
بسم الله الرحمن الرحیم
به نام خدای بخشاینده مهربان
In the name of Allah the Compassionate the Merciful

OSTEOMYELITIS

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- *OSTEOMYELITIS*
  - inflammation of **bone** and **marrow**
    - Generally implies the presence of infection

- Acute diagnosed within 2 weeks of the onset
- Subacute symptoms have been present for more than 2 weeks at the time of presentation

- **Bacteria** # fungi # parasites # other microorganisms

microorganisms can be introduced into bone in three ways

- direct inoculation usually **traumatic**
- during **surgery**
- due to the presence of **orthopedic fixation devices**
- **local invasion** from a contiguous focus of infection
- **hematogenous** delivery
  - In children generally hematogenous

- Incidence
  - 1 in 1000 → 1 in 20,000
  - increased in **sickle-cell disease**
    - Some other immunocompromised
- **Boys** 1.2 to 3.7 times more than girls
- most often in the **first 2 decades** of life
  - 25% younger than 2 years
  - 50% younger than 5 years

- most often ➔ Gram-positive bacteria
  - ***Staphylococcus aureus***
  - ***Streptococcus pyogenes***

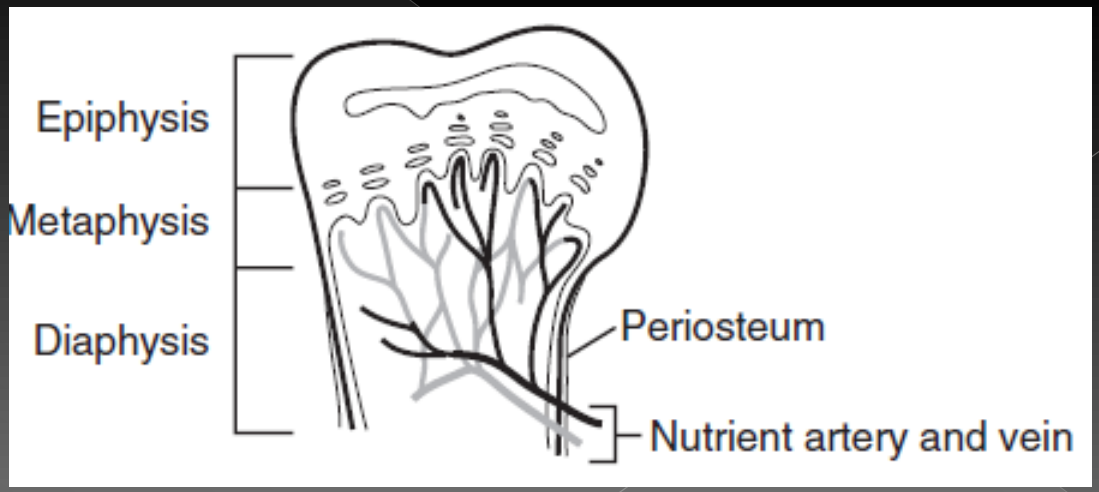
80% to 90% of cases

  - *Kingella kingae* ➔ PCR ➔ important cause in young children
  - *Streptococcus pneumoniae*
  - *Haemophilus influenzae*
  - *Salmonella spp* ➔ immunocompetent & **SCD**
  - *Escherichia coli* aerobic enteric **g-**
  - *Pseudomonas aeruginosa* **injection drug use**
  - *Bacteroides spp.* ***PNS*** & mastoid

Organisms
Gram-Positive Bacteria
Staphylococcus aureus
Coagulase-negative staphylococci
Streptococcus pneumoniae
Other streptococci
Gram-Negative Bacteria
Haemophilus influenzae
Pseudomonas aeruginosa
Salmonella spp.
Escherichia coli
Kingella kingae
Mixed or unusual organisms

Pathogenesis

- Hematogenous osteomyelitis generally begins in the **METAPHYSIS**
- Metaphyseal capillaries
- Trauma or emboli
- Occlusion
- Nidus for infection



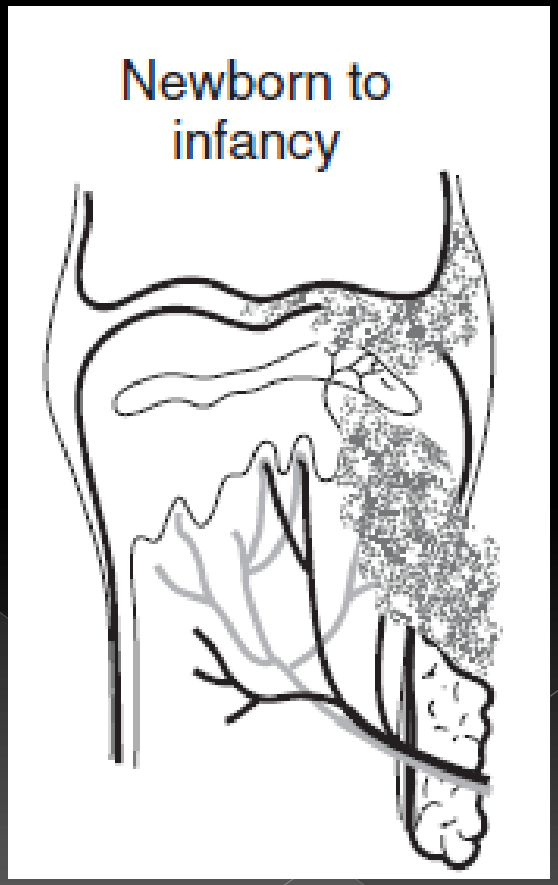
Signs and Symptoms

- may be entirely **subclinical**
  - malaise
  - low-grade fever
- **severe constitutional symptoms**
  - high fevers 39°C to 40°C

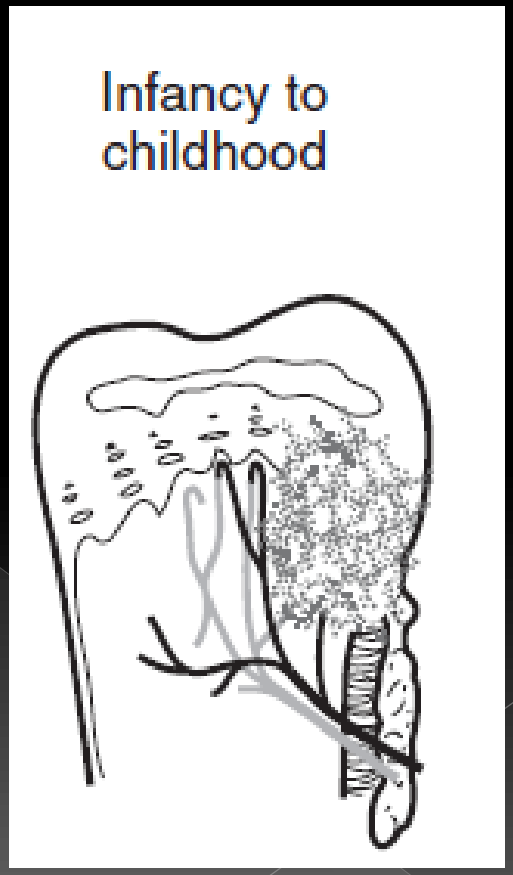
- Subsequent clinical manifestations of osteomyelitis are not related to the severity of initial constitutional signs of infection but are influenced by the
  - **Age Of The Child**

  and
  - **The Etiologic Agent**

- **In newborns, the thin cortex and loosely attached periosteum are poor barriers to the spread of infection**
  - Purulence rapidly ruptures through both of these structures into the contiguous muscle bed
  - dissects the muscle bundles
  - swollen, **discolored limb** taking the appearance of a **sausage**



- In older infants, the cortex is thicker, and the periosteum is slightly denser.
- infection spreads less often to the soft tissues of the extremity.
- **Subperiosteal abscess** and contiguous edema readily develop, generally at the metaphysis, where the cortex is the thinnest.
- The nutrient metaphyseal capillaries present at birth that cross the growth plate in infants are **atrophic by 18 months of age**, but this does not appear to alter the risk of developing septic arthritis at adjacent joints in older children, compared to infants, as once proposed.



- In children and adolescents (4 to 16 years old), the metaphyseal cortex is considerably thicker, with a dense, fibrous periosteum.
- The pathogenesis of the infection is the same in this age group, but the **infection rarely ruptures and spreads to the outer cortical lamellae**.
- As a result, the signs and symptoms of osteomyelitis in these older children and adolescents usually are **more focal**.

- A newborn with osteomyelitis usually is
  - **IRRITABLE**
  - Evidence of **PAIN** when extremity is touched or moved
  - **PSEUDOPARALYSIS**
  - **MASSIVE SWELLING** of the extremity if untreated
- **Plain radiograph** is valuable in newborns;
  most have changes consistent with osteomyelitis on the initial radiograph, including
  - **Soft-tissue Swelling**
  - **Periosteal Changes**
  - **Lytic Lesions Of Bone**
-

- In infants and young children, **pain** is usually accompanied by **LIMPING** because osteomyelitis occurs more commonly in the **lower extremities**.

- The child **often refuses to use the affected extremity** and displays variable constitutional symptoms.

- In older children and adolescents, less restriction of function of the extremity is found compared with infants and young children.
- **POINT TENDERNESS** is often sharply circumscribed and may be found only as a small area of discomfort at rest

- Most commonly, **tubular bones** are involved, but osteomyelitis occurs throughout the skeleton
- The hallmark of the disease is the focal nature of symptoms;
  - **POINT TENDERNESS**
  - **WELL-LOCALIZED PAIN**
- **Percussion of the long bone** away from the area of point tenderness may elicit pain at the site of osteomyelitis in older children and adolescents.

TABLE 55.2 **Site of Involvement in Acute Hematogenous Osteomyelitis**

Location	%
Tubular Bone	
Femur	25
Tibia	24
Humerus	13
Phalanges	5
Fibula	4
Radius	4
Ulna	2
Metatarsal	2
Clavicle	0.5
Metacarpal	0.5
Cuboidal	
Calcaneus	5
Talus	0.8
Carpals	0.5
Cuneiform	0.5
Cuboid	0.3
Irregular	
Ischium	4
Ilium	2
Vertebra	2
Pubis	0.8
Sacrum	0.8
Flat	
Skull	1
Rib	0.5
Sternum	0.5
Scapula	0.5
Maxilla	0.3
Mandible	0.3

Clinical Features Of Organisms

- CA-MRSA
  - **More Complex & Severe** (than MSSA)
  - Life-threatening infections
- Occur more frequently with CA-MRSA (than MSSA)
  - **Myositis**
  - **Pyomyositis**
  - **Intraosseous & Subperiosteal Abscesses**
  - **Pathologic Fractures**
  - **Septic thrombophlebitis**

- *Kingella spp.*
  - children under **36 months** of age
  - **Indolent** course
  - **limb pain** often present for longer than a week before initial medical evaluation
  - complications and sequelae of osteomyelitis are **RARE**
  - Brodie abscess & periosteal abscesses

- *H. influenzae*
  - primarily in the **upper extremities**

Culture-negative osteomyelitis

- Generally **milder**
- Symptoms were of **longer duration**
- Overlying skin changes were seen less frequently
- β-lactam antibiotics generally was successful

  - Suggest a more effective host defense
  - Less Virulent
  - Fastidious Pathogen (*K. Kingae)*

Diagnosis

- suggested by
  - Presence Of Fever
  - Focal Skeletal Pain
  - Warmth
  - Swelling
  - Limp Or Refusal To Use An Extremity
  - ↑↑↑ Serum Acute-phase Reactants (CRP Or ESR)
- Abnormal imaging studies
- Positive blood culture
- Scintigraphy ↑ bone turnover
- Culture or G/S in aspirate ➔ organisms
- Histopathologic evidence of inflammation in surgical specimens

Microbiology

The cornerstone of the diagnosis of osteomyelitis is

Isolation Of Bacteria or other **microbes**

66% to 82% of cases

from bone or from anatomic structures contiguous to bone

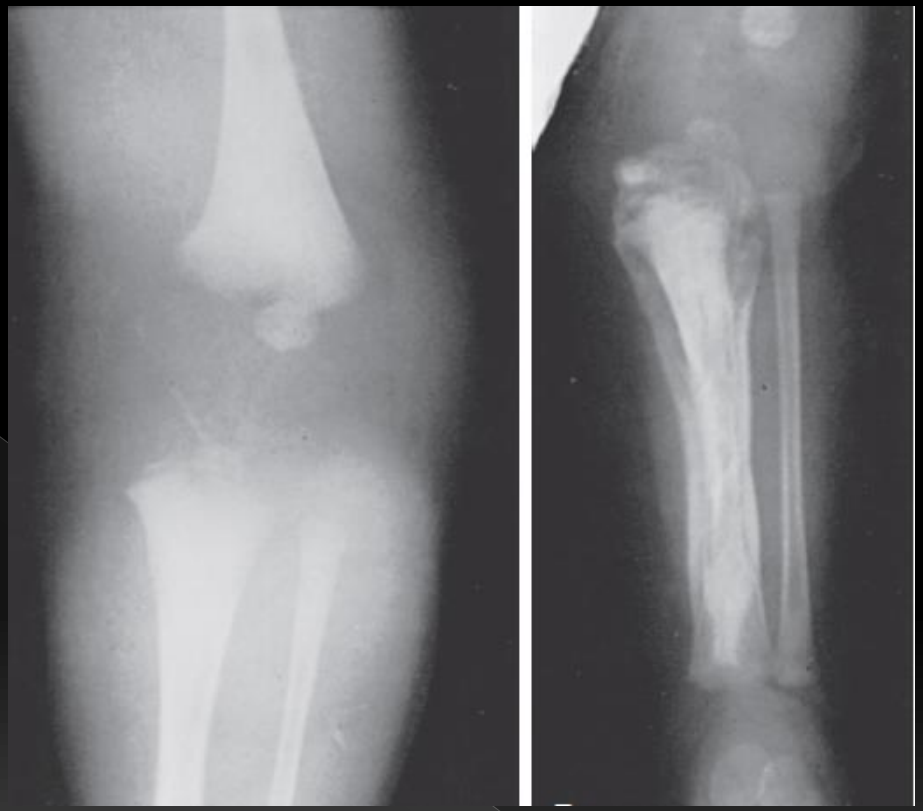
►Aspirates or surgical specimens from bone debridement
►Subperiosteal exudate samples
►Joint fluid

- Blood cultures ➔ **half** of cases (31% to 74%)
- PCR detection➔ fastidious pathogens (*Kingella*)

In neonates, needle aspiration of soft tissue or incision and drainage of bone

Radiology

- ***Plain radiographs***
- ***Conventional radiographs are crucial in establishing*** the diagnosis of pediatric osteomyelitis and **always** should be obtained.
- Because bone density must decrease 50% to be detected by radiographs changes in the less ossified bones of **neonates are detected more readily** than are changes in older children
- in adults ➔ may be
  - no diagnostic value in 23%
  - misleading in 16%



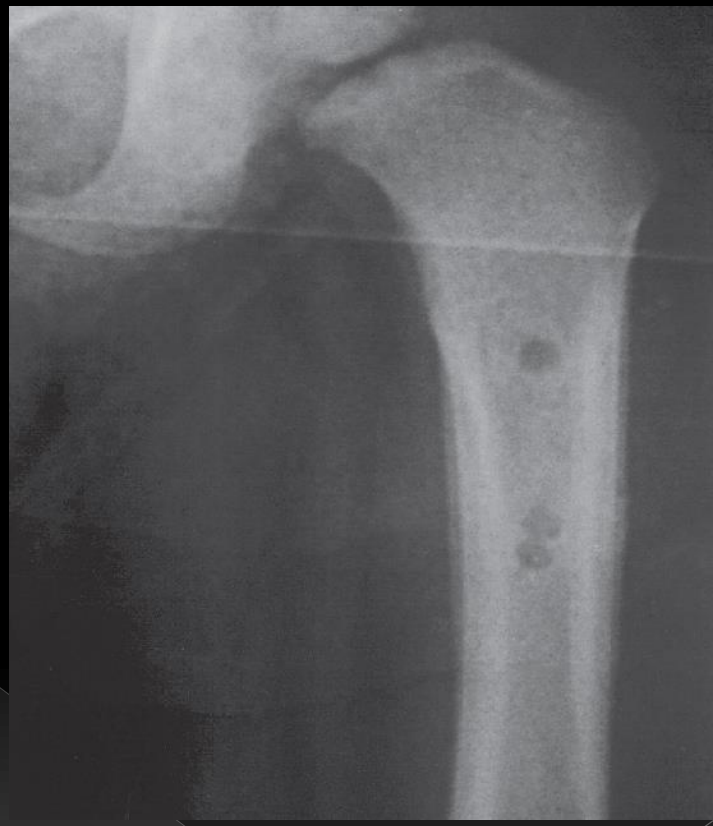
Radiology

- Radiographic changes occur in three stages
- **The first stage** ➔ 3 days after the onset
- formation of a small area of localized, deep soft tissue swelling, usually in the region of the metaphysis
  - Consequently when diagnosis of osteomyelitis is sought soon after onset of symptoms, examination of the radiograph should be directed to the soft tissue rather than the bone.
- **second stage** ➔ 3 to 7 days after the onset of symptoms, swelling of the muscles with obliteration of the interposed translucent fat planes can be noted.
- It is caused by continued spread of edema fluid and can progress, particularly in neonates and young infants, to superficial soft tissue edema; the skin may acquire an "**orange peel**" texture.

- Radiographic evidence of bone destruction usually is not detected **until 10 to 21 days after** the onset of symptoms.

- The first changes detected include
  - **subperiosteal bone resorption**
  - **areas of bone destruction**
  - **periosteal new bone formation**

- The variability depends on the specific bone involved;
  - generally long tubular bones tend to show bony changes 2 to 3 weeks earlier than membranous or irregular bones.



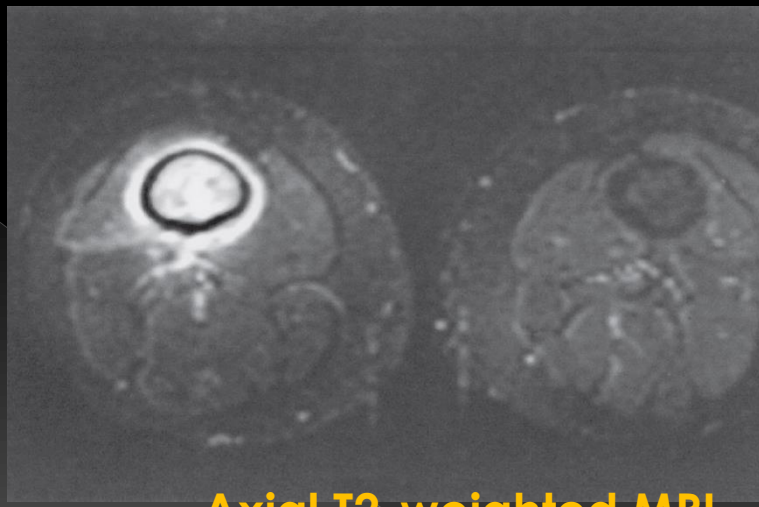
Magnetic resonance imaging

- imaging modality of **choice**
  - when additional imaging is needed beyond plain radiographs
- has **sensitivity in excess of 90%.**

- Advantages over CT & radiographs ; identify
  - **subperiosteal** or **soft tissue** collections of **pus**
    - require surgical drainage without using radiation
  - **Sinus Tracts** for removal
  - spinal osteomyelitis (Loss of vertebral body border)

- T1-weighted ➔ ↓↓ signal
- T2-weighted ➔ ↑↑ signal

- In most cases, **gadolinium** contrast is **not needed**
  - but enhancement may reveal **small abscesses** that would otherwise be missed



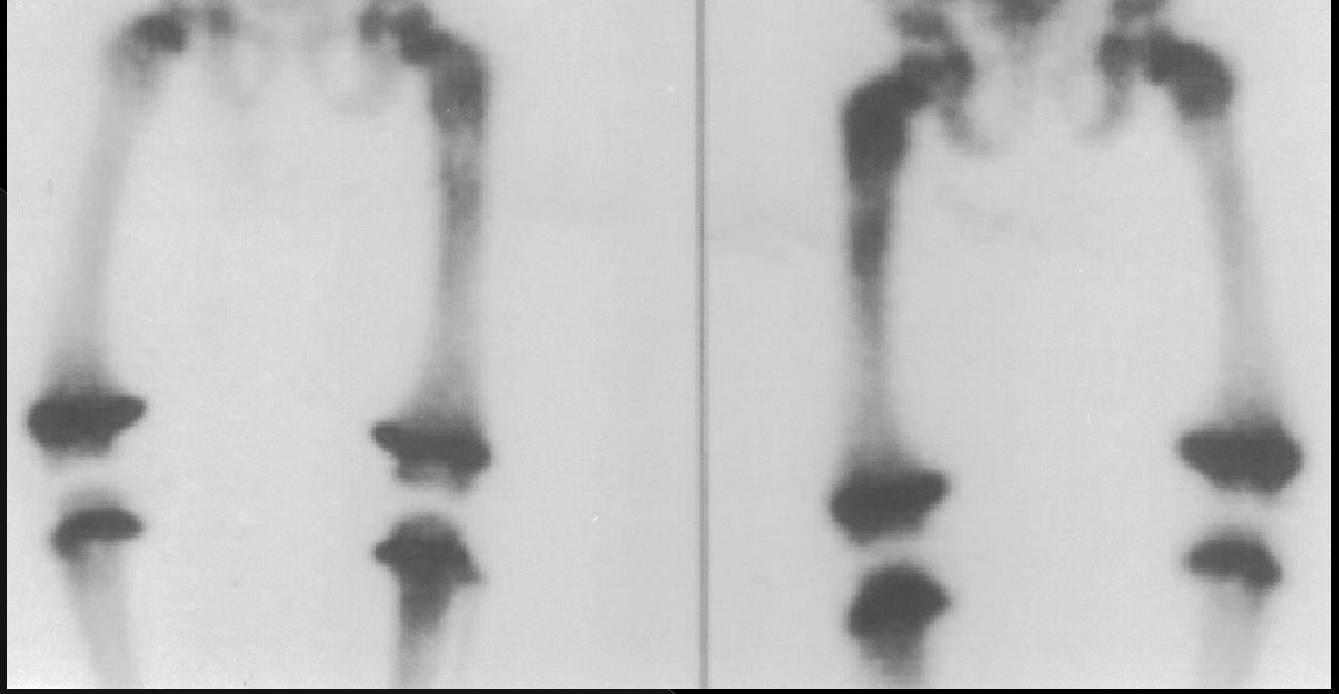
Axial T2-weighted MRI

Radionuclide imaging.

- exposure to ionizing radiation
- detecting multifocal disease
- Technetium 99m (99mTc) diphosphonate scintigraphy
- three-phase bone scan for evaluation
  - flow phase ➔ 2 to 5 seconds (Shortly after)➔ area of suspected osteomyelitis
  - blood pool phase ➔ 5 to 10 minutes after
  - third image ➔ 2 to 4 hours after
  - phosphate adsorbed in bone & Tc 99m concentrated in the junction of osteoid and mineralized bone.

Anything increasing local blood flow (inflammation) ➔ increased general uptake in the first two phases,
but **osteomyelitis** results in **focal uptake** in the **third phase**

- intensity of the signal detected reflecting the level of **osteoblastic activity**



- Acute osteomyelitis in children is **often diagnosed by a 99mTc scan** and treated successfully before bone changes are detected by plain radiographs
- Sensitivity ➔ 95% **reliable for diagnosis**
- in CA-MRSA ➔ 53%
  - acuity of disease
  - more characteristic in longer duration illness
- sensitivity of scans in **neonates** has varied
- False – scans in newborns result from
  - limited spatial resolution,
  - the paucity of mineralization in neonates' bones,
  - ischemia of bone

Gallium 67

- bound to plasma proteins
- localizes in inflammatory foci (increased capillary permeability)
- slower elimination of gallium from blood
- uptake in an inflammatory focus depends less on blood flow
- Delayed elimination often results in poor contrast of bone to soft tissue
- **delays making a reliable interpretation for 24 to 72 hours after injection**
- Combined evaluation with **Ga67** imaging and **Tc99m** scanning may lead to greater diagnostic certainty

Computed tomography

- used occasionally in the diagnosis
- provides excellent definition of **cortical bone**
- high spatial resolution
- detecting **sequestra**
- delineating subperiosteal abscesses
- define infections of the **spine** (now MRI is better)

- CT abnormalities
  - increased density of bone marrow
    - accumulation of purulent material
  - periosteal new bone formation and purulence

Treatment

- ***Surgical Intervention***
  - need for surgical therapy must be considered immediately
- Sequestra should be removed
- contiguous infectious foci are present, they should be debrided adequately
- Immobilization of the affected extremity or splinting may afford relief from pain

Surgical drainage Indications

1. sequestrum is present
2. the disease is chronic or atypical
3. the hip joint is involved
4. spinal cord compression is present.

Antimicrobial Therapy

- **potent activity against**
  - *S. aureus*
  - group A streptococci
- treated initially ➔ **PARENTERAL**
- In areas where most (≥90%) *MSSA*
  1. **penicillinase-resistant, semisynthetic penicillin**
     - **Nafcillin**
     - **Oxacillin** 150 to 200 mg/kg/day div4
  2. **Cefazolin** G1
  3. **Cefuroxime** G2

preferred in infants and young children under 36 mo

- where CA-MRSA is common
  - vancomycin
  - clindamycin
    - (if >90% of CA-MRSA isolates are clindamycin susceptible)
- severely ill at presentation ➔
  - vancomycin + oxacillin /cefazolin

- for younger children
  1.
     - addition of a 3G cephalosporin
     (ceftriaxone or cefotaxime)
     +
     - antistaphylococcal agent
     (vancomycin,clindamycin, oxacillin, or nafcillin)
  2. fourth-generation cephalosporin
     - cefepime

Staphylococci

- penicillin G if susceptible
- penicillinase-resistant penicillin (oxacillin or nafcillin)
- Clindamycin
- Vancomycin
- Ceftriaxone most cases of bone infections caused by MSSA
- Oxazolidinone (linezolid) MRSA MSSA VRE VISA
- streptogramin (quinupristin-dalfopristin) MRSA MSSA VRE VISA
- Trimethoprim-sulfamethoxazole (cotrimoxazole) CA-MRSA
- Lipophilic tetracyclines (minocycline and doxycycline)
- Daptomycin, a bactericidal lipopeptide CA-MRSA
  poor activity in lung tissue AND concerns in osteomyelitis

Route of administration of antibiotics

- sequential use of the **intravenous** and **oral** routes are accepted
  - Which previously was controversial
- Completing treatment with **Oral Therapy** avoids the
  - cost
  - pain
  - Inconvenience IV AB
  - well-known complications of long-term administration of IV AB

- **Oral therapy** when the following criteria are met
  - organism has been identified
  - patient has the ability to swallow
  - retain an appropriate medication
  - patient has a clear clinical response to intravenously
  - peripheral leukocyte count has normalized (if initially abnormal)
  - marked decrease in the serum concentration of CRP

- treatment was continued with Intravenous antibiotics until
  - afebrile
  - until local signs and symptoms of infection were reduced considerably
  - until the patient was maintaining caloric and fluid balances by the oral route
- no evidence that a fixed period of intravenous therapy is beneficial or essential
- **Transition To Oral** therapy **within 7 days** of diagnosis seemed to be equal in outcome to therapy with a fixed initial period of parenteral therapy

- When oral therapy is begun, most antibiotics administered orally for osteomyelitis must be given in doses higher than those used for the treatment of other infections

Drug	Dose
Amoxicillin	100 mg/kg/day divided into 4 doses
Cephalexin	150 mg/kg/day divided into 4 doses
Chloramphenicol	75 mg/kg/day divided into 3 doses
Clindamycin	40 mg/kg/day divided into 4 doses
Dicloxacillin	100 mg/kg/day divided into 4 doses
Linezolid	Age <12 y: 30 mg/kg per day divided into 3 doses; maximum dose 1.8 g/day Age ≥12 y: 600 mg twice per day
Penicillin V	100 mg/kg/day divided into 4 doses
Trimethoprim-sulfamethoxazole	16 mg/kg/day (for trimethoprim component)

- **improvement** is evident **within 3 to 7 days**
- show that effective therapy
  - Monitor acute-phase reactants CRP & ESR
  - ncrease during the first 2 days of therapy
  - CRP
    - begins to decrease rapidly➔ half-life of 1 to 2 days
    - returns to normal in 7 to 10 days

- **Failure of ESR** to decrease during the second week of treatment may indicate
  - a **need for surgical drainage**
  - the development of chronic osteomyelitis

- **3 weeks** or more appears to be the minimal duration of therapy for hematogenous osteomyelitis to achieve a low rate of recurrence
- shorter period of therapy in some studies
  - but no cases of MRSA

- Conservative but individualized approach is to administer antibiotics until ESR and CRP are both within the normal range, which usually requires 4 to 6 weeks of treatment

BOX 55.1 Differential Diagnosis of Osteomyelitis in Children

Fractures
Thrombophlebitis
Scurvy
Septicemia
Cellulitis
Septic bursitis
Myositis
Pyomyositis
Rheumatic fever
Toxic synovitis
Reactive arthritis
Complex regional pain syndrome
Chronic recurrent multifocal osteomyelitis
Osteoid osteoma
Langerhans cell histiocytosis
Leukemia
Ewing sarcoma
Malignant primary bone tumors
Bone infarction (sickle-cell or Gaucher disease)

Chronic recurrent multifocal osteomyelitis (CRMO)

- Special attention in the ddx
  - A chronic illness
  - Multiple chronic,
  - Focal, inflammatory lesions in bone,
  - Periodic exacerbation and remission
  - Moderate bone pain
- most commonly in **GIRLS**
- **Age Of Onset** of **10 years**
- northern European origin
- localized, multifocal bone pain
- gradual onset
- **Fever** ➔ 20% to 50%
- Most ↑ ESR & CRP
- Sporadic illness (may also be foundas part of syndromic illnesses)

- osseous lesions occur primarily in the
  - **Distal femoral**
  - **Distal tibial**
  - **Proximal tibial**
- although lesions are common
  - **Pelvic**
  - **Clavicular**
- vertebral lesions 1/6 to ¼

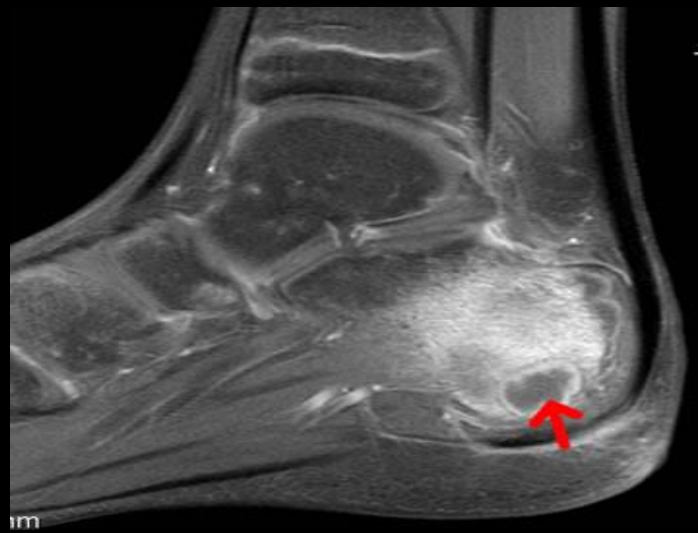
- Patients may have **1 to 20 lesions** at a time
- Biopsy → nonspecific chronic inflammatory process
- Organisms seldom are identified
- Antibiotics → no improvement
- **10% to 20%** → **Pustular Eruption in Palms & Soles**
  Pustulosis palmaris et plantaris
- long-term outlook generally is good
  - numerous relapses
- **Glucocorticoids** and **NSAID** → recurrences are common
- **INF gamma & TNF alfa & bisphosphonates** → long term responses

Special Manifestations of Hematogenous Osteomyelitis

Brodie Abscess

- **subacute** osteomyelitis
- Development of a localized and well-contained **intraosseous abscess**
- most often identified in **adolescents**
  - Complaints of long bone pain and tenderness
  - generally occur in the **Tibia** or **Femur**
  - Fever is generally absent
  - ESR usually is normal
  - A bony defect with sclerotic margins is detected by plain radiography
  - A distinctive "target" lesion has been described in MRI studies

- Concentric layers
  - central abscess cavity
  - Inner ring of granulation tissue
  - outer ring of fibrotic reaction
  - peripheral rim of endosteal reaction➔ hypointense on T1
- *S. aureus*
- gram-positive cocci
- variety of gram-negative



Treatment

- surgical drainage and curettage
- followed by antimicrobial therapy

- Bone grafting may be needed for larger lesions
- prognosis generally is good
- deformities occur in some cases

Osteomyelitis in Patients After Closed Fractures

- A clue to diagnosis is the resumption of pain after the initial postfracture pain has subsided
- usually **1 to 6 weeks after** the injury occurs
- pain differs from fracture
  - being progressive and not being relieved by immobilization
- Patients are **febrile** and may be thought to have another focus of infection
- When the cast is removed, local erythema, fluctuance, and warmth are apparent and out of proportion to the normal healing of fracture
- TX : debridement**+ AB +** external fixation

***S. Aureus* anaerobic superinfection**

Epiphyseal and Apophyseal Osteomyelitis

- acute or subacute
- *S. aureus & K. kingae*
  - **Epiphyses**
  - rarely, **Apophyses** of the tubular bone (e.g., the greater trochanter of the femur)
- **young children**
- pathogenesis is unclear
  - by transphyseal vessels organisms reach to epiphyses
  - After 15 to 18 months of age, these vessels are atrophic
  - via venous sinusoids or by terminal branches of the epiphyseal arteries ➔ **older children**
- Diagnosis : radionuclide bone scan

Nontubular Bones

- calcaneus is the most common
- Pelvis → ischium → ilium → sacroiliac joint

Spinal Osteomyelitis

- different pathophysiology and prognosis

Diskitis

- Capillary network in the annulus fibrosus
  - derived from the terminal radial ramifications of the periosteal vessels
- loss of this vascular supply
  - disk necrosis
    - bacteremia occurs during loss of the blood supply ➔ infection

- Most younger than 3 years
- symptoms for several weeks
- *S. aureus & K. kingae*
- Most **Thoraco lumbar**
- **patient's refusal to walk**
  - **Back pain**
  - **progressive limp**
- **Nonambulatory infants**
  - **Irritable**
  - **refuse to sit or crawl**
- On exam : percussion tenderness
  loss of lordosis of the lower part of the back

- Lesions higher in the spine (T8 to L1) can mimic gastrointestinal disease
  - abdominal pain
  - ileus
  - vomiting

- **Fever** generally is absent or low grade
- Peripheral **leukocytosis** is in one-third
- virtually all have an **increased ESR**

- radiographic findings
  - narrowing of the disk space
    - usually not detectable until 2 to 4 weeks after the onset of symptoms
    - Destruction of the adjacent cartilaginous vertebral endplates
    - herniation of the disk

- overlap of this syndrome with noninfectious disk necrosis,
- Earlier ➔ treating this disease solely by bed rest
- antistaphylococcal therapy
  - Although controversial, oral antistaphylococcal therapy often is administered for a prolonged period (10 days to 4 weeks)
  - Other physicians have suggested giving 5 to 7 days of intravenous antistaphylococcal therapy, followed by 7 to 14 days of a similar oral agent

Vertebral Osteomyelitis

- rare in children
- usually are older than 8 years
- **Hematogenous origin** ➔ *S. aureus.* *Ddx :* TB & brucellosis
- constant back pain
- toxic and have a low-grade fever
  - after an indolent course(2 weeks to several months)
- Percussion of the spinal dorsal process ➔ **exquisite tenderness**
- Paraspinous musclesspasm ➔ with rigidity of the area
- Radiography ➔ localized rarefaction of one vertebral endplate
- **MRI** is the preferred imaging approach
- Technetium 99m and gallium 67
- Therapy ➔ surgical debridement & stabilization, immobilization, + **AB**

NONHEMATOGENOUS OSTEOMYELITIS

Puncture Wound Osteomyelitis

staphylococci
streptococci
Stenotrophomonas maltophilia
Serratia marcescens

- 9 to 18 years
- most commonly ***P. aeruginosa*** (90%)
  - Patella
  - foot
- signs of **OSTEOCHONDRITIS** appearafter another 48 to 72 hours
- joint tenderness
- Localized swelling, erythema, and pain over the entrance of the puncture wound
  - Fever is an infrequent
  - Seldom constitutional symptoms
  - No peripheral leukocytosis
  - ESR is increased minimally
- Surgical debridement of necrotic cartilage is a key element **+ AB**

THANKS FOR YOUR ATTENTION