

Moist wound healing: a review of evidence, application and outcome

Debbie Sharman

ARTICLE POINTS

1 Moist wound therapy has been accepted as a major advance in the treatment of chronic wounds since the 1960s.

2 Chronic wounds do not heal in an orderly and timely fashion, and abnormal wound healing is well recognised in people with diabetes.

3 Hundreds of dressings that help to create a moist wound environment for healing of chronic wounds are currently available. They are an important, but not sole factor, to consider in wound management.

4 There is a need for more evidence-based medicine to encourage best practice management of the diabetic foot; randomised controlled trials are needed to complement consensual experience.

KEY WORDS

- Moist wound healing
- Diabetic foot ulcers
- Evidence-based medicine
- Infection control
- Vascular deficiencies

Debbie Sharman is a Deputy Podiatry Manager and Head of Specialist Podiatry Services at Bournemouth Teaching Primary Care Trust.

Introduction

Over the last 40 years, the moist wound therapy concept has been a major advance in wound treatment. Chronic wounds such as diabetic foot ulcers pose particular treatment challenges, and a moist wound healing environment can contribute significantly to meeting this challenge. Reduced healing times for diabetic foot ulcers lower the cost of management and the risk of further complications such as amputation. This article explores some of the theories surrounding the altered mechanism of healing in people with diabetes. Existing and new dressings that provide a moist wound environment, factors to consider when selecting an appropriate dressing for diabetic foot wounds, and the importance of evidence-based medicine in the management of the diabetic foot are discussed.

Diabetic foot disease is estimated to affect 15% of all people with diabetes (Mancini and Ruotolo, 1997). A recent study has estimated that the annual cost of diabetic peripheral neuropathy in the UK is around £250 million, and that 76% of all diabetic foot ulcers have a neuropathic element (Gordois et al, 2003). As this cost does not include purely ischaemic ulcers, the true costs of diabetic foot complications are likely to be much higher.

Wound healing in people with diabetes

Abnormal wound healing in people with diabetes is well recognised (Bouter et al, 1993). However, there is very little evidence regarding many aspects of foot care in people with diabetes, including wound healing (Pecoraro et al, 1991). The American Diabetes Association (1991) suggested the following predisposing factors to explain the faulty healing of wounds in people with diabetes:

- Abnormal cellular and/or inflammatory pathways
- Peripheral neuropathy
- Vascular disease and/or tissue hypoxia.

Abnormal cellular function, particularly in fibroblasts and neutrophils, have been found in people with diabetes. In vitro, hyperglycaemia may be toxic to these cellular elements; in vivo, it may result in greater susceptibility to infection. Modest

differences in the cellular function of neutrophils, macrophages, and fibroblasts associated with hyperglycaemia have been postulated, but not conclusively shown in vivo. Advanced glycosylation end-products accumulate in diabetes as a result of hyperglycaemia, leading to the non-enzymatic glycosylation of collagen (McInnes, 2001). This process results in the production of abnormal collagen, which is highly inflexible and prone to breakdown, particularly over pressure areas (Elkes and Wolfe, 1991).

The factor most consistently associated with foot ulcers in people with diabetes is peripheral neuropathy. Trauma during walking may not only create a wound but also keep it in a chronic inflammatory phase. This could explain why foot ulcers in people with diabetes fail to heal and become chronic. *Figure 1* shows a typical presentation of chronic diabetic neuropathic ulceration. Motor neuropathy results in



Figure 1. Neuropathic ulcer showing migration of granulation tissue under moist conditions.

PAGE POINTS

1 Animal studies have shown that the defects that occur in diabetic wound healing may be caused by altered collagen metabolism, resulting in reduced collagen levels and abnormal granulation tissue formation.

2 In addition to physiological predisposing factors, there is evidence that psychological stress adversely affects the immune system, and this could impact on wound healing.

3 Patient compliance should always be considered when ulcers fail to heal within expected timeframes; it may be that the patient is not wearing the recommended footwear or is not resting as advised.

4 Research has shown that moist wound environments are associated with: less intense, less prolonged inflammation; more rapid keratinocyte proliferation and migration; earlier differentiation of keratinocytes to restore cutaneous barrier function; increased fibroblast proliferation, increased collagen synthesis; earlier, less prolonged angiogenesis; and earlier full-thickness wound contraction.

weakness and changes in foot structure, which may contribute to continued tissue injury. Sensory neuropathy impairs the neuro-inflammatory response, while autonomic neuropathy impairs the normal maintenance of skin integrity, vascular tone and the thermoregulatory response, all of which can interfere with normal wound repair.

Disturbances in the inflammatory and proliferation phases of wound healing have been suggested in diabetic wound healing (Loots et al, 1999). During the proliferation phase, the extracellular matrix is remodelled and rebuilt. Fibroblasts are the main producers of this extracellular matrix. Loots et al (1999) examined the proliferation of fibroblasts from diabetic ulcers. They concluded that the diabetic process and the ulcer environment itself cause the fibroblasts to age. Overall functional activity is therefore reduced.

Other studies conducted on animals have shown that the defects that occur in diabetic wound healing may be caused by altered collagen metabolism, resulting in reduced collagen levels and abnormal granulation tissue formation (Spanheimer et al, 1988). Hence, even when the wounds do heal they will tend to have reduced tensile strength (Andreassen and Oxlund, 1987). This is seen clinically, as people with healed diabetic ulcers are more prone to future tissue breakdown over previous ulcer sites.

Other factors for consideration

In addition to physiological predisposing factors, there is evidence that psychological stress adversely affects the immune system, and this could impact on wound healing. Ashford et al (2000) showed that foot complications impact further on the psychological effects of chronic illness than living with diabetes alone.

Patient compliance should always be considered when ulcers fail to heal within expected timeframes. It may be that the patient is not wearing the recommended footwear or is not resting as advised (Close-Tweedie, 2002). Again, this could be linked to the psychological effects of living with a chronic disease (McPherson and Binning, 2002). Such issues should be dealt with sensitively so as not to alienate patients and further reduce compliance.



Figure 2. Necrotic burn in a neuropathic foot caused by a foot spa. Rehydration is required to lift the slough.

The body of evidence clearly suggests that people with diabetes are prone to foot wounds. Once formed these are difficult to heal, owing to a combination of physiological and psychological factors.

Effect of a moist environment on chronic wound healing

Overall, research has shown that moist wound environments are associated with:

- Less intense, less prolonged inflammation (Rovee et al, 1972)
- More rapid keratinocyte proliferation (Madden et al, 1989) and migration (Winter, 1962)
- Earlier differentiation of keratinocytes to restore cutaneous barrier function (Vogt et al, 1995)
- Increased fibroblast proliferation (Katz et al, 1991)
- Increased collagen synthesis (Leipziger et al, 1985)
- Earlier, less prolonged angiogenesis (Lydon et al, 1989)
- Earlier full-thickness wound contraction (Pirone et al, 1990).

However, clinically, some caution should be observed with a moist wound environment, particularly in the management of ischaemic and neuroischaemic foot ulcers. Moist wound dressings (e.g. hydrogels) can be used to soften dry hard eschar, often found on such ulcers. Treatment should be on an individual basis after careful assessment because of the increased risk of spreading infection and increasing pain in those with marked ischaemia (Findlow et al, 2001). *Figure 2* shows how a moist environment can assist in the desloughing of a wound.

PAGE POINTS

1 Health professionals should be aware of the characteristics of an ideal moist wound dressing, and able to differentiate between the dressing categories so that the most appropriate decisions for individual patients regarding topical therapy of chronic wounds can be made.

2 Although a moist wound environment is important in wound healing, excessive moisture can contribute to delayed healing and further breakdown of the skin.

3 The properties of dressings may be altered when on the foot.

4 Recent developments in wound healing include new treatments such as skin substitutes, epidermal grafts dermal replacements, composite grafts, and growth factors.

Dressings for use in moist wound healing

Over the past 30 years, hundreds of dressings that help to create a moist wound environment have been developed. *Table 1* summarises the key categories. Healthcare professionals should be aware of the characteristics of an ideal moist wound dressing, and be able to differentiate between the dressing categories so that the most appropriate decisions regarding topical therapy of chronic wounds can be made for the patient (Seaman, 2002).

Characteristics of an ideal moist wound dressing

Seaman (2002) suggested six properties that an ideal dressing should have:

- Maintains a moist wound environment
- Absorbs excess exudate
- Eliminates dead space
- Does not harm the wound
- Provides thermal insulation
- Provides a bacterial barrier.

Considerable care and attention is needed by the healthcare professional in choosing and applying the most appropriate dressing for a chronic wound.

For example, although a moist wound environment is important in wound healing, excessive moisture can contribute to delayed healing and further breakdown of the skin. Unmanaged exudate can contribute to increased wound bacterial counts, skin maceration, wound odour, and increased cost of care as dressings will need to be changed more frequently (Rolstad et al, 2000). Hence, healthcare professionals need to consider the absorptive capacity of the dressing as well as its moisture vapour transmission rate (MVTR) when a high rate of exudate absorption (the capacity to allow the passage of water vapour through a dressing to the outside environment) is required. Dressings with a high MVTR will allow a greater absorption of exudates (Seaman, 2002). *Figure 3* shows an infected ulcer with a high level of exudate.

Consideration should also be given to the fact that the properties of dressings may be altered when on the foot. Dressings are not designed to take the high and repetitive forces exerted on the sole of the foot when walking (Baker, 1997).

Recent advances in dressings

Many modern dressings provide several of the ideal characteristics of moist wound dressings but few (if any) contain all of them (*Table 1*). Recent developments in wound healing include new treatments such as skin substitutes, epidermal grafts dermal replacements, composite grafts, and growth factors. Composite grafts and growth factors have shown some particularly promising initial results in the treatment of diabetic foot ulcers (Page, 2002).

New developments should be considered, particularly in the management of the diabetic foot where standard treatments may be less effective. One novel approach currently being developed for the management of neuropathic diabetic ulcers and leg ulcers is a non-contact boot-shaped plastic film device (Kerraboot®). In clinical investigations to date, this device has been shown to efficiently absorb excess ulcer exudate, reduce wound malodour and, of greatest importance, maintain a warm, moist environment to optimise the healing process (Leigh et al, 2003). Further studies will be required to validate these initial observations.

Evidence-based medicine

There is now an expectation that working practice should aim to be consistent with evidence-based medicine. When it comes to management of the diabetic foot, randomised controlled trials:

- Are uncommon
- Usually only concern the latest biotechnologies
- Have produced confusing results – for a number of reasons.

Many new innovations are presented in glossy brochures with no objective evidence of efficacy. We all believe that neuropathic



Figure 3 Infected ulcer with high level of exudate, which need absorbing to prevent maceration

Table 1. Types and characteristics of occlusive dressings

Category	Characteristics/compositions	Indications/best uses	Advantages	Disadvantages
Films	<ul style="list-style-type: none"> ● Polyurethane based or co-polyester with adhesive backing 	<ul style="list-style-type: none"> ● Split-skin graft donor sites ● Epithelialising wounds ● Abrasions ● Non-draining, primarily closed wounds 	<ul style="list-style-type: none"> ● Transparent: allows wound inspections ● Retains moisture ● Decreases wound pain at donor sites 	<ul style="list-style-type: none"> ● No absorption – fluid retention may lead to excess fluid collection, hence not ideal for exudative wounds ● Cost ● May adhere to some wounds
Foams	<ul style="list-style-type: none"> ● Usually polyurethane, gel film or silicone coated ● Capable of absorbing large volumes of wound fluid ● Some have film outer surface to resist water and bacteria ● Some adhesive, some non-adhesive 	<ul style="list-style-type: none"> ● Heavily exudating wounds especially during the early inflammatory phase following debridement and sloughing when drainage is at its peak ● Some can be used in deep cavity wounds as packing ● Venous leg ulcers 	<ul style="list-style-type: none"> ● Comfortable and conformable ● Highly absorbent ● Claimed not to stick to wound or harm viable tissue ● No dressing residue in the wound bed ● Debrides wound ● Can absorb under compression stockings and bandages 	<ul style="list-style-type: none"> ● May require a second dressing ● Cost ● Opaque ● Cannot be used on dry wounds
Hydrogels	<ul style="list-style-type: none"> ● Available as sheets and amorphous gels ● Contain 80–90% water ● Cross-linked polymer such as polyvinyl ● All donate water to desiccated tissue; some also absorb ● Soothing effect; easily applied and removed without discomfort to patient 	<ul style="list-style-type: none"> ● Rehydrating eschar and slough for easy removal from wound surface ● Semi-transparent ● Diminishes wound pain ● Creating and maintaining a moist not wet micro-environment for cell migration 	<ul style="list-style-type: none"> ● Good for low to moderate exudative wounds ● Soothing to patient ● Simple application and removal ● Maintains intimate contact with the wound surface ● Creates a moist environment for cell migration 	<ul style="list-style-type: none"> ● Amorphous gels always need a secondary dressing ● Cost ● Cannot handle heavily exudating wounds without leakage ● Need frequent application
Hydro-colloids	<ul style="list-style-type: none"> ● Composed of mixture of adhesive, absorbent and elastomeric ingredients ● Carboxymethylcellulose most common absorptive ingredient ● Some contain pectin ● All have top film layer for waterproofing ● Absorb some wound fluid ● Also available as granules and pastes 	<ul style="list-style-type: none"> ● Granulating and epithelialising wounds that are draining low to moderate amounts of exudate ● Promoting autolytic debridement 	<ul style="list-style-type: none"> ● Waterproof and impermeable to bacteria and environmental contaminants ● Comfortable for easy application and comfort at the wound site ● May be left in place for extended periods ● Debrides wound ● Gel creates moist wound healing 	<ul style="list-style-type: none"> ● Moderate to heavy exudate will overwhelm dressing ● Impermeable to oxygen; use with caution in wounds with suspected or known anaerobic infection ● Some hydrocolloids break down ● May have unpleasant odour upon removal – ‘gel and smell’ phenomenon
Alginates	<ul style="list-style-type: none"> ● Composed of soft non-woven fibres derived from brown seaweed ● Available as wound pads and ropes for packing deep cavity wounds ● Absorb fluid and into a gel ● Keep wound bed moist 	<ul style="list-style-type: none"> ● Wounds with moderate to heavy wound exudate ● Granulating and epithelialising wounds where some exudate is present (e.g. leg ulcers) ● Epithelialising wounds generally very low in exudates so would not be suitable for alginate: risk of damaging new tissue 	<ul style="list-style-type: none"> ● Especially useful for packing exuding wounds (absorbent) ● Rope alginates are easy to apply ● Several alginates have good wet strength and can be removed in one piece ● Enhance granulation 	<ul style="list-style-type: none"> ● Always require a second dressing ● Risk of drying wound bed; not recommended for wounds with low volume exudate – can be painful when removed ● Will not debride hard eschar ● ‘Low-tide’ odour is common

Adapted from Eaglstein et al (2001). Reproduced with permission from Blackwell Science.

PAGE POINTS

1 We all believe that neuropathic ulcers will not heal without pressure relief, but other than consensual experience there is little evidence to support this.

2 We could base treatments on clinical experience obtained from treating many patients, indicating that they are cost-effective and benefit patients in terms of healing efficacy and by their ability to reduce pain, odour and wound leakage.

3 If infection is not controlled, pressure not relieved and vascular deficiencies not addressed, then the choice of dressing will be largely irrelevant.

ulcers will not heal without pressure relief, but other than consensual experience there is little evidence for this (Masson, 1999).

Following the development of new materials and devices to create a moist wound environment, there have been very limited data to support their use, if one requires evidence that they have produced more rapid healing in chronic wounds kept moist than in those kept dry. Perhaps this is a problem with the outcome measure, rather than the materials themselves (Harding et al, 2000).

So where does this leave us? Should we join in the cry for more randomised controlled trials? Perhaps we should question the validity of endpoint studies in wound healing research. We could base treatments on clinical experience obtained from treating many patients, indicating that they are cost-effective and benefit patients in terms of healing efficacy and by their ability to reduce pain, odour and wound leakage.

Conclusion

It must be recognised that dressings are not the 'be all and end all' when it comes to the management of diabetic foot ulceration. All too often, non-healing is attributed to the wrong dressing. We must first address the main barriers to healing, as described earlier. If infection is not controlled, pressure not relieved and vascular deficiencies not addressed, then the choice of dressing will be largely irrelevant. However, once these factors are confronted, then wound management becomes important. ■

American Diabetes Association (1991) Consensus development conference on diabetic foot wound care. *Diabetes Care* **22**: 1354-60

Andreassen TT, Oxlund H (1987) The influence of experimental diabetes and insulin treatments on the biomechanical properties of rat skin incisional wounds. *Acta Chirurgica Scandinavica* **153**: 405-09

Ashford RL, McGee P, Kimmond K (2000) Perception of quality of life by patients with diabetic foot ulcers. *Diabetic Foot* **3**(4):150-5

Baker NR (1997) Foot ulcer management. *Journal of Wound Care* **6**(1): Resource file supplement

Bouter KP, Storm AJ, de Groot RRM et al (1993) The diabetic foot in Dutch hospitals: epidemiological features and clinical outcome. *European Journal of Medicine* **2**: 215-18

Close-Tweedie J (2002) Diabetic foot wounds and wound healing: a review. *Diabetic Foot* **5**(2):68-78

Eaglstein WH (2001) Moist wound healing with occlusive dressings: a clinical focus. *Dermatologic Surgery* **27**: 175-81

Elkes RS, Wolfe JHN (1991) The diabetic foot. *British*

Medical Journal **303**: 1053-5

Findlow AH, Oyibo SO, Knowles A et al (2001) The management of infected neuroischaemic diabetic foot ulcers. *The Diabetic Foot* **4**(3):112-18

Gordois A, Scuffham P, Shearer A, Oglesby A (2003) The healthcare costs of diabetic peripheral neuropathy in the UK. *The Diabetic Foot* **6**(2):62-73

Harding KG, Jones V, Price P (2000) Topical treatment: which dressing to choose. *Diabetes Metabolism Research and Reviews* **16** (Suppl 1): S47-S50

Katz MH, Alvares AF, Kirsner RS et al (1991) Human wound fluid from acute wounds stimulates fibroblast and endothelial cell growth. *Journal of the American Academy of Dermatology* **25**: 1054-8

Leigh RD, Rahaman L, Berkers S et al (2003) Management of neuropathic and neuroischaemic leg and foot ulcers: a preliminary assessment of a novel wound dressing device; the Kerraboot. *Ark Therapeutics*: in press

Leipzig LS, Glushko V, DiBernado B et al (1985) Dermal wound repair: role of collagen matrix implants and synthetic polymer dressings. *Journal of the American Academy of Dermatology* **12**: 409-19

Loots MAM, Lamme EN, Mekkes JR et al (1999) Cultured fibroblasts from chronic diabetic wounds on the lower extremity (non-insulin dependent diabetes mellitus) show disturbed proliferation. *Archives for Dermatological Research* **291**: 93-9

Lydon M, Hutchinson JJ, Rippon et al (1989) Dissolution of wound coagulum and promotion of granulation tissue under DuoDERM. *Wounds* **1**(2): 95-106

Madden M, Nolan E, Finkelstein JL et al (1989) Comparison of an occlusive and a semi-occlusive dressing and the effect of the wound exudate upon keratinocyte proliferation. *Journal of Trauma* **29**(7): 924-30

Masson E (1999) Is foot care evidence based? *The Diabetic Foot* **2**(2):44-6

Mancini L, Ruotolo V (1997) The diabetic foot: epidemiology. *Rays* **22**: 511-23

McInnes A (2001) Guide to the assessment and management of diabetic foot wounds. *The Diabetic Foot* **4**(Suppl 1): S1-II

McPherson MV, Binning J (2002) Chronic foot ulcers associated with diabetes; patients' views. *The Diabetic Foot* **5**(4):198-204

Page JC (2002) Critiquing clinical research of new technologies for diabetic foot wound management. *Journal of Foot and Ankle Surgery* **41**(4): 251-9

Pecoraro RE, Ahroni JH, Bpyko EJ et al (1991) Chronology and extremities of tissue repair in diabetic lower-extremity ulcers. *Diabetes* **40**: 1305-13

Pirone L, Monte K, Shannon R et al (1990) Wound healing under occlusion and non-occlusion in partial-thickness and full-thickness wounds in swine. *Wounds* **2**: 74-81

Rolstad BS, Ovington LG, Harris A (2000) Principles of wound management in acute and chronic wounds. In: Bryant RA (ed). *Nursing Management*, 2nd edn. Mosby, St Louis: 85

Rovee ET, Kurowsky CA, Labun J et al (1972) Effect of local wound environment on epidermal healing. In: Maibach HI, Rovee DT (eds). *Epidermal Wound Healing*. Yearbook Medical Publishers, Chicago: 159-84

Seaman S (2002) Dressing selection in chronic wound management. *Journal of the American Podiatric Medical Association* **92**(1): 24-33

Spanheimer RG, Umpierrez GE, Stumpf V (1988) Decreased collagen production in diabetic rats. *Diabetes* **37**: 371-6

Vogt PM, Andree C, Breuing K et al (1995) Dry, moist, and wet skin wound repair. *Annals of Plastic Surgery* **34**: 493-500

Winter GD (1962) Formation of a scab and the rate of epithelialization of superficial wounds in the skin of the young domestic pig. *Nature* **193**: 293-34