Crystal-induced arthritis

Gout and pseudogout

1) Gout (Podagra)

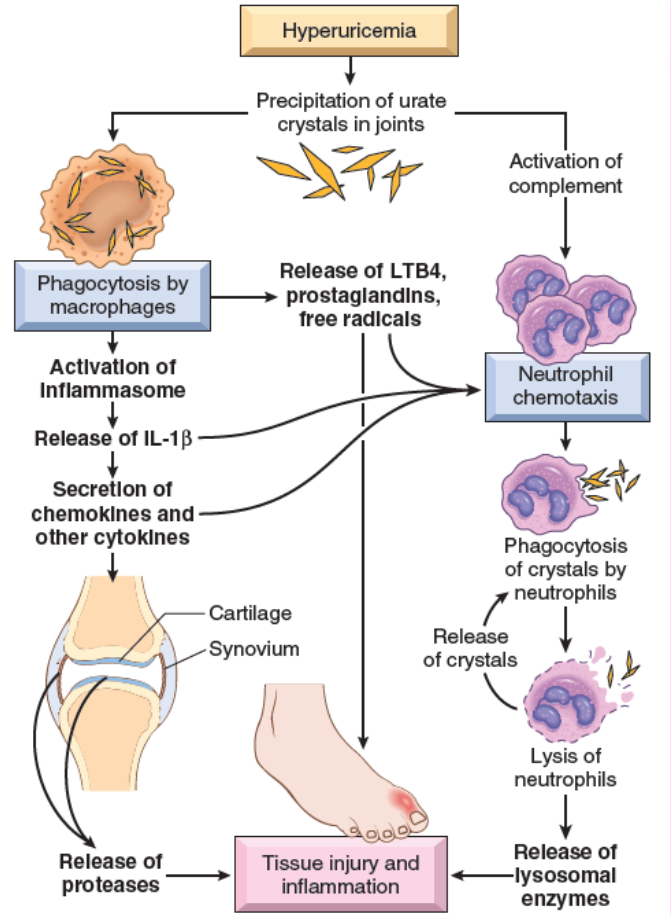
Gout is marked by transient attacks of **acute arthritis** initiated by **urate crystals** deposited within and around joints

- Gout affects about 1% of the population, and shows a predilection for males.
- It is caused by excessive amounts of *uric acid.*
- **Hyperuricemia (plasma urate level above 6.8 mg/dL) is necessary, but not sufficient, for the development of gout.**
- Monosodium urate crystals precipitate from supersaturated body fluids and induce an acute inflammatory reaction.
- Gout is marked by recurrent episodes of acute arthritis, sometimes accompanied by the formation of large crystalline aggregates called *tophi,* and eventual permanent joint deformity.
- Risk factors for the disease include age (more than 30) , genetic, obesity, excess alcohol intake, consumption of purine-rich foods, diabetes, the metabolic syndrome, drugs, and renal failure.

Table 20–3 Classification of Gout

Clinical Category	Metabolic Defect
Primary Gout (90% of cases)	
Enzyme defects—unknown (85% to 90% of cases)	Overproduction of uric acid Normal excretion (majority) Increased excretion (minority) Underexcretion of uric acid with normal production
Known enzyme defects—e.g., partial HGPRT deficiency (rare)	Overproduction of uric acid
Secondary Gout (10% of cases)	
Associated with increased nucleic acid turnover—e.g., leukemias	Overproduction of uric acid with increased urinary excretion
Chronic renal disease	Reduced excretion of uric acid with normal production
Inborn errors of metabolism	Overproduction of uric acid with increased urinary excretion, e.g., complete HGPRT deficiency (Lesch-Nyhan syndrome)

HGPRT, hypoxanthine guanine phosphoribosyl transferase.



Negatively birefringent needle shape crystals

Acute arthritis

- Dense inflammation in synovium and synovial fluid.
- Crystals in cytoplasm of neutrophils and synovium.
- Long, slender, needle, negative birefringence.
- Synovium is edematous and congested with few lymphocytes, plasma cells and macrophages.

Chronic tophaceous arthritis

- Repetitive precipitation of crystals.
- **Chalky deposits** in synovium.
- Synovium: hyperplastic, fibrotic and thickened by inflammatory cells that form PANNUS destroy the cartilage.

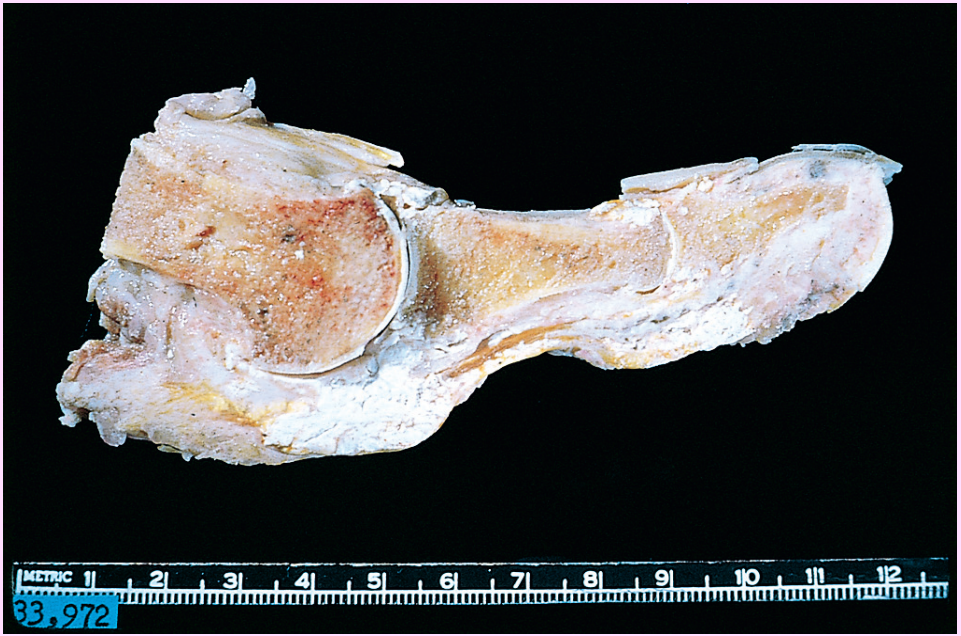
TOPHI

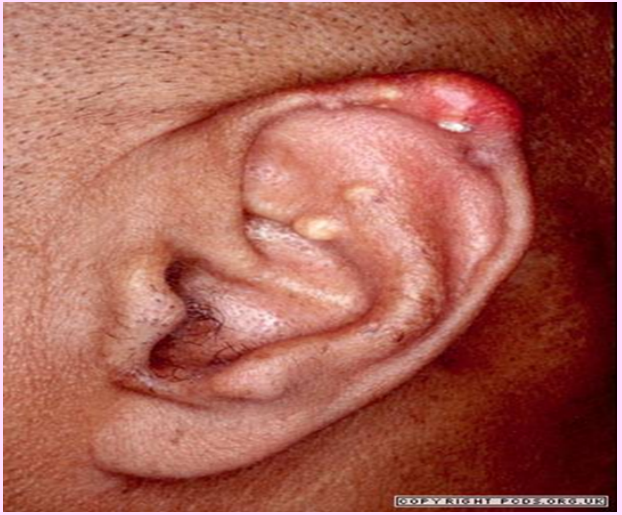
- large aggregations of urate crystals surrounded by an intense foreign body giant cell reaction.
- **cartilage, ligaments, tendons, and bursae are pathognomonic of gout**

Gouty nephropathy

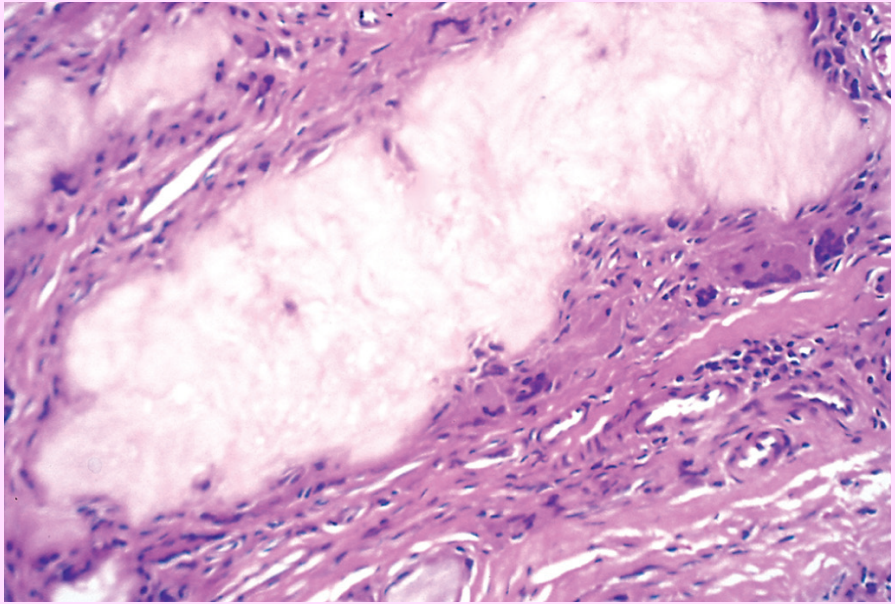
- urate crystals or tophi in the renal medullary interstitium or tubules
- uric acid nephrolithiasis and pyelonephritis.

white tophi involving the
joint and soft tissues





Gouty tophus—an aggregate of dissolved urate crystals is surrounded by reactive fibroblasts, mononuclear inflammatory cells, and giant cells.



Urate crystals are needle shaped and negatively birefringent under polarized light

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Asymptomatic hyperuricemia

- Around puberty in men and after menopause in women.

Acute arthritis

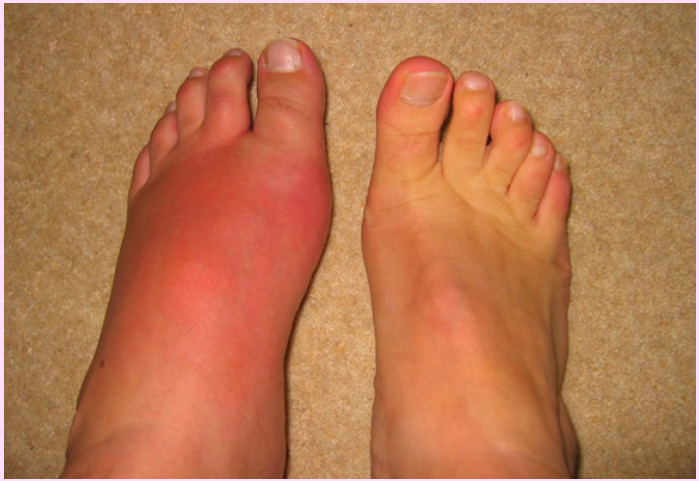
- Sudden, excruciating joint pain, hyperemia, warmth
- 50% metatarsophalangeal joint.
- Last for hours to weeks.

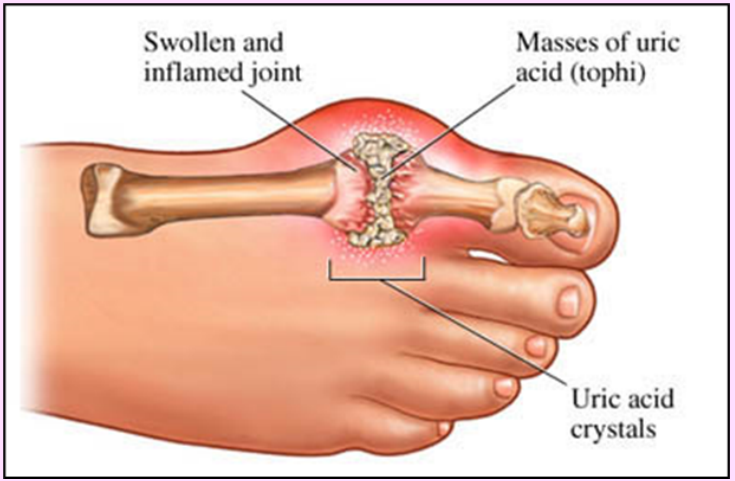
Asymptomatic intercritical period

- Resolution of acute.
- Symptom free.
- Not treated.. Frequent attacks and multiple joints.

Chronic tophaceous gout

- 12 years after initial attack.
- Radiology..loss of joint space.




Swollen and inflamed joint
Masses of uric acid (tophi)
Uric acid crystals

Treatment

- Lifestyle modification
- Reduce symptoms (NSAIDs)
- Lower urate level (medications)

Calcium Pyrophosphate Crystal Deposition Disease (Pseudogout)

- CPPD.
- This condition is due to the deposition of CPPD in the synovium (pseudogout) and articular cartilage (chondrocalcinosis).
- It can occur in three main settings:

1) Sporadic (more common in the elderly).

2) Hereditary.

3) Secondary to other conditions, such as previous joint damage, hyperparathyroidism, hypothyroidism, haemochromatosis and diabetes.

- The crystals first develop in the articular cartilage (chondrocalcinosis), which is usually asymptomatic. From here, the crystals may shed into the joint cavity resulting in an acute arthritis, which mimics gout and is therefore called pseudogout.

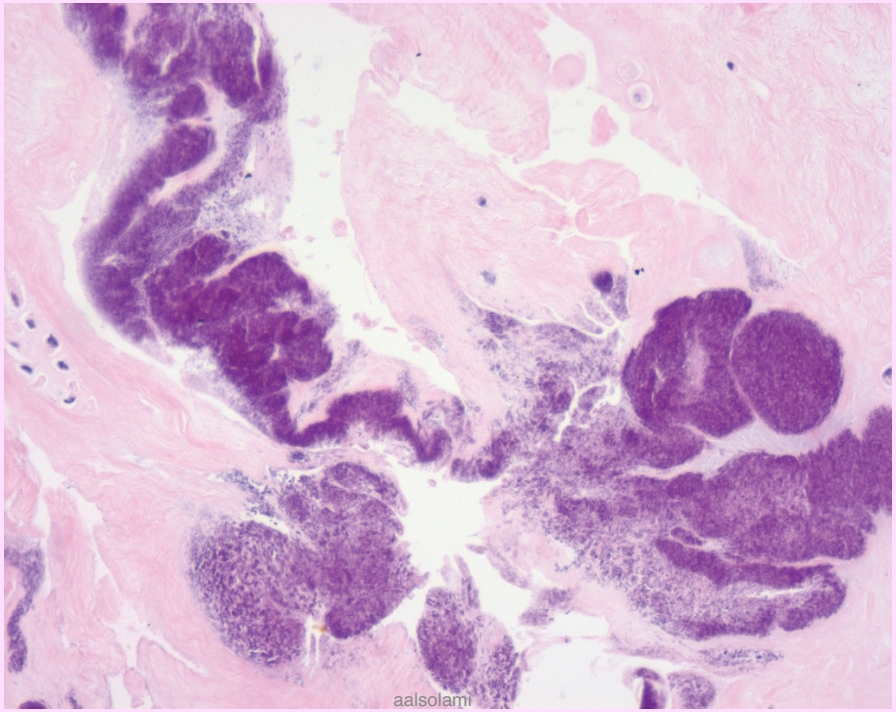
- Pseudogout can be differentiated from gout in three ways:

1) The knee is most commonly involved, wrist, elbow, shoulder, ankle.

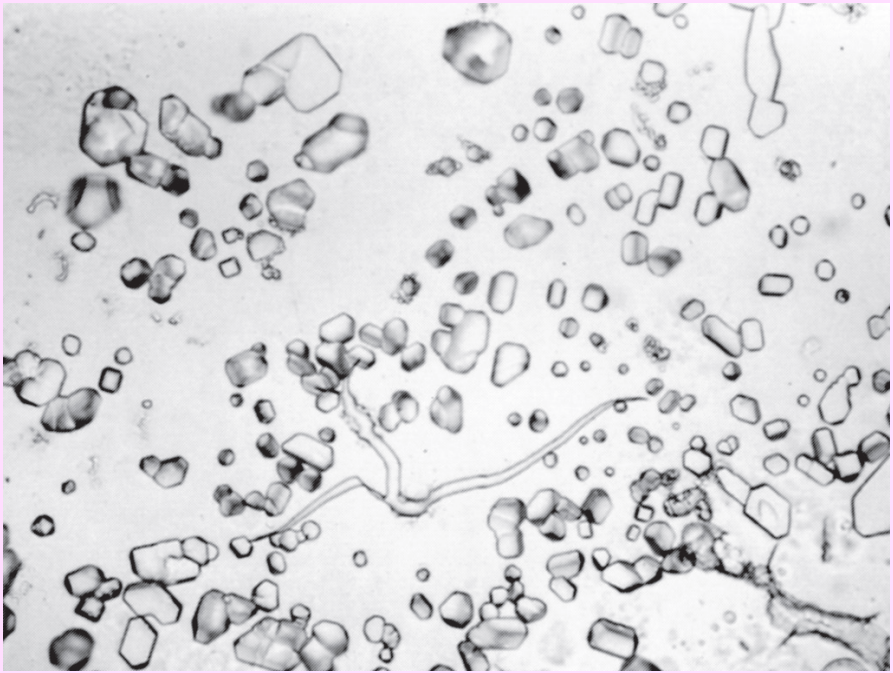
2) X-rays show the characteristic line of calcification of the articular cartilage.

3) The crystals look different under polarizing microscopy, they are rhomboid in shape, positively birefringent .

Deposits are present in cartilage and consist of amorphous basophilic material (blue-purple)



Smear preparation of calcium pyrophosphate crystals.



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OSTEOARTHRITIS (OA)

Type 2 collagen

eburnation

Heberden

Joint mice

osteophyte

Bouchard

RHEUMATOID ARTHRITIS (RA)

CCP

HLA-DR

Ankylosis

Pannus

Swan neck

Boutonniere

GOUT AND PSEUDOGOUT (CRYSTAL-INDUCED)

Tophi

Needle

Rhomboid

birefringence

Reference

Kumar V, Abbas AK, Aster JC. Robbins Basic Pathology. 10th ed. Elsevier; 2017. Philadelphia, PA.
p. 817-821 and 823-826.

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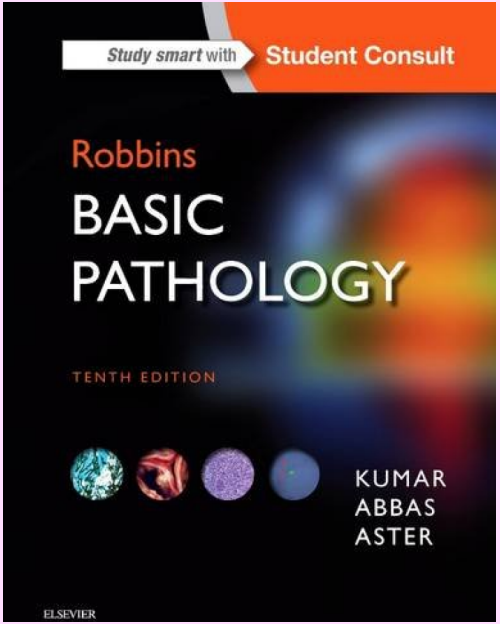

MSK block
Osteomyelitis and Septic arthritis

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Objectives

- Understand the etiology, pathogenesis and clinical features of osteomyelitis.
- Be familiar with some of the terminology used in bone infections like: sequestrum, involucrum, Brodie abscess and Pott's disease.
- Understand the clinicopathological features of tuberculous osteomyelitis
- Identify he bacteria commonly involved in septic arthritis, the clinicopathological features and the characteristics of the joint fluid

Osteomyelitis

- Inflammation of bone and marrow, virtually always secondary to infection.
- Can be: 1) part of systemic infection

  2) primary solitary focus of disease.
- All organisms: viruses, fungi, parasite, bacteria… Pyogenic bacteria and Mycobacteria.

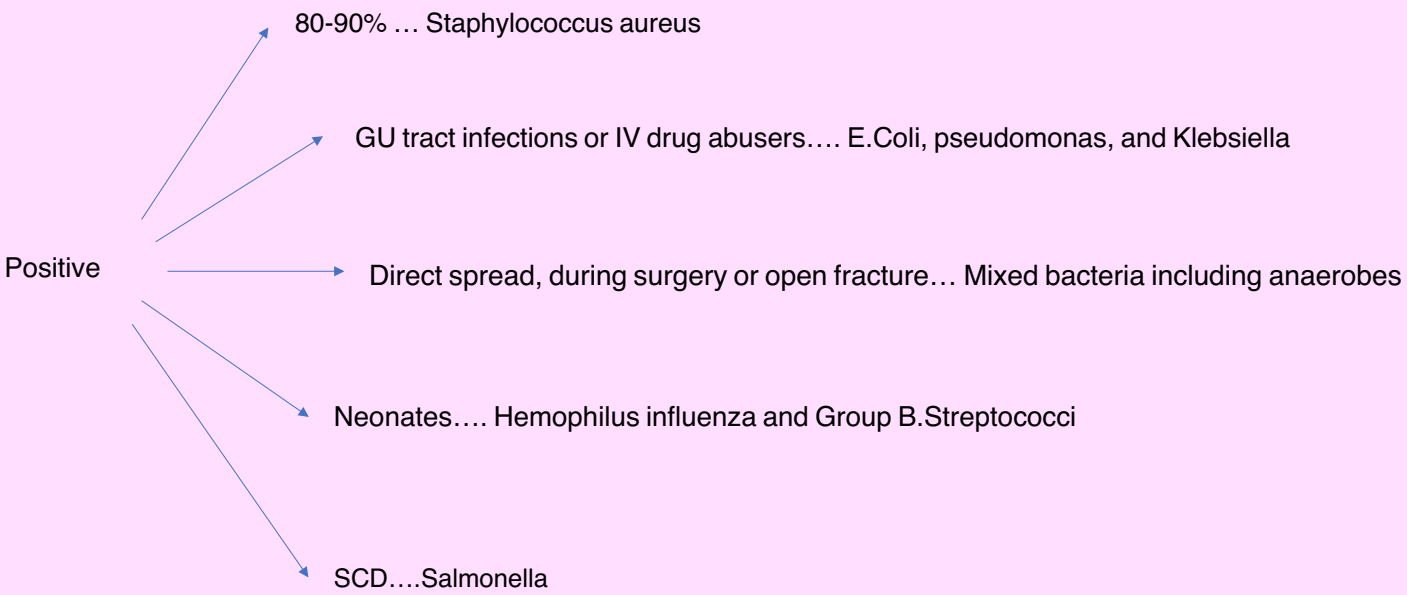
Pyogenic Osteomyelitis

- Almost always caused by bacteria and rarely by fungi.
- Reach bone by: 1) Hematogenous spread
  2) Extension from contiguous site
  3) Direct implantation after compound fractures or orthopedic procedures.

HEALTHY CHILDREN
- Hematogenous.
- Long bones.

ADULTS
- As complication of open fracture, surgical procedures.
- Diabetic foot.

In 50% of cases .. No organisms isolated

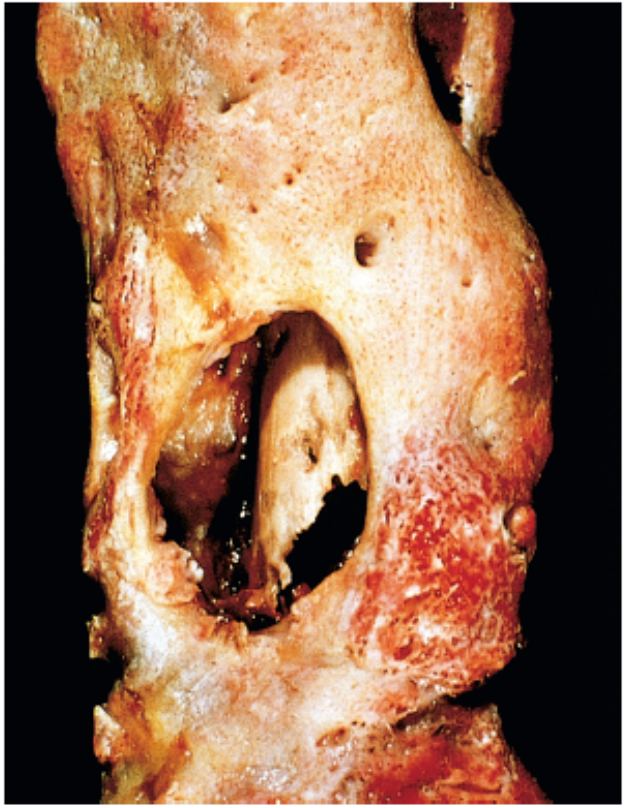


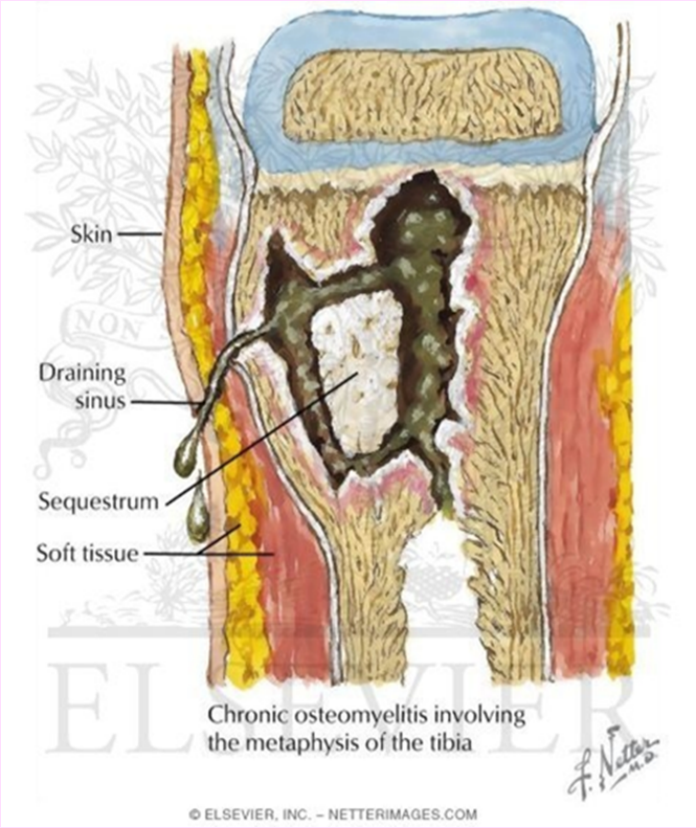
ACUTE

- Bacteria, neutrophil, necrosis (48 hours).
- Spread to reach periosteum.
- Children .. subperiosteal abscess, lift the periosteum and impair blood supply.
- Rupture of periosteum, abscess..skin (draining sinus).
- Dead bone **(SEQUESTRUM).**
- Viable organisms can persist in the sequestrum for years after the original infection

CHRONIC

- After first week.. Chronic inflammatory cell release cytokines..osteoclast, fibrous tissue, deposition of reactive bone at periphery (shell/**INVOLUCRUM**).
- Protean.. Marrow fibrosis, sequestrum, lymphocytes and plasma cell.




Skin
Draining sinus
Sequestrum
Soft tissue
Chronic osteomyelitis involving the metaphysis of the tibia
F. Netter M.D.
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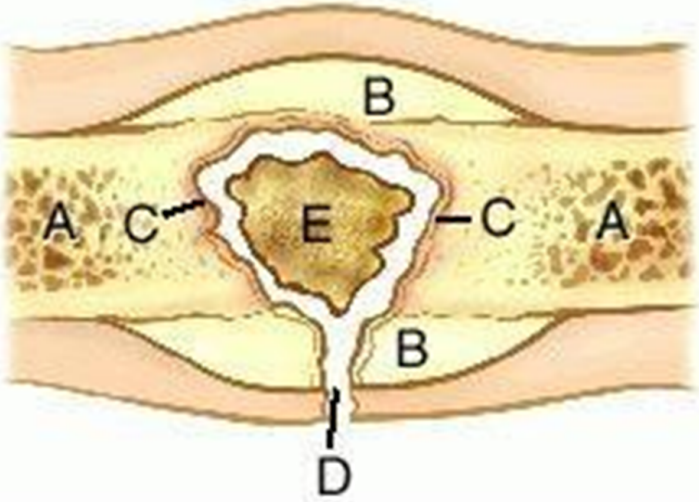
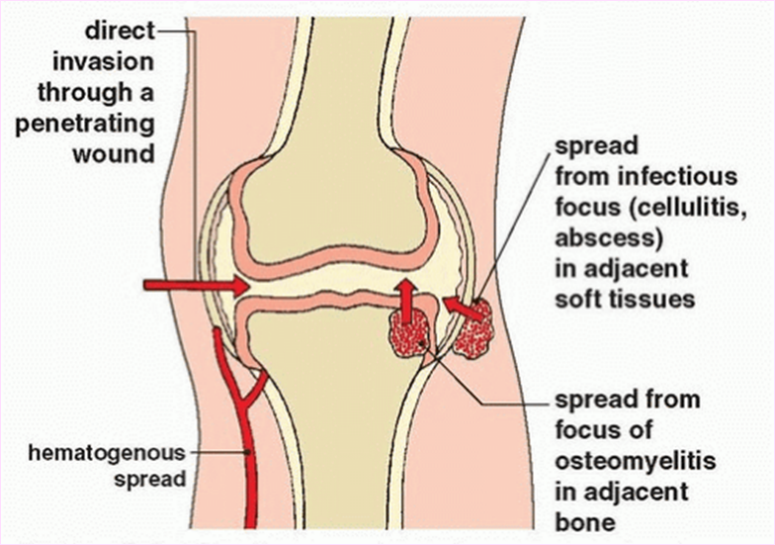


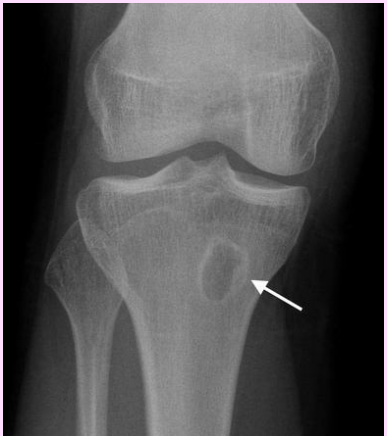
A: healthy bone
B: periosteum
C: involucrum
D: sinus tract
E: sequestrum

Septic (suppurative) arthritis

- Infants (uncommon in adults).
- Infection of epiphysis.. articular surface or along the capsule (tendoligamentous insertion)… Joint.
- Cause destruction to the articular cartilage and permanent disability.



- An analogous process can involve vertebrae, with an infection destroying intervertebral discs and spreading into adjacent vertebrae.
- Brodie abscess is a small intraosseous abscess that frequently involves the cortex



Clinical features

- Acute systemic illness with malaise, fever, chills, leukocytosis, and marked throbbing pain over the affected region.
- Subtle, with only unexplained fever (infants) or localized pain (adults).
- Diagnosis:

1) Signs and symptoms.
2) Radiology (lytic focus of bone destruction surrounded by a zone of sclerosis)
3) Biopsy
4) Bone culture

- Treatment: Treatment requires aggressive antibiotic therapy. Inadequate treatment of acute osteomyelitis may lead to chronic osteomyelitis which is notoriously difficult to manage. Surgical removal of bony tissue may be required.

5-25%.. Chronic osteomyelitis

1. delay in diagnosis
2. extensive bone necrosis
3. inadequate antibiotic therapy
4. inadequate surgical debridement,
5. weakened host defenses.

Acute flare-ups.

COMPLICATIONS:

1. Pathologic fracture.
2. Secondary amyloidosis
3. Endocarditis
4. Sepsis
5. Squamous cell carcinoma if the infection creates a sinus tract.
6. Rarely sarcoma in the affected bone

Mycobacterial Osteomyelitis

Routes of entry:

1. Usually blood borne and originate from a focus of active visceral disease.
2. Direct extension (e.g. from a pulmonary focus into a rib or from tracheobronchial nodes into adjacent vertebrae) or spread via draining lymphatics.

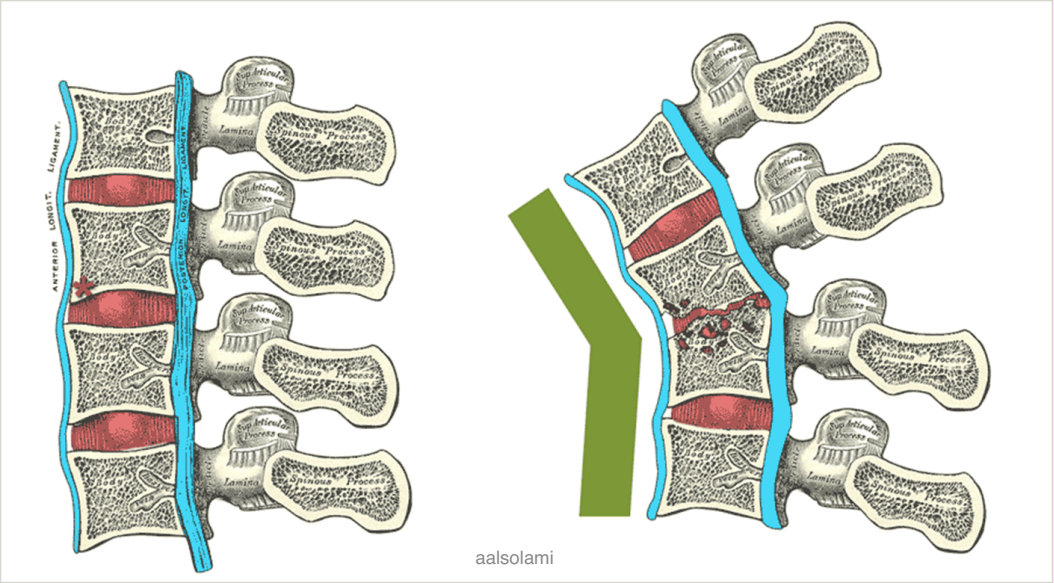
- The bone infection may persist for years before being recognized.
- Approximately 1% to 3% of individuals with pulmonary or extrapulmonary tuberculosis exhibit osseous infection.

- Symptoms: pain, low-grade fever, chills, weight loss.
- Usually solitary except in immunocompromised patients (AIDS).
- Caseous necrosis and granuloma are typical.
- It tend to be more destructive and resistant to control compared to pyogenic osteomyelitis.
- The most common sites of skeletal involvement are:
  - thoracic and lumber vertebrae (40%) followed by the knees and hips
- Pott's disease is the involvement of spine.

Tuberculous spondylitis

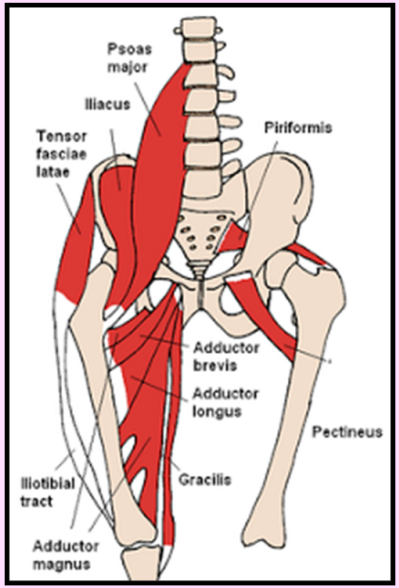
- Pott disease
- Destructive infection of vertebrae.

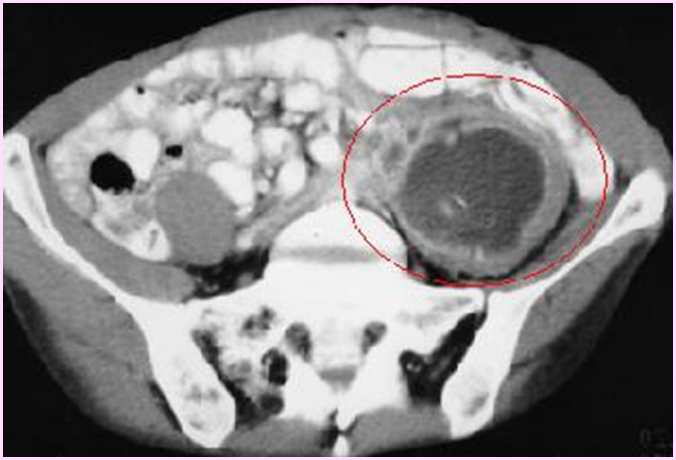
The infection breaks through the intervertebral discs and extends into the soft tissues forming abscesses.



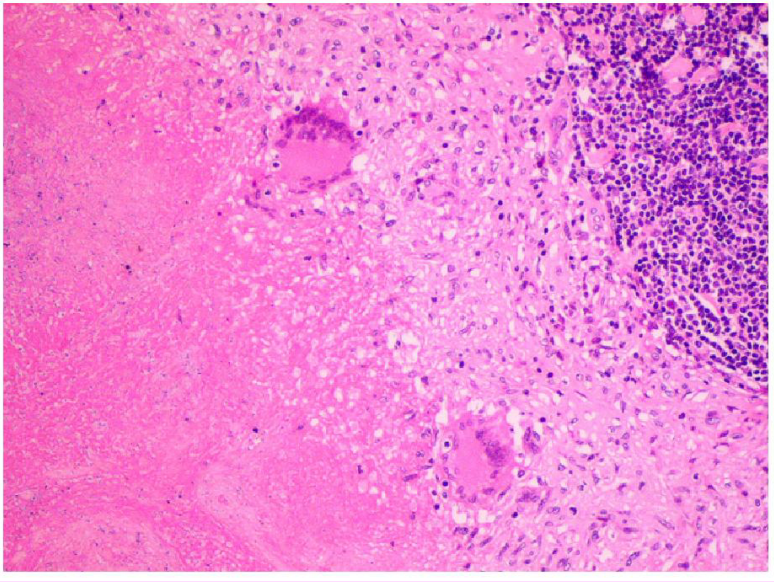
Scoliosis or kyphosis and neurologic deficits secondary to spinal cord and nerve compression

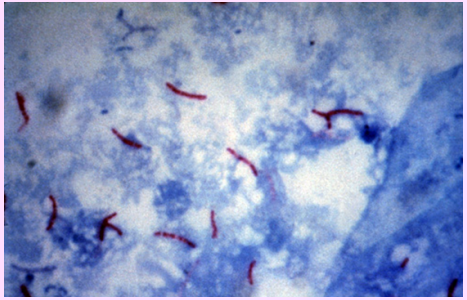
In Pott's disease, the infection may breaks through the intervertebral discs and extends into the muscle forming Psoas abscesses





Histopathology: collections of epithelioid histiocytes and lymphocytes with caseation necrosis





Ziehl Neelsen stain
(ZN or AFB)

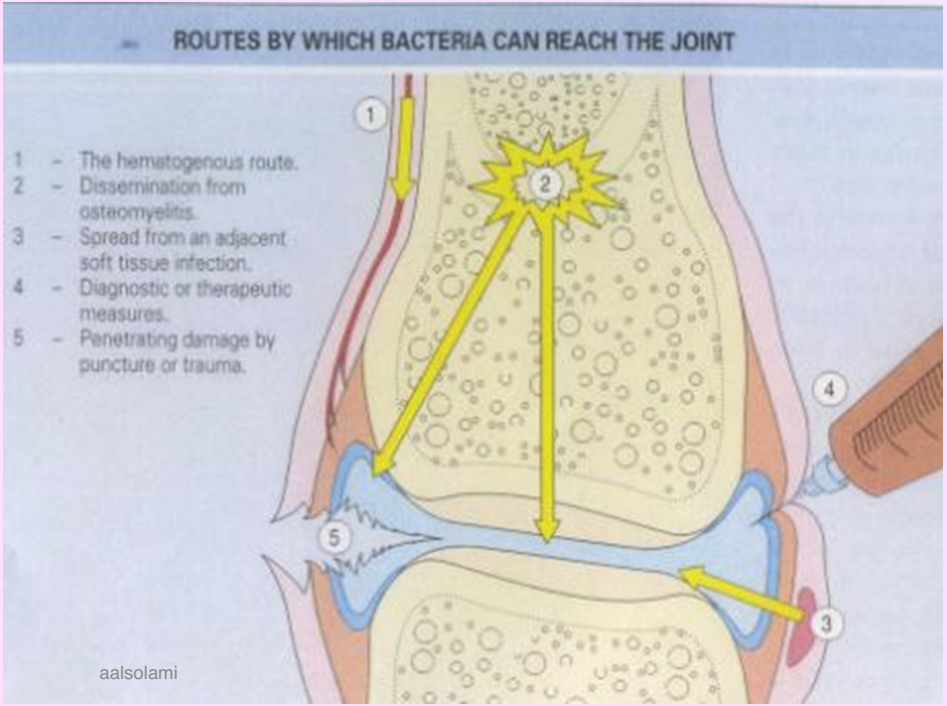
Complications

- Bone destruction
- Tuberculous arthritis
- Sinus tract formation
- Amyloidosis

Infectious arthritis

- Microorganisms of all types can seed joints during hematogenous dissemination.
- In neonates, however, contiguous spread from underlying epiphyseal osteomyelitis may occur
- Articular structures can also become infected by direct inoculation through skin or from contiguous spread from a soft tissue abscess or focus of osteomyelitis.
- Infectious arthritis is potentially serious, because it can cause rapid destruction of the joint and produce permanent deformities

1- hematogenous
2- osteomyelitis
3- adjacent soft tissue infection
4- iatrogenic
5- trauma



Suppurative arthritis

H.Influenza
- Children younger than 2 years.

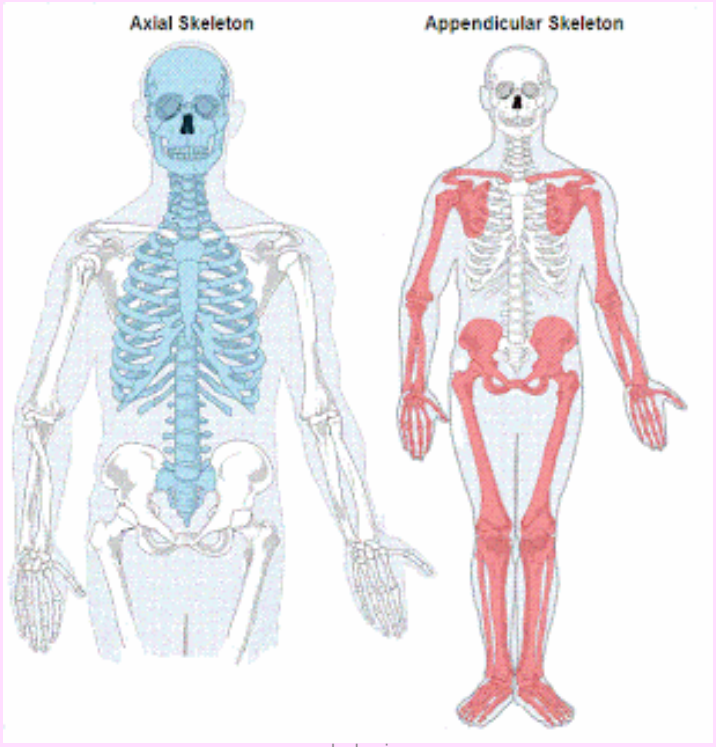
S.Aureus
- Older children and adults.

Gonococcus
- Late adolescence and young adulthood.
- Sexually active women
- Disseminated gonococcal infection in Individuals with deficiencies of complement components (C5, C6, C7, or C9)

.....:
- SCD

Risk factors

1. Immune deficiencies (congenital and acquired)
2. Debilitating illness
3. Joint trauma
4. Intravenous drug abuse (axial joints).


Axial Skeleton
Appendicular Skeleton

- The infection involves only a single joint (in 90% of nongonococcal cases).
- Usually the knee, followed in order by hip, shoulder, elbow, wrist, and sternoclavicular joints.
- Joint aspiration is diagnostic and typically purulent
- Culture allows identification of the causal agent.

Clinical presentation

- Sudden development of an acutely painful, warm, and swollen joint that has a restricted range of motion.
- Systemic findings of fever, leukocytosis, and elevated sedimentation rate are common.
- Cartilage has limited repair potential, so prompt recognition and effective anti-microbial therapy is vital to prevent permanent joint destruction.

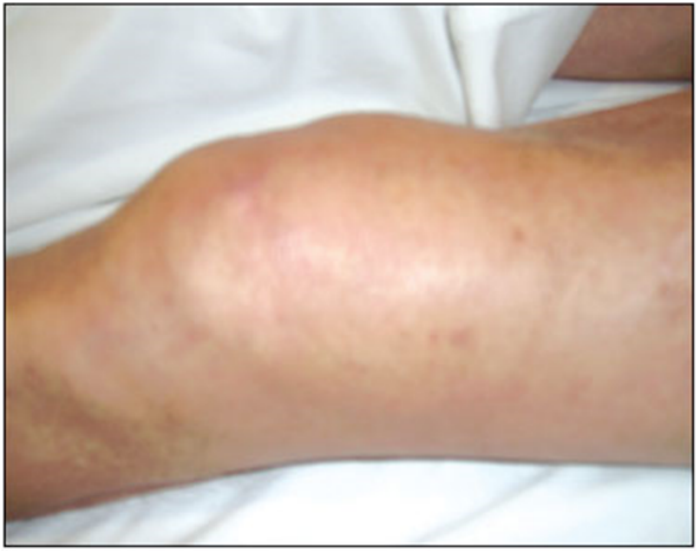
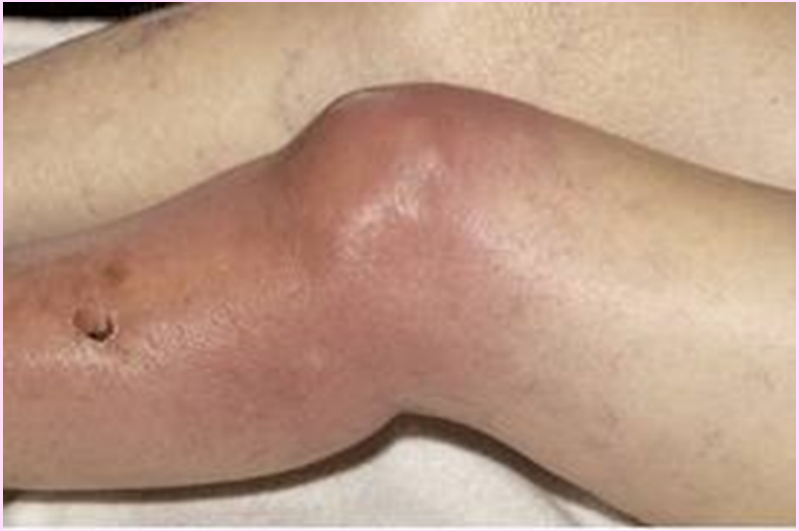
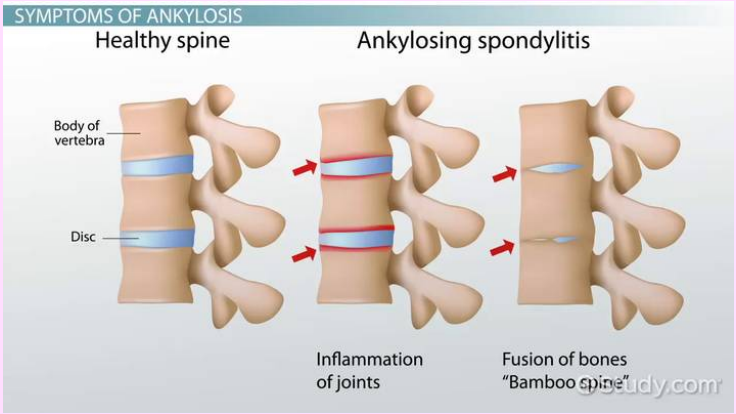


Figure 1
Knee monoarthritis with inflammatory signs.



Complications

- Septic arthritis can lead to ankylosis and even fatal septicemia.
- However, prompt antibiotic therapy and joint aspiration or drainage cures most patients.



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