The relationship between wound, host and bacteria is continuously changing as a result of local, environmental and systemic factors (Templeton, 2014). One of these factors may be the use of antibiotics. However, due to the emergence of many resistant bacteria, the routine use of topical and oral antibiotics is not justified for colonised or infected wounds and should only be considered for wounds that are clinically infected and showing signs of spreading erythema and pyrexia, or if the patient is feeling generally unwell. Therefore, as bacterial colonisation of the wound does not necessarily indicate infection, it should be clear that antibiotics should not be the first choice, although removal of bacteria before it can critically colonise a wound is very important. This places antibacterials in an important position for wound healing if they are effective in reducing colonisation.

Antiseptics are chemicals that can slow or stop the growth of micro-organisms on external surfaces of the body and are mainly used to reduce levels of micro-organisms on the skin and mucous membranes. However, even though it is inevitable that chronic wounds are colonised by micro-organisms, many go on to heal successfully, despite the colonisation. Nevertheless, sometimes bacteria will multiply and invade the tissues and the host, causing damage to tissues, delaying healing and potentially causing systemic illness (International Wound Journal, 2008). Therefore, it is important that any bacteria in a wound is carefully monitored and managed accordingly.

Interest in the use of antiseptics in the management of wound infection has re-emerged in recent years as a result of ongoing and escalating problems with resistance and allergy to topical and systemic antibiotics (World Union of Wound Healing Societies [WUWHS], 2008). However, although antiseptics are commonly used, surprisingly few studies have been conducted to examine the effect on the wound-healing process and efficacy of wound antiseptics. Many of the references in this article are considered older studies but, nevertheless, are relevant to a review such as this.

History of antimicrobials
The earliest documented records of topical wound treatments were found...
in Mesopotamia; these inscriptions on clay tablets have been dated to approximately 2500 BC (Cooper, 2004), and between 14AD and 37AD there is documentary evidence that Cornelius Celsus (a Roman physician) described the four principal signs of inflammation and used ‘antiseptic’ solutions. Claudius Galen (130–200AD) had such an influence on the management of wounds that he is still thought of, by many today, as the ‘father of surgery’. He instigated the ‘laudable pus’ theory, which incorrectly considered the development of pus in a wound as a positive part of the healing process and he would remove pus from one man’s wound and place it in another in order to promote this ‘laudable pus’ theory.

Louis Pasteur was a French chemist and microbiologist renowned for his discoveries of the principles of vaccination, microbial fermentation and pasteurisation. He invented the process of pasteurisation, which is widely used today for milk and beer. The rapid heating process, which kills harmful germs, still bears his name. The importance of antimicrobials has been in the forefront of wound healing since the 19th century.

The use of carbolic acid administered by Joseph Lister in operating theatres from 1865 significantly reduced mortality rates associated with surgical procedures (Cooper, 2004). Lister was a British surgeon who was heavily influenced by Louis Pasteur’s work on bacteria. Certainly, his greatest contribution to medicine was the promotion of the use of carbolic acid as an antiseptic. Lister published the results of his studies in a series of articles in the British Medical Journal and The Lancet, in which he urged surgeons to wash their hands and instruments with a 5% carbolic solution and to wear clean gloves.

**Background to wound antiseptics**

Infection is one of the key reasons why wound healing may stall, leading to increased risks of patient morbidity and mortality with increased treatment costs (NICE, 2008). In the compromised host, there is always an increased risk of wound infection due to the host’s inability to mount a robust immune response to the presence of multiplying micro-organisms within the wound (Vowden et al, 2011). Therefore, infection control is particularly important.

In addition to infection control measures, effective cleansing of the wound is important to reduce bacterial loading and contamination, of the surrounding skin (Bradbury and Fletcher, 2010). Before new granulation tissue and blood vessels can form, the wound microenvironment must be sufficiently clean and organised to facilitate fibroblast migration and interaction via signals sent from the existing fibrin matrix. In addition, keratinocyte migration and proliferation following release of their attachment to the basement membrane is necessary — a course facilitated by matrix metalloproteases (MMPs; Chen and Parks, 2009).

Despite the lack of research on the subject, the practice of wound cleansing or antiseptic management has a dichotomous history anchored in tradition and science (Smith 2005). Nevertheless, history has demonstrated that quality of care is a critical requirement for wound healing and ‘good’ care of wounds has been synonymous with topical prevention and management of microbial contamination.

There is a debate in clinical circles about the potential advantages and disadvantages of cleansing wounds of bacterial contamination because the exudate itself may contain growth elements and chemokines, which contribute to wound healing and for that reason it is not always necessary (Atiyeh et al, 2009). However, if healing is not present, as in a chronic wound, then there are no growth factors present. Therefore, applying something that is slightly irritant to the tissues may increase the inflammatory process and may stimulate the wound to heal. Atiyeh et al (2009) suggested that, when applied at the proper times and concentrations, some classes of antiseptics may provide a tool for the clinician to drive the wound bed in desired directions.

Moscati et al (1998; 2007) suggested that wound cleansing helps to optimise the healing environment and decrease the potential for infection; tap water is recommended as it has the advantages of being efficient, cost effective and accessible (Angeras et al, 1992; Fernandez et al, 2008). Angeras et al (1992) actually found a higher rate of infection in those wounds irrigated with saline. However, this was on a small number — the study population was unknown although a second study of a population of 715 demonstrated similar findings (Moscati et al, 2007). Even where wounds are not clearly clinically infected, they usually have populations of micro-organisms present. It is thought these wounds may heal better if these populations are reduced by antibacterial agents. However, the relationship between infection and micro-organism populations in wounds and wound healing is not very clear (Norman et al, 2016a).

Debridement is an extremely important part of wound cleansing but when debridement of the wound bed is not sufficient to reduce bacterial loads, the application of broad-spectrum antiseptics may be indicated (Thomas et al, 2009).

In two seminal pieces of work, antiseptics directly applied to cultured human fibroblasts were found to be cytotoxic. All of the cytotoxic agents except hydrogen peroxide were subsequently found to adversely affect wound healing in an animal model (Van Den Broek, 1982; Lineaweaver et al, 1985). At the same time, hydrogen
perrno was found to significantly increase the blood flow in ischaemic ulcers in a guinea pig model (Tur et al, 1995) and subsequently increased acceleration of re-epithelialisation in a rat model (Gruber et al, 1975). Macpherson (2004) believed that antiseptics prevent the growth of pathogenic micro-organisms without damaging living tissue.

Topical antiseptics are antimicrobial agents that kill, inhibit or reduce the number of micro-organisms and are thought to be essential for wounds infection control. Although certain skin and wound cleansers are designed as topical solutions with varying degrees of antimicrobial activity, concerns have been raised as wound cleansers may affect normal human cells and may be antimitotic, adversely affecting normal tissue repair (Atiyeh et al, 2009). However, in spite of the in vitro demonstrations of inhibition of healing by some antiseptics, there are increasing data to indicate that healing is inhibited by bacterial infection, and that a reduction in bacterial numbers can reduce inflammation and enhance healing (Pierard-Franchimont et al, 1997).

These antiseptics are available in many different forms: liquids, pastes, creams, ointments, gels, powders, sprays and impregnated dressings. The method of use and frequency of application may influence the practicality of a particular antiseptic. Some are used for one or more short periods each day, some require reappllication several times per day, and others are left in contact with the wound for up to several days (WUWHS, 2008).

The most frequently used topical antimicrobials in modern wound care practice include iodine, silver and honey-containing products. In the past, acetic acid, chlorhexidine, hydrogen peroxide, sodium hypochlorite, potassium permanganate and proflavine have been used (Cooper, 2004), but these are rarely used today.

In one study comparing cadexomer iodine and silver dressings, all participants showed signs of infection or critical colonisation at baseline. The frequency of complete healing at 12 weeks was similar between treatment groups, with 60% of participants healing in the cadexomer iodine group compared with 61% in the silver-impregnated dressing group (Miller 2010). Therefore, no conclusion can be drawn on whether silver or cadexomer iodine is a more powerful antibacterial, or even if the participants would have healed at the same rate without antimicrobials as there was no control to compare. Certainly, the relative effects of systemic and topical antimicrobial treatments on pressure ulcers are not clear. Where differences in wound healing were found, these sometimes favoured the comparator treatment without antimicrobial properties. The trials are small, clinically heterogenous, generally of short duration, and at high or unclear risk of bias (Norman et al, 2016b).

In other studies, hydrogen peroxide and povidone-iodine reduced both migration and proliferation of fibroblasts in a dose-dependent fashion. Treatment with silver-containing antiseptics and chlorhexidine exhibited reductions in proliferation at high concentrations, but enhanced growth at lower doses. Silver-containing compounds and chlorhexidine also proved to be the least detrimental to migration in these assays. MMP release from the cells was differently affected depending on the dosage and class of antiseptic applied (Thomas et al, 2009).

Silver sulfadiazine and chlorhexidine, at levels still proven to be bactericidal, had fewer detrimental effects on fibroblast activity in these assays. The silver-containing antiseptics may even increase the proliferative potential of these cells in culture (Thomas et al, 2009).

To become bactericidal, silver atoms must lose an electron and become positively charged silver ions. Silver ions are highly reactive, affecting multiple sites in bacterial cells. They ultimately cause cell death by binding to bacterial cell membranes and causing disruption of the cell wall and cell leakage (Lansdown, 2002).

There appears to be no robust evidence on the relative effectiveness of any antiseptic, antibiotic or antibacterial preparation evaluated to date. Where some evidence for possible treatment effects was reported, it stemmed from single studies with small participant numbers and was classed as moderate or low-quality evidence. This means it is likely or very likely that further research will have an important impact on confidence in the estimate of effect, and may change this estimate (Norman et al, 2016a).

Current evidence does not support the routine use of honey- or silver-based products and further good quality research is required before definitive conclusions can be drawn about the effectiveness of povidone-iodine, peroxide-based preparations (O’Meara et al, 2013). However, evidence from animal studies and some trials has suggested that honey may actually accelerate wound healing (Jull et al, 2015).

However, like all research findings, the outcome is only ever as good as the design of the research. In the author’s 25-year experience of wound care, antibacterials do make a difference as they quickly remove odour from a wound, which indicates that bacteria is also being removed.

**Biofilms**

It is now understood that many medical conditions are the result of
biofilm formation: cystic fibrosis, periodontitis, endocarditis, kidney stones, tonsillitis, osteomyelitis, and persistent otitis media, to name a few (Keast et al, 2014) However, though common, the nuances of many of the key issues in infection, such as biofilms, critical colonisation are poorly understood (Swanson and Carville, 2014). After attaching to a surface such as a wound bed, bacteria can encase themselves in a gelatinous matrix known as a biofilm. These complex microbial communities can contain numerous bacterial species, protected against the immune system and antimicrobial agents (WUUWHS, 2008). While biofilms can delay wound healing, a routine laboratory test for their detection has not yet been established (Fazli et al, 2009). Nevertheless, there is now strong evidence that biofilms are present in the majority of chronic wounds (Bjarnsholt et al, 2008; James et al, 2008).

The physical barrier of the exopolysaccharide shield protects bacteria in biofilms. Furthermore, bacteria in the biofilm — especially in the periphery — can down regulate their metabolism (a decrease in the number of receptors on the surface of target cells, which makes the cells less sensitive to a hormone or another agent). This makes them less susceptible to antibiotics (Keast et al, 2014) with 60% to 90% of chronic wounds thought to have biofilm formation (Bjarnsholt et al, 2008; James et al, 2008).

Both silver- and iodine-releasing dressings have been shown to kill biofilm bacteria (Percival et al, 2008) whereas normal saline and tap water are possibly ineffective for biofilm management (Cutting et al, 2010).

The beneficial effects of mechanical debridement in infected wounds may be related partly to the removal of bacterial biofilms (International Wound Journal, 2008) which is why mechanical debridement is popular with surgeons.

**Conclusion**

The age of some of the studies reported here means that more recent good quality research is required before definitive conclusions can be drawn about the effectiveness of topical agents, such as povidone iodine, honey-, silver- and peroxide-based products and other topical antiseptics in healing and, in this debate about the role of antiseptics in wound healing, the jury is still out. However, the main arguments are actually between academics who review the research and clinicians who use the products on a daily basis. It is the view of the author that clinicians have a commonsense approach to wound care and if the product did not do what they expected it should do, then they would cease to use the product. This is a simple answer to an age-old question regarding the use of antiseptics.

**References**


