Overview of Wound Healing and Management

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KEYWORDS

• Wound • Healing • Management • Skin • Soft tissue injuries

KEY POINTS

- Wound repair is a coordinated series of phases that have predictable cell types and microenvironments.
- Wound healing is divided into inflammatory, proliferative and maturation phases.
- The pathway of healing is determined by characteristics of the wound on presentation.
- Wounds can heal via primary, secondary or delayed primary healing.
- Debridement and negative pressure wound therapy (NPWT) are important adjuncts to treat contaminated or chronic wounds.
- Soft tissue injuries should be assessed for blood supply, hypoxia, infection, edema and foreign body contamination; and treated based on these characteristics.

PHASES OF WOUND HEALING

Wound healing is a complex, highly developed chain of events that allows people to interact with their environment. The skin is a protective organ, and it provides vital functions like temperature modulation, moisture regulation, as well as sensation, reception, and transmission. The ability to repair and regenerate is central to these functions. Wound repair is a coordinated series of phases that have predictable cell types and microenvironment preparations.

Inflammatory Phase

The initial event when a wound occurs is a platelet plug that limits bleeding and begins cytokine signaling. This event initiates the coagulation cascade and promotes amplification and recruitment of cells for the debridement of nonviable tissue. The platelets create the plug in response to exposed collagen, which then releases ADP promoting continued platelet aggregation. Aggregation is accompanied by release

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Surg Clin N Am 97 (2017) 189–207
http://dx.doi.org/10.1016/j.suc.2016.08.013 **surgical.theclinics.com**

of platelet-derived growth factor (PDGF) and transforming growth factor beta (TGF-β), which is chemotactic for neutrophils in the blood.[1,2]

Neutrophils are drawn to and trapped in the platelet plug in response to PDGF.[1] They are the initial scavengers for debridement. They serve initially to phagocytize dead tissue and bacterial particles as well as create a wound hostile to bacteria by using reactive oxygen species. Neutrophils also provide a key proinflammatory cytokine in interleukin (IL)-1, which has dual effects as a proinflammatory cytokine and a stimulus for proliferation of keratinocytes.[3] The local environment also changes; initially, there is severe vasoconstriction secondary to catecholamine release. This vasoconstriction abates shortly after and there is subsequent vasodilation in response to histamine release from circulating mast cells[4,5] (**Fig. 1**).

As the inflammatory phase progresses, macrophages become the dominant cell type within 24 to 72 hours. Their role in the orchestration of wound healing is critical and changes as wound healing progresses.[6–8] It is widely accepted that macrophages play a central role and their response is key to establishing homeostasis within the wound and downregulating the inflammatory state to avoid pathologic inflammation (**Fig. 2**).

Proliferative Phase

The proliferative phase occurs from days 4 to 21, and is representative of angiogenesis, extracellular matrix (ECM) formation, and epithelialization.[9,10] Although there is considerable overlap between the phases of wound healing, the ability to transition into the next phase can determine whether a wound heals appropriately. ECM formation likely starts with platelet degranulation, because PDGF is a known promoter of proteoglycan and collagen formation. Local fibroblasts respond to PDGF by

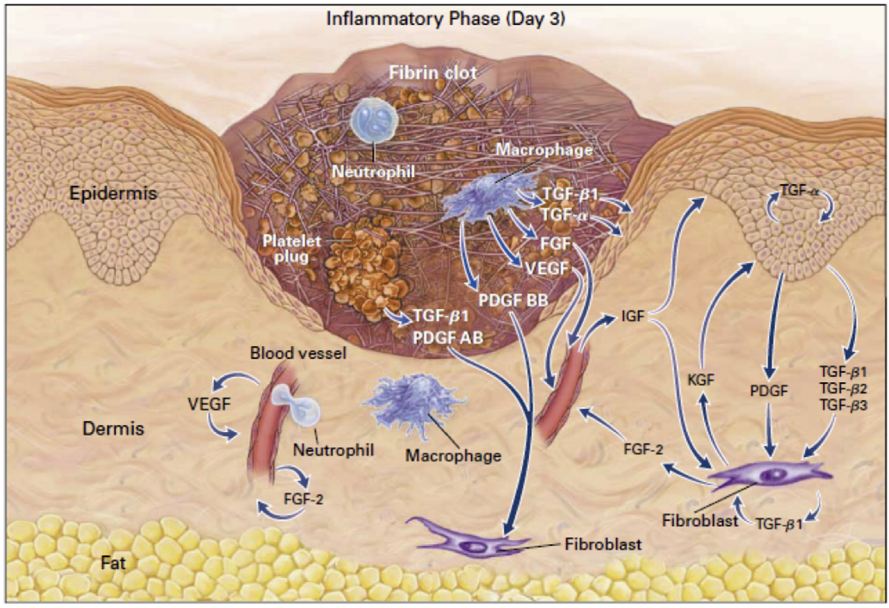

Fig. 1. In the inflammatory phase, the fibrin clot traps the neutrophils which are the first cells in the wound. It invites the macrophage which is involved in orchestrating the process of wound healing. FGF, fibroblast growth factor; KGF, keratinocyte-derived growth factor; VEGF, vascular endothelial growth factor. (*From* Singer AJ, Clark RAF. Cutaneous wound healing. N Engl J Med 1999;341(10):739; with permission. Copyright © 1999 Massachusetts Medical Society.)

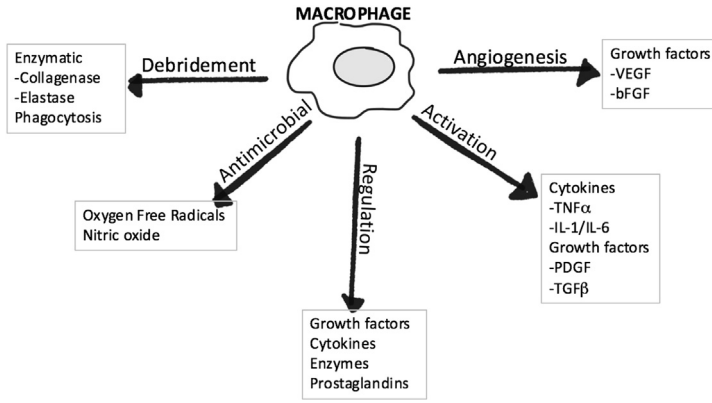

Fig. 2. The macrophage has multiple actions, such as debridement, antimicrobial action, wound regulation, cellular activation via cytokines, and angiogenesis via growth factors. It is the most critical cell involved, and without the action of macrophages there would be no progression in wound healing. bFGF, basic fibroblast growth factor. (*Data from* Broughton G, Janis J, Attinger C. Wound healing: an overview. Plast Reconstr Surg 2006;117:1e-s.)

producing collagen as well as transforming into myofibroblasts to promote wound contraction. Fibroblasts also secrete keratinocyte-derived growth factor (KGF), which stimulates epithelialization from keratinocytes,[11] and endothelial cells produce vascular endothelial growth factor (VEGF), and basis fibroblast growth factor (bFGF) to promote ingrowth of blood vessels. A hallmark of normal wound healing physiology is the ability to cease ongoing collagen production, with maximum deposition at approximately 21 days (Fig. 3).

Maturation Phase

Remodeling phase occurs from 3 weeks to 1 year after injury. It is characterized by wound contraction and collagen remodeling. Macrophages are the principal cell

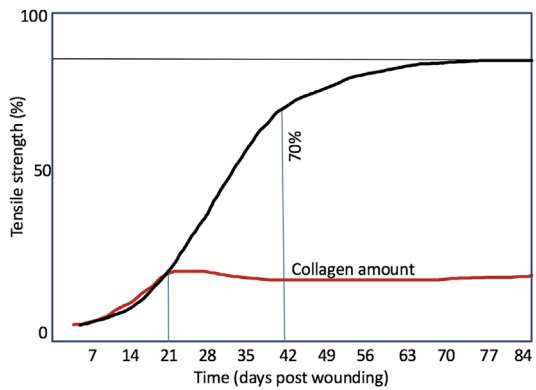

Fig. 3. Collagen accumulation steadily increases till 3 weeks after injury. However, the strength of the wound closure continues to increase after 3 weeks secondary to the cross-linking and alignment of collagen fibers. This strength reaches 70% at 6 weeks and reaches about 80% to 90% at full maturation. (*Data from* Geever EF, Stein JM, Levenson SM. Variations in breaking strength in healing wounds of young guinea pigs. J Trauma Acute Care Surgery 1965;5(5):624–35.)

type in proliferation, and fibroblasts are the principle cell type in remodeling. The hallmark process is the conversion of type III collagen to type I.[12] Equilibrium between type I and type III occurs after approximately 30 days, and maximum strength occurs after roughly 42 to 60 days, hence the traditional recommendation of activity restriction after 6 weeks (see **Fig. 3**). Successful wound healing is contingent on adequate tissue oxygenation at the wound edges. Poor oxygenation can generally be attributed to local strangulation from excessive tension or poor delivery of oxygen to distal tissues. Local measures can be undertaken to improve tissue mobility, because excessive tension is a clinical miscalculation that inevitably fails.

HEALING PROCESSES AND PROBLEMS WITH WOUND HEALING

Wounds generally heal without issue and progress through one of 3 different pathways. The pathway of healing is determined by characteristics of the wound on initial presentation, and it is vital to select the appropriate method to treat the wound based on its ability to avoid hypoxia, infection, excessive edema, and foreign bodies. These factors create an environment that interrupts healing and creates a cycle of hypoxia, inflammation, necrosis, and infection, creating a chronic wound.

Surgical incisions are an example of primary healing, which is an immediate reapproximation of the skin edges, with subsequent epithelialization reconstituting the barrier within 48 to 72 hours. The key component of success with primary healing is limiting tension at the incision line, which can be accomplished by elevating deeper layers, placing progressive tension sutures to distribute the stress, with local tissue rearrangement. If there is too much tension at the suture line, breakdown occurs as a result of local tissue ischemia and necrosis.

Secondary healing is a process that uses contraction and epithelialization to restore the epithelial barrier. The wound is left open, or is in discontinuity, typically because of tension or contamination. The wound bed is kept clean and optimized for keratinocyte migration, which is generally accomplished by using hydrogels and transparent films that are waterproof and impermeable to bacteria. Once again, optimizing the wound bed to prevent hypoxia, necrosis, and infections is key to secondary healing.

Delayed primary healing is used in poorly delineated or contaminated wounds. The principle is to convert a hostile wound into a favorable one that subsequently permits surgical closure. Often adjuncts such as debridement, dressing changes, and placement of negative pressure wound therapy (NPWT) form a bridge to definitive reestablishment of an epithelial barrier. Often this method is used to treat wounds with tissue transfer; however, this can also be used as a bridge to close the wound edges.[13,14] The bridging options that are available depend on the underlying structures (**Fig. 4**).

Molecular Requirements for Wound Healing

Poor oxygenation caused by inadequate delivery is a common occurrence and is often the sequela of patient-derived factors such as smoking, peripheral vascular disease, or poorly controlled diabetes. Although these diseases have a higher prevalence in the adult population, the significance of distal oxygenation must be appreciated in the pediatric population as well. Oxygen is central to many levels of wound healing and can be described as an enzymatic subcellular nutrient critical to oxidative phosphorylation and leukocyte respiratory burst, and integral for collagen synthesis.[15,16]

Proper nutrition is also critical, because wound healing is an anabolic process with increased metabolic demand. Although the physiologic reserve of children is often astounding, establishing and maintaining adequate nutritional stores should be one

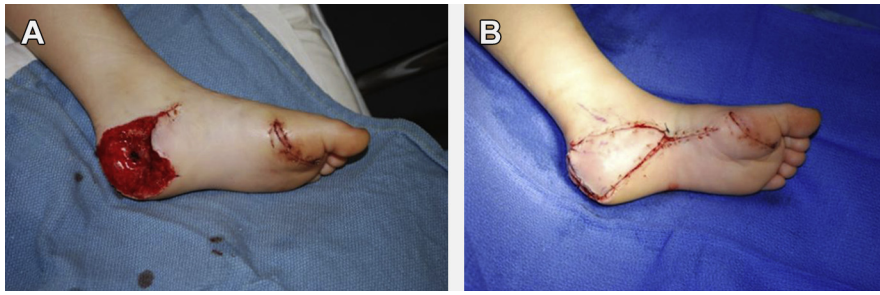

Fig. 4. (*A*) This child had a heel injury secondary to a lawnmower accident with exposed calcaneus. The wound was first debrided to normal, viable tissue and underwent dressing changes for 3 weeks with NPWT. Wound closure should not be attempted in the acute setting in cases of extensive contamination. (*B*) After obtaining a clean wound, a sensate, medial plantar artery flap was used to cover the calcaneus.

of the first interventions when dealing with a chronic wound. In the pediatric burn population, it was shown that early excision and aggressive feeding improved outcomes.[17] It has also been shown in animal models that the tensile strength of wounds is significantly less than that of controls secondary to poor nutrition.[18]

Although protein stores are central to healing, there are specific vitamin and mineral deficiencies that can negatively affect it. The best known is vitamin C because of its role in scurvy. It is a required cofactor for collagen cross-linking but is also implicated in reducing oxidative stress.[19] A deficiency of vitamin C has been associated with a greater susceptibility to wound infection.[20] Vitamin A has been shown to reverse the deleterious effects of steroid use on wound healing, and has demonstrable benefit in other conditions, such as diabetic wound care and tumors.[21,22] Zinc (Zn) is an essential cofactor in DNA and RNA synthesis, and deficiencies lead to poor wound healing. However, the importance of Zn in wound healing was further confirmed when the structure of matrix metalloproteinases was found to have Zn as a cofactor. Zn benefits can be shown topically, but supplementation when levels are normal does not augment healing.[23]

Genetic Disorders in Wound Healing

There are heritable derangements in wound healing. These derangements are generally part of a larger spectrum of disease so effects on healing may be multifactorial. Pseudoxanthoma elasticum is a disease that has both autosomal dominant and recessive pathways. It is characterized by abnormal calcium depositions with hallmark yellowish papules over flexure sites. There can be associated cardiac and ocular disturbances as well as a tendency to form keloids with delayed wound healing.[24] Ehlers-Danlos syndrome is characterized by hyperelastic skin and hypermobile joints. There are 6 major types of Ehlers-Danlos and all but 1 is a heritable disorder of collagen, the exception being a heritable disorder of tenascin.[25,26] It is an autosomal dominant condition often associated with mitral valve prolapse. Because of innate errors in collagen production, wound healing is delayed and disturbed (**Fig. 5**). Type IV is a vascular subtype that has high association with arterial, bowel, and uterine rupture and often results in premature death.[27] Cutis laxa is an inborn error in elastin resulting in severely drooping skin folds. The skin abnormalities are accompanied by cardiovascular and pulmonary comorbidities, all of which result from a nonfunctioning elastase inhibitor.[28]

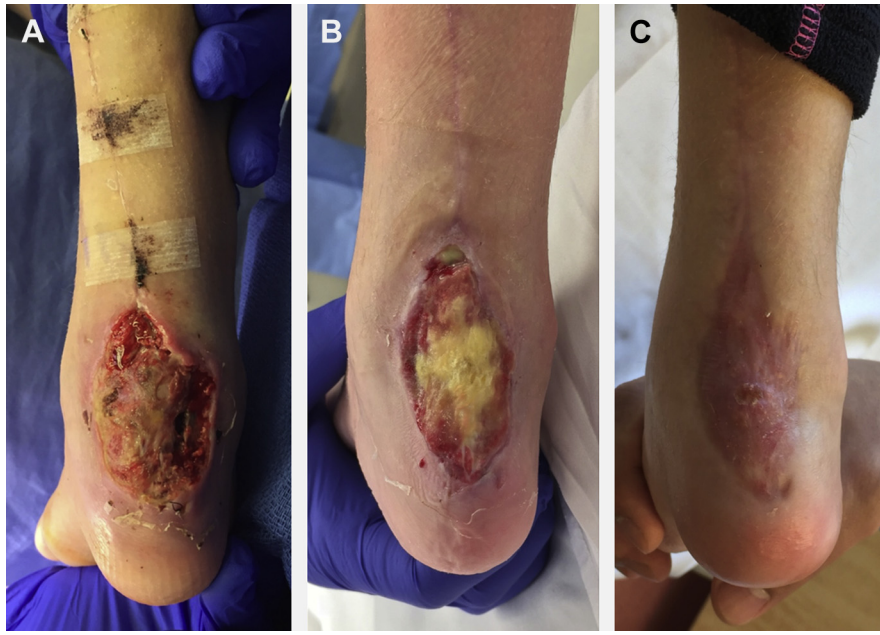

Fig. 5. (*A*) A young woman with Ehlers-Danlos syndrome presented with a complex open wound over the Achilles tendon after trauma. (*B*) After debridement and NPWT for 3 weeks, a bilayer wound matrix (Integra) was used as a bridge to achieving closure. The use of Acticoat (nanocrystalline silver) along with NPWT provides antibacterial coverage and enhances angiogenesis into the scaffold. (*C*) Final outcome with coverage of Achilles tendon. Patients with Ehlers-Danlos have a heritable disorder of collagen and require longer-than-usual times for achieving wound closure.

There are some inherited disorders that are contraindications for elective surgery. Werner syndrome (adult progeria) is autosomal recessive and has plaque-ridden, variably pigmented skin. Affected patients generally are short of stature with premature graying hair or baldness, trophic ulcers, and hypogonadism.[29] The pathologic mutation is of DNA helicase, which leads to chromosomal instability and early death. The error leads to difficulty healing because of poor fibroblast function secondary to poor response to growth factors PDGF and fibroblast growth factor (FGF).[30] Elastoderma is an exceptionally rare disease of excessive elastin fibers in the reticular dermis. It generally presents in young female patients, and the excess skin can be described as pendulous.[31] These conditions are associated with enough morbidity that elective surgery is generally discouraged.

Hypertrophic Scars and Keloids

Common wound healing disorders include hypertrophic scarring and keloids. It is typically taught that if the scar remains within the border of the wound, it is a hypertrophic scar, and if it exceeds the border of the wound it is a keloid. On microscopic examination keloids possess thick eosinophilic collagen bundles,[32] as well as a thickened epidermis and increased mesenchymal density. Often there is a difference in presenting wounds, with hypertrophic scars arising in major incisions or lacerations, whereas keloids arise from minor skin trauma. There is also an increase predilection for both in sites that are exposed to more mechanical forces, such as the sternum, shoulder, and

knee. Foreign bodies and infection also seem to be contributing factors, secondary to lengthening of a proinflammatory state within the wound[33,34] (Fig. 6).

WOUND MANAGEMENT

Suture Types and Postoperative Care

Sutures can be divided into classes based on their makeup, number of strands, and permanence. When suturing in cosmetically sensitive areas, it generally advisable to use layered closures and to use a small monofilament for the most superficial layer of closure. The length of time a suture is retained can predispose to unsightly marks (railroad tracks), because the skin can epithelialize along the suture strand. Another skin closure application is the use of a cyanoacrylate. It has advantages, such as no trauma from needles; however, it alone cannot aid in alignment or support of skin edges. When suturing wounds, using a layered closure helps with final alignment and reduces tension, minimizing scar. For pediatric patients, final closure with delicate sutures, such as 6.0 rapidly absorbable suture, is often recommended for the face or cosmetically sensitive areas. A nonreactive 6.0 nonabsorbable suture can be used, but requires removal in 4 to 6 days, and removal can be difficult in the toddler population.

Postoperative care can be optimized by using a petroleum-based emollient for the first 1 to 3 weeks. After the expected fibroplasia, scar management can be addressed.

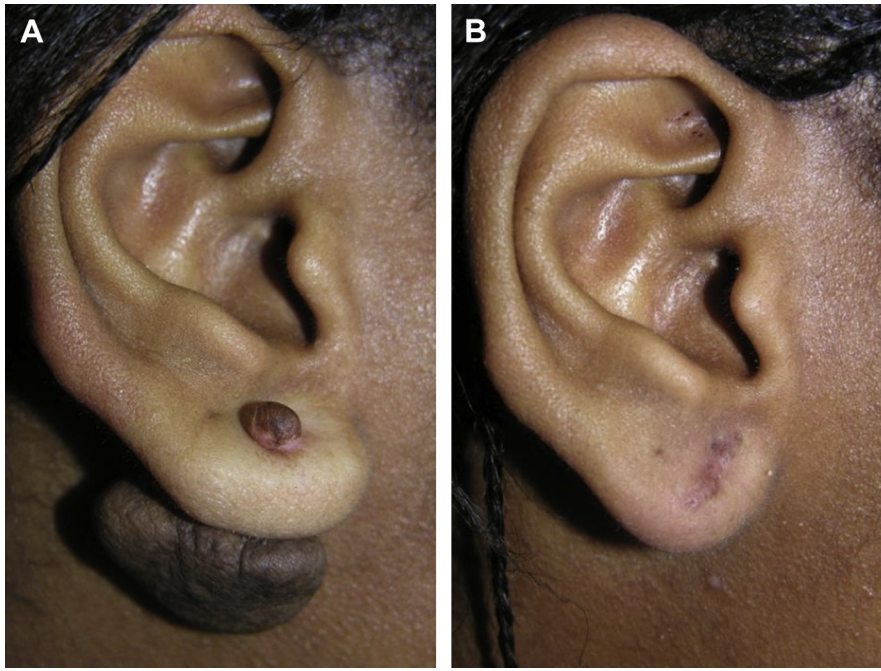

Fig. 6. (*A*) Keloids can occur in areas with no skin tension. The presence of foreign bodies, such as piercings, can be a predisposing factor. Recurrence after excision is common if no adjuvant therapy is performed. (*B*) Treatment commonly is preoperative, serial intralesional triamcinolone injections (usually 6 weeks apart), followed by excision. Low-dose radiation therapy (10–12 Gy) has been shown to ameliorate recurrent keloids that are resistant to corticosteroid therapy.

Often a protocol incorporating silicone-based products and scar massage aid in the aligning of collagen. It is important to convey to the patient that scar maturation can take between 6 and 12 months. Sunscreen during that time can be helpful. A scar initially is hyperemic and this indicates healing. Patience must be counseled to the patient and family because an early intervention rarely results in superior results. After a period of observation, interventions to improve scar appearance can be undertaken. Recently, Donelan and colleagues[35] showed improvement in facial burn scarring using a pulsed dye laser. Other modalities, such as fractional CO_2 lasers, are also being studied for scar management.

Role of Debridement

The goal for any chronic wound is to convert it to an active, healing wound, which is often accomplished by debridement. Whether this is autolytic, mechanical, or enzymatic the goal is to removal all necrotic tissue. Often, adequate debridement unmasks hidden collections, revealing a much more extensive wound than was initially presumed. By removing the necrotic tissue, the wound can optimize the regenerative potential of the bordering tissue. Preservation of the adjacent viable tissue is often critical in areas where there is limited local tissue. Operatively, a limit of debridement has often been to healthy bleeding tissue. This limit often has led to aggressive initial debridement sacrificing otherwise viable tissue. One of the adjuncts that is useful to debride atraumatically, sparing more viable tissue, is the Versajet hydrosurgery system.

After the removal of necrotic tissue, efforts are made to transition to a granulating wound. This transition is accomplished with barrier products that protect neighboring tissue. Some commonly used barrier products are petroleum jelly, zinc oxide, and Cavilon (3M Products). These products maintain peripheral moisture while limiting superficial damage from adhesives. There is an array of topical products available. The appropriate dressing should take into account the frequency of dressing changes as well as the associated edema and moisture of the wound. If the wound is exudative, a more absorbent dressing should be selected. However, if the wound is not excessively moist, using a product that dessicates will limit keratinocyte migration.[36] A dressing ideally provides a level of protection mimicking the epithelium's function. However, this is a difficult function to replicate. In infected wounds, a combination of debridement and silver application is being used in many formulations and delivery. It has broad spectrum of activity against gram-negative bacteria as well as the methicillin-resistant *Staphylococcus aureus* (MRSA) that colonize many chronic wounds.[37]

Negative Pressure Wound Therapy

Having a basic overview of the healing process allows various interventions to either augment or alter the healing process. One of the major advancements in wound healing has been NPWT, or vacuum-assisted closure. The principle of NPWT is its ability to create microdeformation of cells.[38–40] One of its benefits is stimulation of VEGF by creating an area of relative hypoxia, as well as stimulation of other proproliferative cytokines such as TGF-βand basic FGF (bFGF).[41]

NPWT also helps to keep wounds moist, relying on a semiocclusive dressing, which prevents desiccation of wound edges. The suction apparatus also aids in the removal of fluid around the wound, limiting wound edema and maceration, which limits inflammation in chronic wounds.[42] The dressing changes also provide a mechanical debridement.

The application of NPWT has found an increasing number of uses in pediatric surgery. Initially, NPWT was used to aid in closure of pediatric pilonidal disease and was

described as being well tolerated and permitting an earlier return to activities.[43] Subsequent studies expanded on the anatomic regions as well as the age groups to include sternal wounds and complicated neonatal abdominal wounds, and found them to be safe and effective.[44–46]

A key benefit with NPWT is that it minimizes dressing changes. Typically, NPWT dressing changes are 3 times per week as opposed to the daily or twice-daily regimens previously used. The lessened frequency and the continued improvement in the portability of the vacuum device has also allowed faster transition from the hospital setting to home with intermittent nursing visits for dressing changes. Although the up-front cost of NPWT is higher than that of standard dressing care, the overall cost is lessened, specifically when evaluated over increasing lengths of time.[47]

Soft Tissue Wounds to the Face

Facial soft tissue injuries are often a traumatic experience, both for the child and the caregiver. Whenever encountering these injuries, the initial focus should be on identifying and stabilizing more critical issues before addressing soft tissue injuries. Once primary and secondary surveys are complete, attention can be turned to care of soft tissue wounds. An examination assessing the function of motor and sensory nerves should be undertaken as well as documentation of the length, width, depth, and any loss of tissue or presence of contamination. Tetanus vaccine should be administered and antibiotic prophylaxis should be given, especially in bite wounds, contaminated wounds, and patients with comorbidities that predispose them to infections. Initial management should center on cleaning the wound and, if possible, early closure, because delay in closure often worsens the eventual aesthetic outcome.[48] The repair in superficial wounds should be undertaken within 24 hours in areas of good oxygenation and without contamination. Contaminated wounds or regions of poor blood flow should have primary closure within 6 hours if possible.[49] With the exception of dog bites (which are generally clean), bites (cats and humans), ballistic wounds, birds, or barnyard injuries require early debridement with delayed closure to fully assess the extent of damage caused by contamination.

The scalp is a highly vascular region with anastomosis between the external and internal carotid system taking place in the loose fibrofatty region above the epicranium. This region is prone to avulsion and needs to be copiously irrigated because of the presence of emissary veins which may have connections to the dural sinus. The blood supply to the scalp often allows it to survive on a single pedicle in partial avulsion settings, but complete avulsion may require replantation.[50,51] The scalp can also be extended for primary closure using galeal scoring, which involves placing horizontal incisions through the galea to expand the area of coverage. Various rotation and advancement flaps exist for scalp closure. In some cases of cranial bone exposure, the outer cortex can be burred to the diploe space followed by skin grafting, which can be used to achieve pericranial coverage. This grafting can then be treated with subsequent tissue expansion[52] (**Fig. 7**).

Wounds to the ear are challenging, but most can be closed primarily. One of the most important considerations when repairing an ear wound is to prevent chondritis. If the perichondrium is intact, closure of the overlying skin is adequate. Any damaged cartilage should be carefully debrided. If the ear is totally avulsed, surgical replantation should be undertaken. Partial defects are candidates for delayed techniques of reconstruction using local flaps and cartilage grafts[53] (**Fig. 8**). In cases of hematoma or avulsion, it is a general practice to place a bolster to maintain compression and prevent the formation of a hematoma. Formation of a hematoma under the perichondrium can result in anomalous cartilage healing resulting in so-called cauliflower ear.

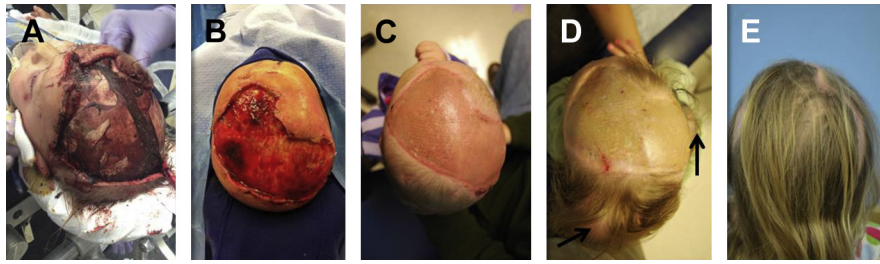

Fig. 7. (*A*) Severe dog bite to the scalp with avulsion of 50% of scalp with gross contamination. (*B*) After repeat debridements, galeal scoring was used to expand native scalp; burring of outer cortex, followed by incorporation of Integra. (*C*) Appearance after skin grafting over Integra. (*D*) Arrow point to tissue expanders in the scalp with recruitment of extra skin. (*E*) Full scalp coverage after 2 rounds of tissue expansion.

Traumatic nasal wounds can be problematic, because the nose has a mucosal lining, along with cartilage structural units and a soft tissue envelope. The nose can be divided into several aesthetic subunits for reconstruction. This approach aids in classification and reconstruction options with local tissue flaps.[54] Total destruction of the nose often requires an axial forehead flap based on the supratrochlear vessels (**Fig. 9**).

Cheek wounds can usually be primarily closed. However, the deeper structures must be assessed, specifically the parotid duct and the facial nerve. It is imperative

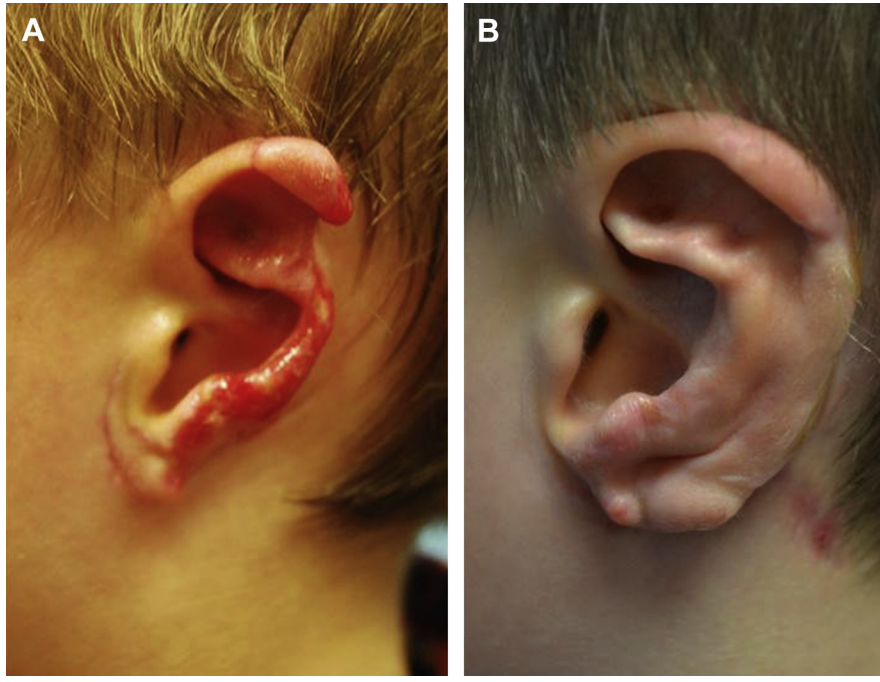

Fig. 8. (*A*) Dog bite with avulsion of posterior half of the ear and ear lobe. (*B*) Appearance after a 2-stage correction with costal cartilage graft and posteriorly based skin flap, followed by division and skin grafting to provide an auricular sulcus.

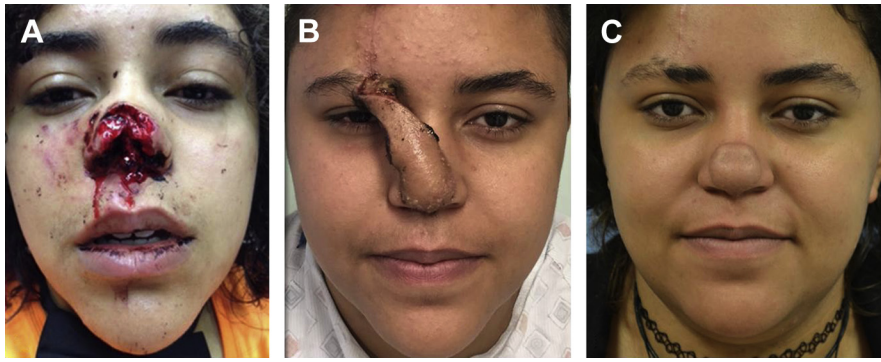

Fig. 9. (*A*) Dog bite with consequent loss of nasal tip subunit. (*B*) Reconstruction with forehead flap. (*C*) Appearance of division and inset of the forehead. The patient can benefit from thinning of the flap at a second stage.

that the branches of the facial nerve are checked for function before administering any local anesthetic. The course of the facial nerve has some variability in anatomy and branching patterns,[55] but some cardinal landmarks can be helpful (**Fig. 10**). The zygomatic and buccal branch can often be found at a line from the midpoint of the root of the helix to the lateral commissure of the mouth.[56] This nerve innervates the zygomaticus major muscle and aids in smiling. The course of the parotid ducts through the cheek has often been described as a line from the tragus to the commissure.[57] The parotid duct exits into the mouth at the level of the first molar. When duct injury is suspected, it can be cannulated with a 24-gauge angiocatheter and injected with methylene blue to assess whether a leak is present in the laceration. If present, the duct needs to be repaired over a stent.

Lip repair can involve direct repair, healing by secondary intent, rotational flaps, or microvascular replantation. Major landmarks such as the philtrum, cupid's bow, white roll, and vermilion-mucosal junction (red line) should be carefully assessed after a laceration in the lip. Discontinuity or the loss of these landmarks requires repair, because alterations of landmarks are conspicuous at conversation distances.[58,59] Small linear lacerations do not require repair because secondary healing in children

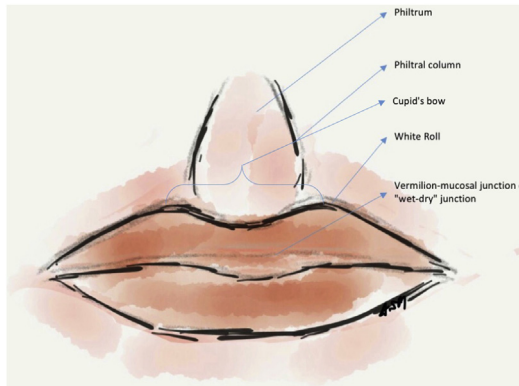

Fig. 10. Major landmarks of the lip.

can produce excellent results. Adhesive closure without sutures has also been used with success.[60] If repair of the lip is to be undertaken, accurate alignment of the landmarks is necessary.

Dog Bites

Dog bites are a common occurrence in the pediatric population. According to the US Centers for Disease Control and Prevention, approximately 4.5 million dog bites occur annually[61] and children aged 5 to 9 years are the most at risk. This number likely understates the actual numbers because some people do not seek treatment. Two large series evaluated morbidity and interventions over a 5-year period at pediatric tertiary care centers[62,63] and both found that more than half of the patients with bites had familiarity with the dog, and 1 study found that 53% were bitten by the family dog.

The location of the injury varied with age because infants and toddlers were more likely to be bitten on the face and older children were more likely to be bitten on the extremity. The studies also showed that pit bulls caused the highest percentage of bites. This finding reinforces previous studies showing that infants and young children are the most at-risk population and the most likely to incur injuries to cosmetically sensitive areas (**Fig. 11**).

Infection rates in dog bites vary, from 1.3% to 45%[64,65]; however, the route and duration of antibiotics varied in studies. It is our practice to ensure that intravenous antibiotics are administered before washout and repair, and generally patients are sent home on an oral course of amoxicillin/clavulanate, to cover the most common bacteria in a dog's mouth (*Pasteurella multocida*).[66] A meta-analysis by Cummings[67] evaluated the role of prophylactic antibiotics and showed a reduced incidence of infection with prophylactic antibiotics.

Necrotizing Fasciitis

Necrotizing fasciitis is a rapidly progressive and destructive infective process that is not frequently seen in the pediatric population; however, because of the speed and extent of injury, it is vital that pediatric practitioners maintain vigilance with soft tissue infections. The diagnosis is clinical and includes severe pain at the site out of

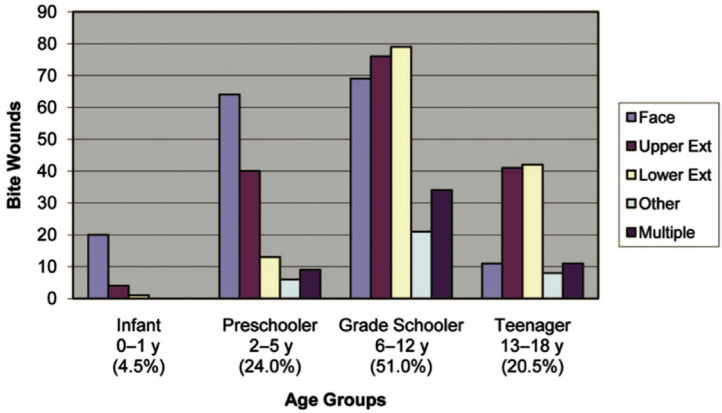

Fig. 11. Distribution of dog bite injuries by anatomic regions in children. Ext, extremities. (*From* Kaye AE, Belz JM, Kirschner RE. Pediatric dog bite injuries: a 5-year review of the experience at the Children's Hospital of Philadelphia. Plast Reconstr Surg 2009;124(2):553; with permission.)

proportion to its appearance. The patient appears toxic, and the skin may appear mottled erythematous or even ecchymotic, and this rapidly spreads. Classically, gray dishwater drainage is described, as is subcutaneous emphysema and large bullae. In children, immune deficient diseases such as acute lymphoblastic leukemia have been implicated. One of the largest case series of pediatric necrotizing fasciitis cited malnutrition as the most common predisposing factor.[68,69]

Microbiology in necrotizing fasciitis is classified into 2 types. Type 1 is polymicrobial and type II is monomicrobial. Type I is often seen after abdominal surgery, rectal perforation, or a spreading infection of the perineum (Fournier gangrene). Microbes in this population are aerobic *Staphylococcus*, *Escherichia coli*, group A *Streptococcus*, and anaerobes of *Peptostreptococcus*, *Prevotella*, *Bacteroides*, and *Clostridium*. Type II is generally *Streptococcus pyogenes*. Necrotizing fasciitis is an emergency with initial management designed for resuscitation, broad-spectrum antibiotics to include clindamycin, and emergent surgical debridement to healthy bleeding tissue.

Exposed Bone/Hardware

Degloving injuries can occur anywhere on the body. The shearing force associated with these injuries can completely denude structures or locally separate, leaving attachments proximally and distally. The initial priority is assessment and repair of deep structures (specifically orthopedic injuries) because there is a significant risk for concomitant injuries.[60] There should be a priority on maintaining any degloved skin because it can be repurposed, and viable pieces can be used as autografts. Other treatment options include tissue substitutes such as Integra and delayed skin grafting.[70]

The need to reconstruct the soft tissue barrier over exposed bone or hardware is critical to heal wounds and prevent infection. Godina[71] recognized that the ability to transfer viable tissue over an injury was beneficial in healing. He showed that coverage of fracture within 75 hours had a lower infection rate and better time to union than coverage between 3 days and 3 months or after 3 months (1.5% and 6 month vs 17.5% and 12.3 months vs 6% and 29 months respectively).[71] Pediatric free tissue transfers have been proved safe and effective.[72] Some benefits of microsurgery in children include the lack of comorbid conditions and anatomy that is generally more favorable than that of their adult counterparts. Neuroplasticity is also greatly improved in children, who have better return of function than adults.[72] It is important to remember that the fourth dimension of time needs to be accounted for in flap design, and although this is rarely a limiting factor it cannot be ignored.

Soft tissue coverage can be attempted for salvage of exposed hardware. The criteria needed for hardware salvage includes no hardware loosening, duration of exposure (<3 weeks), negative wound cultures, and location of the hardware with no signs of instability.[73] Maintaining implants in the spine is key for stability; however, in cases of exposed extremity hardware, removal with external stabilization is still the standard of care (**Fig. 12**). Reconstruction after tumor resection and radiation may result in exposure and complex wounds. Because of the effects of radiation on local tissue, free tissue transfer[74] is required for reconstruction. The benefits of a vascularized graft include accelerated healing and primary bone healing.[75]

Sternal wound infection in pediatric cardiothoracic surgery has been reported to be between 1.5% and 6.7%.[76,77] Different methods to help prevent wound infections with sternotomies have been developed, such as preoperative nasal carriage screening and treatment of MRSA, preoperative chlorhexidine bathing, and optimization of preoperative comorbidities (especially glycemic control).[78] Many of the preoperative adult practices have been adopted in pediatric practice as well.[79]

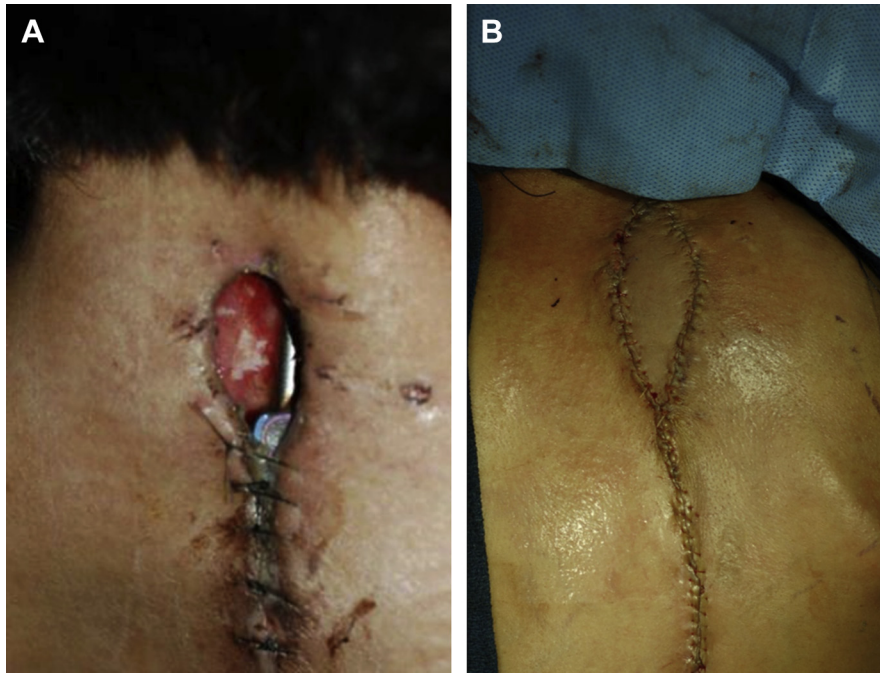

Fig. 12. (*A*) Cervical spinal hardware exposure was seen after correction of scoliosis. (*B*) Trapezius myocutaneous flap was used to cover the hardware, for salvage and stability.

Repair and coverage for sternal wound infections can use many adjacent flaps to provide good stable soft tissue coverage. A pectoralis flap has been used in infants for closure of sternal wound infections.[80,81] Any regional transfer is generally approached in a staged fashion, with initial debridement and dressing changes for a clean wound, followed by flap closure. Rectus muscle can also be used in a vertically based fashion, but the course of the internal mammary artery to the superficial epigastric may be disrupted, so the contralateral side should be used. A regional flap that can be used with success is a pedicled omental flap. Transdiaphragmatic description has been reported in the adult literature.[82]

Abdominal wall disorders such as omphaloceles have well-established protocols for management in infancy. Component separation (which involves separating and advancing certain layers of abdominal muscles, and lengthening their reach to achieve primary midline closure) and tissue expanders are being used to aid in closure of abdominal wall defects when classic methods are unsuccessful. Rohrich and colleagues[83] proposed an algorithm for management of abdominal wall reconstruction, which outlined the size of the defect and an appropriate regional flap or free tissue transfer. Other groups have reported complete reconstruction of the abdominal wall in adults using the lateral circumflex system and a conjoined tensor fascia lata and anterolateral thigh flap.[84]

In extremity reconstruction most bony defects are reconstructed using a fibula graft. Noaman[85] performed a retrospective study in adult patients with an average defect of 8 cm of bone in the extremity. They had a 93% success rate, and, as in the spine, the benefits of vascularized bone grafting included osteogenesis at the fracture site. In the pediatric population requiring lower extremity reconstruction, 75% of patients were

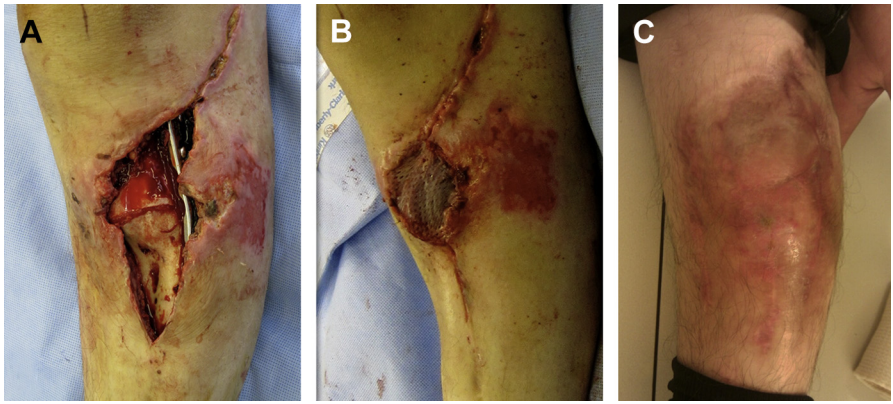

Fig. 13. (*A*) A malnourished young man had exposure of his tibial fracture and hardware. (*B*) After debridement and optimizing nutrition, salvage of hardware (which was found to be stable) was performed with a gastrocnemius muscle flap. (*C*) Final outcome.

able to achieve independent ambulation, and another 20% were able to achieve assisted ambulation.[85] Modifications can be made to the free fibular graft, such as adding cortical allografts to aid in support. Although there is the likelihood of leg length discrepancy, only 14% of patients required surgical correction[86–89] (**Fig. 13**).

Although it may never be possible to eliminate the risk of a wound, the medical armamentarium continues to expand with methods to manage it. The expanded knowledge of cell signaling within a wound may someday allow clinicians to guide healing in a normal cascade even in abnormal conditions.

REFERENCES

1. Goldman R. Growth factors and chronic wound healing: past, present, and future. Adv Skin Wound Care 2004;17(1):24–35.
2. Kim WJ-H, Gittes GK, Longaker MT. Signal transduction in wound pharmacology. Arch Pharm Res 1998;21(5):487–95.
3. Lewis T, Grant R. Vascular reaction of the skin. Part II. The liberation of histamine like substance in injured akin; The underlying cause of factitious urticarial and wheal produced by burning, and observations upon the nervous controls of certain skin reactions. Heart 1924;11:209–65.
4. O'Leary JP, Tabuenca A, Capote LR, editors. The physiologic basis of surgery. Philadelphia: Lippincott Williams & Wilkins; 2008.
5. Raja SK, Garcia MS, Isseroff RR. Wound re-epithelialization: modulating keratinocyte migration in wound healing. Front Biosci 2007;12:2849–68.
6. Schulz C, Gomez Perdiguero E, Chorro L, et al. A lineage of myeloid cells independent of Myb and hematopoietic stem cells. Science 2012;336:86–90.
7. Lech M, Anders H. Macrophages and fibrosis: how resident and infiltrating mononuclear phagocytes orchestrate all phases of tissue injury and repair. Biochim Biophys Acta 2013;1832(7):989–97.
8. Barrientos S, Stojadinovic O, Golinko MS, et al. Perspective article: growth factors and cytokines in wound healing. Wound Repair Regen 2008;16:585–601.
9. Broughton G, Janis J, Attinger C. Wound healing: an overview. Plast Reconstr Surg 2006;117:1e-s.

10. Reinke JM, Sorg H. Wound repair and regeneration. Eur Surg Res 2012;49:35–43.
11. Thorne CH. Grabb and Smith's plastic surgery. Philadelphia: Lippincott Williams & Wilkins; 2013.
12. Romo T Pearson JM Yalamanchili H, et al. Wound healing, skin. E-medicine specialties. Available at: http://www.emedicine.com/ent/topics13.htm. Accessed May 12, 2016.
13. Atiyeh BS, Amm CA, El Musa KA. Improved scar quality following primary and secondary healing of cutaneous wounds. Aesthetic Plast Surg 2003;27(5):411–7.
14. Leininger BE, Rasmussen TE, Smith DL, et al. Experience with wound VAC and delayed primary closure of contaminated soft tissue injuries in Iraq. J Trauma 2006;61(5):1207–11.
15. Tandara AA, Mustoe TA. Oxygen in wound healing—more than a nutrient. World J Surg 2004;28(3):294–300.
16. Hopf HW, Humphrey LM, Puzziferri N, et al. Adjuncts to preparing wounds for closure: hyperbaric oxygen, growth factors, skin substitutes, negative pressure wound therapy (vacuum-assisted closure). Foot Ankle Clin 2001;6(4):661–82.
17. Hart DW, Wolf SE, Chinkes DL, et al. Effects of early excision and aggressive enteral feeding on hypermetabolism, catabolism, and sepsis after severe burn. J Trauma 2003;54(4):755–64.
18. Zaizen Y, Ford EG, Costin G, et al. Stimulation of wound bursting strength during protein malnutrition. J Surg Res 1990;49(4):333–6.
19. Padh H. Vitamin C: newer insights into its biochemical functions. Nutr Rev 1991;49(3):65–70.
20. Arnold M, Barbul A. Nutrition and wound healing. Plast Reconstr Surg 2006;117(7S):42S–58S.
21. Ehrlich HP, Hunt TK. Effects of cortisone and vitamin A on wound healing. Ann Surg 1968;167(3):324.
22. Lansdown ABG, Mirastschijski U, Stubbs N, et al. Zinc in wound healing: theoretical, experimental, and clinical aspects. Wound Repair Regen 2007;15(1):2–16.
23. Lebwohl M, Neldner K, Pope FM, et al. Classification of pseudoxanthoma elasticum: report of a consensus conference. J Am Acad Dermatol 1994;30(1):103–7.
24. Beighton P, De Paepe A, Steinmann B, et al. Ehlers-Danlos syndromes: revised nosology, Villefranche, 1997. Am J Med Genet 1998;77(1):31–7.
25. Burch GH, Gong Y, Liu W, et al. Tenascin-X deficiency is associated with Ehlers-Danlos syndrome. Nat Genet 1997;17(1):104–8.
26. Pepin M, Schwarze U, Superti-Furga A, et al. Clinical and genetic features of Ehlers–Danlos syndrome type IV, the vascular type. N Engl J Med 2000;342(10):673–80.
27. Zhang M-C, He L, Giro M, et al. Cutis laxa arising from frameshift mutations in exon 30 of the elastin gene (ELN). J Biol Chem 1999;274(2):981–6.
28. Salk D. Werner's syndrome: a review of recent research with an analysis of connective tissue metabolism, growth control of cultured cells, and chromosomal aberrations. Hum Genet 1982;62(1):1–15.
29. Bauer EA, Silverman N, Busiek DF, et al. Diminished response of Werner's syndrome fibroblasts to growth factors PDGF and FGF. Science 1986;234(4781):1240–3.
30. Patterson JW. Weedon's skin pathology. China: Elsevier Health Sciences; 2014.
31. Ogawa R, Akaishi S, Izumi M. Histologic analysis of keloids and hypertrophic scars. Ann Plast Surg 2009;62(1):104–5.

32. Butler PD, Longaker MT, Yang GP. Current progress in keloid research and treatment. J Am Coll Surg 2008;206(4):731–41.
33. Ogawa R. The most current algorithms for the treatment and prevention of hypertrophic scars and keloids. Plast Reconstr Surg 2010;125(2):557–68.
34. Attinger CE, Janis JE, Steinberg J, et al. Clinical approach to wounds: debridement and wound bed preparation including the use of dressings and wound-healing adjuvants. Plast Reconstr Surg 2006;117(7S):72S–109S.
35. Donelan MB, Parrett BM, Sheridan RL. Pulsed dye laser therapy and z-plasty for facial burn scars: the alternative to excision. Ann Plast Surg 2008;60(5):480–6.
36. Fonder MA, Lazarus GS, Cowan DA, et al. Treating the chronic wound: a practical approach to the care of nonhealing wounds and wound care dressings. J Am Acad Dermatol 2008;58(2):185–206.
37. Wright JB, Lam K, Burrell RE. Wound management in an era of increasing bacterial antibiotic resistance: a role for topical silver treatment. Am J Infect Control 1998;26(6):572–7.
38. Morykwas MJ, Argenta LC, Shelton-Brown EI, et al. Vacuum-assisted closure: a new method for wound control and treatment: animal studies and basic foundation. Ann Plast Surg 1997;38(6):553–62.
39. Ingber DE. The mechanochemical basis of cell and tissue regulation. Mech Chem Biosyst 2004;1(1):53–68.
40. Ingber DE. Mechanical control of tissue growth: function follows form. Proc Natl Acad Sci U S A 2005;102(33):11571–2.
41. Lu F, Ogawa R, Nguyen DT, et al. Microdeformation of three-dimensional cultured fibroblasts induces gene expression and morphological changes. Ann Plast Surg 2011;66(3):296.
42. Heit YI, Dastouri P, Helm DL, et al. Foam pore size is a critical interface parameter of suction-based wound healing devices. Plast Reconstr Surg 2012;129(3):589–97.
43. Bütter A, Emran M, Al-Jazaeri A, et al. Vacuum-assisted closure for wound management in the pediatric population. J Pediatr Surg 2006;41(5):940–2.
44. Pauniaho S-L, Costa J, Boken C, et al. Vacuum drainage in the management of complicated abdominal wound dehiscence in children. J Pediatr Surg 2009;44(9):1736–40.
45. Lopez G, Clifton-Koeppel R, Emil S. Vacuum-assisted closure for complicated neonatal abdominal wounds. J Pediatr Surg 2008;43(12):2202–7.
46. Othman D. Negative pressure wound therapy literature review of efficacy, cost effectiveness, and impact on patients' quality of life in chronic wound management and its implementation in the United Kingdom. Plast Surg Int 2012;2012:374398.
47. Erba P, Ogawa R, Ackermann M, et al. Angiogenesis in wounds treated by microdeformational wound therapy. Ann Surg 2011;253(2):402.
48. Quinn JV, Drzewiecki A, Li MM, et al. A randomized, controlled trial comparing a tissue adhesive with suturing in the repair of pediatric facial lacerations. Ann Emerg Med 1993;22(7):1130–5.
49. Singer AJ, Hollander JE, Quinn JV. Evaluation and management of traumatic lacerations. N Engl J Med 1997;337(16):1142–8.
50. Hurvitz KA, Kobayashi M, Evans GRD. Current options in head and neck reconstruction. Plast Reconstr Surg 2006;118(5):122e–33e.
51. Kretlow JD, McKnight AJ, Izaddoost SA. Facial soft tissue trauma. Semin Plast Surg 2010;24(4):348–56.

52. Miller GDH, Anstee EJ, Snell JA. Successful replantation of an avulsed scalp by microvascular anastomoses. Plast Reconstr Surg 1976;58(2):133–6.
53. Steffen A, Katzbach R, Klaiber S. A comparison of ear reattachment methods: a review of 25 years since Pennington. Plast Reconstr Surg 2006;118(6):1358–64.
54. Guo L, Pribaz JR, Pribaz JJ. Nasal reconstruction with local flaps: a simple algorithm for management of small defects. Plast Reconstr Surg 2008;122(5):130e–9e.
55. Tzafetta K, Terzis JK. Essays on the facial nerve: Part I. Microanatomy. Plast Reconstr Surg 2010;125(3):879–89.
56. Dorafshar AH, Borsuk DE, Bojovic B, et al. Surface anatomy of the middle division of the facial nerve: Zuker's point. Plast Reconstr Surg 2013;131(2):253–7.
57. Stringer MD, Mirjalili SA, Meredith SJ, et al. Redefining the surface anatomy of the parotid duct: an in vivo ultrasound study. Plast Reconstr Surg 2012;130(5):1032–7.
58. Rhee ST, Colville C, Buchman SR. Conservative management of large avulsions of the lip and local landmarks. Pediatr Emerg Care 2004;20(1):40–2.
59. Smith J, Maconochie I. Should we glue lip lacerations in children? Arch Dis Child 2003;88(1):83.
60. Kudsk KA, Sheldon GF, Walton RI. Degloving injuries of the extremities and torso. J Trauma 1981;21(10):835–9.
61. Available at: http://www.cdc.gov/features/dog-bite-prevention/. Accessed February 23, 2016.
62. Garvey EM, Twitchell DK, Ragar R, et al. Morbidity of pediatric dog bites: a case series at a level one pediatric trauma center. J Pediatr Surg 2015;50(2):343–6.
63. Kaye AE, Belz JM, Kirschner RE. Pediatric dog bite injuries: a 5-year review of the experience at the Children's Hospital of Philadelphia. Plast Reconstr Surg 2009;124(2):551–8.
64. Gurunluoglu R, Glasgow M, Arton J, et al. Retrospective analysis of facial dog bite injuries at a Level I trauma center in the Denver metro area. J Trauma Acute Care Surg 2014;76(5):1294–300.
65. Fleisher GR. The management of bite wounds. N Engl J Med 1999;340:138–40.
66. Bailie WE, Stowe EC, Schmitt AM. Aerobic bacterial flora of oral and nasal fluids of canines with reference to bacteria associated with bites. J Clin Microbiol 1978;7(2):223–31.
67. Cummings P. Antibiotics to prevent infection in patients with dog bite wounds: a meta-analysis of randomized trials. Ann Emerg Med 1994;23(3):535–40.
68. Ferri FF. Ferri's clinical advisor 2013: 5 Books in 1. Philadelphia: Elsevier Health Sciences; 2012.
69. Sudarsky LA, Laschinger JC, Coppa GF, et al. Improved results from a standardized approach in treating patients with necrotizing fasciitis. Ann Surg 1987;206(5):661.
70. Wolter TP, Noah EM, Pallua N. The use of Integra® in an upper extremity avulsion injury. Br J Plast Surg 2005;58(3):416–8.
71. Godina M. Early microsurgical reconstruction of complex trauma of the extremities. Plast Reconstr Surg 1986;78(3):285–92.
72. Upton J, Guo L. Pediatric free tissue transfer: a 29-year experience with 433 transfers. Plast Reconstr Surg 2008;121(5):1725–37.
73. Upton J, Guo L, Labow BI. Pediatric free-tissue transfer. Plast Reconstr Surg 2009;124(6S):e313–26.

74. Viol A, Pradka SP, Baumeister SP, et al. Soft-tissue defects and exposed hardware: a review of indications for soft-tissue reconstruction and hardware preservation. Plast Reconstr Surg 2009;123(4):1256–63.
75. Jandali S, Diluna ML, Storm PB, et al. Use of the vascularized free fibula graft with an arteriovenous loop for fusion of cervical and thoracic spinal defects in previously irradiated pediatric patients. Plast Reconstr Surg 2011;127(5):1932–8.
76. Moran SL, Bakri K, Mardini S, et al. The use of vascularized fibular grafts for the reconstruction of spinal and sacral defects. Microsurgery 2009;29(5):393–400.
77. Woodward CS, Son M, Calhoon J, et al. Sternal wound infections in pediatric congenital cardiac surgery: a survey of incidence and preventative practice. Ann Thorac Surg 2011;91(3):799–804.
78. Tabbutt S, Duncan BW, McLaughlin D, et al. Delayed sternal closure after cardiac operations in a pediatric population. J Thorac Cardiovasc Surg 1997;113(5):886–93.
79. Bryan CS, Yarbrough WM. Preventing deep wound infection after coronary artery bypass grafting. Tex Heart Inst J 2013;40(2):125–39.
80. Sung K, Jun TG, Park PW, et al. Management of deep sternal infection in infants and children with advanced pectoralis major muscle flaps. Ann Thorac Surg 2004;77(4):1371–5.
81. Falagas ME, Tansarli GS, Kapaskelis A, et al. Impact of vacuum-assisted closure (VAC) therapy on clinical outcomes of patients with sternal wound infections: a meta-analysis of non-randomized studies. PLoS One 2013;8(5):e64741.
82. Vyas RM, Prsic A, Orgill DP. Transdiaphragmatic omental harvest: a simple, efficient method for sternal wound coverage. Plast Reconstr Surg 2013;131(3):544–52.
83. Rohrich RJ, Lowe JB, Hackney FL, et al. An algorithm for abdominal wall reconstruction. Plast Reconstr Surg 2000;105(1):202–16.
84. Wong C-H, Lin CH, Fu B, et al. Reconstruction of complex abdominal wall defects with free flaps: indications and clinical outcome. Plast Reconstr Surg 2009;124(2):500–9.
85. Noaman HH. Management of upper limb bone defects using free vascularized osteoseptocutaneous fibular bone graft. Ann Plast Surg 2013;71(5):503–9.
86. Piper M, Irwin C, Sbitany H. Pediatric lower extremity sarcoma reconstruction: a review of limb salvage procedures and outcomes. J Plast Reconstr Aesthet Surg 2016;69(1):91–6.
87. Moran SL, Shin AY, Bishop AT. The use of massive bone allograft with intramedullary free fibular flap for limb salvage in a pediatric and adolescent population. Plast Reconstr Surg 2006;118(2):413–9.
88. Capanna R, Bufalini C, Campanacci M. A new technique for reconstructions of large metadiaphyseal bone defects. Orthoped Traumatol 1993;2(3):159–77.
89. Innocenti M, Abed YY, Beltrami G, et al. Biological reconstruction after resection of bone tumors of the proximal tibia using allograft shell and intramedullary free vascularized fibular graft: long-term results. Microsurgery 2009;29(5):361–72.