BONE AND JOINT INFECTIONS

Chapter 16

OSTEOMYELITIS

Osteomyelitis refers to an infection of bone that is usually bacterial in origin. There are three types of osteomyelitis depending on how the microorganisms were introduced into the bone:

- Haematogenous osteomyelitis: haematogenous delivery (bacteraemia)
  - Primarily a disease of children, with 85% of cases occurring in children younger than 17 years of age
  - In adults most cases are seen in patients over 50 years of age
- Post-traumatic osteomyelitis: direct inoculation usually following trauma or surgery
- Decubitus ulcer or periodontal disease: local invasion from contiguous infection (usually)

HAEMATOGENOUS OSTEOMYELITIS

OSTEOMYELITIS IN CHILDREN

In children, acute osteomyelitis is primarily haematogenous in origin and invariably involves the long bones (e.g. tibia, femur and humerus).

The likely infecting organisms differ with age:

- Neonates to three months of age: usually due to *Staphylococcus aureus*, Gram-negative bacilli and group B streptococci.
- Children more than three months of age: usually due to *Staphylococcus aureus* and group A streptococci.

ANTIBIOTIC TREATMENT

- Antibiotics are recommended for children with clinical features suggestive of osteomyelitis plus characteristic abnormalities on plain X-rays (or MRI or technetium bone scans, in those whose initial plain X-rays are normal).
- Treatment is usually initiated with empiric antibiotics (before the diagnosis is confirmed by culture), which is followed by a specific antimicrobial regimen once the causative organism is identified (from bone, periosteal collection, bone marrow space, joint fluid or blood cultures). In up to 50% of children the causative bacteria are not identified by culture.
- There is limited evidence reporting the relative efficacy of different agents for the treatment of osteomyelitis in children. Current cure rates for osteomyelitis in children are generally above 95% if treated adequately.
- Acute haematogenous osteomyelitis should be treated initially with a parenteral antibiotic.
- The ideal choice for empiric therapy would be a single intravenous agent that has an effective oral counterpart because the response to intravenous therapy is an important consideration when choosing an oral agent for sequential therapy, especially in patients with negative cultures.

There is no minimum duration of IV therapy required for osteomyelitis. Once the patient has demonstrated clinical improvement, been afebrile for 48–72 hours, the local symptoms and signs of infection (i.e. pain, range of movement) have reduced considerably, and the ESR has decreased by 20% or there has been a 50% reduction in the CRP, outpatient and/or oral antibiotic therapy can be considered.

- Sequential therapy (intravenous antibiotics followed by oral therapy) is commonly used in children and generally a total of four to six weeks of antibiotics should be administered.

EMPIRIC ANTIBIOTICS: OSTEOMYELITIS IN NEONATES

Cefotaxime 50 mg/kg/dose IV 8 hourly

AND

Cloxacillin 50 mg/kg IV 6 hourly OR vancomycin IV

Initial vancomycin dosing according to the creatinine is as follows:

- < 0.7 mg/dL: 15 mg/kg every 12 hours
- 0.7–0.9 mg/dL: 20 mg/kg every 24 hours
- 1.0–1.2 mg/dL: 15 mg/kg every 24 hours
- 1.3–1.6 mg/dL: 10 mg/kg every 24 hours
- > 1.6 mg/dL: 15 mg/kg every 48 hours

EMPIRIC ANTIBIOTICS: OSTEOMYELITIS IN INFANTS ONE TO THREE MONTHS OLD

A third-generation cephalosporin (ceftriaxone 75 mg/kg/day IV as a single dose or cefotaxime 50 mg/kg/ IV 6–8 hourly)

AND

Cloxacillin 50 mg/kg IV 6 hourly OR vancomycin 30 mg/kg IV 12 hourly

EMPIRIC ANTIBIOTICS: OSTEOMYELITIS IN INFANTS AND CHILDREN MORE THAN THREE MONTHS OF AGE

Cloxacillin 50 mg/kg IV 6 hourly

OR

Clindamycin 13 mg/kg IV 8 hourly

OR

Vancomycin if the patient has not responded to the regimen containing cloxacillin to cover MRSA

NOTE

- Vancomycin is typically reserved for infection that was acquired in hospital, e.g. neonates in an ICU for more than one week, or when a patient has not responded to a combination regimen including cloxacillin, and/or the patient is seriously ill.
- Ceftriaxone and cefotaxime should not be used alone for the treatment of staphylococcal osteomyelitis since a large number of treatment failures have been described.
- Some advocate the empiric use of vancomycin once the prevalence of methicillin/cloxacillin-resistance in S. aureus is above 15–20%, and/or the patient appears seriously ill. In general, there is no need to cover Haemophilus influenzae type b since immunisation rates in South Africa are high.
- Experience with linezolid in children is limited.

ORAL THERAPY: OSTEOMYELITIS IN INFANTS AND CHILDREN

Contraindications to oral therapy include:

- Age younger than one month. It is recommend to treat neonates parenterally for the full duration of therapy
- Isolate not susceptible to oral antibiotics
- No pathogen isolated and no oral regimen with a spectrum similar to the parenteral regimen that resulted in improvement.
- Patient cannot tolerate the oral agent to which the isolate is susceptible
- Patient and family unlikely or unable to adhere to oral regimen

ORAL TREATMENT: OSTEOMYELITIS IN INFANTS AND CHILDREN

The choice of oral therapy should be based on susceptibility testing of the organism and, in general, is given in higher doses than those used for treatment of other infections. These include:

- Amoxicillin 25 mg/kg/dose every 6 hours.
- Cephalexin 37.5 mg/kg/dose every 6 hours
- Clindamycin 13 mg/kg/dose every 8 hours
- Cloxacillin 50 mg/kg/dose every 6 hours
- Linezolid 600 mg per dose administered every 12 hours for children ≥ 12 years of age; 10 mg/kg per dose administered every 8 hours for children < 12 years of age (maximum 600 mg per dose).

Surgical therapy, which may include drainage of an abscess or removal of devitalised bone, must be initiated promptly when it is indicated.

Immobilisation of the affected extremity may relieve pain, and prevent pathological fractures, especially if the bone involvement is extensive and involves the proximal femur.

OSTEOMYELITIS IN ADULTS

Vertebral joints (usually lumbar, and less commonly thoracic and cervical vertebrae), the sternoclavicular joints and sacroiliac joints are the major joints involved in adults.

Patient characteristics that predispose to bacteraemia include recent gastrointestinal surgery or urinary tract manipulation and intravenous drug use.

Haematogenous osteomyelitis in adults is usually monomicrobic. Staphylococcus aureus remains the most common organism isolated, but Gram-negative bacilli, including Escherichia coli, Klebsiella spp., Pseudomonas aeruginosa and Serratia marcescens occur in about 30% of cases. Unusual organisms such as Candida albicans have been reported in vertebral osteomyelitis.

TREATMENT

Management should include surgical debridement with antibiotic therapy tailored to culture findings. A bone biopsy or subperiosteal abscess aspirate for culture is necessary unless the patient has positive blood cultures.

After cultures are obtained, empiric antibiotics should be selected to cover the most probable pathogens including S. aureus and Gram-negative bacilli.

EMPIRIC TREATMENT: OSTEOMYELITIS IN ADULTS

Cloxacillin 2 g IV every 6 hours

AND

Ciprofloxacin 400 mg IV 12 hourly OR levofloxacin 750 mg IV once daily

FOR PATIENTS AT RISK FOR METHICILLIN-RESISTANT S. AUREUS (MRSA)

Vancomycin 30 mg/kg IV per 24 hours in 2 divided doses (check levels and dose accordingly)

AND

Ciprofloxacin 400 mg IV 12 hourly OR levofloxacin 750 mg IV once daily

Once the aetiological organism is identified and antibiotic susceptibility obtained, the regimen can be modified, if needed.

Duration: For vertebral osteomyelitis, parenteral antimicrobial therapy should be given for four weeks. For non-vertebral osteomyelitis two weeks parenteral antibiotics, followed by two to four weeks oral antibiotic therapy is recommended.

POST-TRAUMATIC OSTEOMYELITIS

Post-traumatic osteomyelitis refers to osteomyelitis that develops as a result of contaminated open fractures or surgical treatment of closed fractures. The microorganisms are introduced into bone in the setting of trauma or via contiguous spread from the injured overlying soft tissue.

The pathogens may include skin flora or nosocomial pathogens in the setting of surgical intervention. The most common pathogens include *S. aureus*, coagulase-negative staphylococci and aerobic Gram-negative rods. Enterococci, anaerobes, mycobacteria and fungi are less commonly implicated.

The hallmarks of post-traumatic osteomyelitis are non-union of the fracture site, poor wound healing after wound closure, fever, surrounding cellulitis and wound drainage.

TREATMENT

The initial management of post-traumatic fractures includes:

- Thorough irrigation and debridement
- Cultures of bone biopsies or fluid collections obtained during debridement
- Tetanus immunisation
- Empiric 'prophylactic antibiotics' should be administered parenterally within six hours after open trauma to reduce the risk of soft tissue infection and osteomyelitis. Initial therapy should be directed against both staphylococci and aerobic Gram-negative bacilli.

PREVENTION OF POST-TRAUMATIC OSTEOMYELITIS

Cefuroxime 1.5 g IV 8 hourly

OR

For patients at risk for methicillin-resistant S. aureus (MRSA):

Teicoplanin loading and maintenance doses of 400 mg IV 12 hourly, then 400 mg IV daily **AND** ciprofloxacin 400 mg IV 12 hourly

OR

Vancomycin 1 g 12 hourly (check levels and dose accordingly) **AND** ciprofloxacin 400 mg IV 12 hourly

'Prophylactic' antibiotics should be given for 3–5 days or for 24–48 hours following wound closure.

Fracture fixation is needed for stabilisation and union. Once union is achieved, fixation hardware can be removed (if possible) with additional debridement and bone grafting (if needed) and wound closure.

Treatment of established post-traumatic osteomyelitis should be tailored to culture and susceptibility results and needs to be continued until union has been achieved.

EMPIRIC TREATMENT OF ESTABLISHED POST-TRAUMATIC OSTEOMYELITIS

Cloxacillin 2 g IV every 6 hours (children: 50 mg/kg 6 hourly) **AND** ciprofloxacin 400 mg IV 12 hourly or ceftazidime 2 g IV 8 hourly

OR

Cefazolin 2 g IV 8 hourly (children: 50 mg/kg 8 hourly) **AND** ciprofloxacin 400 mg IV 12 hourly or ceftazidime 2 g IV 8 hourly

OR

For patients at risk for methicillin-resistant S. aureus (MRSA):

Vancomycin 30 mg/kg per day in 2 divided doses (check levels and dose accordingly) **AND** ciprofloxacin 400 mg IV 12 hourly or ceftazidime 2 g IV 8 hourly

OR

Teicoplanin loading and maintenance doses of 400 mg IV 12 hourly, then 400mg IV daily **AND** ciprofloxacin 400 mg IV 12 hourly or ceftazidime 2 g IV 8 hourly

SEPTIC ARTHRITIS

Bacterial arthritis is the most potentially dangerous and destructive form of acute arthritis. In most cases, it results from haematogenous spread to the joint, but can result from direct inoculation into the joint from trauma, bites, and during joint surgery. Predisposing factors include prior joint pathology such as rheumatoid arthritis, gout, osteoarthritis and recent joint surgery.

Virtually any microbial pathogen is capable of causing septic arthritis. Staphylococcus aureus and streptococci are more common causes of joint infections than Gram-negative bacilli, which typically only produce infection after trauma or in patients with severe underlying immunosuppression. Streptococcus pneumoniae and Haemophilus influenzae may cause arthritis following bacteraemia in children. Gonococcal arthritis may present with an acute monoarthritis, although migratory polyarthritis and tenosynovitis are more typical.

The most common joints involved are the knees, followed by hips, ankles and wrists.

LABORATORY DIAGNOSIS

At the initial suspicion of joint infection, synovial aspiration should be performed and submitted to the laboratory for MCS (Gram stain, polarised microscopy for crystals, white cell count and differential, and culture). Blood cultures should be obtained in any patient presenting with suspected bacterial arthritis.

TREATMENT

Treatment requires both surgical drainage of purulent fluid from the joint and antibiotics. Since no randomised controlled studies have evaluated antibiotic regimens for bacterial arthritis, the initial choice of antibiotics should be based on the Gram stain.

EMPIRIC TREATMENT: SEPTIC ARTHRITIS

GRAM-POSITIVE COCCI

Cloxacillin 2 g IV 6 hourly (children: 50 mg/kg IV 6 hourly),

For patients at risk for methicillin-resistant S. aureus (MRSA):

Vancomycin 30 mg/kg/day IV in 2 divided doses (check levels and dose accordingly)

OR

Teicoplanin loading and maintenance doses of 400 mg IV 12 hourly then 400mg IV daily

OR

Linezolid 600mg IV/PO 12 hourly (children 10mg/kg IV/PO 8 hourly)

GRAM-NEGATIVE BACILLI

Ceftriaxone 2 g IV once daily (children: 50–75 mg/kg/day once daily)

OR

Cefotaxime 2 g IV 12 hourly (children: 50 mg/kg/dose IV 8 hourly)

OR

A quinolone such as ciprofloxacin 400 mg IV 8 hourly

NO ORGANISMS SEEN

Immunocompetent patient:

Vancomycin or teicoplanin or linezolid only.

Immunosuppressed patient or following trauma:

Vancomycin or teicoplanin or linezolid

AND

A third-generation cephalosporin or ciprofloxacin.

Intra-articular antibiotics are not recommended since effective parenteral and oral therapy produce adequate levels of antimicrobial agents in joint fluid. Once the culture and susceptibility results are available, modifications of the initial empiric antibiotic regimen can be made.

The typical duration of therapy is three to four weeks of combined parenteral (approximately two weeks) and oral therapy (to complete the duration of therapy). Joint drainage (usually by single or multiple needle aspirations) should be performed in all patients with bacterial arthritis. Occasionally open drainage is required.

PROSTHETIC JOINT INFECTION

The use of perioperative antimicrobial prophylaxis and a laminar airflow surgical environment has reduced the risk of intraoperative infection to less than one percent after hip and shoulder replacement, and to less than two percent after knee replacement. The management of infection with prosthetic joints is not well standardised due to lack of data from randomised, controlled studies.

The most common microorganisms involved include coagulase-negative staphylococci, Staphylococcus aureus, streptococci, Gram-negative bacilli, enterococci and anaerobes (including Propionibacterium acnes).

Prosthetic joint infections (PJI) are categorised according to the time of onset after implantation:

- Early-onset infection (those that develop within the first three months after surgery) – are usually acquired during implantation and are often due to the more virulent organisms such as Staphylococcus aureus and Gram-negative bacilli.
- Delayed-onset infection (three to 24 months after surgery) – are also usually acquired during implantation. These infections are usually caused by less virulent organisms such as coagulase-negative staphylococci and Propionibacterium acnes.
- Late-onset infection (more than 24 months after surgery) – typically result from haematogeneous seeding. Usually caused by Staphylococcus aureus, coagulase-negative staphylococci, E. coli (typically following urinary tract infections).

TREATMENT

Treatment usually involves both medical (long-term antibiotics) and surgical measures (debridement with or without joint replacement). Since biofilms play an important role, antimicrobial therapy is often unsuccessful unless the biofilm is physically disrupted or removed by surgical debridement. Long-term suppressive therapy alone is sometimes necessary in patients who are elderly, have contraindications to general anaesthesia, or refuse removal or debridement of an infected prosthesis.

- **Early-onset infection** – surgical debridement followed by a long course of intravenous antibiotics is curative in up to 40% of cases, but only if it is performed immediately after the onset of symptoms and if the implant is stable.
- **Delayed-onset infection and late onset infections** – although selected patients who present within one week of the acute onset of symptoms can be managed with the same regimen of debridement followed by intravenous antibiotics, the majority of such patients will not be cured unless the prosthesis is removed.

Both a one-stage and two-stage replacement arthroplasty have been used in patients with prosthetic joint infections with two-stage replacement arthroplasty associated with the highest success rates. With the two-stage replacement arthroplasty, intravenous antibiotics or oral antibiotics with high bioavailability are usually administered for six weeks prior to replacement of the prosthetic joint and continued for minimum six weeks after replacement of the new prosthetic joint.

For those selected patients where retention of the prosthetic joint is an option, suppressive antibiotic therapy should be given for months to even years.

The selection of the specific antimicrobial regimens depends upon the infecting organism and is therefore critically dependent upon definitive microbiological diagnosis and in-vitro antimicrobial susceptibility.

TREATMENT OF PROSTHETIC JOINT INFECTIONS

METHICILLIN-SUSCEPTIBLE STAPHYLOCOCCI

Cloxacillin 2 g IV 6 hourly

OR

Cefazolin 2 g IV 8 hourly

OR

Ceftriaxone 1–2 g IV given daily

METHICILLIN-RESISTANT STAPHYLOCOCCI

Vancomycin 30 mg/kg/day IV in 2 divided doses (check levels and dose accordingly)

OR

Linezolid 600 mg IV/PO 12 hourly (children 10 mg/kg IV/PO 8 hourly)

OR

Daptomycin 6 mg/kg IV given daily

Combination therapy with rifampicin (300 mg orally twice daily or 600 mg once daily) is used in the setting of staphylococcal PJI treated with debridement and retention of the prosthesis and/or in the setting of one-stage arthroplasty.

STREPTOCOCCI

Penicillin G 20 million units IV per day in 6 divided doses or as a continuous infusion

OR

Ceftriaxone 2 g IV given daily

ENTEROBACTERIACEAE

Ceftriaxone 2 g IV given daily

OR

Ertapenem 1 g IV given daily

PSEUDOMONAS AERUGINOSA

Cefepime 2 g IV 12 hourly

OR

Ciprofloxacin 750 mg PO 12 hourly or 400 mg IV 8 hourly

OR

Ceftazidime 2 g IV 8 hourly

ENTEROCOCCUS SPECIES (PENICILLIN-SUSCEPTIBLE)

Penicillin G 20 million units IV per day in 6 divided doses or as a continuous infusion

OR

Ampicillin 12 g IV per day in 6 divided doses or as a continuous infusion

ENTEROCOCCUS SPECIES (PENICILLIN-RESISTANT)

Vancomycin 30 mg/kg/day IV in 2 divided doses (check levels and dose accordingly)

OR

Linezolid 600 mg IV/PO 12 hourly

CULTURE-NEGATIVE PROSTHETIC JOINT INFECTION

Vancomycin 30 mg/kg/day IV in 2 divided doses (check levels and dose accordingly) **AND** ciprofloxacin 750 mg PO 12 hourly or 400 mg IV 8 hourly

OR

Linezolid 600 mg IV/PO 12 hourly **AND** ciprofloxacin 750 mg PO 12 hourly or 400 mg IV 8 hourly

OR

Daptomycin 6 mg/kg IV given daily **AND** ciprofloxacin 750 mg PO 12 hourly or 400 mg IV 8 hourly

NOTE

The oral agents that may be used for suppressive therapy where replacement arthroplasty is not possible should ideally be based on in vitro susceptibilities:

For staphylococci: cephalexin 500 mg 6 hourly or cloxacillin 500 mg 6 hourly PO

For Gram-negatives: ciprofloxacin 500 mg 12 hourly PO

Suppressive therapy combinations with rifampicin are generally not recommended.

SEPTIC BURSITIS

Septic bursitis is inflammation of a bursa that is due to infection. It is almost always due to Staphylococcus aureus. Streptococci are the next most commonly reported cause. It should be treated by aspiration of the bursa and antibiotic therapy. Mild cases can by treated orally and more severe infections intravenously for two to three weeks.

METHICILLIN-SUSCEPTIBLE STAPHYLOCOCCI

Cloxacillin 2 g IV 6 hourly (500 mg PO 6 hourly)

METHICILLIN-RESISTANT STAPHYLOCOCCI

Vancomycin 30 mg/kg/day IV in 2 divided doses (check levels and dose accordingly)

OR

Linezolid 600 mg IV/PO 12 hourly