PHMB made easy

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Introduction

Wound infection continues to be a challenging issue and represents a considerable healthcare burden. If bacterial bioburden is not managed, the progressive states of colonisation, critical colonisation, or wound infection will follow, as outlined in the Wound Infection Continuum (Figure 1). Therefore, managing bacterial bioburden is an essential element of effective wound care. This should be achieved by identifying the correct antimicrobial agent and the most effective mode of delivery for the individual patient and their wound.

Polyhexamethylene biguanide (PHMB) is a compound that has been found to meet the criteria for the ideal antimicrobial agent, having a broad spectrum of activity to reduce bacterial bioburden, while not being associated with toxicity or contributing to bacterial resistance (Gray et al, 2010).

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Identifying wound infection

There are many definitions of wound infection, but a simple definition is: impairment of wound healing by bacteria (Templeton, 2014). Infection not only affects wound healing, which has an associated impact on the patient and their quality of life, but also increases management time for the clinician and thus has practical and financial implications.

As such, infection control is a crucial element of wound care management. Recognising wound infection can be a challenge in clinical practice. Signs and symptoms of possible infection should be monitored and investigated further – i.e. a swab should be taken when these signs are observed – see Table 1.

Vigilance and investigation are also required if:

- The patient shows signs of a systemic infection such as pyrexia, raised white cell count, blood C reactive protein levels (CRP) and/or blood erythrocyte sedimentation rate
- The patient is elderly or immunosuppressed and therefore more susceptible to wound infections, and/or presents with other symptoms exhibiting drowsiness, loss of appetite, nausea, restlessness and confusion.

In recent years, antimicrobial agents have become viewed as the first line of treatment in managing bacterial burden (White et al, 2001). Antimicrobials are agents that kill micro-organisms. Antimicrobial is an 'umbrella' term that includes disinfectants, antiseptics and antibiotics.

Recent advances in antiseptic technology have led to the development of a number of products that are highly effective in destroying pathogens, while being less harmful to healthy tissue. These include antimicrobials such as PHMB, silver, cadexomer iodine and honey; they are generally available in formulations including topical products and impregnated dressings. These antiseptics can successfully be used in topical management to reduce the load of a variety of pathogens, not just bacteria (Vowden et al, 2011).

Figure 1: The Wound Infection Continuum (International Wound Infection Institute, 2016)

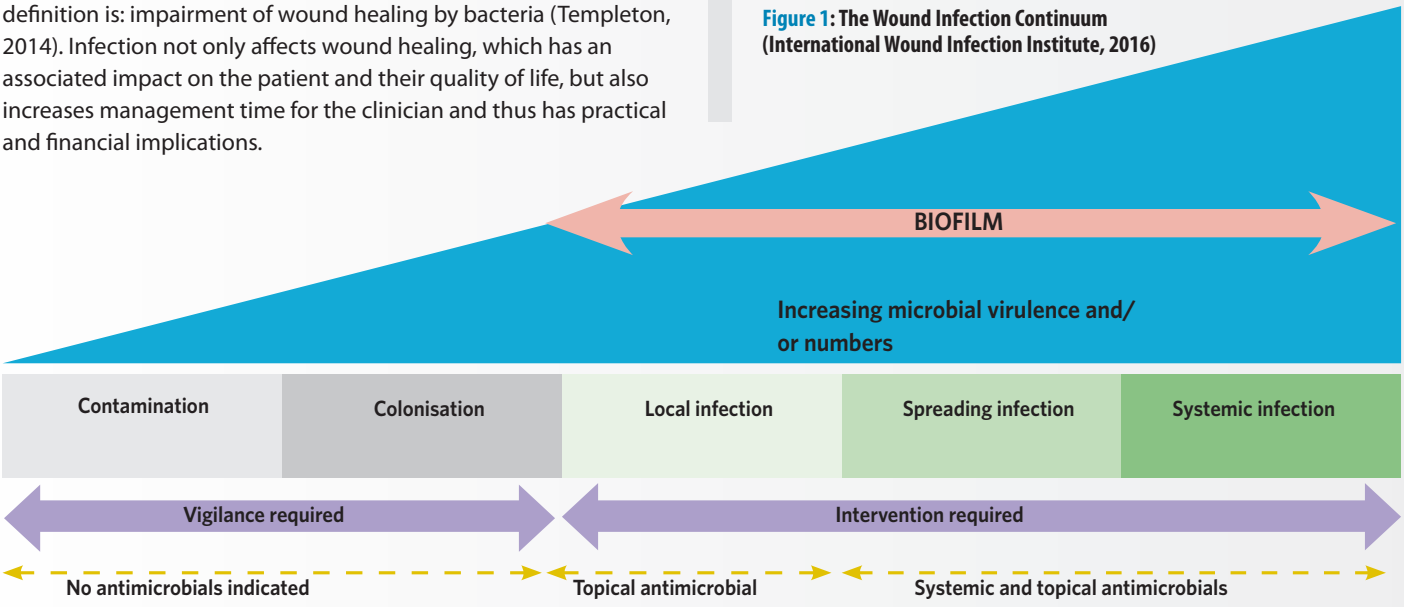

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Table 1: Signs and symptoms associated with stages of the wound infection continuum (International Wound Infection Institute, 2016)

Contamination	Colonisation	Local infection		Spreading infection	Systemic infection
All wounds may acquire micro-organisms. If suitable nutritive and physical conditions are not available for each microbial species, or they are not able to successfully evade host defences, they will not multiply or persist; their presence is therefore only transient and wound healing is not delayed	Microbial species successfully grow and divide, but do not cause damage to the host or initiate wound infection	Covert (subtle) signs of local infection: ■ Hypergranulation (excessive 'vascular' tissue) ■ Bleeding, friable granulation ■ Epithelial bridging and pocketing in granulation tissue ■ Wound breakdown and enlargement ■ Delayed wound healing beyond expectations ■ New or increasing pain ■ Increasing malodour	Overt (classic) signs of local infection: ■ Erythema ■ Local warmth ■ Swelling ■ Purulent discharge ■ Delayed wound healing beyond expectations ■ New or increasing pain ■ Increasing malodour	■ Extending in duration +/- erythema ■ Lymphangitis ■ Crepitus ■ Wound breakdown/dehiscence with or without satellite lesions ■ Malaise/lethargy or non-specific general deterioration ■ Loss of appetite ■ Inflammation, swelling of lymph glands	■ Severe sepsis ■ Septic shock ■ Organ failure ■ Death

All antimicrobials have different properties. The ideal antimicrobial has been described as (Drosou et al, 2003):

- Associated with minimal systemic absorption
- Effective against likely contaminants and pathogens
- Fast-acting, with prolonged residual activity after a single dose
- Inexpensive
- Incapable of promoting bacterial resistance
- Effective at levels that are non-carcinogenic and non-teratogenic (i.e. does not cause DNA damage, which could result in carcinoma or foetal abnormality) to host cells
- Non-toxic
- Widely available.

PHMB is an antimicrobial agent that meets many of these criteria – crucially, with effective broad spectrum mode of action, with minimal toxicity and no recorded bacterial resistance (Gray et al, 2010).

What is PHMB?

PHMB is a synthetic antimicrobial compound that has been in use for over 60 years in various forms, including use in mouthwashes and contact lens cleaners; it has been used more recently in wound care products to reduce bacterial bioburden (Moore and Gray, 2007).

PHMB is structurally similar to naturally occurring antimicrobial peptides (AMPs), which are produced by most living organisms to fight bacteria, viruses and fungi (Gray et al, 2010). PHMB has demonstrated a broad spectrum of efficacy, combined with good safety, minimal toxicity and no association with bacterial resistance (Moore and Gray, 2007). Its broad-spectrum antimicrobial properties combined with its low toxicity make it ideal for managing bioburden while supporting healing (Andriessen and Eberlein, 2008).

How does PHMB work?

PHMB is a positively charged (cationic) polymer, which works against negatively charged micro-organisms. The positively charged molecules bind to bacterial cell membranes, which breaks down the cell integrity and ultimately kills bacteria (Yasuda et al, 2003). This mode of action is quick, so microorganisms are unlikely to develop resistance to PHMB.

PHMB in managing bacterial bioburden

PHMB has a broad spectrum of action against pathogens, including Gram-positive and Gram-negative bacteria, *Staphylococcus aureus*, Methicillin Resistant *Staphylococcus aureus* (MRSA), fungi, and biofilms (Wiegand et al, 2009; Moore and Gray, 2007). See Figure 2 for more information on PHMB's performance in an *in vitro* trial (AMS, data on file).

This is combined with a low cytotoxicity, according to the biocompatibility index(BI; Müller and Kramer, 2008), which is a structured system to compare active antiseptic substances. The antiseptic agent's BI is calculated by taking into account its relative cytotoxicity and microbicidal effect. A BI greater than 1 represents an antiseptic substance with an effective microbicidal activity combined with a relatively low cytotoxicity; a BI less than 1 represents an antiseptic substance with an effective microbicidal activity combined with a relatively high cytotoxicity. When selecting an antiseptic, it is essential to use products with a sustained release of antimicrobial agent at concentrations low enough to minimise toxicity but still able to destroy or inhibit bacterial and fungal growth (International Wound Infection Institute, 2016).

PHMB has a biocompatibility index of approximately 1.45 – meaning that it combines effective microbicidal activity

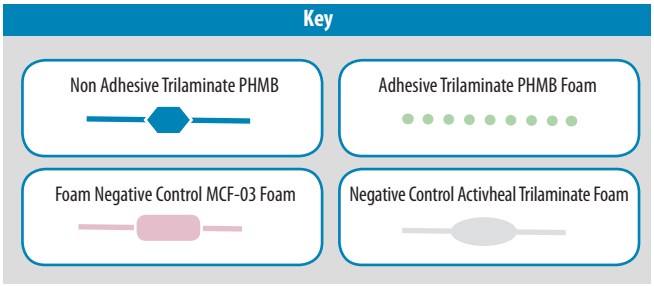
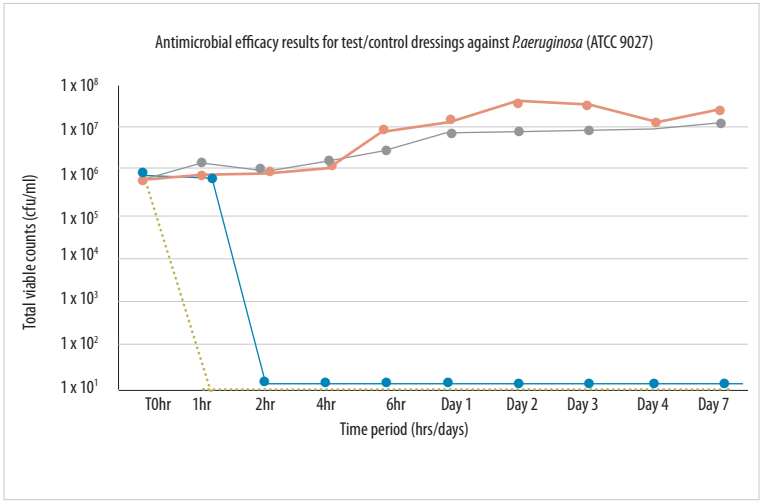
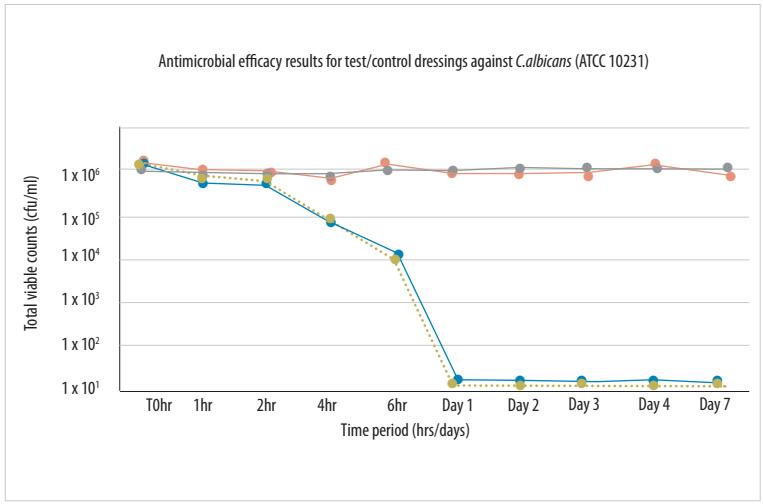
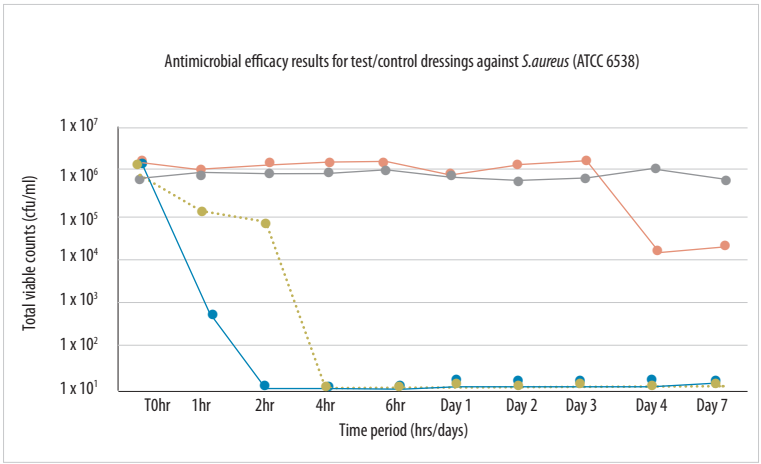


Figure 2: Results of PHMB *in vitro* trial (AMS, data on file)

Figure 2 continued: Results of PHMB *in vitro* trial (AMS, data on file)







compared with low toxicity. Its low toxicity means that PHMB can also be applied over a long period of time (Andriessen and Eberlein, 2008). PHMB has good tissue compatibility, strongly interacting with the acidic lipids within bacterial membranes and only weakly interacting with the neutral lipids of human cell membranes. This helps to prevent damage to the surrounding healthy tissue (Andriessen and Eberlein, 2008; Ikeda et al, 1984).

Crucially, as well as its ideal BI, PHMB does not promote bacterial resistance, which is a growing problem that needs to be taken into account when selecting an appropriate antimicrobial agent (International Wound Infection Institute, 2016).

Concern in recent years over systemic absorption and accumulation of silver has prompted a reappraisal of the antiseptic/antimicrobial measures that clinicians can safely utilise in managing bacterial burden. Used appropriately, PHMB is a highly effective and safe antiseptic/antimicrobial agent, which can be an efficacious alternative to silver and iodine-based antiseptic/antimicrobial wound care products (Gray et al, 2010).

Using PHMB in practice

PHMB should be considered whenever there is a need for the safe and effective treatment of infected or critically colonised wounds, and also when chronic wounds have stopped healing or are enlarging. Chronic wounds are more at risk of complications such as infection, while infection can contribute to delayed wound healing – creating a vicious cycle (World Union of Wound Healing Societies, 2008).

PHMB does not have any specific contraindications for application within the general wound care population. Furthermore, no known bacterial resistance to PHMB has been found (Moore and Gray, 2007).

Testing of PHMB against other commonly used antimicrobial agents has shown that it is an effective alternative to chlorhexidine, povidone-iodine, triclosan, silver and sulfadiazine; its biocompatibility has been shown to be superior to these agents when comparatively tested (Müller and Kramer, 2008). Evidence shows (see Box 1), that PHMB offers an opportunity to incorporate a new method of bacterial control, which has been proven safe, efficient and cost-effective.

PHMB and biofilm management

The principles of wound biofilm management (Figure 3) focus on reducing bacterial burden, disrupting the formed

BOX 1: SUMMARY OF EVIDENCE FOR POLYHEXAMETHYLENE BIGUANIDE (PHMB)

In testing, PHMB has been proven to demonstrate the following benefits:

- Improving healing rates by controlling infection (Müller and Kramer, 2008)
- Encouraging the formation of healthy granulation tissue (Mueller and Krebsbach, 2008)
- Reducing wound-related pain (Daeschlein et al, 2007; Galitz et al, 2009)
- Reducing infection-associated wound malodour (Daeschlein et al, 2007)
- Reducing slough (Mueller and Krebsbach, 2008) and non-viable tissue from the wound (Kaehn, 2009)
- Reducing periwound damage (Cazzaniga et al, 2002)

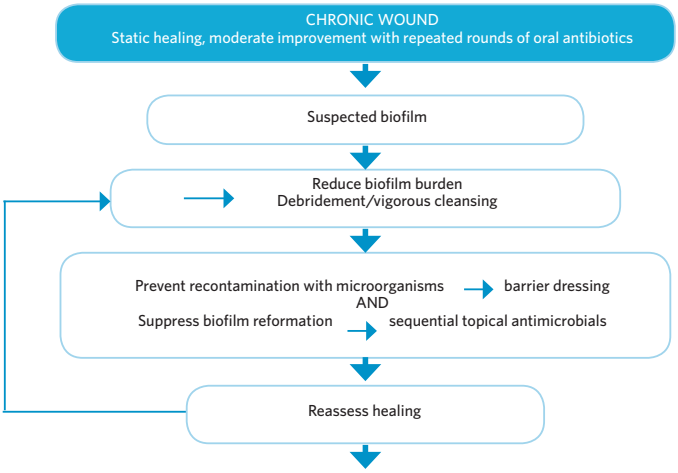


Figure 3: Principles of wound biofilm management (World Union of Wound Healing Societies, 2016)

biofilm and preventing biofilm reformation. This depends on a regimen of debridement and vigorous cleansing, plus the use of antimicrobial products, such as antimicrobial dressings (World Union of Wound Healing Societies, 2016).

PHMB may be used in conjunction with a surfactant – a surface-active substance that lowers the surface tension of a liquid – making it more effective in its ability to penetrate and disrupt difficult coatings (such as slough and debris), and indicating it may be effective in disrupting biofilms (Andriessen and Strohal, 2010; Moore and Gray, 2007).

Biofilm can be particularly challenging to correctly identify and treat (see Box 2), and following debridement the application of a PHMB dressing is a good way of further reducing bacterial bioburden, making PHMB a possible part of management in wounds where biofilm is suspected.

BOX 2: IDENTIFYING AND MANAGING BIOFILMS IN CLINICAL PRACTICE

Biofilms often do not display the classic signs of infection, so identifying suspected biofilms can be a clinical challenge.
The following signs may indicate biofilm and should be further investigated, particularly in chronic wounds:

- Excessive exudate
- Poor-quality granulation tissue
- Signs and symptoms of local infection
- Recurring infection after antibiotic cessation
- Negative wound culture
- No healing despite optimal wound and host support
- Infection lasting >30 days
- Gelatinous material that is easily removed from the wound surface
- Surface reforms quickly (Mahoney, 2015).

When biofilm is identified, the following management steps should be taken:

- It has been demonstrated that frequent debridement should be undertaken to physically remove biofilm. This might be surgical, jet lavage (hydrosurgery), bio-surgical or mechanical.
- Using cleansing products containing a surfactant has been shown to disrupt biofilm production.
- Once the wound has been appropriately cleansed and non-viable tissue removed, it is suggested that an antimicrobial product be usedto prevent reformation of the biofilm; for example, anti-biofilm dressings containing antimicrobial agents such as PHMB (World Union of Wound Healing Societies, 2016).

Mode of delivery: PHMB foam dressings

Typically in the past, PHMB has only been available in gel and solution form; it can now be delivered via foam. Dressings containing PHMB can act as an effective antimicrobial barrier and can reduce bacterial load within wound exudate (Wounds UK, 2010).

Dressings impregnated with PHMB provide an effective means of infection control, while retaining the benefits of a traditional dressing (Joseph and Bhatt, 2015).

Traditional foam dressings are designed to absorb large amounts of exudate if necessary. Therefore, PHMB dressings can be used in wounds with varying exudate levels (from moderate to heavily exuding; foam dressings may not be suitable in wounds that are too dry, as the foam dressing may not adhere to the surface of a dry wound) and can be used in both deep and superficial wounds (Lindholm, 2010). The exudate-handling capability means that dressing change frequency can be reduced, increasing wear time and helping to reduce waste. This also reduces the risk of maceration and damage to the surrounding skin.

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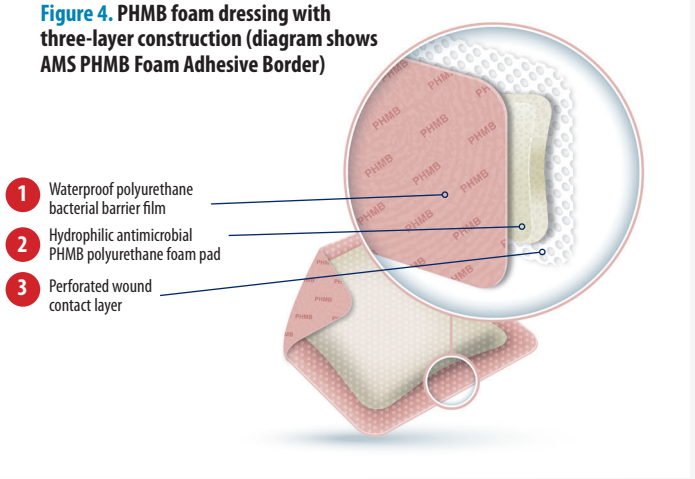
Figure 4. PHMB foam dressing with three-layer construction (diagram shows AMS PHMB Foam Adhesive Border)



The Advanced Medical Solutions PHMB foam dressings, Border and Non-Adhesive, combine the elements of a traditional foam dressing and the antimicrobial action of PHMB. The PHMB Foam border has full adhesive coverage to reduce risk of leakage (see Figure 4 for the dressing's three-layer construction).

The features and benefits of a traditional foam dressing include:

- Waterproof
- Bacterial barrier
- Suitable for moderate to heavily exuding wounds
- Maintains a moist wound healing environment
- Reduces the risk of maceration
- Low friction, reducing rucking
- Kind to skin and easy to remove.

AMS foam dressings are composed of a soft, conformable, microporous, hydrophilic, polyurethane foam with a highly breathable polyurethane membrane or film backing. These are available as both adhesive and non-adhesive foam dressings. The adhesive dressings have a perforated, pressure-sensitive, adhesive wound contact layer. This perforated layer minimises trauma during dressing changes, while the continuous adhesive coverage ensures security, reducing the risk of leakage.

Examples of wound types that can be considered for treatment with PHMB dressings include (Lindholm, 2010):

- Second-degree burns
- Post-surgical wounds
- Traumatic wounds
- Donor/recipient sites
- Leg ulcers
- Pressure ulcers
- Epidermolysis bullosa and scleroderma wounds.

PHMB foam dressings are also suitable for use under compression treatment for venous leg ulcers if necessary. The dressings are available in a range of sizes suitable for different wounds; Table 2 provides a full list of the range of AMS PHMB foam dressings.

Table 2. Product selection guide for AMS PHMB foam dressings

Adhesive Border		Non-adhesive	
7.5cm x 7.5cm	3″ x 3″	5cm x 5cm	2″ x 2″
10cm x 10cm	4″ x 4″	7.5cm x 7.5cm	3″ x 3″
12.5cm x 12.5cm	6″ x 6″	10cm x 10cm	4″ x 4″
15cm x 15cm	7″ x 7″	12.5cm x 12.5cm	6″ x 6″
20cm x 20cm	8″ x 8″	20cm x 20cm	8″ x 8″
10cm x 20cm	4″ x 8″	10cm x 20cm	4″ x 8″
10cm x 30cm	4″ x 12″		

Summary

PHMB is an effective antimicrobial agent, which combines a broad spectrum of antimicrobial activity and low cytotoxicity, resulting in an excellent biocompatibility index of 1.45. PHMB provides an alternative option to comparable antimicrobials when treating patients with an infected wound, or patients who are at risk of infection, without promoting bacterial resistance.

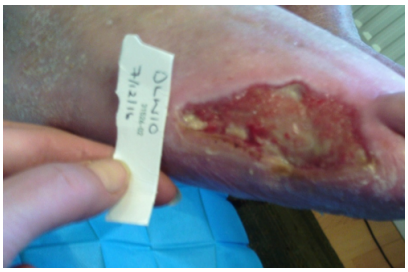
Foam dressings are a novel and effective mode of delivery for PHMB, combining the benefits of a traditional foam dressing with the antimicrobial properties of PHMB. AMS PHMB foam dressings (PHMB Foam Adhesive Border and PHMB Foam Non-Adhesive) use a three-layer construction to provide maximum benefit, which comprises: waterproof polyurethane bacterial barrier film, hydrophilic antimicrobial PHMB polyurethane foam pad and perforated wound contact layer. In practice, this means that the dressings are able to handle large amounts of exudate if necessary, reducing wear time, while simultaneously providing safe and effective infection control.

Case study

Patient history

Patient A, an 82-year-old man, was referred to the diabetic clinic following amputation of the fifth toe and metatarsal head. Mr A had a history of diabetes, peripheral vascular disease and chronic heart disease, and had undergone a recent bypass graft 13 weeks previously. He had been prescribed a course of antibiotics to treat infection/gangrene.

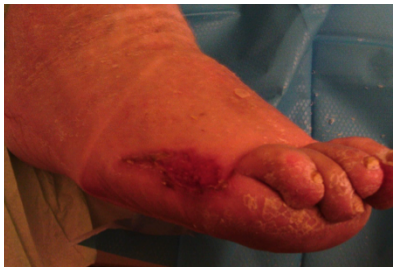
At initial presentation, the wound measured 6.2cm long, 2.7cm wide, with a depth of 0.2cm. On assessment of the wound bed, there was 60% slough and 40% granulation tissue. Exudate levels were classified as moderate and peri-wound skin was normal. The patient's pain level was 3 according to a standard VAS pain score assessment.



Initial presentation

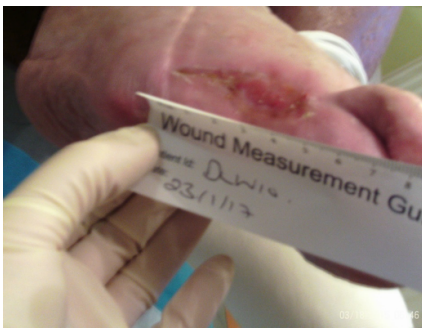
The wound was sharp debrided prior to application of the AMS PHMB Foam 10 x 20cm non-adhesive dressing. It was decided to manage the wound with a PHMB foam to manage exudate levels, prevent maceration, provide a moist wound healing environment and enable wound progression. The PHMB dressing was also selected as bacterial burden was a potential problem. The dressing was secured using a bandage.

Mr A had been in hospital for 4 weeks with gangrene infection to the left foot. The ward nurses had continued to dress the right foot with the AMS PHMB Foam. At assessment, the wound had reduced in size to 6cm long, 3cm wide and 0.1cm deep. There were still areas of sloughy tissue (40%) although superficial, and granulation tissue (60%) along with epithelial tissue, demonstrating wound progression. Exudate levels were low and the peri-wound skin was normal. No clinical signs of infection were noted and no further antibiotics were being administered. The pain level of the patient was 0 according to a standard VAS pain score assessment. The AMS PHMB Foam non-adhesive was reapplied and secured with a bandage. It was noted that the dressing was easy to apply.



Week 5

Following weekly dressing changes, the wound continued to progress and the wound was now 0.2cm long, 0.1cm wide and no depth. There were visible areas of new epithelial tissue and the surrounding skin remained healthy with no signs of infection. The pain level of the patient remained 0 according to a standard VAS pain score assessment. Exudate levels were classified as nil to low. Therefore treatment with the AMS PHMB Foam was discontinued, and the patient changed to a different treatment regimen.



Week 7

Conclusion

The AMS PHMB Foam was found to be an appropriate dressing in the management of a diabetic foot ulcer with moderate exudate levels and at high risk of infection. The dressing produced positive clinical outcomes for the patient. The dressing was able to provide effective exudate handling, while maintaining a moist wound environment and wound progression, with a reduction in wound size.

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