Pathology

Doctor 2017 | Medicine | JU | MSS

Number >>	7
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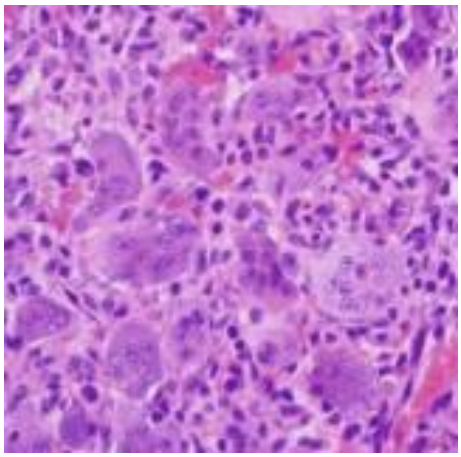
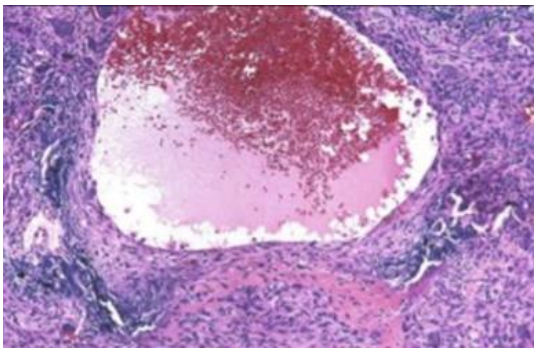
1st system - MSS

Recap

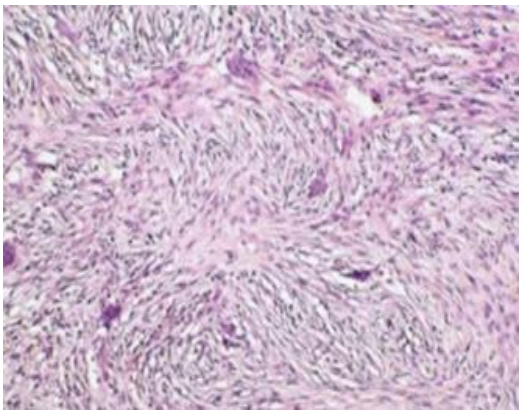
The histological appearance of Giant cell tumor of bone shows only multi-nucleated giant cells.



The histological appearance of Aneurysmal bone cyst shows a sac filled with blood with some fibrous reaction and some multi-nucleated giant cells.



The histological appearance of Nonossifying fibroma shows a benign proliferation of fibroblasts with some multi-nucleated giant cells.

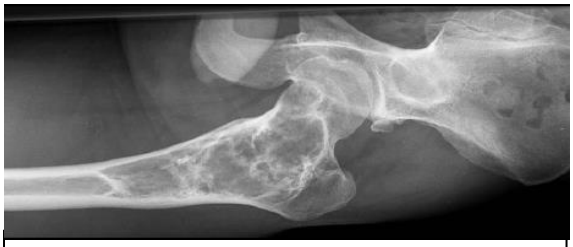


Fibrous Dysplasia (FD)

- Not a real tumor (dysplasia here doesn't mean precancerous).
- It is a developmental dysplastic abnormality of bone genesis due to mutations in GNAS1 gene, so cAMP mediated osteoblast differentiation and bone formation are not normal (has similarities with paget disease of bone but they are not the same).

- A group of multiple diseases:

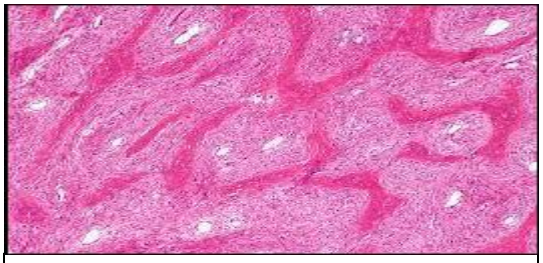
  - ✓ ***Monostotic FD***: affecting one bone (commonly affecting the bones of the skull like the mandible or the maxilla producing protruding jaws or ***Cherubism*** *(abnormal cheeks and bones)*).
  - ✓ ***Polyostotic FD:*** affecting multiple bones.
  - ✓ ***Mazabraud syndrome:*** FD (monostotic or polyostotic) + soft tissue ***myxoma*** (benign soft tissue tumor of myxoid cells). [myxoma is also a common tumor of the heart atria]
  - ✓ ***McCune-Albright syndrome:*** polyostotic FD + ***café-au-lait skin pigmentation*** (dark skin pigmentation) + endocrine abnormalities like ***precocious puberty*** (earlier puberty before the normal age (before 12-15 years for females 15-17 years for males).
    Could cause bone pain, disfigurement or even fractures for sever cases.
    Symptoms start appearing early, so most commonly at a young age the patient will be diagnosed as a McCune-Albright syndrome patient, however it is not easy to diagnose ➔ clinical clues confirmed with a biopsy.



Abnormal bone because of abnormal differentiation of osteoblasts.

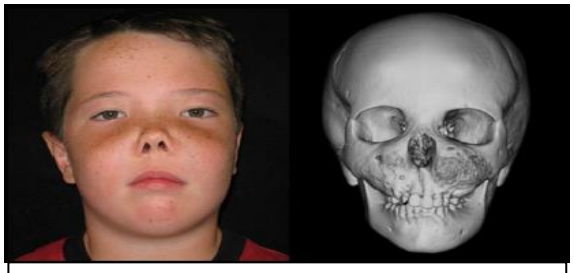
Can be confused with paget.

Biopsy →

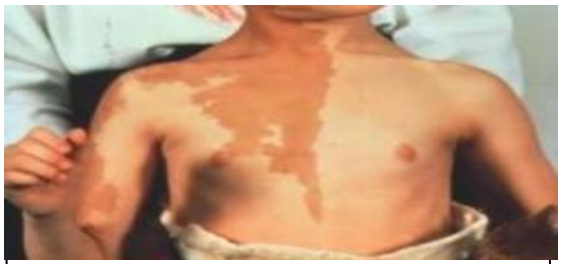


Chinese letter appearance: characteristic of FD

<u>GOOGLE</u>: Curvilinear trabeculae of metaplastic woven bone (never matures) in hypocellular, fibroblastic stroma.



Cherubism



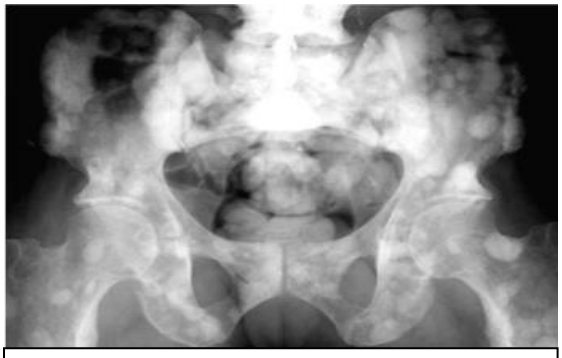
café-au-lait skin pigmentation

Metastatic tumors to bone

- Much more common than primary bone tumors especially in adults.
- In adults, ***carcinomas*** are the most common.
  Carcinomas are the cancers of glandular tissue (adenocarcinomas) which are the most common of metastasizing to bones, and the cancers of the epithelium like squamous cell carcinoma or transitional (urothelial) cell carcinoma.

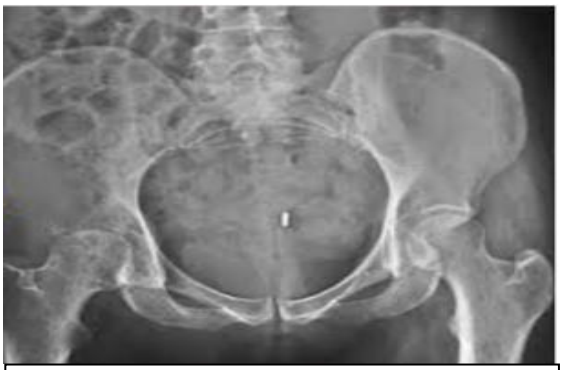
  Most common carcinomas that metastasize to bones:

  - ✓ ***Lung***: the most common especially adenocarcinoma of the lung. (Note: lung cancer is the most common lethal cancer of men and women).
  - ✓ ***Prostate adenocarcinoma:*** in males only (the most common cancer of men). It is very common and with an increasing incidence with age (at the age of 50 there is 50% chance of prostate cancer, and at the age of 100 there 100% chance of prostate cancer) however, fortunately most of them are low grade non-lethal cancers.
  - ✓ ***Breast (mammary adenocarcinoma):*** in females and rarely males (the most common cancer in women).
  - ✓ ***Kidney (renal cell carcinomas):*** both males and females.
  - ✓ ***Thyroid***: follicular carcinoma of the thyroid not the papillary carcinoma.
  - ✓ ***Liver (hepatocellular carcinoma).***
- In children, carcinomas are rare, so the most common ***sarcomas*** are Neuroblastoma, Wilms tumor and rhabdomyosarcoma.
- Usually multiple metastasis and the axial skeleton is more affected. ➔ 70 years Old patient with multiple lytic lesions at the pelvis, shoulder and vertebrae, this is most likely metastatic tumors to bones.
- Mostly by hematogenous spread.
- Can cause Lytic, blastic or mixed lesions (via mediators secretions). The Most common ***are carcinomas caused lytic lesions.***



Multiple blastic lesion.

Most likely of prostate cancer.



Multiple lytic lesion.

Most likely of adenocarcinoma.

Summary

Bone Tumors and Tumorlike Lesions

Primary bone tumors are classified according to the cell of origin or the matrix that they produce. The remainder is grouped according to clinicopathologic features. Most primary bone tumors are benign. Metastases, especially from lung, prostate, kidneys, and breast, are far more common than primary bone neoplasms.

Major categories of primary bone tumors include

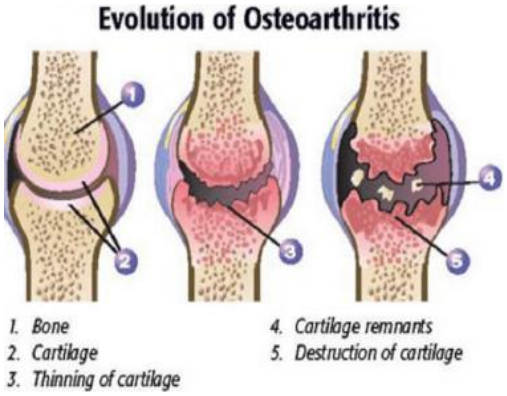
- **Bone forming:** Osteoblastoma and osteoid osteoma consist of benign osteoblasts that synthesize osteoid. Osteosarcoma is an aggressive tumor of malignant osteoblasts, predominantly occurring in adolescents.
- **Cartilage forming:** Osteochondroma is an exostosis with a cartilage cap. Sporadic and syndromic forms arise from mutations in the *EXT* genes. Chondromas are benign tumors producing hyaline cartilage, usually arising in the digits. Chondrosarcomas are malignant tumors of chondroid cells that involve the axial skeleton in adults.
- **Ewing sarcomas** are aggressive, malignant, small round cell tumors most often associated with t(11;22).
- **Fibrous dysplasia** is an example of a disorder caused by gain-of-function mutations that occur during development.

Joints

- Provide motion & stability to our skeleton.
- Synovial (cavitated) joints provide wide motion (knee, elbow…)
- Non-synovial (solid) joints: synarthrosis ➔ minimal movement (skull, sternum…)
- Synovial joints covered by hyaline cartilage (70% water, 10% type II collagen, 8% proteoglycans and chondrocytes).
- Synovial membrane contains:
  - ✓ Type A synoviocytes (differentiated macrophages).
  - ✓ Type B synoviocytes (fibroblast-like).
- Synovial membrane lacks basement membrane.
- Hyaline cartilage: has no blood supply, no nerves, no lymphatics (act as shock absorber).

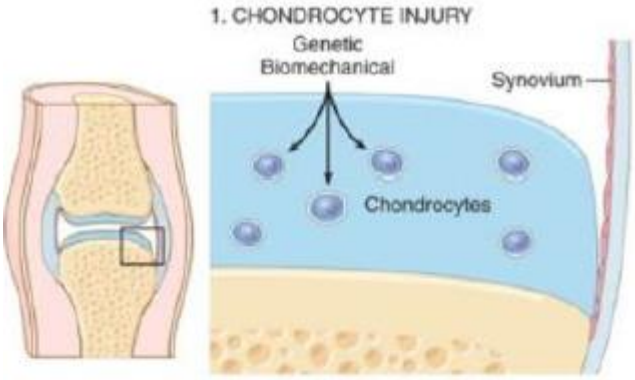
Osteoarthritis

(Degenerative joint disease (DJD))

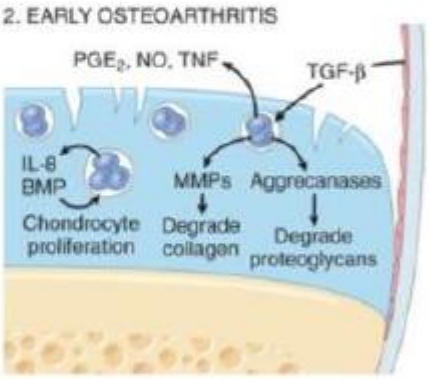


- Degeneration of cartilage occurs in all people, followed by repairing of that cartilage. With increased age, degeneration starts to exceed the repairing and proliferation process which causes DJD (Wear and Tear).
- Insidious; increase with age (>50 yrs.) ➔ very common with 40% of people > 70 years affected.
- Some consider it as not a true inflammation ***(ITIS).*** However, there are some mediators that enhance degradation and chondrocytes injury.
- Two types:
  - ✓ Primary (idiopathic): the most common due to aging process and affecting a few joints.
  - ✓ Secondary: due to preexisting diseases.
- There is some genetic predisposition, but the wear and tear process is more important.

Genetic predisposition with biomechanical wear and tear.

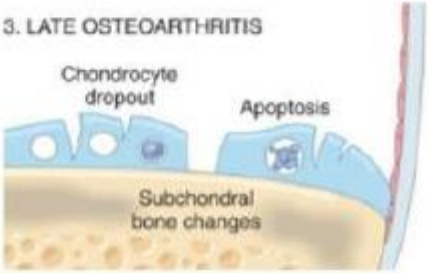


Release of mediators (PGE2, NO, TNF,…) which causes chondrocytes injury.

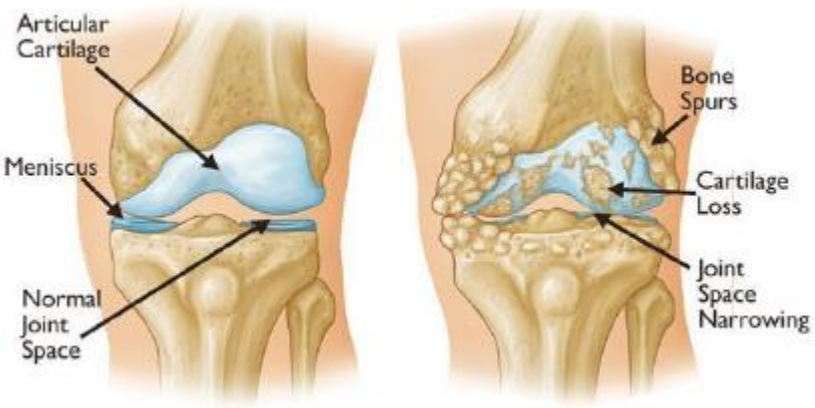


Chondrocytes death (apoptosis) and dropout.

This causes eburnation of the bone.



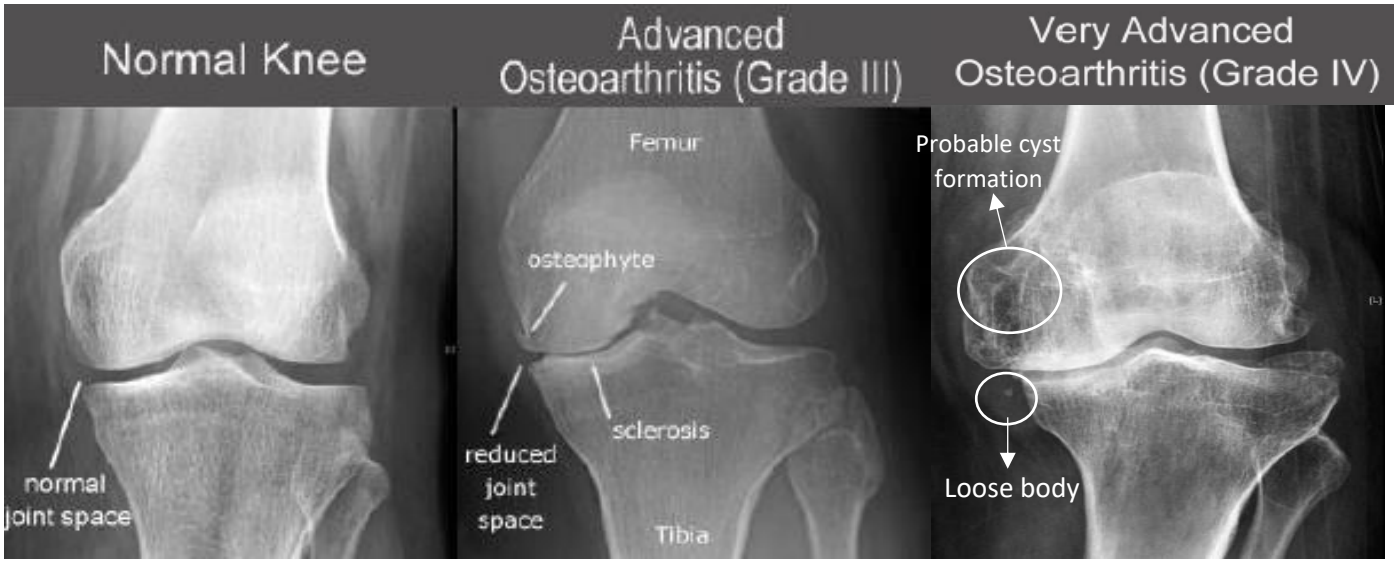
Normal joint.



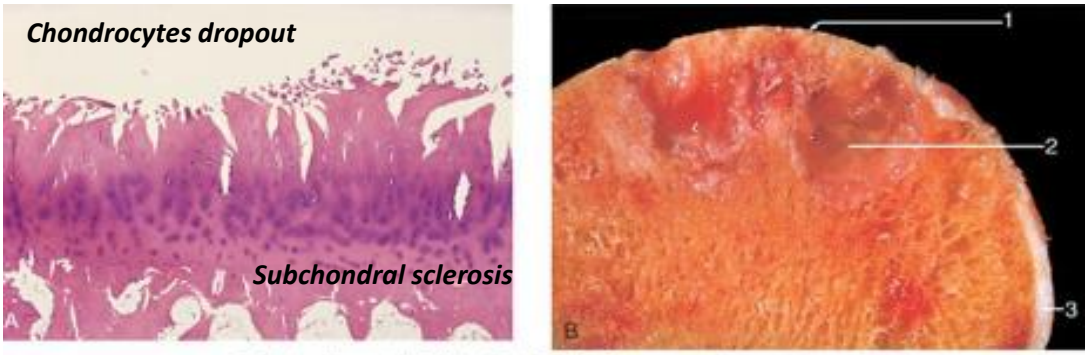
Affected joint.

- ✓ ***Narrowing of joint space.***
- ✓ ***Fragmentation and sever loss of cartilage.***
- ✓ ***Eburnation of the bone.***
- ✓ ***Subchondral sclerosis.***
- ✓ ***Formation of osteophytes (bone spurs) because of friction and injury.***
- ✓ ***bleeding can occur with walking or another trauma.***
- ✓ ***Subchondral cyst formation.***

- Osteophytes are bony outgrowth pieces that may dropout into the joint space forming ***loose bodies***.
- Loose bodies are painful, and if they are big enough, they may cause stiffness of the joint. Loose bodies also produce ***crepitus*** which is cracking or popping sound in the joint and this is for moderate to severe osteoarthritis.



Normal → ***Narrowing, sclerosis osteophyte and cyst formation.*** → ***severe narrowing, sclerosis osteophyte and cyst formation. (Probably need joint replacement)***



- Osteoarthritis. **A,** Histologic demonstration of the characteristic fibrillation of the articular cartilage. **B,** Severe osteoarthritis with 1, Eburnated articular surface exposing subchondral bone. 2, Subchondral cyst. 3, Residual articular cartilage

DJD clinically:

- Morning stiffness then Joint pain that worsens with use and walking and it may cause limping.
- Crepitus, range of motion limitation, radicular pain (sharp pain due to nerve compression), osteophytes impingement on vertebrae, and muscle spasm & atrophy.
- No magic preventive strategies. Weight loss can reduce intensity and severity because there is relation between obesity and osteoarthritis.

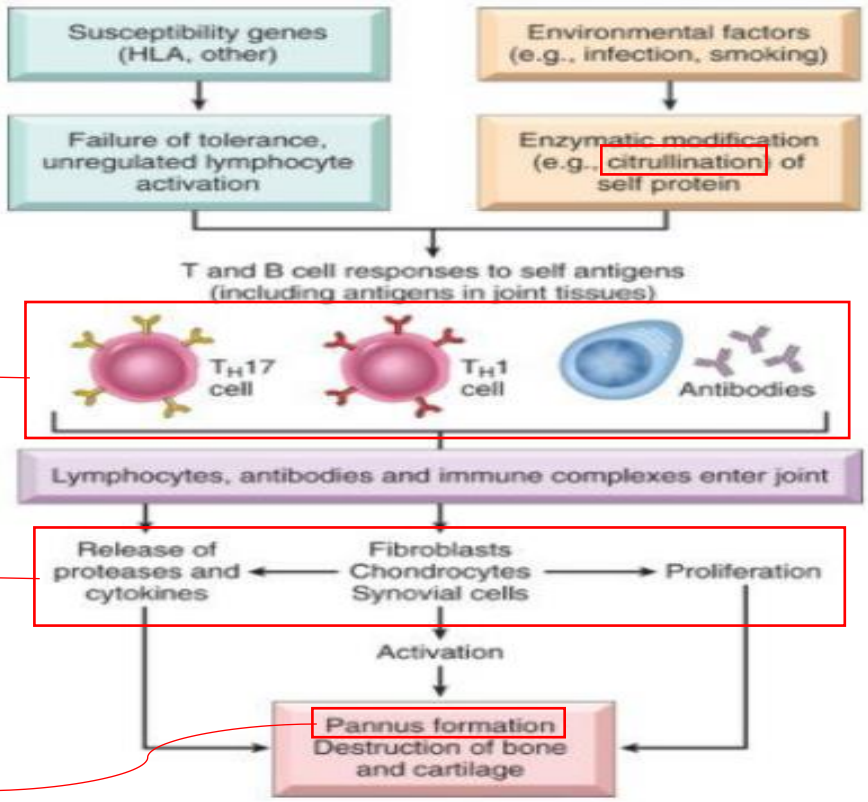
Treatment (Trx):

- Pain control and decrease inflammation by NSAIDs (the most common indication).
- Intra-articular steroids for sever forms. (Not to be used always because of severe side effects).
- Joint replacement for severe cases.

Osteoarthritis has a large health cost on countries because it is very common and needs a lot of medications.

Rheumatoid arthritis

- Called ***proliferative autoimmune synovitis.***
- Much less common then osteoarthritis. And it is a ***true inflammation.***
- **Chronic inflammatory disease**.
- ***Autoimmune in nature*** ➔ (autoimmune means self-antibodies and immune complexes attacking the body).
- Attacks joints with **nonsuppurative** (because it not caused by an infection) proliferative and inflammatory synovitis leading to destruction of joints and adhesions (ankylosis).
- It is **systemic disease** affecting the skin, heart, vessels and lungs (in contrast to DJD which is a joint disease).
- 1% prevalence in USA and it is more common in females than males 3:1 (in the 4th-5th decade of life).
- Genetic predisposition (certain Human Leucocytes Antigens (HLA) types are more exposed to RA than others) + environmental factors plays a role in the development, progression and chronicity of the disease.
- The trigger is not known (viruses, trauma??) ➔ so, it is not really known what makes the imbalance in the tolerant cells (responsible for suppressing the immune reaction) which causes the enticement of the autoimmune reaction.
- Tested by rheumatoid factor test or anti-cyclic citrullinated peptide (anti-CCP) test which looks for citrullinated proteins.



Upregulation of immune cells like (TH17, TH1 and plasma cells)

Destruction and digestion of proteins by the proteases.

The histological appearance of this inflammatory reaction (characteristic of RA).