

# EXAMINING THE MULTIFACTORIAL NATURE OF WOUND INFECTION

Infection is a complex interplay between the host, a potential pathogen and its virulence, and the environment (European Wound Management Association [EWMA], 2005). The diagnosis of infection is a clinical judgement decision (World Union of Wound Healing Societies [WUWHS], 2008) often supported by laboratory analysis. While microbiology results potentially identify specific bacteria present, they cannot predict whether the bacteria will remain colonised or proceed to infection. The important determinant is the host and his or her susceptibility, as well as the ability to mount a robust immune response. This article discusses the multifactorial, yet individual, nature of wound infection and the inherent difficulties in diagnosing infection in many patients' wounds.

*'Controlling pain and bioburden, the hallmarks of infection, necessitates timely and appropriate intervention by clinicians to minimise the risk of a more serious outcome'*

Prevention, early diagnosis and management of infection are central tenets of good wound and patient care, especially in compromised patient groups with chronic wounds. Controlling pain and bioburden, the hallmarks of infection, necessitates timely and appropriate intervention by clinicians to minimise the risk of a more serious outcome, including death. Ongoing assessment and the judicious use of an antimicrobial, such as Suprasorb X + PHMB (Activa Healthcare), are examples of the use of sound clinical judgement in the management of the at-risk wound and patient.

The pivotal role of clinicians in the early detection and management of at-risk wounds is emphasised in this article and the value of antimicrobials, such as PHMB (polyhexamethylene biguanide), as a first-line treatment is reinforced. Benjamin Franklin said: 'A little

neglect may breed great mischief' — the early warning signs of infection should, likewise, not be neglected.

Infection is known to prolong the inflammatory phase and impair wound healing, potentially causing pain, discomfort and distress for the patient. In vulnerable and critically ill patients, infection is also associated with increased risk of morbidity and mortality. Patients who acquire nosocomial wound infections have significantly higher mortality rates than those who do not (Young et al, 2008). Patients who develop surgical site infections (SSI) remain inpatients longer than those who do not develop an infection and this results in an increased cost (Health Protection Agency [HPA], 2009).

## **Defining infection**

Key to understanding wound infection is the knowledge that

all wounds (especially chronic wounds) are contaminated with microorganisms on their surface (Stotts, 2004). The mere presence or multiplication of microorganisms on the wound surface, however, does not necessarily constitute wound infection. Wound bacteria can be acquired from the patient's own endogenous flora, which is present on the skin, mucous membranes or hollow viscera, from the environment or from cross-contamination.

The most common bacteria found in acute and chronic wounds are *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Streptococcus pyogenes*, with anaerobes and various coliforms occurring frequently in chronic wounds (Bowler et al, 2001; Cooper 2005).

Kingsley (2001) described the notion of a continuum in the development of wound infection, using conceptual names to describe the increasingly severe forms of wound bioburden, namely contamination, colonisation, critical colonisation and wound infection (*Table 1*).

Critical colonisation is considered to be the precursor to wound infection and one of the concerns is that even at this stage with high levels of bacteria, there may well be an absence of traditional signs of infection (Edwards and Harding, 2004; Warriner and Burrell, 2005). Uncontrolled localised infection of a wound can lead to deep, more severe infections, such as extensive cellulitis, osteomyelitis, bacteraemia and sepsis.

The balance between colonisation and infection in the wound is tipped, not necessarily by the number of bacteria, but by the ability of the host to mount a

robust immune response against an increasing bacterial virulence. The increasing numbers of bacteria compete with the host's cells for nutrients and oxygen.

**Risk factors for infection**

A detailed and comprehensive patient and wound assessment will enable the clinician to identify factors that may raise the index of suspicion that the patient is at risk of a wound infection. The immune response can be affected by multiple factors, including poor standards of wound-related hygiene (WUWHS, 2008). These factors are depicted in *Table 2* with some specific aspects outlined.

**Systemic factors**

**Comorbidities**

Disorders of the circulatory system will reduce the blood and oxygen delivering capacity within a wound, thus slowing the healing process and increasing the risk of wound infection (Ridgeway et al, 2005). Metabolic disorders, such as diabetes mellitus (often accompanied by peripheral vascular disease), can reduce neutrophil activity in the presence of elevated blood sugar levels, and specifically interfere with the action

of phagocytosis, thus delaying the normal inflammatory response and ingestion of microorganisms.

Neuropathy associated with diabetes can also confound the problem, as it is likely to mask the presence of pain and other signs of inflammation.

**Immunosuppression**

Immunosuppression can arise as a result of concurrent infections and the use of certain drugs, such as chemotherapy, long-term corticosteroids and immunosuppressants, as well as radiotherapy — all of which predispose the individual to the risk of potentially serious infection (Wilson, 2006). Immunosuppression lowers the individual's white blood cell count and/or functionality, resulting in a reduced capacity to fight infection.

**Nutritional status**

Malnourished patients can develop infections and often experience chronic non-healing wounds with decreased tensile strength (Stechmiller, 2010).

**Lifestyle – smoking**

Kean (2010) hypothesised that

**Table 1**  
*The four stages of the wound infection continuum*

Wound stage	Definition
Contamination	Presence of bacteria on the surface of the wound without multiplication
Colonisation	The presence of multiplying bacteria in a wound, which does not result in an immune response or trigger clinical signs and symptoms
Critical colonisation	The individual's immune response barrier is passed and can no longer control the microorganisms
Infection	The multiplying microorganisms within the wound overwhelm the individual's immune response, resulting in associated clinical signs and symptoms

**Table 2**  
*Risk factors for infection*

<i>Systemic factors</i>	<i>Wound characteristics</i>
<i>Inadequate blood supply or hypoxia/poor tissue perfusion</i>	<i>Large in size and/or deep</i>
<i>Metabolic disorder such as diabetes</i>	<i>Prolonged duration</i>
<i>Medication – corticosteroids, cytotoxic agents, immunosuppressants</i>	<i>Anatomical position, e.g. anal area raises potential contamination risk</i>
<i>Alcohol abuse/smoking</i>	<i>Necrotic tissue</i>
<i>Poor nutrition</i>	<i>Foreign bodies</i>
<i>Uncontrolled oedema</i>	<i>Untreated deeper infection, i.e. osteomyelitis</i>
<i>Malignancy</i>	
<i>Renal impairment</i>	
<i>Rheumatoid arthritis</i>	
<i>Renal impairment</i>	

smokers are at increased risk of developing wound infections due to delayed epithelialisation, resulting from a dampened white cell and inflammatory response, which results in a higher bacterial count in the wound bed.

**Signs and symptoms of infection**

The diagnosis of infection can be relatively simple in an otherwise healthy patient with an acute or surgical wound. However, it becomes more of a challenge when the wound is chronic and/or the patient is debilitated (WUWHS, 2008). Assessment of infection tends to be based on the classic signs and symptoms of infection (Table 3).

However, some of these also mimic the markers of inflammation (swelling, pain and erythema) and, therefore, it is vital that clinicians are able to determine whether a change in these indicators is predictive of wound infection. Older people and patients who are immunocompromised, including those taking anti-inflammatory drugs, may not present with the

classic signs as discussed earlier. The WUWHS (2008) has proposed additional criteria to assist the clinician in identifying infection (Table 3).

The signs and symptoms may be more subtle, such as loss of appetite, a general lethargy, malaise and apathy, with the patient seemingly unwilling or unable to undertake normal activities. In patients with diabetes there may also be an accompanying deterioration in diabetes control. Likewise, the changes in the wound may be understated — as the wound bed may appear darker, less vascular or grey in colour. There may also be an increase in slough. Clinicians need to be alert to these warning signs (Figure 1).

Malodour does not necessarily indicate infection but, paradoxically, can be a sign of infection (Gardner et al, 2001), as well as a major cause of anxiety and distress for patients (Jones et al, 2008). Fungating and exuding wounds may produce malodour as a result of fermentation of amino acids in anaerobes to malodorous

organic amines. Fungating wounds may also produce chemical compounds, putrescine and cadaverin, which cause severe malodour. Reducing the levels of bacteria in the wound will, in turn, reduce the odour.

Gardner et al (2001) suggest that pain is the most frequent sign of infection. Indeed, any sudden onset of pain, change in the type of pain, or increase in intensity is a significant indicator for infection. However, it has to be remembered that in patients with nerve damage, such as full thickness burns, or diabetic foot ulceration, pain may be absent.

Wound infection is not just costly to the patient either. Financial costs increase as treatment is prolonged, sometimes resulting in hospital admission (Wounds UK, 2010). Early recognition of wounds at risk of infection is essential to avoid delayed healing and prevent serious infections from occurring (Dissemond et al, 2010).

More subtly, localised wound infection impairs healing and is an important link to wound chronicity. This highlights the need for a thorough, detailed and regular assessment with information provided on the size of the wound, as this is a predictive marker of a wound that is failing to heal (EWMA, 2005). Failure of chronic wounds to reduce in size by 30% over four weeks is an indicator of poor healing (Sheehan et al, 2003).

The presence of microorganisms in wound pus, necrotic tissue, or slough is not evidence of infection. These non-viable substances are known to support bacterial growth due to the availability of nutrients and oxygen (White et al, 2006; Ennis, 2010). Therefore, debridement of sloughy/necrotic tissue is essential to prevent

infection and is recognised as one of the cornerstones of good wound practice (Vowden and Cooper, 2006).

### **Antimicrobials**

One of the key tools for practitioners to help reduce the bioburden in open acute and chronic wounds is the selection of an antimicrobial. If it is suspected that a wound is progressing towards overt infection, or there is an interruption in the healing process, then it is suggested that a topical antimicrobial be considered as first-line of defence to redress the host/bacterial imbalance in favour of the host (Kingsley et al, 2009; Best Practice Statement, 2011).

The early detection and management of infection is key to avoiding complications. It is also incumbent on practitioners to have a working knowledge of appropriate wound dressing regimens and the ideal properties of antimicrobial/antiseptic dressings. Recent studies have demonstrated a reduction in the clinical signs of wound infection when using topical antimicrobials (O'Meara et al, 2001). Antimicrobials alone are recommended to prevent wound infection in a compromised individual or to treat localised infection. Vowden et al (2011) advise the use of antibiotic therapy with an antimicrobial for a spreading or systemic infection.

### **PHMB**

The antiseptic/antimicrobial polyhexamethylene biguanide (also known as polyhexanide or PHMB) is a synthetic analogue of naturally occurring antimicrobial peptides (AMPs), such as keratinocytes and inflammatory neutrophils. AMPs are positively charged molecules with a broad spectrum of activity against bacteria, viruses and fungi

(Moore and Gray, 2007), which bind to bacterial cell membranes and induce cell lysis by destroying membrane integrity.

The structural similarities between AMPs and PHMB enables PHMB to penetrate into bacterial cell membranes and kill bacteria in a similar way to AMPs. It inhibits bacterial cell metabolism and binds to the bacteria's phospholipid (outer) membrane. This prevents bacteria from absorbing nutrients and disposing of waste products, ultimately resulting in microorganism death, while the host cells remain unaffected.

There is also evidence to suggest that PHMB binds to deoxyribonucleic acid (DNA) and other nucleic acids, damaging or inactivating them. Once entry has been gained, PHMB cannot be removed by the bacterium's defence system because it has effectively altered the cell membrane structure (Gilbert, 2006).

PHMB is an antiseptic that has been safely utilised commercially for many years in swimming pools, the brewing industry and as contact lens cleaning solution, with no development of resistance (Moore and Gray, 2007). The long-term use of

PHMB in other areas, without cytotoxicity or the development of resistance, suggests this is unlikely to happen when the antiseptic is used in wound management (Gilbert, 2006). PHMB is active against a number of bacterial pathogens, including methicillin-resistant *Staphylococcus aureus*, *vancomycin-resistant enterococcus*, *Pseudomonas*, *Escherichia coli* and *Staphylococcus epidermis*, as well as yeast and fungi. PHMB is also effective on both planktonic bacteria and biofilm colonies.

It is also noteworthy that, unlike other antimicrobial agents, there is a minimum reduction of the effect of PHMB in the presence of blood and proteins (Dissemond, 2010). PHMB has been successfully incorporated into a range of wound products, including Suprasorb X + PHMB which incorporates 0.3% PHMB.

### **Suprasorb X + PHMB**

Suprasorb X + PHMB is a biocellulose dressing with hydrobalance technology fibres, which is able to regulate the absorption and donation of moisture to the wound bed (Kingsley et al, 2009). This moisture-absorbing and donating capacity is possible within the same



**Figure 1. Infected sacral pressure ulcer.**



**Table 3**  
*Signs and symptoms of wound infection*

<i>Classic criteria</i>	<i>Additional criteria</i>
<i>Pyrexia</i>	<i>Delayed (or stalled) healing</i>
<i>Inflammation</i>	<i>Bridging of skin across a wound</i>
<i>Oedema</i>	<i>Dark/discoloured granulation tissue</i>
<i>Pain</i>	<i>Increased friability (tissue which bleeds easily)</i>
<i>Increase in exudate or pus</i>	<i>Painful/altered sensation to the wound site/surrounding skin</i>
<i>Abscess</i>	<i>Altered odour/malodour</i> <i>Wound breakdown</i> <i>Pocketing at the base of the wound</i> <i>Increased watery/serous exudate rather than pus</i> <i>Erythema extending from the wound edge</i>

wound, removing exudate from wet areas as well as then donating moisture to drier areas. Suprasorb X + PHMB can, therefore, be utilised on light to moderately exuding wounds, as well as dry wounds. The presence of fluid in the dressing means that antimicrobial activity is possible even on dry wounds (Gray et al, 2010).

One of the worst symptoms of infection for the patient is pain (Gardner et al, 2001; Mudge and Orsted, 2010), which often exacerbates the pain already caused by their clinical condition, as in the case of leg ulceration.

In a study of 24 patients with venous leg ulcers, Alvarez et al (2004) reported a significant reduction in pain for patients over a 12-week period, probably linked to the cooling effect of the moist environment promoted by the dressing.

Similarly, Mosti et al (2008) reported a mean reduction in pain experienced by patients with leg ulcers attending an outpatient department within three to four

weeks of treatment with Suprasorb X + PHMB, thus improving their quality of life.

While there is a paucity of evidence from randomised controlled trials (RCTs) on PHMB, nonetheless, there is a plethora of case-study evidence on its overall efficacy in eradicating wound infection, as well as providing marked pain relief (Glover and Wicks, 2009; Gray et al, 2010). These are important factors for clinicians faced with patients with non-healing painful wounds.

Because the PHMB is not bound to the dressing fibres it is able to exert its antimicrobial effect both within the dressing and at the wound-dressing interface. An evaluation of Suprasorb X + PHMB by Cavorsi (2006) featuring 79 wounds of varying aetiology revealed clinical improvement or healing was achieved in more than 80% of cases. In a subset previously unresponsive to silver dressings, a decrease in wound size of 33% was also observed after three weeks.

### **Conclusion**

The pivotal role of clinicians in

preventing and managing wound infection and its consequences cannot be overestimated. It necessitates constantly being on the look out for early warning signs of infection, not only in the patient, but also in the wound itself. Early intervention with an antimicrobial, such as Suprasorb X + PHMB, is key to a good outcome for all concerned. **WE**

### **Declaration of interest**

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