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# Septicemia: The Principal Killer of Burns Patients

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**Abstract:** Burn injury is a major problem in many areas of the world and it has been estimated that 75% of all deaths following burns are related to infection. Burns impair the skin's normal barrier function thus allowing microbial colonization of the burn wounds and even with the use of topical antimicrobial agents, contamination is almost unavoidable. It is therefore essential for every burn institution to determine its specific pattern of burn wound microbial colonization, time related changes in predominant flora and antimicrobial resistance profiles. This would allow early management of septic episodes with proper empirical systemic antibiotics before the results of microbiologic culture becomes available, thus improving the overall infection-related morbidity and mortality. We attempted to examine the factors affecting risk of infection; strategies for infection control and prevention in burn victims.

**Key words:** Burn injury, infection, burn septicemia

## INTRODUCTION

A burn wound has a much higher incidence of sepsis as compared to other forms of trauma, because of extensive skin barrier disruption and an alteration in the cellular and humoral immune responses[1]. A burn injury is known to cause devitalization of tissues and produce extensive raw areas. The wound is moist due to the outflow of serous exudates at a temperature approaching $37^0$C or above. The dead and denatured burn eschar and the moist wound environment favor colonization and proliferation of a variety of microorganisms[2]. Burn injury also causes depression of the immune response and severe catabolism proportional to the extent of injury[3]. The dysfunction of the immune system, a large cutaneous bacterial load, the possibility of gastro-intestinal bacterial translocation[4], prolonged hospitalization and invasive diagnostic and therapeutic procedures, all contribute to sepsis. The infecting organisms may gain access either through cross contamination or they may derive from the patient's own skin and gastrointestinal tract micro-flora. We examine the various aspects of infection in the burn patient including epidemiology, prevention and control.

Infection in the burn patient is a leading cause of morbidity and mortality and continues to be one of the most challenging concerns for the burn team. The importance of preventing infection has been recognized in organized burn care since it's inception and has followed recurring themes through the years. These included strict aseptic technique, use of sterile gloves and dressing materials, wearing masks for dressing changes and spacial separation of patients, either using private rooms or cubicles[5]. However, systemic sepsis continues to endanger life in burn patients. Development of infection depends on three conditions: 1) a source of organisms; 2) a mode of transmission; and 3) susceptibility of the patient.

**Sources of organisms:** These may be endogenous-the patient's own (normal) flora, or exogenous-hospital environment including health-care personnel. Exogenous organisms from the hospital environment are generally more resistant to antimicrobial agents than endogenous organisms. Organisms associated with infection in burn patients include gram-positive, gram-negative and yeast/fungal organisms. The distribution of organisms changes over time in the individual patient and such changes can be ameliorated with appropriate management of the burn wound and the patient. The typical burn wound is initially colonized predominantly with gram-positive organisms, which are fairly quickly replaced by antibiotic susceptible gram-negative, usually within a week of the burn injury. However, if the wound closure is delayed and the patient becomes infected, requiring treatment with broad-spectrum antibiotics, this flora may be replaced by yeasts, fungi and antibiotic-resistant bacteria.

Gram-positive organisms of particular concern include *S. aureus*, enterococci, group A beta-hemolytic Streptococcus and coagulase negative Staphylococcus. Risk factors identified in patients include prior use of third generation cephalosporins and antibiotics active against anaerobes, a critically ill patient with severe underlying disease or immunosupression and a prolonged hospital stay. Gram-negative organisms have long been known to cause serious infection in burns

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Table 1: Physical defenses and their alterations by burn injury

| Organ | Defense Mechanism | Effect of Burn Injury |
|---|---|---|
| Intact skin | Physical barrier; normal flora; low pH maintained by fatty acids; dryness, desiccation, desquamation. | Loss of epidermis and all or part of dermis, depending upon depth of injury; colonization of wound by opportunistic and pathogenic organisms; moist wound, bed and necrotic tissue, eschar. |
| Respiratory tract | Muco-ciliary lining of tract; cough and sneeze reflex; lysosomes in nasal secretions; alveolar macrophages. | Smoke inhalation injury with direct damage to lining of respiratory tract; endotracheal intubation; immobility. |
| Gastrointestinal tract | Peristalsis; hydrochloric acid; mucous gel on epithelial surfaces; normal flora secretory IgA; bile acids and enzymes; fatty acids; bacteriocin. | Adynamic illeus in burn shock period immediately after injury; altered gut permeability with large injury; elevated pH for stress ulcer prophylaxis; altered flora after administration of antibiotics; nasogastric tubes and feeding tubes. |
| Urogenital tract | Flushing action and bacteriostatic pH of urine; normal flora (lactobacilli). | Burns in genital area; Urinary catheter drainage. |
| Eyes and Ears | Flushing action of tears; lysosomes; sebum and ciliary action of ear canals. | Inability to close burned eyelids; accumulation of wound exudates and debris in ear canal. |

patients. Reports reveal that gram-negative bacteremia has been associated with a 50% increase in predicted mortality for patients with bacteremia compared to those without bacteremia[6]. Fungal organisms, especially Candida (yeast) species and true fungi (mold) like aspergillus, Mucor and Rhizopus, have been associated with serious infections in burns. According to the reports, Candida colonization appear to be primarily from endogenous sources while true fungi are ubiquitous in the environment and can be found in air, handling and ventilation systems, plants and soil[7].

**Mode of transmission:** Modes of transmission include contact, droplet and airborne spread. In burn patients, the primary mode is direct or indirect contact, either via the hands of the personnel caring for the patient or from contact with inappropriately decontaminated equipment. Burn patients are unique in their susceptibility to colonization from organisms in the environment as well as in their propensity to disperse organisms into the surrounding environment. In general, the larger the burn injury, the greater the volume of organisms that will be dispersed into the environment from the patient.

**Patient susceptibility:** The patient has three principle defenses against infection: physical defenses, non-specific immune responses and specific immune responses. Changes in these defenses determine the patient's susceptibility to infection. Physical defenses against infection along with changes induced by burn injury are shown in Table 1.

Invasive devices, such as endotracheal tubes, intravascular catheters and urinary catheters, bypass the body's normal defense mechanisms. Infection from intravascular catheters is of particular concern in burn patients, as often these lines must be placed directly through or near burn-injured tissue. Catheter associated blood stream infection is caused by organisms which migrate along the catheter from the insertion site and colonize the catheter tip[8]. Catheter tips are also susceptible to colonization from hematogenous seeding of organisms from the colonized burn wound.

Catheter associated blood stream infection rates for burn intensive care units have been reported to be 8.8 per 1000 central venous catheter days, compared with pool mean rates of 7.4 for pediatric ICUs, 7.9 for trauma ICUs and 5.2 for surgical ICUs[9]. Incidence of infection is also affected by the size of the burn injury (Total Body Surface Area involved). A study from Shriners Burn Hospital, Boston, reported that bloodstream infection increases dramatically as burn wound size increases[5].

Outbreaks of cross colonization and infection are a major challenge on burn units, requiring a clear understanding of how and why they occur. In almost all cases, the colonized patient is thought to be a major reservoir for the spread of infection, while other important sources include contaminated hydrotherapy equipment, common treatment areas and contaminated equipment such as mattresses. Risks associated with care of the burn wound, such as hydrotherapy and common treatment rooms are related to the use of water sources that are frequently contaminated by gram-negative organisms intrinsically and may also be contaminated by organisms from other patients[10]. This aquatic environment is difficult to decontaminate because of continuous reinoculation of organisms from the patient's wound flora and because of the organism's ability to form a protective glycocalyx in water pipes, drains and other areas, making them resistant to the action of disinfectants. Adequate decontamination of this equipment (e.g. tanks, plinths, shower table, straps) is difficult to achieve between patients using this equipment on a daily basis. Furthermore, the patient's own flora may be spread through the water and by care-givers to colonize other sites on the patients that are at increased risk of infection, as for example, the organisms from the wound may migrate to a central venous catheter site or bowel flora may be transferred to the burn wound. In addition to the difficulty in assuring that the common treatment room

is appropriately cleaned between successive patients, necessity of stocking the room with dressing supplies for multiple patients also increases the risk of spread of infection. The other principal modes of transmission in burn units are via the hands of the personnel and contact with inadequately decontaminated equipment or surfaces. The two areas most likely to become contaminated when caring for the burn patient are the hands and apron area of the person, as the surfaces (beds, side rails, tables etc.) are often heavily contaminated with organisms from the patient. Likewise all equipment used on the patient such as blood pressure cuffs, thermometers, wheel chairs, etc. are also heavily contaminated and may transmit infection to other patients if strict barriers are not maintained and appropriate decontamination not carried out.

**Culturing and surveillance:** Culturing and surveillance guidelines are more stringent for the burn patient, particularly those with larger body surface involvement, because of the increased propensity for infection and its transmission. Burn wound flora & antibiotic susceptibility patterns change during the course of patient's hospitalization thus stressing for obtaining routine surveillance cultures:

* To provide early identification of organisms colonizing the wound;
* To monitor the effectiveness of current wound treatment;
* To guide perioperative or empiric antibiotic therapy;
* To detect any cross-colonization, this occurs quickly so that further transmission can be prevented.

Routine surveillance wound cultures should be obtained when the patient is admitted and at least weekly until the wound is closed. Wound cultures twice or three times a week have been recommended for patients with large burn injury. Admission cultures are particularly important for patients transferred from other facilities, as they may be colonized with multiple resistant organisms and serve as an unsuspected reservoir for cross-transmission to other patients on the unit. For pediatric patients, admission throat cultures are also recommended as about 5% of the population will be colonized with Group A beta-hemolytic Streptococcus (*S. pyogenes*) which can have serious consequences if it is transmitted to the burn wound.

Methods of burn wound culturing include obtaining a semi-quantitative swab culture or a quantitative biopsy specimen. Semi-quantitative swab cultures provide information on the type of organisms present on the burn wound as well as the approximate amount and antimicrobial susceptibility. A general rule is to obtain a swab culture for each 10% of open burn to identify organisms of significance on the wound. Quantitative cultures are used to define invasive infection based on bacterial count of 100,000 colonies or more per gram of tissue. However, studies have revealed that this technique is not precise, as 50% of patients with quantitative counts of greater than 100,000 organisms do not have histologic evidence of invasive infection[11]. Furthermore, quantitative culturing is more costly and labor-intensive than swab cultures and their routine use to identify colonizing organisms on appropriately debrided wounds is rarely indicated. Accurate diagnosis of invasive burn wound infection is best determined by clinical criteria, supported when possible by histologic examination if required[10].

Surveillance of infection has been reported to diminish the rate of nosocomial infection[12, 13] as well as reduce cost[14, 15]. At a minimum, surveillance should include collection of data on burn wound infection, pneumonia and bloodstream infection. Systematic collection of data can help the burn unit to monitor changes in infection rates over time, identify trends and evaluate current treatment methods.

**Isolation guidelines:** The effectiveness of simple protective barrier precautions in reducing nosocomial colonization and infection was shown in a study by Klein *et al*.[16] in a pediatric ICU. The open burn wound increases the contamination of environment present around the patient, which is the major difference in burn versus non-burn patients. The degree or amount of contamination is roughly proportional to the size of the open wound and amount of colonization present whereas it is inversely proportional to the distance from the patient. For this reason, appropriate barrier garb is recommended for any patient contact. Patients with greater than 30% total body surface area burn injuries are more immuno-compromised due to the size of their injury. This, in combination with their loss of physical defenses and need for invasive devices, significantly increases their risk to infection. These patients also represent a significant risk for contamination of their surrounding environment with organisms (including multiply resistant organisms when broad spectrum antibiotic treatment has been required) that may then be spread to other patients on the unit. For these reasons, it is recommended that patients with larger burn injuries be isolated in private rooms or other enclosed bed space to ensure physical separation from other patients on the unit[17].

Special attention is also required for patients with smaller burn injuries who are colonized or infected with multiply resistant organisms, especially those with wound drainage that cannot be adequately contained in dry, occlusively wrapped outer dressings, or pediatric patients who cannot comply with hand washing or other precautions[18]. Patients colonized with multiply resistant organisms must frequently have their need for

isolation balanced against their need for rehabilitation and the rehabilitation needs should preferably be met in the private room.

**Infection identification:** Specific sites of infection that are particularly important for burn patients include bloodstream infection, pneumonia, burn wound infection and urinary tract infection. Fever, a highly specific indicator of infection for many patient populations, often does not correlate well with the presence of infection in burn patients, because in burn injuries, the skin and core temperatures increase and there is an increase in heat production, which is associated with the onset of a hyper-metabolic response[19]. Because of this response, fever alone, in the absence of other signs and symptoms, is not indicative of infection.

Causes of burn wound infection relate to the loss of the protective barrier of skin and thrombosis of the subcutaneous blood vessels. The resulting avascular wound bed makes an excellent medium, which can support the growth of microorganisms as well as prevent the penetration of systemically administered antimicrobial drugs. Burn wound infection can be subdivided into 1) local or non-invasive infection characterized by erythema or cellulites, purulent drainage, graft loss, fever (>38.5$^{o}$C) and leukocytosis and 2) invasive wound infection characterized by conversion of partial-thickness to full-thickness injury, rapid eschar separation, necrosis of small blood vessels, edema, erythema and tenderness at the wound edges. Systemically, the patient may be hyperthermic, hypotensive and have decreased urine output and illeus. Laboratory results will reveal leukocytosis and leukopenia, thrombocytopenia, positive blood cultures, hyperglycemia and invasion of organisms into viable tissue on hystopathologic examination of the wound.

The impact of inhalation injury on pneumonia is clinically important, resulting in an incidence rate of 22.2% of ventilated pediatric patients as compared to 7.7% of ventilated pediatric patients without inhalation injury[20]. Onset of pneumonia can either be early, generally within 7 days of the burn injury, or later in the burn course when it usually accompanies generalized systemic sepsis. Diagnosis includes clinical features such as hyperthermia, cough, chest pain, wheezing, etc. or, in intubated patient, progressive respiratory deterioration with a change in the character of sputum (purulent), with changes on the chest radiograph showing a new or progressive infiltrate, consolidation, cavitation, or pleural effusion. Sputum culture is also helpful in diagnosis.

Urinary tract infection may receive little attention in burn patients, but it has been reported to be associated with a 2 to 4% increased risk of bacteremia[5]. Risk factors specific to burn patients includes the presence of perineal burns in certain patients and the increased length of time for which the patient requires catheterization.

**Infection prevention:** Prevention of burn wound infection involves assessment of the wound at each dressing change for changes in the character, odor, or amount of wound drainage, with immediate notification of the physician if any deterioration occurs. Strict aseptic technique should be used when handling the open wound and dressing materials as well as frequency of dressing should be based on the assessment of the wound condition. If the wound has necrotic material present, a debriding dressing should be chosen while a protective dressing is preferable for clean healing wounds. Treatment of an existing wound infection includes consideration of a change of the topical agent being used along with increasing the frequency of the dressing changes. In case an invasive infection is present, surgical excision of the infected wound as well as an appropriate systemic antimicrobial therapy may be required.

Prevention of bloodstream infection centers on appropriate care of the burn wound, to minimize the extent of hematogenous seeding and appropriate handling of intravascular devices. Whenever possible, catheters should be placed through unburned skin, preferably at a sufficient distance from the wound to prevent contamination of the insertion site. Since this is not always feasible in patients with large burn injuries, requiring long-term vascular access, frequent change of the catheter may be attempted. However, the optimum frequency for changing central venous catheters has not been definitively determined and while some advocate change of catheter to a new site every 3 days, others prefer less frequent replacement protocols[20, 21]. Insertion site care of intravenous catheters placed through or near a burn wound presents a challenge, as occlusive dressings cannot be used. A non-occlusive povidone-iodine dressing every 2-4 h depending on the degree of surrounding wound contamination has been recommended in such cases[22].

Treatment of pneumonia should be started promptly, with antibiotic selection modified when culture and sensitivity results are available. Treatment should also include vigorous chest physiotherapy, turning, coughing, deep breathing and suctioning. Newer ventilatory strategies like high frequency ventilation and permissive hypercapnia, to prevent or treat patients with pneumonia and severe respiratory compromise, have also been recommended[23].

Treatment of catheter associated Urinary Tract Infection includes removal of the catheter, if possible and use of systemic antimicrobial agents. Prevention of Urinary Tract Infection includes removal of the catheter as soon as it is no longer required for clinical monitoring of urine output, maintaining a closed urinary drainage system and urinary catheter care.

**Evolution of burn care and trends in outcome:** Burn management has evolved substantially from the earliest documented treatment and burn care depicted in the cave paintings of Neanderthal man and the honey and resin salve used by the ancient Egyptians[24]. Until recently, burn injuries were associated with tragic outcomes and sustained suffering. If burn shock did not claim the life of its victim during the immediate post-burn period, death came from wound sepsis or respiratory insufficiency due to poor understanding of pathophysiology of burn injury[25]. It was not until 1924 when Berkow began to formally express size as a percentage of total body surface area that burn size as a crucial determinant of pathophysiological response was recognized. Lessons learnt from treating the casualties of disastrous accidents such as the Rialto Concert Hall fire of 1930[26] and the Cocoanut Grove fire in 1942[27] instilled the importance of fluid requirement in burn patients, whilst the experiences gleaned during World Wars stimulated Burns Surgeons to attain a better understanding of burn injury[28]. In the 1970s, early excision of small deep burns and immediate auto-grafting resulted in shortened hospital stays, reduced patient suffering and better functional outcomes[29]. To extrapolate this to larger injuries required sophisticated intensive care and blood banking technologies. The principles of burn management evolved with improving technologies and rising sophistication of critical care medicine, including development of positive pressure ventilation, lung protective ventilation strategies, general critical care techniques, improved anesthetic procedures and innovative modes of support[30, 31]. This resulted in the current gold standard of near total early excision with immediate autograft/allograft cover which markedly improved survival probabilities even with major burns (involving >80% total body surface area)[32-34]. Additional reduction in mortality is expected with advancements in the management of inhalation injury and infection.

The wisdom of saving lives of massively burned individuals especially children has been questioned time and again, both from the ethical standpoint as well as the viewpoint of maximizing the use of limited resources. Optimal management of severely burned persons is enormously expensive and even after survival is ensured, may require a protracted period of surgical, medical and psychological rehabilitative measures for many years[35]. Increased survival has led to a shift in focus from mortality to more intermediate and long-term outcome measures such as rehabilitation, reconstruction and reintegration into society[36].

Traditionally, demographic and injury variables such as age, gender, extent of burns and presence of inhalation injury, have been used to predict mortality after severe burns. Scoring systems such as Baux index[37] or the abbreviated burn severity index[38] have attempted to predict the risk of mortality based on these variables. The Baux index is calculated by adding age and burned body surface area. Index values above 100 are regarded as prognostically unfavorable. The abbreviated burn severity index takes age, sex, inhalation injury and burn size and depth into account and sum scores >10 represent a likelihood of survival of less than 40%. These scoring systems, however, have been criticized on the ground that they use demographic and injury variables obtained at admission whereas the treatment efforts for severe burns have improved with early and adequate resuscitation, early excision and grafting, amelioration of the hyper-metabolic response, control of wound infection and improved management of inhalation injury. Therefore, clinical decisions regarding the futility of treatment using variables obtained at admission are essentially inaccurate and addition of variables obtained during hospitalization such as time to establish intravenous access, development of sepsis and organ failure and ventilator dependency has been suggested[39]. A strong association has been reported between persistent hyperglycemia and subsequent mortality in severely burned patients[40].

Hepatic acute phase proteins constitute important predictors for mortality. The acute phase response represents a cascade of events characterized by the up-regulation of type-I and II acute phase proteins and the down-regulation of constitutive hepatic protein production such as albumin, prealbumin and transferrin in response to tissue injury, infection, or inflammation. Pro-inflammatory cytokines mediate these events, which are initiated to restore homeostasis after trauma[41]. Clinical studies have shown that a sustained increased acute phase response can be potentially life threatening, with the uncontrolled and prolonged action of proinflammatory cytokines and acute phase proteins contributing to multi organ failure, hypermetabolism, complications and death[42]. Prealbumin has a short half-life making it more responsive to changes in acute nutritional status. It is therefore used as a clinical marker for potential nutritional status. It also reflects susceptibility to infection[43].

Characteristics of hospital course over a period of about one month seem to contribute much more to the determination of survival than do injury characteristics or other variables obtained during early treatment[34]. However, mortality as an outcome measure suffers from both a 'floor and ceiling effect'. On one hand, its absence says little about any other issue on the continuum of dysfunction; on the other hand, it is an absolute predictor[44]. Management of burn septicemia continues to be a challenge despite various infection control measures, advanced techniques for early detection of microorganisms and the availability of numerous broad-spectrum antibiotics.

## CONCLUSION

The better understanding of burn pathophysiology has resulted in effective fluid resuscitation in the acute

period, but the morbidity and mortality of these patients are mostly linked to the burn wound consequences, once the acute initial phase is over. The burn wound is the source of virtually all ill effects-local and systemic and infection is most undesirable in these patients as it is difficult to control because of the dead and denatured burn eschar, moist environment, dysfunction of the immune system, prolonged hospitalization and invasive diagnostic and therapeutic procedures. Wound sepsis may lead to septicemia, which may occur at any time and endanger the life of the burn patient.

## REFERENCES


1. Winkelstein, A.U., 1984. What are the immunological alterations induced by burn injury? J. Trauma, 24: S72-S83.
2. Lawrence, J.C., 1992. Burn bacteriology during the last fifty years. Burns, 18: S23-S29.
3. Munster, A.M., 1984. Immunologic response of trauma and burns: An overview. Am. J. Med, 76: 142-145.
4. Jones, W.G., J.P. Minei and A.E. Barber, 1990. Bacterial translocation and intestinal atrophy after thermal injury and burn wound sepsis. Ann. Surg., 211: 399-405.
5. Weber, J. and A. McManus, 2004. Infection control in burn patients. Burns, 30: A16-A24.
6. Mason, A.D., A.T. McManus and B.A. Pruitt, 1986. Association of burn mortality and bacteremia: A 25-year review. Arch. Surg., 121: 1027-1031.
7. Becker, W.K., W.G. Cioffi and A.T. McManus, 1991. Fungal burn wound infection. Arch. Surg., 126: 44-48.
8. Goldman, D.A. and G.B. Pier, 1993. Pathogenesis of infection related to intravascular catheterization. Clin. Microbiol. Rev., 6: 176-192.
9. National Nosocomial Infections Surveillance (NNIS) System Report, 2002. Data Summary from Jan 1992-June 2002. Am. J. Infect. Control, 30: 458-475.
10. Weber, J.M., 1998. Epidemiology of infections and strategies for control. In: Carrougher, G.J. Ed. Burn Care and Therapy, St Louis, MO: Mosby Inc, pp: 185-211.
11. McManus, A.T., S.H. Kim and W.F. McManus *et al.* 1987. Comparison of quantitative microbiology and histopathology in divided burn wound biopsy specimens. Arch. Surg., 122: 74-76.
12. Haley, R.W., D.H. Culver and J.W. White *et al.,* 1985. The efficacy of infection surveillance and control programs in preventing nosocomial infections in US hospitals. Am. J. Epidemiol., 121: 182-205.
13. Nicholas, R.L., 1991. Surgical wound infection. Am. J. Med., 91: 54-64.
14. Condon, R.E., W.J. Schulet and M.A. Malangoni, 1983. Effectiveness of a surgical wound surveillance. Arch. Surg., 118: 303-307.
15. Oslen, M.M. and J.T. Lee, 1990. Continuous 10-year wound infection surveillance: Results, advantages and unanswered questions. Arch. Surg., 125: 794-803.
16. Klein, B.S., W.H. Perloff and D.G. Maki, 1989. Reduction of nosocomial infection during pediatric intensive care by protective isolation. New Engl. J. Med., 320: 1714-1721.
17. Burke, J.F., W.C. Quinby and C.C. Bondoc *et al.*, 1977. The contribution of a bacterially isolated environment to the prevention of infection in seriously burned patients. Ann. Surg., 186: 377-387.
18. McManus, A.T., W.F. McManus and A.D. Mason *et al.,* 1985. Microbial colonization in a new intensive care burn unit. Arch. Surg., 120: 217-223.
19. Rieg, L.S., 1993. Metabolic alterations and nutritional management. Crit. Care Nurs., 4: 388-398.
20. Weber, J.M., R.L. Sheridan, M.S. Pastermack and R.G. Tompkins, 1997. Nosocomial infection in pediatric patients with burns: proposed definitions and benchmark rates. Am. J. Infect. Control, 25: 195-201.
21. Sheridan, R.L., J.M. Weber and H.F. Peterson *et al.,* 1995. Central venous catheter sepsis with weekly catheter change in pediatric burn patients: An analysis of 221 catheters. Burns, 21: 127-129.
22. Weber, J.M. and D.D. Tompkins, 1993. Improving survival: Infection control and burns. Crit. Care Nurs., 4: 414-423.
23. Sheridan, R.L., R.M. Kacmarek and M.M. McEttrick *et al.,* 1995. Permissive hypercapnia as a ventilatory strategy in burned: Effect on barotraumas, pneumonia and mortality. J. Trauma, 39: 854-859.
24. Cockshott, W.P., 1956. The history of the treatment of burns. Surg. Gynecol. Obstet., 102: 116-124.
25. Marshall, Jr.W.G. and A.R. Dimick, 1983. The natural history of major burns with multiple subsystem failure. J. Trauma, 23: 102-105.
26. Underhill, F.P., 1930. The significance of anhydremia in extensive superficial burns. JAMA, 95: 852-857.
27. Saffle, J.R., 1993. The 1942 fire at Boston's Cocoanut Grove nightclub. Am. J. Surg., 166: 581-591.
28. Moore, F.D., 1970 The body-weight burn budget: Basic fluid therapy for the early burn. Surg. Clin. North Am., 50: 1249-1265.
29. Janzekovic, Z., 1970. A new concept in the early excision and immediate grafting of burns. J. Trauma, 10: 1103-1108.

30. Hickling, G., J. Walsh, S. Henderson and R. Jackson, 1994. Low mortality rate in adult respiratory distress syndrome using low volume, pressure-limited ventilation with permissive hypercapnia: a prospective study. Crit. Care Med., 22: 1568-1578.
31. Goretsky, M.J., D.G. Greenhalgh, G.D. Warden, F.C. Ryckman and B.W. Warner, 1995. The use of extracorporeal life support in pediatric burn patients with respiratory failure. J. Pediatr. Surg., 30: 620-623.
32. Herndon, D.N., D. Gore, M. Col, M.H. Desai, H. Linares and S. Abston, 1987. Determinants of mortality in pediatric patients with greater than 70% full thickness total body surface area thermal injury treated by early total excision and grafting. J. Trauma, 27: 208-212.
33. Sheridan, R.L., J.P. Remensnyder, J.J. Schnitzer, J.T. Schulz, C.M. Ryan and R.G. Tompkins, 2000. Current expectations for survival in pediatric burns. Arch. Pediatr. Adolesc., 154: 245-249.
34. Spies, M., D.N. Herndon, J.I. Rosenblatt, A.P. Sanford and S.E. Wolf, 2003. Prediction of mortality from catastrophic burns in children. Lancet, 361: 989-994.
35. Fratianne, R.B., C. Brandt, L. Yurko and T. Coffee, 1992. When is enough enough? Ethical dilemma on the burn unit. J. Burn Care Rehabil., 13: 600-604.
36. Sheridan, R.L., M.L. Hinson, M.H. Liang, A.F. Nackel, D.A. Schoenfeld and C.M. Ryan, 2000. Long term outcome of children surviving massive burns. JAMA, 283: 69-73.
37. Baux, S., M. Mimoun, H. Saade, N. Lioret, M. Esteve and X.B. Nolland, 1989. Burns in the elderly. Burns, 15: 239-240.
38. Tobiasen, J., J.H. Hiebert and R.F. Edlich. Prediction of burn mortality. Surg. Gynecol. Obstet., 154: 711-714.
39. Wolf, S.E., J.K. Rose, M.H. Desai, J.P. Mileski, R.E. Barrow and D.N. Herndon, 1997. Mortality determinants in massive pediatric burns: An analysis of 103 children with >80% TBSA burns. Ann. Surg., 225: 554-565.
40. Gore, D.C., D. Chinkes, J. Heggers, D. Herndon, S.E. Wolf and M.H. Desai, 2003. Association of hyperglycemia with increased mortality after severe burn injury. Lancet, 361: 989-1094.
41. Moshage, H., 1997. Cytokines and the hepatic acute phase response. J. Pathol., 181: 257-266.
42. Livingston, D.H., A.C. Mosenthal and E.A. Deitch, 1995. Sepsis and multiple organ dysfunction syndrome: A clinical-mechanistic overview. New Horizon, 3: 276-287.
43. Rodrigueq, D., 1992. Nutrition in patients with severe burns: State of the art. J. Burn Care Rehabil., 13: 254-260.
44. Mossey. J.M. and E. Shapiro, 1982. Self-rated health: A prediction of mortality among the elderly. Am. J. Public Health, 72: 800-808.