Biofilm can simply be described as a community of microorganisms encased in a matrix that provides protection against antimicrobial treatment and the host’s immune system. The National Institutes of Health (2002) estimated that more than 80% of human infections involve bacterial biofilm.

The role that biofilm plays in delayed wound healing is becoming increasingly recognised and researched. At least 78% of chronic wounds contain biofilm (Malone et al, 2017), and its presence contributes to chronicity (Metcalf and Bowler, 2013). The protection that biofilm gives to the microbial community explains why repeated treatment with antibiotics and antiseptics often fails in some hard-to-heal wounds (Bowler and Parsons, 2016).

This article describes what biofilm is, how it forms, and the characteristics that give it protection against host immunity and antimicrobial agents. It presents evidence of its role in wound chronicity, and provides clinical guidance on how to identify and manage wounds with suspected biofilm, using biofilm-based wound care (BBWC).

It also gives an overview of AQUACEL® Ag+ Extra™ dressing, an award-winning dressing that helps to disrupt biofilm, kill infection-causing microorganisms and prevent biofilm re-formation (Parsons and Metcalf, 2014; Bowler and Parsons, 2016; Parsons et al, 2016), and presents clinical evidence to support its use in BBWC.

**MICROORGANISMS IN BIOFILM**

Planktonic microorganisms are single-celled, free-floating cells that are metabolically active and may multiply rapidly within a wound (Bjarnsholt et al, 2016; Bourdillon, 2016). They are the building blocks of biofilm forming an initial attachment to the wound bed within minutes, and, in susceptible patients, can multiply and recruit other species of microorganisms to develop into mature biofilm communities.

As most antibiotics act on single key components of microbial metabolism (Bowler and Parsons, 2016), the metabolic activity of planktonic microorganisms makes them susceptible to the action of these drugs. The exception to this is in the development of antibiotic-resistant strains, such as meticillin-resistant *Staphylococcus aureus* (MRSA) or extended spectrum beta-lactamase (ESBL) producing *Pseudomonas aeruginosa* (Pastar et al, 2013; Bowler, 2018; Percival, 2018).

It is now accepted that microorganisms prefer to exist as biofilm on and in the human body, since this provides protection from environmental threats such as the host immune system and antimicrobial agents, i.e. antibiotics and antiseptics (Bowler and Parsons, 2016).

**BIOFILM CHARACTERISTICS**

Biofilm microorganisms are contained in a protective matrix of self-produced extracellular polymeric substances (EPS).

The EPS consists of a dense matrix of polysaccharides, proteins, lipids and extracellular DNA (of microbial or host origin). It encases the biofilm community and attaches to the wound bed, sometimes below the wound surface (Schultz et al, 2016), protecting the microorganisms.
Now it’s time to confront the biofilm villain

The dressing that gives you the weapons you need to attack the key local barriers to wound healing.

AQUACEL® Ag+ Dressing doesn’t just manage exudate and infection*1-5. It helps destroy biofilm too*6-8.

Find out more about AQUACEL® Ag+ Dressings at www.convatec.co.uk

*As demonstrated in vitro

within from attack and destruction by host immune cells, such as neutrophils and macrophages (Hurlow, 2016).

The EPS also allows microorganisms to withstand nutrient and moisture deprivation, as well as potentially harmful alterations in pH (Hurlow, 2016).

Importantly, the EPS acts as a protective barrier that reduces the effective penetration of antibiotics and antiseptics. It has been estimated that microorganisms in biofilm are 100–1,000 times less susceptible to antimicrobial agents than their planktonic counterparts (Wounds International, 2017).

Furthermore, microbial cells in the deeper layers of biofilm function at a slower metabolic rate. This allows them to be more tolerant of antibiotics, which target metabolically active cell sites (Bjarnsholt et al, 2017; Bowler and Parsons, 2016).

Microorganisms within biofilm use a process called quorum sensing to communicate with each other, promoting their survival as they are able to respond to environmental changes to thrive and replicate (Figure 1).

In biofilm, different microorganisms can group together to form a community. This means biofilm can vary in composition and characteristics, depending on the species involved.

Although a wound may contain a biofilm consisting of different microbial species, individual patches of biofilm may contain only one species (Cooper, 2010; Bjarnsholt et al, 2017). Biofilm is not uniformly distributed across a wound bed and may exist in separate colonies.

CHRONIC WOUNDS AND BIOFILM

A meta-analysis of nine studies by Malone et al (2017) determined that 78% of chronic wounds sampled contained biofilm.

The studies examined biopsy or debridement tissue from chronic wounds and used microscopy, with or without molecular analysis, to identify the presence of biofilm in a variety of chronic wound types. Six of the nine studies demonstrated biofilm in 100% of wounds examined.

‘It is thought that at least 78% of chronic wounds contain biofilm (Malone et al, 2017), and that its presence contributes to chronicity in some patients.’

The authors concluded that biofilm was likely to be present in all chronic wounds, with the lower prevalence in three of the studies being a result of methodology when taking the sample, rather than the absence of biofilm (Malone et al, 2017).

Biofilm can contribute to delayed wound healing by inducing the production of inflammatory mediators, such as neutrophil enzymes of the innate immune system (Watters et al, 2016), pro-inflammatory cytokines (Wolcott et al, 2008), and destructive proteases (Schultz et al, 2016).

Prolonged inflammation can result in damage to healthy tissue and lead to increased wound size, as well as skin maceration through prolonged production of and exposure to wound exudate, which itself may encourage the development of biofilm (Wolcott, 2017).

As well as keeping the wound bed stuck in a chronic inflammatory state, the presence of biofilm clearly increases the risk of full-blown clinical infection developing.

Several in vivo studies have also demonstrated that the physical presence of biofilm in the wound bed can delay healing by impeding granulation tissue formation and epithelial migration (Metcalf and Bowler, 2013; Bjarnsholt et al, 2017).

BIOFILM DEVELOPMENT RISK FACTORS

Systemic and local wound factors
that can result in delayed healing are well recognised (Bjarnsholt et al, 2017).

Systemic factors include co-morbidities such as diabetes, venous disease, malnutrition, malignancy and impaired immune response (James et al, 2008).

Local factors in the wound bed include the presence of slough and necrotic tissue, wound infection, chronic wound exudate that contains potentially harmful enzymes and microorganisms and the presence of biofilm (Table 1).

In some wounds, the presence of biofilm alone will be enough to result in delayed healing, yet in others, healing will eventually occur in the presence of biofilm, if the systemic/local factors delaying healing are addressed (Percival et al, 2015).

This demonstrates the unique interaction between the patient and biofilm (World Union of Wound Healing Societies [WUWHS], 2016), and the need to continually review factors contributing to non-healing.

Although there is limited information regarding specific risk factors for the development of biofilm, many of the same factors that delay wound healing are also thought to predispose to biofilm formation (Keast et al, 2014; Table 2).

IDENTIFYING BIOFILM

Recognising wound biofilm in clinical practice remains a challenge. Currently, the only way to detect biofilm involves advanced microscopy with or without molecular analysis in a laboratory setting (Keast et al, 2014).

Standard clinical microbiology culturing procedures only detect readily culturable organisms. Tissue biopsy or swabbing may miss the area of biofilm entirely due to its non-uniform distribution in the wound bed (Wysocki and Grinnell, 1990; Keast et al, 2014; Hurlow, 2016).

There is currently debate about the visualisation of biofilm in the wound. Some clinicians claim it can be seen as a shiny, translucent layer on the wound surface that re-forms quickly once removed (Dowd et al, 2011; Wolcott, 2015). Others state that biofilm cannot be seen with the naked eye (WUWHS, 2016).

There are indirect indicators for identifying biofilm. Following an algorithm (Figure 2) can help clinicians systematically to assess the potential for the presence of biofilm (Metcalf et al, 2014).

BIOFILM-BASED WOUND CARE

Management of a wound with suspected biofilm should aim to disrupt the biofilm, kill microorganisms and reduce the chances of biofilm re-forming (Wounds UK, 2017). BBWC is a term used for optimising several strategies to manage recalcitrant wounds and address factors that contribute to a delay in healing by targeting biofilm.

<table>
<thead>
<tr>
<th>Challenge</th>
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</tr>
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<tbody>
<tr>
<td>Exudate</td>
<td>Exudate in normal wound healing promotes denaturing of devitalised protein which supports autolysis (Hurlow, 2016). Chronic wound exudate does not have the active growth factors found in acute wound exudate and it can block the healing process, destroy the extracellular matrix (ECM) and become a ‘wounding agent’ itself (Barrett, 2017). Chronic wound exudate can contribute to the integrity of biofilm (Hurlow and Bowler, 2012; Hurlow, 2016)</td>
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<td>Wound infection occurs when microorganisms start to increase in numbers and overwhelm the host’s immune response. This response may be localised within the wound bed or systemic (IWII, 2016). It has also been suggested that infection is the most frequent complication in non-healing wounds (Gottrup et al, 2013; Barrett, 2017)</td>
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There are indirect indicators for identifying biofilm. Following an algorithm (Figure 2) can help clinicians systematically to assess the potential for the presence of biofilm (Metcalf et al, 2014).

It is currently recommended that biofilm should be presumed as a cause of delayed healing in chronic wounds that have not reduced in area >40% (or >50% for diabetic foot ulcers) after four weeks of optimal standard care for the wound type, including management of comorbidities and other factors that may be causing delayed healing (Wounds UK, 2017).

If presence of biofilm is suspected, biofilm-based wound care (BBWC) should be implemented.

Figures 3 and 4 show wounds that are non-healing, with biofilm suspected as a contributing factor to chronicity.

### Table 1: Local barriers to wound healing

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### Table 2: Risk factors for biofilm formation

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This should involve a protocol of care that takes a three-step approach:
- Assessment
- Management
- Monitoring/reassessment.

Assessment
Full holistic patient and wound assessment should be undertaken to determine any underlying factors that may be contributing to delayed healing. These include diseases, e.g. arterial disease, venous disease, diabetes, autoimmune diseases, such as rheumatoid arthritis or underlying cancers, current and previous medication, lifestyle choices and psychological status. In some patients, removing these barriers may result in healing.

Healthcare professionals should also examine the wound and record the findings. This should include wound type, location, duration, tissue type present (with percentages of sloughy, necrotic and granulation tissue being recorded), size (length, depth and width), exudate (colour, consistency and volume), odour, and condition of the wound edge (i.e. is there evidence of maceration). It is also important to identify any signs and symptoms of infection or suspected biofilm and to ask about current and previous wound management regimens (e.g. dressings, devices, antimicrobial agents) (Wounds International, 2017).

Management
Disruption of biofilm can be achieved by cleansing and debriding the wound. However, biofilm may be tolerant to gentle cleansing, so surgical or sharp debridement or the use of debridement pads or wipes to disrupt the biofilm is recommended.

Wound debris, which may contain biofilm fragments and planktonic microorganisms, should be removed from the wound where possible. As biofilm is not evenly distributed on and in the wound bed, regular, multiple attempts may be required to ensure most biofilm is disrupted (Wounds UK, 2017). Biofilm can re-form daily, probably within hours, so regular debridement is key to disrupt and reduce the amount of biofilm present and prevent its re-formation (Metcalf and Bowler, 2013; Hurlow, 2016; Morris et al, 2016; Malone and Swanson, 2017). Currently, debridement every 48–72 hours is recommended (Wolcott et al, 2010).

Following debridement, an appropriate dressing, ideally

Figure 2.
Clinical algorithm to help identify wound biofilm (Metcalf et al, 2014; adapted from the Journal of Wound Care 2014: 23(3): 137–8, 140–2).

Figure 3.
Surgical wound dehiscence, where biofilm is likely to be present. Sloughy tissue is evident around the wound.

Figure 4.
A static ulcer of more than six months’ duration in a patient with diabetes.

Photographs used with kind permission from their respective owners.
with anti-biofilm and an effective antimicrobial agent which can kill the biofilm and planktonic microorganisms released on disruption should be applied (Wounds UK, 2017). As with all dressing selection, other factors for consideration include the dressing’s ability to conform to the wound bed and surrounding skin and manage local wound conditions, such as exudate volume and periwound skin.

Monitoring/reassessment

It is important to continue to monitor/reassess the wound, and use dressings which maintain a moist wound environment while providing an effective antimicrobial agent until the wound shows signs of wound progression. However, antimicrobial agents should not be used indefinitely (WUWHS, 2008).

Wounds should be reassessed at every dressing change for signs of improvement, stasis or deterioration. Action to continue or cease antimicrobial use should be taken according to findings. In wounds where the infection has resolved, the antimicrobial agent can be discontinued. Where the wound has improved but there are also continuing signs of infection, continue treatment with the same or new topical antimicrobial and review again at two weeks (Edwards-Jones et al, 2016). With no improvement or deterioration of the wound, holistic assessment should be repeated and reasons for delayed healing/deterioration identified and addressed where possible.

Ongoing assessment provides the opportunity to identify any changes in a patient’s wound status, so that these can be managed in a timely manner to prevent further wound deterioration (Brown, 2017; Mahoney, 2017).

It is highly unlikely that any protocol of care can eliminate all biofilm, but by carrying out BBWC, antimicrobial agents are able to work more effectively and reduce the bioburden enough to encourage wound healing. Even when the wound appears to be progressing, biofilm may re-form and result in delayed healing in the future, so this should always be considered (Wounds UK, 2017).

AQUACEL® AG+ EXTRA™ DRESSING

AQUACEL Ag+ Extra dressing was specifically developed to meet the challenges of slow-healing, static or deteriorating wounds, which are likely to be compromised by biofilm.

The dressing contains a unique anti-biofilm formulation that is indicated for moderately to heavily exuding, infected chronic and acute wounds, or wounds at risk of infection. However, AQUACEL Ag+ Extra and Ribbon dressings can also be pre-moistened for use on lower exuding or drier wounds. This method should only be used in the absence of a more suitable dressing for the level of exudate being produced.

AQUACEL Ag+ Extra dressing contains two technologies that work together to manage key local barriers to wound healing (i.e. excess exudate, infection and biofilm), namely:

- Ag+ Technology
- Hydrofiber® Technology

Ag+ Technology

The Ag+ Technology used in AQUACEL Ag+ Extra dressing has been specifically designed to help disrupt biofilm and prevent its re-formation (Parsons, 2014; Bowler and Parsons, 2016; Parsons et al, 2016).

Hydrofiber® Technology

The Hydrofiber® Technology in AQUACEL Ag+ Extra dressing transforms into a gel on contact with wound exudate. In action, it:

- Locks in* wound fluid and bacteria to help minimise cross-infection and reduce lateral spread of fluid to help prevent maceration (Bowler et al, 1999; Walker et al, 2003; Newman et al, 2006; Walker et al, 2007; Walker and Parsons, 2010)
- Micro-contours* and forms an intimate contact with the uneven wound bed, helping to minimise the dead spaces in which microorganisms can grow (Jones et al, 2004; Bowler et al, 2010)
- Balances* wound fluid, adding and removing moisture to maintain a moist wound healing environment. The cohesive gel helps minimise pain associated with dressing changes (Barnea et al, 2004; Kogan et al, 2004; Foster et al, 2004).

Clinical efficacy

AQUACEL Ag+ Extra dressing has facilitated wound healing in a number of real life clinical evaluations, studies and in vivo studies.

For example, a real life clinical evaluation of AQUACEL Ag+ dressing was undertaken on 113 cases of challenging, at-risk,
infected acute and chronic wounds, of which 74% had suspected biofilm (Walker et al., 2015). Local standard protocols of care were followed except for the replacement of the current primary dressing with AQUACEL Ag+ dressing. Following an average treatment period of 4.1 weeks, the majority of wounds had either healed or improved (n=107, 94.7%), providing evidence of the benefits of AQUACEL Ag+ dressings for non-healing, chronic and acute wounds which may be impeded by suspected biofilm.

A second study looked at the clinical safety and effectiveness of AQUACEL Ag+ Extra dressing (Metcalf et al., 2017). The dressing was evaluated for a maximum of four weeks in 112 mixed wounds (111 patients), which had been present for an average of 12 months and were thought to be impeded as a result of suspected biofilm or infection. Biofilm was suspected in over half of the wounds (54%). Before the study, while iodine, honey and polyhexamethylene biguanide (PHMB)-containing dressings had been used, silver dressings were the most frequently used, with 16 patients being treated with antibiotics. Following local standards of care but introducing AQUACEL Ag+ Extra dressing to replace the primary dressing previously used, biofilm suspicion fell from 54% to 27% of wounds. Exudate volume reduced from predominantly high or moderate to low or moderate.

The results of this clinical evaluation provide evidence of the benefits of AQUACEL Ag+ Extra dressing for non-healing chronic and acute wounds that may be impeded by suspected biofilm. Seventy-eight percent of wounds progressed towards healing or went on to heal (65% improved, of which 13% healed), with an average management period of 3.9 weeks.

CONCLUSION

Chronic wounds pose a challenge to clinicians delivering wound care.
in the community, and the role of biofilm should be considered in wounds that fail to heal within an expected timeframe despite best practice. For these wounds, BBWC should be implemented.

AQUACEL Ag+ Extra dressing contains two technologies — Ag+ Technology and Hydrofiber Technology — that work in synergy to help disrupt biofilm, exposing microorganisms to broad-spectrum ionic silver and preventing biofilm re-formation (Parsons et al, 2016). Its successful use in clinical practice makes it an attractive option for the management of biofilm in chronic wounds. 

REFERENCES

* As demonstrated in vitro

AQUACEL Ag+ Extra dressing — winner of the World Union of Wound Healing Societies Most Innovative Dressing Award, 2016.


Revalidation Alert

Having read this article, reflect on:

- Factors that result in delayed healing
- The importance of disrupting and preventing biofilm reformation
- The key benefits of using Aqualcel Ag+ Extra dressing to manage hard-to-heal wounds.

Then, upload the article to the free JCN revalidation e-portfolio as evidence of your continued learning: www.jcn.co.uk/revalidation
Wound Care People Ltd

KEY POINTS

- Biofilm has been microscopically observed in 78% of non-healing chronic wounds (Malone et al, 2017).

- Microorganisms prefer to exist as biofilm, since this provides protection from environmental threats such as the host immune response and antimicrobial agents.

- The role of biofilm should be considered in wounds that fail to heal within an expected timeframe despite best practice.

- Management of a wound with suspected biofilm should aim to disrupt and reduce the chances of it re-forming by following a protocol of care involving assessment, management and monitoring/reassessment.

- AQUACEL® Ag+ Extra™ dressing was developed to meet the need for an antimicrobial dressing with anti-biofilm activity, and contains two technologies that work synergistically to achieve this, namely Ag+ Technology and Hydrofiber® Technology.


Wound Care People Ltd