

# Complex Wound Management

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## Abstract

Despite the generous blood supply, and resultant healing capacity within the head and neck, complex wounds in this area may be extremely debilitating and present an obstacle to treatment for the reconstructive surgeon. Delayed, incomplete, or otherwise suboptimal wound healing within this anatomical region may lead to both functional and aesthetically displeasing outcomes, resulting in impaired speech or swallowing, social stigma, and, in severe cases, exposure of critical underlying structures. Due to implications, with regard to wound formation following surgical intervention, the facial reconstructive surgeon, in particular, must be familiar with the multitude of treatment modalities available. This article serves as a review of the underlying pathophysiology of wound healing, local and systemic processes that may influence the healing process, and treatments that facilitate tissue restoration while mitigating future complications.

## Keywords

- ▶ wounds
- ▶ complications
- ▶ wound healing
- ▶ contaminated wounds
- ▶ wound bed preparation

## Physiological Basis of Wound Healing

Whether a wound is formed as a result of a meticulously planned surgical intervention, complication of an underlying systemic disorder, or traumatic injury, early intervention with optimization of the healing process is of paramount importance. Each physiological stage of tissue regeneration has important ramifications on wound formation. A basic understanding of these stages is therefore imperative in regulating the overall process and further augmenting healing.

The restoration of tissue following insult is a complex biological cascade and can best be simplified into several critical phases: the coagulative, inflammatory, proliferative, and remodeling phases.<sup>1–3</sup> If perturbation of any of these phases occurs, delayed healing ensues, thus increasing the risks of poor outcomes and a chronic wound. Immediately following initial injury, a hemostatic cascade is elicited. Vasoconstriction is initiated by thromboxane A<sub>2</sub>. Endothelial cell damage with resultant exposure of collagen activates the coagulation and complement pathways, resulting in a fibrin–

platelet matrix. This aggregate results in clot formation and acts as a substrate, concentrating growth factors.<sup>2</sup> Platelet degranulation and cytokine release induce vasodilation, capillary permeability, inflammation, and edema. Neutrophils, macrophages, fibroblasts, and endothelial cells then migrate to the region of injury. The presence of phagocytes facilitates the removal of bacteria and debris from within the wound. The prolonged presence of these cells within the wound bed, as in the case of contaminated wounds, may result in an extended inflammatory phase, resulting in exacerbated fibrosis and scar formation.<sup>4</sup> Macrophages provide a critical regulatory function, coordinating the transition from a state of inflammation to an active stage of tissue repair.<sup>5</sup> As inflammation subsides, the proliferative phase is initiated during which neovascularization, angiogenesis, collagen deposition, and wound contraction result in increased tissue tensile strength. Reepithelization is critical in establishing a protective barrier overlying healing tissue. Epithelial cell migration is expedited in a moist microenvironment. In stark contradistinction, epithelial cell migration in the setting of tissue desiccation or necrosis has been

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shown to be significantly prolonged and associated with impaired healing.<sup>6</sup> In this regard, a moist occlusive dressing may promote an environment in which reepithelialization occurs more expeditiously, preventing delayed healing or further complications. The final stage of healing, the maturation or remodeling phase, is coordinated by fibroblast remodeling of extracellular matrices, with organized type I collagen replacing type III collagen. Type I collagen fibers align in a more organized parallel fashion, lending more tensile strength and improved appearance to the healing wound. Wound strength subsequently reaches a maximum of 80% of its original tensile strength at approximately 3 months following injury onset.<sup>7</sup>

With the aforementioned physiological pathway in mind, the initial approach to wound management involves recognition of tissue parameters that may potentially contribute to a suboptimal healing state. This delicate interplay of tissue factors and cellular components may be targeted by early interventions aiming to optimize tissue restorative processes while mitigating inflammation.

## Wound Bed Preparation

Given the physiological principles of wound healing, the reconstructive surgeon should be familiar with clinical measures that may optimize the tissue microenvironment to maximize potential healing. Any potential local tissue characteristics that may present an impediment to healing should be identified. These include ischemia, venous congestion, wound dehiscence, infection, desiccation, prior radiation, and necrosis. In chronically nonhealing wounds, a tissue biopsy should be considered to rule out malignancy. Key tenets of local wound care, employed in management of all wounds, aim to minimize the inflammatory component of the healing pathway while augmenting tissue proliferation and remodeling. The International Wound Consensus Panel recommends a systematic approach to the initial treatment of the wound bed.<sup>8</sup> The following four critical steps in the initial preparation of the wound microenvironment are proposed: adequate debridement of the wound bed, decreased inflammation or infection, maintenance of moisture, and optimization of wound edges reepithelialization.<sup>9</sup>

Nonviable cellular debris within the wound bed prolongs the inflammatory phase and impairs phagocytosis, may serve as a nidus for infection, and prevents epithelialization. Prior to reconstructive efforts toward soft tissue coverage, necrotic tissue and eschar must therefore be removed. A multitude of debridement methods are available including surgical, mechanical, enzymatic, and autolytic debridement. The need for aggressive removal of necrotic tissue must be accordingly balanced with the potential damage to underlying viable tissue. With this in mind, more than one debridement method is often employed. In most cases, aggressive debridement techniques are used followed by milder methods for preservation of healthy tissue. These processes effectively restore a healthy wound base and promote formation of functional extracellular matrix proteins that help propagate the healing cascade. Surgical debridement utilizes sharp dissection using

cold instruments in the removal of necrotic tissue. This technique is particularly useful in wounds with large necrotic tissue burden or in the setting of severe infection but results in significant tissue damage. Mechanical debridement comprises removal of tissue using physical force, the most commonly implemented form of which is wet-to-dry dressings. While this method is a milder form of debridement, it may result in limited damage to surrounding tissue. The choice in wound cleanser is of critical importance in wet-to-dry dressings. Generally, sterile saline or antibiotic irrigation may be used in this technique. Cytotoxic skin cleansers such as povidone-iodine, hydrogen peroxide, and sodium hypochlorite should be used with caution due to their deleterious effects.<sup>10,11</sup> Autolytic debridement uses proteolytic enzymes in degrading necrotic debris. A semiocclusive dressing is placed over the wound for 72 hours, and natural enzymatic processes are allowed to ensue. This represents the mildest form of debridement but is a slower process than those previously discussed. Autolytic debridement is not appropriate for exudative, infected, or particularly deep wounds. Hydrogels may be used in combination with occlusive dressings to expedite debridement and soften the wound bed.<sup>11</sup> Enzymatic debridement uses exogenous enzymes to liquefy cellular debris. Papain-urea cream and collagenase ointments are common preparations used in this regard. Papain-urea degrades tissue more rapidly; however, collagenase is more selective toward necrotic debris sparing the underlying viable tissue (→ Fig. 1). This form of debridement is of intermediate strength.<sup>12</sup>

A prolonged inflammatory phase of wound healing may lead to excess exudative debris, delayed healing, and, ultimately, increased scar formation.<sup>13</sup> Infection, in particular, may significantly extend this stage and should be promptly recognized and treated expeditiously. Closed infected wounds should be opened to promote oxygenation and impair obligate anaerobic microbial growth. Wound cultures should be obtained to target antimicrobial therapy and necrotic debris debrided. Optimal treatment for wound infection involves preventative measures and avoidance. Antibiotic prophylaxis decreases surgical site infections in 44% of clean contaminated cases. Prophylactic antibiotics



**Fig. 1** (A) Fibula free flap donor site with dehiscence and resultant chronic wound formation. (B) Same wound after 6 weeks following application of topical collagenase treatment and split-thickness skin graft.

**Table 1** Wound dressings and associated features

Class	Composition	Adhesive	Absorbent	Gas permeable	Fluid permeable	Indications
Gauze	Cotton	–	+	+	+	Debridement, drying
Impregnated gauze	Cotton + antibiotic agent	–	±	+	+	Wound hydration
Adhesive films	Tegaderm	+	–	+	–	Ulcers, skin graft sites, poor for wounds with heavy exudate
Hydrogels	Water + hydrophilic copolymer	–	–	+	–	Cutaneous ulcers, maintains wound moisture, poor for heavy exudate
Hydrocolloids	Colloids	+	+	–	–	Absorptive, for moderate exudate
Foams	Polyurethane based	–	+	+	+	Absorbs moderate amounts of exudates, hydrophilic
Silicone based	Silicone	±	–	+	–	Cutaneous ulcers, hypertrophic scars
Bioengineered skin	Keratinocytes or fibroblasts	–	Variable	+	+	Full-thickness ulcers or burns

Source: Adapted from Pitzer and Patel.<sup>17</sup>

should be administered within 1 hour of incision to reduce bacterial wound burden. There is limited evidence showing the utility in perioperative antibiotics, for more than 24 hours, in reducing surgical site complications in clean contaminated cases and this is therefore generally recommended against.<sup>14</sup>

Maintenance of a hydrated wound microenvironment is also important in amplifying healing potential. Promoting moisture of the wound bed increases the rate of epithelialization twofold.<sup>15</sup> Therefore, desiccation of the wound bed should be avoided with the use of moisture-retentive topical solutions and dressings. Excessive moisture may also represent an impediment to epithelial migration, and excess fluid should be removed with absorbent dressings to avoid maceration.<sup>1,16</sup> ▶ **Table 1** provides a brief overview of available dressing types with their associated features.<sup>7</sup>

## Silver

The use of silver in the treatment of wounds predates to antiquity.<sup>18</sup> Silver products have been shown to have broad-spectrum coverage, particularly in antimicrobial-resistant organisms.<sup>18</sup> Silver has shown bactericidal properties through inhibition of the cytochrome pathway and electron transport in the bacterial respiratory chain.<sup>18</sup> The antimicrobial activity of silver-containing products is dependent on the ionized silver content (Ag<sup>+</sup>). However, delivery to the healing tissue bed may be hindered secondary to the high concentration of negatively charged proteins and ions within this microenvironment. Delivery systems have therefore been developed to facilitate ionized silver transport to the recipient wound bed.<sup>19</sup> Silver sulfadiazine contains silver ion complexed with glycols and alcohols in conjunction with sulfadiazine antibiotic.<sup>20</sup> However, adverse effects include

impaired reepithelialization, eschar formation, and potential bone marrow toxicity.<sup>21</sup> These products should therefore only be used in strict moderation. To address such shortcomings, nanocrystalline silver dressings were developed. These products contain stratified high-density polyethylene between layers of polyester gauze. The outer stratum contains a nanocrystalline coating with uncharged silver (Ag<sup>0</sup>), whereas the deeper segment promotes moisturization within the wound bed. Neutral silver provides longer exposure due to its inert state and lower reactivity to negatively charged wound particles. These dressings also require less frequent changes, as compared with silver sulfadiazine and silver nitrate products, and need only to be changed every few days.<sup>22</sup> This allows for less disruption to the healing wound bed while also decreasing patient discomfort. Additionally, silver has shown broad-spectrum antimicrobial coverage including molds, fungi, and yeast. Studies have noted significant antimicrobial activity toward antibiotic-resistant bacteria including methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococci*.<sup>22</sup> The primary literature has further reinforced the efficacy of nanocrystalline silver over similar silver preparations including silver sulfadiazine and silver nitrate, although there are limited randomized controlled trials (RCTs).<sup>23–25</sup>

However, bactericidal silver concentrations may also be lethal toward healthy native cells. Studies have shown in vitro inhibition of fibroblast proliferation, keratinocyte growth, delay in epithelialization, and cytotoxicity toward skin substitutes.<sup>26,27</sup> However, in vivo studies have yet to confirm these reports, and therefore the exact concentration, duration, and extent of silver-based dressings or topical solutions continue to be controversial. Silver-coated dressings should optimally be employed in burn wounds or deepithelialized wounds infected with multimicrobial-resistant microorganisms.

## Skin Substitutes

Innovations in tissue engineering and advanced biomaterials have facilitated the treatment of composite wound defects, particularly burns, involving a significant body surface area necessitating sizeable tissue coverage. Currently, use of autografts is the preferred technique; however, this can often be limited by tissue availability for grafting or patient factors that may preclude this as an option. Allograft and xenograft cutaneous substitutes pose a possible solution in this setting and may provide temporizing tissue coverage. Biosynthetic skin substitutes and autologous engineered epidermal-dermal tissue are also available but expensive.

Biobrane (UDL Laboratories, Inc.), nylon mesh polymer bound with a thin silicone membrane coated with porcine polypeptides, may be used in wounds extending to the mid-dermis and has shown comparable efficacy with silver sulfadiazine, with decreased necessity for dressing changes.<sup>28,29</sup> TransCyte (Advanced BioHealing, Inc.) dressing consists of nylon mesh polymer with a semipermeable silicone membrane integrated with fibroblasts and porcine collagen.<sup>30,31</sup> Studies have shown equivalency to silver sulfadiazine with respect to healing time, rate of infection, and scar formation.<sup>32</sup> Dermagraft (Advanced BioHealing, Inc.), bioabsorbable polyglactin mesh impregnated with neonatal fibroblasts, has also shown comparable efficacy to allograft with respect to wound infection, healing time, and graft take.<sup>33</sup> Apligraf (Organogenesis Inc.) and Integra (Integra Lifesciences) also represent synthetic semibiological dressings that may be used in complex traumatic composite defects with the exposure of underlying tendon, joint, or bone.<sup>34</sup>

Within the last several years, there has been significant clinical interest in the use of products containing decellularized human amniotic membrane and umbilical cord in treating chronic soft tissue wounds. The composition of human placental membrane includes a collagen-rich extracellular membrane, providing three-dimensional structural framework, growth factors, cytokines, and endogenous mesenchymal stem cells. These properties give this substrate significant potential to further augment the healing process (→ **Figs. 2** and **3**).<sup>35</sup> Although an allograft, amniotic membrane is immunologically inert due to the absence of human leukocyte antigen.<sup>36</sup> Epifix (dehydrated human amnion/chorion membrane), Grafix (placental allograft), and Neox (cryopreserved human amniotic membrane) represent cost-effective and safe options.<sup>35</sup> A detailed review of biologics and synthetic cutaneous substitutes is beyond the scope of this article. Readers are referred to multiple reviews regarding this topic within the references.<sup>30,31,36,37</sup>

## Vacuum-Assisted Negative-Pressure Devices

Vacuum-assisted closure devices have demonstrated considerable utility in the management of chronic wounds and skin grafts. These devices consist of a polyurethane sponge held overlying wounds with adhesive dressing and kept under subatmospheric pressure with the use of a vacuum pump. This mechanism induces granulation tissue formation, removes excess exudate while maintaining appropriate mois-



**Fig. 2** Left: radial forearm free flap donor site with loss of split-thickness skin graft. Right: forearm site after 6 weeks following use of placental graft.



**Fig. 3** (A) Paramedian forehead donor site with incomplete healing. (B) Wound after 6 weeks following placental graft.

ture balance, decreases bacterial load, facilitates debridement, and is thought to improve blood supply to the wound bed.<sup>38</sup> These devices may be used in complex wounds with exposed neurovascular structures or viscera. If intervening muscle and soft tissue cannot be placed between the sponge and the underlying vital structure, Vaseline or silicone mesh may be used allowing for wound closure in patients with multiple comorbidities that may require more definitive reconstruction with free tissue transfer in a delayed fashion. In implementing such a staged approach, wound dimensions are decreased allowing for a less complex composite reconstruction than otherwise originally anticipated.<sup>39,40</sup>

## Hyperbaric Oxygen

Hyperbaric oxygen (HBO) has shown promising results in the management of complex refractory wounds. The patient is placed within a pressurized sealed chamber, with 100% oxygen at 1.5 to 3 ATMs, for approximately 1 to 3 hours over the course of several treatments. A typical treatment course will vary pursuant to the extent of the wound but typically consists of

20 to 40 treatments performed once to twice daily. Favorable anecdotal evidence indicates that HBO may increase angiogenesis and oxygen tissue perfusion, both of which increase overall oxygen-carrying capacity to the hypoxic wound bed, although the exact mechanism is not yet understood.<sup>41–43</sup> Contraindications include pneumothorax, active malignancy, concurrent chemotherapy, and severe reactive airway disease. Potential adverse outcomes include sinogenic or otic discomfort, claustrophobia, and potential neural toxicity due to high oxygen pressures.<sup>43</sup> These adverse reactions may be minimized by parceling treatment courses and providing “air breaks” during treatment. It is the author’s preference to allow at least a 6-month interval, following chemoradiation, prior to implementing HBO to decrease theoretical risk of potentiating growth of the malignant process. Several RCTs have shown that the full effects of HBO are seen up to 1 year following treatment.<sup>44,45</sup>

### Future Considerations in the Management of Complex Wounds

Biosynthetic wound products have been an area of active research and growth as our understanding of the underlying pathophysiology of wound healing improves. As detailed previously, the active wound healing process follows a predictable sequence from inflammation to proliferation and, ultimately, remodeling or maturation. Modulation of the cellular mediators facilitates this pathway and may accelerate wound healing. Eicosanoids, arachidonic, and acid metabolites such as prostaglandins or leukotrienes modulate the early inflammatory phase of wound healing. Their use in chronic wounds has shown early promise, with some laboratory-based studies showing a decrease in size and healing time when compared with controls.<sup>34</sup>

Cytokines similarly play a regulatory role within the inflammatory process, inducing cell proliferation and migration, thereby aiding in the tissue restorative process. Granulocyte-macrophage colony-stimulating factor has shown encouraging results in prospective RCTs.<sup>46</sup>

Recombinant platelet-derived growth factor (PDGF) has shown up to twofold increase in the capacity to augment wound healing when compared with placebo in RCTs and is approved by the U.S. Food and Drug Administration (FDA) for use in diabetic ulcers. Recombinant human PDGF, or Becaplermin, is currently the only FDA-approved product within the United States. Although initially developed for use in diabetic ulcers, there is anecdotal evidence for off-label use in chronic refractory, previously irradiated, wounds of the head and neck.<sup>47</sup> However, a major limitation of growth factor use is the theoretical risk of induced malignancy. This risk should be discussed with the patient prior to implementation of this modality. Biopsy should be considered prior to institution of this treatment in a nonhealing chronic wound at a previously irradiated region to rule out recurrence of neoplasm.

### Conclusion

Poorly healing wounds within the head and neck pose a considerable challenge to the reconstructive surgeon. Prior

to exhaustion of potential reconstructive efforts, any potential barriers that may impede the healing process should be appropriately addressed. Both local and systemic factors that may contribute to poor healing must be identified to maximize healing potential. Wound bed preparation is the initial step involving debridement, control of infection or inflammation, moisture optimization, and maintenance of fresh wound edges so as to promote reepithelialization. Refractory wounds require a multidisciplinary approach with implementation of adjunctive measures such as advanced dressings, application of biologicals, vacuum-assisted devices, HBO, and topical growth factor treatment. However, clinicians must remember that these measures should not serve as replacement of the standard wound care principles of increasing tissue oxygenation, maximization of patient nutrition, debridement of nonviable tissue, and infection control.

Conflicts of Interest  
None declared.

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