ABC of wound healing
Infections

This is the 10th in a series of 12 articles

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Despite optimal treatment some wounds are slow to heal. The challenge clinically and microbiologically is to identify those wounds in which healing is impaired as a result of infection or heavy bacterial burden and in which systemic or topical antimicrobial treatment will be of benefit.

Staphylococci and streptococci are the most commonly encountered pathogenic organisms in community acquired superficial wounds. More unusual organisms may be found in bite wounds, and these reflect the source of the bite. Pathogenic organisms causing surgical wound infections vary according to the anatomical site of surgery. Antibiotic resistant organisms, such as methicillin resistant *Staphylococcus aureus* (MRSA), are more commonly encountered, reflecting the hospital flora.

When to sample

It is inappropriate to swab all wounds: swabs should be taken only from overtly infected wounds and from wounds that are deteriorating, increasing in size, or failing to make satisfactory progress despite an optimal environment for wound healing. Indicators of wound infection include redness, swelling, purulent exudate, smell, pain, and systemic illness in the absence of other foci. Subtle signs of local wound infection include unhealthy "foamy" granulation tissue, contact bleeding, tissue breakdown, and epithelial bridging.

Types of sample

Superficial wound swabs—The ease of obtaining and processing superficial wound swabs, combined with their relatively low cost and non-invasive nature, make them in most instances the most appropriate method for wound sampling. Organisms cultured from a superficial swab may, however, simply reflect the colonising bacterial flora and are not always representative of the pathogenic organisms invading deeper tissue. This is particularly relevant to deep surgical and deep penetrating wounds in which infection from internal sources may occur.

Tissue and pus—Tissue or pus, or both, should be collected whenever possible, as growth from these samples is more representative of pathogenic flora. These are amenable to quantitative microbiological analysis and other techniques used to improve the diagnostic yield. Tissue biopsy should always be carried out when therapeutic debridement of the wound is done, in cases of osteomyelitis, and when superficial sampling methods have been ineffective.

Less invasive techniques—Less invasive sampling techniques—such as dermabrasion and various absorbent pads—have been developed. A wide range of products is available, but no single method is used routinely yet.

Microbiological analysis

Semiquantitative analysis

Most laboratories will perform a semiquantitative analysis on wound swabs. This entails grading bacterial growth as scanty, light, moderate, or heavy. Semiquantitative analysis introduces a bias towards motile and fast growing organisms.

Infection is a major source of failed wound healing

Management of bite wounds

- Carry out meticulous surgical debridement and cleansing of wound
- Send deep tissue specimens for microbiology testing
- Consider empirical treatment with antibiotics
- Consider tetanus prophylaxis
- Seek microbiological advice if bite was by exotic animal

Signs of wound infection

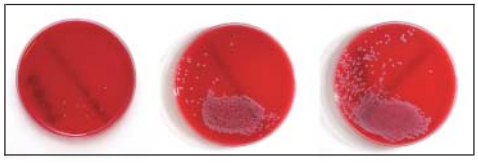
- Redness
- Heat
- Pain
- Swelling
- Exudate (purulent, serous, or serosanguinous)
- Odour
- Poor healing
- Contact bleeding
- Epithelial bridging
- Tissue breakdown
- Presence of unhealthy granulation tissue
- Systemic illness in the absence of other focus of infection

A charcoal swab preserves bacteria during transport to the laboratory

How to take a superficial wound swab

- Removal of superficial debris followed by swabbing of the wound bed is considered to be the best way to obtain a superficial wound swab
- Swabs containing transport media and charcoal should be used as they help to preserve bacteria before laboratory analysis
- Timely delivery of the swab to the microbiology laboratory is essential

Punch biopsy for microbiological analysis



Semiquantitative analysis of swab showing light or scanty, moderate, and heavy growth of *Staphylococcus aureus*

Fastidious organisms such as anaerobes may be under-represented. Semiquantitative counts have been shown to correlate with quantitative tissue counts in both burn wounds and diabetic foot ulcers.

Superficial wound swabs are not always representative of the pathogenic organisms invading deeper tissue

Microbiological analysis

Type of analysis	Suitable samples	Advantages	Disadvantages
Gram stain	Tissue, pus, or swab transported immediately to laboratory	Instant results; good correlation with quantitative counts	Poor sensitivity; no antibiotic sensitivity pattern
Quantitative culture	Tissue, pus, dermabrasion specimens, absorbent pad specimens	Counts $>10^5$ organisms or colony forming units per gram of tissue predict wound infection	Invasive; labour intensive; costly
Semiquantitative culture	All specimens	Practical; can be carried out on swab specimens; some correlation with quantitative analysis	Imprecise; bias towards motile/fast growing organisms; sampling of superficial colonising bacteria

Quantitative analysis

Bacterial load greater than 100 000 organisms or colony forming units per gram of tissue or mm^3 of pus is a predictor of wound infection.

However, some wounds that are more heavily colonised will heal spontaneously, and, conversely, some organisms are able to cause serious infection at much lower levels of colonisation. Infection depends on the pathogenicity of the organism, the type of wound, and the host response.

Interpretation of results

Most wound swabs will yield bacterial growth. Growth of bacteria from wounds is not synonymous with infection, and treatment based on microbiological results alone is not warranted.

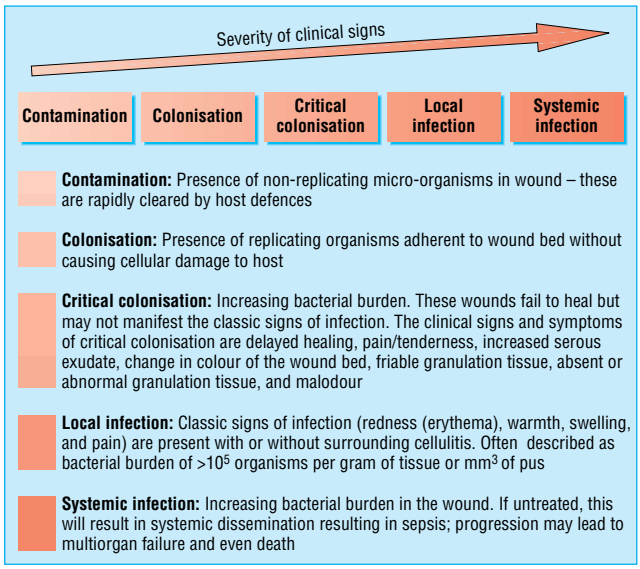
Treatment

Wound infections in association with systemic illness, deep invasion, or cellulitis require empirical systemic antibiotic treatment while culture results are awaited. Choice of treatment will depend on factors such as the type and site of wound; previous microbiological results; and host factors such as drug allergies. Clinicians must always be alert to the possibility of necrotising fasciitis. A high level of suspicion followed by prompt aggressive surgical debridement of devitalised necrotic tissue is essential if the patient is to survive. Important clinical markers include pain disproportionate to clinical signs, anaesthesia over the infected area, and systemic illness.

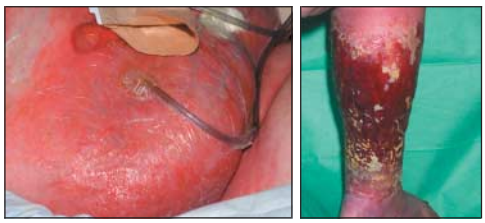
Empirical antibiotic treatment of wound infection in systemically unwell patient*

Type of wound	Antibiotic
Wound infection	Co-amoxiclav
Surgical wound infection	Cefuroxime and metronidazole or co-amoxiclav
Bite wound	Co-amoxiclav
Diabetic ulcer	Co-amoxiclav and ciprofloxacin
Osteomyelitis	Co-amoxiclav or ciprofloxacin and clindamycin
Necrotising fasciitis	High dose benzylpenicillin plus clindamycin (with or without ciprofloxacin)
MRSA infection suspected	Vancomycin or linezolid

*Rough guide only. In general, treatment should be guided by discussion with the local microbiology department. Choice of antibiotics will depend on previous microbiology where available, previous antibiotic treatment, site of surgery, and the local prevalence of MRSA.



Spectrum of interaction between bacteria and host



Left: Extensive cellulitis complicating laparotomy wound. Right: Severely locally infected wound showing unhealthy granulation tissue

Clinical markers of necrotising fasciitis*

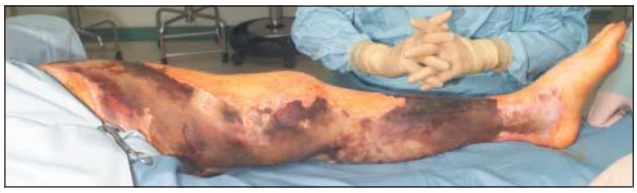
Early presentation
- Pain (may be disproportionate to clinical signs)
- Cellulitis
- Swelling of the affected region
- Induration
- Skin anaesthesia
- Fever
- Tachycardia

Late presentation
- Severe pain
- Skin discoloration (purple or black)
- Blistering
- Haemorrhagic bullae
- Crepitus
- Discharge of "dishwater" fluid
- Severe sepsis or systemic inflammatory response syndrome
- Multiorgan failure

*From Hasham et al, 2005 (see Further Reading box)

Treatment of locally infected wounds with topical antiseptics such as silver compounds or iodine will be sufficient in most instances. Topical treatment avoids the potential side effects of systemic antibiotics, such as *Clostridium difficile* diarrhoea, anaphylaxis, gastrointestinal upset, and, perhaps most importantly, selection of resistant organisms. Systemic treatment may be indicated if topical medication is unsuccessful.

In general, topical antibiotics are not recommended. Reasons for this include inadequate penetration for deep skin infections, development of antibiotic resistance, hypersensitivity reactions, systemic absorption when applied to large wounds, and local irritant effects leading to further delay in wound healing. Short courses of silver sulfadiazine or topical metronidazole can be useful, however, in certain circumstances—for example, with burns and chronic ulcers.



Necrotising fasciitis

Topical antimicrobial preparations

- Iodine releasing agents (povidone-iodine preparations, cadexomer-iodine preparations)
- Potassium permanganate solution
- Silver releasing agents (composite silver dressings, silver sulfadiazine)
- Topical antibiotic (metronidazole)

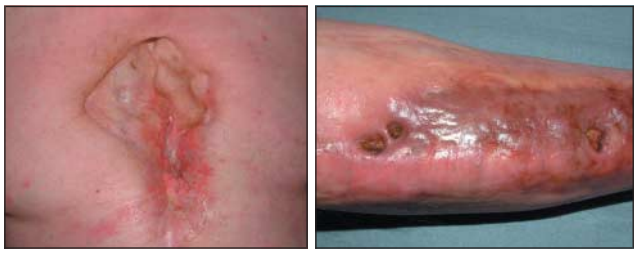
Osteomyelitis associated with wound infection

Osteomyelitis may develop after direct inoculation of bone from a contiguous focus of infection. This can be a devastating complication of wound infection, requiring specialist intervention and management.

Diagnosis

The diagnosis of osteomyelitis should be considered in any chronic wound that does not heal despite optimal treatment or in any wound (especially in those with diabetes) that can be probed to bone. Plain x rays of the affected area should be the first line of investigation.

Radiographic changes, however, can lag behind the evolution of infection by at least two weeks; a single, negative plain x ray film does not, therefore, exclude osteomyelitis. Magnetic resonance imaging is more sensitive than plain radiography. Nuclear scintigraphy—either a technetium bone scan or a labelled white cell scan—may also be helpful but requires careful interpretation. It can be difficult to differentiate osteomyelitis from chronic soft tissue infection.



Left: Osteomyelitis in a chronic, non-healing sternotomy wound. Right: Osteomyelitis arising at the site of a previous traumatic wound to the tibia, previously healed by reconstructive surgery. The sinuses probe to bone

Management

Antibiotics penetrate poorly into devitalised bone, and long courses of antibiotics may be required. It is therefore important to define the infecting organism(s) from the outset so that antibiotic treatment can be targeted. Ideally, in the absence of systemic illness, antibiotics should not be started before microbiological sampling of the infected bone.

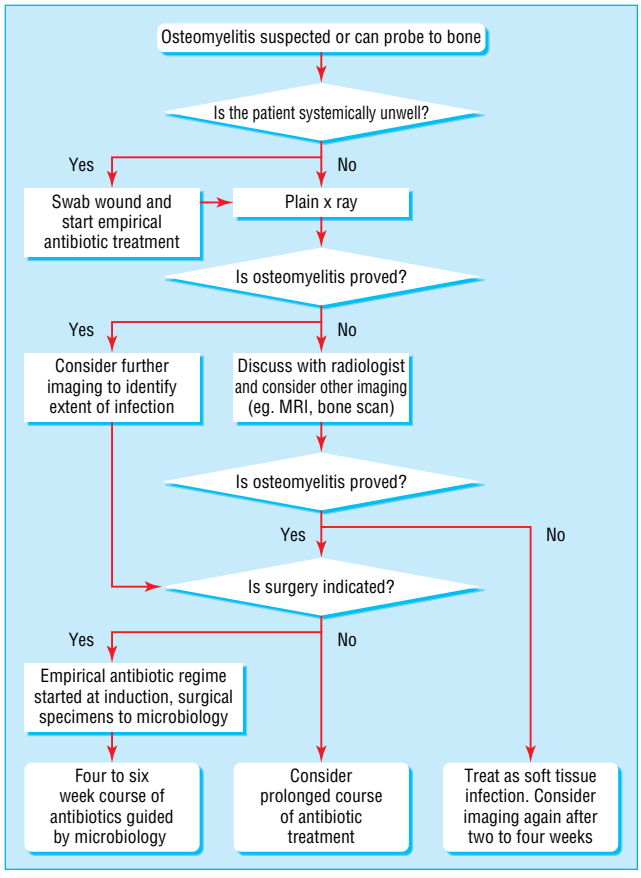
Surgery followed by prolonged intravenous antibiotic treatment (generally a minimum of six weeks), is indicated in selected patients. Periodic antibiotic treatment at times of wound deterioration or of systemic illness may be appropriate if cure is unachievable.

Surgery

Surgery enables debridement of all necrotic bone and tissue and provides deep samples for microbiological analysis. In some patients, surgery is not possible either because of the site of the wound or because of the patient's debility. Under these circumstances, a prolonged course of antibiotics may be warranted.

Antibiotic treatment

Choice of treatment is dependent on the antibiotic sensitivity pattern of the infecting organism(s) along with antibiotic properties, such as bone penetration, and host factors, such as drug allergy. Combination therapy is often used to gain maximal effect. Inflammatory markers (including C reactive



Algorithm for management when osteomyelitis is suspected or if the wound can be probed to bone

protein and erythrocyte sedimentation rate) and radiological images can be used to monitor response.

Methicillin resistant *Staphylococcus aureus*

The incidence of MRSA wound infection and osteomyelitis is increasing. Isolation of MRSA from a wound, however, does not require treatment in the absence of clinical signs of infection. Topical antimicrobial agents, such as iodine and silver compounds, have activity against MRSA and may be used in localised wound infection when there is no evidence of invasion, cellulitis, or systemic upset.

In a systemically unwell individual, a glycopeptide (vancomycin or teicoplanin) should be administered. In all cases of MRSA osteomyelitis and in some MRSA wound infections a second antistaphylococcal agent with good penetration to bone and superficial skin sites should be added—for example, fusidic acid or rifampicin. Both rifampicin and fusidic acid can cause hepatitis and require regular monitoring of liver function tests.

With the exception of linezolid, evidence for the use of oral antibiotics in MRSA infections is lacking. However, when oral antibiotics are used, combinations are recommended to protect against the development of resistance. Combinations of rifampicin or fusidic acid with either trimethoprim or minocycline have been used with some success. The combination of rifampicin with fusidic acid is not advisable because of the increased risk of hepatotoxicity.

Linezolid, an oxazolidinone, is a new agent active against MRSA. It has excellent bioavailability, can be administered orally, and has good skin and bone penetration. Linezolid is generally well tolerated, but can cause bone marrow suppression, and regular haematological monitoring is therefore required. Linezolid use is currently limited by its high cost.

Agents that may be available in the near future include daptomycin, tigecycline, and dalbavancin.

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Competing interests: For series editors' competing interests, see the first article in this series.

Radiological improvement will often lag behind clinical improvement by up to six weeks

Further reading

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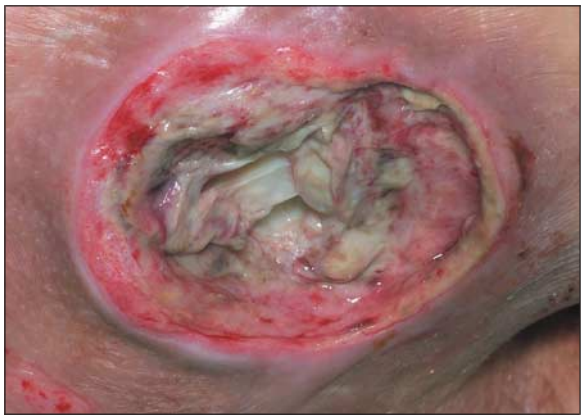

Pressure sore associated with MRSA osteomyelitis. Bone is visible at the base of the ulcer

The figure showing the spectrum of interaction between bacteria and host was supplied by J E Grey and Stuart Enoch.

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Do it yourself thermotherapy

A 75 year old man was found unconscious in his bath. He had had a coronary bypass operation and pacemaker implanted because of syncope with bradyarrhythmia, and, more recently, prostate carcinoma with bone metastases had been diagnosed, for which he was being treated with antiandrogens. Examination revealed an unresponsive patient with a Glasgow coma score of 1-1-1, a rectal body temperature of 41.6°C, a blood pressure of 60/30 mm Hg, a heart rate of 60 beats/min, and a respiratory rate of 20 breaths/min. Biochemical and cardiological investigations did not identify the cause of coma, and the results from a cerebral computed tomography were normal. After the patient had been fully undressed and given saline infusions, his body temperature dropped to 38°C, and his Glasgow coma score became normal within 30 minutes.

At this point his wife told us that her husband had recently been searching the internet for possible treatments for his carcinoma. He had come across information on cooled thermotherapy (TUMT, transurethral microwave thermotherapy) for benign prostate hyperplasia and on hyperthermia treatment for malignant diseases such as melanoma, hepatocellular carcinoma, and metastasised breast and colorectal carcinoma.

On the basis that such treatment would help him, he designed and made a hyperthermia system from spare parts at home. He fitted a large industrial garbage container with the heating element of an old electric frying pan as well as a garden pond pump for circulation. He took hot baths in this device for two hours every other day. All went well until the day of admission, when the water overheated and he lost consciousness.

He was discharged, well, after two days, insisting that he had devised an excellent system apart from forgetting to install a thermostat.

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