Wound bed preparation: TIME in practice

Wound bed preparation is now a well established concept and the TIME framework has been developed as a practical tool to assist practitioners when assessing and managing patients with wounds. It is important, however, to remember to assess the whole patient; the wound bed preparation 'care cycle' promotes the treatment of the 'whole' patient and not just the 'hole' in the patient. This paper discusses the implementation of the wound bed preparation care cycle and the TIME framework, with a detailed focus on Tissue, Infection, Moisture and wound Edge (TIME).

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KEY WORDS
Wound bed preparation
Tissue
Infection
Moisture
Edge

The concept of wound bed preparation has gained international recognition as a framework that can provide a structured approach to wound management. By definition wound bed preparation is 'the management of a wound in order to accelerate endogenous healing or to facilitate the effectiveness of other therapeutic measures' (Falanga, 2000; Schultz et al, 2003). The concept focuses the clinician on optimising conditions at the wound bed so as to encourage normal endogenous healing. It is an approach that should be considered for all wounds that are not progressing to normal wound healing.

Wound healing is a complex series of events that are interlinked and dependent on one another. Acute wounds usually follow a well-defined process described as:

- Coagulation
- Inflammation
- Cell proliferation and repair of the matrix
- Epithelialisation and remodelling of scar tissue.

In the past this model of healing has been applied to chronic wounds, but it is now known that chronic wound healing is different from acute wound healing. Chronic wounds become 'stuck' in the inflammatory and proliferative stages of healing (Ennis and Menses, 2000) which delays closure. The epidermis fails to migrate at the wound margins, which interferes with normal cellular migration over the wound bed (Schultz et al, 2003).

In chronic wounds there appears to be an over production of matrix molecules resulting from underlying cellular dysfunction and disregulation (Falanga, 2000). Fibrinogen and fibrin are also common in chronic wounds and it is thought that these and other macromolecules scavenge growth factors and other molecules involved in promoting wound repair (Falanga, 2000). Chronic wound fluid is also biochemically distinct from acute wound fluid; it slows down, and can block the proliferation of cells, which are essential for the wound healing process (Schultz et al, 2003). Wound bed preparation as a concept allows the clinician to focus systematically on all of the critical components of a non-healing wound to identify the cause of the problem, and implement a care programme so as to achieve a stable wound that has healthy granulation tissue and a well vascularised wound bed.

The TIME framework

To assist with implementing the concept of wound bed preparation, the TIME acronym was developed in 2002 by a group of wound care experts, as a practical guide for use when managing patients with wounds (Schultz et al, 2003). The TIME table (*Table 1*) summarises the four main components of wound bed preparation:

- Tissue management
- Control of infection and inflammation
- Moisture imbalance
- Advancement of the epithelial edge of the wound.

The TIME framework is a useful practical tool based on identifying the barriers to healing and implementing a plan of care to remove these barriers and promote wound healing.

It is important to understand wound bed preparation and TIME within the context of total patient care. If a wound fails to heal there is often a complex mix of local and host factors which

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Table I
TIME – Principles of wound bed preparation

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

will need to be assessed and treated. A full and detailed patient assessment will highlight the underlying aetiology of the wound and other factors that may impede wound healing such as pain and poor nutrition (Dealey, 2000). With this in mind the wound bed preparation 'care cycle' was developed in 2004 (Dowsett, 2004) to provide a care programme that includes the TIME framework. It focuses both on the patient and on the wound in an attempt to address all factors that influence wound healing.

Wound bed preparation care cycle

The care cycle (*Figure 1*) starts with the patient and their environment of care. Individual patient concerns need to be addressed as well as quality of life issues in order to achieve a successful care programme. Patients need to understand the underlying cause of their wound and the rationale for treatments. Assessment and treatment of the underlying condition is essential as the type of wound bed preparation implemented may vary with wound type. For example, sharp debridement is common in the management of patients with diabetic foot ulceration, while compression therapy is the recommended treatment for patients with venous leg ulcers (European Wound Management Association, 2004). The cycle moves from patient assessment and diagnosis to assessing and treating the wound using the TIME framework. The importance of assessment in terms of evaluating the effectiveness of the treatment is highlighted in the cycle. Those patients who have healed come out of the cycle into a 'prevention programme' and patients who have not progressed to healing or who have palliative wounds remain in the cycle and are reassessed, using TIME.

The TIME table has been designed to help the clinician make a systematic interpretation of the observable characteristics of a wound and to decide on the most appropriate intervention:

T — for tissue: non-viable or deficient
I — for infection/inflammation
M — for moisture imbalance
E — for edge, which is not advancing or undermining.

T — Tissue

The specific characteristics of the tissue within a wound bed play a very important role in the wound healing continuum. Accurate description of this tissue is an important feature of wound assessment. Where tissue is non-viable or deficient, wound healing is delayed. It also provides a focus for infection, prolongs the inflammatory response, mechanically obstructs contraction

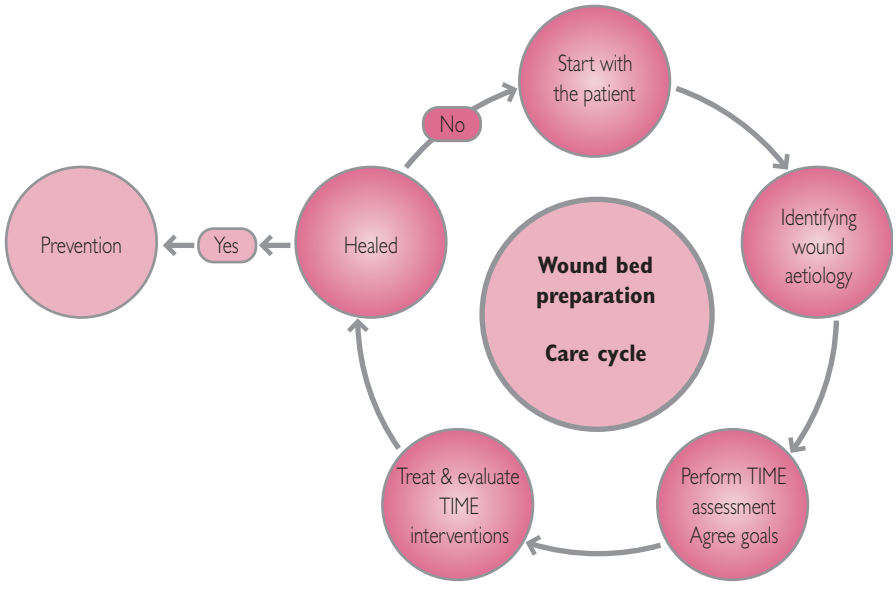

Figure 1. The wound bed preparation care cycle.

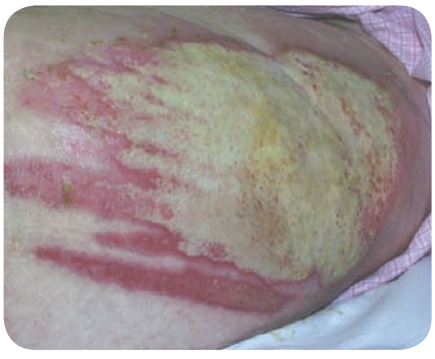

Figure 2. Fixed yellow slough on a wound bed.

and impedes re-epithelialisation (Baharestani, 1999). Necrosis, eschar, and slough are terms that describe non-viable tissue, however, little is known about their constituents.

Work undertaken by Thomas et al (1999) found that devitalised tissue has a defined structure similar to human dermis, however, there are areas of scattered, degraded or disrupted tissue present. For epidermal cells to migrate across a wound surface a well built extracellular matrix is required. Therefore, early interventions to remove devitalised tissue are an essential part of wound management.

Necrosis or eschar on a wound is usually identified through its black/dark grey appearance and, when dried out, is tough and leathery to touch. Wound eschar is full thickness, dry, devitalised tissue that has arisen through prolonged local ischaemia (Gray et al, 2005). It is derived from granulation tissue after the death of fibroblasts and endothelial cells and may also contain inflammatory cells (Thomas et al, 1999) which increases the risk of chronic inflammation of the wound and delays extracellular matrix formation. Necrotic tissue acts as a physical barrier to epidermal cell migration, and hydration at the wound interface is significantly reduced.

Slough is adherent fibrous material derived from proteins, fibrin and fibrinogen (Tong, 1999). It is usually creamy yellow in appearance and can be found dehydrated and adhered to the wound bed (*Figure 2*) or loose and stringy when associated with increased wound moisture.

The presence of devitalised tissue in a wound is often a challenge to health care professionals. It is difficult to accurately assess the depth of a wound that is covered or filled with necrotic or sloughy tissue and, until removed, the true extent of the wound may not be realised. In the majority of clinical cases there is a need to remove the devitalised tissue through a process of debridement, however, it is important to assess the blood flow to the affected area first, particularly if the wound is on the lower leg or foot. In cases where the limb requires revascularisation, it may not be appropriate to undertake tissue debridement until the viability of the limb is determined.

Debridement

Debridement is the process of removing devitalised tissue and/or foreign material from a wound and it may occur naturally. However, in some cases the patient may have an underlying pathology which affects the ability of the body to naturally debride the wound. In a chronic wound, debridement is often required more than once as the healing process can stop or slow down allowing further devitalised tissue to develop. Where debridement is an option for clinicians the following methods may be used:

- Surgical
- Sharp
- Autolytic
- Enzymatic
- Larval
- Mechanical.

Surgical and sharp debridement

Surgical and sharp debridement are the fastest methods of removing devitalised tissue and have the benefit of converting a non-healing chronic wound to that of an acute wound within a chronic wound environment (Schultz et al, 2003) Surgical debridement is normally performed where there is a large extent of devitalised tissue present and where there are significant infection risks.

Sharp debridement is more conservative, but it still requires the skills of an experienced practitioner. Clinical competencies such as knowledge of anatomy, identification of viable or non-viable tissue, ability and resources to manage complications such as bleeding and the skills to obtain patient consent are all essential before undertaking this procedure.

Autolytic debridement

Autolytic debridement is a highly selective process involving macrophage and endogenous proteolytic enzymes which liquefy and separate necrotic tissue and eschar from healthy tissue (Schultz et al, 2003) The natural process is further enhanced by the use of occlusive and semi-occlusive dressings and those which interact to create a moist environment. Phagocytic activity is enhanced and increasing the moisture at the wound interface promotes tissue granulation.

Enzymatic degradation

Enzymatic debridement is a less common method of debridement, however, it is effective in the removal of hard necrotic eschar where surgical debridement is not an option. Exogenous enzymes are applied to the wound bed where they combine with the endogenous enzymes in the wound to break down the devitalised tissue. (Schultz et al, 2005).

Larval therapy

Larval therapy is a quick, efficient method of removing slough and debris from a wound, however, not all patients or staff find this debridement method socially acceptable. Sterile larvae secrete powerful enzymes to break down devitalised tissue without destroying healthy granulation tissue (Thomas et al, 1998).

Mechanical debridement

Mechanical methods of debridement such as irrigation and wet to dry dressings are rarely used as they can cause increased pain and can damage newly formed granulation tissue (NICE, 2001).

If debridement is effective, the T of TIME is removed and wounds can progress through the remaining phases of wound healing.

I — infection/inflammation

Infection in a wound causes pain and discomfort for the patient, delayed wound healing, and can be life threatening. Clinical infections as well as having serious consequences for the patient can add to the overall cost of care. All wounds contain bacteria at levels ranging from contamination, through critical colonisation (also known as increased bacterial burden or occult infection), to infection. The increased bacterial burden may be confined to the superficial wound bed or may be present in the deep compartment and surrounding tissue of the wound margins. Several systemic and local factors increase the risk of infection (*Table 2*). Emphasis is often placed on the bacterial burden, but in fact host resistance is often the critical factor in determining whether infection will occur. Host resistance is lowered by poor tissue perfusion, poor nutrition, local oedema and other behavioural factors such as smoking and drinking excess alcohol. Other systemic factors that impair healing include co-morbidities and medication such as steroid therapy and immunosuppressive drugs. Local factors at the wound bed, such as necrotic tissue and foreign material such as fragments of gauze and dressings, also affect healing and the risk of infection.

Table 2.
Risk factors for infection in chronic wounds

Local factors	Systemic factors
Large wound area	Vascular disease
Deep wound	Oedema
High degree of chronicity	Malnutrition
Anatomic location, e.g. anal region	Diabetes mellitus/rheumatoid arthritis
Presence of necrotic tissue	Smoking/alcoholism
High degree of contamination	Previous surgery or radiotherapy
Reduced tissue perfusion	Use of corticosteroids/immunosuppressants

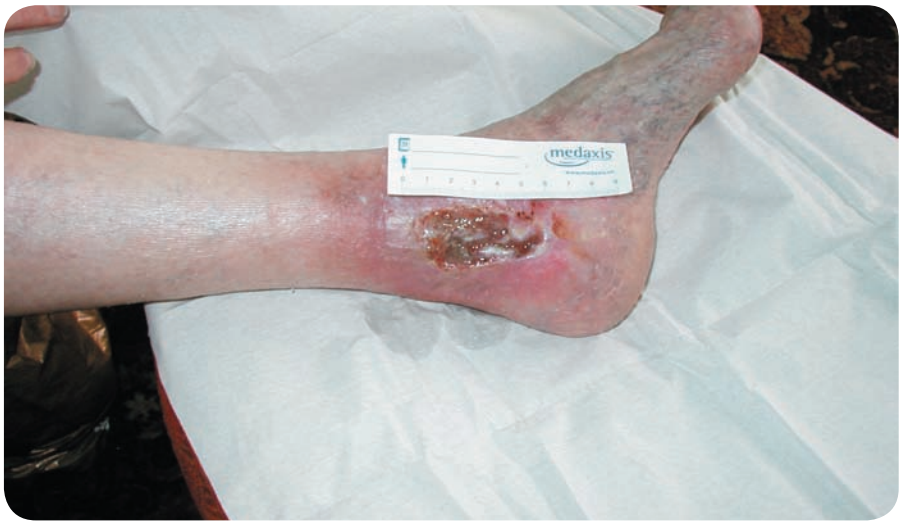

Figure 3. Clinically infected wound.

When a wound is infected (*Figure 3*) it contains replicating micro-organisms which elicit a host response and cause injury to the host. In an acute wound, infection is met by a rapid inflammatory response which is initiated by complement fixation and an innate immune response followed by the release of cytokines and growth factors (Dow et al, 1999). The inflammatory cascade produces vasodilation and a significant increase of blood flow to

Table 3
Differentiating between superficial and deep infection

Superficial infection	Deep infection
Non-healing	Pain: other than usually reported
Friable granulation tissue	Increased size
Exuberant bright granulation tissue	Warmth
Increased exudate	Erythema > 1–2cm
New areas of necrosis in base	Probes to bone or bone exposed
Wound breakdown	
Odour	

(Sibbald et al, 2000)

the injured area. This also facilitates the removal of micro-organisms, foreign bodies, bacterial toxins and enzymes by phagocytic cells, complements, and antibodies. The coagulation cascade is activated isolating the site of infection in a gel matrix to protect the host (Dow et al, 1999). In a chronic wound, however, the continuous presence of virulent micro-organisms leads to a continued inflammatory response which eventually contributes to host injury. There is persistent production of inflammatory mediators and steady migration of neutrophils which release cytolytic enzymes and oxygen-free radicals. There is localised thrombosis and the release of vasoconstricting metabolites which can lead to tissue hypoxia, bringing further bacterial proliferation and tissue destruction (Sibbald et al, 2003).

The presence of bacteria in a chronic wound does not necessarily indicate that infection has occurred or that it will lead to impaired wound healing (Cooper and Lawrence, 1996). Micro-organisms are present in all chronic wounds and low levels of certain bacteria can facilitate wound healing as they produce enzymes such as hyaluronidase which contributes to wound debridement and stimulates neutrophils to release proteases (Stone, 1980).

Diagnosis of infection is primarily a clinical skill and microbiological data should be used to supplement the clinical diagnosis. The classic signs of infection in acute wounds include:

- Pain
- Erythema
- Oedema
- Purulent discharge
- Increased heat.

For chronic wounds it has been suggested that other signs should be added:

- Delayed healing
- Increased exudates
- Bright red discolouration of granulation tissue
- Friable and exuberant tissue
- New areas of slough
- Undermining
- Malodour and wound breakdown (Cutting and Harding, 1994).

These criteria have now been modified according to wound type (Cutting et al, 2005) and are the subject of a position paper (EWMA, 2005). In this document, Cutting et al describe the results of a Delphi approach as a method of developing consensus on the criteria for identification of wound infection. The results of the study indicated that cellulities, malodour, pain, delayed healing or deterioration in the wound/wound breakdown are criteria common to all wounds, but other changes should be noted in different wound types. The Delphi process identified the criteria for six different wound types and should be used as a guide when diagnosing infection in both acute and chronic wounds.

Sibbald et al (2000) suggest that diagnosis should differentiate between superficial and deep infection as outlined in *Table 3*.

Treatment of infection should first of all focus on optimising host resistance by promoting healthy eating, encouraging smoking cessation and addressing underlying medical conditions such as diabetes. Systemic antibiotics are not necessarily the most appropriate way of reducing bacterial burden in wounds, particularly because of the threat of increasing bacterial resistance and should only be used where there is evidence of deep infection or where infection cannot be managed with local therapy (Schultz et al, 2003). Local methods include: debridement to remove devitalised tissue; wound cleansing; and the use of topical antimicrobials such as iodine dressings and silver.

There is renewed interest in the selective use of topical antimicrobials as bacteria become more resistant to antibiotics. Studies show that some iodine and silver preparations have bactericidal effects even against multi-resistant organisms such as methicillin-resistant *Staphylococcus aureus* (MRSA) (Landsdown, 2002; Romanelli et al, 2003; Sibbald et al, 2003). Where infection in the wound has extended beyond the level that can be managed with local therapy, systemic antibiotics should be used. Systemic signs of infection, such as fever, and cellulities extending at least 1cm beyond the wound margin and underlying deep structures, will require systemic antibiotic therapy (Schultz et al, 2003).

M — moisture imbalance

Creating a moisture balance at the wound interface is essential if wound healing is to be achieved. Exudate is produced as part of the body's response to tissue damage and the amount of exudate produced is dependant upon the pressure gradient within the tissues (Trudgian, 2005). A wound which progresses through the normal wound healing cycle produces enough moisture to promote cell

Table 4
Exudate types

Description of exudate	Components of exudate
Serous	Clear and watery. Bacteria may be present
Fibrinous	Cloudy. Contains fibrin protein strands
Purulent	Milky. Contains infective bacteria and inflammatory cells
Haemopurulent	As above but dermal capillary damage leads to the presence of red cells
Haemorrhagic	Red blood cells are a major component of the exudate

(Vowden and Vowden, 2004)

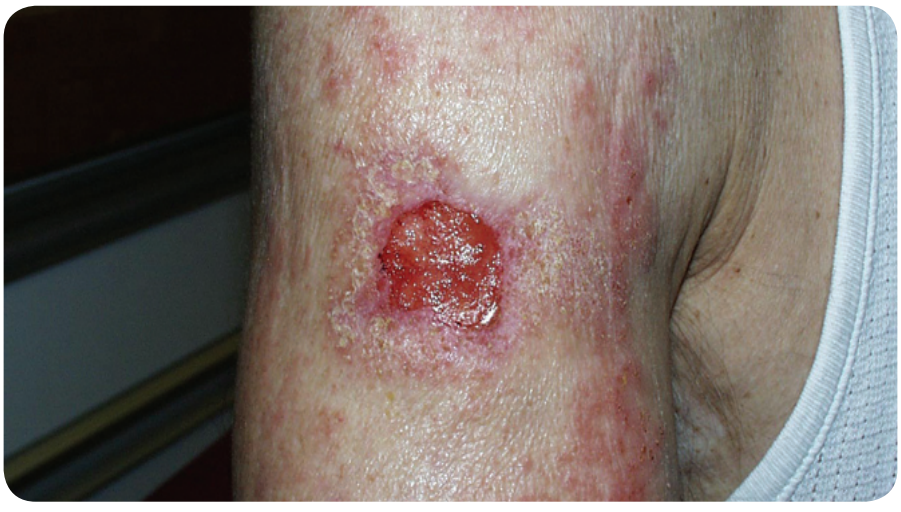

Figure 4. Evidence of irritant dermatitis following dressing application.

proliferation and supports the removal of devitalised tissue through autolysis. If, however, the wound becomes inflamed and/or stuck in the inflammatory phase of healing, exudate production increases as the blood vessels dilate.

A description of the types of exudates can be found in *Table 4*.

Evidence suggests that there are significant differences between acute and chronic wound fluid (Park et al, 1998). Acute wound fluid supports the stimulation of fibroblasts and the production of endothelial cells as it is rich in leukocytes and essential nutrients. Chronic wound fluid, however, has been found to contain high levels of proteases which have an adverse effect on wound healing by slowing down or blocking cell proliferation (Schultz et al, 2003) in particular keratinocytes, fibroblasts and endothelial cells. Increased levels of proteolytic enzymes and reduced growth factor activity all contribute to a poorly developed extracellular wound matrix. This in turn affects the ability of the epidermal cells to migrate across the surface of the wound to complete the healing process.

Factors such as the underlying condition of the patient, the pathology of the wound and the dressing selection all affect the production of exudate (White, 2001). Moisture in a wound enhances the natural autolytic process and also acts as a transport medium for essential growth factors during epithelialisation. If a wound bed becomes too dry, however, a scab will form which then impedes healing and wound contraction. The underlying collagen matrix and the surrounding tissue at the wound edge become desiccated (Dowsett and Ayello, 2004). If a wound produces excessive amounts of exudate the wound bed becomes saturated and moisture leaks out onto the peri-wound skin causing maceration and excoriation. This in turn could lead to an increased risk of infection.

Exudate assessment

Assessment of the exudate is an important part of wound management. The type, amount and viscosity of the exudate should be recorded and dressings selected based on the exudate's characteristics. If a wound is too dry, rehydration should be the principle of management, unless contraindicated as in the case of ischaemic disease. Occlusive dressing products promote a moist environment at the wound interface. As wounds heal, the level of exudate gradually decreases. The management of excess exudate in chronic wounds, however, presents a challenge to many health care professionals. Vowden and Vowden (2004) suggest that an understanding of the systemic and local conditions influencing exudate production and knowledge of the potential damaging chemical constituents of exudates should inform management strategy.

Dressing selection

When selecting a dressing, consideration should be given to the volume of exudate and the viscosity as some dressings absorb a higher volume of fluid than others and some are more efficient when dealing with viscous exudate. There are a variety of dressing products available for the management of exudates ranging from foams, hydrocolloids, alginates, hydrofibres, cadexomer iodine to capillary action dressings. All play a role in the removal of fluid away from the wound surface, however, many of the products, through their ability to gel on contact with wound exudates, maintain a moisture balance on the wound surface itself.

VAC therapy or total negative pressure is a therapy which draws exudates from the wound bed through application of sub-atmospheric pressure via an electronic pump (Mendez-Eastman, 2001). Compression bandages also play a role in the removal of excess

fluid in the lower limbs in patients with venous leg ulcers and lymphoedema. The condition of the surrounding skin is also important as vulnerable skin can react to excess exudate and cause maceration, excoriation, and irritant dermatitis (*Figure 4*). Early application of a protective skin barrier film can minimise these risks. It is important to remember to treat the underlying clinical condition when addressing moisture imbalance in a wound (Newton and Cameron, 2003).

E — edge

When the epidermal margins of a wound fail to migrate across the wound bed or the wound edges fail to contract and reduce in size, consideration needs to have been given to the T,I, and M first to ensure that all aspects of wound bed preparation have been considered. The final stage of wound healing is epithelialisation, which is the active division, migration, and maturation of epidermal cells from the wound margin across the open wound (Dodds and Haynes, 2004).

There are many factors which need to be present in order for epithelialisation to take place. The wound bed must be full of well vascularised granulation tissue in order for the proliferating epidermal cells to migrate. This also ensures that there is adequate oxygen and nutrients to support epidermal regeneration. There needs to be a rich source of viable epidermal cells which can undergo repeated cell division particularly at the edge of the wound. Where cells have become senescent the process slows down or stops completely. Wounds that have a significant number of fibroblasts that are arrested due to senescence, damaged DNA or enduring quiescence do not heal (Vande Berg and Robson, 2003). Other factors, such as bacteria or the presence of devitalised tissue, which interfere with epidermal cell growth, have the potential to influence the rate of wound healing.

There are many reasons why the epidermal margin fails to migrate including hypoxia, infection, desiccation, dressing trauma, hyperkeratosis and callus at the wound margin (Moffatt et al, 2004). For wound healing to be effective, there needs to be adequate tissue oxygenation. Decreased oxygen levels impair the ability of the leucocytes to kill bacteria, lower production of collagen and reduce epithelialisation (Schultz et al, 2003). It is important to remember that wounds rely on both macro- and microcirculation particularly in the lower limb.

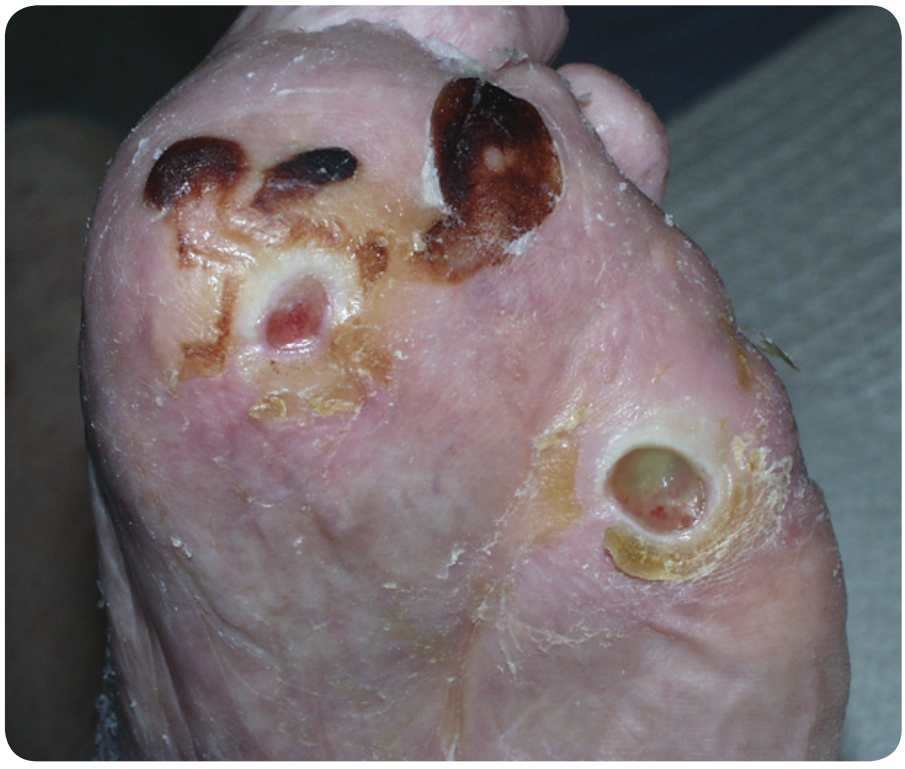

Figure 5. Diabetic foot ulcer.

A baseline assessment needs to be undertaken to determine the degree of ischaemic disease and the ability of the wound to heal without vascular intervention. Wound infection as discussed previously is extremely destructive to a healing wound. Inflammation caused by bacteria causes the extracellular matrix to degrade and therefore epidermal cell migration is interrupted. Wounds become chronic and fail to heal. Dressing products, particularly if adhered or made of fibrous materials, also cause trauma and inflammation of the wound bed which in turn delays healing. It is important to select dressing products which are non adherent, and will not dry out or leave fibres in the wound bed.

In certain clinical conditions such as in diabetic neuropathy, there is an over production of hyperkeratosis and callus formation (*Figure 5)*. It has also been noted that the epidermis of the skin surrounding venous leg ulcers is thicker than normal skin and highly keratinised (Schultz et al, 2005). If this proliferative, thickened tissue is not removed, wounds will fail to epithelialise. Failure of a wound edge to migrate is also thought to be associated with the inhibition of the process of normal programmed cell death (apoptosis) which particularly affects fibrobasts and keratinocytes. Cells undergo a characteristic series of changes following mechanical damage to the cell and on exposure to toxic chemicals. Cells become unresponsive and die.

Undermining or rolling of a wound edge can also influence the ability of the wound to heal. Undermining can be indicative of a chronic wound and in particular, those wounds that are

also critically colonised with bacteria or infected. Rolled edges can present in wounds that have an inflammatory origin such as pyoderma gangenosum or in malignancy. Early diagnosis is important in these cases as failure to provide the appropriate second-line therapy such as oral steroids or tissue biopsy and excision can result in poor healing outcomes.

Measuring a wound at the start of treatment is seen as best practice to enable accurate assessment of the impact of a clinician's intervention. Subsequent measuring can identify whether or not a wound is failing to heal or deteriorating. The edge of the wound will not epithelialise unless the wound bed is well prepared. Always consider the elements of T, I, and M first to ensure that the use of advanced therapies are appropriate and if used are applied to a well prepared wound bed to ensure optimal effect.

Summary and conclusion

The management of chronic wounds has progressed from merely assessing the status of the wound to understanding the underlying molecular and cellular abnormalities that prevent the wound from healing. The concept of wound bed preparation has simultaneously evolved to provide a systematic approach to removing the barriers to natural healing and enhancing the effects of advanced therapies. Wound bed preparation and the TIME framework are most likely to be successful when used alongside the wound bed preparation care cycle.

Key Points

- The TIME framework has been developed as a practical tool for managing patients with wounds.
- The wound bed preparation 'care cycle' focuses care on the patient and their underlying condition.
- Patient progress and response to treatment should be regularly evaluated.

References

Baharestani M (1999) The clinical relevance of debridement. In: Baharestani M et al, eds. *The Clinical Relevance of Debridement.* Springer-Verlag, Berlin

Cooper RA, Lawrence JC (1996) Micro-organisms and wounds. *J Wound Care* **5(5):** 233–6

Cutting KF, Harding KG (1994) Criteria for identifying wound infection. *J Wound Care* **3:** 198–201

Cutting K, Tong A (2003) *Wound Physiology and Moist Wound healing.* Medical Communications Ltd, Holsworthy

Dealey C (2000) *The Care of Wounds.* Blackwell Science, Oxford

Dodds S, Haynes S (2004) The wound edge, epithelialisation and monitoring wound healing. A journey through TIME. Wound bed preparation in practice. *Br J Nurs Supplement*

Dow G, Browne A, Sibbald RG (1999) Infection in chronic wounds: controversies in diagnosis and treatment. *Ostomy Wound Manag* **45:** 23–40

Dowsett C, Ayello E (2004) TIME principles of chronic wound bed preparation and treatment. *Br J Nurs* **13(Suppl 15):** S16–S23

Dowsett C (2004) TIME in Context. The Wound Bed Preparation 'Care Cycle'. Oral presentation at Wounds UK 2004, Harrogate, UK

Ennis WJ, Menses P (2000) Wound healing at the local level: the stunned wound. *Ostomy Wound Manag* **46:** 39S–48S

European Wound Management Association (2004) Position Document: *Wound Bed Preparation in Practice.* MEP Ltd, London

European Wound Management Association (2005) Position Document: *Identifying Criteria for Wound Infection.* MEP Ltd, London

Falanga V (2000) Classifications for wound bed preparation and stimulation of chronic wounds. *Wound Repair Regen* **8:** 347–52

Falanga V (2002) Wound bed preparation and the role of enzymes: a case for multiple actions of therapeutic agents. *Wounds* **4(2):** 47–57

Gray D, White R, Cooper P, Kingsley A (2005) Using the wound healing continuum to identify treatment objectives. Applied Wound Management supplement. Part 2. *Wounds UK* **1(2):** S9–S14

Lansdown AB (2002) Silver: Its antibacterial properties and mechanism of action. *J Wound Care* **11(4):** 125–30

Mendez-Eastman S (2001) Guidelines for using negative pressure wound therapy. *Adv Skin Wound Care* **14(6):** 314–22

Moffatt C, Morison MJ, Pina E (2004) Wound bed preparation for Venous Ulcers. In: Wound Bed Preparation in Practice. EWMA Position Document, MEP, London

National Institute for Clinical Excellence (2001) *Guidance of the Use of Debriding Agents and Specialist Wound Care Clinics for Difficult to Heal Surgical Wounds.* NICE, London

Newton H, Cameron J (2003) *Skin Care in Wound Management.* Medical Communications Ltd. Holsworthy, UK

Park HY, Shon K, Phillips T (1998) The effect of heat on the inhibitory effects of chronic wound fluid on fibroblasts in vitro. *Wounds* **10:** 189–92

Romanelli M, Magliaro A, Mastronicola D, Siani S, et al (2003) Systemic antimicrobial therapies for pressure ulcers. *Ostomy Wound management* **49(5a Suppl):** 25–9

Schultz G, Sibbald G, Falanga V, et al (2003) Wound bed preparation: a systematic approach to wound management. *Wound Repair Regen* **11:** 1–28

Schultz G, Ladwig G, Wysocki A (2005) Extracellular matrix: review of its role in acute and chronic wounds. World Wide Wounds. www.worldwidewounds.com

Sibbald RG, Williamson D, Orsted HL, et al (2000) Preparing the wound bed: debridement, bacterial balance and moisture balance. *Ostomy Wound Manag* **46:** 14–35

Sibbald RG, Orsted HL, Schultz G, Coutts RN, Keast MD (2003) Preparing the wound bed: focus on infection and inflammation. *Ostomy Wound Manag* **47:** 38–43

Stone LL (1980) Bacterial debridement of the burn eschar: the in vivo activity of selected organisms. *J Surg Res* **29:** 83–92

Thomas AML, Harding KG, Moore K (1999) The structure and composition of chronic wound eschar. *J Wound Care* **8(6):** 285–7

Tong A (1999) The identification and treatment of slough. *J Wound Care* **8(7):** 338–9

Trudgian J (2005) Exudate management and wound bed preparation: taking the moist approach. *Wounds UK* **1(suppl 2):** 10–15

Vande Berg JS, Robson MC (2003) Arresting cell cycles and the effect on wound healing. *Surg Clin North America* **83(3):** 509–20

Vowden K, Vowden P (2004) Understanding exudates management and the role of exudates in the healing process. The Exudate Supplement ,Part Two. Br J Nurs

White R (2001) Managing exudates. Part 1. *Nursing Times* **97(9):** XI–XIII