History and Advancement of Burn Treatments

Hai-Fei Liu, MD, PhD,† Feng Zhang, MD, PhD,* and William C. Lineaweaver, MD**

Abstract: Advances in burn care have accelerated within the last 50 years. The principal modalities of and approaches to burn treatment include dressings, antimicrobials, fluid resuscitation, burn wound excision, skin grafting, and use of skin substitutes. This review presents a historical outline of these approaches, their current status, and prospects for the future of burn care.

Key Words: burns, treatments, history

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Burn treatments have been described since ancient times.[1] Burns and their treatments are recognized in cave paintings which are more than 3500 years old. Documentation in the Egyptian Ebers papyrus of 1500 BC advocated a 5-day treatment regimen using a mixture of cattle dung, bees wax, ram's horn, and barley porridge soaked in resin for the topical treatment of burns. In 600 BC, the Chinese treated burn wounds with extracts from tea leaves. Nearly 100 years later, Hippocrates described the use of porcine skin mixed with a resin of bitumen impregnated in bulky dressings which were alternated with warm vinegar soaks augmented with tanning solutions made from oak bark. Celsus recommended a lotion with wine and myrrh for burns in the first century AD. In 300 AD, Hong Ge described a treatment of topical ointment made of old calcarea blended with plant oil or pig fat cooked with willow bark.[2]

In the middle of the 16th century, Ambroise Paré treated burns with onions and probably was the first to describe early burn wound excision. In the early 17th century, Guilhelmus Fabricius Hildanus discussed the pathophysiology of burns and made unique contributions to the treatment of subsequent cicatricial contractures. In 1797, Edward Kentish described pressure dressings as a means to relieve burn pain and blisters. In 1839, Guillaume Dupuytren reviewed the treatment of 50 burn patients with occlusive dressings and developed a classification of burn depth that remains recognizable today.[3] He was also the first to recognize gastric and duodenal ulceration as a complication of severe burns, a concept described in more detail by Curling in 1842.[4]

The recognition of the importance of burn surface area and skin grafting by Reverdin in the 1800s clarified both the diagnostic and surgical understanding of burns.[5] During and after World War I, consensus was reached that the best management of deep burn wounds included excision, skin grafting, and pain management. However, despite a centuries-long history of treatments for burns, many patients still died of shock and infection mainly because the fundamental understanding of the pathophysiological effects of burns was not clear.[6] Research inspired by fire disasters such as the Rialto fire in 1921 and Coconut Grove nightclub fire in 1942 provided the first operational understandings of the pathophysiology of burns.[6]

Based on the index of mortality, it is evident that our ability to treat burn injuries has improved remarkably since World War II. The statistic that 50% lethal area, which is fatal for 50% population, was approximately 40% total body surface area (TBSA) for young adults in the United States in the immediate postwar era. By the 1990s, it increased to approximately 80% TBSA.[7] According to Bull and Fisher,[8] complications such as shock, sepsis, and multi-organ failure resulted in a 50% mortality rate in children with burns covering 50% TBSA between 1942 and 1952. The mortality of children with 80% TBSA or greater burns was only 33% on a large sample study during 1982 to 1996.[9] According to a more recent study, a 98% TBSA injury now has a 50% survival rate in burned children.[10]

Burn treatment is a complex undertaking and involves many components. Elements presented in this brief review include burn dressings, infection control of the burn wound, fluid resuscitation, and burn surgeries. Advances in each of these elements have continued to contribute to survival and functional recovery of burn victims.

BURN DRESSINGS

The application of dressings began in ancient times and included increasingly explicit goals of preventing infection, promoting reepithelialization, avoiding water and heat loss, keeping the wound moist, and decreasing pain. A variety of biological, semibiological, and other dressings can and have been used to cover burn wounds, to aid epithelialization, and to protect the excised wounds from desiccation, infection and mechanical trauma.[11] Biological dressings, such as allograft skin,[12] xenograft (e.g., porcine skin),[11] and human amnion,[13] have been used to cover the wound while reepithelialization occurs. The use of these biological dressings has been associated with problems, including availability, tissue collection, storage, and, importantly, transmission of infection and high costs.[14]

Conventional dressings such as Vaseline gauze or silicone sheets (i.e., Mepitel) and synthetic dressings such as Mepilex, DuoDERM, Omniderm, Tegaderm, and hydrocolloids can be used to cover the wound while reepithelialization takes place.[15]

A number of silver containing dressings are currently used for burn care including ACTICOAT*, Mepilex Ag and Aquacel Ag products. ACTICOAT* is a bilayered polyethylene nanocrystalline silver dressing attached to a soaking coat of polyester that can provide sustained release of silver for up to 7 days.[16] ACTICOAT* was substantiated to have better antimicrobial activity and reduce grafting requirements compared to silver sulfadiazine.[17,18] ACTICOAT* was also demonstrated to have fewer adverse effects and reduce healing times.[19] Mepilex Ag is a soft and highly conformable antimicrobial foam dressing that absorbs exudate and maintains a moist wound environment. The soft silicone layer minimizes the risk for maceration and reduces pain and damage to the area during dressing changes. Mepilex Ag is clinically proven to heal burns faster and with less pain and cost compared to silver sulfadiazine.[20] Aquacel Ag products use a hydrofiber for absorption plus ionic silver. The easy application and low frequency of dressing change make these dressings practical dressings in burn care.

Recent development in dressing and bioengineering technology have introduced dressings and gels containing naturally occurring glycosaminoglycan and chitin,[21–24] with incorporation of growth factors into the gel.[25,26] These dressings have been reported to prevent early extension of burns[27] express antimicrobial properties,[28,29] and promote fibroblast proliferation, angiogenesis, and wound healing.[30] Carbon fiber dressings have been more recently studied and demonstrated to increase

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From the *Joseph M. Still Burn and Reconstructive Center, Jackson, MS; and †Department of Orthopedic Surgery, the Affiliated Hospital of Qingdao University, Shandong, China.
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Reprints: William C. Lineaweaver, MD, Joseph M. Still Burn and Reconstructive Center, Jackson, MS 39216. E-mail: william.lineaweaver@burncenters.com.

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the absorptive capacity of the dressing, reduce inflammation and bacterial growth, and promote wound healing.[31,32]

INFECTION CONTROL

Sepsis has been the most frequent cause of death after burn injury and contributes to almost 75% to 85% of all burn deaths.[33,34] An important advancement in burn care that has dramatically reduced mortality is infection control.

Systemic Antibiotics

The origin of modern scientific infection control in burn patients began with Leonard Colebrook, a physician, bacteriologist, and colleague of Alexander Fleming. Colebrook proposed that burn wounds became infected with bacteria and that strict infection control practices could prevent infection by reducing transfer of organisms between patients in a specially designed burn unit.[35–37] Colebrook also studied the use of dressings impregnated with sulfanilamide and penicillin creams,[35,38] and serum and plasma for burn shock resuscitation at the Glasgow Royal Infirmary.[39]

Lyons et al,[40] managing burn patients at Massachusetts General Hospital, found that hemolytic streptococcal infection responded to sulfa drugs and an effective blood level of sulfonamide offered the most certain control of systemic infection due to the hemolytic streptococcus. However, in 1943, based on a study with 1500 patients, Meleney concluded that neither local nor systemic sulfonamides were effective at controlling local wound infection, and that inadequate surgical excision predisposed to infection.[41]

Emerging resistance by staphylococcus and clostridium to sulfa drugs stimulated research on penicillin. The discovery of penicillin by Alexander Fleming, the Scottish biologist, pharmacologist, and botanist, in 1928 was a major breakthrough but its clinical utility was not appreciated until 1940, when Chain, Florey, and others demonstrated the new drug's life-saving potential against streptococcus, staphylococcus, and clostridium infections in murine and human studies.[42,43]

Organisms associated with infection in burn patients include gram-positive, gram-negative, and viral and fungal organisms. Systemic antimicrobials must be thoughtfully considered for burn patients to prevent the emergence of resistant organisms.

Burn infections caused by the most common gram-positive organisms, streptococci, staphylococci, and enterococci, can be treated with penicillinase-resistant penicillins if the organisms are methicillin-sensitive. Staphylococcal infections resistant to penicillinase-resistant penicillins are termed methicillin-resistant staphylococcus aureus (MRSA) or methicillin-resistant staphylococcus epidermidis (MRSE). Vancomycin has been considered the antibiotic of choice for infections caused by MRSA and MRSE.[44] Linezolid was considered the choice for oral treatment of MRSA and MRSE infections.[45] Most enterococci are susceptible to vancomycin. Vancomycin-resistant enterococci will require treatment with combined medications, such as ampicillin/aminoglycosides, or a quinupristin/dalfopristin combination.

The aminoglycosides were historically the antibiotics of choice for gram-negative infections. However, some gram-negative bacteria in burn patient infections are now resistant to almost all the antibiotic classes and must be treated with the polymixins. Branski et al[46] concluded that colistin, or polymyxin E, was a safe and efficacious antimicrobial drug for adult and pediatric burn population without a marked incidence of toxic side effects, but should be used only with close monitoring of renal function.

The 5 classes of systemic antifungal drugs used in this setting include the polyenes (Amphotericin B), azoles, nucleosides (Flucytosine), echinocandin, and allylamine.[45,47] Drug choices for treating fungal infections should be based on specific organisms isolated or suspected.

Topical Antimicrobials

The high susceptibility of burn wounds to infection, coupled with increased antibiotic resistance among pathogenic bacteria and fungi and the difficulty of systemically administered antibiotics in reaching injured tissue, have contributed to the ongoing development and use of topical antimicrobials in the treatment of burns.

The aim of topical therapies has changed with the increased understanding of the pathophysiology of burns. In the early 20th century, the goal of topical therapies was to counteract the "toxins" released from burn wounds and to minimize fluid loss. In 1925, Davidson asserted that use of tannic acid in burn care not only lessened toxemia, but also provided analgesia, prevented body fluid loss, limited infection, decreased scar formation, and generated a scaffold for healing.[48] Its use was stopped when it was found to lead to lethal liver necrosis.[49]

Sodium hypochlorite (NaClO), one of the first topical antimicrobials, was discovered in the 18th century by Berthollet and was widely used as a disinfectant throughout the 19th century. Its use was hampered by the frequently encountered irritation and topical reactions, but these side effects were later discovered to be due to variables in quality and chlorine in different preparations of the solution.[50] In 1915, Dakin successfully synthesized hypochlorite solutions without irritating contaminants and proposed the concentration of 0.5% NaClO as most effective.[51] During World War I, Dakin teamed up with the famous French surgeon and Nobel Prize winner Alexis Carrel to develop a protocol for wounds and burns. They specified mechanical cleansing, surgical debridement, and topical application of hypochlorite solution.[52] In 1985, Lineaweaver et al[53] found that the cellular toxicity of hydrogen peroxide and acetic acid exceeded their bactericidal potency, but concentrations of povidone-iodine and sodium hypochlorite were identified without fibroblast toxicity but with persistent bactericidal activity. Recently, Heggers et al[54,55] investigated concentrations of sodium hypochlorite for antibacterial activity and tissue toxicity in vitro and in vivo, and found that a modified "Dakin's" solution at a concentration of 0.025% NaClO had sufficient bactericidal properties but eliminated detrimental effects on wound healing.

Pruitt et al[56] achieved a remarkable improvement in postburn mortality in 1964, with the use of a topical antimicrobial, mafenide acetate (Sulfamylon) cream, which was effective against Gram-negative burn wound infections. Meanwhile, mafenide acetate was also adapted for treating burns at the Institute of Surgical Research in San Antonio, Texas, by microbiologist Robert Lindberg and surgeon John Moncrief.[57] This antibiotic could penetrate third-degree eschar and was extremely effective against a wide spectrum of pathogens. Because of its capacity for deep penetration of burn eschars, mafenide acetate appeared particularly effective in the treatment of full-thickness burns with significant devitalized tissue.[58] It is however a carbonic anhydrase inhibitor and can cause systemic acidosis, compensatory hyperventilation, and pulmonary edema. Therefore, the duration and area of mafenide acetate application must be limited to prevent systemic toxicity associated with prolonged or extensive use.[57,58]

A major milestone in topical burn therapy was the application of silver compounds, mentioned above, which remarkably reduced the incidence of burn wound sepsis and death. Silver based topical therapies were especially effective in controlling Pseudomonas aeruginosa infections.

In 1965, Moyer et al[59] used 0.5% silver nitrate solution as an effective topical antibacterial agent for the treatment of burn wounds. Simultaneously, Fox et al[60,61] developed silver sulfadiazine cream (Silvadene), which has become a mainstay of topical antimicrobial therapy due to its success in controlling infection and minimal side effect profile.

FLUID RESUSCITATION

The history of burn resuscitation can be traced back to the treatments and subsequent studies of severely burned patients in large urban fire disasters such as those at the Rialto Theatre (New Haven, Conn) in

1921 and the Coconut Grove nightclub (Boston, Mass) in 1942, when physicians noticed that some patients survived the large burns but died from the secondary shock. As burn size approaches 15% to 20% TBSA, hypovolemic shock sets in if no appropriate fluid resuscitation is conducted.[62] In adults with burns approaching 25% to 30% TBSA, damage to cell membranes also occurs in hypovolemic shock, resulting in a decrease in transmembrane potential and the accumulation of intracellular sodium and water.[63]

It has been advocated that for maximum benefit, fluid resuscitation should begin as early as 2 hours after burn.[9,64] The goal of fluid resuscitation is to prevent hypovolemic shock by maintaining adequate end-organ perfusion. Meticulous attention to details and frequent reassessment is necessary to avoid the dangers of excessive or deficient fluid administration.

Mechanisms that control protein and fluid loss from the vascular space are compromised after severe burns and the subsequent inflammatory reaction that follows the burn injury. The margination of neutrophils, macrophages, and lymphocytes into these areas is associated with the release of a variety of inflammatory mediators, including histamine, serotonin, prostaglandins, platelet products, complement components, and members of the kinin family, which affect and disrupt local and systemic vascular permeability.[65] The end result is an immediate shift of intravascular fluid into the interstitial space.

The foundation of current fluid resuscitation approaches began with the studies of Underhill, who found the composition of burn blister fluid was similar to that of plasma and suggested that early burn mortality might be due to loss of fluid rather than toxins. Underhill identified the significance of loss of the liquid and protein components of the blood in the burn area and proposed the concept of thermal injury–induced intravascular fluid deficits in the 1930s and 1940s.[66,67] Moore et al subsequently developed the concept of the burn edema and introduced an initial formula of infusion therapy in relation to the severity of the injury.[68] At that time, as little as 10% to 20% TBSA burns were associated with high rates of mortality. In the 1970s, a 30% TBSA in burns could lead to nearly 100% mortality in older patients.[69]

In 1930, Underhill proposed blood hemoglobin percentage as an index of resuscitation, and asserted that resuscitation aimed at preventing hemoconcentration is required for 24 to 36 hours postburn. Intravenous sodium chloride solutions were used, supplemented by oral, rectal, and subdermal solutions.[66] Based on hemoconcentration, Harkins proposed a formula of fluid resuscitation for burn patients: 100 mL of plasma for each point when the hematocrit exceeds 45. Furthermore, when hematocrit detecting was unavailable, he recommended the "First Aid Method": 500 mL of plasma for each 10% TBSA burned.[70]

In 1943, Cope et al[71] suggested that the initial dosage of plasma should be determined on the basis of the surface area of the burns. For each 10% TBSA involved, they proposed to give 500 mL plasma in the first 24 hours. The plasma dosage was adjusted subsequently on the basis of repeated hematocrit and serum protein determinations. Meanwhile, the National Research Council (NRC) advocated 1000 mL of plasma for each 10 percent burned area over the first 24 hours.[72]

In 1944, Lund and Browder[73] developed diagrams by which physicians could easily and accurately quantify burn surface area. This quantification led to fluid resuscitation strategies based on TBSA burn calculations. Knaysi et al[74] advocated a simple "rule of nines" for evaluating the percentage of body surface area burned. In the late 1940s, Cope and Moore[75] were able to quantify the amount of fluid for adequate resuscitation based on the percent of the body surface area burned and described a revised NRC formula called the Surface Area Formula in 1947: 75 mL of plasma and 75 mL of isotonic crystalloid solution for one percentage of TBSA, with one half given in the first 8 hours, and one half in the next 16 hours. Urine output was used as the primary index of resuscitation. Moore went on to develop a formula for estimating the amount of fluid for adequate resuscitation based on the burned percentage of body surface area in 1970.[68]

Multiple subsequent formulas included body weight in the calculations and variations in both the volumes per weight per TBSA and the types of crystalloid or crystalloid-colloid combinations administered. Well-known resuscitation recipes included Evans Formula (colloid 1 mL/kg/TBSA, crystalloid 1 mL/kg/TBSA, and 5% glucose 2000 mL for the first day; one half these amounts colloid and salt second day), Brooke Formula (colloid 0.5 mL/kg per TBSA, and crystalloid 1.5 mL/kg per TBSA, plus 2000 mL glucose for the first day; colloid, 0.25 mL/kg per TBSA; and crystalloid, 0.5 mL/kg per TBSA, plus 2000 mL glucose for the next day), and Modified Brooke Formula (crystalloid 2 mL/kg per TBSA, one half for the first 8 hours and one half over the next 16 hours).[76–78]

The use of colloid solutions in the fluid resuscitation of burns could effectively reduce the edema formation and amount of fluid required. Patients with severe burns, preexisting heart disease, and inhalation injuries may benefit the most from lower-volume resuscitations aided by colloid. Colloids used in burn resuscitation have included dextran, albumin and plasma.[79–81]

Baxter and Shires[82] postulated that protein administered in the first 24 hours postburn would leak out of the vessels and exacerbate edema. They therefore developed a crystalloid based formula without colloid, which is now referred to as the Parkland formula and is perhaps the most widely used formula today. The Parkland Formula recommends 4 mL of Lactated Ringer's solution (RL)/kg/% TBSA burned during the first 24 hours of resuscitation after a burn injury. Half the volume is given in the first 8 hours postburn, with the remaining volume delivered over the subsequent 16 hours.[82]

To date, no single recommendation has been established to be the best fluid resuscitation formula for burns.[83,84] Fluid resuscitation formulae are only guides to assist in estimation of fluid requirements, as each patient reacts differently to burn injury and resuscitation. Regardless of the formula or strategy used, the first 24–48 hours require frequent adjustments by clinical indicators of the adequacy of resuscitation.[83] Overresuscitation can be a major source of morbidity for burn patients. Fluid overload during the critical early management can result in unnecessary edema, pulmonary dysfunction, and extended ventilator support.[85,86]

Although the end points for fluid resuscitation are still controversial, the hourly urine output is a well-established parameter for guiding fluid management. The urine output should approach 0.5 mL/kg per hour or approximately 30 to 50 mL/h in most adults and older children (>50 kg), and approximately 1 mL/kg per hour in small children.[87] Yowler and Fratianne[69] suggested that the goal of fluid resuscitation is to maintain urine output in the range of 0.5 to 1 mL/kg per hour for adults and 1% to 1.5 mL/kg per hour in children.

Certain patient populations frequently require higher fluid resuscitation volume. Patients with delayed resuscitation, alcohol abuse, trauma, or inhalation injury may require greater fluid resuscitations than predicted. Patients with inhalation injury sometimes required as much as 30% to 40% higher fluid supplement than calculated by fluid resuscitation formulae for adequate resuscitation.[88]

BURN SURGERY

In 1510 to 1590 AD, Ambroise Pare described early excision of burn wounds. In 1607, Hildanus also recommended removal of burn eschars to facilitate drainage of serous fluid and allow better medication penetration. Limitations of technique, blood replacement, and perioperative support made excision of large burns impossible.[89]

In the 1940s, along with advancements in topical infection control and fluid resuscitation, it was recognized that one of the most effective therapies to reduce mortality in thermal burn injury was the early excision of burn eschar and subsequent skin grafting.[90] Physicians applied pyruvic acid and starch to full thickness burns, followed by grafting as early as 6 days postdebridement.[91] Young, McCorkle and

Silvani, and Saltonstall and Lee[92–94] subsequently reported extensive experience with surgical excision of full thickness burns in the 1940s.

In the late 1950s, Jackson et al[95] advanced the concept of early excision technique in a series of pilot and controlled trials by immediate fascial excision and grafting of small burn areas, and eventually covering up to 65% TBSA with autograft and homograft skin. They concluded that excision and grafting of 20% to 30% TBSA could be carried out on the day of injury safely as long as shock was controlled by red cell volume monitoring. In 1964, Walker et al[96] advocated early excision, starting postburn day 4, for patients with large burns, and immediate coverage with a combination of autograft and cadaver allograft. This technique was not accepted by the majority of surgeons because of controversy over expected outcomes, including mortality, infection, unnecessary blood loss, and total healing time.

It was not until the introduction of tangential excision by Janzekovic[97–99] in the 1970s that early excision in burns achieved greater acceptance. She reported 2615 patients treated for deep second-degree burns by tangential excision of eschar and the damaged dermis down to bleeding tissues and immediate grafting with autograft 3 to 5 days after burn injury.[97] Application of the technique was limited to small burns that could be covered by autografted skin.[100] For the treatment of larger burns, Monafo[101] (early 1970s) was one of the first to advocate the use of tangential excision and grafting. Burke et al[102] treated children with burns over 80% TBSA with a combination of tangential excision for the smaller burns and excision to the level of fascia for the larger burns, and coverage with split-thickness allografts, achieving a remarkable decrease in both hospital time and mortality. In a randomized prospective study, Engrav et al[103] reported that early tangential excision and grafting of deep second-degree burns improved mortality and also reduced hospitalization time when compared with conservative treatment.

In a retrospective study, Tompkins et al[104] reported an improvement in mortality over the course of 1974 to 1984 through the application of prompt eschar excision. Herndon and Parks[105] implemented an early total excision (within 48–72 hours) to fascia with application of 4:1 expanded autograft and cadaver skin for complete closure in the treatment of large burns in children. The results included a decrease in length of stay but not in mortality. In a randomized prospective trial of 85 patients with third-degree burns greater than 30% TBSA, early excision gained significantly decreased mortality in patients who were 17 to 30 years old without inhalation injury, no different mortality in adult patients older than 30 years of age or with a concomitant inhalation injury, and significantly increased mortality in children when compared with therapy of topical antimicrobial and skin grafting after spontaneous eschar separation.[100] In 1988, Tompkins et al[106] also credited the use of prompt eschar excision and grafting for the dramatically decreased mortality in severely burned children. A recent meta-analysis found that early excision of burns was beneficial in reducing mortality in patients without inhalational injury.[107]

SKIN GRAFTING AND SUBSTITUTES

The earliest record of skin grafting can be traced back to the fifth century AD, when Sushrutha, an Indian surgeon, repaired the wounds of noses using reversed skin from forehead and transplanted skin from the buttocks.[108,109] The first documentation of modern skin graft in humans was in 1823, when Carl Bunger treated a nose wound with full thickness skin from the inner thigh. The early success rate of skin grafts was low because of the inefficient harvesting and use of thick grafts.[109] In 1869, Reverdin, a Swiss medical student, introduced "pinch grafts," small circular skin discs, to deal with slowly healing or chronic wounds.[110] The method was soon popularized in England by George Pollock.[111,112] Thiersh et al[113] advocated the use of "razor flaps" in 1874. Generally, these methods were restricted to the treatment of small ulcerated wounds.

In the 1920s, Blair and Brown[114] discovered that deep islands of hair follicles and epithelial cells could be the basis of healing at skin graft donor sites. Split-thickness skin grafts subsequently became popular in the 1930s. After free hand blades with imprecise control over graft thickness, such as the Blair and Catlin knives, tools allowing precise thickness control of skin grafts quickly developed.[115]

Padgett[116] introduced an adjustable dermatome which allowed the harvest of consistent split-thickness skin grafts. Padgett[117] also advocated a categorization of split skin grafts based on thickness. The meshing of grafts was first achieved by Lanz[118] in 1907, who designed a special dermatome consisting of a series of small knives mounted in parallel to make multiple holes in a skin graft, forming a mesh. Meek successfully conducted microdermagrafting using the Meek-Wall microdermatome and prefolded gauzes to expand the graft size as much as nine times the original size.[119,120] Due to its operational complexity, the Meek microdermatome was substituted by the simpler "mesh dermatome" developed by Tanner et al in 1964. This device allowed a three-fold expansion of the harvested graft and other mesh machinery can expand grafts in ratios of 1:1 to 9:1.[121] Recent studies using the modified Meek technique have demonstrated some advantage over mesh grafts when donor sites are limited, especially in extensive burn wounds.[122–124] Furthermore, Lyons and Kagan[125] also recently found that there was great variability in the expected and observed expansion ratios achieved by skin graft meshing devices. Kamolz et al[120] also demonstrated that the micrografting technique provided more reliable and valid expansion rates, when compared with the skin meshing techniques. They recommended using the micrograft technique when large expansion ratios are required, especially in severe and extensive burns.

The first successful use of allogeneic skin graft in burn wound coverage was reported by Girdner[126] in 1881. In 1938, Bettman[127] reported success in the treatment of children with large full-thickness burn injuries covered by allograft skin. Cadaveric allogenic skin grafts were often used to prepare the granulating wound bed for autografting. In 1954, Jackson[128] introduced a combined grafting technique, which used narrow strips of allograft and autograft in a granulating or excised wound. Walker et al[96] advocated an early excision and immediate coverage with a combination of autograft and cadaver allograft for patients with large burns. In massively burned patients with limited donor sites, Alexander et al[129] developed a simple method of applying a widely meshed skin autograft and then covering it with allogenic skin.

With the advance of tissue engineering techniques, skin substitution became a prominent topic in wound-healing research. In the 1970s, Yannas and Burke developed the first bilayer artificial skin, Integra, which consists of a silastic epidermis and a porous collagen-chondroitin dermis. Burke et al[130] were also the first to use this artificial skin on patients with 50% to 95% TBSA burn after prompt excision of burn wounds. Heimbach et al[131] led the first multicenter randomized clinical trial using Integra in 1988. In 1989, Hansbrough et al[132] reported burn wound closure with cultured autologous keratinocytes and fibroblasts attached to a collagen-glycosaminoglycan substrate (composite skin graft, CSS). Further study by Boyce[133] substantiated that the use of CSS in extensive burns reduces the requirement for harvesting skin autografts, and that the quality of grafted skin was similar between CSS and skin autograft after 1 year. Fang et al[134] reviewed the research using cultured epithelial autografts and the acellular dermal matrices in the treatment of extended burn injuries and concluded that the use of acellular dermal matrix with cultured epithelial autografts is becoming increasingly routine, particularly as a life-saving tool after acute thermal trauma. Cultured skin autografts provide possible material for wound closure for patients with extensive burns, although the hospital cost, length of hospital stay, and number of readmissions for reconstruction of contractures is reported to be higher than conventional autografts.[135–137]

After approval by the Food and Drug Administration in 1996, Integra has been widely used in burns and reconstructive surgery. Other artificial skin substitutes include Apligraf (a bilayered bioengineered

skin substitute constructed by culturing human foreskin-derived neonatal fibroblasts in a bovine type I collagen matrix) and Matriderm (a scaffold consisting of native bovine types I, III, and V collagen fiber template incorporating elastin hydrolysate).[138,139]

AMNIOTIC MEMBRANE

Although amniotic membrane has been used for well over a century as a biologic wound cover, in Western medicine its use was first reported for skin transplantation in 1910 by Davis, and as a treatment for burns in 1913 by Sabella.[140,141] In the late 20th century, use of fresh amniotic membrane was precluded due to issues relative to obtaining, preparing, and storing the tissue for use in clinical practice, as well as concern regarding the potential for infectious disease transmission. More recent advanced processing methods to make amniotic membrane available in forms that are convenient and safe allow more widespread use of the tissue in contemporary practice. In 2006, a dehydrated amnion chorion membrane (dHACM) allograft (EpiFix; MiMedx Group, Inc., Marietta, GA), was made available in the market as a HCT/P tissue allograft for the treatment of acute and chronic wounds.

SUMMARY

The advancement of burn treatments has been very significant over the last 75 years. The mortality of severely and extensively burned patients has significantly decreased due to the improvements in infection control, early resuscitation, improved surgical approaches, and other treatments basing on the better understanding of the burn pathophysiology.

Establishment of a standardized, generally accepted, and effective formula of fluid resuscitation of burns still merits further investigation. Limited donor skin and deficiency of eligible skin substitutions in severely burned patients hinders early and effective wound excision and closure, leading to complications and prolonged hospitalizations. Biologic dressings and skin substitutes have contributed to improved outcomes for patients suffering from acute and chronic wounds.[142] Tissue engineered skin substitutes with all the functions of intact human skin and amniotic membrane allografts, such as dHACM, may offer the best opportunity for better outcomes.[142] Better understanding and management of the pathophysiology of burn scar contractures and hypertrophic scarring are also important areas deserving research.[143,144]

Having reviewed the History and Advancement of Burn Treatments, the following articles in this Supplement will address other important topics in the current and future management of burn patients. These will include articles by Herndon and Branski on advances in the use of amniotic membranes as biologic burn dressings; by Tenenhaus on the use of human amnion/chorion membranes in the treatment of burns and complex wounds—current and future applications; by Glat and Davenport on current techniques for burn reconstruction, including the use of dehydrated amnion/chorion membrane; and by Glat on the evolution of burn injury management in clinical practice. Lastly, a series of cases in which dHACM allografts were used in acute and reconstructive burn care are presented by Reilly, Goverman, Glat, and Lineaweaver. Together, these articles provide a comprehensive overview of the current approaches and future considerations in the treatment of these severely injured patients using dehydrated amniotic membrane allografts.

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