Step 1 Musculoskeletal Review
Case 1: An 80 year old male is in clinic because he has a 4-week history of lower back pain. Radiologic image studies are consistent with osteoblastic (bone forming lesions) throughout the lower vertebrae and pelvis.

Labs...

**ESR: 35mm/h** (normal 0-20)
Calcium: 8.6 mg/dl (8.5-10)
Alk Phos: **100 U/L** (normal 20-70)

What is this?
A. Lung Cancer
B. Prostate Cancer
C. Multiple Myeloma
D. Breast Cancer
Take Home Points:

1. Metastatic tumors are more common than primary bone tumors.

2. Metastatic bone tumors are usually osteolytic (bone resorbing) lesions (lung cancer, multiple myeloma).

3. Prostate cancer is the exception, with metastases showing osteoblastic (bone forming lesions) of the axial skeleton e.g. spine, pelvis.

4. Alkaline Phosphatase is an indirect measure of osteoblast activity and is an enzyme that helps to lay down bone by providing an alkaline environment. It will be increased with osteoblastic lesions.

5. Think prostate cancer in an elderly male with new onset back pain and multiple bone lesions on imaging.
Case 2: A 30 year old man with a recent history of bloody diarrhea, is now complaining of a painful, swollen knee. He also has been had difficulty urinating and upon physical exam he is found to have bilateral conjunctivitis with a mucopurulent discharge.

Labs...
Stool Antigen test (from 2 weeks ago): **Positive for Shiga Toxin.**
Serum rheumatoid factor: Negative

What is this?
A. Septic Arthritis
B. Reactive Arthritis
C. Rheumatoid Arthritis
D. Osteoarthritis
“Can’t see, can't pee, can't climb a tree” = Reactive Arthritis (Autoimmune not infectious)

Take Home Points:
1. Spondyl means spine, Arthro means joint, Pathy means something is wrong

2. Rheumatoid factor is an IgM antibody against the Fc portion of IgG antibodies in a patients serum, which is typically found in rheumatoid arthritis.

3. Reiter syndrome (Reactive arthritis) is a seronegative (no rheumatoid factor) spondyloarthropathy.

4. It is classified by the classic triad of urethritis, conjunctivitis, and arthritis.

5. This is an autoimmune disease of young males, and is associated with HLA-B27.

6. It is associated with prior infection of Shigella, Salmonella, Yersinia, Camylobacter, and Chlymadie.
Quick Quiz: What other diseases are associated with HLA-B27?
Quick Quiz: What other diseases are associated with HLA-B27?

Psoriatic arthritis
Ankylosing spondylitis
Inflammatory Bowel Disease
Reactive Arthritis
Case 3: An 85 year old man complains of diffuse bone pain in his lower back, leg, and pelvis. He also has noticed that his had does not fit him anymore, and that he has to turn up the television a lot more to be able to hear. His wife says that his face looks different.

Labs...

Alk Phos: **120 U/L** (normal 20-70)
Calcium: 8.9 mg/dl (8.5-10)
Parathyroid Hormone: 450 pg/ml (230-630)
Urine: **Hydoxyproline** present

What would be a severe complication of this disease?
A. High output cardiac failure
B. Hypocalcemia leading to arrhythmias
C. Hypercalcemia leading to arrhythmias
D. Metastatic calcification
Some Histopathology
Take Home Points:

1. Paget’s Disease is a chronic disorder, primarily affecting elderly males, that results in patterns of enlarged deformed bone. This bone is weak and structurally unsound.

2. Hearing loss can result due to impingement of cranial nerves and a Lion-like face results from increased bone mass. Micro fractures of bone cause chronic pain.

3. A mosaic pattern is seen microscopically on a section of lamellar bone. This pattern refers to the multiple, irregular fracture lines present.

4. Most common cause of isolated elevated alkaline phosphatase in patients >40 years old.

5. Possibly caused by a virus that infects osteoclasts (paramyxovirus). Serious complications include high output cardiac failure due to A-V shunt formation in irregular bone, and increased risk of osteosarcoma.
**More Take Home Points:**

6. 4 Stages of Disease:
   1. Lytic/Osteoclastic
   2. Mixed
   3. Sclerotic/Osteoblastic
   4. Quiescent

7. Can see hydroxyproline in the urine, a major component of type 1 collagen.

8. Can be monostotic (affecting one bone), or polystotic (affecting many bones).

9. Serious complications include high output cardiac failure due to A-V shunt formation in irregular bone, and increased risk of osteosarcoma.
Case 4: A 2 year old boy is has been recently been grabbing onto furniture to help him get up from a seated position. On exam his calf muscles are also enlarged. It was also mentioned that a cousin on his mother’s side is a few years older and has been experiencing progressive muscle weakness.

Labs...
Serum Creatinine Kinase: **130U/L** (25-90)

What genetic mutation doe this boy have?
A. Point mutation in dystrophin gene
B. Frameshift mutation of the dystrophin gene
C. CTG trinucleotide repeat
D. GAA trinucleotide repeat
Take Home Points:
1. Duchenne muscular dystrophy (X-linked muscular dystrophy) is characterized by wasting and replacement of muscle by fat and is typically seen in boys under 6 years old.

2. Weakness begins near the hip and then moves upward to involve the shoulders and arms, and downward to involve the calf muscles.

3. Grower’s sign may be present, which is where patients use their arms to help them stand up.

4. Dystrophin gene is the largest gene in the human genome and is at an increased risk for spontaneous mutation.

5. In Duchenne muscular dystrophy a frameshift mutation leads to the absence of functional dystrophin protein which normally anchors muscle cells to the ECM.
More Take Home Points:

6. Death is due to cardiac or respiratory failure.

7. Becker muscular dystrophy is a milder form of disease where there is a point mutation in the dystrophin gene but the a mutated dystrophin protein is still produced.

8. CTG repeats are associated with myotonic dystrophy

9. GAA repeats are associated with Friedreich ataxia
Case 5: A 75 year old women complains of a swollen, tender, right knee. She is currently taking a thiazide diuretic. Aspiration of synovial fluid reveals basophilic rhomboid crystals that are weakly positive birefringent.

Labs...
Serum uric acid: 5.0mg/dl (3.0-8.2)

What are these crystals made out of?
A. Calcium Pyrophosphate crystals
B. Monosodium Urate Crystals
C. Struvite
D. Cholesterol
**Take Home Points:**

<table>
<thead>
<tr>
<th>Pseudogout</th>
<th>Gout</th>
</tr>
</thead>
<tbody>
<tr>
<td>Affects larger joints like the knee</td>
<td>Typically affects smaller joints first (big toe)</td>
</tr>
<tr>
<td>Crystals are rhomboid and + birefringent</td>
<td>Crystals are needle shape and - birefringent</td>
</tr>
<tr>
<td>Crystals are made out of calcium pyrophosphate</td>
<td>Crystals are made out of monosodium urate</td>
</tr>
<tr>
<td>Affects both sexes equally</td>
<td>Affects males more frequently</td>
</tr>
</tbody>
</table>

Negative birefringence means yellow when parallel(II) to the light.
Case 6: A 7 year old boy is brought to the physician for a 4-cm enlarging mass on the right side of his neck. Biopsy shows poorly differentiated small round and spindle shaped cells.

Labs...

Fluorescent desmin immunoassay of biopsy tissue: **Positive**

What is this?
A. Lipoma
B. Liposarcoma
C. Rhabdoma
D. Rhabdomyosarcoma

H&E stain of tumor biopsy
Take Home Points:

1. Sarcoma means a tumor of connective/mesenchymal tissues

2. Rhabdomyosarcoma is a malignant tumor of striated/skeletal muscle.

3. Most common malignant soft tissue tumor in children, typically found in the head and neck.

4. Can be found in the genitourinary tract of young girls, and would present as a “grapelike” lesion (botryoid rhabdomyosarcoma).

5. Desmin in a component of skeletal muscle cells and is used for tumor identification.
Case 7: A 10 year old boy is brought to the physician because of a pain in his right thigh. A 5cm firm mass in palpable is warm to the touch. X-ray shows a concentric, periosteal reaction surrounding the mass. He has a fever of 99.4F and a pulse of 80 beats/min.

ESR: **35mm/h** (normal 0-20)
Total leukocytes: **13000/mm³** (normal is 3000 to 11000)

What is this?
A.Osteomyelitis  
B.Ewig Sarcoma  
C.Osteosarcoma  
D.Sepic Arthritis

![Tumor biopsy](image-url)
Take Home Points:
1. Ewig’s sarcoma is a highly aggressive, poorly differentiated malignancy of neuroectoderm cells that is found in the diaphysis of long bones in children <15 years old.

2. Systemic signs can be present including, fever, anemia, leukocytosis, and elevated ESR.

3. Small, blue cells with a high nuclear to cytoplasmic ratio, hyperchromatic nuclei, and mitotic figures.

4. Produces a characteristic “onion-skin” appearance on x-ray

5. Responsive to chemotherapy

6. Osteosarcoma would be found in the metaphysics of long bones, not the diaphysis.

Case 8: A young child who is poorly nourished is found to have small firm nodules along the costochondral junction of the anterior chest wall. His legs are also bowed slightly and he has frontal bossing (enlarged forehead).

What laboratory values would you expect to find?

Calcium: (high/low)
PO4: (high/low)
PTH: (high/low)
Alkaline Phosphatase: (high/low)
Take Home Points:

1. Rickets is a condition seen in children due to defective mineralization of osteoid (the connective tissue that osteoblasts lay down made out of type 1 collagen).

2. It is most commonly due to vitamin D deficiency but can also be due to inadequate dietary calcium intake.

3. Labs values:

<table>
<thead>
<tr>
<th>Calcium</th>
<th>PO4</th>
<th>PTH</th>
<th>Alkaline Phosphatase</th>
</tr>
</thead>
<tbody>
<tr>
<td>low</td>
<td>low</td>
<td>high</td>
<td>high</td>
</tr>
</tbody>
</table>

4. Clinical signs will include: bowing of the legs in ambulating children, Rachitic rosary, Frontal bossing, Pigeon-breast deformity.

5. The Rachitic rosary and Frontal bossing result from increased osteoid deposition. The osteoblasts are hyperactive leading to increased alkaline phosphatase.
Quick Quiz: Does Rheumatoid arthritis get better or worse as the day goes on?
Quick Quiz: Does Rheumatoid arthritis get better or worse as the day goes on?

Answer: It gets better with use. This is in contrast to osteoarthritis which gets worse as the day goes on.
Case 9: A 12 year old girl presents to the ED with multiple fractures of her right femur. She has not large bruises as would be expected. She also has mild hearing loss.
What other part of the physical exam should you perform to help confirm the diagnosis?

A. Check the deep tendon reflexes
B. Inspect the conjunctivae
C. Check for hepatosplenomegaly
D. Check for thyroid nodules
Take Home Points:

1. Osteogenesis imperfecta is a heritable disorder that results in a defect in collage synthesis.

2. It is most commonly due to an autosomal dominant defect in collagen type 1 synthesis.

3. Patents presents with multiple fractures because collagen is the main component of osteoid.

4. Osteoid is the scaffold which becomes mineralized to form bone.

5. Thinning of the scleral collagen reveals underlying choridal veins resulting in blue sclera.

6. Involvement of the bones of the middle ear can lead to hearing loss.
Case 10: A 9 year old boy has a history of degenerative joint disease in both knees and the right shoulder.
Labs...
Serum RA factor: negative
Urine analysis: Turned black on after exposure to air.

What is the diagnosis?
A. Phenylketonuria
B. Maple Syrup Urine Disease
C. Alkaptonuria
D. MCAD deficiency
Take Home Points:

1. Alkaptonuria is a metabolic disorder due to a deficiency of homogentisic acid oxidase, an enzyme required for the breakdown of phenylalanine and tyrosine.

2. Homogentisic acid builds up in the joints leading to degenerative changes and causes cartilage to turn blue/black in color (ochronosis).

3. It is an autosomal recessive disorder.

4. Urine will turn black on exposure to air.
Case 11: A 3 year old girl has a broad skull and facial and dental abnormalities. She thought to have a abnormality in the membranous ossification component of bone development.

Which of the following bones would also be affected?

A. Clavicle  
B. Femur  
C. Tibia  
D. Metatarsals  
E. Phalanges
**Take Home Points:**

<table>
<thead>
<tr>
<th>Membranous ossification</th>
<th>Endochondral ossification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Does not use cartilage as a template</td>
<td>Uses cartilage as a template</td>
</tr>
<tr>
<td>Flat bones of the skull</td>
<td>Bones at the base of the skull</td>
</tr>
<tr>
<td>Clavicles</td>
<td>Limbs, hands, feet</td>
</tr>
<tr>
<td>Pelvis</td>
<td>Rest of axial skeleton</td>
</tr>
</tbody>
</table>
Step 1 Musculoskeletal Review

Case presentations:

1. Prostate Cancer
2. Reactive Arthritis
3. Paget’s Disease
4. Duschene Muscular Dystrophy
5. Pseudogout
6. Rhabdomyosarcoma
7. Ewig’s sarcoma
8. Rickets
9. Osteogenesis Imperfecta
10. Alkaptonuria
11. Intramembranous ossification