The Challenge of Biofilms in Chronic Wounds:

Where do we go from here?

By Karen M. Cross, MD, PhD, FRCSC

The etiology of chronic wounds is of course complex, and now that we have more advanced diagnostic techniques available it is time to begin addressing the role that biofilms play in wound healing.

Biofilms are communities of bacteria that are present in as many as 60% of all chronic wounds. Though not all bacteria are pathogenic,[1,2] some do have a major impact on wound environments and healing potentials. Biofilm-based bacteria grow slower than free-living cells (making them intrinsically less susceptible to antibiotics) and produce a protective extracellular polymeric substance (EPS) that shields them from environmental insults and the immune system. The production of EPS is particularly challenging in wounds because it creates a barrier to phagocytosis. As a result, the natural mechanisms for bacterial eradication by the immune system are rendered ineffective. Chronic stimulation of the immune system without effectively eradicating the biofilm/bacteria causes collateral damage to the surrounding tissue, aggravates the wound and slows the healing process.

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Strength in Numbers

We now know that biofilms are the preferred mode of growth for bacteria both in the environment (river rocks, industrial pipelines) and on body surfaces (teeth, skin, catheters, bone, etc.). Biofilms are almost always multi-species, with diverse composition (Gram-negative and Gram-positive genera), and can even include pathogenic yeasts like *Candida albicans*. Many of these species grow better in a symbiotic biofilm than in isolation under standard laboratory conditions because organisms within a biofilm communicate via diffusible signaling molecules to co-ordinate their behaviour ("quorum sensing"). As a result, biofilms should be

thought of as a complex and highly adaptable consortium (akin to a multi-cellular organism), rather than as individual bacterial species.

Because multi-cellularity is a significant factor in virulence, it is important that future therapeutics take a more in-depth approach to diagnosing biofilm species composition using advanced molecular diagnostics rather than historical culture-based methods. Wolcott et al.[3] found that 62.5% of chronic wounds assessed with molecular techniques and treated with targeted antimicrobial therapy healed faster and more completely, versus 48.5% that were assessed with cultures and non-directed therapy. Dowd et al.[4] also showed that 90% of patients receiving personalized topical therapies were more likely to heal their wounds.

The Role of Debridement

Effective debridement, accompanied by the use of antimicrobial dressings to prevent the reformation of biofilm in the wound, is key to wound healing in the presence of a biofilm. Debridement may be by traditional (sharp) methods or through the use of one of several newly developed ultrasound-based debridement tools. Although expensive and sometimes messy, low-frequency ultrasound debridement is the most studied of these modalities and has been tested *in vitro* on single-species biofilms. These studies have shown that ultrasound is effective at breaking up the biofilm but does not affect bacterial viability.[5] However, in an *in vivo* situation, biofilm dispersal is advantageous as it allows for efficient phagocytosis and may make bacteria more susceptible to antibiotic treatment.

What now?

While major advances have been made in the field of basic biofilm biology in the past 10 years, clinical challenges remain. As a first step, we must make efforts to understand what debridement methods are most useful for the initial removal of biofilm (sharp, ultrasound, enzymatic) by comparing them in controlled studies. Once the wound is debrided, we must then endeavour to prevent a pathogenic biofilm from re-forming in the wound. The future of clinical biofilm research lies in understanding that the multi-cellular biofilm lifestyle cannot be treated by traditional antibiotic methods, and that marrying innovative basic science with controlled clinical studies are the way forward. For additional reading about biofilms in wounds, please see the references cited throughout the text and "Ten top tips: Understanding and managing wound biofilm."[6]

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References

1. Percival SL, McCarty SM, Lipsky B. Biofilms and wounds: An overview of the evidence. Adv Wound Care. 2015;4(7):373–81.
2. Peters BM, et al. Polymicrobial interactions: Impact on pathogenesis and human disease. Clin Microbiol Rev. 2012;25(1):193–213.
3. Wolcott RD, Cox SB, Dowd SE. Healing and healing rates of chronic wounds in the age of molecular pathogen diagnostics. J Wound Care. 2010;19(7):272–8, 280–1.
4. Dowd SE, et al. Molecular diagnostics and personalised medicine in wound care: Assessment of outcomes. J Wound Care. 2011;20(5): 232, 234–9.
5. Crone S, et al. A novel *in vitro* wound biofilm model used to evaluate low-frequency ultrasonic-assisted wound debridement. J Wound Care. 2015;24(2):64, 66–9, 72.
6. Keast DH, Swanson T, Carville K, Fletcher J, Schultz, Black J. Ten top tips: Understanding and managing wound biofilm. *Wounds International* 2014;5(2):20–4.

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