Osteomyelitis by Alexander Rabinovich

Definition
Osteomyelitis refers to bone tissue infection leading to inflammation and bone destruction via necrosis and new bone tissue formation.

Epidemiology (Waldvogel Classification)
- Osteomyelitis following hematogenous spread of infection
  - 20% of total osteomyelitis, more common in males of any age, and 85% of pediatric cases.
  - Usually with Hx of URTI, UTI, Skin or Soft Tissue Infection, Immunocompromised
- Osteomyelitis secondary to a contiguous focus of infection
  - 50% of osteomyelitis and is increasing in incidence.
  - Trauma (Open Fractures), Surgery (ORIF), IV Drug Use.
  - Presentation usually 2-4 weeks post event.
- Osteomyelitis associated with vascular insufficiency
  - Diabetes Mellitus is primary cause, and the foot is the primary site.
  - Vascular insufficiency and/or neuropathy.
- Biphasic distribution (Childhood and Adults >50 years old)
- Long bones (Femur, Tibia, Humerus) most often involved in children
- Vertebral column (Lumbar>Thoracic>Cervical), Sternoaviclarial, Sacroiliac bones are most often involved in Adults.
- Sickle Cell Anemia (compromised blood supply to bone due to RBC morphology change)

Etiology

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<th>Infant (&lt;1 y.o)</th>
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Table 1: Pathogens most often associated with osteomyelitis at various age groups. Underlined pathogens are most frequent.

Diagnosis

Acute Osteomyelitis (The phase before sequestrum is developed)
- Presentation within 1 week of symptom onset
- Local signs of infection
  a. Tenderness on palpation over involved bone
  b. Warmth and Swelling
  c. Pain is with or without movement
  d. Decreased range of motion of adjacent joints
- Systemic signs of infection
  a. Fever, Sweating, Chills
  b. Irritability or lethargy

Chronic Osteomyelitis (see image)
- Hallmark Features:
  a. Sequestrum, involucrum, Local Bone Loss and Persistent Drainage
  b. Fever usually absent
  c. High ESR, with Low Leukocyte count
- Localized bone pain
- Erythema and swelling at affected area
- Draining sinus tracts
- Decreased range of motion of adjacent joints
- Diminished blood supply

Table 2: The signs and symptoms of acute and chronic osteomyelitis.
Note 1: A full HPI, PHx, FHx, SHx, Meds, Allergies, Smoking, Alcohol, and O/E are mandatory.
Note 2: Not all s/s have to be present for the diagnosis.
Note 3: If diabetic foot ulcer is >2cm diameter, you have a very high risk of developing osteomyelitis.

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<td>Usually absent in early neonates.</td>
<td>Acute symptomatology of Fever, Sweating, Chills, Irritability, Lethargy.</td>
<td>Decreased limb motion</td>
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<td>Delayed symptomatology for 1 week.</td>
<td>Long bones mainly affected.</td>
<td>Edema in the limb</td>
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<td>If S. aureus, then systemic symptoms, such as Fever, Sweating, Chills, N/V.</td>
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<td>Joint effusion (60 – 70% of cases)</td>
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Table 3: Clinical s/s of hematogenous osteomyelitis in different age groups.
Bone Biopsy

• **GOLD Standard** for the diagnosis of osteomyelitis. Pathological changes in bone tissue and bacterial cultures. Needle biopsy is the most common technique used to obtain the bone sample. (Sensitivity 95%, Specificity 99%)

Probe-to-Bone Test (mostly for Diabetes Mellitus pedal ulcers) (Sensitivity: 66% - Specificity: 85%)

- Insert a sterile blunt probe into ulcer
  - Positive test: probe contacts bone → Suggests Osteomyelitis

Laboratory Tests

- **CBC → Leukocytosis**
  - Blood cultures are positive in 50% of cases
- **ESR > 70 mm/hr → Sensitivity 28%**
- **CRP > 10 mg/L → High Sensitivity, Low Specificity**
  - Acute Phase Reactant
  - Rises more than 6 hours after triggering stimulus
  - Peaks within 50 hours
  - Short half life of 5-7 hours
  - Rapidly declines after condition resolves

Radiological Studies

- **Plain X-Ray** may show: (Sensitivity 62%, Specificity 64%)
  - Early changes, such as haziness and loss of density of the affected bone
  - Soft tissue swelling
  - Periosteal thickening and/or elevation
  - Focal osteopenia.
  - Lytic changes (Osteolysis) tend to occur later (2-3 weeks later)
  - Bone changes may resemble other conditions, such as Charcot Joint, Fracture Healing, Osteopenia, and Cancer
- **CT scan** is good for detecting:
  - Cortical destruction
  - Intraosseous gas
  - Periosteal reaction
  - Soft tissue extension
- **MRI** good for evaluating: (Sensitivity 99%, Specificity 81%)
  - Vertebral involvement
  - Excellent for anatomic detail in planning surgical debridement
  - Difficult to differentiate between cancer and osteomyelitis
  - Excellent for diabetic foot ulcer investigation
- **Ultrasound** can show:
  - Fluid accumulation within the bone
  - Periosteal thickening and/or elevation (> 2mm requires further investigation)
- **Bone Scan with Technetium-99m**: (Sensitivity 86%, Specificity 45%)
  - "Hot Spot" in areas of increased osteoblast activity
  - Abnormal uptake seen 2 weeks before X-Ray changes
  - False positive with: Trauma, Surgery, Septic Arthritis, Cancer, Paget's Disease, and Healed Osteomyelitis
- **Indium-111-labeled Leukocyte scanning** (Sensitivity 89%, Specificity 79%)

Management

- Treatment will vary according to bones involved, severity of infection and immune status of patient (Cierny-Mader Staging)
- **Medical**
  - Empirical high-dose IV antibiotic therapy should be started before all sensitivities are known; the outcome is best if treatment is started within 3 to 5 days of onset of infection and should last for at least 6 weeks.
  - CRP can be used to monitor management, but do not stop treatment if CRP normalizes, finish the 6 week protocol.
- **Surgery**
  - Surgery removes the necrotic tissue, providing both a clean platform for future healing and samples for microbiology to guide the subsequent long-term antibiotic therapy

References

Cierny-Mader Classification

- Allows grading of long bone osteomyelitis and permits the development of a treatment guideline for each of the 12 stages:
  - Classification based on (Anatomy of Bone Infection) + (Physiology of Host/Patient)

**Cierny-Mader Staging System for Long Bone Osteomyelitis**

**Anatomic type**
- Stage 1: Medullary osteomyelitis
- Stage 2: Superficial osteomyelitis
- Stage 3: Localized osteomyelitis
- Stage 4: Diffuse osteomyelitis

**Physiologic class**
- A host: Normal host
- B host: Systemic compromise (B5), local compromise (B1), or both (B5B)
- C host: Treatment worse than the disease

Systemic or local factors that affect immune surveillance, metabolism, and local vascularity

**Systemic**
- Malnutrition
- Renal or hepatic failure
- Diabetes mellitus
- Chronic hypoxia
- Immune disease
- Malignancy
- Extremes of age
- Immunosuppression or immune deficiency

**Local**
- Chronic lymphedema
- Venous stasis
- Major vessel compromise
- Arteritis
- Extensive scarring
- Radiation fibrosis
- Small vessel disease
- Neuropathy
- Tobacco abuse (≥ 2 packs per day)

*Adapted from Cierny, G., Mader, J.T., Pennick, H., Contemp Orthop 1985; 10:17

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**Choice of Antibiotic and Regimen in Osteomyelitis**

<table>
<thead>
<tr>
<th>Organism</th>
<th>Antibiotics of first choice*</th>
<th>Alternative antibiotics*</th>
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<tbody>
<tr>
<td>Staphylococcus aureus (mupirocin sensitive)</td>
<td>Nafcillin 2g Q8h or clindamycin 900mg Q8h</td>
<td>Cefazolin</td>
</tr>
<tr>
<td>Staphylococcus aureus (mupirocin resistant)</td>
<td>Vancomycin 1g Q12h, nafcillin 2g Q8h (if sensitive)</td>
<td>Trimethoprim-sulfamethoxazole or minocycline plus rifampin</td>
</tr>
<tr>
<td>Coagulase negative</td>
<td>Vancomycin 1g Q12h* or Cefazolin, clindamycin †</td>
<td></td>
</tr>
<tr>
<td>Staphylococcus</td>
<td>Cefazolin, clindamycin †</td>
<td></td>
</tr>
<tr>
<td>Group A streptococcus</td>
<td>Clindamycin 900 mg Q8h †</td>
<td>Benzylpenicillin, cefazolin</td>
</tr>
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<td>Group B streptococcus</td>
<td>Clindamycin 900 mg Q8h †</td>
<td>Benzylpenicillin, cefazolin</td>
</tr>
<tr>
<td>Enterococcus spp.</td>
<td>Ampicillin 2g Q6h ± gentamicin 5 mg/kg per day divided Q8h†</td>
<td>Vancocin*</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>Ampicillin 2g Q6h</td>
<td>Cefazolin, gentamicin*, levofloxacin</td>
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<td>Proteus mirabilis</td>
<td>Ampicillin 2g Q6h</td>
<td>Cefazolin, gentamicin*, levofloxacin</td>
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<td>P. vulgaris, P. rettgeri, Morganella morganii</td>
<td>Cefotaxime 2g Q8h ± gentamicin 5 mg/kg per day divided Q8h†</td>
<td>Ticarcillin-clavulanic acid, levofloxacin</td>
</tr>
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<td>Serratia marcescens</td>
<td>Cefotaxime 2g Q6h ± gentamicin 5 mg/kg per day divided Q8h†</td>
<td>Ticarcillin-clavulanic acid, levofloxacin</td>
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<td>Pseudomonas aeruginosa</td>
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<td>Bacteroides fragilis group</td>
<td>Clindamycin 900 mg Q8h †</td>
<td>Metronidazole †, ampicillin-subactam</td>
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<tr>
<td>Peptostreptococcus spp.</td>
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*Antibiotic dose should be adjusted for renal function.
†Dose and interval should be adjusted using drug serum levels.
‡ Clindamycin and metronidazole generally do not require dose adjustment in the presence of renal dysfunction.
| Infants (< 1 y.o): | • Blood vessels cross the epiphyseal growth plate and can cause infection of the epiphysis and joint space.  
  • Cortical bone is thin and loose, which permits release of pressure caused by infection, but promotes rapid spread of infection directly into subperiosteal region.  
  • A large sequestrum (dead bone) is NOT produced, but a large subperiosteal abscess can form. |
|---|---|
| Children (1 – 16 y.o) | • Infection starts in metaphyseal sinusoidal veins and is contained by the avascular growth plate.  
  • The joint is affected only if the metaphysis is intracapsular.  
  • The infection spreads laterally and through the cortex and forms a subperiosteal abscess. |
| Adults (> 16 y.o): | • The growth plate has resorbed and the infection can communicate via blood vessels with the joint space.  
  • Periosteum is firmly attached to bone, and abscess is rarely formed.  But infection can erode through the periosteum and form a draining sinus tract. |

**Pathogenesis**

- **Bacterial adherence**
  - Bacteria adhere to bone by expressing receptors for the components of bone matrix (fibronectin, collagen …)
  - Expression of adhesions permits attachment of the pathogen to cartilage
  - **future treatment → adhesion-derived vaccine**

- **Proteolytic activity**
  - Osteomyelitis → increase proteolytic activity → increase collagen destruction

- **Resistance**
  - When microorganisms adhere to bone, they express phenotypic changes which make them resistant to antimicrobial treatment
  - Eg. S. Aureus makes a protein antigen that inhibits immune function
  - Eg. S. Aureus secretes toxins (exotoxin and toxic shock syndrome toxin) → suppress plasma cell differentiation

**Hematogenous**

- **Long Bone (Tibia, Femur):**
  - Metaphysis more frequently involved. The supply of blood vessels feeding the metaphyseal region leads to slowing of blood flow, and allows bacteria to settle and initiate an inflammatory response.
  - The metaphyseal capillaries lack phagocytic lining cells and allow growth of microorganisms if stasis occurs.
  - The bone is poor at accommodating the pus and inflammation from infection, which means that bone infection leads to a marked increase in pressure.
  - If the increase in pressure is not relieved, it can impinge on the blood supply to wide areas of bone, resulting in ischaemic necrosis.
  - The necrotic avascular areas provide reservoirs of infection largely inaccessible to systemic antibiotics.
  - The periosteum is usually strong enough to prevent expansion and hence a periosteum abscess will form.
  - Once this chronic phase of infection is established, surgical debridement of the sequestra together with appropriate antibiotic therapy is required to eradicate infection.
  - **Infants and Adults** have blood vessel communication from metaphysis to epiphysis, thus infection can potentially spread to the joint space. In children, the growth plate is avascular, thus no spread to the joint space, unless the metaphysis is part of the joint capsule.

- **Vertebral**
  - Preceding Hx of UTI or IV drug use is often present.
  - The segmental arteries supplying the vertebrae usually bifurcate to supply 2 adjacent bony segments. Thus, hematogenous vertebral osteomyelitis usually involves two adjacent vertebrae and the intervertebral disc.
  - May lead to epidural abscess and even meningitis.

**Glossary**

Sequestrum: Dead bone tissue  
Involucrum: Reactive bony encasement of the sequestrum
Chronic Osteomyelitis

Sagittal T1-weighted (left) and T2-weighted (right) MR images of the lumbar spine show marrow and disc edema (darker signal intensity area on T1 and brighter signal intensity area on T2 between arrows) consistent with vertebral osteomyelitis.
Haziness and loss of bone density in osteomyelitis of the arm. Source: Wellcome Photo Library