TREATMENT BURN-WOUND INFECTIONS

The ultimate goal of burn-wound management is closure and healing of the wound. Early surgical excision of burned tissue, with extensive debridement of necrotic tissue and grafting of skin or skin substitutes, greatly decreases mortality rates associated with severe burns. In addition, the four widely used topical antimicrobial agents—silver sulfadiazine cream, mafenide acetate cream, silver nitrate cream, and nanocrystalline silver dressings—dramatically decrease the bacterial burden of burn wounds and reduce the incidence of burn-wound infection; these agents are routinely applied to partial- and full-thickness burns. The bactericidal properties of silver are related to its effect on respiratory enzymes on bacterial cell walls; its interaction with structural proteins causes keratinocyte and fibroblast toxicity that can delay wound healing if silver-based compounds are used indiscriminately. All four agents are broadly active against many bacteria and some fungi and are useful before bacterial colonization is established. Silver sulfadiazine is often used initially, but its value can be limited by bacterial resistance, poor wound penetration, or toxicity (leukopenia). Mafenide acetate has broader activity against gram-negative bacteria. The cream penetrates eschars and thus can prevent or treat infection beneath them; its use without dressings allows regular examination of the wound area. The foremost disadvantages of mafenide acetate are that it can inhibit carbonic anhydrase, resulting in metabolic acidosis, and that it elicits hypersensitivity reactions in up to 7% of patients. This agent is most often used when gram-negative bacteria invade the burn wound and when treatment with silver sulfadiazine fails. The activity of mafenide acetate against gram-positive bacteria is limited. Nanocrystalline silver dressings provide broader antimicrobial coverage than any other available topical preparation, exhibiting activity against methicillin-resistant *S. aureus* (MRSA) and vancomycin-resistant enterococci (VRE), moderate ability to penetrate eschars, and limited toxicity. In addition, this approach provides controlled and prolonged release of nanocrystalline silver into the wound, limiting the number of dressing changes and therefore reducing the risk of nosocomial infections as well as the cost of treatment. Mupirocin, a topical antimicrobial agent used to eradicate nasal colonization with MRSA, is increasingly being used in burn units where MRSA is prevalent. The efficacy of mupirocin in reducing burn-wound bacterial counts and preventing systemic infections is comparable to that of silver sulfadiazine.

In recent years, rates of fungal infection have increased in burn patients. When superficial fungal infection occurs, nystatin may be mixed with silver sulfadiazine or mafenide acetate as topical therapy. A small study found that nystatin powder (6 million units/g) was effective for treatment of superficial and deep burn-wound infections caused by *Aspergillus* or *Fusarium* species. In addition to these products, moisture-retention ointments with antimicrobial properties can promote rapid autolysis, debridement, and moist healing of partial-thickness wounds.

When invasive wound infection is diagnosed, topical therapy should be changed to mafenide acetate. *Subeschar clysis* (the direct instillation of an antibiotic, often piperacillin, into wound tissues under the eschar) is a useful adjunct to surgical and systemic antimicrobial therapy. Systemic treatment with antibiotics active against the pathogens present in the wound should be instituted. In the absence of culture data, treatment should be broad in spectrum, covering organisms commonly encountered in that particular burn unit. Such coverage is usually achieved with an antibiotic active against gram-positive pathogens (e.g., oxacillin, 2 g IV every 4 h) and with a drug active against *P. aeruginosa* and other gram-negative rods (e.g., mezlocillin, 3 g IV every 4 h; gentamicin, 5 mg/kg IV per day). In penicillin-allergic patients, vancomycin (1 g IV every 12 h) may be substituted for oxacillin (and is efficacious against MRSA), and ciprofloxacin (400 mg IV every 12 h) may be substituted for mezlocillin. Oxazolidinone antibiotics like linezolid have demonstrated efficacy in reducing bacterial growth and toxic shock syndrome toxin 1 levels in animal models of MRSA burn-wound infections.

Patients with burn wounds frequently have alterations in metabolism and renal clearance mechanisms that mandate the monitoring of serum antibiotic levels. The levels achieved with standard doses are often subtherapeutic.

Treatment of infections caused by emerging resistant pathogens remains a challenge in the care of burn patients. MRSA, resistant enterococci, multidrug-resistant gram-negative rods, and Enterobacteriaceae producing extended-spectrum β-lactamases have been associated with burn-wound infections and identified in burn-unit outbreaks. Strict infection-control practices (including microbiologic surveillance in burn units) and appropriate antimicrobial therapy remain important measures in reducing rates of infection due to resistant organisms.

In general, prophylactic systemic antibiotics have no role in the management of burn wounds and can, in fact, lead to colonization with resistant microorganisms. In some studies, antibiotic prophylaxis has been associated with increases in secondary infections of the upper and lower respiratory tract and the urinary tract as well as with prolonged hospitalization. An exception involves cases requiring burn-wound manipulation. Since procedures such as debridement, excision, or grafting frequently result in bacteremia, prophylactic systemic antibiotics are administered at the time of wound manipulation; the specific agents used should be chosen on the basis of data obtained by wound culture or data on the hospital's resident flora.

The use of oral antibiotics for selective digestive decontamination (SDD) to decrease bacterial colonization and the risk of burn-wound infection is controversial and has not been widely adopted. In a randomized, double-blind, placebo-controlled trial in patients with burns involving >20% of the total body surface area, SDD was associated with reduced mortality rates in the burn ICU and in the hospital and also with a reduced incidence of pneumonia. The effects of SDD on the normal anaerobic bowel flora must be taken into consideration before this approach is used.

Strategies to reduce or limit systemic spread of wound infections, particularly to the lung, may be useful adjuncts to therapy. Some of these strategies are aimed at reducing neutrophilic inflammation at the site of injury, which can accelerate biofilm formation, particularly by *P. aeruginosa*. For example, in animal models of cutaneous burns with *P. aeruginosa* wound inoculation, a single dose of azithromycin administered early reduces rates of *Pseudomonas* infection and systemic spread to lung and spleen and appears to have effects similar to those of classic anti-*Pseudomonas* agents, such as tobramycin. The extent to which azithromycin can be administered early in humans to prevent dissemination remains to be studied.

All burn-injury patients should undergo tetanus booster immunization if they have completed primary immunization but have not received a booster dose in the past 5 years. Patients without prior immunization should receive tetanus immune globulin and undergo primary immunization.