# Wound bed preparation: a systematic approach to wound management

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The healing process in acute wounds has been extensively studied and the knowledge derived from these studies has often been extrapolated to the care of chronic wounds, on the assumption that nonhealing chronic wounds were simply aberrations of the normal tissue repair process. However, this approach is less than satisfactory, as the chronic wound healing process differs in many important respects from that seen in acute wounds. In chronic wounds, the orderly sequence of events seen in acute wounds becomes disrupted or ``stuck'' at one or more of the different stages of wound healing. For the normal repair process to resume, the barrier to healing must be identified and removed through application of the correct techniques. It is important, therefore, to understand the molecular events that are involved in the wound healing process in order to select the most appropriate intervention. Wound bed preparation is the management of a wound in order to accelerate endogenous healing or to facilitate the effectiveness of other therapeutic measures. Experts in wound management consider that wound bed preparation is an important concept with significant potential as an educational tool in wound management.

This article was developed after a meeting of wound healing experts in June 2002 and is intended to provide an overview of the current status, role, and key elements of wound bed preparation. Readers will be able to examine the following issues; • the current status of wound bed preparation; • an analysis of the acute and chronic wound environments; • how wound healing can take place in these environments; • the role of wound bed preparation in the clinic; • the clinical and cellular components of the wound bed preparation concept; • a detailed analysis of the components of wound bed preparation. **(WOUND REP REG 2003;11:1–28)**

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*This supplement was supported by an unrestricted grant from Smith & Nephew Medical Ltd.*



*ISSN: 1067-1927 $15.00 + 0*

## ACUTE WOUND HEALING

A wound is a breach of the epidermis of the skin that can lead to infection and sepsis. The body has evolved well-defined protective systems to counter this potential threat. Most of the current understanding of wound management has been derived from studies of the healing process in acute wounds. Wounds caused by trauma or through surgery generally follow a well-defined wound healing process that involves four main stages:

- coagulation
- inflammation
- cell proliferation and repair of the matrix
- epithelialization and remodeling of the scar tissue

These stages overlap and the entire process can last for months (Figure 1).

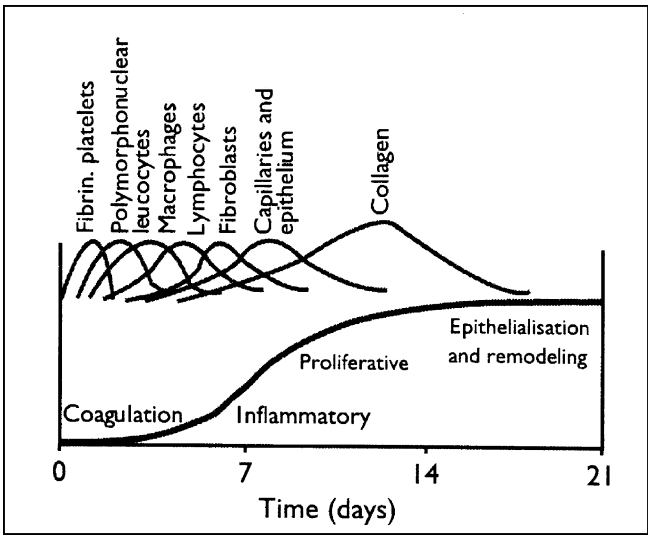


**FIGURE 1.** The processes of wound healing.

### *Cellular activity during wound healing*

During the coagulation phase after injury, platelets initiate the wound healing process by releasing a number of soluble mediators, including platelet-derived growth factor (PDGF), insulin-like growth factor-1 (IGF-1), epidermal growth factor (EGF), fibroblast growth factor (FGF), and transforming growth factor-β (TGF-β). These rapidly diffuse from the wound, and inflammatory cells are drawn to the area of the injury. Table 1 lists growth factors relevant for wound healing and some of their biochemical properties. In general, growth factors are mitogens that stimulate proliferation of wound cells (epithelial cells, fibroblasts, and vascular endothelial cells). Most growth factors are also able to stimulate directed migration of target cells (chemotaxis) and regulate differentiated functions of wound cells, such as expression of extracellular matrix (ECM) proteins.

### *Inflammation*

The inflammatory phase is initiated by the blood clotting and platelet degranulation process. During this phase there is significant vasodilation, increased capillary permeability, complement activation, and migration of polymorphonuclear leukocytes (PMN) and macrophages to the site of the wound. The neutrophils and macrophages engulf and destroy bacteria and release proteases, including elastase and collagenase, which degrade damaged ECM components. They also secrete additional growth factors including TGF-β, TGF-α, heparin-binding epidermal growth factor (HB-EGF), and basic fibroblast growth factor (bFGF). Inflammation is largely regulated by a class of molecules called cytokines, which have powerful stimula-

**Table 1.** Major growth factor families and their biological activities

| Growth factor family | Members | Cell source | Actions |
|---|---|---|---|
| Transforming growth factor beta | TGFβ-1, TGFβ-2 | Platelets | Fibroblast chemotaxis and activation |
| | | Fibroblasts | ECM deposition |
| | | Macrophages | ↑ Collagen synthesis |
| | | | ↑ TIMP synthesis |
| | | | ↓ MMP synthesis |
| | TGFβ -3 | | May reduce scarring |
| Platelet derived growth factor | PDGF-AA, PDGF-BB, VEGF | Platelets | Activation of immune cells and fibroblasts |
| | | Macrophages | |
| | | Keratinocytes | ECM deposition |
| | | Fibroblasts | ↑ Collagen synthesis |
| | | | ↑ TIMP synthesis |
| | | | ↓ MMP synthesis |
| | | | Angiogenesis |
| Fibroblast growth factor | Acidic FGF, Basic FGF, KGF | Macrophages | Angiogenesis |
| | | Endothelial cells | Endothelial cell activation |
| | | Fibroblasts | Keratinocyte proliferation and migration |
| | | | ECM deposition |
| Insulin-like growth factor | IGF-I, IGF-II, Insulin | Liver | Keratinocyte proliferation |
| | | Skeletal muscle | Fibroblast proliferation |
| | | Fibroblasts | Endothelial cell activation |
| | | Macrophages | Angiogenesis |
| | | Neutrophils | Collagen synthesis |
| | | | ECM deposition |
| | | | Cell metabolism |
| Epidermal growth factor | EGF, HB-EGF, TGFα | Keratinocytes | Keratinocyte proliferation and migration |
| | Amphiregulin, Betacellulin | Macrophages | ECM deposition |
| Connective tissue growth factor | CTGF | Fibroblasts | Mediates action of TGF-β on collagen synthesis |
| | | Endothelial cells | |
| | | Epithelial cells | |

Table supplied by Schultz G.

tory and inhibitory actions on inflammatory cells. Table 2 lists cytokines with important wound healing actions and some of their biochemical properties. Cytokines were initially identified according to their influences on chemotaxis, proliferation, and differentiation of inflammatory cells. It is now recognized that cytokines also have important actions on wound cells. For example, interleukin-1 (IL-1) and TNFα stimulate production of proteases by fibroblasts, and TNFα induces apoptosis in fibroblasts. Macrophages attract further macrophages and continue to stimulate migration of fibroblasts, epithelial cells, and vascular endothelial cells into the wound to form granulation tissue around 5 days after injury.

A third important group of regulatory proteins that influence wound healing are listed in Table 3 and are collectively named chemokines, from a contraction of chemo-attractive cytokine(s).[1–3] Chemokines have two primary functions: to regulate the trafficking of leukocyte populations during normal health and development and to direct the recruitment and activation of neutrophils, lymphocytes, macrophages, eosinophils, and basophils during inflammation. The structural and functional similarities among chemokines were not initially appreciated, and this led to an idiosyncratic nomenclature consisting of many acronyms based on their biological functions (e.g., monocyte chemo-attractant protein 1 [MCP-1], macrophage inflammatory protein 1 [MIP-1]), or on their source for isolation (e.g., platelet factor 4 [PF-4]) or their biochemical properties (e.g., interferon-inducible protein of 10 kDa [IP-10], and regulated upon activation normal T-cell expressed and secreted [RANTES]). As their biochemical properties were established, it was recognized that the family of approximately 40 chemokines could be grouped into four major classes based on the pattern of amino acid residues located near the N-terminus.

In summary, growth factors, cytokines, and chemokines are key molecular regulators of wound healing. They are all proteins or polypeptides, are typically

**Table 2.** Cytokine activity in the wound healing process

| Cytokine | Cell source | Biological activity |
|---|---|---|
| Pro-inflammatory cytokines | | |
| TNF-α | Macrophages | PMN margination and cytotoxicity, ± collagen synthesis; provides metabolic substrate |
| IL-1 | Macrophages<br>Keratinocytes | Fibroblast and keratinocyte chemotaxis, collagen synthesis |
| IL-2 | T lymphocytes | Increases fibroblast infiltration and metabolism |
| IL-6 | Macrophages<br>PMNs<br>Fibroblasts | Fibroblast proliferation, hepatic acute-phase protein synthesis |
| IL-8 | Macrophages<br>Fibroblasts | Macrophage and PMN chemotaxis, keratinocyte maturation |
| IFN-γ | T lymphocytes<br>Macrophages | Macrophage and PMN activation; retards collagen synthesis and cross-linking; stimulates collagenase activity |
| Anti-inflammatory cytokines | | |
| IL-4 | T lymphocytes<br>Basophils<br>Mast cells | Inhibition of TNF, IL-1, IL-6 production; fibroblast proliferation, collagen synthesis |
| IL-10 | T lymphocytes<br>Macrophages<br>Keratinocytes | Inhibition of TNF, IL-1, IL-6 production; inhibits macrophage and PMN activation |

**Table 3.** Chemokine families and the immune/inflammatory cells with which they interact

| Chemokines | Member | Cells affected |
|---|---|---|
| α-chemokines (CXC) with glutamic acid-leucine-arginine near the N-terminal | Interleukin-8 (IL-8) | Neutrophils |
| α-chemokines (CXC) *without* glutamic acid-leucine-arginine near the N-terminal | Interferon-inducible protein of 10 kd (IP-10)<br>Monokine induced by interferon-(MIG)<br>Stromal-cell-derived factor 1 (SDF-1) | Activated T lymphocytes |
| β-chemokines (CC) | Monocyte chemoattractant proteins (MCPs): MCP-1,-2,-3,-4,-5<br>Regulated upon activation normal T-cell expressed and secreted (RANTES)<br>Macrophage inflammatory protein (MIP-1)<br>Eotaxin | Eosinophils<br>Basophils<br>Monocytes<br>Activated T lymphocytes |
| γ-chemokines (C) | Lymphotactin | Resting T lymphocytes |
| δ-chemokines (CXXXC) | Fractalkine | Natural killer cells |

synthesized and released locally, and primarily influence target cells by paracrine actions. The initial concepts that growth factors were mitogens only for wound cells, that cytokines regulated differentiation of inflammatory cells, and that chemokines only regulated chemoattraction of inflammatory cells were too narrow and it is now recognized that there are substantial overlaps in target cell specificity and actions between these three groups.

### Cell proliferation and repair of the matrix

As the number of inflammatory cells in the wound decreases, the fibroblasts, endothelial cells, and keratinocytes take over synthesis of growth factors. Keratinocytes synthesize TGF-β, TGF-α, and IL-1. Fibroblasts secrete IGF-1, bFGF, TGF-β, PDGF, keratinocyte growth factor (KGF), and connective tissue growth factor (CTGF). Endothelial cells produce bFGF, PDGF, and the important angiogenic factor, vascular endothelial cell growth factor (VEGF). These continue to promote cell migration, proliferation, new capillary formation and synthesis of ECM components.

Initially, the injury defect is filled by a provisional wound matrix consisting predominantly of fibrin and fibronectin. As fibroblasts are drawn chemotactically into the matrix, they synthesize new collagen, elastin and proteoglycan molecules that form the initial scar, and secrete lysyl oxidase, which cross-links collagen of the ECM. However, before the newly synthesized matrix components can properly integrate with the existing dermal matrix, all damaged proteins in the matrix must be removed. This is carried out by proteases (Table 4), secreted by neutrophils, macrophages, fibroblasts, epithelial cells, and endothelial cells. Key proteases include collagenases, gelatinases, and stromelysins, which are all members of the matrix metalloproteinase (MMP) super family, and neutrophil elastase, a serine protease. Cell proliferation and synthesis of new ECM places a high metabolic demand on the wound cells, which is met by a dramatic increase in vascularity of the injured area. Epithelial cells proliferate and migrate across the highly vascularized, new ECM (granulation tissue), and reform the epidermal layer. Proliferation and repair typically last several weeks.

### Remodeling of scar tissue

Synthesis of new ECM molecules continues for several weeks after initial wound closure, and the scar is often visibly red and raised. Over a period of several months, the appearance of the scar usually improves, becoming less

**Table 4.** Proteases and tissue inhibitors important in wound healing

| Name | Pseudonym | Substrates |
|---|---|---|
| MMP-1 | Interstitial collagenase<br>Fibroblast collagenase | Type I, II, III, VII, and X collagens |
| MMP-2 | 72 kDa gelatinase<br>Gelatinase A<br>Type IV collagenase | Type IV, V, VII, and X collagens<br>α1-protease inhibitor |
| MMP-3 | Stromelysin-1 | Type III, IV, IX, and X collagens<br>Type I, III, IV, and V gelatins<br>Fibronectin, laminin and pro-collagenase |
| MMP-7 | Matrilysin<br>Uterine metalloproteinase | Type I, III, IV, and V gelatins<br>Casein, fibronectin and pro-collagenase |
| MMP-8 | Neutrophil collagenase | Type I, II, and III collagens |
| MMP-9 | 92 kDa gelatinase<br>Gelatinase B<br>Type IV collagenase | Type IV and V collagens<br>Type I and V gelatins<br>α1-protease inhibitor |
| MMP-10 | Stromelysin-2 | Type III, IV, V, IX, and X collagens<br>Type I, III, and IV gelatins<br>Fibronectin, laminin and pro-collagenase |
| MMP-11 | Stromelysin-3 | Not determined |
| MMP-12 | Macrophage<br>Metalloelastase | Soluble and insoluble elastin |
| MMP-14 | Membrane type MMP-1 (MT-MMP-1) | Pro-MMP-2, gelatin, fibronectin |
| MMP-15 | Membrane type MMP-2 (MT-MMP-2) | Pro-MMP-2, gelatin, fibronectin |
| TIMP-1 | Tissue inhibitor of metalloproteinases-1 | Inhibits all MMPs except MMP-14 |
| TIMP-2 | Tissue inhibitor of metalloproteinases-2 | Inhibits all MMPs |
| TIMP-3 | Tissue inhibitor of metalloproteinases-3 | Inhibits all MMPs, binds pro-MMP-2 and proMMP-9 |
| Elastase | Neutrophil elastase | Elastin, type I, II, III, IV, VIII, IX, XI collagens, fibronectin, laminin, TIMPS<br>Activates pro-collagenases, pro-gelatinases and pro-stromelysins |
| α1-protease inhibitor | α 1-PI<br>α 1-antitrypsin | Inhibits elastase |

raised and red. On a cellular and molecular level, the scar is remodeling, with a new equilibrium being reached between synthesis of ECM components in the scar and their degradation by proteases. The increased density of fibroblasts and capillaries present in the early phase of healing declines, primarily through apoptosis. In the final remodeling phase, tensile strength reaches a maximum as cross-linking of collagen fibrils plateaus.

### Converting chronic wounds to healing wounds

With this understanding of the wound healing process, principles of acute wound management were established that usually result in rapid and clean healing of the wound. Debridement and appropriate dressings are often used to accelerate healing, although in a healthy individual, healing will normally take around 21 days without further clinical intervention. When wounds fail to heal, the molecular and cellular environment of a chronic wound bed must be converted into that of an acute, healing wound so that healing can proceed through the natural sequential phases described above. This is the aim of wound bed preparation.

### Acute wound healing: role of debridement

Debridement is widely used to clear wounds of necrotic tissue and bacteria to leave a clean surface that will heal relatively easily. Devitalized, necrotic tissue provides a focus for infection, prolongs the inflammatory phase, mechanically obstructs contraction and impedes reepithelialization.[4] Nondebrided tissue may also mask underlying fluid collections or abscesses and make it difficult to evaluate wound depth.

In the early stages of wound healing, debridement occurs autolytically through the action of neutrophil-derived enzymes including elastase, collagenase, myeloperoxidase, acid hydrolase, and lysosomes. Protease inhibitors are also released by wound cells to restrict protease action to the wound bed, minimizing damage to intact tissue at the wound edge.

Debridement using surgical, enzymatic, autolytic, or mechanical methods is often all that is required to promote the first step in the healing process. Although debridement occurs naturally, assisted debridement accelerates the wound healing process.[5]

### Acute wound healing: role of dressings

The role of occlusive dressings in wound healing is often misunderstood with many clinicians fearing that a moist environment will promote infection. Numerous clinical trials have shown that this is not the case: indeed, wounds treated with occlusive dressings are less likely to become infected than wounds treated with conventional dressings.[6] Occlusive dressings are relatively impermeable to exogenous bacteria and they encourage the accumulation of natural substances in wound fluid that inhibit bacterial growth and reduce the burden of necrotic tissue in the wound.

A moist wound environment has been shown to accelerate wound healing by up to 50% compared with exposure to air.[7] Wounds that are allowed to dry develop a hard crust, and the underlying collagen matrix and surrounding tissue at the wound edge become desiccated. Keratinocytes must burrow beneath the surface of the crust and matrix if reepithelialization is to occur, as they can only migrate over viable nutrient-rich tissue and intact ECM. By contrast, a moist environment physiologically favors migration and matrix formation and accelerates healing of wounds by promoting autolytic debridement. Moist wound healing also reduces wound pain and tenderness, reduces fibrosis, decreases wound infection rates, and produces a better cosmetic outcome.

## CHRONIC WOUND HEALING

Chronic or nonhealing ulcers are characterized by defective remodeling of the ECM, a failure to reepithelialize, and prolonged inflammation.[8–10] The epidermis fails to migrate across the wound tissue and there is hyper-proliferation at the wound margins that interferes with normal cellular migration over the wound bed, probably through inhibition of apoptosis within the fibroblast and keratinocyte cell populations. Fibroblasts obtained from chronic ulcers show a decreased response to exogenous application of growth factors such as PGDF-β and TGF-β[8,9] possibly due to a form of senescence.[11,12] In chronic wounds, cells accumulate that are unresponsive to wound healing signals, therefore topical application of growth factors is unlikely to lead to wound closure until adjacent cells that are capable of responding to growth factors migrate into the wound.

### Non-progressive or "stuck" wounds

Venous and foot ulcers in a person with diabetes are believed to be "stuck" at the inflammatory and proliferative phases, respectively.[13] (Figure 2) In acute wounds, the expression of ECM molecules such as fibronectin and thrombospondin follows a defined temporal course. In chronic wounds there appears to be an over-expression of these matrix molecules, which is believed to result from cellular dysfunction and disregulation within the wound.[14] It is also known that proteinaceous molecules are present which emanate from the circulatory system.

Fibrinogen and fibrin are common in chronic wounds and it has been hypothesized that these and other

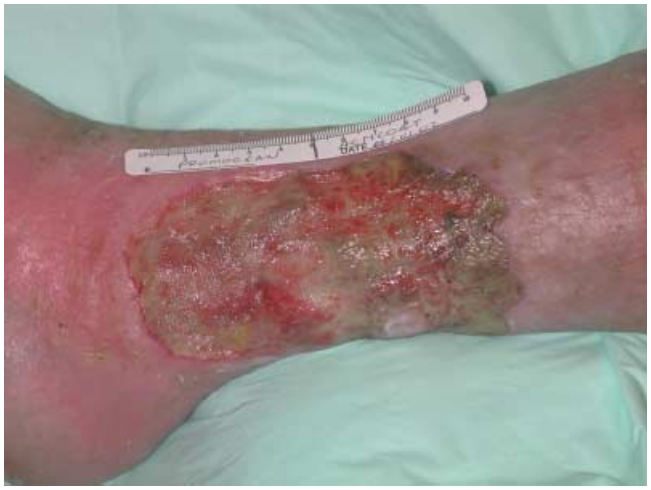

**FIGURE 2.** Leg ulcer stuck in the inflammatory phase. Note yellow slough on the surface. (© R. Gary Sibbald, MD).

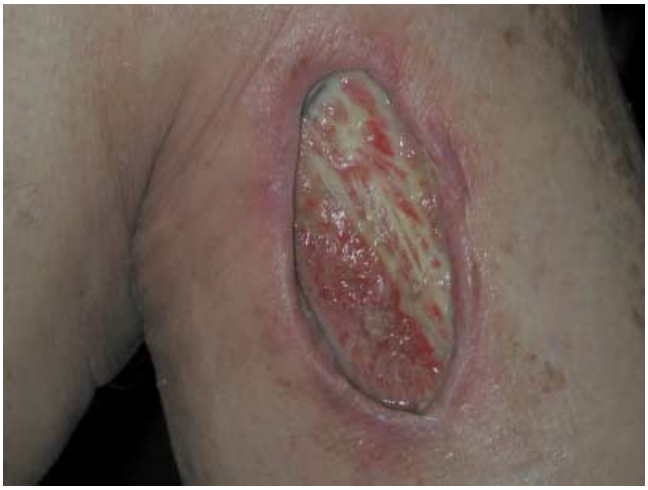

**FIGURE 3.** Lateral knee wound postdrainage of an abscess with exposed fascia and new granulation tissue. (© R. Gary Sibbald, MD).

extravasated macromolecules scavenge growth factors and certain signal molecules involved in promoting wound repair.[14] So while there may be a large number of growth factors within the wound, these can become sequestered and unavailable to the wound repair process.

### *Role of wound fluid in chronic wounds*

Chronic wound fluid is biochemically distinct from acute wound fluid: it slows down, or even blocks, the proliferation of cells such as keratinocytes, fibroblasts, and endothelial cells and has a detrimental effect on wound healing.

Stanley et al.[15] demonstrated that dermal fibroblasts cultured from the edges of chronic venous leg ulcers grew more slowly than fibroblasts from healthy skin in the same patient. Cells at the wound margin appeared senescent, that is, with loss of proliferative capacity, and were larger and less responsive to growth factors. Dermal fibroblasts produce matrix proteins such as fibronectin, integrins, collagen, and vitronectin to form a basal lamina over which keratinocytes migrate. Laminin, on the other hand, a component of the basement membrane, inhibits keratinocyte migration.[16–18] While a moist environment is conducive to wound healing, chronic wound fluid from leg ulcers contains extensively degraded vitronectin and fibronectin, which may prevent cell adhesion. Other studies have shown that chronic wound fluid may inhibit proliferation of fibroblasts[19].

Another major difference is the level of inflammatory cytokines.[20,21] In acute healing, levels of two pro-inflammatory cytokines, TNFα and IL-1, peak after a few days and return to very low levels in the absence of infection. Levels in nonhealing wounds, however, are persistently elevated. As nonhealing wounds begin to heal, the concentrations of the inflammatory cytokines decrease to values approaching those in acute healing wounds, indicating a close correlation between low levels of inflammatory cytokines and progression of wound healing.

Acute wound fluid contains factors that induce cell proliferation such as platelet-derived growth factor-like peptides, interleukin-6 (IL-6) and TGF-α and TGF-β; chronic wound fluid contains lower amounts of these growth-promoting cytokines. The growth inhibitory effect of chronic wound fluid clearly must be overcome to stimulate wound healing and tissue regeneration (Figure 3).

In chronic wound fluid there is a very low level of glucose and heightened proteolytic activity, both important factors in impaired epithelialization and healing. The higher concentration of MMPs and serine proteinases in chronic wound fluid result in chronic tissue turnover, leading to the breakdown or corruption of matrix material essential for reepithelialization, and hence to failed wound closure. It is also known that macromolecules in the wound fluid can bind growth factors, making them unavailable to the regeneration process.

Proteases can also degrade growth factors and cytokines essential for wound healing.[22] Recently, measurements of MMPs and their natural inhibitors, tissue inhibitor of metalloproteinases (TIMPs) in fluid from chronic wounds showed there was a close correlation between high ratios of TIMP/MMP-9 and healing of pressure ulcers.[23] The elevated levels of inflammatory cytokines and proteases, along with low levels of mitogenic activity and poor response to cells in chronic wounds, led to the concept that the molecular environment of chronic wounds must be rebalanced to levels seen in acute healing wounds (Figure 4).

## HOLISTIC APPROACH TO WOUND HEALING

Before deciding on local wound applications, it is vital to consider the possible causes of a nonhealing wound and to review and correct, if possible, patient factors that may impede healing:

- Assess and correct causes of tissue damage.
- Tissue perfusion: ensure adequate blood supply.
- Assess and monitor wound history and characteristics.

### *Assess and correct cause of tissue damage*

The first step in wound bed preparation is treatment of the cause and patient-centered concerns (Table 5).

The overall health status of a patient has a significant impact on the wound healing process. A general medical history, including a medication record, is invaluable in identifying causes that may prevent wound healing.

Systemic steroids, immunosuppressive drugs, and nonsteroidal anti-inflammatories will deter wound healing, as will rheumatoid arthritis and other autoimmune diseases such as systemic lupus, uncontrolled vasculitis, or pyoderma gangrenosum. Inadequate or poor nutrition will delay healing, particularly if the patient's protein intake is low.

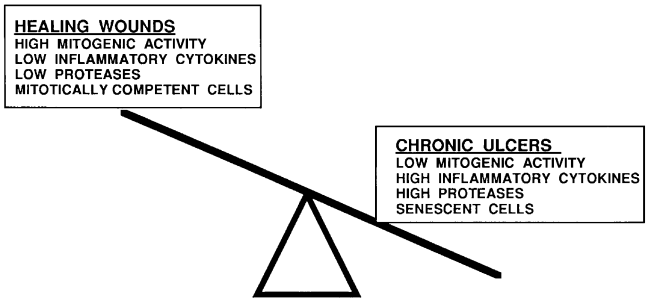


**FIGURE 4.** The molecular environment of healing and nonhealing chronic wounds.

### *Ensure adequate tissue perfusion*

Wound healing can only take place if there is adequate tissue oxygenation. A well-vascularized wound bed provides nutrients and oxygen to sustain newly formed granulation tissue and maintain an active immunological response to microbial invasion. Oxygen is available in two forms: bound to hemoglobin or dissolved in plasma. In chronic wounds and skin, unlike in active muscle, the oxygen dissolved in plasma can be adequate for healing, assuming that perfusion of the tissue itself is satisfactory. Decreased oxygen levels impair the ability of leukocytes to kill bacteria, lower production of collagen, and reduce epithelialization. However, low oxygen tension coupled with adequate oxygen tension to heal stimulates the release of angiogenesis factor from macrophages.

Wounds of the lower extremities may be particularly affected by poor blood supply (Figure 5). External factors such as hypothermia, stress, or pain can all increase sympathetic tone and decrease tissue perfusion; smoking reduces microcirculatory flow while certain medications increase it. In arterial ulcers, macrovascular or microvascular disease leads to tissue ischemia; in pressure ulcers base tissues become compressed and capillaries close. Vascular resistance is inversely proportional to the fourth power of the vessel radius, therefore cross-sectional vessel area is the most significant factor in blood flow resistance. In infected ulcers, deposition of neutrophils in the wall and lumen of small vessels leads to ischemia. In venous stasis ulcers, fibrin cuffs round capillaries may cause local hyperperfusion. In diabetic foot ulcers, glucose inhibits proliferation of endothelial cells, and angiogenic mediators are deficient.

A laser Doppler perfusion imaging is a noninvasive method for investigating skin microvasculature. A two-dimensional flow map of specific tissues and visualization of the spatial variation of perfusion can be created with this technique.[24]

**Table 5.** Treating the cause of chronic wounds

| Cause | Tissue stress | Correction |
|---|---|---|
| Venous insufficiency | Local edema | Compression therapy |
| Diabetic or other foot ulcer | Vascular supply compromised | Dilation for healability |
| | Deep infection | Ulcer <1 month (Dow et al)<br>Antimicrobials for gram-positives<br>Ulcer >1 month<br>Antimicrobials for gram-positives, gram-negatives, anaerobes |
| | Increased pressure with hyperkeratotic callus on ulcer rim | Sharp debridement and pressure downloading, orthotics |
| Pressure ulcer | Increased local pressure | Pressure reduction or relief surfaces |
| | Low albumen | Dietary assessment and nutritional correction |
| | Friction and shear | Head of the bed not above 30° |
| | Immobility | Turning program, increase physical activity |
| | Incontinence of faeces/urine | Stool bulk agents/bowel routine/ catheterization-condom, intermittent, permanent |

Tissue warming and the application of hyperbaric oxygen have both been evaluated as measures to improve perfusion[25–27] as has the use of electrical stimulation to enhance microcirculatory flow.[28]

### *Assess wound history and characteristics*

If the wound is recurrent, patient education or treatment of an underlying condition may be the critical step in bringing about wound healing.

The size, depth, and color of the wound base (black, yellow, red) should be recorded to provide a baseline against which healing can be assessed. The amount and type of exudate (serous, sangous, pustular) should also be assessed: a heavy exudate may indicate uncontrolled edema or may be an early sign of infection.

The wound margin and surrounding skin should be checked for callus formation, maceration, edema, or erythema and the causes corrected. Patients with neuropathy often display hyperkeratotic calluses on the plantar aspect of the foot, which lead to increased local pressure. The callus should be removed to reduce pressure. White hyperkeratosis of the surrounding skin or ulcer margin and an over-hydrated wound surface often suggest excess fluid, which may be due to local dressings that keep the ulcer too moist or that do not absorb exudate. Limb edema or uncorrected pressure may also be causes of local edema, while maceration may be a sign of infection. Local erythema is a sign of inflammation or infection: warm, hot, tender erythema suggests infection, while discreet erythema with well-demarcated margins and co-existing epidermal changes probably indicates contact allergic dermatitis due to applied dressings or topical treatments. Contact allergic dermatitis requires treatment with topical steroids, while chronic irritant dermatitis can be treated with protectants such as petrolatum, zinc oxide ointment, or commercial barrier preparations around the wound margin.

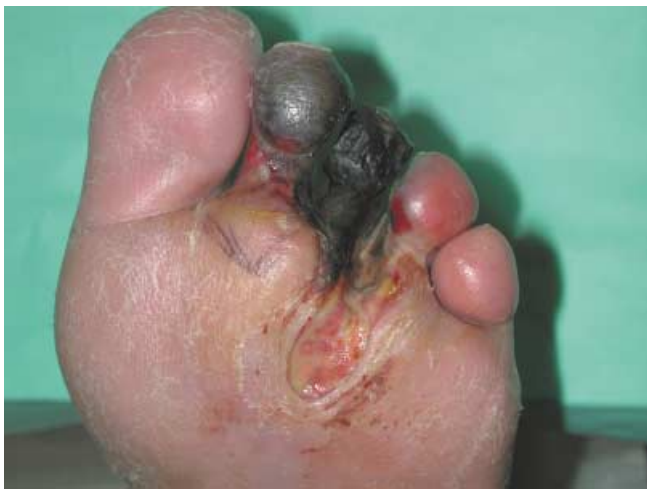

**FIGURE 5.** Necrotic toes with dry gangrene as the end result of ischemia and deep tissue infection. If the peripheral vasculature is insufficient, there is not enough blood to supply to promote healing. Aggressive debridement and moist interactive dressing are contra-indicated. Topical antiseptics may be used to decrease bacterial burden and dry the tissue, facilitating elimination of the gangrene. (© R. Gary Sibbald, MD).

While pain can be experienced during debridement or dressing changes, continuous pain may be due to an underlying cause, local wound irritation, or infection. It is important to assess continuous pain to determine whether its origin is in the wound or in the surrounding anatomical region.

## WOUND BED PREPARATION

In most cases it is not possible to apply the principles of acute wound healing to chronic wounds without considering the biochemical environment present in the latter. Chronic wounds have a complex, inflammatory nature and produce substantial amounts of exudate, which interfere with the healing process and the effectiveness of advanced therapeutic healing products. The normal pattern and time frame of the cellular and biochemical events is disrupted and the wound is prevented from entering the proliferative phase of healing.

There is often a pro-inflammatory stimulus due to necrotic tissue, a heavy bacterial burden, and tissue breakdown that causes cellular and biochemical changes in the wound bed such as increased levels of MMPs, which degrade the ECM and result in impaired cell migration and deposition of connective tissue.[29] MMPs also degrade growth factors and their target cell receptors, preventing healing and perpetuating the chronic inflammatory phase.

The management of chronic wounds needs to be freed from the acute wound model to optimize their clinical management.[13] Wound bed preparation is an approach for achieving this objective: wound bed preparation focuses on all of the critical components, including debridement, bacterial balance, and management of exudate (Figure 6) and takes into account the overall health status of the patient and how this may impinge upon the wound healing process. The ultimate aim is to ensure formation of good-quality granulation tissue leading to complete wound closure, either naturally or through skin products or grafting procedures.

By analyzing the components of chronic wounds, more effective management strategies can be developed. Tarnuzzer and Schulz[21] suggest that the treatment of chronic wounds should focus on reestablishing the balance of growth factors, cytokines, proteases, and their natural inhibitors as found in acute wounds. This can be achieved through attention to necrotic burden (debridement),

bacterial imbalance, and excess exudate, and to the overall health status of the patient to ensure that systemic factors are identified and corrected.

### *Definition of wound bed preparation*

Wound bed preparation is the management of the wound to accelerate endogenous healing or to facilitate the effectiveness of other therapeutic measures. Local management of a nonhealing wound involves:

- an ongoing debridement phase,
- management of exudate, and
- resolution of bacterial imbalance.

At a meeting in June 2002, the expert working group responsible for this article summarized the clinical components of wound bed preparation along with the underlying cellular environment at each stage. A table was designed (Table 6) to illustrate in a simple way the link between clinical observations and underlying cellular abnormalities and to link clinical interventions with their effects at a cellular level.

## *ONGOING DEBRIDEMENT IN CHRONIC WOUNDS*

Efficient debridement is an essential step in acute and chronic wound management. Chronic wounds are likely to require ongoing maintenance debridement rather than a single intervention. The underlying pathogenic abnormalities in chronic wounds cause a continual build-up of necrotic tissue, and regular debridement is necessary to reduce the necrotic burden and achieve healthy granulation tissue (Figure 7). Debridement also reduces wound contamination and therefore assists in reducing tissue destruction. Dead spaces that may otherwise harbor bacterial growth must be exposed during debridement.

Five methods of debridement are available, each with its own advantages and limitations. Those methods that

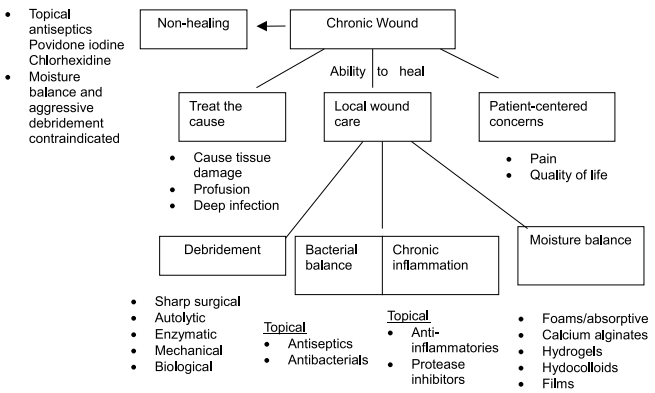


**FIGURE 6.** Paradigm for preparing the wound bed.

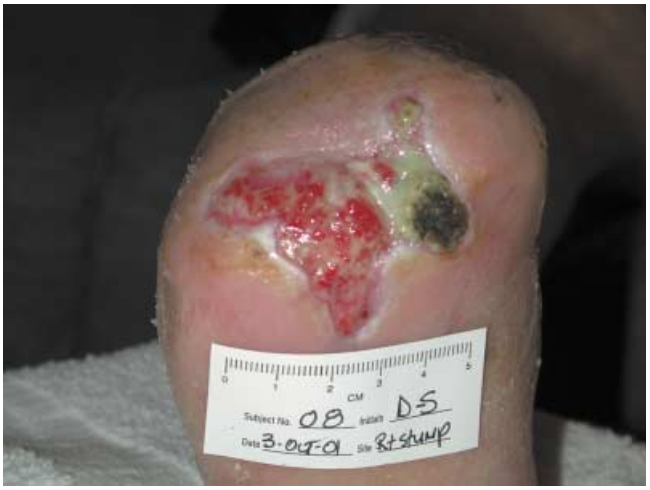

**FIGURE 7.** Amputation stump with necrotic, yellow fibrinous and granulation tissue base. (© R. Gary Sibbald, MD).

are most efficient at removal of debris may, at the same time, be the most detrimental to fragile new growth, and more than one method may be appropriate.

### *Autolytic debridement*

This occurs spontaneously to some extent in all wounds. It is a highly selective process involving macrophages and endogenous proteolytic enzymes, which liquefy and spontaneously separate necrotic tissue and eschar from healthy tissue. Moist dressings such as hydrogels and hydrocolloids can enhance the environment for debridement by phagocytic cells and can create an environment capable of liquefying slough and promoting tissue granulation.[30,31] If tissue autolysis is not apparent within 72 hours, another form of debridement should be used. If persistent eschar contributes to the delay in autolysis, the hard eschar surface can be scored with a scalpel blade, without penetrating to underlying viable tissue. This procedure facilitates the autolytic process of moist dressings.

### *Surgical and sharp debridement*

This is the fastest and most effective way to remove debris and necrotic tissue (Figures 8A and B). The scalpel decreases bacterial burden and removes old and senescent cells, converting a nonhealing chronic wound into an acute wound within a chronic wound. Surgical debridement that leaves a bleeding base has been shown to increase the healing rate of diabetic neurotropic foot ulcers.[5]

Surgical debridement is normally performed where there is a large wound area, widespread infection, where bone and infected tissue must be removed, or where the patient is septic.[32] It is also the treatment of choice for diabetic neurotropic foot ulcers with hyperkeratosis callus on the ulcer rim.

**Table 6.** The principles of wound bed preparation (WBP)

| Clinical observations | Proposed pathophysiology | WBP clinical actions* | Effect of WBP actions | Clinical outcome |
|---|---|---|---|---|
| Non-viable or deficient tissue | Defective matrix and cell debris impair healing | Debridement (episodic or continuous)<br>■ Autolytic, sharp surgical, enzymatic, mechanical or biological | Restoration of wound base and functional extracellular matrix proteins | Viable wound base |
| Infection or inflammation | High bacterial counts or prolonged inflammation:<br>↑ inflammatory cytokines<br>↑ protease activity<br>↓ growth factor activity | ■ Remove infected foci<br>Topical/systemic:<br>■ Antimicrobials<br>■ Anti-inflammatories<br>■ Protease inhibitors | Low bacterial counts or controlled inflammation:<br>↓ inflammatory cytokines<br>↓ protease activity<br>↑ growth factor activity | Bacterial balance and reduced inflammation |
| Moisture imbalance | Desiccation slows epithelial cell migration<br>Excessive fluid causes maceration of wound margin | Apply moisture balancing dressings, compression, negative pressure or other methods of removing fluid | Restored epithelial cell migration, desiccation avoided<br>Oedema, excessive fluid controlled, maceration avoided | Moisture balance |
| Non-advancing or undermined epidermal margin | Non-migrating epidermal margin<br>Non-responsive wound cells and abnormalities in protease activity | Re-assess cause or consider corrective therapies:<br>■ Debridement<br>■ Skin grafts<br>■ Biological agents<br>■ Adjunctive therapies | Migrating keratinocytes and responsive wound cells<br>Restoration of appropriate protease profile | Advancing epidermal margin |

*Suggested clinical treatments by the © International Wound Bed Preparation Advisory Board.

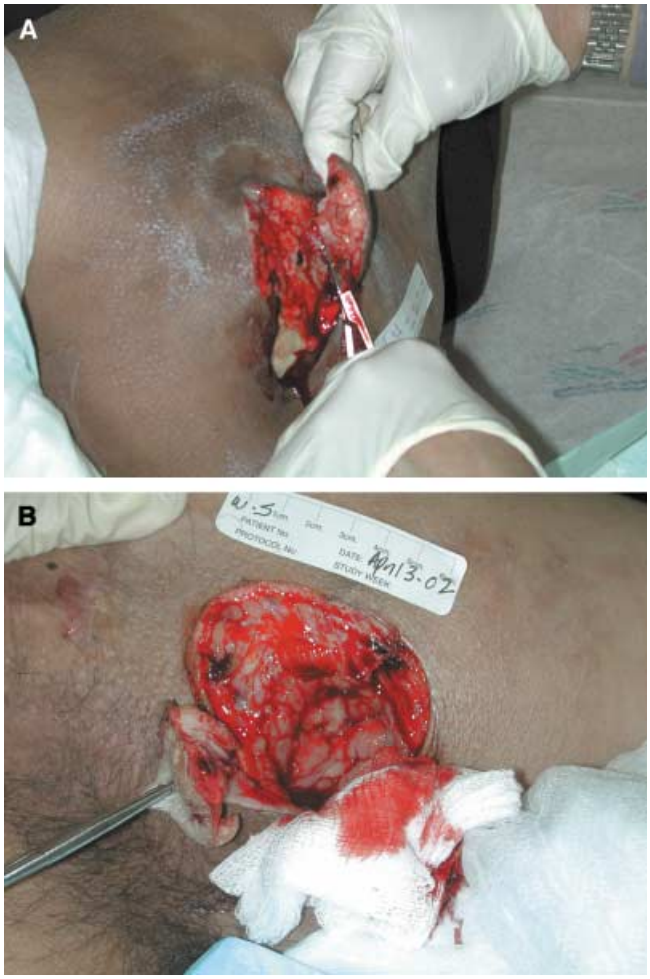


**FIGURE 8.** Debridement of buttock ulcer. (A) Interoperative. (B) Buttock ulcer post-surgical debridement. (© R. Gary Sibbald, MD).

This method can be painful and can lead to bleeding (although this can be beneficial as it stimulates release of growth factors from platelets) and can damage tendons and nerves.[4] Various topical, intralesional, oral, or intravenous pain relief agents are available and the most appropriate method should be chosen for the wound. Topical creams can be applied and occluded in a thick coat on the wound, or intralesional xylocaine can be placed around the periphery if a deeper anesthetic effect is required.

Surgical and sharp debridement must be performed by an experienced clinician and caution must be exercised in patients with compromised immunity to avoid the creation of large open wounds that may favor opportunistic infection. This procedure is inappropriate for a nonhealable ulcer—one with insufficient vascular supply to allow healing—and must be used with extreme caution in patients on anticoagulants.

### *Enzymatic debridement*

Autolytic debridement occurs through the action of endogenous enzymes including elastase, collagenase, myeloperoxidase, acid hydrolase, and lysosomes. Enzymatic methods use topical application of exogenous enzymes to the wound surface where they work synergistically with endogenous enzymes to debride the surface. This method appears to be most useful in the removal of eschar from large wounds where surgical techniques can not be used. Cross-hatching or scoring of the eschar may be necessary prior to application of the enzyme. Excess exudate may be produced with these agents, and local irritation to the surrounding skin or infection sometimes occur.

Several agents are available, although not in all markets, including fibrinolysin/desoxyribonuclease (fibrinolysin/DNase), collagenase and papain/urea (Table 7).

Fibrinolysin/DNase breaks down fibrin, inactivates fibrinogen and several coagulation factors, and dilates blood vessels in the wound bed, all of which allow macrophages to enter the wound and degrade necrotic tissue. The products of fibrinolysin degradation are not resorbed and must be removed from the wound by irrigation. DNase cleaves nucleic acids, leading to liquefaction of exudate and decreased viscosity.

Bacterial collagenase isolated from *Clostridium histolyticum* displays great specificity for the major collagen types in the skin (type I and type II collagen) and has been successfully used as an enzymatic debrider.[33,34] It cleaves glycine in native collagen and digests collagen, but is not active against keratin, fat, or fibrin. The wound healing process is promoted by the digestion of native collagen bundles which bind nonviable tissue to the wound surface, and by the dissolution of collagen debris within the wound.

Papain is a proteolytic enzyme derived from the papaya fruit. It is inactive against collagen and digests necrotic tissue by liquefying fibrinous debris. Papain requires the presence of activators in order to function: urea is used as an activator and it also denatures nonviable protein matter, making it more susceptible to proteolysis.

### *Mechanical debridement*

Methods such as wet-to-dry dressings, wound irrigation, and whirlpool techniques are used to physically remove debris from the wound.

Wet-to-dry dressings macerate eschar and induce mechanical separation as the dressing is removed from the wound bed.[35] However, this can be uncomfortable for the patient and can damage newly formed tissue. High- or low-pressure streams of water are used to remove bacteria, particulate matter, and necrotic debris from wounds, but bacteria may be driven even further into soft tissue with this technique.

**Table 7.** Products available for enzymatic debridement

| Enzyme | Action | pH range required for activity |
|---|---|---|
| Bacterial collagenase | Degrades native collagen<br>Does not attract fibrin | 6.0 to 8.0 |
| DNase/fibrinolysin | Acts on DNA of purulent exudate | 7.0 to 8.0 |
| | Breaks down fibrin components of blood clots and fibrinous exudate | 4.5 to 5.5 |
| Papain/urea | Relatively ineffective alone, indiscriminate and requires urea | 3.0 to 12.0 |
| Trypsin | Dissolves blood clots | – |

Table adapted from Falabella AF 1999.[105]

Whirlpools or foot soaks are used to loosen and remove surface debris, bacteria, necrotic tissue, and wound exudate. This technique is suitable for necrotic wounds at the inflammatory phase but not for granulating wounds where fragile endothelial and epithelial cells may be removed. It may also spread infection to susceptible areas such as the toe webs, nail folds, and skin fissures.

### *Biological therapy (larval therapy)*

A reemerging technique of debridement is the use of maggots. As far back as the First World War it was noticed that wounds infested with maggots were cleaner and less infected than uninfested wounds. Today, sterile larvae of the *Lucilia sericata* fly are used, which produce powerful enzymes to break down dead tissue without harming healthy granulation tissue.[36] The enzymes also appear to combat clinical infection[37] with reduced bacterial counts noticed in infested wounds, including methicillin-resistant *Staphylococcus aureus* (MRSA).[38]

Hard eschar may need to be softened first and the moisture content of the wound needs to be monitored. The larvae can "drown" in excess exudate but need to have some moisture; otherwise they will dry out and die. Table 8 summarises the characteristics of the major methods of debridement.

## MANAGEMENT OF EXUDATE IN CHRONIC WOUNDS

The role of moisture in wound healing has often been misunderstood. When the science of wound healing began to develop, the concept of moist dressings took hold[39] and occlusive dressings are now widely used in the treatment of acute wounds. The benefits of occlusion seem to be:

- the presence of a moist wound healing environment that assists epidermal migration
- alterations in pH and oxygen levels
- the maintenance of an electrical gradient
- the retention of wound fluid.[40]

It was assumed that as contact with wound fluid was beneficial to the healing process, occlusive dressings would therefore be suitable in the management of chronic wounds. It is now known that chronic wound fluid contains substances detrimental to cell proliferation, and maintaining contact between a chronic wound and its fluid is likely to delay wound healing. Chronic wound fluid leads to the breakdown of ECM proteins and growth factors and the inhibition of cell proliferation.[14,41]

Occlusive dressings may be beneficial in some respects—such as preventing crust formation, encouraging migration of inflammatory cells into the wound—but treatment may be better carried out with dressings that remove some of the wound exudate.

The build-up of chronic wound fluid must be managed to minimize the negative biochemical factors. Compression bandaging or highly absorbent dressings are helpful in removing wound fluid, enabling growth factors to promote an angiogenic response, leading to wound closure. An appropriate wound dressing can remove copious amounts of wound exudate while retaining a

**Table 8.** Selecting a method of debridement

| | Debridement method | | | |
|---|---|---|---|---|
| **Characteristic** | **Autolytic** | **Surgical** | **Enzymatic** | **Mechanical** |
| Speed | 4 | 1 | 2 | 3 |
| Tissue selectivity | 3 | 2 | 1 | 4 |
| Painful wound | 1 | 4 | 2 | 3 |
| Exudate | 3 | 1 | 4 | 2 |
| Infection | 4 | 1 | 3 | 2 |
| Cost | 1 | 4 | 2 | 3 |
| 1 = most appropriate; 4 = least appropriate | | | | |

Table from Sibbald et al. 2000.[44]

moist environment that can accelerate wound healing.[7] The choice of wound dressing at one stage of the wound process may well influence subsequent events in the later phases of healing.[42] The Agency for Health Care Policy and Research published guidelines in 1994 for the selection of dressings. These were published in Ostomy Wound Management in 1999 and reevaluated by Liza Ovington[43] (Table 9).

A simple alternative to the use of specialized dressings is to thoroughly clean and irrigate a chronic wound with saline or sterile water, which removes exudate and cellular debris and reduces the bacterial burden of the wound. Indirect methods of reducing exudate should not be forgotten: wound fluid may be a result of extreme bacterial colonization or may simply involve relief of pressure or elevation of the affected limb.

No single dressing meets all the requirements, and today a number of advanced dressings are available for various types of wound. Table 10 provides guidance on selecting the most appropriate.

### Foams, hydrofibers, crystalline sodium chloride gauze

Foams, hydrofibers, and crystalline sodium chloride gauze are the most appropriate for sloughy or exudative wounds.[44] Foams provide thermal insulation, high absorbency, a moist environment, and are gas permeable. They can easily be cut to shape and do not shed fibers. Some foams have additional wound contact layers to avoid adherence when the wound is dry and polyurethane backing to prevent excess fluid loss. Hydrofibers are highly absorbent and contain the fluid within the fiber as well as possessing good tensile strength. Both of these groups can be worn for up to 1 week. Crystalline sodium chloride gauze is used for highly exudative wounds, mechanical debridement, and has antibacterial properties. This dressing needs to be changed daily.

### Calcium alginates

Calcium alginates, which form a gel upon contact, promoting moist interactive healing, are ideal for exudative and infected wounds.[45,46] They are derived from brown seaweed. Some have a high mannuronic acid content, which gives a high gelling property for autolytic debridement, and others have a high galuronic acid content, which provides good fiber integrity for packing sinuses. Post-debridement, they can donate calcium, facilitating hemostasis, and accept sodium, converting the calcium alginate fiber to a sodium alginate hydrogel. No crust is formed and the wound can progress from the inflammatory to the proliferative stage.

**Table 9.** Guidelines for the use of wound dressings

| |
|---|
| Use a dressing that will maintain a moist wound environment. |
| Use clinical judgment to select a moist wound dressing for the wound being treated. |
| Choose a dressing that will keep the peri-ulcer skin dry while maintaining the moisture within the wound. |
| Use a dressing that will control the wound exudate without leading to desiccation of the wound bed. Uncontrolled exudate can lead to maceration of the surrounding skin and lead to further deterioration of the wound. |
| If possible, use dressings that are easy to apply and do not require frequent changes as this will decrease the amount of health care provider time required. |
| Fill any cavities within the wound to avoid impaired healing and increased bacterial invasion. Overpacking must be avoided to prevent damage to newly formed granulation tissue, which could delay healing and may also decrease the absorbent capacity of the dressing. |
| Monitor all dressings, particularly those near the anus, which are difficult to keep in place. |

**Table 10.** Selection of an appropriate dressing for a nonhealing wound

| | Appearance of wound bed | | | | Appearance of granulation tissue | | |
|---|---|---|---|---|---|---|---|
| **Dressing** | **Black (necrotic)** | **Yellow (dry)** | **Sloughy (moist)** | **Red (infected)** | **Red (wet)** | **Red (bleeding)** | **Pink/purple (healthy granulation/ reepithelialization** |
| Foam | | | ++ | ++ | +++ | | |
| Hydrofiber | | | +++ | ++ | +++ | + | |
| Crystalline NaCl gauze | | | +++ | +++ | ++ | | |
| Calcium alginate | | | + | +++ | +++ | +++ | |
| Hydrocolloid | + | ++ | ++ | | ++ | | ++ |
| Hydrogel | ++ | +++ | | + | | + | +++ |
| Adhesive film | | | | | | | +++ |
| Non-adhesive film | | | ++ | | | | |
| Enzymes | +++ | +++ | | | | | ++ |

Table from Sibbald et al. 2000.[44]

### Hydrogels

Hydrogels provide a high concentration of water (70–90%) contained in insoluble polymers (backbones are often propylene glycol saline, hydrocolloids, etc.) and are the best choice for dry, sloughy wounds with low levels of exudate. They need changing every 24–72 hours, however, as they are not strongly anti-infective.

### Hydrocolloids

Hydrocolloids form a linked matrix gel on contact with the wound exudate and are suited to autolytic debridement for mild to moderately exudating wounds.[47] They are occlusive, providing an anaerobic environment that may sometimes assist in correcting hypertropic granulation. Carboxymethylcellulose provides both hydrophilic and hydrophobic terminals. These dressings also contain adhesives, other polysaccharides, and proteins. Adhesives related to colophony (pentolin H) in some hydrocolloids can cause allergic contact dermatitis, especially with prolonged use in susceptible patients.[48] Pectin contributes to the fibrinolytic activity and the low pH provides some antibacterial properties. Occlusion is achieved with a foam or film sheet backing and these dressings have a wear time of 2 to 7 days.

### Film dressings

Film dressings are ideal at the later stages of wound healing when there is no significant exudate. Many are permeable to water vapor and oxygen but impermeable to water and microorganisms. Film dressings are available in adhesive and nonadhesive forms and can be left in place for long periods.

## BACTERIA IN WOUND MANAGEMENT: RESOLUTION OF BACTERIAL IMBALANCE

Most clinicians are concerned about infection in healing wounds; however, the presence of bacteria in a chronic wound does not necessarily indicate that infection has occurred or that it will lead to impairment of wound healing.[42,49] Microorganisms are present in all chronic wounds, and it has been suggested that certain low levels of bacteria can actually facilitate healing.[50,51] Bacteria produce proteolytic enzymes such as hyaluronidase, which contribute to wound debridement and stimulate neutrophils to release proteases.[52]

Organisms are acquired from the indigenous flora of the human host or from the environment. Bacterial involvement in wounds can be divided into four categories:

1. wound contamination
2. wound colonization
3. critical colonization
4. wound infection

Wound contamination is the presence of nonreplicating microorganisms in the wound. Most organisms are usually incapable of developing replicative infection due to the hostile environment of human soft tissue. Examples include contamination by soil organisms in an open wound.

Wound colonization is the presence of replicating microorganisms adhering to the wound that are not causing injury to the host. This includes skin commensals such as *Staphylococcus epidermidis* and *Corynebacterium* species, which in most circumstances have been shown to increase the rate of wound healing.[53]

Critical colonization/increased bacterial burden occurs when bacteria cause a delay in wound healing.[54,55] Bacteria can release MMPs and other pro-inflammatory mediators that impair healing. Clinically, nonhealing can first be detected when the wound margins fail to change. An increased serous exudate may be accompanied by friable bright red granulation tissue, often exuberant. Bacteria can stimulate angiogenesis and lead to the production of a deficient or corrupt matrix. The increased vascularity often leads to an abnormal bright red color and a friable corrupt matrix. When a dressing is removed, the wound surface may bleed easily. An unpleasant or putrid odor may also be accompanied by new areas of necrosis or breakdown in the wound base.

The concept of critical colonization was demonstrated by Sibbald et al.[54] in a study where a nanocrystalline silver dressing was applied to patients with chronic wounds. The wounds did not have clinical signs of infection, but the use of the silver dressing resulted in clinical improvement and accelerated healing, with decreased exudate in many patients and improvement in surface semiquantitative bacterial swab results. There was no change in the bacterial burden of the deep component as measured by deep quantitative bacterial biopsy. Surface antimicrobial agents can change the superficial bacterial burden, but if imbalance is noted in the deep compartment, systemic antibacterial agents are needed.

In a second study,[55] patients with nonhealing diabetic neurotropic foot ulcers were treated with a living skin equivalent, combining viable human dermal neonatal fibroblasts and a vicryl matrix. Patients were assessed for VIP (Vascular supply adequate to heal; absence of clinical signs of deep Infection; and Pressure downloading with orthotics and deep-toed shoes). Quantitative bacterial biopsies were taken prior to the onset of weekly skin substitute application for 8 weeks and the healing rates of the ulcers were measured (Table 11).

For ulcer closure, healing rates of 0.065 cm/week or greater are required.[56,57] Only those ulcers in bacterial balance with less than $1.0 \times 10^6$ colony-forming units per gram (CFU/g) of tissue were stimulated to heal with the application of the skin substitute. This is similar to the results of Robson and Krizek,[58] who predicted split-thickness skin graft failure in patients with $> 10^5$ CFU/g of tissue on quantitative biopsy, but other investigators were not able to confirm these findings. The concept of infection, however, is more complex:[49]

$$\text{Infection} = \frac{\text{Bacterial load} \times \text{virulence}}{\text{Host resistance}}$$

In a person with diabetes, host resistance is decreased and bacteria have a relative advantage, while nondiabetic patients may be able to handle an increased bacterial burden and still heal (Figures 9A and B). Clinical signs and symptoms that may be useful in determining superficial and deep tissue infection are outlined in Table 12.

Wound infection is the presence of replicating microorganisms within the wound and the presence of injury to the host. As the bacterial burden increases, the colonized wound is transformed into a covert infection[59] which may not involve extensive tissue invasion but is sufficient to inhibit wound healing. As the bacterial burden increases wound infection or systemic dissemination (sepsis) can occur.[49] Infection often is accompanied by local pain, warmth, dermal or deeper erythema, swelling, and frank pus.

Cutting and Harding[60] identified friable bright red granulation, exuberant granulation, increased discharge, and new areas of slough within the wound base as possible signs of infection. Gardner et al.[61] validated pain, increased wound size, new areas of breakdown, and odor as signs with a high correlation with $> 10^5$ colony-forming organisms of bacteria per gram of tissue. Grayson et al.[62] validated the exposure or probing to bone of foot ulcers in people with diabetes as a useful bedside test (sensitivity 66%; specificity 85%; positive predictive value 89%; and negative predictive value 56%).

**Table 11.** Wound healing rates as a function of wound bacterial load*

| Bacterial burden | Number of patients | Wound healing rates |
|---|---|---|
| $>10^6$ | 3 | 0.055 cm/week |
| $10^5$–$10^6$ | 3 | 0.15 cm/week |
| No growth | 2 | 0.20 cm/week |

*Data from Browne et al. 2001.[55]

**Table 12.** Signs and symptoms of superficial and deep tissue infection

| Tissue depth | Signs/symptoms |
|---|---|
| Superficial | Nonhealing<br>Friable granulation<br>Exuberant bright red granulation<br>Increased exudate<br>New areas of necrosis in base |
| Deep | Pain<br>Increased size<br>Warmth<br>Erythema >1–2 cm<br>Probes/exposed bone |

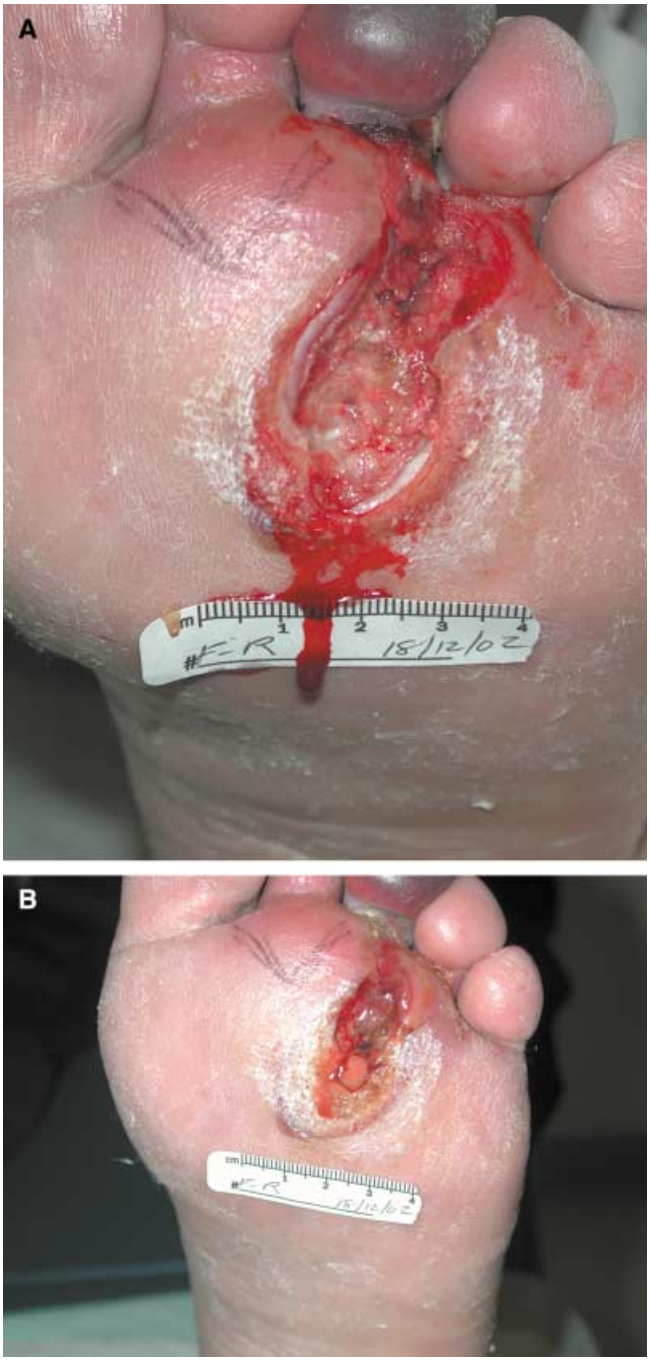


**FIGURE 9.** Foot with distal infection leading to early gangrene of the toe. (A) Pre-operative. (B) Post-debridement of sinus tract on the distal foot.

In an acute wound, a rapid inflammatory response is initiated by the release of cytokines and growth factors. The inflammatory cascade produces vasodilation and a significant increase of blood flow to the injured area. At the same time, enhanced vascular permeability allows the removal of microorganisms, foreign debris, bacterial toxins, and enzymes by phagocytic cells, complement, and antibodies. The coagulation cascade is also activated, which isolates the site of infection in a gel-like matrix to protect the host.[49]

In a chronic wound, the continuous presence of virulent microorganisms can lead to a massive and continued inflammatory response that may actually contribute to host injury. There is persistent production of inflammatory mediators such as prostaglandin E2 and thomboxane and steady ingress of neutrophils, which release cytolytic enzymes and oxygen free radicals. There is localized thrombosis and the release of vasoconstricting metabolites, which can lead to tissue hypoxia, bringing about further bacterial proliferation and tissue destruction.[49]

In infected wounds, the occlusion of larger vessels leads to wound hypoxia, the proliferation of small vessels leads to the formation of fragile granulation tissue, and fewer fibroblasts are associated with disorganized collagen production.[49]

### Diagnosis of wound infection

Although diagnosis of infection may be difficult, one common feature is the failure of the wound to heal, often with progressive deterioration of the wound. The diagnosis of infection in a chronic wound is hampered by the often subtle nature of the transformation from colonization to infection and by the difficulty in assessing all the factors that contribute to the development of infection.

### Bacterial burden

Quantitation of bacteria using tissue biopsy can predict host injury and wound infection but is costly, time-consuming, and causes further trauma to the patient. There is also the drawback that bacteria have variable virulence: beta-hemolytic streptococci can induce significant injury at $10^2$–$10^3$ colony-forming units per gram of tissue, whereas wounds with more than $10^6$ colony-forming units can often heal without trouble.

A semiquantitative swab technique is a practical means of assessing bacterial burden on a routine basis. The wound bed is first cleaned with saline irrigation and debridement and a swab is taken by rolling the swab across the exposed bed. The swab is inoculated onto solid media and streaked into four quadrants. It has been shown that 4 + growth or growth in the fourth quadrant (> 30 colonies) corresponds to approximately $10^5$ or greater organisms per gram of tissue as measured by quantitative biopsy.[63] This technique samples a large area of the wound surface but may also lead to an increased number of false-positive results. Techniques for sampling are summarized in Table 13.

### Pathogen characteristics

In chronic wounds the pathogen species may be much more important than the number of organisms. Beta-hemolytic streptococci are almost always significant regardless of quantity, and other pathogens that require treatment at any level include *Mycobacteria*, *Bacillus anthracis*, *Yersinia pestis*, *Corynebacterium diphtheriae*, *Erysipelothrix* species, *Leptospira* species, *Treponema* species, *Brucella* species, Herpes Zoster, Herpes Simplex, invasive dimorphic fungi (*Histoplasma* species, *Blastomyces* species, *Coccidioides immitis*) and parasitic organisms such as leishmaniasis.

The microbial flora of a chronic wound changes over time. In an early acute wound, normal skin flora are the predominant organisms. Gram positives including *S. aureus* and beta-hemolytic streptococci are usually present. After about 4 weeks a chronic wound usually becomes colonized with facultative anaerobic gram-negative rods such as *Proteus*, *E. coli* and *Klebsiella* species. As the wound deteriorates and deeper structures become involved, anaerobic flora become part of the local microbial population.[64] Wounds of several months' duration will have on average four to five different microbial pathogens including anaerobic and aerobic gram-negative rods, which are often detected late in the course of chronic wound infection. These may be introduced into the wound from exogenous sources such as bath water and footwear,

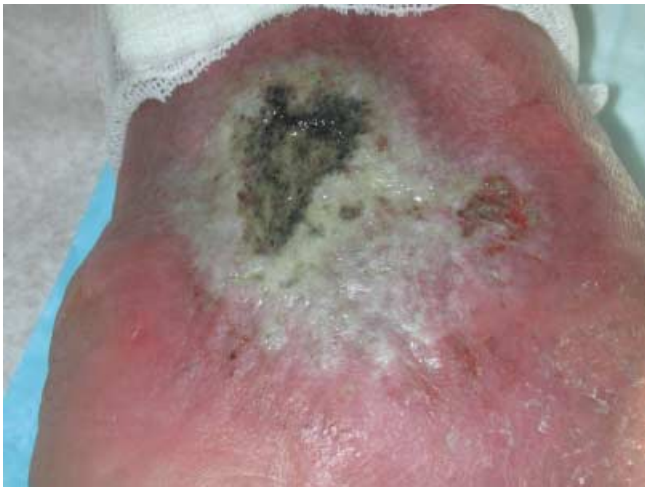

**FIGURE 10.** Superficial *Pseudomonas* infection. (© R. Gary Sibbald, MD).

**Table 13.** Techniques for assessing bacterial burden

| Technique | Description | Strength | Weakness | Indications/ recommendations |
|---|---|---|---|---|
| Quantitative biopsy | Tissue is biopsied, weighed, homogenized to free microorganisms from tissue matrix. Homogenate is serially diluted and plated. After incubation, colonies are enumerated and identified and colony counts calculated | Evaluates presence of microorganisms within tissue as opposed to surface colonization | Invasive. Punch wounds may be slow to heal. Time-consuming, expensive, possibly reduced sensitivity. | Reserve for clinical trials and research settings |
| Quantitative swab | Swab twirled over 1cm$^2$ surface of wound and agitated in 1 ml transport media. Serially divided and cultured on pour plates. | Approximates quantitative biopsy. | Time-consuming, expensive. Less rigorously studied than biopsy. Overestimates colony counts by 1 log relative to biopsy. | Requires further study to define role. |
| Semi-quantitative swab | Swab rolled across wound bed and inoculated on standard media in Petri dish, then streaked into four quadrants. | Quick, inexpensive, reproducible. Correlates with biopsy results. | Some reduction in specificity. Inadequate wound bed preparation results in excess of surface colonizers. | Consider use if appropriate or in liaison with hospital laboratory |
| Rapid slide technique | Wound bed biopsy is weighed, diluted 10-fold, and homogenized. 0.02 ml aliquot is placed on a slide, heat-fixed, and stained. A single bacterium per total field corresponds to >$10^6$ CFU/g of tissue. | No delay between collection and reporting. Organism morphology and gram stain characteristics may be identified. | Organisms cannot be specified. Highly operator sensitive. | Rapid technique for determining when primary or delayed closure can be performed. |
| Irrigation-aspiration | Would fluid is aspirated after irrigation, then cultured. | Atraumatic, noninvasive technique. | Does not quantitate bacterial burden. | Research technique requiring further study. |

Adapted table from Dow et al. 1999.

**Table 14.** Risk factors for infection in chronic wounds

| |
|---|
| Large wound area: greater host impairment |
| Increased wound depth (subdermal) |
| Degree of chronicity |
| Anatomic location (distal extremity, perineal) |
| Presence of foreign bodies |
| Necrotic tissue |
| Mechanism of injury (bites, perforated viscous) |
| Degree of post-wounding contamination |
| Reduced perfusion |

including *Pseudomonas* species, *Acinetobacter* species, and *Stenotrophomonas* species. These seldom cause soft tissue invasion unless the host is highly compromised (for example, malignant otitis externa due to *Pseudomonas* in persons with diabetes) (Figure 10).

### Host resistance

Local factors that increase the risk of infection in chronic wounds are summarized in Table 14. Host resistance is the single most important determinant of wound infection and should be rigorously assessed whenever a chronic wound fails to heal.

Systemic host resistance can be affected by many variables, some of which may be behavioral and lead to noncompliance. Inability to control blood sugar levels, smoking, drug and alcohol abuse, malnutrition, and depressive illness can all diminish host resistance and increase the likelihood of infection. Other factors such as right-sided heart failure can lead to infection, as edema reduces lymphatic flow and increases the risk of gram-positive infection. In such cases, wound management will involve not just treatment of the wound, but also treatment of the underlying disease. The use of cytotoxic agents and corticosteroids can totally mask all signs of local or systemic infection. Table 15 lists some of the systemic factors that increase the risk of infection in chronic wounds.

### Treatment

Systemic antibiotics are not necessarily the most appropriate way of reducing bacterial burden in wounds, particularly with the development of increasing bacterial resistance. Other methods may be more suitable, including:

- enhanced host defense mechanisms
- debridement
- wound cleaning
- wound disinfection
- topical antibiotics

**Table 15.** Host risk factors that increase the risk of infection in chronic wounds

| |
|---|
| Vascular disease |
| Edema |
| Malnutrition |
| Diabetes mellitus |
| Alcoholism |
| Prior surgery or radiation |
| Corticosteroids |
| Inherited neutrophil defects |

Host defense mechanisms may be enhanced by a number of methods appropriate to the particular condition of the patient—some of which were mentioned above. An infected chronic wound in the presence of critical limb ischemia may be improved by reconstructive vascular surgery, for example, and bacterial burden may be reduced by measures designed to control blood sugar, reduce smoking, and so on.

Debridement has not been scientifically studied until quite recently[5] but has long been regarded as a technique that enhances wound closure. Debridement removes foreign bodies from the wound, an intervention that improves local host defense mechanisms and reduces active infection.[65] When foreign material is present in the wound, fewer microorganisms are required to produce an infection.[66]

The removal of devascularized tissue and necrotic material (soft tissue, bone fascia, muscle, and ligament) has a similar beneficial effect. Debridement also produces a more active wound and the release of tissue cytokines and growth factors (Figures 11A and B).

Wound cleaning is an important technique in which organisms are physically removed from the wound bed. Physiologic saline is applied at pressures that will remove microbes without disturbing tissue, usually between 8 and 15 psi. Surfactants have also been used but may be toxic to the granulation tissue and do not necessarily have any benefits over saline.

Wound disinfection has been an area of controversy because in vitro many of these agents have shown toxicity to human fibroblasts. Commonly used disinfectants include:

- povidone-iodine
- ionized silver
- chlorhexidine
- alcohol
- acetic acid
- hydrogen peroxide
- sodium hypochlorite (Dakin's solution)

However, despite the apparent toxicity in vitro, these agents may not significantly delay wound healing in vivo. The type of evaluation used in vitro is markedly different from that encountered in the normal wound


**FIGURE 11.** (A) Debridement of necrotic eschar. (B) Removal of eschar leaving prepared wound bed. (© R. Gary Sibbald, MD).

environment[67,68] and in vivo studies have shown that toxicity varies between agents and is highly dependent on the concentration used.[69,70]

Toxicity can also be modified through sophisticated delivery methods. One example is cadexomer iodine, which consists of a modified starch matrix that absorbs moisture up to six times its own weight. Swelling of the lattice increases the size of its micropores, which slowly release iodine in a controlled fashion. This product has been shown to accelerate wound healing in chronic leg ulcers.[71]

Nanocrystalline silver dressing slowly releases silver within the dressing, which has a broad spectrum of antibacterial activity and is combined with an absorptive polyester pad that can decrease friable exudative tissue on the wound surface. Silver has recently been combined with other moist interactive dressings including foams, calcium alginates, hydrocolloids, and films.

Dilutions of antiseptic solutions (e.g., sodium hypochlorite, 0.005%; acetic acid, 0.0025%) during the most active stage of infection are beneficial but will only treat the wound surface rather than deep infection and have considerable tissue toxicity.

Topical antimicrobials are most appropriate when used to decrease the bacterial burden in chronic wounds with active but localized infection. They are not suitable for highly infected wounds with soft tissue invasion or systemic sepsis and should not be used as a substitute for debridement. Increasing antimicrobial resistance means these agents should not be used for extended periods of time and should be followed by an appropriate dressing once the bacterial burden has been reduced to acceptable levels. In general, topical antimicrobials should have a low sensitization potential, not be used systemically (emergence of resistant organisms), and have a low tissue toxicity.[72] They can be used for a finite period (e.g., 2 weeks) to control superficial increased bacterial burden, but should not replace systemic agents if the deep compartment is not in bacterial balance.

Systemic antimicrobial therapy should be used in all chronic wounds where there is active infection beyond the level that can be managed with local wound therapy. Systemic signs of infection such as fever, life-threatening infection, cellulitis extending at least 1 cm beyond the wound margin, and underlying deep structure infections indicate the use of systemic therapy. Table 16 summarizes the choices available based on the severity of infection and the duration of the chronic wound.

Occlusive wound dressings can be used to treat most wounds if there are no signs of exudative infection, and if the wound is largely confined to the level of the dermis. Occlusion can actually accelerate wound healing in the presence of a viable microbial population, which even increases during the period of occlusion. The wound fluid beneath an occlusive dressing is anaerobic and *Pseudomonas* species tend to disappear while there is an increase in skin colonizers such as *Enterococcus* species and anaerobic flora. However, infected, exudative wounds do not respond well to the use of occlusive dressings and can lead to rapid wound deterioration. In these cases, it is more appropriate to follow debridement with calcium

alginate dressings, foams, hydrofibers, or salt-impregnated gauze.

## THE CLINICAL RELEVANCE OF WOUND BED PREPARATION

Wound bed preparation should be considered for chronic wounds that are not progressing to normal wound healing. Some might argue that the concept of wound bed preparation is too simple or that there is nothing new about it. However, wound bed preparation as a strategy allows clinicians to break down into individual components various aspects of wound care while maintaining a global view of the objective.

Wound bed preparation allows us to define the steps involved in the management of chronic wounds and to understand the clinical problems and the basic science underpinning the problems.

A critical point is the differentiation of wound bed preparation from wound debridement alone. In acute wounds, debridement is a good way to remove necrotic tissue and bacteria after which one should have a clean wound that can heal with relative ease. In chronic wounds, much more than debridement needs to be used for optimal results. Not only do we need to concern ourselves with removal of actual eschars and nonviable tissue but also with exudate (Table 17). There is also increasing realization that the resident cells in chronic wounds may be phenotypically altered and no longer able to respond to certain signals, including growth factors.

The relevance of wound bed preparation to clinical practice is that time and money will not be spent on expensive advanced products that do not work. A poorly prepared wound cannot be treated with a growth factor or bioengineered skin with the expectation of success.

**Table 16.** Systemic antimicrobial therapy for chronic wounds

| Presentation | Severity | Organisms | Antibiotic and dose | Route | Duration |
|---|---|---|---|---|---|
| Wound <4 weeks old<br><2 cm rim of cellulitis<br>Superficial infection<br>No systemic response<br>No bone involvement<br>Outpatient management | Mild | *S. aureus*<br>*Strepto-coccus* sp | • Cephalexin 500 mg qid, or<br>• Clindamycin 300 mg tid | PO | 14 days |
| Wound <4 weeks old<br>Superficial infection<br>Extensive cellulitis<br>Systemic response<br>Inpatient management | Severe | *S. aureus*<br>*Streptococci* | • Cloxacillin, or<br>• Oxacillin 2 g q6h | IV (step down to oral) | 14 days total |
| Wound >4 weeks old<br>Deep tissue infection<br>No systemic response<br>Outpatient management | Mild to moderate | *S. aureus*<br>*Streptococcus* sp<br>Coliforms<br>Anaerobes | • Amoxicillin-clavulanate 500/125 mg tid, or<br>• Cephalexin 500 mg qid + metronidazole 500mg bid, or<br>• Cotrimoxazole 160/800 mg bid + metronidazole (or clindamycin), or<br>• Clindamycin 300 mg po tid + levofloxacin 500 mg po od | PO | 2 to 12 weeks |
| Wound >4 weeks old<br>Deep tissue infection<br>Systemic response with fever, rigors<br>Limb or life threatening<br>Inpatient management | Severe | *S. aureus*<br>Streptococcus species<br>Coliforms<br>Anaerobes<br>*Pseudomonas* | • Clindamycin 600 mg q8h + cefotaxime 1g q8h (or ceftriaxame 1gm q24h), or<br>• Piperacillin 3g q6h + gentamicin 5mg/kg q24h, or<br>• Piperacillin-tazobactam 4.5g q8h, or<br>• Clindamycin 600mg q8h + levofloxacin 500mg q24h, or<br>• Imipenem 500mg q6h | IV | 14 days iv (prolonged oral therapy if bone or joint involvement) |

Table from Dow et al. 1999.

**Table 17.** Wound bed preparation

| **Wound abnormalities and suggested corrective measures** | | | |
|---|---|---|---|
| Necrotic tissue<br>Edema<br>Infection<br>Hemodynamics | Biofilms<br>Necrotic tissue and exudate (necrotic burden) | Corrupt matrix<br>Fibrin<br>Growth factor-trapping MMPs | Cellular burden<br>Phenotypic changes in wound cells |
| ↓ | ↓ | ↓ | ↓ |
| Debridement<br>Antibiotics<br>Surgery | Slow-release antiseptics<br>Dressings<br>Enzymes<br>Maintenance debridement | Matrix materials<br>Fibrinolysis<br>Growth factors<br>MMPs inhibitors<br>Gene therapy | Cell chemotherapy<br>Bioengineered skin<br>Cell therapy<br>Stem cells |

Table from Falanga V 2000.

### *Evaluation of wound bed preparation*

Wound bed preparation is a valuable concept that attempts to systematize the approach to the treatment of chronic wounds. It has been shown that the clinical interventions can be justified in terms of the underlying cellular wound environment. The next stage is to show that a systematic approach works more effectively and more consistently than either a trial-and-error approach or an approach based on acute wound management.

To compare the efficacy of interventions, an accepted system of assessment and staging for wounds is needed. Falanga[13] developed a staging system for wound bed preparation that takes into account two critical aspects: wound bed appearance and the amount of wound exudate (Table 18). He suggests that this system will need validation but could be a useful starting point for judging wound preparedness and for correlating it with the ultimate outcome of complete wound closure.

In assessing the value of wound bed preparation, we need to test the hypothesis that the cellular environment is indeed responsible for delaying wound healing and that our interventions correct the cellular imbalance. If wound bed preparation is carried out properly we should see:

- a decrease in cytokines
- a decrease in MMPs
- an increase in growth factors and a positive clinical effect on healing. Evaluation tools for wound bed preparation are currently being developed and should provide more insight into the interventions used in wound management.

## ADVANCED WOUND HEALING TECHNIQUES

In recent years there have been many exciting developments in products designed to assist wound healing, such as tissue engineering and the use of growth factors. If the underlying cause, local wound care, and patient concerns have all been addressed but a wound still fails to heal, these and other advanced products may stimulate wound healing. However, it must be stressed that they will only be successful if applied to a well-prepared wound bed. The optimal preparation of the wound bed requires complete debridement of devitalized tissue, bacterial balance, and moisture balance. Skin grafts fail if there are $\geq 1.0 \times 10^6$ organisms in the wound bed.[73]

**Table 18.** Assessing wound bed characteristics

| | **Wound bed characteristics** | | |
|---|---|---|---|
| **Wound bed appearance score** | **Granulation tissue** | **Fibrinous tissue** | **Eschar** |
| A | 100% | − | − |
| B | 50 to 100% | + | − |
| C | <50% | + | − |
| D | Any amount | + | + |
| **Wound exudate** | **Extent of control** | **Exudate amount** | **Dressing requirement** |
| 1 | Full | None/minimal | No absorptive dressings required. If clinically feasible, dressings can remain for up to 1 week |
| 2 | Partial | Moderate amount | Dressing changes required every 2 to 3 days |
| 3 | Uncontrolled | Very exudative wound | Absorptive dressings changes required at least daily |

Table from Falanga V 2000.

### Tissue engineering

With autologous skin grafts, large areas of the patient's own skin are taken—usually from the back or thigh—to cover the injured area. Skin grafts and rational flaps have been used to heal large wounds and those that fail to heal by conservative therapies. Skin grafts require the creation of a donor site or second wound along with anesthetics. Attempts have been made for years to culture and grow keratinocytes in the laboratory to reduce the need for skin grafting.

In one autografting system, the patient's own cells are cultured onto a hyaluronic acid scaffold for grafting. The cells are harvested from an 8-mm skin biopsy and the keratinocytes are cultured and migrate through a laser-cut membrane. Within 1 month, the single biopsy can provide sufficient epithelial cells to cover an adult body.

Reinwald and Green[74] made an important advance in the management of burn patients by demonstrating how to rapidly expand an epidermal cell population in vitro over a period of 3–4 weeks. They produced the best skin graft take with noninfected, well-vascularized wounds. The procedure uses trypsinized cells that have been irradiated and placed in a Petri dish. The cells are grown to confluence, enzymatically separated, and grafted.

Bioengineered products replace the patient's damaged or destroyed dermal tissue and stimulate the patient's own epithelial cells. Human fibroblast cells are cultured from the foreskins of neonates onto a bioabsorbable scaffold. As they proliferate, they secrete dermal collagen, growth factors, and ECM proteins to create a living dermis, which is then implanted into the wound to facilitate healing.[75]

Allogenic, bilayered tissue consisting of a layer of viable keratinocytes and a dermal layer of viable fibroblasts dispersed in a type I collagen matrix has been used successfully in venous leg ulcers and neuropathic diabetic foot ulcers.[76]

Another artificial skin consists of a three-dimensional collagen dermal matrix and a temporary silicone epidermal layer. Moisture loss from the wound is controlled, and infiltration of the wound bed by the new dermis scaffold assists in wound closure.[77]

### Growth factors

Sometimes proper management of a chronic wound still does not result in healing, despite excellent attention to the underlying disease and to the wound environment. The application of topical growth factors to a persistently nonhealing, but well-granulated, wound is often considered in order to stimulate some aspect of the healing process.

The application of growth factors to chronic wounds is based on the assumption that there is an underlying cellular disorder in wounds that fail to heal, resulting in a shortfall of the specific growth factors required for the normal wound healing process. The role of topical growth factors is being assessed in wounds at various stages of healing and much new data on their contribution has emerged over the past decade. There are several problems with supplying an excess of a single growth factor in high concentrations. Each growth factor is part of an orchestra for healing signals and other components may be missing, or alternatively, high concentrations of some growth factors may even be harmful. Growth factor response may also be healing stage-specific.

The growth factors that have been most actively studied include:

- bFGF, which stimulates endothelial cell proliferation and migration
- TGFβ, which stimulates the growth of fibroblasts and keratinocytes and the production of extracellular matrix, particularly collagen
- EGF, which supports the growth of keratinocytes and assists the migration of keratinocytes, fibroblasts and endothelial cells
- PDGF, which is chemotactic for polymorphonuclear cells and macrophages

### PDGF

PDGF has a wide range of effects on other cells in the wound healing process and is felt to have considerable promise. It has been studied in a number of clinical trials. In an early study by Knighton et al.[78] chronic nonhealing ulcers were treated with autologous platelet-derived wound healing formula (PDWHF), which contained PDGF. Forty-nine patients with 95 wounds were treated with the autologous extract resulting in a mean time to 100% healing of only 10.6 weeks. A second trial by Knighton was carried out in 1990 using PDWHF for chronic ulcers. In this prospective, randomized, blinded study, 32 patients were treated for 8 weeks with either PDWHF or placebo. Eighty-one percent of the active treatment group reached complete epithelialization within the study period, compared to 15% of the controls. After crossover, all controls healed in an average of 7.1 weeks.[79]

In 1992, a study using recombinant human PDGF was carried out by Robson et al.[80] In this double-blind, placebo-controlled, randomized study, 45 patients with pressure ulcers were treated with varying concentrations of rhPDGF or placebo. The ulcer size reduction of the rhPDGF-treated patients was greater than the reduction in the placebo group.

Since then, many other studies have confirmed the efficacy and safety of this topical growth factor in pressure

ulcers[81] and chronic diabetic ulcers,[82–84] and the product is now available as a commercial gel that contains rhPDGF in an aqueous-based sodium carboxymethylcellulose gel. Topical gene therapy is another approach to delivering growth factors to chronic wounds. Studies in ischemic skin wounds in rabbit and rat models suggest that a single application of adenoviral vectors expressing PDGF accelerates healing, as do daily topical applications of Becaplermin (PDGF). Clinical trials are currently under way evaluating localized gene therapy of chronic diabetic foot ulcers treated with replication-incompetent adenoviral vectors that transiently express PDGF. Transient, local gene therapy with adenoviral vectors may provide several advantages over daily, topical treatment with growth factors, including lower cost, better patient compliance, and better response due to a lower physiological level of the growth factor surrounding wound cells.

The wound healing process is very complex and different growth factors emerge at different times in the healing process. In the future, the application of more than one growth factor may be beneficial, with different growth factors being added at different times.

### Adjunctive therapies

An additional option for nonhealing wounds is the use of adjunctive therapies for chronic recalcitrant wounds. Electrical stimulation will activate fibroblasts (↑ DNA, collagen synthesis, ↑ growth factor receptor sites) and stimulate migration of other key cells.[85] There are 25 reports of electrical stimulation use in chronic wounds, including 10 positive outcomes in randomized, controlled trials.

In vitro studies of therapeutic ultrasound have shown the release of chemo-attractant and mitogenic factors from inflammatory cells and enhanced fibroblast proliferation along with increased collagen synthesis. A total of 16 published studies include 12 randomized, controlled trials of which 8 had positive outcomes. Evidence for the VAC (vacuum-assisted closure) system (KCI, Inc.), electromagnetic fields, pneumatic compression, therapeutic heat, hydrotherapy, and laser is less complete.

The VAC has enjoyed an increased popularity in the last few years for chronic wounds. The VAC pump and wound contact sponge remove excess wound fluid, stimulate angiogenesis, increase the rate of granulation tissue, and potentially decrease bacterial colonization. The decrease in local edema may increase regional blood flow and the VAC can prepare the wound bed to increase the take rate of local skin grafts. Several chronic wound care case series have been reported and large multicenter randomized, controlled trials are currently being conducted.

Although adjunctive therapies may provide additional treatment options, translating them into standard clinical practice has been limited by lack of their widespread availability and relatively few standardized conditions and procedures.

## COMMUNICATION AND EDUCATION CHALLENGES IN WOUND BED PREPARATION

Clinical studies have shown that a systematic approach to the management of leg ulcers can reduce both healing time and costs.[86–89] Diagnosis and treatment of the underlying condition are as important, if not more so, than treatment of the ulcer itself. However, much ulcer management—particularly in community nursing—is based on experience rather than research-based knowledge, and research findings are often not implemented in practice.[90,91]

We anticipate that there will be similar obstacles in adopting the principles of wound bed preparation by the wound care community. Although the concept of wound bed preparation can be substantiated with reference to underlying biochemical factors, many different health care professionals are involved in the management of wounds—increasing the difficulty of the education process—and ulcer and wound management receives very little attention in training curricula.

### Education on the management of ulcers

In the United States, a study of academic deans of US medical schools found that comprehensive coverage of many important topics is impossible because of the limited duration of undergraduate medical courses.[92] Seventy percent of the 143 deans approached responded to a survey and the most significant barrier to change in the curriculum was thought to be an "already overcrowded curriculum." The case for adding new material is determined by the importance attached to the topic by teaching staff.[93] Teaching on subjects such as pressure ulcers may vary between courses leading to the same professional qualification, and may not even be included if teachers do not consider the topic to be of sufficient importance.[94]

One study of UK medical school curricula about the care and prevention of chronic wounds found that teaching time ranged from 0 to 3.5 hours per week, with 6 hours per term being the average.[95]

A survey in the United Kingdom[94] examined the provision of education on the prevention of pressure ulcers within radiography courses. Radiography environments are a potential cause of pressure ulcers. Twenty-four

institutions in the United Kingdom provide radiography courses and 23 of their course prospectuses were examined. There was no mention of any information about the prevention or management of pressure ulcers.

Fourteen of the 24 also replied to a questionnaire survey. Nine of the 14 provided classroom teaching on pressure ulcers, four did not provide any teaching, and one was unsure. Of the nine who provided teaching, eight provided teaching in the first year: four provided less than 1 hour, three provided 1 hour, and one provided more than 2 hours. The ninth respondent provided 2 hours in year 2. Two of the institutions that provided less than 1 hour of teaching in the first year provided additional material in the following years. The teaching time allocated is not very great and unless the care concepts are revisited in later years, the importance of general care may be overlooked in favor of technical aspects of radiography.[94]

### Responsibility for the management of ulcers and chronic wounds

The care and management of pressure ulcers has for many years been seen as a nursing responsibility.[97] In radiography, references to pressure ulcers in radiography texts support this view.[98] The prevention of pressure ulcers and the management of people with them is multidisciplinary but in many places it is still considered to be a nursing problem. All of the teaching in the radiography courses is provided by radiographers rather than nurse specialists, however.

There is little published material on wound management in the developed world, but some information is available for the United States, Canada, United Kingdom, France, and Australia.

A curriculum in competencies on pressure ulcer prevention and treatment is available through the National Pressure Ulcer Advisory Panel (www.npuap.org). One of the accrediting organizations for nursing programs in the US—the American Association of Colleges of Nursing (AACN)—has competencies which include wound care. Depending on the textbooks that a student nurse is assigned, she could read as little as 40 lines of text on wound management.[99]

### Wound management in Canada

The treatment of chronic wounds in Canada has shifted from acute and chronic hospital or institutional care to home care. In two surveys of Peel region home care, open wounds represented 32–38% of all clients. Management of chronic wounds is shared among many health care professionals: family doctors, dermatologists, plastic surgeons, infectious disease specialists, and diabetologists take part in interdisciplinary wound clinics. Nursing expertise may come from enterostomal therapists, clinical nurse specialists, home care registered nurses, or registered practical nurses.

The concept of an organized approach to local wound care was first discussed by Krasner and Sibbald in Nursing Clinics of North America (1999)[100] and developed as wound bed preparation in early 2000 at a strategic retreat and at the Symposium on Advanced Wound Care. The template for the Canadian Association of Wound Care was published in Ostomy Wound Management in November 2000[44] and can be found in the website http://www.cawc.net. This template is currently undergoing revision and will be updated in 2003.

### Wound management in the United Kingdom

In a 1998 survey, Hickie and colleagues found that general practitioners (GPs) see significantly fewer leg ulcer patients than either district nurses (DNs) or practice nurses (PNs).[101] DNs and to a lesser extent PNs are the principal health care professionals involved in the care of leg ulcers. GPs and PNs tended to carry out a joint assessment, while DNs tend to make their own initial assessment. Regarding the choice of dressing or treatment, DNs were more likely to work independently, with 52 (64%) stating that they were responsible.

The progress of the wound was monitored by measurement of the lesion (93%) and the amount of exudate (70%). The level of pain was less important than these two factors.

In the same survey, the authors found that protocols for leg ulcer management were unusual, with only 12 DNs (15%) and 12 PNs (15%) reporting that their practice used one. The choice of treatment would be based on a number of factors, the most common being: presence of infection (99%), type of ulcer (97%), and previous treatment (88%). The availability of dressings was also a factor in some cases (44%), and frequency of visits to change were important to PNs (71%). DNs were more likely to prescribe dressings and treatments individually for the patient, while PNs would be more likely to use a dressing that was in stock.

Hickie et al. believe that their results are likely to present an optimistic view of the quality of care in the United Kingdom on the basis that the results returned in their survey originate from groups with an interest in leg ulcer management.

### Wound management in France

There are no wound care centers in France.[102] Reimbursement is usually available for nursing time and wound dressings but not for growth factors and skin substitutes.

Most pressure ulcers (49%) are treated by primary care physicians or geriatricians in the acute care setting. Thirty percent are treated in nursing homes, and 21% at home, with most venous leg ulcers (60%) treated in the home.

A survey of nurses at the Civil Hospital of Colmar[103] on the management of chronic wounds found that 58% of nurses carried out the care after medical consultation, 31% did so without medical advice, and 11% carried out the care in collaboration with a doctor. In France, 70% of wounds are treated with conventional dressings and only 30% with modern dressings (30% of these are hydrocolloids).[104]

In France, nurses are legally authorized to use sharp debridement for venous ulcers but not pressure ulcers. Autolytic debridement is the most common form of nonsurgical debridement used.[102]

The survey by Couilliet et al.[103] found that only 5% and 14%, respectively, of the nurses knew all the classical clinical characteristics of venous and arterial leg ulcers. Important risk factors for pressure sores were not well known and only 15% of nurses regularly used an evaluation scale of risk. In this survey, 82% of the nurses thought that the use of antiseptics was more important than compression in the treatment of venous leg ulcers. Knowledge of new dressings was inadequate.

### *Wound management in Australia*

A survey of current practice carried out in Australia for the prevention and management of pressure ulcers[105] found a variety of approaches in common use. There was a range of inconsistencies across the various nursing domains with regard to risk assessment, prevention, and treatment of ulcers. Most nurses seemed to be familiar with modern wound dressings (e.g., hydrocolloids, foams, alginates) but often did not use them in appropriate circumstances. Overall, the authors report, there is an absence of guidelines and a coordinated approach with the result that current practice is diverse, inconsistent, and sometimes outdated.

### *Other European countries*

The situation in other European countries is similar to that in France and the UK but is not as well researched or documented. Information about wound management in Italy and Germany is based on experience supplied by specialists working in these countries.

In Italy there are a number of different specialists involved in chronic woundcare. However, the majority are split between geriatricians (approx 30%) and vascular surgeons (approx 30%). Dermatology is not a speciality within chronic woundcare but at least 50% of dermatologists have to deal with woundcare issues. GPs are in charge of patient treatment and are becoming more aware of wound management issues. On the other hand, complete reimbursement is only available to patients with pressure ulcers.

Educational courses for doctors and nurses have recently become more available, and there are a number of courses for nursing schools in Italy. However, academic educational programs are not so well developed.

In Germany more than 95% of patients are currently treated by non-specialist medical staff who have little understanding about wound bed preparation or similar wound management approaches. Insurers seldom provide reimbursement for new woundcare products or treatments and therefore the field of advanced wound management is limited to specialist centers. These centers tend to be associated with universities from where they derive their funding.

Medical education is limited, with some medical degrees allocating just one hour in total to woundcare, and limited time is allocated in many postgraduate courses for dermatologists or surgeons. Many specialist medical and nursing staff have a great deal of interest in this field but education must catch up with demand in order for wound management to move forward in Germany.

Italy and Germany have a lower percentage of their population aged over 65 than other countries such as the UK and The Netherlands. As a result there appear to be a smaller percentage of patients in long term hospital care with pressure sores.[107]

## CONCLUSION

The conclusion of the wound management experts who attended the meeting in France (June 2002) was that wound bed preparation provided a rational and systematic approach to the management of nonhealing wounds, which could be supported with reference to the underlying cellular environment. However, given the low priority that wound management receives in medical teaching programs and the number of disciplines that are, or can be, involved in chronic wound management, it will be a challenge to communicate these concepts to the wound management community. It is hoped that this document will contribute to informing the medical community about the potential benefits of wound bed preparation as part of a more systematic—and ultimately, more effective—approach to wound management.

## ACKNOWLEDGMENT

We are grateful to Jude Douglass for her assistance in the collation and organization of the content of this supplement.

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