Understanding biofilm formation and biofilm-based wound care

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This paper explores the science that underpins the formation of biofilms in wounds and the techniques that are most effective when providing biofilm-based wound care. Wound bed preparation, debridement and dressing choice are extremely important when managing wounds with biofilms and each should be adapted according to the extent to which the biofilm dominates the wound bed. Methods for disrupting and suppressing biofilms are discussed as well as appropriate dressing choices.

The presence, attributes and effects of microorganisms in chronic wounds produce significant barriers to healing through increases in microbial load, increased exudate production and development of non-viable tissue[1]. Microbes are present on the wound beds of all wounds and, although not all wounds become chronic, microbial presence (with or without factors that impair the host's immune response) is at least partly responsible for all wounds that become chronic[2,3].

Microbes on the wound bed surface grow in both a planktonic phenotype (free-floating mobile single cells) and biofilm phenotype (attached sessile polymicrobial communities[4]. A wound biofilm — comprising a number of diverse microbial species that live in a protective, self-secreted matrix — is much more difficult for host immunity to handle and much more recalcitrant to treatment[5,6] *[Box 1]*.

Biofilm formation

After a microbe has attached to the wound bed or another microbe, biofilm begins to form. The microbes secrete polymeric substances (mainly sugars) that encase the rapidly growing microcolony. Within minutes, the microbial colony is securely encased in a self-secreted matrix that blocks penetration of antibodies, white blood cells, complement or other host immune responses[10,11]. This early biofilm is resistant to antibiotics and biocides[12,13]. Where a patient has a reduced immune response, such as immunocompromise, a metabolic disorder or vascular compromise, the microbes are able to build their protective shelter with little resistance[14].

Box 1.How biofilms delay healing

- Inflammation[7]
- Increased exudate[8]
- Host-cell senescence (a state of permanent cell-cycle arrest)[9]

Biofilm can comprise a wide range of microbial species, including bacteria and fungi, and becomes more difficult to eradicate as diversity increases[15]. This is because the different microorganisms can share metabolic substances[16], produce resistance molecules such as beta-lactamases[17] to protect their neighbours, and act in tandem (known as quorum sensing),[5,18] enhancing the individual microbes' abilities to function as pathogens against the host.

The presence of a protective matrix, quorum sensing that regulates microbial gene expression and the synergies posed by microorganisms all contribute to a biofilm's many defences. These include slow penetration of antimicrobials, depletion of antimicrobials, the ability to trigger an excessive stress response from the host's cells and altering the microenvironment to be less favourable towards healing.[19] Biofilms are difficult to eradicate due to these factors and the speed of their development and redevelopment after they are disrupted.

One particular challenge when treating wounds with biofilms is the slow penetration of biocidal substances into biofilm[20]. Dodds et al proposed that reactive substances such as hydrogen peroxide, gluteraldehyde, bleach, vinegar, non-bound iodine and soaps need hours of contact with a biofilm to even begin to reduce the microbial load[21].

Clinical characteristics of wound biofilm

In one study, the presence of biofilm was identified in 60% of biopsies of chronic wounds[2]. Although biofilm cannot be detected with the naked eye, performing a thorough assessment can help determine whether

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the microbial load has formed a biofilm and whether the wound has become — or is in danger of becoming — chronic[22]. A biofilm-dominated wound will demonstrate characteristics such as:

- Significant exudate
- Tenderness
- Reactive hyperaemia around the wound
- Progressive necrosis of the edge of the wound bed[23].

The wound bed will usually show secondary signs of infection such as friability or fibrosis, maceration, undermining/tunnelling and slough associated with chronic wounds[24].

Patients who experience these symptoms and accompanying delayed healing often believe there are responsible microbes that need to be 'cleansed' from the wound. In clinical practice, it has been observed that patients may 'manage' their own wounds with antimicrobial soap, peroxide, alcohol, acetic acid and dilute bleach (or even full-strength bleach). There have also been anecdotal reports of kerosene, mercurochrome, dimethyl sulfoxide, aspirin solution and other extremely harsh agents being used.

It is, therefore, important that clinicians provide appropriate biofilm-based wound care in order to optimise care of both the wound and the patient's wellbeing. Biofilm-based wound care employs multiple simultaneous strategies that suppress the biofilm below a level that causes disease which lets the host clear the chronic infection and heal the chronic wound[25].

Biofilm disruption and suppression

Biofilm-based wound care comprises interventions designed to break up biofilm, inhibit microbial cell-to-cell communication and prevent biofilm redevelopment[26]. It should be tailored to each patient based on a thorough holistic assessment of their medical history and status and of the wound and its characteristics in order to determine the extent to which biofilm-based wound care is required.

Debridement

In a wound dominated by biofilm, aggressive debridement of slough and the underlying tissue that contains biofilm is a key initial intervention to disrupt biofilm cells. It can also be used as an ongoing strategy for suppressing microbial regrowth and biofilm reformation[27].

Current opinion is that the biofilm must first be physically disrupted before cleansing can be effective. Disruption techniques include sharp debridement, energy-transfer methods (ultrasound[28] or pulse lavage[29]) or newer methods using hydrosurgical or radio frequency tools[30].

Cleansing

Antiseptic cleansing solutions — including common options such as hypochlorous acid, polyhexamethylene biguanide and phenoxyethanol — have, on their own, very little effect on an intact, mature biofilm[31]. The protective matrix of a mature biofilm will either counteract or retard penetration of these antiseptic wound-cleansing solutions and render them as effective as normal saline or tap water in combatting antimicrobial activity[32,33].

However, once a mature biofilm has been physically disrupted, it is significantly more susceptible to biocides and antibiotics during the period in which it tries to reconstitute[30]. Wound cleansing is performed to remove surface contaminants, loose debris, slough, softened necrosis, bacteria and/or remnants of previous dressings from the wound surface and its surrounding skin[34].

Dressing choice

After debridement and cleansing, the wound should be dressed with an appropriate antimicrobial dressing according to clinical indications (such as exudate levels and the need for odour management)[7,18,26,27]. This is particularly important during the first 24 hours after debridement and cleansing or after the first 24 hours of the initial development of biofilm. This period provides a 'therapeutic window for the application of topical antimicrobials,' as microbial cells involved in biofilm formation and reformation 'demonstrate increased sensitivity to antimicrobials and anti-biofilm agents at this time'[22]. Thus, in chronic wounds and even in wounds that are showing a normal or a sustainable wound-healing trajectory, it is important to protect the wound bed from the establishment of biofilm.

Conclusion

Biofilms contribute to non-healing in chronic wounds and they can be challenging to detect and remove. Targeting biofilms through wound cleansing is an important method for managing chronic wounds. For the uncontrolled chronic wound dominated by wound biofilm, more aggressive cleansing, energy transfer and/or sharp debridement is necessary to disrupt the protective matrix of

the biofilm. Antimicrobial cleansers can then be used to remove loose material and act against the newly exposed bacterial and fungal cells. Finally, an antimicrobial wound dressing should be applied to prevent reformation of biofilm. This provides some antimicrobial protection to the healing wound as it moves toward full re-epithelialisation. WME

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