The Epidemiology of Burn Wound Infections: Then and Now

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Burn wound infections are a serious complication of thermal injury. Although pneumonia is now the most important infection in patients with burns, burn wound infection remains a serious complication unique to the burn recipient. The methods for managing thermal injury have evolved during the past 50 years. This evolution has been accompanied by changes in the etiology, epidemiology, and approach to prevention of burn wound infections. In the 1950s, 1960s, and 1970s and into the mid-1980s, burn wounds were treated by the exposure method, with application of topical antimicrobials to the burn wound surface and gradual debridement with immersion hydrotherapy. As early burn wound excision and wound closure became the focal point of burn wound management, accompanied by a change from immersion hydrotherapy to showering hydrotherapy, the rate of burn wound infection appeared to decrease. Few epidemiologic studies have been done since this change in the approach to management of thermal injury. There are few data on the epidemiology of burn wound infections from the era of early excision and closure. Data are needed on infection rates for excised and closed burn wounds, the etiologies of these infections, and the epidemiology and the prevention of such infections. Additional studies are needed on the indications for topical and antimicrobial prophylaxis and selective decontamination of the digestive tract.

Thermal injury is a serious type of trauma requiring care in specialized units. It is estimated that ~2.5 million persons in the United States sustain burns requiring medical attention each year [1]. More than 100,000 of these patients are hospitalized, and there are ~12,000 deaths per year due to thermal injury.

Although presently more patients with burns die of pneumonia than of burn wound infection, burn wound sepsis remains an important infectious complication in this population. Thermal injury to the skin causes a massive release of humoral factors, including cytokines, prostaglandins, vasoactive prostanoids, and leukotrienes [2]. Accumulation of these factors at the site of injury results in "spillover" into the systemic circulation, giving rise to immunosuppression. All arms of the immune system are involved in this immunosuppression. Chemotaxis of neutrophils is decreased, as are phagocytic and bactericidal activity [3]. Thermal injury results in less phagocytic

activity and lymphokine production by macrophages. The effect on T lymphocytes is to increase the number of suppressor cells and to decrease the number of helper cells. Natural killer cell activity is also diminished.

In addition to loss of the natural cutaneous barrier to infection, coagulated protein and other microbial nutrients in the burn wound, combined with avascularity of the wound, lead to microbial colonization. In some patients, colonization is followed by invasion of microorganisms, giving rise to burn wound infection.

After the development of effective therapy for fluid and electrolyte abnormalities caused by severe burns, infection and septicemia became the leading causes of mortality [4]. In the first of 2 studies published in 1965 on the effect of topical application of the antimicrobial agent *p*-aminomethylbenzene sulfonamide (mafenide acetate) to the burn wound surface, Lindberg et al. [4] observed a 50% reduction in the rate of infection of burn wounds of <50% of total body surface area (TBSA). Burn wound sepsis in patients with burns on 30%–60% of the TBSA was almost eliminated as a cause of death.

Silver nitrate (0.5% solution) was also introduced as a topical antimicrobial agent in 1965 [5]. It was applied as a liquid and

had a broad spectrum of antimicrobial activity. Because application of silver nitrate results in black or brown staining of everything with which it has contact, the most-used topical antimicrobial agent is silver sulfadiazine, which was synthesized from silver nitrate and sodium sulfadiazine [6]. It is produced as a 1% concentration in a water-soluble cream base.

EPIDEMIOLOGY OF BURN WOUND INFECTIONS DURING THE EARLY APPROACH TO TREATMENT OF THERMAL INJURY

At the time that topical antimicrobial therapy was introduced, thermal injury was treated with conservative therapy. The controlled growth of bacteria on the wound surface was permitted, to break down the burn eschar, and debridement was achieved by daily treatment with immersion hydrotherapy. When the eschar had been removed, the underlying bed of granulation tissue was covered with skin grafts. This type of therapy was used in 1950s, 1960s, and 1970s and into the 1980s. Much of the information on the epidemiology of burn wound infections was published in these decades [7–33]. The most important reservoirs for microorganisms that colonized the burn wounds of new patients were the collective burn wound surfaces and the gastrointestinal (GI) tracts of patients [7–10, 12, 15, 16]. Microorganisms were transmitted by the hands of health care workers, by fomites and hydrotherapy water [7, 9, 20–24, 27, 29, 30, 33], and, according to some reports, by the air [14, 23, 26, 30].

Risk factors for burn wound colonization or infection were the size of the burn wound (the percentage of TBSA burned) and the duration of hospitalization [7, 16, 19]. Outbreaks of infection in burn units occurred and were related to contaminated mattresses [29, 33] and to contaminated hydrotherapy water [21, 26, 27]. In each of the outbreaks related to hydrotherapy, the outbreak microorganism was resistant to the topical antimicrobial agent in use at the time of the outbreak. Other outbreaks due to microorganisms that were resistant to topical antimicrobial agents have also been reported [20, 25].

The most common causes of burn wound infections were bacteria, with *Pseudomonas aeruginosa* being the most important species [7–16, 20–27, 30]. Less common causes of burn wound infection were yeasts [34–38], filamentous fungi [39–42], and viruses [43, 44].

Diagnosis of burn wound infection. During the decades of exposure burn wound treatment, burn wound infections were diagnosed by symptoms and signs, by the appearance of the burn wound, and by a full-thickness biopsy of the burn wound in an area that appeared infected on clinical examination. Tissue biopsy specimens were examined histopathologically and cultured quantitatively [31]. Burn wound infection was diagnosed by histopathological examination when microorganisms were observed to be invading viable tissue beneath the eschar [31]. Burn wound infection was also diagnosed by quantitative cultures that yielded $\geqslant 10^4$ cfu/g of tissue [45] or $\geqslant 10^5$ cfu/g of tissue [46]. However, in a study published in 1981, significant doubt was raised about quantitative cultures because of substantial variability in quantitative counts from tissue biopsy specimens that had been divided and each cultured separately [47]. Only 38% of paired quantitative results agreed within the same $\log_{10}$ unit, whereas 44% differed by ± 2 $\log_{10}$ U or more. Table 1 shows the definitions used to diagnose burn wound infections in patients with unexcised burn wounds treated by the exposure method [49].

Prevention of burn wound infections. At the time topical

Table 1. Criteria for diagnosis of burn wound infections.

Criterion	Description
1	Patient has a change in burn wound appearance or character (such as rapid eschar separation; dark brown, black, or violaceous discoloration of the eschar; or edema at wound margin) **and** histological examination of burn biopsy specimen reveals invasion of organisms into adjacent viable tissue.
2	Patient has a change in burn wound appearance or character (such as rapid eschar separation; dark brown, black, or violaceous discoloration of the eschar; or edema at wound margin) **and** at least 1 of the following: (1) organisms cultured from blood samples in the absence of other identifiable infection, or (2) isolation of herpes simplex virus, histological identification of inclusions by light or electron microscopy, or visualization of viral particles by electron microscopy in biopsy specimens or lesion scrapings.
3	Patient with a burn has at least 2 of the following signs or symptoms with no other recognized cause: fever (temperature, >38°C) or hypothermia (temperature, <36°C), hypotension, oliguria (urine output, <20 mL/h), hyperglycemia at previously tolerated level of dietary carbohydrate, or mental confusion, **and** at least 1 of the following: (1) histologic examination of burn biopsy specimen showing invasion of organisms into adjacent viable tissue, (2) organisms cultured from blood specimens, or (3) isolation of herpes simplex virus, histological identification of inclusions by light or electron microscopy, or visualization of viral particles by electron microscopy in biopsy specimens or lesion scrapings.

NOTE. Burn infection must meet 1 of the criteria. Adapted from [48], with permission.

antimicrobial agents were being introduced, plastic isolators with filtration of air were being tested with variable success [8, 12, 13, 50]. Such isolators were never widely used. Patients were generally treated by personnel wearing barrier apparel, including caps, masks, gowns, shoe covers, aprons, and gloves [23, 24, 33, 51].

Immersion hydrotherapy was used by most burn care facilities in the earlier decades of burn wound care. By 1990, 81.4% of burn centers continued to use immersion hydrotherapy; 82.8% performed hydrotherapy on all patients, without regard for size of the burn wound; and 86.9% of the centers continued hydrotherapy throughout hospitalization [52]. Hydrotherapy treatments were associated with transmission of microorganisms between patients. One of the major problems with hydrotherapy equipment was the difficulty in decontaminating the agitators and aerators in the tubs [21]. Aerators and agitators were removed from hydrotherapy tubs and replaced with plastic disposable tub liners, and water agitation was produced by compressed air emitted from channels in the plastic liner [27]. Even with this modification, hydrotherapy water continued to be cross-contaminated between patients by inadequate hand washing and use of barriers by caregivers [27].

In an attempt to decrease the risk of transmission of microorganisms by hydrotherapy treatments, investigators added antimicrobial agents to hydrotherapy water [53–55]. It was observed that sodium hypochlorite lowered the number of microorganisms on burned and unburned skin [53, 55]. Chloramine-T in hydrotherapy water was effective in eliminating gram-negative microorganisms from wounds after 5 days of treatment [54]. No side effects were noted. In one study in which sodium hypochlorite was added to hydrotherapy water, patients noted more discomfort than they did with immersion in water without sodium hypochlorite. The release of chlorine vapors from sodium hypochlorite in hydrotherapy water irritated the conjunctivae and nasal mucosae of personnel [55]. Currently, it is unknown how many burn centers use disinfectants in hydrotherapy water.

EPIDEMIOLOGY OF BURN WOUND INFECTIONS IN THE 21ST CENTURY

From the mid-1980s through the present, burn wound excision and grafting have replaced the earlier exposure therapy that made use of hydrotherapy and gradual debridement until a bed of healthy granulation tissue was developed, followed by coverage with autologous skin grafts. In some burn centers, early burn wound excision is accomplished in the first few days after burn injury. The latter approach often involves use of temporary wound coverings, such as allograft, xenograft, and synthetic materials. In other burn centers, burn wound excision

and wound closure of large burns are staged over several weeks, and grafting is done with autologous skin [56, 57].

The major goals of early burn wound excision included decreasing mortality, reducing scar tissue formation to improve the cosmetic outcome, and decreasing the incidence of burn wound infection and systemic sepsis. At one burn center, it was noted that after 1978, when early excision and skin grafting were instituted for treatment of burn wounds judged to require >3 weeks to heal, the incidence of documented systemic sepsis originating from the burn wound decreased from 6% to just over 1%. During the same period, the author noted that the rate of death due to burn wound sepsis decreased from 40% to 18% of all patient deaths [56].

However, only 2 randomized, controlled trials of early excision versus conservative exposure therapy have been done, and neither showed a significant reduction in burn wound infections in burns of >15% of TBSA [58, 59]. Whether early excision reduces burn wound infection, burn wound excision seems to have replaced conservative exposure therapy for most patients. Such therapy may reduce the rate of burn wound infection, and it would be expected that excision and closure of burn wounds would reduce the reservoir of bacteria made up by the collective burn wound surfaces of patients in a burn treatment facility.

Another important aspect of the change in therapy of burn wounds is that, with early excision and skin grafting, it has been necessary to develop new definitions for burn wound infections. The new definitions were developed by a subcommittee of the Committee on the Organization and Delivery of Burn Care of the American Burn Association [60] and are shown in table 2.

Another observation that needs additional study is that blood transfusions appear to be a risk factor for infection in patients with burns [61]. This untoward effect of blood transfusion appears to be mediated by immunosuppression in addition to that caused by thermal injury. Because early excision is associated with substantial blood loss requiring transfusion of multiple units of blood, it is unclear how much the advantages of early wound excision and closure are offset by further immunosuppression of the patient.

Another area that seems to be evolving is the technique for cleansing and debriding burn wounds. Although some burn treatment facilities still use immersion hydrotherapy, most burn facilities now shower patients with a hand-held sprayer [62]. This reduces the risk of transferring surface bacteria to open burn wounds. The change from immersion to showering hydrotherapy may also have had an effect on the epidemiology of burn wound infections. In the absence of immersion hydrotherapy equipment, such equipment would be eliminated as a potential reservoir for microorganisms that colonize the burn wound surface, and cross-contamination of patients' burn

Table 2. Proposed definitions for burn wound infections, including burn wound impetigo, open burn-related surgical wound infections, cellulitis, and infection of unexcised burn wounds.

Infection	Criteria
Burn wound impetigo	Infection involves loss of epithelium from a previously reepithelialized surface, such as grafted burns, partial-thickness burns allowed to close by secondary intention, or healed donor sites; **and** is not related to inadequate excision of the burn, mechanical disruption of the graft, or hematoma formation; **and** requires some change of or addition to antimicrobial therapy. Infection may or may not be associated with systemic signs of infection, such as hyperthermia (temperature, >38.4°C) or leukocytosis (WBC count, >10,000 cells/mm^3).
Open burn-related surgical wound infection	Infection occurs in surgically created wounds, such as excised burns and donor sites that have not yet epithelialized; **and** has a purulent exudate that is culture positive; **and** requires change of treatment (which may include change of or addition to antimicrobial therapy, removal of wound covering, or increase in frequency of dressing changes); **and** includes at least 1 of the following: (1) loss of synthetic or biological covering of the wound, (2) changes in wound appearance (such as hyperemia), (3) erythema in the uninjured skin surrounding the wound, or (4) systemic signs, such as hyperthermia or leukocytosis.
Burn wound cellulitis	Infection occurs in uninjured skin surrounding the burn wound or donor site, **and** is associated with erythema in the uninjured skin progressing beyond what is expected from the inflammation of the burn, **and** is not associated with other signs of infection in the wound itself, **and** requires change of or addition to antimicrobial therapy, **and** includes at least 1 of the following: (1) localized pain or tenderness, swelling, or heat at the affected site; (2) systemic signs of infection, such as hyperthermia, leukocytosis, or septicemia; (3) progression of erythema and swelling; or (4) signs of lymphangitis and/or lymphadenitis.
Invasive infection in unexcised burn wounds	Infection occurs in deep partial- or full-thickness burn that has not been surgically excised, **and** is associated with change in burn wound appearance or character (such as rapid eschar separation or dark brown, black, or violaceous discoloration of the eschar), **and** requires surgical excision of the burn and treatment with systemic antimicrobials, **and** may be associated with, but not dependent upon, any of the following: (1) inflammation of the surrounding uninjured skin, such as edema, erythema, warmth, or tenderness; (2) histological examination of the burn biopsy specimen shows invasion of the infectious organism into adjacent viable tissue; (3) organism isolated from blood culture in absence of other identifiable infection; or (4) systemic signs of infection, such as hyper- or hypothermia, leukocytosis, tachypnea, hypotension, oliguria, hyperglycemia at previously tolerated level of dietary carbohydrate, or mental confusion.

NOTE. Adapted from [60], with permission.

wound surfaces by such treatments would no longer occur. However, 2 outbreaks related to showering hydrotherapy have been reported [63, 64].

In one outbreak, patients were initially immersed in tap water to remove adherent dressings and then washed further with a gentle stream of water from a hand-held device [63]. Although patients were initially immersed in tap water to remove adherent dressings, the hydrotherapy treatments were completed by showering. The authors recovered *Pseudomonas* species from 2 hydrotherapy tubs. The outbreak cleared when hydrotherapy was replaced by local wound care in patients' rooms.

Another outbreak occurred in a burn care facility where hydrotherapy treatments were done entirely by showering. Methicillin-resistant *Staphylococcus aureus* was recovered from cultures of samples from the stretcher used for showering and the pistol grip on the hand-held shower [64]. Hydrotherapy treatments were also discontinued in this unit and were replaced by wound care in each patient's room. Institution of these

measures cleared the outbreak. It is unclear what the comparative risks are for transmission of microorganisms to patients' burn wounds by immersion hydrotherapy, hydrotherapy by showering, and wound care provided in each patient's room.

The epidemiology of burn wound infections today. In the past 2 decades, important changes in burn wound treatment may have changed the epidemiology of infections in patients with burns. Central to the possible changes in epidemiology are early excision and closure of the burn wound and replacement of immersion hydrotherapy by showering hydrotherapy or local burn wound care in patients' rooms.

Although the causative microorganisms of burn wound infections have changed little over the past 2 decades (tables 3 and 4) [49], in at least 1 health care center with very effective infection control, the rate of burn wound infections has markedly decreased, and bacteria are less often the cause than fungi [65]. The very effective infection control was brought about by moving the patients from an intensive care ward without

Table 3. Bacteria and fungi that constituted ≥1.0% of 1984 isolates recovered from 1267 burn wound infections: National Nosocomial Infections Study of the Center for Disease Control, July 1974 to July 1978.

Species	Percentage of isolates
Staphylococcus aureus	22.9
Pseudomonas aeruginosa	20.9
Pseudomonas species	7.2
Escherichia coli	6.7
Group D streptococci	5.0
Streptococcus faecalis	4.2
Klebsiella pneumoniae	3.7
Serratia marcescens	3.1
Enterobacter cloacae	3.0
Proteus mirabilis	2.8
Enterobacter species	2.5
Klebsiella species	2.2
Staphylococcus epidermidis	1.4
Group A streptococci	1.1
Enterobacter aerogenes	1.0
Candida albicans	1.3

separate enclosures to a renovated unit with separate bed enclosures [66]. Care of patients in the new unit reduced the incidence of infections from 58.1% to 30.4%, and the overall proportion of patients with bacteremia was reduced from 20.1% to 9.4%. The incidence of bacteremia due to *P. aeruginosa* in the new unit was reduced to 1.4% from 8.1% in the old open-ward facility [67].

Microorganisms are probably still transmitted to the burn wound surfaces of recently admitted patients by the hands of personnel, by fomites, and perhaps, to some extent, by hydrotherapy. The GI tract continues to be a potential reservoir for microorganisms that colonize the burn wound surface. It is likely that endogenous microorganisms continue to be transmitted to burn wound surfaces by feces.

As a result of the extensive bleeding that occurs during early burn wound excision, blood transfusions remain a potential risk factor for infection because of their immunosuppressive effect. In the era of early excision and closure, it is unclear to what extent size of burn wound, duration of hospitalization, and resistance to topical and systemic antimicrobial agents are risk factors for burn wound colonization and infection.

Diagnosis of burn wound infections. Quantitative cultures of burn wound tissue specimens are no longer used for diagnosis of burn wound infection. This is because of their imprecision and poor specificity [47, 68]. However, when quantitative cultures yield <10^5 cfu/g of burn wound tissue, it has been found that 96.1% of patients do not have a burn wound

infection. Quantitative cultures are useful for indicating the predominant microorganism(s) in the burn wound, identifying the species, and providing susceptibility data. In addition, in one study, the results of cultures agreed with all histologically diagnosed bacterial infections and 5 of 8 histologically diagnosed fungal infections [68].

Diagnosis of burn wound infections by biopsy showing microbial invasion of viable tissue is seldom used today [60]. It is, however, the "gold standard" for diagnosis of infection in unexcised burn wounds. Burn wound infections are now diagnosed largely on the basis of clinical symptoms and signs and by clinical examination of the burn wound (table 2). This is supplemented, when possible, by blood cultures and cultures of purulent exudates from the burn wound.

Prevention of burn wound infections. Barriers to prevent transmission of microorganisms to patients were used in the earlier decades and continue to be important elements of infection control in modern burn care. In one burn care facility, a study was performed to determine how patients with burns could most effectively be isolated to prevent transmission of microorganisms [69]. During phase 1 (baseline) of a phased study, the authors determined that 63% of patients were colonized with marker microorganisms appearing on days 4–8 of the study. Phase 2 followed education of the burn center personnel on the use of proper isolation technique. This approach resulted in no change in the colonization rate. In phase 3, a simplified isolation protocol was adopted, the rate of colonization decreased from 63% to 33%, and a significant delay in colonization (from 7.8 to 21 days) was observed in patients colonized with *P. aeruginosa*. The effectiveness of the simplified isolation protocol was confirmed when it was again evaluated in phase 4.

Table 4. Bacteria and fungi that constituted 1830 isolates recovered from 1234 burn wound infections: National Nosocomial Infections Study System, Centers for Disease Control and Prevention, 1980–1998.

Pathogen	No. (%) of isolates
Staphylococcus aureus	420 (23.0)
Pseudomonas aeruginosa	353 (19.3)
Enterococci	202 (11.0)
Enterobacter species	176 (9.6)
Escherichia coli	131 (7.2)
Coagulase-negative staphylococci	78 (4.3)
Candida albicans	64 (3.5)
Serratia marcescens	64 (3.5)
Klebsiella pneumoniae	48 (2.6)
Others	294 (16.0)

NOTE. Data from R. P. Gaynes (Centers for Disease Control and Prevention, personal communication, 1998).

The intent of changes in the hydrotherapy technique from immersion to showering was to decrease the transmission of microorganisms to the burn wound. It is unclear what effect the changes in hydrotherapy technique have had on the epidemiology of burn wound infections.

Although topical antimicrobial agents continue to be used, their role is unclear for wounds created by early excision and wound closure. They may be applied to the burn wound before excision and to wounds that have delayed excision or cannot be excised. Given the untoward effects of topical antimicrobial agents and their selection of fungi and resistant bacteria for colonization of the burn wound surface, the use of topical antimicrobials in the era of burn wound excision needs further study [32].

The effect of burn wound excision on the epidemiology of burn wound infections is unclear. By reducing the portal of entry, wound excision and closure could decrease the occurrence of burn wound infections, but such an effect has not been proven by prospective randomized clinical trials except in the case of burn wounds of ≤15% of TBSA [58].

It is possible that, when burn wounds are excised and the site of excision is closed by autografting or temporarily covered by allograft or other materials, the density of microbial colonization in the areas of thermal injury would be diminished. This would decrease the reservoir of microorganisms made up by the collective burn wounds of patients in the burn care facility. To my knowledge, this has never been studied.

The GI tract remains a potentially important reservoir and mode of transmission for microorganisms that colonize the burn wound. This is particularly true for large burn wounds [7, 70]. The sources of *P. aeruginosa* that colonize the GI tracts of patients with burns include the hands of health care workers, the environment, and food [7, 71–73].

Other than use of barriers, the approach to control of the GI tract as a reservoir and mode of transmission has been the attempted suppression or elimination of microorganisms in the GI tract. The approach has been to administer combinations of oral antimicrobial agents. This prophylaxis is termed "selective intestinal decontamination" (SDD).

Several studies of SDD involving patients with burns have been published [74–79]. The most common antimicrobial agents used in combination were neomycin, erythromycin, polymyxin, tobramycin, trimethoprim-sulfamethoxazole, amphotericin B, and nystatin. Two antibacterial antimicrobials were usually combined with an antifungal agent. Four of the 6 studies were prospective, but only 1 was a prospective, randomized, placebo-controlled, double-blind study [79]. Unfortunately, the latter study was likely underpowered to detect a clinically significant difference between the 11 patients who received prophylaxis and the 12 control subjects who received placebo. The authors did not report the α level, the power of the study, or the differences that they were trying to detect between the treated group and the placebo group.

CONCLUSIONS

Modern burn wound therapy is centered on early excision and closure of the wound. Accompanying the change from the conservative exposure method of burn wound therapy to early excision and closure has been the change from immersion hydrotherapy to showering hydrotherapy. The definitions for burn wound infections have also changed. Questions that need to be addressed in future studies include the following: (1) Does early excision and closure reduce burn wound infection rates? (2) Is the closed wound less likely to be colonized and, therefore, less likely to be a reservoir for microorganisms? (3) Does showering hydrotherapy decrease the likelihood of burn wound contamination? (4) What is the current role of topical antimicrobial agents? The role of SDD in preventing burn wound colonization and infection is unclear, and large, prospective, randomized, placebo-controlled, double-blind clinical trials are needed to determine whether SDD is effective in preventing burn wound infections. The only documented effective control measure is the use of barriers to prevent cross-contamination.

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