Wound infection made easy

Introduction

Wound healing is a complex, multifaceted process influenced by intrinsic and extrinsic factors, some of which can be controlled. When healing stalls and certain signs and symptoms are present, the wound may be critically colonised or infected. There is no single scientific test to definitively diagnose infection; wound infection is diagnosed by clinical assessment of the wound and the whole patient. It is therefore important that clinicians understand how infection develops, how signs and symptoms manifest in various aetiologies, and how and when to initiate use of topical antimicrobials and systemic antibiotics in wounds clinically diagnosed as infected.

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Wound healing and infection

Wound healing is a complex process that follows a progressive three-step sequence: inflammatory, proliferative and remodelling. These phases can overlap[1], and each stage's duration will be influenced by a variety of factors. When a wound fails to progress to healing or respond to treatment over the expected healing time frame (depending on the patient and wound type), it usually stalls in the inflammatory phase. This non-healing phase, called 'chronicity', has various causative factors[2]. Wound infection often causes chronicity and, therefore, it is important to understand why wound infection occurs, and how to identify and manage it.

Assessing the risk of wound infection

Patient assessment should include the general medical condition and risk factors for wound infection. Age (e.g. neonatal and elderly patients), certain chronic medical conditions (e.g. diabetes, pulmonary disease, vascular disease), medications (e.g. oncology drugs, anti-platelet drugs, glucocorticoid steroids) and lifestyle factors (e.g. smoking, alcohol consumption) put patients with wounds at greater risk for the development of infection[3].

Recognising colonisation and infection

There is no single test to definitively diagnose infection; wound infection is diagnosed by clinical assessment of the wound and the whole patient. Swabbing a wound helps determine sensitivities or resistance to empirical treatment[4]. However, wound swab culture results may be misleading, as clinical microbiology laboratories use methods that select for planktonic bacteria or are not always suitable for culture of anaerobic species. Thus a wound culture might not capture bacteria protected within a biofilm, nor will it detect biofilm, so the result is often inconclusive[5,6].

If a swab is needed to determine whether bacteria are present in deeper wound bed tissues, the wound should first be irrigated with normal saline, to remove surface debris and avoid detection of only surface contaminants. The swab should be performed according to solid clinical rationale, per local protocol (Table 1).

Clinical judgement is therefore needed to interpret signs and symptoms. The classic signs and symptoms of wound infection include inflammation, new or increasing pain, local heat, swelling, advancing redness and purulence[5]. However, these indicators are more likely to appear in acute rather than chronic wound infection and, therefore, clincians must be familiar with the secondary signs of infection. The secondary signs of infection are suggestive of a local wound infection, critical colonisation or high bioburden in a chronic wound[10–12].

It can be particularly difficult to diagnose bioburden levels in wounds with persistent inflammation, such as mixed-aetiology leg ulcers. In such wounds, it is more likely to be critical colonisation or local infection (Figure 1), the key criteria for which include malodour, friable/bleeding tissue, breakdown/increase in size of wound, discolouration, spreading erythema, change in the nature of pain, bridging of the wound, pocketing at the base of the wound, and development of pus/slough or an abscess[11]. In addition, increased exudate or exudate that has become purulent can be signs that the microbial burden in the wound may be a factor adding to chronicity[5].

Critical colonisation and local infection can also be difficult to diagnose in diabetic foot ulcers (DFUs), because vascular compromise and neuropathy in the foot often mean that the classic signs of infection are not present[13]. The high morbidity and mortality associated with infection in DFUs mean that early and aggressive treatment — in the presence of even subtle signs of infection — is more appropriate than for wounds of other aetiologies[14] (Table 2).

Role of biofilms

Biofilms will often be present — up to 60% of the time — in wounds with chronicity, and may be responsible for the state of persistent inflammation that makes diagnosing wound infection difficult[21]. Biofilms are dynamic communities of bacteria and fungi

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Table 1 When to initiate a wound culture swab[7–9]

When to swab	Rationale
Initial presentation of symptoms of infection	To determine resistance to empirically commenced antibiotic; to assess virulence and type of wound microbes
Wound(s) not progressing after 2 weeks of treatment	To determine if another causative microbe is active or if antibiotic resistance has occurred
Normal surveillance protocol	Per protocol to screen for certain resistant microbes
Treatment completion (if local protocol advises)	To determine clearance of microbes

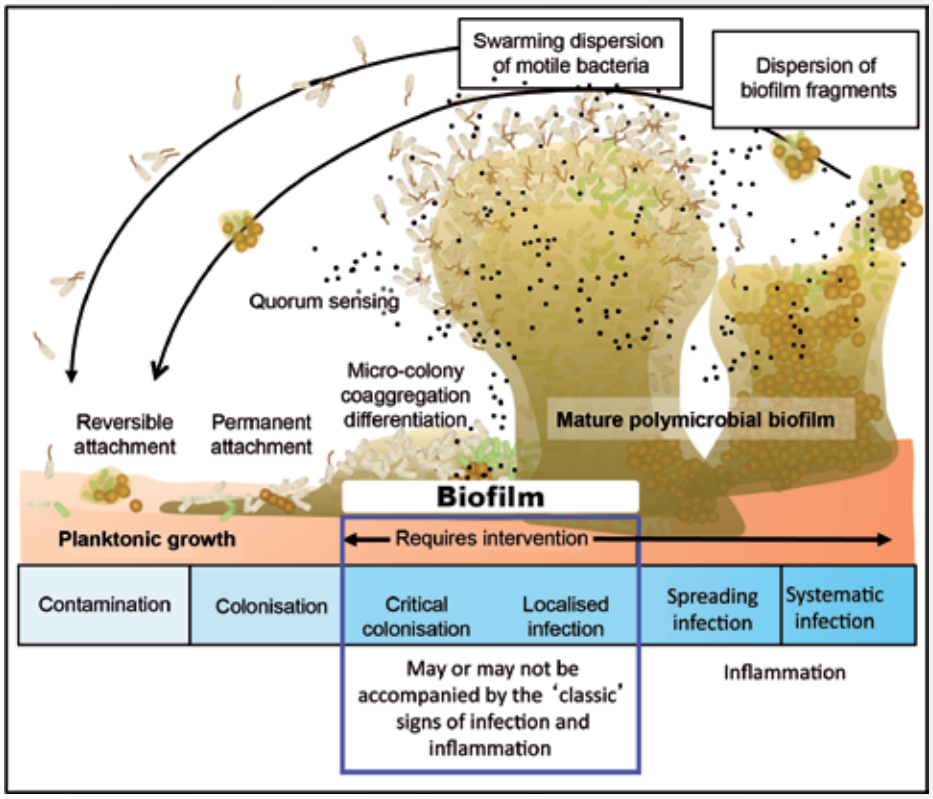


Figure 1. The continuum of wound infection (illustration courtesy G Schultz)

living within a protective self-secreted matrix of sugars and proteins[22]. They can develop within 2–4 days of initial colonisation, and become very tightly attached to extracellular matrix components or the wound bed, making them difficult to remove by surface irrigation or superficial debridement[23].

Goals of treatment

The wound management plan should be tailored according to the patient's individual situation. Perform a thorough holistic assessment of the patient's medical history and status, and of the wound and its characteristics to determine the extent to which critical colonisation or local infection is a risk.

Where there is a high risk, but the signs and symptoms of critical colonisation and local infection are absent, the goal of treatment should be to prevent onset of infection. Non-viable and devitalised tissue provides an opportunity for microbial growth and should therefore be removed from the wound bed and wound edge through irrigation or debridement[3]. Moisture imbalance should be rectified to optimise a moist wound-healing environment in which exudate is managed and drying out prevented[3]. In addition, the use of a topical antimicrobial in certain high-risk individuals/wounds (Box 1) can also help prevent an increase in microbial bioburden and the possible onset of infection; the rationale for application of the topical antimicrobial should be clearly documented in the patient's wound management plan and a review date set[3].

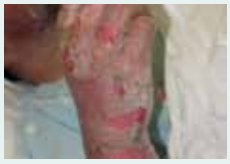
Box 1 Potential triggers for use of a topical antimicrobial as prophylaxis[3]

- Patient history of delayed wound healing/infection
- Gross contamination that presents risk of cross-infection with multidrug-resistant bacteria
- Anatomical location of the wound that increases risk of contamination (e.g. sacrum)
- Wound of 4+ weeks' duration at initial presentation for treatment, with no visible signs of healing, or with signs of continued deterioration
- Evidence of pathologies or activities likely to compromise immunity (e.g. in diabetes with poorly controlled blood glucose, smoking, regular alcohol use beyond recommendations)
- Significantly compromised blood flow where healing is unlikely without vascular intervention
- Odour that affects quality of life

In wounds exhibiting signs and symptoms of critical colonisation or local infection, the treatment goal must be to reduce the bioburden and/or eradicate potential biofilm in the wound bed. The first step in these wounds is aggressive debridement of slough and the underlying tissue, to disrupt the microbial burden and supress biofilm regrowth[24].

Once the microbial burden has been physically disrupted, it is significantly more susceptible to biocides and antibiotics while the biofilm works to reconstitute[25]. Wound cleansing may be performed at this stage to remove surface contaminants, loose debris, slough, softened necrosis, bacteria and

Table 2 Considerations for diagnosing critical colonisation and localised infection in wound aetiologies (photos courtesy T Swanson)

Wound aetiology	Tips for diagnosis	Tips for management
Leg ulcer 	Can be distinguished from chronic inflammation by being unilateral, warm to touch, increase in pain, and increased size of wound despite use of a therapeutic level of compression At least 3 of these 5 clinical signs of local infection: ▪ Pain between dressing changes ▪ Periwound skin erythema ▪ Oedema ▪ Malodour ▪ High levels of exudate[5]	Topical antimicrobial agents should be used with standard management practices such as graduated compression therapy Manage the increased exudate with an absorbent dressing suitable for use under compression therapy
Diabetic foot ulcer 	Signs and symptoms may be subtle (and up to half of infected DFUs will show no signs and symptoms), so it is important to be proactive in exploring if the wound is not progressing, particularly if 2 or more of these are present: ▪ Local swelling or induration ▪ Erythema ▪ Local tenderness or pain ▪ Local warmth ▪ Presence of/increased exudate or purulent discharge[14,15] Probe to bone or exposed bone is likely indicative of osteomyelitis[14]	Listen to the patient regarding his/her subjective symptoms Manage factors such glycaemic control and offloading in consultation with a specialist (e.g. podiatrist) Use appropriate topical antimicrobial and/or systemic antibiotics for prevention and treatment per local protocol[16], in consultation with a specialist
Pressure ulcer 	Local infection is likely in the presence of: ▪ Lack of healing for 2 weeks ▪ Friable granulation tissue ▪ Malodour ▪ Increased pain in wound ▪ Increased periwound warmth ▪ Negative change in the nature of the wound drainage ▪ Increased necrotic tissue in the wound bed ▪ Pocketing or bridging of the wound bed ▪ No improvement/deterioration despite implementation of appropriate relief of pressure, shear and friction	Manage factors such as nutrition and pressure reduction/relief Reduce bacterial load and biofilm through cleansing, debridement and appropriate antimicrobial dressings[17]
Surgical site wound 	Post-operative symptoms include: ▪ Redness and pain around the surgical area ▪ Drainage of cloudy fluid from the surgical wound ▪ Fever[18] ▪ Wound breakdown/dehisence	Identify risk factors before elective surgery and manage per local protocol Use an appropriate antimicrobial dressing or device (e.g. negative pressure wound therapy) to manage symptoms, exudate and bacterial burden[19]
Superficial partial-thickness burn 	It is important to differentiate between burn wound erythema (a normal process characterised by painless, blanchable redness <2cm from the burn edge for 3–5 days post-injury) and cellulitis, which presents with: ▪ Advancing redness ▪ Warmth ▪ Tenderness[20]	Reassess within 24–72 hours of injury to monitor for increased depth (due to burn conversion) or infection Closely monitor for signs and symptoms of infection and response to treatment Use appropriate topical and/or systemic antimicrobial per local guidelines

other microbes from the wound surface and surrounding skin[26]. After debridement and cleansing, application of an antimicrobial dressing that is appropriate for the clinical indications (e.g. exudate and odour management), as well as safe for and acceptable to the patient, is recommended[22,24,27,28] (Table 3). This is particularly important during the first 24 hours after debridement and cleansing, to protect the wound from the re-establishment of the microbial burden[29].

Role of antibiotics

Indiscriminate use of antimicrobials — antibiotics in particular — has made resistant organisms more prevalent[31]. During the next 50 years, microorganisms' drug resistance will increase, and new strains with resistance to a wide variety of agents will emerge, rendering many drugs ineffective[32]. In several countries that have launched large-

Table 3 Overview of topical antimicrobials[3]

Agent to reduce/ prevent microbial burden	Additional rationales for use	Wound types	General guidance for use*
Enzyme alginogel	▪ Autolytic debridement ▪ Moisture balance ▪ Wound edge and epithelial cell protection	▪ PU ▪ DFU ▪ Acute wound ▪ Arterial ulcer ▪ Superficial partial-thickness burns	▪ Apply to wound and cover with a secondary dressing ▪ Can be used long-term due to no body absorption ▪ Contraindicated in patients with known sensitivity to alginate dressing or polyethylene glycol
Iodine (povidone, cadexomer)	▪ Effective against MRSA[30] ▪ Reduced selection for bacterial resistance[30]	▪ VLU ▪ DFU ▪ Cavity wounds (cadexomer only)	▪ Use for 1 week, with dressing changes 2 to 3 times weekly ▪ If there are signs of improvement, continue use up to 2 weeks. If the wound does not improve after 1 week, discontinue use ▪ Contraindicated for long-term use, and in patients with known/suspected iodine sensitivity, and renal or thyroid diseases
Medical-grade honey	▪ Autolytic debridement ▪ Odour management	▪ Leg ulcer ▪ Superficial or partial-thickness burn ▪ DFU ▪ PU ▪ Surgical wound ▪ Graft site	▪ Change dressing based on how quickly honey is diluted by exudate ▪ Ensure direct contact with the wound bed and use with a secondary dressing to manage exudate ▪ Monitor blood sugar levels in patients with diabetes ▪ Use with caution in patients with bee venom allergy ▪ Do not let the dressing dry out
Octenidine dihydrocholoride	▪ Autolytic debridement ▪ Donate moisture to the wound bed ▪ Wound cleansing	▪ Superficial or partial-thickness burn ▪ PU ▪ Leg ulcer ▪ DFU	▪ Apply directly to the wound bed and leave in contact for ≥5 minutes ▪ Can be used to soften dressings and loosen encrusted coatings before removal ▪ Contraindicated in patients with octenidine sensitivity, on exposed structures underlying the dermis
Polyhexamethylene biguanide (PHMB)	▪ Odour management (dressing) ▪ Removal of encrusted dressings (solution) ▪ Debridement (gel) ▪ Wound bed preparation (gel and solution) ▪ Wound cleansing	▪ Partial-thickness burn ▪ Surgical wound ▪ Graft site ▪ Leg ulcer ▪ PU ▪ DFU	▪ Warm solution to body temperature, apply to gauze, then the wound, and cover and leave in contact for 10 minutes ▪ If using gel in dehydrated, deep, tunnelling or cavity wounds, first apply to a ribbon gauze ▪ Dressing can be left in place 5–7 days ▪ Contraindicated in patients with PHMB sensitivity ▪ Do not combine with other wound cleansers or ointments
Silver (metallic, nanocrystalline, ionic)	▪ No known bacterial resistance in wounds ▪ Manage exduate, fill cavity wound, protect vulnerable tissue (combined with alginates or contact layers)	▪ All wound types ▪ With caution in children	▪ Use for 2 weeks. If there are signs of improvement, continue use up to 4 weeks. If there are no signs of improvement, discontinue use ▪ Do not use >4 weeks without strong clinical rationale ▪ Contraindicated for long-term use, over large surface areas and in patients with sensitivity to silver ▪ Use with caution in heavily exuding wounds (risk of maceration)
Silver sulfadiazine	▪ Soothe painful wounds	▪ Partial- or full-thickness burn ▪ Leg ulcer ▪ PU	▪ Use for 1 week. If there are signs of improvement, use up to 2 weeks. If there are no signs of improvement, discontinue use ▪ Do not use >2 weeks ▪ Clean wound, and cover with 0.3–0.5cm thickness of cream and a secondary dressing ▪ Contraindicated in patients with sensitivity to silver sulfadiazine and sulfa drugs ▪ May result in the development of a false eschar

scale, coordinated efforts to reduce antibiotic usage, reports of incidences of resistant strains of bacteria, such as *Staphylococcus aureus* and *Clostridium difficile*, have decreased significantly[33].

It is therefore recommended that systemic antibiotics be used cautiously. In addition, where possible, the choice of antibiotic prophylaxis should be matched to the organisms most likely to cause infection, using the local antibiotic formulary guidelines to ensure the most appropriate antibiotic, dose, timing of administration and duration of use[34]. Antibiotic prophylaxis is indicated in patients who have systemic risk factors that make infection likely (e.g. poor vascularity, compromised immune systems), particularly in wounds at high risk of becoming infected, such as contaminated wounds, wounds with large areas of necrotic tissue, and high-risk anatomical sites such as the sacrum,

Box 2 Potential triggers for systemic antibiotic use[34]*

- Abnormal/absent granulation or necrosis
- Pocketing, tunnelling, maceration
- Static or enlarged wound size
- Erythema spreading >2cm around the wound
- Appearance of or changes in nature of pain
- Wound deepening to involve structures under the skin and subcutaneous tissues†
- Body temperature >37°C†
- Heart rate >90 beats per minute†

*Not exhaustive
†Systemic infection only

hand or foot (Box 1)[31,35]. For example, if a DFU shows signs of critical colonisation or local infection, antibiotics should be initiated due to the potential for rapid onset of infection, as well as the risk of amputation if infection settles in[13].

If there are signs of systemic infection, systemic antibiotics should be initiated; a topical antimicrobial can also be used if localised effect is desired, and the wound status allows dressing application and change without further damage to surrounding structures (Box 2). If the patient and wound are showing signs of spreading infection, use of systemic antibiotic therapy may be considered in addition to a topical antimicrobial (Box 2).

Monitoring progress

A multidisciplinary approach, coupled with a treatment pathway that enables timely referral to specialists, is important for optimal outcomes. Thorough, ongoing assessment should be employed to evaluate the progression of the wound (according to treatment goals) and the effect of the current treatment on meeting these goals[36]. The results of assessment should be clearly documented in the patient record and care plan, with any changes and a clear rationale for such changes recorded[36].

Outcomes can be measured by improvement of wound and periwound conditions, and quality-of-life indicators (e.g. pain, odour)[37]. Healing trajectories are noted in the literature:

- **It is reported that most wounds should heal within about 4 weeks[37]**
- **Burns healing 2% per day have positive indications for healing and patient survival[38]**
- **DFUs that do not reduce in area by ≥50% within 4 weeks are unlikely to heal by 12 weeks[39]**

The clinician should review the wound 1 week after presentation (or per local protocol), looking for positive indicators such as decreased pain, exudate (level and type), odour and oedema; and improved periwound skin (intact, decreased erythema and oedema), wound edges (intact, non-inflamed) and wound bed (increased granulation tissue, decreased non-viable tissue).

If these positive indicators and improvements are not being seen, it is important to investigate whether infection or an underlying condition is the cause. If antibiotics have been initiated, a positive indicator within 24–48 hours should be expected.

Frequency of dressing change should be based on regular, ongoing assessment, dressing indications (e.g. exudate, odour, infection management), manufacturer instructions and patient factors (e.g. sensitivity to materials, concordance with dressing choice). Change treatment if dressing performance does not meet expectations for the clinician or patient, or if the patient experiences any adverse effects from treatment. The changing condition of the wound may also initiate a change in the care plan (e.g. if symptoms have resolved or if new symptoms present).

Where wound healing is not an achievable outcome, it is as important to manage the wound locally as it is to implement holistic assessment and management, including nutrition, stress (physical and emotional/psychological), lifestyle factors, quality of life and medication, in concordance with the wishes of the patient and their families.

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Summary

Wounds that have been clinically diagnosed as infected could be treated with a topical antimicrobial that is appropriate for the clinical indications (e.g. exudate and odour management) as well as safe for and acceptable to the patient. Systemic antibiotics should be considered and used cautiously and in consultation with a specialist member of the multidisciplinary team. A multidisciplinary approach, coupled with a treatment pathway that enables timely referral to specialists, is important for optimal outcomes. Thorough, ongoing assessment should be employed to evaluate the progression of the wound (according to the treatment goals) and the effect of treatment on meeting treatment goals.

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