Chronic long bone osteomyelitis: diagnosis, management and current trends

Osteomyelitis is an inflammatory process in bone, caused by an infecting microorganism, which leads to bone destruction (Lew and Waldvogel, 2004).

Osteomyelitis was initially described by Hippocrates in 460–370 BC. However, 20th century advances in surgery and the development of antibiotics laid the foundations for current osteomyelitis treatment (Klenerman, 2007).

This article considers chronic osteomyelitis related to bacterial infection of long bones.

Epidemiology

Osteomyelitis is more common in males. It has a bimodal age distribution, being most common in children and the elderly (Kremers et al, 2015). It rarely presents in adults unless they have a predisposing risk factor such as diabetes, decubitus ulcers, sickle cell, surgery, open fractures, trauma or intravenous drug use (Chihara and Segreti, 2010). It is more common in summer months, when the weather is hot (Gillespie, 1985).

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Classification

Osteomyelitis can be classified by the source of the infecting organism (Waldvogel et al, 1970):

Haematogenous route

This is osteomyelitis resulting from bacteraemia, most commonly from small skin boils and lesions. This accounts for 80% of cases of osteomyelitis worldwide (Bickler and Sanno-Duanda, 2000). It is six times more common in tropical regions (Meier et al, 1993). It most commonly affects metaphyseal bone; common sites include the distal femur and proximal tibia, and as the infection spreads it can lead to infection of the adjacent joint and a septic arthritis.

Direct route

This is osteomyelitis caused by inoculation of the bone from an adjacent infective source. Examples include open fractures, bone surgery and contiguous spread through soft tissue defects like pressure ulcers. This route always compromises the surrounding soft tissues.

Classification systems are of limited use because they cannot reliably inform the clinician as to the best management of each case. The current trend now is for a case by case assessment and discussion with the multidisciplinary team. Several classification systems exist, the most widely used include:

- The Waldvogel classification system. This is based on the aetiology of osteomyelitis but does not give therapeutic guidance (Waldvogel et al, 1970)
- The Cierny–Mader classification looks at both the anatomical area of infection and the physiological status of the patient. It guides whether a patient is suitable for extensive surgery and prolonged reconstruction (Mader et al, 1997).

Organisms

Staphylococcus aureus is the most common bacteria isolated in any type of osteomyelitis. Other common pathogens include *Streptococcus pyogenes*, *Escherichia coli*, group B Streptococcus and *Haemophilus influenzae*. Anaerobes are also isolated after open fractures.

The bacteria attach to the surface of dead bone by a series of complex cellular interactions controlled by bacterial adhesins. These adhesins recognize host proteins on the dead bone or implant coatings. Once they attach, the bacteria produce a biofilm composed of a polysaccharide extracellular matrix that allows micro-colonies to develop and mature (Chihara and Segreti, 2010). This biofilm is very resistant to antibiotic penetration.

Pathology

Bone infection evolves over time and is often differentiated into acute and chronic osteomyelitis. This can be thought of as a progressive scale, with the appearance of dead bone signalling the start of chronic osteomyelitis (*Figure 1*).

Bone death occurs as a result of extensive periosteal stripping and medullary ischaemia secondary to the infection. This then leads to activation of inflammatory cells (pus) and the separation of dead bone (known as 'sequestrum'). Pus is discharged through sinuses (McNally and Nagarajah, 2010).

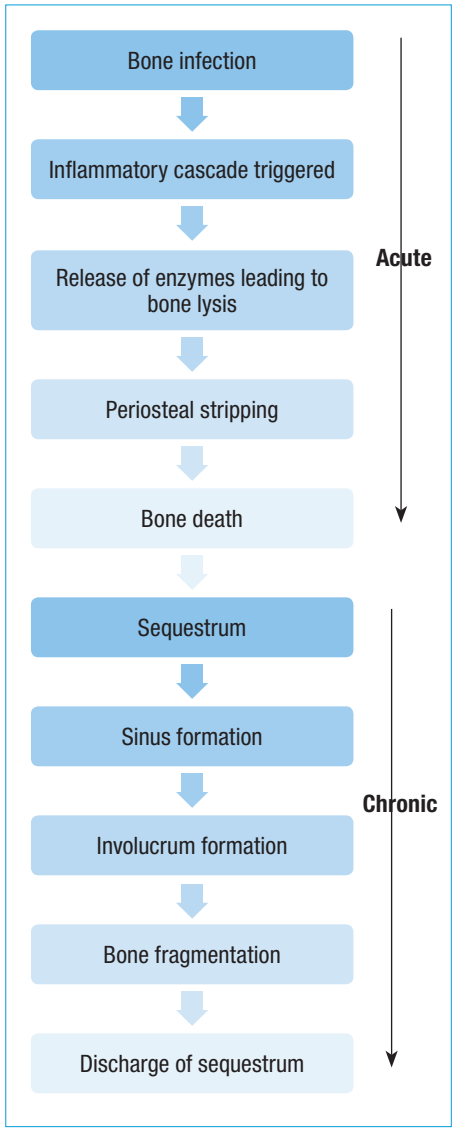
The surrounding bone then produces new bone within the medulla or under the elevated periosteum. This new bone is termed 'involucrum' – this is thick cortical bone which often traps the sequestrum within the intramedullary canal, leading to persistent infection. Osteomyelitis can involve the whole length of the bone.

Diagnosis

Diagnosis of osteomyelitis is mainly a clinical one. Patients most commonly present with a history of pain, fever and rigors. In chronic osteomyelitis the patient may describe pain that is relieved as a sinus opens and discharges.

On examination the affected limb may show redness, swelling or warmth. There may be obvious signs such as discharging sinuses, scars from previous surgery or exposed metalwork.

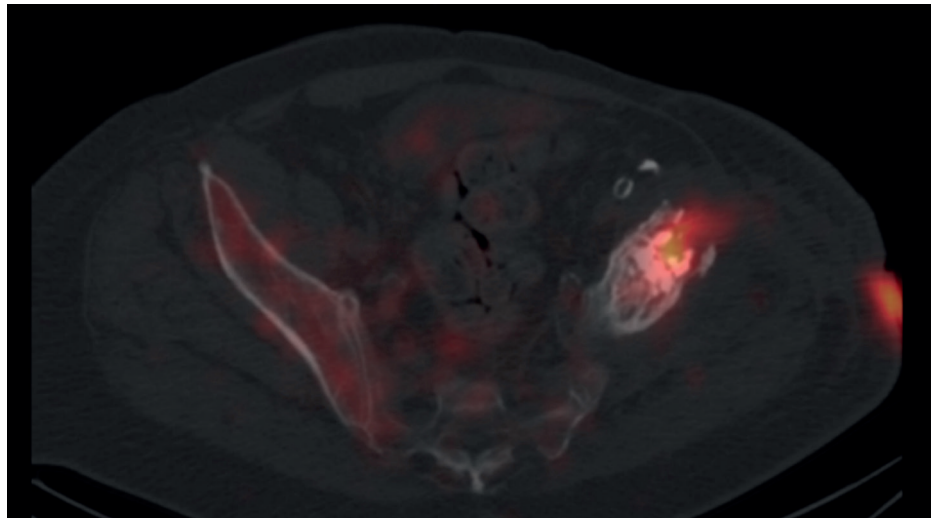
Figure 1. Progression of osteomyelitis.



In chronic presentations, diagnosis can be difficult as patients may have minimal clinical signs. Often the only symptom is a diffuse pain in the affected limb. There is no specific blood test that leads to a diagnosis but C-reactive protein, erythrocyte sedimentation rate and full blood count are useful as markers of infection.

Blood cultures are indicated in the pyrexial patient and are very helpful in haematogenous osteomyelitis but they have low sensitivity. Swabs from sinus tracts are rarely concordant with the pathogen causing osteomyelitis (Sheehy et al, 2010). Osteomyelitis patients who are not septic should not be started on antibiotics until bone and tissue samples are obtained in theatre for culture and sensitivity. Bone biopsy is the gold standard for identifying the causative organism.

Figure 2. Indium 111 single-photon emission computed tomography showing chronic osteomyelitis of the left iliac crest with a draining sinus.



Imaging

Plain films are usually the first-line imaging for patients with suspected chronic osteomyelitis. The key features seen on plain film are periosteal reaction and osteopenia. Often plain films do not show early infection as it takes weeks for osteomyelitis to show signs on an X-ray.

Computed tomography scans give a good view of cortical bone and are useful in locating sequestration and for surgical planning. The soft tissues are not seen in detail.

Magnetic resonance imaging is very good at differentiating between bone and soft tissue infection. It is also useful in identifying abnormal bone marrow and can detect osteomyelitis as early as 3–5 days (Chihara and Segreti, 2010). However, it can be difficult to differentiate between postoperative changes and recurrent chronic infections on magnetic resonance imaging.

Ultrasound scanning has a role in early identification of soft tissue abscesses and guided drainage of sub-periosteal collection.

Nuclear medicine scanning, such as white cell-labelled In111 single-photon emission computed tomography, is the gold-standard test in the authors' unit (*Figure 2*). It uses functional assessment of the labelled white cells to show the infection and co-registers this with a high fidelity computed tomography scan (Lew and Waldvogel, 2004). This has the advantage of showing where the sequestrum is and what the best approach would be to remove it. This allows the authors to plan the approach for a window that will remove the least amount of structural bone.

Treatment

Treatment of osteomyelitis should take a combined multidisciplinary team approach with medical management guided by infectious diseases physicians and surgical management guided by orthopaedic and plastic surgeons. Patient factors and comorbidities should be optimized, for example strict glycaemic control in patients with diabetes.

Antibiotics

Antibiotics can be given both locally and systemically and should be selected based on their ability to attack the causative organism. It is therefore vital to try and identify the causative organisms. One way of doing this is by stopping antibiotics for 2 weeks before definitive surgery in order to maximize the chance of isolating the pathogen during intraoperative tissue biopsy. Despite this, many cases will be culture negative. In this setting the antibiotic choice must cover the likely causative organisms mentioned earlier.

The chosen antibiotic must provide adequate bone penetration to achieve antibiotic levels in the bone that exceed the minimum inhibitory concentration to kill bacteria. For some antibiotics this can only be achieved by using the intravenous route. For example, beta-lactam antibiotics (penicillins, cephalosporins and carbopenems) penetrate bone at levels 5–20% of the serum level (Spellberg and Lipsky, 2012). The serum concentrations with intravenous administration are high enough that adequate levels are achieved in bone. This is not the case with oral

preparations. Some oral antibiotics, such as linezolid, ciprofloxacin, clindamycin, cotrimoxazole, rifampicin and fusidic acid, achieve excellent concentrations in bone, and therefore can be used in the oral form (although rifampicin and fusidic acid should always be used in conjunction with another agent because of the potential for bacterial resistance to develop).

To date only small studies have compared oral and intravenous therapy for osteomyelitis. The results of the OVIVA study, a large UK multicentre randomized controlled study comparing oral *vs* intravenous therapy for bone and joint infections, are eagerly awaited (Li et al, 2015). For osteomyelitis associated with metal, where organisms may exist in a biofilm, rifampicin is a useful agent to penetrate biofilm.

Local antibiotics such as vancomycin and gentamicin can be administered through antibiotic-impregnated cement or biodegradable calcium-based carriers. Biodegradable calcium-based carriers have the advantage of allowing tissue and bone ingrowth as they degrade. Because they degrade, they do not necessarily require a second procedure to remove them.

The usual duration of antibiotic treatment is 4–6 weeks, based on historical data, with relapse of infection associated with shorter courses (Spellberg and Lipsky, 2012).

Surgical principles

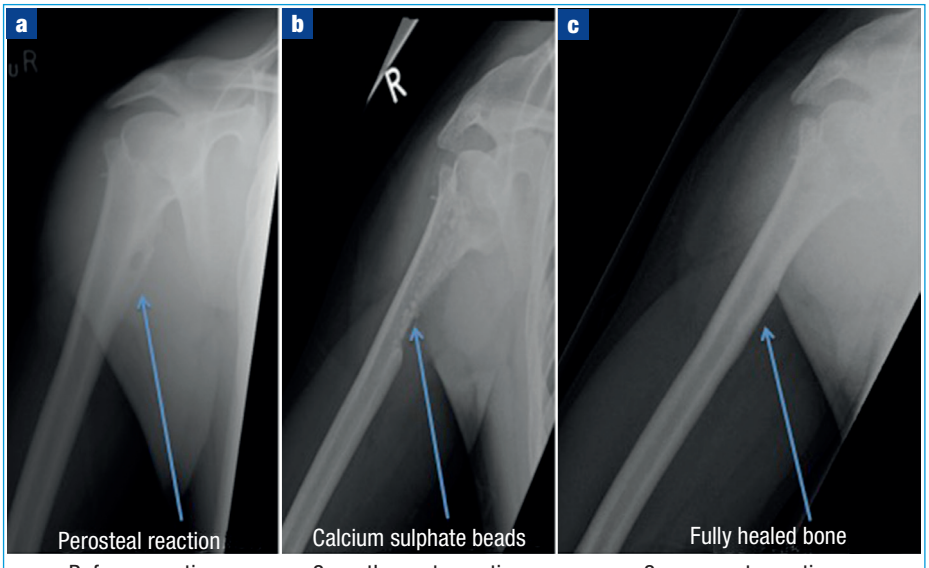
The goal of surgery is to achieve a viable vascularized environment free of dead bone (*Figure 3*). Antibiotics alone cannot eradicate chronic osteomyelitis; surgical debridement and sequestrectomy is required to debride all necrotic and infected bone, soft tissue and sinuses.

Before administering antibiotics, biopsies are performed via a small window through the planned surgical incision. Multiple samples are taken and sent to the lab for culture and sensitivity.

The excision margins should be at least 5 mm clear of infection. Simpson et al (2001) compared cure rates based on surgical margins and showed that excision with less than a 5 mm margin had a recurrence rate of 28% compared to a 100% cure rate with excision margins greater than 5 mm.

After excision of infection there is often a large defect. It is important to fill this dead space to prevent the recollection of infection. Dead space options include muscle flaps, cement spacers and biodegradable calcium beads that also act as a method of local antibiotic release.

Figure 3. Radiographs of a 28-year-old man suffering from chronic osteomyelitis of the proximal humerus. **a.** The preoperative radiograph shows the typical appearance of infection. He underwent sequestrectomy and **(b)** the 2-month postoperative radiograph shows evidence of the calcium sulphate beads for local antibiotic administration and dead space management. **c.** The final radiograph shows the beads have resorbed and the bone has healed.



The next step is to assess the stability of the bone. Sequestrectomy alone can leave a structural involucrum that is stable enough to allow the patient to weight-bear.

Bone loss secondary to debridement will need reconstruction. There are several techniques described for reconstruction of bone defects after excision of bone infection.

The Papineau technique involves radical debridement, staged bone grafting and delayed coverage, either by granulation or delayed skin grafting. This technique is rarely indicated today as modern plastic surgical techniques allow immediate one-stage reconstruction.

Bone transport using circular frames such as the Ilizarov technique are useful in filling segmental bone defects, working by distraction osteogenesis. As the bone is gradually distracted it stimulates neovascularization and new bone formation.

The Masquelet technique is a two-stage technique for the treatment of segmental bony defects. It involves initial wide debridement and the placement of an antibiotic-loaded cement spacer with temporary stabilization using intramedullary nailing, plating or external fixation. The cement spacer allows formation of a membrane rich in growth factors. At the second stage 8 weeks later, the spacer is removed; careful placement of bone autograft into the induced membrane improves healing and reduces the amount of graft that is resorbed (Masquelet and Begue, 2010).

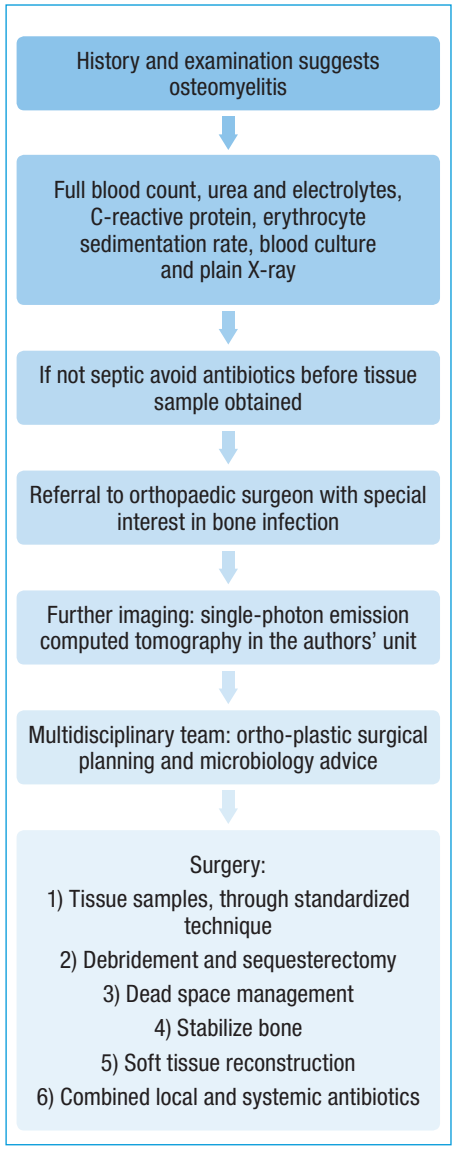
Vascularized bone flaps can be considered for large bone defects, but are only really suitable for patients fit enough for a prolonged single stage reconstruction. An example of this technique is the use of free fibula allograft.

Reconstruction of soft tissue defects is planned and performed by plastic surgeons in a combined surgical approach with orthopaedic surgeons. This makes it possible to achieve soft tissue coverage in a single stage. Reconstruction follows the reconstructive ladder with a combination of split skin grafts, local and free flaps used. *Figure 4* shows the treatment pathway in the authors' unit.

Conclusions

Chronic osteomyelitis remains one of the most difficult conditions to treat and patients should ideally be referred to a specialist centre for bone infection and follow a multidisciplinary team approach. Diagnosis can be difficult in early osteomyelitis, magnetic resonance imaging is the most accurate imaging modality for early diagnosis.

Figure 4. Flow chart showing treatment pathway in the authors' unit.



Antibiotics should be paused for 2 weeks, if it is safe to do so, until tissue samples are taken. A joint procedure involving plastic and orthopaedic surgeons is often required for limb salvage. This is often followed by a minimum 6-week course of antibiotics. The aim of treatment is to give the patient a functional infection-free limb. **BJHM**

Conflict of interest: none.

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KEY POINTS

- Chronic osteomyelitis is characterized by bone infection in the presence of necrotic bone.
- It remains one of the most difficult conditions to treat and should ideally be referred to a specialist centre for bone infection and follow a multidisciplinary team approach.
- Delaying antibiotic administration until intraoperative tissue samples are taken allows for targeted antibiotic therapy to maximize efficacy.
- A joint surgical approach requiring orthopaedic and plastic surgeons is often required for limb salvage.
- The aim of treatment is to give the patient a functional, infection-free limb.

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