References

1. Lipsky BA, Berendt AR (2010) Hyperbaric oxygen therapy for diabetic wounds: has hope hurdled hype? *Diabetes Care* 33(5): 1143–5
2. Abbott CA, Carrington AL, Ashe H, North-West Diabetes Foot Care Study et al (2002) The North-West Diabetes Foot Care Study: incidence of, and risk factors for, new diabetic foot ulceration in a community-based patient cohort. *Diabet Med* 19: 377–84
3. Centers for Disease Control and Prevention (2005) Lower extremity disease among persons aged ≥40 years with and without diabetes: United States, 1999–2002. *MMWR Morb Mortal Wkly Rep* 54: 1158–60
4. Lauterbach S, Kostev K, Kohlmann T (2010) Prevalence of diabetic foot syndrome and its risk factors in the UK. *J Wound Care* 19: 333–7
5. Moxey PW, Gogalniceanu P, Hinchliffe RJ et al (2011) Lower extremity amputations—a review of global variability in incidence. *Diabet Med* 28: 1144–53
6. Latham E (2013) Hyperbaric oxygen therapy: enhancement of healing in selected problem wounds. Medscape. Available at: http://bit.ly/1f3TBdt (accessed 10.12.13)
7. Roeckl-Wiedmann I, Bennett M, Kranke P (2005) Systematic review of hyperbaric oxygen in the management of chronic wounds. *Br J Surg* 92: 24–32
8. Chen SJ, Yu CT, Cheng YL, Yu SY, Lo HC (2007) Effects of hyperbaric oxygen therapy on circulating interleukin-8, nitric oxide and insulin-like growth factors in patients with type 2 diabetes mellitus. *Clin Biochem* 40: 30–6
9. Steed DL, Attinger C, Colaizzi T et al (2006) Guidelines for the treatment of diabetic ulcers. *Wound Repair Regen* 14(6): 680–92
10. Katsilambros N, Dounis E, Makrilakis K, Tentolouris N, Tsapogas P (2010) *Atlas of the Diabetic Foot*. 2nd edn. Wiley-Blackwell: 220. Available at: http://bit.ly/1jlqz6A (accessed 10.12.13)
11. Gesell L (2008) *Hyperbaric Oxygen Therapy Indications*. 12th edn. The Hypberbaric Oxygen Therapy Committee report. Undersea and Hyperbaric Medical Society, Durham, NC
12. European Committee for Hyperbaric Medicine (2004) 7th European Consensus Conference on Hyperbaric Medicine. ECHM, Lille. Available at: http://bit.ly/ICQ7E8 (accessed 10.12.13)
13. CMS.gov (2003) Medicare national coverage determination for hyperbaric oxygen therapy (20.29). Available at: http://go.cms.gov/1jlu5Oq (accessed 10.12.13)
14. Robson MC, Barbul A on behalf of the Wound Healing Society (2006) Guidelines for the best care of chronic wounds. *Wound Regen Repair* 14(6): 647–8
15. Faglia E, Favales F, Aldeghi A et al (1996) Adjunctive systemic hyperbaric oxygen therapy in treatment of severe prevalently ischemic diabetic foot ulcer. *Diabetes Care* 19(12): 1338–43
16. Heyneman CA, Lawless-Liday C (2002) Using hyperbaric oxygen to treat diabetic foot ulcers: safety and effectiveness. *Crit Care Nurse* 22(6): 52–60
17. Chen C-E, Ko Y-H, Fong C-Y, Juhn R-J (2010) Treatment of diabetic foot infection with hyperbaric oxygen therapy. *Foot Ankle Surg* 16: 91–5

Advances in wound dressing technology

Author: Professor Geoff Sussman

Over the past 50 years or so, the emphasis in wound care research has been on developing a range of wound dressings with properties of absorption, hydration and more recently antibacterial activity[1]. The new developments have lead to a shift from simple dressings to more advanced devices and products that incorporate pharmaceutically active ingredients.

There is a need to improve the condition of wound bed tissue and provide products that repair and regenerate damaged tissue and optimise healing. This can be achieved either by the addition of essential healing components or by removing or neutralising elements that retard healing or lead to ongoing tissue damage.

An urgent requirement is to develop effective point-of-care diagnostic tests to identify and define the underlying cause of wound breakdown. A point-of-care test that can detect elevated protease levels is now available[2,3], but much could be done if we had a better understanding of the presence of inflammatory cytokines, wound pH, autoimmune antibodies and other markers of infection.

There are cost implications with these newer treatments and diagnostic tests, and it is important to not only look at the unit cost of a product but also to explore the cost-effectiveness of the intervention in relation to associated and long-term costs, as well as cost savings[4,5]. If newer methods of treatment prevent or reduce the length of hospital stay and speed healing, then in the long term it is possible to make an economic case for using them.

KERATIN-BASED WOUND MANAGEMENT

An interesting example of a new wound treatment is the development of keratin-based wound care products. The ability of keratinocytes to migrate is critical for wound re-epithelialisation[6,7]. Keratins are the major proteins in keratinocytes and are essential for many cellular functions (e.g. cell migration), and upregulation of keratin expression has been observed in response to wounding[8,9].

Keratin-based products have been approved for use in several regions of the world, including Australia, New Zealand and the USA. A robust keratin matrix (Keramatrix®; Keraplast Technologies LLC), designed for use on wounds with moderate exudate levels or for use as an interface with negative pressure wound therapy, has shown positive results[6,8]. As the wound heals, the keratin matrix

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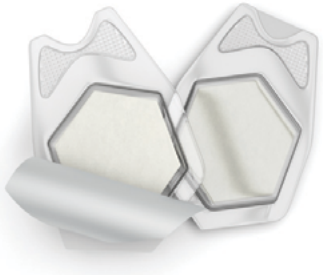

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is absorbed into the wound and does not need to be removed at dressing change[6,8].

The matrix is also available as a hydrogel (Keragel™; Keraplast Technologies LLC), which is designed for use in chronic dry wounds, acute wounds and for the treatment of certain skin conditions, such as epidermolysis bullosa[10–12]. Keragel provides moisture to a dry wound as well as a keratin-rich environment to encourage cell growth, leading to excellent healing outcomes[13]. The author has used both forms of the keratin matrix with good results at the Wound Clinic, Austin Hospital, Heidelberg, Australia.

PHARMACOLOGICAL THERAPIES

The adjunctive use of pharmacology also has benefits in wound management, with some interesting agents being used including angiotensin-converting enzyme (ACE) inhibitors, monoclonal antibodies, topical immunosuppressants and xanthine oxidase inhibitors. An example was presented at the European Cardiology conference held in Munich, August 2013, by Ahimastos et al[14], whose randomised controlled trial demonstrated that ACE inhibition improved walking ability and quality of life in patients with peripheral arterial disease; an improvement that impacts on wound healing and is substantially beyond that reported with conventional medical therapies.

Biologics, including monoclonal antibodies and in particular tumour necrosis factor alpha-antagonists, are now being extensively evaluated in the setting of chronic wound healing. Preliminary studies and case reports provide evidence of the clinical potential of these compounds in treating *Pyoderma gangrenosum*[15,16].

The author's facility has used calcineurin inhibitors such as tacrolimus successfully for the induction or maintenance of remission in immune and inflammatory disorders, such as *Pyoderma gangrenosum*, necrobiotic xanthogranuloma and vasculitic wounds[17–19]; it is applied topically as a 0.1% ointment. Topical tacrolimus does not negatively impact acute cutaneous wound healing[20].

Tacrolimus promotes melanocyte and melanoblast growth and creates a favourable milieu for cell migration via keratinocytes, which are possible mechanisms of how tacrolimus ointment induces repigmentation in patients with vitiligo[21].

Tacrolimus forms complexes with cytoplasmic immunophilins, which block the action of calcineurin in activated T-cells. This prevents the production of interleukin-2 and other cytokines, which normally stimulate T-cell proliferation and differentiation. Tacrolimus is used for the prevention of solid organ transplant rejection and the prevention and treatment of graft-versus-host disease in stem cell transplants[22,23]. It is normally administered intravenously or orally.

INNOVATIVE DEVELOPMENTS

These are some examples of innovative developments for advanced wound management. These interventions offer promising additions and new possibilities, and suggest that the future is bright for improved wound healing as we uncover the mystery of tissue repair and develop new ways of restoring tissue balance. ■

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References

1. Queen D et al (2004) *Int Wound J* 1(1): 59–77
2. Expert Working Group, *Wounds International* (2011) International consensus. The role of proteases in wound diagnostics. Available at: http://bit.ly/1bcAhdK (accessed 03.12.2013)
3. Dissemond J et al (2013) EPA made easy. Available at: http://bit.ly/1d1VaqZ (accessed 05.12.2013)
4. Vu T et al (2007) *Fam Practice* 24(4): 372–9
5. Expert Working Group, *Wounds International* (2013) International consensus. Making the case for cost-effective wound management. Available at: http://bit.ly/1k6g7Dg (accessed 03.12.13)
6. Pechter PM et al (2012) *Wound Rep Reg* 20: 236–42
7. Davis S et al (2009) *J Am Acad Dermatol* 60(3, Suppl 1): AB201
8. Tang L et al (2012) *Exp Dermatol* 21(6): 458–60
9. Perez R et al (2009) Evaluation of the effects of two keratin formulations on wound healing and keratin gene expression in a porcine model. Presented at the Symposium on Advanced Wound Care Conference, 26–29 April, Dallas, TX
10. Kirsner R (2009) *J Am Acad Dermatol* 60(3, Suppl 1): AB202
11. Arbuckle A (200) A case study series of the management of Epidermolysis bullosa using Keragel T. Society of Paediatric Dermatology, Portland, OR, USA
12. Balance K et al (2008) Improved healing of a diabetic foot ulcer using new keratin dressing technology. Australian Wound Management Association Conference Proceedings, 7–10 May, Darwin, NT
13. Hammond C et al (2010) *Wound Pract Res* 18(4): 189–95
14. Ahimastos AA et al (2013) *JAMA* 309(5): 453–60
15. Fonder MA et al (2006) *J Burns Wounds* Nov 20; 5:e8. Available at: http://1.usa.gov/1aPcoVw
16. Juillerat P et al (2007) *Dermatology* 215: 245–51
17. Altieri M et al (2010) *Ostomy Wound Management* 56(9): 32–6
18. Tzellos TG, Kouvelas D (2008) *Eur J Clin Pharmacol* 64: 337–41
19. Khurrum Baig M et al (2004) *Colorect Dis* 6: 250–3
20. Namkoong S et al (2013) *Exp Dermatol* 22(5): 369–71
21. Lan CC et al (2005) *Br J Dermatol* 153(3): 498–505
22. Dayton JD et al (2011) *J Heart Lung Transplant* 30(4): 420–5
23. Watkins KD et al (2012) *J Heart Lung Transplant* 31(2): 127–31