Biofilms: A practice-based approach to identification and treatment

KEY WORDS
- Biofilm
- Chronic wound
- Debridement
- Identification
- Management pathway
- Treatment

A growing body of research evidence suggests that biofilms play an important role in chronic wounds and are often one of the causes of delayed wound healing. Biopsies from chronic wounds found that 60% of the specimens contain biofilm structures in comparison to only 6% of biopsies from acute wounds (James et al, 2008). Here, the author discusses the clinical relevance of biofilms and offers a practice-based approach to their identification and treatment with a suggested management pathway, utilising case study examples. The aim of care should be to prevent biofilm formation in the first instance, treat if biofilm present, and prevent reconstruction.

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Chronic wounds are a burden to the healthcare economy and have a significant impact on patients' quality of life. Wound complications are associated with longer and more intensive treatment, extended hospital stays or readmission, and specialist intervention. The experience of living with a chronic wound can have a significant impact on patient wellbeing (Wounds International, 2012).

The prevalence of people with at least one chronic or acute wound is 3.7 per 1000 of the population, with estimated treatment costs of £2.5–3.1 million per 100 000 people in the population, and approximately 79% of these wounds are treated in the community (Posnett et al, 2009). The cost of dressings and other materials account for only 17–22% of the total cost of providing wound care in the NHS, with hospital admissions from wound complications (e.g. infection) being the most expensive element of care (Drew et al 2007).

There are many reasons why wounds fail to heal, including multiple comorbidities, poor nutrition, and often failure by healthcare professionals to recognise and treat the underlying cause. Additionally, poor communication with patients and lack of engagement can lead to noncompliance with recommended treatment regimens. Localised problems at the wound bed also play an important role in nonhealing. The TIME framework (tissue, infection/inflammation, moisture balance and edge of wound) has been shown to be a useful tool in the management of chronic wounds (Schultz et al, 2003; Dowsett, 2008).

Recently, there has been a renewed interest in the concept of biofilms in chronic wounds (Leaper et al, 2012). A growing body of evidence suggests that biofilms play an important role in wound chronicity; one study found that 60% of chronic wound biopsies contained biofilm structures, but these structures were found in only 6% of biopsies from acute wounds (James et al, 2008). Biofilm may be an unrecognised but important barrier to healing in chronic wounds even where clinical infection is not evident (Edwards and Harding, 2004).

BIOFILM RECOGNITION

A biofilm is a microbially derived sessile community characterised by cells that are irreversibly attached to a substratum or interface or to each other, are embedded in a matrix of extracellular polymeric substances that they have produced, and exhibit an altered phenotype with respect to growth rate and gene transcription (Donlan and Costerton, 2002). The nature of biofilms make them less susceptible to immune defence, thus biofilm-associated infections can persist for extended periods (Percival et al, 2012).

While many studies confirm that chronic wounds often contain a poly-microbial flora, controversy remains with regard to whether these organisms directly contribute to nonhealing. It seems most likely that individual bacteria themselves are not directly responsible for nonhealing wounds.

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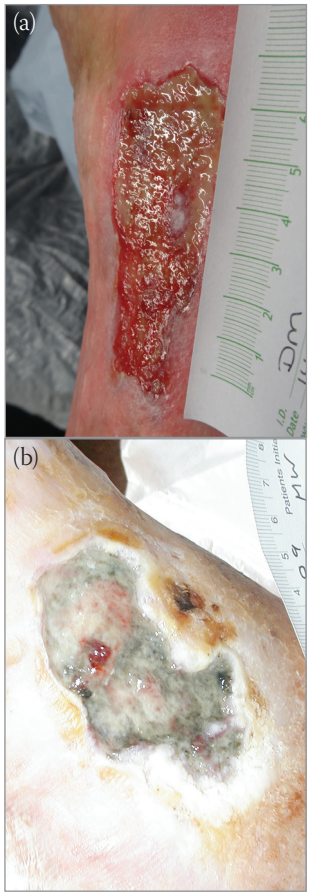


Figure 1. Examples of wounds in which biofilm communities have become large enough that they can be seen as (a) "shiny" or "slimy" structures on the wound surface, often with (b) the build up of slough despite frequent debridement.

Rather, there is a direct correlation between the presence of four or more distinct bacterial species in a wound and nonhealing – suggesting that mixed microbial populations are a cause of pathology (Dowd et al, 2008).

The most reliable method to confirm the presence of a biofilm is specialised microscopy. Many clinicians – especially those undertaking wound care in the community – will not have access to specialised microscopy for wound biofilm diagnosis. It is envisaged that diagnostic point-of-care testing for wound biofilms will ultimately be developed. However, until such tools exist, decisions about how to recognise and treat biofilms in chronic wounds remain a challenge for clinicians.

The author's clinical experience suggests that early identification and treatment of a biofilm in a wound can increase healing rates and improve patient wellbeing. Because they are microscopic structures, naked-eye identification of a biofilm poses a challenge. However, if biofilm communities become sufficiently extensive their presence may be indicated by the observation of "shiny" or "slimy" structures on the wound surface (*Figure 1a*). Wounds on which a large amount of slough builds up, despite frequent debridement, may be indicative of a biofilm (*Figure 1b*). Factors that may lead the clinician to suspect a wound biofilm include (Percival et al, 2012):

- Failure to close or progress to healing despite appropriate therapy/s.
- Exudate and malodour.
- Shiny, slimy wound surface.
- Persistent necrotic tissue.
- Persistent slough.
- Unresponsive to antimicrobials.
- Polymicrobial microbiology.

MANAGEMENT PATHWAY

Biofilm management needs to be addressed within the context of the holistic care of the patient, including wound assessment, addressing patient concerns, treatment of the underlying conditions, local wound management and wound bed preparation. The aim should be to prevent biofilm formation in the first instance, treat if a biofilm is present and prevent reconstruction. This multiple dynamic concurrent strategy approach is known as biofilm-based wound care (Wolcott R 2013; *Figure 2*).

Wound bed preparation is considered a significant component of strategies to prevent and control biofilm (Leaper et al 2012). Cleansing, debridement, and topical antimicrobials need to be considered in addressing wound biofilm.

The method of debridement selected should depend on the wound type, knowledge and skills of the clinician, and patient preference. Research into the management of wound biofilms to-date has focused on the use of sharp debridement and ultrasonic debridement (Wolcott et al 2008). Correctly performed, debridement removes devitalised tissues and their associated bacterial communities. While no single method of debridement has yet been shown to perform better than another in managing biofilm, it is clear that the disruption of biofilm that occurs during debridement is essential and should be undertaken regularly. Once a biofilm has been disrupted through debridement it is more vulnerable to treatment agents such as antimicrobials (Leaper et al, 2012).

Vigorous wound cleansing is also recommended for the removal and prevention of biofilm (Phillips et al, 2010a; Leaper et al, 2012). Some products – solutions containing surfactants and antimicrobials – are designed to aid physical cleansing by removal of debris and disrupting of biofilm.

Due to their polymicrobial nature, topical, broad-spectrum antimicrobial agents that kill – rather than inhibit – microorganisms are recommended for the local management of biofilms. These agents include nanocrystalline silver (Phillips et al, 2010b), iodine, polyhexamethylene biguanide (PHMB), and honey (Phillips et al, 2010a). There is currently not enough evidence to suggest conclusively which of the antimicrobials is most effective in managing biofilms, however one study demonstrated that cadexomer iodine penetrated biofilms more effectively than either silver or PHMB (Schultz et al, 2009). There is also evidence to suggest that healing rates are higher with the use of cadexomer iodine than with standard care (O'Meara, 2008).

It is recommended that antimicrobial dressings be used for 2 weeks initially and then the wound, patient, and management plan should be re-evaluated (Wounds UK, 2011). An emerging principle for the use of topical antimicrobials is

to change to a different antimicrobial if there has been no evidence of wound progress following an adequate period of exposure to a given agent (Phillips et al, 2010a). Some wounds respond well to topical antimicrobials but when the antimicrobial is discontinued the wound becomes static and symptoms (e.g. slough) return. It is not unusual for clinicians to repeat the use of an antimicrobial dressing in these patients or prolong their use, however long-term use of a topical antimicrobial should be avoided.

The enhanced ability of biofilms to resist traditional treatments has led to specific research into novel techniques to manage biofilms. For example, because bacterial growth is dependent on the availability of iron, interruption of bacterial iron metabolism is another potential mechanism to deter biofilm formation and growth. Thus, lactoferrin has been reported to inhibit bacterial growth by sequestrating available iron (Phillips et al, 2010a), but such agents are not widely available and their applicability in clinical practice continues to be investigated.

Two case studies are provided here (*Boxes 1–2*). They provide examples of biofilm management that were successfully applied in practice and resulted in wound progression.

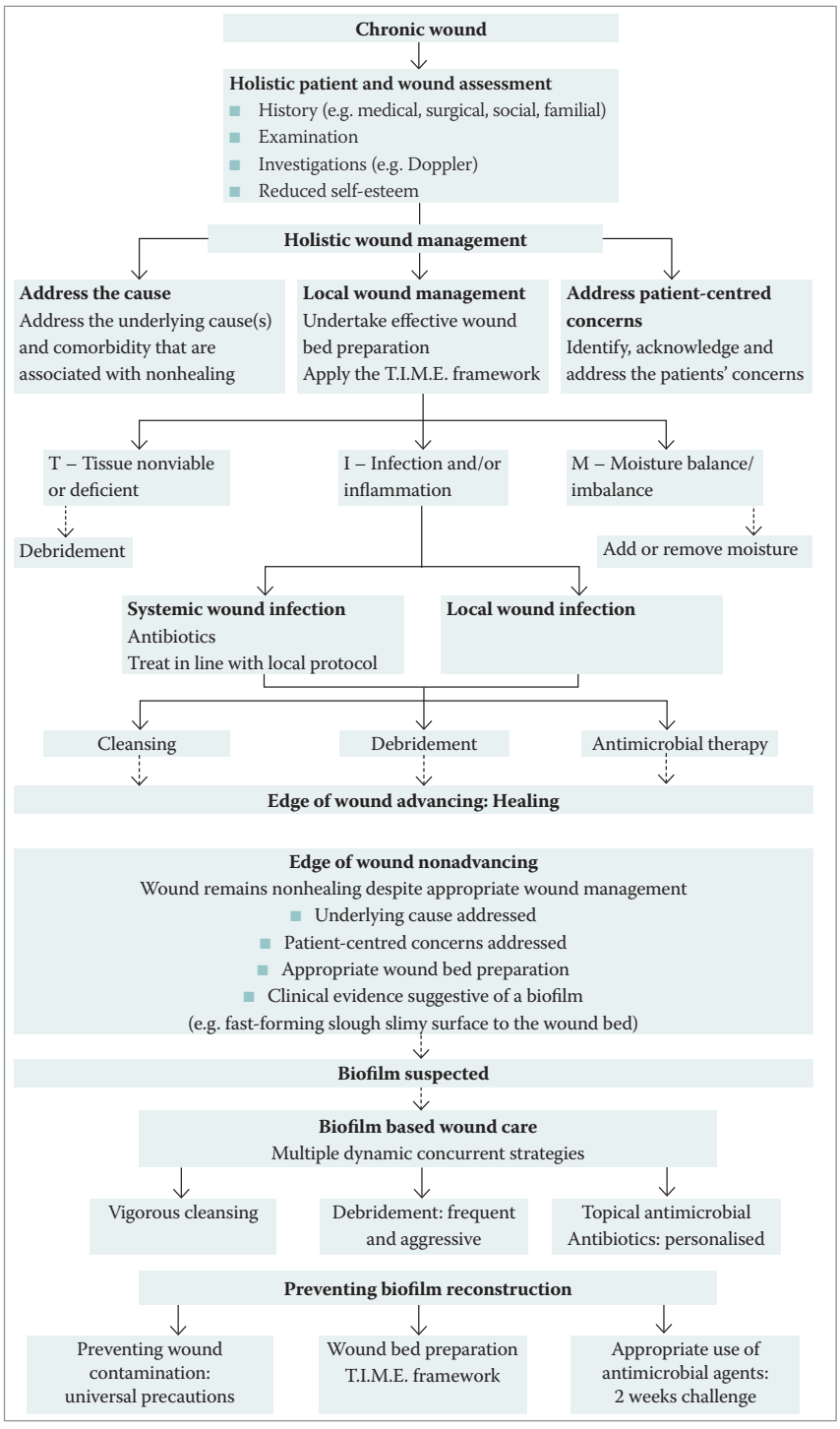
CONCLUSION

Measuring outcomes is becoming increasingly important in health care; services must demonstrate the quality improvement – both in terms of outcomes and cost-effectiveness – achieved by the interventions delivered. Appropriate use of antimicrobials in the treatment of wound infection and biofilm is an essential element of meeting this agenda and reducing the burden of chronic wounds, both for patients and the health economy.

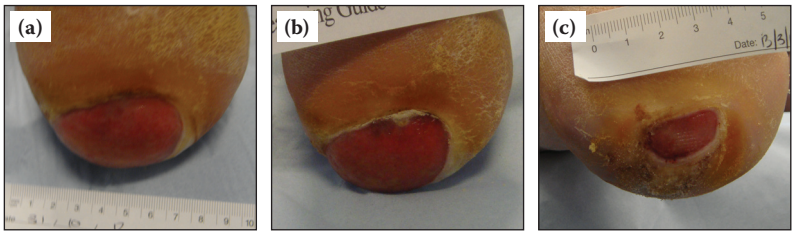
It is important to remember that there are many reasons why a wound may fail to heal. It is essential to reassess the patient and the wound frequently, ensure the underlying cause of the wound has been addressed, and apply the principles of good wound bed preparation to prevent or disrupt biofilm development. Cadexomer iodine has been shown to be effective in these circumstances.

It is equally important to remember that chronic wounds can affect patients' wellbeing, and this can further delay wound healing (Wounds International, 2012). Patients who have wounds that fail to progress to healing following the application of these principles should be referred for specialist wound assessment and advice. WUK

Figure 2. Management pathway to prevent and treat biofilms (adapted from Schultz et al, 2003).

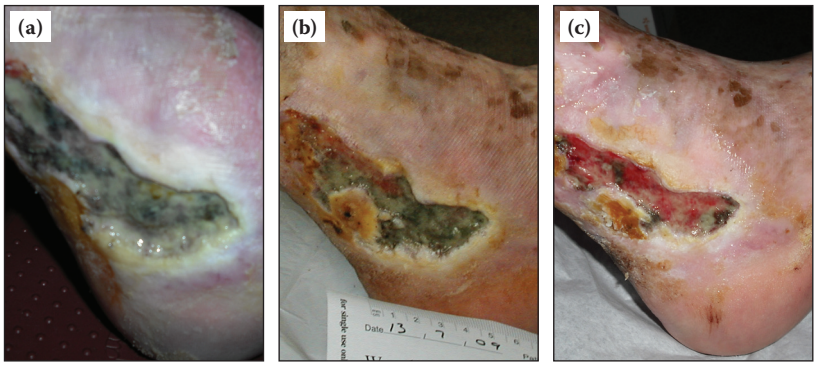


Case Study 1 – A diabetic foot ulcer



- A 63-year-old man with a diabetic foot ulcer **(a)** static for 7 months (7 cm × 5 cm).
- Red, friable granulation tissue was covered with a slimy structure.
- Silver dressings had been applied for 2 weeks without improvement **(b)**.
- A care plan was devised to improve the patient's glycaemic control, offload the ulcerated foot, and provide sharp debridement.
- A cadexomer iodine sheet dressing was selected to address the suspected biofilm and excess exudate; a hydrocellular heel dressing was selected as the secondary dressing.
- Within 3 weeks the ulcer reduced 40% (4 cm × 5 cm) in size **(c)**, the quality of the wound bed improved, and the wound was progression to healing.
- The patient was able to return to work.

Case Study 2 – A nonhealing venous leg ulcer



- A 68-year-old man with a nonhealing venous leg ulcer, unresponsive to compression therapy.
- The wound was covered by slough (100%), painful, and malodourous.
- Local wound infection was diagnosed and treated with silver for 2 weeks and multilayer compression bandages.
- Pain levels and exudate volume decreased and slough in the wound bed was reduced by 50%.
- Wound size remained static with slough rapidly reappearing; biofilm was suspected.
- A regimen of vigorous cleansing followed by dressing with a cadexomer iodine sheet dressing to address the suspected biofilm, and a foam dressing as a secondary dressing, was undertaken for a period of 4 weeks.
- The wound progressed to healing.

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