Non-Neoplastic Bone & Joint Lesions

Infectious

Acute Osteomyelitis

*aka Suppurative or Pyogenic osteomyelitis*

**Acute Inflammation with Bone Destruction**

Necrotic bone with empty osteocyte lacunae. May see brisk osteoclast activity. Bone often appears “moth eaten” (irregular erosions) with lots of “rat bites.”

Often caused by **bacteria** (usually **Staph**)

Can get from hematogenous spread (“primary,” often in kids in metaphysis of long bones or adults in spine).

Can also be from direct inoculation, often from trauma or ulceration (“secondary,” often adults)

Chronic Osteomyelitis

**Chronic Inflammation with Bone Destruction**

Marrow replaced by fibrosis with plasma cells and lymphocytes

Often bone remodeling with osteoclasts and osteoblasts

Plasma cells are polytypic (mixture of kappa and lambda)!

Similar irregular rat/moth-eaten appearance

Often granulation tissue

Necrotizing granulomas ➔ consider Tuberculosis (“Pott’s disease” in spine),

Can have sinus tract to surface line by squamous epithelium ➔ can turn into squamous cell carcinoma.

Septic Arthritis

Neutrophilic inflammation of synovium with accumulation of pus in joint space. Often clinical/lab Dx.

Caused by bacteria, often **Staph** (esp. *S. epidermidis* with prosthetic joints).

Leads to rapid cartilage destruction ➔ acute medical emergency that needs rapid treatment.

Periprosthetic Joint Infection

Can cause prosthetic loosening, requiring revision arthroplasty

If there is concern for infection, will often send joint capsule for frozen section neutrophil count (cutoff often >5 neutrophils/single HPF in 5 separate HPFs, excluding surface fibrin).

**Be SURE it is PMN**—lymphocytes can be twisty and mimic PMNs. Treatment = prosthesis removal and subsequent reimplantation after eradiation.

Also evaluated for clinically based on physical exam, culture, ESR, CRP, and synovial fluid studies.
Degenerative/Reparative Changes

Degenerative Joint Disease

*aka “DJD” or Osteoarthritis (“OA”)*

Non-inflammatory loss joint cartilage, subchondral bone sclerosis, periarticular bone cysts (Geodes), osteophyte formation, and synoviocyte hypertrophy/hyperplasia.

Common result of a variety of factors including trauma, “wear and tear,” metabolic diseases, avascular bone necrosis, and altered loading/anatomy.

If treated surgically → joint arthroplasty

Ganglion Cyst

Cysts composed of fibrous tissue without a lining.

Contain myxoid/mucous material.

Can be unilocular or multilocular.

Seems to arise from joint capsule.

Most often on wrists and hand/feet.

Most common in young adults.

Can surgically excise if bothersome.

Historically, could strike and rupture with a large heavy book (e.g., a Bible) → “Bible bump”

Fracture Callus

Reparative changes seen at a site of prior bone fracture

Immediately after fracture → hemorrhage and hematoma → gradually replaced by organization and granulation tissue

Woven bone, fibrosis, and cartilage with ossification

Prominent osteoblastic rimming and bone remodeling

Fracture can be seen on imaging.

Should NOT see: atypical mitoses, significant cytologic pleomorphism
Avascular Necrosis

Geographic area of subchondral bone and marrow necrosis with partially separated articular cartilage surface ("crescent sign").

Risk factors: Trauma, Steroids, Alcohol, Chemotherapy, Collagen vascular disease, Pregnancy, etc...

→ Leads to DJD/OA → requires joint replacement

Aseptic Joint Loosening

Foreign material wear particles (fragments of prosthetic that have broken off: metal, polyethylene glycol, cement, ceramic, etc..) are ingested by macrophages → causes inflammation around joint → Osteolysis → Joint loosening

Abundant foamy histiocytes, Foreign body giant cells, and inorganic particles.

Wear particles from metal articular surfaces are small and appear black. Accumulate in macrophages and fibrous tissue → “Metallosis”

Metal can even make its way to regional lymph nodes!

Aseptic Lymphocytic Vasculitis-associated Lesion (AVAL)

Seen with metal-on-metal articulations.

Despite name, no true vasculitis.

Three defining features:
1) Prominent lymphoid aggregates, often near venules
2) Absence of obvious metal debris
3) Necrosis of synovium
**Autoimmune Diseases**

**Rheumatoid Arthritis**

Most common primary inflammatory arthropathy. Chronic, idiopathic erosive symmetric polyarthritis. Impacts all joints, but worst impacted are small joints of hands (MCP & PIP), feet, and C-spine. Many extra-articular manifestations (e.g., Lung disease) Serology: Positive Rheumatoid Factor (RF)

- **Chronic Synovitis:**
  Expands synovium with chronic inflammation (lymphocytes and plasma cells), often with lymphoid aggregates. Often reactive/hyperplastic synovium with surface fibrin/fibrinoid necrosis and granulation tissue. May erode nearby bone. Sometimes occasional neutrophils.

- **Pannus**
  Synovium that erodes cartilage and other joint structures → characteristic marginal erosions of bone on X-ray.

- **Rheumatoid nodule:**
  Necrotizing granulomas with central necrobiosis

**Loose Bodies**

Loose fragments of tissue found free within the joint space Can result from trauma, DJD, or neoplasm. Most common in knee → cause locking and pain

- **Fibrinous Loose bodies ("Rice Bodies")**
  Consist of laminated fibrin. Grossly resemble rice grains.

- **Osteochondral or Cartilaginous Loose bodies**
  Detached fragments of articular cartilage ± bone. Result from trauma. Often solitary.

- **Synovial Chondromatosis**
  Locally aggressive neoplasm. Multiple hyaline cartilage nodules within synovium or loose in joint space. Chondrocytes cluster together in groups. FN1-ACVR2A fusions.

**Loose Bodies**

Loose fragments of tissue found free within the joint space Can result from trauma, DJD, or neoplasm. Most common in knee → cause locking and pain

- **Fibrinous Loose bodies ("Rice Bodies")**
  Consist of laminated fibrin. Grossly resemble rice grains.

- **Osteochondral or Cartilaginous Loose bodies**
  Detached fragments of articular cartilage ± bone. Result from trauma. Often solitary.

- **Synovial Chondromatosis**
  Locally aggressive neoplasm. Multiple hyaline cartilage nodules within synovium or loose in joint space. Chondrocytes cluster together in groups. FN1-ACVR2A fusions.

**Loose Bodies**

Loose fragments of tissue found free within the joint space Can result from trauma, DJD, or neoplasm. Most common in knee → cause locking and pain

- **Fibrinous Loose bodies ("Rice Bodies")**
  Consist of laminated fibrin. Grossly resemble rice grains.

- **Osteochondral or Cartilaginous Loose bodies**
  Detached fragments of articular cartilage ± bone. Result from trauma. Often solitary.

- **Synovial Chondromatosis**
  Locally aggressive neoplasm. Multiple hyaline cartilage nodules within synovium or loose in joint space. Chondrocytes cluster together in groups. FN1-ACVR2A fusions.
## Crystalline Diseases

<table>
<thead>
<tr>
<th></th>
<th>Gout</th>
<th>Pseudogout</th>
<th>Tumoral calcinosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>30-50 yrs (middle age)</td>
<td>&gt;50 yrs (older)</td>
<td>10-40 yrs (young)</td>
</tr>
<tr>
<td><strong>Site</strong></td>
<td>1st MTP</td>
<td>Knee</td>
<td>Shoulder, Hips</td>
</tr>
<tr>
<td><strong>Crystal Shape</strong></td>
<td>Needle</td>
<td>Rhomboid</td>
<td>Irregular gritty plates</td>
</tr>
<tr>
<td><strong>Type</strong></td>
<td>Urac acid</td>
<td>Calcium pyrophosphate</td>
<td>Calcium hydroxyapatite</td>
</tr>
<tr>
<td><strong>Polarizable</strong></td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td><strong>Seen on H&amp;E</strong></td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><strong>Inflammatory reaction</strong></td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
</tbody>
</table>

### Gout

**Uric acid metabolic disorder** → hyperuricemia → deposit monosodium urate crystals in joint fluid and tissues

Classically middle-aged males
Most common joint: 1st MTP, but can get anywhere

Uric acid dissolves in water during staining process (so often not seen well on H&E slides), but can be seen on fresh touch preps or unstained slides → *needle-shaped* yellow, negatively birefringent crystals. Joint fluid often neutrophil-rich.

On H&E: See fluffy pink deposits with associated granulomatous inflammation and giant cells. Soft tissue deposits = *“Tophi”*

### Pseudogout

**Calcium Pyrophosphate Dihydrate** (CPPD) deposits in cartilage and joint soft tissue.

Appear as rhomboidal purple positively birefringent crystals. On H&E: well-demarcated basophilic material with virtually no inflammatory response

Often associated with degenerative joint disease.

Often *incidental* finding in arthroplasty finding.

### Tumoral Calcinosis

**Calcium hydroxyapatite deposits**

Common locations: shoulder, sites of pressure

Can be localized in relation to *trauma* or due to a *systemic disorder* (e.g., renal failure or hyperphosphatemia)

Lobules of apatite-type calcifications surrounded by chronic inflammation with a prominent foreign body giant cell reaction

---

Modified from a presentation by Scott Kilpatrick, Cleveland Clinic, USCAP 2021
**Metabolic/Endocrine/Idiopathic**

**Paget Disease**

Localized disorder of bone remodeling characterized by focal areas of increased turnover with excess bone synthesis and resorption.

Often localized to a single bone in elderly men. Early → more resorptive; Late → more synthesis.

Unusually large osteoclasts with increased nuclei and prominent nucleoli. Prominent osteoblastic rimming. Paratrabecular marrow fibrosis.

Unusually thick and thin bone trabeculae

Numerous irregular reversal cement lines and bone scalloping. Mosaic pattern.

Etiology poorly understood

Increased risk of osteosarcoma

**Brown Tumor of Hyperparathyroidism**

Forms a mass lesion. Most common in Mandible and Maxilla.

Hyperparathyroidism (often due to adenoma) → stimulates a proliferation of osteoclasts with fibrous tissue and hemorrhage (resembles many other giant cell-rich lesions, like reparative granuloma), so knowing PTH is key. Treat with parathyroidectomy.

Also can see generalized bone changes with cortical bone loss → osteitis fibrosa cystica

**Osteoporosis**

Decrease in mass of mineralized bone → increased risk of fracture.

Frequent in postmenopausal women (due to estrogen loss) and with general aging. Can also be secondary to a variety of conditions (e.g., hyperparathyroidism, malnutrition) and medications (esp. Steroids).

**Renal Osteodystrophy**

Seen in setting of chronic renal failure.

Increased osteoclast activity → osteoporosis

With renal failure → hyperphosphatemia → secondary hyperparathyroidism → increased osteoclast activity

Also, Vit D deficiency → Hypocalcemia