Chronic Wounds

Kourosh Izadi, MD, DDS*, Parham Ganchi, MD, PhD

Division of Plastic Surgery, Department of Surgery, New Jersey Medical School–UMDNJ, 90 Bergen Street, Newark, NJ 07103, USA

The definition of a chronic wound is not clearly outlined in the literature. Chronic wounds develop when there is a disruption in the normal healing process. They fail to heal within a “normal” period of time when similar wounds would otherwise have healed. Wounds that have failed to progress through a normal sequence of repair in 4 to 8 weeks are generally presumed to be chronic. Chronic wounds can be a challenge to the patient, the health care professional, and the health care system. Venous leg ulcers, pressure sores, ischemic ulcers, and diabetic foot ulcers are examples of chronic wounds. There are over 4 million Americans afflicted with these types of wounds, with an annual treatment cost of 9 billion dollars. A large percentage of these wounds occur in the growing elderly population. This becomes a large burden to society because of the loss of productivity and escalating health care costs [1].

Many factors can impair wound healing. Some of the local or intrinsic factors that impair wound healing include ischemia, infection, presence of necrotic tissue, and foreign bodies in the wound. The extrinsic or external factors that need to be considered in the evaluation of a chronic wound are diabetes mellitus, cancer, chronic disease (chronic renal failure), steroid use, radiation injury, and malnutrition. It is often a combination of these factors that plays an important role in the chronic wound. The clinician needs to break the cycle in these circumstances to be able to manage the chronic wound successfully. Factors that are known to impair wound healing must be identified and corrected [3].

Impairment of wound healing

There are many factors that impair the healing process and delay or alter the normal sequence of wound healing. These factors are usually classified as intrinsic and extrinsic. The intrinsic, or local factors, that may alter wound healing include ischemia, infection, presence of necrotic tissue, and foreign bodies in the wound. The extrinsic or external factors that need to be considered in the evaluation of a chronic wound are diabetes mellitus, cancer, chronic disease (chronic renal failure), steroid use, radiation injury, and malnutrition. It is often a combination of these factors that plays an important role in the chronic wound. The clinician needs to break the cycle in these circumstances to be able to manage the chronic wound successfully. Factors that are known to impair wound healing must be identified and corrected [3].

Intrinsic factors

Ischemia and wound hypoxia

The transport of oxygen to the injured tissue is one of the most important steps in wound healing [4,5]. There are a variety of vascular and systemic disorders that unfavorably affect the delivery of
oxygen and nutrients to the injured tissue. These include arterial occlusive disease and chronic venous insufficiency, which are the most common etiologies in this group of patients. These disorders consist of vaso-occlusive disease, such as atherosclerosis and thrombosis of blood vessels, loss of endothelial integrity by autoimmune disorders, and disruption of vessels by trauma [6].

Obstruction of blood flow to the wound results in a relative decrease in the perfusion pressure of oxygen and a hypoxic wound. The chronic hypoxia results in a nonhealing wound and a host that is susceptible to infection [7]. The combination of hypoxia and infection leads to a vicious cycle that is hard to break. Wounds with oxygen tensions of 35 mm Hg or less in the adjacent skin of the extremities do not heal. Low tissue oxygen levels have been demonstrated in nonhealing wounds [8]. In settings when wound hypoxia can be verified, hyperbaric oxygen is an effective way to improve oxygen delivery [9]. Supplemental oxygen may also improve wound healing. This can affect replication of fibroblasts and collagen synthesis. Advances in vascular surgery allow for bypass of occluded blood vessels and improvement in oxygen delivery, allowing wounds to heal.

Venous ulcers are another source of chronic, nonhealing wounds that are difficult to treat. The exact mechanism is not well understood. Chronic venous insufficiency is caused by abnormalities of the venous walls and valves that lead to obstruction or reflux of blood flow in the veins [10,11]. Impairment of oxygen delivery to tissues from capillaries is thought to be the underlying mechanism leading to venous ulcers. Accumulation of proteinaceous exudates and subsequent fibrosis of this fluid around the capillaries and within the interstitium creates a barrier to the diffusion of oxygen and nutrients to the tissues. Lysosomal enzymes and proinflammatory mediators are released, exacerbating the problem and causing tissue breakdown [5,12].

Anemia alone is not thought to affect wound healing [13], although patients with anemia usually suffer from other systemic and local conditions that may affect wound healing. Proper evaluation and work-up of the patient with a chronic wound may reveal hematologic abnormalities that must be corrected for successful comprehensive management of the patient. In summary, reversible vascular disorders must be diagnosed and managed with appropriate surgical or interventional care. Vasculitis is usually treated medically. With the appropriate surgical and medical interventions, blood flow and oxygen delivery to the wound should be optimized.

### Infection

Open wounds have lost their protective skin barrier and are invariably colonized with microbes. Contamination is defined as the presence of non-replicating organisms within a wound [14]. Colonization is defined as the presence of replicating organisms in the wound without host tissue damage [14]. Wound infection is defined as the presence of replicating organisms in a wound with local tissue damage [14]. Biofilm is a slimy layer of bacteria encased in a hydrated matrix of polysaccharides and proteins that attach to necrotic tissue and surgical implants [15,16]. Biofilm is a structurally complex, dynamic system that provides bacteria a protected mode of growth that allows cells to survive and thrive in chronic wounds [17]. Antibiotic resistance of bacteria in the biofilm contributes to the chronicity of infections [18].

In contrast to acutely injured contaminated wounds, all chronic wounds contain a tissue level of microbial flora [19,20]. Infection can alter the healing process by prolonging the inflammatory phase of wound healing. The mechanism by which this occurs is believed to be due to the effect of bacterial enzymes. The enzymatic action of bacterial byproducts is believed to degrade fibrin and growth factors that are essential for healing [21–23]. The decrease in host defenses and relative lack of oxygen in the tissues results in a host that is unable to successfully propagate an immune response to combat the infection. Wound infection is defined as a bacterial count > 10⁵/g of tissue for most bacteria [24–27]. Successful closure of wounds (eg, burns and pressure sores) and techniques such as skin grafting and flap coverage have been shown to be dependent on maintaining a level below 10⁵ organisms per gram of tissue on biopsy [28–32]. Factors that may increase the likelihood of infection include immune suppression (organ transplant recipients), malnutrition, hypoxia (arterial or venous insufficiency), and the presence of a foreign body and necrotic tissue that serves as a nidus for infection. The risk of developing chronic fungal or unusual bacterial infections should be kept in mind and investigated if the initial cultures yield negative results.

A thorough evaluation of the wound must be made to rule out infection. The initial step involves a thorough history, inspection of the wound, and thorough physical evaluation. Cultures and tissue biopsy are obtained only on select cases. Deeper infections may not be diagnosed as easily and may require more sophisticated methods such as CT or MRI. Skeletal involvement may need to be ruled out at the onset of treatment to determine the extent of
the problem. Radioisotope scanning may be useful in these situations.

Foreign body
The presence of avascular foreign material creates an environment where bacteria can thrive. Exposure of orthopedic hardware, vascular grafts, or devitalized bone in an open wound predisposes it to infection and a protracted healing period. Generally, exposed foreign bodies must be removed from open wounds. It may be possible to salvage some foreign bodies, such as orthopedic hardware, with the use of the vacuum assisted closure (VAC) device [33,34]. Devitalized bone or necrotic tissue must be removed to allow the host to repair the wound. It may be difficult to remove all nonviable tissue in one operation. Multiple debridements may be necessary to obtain a healthy viable tissue bed ready for closure. In a recalcitrant wound, radiographic examination may prove beneficial in identifying foreign bodies.

Radiation
Radiation therapy can have a devastating impact on wound healing. The effects are dependent on the dose of radiation, the site of the wound, and concomitant surgery or chemotherapy. Radiation effects on normal tissues can be divided into acute and chronic. Acute or early radiation effects are changes observed during or immediately after radiation therapy. The late or chronic effects are seen weeks to years after therapy. Although acute effects can be severely disabling to the patient, it is the chronic progressive late effects that permanently alter a patient’s ability to heal (Fig. 1). The acute effects include erythema, mucositis, and frank ulceration at the site of injury. Fibrosis, lymphedema, osteorradionecrosis, and vascular changes can develop in the chronic stages of injury. The most important of these detrimental effects is damage to the blood vessels and the cells in the vicinity of the radiation portal. Histologic examination of irradiated tissue has shown endarteritis obliterans of the microvasculature [35,36]. Radiation injury causes endarteritis that inhibits wound healing by interrupting the normal angiogenesis that takes place when tissues are injured [37]. There is damage at the cellular level and to oxygen delivery. This may be improved by hyperbaric oxygen therapy. The hypoxic, hypocellular, avascular nature of irradiated skin makes it prone to ulceration and delayed healing. Post radiation injury poses difficult challenges to the clinician. The high-energy megavoltage portals used by radiation oncologists decrease the dosage delivered to the normal adjacent tissues and minimize the untoward effects of radiation that were more commonly seen with the low-energy orthovoltage therapy in the past. Any wound present in a radiation field must be biopsied to rule out recurrent or persistent tumor.

Cancer
The patient with cancer often has abnormalities of wound healing. There are a number of variables that need to be considered in this setting. These include malnutrition and catabolic conditions that impair the wound healing process. The administration of chemotherapy and radiation may directly and indirectly affect wound healing as well. Occasionally, neoplasms can mimic or develop in chronic wounds. A high level of suspicion is prudent. These neoplasms include squamous cell carcinomas and basal cell carcinomas and tend to be more aggressive varieties [38]. Systemic disorders such as lymphoma may initially present as a nonhealing skin ulcer. Biopsies of these lesions are performed to determine the presence of tumor in the wound. The presence of a malignancy within a wound precludes the wound from healing.

Extrinsic factors
Diabetes mellitus
Diabetes mellitus has been estimated to afflict 15 to 20 million patients in the United States, half of whom are undiagnosed [39]. The effects of uncontrolled diabetes on wound healing are well known to most clinicians [40–44]. Patients with diabetes mellitus make up a large percentage of patients with chronic wounds. The diabetic foot is characterized by sensory, motor, and autonomic neuropathy and macrovascular disease, which can lead to ulceration, infection, gangrene, and eventual amputation [45].
Diabetic ulcers usually occur due to the patient’s inability to sense pressure because of neuropathy [46]. The effects of neuropathy are many and include an increase in repeated trauma and eventual skin breakdown and ulceration. Patients with diabetes are also at higher risk for peripheral vascular disease, especially of the infrapopliteal system. Large-vessel disease can be a source of ischemia in this patient population. The combination of poor blood flow [47,48] and altered collagen metabolism can exacerbate the chronic wound in patients with diabetes. Wounds in patients with diabetes have been shown to have reduced tensile strength [49]. A decrease in the immunologic defense mechanism is thought to be present in patients with diabetes. Granulocytes have been shown to have decreased chemotaxis, adhesion, phagocytosis, and, as a result, a defect in bactericidal activity [50–52]. Epithelialization is impaired and further aggravates the poor healing noted in these patients.

Cardiovascular insufficiency
Patients with impaired cardiovascular function present a challenge. The decrease in the perfusion pressure of organs, which include skin and healing wounds, may prolong and jeopardize the process of repair. Because the cardiovascular disease may be life threatening, primary therapeutic attention is directed toward perfusion of viscera and not skin perfusion and integrity. A concerted effort to optimize the patient’s cardiovascular status and alleviate the immediate risk allows the wound specialist to concentrate on the problem and pursue the means to allow the patient to heal.

Steroids
Glucocorticoids have been used for many years to treat a number dermatologic disorders, transplant recipients, and autoimmune disorders. The effects of steroids are dose and time dependent. Short treatment protocols are not associated with significant delays in wound healing. Systemic steroid administration has been shown to decrease the inflammatory response and affect almost all phases of wound healing [53–58]. The effects on wound healing may be long lasting when steroids are administered on a daily basis and may impair the repair process for up to 1 year after the administration of the medication [12]. Steroids alter the inflammatory phase of wound healing by inhibiting macrophage activity, angiogenesis, fibrogenesis, and wound contraction [12,59,60]. The effects of steroids on wound healing may be reversed with the administration of vitamin A [7,53,61,62]. Steroids inhibit the release of lysosomal enzymes that are essential in the inflammatory phase of wound healing. Vitamin A is thought to antagonize this effect and allow the release of lysosomal enzymes [12].

Chemotherapy
Antineoplastic agents are being used widely for the management of malignant disease, autoimmune disorders, and dermatologic conditions. These drugs disrupt tumor growth and affect wound healing because they target rapidly dividing cells [63]. The effects of these medications are widespread, and the resultant anemia, granulocytopenia, and thrombocytopenia alter the balance that is essential for proper wound healing. The inhibition of immunologic defense mechanisms makes the host more susceptible to infection, and a vicious cycle ensues. Each antineoplastic agent has a different mechanism of action. Administration of chemotherapeutic agents 2 weeks after wound closure minimizes the risk of complications from these medications [61,64]. Pre-operative administration of antineoplastic agents is believed to be more significant in impairing wound healing. Appropriate coordination of surgical care is mandatory in a patient that is undergoing chemotherapy so that optimal timing is chosen for treatment [65].

Iatrogenic agents
Some of the agents used for wound care may have a detrimental effect on wound healing. Alcohol containing agents, antimicrobials such as Dakin’s solution, and povidone iodine are known to be toxic to the cellular components of the wound and to alter the balance toward a nonhealing wound [66,67]. A complete history of wound care products is an important component of management. Once an agent is identified, the patient or the caregiver needs to be educated regarding its use or misuse.

Factitious disorders (Munchausen syndrome and Munchausen syndrome by proxy) are difficult to diagnose and may present a dilemma to the physician. The diagnosis is usually one of exclusion, and, once diagnosed, treatment should be rendered by a psychiatrist familiar with these disorders.

Malnutrition
The optimal conditions for wound healing require a thorough assessment of the nutritional status of the patient [68]. Before initiation of any heroic efforts to manage wounds that have been present for an extended period of time, one must thoroughly search for causes that may explain the presence of the wound in the first place. To optimize the nutritional status of a patient, a clear understanding of the
patient’s caloric requirements and a facility with nutritional supplements and vitamins are a must. Protein malnutrition is associated with suboptimal wound healing, cell synthesis, wound remodeling, angiogenesis and fibroblast proliferation [69,70]. Protein and vitamin deficiency is known to impair the immune system, making the host more susceptible to infection. It has been shown that as little as 4 weeks of malnutrition may alter the function of the inflammatory cells that are vital to wound healing [71]. Patients with diabetes are often maintained on caloric restriction, which may be insufficient energy to promote healing.

As part of a multidisciplinary approach to manage a patient with a chronic wound, every effort should be made to obtain a thorough history regarding weight loss, appetite, vomiting, diarrhea, and eating habits [72,73]. Physical examination includes evaluation of muscle, fat, and subcutaneous fat loss. Edema can be seen in hypoproteinemia. Laboratory studies include serum protein and albumin and other specific nutritional parameters [12].

Depletion of vitamin C, which is rare in the United States, may result in disruption of collagen formation. Vitamin C serves as a cofactor in the hydroxylation of proline in the production of collagen, and its deficiency results in delayed wound healing. Deficiencies in zinc, iron, copper, and magnesium also affect wound healing. Wound patients should receive multivitamins and appropriate nutritional support.

Tobacco

Cigarette smoking has long been known to impair wound healing. Tobacco is a potent vasoconstrictor, decreasing oxygen delivery to healing wounds [74]. Nicotine acts via the sympathetic nervous system to cause systemic vasoconstriction. Tobacco smoke contains carbon monoxide that binds to hemoglobin and reduces the oxygen-carrying capacity of hemoglobin [75]. Hydrogen cyanide is one of the components of cigarette smoke and is known to interfere with cellular respiration. Nicotine is known to be detrimental to flaps [76] and to dramatically increase the failure rate of microvascular surgery [77,78]. The healing potential for patients who smoke has been found to be equal to that of nonsmokers when cessation of smoking is encouraged as little as 2 weeks before surgery.

Psychologic factors

The burden and disability experienced by patients who have chronic wounds alters their way of life. Motivating such a patient to follow a wound care protocol can pose a challenge for the clinician. The patient needs to be optimized not only medically and surgically but also socially. There must be a complete review of the patient’s support system to identify any difficulties that may be encountered during the course of treatment. A social worker should assess the social environment and help facilitate patient compliance with the treatment protocol. The ability of the patient and his family/caregiver to comply with the treatment protocol is one of the most important factors in determining the overall success of treatment.

Chronic disease

Advances in medicine have allowed a comprehensive approach to the management of patients with debilitating, chronic diseases. The wound management team plays a critical role in this era of comprehensive care. As the aging population increases, there will be an increase in the number of patients that will develop chronic wounds. The pathophysiology of chronic wounds in this patient population is multifactorial. Patients with chronic diseases such as cardiac, renal, and hepatic pathology develop a multitude of physiologic abnormalities that make them susceptible to developing chronic wounds. The constant chronic nature of these pathologic systemic conditions also negatively alters the patient’s social and environmental status.

Evaluation and management

Psychosocial aspects

One of the most important issues in managing patients with chronic wounds is the integration of social and physical ailments. There are a variety of social and psychologic issues that need to be addressed in this patient population. The chronically ill patient is prone to suffering from depression and a lack of motivation. The combination of chronic disease and a wound that fails to heal further undermines the motivation of the patient to provide self-care and remain compliant with the physician’s treatment plan. A thorough evaluation of the patient’s social and medical status can have a significant impact on the success of the wound care protocol. Further optimization of the patient’s current social and psychological status is beneficial as therapy progresses. A clear goal must be set and explained to the patient and the caregiver from the beginning of treatment so that there are no misconceptions or misunderstandings regarding the plan. In cases of
recalcitrant wounds, the possibility of failure must be discussed so that the patient is not disappointed after a long and labor-intensive effort.

The management of extrinsic factors in patients with chronic wounds is of utmost importance. There are some extrinsic factors that can be controlled by the physician, such as strict glucose control for the diabetic patient, tapering of steroid use in a patient who suffers from autoimmune disorders, and optimizing the nutritional status of a patient who is malnourished. Close cooperation with the patient’s medical doctor can be valuable in these cases.

**Intrinsic factors: wound bed preparation**

**Debridement**

The initial management of a patient with a chronic wound involves a close and thorough examination of the wound to outline a surgical strategy and to determine if the wound is ready for closure. Thorough debridement of all necrotic tissue is the initial step in generating an environment that allows healing to occur [79]. The process of debridement reduces the bacterial load and their byproducts allowing the wound to enter a more favorable phase of healing [80]. The presence of necrotic, nonviable tissue inhibits wound healing and renders the wound susceptible to infection, which further retards wound healing. The removal of all necrotic tissue and exposure of the whole wound allows one to more predictably examine and plan future coverage of the wound. We prefer to perform all debridements in the operating room where complete access, proper instrumentation and lighting, and patient comfort may be optimally delivered. Electrocautery is also available in the operating room, allowing for meticulous hemostasis. It is difficult to adequately debride a wound at the bedside. The exceptions are diabetic plantar ulcers, which can be painlessly debrided of the typical keratinacious debris at the bedside. There are a variety of ways to remove necrotic tissue. Many have proven useful when used properly.

Scalpel or scissors are usually used to sharply debride necrotic skin and subcutaneous tissue. In

![Fig. 2. (A) Sacral decubitus ulcer with necrotic tissue. (B) Methylene blue applied to the wound. (C) Appearance of the wound after debridement with Versajet.](image-url)
cases where more refined, controlled removal of necrotic tissue is important, such as around vital structures, we have found the high-pressure parallel water jet system to be useful. This is a high-pressure water jet/vacuum evacuator (Versajet; Smith & Nephew, Tampa, FL) with an adjustable control that allows precise, controlled, thin-layer excision of nonviable tissue (Fig. 2). This system is useful in situations where nearby structures must be protected or in wounds where minimal healthy tissue remains and must be preserved. This tissue may allow for coverage of the wound with a skin graft where a flap may have otherwise been necessary. The water jet serves to irrigate the wound and remove necrotic debris and bacteria.

High-pressure pulse lavage has been shown to decrease bacterial counts and remove some necrotic material from the wound, improving the wound environment. Treatment of infection is an important adjunct in the management of chronic wounds.

**Wound dressings**

After the eradication of necrotic tissue and control of infection in a wound, the appropriate dressing must be chosen. A moist environment has been found to provide the best condition for wound healing. Wound desiccation is known to be detrimental to wound healing [81,82]. Most clinicians use wet-to-dry dressings to manage chronic wounds. The advantage of this dressing is repeated debridements after each dressing change. However, healthy tissues are sacrificed when these dressings are allowed to dry. For clean wounds, moist-to-moist dressings provide a more ideal environment that prevents desiccation and promotes healing. Ideally, a wound is debrided early in its management and is treated with moist dressings to optimize healing. There are many dressings available to the clinician. An understanding of the basic requirements of wound healing allows the clinician to choose the dressing that best suits his patient’s needs.

Compression therapy is usually chosen for patients who have chronic venous insufficiency or impairment of healing secondary to edema. Compression dressings reduce fluid extravasation into the extracellular space, allowing for better diffusion of oxygen and nutrients to the wound [83].

The introduction of the vacuum assisted closure (VAC) (KCI, San Antonio, TX) device has revolutionized the management of chronic wounds [84]. The VAC dressing is a sponge and suction drainage system that is applied to the wound and covered with an airtight adhesive plastic dressing. Suction is continuously applied to the affected wound, and the dressing is changed every 2 to 5 days. The VAC dressing needs to be changed more frequently in the pediatric population due to the more rapid rate of granulation tissue formation that can grow into the sponge dressing. The VAC dressing allows for less frequent dressing changes, reduces edema in the wound, and augments formation of fine granulation tissue receptive to flap or skin graft closure. It maintains a moist environment that is optimal for wound healing. Studies have shown that this method allows granulation tissue formation even in extreme cases such as overexposed bone and orthopedic hardware [85–88] (Fig. 3). The bacterial load in wounds that are managed with the VAC dressing is under investigation, and contradictory evidence exists as to whether there is an increase or decrease in the number and type of bacteria [89,90]. The VAC dressing acts as a temporary cover for open wound so that closure can be performed in a more controlled setting. The VAC can be thought of as a semi-occlusive dressing that is continuously drained via the suction system. Complications associated with the VAC dressing are uncommon in experienced hands, but toxic shock syndrome, hematoma, bleeding, and pain have been reported in the literature [91,92].

**Edema control**

Persistent edema is detrimental to wound healing. There are a variety of dressings that can be applied to aid in the control and relief of edema. Compression stockings, Unna’s paste boots, elastic wrapping, multilayer compression wraps, and pneumatic compression devises are useful modalities to treat chronic venous insufficiency and edema [10]. Compression has been shown to increase healing rates in venous leg ulcers [93]. Elevation of the extremity is a simple and cost-effective method to decrease edema. The VAC dressing has been shown to decrease edema, likely by removing extracellular fluid. Proper education of the patient is mandatory when this type of therapy is prescribed. Patient cooperation is an important factor in determining the efficacy of these treatment modalities.

**Pharmacology**

The pharmacologic aspects of wound management include replacement of nutrients and blood products, institution of antibiotics to treat clinically
significant infections, management of the patient’s underlying medical condition, and topical agents to treat the wound. The replacement of nutrients, vitamins, and trace elements assures adequate substrate to allow wound healing to occur unhindered. Optimizing the nutritional status of the patient is not a static protocol and needs to be assessed frequently to assure a benefit. The advice and assessment of a nutritionist can be beneficial. Replacement of blood products should be done cautiously. There are risks with transfusion therapy, and only in select cases where a clear benefit exists should this be considered. The decision to transfuse a patient is controversial and needs to be individualized. Surgical procedures should be planned and executed meticulously to minimize blood loss, which can compound underlying anemia. Treatment with erythropoietin and iron can help reverse anemia.

All open wounds are contaminated, and attempts should be made to remove all nonviable tissue and

Fig. 3. (A) A 65-year-old man with circumferential wound of the lower extremity underwent bypass surgery. (B) Debridement of the wound. (C) VAC treatment completed over a 2-month period. (D) Healed wound after application of skin graft.
reduce the bacterial load. Indiscriminate use of topical agents is not recommended because adjacent healthy tissues may be damaged by these medications. Acetic acid, Povidone-iodine solutions, hydrogen peroxide, and Dakin’s solution are known to cause damage to healthy granulation tissue.

One of the interesting pharmacologic modalities being promoted for the management of chronic wounds is anabolic steroids. Persistent weight loss is seen in some patients despite satisfactory medical and nutritional management. These patients may be candidates for anabolic steroid therapy to reverse their hormonal discrepancy. Anabolic agents such as oxandrolone have been used with success to halt this catabolic process and are worth considering for select patients [88].

Pentoxifylline has been used for many years for the treatment of intermittent claudication and to improve blood flow to ischemic wounds [94]. The mechanism of action of this medication is not clearly understood. It is hypothesized to increase fibrinolysis, reduce leukocyte adhesiveness, and increase red blood cell deformability [95].

**Hyperbaric oxygen therapy**

Hyperbaric oxygen (HBO) chambers were developed for the treatment of diving decompression sickness. The use of HBO has expanded to treat a variety of conditions and ailments, including chronic wounds. Hyperbaric oxygen may be of benefit to tissues that are hypoxic and problematic wounds [96]. The definitive indications for the treatment of wounds with hyperbaric oxygen are controversial. It is well known that optimal delivery of oxygen to the wound is pivotal in creating an environment conducive to healing. Optimizing oxygen delivery to ischemic wounds should be addressed in a comprehensive manner, including appropriate investigations to diagnose arterial disease that may be amenable to surgical intervention. In patients with hypoxia that cannot be corrected surgically, one may take advantage of intermittent HBO to increase the oxygen tension in the wound [91,97,98]. HBO in patients with limited arterial delivery is beneficial but does not supplant revascularization. Oxygen delivery in these cases is most significantly improved by bypass surgery or by the introduction of a well-vascularized free tissue transfer [99]. Cost and access to hyperbaric chambers makes routine use difficult for the majority of patients.

In a systematic review, Chang et al [100] suggest that HBO therapy may be beneficial in chronic non-healing diabetic wounds, compromised skin grafts, osteoradionecrosis, soft tissue radionecrosis, and gas gangrene compared with standard wound care alone. However, the HBO literature has not provided definitive proof of its efficacy and cost effectiveness.

**Coverage**

**Wound dressings**

A plethora of wound dressings exist to address almost all conceivable wound types. Many wounds proceed to full healing with proper dressings in addition to patient optimization and wound preparation.

**Skin grafts**

Less complicated, well-vascularized wounds can be covered with skin grafts. Most wounds can be covered with split thickness skin grafts. There are instances when there are advantages to performing a full-thickness skin graft, such as wounds of the face where local flaps are not applicable and over hand and joint surfaces. Full-thickness skin grafts tend to retain more of the characteristics of normal skin and thus may allow a more cosmetic and functional graft for reconstruction. The availability of split thickness grafts and the ability to mesh the graft allows for coverage of larger areas as compared with full-thickness skin grafts. Full-thickness skin grafts are preferred in children where growth occurs as the child matures. Although all skin grafts require a well-vascularized bed, split-thickness skin grafts are able to tolerate suboptimal conditions better than full-thickness grafts. Furthermore, the supply of full-thickness skin grafts is somewhat limited, and closure of the donor site can be problematic.

**Skin substitutes**

A variety of biologically active modalities are available to cover open wounds. Transcyte (Smith & Nephew, Largo, FL) stabilizes wounds and cuts down on fluid and protein loss [101,102]. Integra (Integra neurosciences, Plainsboro, NJ) provides a neodermis in preparation for STSG. This approach minimizes contracture in burn injuries. Apligraf (Novartis, Basel, Switzerland) and Dermagraft (Smith & Nephew) are skin substitutes that consists of artificial dermis seeded with live fibroblasts [103,104]. This has been shown to facilitate healing
of diabetic foot and venous leg ulcers. Regranex (Ortho McNeil, Ethicon Inc., Somerville, NJ) is a gel containing recombinant PDGF and has been shown to be effective in treating diabetic ulcers [105,106].

Local flaps

Local flaps have several advantages in more complicated wounds. There is better color and quality match as compared with free flaps and skin grafts. The donor site is usually repaired linearly or covered with a skin graft as needed. The appearance of the scar can be improved by placing the incisions in the natural skin folds or by hiding them in inconspicuous locations. The clinician needs to be experienced in performing these procedures to obtain optimal functional and cosmetic results. The quality and quantity of adjacent tissue also needs to be evaluated before committing to local flap coverage. This holds true especially in cases where infection and radiation have damaged the surrounding tissues making them unusable for this purpose. Fig. 4 shows an example of local flap coverage.

Distant flaps

Complex wounds may be covered with free flaps when simpler options (eg, local flaps and skin grafts) are not possible or available. Microvascular reconstruction can be technically challenging and can require prolonged operative time. Patient selection is important in optimizing outcome. The patient needs to be in optimal medical condition to be able to tolerate a long procedure with many inherent risks. Advancements made in recent years offer a wide variety of options for reconstruction that were otherwise not possible in the past. Flaps are chosen on the basis of the anatomy to be reconstructed and the quality and quantity of tissue that is needed. Wounds with significant tissue loss and lack of local donor sites are candidates for distant tissue transfer. The

Fig. 4. (A) Infected open tibia/fibular fracture. (B) Wound after debridement and VAC dressing. (C) Coverage with local sural flap.
patient and family need to be well informed regarding all the risks of the procedure.

Prevention of recurrence

Risk of recurrence must be thoroughly assessed before committing a patient to a long and lengthy surgical treatment plan. The possibility of recurrence is always on the mind of the reconstructive surgeon and needs to be emphasized to the patient. Patients should be instructed to avoid trauma and to comply with their medical regimen to prevent recurrence. Compliance with treatment is important in preventing recurrence.

Nonsurgical treatment

Patients who are unstable, those with multiple medical problems and those with intractable chronic or terminal diseases are poor candidates for surgical therapy. The goals for managing these patients are generally to eliminate infection, alleviate pain, and optimize a wound care regimen. The patient should be made comfortable, and frequent examination is mandatory to assure infection is not present.

Summary

The management of chronic wounds can be a challenging endeavor especially in this era of managed care and reduced reimbursements for physicians. A thorough understanding of the problem involves a well-trained, multidisciplinary group of physicians, nurses, therapists and social workers that work well together. The search for an answer to the problem begins with a thorough history and physical examination to arrive at a diagnosis. This leads to a comprehensive wound care plan that includes local wound care, surgical closure when appropriate, and consultation of appropriate services on a case-by-case basis to assure an optimal outcome.

References

[22] Ladwig GP, Robson M, Liu R, et al. Ratios of activated matrix metalloproteinases-9 to tissue inhibi-
tor of matrix metalloproteinases-1 in wound fluids are inversely correlated with healing of pressure sores. Wound Repair Regen 2002;10:26–37.

[65] Lawrence WT, Talbot TL, Horton JA. Preoperative or postoperative doxorubicin hydrochloride (Adria- mycin): which is better for wound healing? Surgery 1986;100:9–13.


[102] Pave SA, Byrne PO. Safety and efficacy of TransCyte...


