CME

A Practical Guide to Wound Healing

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Learning Objectives: After reading this article, the participant should be able to: 1. Understand the basic stages of wound healing. 2. Apply current techniques to achieve wound closure. 3. Manage patients with simple and complex wounds effectively.

Summary: While wound healing can still be divided into stages, numerous intrinsic and extrinsic factors must be considered as well if clinical success is to be reliably achieved. While a routine wound may require nothing more than a simple dressing, the more complex and challenging wounds may benefit from more advanced therapy, such as growth factor applications, specialized dressings, or adjunctive therapy. This article will attempt to provide a concise summary of the advances in the basic and clinical science of wound healing. (*Plast. Reconstr. Surg.* 125: 230e, 2010.)

Although most wounds can be expected to heal uneventfully, infection, dehiscence, and delayed healing continue to be problems, with significant associated morbidity, mortality, and economic cost.[1,2] Advances in the basic science of wound healing and its clinical application have led to numerous new therapies, products, and modalities that are constantly changing our approach to wound management.[3]

BASIC SCIENCE OF WOUND HEALING

Wound healing is a complex process, involving a daunting array of cell variants, cytokines, growth factors, and matrix elements, the most relevant of which are listed in Table 1. Although a simplification, the classic division of wound healing into inflammatory, proliferative, and remodeling phases is still useful in understanding both routine and pathologic wound healing.[4]

Hemostasis (Seconds to Minutes)

The immediate response to injury is vasoconstriction caused by the release of thromboxane and prostaglandins. Platelets adhere to exposed collagen and release the contents of their granules, whereas tissue factor activates both platelets and the coagulation cascade.[5] The resulting fibrin-platelet matrix, in addition to controlling hemorrhage, concentrates growth factors and serves as a scaffold for wound healing.[6,7]

Inflammation (3 to 5 Days)

Prostaglandins, histamine, serotonin, kinins, and bacterial products cause vasodilatation and capillary permeability, resulting in edema. A wide variety of factors and cytokines, including fibronectin, interleukin-1, tumor necrosis factor-α, and platelet-derived growth factor, attract granulocytes to the wound.[8,9]

Neutrophils appear in the wound shortly after injury and phagocytize debris and bacteria. Proteases secreted by neutrophils digest debris and injured tissues, whereas oxygen-dependent killing mechanisms are used to control bacterial contamination. Within 24 to 48 hours, local monocytes migrate into the wound and become macrophages. Although macrophages have a phagocytotic role, they also produce a wide array of growth factors. Experiments reveal that although wound healing

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Related Video content is available for this article. The videos can be found under the "Related Videos" section of the full-text article.

Table 1. Cytokines Involved in Wound Healing

Factor	Source	Effect
Epidermal growth factor	Platelets, macrophages, endothelium	Chemotaxis, stimulates angiogenesis, wound contraction, fibroblast proliferation
Transforming growth factor-α	Macrophages, lymphocytes, keratinocytes	Stimulates keratinocyte and fibroblast proliferation, migration
Transforming growth factor-β	Platelets, lymphocytes, macrophages, endothelium, keratinocytes	Chemotactic, stimulates angiogenesis and fibroblast proliferation
Fibroblast growth factor	Macrophages, lymphocytes, endothelium, mast cells	Stimulates angiogenesis, keratinocyte and fibroblast proliferation, migration
Keratinocyte growth factor	Fibroblasts	Stimulates keratinocyte migration, differentiation, and proliferation
Tumor necrosis factor	Macrophages, lymphocytes, mast cells	Causes fever and corticotropin-releasing hormone secretion, suppresses appetite, stimulates acute-phase responses, stimulates macrophages, fibroblasts, angiogenesis
Interleukin-1	Macrophages, lymphocytes, mast cells	Causes fever, stimulates acute-phase response, stimulates neutrophils, macrophages, TNF, interferon release
Interleukin-2	Macrophages, lymphocytes, mast cells	Causes fever, stimulates macrophages, causes lymphocyte differentiation and proliferation
Interleukin-6	Macrophages, lymphocytes, mast cells	Causes fever, stimulates acute-phase response, up-regulation of Toll-like receptors
Interleukin-8	Macrophages, lymphocytes, mast cells	Chemotactic, stimulates neutrophils
Platelet-derived growth factor	Platelets, macrophages, endothelium	Chemotactic, stimulates fibroblasts, angiogenesis, wound contraction
Vascular endothelial growth factor	Keratinocytes, hypoxic cells	Stimulates angiogenesis
Endothelium-derived growth factor (nitric oxide)	Endothelium	Vasodilatation, antibacterial action, angiogenesis, apoptosis

progresses normally in the absence of neutrophils, macrophages are essential to the process.[10,11]

Although inflammation is important in both controlling contamination and inducing the proliferative phase of wound healing, prolonged or intense inflammation can cause injury to viable tissues. In addition to their local effects, inflammatory mediators can result in a systemic inflammatory response. Failure to progress to proliferation results in a chronic wound.

Proliferation (4 to 14 Days)

The process of reepithelialization occurs soon after injury. Reepithelialization relies on the migration of epithelial cells from the wound margins and from any remaining adnexal structures in the dermis, such as hair follicles, sebaceous glands, and sweat glands. Epithelial migration and proliferation continue until the wound is covered and an intact epithelial barrier is reestablished.[12] Although many surgeons prefer to keep wounds dry, a moist environment helps promote more rapid epithelialization,[13] and washing a surgical incision the day after surgery does not appear to increase the incidence of complications.[14]

The low oxygen tension and high lactate levels characteristic of the poorly perfused wound stimulate the production of angiogenic factors, which encourage new capillary growth.[15,16] Matrix metalloproteinases break down the extracellular matrix to allow the penetration of these new vessels.[17] As local oxygen tension increases, the stimulus for angiogenesis declines, and vessels that are no longer needed undergo apoptosis.

Within 2 to 3 days, activated fibroblasts have migrated into the wound. The initial wound matrix, composed primarily of fibrin and fibronectin, is supplemented by glycosaminoglycans, proteoglycans, and other proteins produced by fibroblasts. Fibroblasts begin secreting disorganized collagen, high in immature type III collagen, into this provisional matrix.[18] Some fibroblasts are stimulated to become myofibroblasts, which are responsible for wound contraction.[19–21] As collagen production does not begin for several days after initial wounding, early motion rehabilitation protocols that wait until this point to start range of motion may reduce the risk of additional bleeding while still minimizing the degree of adhesion formation.

Remodeling (Day 8 to 1 Year)

Fibroblasts continue producing collagen even as various proteases are produced to digest it. Net collagen synthesis lasts approximately 4 to 5 weeks, but increased collagen turnover continues for up to 1 year following injury.[22,23] Over time, the frac-

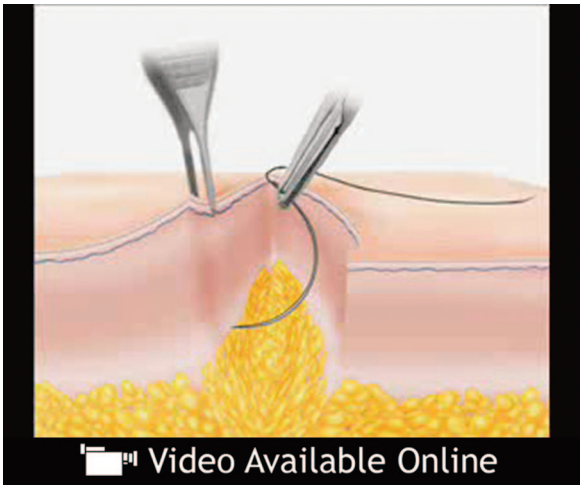
tion of type III collagen decreases as it is replaced by stronger type I collagen and collagen fibrils become increasingly organized. After 1 week, the wound has only 3 percent of its preinjury breaking strength, increasing to 30 percent at 3 weeks, and peaking at roughly 80 percent approximately 3 months following injury.[24] Depending on the stresses across the wound, suture selection should vary accordingly. Poliglecaprone suture retains only 20 to 30 percent of its breaking strength in vivo after 2 weeks, whereas polyglactin lasts twice as long and polydioxanone lasts longer still.[25,26]

BASIC SKIN SUTURING FOR MEDICAL STUDENTS AND RESIDENTS

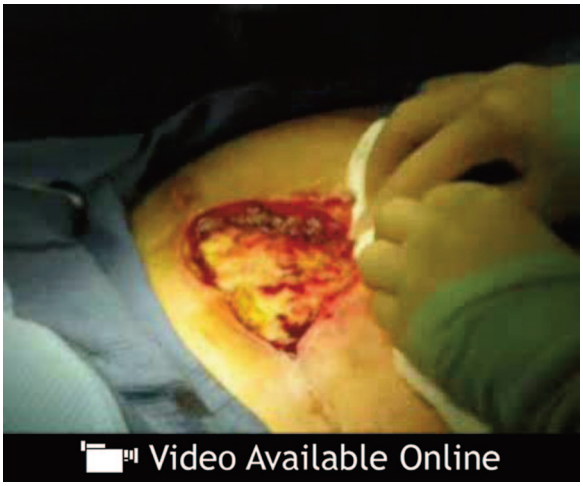
For a video explaining basic suturing, the avoidance of sutures marks (scars), painless suture removal, and optimal cosmetic results, a video has been provided. (**See Video 1,** which demonstrates basic skin suturing, available in the "Related Videos" section of the full-text article on www.PRSJournal.com.)

BASIC WOUND MANAGEMENT

Performing proper débridement and control of infection and ensuring adequate blood flow, using arterial bypass or angioplasty if necessary, remain the keys to initial wound management regardless of what reconstruction may ultimately be required.[27] (**See Video 2,** which demonstrates basic soft-tissue débridement; **Video 3,** which demonstrates acute burn débridement; and **Video 4,** which demonstrates hard-tissue débridement, all available in the "Related Videos" section of the full-text article on www.PRSJournal.com.)



Video 1. Video demonstrating basic skin suturing is available in the "Related Videos" section of the full-text article on www.PRSJournal.com.

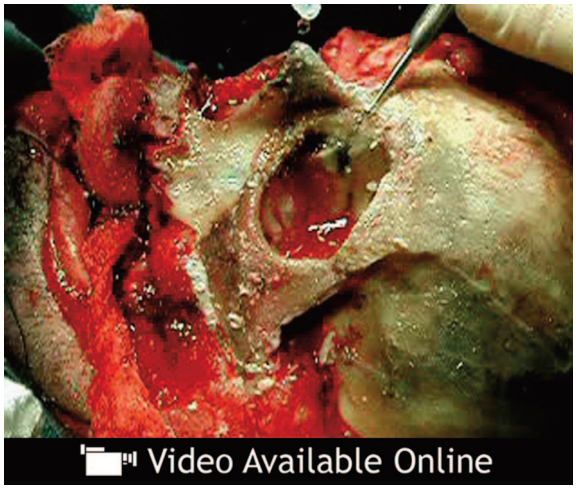


Video 2. Video demonstrating basic soft-tissue débridement is available in the "Related Videos" section of the full-text article on www.PRSJournal.com.

Video 3. Video demonstrating acute burn débridement is available in the "Related Videos" section of the full-text article on www.PRSJournal.com.

Systemic factors, such as the patient's underlying medical conditions and their nutritional status, should also be evaluated and addressed. Albumin and prealbumin, with half-lives of approximately 20 and 3 days, respectively, are useful indicators of overall nutritional status, although they must be interpreted cautiously in the setting of liver disease, sepsis, or inflammatory states. Malnutrition in the massive weight loss patient after gastrointestinal bypass is common and can present with deficiencies of protein, fat-soluble vitamins (A, D, E, and K), vitamin B_{12}, folate, thiamine, iron, and zinc, even with supplementation.[28,29]

Often, when called on to evaluate a chronic, nonhealing wound, these basic principles have



Video 4. Video demonstrating hard-tissue débridement is available in the "Related Videos" section of the full-text article on www.PRSJournal.com.

been neglected in favor of the various adjuncts discussed later in this article. Whatever their value, no amount of topical antiseptic or negative-pressure therapy will heal a wound in a patient with inadequate circulation or a prealbumin value in the single-digit range.

COMPLEX WOUNDS

Radiation and Chemotherapy

Radiation has deleterious effects on local vascularity, fibroblast activity, growth factor levels, and mesenchymal stem cell populations.[30–34] Microscopic examination of irradiated tissue reveals microvascular thrombosis and abnormal vasculature. Clinically, irradiated wounds are associated with slower epithelialization, decreased tensile strength, and higher infection and dehiscence rates.[35,36] A multitude of agents are currently under investigation, both as prophylaxis and treatment of radiation-induced injury, including hyperbaric oxygen, pentoxifylline, and topical growth factors, although none has achieved widespread use. Irradiated skin heals poorly, even when sutured to a vascularized flap. Often, a better strategy is to excise the irradiated skin and subcutaneous tissue and cover the whole

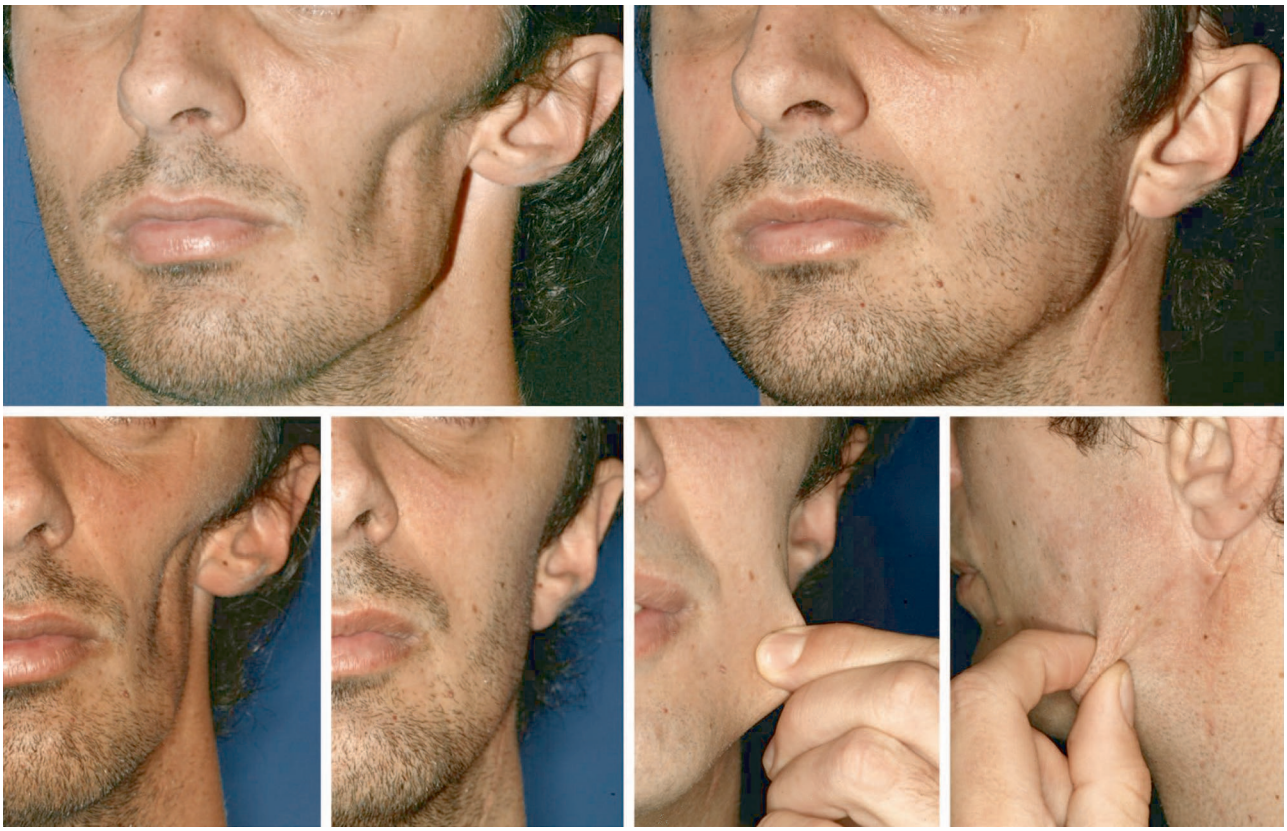


Fig. 1. A 23-year-old man presented 15 years after radical local excision of a rhabdomyosarcoma of his left masseter followed by irradiation (*left*). Seven months after one fat injection procedure, the volume is increased and the skin appears softer and healthier (*right*). (Reproduced from Coleman SR. Structural fat grafting: More than a permanent filler. *Plast Reconstr Surg.* 2006;118:108S–120S.)

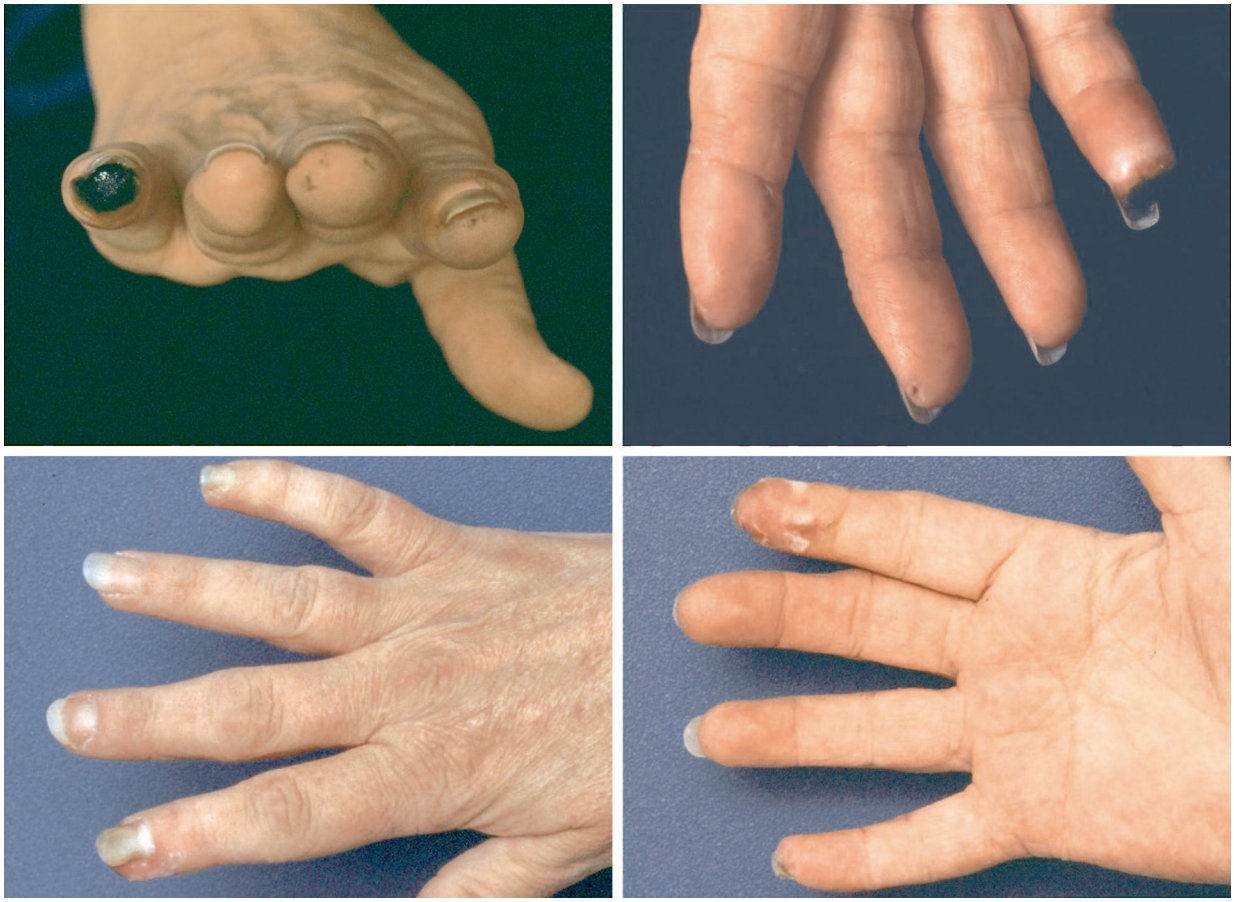


Fig. 2. (*Above*) Patient before injection of the ulnar border of the hand. The small finger has distal tip infarction. (*Below*) At 3 months after the first botulin toxin type A (Botox; Allergan, Inc., Irvine, Calif.) injection, the small finger has healed. One month after the first Botox injection, the radial side also became ischemic, and the index finger developed superficial infarction and skin loss. Botox injections at that time reversed ischemia. (*Below*, *right*) Early healing of those ulcerations. The index finger healed without débridement. (Reproduced from Van Beek AL, Lim PK, Gear AJ, Pritzker MR. Management of vasospastic disorders with botulinum toxin A. *Plast Reconstr Surg*. 2007;119:217–226.)

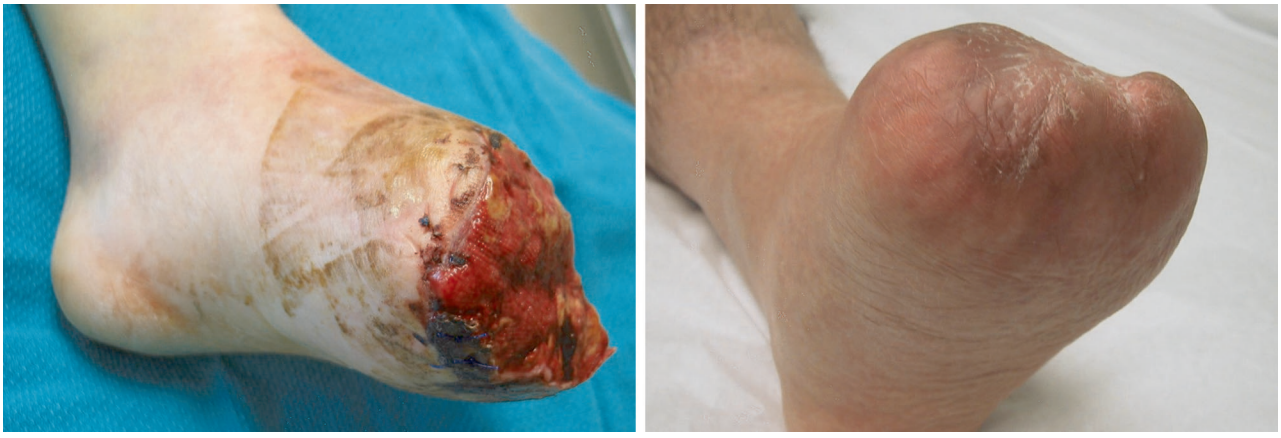


Fig. 3. Distal foot amputation (no joint involvement) healed with secondary healing with excellent results. Video of the patient ambulating is included in the video on wound healing by secondary intention in the "Related Videos" section of the full-text article on www.PRSJournal.com.

defect with a well-vascularized flap sewn to well-vascularized skin.[37–39] Although data are still limited, marked improvements in irradiated tissues have been reported with autologous fat injection[40,41] (Fig. 1).

Antineoplastic drugs may also have harmful effects on wound healing. Multiple animal models have demonstrated decreased inflammation, fibroblast function, and wound breaking strength in wounds subjected to various chemotherapeutic agents.[42–44] When combined with radiation, these effects may be cumulative.[45] Although some studies reveal a significantly increased complication rate in the setting of adjuvant therapy,[43,45] many others did not find them to be a factor.[46–48] The timing of administration may determine the extent of the effect on wound healing.[49] In general, however, it seems prudent to wait until adjuvant therapy is complete before embarking on complex reconstruction.

Diabetes

Many of the deleterious effects of diabetes are attributable to the formation of advanced glycosylation end products, which affect the extracellular matrix, cell signaling pathways, and gene expression in diabetic wounds.[50,51] This manifests as a decreased inflammatory response, decreased granulocyte response, and slower epithelialization.[52] In humans, increased hemoglobin A1c levels have been correlated inversely with ability to heal foot ulcers.[53]

In addition to its deleterious effects on wound healing, diabetes in associated with multisystem dysfunction, including neuropathy and vasculopathy.[54] Proper footwear, regular inspection, and prompt attention to even minor complaints are all important in minimizing the risk of ulcer development. Offloading diabetic foot ulcers with foot orthoses or total contact casting is an effective treatment that is frequently overlooked.[55] There is also an increase in interest in Achilles tendon lengthening to offload the forefoot for distal plantar ulcers in this group of patients.[56]

Steroids

Steroids have a direct inhibitory effect on macrophages, leukocytes, and fibroblasts, greatly decreasing the inflammatory reaction to injury. This results in decreased collagen deposition, impaired angiogenesis, delayed epithelialization, decreased wound contraction, and increased infection.[57,58] The effects of steroids can be partially reversed with high-dose vitamin A, 25,000 international units per day for 3 days.[59] Although this restores the inflammatory response and promotes collagen synthesis, wound contraction is still impaired and the risk of infection is still elevated.[60]

Patients on chronic steroids have thin dermis that avulses easily, resulting in large wounds from minor abrasions. Skin grafting can be difficult, as sutures hold poorly in this thin skin.[61] One effective solution is to unfurl the skin as far as possible and secure it with paper tape, elevate the extremity, and perform meticulous wound care. Much of the avulsed skin will often survive as a graft, and the residual raw area can heal secondarily.

Wounds Secondary to Medical Conditions

Wounds such as erythema nodosum caused by underlying medical conditions such as inflamma-

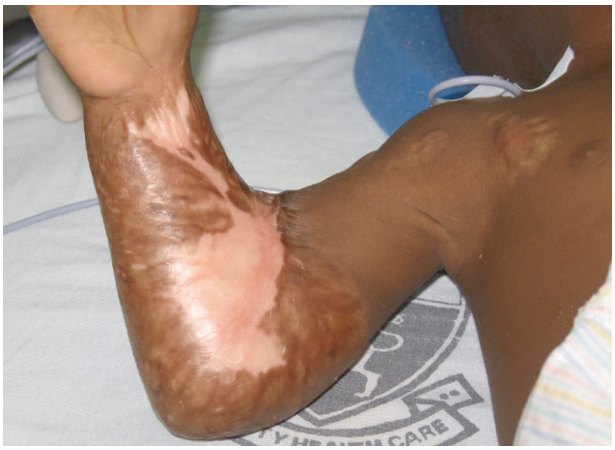


Fig. 4. Secondary healing across an elbow joint, resulting in severe contracture.

Video 5. Video demonstrating healing by secondary intention is available in the "Related Videos" section of the full-text article on www.PRSJournal.com.

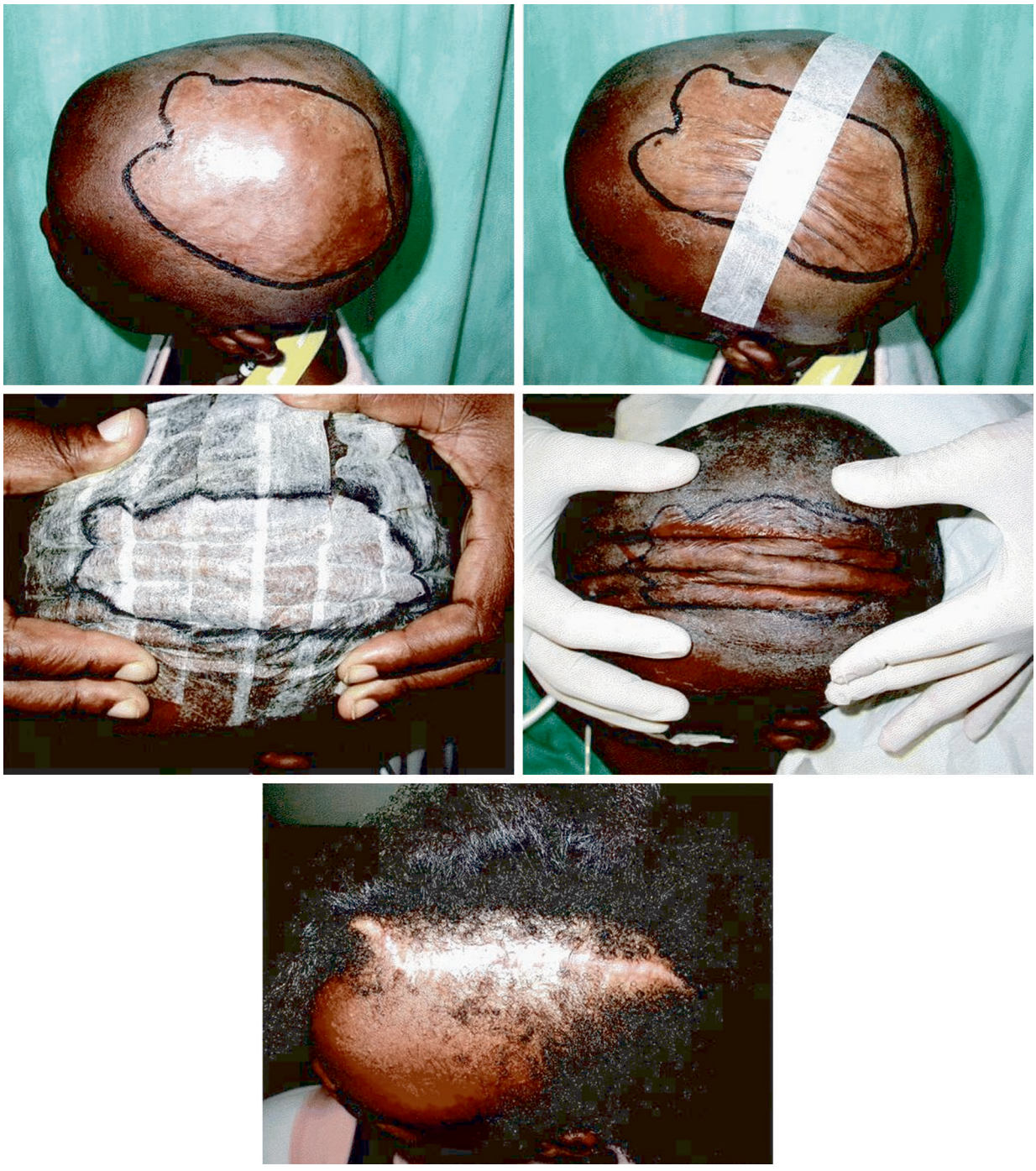


Fig. 5. Preoperative skin creep induced with paper tape. This same creep phenomenon can be used with tape, sutures, and other methods in open wounds to recruit skin in areas with tight skin such as the pretibial region. (Reproduced from Daya M, Nair V. Traction-assisted dermatogenesis by serial intermittent skin tape application. *Plast Reconstr Surg*. 2008; 122:1047–1054.)

tory bowel disease or leprosy can be resolved successfully with systemic steroids.[62] Fingertip ulcers in patients with vasospastic disorders such as Raynaud syndrome and scleroderma can be treated successfully using vasodilators or chemical denervation[63] (Fig. 2).

Open Wounds and Healing by Secondary Intention

Secondary healing can be very effective in specialized skin areas such as the glabrous skin of hands and feet, provided that the wound does not cross joints, as this may lead to contracture (Figs.

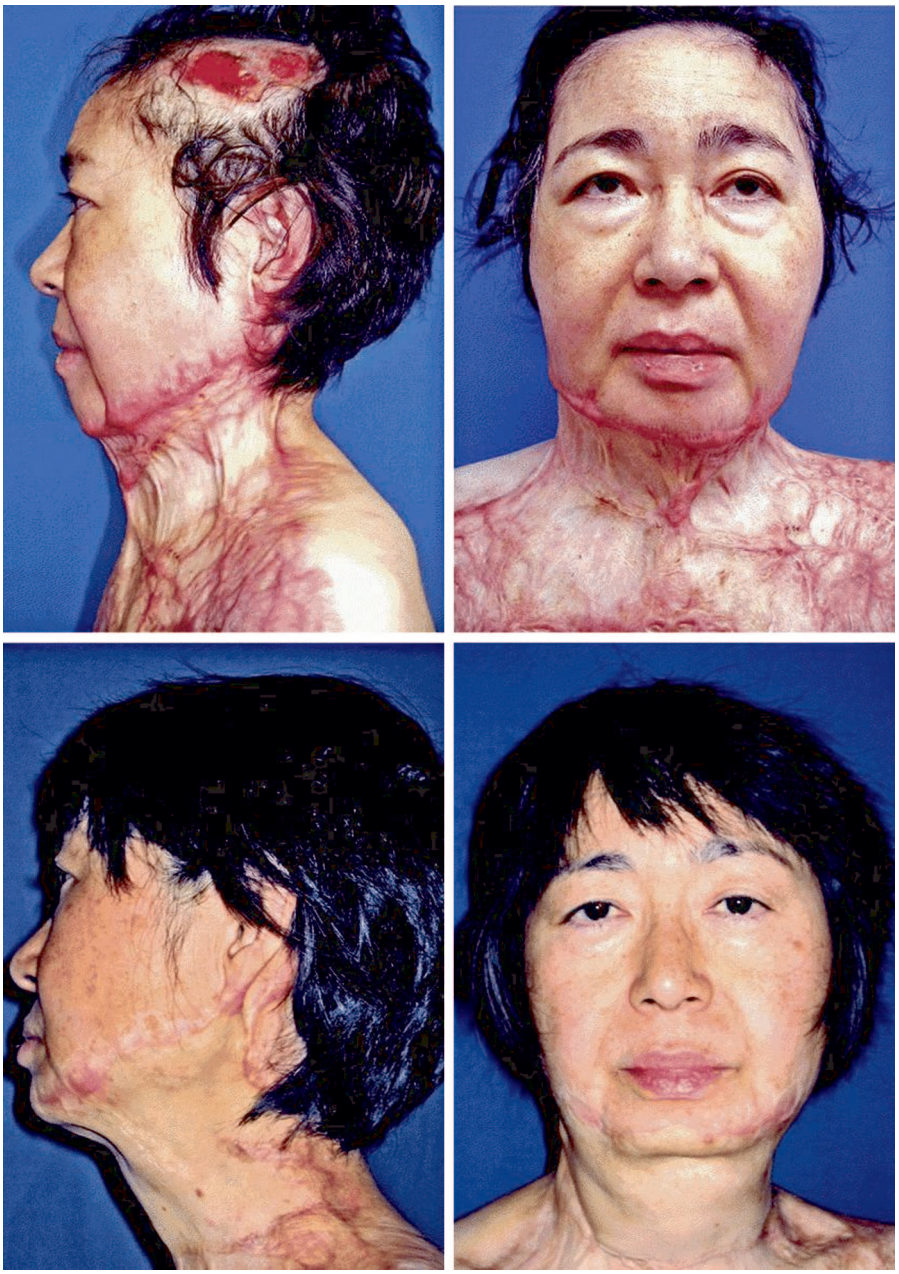


Fig. 6. Flap coverage of neck wound contracture. Flap reconstruction of joint contracture is more effective than skin grafts. (Reproduced from Matsumine H, Sakurai H, Nakajima Y, Kubo K, Higuchi R, Nozaki M. Use of a bipedicled thin groin flap in reconstruction of postburn anterior neck contracture. *Plast Reconstr Surg*. 2008;122:782–785.)

3 and 4). (**See Video 5,** which demonstrates healing by secondary intention, available in the "Related Videos" section of the full-text article on www.PRSJournal.com.)

Most fasciotomy defects can be closed by drawing the wound margins closer together with elastic, sutures, or tape without the need for skin grafting[64–66] (Fig. 5).

Contractures

In general, flaps fare better than grafts to satisfy dermal insufficiency in wounds that heal with joint contracture. If thin skin grafts are used to reconstruct joint contractures, recurrence is common. The take of thicker, more effective skin grafts is less reliable (Fig. 6).

Simple local circumferential scar release without large distant flaps may be an elegant solution

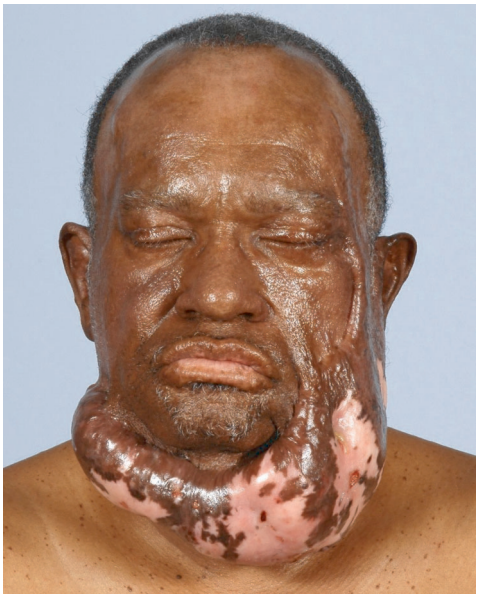


Fig. 7. Patient with a large keloid of the anterior neck secondary to flame burns that required surgical excision.

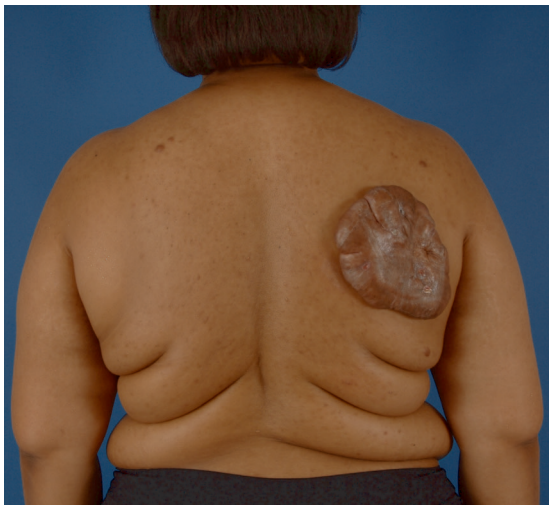


Fig. 8. Recurrent keloid on the back despite prior multimodality treatment with excision, steroid injection, and oral therapy.

Table 2. Dressings

Class	Characteristics
Gauze	Cotton fiber, inexpensive Labor intensive, requires frequent changes Nonspecific débriding action
Impregnated gauze	Nonadherent Maintains wound bed moisture May contain antibacterial agents
Adhesive films	Impermeable to bacteria, contaminants Not suitable for wounds with heavy exudates May damage delicate skin
Hydrogels	Water- or glycerin-based polymer gels, generally translucent Maintains wound bed moisture, encourages autolysis Nonadherent Not suitable for wounds with heavy exudates
Hydrocolloids	Carboxycellulose, pectin, or gelatin colloids Occlusive, encourages autolysis Adherent, may damage delicate skin Not suitable for wounds with heavy exudates
Foams	Hydrophilic, generally polyurethane based Can absorb moderate amounts of exudates Nonadherent
Alginates	Made from seaweed, forms hydrophilic gel on contact with moisture Suitable for wounds with heavy exudates Some antibacterial activity Some hemostatic activity
Debriding agents	Selectively débrides necrotic tissue Specific preparations have different targets, associated with variable speed of action, pain on application Chlorophyllin-containing compounds increase epithelialization
Silver dressings	Commercially available, added to a wide variety of dressings Broad-spectrum antimicrobial activity Like other antimicrobials, may have toxic effects on host tissue Should be reserved for critically colonized or infected wounds

to the problem of joint contracture in selected instances.[38] Z-plasties are useful in correcting the webbing that results from scar contracture in concave surfaces such as the medial canthus and axilla. It is useful to remember that large Z-plasty flaps are often more effective than small ones.

Hypertrophic and Keloid Scars

Hypertrophic scars are often defined as scars that remain within the boundaries of the original injury, whereas keloids grow beyond those boundaries. A recent metaanalysis revealed an overall response rate to treatment of 70 percent, with a mean improvement of only 60 percent.[67] All forms of treatment including excision with or without postoperative irradiation, steroid injection, silicone gel sheeting, laser, and other forms of chemotherapy have a significant recurrence rate, and data comparing these modalities are limited. Patients are educated that this type of wound healing is poorly understood and there is no guarantee of cure. A subset of hypertrophic scars that are amenable to surgical treatment are the hypertrophic scars arising from burn wounds that have healed secondarily and are surrounded with normal supple skin. These are often amenable to serial excision (Figs. 7 and 8).

WOUND-HEALING ADJUNCTS

Dressings

Traditional wet-to-dry dressings are associated with significant pain, and although they can débride effectively, healthy tissue and granulation are removed in addition to necrotic tissue.[68] These dressings may also aerosolize bacteria from the wound.[69] Allowing the wound to dry even though wound healing proceeds best in a moist environment is also counterproductive. Wet-to-dry or moist gauze dressings have been supplemented with a vast array of dressing materials (Table 2) and antiseptic agents (Table 3).

Many patients cannot afford sterile or sophisticated dressings for smaller open wounds that will take weeks to heal secondarily. A recent study has shown that clean dressings can be made of sanitary napkins, panty liners, diapers, or Coban tape for this group of patients who cannot afford sterile dressings.[70] For these patients, daily washing with clean water is likely the most important part of management to decrease the amount of nonviable tissue available to support bacterial growth.

Staphylococcus aureus and *Staphylococcus epidermidis* have such a low sensitivity to topical antibiotics such as bacitracin (25 percent sensitive in one recent study[71]) that the effectiveness in such ointments is questionable. The fact that they keep wounds moist may be more important than their antibacterial properties. However, topical greases such as petrolatum jelly achieve the same goal at much less expense.[72] If patients can afford them, transparent films, hydrogels, and impregnated gauzes all serve to keep a wound moist and have minimal débriding action, and are well suited to epithelializing wounds.[73,74] Occlusive dressings work well when there is minimal exudate. Hydrogels, hydrocolloids, foams, and alginate dressings may be more appropriate when there is a great deal of exudate.[68,74,75] Alginates also have some antibacterial and hemostatic activity.[76–79]

Wounds with a fibrinous, nonviable base or small amounts of necrotic tissue may be treated effectively with enzymatic débriding agents. Although these agents are no substitute for surgical débridement, they are simple to apply and cause minimal discomfort to the patient. Some preparations also encourage epithelialization.[80] Recently, the popular papain-containing débriding agents were removed from the market, although collagenase is still available commercially.

Negative-Pressure Wound Therapy

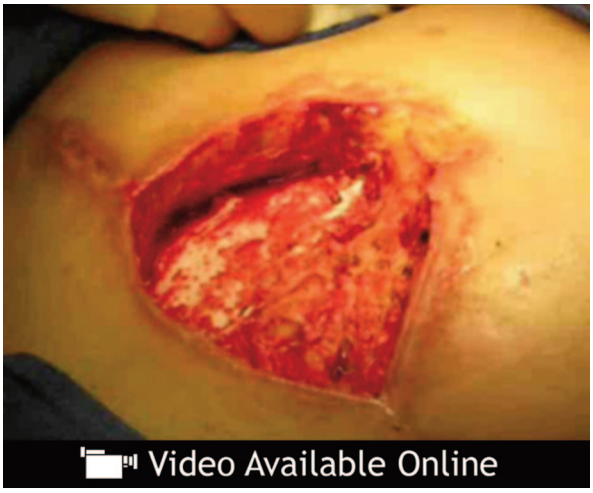
Negative-pressure wound therapy has been a major innovation in wound care. In addition to acting as an occlusive dressing, it may increase blood flow to the wound, decrease edema, decrease bacterial contamination, and promote wound contraction.[81–84] This type of vacuum sponge dressing is particularly well suited to large deep wounds with soft tissue at the base, such as abdominal, chest, perineal, and fasciotomy wounds. They are contraindicated in wounds containing freshly repaired blood vessels, as the vacuum can disrupt the anastomoses.[85] Otherwise, structures such as blood vessels, tendons, and bones can be protected by nonadherent gauze or polyvinyl alcohol (white) foam sponge before application of the standard polyurethane sponge and will eventually granulate.[84]

Initial investigations focused on the level of negative pressure and variations on blood flow.[83] However, the mechanism of action of negative-pressure dressings is likely more complex than originally thought. Micromechanical stresses, edema reduction, and even the chemical properties of the polyurethane foam used in the dressing sponge may also play a role in promoting cell proliferation and granulation.[86] Although clinical use varies widely, this type of dressing is perhaps best considered a tool with which to prepare wound beds and accelerate wound healing rather

Table 3. Topical Antiseptics

Agent	Formulations	Notes
Iodine	Povidine or cadexomer iodine; cream, solution, ointment, impregnated dressings	Broad-spectrum antimicrobial, inhibits fibroblast activity at higher concentrations
Chlorhexidine	Solution, powder, impregnated dressings	Broad-spectrum antimicrobial, inhibits granulocyte migration
Acetic acid	Solution	Specifically effective against *Pseudomonas*
Hypochlorite	Solution	Broad-spectrum antimicrobial, fibroblast toxic at higher concentrations
Hydrogen peroxide	Solution, cream	Conflicting studies on effects on wound healing, rare case reports of gas embolism when use as irrigant
Honey	Liquid, impregnated dressings	Primary use has been in burns

than a reconstructive method by itself. For example, recent data reveal that wounds treated with negative-pressure therapy still require prompt coverage of bone or other poorly vascularized tissues or they suffer from an increased risk of infection and potential osteomyelitis.[87] (**See Video 6,** which demonstrates vacuum-assisted closure application, available in the "Related Videos" section of the full-text article on www.PRSJournal.com.)



Video 6. Video demonstrating vacuum-assisted closure application is available in the "Related Videos" section of the full-text article on www.PRSJournal.com.

Growth Factors

Recombinant platelet-derived growth factor (Regranex; Ortho-McNeil-Janssen Pharmaceuticals, Inc., Raritan, N.J.) is the only topical growth factor approved by the U.S. Food and Drug Administration. It has been shown to modestly increase the rate of wound healing in chronic wounds, pressure ulcers, and diabetic foot wounds, and should not be used in patients with systemic malignancies because of reports of increased death rates in this population.[88–91] Platelet gels, which presumably contain a wide array of growth factors, have been reported to be effective in many arenas, including orthopedic, dental, cardiac, and plastic surgery, although evidence is limited at this time.[92–94] Several other factors, including epidermal growth factor and macrophage colony-stimulating fac-

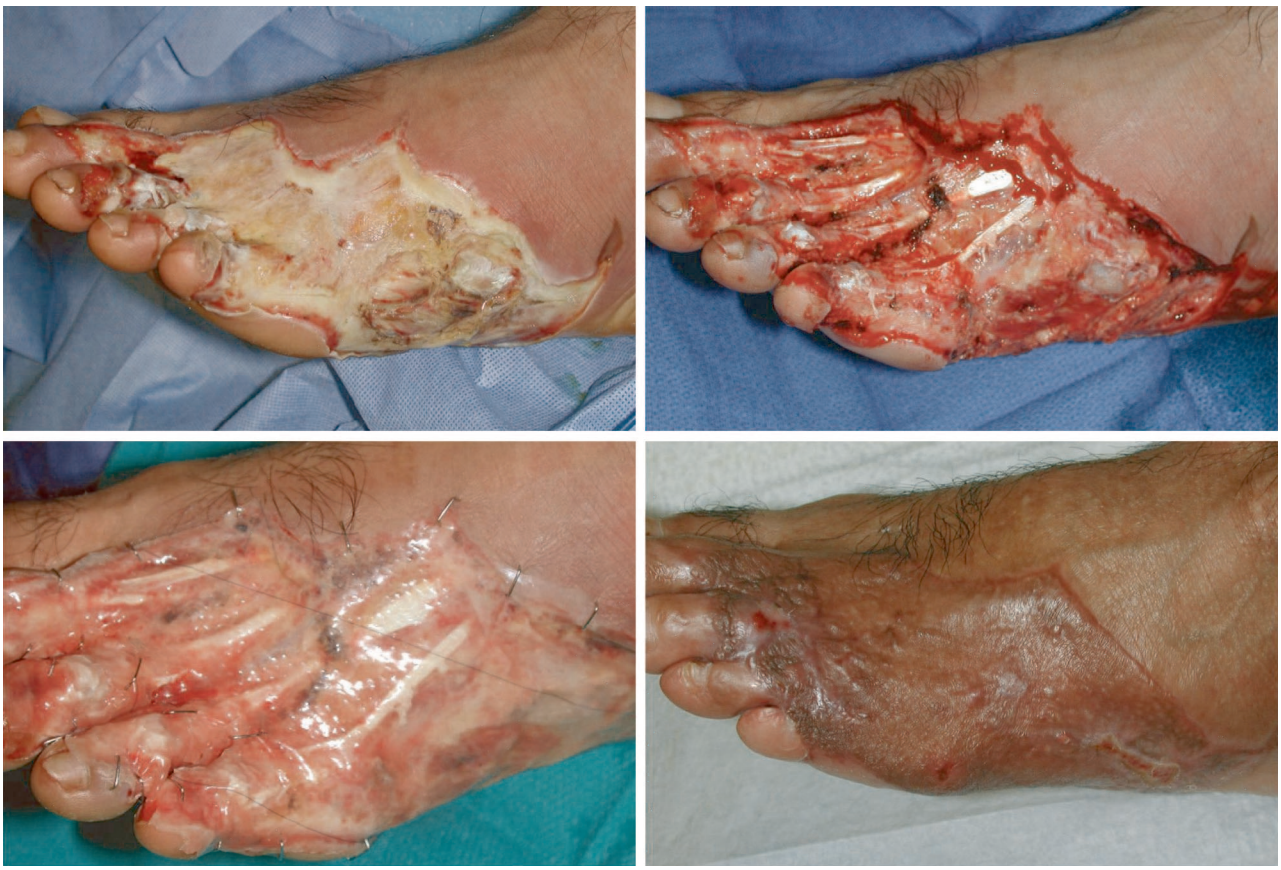


Fig. 9. Use of Integra to cover burn wound of the foot. (Reproduced from Lee LF, Porch JV, Spenler W, Garner WL. Integra in lower extremity reconstruction after burn injury. *Plast Reconstr Surg*. 2008;121:1256–1262.)

tor, are under investigation. Fibroblast growth factor-2, which showed initial promise, has been discontinued by the manufacturer.

Apligraf

Apligraf (Organogenesis, Inc., Canton, Mass.) is an engineered composite dermal/epidermal graft cultured from neonatal foreskin. Apligraf contains living cells, which in theory produce growth factors that promote wound healing, in addition to its role as a skin substitute.[95,96] Several small studies have shown its effectiveness in healing chronic wounds, including diabetic foot ulcers, venous ulcers, and heel ulcers.[96–98]

Bilaminate Neodermis

Integra (Integra LifeSciences Corp., Plainsboro, N.J.) is an engineered skin substitute composed of bovine collagen and shark chondroitin-6-sulfate covered by a silicone membrane. Initially used in burn reconstruction, it has found use in a wide variety of scenarios.[99] Wounds with exposed bone or tendon, even without associated periosteum or paratenon, can be successfully covered with Integra.[100–102] The matrix becomes vascularized over the course of weeks, and completion of reconstruction may eventually require a thin split-thickness skin graft. This may obviate the need for a free flap in the distal third of the leg, for example. However, the expenses in terms of both material and wound care are considerable, and the cost effectiveness of this approach has yet to be validated. This technique can also add a dermis-like pliability to grafts, which are generally quite stiff (Figs. 9 and 10). (**See Video 7,** which demonstrates application of Integra, available in the "Related Videos" section of the full-text article on wwwPRSJournal.com.)

Hyperbaric Oxygen

Hyperbaric oxygen exposes patients to supernormal oxygen concentrations. This causes vasoconstriction and increased partial pressures of oxygen in the blood, stimulates angiogenesis and fibroblast proliferation, and acts in synergistic fashion with certain antibiotics.[103] It is an established treatment for carbon monoxide poisoning and osteoradionecrosis,[104,105] and may have a role in

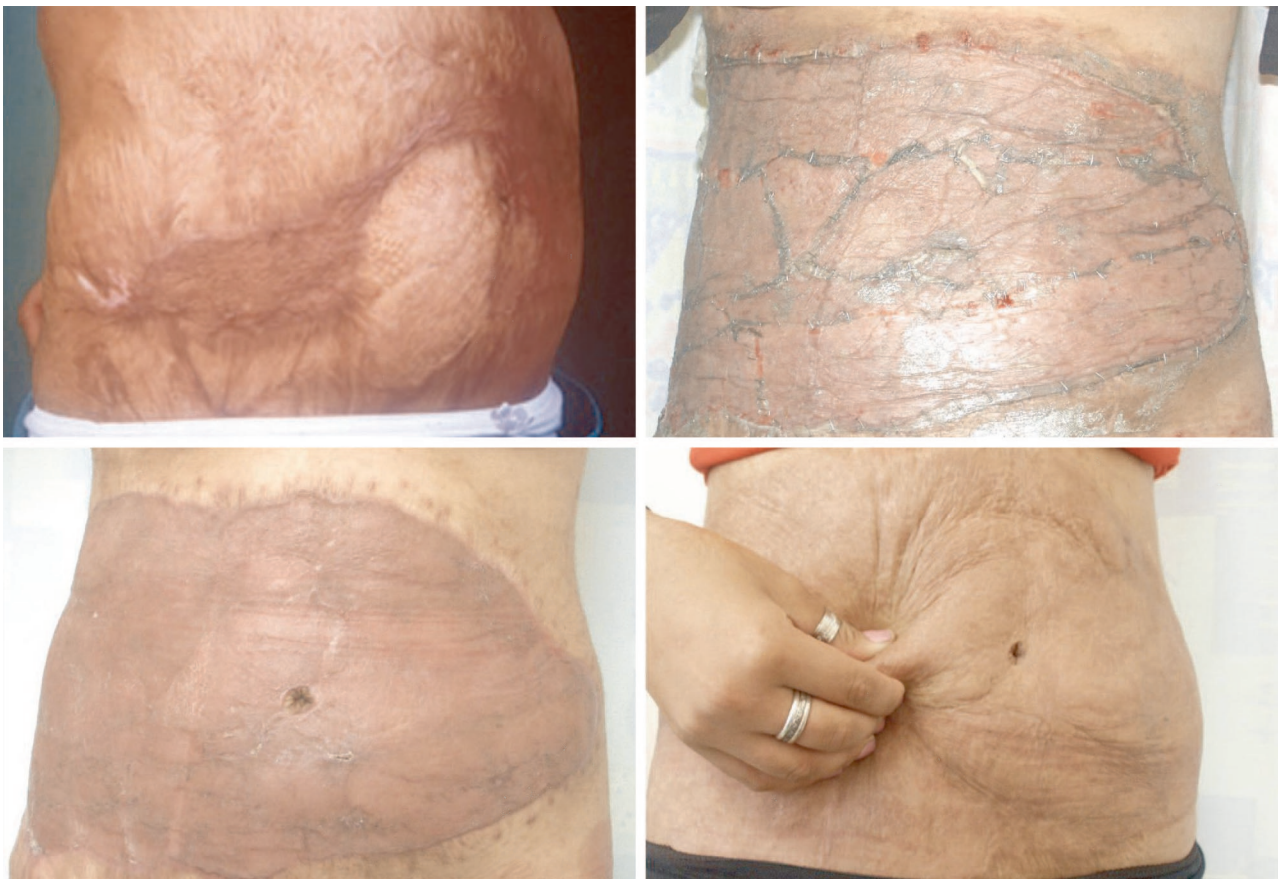


Fig. 10. Postoperative views demonstrating the skin graft flexibility of Integra.

Video 7. Video demonstrating Integra application is available in the "Related Videos" section of the full-text article on www.PRSJournal.com.

the treatment of diabetic foot ulcers and severe anaerobic infections. Complications include barotrauma to the ears and lungs, seizures, nausea, and aggravation of congestive heart failure. Although there are animal data to support the use of hyperbaric oxygen therapy in chronic wounds and to improve flap and graft survival,[106] the need for highly specialized equipment, complications, and limited human data have limited its clinical application.

CONCLUSIONS

As our understanding of wound healing advances, our therapeutic options expand apace. As the complexity of the wound-healing process becomes evident, it becomes clear that no single agent or modality will heal every wound. Instead, each patient and each wound must be evaluated systematically to identify those factors that must be addressed to optimize the wound-healing process. Although bioengineered tissue substitutes, mechanical dressings, and growth factors may be exciting and indeed improve outcomes, they should be adjuncts and not substitutes for basic wound care. Optimizing the patient's medical status and, above all, adequate, timely débridement and close monitoring of the wound's response to therapy still constitute the foundation of wound healing. Even as new advances present themselves, these core principles should not be forgotten.

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PATIENT CONSENT

Patients provided written consent for use of their images.

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