Wound infection in clinical practice
An international consensus
Wound infection continues to be a challenging problem and represents a considerable healthcare burden. Early recognition along with prompt, appropriate and effective intervention are more important than ever in reducing its economic and health consequences, especially in the context of growing resistance to antibiotics.

This important document represents the consensus opinion of an international panel of experts who met in 2007. A major strength of this meeting was the open sharing of the realities and practicalities of treating wound infection in many different situations.

The content of this document has been carefully considered to relate directly to daily clinical practice. In particular, it provides broad, clear and safe guidance on the areas of diagnosis and the topical/systemic treatment of bacterial wound infection. The wide disciplinary and geographical representation of the panel ensures that the principles presented are both practical and adaptable for use in local settings worldwide. Research will continue to provide greater understanding of wound infection and to shape future practice.

Professor Keith Harding
Even though it is virtually inevitable that most wounds contain micro-organisms, many heal successfully. However, sometimes micro-organisms (particularly bacteria) multiply, invading and damaging tissues, delaying healing and occasionally causing systemic illness.

The potential for bacteria to produce harmful effects is influenced by the:
- ability of the patient's immune system to combat the bacteria (host resistance)
- number of bacteria introduced – higher numbers are more likely to overcome host resistance
- type of bacteria introduced:
  - some bacteria have greater disease-producing ability (virulence) than others, and may be able to cause disease in relatively low numbers
  - benign residents in one body site may cause disease if transferred elsewhere.

Wounds usually contain bacteria – often without detrimental effect

DEFINITIONS
The presence of bacteria in a wound may result in:
- contamination – the bacteria do not increase in number or cause clinical problems
- colonisation – the bacteria multiply, but wound tissues are not damaged
- infection – the bacteria multiply, healing is disrupted and wound tissues are damaged (local infection). Bacteria may produce problems nearby (spreading infection) or cause systemic illness (systemic infection) (Figure 1).

Localised infection is often characterised by the classical signs and symptoms of inflammation – pain, heat, swelling, redness and loss of function. However, particularly in chronic wounds, bacteria may cause problems, eg delayed (or stalled) healing, in the absence of such obvious indicators of inflammation. Some clinicians refer to this more subtle state of localised infection as 'critical colonisation', or 'covert' or 'occult' infection. Whatever term is used, when the bacteria in a wound cause problems, intervention is required to prevent deterioration and to facilitate wound healing.

Further research is required to fully understand the factors involved in the transition from colonisation to localised infection. This may facilitate future guidance regarding the timing and nature of intervention.

APPLICATION TO PRACTICE
Intervention is usually required only when the patient is at a high risk of wound infection (see page 2) or when the interaction between the bacteria in a wound and the host's defences impairs healing, causes further damage, and results in localised, spreading or systemic infection.
The diagnosis of wound infection is made mainly on clinical grounds. Assessment should include evaluation of the patient, the tissues around the wound and the wound itself for the signs and symptoms of wound infection, as well as for factors likely to increase the risk and severity of infection. Incorporation of assessment for wound infection into routine wound practice will aid early detection and subsequent treatment.

**RISK OF INFECTION**

The risk of wound infection is increased by:

- any factor that debilitates the patient, impairs immune resistance or reduces tissue perfusion, eg:
  - comorbidities – diabetes mellitus, immunocompromised status, hypoxia/poor tissue perfusion due to anaemia or arterial/cardiac/respiratory disease, renal impairment, malignancy, rheumatoid arthritis, obesity, malnutrition
  - medication – corticosteroids, cytotoxic agents, immunosuppressants
  - psychosocial factors – hospitalisation/institutionalisation, poor personal hygiene, unhealthy lifestyle choices

- certain wound characteristics (Box 1) or poor standards of wound care related hygiene.

Clinicians must maintain a high level of clinical suspicion for wound infection, particularly in patients with diabetes mellitus, autoimmune disorders, hypoxia/poor tissue perfusion, or immunosuppression.

**BOX 1 | Wound characteristics that may increase the risk of infection**

<table>
<thead>
<tr>
<th>Acute wounds</th>
<th>Chronic wounds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contaminated surgery</td>
<td>Necrotic tissue or foreign body*</td>
</tr>
<tr>
<td>Long operative procedure</td>
<td>Prolonged duration</td>
</tr>
<tr>
<td>Trauma with delayed treatment</td>
<td>Large in size and/or deep</td>
</tr>
<tr>
<td>Necrotic tissue or foreign body*</td>
<td>Anatomically situated near a site of potential contamination, eg anal area</td>
</tr>
</tbody>
</table>

*Particularly in the presence of hypoxia

**SIGNS AND SYMPTOMS**

Infection in acute or surgical wounds in otherwise healthy patients is usually obvious. However, in chronic wounds and debilitated patients, diagnosis may rely on recognition of subtle local signs or non-specific general signs (such as loss of appetite, malaise, or deterioration of glycaemic control in diabetic patients). The extent and severity of a wound infection will impact on management. It is important to recognise and differentiate the signs and symptoms of localised, spreading and systemic infection (Figure 4).

Infection may produce different signs and symptoms in wounds of different types and aetiologies. Scoring systems and diagnostic criteria have been developed to aid identification of infection in acute wounds, such as surgical site infection, eg ASEPSIS and the Centers for Disease Control and Prevention (CDC) definitions. Validated scoring systems that aid diagnosis of wound infection in the various types of chronic wound are awaited. However, there is sufficient evidence for clinicians to integrate selected signs and symptoms of infection (Figure 4) into general wound assessment.

Clinicians need to act promptly if a patient with a wound shows signs of a potentially fatal infection, eg signs of sepsis or extensive tissue necrosis (necrotising fasciitis or gas gangrene).

Clinicians must be familiar with the signs and symptoms characteristic of infection in the wound types they see most frequently, eg in diabetic foot ulcers.
### Acute Wounds

**Localised infection**
- Classical signs and symptoms:
  - new or increasing pain
  - erythema
  - local warmth
  - swelling
  - purulent discharge
- Pyrexia – in surgical wounds, typically five to seven days post-surgery
- Delayed (or stalled) healing (Box 5, see page 10)
- Abscess
- Malodour

**Spreading infection**
- As for localised infection PLUS:
  - Further extension of erythema
  - Lymphangitis (Box 5, see page 10)
  - Crepitus in soft tissues (Box 5, see page 10)
  - Wound breakdown/dehiscence

**Notes**
- Burns – also skin graft rejection; pain is not always a feature of infection in full thickness burns
- Deep wounds – induration (Box 5, see page 10), extension of the wound, unexplained increased white cell count or signs of sepsis may be signs of deep wound (ie subfascial) infection
- Immunocompromised patients – signs and symptoms may be modified and less obvious

### Chronic Wounds

**Localised infection**
- New, increased or altered pain*
- Delayed (or stalled) healing* (Box 5, see page 10)
- Periwound oedema
- Bleeding or friable (easily damaged) granulation tissue
- Distinctive malodour or change in odour
- Wound bed discoloration
- Increased or altered/purulent exudate
- Induration (Box 5, see page 10)
- Pocketing (Figure 2)
- Bridging (Figure 3)

**Spreading infection**
- As for localised infection PLUS:
  - Wound breakdown*
  - Erythema extending from wound edge
  - Crepitus, warmth, induration or discoloration spreading into periwound area
  - Lymphangitis (Box 5, see page 10)
  - Malaise or other non-specific deterioration in patient’s general condition

**Notes**
- In patients who are immunocompromised and/or who have motor or sensory neuropathies, symptoms may be modified and less obvious. For example, in a diabetic patient with an infected foot ulcer and peripheral neuropathy, pain may not be a prominent feature*
- Arterial ulcers – previously dry ulcers may become wet when infected
- Clinicians should also be aware that in the diabetic foot, inflammation is not necessarily indicative of infection. For example, inflammation may be associated with Charcot’s arthropathy

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*Individually highly indicative of infection. Infection is also highly likely in the presence of two or more of the other signs listed.
INVESTIGATIONS
Initial assessment may indicate the need for microbiological analysis, blood tests or imaging investigations to confirm the diagnosis, detect complications such as osteomyelitis, and guide management.

Microbiology
In practice, the use of microbiological analysis to guide management will be heavily influenced by local availability of microbiology services. Even where readily accessible, microbiological tests should not be performed routinely (Box 2).

BOX 2 | Indications for wound specimen collection for microbiological analysis

- Acute wounds with signs of infection
- Chronic wounds with signs of spreading or systemic infection (Figure 4, see page 3)
- Infected chronic wounds that have not responded to or are deteriorating despite appropriate antimicrobial treatment
- As required by local surveillance protocols for drug resistant micro-organisms

*In patients showing signs of sepsis, blood cultures are important, and cultures of other likely sites of infection should be considered
†Also consider for high-risk chronic wounds with signs of localised infection, eg delayed (or stalled) healing, in patients who have diabetes mellitus or peripheral arterial disease, or who are taking immunosuppressants or corticosteroids

Sampling techniques include wound swabbing, needle aspiration and wound biopsy. Wound swabbing is most widely used, but may mislead by detecting surface colonising microorganisms rather than more deeply sited pathogens. Wound biopsy provides the most accurate information about type and quantity of pathogenic bacteria, but is invasive and often reserved for wounds that are failing to heal despite treatment for infection.

The best technique for swabbing wounds has not been identified and validated. However, if quantitative microbiological analysis is available, the Levine technique may be the most useful. In general, sampling should take place after wound cleansing (and, if appropriate, debridement), and should concentrate on areas of the wound of greatest clinical concern.

Bacteria are usually identified and quantified using culture techniques. When very rapid identification is required, eg in sepsis, microscopic examination by experienced personnel of clinical specimens treated with a Gram stain may be useful in guiding early antimicrobial therapy. Samples sent for analysis should be accompanied by full clinical details to ensure that the most appropriate staining, culture and antibiotic susceptibility analyses are performed and that the laboratory is able to provide clinically relevant advice.

Beware of interpreting a microbiology report in isolation – consider the report in the context of the patient and the wound and, if appropriate, consult a microbiologist or infectious disease specialist

APPLICATION TO PRACTICE
Assessment of wounds for infection incorporates a full evaluation of the patient and should consider how immune status, comorbidities, wound aetiology/status and other factors will affect the risk, severity and likely signs of infection.

The classical signs of infection are not always present, particularly in patients with chronic wounds or diabetes mellitus.

The diagnosis of wound infection is based mainly on clinical judgement – appropriate investigations (eg microbiology of wound samples) can support and guide management.
Effective management of wound infection often requires a multidisciplinary approach and may involve specialist referral (Figure 5). It aims to readjust the interaction between the patient and the infecting micro-organism(s) in favour of the patient by:
- optimising host response
- reducing the number of micro-organisms.

**OPTIMISING HOST RESPONSE**

Implementation of measures to optimise host response will enhance the ability of patients to fight infection and improve their healing potential. Systemic factors that may have contributed to the development of the wound infection (and often in the case of chronic wounds, the wound itself) should be addressed, eg optimisation of diabetic glycaemic control and the use of disease-modifying drugs in rheumatoid arthritis.

**REDUCING BACTERIAL LOAD**

*Effective hygiene and preventative measures*

Infection control procedures should be followed to prevent further contamination of the wound and cross-contamination. Good hygiene practice includes paying particular attention to thorough hand cleansing/disinfection and suitable protective working clothes, including gloves.

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**Figure 5 | Effective management of wound infection**

Prompt, effective management of wound infection may reduce time to healing and minimise impact on patients, healthcare systems and society

Treatment of an infected wound should follow a clear, decisive plan

Management of comorbidities may require specialist input

Good hygiene, wound debridement and wound cleansing will aid reduction in wound bacterial load

When the problems caused by bacteria remain localised to a wound, antibiotics are often unnecessary and topical treatment with antiseptics is usually sufficient

Regular re-evaluation of the wound, the patient and the management plan is essential
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. Many antiseptics are relatively easy to use (including by patients and carers), are widely available, frequently cost less than antibiotics, and can often be administered without prescription.

Topical antibiotics should only be used in infected wounds under very specific circumstances by experienced clinicians (eg topical metronidazole might be used for the treatment of malodour in fungating wounds)

**USING ANTISEPTICS**

Antiseptics generally have a broad spectrum of antibacterial activity. Their action at multiple sites within microbial cells reduces the likelihood of bacteria developing mechanisms to avoid their effects and so may explain their relatively low levels of bacterial resistance. Factors influencing the choice of antiseptic for an infected wound include:

- clinician familiarity
- availability, cost and reimbursement issues
- ease of use and implications for pattern of care
- efficacy and safety.

**Possible toxic effects**

In the past, concerns about the toxic effects of some antiseptics on animal tissues in laboratory tests have limited their clinical use. Although research evidence determining whether this effect also occurs in clinical practice is lacking, some antiseptics, eg cadexomer iodine and some newer silver formulations, do appear to have beneficial effects on wound healing. Even so, for many antiseptics, research demonstrating their effects on wound healing is awaited and so antiseptics should not be used indiscriminately or indefinitely.

For an antiseptic with an unknown impact on wound healing, clinicians need to consider whether, for a particular wound in a particular patient, the clinical benefit of its use outweighs any possible negative effect on wound healing.
Clinical evidence

As discussed, there is a growing body of clinical evidence supporting the use of the antiseptics silver\textsuperscript{12} and iodine\textsuperscript{13} in infected wounds, and there is interest in alternatives such as honey\textsuperscript{14} and larval therapy (maggots)\textsuperscript{15}. Current clinical evidence is strongest for some silver products. Despite the use of many other antiseptics in a wide range of situations (Table 1, see page 10), evidence supporting their efficacy in the treatment of wound infection is more limited. Unless suitable alternatives are unavailable, sodium hypochlorite and hydrogen peroxide solutions are not usually recommended.

Over the years, many natural remedies have been used on infected wounds. Caution is advised until clinical evidence of their efficacy and safety becomes more robust.

Roles and formulation

Antiseptics are used mainly in the treatment of infected open acute and chronic wounds (Box 3, see page 7). If there are signs of spreading or systemic infection, antiseptics should be used in conjunction with systemic antibiotics.

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 reapplication several times per day, and others are left in contact with the wound for up to several days.

To maximise the potential impact of antiseptics on bacterial load, clinicians may consider that there is a carefully controlled role for:

- using an antiseptic solution for cleansing an infected wound \textit{in addition to}
- applying an antiseptic preparation/dressing until the next dressing change.

Clinicians are advised to review evidence of efficacy and safety, and to consult local regulatory information before using a particular antiseptic to treat an infected wound.

The formulation of an antiseptic may determine its use and may contribute to other facets of wound care. For example, a solution would be required for cleansing. Also, a highly absorbent formulation would be preferable in a heavily exuding wound; conversely, an antiseptic-containing dressing of low absorbency may be more suitable for a low to moderately exuding wound.

More extensive clinical research is needed to evaluate the best methods for using antiseptics and to clarify the impact of antiseptic delivery systems on efficacy.

APPLICATION TO PRACTICE

Treatment of infected wounds with antiseptics is often necessary – clearly define reasons for use, treatment goals and duration of use

Use antiseptics in the context of a management plan that incorporates optimising host immune response and other methods of reducing bacterial load (Figure 5, see page 5)

Consider how the formulation of an antiseptic could contribute to other aspects of wound care and accommodate local resources or patterns of care

When using topical antimicrobials, clearly define and regularly review reasons for use, goals and duration of treatment; do not use indefinitely
In some parts of the world, indiscriminate use of antibiotics has contributed to the development of antibiotic-resistant strains of bacteria (e.g., meticillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Staphylococcus aureus* (VRSA) and multi-drug resistant *Pseudomonas* and *Acinetobacter* species), and to the emergence of healthcare-associated infections such as *Clostridium difficile* associated diarrhoea. However, used appropriately, systemic antibiotics do have an important and potentially life- or limb-saving role in the management of wound infection (Box 4).

The choice of systemic antibiotic for an infected wound will be influenced by the:
- most likely or confirmed antibiotic susceptibilities of the suspected or known pathogen(s)
- patient – e.g., allergies, potential interactions with current medication, comorbidities, ability and willingness to comply with treatment
- guidelines for the treatment of infection in specific wound types – e.g., for diabetic foot infections
- severity of the infection – e.g., degree of spread, systemic symptoms
- availability, cost and safety.

Administration of a combination of antibiotics may be necessary. Intravenous antibiotics are usually reserved for serious or life-threatening infections.

### BOX 4 | Using systemic antibiotics in wound infection

**Indications for systemic antibiotics**
- Prophylaxis where risk of wound infection is high, e.g., contaminated colonic surgery or ‘dirty’ traumatic wounds
- Spreading or systemic wound infection
- When culture results reveal β-haemolytic streptococci, even in the absence of signs of infection

**Review antibiotic regimen**
- If there is no improvement of systemic or local signs and symptoms, re-evaluate the patient and the wound; consider microbiological analysis and changing antibiotic regimen
- If the patient has an antibiotic-related adverse event; discontinue causative antibiotic

**Discontinue/review systemic antibiotics**
- At the end of the prescribed course (according to type of infection, wound type, patient comorbidities and local prescribing policy)

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- guidelines for the treatment of infection in specific wound types – e.g., for diabetic foot infections
- severity of the infection – e.g., degree of spread, systemic symptoms
- availability, cost and safety.

Administration of a combination of antibiotics may be necessary. Intravenous antibiotics are usually reserved for serious or life-threatening infections.

Empirical antibiotic treatment must take into account the local antimicrobial susceptibility patterns of the possible pathogens.
in open surgical wounds healing mainly by epithelialisation, the epithelial margin advances at about 5mm per week\(^2\). Currently used mainly for burns.

- Antimicrobial effects have been attributed to some
- Used as a soak to reduce wound bacterial load
- Available in several forms including silver sulfadiazine

Povidone iodine (polyvinylpyrrolidone iodine – PVP-I)
- Staining of the wound bed or surrounding skin by ionic
- Also known as polyhexanide and polyaminopropyl

A reduction in venous leg ulcer surface area of >30% during the first two weeks of treatment is predictive of healing\(^1^9\).
- Mainly used as a skin disinfectant or surgical scrub
- Considered for its effect against

Cadexomer iodine releases iodine from highly
- Caution is advised when using the solution because
- Consider protecting periwound skin during use

Cautionary note

Further research is required to clarify the suitability of individual antiseptics for particular wound types and to provide clear guidance on appropriate duration of use. Clinicians should carefully consider the potential risks and benefits of using an antiseptic. Clinicians are also strongly advised to consult research evidence and local prescribing/ regulatory information for recommended methods of use and safety information before using a particular antiseptic formulation for the treatment of an infected wound.

Critical colonisation – A potentially important concept that is widely applied to chronic wounds but lacks clarity. It arose to differentiate problems caused by bacteria that are not always accompanied by the classical signs of infection, eg delayed (or stalled) healing, from more obvious infection. However, the concept and a clear understanding of its meaning and implications are not universally accepted.

Delayed healing – Healing progresses at a slower rate than expected. As a guide:
- in open surgical wounds healing mainly by epithelialisation, the epithelial margin advances at about 5mm per week\(^2\)
- clean pressure ulcers with adequate blood supply and innervation should show signs of healing within two to four weeks\(^1^8\)

Induration – Hardening of the skin and subcutaneous tissues around a wound due to inflammation, which may be secondary to infection.

Lymphangitis – Inflammation of lymph vessels, seen as red skin streaks running proximally from a site of infection.

Table 1 | Antiseptics that may be used in the management of wound infection

<table>
<thead>
<tr>
<th>Antiseptic</th>
<th>Formulation(s)</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetic acid</td>
<td>Solution</td>
<td>Considered for its effect against <em>Pseudomonas aeruginosa</em></td>
</tr>
<tr>
<td>Chlorhexidine</td>
<td>Solution, powder, impregnated dressings</td>
<td>May be used as an alternative in patients allergic to iodine preparations</td>
</tr>
<tr>
<td>Honey</td>
<td>Available for direct application, impregnated dressings</td>
<td>Antimicrobial effects have been attributed to some components and physical properties. However, composition (and hence antibacterial activity) is highly variable, making comparison of clinical trials difficult</td>
</tr>
<tr>
<td>Hydrogen peroxide</td>
<td>Solution, cream</td>
<td>Caution is advised when using the solution because cases of gas embolism have been described</td>
</tr>
<tr>
<td>Iodine</td>
<td>PVP-I: solution, cream, ointment, spray, impregnated dressings Cadexomer iodine: ointment, paste, powder, impregnated dressings</td>
<td>Modern products slowly release relatively low levels of iodine, reducing the likelihood of toxicity and staining</td>
</tr>
<tr>
<td>Potassium permanganate</td>
<td>Solution, tablets for dissolving in water</td>
<td>Used as a soak to reduce wound bacterial load</td>
</tr>
<tr>
<td>Polyhexamethyl biguanide (PHMB)</td>
<td>Solution, impregnated dressings</td>
<td>Also known as polyhexanide and polyaminopropyl biguanide; related to chlorhexidine</td>
</tr>
<tr>
<td>Silver</td>
<td>Silver sulfadiazine: cream, impregnated dressings Ionic silver: impregnated dressings, nanocrystalline silver</td>
<td>Available in several forms including silver sulfadiazine (silver–antibiotic combination)</td>
</tr>
<tr>
<td>Sodium hypochlorite</td>
<td>Solution</td>
<td>Not usually recommended unless suitable alternatives are unavailable</td>
</tr>
<tr>
<td>Triclosan</td>
<td>Solution, impregnated dressings</td>
<td>Mainly used as a skin disinfectant or surgical scrub</td>
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</table>