Management of acute and chronic osteomyelitis

Pinak S Ray, Robert B Simonis

The incidence of acute and subacute osteomyelitis is declining. Vaccination has almost eradicated* Haemophilus *bone infection in infants. However, chronic traumatic osteomyelitis is becoming more frequent following an increase in motorcycle accidents and infected internal fixation of fractures. There are now effective means of treating this using the Ilizarov external circular frame.

Osteomyelitis is an infection of the bone and bone marrow caused by blood-borne organisms (haematogenous), or by direct inoculation from an open traumatic or surgical wound. Antibiotics have dramatically reduced the incidence of osteomyelitis and the mortality resulting from it, but morbidity from osteomyelitis still persists. The term osteomyelitis also describes granulomatous infections such as tuberculosis or fungal infections.

CLASSIFICATION

Osteomyelitis is classified as acute (either acute haematogenous or following open fracture or surgery); subacute or chronic.

ACUTE HAEMATOGENOUS OSTEOMYELITIS

Children are most commonly affected. Blood-borne organisms settle in the metaphysis or the epiphysis of long bones, most commonly around the knee.

Certain anatomical factors have been suggested for the prevalence of infection around the juxta epiphyseal areas:

1. The vascular architecture in the metaphysis has nutrient arteries and venous sinusoids forming sharp 'hair-pin' loops, favouring stagnation of blood flow and multiplication of bacteria (*Figure 1*).
2. These large calibre venous sinusoids are vulnerable to minor trauma, predisposing to thrombosis and haemorrhage, forming an ideal site for the multiplication of bacteria.
3. Certain metaphyses are intracapsular, e.g. the hip and knee. This facilitates direct spread of pus from the long bone into the adjacent joint.
4. In children under 1 year of age there is a free vascular anastomosis between the metaphysis and the epiphysis. Infection can start in the epiphysis.

Organisms

The commonest isolated organism is *Staphylococcus aureus*. It is responsible for approximately 60% of such infections in children between the age of 1 month and 5 years (Jackson and Nelson, 1982). Methicillin-resistant *Staph. aureus* (MRSA) has increased in prevalence in the last few years. The second commonest organism is streptococci, both group A and group B. Group B is particularly prevalent in the first 2 months of life. *Haemophilus influenzae* osteomyelitis has almost been eradicated by vaccination (Howard et al, 1999). Other gram-negative organisms implicated are *Escherichia coli*, *Proteus*, *Pseudomonas* and *Brucella*. Sickle cell anaemia is known to predispose to *Salmonella* osteomyelitis (salmonella is a bowel commensal) (Piehl et al, 1993); however, the commonest organism in this group is still *Staph. aureus* (Golding et al, 1959). *Pseudomonas* is often the causative organism in drug addicts.

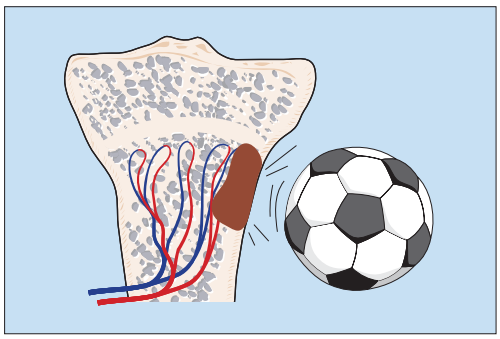


Figure 1. Vascular anatomy of the metaphysis and the epiphysis of long bone, haemorrhage from minor trauma.

Mr Pinak S Ray is Ilizarov Research Fellow and **Mr Robert B Simonis** is Consultant Orthopaedic Surgeon, Rowley Bristow Orthopaedic Unit, Ashford and St Peter's Hospitals NHS Trust, Chertsey, Surrey KT16 0PZ

Correspondence to: Mr RB Simonis

Infectious process and its consequences

Pus under pressure is formed within the metaphysis and tracks through the Haversian system and the cortex, elevating the periosteum and forming a subperiosteal abscess. The rising pressure, vascular stasis, infective thrombosis and periosteal stripping compromise the blood supply and the shaft becomes necrotic. Portions of dead bone are often separated from surrounding viable bone by granulation tissue. These are called sequestra (Latin: sequester – standing apart) (*Figure 2*).

The pus either re-enters the bone at another level or bursts out into the soft tissues and through the skin. The elevated periosteum responds by laying down new bone called the involucrum (Latin: involucre – to envelope), which surrounds the dead and infected bone.

In an established infection, defects in the involucrum become cloacae (Latin: cloaca – sewer), through which pus drains, establishing sinus tracts. The osteomyelitis then becomes chronic.

Clinical features

Effective treatment depends on early diagnosis, which in turn depends on a careful history and examination. Pain is the first symptom. It is usually continuous and may be related to recent trauma.

Figure 2. Sequestrum, excised from plated tibia.

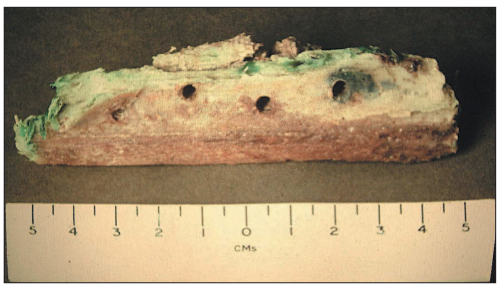
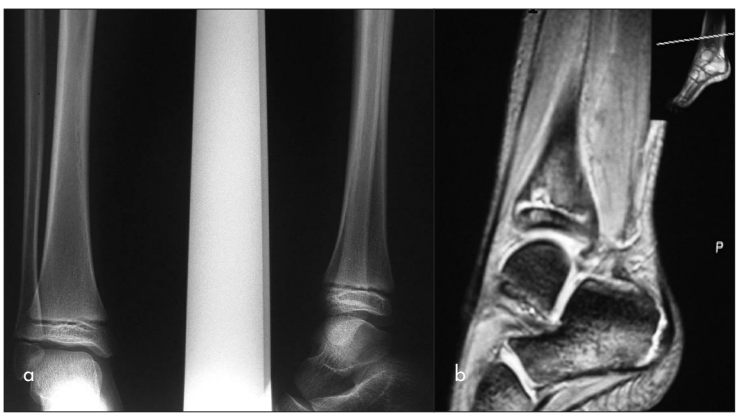


Figure 3. a. Normal X-ray in a 7-year-old girl with painful distal tibia. b. Magnetic resonance imaging scan of the ankle at the same time showing metaphyseal osteomyelitis.



The child looks ill and has a fever. He/she often refuses to use one limb but usually allows some movement with gentle encouragement, in contrast to septic arthritis, where movement is nil and extremely painful. Local tenderness and swelling can be found if the bone is superficial (tibia and ulna). Cellulitis in a child is often a sign of osteomyelitis. Infants may present just as 'failure to thrive'. They may have a 'pseudoparalysis' of the affected limb. In infants it is not uncommon for several bones to be infected at the same time.

It is important to be aware that previously administered antibiotics can mask the symptoms and signs.

Fortunately the incidence of acute and subacute haematogenous osteomyelitis is declining. This is most probably a result of reduced virulence of responsible pathogens, increased host resistance and increasing effectiveness of community-administered antibiotics (Blyth et al, 2001).

Investigations

Measurement of erythrocyte sedimentation rate (ESR), often not done in the initial stages, is a useful blood test. It rises rapidly and can reach but rarely exceeds 100 mm/hr. It is a useful indication of the response to treatment, but its decline is slow, tending to remain elevated for some time after infection has subsided. The most sensitive monitor of the course of the infection is C-reactive protein level. White blood cell count (WBC) is elevated with an increase in the number of neutrophils. The WBC count can vary from 7000 to 26000/mm^3 (Sullivan et al, 1981). Blood cultures are positive in 50–70% of cases (Blockley and Watson, 1970). Blood for culture should always be obtained before administration of antibiotics.

X-rays are completely normal for the first 10 days after the infection starts (*Figure 3a*). The first signs will be osteoporosis, which may be patchy. Periosteal new bone is not seen for 3–6 weeks. When it is present, remember that pus has already penetrated the cortex, formed a subperiosteal abscess and thrombosed the nutrient vessels.

Bone scans are useful for localizing the lesion before surgery, but they do not specify the pathology. Gallium-67 labelled gallium citrate uptake related to local accumulation of polymorphonuclear leucocytes can be used sequentially following a 99^m-technetium scan to increase the specificity (Merkel et al, 1984).

A magnetic resonance imaging (MRI) scan shows changes in the bone long before plain X-

ray films (*Figure 3b*). It is more useful than computed tomography (CT) scanning at making the diagnosis.

Treatment

The first priority is resuscitation of the dehydrated child with fluids. After blood has been taken for culture and laboratory tests, intravenous 'best-guess' antibiotics are started. In most cases the primary antibiotic of choice is flucloxacillin (Gillespie and Mayo, 1981). MRSA is treated with teicoplanin or vancomycin. Antibiotics are given in doses adequate to provide satisfactory blood and bone levels. The C-reactive protein and haemoglobin level, ESR and WBC count are monitored regularly.

During treatment the patient is rested in bed with the affected limb immobilized.

In early cases (under 48 hours), the infection can often be abated with large doses of intravenous antibiotics. However, if the child has been ill for a longer period of time, or if he/she is not improving with antibiotic treatment, surgery is indicated. The objective is to release the pressure inside the bone, and prevent the formation of a subperiosteal abscess. It is better to operate too early than to wait until the nutrient vessels have thrombosed and the shaft is dead.

Under general anaesthetic the affected bone is exposed and the periosteum is incised longitudinally. Any pus evacuated is sent for gram staining, aerobic and anaerobic culture, and antibiotic sensitivity. The cortex should be drilled to decompress the metaphysis and the entire area irrigated with saline. One to three cortical drill holes are sufficient. The skin is loosely closed. The value of closed suction drainage with continuous intramedullary irrigation remains to be proved. Inspite of careful precautions, this technique could invite the possibility of secondary infection. A drain is therefore not used in acute osteomyelitis, although it certainly has a place in the treatment of more chronic infection.

OSTEOMYELITIS FROM DIRECT INNOCULATION OF BACTERIA

Post-traumatic osteomyelitis is a common clinical problem now. The infection is often polymicrobial; isolated organisms can be *Staphylococcus*, *Streptococcus*, gram-negative or even anaerobic organisms. Most infections occur after open reduction and often inadequate internal fixation of fractures, following high energy open injuries. To obliterate infection, it is essential to rigidly immobilize the fracture fragments. The safest method is to remove all internal fixations, debride the infected bone and fix the fracture rigidly using an external fixator. This is attached to the bone by pins, situated well away from the fracture site. It is also essential to ensure that the soft tissue cover is adequate.

Total joint replacements can get infected acutely or many years later following a bacteraemia from a focus of infection elsewhere in the body. Patients with hip or knee replacements should be given prophylactic antibiotics during urinary catheterization, in an attempt to prevent late infection.

SPINAL OSTEOMYELITIS

In adults the commonest site of infection is the spine, with *Staphylococcus* and *Streptococcus* being the commonest organisms. Haematogenous seeding of gram-negative organisms may occur from intra-abdominal infections, such as cholecystitis or appendicitis, or from urinary tract infection after catheterization (Smith and Blaser, 1991). The organisms gain access to the spine via Batson's venous plexus which anastomose with both the systemic veins and the portal venous system. They lack valves and so retrograde flow can lead to metastatic infection. The organisms settle on the vertebral end plate. Infection spreads from one vertebra to the next through intermetaphyseal anastomoses. The intervertebral disc is avascular and becomes involved in the infectious process. As the infection continues progressive bone destruction occurs.

Deep boring back pain, unrelieved by rest or position, is the commonest symptom from pyogenic vertebral osteomyelitis. It is notoriously difficult to diagnose. It is not uncommon for patients to be in hospital for weeks before the diagnosis is made.

ESR is usually raised. WBC is often normal or slightly elevated. Blood culture is positive in about 25% of cases (Sapico and Montgomerie, 1979). There are no X-ray changes in the first 2–3 weeks. Initial X-rays show a loss of disc height and of paravertebral soft tissue shadow. This is followed by loss of cortical integrity of the end plate with progressive vertebral destruction. Resolving infection usually goes onto spontaneous anterior vertebral fusion.

A technetium bone scan is a useful investigation but is not specific, making a MRI scan the investigation of choice. A MRI scan can show marked vertebral destruction even though the X-rays look normal (Kerslake and Worthington, 1972).

Once the site of the infection has been determined, a needle biopsy obtained under fluoroscopic control is sent for microbiological and histological examination. The majority of cases respond to non-operative treatment. The main-

stay of treatment is appropriate antibiotic in adequate doses, for a prolonged period of time; preferably intravenously for 6–8 weeks. This is followed by oral antibiotics for up to 6 months. Spinal immobilization and rest are also an important part of the treatment. Adults with vertebral osteomyelitis rarely need surgery. Spontaneous spinal fusion occurs in about 60% of cases (Sapico and Montgomerie, 1979).

Spinal tuberculosis still occurs in the UK, commonly in the immunocompromised and in patients with acquired immunodeficiency syndrome (AIDS). It usually affects the lower thoracic and upper lumbar vertebra. It starts in one vertebral body and then spreads under the longitudinal ligaments to affect other levels. Pain may be deceptively slight so consequently it is picked up late and not treated until vertebral collapse, which leads to a localized kyphosis. The infection can track down the psoas muscle presenting as a cold abscess in the groin.

SUBACUTE OSTEOMYELITIS

Subacute haematogenous osteomyelitis is difficult to diagnose because the characteristic signs and symptoms of acute infection are absent. The patient presents with pain at the end of a long bone and occasionally with a limp. The femur and the tibia are the commonest bones involved. There is usually no systemic illness, no previous complaints and no local signs of infection. The illness is mild, presumably because the organisms are less virulent and the patient is more resistant. Laboratory tests are usually normal, although the ESR may be slightly raised.

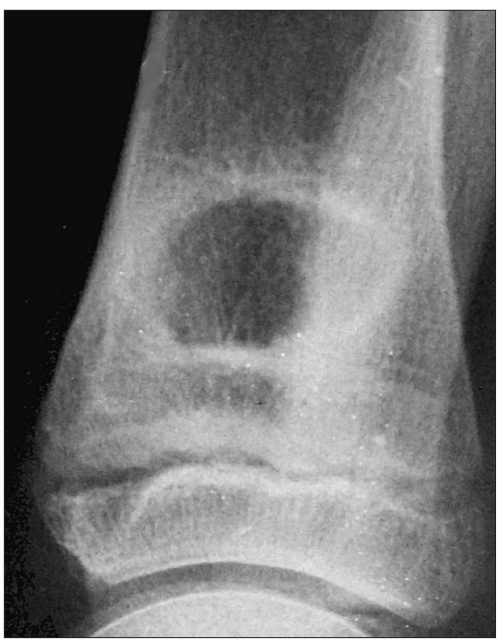


Figure 4. Brodie's abscess.

The radiograph usually shows a well-established lesion in the bone. They can mimic various benign and malignant bone tumours and non-pyogenic infections.

Classification

Subacute osteomyelitis has been classified by Gledhill (1973):

- Type 1: Solitary metaphyseal lesion walled off by a sclerotic reactive bone. There is normal bone around the sclerosis, without any periosteal reaction (Brodie's abscess) (*Figure 4*)
- Type 2: Solitary metaphyseal lesion with cortical erosions resembling osteosarcoma
- Type 3: Diaphyseal lesion with cortical hypertrophy. This can be confused with an osteoid osteoma
- Type 4: Diaphyseal lesions with layers of periosteal new bone formation, giving an onion-skin appearance similar to Ewing's sarcoma.

Management

It is best to be certain of the diagnosis with a biopsy followed by a curettage. A bacteriological culture is positive in under 50% of cases, usually *Staph. aureus*. A prolonged course of antibiotic (6–12 weeks) usually cures this condition.

CHRONIC OSTEOMYELITIS

Inappropriately treated acute osteomyelitis can become chronic, but now it more frequently follows an open fracture or an operation.

The organisms are the same as from the original haematogenous osteomyelitis, *Staph. aureus* being the commonest. Following trauma or surgery the organisms are polymicrobial, *Staph. aureus* and gram-negative organisms being the commonest.

Classification

Chronic osteomyelitis has been classified by Cierny and Mader (1984):

- Type 1: Intramedullary osteomyelitis
- Type 2: Superficial osteomyelitis, as a result of a skin infection extending to the bone
- Type 3: Both endosteal and cortical involvement of a segment of the bone
- Type 4: Diffuse involvement of a section of the bone. The bone and the limb will become unstable after debridement.

A physiological classification of the host has been suggested (Cierny and Mader, 1984). This determines the risk of infection and also gives a yardstick for prognosis following chronic osteomyelitis:

- Host type A: normal immune system, non-smoker
- Host type B: immunologically compromised
  B1: locally (lymphoedema, varicose veins, arteritis)
  B2: systemically (diabetics, renal and liver failure, drug addicts, and smokers)
  B3: both locally and systemically
- Host type C: major nutritional and systemic disorders.

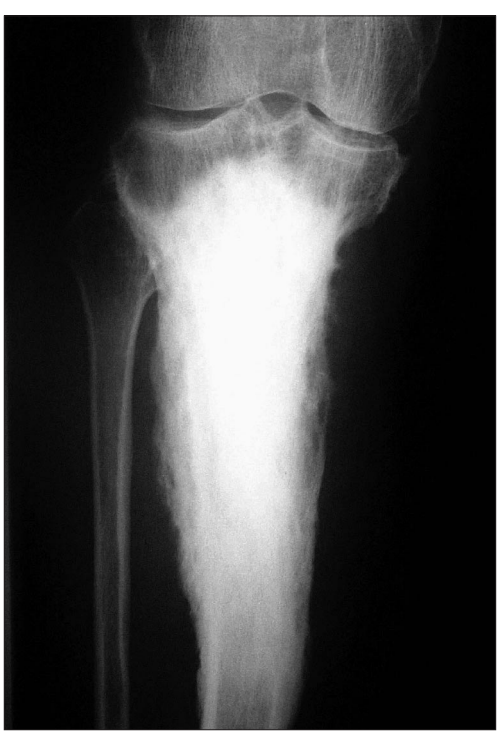
The chances of curing a B3 or C type host with surgery and antibiotics is slim.

Chronic sclerosing osteomyelitis of Garre

This condition is increasing in frequency. The patient is usually a young adult with a long history of low grade pain. It is gradual in onset, eventually producing a locally enlarged tender segment of bone. Rarely is there a fever. C-reactive protein and ESR levels are raised in the more active phase. The process is usually self resolving, but may recur a number of years later. The metaphyses of long bones and the mandible are the commonest bones involved. The X-ray shows cortical thickening and sclerosis, with no intramedullary cavity (*Figure 5*). This sometimes resembles a bone tumour, such as osteoid osteoma or sarcoma (Macnicol, 2001).

The diagnosis is made by a bone biopsy, which shows inflammation but no pus. Rarely is an organism isolated. Symptoms can be relieved by intermittent administration of non-steroidal anti-inflammatory drugs. Prolonged antibiotic therapy does not change the clinical course of the disease. If a small segment of bone is affected, the diseased bone can be excised and replaced with bone transport. If a large area is involved it is not treatable.

Figure 5. Chronic sclerosing osteomyelitis of Garre.



Management

Antibiotics alone do not eradicate chronic infection. However, they do have a place in:

1. Preventing acute flares by taking a low dose of antibiotics
2. Attempting a complete cure of the infection by giving systemic and local antibiotic irrigation, combined with an aggressive surgical debridement of all dead and infected bone.

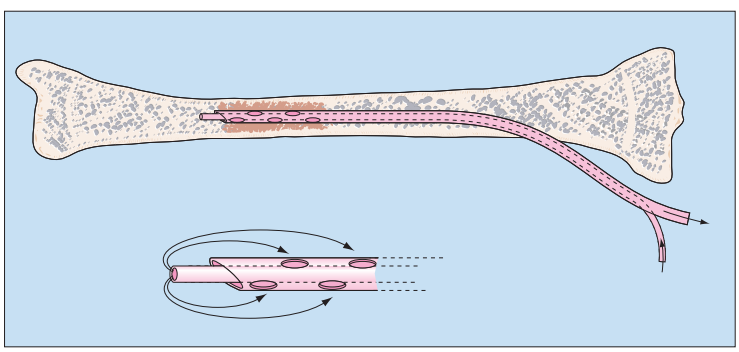
Bone biopsy is required to identify the appropriate antibiotics, as sinus tract cultures are not adequate. The choice of antibiotic should be guided by a microbiologist. Teicoplanin, vancomycin, clindamicin and rifampicin have good bone penetration, and can be useful in MRSA osteomyelitis. They should be given in high enough doses to make the serum concentration eight times the minimal bactericidal concentration (Quintiliani and Nightingale, 1984). Antibiotics should be continued for at least 3 months after surgery, the first 2 weeks at least being intravenous.

Surgery

Intramedullary reaming: Intramedullary osteomyelitis (Cierny type 1) can sometimes be cured by intramedullary reaming followed by antibiotic irrigation. The reaming is performed as when inserting an intramedullary nail, but reaming out as wide as possible, up to the cortex. All loose and infected bone must be washed out of the medullary cavity with pulsed lavage.

Antibiotic irrigation (Lautenbach): Double lumen tubes are inserted into the cavity, which is initially filled with 50 ml of saline, containing antibiotic and Varidase (Wyeth Laboratories, Princeton, NJ) to prevent clotting (*Figure 6*). This

Figure 6. Lautenbach irrigation, using double tubing of medullary cavity following intramedullary reaming.



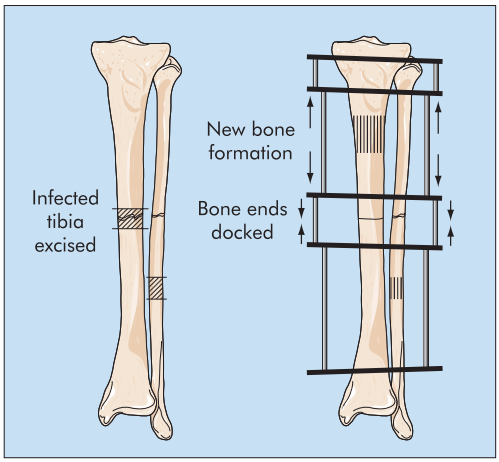


Figure 7. Excision of infected non-union, and replacement of gap by proximal bone transport, using an Ilizarov circular frame.

small volume is left in the intramedullary cavity for 1 hour and then cleared by low pressure suction. The cavity is then filled up again and the procedure repeated, 24 hours per day, for a period of up to 2 weeks assuming the tubes do not block. The volume of the antibiotic solution diminishes as the cavity gets smaller. Systemic antibiotics are continued at the same time.

This is a more effective method of instilling antibiotics into an infected cavity, than by the insertion of gentamicin-laden cement beads. These beads become difficult to remove after a few weeks. A more recent development is the collagen-based drug delivery system like the Collatamp-G (Syntacoll, Herisau, Switzerland). These are fully biodegradable implants containing antibiotics such as gentamicin. They show excellent pharmacokinetic properties ensuring adequate local concentration of antibiotic. All these products are biocompatible and biodegradable thus avoiding a need for a second removal operation.

Surgical debridement: Chronic osteomyelitis following infected internal fixation after trauma has a better chance of a 'cure' than when following a haematological infection. Traumatic osteomyelitis is often localized to a small section of a long bone, whereas haematological osteomyelitis can affect the whole bone. Traumatic osteomyelitis is often combined with an infected non-union.

To achieve a cure it is vital that all dead and devitalized bone be resected, that the cavity is irrigated until 'clean', and then filled in with bone. This used to be performed by open autogenous bone grafting (Papineau technique). In the last 10 years this technique has been replaced by bone transport using an Ilizarov circular frame, which has revolutionized the management of chronic osteomyelitis.

Ilizarov treatment of chronic osteomyelitis: A minor infected non-union with no obvious radiological sequestrum can be treated by rigid stabilization and compression of the fracture using the Ilizarov frame. Stabilization increases the vascularity at the fracture site, producing repair callus, which allows antibiotics to reach the infected area. This heals the non-union and also eliminates the infection.

However, if there is massive infection, diffuse spread of infection along the bone, or a sequestrum present, then the dead and infected bone must all be excised, resulting in a loss of substance of the bony shaft. The bone is then sta-

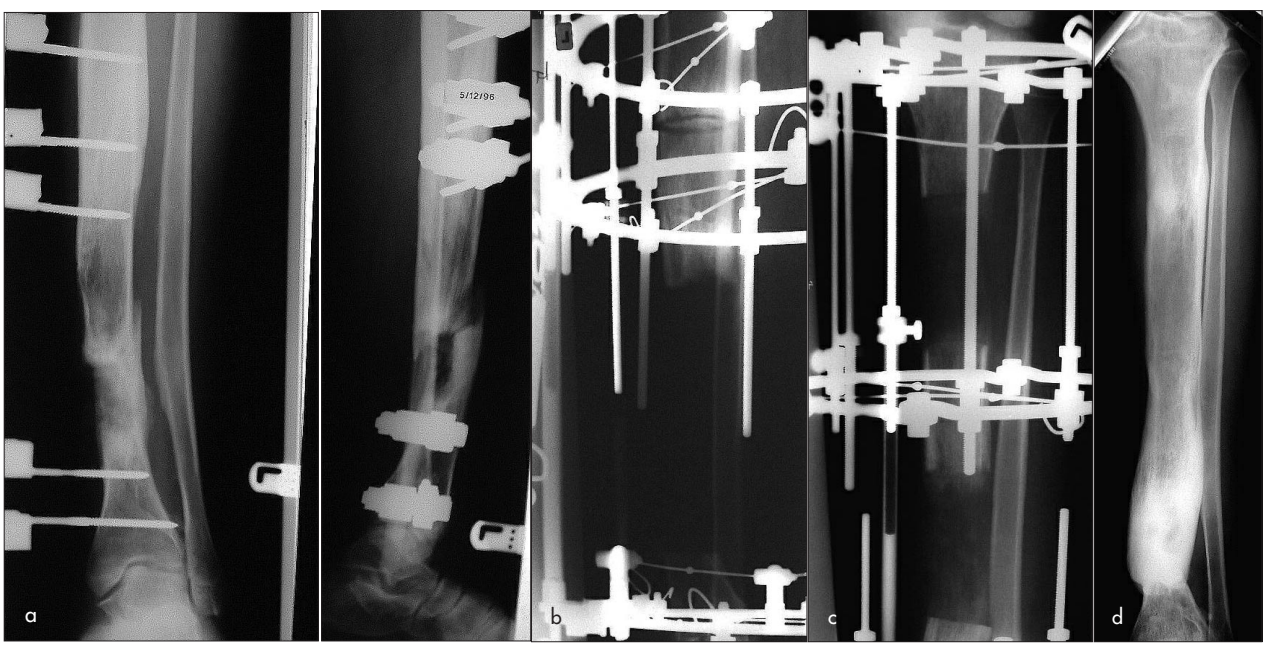


Figure 8. a. Infected tibial non-union, unsuccessfully treated by a monolateral external fixator. b. 9 cm of infected tibia excised. Ilizarov frame applied with a single proximal corticotomy for bone transport. c. Halfway through bone transport. d. Final reconstruction of the tibia. No residual infection.

bilized with an Ilizarov frame and the long bony gap is slowly closed using bone transport from a distant corticotomy site (Dendrinos et al, 1995) (*Figure 7–9*). The maximum length that can be restored by one corticotomy is about 6 cm. Bone transport would need to be performed at two separate sites if the bone loss is much greater than this (Cattaneo et al, 1992).

Amputation: Before planning any surgical treatment on these patients it is important to counsel them and carefully evaluate their personality. They may already have undergone many surgical procedures. In difficult cases with severe infection, prolonged pain and suffering, as well as economic and family problems, it may be more appropriate to offer an amputation, rather than further prolong their treatment without any guaranteed success.

Complications

Patients with chronic osteomyelitis can have recurrent flares and pathological fractures. Amyloid deposition is also a known complication of chronic osteomyelitis. A long-standing osteomyelitis can predispose to a squamous cell carcinoma of the sinus (Marjolin's ulcer) (*Figure 10*). HM

Conflict of interest: none.

Apley AG, Solomon L (1993) Infection. In: Apley AG, Solomon L, eds. *System of Orthopaedics and Fractures.* Butterworth-Heinemann Ltd, Oxford: 31–53

Blockley NJ, Watson TT (1970) Acute osteomyelitis in children. *J Bone Joint Surg* **52B:** 77–87

Figure 9. Ilizarov frame on an infected tibia.

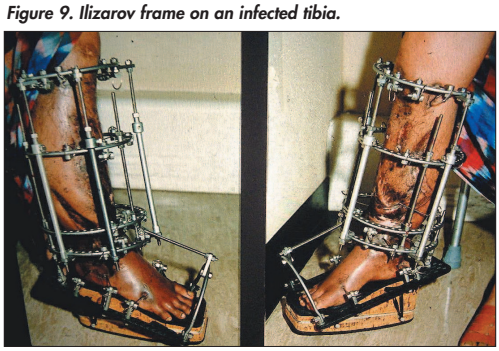
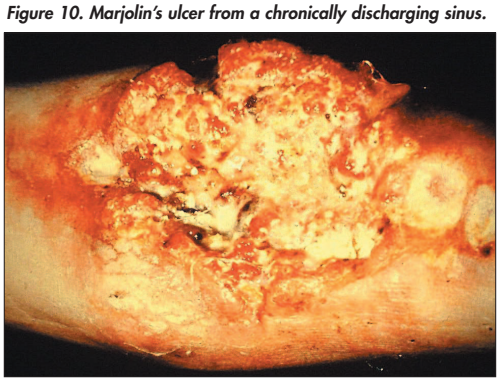


Figure 10. Marjolin's ulcer from a chronically discharging sinus.



Blyth MJG, Kincaid R, Craigen MAC, Bennet GC (2001) The changing epidemiology of acute and subacute haematogenous osteomyelitis in children. *J Bone Joint Surg* **83B:** 99–102

Bullough PG, Vigorita VJ (1984) Bone and joint infections. In: Bullough PG, Vigorita VJ, eds. *Atlas of Orthopaedic Pathology.* Gower Publishing Ltd, London: 9.2–9.17

Cattaneo R, Catagni M, Johnson EE (1992) The treatment of infected non-union and segmental defects of the tibia by methods of Ilizarov. *Clin Orthop* **280:** 143–52

Cierny G III (1990) Chronic osteomyelitis: results of treatment. *AAOS Inst Course Lect* **39:** 495–508

Cierny G III, Mader JT (1984) Adult chronic osteomyelitis. *Orthopaedics* **7**: 1557–64

Dendrinos GK, Kontos S, Lyntsis E (1995) Use of Ilizarov technique for treatment of non-union of the tibia associated with infection. *J Bone Joint Surg* **77A:** 835–46

Gillespie WJ, Mayo KM (1981) The management of acute haematogenous osteomyelitis in the antibiotic era. A study of the outcome. *J Bone Joint Surg* **63B:** 126–31

Gledhill RB (1973) Subacute osteomyelitis in children. *Clin Orthop* **96:** 57–69

Golding JSR, MacLver JE, Wint LN (1959) The bone changes in sickle anaemia and its genetic variants. *J Bone Joint Surg* **41B:** 711–18

Howard AW, Viskontar, Sabbagh C (1999) Reduction in osteomyelitis and septic arthritis related to *Haemophilus influenzae* type b vaccination. *J Pediatr Orthop* **19:** 705–9

Jackson MA,Nelson JD (1982) Etiology and medical management of acute suppurative bone and joint infection in paediatric patients. *J Pediatr Orthop* **2:** 313–23

Kawashima M, Tamura H (1984) Topical therapy in orthopaedic infection. *Orthopaedics* **7:** 1592–8

Kerslake RW, Worthington BS (1972) MRI of the spine. *Clin Radiol* **43:** 227–33

Macnicol MF (2001) Patterns of musculoskeletal infection in childhood. *J Bone Joint Surg* **83B:** 1–2

Merkel KD, Fitzgerald RH Jr, Brown ML (1984) Scintigraphic evaluation of musculoskeletal sepsis. *Orthop Clin North Am* **15:** 401–16

Piehl FC, Davis RJ, Prugh SI (1993) Osteomyelitis in sickle cell diease. *J Pediatr Orthop* **13**(2): 225–7

Quintiliani R, Nightingale C (1984) Principles of antibiotic usage. *Clin Orthop* **190:** 31–5

Sapico FL, Montgomerie JZ (1979) Pyogenic vertebral osteomyelitis: report of 9 cases and review of literature. *Rev Infect Dis* **1:** 754–76

Smith AS, Blaser SI (1991) Infections and inflammatory process of the spine. *Radiol Clin North Am* **29:** 809–27

Sullivan JA, Vasileff T, Leonard JC (1981) An evaluation of nuclear scanning in orthopaedic infection. *J Pediatr Orthop* **1:** 73–9

KEY POINTS

- The incidence of acute osteomyelitis has declined over the last decade.
- The commonest organism isolated in acute osteomyelitis is *Staphylococcus aureus* (60% of cases in children between the age of 1 month and 5 years).
- C-reactive protein is the most sensitive monitor of the course of infection.
- A magnetic resonance imaging scan shows bone changes before plain X-rays.
- Early cases of acute osteomyelitis can be 'cured' with rest and prolonged high dose of antibiotics.
- Late cases need decompression by drilling through the cortex, as well as antibiotic treatment.
- Age, virulence of infecting organisms, type of host, duration of disease and extent of bony involvement are factors which determine the severity of the disease in chronic osteomyelitis.
- Infected non-union is best treated by stable fracture fixation using an external fixator.
- The Ilizarov circular frame has revolutionized the management of post-traumatic chronic osteomyelitis.