Defining a holistic pain-relieving approach to wound care via a drug free polymeric membrane dressing

Wound care practice continuously demonstrates that healing cannot be adequately controlled if a patient's experience of pain is not managed effectively. Current pain management guidelines do not account for the holistic treatment of pain emanating from a wound — an environment of uncontrolled or rogue inflammation, neuropathy and neuroischaemia. This article investigates how polymeric membrane dressings can interact with the pathology of wounds to correct abnormalities in pain pathways of the nervous system and dampen problematic ongoing pain to enhance the clinical picture of wound healing.

polymeric membrane dressing; wound pain

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Several studies have demonstrated strong links between patient pain experiences and healing outcomes.[1,2,3] This topic has been the focus of intensive research over the past decade, resulting in three 'Best Practice' statements[4, 5, 6] and two books dedicated to the ongoing research and teaching.[7]

It is clear that practitioners must consider wound-related pain as important an issue as their patients do, for it impacts on treatment, and on clinical outcomes. However, practice will only change if all professionals actively engage in care strategies that are proven to minimise trauma and pain in wound care.[8]

A variety of measures may be taken to reduce or even avoid pain during the period of wound management — for example, the administration of pharmacologically active agents (including opioid analgesics, topical anaesthetics, non-steroidal anti-inflammatory drugs [NSAIDS], anticonvulsants or antidepressants) [9]. However, recommended pharmacological strategies can be inadequate and often have associated dose-limiting side-effects. Where the origin of wound pain is multifaceted — at times involving a vicious combination of neuropathy, uncontrolled inflammation, oedema and neuroischaemia — it is reasonable to suggest that such pharmacological agents do not offer holistic treatment.

Pain at dressing change must also be considered. Such pain may arise through the removal of adherent dressings,[10] which can cause damage to the surrounding skin and the wound bed. Such trauma will increase the time to healing[11] and so involve extra time and materials. Pain responses are affected not only by physical injury, but also by the psychological, social, and environmental conditions at any given time[12] — thus, apprehension at wound cleansing can also give rise to unnecessary pain in wound patients.[3]

Fig 1 depicts a rudimentary summary of how pain levels may fluctuate during wound care. In healthy patients, an acute wound (such as an abrasion) can progress to healing within days; however, the more complex pathology seen in a 'chronic' ulcer or in a burn wound can be more difficult to control and/or treat and will typically take months to heal. In the long term, this can lead to adverse modifications to the delivery of pain messages to the brain (nociception), which can result in pain symptoms that linger, chronically, in the background (dysaesthesia) or that appear on mechanical or thermal stimulation of the affected area (hyperalgesia and allodynia).[13]

In a context of background pain, the process of dressing change can impair wound care and pain management, and have a highly detrimental effect on healing[3]. It is important, therefore, that when considering the treatment of wound-related pain, a holistic perspective be adopted, which demands

References:
1 McGuire, L., Heffner, K., Glaser, .R et al. Pain and wound healing in surgical patients. Ann Behav Med. 2006; 31: 2, 165-172.
2 Woo, K.Y., Sibbald, R.G. The improvement of wound-associated pain and healing trajectory with a comprehensive foot and leg ulcer care model. J Wound Ostomy Continence Nurs. 2009; 36: 2, 184-191.
3 Woo, K.Y. Wound-related pain: anxiety, stress and wound healing. Wounds UK 2010; 6: 4, 92-98.

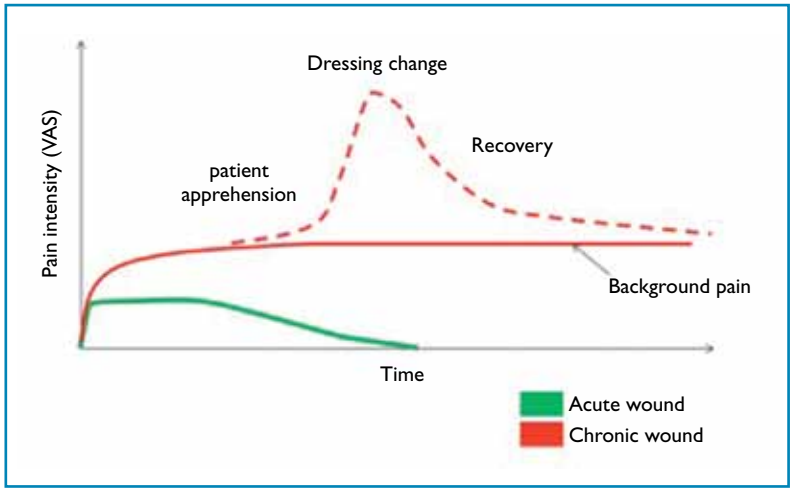


Figure 1. If we could depict the progression of pain levels in wound care patients over time would they look like this?

Box 1. Factors that may result in wound pain*

- Trauma during dressing change
- Products used
- Skin excoriation
- Infection
- Lack of empathy
- Poor bandaging technique
- Previous experience of pain
- Cleansing procedures
- Paediatric patient

*adapted from Hollinworth and Collier 2000

consideration of the potential for wound dressings to reduce background pain, and acknowledgement of how pain can be exacerbated by dressing changes. It is necessary to consider the wound's aetiology, when pain occurs, any associated procedures and the impact that pain has on clinical outcomes.

Recent research has identified specific dressings that impact on wound-related pain, notably at dressing change.[10] Polymeric membrane dressings (PolyMem, Ferris Mtg. Corp.) have been shown to be effective in the reduction or avoidance of wound pain. Furthermore, their non-adherent properties [14, 15] mean that these dressings can be successfully used in the fragile skin disorder epidermolysis bullosa.

This review will consider how polymeric membrane dressings impact on the modulation of nociception in chronic wounds, wound-related pain and clinical outcomes.

Could a drug-free polymeric dressing dampen background somatic pain?

It is widely recognised that wound infection,[16] neuroischemia,[17] and neuropathy[18,19] cause pain. It is also acknowledged that there is an association between pain and stress,[20] and that psychological stress interferes with healing[21] (Box 1).

Inflammation, an inevitable consequence of tissue injury, is essential for the re-establishment of cutaneous homeostasis following injury, and a prerequisite for tissue repair. In recent years, our knowledge of specific subsets of inflammatory cell lines and the cytokine network that orchestrates the inflammation associated with tissue repair has increased.[22] However, uncontrolled inflammation has been shown to disperse swelling and cause secondary damage, delaying healing[23] and causing an increase scarring,[24] possibly as a result of the modulation of nociception.

When applying this theory to chronic wounds, there are two foci in the nervous system that should be considered:

- Nociceptors (pain sensors) in the tissue bed — at the peripheral level
- The spinal cord — at the central level.

Pain messages themselves are transmitted through the nervous system via action potentials (electrical activity across nerve membranes), which move from peripheral nociceptors to the spinal cord, from which they move to higher centres of the brain where pain is registered. Action potentials are generated by the influx of sodium ions in to nerve cells, which causes electrical activity to move along nerve fibres.

The augmented pain sensations observed in patients with injured or inflamed tissue or nerves are associated with ectopic augmented levels of action potentials being sent from the site of damage [25]. Hence, researchers have investigated the role of sodium ion exchange in this response.[26,27] Preclinical studies in animal models of tissue inflammation, neuropathy and neuroischemia, together with investigations using clinical biopsies of damaged tissue [28] have demonstrated that sodium channels — which facilitate the movement of sodium ions during the generation of an action potential — cluster to abnormally high levels in injured tissue. This is associated with a lowering of the threshold of sensory input (mechanical or thermal) needed to evoke an action potential — nociceptors within tissue become 'sensitised'. This might also explain why abnormal pain symptoms continue to be reported post-healing.

If the contribution that sodium ions make to this pain signal could be dampened, chronic pain symptoms may be reduced (potentially the background pain that exists in chronic wounds). Preliminary data suggest that polymeric membrane dressings elicit their effects by absorbing sodium ions from the outer layers of the epidermis[29] — if not removed, these sodium ions may exacerbate the generation of

4 European Wound Management Association. Pain at wound dressing changes (position document). Medical Education Partnership, London.

5 World Union of Wound Healing Societies. Principles of Best Practice: Minimising Pain at Wound Dressing-related Procedures. A Consensus Document. MEP, 2004.

6 World Union of Wound Healing Societies. Principles of Best Practice: Minimising pain at dressing-related procedures: "Implementation of pain relieving strategies" - a consensus document. WUWHS, 2008. http://www.wuwhs.com/pdfs/final%20pain%20supplement.pdf Accessed 12th April 2011.

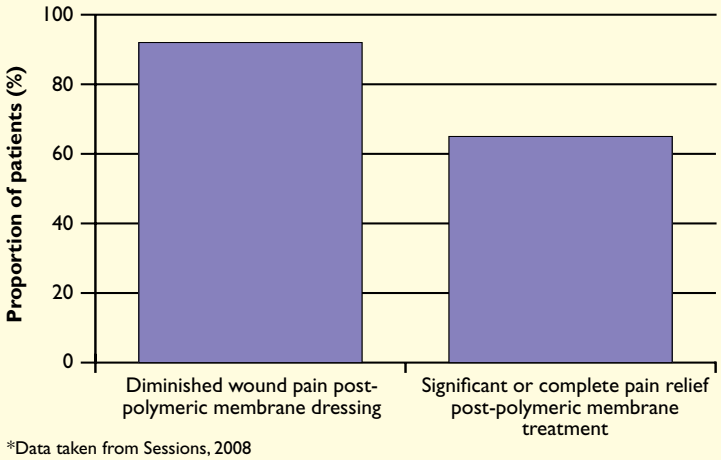
7 White, R.J., Harding, K.G. Trauma and Pain in Wound Care: Volume II. Wounds UK, 2006.

8 Hollinworth, H., White, R.J. The clinical significance of wound pain. In: White, R.J., Harding, K.G. (eds). Trauma and Pain in Wound Care. Wounds UK, 2006.

9 Tan, T., Barry, P., Reken, S., Baker, M. Guideline Development Group. Pharmacological management of neuropathic pain in non-specialist settings: summary of NICE guidance. BMJ. 2010; 340: c1079.

10 Bell, C., McCarthy, G. The assessment and treatment of wound pain at dressing change. Br J Nurs. 2010; 19: 11, S4-S8

Fig 2. A pooled analysis of pain relief achieved post polymeric membrane wound dressing*



*Data taken from Sessions, 2008

11 Hollinworth, H. The management of patients' pain in wound care, Nursing Stand 2005; 20: 7, 65-73.

12 Melzack, R. From the gate to the neuromatrix. Pain Suppl 1999; 6: S121–S126.

13 Kuner, R. Central mechanisms of pathological pain. Nat Med. 2010; 16: 11, 1258-1266.

14 Foresman, P.A., Ethridge, C.A., Rodeheaver, G.A wound healing evaluation on partial-thickness rat wounds. Symposium on Advances in Skin and Wound Care. 1991 Annual Meeting. Poster Presentation. Health Management Publication

15 Benskin L. Complete closure of extensive third-degree burn wound using PMD (Hand Burn). Presented at 8th Ann American Professional Wound Care Assoc. Poster 4. Apr 2-5, 2009. Philadephia, PA USA

16 Bjarnsholt, T., Kirketerp-Moller, K., Jensen, P. et al. Why chronic wounds won't heal: a novel hypothesis. Wound Repair and Regeneration 2008; 16: 2, 1-10.

17 Vora, A., Myerson, M.S. Crush injuries of the foot in the industrial setting. Foot Ankle Clin. 2002; 7: 2, 367-383.

action potentials, leading to the generation of background (somatic) pain.

Uncontrolled, or 'rogue' inflammation at the wound site — caused by an infiltration of immune cells such as macrophages and neutrophils arriving to deal with infection and debris and initiate healing — can also augment neural input, thereby enhancing the delivery of pain messages to the spinal cord. Some of the inflammatory mediators, released by these cells during the debridement of necrotic or infected tissue have been shown to promote abnormal nociceptor activity, also via 'sensitisation' [22].

Investigations in rodents — wrapping incisions in polymeric membrane dressing — have demonstrated that the dressing can reduce the spread of macrophages and neutrophils to areas outside of the direct injury, without interfering with the local inflammation that is necessary for healing.[30] The dressing has also been shown to significantly reduce the visible effects of inflammation, oedema and bruising in a rabbit model of mechanical injury.[31]

It may be possible to dampen background pain as action potentials extend to the spinal cord. Here pain signals are filtered by 'gate-keeper cells'[32] before the pain message is packaged up and processed by higher brain centres.

The arrival of pain messages at the spinal cord can be monitored via c-fos, a protein marker of neuronal activity. In a rodent model of incision pain, c-fos expression in the spinal cord has been analysed, demonstrating that applying polymeric membrane dressing to the site of injury can significantly reduce spinal neuronal cell activation versus both gauze and placebo foam, thus dampening the pain message arriving at the spinal cord.[30] Further data in control animals (without incision) highlighted a particularly interesting observation regarding the mechanism by which these dressings might dampen nociceptive transmission to the spinal cord, as c-fos expression was also seen in control animals wearing the dressing.[30] This may suggest that the polymeric membrane also activates non-nociceptive nerve fibres, to trigger a phenomenon known as descending inhibition — effectively closing the filter gates in the spinal cord and limiting the infiltration of pain messages to higher brain centres.[32] This has been likened to the action of acupuncture and transcutaneous electrical nerve stimulation (TENS). Behavioural observations in animal models have confirmed that these changes, at a cellular level, translate to significantly reduced mechanical and thermal hyperalgesia[30] — but how does this translate to the clinical situations of wound care?

How does a drug-free polymeric membrane dressing perform in clinical wound-related pain?

Researchers in Korea have demonstrated positive results for a polymeric membrane dressing in 72 patients with either second degree burn wounds or skin graft donor sites. Versus a conventional petrolatum gauze dressing, there were significantly reduced levels of wound site pain when polymeric membrane dressings were used. In addition, healing times were significantly faster and patients reported improved levels of comfort.[32]

A later randomised, controlled study of wound healing following arthroscopic knee surgery, indicated that versus standard dressings, polymeric dressings significantly reduced pain scores on days 1–10 post-operatively, together with a reduction in mean overall pain score on a 0–10 scale (this dropped from 4.5 with standard dressings to 2.2 with polymeric membrane dressings). To assess how pain levels may correlate to underlying inflammation, the researchers also compared skin temperature with both dressings, revealing that wounds treated with polymeric dressings achieved an approximate 2.5°F mean reduction in skin temperature.[34]

There are published peer-reviewed case studies that demonstrate the effects of polymeric dressings on a wide range of wounds,[35-38] and a recent pooled analysis of data from 32 patients reporting significant wound pain pre-treatment has been made possible.[39] As shown in Fig 2, pain relief — significant or complete — was reported by a large proportion of those treated with polymeric dressings. This was accompanied by a general reduction in the use of pharmacological pain medication.[39]

Long-term data is now available from specialised units worldwide, with large patient populations, providing evidence that polymeric membrane dressings offer reproducible pain relief during dressing change, rapid healing and a reduction in the need for pain medication.[40-43]

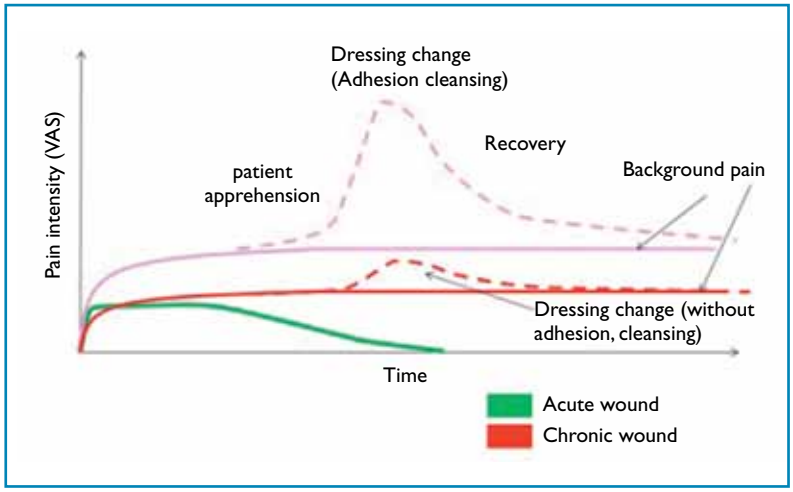


Fig 3. The original depiction of pain progression in wound care is shown in purple (taken from Fig 1). The new clinical picture, taking in to account polymeric membrane dressing data, is shown in red. If background pain can be reduced together with dressing changes involving no adhesion or cleansing requirements, this new depiction could explain why these dressings reduce pain and promote fast healing.

Certainly, the removal of dressings that have adhered to the wound bed causes trauma and significant pain to the patient. Further, this extends time to healing as the wound reverts back to the inflammatory stage at each dressing change. Traditional gauze and paraffin tulle products (such as Jelonet) have repeatedly been shown to adhere to the wound bed in this way, and if left *in situ*, granulation tissue grows into the product mesh, exacerbating adherence, with wound pain and trauma on removal.[44,45,46]

It is a professional concern that, patients are still subjected to wound cleansing and dressing strategies that exacerbate their existing pain, and which often cause further trauma to delicate healing tissues. Wounds do not routinely require cleansing. Wiping the wound bed with gauze traumatises fragile granulation tissue, and on virtually every occasion it is a painful, unpleasant experience for the patient. To use a genuinely non-adherent dressing and limit unnecessary traumatic wound cleansing at dressing change could also lower patient apprehension and their experience of pain. These attributes are recognised characteristics of polymeric membrane dressings.[14,15,47]

To refer back to the issue of exacerbated pain responses at dressing change — compounded by the continuous background pain associated with chronic wounds (see Fig 1) — this review article has presented data indicating that polymeric membrane dressings could impact on inflammation, its dissemination beyond a site of injury, nociceptor activation and the neuromodulation that is linked to tissue damage — there is certainly evidence that they are linked to pain relief. If we relate this to a 'dampening' of background wound pain, and also consider the non-adherence and self-cleansing characteristics of polymeric membrane dressings, we might propose an amendment to the clinical picture (Fig 3). ■

18 Bengtsson, L., Jonsson, M., Apelqvist, J. Wound-related pain is underestimated in patients with diabetic foot ulcers. J Wound Care. 2008; 17: 10, 433-435.

19 Boulton, A.J. What you can't feel can hurt you. J Vasc Surg. 2010; 52: 3 (Suppl): 28S-30S.

20 Soon, K., Acton, C. Pain-induced stress: a barrier to wound healing. Wounds UK 2006: 2: 4, 92–101.

21 Gouin, J.P., Kiecolt-Glaser, J.K The impact of psychological stress on wound healing: methods and mechanisms. Immunol Allergy Clin North Am 2011; 31: 1, 81-93.

22 Eming, S.A., Krieg, T., Davidson, J.M. Inflammation in wound repair: molecular and cellular mechanisms. J Invest Dermatol. 2007; 127: 3, 514-525.

23 Menke, N.B., Ward, K.R., Witten, T.M. et al. Impaired wound healing. Clin Dermatol. 2007; 25: 1, 19-25.

24 Satish, L., Kathju, S. Cellular and Molecular Characteristics of scarless versus fibrotic wound healing. Dermatol Res Pract. 2010; 790234.

25 Papir-Kricheli, D., Devor, M. Abnormal impulse discharge in primary afferent axons injured in the peripheral versus the central nervous system. Somatosens Mot Res. 1988; 6: 1, 63-77.

26 Matzner, O., Devor, M. Hyperexcitability at sites of nerve injury depends on voltage-sensitive Na+ channels. J Neurophysiol. 1994; 72: 1, 349-359.

27 Coggeshall, R.E., Tate, S., Carlton, S.M. Differential expression of tetrodotoxin-resistant sodium channels Nav1.8 and Nav1.9 in normal and inflamed rats. Neurosci Lett 2004; 355: 1-2, 45-48.

28 Cummins, T.R., Sheets, P.L., Waxman, S.G. The roles of sodium channels in nociception: Implications for mechanisms of pain. Pain. 2007; 131: 3, 243-257.

29 Kahn, A.R. A superficial cutaneous dressing inhibits pain, inflammation and swelling in deep tissues. Presented at: American Pain Society 18th Annual Scientific Meeting; October 21-24, 1999.

30 Beitz, A.J., Newman, A., Kahn, A.R. et al. A polymeric membrane dressing with antinociceptive properties: analysis with a rodent model of stab wound secondary hyperalgesia. J Pain. 2004; 5: 1, 38-47.

31 Kahn, A.R. A Superficial cutaneous dressing inhibits pain, inflammation and swelling in deep tissues. presented at the World Pain Conference, July 15–21, 2000. Pain Medicine 2000; 1: 2, 187.

32 Melzack, R., Wall, P.D. Pain mechanisms: a new theory. Science 1965; 150: 699, 971–979.

33 Kim, Y.J., Lee, S.W., Hong, S.H. The effects of PolyMem on the wound healing. J Korean Soc Plast Reconstr Surg 1999; 109: 1165-1172.

34 Hayden, J.K., Cole, B.J. The effectiveness of pain wrap compared to standard dressing on the reduction of post-operative morbidity following routine knee arthoroscopy: a prospective randomized single blind study. Orthopedics 2003; 26: 59-63.

35 Blackman, J.D., Senseng, D., Quinn, L., Mazzone, T. Clinical evaluation of a semipermeable polymeric membrane dressing for the treatment of chronic diabetic foot ulcers. Diabetes Care. 1994; 17: 4, 322-325.

36 Yastrub, D.J. Relationship between type of treatment and degree of wound healing among institutionalized geriatric patients with stage II pressure ulcers. Care Manag J. 2004; 5: 4, 213-218.

37 Yastrub, D.J. Getting the stalled wound back on the road to healing. Ostomy Wound Manage. 2009; 55: 1, 8.

38 Spillo, N.M. Managing Stage IV pressure ulcers in the home. Ostomy Wound Manage. 2009; 55: 3, 6.

39 Sessions, R.C. Examining the evidence for a drug-free dressing's ability to decrease wound pain. 23rd Annual Clinical Symposium on Advances in Skin and Wound Care. Poster 134. Oct 26-30, 2008. Las Vegas, NV USA.

40 Wilson D. Skin tear healing improved through the use of polymeric membrane dressings. 21st Clinical Symposium on Advances in Skin and Wound Care. Poster 341. 2006; 373

41 Stenius M. Fast healing of pressure ulcers in spinal cord injured (SCI) people through the use of Polymem(R) dressings. 10th Anniversary EPUAP open meeting. Poster 21. Aug 30-Sept 1, 2007. Oxford, England.

42 Benskin, L., Bolhuis, J. Evidence-based skin tear protocol yields phenomenal results. WOCN Society 40th Annual Conference. Abst 2403, June 21-25, 2008. Orlando, Fl USA.

43 Tamir, J. Polymeric foam dressing for skin graft donor sites: 3 years experience on 800 cases. 23rd Clinical Symposium on Advances in Skin and Wound Care. Poster 49. Oct 2008. 27-30. Las Vegas, NV USA.

44 Hollinworth, H., Collier, M. Nurses' views about pain and trauma at dressing changes: results of a national survey, J Wound Care 2000; 9: 8, 369-373.

45 Bethell, E. Why gauze dressings should not be the first choice to manage most acute surgical cavity wounds, J Wound Care, 2003; 12: 6, 237-239.

46 Jones, A, San Miguel, L. Are modern wound dressings a clinical and cost-effective alternative to gauze? J Wound Care, 2006; 15: 2, 65-69.

47 Harrison J. Wound Cleansing for the 21st Century. Ostomy Wound Management 2008, 54: 12, 14.