UrgoClean Ag made easy

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Introduction

In a chronic or deteriorating wound, there are barriers and factors that delay timely wound healing, which combined encourage microbial proliferation, microbial attachment and biofilm formation. Biofilms are found in both chronic and acute wounds and are considered to be the underlying cause of prolonging inflammation and increasing a wound's propensity to infection (Percival et al 2012). This Made Easy focuses on UrgoClean Ag: a dressing that combines the cleaning and desloughing action of polyabsorbent fibres with antimicrobial ionic silver, which can be used for locally infected, and 'at risk' acute and chronic wounds.

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Understanding chronic wounds

Chronic wounds exist in a state whereby cells in the wound enter an unresponsive and dormant/senescence state of growth (Williams, 1998). In a deteriorating wound there are many barriers and factors that, in conjunction with cellular suppression, delay timely wound healing and encourage microbial growth, microbial adhesion, microcolony formation and biofilm formation. These barriers include high levels of exudate, slough, eschar and inflammation, which affect normal cell function and growth and cause an increase in pH and matrix metalloproteinases (MMPs) levels.

Chronic wounds are often 'stuck' in a state of inflammation, which increases the risk of the wound developing an infection. Local infection affects wound healing in a number of different ways (Figure 1). The classic signs of infection include local heat, inflammation, redness, purulence and pain (World Union of Wound Healing Societies, 2008).

It is estimated that over 50% of patients with a chronic wound will develop a localised infection (Gomes et al, 2017). For patients that have numerous underlying pathologies and a poorly functioning immune response, the risk of a wound becoming chronic and infected is high. Such high-risk patients represent a major concern for the healthcare professional (HCP) with potential infection-related complications possible. Therefore, infection prevention is one of the most important elements of a wound management strategy.

Prolonged inflammation

Prolonged elevation of proinflammatory cytokines, such as:
- Interleukin 1 (IL-1)
- TNF-alpha

▶ Elongation of the inflammatory phase

Imbalance of proteases (human and bacterial) and inhibitors

Prolonged inflammation leads to:
- increased levels of MMPs (particularly MMP 2 and MMP 9)
- Decreased level of naturally occurring protease inhibitors (e.g. tissue inhibitors of matrix metalloproteinases [TIMPs])

Degradation of growth factors

The shift in a protease imbalance can cause growth factors in chronic wounds to be rapidly degraded

Figure 1. The effects of infection on wound healing in chronic wounds

The visible and hidden barriers to wound healing

Wounds that are showing signs of deterioration and infection will also develop increasing levels of exudate, biofilm, eschar and slough – these barriers to wound healing can hide the signs of an infected wound and represent a hidden issue (Figure 2). Eschar and slough in particular are considered problematic. Both are composed of a complex mixture of fibrin, elastin, collagen, dead and living human cells (i.e. fibroblasts, keratinocytes, leucocytes), and microbial cells that reside in planktonic and sessile (attached) states that can increase the risk of infection. Slough especially can enhance and prolong inflammation (Percival and Suleman, 2015).

Therefore these barriers of slough, debris, eschar, exudate and biofilm need to be managed and removed effectively to avoid wound deterioration, a more complex infection and associated complications. Cleaning the wound is a very important step that should be part of all standard protocols of care, especially before antimicrobial usage as an antimicrobial's performance can be significantly reduced in highly biological systems.

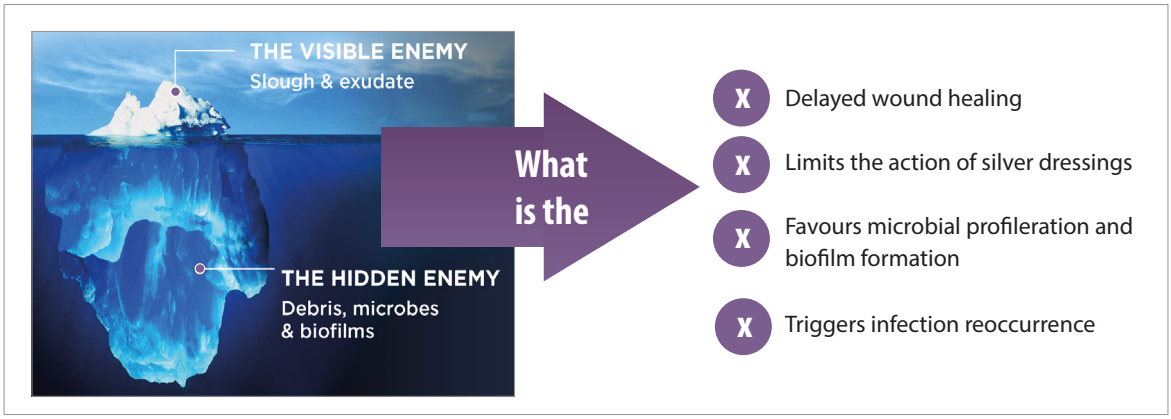


Figure 2. **The visible and hidden barriers to wound healing – both need to be addressed to fight local wound infection**

Wound management

Wound cleaning

Wound cleaning is akin to brushing our teeth; we ensure that our oral hygiene is up to a high standard to help both the prevention and the management of biofilms and inflammation thereby lowering the risk of infection. Unfortunately, if good oral hygiene is not maintained, biofilm growth and regrowth can occur, along with inflammation and infection. It is important that a wound cleaning strategy is in place for each wound and patient to:

- **Reduce microbial levels, bioburden and risk of local infection**
  - by removing support for microbial adhesion (slough, biofilm, exudate etc.) and eliminating pathways of microbial dissemination (i.e. inflamatory pathways and materials whereby microorganisms may attach, disseminate and form biofilm).

- **Facilitate complete action of antimicrobial agents**
  - by removing all barriers (microorganisms, biofilms, slough, exudates etc.) and exposing the wound bed directly to antimicrobial agents.

Desloughing and debriding, or a combination of both, are commonly adopted wound cleaning approaches (Rhoades et al, 2008; Malone et al, 2017). Cleaning also aids autolytic debridement, which helps to develop a more conducive environment for healing and wound remodelling. Other cleaning approaches include the use of non-antimicrobial and antimicrobial-based irrigating solutions, desloughing cloths and pads to remove the more loosely attached slough. Surfactants can be beneficial as they alter the surface tension between surfaces and also increase the 'wettability' – the ability of a liquid to maintain contact with a solid surface – increasing solubility for easier removal (Rodeheaver and Ratliff, 2014).

Wound dressings

Both at risk and infected wounds should be managed with a wound dressing that is impregnated with an antiseptic – a substance that can be applied to living skin and tissue, which has the ability to prevent, kill or slow down the growth of microorganisms.

There are many different wound dressings available to the HCP that can be employed for the treatment of at-risk and infected wounds, each with their own features and benefits. For use in high-risk wounds, topical antimicrobials are often employed. Silver, and more specifically ionic silver (Ag^+), is considered a very effective antimicrobial when used in the right environments and the barriers to its inactivation are removed. It works at low concentrations, over a wide pH range and exhibits broad-spectrum activity against fungi, yeasts, and a range of bacteria including antibiotic-resistant and anaerobic bacteria.

The efficacy of ionic silver has been well documented in many scientific publications highlighting its efficacy on microbes that reside within the planktonic state and microbes growing or residing in the sessile state (Paladini and Pollini 2019; Percival et al, 2019). Ionic silver should form part of a combination therapy approach, and used in conjunction with an appropriate wound dressing material in order to achieve maximum efficacy on both planktonic or free-floating bacteria, sessile microbes or attached bacteria and biofilm.

Despite the evidence regarding the efficacy and effectiveness of ionic silver, when it comes to wound care, the performance and success of any antimicrobial-based wound dressing must not be based solely on its antimicrobial ability. This is because the dressing format and material that carries the antimicrobial often has inherent characteristics and capabilities that are an important addition in both the prevention and the

management of local infection. It is vital that the dressing format that delivers the active agent into or onto a wound should, firstly, support the wound healing continuum and, secondly, help to enhance the delivery of the antimicrobial agent at the point of contact. Some wound dressings such as UrgoClean Ag have inherent abilities to sequester and immobilise microbes both within the free-floating planktonic state and when they have been detached from the biofilm. This represents an important component of an infection control strategy as the wound dressing itself will prevent the dissemination of microbes and toxins and, therefore, help to reduce the infection risk to the patient.

UrgoClean Ag

UrgoClean Ag has inherent characteristics that have been shown to be effective in wound 'cleaning' by physically binding onto debris (e.g. slough, necrotic tisse) so once the dressing is removed the debris that is bound onto it are also effectively removed. (Figure 3). The combined cleaning and antimicrobial action helps to support the use of UrgoClean Ag in both the prevention and management of a localised wound infection and support the strategy for progression of a chronic wound to healing.

Anti-biofilm activity

The importance of combined cleaning and antimicrobial action

The polyabsorbent fibres of UrgoClean Ag have been shown within *in vitro* studies to assist the deeper penetration of ionic into the biofilm to kill the microorganisms found within it (Percival, 2018; Figure 4), which may translate to the positive outcomes being observed in the *in vivo* environment.

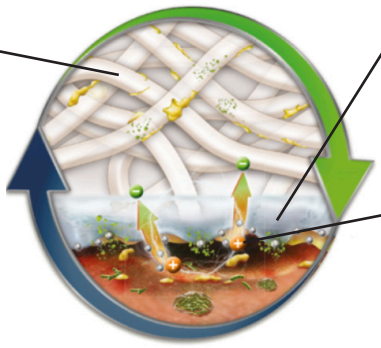
Additionally, Desroche et al (2016) demonstrated that UrgoClean Ag exhibited better anti-biofilm activities against *in vitro* biofilms of Methicillin-resistant *Staphylococcus aureus* (MRSA) and *Pseudomonas aeruginosa* than a carboxymethylcellulose (CMC) dressing, which combined silver, ethylenediaminetetraacetic acid (EDTA) and Benzylkonium chloride after 24 hours of exposure.

Cleaning, mechanical disruption and desloughing

Desroche et al (2016) also showed that the polyabsorbent fibres in UrgoClean Ag have the ability to bind onto and remove sections of the biofilm matrix. It is believed that the breakdown of the biofilm matrix occurs particularly when the dressing is removed, a process known as 'mechanical disruption', (Alhede et al, 2011).

Unique polyacrylate (polyabsorbent) fibres with an acrylic core

- Desloughes and cleans the wound: Polyacrylate fibres trap, absorb vertically and retain the sloughy residue within the dressing.
- 'Mechanical disruption' – particularly when the dressing is removed – of the extracellular matrix of a biofilm (Desroche et al, 2016)

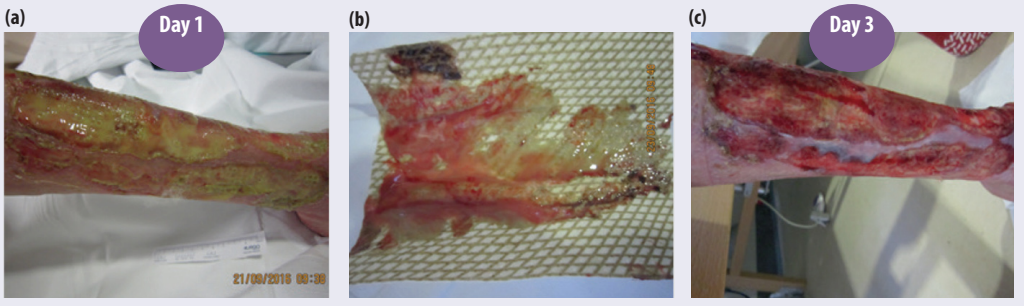


TLC healing matrix

- Helps atraumatic care and pain-free dressing change to protect the surrounding skin from damage (Dalac et al, 2016)

Silver sulphate

- Readily soluble and delivers effective levels of ionic silver that is necessary to kill microorganisms.



(a) Leg ulcer on day 1;
(b) UrgoClean Ag on removal;
(c) Leg ulcer on day 3.

Figure 3. Composition and mode of action of UrgoClean Ag.

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To cite this document:
Wounds UK (2020) *UrgoClean Ag Made Easy.* Wounds UK, London. Available from: www.wounds-uk.com/made-easy

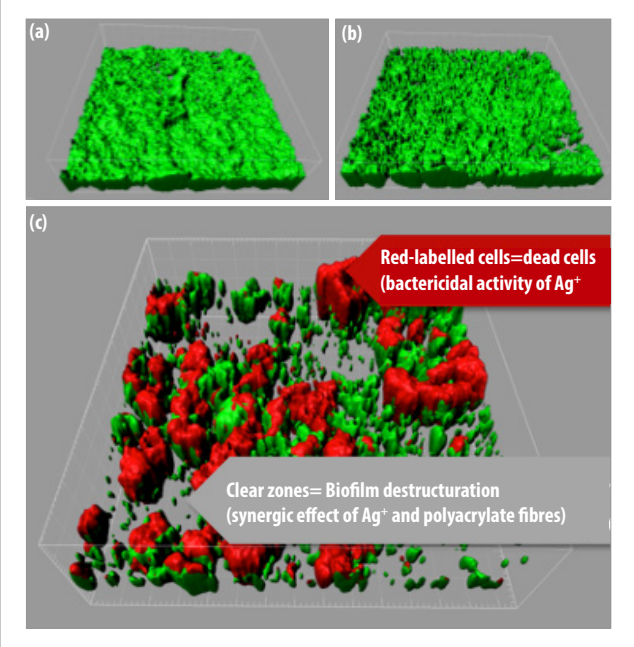

Figure 4. Confocal images (a) Untreated biofilm (b) Neutral dressing with poly-absorbent fibre (c) The efficacy of the combined action of poly-absorbent fibres and TLC-Ag healing matrix of UrgoClean Ag on biofilm. UrgoClean Ag significantly reduced the biofilm volume and disrupts the integrity of the biofilm after 24 hours of exposure (Percival et al 2018).

Clinical data from a prospective, multicentre, non-comparative clinical trial of UrgoClean Ag dressing of 37 patients with wounds showed a 75% reduction in patients with heavy exudate, and a 62.5% reduction in sloughy tissue and wound debris. All signs of localised infection resolved and continuous cleaning was achieved for up to 7 days (Dalac et al, 2016).

However, within any anti-biofilm strategy in wound care it is important to understand that a biofilm-based management approach involves a combination of approaches and technologies. A combination of therapies is needed to prevent biofilms, kill the microbes within the biofilm, reduce and break down the biofilm matrix, prevent the reattachment of microbes and also have the ability to sequester both planktonic microbes and those that have just detached from a biofilm.

Conclusion

Wound healing and the effectiveness of an antimicrobial-based wound dressing are impaired if there are barriers to wound healing, such as slough, debris, exudate and eschar. These barriers reduce the effective action of ionic silver once it is released into the wound. Furthermore, the research suggests that it is not just the type or amount of silver that is delivered into the wound, but also the wound dressing material that determines the clinical effectiveness of a silver-impregnated wound dressing. Therefore, a dressing that has the combined approach to clean the wound of barriers to healing, thereby supporting the effectiveness of silver will lead to improved clinical outcomes. The ability of UrgoClean Ag to continuously clean the wound of exudate, slough and microorganisms, in combination with the strong antimicrobial impregnated action of ionic silver, confirms that UrgoClean Ag is an effective antimicrobial wound dressing for locally infected and 'at risk' wounds, and wounds that are not progressing to healing.

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