

Approaches to wound management

Basically, all traumatic or surgical patients have one thing familiar, namely, the presence of a wound. The wound becomes a potential source of considerable morbidity and mortality as a result of subsequent tissue inflammation and infection. A non healed wound becomes quickly colonized with bacteria from the environment eliciting further inflammation and subsequent organ injury. The long term effects of the healing process, namely, contractures and scar formation, can also have an significant impact not only cosmetically but also on function, for example, the pulmonary fibrosis after acute lung injury or intra-abdominal adhesions after peritonitis (Dulmovits and Herman, 2012). New wound care technologies are being developed at an increasingly rapid pace in recent years. These innovations could significantly reduce the overall costs for treating complex and chronic wounds, while offering greater savings in preventing wounds and their recurrence. It is well documented that anaerobic bacteria constitute, one-third of the total number of microbial species in colonized wounds, and this number increases to approximately 50% in infected wounds. Therefore, antimicrobial treatment of clinically infected and/or non-healing polymicrobial wounds should cover a variety of potentially synergistic aerobic or facultative anaerobic microorganisms and should not simply target specific pathogens that are often perceived to be the causative agents (e.g., *S. aureus* and *P. aeruginosa*). Clinical studies have demonstrated that a measure of the tissue microbial load in a wound can predict delayed healing or infection (Percival *et al.*, 2010). The quantitative tissue biopsy specimen technique is probably most useful in traumatic or surgical wounds to determine the correct time for wound closure or grafting. Antimicrobial agents (broad-spectrum antibiotics) are primarily used either prophylactically in the treatment of wounds that are likely to be heavily contaminated following surgery or in the treatment of clinically infected wounds. Wounds that are heavily contaminated (chronic or acute traumatic), failing to heal and possibly deteriorating, but have only local or no clinical signs of infection may benefit from topical antibiotic or antiseptic therapy. Surgical debridement of compromised (nonviable) tissue not only exposes the healthy, perfused tissue required to initiate wound healing but also effectively removes the majority of microbial contaminants, thus reducing the risk of infection. Biosurgical debridement,



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involving the use of fly larvae (maggots), has also regained popularity in recent years and is proving efficacious in the treatment of both infected and necrotic wounds. Wounds in which pressure is not off-loaded appropriately may take longer to heal and therefore may be exposed to a greater risk of infection. Therefore, mitigation of these stresses is important in the healing of these wounds. Another recently introduced perspective to pressure reduction in wounds involves the application of subatmospheric pressure. Essentially, a sterile open foam dressing is applied to a wound, which is then closed to the external environment to enable the application of a low-level vacuum (125 mm Hg). This type of system has been shown to reduce interstitial pressure, restore blood flow, and remove cell-inhibitory factors within chronic wound fluid. Additionally, vacuum-assisted wound closure has been shown to reduce the bacterial load in tissue 1,000-fold after 4 days of treatment in an experimental infected wound model. In recent years there have been many developments in products designed to assist wound healing, such as tissue engineering and the use of growth factors. However, it requires well-prepared wound bed. The optimal preparation of the wound bed requires complete debridement of devitalized tissue, bacterial balance, and moisture balance. Skin grafts fail if there are $\geq 1.0 \times 10^6$ organisms in the wound bed. Skin grafts require the creation of a donor site or second wound along with anesthetics. Attempts have been made for years to culture and grow keratinocytes in the laboratory to reduce the need for skin grafting. In one autografting system, the patient's own cells are cultured onto a hyaluronic acid scaffold for grafting. The cells are harvested from an 8-mm skin biopsy and the keratinocytes are cultured and migrated through a laser-cut membrane.

Within 1 month, the single biopsy could provide sufficient epithelial cells to cover an adult body. Bioengineered products replace the patient's damaged or destroyed dermal tissue and stimulate the patient's own epithelial cells. Human fibroblast cells are cultured from the foreskins of neonates onto a bioabsorbable scaffold. As they proliferate, they secrete dermal collagen, growth factors, and ECM proteins to create a living dermis, which is then implanted into the wound to facilitate healing. Allogenic, bilayered tissue consisting of a layer of viable keratinocytes and a dermal layer of viable fibroblasts dispersed in a type I collagen matrix has been used successfully in venous leg ulcers and neuropathic diabetic foot ulcers. The application of topical growth factors to a persistently nonhealing wound is often considered in order to stimulate some aspect of the healing process. The growth factors that have been most actively studied include: Basic fibroblast growth factor (bFGF), which stimulates endothelial cell proliferation and migration, transforming growth factor beta (TGF β), which stimulates the growth of fibroblasts and keratinocytes and the production of extracellular matrix, particularly collagen, epidermal growth factor (EGF), which supports the growth of keratinocytes and assists the migration of keratinocytes, fibroblasts and endothelial cells, platelet derived growth factor (PDGF), which is chemotactic for polymorphonuclear cells and macrophages. The PDGF, efficacy and safety have been confirmed in pressure ulcers and chronic diabetic ulcers, and the product is now available as a commercial gel that contains recombinant human PDGF in an aqueous-based sodium carboxymethylcellulose gel. Topical gene therapy is another approach to deliver growth factors to chronic wounds (Boateng *et al.*, 2008; Fan *et al.*, 2010). The gene-based strategies for treating and repairing tissue defects appear particularly bright. Numerous experimental investigations have demonstrated the feasibility of delivery and expression of gene products to various cell types involved in tissue repair. Over expression of certain gene products by viral and non-viral methods can stimulate a number of cell types toward desired differentiation or biosynthesis pathways. Certain transgenes appear to enhance tissue repair in some animal models, suggesting that the strategy is feasible and efficacious. Clinical trials are currently under way evaluating localized gene therapy of chronic diabetic foot ulcers treated with replication-incompetent adenoviral vectors that transiently express PDGF. The stem cells therapy is also gaining momentum. Chronic ischemic wounds treated with bone marrow derived stem cells revealed complete closure in more than 50% of the patients. Also CD34+ cells applied on diabetic ulcers resulted in improved blood circulation and revealed higher values of transcutaneous oxygen partial pressure (Gunter and Machen, 2012). An additional option for non healing wounds is the use of adjunctive therapies for chronic recalcitrant wounds. Electrical stimulation will activate fibroblasts (increase DNA, collagen synthesis, increase growth factor receptor sites) and stimulate migration of other key cells.

Silver is widely used to prevent bacterial contamination in wound dressings, but these dressings deliver a very large load of silver, and that can kill a lot of cells in the wound. New approach for using silver has been recently developed; the material is made from polyelectrolyte multilayers -a sandwich of ultra-thin polymer that adheres through electrical attraction, carrying a precise dose of silver which can be designed to release ions for days or weeks as needed. The final sandwich range from a few nanometers to several hundred nanometers in thickness. One square inch contains just 0.4 percent of the silver that killed 99.9999 percent of the bacteria but did not damage fibroblasts cells that are needed to repair a wound (Agarwal, 2012). Wound healing is a multistep process requiring the interaction and coordination of many different cell types and molecules—including growth factors and proteases. Recent advances in molecular biology, nanotechnology and functional genomics, coupled with an increased understanding of the pathophysiology of chronic wounds have resulted in the development of novel therapies such as tissue engineered substitutes and growth factors. In addition, promising developments in the areas of stem cells and gene therapy have given rise to new hope in modulating non-healing wounds. There is heterogeneity within wound types; identification of the cellular and molecular dysfunction in individual wounds and targeting or supplementing them is one of the goals for the future. Therefore a rationale and systematic approach to the wound management will significantly improve the quality of life patients as well as reduce burden on health care budget.

REFERENCES

- Agarwal A. New approach to wound healing easy on skin, tough on bacteria. 2012. Available from: <http://www.med.wisc.edu/news-events/new-approach-to-wound-healing-easy-on-skin-tough-on-bacteria/1338>.
- Boateng JS, Matthews KH, Stevens HN, Eccleston GM. Wound healing dressings and drug delivery systems: a review. *J Pharm Sci.* 2008; 97: 2892-923.
- Fan WL, Rashid M, Enoch S. Current advances in modern wound healing. *Wounds UK.* 2010; 6: 22-36.
- Gunter CI, Machens HG. New strategies in clinical care of skin wound healing. *Eur Surg Res.* 2012; 49:16-23.
- Percival SL, Thomas JG, Williams DW. Biofilms and bacterial imbalances in chronic wounds: anti-Koch. *Int Wound J.* 2010; 7:169-75.
- Dulmovits BM, Herman IM. Microvascular remodeling and wound healing: A role for pericytes. *Int J Biochem Cell Biol.* 2012; 44:1800-1812.

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