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The Changing Epidemiology of Infection in Burn Patients

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Topical chemotherapy, prompt excision, and timely closure of the burn wound have significantly reduced the occurrence of invasive burn wound infection and its related mortality. Since wound protection is imperfect and invasive wound infection may still occur in patients with massive burns in whom wound closure is delayed, scheduled wound surveillance and biopsy monitoring are necessary to assess the microbial status of the burn wound and identify wound infections caused by resistant bacteria or non-bacterial opportunists at a stage when therapeutic intervention can control the process.

As a reflection of the systemic immunosuppressive effects of burn injury, infection remains the most common cause of morbidity and mortality even though the occurrence of wound infections has been significantly decreased. Pneumonia is the most frequent infection occurring in burn patients today but the improvements in patient management, wound care, and infection control have made bronchopneumonia the most common form of this infection and gram-positive organisms the most common causative agents. The organisms causing bacteremia that exert a species specific effect on the mortality related to extent of burn injury and patient age have changed in concert with changes in wound flora.

Infection control procedures, including scheduled surveillance cultures, utilization of cohort patient care methodology, strict enforcement of patient and staff hygiene, and patient monitoring have been effective in eliminating endemic resistant microbial strains, preventing the establishment of newly introduced resistant organisms, diagnosing infection in a timely fashion, instituting antibiotic and other necessary therapy in a prompt manner, and documenting the effectiveness of present day burn patient care and the improved survival of burn patients.

Infection has always been the predominant determinant of wound healing, incidence of complications, and outcome of burn patients. The marked decrease in shock and acute renal failure as causes of death that has resulted from the use of effective fluid resuscitation regimens in patients with extensive burns has only served to increase the relative importance of infection in that subset of burn patients [1]. Other improvements in care that protect organ function and prevent complications, such as exsanguinating hemorrhage from stress ulcers, have further accentuated infection as the most frequent cause of burn patient morbidity and mortality [2]. Additionally, the changes in wound care that have occurred over the last 3 decades and significantly reduced the occurrence of bacterial burn wound infection have altered the site, type, causative agent, and time of onset of the infections that do occur and so frequently determine the fate of burn patients.

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Burn Wound Infection

The incidence of infectious complications in burn patients is increased in proportion to the fraction of the body surface injured [3]. The direct effects of heat on skin and underlying tissue make the burn wound particularly susceptible to infection as evidenced by the frequent occurrence of invasive burn wound infections prior to the development of topical chemotherapy [4]. The denatured protein in burn injured tissue is a rich pabulum for microbial growth and proliferation. Additionally, the thermal thrombosis that renders the eschar avascular further promotes infection by precluding delivery of the cellular components of the host defense system and limiting delivery of bloodborne antibiotics to the microorganisms within the burn wound [5]. If the burn wound is not protected by topical chemotherapeutic agents and the eschar is unexcised, the proliferating microorganisms penetrate the eschar migrating preferentially along hair follicles and sweat glands to reach the interface between non-viable and viable tissue [6]. In that location, commonly termed the subeschar space, further microbial proliferation occurs which, if host defenses are adequate, simply promotes eschar slough but, if host defenses are deficient, promotes invasion of the underlying viable tissue.

There are also time related changes in the microbial flora of an untreated burn wound which are the same as those that occur in any open wound or the intubated airway and recapitulate the history of surgical infections [7]. The initially sparse predominantly gram-positive flora is rather rapidly replaced by a progressively dense, predominantly gram-negative flora (more tolerant to the antimicrobial agents in use) that in turn may be supplanted by a non-bacterial flora if wound closure is delayed and the patient requires treatment with broad spectrum antibiotics [8].

The intraeschar proliferation and penetration of bacteria can be retarded and even prevented by the use of topical antimicrobial chemotherapy. There are three commonly used topical agents each of which has been demonstrated to be effective in reducing the occurrence of invasive burn wound infection [9]. Sulfamylon® burn cream is an 11.1% suspension of the acetate salt of mafenide, an N′ unsubstituted sulfonamide, in a hydro-

philic base. Mafenide acetate is water soluble and freely diffuses into the eschar. That solubility and the high activity of mafenide against gram-negative organisms, particularly *Pseudomonas aeruginosa*, make Sulfamylon® burn cream particularly effective in limiting proliferation of bacteria that have penetrated the eschar and preventing the development of invasive burn wound infection. The other topical agents, silver sulfadiazine burn cream, a 1% suspension of silver sulfadiazine in a hydrophilic base, and 0.5% silver nitrate soaks, are both effective in preventing microbial penetration of the eschar when treatment is begun immediately after burning but less effective, because of limited or no diffusibility, in controlling the proliferation of microorganisms already colonizing the eschar. 0.5% silver nitrate soaks are generally reserved for use in patients who are allergic to sulfonamides. The authors currently apply mafenide acetate burn cream following the daily chlorhexidine cleansing and silver sulfadiazine burn cream 12 hours later in order to realize the benefits of each agent and minimize the side effects of both.

The type of organisms present in the eschar strongly influences the incidence of invasive infection and patient outcome. The risk of invasive wound infection and the characteristics of that infection are determined by the type of organisms predominant in the eschar. Enzymes and other metabolic products produced by Pseudomonas species as well as their flagellum-imparted motility enhance the invasive potential of those organisms and the rapid spread of the infections they cause [6, 10]. In contradistinction, wound infections caused by the Staphylococci tend to remain superficial and localized [3]. The invasive potential and characteristics of non-bacterial wound infections are also organism specific. Candida species seldom invade and commonly remain confined to the wound surface [11]. Aspergillus species are more likely to cause invasive infection but the infections are commonly superficial and rarely cross fascial planes [12]. The Phycomycete species have a propensity to invade and thrombose small vessels and thus cause rapidly expanding ischemic necrosis. Phycomycotic infections are characterized by deep invasion and by rapid spread along and across fascial planes [13].

The widespread use of burn wound excision, as described elsewhere in this symposium, has defined the role of topical chemotherapy as that of controlling the density of intraeschar microorganisms during the typically brief interval between injury and surgical removal of the burned tissue and graft closure of the wound. Even so, there are patients in whom supervening complications or a disparity between extent of burn and available donor sites delay excision and wound closure and thereby require prolonged topical chemotherapy [14]. Since all topical agents provide imperfect protection and none sterilize the burn wound, invasive infection may occur in such patients. In the period 1983 to 1987 only 54 invasive burn wound infections were diagnosed in 42 of the 998 burn patients admitted to the U.S. Army Burn Center. To identify that complication in a timely fashion and institute specific therapy promptly, a program of scheduled wound surveillance and biopsy monitoring is necessary.

The burn wound is best examined at the time of the daily cleansing when all dressings and topical agent have been removed from the wound. The local signs of burn wound infection include focal dark discoloration of the burn, conversion of an area of partial-thickness injury to full-thickness necrosis, green discoloration of the subcutaneous fat, the appearance of vesicular lesions in healing or recently healed partial-thickness burn, and unexpectedly rapid separation of the eschar. Identification of one or more of those signs suggests that the patient's host defenses have been overwhelmed by the microorganisms in the wound and that an invasive burn wound infection has occurred (Fig. 1). Since many of the signs of wound infection can be mimicked by other conditions, the microbial status of any wound showing such changes must be assessed [15]. Quantitative cultures of the wound surface or of a wound biopsy, advocated by some as a means of diagnosing a burn wound infection, appear to be helpful in confirming the absence of wound infection but of little help in confirming the presence of such. Quantitative cultures of wound biopsy specimens that show bacterial counts of less than 10^6 organisms per gram of tissue correlate well with absence of infection on histologic examination. Conversely, <50% of quantitative cultures, showing growth of 10^6 or more bacteria per gram of tissue, are associated with histologic evidence of infection and such a lack of specificity of high bacterial counts severely compromises their usefulness in diagnosing the presence of invasive infection [16].

Fig. 1. The multiple rounded foci of black discoloration in the burn wound as well as the edema and less intense discoloration of the unburned skin at the margins of the burn wound are characteristic of invasive burn wound infection. These lesions, evident on the 13th postburn day, prompted a burn wound biopsy which confirmed the diagnosis of invasive Pseudomonas burn wound infection in this 72 year old male with a burn involving 69% of the total body surface. A blood culture obtained on that day was reported as showing growth of *Pseudomonas aeruginosa*.

The histologic examination of a burn wound biopsy is the only reliable means of differentiating microbial colonization of non-viable tissue from microbial invasion of viable tissue and making the diagnosis of invasive burn wound infection. The biopsy specimen should be obtained from that area of the wound showing the most marked changes characteristic of burn wound infection and must include viable tissue that underlies the eschar [17] (Fig. 2). The specimen can be processed within 30 minutes by a frozen section technique or within 3 to 4 hours by a rapid section technique [18, 19]. The pathologist must identify microorganisms present in viable tissue to confirm the

Fig. 2. A scalpel is used to obtain a biopsy from an area of dark discoloration of the burn wound. The lenticular tissue specimen must include underlying unburned tissue so that the nonviable/viable tissue interface can be examined histologically.

diagnosis of invasive burn wound infection (Fig. 3). Other signs of inflammation in viable tissue, including hemorrhage and microvascular thrombosis, are non-specific and should prompt a meticulous search for microorganisms in the viable tissue of the biopsy material being examined or even performance of another biopsy if the initial biopsy is negative and discordant with either wound appearance or the patient's general condition.

On the basis of the histologic findings, the pathologist can stage the microbial status of the wound according to the schema depicted in Table 1. The mortality of burn patients increases as the numerical stage increases. As would be anticipated, a markedly higher mortality is associated with Stage II as compared to Stage I [17]. If only colonization is evident on the histologic sections, the depth of eschar penetration should be determined. If, in subsequent biopsies, histologic findings of increased proliferation and eschar penetration by the microorganisms give evidence of inadequate control of the intraeschar microorganisms, the wound care regimen should be changed even if invasion is not present. If invasion has occurred, the sections should be examined to identify microvascular involvement (Stage IIC) which indicates increased risk of remote dissemination and mandates close monitoring to identify such [20] (Fig. 4).

When invasive bacterial burn wound infection is diagnosed both general care and wound care must be changed. Systemic antibiotic therapy should be started using full doses of the antibiotic to which the predominant flora of the treatment unit are sensitive as determined by the microbial surveillance program. Antibiotic therapy is later adjusted as indicated by culture and sensitivity results from the biopsy specimen. Scheduled monitoring of the peak and trough serum levels of the antibiotics allows one to adjust the dosage schedule to compensate for the elevated metabolic rate of the burn patient or, conversely, for sepsis related impairment of hepatic and renal function [21]. If the infection is bacterial, one-half the daily dose of a broad spectrum penicillin, such as piperacillin, suspended in 1,000 ml of normal saline should be immediately infused into the subeschar tissues beneath all infected areas of the wound using a number 20 spinal needle to minimize the number of injection sites [22]. Surgical excision of the infected tissue

Fig. 3. Photomicrograph of a burn wound biopsy specimen showing hyphae typical of Aspergillus species (45° branching angle) in unburned tissue. Depth of penetration, indexed by presence of hyphal elements in the central portion of the lower one-third of the field is indicative of stage IIB invasion.

Table 1. Criteria for staging the microbial status of burn wounds.

Stage I: Colonization	
A. Superficial	Sparse microbial population on burn wound surface
B. Penetration	Microorganisms present in variable thickness of eschar
C. Proliferation	Dense population of microorganisms at nonviable/viable tissue interface
Stage II: Invasion	
A. Microinvasion	Microscopic foci of microorganisms in viable tissue immediately subjacent to subeschar space
B. Generalized	Widespread penetration of microorganisms deep into viable subcutaneous tissues
C. Microvascular	Involvement of lymphatics and microvasculature

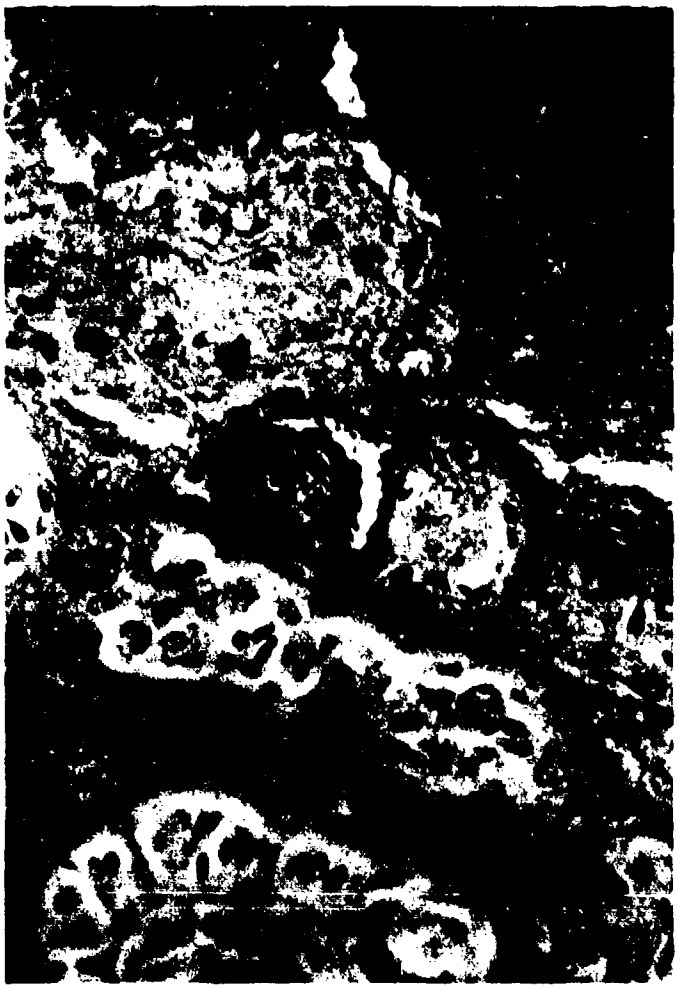

Fig. 4. Photomicrograph of burn wound biopsy specimen showing dense palisading of dark staining gram-negative bacilli around a capillary and vein adjacent to a sweat gland in unburned tissue beneath the eschar. Stage IIC. Note thermally coagulated tissue of the eschar in upper right quadrant of the photo.

should be carried out within the next 6 to 12 hours and just prior to that procedure a second subeschar injection of the broad spectrum penicillin should be performed to protect the patient from hematogenous dissemination of viable bacteria during the excision. The excised wound is covered with antibacterial soaks or a biologic dressing, depending upon the assessed adequacy of the excision. Twenty-four to 48 hours thereafter, the patient is returned to the operating room for reexamination of the excised wounds. If residual infection is evident, further debridement is carried out and the wounds are treated as before but, if no residual infection is noted, the wound can be closed by autografting.

Fungal Burn Wound Infections

During the past two decades, a striking change in the microbial ecology of the burn wound has occurred. The recovery of Pseudomonas species from the wounds of burn patients has markedly decreased since 1977 and in concert invasive Pseudomonas burn wound infection has virtually disappeared [23]. That epidemiologic change is reflected in the data in Table 2 confirming that, in a recent 5 year period, invasive burn wound infection was present in only 15% and was considered to be the cause of death in only 8% of the 166 burned patients who were treated and died at this Institute. Bacteria were the causative organisms in only 8 of the 25 fatally burned patients who developed invasive burn wound infection during that period while fungi and Candida were the causative organisms in 18 (72%) patients (one patient had both bacterial and fungal infections).

Table 2. Invasive burn wound infections in fatal burns: 1983–1987.

Number of fatal burns		166
Invasive burn wound infection as primary cause of death		13 (8%)
Invasive burn wound infection present at any time		25 (15%)
Bacterial	8	
Fungal[a]	18	

[a]One patient had both bacterial and fungal infections.

Table 3. Invasive non-bacterial burn wound infections, January, 1983–May 1989.

Causative organism	Number of patients
Candida species	13
Filamentous fungi:	
Aspergillus species	26
Unspeciated	12
Alternaria species	1
Mucor species	5
Herpes simplex virus	5

Total number of burn patients treated = 1318.

A recent review of 1,318 burn patients admitted from January, 1983 to May, 1989 reveals that Candida burn wound infections occurred in 13 patients and filamentous fungi were the causative agents of 44 histologically documented invasive burn wound infections. Aspergillus species were the causative agents of 26 of those 44 fungal wound infections, unspeciated fungus the cause of 12, Alternaria species the cause of 1, and Mucor species the cause of 5 infections (Table 3). These non-bacterial infections occurred late in the hospital course of patients with extensive burns as indicated by the finding that postburn day 31 was the mean time of burn wound colonization by Candida species. This late occurrence of fungal and candidal infections reflects both the general success of current burn wound care techniques in effecting closure of the wounds of patients with burns $\leq$50% of the total body surface and the consequences of broad spectrum antibiotic therapy used in the treatment of other infections in patients with more extensive burns in whom unavailability of donor sites prevents closure of their burn wounds within the first postburn month [24] (Fig. 5).

The treatment of candidal or fungal invasive burn wound infection is similar to that of invasive bacterial infection. The topical agent being used should be discontinued and twice daily topical applications of clotrimazole cream begun. If the fungal infection involves deep tissue, such as fascia or muscle; has invaded the microvasculature of the underlying viable tissue; has spread to remote tissues; or is associated with systemic signs of sepsis, parenteral administration of amphotericin-B

Fig. 5. Generalized invasive fungal infection evident on postburn day 40 in the extensive full-thickness burns of this 33 year old male with burns of 84% of the total body surface who required early amputation to remove an incinerated left forearm. Black discoloration and caseous necrosis of the exposed subcutaneous tissue are characteristic of the Aspergillus infection that was confirmed by biopsy. Note typical sharp demarcation of the margins of the infected wounds and the edema of the skin edges.

therapy should be started and continued until the infection has been eradicated or a full course of treatment completed. The infected tissue should be widely debrided and the wound treated by application of a biologic dressing or with a topical anti-fungal agent beneath occlusive dressings changed twice daily, depending upon the assessed adequacy of excision. The patient is returned to the operating room 24 to 48 hours later for further debridement, if necessary, or closure of the wound by autografting if the infection has been controlled.

The previously noted invasiveness of phycomycotic infections may necessitate radical debridement of involved fascia and muscle and even amputation of an extensively involved limb to encompass the infection [25]. During the period 1954 to 1983 invasive phycomycotic infections occurred in 75 patients and in 26 (35%) patients amputation, ranging from removal of a digit to a glenohumeral disarticulation, was necessary to control the infection. In 32 patients with a mean burn size of 45% of the total body surface, the phycomycotic infection was controlled by excision of the infected tissue and those patients survived both the infection and their burn injury. The other 43 patients with a mean burn size of 59% of the total body surface, died either because of inability to control the infection or some other complication of their extensive injury. The true fungi, especially Aspergillus species, may also cause infection in previously excised burn wounds that have been covered by meshed split-thickness skin grafts. These infections are typically superficial and should be treated by prompt excision of the foci of infection and twice daily application of clotrimazole cream to prevent progressive graft loss.

Viral Infections

Viral infections have also been recognized in burn patients with increasing frequency over the past 2 decades [26]. Herpes simplex virus Type I has been the most commonly identified

Table 4. Primary cause of death in 166 fatal burns: 1983–1987.

Primary cause of death	Number of patients
Pneumonia	83
Invasive burn wound infection	13
Myocardial infarction and insufficiency	25
Inhalation injury with acute pulmonary insufficiency	11
Anoxic encephalopathy	5
Aspiration	4
Miscellaneous[a]	25

[a] Three or less cases of each of 16 causes.

Table 5. Type of pneumonia in burn patients.

	Airborne (%)	Hematogenous (%)
Before topical chemotherapy	33	67
With topical chemotherapy	65	35

virus causing infections [27]. During the period 1982 to 1988 there was herpetic infection of the airway in 9 burn patients and of the burn wound in 5 patients (Table 3). During that same period, 6 cytomegalovirus (CMV) infections of the airway were identified. The identification of persistent temperature elevation, lymphocytosis without abnormal lymphocytes, and anicteric hepatitis as the clinical manifestations of a viral infection will forestall the administration of ineffectual antibiotics. In a recent prospective study Bale and coworkers [28] found that seroconversion or a more than fourfold increase in CMV antibody titer occurred in 35.6% of 87 burn patients but that such evidence of CMV infection did not appear to affect either the morbidity or mortality of those patients. Evidence of systemic viral infection in a patient with a progressively deteriorating hospital course justifies the administration of antiviral agents such as adenine arabinoside or gangcyclovir.

Pneumonia

Even though invasive burn wound infection has been significantly reduced, infection remains the most common cause of morbidity and mortality in burn patients (Table 4). Pneumonia is now the predominant type of infection in burn patients as it is in other critically ill patients [3, 29]. In the 5 year period 1983 to 1987 pneumonia occurred in a total of 169 (17%) of the 998 burn patients admitted. In 43 of those patients more than one episode of pneumonia was diagnosed and treated. The clinical impact of pneumonia is indexed by its presence in 91 (55%) of the 166 fatally burned patients cared for at the U.S. Army Institute of Surgical Research during that period and its classification as the primary cause of death in 83 (50%) patients. Improved wound and general care have changed the prevalent form of pneumonia from hematogenous to airborne and altered the predominant causative organisms [30]. In the 1960's, the introduction of topical antimicrobial chemotherapy was associated with the reversal in frequency of the two forms of pneumonia shown in Table 5.

The organisms that cause infections at any given burn center change with time such that the predominant organisms form a

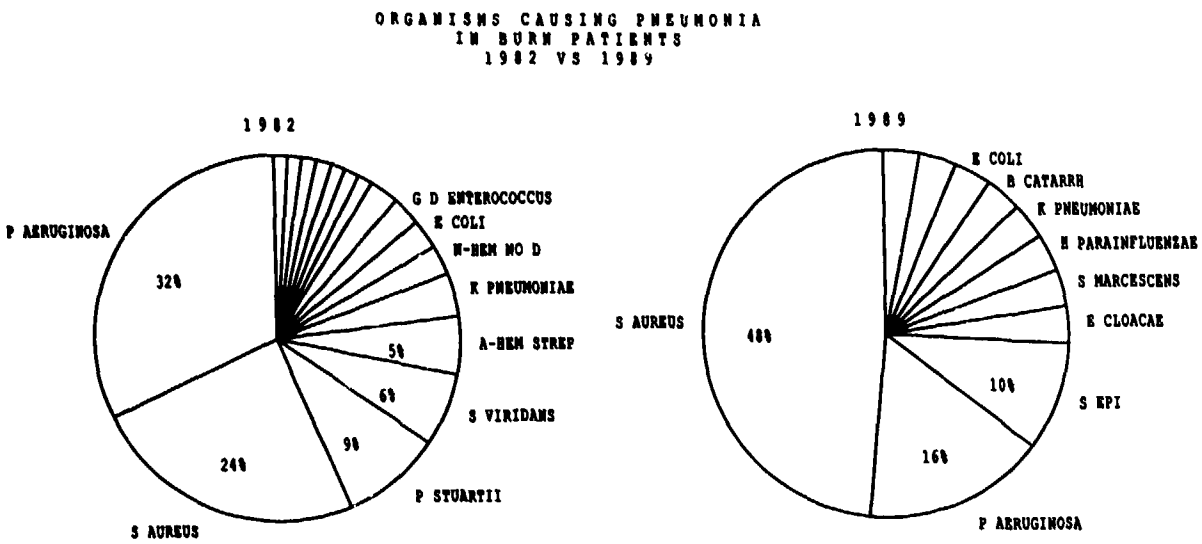

Fig. 6. The predominant organisms causing pneumonia in burn patients have changed markedly during the past decade.

succession of mini-epidemics [31]. The dynamic nature of the continual change in the predominant organisms causing infection in burn patients has been documented over the past decade. In 1982 *Pseudomonas aeruginosa* was the organism most often present in cultures of airway secretions (21% of the organisms recovered) and *Pseudomonas aeruginosa*, *Providencia stuartii*, and *Klebsiella pneumoniae* constituted 40% of the organisms recovered from cultures of the airway. *Pseudomonas aeruginosa* was considered to be the organism causing 32% of the pneumonias that occurred that year and *Staphylococcus aureus* the cause of only 24% of the pneumonias. In contrast, *Staphylococcus aureus* was the cause of 48% and *Pseudomonas aeruginosa* the cause of only 16% of the pneumonias in burn patients treated in 1989 (Fig. 6).

The similarities of the systemic response to burn injury and infection make the diagnosis of infections in sites other than the burn wound difficult [15]. The febrile and leukocytic responses to either pneumonia or tracheobronchitis characteristically exaggerate to some degree the fever and leukocytosis evoked by burn injury *per se* that at least partially obscure those clinical signs of superimposed infection. The diagnosis of tracheobronchitis is made on the basis of such clinical findings as well as the identification of microorganisms on a Gram stain preparation of the endobronchial aspirate and findings of > 25 neutrophils and < 10 squamous cell per low power field on histologic examination of the endobronchial aspirate, all in the absence of roentgenographic infiltrates. In the early stages of tracheobronchitis, respiratory insufficiency may be minimal or even absent and treatment consists of systemic administration of an antibiotic active against the organisms that predominate in the endobronchial flora. Tracheobronchitis is a common precursor of bronchopneumonia, particularly in patients with inhalation injury, of whom 46% develop pneumonia within 12 days of injury [32]. If pneumonia does not develop, the mortality associated with tracheobronchitis is much less than that associated with pneumonia as evidenced by the increased survival associated with the decreased incidence of pneumonia in burn patients with inhalation injury treated with prophylactic high frequency ventilation [33].

Table 6. Diagnostic criteria for pneumonia.

I. Clinical findings
A. Fever
B. Purulent sputum
C. Progressive ventilatory impairment
II. Roentgenographic infiltrate
III. Endobronchial aspirate
A. Histologic findings
1. Microorganisms present
2. >25 neutrophils and < squamous cells per high power field
B. Positive culture

The diagnosis of pulmonary infection is made on the basis of what may be rather subtle clinical signs, roentgenographic changes, and laboratory test results (Table 6). Bronchopneumonia typically begins as a bronchiolitis that spreads distally and involves a variable volume of adjacent parenchyma. This form of pneumonia occurs relatively early in the postburn period (the mean time of diagnosis is postburn day 10) and is often first manifested by the appearance of irregular linear roentgenographic densities in the dependent portions of the lung or areas of the lung damaged by inhalation injury. If untreated, progressively greater amounts of lung tissue become opacified and ventilatory insufficiency becomes progressively more severe. Examination of the endobronchial aspirate establishes a tentative diagnosis if >25 neutrophils and <10 squamous cells are present per low power field and ≥10 organisms are present per high power field [34]. Cultures of the endobronchial secretions should be obtained to identify the predominant organism and its antibiotic sensitivities. Although endoscopically directed bronchial lavage has been recommended by some as a means of enhancing culture specificity [35], in the authors' experience such culture techniques have not increased diagnostic accuracy in burn patients. Systemic antibiotic therapy, initiated at the time of clinical diagnosis and based on surveillance data, is adjusted according to culture and

Fig. 7. Chest roentgenogram showing rounded infiltrate characteristic of hematogenous pneumonia in the left lower lobe of a 20 year old female with burns of 59% of the total body surface. This lesion appeared on postburn day 60 and was caused by organisms originating in an infected burn wound that was still open.

Fig. 8. Recovery of Candida species from a blood culture obtained on postburn day 16 in the absence of any other obvious source led to exploration of the previously cannulated vein in the forearm of a 68 year old male with a burn of 33% of the total body surface. Note the edema and dark erythematous discoloration of the vein proximal to the site of cannulation and the smaller caliber uninvolved segment of the vein at the base of the incision to the right of the cannulation site. Candida species were cultured from the purulent material present within the vein.

sensitivity test results as necessary. Mechanical ventilatory support is provided as required.

The other form of pneumonia, hematogenous, begins as a capillaritis which, if uncontrolled, spreads to involve adjacent parenchyma. This form of pneumonia occurs relatively late in the postburn period (the mean time of diagnosis is postburn day 17) and is typically first manifested by the appearance of a rounded density on the chest roentgenogram (Fig. 7). If untreated, the original density will increase in size and other similar densities may appear in a random distribution throughout the lung fields. This form of pneumonia is associated with a higher mortality than airborne or bronchopneumonia but, as a reflection of its metastatic nature, is less often a principal cause of death. Current wound care techniques that have significantly reduced the occurrence of invasive burn wound infection and the meticulous intravascular cannula management that has reduced suppurative thrombophlebitis have combined to make hematogenous pneumonia an infrequent complication. Even so, wound and intraluminal vascular infections still account for the majority of the few cases of hematogenous pneumonia that occur today. An occult visceral perforation or an inapparent soft tissue infection are relatively rare sources of bacteria causing hematogenous pneumonia and in a small number of cases the primary site of infection remains unidentified. The appearance of the roentgenographic signs typical of hematogenous pneumonia mandates a careful search for and control of the primary source of infection as well as initiation of systemic antimicrobial therapy effective against the organism causing both the primary infection and the pneumonitic process.

Suppurative Thrombophlebitis

The incidence of suppurative thrombophlebitis increases as the duration of cannulation increases but infection may occur in any previously cannulated vein no matter how brief the duration of cannula residence [36]. Other factors that influence the incidence of suppurative thrombophlebitis include composition of the cannula, the pH and content of the infusate, contamination of the infusate or infusion system, and the frequency of bacteremia resulting from manipulation of the burn wound [37]. The suppurative process most commonly arises at the site where the cannula tip lay and then extends principally in a proximal direction with typically limited if any distal extension.

The roentgenographic signs of hematogenous pneumonia or the repeated recovery of a single organism (particularly *Staphylococcus aureus*) from blood cultures in the absence of another obvious cause suggest that a focus of intravascular infection is the source. In recent years Staphylococci have replaced the previously prominent gram-negative wound flora as the predominant cause of suppurative thrombophlebitis and, in the last 8 years, 3 cases of suppurative thrombophlebitis have been caused by Candida species and one by Aspergillus species. Because of burn related immunosuppression and the presence of overlying burn which may attenuate or obscure signs of inflammation, respectively, local signs of suppurative thrombophlebitis are present in <50% of patients with the disease [38]. Consequently, when the diagnosis is entertained it is necessary to evaluate every previously cannulated vein even in the absence of local signs. A markedly indurated or tender vein should be surgically exposed from the site of percutaneous cannulation to the site where the cannula tip resided within the lumen. Induration and edema of the vein wall are consistent with infection within the vein (Fig. 8). The diagnosis is confirmed if incision of the vein wall reveals intraluminal suppuration. If no grossly purulent material is evident, the inflamed segment of vein and its contents should be excised, cultured, and subjected to histologic examination to identify microorganisms and signs of infection within the lumen or wall of the vein.

Suppurative thrombophlebitis is treated by surgical excision of the involved segment of vein extending from a point of unequivocally normal vein wall distal to the infection to a point

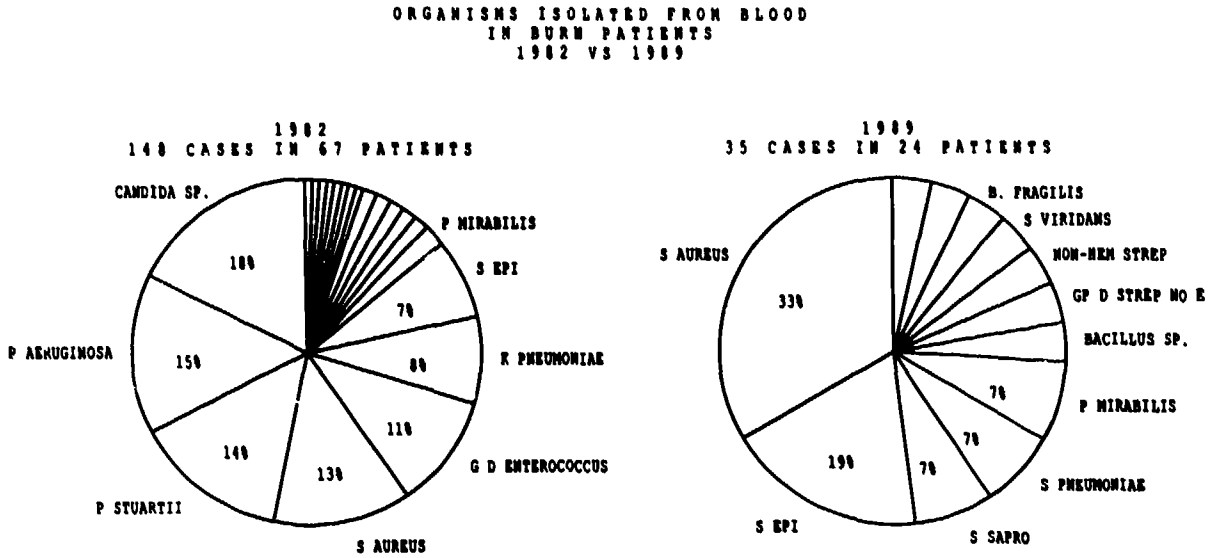

Fig. 9. Organisms isolated from blood cultures of burn patients in 1982 and 1989. Note the marked decrease in number of patients with bacteremia in 1989 as well as the temporal change in predominant organism.

of unequivocally normal vein wall proximal to the suppurative process. Since there may be skip areas of relatively normal vein between multiple areas of suppuration that are situated proximal to the primary site of infection, it is necessary to excise the vein up to the point where unaltered back bleeding is evident from a vein unequivocally free of inflammatory change or up to the point where it becomes a tributary of a higher order vein and the wall of that vein is uninvolved in the septic process [39]. Tributary veins with intraluminal suppuration should also be excised. The wound is then loosely packed open and the dressing is changed daily beginning 48 hours following excision. When the infection has resolved, the excision site can be closed secondarily or by skin grafting.

Early diagnosis and prompt surgical extirpation of suppurative thrombophlebitis prior to hematogenous dissemination of the infecting organisms to remote organs and tissues decreases the mortality associated with this complication. Persistence of sepsis following excision of an infected vein may be due to inadequate excision, residual septic foci either proximal or distal to the extent of the original excision, suppuration within another previously cannulated vein, or the presence of hematogenous pneumonia or acute bacterial endocarditis due to microbial dissemination prior to the surgical excision of the focus of intraluminal suppuration. Each of those possibilities should be considered and treated as necessary, if present. Far more important than even prompt diagnosis and treatment is prevention of the disease by limiting the duration of intraluminal residence of each intravascular cannula. Strict limitation of cannula residence to a maximum of 72 hours reduced the incidence of suppurative thrombophlebitis from a level of 6.9% during 1969 and 1970 to 1.4% of burn patients treated during 1977 and 1978 [40]. Such cannula discipline and the wound care described above have further reduced the incidence of suppurative thrombophlebitis, 16 (0.71%) cases in 2268 burn patients admitted from June, 1982 to December, 1990.

Bacteremia and Septicemia

The significance of a positive blood culture in a burn patient depends upon the temporal relationship of the blood culture to the time of wound cleansing or debridement, the presence of other signs of infection, and the patient's general condition. Sasaki and coworkers [41] documented that 20.6% of wound care procedures caused bacteremia and that the incidence of positive blood cultures increased as the extent of the burn wound increased and as the extent of wound manipulation increased. Bacteremias associated with daily wound cleansing are typically brief and require no treatment but those associated with surgical excision justify perioperative antibiotic therapy with agents active against both gram-positive and gram-negative organisms. If two successive blood cultures are positive for the same organism and exogenous contamination can be excluded, systemic antibiotic therapy directed against the organisms recovered should be started, even if the patient does not appear to be septic. As is the case in other immunocompromised patients, multiple organisms may be recovered from a single blood culture or from successive blood cultures drawn from burn patients who are critically ill with life threatening complications [42]. Consequently, such culture findings, when consistent with the patient's clinical status, should not be discounted as "contaminants" but treated by the institution of antimicrobial therapy using agents active against all of the recovered organisms.

The previously noted changes in wound care and patient management have not only altered the predominant causative organisms but have also reduced the overall occurrence of bacteremia in burn patients (Fig. 9). The recession of gram-negative bacteremia and the increased prevalence of gram-positive bacteremia have had an apparently favorable effect on the outcome of patients with burns of 30% to 80% of the total body surface. A 25 year review of burn patients treated at this Institute has documented that the effect of bacteremia on

mortality is organism specific. Gram-negative bacteremia and Candidemia significantly increased the mortality of burn patients above that predicted on the basis of extent of burn and patient age, while gram-positive bacteremia exerted no identifiable effect on the predicted mortality of burn patients [43]. Even multiply resistant *Staphylococcus aureus* appears to exert little effect on the outcome of patients in burn centers and other "acute" hospitals [44, 45].

Table 7. Improvement in burn patient survival 1945–1989.

	Extent of burn associated with 50% survival	
Age group	1945–1957	1985–1989
Pediatric (0–14 years)	51.0%	53.4%
Young adult (15–40 years)	43.0%	75.6%
Older adults (41+ years)	23.0%	44.0%

Infection Control Procedures

In a very real sense, the described changes in burn patient infections are consequences of medical progress. Improved care of critically ill patients in general, and improvements in burn wound care in particular, not only salvage more burn patients but even prolong the survival of patients who, because of the extent of their burn, would previously have expired relatively early in their postburn course. The time of death of those burn patients who died in 1970 was postburn day 17 while in 1987 that had increased to postburn day 24. Those patients who have had one or more courses of broad spectrum antibiotics as treatment for bacterial infection and have extensive areas of unclosed burn wound are those who develop late occurring infections caused by the residual flora of the burn wound. By virtue of treatment, those organisms are predominantly nonbacterial opportunists and multiply resistant bacteria (especially *Staphylococcus aureus*) that have colonized not only the open burn wound but the unburned skin, the airways, and even the gastrointestinal and urinary tracts.

Vigorous enforcement of an infection control program has minimized the clinical impact of these changes. Scheduled microbial surveillance, biopsy monitoring of the burn wound, environmental control procedures, including cohort patient care as necessary, and an actively functioning infection control committee have permitted prompt identification of and adaptation to these recent epidemiologic changes. McManus and associates [46] have documented that cohort patient care was effective in eliminating a multiply resistant endemic strain of Pseudomonas from the U.S. Army Institute of Surgical Research burn center in the mid-1980's. Since that time, the infection control program has included 3 time per week culturing of the burn wound surfaces and sputum and 2 time per week culturing of the urine and stool. Antibiotic sensitivities are determined for all Staphylococci and Pseudomonas species as well as the predominant gram-negative organisms recovered from those routine cultures. A daily written report and computer display of each patient's culture and sensitivity testing results is provided to each attending physician so that, should an infection be diagnosed, the initial empirical selection of antibiotics can be made on the basis of those results.

Environmental control includes strictly enforced hand washing, gowning (including use of disposable plastic aprons to prevent soilage of the clothing of attending personnel during wound care procedures), and gloving policies. Cohort patient care is a component of environmental control that is utilized to some degree at all times. The assignment of care personnel as teams to provide care for only a specific patient or patients, and strict limitation of movement of convalescent patients who represent a reservoir of resistant organisms prevent establishment and perpetuation of endemic microbial strains. When a patient is admitted bearing an organism that possesses broad antibiotic resistance, physical separation of that index patient from other patients should be maintained. Utilized in selective and graduated fashion, the infection control program has been effective in eliminating endemic organisms that possess broad antimicrobial resistance, preventing the establishment of newly introduced resistant organisms as predominant members of the burn center flora, and preventing reintroduction into the intensive care unit of resistant strains from recovering patients in the convalescent ward.

The activities of the infection control committee form an integral part of any burn center's infection control program. Antibiotic use should be monitored and restricted when necessary to delay the development of microbial resistance. Rigorous criteria for the definition and identification of the infections that occur in burn patients must be established to permit generation of reliable epidemiologic data. The results of surveillance cultures must be reviewed on a scheduled basis to identify potentially epidemic strains and institute control measures to eliminate such strains. Finally, culture results must be correlated with outcome and the improvements in survival that accompany observed changes in type, site, and causative agents of infections must be documented to validate the effectiveness of both the infection control program and present day burn center care [47] (Table 7).

Résumé

Des antibiotiques locaux, une excision rapide et une couverture cutanée ont contribué à réduire de façon significative la fréquence des infections des plaies et la mortalité qui en découle. La protection des plaies est cependant encore imparfaite et l'invasion massive des plaies est un risque réel chez les brûlés dont la fermeture cutanée est retardée. Une surveillance des plaies avec prélèvements systématiques à intervalles répétés est nécessaire pour évaluer la flore microbienne de la brûlure et identifier les infections provoquées par des souches bactériennes résistantes ou des germes opportunistes non bactériens à un stade où l'intervention thérapeutique peut être utile. Du fait de la dépression des fonctions immunologiques chez le brûlé, l'infection reste la cause la plus fréquente de morbidité et de mortalité même si la fréquence de survenue même des infections a diminué. Les infections pulmonaires sont la complication la plus fréquente chez le brûlé aujourd'hui malgré les améliorations dans le traitement global des plaies et surtout dans celui de l'infection. Les germes gram positif sont le plus souvent en cause. Le type de germes provoquant une bactériémie, responsable d'une mortalité variable suivant l'âge et l'étendue des lésions, a changé en même temps que la flore des plaies s'est modifiée. Les procédés de maîtrise de l'infection,

comme mises en culture systématique des prélèvements, l'utilisation d'une méthodologie de cohortes, l'exigence d'une hygiène stricte pour les patients et le personnel ainsi que la surveillance des patients ont permis de gros progrès. L'élimination des souches microbiennes endémiques résistantes, la limitation de l'introduction de nouveaux germes résistants, la précocité du diagnostic d'infection, l'institution d'un traitement antibiotique approprié et l'évaluation de l'efficacité des soins quotidiens ont ainsi amélioré la survie des brûlés.

Resumen

La terapia tópica, la resección temprana y el oportuno cierre de la quemadura han reducido en forma significativa la infección invasiva de la herida y su concomitante mortalidad. Puesto que la protección de la herida es imperfecta y la infección invasiva puede ocurrir en los pacientes con quemaduras masivas en quienes el cierre de la herida se ha retardado, se hace necesario realizar vigilancia programada de la herida y monitoría mediante biopsia para determinar el estado microbiológico de la quemadura e identificar infecciones por bacterias resistentes o por organismos oportunísticos no bacterianos en una etapa en que la intervención terapéutica pueda controlar el proceso.

Como un reflejo de los efectos immunosupresores sistémicos de la lesión térmica, la infección se mantiene como la causa más común de morbilidad y mortalidad, a pesar de que la incidencia de infección de la quemadura ha disminuido en forma significativa. Actualmente la neumonía es la infección más frecuente en el paciente quemado, pero los avances en el tratamiento total del paciente, en el manejo de la herida y en el control de la sepsis han hecho de la bronconeumonía la forma más común de este tipo de infección y de los microogranismos gram positivos los agentes causales más comunes. Los gérmenes causantes de bacteremia que ejercen un efecto específico sobre la mortalidad relacionada con la extensión de la quemadura y la edad del paciente han variado en concierto con los cambios en la flora de la herida.

Los procedimientos de control de la infección, incluso la vigilancia programada mediante cultivos, la utilización de metodologías basadas en cohortes de pacientes, la estricta implementación de medidas de higiene del paciente y del personal y la monitoría del paciente han resultado eficaces en eliminar las cepas endémicas resistentes, en prevenir el establecimiento de gérmenes resistentes recientemente introducidos, en diagnosticar la infección en forma oportuna, en instituir antibioticoterapia y otras formas de terapia precozmente y en documentar la eficacia del manejo actual del paciente quemado y mejorar su supervivencia.

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