A research roundup of recent papers relevant to wound care

In this section, we bring together information found online and published in other journals about wound healing research. There is a lot happening and this is a great opportunity to highlight research that may have an impact on your practice now or in the future. The aim of this roundup is to provide an overview, rather than a detailed summary and critique, of the research papers selected.

**WOUND DURATION AND HEALING RATES: CAUSE OR EFFECT?**

Multiple factors affect wound healing rates. One of these factors, wound duration at presentation, is known to be related to prolonged healing rates and likeliness of healing. Untangling the effect of this factor on wound healing rates is complex. Is this simply an observation of the obvious; wounds of longer duration will be harder to heal? Or does time represent an independent factor, implying that if treatments were given earlier in the disease process, better outcomes may result? This review summarises the available evidence of the effects of wound duration on healing rates and examines potential biological abnormalities identified in chronic wounds, which may be significant in making chronic wounds difficult to heal.

*What this study might mean for wound care*
Wounds of longer duration are associated with excessive inflammation, fibroblast senescence, and alterations in wound-bed flora, which appears to have a progressive relationship. Early and aggressive treatment of ulcers that fail to respond to standard care may well aid in reducing the burden of wounds that become chronic.

**A RANDOMIZED CONTROLLED TRIAL OF LARVAL THERAPY FOR THE DEBRIDEMENT OF LEG ULCERS: RESULTS OF A MULTICENTER, RANDOMIZED, CONTROLLED, OPEN, OBSERVER BLIND, PARALLEL GROUP STUDY**

This study compared the clinical effectiveness of a larval therapy dressing (BioFOAM) with a standard debridement technique (hydrogel) in terms of time to debridement of venous or mixed arterial/venous leg ulcers. Data analyses were conducted on 88 subjects. Sixty-four subjects completed the full study. A total of 96.9% patients who completed treatment in the larval group debrided fully, compared with 34.4% patients who completed the hydrogel group. During the 21-day intervention phase, 67.4% from the larval group, and 26.2% from the hydrogel group debrided fully ($p=0.001$ in support of larvae). Subjects in the larval group required significantly fewer dressing changes (mean 2.83 vs. 5.40, $p=0.001$). There were no statistically significant differences in the clinical condition of the wound bed and surrounding skin by intervention. Subjects in the larval group experienced more ulcer-related pain or discomfort than subjects in the hydrogel group ($p<0.001$).

*What this study might mean for wound care*
It is well accepted that larvae is a useful tool to assist healing in certain wounds by facilitating debridement of necrotic tissue and this study provided good evidence to show that larval therapy debrided venous and mixed arterial/venous leg ulcers effectively. The overall time to healing, however, is not reported.

**CONTRASTING HOST IMMUNO-INFLAMMATORY RESPONSES TO BACTERIAL CHALLENGE WITHIN VENOUS AND DIABETIC ULCERS**

This study prospectively examined the interrelationship between clinical, microbiological, and proinflammatory biomarker levels and chronic venous leg ulcers (CVLUs) and diabetic foot ulcers (DFUs). Wound swabs and fluids were collected from CVLUs ($n=18$) and...
DFUs \( (n=15) \) and diagnosed clinically as non-infected or infected; and qualitative/quantitative microbiology was performed. CVLU and DFU fluids were also analysed for cytokine, growth factor, receptor, proteinase/proteinase inhibitor; and oxidative stress biomarker (protein carbonyl, malondialdehyde and antioxidant capacity) levels. There was no difference between clinical diagnosis, microbiology, or biomarker profiles, however increasing bacterial bio-burden \( (\geq 10^7\text{ colony-forming units/ml}) \) was associated with significant alterations in cytokine, growth factor, and receptor levels. These responses contrasted between ulcer type, with elevated cytokine, growth factor, and receptor levels in CVLUs, these were all decreased in DFUs with increasing bio-burden. Proteinase biomarkers exhibited few differences between CVLUs and DFUs, however significant elevations in antioxidant capacities correlated with increased bio-burden in CVLU fluids, but not in DFUs. Furthermore, oxidative stress biomarker levels were significantly elevated in all DFU fluids compared with CVLUs. 

**What this study might mean for wound care**

This study provides further insight into the contrasting disease-specific host responses to bacterial challenge within infected CVLUs and DFUs. The study provides evidence to support the use aggressive management strategies in the care of infected DFU.

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**A CHEMICAL BIOLOGICAL STRATEGY TO FACILITATE DIABETIC WOUND HEALING**


A team of researchers from Notre Dame’s Department of Chemistry and Biochemistry, searched for matrix metalloproteinases (MMPs) in the wounds of healthy and diabetic mice. Gelatinases, a class of enzymes, have been implicated in a host of human diseases from cancer to cardiovascular conditions. MMPs remodel the extracellular matrix in tissue during wound healing. The study shows that MMP-9 is detrimental to wound healing, while MMP-8 is beneficial. The team treated diabetic mice with an inhibitor of MMP-9 and discovered that wounds were healed 92\% after 14 days, as compared to 74\% healing in untreated mice. The identification of the enzyme that interferes with diabetic wound healing and that which repairs the wound, opens the door to new, novel treatment strategies.

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**STRESS-INDUCED HORMONES CORTISOL AND EPINEPHRINE IMPAIR WOUND EPITHELISATION**


Stress-induced disruption of hormonal balance in animals and humans has a detrimental effect on wound healing. After injury, keratinocytes migrate over the wound bed to repair a wound. However, their nonmigratory phenotype plays a role in the pathogenesis of chronic wounds. Despite many therapeutic approaches, there is a dearth of treatments targeting the molecular mechanisms mediated by stress that prevent epithelisation. Recent studies show that epidermal keratinocytes synthesise stress hormones. During acute wound healing, cortisol synthesis in the epidermis is tightly controlled. Additionally, keratinocytes express beta-2-adrenergic-receptor \( (\beta2AR) \), a receptor for the stress hormone epinephrine. Importantly, migratory rates of keratinocytes are reduced by cortisol and other \( \beta2AR \) agonists, thus indicating their role in the inhibition of epithelisation. Inhibition of local agonists with antagonists could be used to promote wound epithelisation.

**What this study means for wound care**

Modulation of local stress hormone production may represent an important therapeutic target for wound healing disorders. Topical administration of inhibitors of cortisol synthesis, statins, \( \beta2AR \) antagonists, and systemic beta-blockers can decrease cortisol synthesis, farnesyl pyrophosphate, and epinephrine levels, respectively, thus restoring keratinocyte migration capacity. These treatment modalities could represent a novel therapeutic approach for wound healing disorders.