Advances in resuscitation and critical care have significantly improved survival after thermal injury. Ultimately, survival remains contingent on effective wound management and complete wound closure. Current approaches to burn management are based on an understanding of the biology and physiology of human skin and the pathophysiology of the burn wound.

Anatomic and Physiologic Considerations

Biology of the Skin

The skin is a complex organ composed of two distinct layers, the epidermis and the dermis; these layers are integrated by a structure known as the basement membrane zone (BMZ) [see Figure 1]. It provides containment, structure, protection, homeostasis, excretion, temperature regulation, biosynthesis, sensory perception, and appearance.

The epidermis is the outer layer and acts as the barrier between body tissues and the environment. This layer protects against infection, ultraviolet light, and evaporation of fluids and provides thermal regulation. The epidermis is derived from fetal ectoderm and, thus, like other ectodermal derivatives, is capable of regeneration. Repair of epidermal wounds is achieved through regeneration of epidermal cells both from the perimeter of the wound and from the adnexal structures of the epidermis (i.e., hair follicles, sweat glands, and sebaceous glands). Accordingly, pure epidermal injuries heal without scarring.

The principal cell of the epidermis is the keratinocyte. These cells are arranged into five progressively differentiated layers, or strata: the stratum basale, the stratum spinosum, the stratum granulosum, the stratum lucidum, and the stratum corneum. The outermost of these layers—the relatively impermeable stratum corneum—provides the barrier mechanism that protects the underlying tissues. These layers are derived from continued cell division and maturation of the basal keratinocyte stem cells at the stratum basale, the deepest level of the epidermis.

Besides keratinocytes, the epidermis contains cells from other embryologic layers that carry out specific functions. These cells include melanocytes and Langerhans and Merkel cells. Melanocytes, derived from fetal neuroectoderm, migrate to the ectoderm during normal embryogenesis and populate the interfollicular stratum basale and hair follicles. These send dendritic processes between the basal cells to the epidermis, anchoring them to the keratinocytes. Through these dendritic processes, melanosomes are transferred via phagocytosis to the adjacent keratinocytes. The melanosomes synthesize the pigment melanin through the action of the enzyme tyrosinase. Melanin provides the skin with its pigment and absorbs harmful ultraviolet radiation. Melanocytes are terminally differentiated cells without reproductive ability. Hence, deep dermal injuries often lead to cutaneous hypopigmentation.

Langerhans cells, derived from bone marrow cells, play a critical role in the immune function of the skin. These cells recognize, phagocytize, process, present foreign antigens, and, through their expression of class II antigens, initiate the rejection process in skin transplantation. Merkel cells are neuroendocrine cells that reside near hair follicles and nerve endings. These cells are transducers of fine touch. Their embryonic origin and homeostasis are a source of great debate. However, their presence in the hand and feet must be considered when deciding whether to excise and graft the volar and plantar surfaces.

In contrast to the epidermis, the dermis is a complex network comprising cellular and acellular components. This layer provides skin with its durability and elasticity. Structurally, the dermis consists of two sublayers, a superficial one (the papillary dermis) and a deeper one (the reticular dermis). Collagen is the major structural matrix molecule, constituting approximately 70% of the skin’s dry weight. Elastic fibers account for approximately 2% of the skin’s dry weight and play an important role in maintaining the integrity of the skin after mechanical perturbation. Glycosaminoglycans (GAGs) and adhesion molecules are the third major extracellular components of the dermis. These molecules help regulate intracellular and extracellular events by binding to, releasing, and neutralizing cytokines and growth factors. Adhesion molecules are crucial for cellular migration and chemotaxis in and out of the wound.

The fibroblast is the principal cell of the dermis and is responsible for synthesis and degradation of fibrous and elastic dermal proteins. The dermis also contains various bone marrow–derived inflammatory cells and other poorly understood mesenchymal stem cells, mast cells, and cells associated with vascular, lymphatic, and nervous tissue.

The BMZ is a complex region of the extracellular matrix connecting the basal cells of the epidermis with the papillary dermis. At the light microscopic level, the dermal-epidermal junction consists of protrusions of dermal connective tissue known as dermal papillae, which interdigitate with epidermal projections known as rete ridges. The structure of the BMZ is best appreciated on electron microscopy, where it appears as a trilaminar zone consisting of a central electron-dense region (the lamina densa) flanked on both sides by regions of lower electron density [see Figure 2]. Within the basal cells of the epidermis are multiple sites of attachment to the basal lamina, which are known as hemidesmosomes. On the dermal
side of the basal lamina are numerous anchoring fibrils, which reach from the lamina into the connective tissue of the dermis. The BMZ plays a significant role in burn wound healing: epithelialized wounds undergo blistering until the anchoring structures of the BMZ mature and provide protection from shearing.6

PATHOPHYSIOLOGY OF THERMAL INJURY

Jackson’s 1953 classification of burn wounds remains the foundation of our understanding of the pathophysiology of thermal injury to the skin.7 In this classification, there are three zones of tissue injury resulting from a burn [see Figure 3]. The central, most severely damaged area is called the zone of coagulation because the cells in this area are coagulated or necrotic. Tissue in this zone must be débrided. The zone of coagulation is surrounded by the zone of stasis, an area characterized by vasoconstriction and ischemia. Tissue in this zone is initially viable; however, it may convert to coagulation as a consequence of the development of edema, infection, and decreased perfusion. With good wound perfusion, tissue in the zone of stasis generally remains viable. Surrounding the zone of stasis is the zone of hyperemia, an area characterized by vasodilatation resulting from the release of inflammatory mediators from resident cutaneous cells. Tissue in this zone typically remains viable.

Clinical Evaluation and Initial Care of Burn Wound

After admission to the burn center, the burn wound is cleaned with soap and water, blisters and debris are removed, and the extent and depth of the wound are assessed. Management of tar burns warrants special mention. When tar that has been heated to maintain a liquid form comes into contact with skin, it can transfer sufficient energy to cause a significant burn injury. As the tar cools on the skin, it solidifies, thereby becoming difficult to remove. Solvents such as petrolatum, petrolatum-based ointments, lanolin, and Medi-Sol (Orange-Sol, Inc., Gilbert, Arizona) are useful for tar removal. For optimal effect, 10 to 15 minutes should be allowed after
solvent application before removal of the tar is attempted. Repeat applications may be necessary for complete removal.

**ASSessment of Burn Depth**

Thermal injury can damage the epidermis alone, the epidermis along with a portion of the dermis, or the entire skin and can even extend into the underlying subcutaneous tissue. The depth of the injury affects the subsequent healing of the wound; thus, assessment of burn wound depth is important for selection of wound dressings and, ultimately, for determination of the need for surgery [see Table 1].

Superficial burns involve only the epidermis. They typically are erythematous and painful, much as a sunburn would be. Most such burns heal within 3 to 4 days, without scarring. The usual treatment is a soothing moisturizing lotion (e.g., one containing aloe vera), which both optimizes the rate of epithelialization and provides comfort to the patient.

Partial-thickness burns extend through the epidermis and into the papillary dermis. Blistering is their hallmark [see Figure 4]. These burns can be further categorized as superficial or deep. Superficial partial-thickness burns are typically pink, moist, and painful. They usually heal within 2 to 3 weeks, without scarring or functional impairment. Deep partial-thickness wounds extend into the reticular layer of the dermis. They are typically a mottled pink-and-white, dry, and variably painful. In some cases, they may be difficult to distinguish from full-thickness burns. Deep partial-thickness burn wounds, if they do not become infected, typically heal in 3 to 8 weeks, with severe scarring, contraction, and loss of function. Therefore, if a partial-thickness burn has not healed by 3 weeks, surgical excision and skin grafting may be required.

Full-thickness burn wounds extend through the entire dermis and into the subcutaneous tissue. These burns are typically white or black, dry, and painless [see Figure 5]. Some full-thickness burns appear red, but they can be distinguished from superficial burns because they are not moist and do not blanch with pressure. Because all skin appendages are burned away, full-thickness burns can heal only by contraction or migration of keratinocytes from the periphery of the wound. Accordingly, all full-thickness burns, unless they are quite small (e.g., the size of a quarter or smaller), must be treated with excision and grafting.

As a rule, both superficial and full-thickness burns are easily recognized, and treatment decisions are relatively straightforward. It is frequently difficult, however, to determine the ultimate fate of intermediate partial-thickness burns soon after injury. For this reason, these wounds are often referred to as indeterminate-thickness wounds. Over the course of the first several postburn days, it usually becomes easier to determine which indeterminate-thickness wounds are likely to heal in a timely manner, without the need for grafting.

Various techniques for assisting the assessment of burn depth have been described, including the use of vital dyes, laser flowmetry, thermography, and magnetic resonance imaging. However, none of these adjuncts have been shown to replace the clinical evaluation of an experienced burn care provider.
Determination of Need for Escharotomy

Burn wound eschar consists of dead skin, has the consistency of leather, and may restrict limb perfusion by creating a nonelastic exoskeleton. A key issue in assessing burn wounds is whether escharotomies are necessary. In general, escharotomies are required only for circumferential full-thickness extremity burns in which distal perfusion has been compromised or for chest burns in which eschar poses an external mechanical barrier to respiration. Escharotomies can be performed at the bedside with either a scalpel or an electrocautery. They should extend through the eschar only, not through the muscle fascia. Adequate release is signaled by separation of the eschar, improved distal perfusion, and, sometimes, a popping sound. Because an escharotomy is a superficial incision through dead tissue, only minimal doses of analgesics and anxiolytics are required.

Daily Burn Wound Care

The use of hydrotherapy tanks, previously a standard component of burn unit wound care, has fallen from favor somewhat because of the risks of cross-contamination between one burn wound area and another. It is preferable to place the patient on a shower table, which is inclined so that water runs off the wounds and into a drain (see Figure 6). Smaller wounds can often be managed with bedside wound care after a shower. Increasingly, partial-thickness burns are treated with biosynthetic and or silver-impregnated materials that do not require daily wound care. Washing with tap water and regular soap suffices for daily burn wound cleansing. It is important to be cognizant of the need to provide adequate sedation and analgesia while performing daily wound care—a particularly challenging task with infants and elderly patients.

Topical Burn Wound Treatment

General Principles

Because thermal injury disrupts the protective barrier function of the skin, dressings are needed to protect the body against environmental flora. Burn dressings also protect against evaporative heat loss. The ideal burn dressing would be inexpensive and comfortable and would not require frequent changing. Daily dressing changes allow the burn care provider not only to apply clean dressings but also to clean the wounds and débride fragments of separated eschar and devitalized tissue.

Numerous topical agents and dressings are available for use in burn patients; we limit our discussion to the ones that are most commonly employed and have proved most effective. Selection of an appropriate dressing for a given wound is governed by the specific goals of management. With purely superficial wounds, the goal is to create a moist environment that will optimize epithelialization. Typically, this is achieved by applying ointments or lotions. With partial-thickness and full-thickness wounds, however, it is necessary to include agents that protect against microbial colonization (see below). Once a partial-thickness burn demonstrates evidence of epithelialization, dressings should be changed to a regimen that facilitates healing (e.g., greasy gauze with ointment).

Antimicrobial Agents

It must be emphasized that systemic antibiotic prophylaxis plays no role in the management of acute burn wounds and provides no protection against microbial colonization of burn eschar\(^{15}\); in fact, use of prophylactic antibiotics in burn patients increases the risk that opportunistic infections will...
Because eschar has no microcirculation, it is impossible for systemically administered antibiotics to reach the eschar surface, where colonization occurs. Therefore, topical preparations, which are capable of supplying high concentrations of antimicrobial agents at the wound surface, must be used. In the early postburn period, the dominant colonizing organisms are staphylococci and streptococci—typical skin flora. Over time, however, the burn wound becomes colonized with gram-negative organisms. Thus, topical antimicrobial agents used in early burn care should have broad-spectrum coverage to minimize colonization of the wound, but they need not be able to penetrate the burn eschar deeply.

Of the antimicrobial agents used in this setting [see Table 2], silver sulfadiazine is the one most commonly employed for partial-thickness and full-thickness burns. Silver sulfadiazine is soothing on application and is active against a broad spectrum of microorganisms. Because it does not penetrate eschar, very little is systemically absorbed; therefore, it is ineffective against already established burn wound infections. Wounds treated with silver sulfadiazine may form a tenacious yellow-gray pseudoeschar, which can be mistaken for true eschar. This pseudoeschar develops when silver sulfadiazine combines with the wound exudates; it can be gently débrided during daily wound care. It has been suggested that silver sulfadiazine may be responsible for the leukopenia that sometimes develops during the first week after a major burn. This attribution may not be entirely accurate, however, given that this leukopenia may also develop in patients treated with silver nitrate. It is possible that the leukopenia results not from either agent but from the margination of neutrophils secondary to the pathophysiology of the burn injury itself. In any case, the leukopenia is typically self-limited and necessitates no change in therapy. Patients with a history of sulfa allergy typically do not have adverse reactions to silver sulfadiazine; however, if there is concern about a possible reaction, a test patch can be applied to a small area of the wound. If the patient is allergic, silver sulfadiazine will cause pain on application or, in some cases, a rash.

Mafenide acetate is also commonly used in the management of burn wounds. It provides excellent coverage against gram-negative organisms, but it is not as active against staphylococci and has no antifungal activity. Unlike silver sulfadiazine, mafenide penetrates eschar very well, and this ability makes it effective in treating as well as preventing burn wound infections. Mafenide does, however, have some drawbacks. Because it is a potent carbonic anhydrase inhibitor, regular use and the consequent ongoing systemic absorption can lead to metabolic acidosis. In addition, because it is so well absorbed, twice-daily administration is necessary. Finally, topical application of mafenide, particularly to partial-thickness burns, is painful, which limits its utility in the routine management of burn wounds. Mafenide is frequently used on the ears and the nose because of its ability to penetrate eschar and protect against supplicative chondritis; however, silver sulfadiazine appears to be equally effective in this setting. Mafenide is available both as a cream and as a solution. The solution is useful as a topical agent for skin grafts when the wound bed is considered likely to benefit from postoperative antimicrobial treatment.

Silver nitrate provides broad-spectrum antimicrobial coverage, including good activity against staphylococci and gram-negative organisms (e.g., Pseudomonas). It is relatively painless on administration and must be reapplied every 4 hours to keep the dressings moist. It does not readily penetrate eschar. Silver nitrate is used in the form of a 0.5% solution, which is bacteriostatic but is not toxic to epithelial cells. The hypotonic formulation (it is reconstituted in water) can cause osmolar dilution, resulting in hyponatremia and hypochloremia. Therefore, careful electrolyte monitoring and diligent replacement are necessary. In rare cases, use of silver nitrate solution can also lead to methemoglobinemia; if this condition is detected, administration of silver nitrate should be discontinued. A principal disadvantage of silver nitrate solution is that it stains everything it touches black.

Newer silver-containing dressings are now manufactured, improving care by decreasing the need for daily wound care. Some dressings contain nanocrystalline silver embedded on a high-density polyethylene mesh (Acticoat, Smith & Nephew, New Zealand).

### Table 2  Topical Antimicrobial Agents Used in Burn Care

<table>
<thead>
<tr>
<th>Agent</th>
<th>Antimicrobial Coverage</th>
<th>Advantages</th>
<th>Disadvantages/Precautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacitracin</td>
<td>Gram-positive bacterial</td>
<td>Soothes and moisturizes; good for facial care and epithelializing wounds</td>
<td>Not appropriate for deeper wounds</td>
</tr>
<tr>
<td>Mafenide</td>
<td>Broad-spectrum antibacterial; anticostral</td>
<td>Penetrates eschar well; available as solution or cream</td>
<td>Painful on application; causes metabolic acidosis (via carbonic anhydrase inhibition)</td>
</tr>
<tr>
<td>Mupirocin</td>
<td>Anti-MRSA</td>
<td>Effective against MRSA</td>
<td>Narrow (poor gram-negative) antimicrobial coverage</td>
</tr>
<tr>
<td>Nystatin</td>
<td>Antifungal (Candida)</td>
<td>Provides fungal prophylaxis with swish-and-swallow solution</td>
<td>May interfere with activity of mafenide</td>
</tr>
<tr>
<td>Silver nitrate</td>
<td>Broad-spectrum antibacterial</td>
<td>Effective for both prophylaxis and treatment of wound infection</td>
<td>Penetrates eschar poorly; causes hyponatremia; stains linen and dressings; induces methemoglobinemia</td>
</tr>
<tr>
<td>Silver sulfadiazine</td>
<td>Broad-spectrum antibacterial; antipseudomonal</td>
<td>Soothes on application and causes no pain</td>
<td>Penetrates eschar poorly; causes leukopenia</td>
</tr>
</tbody>
</table>

MRSA = methicillin-resistant Staphylococcus aureus.
London, England), embedded in hydrofibers (Aquacel AG, ConvaTec Bristol-Meyers Squibb Company, Skillman, New Jersey), or attached to a soft silicone dressing (Mepilex Ag, Mölnlycke Health Care US, LLC, Norcross, Georgia). It is speculated that the nanocrystalline silver provides a sustained release of elemental silver, contributing to aerobic, anaerobic, gram-positive and gram-negative antimicrobial activity.13 Acticoat has been successfully used for coverage of partial-thickness burns, as well as for coverage of donor sites and meshed skin grafts.14 With burn wounds, the Acticoat dressing is typically changed every 3 days. The reduced frequency of dressing changes simplifies burn care somewhat but can hinder evaluation of evolving partial-thickness burns. With donor sites, Acticoat can be left in place until the underlying partial-thickness wound heals. Typically, an adhesive tape such as Hypafix (Smith & Nephew) is used to secure the dressing to the donor site for 7 days. Once the tape has been removed, the Acticoat usually is sufficiently adherent to allow patients to shower daily and towel-dry the dressing until it eventually peels off the healed wound. The development of nanocrystalline silver–embedded products has increased the treatment modalities of the burn patient.

Bacitracin, neomycin, and polymyxin B have all been used for coverage of superficial wounds in conjunction with Xeroform or petrolatum gauze to accelerate epithelialization and minimize colonization. These ointments also are commonly administered several times daily in the care of superficial face burns. Mupirocin has proved effective in treating methicillin-resistant Staphylococcus aureus (MRSA) colonization; however, because of the potential for the development of bacterial resistance, it should be employed only in MRSA-positive wounds.

Surgical Burn Wound Management

As noted [see Clinical Evaluation and Initial Care of Burn Wound, Assessment of Burn Depth, above], superficial burns and superficial partial-thickness burns typically heal without any need for surgical excision and grafting. Dressing changes and wound care can remove necrotic debris and provide an environment conducive to healing in a timely fashion (2 to 3 weeks), with minimal scarring. For deep partial-thickness and full-thickness burns, however, operative débridement with subsequent skin graft coverage is necessary. Timely removal of eschar is critical for successful management. Surgical excision removes necrotic tissue that serves as a nidus for microbial proliferation and the development of burn wound sepsis.15,16

EARLY EXCISION AND GRAFTING

Surgical excision of burn wounds is a concept whose importance was not fully appreciated until the 1970s. Previously, the usual practice was to leave eschar intact over the wound surface, the idea being that proteolytic enzymes produced by migrating neutrophils and bacteria within the contaminated eschar would cause a natural separation of the eschar from the wound bed (sloughing) and that the resulting granulating wound would serve as the bed for grafting. The rationale for delaying surgical management was that it would presumably allow the burn care provider time to determine which wounds would heal spontaneously and which would have to be covered with skin grafts. It has since become clear, however, that in cases of extensive burn injury, delayed management results in more extensive bacterial colonization, as well as an increased likelihood of burn wound sepsis, multiple organ failure, and, ultimately, death.

Early excision and skin grafting of small burn wounds were first described by Lustgarten in 1891.15 After the Cocoanut Grove fire in 1942, Cope and colleagues suggested that patients treated with early excision and grafting had better overall outcomes.18 In 1960, Jackson and colleagues reported discouraging results with early burn wound excision,19 and it was not until 10 years later, when Janzekovic reported good results with surgical burn wound excision,20 that enthusiasm for early excision was rekindled. As clinical experience with early excision was accumulated, the benefits became clear.

Since Janzekovic’s report, studies have repeatedly shown that early wound excision and closure improve survival, reduce the infection rate, and shorten hospital stay. Other studies have demonstrated that early removal of dead and severely damaged tissue interrupts and attenuates the systemic inflammatory response syndrome (SIRS).15,16,21–24 Early excision of deep burn wounds also appears to decrease hypertrophic scarring. Similarly, early excision and grafting have been shown to be beneficial for burns of indeterminate depth. In a study of patients with burns covering less than 20% of their total body surface area (TBSA), early excision and grafting reduced length of stay, cost of care, and time away from work in comparison with nonoperative treatment.25

WOUND EXCISION

Early staged excision, beginning as early as postburn day 3 if feasible, is now conventional treatment for major burns. Operations are spaced 2 to 3 days apart until all eschar is removed and full wound coverage is achieved. Débrided wounds can be temporarily covered with biologic dressings or cadaveric allograft until autogenous donor sites are available.26,27

Generally, the decision whether to perform operative wound excision is guided by whether spontaneous wound healing is likely to occur in a timely fashion (i.e., within 2 to 3 weeks after the burn). Burn wounds over joint surfaces, however, should undergo excision and grafting sooner so as to minimize healing by wound contraction, which can ultimately lead to disabling contractures. In patients with extensive burns, hemodynamic and pulmonary status must be considered in deciding on the timing of operation. Any critically ill burn patient will have some degree of respiratory dysfunction, but the patient should at least be capable of being safely transported from the intensive care unit to the operating room and back. The risk of hypothermia and the need for blood transfusion must be anticipated before operation and clearly communicated to the anesthesiologist.

There are two main technical approaches to surgical excision of the burn wound: fascial excision and tangential excision. Fascial excision, as the name suggests, involves excising the burned tissue and the underlying subcutaneous tissue down to the muscle fascia [see Figure 7]. A major advantage of fascial excision is that it yields an easily defined plane that is well vascularized and therefore can readily accept a graft. In addition, bleeding is generally easier to control at the fascial level of dissection because the vessels are easier to identify and coagulate. Furthermore, the entire excision can
be performed with the electrocautery, and blood loss is thereby minimized. The principal drawback of this approach is that the excision inevitably includes some healthy, viable subcutaneous tissue. Another disadvantage is that the removal of subcutaneous tissue may create an unaesthetic contour deformity.

Tangential excision, as the name suggests, involves sequentially excising the layers of eschar in a tangential fashion until a layer of viable bleeding tissue capable of supporting a skin graft is encountered [see Figure 8]. The goal is to remove only the nonviable tissue, particularly in the case of deep dermal wounds. Typically, tangential excision is performed with a handheld knife (a Watson knife or a Weck/Goulian blade). A back-and-forth carving motion is used, and very little force is applied. The guard on the knife can be used to control the depth of excision. The appearance of diffuse punctate bleeding signals that viable tissue has been reached. The main disadvantages of tangential excision are that (1) it may be difficult to control the diffuse bleeding from the wound bed, and (2) it may be difficult to assess the suitability of the underlying fat for accepting a graft.

A water jet–powered instrument (VersaJet Hydrosurgery System, HydroCision, Andover, Massachusetts) is available that can be used for tangential burn wound excision. This device offers an easy and relatively precise way of excising eschar and is particularly useful for excising nonviable tissue from the concave surfaces of the hands and feet, as well as the eyelids and ears.

To minimize hematoma formation and graft loss, it is critical that adequate hemostasis be achieved before the placement of skin grafts, cadaveric grafts, or skin substitutes. Telfa pads (Kendall, Mansfield, Massachusetts) soaked in an epinephrine solution (1:10,000) are a mainstay of hemostasis, combined with topical pressure and cauterization when necessary. A fibrinogen thrombin delivery system (Tisseel Fibrin Sealant, Baxter, Deerfield, Illinois) is commercially available that improves the ability to control bleeding after excision.

Regardless of which excision technique is used, blood-conserving strategies should be used routinely to minimize transfusion requirements. These strategies include manual pressure, use of topical epinephrine and/or fibrin sealant, tumescence of burn wounds with vasoactive medications, and the use of tourniquets. The extremities can be suspended from operating room ceiling hooks [see Figure 9] to provide access to their entire circumference.

SKIN GRAFTING

The best replacement for lost skin is clearly skin itself. The first known report of skin grafting comes from the *Sushruta Samhita*, an ancient Indian surgical treatise that may date back as far as the seventh century BC. This text describes the use of both skin flaps and grafts for the repair of mutilations of the nose, the ears, and the lips. The Indian method of grafting was first introduced to Western medicine by English surgeons, who observed it during the late 18th century.
It was not until 1804 that successful transplantation of free skin grafts was reported by Baronio of Milan, who successfully grafted large pieces of autogenous skin onto different sites on sheep.\textsuperscript{34} In 1869, Jacques Reverdin, in a report to the Société Imperiale de Chirurgie, described the use of a small epidermal graft, which became known as the pinch graft.\textsuperscript{35} This technique did not, however, gain wide recognition until 1870, when successful experiments in skin grafting for the treatment of burn patients were performed by George David Pollock.\textsuperscript{36} In 1872, Ollier described the use of both full-thickness and split-thickness skin grafts and realized the possibility of covering large areas with such grafts if a satisfactory method of cutting them could be devised.\textsuperscript{34}

Currently, a 95\% success rate is the standard of care for skin grafting. To achieve this level of success requires adequate wound bed preparation (see above), careful selection of suitable donor sites, and appropriate postoperative care.

Skin grafts are broadly classified as either full-thickness or split-thickness grafts, depending on whether they contain the full thickness of the dermis or a partial thickness. Split-thickness grafts are further categorized as thin, intermediate, or thick, depending on the amount of dermis harvested with the graft. The thinner the skin graft, the greater the degree of contraction that occurs at the recipient site after engraftment. Although thicker grafts have the advantage of contracting less, they leave a greater dermal deficit at the donor site, which can lengthen the time needed for healing and increase the risk of hypertrophic scarring at that site.

Full-thickness skin grafts can be harvested either through use of a dermatome or through direct excision of skin from the flank, the groin crease, the hypothenar eminence, or the forearm, which can be used for coverage of small defects of the hand or the face. Standard (intermediate) split-thickness grafts are typically harvested at a thickness of 0.010 to 0.012 in. Thin (0.006 in.) split-thickness skin grafts are generally used in conjunction with skin substitutes, whereas thick (0.018 to 0.025 in.) split-thickness grafts are typically used in grafting of the hand and the face. The thickness of the graft depends both on the dermatome setting and on the pressure the harvester applies to the dermatome during harvesting.\textsuperscript{37}

Donor-site selection for split-thickness skin grafts is based on the distribution of the burn. The anterolateral thigh, when available, is the donor site of choice for most adult patients: it can be harvested in the supine position, it can easily be left open to the air so the donor-site dressing can dry, and it can be covered by shorts if desired. When larger grafts are needed or the thighs are burned, the back, the buttocks, and the abdomen can serve as donor sites. Subcutaneous infiltration of a physiologic salt solution yields a smooth, firm surface that facilitates the harvesting of these areas. If this is done, the anesthesiologist should be informed that additional fluid is being administered. In children, the buttocks and the scalp are commonly employed as donor sites. Once healed, these sites are usually inconspicuous: the buttock donor site can be harvested in such a way that it can be covered by a bikini, and the scalp donor site is typically covered by regrown hair. It is important to reassure the patient’s parents that if the graft is harvested appropriately, the donor site will not exhibit alopecia and the recipient site will not grow hair. Generally, however, these sites are sufficient only for the grafting of small wounds.

Skin grafts can be applied as sheet (or unmeshed) grafts, or they can be meshed at ratios ranging from 1:1 to 4:1. Meshing allows the egress of serum and blood from wounds, thereby minimizing the risk that hematomas or seromas will form that could compromise graft survival. In addition, meshed grafts can be expanded or stretched to cover larger surface areas. When grafts are meshed at ratios of 3:1 or higher, allograft skin or another biologic dressing can be applied over them to prevent the interstices from becoming desiccated before they close.\textsuperscript{38} Because of the lack of dermis in the interstices, widely expanded mesh always scars, takes a long time to close, and results in permanent unattractive mesh marks. In our center, widely spread mesh is never used unless it is grafted onto a dermal template to minimize scarring (see below).

Sheet grafts should be used on the face, the neck, the hands [see Figure 10], and, whenever possible, the forearms and the legs. In these exposed areas, the superior cosmetic and functional results obtainable with sheet grafts make such grafts preferable. Because sheet grafts have no interstices, they must be closely monitored and periodically rolled with a cotton-tipped applicator to drain any fluid collection. Any serous or bloody blebs that form beneath the graft should be incised with a No. 11 scalpel and drained expeditiously. A common practice known as pie-crusting, which involves making incisions in a sheet graft at the time of surgery, actually does not yield much improvement in graft survival, because blebs often form in areas without incisions. Use of fibrin sealant at the time of grafting may lower the incidence of blebs.\textsuperscript{39}

**Graft and Donor-Site Dressings**

Once the graft is secured in place, a dressing may be applied to protect it from shearing, as well as to accelerate closure of meshed graft interstices. Numerous options for graft dressings exist, including wet dressings and greasy gauze. The use of a nonadherent dressing such as Conformant 2 (Smith & Nephew) along with an outer antimicrobial wet dressing allows the overlying dressings to be periodically removed without dislodging the graft from the wound bed. Bolsters consisting of cotton and greasy gauze are employed to help grafts conform to concave wound surfaces, and splinting of extremities may be necessary for safe graft immobilization, especially over joints. A vacuum-assisted closure system can

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**Figure 10** Sheet grafts are the gold standard for skin grafting of the face, the neck, and, whenever possible, the forearms and the legs. This 1-month follow-up demonstrates the aesthetic superiority of sheet grafts.
be used as another option for promoting graft healing. Alternatively, an Unna boot can be placed on both the upper and the lower extremity to immobilize the graft and provide vascular support, allowing mobilization of the extremity in the immediate postoperative period.\(^{40}\)

Sheet grafts can be either left open to the air to allow continuous monitoring or wrapped with dry dressings, which can be removed if necessary to allow interval inspection and deblebbing.

There are also various options for donor-site dressings. The ideal donor-site dressing would not only minimize pain and infection but also be cost-effective. Greasy gauze or a nanocrystalline silver-embedded material is often employed for this purpose. Typically, these dressings are left in place until the donor site epithelializes, at which time the dressing is easily separated from the healed wound. Op-Site (Smith & Nephew), a transparent polyvinyl adhesive film, is also commonly used. With Op-Site, the underlying wound is easily examined without removal of the dressing; however, intermittent drainage of the wound fluid that accumulates is necessary. Op-Site does not work well over joint surfaces and concave or convex areas (e.g., the back). Silver sulfadiazine in a diaper is an excellent covering for buttock donor sites in children; dressing changes can be done with each diaper change.

### POSTOPERATIVE WOUND CARE

Even with complete graft take and timely donor-site epithelialization, several wound management issues may still arise in the early postoperative period. Physical therapy must be initiated in this period, and management of scarring must be addressed. Blisters are common on newly healed donor sites and ungrafted wounds. The new epithelial layer of these wounds lacks the connections to the underlying wound bed normally provided by the BMZ, which protect the epidermis from shearing. During the months it takes for these structures to reconstitute, their absence frequently leads to blistering. These blisters are usually best managed by draining them with a clean pin, reapplying the epithelial layer to the wound surface, and covering the site with adhesive bandages. The bandages can be soaked off in the shower to ensure that the adhesive causes no additional injury.

Inclusion cysts may develop in healed grafts that were placed over excised wound beds that still contained a thin layer of dermis with adnexal structures. The secretions from the adnexal structures collect beneath the skin graft to form the cysts. Inclusion cysts are treated by unroofing the affected area with a needle.

A condition known as sponge deformity (so called because the skin looks like a bridge of coral sponge [see Figure 11]) may occur if a skin graft is placed over a wound that heals underneath the graft in multiple small areas, with or without sloughing of the overlying graft.\(^{41}\) Where the graft does not slough, a bridge forms. This unsightly deformity can be treated by incising the bridges over the healed tissue with sharp scissors.

Healed donor sites, skin grafts, and ungrafted burns can also break down as a result of infection—a process referred to as melting. Such melting can occur quite rapidly: a graft or healed wound that demonstrates complete take one day may exhibit significant breakdown the next day. Wound cultures should be obtained from these areas, and the open sites should be treated with topical antibiotic ointment and, if the problem worsens, systemic antibiotics.\(^{41}\)

Malignant degeneration can occur in healed burn wounds decades after the initial injury. These tumors—known as Marjolin ulcers—are usually squamous cell carcinomas and are more aggressive than typical skin cancers. Marjolin ulcers have a high metastatic potential and are associated with a high mortality. New or chronic ulcers in burn wounds should raise the suspicion of malignancy and be considered an indication for biopsy.\(^{43}\)

### BIOLGIC DRESSINGS AND SKIN SUBSTITUTES

As noted [see Early Excision and Grafting, above], conventional burn wound management dictates early, aggressive excision of burn wound eschar to minimize the chances of sepsis or progression of burn wound depth.\(^{15,16,21-24}\) In some cases, the body surface area to be excised is larger than can be covered by autografts from the available donor sites. The solution is to strategically select areas for autograft coverage and then temporarily cover the remaining open areas with biologic dressings. Donor sites typically epithelialize within about 2 weeks, after which time they can be reharvested, allowing temporary dressings to be serially removed and covered with new autograft.\(^{26,44}\)

Biologic dressings perform several important functions. By adhering to the wound bed, they provide a physical covering that controls water vapor transmission, thus minimizing loss of water, electrolytes, and proteins and preventing desiccation and maceration of wounded tissue (which can lead to extension of the depth of injury). In addition, biologic dressings help prevent microbial invasion from the environment.\(^{26,45,46}\)

### ALLOGRAFT AND XENOGRAFT SKIN

Although the technique of skin grafting is thousands of years old, skin grafting between individuals was not reported until the late 19th century. In 1869, Reverdin published a report on the transplantation of small epidermal grafts from his own arm onto a patient’s burn wound.\(^{39}\) In 1881, Girdner described transplantation of skin grafts from a cadaver to a
burn patient and reported a 75% immediate take rate. It was widely noted that these grafts initially performed well but survived for only 6 to 8 weeks. The mechanisms underlying the rejection of these grafts were eventually elucidated by the efforts of Sir Peter Medawar, who received the Nobel Prize in 1960 for his seminal work on defining the basis of allograft rejection and tolerance induction.

The use of allograft was popularized by James Barrett Brown in the 1940s and 1950s, and with the subsequent development of skin banking, allograft became the standard temporary graft for excised burn wounds when sufficient autograft is unavailable or autografting is not indicated.

Ultimately, allograft skin is always rejected unless the donor and the recipient are immunologically identical. The rejection process usually begins within 10 days in an immunologically competent host, but allografts can be tolerated for up to 1 month in a host who is severely immunocompromised (e.g., as a result of extensive burn injury). The use of immunosuppressive agents such as cyclosporine has led to the achievement of prolonged allograft tolerance, but it also exposes the burn patient to the risks inherent in prolonged systemic immunosuppression.

In addition to providing temporary wound closure, allograft has been used as an overlay for meshed autograft with the aim of accelerating epithelialization of the interstices. Allograft has also been used to cover donor sites after autograft harvesting and to cover wounds after excision as a means of assessing the suitability of a bed for autograft placement.

Recognition of the weaker immunogenicity of the dermal layer of cadaver allograft stimulated various attempts to employ allograft for permanent dermal replacement. Jackson and colleagues were the first to report the use of alternating strips of autograft and allograft for definitive closure of large burn wounds. In 1985, Heck and colleagues constructed the first deliberate combination of allogeneic dermis with autologous epidermis. This basic idea was subsequently expanded on by Cuono and colleagues, who used cryopreserved allogeneic dermis as a bed for autologous keratinocyte cultures. These investigators demonstrated long-term survival and documented the reconstitution of a normal-appearing BMZ with anchoring fibrils.

Use of allograft skin as a temporary cover or as the permanent dermal replacement in the composite technique does have several drawbacks, including the limited availability of suitable skin, the variable quality of the skin obtained, the substantial cost of allograft procurement and preservation, and the significant potential for disease transmission.

Xenografts from a number of species have also been used as biologic dressings. Porcine xenograft has been used in the management of exfoliative skin disorders (e.g., toxic epidermal necrolysis) as well as for temporary wound coverage after excision and before definitive autografting.

Since the 1980s, research efforts have focused on the development of skin replacements that could serve as either a temporary or a permanent substitute for human skin. Conceptually, any skin replacement must recapitulate the native skin biology—that is, it must include an epidermal component, a dermal component, and a BMZ equivalent linking the two.

CULTURED EPIDERMAL AUTOGRAFTS

Replacement of the epidermis alone was successfully accomplished in the 1970s with the development of cultured epidermal autografts (CEAs). In 1975, Rheinwald and Green reported the successful isolation and culture of epidermal keratinocytes, and several years later, O’Connor and colleagues reported the first clinical use of CEAs to cover burn wounds. In 1984, Gallico and colleagues described the use of CEAs to resurface the burn wounds of two children who had sustained injuries over 95% of their TBSA. CEAs are grown in the laboratory from a biopsy of the patient’s own skin. A current example is Epicel (Genzyme Biosurgery, Cambridge, Massachusetts), which has been approved by the Food and Drug Administration (FDA) for use in the United States but requires Institutional Review Board approval and separate informed consent because of concern that the feeder layer for the keratinocytes is of murine origin.

CEAs are most commonly applied to the granulation tissue of chronic wound beds. As more clinical experience with CEAs was amassed, the drawbacks of using epidermal components alone to replace full-thickness skin loss became evident. The lack of a dermal component made the CEAs extremely fragile and led to high rates of sloughing and infection. Even when CEA engraftment occurred, the BMZ structures critical to graft durability were poorly reconstructed. Compton and colleagues compared the outcome of wounds covered with CEAs alone with the outcome of wounds covered first with allograft dermis and then with CEAs. They found that in wounds containing the allograft dermal component, there was greater initial take, better long-term durability, and accelerated formation of important BMZ structures. It is now well recognized that CEAs are capable of replacing the epidermis but are not effective when used alone to resurface deep partial-thickness and full-thickness wounds. Bilayer skin substitutes consisting of both dermal and autologous epidermal cultured cells are being developed to reduce the time for maturation on the patient. Although the theoretical applications are vast, the successes of these products have never been demonstrated in prospective randomized trials. Another potentially promising concept is use of dispersed cells in conjunction with widely meshed grafts to decrease time to closure and decrease scarring.

In vitro development of an epidermal replacement was made possible by the simpler biology of the epidermis. Development of a dermal replacement has proved a more formidable challenge. Dermis consists mainly of extracellular matrix, and its complex structure is not amenable to growth in culture.

SKIN SUBSTITUTES

The drawbacks of allograft and xenograft skin have further underscored the need for an off-the-shelf dermal replacement. Yannis, Burke and colleagues described a pioneering approach to the development of a skin replacement containing both an epidermal and a dermal component in the early 1980s. Recognizing the importance of the dermis in skin replacement, they developed a bilayer construct that is now commercially available under the name Integra (Integra LifeSciences Corporation, Plainsboro, New Jersey). The epidermal component of this construct consists of a layer of Silastic film, which acts as a protective barrier against infection and evaporation from the wound bed; the dermal layer
Integra consists of a porous matrix of fibers composed of cross-linked bovine collagen and a single type of GAG (chondroitin-6-sulfate). Integra can be placed on a completely excised, noninfected wound bed. Initial studies indicated that a neodermis forms, created by the ingrowth of fibroblasts and endothelial cells into the dermal matrix template provided by the Integra. Once this neodermis forms and the dermal scaffold is well incorporated into the wound (typically, after 14 days), the Silastic component is removed. A thin (0.006 in.) split-thickness autograft is then placed on the neodermis [see Figure 12].\textsuperscript{27,78,79} Integra not only is a useful adjunct in the management of large burn wounds but also can play an important role in the management of hand and facial burns requiring excision and grafting.\textsuperscript{80–82} It must be emphasized, however, that for Integra to vascularize completely, it must be applied to a viable, noninfected wound bed. In addition, meticulous surgical technique and appropriate postoperative care are critical for a successful outcome.

Another product marketed for dermal replacement is Alloderm (LifeCell, Branchburg, New Jersey), which is an acellular dermal matrix produced from human cadaveric skin. The cadaveric skin is first stored in normal saline for 15 hours to remove the epidermal component. The cadaveric dermis is then incubated in sodium dodecyl sulfate to extract any remaining cellular components. The decellularized substrate is freeze-dried and reconstituted by soaking it in crystalloid solution before use.\textsuperscript{26} Alloderm can be used for immediate wound coverage in combination with a thin split-thickness autograft. Data from multicenter trials indicate that Alloderm works best with thin (0.006 to 0.008 in.) autografts: the thicker the autograft, the lower the take rates.\textsuperscript{26,27,83} Alloderm has also been used for abdominal wall reconstruction and for soft tissue augmentation in the face.

A product known as TransCyte (Smith & Nephew)—formerly Dermagraft-TC—is approved by the FDA as a temporary (as opposed to permanent) cover for full-thickness wounds after excision. TransCyte is produced by seeding neonatal fibroblasts isolated from foreskin onto Biobrane, a synthetic dressing consisting of Silastic attached to a nylon mesh, which is coated with porcine peptides prepared from type I collagen. The Silastic layer of Biobrane serves as a temporary permeable barrier, whereas the fibroblast-impregnated nylon mesh serves as a dermal component.\textsuperscript{26,27} Dermagraft (Smith & Nephew), in contrast, is employed as a permanent dermal replacement. Dermagraft consists of human neonatal fibroblasts seeded onto an absorbable polyglactin mesh scaffold, which is intended to mimic the native dermal architecture.\textsuperscript{26,27} It is approved by the FDA for treatment of venous stasis ulcers, but it was developed for coverage of excised burn wounds in conjunction with a split-thickness autograft.

Although a permanent off-the-shelf skin replacement has yet to be developed, the available products have already significantly influenced the management of burn wounds. In addition, the shortcomings of each product and strategy have improved our understanding of skin biology and physiology and confirmed the importance of both the epidermis and the dermis in the structure and function of skin.

Financial Disclosures: None Reported

References


Acknowledgments

Figure 1  Tom Moore
Figure 2  Seward Hung