Conferences and Reviews

Prognosis and Treatment of Burns

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Survival rates for burn patients in general have improved markedly over the past several decades. The development of topical antibiotic therapy for burn wounds, the institution of the practice of early excision and grafting, and major advances in intensive care management have all contributed to this success. In this review we address these 3 important advances in the modern treatment of burn injuries and provide a brief historical overview of these accomplishments and others, emphasizing specific achievements of note and promises for the future. We also discuss 3 topics of interest to burn physicians, including the special problems and high mortality of elderly burn patients, the disturbingly high mortality in burn patients with inhalation injury, and the possible use of artificial skin to facilitate rapid wound closure.

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The progress that has been made in burn care over the past four decades has dramatically increased survival rates for burn victims.[1,2] The advances that led to this success accompanied the following three giant steps in the history of modern burn care:

- The introduction of topical antibiotic therapy into the wound care armamentarium;
- The adoption of the technique of excising the burn eschar of large burns; and
- Improvements in the technology and clinical skill in the management of burn wounds, resuscitation, and nutrition and the prevention and management of associated pulmonary problems.

These three areas of clinical advancement have merged to produce an LA_{50} of 70% (half of patients with 70% of the total body surface area burned will survive) compared with an LA_{50} of less than 50% in 1952 (Figure 1).[3]

In this review, we address the three most important advances in the modern treatment of burn injuries. The contribution to improved mortality made from these three giant steps has changed the prognosis of burn injuries substantially. Next, we provide a brief historical overview of the progress of mortality of burn injuries. Finally, we discuss three topics of interest to those who routinely care for patients with burns, including the special problems and high mortality of elderly burn patients, the disturbingly high mortality in burn patients with inhalation injury, and the possible use of artificial skin for facilitating rapid wound closure when donor site healing is problematic.

Three Giant Steps

Topical Antibiotic Therapy

Safe, effective topical antimicrobial therapy for burn wounds was first introduced in the mid-1960s.[4] By the early 1970s, decreased mortality was reported in burn patients treated with topical antibiotic therapy.[5–7] Over a ten-year period, the treatment of burn wounds with either 0.5% silver nitrate solution, mafenide acetate cream, or silver sulfadiazine cream became the standard method of care for controlling the microbial environment of burn wounds. The limitations of topical antibiotic therapy were discussed in 1974, when it was observed that all topical agents are roughly similar in their ability to control burn wound sepsis and that all reduce mortality by about the same degree.[8] Furthermore, the development of topical antibiotic therapy for burn wounds served more to delay the onset of wound sepsis than to prevent it, and the benefits applied to only small and moderate-sized burns, with seemingly no effect on the mortality of massive burns. At the same time, these drawbacks were specifically addressed with the introduction of a technique of primary burn wound excision, and a convincing argument was made about why burn eschars should be separated from the healing wound. The plan was to develop a system of burn care that is directly based on the surgical principle of immediate debridement of necrotic tissue and primary wound closure.[8]

Primary Excision and Grafting of the Burn Wound

The first favorable report of the use of primary excision of burn wounds came in the mid-1940s, in the aftermath of the Boston, Massachusetts, infamous Coconut Grove fire.[9] The technique did not merit high acclaim during the 1950s, however, because of clinicians' limited ability to support the huge metabolic demands that inevitably accompanied the procedure.[10,11] In fact, in 1960 the procedure fell into disrepute when the cases of 25 patients with large burns who underwent fascial excision and grafting were compared with those of patients

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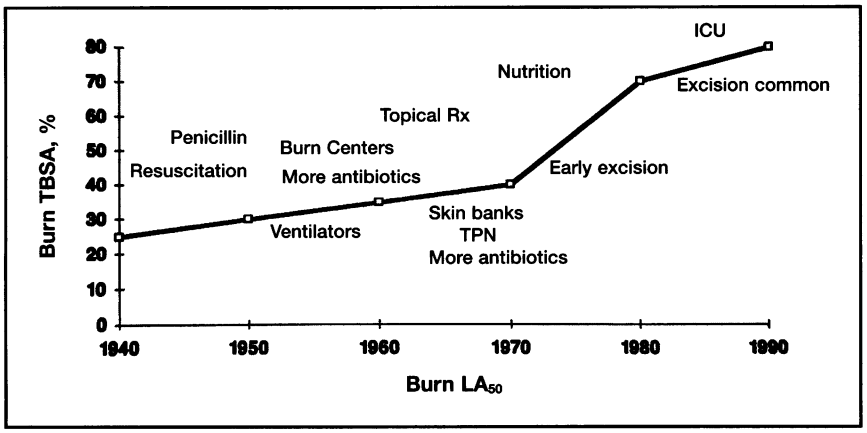

Figure 1.—A schematized time line of important advances in burn care is shown. ICU = intensive care unit, LA_{50} = survival of half of patients, depending on the percentage of total body surface area (TBSA) burned, Rx = therapy, TPN = total parenteral nutrition

who had delayed grafting and grafting on granulation tissue. Mortality was not increased, but neither was it decreased, thus safety if not effectiveness was ensured.[12] In 1970, concurrent with pronounced advances in critical care management of burn patients, the concept of early excision and grafting was reintroduced with a classic description of the tangential excision procedure.[13] In 1974, improved survival and a shorter time to wound closure were reported in patients with burns of 10% to 65% of total body surface area when treated with excision and grafting (with silver nitrate dressings) versus silver nitrate alone.[8] In 1988 the mortality of children with burn injuries was substantially reduced through the use of prompt eschar excision.[14] In 1989 patients were randomly assigned to receive either early excision or topical antimicrobial therapy and skin grafting after spontaneous eschar separation. Mortality from burns without inhalation injury was decreased by early excision from 45% to 9% in patients who were 17 to 30 years of age ($P < .025$).[15] These and many other studies confirm the improvements in survival and decreased length of hospital stay that can be achieved with the practice of early excision, even for large burns.

Advances in Technology and Clinical Skill

Although the practice of early excision and grafting has had considerable effect on survival for patients with massive burns, other factors have contributed substantially to its success. These include the somewhat intangible gains in clinical insight that come from years of experience in caring for burn patients. More tangible factors include advanced intensive care unit monitoring and nursing protocols, better ventilators, and better skill in surgical departments. In one series, the cases of 57 adults patients with massive burns (≥50% of total body surface area) from 1980 to 1989 were compared with those of 56 patients with similar massive burns in the period between 1970 and 1979. The results show a significant improvement ($P < .01$) in the survival rate of the more recent patients, attributed to improvements in the early treatment of inhalation injury, sepsis, and multiorgan failure.[1] The cases of 15 patients from 1978 to 1979 were compared with those of 16 patients treated in 1980 to 1981. Early excision was practiced in both groups, but during the first week in the later group. Factors noted to contribute to improved survival were early endotracheal intubation with the application of positive end-expiratory pressure before evidence of pulmonary dysfunction; the elimination of Swan-Ganz and central venous lines for early volume restoration unless absolutely necessary; the addition of hypertonic saline solution and protein infusions during the first 24 hours of resuscitation along with Ringer's lactate alone, resulting in a 30% decrease in fluid requirements; the rapid institution of nutritional support beginning day 3 using a combination of peripheral hyperalimentation and tube feeding; and early eschar excision and grafting beginning in the first week rather than the second or third week, as previously practiced.[16] General improvements in the management of critically injured patients have contributed substantially to the improved mortality rates of burn patients.

The benefits and limitations of burn wound excision were discussed in 1992, when the technique was viewed in the larger context of the total care and rehabilitation of patients with burn injury. Several factors were named that may have contributed to the decreased mortality seen after the institution of early excision and grafting, including improved antibiotic regimens, improved modes of ventilatory support, and improved methods of managing the postburn hypermetabolic response, such as better nutrition. It was also stressed that the benefits of excisional therapy lie not in the excision itself, but in the ability to accomplish rapid wound closure with skin grafts. Attention was called to the major unresolved problem in burn wound care today: the unsatisfactory appearance and functional impairment that may attend the scars of deep burns.[17]

Historical Overview of Burn Mortality

The most important factors associated with mortality,

namely, patient age and extent of burn, have not changed. As early as 1902, it was shown that the survival of burned patients was related to patients' age and extent of total body surface area burned.[18] In 1961 the prognostic value of the simple addition of age plus the percentage of burn surface area was shown. Although this finding was not published in the surgical literature, it gained wide acceptance and became the most common method used in predicting mortality in burn patients.[19] In 1982 other factors were found that substantially influence survival, including the admission leukocyte count, admission serum osmolality, the involvement of inflammable liquid, and the presence of preexisting mental disorders, circulatory disease, and digestive disease.[20] Still other factors found that significantly affected survival in a series of patients included the arterial pH and serum protein concentration at the beginning of treatment.[21] Despite these later attempts to better identify patients at high risk of dying, it was again shown in 1991 that mortality from burns was directly proportional to the extent of injury and the patient's age.[22]

In the 1960s, burn shock was the leading cause of in-hospital death after major burns.[23] Due to the release of neuroendocrine factors at the time of injury, extensive burns evoke circulatory derangements at both local and systemic levels, which may quickly lead to cardiovascular collapse.[24] The term "burn shock" describes the rapid onset of circulatory failure that occurs over the first 72 hours after injury if inadequately treated. The most important breakthrough in the successful management of burn shock proved to be the discovery that the expeditious administration of fluid could prevent its disastrous course.

In 1923, after the cases of 21 victims of the 1921 Rialto Theater fire in New Haven, Connecticut, were analyzed, it was noted that burn shock was due to intravascular fluid loss.[25] Since then, debate has raged over the optimal fluid resuscitation regimen to be used to prevent burn shock. The 1978 Consensus Development Conference on burn care issued a statement that fluid restoration in the first 24 hours should be with a balanced isotonic salt solution such as Ringer's lactate, that such a solution was as effective as colloid-containing fluids for the initial resuscitation, that colloid was of value in the period beginning 24 hours after a burn, and that the complete restoration of plasma volume as soon as possible after capillary leakage was resolved was beneficial.[26] As a result, burn shock is now prevented or reversed in 70% to 95% of cases when applied in a burn referral center.[27,28]

As the pathophysiology of burn shock was finally being understood and conquered, infection became the great killer of burn patients. The "conservative" method of burn wound management that was widely used consisted of topical antimicrobial therapy until spontaneous eschar separation, followed by autografting. Eschar separation is caused by the process of bacterial enzymatic digestion at the surface of the wound. Although topical antibiotics are helpful in maintaining microorganism counts below an invasive level, they also slow the natural process of eschar separation by decreasing the concentration of enzymatic lysins available in the wound. Morbidity is prolonged as weeks are spent waiting for the eschar to separate and fall off so that skin grafts can be placed on granulation tissue. Furthermore, even though the burn wound itself may remain free of invasive infection, the eschar remains present as a source of seeding to other vulnerable areas, particularly the respiratory tract. In 1962 respiratory tract damage was targeted as the principal killer of burned patients.[29] This was confirmed in 1970 when it was shown that pulmonary sepsis was the principal cause of death among a series of burn patients.[30] In 1979 late infectious complications were reported to have supplanted circulatory collapse as the leading cause of in-hospital death.[31] These late infectious complications are more commonly from a pulmonary source than from the burn wound itself.

In summary, a comprehensive review of the literature reveals that in 1996, the major factors associated with mortality in burn patients are age and percentage of total body surface area burned. The presence of inhalation injury and comorbidity are other crucial factors. Early excision and grafting have supplanted conservative management as the recommended treatment of large burns, except perhaps in elderly patients.[32] The fatal consequences of pulmonary complications are emphasized in the literature, and aggressive methods of pulmonary management are recommended.[33]

Special Considerations

Elderly Burn Patients

Older adults (in general, those older than 60 years) constitute a special population of burn patients. For any given burn size, their mortality is higher than for younger persons. Older patients have decreased physiologic reserve, which renders them less able to tolerate the metabolic demands of serious injury.[34] The thinner skin of older adults leads to larger and deeper burns and deeper donor sites. Delayed donor-site healing is a major cause of postburn morbidity in older patients that is related to an age-dependent slow rate of epidermal proliferation.[35] The threat of pneumonia is ever present in older patients and has been shown to be a significant factor affecting mortality in all burn patients.[30] Impaired senses and slow reaction time—often the factors that cause the injury in the first place—contribute to the difficulty in managing the logistics of wound care and activities of daily living for these patients. Older people who were living alone when they were injured seldom return to their former level of functioning and commonly require alterations in living arrangements, a situation that can be psychologically devastating to burn survivors.

In 1955, it was noted that there were no reports of patients older than 60 years surviving with greater than 10% burns.[36] Sixteen years later, it was again noted that no patients older than 60 years with burns over greater than 30% of the total body surface area survived.[37] In a

series of burned aged patients, survival was improved with the use of 0.5% silver nitrate solution. In 1983, the concept that adequate urine output is an indicator of adequate volume status during burn resuscitation, especially in elderly patients, was challenged. It was concluded that physiologic profile monitoring (pulmonary artery catheterization) in older patients is a useful guide to the precise management of fluid restoration and the early detection and treatment of ventricle dysfunction and that these result in improved survival.[38] In 1995, the mortality of a group of 111 octogenarians was reported to be 26%, the patients on average faring better than their predicted mortality rates as derived using either the Baux Index, the Bull Table, or the Abbreviated Burn Severity Score.[39] This improvement in mortality has not been reported elsewhere, however, and the literature suggests that survival rates have not improved substantially over the past 20 years in elderly patients with large burns.[40]

There is a positive note regarding the outcome of elderly burn patients. In 1992, decreased mortality was reported in patients older than 65 years at a burn center, achieved by increasing the number of nurses, changing local burn wound treatment, improving the documentation of wound status and general conditions, and improving nutritional support. As the general population ages, more experience is gained in the management of the special problems of older patients. Literature reports compare traditional with nonstandard treatment methods to ensure that results improve.[32,41,42] Social and rehabilitation services have become standard components of burn care for elderly patients and provide more today in the way of services and facilities than ever before. The stage is set for making noticeable improvements in the mortality of older burn patients. Because older patients often survive the resuscitation phase only to die of complications during the prolonged wound healing phase, early wound closure with artificial skin may indeed prove lifesaving for these vulnerable patients.

Inhalation Injury

As many as a third of patients with major burns have associated inhalation injury, often a lethal concomitant insult to otherwise less serious burn injuries.[43] In 1973, investigators labeled inhalation injury as the major threat to burn patients. In a series of 100 patients with smoke inhalation, pulmonary complications developed in 22, with 86% mortality.[44] In a review of the literature in 1981, it was concluded that inhalation injury was still a primary determinant of survival following major burns.[45] Further literature reviews in the 1990s confirmed the fact that not much progress has been made in improving the survival rates of patients with smoke inhalation in combination with major burns.[46]

Inhalation injury may be described as an acute respiratory tract injury caused by steam or toxic inhalants such as fumes, gases, or mists.[47] Thermal inhalation injuries per se are rare due to the efficient cooling mechanisms of the respiratory tract. Severe chemical injuries from smoke inhalation are common, however, due to the caustic nature of incomplete products of combustion that are released by burning compounds.[48] The extent of inhalation damage depends on the composition of the burning material, the concentration of fumes given off (whether in a closed space or not), the temperature of the gases (rarely an important component), and the duration of exposure of the patient to the caustic fumes. The result is some degree of tracheobronchitis.[49] In severely affected patients, tracheobronchial mucosal slough and airway obstruction from cellular debris subsequently develop, followed by pneumonia and the potential for invasive sepsis. The burn induces inflammatory cascades that result in pulmonary leukocyte and macrophage activation, thereby worsening the injurious effect on the lungs. This inflammatory response persists until final wound closure is achieved.

Optimism is expressed in the literature that mortality for patients with combined burn and inhalation injuries is improving. Much of the credit is attributed to general advances in intensive care management, improved infection control measures, and better antibiotic combinations for the treatment of pneumonia. Improvements in the ventilatory management of these patients have been shown with the use of high-frequency ventilation[33] and extracorporeal membrane oxygenation, a treatment method that has shown promise in children with burns.[50]

Carbon monoxide toxicity is a type of inhalation injury that deserves special mention, as it is one of the leading causes of deaths from fires.[51] Carbon monoxide is a tasteless, odorless, and colorless gas with an affinity for hemoglobin 200 times that of oxygen. As oxygen is consumed during the burning process, carbon monoxide is released. It then binds preferentially to the hemoglobin molecule in place of oxygen, shifting the hemoglobin-oxygen saturation curve to the left and resulting in major impairments in oxygen delivery. The goal of the treatment of carbon monoxide toxicity is the total displacement of carbon monoxide on the hemoglobin molecule by oxygen as early as possible (the half-life of carboxyhemoglobin is 30 minutes in a patient breathing 100% oxygen) to prevent devastating neurologic sequelae (anoxic brain injury). Oxygen is usually administered in concentrations of 90% to 100%. Hyperbaric oxygen (2 to 3 atm) produces an even more rapid displacement of carbon monoxide and may be useful when exposure has been extensive. Although hyperbaric oxygen therapy is commonly used for persons who have sustained carbon monoxide poisoning without burn injury, there is less acceptance of its use in patients with considerable burns.[52–54]

Skin Substitutes

Burn specialists continue to await the development of the ideal skin substitute. Cultured epithelial autografts, at one time thought to be the answer to the wound coverage problem,[55] have proved to be disappointing. They have been presented as lifesaving therapy,[55] but long-term results have not yet been reported. Furthermore, recent reports of the use of these allografts describe poor

graft take when used for the treatment of massive burns.[56,57] The lack of dermis available beneath these thin autografts prevents the development of sturdy skin. The result is a fragile scar surface that bears little resemblance to normal skin for many months. This situation was described histologically in 1988.[58] The use of these autografts for smaller or shallower burns is an avenue that remains to be explored and one in which cost-effectiveness analyses are critical.

In a 1988 multicenter randomized clinical trial, increased survival was reported in patients with life-threatening burns, associated with the use of artificial skin.[59] Two years later, a histologic study of the product the investigators in that study used, now called Integra, was published.[60] Integra consists of a dermal substitute of bovine collagen and chondroitin-6-sulfate and an epidermal layer of synthetic polysiloxane polymer (Silastic). It was reported that with rare exceptions, an intact dermis was achieved as well as definitive closure of a complete epidermal layer with a minimum of scarring. Integra is now available for clinical use, and the results of clinical studies are anticipated. Many synthetic products have been developed as skin substitutes, but their clinical efficacy and cost-effectiveness have yet to be established.[61–63]

Conclusions

We have presented a brief overview of the accomplishments made in burn therapy over the past several decades. The following conclusions can be drawn from the preceding review:

- Pronounced improvements have been made in the mortality statistics of burn patients in general over the past several decades. The LA_{50} is currently 70% of the total body surface area.
- Infectious complications, mainly pulmonary, have supplanted burn shock as the main killer of burn victims.
- Early excision and grafting have replaced conservative management as the recommended method of treating large burns, except perhaps in elderly patients.
- Despite a revolution of advances in critical care medicine and surgical treatment, burn patients older than 60 years and those with inhalation injury continue to have disproportionately high mortality.

The development of a satisfactory skin substitute is on the horizon. Measures of success must include clinical effectiveness in achieving wound closure and cost-feasibility studies.

REFERENCES

1. Xiao J, Chai BR, Kong FY, et al: Increased survival rate in patients with massive burns. Burns 1992; 18:401–404

2. Tompkins RG, Burke JF, Schoenfeld DA, et al: Prompt eschar excision: A treatment system contributing to reduced burn mortality—A statistical evaluation of burn care at the Massachusetts General Hospital (1974–1984). Ann Surg 1986; 204:272–281

3. Herndon D: Total Burn Care. London, England, WB Saunders, 1996

4. Moyer C, Brentano L, Gravens D, Margraf H, Monafo W: Treatment of large human burns with 0.5% silver nitrate solution. Arch Surg 1965; 90:812–867

5. Baxter C: Topical use of 1.0% silver sulfadiazine, *In* Polk HJ, Stone H (Eds):Contemporary Burn Management. Boston, Mass, Little, Brown, 1971, pp 217–225

6. Moncrief J: The status of topical antibacterial therapy in the treatment of burns. Surgery 1973; 63:862–867

7. Polk HC Jr: Treatment of severe burns with aqueous silver nitrate (0.5%). Ann Surg 1966; 164:753–770

8. Burke JF, Bondoc CC, Quinby WC: Primary burn excision and immediate grafting: A method shortening illness. J Trauma 1974; 14:389–395

9. Cope O, Langhor J, Moore F, Webster R: Expeditious care of full thickness burn wounds by surgical excision and grafting. Ann Surg 1947; 125:1–22

10. Moncrief J: Burns. N Engl J Med 1973; 288:862–867

11. MacMillan B, Artz C: A planned evaluation of early excision of more than 25% of the body surface in burns. Surg Forum 1957; 7:88–93

12. Jackson D, Topley E, Cason J, Lowbury E: Primary excision and grafting of large burns. Ann Surg 1960; 152:167–189

13. Janžekovič Z: A new concept in the early excision and immediate grafting of burns. J Trauma 1970; 10:1103–1108

14. Tompkins RG, Remensnyder JP, Burke JF, et al: Significant reductions in mortality for children with burn injuries through the use of prompt eschar excision. Ann Surg 1988; 208:577–585

15. Herndon DN, Barrow RE, Rutan RL, Rutan TC, Desai MH, Abston S: A comparison of conservative versus early excision therapies in severely burned patients. Ann Surg 1989; 209:547–553

16. Demling R: Improved survival after massive burns. J Trauma 1983; 23:179–184

17. Monafo WW, Bessey PQ: Benefits and limitations of burn wound excision. World J Surg 1992; 16:37–42

18. Weidenfeld S: Über den Verbrennungstod: I. Äbhangigkeit des Verbrennungstods von der Grosse der Verbrannter Hautflache. Arch Dermatol Syph 1902; 61:33–56

19. Baux S, Mimoun M, Saade H, et al: Burns in the elderly. Burns 1989; 15:239–240

20. Berry CC, Wachtel TL, Frank HA: An analysis of factors which predict mortality in hospitalized burn patients. Burns Incl Therm Inj 1982; 9:38–45

21. Kaukinen L, Pasanen M, Kaukinen S: Prognostic indicators in burned patients. Ann Chir Gynaecol 1985; 74:86–99

22. Benmeir P, Sagi A, Greber B, et al: An analysis of mortality in patients with burns covering 40 per cent BSA or more: A retrospective review covering 24 years (1964–88). Burns 1991; 17:402–405

23. Fozzard H: Myocardial injury in burn shock. Ann Surg 1961; 154:113–119

24. Carleton SC: Cardiac problems associated with burns. Cardiol Clin 1995; 13:257–262

25. Underhill E, Carrington G: Blood concentration changes in extensive superficial burns, and their significance for systemic treatment. Arch Intern Med 1923; 32:31

26. Baxter C: Supportive therapy in burn care: Guidelines for fluid resuscitation. J Trauma 1981; 21(suppl):687–692

27. Demling R: Fluid replacement in burned patients. Surg Clin North Am 1987; 67:15–30

28. Baxter C: Fluid resuscitation, burns percentage, and physiologic age. J Trauma 1979; 19(suppl):864–870

29. Phillips A, Cope O: Burn therapy: The revelation of respiratory tract damage as the principal killer of burned patients. Ann Surg 1962; 155:1–19

30. Pruitt B, Flemma R, DiVencenti F, Foley F, Mason A: Pulmonary complications in burn patients. J Thorac Cardiovasc Surg 1970; 59:7–20

31. Sevitt S: A review of the complications of burns, their origin and importance of illness and death. J Trauma 1979; 19:358–369

32. Housinger T, Saffle J, Ward S, Warden G: Conservative approach to the elderly patient with burns. Am J Surg 1984; 148:817–820

33. Rue LW 3d, Cioffi WG Jr, Mason AD, McManus WF, Pruitt BA Jr: Improved survival of burned patients with inhalation injury. Arch Surg 1993; 128:772–780

34. Scalea TM, Simon HM, Duncan AO, et al: Geriatric blunt multiple trauma: Improved survival with early invasive monitoring. J Trauma 1990; 30:129–137

35. Cameron I: Cell proliferation and renewal in aging mice. J Gerontol 1972; 27:162–169

36. Ziffren S: Management of the burned elderly patient. J Am Geriatr Soc 1955; 3:36

37. Hartford C, Ziffren S: Improved survival of burned aged patients with 0.5% silver nitrate. J Am Geriatr Soc 1971; 28:118–123

38. Agarwal N, Petro J, Salisbury R: Physiologic profile monitoring in burned patients. J Trauma 1983; 23:577–583

39. Cadier MA, Shakespeare PG: Burns in octogenarians. Burns 1995; 21:200–204

40. Forjuoh SN, Smith GS: Case-fatality rates by body part affected and trends in hospitalized burns in Maryland, 1981–90. Burns 1993; 19:387–391

41. Kara M, Peters W, Douglas L, Morris S: An early surgical approach to burns in the elderly. J Trauma 1990; 30:430–432

42. Ikeda J, Sugamata A, Jimbo Y, Yukioka T, Makino K: A new surgical procedure for aged burn victims: Applications of dermolipectomy for burn wounds

and donor sites. J Burn Care Rehabil 1990; 11:27–31

43. Heimbach DM, Waerckerle JF: Inhalation injuries. Ann Emerg Med 1988; 17:1316–1320

44. Achauer BM, Allyn PA, Furnas DW, Bartlet R: Pulmonary complications of burns: The major threat to the burn patient. Ann Surg 1973; 177:311–319

45. Moylan JA: Inhalation injury—A primary determinant of survival following major burns. J Burn Care Rehabil 1981; 2:78–84

46. Smith DL, Cairns BA, Ramadan F, et al: Effect of inhalation injury, burn size, and age on mortality: A study of 1447 consecutive burn patients. J Trauma 1994; 37:655–659

47. Fitzpatrick J, Cioffi WG Jr: Diagnosis and treatment of inhalation injury. *In* Herndon DN (Ed): Total Burn Care. London, England, WB Saunders, 1996, pp 184–192

48. Prien T, Traber D: Toxic smoke compounds and inhalation injury—A review. Burns Incl Therm Inj 1988; 14:357–364

49. Moritz A, Henriques FJ, McLean R: The effects of inhaled heat on the air passages and lungs: An experimental investigation. Am J Pathol 1945; 21:311–331

50. Ombrellaro M, Goldthorn JF, Harnar TJ, Shires GT: Extracorporeal life support for the treatment of adult respiratory distress syndrome after burn injury. Surgery 1994; 115:523–526

51. Demling R: Smoke inhalation injury. New Horizons 1993; 1:422–434

52. Grube BJ: Therapeutic hyperbaric oxygen: Help or hindrance in burn patients with carbon monoxide poisoning? (Letter) J Burn Care Rehabil 1989; 10:285

53. Hart GB, Strauss MB, Lennon PA, Whitcraft DD 3d: Treatment of smoke inhalation by hyperbaric oxygen. J Emerg Med 1985; 3:211–215

54. Myers RA, Snyder SK, Linberg S, Cowley RA: Value of hyperbaric oxygen in suspected carbon monoxide poisoning. JAMA 1981; 246:2478–2480

55. Coleman JJ 3d, Siwy BK: Cultured epidermal autografts: A life-saving and skin-saving technique in children. J Pediatr Surg 1992; 27:1029–1032

56. Rue LW 3d, Cioffi WG Jr, McManus WF, Pruitt BA Jr: Wound closure and outcome in extensively burned patients treated with cultured autologous keratinocytes. J Trauma 1993; 34:662–667

57. Herzog SR, Meyer A, Woodley D, Peterson HD: Wound coverage with cultured autologous keratinocytes: Use after burn wound excision, including biopsy followup. J Trauma 1988; 28:195–198

58. Woodley DT, Peterson HD, Herzog SR, et al: Burn wounds resurfaced by cultured epidermal autografts show abnormal reconstitution of anchoring fibrils. JAMA 1988; 259:2566–2571

59. Heimbach D, Luterman A, Burke J, et al: Artificial dermis for major burns—A multi-center randomized clinical trial. Ann Surg 1988; 208:313–320

60. Stern R, McPherson M, Longaker M: Histologic study of artificial skin used in the treatment of full-thickness thermal injury. J Burn Care Rehabil 1990; 11:7–13

61. Pruitt BJ, Levine N: Characteristics and uses of biologic dressings and skin substitutes. Arch Surg 1984; 119:312–322

62. Cuono CB, Langdon R, Birchall N, Barttelbort S, McGuire J: Composite autologous-allogeneic skin replacement: Development and clinical application. Plast Reconstr Surg 1987; 80:626–637

63. Hull BE, Finley RK, Miller SF: Coverage of full-thickness burns with bilayered skin equivalents: A preliminary clinical trial. Surgery 1990; 107:496–502