

Evidence in venous ulcer management: a new consensus recommendation

The estimated UK prevalence of venous leg ulceration (VLU) is 0.1–0.3%, increasing with age (Scottish Intercollegiate Guidelines Network [SIGN], 2010). The anticipated annual cost of treating a VLU in the UK has been estimated to be between £1,298 and £1,526 based on 2001 prices (Iglesias et al, 2004), and accounts for 30–50% of home nursing visit resources (Lees and Lambert, 1992; van Hecke et al, 2008). Most VLU treatments are carried out in the outpatient setting, with 50% of ulcers healing within ten weeks. However, some VLUs may take up to ten years to heal, with a 70% recurrence rate. Of those patients hospitalised because of poor or non-healing, most demonstrated recurrence of the ulcer within two months (Reeder et al, 2010).

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KEY WORDS

Hard-to-heal wounds
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Factors involved in clinical outcomes

Hard-to-heal wounds are commonly defined as those that do not heal within the anticipated timeframe or sequence, despite an appropriate treatment (Ballard and Baxter, 2000; Margolis et al, 2004) — for example, a venous leg ulcer (VLU) treated with a moist wound dressing and graduated compression that has not shown any demonstrated healing outcomes within four weeks (van Rijswijk, 1993; Ballard and Baxter, 2000; Phillips et al, 2000). These outcomes are supported by an international study (White, 2011), where practitioners reported that only one-fifth of all

ulcers healed in one month, and only 40–50% healed in three months.

The non-healing or hard-to-heal wound is now a burden — not only to the patient and carer, but also to the wider health system and economy.

The term 'hard-to-heal wounds' is open to interpretation and poses complex challenges to the clinician as, despite their best efforts, wound healing in these cases is either prolonged or never achieved. This is of particular interest in the current environment, where clinicians are under great pressure to justify their actions in terms of clinical outcomes and cost-effectiveness. When examining percentage reduction of the area of venous ulcers, Phillips et al (2000) suggested that, in approximately 77% of cases, healing outcomes could be predicted based on a reduction in wound size by 44% or more at three weeks. In addition, Margolis et al (2004) demonstrated that a simple scoring system, based

on ulcer size and duration, can provide a good indication of the outcomes likely at 24 weeks.

The complexity of the wound has a major impact on healing progression, and can be related directly to five key areas (Vowden et al, 2008):

- ▶▶ Wound-related factors
- ▶▶ Patient-related factors
- ▶▶ Skill and knowledge of healthcare professionals
- ▶▶ Resources and treatment-related factors
- ▶▶ Environmental factors (both primary and secondary).

The non-healing or hard-to-heal wound is now a burden — not only to the patient and carer, but also to the wider health system and economy. The impact on patients and carers is significant and can be seen, for example, in lost employment, ongoing pain and suffering, and a reduced quality of life.

Many clinicians feel that their treatment choices are restricted and that their ability and clinical freedom to choose the dressings

All authors were members of the consensus group
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most appropriate for an individual patient are limited (Bjarnsholt et al, 2008). Even with an increasing knowledge base and newer and more sophisticated treatments, many clinicians who encounter the hard-to-heal wound will rely upon clinical guidelines to scope the assessment regimen, a treatment pathway and a monitoring schedule that allows for a consistent, evidence-based approach across all care settings.

Guidelines for the management of VLUs: a gap analysis

A significant change to the management of VLUs occurred in 1997, when a systematic review demonstrated the benefit of compression therapy in this area (Fletcher et al, 1997). The Royal College of Nursing (RCN) and the Scottish Intercollegiate Guidelines Network (SIGN) published the first guidelines in 1998. Currently, international clinical guidelines describe the assessment and treatment of VLUs, with great attention being paid to vascular assessment — specifically, peripheral perfusion as measured by the ankle brachial pressure index (ABPI). The stratification of care pathways offers practitioners a choice of treatments, with compression bandaging recognised as the gold standard (European Wound Management Association [EWMA], 2003).

In the opinion of the consensus group, the most respected wound management guidelines in the UK have been produced by the National Institute for Health and Clinical Excellence (NICE) (2003), EWMA (2002), the RCN (2006) and, most recently, SIGN (2010).

The consensus group examined the RCN and SIGN guidelines and noted that neither were prescriptive for wound dressings for VLUs. The most recent SIGN guidance states that 'no evidence was identified to support superiority of any dressing type over another when applied under appropriate multilayer bandaging' (SIGN, 2010).

BOX 1

Members of the consensus group

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As a UK-based panel of wound management specialists, the authors are aware that although it is common practice to adapt national guidelines for use at local level, a core population with hard-to-heal wounds may not be receiving optimal wound therapy.

While each document provides excellent guidance as to appropriate compression therapy, there is no definition of hard-to-heal wounds and, furthermore, little or no advice on how to manage them. As such hard-to-heal wounds will, by definition, constitute at least 20% of all VLUs, this lack of guidance must be regarded as a deficiency. The ongoing treatment of hard-to-heal

wounds is a constant challenge to practitioners: survey data show that 80% regularly treat patients with hard-to-heal ulcers, and 74% monitor the wounds on a weekly basis to detect any changes in the wound that may identify delayed healing, thus allowing alternative treatments to be initiated (White, 2011).

As a UK-based panel of wound management specialists, the authors are aware that although it is common practice to adapt national guidelines for use at local level, a core population with hard-to-heal wounds may not be receiving optimal wound therapy. This is supported by the literature review conducted by Rippon et al (2007), which showed that even after two years of 'standard of care' treatment (that is, high compression bandaging), approximately 20% of VLUs were still unhealed.

The challenge for practitioners centres on the holistic assessment of the patient. This not only comprises management of the wound bed, but also the impact of comorbidities, lifestyle factors, symptom management (for example, pain, odour and exudate) and compliance with treatment and available resources.

What is the hard-to-heal wound, and how do practitioners make decisions regarding them?

Leg ulcer guidelines have been developed and refined since the 1990s, ensuring availability of information on current, evidence-based treatments to support clinical practice. van Hecke et al (2008) report uncertainty regarding the manner or process by which research findings relating to leg ulcer treatment are implemented in community nursing practice. The consensus group proposed that the variation in both healing and recurrence rates highlights the need to re-examine the current guidelines and investigate their recommendations for hard-to-heal wounds.

While non-healing patients can be placed on a long-term management plan or pathway as early as six weeks, there is often geographical variation in knowledge base, clinical practice and treatment. Factors include the availability of dressings in the local wound care formulary, and differing levels of knowledge and experience. Less than favourable dressing 'trials' can result, with practitioners often 'swapping and changing' treatments in long-term patients in an attempt to try to heal the wound (Guidelines Working Group, 2011), but with very little resultant improvement in patient outcome. These issues, that is, the timely assessment and initiation of appropriate compression, availability of suitable wound management materials and education as to their correct use, must be addressed.

The treatment of chronic wounds is dependent on an objective diagnosis that, as Stremitzer et al

(2007) suggest, is usually based on the visual impression of the wound. However, an appropriate wound assessment should be based on:

Correction of the underlying wound pathology (wherever possible) and comorbidities is a key priority in proactive wound management. If any underlying disease is not, or cannot, be corrected, it will have a direct impact, delaying or preventing wound healing.

- ▶▶ Accurate assessment of the underlying condition and blood supply
- ▶▶ Accurate diagnosis
- ▶▶ Size and depth of the lesion
- ▶▶ Presence and recognition of normal or abnormal granulation tissue
- ▶▶ Presence of fibrin debris, necrosis or wound exudate
- ▶▶ Judgement of condition of the edge of the wound
- ▶▶ Presence of infection.

The hard-to-heal wound is usually arrested in the inflammatory stage, with an influx of neutrophils causing 'uncontrolled' inflammation and, consequently, extensive damage to the host tissue (Bjarnsholt et al, 2008).

A key factor is the ability of the practitioner to differentiate between different types of wound tissue, with progress monitored by accurate and timely evaluation of the prescribed treatment. Stremitzer et al (2007) identified a knowledge gap in the recognition of tissue types and an inability to classify these correctly. They suggest that it is not enough to measure the size of the wound; tissue evaluation will allow the practitioner to determine changes in principal tissue types (for example, an increase in the amount of necrosis, fibrin deposits and granulation tissue)

which, in turn, will indicate whether the wound is healing or whether treatment needs to be adjusted.

Why chronic wounds will not heal

The successful management of non-healing wounds relies on the identification and treatment of factors that act as 'brakes on the healing process' (Bjarnsholt et al, 2008). It is suggested that the 'chronic wound' will not heal due to the healing and destructive processes being 'out of balance', and it is only by the manipulation and counterbalancing of these processes that healing can be initiated (Bjarnsholt et al, 2008). Correction of the underlying wound pathology (wherever possible) and comorbidities is a key priority in proactive wound management. If any underlying disease is not, or cannot, be corrected, it will have a direct impact, delaying or preventing wound healing.

The inflammatory process is an integral part of acute wound healing as, in chronic wounds, there is a tendency to see an exaggerated inflammatory response, resulting in increases in pro-inflammatory cytokines, proteolytic enzymes (such as the cleansing proteases often referred to as matrix metalloproteinases [MMPs]) and reactive oxygen species. During the granulation phase of healing, the extracellular matrix (ECM) is degraded by a number of proteases. The increased protease activity breaks down the newly formed granulation tissue. The levels of these proteases increase within the wound after injury and decrease when the inflammation resolves. It is thought that, in normal healing, protease levels peak at day 3, reducing at day 5. However, in the chronic, non-healing wound, the proteases reach higher levels and persist for longer, thus impairing healing and destroying any normal tissue (International Consensus, 2011).

Tissue MMPs degrade several components of the ECM — including tendons, cartilage and fibrin —

facilitating the migration of cells, the accumulation of new ECM and the development of new tissue. It can be said that MMPs are involved in any process linked with inflammation, tissue reorganisation and modelling (Armstrong and Jude, 2002).

Wound exudate is also problematic, as the MMPs destabilise the wound environment by breaking down the peptide links within the growth factors and affecting the ECM (Powell, 2009). The imbalance of MMPs in chronic wounds has been identified as having a negative effect on healing (Armstrong and Jude, 2002; Widgerow, 2011). Schultz et al (2003) suggest that the molecular environment of the chronic wound should be re-balanced to levels seen in the acute wound, to promote further healing. This would result in a move from low to high mitogenic activity, high to low inflammatory cytokines, high to low proteases and senescent to mitotically competent cells.

When clinically assessing wounds, the practitioner should always be mindful of the presence of infection, identifiable by the following criteria (EWMA, 2005):

- ▶▶ Cellulitis
- ▶▶ Delayed healing despite appropriate compression therapy
- ▶▶ Increase in local skin temperature
- ▶▶ Increase in ulcer pain or change in nature of pain
- ▶▶ Newly formed ulcers within inflamed margins of pre-existing ulcers
- ▶▶ Wound bed extension within inflamed margins
- ▶▶ Discolouration (for example, dull, dark brick-red)
- ▶▶ Friable granulation tissue that bleeds easily
- ▶▶ Increase in exudate viscosity
- ▶▶ Increase in exudate volume
- ▶▶ Malodour
- ▶▶ New-onset dusky wound hue
- ▶▶ Sudden appearance or increase in amount of slough
- ▶▶ Sudden appearance of necrotic black spots
- ▶▶ Ulcer enlargement.

However, these signs are also indicative of clinical inflammation resulting from high protease activity. The inflammatory response can become exaggerated, thus increasing production of pro-inflammatory cytokines, proteolytic enzymes (MMPs, elastase and plasmin) and reactive oxygen species, with the excessive activity causing growth factor inactivation and ECM destruction (Vowden et al, 2008).

There is a gap in the guidelines regarding wound assessment and how to prevent wounds from becoming chronic and hard-to-heal.

The chronic wound bed is characterised by high bacterial content (of more than one strain), the presence of biofilms and an increased tendency to harbour drug-resistant organisms (Vowden et al, 2008). It is proposed that 'biofilm based management is becoming fundamental to non-healing wounds' (Percival et al, 2010). However, it should be noted that not all bacterial infections are considered treatable via antibiotics, with a distinct lack of evidence concerning optimal regimens or clinical hallmarks for efficient treatments (Bjarnsholt et al, 2008).

Bjarnsholt et al (2008) suggest that boosting the cellular immune system using MMP inhibitors and growth factors, as well as the modulation of invading bacteria, might also promote healing.

Looking to the future

The primary aim of treating a VLU is to promote healing. Future successes in the hard-to-heal population will require early identification, assessment of chronicity factors (Boyd et al, 2004, Stremitzer et al, 2007), understanding of the impact of MMPs and the early implementation of timely and appropriate therapy (which will

always include high compression therapy in the treatment of VLUs) (EWMA, 2003). In practice, this will require the practitioner to have a comprehensive knowledge of various methods of wound assessment and risk factors for delayed healing, as well as good observational techniques, to predict the need for a change in treatment (White, 2010).

Conclusion

Wound healing usually follows a predictable sequence. However, in some individuals it can be prolonged, or may never be fully achieved. The non-healing or hard-to-heal wound has become an ongoing burden to the VLU patient, the practitioner and the health economy, resulting in poor health outcomes and decreased quality of life for the patient, coupled with an increased cost to the economy (White, 2011).

Current clinical guidelines make no specific reference to this complex group of patients, thus providing no backup or information for practitioners to base their complex treatment regimens on. There is a gap in the guidelines regarding wound assessment and how to prevent wounds from becoming chronic and hard-to-heal. In February 2011, an expert panel advised that there was a need for evidence to address the assessment and treatment of the hard-to-heal VLU population, with specific attention being paid to causation, dressing choice and treatment outcomes, using robust clinical evidence as advocated by the EWMA Patient Outcomes Group (2010). The panel recommended that a comprehensive review of the new literature be undertaken and incorporated into the existing guidelines to determine which direction practitioners should take to address the unmet needs of patients with these painful and debilitating wounds. **WUK**

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References

- Armstrong DG, Jude EB (2002) The role of matrix metalloproteinases in wound healing. *J Am Podiatr Med Assoc* 92(1): 12–18
- Ballard K, Baxter H (2000) Developments in wound care for difficult to manage wounds. *Br J Nurs* 9(7): 405–8, 410, 412
- Bjarnsholt T, Kirketerp-Moller K, Jensen PO et al (2008) Why chronic wounds will not heal: a novel hypothesis. *Wound Repair Regen* 16(1): 2–10
- Boyd G, Butcher M, Glover D, Kingsley A (2004) Prevention of non-healing wounds through the prediction of chronicity. *J Wound Care* 13(7): 265–66
- European Wound Management Association (2002) *Position document. Pain at wound dressing changes*. MEP Ltd, London. Available online at: <http://ewma.org/english/position-documents/all-documents.html#c507> [last accessed 27/07/2011]
- European Wound Management Association (2003) *Position document. Hard-to-heal wounds: a holistic approach*. MEP Ltd, London. Available online at: <http://ewma.org/english/position-documents/all-documents.html#c319> [last accessed 26/07/2011]
- European Wound Management Association (2005) *Position document. Identifying criteria for wound infection*. MEP Ltd, London. Available online at: <http://ewma.org/english/position-documents/all-documents.html#c500> [last accessed 15/08/2011]
- EWMA Patient Outcome Group (2010) Outcomes in controlled and comparative studies on non-healing wounds: Recommendations to improve the quality of evidence in wound management. *J Wound Care* 19(6): 237–68
- Fletcher A, Cullum N, Sheldon TA (1997) A systematic review of compression treatment for venous leg ulcers. *Br Med J* 315(7108): 576–80
- Iglesias CP, Nelson EA, Cullum N, Torgerson DJ (2004) Economic analysis of VenUS I, a randomized trial of two bandages for treating venous leg ulcers. *Br J Surg* 91(10): 1300–06
- International Consensus (2011) The role of proteases in wound diagnostics. An expert working group review. Wounds International, London. Available online at: www.woundsinternational.com/article.php?contentid=127&articleid=9869&page=1 [last accessed 26/07/2011]
- Lees TA, Lambert D (1992) Prevalence of lower limb ulceration in an urban health district. *Br J Surg* 79(10): 1032–34
- Margolis DJ, Allen-Taylor L, Hoffstad O, Berlin JA (2004) The accuracy of venous leg ulcer prognostic models in a wound care system. *Wound Rep Regen* 12(2): 163–8
- National Institute for Health and Clinical Excellence (2003) *Pressure ulcer prevention*. NICE, London. Available online at www.nice.org.uk/page.aspx?o=CG007NICEguideline [last accessed 10 December 2010]
- Percival SL, Cutting KF, Williams D (2010) Biofilms: possible strategies for suppression in chronic wounds. *Nurs Standard* 24(23): 16–21
- Phillips TJ, Machado F, Trout R, Porter J, Olin J, Falanga V (2000) Prognostic indicators in venous ulcers. *J Am Acad Dermatol* 43(4): 627–30
- Powell G (2009) The new Start dressing range — Urgotul Start, UrgoCell Start. *Br J Nurs* 18(6): S30, S32–S36
- Reeder SWI, de Roos K-P, de Maeseneer M, Sommer A, Neumann HAM (2010) Hospital admission for venous ulcers: what is it worth? (Paper 5.4). *Phlebology* 25(6): 309
- Rippon M, Davies P, White R, Bosanquet N (2007) The economic impact of hard-to-heal leg ulcers. *Wounds UK* 3(2): 58–69
- Royal College of Nursing (2006) *Clinical practice guidelines. The nursing management of patients with venous leg ulcers*. RCN, London. Available online at: www.rcn.org.uk/data/assets/pdf_file/0003/107940/003020.pdf [last accessed 27/07/2011]
- Schultz GS, Sibbald RG, Falanga V, et al (2003) Wound bed preparation: a systematic approach to wound management. *Wound Rep Regen* 11(Suppl 1): S1–S28
- Scottish Intercollegiate Guidelines Network (2010) Management of chronic venous leg ulcers. A national clinical guideline. SIGN, Edinburgh. Available online at: www.sign.ac.uk/guidelines/fulltext/120/index.html [last accessed 26/07/2011]
- Stremitzer S, Wild T, Hoelzenbein T (2007) How precise is the evaluation of chronic wounds by health care professionals? *Int Wound J* 4(2): 156–61
- van Hecke A, Grypdonck M, Defloor T (2008) Guidelines for the management of venous leg ulcers: a gap analysis. *J Eval Clin Pract* 14(5): 812–22
- van Rijswijk L (1993) Full-thickness leg ulcers: patient demographics and predictors of healing. Multi-Center Leg Ulcer Study Group. *J Fam Pract* 36(6): 625–32
- Vowden P, Apelqvist J, Moffatt C Wound complexity and healing. In: European Wound Management Association (2008) *Position document. Hard-to-heal wounds: a holistic approach*. MEP Ltd, London
- White R J (2010) Delayed wound healing: Who, when, why, and in whom? *Nurs Standard Autumn Suppl* 1(1): 24–32
- White R (2011) Hard-to-heal wounds: results of an international survey undertaken. *Wounds UK* 7(4): 22–31
- Widgerow AD (2011) Chronic wound fluid — thinking outside the box. *Wound Rep Regen* 19(3): 287–291

Key points

- ▶▶ A GAP analysis has been conducted on guidelines for the management of venous leg ulcers.
- ▶▶ The non-healing or hard-to-heal wound has become an ongoing burden to the VLU patient, the practitioner and the health economy.
- ▶▶ While non-healing patients can be placed on a long-term management plan or pathway as early as six weeks, there is often geographical variation in knowledge base, clinical practice and treatment.
- ▶▶ The panel have identified shortcomings in guidelines with respect to identification and management of hard-to-heal VLUs.
- ▶▶ A comprehensive review of the new literature needs to be undertaken and incorporated into the existing guidelines.