Next-generation antimicrobial dressings
AQUACEL™ Ag+ Extra™ and Ribbon

antimicrobial tested infection control
absorbency strength
comfortable advanced
exudate control evidence customizable
healing protection
conformable quality of life
biofilm control
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Understanding Local Barriers to Wound Healing

The Impact of Delayed Wound Healing

In developed countries, about 1–2% of the population can expect to experience a chronic wound during their lifetimes. There is a high associated expense: for example, the UK National Health Service estimated the cost of caring for patients with chronic wounds as £2.3–3.1 billion per year based on 2005–6 figures. Wounds that are deteriorating (ie increasing in size, exude or odour) or severe (infected or with other complications that require hospital admission) cost two to six times more per week to treat than do wounds that are progressing to healing.

Excess Exudate

Wounds invariably contain bacteria and other microorganisms, and in well cared for healthy individuals, most heal without problems. However, the presence of microorganisms in a wound, even in the absence of signs of local or systemic infection, has long been recognised as a potential cause of delayed healing. Bacteria in wounds exaggerate the inflammatory response, inducing the release of protein-digesting enzymes and reactive oxygen species which, in excess, can damage tissue. Inflammation increases the permeability of blood vessels in the wound, increasing exudate production, which in turn may cause pain, wound enlargement, and maceration and excoriation of the wound bed and periwound skin. These effects can slow or stall the healing process, or even lead to deterioration and enlargement of the wound. Underlying comorbidities can also result in inflammation and production of excess exudate, so patient assessment should be holistic (Box 1).

Infection

When a wound becomes infected, microbes invade and damage deeper tissues. Bacteria can produce localised problems — eg pain, erythema, inflammation, excess exudate — or result in systemic illness (sepsis). Infection can turn an acute wound into a chronic wound, prolonging treatment or resulting in hospital admission, both of which can significantly increase the costs of care.

Biofilm

In recent years, research has recognised that, in addition to existing in a free, planktonic form, microorganisms in wounds can exist as biofilm, which is increasingly implicated in delayed wound healing. The inter-relationship between biofilm, excess exudate and infection will be explored in this article. (See Table 1, page 4, for a summary of key biofilm studies.)

What is biofilm?

Biofilm comprises communities of microorganisms that secrete a hydrated matrix of polysaccharides, proteins and DNA (extracellular polymeric substance; EPS). The matrix varies in composition and characteristics depending on the microorganisms involved, but provides protection and attachment to a surface such as the wound bed. In environmental, industrial and medical settings, biofilm is prevalent and the predominant form in which bacteria exist. In humans, biofilm contributes to a range of infections, and is implicated in at least 80% of bacterial infections. In the United States, an estimated 17 million people annually are affected by chronic biofilm-related infections, costing approximately USD94 billion. A study that used light microscopy and electron microscopy to identify biofilm in wounds found that 60% of chronic wound debridement samples contained biofilm, although biofilm was found in only 6% of acute wound biopsies.
How does biofilm form?
Most wound pathogens are biofilm-producers. Planktonic bacteria attach to a surface such as a wound bed, and start to multiply and secrete the surrounding EPS matrix (Figure 1). As they multiply, bacteria adapt to their environment to promote survival. For example, biofilm formation is controlled by a type of bacterial communication known as quorum sensing. As biofilm develops and matures, it attaches more firmly to the surface and can shed planktonic bacteria and fragments of biofilm to seed biofilm elsewhere.

How biofilm protects bacteria
Microorganisms within biofilm exhibit greater tolerance to the immune response and antimicrobial agents. Mechanisms for this are understood to be:

- **Blocking** — the matrix prevents antimicrobial agents and inflammatory cells from penetrating the biofilm efficiently, may inactivate antibodies and inhibits envelopment of bacteria by immune cells.
- **Mutual protection** — the different species of bacteria may cooperate, e.g., antibiotic-resistant bacteria may secrete enzymes that protect other bacteria and transfer genes that confer resistance.
- **Reduced growth rate** — the metabolic rates of some of the bacteria in biofilm slow considerably as the biofilm matures, to the point they ‘hibernate’ (quiescence), protecting them from some antibiotics, which require metabolic activity and microbial growth to work.

How biofilm can delay healing
There are many mechanisms by which biofilm may be implicated in delayed healing, with a key mechanism being the persistent low-grade inflammatory response. The immune system attempts to attack biofilm by secreting high levels of proteases (e.g., matrix metalloproteinases, elastase), antimicrobial enzymes (e.g., myeloperoxidase, lysozyme) and reactive oxygen species (ROS), which may not be effective. These factors stimulate the production of excess exudate, which may encourage biofilm growth and, as a result, increase the risk of infection. The ROS and enzymes in the exudate may also have unintended effects and damage healing and normal tissue, slowing healing and possibly enlarging the wound. In controlled in vivo studies, biofilm has been found to impair granulation tissue formation and epithelialisation, acting as a physical barrier to the wound healing process. Biofilm may also shed bacteria, which can also cause localised and systemic infection if invasive, and encourage development of further areas of biofilm within the wound.

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FIGURE 1: Development and maturation of biofilm in a wound
Identification of biofilm is a major challenge. Currently only specialised microscopy can definitively detect biofilm; as such, the development of a point-of-care test is needed. However, clinical studies have suggested it may be possible to differentiate biofilm from slough by appearance and behaviour:

- **Slough** — comprises dead or devitalised wound tissue that is continuous with the underlying viable tissue.
- **Biofilm** — is derived largely from microorganisms and may form shiny, gel-like, translucent substances, or slimy patches or layers in the wound bed, and reforms often daily, but sometimes within hours, after debridement. The finding that at least 60% of chronic wounds contain biofilm suggests that a high index of suspicion for biofilms is warranted in wounds that are not healing in a timely manner, even with the most appropriate wound management and use of antimicrobial agents. Mature biofilm is also tolerant of antimicrobial therapy and can reform quickly when physical removal is attempted. However, biofilm tolerance appears to be reduced for a day or so after debridement, as remaining bacteria are exposed and more vulnerable.

Managing wounds containing biofilm

Biofilm-based wound care is a term for using multiple strategies to manage chronic wounds suspected of containing biofilm. Such strategies aim to reduce the amount of biofilm in the wound and encourage a state where it is more susceptible to antimicrobial agents, and prevent reformation of the biofilm. The principles of standard wound care must also be employed. Clinical observation has suggested that wound biofilm is linked to underlying pathophysiological factors such as peripheral arterial disease, wound infection, osteomyelitis and moisture imbalance, making it crucial that clinicians assess and address all factors that may be contributing to wound chronicity. Further, it is important to follow a protocol of care that incorporates cleansing and/or debridement, and focuses on selection of the appropriate antimicrobial dressing to manage excess exudate, infection and biofilm (Box 2).

Reducing biofilm

Debridement does not eradicate biofilm, but can remove the bulk and temporarily disrupt what remains.
TABLE 1: Key studies on biofilm in wounds

<table>
<thead>
<tr>
<th>Reference</th>
<th>Title</th>
<th>Study type</th>
<th>Main conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>General review</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>■ A growing body of evidence shows biofilm exists in at least half of chronic wounds and are implicated in delayed healing</td>
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<td></td>
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<td>■ Biofilm could be contributing many billions of dollars to the cost of chronic wounds worldwide</td>
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<td>■ Biofilm creates a low-grade, persistent inflammatory response and impairs epithelialisation and granulation tissue formation</td>
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<td></td>
<td>■ The best available protocol to care for wounds with suspected biofilm is debridement, cleansing and antimicrobial dressings</td>
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<td></td>
<td></td>
<td></td>
<td>■ A point-of-care biofilm detection test is needed</td>
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<tr>
<td>Presence in chronic wounds</td>
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<tr>
<td>James, et al. Wound Repair Regen 2008; 16: 37–44&lt;sup&gt;10&lt;/sup&gt;</td>
<td>Biofilms in chronic wounds</td>
<td>Microscopic, culture and molecular examination of 66 wound tissue samples for biofilm</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>■ Microscopy revealed biofilm in 60% of chronic wound debridement samples and 6% of acute wound biopsies (P&lt;0.001)</td>
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<tr>
<td></td>
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<td></td>
<td>■ All chronic wound types are equally likely to contain biofilm</td>
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<td></td>
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<td>■ The biofilms contained polymicrobial communities; no two specimens had the same mix of microorganisms</td>
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<td></td>
<td></td>
<td>■ Culture analysis showed that 86% of wounds were colonised by bacteria (60% by S. aureus and &lt;30% by P. aeruginosa)</td>
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<td></td>
<td>■ Large bacterial aggregates were detected in 59% of samples; as 70% were P. aeruginosa, S. aureus is overrepresented in culture analysis</td>
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<tr>
<td>Animal model of biofilm management</td>
<td></td>
<td></td>
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<tr>
<td>Seth, et al. Plastic Reconstr Surg 2012; 129(2): 262e–74e&lt;sup&gt;24&lt;/sup&gt;</td>
<td>Treatment of Pseudomonas aeruginosa biofilm–infected wounds with clinical wound care strategies: a quantitative study using an in vivo rabbit ear model</td>
<td>Rabbit ear wounds colonised with P. aeruginosa and (I) alternate day debridement, (II) lavage, (III) Silvadene, (IV) lavage + Silvadene, or (V) initial debridement, daily lavage and Silvadene</td>
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<td></td>
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<td>■ Controls healed better than biofilm-colonised wounds (P=0.01)</td>
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<td></td>
<td></td>
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<td>■ Protocols (I), (II) and (III) showed no improvement in bacterial counts or healing</td>
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<td></td>
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<td></td>
<td>■ Protocols (IV) and (V) achieved decreased bacterial counts (p=0.05) and better healing (p=0.05) compared with untreated biofilm</td>
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<tr>
<td></td>
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<td></td>
<td>■ Scanning electron microscopy (SEM) of wounds treated with protocol (V) showed biofilm was temporarily disrupted and reformed within 24 hours</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>■ Biofilm delays wound healing</td>
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<tr>
<td>Clinical management</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wolcott and Rhoads. J Wound Care 2008; 17(4): 145–55&lt;sup&gt;25&lt;/sup&gt;</td>
<td>A study of biofilm-based wound care (BBWC) in subjects with critical limb ischaemia</td>
<td>Retrospective study of healing in patients with critical limb ischaemia and a wound requiring &gt;5 visits to the clinic; n=190</td>
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<td></td>
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<td></td>
<td>■ Patients had received BBWC that included sharp or ultrasonic debridement and anti-biofilm strategies, eg lactoferrin, xylitol and antimicrobial agents</td>
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<td></td>
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<td>■ 77% of patients showed complete healing, and 23% were non-healing</td>
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<tr>
<td></td>
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<td>■ When compared with a study of similar patients who did not receive BBWC, healing rates in this study were significantly higher (P&lt;0.05)</td>
</tr>
<tr>
<td>Hurlow and Bowler. Ostomy Wound Manage 2009; 55(4): 38–49&lt;sup&gt;26&lt;/sup&gt;</td>
<td>Clinical experience with wound biofilm and management: a case series</td>
<td>Case series; n=4</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>■ All patients presented with or developed suspected wound biofilm</td>
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<tr>
<td></td>
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<td></td>
<td>■ Suspected biofilm differed from slough: it had a cloudy, translucent, viscous, gel-like appearance, and could be debrided from the wound bed with minimal trauma</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>■ Different strategies are required to manage slough and biofilm, and perseverance is required when managing biofilm</td>
</tr>
<tr>
<td>Kennedy, et al. Burns 2010; 36: 49–56&lt;sup&gt;27&lt;/sup&gt;</td>
<td>Burns, biofilm and a new appraisal of burn wound sepsis</td>
<td>Microscopic examination of severe burn tissue samples from 11 patients</td>
<td></td>
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<tr>
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<td>■ Light microscopy revealed multiple large aggregates of bacteria (biofilm) on the wound surface and penetrating the wound bed</td>
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<td></td>
<td>■ SEM revealed mixed biofilm, particularly on the surface of the escharotomy sites</td>
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<tr>
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<td></td>
<td></td>
<td>■ Finding of biofilm in an escharotomy site as early as 7 days is evidence for the early excision and coverage of burn wounds</td>
</tr>
<tr>
<td>Hurlow and Bowler. J Wound Care 2012; 21(3): 109–19&lt;sup&gt;27&lt;/sup&gt;</td>
<td>Potential implications of biofilm in chronic wounds: a case series</td>
<td>Case series; n=9</td>
<td></td>
</tr>
<tr>
<td></td>
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<td></td>
<td>■ This case series considered the presence of biofilm in relation to other pathophysiological factors, eg peripheral arterial disease, wound infection, osteomyelitis and moisture imbalance</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>■ Infection — biofilm may be linked to acute and chronic wound infection, and may be a precursor to an infection state or osteomyelitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>■ Moisture imbalance — poor exudate management, biofilm formation, infection and increased exudation may form a self-perpetuating cycle</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>■ Peripheral arterial disease — the hypoxic wound environment may encourage biofilm formation</td>
</tr>
</tbody>
</table>
This stimulates biofilm metabolic activity, reducing the tolerance of the remaining biofilm and increasing susceptibility to antimicrobial agents and the immune response. Cleansing with a wound irrigation solution may also reduce biofilm burden by aiding removal of biofilm and other wound debris. Biofilm can be further reduced by applying topical agents that have proven anti-biofilm activity.

Preventing biofilm reformation

Biofilm may reform in a cleansed/debrided wound due to growth of biofilm fragments that remain after initial biofilm removal. Preventing reconstitution involves preventing reintroduction of microorganisms by using barrier dressings, managing exudate and using topical antimicrobial agents to kill planktonic bacteria and manage remaining biofilm bacteria (e.g., silver, iodine, polyhexamethylene biguanide). Agents that interfere with biofilm formation (e.g., lactoferrin or xylitol) may become options, but require further investigation.

AQUACEL™ Ag+ dressings (Extra™ and Ribbon options) are next-generation antimicrobial dressings designed specifically to address excess exudate, infection, and biofilm, three of the key local barriers to wound healing.

REFERENCES


NEXT-GENERATION ANTIMICROBIAL DRESSINGS: AQUACEL™ AG+ EXTRA™ AND RIBBON | 5
DESIGNING A DRESSING TO ADDRESS LOCAL BARRIERS TO WOUND HEALING

FROM BARRIER TO BIOFILM
The skin provides a very effective barrier against the environment but, once the skin has been damaged and a wound established, microbial contamination is inevitable. Contamination can lead to colonisation and, if unchecked by the patient’s immune system or appropriate treatment, to the formation of biofilm. The effect of biofilm varies, but generally is known to cause inflammation¹ and the consequent continuous generation of excess exudate, which can lead to delayed healing and local or spreading infection².

DEVELOPMENT OF AN ENHANCED ANTIMICROBIAL DRESSING
A growing understanding of the role biofilm plays in delayed wound healing, and knowledge of the composition and structure of biofilm (see pp1–5), has led researchers to develop Ag+ Technology³. This has strong synergistic effects between the broad-spectrum antimicrobial activity of ionic silver (as contained in AQUACEL™ Ag dressing; Figure 1, Box 2) and specific compounds that aid biofilm disruption and removal efficacy. The combination of Ag+ Technology and established Hydrofiber™ Technology (to manage exudate and the wound environment; Figure 1) has resulted in next-generation AQUACEL™ Ag+ dressings (Extra™ and Ribbon options).

EVIDENCE OF ENHANCED DRESSING PERFORMANCE
These dressings manage exudate and boost the effectiveness of the ionic silver against biofilm, thereby reducing infection risk without the need to increase the silver content (see Figure 1, Box 4). A series of laboratory in vitro and in vivo experiments and clinical studies demonstrate the efficacy of AQUACEL Ag+ dressings.

Disrupts, kills, removes and prevents biofilm reformation (in vitro)
A laboratory model was developed to evaluate the antimicrobial activity of AQUACEL Ag+ Extra dressing against pathogenic wound bacteria in biofilm⁹,¹⁰. Biofilm was grown on cotton gauze by agitating microbes in a low-nutrient medium over 48 hours. The presence, maturity and structure of the biofilm was confirmed by confocal laser-scanning microscopy. Gauze–biofilm substrates were then transferred to agar plates mounted in a leather-surfac ed holder to create a simulated biofilm-colonised wound model (Figure 2). Dressings were applied to the biofilm surface, hydrated and covered with an appropriate secondary dressing. After incubation, the killing effect of the dressing on biofilm bacteria was assessed at several points over five days.

Author: Dave Parsons, Director, Science and Technology, Global R&D, ConvaTec

FIGURE 1: Progress in Hydrofiber™ dressing technology

FIGURE 2: Simulated biofilm-colonised wound model

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1. Hydrofiber™ Technology in dressings:
- Adapts to the wound*
- Readily cut to size, folded or packed
- Gels instantly, absorbing exudate and preventing it from spreading*
- Traps exudate and its bacterial and inflammatory contents*
- Conforms to the wound bed, eliminating free fluid*
- Provides a moist, non-adhesive contact layer which encourages autolytic debridement and facilitates the removal of foreign matter

2. Ionic silver added:
- Exhibits broad-spectrum antimicrobial activity⁴–⁷*
- Helps treat wound infection
- Helps prevent cross-contamination/infection

3. Strengthening yarns added and dual-layer design developed:
- Absorption increases by 50%*¹
- Enhanced strength allows complete dressing removal, even when saturated (nine times stronger)²

4. Ag+ Technology developed:
- Kills bacteria⁹,¹⁰*
- Disrupts and removes biofilm*¹¹
- Prevents reformation of biofilm⁹,¹⁰*

*as demonstrated in vitro
Biofilm reformation was also assessed by inoculating fresh bacteria onto the gauze substrate beneath the dressing, followed by incubation and assessment of bacterial viability over subsequent days.

A single dressing application eradicated mature *Pseudomonas aeruginosa* biofilm in four days (Figure 3) and community-associated meticillin-resistant *Staphylococcus aureus* (CA–MRSA) biofilm in five days (Figure 4), confirming killing and inferring disruption of biofilm. The same dressing subsequently was shown to control bioburden after a simulated contamination event, proving the dressing’s ability to prevent biofilm reformation (Figures 3 and 4).10

To further investigate the physical disruption and removal of biofilm, a chemical assay was devised11. *S. aureus* biofilm was grown for 24 hours on a filter disc; planktonic bacteria were removed by rinsing with saline, and then the filters were dressed with saline-hydrated dressings. At 24 hours, dressings were removed and the residue on the filter disc assayed for potassium (as a marker of mass of biofilm removed) and silver (as an indicator of transferred antimicrobial activity and hence biofilm disruption) (Table 1).

Hydrofiber Technology has some effect on biofilm, one that is enhanced by the addition of ionic silver. Ag+ Technology not only further increases the dressing’s ability to physically remove biofilm, but also disrupts the structure of the residual biofilm so that ionic silver can more efficiently apply its antimicrobial effect.

**TABLE 1: Biofilm removal and silver penetration into residual biofilm after a single dressing application for 24 hours**

<table>
<thead>
<tr>
<th>Dressing</th>
<th>% biofilm removed</th>
<th>Relative concentration of silver</th>
</tr>
</thead>
<tbody>
<tr>
<td>AQUACEL™</td>
<td>37</td>
<td>0.0</td>
</tr>
<tr>
<td>AQUACEL™ Ag</td>
<td>66</td>
<td>1.0</td>
</tr>
<tr>
<td>AQUACEL™ Ag+*</td>
<td>78</td>
<td>4.0</td>
</tr>
</tbody>
</table>

**Note**

* Dressing did not contain strengthening yarn or have the additional absorptive capacity of AQUACEL™ Ag+ Extra™ dressing.

**Removes the biofilm barrier to enable healing (in vivo)**

Using an independent medical research laboratory and a scientifically validated *in vivo* biofilm-colonised full-thickness wound model12, the ability of dressings to promote healing in the presence of established biofilm was studied. Compared to an antiseptic control dressing (a commercially-available polyhexamethylene biguanide [PHMB] gauze dressing), AQUACEL Ag+ dressing* showed a 95% greater reduction in biofilm after six days of bi-daily dressing changes.
This treatment allowed more rapid wound healing and wounds had an average (by area) of 48% more granulation tissue and 24% more epithelial tissue than with the PHMB gauze dressing in the same six-day period (Figure 6)\(^13\). Similar observations of faster healing — compared to a PHMB gauze dressing — were observed in a further study in which the wounds contained a mixed-species \textit{P. aeruginosa} and \textit{S. aureus} biofilm (Figure 7)\(^14\).

\textbf{FIGURE 5: Reduction in biofilm after six days of bi-daily dressing changes. Key: }\textcolor{blue}{\textbullet} = polyhexamethylene biguanide gauze; \textcolor{green}{\textbullet} = AQUACEL\textsuperscript{TM}; \textcolor{red}{\textbullet} = AQUACEL\textsuperscript{TM} Ag\textsuperscript{+}; n=6

\textbf{FIGURE 6: Granulation and epithelial tissue growth after six days of bi–daily dressing changes. Key: }\textcolor{blue}{\textbullet} = polyhexamethylene biguanide (PHMB) gauze; \textcolor{green}{\textbullet} = AQUACEL\textsuperscript{TM}; \textcolor{red}{\textbullet} = AQUACEL\textsuperscript{TM} Ag\textsuperscript{+}; n=6

\textbf{FIGURE 7: Healing of wounds colonised with a mixed-species \textit{Pseudomonas aeruginosa} and \textit{Staphylococcus aureus} biofilm beneath polyhexamethylene biguanide (PHMB) gauze and AQUACEL\textsuperscript{TM} Ag+ dressing*}

\textbf{Note}

Dressing did not contain strengthening yarn or have the additional absorptive capacity of AQUACEL\textsuperscript{TM} Ag Extra\textsuperscript{TM} dressing.

\textbf{Finally, when tested in a controlled, non-comparative clinical study of human subjects with venous leg ulcers that were either clinically infected (n=10) or showing at least three of the five classic signs of infection (pain, erythema, oedema, heat, and purulent exudate) (n=32), AQUACEL Ag+ dressing* supported healing in both groups (Figure 8). Improved healing rates were accompanied by reductions in reported pain scores both during wear and on dressing change}\(^15\). Further clinical examples are provided beginning on page 12, including a series of case studies.
FIGURE 8: Healing in venous leg ulcers treated with AQUACEL™ Ag+ over 8 weeks. Key: ▼ = all wounds (n=42); ■ = clinically infected subset (n=10)

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8. WHRI3817 TA297. Assessment of the in vitro physical properties of AQUACEL Ag, AQUACEL Ag EXTRA and AQUACEL Ag+ EXTRA dressings. ConvaTec data on file.
10. WHRI3875 MA239. Antimicrobial activity against CA-MRSA and prevention of biofilm reformation by AQUACEL Ag+ EXTRA dressing. ConvaTec data on file.

CONCLUSION
The ideal dressing needs to be simple to use and effective. It must manage key local barriers to healing — excess exudate, infection, biofilm — and provide both wound protection and an environment that is conducive to healing. AQUACEL Ag+ dressings (Extra and Ribbon options) offer advanced wound dressing design and provide a potential solution to each of these challenges for the clinician (Figure 9).
AQUACEL™ Ag+ DRESSINGS: IN PRACTICE

CHRONIC WOUNDS AND TOPICAL ANTIMICROBIALS
Systemic antibiotics are often prescribed to treat wound infection, but only half of patients with uncomplicated chronic wounds receive appropriate antibiotic therapy. Furthermore, prolonged and excessive uses of systemic antibiotics often lead to undesirable adverse effects (e.g., *Clostridium difficile* colitis) and promote emergence of resistant bacteria.

The alternative approach involves early and judicious use of topical antimicrobial agents — including those containing antiseptics and antibiotics — to limit the formation of biofilm and spread of infection into the deeper tissue compartment (Box 1, page 11). When deciding whether to use a topical antimicrobial dressing to treat wound infection, a systematic approach is required (Figure 1). Treatment of wound infection must involve three key components: assessment of wound infection, management of active infection, and prevention of recurring infection.

ASSESSMENT OF WOUND INFECTION
Wound infection is best diagnosed by assessing the presentation of clinical signs and symptoms. Comprehensive assessment should include patient factors such as malnutrition, immunosuppression, diabetes and poor vascular supply that compromise host defense against pathogens, in addition to wound characteristics.

No one particular sign or symptom will accurately confirm a diagnosis of wound infection. As such, clinicians should seek to evaluate a combination of these possible signs and symptoms to determine bacterial damage in wounds. Based on a literature review, the proposed wound infection checklists differentiate the clusters of signs and symptoms associated with superficial/localised wound infection (Table 1) and deep soft tissue infection (Table 2).

MANAGEMENT OF ACTIVE INFECTION
Systemic antibiotics should be used in wound infections that involve soft tissue. Wounds are best treated with systemic antibiotics when healing is not immediately achievable (uncontrolled deep infection) or topical antimicrobials when bacterial burden is more of a concern than tissue toxicity. Topical antimicrobials can also be used to control microbial burden in individuals who are very high-risk due to patient factors.

However, treatment of wounds that are superficially infected should follow a different path. Debridement and/or vigorous cleansing should be used to disrupt resilient biofilm, remove devitalised tissue, eliminate foreign material and reduce bacterial debris. After biofilm disruption, consider using topical antimicrobial agents to prevent biofilm reformation, which could occur within 24 to 48 hours of debridement.

PREVENTION OF RECURRING INFECTION AND MAINTENANCE OF WOUND
Cleansing and/or debridement and application of topical antimicrobial agents are generally accepted as good clinical practice to address biofilm and accelerate wound healing. Once the bacterial burden is controlled (e.g., improved wound characteristics and healing), a moist interactive dressing, such as AQUACEL™ Extra or AQUACEL™ Foam, may replace antimicrobial dressings.

ABOUT THE CASE SERIES
The case series evaluated AQUACEL Ag+* dressings in patients with wounds that were infected or at risk of infection. The dressing was used on 17 patients (18 to 85 years old) with 18 wounds during a prospective four-week trial. Wounds included pressure ulcers (PUs), surgical wounds, venous leg ulcers and skin tears. All wounds exhibited signs and symptoms of wound infection, with impaired healing but without tissue invasion or systemic immunological response.
Underlying wound causes were addressed (eg compression therapy for venous disease and therapeutic support surfaces for PUs). Patients with uncontrolled systemic diseases and medical therapies that could impair healing were excluded from the study.

Wound surface areas ranged from 0.72cm² to 56cm² at baseline. Improved healing was observed in 17 of 18 wounds after four weeks, at which time surface areas ranged from 16.8cm² to complete closure, an overall 66% reduction in wound surface areas. The AQUACEL Ag+* dressing was rated excellent by clinicians in terms of fluid handling capacity, ease of removal and periwound protection. The findings substantiate the combination of Hydrofiber® Technology and Ag+ Technology as part of an effective antimicrobial armamentarium for treating wound infection. Details of six of the case studies begin on page 12.

**CONCLUSION**

Treatment of wounds that are infected or at risk of infection must involve assessment, management and prevention. The ideal antimicrobial dressing used as part of this systematic approach should destroy biofilm, kill infection–causing bacteria, and handle excess exudate. The following case study evaluations describe the use of AQUACEL Ag+* dressing in a range of wound types, and demonstrate its positive effects in removing barriers to wound healing.

### TABLE 1: Clinical signs and symptoms of superficial wound infection: UPPER

<table>
<thead>
<tr>
<th>UPPER wound compartment infection</th>
<th>Signs and symptoms related to infection in the upper wound compartment</th>
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<tbody>
<tr>
<td>U: unhealthy tissue</td>
<td>Presence of &gt;50% of debris, red friable tissue or abnormal discolouration of granulation tissue</td>
</tr>
<tr>
<td>P: pain</td>
<td>Sudden emergence of increase in pain</td>
</tr>
<tr>
<td>P: poor healing</td>
<td>Changes in wound size of less than 10% in last 7 days</td>
</tr>
<tr>
<td>E: exudate</td>
<td>Moderate to heavy amount of exudate</td>
</tr>
<tr>
<td>R: reek</td>
<td>Presence of foul odor</td>
</tr>
</tbody>
</table>

### TABLE 2: Clinical signs and symptoms of deep wound infection: LOWER

<table>
<thead>
<tr>
<th>LOWER wound compartment infection</th>
<th>Signs and symptoms of wound infection related to bacterial damage in the lower or deeper wound compartment</th>
</tr>
</thead>
<tbody>
<tr>
<td>L: larger in size</td>
<td>Increase in wound size or new areas of satellite breakdown</td>
</tr>
<tr>
<td>O: osseous tissue</td>
<td>Wound that probes to bone</td>
</tr>
<tr>
<td>W: warmth</td>
<td>Increased periwound temperature of more than 1.11°C (2°F) compared to temperature in proximal area</td>
</tr>
<tr>
<td>E: (o)edema</td>
<td>Mild to moderate oedema</td>
</tr>
<tr>
<td>R: redness</td>
<td>Redness of &gt;2cm beyond wound margin</td>
</tr>
</tbody>
</table>

**REFERENCES**


**BOX 1: Defining the compartments**

- **Upper compartment** — Extends to approximately 1-3mm below the wound surface
- **Lower compartment** — Begins at approximately 3mm below the wound surface
CASE 1: PRESSURE ULCER IN THE THORACIC VERTEBRAL REGION

INTRODUCTION
A 23-year-old male presented with a pressure ulcer of three to six months’ duration in the thoracic vertebral area. Baseline measurements were 1.5cm x 1.3cm, with no measurable depth. The wound bed had 50% granulation tissue and 50% slough. The periwound skin was healthy.

The patient had a medical diagnosis of spina bifida. He had recurrent ulcers to his exterior spine region, and an area that protruded due to deformity. His mobility was impaired and he spent most of the day in his wheelchair.

The wound showed the following signs and symptoms of clinical infection:
- Large amounts of purulent exudate
- Suspected presence of biofilm as determined by clinical opinion
- Discolouration of granulation tissue.

Prior wound management routines had included povidone iodine and silicone dressings that were changed three times per week.

METHODOLOGY
On 16 August 2013, a new wound management routine was initiated. The wound was cleansed with normal saline. AQUACEL™ Ag+ dressing (5cm x 5cm) was applied as the primary dressing. This was covered with an absorbent secondary dressing and secured with a transparent film dressing. Dressings were changed twice per week with evaluations completed weekly in the outpatient clinic. The wound received regular mechanical debridement.

Week 1 results
Wound measurements had decreased to 1.2cm x 0.5cm (a 70% reduction in surface area). Management of exudate by the dressing was rated as good. There was complete debridement of slough with conversion to healthy granulation tissue and partial epithelialisation of the wound bed.

Week 2 results
Wound measurements had decreased to 0.8cm x 0.3cm (an 88% reduction). The dressing’s management of exudate continued to be rated as good. The wound bed showed 90% epithelialisation and a small scab. Based on wound appearance and lack of exudate, the treatment regimen was discontinued.

DISCUSSION
Within two weeks, this chronic wound — which had been present for 3–6 months and showed little sign of healing — had reduced in size by more than 85%. Clinical signs of local infection, including suspected presence of biofilm, improved within seven days of introducing AQUACEL Ag+ dressing.

Note
- Dressing did not contain strengthening yarn or have the additional absorptive capacity of AQUACEL™ Ag+ Extra™ dressing.
CASE 2: SACRAL PRESSURE ULCER IN ELDERLY PATIENT

INTRODUCTION
An 88-year-old female presented with a sacral pressure ulcer (PU) of three months’ duration. Baseline measurements were 1.8cm x 0.4cm x 0.5cm. The wound bed had 80% granulation tissue and 20% slough. The periwound skin was healthy. Multiple comorbidities were present including pulmonary oedema, chronic obstructive pulmonary disease, peripheral vascular disease, chronic atrial fibrillation, ventricular tachycardia and amputation of the left leg due to ischaemia.

The patient had developed a sacral PU after surgery due to prolonged immobilisation. The wound showed the following signs and symptoms of clinical infection:

- Small amounts of purulent exudate
- Suspected presence of biofilm as determined by clinical opinion
- Discolouration of granulation tissue.

Prior wound management routines had included AQUACEL™ as a primary dressing and an absorbent secondary dressing secured with a transparent film dressing.

METHODOLOGY
On 26 July 2013, a new wound management routine was initiated. The wound was cleansed with normal saline and AQUACEL™ Ag+* dressing (5cm x 5cm) applied as the primary dressing. This was secured with a transparent film dressing. This management routine was repeated three times a week. Evaluations were completed weekly in the outpatient clinic.

Week 1 results
Wound measurements had decreased to 0.8cm x 0.3cm x 0.3cm (an 80% reduction in volume). The dressing’s management of exudate was rated as excellent. There was complete debridement of slough achieved by the dressing, with conversion to healthy granulation tissue and partial epithelialisation of the wound bed.

Week 2 results
Wound size had decreased to 0.4cm x 0.2cm x 0.1cm (a 98% reduction). Periwound skin was healthy, and the wound bed was mostly epithelialised with some healthy granulation tissue. The bottom portion of the wound was covered with a stable dry scab, which was not removed because there was no sign of further damage beneath it. Management of exudate continued to be rated as excellent.

Week 3 results
The wound had healed and the periwound skin was intact and healthy.

DISCUSSION
Despite multiple comorbidities, this sacral PU healed within three weeks. For this wound, the dressing properties that contributed to wound healing were effective debridement of slough and excellent management of wound exudate.

Note:
- Dressing did not contain strengthening yarn or have the additional absorptive capacity of AQUACEL™ Ag+ Extra™ dressing.
CASE 3: LOWER RIGHT LATERAL LEG TRAUMATIC WOUND

INTRODUCTION
An 86-year-old male presented with a history of venous insufficiency and chronic oedema. During a fall, his walker had fallen on his lower right leg, leading to a traumatic wound on the lateral aspect. The wound was progressive, increasing in size and had not improved for three weeks.

Baseline measurements were 2.8cm x 2.0cm. The wound bed had 95% granulation tissue and 5% slough. Periwound skin was healthy. Multiple comorbidities were present including severe chronic obstructive pulmonary disease, congestive heart failure, atrial fibrillation, mitral regurgitation with preserved left ventricular ejection fraction, and sleep apnoea. Due to shortness of breath, the patient’s exercise tolerance was poor and his nutrition status was less than optimal (albumin 30mg/g).

The wound showed the following signs and symptoms of clinical infection:
- Friable, discoloured granulation tissue
- Suspected presence of biofilm as determined by clinical opinion
- Small amounts of purulent exudate.

The prior wound management routine had included AQUACEL™ Ag dressing, secured with a transparent film dressing, changed three times per week.

METHODOLOGY
On 26 July 2013, a new wound management routine was initiated. The wound was cleansed with normal saline. AQUACEL™ Ag+ dressing (5cm x 5cm) was applied as the primary dressing and secured with a transparent film dressing. Dressings were changed three times a week. The wound received regular mechanical debridement. Weekly evaluations were done in the outpatient clinic.

Week 1 results
Wound measurements had decreased to 2.8cm x 1.0cm (a 50% reduction in area). The dressing’s management of exudate was rated as excellent. There was active debridement of slough.

Week 2 results
Wound size had decreased to 2.1cm x 1.2cm (a 57% reduction). The periwound area was healthy, and active debridement of slough had continued. Exudate management continued to be rated as excellent.

Week 3 results
Wound size had decreased to 2.0cm x 1.0cm (a 64% reduction). The periwound skin was healthy, granulation tissue had improved in colour, and active debridement of slough had continued. The dressing’s ability to manage exudate was again rated as excellent.

Week 4 results
Wound size had remained at 2.0cm x 1.0cm. The periwound skin was healthy, active debridement of slough had continued, and management of exudate remained excellent.

Week 5 results
The wound had decreased in size to 1.0cm x 0.8cm (an 86% reduction). Periwound skin was intact and healthy. A clinical decision was made to leave the scab intact due to the presence of healthy epithelial tissue.

DISCUSSION
Despite multiple comorbidities, this traumatic leg wound decreased in size by over 85% within five weeks. For this wound, the dressing properties most important to healing were effective debridement of slough and excellent management of wound exudate.

Note
Dressing did not contain strengthening yarn or have the additional absorptive capacity of AQUACEL™ Ag+ Extra™ dressing.
CASE 4: TRAUMATIC WOUND ON DORSUM OF THE LEFT HAND

INTRODUCTION
A 90-year-old female presented with a traumatic skin tear wound on the dorsum of her left hand. This had resulted from a fall during which her hand had become caught on a side rail. The wound had been present for two weeks and was considered to be at high risk of infection. Contributing medical history included Parkinson’s disease, anaemia, diabetes, hypertension, congestive heart failure, myocardial infarction and osteoarthritis.

Baseline measurements were 3.0cm x 2.2cm and no measurable depth. The wound showed the following signs and symptoms of clinical infection:
- Moderate amounts of purulent exudate
- Discoloured granulation tissue
- Pain (rated as a 2 on a visual analogue scale [VAS] during dressing changes and while the dressing was in situ)
- Suspected biofilm presence as determined by clinical opinion.

Before the dressing trial, the wound had been cleansed with saline and covered with an absorbent silicone and soft foam dressing twice weekly.

METHODOLOGY
On 7 August 2013, a new wound management routine was initiated. The wound was cleansed with normal saline. AQUACEL™ Ag+* dressing (10cm x 10cm) was applied as a primary dressing and secured with an absorbent secondary dressing and transparent film. Dressings were changed once per week in the hospital. Evaluations were undertaken at dressing changes.

Week 1 results
All clinical signs and symptoms of infection had resolved. Wound measurements had decreased to 2.0cm x 1.0cm (a 70% reduction in area). Pain ratings had also decreased to a 1 on the VAS during dressing change and 0 with the dressing in situ.

Week 2 results
The wound had closed and was covered with a dried scab. There was no exudate present and the wound was epithelialised.

DISCUSSION
The use of AQUACEL Ag+ dressing provided sustained antimicrobial activity against this superficial wound and aided debridement of the necrotic slough, allowing total wound closure within two weeks.

Note
Dressing did not contain strengthening yarn or have the additional absorptive capacity of AQUACEL™ Ag+ Extra™ dressing.
CASE STUDIES

CASE 5: SACRAL PRESSURE ULCER IN PATIENT WITH MUSCULAR DYSTROPHY

INTRODUCTION
A 36 year–old–male presented with a sacral pressure ulcer of one to three months’ duration. Primary medical diagnoses included Duchenne muscular dystrophy, chronic respiratory failure with tracheostomy ventilation and urosepsis. Contributing factors to the wound’s development included compromised mobility and impaired tissue oxygenation due to chronic respiratory failure.

The wound showed the following signs and symptoms of clinical infection:
- High amounts of purulent exudate
- Suspected presence of biofilm as determined by clinical opinion
- Discoloured, friable granulation tissue.

Baseline wound measurements were 3cm x 2cm x 1.2cm, with 0.7cm undermining at 12 o’clock. The wound bed comprised 20% necrotic tissue, 10% slough and 70% granulation tissue. The periwound skin was macerated and wet. Before the dressing trial began, this wound had been managed with povidone iodine and ribbon gauze that was changed daily.

METHODOLOGY
On 26 July 2013, a new wound management routine was initiated. The wound was cleansed with normal saline. AQUACEL™ Ag+* dressing (10cm x 10cm) was lightly packed into the wound and secured with an appropriately sized absorbent dressing.

Week 1 results
Wound measurements had decreased to 2cm x 1.8cm x 0.4cm (a 80% reduction in volume). There was no change in the undermining measurement of 0.7cm. There was some slight discolouration of granulation tissue. Exudate management was rated as excellent.

Week 2–3 results
Wound measurements had decreased to 1.8cm x 1cm x 0.6cm (a 85% reduction), undermining to 0.4cm. Discolouration of granulation was again observed to be slight. The dressing’s exudate management continued to be rated as excellent.

One week later, the wound had decreased significantly, to 1.2cm x 1.0cm x 0.3cm (95% reduction), with undermining of 0.3cm. Granulation tissue was no longer discoloured or friable.

Week 4 results
Wound size had decreased to 0.8cm x 0.4cm x 0.2cm (a 99% reduction), and undermining had maintained at 0.3cm. Healthy granulation was noted in the wound bed. The dressing’s ability to manage exudate was again rated as excellent.

Week 5 results
Wound size had decreased to 0.8cm x 0.4 cm with no measurable depth. All undermining had resolved. Healthy granulation was noted, and exudate management by the dressing remained excellent.

DISCUSSION
After five weeks’ treatment, significant progress towards healing of the wound was noted. The undermining had resolved, and the wound measurements had decreased by at least 99%. The dressing’s ability to manage exudate was rated as excellent throughout the dressing trial period. All necrotic tissue and slough were debried autolytically by the dressing, and the wound bed had converted to healthy granulation tissue.

Note
- Dressing did not contain strengthening yarn or have the additional absorptive capacity of AQUACEL™ Ag+ Extra™ dressing.
**CASE 6: SACRAL PRESSURE ULCER WITH SIGNIFICANT UNDERMINING**

**INTRODUCTION**
A 63-year-old male presented with a sacral pressure ulcer that had been present for three to six months. A primary medical diagnosis of West Nile virus with associated paralysis was made. Contributing factors to wound development included compromised mobility, shear, friction and heat accumulation in the sacral area, creating a local microclimate associated with a high risk of skin breakdown.

Baseline wound measurements were 2cm x 1.3cm, with 0.4 cm depth and 2.8 cm undermining at 12 o’clock. The wound bed was covered with 100% friable granulation tissue. The periwound skin showed some redness. The wound had the following signs and symptoms of clinical infection:
- High amounts of purulent exudate
- Suspected presence of biofilm as determined by clinical opinion
- Discoloured, friable granulation tissue.

Before the dressing trial began, the wound was managed with polyhexamethylene biguanide (PHMB)-impregnated ribbon gauze dressing, covered by an absorbent secondary dressing and secured with a transparent film.

**METHODOLOGY**
On 26 July 2013, a new wound management routine was initiated. The wound was cleansed with normal saline. An AQUACEL™ Ag+® dressing measuring 5cm x 5cm was lightly packed into the wound, then secured with an absorbent secondary dressing. Dressings were changed three times per week.

**Week 1 results**
The wound measured 2cm x 1.0cm x 0.9cm which, although an overall increase in volume, was accompanied by a decrease in undermining to 2cm. Discolouration of granulation tissue and continued presence of biofilm were observed. Management of exudate was rated as excellent.

**Week 2 results**
The wound had decreased to 1.8cm x 1cm x 0.6cm (a 40% reduction). Undermining had further decreased to 1.6cm. Discolouration of granulation tissue and presence of biofilm were observed to be small during the assessment. The dressing’s exudate-management ability was again rated excellent.

**Week 3 results**
Wound measurements were unchanged, though undermining had decreased to 1.5cm. Healthy granulation was noted. Exudate management continued to be rated excellent.

**Week 4 results**
The wound had decreased to 1.5 cm x 0.8 cm x 0.3cm (a 65% reduction from baseline). Undermining was unchanged; healthy granulation tissue was noted. Management of exudate remained excellent.

**Week 5 results**
The wound had decreased to 1.3cm x 0.7 x 0.3cm (a 73% reduction from baseline), and undermining to 1.2cm. There was healthy granulation tissue and no biofilm present.

**DISCUSSION**
After five weeks’ treatment, significant progress towards healing was noted. Undermining had decreased by 57% and wound dimensions by over 70%. Management of exudate was rated as excellent throughout the dressing trial period.

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**Note**
* Dressing did not contain strengthening yarn or have the additional absorptive capacity of AQUACEL™ Ag+ Extra™ dressing.