166e Infectious Complications of Burns

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The skin is an essential component of immunity, protecting the host from potential pathogens in the environment. Breaches in this protective barrier thus represent a form of immunocompromise that predisposes the patient to infection. Thermal burns may cause massive destruction of the integument as well as derangements in humoral and cellular immunity, permitting the development of infection caused by environmental opportunists and components of the host's skin flora.

EPIDEMIOLOGY

Over the past decade, the estimated incidence of burn injuries in the United States has steadily declined; still, however, >1 million burn injuries are brought to medical attention each year. While many burn injuries are minor and require little or no intervention, 183,000 cases were reported between 2002 and 2011 to the National Burn Repository from specialized burn care facilities; of the 45,000 persons hospitalized for these injuries, 60% required intensive care and 20,000 had major burns involving at least 25% of the total body surface area. The majority of burn patients are men. Children under the age of 5 account for ~20% of all reported cases. Scalds, structural fires, and flammable liquids and gases are the major causes of burns, but electrical, chemical, and smoking-related sources also are important. Burns predispose to infection by damaging the protective barrier function of the skin, thus facilitating the entry of pathogenic microorganisms, and by inducing systemic immunosuppression. It is therefore not surprising that multiorgan failure and infectious complications are the major causes of morbidity and death in serious burn injury. More than 3000 patients in the United States die of burn-related infections each year, and 6 of the top 10 complications recently identified by the American Burn Association's 10-year review are infectious: pneumonia (4.6%), septicemia (2.7%), cellulitis/traumatic injury (2.6%), respiratory failure (2.5%), wound infection (2.2%), another infection (2.0%), renal failure (1.5%), line infection (1.4%), acute respiratory distress syndrome (1.2%), and arrhythmia (1.0%).

PATHOPHYSIOLOGY

Loss of the cutaneous barrier facilitates entry of the patient's own flora and of organisms from the hospital environment into the burn wound. Initially, the wound is colonized with gram-positive bacteria from the surrounding tissue, but the number of bacteria grows rapidly beneath the burn eschar, reaching ~8.4×10^3 cfu/g on day 4 after the burn. The avascularity of the eschar, along with the impairment of local immune responses, favors further bacterial colonization and proliferation. By day 7, the wound is colonized with other microbes, including gram-positive bacteria, gram-negative bacteria, and yeasts derived from the gastrointestinal and upper respiratory flora. Invasive infection—localized and/or systemic—occurs when these bacteria penetrate viable tissue. In addition, a role for biofilms has been recognized in experimental animal models of burn-wound infection. (*Biofilms* are surface-associated communities of bacteria, often embedded in a matrix, that allow the microbes to persist and to resist the effects of host immunity and antimicrobial agents.)

Streptococci and staphylococci were the predominant causes of burn-wound infection in the preantibiotic era and remain important pathogens at present. With the advent of antimicrobial agents, *Pseudomonas aeruginosa* became a major problem in burn-wound management. In animal models of cutaneous thermal injury and wound infection with *Pseudomonas*, there is an early, steady increase of neutrophils in the skin and bacterial dissemination to lungs and spleen within 72 h. Less common anaerobic bacteria are typically found in infections of electrical burns or when open wound dressings are used. The widespread use of topical and more effective antimicrobial agents has resulted in a decline in bacterial wound infections and the emergence of fungi (particularly *Candida albicans, Aspergillus* species, and the agents of mucormycosis) as increasingly important pathogens in burn-wound patients. Herpes simplex virus also has been found in burn wounds, especially those on the neck and face and those associated with inhalation injury. Cytomegalovirus viremia has been described in up to 71% of seropositive burn patients in prospective studies, and high levels (>1000 copies/mL) have been associated with increased duration of mechanical ventilation and longer stay in the intensive care unit (ICU).

Autopsy reports from patients with severe thermal burns over the last decade have identified *P. aeruginosa, Escherichia coli, Klebsiella pneumoniae*, and *Staphylococcus aureus* in association with mortality, independent of the percentage of total body surface area burned, the percentage of full-thickness burn, inhalation injury, and day of death after the burn. Indeed, burn trauma patients who acquire secondary *P. aeruginosa* infection have a fourfold greater mortality rate than those without *P. aeruginosa*. Historically, mortality rates among burn patients infected with *P. aeruginosa* have been as high as 77% over a 25-year period. In addition, *Acinetobacter calcoaceticus-baumannii* is among the top pathogens in some burn centers.

The cascade of events that follow a severe burn injury and that lead to multiorgan system failure and death is thought to represent a two-step process. The burn injury itself, with ensuing hypovolemia and tissue hypoxia, is followed by invasive infection arising from large amounts of devitalized tissue. The frequency of infection parallels the extent and severity of the burn injury. Severe burn injuries cause a state of immunosuppression that affects innate and adaptive immune responses. The substantial impact of immunocompromise on infection is due to effects on both the cellular and the humoral arms of the immune system. For example, decreases in the number and activity of circulating helper T cells, increases in suppressor T cells, decreases in production and release of monocytes and macrophages, and diminution in levels of immunoglobulin follow major burns. Neutrophil and complement functions also are impaired after burns. The increased levels of multiple cytokines detected in burn patients are compatible with the widely held belief that the inflammatory response becomes dysregulated in these individuals; bacterial cell products play a potent role in inducing proinflammatory mediators that contribute to this uncontrolled systemic inflammatory response. Increased permeability of the gut wall to bacteria and their components (e.g., endotoxin) also contributes to immune dysregulation and sepsis. Thus, the burn patient is predisposed to infection at remote sites (see below) as well as at the sites of burn injury. Another contributor to secondary immunosuppression after burn injuries is the endocrine system; increasing levels of vasopressin, aldosterone, cortisol, glucagon, growth hormone, catecholamines, and other hormones that directly affect lymphocyte proliferation, secretion of proinflammatory cytokines, natural killer cell activity, and suppressive T cells are seen.

CLINICAL MANIFESTATIONS AND DIAGNOSIS

Since clinical indications of wound infection are difficult to interpret, wounds must be monitored carefully for changes that may reflect infection. A margin of erythema frequently surrounds the sites of burns and by itself is not usually indicative of infection. Signs of infection include the conversion of a partial-thickness to a full-thickness burn, color changes (e.g., the appearance of a dark brown or black discoloration of the wound), the new appearance of erythema or violaceous edema in normal tissue at the wound margins, the sudden separation of the eschar from subcutaneous tissues, and the degeneration of the wound with the appearance of a new eschar.

Early surgical excision of devitalized tissue is now widely used, and burn-wound infections can be classified in relation to the excision site as (1) burn-wound impetigo (infection characterized by loss of epithelium from a previously re-epithelialized surface, as seen in a partial-thickness burn that is allowed to close by secondary intention, a grafted burn, or a healed skin donor site); (2) burn-related surgical-wound infection (purulent infection of excised burn and donor sites that have not yet epithelialized, accompanied by positive