MUSCULOSKELETAL

PART I
A 63yo female presents with bony swelling in her distal interphalangeal joints without erythema. Her proximal interphalangeal joints, hands, and wrists are normal. What is the underlying cause of her condition?

a. Bacterial infection  
b. Crystal deposition  
c. Wear and tear  
d. Viral infection  
e. Autoantibodies
QUESTION #1
A 63yo female presents with bony swelling in her distal interphalangeal joints without erythema. Her proximal interphalangeal joints, hands, and wrists are normal. What is the underlying cause of her condition?

a. Bacterial infection- septic arthritis
b. Crystal deposition- gout and pseudogout
c. Wear and tear- osteoarthritis
d. Viral infection- transient arthralgia/arthritis
e. Autoantibodies- rheumatoid arthritis
WHY CAN WE RULE OUT GOUT/PSEUDOGOUT?

• The joints are usually swollen, painful, and red in these conditions.

HOW DO WE DIFFERENTIATE BETWEEN RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS?

• There is usually no redness or tenderness of joints in osteoarthritis.
• Rheumatoid arthritis can present with swelling of joints, but redness is not always seen.
OSTEOARTHRITIS

- **Who:** Elderly (usually >60yo), obese, those with trauma to a joint, women
- **What:** Non-inflammatory bone disease involving degeneration of articular cartilage
- **Where:** Hip, knee, cervical and lumbar vertebrae, DIP and PIP
- **Why:** Next slide
- **How (to diagnose):** Imaging

**Other facts**
- Most common type of arthritis
- Enlargement of DIPs = Herbeden’s nodes
- Enlargement of PIPs = Bouchard’s nodes
- Pain in joints after use
- Cartilage loss usually begins on the medial side
THE "WHY" OF OSTEOARTHRITIS

• The mechanical trauma leads to degradation of articular cartilage*
  • Components of cartilage: proteoglycans and type II collagen

Findings

• Fraying of cartilage ("joint mice")
• Eburnation (erosion of overlying cartilage → polished appearance of bone)
• Osteophyte formation (reactive bone formation)
• Subchondral cysts
• NO ANKYLOSIS (fusion)
OSTEOARTHRITIS

1) Eburnation
2) Subchondral cyst
3) Normal articular cartilage

Bouchard node (PIP)
Heberden node (DIP)
RHEUMATOID ARTHRITIS

- **Who:** Women 20-50yo
- **What:** Chronic, autoimmune systemic disease (Type III)
- **Where:** symmetric MCP and PIP joints, wrists, elbows, ankles, knees
- **Why:** Next slide
- **How (to diagnose):** based on clinical presentation and lab findings
  - Can include rheumatoid factor, anti-CCP, antinuclear antibody

Other facts

- Association with HLA-DR4
- Extra-articular manifestations
  - Pleural/pericardial effusions
  - Pulmonary fibrosis
  - Anemia of chronic disease
  - Rheumatoid nodules
    - Extensor surface of the forearm, lungs
    - Central necrosis surrounded by histiocytes
  - Fever, malaise, weight loss
  - Baker’s cyst
    - Swelling of bursa behind knee
THE “WHY” OF RHEUMATOID ARTHRITIS

- Initial inciting agent (virus?) → B cell activation → autoantibodies → immune complex deposition → chronic synovitis and pannus formation → ankylosis

Joint Findings
- Ulnar deviation of fingers
- Usually polyarticular
- **Morning stiffness** (usually >30 minutes that improves with use)
- Swan neck deformity
  - PIP hyperextends while DIP flexes normally
X-Ray: Joint-space narrowing, osteopenia, ulnar deviation of fingers

Swan-neck deformity (flexion of DIP, hyperextension of PIP)
<table>
<thead>
<tr>
<th></th>
<th>Osteoarthritis</th>
<th>Rheumatoid arthritis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Incidence</strong></td>
<td>Elderly, women &gt; men</td>
<td>Women of childbearing age</td>
</tr>
<tr>
<td><strong>Frequent sites</strong></td>
<td>Weight-bearing joints; DIP and PIP</td>
<td>Symmetric involvement; PIP and MCP</td>
</tr>
<tr>
<td><strong>Etiology</strong></td>
<td>Mechanical injury</td>
<td>Autoimmune (type III)</td>
</tr>
<tr>
<td><strong>1° site of destruction</strong></td>
<td>Articular cartilage</td>
<td>Synovial fluid</td>
</tr>
<tr>
<td><strong>Notable features</strong></td>
<td>Osteophytes; joint mice; eburnation</td>
<td>RF; systemic symptoms; HLA-DR4</td>
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<tr>
<td><strong>Treatment</strong></td>
<td>NSAIDs, Tylenol, heat, viscosupplementation (hyaluronic acid injections), intra-articular glucocorticoids, joint replacement</td>
<td>NSAIDs, corticosteroids, disease-modifying agents (e.g. methotrexate), biological agents (e.g. TNF-alpha inhibitors)</td>
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</table>
A 45yo woman presents with swelling, stiffness, and pain involving multiple joints, especially in her hands. Symptoms began 6-7 months prior and have led to significant restriction of her daily activities. She experiences prolonged morning stiffness and generalized fatigue. Tylenol and ibuprofen have provided only minimal relief. Which of the following drugs would provide most rapid and complete relief of her symptoms?

- First, is this osteoarthritis or rheumatoid arthritis?
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d. Sulfasalazine
e. Minocycline
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a. Colchicine- for acute gout
b. Methotrexate- preferred in moderate or severe RA but takes weeks
c. Prednisone- corticosteroid
d. Sulfasalazine- for mild, early seronegative RA
e. Minocycline- for mild, early seronegative RA
QUICK REVIEW: METHOTREXATE

- Inhibits dihydrofolate reductase
- Side effects to know: myelosuppression, fatty liver (ALT/AST elevations), mucositis (painful mouth ulcers), teratogenic
A 35 yo man comes in complaining of severe left hip pain that is terrible when he awakens but improves throughout the day. He also has occasional swelling of his hands and fingers. On physical exam, you notice a gray, dry scaly rash on his knuckles and elbows. X-rays of his lumbar spine and hips show sacroiliitis on the left side. Hand X-rays show severe erosions of the DIP joints on the right. He is HLA-B27 positive. What is the most strongly associated condition?

a. Reiter’s syndrome
b. Budd-chiari syndrome
c. Sjogren syndrome
d. Reye’s syndrome
e. Goodpasture’s disease
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SERONEGATIVE SPONDOYLOARTHROPATHIES ["PAIR"]

What they all have in common: no RF, association with HLA-B27, M>F, axial skeleton involvement

• Psoriatic arthritis
  • Sausage-shaped DIP joints
  • “pencil-in-cup” x-ray
  • Asymmetric, patchy involvement

• Ankylosing spondylitis
  • Sacroiliac joints/spine inflammation
  • Ankylosis ("bamboo spine")
    • Can’t bend forward
    • Restrictive lung disease
  • Also uveitis, aortic regurgitation

• IBD + arthritis/spondylitis

• Reiter’s syndrome (reactive arthritis)
  • Post GI (Shigella, Salmonella, Yersinia, Campylobacter) or post-chlamydia infection
  • “Can’t see, can’t pee, can’t climb a tree” (conjunctivitis/uveitis, urethritis, arthritis)
A 64 yo Caucasian male with repeated episodes of ankle arthritis notices a nodule near his right knee joint. Biopsy reveals many inflammatory cells that are negatively birefringent under polarized light. The crystals most likely represent:

a. Uric acid
b. Calcium oxalate
c. Calcium pyrophosphate
d. Monosodium urate
e. Calcium hydroxyapatite

+ birefringence = ___________ when parallel
- birefringence = ___________ when parallel
GOUT

- Needle-shaped monosodium urate crystals
- Negative birefringence
- Associated with Lesch-Nyhan, leukemia, renal insufficiency, Von Gierke’s disease
- Radiolucent

PSEUDGOUT

- Rhomboid-shaped calcium pyrophosphate dehydrate (CPPD)
- Positive birefringence
- Associated with hemochromatosis, hemosiderosis, 1° hyperparathyroidism
- Can be radiopaque

Rx for acute:
- NSAIDs, steroids, colchicine

Crystal uptake by neutrophils → free radical release, cytokine production, and inflammatory response

Joint is painful, swollen, and red
QUESTION #5

A 35yo male with a history of peptic ulcers develops sudden onset pain, swelling, and redness of his 1st right metatarsophalangeal joint. Needle aspiration shows needle-shaped, negatively birefringent crystals. (Stop here... gout or pseudogout?) He is prescribed a medication, but calls you back in one day saying he developed nausea, vomiting, and diarrhea. What is the mechanism of action of the drug prescribed?

a. Inhibit microtubule formation
b. Inhibit xanthine oxidase
c. Inhibit reabsorption of uric acid in proximal convoluted tubule
d. Inhibit cyclooxygenase
e. Inhibit TNF-alpha
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a. Inhibit microtubule formation- colchicine
b. Inhibit xanthine oxidase- allopurinol
c. Inhibit reabsorption of uric acid in proximal convoluted tubule- probenecid
d. Inhibit cyclooxygenase- NSAIDs
e. Inhibit TNF-alpha- etanercept, infliximab
TREATMENT OF GOUT

• **Acute gout attacks**
  • **NSAIDs are 1st line**
  • **Colchicine** is 2nd line (due to GI side effects)
    • Binds tubulin, inhibiting polymerization which impairs leukocyte migration and phagocytosis
    • Recommended for those who can’t take NSAIDs
  • **Glucocorticoids** if NSAIDs and colchicine contraindicated (e.g. renal failure)

• **Chronic - contraindicated in acute gout**
  • **Allopurinol**
    • inhibits xanthine oxidase, decreasing conversion of xanthine to uric acid
  • **Febuxostat**
    • inhibits xanthine oxidase
  • **Probenecid**
    • inhibits reabsorption of uric acid in PCT
A mother brings her 3yo son to the physician for an annual check-up. The doctor notes that the child has had 5 bone fractures, 3 of which resulted from minimal trauma. Her pregnancy was normal. The child has been in the 50th percentile for both height and weight since birth. On exam, this is a pleasant child with normal stature, small teeth, and no bruising. His eyes appear as below. What is the primary impairment?

a. Endochondral ossification
b. Bone matrix formation
c. Epiphyseal vascular supply
d. Intramembranous ossification
e. Nothing because this is child abuse
OSTEOGENESIS IMPERFECTA

• “Brittle bone disease”

• Most common: Autosomal dominant, deficiency/abnormality with type 1 collagen → bone matrix formation impairment
  • Type 1 collagen in bones, teeth, ligaments, skin, and sclera
  • Usually gives flexibility to bone

• Clinical findings
  • Pathologic fractures (Mimics child abuse, but no bruising)
  • Blue sclera (actually seeing underlying choroidal veins due to thinning of collagen)
  • Hearing loss (middle ear bones are abnormal/fracture easily)
  • Dental problems (lack of dentin)

• Treatment: bisphosphonates to increase mineralization
QUESTION #7

A 24 year old African American female presents with constant left hip pain exacerbated by weight-bearing but also present at rest. She has a history of acute chest syndrome and pneumococcal pneumonia. Her vital signs are listed below. There is restriction of movement at the left femoral joint, without redness or warmth. What is the most likely cause of pain?

- Temperature: 99 F  
- BP: 110/65  
- Pulse: 110  
- Respiration: 15

a. Osteomyelitis  
b. Osteoporosis  
c. Paget’s disease  
d. Avascular necrosis  
e. Osteochondritis dissecans
AVASCULAR (ASEPTIC) NECROSIS

- Most common location: femoral head
- Infarction of bone and marrow due to impaired blood supply
- Most common cause: trauma or fracture
- Also associated with:
  - Sickle cell disease
  - Alcoholism
  - Long-term corticosteroid use
  - Decompression sickness (Caisson disease)
- Diagnosis: MRI most sensitive

Presentation: Groin pain worsened by weight bearing; painful, restricted passive and active movement, no swelling or erythema
An 80yo male presents with bone pain and changes in facial features. He has had progressive deformities of his legs and arms with chronic, diffuse bony pain. Lab studies show elevated alkaline phosphatase and urine hydroxyproline. X-rays suggest Paget disease. What is the possible underlying mechanism?

a. Generalized reduction in bone mass
b. Genetic deficiency of carbonic anhydrase II
c. Paramyxovirus infection of osteoclasts
d. Monoclonal proliferation of plasma cells
e. Overproduction of growth hormone
QUESTION #9

An 80yo male presents with bone pain and changes in facial features. He has had progressive deformities of his legs and arms with chronic, diffuse bony pain. Lab studies show elevated alkaline phosphatase and urine hydroxyproline. X-rays suggest Paget disease. What is the possible underlying mechanism?

a. Generalized reduction in bone mass - osteoporosis
b. Genetic deficiency of carbonic anhydrase II - osteopetrosis
c. Paramyxovirus infection of osteoclasts
d. Monoclonal proliferation of plasma cells - multiple myeloma
e. Overproduction of growth hormone - acromegaly
PAGET DISEASE
AKA OSTEITIS DEFORMANS

Who: Primarily middle-aged to elderly males

What: Increased osteoclast and osteoblast activity → disorganized bone remodeling → mosaic bone pattern that fractures easily

Where: spine, pelvis, skull, femur, tibia

Why: recent technique shows paramyxovirus in osteoclasts of affected bones, but still unknown

How (to diagnose): radiology
PAGET DISEASE

• Clinical features
  • Bone pain
  • **Increasing hat/shoe size**
  • Hearing loss
  • **Elevated alk phosp** (normal Ca, PTH, phosphorus)
  • Lion-like facies

• Complications
  • High-output cardiac failure
    • AV shunts within vascular lesions
  • **Osteosarcoma**
A QUICK NOTE ON SOME THE OTHER ANSWERS...

• **Osteopetrosis:** “marble bone disease”
  - poor osteoclast function → thick, dense bones
  - Often mutation in carbonic anhydrase II
  - X-ray: bone-in-bone appearance, very dense (bright white)
  - Sx: bone fractures, pancytopenia, blindness, deafness, hydrocephalus
  - Rx: bone marrow transplant

• **Acromegaly**
  - Overproduction of growth hormone
  - Big head, hands, feet
  - Hypertension, 2° diabetes, cardiomegaly, osteoporosis
OSTEOPOROSIS

- Decreased trabecular bone mass and density
  - Due to loss of organic bone matrix and minerals
- Women > men
  - Related to peak bone mass
- **Normal lab values** (calcium, phosphate, PTH, alk phosphatase)
- X-ray: diffuse radiolucency of bone
- Prone to **vertebral crush fractures**
  - Acute pain, shortened stature, kyphosis
- May be primary or secondary
  - Secondary causes: hypercortisolism, hyperthyroidism, anorexia nervosa
PRIMARY OSTEOPOOROSIS

Postmenopausal

- Decreased estrogen leads to increased bone resorption
- Associations: femoral neck fracture, Colles’ fractures

Senile

- Decreased ability of osteoblasts to divide/produce osteoid
- Usually seen in >70 yo

Prevention

Weight-bearing exercise, adequate Vit D and Calcium, smoking cessation

Treatment

Bisphosphonates
Estrogen replacement is debatable
RISK FACTORS FOR OSTEOPOROSIS

- Menopause
- Caucasian female
- Smoking
- Alcohol
- Physical inactivity
- Corticosteroid therapy

Menopause Sucks
<table>
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<tr>
<th>Disease</th>
<th>Calcium</th>
<th>Phosphate</th>
<th>PTH</th>
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<tr>
<td>Osteoporosis</td>
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<tr>
<td>Paget disease</td>
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<td>Normal</td>
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<tr>
<td>Osteopetrosis</td>
<td>↓</td>
<td>normal</td>
<td>normal</td>
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<tr>
<td>Osteomalacia/Rickets*</td>
<td>↓</td>
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<tr>
<td>Von Recklinghausen disease**</td>
<td>↑</td>
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*Vit D deficiency → decreased calcium → increased PTH → decreased phosphate; hyperactivity of osteoblasts → increased alkaline phosph

**also known as osteitis fibrosa cystica: widespread osteolytic lesions due to hyperparathyroidism, can manifest as brown tumors and diffuse radiolucency of bone
A 16 year old boy presents with left knee pain and swelling that has been present for a month. He thought the pain was from an old basketball injury, but it has persisted and caused him to limp. X-rays of the knee show a sunburst pattern next to lifting of the periosteum. What is the most likely diagnosis?

a. ACL tear with avulsion
b. Ewing sarcoma
c. Giant cell tumor
d. Osteosarcoma
e. Chondrosarcoma
MALIGNANT BONE TUMORS

- **Multiple myeloma** - Most common 1° malignant
  - Proliferation of plasma cells in bone marrow
  - Monoclonal M protein spike, other systemic sx
  - Punched-out lytic bone lesions

- **Osteosarcoma** - 2nd common 1° malignant
  - Males 10-20yo
  - Risk factors: retinoblastoma, Paget’s disease, radiation
  - X-ray: sunburst appearance, lifting of periosteum (Codman triangle)
  - Metaphysis, usually around knee
  - Aggressive, requires chemo and surgical resection
MALIGNANT BONE TUMORS

- **Ewing sarcoma**
  - Anaplastic “small blue cell” tumor usually in diaphysis
  - Boys <15 yo (can mimic acute osteomyelitis in this age group)
  - (11;22) translocation
  - X-ray: “onion skin”
  - Often metastasizes, responds to chemotherapy

- **Chondrosarcoma**
  - Men 30-60 yo
  - Glistening mass within medullary cavity

- **Metastatic**
  - More common than primary tumors
  - Punched-out lesions
EWING SARCOMA

“ONION SKIN” = DUE TO PERIOSTEAL REACTION
BENIGN BONE TUMORS

- **Osteochondroma**
  - Most common benign
  - Tumor of bone with overlying cartilage cap
  - Usually grows laterally from metaphysis
  - Males <25 yo

- **Giant cell tumor (osteoclastoma)**
  - 20-40yo, females slightly more than males
  - “soap bubble”/”double bubble” on X-ray
  - Epiphyseal end, often around knee
  - Multinucleated giant cells and oval/spindle-shaped cells
OTHER BENIGN BONE TUMORS

- **Osteoma**
  - usually on facial bones
- **Osteoid osteoma**
  - osteoblast tumor usually in femur
- **Chondroma**
  - usually in small bones of hands/feet
**Skeletal Muscle Inflammatory Disorders**

**Polymyositis**
- Progressive symmetric proximal muscle weakness
  - Most often shoulders
- T cell-mediated damage
  - **Endomysial inflammation** with CD8+ T cells

**Dermatomyositis**
- Polymyositis + **skin involvement**
  - heliotrope rash, Gottron papules, malar rash
- Antibody-mediated damage
  - **Perimysial inflammation** with CD4+ T cells

- Inflammatory disorders of skeletal muscle +/- skin
  - Increased CK, positive ANA, positive anti-Jo-1 antibodies*
  - Women 40-60 years old
  - Rx: steroids
A 48yo man presents with worsening knee pain. X-rays show fine, radiographically dense crystals in the tissues of the knee joint. What is the most likely diagnosis?

A. Gonococcal arthritis
B. Osteoarthritis
C. Gout
D. Rheumatoid arthritis
E. Pseudogout
A woman presents with lower back pain. Physical exam shows coarse facial features and kyphosis. Lab results are significant for increased alkaline phosphatase. A bone biopsy shows a mosaic pattern of bone spicules with prominent osteoid seams. What kind of cancer is she at an increased risk of developing?

A. Hodgkin lymphoma
B. Osteochondroma
C. Ewing sarcoma
D. Osteosarcoma
E. Non-Hodgkin lymphoma
A 34 yo Caucasian male has mild urethritis that resolves. Swabs are negative for gonococcal infection. Two weeks later, he experiences conjunctivitis, right knee pain, and a vesicular rash on his palms and soles. What else is this associated with?

A. periostitis
B. hyperuricemia
C. sacroiliitis
D. infectious arthritis
E. pancreatitis
POST-TEST

What factor is most consistent with curve A?

A. Menopause
B. Physical inactivity
C. Black race
D. Smoking
E. Steroid use