Osteomyelitis

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Author
Charalampos Zalavras, MD, PhD, FACS

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1. Prevention

Institute preventive measures in patients at risk for osteomyelitis.

1.1 Inform all patients with diabetes or peripheral vascular disease about proper foot care. 

Recommendations
- Stress the importance of meticulous attention to foot care and proper management of minor foot injuries.
- Tell patients to perform daily foot inspection.
- Advise a yearly foot exam by a health care provider.
- Recommend gentle cleansing with soap and water followed by application of topical moisturizers.
- Suggest custom-made footwear to accommodate a foot deformity.

Evidence
- A 2013 Cochrane review of pressure-relieving interventions to treat diabetic foot ulcers included 14 trials with 709 participants. Seven studies comparing nonremovable casts to removal devices to relieve pressure found more healed ulcers in patients receiving nonremovable casts (RR, 1.17 [CI, 1.01 to 1.36]) (1).
- A 2008 systematic review of footwear and offloading interventions to prevent and heal diabetic foot ulcers included 21 controlled and 108 uncontrolled studies and found little evidence that footwear or interventions can prevent diabetic foot ulcers (2).
- A randomized trial compared multidisciplinary care plus education to education alone in 145 patients with a history of diabetic foot ulcers. After 2 years of follow-up fewer patients in the multidisciplinary group had recurrent foot ulcers (30.4% vs. 58.4%, P<0.001) (3).

Rationale
- Neuropathy may prevent normal pain stimuli that would alert patients to trauma.
- Ulcers of the lower extremities are often secondary to minor abnormalities, which are preventable.
- Untreated lower extremity ulcers can progress to osteomyelitis.

1.2 Consider antimicrobial prophylaxis before invasive dental procedures in select patients with hip or knee arthroplasty. 

Recommendations
- Do not routinely give antimicrobial prophylaxis to patients who have had hip or knee arthroplasty.
- Consider antimicrobial prophylaxis patients with joint replacement within the last 2 years or a prior prosthetic joint infection who undergo high-risk dental procedures, such as:
  - Dental extraction
  - Periodontal procedures
  - Dental implants
  - Reimplantation of avulsed teeth
  - Root canal or surgery only beyond the apex
  - Initial placement of orthodontic bands
  - Intraligamentary local anesthetic
  - Prophylactic cleaning when bleeding is anticipated
- In patients receiving antibiotic prophylaxis for dental work, administer a single antibiotic dose within 60 minutes of the procedure:
  - In patients not allergic to penicillin, use amoxicillin, cephalexin, or cephradine, 2 g orally
In patients not allergic to penicillin and unable to take oral medication, use ampicillin, 2 g, or cefazolin, 1 g, intramuscularly or intravenously.

In patients allergic to penicillin, use clindamycin, 600 mg orally.

In patients allergic to penicillin and unable to take oral medication, use clindamycin, 600 mg intravenously.

Recognize that there is no evidence to suggest that patients with an orthopedic implant other than a total joint arthroplasty should receive antimicrobial prophylaxis before dental work.

**Evidence**

A case-control study compared 339 patients with total hip or knee infection to 339 control patients with arthroplasty but without joint infection. Antibiotic prophylaxis in high-risk dental procedures did not decrease the risk for subsequent total hip or knee infection (adjusted OR, 0.9 [CI, 0.5 to 1.6]) (4).

A 2012 guideline from the American Academy of Orthopaedic Surgeons and the American Dental Association recommended that clinicians consider not prescribing antibiotic prophylaxis for patients with prosthetic joints who undergo dental procedures (5).

**Rationale**

Bacteremia can occur following dental and other invasive procedures; antimicrobials can prevent transient bacteremia.

Most prosthetic joint infection is due to microorganisms that are not the normal flora of the oral cavity.

Antimicrobial prophylaxis in all patients with a total joint arthroplasty may be associated with increased cost and antimicrobial resistance.

**Comments**

There is no evidence to demonstrate a direct link between bacteremia due to dental procedures and prosthetic joint infection.

### 1.3 Administer antimicrobial prophylaxis in patients undergoing general orthopedic surgery, particularly arthroplasty.

**Recommendations**

- Consider prophylactic antibiotics directed against staphylococci and streptococci, such as penicillinase-resistant penicillins or first- or second-generation cephalosporins.
- Use antimicrobials with anaerobic activity, such as cefoxitin, for surgical prophylaxis in patients with lower-extremity ischemia.
- Administer the first dose of antimicrobial upon induction of anesthesia and within 1 hour before incision.
- In patients with type 1 hypersensitivity to a β-lactam (cephalosporins or penicillins), consider vancomycin as an alternative.
- Do not continue antimicrobial therapy for more than 24 hours after an operative procedure.
- In patients with prolonged surgical procedures, provide additional intraoperative dosing every one to two half-lives of the antimicrobial used.

**Evidence**

- A 2004 advisory statement from the National Surgical Infection Prevention Project recommended antibiotic prophylaxis for arthroplasty with cefazolin or cefuroxime in patients without penicillin allergy, and with vancomycin or clindamycin in patients with penicillin allergy (6).
- A randomized trial compared cefazolin to placebo in 2097 patients undergoing total hip replacement. The cefazolin group had fewer postoperative hip infections than the placebo group (0.9% vs. 3.3%, P<0.001) (7).
- In a randomized, placebo-controlled trial using cefoxitin vs. placebo for surgical prophylaxis in patients undergoing amputation of the lower extremity, the incidence of wound infection was significantly lower in the cefoxitin arm when compared to placebo (38.7% vs. 16.9%) (8).
Rationale

- Antimicrobials used for prophylaxis should have activity against staphylococci and streptococci, because they are the most common organisms to cause foreign body-associated osteomyelitis.
- Prolonged prophylaxis for more than 24 hours does not improve efficacy and may increase toxicity and microbial resistance.
- Antimicrobials with anaerobic activity may provide better anaerobic coverage in patients with ischemia.

1.4 Administer antimicrobial prophylaxis and perform surgical debridement in patients with open fractures.

Recommendations

- Always perform thorough debridement with removal of foreign material, excision of nonviable tissue, and low pressure irrigation of the open fracture wound.
- Start a broad-spectrum antimicrobial regimen with activity against staphylococci, streptococci, gram-negative bacilli, and anaerobes (if ischemia or contamination with soil is present) as soon as possible following the trauma.
- Consider the use of local antibiotic polymethylacrylate beads in open fractures with soft tissue defects, bone defects, or severe contamination.
- Continue antimicrobial prophylaxis typically for 3 days, although the optimal duration of therapy is unknown.
- Reconstruct the soft tissue envelope when a soft tissue defect is present.

Evidence

- Two randomized trials found that the use of prophylactic antimicrobials in patients with open fractures reduced the rate of posttraumatic osteomyelitis when compared to placebo (9; 10).
- In a study involving 1102 open fractures, the infection rate was 24% in patients receiving no prophylactic antibiotics, whereas the infection rate was 4.5% in the patients receiving prophylactic antibiotics (11).
- In a study of 70 patients with open fractures, the degree of bacterial contamination of the wound during surgical debridement of patients with open fracture strongly correlated with subsequent infection (12).
- A randomized, controlled trial found that among 89 patients with open fractures who completed the 1-year follow-up, the reoperation rate for complications was 28% in the high-pressure pulsatile lavage group and 19% in the low-pressure group (P=0.17) (13).
- In one unblinded retrospective study involving 1085 limb fractures, treatment with systemic antimicrobial therapy and adjuvant local use of aminoglycoside polymethylmethacrylate beads showed a lower incidence of infection when compared with systemic antimicrobial therapy alone (3.7% vs. 12%, P< 0.001) (14).

Rationale

- Debridement and antimicrobial prophylaxis reduce the degree of bacterial contamination, thus reducing the risk of subsequent posttraumatic osteomyelitis.
- Open fractures are usually contaminated with multiple organisms, mainly aerobic gram-negative bacilli and staphylococci.
- High-pressure pulsatile irrigation may create bone damage and propagate bacteria into soft tissues.
- Soft tissue coverage prevents secondary contamination and improves local vascularity, thereby enhancing local host defenses and delivery of antibiotics at the fracture site.
2. Diagnosis

Use clinical exam and lab and imaging studies to diagnose osteomyelitis.

2.1 Evaluate for osteomyelitis in patients with pain contiguous to a bone and drainage from a fistulous sinus tract, including patients with diabetic foot ulcers.

Recommendations

- Ask patient about:
  - Type, duration, and date of onset of pain
  - Type of discharge:
    - Purulent
    - Serous
    - Serosanguineous
  - Presence of fever or chills
  - Predisposing factors, such as:
    - Previous surgery or trauma, especially when orthopaedic implants are present
    - Diabetes
    - Rheumatoid arthritis
    - Peripheral vascular disease
    - Intravenous drug abuse
    - Long-term intravenous catheter placement
  - Prior antimicrobial use
  - Drug allergy

- Ask patients with prosthetic joints about loosening or pain.
- Ask patients with diabetes about lower extremity ulcers, neuropathy, and trauma.

Evidence

- A retrospective study of patients with osteomyelitis at a single institution found that fever was present in 20 of 21 patients with hematogenous osteomyelitis and in no patients with chronic osteomyelitis (15).
- A case-control trial compared patients with and without postoperative osteomyelitis to identify risk factors. Wound dehiscence (OR, 21.5 [CI, 2.9 to 160]) and surgical site infection (OR, 27.5 [CI, 6.7 to 112.8]) were potent risk factors for osteomyelitis in the multivariate analysis (16).
- A study of patients with *S. aureus* prosthetic joint infection following total hip or knee arthroplasty found prosthesis removal and delayed reimplantation to be an effective treatment to limit recurrence of the infection, provided there was none present at reimplantation (17).

Rationale

- Purulent discharge is more likely to be associated with some organisms, such as *Staphylococcus aureus* or β-hemolytic streptococci, than with other organisms such as coagulase-negative staphylococci and enterococci.

Comments

- Patients with acute hematogenous osteomyelitis are more likely to present with acute pain and fever than are patients with chronic contiguous osteomyelitis, though patients with chronic osteomyelitis and concomitant soft tissue infection can present with pain and fever.
• Patients who underwent a total joint arthroplasty and have had periprosthetic pain since surgery are more likely to have a periprosthetic infection than patients who had a pain-free period.
• Periprosthetic loosening in the first 2 years after arthroplasty should raise the index of suspicion for the presence of a prosthetic joint infection.

2.2 Perform a physical exam on all patients with suspected osteomyelitis.

Recommendations
• During physical exam, note:
  - Temperature
  - Presence or absence of a sinus tract
• In patients with diabetic or vascular ulcers:
  - Look for exposed bone.
  - Note ulcer size.
  - Look for erythema, edema, and drainage around the ulcer.
  - Consider performing a probe-to-bone test, in which the wound is examined with a sterile probe. The test is positive if the probe reaches a hard surface without intervening soft tissue.

Evidence
• A 2008 systematic review evaluated the accuracy of the history and physical exam for osteomyelitis in diabetic foot ulcers. No elements of the history were accurate. Exposed bone (LR, 9.2) was predictive of osteomyelitis, but the absence of exposed bone did not rule it out (LR, 0.70). Ulcer area >2 cm² (positive LR, 7.2; negative LR, 0.48) and the probe-to-bone test (summary positive LR, 6.4; negative LR, 0.39) had moderate diagnostic performance (18).
• A 2012 guideline from the Infectious Diseases Society of America for the diagnosis and treatment of diabetic foot infections recommended that clinicians assess the vascular and neurologic integrity of the foot and look for inflammation and erythema. In addition, the guideline recommended the probe-to-bone test in patients with ulcers and suspected osteomyelitis (19).

Rationale
• The presence of a sinus tract overlying a bone structure is highly associated with the presence of osteomyelitis.
• Exposed bone in the depth of a foot ulcer is almost always associated with the presence of osteomyelitis.
• Ulcer area >2 cm² and a positive probe-to-bone test are associated with osteomyelitis in patients with diabetic foot ulcers.

2.3 Characterize the osteomyelitis based on the duration of illness (acute vs. chronic), the mechanism of infection (hematogenous vs. contiguous), the affected part of the bone, the physiologic status of the host, and the presence of orthopedic hardware.

Recommendations
• Be aware of the following when characterizing osteomyelitis:
  - Hematogenous acute osteomyelitis occurs most often in children and the elderly
  - Hematogenous osteomyelitis:
    o In children frequently occurs in the metaphysis of the femur, tibia, and humerus
    o In adults often seeds the intervertebral disc space and two adjacent vertebrae
  - Contiguous focus osteomyelitis:
    o Is much more common in adults than in children
    o Is typically seen in persons over age 50 who have diabetes or severe peripheral vascular disease
Osteomyelitis

- Occurs secondary to the spread of infection from adjacent soft tissue or joints, or due to direct inoculation of microorganisms due to trauma or surgery
  - Fever and erythema is often absent in chronic and contiguous osteomyelitis

**Evidence**
- Consensus.

**Rationale**
- Medical and surgical therapies vary depending on the type of osteomyelitis.

### 2.4 Look for unusual sites of osteomyelitis after specific activities and procedures.

**Recommendations**
- Evaluate patients with:
  - Suprapubic discomfort and a wide-based, waddling gait following urogynecologic surgery for the presence of osteomyelitis of the pubic symphysis (osteitis pubis)
  - Wound healing complications, unstable sternum, and fever after thoracic surgery for the presence of sternal osteomyelitis
  - Pain, cellulitis, or drainage in the sternoclavicular area after subclavian vein catheterization for the presence of clavicular osteomyelitis
  - Sudden onset of groin pain and fever for osteomyelitis of the pubis in athletic individuals

**Evidence**
- A retrospective chart review showed that 15 of 2030 patients (0.74%) undergoing Marshall-Marketti-Krantz retropubic urethropexy developed osteitis pubis (20).
- A retrospective chart review showed that 33 of 7136 patients (0.46%) undergoing open-heart surgery developed sternal osteomyelitis (21).
- A narrative review described clavicular osteomyelitis as a well-recognized, albeit rare, complication of subclavian catheter insertion (22).

**Rationale**
- Sutures placed in the periosteum or the cartilage of the symphysis pubis along with surgical trauma after selected urogynecologic procedures might predispose to the development of osteitis pubis.
- Sternotomy as well as the use of the internal mammary artery can deprive the sternum of its vascular supply and, therefore, can lead to necrosis and infection of the sternum wound edges.
- Some athletes develop pelvic osteomyelitis following strenuous exercise, such as football or running, for unclear reasons.

### 2.5 Use lab testing, including ESR and deep cultures, to assist in the diagnosis and to identify specific organisms.

**Recommendations**
- Order ESR to aid in the diagnosis of osteomyelitis; consider CRP as an alternative test.
- Order CBC and blood cultures in patients with systemic infection, but recognize that leukocyte count is not helpful in the diagnosis.
- Obtain deep surgical cultures, if possible.
  - Ensure that cultures are incubated in anaerobic and aerobic media.
  - Consider special culturing techniques for organisms, such as fungi, mycobacteria, mycoplasma, or Brucella species, in the following situations:
    - Culture-negative cases
    - History of exposure
    - Living in an endemic area
Osteomyelitis

1. **Immunocompromised hosts**
   - Hold cultures for at least 10 days when infection with *Propionibacterium acnes* is possible (e.g., after shoulder arthroplasty).
   - Recognize that there is a poor correlation between superficial culture (e.g., sinus tract and wound drainage) and deep culture.
   - In hemodynamically stable patients without overt sepsis, hold antimicrobials until surgical cultures are obtained.
   - See table [Laboratory and Other Studies for Osteomyelitis and Periprosthetic Joint Infection](#).

2. **Evidence**
   - A 2008 systematic review evaluated the accuracy of diagnostic tests for osteomyelitis in patients with diabetic foot ulcers. At a cut-off of 70 mm/h, ESR had pooled positive LR of 11 (CI, 1.6 to 79) and negative LR of 0.34 (CI, 0.06 to 1.9). Elevated leukocyte was evaluated in only one study and had poor sensitivity. Swab culture had very poor utility, with both positive and negative LRs of 1 (18).
   - A case-control study evaluated the diagnostic accuracy of physical exam features and lab tests for osteomyelitis in patients with diabetic foot ulcers. In the multivariate analysis, the strongest predictors were ulcer depth >3 mm (adjusted OR, 13 [CI, 2.97 to 58.4]), ESR >80 mm/h (OR, 19 [CI, 1.75 to 213]), and CRP >3.2 mg/dL (OR, 23 [CI, 2.45 to 217]) (23).
   - Sinus tract cultures were compared with cultures of operative specimens from 40 patients with chronic osteomyelitis. Only 44% of the sinus tract cultures contained the operative pathogen. Isolation of *S. aureus* from sinus tracts correlated with the presence of *S. aureus* in the operative specimen (24).
   - A retrospective review of 11 patients diagnosed with *P. acnes* infection after shoulder arthroplasty found that the average number of days from collection to a positive culture was 9 (range, 8 to 10 days) (25).
   - In 2012, the Workgroup of the Musculoskeletal Infection Society published a consensus definition of periprosthetic joint infection, which required the presence of a sinus tract communicating with the prosthesis, two positive cultures from the affected prosthetic joint, or four of six minor criteria (26).
   - A 2010 guideline from the American Academy of Orthopedic Surgeons for the diagnosis of periprosthetic joint infections of the hip and knee recommended ESR and CRP testing in patients with suspected infection, with further testing done in patients in whom either test is positive (27).
   - A 2012 guideline from the Infectious Diseases Society of America for the diagnosis and treatment of diabetic foot infections recommended obtaining cultures prior to initiating antibiotic treatment (19).

3. **Rationale**
   - A low ESR or CRP level can rule out the diagnosis of osteomyelitis.
   - Antimicrobial therapy is based on the identification of the organisms and their antimicrobial sensitivities.
   - Superficial cultures obtained from drainage site are usually contaminated with skin flora.
   - Use of antimicrobials before culture is obtained reduces the sensitivity of the culture.

4. **2.6 Perform imaging, generally with radiographs and MRI, in patients with suspected osteomyelitis.**

   **Recommendations**
   - Check radiographs in patients with suspected osteomyelitis to look for bone deformities, recognizing that radiographs are not sensitive or specific for osteomyelitis.
   - Perform MRI as the next test in most patients with suspected osteomyelitis.
   - Consider nuclear imaging, including bone scans and tagged white cell scans, as alternative diagnostic tests.
   - See table [Laboratory and Other Studies for Osteomyelitis and Periprosthetic Joint Infection](#).
• See figure Plain Radiograph of Left Total Hip Arthroplasty.
• See figure Radiograph of Left Total Knee Arthroplasty.
• See figure MRI of Vertebral Osteomyelitis.
• See figure MRI of Osteomyelitis in the Foot.
• See figure MRI of Increased T2 Signal Abnormality.

Evidence

• A 2012 guideline from the Infectious Diseases Society of America for the diagnosis and treatment of diabetic foot infections recommended radiography to look for bone deformities and MRI to look for evidence of osteomyelitis (19).
• A 2008 systematic review evaluated the accuracy of diagnostic tests for osteomyelitis in patients with diabetic foot ulcers. Plain radiographs had moderate accuracy for lower extremity osteomyelitis, with positive LR of 2.3 (CI, 1.6 to 3.3) and negative LR of 0.63 (CI, 0.51 to 0.78) (18).
• A 2007 meta-analysis of the accuracy of MRI for osteomyelitis of the foot included 16 studies. Sensitivity was 90% and specificity was 82.5%. In studies comparing MRI to other modalities, MRI was found to be more accurate than bone scans, radiographs, and white blood cell studies (28).
• A 2006 meta-analysis of nuclear imaging for osteomyelitis in patients with diabetic foot infections included 50 original studies. Overall, three-phase bone scan had sensitivity of 90% and specificity of 46%; tagged white-cell scans had sensitivity of 86% and specificity of 74% to 84%, depending on the tracer used; MRI had sensitivity of 90% and specificity of 74% (29).

Rationale

• Radiographs are not sensitive or specific for osteomyelitis but they can detect other abnormalities.
• MRI is the most accurate test for osteomyelitis.

2.7 Differentiate osteomyelitis from other disorders with similar manifestations.

Recommendations

• Consider the broad differential diagnosis of osteomyelitis, which includes a variety of degenerative, inflammatory, and neoplastic diseases affecting the bone.
• Use clinical and lab evaluation to narrow the differential diagnosis:
  • Use history and physical exam to help differentiate between soft tissue infection and osteomyelitis.
  • Consider the presence of a predisposing factor to osteomyelitis.
  • Use imaging studies to help differentiate between neuropathic arthropathy and osteomyelitis in patients with diabetes.
• See table Differential Diagnosis of Osteomyelitis.

Evidence

• A study of the accuracy of diagnostic tests for osteomyelitis included 23 patients suspected of having spinal osteomyelitis. Ten were diagnosed with osteomyelitis; others were diagnosed with epidural abscess, spinal stenosis, displaced bone graft, metastasis, compression fracture, disk herniation, spondylolisthesis, nonspecific arthropathy, and sickle cell disease (38).
• Among 16 diabetic patients with a hot swollen foot who were studied prospectively, 25% had osteomyelitis. The others were diagnosed with conditions such as neuropathic fractures, and soft tissue swelling (45).

Rationale

• Neoplastic diseases, degenerative diseases, and a number of inflammatory diseases can mimic osteomyelitis.
• Accurate diagnosis is crucial in selecting therapy.
3. Consultation

Consider obtaining consultation with appropriate specialists when the diagnosis of osteomyelitis is unclear. Consider consultation for management in all patients with osteomyelitis.

3.1 Consider consulting an infectious disease specialist, vascular surgeon, or orthopedic surgeon when there is diagnostic uncertainty, a need for bone biopsy, or ischemia.

Recommendations
- Consider referral to:
  - A vascular surgeon in diabetic foot osteomyelitis or osteomyelitis with decreased peripheral pulses for vascular Doppler, transcutaneous oxygen tension, blood pressure measurements in the lower extremities, and angiography as needed
  - An orthopedic surgeon when considering a diagnostic bone biopsy or surgical exploration
  - An infectious disease specialist to help guide appropriate testing, including microbiologic culture data, and antibiotic selection
  - A radiologist to help interpret the imaging data and to perform a diagnostic aspiration

Evidence
- Consensus.

Rationale
- Bone biopsy cultures and pathology are considered the gold standard for the diagnosis of osteomyelitis.
- Prompt revascularization by a vascular surgeon will improve oxygen tissue tension and optimize the delivery of systemic antimicrobials to infected tissue and bone.
- Special surgical expertise is needed for a thorough debridement of all necrotic tissue and the removal of all infected hardware and cement.
- Special knowledge in antimicrobial regimens and proper interpretation of microbiologic data are crucial for a successful outcome in patients with osteomyelitis.
- Special expertise by interventional radiology is needed in order to maximize the outcome of diagnostic and therapeutic aspirations and drainage of associated abscesses.

3.2 Obtain consultation with an orthopedic surgeon, an infectious disease specialist, and other appropriate specialists for help in the medical and surgical management of patients.

Recommendations
- Obtain orthopedic surgery consultation for:
  - Implant-related osteomyelitis
  - Chronic osteomyelitis
  - Recurrent osteomyelitis
  - Complicated vertebral osteomyelitis
  - Diabetic foot osteomyelitis
- Obtain infectious diseases consultation for:
  - Implant-related osteomyelitis
  - Chronic osteomyelitis
  - Recurrent osteomyelitis
Osteomyelitis

- Diabetic foot osteomyelitis
- Osteomyelitis associated with multidrug-resistant organisms
- Nonbacterial osteomyelitis
- Patients with multiple drug allergies

- Obtain vascular surgery consultation in diabetic foot osteomyelitis and in osteomyelitis associated with peripheral vascular disease, because revascularization may be needed.
- Obtain a plastic surgery consultation for soft tissue coverage.
- Obtain a cardiothoracic surgery consultation in sternal osteomyelitis following median sternotomy.

Evidence
- Consensus.

Rationale
- Because several aspects of the medical and surgical treatment of osteomyelitis are not based on randomized clinical trials, the personal expertise of an infectious diseases specialist and an orthopedic surgeon can be valuable.
- Complete surgical debridement and removal of all infected hardware is dependent on the experience of the orthopedic surgeon.
- Patients with recurrent infections might need more aggressive surgical debridement, prolonged antimicrobial therapy, and a search for unusual or fastidious microorganisms.

Comments
- Patients with orthopedic implant-related osteomyelitis should be managed on a case-by-case scenario, weighing the high risk for recurrence against the functional outcome if the implant were to be removed.
- A neurosurgical consultation can be obtained in place of or in addition to orthopedic consultation for spine-related infections.
4. Hospitalization

Hospitalize most patients with osteomyelitis.  

4.1 Hospitalize most patients with osteomyelitis for initial therapy.  

**Recommendations**

- Hospitalize patients when:
  - Surgical intervention is planned, such as extensive debridement, bone excision for culture, resection of foreign bodies, soft tissue coverage, and bone grafting
  - Patients have systemic signs and symptoms of sepsis syndrome associated with osteomyelitis
  - There is associated soft tissue infection such as cellulitis or abscess
  - The physician is planning to initiate parenteral antimicrobial therapy

**Evidence**

- A 1997 guideline from the Infectious Diseases Society of America recommended that parenteral antimicrobial therapy be initiated in a controlled setting, preferably an inpatient setting, to carefully monitor for the occurrence of serious side effects (immediate hypersensitivity to a β-lactam) (48).
- A 2012 guideline from the Infectious Diseases Society of America for the diagnosis and treatment of diabetic foot infections recommended hospitalization for patients with severe infection, those who are worsening despite outpatient therapy, and those with complicating features such as peripheral arterial disease or unstable home situation (19).

**Rationale**

- Patients undergoing surgical debridement require inpatient management of postoperative anesthesia, pain, and immobility.
- Patients with local soft tissue infection, fever, or chills could be bacteremic and should be hospitalized for prompt initiation of antimicrobial therapy.
- Initiation of parenteral antimicrobial therapy should be done in a controlled setting, preferably an inpatient setting, to carefully monitor for the occurrence of serious side effects.
5. Therapy

Consider antimicrobial therapy and surgery to be the mainstays of treatment for osteomyelitis.

5.1 Perform surgical debridement in patients with chronic osteomyelitis, orthopedic implant-associated osteomyelitis, and ulcer-related osteomyelitis.

Recommendations

- Perform complete drainage and debridement of all necrotic soft tissue and bone resection of dead and infected bone.
- Remove foreign bodies from infected areas when technically possible.
- Provide adequate soft tissue coverage.
- Restore effective blood supply by surgical or percutaneous transvascular angioplasty.
- When debridement, stable reconstructive surgery, or revascularization cannot be successfully accomplished, consider other options such as limb amputation or the use of chronic antimicrobial suppression.

Evidence

- A 2010 Cochrane review of debridement of diabetic foot ulcers included six randomized trials. Surgical debridement was equivalent to standard treatment and hydrogels were not superior to standard wound care (49).
- A 2012 systematic review of surgical treatment of infected hip arthroplasty included 62 trials with 4197 patients. Rates of reinfection after 1-stage or 2-stage revision were similar (8.6% to 10.1%) (50).
- A 2012 guideline from the Infectious Diseases Society of America for the diagnosis and treatment of diabetic foot infections recommended either a primary surgical (i.e., debridement) or primary medical (i.e., antibiotics) therapeutic strategy (19).

Rationale

- Debridement reduces the bacterial load, removes dead tissue and foreign bodies, and allows for a more thorough exam of the wound for the presence of underlying infection.
- Failure to remove an infected orthopedic implant would allow the offending microorganisms to form a biofilm and therefore escape the effect of antimicrobials.
- Soft tissue coverage performed by a plastic surgeon provides wound protection, prevents secondary contamination, allows revascularization of the affected site, and promotes bone healing.
- Revascularization is extremely important to allow adequate oxygenation to soft tissue and bone in order to allow healthy healing. In addition, this would allow antimicrobial delivery and access of host humoral response to the infected area.

Comments

- There is an increased risk for squamous cell carcinoma at the sinus tract site in patients with longstanding untreated chronic draining sinus due to an underlying osteomyelitis.
- The risk for systemic amyloidosis is increased in patients with longstanding untreated chronic osteomyelitis.

5.2 Treat patients with osteomyelitis with antibiotics, targeting the documented or likely infecting agent.

Recommendations

- Use effective antimicrobial therapy for 4 to 6 weeks in patients with osteomyelitis following appropriate surgical debridement.
In patients with chronic osteomyelitis and without acute soft tissue infection or sepsis syndrome, withhold antimicrobial therapy until deep bone cultures have been obtained.

For patients with osteomyelitis associated with diabetic foot ulcers:

- Target therapy based on antimicrobial sensitivity of cultured organisms.
- Include coverage of *S. aureus* if choosing empiric therapy.
- Cover MRSA empirically in patients with a history of MRSA infection, MRSA colonization in the last year, severe infection, or if the local prevalence of MRSA is high.
- For patients without suspected MRSA, consider empiric treatment with ampicillin-sulbactam, cefoxitin, ceftriaxone, moxifloxacin, or others.
- For patients with suspected MRSA, treat empirically with vancomycin, considering linezolid and daptomycin as alternative therapies.

In patients already receiving antimicrobial therapy, withhold antimicrobials for at least 1 to 2 weeks before surgical debridement and culture ascertainment.

See table Drug Treatment for Osteomyelitis.

See table Drug Treatment for Osteomyelitis Caused by Unusual Organisms.

**Evidence**

- A 2012 guideline from the Infectious Diseases Society of America for the diagnosis and treatment of diabetic foot infections recommended a variety of possible antibiotics. The guideline recommended at least 4 weeks of antibiotic therapy for osteomyelitis associated with diabetic foot ulcers, though in patients who receive curative surgery with no residual infected material, the guideline recommended only 2 to 5 days of antibiotic therapy (19).
- A 2010 narrative review of MRSA in diabetic foot infections noted that the rate of MRSA infection among patients with diabetic foot ulcers ranged from 15% to 30%, with higher rates among patients with frequent hospitalizations, chronic ulcers, and possibly osteomyelitis (51).
- A randomized, double-blind, placebo-controlled trial compared the efficacy of long-term quinolone with rifampin vs. quinolone alone in the treatment of patients with orthopedic implant-related infection treated with debridement and retention of the hardware. Combination therapy was superior to therapy with quinolone alone (52).
- A randomized, controlled trial showed that outcomes were comparable among patients with *S. aureus* chronic osteomyelitis receiving oral rifampin-cotrimoxazole vs. intravenous cloxacillin. Retention of implants was significantly associated with recurrence of infection (53).
- A 2005 systematic review of antibiotic treatment of osteomyelitis included 93 noncomparative and comparative clinical trials in both children and adults. Patients identified as having prosthetic joint infections or infected hardware or implants were excluded. Studies involved a variety of antibiotics; most found that the compared regimens were equivalent. In the preponderance of studies, patients with acute osteomyelitis had a higher cure rate than patients with chronic infection. The optimal duration of therapy remains uncertain, but most investigators treated patients for 6 weeks. Investigators treated chronic osteomyelitis for 20 days to 6 months (54).

**Rationale**

- Antimicrobial therapy is directed against microfoci of osteomyelitis that are left behind after surgical debridement and at distant metastatic foci of infection.
- Antimicrobials should be used for 4 to 6 weeks in order to allow the debrided bone to be covered by vascularized soft tissue.

**Comments**

- The available literature is inadequate to determine the best antibiotics, route, or duration of treatment. Unless the antimicrobial sensitivities of the causative organisms dictate otherwise, the choice of antibiotics should be based on safety, cost, and practicality.

**5.3 Consider antimicrobial therapy alone in patients with an uncomplicated acute hematogenous osteomyelitis.**
**Recommendations**

- Recognize that in prepubertal children, hematogenous osteomyelitis is usually located in the metaphyseal area of long bones and is best treated with parenteral antimicrobial directed against *S. aureus* or streptococci.
  - Continue therapy for the acute hematogenous osteomyelitis of the long bones in children for 3 to 4 weeks.
  - After 7 to 10 days of intravenous antimicrobial therapy, consider switching to an oral agent for the remaining 2 to 3 weeks.
- Consider surgical intervention when there is:
  - Involvement of the femoral head
  - Failure to make a specific microbiologic diagnosis with noninvasive techniques
  - Neurologic complication
  - Sequestra and failure to improve while on appropriate antimicrobial therapy
- Treat adult patients with uncomplicated acute hematogenous vertebral osteomyelitis with 4 to 6 weeks of effective antimicrobial therapy.
- See table [Drug Treatment for Osteomyelitis](#).

**Evidence**

- Treatment with parenteral antimicrobial therapy followed by an early switch to an oral agent was successful in 100% of 116 children diagnosed with acute osteomyelitis ([55](#)).
- A case series of patients with uncomplicated adult vertebral osteomyelitis found that the urinary tract was the most common source of infection ([56](#)).
- A 10-year retrospective study of patients with vertebral osteomyelitis observed that patients who received 6 weeks of antibiotic therapy had similar outcomes to patients receiving longer courses ([57](#)).
- A randomized, controlled trial compared 20 days to 30 days of antimicrobial therapy in children with acute hematogenous osteomyelitis and found similar outcomes in the two groups ([58](#)).
- Treatment with short- or long-term intravenous antibiotics after surgical drainage of acute hematogenous bone or joint infection in children showed similar results in both groups, with the added benefit of a shorter hospital stay for children with blood-borne musculoskeletal infection ([59](#)).
- A retrospective study of 1969 children with acute osteomyelitis treated at 29 hospitals showed that early transition to oral therapy was not associated with a higher risk for treatment failure (4% vs. 5% for prolonged intravenous therapy). Readmissions for antibiotic-related complications were significantly higher among the patients receiving prolonged intravenous therapy (1.6% vs. 0.4%, *P*=0.005), 3% of whom were readmitted for a catheter complication ([60](#)).
- A prospective study compiled the results of compassionate use of linezolid in 55 patients, but only 22 were available for long-term follow-up, which averaged 195 days. The clinical cure rate in these 22 patients was 82% ([61](#)).
- A retrospective review of 20 consecutive patients with orthopedic infections caused by gram-positive cocci treated with linezolid observed a 55% clinical cure rate with an average follow-up of 276 days. All of these patients underwent surgical debridement, but only 10 of the 15 patients with orthopedic hardware had their hardware removed ([62](#)).
- A retrospective review of 22 patients with chronic implant-related osteomyelitis, treated with linezolid and surgical debridement with implant removal in all cases, reported no recurrence of infection in the 14 patients who were followed for a mean time of 22 months ([63](#)).

**Rationale**

- The metaphyseal area of long bones in prepubertal children and vertebral bodies are highly vascularized and antimicrobial therapy alone is effective in curing this disease.

**Comments**
Vancomycin therapy for MRSA bacteremia may not prevent the development of hematogenous vertebral osteomyelitis, and vancomycin monotherapy may not prevent the progression of MRSA vertebral osteomyelitis (64).

5.4 **Adjust the duration of antimicrobial therapy in implant-related osteomyelitis according to the surgical therapeutic modality.**

**Recommendations**

- In most cases, attempt removal of all infected implants and debridement of infected bone followed by 4 to 6 weeks of effective antimicrobial therapy based on the results of deep cultures and in vitro antimicrobial sensitivity data.
- If removal of implants is not possible due to mechanical instability or contraindications to surgery, follow parenteral antimicrobial therapy with prolonged suppression using an oral antimicrobial agent with low toxicity profile.
- If removal of implants is not possible in patients susceptible to staphylococcal infections, consider an antimicrobial regimen using rifampin along with another antistaphylococcal agent for 3 to 6 months.
- In patients with acute periprosthetic joint infections (less than 1 month of symptom duration), consider debridement, polyethylene exchange, and retention of the components, followed by combined quinolone and rifampin therapy for 3 to 6 months.
- In patients with acute infections following fracture fixation, consider debridement with retention of the implants if the implants are providing stability of the fracture. Remove the implants and perform debridement when the fracture is healed.
- See table Drug Treatment for Osteomyelitis.

**Evidence**

- A randomized, double-blind, placebo-controlled trial compared the efficacy of quinolones with rifampin vs. quinolone alone in the treatment of patients with orthopedic implant-related infection and found that combination therapy was superior to therapy with quinolone alone in susceptible staphylococcal infections (52).
- A retrospective study showed that when early deep infections after internal fixation of a fracture were treated with debridement, antibiotic suppression, and retention of hardware, fracture union occurred in 71% of cases (65).

**Rationale**

- Microorganisms attached to foreign bodies are often resistant to antimicrobials.
- Antimicrobial therapy is directed against microfoci of osteomyelitis that are left behind after surgical debridement and at distant metastatic foci of infection.
- Fractures may heal in the presence of infection provided there is stability at the fracture site.

5.5 **Consider using local antimicrobial delivery devices such as antibiotic-impregnated polymethylmethacrylate spacers and beads to reduce the risk of recurrence.**

**Recommendations**

- Consider using vancomycin and/or aminoglycoside-impregnated cement spacers and beads during surgical debridement (local delivery of antimicrobials).
- Use local antimicrobial delivery devices, such as cement spacers and beads, to reduce the risk for recurrence in patients with implant-associated osteomyelitis or chronic recurrent osteomyelitis.
- Do not add vancomycin or gentamicin to polymethylmethacrylate in infections due to vancomycin-resistant enterococci, candida, and multidrug-resistant Enterobacteriaceae.
- See figure Plain Radiograph Showing Antimicrobial-Containing Spacer Material.
- See table Drug Treatment for Osteomyelitis.

**Evidence**
• A prospective, single-blind, randomized study evaluated the role of antibiotic-impregnated cement in the prevention of deep infection at primary total knee arthroplasty in patients with diabetes mellitus. No patient randomly assigned to cefuroxime-impregnated cement had infections, compared with 13.5% in the control group (66).
• In one study, none of the patients with a total knee arthroplasty infection treated with an insertion of a prosthesis using antibiotic-impregnated bone cement developed recurrent infection (67).
• A prospective, randomized clinical trial compared use of bioabsorbable tobramycin-impregnated calcium sulfate with standard antibiotic-impregnated cement beads in the treatment of chronic osteomyelitis and infected nonunion and found that the cure rate was the same (86%) between the two groups (68).

Rationale
• Most microorganisms causing osteomyelitis are sensitive to a combination of vancomycin and aminoglycoside.
• Antimicrobial delivery devices can deliver high local levels of antimicrobials well above those achieved with parenteral therapy.
• Antibiotic-impregnated bioabsorbable bone substitutes may be an alternative to antibiotic-impregnated cement.

Comments
• When microbiology is known preoperatively, antimicrobials in cement can be tailored to culture results.
• When antimicrobials are used in high dosages locally, systemic absorption may occur, resulting in systemic adverse events. These adverse events may be more pronounced in elderly patients with renal impairment.
• There are insufficient data to guide the use of other antimicrobials in patients with infections due to vancomycin-resistant enterococci, candida, and multidrug-resistant Enterobacteriaceae.

5.6 Consider hyperbaric oxygen therapy as an adjunctive measure for patients with chronic refractory osteomyelitis.

Recommendations
• Reserve hyperbaric oxygen as an adjunctive therapy in patients with recurrent posttraumatic or chronic osteomyelitis.
• Administer hyperbaric oxygen once daily for 90 to 120 minutes at two to three atmospheres at 100% oxygen tension for 15 to 20 separate sessions.

Evidence
• A 2012 guideline from the Infectious Diseases Society of America for the diagnosis and treatment of diabetic foot infections did not recommend hyperbaric oxygen therapy (19).
• A case series of 13 patients with refractory osteomyelitis treated with hyperbaric oxygen observed cure of infection in 12 of the patients (69).
• A retrospective, nonrandomized study of 115 patients with diabetic foot ulcers with and without osteomyelitis found that hyperbaric oxygen therapy decreased the rate of major amputations (70).

Rationale
• Hyperbaric oxygen increases the oxygen tension in infected tissue, including bone.
• Hyperbaric oxygen has a direct bactericidal or bacteriostatic effect on anaerobic organisms.

Comments
• Hyperbaric oxygen therapy is only available in selected centers in the United States.
6. Patient Education

Inform patients about the natural history of osteomyelitis and its management.

6.1 Discuss with patients the pathophysiology, symptoms, therapeutic modalities, and outcome of osteomyelitis.

Recommendations
• Explain to patients the distinction between hematogenous osteomyelitis, implant-related osteomyelitis, and contiguous osteomyelitis.
• Advise patients that pain, drainage, or fever could be associated with recurrence of the disease and should be reported promptly to a health care provider.
• Discuss surgical, medical, and adjunctive measures, and decide on the optimal therapeutic strategy.

Evidence
• Consensus.

Rationale
• Informed patients are better able to make decisions regarding treatment with consideration of medical facts and other psychosocial factors.

6.2 Inform patients about the possible side effects of antimicrobial therapy and how to maintain venous access.

Recommendations
• Explain to patients the well-recognized side effects associated with certain antimicrobial agents:
  • Ototoxicity or nephrotoxicity with aminoglycoside and vancomycin therapy
  • Diarrhea, including *Clostridium difficile* diarrhea, with β-lactams and clindamycin
  • Rash with β-lactams
  • Leukopenia, thrombocytopenia, and eosinophilia with β-lactam antimicrobials
• Teach patients the proper maintenance of the venous access line and the administration of antibiotics:
  • Carefully examine the venous access site every 3 to 4 days
  • Change the dressing overlying the insertion site of the venous access weekly

Evidence
• A retrospective review of patients on home intravenous antibiotic therapy noted that 8% required rehospitalization due to therapy-related complications. Toxicities included leukopenia (16%), thrombocytopenia (4%), nephrotoxicity (8%), diarrhea (7%), and rash (4%) [71].

Rationale
• Early recognition of side effects by a patient might lead to early intervention and therefore the avoidance of more serious side effects.
• Poor maintenance of access line can predispose to the failure of function as well as infection of the access device.
7. Follow-up

Schedule follow-up to monitor for drug-related toxicity, vascular access complications, and disease recurrence.

7.1 Use clinical and lab data selectively in follow-up of patients with osteomyelitis.

Recommendations

- See patients every week if they are receiving parenteral antibiotics, and every several weeks if they are receiving oral antibiotic therapy.
- Ask patients about:
  - Persistent pain at the osteomyelitis site
  - Side effects (depending on drug used), and adjust therapy
  - Fevers or other signs of systemic illness
- Closely monitor the surgical incision for drainage, hematoma, and superficial surgical site infection.
- In patients on long-term parenteral antibiotics, examine the venous access site and device for local tenderness, phlebitis, infiltration, erythema, or purulence at the exit site on a regular basis (every 3 to 4 days).
- Monitor the leukocyte count in patients in whom it was initially elevated.
- Check ESR or CRP after 1 month of follow-up in patients with chronic or vertebral osteomyelitis in whom values were initially abnormal.
- Monitor drug levels when using potentially toxic agents, such as vancomycin or an aminoglycoside, at the onset of therapy and at intervals thereafter according to renal function and dosage adjustments; in stable patients without dosage changes, antimicrobial levels need not be determined more frequently than weekly.
- Consider checking serum bactericidal levels in difficult cases or when switching to oral therapy.
- Do not routinely obtain imaging studies in follow-up of patients appropriately treated for osteomyelitis.
- When there is no response to drug therapy, consider need for debridement, removal of foreign bodies, or revascularization.

Evidence

- A study showed that a decrease of >50% in the ESR within the first month was rarely associated with treatment failure in patients with vertebral osteomyelitis (72).
- Sixty-three children with acute hematogenous osteomyelitis were followed with serial CRP measurements. Patients with persistently elevated CRP levels beyond the fourth day had a complicated course (73).
- Six of eight patients treated medically for pyogenic vertebral osteomyelitis showed evidence of progressive disease on an MRI performed within 6 weeks, despite obvious clinical improvement (74).

Rationale

- Persistent pain at the site of osteomyelitis after therapy may indicate persistent infection.
- An elevated temperature might reflect a persistent infection or might be related to drug fever.
- Early postoperative wound healing problems and infection have been associated with subsequent deep surgical site infections.
- Central venous catheter infection is a common complication that could be avoided by removing the catheter if local problems occur.
- Persistent elevation of ESR or CRP levels after medical and surgical therapy in patients with chronic or vertebral osteomyelitis could reflect the presence of a persistent focus of infection.
- Optimal serum antimicrobial levels may maximize efficacy and minimize toxicity.
Osteomyelitis

Comments

- A decrease of more than 50% in the ESR is rarely associated with treatment failure in patients with vertebral osteomyelitis.
- Interpretation of imaging studies could be confusing and difficult following surgical therapy of osteomyelitis because postoperative changes could be confused with radiologic signs of disease progression. Plain radiographs help assess bone healing in infected nonunions.
- Baseline and repeat MRI, along with clinical status and inflammatory biomarkers, may be useful in predicting treatment failure and guiding further management of patients with vertebral osteomyelitis.
References


6. Bratzler DW, Houck PM; Surgical Infection Prevention Guidelines Writers Workgroup; American Academy of Orthopaedic Surgeons; American Association of Critical Care Nurses; American Association of Nurse Anesthetists; American College of Surgeons; American College of Osteopathic Surgeons; American Geriatrics Society; American Society of Anesthesiologists; American Society of Colon and Rectal Surgeons; American Society of Health-System Pharmacists; American Society of PeriAnesthesia Nurses; Ascension Health; Association for periOperative Registered Nurses; Association for Professionals in Infection Control and Epidemiology; Infectious Diseases Society of America; Medical Letter; Premier; Society for Healthcare Epidemiology of America; Society of Thoracic Surgeons; Surgical Infection Society. Antimicrobial prophylaxis for surgery: an advisory statement from the National Surgical Infection Prevention Project. Clin Infect Dis. 2004;38:1706-15. (PMID: 15227616)


Osteomyelitis


Osteomyelitis


**Glossary**

**bid**
twice daily

**CBC**
complete blood (cell) count

**CI**
confidence interval

**CRP**
C-reactive protein

**ESR**
erythrocyte sedimentation rate

**LR**
likelihood ratio

**MRI**
magnetic resonance imaging

**MRSA**
methicillin-resistant *Staphylococcus aureus*

**OR**
odds ratio

**PET**
positron emission tomography

**po**
oral

**RNA**
ribonucleic acid

**RR**
risk ratio

**tid**
three times daily
### Laboratory and Other Studies for Osteomyelitis and Periprosthetic Joint Infection

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukocyte count</td>
<td>20-26</td>
<td>96</td>
<td>Normal leukocyte count does not rule out infection (30; 31)</td>
</tr>
<tr>
<td>ESR (cutoff, 70-80 mm/h)</td>
<td>50-90</td>
<td>85-100</td>
<td>More sensitive in acute hematogenous vs. chronic osteomyelitis. Helpful to monitor response to therapy (15; 31)</td>
</tr>
<tr>
<td>CRP</td>
<td>71-96</td>
<td>92</td>
<td>More sensitive in acute hematogenous vs. chronic osteomyelitis (30). Very sensitive in periprosthetic joint infection (31)</td>
</tr>
<tr>
<td>Interleukin-6</td>
<td>97</td>
<td>91</td>
<td>Appears accurate in the setting of prosthetic joint infection (32)</td>
</tr>
<tr>
<td>Sinus tract culture</td>
<td>44</td>
<td></td>
<td>Correlation between sinus tract cultures and surgical cultures is high for <em>S. aureus</em> (80% sensitivity) but poor for other microorganisms (24)</td>
</tr>
<tr>
<td>Blood cultures</td>
<td>10-26</td>
<td></td>
<td>Should be done in patients with associated fever or systemic signs of sepsis. Less sensitive in chronic or implant-associated osteomyelitis (15; 33). Infectious endocarditis may be associated with spontaneous pyogenic vertebral osteomyelitis (34)</td>
</tr>
<tr>
<td>Plain bone X-ray</td>
<td>62</td>
<td>64</td>
<td>May be negative early in the disease; early findings include soft tissue swelling and subperiosteal elevation. Lytic lesions typically do not appear for 2-6 weeks. Sclerotic changes with periosteal new bone formation suggest chronic infection. Should be done in all patients (15; 35)</td>
</tr>
<tr>
<td>MRI</td>
<td>90-98</td>
<td>74-88</td>
<td>Considered the preferred imaging modality for pediatric osteomyelitis (36) and is diagnostically useful even after recent intervention (37). Contraindicated with selected hardware</td>
</tr>
<tr>
<td>99mTc methylene diphosphonate scan</td>
<td>69-100</td>
<td>38-82</td>
<td>May be helpful early in the course of the disease, but specificity is low (bone tumor, neuropathic arthropathy, surgery) (38; 39)</td>
</tr>
<tr>
<td>Fluorodeoxyglucose PET</td>
<td>88-99</td>
<td>81-95</td>
<td>PET has high diagnostic accuracy for chronic osteomyelitis (40) and periprosthetic infection (41)</td>
</tr>
</tbody>
</table>
### Gallium citrate GA67 scan

|   |   |   | Often combined with a technetium scan to increase accuracy. More sensitive than technetium scan in patients with disc space infection (38; 39) |

### ¹¹¹In-labeled white cell scan

|   |   |   | Sensitivity and specificity are increased with a technetium scan. Cannot differentiate between septic and aseptic loosening of total joint arthroplasty |

### Percutaneous bone biopsy and cultures

|   |   |   | Not as invasive as an open biopsy (42; 43). Mainly used in disc space infection or diabetic foot infection. Lower sensitivity with previous antibiotic treatment (44) |

### Surgical bone biopsy and cultures

|   |   |   | Considered the gold standard for diagnosing osteomyelitis; usually obtained before or during surgical debridement. Specimens must be sent for cultures and histopathology |

---

CRP = C-reactive protein; ESR = erythrocyte sedimentation rate; MRI = magnetic resonance imaging; PET = positron emission tomography.
## Differential Diagnosis of Osteomyelitis

<table>
<thead>
<tr>
<th>Disease</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteomyelitis</td>
<td>Appropriate clinical situation, possibly pain and fever. In the case of ulcers, visible involvement of bone, high ESR or CRP, positive probe-to-bone test. May require bone biopsy to guide therapy.</td>
</tr>
<tr>
<td>Soft tissue infection</td>
<td>Imaging studies show sparing of the bone. Probe-to-bone test is negative. Surgical exploration usually able to determine the integrity of cortical bone.</td>
</tr>
<tr>
<td>Infectious arthritis</td>
<td>Severe functional limitation and joint swelling on exam is often present. Adjacent osteomyelitis may be present if clinical signs of infection persist after surgical management of septic knee arthritis, especially in patients with comorbid conditions (46).</td>
</tr>
<tr>
<td>Ewing's sarcoma or primary bone tumors</td>
<td>Mainly occurs in children and young adults. Diagnosis often made after biopsy and microbiologic studies.</td>
</tr>
<tr>
<td>Metastatic malignancy to the bone</td>
<td>Usually associated with a primary lesion: breast, prostate, lung. Metastasis usually multifocal.</td>
</tr>
<tr>
<td>Neuropathic arthropathy in diabetes</td>
<td>Radiologic features should be suggestive. Absence of systemic signs and symptoms of infection. May be quite difficult to distinguish from infection.</td>
</tr>
<tr>
<td>Vaso-occlusive crisis in sickle cell anemia</td>
<td>A combination of sequential bone marrow and bone scintigraphy may be useful. May be difficult to distinguish from infection clinically. Vaso-occlusive crisis is more likely to affect more than one site and is less likely to present with limb swelling and a prolonged course of fever and pain (47).</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>Radiologic features should be suggestive. Absence of systemic signs and symptoms of infection. CRP level, ESR, and leukocyte count should be normal.</td>
</tr>
</tbody>
</table>

CRP = C-reactive protein; ESR = erythrocyte sedimentation rate.
### Drug Treatment for Osteomyelitis

<table>
<thead>
<tr>
<th>Drug or Drug Class</th>
<th>Dosing</th>
<th>Side Effects</th>
<th>Precautions</th>
<th>Clinical Use</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Penicillins</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ampicillin/sulbactam (Unasyn)</td>
<td>1.5-3 g IV q6hr</td>
<td>Hypersensitivity reactions, hematologic toxicity, vomiting, diarrhea</td>
<td>If CrCl&lt;30, extend dosing interval</td>
<td>Complicated infections without MRSA</td>
</tr>
<tr>
<td>Nafcillin (Nalipen)</td>
<td>0.5-2 g IV q4hr</td>
<td>Phlebitis, infrequent nephrotoxicity</td>
<td>May need to decrease dose with CKD or hepatic disease</td>
<td>MSSA, coagulase(-) staphylococci</td>
</tr>
<tr>
<td>Oxacillin (Bactocill)</td>
<td>0.5-2 g IV q4hr</td>
<td>Hepatotoxicity</td>
<td></td>
<td>MSSA, coagulase(-) staphylococci</td>
</tr>
<tr>
<td>Penicillin G (Pfizpen)</td>
<td>20 million U/24hr IV continuously or in 6 equally divided doses</td>
<td>Rash, phlebitis</td>
<td>Decrease dose with CrCl&lt;50</td>
<td>Penicillin-susceptible streptococci, enterococci</td>
</tr>
<tr>
<td><strong>Cephalosporins</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cefazolin (Kefzol, Ancef)</td>
<td>1-2 g IV q8hr</td>
<td>Hematologic toxicity, hypersensitivity reactions, nephrotoxicity, hepatotoxicity, diarrhea</td>
<td>If CrCl&lt;35, decrease dose and extend dosing interval</td>
<td>MSSA, coagulase(-) staphylococci, β-hemolytic streptococci</td>
</tr>
<tr>
<td>Ceftriaxone (Rocephin)</td>
<td>1-2 g IV or IM q24hr</td>
<td></td>
<td>Caution with severe CKD</td>
<td>Active against many Enterobacteriaceae, β-hemolytic streptococci</td>
</tr>
<tr>
<td>Cefepime (Maxipime)</td>
<td>1-2 g IV q12hr</td>
<td>Neurotoxicity</td>
<td>If CrCl&lt;60, extend dosing interval</td>
<td>P. aeruginosa, Enterobacter sp</td>
</tr>
<tr>
<td><strong>Fluoroquinolones</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ciprofloxacin (Cipro)</td>
<td>400 mg IV q12hr or 500-750 PO q12hr</td>
<td>Hypersensitivity reactions, hepatotoxicity, seizures, QT prolongation, photosensitivity, nausea, diarrhea, neuropathy</td>
<td>Tendon rupture and tendonitis, myasthenia gravis, exacerbation. Caution with: diabetes, warfarin. Ensure adequate hydration. Separate antacids, iron, dairy by 2 hr</td>
<td>Empiric treatment of gram(-) bacteria</td>
</tr>
<tr>
<td>Moxifloxacin (Avelox)</td>
<td>400 mg PO qd</td>
<td></td>
<td>Caution with hepatic disease</td>
<td>Chronic osteomyelitis</td>
</tr>
<tr>
<td><strong>Additional agents</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vancomycin (Vancocin)</td>
<td>15 mg/kg IV q12hr</td>
<td>Ototoxicity, nephrotoxicity, neutropenia, nausea, hypokalemia</td>
<td>Avoid rapid infusion (causes histamine release). Avoid extravasation. Monitor trough concentrations. In CKD, individualize dose</td>
<td>MRSA, coagulase(-) staphylococci. Goal trough serum level: 5-10 μg/ml</td>
</tr>
<tr>
<td>Linezolid (Zyvox)</td>
<td>600 mg PO or IV q12hr</td>
<td>Hematologic toxicity-particularly thrombocytopenia. Vomiting, diarrhea, seizures, hypoglycemia</td>
<td>Avoid: MAOI therapy, large amounts of foods with high tyramine content. Monitor blood pressure</td>
<td>MRSA, VRE. Alternative to vancomycin</td>
</tr>
<tr>
<td>Daptomycin (Cubicin)</td>
<td>6 mg/kg IV qd</td>
<td>Diarrhea, abdominal pain, increased CPK, eosinophilic pneumonia, ototoxicity, neuropathy, hepatotoxicity</td>
<td>If CrCl&lt;30, extend dosing interval</td>
<td>Alternative to vancomycin</td>
</tr>
<tr>
<td>Trimethoprim-sulfamethoxazole (Septra DS, Bactrim DS)</td>
<td>1 double-strength tablet (160/800 mg) q12hr</td>
<td>Hypersensitivity reactions, vomiting, hyperkalemia, CNS effects</td>
<td>Avoid with: pregnancy near term, sulfonamide sensitivity. If CrCl&lt;30,</td>
<td>Chronic osteomyelitis</td>
</tr>
<tr>
<td>Drug</td>
<td>Dose</td>
<td>Common Side Effects</td>
<td>Precautions</td>
<td>Microorganisms</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>-----------------------</td>
<td>-------------------------------------------------------------------------------------</td>
<td>-----------------------------------------------------------------------------</td>
<td>-------------------------------------------------------</td>
</tr>
<tr>
<td>Sulfamethoprim DS)</td>
<td></td>
<td>photosensitivity. Rare: hematologic toxicity, methemoglobinemia</td>
<td>decrease dose. Caution with hepatic disease. Inhibitor of CYPs 2C8 and 2C9</td>
<td></td>
</tr>
<tr>
<td>Rifampin (Rifadin, Rimactane)</td>
<td>600 mg PO qd or 300-450 mg PO bid</td>
<td>GI or CNS effects, hypersensitivity reactions, nephrotoxicity, hepatotoxicity, thrombocytopenia, menstrual disturbances, edema, orange body fluids and contact lenses, flu syndrome when taken intermittently</td>
<td>Do not exceed 8 mg/kg/day with hepatic disease. If CrCl&lt;10, decrease dose by 50%. Potent inducer of CYP3A4, inducer of other CYP isoenzymes (many drug interactions)</td>
<td>MRSA, coagulase(-) staphylococci. Always use in combination with another agent</td>
</tr>
<tr>
<td>Meropenem (Merrem)</td>
<td>1 g IV q8hr</td>
<td>Vomiting, diarrhea, constipation, injection site reactions</td>
<td>Caution with seizure disorder. Decrease dose with CrCl&lt;50</td>
<td>P. aeruginosa, Enterobacter sp</td>
</tr>
</tbody>
</table>

**Notes:**
- **bid =** twice daily;
- **CKD =** chronic kidney disease;
- **CNS =** central nervous system;
- **CPK =** creatine phosphokinase;
- **CrCl =** creatinine clearance;
- **CYP =** cytochrome P450 isoenzyme;
- **GI =** gastrointestinal;
- **IM =** intramuscular;
- **IV =** intravenous;
- **MAOI =** monoamine oxidase inhibitor;
- **MRSA =** methicillin-resistant *Staphylococcus aureus*;
- **MSSA =** methicillin-susceptible *Staphylococcus aureus*;
- **PO =** oral;
- **q12hr =** every 12 hours;
- **qd =** once daily;
- **qid =** four times daily;
- **SC =** subcutaneous;
- **tid =** three times daily;
- **VRE =** vancomycin-resistant enterococci.

PIER provides key prescribing information for practitioners but is not intended to be a source of comprehensive drug information.
### Drug Treatment for Osteomyelitis Caused by Unusual Organisms

<table>
<thead>
<tr>
<th>Organism</th>
<th>Antimicrobial Agent</th>
<th>Duration of Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Mycobacterium tuberculosis</em></td>
<td>Combination of:</td>
<td>Combination regimen for the initial 2 mo of therapy; continue isoniazid and rifampin an additional 10 mo thereafter</td>
</tr>
<tr>
<td></td>
<td>Isoniazid, rifampin, and pyrazinamide; isoniazid, rifampin, pyrazinamide, and ethambutol; or isoniazid, rifampin, pyrazinamide, and streptomycin</td>
<td></td>
</tr>
<tr>
<td>Nontuberculous mycobacteria</td>
<td>Combination of antimycobacterial agents, depending on drug susceptibility</td>
<td>6-9 mo from resolution of all symptoms</td>
</tr>
<tr>
<td><em>Candida sp</em></td>
<td>Amphotericin B, fluconazole</td>
<td>Initial course of amphotericin B for 2 to 3 weeks; then fluconazole for a total of 6 to 12 mo of therapy</td>
</tr>
<tr>
<td><em>Blastomyces dermatitidis osteomyelitis</em></td>
<td>Itraconazole</td>
<td>1 year</td>
</tr>
<tr>
<td></td>
<td>For patient whose disease progresses during treatment with an azole, or who is unable to tolerate an azole because of toxicity, consider amphotericin B as an alternative</td>
<td></td>
</tr>
<tr>
<td><em>Sporothrix schenckii</em></td>
<td>Itraconazole, amphotericin B</td>
<td>Itraconazole for 12 mo. Amphotericin B may be indicated for treating patients with extensive involvement, or for those patients for whom itraconazole therapy fails</td>
</tr>
<tr>
<td><em>Aspergillus</em></td>
<td>Itraconazole or amphotericin B</td>
<td>The optimal duration of therapy is unknown and dependent on the extent of invasive aspergillosis, the response to therapy, and the patient’s underlying illness or immune status</td>
</tr>
<tr>
<td><em>Candida sp</em></td>
<td>Amphotericin B</td>
<td>2 to 3 weeks, followed by fluconazole for a total duration of therapy of up to 12 mo</td>
</tr>
<tr>
<td><em>Coccidiodes immitis</em></td>
<td>Amphotericin B or fluconazole</td>
<td>At least 12 mo</td>
</tr>
<tr>
<td><em>Scedosporium apiospermum</em></td>
<td>Voriconazole</td>
<td>Months or years and may require chronic suppressive therapy (75; 76)</td>
</tr>
<tr>
<td><em>Brucella sp</em></td>
<td>Doxycycline and streptomycin</td>
<td>Doxycycline for 45 days plus streptomycin for the first 15 days</td>
</tr>
</tbody>
</table>
Figures

Plain Radiograph of Left Total Hip Arthroplasty

Cerclage wires are seen around the femoral component. A periprosthetic fracture of the proximal shaft of the left femur is noted. Marked periprosthetic lucency around the proximal left femoral component, consistent with loosening is also noted. Periprosthetic loosening is a radiologic finding that is sometimes associated with prosthetic joint infection.
Radiograph of Left Total Knee Arthroplasty

Periprosthetic lucency is seen around the tibial component. Old fracture deformity of the distal left femur with plate and screw fixation. The total knee arthroplasty was resected. Intraoperative cultures grew methicillin-resistant, coagulase-negative staphylococci.
MRI of Vertebral Osteomyelitis

MRI shows moderate destruction of the inferior L3 and superior L4 vertebral bodies compatible with diskitis/osteomyelitis. There is moderate to marked narrowing of the thecal sac at this level due to retropulsion of an enhancing bony fragment.
MRI of Osteomyelitis in the Foot

MRI of the right foot shows an ulcer along the medial aspect of the foot near the metatarsophalangeal joint. There is abnormal soft-tissue thickening and edema deep to this ulcer with loss of the bony cortex and abnormal signal along the medial aspect of the head of the right first metatarsal. These findings suggest a localized area of osteomyelitis at this site.
MRI of Increased T2 Signal Abnormality

MRI image shows an increase in the amount of T2 signal abnormality and enhancement within the L3 and L4 vertebral bodies and disc, consistent with increased involvement with osteomyelitis.
Plain Radiograph Showing Antimicrobial-Containing Spacer Material

This plain radiograph shows postoperative changes that are consistent with resection arthroplasty. This procedure was done to treat a *Staphylococcus aureus* total knee arthroplasty infection. Spacer material containing antimicrobial agents is placed in the joint.