. An external fixator with two-pin, four-cortex fixation above and below the joint will provide stability and will permit access to the wound. For the elbow, it allows fine adjustment to the normal carrying angle as well. If the knee is accurately reducible at the time of application of the fixator, there is a good possibility that the reduction can be maintained. If the tibia cannot be brought forward completely by manual manipulation, it may be necessary to suspend the tibia through a transverse pin at the level of the tibial tubercle. For static vertical traction, the extremity must be elevated from the bed. For dynamic traction, enough weight must be used to accomplish the same elevation. If the tibia can be brought forward by this means, an external fixator will hold the reduction. For the knee to remain stable with the tibia forward, the patellar tendon must be reattached and quadriceps integrity reestablished; otherwise, when the fixator is removed, the tibia will once again begin an incremental posterior shift toward its own point of stability. No amount of external splinting or bracing is likely to prevent that shift.

The proximal interphalangeal joints of the hands are more frequently exposed by burn than any others. If the central extensor slip remains intact, there is less risk for subluxation of the joint. Even if there is loss of continuity of the central slip but preservation of the lateral bands, subluxation is easily prevented if the joint is maintained in extension while soft tissue cover is being achieved. It is with loss of the support of lateral bands and collateral ligaments that the joints become liable to dislocation. With the metacarpophalangeal joints, the tendency to displacement or subluxation may be greater because these joints are functionally multiplanar, while the interphalangeal joints are uniplanar. Fortunately, metacarpophalangeal joints are less often exposed than the interphalangeal ones.
The protecting position for the proximal interphalangeal joints is full extension. If only the central slip is lost, the position may be held with an external splint. In states of greater instability it may be necessary to use intramedullary transarticular Kirschner wires to hold the position. The wires, although reasonably efficient, do not control rotation, and they carry with them a risk for post-treatment joint stiffness. In small children it is impossible to introduce the Kirschner wires through the distal phalanx; thus, it is better, with the proximal phalanx flexed to 90 degrees, to place the wire through the corresponding metacarpal head into the proximal and middle phalanges. Short-term transfixed does not harm the joint, and metacarpophalangeal flexion is the favored position for functional restoration. Pin traction through the distal phalanges in a skeletally stabilized metal splint is another method for maintaining extension of threatened digital joints. It has the advantages of patient comfort and mobility, secure positioning of hand and upper extremity, easy maintenance of elevation, and easy access for dressings, for additional surgery, and for exercise of lesser affected joints. The system likewise makes it possible to keep digits separated, thus facilitating local care. Traction should not be used if collateral ligaments are not intact. By whatever means attained, the corrected position must be maintained until the joint is covered with graft. Protection should continue with a standard splint or brace until the joint is sound.

The two joints most likely to dislocate because of faulty positioning are the shoulder and the hip. These two ball and socket, multiplanar joints sacrifice stability in favor of mobility. This is particularly true of the shoulder, where the shallow glenoid contains at any one time only one third of the head of the humerus. In burns, the head of the humerus may begin to subluxate forward if, during prone positioning for management of back and buttock wounds, the arms are maintained in full abduction in the coronal plane. In this position the arms are in at least 15–20 degrees of extension from the more secure neutral position in line with the scapulae and the humeral heads are forced forward against the anterior capsule. Even when the patient is supine, full abduction and extension of the arms should be avoided. For short-term management, particularly when the patient gets out of bed each day, this position probably does not threaten the joint. But if the patient is to be bed confined and the position unrelied for days or weeks, the head of the humerus may begin to subluxate forward. In the extreme situation, the head of the humerus will dislocate to a medial subcoracoid position. In patients with deep burns extending from chin to axillae to chest, the common posture of elevation and position. To maintain ankle position it is sometimes appropriate to insert a large vertical Steinmann pin through the calcaneus and talus into the tibia. The position should be maintained until the exposed joint is covered with epithelialized granulation tissue or skin graft. Exposed adjacent bone can be shaved or drilled, as previously described, to encourage surface granulation. Drilling is particularly useful at the elbow where the olecranon is regularly exposed. Often, however, granulation tissue will quickly extend the wound margins and effectively close the wound so as to allow split-thickness skin grafting. If the burn is isolated to the joint or if the extremity is not otherwise seriously burned, a local muscle, skin or compound flap may be used to close the joint. Free vascularized flaps are useful and should always be considered if it is anticipated that nerve graft or tendon graft or transfer at the site will be required in the future. Incremental remobilization of the joint may proceed when wound closure is sound. Culture of material from an exposed joint will likely yield a variety of organisms consistent with those of the general burn wound, thus requiring broad-spectrum antibiotic management.

The incidence of hematogenous septic arthritis is obscured by its frequent association with severe burns and because there are rarely separable clinical signs such as local heat and swelling, elevation of temperature, and elevation of sedimentation rate. Local tenderness and greater than usual pain with motion may focus attention on the affected joint. Aspiration of the joint will confirm a diagnosis. A radiograph is helpful, but in the early phases of infection will show only local cellulitis as increased periarticular soft tissue density. If

The head of the humerus is most secure in the glenoid fossa when the arm is adducted to neutral and internally rotated, a position that is incompatible with wound management of burns of the trunk, neck, and upper extremities. The protecting position that accommodates the need for abduction for axillary burns is elevation of the arms in line with the scapulae. The arm is then approximately 20 degrees forward of the coronal plane or in 20 degrees of horizontal flexion. When the patient is prone, the protecting position can be gained only if the chest is supported on a chest width mattress, folded blankets or towels, or a foam rubber pad, any of which will allow the arms to drop forward. When the patient is positioned this way, whether supine or prone, the forearms will be pronated and the arms will be in sufficient internal rotation to favor seating of the head of the humerus in the glenoid.

The hip will tend to subluxate posteriorly if the thigh is persistently allowed to remain flexed, adducted, and internally rotated during the acute burn phase. For the most part, however, the protecting position of extension to neutral or 180 degrees and 15–20 degrees of symmetric abduction is easy to attain and maintain and is, in fact, the most desirable position for wound management.

Infection of a joint may result in its subluxation or dislocation. Hip displacement because of apparent spontaneous dissolution has been described by Evans and Smith. Eszter and Istvan56 and Cristallo and Dell’Orto57 reported similar cases. In none of these cases, however, could it be determined that the joint destruction was due to infection.
a patient has been receiving broad-spectrum antibiotics, material aspirated from the affected joint may not grow an organism in culture. Clearly, without organism identification and sensitivity determinations, specific antibiotic therapy cannot be initiated.

We have been of the opinion that debridement and exterozation of the joint and regular vigorous lavage are as important as antibiotics in the treatment of closed infected joints.

We believe now that arthroscopic debridement and closed irrigation should be considered as an alternative method of management whether or not skin over the affected joint is burned. Rarely in burns, a joint may become infected from adjacent metaphyseal osteomyelitis. In this situation joint preservation is the treatment priority, and measures are the same as for septic arthritis of strictly hematogenous origin.46 In children, most infected joints can be salvaged. Adult joints are less resilient. Persistent joint infection will destroy cartilage and lead to ankylosis.58,59 All chronically infected joints are liable to dislocation because of surface destruction and capsular laxity.

Amputations

In thermal burns, major amputations are most often performed because of non-viability of the extremity or because a surviving extremity is rendered useless by scar, deformity, or insensitivity. Occasionally, in an extensive burn, a severely burned extremity that might be salvaged in part is sacrificed to reduce the extent of the burn or as a lifesaving measure. In thermal burns, the level of extremity amputation is determined by the viability of muscles and tendons. The more distal the site the better, and it is important to retain joints even if motion will be restricted. For example, if a forearm or leg must be sacrificed, the elbow or knee should be spared if the more proximal muscles controlling that joint are intact, if the bone bleeds, and if there is the possibility that the remaining tissue of the stump has sufficient blood supply to produce granulations for grafting. Aside from affording a better functional prospect, sparing the joint will provide the surgeon opportunity at a later time to choose an appropriate revision level if the joint does not function. The patient will at that time be healthier and stump closure will be routine. Jackson suggests that it may be technically feasible to cover even non-viable bone with a free flap in order to maintain extremity length.24

In electrical burns, the level of amputation is most often determined by muscle viability. Stump care is the same as with thermal injury.

Prostheses can be easily fitted over stumps covered with split-thickness grafts. Ridges of hypertrophic scar will break down if there is friction within the socket of the prosthesis, but scar often softens and flattens with the constant, even pressure of a well-fitted socket; prostheses fitted early over grafted stumps may prevent scar thickening. Breakdown may occur at points where the graft is adherent to bone. This problem may require surgical freeing of the adherent graft and reshaping of the bone. Minor hip and knee flexion contractures complicate the fitting and function of a prosthesis; thus, every effort should be made to maintain full extension of these joints. Late revisions of amputations in children are required when the bone overgrows in length and when offensive terminal exostoses develop. The overgrowing bone can be shortened and the exostoses removed.

It is important in the early management of upper extremity amputations in infants and young children to supply temporary prosthetic extensions. This provides functional orientation to a prosthesis, maintains muscle bulk and tone, and encourages continuing bimanual activity at normal extremity length until a prosthesis with appropriate terminal device can be applied. Children quickly acquire prehension and transfer skills if they have an opposable stump and they may reject prostheses if they are not applied early. It is equally important to restore bipedal function as soon as possible. If delay of healing or ulceration of a lower extremity stump prevents early prosthetic fitting, an ischial weight-bearing device that suspends the stump will permit the child to walk in advance of prosthetic fitting. Inflatable plastic air bags provide both even pressure and accurate fit for weight-bearing in container sockets. Early prosthetic fitting is desirable in teenagers and adults as well, but is not as critical as it is in children. As in non-burned persons, an upper extremity prosthesis may be rejected at any age if the opposite extremity is fully functional.50

Alterations in growth

In 1959, Evans and Smith reported that a patient who was 24 years of age when burned had a subsequent 1½ inch increase in height. It was suggested that one explanation for this growth spurt might be local change in hemodynamics with stasis, passive hyperemia, and chronic inflammation. We have not since documented height changes in burned adults, but we have observed children whose growth after burn has seemed to be retarded. If growth plates remain open, it is difficult to explain overall growth retardation except on an endocrine or humoral basis. It is easy, however, to explain extremity length differences on the basis of premature closure of growth plates due to direct involvement of the bone or to severity of overlying burn. Frantz reported lower limb length discrepancy in four patients with foot and ankle burns.61 Growth plates closed prematurely in only two of the cases. Jackson described two patients with digital and lower extremity deformity, respectively, due to partial closure of growth plates.24 In Ritsilä et al’s case, contracture alone was apparently the cause of growth retardation in an upper extremity.62 It seems reasonable, although hard to prove, that growth in a severely burned extremity would be retarded because of functional impairment. One patient, a 3-year-old boy with 80% total body surface burn and sufficiently deep burns of the right upper extremity to require mid-humerus amputation, demonstrated, 4 years after the burn, failure of development of the right shoulder girdle. The factors operant in this case could be premature closure of the growth plates of scapula and clavicle, restrictive scar, and disuse atrophy.

There is yet another confusing aspect of premature closure of growth plates in that within an extremity with total full-thickness burn, only a few of the growth plates will close prematurely. The explanation for this capricious selectivity is at best obscure. Evans and Calhoun recorded an example of spotty closure of growth plates in a 14-year-old male with 90% total body surface burn.12 There was complete closure of distal tibial and fibular epiphyses 1 year after burn together
with closure of all digital epiphyses in the feet and of several digital epiphyses in the hands. Other major epiphyses were spared (Fig. 48.2).

In early experience, abnormal growth plate closure was observed in a 6-year-old girl with 50% third-degree burn that did not involve legs or ankles. Rapidly destructive septic arthritis of one ankle resulted in closure of the adjacent tibial growth plate.

Only occasionally can growth changes be anticipated because of obvious affection of the bone. More often the changes are subtle. It seems clear, thus, that among seriously burned children, regular height and extremity length measurements must be part of ongoing post-burn assessment until it is determined that the extremities and trunk are developing symmetrically and on schedule. Extremity and trunk alignment must likewise be part of the assessment as subtle angular deformity can occur because of partial closure of a growth plate. Jackson’s report addresses this problem.24

So-called growth arrest lines seen in the radiographs of non-burned children, who have serious illness or major trauma other than burns, are commonly observed in burned children. In burns, as in other conditions, these transverse markers of relatively increased mineralization represent normal recovery from an insult to enchondral bone formation due to serious stress. They are of no clinical or functional significance. They are more related to total burn than to involvement of select burned extremities as all major long bones are affected. There is no evidence that growth arrest lines per se have any effect on growth.

Further reading


The most recent comprehensive review of the subject of heterotopic bone.


A detailed discussion of heterotopic bone and a comprehensive cover of the subject.


Descriptions of burn-related deformity and management, with the important inclusion of the concepts of Barbara Willis.


The earliest description of burns related to heterotopic bone.


A comprehensive discussion of causes and persistence of mineral loss.


With an introduction of the concept of superimposed trauma in burns.


Traction system in the management of wound burns.

Access the complete reference list online at http://www.expertconsult.com
References

Mitigation of burn-induced hypermetabolic and catabolic response during convalescence

Oscar E. Suman, David N. Herndon, Celeste C. Finnerty, Elisabet Borsheim

Background

Advances in burn management and critical-care have greatly improved acute outcomes following severe burn injuries in recent decades. This has led to an increased focus on measures to improve long-term outcomes by enhancing rehabilitation and reintegration of burn survivors back into fulfilling and productive roles in society. Long-term debilitation following severe burns results from a combination of physical and psychological factors, including persistent hypermetabolism and physiological derangements, severe skeletal muscle wasting, deformity, scar contracture, pain and itch, limb amputation, multiple operative interventions over the course of years, and psychological and social factors related to loss, disfigurement, identity, and bereavement. Burn team scientists and clinicians have barely begun to gain knowledge into what the long-term quality of life for these survivors can be.\(^1\)\(^2\) Rehabilitative challenges for such children are numerous, and the best methods of achieving good outcomes in children with severe burns are still being developed.\(^3\)

Despite the similarities in treatment of pediatric and adult burns, pediatric injuries present unique challenges, both at the time of acute treatment and throughout rehabilitation. Increased experience and new data, gathered in large part from courageous young survivors, have allowed burn team clinicians and scientists to identify many long-term problems associated with large burns. A major problem during convalescence of the pediatric burn patient is the prolonged hypermetabolic state associated with catabolism and growth delay. Recent gene expression studies have demonstrated that, of the thousands of genes which are altered by a severe burn injury in peripheral blood leukocytes, the expression of 21% of the genes are age-specific.\(^4\) Many of these genes play important roles in mitochondrial and immune function. These studies demonstrated that there is a temporal component of the response to burn injury as well, with complete resolution of the genomic response to injury taking up to (and in some cases beyond) 1 year. Although the direct role that these genes play in mediating age-specific manifestations of burn-induced sequelae, on-going studies will improve our ability to personalize treatment in pediatric and adult burn patients.

In response to a severe burn, afferent stimuli are activated causing a hypothalamic thermoregulatory re-set to occur. This results in increased heat production, a faster heart rate and a greater cardiac output, in addition to an exaggerated increase in resting energy expenditure.\(^5\) The control and treatment of prolonged postburn hypermetabolism remain an unsolved problem.\(^6\) Whereas the cause is still not well understood, catecholamines are the major mediators.\(^7\) Catecholamine and cortisol levels can be elevated for up to 1 year post-burn.\(^8\) With this elevation in stress hormones, there is a long-lasting increase in resting energy expenditure, glucose production and catabolism. The effect of this hypermetabolic, hypercatabolic state is rapid muscle breakdown.\(^9\)

The self-catabolism, which is manifested as an increase in protein degradation with a lesser increase in synthesis, persists, despite state-of-the-art nutritional care.\(^10\) As a result, the rate of protein degradation continues to exceed that of synthesis. The protein catabolic response to injury leaves patients debilitated for months and severely delays the rehabilitation process. Protein is degraded to provide amino acids for energy as well as building blocks for host defense protein synthesis. Most of the required amino acids are taken from active muscle which serves as a pool for amino acids. The increase in amino acid loss from muscle causes muscle wasting and loss of strength. Severe muscle wasting is closely related to overall morbidity and mortality in the burned patients.

Finally, associated with the prolonged hypermetabolic, hypercatabolic state, there is also reduced bone formation, resulting in severe osteopenia or osteoporosis\(^11\) as well as linear growth retardation.\(^12\)\(^-\)\(^14\) This may partly be caused by the continuous elevation in endogenous glucocorticoids that decrease osteoblasts on the mineralization surface of bone, blocking of osteoclastogenesis leading to low bone turnover and bone loss, and a reduced synthesis of vitamin D from skin from burned patients.\(^15\)

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Mitigation of hypermetabolism

Propranolol

Herndon et al. proposed that beta-blockade would mitigate the catecholamine driven hypermetabolic response.16 Their initial study demonstrated that propranolol, given to decrease severe burn-induced tachycardia, attenuates catabolism of skeletal muscle, reduces resting energy expenditure, and decreases hypermetabolism during the acute hospitalization period in severely burned children.16 This mitigation of the catabolic response is associated with alterations in genes for key proteins, including dynein, heat shock protein 70, and myosin.17 Decreases in free fatty acid availability by inhibition of peripheral lipolysis and reduction of hepatic blood flow through the use of propranolol lead to the reduction of fatty infiltration of the liver.18,19 These studies of short treatment regimens of beta-blockade (2–4 weeks) have been extended up to 2 years. Preliminary analysis demonstrates that reduction in cardiac work is the major benefit noted 6 months following the injury. Long-term improvements in lean body mass, increased bone mineral content, and decreased formation of hypertrophic scar persist as well, indicating that extended treatment of severely burned children with propranolol continues to improve patient recovery. Studies to determine the impact of beta-blockade on muscle strength, cardiopulmonary function, and growth will elucidate whether propranolol in combination with exercise can cause even greater improvements in post-burn recovery.

Mitigation of catabolism

As mentioned previously, the catabolic response decreases lean mass, muscle strength and cardiopulmonary function. Appropriate levels of lean mass, muscle strength and cardiopulmonary function are essential for normal daily activities. Several treatment options for improving these outcomes have been investigated at our institution.

Exercise

Resistance exercise has an established influence on muscle strengthening and muscle protein synthesis. The beneficial effects of resistance training have been well documented in healthy adults, adolescents, and older children.20–24 Ferrando et al. demonstrated in healthy adults that moderate resistance exercise is capable of ameliorating the decreases in skeletal muscle protein synthesis and strength that accompany inactivity.25 The acute stimulatory effects of resistance exercise may last up to 48 h.26

Most of our experience with exercise has been in children and adolescents older than 7 years of age. In burns, resistance exercise alone is also capable of inducing increases in lean mass, muscle strength and aerobic capacity. Suman et al. demonstrated in severely burned children and adolescents that a 12-week exercise program of resistive and aerobic exercise significantly improved lean mass, muscle strength and aerobic capacity relative to standard of care treatment (Fig. 49.1).27,28 We should note that a 12-week exercise program of resistive and aerobic exercise does not reduce REE. However, this is due to the increased lean mass. Furthermore, it should be noted that exercise training in burned children does not further exacerbate REE.27

Exercise and younger children

Because of the difficulties with young children (i.e. under 7 years of age) using the exercise equipment or cooperating in obtaining certain measures, the exercise studies described above were conducted with children ages 7–18. However, as exercise treatment has proven incredibly beneficial, we have now begun a program using music and movement for young children. Movements are chosen to increase strength, flexibility, and endurance. Children enjoy this ‘play,’ and preliminary data indicate the program to be beneficial to overall development and specifically to maintaining or improving joint range of motion beyond standard of care (prescribed occupational–physical therapy exercises).29

Exercise and adults

To our knowledge there is only one published prospective, randomized study involving adults with severe burns and exercise training. One of these studies investigated the
Mitigation of burn-induced hypermetabolic and catabolic response during convalescence

Efficacy of a 12-week exercise program in producing greater improvement in aerobic capacity in adults with burns relative to the usual care. This randomized, controlled, double-blinded trial had patients completing a 12-week, 36-session, aerobic treadmill exercise program. Some patients were in the work-to-quota (WTQ) program, and intensified their exercise according to preset quotas. Other participants were in the work-to-tolerance (WTT) program and exercised to their tolerance. Participants completed a maximal stress test at baseline and at the 12 weeks to measure physical fitness. The authors reported that the WTT and the WTQ exercise groups both made significant improvements in aerobic capacity from baseline to 12 weeks. However, the control (usual care) group did not. WTT and WTQ participants demonstrated significantly greater improvements in aerobic capacity in comparison to the usual group patients. The WTT and WTQ groups did not differ significantly from each other with regard to their improvements in aerobic capacity. This very well designed study demonstrated that the aerobic capacity of adult burn can be improved with participation in a structured, 12-week exercise program after injury.30

Anabolic agents

Growth hormone

Anabolic agents studied at our institution have included recombinant human growth hormone (rhGH), and oxandrolone, a synthetic testosterone analogue. Both have shown promising results, significantly improving growth and muscle gain following severe burns in children.31 However, a multicentre trial of adult critical-care patients reported increased mortality in patients treated with growth hormone,32 and its use is presently therefore only considered in children.

Przkora et al. studied the effects of administering 0.05 mg/kg per day of rhGH to children from hospital discharge until 12 months after burn injury. The investigators showed that growth and bone mass as well as lean mass were significantly increased in patients receiving rhGH compared with the placebo group. Furthermore, both lean mass and muscle strength improved significantly in the treatment group. The observed beneficial effects on body composition were associated with significant elevations in anabolic hormones such as insulin-like growth factor-1 (IGF-1). Additionally, serum cortisol, a catabolic hormone, was significantly lower with rhGH treatment when compared with placebo. The enrolled patients were followed for an additional year once rhGH use was discontinued and the authors demonstrated a persisting effect on growth and on bone mass in the rhGH group during this period. No rebound phenomena on body composition or on hormone metabolism were noted during the year following cessation of rhGH.33

Because of the positive results obtained with exercise intervention alone and with rhGH alone, we rationalized that an exercise program that included resistance exercise in combination with rhGH would provide for a synergistic effect on skeletal muscle protein synthesis by addressing separate stimulatory mechanisms for an extended period of time. Suman et al. studied 44 severely burned children and adolescents who received rhGH (0.05 mg/kg per day) or placebo for 9 months and either participated in a 12-week exercise program or received standard of care treatment (daily physical and occupational therapy).34 In this study, the mean percentage change in lean body mass after 12 weeks was similar for the groups of participants receiving GH alone, exercise alone, or the combination of both. On the other hand, the mean percentage change in muscle strength was significantly greater only in the groups receiving exercise, independent of rhGH. Preliminary results using a higher dose of rhGH (0.1 mg/kg per day) also yielded similar results; lean mass increased by GH alone, exercise alone, or the combination. However, similar to low-dose rhGH, muscle strength was only increased via exercise. Similarly to muscle strength, peak aerobic capacity was only improved by exercise. It is presently unknown what are the effects of higher doses of rhGH on muscle mass of severely burned children.

A difficulty confronted in these studies using rhGH is that rhGH is administered via daily injections. Although these injections are relatively painless (the investigators have first given them to themselves to be sure of this), they present a daily source of irritation and tension to parent and child. Therefore, we searched for a less-intrusive means to improve body composition.

Oxandrolone

Oxandrolone is an anabolic steroid that has been used in catabolic situations such as hepatitis and AIDS patients and can be administered orally, thus eliminating one source of stress for children and families. In a randomized trial Przkora et al. treated severely burned children with oxandrolone (0.1 mg/kg twice daily per os) or placebo from hospital discharge up to 12 months after trauma. They found a significant improvement in body composition, including linear growth, bone density, and lean mass. Muscle strength was also significantly improved with oxandrolone. As with long-term rhGH treatment, no adverse side-effects were observed in the year following treatment. Beneficial effects on growth were noted even 1 year after treatment.35

We have also recently studied the effects of oxandrolone in conjunction with the exercise program.36 Oxandrolone in combination with exercise increased lean mass significantly more than either the drug or exercise treatment alone. Muscle strength and functional improvement were significantly improved with the combination of oxandrolone and exercise as well as with exercise alone. A surprising, but welcome finding was that oxandrolone alone improved muscle mass and strength. Finally, aerobic capacity was significantly improved with the combination of oxandrolone and exercise as well as with exercise alone. We have planned future studies that will introduce propranolol instead of rhGH or oxandrolone and will follow a similar design as described above.

Mitigation of growth delay

One can think of this physical state as the body running at almost twice its normal rate even though the individual is at rest. The patient requires enormous amounts of nutritional intake to keep up with the energy expenditure. Even with adequate caloric intake, individuals in this state lose
Our progress in developing such strategies is the subject of problems and devising methods of improving treatments. In the early stages of this process; we are still learning about most of the issues evolving from massive burn, we are still during and after discharge from acute hospitalization. For of severely burned children demand that we develop strat

time extending far beyond wound healing. However, in clinical work, we observed that the children fail to develop muscle, to grow, and to gain weight for a period of time extending far beyond wound healing.

We followed systematically 25 severely burned children for 1 year to ascertain the duration of the hypermetabolic–catabolic state. Stable isotope methodology and body composition studies were performed during acute hospitalization, at initial hospital discharge, and at 6, 9, and 12 months post-burn. The resting energy expenditure of these children peaked at 1-week post-injury with a metabolic rate of 180% of normal and progressively declined with time. At the 12-month exit from the study, their resting energy expenditure remained 15% above basal metabolic rate. Catabolism persisted for at least 9 months, which was 7 months after complete wound healing. As muscle catabolism and the hypermetabolic response persists well into the rehabilitative phase, strategies to counter these effects should similarly extend during rehabilitation.

Knowledge of the duration and extensive harm resulting from the catabolic effects of trauma has also led to efforts to better delineate mechanisms of catabolism and to a vigilant pursuit of early interventions that could attenuate the effects of the hypermetabolic–catabolic response. Factors affecting the convalescence of severely burned children are shown in Figure 49.2. The effect of the hypermetabolic–catabolic response 6 months after burn is displayed in Figure 49.3. Such long-lasting deleterious effects upon the recovery of severely burned children demand that we develop strategies to attenuate the hypermetabolic–catabolic response during and after discharge from acute hospitalization. For most of the issues evolving from massive burn, we are still in the early stages of this process; we are still learning about problems and devising methods of improving treatments. Our progress in developing such strategies is the subject of this chapter.

In 1990, Rutan and Herndon demonstrated a dampened growth curve for both height and weight in male and female pediatric patients who had sustained major thermal injury. The growth velocities were delayed up to 3 years after burn injury. Even after the return to normal growth velocities, the burned patients lagged behind age- and sex-matched peers.

Normal linear growth and weight gain in children are dependent upon a number of factors. The prenatal environment, adequate nutritional intake, and an emotionally nurturing household environment are crucial. Long hospitalizations alone have been known to produce profound arrests in growth and development in children. The management of massively burned children includes multiple operations and prolonged hospitalization. In cases of fascial excision, subcutaneous fat layers in the injured area are also removed. Fat stores are further depleted in providing energy for the process of gluconeogenesis from existing protein stores for dietary supply. All the reasons for the growth delay following severe burns are not currently known.

**Growth hormone**

Growth hormone (GH) levels have been shown to decrease in severely burned adults, and it is likely that children experience a similar decrease. In children, measured serum growth hormone levels remain depressed during both the acute phase following severe burns, and may remain so for at least 2 years.

Administration of an anabolic agent such as recombinant human growth hormone (rhGH) during the acute treatment of severely burned children has been demonstrated to be extremely beneficial in promoting healing and normalizing growth. Studies of GH demonstrate that it can be given safely to severely burned children and that it accelerates wound healing and reduces tissue wasting commonly seen in the catabolic patients. Using rhGH in the acute treatment of children with severe thermal injuries has been shown to improve net muscle protein synthesis as well as to accelerate wound healing and reduces length of hospital stay. Knowledge gained from such studies suggests improved treatment approaches that can be evaluated. Improvement in each of these areas could contribute to improved growth and weight gain; therefore, administration of GH was perceived as a probably advantageous tool in the management of pediatric burn patients toward normal growth.

Treatment with low dose rhGH (0.05 mg/kg per day) has previously been shown to improve growth, lean body mass, and bone mineral content when given to children following severe burns. This low dose treatment with rhGH, however, did not appear to reduce elevated metabolic rates, reflected in resting energy expenditure and cardiac output measurements. Furthermore, while both lean mass and muscle strength were significantly improved at 12 months, when treatment was discontinued, these were not significantly different by two years post-burn compared to controls. Beneficial effects of low-dose rhGH have also included a reduced number of operative reconstructive procedures.

More recently, Branski et al. reported on the effects of low-dose rhGH treatment at three different dosing levels in children with severe burns over 40% TBSA, as part of a single-center randomized controlled trial at our unit. Patients received 0.05, 0.1 or 0.2 mg/kg per day for 12 months after injury and were followed up for 2 years, with analysis reported for 195 patients (n = 101 treatment groups, n = 94 controls).

Low et al. tested the hypothesis that rhGH would ameliorate the growth delay by following, for 3 years, 49 children
in a prospective, randomized, masked study. A total of 26 children received 0.2 mg/kg GH during their acute hospitalizations and 23 children received 0.9% saline as placebo during the same time periods of acute hospitalization. Children who were treated with GH during their acute care maintained stature (height for age percentile and height-velocity), whereas untreated children who were not in a growth spurt at the time of burn remained delayed in linear growth at the end of the study, 3 years post-injury. Continuing with this study, Low et al. found that the differences in height percentiles had nearly resolved at 5 years post-burn.44 Short-term (average of 6 weeks) administration of GH did not attenuate the hypermetabolic state; resting energy expenditures remained elevated for both groups of children during the time they were being treated acutely. However, the administration of GH apparently made up for a deficit that commonly occurs following severe burn injury. Children burned during a growth spurt are thought to have the advantage of higher levels of growth hormone available and thus, can maintain normal growth without exogenous hormone.

**Summary**

In this chapter, we have described various interventional strategies used in counteracting the hypermetabolism, catabolism and growth delay (in children) which is present after severe burns. These burn-induced sequelae can continue for many years, thus mitigation of these responses is of vital importance. Methods used to mitigate some of these responses include aerobic and resistive exercise, as well as the use of anabolic agents, such as growth hormone and oxandrolone. Beta-adrenergic blockade to reduce cardiac work is a promising interventional strategy, but needs further evaluation. Strategies to attenuate catabolism, hypermetabolism, and other burn-induced problems should also result in improvements in the quality of life of the

**Figure 49.3** (a–c) The ravaging effects of a severe burn are illustrated in these photos. The body is in a hypermetabolic and catabolic state. This results in loss of muscle mass and bone mass, and is worsened by prolonged inactivity. In addition, there are physical limitations sometimes caused by the loss of digits or extremities and of burn scar contractures.
The ultimate objective of strategies to attenuate catabolism, hypermetabolism, and other burn-induced problems should be to improve the quality of life of burn victims. This may be accomplished by offering the burn victims physical and psychosocial rehabilitation strategies to enhance their potential of a full and effective re-incorporation into society.

Further reading


Access the complete reference list online at [http://www.expertconsult.com](http://www.expertconsult.com)
References


Reconstruction of burn deformities: an overview
Lars Peter Kamolz, Ted Huang

The severity of burn injuries is usually assessed, if not by patient survival, by the consequence of burn injuries, i.e. scar hyperplasia/hypertrophy, scar contracture, and structural deformities due to loss of bodily components. Since the bodily deformity is closely related to the magnitude of injuries, restorative procedures are seldom indicated if the depth of injury is superficial and the burned area limited (Fig 50.1) but are required for deep burns (Fig 50.2).

The possibility of surviving burn injuries has changed dramatically over the past 30 years, attributable singularly to an aggressive approach in surgical treatment of burn wounds, i.e. early wound debridement and wound coverage.1–3 It is ironic that the success attained in burn treatment has resulted in a higher number of patients who will need to undergo reconstruction because of an aggressive ‘life-saving’ surgical treatment.

Formation of scar tissues at a wound site and contraction of the scar tissues are the normal consequence of an injury. Although the exact mechanisms accounting for the sequential changes in wound healing and scar formation remain incompletely understood, wounds with infection and/or those allowed to heal spontaneously, for instance, tend to result in a thickened scar that is contracted circumferentially; an observation suggestive that various fibrogenic cytokines such as transforming growth factor β could play an important role in the pathogenesis of otherwise clinically undesirable consequences.4,5

Thickened and contracted scar tissues, i.e. the changes that are ‘normal’ and ‘expected’ consequence of the wound healing processes, are microscopically composed of collagens arranged in whorls and nodules. The changes may be observed as early as 3–4 weeks following the injury and they are cosmetically unsightly and functionally disturbing (Fig. 50.3).

Reconstruction of burn deformities

General principles

Burn injuries are a traumatic illness resulting in aberrant body physiologic processes caused by thermal destruction of the skin. The altered physiologic processes will affect not only the healing of the original burn wounds but also healing processes of the secondary surgical procedures aiming to restore the consequence of the original injuries. The treatment, under an aberrant physiologic circumstance, should aim to repair the burn wounds first. Attempts to restore deformities should be delayed until recovery from the initial phase of injury is complete.6

Early treatment of deformity

Of the consequences of burn injuries, hyperplasia and contracture of resultant scars at wound sites and the contraction of mobile bodily parts, i.e. eyelids, neck, axilla, elbow, hands-fingers, groin, knee and ankle-foot, are two most common problems that are in need of attention. The regimen of applying pressure upon scar tissues and of immobilizing joint structures has been advocated to minimize the undesirable consequences of scarring and scar contracture (Fig. 50.4).

Although the true efficacy of a non-surgical regimen to control the deformities has not been established, the frequency of secondary joint release among individuals who ‘endured’ the morbidities associated with proper joint splinting for a period of no less than 6 months has been noted.7,8 The use of pressure dressing, especially in the areas such as upper and lower limbs, with proper splinting of the hand and fingers is strongly recommended soon following the injury. The regimen of non-surgical management of burn deformity must include daily physiotherapy and exercise to maintain joint mobility and to prevent muscle wasting.

Assessment of burn deformities

Objective assessment of deformities by the patient is neither physically nor psychologically possible soon after the accident. Restoration of physical changes resulting from the injury, in addition to the need of obtaining relief of pain and discomfort, are the primary concerns of the patient. Medical assessment of physical problems caused by scarring and scar contracture will require a detailed understanding of the extent of original injury and the precise treatment approach used to manage the burn wound. Formulating a realistic plan to restore physical problems and to alleviate pain and discomfort in the area of injury requires an in-depth analysis of the physical deformities and psychological disturbance sustained by the patient. Psychiatric, psychosocial, and
physiotherapeutic care, in this sense, must be continued while the surgical treatment plan is instituted.

**Indication and timing of surgical intervention**

For a surgeon, making a decision of ‘how’ to operate on a patient with burn deformities is quite simple. In contrast, deciding ‘when’ to operate on a patient with burn deformities can be difficult.

The basic principle of restoring bodily deformities that impose functional difficulties before surgical efforts are directed to restoring appearance should be followed. The surgeon’s efforts should be concentrated upon restoring the deformed bodily parts essential for physical functions. An exposed skull or a calvarial defect, contracted eyelids, constricted nares, contracted major joints, and a urethral and/or anal stricture in individuals with severe perineal burns, are the prime indications for early surgical intervention. In contrast, restoration of contour deformity can be delayed. In fact, reconstruction of the nose and the ear, for instance, should not be initiated until its growth pattern has reached the growth peak; ear reconstruction may be initiated once the child has reached 6–8 years of age, while nasal reconstruction should be delayed until 16–18 years.

Although the exact scientific basis remains unclear, it has been advocated that attempts at reconstructing burn deformities should be delayed for at least 2 years post-burn injuries; the time needed for scar maturation. During the interim, the use of pressure garments and splinting is recommended to ‘facilitate’ scar maturation and to ‘minimize’ joint contracture. The true efficacy of pressure garments in ‘facilitating’ scar maturation remains undefined. Lack of a reliable method to determine various stages of scar maturation and personal difference in assessing scar appearance could...
account for the controversy. Splinting a joint imbedded in burned scars with an external device to maintain a proper joint angulation, on the other hand, was found to be effective in reducing the need for re-operation to achieve joint function. However, this was possible only if the patient would wear the splint faithfully for a minimal period of 6 months. A physical exercise regimen to provide vigorous movements of a burned joint was found to be effective in reducing the need for surgical intervention.

The 2-year ‘moratorium’ on early burn reconstruction, in some ways, is justifiable. Operating on an ‘immature’ scar characterized by redness and induration is technically more cumbersome; hemostatic control of the wound is difficult and inelasticity and lack of tensile strength noted in scar tissues render tissue manipulation more difficult. A high rate of contracture noted in instances where a partial-thickness skin graft is used for releasing a wound showing active inflammatory processes may further support the advocacy of two years of delay in initiating burn reconstruction.9

Our recent change in handling individuals who were in need of reconstruction followed the finding that contracted bodily parts can be effectively reconstructed in the first 2 years post-burn if skin flap, fasciocutaneous flap or musculocutaneous flap techniques are used. Reconstruction is initiated in individuals as early as 3–6 months following the initial injury. The approach is well-suited for those encountering functional difficulties because of scarring and scar contracture.10

The techniques of reconstruction

There are several techniques routinely used to reconstruct bodily deformities common to burn injuries, i.e. unsightly scar, scar contracture, and joint contracture. Principally, they are: (1) excision of scars with primary closure technique; (2) wound closure following scar excision with a piece of free skin grafting technique with or without the use of dermal template; (3) an adjacent skin flap technique; (4) an adjacent fasciocutaneous (FC) flap technique; (5) an adjacent musculocutaneous (MC) flap technique, and (6) a distant skin, fasciocutaneous (FC) flap, or musculocutaneous (MC) flap via microsurgical technique.

Primary wound closure technique

Excision of an unsightly scar with layered closure of the resultant wound is the simplest and the most direct approach in burn reconstruction. The technique is also useful in handling scars that are hyperesthetic and pruritic.

The margins of scar requiring excision are marked. It is important to determine the amount of scar tissue that can be removed, yet the resultant defect could be closed directly. ‘Pinching’ the edge of scar at three or four different sites along the length of scar to determine the mobility of the wound edges is the simplest yet most reliable method to determine the amount of scar tissues that can be removed safely. Leaving a rim of scar tissue is generally necessary unless the size of scar is so small that removal and direct closure of the resultant wound would not lead to contour deformity. A circumferential incision is made in the line marked and is carried through the full thickness of the scar down to the subcutaneous fatty layer. While the outer layer of the scarred tissue is excised, 4–5 mm of collagen layer is left attaching to the base. The conventional approach of wedged scar excision will result in depression along the site of scar excision, an iatrogenic consequence that could be difficult to amend secondarily. In order to minimize vascular supply interference along the wound edges, undermining of scar edge should be kept minimal. In some ways, is justifiable. Operating on an ‘immature’ scar characterized by redness and induration is technically more cumbersome; hemostatic control of the wound is difficult and inelasticity and lack of tensile strength noted in scar tissues render tissue manipulation more difficult. A high rate of contracture noted in instances where a partial-thickness skin graft is used for releasing a wound showing active inflammatory processes may further support the advocacy of two years of delay in initiating burn reconstruction.9

Skin grafting technique

Free skin graft without incorporating a dermal template

Covering an open wound with a piece of skin graft harvested at an uneven thickness is the conventional approach of wound closure. While the whole structure of the skin removed as an intact unit, i.e. epidermis and dermis, is defined as a full thickness skin graft, a piece of skin cut at a thickness varying between 8/1000th of an inch (0.196 mm) and 18/1000th of an inch (0.441 mm) is considered to be a partial- or a split thickness skin graft. The thickness of a full thickness skin graft is quite variable depending upon the body site. A full thickness skin graft harvested from the back, for instance, will be 16/1000th of an inch (4 mm) in thickness, while one harvested from the upper eyelid will be around 35/1000th of an inch (0.8 mm). The difference is attributable to the difference in the thickness of the dermis.

While a power-driven dermatome is usually used to harvest a partial- (split-) thickness skin graft, a free hand knife could be used to cut a piece of full thickness skin graft. A paper template may be made to determine the size of skin graft needed to close a wound. The skin graft is laid onto the wound, colloquially known as the ‘wound bed’, and is anchored into place by suturing the graft to the wound edge-to-edge at various sites. An apposition of the skin graft with the ‘wound bed’ is essential to ensure an in-growth of vascular network in the graft within 3–5 days for graft survival, as any mechanical barriers, i.e. blood clot or pool of serous or purulent fluid, will prevent vascularizing processes, leading to graft loss. A gauze or cotton bolster tied over a graft has been the traditional technique to anchor and to prevent fluid accumulating underneath a graft even though no objective evidence supports the efficacy of this maneuver. A quilting technique instead of bolstering technique has been found to be more effective in immobilizing a skin graft and is associated with fewer morbidities (Fig. 50.6).

The basis for using a free skin graft of various thicknesses to close all wounds is not entirely clear. It is, however, clear that the use of a thin graft is more appropriate for closing wounds with unstable vascular supplies, particularly if skin graft donor sites are scarce. Although the exact reasons remain undefined, the quality and the presence of dermis could influence the extent of wound contraction. That is, the extent of contraction noted in a ‘wound bed’ is more if a piece of skin graft with minimal dermal inclusion, i.e. a thin partial thickness skin graft, is used. By inference, the presence of dermal structure in the ‘wound bed’ could affect wound contraction.

Free skin graft with prior incorporation of a dermal regenerative template

For the past several years, artificial dermal substitutes that have been manufactured from allograft or xenograft materials, e.g. AlloDerm™, Integra™, etc. (the manufacturing
an open wound has been found to form a layer of parenchymal structures resembling a dermis rendering wound coverage with an autologous skin graft where an immediate closure is not possible. The need for a staged approach to graft a wound, however, is considered cumbersome (Fig. 50.7).

**Skin flap technique**

The approach of using a segment of skin with its intrinsic structural components attached to restore a destroyed and/ or absent bodily part follows the fundamental principle of reconstructive surgery. The technique, however, will not only cause skin scarring in the flap donor site but also a donor site contour alteration that may be considered cosmetically unsightly. Loss of a skin flap, more commonly encountered in burn patients when the altered vascular supplies to the skin are altered by injuries and surgical treatment, could render this technique unsuitable, if not even undesirable. Despite the drawbacks, the approach to restoring a damaged bodily part with a piece of analogous-tissue is technically sound and the procedure will provide an outcome to restore bodily function and contour. The recent technical innovation of incorporating a muscle and/or fascial layer in skin flap design, especially in burned areas further expanded the scope of burn reconstruction as more burned tissues could be used for flap fabrication.

**Figure 50.5** (a) The scar formed in the left submental area was pruritic and unsightly. The extent of the excision was marked and the area was infiltrated with 0.25% lidocaine containing 1:400,000 epinephrine to achieve hemostasis. (b) The epidermal layer was sharply excised leaving the dermal layer intact. (c) The wound edges were closed primarily in layers using nylon sutures. (d) The extent and appearance of scarring noted before excision, 10 months following the initial burns. (e) The appearance of the operative site five years following partial scar removal.

**Figure 50.6** A partial thickness skin graft was used to cover an open wound resulted from releasing of a contracted lower lip.

process was initially described by Yannis and Burke in 1980), are biosynthetic two-layered membranes composed of a three dimensional porous matrix of fibers and of cross-linked bovine tendon and glycosaminoglycan (chondroitin-6-sulfate). The material when implanted over
Reconstruction of burn deformities: an overview

Figure 50.7  (a) A 6-year-old girl bothered by recurrent infection caused by scar-imbedded inclusion cysts in the left flank area extending from the lower axilla to the upper trochanteric region. (b) A piece of Integra™ was used to cover a wound of 25–30 cm x 10–15 cm. (c) The vascularized Integra™-covered wound was covered with a partial thickness skin graft of 8/1000th of an inch in thickness 3 weeks later. (d) The appearance of the grafted area a year following the operation. The scar was noted to be soft and pliable.

Figure 50.8  (a) A triangular skin mark made over the right nasolabial area to mark an axial skin flap fabricated for left lower eyelid ectropion reconstruction. (b) The size of skin flap was equal to the size of the lower eyelid defect to cover an open wound that had a cartilage graft for tarsal replacement. (c) The triangular flap was rotated cephalad and laterally to fill the left lower eyelid tissue defect. (d) The left lower eyelid ectropion consequential to the loss of eyelid skin and the tarsus. (e) Appearance of the left lower eyelid 3 years following the reconstructive procedures.

The axial skin flap
The skin in many areas is nourished directly by known cutaneous arteries. A skin flap, regardless of its length-to-width ratio requisite, may be fabricated if the vascular trees are included in the flap pattern (Fig. 50.8).

The z-plasty technique
This technique, in short, is based upon the principle of mobilizing a full segment of skin, with its vascular supplies undisturbed, from an area adjacent to the site needing tissue replacement. This is conventionally achieved by interposing two skin flaps of an equilateral triangle, i.e. 60° that has a common limb drawn along the scarred area. A scarred and contracted area is released as the flaps are interposed in an opposite direction. Any space defect due to skin and underlying tissue movement is made up by mobilizing tissues from an adjacent area (Fig. 50.9).

The modified z-plasty technique; alias $\frac{3}{4}$ z-plasty technique
Two flaps are used, as in the conventional z-plasty technique, of a right angled triangle, i.e. one internal 90° angle and the other with a ‘modified’ 45° angle; the angle for the triangular flap has decreased from a conventional 60° to 45°, hence the $\frac{3}{4}$ z-plasty technique. The limb of the 90° triangle is made in the scarred area resulting from the tissue loss. The second limb of the triangle is made perpendicular to the first one. The angle formed by the second limb of the right-angled triangle and the hypotenuse of the second right-angled triangle is 45°. A triangular skin flap fabricated in this manner is rotated to fill a tissue defect formed from surgical releasing of the contracted scarred area. The procedure, in this sense, is a variant of the conventional rotational/interpositional skin flap technique by rotating the 45° triangular skin flap singularly to make up the defect (Fig. 50.10).

Despite its geometric advantage in flap design, fabricating a skin flap or skin flaps for z-plastic reconstruction of burn deformities is not infrequently plagued with skin necrosis. Aberrant vascular supplies to the skin attributable to the original injury and/or surgical treatment could be the factor responsible for the problems. The use in recent years of a skin flap designed to include muscle or fascia, has further expanded the usefulness of conventional z-plasty and $\frac{3}{4}$ z-plasty techniques in burn reconstruction.
Figure 50.9 (a) Neck scar. (b) Two equilateral triangles were marked into a ‘z’ and incisions were made to free up two triangle skin flaps. (c) Two flaps were interposed to achieve the release. (d) Before release, the patient, a 13-year-old boy, complained of tightness over the neck area caused by a tight scar band. (e) The appearance of the neck 4 years following releasing procedures. The z-plasty procedure alleviated the neck tightness.

Figure 50.10 (a) A horizontal line was drawn along the site of tightness. A triangular skin marking was also drawn with its cathetus perpendicular to the line of release. (b) The triangular flap was rotated cephalad and medialward to make up the wound defect resulted from release. (c) The flap donor site closure as well as the inset of flap was achieved primarily.
Musculocutaneous (MC) or fasciocutaneous (FC) flap technique

Inclusion of not only the skin but also the subcutaneous tissues and the fascia and the muscle is necessary to fabricate a skin flap to reconstruct tissue defect in individuals with deep burn injuries. That is, fabricating a flap in a burned area is possible if the underlying muscle or the fascia is included in the design.

**Musculocutaneous z-plasty technique**

While the skin pattern is identical to the conventional z-plasty technique, the muscle underneath must be included in the flap fabrication. Although physical characteristics of normal skin, i.e. the skin pliability and expandability, are absent if scarred skin is included in the flap design, a 'scarred-skin' MC or FC flap could be safely elevated and transferred to close an open wound. In practice, the MC z-plasty technique is useful in neck release and in the eyelid because of the character of underlying muscle; i.e. the platysma and orbicularis oculi muscles are thin, pliable and easily movable (Fig. 50.11).

**Fasciocutaneous z-plasty technique**

This is a technical modification of the MC z-plasty technique, by including the muscular fascia only. Separation of skin and its subcutaneous tissues from the underlying fascia
must be avoided in order not to impair the blood supply to the flap. In practice, the technique is useful in reconstructing contractural deformities around the knee and ankle areas.

3/4 Fasciocutaneous z-plasty technique
A 45° triangular FC flap that includes the fascial layer may be fabricated anywhere in the body. The flap is elevated and then turned 90° to cover a tissue defect resulting from releasing a contracted wound. Although an unburned skin when used to fabricate a triangular flap is more versatile, a scarred skin with or without subcutaneous tissues may be used also for flap fabrication. Suturing the fascia to the skin edge is a useful maneuver to avoid accidental separation of the fascia from the overlying skin, and impairing the vascular supplies to the dermal structures (Fig. 50.12).

Paratenon cutaneous z-plasty and 3/4 paratenon cutaneous z-plasty techniques
In instances where fabrication of a composite skin flap is indicated in the distal section of the upper and lower extremities, i.e. wrist and ankle, the paratenon, a fascial extension of the voluntary musculatures, should be included in the flap design and fabrication (Fig. 50.13).

### Tissue expansion technique
An extreme stretching of the integument is quite commonly observed in human bodies. The tissue expansion technique follows the same principle, except it is carried out intentionally with an inflatable device, i.e. a tissue expander. Because of excessively active scarring processes more frequently observed in burn victims, especially during the period soon following the accident, timing to initiate the procedure could be difficult. Use may be limited because of pain and discomfort associated with expansion (Fig. 50.14).

### Free composite tissue transfer via microsurgical technique
With the advent of microsurgical technique, transplanting a composite tissue can be carried out with minimal morbidities. Opportunities for this regimen, however, may be limited in burn care because of a paucity of donor materials. It is ironic that burn patients with suitable donor sites seldom require such elaborate treatment. Those who are in need of microsurgical tissue transplantation are inevitably those with no appropriate donor sites because of extensive tissue destruction.

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**Figure 50.12** (a) A triangle skin marking was made with its cathetus drawn along the line of contracture and perpendicular to the inferior wound edge resulting from the release. (b) Incisions were made along the skin marking for flap fabrication. (c) The triangle skin flap was elevated to include the fascial layer to form a random fasciocutaneous flap. (d) The appearance of flap and the wound 10 days following the release and flap reconstruction.

**Figure 50.13** (a) Two equilateral triangles were marked over the left heel cord, the area felt to be tight. (b) The skin flap was fabricated to include the fascial layer underneath. (c) Two FC flaps were interposed to achieve the release. (d) The inset of two flaps completed. (e) The appearance of left heel cord before release. (f) The appearance of left heel cord 4 years following release.
Reconstruction of burn deformities: an overview

Figure 50.14 (a) The patient was a 4-year-old with scalp alopecia resulting from extensive burns involving the scalp and the face area. (b) No attempt was made to reconstruct the scalp alopecia until she was 8 years of age. The tissue expander technique was used to expand the left side of scalp for wound coverage. (c) The appearance of right temporal scalp following two scalp expansion-advancement procedures.

Comments

The regimen of burn treatment has changed drastically over the past 50 years. The central focus of burn treatment was moved from understanding the pathophysiology of burn injuries and mastering patient resuscitation in the 1950s, to learning how to cover a burn wound in the 1960s, even though the principle of early debridement of burn wound was clear to the physicians. Reconstructive efforts offered to those who had survived the trauma were mostly limited to restoration of lost physical functions. Cosmetic reconstruction was simply seldom offered. The treatment outcome, however, was in most instances suboptimal because of excessive scarring and scar contracture, two consequences which continue to limit the outcome of burn reconstruction.

A more aggressive approach in managing burned wounds came in the 1980s. Various pharmacological agents have been used to control aberrant metabolic processes induced by the trauma to control infectious consequences and safer anesthetic agents have contributed substantially to the survival of burn victims. The regimen of an early debridement and wound coverage initially with biological dressing and later with autologous skin grafts, had further enhanced the survival rate. It is, however, ironic that this improved survival has caused an upsurge of patients in need of reconstruction. That is to say that everyone who had survived burns would be in need of reconstruction, functional or otherwise.

Unsightly hypertrophic scar, scar contracture affecting particularly the joint structures, and destroyed body parts are still the most common sequelae of burn injuries today. Although the use of skin grafting and skin flaps have remained the mainstay of burn reconstruction, the outcome can still be suboptimal because of techniques that cannot meet the therapeutic objectives to correct the three problems listed.

The exact timing to initiate reconstruction of burn deformities remains unsettled. Difficulty in obtaining suitable tissues for replacement, morbidities associated with surgical procedures that involve scar tissues that are active, and outcomes that cannot be assured, could account for the controversy. The predicament, on the other hand, could be due to the techniques used. The use of flap techniques, particularly the use of techniques such as fasciocutaneous z-plasty and paratenon cutaneous z-plasty, enable us to reconstruct contractural deformities that involve the major joints as well as eyelid deformities as early as 4–6 months following the injuries.

Questions concerning the ideal approach in managing burn deformities remain unanswered. Although surgery has been the mainstay of reconstructive approach for the past half century, these problems perhaps, should be handled completely non-surgically or with limited use of surgical means. That is, reducing the inflammatory phase following injury and controlling the level of various fibrogenic cytokines could be useful in forming scar tissues considered to be physiomechanically, sound yet cosmetically pleasant. The science of tissue engineering could lead to the formation of bodily parts that could be used to replace absent or destroyed body components.

Summary

Reconstruction of bodily deformities due to burns is difficult, if not impossible. The difficulty is largely due to the lack
of understanding of the pathomechanism of wound healing and scar tissue formation. Furthermore, technical limitations to replacing bodily parts further fuels the psychological frustrations for reconstructive surgeons.

The use of a musculocutaneous flap and/or fasciocutaneous flap, particularly as modified to follow the principles of z-plasty or $\frac{1}{2}$ z-plasty, has been found to be effective in restoring functions lost because of scarring and scar contracture. Furthermore, it is conceivable that refinement in microsurgical tissue transfer techniques in conjunction with advances that will be made in tissue engineering/body parts formation, would render the task of reconstructing burn deformities easy and simple.

Further reading


References

The use of skin grafts, skin flaps and tissue expansion in burn deformity reconstruction
Ted Huang, Manuel Dibildox

Introduction

Although the magnitude varies, scars formed around injury sites and/or structural deformities are the common sequelae of burn injuries. Secondary surgical treatment of the consequences, whether it is for function or appearance is usually necessary. Secondary reconstruction of bodily deformities requires the use of autologous uninjured tissues harvested as a free skin graft, a pedicled skin flap with or without fascia and/or muscle layer attached, and a free composite graft.

Skin grafts

The skin thickness varies depending upon the bodily locations; the eyelid skin, especially the upper eyelid, and the skin located behind the ear is thin, while the scalp, trunk, the palmar skin, and the sole of the foot are thick.1–3

A skin graft is classified into two types depending upon the amount of skin structures included, i.e. a piece of skin shaved to contain epidermis and various layers of dermis is said to be a split-(partial-) thickness skin graft (STSG). The graft can be harvested in different thicknesses; a thin graft is 6–8/1000th of an inch (0.15–0.20 mm) in thickness, while a graft with a thickness of 16–18/1000th of an inch (0.40–0.45 mm) is a thick split-thickness skin graft. A skin cut to contain all components of the skin, i.e. epidermis and dermis, is classified as a full-thickness skin graft (FTSG) (Fig. 51.1).4,5

Skin flaps

A skin flap is a graft composed of all skin elements, i.e. epidermis, dermis and subcutis that includes fatty tissues and neurovascular structures. Depending upon the type, it may include the fascial layer or the muscles underneath. The flaps are classified into: (1) a random cutaneous flap; (2) an axial (arterialized and/or neuroarterialized) skin flap; (3) a fasciocutaneous flap; (4) a musculocutaneous flap, and (5) a free composite flap attached with neurovascular structures.

The techniques to fabricate various skin flaps

A random cutaneous flap

Design and fabrication of a random cutaneous flap could be made anywhere in the body surface. The shape and the form of a random skin flap can vary depending upon the treatment plan; a flap is configured according to the outline of the wound defect. A fabricated skin flap is advanced to complete wound closure. The flap mobility, however, could be restricted if the layer of underlying subcutaneous tissues is thick or fibrous. The length and the width of a random cutaneous flap are determined according to the pattern of vascular supplies to the skin; the ratio of flap length and the width is limited to 2:1. Necrosis of the skin at the end is common for a long and narrow skin flap (Fig. 51.2).6–8

An axial or an arterialized skin flap

As shown, a nasolabial flap can be fabricated with a length versus width ratio in excess of 2:1; this is a skin flap formed along the side of nose. The Bakamjian flap, a deltopectoral flap, basing its vascular supplies upon the branches of intercostal vessels, has been used frequently to reconstruct deformities that involve the lower face and the neck (Fig. 51.2).9–12

Z-plasty

Surgical release of a tight band can be achieved by switching right angularly two triangular skin flaps 60° with their catheti formed in continuity along the axis of a tight scar, i.e. the z-plasty technique.13–15 Although the technique is suited for releasing a tight scar band across a joint surface, in practice a scarred area is seldom left with unburned skin on both sides of a burn scar band. Consequently, the relief of contraction obtainable by means of classic z-plasty technique may be limited.

Modified z-plasty alias ¾ z-plasty

The flap configuration of z-plasty may be modified by changing the angle of two opposing triangles, i.e. from 60° to 90° and 45°, respectively. The technique is also known as a
Easily fabricated to make up an open wound that is long (Fig. 51.4).

Flap techniques to reconstruct common burn deformities

The eyelid deformities

Although the use of a skin graft has been advocated as the method to reconstruct eyelid deformities, i.e. eyelid ectropion and entropion, recurrence of contraction is quite common. The use of a nasolabial skin flap is a preferred technique to reconstruct ectropic or entropic deformities of the lower eyelid. It provides the tissue bulk needed and the means for a complex eyelid reconstruction that requires the use of cartilage graft (Fig. 51.5).
Figure 51.2 (a) A segment of skin, oblong in shape, is dissected out in the area along the nasolabial fold on the left. (b) The skin and its subcutaneous layer is separated at the level just above the muscle to assure the inclusion of the vasculatures. (c) The flap with the skin left upon the subcutaneous tissues, i.e. an island skin flap, is rotated laterally to cover an open wound located underneath the ciliary border. (d) The wound edges are closed primarily.

Figure 51.3 (a–c) The technique of z-plasty may be modified by changing the flap angle from 60° to 90° for one and 30–45° for the other to achieve the tight scar release.
Neck contracture
A ¾ musculocutaneous (MC) z-plasty is a modified transpositional composite skin flap technique. A triangular skin flap with its underlying musculature, i.e. platysma muscle attached, is fabricated in the area adjacent to the opened wound resulted from neck release. Cathetus of the triangular skin flap is made perpendicular to the corner of the wound. The flap, with its dimension fitting the wound defect, is fabricated as an MC flap. The flap is rotated 90° to close the wound defect (Fig. 51.6).

Axilla contracture
Although the exact reasons remain unclear, the axilla is the joint among the large joints most commonly plagued with contracture. Splinting has been advocated as the method to manage the problem, but the efficacy of this treatment modality remains undefined. Similarly, outcomes obtainable with the conventional approach of surgical release and skin grafting are unpredictable.

A ½ fasciocutaneous (FC) z-plasty is a modified transpositional or interpositional composite skin flap technique. The fascial layer is included in the flap fabrication. The flap donor defect is closed primarily, or with the use of skin graft (Fig. 51.7). Neither the use of splint nor physiotherapy are prescribed following the surgery.

Elbow and wrist contracture
The indication and the technique are similar to the approach used to attain release of axillary contracture. The patient is encouraged to move the joints within 1–2 weeks following the release.

Knee contracture
The contracture is noted to involve the popliteal area more often than the patellar surface of the knee. As in other joints, a modified transpositional skin flap technique is suited for reconstructing the deformity. The technical details are similar to those used in the axilla and elbow joint release.

Ankle contracture
Contractural deformities involving an ankle joint are quite common among individuals sustaining extensive burn injuries. Although reconstruction of ankle deformities is indicated in instances where non-surgical maneuvers to control the consequence are ineffective, closure of a surgical wound in the ankle area can be difficult because of limited available tissue suitable for wound repair. A composite skin flap that includes the fascia/paratenon and the overlying skin structures fabricated from the area adjacent to the ankle, a ½ FC z-plasty technique, has been used to cover the wound resulting from surgical release of the contraction (Fig. 51.8). Splinting of the ankle by wearing a high-top shoe for a period of 3–6 months following the procedure is strongly recommended.

Tissue expansion
Bodily deformity reconstruction by means of a tissue expander is based upon the principle of utilizing the excess skin resulting from stretching of normal skin. A silicone balloon is placed in a tissue pocket mostly above the muscle layer, inflated to a designated volume via an injection port placed in the adjacent area. An expanded skin is suited for replacing a scarred skin as it retains the color and
Figure 51.5  (a) Blepharophimosis resulted from the loss of the eyelids. (b–d) A nasolabial island skin flap was fabricated to reconstruct the lower eyelid deformity. (e) The appearance of the left eyelid 4 years following reconstruction.
Figure 51.6 (a–e) The muscle is incorporated in the fabrication of triangular flaps used to release this neck contracture 6 months following the injury. The muscle-skin flap donor site is closed primarily.
The use of skin grafts, skin flaps and tissue expansion in burn deformity reconstruction

Figure 51.7 (a–e) MC z-plasty technique is utilized to achieve contractural release; contracture developed within 4–5 months following the injury. (e) Denotes the appearance of leased right axilla 2 years later.

texture, and in some instances, the hair and sensation, of the donor skin.

The use of a tissue expander in reconstructing burn deformities

Indications for tissue expansion

The technique is considered useful for instances where a deformity requires a large segment of uninjured skin to restore structural deformities, provided that an ample amount of unburned skin is available in the locale adjacent to a proposed flap recipient site. The skin over the flap donor site must be sufficiently pliable for expansion.

Contraindications for tissue expansion

Skin elasticity is often altered with burns because of scarring. Loss of skin elasticity essentially renders the mechanical stretching of scarred skin difficult, if not impossible. Although the exact reasons remain unclear, scarred skin can be broken easily with the force of traction resulting in wound
disruption and consequently, expander extrusion. The use of the tissue expansion technique in an area with extensive scarring is therefore, contraindicated, if not impractical.

**Description of a tissue expander (TE) placement technique**

The subcutaneous layer is infiltrated with local anesthetics, i.e. 0.25% lidocaine containing epinephrine in 1:400000 concentration is used. A subcutaneous tissue pocket is surgically created with a size that will house an implant. Instilled into the lumen is 30–40 cc of physiologic saline solution to stretch out the implant. A second subcutaneous tissue pocket is located adjacent to the incision site to house the accompanying injection port.

**After care of TE**

Balloon expansion should be delayed for 3–4 weeks. Once the healing processes are complete, 30–45 cc of physiologic saline solution is injected into the expander via an injection port. The injection is repeated at a rate of once or twice a week until the desired extent of skin stretching is attained.

**TE in clinical use**

**The use of TE in scalp alopecia reconstruction**

The method of scalp alopecia reconstruction centers upon the principle of replacing scalp alopecic tissues; a hair-bearing scalp flap mobilized from the area adjacent is advanced directly or with rotation of the flap. It is important to assess the density of hair follicles in the scalp planned for expansion. The hair density may decrease with scalp stretching and aesthetic appearance of a reconstructed scalp deformity may be suboptimal.

The outcome of scalp alopecia reconstruction can be satisfactory for a defect that is less than one-third of the total scalp area. An acceptable outcome is attainable with two or three procedures. In contrast, the outcome is judged to be
The use of skin grafts, skin flaps and tissue expansion in burn deformity reconstruction

The lower one-third of the face is injured frequently; it can result in contractural deformities that involve the lower cheek, the lip, the chin and the upper neck. Results obtainable with the conventional techniques of skin grafting and local flap are not always satisfactory, unless the scarred deformities can be replaced with a piece of thin and unburned skin. Expansion of the skin located in the neck area, if feasible, is the choice. The expander is placed usually in the upper neck area underneath the skin but above the platysma muscle and is expanded to gain sufficient flap dimension to allow cephalic advancement to cover the scarred area, i.e. the lower cheek, lower lip and the chin that includes the submentum. The outcome is cosmetically acceptable in most instances (Fig. 51.10).

**Figure 51.9** (a) Electrical burns caused not only the loss of scalp but also the calvarium. (b) Two expanders were inserted over the temporoparietal area on both sides for scalp expansion. The calvarial defect was repaired with a free bone graft while the scalp defect was restored with expanded scalp tissue. (c) The appearance of scalp 1 year following the procedures.

**Figure 51.10** (a) A moderate degree of scar hypertrophy developed in the lower face around the mouth. (b) A tissue expander of 350 cc was inserted in the mid-neck area. (c) The expanded skin was advanced to replace the scarred area around the mouth and the upper neck area.

**The use of TE in reconstructing lower face deformities**

Grafting a skin defect is the simplest technique to repair an open wound. It is, however, ineffective in restoring cosmetic appearance of the injured bodily structures. Furthermore, recurrence of scar thickening and contraction of scar tissues is less likely with the use of full-thickness skin graft, the outcome is at best, unpredictable and unreliable. The paucity of full-thickness skin graft donor site in individuals with extensive burns could furthermore, render the lower cheek, lower lip and the chin that includes the submentum. The outcome is cosmetically acceptable in most instances (Fig. 51.10).

**Comments**
treatment modality ineffective. The use of a skin flap is the recommended approach because of its reliability and predictability.

The task of fabricating a random cutaneous flap, i.e. a skin flap with a random pattern of vascular supply, is technically simple. Survival of the flap, on the other hand, may be compromised if the flap length to width ratio exceeds 2:1.6,7 The dilemma of circulatory embarrassment in a skin flap is circumvented by inclusion of known arterial supplies and/or underlying fascia or muscle in flap design and fabrication, i.e. an axial skin flap and a fasciocutaneous or musculocutaneous flap.20 The ease of flap mobilization, that is the function of flap arc rotations can be facilitated if the flap length–width ratio is increased from 2:1 in a random skin flap to 4–5:1 in a FC or MC flap. For an axial skin flap, the length of arterial tree will be the governing factor in determining the flap length.

The classic z-plasty is executed technically by rotating 90° in the opposite direction of two triangular skin flaps of 60° angle formed on either side of a contracted scar band. Although the increment in tissue dimension, i.e. release of tightness in a scar band gained with the technique has been calculated mathematically to be 1.6-fold of the original scar length, the exact extent of release achievable in practice is less optimal.15 Differences in skin elasticity and the magnitude of scarring surrounding the skin flaps, the factors affecting the flap advancement, and rotation are the probable factors responsible for the discrepancy in efficacy of the technique.

The most important factors governing the efficacy of the technique in clinical use are the pliability of the skin in the site of expansion and the pattern of vascular supplies to the skin in the proposed expansion site. In this regard, the technique may not be suited to expand the skin in a burned area as the skin is unpliant and the vascular supply pattern is aberrant. Incidents of extrusion, the ultimate sign of technical failure in the TE technique, are common for an implant placed in the extremity and/or in an area with extensive scarring.

With the advent of a microsurgical technique of composite tissue transfer, the students of burn reconstructive procedures have become ignorant of the approaches in fabricating a random skin flap and/or an axial flap at various bodily sites described in the past. The flaps such as the Bakamjian flap; the deltopectoral skin flap;9,10 the deltoid flap;21 the Song radial arm flap,22 etc. are useful, particularly for burn deformity reconstruction in children; unburned bodily sites suitable as flap donor sites are scarce and the vessel size and length are small – the factors predestined for graft transfer failure if ignored.

Summary

It is essential for a surgeon to be versed in the knowledge of techniques described for burn deformity reconstruction. The use of a given technique may not be feasible because of structural alteration induced by the injuries causing the bodily deformity requiring reconstruction. It is similarly important and essential for a surgeon to be familiar with the technical limitations and outcomes derivable with the techniques used. The techniques based upon modification of the classic interpositional skin flap technique, i.e. 3/4 z-plasty, 1/4 FC z-plasty, 1/4 MC z-plasty, and 1/4 axial z-plasty techniques are in our experience the most useful approaches in alleviating contractural deformities noted in burn patients. The procedures could be used to reconstruct deformities at any time and the morbidities are nil.

Further reading

References

Introduction

Free tissue transfers using a microvascular technique have been firmly established since the operating microscope revolutionized the method of flap movement in the 1970s. They have been used more often in reconstruction after extirpation of head and neck cancers, breast cancers, and upper and lower limb trauma. Although skin grafts are generally used for post-burn reconstruction, the flap coverage is superior in both functional and aesthetic standpoints under certain situations. Therefore, burn care has also been included in this expanding role of the free tissue transfer.

On the other hand, severe burn patients, to whom the free flap transfers are often adapted, are characterized by a shortage of available donor tissue for flap elevation. In addition, one of the major drawbacks of the conventional free flap is the bulk of the tissue. The technique of tissue expansion first introduced in the early 1980s1,2 can reduce the donor site morbidity and the bulkiness of the flaps. In burn patients, this technique has been well indicated for alopecic deformities of the scalp. Moreover, it can extend the indication of the free flap transfer for severe burn patients.3–5

Prefabricated flap is another versatile reconstructive option, especially in patients with severe burn injuries. In this method, a vascular carrier is implanted to a new skin territory. Following a period of maturation and neovascularization, the prefabricated flap can be transferred, based on the implanted pedicle. Washio6 reported the very first attempt of prefabricated flap in a canine model using an intestinal seromuscular patch as the vascular carrier. Thereafter, various types of tissue, such as muscle,7 fascia,8 and vascular pedicle alone, have been developed for the same purpose. In severe burn patients, the limited donor site for free flap elevation can be maximized using these techniques.

Usage of the microvascular technique for acute burn care

Because the thermal injury induces the damage primarily to the skin surface, the necessity of microvascular technique is quite rare for acute burn care. The majority of burn patients require only debridement and coverage with split-thickness skin grafts. The exceptional situation necessitating the microvascular technique is the extremely deep burn involving underlying structures such as bone, tendon, major vessels and internal organs. These local conditions cannot support skin grafts for coverage. Historically, these wounds were managed with preservation of eschar in expectation of generating granulation tissue or decortication of bone cortex to prepare a bed for skin grafts.3 These techniques often led to long-term morbidity, including extensive necrosis of underlying structures, persistent skin ulceration and resultant infections. Therefore, microvascular free tissue transfer should be considered as a primary method of reconstruction for extremely deep thermal injury whenever clinically feasible (Fig. 52.1). These reconstructive techniques offer an early, reliable means of definitive reconstruction, preserving function, providing uncomplicated healing, and promoting early rehabilitation.10,11

Free flap to the post-burn neck contracture

Thermal injuries to the anterior neck region are prone to induce a severe contracture, especially in a case with flame burn, because the skin of this area is relatively thin and pliable. The optimal reconstructive method for skin supplementation, namely skin grafting versus flap coverage, is still controversial. The flap coverage takes advantage regarding pliability of the reconstructed skin, not necessitating a long-term splinting, which is mandatory after skin grafting to the anterior neck region. However, the primary shortcomings of conventional free flaps have been their bulkiness and the unavoidability of a secondary defatting procedure. To obtain a natural neck appearance, particularly the mentocervical angle, thinning of the flap is essential for achieving an aesthetically satisfactory result. A large number of thin free flaps have been developed for anterior neck reconstruction.12–14 These flaps with a thin layer of fat not only without deep fascia and fat but also without much of the superficial layer, are well suited for this purpose. Dense vascular network located in the subdermal layer can provide reliable vascularity in relatively large flaps, leaving the suprafascial axial vessels skeletonized from surrounding fat tissue.

The groin flap is the oldest free flap, which is considered to have minimum donor site morbidity. In 1972, McGregor and Jackson15 first described the vascular basis of the groin flap, based on the superficial circumflex iliac vessels, and
In recent years, the advancement of imaging with multidetector-row computed tomography angiography (MDCTA) has allowed for preoperative determination of vessels most suitable for flap vascular supply. These images provide three-dimensional information on the course of the target vessels leading to a significant reduction in surgical time and a safer elevation of the thin flap.

Post-burn facial reconstruction using microvascular technique

Severe post-burn scarring of the face presents a formidable challenge for the reconstructive surgeon. A constriction of cicatricial tissue may lead to a functional disability with ectropions of lips and eyelids, oral incontinence and drooling. In addition to functional considerations, the face needs to be reconstructed with the concept of an aesthetic unit. The effort to leave unburned small areas often results in a rather patchwork result and thus a cosmetically unacceptable
appearance. Each aesthetic unit has an individual preference for reconstructive options. For example, eyelids are best reconstructed with skin grafting from the retroauricular region. Because of the thinness of the skin of eyelids, flap coverage is less optimal than skin grafting. On the other hand, flap coverage is mandatory for nasal unit reconstruction, because the three-dimensionally complicated shape needs to be maintained overlying nasal support. For this reason, the median forehead flap is the standard reconstructive method for nasal deformity following thermal injury.

The indication of the free flap transfer is mostly addressed to the lower part of the face among patients with severe burn. Cicatricial deformities that involve the perioral region are not uncommon consequences of flame burns. Surgical release of offending scar tissues around the mouth; covering the resultant defect with a full thickness skin graft (FTSG) is the mainstay of surgical management. However, FTSG has some drawbacks, such as frequent partial skin loss, visible marginal scar, postoperative dark pigmentation, and contracture. Mismatching of the skin color renders the surgical outcome cosmetically unacceptable. In addition, there are more limitations of chin movement in FTSG than flap. Because full supplementation of dermis and soft tissue are required to solve a fundamental problem, various types of free flaps have been used in reconstructing the perioral area.4,22,23

While severe burn injury is characterized by a shortage of available donor tissue for reconstruction, the scalp is often preserved as a precious donor site in this circumstance: the skin is thick and, when burned, heals faster than other anatomic areas. Since the first report of the frontal visor flaps by Leon Dufourmentel24 in 1919, usage of scalp flap for lower face reconstruction had been sporadically reported in male patients. A study of the vascular supply of the scalp with a
particular emphasis on the posterior branch of the superficial temporal artery revealed that it was possible to transpose the hair-bearing flap on a long, highly mobile, narrow pedicle containing this vessel. The major criticism of the classic scalp flap was its donor site morbidity and resultant alopecia. Free scalp flap combined with tissue expansion technique virtually eliminated morbidity at the donor site (Fig. 52.3).4 However, the usefulness of this method may be curtailed in a woman because transferring of hair-bearing tissues to the face could create a cosmetically unacceptable result. A complete laser depilation is required when utilizing this method for female patients.

The prefabricated flap is a versatile reconstructive option, especially in patients with severe burn injuries, because it can create new donor sites without limitation of natural vascular territories. Prefabricated flaps have been utilized for reconstruction of individual aesthetic units such as nose, ear, cheek, lip and neck.25–27 However, in the case of a composite units defect, a single vascular carrier may not be sufficient to perfuse all units to be reconstructed. In these cases, separated vascular carriers that can nourish each unit independently are desirable. Within this paradigm, the jejunal seromuscular patch6 is a good candidate for the vascular carrier, because the jejunum can be divided into multiple segments, based on the arcade structure of the vessels. Using this method, the composite facial defect including the nose, upper lip, and lower lip can be reconstructed (Fig. 52.4).3

**Total face reconstruction using the microvascular technique**

When an entire face needs to be covered, a remarkable amount of skin is required. The area is deceptively larger than one expects, because the graft must wrap over a curved rather than flat surface. From a conceptual point of view, if
**Figure 52.4** (a) A 72-year-old man sustained a 37.5% body surface area burn. After complete wound closure, the patient presented with severe facial deformities including partial loss of the nose. (b) Jejunal seromuscular patches were transplanted to the supraclavicular region using microvascular anastomoses. (c) Prefabricated flap created in the left anterior chest. Segment 1: Prefabrication for nasal reconstruction. The costal cartridge was transplanted between skin and transferred seromuscular layer. Segment 2: Prefabrication for upper lip reconstruction. Segment 3: Prefabrication for lower lip reconstruction. (d) At 3 years after reconstruction. (From Sakurai H, Takeuchi M, Nakamori D, et al. Prefabricated flap for multiple facial units reconstruction using a jejunal seromuscular patch as a vascular carrier. Burns 2010; 36:e31–e35.)

**Figure 52.5** (a) A 57-year-old patient with severe contracture of the face after burns. (b) Reshape of the transferred flap succeeded in achieving total face reconstruction. (c) Donor site for the total face reconstruction. (Patient in: Sakurai H, Takeuchi M, Fujiwara O et al. Total face reconstruction with one expanded free flap. Surg Technol Int 2005; 14:329–333.)
a total face needs to be resurfaced, the color and texture matching to the original facial skin is less important. Although each aesthetic unit has an individual preference for reconstructive options as mentioned before, it is more important to use a sole donor site that can provide a large amount of skin flap in the case of total face reconstruction. When the whole face needs to be reconstructed with a single skin flap, openings for eyes, nostrils, and a mouth have to be made. It is well known that a surgical delay and tissue expansion can lead to vascular ingrowths to the transferred tissue. Therefore, a tissue-expansion technique is well adapted for total face reconstruction, not only to reduce the donor site morbidity, but also to ensure vascular reliability to the central portion even after the fenestrations. Even though the abundant tissue can be transferred to the face as a single free flap, it becomes flattened when transferred to the face. However, once the skin is reconstructed as a vascularized tissue, it can be readily moved and shaped again. It is another superiority of the free flap in contrast to skin grafting. The shaping of the free flap to the face can be achieved as either local flap or axial flap, in conjunction with tissue expansion and prefabrication (Fig. 52.5).

**Further reading**


References

Introduction

Reconstruction of the head and neck following burn injuries presents great challenges and great opportunities. Successful treatment requires sound surgical judgment and technical expertise, as well as a thorough understanding of the pathophysiology of the burn wound and contractures. Many disciplines are required to successfully care for patients with burns of the head and neck. These include skilled nursing, experienced occupational and physical therapy, and psychological and social support systems. The surgeon must also have familiarity and expertise with non-surgical treatment modalities such as pressure therapy, steroids, and laser therapy. Realistic expectations on the part of both patients and surgeons are essential to achieve successful treatment outcomes. Burns to the head and neck of a serious nature result in tissue injury with scarring and complete removal of scars is not possible. A scar can only be modified or exchanged for a scar or scars of a different variety. Despite this fundamental limitation, reconstruction of the burned face and neck creates great opportunities for plastic surgery to significantly improve functional and aesthetic deformities resulting in profound improvement for this large group of challenging patients.

Burn injuries constrict and deform the face, distorting its features, proportions and expression.1 Burns also alter the surface of the facial mask by causing scars and altering texture and pigmentation. The changes to the surface of the skin are deforming but are much less important to facial appearance than are the changes in proportion, features, and expression. The removal of scars should not be the primary goal of facial burn reconstruction. A normal looking face with scars is always better looking than an even slightly grotesque looking face with fewer scars. Mature scars that result from burn injury will often be less conspicuous than surgically created scars or surgically transferred flaps or grafts. The subtle and gradual transition between unburned skin and burn scar is an excellent example of nature’s camouflage and can render scarring remarkably inconspicuous. The principal goal of facial burn reconstruction should be the restoration of a pleasing and tension-free facial appearance with appropriate animation and expression.2 If this goal is kept in mind and pursued with persistence and determination, the amount of improvement that can result after severe facial burn injury can be remarkable. Ignoring this basic principle can result in iatrogenic catastrophes during reconstructive surgery of the head and neck following burn injury.

Successful reconstruction of burn deformities of the head and neck requires a well-functioning and extensive team.3 Major burn deformities in this area can be intimidating and overwhelming. Experience and a specialized infrastructure are required to take care of these patients comfortably and successfully. Familiarity with their unique problems and a firm commitment to correcting their challenging deformities is required from all members of the reconstructive team. The care of a patient from the onset of a major burn involving the head and neck to a successful reconstructive outcome requires skill, patience, determination, and enthusiasm from all who are involved.

Acute management

Although the main focus of this chapter is the reconstruction of established facial burn deformities, an understanding of the acute care of facial burn injuries is necessary in order for the surgeon to have an accurate perspective. Excision and grafting of deep second-degree and full-thickness burns has become the standard of care since it was first proposed in 1947.4–6 It remains controversial whether this is the optimum treatment for facial burn injuries. Early excision and grafting of the face is problematic because of the difficulty in diagnosing the depth of the facial burn and accurately predicting an individual patient’s long-term prognosis both functionally and aesthetically. The overwhelming majority of facial burns treated conservatively with a moist regimen of topical antibiotics will be healed within 3 weeks. Burns which are clearly full-thickness are best treated by early excision and grafting within 7–10 days to promote early wound closure and minimize contractile forces (Fig. 53.1). The problem cases are those where healing has not occurred by 3–4 weeks or longer. Early tangential excision and grafting has been proposed for these patients in order to achieve more favorable healing with less eventual contracture deformities.7 Proponents of conservative therapy argue that early excision and grafting may result in a patient with a grafted face who would otherwise have healed favorably by successfully epithelializing their partial-thickness burn from skin appendages.8 Conservative management has been facilitated by the myriad ancillary techniques currently available to favorably influence the healing of facial burns such as pressure,
Pathogenesis

Superficial second-degree burns usually heal without scarring or pigmentary changes. Medium-thickness second-degree burns which epithelialize in 10–14 days usually heal without scarring, although there can be long-term changes in skin texture and pigmentation. Deep second-degree burns which epithelialize after 21 days or longer must be carefully managed for they have a propensity to develop severe late
Reconstruction of the head and neck

in the development of early hypertrophic scarring, relief of the tension with either focal z-plasty or judicious release and grafting can be very helpful. Full-thickness facial burns should usually be excised and grafted unless focal and small.

Evaluation of facial burn deformities

Facial burn reconstruction should be based on an overall strategy and a clear understanding of the fundamental problems. Many reconstructive techniques have been described in the literature and most can be successful if the strategic goals are appropriate. The best reconstructive plan is usually a judicious combination of contracture releases by z-plasty, grafts, and flaps, followed by appropriate scar revision.

Deep second- and third-degree burns heal by contraction and epithelialization. The more severe the burn injury, the more contraction takes place during the healing process. The changes in facial appearance following a deep second-degree burn injury are dramatically demonstrated in Figure 53.5. Three weeks following a deep second-degree burn, the patient’s facial features and proportions remain essentially normal. Six months later, contractile forces have deformed the facies in a pattern that is repeated to a variable degree in virtually all severe facial burns. These changes make up the stigmata of facial burn injury and are listed in Box 53.1. The eyelids are distorted with ectropion, the nose is foreshortened with ala flaring, the upper lip is shortened and retruded with loss of philtral contour, the lower lip is everted and inferiorly displaced, the lower lip is wider than the upper lip in anterior view. The tissues of the face and neck are drawn into the same plane with loss of jawline definition. The severity of these changes is proportional to the severity of the injury.

Fortunately, the majority of facial burn injuries are not severe and do not involve the entire face. A relatively small hypertrophic scarring (Fig. 53.3). These patients should be closely monitored after initial healing and at the first sign of hypertrophy must be managed with all available ancillary treatment modalities. Pressure garments have been shown over several decades to be effective in suppressing and reversing hypertrophic scarring. Adding silicone to pressure therapy seems to increase its efficacy. Computer-generated clear face masks lined with silicone have improved the ability to deliver pressure to facial hypertrophic scars and are better tolerated by patients (Fig. 53.4). When tension plays a role
number of patients sustain injuries which deeply involve the entire face such as shown in Figure 53.5. It can be helpful to separate patients with facial burn deformities into two fundamentally different categories as described in Box 53.2. Type I deformities consist of essentially normal faces that have focal or diffuse scarring from their burns and may have associated contractures. Type II deformities make up a much smaller number of patients who have 'pan-facial' burn deformities with some or even all of the facial burn stigmata. Although these categories are not rigidly defined and there are some patients who do not fit neatly into one or the other, understanding the fundamental difference between these two groups of patients can help define treatment goals. It can also aid in selecting the most appropriate methods for reconstructive surgery.

Patients with type I deformities have an essentially normal facial appearance despite scars from their burns. In these patients, one must be certain that surgical intervention does not adversely alter normal facial features or create distortion from iatrogenically induced tension. Overall facial appearance should not be sacrificed in an effort to 'excise scars.' The best reconstructive options for patients with type I facial burn deformities are usually scar release and revision with z-plasties, full-thickness skin grafts, or tissue rearrangement with local flaps. The pulsed-dye laser can be helpful for decreasing post-burn erythema and treating persistently erythematous burn scars. Full-thickness skin grafts are excellent for focal contractures. Z-plasties in combination with the pulsed-dye laser can be a powerful scar-improving combination (Fig. 53.6). Excision of scars and resurfacing operations in aesthetic units and major flap transpositions with or without tissue expansion are rarely indicated.

The much less frequently encountered group of patients with type II facial burn deformities presents a completely different clinical situation. Examples of patients falling into the type II category are shown in Figure 53.7. The surgical goals for this group of patients should be the restoration of normal facial proportion and as much as possible the restoration of the position and shape of normal facial features. The intrinsic and extrinsic contractures that exist in these patients require large amounts of skin. The correction of these contractures should be carried out in a carefully planned and staged fashion. The sequence of operations is usually the following: eyelids, lower lip and chin, upper lip, cheeks, nose, and then other residual deformities. As each area is reconstructed, the addition of skin results in the relief of tension, which benefits other areas of the face. Excision of normal skin or elastic healed second-degree burned skin is almost never indicated. After facial proportion has been

**Box 53.1** Stigmata of facial burns

- Lower eyelid ectropion
- Short nose with ala flaring
- Short retruded upper lip
- Lower lip eversion
- Lower lip inferior displacement
- Flat facial features
- Loss of jawline definition

**Box 53.2** Facial burn categories

**Type I**
Essentially normal faces with focal or diffuse burn scarring with or without contractures.

**Type II**
Pan-facial burn deformities with some or all of the stigmata of facial burns.

Figure 53.5 (a) Three weeks following a deep second-degree burn with essentially normal facial features and proportions. (b) Six months later, contraction and hypertrophy have created facial burn stigmata.
achieved and facial features have been restored to their normal location and shape without tension, scar revision can be carried out to smooth and blend the remaining functional scars (Fig. 53.8).

Normal faces are a mosaic of colors, textures, wrinkles and irregularities. In a face which has undergone major burn injury, a mosaic appearance of scars, grafts, pigmentary abnormalities and other flaws can be attractive as long as the facial features are restored to a normal location and are sufficiently loose and mobile for normal and appropriate facial expression. Cosmetics can be useful for blending and camouflaging areas of pigmentary and texture abnormalities, particularly in females.

**Fundamental principles and techniques**

**Contractures**

Burn injuries result in open wounds which either heal by contraction and epithelialization, or are closed by skin grafting. Contractures result from both of these forms of wound healing. Contractures are either intrinsic or extrinsic. Intrinsic contractures result from loss of tissue in the injured area with subsequent distortion of the involved anatomic part. Extrinsic contractures are those in which the loss of tissue is at a distance from the affected area but the distorted structures such as eyelids or lips are not injured themselves.
Corrective measures should be directed at the cause of the contracture in order to provide optimal benefit and prevent iatrogenic deformities. It is helpful to minimize the amount of skin and scar which is excised when correcting facial contractures. When tension is released, many scars will mature favorably and become inconspicuous. Even long-standing scars will respond to a change in their environment. Healed second-degree burns under tension may be unattractive but when restored to a tension-free state can be superior in function and appearance to any replacement tissue. Minimizing excision also decreases the amount of new skin which must be provided in the reconstruction. Every effort should be made to relieve tension from the face when performing burn reconstruction. Tight faces are never attractive. Tight scars are always hypertrophic and erythematous. Relaxed scars are ‘happy’ scars.

**Aesthetic units**

The concept of facial aesthetic units has profoundly affected plastic surgical thinking since its introduction by Gonzalez-Ulloa. Initially conceived as the ideal approach for resurfacing the face following burn injury, this important concept has been emphasized in virtually all subsequent writings about facial burns. It is important to keep facial aesthetic units in mind during burn reconstruction but the desire to adhere to this concept should not supersede common sense. When small unburned and unimportant islands of skin are in an aesthetic unit that is being resurfaced, they can be sacrificed. Otherwise, the excision of normal facial skin is rarely indicated in burn reconstruction. All burned faces to some degree are mosaic. Scar revision with z-plasties is an excellent technique to camouflage scars in a burned face. Mosaic faces which are proportional, tension free, and normally expressive appear much better in real life than they do in images.

**Z-plasty**

The z-plasty operation is a powerful tool in the surgeon’s armamentarium for facial burn reconstruction. The z-plasty has been used for over 150 years to lengthen linear scars by recruiting lax adjacent lateral tissue. Z-plasty can also cause a profound beneficial influence on the physiology of scar tissue when it is carried out within the scarred tissues rather than after excising them. The physiology of this phenomenon is related to the immediate and continuing breakdown of collagen which occurs in hypertrophic scars following the relief of tension. Z-plasty also narrows scars at the same time that it lengthens them. In addition, the z-plasty adds to scar camouflage by making the borders of the scar more irregular. In order for z-plasties to lengthen a burn scar and restore elasticity, the lateral limbs of the z-plasty must extend beyond the margins of the scar. The improvement in the appearance of facial scars following z-plasty and without any scar excision can be dramatic, particularly when combined with pulsed-dye laser treatment (Fig. 53.6).

**Laser therapy**

Hypertrophic scarring is a frequent complication after partial-thickness facial burn injuries which take longer than 3 weeks to completely epithelialize. Despite conservative management and close monitoring, hypertrophic scarring can become severe during the first two years after the burn (Fig. 53.3). The pulsed-dye laser (PDL) has emerged as a successful treatment modality during this period of scar proliferation and is an effective alternative to scar excision in patients with hypertrophic facial burn scars. Multiple studies have demonstrated its beneficial effect on scar erythema and hypertrophy. The PDL also rapidly decreases pruritus and pain and provides an additional, low-morbidity, therapeutic intervention for patients and their families during the often prolonged period of scar restoration.
maturation. Restoration of hypertrophic facial scars to their previous state of a flat, epithelialized surface is a superior outcome to surgical excision with its concomitant increase in facial tension.\(^2\) The development of fractional ablative and non-ablative laser therapy using various types of lasers including CO\(^2\) and Erbium-YAG offer promising new options for the management of facial burn scars in the future (Fig. 53.9).\(^2\)

**Grafts**

Skin grafts are an essential part of facial burn reconstruction. Surgical decisions regarding donor site selection, the use of split-thickness versus full-thickness grafts, the timing of intervention and the postoperative management of grafts often determine the success or failure of facial burn reconstruction. Split-thickness skin grafts contract more than full-thickness grafts, wrinkle more, and always remain shiny with a ‘glossy finish’ look. Split-thickness skin grafts should be used primarily in the periphery of the face unless the limited availability of donor sites requires their use in more prominent areas. Split-thickness skin grafts can be excellent for upper eyelid releasing and resurfacing. Hyperpigmentation of split-thickness grafts on the face is a frequently occurring problem in dark-skinned patients, particularly of African descent.

The full-thickness skin graft is a reliable workhorse in facial burn reconstruction. The broad, central, conspicuous
areas of the face such as the cheeks, upper and lower lips, and dorsum of the nose are excellent sites for the use of full-thickness grafts. The missing or damaged parts in the vast majority of even severe facial thermal burns are the epidermis and the dermis and that is what full-thickness skin grafts provide. After facial burns, the subcutaneous fat may be compressed or distorted by contractures but it is rare that it is lost or injured. Adequate skin must be provided when doing definitive resurfacing operations with full-thickness grafts. Contractures must be overcorrected and postoperative management with conformers and pressure is essential. Full-thickness skin grafts are very reliable when used electively in the face for reconstruction after burns.²⁹

Flaps

Flaps can be useful for facial burn reconstruction but they must be used judiciously and skillfully, recognizing their problems and limitations. The thickness of skin flaps from all distant donor sites is greater than that of the normal facial skin. The face is tight following burn injury and flaps tend to contract when transferred. They can, therefore, compress or obscure underlying tissue contours. Transposing or advancing flaps from the neck and chest up to the face can easily create extrinsic contractures that adversely affect facial appearance. When flaps have been enlarged by tissue expansion, they are even more dangerous in this regard. Contractures with a downward vector create a 'sad' facial appearance that is distressing to patients. Cervicopectoral flaps provide the best color match in color and texture to facial skin. Distant flaps, whether transferred by traditional technique or microsurgery, share the common flaw of poor match in terms of color and texture.

Tissue expansion

Tissue expanders must be used with caution in the reconstruction of the head and neck. The underlying theme of almost all burn deformities is tension secondary to tissue deficiency. Stretching adjacent tissue in order to carry out
Reconstruction of the head and neck

Timing of reconstructive surgery

The timing of reconstructive plastic surgery following facial burn injury falls into three separate phases: acute, intermediate, and late. Specialized burn centers create an ideal patient-care environment where acute care and reconstructive surgery can be planned and carried out in optimal circumstances with collaboration among acute and reconstructive physicians and surgeons. The reconstruction of facial burn injuries to the head and neck should optimally begin with the acute care.

Acute reconstructive surgery occurs during the first months following the burn injury and includes urgent procedures which are required to facilitate patient care or to prevent acute contractures from causing permanent secondary damage. Acute reconstructive intervention is most frequently indicated in the eyelid, perioral, and cervical areas. Intermediate reconstructive surgery takes place during the months to years after wounds are closed and the scar maturation process is proceeding. During this phase of recovery, some patients will present to the reconstructive surgeon after having received their acute burn care at another facility. Timely intervention when indicated is important in this group of patients as it can positively influence further maturation of scars and grafts. Late-phase reconstructive patients present to the reconstructive surgeon with established facial burn deformities many years following their acute injury.

Acute-phase reconstruction

Eyelids

Upper and lower eyelid ectropion can occur from burn injuries to the periorbital region (intrinsic contracture) or may arise secondarily as a result of the contracture of open wounds and skin grafts at more distant sites (extrinsic contracture). With severe ectropion such as shown in Figure 53.10a, early intervention is mandatory in order to prevent irreversible injury to the cornea. Conservative measures to protect the cornea, such as temporary sutures or contact lenses, are often ineffective. Tarsorrhaphy can cause irreversible iatrogenic injury and should not be used. The best treatment is early intervention with release of contracture and resurfacing with split-thickness skin grafts (Fig. 53.10b). Release of even extreme contractures with grafting can be done in the presence of open wounds and effectively restores protective eyelid function.

Perioral deformities

Microstomia occurs from circumferential scarring at the junction between lips and cheek. Perioral scarring from either open wounds or contraction of skin graft suture lines can act as a pursestring, resulting in diminished oral opening (Fig. 53.11). This can compromise alimentation and airway access. Microstomia is best addressed by the acute release of the oral commissures taking care to avoid extensive transverse releasing incisions in the aesthetic units of the cheek. Overcorrection can easily result in macrostomia. As soon as adequate oral opening is achieved for feeding and airway access, definitive reconstruction is best left for the post-acute period.

Macrostomia is caused by rapid contraction of open wounds or grafts in the cheek and perioral region, resulting in eversion of the upper and lower lips and lateral movement of the oral commissures (Fig. 53.12). The loss of an effective oral sphincter causes drooling and desiccation of the oral mucosa, and can result in irreversible damage to the dentition. Early intervention with release and grafting of the lower and/or upper lips should be carried out as soon as possible. Definitive reconstruction is best carried out at a later period.

Cervical deformities

Anterior neck contractures in the acute period are best prevented by aggressive splinting and incisional releases and grafting when indicated. When severe anterior neck flexion contractures occur, early release and grafting is necessary to allow for adequate airway access and to minimize
acute wound closure. The treatment options during this period are multifaceted and are continuing to evolve. Significant progress is being made with these types of interventions.

It is often recommended that definitive reconstructive surgery be carried out after facial scars and skin grafts are mature, soft, and supple. This process takes at least a year and frequently takes many years to fully occur. The maturation of facial burn scars takes much longer than is generally appreciated by patients and reconstructive surgeons alike. If scars are continuing to improve, it is usually best to allow them to continue to mature. If scars are not maturing favorably, well-timed and well-conceived surgical intervention to favorably influence the scar maturation process can be beneficial. The scar maturation process after facial burns is influenced by multiple factors. The most important factor other than the initial severity of the injury is the amount of tension present in the face and acting on the scars. Surgical procedures to decrease tension and to favorably alter the direction and contour of scars can achieve significant improvement in scar maturation for many years following a burn. Whenever healing burns cross concave surfaces, there is a tendency for hypertrophic scarring to develop. Examples in the face are the glabella, the nasojugal groove, the crus helicis of the ear, and the infra-commissural folds. Relieving tension with z-plasties without scar excision is very effective in correcting hypertrophy (Fig. 53.14). Steroids, both topically and intralesionally, can be helpful during this period but must be used sparingly to avoid atrophy, telangiectasias, and erythema. Tension can also be relieved by judiciously placed releases and skin grafts. The skin grafts can be of either split-thickness or full-thickness variety. Split-thickness skin grafts are best used where the location of the graft will be inconspicuous or where large amounts of skin are required to relieve the contractures. This is frequently indicated when there are associated neck contractures. Tension from the neck must be eliminated as much as possible to allow for favorable maturation of facial burn scars. The use of full-thickness skin grafts during the intermediate phase of reconstruction should be rare and limited to circumstances where definitive repair is being carried out and there is little chance that further skin will be required in that region. The pulsed-dye laser is a promising adjunctive therapy which can decrease erythema and speed the rate of scar maturation (Fig. 53.6).

Late-phase reconstruction

Late-phase reconstructive surgery takes place when scars are mature and the patient’s deformities are essentially stable. In some patients, scars will be soft and supple, but in others, even long-standing scars may be hypertrophic and hyperemic many years following the burn injury because of persisting tension or unfavorable orientation. Scars can remain indurated and hyperemic for decades following a facial burn. Reorientation in this late phase with z-plasties and treatment with the pulsed-dye laser can result in remarkable improvement (Fig. 53.15). Scar excision can often be avoided with its concomitant increase in facial skin tension and distortion of facial features.
Previously described reconstruction techniques include serial excision, rotational scalp flaps, free hair follicle transplantation, and staged scalp tissue expansion. Of patients with scalp injuries, associated adjacent burn deformities were commonly found involving the ear, nose, and eyebrow. These injuries included ear deformity (46%), nasal deformity (27%), and eyebrow deformity (46%). Therefore, in planning the surgical reconstruction for pediatric scalp alopecia, it is helpful to evaluate each patient for adjacent structure burn injuries requiring reconstruction. Therefore, as one plans the stages of tissue expansion procedures, one can plan concurrent reconstruction of associated burn injuries, sometimes taking advantage of the region of expected alopecia excision.

Reconstruction of specific areas of the head and neck

Scalp

Scalp alopecia is seen in as many as 25% of children who suffer burn injuries of the head and neck. McCauley et al. devised a system of classification for burn alopecia based on the pattern and extent of deformity. They describe the pattern of alopecia as uniform, segmental, patchy, or total (types I–IV, respectively) and the extent of alopecia as 25% of the scalp, 25–50%, 50–75%, or >75% (subtypes A–D, respectively). Their system serves as both the means of description and an initial step in planning operative care.

Figure 53.13 (a,b) Extreme anterior cervical contracture secondary to burns of the entire chest and neck. (c,d) At 23 years post-burn after release and split-thickness skin grafting. Two additional releases and grafts were required.
artery island flaps for eyelid or eyebrow reconstruction have been used for many years.\textsuperscript{41–43} When used for eyebrow reconstruction, they can be bushy and conspicuous and should be used with caution, particularly when carrying out unilateral eyebrow reconstruction.

Burn injuries of the scalp and upper face often result in scars that distort the relative positions of the anterior hairline, eyebrows and upper eyelid. Contour of the brow is distorted with exaggerated elevation of the central peak. Further, scar contracture involving the upper eyelid can result in cicatricial ectropion, associated with effacement of the supratarsal fold and corneal exposure. This stereotypic set of upper facial deformity can be treated with tissue expansion.

Eyebrows

Eyebrow reconstruction following complete loss is an unsolved surgical problem. Composite grafts of hair-bearing scalp from carefully selected sites in the retroauricular area can satisfactorily transfer hair.\textsuperscript{39–41} Unfortunately, the hair is scalp hair which grows rapidly and is more projecting than the tangential delicate hair of the normal eyebrow. For complete eyebrow replacement, the technique of composite grafting as described by Brent\textsuperscript{39} is most useful. For partial eyebrow loss, micro- and mini-grafting of scalp hair can be efficacious. Occasionally, borrowing composite grafts from a contralateral unburned eyebrow is appropriate. Temporal

\textbf{Figure 53.14} (a,b) Diffuse, hypertrophic scarring of cheeks, chin, and lips 8 months following flame burn injury. (c,d) At 12 years post-burn after treatment with pressure therapy, steroid injections, and multiple z-plasties within the scar tissue. No scar tissue was excised.
and antegrade foreheadplasty. In this technique, the scalp and forehead areas are tissue expanded. The tissue expander is removed and the scalp aponeurosis is advanced antegrade and loaded in redundant fashion over the brows at the level of the arcus marginalis. Accounting for the fourth dimension of time and tissue recoil, the brows are returned to a natural contour and improved position (Figs 53.16, 53.17).

**Eyelids**

Correction of upper and lower eyelid contractures in the late reconstructive period can be a daunting and humbling challenge. The periorbital region is made up of complex three dimensional anatomy and requires abundant skin to appropriately drape the contours of both the upper and lower eyelids. The slightest amount of excessive tension from either the eyelid skin itself or contractures in adjacent regions such as the forehead or cheek can profoundly and adversely effect eyelid function and appearance. Reconstructive goals should be restoration of a normally shaped palpebral fissure with appropriate orientation of upper and lower eyelashes at rest and in the open position whenever possible. This often requires extensive releasing incisions extending medial to the medial canthus and lateral to the lateral canthus in order to adequately release all the contracted tissues. When ectropion is the result of a distant contracture, the normal eyelid skin should always be returned to its normal location. Incisions should not be made at the eyelid margin, thereby separating the normal eyelid skin from the ciliary line and replacing it with a graft. When overlying scar is released, care must be taken to prevent injury to the underlying orbicularis oculi muscle. This is often rolled up and contracted and is rarely completely lost. It must be unfolded to its normal flat broad shape and the resulting defect resurfaced with abundant skin graft. Upper eyelid resurfacing is best carried out with split-thickness skin grafts from the best available donor site. Full-thickness skin grafts in the upper eyelid usually transfer a thick dermal component which compromises the delicate contour of the supratarsal fold. Lower eyelid resurfacing may be done with either split-thickness skin grafts or appropriate full-thickness grafts when indicated. For minor contractures of either upper or lower eyelids, the perfect reconstructive material can be obtained from an unburned contralateral upper eyelid. Medial canthal folds are best corrected with z-plasties when there is not a significant tissue deficiency.

**Lower lip and chin**

Deformities of the lower lip and chin usually occur in combination. Contracting forces result in inferior dislocation and eversion of the lower lip. In addition, there is compression of the soft-tissue contours of the chin prominence. Release should be carried out at the vermilion scar junction and the lower lip carefully unfurled taking care to prevent iatrogenic injury to the underlying orbicularis oris muscle. The resulting defect is then resurfaced with split-thickness skin grafts or full-thickness grafts when indicated. Restoration of chin contour can be improved with chin implants.

**Upper lip deformities**

The upper lip is usually shortened and retruded by severe facial burn injuries. Releasing and grafting should be carried out, taking care not to overcorrect the deformity and create a long upper lip. Full-thickness grafts from the best available donor sites are usually the best option for resurfacing. Reconstruction of the philtrum when indicated is best

Figure 53.15 (a) A 16-year-old female 11 years following contact burn. Right cheek scar remains erythematous, indurated, and conspicuous. (b) Relaxation and reorientation of scar tissue with z-plasty. (c) Five years later after six treatments with the pulsed-dye laser.
Figure 53.16 Tissue expanded antegrade forehead-plasty. This patient suffered flame burn injury to the scalp and forehead. The hyperpigmented skin graft on the scalp serves as a marker illustrating movement of the expanded scalp and forehead tissue. Before the forehead-plasty, the patient suffered from upper lid ectropion and exposure of the left cornea. Note the over-elevated eyebrows and effacement of the supratarsal fold in the left upper eyelid (a). A tissue expander was placed (b). Antegrade forehead plasty was performed and forehead tissue was loaded in a redundant fashion above the brows, with overcorrection to account for tissue recoil (c). At 1 month post-operation, note the extent of antegrade forehead movement, where the hyperpigmented skin graft is observed to move from the scalp to mid-forehead region. At 2 years following the operation, the forehead tissue has flattened out and the eyebrows restored to an improved position over the orbital rims. Note the restoration of the supratarsal fold to the left upper eyelid, and partial recoil of the hyperpigmented skin graft (d).

Figure 53.17 Diagram illustrating tissue movements of antegrade forehead-plasty. Scalp tissue is maximally expanded, with consequent further exaggeration of eyebrow elevation (left). Tissue expander is removed and the expanded scalp and forehead skin are advanced anteriorly, loaded in redundant fashion over the eyebrows (middle). Over time, the redundant skin recoils, restoring the eyebrows to a more natural position (right).
Nasal deformities

Burn injuries to the nose result in a broad range of deformities which can be focal and minor or can result in complete nasal amputation. Minor deformities are best dealt with by local scar revision, particularly with z-plasties to relieve contractures, or releases in combination with full-thickness skin grafting. Shortening of the nose with flaring or partial loss of the alar rims is common in more severe facial burns. Local release of the alar lobules with full-thickness skin grafts is a useful technique for minor to moderate contractures. Complete excision of dorsal scar and graft in an aesthetic unit with a full-thickness skin graft is useful for more severe shortening. When the lower third of the nose has been amputated by the burn injury, inferiorly-based, turn-down flaps of the dorsal nasal tissues can provide satisfactory lengthening and improved contour to the tip and alar lobules. More severe cases of nasal deformity can be treated...
by either dorsal turn-down flaps or other forms of total nasal reconstruction. The dorsal turn-down flap usually requires at least two stages but can be effective in even near total nasal amputation (Fig. 53.18). Forehead flaps are usually unavailable in patients who have sustained facial burns severe enough to result in total nasal amputation. Distant flaps can be used with either microsurgical transfer using a radial forearm flap or using the frequently unburned skin of the upper inner arm for a Tagliacozzi flap. If the face is otherwise composed of burn scar and graft, these distant flap nasal reconstructions have the disadvantage of appearing to be ‘stuck on’ and stand out in the midst of the otherwise mosaic appearance of the face. When the face has required resurfacing with flaps, a nasal reconstruction with flap tissue is the best option (Fig. 53.21).

**Ear deformities**

Improved care in the acute phase of burn injury has greatly decreased the incidence of helical chondritis and the resulting associated deformities of crumpled or lost cartilage. Minor ear deformities are often seen in patients with little or no hair loss and can easily be camouflaged. Larger defects can be treated by myriad local reconstructive techniques. Subtotal ear amputation (Fig. 53.22) often lends itself to reconstruction with a conchal transposition flap and skin graft. Complete ear loss can be masked by the use of a prosthesis. Fixation has been improved by the use of osteo-integrated implants but cost and color changes remain problematic. Selected patients can be appropriate candidates for total ear reconstruction using autologous cartilage and soft-tissue coverage from either temporalis fascia flaps, or expanded local tissue. Alloplastic materials should not be used in the reconstruction of postburn ear deformities due to an acceptably high extrusion rate.

**Figure 53.19** (a) Severe oral commissure burns destroy vermilion, mucosa, muscle, and the skin of the lip and cheek. (b) Extensive contracture results with thickening of the leading edge of the commissure.

**Figure 53.20** (a) At 16 years following devastating right oral commissure electrical burn. Some 40% of lip circumference is lost and the commissure is thick and immobile. (b) Following tongue flap reconstruction, the commissure is thin and mobile and facial expression is restored.
Figure 53.21 (a,b) Pan-facial burn deformity in a 14-year-old male. Cervicopectoral flap resurfacing was chosen for reconstruction of the cheeks and chin. (c,d) Nasal appearance following reconstruction with a Tagliacozzi flap. A scalp flap was used to reconstruct the upper lip and create a moustache.

Figure 53.22 (a) Typical post-burn pattern of peripheral helical loss. (b) Reconstructed ear following expansion with conchal transposition flap and skin grafts.
Cervical contractures during the acute period as burn scars and grafted areas contract include splinting, physical therapy, neck collars, and the use of a three-quarter mattress to encourage neck extension.

### Prevention

Cervical contractures are a major problem in burns involving the chest, neck, and face. The anterior neck skin is thin and the neck is a highly mobile flexion area easily prone to contracture. As noted previously, severe neck flexion neck contractures in the acute phase often require early reconstruction to aid in airway management. Neck contractures should usually be dealt with prior to carrying out facial burn reconstruction as the extrinsic contractile forces from the neck cause facial deformities and can adversely affect the maturation of scars on the face. Preventive methods to minimize cervical contractures during the acute period as burn scars and grafted areas contract include splinting, physical therapy, neck collars, and the use of a three-quarter mattress to encourage neck extension.

### Release and grafting

The majority of anterior neck contractures can be satisfactorily treated with release and skin grafting. Extensive contractures usually require split-thickness skin grafting. Focal contractures can be appropriate for full-thickness grafting, which will result in a superior outcome from both a functional and aesthetic standpoint. When neck contractures are extensive, the lower face and chest are usually a

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**Figure 53.23** (a,b) Persistent, anterior neck contracture following repeated inadequate split-thickness skin grafting. (c,d) Release and anterior neck resurfacing was carried out with bilateral shoulder flaps. Secondary midline z-plasties improved the vertical release and created an aesthetic neck contour. Chin augmentation improved the patient’s profile.
Local flap reconstruction

When split-thickness skin grafting is unsuccessful because of recurrent contracture or does not provide a satisfactory aesthetic result, local flap reconstruction of the anterior neck is an excellent technique if there is available tissue. Flaps can either be unilateral or bilateral. When bilateral flaps are available, midline z-plasties secondarily can help to improve neck contour (Fig. 53.23). Donor site morbidity is usually minimal as the upper chest in these patients has frequently been disfigured to some degree by the burn injury.

Distant flap reconstruction

Free flaps have been advocated for the treatment of anterior neck contractures. Excellent outcomes can be obtained but require microsurgical technique and create the possibility of complete flap loss. Another potential negative of free flaps to the anterior neck is that they can be thick and bulky, requiring multiple defattings and secondary revisions. The free flap can also appear to be an island in the midst of a broad area of healed graft and burn scar.

Further reading

- Davis JS. The relaxation of scar contractures by means of the z-, or reversed z-type incision: stressing the use of scar infiltrated tissues. Ann Surg. 1931;94:871-884.

Access the complete reference list online at http://www.expertconsult.com
References


Correction of burn alopecia

Robert McCauley

Introduction

Patients who sustain large total body surface area burns have involvement of the head and neck between 25% and 45% of the time. Since human skin does not regenerate itself, scarring is the end result of the healing process. Such scarring can not only be disfiguring but also can lead to contractures which can affect function. The ultimate effect of deep burns to the scalp is loss of hair leading to cicatricial alopecia. The management of this problem is multifactorial. It includes the analysis of the size of the defect, its location, the surface area of the remaining scalp and the condition of the remaining hair-bearing scalp. The treatment can range from excision with primary closure to the use of multiple tissue expanders.

The scalp is a popular donor site for the harvesting of split thickness skin grafts to resurface patients with large total body surface area burns. Multiple harvestings of skin grafts from the scalp may also lead to cicatricial alopecia. However, the incidence of alopecia associated with graft harvesting remains controversial. In 1990, Brou et al. reported a 61% incidence of alopecia in patients with existing scalp burns, in which skin grafts were harvested from the injured scalp. Yet, only a 2.2% incidence of alopecia was noted in patients without burns to the scalp who underwent harvesting of scalp grafts for closure of burn wounds. Reconstructive surgeons have a number of tools available to address the correction of problems associated with burn patients. However, one must keep in mind that inherent in all techniques can be problems associated with color match, texture, and donor site disfigurement. Certainly, primary closure of burn alopecia can eliminate these problems using local flap advancement. Now, tissue expansion is an example of how skin responds to mechanical stress. It offers a number of advantages when compared with other modalities of reconstruction. Such advantages as color match, sensation and minimal donor site morbidity are not to be taken lightly. However, tissue expansion is not for everyone. But, it is such a valuable technique that it has become an integral part of the armamentarium for reconstruction surgeons who are charged with the reconstruction of burn patients.

Histomorphology of tissue expansion

It is noted that tissue expansion occurs under natural conditions (i.e. pregnancy, breast development) and in abnormal circumstances (expansion of the neck, earlobes). As part of the aesthetics in various societies, tissue expansion has been noted to document positions of social hierarchy. The first clinical case of soft tissue expansion was reported by Neumann in 1957. In a case of partial traumatic ear loss in a 52-year-old man, Neumann inserted a rubber balloon above the ear to create an expanded flap to cover his cartilaginous framework. However, in spite of this remarkable case, the idea of soft tissue expansion to correct traumatic defects remained dormant for another 20 years. In 1975, both Austad et al. and Radovan began pioneering work on soft tissue expansion. Experimental data on the histomorphology of tissue expansion largely came from animal data. Although Austad reported the laboratory experience with tissue expansion prior to clinical use, Radovan is noted as the first surgeon to claim extensive use with tissue expanders clinically.

Epidermis

The response of the epidermis to tissue expansion is quite interesting. The examples of tissue from both guinea pigs and humans reveal epidermal thickening. Additional studies by Pasyk et al. noted that epidermal thickening can last up to two years after expansion. Pasyk also showed that the epidermal thickening occurred in the stratum spongiosum. However, there is no correlation between epidermal thickening with expansion time, location, volume or patient age. Interestingly, with expansion, light microscopy reveals an undulated basal lamina. The basal and prickle cells show an increase in the bundles of tonofibrils within the tonofilaments. Such findings align with a decrease in the intracellular spaces, in all of the epidermal layers, suggest increased mitosis. These findings were later supported by Austad, who documented increased mitotic activity using tritiated thymidine. The three-fold increase in epidermal mitosis occurred during expansion but returned to baseline in 2–5 days.

Dermis

The expansile and recoil properties of the skin are related to the amount of collagen and elastin fibers in the dermis. Similarly, the epidermis, like the dermis, undergoes significant changes during the expansion process. However, the thickness of the dermis is reduced dramatically. This is not related to expander volume or anatomic location. Most of the dermal thinning occurs in the reticular dermis, with thinning of the papillary dermis being less dramatic. During the
first few weeks of expansion, the dermis thins significantly but less so towards the end of the expansion process. After expansion, the reticular dermis is noted to have increased amounts of thick bundles of collagen fibers parallel to the skin. In addition, the elastic fibers in the expanded dermis were thicker and longer. It is believed that the presence of increased numbers of active fibroblasts in the dermis is responsible for the immature collagen fibers. Collagen bundles populate both the reticular and papillary dermis from the multiplication of fibroblasts.12,13

Skin has the ability to stretch and recoil. Elastin fibers are linked to each other by end-to-side junctions, and interspersed among collagen fibers, which are often larger and unlinked to another. Elastin fibers, unlike collagen, have the ability to stretch and retract. Collagen fibers in their relaxed state are disoriented and unparalleled. These fibers, in the presence of applied stress, align in a parallel fashion.10 This response is believed to be linearly proportional to the magnitude of the applied stress. However, too much stress during expansion of skin can cause constriction in the tiny blood vessels, inducing ischemia. The goal of reconstructive surgeons is to take advantage of this regenerative process without causing flap loss secondary to ischemia. It should be noted that sebaceous glands and sweat glands, and sensory nerves might undergo subtle changes. Hair follicles remain unchanged qualitatively but remain active. The lumens of various glands remain open even though adjacent structures have been compressed.12,13 It is believed that sensory fibers do not undergo any appreciable structural changes.10

Blood vessels
Several investigators have noted a significant proliferation of blood vessels associated with tissue expansion. This proliferation occurs primarily at the junction of the capsule and host tissues. Within days of expansion, small capillaries become distended, and in addition, the number of arterioles and venules increase. Cherry et al. noted an increase in the surviving length of expanded random-patterned skin flaps when compared with delayed skin flaps.14 Sasaki and Pang confirmed previous studies by documenting increased blood flow in expanded flaps.15 Lantieri et al. later suggested that vascular endothelial growth factor (VEGF) may play a part in the development of the increased vascularity of expanded flaps as VEGF was only expressed in expanded flap.16

Molecular basis of tissue expansion
Clearly, several studies have documented an increased mitotic index in the epidermis with tissue expansion.15,17 Yet, Takei et al. thought the mechanism of action was through the activation of growth factors.18 This group postulated that platelet derived growth factors and other growth factors could stimulate cutaneous cellular activity. It is well known that transforming growth factor-B (TGF-β) can not only influence extracellular matrix production but can also enhance fibroblast proliferation. In addition, it is felt that membrane bound molecules can play a role in the regulation of signal transduction pathways (Fig. 54.1). Although it is clear that strain has an effect on skin biology, whether or not we can modulate its effects chemically may be a rich source for future research.

Clinical application: correction of burn alopecia
Primary closure
In 1978, Huang et al. categorized the extent of burn alopecia as it related to correction of this problem. At this time, the authors used primary excision and rotation flaps as a means to either eliminate or camouflage burn alopecia.19 This group discovered that alopecia greater than 15% of the hair-bearing scalp was not amenable to correction using serial excision. The next stage in the evolution of closure of scalp defects came from Orticochea. The use of three and four limb Orticochea flaps was successful in the closure of scalp defects greater than 15%.20 The Juri flap, a pedicled, laterally-based scalp flap, was described to re-establish the anterior hairline in bald patients. The use of the Juri flap along with tissue expansion has also been described.21,22 It is clear that the use of primary closure in the correction of burn alopecia without the use of tissue expansion is possible. However, the extent of closure is less than 20–25% (Table 54.1). In general, if more than two operations are required to close a scalp defect, tissue expansion should be given serious consideration.

Burn alopecia classification
Many investigators have demonstrated the safety and efficacy of tissue expansion in the correction of burn alopecia.23–25 McCauley et al. developed a classification based on both the pattern of alopecia and the extent of alopecia.25 This classification system was designed as a template by which
Correction of burn alopecia

As previously noted, if primary closure of burn alopecia requires more than two operations, tissue expansion should be the operation of choice to achieve closure. Not only is patient selection crucial, so is individualized preoperative planning. Although some authors claim that subgaleal expansion yields better results with greater ease of expansion, most authors routinely use the supragaleal approach.26 The expectations of the patient and those of the surgeon should match. Patient acceptance of the weekly or biweekly injection processes and the progressive deformity caused by the expander is essential. Several parameters must be considered prior to expansion. Issues related to the insertion

### Table 54.1 Classification and sex distribution of burn alopecia

<table>
<thead>
<tr>
<th>Group</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A (&lt;15%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adults</td>
<td>3</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Children</td>
<td>29</td>
<td>17</td>
<td>51</td>
</tr>
<tr>
<td>Group B (16–30%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adults</td>
<td>6</td>
<td>0</td>
<td>12</td>
</tr>
<tr>
<td>Children</td>
<td>11</td>
<td>19</td>
<td>36</td>
</tr>
<tr>
<td>Group C (31–60%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adults</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Children</td>
<td>10</td>
<td>8</td>
<td>18</td>
</tr>
<tr>
<td>Group D (&gt;61%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adults</td>
<td>4</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Children</td>
<td>3</td>
<td>3</td>
<td>6</td>
</tr>
</tbody>
</table>


### Table 54.2 Classification of burn alopecia

<table>
<thead>
<tr>
<th>Type</th>
<th>Single alopecia segment</th>
<th>Multiple alopecia segments amenable to tissue expansion placement</th>
<th>Patchy burn alopecia not amenable to tissue expansion placement</th>
<th>Total alopecia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type I</td>
<td>A. Less than 25% of the hair-bearing scalp</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type IIA</td>
<td>B. 25–50% of the hair-bearing scalp</td>
<td></td>
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<td></td>
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<tr>
<td>Type IIB</td>
<td>C. 50–75% of the hair-bearing scalp</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type IIC</td>
<td>D. 75% of the hair-bearing scalp</td>
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</tbody>
</table>


reconstruction efforts could be designed to address specific problems with burn alopecia. (Table 54.2) The classification scheme is based on the type of alopecia (type 1–type 4) and the extent of alopecia (A, B, C, or D). Such classification is useful in the preoperative planning for correction of this problem.

Patients with type 1A or 1B burn alopecia can be corrected with a single expansion, although over-inflation may be necessary. Patients with type 1C and 1D burn alopecia may require multiple expanders either together and/or sequentially to correct these large areas of alopecia (Figs 54.2, 54.3). Patients with type IIA or IIB alopecia may also be corrected with a single expansion. However, patients with type IIC and IID alopecia require intricate flap designs to correct the problem. It is important to note that scalp expansion only allows redistribution of a healthy scalp tissue without creating new hair follicles. It has been noted that the interfollicular distance can increase two-fold without noticeable thinning of the hair.24 Several investigators have been reluctant to address burn alopecia >50% of the hair-bearing scalp, citing poor results. However, alternatives to resurfacing of the scalp are limited and some patients feel that some hair is better than no hair (Fig. 54.4).

### Principles of tissue expansion

(relevant content cut off)
process are less controversial. Most surgeons feel that the use of perioperative antibiotics is crucial. However, other issues are more debatable. The type of incision, paralesional or remote, is still under scrutiny. The orientation and the number of expanders have also been scrutinized. What size expander should one use and how much flap advancement can be expected? These are still debated issues. Internal versus external port placement may be individualized based on circumstances. How this affects the success of expansion is not always clear.

Techniques of tissue expansion

The type of incision used to insert a tissue expander is still an issue. One issue that does not appear to be controversial is size: regardless of the type of incision used, it should be as small as possible. Proponents of paralesional incisions (i.e. incisions at the junction of normal tissue and the scarred area) believe that minimal undermining of tissues is required for insertion of expanders. In addition, no statistically sound data has proven that infection rates, wound dehiscence rates, and implant exposure rates are significantly different. Proponents of the remote incision believe that healthy tissue approximated to healthy tissue affords better healing. The migration of expanders during the expansion process will not interfere with the weakest point in the skin, the incision. Complication rates have been cited to be less. However, several factors may influence this data. Currently, no controlled, randomized studies exist on site-specific expansion to settle this controversy. Complications may simply be related to the quality and quantity of tissues undergoing expansion.

Tissue expanders come in all shapes and sizes. They can be bought 'off the rack' or custom made. The choices of remote versus in situ ports are also available. In addition, differential expanders are also currently utilized. In 1984, Gibney recommended the use of expanders with a base width that is 2.5–3 times the width of the defect to be covered. Later, Manders et al. recommended the use of as
large an expander as possible. Brobmann and Huber, in an experimental study on pigs, addressed the issue of expander size and shape relative to the amount of expansion obtained. It was determined that less time, pressure, and volume are needed in a larger expander to achieve gain in the same surface area when compared with smaller implants. Several investigators have proposed the use of a mathematical model for determining the size, amount of inflation required, and expected advancement. However, the complexity of this model has not led to widespread use. When expanders are placed over rigid flat surfaces, predicting the amount of flap advancement is straightforward. It is only when expanders are placed under soft tissues with the tendency toward inward compression (i.e. the abdomen in children) or in areas of concavity (i.e. the neck) that the prediction of advancement is less reliable. In the scalp, prediction of flap advancement is reliable. In the author’s experience, measuring the dome of the expander and subtracting the width of the expander is fairly accurate in determining the length of flap advancement.

Some investigators have looked at the issue of external port placement in the pediatric population; the use of external ports can alleviate pain and anxiety associated with weekly injects. However, as long as safety issues are addressed, individualized circumstances best determine how and where ports are placed. If internal ports are used, placement should be in normal tissue to avoid exposure. If this is not possible, the best tissue possible should be used for port placement, preferably in an area that will be excised once the expansion process is complete.
Complications of tissue expansion

Major

Reports of complications with tissue expansion are numerous. Manders et al. published their experience with 41 expanders in 35 patients as a multi-site review. They defined complications as major and minor. Major complications of expansion were those that interrupted the expansion process (Table 54.3). In their review, 25% of patients had major complications requiring alterations in the treatment plan. Zellweger and Küni had similar problems with 5 of 21 expansions attended by major complications. In their review, 25% of patients had major complications as major and minor. Major complications of expansion were those that interrupted the expansion process (Table 54.3). In their review, 25% of patients had major complications requiring alterations in the treatment plan.

Zellweger and Küni had similar problems with 5 of 21 expansions attended by major complications. In their review, 25% of patients had major complications as major and minor. Major complications of expansion were those that interrupted the expansion process (Table 54.3). In their review, 25% of patients had major complications requiring alterations in the treatment plan.

Complications occurred in 27.9% of the expanders. However, 41% of these problems could not be solved and may be classified as major complications (12.6%). Although it is important to note expander complications, the number of patients who experience major complications is more important. This study suggests failure in 10 of 157 patients.

Minor

Minor complications were defined as problems that were resolved without failure of the procedure. Manders reported 17% minor complications in his study. In a retrospective review of 346 expanders in 132 patients, Pitanguy addressed the issue of re-expansion. Although the overall complication rate was only 7.5%, it is unclear as to whether repeat expansions were associated with increased complication rates. In 1998, Pisarski et al. shed a different light on multi-site expansion studies by detailing their complication rates over two separate time periods. Refinements in techniques, protocols, and surgeon maturity, when all sites are included, reduced complication rates from 30% to 18%. To date, it appears that the overall complication rate for tissue expansion is around 15–20% despite advances in techniques and strict protocol procedures.

The number of site-specific studies lends crucial insight into complications associated with expansion of different regions in the body. Scalp expansion for correction of burn alopecia is well documented. As noted in scalp expansion reviews, the use of expanders for the correction of burn alopecia has virtually solved this problem.

Conclusion

Burn alopecia remains a significant problem in patients with large total body surface area burns. Even with refinements in technique, complication rates remain moderate. Direct closure of this problem without tissue expansion removes around 15% of the scalp. Even with the use of Orticochea flaps, coverage of large scalp alopecia beyond 25% is limited. Tissue expansion has numerous advantages: color match, texture match and minimal donor site morbidity. The disadvantages are well known and include a protracted time period for completion of the expansion process and a significant complication rate. All patients who are victims of burn injury want to look and function at their best. Tissue expansion in certain patients offers this advantage. As we continue to refine our approach to certain problems using tissue expansion, it is important to communicate to our patients that although the process may be long and complicated, the end results can be quite beneficial.

Further reading


References

Reconstruction of the burned breast

Peter Dziewulski, Jorge Leon Villapalos

Introduction

The breast is important in both function and appearance in females and males. The prominent anatomic location of the breast and the nipple-areolar complex makes these structures prone to damage in all types of burn injury to the anterior chest wall. Burns to the breast can potentially impair and destroy both function and aesthetics. Due to its anatomical location, the breast is commonly injured in both small and large burn injuries, commonly scald injuries in children and as part of an injury to the whole trunk in major full-thickness flame injuries.

The management of the burned breast is undertaken concurrently with the management of the patient and their injury as a whole. Initially, stabilization, airway control, and resuscitation are a priority followed by wound management and optimization of healing potential depending on the depth and extent of injury. After healing, scar management and surveillance become important particularly in the female child to monitor development and growth of the breast during puberty.

The later effects of burns injury, which are related to loss of normal tissue and scarring, include limitation of movement, pain, disfigurement, and social embarrassment. Damage to the breast is particularly important in the prepubescent young girl. Absence of a nipple is a noticeable and striking concern to both male and female burn patients, even when more extensive burns and scarring are present elsewhere. Reconstruction of the burned breast is dependent on optimal early wound healing to prevent deformity. Once disfigurement and deformity are established accurate assessment, characterization, and planning are crucial to timely and successful reconstruction.

Breast anatomy

The breast is made up of both fatty tissue and glandular milk-producing tissues. The ratio of fatty tissue to glandular tissue varies among individuals. The relative amount of fatty tissue changes over time as the glandular tissue initially grows then diminishes. The glandular tissue is arranged in a series of lobules and ducts which are connected to the nipple-areolar complex (NAC). The gland in children lies 4–8 mm beneath the skin and is attached to the nipple by the pars infundibularis of the milk ducts. The ducts themselves are lined by epithelial cells which can act as a source of proliferating cells to resurface the nipple and areolar area. In addition, there is an intimate approximation of the NAC and breast gland bud in children which is important as excisional surgery may result in unnecessary removal of the breast bud with subsequent damage to the growth potential of the breast.

The breast overlies the pectoralis major muscle as well as the uppermost portion of the rectus abdominis muscle inferolaterally. The nipple should lie above the inframammary crease and is usually level with the fourth rib and just lateral to the mid-clavicular line. The average nipple-to-sternal notch measurement in a youthful, well-developed breast is 21–22 cm; an equilateral triangle formed between the nipples and sternal notch measures an average of 21 cm per side.

Epidemiology

Burn injury to the trunk is common and can lead to significant problems. It has been reported as the second most commonly injured area following the upper extremity, with the breast being the most frequently injured area on the trunk.

Burn injury to the breast can occur at any age and to either sex but causes most problems in the female. Aetiology is varied but in one study 66% of injuries to the female breast were due to scald injury with a significant number having isolated breast burns.

In particular two patterns of injury emerge. Scald injury usually affecting the upper torso and breast in children and trunk burns involving the breasts in patients who have extensive flame burn injury.

In prepubescent females, most of the burns to the anterior chest wall are scalds, and depending on burn depth, the subcutaneous tissue may remain viable, thus preserving the breast bud. During puberty, if healing has led to abnormal scarring, the breast parenchyma develops under the scar and can result in breast contracture and disfigurement. The breast mound and the nipple-areolar complex are displaced, the contours are ill-defined, and the inframammary fold is effaced.

Chest wall burns in the prepubescent female can be devastating to both the child and the parents, as normal breast growth and development may be compromised. Attention to detail and avoidance of excision of the breast bud is required to preserve the development of the breast in prepubescent
girls. Young girls with burns to the anterior chest wall must have long-term care to help ensure proper development and aesthetic appearance of the breasts during and after puberty.6

There are no prospective trials available on the longitudi- nal results of burns to the anterior chest wall in prepubescent females, nor are there any retrospective reviews with large numbers of young girls.

In a retrospective review of anterior chest wall burns in prepubescent girls treated with surgical debridement and split-thickness skin grafts, long-term problems with scarring and impaired breast development requiring reconstructive surgery many years after the initial burn were identified. In this single-institution study, 193 prepubescent girls were treated for anterior chest wall burns over 20 years; 52 (27%) were treated with surgical debridement and split-thickness skin grafts, and 11 with documented burns to the breast and nipple-areolar complex were available for long-term follow-up. In this small sample, the mean timeframe from burn to follow-up was 26.5 years (range 19–32 years). All 11 women required reconstructive procedures after the onset of breast development to improve breast appearance. Complications of the burns included breast asymmetry, distortion, banding, and unpleasant skin texture.1

In a longitudinal assessment of 28 prepubescent girls with severe burns to the anterior chest wall, 17 (61%) lost the nipple-areolar complex, but all developed breast tissue at puberty. However, 20 (71%) of these young patients experienced entrapment of the breast and required surgical intervention and incisional releases of the anterior chest wall to allow for proper breast development.7

**Acute care**

Burns to the breast are initially gently washed and debrided and dressed with topical antimicrobials and dressings prior to surgical excision if the burns are too deep to warrant spontaneous healing. The burn eschar should not be excised from the nipple-areolar complex, as healing occurs from the deep glandular structures. The eschar should be allowed to separate spontaneously.1

Minor and superficial partial-thickness burns to the anterior chest wall are treated with local antimicrobial agents and dressings, while deeper burns are treated with excision and soft tissue coverage. Spontaneous eschar separation and grafting versus tangential excision of the eschar and grafting after burn demarcation are two options for the management of the burned breast. Surgical experience, the overall condition of the patient, and the extensiveness of the burn will help determine the best approach.8

It is well recognized that even with nipple loss, breast development can occur and that conservative management of the NAC is beneficial as the breast bud underneath is viable and retains the potential for growth and development.

If surgery is required, care should be taken not to excise the breast bud from the anterior chest wall of pre-pubertal girls during the debridement of the burned skin.9 The mamma gland in children is located 4–8 mm deep in the subcutaneous tissue.4 Nor should the breast mound be excised, if at all possible, in adult females. The relative avascular adipose tissue and connective tissue of the non-lactating breast requires a very careful excision of all non-viable tissue.

Debridement and grafting of the breast, especially the large pendulous breast, is a technically challenging undertaking. Debridement of a complex convex surface while trying to avoid injury to the nipple areolar complex needs a judicious approach. In the pendulous breast, tissue traction may be applied by tissue forceps or towel clips to allow an even tangential excision plane. Resurfacing of the breast must be undertaken with prevention of future deformity in mind. Cosmetic units of the breast must be preserved and grafts placed to avoid future disfiguring contractures. Sheet grafts often do not contour well and a narrowly meshed unexpanded autograft (1:1.5, 1:2) is preferred.

Post-skin grafting positioning of the patient and the breast is important to avoid shearing of grafts on the lateral border and the inframammary area where friction can be significant. Abduction of the upper limb is important for this reason as well as preventing axillary contracture. In addition tie-over bolsters can be used on the breast to reduce graft shear. Despite all these measures, the take of grafts on the large pendulous breast is often unsatisfactory in the inframammary and lateral borders leading to graft loss, re-grafting and suboptimal outcome, which can give rise to post-burn contracture and deformity.

**Burns during pregnancy and lactation**

Burns to the breast during pregnancy are in general uncommon but have increased incidence in certain societies.10 The use of topical agents can be limited due to concerns regarding absorption and toxicity and in general the use of silver sulfadiazine, cerium nitrate, and povidone-iodine are not recommended during pregnancy or lactation. Combination antibiotic ointments provide the best local care until wounds can be treated by tissue coverage. Early coverage of the burns by tangential excision and split-thickness skin grafts facilitates healing of the wounds and minimizes septic complications, thus improving maternal and fetal outcome.11

If residual breast tissue is preserved, successful breast-feeding after sustaining burns to the breast while pregnant has been reported.12 Absence of a nipple-areolar complex precludes breast-feeding; distortion of the complex does not. Split-thickness skin grafts and customized pressure therapy is used to correct a contracture deformity.

In a retrospective review of 25 pregnant burned patients, the prognosis was the same as that of other burned patients. Pregnancy does not adversely affect maternal outcome.13

Prophylactic management of burned lactating breasts with bromocriptine produced cessation of lactation and induced breast involution. Once the engorgement is dissipated, surgical excision of the burn and tissue coverage can proceed as previously described.14

**Burns to large breasts**

The current system for determining the percentage of total body surface area (TBSA) burned may underestimate that percentage for burns of the anterior trunk in women with large breasts. In a review of 60 volunteers to determine the difference in TBSA of the anterior trunk between men and women, large-breasted women (cup size D and greater) were
In order to plan reconstruction, the post-breast-burn deformity must be evaluated and analysed so that a systematic approach may be undertaken. However, in major burn injury, donor sites may be sparse and the tissue available for reconstruction may be less than optimal. With limited donor sites, a systematic approach may not be possible and the patient’s requests and desires, coupled with judicious use of tissue and realistic expectations, may be the optimal solution. Post-burn breast sequelae can be classified according to the description in Table 55.1.

Burn scar and deformity of the breast can affect one or both breasts and can affect part or the whole of the breast. It can involve development of the breast mound leaving discrepancies in shape, size and position of the mound and can also affect the nipple-areolar complex in a similar way. Deformity can be classified according to its causes, including scar contracture within and without the boundaries of the breast giving rise to intrinsic and extrinsic contracture. A pathognomonic feature of burn scar that crosses the inframammary fold area is loss of definition and flattening of the inframammary fold. Complete entrapment of the breast can prevent breast growth and mimic hypoplasia or aplasia of the breast gland. Similarly, if the gland has been partially or totally destroyed or removed, this can lead to hypoplasia or aplasia of the breast.

Finally, symmetry of the breast is an important issue as no matter how good the shape or size of the breast, significant asymmetry will always be apparent and distressing.

<table>
<thead>
<tr>
<th>Location</th>
<th>Unilateral</th>
<th>Bilateral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extent</td>
<td>Total</td>
<td>Subtotal</td>
</tr>
<tr>
<td>Anatomical</td>
<td>Breast mound</td>
<td>NAC</td>
</tr>
<tr>
<td>Deformity</td>
<td>Contracture – intrinsic/extrinsic</td>
<td>Hypoplasia</td>
</tr>
<tr>
<td>Symmetry</td>
<td></td>
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</tr>
</tbody>
</table>

When assessing a patient with post-burn breast deformity all the above must be taken into account when formulating a treatment plan to restore breast size, shape, NAC and symmetry.

**Principles of reconstruction**

The basic aim of any burn reconstruction is to improve function, comfort, and appearance. A realistic approach is necessary to counsel patients’ expectations to the probable outcomes of reconstructive surgery. A strong patient–surgeon relationship is necessary in order to negotiate a master plan and agree on priorities.

The ideal time to reconstruct the burned prepubescent breast is once breast maturity is attained. Growth, development, and patient cooperation must be considered when planning reconstructive procedures. It is generally best to allow the scar to mature prior to reconstructing the breast and to perform the procedures during early adulthood. If the release of the contracture is ill-timed, the post-pubertal development and growth of the breast parenchyma acquires a splayed, hypoplastastic, and flattened form. In severe cases, however, staged procedures throughout puberty may be required to optimize the aesthetic result.

In addition to the general measures above, other specific assessments would be to identify the problems described above as post-burn sequelae in the breast. In particular it is important to elucidate the patient’s concerns about the breast, which breast is preferred and what the perceived goals of reconstruction are.

Specifics to note on physical examination include the quality of the skin and scar, intrinsic or extrinsic scar contracture, the position of the NAC, the sternal notch to nipple distance, the breast base size in cm and any differences between the breasts in terms of symmetry, shape and size. In addition it is important to note what tissues are left, what parts are missing, and what sort of donor sites are available.

Analysis of donor sites is crucial and must include areas for harvesting both full- and split-thickness skin grafts, the back to examine the latissimus dorsi donor site and all areas where potential flaps can be harvested for free tissue transfer such as the lower abdomen (DIEP flap), inner thigh (TUG flap) and the buttock (SGAP flap). In addition areas of fat deposition on flanks, buttocks, and upper abdomen must also be examined as potential sites of fat harvest for autologous fat transfer.

This will help to determine the techniques available for burn reconstruction. Reconstructive techniques to improve breast development and appearance include simple contracture releases, z-plasty, skin grafting, nipple reconstruction, breast augmentation with an implant, replacement of lost breast volume with autologous fat transfer or with free tissue transfer, and reduction of the contralateral unburned breast to match the under-developed burned breast.

The principles used to reconstruct the burned breast are described in Box 55.1.

**Release and resurfacing scar**

Release of scar contracture will entail expansion of breast skin surface either by release contractures and split-thickness
skin grafting or the use of dermal regeneration templates combined with skin grafting at the infra-mammary fold, peri-areolar area, sternal area, and anterior axillary line. Release of such contractures and resurfacing of the breast skin can allow near-normal mammary gland development and will improve shape and volume (Fig. 55.1). The expansion of breast skin may sometimes need tissue expansion or the use of distal or free flap tissue cover.3,17-19

The distortion of the inframammary fold is functionally disabling and aesthetically disfiguring.20 The reconstruction and redefinition of the inframammary fold as a major landmark in successful breast reconstruction can be performed by simple scar release and grafting of the area. Replacement of scarred skin and subdermal tissue with a normal skin advancement flap provides a natural and aesthetic solution. Flap reconstruction provides well vascularized tissue with superior pliability, elasticity and durability when compared to skin grafting. The expanded reverse abdominoplasty can recreate the inframammary crease in a multi-staged process.20,21 The possibility of pre-expansion allows extra tissue to recreate this breast anatomical landmark with healthy pliable skin. This technique can provide an optimal aesthetic result, but its use is limited if burn scars involve the abdomen. Infection, hematomata, seroma, fat necrosis, flap loss, and abnormally shaped umbilicus and breast are complications of this procedure.

The use of dermal regeneration templates in breast reconstruction following burns are reported to reduce the recurrence of scar contracture and to provide pliability to the reconstruction. Prevention of infection of the template is fundamental to success. There should be regular reviews until the second stage of reconstruction is achieved. Topical negative pressure therapy can be used to keep the template and the graft in place.22

**Box 55.1 Principles of post-burn breast reconstruction**

- Release scar contracture
- Resurface unsightly or painful scar
- Replace missing parts including breast mound and NAC
- Re-establish symmetry.

Replacement of missing parts

**Breast mound reconstruction**

In addition to contracture release, volume replacement is the key to restoration of breast symmetry and appearance. Volume replacement can be achieved by the two broad categories of technique used for traditional post-oncological breast reconstruction. These include prosthetic implant-based reconstruction and autologous tissue reconstruction to restore shape and volume.2

The generally held convention that scar tissue lacks elasticity and pliability, cannot be expanded with tissue expanders and limits adequate volume reconstruction of the breast mound has been challenged. It is recognized that burn scar can be stretched and expanded and this allows the use of tissue expanders for volume (Fig. 55.2).23,24

In a retrospective review of 15 women with burns to the breasts reconstructed with contracture release and tissue expanders, there were no significant differences in major complications, operative time, and amount of time to expansion, compared with the same reconstruction procedures in 20 women with congenital breast anomalies.25 Endoscopically assisted tissue expanders had significantly fewer major complications, required less operative time, and required less time to expand for the burn patients compared with expanders placed by the traditional open method.26

Tissue expanders and breast prostheses used to perform breast volume augmentation must always be covered by an adequate tissue envelope to prevent exposure and extrusion of the implant. This usually requires submuscular placement of the implant and will occasionally require importing of muscle and uninjured skin to provide more substantial soft tissue cover using a pedicled latissimus dorsi flap.

The use of a dermal regeneration template (Integra) followed by tissue expansion as a staged procedure for post-burn breast hypoplasia appears to be reliable and safe.27,28 The first stage includes release and excision of contractures and scars, submuscular insertion of anatomical tissue expander, and coverage of the anterior chest wall with Integra. The second stage is performed 1 month later and involves removal of the outer silicone layer of Integra, applying a split-thickness skin autograft to the areas, and partially inflating expander. The expander is then overinflated, removed, and replaced with a permanent silicone implant in the third stage of reconstruction. Patient satisfaction and short-term evaluation of this technique is promising,27,28 but no long-term studies or clinical trials are available for further assessment.

In the uncommon event of breast aplasia following destruction or more commonly unintended excision of the breast bud a total breast reconstruction will be required. This will usually involve replacement of both skin and breast volume, though submuscular tissue expansion can provide satisfactory reconstruction. If the breast bud has been destroyed and skin graft scar is adherent to the pectoralis fascia or muscle then extra tissue must be imported into the area. As described above, a pedicled latissimus dorsi flap with a submuscular tissue expander will give good volume replacement.

The other option is to undertake autologous reconstruction using free tissue transfer. The free flap of choice is the deep inferior epigastric perforator (DIEP)29,30 flap or the transverse rectus abdominis myocutaneous (TRAM) flap,31 which require uninjured abdominal tissues. Other alternatives include the superior gluteal artery perforator (SGAP) flap32 and the transverse upper gracilis (TUG) flap.33 Although technically more demanding, the use of free tissue transfer flap reconstruction provides autologous volume replacement and obviates the need for a prosthetic implant with the inherent risks of infection and extrusion. Occasionally, both free tissue transfer and an implant may be required for reconstruction (Fig. 55.3).34 In addition to the technical demands of the surgery free tissue transfers are longer operative procedures and are potentially not suitable for medically unfit patients. In addition, failure of autologous reconstruction deprives the patient of healthy tissue and increases the possibility of unsightly donor site scarring.

Autologous fat transfer has become increasing popular as a method of volume replacement in the breast, particularly for aesthetic volume augmentation and for post-oncological
Figure 55.1 Breast contracture release. (a.i) Planned release of symmastia and inframammary fold contractures to release breast mound. (a.ii) Following incisional release – note skin deficit. (a.iii) Resurfacing with dermal template. (a.iv) Use of topical negative pressure to secure dermal template and prevent shearing. (a.v) Dermal template ready for autografting. (a.vi) Second stage resurfacing of dermal template with sheet autograft. (b.i–b.iii) Preoperative views. (b.iv–b.vi) Postoperative views following NAC reconstruction showing improvement in projection, cleavage, inframammary fold.
reconstruction. \textsuperscript{35} Non-autologous substances have also been used for cosmetic augmentation but their effects are temporary. The steps involved in autologous fat transfer include identification of donor sites, harvesting, preparation, and injection of the fat. The implications for burn patients center around choice of donor sites where adequate amounts of fat may be sparse. The procedure can be lengthy and may not be suitable for high anesthetic risk patients. Complications include pain, infection, bruising, edema, contour irregularity and defect. The potential use of adipose derived stem cells opens an exciting prospect for the use of fat in the reconstruction of the burned breast in addition to potential benefits in scar modulation.\textsuperscript{36–39}

**Nipple-areola complex reconstruction**

Reconstruction of the nipple-areola complex (NAC) can be divided into subtotal or total reconstruction depending on how much of it is preserved following burn injury. Nipple-areolar complex reconstruction is usually performed at a second stage once breast mound volume and shape have been addressed.

Subtotal reconstruction of a partially preserved NAC can be challenging due to excessive nipple flattening and surrounding peri-areolar scarring. Split-thickness skin grafts and pressure therapy have been described to release the contracture.\textsuperscript{40}

Total NAC reconstruction is based on principles and techniques used in post oncological reconstruction.\textsuperscript{41} Nipple reconstruction can be achieved using local flaps but is limited by the lack of pliability of scarred skin. There are many techniques described for post-oncologic reconstruction, including the skate flap\textsuperscript{42} and the C-V flap;\textsuperscript{43} however all suffer from loss of nipple projection. Despite there being many techniques there have been very few comparative studies.\textsuperscript{44} A modification of the star flap has produced promising results in terms of maintenance of nipple projection.\textsuperscript{45} The burn scar in and around the NAC area is not pliable and leads to loss of projection of the nipple and potential flap necrosis of the reconstruction. Nipple sharing or the insertion of composite grafts subcutaneously are alternative options.\textsuperscript{41}

The areola can be reconstructed by using full-thickness skin grafts from the inner thigh or labia.\textsuperscript{41} These areas usually give a darker graft mimicking the pigmentation of the areola. However, this technique has significant donor site morbidity in terms of wound healing and infective complications and usually results in a colour mismatch with the contralateral NAC.

A good alternative is to tattoo both the reconstructed nipple and surrounding areolar area to match colour to the...
contralateral unburned nipple-areolar complex. Tattooing of scar is unpredictable and probably best done once the scar is mature. Tattooing provides an excellent option to enhance the appearance of the nipple-areolar complex (Fig. 55.1b).

**Asymmetry**

The correction of asymmetry plays an important part in post-burn breast reconstruction. Asymmetry following burn injury to the breast can be due to pre-existing asymmetry, scar contracture or impaired maturation of the breast gland. Attempts to improve appearance and symmetry can focus on the injured breast or on the contralateral uninjured breast.

Symmetrization procedures performed on the contralateral breast can be aimed at matching size using breast augmentation or reduction and shape using mastopexy/reduction techniques. Burned breasts are less likely to develop a natural ptosis so mastopexy and breast reduction techniques undertaken on the contralateral breast will restore balance and symmetry.

Post-burn deformity of the large breast can produce nipple areolar complex displacement, burn scar contracture, and scarring. In a retrospective review of 11 women with deep thermal burns to ptotic and hypertrophied breasts with post-burn deformities, reconstruction with the inferior pedicle dermal flap resulted in reduction of the large breast size, elimination or reduction of burn scars and relocation of the nipple areolar complex to a normal position.46

Mammary hyperplasia can occur in patients with previous full-thickness burns of their breasts. Reduction mammoplasty has been generally avoided due to concern regarding devascularization of the skin graft or the nipple-areolar complex. In a retrospective review of six patients with full-thickness burns of the breasts and subsequent skin graft coverage, there was no nipple loss, hematoma, infection, or major loss of skin flaps. Reduction mammoplasty in this group of patients is safe and carries minimal risk.47

**Summary**

Initial care of burns of the breast should follow general principles of burn management, including resuscitation, judicious wound debridement to maximize tissue preservation followed by periodic review to monitor development of breast anatomy. This approach should ensure that post-burn deformity is minimized and that developmental and reconstructive potential is maximized. In particular, care in...
treatment should avoid permanent loss of breast volume and cosmetic deformity.

The initial debridement must ensure preservation of the nipple-areola complex to allow breast development. Excessive debridement of this area will lead to permanent breast mound underdevelopment.

Deep burns of both the developing and adult breast will inevitably lead to contracture and deformity of breast mound, inframammary fold, and nipple-areola complex. Adequate timing of reconstruction of the prepubescent burned breast will avoid lasting deformity.

The principles of reconstruction include preservation and restoration of: breast mound volume, breast mound shape, the inframammary fold, and nipple-areola complex and breast symmetry. Breast shape and volume restoration depend on the availability of remaining breast tissue, and local and distant unburned tissue. Following excision of burn scar or contracture, cover can be achieved by applying reconstructive ladder principles of ascending complexity. These include skin grafting with or without dermal templates, local, regional, distal and free flaps and tissue expansion techniques. Symmetrization procedures, either reduction or augmentation, may be necessary in the contralateral unburned breast.

Multidisciplinary involvement and psychological support are fundamental in achieving success, especially in the young developing female.

Further reading


References

47. Coleman SR. Structural fat grafting: more than a permanent filler. Plast Reconstr Surg. 2006;118(3 Suppl):1085S-1205S.
Management of contractural deformities involving the shoulder (axilla), elbow, hip and knee joints in burned patients
Ted Huang, Jui-Yung Yang

Introduction
Burn injuries, regardless of the etiology, rarely involve a joint itself. However, the joint function is often impaired because of burns. The joint problems and joint deformities noted in burn patients are mostly due to physical inactivity combined with limitation of joint movement because of scar contracture.

The regimen of burn management, especially during the period immediately following the injury, seldom includes plans to care for the joint. Instead, the treatment is focused upon resuscitative efforts to restore fluid balance and to maintain functional integrity of the circulatory and the pulmonary systems. The consequence of joint dysfunction is usually left for later reconstruction.

Contractural deformities of the shoulder (axilla), elbow, hip and knee observed in a burned patient

The factors leading to formation of the contractural deformities
Folding bodily joints in flexion, a so-called posture of ‘comfort’, is a characteristic body posture seen commonly in a distressed individual. Although the exact reasons are not entirely clear, contraction of muscle fibers at rest and contractile force difference between the flexor muscle and the extensor muscle play an important role in the genesis of this body posture. The magnitude of joint flexion, furthermore, increases as an individual loses voluntary control of muscle movement, as frequently occurs in a burn victim (Fig. 56.1). A prolonged period of physical inactivity associated with burn treatment and scar tissue contraction around the joint structures as the recovery ensues, further impedes the joint mobility.

Incidence of burn contracture involving the shoulder (axilla), elbow and knee joints

Burn treatment that requires a long period of bed confinement and physical inactivity as well as restriction of joint movement will lead to joint dysfunction. Consequently, every bodily joint, i.e. the vertebral, mandibular, shoulder, elbow, finger, hip, knee and toe joints, are susceptible to changes. Of various bodily joints involved, the contractural deformities of the shoulder (axilla), elbow and the knee are relatively common. Factors such as a wide range of joint movement and an asynchronous muscular control characteristic features of these joints, when combined with a high vulnerability to burn injuries, are the probable reasons accounting for the high incidence encountered. Recent review of the records of 1005 patients treated at the Shriners Burns Hospital in Galveston, Texas, over the past 25 years, indicated that the elbow was the joint most commonly affected. There were 397 patients with elbow joint deformity followed by 283 knee contractures. There were 248 axillary deformities. The hip joint contracture was the deformity least encountered and was noted in only 77 patients (Table 56.1).

The efficacy of splinting in controlling burn contractures of shoulder (axilla), elbow and knee joints
Although Cronin in 1955 demonstrated that the neck splint was effective in preventing recurrence of neck contracture following surgical release, the routine use of splinting for burn patients did not become a part of the regimen of burn wound care in Galveston until 1968 when Larson, the former Surgeon-in-Chief and Willis, the former Chief Occupational Therapist at the Shriners Burns Institute, began to fabricate splints with thermoplastic materials to brace the neck and extremities.2–5
The effectiveness of splinting was diminished to 55% if splinting was discontinued within 6 months. For comparison, the incidence of contractural deformity ascertained in 219 patients who had never worn the splint was 62% (Table 56.2). Although splinting and bracing were shown to be effective in minimizing joint contracture, it was not entirely clear if restriction of joint movement would affect the quality of scar tissues formed across the joint surface. The effects were assessed by determining the frequency of secondary surgery performed in this group of patients. Over 90% of 219 individuals who did not use the splint/bracing, required reconstructive surgery. In contrast, the need for surgical reconstruction in individuals who wore splints was 25%.

Management during the acute phase of recovery

It is believed that inadequate physical exercise and lack of joint splinting and bracing, while allowing a patient to assume the posture of ‘comfort,’ are the main factors responsible for the genesis of contractural deformities seen in burn patients during the acute phase of recovery from burn injuries. The deformities, furthermore, are made worse because of skin involvement and burn scar contracture. In order to minimize this undesirable consequence of burn injuries, proper body positioning and splinting of the joint structures must be incorporated in the regimen of burn treatment. The treatment should be implemented as soon as the patient’s condition becomes stable.

Body positioning and joint splinting

Bodily position

Although a supine position is preferred, the patient may be placed in a lateral decubitus position while confined in bed. The head should be placed in a neutral position with the neck slightly extended. For a patient placed in a supine position, neck extension is achieved by placing a small pad between the scapulae to facilitate the scapular traction. A neck brace may be used if a patient is placed in other body positions.

Table 56.1 The distribution of joint deformities

<table>
<thead>
<tr>
<th>Joint involved</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shoulder (axilla)</td>
<td>248</td>
</tr>
<tr>
<td>Elbow</td>
<td>397</td>
</tr>
<tr>
<td>Hip</td>
<td>77</td>
</tr>
<tr>
<td>Knee</td>
<td>283</td>
</tr>
<tr>
<td>Total</td>
<td>1005</td>
</tr>
</tbody>
</table>

Table 56.2 The incidence of contractures across the shoulder (axilla), elbow and knee joints

<table>
<thead>
<tr>
<th>Joint involved</th>
<th>With splint</th>
<th>Without splint</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;6 months</td>
<td>&gt;6 months</td>
</tr>
<tr>
<td>Shoulder</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe/moderate</td>
<td>137</td>
<td>24</td>
</tr>
<tr>
<td>Mild/none</td>
<td>37</td>
<td>6</td>
</tr>
<tr>
<td>Elbow</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe/moderate</td>
<td>75</td>
<td>17</td>
</tr>
<tr>
<td>Mild/none</td>
<td>61</td>
<td>33</td>
</tr>
<tr>
<td>Knee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe/moderate</td>
<td>26</td>
<td>4</td>
</tr>
<tr>
<td>Mild/none</td>
<td>45</td>
<td>16</td>
</tr>
</tbody>
</table>

Figure 56.1 The posture of ‘comfort’ characterized by flexion of shoulder (axilla) and elbow joints, plus hip and knee joints is assumed by patients under distress, as in burn patients.
Management of contractural deformities involving the shoulder (axilla), elbow, hip and knee joints in burned patients

Shoulder (axillary) joint
The shoulder joint is kept at 90–120 degrees of abduction and 15–20 degrees of flexion. This generally results in 60–80 degrees of arm elevation. The position is not only useful in protecting the brachial plexus from traction injury but also effective in maintaining the stability of the glenohumeral joint. The position is best kept with the use of foam wedge, trough, and/or airplane splint. A ‘figure-of-eight’ wrapping over a pad around the axilla, more frequently used for patients during the intermediate phase of recovery from the injury, is effective in maintaining shoulder abduction. It is also useful in preventing excess shoulder flexion.

Elbow joint
Elbow flexion is commonly seen in a distressed patient. Rigid flexion contracture of the elbow is a common sequela if the elbow is left unattended. With burns of the skin around the olecranon, exposure of the elbow joint is a common sequela if the elbow is allowed to contract freely. Maintaining the elbow in full extension therefore is essential. An extension brace (Fig. 56.2), or a three-point extension splint across the elbow joint is effective for this purpose (Fig. 56.3).

Wrist joint
A contractural deformity involving a wrist joint is relatively common in individuals with hand burns that were not splinted properly. A cock-up hand splint should be applied to maintain a 30° wrist extension (Fig. 56.4).

Hip joint
A contractural deformity of the hip is relatively uncommon unless the hip joint is allowed to remain flexed for a long period of time. Hip extension can be achieved by placing the patient in a prone position. In a supine position, 15–20 degree of abduction is maintained with the use of brace or anklet.

Knee joint
Flexion of the knee is another posture commonly assumed by a burned victim. Similar to the elbow, uncontrolled flexion of the knee joint will lead to exposure of the joint structure, especially in instances where the injuries involved the patella surface. Maintenance of knee in full extension is, in this sense, an essential component of therapeutic regimen. This is accomplished by means of a knee brace or a three-point extension splint to assure a full extension of the knee joint (Fig. 56.5).

Exercise
Although exercising a burned victim is an integral part of burn therapy, it is seldom implemented until the resuscitative measures are completed and the condition of the patient is considered stable. The primary goal of exercise is to maintain functional integrity of the joint structures and the muscle strength. This is attained by, in most instances, moving the joint manually and muscles passively. Frequency and intensity of an exercise regimen, however, may vary depending upon the magnitude of injury and the extent of joint involvement. The treatment, if possible, should be intensive and is rendered as frequently as possible.
Management during the intermediate phase of recovery

A period starting from the 2nd month following the injury through the 4th month is considered as the intermediate phase of recovery from burn injuries. The burn victims typically will have full recovery of physiologic functions with integumental integrity restored. The cicatricial processes around the injured sites, on the other hand, are physiologically active though healing of the burned wound is considered satisfactory. That is, the process is characterized by, in addition to a maximal rate of collagen synthesis, a steady increase in the myofibroblast fraction of the fibroblast population in the wound; the cellular change believed to account for contraction of the scar tissues. Continuous use of splinting and pressure to support the joints and burned sites, in this sense, is essential in order to control changes caused by ensuing scar tissue formation and scar contracture.

Bodily positioning and joint splinting

Joint splinting and bodily positioning are similar to the regimen used during the acute phase of burn recovery. That is, the shoulder is kept at 15–20 degree flexion and 80–120 degree abduction. A 'figure-of-eight' wrapping over an axillary pad is used to maintain this shoulder joint position (Fig. 56.6). The elbow and knee joints are maintained in full extension by means of a three-point extension splint or brace. A pressure dressing or garment is incorporated in the splint. In instances where the use of 'figure-of-eight' bandage, pressure dressing and/or garment, is not feasible because of recent surgery, devices such as an 'airplane splint' device (Fig. 56.7), or a three-point extension splint may be used to splint the axilla, elbow and the knee joints.

Pressure dressing

A compression dressing, originally incorporated in the treatment of burned wounds of the upper and lower extremities at the Shriners Burns Hospital in 1968 as a means to provide mechanical support to healing wounds, is effective in reducing tissue swelling and in promoting softening of a burned scar. Compression of a burned wound even though healing
is still in progress, is most easily achieved by means of wrapping the extremity with an elasticized bandage. Wrapping of the extremity should begin at the hand or foot. The bandage is moved cephalad in a criss-cross fashion. The splint is reapplied over the bandage. It is important to rewrap the extremity three to four times daily. Wrapping an extremity with an elasticized bandage can produce a pressure ingredient of 10–25 mm Hg. The use of a pressure dressing should be continued for 12 to 18 months.

**Surgical management of established contractural deformities**

Contraction of the shoulder, elbow, hip and knee joints can occur despite proper splinting and intensive physical therapy. Surgical reconstruction of contractural deformities, in this sense, remains an essential component of patient care and patient rehabilitation. The task of deciding the timing of surgical intervention, however, can be difficult and it requires detailed evaluation of the patient and the deformity. The following are ascertained before surgery:

1. The causes of joint immobility
2. The extent and the availability of uninjured skin that could be used for reconstruction
3. The extent of maturation of scar tissues that surround the joint.

**Patient evaluation**

There are numerous factors that will affect joint movements in burn patients. Although hypertrophy and contraction of scar tissues and/or contracted skin graft around a joint are the most common causes of joint impairment, changes in the ligamentous structures or the joint itself due to burn injuries could also limit the joint mobility. Detailed examination that includes radiographic assessment of the joint structures is essential in order to formulate a definitive treatment plan.

**Non-operative or minimally invasive approach to correct a contracted and/or stiff joint**

Restoration of movements in a contracted and/or stiff joint could be attained by minimally invasive or non-surgical means. ‘Pushing’ and ‘pulling’ of an extremity that in turn, ‘stretches’ contracted scars and tissues around an affected joint is the principle behind this modality of managing a contracted and/or stiff joint. The treatment is found to be especially effective in mobilizing a contracted joint caused by a long period of physical inactivity or in some instances, of scar contracture.

Although the morbidities associated with this modality of treatment are minimal, breakdown of the skin due to pressure and/or friction resulting from ‘pushing’ and ‘pulling’ of a limb can occur.

**Shoulder (axillary) contracture**

Tight scars formed across the shoulder joint, usually in the area along the axillary folds, often limit the joint movement. The joint stiffness caused by scar contracture may be further aggravated by physical inactivity, especially if the patient is allowed to remain in the posture of ‘comfort’.

There are two non-surgical methods commonly used to mobilize a contracted shoulder (axilla) joint. One is ‘figure of eight’ compression dressing technique and the other an ‘airplane’ splinting technique:

**A ‘figure-of-eight’ compression dressing**

An elasticized bandage is used to wrap over a pad placed in the axillary fold around the shoulder joint in a ‘figure-of-eight’ fashion to extend and abduct the shoulder. The dressing must be worn continuously and it is removed only for cleansing. Continuous wear of the dressing for a period of 3–6 months is necessary to obtain the release. The mobility of the joint increases as the scar tissues across the axilla softens. The extent of relief may be limited if the scar is thick and unyielding to the pressure (Fig. 56.8).

**An airplane splint**

The splint is fabricated with a thermoplastic material. The spreading angle of the splint is conformed to the extent of the shoulder (axilla) joint held at maximum abduction plus 10–15 degrees of extension. Abduction and extension of the joint, that is elevation of the arm, will be maintained by ‘pushing’ the arm away from the upper thorax. Care is needed to protect the skin over the inner aspect of the arm and the side of the chest. The splint is changed regularly as the angle of joint abduction increases. To achieve the needed release in most instances, 1–3 months of continuous use of this device is usually necessary (Fig. 56.7).

**Elbow and knee contracture**

Flexion contracture is the most common deformity encountered in these two joints. The scar formed across the antecubital and the popliteal fossae frequently aggravates the magnitude of contractural problems in these joints. The following techniques are frequently utilized before surgery to obtain joint movement and joint extension:

**A three-point extension splint**

The splint is assembled similarly to a prosthetic/orthotic device. Two sidebars hinged at the middle are connected with a bracing trough at the end. A cap pad is attached at the mid-section of the sidebar to fit over the elbow or the kneecap. The splint is placed across the antecubital fossa or the popliteal fossa. Fitting of the splint is adjusted with the Velcro straps (Figs 56.2, 56.3).

The amount of extension achieved by the joint is determined by the extent of pre-existing joint stiffness. The angle of extension is initially determined by the angle of joint contracture. The magnitude of extension is controlled by tightening the olecranon or patellar pad. It is increased gradually as the joint gains its mobility. The problems encountered with the use of a ‘three-point extension splint’ are uncommon. However, breakdown of the skin can occur. Leverage attainable from 3-point pressure application may be limited in a young individual because of short limb length. The skeletal traction technique, in such instances, may be used.
A 6-year-old boy sustained burns of the right side of his body extending from the lower neck to the upper thorax that included the axillary crease. (b) He experienced difficulty in extending both the neck and the right arm because of ensuing contraction of scar tissues around the neck and the axilla. (c) A 'figure-of-eight' dressing was used to maintain the shoulder extension and abduction. The dressing was used for 12 months. (d) He regained the shoulder extension and mobility with the use of pressure dressing.

A skeletal traction technique

Utilizing a skeletal traction technique to restore movements in a contracted joint typically requires percutaneous insertion of a Steinman’s pin through the radius for the elbow joint and the tibia for the knee joint. The pin is inserted through both cortices at the junction of proximal two-thirds and the distal third of the radius or the tibia. A contracted joint can be mobilized by continuous and constant ‘pull’ of the long bone utilizing gravitational force generated with 10–15 pounds of weight placed through a pulley device.

For a flexion deformity of the elbow, the patient is placed in a supine position. The pulley traction device will provide a horizontal and then a vertically downward pull (Fig. 56.9).

A weight placed around the ankle with the patient being placed in a prone position, instead of a skeletal traction device, may be used to pull the foreleg to loosen a contracted knee. This technique is especially useful in treating individuals with a limited knee flexion contracture. Traction is continued for a period of time and is repeated several times a day (Fig. 56.10).

Although the morbidities due to infection are uncommon, continuous and constant force of pull can cause break down of the skin typically located in the area across the joint surface. The wound can be temporarily covered with surgical dressing or biological dressing. Closure of the wound is contemplated once the joint contracture is fully corrected.
Management of contractural deformities involving the shoulder (axilla), elbow, hip and knee joints in burned patients

Figure 56.9 A contractural deformity had developed involving the left elbow joint. There were no direct injuries involving the joint. A Steinmann’s pin was inserted through the distal third of the radius for traction. A 500 g weight was used. A full extension of the contracted elbow joint was completed in 3–4 days.

Figure 56.10 A knee contracture developed in an 8-year-old boy due to improper positioning and immobilization of the knee joint. There were no direct injuries involving the knee area. With the patient being placed in a prone position, the ankle was strapped with a 10–15 pound weight. The flexion contracture was relieved in 3 days.

Surgical treatment of a contracted joint
Surgical treatment of a contracted joint is contemplated in individuals where the use of non-surgical treatment is ineffective and where functional integrity of a joint is at jeopardy. Surgical intervention, in this regard, is relatively unusual during the acute phase of recovery. Instead, the reconstruction is delayed until the scar tissue becomes fully ‘matured’, i.e. with flattening and softening of the scar tissue.

Pre-surgical evaluation
The patient is seen and the involved joint is examined before surgery. The following features are assessed:
- The extent of joint contracture is determined and the passive and active range of joint motion is assessed. Radiographic evaluation may be obtained to delineate structural integrity of the joint.
- The magnitude of scarring and scar thickness is assessed. The scar is usually thickest across the joint surface.
・The location and the size of uninjured skin are delineated. The availability of uninjured skin frequently determines the technique of reconstruction. Skin graft and skin flap donor site is also ascertained.
・The point and the axis of joint rotation are located. The line of incisional release is in alignment with the axis of joint movement.

Techniques of joint contracture release
Despite detailed examination before surgery, exact cause of joint stiffness can only be delineated with surgery. In practice, contraction of the scar tissues across the joint structure is the most common cause of contractural joint deformities.

Release of joint contracture by incising the scarred tissue
A contracted joint is freed by making an incision in the scar across the joint surface. The incision is placed in line with the axis of joint rotation. The incision is confined within the width of the scar initially and is lengthened as necessary to achieve the intended release. Prior infiltration of the area with lidocaine containing epinephrine in 1:400,000 concentration is useful in obtaining hemostasis and later pain control. The incision, however, must be made with caution to avoid injuring major vessels and nerves. This is achieved by ‘pushing’ instead of ‘slicing’ motion of a surgical blade to free the scarred tissues. The extent of release is assessed by the improvement of joint motion gained as the scarred tissue is severed.

In rare instances, cicatricial changes could involve the joint capsule. Reconstruction of the capsular structure will be necessary.

The z-plasty technique
A contracted wound is lengthened by interposing two triangular skin flaps mobilized from an unburned area immediately adjacent to the area of release. The lengthening of the wound is maximally attained by interposing two triangular flaps of 60° angle. While the z-plasty technique is an excellent means to ameliorate the problem of wound contracture; it is not possible if the amount of uninjured skin adjacent to the wound is limited.

Wound coverage
There are six basic techniques of wound coverage. Namely:
1. Primary closure of the wound
2. A full-thickness or partial-thickness skin graft
3. An interposition skin flap mobilized from the area adjacent
4. Combination of an interposition skin flap and skin grafting
5. A muscle or skin-muscle flap mobilized from the adjacent area
6. A free skin or skin-muscle flap harvested from a distant site and transferred via a microsurgical technique.

Primary closure of the wound
Wound closure per primum following burn scar excision is difficult if not entirely impossible. Inelasticity of the skin surrounding the wound and an inadequate amount of uninjured skin available for mobilization and closure preclude the use of this method of wound closure. Closure of a resultant wound following release, in practice, would defeat the original objective of contractural reconstruction.

Skin grafting technique
The use of a piece of skin graft, full or partial thickness, to cover a wound is the most fundamental technique of wound coverage that is technically simple with minimal morbidities.

Operative technique
A partial-thickness skin graft of 15/1000th to 20/1000th in thickness is harvested from an unburned area using a dermatome. The scalp, lower abdomen, and the anterior surface of the upper thigh are the common donor sites. A piece of full-thickness skin graft can be harvested from the lower abdomen, above the suprapubic or inguinal area, without leaving unsightly donor site defects. The subdermal fatty tissues are removed but attempts should be made to preserve the subdermal capillary plexus (Fig. 56.11). The donor defect is usually closed primarily.

The graft is cut to fit the defect and the edges are anchored with 3–0 silk sutures. The ends are left sufficiently long to tie over a bolster to immobilize the graft. Several anchoring ‘mattress’ stitches using 4-0 or 5-0 chromic catgut sutures may be placed in the center of the graft to immobilize the skin graft against the base. Hemostasis around the recipient site is essential. Hematoma formed underneath the graft will hinder the ‘take’ of the graft.

After care
The bolster is usually removed in 4–5 days after the procedure. Bodily fluid or blood elements accumulated underneath the graft, i.e. seroma and/or hematoma are evacuated. This is achieved by making a small ‘nick’ in the graft with a pair of surgical scissors. The fluid is ‘rolled’ out with a cotton tip applicator. The joint is immobilized immediately and pressure dressing is used to minimize the consequence of contracture. Physical exercise is resumed 3 weeks after the surgery.

An interposition flap technique
This technique, known by various names such as ¾ z-plasty technique, a ‘banner’ flap interposition technique, etc., is the most useful method of wound coverage following a releasing procedure for a contracted joint. The technique is based upon a principle that an open wound consequential to surgical release may be covered with a skin flap mobilized from an adjacent area. While designing of a flap is technically simple, it requires an area of unburned skin adjacent to the released wound.

Operative technique
A triangular skin flap is designed in an unburned area adjacent to the wound following release. A vertical limb of the flap begun at the end of released wound edge is set at a 90° angle to the end of the wound. The limb length is equal to
Management of contractural deformities involving the shoulder (axilla), elbow, hip and knee joints in burned patients

The use of a free flap or muscle flap
Although most of the major joint deformities could be reconstructed with the techniques described, the use of microsurgical technique may be occasionally necessary to transfer a segment of soft tissue from a distant donor site.

Of the varieties of flap available, we prefer the use of an anterior lateral thigh (ALT) perforator flap. The vascular supplies to the skin around the anterior section of the upper thigh are consistent. Preparation of a flap is therefore, technically simple. While the morbidities attributable to flap harvest are generally minimal, the flap can be bulky; secondary procedures to thin down a flap are often necessary (Fig. 56.16). Instead, a muscle flap may be used. The tissue bulkiness may be curtailed by using a piece of skin graft (Fig. 56.17).

Summary
Contractural deformities of the shoulder (axilla), elbow, hip and knee joints are not uncommon sequelae of burn injuries. Although the injury involving the limbs and the joint structures could account for the deformities encountered, lack of proper positioning and inadequate physical exercise while recovering from the injuries could further contribute to genesis of the problems.

The use of brace, splint and pressure dressing is important in minimizing such an undesirable consequence of burn injuries. The treatment for an established joint deformity, on the other hand, requires surgical release of the contracted skin and scars. Various methods of reconstruction have been...
Figure 56.12. (a) An interpositional skin flap technique, i.e., a modified z-plasty technique as useful in reconstructing a flexion deformity around the joint, as seen in this 12-year-old individual who had sustained burn injuries around the right axilla. (b) An incision made across the area with maximal contraction resulted in a large tissue gap of 12 cm × 5–6 cm. (c) A triangular skin + fascia flap was mobilized from the lateral upper chest area and was rotated 90° posteriorward to cover the wound. (d) The donor site was closed primarily. (e) The appearance of the wound 2 years following the reconstruction.
Figure 56.13  (a) An interpositional skin flap technique of wound closure may be modified as in this 5-year-old girl who had sustained burns around the right axilla that caused contracture of the axillary joint. (b) The skin defect was so extensive that it could not be covered completely with a single flap. (c) The uninjured skin raised as a flap was transferred to the middle of the wound leaving the areas proximal and distal to the flap to be covered with skin grafts. (d) The appearance of the wound 10 days following the surgery. (e) The appearance of the wound 10 years after the surgery. The flap placed in the middle of the wound had increased in size because of body growth and stretching of the scar tissues.
Figure 56.14 (a) Flexion of the knee was limited because of tight scars around the patella. (b) An incisional release of the tight area across the patella provided the relief of knee contracture. However, it resulted in an open wound of 4–5 cm in size. (c) A medial segment of the soleus muscle was used to cover the defect. (d) The appearance of the knee area three months following the procedure.

Figure 56.15 (a) A moderate degree of flexion contracture involving the right ankle of a 6-year-old boy required release. A triangularly shaped skin + fascia flap was marked over the medial side of the lower leg. (b) A fasciocutaneous flap was fabricated and was rotated 90° anteriorly to cover a tissue defect consequential to contractual release.
Figure 56.16, cont’d (c) The closure of flap donor site required the use of a skin graft. Healing was uneventful. (d) The appearance of right ankle area 18 months following the surgery.

Figure 56.16 (a) An ALT perforator flap was used to reconstruct an ankle contracture deformity. (b) While wound coverage was achieved, the tissue was noted to be bulky, requiring secondary debulking procedures.
described to manage the problems encountered. Attempts have been made to outline the approach of managing contractural deformities involving the shoulder (axilla), elbow, hip and the knee joints.

**Further reading**


**Figure 56.17** (a) The patient had sustained electrical burns resulting in tissue loss over the right heel area. (b) The wound debridement resulted in a large soft tissue deficit exposing the Achilles tendon. A muscle flap was transferred via microsurgical means to cover the wound. The muscle was covered with a piece of skin graft. (c) Healing was uneventful.

Access the complete reference list online at [http://www.expertconsult.com](http://www.expertconsult.com)
References

11. Mardini S, Tsai FC, Yang JY. Double free flaps harvested from one or two donor sites for one or two-staged burn reconstruction: models of sequential-link and independent-link microanastomoses. Burns. 2004;30:729-738.
Introduction

The human hand is not only an organ to handle tools but also the apparatus to express emotion. Although it accounts for only 2.5–3% of the total body surface area, a hand can become involved in up to 80% of the treated burn injuries. A hand may be burned as an isolated injury, or in conjunction with other body areas. It is rarely spared from injuries if burns involved >60% TBSA. Hand burns occur more frequently at the workplace and are more likely to be flame burns or electrical burns. Scalds, explosions or open flames are the likely causes of injuries occurred at home and contact burns to the hand and scald injuries are common in small children.

Functional recovery of an injured hand, in short, depends upon early stable wound coverage, an adaptable skeletal framework, movements and strength of musculotendinous structures restored while the magnitude of original injuries governs functional impediment; loss of the thumb, for instance, accounts for a 50% function loss of the whole hand.

Management of a burned hand

Initial care of a burned hand

Cooling the burned hand, an effective means to provide pain relief and the possible curbing of further tissue damage, is instituted on-site soon after the accident. The injured hand is submerged in cool running water, if not iced, and is continued until a definitive therapy can be rendered. For chemical burns, the injured site is continuously irrigated with cool water if not iced. It is continued until the wound surface pH value, if the measurement is possible, returns to near neutral.

Restoration of hand function is the ultimate objective in managing the injured hand. Treatment follows the principles that would prevent additional tissue damage and provide quick recovery and restoration of hand function. Delayed or ‘conservative’ burn wound treatment inevitably leads to further wound complication as it could involve tendinous structures as well as the underlying bony skeleton, the
features which could indicate a poor prognosis for the victims. Surgical intervention is contemplated in all hand burns unless the magnitude of injuries are obviously and definitely superficial.

Escharotomies are carried out either at bed side using an electrical cautery or a cold knife once the vascular status of the involved limb is judged to be compromised. Incisions are made over the medial and the lateral mid-axial lines through the skin down to the muscle layers. The line of release extends both caudad and cephalad beyond the margin of tissue swelling to assure complete release. The incisions on fingers are made along the mid-lateral line just dorsal to the digital neurovascular bundle that may include the Cleland’s. A single incision is made in the radial side of the thumb and the ulnar side for the fingers. Releasing incisions may be extended into the web spaces to assure the integrity of vascular supplies to the intrinsic musculatures of the hand. Incisional releases may be carried out to involve the forearm muscle compartment and the carpal as well as the Guyon canals in electrical burns (Fig. 57.2).

The wounds following decompressive maneuvers are covered with cadaveric skin graft or non-adhesive dressing impregnated with antimicrobial ointment. Continuous elevation of the injured limb is important to curtail

Figure 57.1 (a) A hand that has sustained superficial burns. (b) Pallor mixed with erythematous changes, i.e. mottling, noted in a hand that has sustained flame burns. (c) Findings of skin anesthesia and vessel thrombosis suggest full-thickness skin injuries. (d) Carbonization suggests a complete destruction of the structures.
Care of a burned hand and reconstruction of the deformities

Wound coverage. The resultant wound, with fully vascularized dermal template in place, is covered with a partial-thickness skin graft. Similarly, Aldoderm®, an inert cadaveric dermis, may be used.

The depth of burn wound that involves the palm, in most instances, is superficial, as it is protected by the thick epidermal layer of the palmar skin. The recovery is consequently much quicker and less eventful in comparison with an open wound of the dorsum of the hand. A conservative regimen of treatment when and if used to manage an open wound involving the dorsum of the hand results in a much longer time to heal than an injury that involves the palmar surface. The use of full-thickness skin grafting appears to provide excellent results but may be limited to wounds of a small area. On the other hand, the efficacy of FTSG as reported by others, could not be ascertained.

Finger joints, especially over the dorsum, tend to become exposed because of thinness of the skin and high vulnerability to injury. In order to minimize boutonnière deformities, the DIP and PIP joints are maintained at full extension with the Kirschner wires placed intramedullarily for a period of time. The use of skin flaps will be necessary in instances where the joint, the tendinous as well as neurovascular structures become completely devoid of soft tissue coverage. The results with the use of skin flap, especially mobilized from a distant site, on the other hand, are not entirely satisfactory because of the thickness of skin over the joint structures.

After care

The care of a burned hand soon after the treatment consists of hand elevation to minimize tissue swelling and pain. Persistent edematous swelling of the hand is believed to result in a loss of joint mobility and dorsal skin laxity impairing joint movements, especially at the metatarsophalangeal (MTP) joints level. A protective splint that will maintain MCP joint flexed at 70° and the PIP, as well as DIP joints kept at full extension, with the hand in a position of ‘safety’, is used (Fig. 57.3). Otherwise, a contracted palm, stiff and edematous changes. The wounds are managed during the following 10–14 days by performing additional wound debriddment if indicated, and wound closure by means of skin grafting and/or skin flap techniques.

**Definitive surgical care of burned hand wound**

Any wounds judged to be unequivocally third-degree burns, or those showing no progressive signs of healing, require surgical intervention. The procedure may be delayed for victims with extensive injuries; surgical care of other vital sites takes place ahead of the hand wound coverage, even though such a delay in caring for hand wounds often results in deformities caused by thickening of the scar and contraction of the joints. Diligent exercise and physiotherapy could minimize the undesirable consequences.

Tangential excision of the burn wound with immediate skin grafting of the resultant wound is the ideal approach in managing the burned hand. The definitive procedure of wound coverage may be delayed in instances where the exact depth of injuries, especially in electrical injuries and crush injuries, or the exact magnitude, could not be ascertained with assurance. A second-look procedure is needed to assess the wound; additional removal of devitalized tissues, in practice, is often necessary.

The use of a sheet of skin graft, partial in thickness, is preferred to cover an open wound of the dorsum of the hand because of a better achievable outcome, i.e. pliable scars and good color match. However, the use of a meshed skin graft in 1:1 or 1.5:1 in ratio, a minimally meshed graft, has been reported to provide a similarly good outcome. In addition, artificial dermal regeneration template materials such as Integra®, Pelnac® and Terudermis®, may be used for initial wound coverage. The resultant wound, with fully vascularized dermal template in place, is covered with a partial-thickness skin graft. Similarly, Aldoderm®, an inert cadaveric dermis, may be used.

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Finger joints, especially over the dorsum, tend to become exposed because of thinness of the skin and high vulnerability to injury. In order to minimize boutonnière deformities, the DIP and PIP joints are maintained at full extension with the Kirschner wires placed intramedullarily for a period of time. The use of skin flaps will be necessary in instances where the joint, the tendinous as well as neurovascular structures become completely devoid of soft tissue coverage. The results with the use of skin flap, especially mobilized from a distant site, on the other hand, are not entirely satisfactory because of the thickness of skin over the joint structures.

**Figure 57.2** Release of the carpal tunnel as well as the Guyon’s canal may be necessary.

**Figure 57.3** A hand splint that will maintain the DIP-PIP joints at full extension, MCP joints at 70° while keeping the wrist joint at 30° extension, i.e. the hand in a position of ‘safety’.
contracted PIP and extended DIP joints, the classic boutonnière’s deformity, is a common sequela noted in a hand improperly positioned. A temporary pre-manufactured splint can be placed on the patient with the initial dressing application and continued after the initial assessment. A customized hand splint should be used to support hand position over 2–3 days post-injury since a pre-manufactured splint may cause unwanted pressure points in the hand. Removal of the splints for range of motion exercise at least twice a day is recommended. The hand is kept in a protective posture and elevated for 4–5 days following surgical treatment.

Although a partial-thickness skin graft is the most common material used for wound coverage and wound resurfacing, contraction of a graft site is common. Splinting of the hand and fingers in a protective configuration is preferred; the patients would assume the usual posture once the post-surgical exercise regimen is completed. Pressure garments are used often for patients soon after the wound closure to control excess swelling and scar formation. Wrapping the injured fingers with Coban is also used to control tissue edema.

Management of established burned hand deformities

General principles

Although the primary objective of reconstructing burned hand deformities is to restore hand function, recurrent problems of joint contractures and stiffness can ensue, despite early wound coverage, continuous use of hand splinting and physiotherapy. This is particularly true if the hand injury was not the only site of burns, when reconstructive measures are delayed or deferred for individuals with extensive burns or when reconstruction of structural deformities such as eyelids, mouth and neck takes precedence over hand deformities. The procedures may be modified because of the paucity of donor tissues that could be used for reconstruction.

Two years of waiting following recovery from the injury has been the precept and the practice in hand reconstruction followed for the past 50 years. An early reconstructive endeavor has been advocated in recent years, especially for those who have shown full recovery from the injury and whose deformities are limited to the hand. It is important for both the surgeon and the patient to have a clear understanding of therapeutic objectives, technical details and consequences one may encounter while recovering from the procedures. It is important to inform the patient of the truth about the procedures and for the surgeon to learn if his/her patient has a realistic expectation about the outcome of reconstruction.

Reconstructive methods

The following are the methods used most commonly for correcting hand deformities:

1. **Primary closure of the wound:** This technique is used to close a wound resulting from the excision of scar tissues.

2. **Grafting of a wound:** In instances where primary coaptation of wound edges is not possible because of extensive tissue deficit, that is, primary wound closure is not possible, a skin graft may be harvested from a distant site to cover the wound. Skin grafts are classified as split thickness or full-thickness. A piece of skin that contains all layers of common integument is called a full-thickness skin graft (FTSG), while one with only the epidermis and the outer layer of the dermis is termed a partial/split-thickness skin graft (STSG). It is said that functional and cosmetic outcome of an open wound grafted with a piece of full-thickness skin graft is better than one grafted with a partial-thickness skin graft. The outcome, in practice, is not predictable. Grafting is, furthermore, contraindicated if a wound bed lacks vascular supplies and structures such as tendons, bones and neurovascular bundles are devoid of soft tissues (Fig. 57.4).

3. **Skin flaps:** A segment of skin with its vascular supplies left intact in the subcutaneous layer of the skin, is fashioned to form a pedicle. When a skin flap is transferred to make up a tissue deficit caused by scar excision and/or release, a resultant wound of flap fabrication is closed in most instances primarily. In rare occasion, a piece of skin graft is used for wound closure.

4. **Z-plasty and modified z-plasty techniques:** A scarred area with tight scar bands mostly in one direction is released by interposing two triangular skin flaps. A contracted scar is released and the resultant wound is closed by two flaps mobilized from the sides (Fig. 57.5).

5. **Musculocutaneous (MC) flap and fasciocutaneous (FC) flap:** The vascular supplies to the skin are enhanced by incorporating either the muscle or muscular fascia underneath. The flap is mobilized to make up a defect resulting from scar release (Fig. 57.6).

6. **Other techniques of flap fabrication:** There are several techniques used to fabricate a composite skin flap for burned hand deformity reconstruction. They include an arterialized skin flap, an axial flap, and distant composite skin flaps. The design of skin flap, harvesting and transfer are technically cumbersome. The bulkiness of tissues transferred, furthermore, often restricts the joint movements.

Reconstruction of phalangeal deformities

**Flexion contractural deformities**

Flexion contracture of an involved finger and hand formed over the joint surface is attributable to scar contraction and aided by contraction of the hand flexor musculatures. Release of a contracted joint may be achieved by z-plasty or by incising the contracted scar. The resultant wound is, if feasible, repaired by utilizing an interpositional skin flap technique, i.e. $\frac{3}{4}$-z-plasty. Skin grafting will be the option available for wound closure if the tissue around the operative site is not suitable for flap fabrication. On rare occasions, complete relief of contracture may require release of tight tendinous structures and neurovascular bundles as well as the joint structures. The use of a distant skin flap technique, i.e. a
Figure 57.4  (a) The wound defects around the palmar surface and the thumb base resulted from release of the contracture. (b) A partial-thickness skin graft of 16/1000th of an inch in thickness was used to cover the wound. The fingers were maintained at angles with K-wires. (c) The appearance of the operative site 18 months later.

Figure 57.5  (a) A line drawn indicated the line of release and fabrication of a triangular skin flap. (b) A triangular skin flap was elevated, i.e. a modified z-plasty.
Figure 57.5, cont’d  (c) The flap was transposed and the wound was closed primarily. (d) The appearance of the left hand 2 years following release.

Figure 57.6 (a–e) A distally-based fasciocutaneous flap was harvested from the radial side of the distal forearm to cover a defect resulting from wrist flexion contracture release. The flap donor site was covered with a piece of partial-thickness skin graft of 14/1000th of an inch in thickness.
The wrist joint became fully extended with the releasing procedures.

Figure 57.6, cont'd
cross-finger flap technique, will be necessary to cover the exposed tendons, digital neurovascular bundles and the joint. The use of an axial lateral digital flap, a neurovascular island flap, may be necessary for a finger that has lost sensory supply to restore not only the soft tissue deficit but also the sensory supply. The finger is maintained at full extension by inserting an intramedullary Kirschner wire or a wire placed underneath the flexor tendon sheath to maintain finger position for a period of 10–14 days (Fig. 57.7).

**Extension contractural deformities**

An isolated extension contracture of the fingers that involved the PIP and MCP joints is attributable to scarring formed over the area of these joints. In practice, the deformities usually extend distally as well as proximally to include the entire digit and the wrist joint surface. Although the use of hand and finger splints could prevent the genesis of deformities, the task of splinting injured joints soon after the injury is difficult and true efficacy is difficult to ascertain. Surgical intervention may be necessary to correct an established deformity (Fig. 57.8).

The contracture is released by incising the scar over the deformed finger joint(s), i.e. the deformed DIP, PIP and the MCP joints. Inserting a K-wire from the proximal phalanx through the MCP joint into the metacarpal bone while the MCP joint is flexed at 90° will maintain the PIP and DIP joints flexed. While a transpositional skin flap, i.e. $\frac{1}{2}$-z-plasty technique, may be used to cover the wound defect over the finger joint defect, STSG is needed for the wound coverage.
over the MCP joint. While a distant skin flap may appear beneficial, its bulkiness inevitably limits the finger movements necessitating secondary procedures such as excision of fatty tissues and re-grafting or defatting maneuvers.

Web space contracture

Narrowing of the web space, i.e. cicatricial syndactyly, is a common sequela of burn hands. Although numerous varieties of techniques have been described for correction, placement of unburned tissues in the dorsal aspect of the web is the key of reconstruction. This is most easily achieved by use of a triangular skin flap mobilized from either the radial or ulnar side of the fingers, rotated into a contracted web space, especially to the second, third and the fourth, to achieve the release. No additional physiotherapy is necessary. Daily unrestricted use of the hand will restore the web space and the movements of the fingers (Fig. 57.9).

The first web space contracture

The first web space contracture, i.e. the widest hand web space, between the thumb and the index finger, is similarly quite common. While conventional techniques such as z-plasty, skin grafting, etc. may be used to reconstruct the deformity, the technique consisting of combining two
Figure 57.9 (a) Contracture involving the right second web space. A \( \frac{1}{2} \)-z-plasty, with its triangular skin flap donor site on the radial side of the middle finger proximal phalanx. (b) The flap was rotated dorsally and the wound was closed primarily. (c) The appearance of the operative site 3 years following the release. Healing was uneventful.

z-plasty and one central Y-to-V plasty, commonly known as the trident flap technique, the 'jumping-man' technique, seagull-wing flap technique or five-flap technique, is a simple and effective approach in providing the release. Approximately 30–40% increase in the web space is obtainable with this technique of release (Fig. 57.10).

Reconstruction of a deformed thumb

It is estimated that 45–50% of hand functions are lost with the loss of a thumb. A patient can regain the basic hand function of pinching with partial grasping of an object if a digital knob can be restored. Although techniques of thumb elongation such as bone-grafting, skeletal traction and toe-to-thumb transplantation have been advocated, they are unsuitable for thumb replacement in a burned hand, especially in children. Paucity of donor sites, inelastic skin unyielding to traction, a high rate of technical failure and the morbidities inherent in these regimens are the factors that account for the difficulties noted in practice.

Digital stacking technique of thumb reconstruction

The technique of stacking a remnant of the second digit to the first to elongate the thumb remnant has been in use in Galveston for the past 30 years. The remnant of the second digit is transected at the mid-carpal level. The distal segment is fabricated as a composite tissue graft with its neurovascular bundle kept intact. The bony end is ‘stacked’ upon the distal end of the thumb remnant. Resection of the second digit remnant in practice creates a deeper first web space while elongating the thumb remnant. The procedure, though technically cumbersome, carries low morbidities and could be performed in an outpatient surgical facility (Fig. 57.11).

Reconstruction of deformities involving the dorsum of the hand

Incisinal release of contracted scar tissues affecting the joint movement and covering of the resultant wound with skin grafting or skin flap techniques is the basic principle used for deformity reconstruction. Freeing of the periarticular structures of the MCP, PIP and DIP joints is sometimes necessary. K-wire fixation of the released joint at 90° for a period of 10–12 days following surgical release is necessary.

The technique of skin grafting is the most common method used to cover an open wound resulting from scar tissue removal or contractural release. A distant skin flap may appear to circumvent the undesirable sequelae of skin grafting technique, i.e. scar hypertrophy and scar contracture, but the bulkiness of tissues used inevitably interferes with finger and hand motion. Repeated procedures are usually needed to thin down flaps to gain joint mobility.

Electrical injuries involving the upper limb

The exact mode of tissue injuries caused by electricity remains incompletely understood. Although cell damage directly caused by electrical current may account for some of the
injuries noted, most of the tissue damage is believed to be due to heat generated by electrical current flowing through the tissues with extreme resistance; it follows Ohm’s Law and Joule’s Law of electricity, respectively, i.e. Current (I) = Voltage (E) ÷ Resistance (R); Power (J) = (Current) I² × Resistance (R).

The upper limb is a common site of injuries sustained at work sites for adults and while playing in areas with high voltage electrical lines for children. Although the precise mode of injuries is unclear, the affected area often includes the entire extremity, i.e. the shoulder to the hand. The damaged structures noted are mostly the muscles in the arm, neurovascular bundles, and the skin over a contact point in the forearm and in the hand. The magnitude of structural damage observed is believed to be related to the long bones. The heat generated in the bone with the flow of electricity is the major culprit responsible for muscle and neurovascular bundle destruction. Electrical burns of the upper extremity, unlike other thermal injuries, are deep third-degree burns if not a ‘fourth’-degree injury. The regimen for electrical burns of the upper extremity and the outcome of treatment differ from thermal injuries involving other organs.

The classification of upper limb electrical burns

The gross appearance of the injured site, the operative findings, the magnitude of tissue damage, and the location of electrical contact play an important role in governing the healing processes and the outcome of treatment rendered. The wounds are classified into four categories: the location of injuries; the magnitude of arm involvement; the magnitude of impairment and the involvement of

Figure 57.10 (a) A moderate degree of web space contraction developed in the first web space 9 months following the accident. Skin markings were for a trident technique of contracture release, alias a 5-flaps release technique, a jumping-man releasing technique. (b) A trident technique is composed of z-plasties and Y-to-V releasing technique. (c) An increase of 30–50% in arc length with the multi-flap technique. (d) The appearance of released web space 3 years later.
neurovascular structures are the key features used for the classification.

Type I: A wound which involves the superficial digital flexor musculatures but spares the deep digital flexors, with minimal or no ulnar nerve impediment, and a grossly normal vascular supply to the hand (Fig. 57.12a).

Type II: A wound which involves the entire flexor surface but a portion of the lateral side of the forearm; extensive but moderate damage involving the superficial and deep digital flexor musculatures respectively; pronator muscle damage; no or minimal median nerve injury but a moderate degree of ulnar neurosensory impediment; variable circulatory disturbances but improving with wound decompensation (Fig. 57.12b).

Type III: A wound with circumferential burns; gross impairment of both superficial and deep flexor musculatures; loss of pronator musculature movement; a moderate degree of both median and ulnar nerve sensory impediment; gross circulatory impairment to the hand; rapid wound deterioration (Fig. 57.12c).

Type IV: A wound with circumferential arm involvement with accompanied hand involvement; hand vascular circulation is nil (Fig. 57.12d).

**Diagnosis of arterial injuries secondary to upper limb electrical injuries**

The probability of tissue necrosis caused by high voltage electricity soon after the accident may vary between 10% and 60%. The incidence of extremity amputation among those diagnosed to have a Type III injury can be in the range 25–80%, attributable to vascular injuries. Assessing and delineation of vascular injuries for patients with electrical burns
Decompressive escharotomy and fasciotomy

Tissue destruction that particularly involves deep structures inevitably leads to interstitial extravasation of tissue fluid and the consequences of tissue swelling. Decompression of tight tissue compartment by incising the skin tightened because of burns and/or loss of elasticity is essential to restore both arterial and venous flow. The release of muscle compartments is furthermore, necessary in instances where the muscle compartments are swollen. Without releasing procedures, ischemia can cause the demise of other structures such as nerves. Necrotic muscles should be removed as soon as possible to prevent systemic toxicity.

Early debridement

It is appropriate for patients whose general condition is stable and without obvious limb vascular impediment to undergo wound debridement procedures from 1–2 days following injury. The procedures should include removal of all devitalized tissues, ascertaining the viability of digital musculatures, pronator and supinator muscles. All efforts are made to preserve all forearm nerve structures, unless nerve viability is clearly lost. Vascular continuity, in instances

The management of limb electrical burns

Patients sustaining electrical burns of the upper limb are not infrequently found to suffer other injuries. Surgical debridement of burn wounds is planned once the condition of the burn victims is stabilized.
where the patency of both radial and ulnar arteries is compromised, may be restored by means of a vein-grafting technique. The use of anticoagulants, i.e. low molecular Dextran or heparin, will be necessary for a period of time to minimize the recurrence of vascular thrombosis.

**Wound management**

The magnitude of tissue damage in high voltage electrical burns is often so extensive that it involves muscles and blood vessels. Limb removal, in such instances, is the sole treatment option left in order to minimize lethal consequences of the injuries. The conventional regimen of a split-thickness skin graft for wound coverage is generally not feasible because of wound beds devoid of vascular supplies and/or tissue loss (Fig. 57.13). Instead, a skin flap mobilized from an area adjacent or distant is used for not only the wound coverage but also for nurturing the nerves. Because of the injuries, an axial skin flap fabricated in the forearm, i.e. a radial forearm flap, abdominal flap, musculocutaneous flap, or free flap/perforator flap transferred via microsurgical means, is preferred (Fig. 57.14).

**Functional reconstruction of limb deformities**

Loss of limb function is not uncommon following electrical injuries. Insufficient vascular supply, extensive nerve and musculotendinous damages, loss of muscle functions involving the shoulder girdle and the forearm, as well as loss of intrinsic musculatures of the hand are the factors responsible for the difficulties encountered.

Maintaining joint mobility and replacement of lost soft tissue in the forearm and the hand are two key features necessary for functional reconstruction. Patients are encouraged to follow a physical exercise regimen to maintain joint mobility, particularly of the finger joints. Successful nerve grafting for sensory restoration and/or tendon transferring procedures for digital movements requires prior skin flap procedures mobilized from an adjacent area or a free flap transferred via microsurgical means to restore the soft tissue coverage of the injured site. Restoration of the tendon activities is contemplated once these procedures are completed. The rehabilitative regimen in general takes minimally 2–3 years to complete.

**Comments**

Effective hand reconstructive procedures rely not only on the surgeon’s surgical judgment and skill but also on patients’ compliance with rehabilitative treatment following the operation. Although sensitivity to the needs of patients with burned hand deformity is not infrequently overlooked in the presence of other problems, the support for this group of patients cannot be minimized. Care for injured hands must be instituted as soon as possible and should continue for a

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**Figure 57.13** (a,b) Once the wounds are judged to be ‘clean’, a skin flap mobilized locally or from a distant site is used to cover the wound. An 18-year-old man sustained high-voltage electrical injury. The exit wound located in the forearm was covered with a flap mobilized from the lower abdomen. (c) An elbow wound was covered with a local skin flap.
long period of time. The task of reconstructing a deformed hand if its needs are neglected during the initial phase of injury treatment is quite difficult. The preparation of an injured patient for his/her return to society can be hampered by delay in restoring hand deformities and functions. A well-planned regimen is essential for an early restoration of these individuals to their former lives.

**Summary**

Reconstruction of a burned hand deformity begins with care at the time of hospital admission. Early surgical attention, with control of edema and proper hand positioning is essential for a satisfactory outcome of treatment. A satisfactory outcome is, however, is governed by a treatment plan organized with inputs from all people concerned. A team approach is essential for handling the problems of the burned hand.

**Further reading**


**Figure 57.14** (a-c) A composite skin flap, i.e. an ALT flap, harvested from the anterior thigh area, may be used via microsurgical means to cover an extensive wound.
References

Introduction

Burns of the perineal area are quite uncommon even though the lower trunk and the lower extremities are vulnerable to burn injury. Alghanem et al. reported the incidence of perineal burns to be about 12/1000 admissions, more than 20 years ago. While the occurrence of perineal burns has remained fairly consistent at 1.0–1.5% at our hospital, 35 children underwent genito-perineal reconstruction, out of 1133 presentations between 2002 and 2009. An increase in the number of children who have survived extensive burns of a total body surface area (TBSA) involvement of more than 40%, could account for the increase in the number of children requiring secondary reconstruction.

Management of burns of the perineum during acute phase of injury

A conservative approach is used to manage perineal burns. The perineal area is cleansed daily and the wound is covered with antibiotic dressing. The urethral tract is stented with an indwelling Foley catheter as it is also used to decompress the urinary bladder. The perineal area is neither splinted nor braced. The thighs are maintained at 15 degrees of abduction using a wedge splint to minimize contracture of the hip joint. The extent of burns is allowed to demarcate in time and the wound is often left to heal spontaneously. A non-healing wound is managed with the use of a partial-thickness or a full-thickness skin graft. On rare occasions, a skin flap may be mobilized from the area adjacent to reconstruct defects consequential to full thickness skin loss of the penis and the scrotum.

Other possible problems seen with burns of the perineum during the acute phase of injury, include necrosis of the penile shaft, testicular necrosis, urethral stricture, and rectal prolapse. Although the Shriners Burns Hospital and the University of Texas Medical Branch Hospitals in Galveston, Texas, have adopted a relatively conservative regimen to manage perineal burns, the approach of wound care is in practice, quite variable, and the exact regimen is often modified depending upon the structures involved.

Burns of the penis

Burn injuries limited to the penis, though possible, are quite rare (Fig. 58.1). Concomitant involvement of the penis with burn injuries of the lower trunk and the perineal area, on the other hand, is quite common. The initial regimen of patient management, in addition to resuscitative measures, consists of wound care and urethral stenting. An indwelling Foley catheter of appropriate size is inserted into the urinary bladder to stent the urethral tract and at the same time, to monitor the urinary output. The catheter is removed once the swelling around the penile shaft has subsided and status of the wound becomes delineated. No attempt is made to debride the burned wound early. Instead, it is allowed to demarcate and is often allowed to heal spontaneously.

Loss of skin over the penile shaft and the scrotum

Spontaneous healing is expected in most instances with burn injuries of the penis and scrotum, since full thickness injury of the penile and scrotal skin is relatively uncommon. Skin grafting, a partial thickness or a full thickness graft could be used to cover the wound if healing is delayed (Fig. 58.2).

In rare instances, a skin flap may be needed to reconstruct structures such as urethral tract and/or scrotal sac because of loss of skin coverage. An inguinopudendal skin flap mobilized from the inguinal crease area may be used if the use of skin graft is judged not to be feasible. The use of muscle-skin flap such as a gracilis MC flap is not recommended because of subsequent high tissue temperature evolving in a skin flap that may interfere with spermatogenesis.

Burn wound of labia majora

Isolated burns of the labial structures are rare. Instead, labial burns are often associated with injuries of surrounding areas such as abdomen andinguinal folds. As in the management of burns of male genitalia, the injured areas are allowed to heal spontaneously (Fig. 58.3). Distortion of the labial structures mostly due to contraction of scar tissues in the pubic and inguinal areas is left for later reconstruction.
Perineal wound coverage

An isolated burn injury of the perineal area is extremely rare. On the other hand, the area will become involved if the lower trunk/buttock is injured. The extent of scar contracture varies depending upon the depth of burns. While it may heal spontaneously with minimal scarring, contracture of the perineal area is a common sequela, regardless of methods used to care for the wound (Fig. 58.4). The natural inclination to keep the thighs together and hip adducted during the recovery phase of acute burn injuries seems to aggravate scar contraction.

Anal burns

Burns of the anus are rare, though it could become involved because of extensive burns of the perineum. If the skin injury around the anal opening is full-thickness, the use of a skin flap may be necessary to minimize the consequence of stricture. A skin flap mobilized from the area adjacent will be necessary to graft the perianal area. Wound coverage with a skin graft is technically difficult and will lead to anal stricture because of graft contracture.

Rectal prolapse

Rectal prolapse occurs occasionally in young children with extensive burn injuries with or without perineal involvement. The exact reasons for rectal prolapse occurring in burned infants remain unclear. Redundant rectal mucosa, structural relationship of the rectum to other pelvic organs such as sacrum and coccyx, urinary bladder and uterus, and lack of muscular support provided by the pelvic musculature, anatomical features unique to infants of 1–3 years of age could account for the incident. Sudden increase in intra-abdominal pressure and malnutrition and constipation due to response to the burn injuries could conceivably aggravate the magnitude of the rectal mucosa descending through the anal opening.

Clinically, in addition to eversion of rectal mucosa, the finding of edematous swelling around the buttocks and perianal area is quite common, even though the area is spared of burns. The onset can be quite sudden without any obvious precipitating event. However, grunting or the Valsalva maneuver can precipitate an eversion of the rectal canal through the anal opening.
Management of burn injuries of the perineum

The regimen of treatment consists of rectal padding, and daily cleansing of the perineal and perianal area. A stool softener is added to the dietary regimen to facilitate bowel movement. Spontaneous regression of the prolapse is likely as the nutrition improves and tissue swelling subsides (Fig. 58.5). Surgical intervention, though in most instances unnecessary, is indicated if the prolapse is not readily reducible due to anal sphincteric dysfunction and/or intussusception.4,5

Reconstruction of established deformities of the perineum and the perineal structures

Cicatricial contracture around the perineum is the most common sequela of perineal burns.1,6 The magnitude of contracture is, furthermore, exaggerated because of contraction of burn scars in the inguinal crease and inferomedial gluteal folds. Other problems, though relatively uncommon, included complete loss of penis, anal stenosis, and intractable rectal prolapse.

There are numerous methods such as the z-plasty technique, the interpositional skin flap technique, incisional release of scarred tissues closed with local skin flap or skin graft available to reconstruct the deformities. In practice, the technique used to reconstruct perineal and genital deformities varies depending upon the magnitude of scarring around the perineum and the extent of functional impediment encountered.

Reconstruction of penile deformity

The task of assessing the exact extent of penile deformities can be difficult. Distortion of the penile configuration attributable to scar contracture could be due to loss of the skin or a combination of the skin and Buck's fascia. In addition,
The skin defect resulting from incisional release of the scar is covered with a full thickness skin graft if the Buck’s fascia is spared of scar injury. In rare instances with injury that has involved the Buck’s fascia, surgical release of the fascial deformity is necessary. A dermal graft harvested from the lower abdomen may be used to reconstruct burn fascial defect. A skin flap mobilized from the area along the groin crease, as an island skin pedicle flap, may be needed to cover the skin defect.

Complete loss of the penis, though devastating, is extremely rare (Fig. 58.6). Reconstruction of the penis is

**Figure 58.5** (a) The patient was a 2-year-old girl who had sustained 65–70% total body surface burns. (b) Prolapse of the rectum appeared 12 days after the accident. The problem was managed nonsurgically. (c) The prolapse receded spontaneously 2 months later as she recovered from the burn injury.

Engorging the penile shaft is necessary to assess precisely the extent of penile deformity, as the gross appearance of a flaccid penis can be misleading. Artificial penile erection is created under anesthesia by placing a tourniquet at the base of the penis using a piece of $\frac{1}{8}$ inch Penrose drain. Physiologic saline solution is injected into the corpus cavernosum in sufficient amount to induce congestion. The shaft deformity attributable to skin loss and/or fascial loss will be delineated once the corpus becomes engorged.

Scarring in the pubic area and/or the inguinal fold can further exaggerate the extent of penile deformity.
Management of burn injuries of the perineum

Even though contractural deformity is likely to recur, a skin graft can be used to cover the defect.

Reconstruction of labial deformity

An isolated contour deformity of the labia majora is relatively uncommon. On the other hand, scar contracture occurring in the suprapubic and pubic area, as well as the inguinal fold could distort the normal configuration of the labia. Prior surgical release of the contracted scar tissues around the pubic and inguinal fold areas is an essential step in order to determine the extent of labial deformity and the method to reconstruct the deformed labia.

To restore a contour deformity caused by skin and subcutaneous tissue loss, a skin flap may have to be mobilized from the area adjacent. To reconstruct a contour deformity due to parenchymal tissue loss, injection of free fat cells, i.e. lipoinjection, could be useful. To inject free fat cells to augment the labial contour, the cells are aspirated from the lower abdomen using the inner cannula of #14 Intracath® needle attached to a 3 cc syringe. The syringe is moved in a 'back-and-forth' piston-like manner. The fat cells are injected into the labia using the same syringe but connected with a 19 gauze blunt needle.

Reconstruction of scrotal deformities

Full thickness burn injuries of the scrotum often result in scar encasement of testicular structures. Reconstruction requires surgical release of the scarred areas. A thin skin flap such as the inguinopudendal flap or a flap mobilized from the area adjacent is needed to cover the resultant defect. A musculocutaneous flap such as a gracilis MC flap is not suitable for scrotal reconstruction because of the thickness of the flap and possible impeding decrease in spermatogenesis due to high tissue temperatures exerted from the flap. Even though contractural deformity is likely to recur, a skin graft can be used to cover the defect.

Reconstruction of band deformity around the perineum

Scarring and scar contracture of the perineum is a common sequela of perineal burns, especially if it is allowed to heal spontaneously. Although it seldom causes any difficulty at a
spreading of the buttock and is responsible for discomfort with sitting. Although a contracted perineal band may be incised to gain release, the task of closing the resultant wound can be difficult. Recurrence of contracture is a common sequela with the use of skin graft. Instead, a multiple z-plasty technique is a preferred method of reconstruction to release scar bands around the perineum.

Figure 58.7 (a) There are various techniques available to reconstruct a penile shaft. A forearm composite flap, one of the methods currently in use, was chosen to reconstruct a phallic structure for a 51-year-old man who lost his penis because of cancer. (b) As shown in a schematic drawing, a section of the skin with radial artery attached is harvested from the volar surface of the forearm was utilized for penile reconstruction. A tube-inside-the-tube was used to reconstruct the urethral tract. In addition, the pulp from the big toe was also used to reconstruct the glans penis. (c) The tissues were assembled with vessels and nerve structures set for ‘hook up’. (d) The appearance of genitalia before reconstruction. (e) The appearance of reconstructed penis in a 50-year-old man who had lost the penis because of cancer. (a,b,e Courtesy of Dr Kenji Sasaki. Penile reconstruction: combined use of an innervated forearm osteocutaneous flap and big toe pulp. Plast Reconstr Surg 1998; 104:1054–1058 and reprinted with permission.)

young age, the scars around the perineum could eventually interfere with sitting because of tightness or contraction around the buttock. In addition, the patient may encounter difficulty with bowel movement because of gluteal contracture and cicatricial changes involving the anal opening.

The deformity resulting in the perineal area is usually a tight band developed in the suprapubic area, or between the ischial tuberosities. Inelastic scars cause inadequate spreading of the buttock and is responsible for discomfort with sitting.

Although a contracted perineal band may be incised to gain release, the task of closing the resultant wound can be difficult. Recurrence of contracture is a common sequela with the use of skin graft. Instead, a multiple z-plasty technique is a preferred method of reconstruction to release scar bands around the perineum.
Management of burn injuries of the perineum

Figure 58.8 (a) A tight scar band in the perineal area consequential to burn injuries involving the perineum and the lower extremities. (b) Releasing incisions were placed in the areas away from the anal opening to avoid injuring the anal sphincter. A triangular flap was designed in the uninjured area at each end of the scar band. A releasing incision was set perpendicularly to the direction of the scar band. (c) Each triangular flap was rotated 90° to close the open wound resulting from incisional release. (d) Tight bands develop in the perineal area.

The technique of multiple z-plasty

The patient is placed in a lithotomy position. Tightness and scar band can be delineated with abduction of the hip joint (Fig. 58.8a). A line is drawn in the scar band along the horizontal direction of the band. The length of the horizontal line may extend from one side of the scarred area to the other. A triangular flap with its apex at the end of the horizontal line is marked. The angle may vary between 30° and 60° depending upon the uninjured tissues available at both ends of the horizontal line. The length of the limb of each triangle will be the same as the incision made perpendicular to the horizontal line to release the tight band (Fig. 58.8b). Two z-plasties, i.e. two triangular flaps with 30–60° and 90° angle, respectively, are formed as the flaps are raised along the skin markings made. Release of a contracted scar band is achieved by rotating these two flaps at each end (Fig. 58.8c). The release of a tight band across the perineal area was maintained by interposing a segment of soft tissues mobilized. Figure 58.8d shows the appearance of a perineum 4 years following the releasing procedure.

Although the extent of perineal release may be limited because of scarred tissues surrounding the triangular flaps fashioned, the z-plasty technique is useful in changing the pulling direction of scar tissue, thus diminishing tightness around the perineum.

Reconstruction of anal stricture

While burn injuries rarely involve the entire anorectal canal, it is not unusual to involve the perianal skin and the external sphincter ani muscle. Stricture of the anal opening due to scar contracture and the cicatricial involvement of the external sphincter ani muscle are common sequelae. Cicatricial changes around the anal opening can and will interfere with bowel movement.

The treatment requires surgical release of constricted scar bands around the anal opening. An interpositional skin flap fashioned as an island flap or a modified z-plasty with skin flaps mobilized from the area adjacent, is used to make up the tissue defect (Fig. 58.9). The method of using a piece of skin graft to reconstruct the defect is not useful. Application of the graft is difficult and recurrence of stricture is common because of scar contracture.

Reconstruction of rectal prolapse

Although the problem, in most instances, is self-limiting and the prolapse will recede spontaneously as nutritional status of the patient and healing of the burned perineum improves, surgical intervention will be necessary if the rectal prolapse becomes intractable (Fig. 58.10).
Figure 58.9 (a) A 4-year-old boy developed, in addition to a tight scar band across the perineum, anal incontinence because of cicatricial changes that had involved the entire perineal area. (b) A modified multiple z-plasty technique was utilized to reconstruct perineal contracture and anal stenosis. (c) Skin flaps were rotated into the areas to reconstruct the deformity following the surgical release. (d) The appearance of the anal area before release. (e) The appearance of the anal area 9 months following release.
Management of burn injuries of the perineum

Figure 58.10 (a) A 2-year-old boy who had sustained a third-degree scalding burn that mostly involved the lower extremities. He developed rectal prolapse 10 days after the accident. (b) He underwent a rectopexy procedure because of persistent eversion of the rectal mucosa. (c) The patient regained anal continence 6 months after the surgery.

Summary

Burn injuries of the perineum are relatively uncommon. The regimen of treatment during the acute phase of recovery is conservative. The urethral tract is stented with an indwelling Foley catheter and the wound is cleaned daily. Neither a splint nor a brace is used to immobilize the perineal area. The wound is usually left to heal spontaneously. The resultant deformity, with rare exception of total loss of the penis, is limited. Instead, disfigurement of the scrotal/labial contour and/or scar bands around the genitalia are the common complaints presented by the patients.

The approach in reconstructing scarred deformities is centered upon release of tight scar bands around the perineal structures as it interferes with sitting and/or bowel movement. Incisional release and reconstruction utilizing a z-plasty technique or an interpositional skin flap technique is effective in correcting the deformities.

Further reading


Access the complete reference list online at http://www.expertconsult.com
References

Reconstruction of burn deformities of the lower extremity
Jui-Yung Yang, Ted Huang

Introduction

Although the exact incidence remains undefined, the likelihood of lower extremity burns is strictly related to the magnitude of injury. The management of lower limb burns is essentially identical to the regimen used for other bodily sites. That is, the principle of debridement and wound coverage is followed.

Individuals with complete wound coverage may have survived the injury. True survivors are, however, those who can ambulate at the time of discharge, as burn victims’ successful re-entry to the society is enhanced by the success in restoring limb configuration to regain walking posture, and efforts are aimed to restore weight bearing and joint movement.

Reconstruction of knee, ankle and foot deformities

General principles

Releasing contracted joints to restore the usefulness of the foot is the fundamental approach in reconstruction. The resultant tissue defect is covered with skin grafts and/or skin flaps. A Kirschner’s wire of 0.025–0.035 inch in size for small joints and a Steinmann pin of 0.045 inch or larger caliber for a large joint is used for joint immobilization and structural alignment. The position of released joint structures is maintained for a period of 10–14 days. The pins and wires are removed and external appliances or shoes are used to maintain the foot position. The techniques of skin grafting and/or skin flap wound coverage may be plagued with problems of graft and flap loss.

Scar deformities involving the knee joint, dorsum of the foot and the ankle

Hypertrophic scar deformities

In addition to unsightliness, thickened scars can limit joint movements. While symptomatic and unsightly scars can be partially or completely removed surgically, non-surgical regimens designed to provide proper joint alignment may be attained with the use of splinting and scar compression; a knee splint and a high-top shoe, for example, are the most common tools used.

Contractural deformities involving the toes

An extension deformity of the toes at the metatarsophalangeal (MTP) joint level with or without associated dorsiflexion contracture of the ankle is common if the dorsum of the foot and the ankle are involved.

Reconstruction of the dorsally contracted toes

Contracted toes are released by incising the scar at the level of metatarsophalangeal (MTP) joint and/or proximal interphalangeal (PIP) joint. Release of the scar tissues at the web space is usually delayed to minimize morbidities associated with aberrant wound healing.

In children with recent onset of toe extension contracture, surgical manipulation of the volar plate of the MTP joint capsule is usually unnecessary. A Kirschner’s wire of 0.020–0.035 inch size is inserted through the proximal phalanx to keep the digit in full extension while maintaining the MTPJ in 45–60° plantar flexion. The wires are removed 10–14 days later, once the take of skin graft or flap is established (Fig. 59.1).

While seldom indicated in children, joint capsuloplasty that involves the volar plate of the MTP joint may be necessary in adults or in a joint that has subluxed for a long period of time. Mere release and skin graft/flap coverage of the wound over the joint structures may not restore joint alignment.

In order to minimize recurrent contracture of the toe joints commonly associated with the use of skin grafting technique, a skin flap mobilized from the area adjacent may be used, particularly in instances where the joint structure is exposed. A ⅓ z-plasty technique is useful in achieving coverage of the joint structures and the wound defect (Fig. 59.2).

Contractural deformities of the anterior ankle

Tightness of the ankle joint with a dorsiflexion of the foot is a common consequence of burn injury that is limited to the anterior surface of the ankle. As in other deformities noted in the foot, improper splinting of the foot and the ankle joint, plus scar contracture, are the probable cause...
Instead, the technique to fabricate a paratenon cutaneous flap may be used. The technique of paratenon cutaneous (PC) z-plasty, a variant of paratenon cutaneous z-plasty technique, is useful for instances with extensive scarring with an uninjured skin available for flap fabrication. A right-angled triangular skin flap is marked with its cathetus perpendicular to the line of scar release. The paratenon is included for flap fabrication. The flap is rotated 90° to fill the defect resulting from release (Fig. 59.3).

Scar deformities involving the sole of the foot

Plantar flexion of the toes at all joint levels, i.e. the clawing toe deformity, is the common deformity encountered in instances where the dorsal surface of the toes is spared of injuries. Plantar flexion of the toes compounded by contraction of the scar formed in the area is the probable cause of this deformity.
Figure 59.2 (a) A skin marking indicated the incision line required to release a contracted right fifth MTP joint. A triangular skin marking indicated the skin flap. (b) A distally-based flap was elevated with the underlying fascial layer attached. (c) The flap was rotated medially to cover the wound resulting from contractural release. (d) The wound edges were closed.
Figure 59.3 (a) Anterior surface of the left ankle showed the formation of moderately hypertrophic scar limiting ankle movement. (b) A skin marking indicated a line of contractural release over the ankle joint; a triangular skin drawing marked a skin flap with underlying fascial and paratenon structures attached. (c) The fascio-paratenon structures were identified. (d) A distally based paratenon cutaneous flap was fabricated. (e) The appearance of operative site 1 year following the procedure.
Reconstruction of plantar flexion deformities of the toe

Surgical release of the contracted scar at the site of contraction may not be necessary unless the magnitude of contraction interferes with the wearing of shoes.

The use of a composite skin flap mobilized from the dorsum of the foot

Skin grafting technique is the best modality for reconstruction. Splinting of the foot and toes immediately following surgery is an essential component of the post-surgical care plan. Recurrence of the contracture is very likely without an effective toe splinting maneuver.

Reconstruction of the deformities involving the plantar surface of the foot

The problems are mostly related to breakdown of the graft caused by pressure and shearing forces exerted by walking. Although a local composite skin flap could be used to reconstruct a small defect, breakdown of the skin with ulcer formation is inevitable unless the flap is sensate. Restoration of skin sensation to the pressure points is a pre-requisite for successful patient rehabilitation.

Reconstruction of specific ankle deformities

Extensive burns of the foot and ankle area can lead to talipes-like deformities of the foot, e.g. talipes equinus, varus and valgus (Fig. 59.4). Reconstructive procedures will involve not only the release of the capsular structure around the ankle joint but also lengthening of the tendon of Achilles for an equinus deformity, to restore the joint. In practice, the extent of ankle restoration may be limited because of difficulty in closing an open wound resulting from soft tissue release. Use of skin flap in conjunction with skin graft is considered for covering a wound with exposed tendinous and capsular elements.

Reconstructing a talipes equinus-like deformity

A plantar flexion deformity that is most commonly caused by an injury involving the heel of the lower leg. While contraction of the resultant scar could be the factor responsible for the deformity, tendo-Achilles shortening could further aggravate it. Surgical restoration of ankle mobility will require lengthening of the Achilles tendon. The plan in lengthening the heel-cord must include measures such as fasciocutaneous z-plasty or \( \frac{1}{3} \) fasciocutaneous z-plasty technique to close the heel wound that tendon structures expose.

Reconstructing a talipes vera and valgus-like deformity

Although delineation of the exact extent of tissue destruction and scarring to cause an ankle deformity may be difficult, releasing maneuvers can result in a wound with exposed tendon and joint structures. Inclusion of a surgical plan for wound coverage is essential to minimize morbidity. The use of transpositional fasciocutaneous flap technique; alias \( \frac{1}{3} \) fasciocutaneous z-plasty, is useful. The technical details of fasciocutaneous z-plasty and the \( \frac{1}{3} \) fasciocutaneous z-plasty technique are described as follows:

The modified z-plasty technique that includes the paratenon in flap fabrication; alias \( \frac{1}{3} \) paratenon cutaneous z-plasty technique

Both techniques are essentially identical to the FC z-plasty and \( \frac{1}{3} \) FC z-plasty. They are so termed because of inclusion of the paratenon of the underlying tendon structures in flap fabrication to assure vascular supply. In fabricating a flap, the dissection of the tissue must include the paratenon overlying the tendinous structures. A composite triangular skin flap, i.e. the skin and the paratenon located underneath, are transposed (Figs 59.3, 59.5).

Reconstruction of flexion knee deformities

A knee joint contracture is mostly that of flexion. The incidence, in comparison with other large joints, is relatively uncommon. The deformities noted are usually caused by improper use or lack of splinting. The deformities vary from a tight scar band across the popliteal fossa to a frank knee joint contraction. The treatment options vary according to the deformities noted.

Non-surgical management

Although mechanical traction by pulling on an ankle is effective in correcting a contracted knee joint, splinting and/or casting with progressive extension is a more common approach used to correct a slight to mild joint contracture. Long-term use of a knee splint, however, is needed to prevent recurrence. In practice, patient compliance is low and tightness across the popliteal fossa can persist. Surgical intervention will therefore, be necessary.

Surgical management

The treatment options available to correct the deformity are: (1) skin grafting; (2) z-plasty; (3) interpositional z-plasty alias \( \frac{1}{3} \) z-plasty, and (4) interpositional random fasciocutaneous z-plasty alias \( \frac{1}{3} \) FC z-plasty.

Reconstruction of a contracted knee joint with skin grafting technique

Scars that are contractive and thickened may be best managed with excision and skin grafting. Complete removal of fibrous tissues is necessary. On the other hand, the use of a skin grafting technique may not be feasible if the popliteal vessels and neural structures become devoid of overlying soft tissues.

A partial thickness skin graft of 14–16/1000th of an inch in thickness (STSG) is used most commonly for wound coverage. Immobilization of the knee joint in full extension for a period of 3 weeks followed by continuous use of posterior knee splint for 9–12 months is necessary to minimize recurrence of joint contracture (Fig. 59.6).

Reconstruction of a contracted knee joint with an interpositional skin flap technique, alias \( \frac{1}{3} \) z-plasty technique

Skin markings triangular in shape are made in the area with unburned skin or pliable skin adjacent to the site of release.
Figure 59.4  Showing examples of cicatricial ankle deformities caused by scarring and contraction of scars formed around the ankle joint. (a) Calcaneus deformity. (b) Equinus deformity. (c) Valgus deformity. (d) Varus deformity. (e) Equinovarus deformity. (f) Equinovarus deformity.
The cathetus of the triangle is made perpendicular to the distal end of released wound. The flap length to width ratio should be less than 2:1. The skin flap is rotated 90° to complete the wound closure. The flap donor site is closed primarily (Fig. 59.7).

**Reconstruction of a contracted knee joint with an interpositional fasciocutaneous (FC) flap, alias 3/4 FC z-plasty**

Inclusion of the underlying fascial layer is useful in fabricating a triangular flap with a flap length to width ratio in excess of 2:1. Release of the joint surface may become necessary if a scarred skin is used to fabricate the flap.

**Other methods to reconstruct a contracted knee joint**

A composite skin flap may be converted into an island flap if the vascular supply to the area is readily known. The arc of flap rotation is wider and the inset of the flap is technically simpler and easier (Fig. 59.8).

**The anterior lateral thigh perforator (ALT) flap**

The flap can be thinned and trimmed as well as modified to fit the wound contour. Harvesting a flap is technically simple as the location of the vascular pedicle is consistent and the vascular territory is large. Donor site morbidity is nil. The ALT flap unfortunately has its anatomical limits; the size of flap may not be sufficient to cover the whole defect; variations occasionally are noted in the vascular patterns; the flap may be bulky. Flap dissection may be technically cumbersome (Fig. 59.9).

**Free muscle flap**

A muscle flap harvested from a distant site and transferred via microsurgical means is another treatment option available for deformity reconstruction.

**Medial thigh perforator (MTP) flap or ALT-MTP combination flap**

Combining an ALT flap with MTP flap linked in sequence and/or independently has been found to be useful in fabricating a composite flap with its size sufficient to cover a large wound. A MTP flap derives its vascular supplies from the perforator of the superficial femoral artery.

**After care and rehabilitation**

The patient’s recovery from devastating injuries may depend upon the effectiveness of reconstruction procedures. This in turn is governed by the timing of surgical intervention.
Figure 59.5  (a) A moderate degree of left ankle contracture was noted. (b) The technique of transpositional fascio-paratenon-cutaneous flap, alias fasciocutaneous z-plasty, was used for contracture involving the ankle joint. (c) The flaps were fabricated. (d) The flaps were moved into place to make up the tissue defects resulting from releasing procedures. (e) The appearance of operative site 2 years following the operation.
Figure 59.6. (a) A persistent ulcer developed in the left popliteal fossa area for 3 years following burn injuries involving 65% of total body surface area. (b) An open wound measuring 10 cm x 7 cm resulted from the scar and ulcer excision. (c) A partial thickness skin graft of 15–16/1000th of an inch in thickness was used to cover the open wound. (d) Healing of the grafted area was uneventful. The appearance of grafted popliteal fossa 2 years later.
Figure 59.7  (a) Tightness was noted over the right popliteal fossa laterally. (b) The transpositional flap technique alias \( z \)-plasty was used to achieve the release. (c) The appearance of released site 3 years later.

Figure 59.8  (a) An island skin flap with its vascular supplies, based upon the medial geniculate vessels, was fabricated to cover a chronic non-healing wound located over the patella. (b) The appearance of knee. Healing was uneventful.
Figure 59.9  (a) A large wound resulted from electrical injuries. (b,c) A large piece of soft tissue was harvested from the anterior thigh area, i.e. an anterolateral thigh flap, and transferred via microsurgical means to cover the wound. (d) Although the wound was covered, additional revision will be needed to debulk the excess tissues.
and the postoperative rehabilitative therapy. The outcome of toe-release, for instance, is affected by a treatment that requires the use of pressure garment and shoe inserts for a minimum of 6 months. Recurrence of toe deformity could be drastically reduced by using the Otoform insert as a metatarsal bar for a minimum of 2 months. The modification is instituted once the positioning K-wires are removed from the toes.

Other post-surgical care regimens must include a physical therapy treatment plan with a treatment duration varying according to the magnitude of injury and the limb deformities and executed under the supervision of trained staff.

Comments

The task of managing knee, ankle and foot deformities consequent to burn injuries can be difficult. Initially, a physical therapist is given the task of providing care to regain muscle strength and joint mobility. Attainable therapeutic goals with physical therapy may be curtailed in individuals with permanent structural destruction of the foot and ankle joints. That is, the foot and ankle will remain stiff and walking will be difficult regardless of the intensity of the therapy and the duration of therapy rendered. It is therefore, essential for a surgeon’s continuous involvement in the care of patients.

Scar contracture is the most common cause of flexion contraction, stiff foot and ankle joints and in some instances various talipes-like deformities. Surgical release of contracted scar around the joint is the most fundamental and the most common approach used to restore the mobility of the joints. In practice, maintaining a proper joint alignment is difficult even though the release of scar tissues around the joint structures is complete. The difficulty in restoring joint alignment could be due to structural alterations in the joint capsule because of burn injuries and/or protracted abnormal joint positioning. Release of ligamentous structures surrounding the joint, however, is seldom needed. Instead, joint alignment can be easily maintained with the use of Kirschner’s wires of 0.025–0.035 inch in size inserted percutaneously to ‘re-shape’ altered capsular elements.

Skin grafting is the technique most commonly used to cover an open wound resulting from scar release or joint realignment. The usefulness may be compromised if the wound is located in a pressure bearing area of the foot, i.e. the sole of the foot. Incomplete or inadequate graft sensory re-innervation in a pressure-bearing area can lead to breakdown of the graft. Although various techniques to resurface burned sole have been advocated, usefulness in burned foot reconstruction is limited. Similarly, the skin materials suitable for covering an exposed tendon and joint structure must have the components of subcutaneous fatty tissues. A skin flap with assured vascular supplies that can be mobilized from an adjacent area will be an ideal approach for wound coverage. In practice, burns would damage not only the foot but also the tissue adjacent, thus negating the possibility of using the tissues from the area as a flap donor site. A composite tissue transfer via a microsurgical technique, though clinically appealing, may not be feasible because of lack of suitable donor sites. In contrast, a local flap technique, i.e. a rotational flap technique and/or an interpositional flap technique, has a logistical advantage over other techniques. However, a flap fabricated in the leg, especially in the area below the knee, can be plagued with problems of flap necrosis attributable to disruption of the vascular supplies to the skin with flap dissection. Techniques utilizing a musculocutaneous (MC) flap, a perforator flap or reverse flow skin flap, advocated more recently appeared to have technical advantages over a random skin flap. The tissue mobilized, however, is generally speaking bulky for the wound coverage, and excursion of the flap may be limited. A random fasciocutaneous flap and a random paratenon cutaneous flap, a composite skin flap that includes the underlying fascia and/or paratenon, appeared to circumvent the anatomical limitation of flap fabrication. The skin in almost any location in the foot and in the lower leg can be used for designing a skin flap for wound coverage. As we have noted, the use of this technique is possible in a scarred area unless the underlying fascia and/or paratenon has been destroyed.

Summary

Although the task of reconstructing foot and ankle deformities is difficult, the basic technique of incisional release with skin graft may be useful. On the other hand, the use of a local rotational skin flap technique, alias bi-flap, is preferred, especially in instances where a flap is needed to cover a wound with exposed tendon and joint structure. The viability of skin flap is enhanced by including the fascia and/or paratenon in flap design.

Further reading

References

2. Mardini S, Tsai FC, Yang JY. Double free flaps harvested from one or two donor sites for one or two-staged burn reconstruction: models of sequential-link and independent-link microanastomoses. *Burns*. 2004;30:729-738.
The ethical dimension of burn care

Arthur P. Sanford

Introduction

In seeking optimum health for each patient, contemporary burn care aspires to integrated excellence in multiple dimensions. It is a ‘bio-psycho-social-economic-legal-and-ethical’ enterprise, and the many hyphens indicate that all the dimensions of care are connected. Too often, the bio-psycho-social-etc. dimensions are assumed to be interconnected like railway cars with the biological dimension in front, and the ethical hooked on only if necessary at the end, like an optional caboose. This is a misleading assumption.

Optimal burn care is most frequently achieved when it is assumed that all the dimensions of burn care are always present and in need of regular attention. Moreover, highly integrated, team-oriented, interdisciplinary burn centers practice as if all the dimensions of care are always interpenetrating, just like the length, width and height of a solid object. In their daily work, they assume that no one dimension may be changed without affecting all the others, and they depend on frequent detailed rounds, interdisciplinary staff meetings, and ongoing interviews with patients and families to keep all the dimensions of care coordinated and up-to-date.

In part because the multiple dimensions of burn care are so intimately interrelated, decisions involving the ethical dimension of burn care are extremely common. They are so common, in fact, that care-providers are usually unaware of them. Ethics, after all, is critical thinking about right and wrong, what should or should not be done, etc. The words ‘should,’ ‘should not’ and similar words, indicate that ethical matters are being addressed. For example, whenever we decide which of several therapeutic alternatives should be recommended, we are making an ethical decision.

What is ‘an ethical problem?’

An ethical problem is present when it involves a conflict of two or more of the following: rights or rights-claims, obligations, goods and/or values. For example, disputes about writing a ‘comfort-measures-only’ order for a patient without decision-making capacity and with a very low probability of survival commonly involve a conflict between a obligation and a good: the obligation not to abandon aggressive therapy prematurely, and the good of a maximally pain-free and unprotracted death. In this case, the burn team and the patient/surrogate are ordinarily the major stakeholders and appropriate decision-makers, and they are addressing a problem in clinical ethics. On the other hand, consider the burn center’s or healthcare organization’s (HCO’s) responsibility to ICU patients when a safe nurse-to-patient ratio cannot be consistently met, despite the burn center’s best efforts? If discerning what should be done in such circumstances requires decision-making at the managerial level of the burn center or HCO, a problem in organizational ethics is the correct term to use.

As indicated, conflicts among rights, obligations, etc. are very common and vary greatly in difficulty. When should they be taken seriously? An ethical problem is serious when there are stakeholders involved who stand to be seriously affected by the problem or its outcome. Stakeholders working collaboratively without outside help can successfully manage the vast majority of such problems. When are such problems so serious that assistance should be sought from a healthcare ethics committee/consultant (HEC) or its equivalent? An ethical problem is serious enough to refer to an HEC:

1. When you suspect the Smell Test would be positive, i.e. ‘What would the action or situation we are considering smell like if we read about it in a front page news article or in a popular blog? Would I be comfortable explaining it to my spouse, or my grandmother?’ The problem with this, as the olfactory image reminds us, is that living with bad smells or unethical conduct for a long time may dull a person’s ability to notice them.

2. When there is persistent disagreement among the major stakeholders; and codes, rules, laws and more discussions fail to lead to a resolution within generally acceptable ethical boundaries in a reasonable amount of time.

How should clinical ethics problems be managed?

In the United States, the informed consent process was developed by the American judiciary to safeguard the legal rights and welfare of all the stakeholders participating in
bedside decision-making. Throughout the USA, this legal process has become the foundation of the healthcare provider's approach to avoiding and managing serious ethical problems at the bedside. Its application in the burn center was explained and diagrammed in detail in the first edition of this book, and what follows should be considered an update and development of what is stated there.

On the vast majority of occasions, there is little or no difficulty achieving agreement and patient consent about a proposed course of burn management. There are many predictors of clinical outcomes that are without controversy. Occasionally, however, the process of obtaining informed consent leads to problems involving disagreements, anxieties and/or controversies about what should be done. At this point, the participants must give careful attention to the quality of the discussion in attempting to resolve the problem.

Ethical discourse is a skill requiring practice. No one becomes good at participating in ethical discourse simply by reading books about the subject, or by letting a consultant take over when things get difficult. Avoidance of, or reluctance to participate in, discourse with stakeholders about ethical problems is a suboptimal recourse when at last a care-provider is forced by circumstances to act.

Contrary to very common practice, ethical discourse at its best is not merely filling your 'opponents' heads with what you want them to know so they will say what you want to hear. Nor is it simply getting your discourse partners to effectively 'get things off their chests' so they will feel better and then say what you want to hear. This may make them feel better, but will do nothing for you. Least of all is it engaging in verbal warfare to win an argument. At its best, ethical discourse begins by building a safe place for ethical dialogue, i.e. establishing an interpersonal 'relationship' made safe for transparent and self-critical honesty by making active listening and openness-to-learning the norm.

The role of the care-provider in ethical dialogue

1. The care-provider should develop the trust necessary to establish the safe place for ethical dialogue described above. To do this the care-provider should learn the bio-psycho-social-economic-and cultural/religious information required to approach the patient and his family and/or surrogate with empathy for their lives and values. Our western religious backgrounds teach us that we have certain limitations to this life and look to the future beyond. The eastern religious backgrounds teach us that within our lives we will come back and reflect on what our previous lives have been and also place extreme respect on the departed spirit. Finally, there are people who do not have a religious background that live for different goals and different aspirations. All of these must be considered early on when determining what the caregiver's relationship and position will be with the patients and their families. Many patients, given the opportunity and fully understanding their condition, will decide against extremes of treatment and continuing care with the hope of not burdening their family with large hospital bills. All of these issues must be explored with the patient before one can feel 100% comfortable with the decision and where they are coming from.

2. The care-provider must discover if the patient has decision-making capacity sufficient to participate meaningfully in deliberation. To have decision-making capacity, the patient's (or if necessary, the patient's/surrogate's) consent to, or refusal of, the care-provider's recommendations must be: informed (i.e. comprehending and appreciating relevant information); free (substantially free of distorting non-rational/emotional influences); deliberate (decided after weighing pros and cons in the light of his/her own value system); voluntary (reflecting his/her own intentions); and expressed (communicated verbally or non-verbally). Decision-making capacity is enhanced by optimizing the patient's physiological stability, consciousness and pain control as much as possible. It is typically verified by ascertaining orientation, and by asking the patient to rephrase the information provided to him in his own words and to say why he has made the decision he has. Determination of decision-making capacity by judicial process (i.e. determination of legal competency) is rarely necessary. If despite all efforts, the patient is found to be without decision-making capacity, an appropriate surrogate should be sought among the patient's family or friends, depending on local laws to determine priority.

3. The care-provider should provide appropriate information about the patient's diagnosis and the therapy proposed, its nature, prognosis, pros and cons, and similar information about plausible alternatives including forgoing the therapy proposed. This should be continuously updated as the patient's condition changes throughout hospitalization. Prior investigation of the patient's and/or surrogate's bio-psycho-social-economic-cultural-etc. background is particularly helpful in the effort to assure clear communication and a common understanding among dialogue partners.

The role of the patient or surrogate

The role of the patient is to assimilate this information given by the caregivers. One cannot expect an unfamiliar patient in the middle of an acutely injured situation to understand or have complete background in understanding what medical information is being given to them. There are limitations in their understanding and the assimilation of this information must be taken into account. Also, the patients have the duty within their own value system to make a decision with their own best interest at heart. This includes their aforementioned religious or non-religious background, their family and what the needs and wants of their family are. It becomes an obligation of the patient or their surrogate to become a member of the team responsible for the individual. This obligation includes the necessity to reveal information completely and honestly, to become actively involved in their care, and participate constructively and sincerely in ethical dialogue about the issues at hand.

We must also consider previous life experiences. For example, the patient may have had family members or relatives with severe or terminal illnesses, themselves. Such terminal illnesses are going to influence people greatly in not
wanting to see suffering or experience it, thus, desiring to relieve the family of this burden if they have had a previous bad experience. A religious background is also mentioned, which is a large factor in people’s decision. Clergy might be involved at any step of the way to involve the patient’s religious resources or spiritual support background in order to try to make the decisions about care and continuing treatments. Finally, there is the perception of what it would be like to survive a significant burn. Many people feel that this is not something that you would wish on anyone, let alone suffer themselves. Patients may feel that they are not going to be a functional member of society, or that they will lose out on many of the things that they had been previously involved in or hope to achieve. It has been reported that children with large burn injuries who survive end up at least as well off as their peers.\textsuperscript{11} The men when they reach maturity perform better scholastically and have a better self-image than their peers. The women perform at least on an equal level with their peers. So, what we are finding is, as more patients survive massive burns, that these people do not become shut-ins but survive and thrive. The philosophy is that if you help the person get through the crisis, their own internal tools dictate whether they are going to fail or succeed. If the patient was going to succeed, they will succeed. If the patient fails, they were going to fail, regardless of the burn injury. The burn injury only magnifies their ability to cope with difficult events.

### How should persistent ethical conflict be managed?

Even when participants make a sincere effort to establish rational discussions, disagreements about conscientiously held positions occasionally persist. At this point, patience and the setting aside of adequate time to walk through carefully considered steps in ethical decision-making are necessary. Often, to build up their own skills and enhance chances of success, the patient/surrogate or care-providers will ask a HEC to coach them in pursuing a consensus collaboratively arrived at.

In any serious ethical inquiry, three questions must be answered: What seems to be the problem? What can be done? What should be done? A seven-step decision-making model has been found helpful in answering these questions and is illustrated in Table 60.1. \textsuperscript{12}

- **Step 1.** Discover conflicting values of stakeholders
- **Step 2.** Discover the relevant information
- **Step 3.** Identify principles, laws, other values relevant to the decision
- **Step 4.** Identify alternative courses of action
- **Step 5.** Compare alternatives and values; is decision clear?
- **Step 6.** If not, assess consequences
- **Step 7.** Make decision, collaboratively, if possible

Table 60.1. Three questions to be addressed when a clinical ethics problem is serious and persistent, and the steps appropriate for answering each question

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<td>1. What seems to be the problem?</td>
<td><strong>Step 1.</strong> Discover conflicting values of stakeholders</td>
<td><strong>Step 2.</strong> Discover the relevant information</td>
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<td>2. What can be done?</td>
<td><strong>Step 3.</strong> Identify principles, laws, other values relevant to the decision</td>
<td><strong>Step 4.</strong> Identify alternative courses of action</td>
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<tr>
<td>3. What should be done?</td>
<td><strong>Step 5.</strong> Compare alternatives and values; is decision clear?</td>
<td><strong>Step 6.</strong> If not, assess consequences</td>
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Modified from May 1990. \textsuperscript{12} (With permission of the American Accounting Association and the author)

The ethical dimension of burn care

In such cases, care-providers typically have no way of knowing or deducing with confidence what the patient’s wishes might be in a given set of circumstances. In general, the decision made must seek the best interest of the patient, but the process required may vary. In some jurisdictions, consultation with another physician, the healthcare
institution’s administration, and/or HEC is mandatory. In others, a court appointed conservator might be required. In all such cases: (1) the search for a surrogate should be diligent; (2) all relevant medical information must be obtained and reviewed; (3) real or apparent conflicts of interest must be disclosed; (4) the opinions of the healthcare team and of one or more physicians in addition to the responsible attending should be reviewed; (5) burden versus benefit must be weighed from the patient’s point of view; and (6) steps should be taken to ensure the benefit of continued life to a disabled patient is not devalued or underestimated. Some institutions also require that consideration of economic impact on healthcare providers and the healthcare institution be excluded from consideration in such cases. Eventually a surrogate decision-maker is identified and, hopefully, this is a person who has previously known the patient and their values prior to the accident, who has possibly had discussions about extreme end-of-life issues and can speak on the patient’s behalf. The surrogate decision-maker must not make the decision based on what they would want for the patient. However, the surrogate decision-maker must know what that patient would prefer and act as an advocate in this situation, since the patient is not able to participate in the decision. They should be expressing the patient’s views, not projecting their own views onto the patient.

How should organizational ethics problems be managed?

Currently, healthcare decision-making affecting burn care occurs at three levels: in the clinic, in the organization, and in society. The disciplines designed to improve ethical decision-making at the first and last levels are called clinical and societal ethics, respectively. They discern facts and values for guiding clinical or societal decisions that affect patient care and have received wide attention in both the media and scholarly journals for years. Recently, attention has been called to the need for discernment of facts and values for guiding managerial decisions that affect patient care. For example, at times, problems present as difficulties in clinical decision-making, but have their root causes in areas that require decision-making at the managerial level. With dwindling numbers of nurses entering training, fewer and fewer nurses will be available to provide intensive care, and managerial decisions will be required to produce or recruit more nurses and to judge just when it is no longer safe to admit new patients to beds without adequate staffing. Perhaps rehabilitation services in a given geographical area have not kept up with the ever increasing numbers of patients with large burns who survive but require longer and more expert rehabilitation. Managerial decisions about the distribution of scarce resources will have to be made if adequate rehabilitation is to be available.

Such decisions are ethical: they involve conflicts of rights, obligations, goods and/or other values. They tend to be less dramatically immediate and more deferrable, but they usually affect more persons and require more resources and follow-up than clinical ethics decisions. They sometimes appear to be made in the front office, apparently without satisfactory input from care-providers, patients or other stakeholders, and without availability of extensive literature or assistance from a committee or consultant skilled in ethical analysis and critique applied at the organizational level.

The development of the discipline of ‘organizational ethics’ is just beginning, and overdue in the judgment of JACHO and other authorities. The obligation to be ethical at every level of healthcare decision-making will become increasingly obvious and pressing, with continuing changes in the ways healthcare is delivered. More and more, we are holding our leadership at the institutional level to be transparent in their decisions and ultimately to be held accountable for their actions.

Specific problems

Human research

Many of the modern progresses in healthcare, particularly burns, have come through active research protocols. Many advances including fluid resuscitation, excision and grafting, temperature and nutritional control, and modulation of hypermetabolic response are all based on active research in a clinical setting on human patients. It must be remembered that these are volunteers first and patients must not be coerced into the treatment. Institutions that are involved in human research must have Institutional Review Boards in place to monitor approved protocols and follow-up on patients and complaints with their research driven caregivers. Childhood research is an even more scrutinized area because it is now the surrogate, as a parent, who is giving consent for the research. It is a difficult area to approach, however, with the thorough monitoring of institutional review boards and the realization that those children have a great deal to benefit from progress in healthcare. Children should be included in research so that they can get the benefits of progress in medicine and science at the earliest possible opportunity. However, this should not be at the expense of their own rights. Many patients feel, when asked to participate in research protocols, that they have a duty to those who preceded them, who got the physicians to the level of care they can provide to them now. They feel they should try to give something back to the science of medicine. Patients realize that they cannot do that to the caregivers who got them to where are now and feel a duty to participate to help future victims who will also need their assistance. We must not use such leverage to coerce unsure patients to participate in investigations.

Futility

The concept of futility and hopelessness in the care of a patient has changed drastically over the recent past. At one time, any burn over a significant size offered no hope for survival. Through our efforts in resuscitation, we have pushed this survivability to current levels, where in the youngest of age groups, patients with extremely large burns can function and survive. At the same time, we are finding that there is no simple definition of futility, making simple pronouncements of futility impossible.
The ethical dimension of burn care

Summary

As conceived in ancient Athens and during most of its history, Western ethics has been an effort to: (1) achieve the ethical life, i.e. life in all its important dimensions, lived at its most flourishing, and (2) solve any problems about what should or should not be done during that quest. The sustained pursuit of excellence in total burn care first achieved momentum in the USA in the mid-twentieth century. It has always drawn its most primal motivation from the fact that burn patients are among the most severely injured and utterly vulnerable of human beings, and therefore deserving of the most tender, skillful and comprehensive care. Commitment to the safety, healing, rehabilitation and growth of patients during their return to as flourishing a life as possible, has been the spearhead of the quest since its beginning, and both the fire in its belly and the steel in its resolve ever since. Clearly, burn care is an ethical endeavor through and through, not just when and where difficult patients or ethical problems become evident. It is never just a burn, but a patient we may not have known previously, but will have touched for the rest of their life.

Further reading


References

5. May WW. Discerning what's right in health care at the clinical level. Lecture at USC Keck School of Medicine, Los Angeles, CA, May 8, 2000.
Introduction

Deliberate injury by burning is often unrecognized. According to the US Department of Health and Human Services Administration for Children and Families, child abuse and neglect are defined as any recent act or failure to act on the part of a parent or caretaker, which results in death, serious physical or emotional harm, sexual abuse or exploitation, or an act or failure to act which presents an imminent risk of serious harm. Within the USA alone, 1.5 million children are abused or neglected each year, with 4–39% of these occurrences being reported as intentional burn injuries and less than half ever being substantiated. It is imperative that all clinicians are aware of the importance of recognizing signs and symptoms of intentional injury presentations, as the opportunity for intervention is critical when taking into account that 50% of children experience recurrent abuse and 30% are ultimately fatally injured. Reporting suspicious injuries to child protective services is mandated by law for all clinicians working with children. Some treating facilities identify specific treatment team members (i.e. psychologist or social workers) to be responsible for all reporting. In these situations it may be necessary to follow the protocol of the hospital or treating facility first; however it is important to note that any physician, medical professional or mental health professional that encounters a suspicious injury must insure that the injury is reported to the appropriate authorities. At other times, the concern of reporting is more a result of ambiguity or vagueness in the information, which can cause hesitation to report the suspicious injury. In these incidents of doubt, the most salient point to remember is that the clinician is responsible to report suspicious injury not to prove or validate the abuse. It is always better to report the suspicion than to ignore it. Most state agencies also have hotlines that are available to call 24 h a day to ask specific questions regarding reporting suspicious injuries. Although it is overwhelming to imagine that so much abuse occurs, statistics show that it does occur not only with children but with adults and our elderly population.

Intentional injuries can occur in the form of neglect, physical abuse, sexual abuse, and emotional abuse. All of these injuries can occur independently but they often occur simultaneously. Neglect is the most common form of intentional injury. Of the average 5.5 million referrals made to Child Protective Services each year, 64.5% of these children are neglected. Physical abuse occurs in 25% of intentional injury cases. More than 15% of victims of abuse suffer more than one type of abuse and more one-third of child fatalities are attributed to neglect (Fig. 61.1). Burn injury is frequent in both neglect and physical abuse of children. Severe burns in children are between 10% and 12% of all intentional injuries.

Since the last edition of this book, intentional injuries to adults have increased. It is frequently debated within the literature as to whether the increase is a valid increase or if there is an increase in reporting. Violence specifically against women and young girls has now become a universal phenomenon. The World Health Organization reported that of the women who were partnered at some point during their lifetime, 15–71% reported experiencing physical or sexual violence by their partner. Within this realm of violence against women and young girls, acid violence is the worst form of violence and violation of human rights. Though steps are being taken to control the widespread free sale of acids to the public, this act of violence is still on the rise and warrants discussion in the burn care literature and sensitivity to this overwhelming problem by all burn care professionals. Another vulnerable population of intentional burn injuries are the elderly. In the past 10 years, burns in the elderly have increased secondary to increase in size of the aging population.

In this chapter, we have integrated our experience with current literature to classify risk factors in the total population and to propose validated therapeutic interventions to treat the burn wounds and the complex social and psychological familial concerns that both create injury and complicate the recovery, and rehabilitation of the patient. It is essential that the burn team clinicians understand their role and responsibility in assisting not only burn patients but the perpetrators as well because history and statistics have shown us that the outcome can be fatal if intervention and prevention methods are not implemented with sensitivity to maintain positive relationships with burn patients as well as the perpetrators.

The authors are well versed in clinical experience and research experience of child abuse and pediatric burn injuries; however, our experience of intentional burn injuries within the adult population is limited. The literature and our extensive knowledge of information regarding intentional injuries against children are reflected in this chapter. We have included the most recent literature on adult injuries.
but it is not exhaustive. It is important to note that the pediatric population is not the only target for intentional injuries.

**Prevalence rates of intentional burn injuries**

Despite the improvement and use of smoke detectors, investment in sprinkler systems and improvement in building codes in developing countries, burns continue to cause significant intentional and unintentional injuries. Smoking remains the leading cause of death by fire. Cooking is the number one cause of residential fires. Annually, fire-related injuries claim more than 300,000 deaths and 10 million ‘disability-adjusted life years’ worldwide. Middle and low-income countries exceed 95% of fire-related burns. Approximately half of these countries are in southern parts of Asia. In the USA, burn injuries result in approximately 1 million emergency department visits and 50,000 hospital admissions, with a 5% mortality rate. Fire and burns represent 1% of the incidence of injuries. Fatal home injury burns and fire deaths rank fifth and third, respectively in the USA. The incidences of the causes of burns are: flame/fire 46%; scalds 32%; hot objects 8%; chemicals 3%, and other forms 6%. Fires/burns occur frequently in the home 43%; street/highway 17%; occupational 8%, and other 32%. Burn injuries inflicted in Pakistan occur mostly to adult women: approximately, one-third are secondary to stove burns and 13% are acid burns. Husbands inflict more than 52% of these injuries and in-laws one-quarter of the injuries. Victims who are at highest risk of fire-related injuries and deaths are children ≤4; adults over 65 years; African-Americans and Native Americans, and the poor or those living in rural areas. A literature review of hospital-based studies of the prevalence of burn injuries in China, revealed similar results with children <3 years more vulnerable; males more than females; those living in a rural setting, and incidence occurring between the hours of 17:00 and 20:00.

**Prevalence of childhood burns**

Over the past 50 years, child abuse has been documented especially in the USA. Child abuse characteristics are composed of physical abuse, neglect, sexual abuse, psychological abuse and other, which include Munchausen by proxy and abandonment. Child abuse may present with multiple characteristics. Major forms of injuries to children include falls, poisonings, car accidents, foreign body and fires/burns. Ten percent of child abuse is burns and 20% of burns are child abuse. The child abuse death rate in the USA is approximately 1000 children annually, with burns and scalds as the most frequent cause of death. In China, the mortality rate from abuse ranges from 0.49% to 3.14%. In Hong Kong, it is 2.3%; in Singapore 4.61%, and in Iran 6.4%. The lowest rates are in the UK and the highest rates are in the USA, where the majority of the studies have been completed. In many cases of burn injuries, it may be difficult to conclude if the burn injury is an incidence of neglect, intentional or truly an accidental event. More recent studies have begun to analyze hospital cases of burns to delineate if intentional or non-intentional. The characteristics of types of burns include scalding (70%); flame burns (50%), or electrical (3–4%). Bathtub submersions peak at 6–11 months, then again at 12–14 months and remain high until 33–35 months of age. Most studies calculate the mean ages of children with intentional burns from 2 to 4 years of age. Boys are 2–3 times more afflicted than girls with the youngest of multiple siblings suffering most often. There is no ethnic predilection. Of children who are victims of physical abuse 10–12% suffer severe burns. In 2007, Hicks and Stolfi concluded children with burn injuries are at risk for occult fractures at a significant rate. Therefore, a skeletal survey should be routine in burn patients presenting to the emergency department, as recommended by the American Academy of Pediatrics. Men are convicted at a greater rate than female perpetrators, despite an equal rate as perpetrators.

**Prevalence in elderly**

Over the past 10 years, prevalence data of burns in elderly has increased secondary to recent emerging studies in this area. As in pediatric burns, geriatric burns are higher in the developed countries at a rate of 20%, yet in the developing world it is 5%. Results of the review of data from the US National Burn Repository demonstrated an increase in rate...
of elderly abuse from 1991 to 2005. Of those burned, 14% are over 55 years of age (with 6.2% between 55–64 years; 3.3% between 65–74 years, and 4.4% >75 years of age). There is a male predominance of burns of 1.4:1. However, this decreases with age and is thought to be secondary to the decrease in life expectancy of males to females. The most common injuries are flame burns, accounting for 37%, and scalds at 22%. The total body surface area (TBSA) was 9.6% and the majority of injuries were residential. In the UK, residential settings are the leading site for burn injuries to the elderly at a rate of 18.6%. The occurrences had a 32% higher mortality rate and 33% more TBSA affected than like-sized burns in aged patients from other causes than abuse. Over a 4-year period, Bortolani and Barisoni27 investigated 53 patients aged ≥60 years who were admitted to a local Italian hospital. It was noted 85% of these burns occurred in the home and 11% in nursing homes. Flame burns were the most common at 55%. The incidences were attributed to pre-existing diseases in 85% of patients. These diseases included cardiovascular accidents, neurological problems and diabetic comas. In addition to illness, lack of adequate supervision is another major etiology for burns in this age group. In the USA, residential care settings accounted for one-fifth of geriatric burns. With increase in an aging population, there is concern about an increase of domestic elderly abuse and proportionately an increase in burn victims. In the USA, elderly physical abuse was underreported, with a rate of 2.8% of total cases of abuse in 1988. However, in 1996, residential institutions estimated only one-fourth to one-fifth of abuse was reported. Another study, from Canada, estimated the institutions estimated only one-fourth to one-fifth of abuse in 1988. However, in 1996, residential institutions estimated only one-fourth to one-fifth of abuse was reported. Another study, from Canada, estimated the prevalence of abuse at 1%. The abuse is usually kept secret owing to guilt, shame and fear of reprisal, especially if the perpetrator is the victim’s adult child (Box 61.1).

The literature reports controversial results on the most likely perpetrator, spouse vs adult children. As in child abuse, disabled adults and those who suffer from dementia are at higher risk for abuse. Drugs and alcohol abuse in caretakers also increase the rate of abuse. Other characteristics in caretakers are mental disorder, financial difficulties and deviant behavior.

### Box 61.1: Premorbid indicators of intentional burn injuries of adults

- Physical dependence
- Psychological dependence
- Accessibility as a target for abuse as in institutional living or living with a ‘caretaker’
- Caretaker(s) with a history of substance abuse, and/or other psychopathology
- Social isolation
- An injury that is not consistent with the story described
- Conflicting reports of the injury
- Scalds with clear-cut immersion lines and no splash marks
- Scalds that involve the anterior or posterior half of an extremity and/or the buttocks and genitals, or a flexion pattern
- Other physical signs of abuse/neglect
- History of related incidents

### Distinctive characteristics of perpetrators and families

Perpetrators are frequently individuals responsible for the care and supervision of their victims. In 2007, one or both parents were responsible for 69.9% of child abuse or neglect fatalities. More than one-quarter (27.1%) of these fatalities were perpetrated by the mother acting alone. Child fatalities with unknown perpetrators accounted for 16.4% of the total. According to the National Child Abuse and Neglect data system in 2008, 56.2% of perpetrators were women and 42.6% were men and 1.1% were unknown. Of the reported women perpetrators 45.3% were younger than 30 years of age compared to 35.2% of men younger than 30. These percentages have remained consistent for several years in a row. Some 61% of all perpetrators were neglected as children. Approximately 13.4% of all perpetrators were associated with multiple types of abuse. Ten percent of perpetrators experienced physical abuse as children and 6.8% were sexually abused as children. The children who are abused, 80% were abused by their parents. Other relatives accounted for an additional 6.5%. Unmarried partners of parents were 4.4% of perpetrators. Of those parents who were perpetrators, more than 90% were biological parents, 4% were step-parents and 0.7% were adopted parents.

Other characteristics of perpetrators include being commonly adolescent parents, single parents, often maintaining inconsistent expectations for a child’s development, experiencing a lack of external supports, stressors such as substance abuse, poor education (no high school diploma), unemployment, poor housing, mental illness, and being reliant on children for emotional support (Box 61.2). Most fatalities from physical abuse are caused by fathers or other male caregivers. Mothers are most often held responsible for deaths resulting from child neglect. In some situations there are two ‘perpetrators’, i.e. the actor and the overtly passive observer who does not stop the abuse. Justice and Justice, in their work with families who mistreat children, identified several erroneous belief systems that are commonly held by perpetrators; these are listed in Box 61.3. Since, as most authorities believe, violence is a multigeneration intra-family pattern, then it is likely that the belief systems attributed to child perpetrators can be extrapolated to perpetrators of adult abuse as well.

Often in homes where abuse occurs, there is little to no emotional support for the perpetrators. They are often dealing with tremendous life stressors and unfortunately resort to immature coping styles to deal with frustrations. Perpetrators resort to abuse as a result of complex behaviors derived from a dysfunctional family history, lack of education, desperation and at times substance abuse. Children and elderly are usually dependent upon the perpetrator and ironically are a source of stress and therefore become the victim of intentional injuries. Corporal punishment is ‘the use of physical force with the intention of causing a child to experience pain but not injury for the purpose of correction or control’. Some perpetrators will use this explanation as a form of justification for intentional injuries. In young children learning toilet training, a hot bath to clean after a toileting accident is often a form of punishment. Usually,
Box 61.2 Risk factors for abuse/neglect by burning

**Forced-immersion demarcation**
- Symmetrical, mirror image burn of extremities
- Glove-like (burned in web spaces)
- Circumferential
- Minimal splash marks
- Uniform depth
- Full-thickness
- Clear line of demarcation, crisp margin
- Doughnut-shaped scars on buttocks/perineum (spared area forcibly compressed against container, decreasing contact with hot liquid, if container is not a heated element)
- Flexion burns, ‘zebra’ demarcation to popliteal fossa, anterior hip area, or lower abdominal wall
- Injuries of restraint (e.g. bruises mimicking fingers and hands on upper extremities).18

**Injury demarcation, other**
- Incongruent with history of event
- Pattern of household appliance – note whether even pattern versus brushed, imperfect mark
- Scald
- Location of injury: palms, soles, buttocks, perineum, genitalia, posterior upper body
- Cigarette burn, if more than one on normally clothed body parts and if impetigo ruled out.

**History of injury**
- Evasive, implausible explanation
- Incompatible with child’s developmental age
- Changes in story; discovered to be burned – rule out dermatologic epidermolysis bullosa (EB), dermatitis herpetiformis, chemical burn due to analgesic cream, phytophotodermatitis,17 and birth marks, including Mongolian spots18
- Under-supervised – inadequate monitoring, impaired person supervising, inordinately young babysitter (<12 years of age)
- Burn is older than history given
- Water outlet temperature greater than 120°F
- Mechanism of burn is incompatible with injury (e.g. exposure time, history of event, and degree of burn are inconsistent)
- Patient’s per-event behavior displeasing to caregiver (e.g. inconsolable, failed to meet caregiver’s expectations)
- Toileting events related to history of injury19
- Burn attributed to:
  - Child or patient, as per caregiver
  - Caregiver who is not present at the healthcare facility
  - Caregiver, as per patient
  - Delay in seeking medical treatment – note estimated time of delay.

**Developmental associations**
- Pre-verbal, non-verbal person
- Vulnerable person (e.g. special need, failure to thrive, elderly)
- Caregiver expectations are inconsistent with patient’s development; caregiver overestimates child’s developmental skills and safety knowledge; caregiver unaware of patient’s developmental capacity
- Patient has symptoms of mental disorder (e.g. ruminating, aggressive)
- Patient displays disturbing behaviors related to attachment (e.g. excessive crying, clinging, apathy/lethargy, excessively withdrawn, listless, unemotional, submissive, polite, fearful, vacant stare)
- Hyper-sexualized language or behavior, as compared to same age peers.

**Caregiver–patient relations**
- History of interrupted caregiver–child bonding
- Adolescent caregiver(s) (e.g. child–child versus adult–child interactions)
- Strained interactions; inappropriate expectations of the patient by the caregiver
- Role reversal (rely on patient for support)
- Inappropriate or lack of caregiver concern:
  - Detached
  - Lack of sympathy
  - Lack of physical contact (e.g. fails to hold or pick up child)
  - Inebriated during visits
  - Infrequent visits.

**Other physical signs of abuse or neglect**
- Unrelated injuries:
  - Fractures, dislocations; rupture to spleen, liver, or pancreas; point tenderness; impaired range of motion or function
  - Signs of poisoning
  - Ocular insult (edema, scleral hemorrhage, hyphema, bruise, blue sclera)
  - Swelling, bogginess, depressions, cephalohematomas palpable on head or increased intracranial pressure at fontanelle
  - Blood, infection, or foreign body in ear
  - Edema, bleeding, septal deviation of nose; foreign bodies in nose; cerebrospinal fluid rhinorrhoea from nose
- Unrelated injuries involving the skin: hematomas, soft tissue swelling, lacerations, fingernail markings, scars, bruises (check behind ear), welts, rope burns, strangulation marks, bites, alopecia – note color, size, shape, and location of each (scalp most visible while shampooing)
- Abdominal tenderness, guarding, rebound tenderness, or bruises
- Cardiac instability, tachycardia, murmurs, flow murmurs secondary to anemia, or palpable rib fractures
- Dehydration or malnutrition – note weight, height, and head circumference
- Previous burns
- Unkempt, e.g. severe diaper rash, dirt under nails or in axillae, odoriferous, dirt on plantar surfaces of feet in cold weather
- Inadequate or no immunization record
- Inadequate dental care (e.g. caries); trauma to lips, tongue, gums, frenula, palate, pharynx, or teeth
- Inadequate medical care
- Inappropriate dress
- Assess prior to invasive medical procedures
- Genital, urethral, vaginal, or anal bruising, bleeding
- Swollen, red vulva or perineum
- Foreign body in genital area
- Positive cultures for sexually transmitted diseases – if herpes develops, note whether lesions are on unburned body surface area, on genititals of type II
- Pregnant minor
- Recurrent urinary tract infections, streptococcus pharyngitis, abdominal pain.

**Family**
- Caregiver abused or emotionally deprived during childhood
- Limited disciplinary practices (e.g. only physical punishment)
- Lack of external supports; isolation
- Mental illness; substance abuse; criminal history
- Lack of financial self-sufficiency
- Poor employment history
- Dependent caregiver; unable to cope with daily responsibilities; unorganized
- Violent couples; impulsive; easily frustrated
- Previous Department of Protective and Regulatory Services involvement19
- Prior accidents to dependents
- Acute family stressors
- No primary caregiver.
the perpetrator’s intent is to clean the child well, not to burn; however, serious burns often occur. They often fail to seek appropriate and timely medical treatment for an injured child, not only because they fear punishment but also because of their learned helplessness and passivity. They discount the seriousness of the injury, as well as their ability to take care of the injury. ‘I didn’t think it was that bad’ is an explanation often given for delay in seeking treatment. By diminishing the significance, they relieve themselves of responsibility to act. When the perpetrator does take the child for help, the perpetrator commonly seeks first a relative or neighbor rather than a physician because perpetrators do not believe in their own ability to decide whether to seek medical treatment. Perpetrators are observed to interact inappropriately with their children because they are preoccupied with having their own needs met. A child who is hurt and demanding is unlikely to reward the perpetrator with feelings of comfort that the perpetrator seeks, and so the perpetrator withdraws from the child. If the child is quiet and compliant, the perpetrator may be observed to ignore the child and sit passively, watching television for long periods until some external force acts as a stimulus to motivate the adult into action.26

### Indicators of intentional injuries

In approaching pediatric/adult burn victims, indicators of possible inflicted burns injuries should be considered (Table 61.1). Patterns of scald burns are highly suggestive of inflicted injuries and healthcare providers have a general agreement of these indicators (Box 61.2).22 (1) During scald burns, it is implied that the absence of splash is suggestive of the victim being held down. Some children who jump into a hot tub of water may panic or freeze and just remain still and not have splash burns. There are predominantly symmetric clear upper margins. The burns involve lower extremities, buttock sparing (doughnut ring pattern) at the highest level and sparing buttocks (doughnut ring pattern) at the lowest level. (2) If there is uniformity of burn consider that the patient was held still during the incident. (3) Symmetric bilateral burns (glove and stocking distribution) are highly suggestive of forcible immersion (Fig. 61.3b). (4) In submersion burns, there may be skin sparing secondary to joint flexion or victim forcibly held against the receptacle. This gives an appearance of a doughnut appearance (or ‘halo sign’). (5) In an Australian study authored by Heaton in 1989,10 bilateral burns of extremities are between 2.4 and 4.8 times more common in inflicted burns.22 (6) Accidental cigarette burns are superficial and ill defined. Yet inflicted wounds are superficial circular or ovoid macular wounds with distinct depigmented lesions and hyperpigmented edges. (7) Heated metal objects cause deeper burns (Fig. 61.3a). (8) Electric shock burns are revealed based on the size of the device and entrance and exit wounds. Areas will vary from full-thickness necrotic areas to superficial wounds that are erythematous. One cannot evaluate these lesions in isolation (Box 61.2). Review of medical records is

### Table 61.1 Triage tool for diagnosis of intentional scalds

<table>
<thead>
<tr>
<th>Evaluate for intentional scald</th>
<th>Intentional scald should be considered</th>
<th>Intentional scald unlikely</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanism</td>
<td>Immersion</td>
<td>Spill injury; flowing water injury</td>
</tr>
<tr>
<td>Agent</td>
<td>Hot tap water</td>
<td>Non-tap water; other liquids (beverage)</td>
</tr>
<tr>
<td>Pattern</td>
<td>Clear upper limits; Uniformed depth scald symmetry (extremities)</td>
<td>Uniform scald depth; skin fold sparing; central sparing buttocks (doughnut ring pattern)</td>
</tr>
<tr>
<td>Distribution</td>
<td>Isolated buttock/perineum, ± lower extremities; isolated lower extremities; rarely the face</td>
<td>Glove and stocking; 1 limb glove/stocking</td>
</tr>
<tr>
<td>Clinical features</td>
<td>Associated unrelated injury (recent or old fractures); history incompatible with examination findings</td>
<td>Previous burn injury; neglect/faltering growth; history inconsistent with assessed development</td>
</tr>
<tr>
<td>Historical/social features</td>
<td>Passive, introverted, fearful child; previous abuse; domestic violence; numerous prior accidental injuries; sibling blamed for injury</td>
<td>Trigger, such as soiling/enuresis/misbehaviour; differing historical accounts; lack of parental concern; unrelated adult presenting child; child known to social services</td>
</tr>
</tbody>
</table>


### Box 61.3 Erroneous beliefs of abusers

Erroneous belief systems commonly contributing to the family system in which abuse occurs:27
- If my child cries, misbehaves or does not do what I want, he or she does not love me and I am a bad parent
- My child should know what I want and want to do it
- My child should take care of me like I took care of my parents
- My spouse/lover should know what I want and meet all of my needs
- If I have to ask, it does not count
- You cannot trust anyone.
Figure 61.2 Newborns who were burned in hospitals by improperly trained hospital personnel.

Figure 61.3 (a) Abuse. Contact burn in which the markings of an iron are clearly visible. (b) Abuse. Classic ‘stocking’ pattern resulting from feet being immersed in very hot water. The initial history given by the mother of the 21-month-old infant was that an older sibling had turned on the hot water, and the patient herself dipped her feet into the tub.
necessary to assure presence of a pattern of repeated abuse. Also be aware patients may frequent a variety of hospitals in the areas to decrease suspicion by medical providers. Corroboration of history to physical exam is essential and may suggest indicators of intentional burns.

**Intentional acid burn injuries against women**

Violence against women is a growing concern worldwide. According to the World Health Organization on women's health and domestic violence, acid-throwing constitutes a special case of intentional injury displaying an alarming increase in cases over the past 2 decades in 48 different countries including Bangladesh, Pakistan and other South Asian countries. In 1993, the United Nations adopted a Declaration for the ending of violence against women and equal rights of men and women. However, the gender-based violence continues to be a pervasive global issue that contributes significantly to preventable morbidity and mortality for women across diverse cultures. Women are not only subjected to burning but they are often tortured, disfigured with acid, endure beatings, sexual violence and ritual honor killings. The most severe and excessive form of gender based-violence in Pakistan is stove burning by husbands and in-laws as a result of inadequate dowries.

Acid burning is the most common form of violence against women. Acids (hydrofluoric acid, sulfuric acid and nitric acid) are readily available in schools, textile mills, jewelry making, battery manufacturers and fertilizer factories and are easily affordable. These acids are used against females usually aged between 12 and 15, again in low socioeconomic situations. Attacks are often perpetrated by men against women, with a reported 47 cases in 1996 increasing to 228 in 2001. The frequent reasons for acid burning include disputes over rejected sexual advances or marital disputes (41%), land and family disputes (32%) and dowry dissatisfaction (13%). Isolated cases of disputes between neighbors have culminated in acid attacks on babies.

Acid burn victims who survive encounter deeper wounds that often affect muscle tissue, longer hospitalization and permanent physical disfigurement. The contact of acid on the skin and body is devastating. The acid often causes corrosion upon impact. Permanent damage can occur to eyes causing blindness or death. The psychological trauma that subsequently follows these burn injuries is overwhelming. The women experience social isolation, difficulty with body image, depression, anxiety and public humiliation. The increase in these violent acts against women indicates a need for improvement in legal provisions and protection for women worldwide.

**Self-inflicted burn injuries**

One of the most violent means of self-immolation is suicide by burning. It can also be an act as a part of a deliberate self-harm syndrome, consisting of continual, sudden urges towards self-harm. There has been an increase in the literature on self-immolation. It is unclear as to whether this emphasis is a result of increased rate of recurrence or increase in reporting. Historically, there is a debate as to whether self-immolations are more acceptable if they are religiously or politically motivated. Characteristics of females who self-immolate include substance abuse, a lack of social support, younger age and diagnosed eating disorders.

Males who self-immolate are also younger with severe mental illness or pathological family dynamics or possibly an adherence to fundamentalist religious convictions. Regardless of sex, self-inflicted burn patients usually have some previous psychiatric problems, often depression or borderline personality disorder, previous failed suicide attempts with a poor response by others to suicidal ideation, recent life stressors with feelings of helplessness. One of the highest rates of this behavior is in Iran among young females where marital conflict is a significant risk factor. Others include low-literacy, low socioeconomic status, limited access to mental health services and post-traumatic stress disorder.

Although self-inflicted burn injuries are less frequent in Western culture, studies report a rate of 0.5–2% in adolescents and up to 25% in adults. In Africa, south Asia and the Middle East self-inflicted burn injury rates are up to 28% of all burn injuries. There is an estimated range of self-immolation counting for 9–32% of all suicides in India, Zimbabwe, and Iran with rates of Iranian and Brazilian women being as high as 46% of suicides. Some studies have found that there are no gender differences in the rates of self-immolation but some have determined that it is most common in females, specifically Asian and Latin females while others have found that it is more common in males. Other risk factors for self-immolation in Western culture include previous psychiatric treatment, diagnosis of a psychotic disorder, unemployment or non-intentional. Obtaining a detailed history from the patient and family is of particular importance in assessing whether the burn is likely to be intentional or accidental. Evaluating for intentional burn injuries requires a multidisciplinary team effort (Box 61.4).

**Clinical evaluations of suspicious injury with pediatric patient and family**

The history of the burned child is of particular importance in assessing injuries of patients and providing an accurate assessment of incident to determine if suspicious injuries are intentional or non-intentional. Obtaining a detailed history from patient and caretaker is foremost in assessing creditability or
Social workers are advocates for referral and follow-up care. Both are skilled at assessing family dynamics and social situations in greater detail and should be your focal point for referral to appropriate government agencies. Psychosocial assessment and interview with the patient separately {when possible} from the caretaker will provide a more accurate picture of the injury events. Inconsistency is a marker of discrepancies in the history, which may alert an examiner to possible abuse. The patient and caretaker must have a detailed interview documented verbatim by the historian. Paraphrasing information increases the likelihood of personal interpretation of history. The presence of witnesses and the exact timing must be confirmed and these persons interviewed to assess for correlation in narratives. A thorough event reconstruction soon after admission should be conducted and documented. This limits the room the suspect has to alter the events and timeline related to the burn or the opportunity to collude with witnesses. The pattern of circumstances is extremely important, with suspicions raised when the adult responsible claims not to have seen the incident, attributes the injury to a sibling, or presents late, or when relatives other than the adult supervising at the time of the burn bring the child for assessment. The clinician conducting the interview must be well versed in child development to ascertain normal developmental response to those that are suspicious of abuse. Observations of interactions and behavior are equally as important as the specific questions that are asked during the interview process.

Abused children often have similar characteristics; they are under the age of two making them vulnerable to their caregivers. Other characteristics include inconsolable crying, difficulty toilet training or associated toilet training accidents, insufficient or strained parent–child attachment, inappropriate behavior such as apathy or apparent tolerance to invasive procedures. Severely abused children will demonstrate exaggerated responses by either being overly fearful or overly affectionate with medical team. When requested to provide immunization records parents or caregivers suspicious of abuse will often fail to provide or will avoid providing accurate medical records and record of immunizations.

The interview with a child is an essential component to determining if the injury was intentional. The rapport that is established through a therapeutic relationship is the key factor to a successful interview. Warm-up questions or non-threatening questions should be asked first to establish rapport: When is your birthday?; questions about school, friends, or asking the child to verbalize a story of their best day. Once sufficient rapport is established asking open-ended questions about the injury is most effective, i.e. What happened? How did you get hurt? The child should be encouraged to tell the story freely. Specific questions for clarification should be asked only after the child has told the story. If the child seems unwilling to talk about what happened, the interviewer can suggest the child raise a hand or wiggle a finger to signal that they know something but do not yet want to talk about it. When interviewing younger children short sessions with breaks will allow rapport building and trust to develop for the child to feel safe to share his/her story. The suspicious injury assessment should be discussed confidentially with the family members, including the suspected

**Box 61.4 Documentation for reporting**

In addition to the documentation of first-hand observations, the following tasks should be delegated:

- Examine the patient for other signs of maltreatment, including a skull and long-bone radiological scan. Clearly state that the radiology consultation is for assessment of occult trauma.
- Photograph injuries and any possible evidence.
- If the patient has been referred from another hospital, access information from the staff at that hospital to determine whether they identified suspicious aspects of the injury and whether the injury was reported to an investigating agency. If so, ascertain the number assigned to the patient’s case by the investigating agency. This number is needed for subsequent calls related to the patient.
- Interview the patient.
- Interview family members or caretakers individually and together for thorough histories of the event, sensitive to the differences in the story or changes across time.
- Obtain a thorough family history, the patient’s medical history and the developmental capacity of the patient.
- Gather other available collateral information, e.g. medical records from other places of treatment.

Stating that fracture is less likely in children under 2 years is misleading. In addition to the documentation of first-hand observations, the following tasks should be delegated:

- Examine the patient for other signs of maltreatment, including a skull and long-bone radiological scan. Clearly state that the radiology consultation is for assessment of occult trauma.
- Photograph injuries and any possible evidence.
- If the patient has been referred from another hospital, access information from the staff at that hospital to determine whether they identified suspicious aspects of the injury and whether the injury was reported to an investigating agency. If so, ascertain the number assigned to the patient’s case by the investigating agency. This number is needed for subsequent calls related to the patient.
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- Obtain a thorough family history, the patient’s medical history and the developmental capacity of the patient.
- Gather other available collateral information, e.g. medical records from other places of treatment.

plausibility of history to what is seen on physical exam (Box 61.2). It is essential that providers are familiar with child development in order to incorporate child development into the assessment process. Trust issues may interfere in obtaining a precise history. The assessment always requires an open mind for the possibility of intentional injury, which should be thoroughly investigated when clinical features are present in the history and examination. Features of the physical exam consist of identifying the pattern of burn injury, the distribution and associated features being the more important aspects to distinguish. The reported method of injury must be clearly associated with the observed pattern of injury, burn depth and appearance on physical examination (Box 61.2). Children who are burned are also in a high risk group of being subjected to other forms of abuse. Although a few studies have indicated that pediatric burn patients are at a lower risk for related fractures from abuse, approximately 18.6% of children in this subgroup had fractures on their skeletal survey. Another study found pediatric burns have a 14% risk of fractures. This rate may be underestimated since all patients did not receive a skeletal survey. These fractures are occult and may not have physical evidence of their existence. Further evidence has also revealed that children with burns are less likely to be evaluated for fractures reflecting the erroneous belief that they are a lower risk group. All children 2 years and under should receive a skeletal survey. Another study found pediatric burns approximately 18.6% of children in this subgroup had fractures on their skeletal survey. The clinician must also be mindful at this time and assess for signs of abusive head trauma such as intracranial and retinal hemorrhage.

**Psychosocial assessment**

Multidisciplinary work is essential for appropriate management of children or adult burn/abuse victims. Psychologists are critical in the initial evaluation to assist in interviewing,
perpetrator.36 Perpetrators should be allowed time to process their concerns in a non-judgmental and therapeutic manner. The family should remain informed of the process and potential Child Protective Services interventions. It is important to share with families an understanding that often Child Protective Services is seen as a punitive agency but essentially the main goal is the safety and protection of all children. Sharing information will initiate a therapeutic relationship. Most perpetrators are reluctant to trust medical teams especially when they feel as if they are being judged. Being honest about the process and the information shared with child protective services minimizes mistrust. As stated previously, perpetrators often have limited emotional support. When an intentional burn injury occurs, psychologists are an essential component to providing the initial support and addressing fears, sadness and helplessness those perpetrators may feel. Regular psychotherapy sessions are critical to making a positive change in the family dynamics.

Reporting suspected intentional burn injury

In 1967, State legislatures in every state had laws mandating that any reasonable suspicion of intentional injury be reported to the appropriate authorities.36 In 1974, the Federal Child Abuse Prevention and Treatment Act was passed. These laws require professionals to report suspected intentional injuries to a child when there is sufficient information that would lead a ‘competent professional to believe maltreatment is reasonably likely.’36 It is important to be knowledgeable of not only state laws but local governing agencies’ policies on reporting suspicious injuries. Most hospitals have risk management or legal teams that are well versed in the federal and state laws as well as the policies, rules and regulations of the hospital. Methods of communications regarding intentional injuries should be clearly outlined and reviewed prior to sharing any information regarding intentional injuries.

Providers who suspect abuse should report to the appropriate agency as designated by the state in which you practice. As you interview note interaction between caregiver and patient. Providers should document inappropriate concerns, lack of sympathy, detachment, delay in seeking care, or use of drugs or alcohol (Box 61.2). If you suspect that inconsistency exists, without being confrontational, alert caregiver and give them the opportunity to give a more truthful history. Detailed documentation of history and physical exam may be used in litigation charges and should be clear, concise and accurate. It is imperative for clinicians responsible for reporting suspected abuse to be as accurate as possible as there are significant consequences for inaccurate assessment and diagnosis of suspected abuse. Some 50% of children who sustain intentional injuries have recurrent injuries that are eventually fatal.3

Ultimately, it is not the hospital or any of the medical staff’s obligation to prove that a suspicious injury was intentional. It is important to report the suspicion and ensure continuity of care and cooperate with the legal process.3 While the child is receiving medical treatment it is imperative to keep accurate records and document all treatment and interactions among family members. The prosecuting attorney is responsible for proving intentional injuries; however, medical records are often a key element. Physician reporting and cooperation is invaluable to legal prosecution. The physician’s opinion on likelihood of intentional injury strongly influences CPS workers and prosecutors.3 Salient to remember with intentional injury cases is that most attorneys have limited to no experience with burn injuries and the expertise of medical investigators, burn psychologist and social workers are the foundation for proving allegations and protecting the child from future injuries.

There are no federal programs to specifically address reporting of suspected abuse in adults. All states have individual laws, reporting guidelines and penalties for adult abuse. It is best practice to be aware of your state laws if you work with adults but if unsure following the same guidelines as for children until the exact information can be obtained is acceptable. Most states have a statewide intake office that can be located online and most states have online reporting. The National Center on Elder Abuse provides information and assistance on elder abuse, including a listing of state elder abuse hotlines. Child Help USA is a private charity that established and maintains the National Child Abuse Hotline (800)-4-A-CHILD (800–422–4453) and provides a listing of statewide reporting numbers at their website at: http://www.childhelpusa.org/report. Telecommunications Device for the Deaf number is (800)-2-A-CHILD. The US Department of Health and Human Services Administration for Children and Families provides a listing of statewide reporting phone numbers at their website: http://nccanch.acf.hhs.gov/topics/reporting/report.Cfm.

Clinical interviewing with other vulnerable populations

When interviewing vulnerable patients, it is important to provide a safe and confidential environment that is non-confrontational or judgmental. Developing rapport and trust is an essential component of the interview process. The older adult is likely to be dependent upon the abuser in matters of daily living. Often the perpetrator is a family member or loved one. Whether the patient is able to express their emotions or not, they will likely experience fear, worry, shame, and a desire to protect the perpetrator. The therapeutic relationship developed will allow the patient to trust that the medical team will work in their best interest as well as the best interest of the perpetrator.

Maintaining professional relationships with patient and family

When approaching a child/adult who is an abuse victim, the provider must maintain professionalism, self control and remain non-accusatory. Clinicians within the healthcare profession are natural protectors of children with the desire to automatically align with the child. Addressing one’s own feelings is vital to providing the best care for the patient. Establishing a therapeutic relationship with the family may be difficult but it is imperative as many of these children are reunited with their family at discharge or at some point during outpatient burn care.
removing lids do not forget steam can burn the face or arms; wear tight fitted clothing or short sleeves; for those with mobility impairment use a sturdy, large lap tray to carry hot liquids. Microwave scald burns have risen significantly since the 1980s. Proper placement where the face is higher than the door of the microwave is recommended. Children under 7 years of age should never operate this appliance. Never heat baby formula in the microwave due to unevenness of heating. Always allow microwave cooked items to sit for 1 minute prior to opening. Prevent tap water scalds by setting hot water heater below 120°F (Table 61.2); ‘adequate and constant supervision is the single most important factor in preventing tap water scalds’ (American Burn Association); if a single faucet handle always place in cold water position; avoid sudden fluctuation of water, e.g. flushing toilet. The CDC has free material that can be downloaded from the web (/safechild/Fact Sheets/Burns-Fact-Sheet-a.pdf).

Prevention of non-accidental burn injuries is a little more difficult. Further research and education of physicians and maltreatment teams are imperative. Since the establishment of the National Burn Repository (NBR) by the American Burn Association, a Burn Registry was established to create a national database. Physicians need to recognize suspicious burns and document exam and history in detail. Further research will assist in identifying clearer indications and patterns to determine intentional injuries.

### Table 61.2 Exposure time to receive a severe burn in hot water; time and temperature relationship

<table>
<thead>
<tr>
<th>Water temperature</th>
<th>Time for a third-degree burn to occur</th>
</tr>
</thead>
<tbody>
<tr>
<td>155°F 68°C</td>
<td>1 second</td>
</tr>
<tr>
<td>148°F 64°C</td>
<td>2 seconds</td>
</tr>
<tr>
<td>140°F 60°C</td>
<td>5 seconds</td>
</tr>
<tr>
<td>133°F 56°C</td>
<td>15 seconds</td>
</tr>
<tr>
<td>127°F 52°C</td>
<td>1 minute</td>
</tr>
<tr>
<td>124°F 51°C</td>
<td>3 minutes</td>
</tr>
<tr>
<td>120°F 48°C</td>
<td>5 minutes</td>
</tr>
<tr>
<td>100°F 37°C</td>
<td>Safe temperature for bathing</td>
</tr>
</tbody>
</table>

Note: Downward adjustments to time needed for young children.


### Future burn prevention and child safety

Burns and scalds are a significant cause of morbidity and mortality in children. Some studies have shown successful counter-measures to prevent burn and scald related injuries. To prevent accidental burns the American Burn Association Scald Injury Prevention Educator’s Guide has published steps by which physicians can instruct their patients to assist in burn and scald prevention. Hot food and beverage scalds are the most common causes of scald injuries in both children and adults. Providing a safe cooking area and a supervised environment is foremost in prevention. Suggested examples are: do not carry hot liquids when carrying your child; place children in the playpen or high chair away from the stove; no child walkers; cook on back burner and remember to turn the pot handle to the inside; appliance cords kept coiled and out of reach from counter; when

### Further reading


Access the complete reference list online at http://www.expertconsult.com
References

Introduction

Advances in acute burn care during the past 25 years, in terms of decreased mortality and decreased length of hospital stay, have been truly outstanding and amazing. In 1971, survival statistics at the Institute of Surgical Research in San Antonio demonstrated an LD$_{50}$ (lethal dose resulting in a 50% survival rate) with approximately 40% TBSA (total body surface area) burn. Thus 50% of the patients with burns of only 40% died. Now, the LD$_{50}$ approaches 80% TBSA, and, if no inhalation injury is involved, patients with burn injuries greater than 80–90% of their TBSA routinely survive. In almost every burn unit in the United States, the length of stay has decreased from nearly 3 days/% burn to less than 1 day/% burn. The success can be stated simply: patients with larger, more severe burns are surviving; however, are these patients returning to society to become productive citizens? What is the real outcome of massively burned patients? Do pediatric burned patients become functional adults? How do they function socially later in life? What is the long-term effect on the patient’s families and society? Are survival and decreased length of stay really the measure of productivity for our specialty? Unfortu-
nately, the answer is clearly ‘yes’. Are we returning our patients to a society which is not ready financially, psychologically, or socially, to accept them? Again, unfortunately, the answer is clearly ‘yes’.

Although the American Burn Association has made rehabilitation a major emphasis, quality work still remains to be done. It is important and imperative that burn centers evaluate the functional outcome of a thermally injured patient. This is important not only for disability assessment but also for evaluation of our medical management. Outcome studies in the 20th century will not only emphasize survival and hospital stay but also patient satisfaction and ability to return to work. The purpose of this chapter is to review the functional sequelae and disability assessment following thermal injury.

Basic considerations: impairment, disability, handicap

The various terms such as ‘impairment’, ‘disability’, and ‘handicap’ appear in laws, regulations, and policies of diverse origin without proper coordination of the ways in which they are used.

‘Impairment’ refers to an alteration of an individual’s physiological, psychological, and anatomical structure or function that interferes with activities of daily living or a significant deviation, loss, or loss of use of any body structure or function in an individual with a health condition, disorder, or disease.2

‘Disability’, which is assessed by non-medical means, means an alteration in an individual’s capacity to meet personal, social, or occupational demands or to meet statutory or regulatory requirements or activity limitations and/or participation restrictions in an individual with a health condition, disorder, or disease.2

‘Handicap’ is independent of both impairment and disability, although it is sometimes used interchangeably with either of those terms. Under the provision
of federal laws, an individual who is defined as handicapped has an impairment that substantially limits one or more life activities, including work, has a record of such impairment, or is regarded as having such an impairment. As a matter of practicality, however, a handicap may be operationally understood as being manifest in association with a barrier obstacle to functional activity. An individual of limited functional capacity is handicapped if there are barriers to accomplishment of tasks or life activities that can be overcome only by compensating in some ways for the effect of an impairment. If an individual is not able to accomplish a task or activity despite accommodation, or if there is no accommodation that will enable the accomplishment, then in addition to being handicapped, the individual is also disabled. On the other hand, an impaired individual who is able to accomplish a task or activity without accommodation is, with respect to the task or activity, neither handicapped nor disabled. The concept of ‘employability’ deserves special attention, for, in an occupational setting, if an individual within the boundaries of medical condition has the capacity, with and without accommodation, to meet a job’s demands and conditions of employment as designed by the employer, the individual is employable and consequently not disabled. On the other hand, an individual who does not have the capacity or who is unwilling to travel to and from work, to be at work, and to perform assigned tasks and duties, is not employable.

The first critical task in carrying out a medical determination related to employability is to learn about a job, specifically the expectations of the incumbent, with respect to performance, physical activity, reliability, availability, productivity, expected duration of useful service life, and any other criteria associated with qualifications and suitability. Sufficient detailed information from a job analysis will provide a basis upon which a physician determines exactly what kinds of medical information are needed and to what degree of detail to assess an individual’s health with respect to demand criteria.

Impairment assessment

Before discussing the medical aspects of evaluating thermally injured individuals, it must be pointed out that no Social Security and Worker’s Compensation disability program medical listing exists for burns. Instead, burns must be evaluated under the appropriate body system. Often, more than one system is involved: in other words, musculoskeletal, respiratory, and skin all must be considered in the final decision. Claims must be aimed primarily at resolving the question of onset, whether the impairment can be expected to last 12 months or end in death. The medical evidence needed to document the existence and severity of a medically determinable impairment due to burns must include a history of the impairment, which describes the origin and course of the condition, dates of confinement, nature of treatment, and the claimant’s response; current objective findings such as results of examinations, laboratory tests such as blood pressure, electrocardiogram, x-rays, blood tests, range of motion, medical factual data upon which diagnoses are based; and a description of the objective findings of the claimant’s limitations and remaining capacities. In other words, how far can the patient walk, which activities cause breath or chest pain, what extent of motion is there in affected parts of the body. Regional specialized burn centers treat many serious burns annually. These centers are excellent sources of medical evidence as they maintain complete detailed records regarding the nature of an injury, treatment, complications, and prognosis. Advances in burn care have improved the survival rate in major burns. Efforts to rehabilitate these survivors and improve their quality of life represent a significant challenge for those involved in their care. The rehabilitation of these survivors is unique and multifaceted, and rarely limited to one system. Many individuals will experience some type of long-term physical impairment or mental limitation, and the rehabilitation process may take years to complete. It must be emphasized that impairments resulting from a burn are not restricted to the skin. Complications may affect any body system; thus, the examiner who is assessing individuals for disability must be attentive to the systemic sequelae of burn injury. The evaluation of a burn victim has some unique features. The necessity to consider such subjective factors as heat and cold intolerance, sensitivity to sunlight, pain, chemical sensitivity, and changes in sweating pattern, as well as the more objective considerations of decreased coordination, sensation, strength, and contracture, lends itself to a unique evaluation.

Disfigurement from scarring, a frequent sequela of burns, may not affect performance and thereby, in and of itself, causes no impairment. Scarring represents a special type of disfigurement. Again, no percentage of impairment is assigned for the existence of a scar per se; however, scars affect sweat glands, hair growth, and nail growth, and cause pigment changes or contractures and may affect loss of performance and cause impairment. Sensory deficit, pain or discomfort from scars needs to be evaluated, as well as the loss of motion of a scar area. An impairment due to disfigurement from scarring may also create behavioral or
psychological impairments which subsequently may be rated. The need for intermittent or continuous treatment of the skin with topical agents and pressure garments can impair a person’s function and needs to be considered. There is a surprising lack of published literature which relates to the impairment evaluation of a burned patient. The following are concepts which must be kept in mind when evaluating a post-burn patient for impairment and resulting deformities.

Skin

Scars and cutaneous abnormalities which result from the healing of burned tissue may represent a special type of disfigurement. Scars should be described by giving their dimensions in centimeters, and by describing their shape, color, anatomical location, and evidence of ulceration; their depression or elevation, which relates to whether they are soft and pliable or hard and indurated, thin or thick and smooth or rough; and their attachment, if any, to underlying bone, joints, muscle and other tissues. Good color photography with multiple views of a defect enhances the description of scars.

The tendency of a scar to disfigure should be considered in evaluating whether impairment is permanent or whether the scar can be changed, made less visible, or concealed. Function may be restored without improving appearance and appearance may be improved without altering anatomical or physiological function. If a scar involves loss of sweat gland function, hair growth, nail growth, or pigment formation, the effect of such loss on performance of an activity of daily living should be evaluated. Furthermore, any loss of function due to sensory pain, any sensory defect, pain or discomfort in a scar should be evaluated.

Burn scar contracture is probably the most frequently seen cause of impairment in a post-burn individual. Every burn, regardless of the depth of injury, heals with some element of contracture. Contractile forces continue long after a wound is healed and can result in severe skin shortage. Inadequate skin prohibits movement to a joint’s normal arc of motion and will influence not only the joint underlying the contracture but also those adjacent to the scar. In the early stages of development, burn scar contractures may often be corrected through the use of splints and pressure garments designed to force developing scar tissue into more normal configurations. In spite of the benefits derived from these modalities, they may also function as a type of impairment, both physically and cosmetically. Understanding the splints which individuals must wear and their limitations are important factors in the assessment of disability. Often, surgical means must be employed in order to restore function. When a surgical release of a contracture is performed, the resultant defect can be of considerable size and will require closure by means of a skin graft or flap of tissue. Burn scar contracture frequently requires a series of staged surgical procedures before optimal function and cosmesis are achieved. Recovery from surgical intervention must be followed by an extensive rehabilitation program. If an individual does not participate in a rehabilitation program, contractures will reoccur.

The definition of functional impairment should not be limited to an individual’s ability or inability to perform joint range of motion. An extremity can exhibit full active range of motion and still be considered impaired due to poor skin quality. Although much can be done to restore function, the skin is never restored to normal. Scar tissue is less tolerant of the everyday stress imposed on it than normal skin. Scar epithelium is thin, fragile, and prone to chronic ulceration. Regardless of the location, these chronic open areas will not heal and eventually require skin grafting. This type of lesion can occur at any time, even years after the initial hospitalization. Skin grafts have the same abnormalities as burn scars in that they all involve contracture formation, have loss of sweat gland function, hair growth, and altered pigment formation. Although frequently cosmetically more acceptable, skin grafts are still not normal skin. Physical limitations such as cold and heat intolerance, difficulty with sun exposure, altered sensation, or painful scars may prohibit individuals from performing their past work or other work.

Musculoskeletal

Functional limitation secondary to burn injury usually results from an anatomical alteration about a major joint. The degree to which the function of a joint is affected is greatly influenced by the amount of soft-tissue loss and the degree of pain associated with movement. Full-thickness burns, those involving all layers of skin, may also result in secondary damage to muscle, bone, tendon, and ligaments. In the acute phase of treatment of such injuries, a joint may be exposed, making it vulnerable, and susceptible to a chronic infection (osteomyelitis), instability, and arthritic changes. Ectopic calcification, the abnormal deposition of calcium around the joints, is usually seen in the elbow, but it can occur in any joint. Symptoms include pain with a significant decrease in motion. These changes in joint structure can be verified by X-ray and will require surgery at a later date for correction. Extensive soft-tissue destruction involving the loss of muscle mass, as seen in electrical injuries, will require numerous staged procedures in order to restore function. An individual may never be restored to full function and may be excluded from performing certain types of work which exist in the national economy.

Restriction of normal movement by contracture is not limited to the extremities. When a scar occurs over the trunk or anterior chest, severe and chronic postural changes can result which may cause secondary spinal deformity or altered respiratory functions. Amputations are another leading contributor to post-burn impairment. Unlike amputations which are performed for other medical conditions such as peripheral vascular disease, amputation following an extensive thermal injury will often require several staged surgical procedures in order to produce a stump capable of accommodating a prosthesis. It is also important to realize that amputations are not confined to the extremities alone but may also involve skin appendages such as the ears and nose. Complicated stage procedures using local or distant full-thickness skin or muscle-skin flaps are required in order to restore function and cosmesis in these areas. An understanding of how long it will take for an individual’s function to be restored is an important factor in deciding about the issue of disability.
Special senses and speech
Impairment to the senses of hearing or vision can occur as a result of a thermal insult, secondary to life-sustaining treatments or as a complication of a healing burn. The loss of central or peripheral vision may begin at the time of contact with a burning agent and can cause the destruction of the eyelids and damage to the cornea. A series of surgical procedures must be performed in order to create a functional eyelid. Contracture of the eyelids, more commonly the lower, may develop quickly, resulting in incomplete closure of the eyelid, and potential damage to the cornea can result in conjunctivitis or corneal ulceration. In spite of adequate surgical correction, it is common for such injured individuals to have repetitive episodes of recontracture for up to 2 years post-healing, due to ongoing scar contracture process. Perioral burns that result in lip eversion and microstomia, or contracture of the mouth, may eventually impair mastication and result in drooling as well as inhibiting an individual from producing speech which can be heard or understood. Hearing impairment due to the acute burn is rare, but there may be a loss of the external ear, or deafness secondary to the treatment of life-threatening infections with antibiotics.

Respiratory system
Burns that occur in an enclosed space, such as a building structure, often result in some form of inhalation injury to the respiratory system. Impairment may be limited to a temporary need for ventilatory support or extend to permanent respiratory disease. Chronic and recurrent respiratory infections and pulmonary insufficiency may limit an individual’s ability to perform their past work or other work in the national economy, especially when toxic chemicals or dust are present in the workplace. Exposure to irritating gases can also worsen preexisting asthma or result in irritant-induced asthma. Although this form of reactive airway disease usually resolves with time, some individuals may have persistent respiratory impairment that also may require a change in vocation in order to avoid continued exposure to irritants and exacerbation of symptoms. Furthermore, patients with severe inhalation injuries may require a tracheostomy long after the burn has healed. Closure of the stoma is often delayed for the purpose of intubation and anesthesia in future reconstructive surgeries. Pulmonary function tests are essential in determining respiratory impairment.

Cardiovascular system
A cardiovascular evaluation should include a good history and electrocardiogram. Patients complaining of chest discomfort thought to be of cardiac origin should have a more extensive work-up. There is some evidence of increased incidence of cardiovascular disease in the long-term follow-up of survivors of large thermal injuries.

Neurological system
Neurological impairment caused by a burn may be obvious at the time of admission to a burn center or become clinically apparent up to 2 years following the injury. Patients who are considered at risk include those who have sustained an electrical injury, are predisposed to stroke, or who exhibit signs of peripheral neuropathies secondary to thermal damage. Such patients should be closely monitored for signs of progressive neurological deficit. Electromyography studies will chart the development of degenerative peripheral nerve or spinal cord dysfunction. Dysfunction may be demonstrated in the form of paresis, paralysis, tremor, involuntary movement, or ataxia. Individuals who have suffered an electrical injury may develop a condition characterized by progressive degeneration of fine and gross motor coordination. Resultant complications can range from inability to perform work-related tasks safely to an inability to perform the routine activities of daily living. It is a disease process which takes place over a significant period of time, and may worsen after an individual has returned to work. In addition to the motor deficits caused by electrical injury, those individuals in whom a current passed above the level of the clavicle have a high incidence of cataract formation with the first 3 years post-injury.

Heme and lymphatic
Full-thickness or deeper burns, particularly of the lower extremities, will also cause damage to the lymphatic system. Such injured individuals often demonstrate a lack of normal lymphatic drainage, resulting in chronic edema and the development of stasis ulcers. There can be little or no improvement expected post-healing. External support in the form of elastic garments is necessary to help replace the normal activity of the lymphatic system in reabsorption of fluid. These individuals frequently have difficulty in standing for long periods of time or working in a hot and humid environment.

Digestive system
The digestive system is not usually a problem except in those individuals who have had superior mesenteric artery syndrome, cholecystitis, or peptic ulcer disease during the acute admission. The post-discharge clinical course of these individuals is never predictable; if affected individuals become symptomatic, they should be followed up by a specialist.

Genitourinary system
The genitourinary system may be a problem if deep perineal or buttock burns occurred. Aside from the obvious psychological problems, partial loss of the penis or scarring of the external genitalia may result in difficulty voiding. A badly scarred perineum or buttocks may make sitting in one position for prolonged periods painful and difficult.
Psychological

The advances of surgical techniques involving early excision and grafting as well as the increased ability to prevent infection allow many patients who would otherwise perish to face life shattered by psychological problems as a result of disfigurement. The onset of a thermal injury is a sudden and frightening experience not only to a patient but also to his family members. Because of the unexpected nature of onset, all phases of the patient’s lifestyle are abruptly changed. Often, the full emotional impact is not felt until the time a patient is discharged from the protected environment of a hospital. At this time, the reality of the emotional, physical, and financial burden of a thermal injury are apparent and must be faced. The extent to which a person can psychologically deal with his injuries varies, as do individual personalities. Each case is unique and must be evaluated as such. Studies on the psychological adjustment of survivors of burns generally reflect a biased adjustment to moderate injuries. Few quantifiable data are available concerning the psychological well-being of long-term survivors of severe injuries. Although most authors conclude that victims of burns make satisfactory adjustments, others report symptoms of the psychopathological sort which contradict this optimism. Public acceptance is an important problem facing a burn patient. Goffman, in 1963, stated that the way that burn disfigured patients have dealt with the world has generally been shown to be affected by society showing negative responses to visible scars. The burn-disfigured person has to contend with their body image as well as the attitudes of the people and the culture around them. TV and radio have altered not only family standards, but standards of self-perception as well. The young and the beautiful are emphasized. Everyone must be a ‘10’. Patients with burns, like paraplegic or quadriplegic persons, have injuries which can be seen and understood by the public; however, there is also marked ambivalence about a patient with burns as emphasized by the movie industry which has frequently characterized the evil person as being deformed. The ‘Phantom of the Opera’ is a burn victim, while ‘A Nightmare on Elm Street’ depicts Freddie Krueger as evil, deformed, and scarred. The burned patient must deal not only with his burn injury but also with society’s built-in impressions which are fostered early in life through cartoons, advertising, television, and movies. This is especially important in the pediatric burned patient for whom returning to school can be difficult, to say the least. Recent studies from the Shriners Burns Institutes in Boston and Galveston emphasize that, in pediatric patients with large thermal injuries, most children appear to be satisfied with their quality of life. This finding was especially true in children with sup

Impairment evaluation

The physical examination of a burn victim is much the same as the disability evaluation for any patient. With the information gathered from the history and physical examination, and using the tables in the American Medical Association’s Guide to the Evaluation of Permanent Impairment, 6th edition, the physician can arrive at an impairment rating. In addition to the usual range of motion form, a questionnaire regarding the special problems related to burns is useful (Table 62.1). The 6th edition of the American Medical Association’s Guide to the Evaluation of Permanent Impairment is changed from the previous editions in the following ways.

Standardized methodology is applied to each chapter to enhance the relevancy of impairment ratings, improve internal consistency and promote ease of application to the rating process. This ordered method enables busy physicians to become proficient with the ratings for multiple organ systems and anticipate how each chapter is organized and assimilates information.

The 6th edition applies both terminology from and an analytical framework based on the International Classification of Functioning, Disability and Health (ICF), to generate five impairment classes which permit the rating of the patient from no impairment to most severe. A diagnosis-based grid has been developed for each organ system. The grid arranges commonly used ICD-9 diagnoses within the five classes of impairment severity, according to the consensus-based dominant criterion.

Using the latest evidence in diagnosis and clinical tests, the 6th edition offers the following key features:

- Standardized approach across organ systems and chapters
- Expanded use of diagnostic approach to help physicians consider relevant clinical tests and patient outcomes in performing the rating
- Required clinical information needed to rate a given condition
- Clear step-by-step grading instructions in each chapter to promote consistent scoring of impairment ratings and to improve physician consistency
- Simplified methodology presented between chapters
- Contemporary, evidence-based concepts and terminology of disablement from the ICF
- The latest scientific research and evolving medical opinion provided by nationally and internationally recognized experts
- More comprehensive and expanded diagnostic approach
- Transparent process to allow the evaluator to document functional assessment, clinical tests and physical findings
- Uniform grids to help physicians calculate impairment ratings.

It is helpful to have members of a rehabilitation department, namely physical therapy and/or occupational therapy, be familiar with this evaluation. A combined approach with either an occupational therapist or a physical therapist to evaluate actual objective determination such as range of motion, and a burn surgeon performing the subjective rating
Total Burn Care

Class 2 impairment of the whole person is 11–27%. Skin disorder signs and symptoms are present >30–60% of the time AND often require treatment with topical or systemic medications AND when signs and symptoms are present, there is minimal interference with ADLs.

Class 2 impairment of the whole person is 11–27%. Skin disorder signs and symptoms are present >30–60% of the time AND often require treatment with topical or systemic medications AND when signs and symptoms are present, there is minimal interference with ADLs.

Class 3 impairment of the whole person is 30–42%. Skin disorder signs and symptoms are present >60–90% of the time AND require intermittent to constant treatment with topical or systemic medications AND when signs and symptoms are present, there is mild interference with some ADLs.

Class 4 impairment of the whole person is 45–58%. Skin disorder signs and symptoms are present >90% of the time AND require treatment with topical or systemic medications on a regular basis AND there is severe interference with most ADLs to the extent that confinement may be required.

The impairment evaluation is somewhat subjective; however, individual patients can be placed into various categories. The final impairment rating is a combination of the

<table>
<thead>
<tr>
<th>Table 62.1 Patient questionnaire related to burn sequelae</th>
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<tbody>
<tr>
<td>Decreased sensation</td>
</tr>
<tr>
<td>Heat intolerance</td>
</tr>
<tr>
<td>Cold intolerance</td>
</tr>
<tr>
<td>Sensitivity to sunlight</td>
</tr>
<tr>
<td>Sensitivity to chemicals</td>
</tr>
<tr>
<td>Restricted chest motion</td>
</tr>
<tr>
<td>Restricted abdominal motion</td>
</tr>
<tr>
<td>Loss of hair</td>
</tr>
<tr>
<td>Loss of nails or malformed nails</td>
</tr>
<tr>
<td>Dysesthesias</td>
</tr>
<tr>
<td>Hypopigmentation</td>
</tr>
<tr>
<td>Hyperpigmentation</td>
</tr>
<tr>
<td>Drug use</td>
</tr>
<tr>
<td>Increased alcohol use</td>
</tr>
<tr>
<td>Donor site scarring</td>
</tr>
<tr>
<td>Approximate body surface area of donor</td>
</tr>
<tr>
<td>Gastric pain</td>
</tr>
<tr>
<td>Joint pain</td>
</tr>
<tr>
<td>Tearing, photophobia</td>
</tr>
<tr>
<td>Decreased vision</td>
</tr>
<tr>
<td>Shortness of breath</td>
</tr>
<tr>
<td>Lack of endurance</td>
</tr>
<tr>
<td>Hoarseness or other vocal cord problem</td>
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</tbody>
</table>

for the skin or psychological status, is useful. The objective measurements due to restriction of active motion and amputations are well outlined in the Guide to the Evaluation of Permanent Impairment. The techniques of measurement are simple, practical, and scientifically sound. For the examination of upper and lower extremities, a large and small portable goniometer are used. The upper extremity, lower extremity, the spine, and the pelvis are considered a unit of the whole person; and tables are available in the manual to determine impairment ratings of the whole person. The subjective rating for skin or psychological determination is not precise. The criteria for evaluating permanent impairment of the skin are divided into five classes and are different from previous editions of the Guides to the Evaluation of Permanent Impairment:

Class 0 impairment of the whole person is 0%. Skin disorder signs have been present in the past but are currently present <1% of the time AND no medication is necessary AND there is essentially no interference with activities of daily living (ADLs).

Class 1 impairment of the whole person is 1–9%. Skin disorder signs and symptoms are present 1–30% of the time AND may intermittently require treatment with topical medications AND when signs and symptoms are present, there is minimal interference with ADLs.

Class 2 impairment of the whole person is 11–27%. Skin disorder signs and symptoms are present >30–60% of the time AND often require treatment with topical or systemic medications AND when signs and symptoms are present, there is minimal interference with ADLs.

Class 3 impairment of the whole person is 30–42%. Skin disorder signs and symptoms are present >60–90% of the time AND require intermittent to constant treatment with topical or systemic medications AND when signs and symptoms are present, there is mild interference with some ADLs.

Class 4 impairment of the whole person is 45–58%. Skin disorder signs and symptoms are present >90% of the time AND require treatment with topical or systemic medications on a regular basis AND there is severe interference with most ADLs to the extent that confinement may be required.

The impairment evaluation is somewhat subjective; however, individual patients can be placed into various categories. The final impairment rating is a combination of the

<table>
<thead>
<tr>
<th>Table 62.1 Patient questionnaire related to burn sequelae</th>
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<tbody>
<tr>
<td>Decreased sensation</td>
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<tr>
<td>Heat intolerance</td>
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<tr>
<td>Cold intolerance</td>
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<tr>
<td>Sensitivity to sunlight</td>
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<tr>
<td>Sensitivity to chemicals</td>
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<tr>
<td>Restricted chest motion</td>
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<tr>
<td>Restricted abdominal motion</td>
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<tr>
<td>Loss of hair</td>
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<tr>
<td>Loss of nails or malformed nails</td>
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<tr>
<td>Dysesthesias</td>
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<tr>
<td>Hypopigmentation</td>
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<tr>
<td>Hyperpigmentation</td>
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<tr>
<td>Drug use</td>
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<tr>
<td>Increased alcohol use</td>
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<tr>
<td>Donor site scarring</td>
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<tr>
<td>Approximate body surface area of donor</td>
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<tr>
<td>Gastric pain</td>
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<tr>
<td>Joint pain</td>
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<tr>
<td>Tearing, photophobia</td>
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<tr>
<td>Decreased vision</td>
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<tr>
<td>Shortness of breath</td>
</tr>
<tr>
<td>Lack of endurance</td>
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<tr>
<td>Hoarseness or other vocal cord problem</td>
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actual objective determinations and the subjective rating for skin and psychological impairment.

Functional outcome

Outcome from thermal injury depends upon many factors other than severity of illness; this may include social status, family support, and patient motivation. A determination of impairment combined with disability is an excellent modality to determine outcome. Presently, we perform formal impairment ratings only when asked by insurance companies, social security, worker’s compensation, or the legal system. With emphasis on continuous quality improvement and insurance companies evaluating care by outcome determinations, it is important for burn surgeons to document their outcome. Impairment ratings are time consuming; however, they are an excellent way to evaluate outcomes of care. A systematic approach to evaluating outcomes in this manner should be initiated.

Summary

Disability determination is a difficult and by no means objective procedure. It is not within the scope of this chapter to present all the possible complications and resulting impairments secondary to burn injury. There are certain concepts which must be kept in mind when evaluating a post-burn patient for impairment and resulting deformity. Most burn injuries which are significant enough to require admission to a specialized burn care facility will likely result in some type of temporary or permanent disability. Concepts unique to burn patients:

- The most common complications arise from burn scar contracture and cosmetic deformity, and will require staged surgical procedures for correction.
- Rehabilitation may take several years to return a patient to an acceptable level of functioning.
- Post-burn cosmetic deformity needs to be confined to areas which are socially acceptable.
- Resulting disabilities are not proportional to the extent of cutaneous injury.
- Certain complications, such as neurological degeneration, may not arise until a few years following an injury and are fairly unpredictable.

Many burned patients will have limitations which, individually, fall short of the criteria needed for evaluating disability. It is important to evaluate the comprehensive result of all limiting factors in order to accurately assess the level of disability.

Further reading


References


Cost-containment and outcome measures

Juan P. Barret

Introduction

Medicine is a continuous evolving science. Several developments in medicine and burn care have occurred during the last 6 decades, but so has the increase in financial costs of this delivery of care. The nature of burn injury requires the participation of many different specialties, thus leading to the development of ‘burn teams’ and ‘burn centers.’ The result of such collegial effort is state-of-the-art burn care that gathers well-trained personnel with ultimate technology. The complexity of burn care in the context of the current health economic era has made outcome measurement, quality assurance, and cost-containment in the burn unit extremely important components of burn care. Current financial restraints, objectivity of limited economical resources, and in-depth critical evaluation of the provision of health in modern society make evidence-based burn care mandatory. Unfortunately, the continuous appraisal that this new approach has introduced in current medicine evidences the lack of available data in many, otherwise, widely accepted therapies.

The present chapter gives an insight into the relevance of outcome measurement as an objective reflection of the quality of care that is provided in burn centers. The development of quality assurance programs and the provision of evidence-based burn therapy are necessary to maintain excellent outcomes, while improving cost-containment. How programs of quality assurance function and how costs are contained with overall improvement of the quality of care are explained below.

Socioeconomic impact of burns

The first step for any system for self-evaluation and control is the recognition of the scope of the problem being evaluated. Knowledge of the incidence, prevalence, and all relevant data of the disease or condition investigated is necessary to put the health impact into perspective and to determine the background from which all interventions are instituted, and audit their performance.

Burn injuries continue to plague the economic systems of both developed and underdeveloped countries. In developed countries, severe disabilities secondary to burns produce significant financial losses; in the developing world, loss of life from burns is extremely high. The death toll is highest at the extremes of age; young adults more frequently survive with disabilities that truncate their production in society. Minor burns represent economic loss in the form of sick leaves, and their sequelae sometimes interfere with the productivity of the victim. Survivors of massive burns are more prone to develop long-term sequelae, and consequences to their families and to society can be devastating.

The overall incidence of burns in developed countries is still relatively high, while the numbers of persons who die from burns is remarkably low. It is reported that 820/100 000 persons per year are burned, with 30/100 000 persons per year requiring specialized treatment. Admissions to burn centers account for 6.5/100 000 persons per year. The gross burn mortality in developed countries (people who die at the scene of the accident plus people who die in specialized units) is only 0.6/100 000 persons per year. LD50 (the body surface area burned that kills 50% of people) in the pediatric population and in young adults is over 90% total body surface area (TBSA) full-thickness burns, and over 40% TBSA full-thickness burns in the elderly. Burn mortality indices under 4% are common among inpatient populations.

The social cost of minor burns in developed countries is significant. In Western Europe, these costs, including the loss of production at work of the individual, social security cost, and the cost of the entire treatment is around 7000 Euros. For severe burns, social costs are much higher and are to be estimated over 40 000 Euros per patient. These are underestimates because the true social costs of long-term disabilities resulting from burn injuries are not yet well determined.

The world estimate is more dismal. World statistics put burn injuries to the level of a major health problem. Burns described as ‘minor’ in developed countries produce severe disabilities or even death in developing countries. There are more than 150 000 fire deaths every year in the world, and approximately 30 000 000 people in the world require admission to specialized units. In developing countries, survival of patients with burns over 40% TBSA burned is minimal.

Outcome measures

Outcome measures are the cornerstone of cost-containment and continuous quality improvement in any given health system. They serve to evaluate what works and what does not, they are used for research and for the improvement of clinical practice and to provide higher quality care in a cost-effective manner.
For a long time, burn mortality has been considered a major outcome measure of the quality of burn care. Improvements in burn mortality, though, have produced a change in the expectations of burn care providers. No longer is survival per se a sufficient outcome measure; mortality is being questioned as a true outcome measure in current burn practice, but psychosocial adaptation and physical rehabilitation are of prime importance. The need for some supportive services, therefore, may extend throughout the patient’s lifetime.

Paralleling the development of modern societies, outcome measurements in healthcare systems focus more on rehabilitation and quality of life than on raw incidence, prevalence and survival rates. When this principle is applied to trauma and burn care systems, there are four main outcome measurements that are to be considered:

1. Burn mortality (raw and relative mortality);
2. Length of stay (LOS);
3. Modulation of the hypermetabolic response;
4. Quality of life.

**Burn mortality**

Survival is still one of the major outcome measures in burn centers. It is the most frequently used measure because data is easily retrieved and easy to compare among different centers. Although every burn center has its own particular limitations, it is clear that there exists a minimum standard of burn survival (i.e. LD50 of 90% TBSA burned in children and young adults) that should be met given the social and economic situations provided. In order to achieve the minimal standards of care, it is important to analyze the comparability of results of every burn center. Local geographic and social parameters vary, thus the generation of models of probability of death or probit analysis with statistical logistic regression has proven useful for surveying the outcome of burn victims (Fig. 63.1). It has the benefit of comparability, but it presents also the benefit of internal control of the burn center, since the logistic model represents the standard of care for that given center. Ideally, the probability of survival should increase with time, reflecting the continuous improvement of the quality of care. The responsibility of the burn team is to continuously improve those results and generate new revised models of probit analysis. The advantage of this analysis is that it includes all the particular social and economic situations of the local geographic area, and on the other hand it is comparable with the results of other centers. One of the main disadvantages is that the prediction is based only on age and TBSA burned.

Other indexes, such as the abbreviated burn severity index (ABSI), includes the patient’s sex, depth of the injury, and inhalation injury as risk factors that determine the severity of the burn, achieving a more accurate predictive factor. If additional factors are considered, such as pre-existing disease or the abuse of toxic substances, the specificity and sensitivity of the predictors improve. However, even though survival after burn trauma is one of the primary objectives of burn centers, raw mortality and relative mortality (mortality index corrected per age and sex groups in the general population) are no longer the only outcome measures in burn health systems.

![Figure 63.1](image_url)

Likewise, the performance of any given burn centre has to be analyzed. Probit analysis, subgroup mortality audit, catheter related bacteremia, nosocomial pneumonia, urinary sepsis, and multiple resistant organism outbreaks are some of the data to be monitored overtime.

**Length of stay (LOS)**

Length of stay (number of days admitted to hospital) is a relevant indicator for hospital administrators. It is a direct indicator of cost of treatment and its relevance applies to all patients, regardless their final outcome. As pointed out by Pereira et al., data on burn survival have been available for decades, but less information has been published on LOS. Length of stay is an indirect indicator of morbidity (uncomplicated patients should leave hospital sooner than complicated patients), although it must be interpreted with caution. Patients may stay longer for rehabilitation despite being healed completely, or, conversely, patients may be discharged home and readmitted soon after as rehabilitation patients to change insurance coding and reimbursement. The best way to standardize LOS to allow easy access and comparison is to express it as a function of burn size (days/%TBSA). It can be then used as an efficiency indicator of burn care provided, with the ratio below 1 (<1 day per 1% burn) as a goal for burn treatment. However, it works very efficiently and as a good comparison method for massive burns, but it can produce important bias when considering small burns with specific locations (hands, face, genitalia, feet); depths (deep burns requiring flaps), or age (pediatric or geriatric population). We have to assume that certain populations will stay longer than the ‘ideal’ ratio and administrators and insurance companies should be aware of that.
Modulation of the hypermetabolic response

Burn patients exhibit a florid inflammatory and hypermetabolic response that is more intense and prolonged than the response of similar critical care and trauma patients. The metabolic rate of a burned person is twice that of an injured one. It causes a hyperdynamic circulatory response with increased body temperature, oxygen and glucose consumption and carbon dioxide production, glycogenolysis, proteolysis, lipolysis and futile substrate cycling. This will lead to wasting of lean body mass, muscle weakness, immunodepression and poor wound healing. It has been an area of intense research in the past 2 decades, and the modulation of this response and the maintenance of lean body mass, a competent immune system, and muscle tone and strength are current outcome measures that can be quantified during hospital course and late in the recovery phase. They are important end-points that indicate the efficacy of the treatment received and predictive tools for the assessment of new therapeutic interventions. Furthermore, the modulation of the hypermetabolic response is one of the few areas in burn care with evidenced-based data. How to measure this response and strategies for modulation and abrogation of the catabolic effects of burn injury can be found elsewhere in relevant book chapters.

Quality of life

The grade of disability and the quality of life achieved by burn survivors are also considered main outcome measures. In modern society, it is not only survival that is important, but also the quality of life achieved. Survival at any price may lead to subtotal or total disability, which may or may be not acceptable for all persons. The latest reports of psychosocial adaptation of patients surviving severe or massive injuries show an optimal response and adaptation in society. Moreover, most burn survivors achieve social adjustment that is within normal limits. Physical disabilities are certainly common and so is change in body image acceptance. Location of the injury (hands, face, etc.) and background personality and premorbid psychological status are also extremely relevant for coping with the new situation (Box 63.1).

The physical examination of a burn victim is much the same as the disability evaluation for any patient. With history and physical examination, and using the tables of the American Medical Association’s Guide to the Evaluation of Permanent Impairment, a rating of impairment can be made. The techniques of measuring, although complex and time-consuming, are practical and scientifically sound. A combined approach, with an occupational or physical therapist who makes the objective determination of physical impairment and a burn surgeon who makes the subjective determinations, is advisable; and, once thorough assessment has been performed, the patient will be placed in one of the categories for permanent impairment and disability (Box 63.1). Impairment and disability assessments are most relevant for insurance companies, social security, worker’s compensation, and the legal system. Since the burn team is not only responsible for the acute care, but also for continuous quality improvement and the evaluation of outcome characteristics, disability determination is an integral part of modern burn care. Only with such evaluation can the quality of outcomes be improved.

Although disability and impairment assessment is one of the main outcome measures, it alone does not describe the quality of life that patients achieve after burns are healed and all formal treatment is finished. One of the measures that adapts to healthcare systems is the Quality Adjusted Life Years (QALY) introduced by Torrance in 1986. One QALY is a measure of all benefits of health treatment that include increase in life expectancy and enhanced quality of life. The increase in life expectancy is measured in number of years, while quality of life is measured in a scale with a maximum of 1 (perfect health). In this scale, 0 corresponds to death. There are negative numbers, since there are health situations that are considered by patients to be worse than death. The QALY are, therefore, the number of years with perfect health which are also compared to the number of years lived in a specified state of health. For example, if a person lived for 70 years in perfect health and died, they would accomplish 70 QALY. Conversely, if a person lived 45 years in perfect health, and then acquired chronic renal failure, with a quality of life of 0.4 and died at age 70, they would accomplish 55 QALY [45 QALY+25(0.4)]. There are two sorts of methods to calculate QALY, the ‘standard gamble’ and the ‘time trade-off’. The second method is the simplest and the most used. Patients are confronted with two situations: the situation of disease and/or sequelae for t years and the situation of perfect health for x years followed by death. The utility of any treatment of a chronic condition is represented by x/t. Life expectancy under a certain chronic condition is compiled from medical literature. This time is converted to QALY under perfect health, and the risks of the medical treatment are then evaluated in terms of the effectiveness in producing QALY.

When QALY are applied to burn patients, it is easy to assume that the treatment of severe injuries, which will result in death without treatment, will produce an important number of QALY. Nevertheless, many burn injuries heal with sequelae, so that the quality of life achieved is not that of perfect health, but sometimes quite less than that. Patients that survive life-threatening injuries acquire a high number of years in terms of life expectancy, whereas the total number of QALY is often less than the optimal number. This is
confusing since the overall assessment of quality of life that burn patients express in the long run is usually higher than expected.2,3 One of the main problems of QALY assessment as a measure of cost-efficacy and cost-utility is that patients tend to make a short-term estimation of life expectancy and quality of life.22 Burn sequelae are more dramatic in the first months and years after the injury, resulting in a low estimation of QALY.

The overall assessment of quality of life has to include few core domains, which, as a whole, gather more information on how we do perform in quality of life issues and on how this is appreciated by burn survivors; these domains, aside from perceived quality of life, include psychological function (including pain and sensory alterations), skin integrity together with neuromuscular function, and physical role function (disability scoring). Unfortunately, the quality of life and the quality of delivery of healthcare perceived by patients often differs from that assumed or measured by health-careers and providers.

Other widely used tools are the Short form 36 (SF-36),21 which measures global reintegration and socialization and the Vineland Adaptive Behavior Scales-Survey Form,22 which measures a broad range of functioning in communication, daily living skills, socialization, and motor skills.

Burn specific measures that are also helpful in categorizing the status of health in burn survivors and their appreciation of such recovery are the Burn Specific Health Scale (BSHS), the Coping with Burns Questionnaire (CBQ), and the Satisfaction with Appearance Scale (SWAP).

**Cost-containment in the burn unit**

Over the last 2 decades, there has been a continuous change and evolution in health economy. The continuous increase in world population has been joined with an increase in life expectancy, which, along with the decrease in births has led to an increase in the mean age of population. This is particularly true in developed countries where the population pyramids have reversed their shape. The increasing population of ‘elders’ (along with the economic crisis and the expected increase in costs of healthcare technology and specialists) has provoked an exponential increase in health costs. Economical analysis and cost-containment with an emphasis on cost-efficacy and cost-utility are principal pillars of health economy.

Assessing the maintenance of good outcomes assures that all economic efforts invested in burn centers produce the expected benefits with a positive cost-efficacy effect. Our resources in contemporary society have become limited, so the best outcomes with good cost-efficacy and cost-utility ratios are essential. It is clear that insurance companies and society seek healthcare systems where less investment still results in the best outcome. It is particularly true in burn centers; reimbursement will peak in centers that provide the best functional outcome in a standard period of time. Contracts flow when good return to productive life is achieved.

In order to maintain a dynamic and viable center, a cost-containment program must be instituted. These programs are defined as all measures directed to produce the best cost-efficacy and -utility ratios, i.e. to maintain costs within expected margins and optimize burn care providing the best outcomes. The main steps of cost-containment programs are:

1. Data acquisition, quality assurance, and outcome measurement
2. Treatment protocols
3. Optimization of resources

**Data acquisition, quality assurance, and outcome measurement**

The first step to control costs in burn centers is the development of a QA program to include data acquisition and outcome measurement. The flow of economic efforts is then bi-directional, from society to patient care and from burn centers to society. All investments made in the burn center are returned to society in the form of excellent outcomes and social reintegration. On the other hand, the knowledge of the most recent outcome figures for the burn unit alert the burn team to know the point of futility of treatment. Expensive efforts to save patients whose burn injuries are fatal increase costs exponentially, decreasing the resources available for other burn patients. It is particularly true in developing countries, where all efforts need to be concentrated only in those patients who will survive.

However, the equal responsibility of the burn team to improve the outcome of burn patients mandates that they push ahead to achieve better survival and better quality of life for their patients. The line that separates futility from constant improvement is vague. The only way to define it and to improve outcomes without increasing futile efforts is with burn research. Experimental and clinical burn research produces new data, which, after critical evaluation of results, will impact and change clinical protocols and pathways.

**Quality assurance**

Quality assurance (QA) means a critical appraisal of data collected in the specific system to give assurance to users and to healthcare providers that quality is achieved. Such appraisal should also result in better management, lower complication rates, and better outcomes. The essence of QA is the idea that real quality improvements involve the continuous search for opportunities for all processes to get better.23 Quality assurance is essential in the modern healthcare system where cost-containment and cost-efficacy are primary end-points. QA programs provide data to support requests for funding of burn patient care at an appropriate level. They are primordial to suffice the minimal requirements that are to be met by burn centers in order to be endorsed by national societies and state agencies.

The standard QA program is depicted in Figure 63.2. All members of the multidisciplinary burn team (Box 63.2) join together to satisfy common goals and to target all possible problems encountered in day-to-day work. Should problems arise, an assessment is made; and committees are organized to respond if such a formal response is needed. Actions are carried out in order to solve the problem, and the results of such actions measured. When responses are shown to be effective, the actions and changes in protocols are sustained. Otherwise any new problem that was encountered with the process is targeted for improvement, and actions carried out to address those problems.
Developing a functional QA program requires the production of clinical protocols and critical care pathways. Although time-consuming at first, this planning saves much time in the long-term. Members of the burn team are well acquainted with clinical protocols that begin at an exact time point during patient care. Time points, red flags, and self-stopping parameters are necessary. Protocols are essential for a QA program, since deviations from protocols are easily detected, facilitating evaluation and assessment of the deviations.

Clinical indicators of the overall performance of the unit must be established. It is the responsibility of every member and every department involved in the burn care system to provide the burn team and the QA program with indicators of the well-functioning unit, essentially defining what the unit would be if everything performs properly. Deviation from these performance goals are detected and included in the evaluation system. Outcome measures are main clinical indicators of the performance of the burn unit as a whole and should be evaluated periodically. Changes in outcomes must be evaluated carefully to detect any malfunction or deviation and develop an appropriate action. Mortality, probit analysis, disability, and quality of life are outcome measures that need to be surveyed constantly. Every specialty involved in burn care must develop their own specific outcome measures that contribute to overall outcome in order to assess, maintain, and constantly improve their contribution to care. Examples of these secondary outcome measures are graft take, pain control, or infection control.

At the Shriners Burns Hospital in Galveston, Texas, QA staff members are active and indispensable members of the burn team. Their constant surveillance helps burn patients and burn team members by assisting to develop protocols and by monitoring achievements according to protocols. They promptly detect deviations so that adequate action can be immediately taken. Their effort assures that no variables will be left to flow without control, so the expected outcome will result. The author finds QA staff to be important back-up aids in helping to prevent unwanted surprises.

Finally, QA programs help to maintain cost-efficacy in the burn center. By maintaining outcomes, the investment that society and insurance companies make in the expensive treatment of burn patients is rewarded by provision of state of the art treatment and excellent outcomes. Documentation of such standard of care should result in reimbursement and funding that are maintained if not increased.

Evidence-based medicine in burn care

As it has been outlined in previous sections, there has been a burst in wound technology, critical care, and biotechnology during the past 2 decades. It is not uncommon to be confronted on a daily basis with new technology, pharmaceutical novelties, and expensive new treatments. There has been an exponential improvement in burn care when we compare current survival outcomes with those published 30 years ago. However, paralleling this exponential improvement there is an escalation in treatment expenses, which is not always accompanied by clear data supporting the use of such new technology. In the new era of healthcare, we are confronted with the necessity of providing state of the art burn care while containing burn care expenses. The answer to this ethical and pragmatic dilemma consists in the rationalization of treatment provided supported by clear outcome data. Evidence-based medicine plays a central role in this model of new healthcare, and consists in the provision of treatment based on clear protocols supported by data that warrants cost-efficiency of the therapy used.

Unfortunately, few treatments are evidence-based in burn care, and, most surprisingly, some evidence-based burn care that presents with strong data supporting outcome are not followed by burn practitioners. The basis of care should be that simple things should always be performed well.’ It is not always so, and even in pre-hospital medicine and accident retrieval, we find important differences throughout the world, despite being important outcome data supporting what should be done in the accident scene and transport.

Another of the few areas where evidence-based burn care has exploded is resuscitation of burn shock. Resuscitation end-points and monitoring strategies have produced data determining when futility of treatment has been reached, by shifting from fluids and urine-output to adequate end-point monitoring, edema control, adjuvant therapies, and tissue perfusion and oxygenation. This suggests
that traditional methods of monitoring are not supported by scientific data, and should be replaced by constant physiologic monitoring.\textsuperscript{26,27} However, despite emerging data on the necessity of shifting to a more monitor based resuscitation, most burn centers in the world continue to resuscitate based on tradition and old resuscitation formulas. Similar behaviors are encountered in the use of human albumin solutions and hyperbaric oxygen treatment. Strong epidemiological data suggests an increase in mortality with the use of albumin among patients with burns,\textsuperscript{28} and the beneficial effect of hyperbaric oxygen in several surgical conditions is an evidence-based therapy.\textsuperscript{29} In spite of all this data, albumin is liberally used, and few facilities use hyperbaric oxygen therapy. Further evidence exists on the use of diagnostic technology (laser Doppler imaging),\textsuperscript{30} external pulse shock wave therapy,\textsuperscript{31} alternative wound covers,\textsuperscript{32} etc. However, few centers use this technology, despite the existing data that supports their efficacy. It seems that tradition and personal belief is stronger than evidence-based therapy in the burn community. A shift in burn treatment towards evidence-based practice is necessary to become cost-effective and provide optimal care.

Treatment protocols and rationalization of pharmaceutical costs

State of the art technology, pharmacological treatments, and skin substitutes are at the top of the price ladder in health treatment. A judicious and clear use of these technologies is clearly indicated for such costs to provide benefit. Clinical protocols and critical care pathways are essential elements to control costs. Protocols and pathways are tools developed after consensus conferences over treatments and diagnostic tests. Experts review the quality and effectiveness of these treatments and techniques, and a consensus is generated about the rationale for the use of old, current, and new technology.\textsuperscript{33} Consensus declarations are included in clinical pathways. In this way, well thought-out methodology with predicted costs is used to generate outcomes. If no deviations are made and new techniques are not tried without thoughtful consideration, the overall costs of the burn center are contained – provided the annual number of admissions is maintained.

The introduction and testing of new techniques need to be carried out within well-controlled research protocols, and all results need to be critically reviewed. New treatments must be tested versus the standard of care at any given time, and results compared. When better outcomes are achieved with good cost-efficacy results, the new treatment protocol can be general and become standard. As an example, advances that were possible thanks to research supported by the Shriners of North America are prompt eschar excision and immediate wound closure, pressure garments, fluid resuscitation, bacterial translocation control, early enteral nutrition, and improvements in inhalation injury treatment among others. This research was conducted as a comprehensive program of experimental research followed by clinical application in clinical research protocols. Positive results were then applied to routine clinical protocols improving standard patient care.

Cost-containment, besides QA programs and clinical protocols, is based in rationalization of pharmaceutical costs and optimization of resources. More than 60\% of all costs in burn centers result from the use of topical and systemic treatments, as opposed to costs in some other surgical subspecialties, including plastic surgery. The utilization of these expensive treatments should follow evidence-based guidelines and strict clinical protocols. However, decisions so as to whether a specific treatment ought to be used or not are not based solely on economic reasons. Prospective cost-efficacy research nursing and medical trials are nowadays key elements in modern burn centers. In such manner, limited resources are tested against standards of care. The impact of topical treatment expenses, specific hospital stay for that given treatment, human resources implications (i.e. nursing requirements), and quality of delivered care in terms of wound healing and patient satisfaction is taken into account. Decisions are then made based on clinical results of best practice together with the excellency of patient-delivered treatment.\textsuperscript{32}

Optimization of resources

The optimization of resources begins with the organization and calculation of burn unit requirements. In order to calculate the number of personnel required to treat all burns in a determined area, the method of necessity is very helpful. To determine the desired number of personnel (RT), one must obtain the catchment population (P), the incidence of burns (I) in persons/year, the number of hours of treatment per day (A), the mean hospital stay in days (L), and the mean number of hours that personnel work in the burn unit (W).\textsuperscript{35} The basic formula is as follows:

$$RT = \left[ \frac{P \times I \times A \times L}{W} \right]$$

For example, in a geographic area with a population of 5 million people, a raw burn incidence (patients admitted to the burn center) of 6.5/100,000 persons per year, and 1 admission/patient per year, a mean hospital stay per patient of 16.5 days with full-time (40 h/week) personnel working a total of 1960 h/year to provide continuous care of a patient per 24 h, the total number of personnel required for the complete treatment of burn patients is 65.6, calculated as follows:

$$RT = \left[ \frac{5000000 \text{ people} \times 6.5/100000 \text{ persons/year} \times 24 \text{ h} \times 16.5 \text{ days}}{1960 \text{ h}} \right] = 65.6$$

The number of beds (NB) dedicated to burn treatment is based on the incidence of burn injuries (I), the mean hospital stay (L), and the ideal index of admissions (IO) estimated as 0.85 (85\% of beds used for burn treatment, 15\% of beds unoccupied),\textsuperscript{36} resulting in:

$$NB = \left[ \frac{I \times L}{365 \times IO} \right]$$

When this formula is applied to the same example, the number of beds required are 17.3 beds for a geographic area with 5000000 population and a burn incidence (admissions to burn center) of 6.5 per 100000 persons/year:

$$NB = \left[ \frac{5000000 \text{ people} \times 6.5/100000 \text{ persons/year} \times 16.5 \text{ days}}{365 \times 0.85} \right] = 17.3$$

Although all parameters are well known for all countries and the theoretical burn care needs can be calculated with
them, it is common knowledge that burn incidence and the index of admissions suffer important oscillations throughout the year. The calculation of an optimal burn center occupation at 0.85, which is the index for optimal outcome and cost-efficacy. Even though it does not affect the actual function of the burn center (it does affect it if the index is calculated at 1, with periods of bed occupation over 100%), it makes an important impact in cost-containment, since the maintenance of a full functioning burn center with minimal admissions lowers cost-efficiency, and may produce an important financial loss.

In order to optimize the index of occupation of the burn center, and maintain it at 0.85, it is possible to admit patients at the burn center who present with a spectrum of injuries suitable for treatment at the burn center. Given the nature of burn injuries, the burn team is capable of managing patients with a spectrum of trauma and extensive cutaneous or soft-tissue losses. Box 63.3 lists all patients suitable to be treated at the burn center. It must be borne in mind, however, that the burn center is a super-specialized unit created for the care of burns, and that, as such, it may be the only facility for such injuries in that particular area. It is imperative to reach a balance between optimal function and cost-containment with optimal treatment of burn injuries. To achieve that, a set of priorities have to be created for admission to the burn center so the treatment of other injuries and patients do not challenge the admission of severe burn injuries. In Box 63.4, all patients suitable for treatment in the burn unit are divided into three types of priorities. Priority 1 patients include all burn patients whose injuries are categorized as major injuries by ABA standards. These patients have priority over all other patients. Patients included in priority 2 are patients who may be treated in other specialized units of the hospital, but also can be treated with the same standard of care in the burn unit and will benefit from care by the burn team. These patients are admitted on a bed availability basis, with the main idea of maintaining an optimal IO. Patients included in priority 3 are patients who do not present with acute injuries but who may benefit from treatment in the burn center. These patients are admitted as elective cases.

Other programs of cost-containment that are very effective in maintaining low costs and improving the quality of care are programs to optimize human resources and programs of day care. Human resources in the burn center can be optimized by planning nurses’ shifts. Morning shifts are usually the busiest and 8-h shifts are the most effective. Therefore, morning shifts can be scheduled with the largest number of nurses, while afternoon and night shifts can be staffed by fewer. On the other hand, nurses’ shifts with flow capabilities increase the overall performance of personnel in the burn center. Personnel that can staff the nursing wards, outpatient clinics, and social services provide more freedom in the organization and optimization of resources, diminishing costs in the burn center.

Another important change in modern healthcare is the development of day-care programs, i.e. major wound care on an outpatient basis and day surgery. Both types of programs diminish the need of admission to the burn center, thereby decreasing costs and increasing performance. This also allows the treatment of other injuries in the burn center, which increases reimbursement via third party payers and via the budgets of other departments. Patients who present with burn wounds, even large wounds, who do not need admission for other causes and whose injuries at not at risk of infection at home may be treated as outpatients with daily or periodic dressing changes in the day-care unit of the burn center. On the other hand, minor burns, with the advent of new and safer techniques of anesthesia, can be successfully treated surgically in day surgery. These two programs require a strict standardization of protocols so only patients who fit the program are included in the day care unit protocol. Patients must be able to reach the burn center at any time, and all risk factors and warning signs need to be explained verbally and provided in writing to the patient and/or to the person who will take responsibility for the care of the patient.

### Box 63.3 Patients suitable for treatment in a burn center
- Acute burns
- Rehabilitation and reconstructive burn patients
- Toxic epidermal necrolysis and other life-threatening dermatosis
- Blunt and penetrating trauma patients
- Brain trauma
- Maxillofacial injuries
- Upper and lower limb reconstruction
- Craniofacial surgery
- Free flap reconstruction
- Traumatic soft-tissue avulsions
- Pressure sores
- Chronic wounds
- Diabetic and vascular ulcers.


### Box 63.4 Priority of admissions to the burn center

**Priority 1**
1. Severe burns
2. Electrical injuries
3. Burns with inhalation injury
4. Burns in infants
5. Burns in the elderly
6. Burns in patients with chronic or debilitating disease
7. Toxic epidermal necrolysis

**Priority 2**
1. Multiple blunt or penetrating traumas
2. Brain trauma
3. Maxillofacial injuries
4. Upper and lower limb reconstruction following trauma

**Priority 3**
1. Free flap surgery
2. Craniofacial surgery
3. Other plastic surgery procedures.

Every effort should be made by the burn team to start a program of day-care, since the benefits in patient care, quality of life, and cost-containment are spectacular when the program is fully functioning. Optimization of resources at the UHVH Burn Center by means of the implementation of a comprehensive day-care program, optimization of bed occupancy by patients with large wounds other than burns and upper and lower limb open fractures and soft tissue trauma has made an important impact in the cost-efficiency of the center. A bed occupancy of 0.85 and/or time of 95% has been achieved. Furthermore, the day-care program allowed a decrease in the number of physical beds from 39 to 26, while maintaining the quality of care and the provision of excellent and timely burn service, thus achieving optimal cost-efficiency.

**Telemedicine**

The past decades have witnessed one of the most important developments in human history. With the advent of the digital era, globalization and the widespread availability of internet have provided modern medicine with new tools for optimal delivery of healthcare. In general terms, burn centers are responsible for the health of a determined geographical area with a matched catchment population. Burns happen anytime, anywhere to anybody. All burn victims should have treatment granted by experienced and dedicated burn teams. However, even with specific guidelines for burn injury retrieval, optimal burn care delivery may implicate, in many instances, transportation of the patients long distances with an escalation of costs. The utilization of high speed digital connection and/or robotics (telemedicine) allows for the evaluation and treatment of patients without the need for transportation. During the initial consultation through a physician to physician connection, a complete medical history and examination, diagnosis and treatment plan can be performed and a final decision to evacuate the patient can be made. Follow-up of patients in outreach digital outpatients’ clinics is also possible. In this manner, the patient receives optimal treatment directed by the burn team at the local hospital facility, limiting transportation and loss of working hours in a cost-efficient manner. At the University Hospital Vall d’Hebron, such protocol is an ongoing research project that will modernize burn treatment in our area. Although initial cost for the setup of the telemedicine project is high, it is quickly reimbursed by the decreased number of burn evacuations to the burn centers. Telemedicine projects need to be organized with the inclusion of third-party payers, which, eventually, benefit from the limitation of the cost of treatment per patient.

**Summary**

The relevant socioeconomic impact of burns and the particular characteristics of burn injuries made necessary the development of teams to provide dedicated and specialized treatment of burn injuries. The achievement of total burn care and the current excellent outcomes in burn patients have paralleled a continuous increase in the complexity of treatment of burn victims and concomitant increase in costs of treatment. To contain costs and to prevent decline in standard of treatment, it is necessary to develop clinical protocols providing strict guidelines to healthcare providers. Thus, quality assurance programs are developed. Outcome measurement is also a part of quality improvement, since it is the main indicator of the quality of care that is performed at the burn center. Outcome data are part of the data acquisition of QA programs, and outcomes are also improved by the actions of such programs. The climb in costs must be contained with specific measures following an overall plan and by implementation of evidence-based medicine. QA programs provide the tools to insure that measures to control expenses are applied while maintaining the quality of care so excellent cost-efficacy can be obtained. In the modern era of healthcare management, programs of day care, admission of patients without burn injuries to the center, optimization of resources (technical and human), and programs of telemedicine are of paramount importance to maintain the gold standard of burn care while containing costs.

**Further reading**


Access the complete reference list online at [http://www.expertconsult.com](http://www.expertconsult.com)
References

Management of pain and other discomforts in burned patients

Walter J. Meyer III, Shelley Wiechman, Lee Woodson, Mary Jaco, Christopher R. Thomas

Introduction

The words ‘burn injury’ trigger immediate and vivid images of excruciating pain and suffering. Children are conditioned from early childhood that burn injuries are painful and can cause great harm. Until recently, debate continued over the importance of pain management in the burn survivor. Many practitioners believed that the treatment of pain, especially in children, was more dangerous than leaving it untreated. The past 15 years have shown that children’s pain can be effectively and safely managed.1–3 There is mounting evidence that effective pain management leads to a better long-term outcome. Kavanagh et al.4 demonstrated that pain in a burned patient adds significantly to the physiologic demands caused by stress. Successful pain management can significantly reduce the occurrence of psychological disorders such as depression and post-traumatic stress disorder.2,5,6

A series of therapeutic approaches have been developed to address both the pain and its associated anxiety. There is of course some concern about potential risk for dependence and addiction with opiates or benzodiazepines but this is offset by the importance of treating pain aggressively. In addition to pain and anxiety, practitioners are now focused on pruritus as well. Scales have been developed to measure pain, anxiety and itch separately.

Pathology of a burn injury as it relates to pain

All burn injuries are painful. Even first-degree burns can produce at least mild pain and discomfort, especially when something such as clothing rubs against the burned area. Second-degree moderate to deep partial-thickness burns result in variable amounts of pain depending on the amount of destruction to the dermis. Superficial dermal burns are the most painful initially. Even the slightest change in air currents moving past the exposed superficial dermis usually causes a patient to experience excruciating pain. Without the protective covering of the epidermis, nerve endings are sensitized and exposed to stimulation. In addition, as the inflammatory response progresses with the increase in swelling and the release of vasoactive substances, pain is increased and begins to involve the surrounding area.7

Areas of deeper partial-thickness burns may display a confusing pattern of pain over the first few days. These areas may show little or no response to sharp stimuli such as a pin-prick; yet a patient may complain of deep soreness related to the inflammatory response. These wounds are more like full-thickness burns with respect to the pain they cause. In a full-thickness burn, the dermis, with its rich network of nerve endings, is completely destroyed. This leads to an initial response of a completely anesthetic wound when a sharp stimulus is present. Yet, patients often complain of a dull or pressure type of pain in these areas. Once the devitalized tissue, i.e. eschar, sloughs and is replaced by granulation tissue a patient again experiences the sensation of sharp pain to noxious stimuli. While not completely understood, it appears that some deep burn injuries have a neuropathic pain component, where regeneration of nerves and or nerve damage creates a form of pain different from that resulting from tissue damage.

Pain-generating mechanisms during an initial injury

Studies of humans and monkeys confirm that burn injuries not only make an injured area and surrounding tissue more painful, but also cause hyperalgesia.7–9 Sensory nerve damage may also play a role in excessively difficult to treat pain. Burn injury is characterized by release of large amounts of inflammatory factors such as interleukins, which probably add to the perception of pain and the hyperalgesia. The hyperalgesia is further enhanced because the burn wound heals slowly over days or weeks.

Ptacek et al.10 found that, while there was a general trend for pain to decrease over time, there was also considerable variability in the course of pain among adult burn survivors. Persons with large burns showed a higher affective (suffering) component to the pain, but there is no reliable correlation between the pain scores and burn size. A source of confusion concerning the amount of pain expressed by burn patients is the role played by psychological problems such as anxiety and depression. Choinière et al.11 noted that pain at rest was significantly and positively related to levels of anxiety or depression, i.e. with elevated anxiety or depression, pain scores at rest increased. Although these studies demonstrate the great variability in pain expression in burned patients, they do not identify pain-generating mechanisms, either physiologically or psychologically, in a burn-injured patient. Charlton et al.12 used the State/Trait Anxiety Inventory to measure anxiety and reported that the study sample of adult burned patients was not particularly anxious. Other studies have suggested that burned patients have increased levels of anxiety, especially related to...
treatment and outcome and that these levels may increase over time.\textsuperscript{13–16} Anticipation of pain related to wound care that occur at least daily can increase a patient’s perception of pain which in turn can lead to greater anxiety. This reaction may explain some findings which suggest that pain increases over time in burned patients.\textsuperscript{17–19} Depression also plays a similar role in enhancement of pain.\textsuperscript{20} Pain leads to depression and depression enhances the perception of pain.\textsuperscript{5,6} In burn care units, where very aggressive pain management is practiced, depression is not a major problem.\textsuperscript{21}

**Pain as a function of the healing process**

As a deep dermal or full-thickness burn wound heals, either by primary intention from excision and grafting or by secondary intention through granulation tissue and scar formation, the injured neural tissue is reorganized.\textsuperscript{18} Reflex neural function returns to grafted burn skin approximately 5–6 weeks after the burn has been covered by autografted skin.\textsuperscript{19} Active vasodilatation, vasoconstriction, and pain sensation all return at this time. These functions also return to the burn wound which heals through scar formation but may take up to 6 months for complete neural reorganization. This is the basis of neuropathic pain in the burn wound site.

Although rare, causalgia, dysesthesia, and phantom pain syndrome can sometimes develop in healing skin. Phantom limb sensation and pain is more common following amputation, which is often associated with large burn injury or electrical injury. The incidence of these chronic pain syndromes seems to be related to the healing process. Burns that have been excised and grafted on a clean and uniform vascular bed rarely develop one of these chronic pain syndromes. Wounds that heal by granulation and scar formation seem to be more apt to develop a chronic pain problem because of the continued stimulation of nerve fibers in the area with enhancement of the hyperalgesia. Skin biopsies of granulation tissue have clearly shown neuronal tissue entrapment.\textsuperscript{15} Pain, in scar tissue, subsides over time as the scar tissue matures.

**Measurement of pain in burned patients**

In many studies, patients have been asked to rate overall pain, pain at rest, overall procedural pain, and worst pain during the procedure. Such perplexing instructions may account for some of the variability in pain reports. A more reasonable approach may be to ask a patient to rate pain as either procedural or non-procedural (background) pain, with each given an operational definition. Procedural pain can be defined as that related to wound care or stretching of the patient’s scar tissue, activities that seem to cause the worst pain for burned patients. Background pain is the discomfort experienced at rest or during mild activity.

Although pain cannot be measured directly, it can be quantified by using one of the standardized tools described below. Using reliable and valid tools allows us to gauge the effectiveness of our treatment for any one patient. Assessing pain on a scheduled basis and using the same tool for each assessment gives us information about how pain is experienced by a single patient throughout the burn treatment; we can note patterns that emerge, and schedule medications accordingly. Furthermore, standardized tools allow us to compare pain management of one patient with another as well as one burn unit pain management with that of other burn units in order to determine, for example, the effectiveness of a new protocol for pain management. Another important reason for assessing pain regularly and in a standardized way is that it communicates to the patient that we believe she/he has pain, and we are trying to do something about it. This communication reassures the patient, thereby reducing the likelihood that the patient will escalate pain, anxiety and other related behaviors.

In an attempt to understand how pain is modulated, several experimental tools have been employed to further elucidate the exact pathways involved in pain transmission and to better understand the therapies used to relieve pain. Some of these tools are: cortical evoked potentials; functional brain imaging (PET or positive emission tomography); functional magnetic resonance imaging (fMRI); source analysis of evoked activity; and electrophysiologic recording from the human brain. Comparison with verbal judgments of pain magnitude validates these physiologic measures.

**Pain measurement techniques for an adult burned patient**

A variety of pain measurement techniques have been used with adult burned patients. The more common measures include adjective scales (Table 64.1), numeric scales (i.e. rating pain on a scale of 0–5, 0–10 or 0–100), and visual analog scales (Fig. 64.1). Each of these scales measures the sensory component of a patient’s pain. Adjective scales and numeric scales are quick and easy to administer because they do not require a visual representation of the scale. The visual analog scale requires a visual representation of the scale to be presented to a patient. Patients must mark or point to the place on the scale that represents their level of pain. The demonstrated validity of the scale allows for comparisons of visual analog pain assessments between studies with different patient samples.

Motivational-affective and cognitive-evaluative components of pain are most frequently measured using the McGill Pain Questionnaire (MPQ).\textsuperscript{22} The MPQ takes 10–20 min

<table>
<thead>
<tr>
<th>Table 64.1 Adjective scales in English and Spanish</th>
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<tbody>
<tr>
<td>0  No pain</td>
</tr>
<tr>
<td>1  Slight pain</td>
</tr>
<tr>
<td>2  Moderate pain</td>
</tr>
<tr>
<td>3  Severe pain</td>
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</tbody>
</table>

**Figure 64.1** Visual analog scale (VAS) for children to rate their levels of pain. (From the Varno/Thompson Pediatric Pain Questionnaire. With permission from the American Society for Clinical Pharmacology and Therapeutics.)
and consists of 20 sets of adjectives which describe all three components of pain: sensory, affective, and evaluative. Qualitative profiles and quantitative scores for each dimension as well as a total pain score can be derived from the selected adjectives. The MPQ has been translated into several languages and has been shown to be a reliable and valid measurement tool. Gordon et al.23 in a prospective multicenter study, asked 40 adult burned patients to rate their pain on four scales: a visual analog scale; an analog chromatic scale;24 an adjective scale, and a faces scale.25 At the end of the study patients were asked to choose their preferred scale. The majority of subjects preferred the faces and analog chromatic scales. Although further research is needed to validate these findings, the preference of patients is another variable to be considered.

Pain measurement techniques for pediatric burn patients

The measurement of children’s pain is much more complex than it is for adults, especially for pre-verbal children. The assessment of pain in children has included physiologic measurements, behavioral assessment, and patient reports of pain. The physiologic indicators which have been evaluated are heart rate,26 respiratory rate,26 blood pressure,26 endocrine changes,26,27 and changes in PO2.28 None of these shows promise as an indicator for measuring pain in sick children, since all are affected by a variety of stressors, metabolic changes related to a burn, and medications, in addition to pain.

Behavior scales have been devised to measure pain by providing standardized instructions and guidelines for observing behaviors thought to be specific to pain. A number of investigators25–31 have looked at infants’ cries as measurable behaviors that can be observed in order to evaluate pain. These studies demonstrate that length of cry, pitch, intensity, and other characteristics of crying may be used to evaluate pain in infants. Likewise, infant facial expressions may be used to code pain; a system was developed which characterizes nine facial actions involved in the expression of pain, but its use requires videotaping and detailed analyses of an infant’s facial movements.31–33 Both the measurement of crying and facial expression require too much time and special equipment to be appropriate for the clinical setting. Other investigators have devised multidimensional scales that include length of cry, facial expressions, and behavioral states in order to measure pain in infants.34,35 These scales are easier to use and allow an observer to assess pain as either present or absent without further quantification.

Examples of observational scales, which allow for quantification and may be used with toddlers and pre-verbal children, are the CHEOPS (Children’s Hospital of Eastern Ontario Pain Scale)36 and the Observer Scale.37 The CHEOPS is a scale of six behaviors, each scored on a numeric range; it yields a total numeric score for pain. This scale has been shown to be valid and to have good interrater reliability. The Observer Scale is another standardized instrument that categorizes overall pain or comfort behaviors on a scale of 1–5. The Observational Pain Assessment Scale (OPAS), a burn specific observational tool, was developed by Barone et al. at Shriners Hospital for Children, Cincinnati and is very useful in children 0–3 years of age.38 The scale is depicted in Table 64.2.39

Research suggests that simple self-report scales can be used with preschool children. Examples of such scales include the Oucher Scale (photographs of children with various facial expressions).40–42 Drawings of faces25,43 have also been used with preschool age children44 and school age children (8 years).39 Preschool children have also used the Poker Chip Tool,45 color scales,46,47 and a thermometer47 to report the degree of pain or hurt. These simple tools allow a preschooler to report pain and are easy to use. One caution with the face scales is that a practitioner must help a child differentiate between physical pain and sadness unrelated to pain. Since there is no evidence that any one of these is more valid than another, it is recommended to pick one and use it consistently. When self-report scales are used in conjunction with observational scales, a practitioner gets a better picture of a child’s response to pain and pain therapies.

A school-aged child’s cognitive development allows more abstract thinking. In addition to the Faces Pain Rating Scales which they enjoy;25 they can use simple numeric scales 0–5 in the early school years (ages 7–8) and more complex scales 0–10 or 0–100 in the later years (age 9–12). Visual analog scales anchored with happy and sad faces and simple adjective scales also can be used with this age group.47,48 In addition to self-reports of pain, observational scales such as the CHEOPS36 or the Procedure Behavior Check List49 can be used with a school-aged child. Again, the important issue is to use one selected scale consistently since no one has been shown to be more valid than others.

Adolescents can think abstractly and can quantify and qualify phenomena and so can use the same scales as adults. One concern with adolescents is that, when they are ill, they tend to regress and thus may require the use of a simpler scale during such times.

<table>
<thead>
<tr>
<th>Table 64.2 Observational Pain Assessment Scale (OPAS)39</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assess each of the areas identified in the ‘Observed behavior’ column rating each behavior using the 0, 1, or 2 rating. Add the ratings together for each observed behavior. Document your total score.</td>
</tr>
<tr>
<td><strong>Observed behavior</strong></td>
</tr>
<tr>
<td>Restlessness</td>
</tr>
<tr>
<td>Muscle, tension</td>
</tr>
<tr>
<td>Facial expression</td>
</tr>
<tr>
<td>Vocalization</td>
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<tr>
<td>Wound guarding</td>
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</tbody>
</table>

Used with permission of authors.39
Intubated and sedated children provide more challenges in the assessment of pain. The more disabilities that a child has and the more medications that are being given to the patient create challenges to the clinician. A 2-year-old child who is blind, with only one extremity that is functioning and who is on numerous medications, presents a huge assessment challenge to the clinician. Box 64.1 presents a list of clinically useful tools according to patient age.

‘Pain is what the child says it is.’ What about the case where the care-provider documents a lower number than the child says it is because the care-provider believes the child is over-rating the score? Reiman et al. surveyed nurses’ knowledge and attitudes regarding pain and their ability to manage pain. The modified Pediatric Nurses’ Knowledge and Attitude Survey regarding pain tool (PNKAS – Shriners Version 2002) needs further validation but demonstrates the need to consider the healthcare provider’s attitude and knowledge of pain.

### Measurement of anxiety

Anxiety is measured in a variety of ways. In 2000, Robert et al. surveyed 64 burn treatment centers to determine how they evaluated and treated anxiety, especially in children. They found that most centers did not use standardized measures of anxiety. Based on that survey and other information, the Shriners Hospital for Children in Galveston has been using the Fear Thermometer adapted by Silverman and Kurtines to measure anxiety associated with anticipated procedural pain.

### Measurement of itching

Itching is very common in burn survivors. Even in small burns, the prevalence is 35% with moderate pruritus and 14% with severe and in many cases the pruritus impacts daily living. Another series of 310 burns reported a prevalence of 87%. Patients who experience such itching often excoriate new grafts or recently healed skin, thus enhancing their susceptibility to infections. When the pruritus is severe, patients can focus on nothing else. Field et al. reported using a visual analog scale of 1 to 10 to assess itching. Pat Blakeney, PhD and Janet Marvin, RN at the Shriners Hospital for Children in Galveston teamed up to develop an instrument to measure itchiness, called ‘itch man’ (Fig. 64.3). This instrument was based on a patient’s drawing of his experience in the hospital. Children seem to be able to relate to ‘itch man’, and validation has been completed. A similar tool is needed for children.
Comparison effectiveness of shower and bath oil treatments for severe itch, but that scale does not seem suitable for children and is not validated.53

In summary, symptom assessment and management are very important in burn care. The experience of pain may affect the perceptions of other symptoms, including anxiety, fear or itch. Each symptom should be assessed within the context of other symptom assessments. Further studies need to be completed in all these areas.

**Treatment considerations**

Once the pain has been assessed and quantified, treatment can be considered. Three modalities of treatment are effective with pain secondary to burn injury. They include surgical, pharmacological and behavioral treatment. The type of treatment depends on the time since burn. The following will consider the types of treatment by time after burn:

- Emergency or resuscitative phase (0–72 h after injury)
- Acute phase (72 h to 3 or 5 weeks, until the wounds are closed)
- Rehabilitative phase (from the time of wound closure to scar maturity). This phase may last months to years.

**Pharmacologic management of pain**

Pharmacologic management of burn pain is the mainstay of therapy. General rules are helpful in governing the use of pain medication. The first tenet is that if the patient says he/she is having pain, he/she is suffering. The second tenet is that analgesics are most effective when given on a regular schedule (not ‘as needed’ or PRN). Third, pain medication should be given on a regular basis. Whether more or less morphine ends up being given is not clear. However, many patients especially adolescents, greatly prefer being in charge with a PCA.

Many patients also require anxiolytic medication along with the analgesic medication. Therefore, included in Table 64.3 are the anxiolytic agents which are suggested for use by several authors. In a recent review of the practices of three pediatric burn hospitals it is clear that the vast majority of children with moderate and large burns receive both opiates and benzodiazepines.72 This is also the experience in the Shriners Hospital for Children in Galveston Texas.2

**Emergency phase**

If the initial burn injury can be closed surgically, that gives the best relief of pain. The pain is predominantly related to the open wound. Once the wound is closed, the pain subsides. The use of resection and grafting of open burn wounds significantly reduces the burn pain. Open wounds should be grafted as soon as they are clean enough to do so. Even temporary coverage with cadaver skin or pigskin reduces pain in the area of the burn. In the case of second-degree wounds, the use of BiobraneRX, OpsiteRX, TegadermRX DuodermRX or other wound-covering dressings almost immediately eliminates pain in the burn wound site.73–77 Cultured allogeneic keratinocyte sheets accelerated healing and thereby reduced pain and suffering compared to OpsiteRX treatment.78

Sometimes the pain can be managed by topical agents. Aloe vera has been used as a home remedy for many generations. Recently, there have been several studies to examine its efficacy more thoroughly. Maenthaisong et al. did a systematic review with a meta-analysis and concluded from the
### Table 64.3 Pharmacologic therapies for burn pain relief

<table>
<thead>
<tr>
<th>Phase</th>
<th>Procedural analgesics</th>
<th>Background analgesics</th>
<th>Anxiolytics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Emergent phase</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Procedural analgesics</td>
<td>Morphine (IVB, IVCI)</td>
<td>Morphine (IVCI, PCA)</td>
<td>Diazepam (IV)</td>
</tr>
<tr>
<td>Meperidine (IVB)</td>
<td>Meperidine (PCA)</td>
<td>Meperidine (IVCI, PCA)</td>
<td>Lorazepam (IV)</td>
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<tr>
<td>Fentanyl (IVB, IVCI)</td>
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<td></td>
<td>Midazolam (IV)</td>
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<td>Hydromorphone (IVB, PO)</td>
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<td></td>
<td>(IVCI) (Versed)</td>
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<tr>
<td>(Dilaudid)</td>
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<tr>
<td>Naltrexone (IVB)</td>
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<td>Ketamine (IV, IM)</td>
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<tr>
<td>(Percocet)</td>
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<tr>
<td><strong>Acute phase</strong></td>
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<tr>
<td>Procedural analgesics</td>
<td>Morphine (IVB, IVCI, PCA), Roxanol (oral morphine)</td>
<td>Morphine (IVCI, PCA)</td>
<td>Diazepam (PO)</td>
</tr>
<tr>
<td>Meperidine (IV, IM)</td>
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<td>Lorazepam (PO)</td>
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<td>(Xanax)</td>
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<td>Oxycodone (PO)</td>
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<td>(Percocet)</td>
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<td><strong>Rehabilitative phase</strong></td>
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<tr>
<td>For severe pain</td>
<td>Hydromorphone (PO)</td>
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<td>Diazepam (PO)</td>
</tr>
<tr>
<td>Fentanyl (transmucosal)</td>
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<td>Lorazepam (PO)</td>
</tr>
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<td>Morphine (IVB, IVCI, PCA)</td>
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<td>(Ativan)</td>
</tr>
<tr>
<td>For mild to moderate pain</td>
<td>Oxycodone (PO) (Percocet)</td>
<td>Non-steroidal anti-inflammatory drugs (NSAIDs) with or without narcotics</td>
<td>Alprazolam (PO)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Usually not necessary: Acetaminophen NSAIDs</td>
<td>(Xanax)</td>
</tr>
</tbody>
</table>

Published studies of first- and second-degree burns that aloe vera was more effective than the control. It was associated with a shorter healing time by 8.79 days. A more recent randomized controlled study in 2009 by Khorsaniet al. confirmed the greater efficacy of aloe over silver sulfadiazine.

As noted under above, physical coverage of the burn wound decreases pain. For instance, leaving blisters intact leads to less pain. But this practice is questionable because of possible infection associated with the blisters. One additional issue concerning procedures is the amount of pain created from removing a dressing over the burned area. These removals are usually facilitated by soaking the dressings off but the soaks are sometimes painful. Some of the newer dressings are easy and painless to remove; moist exposed burn ointment dressings are being developed to reduce that pain.

Acticoat was found to be much less painful than silver sulfadiazine in the treatment of partial thickness burns by Varas et al. Several new lipidocolloid dressings seem to show promise for reducing pain. Cellulose dressings also reduce pain. Several new products are adherent to dry skin but not moist skin and therefore cause much less pain. Suprathel is a reabsorbable skin substitute which goes even further in reducing the pain of dressing.

One more novel technique of painlessly cleaning the burn wound is to use an ultrasound mist. There are two short reports advocating this.

Sometimes nerve blocks, either local or regional, work; they are usually done with lidocaine or related compounds. Pedersen et al. reported the use of EMLA cream, a prilocaine and lidocaine mixture, to burn wounds in a double-blind randomized manner for 8 h to reduce pain but it did not reduce late hyperalgesia. Whenever EMLA cream is applied to disrupted skin or large areas, caution should be taken to avoid toxicity from systemic absorption. Seizures and other CNS toxicity have been reported from these circumstances.

Both bupivacaine and lidocaine infiltration of the burn wound eschar site or the grafting site have been successfully used to reduce pain. In non-randomized and non-controlled studies, sympathetic nerve blocks with lidocaine are effective for blocking thermal pain.

Physiological changes and treatment occur in patients with burns >10% total body surface area (TBSA). During the emergency phase, the preferred route for most medications is the intravenous route because of potential problems with absorption from the intramuscular site and stomach due to decreased perfusion. Of the agents recommended for the relief of procedural pain, morphine is the most widely used. For procedures, IVB and IVCI are the most common methods of administration used. For extremely painful procedures in both the emergency and acute phase, fentanyl has a major advantage, in that it is shorter acting and avoids over sedation following a procedure, as might occur with repeated doses of morphine. Higher opiate doses during the initial resuscitations are associated with higher resuscitation volumes; this is probably secondary to the vascular effects of the opiates. As noted above, we have few studies of the pharmacokinetics of opioids and anti-anxiety drugs in burned patients. Martyn, in a review of pharmacologic studies in burned patients, describes a variety of pathophysiologic changes accompanying burn injury, which can alter drug deposition. These changes include cardiovascular...
changes, alteration in renal and hepatic function, and fluctuations in plasma protein concentration, which may render pharmacokinetic studies of non-burned patients not applicable to burned patients. Since it is difficult to predict precisely how drug responses will be altered, it is important to monitor responses on drug levels more closely so that dosage can be titrated to the individual patient’s needs. In addition to opioid analgesics, anesthetic agents such as ketamine and nitrous oxide may be used for procedural pain and are discussed in more detail below.

**Acute phase: background pain and anxiety**

During the acute phase, the choice of pharmacological agents used to manage procedural pain encompasses a number of orally administered opioid analgesics. The pain management is divided into background pain and procedural pain. To control background pain during the acute phase, the use of PCA or NPC (non-pain-contingent) medication regimen is far superior to the PRN (as requested) method. Allowing a patient to medicate himself as needed usually results in better and smoother pain control as well as better staff and patient relationships. For a burned patient with extensive hand burns, the control cord can be fitted with a padded pedal-type apparatus that can be positioned so that the patient can press it with a foot, elbow, etc. Occasional patients will use the highest dose allowed in order to withdraw from the entire treatment setting. If this occurs, confrontation and negotiation are important to get the patient back to the task at hand.

Important caveats for the use of PCA should include:

1. An initial bolus in adults of 0.1 mg/kg of morphine or equivalent dose of other drugs.
2. Increasing the patient-controlled dose as needed to achieve pain relief (recognizing that tolerance develops at varying rates in individual patients).
3. Planning for a change in dosing regimens at night to include:
   a. giving a bolus dose at bedtime;
   b. doubling the patient controlled dose and lengthening the time interval between doses so that when a patient awakens in pain, he or she does not have to lie awake to push a button several times in order to get adequate medication;
   c. if the increased intermittent dosing is not adequate, being lenient with bolus doses or to start a patient on a continuous morphine drip at night.

Opioid analgesics have been the mainstay of burn pain drug therapy. Among the opioids, morphine is the most commonly used for background pain. Morphine can be given orally or parenterally but bioavailability of oral doses is reduced by first pass hepatic metabolism and the dose must be two- to three-fold higher than the IV dose. For procedural pain, other opioids with more rapid onset and shorter duration may be more appropriate for procedural pain. Treatment with narcotics has been associated with tolerance and a hyperalgesic state that makes pain more difficult to treat.

Of these agents, morphine has continued to be the mainstay for both background and procedural pain management. Long-term use of morphine has several inherent problems. Morphine binds to more than one receptor class. Although the main effect is on the µ-opiate receptor which alleviates pain, it also stimulates the N-methyl-D-aspartate (NMDA) receptor, which causes the development of a hyperalgesic state associated with morphine tolerance and complications such as bowel obstruction. Changing to other opiates, such as methadone, or other compounds, such as ketamine, which block the NMDA receptor pathways can improve the management of pain no longer controlled with morphine. Other opiates such as hydromorphone (Dilaudid), levorphanol (Levo-Dromoran), fentanyl, and methadone are all excellent oral agents for the relief of moderate to severe pain when given in equianalgesic doses to morphine. Fentanyl comes in a convenient flavored Oralet, especially attractive for use with children. The combination of lorazepam, given with hydromorphone 45–60 min before a procedure, results in reasonable pain control for the majority of adult patients. As with other opioid analgesics, tolerance may develop rapidly, so the dose of hydromorphone may need to be adjusted frequently. Opiate clearance seems to be faster in individuals with burn injury. Methadone has a longer half-life than morphine and therefore can provide coverage for a longer time between doses. Also methadone has been noted to give smoother pain relief for children postoperatively than morphine. Methadone is different from morphine both pharmacokinetically and pharmacodynamically and has been reported to be effective in patients tolerant to and poorly-controlled by morphine. In addition, methadone is a fraction of the cost of most other opioid analgesics. We do not use meperidine because many individuals report a rush with IV meperidine, thereby adding to its addictive qualities.

Pain associated with dressing change is very important to manage well. Finn suggested adding patient PCA intranasal fentanyl versus oral morphine. In a randomized double blind placebo controlled study of 26 adults, they concluded that intranasal fentanyl was as effective and safe as oral morphine. Also Prakash et al. reported using PCA with fentanyl as an effective alternative.

From the published literature concerning the use of opioids in patients with burn injury, one would have difficulty making decisions about the best drug, the best dosage range, or the best route or method (i.e. PCA, or continuous infusion) of administration of these drugs. Morphine or other opioid analgesics are considered mainstays of pain relief for burned patients, but many reviewers report less than adequate pain relief for burned patients with the use of such agents. The line between enough opioid analgesics to provide pain relief and too much causing respiratory depression is difficult to find. Also, the experience of the authors has shown that even a PCA regimen must be individualized and frequently adjusted.

More recently, gabapentin has been advocated for acute burn pain. It may be effective because the nature of a burn injury is destruction of nerve endings in the skin. Studies by Cuignet et al. documented that if 2400 mg of gabapentin is given to adult burn survivors per day, the amount of morphine needed is less and the pain control better. Anxiety medication should be considered only after the patient’s pain has been aggressively treated. The medical staff can inappropriately attribute the patient’s complaint to anxiety (‘just anxious’ is a frequently used phrase) when, in
These drugs are distinguished by several unique features. Profound sedation is possible with minimal effects on respiration.149 Patients sedated with dexmedetomidine can often be aroused. The α-2 adrenergic agonists are not controlled substances and there are no reports of substance abuse with clonidine or dexmedetomidine. Use in the ICU has not been associated with withdrawal symptoms even when dexmedetomidine was infused for up to 168 h at 0.21–0.49 µg/kg per hour.149 Long-term administration of dexmedetomidine infusions in burn patients achieved adequate sedation.146,150,149 No tachycardia and no rebound hypertension or tachycardia were observed when the drug was discontinued.

In our institution, pediatric burn patients poorly controlled with morphine and lorazepam have been found to respond to orally administered (nasogastric tube) clonidine in doses of 2–5 µg/kg (unpublished observations). When more profound sedation of intubated patients is required, we have used continuous infusion of dexmedetomidine 0.3–0.7 µg/kg per hour after a loading dose of 1 µg/kg intravenously over several minutes.

**Acute phase: procedural pain and anxiety**

During the course of the acute phase of injury, burn patients must endure numerous painful procedures that produce intense physical and psychic stress. Among others, these include initial wound debridement, daily dressing changes, range of motion and exercise therapy, wound staple removal, and placement of intravascular catheters. For a number of reasons, adequate control of the pain and anxiety associated with these procedures is especially challenging (Box 64.2). Poorly-controlled pain can make it difficult to accomplish a procedure effectively or safely and increases anticipatory anxiety that can impair patient compliance and may contribute to behavioral morbidity such as post traumatic stress syndrome.151 In addition, increased sympathetic tone which is associated with exaggerated catabolism, impaired wound healing and immune function are associated with pain and can contribute to prolonged hospitalization.152,155 Effective pain control in adults can often be sufficient to reduce anxiety. In pediatric patients, however, anxiety is also needed. For especially stressful procedures, most pediatric patients must be rendered insensible. For this reason, the popular term ‘conscious sedation’ is usually inaccurate and misleading when treating pediatric patients. A very young patient who is aware of the procedure will resist enough to make the procedure difficult or less safe and the anxiety associated with this experience makes future procedures more difficult. The level of sedation and analgesia required in this situation cannot accurately be described as ‘conscious.

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**Box 64.2 Challenges associated with sedation and analgesia for procedures in burn patients**

1. Intense but brief pain
2. Risks of complications with deep sedation
3. Controversy over who should administer deep sedation
4. Prolonged effects of deep sedation
5. Frequent NPO periods disrupt nutritional needs of burn patients.
sedation. A more accurate descriptive term is moderate or deep sedation for procedures. The depth of sedation must be individualized depending on the intensity of the pain associated with the procedure and the patient’s maturity, level of anxiety, and pain tolerance.

Several effective protocols for delivery of moderate sedation for procedures have been published, involving a variety of drugs and routes of administration.114,154-156 The ideal pharmacological treatment would be easily administered in a palatable form, produce intense analgesia with a rapid onset, relatively short duration of action, and with minimal side-effects. Most drugs in current use will produce prolonged sedation when given in doses that prevent most of the intense pain during wound care. On a daily basis, this prolonged period of sedation can interfere with nutritional support and other therapies. In the outpatient setting without an intravenous catheter, the most common technique is to give a pre-procedural fixed dose of an analgesic with or without an anxiolytic by the oral, transmucosal, or intranasal route. Fentanyl citrate is available as a flavored Oralet to administer by the oral transmucosal route. The oral transmucosal route has the advantage of direct absorption into the systemic circulation which bypasses the first pass hepatic metabolism which results in less systemic side effects as compared to an intravenous bolus. 

In pediatric patients prior to dressing change, Borland and colleagues compared analgesia and sedation with morphine administered orally and fentanyl given intranasally.155 Although both were effective, intranasal fentanyl was more palatable and had a much more rapid onset. Although these regimens provide significant analgesia, pain control is often not optimal. It is difficult to provide sufficient analgesia with enteraly administered drugs to control the intense pain without unacceptable risk of adverse effects, especially prolonged sedation. Remifentanil administered intranasally is an attractive alternative. Remifentanil is an ultra short acting opioid rapidly metabolized by plasma esterase.160 In our institution 5–10 µg/kg of intranasal remifentanil enhanced the effectiveness of oral transmucosal fentanyl as judged by pain scores and the subjective evaluations of nurses and patients (unpublished observations) and did not delay recovery. The ultra short duration of action allows rapid recovery which reduces risks of sedation and may improve patient satisfaction.

When patients have an intravenous catheter in place there are many more treatment options that allow more profound analgesia, more rapid onset with shorter duration of action, and depending on which drugs are administered, reversal of drug toxicity with antagonists. Sedative and analgesic drugs can be given as a bolus with supplemental doses given as needed, as an infusion to be titrated or supplemented with bolus doses, and by patient controlled analgesia (PCA).

Deep sedation can be associated with the risk of serious morbidity and even mortality. Deep sedation can be associated with airway obstruction, depressed airway reflexes and respiratory drive, and hemodynamic instability. Loss of consciousness causes reduced pharyngeal tone and airway obstruction of varied degree depending largely on the patient’s anatomy. If this is not recognized or attempts to open the airway are not successful (operator skill or difficult patient anatomy) hypoxia can result. An airway exam is a critical part of the pre-procedure evaluation and a sedation plan must take into consideration potential difficulties with airway and respiration. Obstruction due to laryngospasm can be very difficult to relieve and in extreme cases may require muscle relaxation and intubation. Hypoxia can also result from hypoventilation due to depressed respiratory drive. If airway reflexes are depressed aspiration of gastric contents may occur when passive reflux or active vomiting occur. In addition, deep sedation can cause loss of sympathetic tone or direct cardiovascular depression. These effects can lead to morbidity due to hemodynamic instability.

Adverse events associated with deep sedation during endoscopy161 led the Joint Commission to set guidelines for sedation that included restrictions regarding who can administer deep sedation. A controversy developed since the American Society of Anesthesiologists (ASA) defines general anesthesia as a condition induced by medication that results in the patient’s inability to respond purposefully to commands.162 Since hospital guidelines restrict administration of general anesthesia to anesthetists, this interpretation precludes personnel other than anesthetists from administering deep sedation. Although the Joint Commission adopted the ASA definition of general anesthesia, other medical specialties developed their own guidelines whereby formal training in anesthesiology is not required to administer drugs and monitor patients for moderate or deep sedation.163 Requiring the presence of an anesthesiologist or certified nurse anesthetist during moderate or deep sedation creates problems in that there are not enough anesthetists available to provide coverage for all procedures and the added professional fees significantly increases the costs of these procedures often, it is argued, without proportional added benefit. Numerous studies have demonstrated that with competency based credentialing along with appropriate planning and organization, moderate and deep sedation can be administered safely by non-anesthetists. Components of a suitable program are listed in Box 64.3. Currently (Joint Commission update from July 10, 2010), Joint Commission standards require that personnel “permitted” to administer sedation must be able to rescue patients from the effects of sedation that intentionally or unintentionally result in a state of general anesthesia. The Joint Commission now leaves it up to each organization to decide how to determine which

Box 64.3 Organizational recommendations for provision of moderate or deep sedation for procedures

1. Pre-procedural evaluation of the patient including airway exam
2. A documented plan for sedation and monitoring
3. Availability of equipment for continuous monitoring of breathing effort, airway patency, oxygenation, and circulation
4. A designated practitioner with documented airway skills whose primary responsibility is to administer the sedative drugs and monitor the patient during the procedure and during recovery
5. Personnel administering and monitoring sedation cannot be the individual performing the procedure, and can do other tasks only for brief intervals
6. Resuscitation equipment must be immediately available.
personnel are permitted to administer moderate or deep sedation.

Departments of anesthesia are a logical and convenient resource for training, organizing, and monitoring sedation programs. In our institution (Shriners Hospital for Children, Galveston), competency-based credentialing for sedation privileges requires knowledge of hospital policy regarding sedation guidelines, current ACLS or PALS training, passage of a written exam over self-study didactic material, and successfully managing the airway of a minimum of five patients in the operating room under general anesthesia each year. Educational material, supervision of airway training, and oversight of adverse events is provided by personnel from the Anesthesiology Department. Medication errors and adverse events are monitored and adverse events are to be reviewed during monthly hospital morbidity and mortality conferences.

The anxiety medication often used for procedures is midazolam, which has pharmacokinetic characteristics that make it an attractive anxiolytic agent for procedural sedation. It has a rapid onset, which facilitates titration. The elimination half-life of 2.5 h is considerably shorter than that of lorazepam (13 h) or diazepam (36 h) and results in a shorter recovery time. It is better tolerated when given intravenously. The amnesic effect of midazolam is greater than diazepam. Elderly patients have a more consistent response to a given dose. Either lorazepam or midazolam would be more appropriate than diazepam for repeated use in burn care.

Other pharmacologic agents often used for procedural pain include ketamine, propofol, and nitrous oxide. Ketamine has been widely used as a sedative and analgesic for painful procedures in burn patients. Ketamine has recently been described as possibly the first choice for anesthesia in burn patients. Several qualities make ketamine an effective drug for these procedures. It is a potent analgesic and its inhibition of NMDA receptors reduces hyperalgesia associated with morphine tolerance. In higher doses, patients experience profound analgesia, become insensitive (dissociated) from their surroundings, and are amnesic to the procedure. Ketamine preserves respiratory drive and airway reflexes, and increases sympathetic tone which generally supports blood pressure. Dysphoria, hallucinations and even delirium may occur, which has limited its use in some cases. Emergence problems are less frequent in pediatric patients, but often occur in adolescent males. Midazolam has been found to provide some relief of these reactions. Another potential problem with ketamine is increased oral secretions but this can be controlled by glycopyrrolate. Ketamine can be given orally, intramuscularly, and intravenously. Ketamine causes pain on injection. This can be prevented by administration of lidocaine through the IM needle or the IV tubing prior to ketamine injection. Tachycardia and hypertension may be poorly tolerated by older patients with hypertension or coronary artery disease. Ketamine has been avoided in patients with increased intracranial pressure because it has been reported to cause increased cerebral blood flow that might further increase intracranial pressure. More recent evidence contradicts this dogma. Clinical and experimental data suggest that, especially for patients who are mechanically ventilated, ketamine may offer neuroprotective, decreased intracranial pressure, and improved cerebral perfusion.

A combination of ketamine and the α-2 adrenergic agonist dexmedetomidine is particularly effective for procedures. The analgesic effect of ketamine is enhanced by dexmedetomidine allowing lower ketamine doses while at the same time increased heart rate and blood pressure produced by ketamine are moderated. Clonidine has also been found to reduce emergence problems associated with ketamine sedation.

Propofol is a non-barbiturate hypnotic agent without analgesic activity. It is administered intravenously and is most commonly used as a general anesthesia induction agent. Advantages include a rapid onset of action and a rapid emergence with little cumulative effect after prolonged infusion periods. Disadvantages of propofol include pain on injection and loss of consciousness; propofol causes loss of pharyngeal motor tone which may cause airway occlusion. Propofol also causes depressed respiratory drive, loss of airway reflexes, and hypotension. These changes increase the risk of respiratory complications. As a result, propofol sedation in non-intubated patients should be used only by practitioners with credentials for moderate and deep sedation for procedures. At room temperature, the lipid emulsion formulation of propofol is an ideal growth medium for bacteria. Endotoxic shock and wound infection have been reported in patients after administration of propofol left at room temperature for prolonged periods of time. Since it lacks analgesic activity, when given alone propofol must be given in doses large enough to cause loss of consciousness to prevent response to painful procedures. It has also been given by continuous infusion in combination with analgesics such as opiates or ketamine. Coimbra et al. reported its use as an adjunct to morphine in a patient-controlled sedation protocol for burn patients undergoing their first dressing changes. After premedication with morphine (0.1 mg/kg plus a set fraction of the dose needed for background pain), an effective intravenous sedative dose of propofol was determined (0.3 mg/kg plus additional titrated doses of 0.1 mg/kg). This dose of propofol was used as a patient controlled dose without lockout. Pain control was judged good by a pain score of 3 ± 1.8 and satisfaction scores by patients and nurses were 5.8 ± 0.2 and 5.9 ± 0.3, respectively (maximum score 6.0). In this small group of patients, no problems with respiration or circulation were experienced. The rapid onset and short duration of action of propofol make it an easy drug to titrate for sedation. For this reason, propofol has become a favored sedative drug for non-anesthetists, especially GI endoscopists, pulmonologists, and intensivists.

Nitrous oxide is the only non-halogenated anesthetic gas still in clinical use. Its low potency requires 50–70% inhaled concentrations to provide significant analgesia. Filkin et al. have reported effective analgesia during burn wound care with self-administered nitrous oxide. More recently, Ozil et al. used 50% nitrous oxide in oxygen in combination with morphine premedication to provide analgesia for 33 children with small (≤10% TBSA) burns. In these cases pain scores and patient/parent satisfaction were favorable. Brief intermittent exposure to nitrous oxide and chronic exposure to trace amounts appear safe, but repeated exposure to higher concentrations can result in significant hematopoietic and neurological toxicity. This results from oxidation by nitrous oxide of the cobalt in vitamin B12 which impairs its coenzyme function. Synthesis of methionine and
tetrahydrofolate needed for DNA synthesis and metabolic reactions involving methylations is inhibited by nitrous oxide inactivation of vitamin B12. Clinical presentation mimics pernicious anemia with megaloblastic anemia and subacute combined degeneration of the spinal cord. Hayden and colleagues reported a case of myeloneuropathy in a burn patient exposed to high concentrations chronically when he was given 50% nitrous oxide in oxygen to self-administer ad lib over approximately 4 months. Chronic exposure is also possible for workers exposed to nitrous oxide chronically. Sweeny et al. found bone marrow changes consistent with nitrous oxide toxicity in 3 of 21 dentists who used nitrous oxide for sedation and analgesia for their patients during long procedures. Ambient nitrous oxide concentrations were as high as 4600 ppm in their work areas. With modern scavenging systems, operating room personnel are not considered at risk. If nitrous oxide is used for analgesia for burn patients, adequate consideration must be given to chronic exposure of personnel.

**Ventilator patient**

Special consideration should be given to managing the pain of a patient requiring mechanical ventilation. The endotracheal tube causes significant discomfort, and sedation and analgesia are required to facilitate synchrony with mechanical breaths and minimize ventilator associated injury from increased airway pressures. Morphine or fentanyl along with midazolam are first-line drugs in most ICUs for ventilated patients. In some burn patients, opiate tolerance develops rapidly and is associated with hyperalgesia and poor pain control. Methadone has been found useful in burn patients poorly controlled with morphine. NMDA receptor antagonism by methadone has been used to explain this effect. Alpha-2 agonists (clonidine and dexmedetomidine) and low dose ketamine have been found in other patients. When muscle relaxants are used to facilitate mechanical ventilation it is necessary to ensure that adequate sedation and analgesic medications are also continuously administered.

**Rehabilitative phase**

There are several types of pain that patients report during the rehabilitative phase. First, patients report an aching type of pain, similar to arthritic pain. In this case, mild opioid analgesics, acetaminophen, or nonsteroidal anti-inflammatory drugs (NSAIDs) may be used for either procedural (exercise) or background pain. In addition ibuprofen may reduce the hypermetabolic state. There is disagreement between providers concerning the risk of ibuprofen in causing bleeding from grafts. Now ibuprofen is available in an intravenous form so it may be more useful. At the Shriners Hospital in Galveston, Ibuprofen is used a lot in the rehabilitation phase to help with muscle pain and seems to be more efficacious than opiates, which increase somnolence.

Because of the significant side-effect profile of nonsteroidal and anti-inflammatory drugs (NSAIDs) such as ibuprofen, acetaminophen has been considered for the management of chronic pain. Acetaminophen at a dose of 10–15 mg/kg of body weight given every 4 h (up to a maximum of 4000 mg/day) is equal in efficacy to Ibuprofen at a dose of 10 mg/kg of body weight given every 4 h (up to a maximum of 2400 mg/day). In addition, acetaminophen is well tolerated and causes almost no side-effects, although there is some concern about long-term liver problems with this medication.

The best response was with the younger children and the smaller burns, but acetaminophen levels should be monitored in very young or extremely ill children. One should be aware that, because acetaminophen is packaged in conjunction with hydrocodone in the form of Vicodin RX and Loratadine, one should be careful not to give acetaminophen in addition to either one of these combination medications.

We have found diazepam to be very useful in providing background anxiety control when muscle relaxation is desired (e.g. to facilitate rehabilitative exercise) in addition to attenuating anxiety. Because of its long half-life, it is ideal for treating the patient during the rehabilitative period when the healing burn wound is very uncomfortable and seems to inhibit doing any activities including sleep.

The second type of pain is neuropathic pain. This type of pain may either be due to the regeneration of nerve endings, or may be phantom pain from the loss of digits or limbs. Individuals with phantom limb pain often have sensations of the existence of these digits or limbs for many years after their loss. Neuropathic pain can also be associated with the damage to the nerve endings in the skin. The neuropathic pain has many descriptions: pins and needles, like someone walking on your skin with cleats, burning or the sensation of having multiple bites of fire ants. The only thing the patient can do to reduce the pain is to move around or rest. The pain is brought on sometimes by temperature change, dependent position, or weight-bearing activities. Often the pain will not start for many months after the injury (4.3 ± 0.5 months) but some have the pain immediately, especially if a limb or digit is lost.

This type of pain will often last more than a year and usually does not respond to traditional pain management with nonsteroidal acetaminophen or opioid analgesics. This neuropathic pain often does respond to the use of tricyclics or anticonvulsants. Doses of imipramine or amitriptyline of 1 mg/kg body weight often are effective. Phantom limb pain is more common in those with electrical injury than following flame injury. If the pain does not respond to this, then carbamazepine might be utilized in doses which are therapeutic for seizures. Gabapentin has been used for neuropathic pain with good effect with few side-effects. Most recently, pregabalin, which was developed for the treatment of the neuropathic pain of diabetes, has been used successfully for neuropathic pain of burns. Some patients have required the simultaneous use of several of these agents to get control of their pain. Over time, this neuropathic pain seems to become more tolerable and slowly dissipate. Gabapentin is not sedating for most patients but amitriptyline is. Both amitriptyline and pregabalin are associated with excessive weight gain.

**Itch medications**

Itch is one of the most common sequelae of burn injury. Field et al. reported that pruritus occurs in 87% of patients who have a burn injury. Although it is thought to be
secondary to the injury of the skin, the possibility that morphine is adding to the itch needs to be kept in mind. Itch can definitely influence the quality of life and duration of rehabilitation required. Scratching further injures the skin leading to graft loss and skin breakdown, sometimes requiring further grafting. In addition, it is very common for the patient to have a significant problem exercising or sleeping if the itching is intense. Several classes of medications can be used to treat itch but very few real comparative studies have been done. The approaches to treatment are as varied as the presumed causes of the itching. Pruritus associated with burns is poorly understood, so blocking histamine, kinins, proteases, prostaglandins, substance P and 5HT release and receptors have all been tried.

The first-line of defense is a series of moisturizing body shampoos and lotions to alleviate itching due to dry, scaly skin. Then, failing that, Preparation H, which contains a caine, has been advocated. Topical steroids are not usually used because of the infection risk, until the skin is well healed. They are effective in controlling the itching. Only a small area of skin should be treated with steroids in order to reduce the risk of systemic adrenal suppression. Antihistamine creams such as Benadryl (diphenhydramine) cream are available. Other topical medications include colloid and oatmeal baths. Newer topicals are tricyclic antidepressants such as doxipin. The major side-effect of this preparation is that too much is absorbed with resultant over sedation.

Several non-medication approaches have been used. Massage seems to have a very beneficial effect. In addition Hettrick et al. reported that Transcutaneous Electrical Nerve Stimulation (TENS) considerably reduced the perception of itching in 9 adult patients compared to control. The most recent is the use of pulse dye laser to reduce pruritus in burn scar. Silicone gel sheeting has been reported to also be effective.

Usually the antihistamines are given orally. Using only one antihistamine results in complete relief for only 10% of the patients. Diphenhydramine PO 1.25 mg/kg q.6 h is often the first oral medicine used because of its sedative effect as well as helping control the itch. A few children respond better to loratadine, which is much longer lasting. If the itch is not well controlled using only one, then another class of antihistamines can be added such as hydroxyzine PO 0.5/kg q.6 h. Lastly, if the itch is still not well controlled, an antiserotonergic agent, such as cyproheptadine 0.1 mg/kg q.6 h, can be added, scheduled so that one of the medications is given every 2 h. This is targeted against the 5HT1 receptors. Care must be made to not use the cyproheptadine with patients who are on serotonergic antidepressants.

Recently, gabapentin (10–35 mg/kg per day in divided doses) has been found in a pilot study to help with itching produced by burns. Typical individual dose is 5 mg/kg during the day and 10 mg/kg for bedtime. Comparative studies using gabapentin have demonstrated its efficacy. Goutos et al. demonstrated that it was usually more effective than antihistamines. If this holds, then gabapentin may move up to be tried if diphenhydramine fails. Like the other anti-itch medications the main side effects are central nervous system related, such as sedation and neuropsychiatric symptoms.

Another new class of medications to be used in chronic itching is naltrexone. First, LaSalle et al. reported suggesting some improvement in itch with naltrexone. Then, Jung et al. reported a significant decrease in itching sensation and scratching from 9 to 5.9 on a 10-point scale after 2 weeks of treatment with 50 mg of naltrexone at night when it was given with the usual antihistamines. Side-effects of headache and nausea were noted in many of the patients.

### Development of protocols for comfort

Interest in pain management of burned patients has been a high priority in the treatment of burns only in the last 10–15 years. Beginning in 1995, multiple institutions have published their pain protocols. The protocol currently used in the Shriners Burns Hospital in Galveston has been reviewed and up-dated every few years; the most recent version is shown in Box 64.4, and includes management of the most common discomforts of burned patients.

### Non-pharmacologic therapies in burned patients

As has been discussed, there is a strong interaction between psychological and physiological factors contributing to the pain experience. Anxiety in particular is prevalent among patients with burn injuries and is known to exacerbate acute pain. Non-pharmacologic therapies play an important role in addressing the psychological factors that exacerbate pain, as well as having a direct impact on the pain itself.

In understanding how non-pharmacologic approaches can be used with burn pain, it is important to discuss how behavioral principles contribute to the patient’s experience. In terms of classical (stimulus-response) conditioning, patients (particularly children) often will develop a conditioned anxiety response to stimuli associated with painful burn procedures. One study demonstrated that the simple event of a healthcare worker wearing scrubs was enough to elicit a fearful response in children with burns. In terms of operant (reinforcement) conditioning, patients can be thought to gain reinforcement by avoiding or escaping painful procedures, perhaps by screaming enough to terminate treatment or to obtain some sort of reinforcement from the staff by showing pain behaviors. Between the stimulus that precedes pain and the pain response that follows, there is the cognitive processing of pain. Such cognitions can be modified, as can behavior, and can influence how much pain a patient experiences. Classical and operant conditioning principles and modifying internal cognitions have a bearing on how non-pharmacologic approaches are applied to burn pain. Martin-Herz et al. and Thurber et al. provide an excellent overview and extensive discussion of the theory and application of such principles in pain management in pediatric wound care.

### Classical conditioning

If the stimuli associated with a painful procedure can be conditioned to evoke anxiety or pain, then a logical goal is to reduce the impact that pre-wound care stimuli have on the fear/pain response. An obvious environmental intervention is to make the wound care procedure setting as minimally threatening as possible. For children this might involve...
making the hydrotherapy tank a ‘bath tub play area’ with age appropriate floating toys, etc. Cheerful or relaxing music, a warm room and pleasing art on the walls can also lessen the threatening nature of a typical tank room. Our understanding is that some clever children’s hospital staffs have turned their MRI scan into a ‘cave in a jungle’; obviously such a setting will be less threatening to a child than will be the typical location of such radiological procedures. Similar setting will be less threatening to a child than will be the typical location of burn care can be quite complicated and the medical procedures they will undergo and their daily schedule. In addition, burn care can be quite complicated and the medical information that patients are required to process can be overwhelming. When an adult or child feels out of control, anxiety increases. We can enhance a patient’s sense of control over the hospital environment by allowing them to have input into their care as much as possible. For example, adults and adolescents may be able to work with the nurse to determine the day’s schedule, to specify techniques that they have found make wound care go smoother, choose to eat in the cafeteria instead of having meals served in their room, and choose the music that is played in wound care. Children should be offered forced choices as often as possible to create a sense of control. Forced choice is a technique whereby a child is give two reasonable options and allowed to choose the one they prefer. For example, a child might be offered forced choices as often as possible to create a sense of control. Forced choice is a technique whereby a child is given two reasonable options and allowed to choose the one they prefer. For example, a child might be given a choice of whether to have wound care before lunch or after dinner.

### Box 64.4 Shriners Burns Hospital (Galveston): comfort protocol for children

**Background pain**

**Inpatient**
- IV morphine sulfate 0.03–0.05 mg/kg every 2–4 h if awake; usually every 2 initially and then every 4.

*Note: Begin bowel prep program simultaneously with beginning opioids.*

**Outpatient**
- Oral acetaminophen 15 mg/kg q.4 h or Ibuprofen 10 mg/kg q.8 h
- If inadequate, add hydrocodone 0.2 mg/kg usually in combination with acetaminophen.

**Pre-wound cleaning**

**First choice**
- Hydrocodone 0.2 mg/kg in combination with acetaminophen 10–15 mg/kg usually given with lorazepam or 0.1 mg/kg diazepam
- If inadequate, fentanyl buccal mucosa (lollipop) 10 µg/kg.

**If NPO:**
- IV morphine 0.05–0.1 mg/kg (if >15 kg) with IV lorazepam 0.5 mg/kg.

**Pre-rehabilitation therapy**

- On request of therapist, hydrocodone 0.2 mg/kg in combination with acetaminophen 10–15 mg/kg usually given with benzodiazepine 0.5 mg/kg lorazepam or 0.1 mg/kg diazepam.

**Postoperative pain**

**Option A**
- IV morphine infusion via PCA pump (if >5 years), total dose 10–20 mg/kg per 4 h

**Option B**
- Attendant administered bolus, slow IV push morphine 0.03–0.05 mg/dose q.2 h (hold if level of responsiveness is decreased).

Update of Ratcliff et al. 2006.

**Anxiety**

**Inpatient**
- Lorazepam PO 0.05 mg/kg q.4–6 h

**Outpatient**
- If muscle relaxation is also desired, diazepam 0.1 mg/kg usually initially every 8 h.

*Note: Taper benzodiazepines slowly by reducing the dose by 50% every 2 days.*

**Acute stress disorder or post-traumatic stress disorder symptoms**
- Fluoxetine 5 mg if under 6 years of age; for the older person, begin with 5 mg and increase slowly to 20 mg as needed or
- Imipramine 1 mg/kg and increase slowly to 3 mg/kg as needed (usually used in young children where fluoxetine could not be easily dosed).

**Itch**
- Use skin moistening shampoos and lotions, topical ointments (not hydrocortisone creams)
- Begin with diphenhydramine PO 1.25 mg/kg q.4–6 h; if itch not well-controlled, add hydroxyzine PO 0.5/kg q.4–6 h
- If itch still not well-controlled add gabapentin begin 5 mg/kg once per day then titrate up to 10–35 mg/kg in three divided doses.
- Other meds that may be tried are the following:
  - Cyproheptadine 0.1 mg/kg q.6 h so that one of the medications is given every 2 h.
  - Loratadine 10 mg q.day.
  - Topical doxepin 5% cream to small areas.

**Note:** Taper benzodiazepines slowly by reducing the dose by 50% every 2 days.
or after lunch, or whether they prefer to take their medicine with apple juice or milk. The key is to only provide two options and to ensure that the healthcare provider and parent are agreeable to whichever option they choose. Kavanaugh and colleagues described how giving children more control during procedures can reduce the effects of learned helplessness, and enhance pain tolerance. He reported that children who were provided with the opportunity to participate in and make decisions about their wound care showed lower depression, anxiety, hostility and stress scores than did controls.

Finally, psychological preparation can also play an important role in enhancing control and minimizing anticipatory anxiety. Patients can be provided with procedural or sensory preparatory information. With procedural-based preparatory information, patients are explained the mechanics of their procedure (e.g. ‘we will unwrap your bandages, wash your wounds and debride necrotic skin, apply silver sulfadiazine cream and then rewrap your dressings’). With sensory information patients are prepared as to what they might feel during a procedure (‘You will likely feel a pulling sensation as we remove your dressings and a stinging sensation when we wash your wounds with an antiseptic’). Such information is usually helpful to patients, but we should stress that some patients prefer to have as little information as possible, given their particular coping styles. It is best to follow a patient’s lead in determining how much detail to provide when explaining upcoming procedures.

Another approach based on classical conditioning is relaxation training. Patients can be taught deep relaxation and imagery prior to undergoing painful procedures. The rationale is to counteract the anxiety stimulated by pre-procedural stimuli with the relaxation response. If anticipatory anxiety is minimized with deep relaxation, the potential for a cyclical interaction between anxiety and acute pain is reduced. Clinicians have also reported success administering massage therapy on non-burned areas immediately prior to wound care. Children who received 15 min of massage therapy reported lower pain scores during wound care than a control group. A number of studies have applied relaxation training and stress inoculation techniques, as well as some of the behavioral techniques discussed below to reduce burn pain.

Operant conditioning

The consequences that patients receive for showing pain can have implications for pain control. Since almost all burn procedures are extremely aversive, it will be the natural tendency of patients, particularly children, to be motivated to escape such events. Staff members who allow patients to terminate procedures might be reinforcing, and potentially exacerbating, such as escape behaviors. When left unchecked, this process can lead to a distressed patient becoming combative rather than tolerating procedures. While such avoidance behavior should (more importantly) alert the staff that analgesia is inadequate, and the many potential pharmacologic protocols discussed above should be invoked, it can also occasionally suggest a need for further limit setting. Rewarding a patient with rest once a stage of wound care is completed rather than based on pain behavior can be a useful means to minimize such escalating behavior.

Children can also be given a predetermined number (usually five is adequate) of ‘timeout cards’ that they can present at any time during wound care and it is worth a 1-min timeout or rest period. Once the cards are used up, they no longer have any timeouts. This technique can enhance their sense of control over the environment as well as ensuring that rest periods do not reinforce pain behaviors. Again, however, the goal of a burn team should be to provide enough preparation and analgesia in a pre-emptive fashion that the need for such escape behaviors do not develop in the first place.

Another common application of operant principles has to do with token economies for children. It can be extremely useful to reward children for successful completion of procedures by using star charts, prize boxes or reinforcement schedules of this nature. Thus, a child, upon completing a procedure, may receive a star in a grid that covers a week of burn care. Older children can use an accumulation of points to purchase a desired reward. Courage beads have also become popular in pediatric hospital settings. Different colored beads are assigned to various painful or unpleasant procedures (e.g. wound care, physical therapy, X-ray, blood draws, etc). Each time a child completes one of these unpleasant procedures, they receive the corresponding bead and add it to a necklace. Both boys and girls have responded positively to these necklaces and often wear them or display them as a source of pride. It is important that children are rewarded for completing procedures rather than for ‘being brave’ as the latter can serve as a subtle form of punishment to children; in other words, reinforcement should not be withheld if children act out and have a bad day during wound care, as long as wound care is completed (see before).

One final application of operant principles that is borrowed from the chronic pain literature is the use of a quota system that rewards activity with rest. This is particularly useful with patients who are overwhelmed by therapies or who appear to have poor motivation. Patients complete predetermined quotas of activity that are within their capacity, and then are allowed to rest. A baseline assessment determines what is within their capacity. For example, a patient who is trying to walk with burned legs might be instructed to walk until tired for three therapy sessions. The distance walked is recorded for those three sessions, the average is taken, and 80% of that average becomes the starting point. For example, the patient walks 50, 150, and 100 feet during three sessions. The average is 100 feet and 80% of that is 80 feet. This (80 feet) becomes the starting point. Patients start at 80 feet and increase that amount by 5% (about 5 feet) each session. If they fail to meet a quota, they return to the last successful one. However, they also quit when they reach the goal. They do not keep exercising even when they are having a ‘good day.’ This addresses the problem of pacing and over-fatigue. Ehde et al. have reported the successful use of the quota with a number of patients with burn injury, both in terms of increasing therapy performance and reducing depression.

Cognitive interventions

How patients think about their pain can be regarded as a behavior that can be modified and, in turn, can influence the degree of suffering they experience. As such, an
important nonpharmacologic approach is to draw out the thoughts patients have about their pain and teach them to modify accordingly. A particularly salient example is catastrophizing about pain. Catastrophizing thoughts include those such as ‘I cannot stand this pain,’ ‘I will never get better,’ or ‘The pain means I will die.’ Such catastrophizing thoughts have been associated with greater amounts of pain and less favorable health outcomes in a variety of studies. Patients can be taught to challenge and reinterpret such thoughts. Along the same lines, it can be useful to teach patients to reinterpret the meaning of their pain sensations. For example, the appearance of skin buds and enhanced pain sensation may indicate that a wound is healing and skin grafts may not be necessary.222

Under the rubric of cognitive interventions patients may be taught techniques to enhance their ability to cope with pain. Positive self-talk and imagery designed to facilitate coping during periods of pain are examples of this. Thurber et al.215 and Martin-Herz et al.214 have published a two part series on a conceptualization of psychological approaches to burn pain, as well as specific examples for treatment. Crucial in choosing an approach is the assessment of a person’s coping style. At one end of the continuum is the avoidant coping style where patients prefer to turn away or be distracted during painful procedures. Any distraction technique described in this chapter would be appropriate for this group of patients. On the opposite anchor of the continuum are those with an approach coping style who seek information and like to be involved as much as possible in their care. In this group, having them participate in wound care, and giving them as much information as they request will help to decrease their anxiety. If they are told to close their eyes, turn away and distract themselves from the procedure at hand, their anxiety will only increase.

Distraction is another cognitively based approach to pain control. Processing pain requires a certain amount of conscious attention and distracting such patients’ attention can enable patients to tolerate pain better. Movies, music therapy and games have all been used with some success as distraction techniques for burn pain.222,226,228 Music has the additional benefit of inducing a relaxation response.223,229

Virtual reality

Another form of distraction gaining attention is the use of virtual reality technology. Several researchers have reported on the use of immersive virtual reality (VR) as a powerful analgesic.230,231,238 Virtual reality can immerse patients’ attention in a computer-generated world, and engage them in interaction with that world. These investigators indicate that VR can significantly reduce pain during wound care and physical therapy,230,238 even relative to computer game distraction and television.231,239 Recently, Morris et al.230,239,239a conducted a systematic review on the use of virtual reality distraction for reducing both pain and anxiety in acute burn pain. They found nine studies that met their rigorous inclusion criteria. Results showed that virtual reality distraction is most often used for burn wound care and physical therapy and is an adjunct to pharmacotherapy. When compared to pharmacotherapy alone, it appears that virtual reality distraction is superior in reducing pain. However, there is equivocal evidence for the effect of virtual reality on reducing anxiety during these procedures.

Hypnosis

Hypnosis involves a blend of relaxation, imagery and cognitive based approach. The technique deserves special attention because there are a number of reports on its use with burn pain and, when it is effective, its impact on burn pain can be quite dramatic. There are over 100 anecdotal reports in the literature that indicate that hypnosis can dramatically reduce pain and at least a dozen have been done with pain from burn injuries; such studies however lack control groups, standard measures of pain or information about pain medications.241 More recently, tightly controlled studies with reliable measures of pain have supported hypnosis as an effective nonpharmacologic approach to burn pain.242,243 Patterson and Jensen have reported 12 controlled studies on chronic pain and 17 with acute pain, indicating pain reduction; indeed, this modality is becoming far more scientifically acceptable.244

Patients with burn injuries are ideal candidates for hypnosis for a number of reasons. In a review of such factors, Patterson et al.245 listed motivation, regression, dissociation and hypnotizability as factors that promote hypnotic analgesia on the burn unit.245 Specifically, patients who are faced with the excruciating nature of burn pain are motivated to engage in techniques such as hypnosis. The nature of a burn and its resulting care can cause a patient to become emotionally regressed (i.e. more dependent on the burn staff) and dissociated (i.e. removed from their emotions), and both of these factors seem to be associated with hypnotizability. Such factors likely account for the frequent dramatic effects that are seen with hypnosis and burn care. On the other hand, hypnosis clearly will not benefit some burn patients, and the degree to which patients are inherently hypnotizable (or not hypnotizable) almost certainly has some bearing on this issue.245

Ewin246,247 has strongly argued for providing hypnosis within 2–4 hours after a patient sustains a burn injury. He maintains that this approach can serve to impede the progression of the burn as well as facilitate pain control. Unfortunately, it is difficult to have a clinician available during this stage of burn care, and Ewin’s findings have yet to be tested in other settings. The protocol used by Patterson and colleagues248–250 is to provide hypnosis prior to wound care and have nurses provide standard post-hypnotic suggestions during wound care. This approach is efficient for both the hypnotist and the nurses. Patterson et al. have recommended that hypnosis used in this fashion be an adjunct to, rather than replacement for, pain medication.245 A randomized controlled trial by Wiechman et al.248 used this protocol for burn wound pain and found that hypnosis significantly reduced the affective component of pain when compared to an attention-only control group. Further, Shakibaei et al. conducted a randomized controlled trial of hypnosis for reducing pain and reducing flashbacks in burn patients.249 They also showed that the hypnotherapy group had significantly lower pain ratings and fewer flashbacks than the control group.
Virtual reality hypnosis

More recently, investigators have combined immersive virtual reality with hypnosis in order to control burn pain. This approach has the advantage of not requiring a trained hypnotist to be present and appears to work as well as ‘live hypnosis’.252,250 The technology simply requires patients to open their eyes and watch the induction presented before them; minimal cognitive effort or skill is required. Delivering hypnosis in this addressed several concerns of standard, therapist induced hypnosis. First, this standardized procedure allows for greater use in that it does not require a trained therapist to be present at each session. Second, with the visual images in front of them, it decreases the extent of cognitive effort that is required. This is important for patients who are taking opiate medications and cannot concentrate as effectively. It also helps those who are lower in visual imagery skills and, therefore, unable to visually imagine the scenes described by the therapist during traditional hypnosis.

Empirical support

Recently, there have been several rigorous systematic reviews of studies that have focused on both pediatric and adult nonpharmacological pain management strategies. Hanson and colleagues conducted a systematic review of nonpharmacological interventions for acute procedural pain in pediatric patients with burn injuries.253 Using systematic review methods of the US Preventative Services Task Force, they found 12 articles that met the study criteria and seven of the 12 articles were rated as ‘fair or good’. They categorized these 12 articles into child mediated interventions, parent mediated interventions and healthcare provider mediated interventions. Of the child mediated interventions, both virtual reality distraction and stress management showed promising effects. Of the healthcare provider interventions, massage therapy, and optimizing patient control during wound care were effective at relieving wound care pain when compared to a control group. Parent mediated interventions were not found to be effective, and in fact, one study showed an increase in children’s distress when parents were present.254 Although the study designs in these interventions were rated as poor, the findings are consistent with those reported by clinicians, in that parental presence during painful procedures can either help a child or hurt a child depending upon the parents’ affect and ability to soothe their child. This is a difficult intervention to study, but one that deserves more attention in this era of family-centered care and the emphasis on increased parental involvement in a child’s care. It would be a tremendous benefit to the field if we could determine which variables are necessary to facilitate a positive parental presence, and which variables serve as barriers to the success of this practice. Hanson et al.255 acknowledged that it is very difficult to conduct randomized controlled trials with adequate sample sizes in this population, but we need to strive to find empirical support for the techniques that we choose.

de Jong et al. also conducted a systematic review of the literature for non-pharmacological interventions for acute burn pain in adults.255 They found that hypnosis was the most frequently studied intervention and that the majority of the studies on hypnosis showed a beneficial effect when compared to a control group. They concluded that hypnosis seems to have a strong impact on the affective component of pain. Their review also showed beneficial effects of distraction relaxation and found that any technique that enhances a patient’s control over the situation is beneficial.

The authors of these systematic reviews provided directions for future researchers that would advance our knowledge of the effectiveness of nonpharmacological interventions. These suggestions included the need for large sample sizes, documentation regarding study response rates and randomization methods, experimental control for premorbid psychosocial variables, details on instructions given to patients, cost outcomes, and assurance of treatment integrity/ adherence.253,255

Summary

The current practice of burn pain management would seem to be based more on personal bias and tradition than on a systematic, scientific approach. In addition, the number of pharmacokinetic studies of pain-relieving drugs of any kind in young children is sparse. Since approximately 35% of all burn injuries occur in children under 16 years, with a great majority of these occurring in children under 2 years, we have almost no information on which to base the use of pain-relieving drugs in burned children. It is no wonder that Perry and Heidrick256 found great disparity in which burn care staff would order or administer to a young child as compared to an adult with burns of similar size and area of distribution on the body. More pharmacokinetic studies in both adults and children with burn injuries must be initiated.

However, significant progress has been made since the last edition of this book. Both Faucher and Furukawa109 and Sumner et al.257 have published comprehensive reviews of burn pain management and have offered some protocols for clinical use. Another standardized protocol offering guidelines for starting doses of medication from the Shriners Burn Hospital in Galveston is given in Box 64.4. Nonpharmacologic techniques are more frequently included in a center’s repertoire of tools for managing anxiety, recognized as a definite adjunct to pharmacotherapy. Most burn centers recognize anxiety as contributing to patient discomfort and are beginning to treat both anxiety and pain. The major problem currently with these techniques is that they are personnel intensive and therefore are often not offered or reimbursed in the current managed care environment in the USA.

Appropriate pain management depends on vigilance in assessment and flexibility in treatment. Patients show great individual variation in their responses to the variety of agents and modalities presented. A fixed and inflexible approach to treatment is likely to over-medicate on one day and under medicate the next.

To avoid over- and under-medication in adults, regimens which allow patients to control their own therapy seem most appropriate. This is very important for adults and teenagers, but children also can benefit from having this control. PCA can be used safely by many children and should not be disregarded as a tool on the basis of age alone. For procedural pain, patient control regimens may include
Management of pain and other discomforts in burned patients

• feel comfortable with a process that never ends, but which can bring many moments of relief for the patient and satisfaction for the caregivers.

Further reading


self-administered nitrous oxide, PCA, hypnosis, a variety of behavioral approaches, or a combination of these approaches. For background pain, the best control seems to be the use of slow release opioids or other pain cocktails given on a non-pain contingent basis (i.e. scheduled every 4–6 h), with the flexibility to supplement this with PRN or ‘as desired’ medication. Another approach would be to use PCA with or without a continuous low-dose infusion of narcotics. A variety of non-pharmacologic therapies may also help relieve background pain. The most important aspect to remember with all of these regimens, as mentioned before, is flexibility. The other obvious aspect is to remember that a patient is not only the best person to assess his pain, but he is also the best to evaluate the success of the therapies provided.

Burn care professionals who desire to keep their patients as comfortable as possible can perhaps best prepare themselves by learning to:

• watch and listen to their patients with vigilance;
• use a standardized assessment tool for measuring discomfort on a scheduled basis as well as during moments when the patient is complaining, either verbally or behaviorally, pre- and post-administration of treatment;
• know how discomforts are likely to change as the patient recovers;
• include a variety of pharmacologic and non-pharmacologic methods for managing discomforts and be prepared to change as the patients’ needs change;

Access the complete reference list online at http://www.expertconsult.com
References


Psychiatric disorders associated with burn injury

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Introduction

All members of the treatment team should have a basic knowledge of psychiatric problems, as they commonly occur and often play a central role in burn recovery. It is useful to have mental health professionals as integrated members of the team, as their expertise and skills are often needed in the management of patients with burns, to screen and identify and assist in the treatment of the multitudes of psychiatric and psychological issues concomitant to burns.

Pre-existing psychiatric disorders and symptoms are relatively common in the histories of burned patients, and frequently appear to have contributed significantly to the etiology of the injury itself.1–4

Besides premorbid disorders, a number of patients will develop psychiatric symptoms during acute treatment for burns, as also can be seen after other major trauma.4 Pain, itching and stress during hospitalization can contribute to problems during acute treatment such as sleep disorders and depression, starting a vicious circle. Dissociation and anxiety experienced during the burn have been shown to predict later psychopathology.5,6 While it is understandable to expect patients with major burns to be at risk, even minor burns can result in significant psychological distress and psychiatric symptoms.7

At the present time, there is no profile that can reliably predict and identify which patients will suffer psychiatric symptoms following burns. Furthermore, patients will seldom actively seek help for psychological distress or psychiatric symptoms, although this can have a strong effect on outcome and rehabilitation. All members of the burn team should be aware of this dilemma and be observant of signs or symptoms.

This chapter will focus on the recognition and treatment of common mental disturbances that can be expected to occur in patients suffering serious burns. This includes specific attention to both pediatric as well as adult patients, as symptoms and signs may differ between ages. Although pre-existing psychopathology alters the expression of a patient’s distress and complicates medical management of the patient, the common symptoms described in this chapter are not necessarily indicative of premorbid psychopathology.

Premorbid adult psychiatric disorders

Although a burn can occur to anyone, psychiatric morbidity greatly increases the risk of sustaining an injury, either directly (e.g. self-inflicted burns or suicide attempts) or indirectly by reducing vigilance or affecting judgment (e.g. substance abuse, depression).1,7,8 The knowledge of pre-existing psychiatric problems is important for burn care mainly for two reasons: first, to better understand and identify psychiatric symptoms occurring during treatment and to recognize them as ongoing or reactivated problems instead of reactions to the injury and second, to increase awareness of potential difficulties during rehabilitation (for a comprehensive review refer to McKibben et al. 20091).

Patients with pre-injury psychiatric disorders have been observed to require longer hospitalization, they more frequently experience complications during treatment, problems with rehabilitation and post-burn adjustment, and have a higher risk of developing other psychiatric disorders, e.g. post-traumatic stress disorder (PTSD).3,4,9–11

Psychiatric disorders

Psychiatric morbidity is common in burn patients. Two-thirds of all patients with burns have at least one psychiatric disorder, 50% had a psychiatric disorder in the year before injury, and one third have an ongoing psychiatric disorder at the time of injury.1

The most frequent preexisting psychiatric disorder in burn patients is the mood disorder major depression, which is present in up to 42% of individuals, a proportion much higher than in the general population.1 Smoking (more than 10 cigarettes daily) has been shown to increase the risk of burns by up to six-fold. In the use of certain drugs, e.g. the stimulant drug methamphetamine, highly volatile and flammable substances, which further increases the risk of getting burned.12

Patients with pre-existing psychiatric morbidity have a higher risk of sustaining a preventable injury and in individuals with psychotic disorders self-inflicted burns are over-represented.1 Personality disorders are also over-represented in burn patients compared to the general population and
persons who score high on the personality traits neuroticism and extraversion appear to have a higher risk of injury.1

Self-inflicted burns and suicide attempts

Of patients with self-inflicted burns, those attempting suicide are more likely to have larger burns and longer hospitalizations than those with the intent of self-mutilation.13

The proportion of self-inflicted burns differs across the world: whereas it is between 1% and 9% in North America and Europe with no clear gender distribution, it is a major cause of burns in females in the Middle East, Africa and south Asia with a prevalence of up to 28%. Across cultures psychiatric morbidity is an important risk factor, often in conjunction with social stress factors such as marital problems or unemployment.1

Pediatric disorders (ADHD, conduct)

Prior psychological problems can increase risk for pediatric burns and specific psychiatric disorders have been found to occur more frequently in pediatric burn survivors than the general population. Children with attention deficit hyperactivity disorder (ADHD) appear to be at greater risk for burns.14–16 Playing with fire and fire setting are symptoms of conduct disorder17 and can result in burns. In addition, certain types of inhalant abuse (sniffing) can result in burns. Commonly, pediatric burn survivors may not exhibit symptoms of prior psychiatric disorders during the acute phase of treatment due to the impact of injuries and other treatments. When symptoms are evident, continuation of prior treatment or implementation of indicated treatment for a pre-existing psychiatric disorder may not only control symptoms but also facilitate patient participation and cooperation with acute care and long term rehabilitation.

Social (family)

Clearly, parental and family characteristics can both increase the risk for burns in children as well as influence the subsequent recovery and outcome. The presence of child abuse or neglect can directly result in pediatric burns.1,18,19 The presence of parental anxiety, depression, poor coping skills or lack of social support at the time of injury were associated with poorer child functional outcome in pediatric burn survivors.20,21 Possibly, high parent anxiety in combination with ineffective coping strategies, rather than family functioning or burn severity, is most predictive of pediatric burn outcome.22

Parents are psychologically traumatized by the burns of their children and face numerous emotional challenges during subsequent treatment and recovery. Parents report more feelings of anxiety and being stressed, depressed and guilty than the normal reference population, not only by their children’s behaviors but in areas unrelated to their children.23,24 These stresses can result in psychiatric disorders in parents up to 2 years following the injury, with mothers at greater risk for developing mental health problems and depressive and post-traumatic stress symptoms.24–26 Increased risk for depression was associated with having an only child or multiple offspring injured, low family socioeconomic status and complicated burn injuries (secondary infection or amputation). Larger burns and the presence of parent–child conflict, parental dissociation, or PTSD symptoms in the child were strongly correlated with parental PTSD symptoms.27,28 This emphasizes the need for psychological attention to parents of burned children, as well as to the children themselves.

In-hospital contributing factors and disorders

Several problems during acute burn treatment can affect the course of treatment and eventually outcome after burns. Pain, itching and sleep disorders are caused by both the injury and its treatment. High levels of stress and anxiety may contribute to the development of psychiatric morbidity, e.g. PTSD. In patients with substance dependence, withdrawal symptoms can occur during acute care and patients with pre-injury substance abuse have a higher risk of developing psychiatric symptoms during and after acute care. There is evidence that in the case of comorbidity of PTSD and substance abuse concurrent treatment of both disorders is necessary to achieve improvement.29

After the initial post-burn period, a patient progresses through a series of operative procedures interspersed with days of physical therapy. A patient’s world is one of pain or the sure knowledge of repeated pain in the near future and feelings of anxiety and powerlessness are predominant.30–33 Every movement, e.g. shifting position and change of bedclothes, is painful. Treatment and experience of hospitalization may be as traumatic psychologically as the original burn, and patients who experience high levels of pain not only have a higher risk of poor adjustment and psychiatric problems after discharge, but also wound healing can decrease due to stress.32,34 Furthermore, high levels of stress and anxiety and PTSD decrease pain tolerance.31

Itching is a common problem during wound healing and scar maturation, and it can cause considerable distress and anxiety.33,35,36 Persistent itching can disrupt sleep, which increases stress levels and also impairs everyday functioning and participation in rehabilitation.37 Anxiolytic, antidepressant and antipsychotic agents have been used successfully to treat itch.36

Significant sleep problems are common during and after treatment for acute burns.38–40 The noise and light on the unit and interruptions for treatment will disrupt sleep.41 Pain, anxiety and itching can disrupt sleep or affect sleep quality, and symptoms of stress and PTSD, e.g. nightmares, can cause both awakening and a fear of going back to sleep.39,42 Pain severity during hospitalization has been shown to predict insomnia after discharge and insomnia in turn predicted long-term pain.40 Burn patients who experience poor sleep at night will also have lower pain tolerance during the day.42

In-hospital adult disorders

During treatment for acute burns disorientation, confusion, delirium, transient psychosis, depression and anxiety, stress and sleep disorders are commonly observed.3 Causes of these symptoms are multifactorial: hypoglycemia, sepsis, and/or a variety of other organic problems can contribute.
The altered state of consciousness may be transitory, wax and wane over several days, or, with large burns, persist for weeks.

A significant number of burn survivors will experience acute or post-traumatic stress disorder symptoms, including intrusive memories of the injury, during their acute recovery.1,43

Symptoms of depression and agitation related to excessive pain will subside with adequate pain management. The experience of pain has been found to be a mediating risk factor for PTSD in both pediatric and adult burn patients.32,44

After severe burns patients are at risk for the development of substance abuse in the wake of PTSD.3,29 In contrast, the use of opioids and other pain medication will not cause dependence per se if adequately administered and tapered when pain levels decrease.31,45

**Delirium**

Delirium is a state of acute brain dysfunction. It is a transient and usually reversible syndrome with disturbance of consciousness and cognition compared to previous levels of functioning. Hallucinations and delusions can occur and patients in delirium can become suicidal or combative. Early symptoms can be restlessness, anxiety, disorientation or sleep disorders.

Delirium in burn patients has been found to occur more often in individuals with a history of substance abuse or other psychological problems and with larger burns.46,47

Another potential cause of disorientation, hallucinations, and agitation may be medications used in the treatment of the acute burn patient.37 Sleep deprivation has also been discussed as a cause for delirium in ICU-patients.38

Sepsis and metabolic conditions can also result in hallucinations.

**Acute stress disorder (ASD)**

Acute stress disorder is the most common psychiatric disorder seen in survivors of major burns besides post-traumatic stress disorder (PTSD), with a prevalence as high as 19%.5,33,43,49 Acute stress disorder symptoms appear immediately following the trauma, last for at least two days and usually resolve within 4 weeks after the trauma. The criteria for ASD and PTSD according to DSM-IV-TR are shown in Table 65.1.17

The presence of avoidant symptoms during the acute phase of recovery is reported to predict chronic

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**Table 65.1 Criteria for post-traumatic stress disorder (PTSD)**

<table>
<thead>
<tr>
<th>A.</th>
<th>The person has been exposed to a traumatic event in which both of the following were present:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>The person experienced, witnessed, or was confronted with an event or events that involved actual or threatened death or serious injury, or a threat to the physical integrity of self or others.</td>
</tr>
<tr>
<td>2.</td>
<td>The person’s response involved intense fear, helplessness, or horror. <strong>Note:</strong> In children, this may be expressed instead by disorganized or agitated behavior.</td>
</tr>
<tr>
<td>B.</td>
<td>The traumatic event is persistently re-experienced in one (or more) of the following ways:</td>
</tr>
<tr>
<td>1.</td>
<td>Recurrent and intrusive distressing recollections of the event, including images, thoughts, or perceptions. <strong>Note:</strong> In young children, repetitive play may occur in which themes or aspects of the trauma are expressed.</td>
</tr>
<tr>
<td>2.</td>
<td>Recurrent distressing dreams of the event. <strong>Note:</strong> In children, there may be frightening dreams without recognizable content.</td>
</tr>
<tr>
<td>3.</td>
<td>Acting or feeling as if the traumatic event were recurring (includes a sense of reliving the experience, illusions, hallucinations, and dissociative flashback episodes, including those that occur on awakening or when intoxicated). <strong>Note:</strong> In young children, trauma-specific reenactment may occur.</td>
</tr>
<tr>
<td>4.</td>
<td>Intense psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event.</td>
</tr>
<tr>
<td>5.</td>
<td>Physiological reactivity on exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event.</td>
</tr>
<tr>
<td>C.</td>
<td>Persistent avoidance of stimuli associated with the trauma and numbing of general responsiveness (not present before the trauma), as indicated by three (or more) of the following:</td>
</tr>
<tr>
<td>1.</td>
<td>Efforts to avoid thoughts, feelings, or conversations associated with the trauma</td>
</tr>
<tr>
<td>2.</td>
<td>Efforts to avoid activities, places, or people that arouse recollections of the trauma</td>
</tr>
<tr>
<td>3.</td>
<td>Inability to recall an important aspect of the trauma</td>
</tr>
<tr>
<td>4.</td>
<td>Markedly diminished interest or participation in significant activities</td>
</tr>
<tr>
<td>5.</td>
<td>Feeling of detachment or estrangement from others</td>
</tr>
<tr>
<td>6.</td>
<td>Restricted range of affect (e.g. unable to have loving feelings)</td>
</tr>
<tr>
<td>7.</td>
<td>Sense of a foreshortened future (e.g. does not expect to have a career, marriage, children, or a normal life span)</td>
</tr>
<tr>
<td>D.</td>
<td>Persistent symptoms of increased arousal (not present before the trauma), as indicated by two (or more) of the following:</td>
</tr>
<tr>
<td>1.</td>
<td>Difficulty falling or staying asleep</td>
</tr>
<tr>
<td>2.</td>
<td>Irritability or outbursts of anger</td>
</tr>
<tr>
<td>3.</td>
<td>Difficulty concentrating</td>
</tr>
<tr>
<td>4.</td>
<td>Hypervigilance</td>
</tr>
<tr>
<td>5.</td>
<td>Exaggerated startle response.</td>
</tr>
<tr>
<td>E.</td>
<td>Duration of the disturbance (symptoms in Criteria B, C, and D) is more than 1 month.</td>
</tr>
<tr>
<td>F.</td>
<td>The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.</td>
</tr>
</tbody>
</table>

Specify if:

**Acute:** if duration of symptoms is less than 3 months

**Chronic:** if duration of symptoms is 3 months or more

With delayed onset: if onset of symptoms is at least 6 months after the stressor.

post-traumatic disorder in burn patients.\textsuperscript{50,51} It is of great importance to recognize symptoms of ASD and PTSD at an early stage, as ASD has been shown to be a predictor for PTSD and once PTSD is established it usually will persist.\textsuperscript{55}

**Depression**

Although depression is a reaction most observers would expect of burned patients, only a relatively small number of patients with burns have been observed to have symptoms of severe depression.\textsuperscript{49,52,53} In most studies pre-injury depression or lower levels of well-being were stronger predictors than burn size for subsequent depression. All the same, those individuals who experience symptoms of depression during hospitalization will continue to do so after discharge, so that early recognition and treatment may improve their situation considerably.\textsuperscript{52}

The criteria for major depression according to DSM-IV-TR can be found in Table 65.2.\textsuperscript{17} This is an extremely difficult diagnosis to make during the acute burn period, since many of the criteria are linked to physical symptoms. Even beyond the acute phase, the diagnosis is often complicated by grief. The critical symptoms in a burned patient are depressed mood and anhedonia.

**In-hospital pediatric disorders**

Symptoms of delirium and transient psychosis rarely occur among children under the age of 10 years.\textsuperscript{56} True hallucinations are uncommon in children, but when they do occur, the most likely cause is stress, followed by pain and medications.\textsuperscript{54} Sepsis and metabolic conditions can also result in hallucinations, and are a more frequent cause of this than psychiatric disorder in young burn patients.

In contrast to delirium and psychosis, burn encephalopathy is often observed in children,\textsuperscript{56,57} characterized by lethargy, withdrawal, or coma. EEGs in such cases typically reveal diffuse, nonspecific slow waves. Causative factors probably are the same as those for delirium.\textsuperscript{58}

Even young children can experience severe anxiety following burns, with up to a third of patients reporting symptoms of acute stress disorder in the immediate aftermath of burns.\textsuperscript{59} Mediating factors for the appearance of anxiety symptoms appear to be size of burn, parental stress and the experience of pain. In a study of pediatric burn patients, a high resting heart rate, lowered body image and parental stress symptoms were found to be significant risk factors in development of ASD.\textsuperscript{60}

Pain in children appears to dramatically increase the risk for development of anxiety symptoms and subsequent anxiety disorders; appropriate pain management can reduce or resolve anxiety symptoms.\textsuperscript{61,62} A smaller but still significant number of burn survivors will experience post-traumatic stress disorder symptoms, including intrusive memories of the injury, during their acute recovery.\textsuperscript{63,64}

**Long-term post-burn disorders**

The main factors that have been suggested as reasons for psychiatric problems beyond the time of the discharge from the burn care center are pain and previous psychiatric illness. Pain and depression seem to be linked in such a way that they can cause each other.\textsuperscript{65} Also acute pain at the time

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### Table 65.2 Criteria for major depressive episode

| A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning: at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.  |
| Note: Do not include symptoms that are clearly due to a general medical condition, or mood-incongruent delusions or hallucinations. |
| 1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g. feels sad or empty) or observation made by others (e.g. appears tearful). Note: In children and adolescents, can be irritable mood. |
| 2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation made by others). |
| 3. Significant weight loss when not dieting or weight gain (e.g. a change of more than 5% of body weight in 1 month), or decrease or increase in appetite nearly every day. Note: In children, consider failure to make expected weight gains. |
| 4. Insomnia or hypersomnia nearly every day. |
| 5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down). |
| 6. Fatigue or loss of energy nearly every day. |
| 7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick). |
| 8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others). |
| 9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide. |

| B. The symptoms do not meet criteria for a Mixed Episode. |
| C. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning. |
| D. The symptoms are not due to the direct physiological effects of a substance (e.g. a drug of abuse, a medication) or a general medical condition (e.g. hypothyroidism). |
| E. The symptoms are not better accounted for by Bereavement, i.e. after the loss of a loved one, the symptoms persist for longer than 2 months or are characterized by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, or psychomotor retardation. |

American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Text Revision (DSM-IV-TR), 4th edn. 2000.\textsuperscript{17}
of discharge from the hospital seems to produce long term suicidal ideation.66,67 There is a reciprocal relationship between pain and depression or anxiety.57

Another predictor of psychiatric problems is the presence of psychiatric or personality disorders pre-burn.2 Cognitive processes may play an important role as, for example, burn-related attentional bias has been shown to be strongly associated with PTSD 1 year post-injury.68 Skull burns are associated with cognitive as well as affective disorders post-burn,69 but there does not seem to be a relationship to facial burns or even very large burns.

**Post-traumatic stress disorder (PTSD)**

Post-traumatic stress disorder (PTSD) is the most common psychiatric disorder seen in survivors of major burns70 with a prevalence as high as 45%.33,43,70,71 The diagnostic criteria for PTSD are shown in Table 65.1. About one-third of burn survivors develop post-traumatic stress disorder within 2 years of their injury72 and this was true for even small burns.73 ASD seems to predict PTSD in most adult burn survivors.43,74

The patient should be interviewed about sleep patterns and startle response, as nightmares and altered sleep patterns are usually the symptoms first noted. In fact, one of the most important pieces of information for screening for PTSD is nightmares in adults.75 A significant number of burn survivors will experience post-traumatic stress disorder symptoms, including intrusive memories of the injury, during their acute recovery.83,84 The presence of avoidant post-traumatic disorder symptoms during the acute phase of recovery is reported to predict chronic post-traumatic disorder in burn patients.30,43,72,74,78 Patients should be given ample opportunity to explore their feelings and fears about the traumatic event. Concerns that midazolam administration might interfere with this process and actually enhance PTSD could not be substantiated.77

**Other anxiety disorders**

Many patients continue beyond acute hospitalization to have periods during which they appear extremely anxious and express fear. These periods often recur in association with return to a hospital for reconstructive surgeries. General anxiety is characterized by excessive worry for more days than not, for at least 6 months, difficulty in controlling the anxiety, clinically significant distress or impairment in social occupation or other important areas of functioning, and anxiety with three or more of the following: restlessness, feeling on edge, easily fatigued, difficulty concentrating – mind going blank, irritability, muscle tension or sleep disturbance.

In the literature, the prevalence of anxiety disorders in adults during the year after burn – usually generalized anxiety disorder or agoraphobia without panic – is below 20% and those with very small burns had even less anxiety.7,78 Avoidant coping style was significantly correlated with the level of anxiety at 3 months.7 In a study of young adults burned as children and with much larger burns than the other studies all the anxiety disorders were found and they were twice as common as in matched controls: 12.9% of the subjects had a specific phobia, 6.9% had generalized anxiety and 20.8% had PTSD.79

Not infrequently, anxiety spills over to other situations and/or becomes focused on specific objects; thus, phobias develop that are characterized by excessive persistent fear in response to specific stimuli. In a burned patient, difficulty controlling anxiety which is so distressful that it interferes with important functioning, restlessness, and difficulty in concentrating, are diagnostic of anxiety disorders since some other symptoms can be related to burn injuries specifically, e.g. being easily fatigued.

Although adults may express anxiety through ‘panic’ symptoms such as sweating, palpitations, trembling, or nausea, children may express anxiety by crying, tantrums, freezing, or clinging. A differential diagnosis of these anxiety disorders distinct from post-traumatic stress disorder is difficult and requires a careful interview. An over-anxious patient is afraid of what might happen: the post-traumatic stress disorder patient re-experiences and fears what has happened.

**Major depression**

The critical symptoms in a burned patient are depressed mood and anhedonia and sometimes the mood is seen as irritable rather than depressed. Due to an overlap in symptoms of depression and somatic problems caused by the burn itself (fatigue, sleeplessness) it can be difficult to assess the ‘true’ proportion of patients with depression after burns. A number of approaches have been used to determine the incidence among adult survivors of major burns using self report measures like the Beck Depression inventory.80

A review of the literature on depression in burn survivors found a prevalence of major depression at 1 year post-discharge of between 4% and 7%. At more than 1 year post-discharge the prevalence ranged between 9% and 23% (for a comprehensive review refer to Thombs et al. 2006).80

It has been observed that depressive symptoms were linked to physical limitations at 5 years after injury.43 The appearance and location of the burn scar may be predictive for post-traumatic stress disorder symptoms of avoidance and emotional numbing82 or depression, especially in women.83 In contrast, other studies found that neither the severity nor the visibility of burn scars influence long-term adjustment, but rather social introversion, which predicted the development of pathological shame.84,85 Many patients with PTSD have comorbid depression,86 both are sequelae of trauma and they share many symptoms, but they develop independently of each other.87

**Dysthymia**

A smaller percentage of burned patients, around 4%, will develop a milder but more protracted type of depression called ‘dysthymia’.80,88 This condition is characterized by a depressed or irritable mood on most days and must be present for at least 2 years in adults in order to be diagnosed. Patients often report chronic anger, appetite changes, sleep difficulties, fatigue, low self-esteem, poor concentration, difficulty making decisions and feelings of hopelessness. The same combination of medication and psychotherapy is recommended for dysthymic patients as for major depression.
Substance and alcohol abuse

There are almost no studies that indicate the prevalence of substance abuse or alcohol abuse in adults. Maes et al. reported an incidence of new onset psychoactive substance use disorders of 6%. Certainly prior abuse leads to present abuse. In a study in young adults who were burned as children the prevalence of the use of alcohol and substances was 7.9% for alcohol and 35.7% for other substances; however this rate later fell to 3% for alcohol and 9.9% for other substances. These young adult prevalence rates are lower than the reference population in the USA for alcohol but were higher for substance abuse/dependence, which may reflect the socioeconomic background of the subjects studied.

Comorbidity and problems beyond psychiatric illness

PTSD and depression are both linked to poor long-term outcomes in adults. PTSD and pain together predicted PTSD and depression are both linked to poor long-term poor functional outcome and increased disability after major burns. PTSD symptoms led to greater physical and psychic social disability, poorer social functioning and less vitality. Pain is linked to poor concurrent physical functioning and depression can predict decreased physical health 2 months post-discharge.

Pediatric: psychiatric disorders and social adjustment

A significant number of the children and adolescents who survive major thermal injury develop a variety of significant behavioral and emotional problems at some point in their lives, but good adjustment is achieved by the majority of individuals. In studies in adolescent and young adult survivors of pediatric burns about half of the individuals met criteria for one or more psychiatric disorders. Compared to a group of survivors of flood trauma, a community sample of burned children had significantly more phobic disorders, over-anxious disorders, enuresis, encopresis, major depression, PTSD, and substance/ethanol abuse. Sleep disorders and psychotic disorders were also slightly more common among the burned children. Parents usually report more problems than do the children themselves or the teachers. This observation could be explained by increased problems of the children following severe burns that would not be easily observed by persons who do not live with the patient, or by the fact that parents became overly sensitive to any indication of difficulty for their children following burns. Children may express anxiety differently to adults, and their anxiety is often evidenced by crying, tantrums, freezing, or clinging. A differential diagnosis of anxiety disorders distinct from post-traumatic stress disorder is difficult and requires a careful interview. Depression is a rare long-term sequela of burns in children; fewer than 50% of the children had ever suffered symptoms of major depression and in a sample of adolescent survivors only 6% met criteria for a major depressive disorder.

Another area of long-term psychiatric outcome following pediatric burns that has received little attention, is the development of personality disorders. In the same sample of young adults mentioned above, personality disorders were common and significantly associated with comorbid Axis I diagnoses.

Diagnosis (screening instruments, SCID)

The psychiatric diagnoses that have been noted as part of the long-term process of recovery from burns are usually acute stress disorder, post-traumatic stress disorder, generalized anxiety, depression and dysthymia. These diagnoses may be affected by major psychological issues directly related to the burn, e.g. loss, pain, anxiety, grief, loss of self-esteem, loss of job or society role, disfigurement, major financial issues and major legal problems.

Two techniques are used to determine the prevalence of psychiatric disorders in burn survivors. The one most commonly used has been the self report questionnaire, e.g. Beck Depression Inventory, Impact of Event Scale-Revised, Davidson Trauma Scale, Brief Symptom Inventory, McGill Pain questionnaire and Quality of Life surveys such as the Short Form 36 (SF-36) or the EQ-5D, which has been validated with burn survivors.

For a more complete diagnostic survey the gold standard is the Structured Clinical Interview for DSM-IV-Axis I Disorders (SCID I) interview.

Treatment

Delerium and agitation

Due to the problems which have been associated with phenothiazines, benzodiazepines have been used to a greater extent in recent years for the combative, delirious patient. The two most commonly used benzodiazepines are diazepam and lorazepam. Lorazepam (0.03 mg/kg) intravenously or intravenously can usually be given every 4–8 h; for a very combative patient it can be given hourly. A third benzodiazepine which is frequently used is midazolam at 0.05 mg/kg IV, typically used in conjunction with morphine for procedures such as tubbing and staple removal. Midazolam is also used for sedation as a continuous infusion for intubated patients. When using the benzodiazepine class of medications, a clinician must balance the desired effects of relaxation with oversedation. Visual and auditory hallucinations may occur if the dose of benzodiazepine is too high. In cases of excessive anxiety in the presence of adequate pain control, lorazepam can be added to a patient’s treatment. Nighttime doses usually enhance sleep. Diazepam may be used in place of lorazepam if simultaneous muscle relaxation is desired. Diazepam has an extremely long half-life, 40 h, and therefore should be used sparingly. To avoid excessive sedation by benzodiazepines, a patient should not be awakened for the next dose.

ASD and PTSD

Therapy is the same for the two disorders and usually includes a combination of psychotherapy and pharmacotherapy. Cognitive behavioral therapies have been specifically developed for treatment of anxiety disorders. They assist patients in mastering PTSD symptoms and typically
include techniques such as role play, imagined exposures and most recently virtual reality. Also training in anxiety management using stabilizing and calming techniques are important for recovery from PTSD.

Pharmacotherapy developed over the past 2 decades with the use of SSRIs such as sertraline and fluoxetine as first line drugs. Other useful medications are tricyclic antidepressants (TCAs), antipsychotics such as risperidone and quetiapine fumarate, and α-2 adrenergic agonists such as clonidine. Antidepressants such as selective serotonin re-uptake inhibitors (SSRIs) like fluoxetine, or a TCA like imipramine should be considered for ASD.109 Both SSRIs and TCAs are helpful in reducing the nightmares and improving the sleep pattern. Treatment with a SSRI or TCA should be continued for at least 9 months to 1 year following the improvement of symptoms because of the risk of relapse.

One of the major issues for TCAs is that cardiac arrhythmias, associated with a prolonged PR interval, can be life-threatening.107 When medication is discontinued, it should be reduced over time, to avoid uncomfortable, although not medically threatening, discontinuation symptoms. The relatively long half-life of fluoxetine usually protects patients from any discontinuation symptoms, but requires extended vigilance for any drug–drug interactions.

Typically, the SSRIs are given in the morning rather than the evening as they may interfere with sleep onset. Side-effects of SSRIs include gastrointestinal upset, increased agitation, headaches, and sweating. A rare but potentially life-threatening side-effect is serotonin syndrome,108 characterized by at least three of the following symptoms: delirium, agitation, sweating, fever, hyperreflexia, myoclonus, tremor, incoordination, diarrhea and shivering. Severe cases can result in hyperpyrexia, shock or death. The risk of serotonin syndrome increases when patients are on multiple medications that potentiate central nervous system serotonin, such as an SSRI and a monoamine oxidase inhibitor. There is a reported case of serotonin syndrome in a pediatric burn patient who was receiving fluoxetine and linezolid, a broad spectrum antibiotic with monoamine oxidase inhibition.109

In an emergency room setting, propranolol has been tried with some success for those with minor injuries. It has been reported to be very helpful in the treatment of PTSD and ASD and to prevent their occurrence following a variety of different types of trauma. Longer term studies with larger injuries have not shown propranolol to be helpful for the prevention or treatment of ASD or PTSD.108 Benzodiazepines will control some immediate symptoms but are not useful long term.

Other anxiety disorders

Most burn patients, certainly those who qualify for the diagnosis of generalized or overanxious disorder, will benefit from lorazepam therapy in addition to supportive psychotherapy. If anxiety is associated with other symptoms of post-traumatic stress, such as hypervigilance or poor sleep, antidepressants such as a SSRI106 or a TCA112 should be considered. The SSRIs have the advantage of being safer drugs for outpatient treatment since an overdose is unlikely to cause significant cardiac problems as have been attributed to the TCAs.113

These disorders like PTSD can be treated with a combination of antidepressant and psychotherapy, with psychotherapy being the most useful.

Major depression

Major depression, with or without grief reaction, should be treated by a team approach. A patient should be involved in scheduled daily activities. Psychotherapy should begin to identify and address appropriate issues. Medication with SSRIs or TCAs, as described for acute and post-traumatic stress, is often helpful. Once the symptoms have responded to medication, treatment should continue for nine months to a year in order to avoid relapse on discontinuation.

Often, the depression is comorbid with PTSD. Therefore medications which affect both are preferred. Fluoxetine and the other SSRIs are the first-line medications for treatment of patients with depressive symptoms.107,114

Sleep disturbances

After discharge, many burn survivors have significant sleep problems. Like in the hospital setting this may be secondary to PTSD symptoms, depression, itch or pain. Pain in the hospital before discharge will predict insomnia.40 When sleep disturbance with nightmares is associated with post-traumatic anxiety, as described above, antidepressant medications are the drugs of choice. Imipramine and doxepin are both sedating antidepressants that are effective treatments for sleep problems in burn patients. Trazodone and nefazodone are alternative medications for insomnia and do not appear to alter sleep architecture as much as other antidepressants. Mirtazapine is another antidepressant that has been used for insomnia although little is known about its effects on sleep architecture. Pain and itch are other problems that can interfere with sleep and should be addressed with appropriate analgesic or antipruritic medications.115 If a patient continues to have significant sleep problems, sleep can be induced with diphenhydramine. Diphenhydramine doses of 1.5 mg/kg are often used throughout the day for itching and may be used alone for sleep at night or as an adjunct to other sleep medications. Usually, doses of 25 or 50 mg in the evening are adequate. Recently, Quetiapine fumarate (Seroquel XR) PO has been found to be safe and useful in this setting.

Special aspects in pediatric treatment

As with adults, pediatric patients suffering with psychiatric symptoms can benefit from psychotherapy, with appropriate indicated treatment for their specific problems. A number of specific therapies have been adapted for treatment of anxiety, PTSD and depression in children and adolescents. In addition, specific treatments for pediatric burn survivors have been developed, such as social skills training addressing disfigurement.116

Pediatric burn patients appear to have a much higher rate of adverse reactions to haloperidol and alternative management of agitation should be considered.117 Chlorpromazine and thioridazine may be used in place of haloperidol in the dosage range of 25–100 mg per dose. Chlorpromazine and thioridazine have strong sedative effects and interfere with
learning, but are less likely than haloperidol to produce associated dystonia, pseudo-Parkinsonism, and akathisia. If more than 2 mg of haloperidol per day are used, attention must be given to simultaneous administration of I or 2 mg/day of benztropine or 2–5 mg/day of trihexyphenidyl in divided doses. Benztropine or trihexyphenidyl are used to avoid dystonia, pseudo-parkinsonism, and akathisia.102 Occasionally, dystonia takes the form of an oculogyric crisis, which resembles an acute neurological catastrophe118 and can be a true medical emergency if respiration is impaired. These reactions are usually alleviated by 50 mg IV diphenhydramine.

The treatment of anxiety and depression in children with SSRIs and TCAs requires closer attention to dosage and potential side effects. The usual starting dose of fluoxetine is 5 mg for children <40 kg; 10 mg for children between 40 and 60 kg; and an adult dose for any children >60 kg. The usual starting dose of imipramine is 25 mg/day unless the patient weighs <25 kg. The beginning dose is 12.5 mg for those under 25 kg. The dose can be increased rapidly over the next few days to a dose of 1 mg/kg. If the symptoms are still uncontrolled, the dose may be increased stepwise to 3 mg/kg, but only with frequent checking of the plasma level and EKG changes with each increment of dose. A steady state is usually not reached until a given dose is maintained for 3–5 days. The preferable time of administration is in the evening to aid with sleep. Major side-effects of the TCAs are anticholinergic effects (dry mouth and dry nasal passages, constipation, urinary hesitance, and occasional esophageal reflux).102 Autonomic complications such as orthostatic hypotension, palpitations, and hypertension have been reported in adolescents with this medication.119 Cardiac arrhythmias, associated with a prolonged PR interval, can be life-threatening.107,114 Sudden death has been reported for teenagers and children receiving desipramine and other TCAs.120 Amitriptyline or doxepin may be used in place of imipramine. The dosages are similar; however, both these medications may cause more sedation than imipramine.102

Following clinical reports of increased suicidal ideation in pediatric patients treated with certain antidepressant medications and a review of clinical trial data, the US Food and Drug Administration instructed all manufacturers to include a ‘black box’ warning with all antidepressant medications.121 Pediatric patients and their caretakers must be aware of these risks and clinicians should closely monitor children and adolescents on these medications for possibly increased suicidal ideation and behavior.122

Resilience, post-traumatic growth

Although it has become generally accepted knowledge that trauma and injury can lead to psychological and psychiatric problems, the fact that a considerable proportion of individuals do not develop problems after trauma and injury has found much less attention and to date, there are only an extremely small number of studies in burn patients. Resilience and post-traumatic growth are two separate constructs. Resilience is a trait that exists before exposure to trauma or adverse events that enables posttraumatic growth.123 Resilient individuals have an ability to ‘bounce back’ and regain balance in all aspects of life, as well as endurance in the face of adverse events.123–126 Three categories of protective factors, which also are predictive of resilience, have been identified.125 Individual characteristics, relationships and social network.

In contrast, post-traumatic growth (PTG) is the development of new behavior and attitudes that were not present before the event. It is a positive psychological development as the result of struggles in the face of hardship or traumatic events.123,127 The Post-traumatic Growth Inventory127 identifies five different aspects of post-traumatic growth: ‘New Possibilities, Relating to Others, Personal Strength, Spiritual Change, and Appreciation of Life’. Post-traumatic growth appears to be somewhat related to the personality traits optimism and extraversion. Female gender and social support are strongest predictors of PTG and higher levels of education and higher socioeconomic status also are predictive.123

Resilience and PTG can both occur concurrently with distress and lower quality of life, in fact PTG may not occur without some level of distress, but distress diminishes over time in individuals who experience PTG. Longitudinal studies show that PTG levels out at about 6 months after trauma.123

Interventions to foster PTG

While alleviating distress does not foster PTG, growth can protect from further distress. The patient’s own experiences and psychological development appear to play a central role in PTG. The caregiver’s role should be to support and improve coping, strengthen self-image and enhance social support; caregivers ‘must be comfortable in allowing the patient to struggle with the event’.123,128 Common aspects of PTG in burn patients appear to be the use of active and flexible coping, social support, enhanced self-image and the successful search for meaning.129,130

Summary

Pre-injury psychiatric morbidity can have a major effect on outcome after a burn. Furthermore, psychiatric symptoms occur commonly as part of the complex systemic response to burn injuries. Psychological and pharmacologic response is important in the successful recovery of a burned person, and may reduce the risk of long-term psychiatric sequelae of the injury. It is important to note that psychological adaptation is a lengthy process occurring over months or years. During the post-burn years, it is imperative that the burn team assesses the mental and affective states of patients while assessing their physical recovery. In most cases, patients with sleep disorders, depression or withdrawal from previous activities will not seek psychiatric attention and treatment, although these problems can be ameliorated by treatment. It therefore becomes a responsibility of the expert in burn care and the entire burn team to be aware of frequently occurring problems, to ask the right questions to assess a patient’s status, and to assist a patient in receiving psychological and psychiatric assistance.
Further reading


Access the complete reference list online at [http://www.expertconsult.com](http://www.expertconsult.com)
References

5. Taal IA, Faber AW. Dissociation as a predictor of psychopathology following burns injury. Burns. 1997;23(5):400-403.
71. Zatzick D, Roy-Byrne PP. From bedside to bench: how the epidemiology of clinical practice can inform the secondary prevention of PTSD. *Psychiatr Serv. 2006;57(12):1726-1730.
92. LeDoux J, Meyer WI 3rd, Blakeney PE, et al. Relationship between parental emotional states, family environment and the
Psychosocial recovery and reintegration of patients with burn injuries
Laura Rosenberg, John W. Lawrence, Marta Rosenberg, James A. Fauerbach, Patricia E. Blakeney

Introduction

The process of psychosocially adapting to a severe burn is complex. Common issues faced by burn survivors include traumatic stress, depression, body image disturbance, social anxiety, grief, pain, itching, sleep disturbance, substance abuse, adapting to physical limitations and coping with permanent burn scarring. In addition, burns often interfere with a person’s ability to work and perform familial responsibilities. Sometimes the survivor’s family is also traumatized, and the family’s material and social resources can be greatly taxed during the course of burn recovery. Despite the sudden life-altering nature of burn injuries, studies of the psychological morbidity for burn survivors suggest that most burn survivors are resilient and adjust well over time. However, approximately 30% of both adult and children burn survivors experience moderate to severe long-term psychosocial difficulties. The current chapter reviews the challenges of providing quality psychosocial treatment for burn survivors through the course of recovery. The goal is to assist individuals in attaining optimal psychological, emotional and social functioning (Figs 66.1, 66.2).

Integrating psychological treatment with physical treatment

Comprehensive burn treatment requires a coordinated interdisciplinary team. Usually the burn team consists of physicians, nurses, care coordinators, physical and occupational therapists, and mental health professionals such as child life specialists, social workers, and psychologists. It may be convenient to think of physical and psychosocial recovery as being two different processes overseen by different sets of professionals, but the two are so intertwined that a team approach to burn recovery is essential. The mental health professionals both consult with other caregivers about the patient’s psychological and social issues and implement psychosocial interventions psychotherapy, and a community reintegration plan. Thus, the mental health professionals on a burn team work both indirectly through consultation and provide patient direct care.

Integrating the patient’s family into the treatment plan from the beginning also facilitates successful outcomes. For the psychotherapist on the burn team, the family unit is often the patient. Each individual within the family, including the burn survivor, is an essential element of this unit whose needs must be addressed as they all adapt to the changes in the family.

Assisting with grief following trauma

Traumatic events are frightening experiences that create uncertainty, anxiety, and a sense of threat for victims and their families. An individual who experiences a burn injury may face multiple changes and losses including separation from one’s support network and home environment, uncertainty regarding the length of hospitalization and process, changes with physical appearance, and in certain circumstances death of loved ones. On the burn unit, these issues often become the focus of psychosocial intervention. Successful grief therapy requires mental health professionals to have an understanding of the traumatic event, knowledge of the individual’s past experiences with loss and coping styles, and cultural and religious beliefs. Mental health professionals can assist re-establishing a sense of equilibrium following trauma by facilitating the grieving process.

The terms bereavement, grief, and complicated grief may be confusing and merit clarification. Bereavement refers to coping with the death of a loved one; whereas grief is a broader term referring to coping with loss in general. For example, a burn survivor may grieve the loss of his or her physical abilities or his or her pre-scarred skin. Grief reactions are individually unique and age dependent. Complicated grief occurs in adults when the grieving process is compromised by trauma. Prigerson and Jacobs (2001) described complicated bereavement as difficulty comprehending and accepting the death of a loved one, persistent and intense longing for the deceased, intrusive thoughts about the deceased, and avoidance of painful memories. Children can also experience childhood traumatic grief when there is traumatic loss or bereavement. This construct evolved from the literature in child development and trauma and occurs when trauma symptoms interfere with the child’s ability to grieve normally. The child may engage in avoidance behaviors which interfere with the normal grieving process. Traumatic grief can co-occur with psychiatric disorders such as depression and posttraumatic
children and adolescents who experienced the death of a loved one and found significant correlations between childhood traumatic grief scores and PTSD, depression, and anger. In addition, the severity of the traumatic grief response was associated with the view of the death as traumatic.10

On the burn unit, mental health professionals may need to inform the burn survivor about multiple losses and life changes which may include changes in appearance, loss of body parts, the death of others such as family and friends, loss of a pet, loss of a home, etc. In some circumstances, it requires informing, supporting, and preparing the family for bereavement of the burn trauma victim. This is a delicate process that requires appropriate timing and psychosocial planning. Important factors to consider when planning the disclosure process with patients and families include the patient’s medical stability and ability to participate in conversations; the readiness of the patient and family to hear the news; identification of what they know about the trauma and the factors related to the traumatic event; their wishes regarding disclosure; and knowledge of their cultural, religious and spiritual needs.12 Bronson and Price (2007) in their article for the Phoenix Society discussed important principles to keep in mind when working with grieving children after burn trauma. They suggest a process which includes supportive and compassionate truth-telling, acceptance, respectfulness of individual differences and feelings, and giving the individual an opportunity to say good-bye.13

If death occurs on the burn unit, staff can psychologically support the family by obtaining desired spiritual assistance, assisting them with paperwork for the burial process, allowing them quiet, private time with the deceased, and providing distraught family with memory items if they wish to have them.

**Cultural sensitivity**

Burn patients come from diverse cultures, and burn care teams must be sensitive as to how cultural issues can affect patients and families in all the phases of the recovery process. ‘Culture’ refers to the socially transmitted expectations, beliefs, traditions, and behavioral patterns typical of a given community at a point in time.14 Some of the factors influencing culture include country of origin, geographical location within the country, ethnicity, and socioeconomic background. Staff must also be aware of their own biases, values, and assumptions that stem from their cultures.15,16

**Acculturation** is the process in which individuals from one culture embrace patterns, customs, beliefs, values, and the language of the dominant culture.17,18 Patients and their families on first arriving at a burn care facility must rapidly adapt to the culture of the hospital environment. Even if the hospital is within their own community, they experience some level of culture shock and acculturation. This process is even more complicated for those who are transported for care to communities far removed from their homes and perhaps in another country. For some patients, this traumatic situation is also the first time they have traveled to another country, and the first time they have had to deal with differences in language, currency, living accommodations, and foods. Individuals’ concepts of time and space, appropriate hospitality, importance of greetings, how non-verbal
gestures are interpreted, and ways of expressing gratitude may differ greatly among cultures. Ideas of what caused the burn injury and what is necessary for healing to occur also are determined by cultural values.\textsuperscript{19,20}

Coping with such a multitude of unfamiliar experiences in a traumatic situation is an extraordinary challenge that can inhibit a patient’s or family’s ability to participate in the recovery process. The burn team must be aware of cultural differences and make culturally appropriate accommodations to a patient’s treatment plan. Cultural traditions can be incorporated into treatment plans to enhance participation toward recovery. For example, if a Latino family believes that the burn incident was a result of ‘evil eye’ they may request a cleansing ritual.\textsuperscript{17} It is impossible for providers to know the beliefs and expectations of every culture; however, cultural sensitivity and a willingness to learn are necessary for good patient–provider communication and improves outcomes. Staff can acknowledge their lack of familiarity and pose a question to the patient/family of whether there is anything the team can do to help meet their cultural, spiritual, and religious needs. The question conveys respect for cultural differences and a desire to help through the acculturation process.

Knowledge and sensitivity of cultural practices is also important when focusing on safety and prevention education with patients and their families. Epidemiological research has focused on identification of sociodemographic risk factors and cultural practices that have contributed to burn injuries in developed and developing countries and found differences among these countries.\textsuperscript{21-24} The highest incidence of severe burns occurs in low and middle income countries\textsuperscript{25} with children being at highest risk.\textsuperscript{21} In developing countries, factors such as poverty, crowding, food preparation practices, unstable cooking methods, and inconsistent supervision practices place young children at high risk for scald burns.\textsuperscript{22,26,27} Identification of these modifiable risk factors and cultural practices during the course of treatment can facilitate prevention education for the patient/family and hopefully this education will be disseminated throughout their communities.

**Approach to assessment and intervention**

Our general approach to assessment and care of burn survivors is described throughout the chapter as we suggest interventions to deal with specific difficulties commonly experienced at each phase of recovery. It is basically a behavioral approach based on learning principles (e.g. operant conditioning, cognitive restructuring, and social learning theories) where maladjusted behavior is the target of intervention. Assessment and treatment are integrally related and both occur simultaneously throughout the recovery and rehabilitation process.

**The longitudinal pattern of psychological recovery**

Psychological healing occurs across time commensurate with physical healing in a relatively predictable and consistent pattern.\textsuperscript{28} Awareness of this process permits family members and patients to anticipate the development of psychosocial issues, view concerns as normal reactions to the trauma instead of symptoms of psychological impairment, and facilitate coping with these issues. The following sections address psychosocial issues patients deal with in each phase of the recovery process.

**Pre-injury adjustment**

Shortly after being admitted to the burn unit, a psychosocial assessment is done through a clinical interview with the patient and/or family to gather information regarding variables which may influence the patient’s recovery and treatment plan. These variables include previous stressful events, risk factors, pre-burn physical and psychological health, coping skills, family and social support, and family’s strengths and weaknesses.\textsuperscript{29,30} Gathering information about factors which contributed to the circumstances of the burn is emphasized in instances of suspected abuse and neglect. Part of the clinical interview involves initiation of a therapeutic alliance with those who are most likely to be involved in assisting a patient’s recovery.

Because patients will be dependent to some extent on family or other caretakers during recovery, it is essential to identify risk factors in the family system. Historical risk factors which may predispose individuals to burn injury and which may affect post-burn recovery include: physical illness, substance abuse, psychiatric illness, behavioral problems, poverty, inadequate social support, and heightened family disruption.\textsuperscript{30-33}

**Admission crisis**

On admission to the ICU, individuals with burns may experience terror, confusion, shock, disbelief, pain, anxiety, and may believe death is imminent. The hospital environment can be confusing and frightening. While the physiological emergency is treated medically, the psychological crisis must be addressed. The goals at this time are to establish therapeutic rapport with the patient, help decrease anxiety, and assess strengths and needs of the patient. The first two tasks are addressed immediately by orienting the patient, assisting the patient to focus on immediate priorities, and assuring the patient the burn team is composed of knowledgeable experts who will provide excellent care. The patient’s heightened anxiety can be expected to interfere with his/her comprehension, so it is usually necessary to repeat statements of reassurance. ‘To prevent a patient from becoming emotionally overwhelmed, it may be necessary initially to avoid or limit talking about trauma-related content. Patients, especially children, in this early stage of recovery, may exhibit signs of cognitive and emotional regression, and it is important to respond to them on that level. Techniques such as hypnotherapy and relaxation with focused imagery can help decrease patients’ anxiety.

Family members are also traumatized and typically experience difficulty eating and sleeping for the first days. Other symptoms of trauma response often experienced by family members include problems focusing and concentrating, a feeling of loss of control, and a generalized sense of incompetence and helplessness. They may need frequent repetition of information and direction in providing comfort to the
patient. The psychotherapeutic tasks to be accomplished with the family are similar to those for the patient, i.e. to establish a therapeutic relationship and diminish anxiety. This can be done by assisting with orientation to the hospital, and providing information about the normal reactions and responses to trauma. Validating that their distress is normal and temporary helps communicate empathy and understanding. Learning about the injury and its treatment helps restore a family's sense of competence and provides opportunities for them to experience the reality of their roles in helping the patient. The manner in which an individual and family will ultimately adjust to long-term sequelae of a burn is often determined in the early stages of recovery.

Critical care phase

In this phase, intensive medical and surgical care is provided until the majority of open wounds are covered. This period is important psychologically. Patients experience pain, anxiety, and fear of treatment procedures. Organic factors stemming from the injury and its treatment can contribute to psychological symptoms of disorientation, confusion, sleep disturbance, transient psychosis, and delirium. Helpful interventions include repeated orientation to person, place and time; placing comforting objects in the patient's view or so that he/she can touch them; and making the patient's environment as soothing as possible. Visits from family and friends can provide familiarity and reassurance to a patient. A schedule that approximates a regular wake/sleep cycle helps a patient begin to feel normal.

Reassurance from staff about the normal aspects of recovery can help decrease a patient's anxiety. Information about the recovery process, treatment plan, and how staff plan to help improve function can provide a sense of hope. When a patient is alert, the psychotherapist can facilitate grief work to help the patient adjust to the effects of the burn. Patients with altered mental states may be hearing although not responding and discretion should be used regarding what is said near them. Psychological interventions are aimed at diminishing anxiety and increasing comfort instead of correcting the person's perception of reality.

Pain and anxiety management are crucial in this stage of recovery. Providing good pain control enhances the burn care staff's effectiveness in promoting psychological recovery. Routine and scheduled assessments of background and procedural pain, and anxiety, validates a patient's concerns but also sets an expectation of relief. The use of standardized scales provides the message that to experience a range of pain is normal, and allows the patient to participate to some degree in mastering discomfort. When staff assess comfort as routinely as vital signs, patients are less likely to feel anxious about their pain management.

Psychological interventions should be used in conjunction with pharmacological management for both pain and anxiety. The perception of pain can be influenced by anticipatory anxiety over procedures. Cognitive and behavioral interventions which enhance a patient's mastery or control can help decrease pain and anxiety. Patients often tolerate procedures better when the reasons for each procedure are explained. They may feel more comfortable by participating in their own care; they may gain some mastery over pain when they are allowed to remove their own dressings or participate in wound debridement. The presence of a supportive person can be effective in decreasing pain as well. Instructing a family member on how to comfort their loved one is important during these procedures.

Interventions which redirect a patient's attention away from painful procedures can facilitate pain and anxiety management. Music therapy is an excellent adjunct to analgesia during burn care with pediatric patients. Fratianne et al. (2001) found that music therapy interventions significantly decreased the perception of pain in children during wound care. Although anxiety also decreased, results were not significant. On the other hand, Haythornthwaite et al. (2001) reported a sensory focused intervention was more effective in reducing pain in comparison to music distraction with adult burn survivors.

Other interventions which have been effective in decreasing pain and distress associated with burn treatment include deep breathing, progressive relaxation, visual imagery, biofeedback, hypnosis and virtual reality. Hypnosis induces a relaxed and focused state of awareness which can be extremely helpful in facilitating comfort for adult and pediatric patients. Hypnotic inductions and suggestions must be modified to facilitate a patient's use of imagery. Some patients will respond well to suggestions of imagining a 'favorite place'. Children aged 3 and over respond well to storytelling, with suggestions for comfort and mastery interwoven into the story. Recent research reported that immersive virtual reality, in which individuals' attention was immersed in a computer generated world, was effective in reducing pain during wound care. This intervention may also be helpful during physical therapy. Mott et al. (2008) found that augmented reality, where a character is viewed on a screen, was also effective in decreasing pain ratings of pediatric burn patients during prolonged wound care.

In addition, child life interventions such as medical play which gives children control by having them role play and manipulate medical equipment, preoperative preparation about procedures or surgeries, and procedural support can facilitate coping in children and decrease anxiety during burn care. The child's age and development need to be considered when selecting the intervention.

Although over time family members may become more at ease with hospital routines, they will continue to have difficulty coping, feel anxious, and need updates about their patient's present and future status, and may develop new concerns as they are placed in new roles and responsibilities. Being away from support systems can be difficult. It is helpful to provide information about what to expect in the immediate future, to facilitate patient interaction, and to provide honest information while allowing family members to protect themselves from overwhelming despair. Family may be reluctant to touch the patient for fear of causing pain and may feel uncomfortable talking aloud to a non-responsive patient. Staff can find ways to allow family members to nurture their loved one and can assist them in becoming comfortable in caring for their patient's needs. Taking the time to treat the family is a very important part of treating the patient. In addition, this treatment facilitates the family's resumption of feelings of competence and control, desensitizes them to the sights and odors in the room, and encourages them to join with the burn team in the healing and rehabilitation of the patient. A family must find reason to
hope, and staff can assist them by suggesting realistic and optimistic outcomes. Psychotherapeutic work with the family should also identify and plan for management of family issues which may impede a patient’s recovery and rehabilitation, such as financial support, family alliances, historical family events, and beliefs that influence current perceptions and behaviors.

In-hospital recuperation phase

In this phase of recovery, patients become physically stronger yet face new challenges. Patients often reminisce about the past, begin to comprehend the extent of their injury, and experience difficulty adapting to physical limitations and changes in their appearance. They may feel anxious about the future and grieve losses. They can also experience a loss of control and autonomy because they have now become dependent on others for their care, yet be ambivalent about resuming self-care to increase independence. The team can help motivate the patient to participate in treatments and assume responsibility for his/her recovery. Patients who desire optimal recovery need to comply with the medical team’s instructions, many of which require significant physical discomfort. Pain continues to be a concern as patients become increasingly active in rehabilitative exercises, and pain and anxiety management are important to regain optimal physical functioning. As in the previous phase of recovery, music therapy, hypnosis, relaxation techniques, and virtual reality can facilitate pain and anxiety management.

Emotional lability and cognitive and behavioral regression may also occur, especially with younger children. Because children often have difficulty expressing verbally their feelings and frustrations, they may exhibit behavioral outbursts. Parents may be relieved to find out such behaviors are normal, and often require guidance with implementation of treatment plans that target and positively reinforce desirable behaviors (e.g. reinforcement plans with short-term goals such as star charts). Patients may feel frustrated, angry, hopeless, and depressed. These emotional reactions can be difficult for family members to cope with. Hopelessness is more likely to result when patients feel a lack of control and eventually give up trying, which can lead to chronic depression. Although depressive symptoms may decrease during the initial hospitalization, Ullrich et al. (2009) found depression during hospitalization was related to physical functioning of patients up to the first year post-burn. Psychotherapeutic work with the patient may involve helping the patient experience control, combat feelings of hopelessness and helplessness, facilitate healthy expression of emotions, achieve success, and feel rewarded while progressing through difficult procedures. Desired behaviors (e.g. pressure garment use or walking on treadmill) can be reinforced through verbal praise.

A psychotherapeutic challenge of this phase is to accept and validate the patient’s emotional demonstrations as normal behaviors in the recovery process while also setting limits on the ways in which emotions are expressed. Early in this phase, as the patient begins to ask about the future, the psychotherapist can describe the predictable pattern of emotional vicissitudes indicating they are normal and can be endured and managed. Staff can demonstrate positive regard and acceptance of the patient while also helping the patient to exercise control over destructive behaviors. Responses to questions should be honest but hopeful regarding the expectations of treatment and recovery. Interventions aimed at facilitating grief work, coping with body image concerns, management of anxiety and depression, and social skills training to facilitate social interactions are helpful during this phase of recovery.

Much psychotherapeutic work during this phase is accomplished with patient and family together. Families must learn how to assist a patient in adjusting to the new situation, and the family system must accommodate to the changed situation. Research has shown the high importance of strengthening the family unit, facilitating family closeness, and supporting their attempts to organize their lives to incorporate the additional duties involved in providing continued care for their patient. Families must plan and implement adjustments in their relationships and in their home environments that will be necessary for the continuation of the patient’s recovery and rehabilitation after discharge.

Reintegration phase

Preparing for a patient’s discharge to outpatient status and eventually home begins upon admission to the burn unit. A major objective is to facilitate a patient’s reintegration to life at home and his/her community. Community reintegration is the process of becoming involved in the community, in school and work, and in leisure activities. Returning home signifies social interactions with the larger community of extended family, friends, and strangers. Patients as well as family must prepare for those encounters. Patients often feel ambivalent and anxious, fear social rejection, worry about being accepted and receiving social support. Returning to a cohesive and supportive family environment and loyal friends can make this transition easier.

Psychotherapeutic activities in this phase involve education and preparation of patient and family about difficulties which may be anticipated at discharge. Coping skills that can help are discussed and practiced. Patients and families often deny that they will have problems; however, psychotherapists can help prepare such patients by offering suggestions to address problems that other people have experienced. Issues such as recurrence of posttraumatic stress symptoms, sleep disturbance, irritability, or fear of resuming sexual activities should be discussed prior to discharge.

Social skills programs are available to facilitate positive reintegration to society, improve social comfort, and increase confidence in social interactions. The program Be Your Best by Barbara Kammerer Quayle and The Phoenix Society for Burn Survivors Inc. (2006) was developed to help burn survivors with community reintegration. Another program Changing Faces by James Partridge, an organization dedicated to assisting persons with facial disfigurement, recommends a brief social skills training program called ‘3–2–1–GO!’ Both programs provide strategies to prepare patients to answer questions related to the burn, and for dealing with staring and stigmatizing behaviors. The patient may benefit from rehearsal using these skills on brief outings outside the hospital. If difficulties are encountered, the patient can consult with the burn team for direction and support to develop an alternate plan. Groups of inpatients, outpatients,
and their families can be extremely helpful in the process of anticipating difficulties at discharge and rehearsing solutions while also providing emotional support.

The burn team may prepare the community to which a patient will return (e.g., extended family, neighbors, church groups, social clubs, a patient’s workplace, and for pediatric patients, the school). Instructing those unfamiliar with burns in what to say or do to ease a survivor’s re-entry may assist with reintegration. Variables that may affect burn survivors’ ability to return to work once they are discharged from the hospital include size and severity of burn, duration of hospitalization, location of burn, physical impairment, pain, prior employment history, lack of vocational training, work environment impediments, and psychosocial difficulties. Variables found to assist with return to work were psychosocial support, positive thinking and vocational training. A recent literature review reported 66% of burn survivors returned to work within the first 2 years post-burn. In a study of young adults who sustained burns during childhood, Meyer et al. found that 63% of the sample were employed either full-time or part-time. Individuals who do work report improved quality of life.

Factors that affect adults’ return to work can also influence school re-entry for pediatric burn survivors. Staley et al. (1998) reported children with small burns returned to school within the first week or month post-burn, and most performed well academically. However, pediatric burn survivors often require assistance to return to school so they can learn, develop, and form peer relationships. Many burn centers in the USA have developed school re-entry programs. These programs are designed to educate staff and students about aspects of burns, provide generic information about treatment and recovery, emphasize the child’s abilities and needs, clarify ways in which the child may require assistance, and address the importance of normalizing school activities and providing support. Working with the family and the school, burn professionals develop a plan to integrate the child burn survivor back into school. Usually, part of the process includes the burn professionals visiting the child’s classroom, explaining the nature of burns and burn rehabilitation, engendering compassion and support for the burn survivor, and answering questions. Burn professionals running school re-entry programs have received a good deal of positive feedback from schools and families; however, the long-term efficacy of school re-entry programs has not been empirically demonstrated. A few studies have reported that interventions developed around specific children, on-site school visits and educational videos/DVDs are beneficial. The Journey Back by The Phoenix Society for Burn Survivors (2006) is a comprehensive program providing generic materials designed to help pediatric burn survivors, families of burned children, and school communities with the re-entry process.

Rehabilitation phase, post-discharge

Discharge from acute inpatient treatment does not signify that a patient is well. Rehabilitation may require several months to years. Burn survivors’ wounds may be vulnerable to breakdown and may require dressing changes, exercises, and application of special splints and pressure garments. Grief work continues as burn survivors cope with losses; delayed grief reactions occur. Symptoms of post-traumatic stress may recur upon leaving the protective hospital environment. Body image concerns may become more acute as burn survivors confront stigmatizing reactions to their scars. Also, the family’s social and emotional resources may become taxed as the family transitions into becoming the patient’s primary caregivers.

Factors to consider during rehabilitation in burn care are the patient’s functional impairment and/or disability. Injury, impairments and functional limitations represent potentially disabling conditions, while disability itself is a function of the interaction between the person’s limits and the environment. Factors that moderate the relationship of injury to disability are biology (e.g., genetic, congenital), environment (e.g., physical, social, psychological), and lifestyle (e.g., expected behaviors). The goal of rehabilitation is to enable full social-environmental integration, including access to social opportunities (e.g., roles) and physical space (e.g., absence of physical barriers). The National Institute of Disability and Rehabilitation Research (NIDRR) presents a paradigm for conceptualizing and conducting rehabilitation research that places environmental factors on an equal footing with person factors.

Regarding burn injury, there are some data to suggest that the most important long-term (>2 years post-injury) disability is at the interface of the burn survivor and social environment. A study of young adult survivors of childhood burns (mean years post-burn, 14 years) found that on standardized behavioral scales the young people were rated by others to be doing well. However, in individual standardized psychiatric interviews, an unexpectedly high percentage reported psychiatric disorders, specifically anxiety related to social situations, and personality disorders severe enough to warrant diagnoses. Similar results were found in a study of adolescents (mean years post-burn, 10 years). In these studies, the young people were rated by a physical therapist to have no physical limitations that prevented their abilities to care for themselves and to participate in ordinary activities, but their anxieties were severe enough to limit their achievement of full capacity. Even if most burn survivors eventually function satisfactorily by external criteria, clinically they may be suffering significant distress that is not easily observable. A goal of psychosocial care providers in working with survivors is to understand the sources of survivors’ distress and to develop interventions that enable survivors to become full participants in society.

It would be extremely valuable to patients leaving the hospital, as well as their social network, employers, and care providers, if there were a set of predictors that could reliably estimate when and to what degree functional improvement could be expected over time. Fauerbach et al. (2006) evaluated functional impairment of burn survivors from discharge and across 2 years. They found that psychological impairment was predicted by prior alcohol abuse, psychological distress, and psychological function both before the burn and at discharge. These data can inform providers and adult patients about factors that could be modified to effect more desirable outcomes. Conducting such studies in burn care requires multisite studies over several years to gather sufficient data. For pediatric patients, such studies are underway but take many years because they must also consider
Among the most common manifestations of psychosocial distress are: sleep disturbance, depression, body image dissatisfaction, acute and posttraumatic distress, as well as more heterogeneous symptoms. The mean level of psychological distress among those with major burn injuries is reported to be significantly higher than that of a normative sample. Evidence indicates that psychological distress in the hospital can have an enduring impact on physical and psychological health and function. In one study, psychological distress while in the hospital was found to be associated with significantly greater impairment of physical and psychological function and slower rates of recovery over the course of the first year following a major burn injury, even when pre-burn physical and psychological health and function were statistically controlled. In a second longitudinal study following burn survivors over the first year of recovery, psychological distress was highly correlated with poor quality of life throughout the study. Previous research has used questionnaires and standardized measures to evaluate long-term distress of burn survivors. Recently, Wiechman Askay et al. (2009) used ‘QMethodology’, a qualitative approach, to identify the primary reasons of distress experienced by adults post-burn. Participants were asked to rank order a list of 50 possible causes of distress. Four main categories emerged: physical difficulties; physical concerns and family's adjustment; body image, social issues and concerns about the future; and a combination of physical and psychosocial difficulties. Future studies should focus on qualitative methodology to identify patterns of distress among burn survivors.

Acute and post-trauma distress

Acute stress disorder (ASD) and posttraumatic stress disorder (PTSD) following exposure to trauma are common. ASD and PTSD are characterized by three symptom clusters: re-experiencing, avoidance, and increased arousal symptoms. In various studies, the prevalence rate of ASD among adult burn survivors has varied between 10% and 23%, whereas the rate among pediatric survivors has been between 8% and 31%. It is estimated that 15% and 45% of adult burn survivors meet the criteria for PTSD in the first year post-burn, and almost 50% meet the criteria for at least one of the PTSD symptom clusters. The current and lifetime incidence of PTSD in pediatric burn survivors are 7% and 30%, respectively, whereas Meyer et al. (2007) found these rates in young adults who sustained childhood burns to be 9% and 21%, respectively.

Post-trauma distress has been found to be associated with greater lengths of acute hospitalization, enhanced sense of distress, and impaired adjustment to injury. In the population of patients surviving severe burns, certain aspects of pre-trauma adjustment (e.g. history of mood disorder) and coping style can influence the risk of developing PTSD following trauma exposure. Individual factors (e.g. avoidance of reminders) and aspects of the injury (e.g. injury severity, facial injury) have been associated with poorer outcome. High levels of trait neuroticism appear to be at greater risk of PTSD symptomatology following burn injury while high levels of extraversion appear protective against PTSD.

It might be assumed that PTSD is related to greater initial injury; however, PTSD among burn survivors has not been found to be related to severity of injury. On the other hand, high levels of acute post-trauma stress symptomatology have been shown to be positively related to perception of more intense pain among hospitalized burn patients. High emotional distress and acute stress disorder symptoms during hospitalization are risk factors for PTSD 2 years post-burn.

Body image, stigmatization, and social integration

Body image is one's self-evaluation of one's physical appearance. Negative body image or body dissatisfaction is the belief that one is unattractive or 'ugly.' Body image is highly correlated with self-esteem particularly among adolescents and young adults. Negative body image is a component of or is highly associated with a number of psychiatric disorders including depression, social anxiety, eating disorders and drug abuse. Due to the fact that burn survivors are permanently scarred by their injuries, it is commonly hypothesized that burn survivors are at high risk of developing a negative body image.

Like disability, body image is a consequence of the interaction between a person and his/her social environment. In order to understand the challenge of adapting one's body image to having burn scars, it is necessary to be familiar with the appearance norms of the burn survivor's culture. These sociocultural norms establish criteria for the importance of appearance, how one should appear, and the room for deviation from the norms. In the USA and in most industrialized nations, there is a cultural obsession with physical appearance, especially for women, which is driven by the cosmetic industry and the commoditization of appearance. Consequently, there is great deal of social pressure to be beautiful and what constitutes 'beauty' is narrowly defined as: a thin body shape, angular facial features, tall, young, and unblemished, smooth, light-colored skin. Appearance norms are communicated to the individual both through the mass media and interpersonal behavior. Via the mass media (e.g. magazines, television, and the internet) people are exposed to hundreds of images daily of 'beautiful people' technologically enhanced through processes such as airbrushing, soft-focus camera shots, and manipulated digital images. The message, implicit or explicit, of cosmetic product advertisements is that you are an inadequate person unless you are very attractive, and this product will enhance your appearance. There is also interpersonal pressure to conform to appearance norms. One review of the literature on appearance concluded that people tend to both make positive assumptions about 'good looking' people and treat them more favorably than less attractive people. On the other hand, people that deviate from the beauty standard are more likely to experience stigmatization and discrimination behavior. For example, children are most frequently
teased about their appearance in comparison to all other aspects of their person or behavior.

Social stigmatization is a process in which people are socially rejected and ostracized based on a negative stereotype. People with visible differences have long been stigmatized in the mass media. In many movies and video games, the villain is a person with a physical difference, often burn scars. Thus, the scars of villains such as ‘Two-Face’ in the Batman series are the physical mark of the dehumanized ‘other.’ Stigmatizing interpersonal behaviors experienced by burn survivors include: an absence of friendliness and courtesy, staring, pointing, startled and disgusted reactions, ignoring, avoidance, confused behavior, teasing, bullying, and discrimination.110,111,116,118 There is evidence that people with visible differences are more likely than people without visible differences to experience stigmatizing interpersonal behavior. For example a number of studies have investigated whether people’s behavior differed when they interacted with an actor who had or did not have a made-up facial disfigurement. When interacting with the actor with a mock disfigurement, participants were less likely to offer assistance, sit or stand close to the actor, and limit their interactions with the actor.119–121

What are the psychosocial consequences for burn survivors to live in a highly beauty conscious society? Few studies have investigated the frequency of body image dissatisfaction and perceived stigmatization and their correlates among burn survivors. Studies that have compared the body image of burn survivors to a non-burn comparison group have found no normative differences.122,123 For example, in one study comparing a group of long-term pediatric burn survivors between the ages of 8 and 18 (M age = 14.7) to an age-matched non-burn comparison group on a body image measure, there was no difference between the males in the two groups. Among the females, on average the burn group had higher body image scores than the comparison group.123 This surprising finding needs to be interpreted with caution given that it has not been replicated. Further research is required to determine if burn survivors as group have different rates of body image dissatisfaction than the general population.

In regard to risk factors for negative body image, severity of burn scarring has proven to have a modest relationship with body image among both adult and child burn survivors. Across studies, the correlation between burn severity and body image has ranged from 0.00 to 0.40.87,123–125 One study suggested that the relationship between perceived scar severity and body image is moderated by importance of appearance.126 For those burn survivors who placed little value on physical appearance, self-rated scar severity had no relationship with body image. For those burn survivors who highly valued physical appearance, scar severity was highly predictive of body image. All studies investigating the relationship between scar severity and body image have been limited by the fact that there is no reliable standardized measure of scar severity. Studies to date have used proxy variables to measure scar severity such as total body surface area (TBSA) burned or numbers of burn-related surgeries.

Within the literature there has been a theoretical debate regarding the relationship between burn scar location and body image. The ‘visible hypothesis’ poses that socially visible scars, such as scars on the face, will be highly related to body image dissatisfaction because burn survivors with visible scars will experience more frequent stigmatizing reactions from others. The ‘hidden scar’ hypothesis posits that because the person has fewer opportunities to learn how to deal with the reactions of others, he or she will live in fear of the scar being revealed and thus have a negative body image. There is little empirical evidence for either hypothesis. In the studies that have been completed, the correlation between facial scarring and body image has ranged from 0.00 to 0.20.124 Gender has also been investigated as a possible risk factor. In comparison to men, women burn survivors tend to have lower body image; however, the gender difference in burn survivors has not been as great or as consistent across studies as it is in the general population. Across studies, the strongest correlates of body image among burn survivors have been social and emotional variables such as social support, perceived social stigmatization, importance of appearance, and depression (r ranging from 0.30 to 0.60).87,123–125,127

In regards to stigmatization of burn survivors, the few studies that have been completed have focused on pediatric burn survivors. Among pediatric burn survivors, there is some evidence that appearance-related stigmatization is a common concern. In a survey of 250 pediatric burn survivors, 60% of participants reported being bullied within the last 6 months. A total of 25% of the sample indicated that bullying was a ‘big problem’.128 However, to date, there is not enough evidence to conclude that burn survivors experience stigmatizing interpersonal behavior more frequently than the general population. First of all, appearance-related teasing appears to be very common in the general population. In a survey of adolescents in Britain, 52% of the sample had experienced distress related to appearance-related teasing and 10% reported at least one incidence of avoiding going to school fearing appearance-related teasing.112 No studies compare burn survivors’ experience of stigmatizing behaviors to that of a comparison group. Two studies comparing the frequency with which children with craniofacial differences experienced teasing and other victimization behavior to a comparison group found no differences between groups.129,130

To date, there is no empirical evidence that burn survivors as a group experience higher levels of negative body image or more stigmatizing behavior than non-burn comparison groups. However, relatively few studies have been completed and these findings need to be replicated before they are accepted as fact. Over the last decade, a number of new questionnaires have been validated to measure body image, perceived stigmatization, and social comfort among people with visible differences.126,131–133 Hopefully, these instruments will facilitate future body image research among burn survivors. Clinical experience suggests that approximately 20–30% of burn survivors struggle with body image and social integration issues. For these burn survivors, the emotional pain that results from body image dissatisfaction and the social discomfort can be very intense.

Distress of families of burn survivors

Long-term impact on families of burn survivors has not been well studied, but clinical experience and scanty empirical data indicate the sequelae to be significant. Family members
may continue to experience symptoms of posttraumatic stress after a patient has returned home.\textsuperscript{50} Parents of survivors of massive injuries appear extraordinarily stressed even several years after their children’s recoveries.\textsuperscript{29,134} A series of studies at the Shriners Hospital for Children in Galveston found that parents of recovering pediatric burn patients reported significant depressive symptoms at 2 years post-injury, and they attributed their distress to their burned children.\textsuperscript{29,135} Although parental distress appears to improve with time for most, parents of the most troubled burned children continued across time to be troubled themselves.\textsuperscript{135} Parents also express concern for their unburned children whom some felt had been deprived of attention and time while the burned sibling presented an extensive drain on the family system. Even free medical and surgical care did not eliminate the burden of direct and indirect costs of burn injury, and many families experience financial difficulties attendant to the injury and treatment of their child.\textsuperscript{29}

**Long-term outcome: quality of life**

After survival is assured, quality of life is arguably the most important outcome to individuals who are seriously ill or injured. Health-related quality of life has been defined as a multifactorial construct that involves an individual’s degree of satisfaction and level of health and functioning in several core domains including: physical-behavioral (e.g. ability to perform self-care behaviors) and psychological wellbeing (i.e. subjective sense of contentment and the absence of emotional distress); social and role functioning (e.g. ability to fulfill family, work, and community responsibilities), and personal perception of health (i.e. satisfaction with one’s health status).\textsuperscript{136}

Quality of life has been investigated using general health questionnaires or measures that focus on specific behaviors. Recent research has begun to focus on the overall quality of life.\textsuperscript{137–139} As with self-report behavioral scales, most long-term (over 2 years) burn survivors appear to have eventually developed satisfactory adjustment and are within normal range on domain subscales of the SF-36, a widely used measure which assesses general health quality of life.\textsuperscript{136,137,139} Rosenberg et al. (2006) examined quality of life of young adults who sustained burns as children using the Quality of Life Questionnaire by Evans et al.,\textsuperscript{140} which measures specific behaviors. They found that young adults rated their overall quality of life and general wellbeing lower than the normal population. In a study with the same sample, Meyer et al. examined sexual attitudes and behaviors of burn survivors and found that overall they felt positive about their sexual experiences.\textsuperscript{141}

A number of studies suggest that early psychological distress predicts poor quality of life outcomes. Fauerbach et al. (1997) found that pre-burn psychiatric disorder predicts poorer psychosocial adjustment and health-related quality of life after the burn.\textsuperscript{98} Body image dissatisfaction at time of discharge is associated with prolonged periods of poorer mental health-related quality of life among adult patients following disfiguring injuries.\textsuperscript{142} The impact of body image dissatisfaction on psychosocial quality of life is independent of distress, injury, and pre-injury adjustment variables. Post-trauma distress during the reintegration phase is predictive of significant extended problems with adjustment during subsequent phases of recovery.\textsuperscript{143,144} In conclusion, the quality of life research points to the importance of early detection and treatment of psychosocial problems among burn survivors.

**Interventions for burn survivors beyond acute care**

Moving beyond general social support, psychologists and psychiatrists specializing in burn recovery have been working to develop theoretically-based empirically-testable interventions that can be tailored to the individual needs of both pediatric and adult patients. As stated above, the psychosocial sequelae of a burn are quite varied. Survivors may experience PTSD, body image concerns, social anxiety, depression, guilt, anger, grief, substance abuse, family conflict, homelessness, joblessness, etc. In order to create effective individual treatment plans, there need to be effective treatment protocols for treating specific common problems. Within recent years detailed psychotherapy treatment programs have been described to treat PTSD,\textsuperscript{145} acute stress disorder,\textsuperscript{146} and social skills training for coping with disfigurement.\textsuperscript{147,148} However, much more research is needed to empirically demonstrate the efficacy of these interventions among burn survivors and other groups with physical differences.\textsuperscript{149}

Cognitive therapy for the treatment of body image and social integration concerns of people with visible differences is an example of a tailored psychotherapy.\textsuperscript{147,148,150,151} Though much has been learned about the risk and protective factors for body image issues and social adjustment, there remain few empirically validated treatments.\textsuperscript{152} The therapy is based on a detailed conceptualization of how a survivor’s social environment, thoughts, behaviors and emotions interact to maintain the survivor’s distress. Given the sociocultural premium placed on appearance, it is understandable that some burn survivors adopt personal values that prioritize physical appearance. Consequently, these individuals often ruminate about the discrepancy between their appearance and the ideal (or their lost appearance). Self-conscious about their appearance, the burn survivor may act in ways that confirm their belief that their appearance is socially unacceptable. For example, they may minimize or avoid social interactions with others. This social avoidance may be interpreted by others as curt or rejecting behavior by the burn survivor. Thus, brief awkward social encounters turn into self-confirming experiences which validate the survivor’s belief that their burn scars make them a socially inadequate person.

Based on this model, cognitive behavioral therapists have developed several techniques for treating negative body image and social anxiety related to a physical difference. Likely, the most important is teaching a specific set of social skills.\textsuperscript{147,148,153} As mentioned previously, these social skills include having a short precise answer to explain ‘what happened,’ guiding the topic of conversation, using confident body language and eye contact, and assertively confronting confused and rude behavior. After mastering these skills through in-therapy practice, the survivor is encouraged to practice the skills by engaging in social activities. This
practice helps break the social avoidance-depression cycle which maintains the burn survivor’s negative body image.

Though promising psychosocial interventions are being developed, many burn survivors lack access to mental health care in general and access to mental health providers with expertise in treating burn survivors in particular. Most burn survivors who suffer psychological symptoms of distress following discharge from a burn center and who desire treatment must rely on mental health professionals in the community. However, it may be difficult for them to find helpful resources. Of the 101 young adults who had been burned as children in the Meyer et al. (2007) study, none were receiving professional help for their difficulties. Such treatment is expensive and often not affordable by an individual without insurance or other financial assistance. In the USA, there is no universal healthcare. Many burn survivors do not have health insurance because they cannot afford the premiums. In addition, burn survivors do not always qualify for financial assistance because their ‘disabilities’ are declared insufficient to require such aid. Even when they can afford such treatment, they may be unable to find a mental health professional to work with them. Mental health professionals who are naïve regarding burn survivors’ needs sometimes believe that it is inevitable that scarred survivors will feel depressed and/or anxious; thus, they act as if the survivor (and the helper) cannot expect much in the way of improvement.

Given the limited access to effective psychotherapy, perhaps a more effective strategy for improving psychosocial outcomes for burn survivors are interventions that create more accepting and tolerant social environments. Programs or organizations with the mission of engendering social acceptance for burn survivors and other people with physical differences include school re-entry programs, burn camps, the ‘Phoenix Society for Burn Survivors’ in the United States and ‘Changing Faces’ based in the United Kingdom. School re-entry programs were previously discussed. Burn camps provide an opportunity for pediatric burn survivors to socialize with other burn survivors, participate in recreational activities in a supportive environment, and may increase self esteem. There are different types of burn camps and the goal depends on the purpose of the camp. For example, some camps were designed to provide mental health and rehabilitation services to children once they have left the hospital; whereas, other camps are for recreational purposes only.

The Phoenix Society for Burn Survivors is ‘a nonprofit organization dedicated to empowering anyone affected by a burn injury.’ In conjunction with regional burn centers, the Phoenix Society coordinates over 30 burn support groups.
Psychosocial recovery and reintegration of patients with burn injuries

In addition, they host the annual World Burn Congress, a conference that brings together burn survivors, their families, firefighters, and burn care professionals to address the aftercare and reintegration issues of burn survivors. Recently, the Phoenix Society for Burn Survivors and the American Burn Association have formed a joint committee, The Aftercare and Reintegration Committee, devoted to improving psychological health and social reintegration following burns.

Changing Faces is a charity based in the UK dedicated to creating ‘a culture of inclusion for people with disfigurement’. In addition to providing counseling and supporting research, they organize sustained political campaigns in support of the civil and human rights of people with visible differences. For example, they have organized the ongoing ‘face equality’ campaign with the goal of challenging ‘media, advertisers, and the film industry [to] adopt more factual and unbiased portrayals of people with disfigurements, actively avoiding language and imagery that creates prejudice.’ In addition, the campaign has asked politicians and policymakers to ‘ensure that facial prejudice and discrimination are effectively outlawed by improving anti-discrimination law and promoting best practice.’

Summary

Most burn survivors do eventually adapt well and resume lives of productive activity with satisfactory self-esteem and social interactions. Empirical data indicate that the first year or so post-burn is fraught with discomfort and distress, but much of the difficulty is transient. The process of psychological adaptation often continues for several years. Symptoms of disturbance that linger among burn survivors are likely to be such that only intimate friends and family members will observe them (e.g. nightmares, flashbacks, body image dissatisfaction, social anxiety), so it is valuable for persons with expertise in burn adaptation to periodically assess survivors (especially pediatric survivors who change constantly) to ask about such common symptoms and to provide an opportunity for intervention.

That most burn survivors do amazingly well should never be interpreted as indicative of ease in adaptation. We would never want to diminish the pain and suffering they endure from physical and psychological wounds. As psychotherapists to a large number of burn survivors, we know very well the struggles of survivors. They have moments of true despair and hopelessness, moments of rage, and moments of joy. Probably at some level, burn survivors always feel some sadness about their scars; eventually they attend to other things most of the time and do not obsess over their scars. Fortunate psychotherapists can know them through all extremes, looking for glimmers of hope, validating anger, celebrating victories, and gaining deep respect for the resilience of human beings (Fig. 66.3).

Further reading


Access the complete reference list online at http://www.expertconsult.com
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To save space in the index, the following abbreviations have been used: SIRS – systemic inflammatory response syndrome

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Clip 13.02, Tangential Excision. Procurement of Skin grafts. Application Autografts
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Clip 13.04, Fascial Excision of Necrotic Burn Eschars
Clip 13.05, Tangential Excision and Application of Allograft to Burn Wounds Followed by 4:1 Autografting

Clip 19.01, General features of smoke inhalation injury
Clip 19.02, Inhalation injury viewed through the endotracheal tube
Clip 19.03, View of swollen supraglottic structures due to thermal injury
Clip 19.04a, Bronchoscopic evidence of intense smoke exposure and severe injury to large airways in a patient with minimal pulmonary parenchymal dysfunction
Clip 19.04b, Chest radiograph obtained at the time of the bronchoscopic exam shown in Clip 19.04a
Clip 19.05, Acute lung injury associated with scald injury mimics effects of smoke injury
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Clip 19.09, Endoscopic view of inflammatory changes in a pediatric larynx
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Clip 61.01, Video of Brief Physical Exam to Assess for Potential Intentional Injury
Clip 66.01, Psychosocial Recovery and Reintegration of Patients with Burn Injuries

Additional video clip (Courtesy of General Reconstructive Surgery by Gregory RD Evans and Garrett A Wirth)

Evans & Wirth Clip 2.01, Tangential Excision and Skin Grafting
PowerPoint presentations

Chapter 10, Evaluation of the Burn Wound: Management Decisions
Chapter 11, Enzymatic Debridement of Burn Wounds
Chapter 12, Treatment of Infection in Burns
Chapter 13, Operative Wound Management
Chapter 14, Anesthesia for Burned Patients
Chapter 15, The Skin Bank
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Chapter 19, Diagnosis and Treatment of Inhalation Injury
Chapter 20, Respiratory Care
Chapter 23, Hematologic and Hematopoietic Response to Burn Injury
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Chapter 27, Vitamin and Trace Element Homeostasis Following Severe Burn Injury
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Chapter 31, Etiology and Prevention of Multisystem Organ Failure
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Chapter 40, Cold-Induced Injury: Frostbite
Chapter 41, Chemical Burns
Chapter 42, Radiation Injuries and Vesicant Burns
Chapter 43, Exfoliative Diseases of the Integument and Soft Tissue Necrotizing Infections
Chapter 44, The Burn Problem: A Pathologist’s Perspective
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Chapter 47, Comprehensive Rehabilitation of the Burn Patient
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Chapter 61, Intentional Burn Injuries
Chapter 63, Cost-Containment and Outcome Measures
Chapter 64, Management of Pain and Other Discomforts in Burned Patients
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