Bones and Joints
Part 1

APPROVED

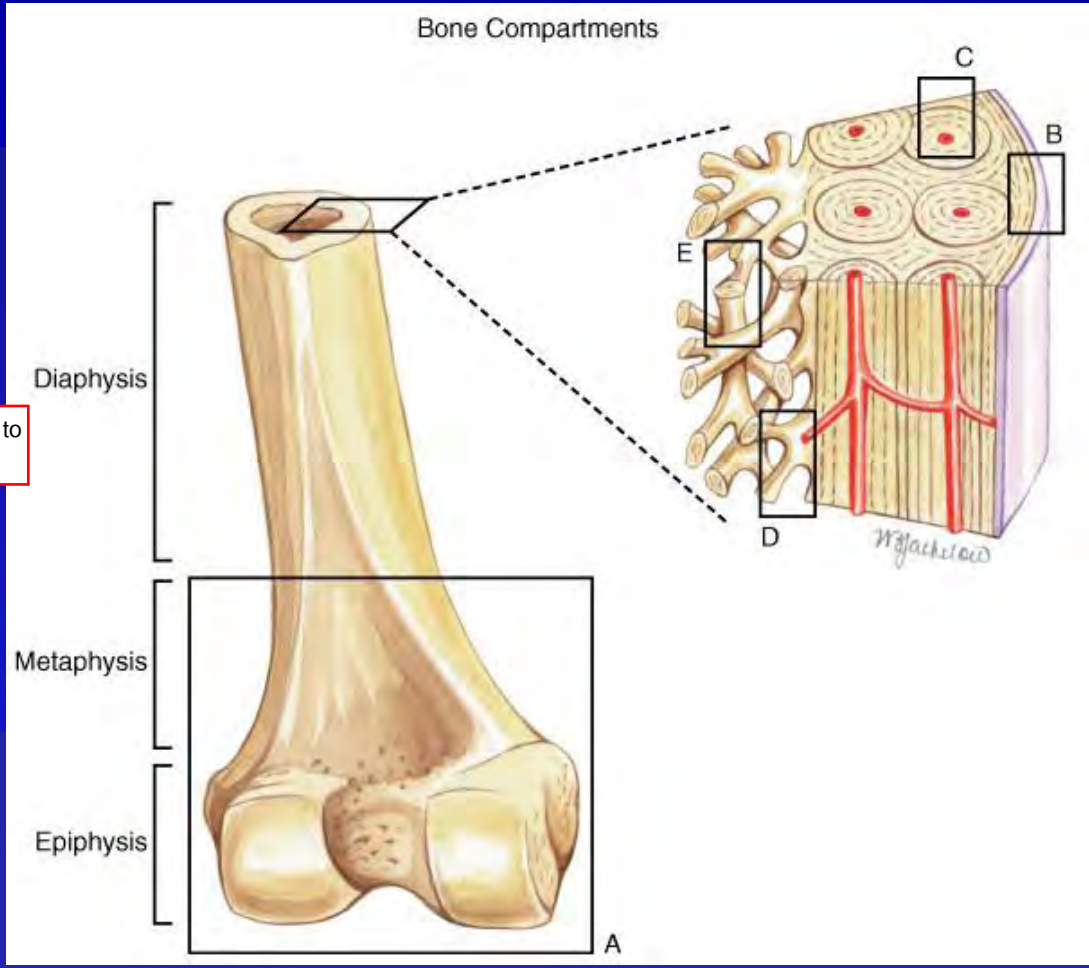
Leslie G Dodd, MD

Outline

- Review of normal anatomy, histology and landmarks
- Growth and repair
- Congenital/hereditary disorders
- Metabolic disorders
- Inflammatory disease
- Arthritis/Pathology of the Joint

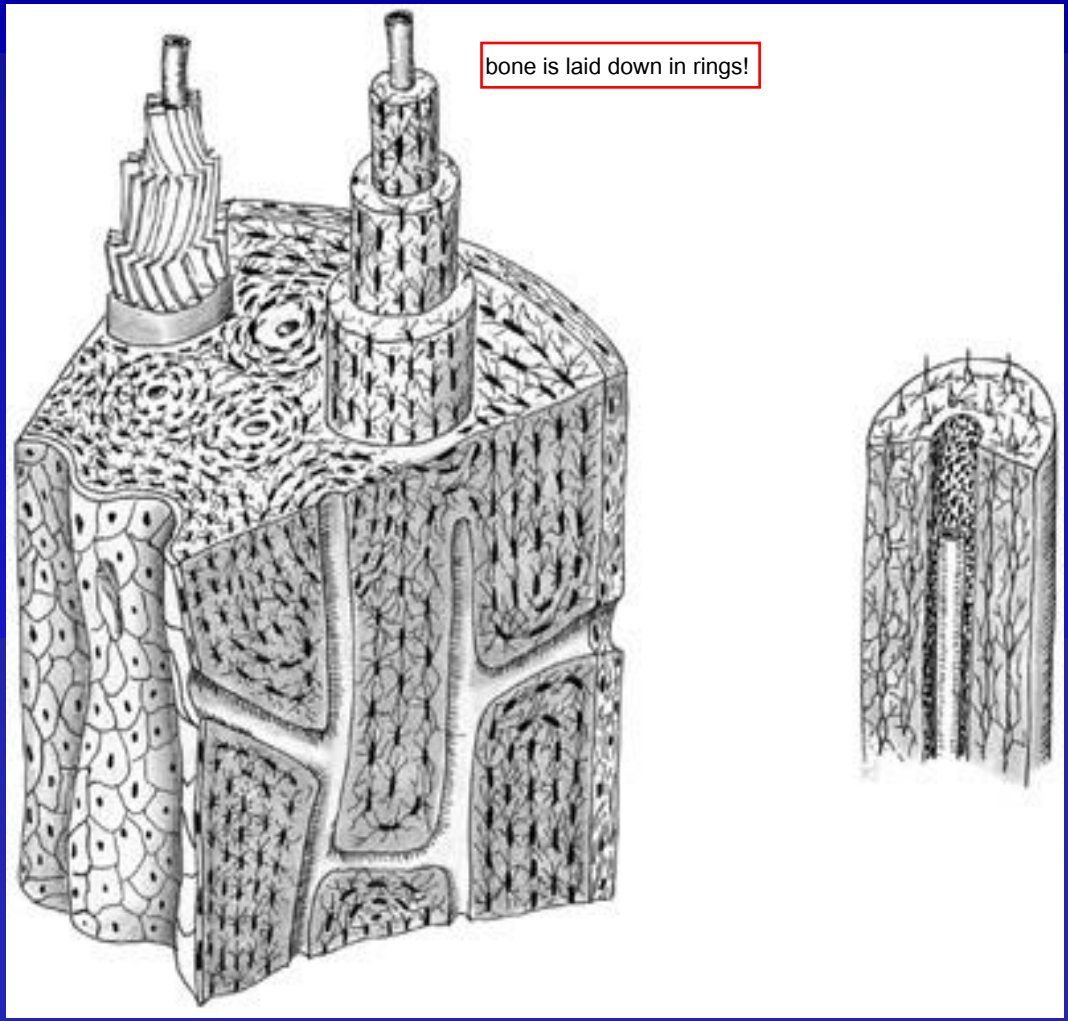
Bone Landmarks/ A &H

- Anatomic landmarks:
  - Diaphysis — central area
  - Epiphysis — growth plate
  - Metaphysis — active turnover; adjacent to growth plate
- Cortex
- Medullary cavity
  - Cancellous/trabecular bone



circumferential bone -- cortical; provides strength
internal bone -- trabecular; provides large SA for hematopoiesis function
function of bone:
strength from cortex
lightness from trabecular

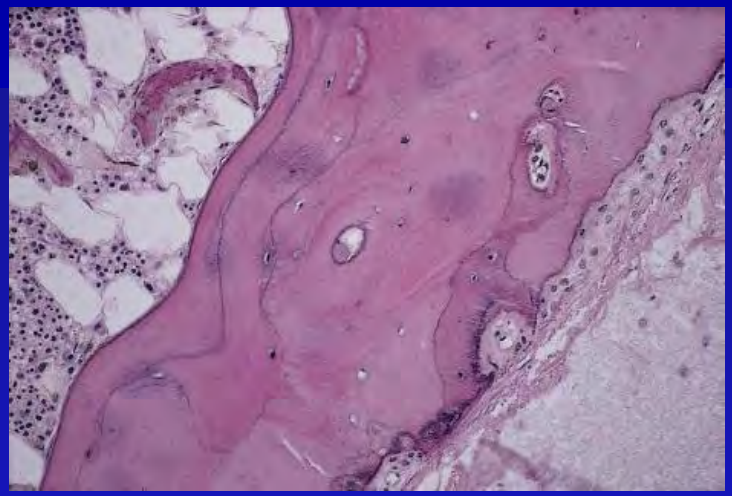
Bone– Organization and structure

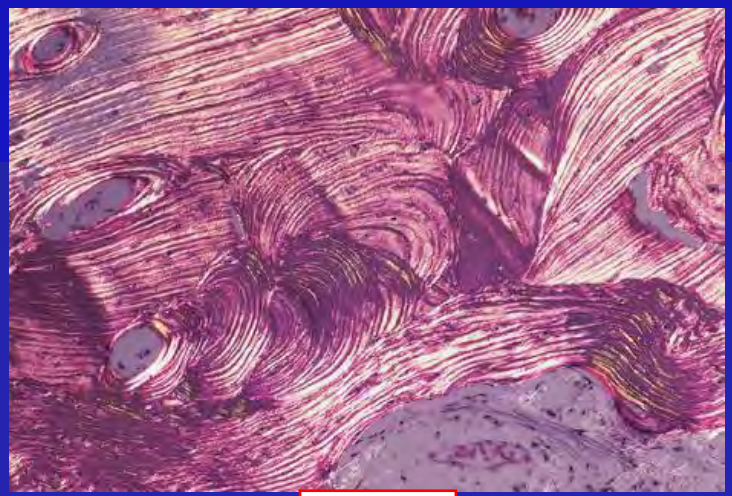


Bone A/H

polarized light shows bone striations; is laid down concentric rings 'appositional growth'

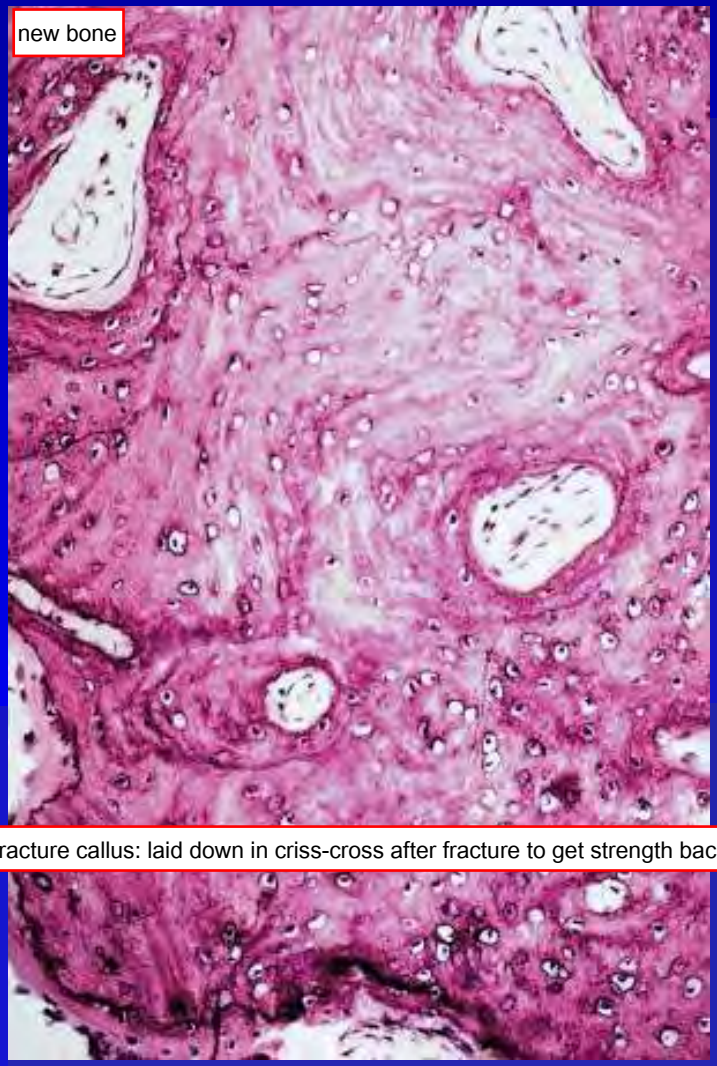
- Trabecular (mature) bone laid in lamellar fashion
- Immature bone is woven; associated with fracture, repair, tumor,etc.



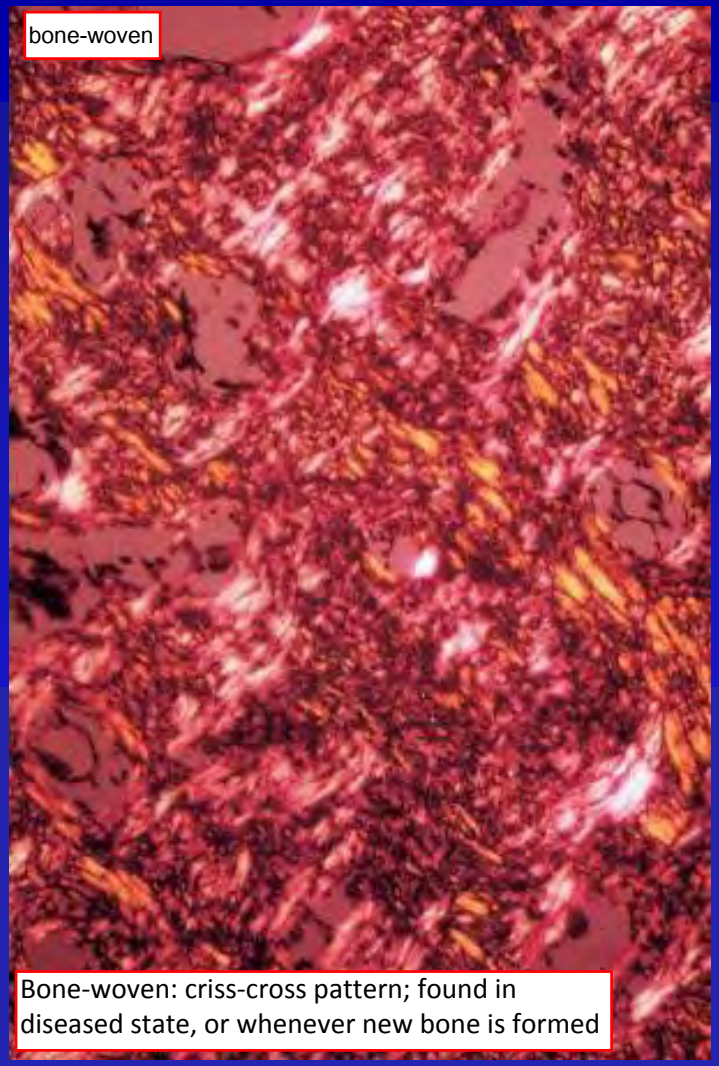


polarized light

Bone-woven bone vs lamellar



fracture callus: laid down in criss-cross after fracture to get strength back



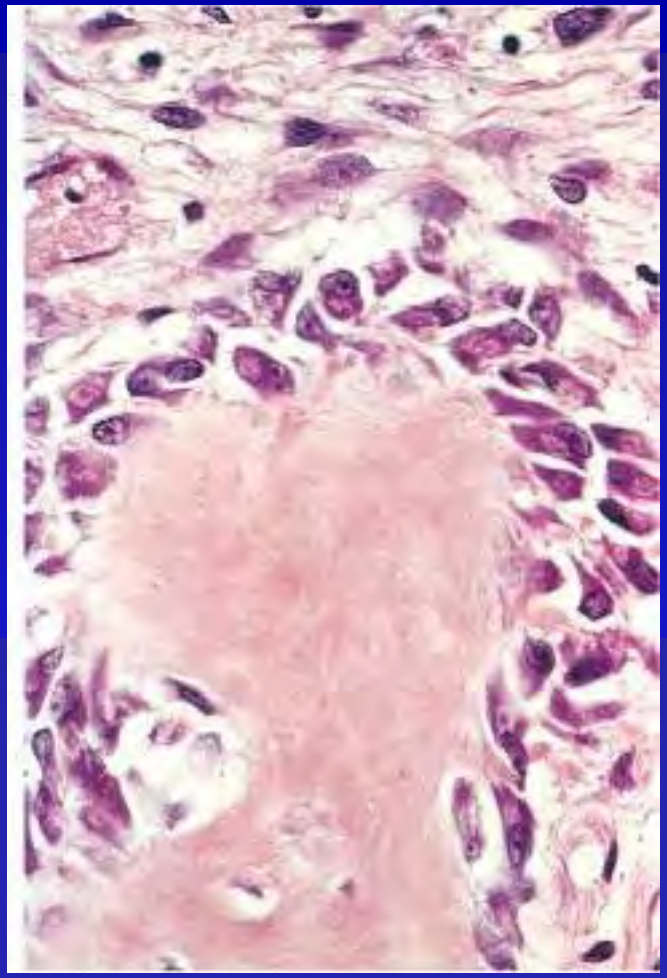
Bone-woven: criss-cross pattern; found in diseased state, or whenever new bone is formed

Osteoblast

Blasts = Build

Osteoblast: lays down matrix: bone matrix is Ca; most dry weight is collagen. Form line around edge of advancing bone. When bone is mature they become trapped as osteocytes

- Responsible for synthesizing bone and mineralization
- In active growth or remodeling at edge of advancing bone formation
- Entrapped to become osteocytes

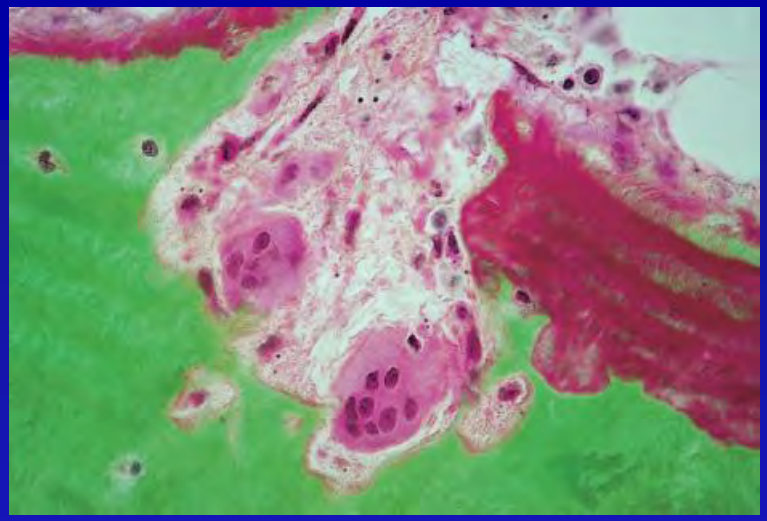


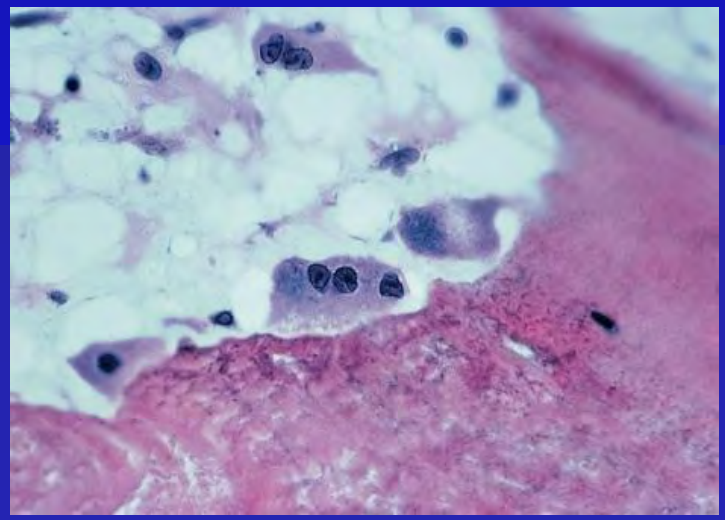
Osteoclasts

Clasts = Cut

Osteoclasts: constantly functioning; use 'enzymes and collagenases.' Sit in holes in bone called Howship's lacunae

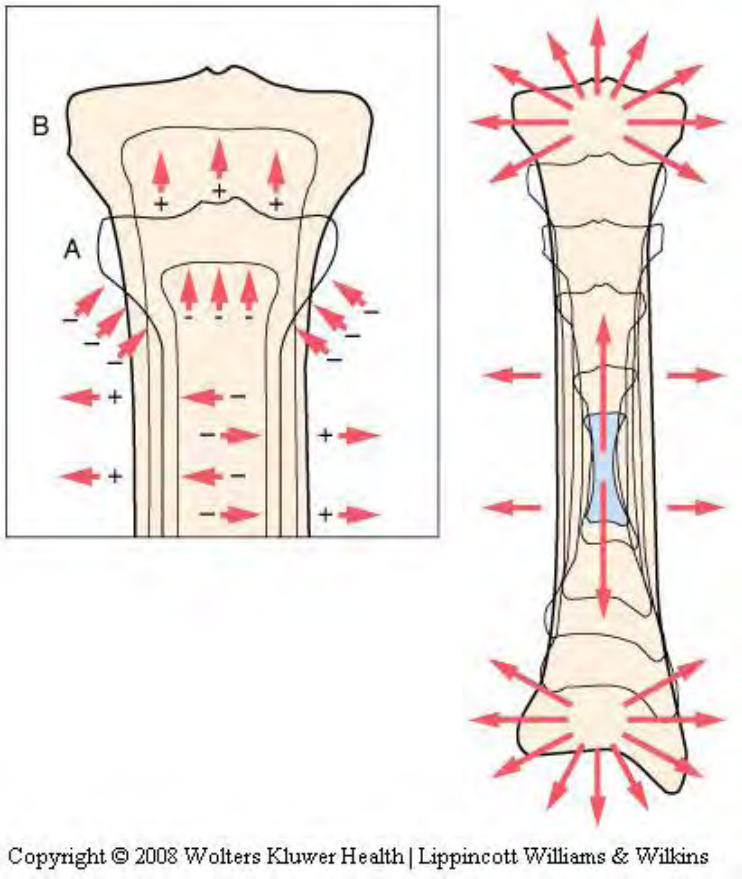
- Responsible for bone resorption
- Attach to bone matrix protein
- Form Howship's lacunae





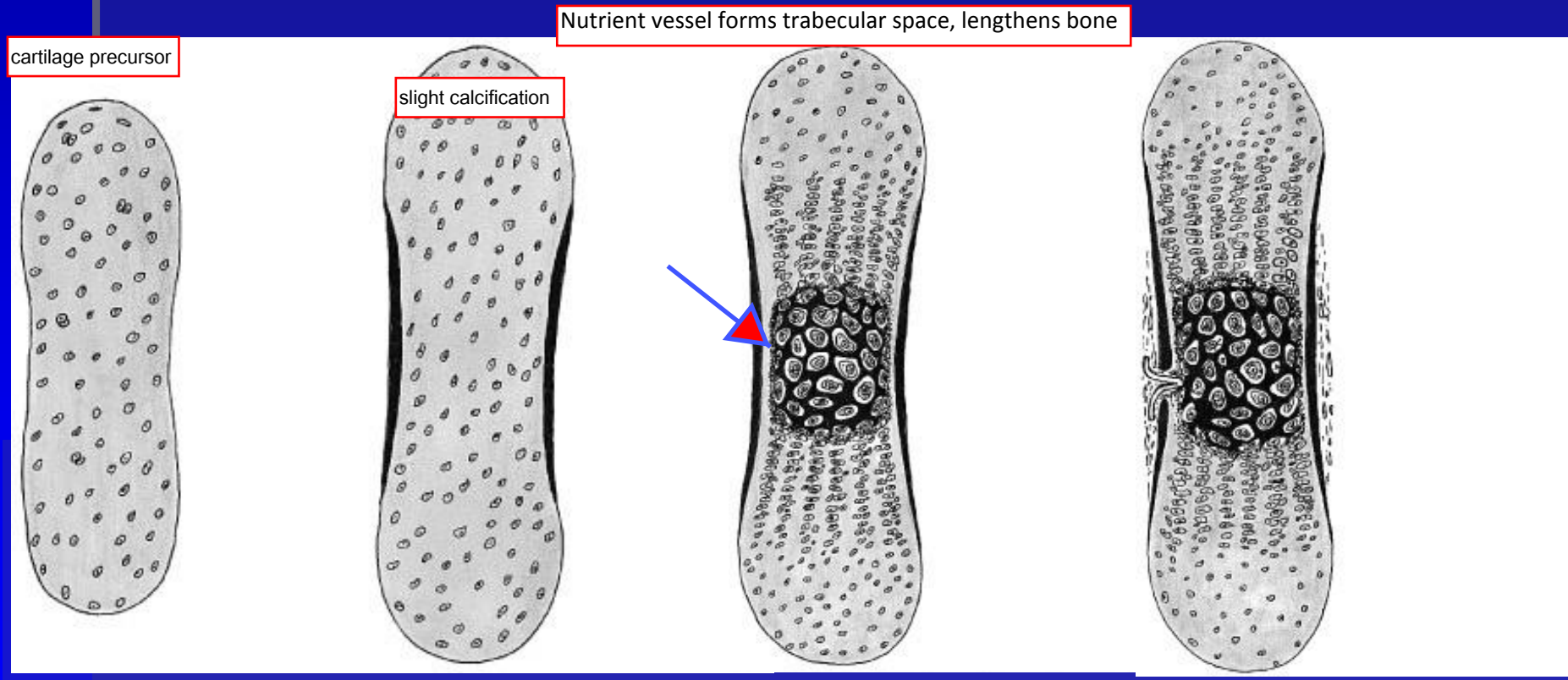
Bone development and growth

Intrachondral (long-bone) development: has to grow both in length and circumference



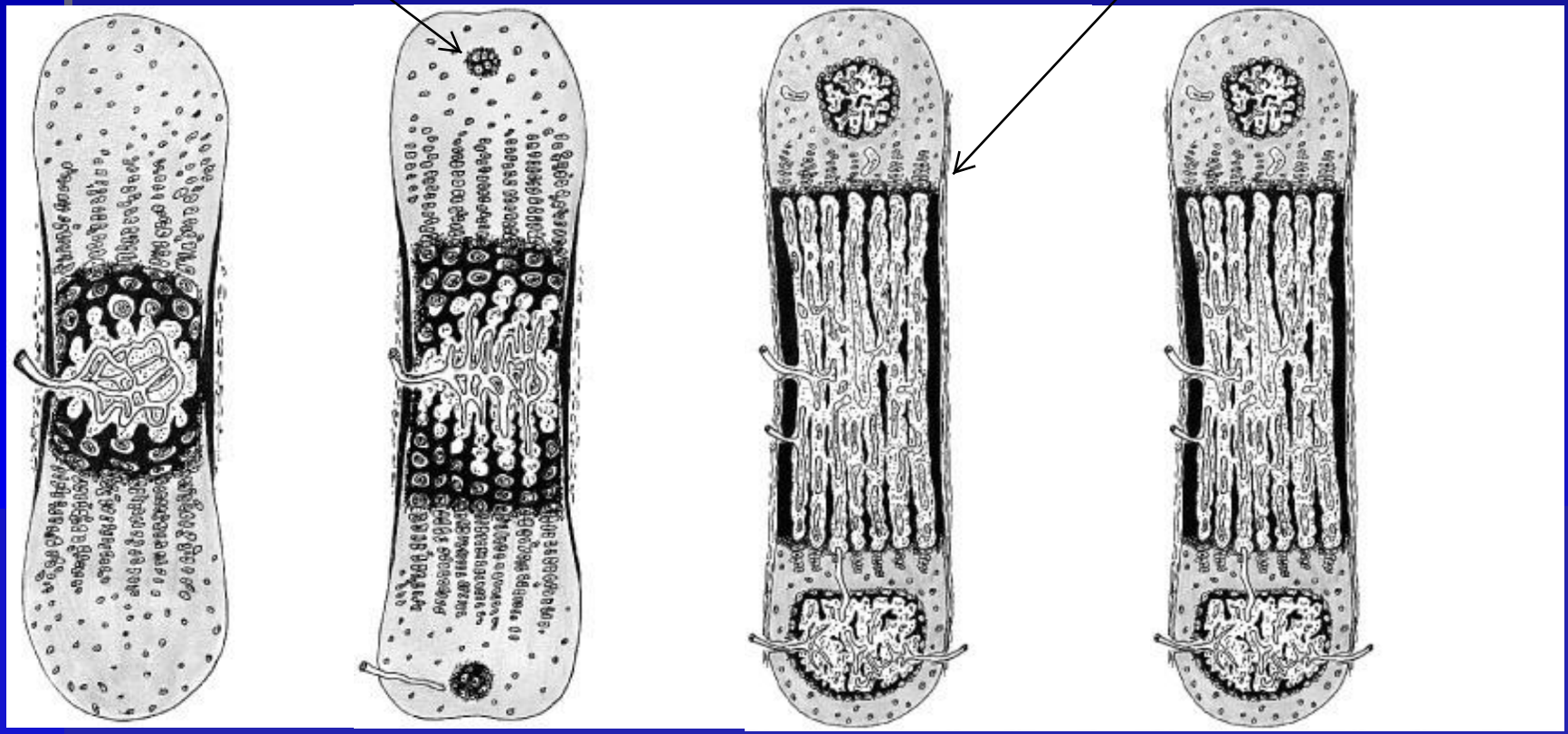
- Growth
  - Enchondral ossification
  - Membranous ossification
- Remodeling
  - Physical/mechanical forces
  - Mineral deposition and collagen
  - Hormones and paracrine/autocrine functions

Bone growth—enchondral ossification



Enchondral ossification

Get secondary cavity with, above, epiphyseal line (where growth occurs once you're born), have secondary centers of ossification (important for some pathophys and tumors)



Skeletal maturity: 16-17yo (female), 17-19yo (male)

Modeling and Remodeling

As juvenile, longitudinal growth occurs in epiphyses.
As adult, no longer capable of longitudinal growth b/c of fusions; epiphyseal line is where secondary growth occured

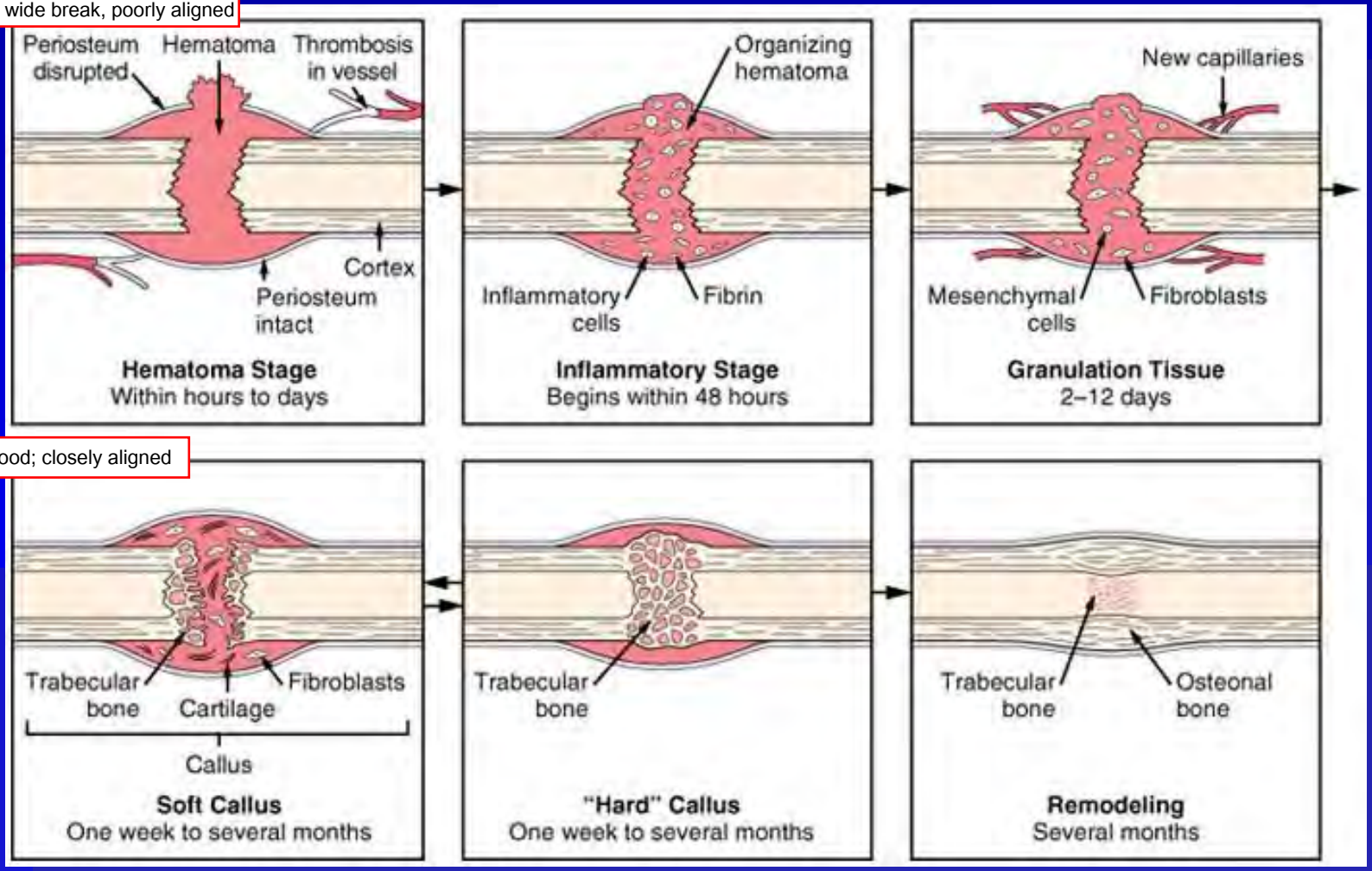
juvenile; no epiphyseal line

adult: epiphyseal lines present

healing -- blood collects at site of trauma (hematoma). hematoma organizes region -- nutrients, cartilage precursors, come in, makes woven bone (lacks tensile strength). if ends align, healing occurs quickly. if ends are NOT aligned, very large callus forms. if any wiggling, wont form callus all the way. this is why you have to mobilize the fracture

Fracture Callus

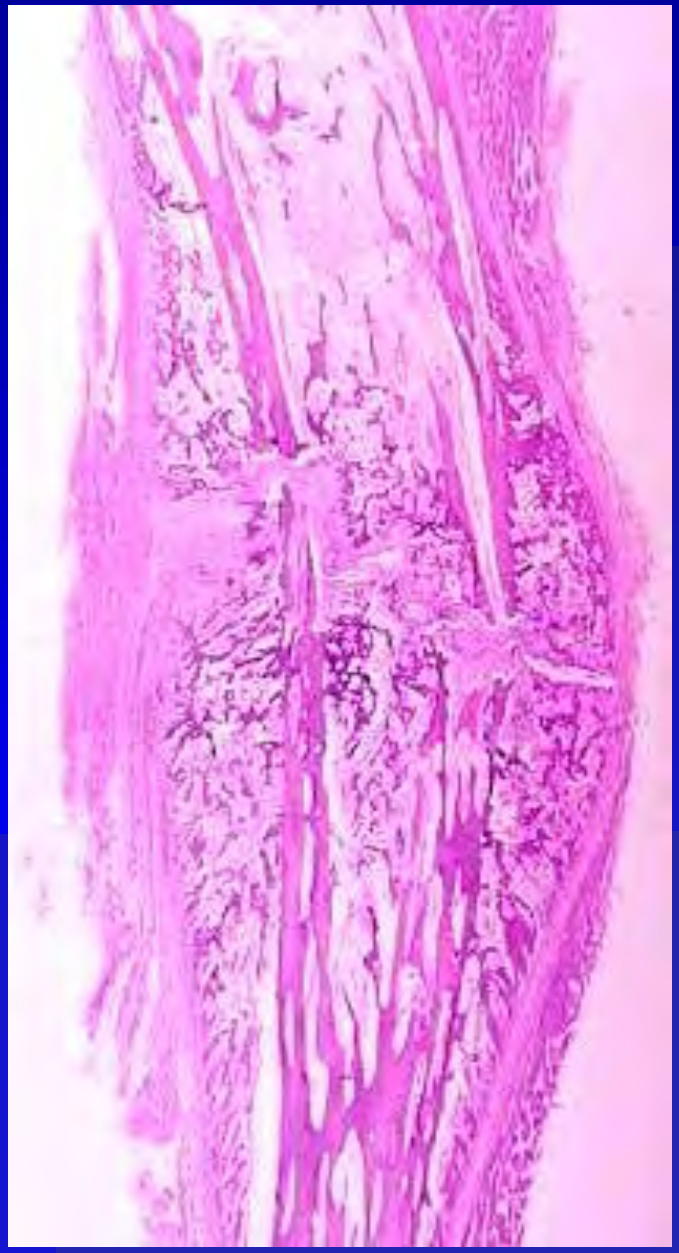
bad; wide break, poorly aligned



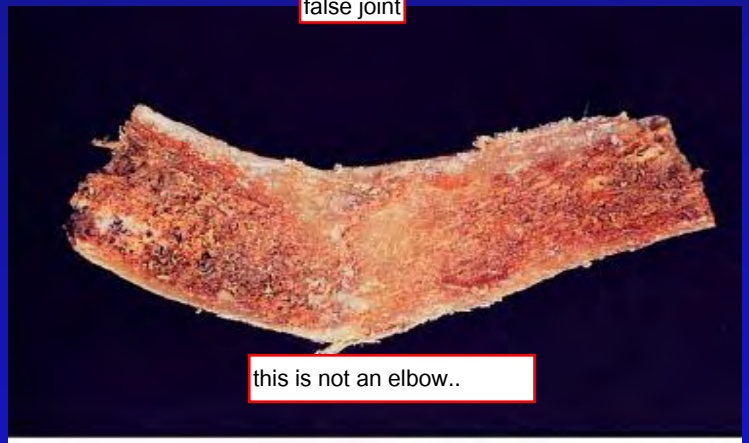
good; closely aligned

example of a bad fracture w/o treatment: callus doesnt form all the way; get bending/wiggling. get psuedoarthrosis ('false joint') predisposes to mech problem and infection

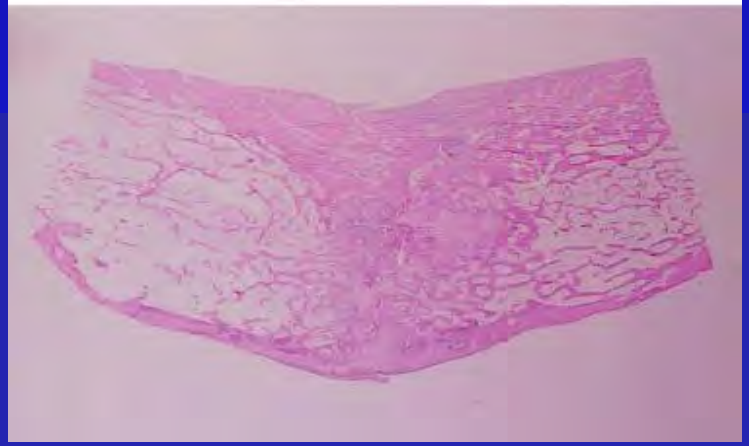
Fracture repair



false joint



this is not an elbow..



LETS TALK ABOUT HEREDITARY DZS

Achondroplasia

long-bones dont grow; membranous bones DO grow. look short in stature and have short limbs, but normal sized head and trunk

- Achondroplasia (from the Greek for "without cartilage") is the most common form of dwarfism, occurring once every 14,000 births .
- Symptoms of achondroplasia include a large head; shorter arms and legs, especially upper arms and thighs; prominent forehead; protruding jaw

Osteogenesis Imperfecta

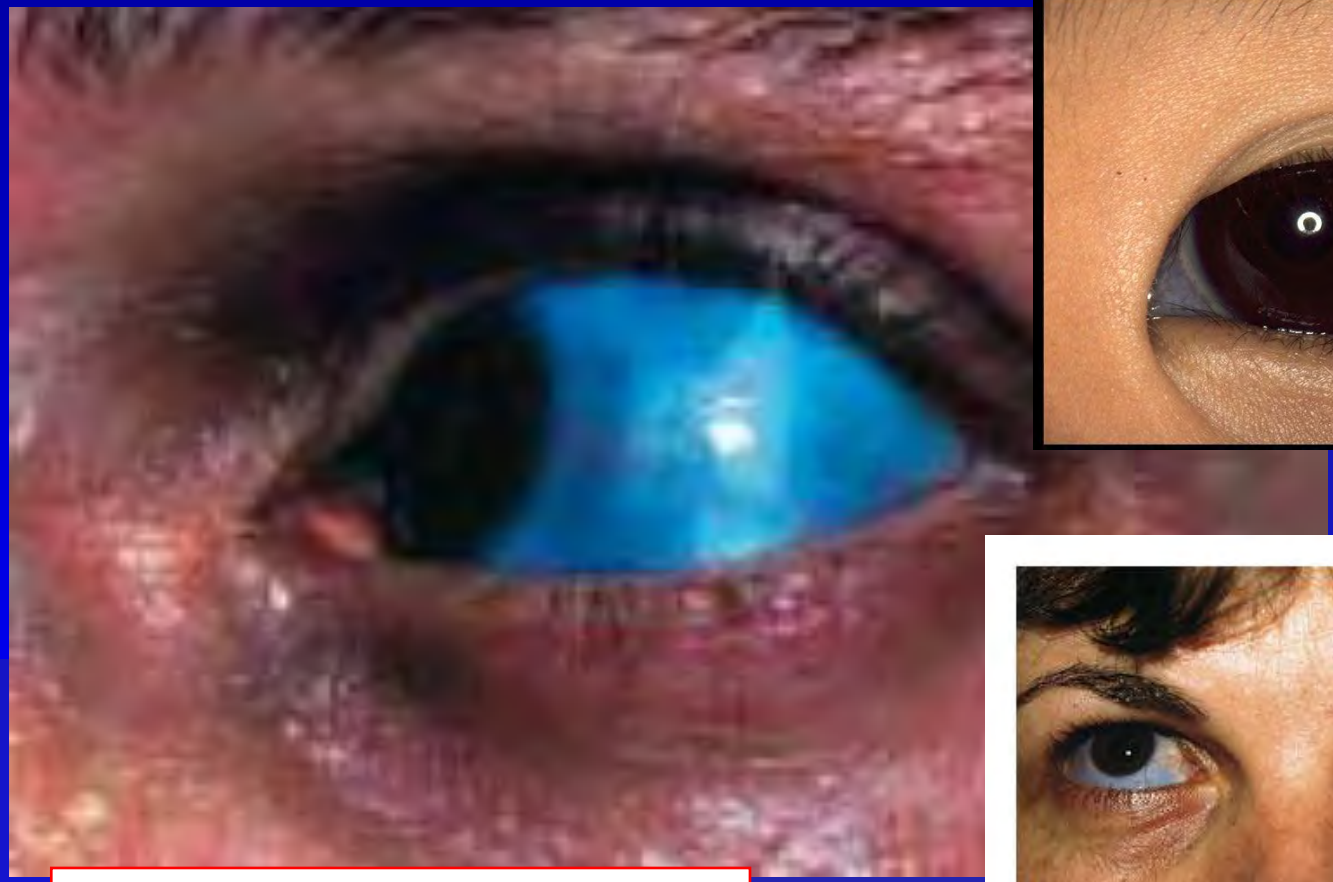
defect in type I collagen

- OI an inherited disorder of collagen maturation which results in abnormal skeletal, ligament, skin, sclera and dentin formation
- Major clinical criteria:
  - Osteoporosis
  - Blue sclera
  - Dentigenesis imperfecta
  - Premature otosclerosis

bad teeth

overgrowth of bones responsible for hearing

OI Blue Sclera



Q: why is the sclera blue?

A: blue-gray color of the sclera is due to the underlying choroidal veins which show through. This is due to the sclera being thinner than normal because of the defective Type I collagen not forming correctly. Dr. H

Osteogenesis Imperfecta

osteogenesis imperfecta Type II (fetal) is lethal; autosomal recessive. in utero, babies have such fragile bones they fracture, dont survive the birth process

Osteopetrosis

several different types: range from not severe (autosomal dom) to severe (autosomal recessive).

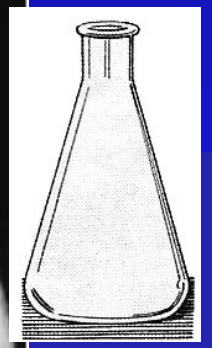
auto dominant not severe usually just have brittle bones

- Aka “Marble bone disease”
- Heterogeneous group of inheritable conditions characterized by defect in bone resorption by osteoclasts
- “types” based on severity:
  - “Malignant”/infantile form
  - Intermediate
  - “Benign”/adult form

Osteopetrosis

- Pathologic features:
  - Increased susceptibility to fracture
  - Decreased marrow space = anemia, neutropenia
- Radiographic features:
  - Sclerotic bone
  - Erlenmeyer flask deformity

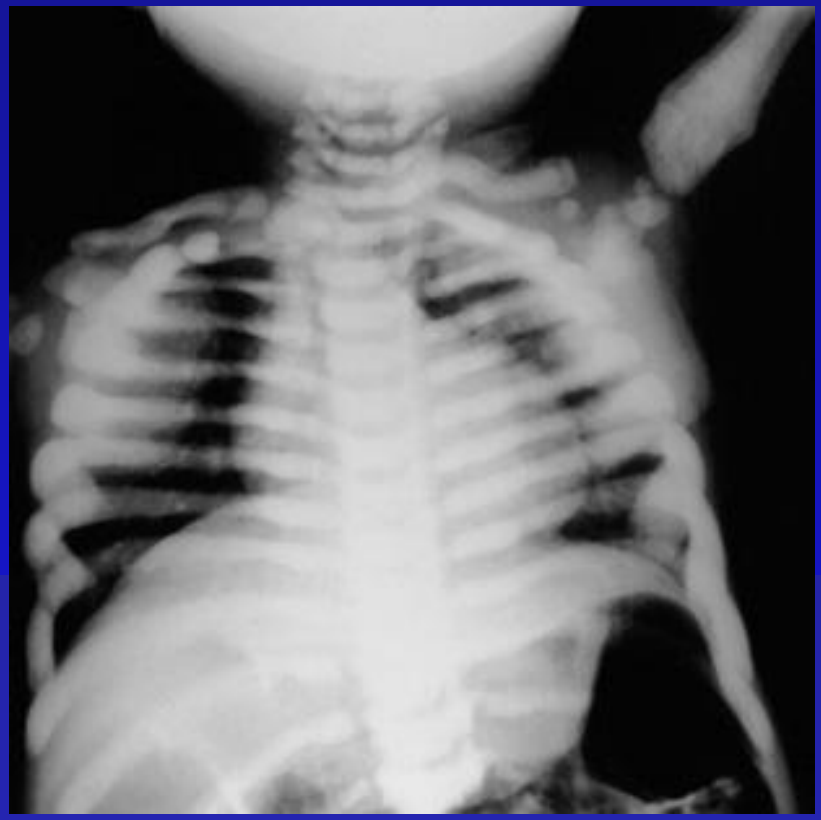
'erlenmeyer flask deformity'



bone and hard, but are brittle and break easily

Osteopetrosis—Infantile form

- Lack of bone remodeling = insufficient marrow cavity for hematopoiesis
- Extramedullary hematopoiesis = hepatosplenomegaly
- Failure to thrive, compression effects or severe anemia and thrombocytopenia



infantile is most severe form (auto recessive). fetus is affected with bony overgrowth in utero
most severe symptom / problem: marrow cavities dont form, so have to have hematopoiesis occur in spleen / liver.
get massive hepatosplenomegaly. get anemia, thrombocytopenia. usually expire at birth or shortly after.

adult is less severe form, will have multiple fractures; 'inconvenient but compatible w life'

'no matter what you go into, you'll encounter this problem'

Osteoporosis

peak bone mass: 30 years; everyone gets it, slowly. but older white women get it the worst

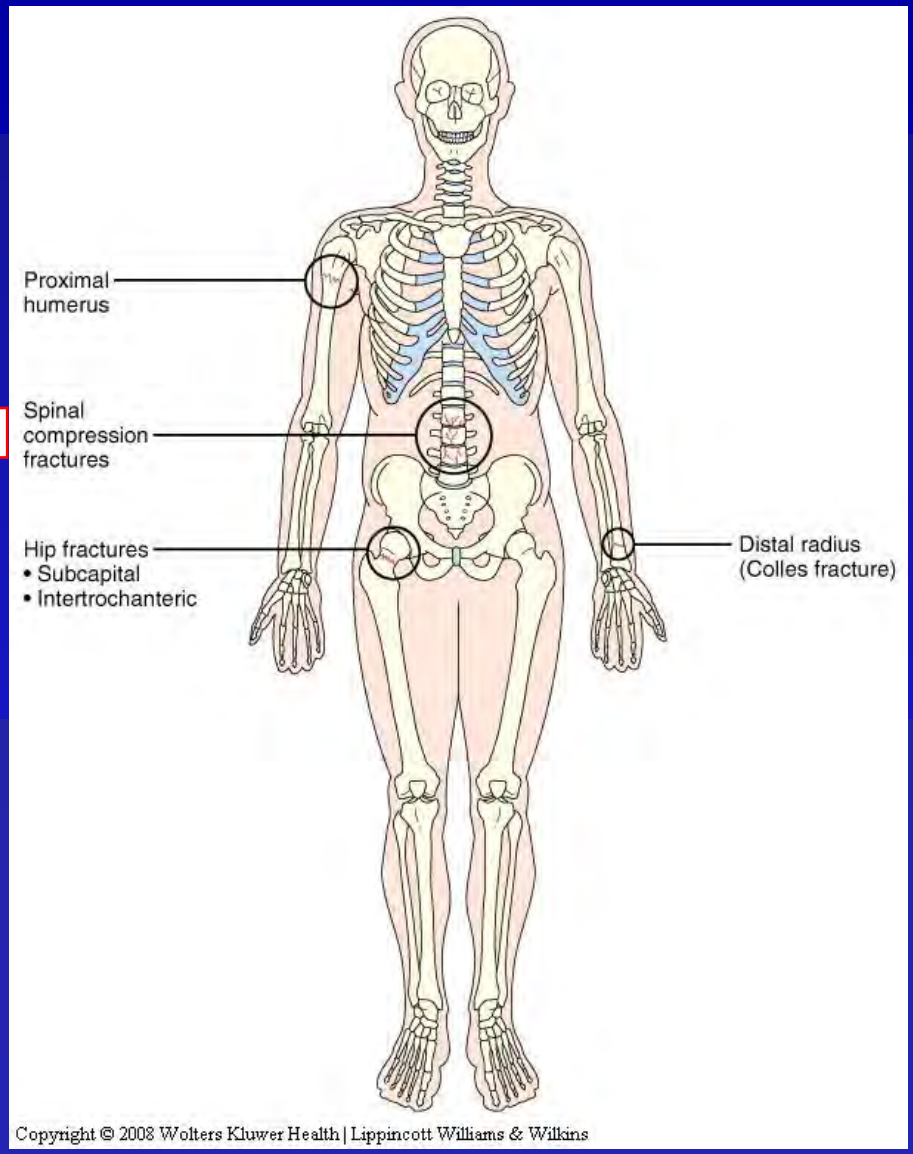
- Decrease in amount of bone to the point of spontaneous fracture or fracture after minimal trauma
- In U.S. are 1.5 million osteoporotic fractures with est health care cost of $18 billion
- Older white women most frequently affected
  - Begins as early as 35; 0.2 percent loss per year
  - After menopause loss accelerates

Osteoporosis

continued bone loss to the point that they can fracture spontaneously or w/ miminum trauma

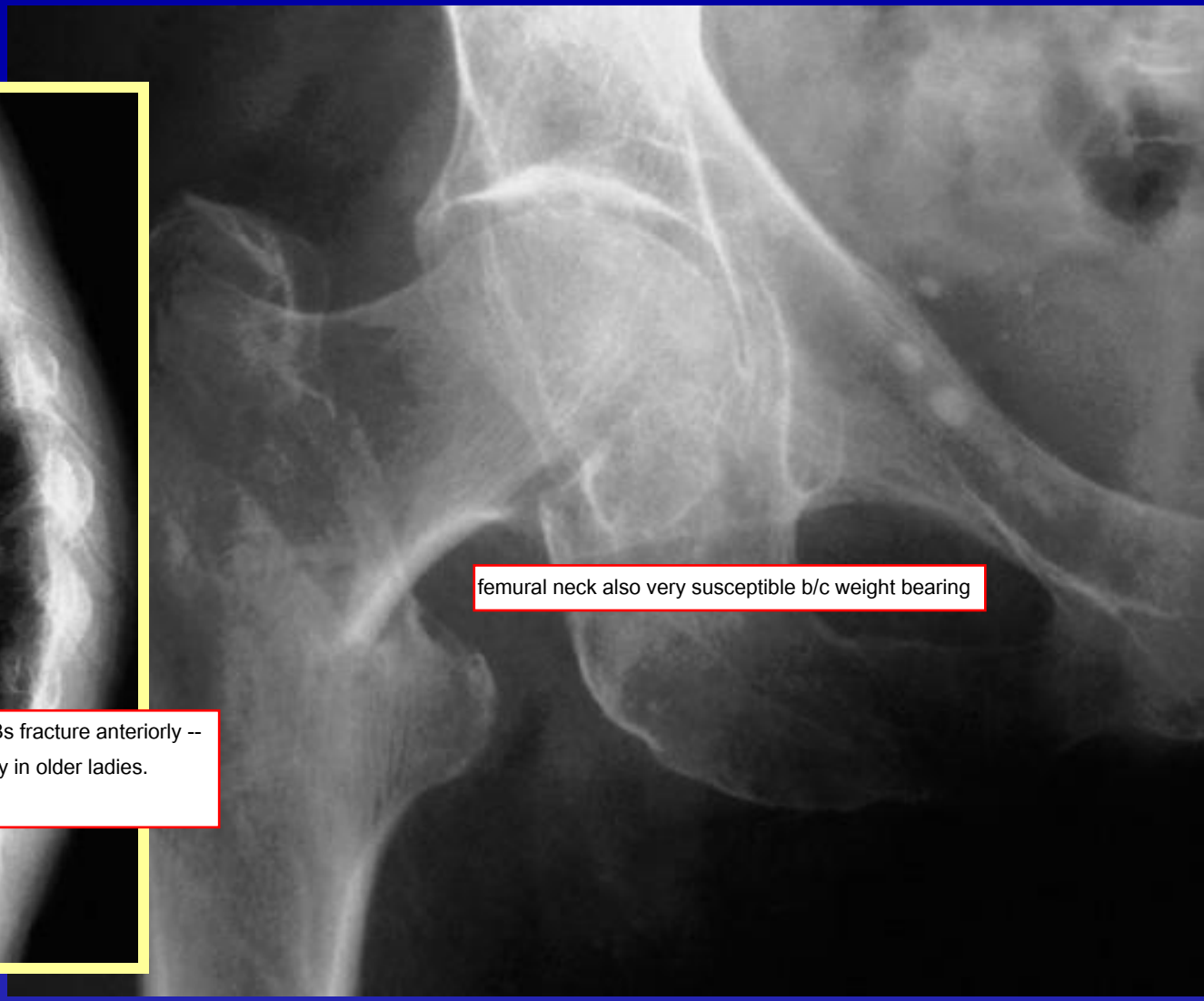
- Common fracture sites:
  - Proximal humerus
  - Distal radius — 'colles' fracture; very common
  - Hip fracture — susceptible b/c big, weight bearing joint
  - Spinal compression fracture — get multiple microfractures, compresion type fractures

in long bones: you have a fall where you use your arms to catch yourself. 'colles' fracture

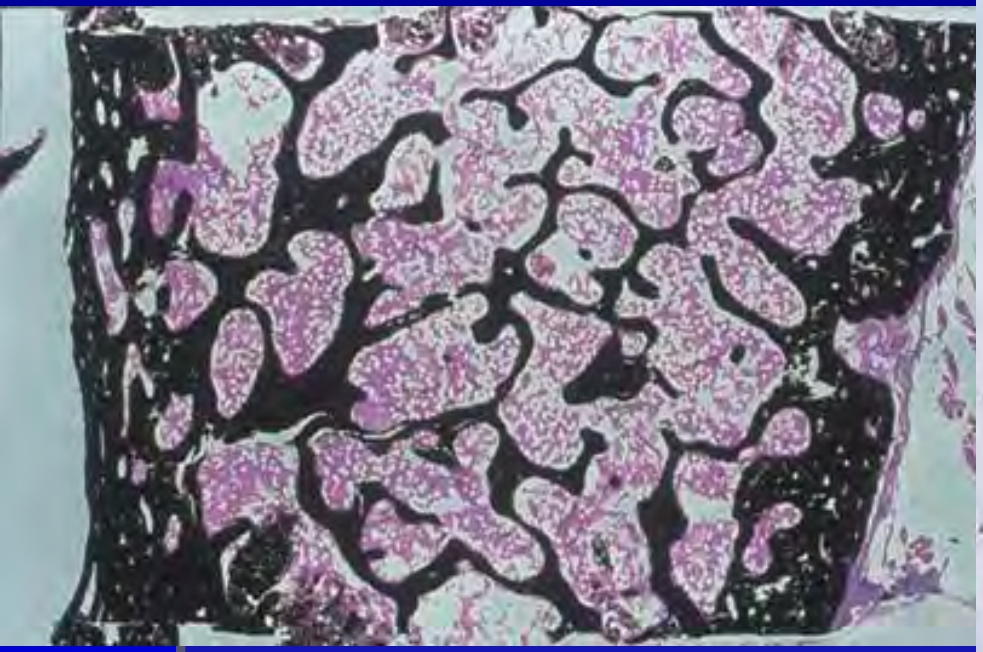


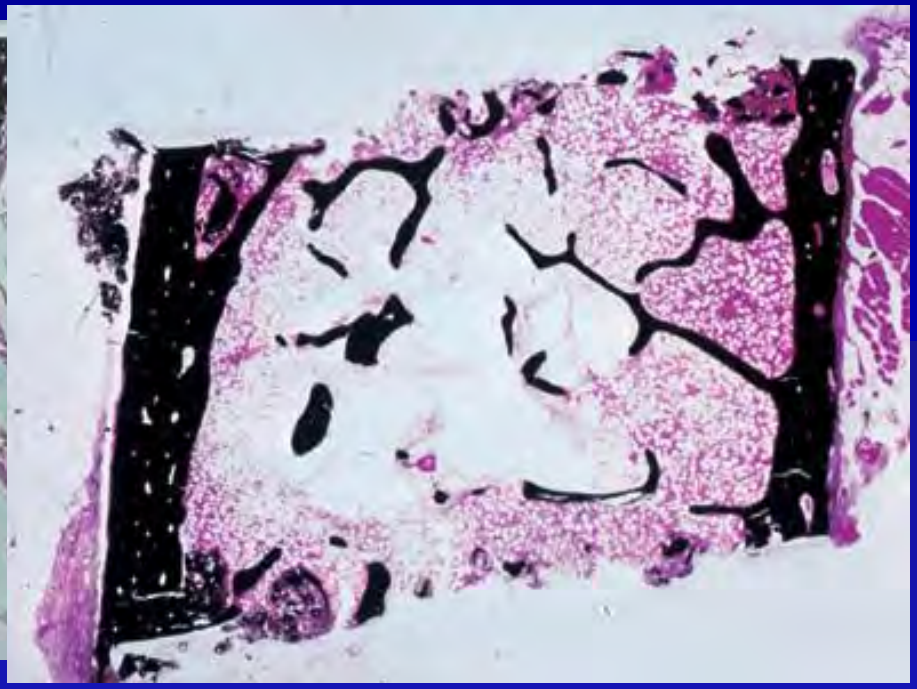
Osteoporosis

vertebral bodies have big marrow space. VBs fracture anteriorly -- get curvature of spine. see it most commonly in older ladies. known as 'dowajer's hump.'



femural neck also very susceptible b/c weight bearing



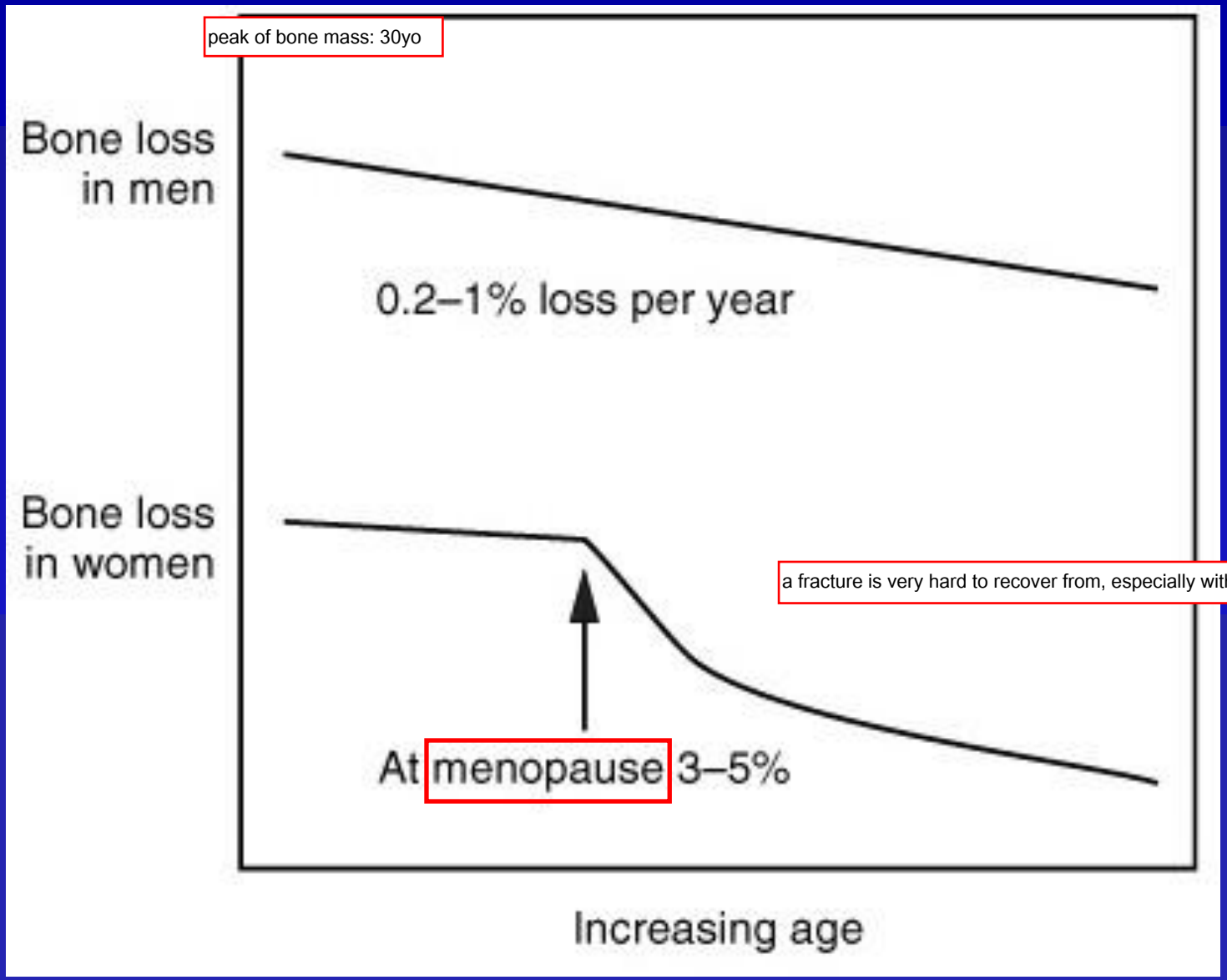


- Iliac biopsy revealing Microarchitectural deterioration: loss of bone, thinning of remaining bone and lack of trabecular connectivity

histo: L: relatively normal. see cortical area and trabeculae line up, give structural integrity.
R: cortices thinner, trabeculae dont line up or touch, so very weak
so, **lose the actual bone mass from both cortical bone and trabecular bone**

Osteoporosis

there are genetic and env components.
AAs dont lose bone as quickly as Cs.
if you live to 90yo as a woman, you are losing a LOT of bone density along the way



Paget's Disease

genetic: northern european

- Skeletal disorder with characteristic clinical, x-ray and histologic changes
- Rare before age 40
- Est to involve 2-3% of population over 50.
- Common in individuals of English/Euro descent and of areas settled by immigration: US, Australia, New Zealand, Argentina, South Africa

note that not everyone will have symptoms as severe as what she will describe

Paget's Disease

for unknown reason, will have discoupled bone remodeling. alternating phases of osteoblastic w/o osteoclastic, vice versa, and a quiescent phase causing sclerosis.
effects: early phase: intense blood supply can cause high output cardiac failure, bone deformity can impinge of nerves, bone pain
lab tests are not sensitive or specific

- Activation of osteoblasts and osteoclasts resulting in abnormal remodeling of bone.
- High tissue turnover manifests as abnormal lab results
  - Elevated alkaline phosphatase
  - Urinary hydroxyproline (collagen breakdown)

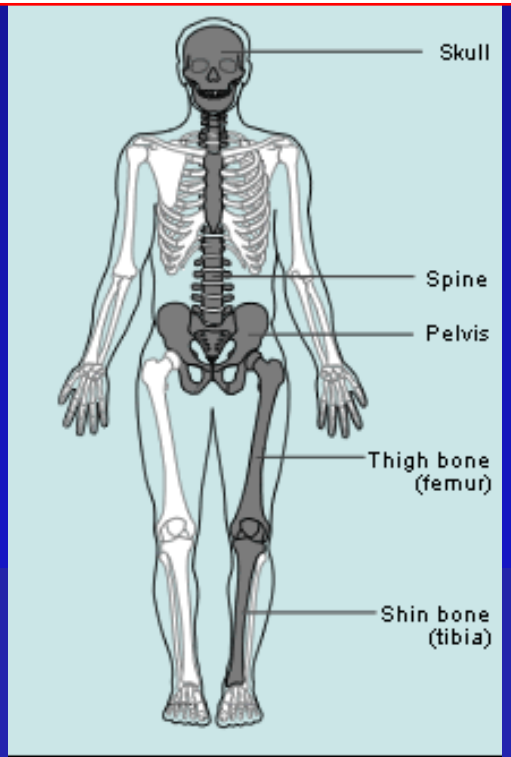


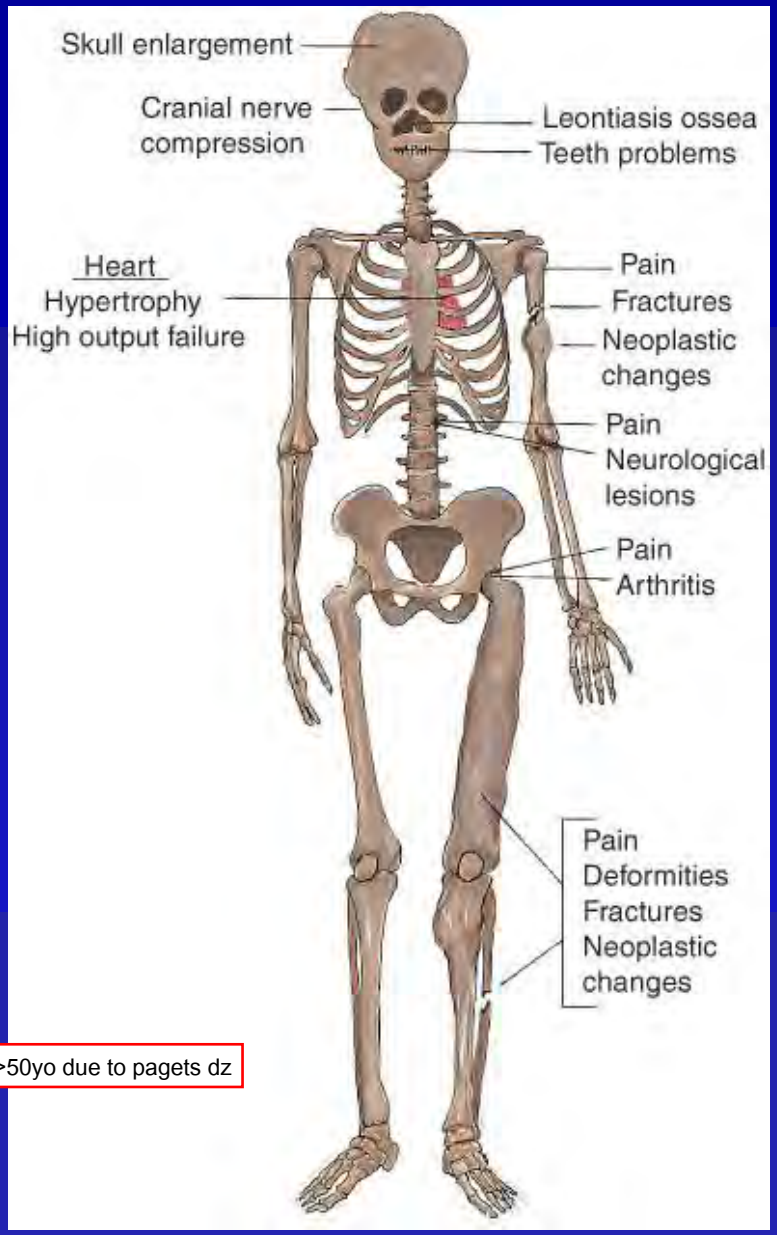
Figure 2. The bones commonly affected by Paget's disease

Paget's Disease

fracture is one of the first symptoms

- Bone pain
- Paget bone is prone to fracture
- Neurologic symptoms
- Increased risk of sarcoma

osteosarcoma. normally a dz of infants to adolescents. but second peak in >50yo due to pagets dz



Paget's Disease

can be multi or uni focal
can be severe or clinically asymptomatic

evidence of deformity, thickening, radiolucency

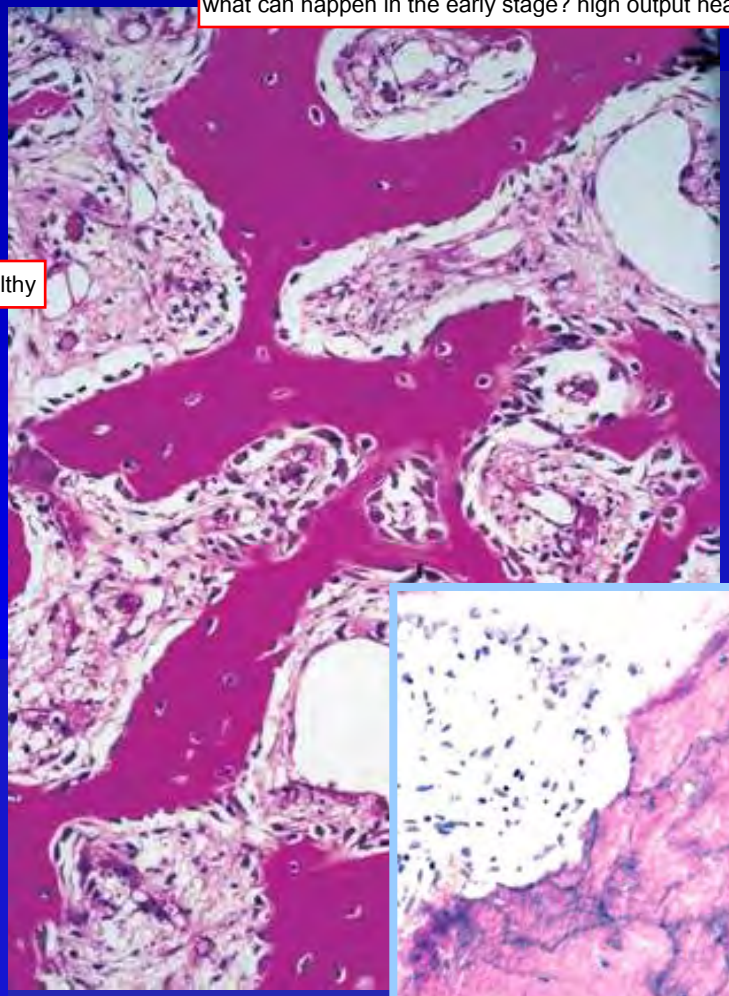
- Imaging findings depend on phase of disease
- Deformity, thickening and coarsening
- Weak, "brittle" bones

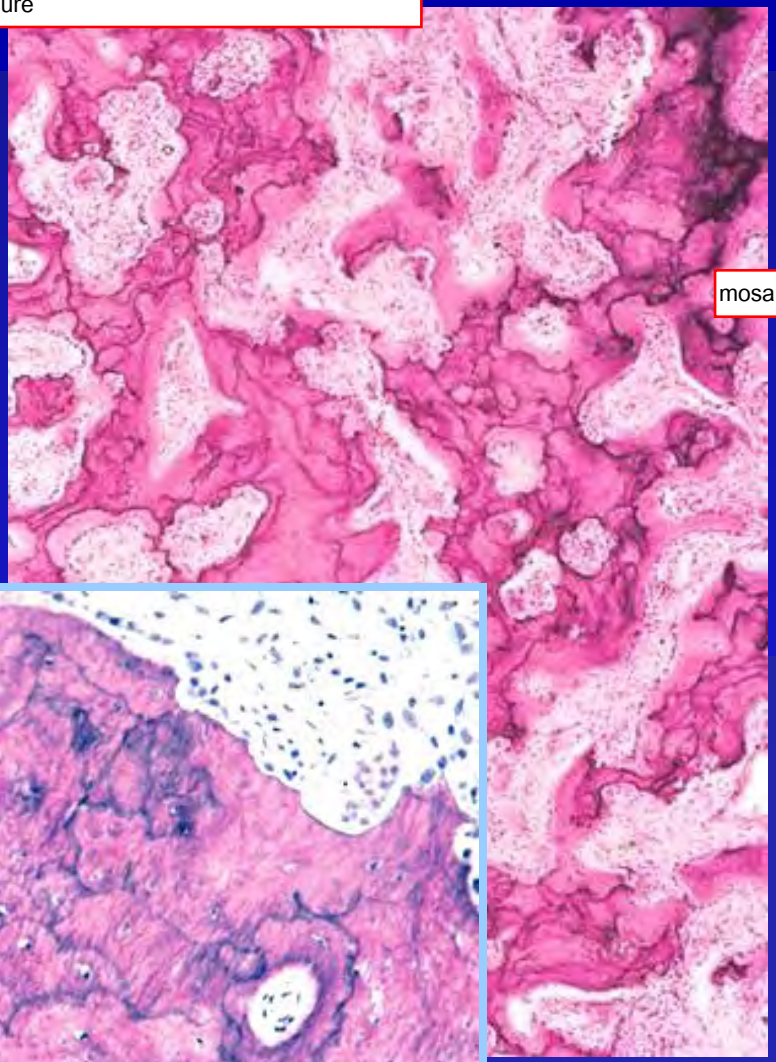
what are the three phases?
blastic phase
clastic phase (resorbed)
sclerotic phase

Paget's histology

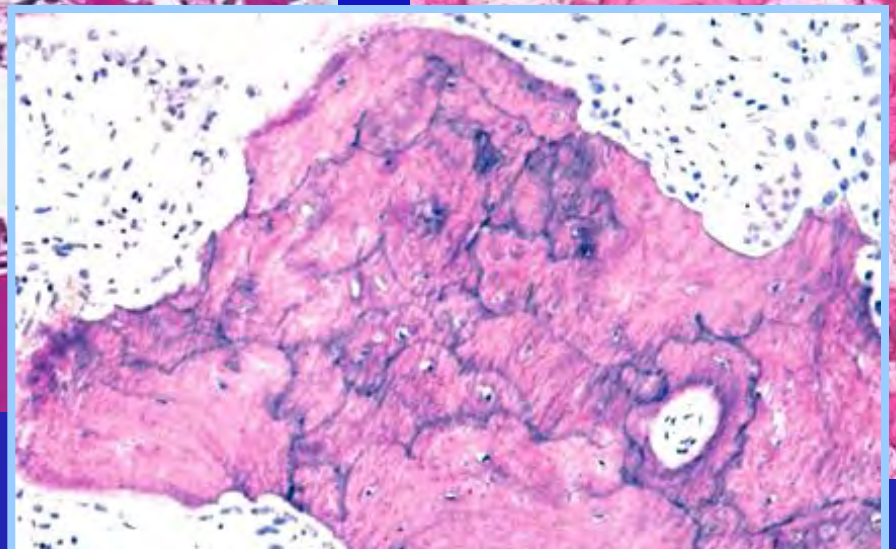
histo doesn't help to diagnose except for mosaic pattern of bone formation in burnt out, end stage.
what can happen in the early stage? high output heart failure

healthy





mosaic

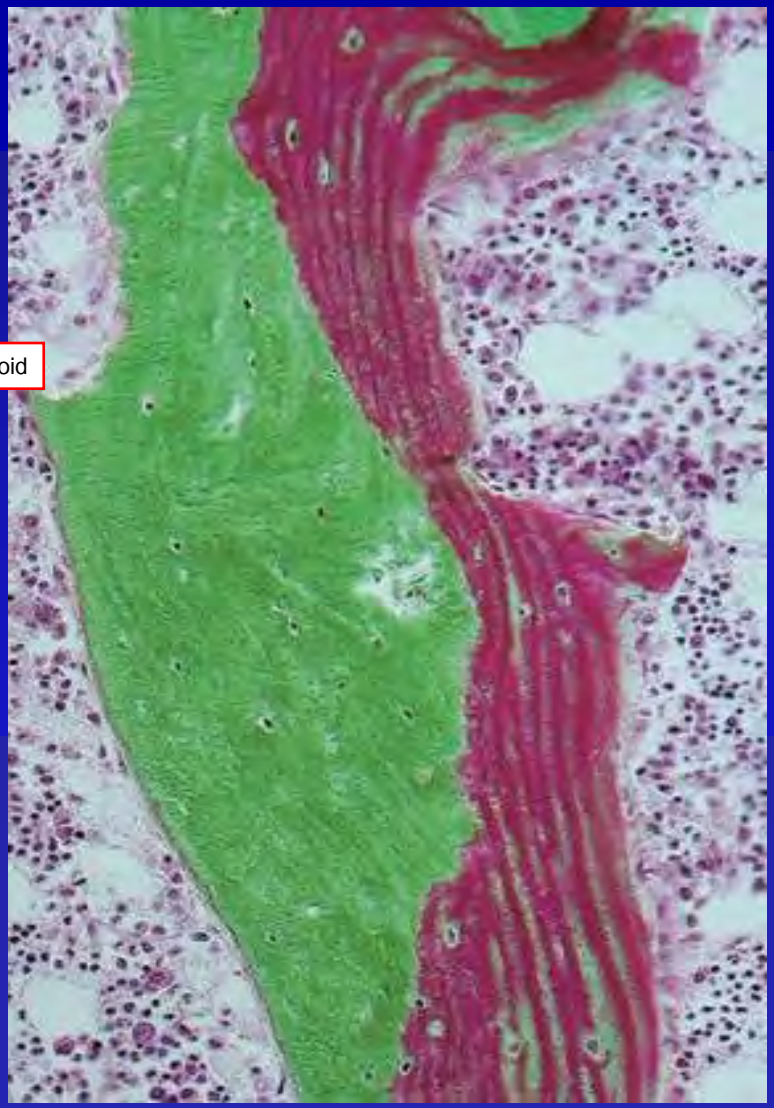


NOW STARTING METABOLIC DZS

Osteomalacia

collagen precursor does not get mineralized, so have a lack of osteoid
green = unmineralized
red = bone being laid down in a nice lamellar pattern

- Defect in mineralization of bone = increase in unmineralized osteoid = lack of osteoid
- Numerous mechanisms:
  - Dietary deficiencies
  - Renal tubule leak (Ph)
  - Hepatobiliary disease
  - Metal poisoning
  - Drugs
  - Malabsorption



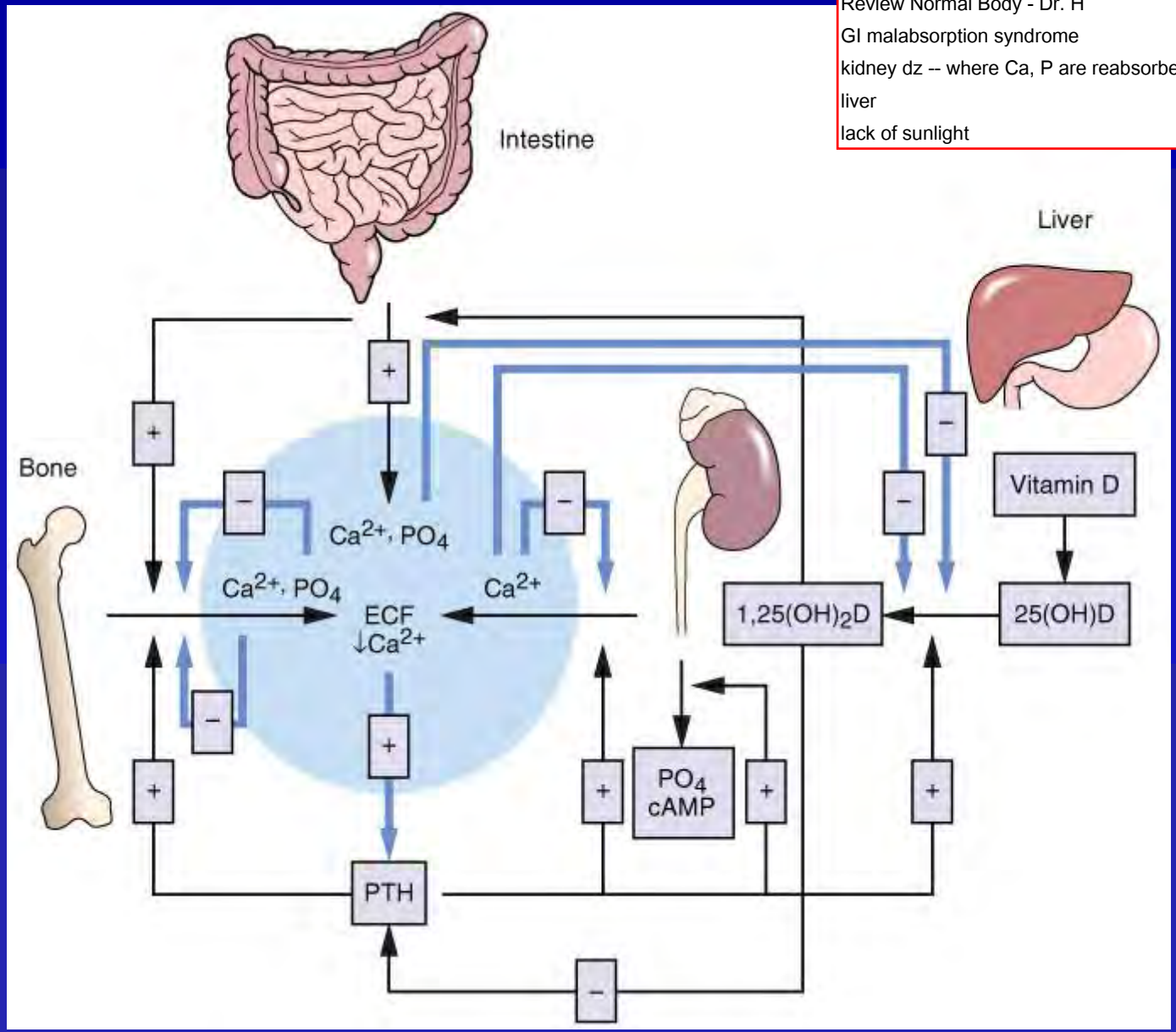
Rickets

reached peak incidence in early industrial era in the UK, where lots of malnutrition and lack of exposure to sunlight. in developing infant / newborn, affects of osteomalacia are very profound. get irreversible deformity and bowing of the legs. rickets not 'just historic' due to food fat-ism, continued malnutrition

- Osteomalacia of childhood
- Skeletal effects more profound on developing skeleton
- Disturbances of growth plate = deformity and dwarfism

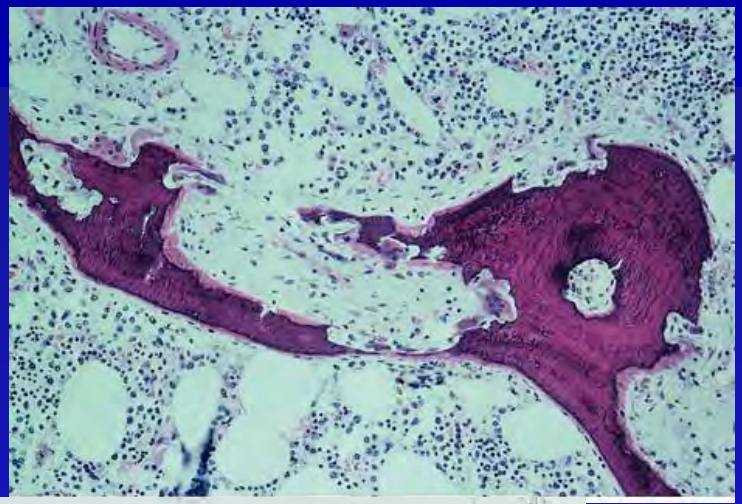
Regulation of calcium homeostasis

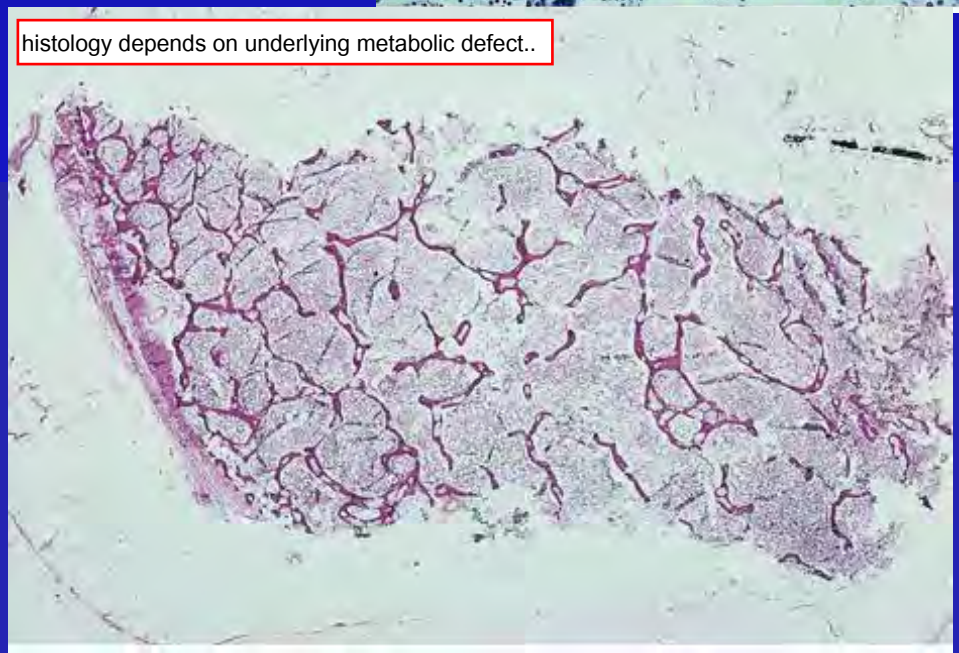
Review Normal Body - Dr. H
GI malabsorption syndrome
kidney dz -- where Ca, P are reabsorbed
liver
lack of sunlight



Hyperparathyroidism

- Primary and secondary there is 1ary, 2dary, 3iary forms.
- Increased PTH leads to osteoclastic bone resorption

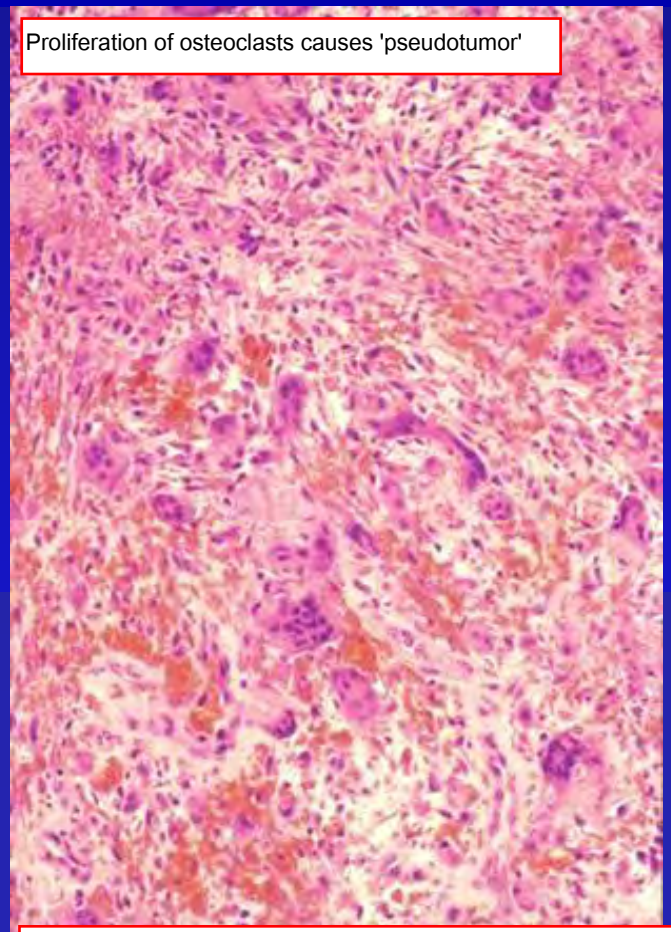




Hyperparathyroidism—Brown tumor

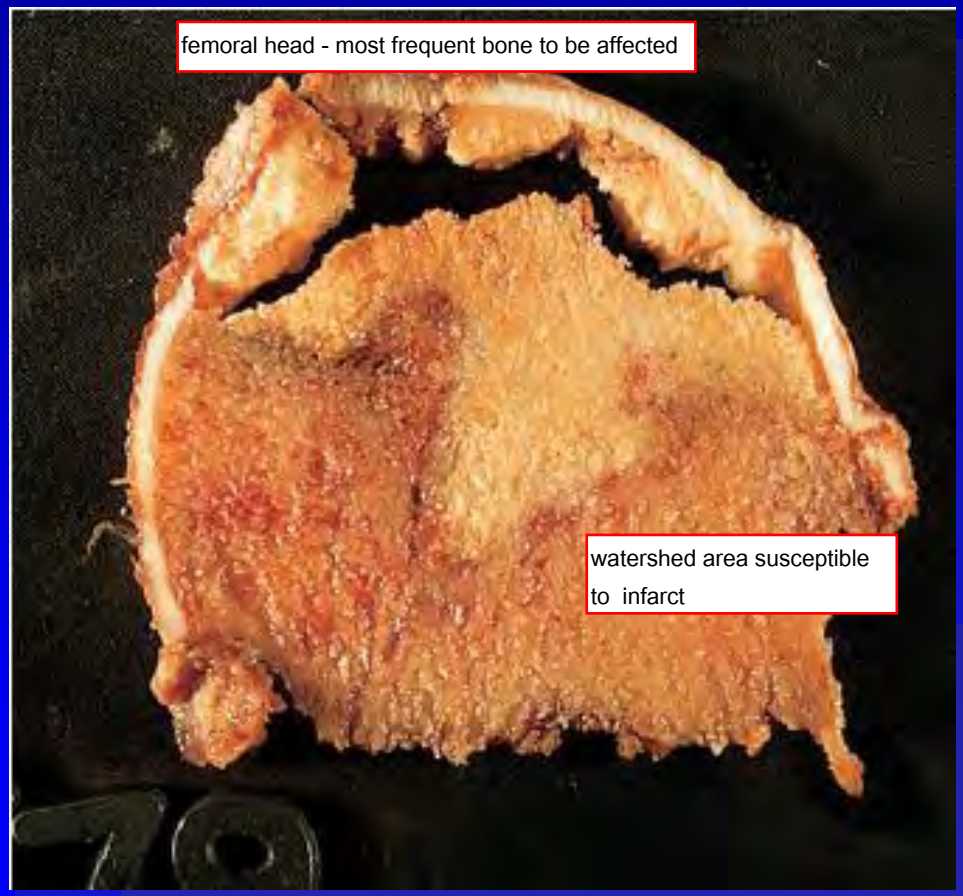
unusual presentation: localized defect in bone where it simulates a tumor. HPTism will give bone pseudotumors that mimic bone tumor

Proliferation of osteoclasts causes 'pseudotumor'



bone is just full of osteoclasts. giant cell tumor looks almost identical -- look out for it on next lecture!

Osteonecrosis



Causes:

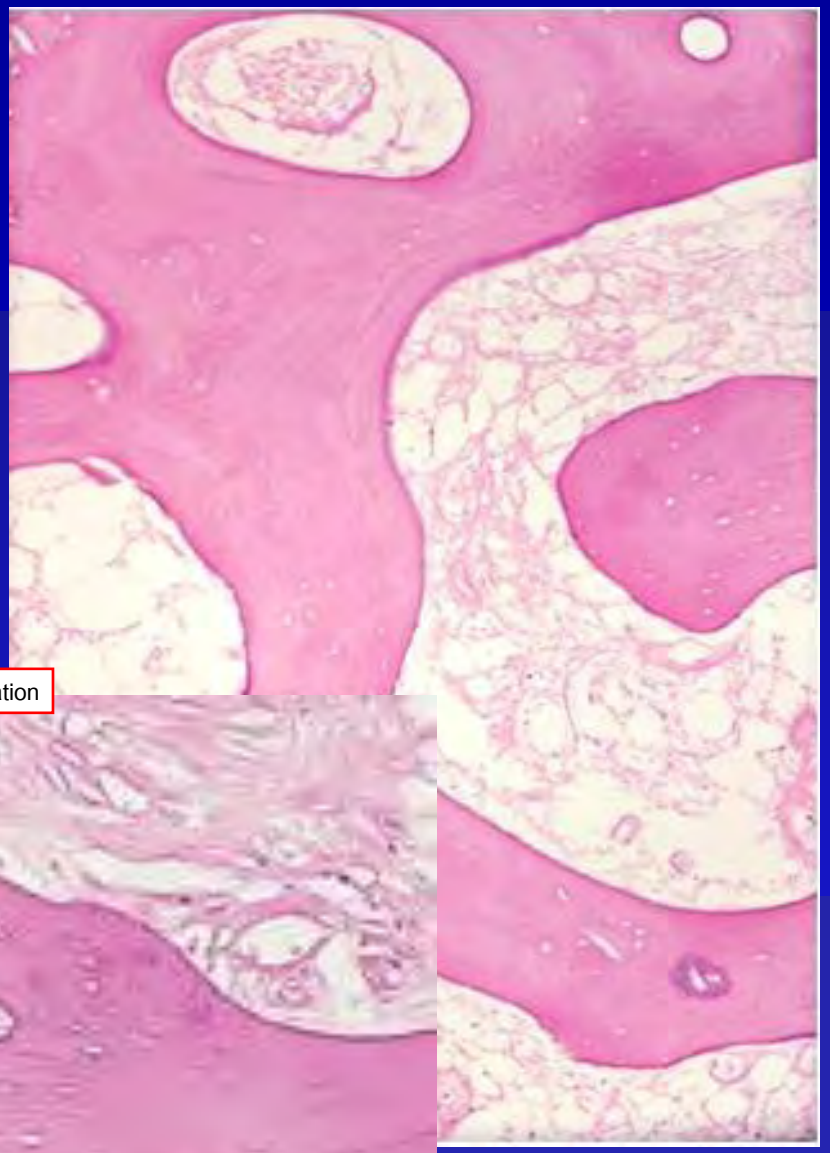
- Traumatic
- Iatrogenic:
  - Radiation
  - Corticosteroids
- Sickle cell disease
- Gaucher Disease
- Alcohol
- Idiopathic

long-term steroid use

large number of cases are idiopathic; unclear

Osteonecrosis

- Histologic changes:
- Loss of marrow and fat saponification
- Loss of osteocyte nuclei

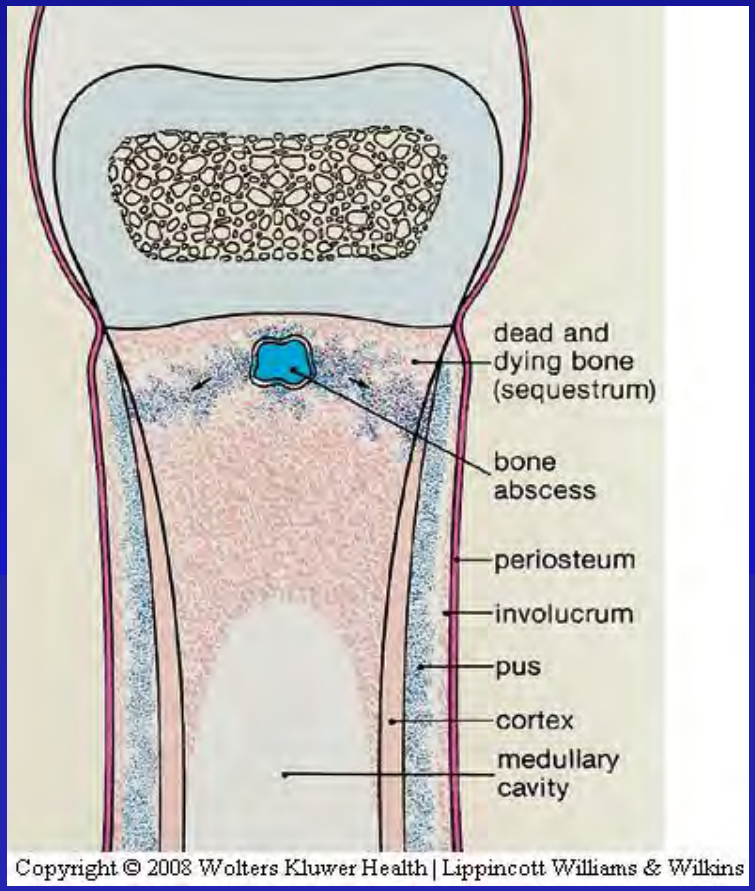


bone dies, marrow becomes fibrotic, get fat saponification

Osteomyelitis

- Pyogenic/bacterial
- Routes of spread
  - Hematogenous
  - Extension from contiguous site
  - Direct implantation (trauma)

usually bacterial; any systemic infection is a risk factor.
systemic ie UTIs,
commonly due to really bad trauma / fractures (especially that involve a break in the skin)



Ostoemyelitis –organisms

- 50% -- no organism is ever isolated
- Other:
  - *Staphylococcus aureus*
  - *E Coli, Pseudomonas, Klebsiella*
  - *Haemophiles influenza, Group B strep*
  - *Salmonella*

even if you do isolate, can be polybacterial

very commonly isolated

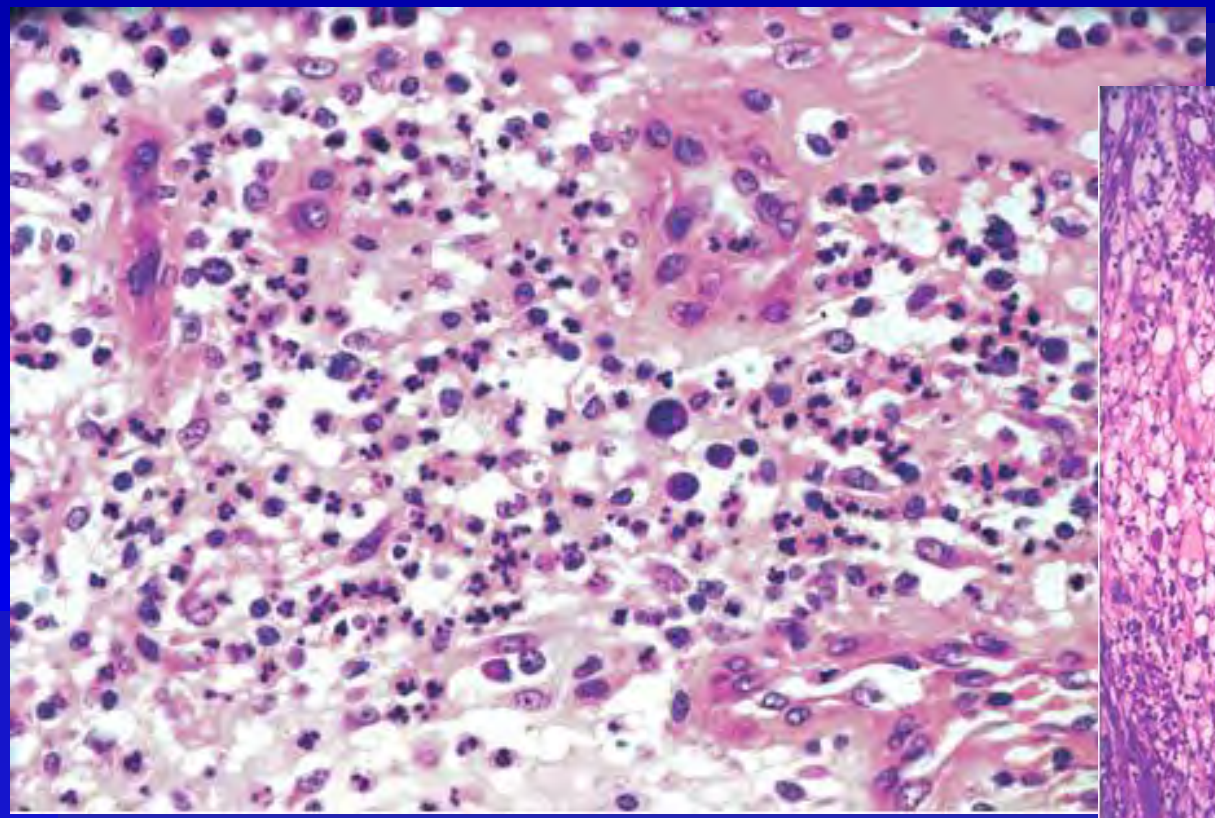
also commonly isolated

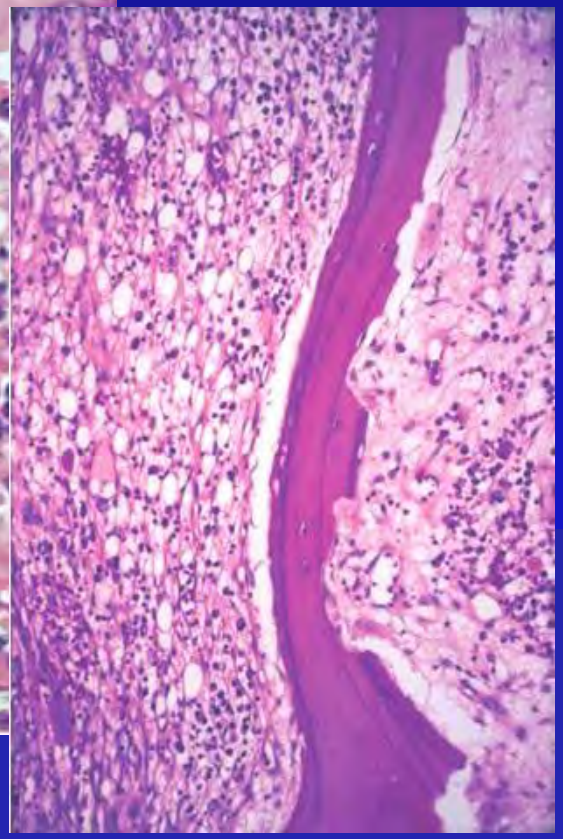
in peds

in sickle cell patients

'this makes a good test q'

Osteomyelitis

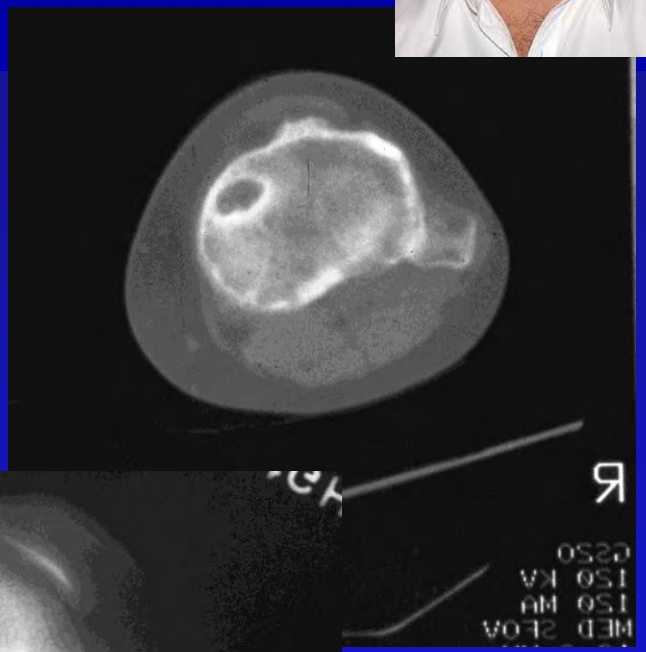




Osteomyelitis-Brodie's Abscess

Brodie's Abscess describes a small, focal area of osteomyelitis: seen especially in children; painful patients can can have increased sed rate. 'just go in and evacuate them.'

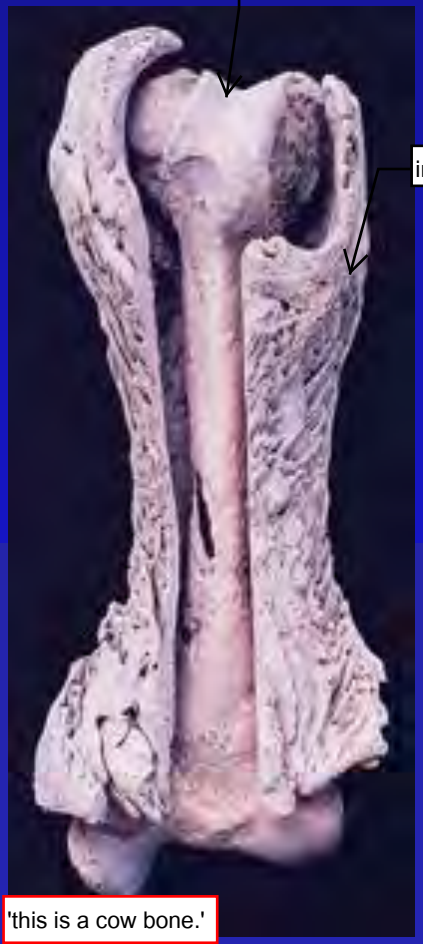
- Possible outcomes of untreated/undertreated osteomyelitis
  - Low-grade, well localized bone abscess



Osteomyelitis- sequestrum and involucrum

dead bone that is a nidus of infection; used clinically to describe an area of concern

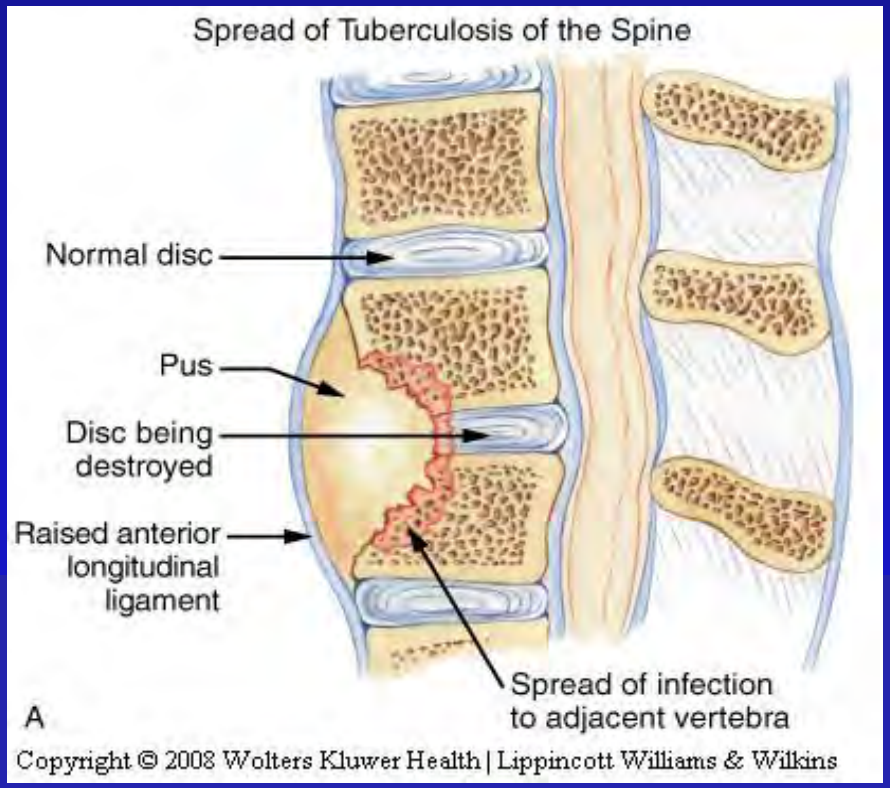
native, healthy bone that forms around the sequestrum to seal it off from the rest of the body; not really used clinically



'this is a cow bone.'

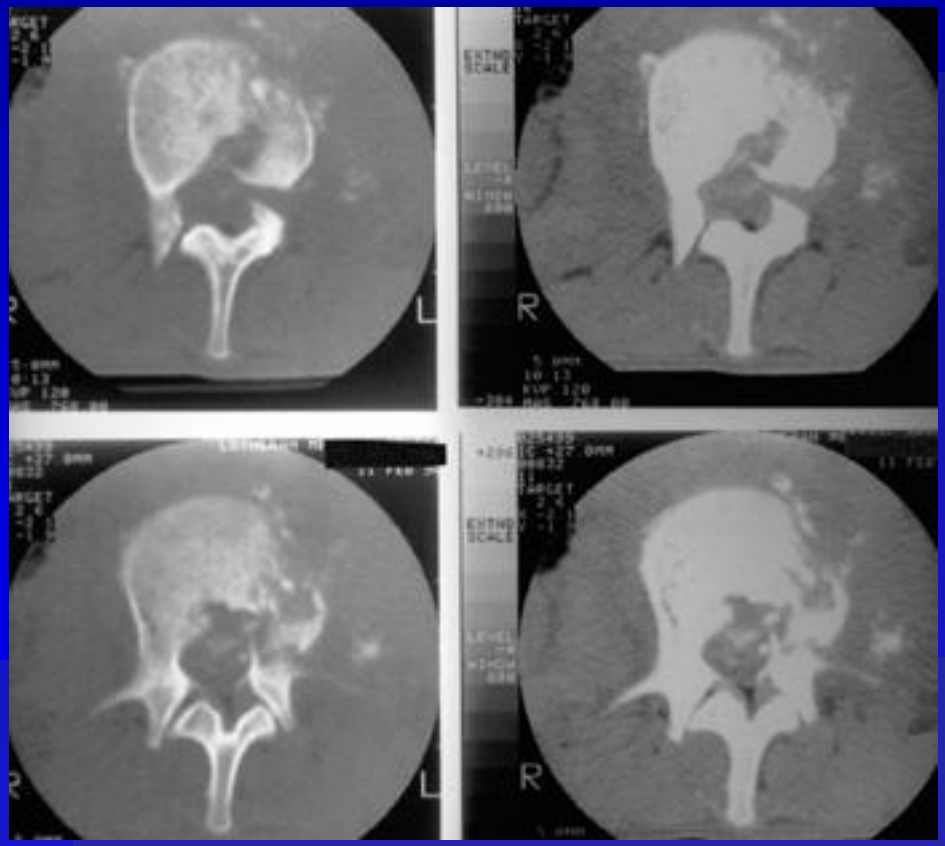
Potts Disease

- Increasing incidence with globalization and increase in iatrogenic or acquired immunosuppression
- Pulmonary disease is most common but subset will form osteomyelitis



special type of osteomyelitis due to TB. tuberculoid osteomyelitis is a bad dz -- likes to infect the spine, is very destructive. causes all types of destructive foci, causes soft tissue calcification, can get ankylosis of vertebrae.
'if you see an infection of the spine, think potts dz.'

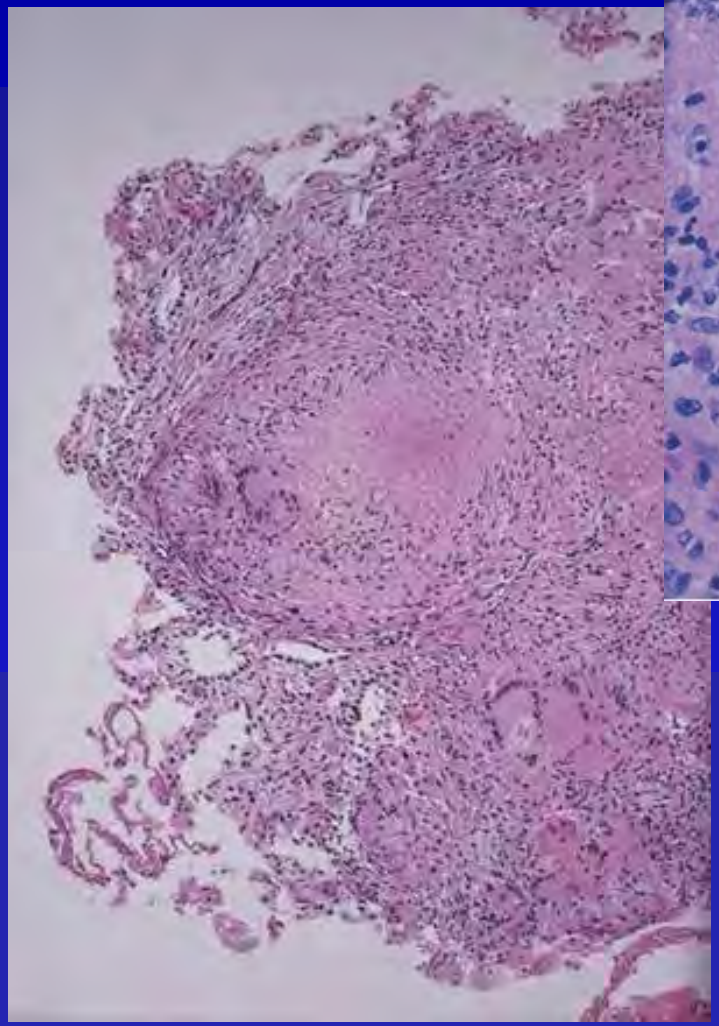
Potts Disease

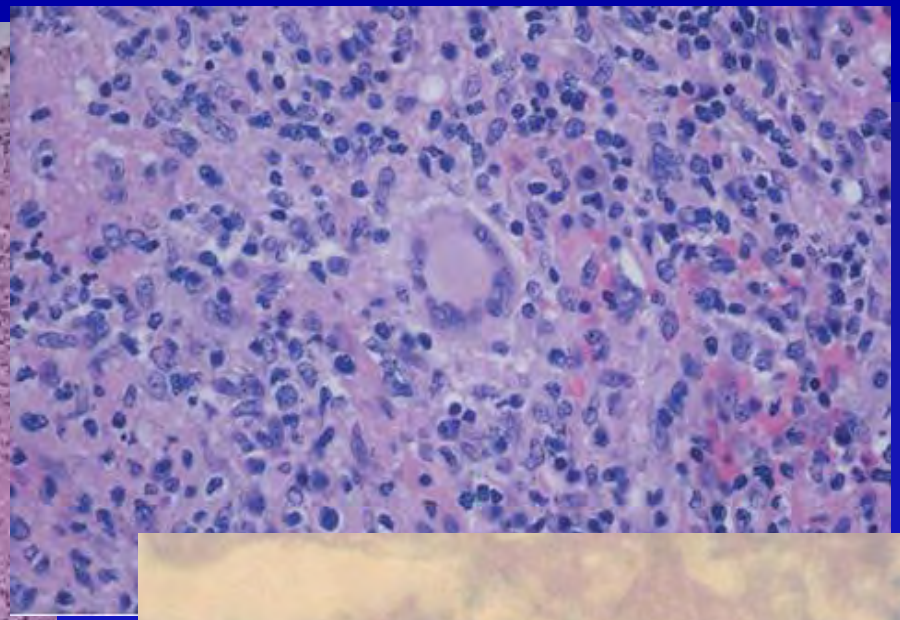


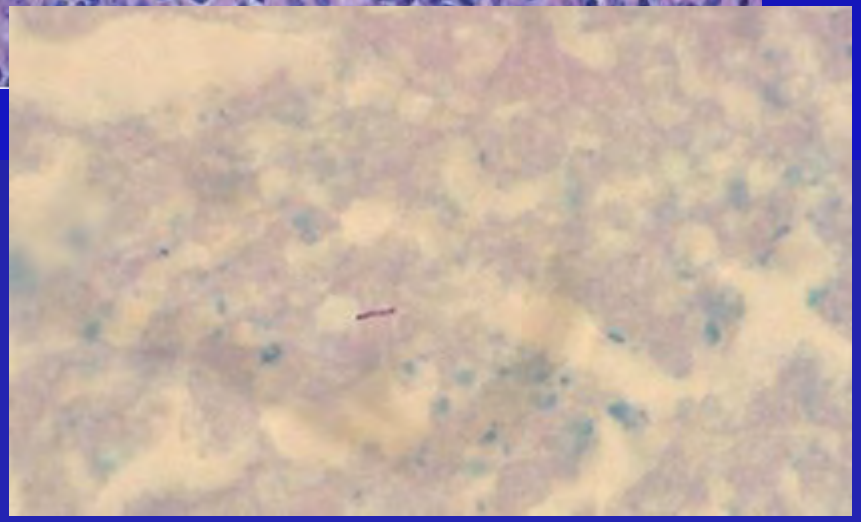
- Fragmentation of vertebral bodies
- Obliteration of disc space
- Calcified soft tissue masses
- Encroachment on spinal canal

TB infection in soft tissue!!

Mycobacteria







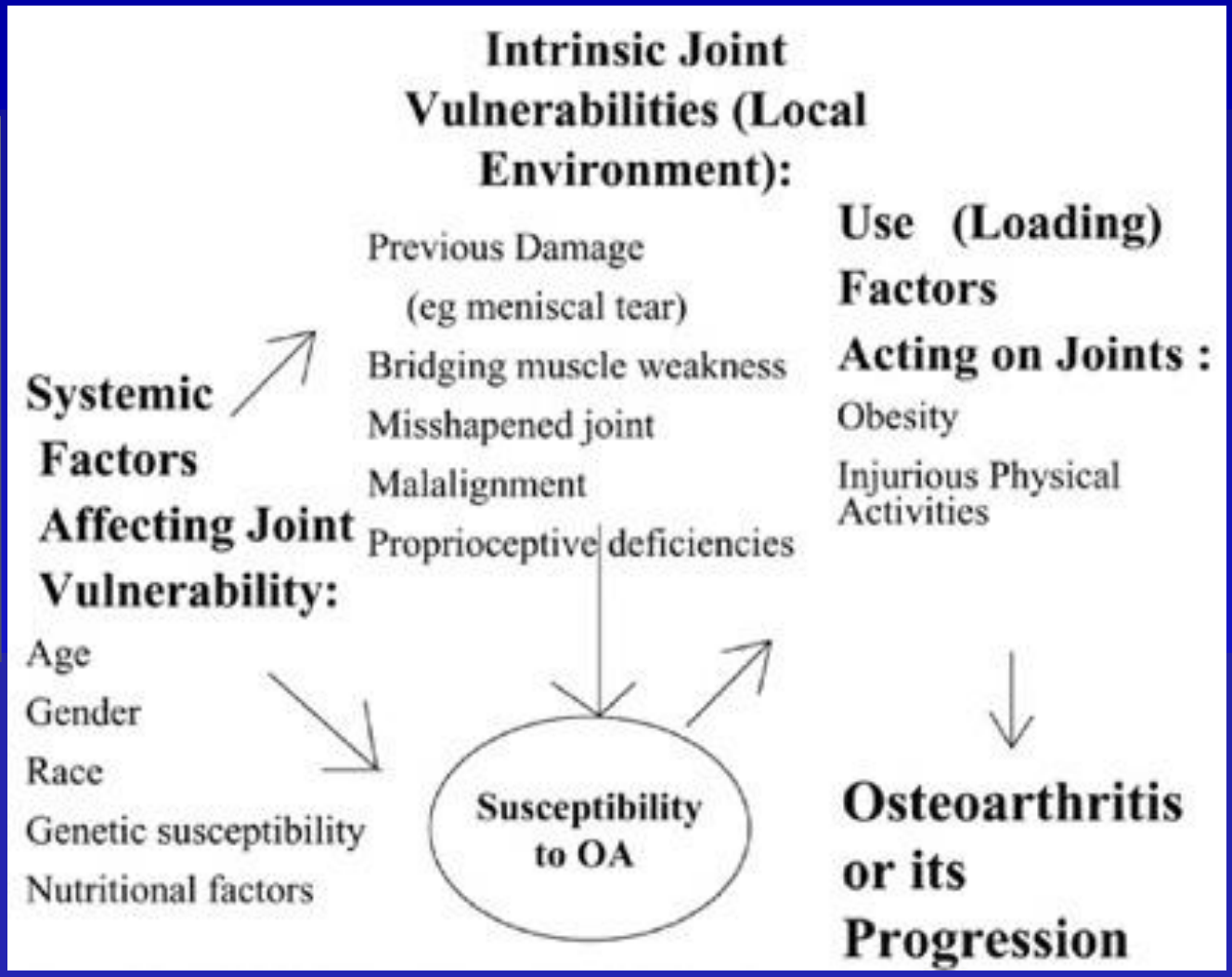
Osteoarthritis

happens to all of us: degeneration and process of wear and tear helps to cause this.
secondary effects -- repeated trauma (athlete), overweight, malalignment in joint, etc.

- AKA “Degenerative joint disease”
- Ubiquitous process with increasing prevalence relative to age
- Different manifestations in depending on location, severity
- Clinical: Pain and stiffness, lack of mobility
- Primary osteoarthritis– “wear and tear”
- Secondary OA-congenital deformity, repeated mechanical trauma, obesity, other underlying disease

Osteoarthritis

'probably genetic underpinning and env, but is ubiquitous; just wear and tear'



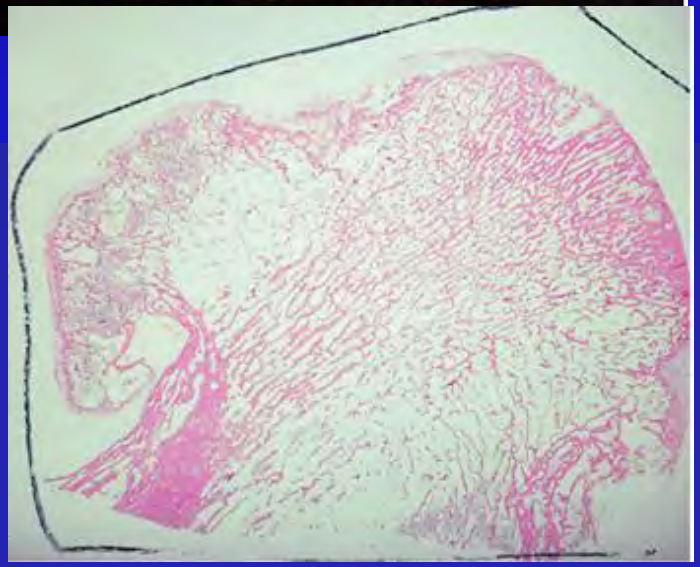
Osteoarthritis

large weightbearing joints are most affected. the articular surface is fibrillated ('torn up'). get pieces of cartilage that fall off due to degenerative process, fall into the joint, called joint mice. joint mice move around, cause some clicking, popping, immobalization. accounts for some, but another process also occurs -- see next slide

- Histologic changes:
  - Fibrillation and cracking of the of the surface articular cartilage
  - Loss of cartilage and formation of “joint mice”

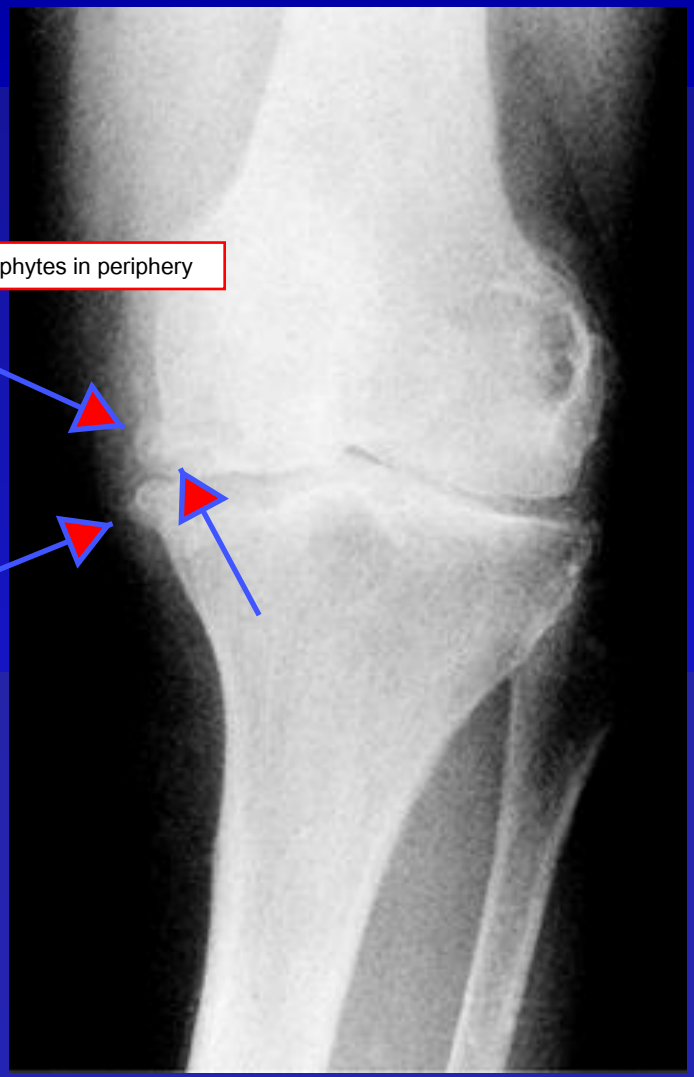
Osteoarthritis—histologic changes

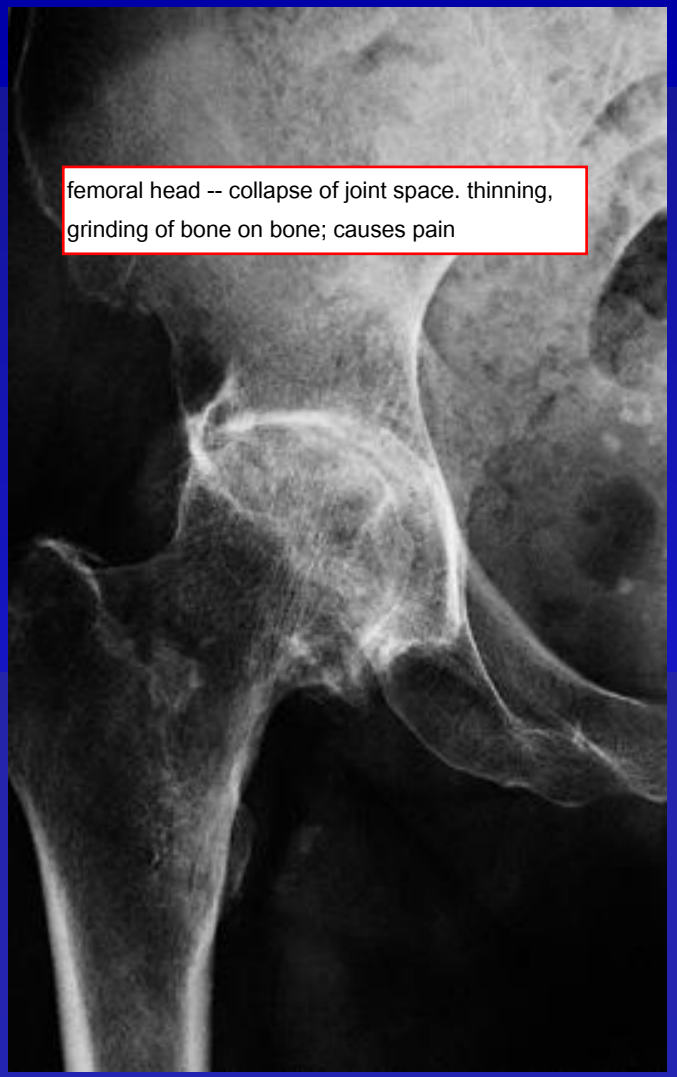
- Exposure of underlying bone (eburnation)
- Formation of osteophytes and cysts within the subchondral bone



as that happens, get intensively painful bone-on-bone grinding. bone tries to remodel itself, but has poor architecture, causing osteophytes -- irregular protrusions of bone. this exacerbates the problems -- decrease in range of motion and increased pain

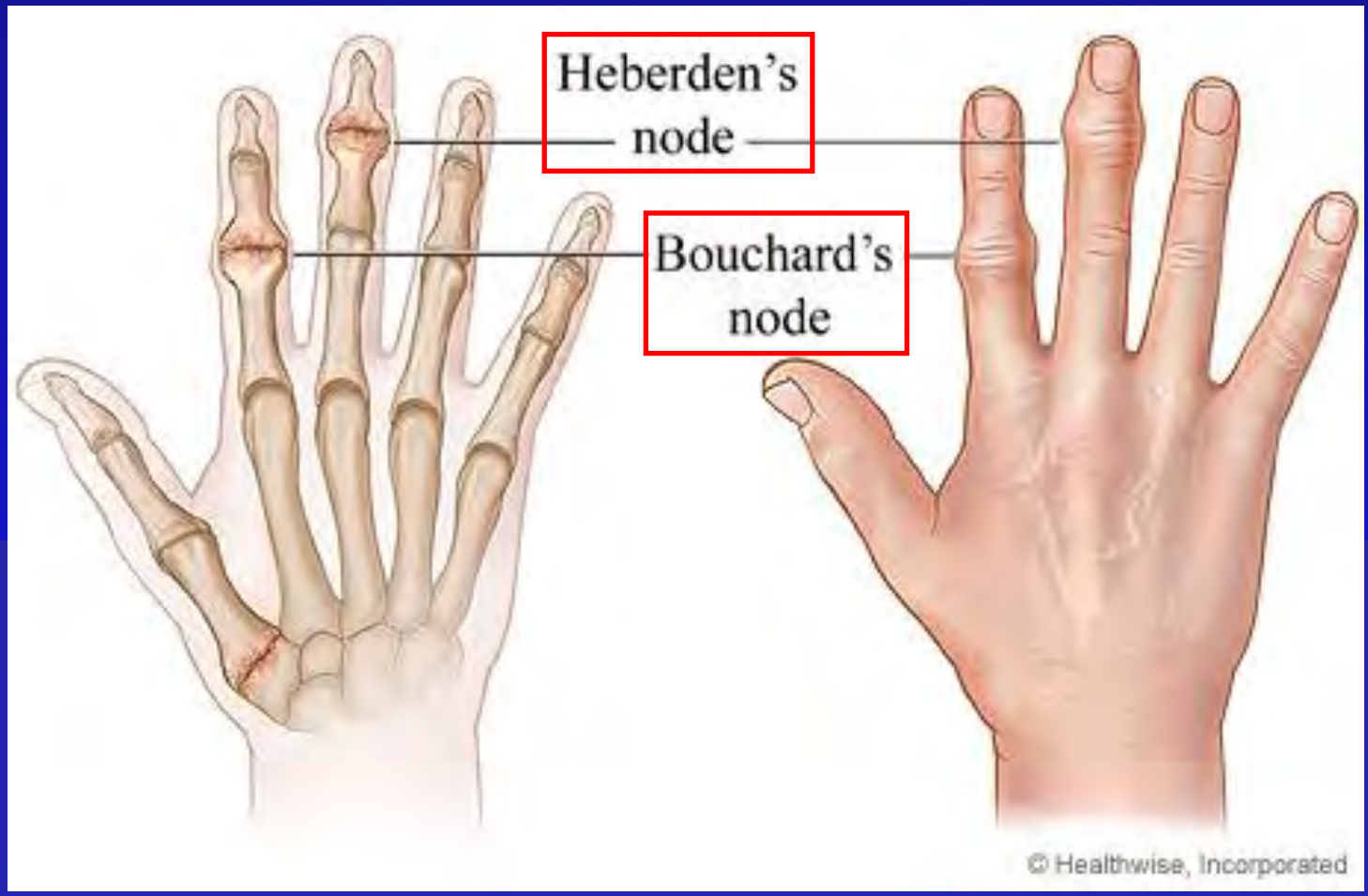
Osteoarthritis



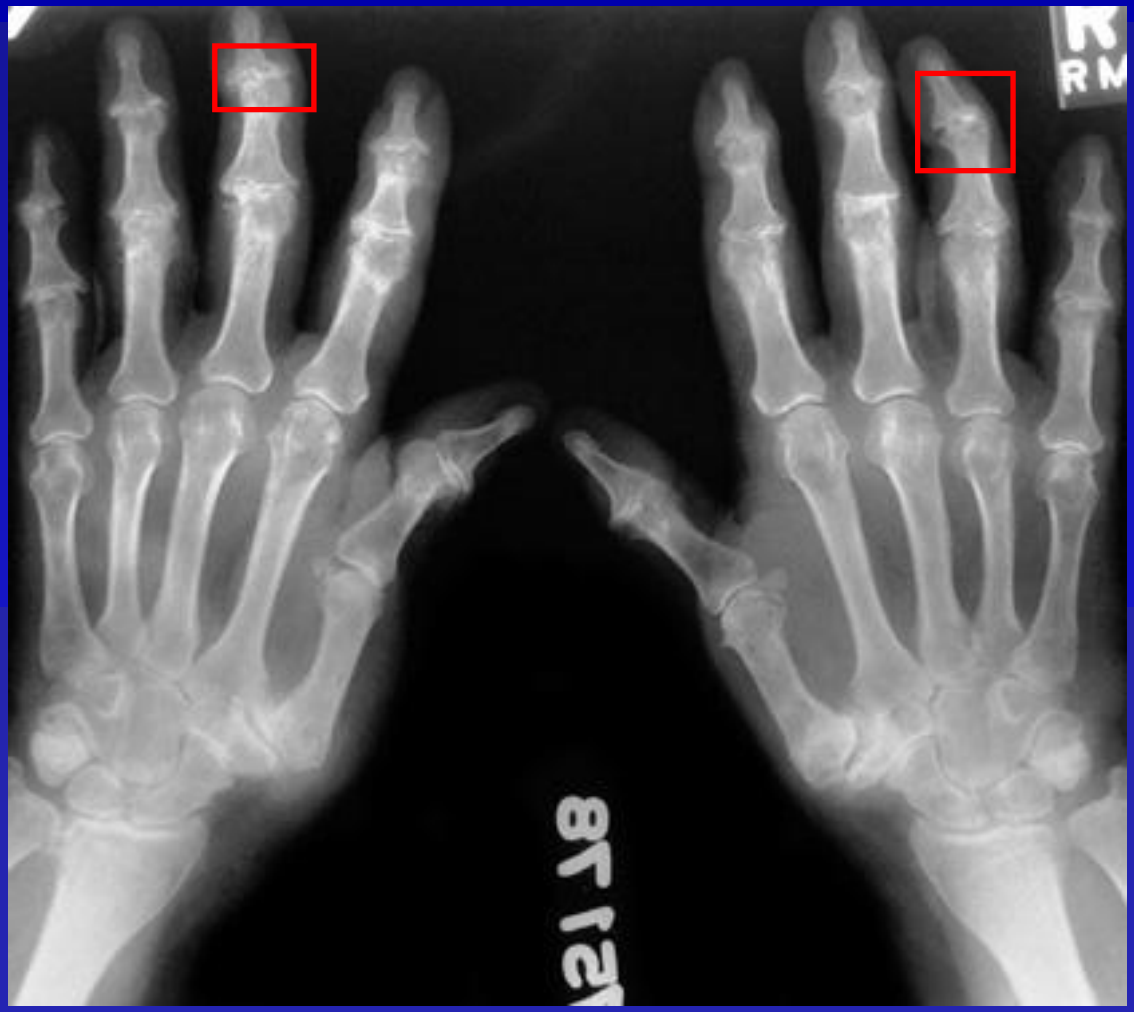


Manifestations of osteoarthritis

sometimes get first in hands. get inflam and deformity in hands. notice that THIS deformity in hands is different that seen in RA.



Osteoarthritis



Osteoarthritis

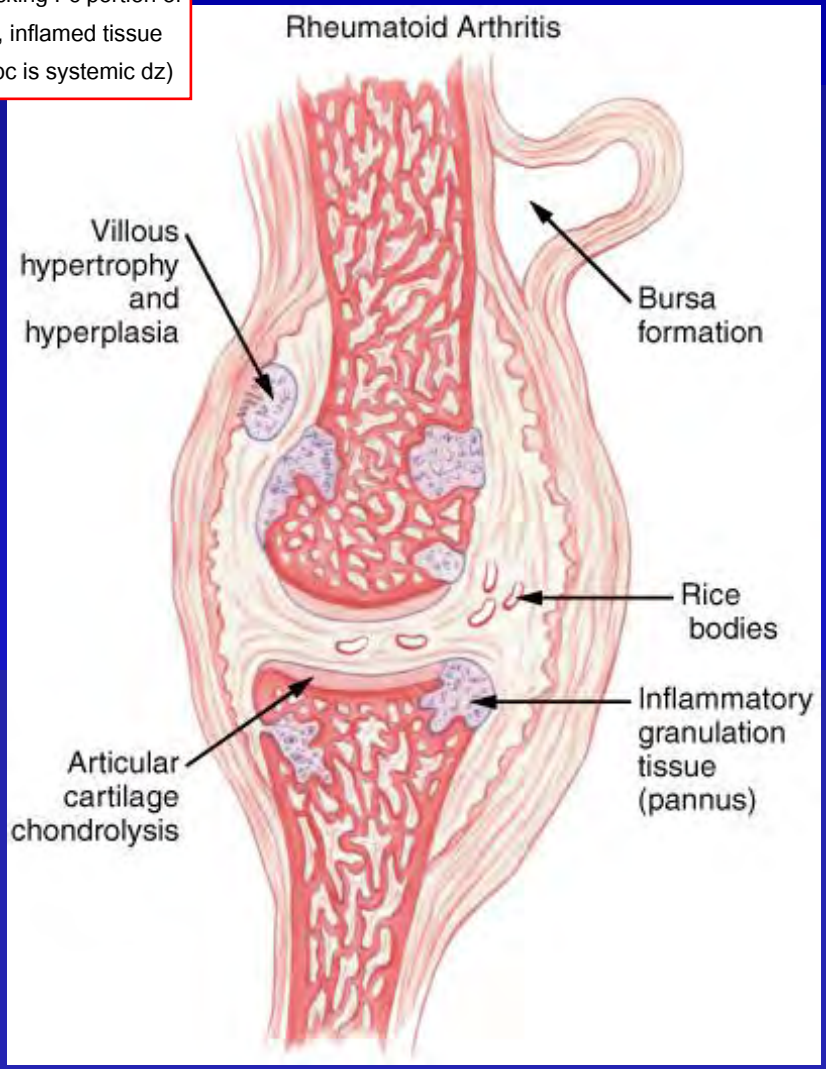
- Laboratory findings — non-specific except for 'joint mice'
  - Normal sedimentation rate
  - Synovial fluid is clear/viscosity normal
  - Fragments in fluid — have joint mice in synovial fluid. can be small or can be macroscopic
- Treatment — 'fortunately very good'
  - Anti-inflammatory/Analgesics
  - Surgical — lots of anti-inflam and analgesics. once they stop working shift to surgical tx. 'we have an epidemic of hip and knee replacements'.

Must be able to differentiate RA from OA.

Rheumatoid arthritis

RA: small joints (hands and feet) first. is inflammatory, systemic dz. caused by autoantibody IgM attacking Fc portion of normal Ig. in RA, get 'villus hypertrophy' -- lining of joints get inflamed, get influx of inflammatory cells, inflamed tissue grows, starts to invade into the bone, causes deformity. also get changes in soft tissue and vessels (bc is systemic dz)

- Chronic, systemic inflammatory disorder associated with autoimmune factors
- Manifests as joint disease but to lesser extent skin/soft tissue (rheumatoid nodules) and vessels



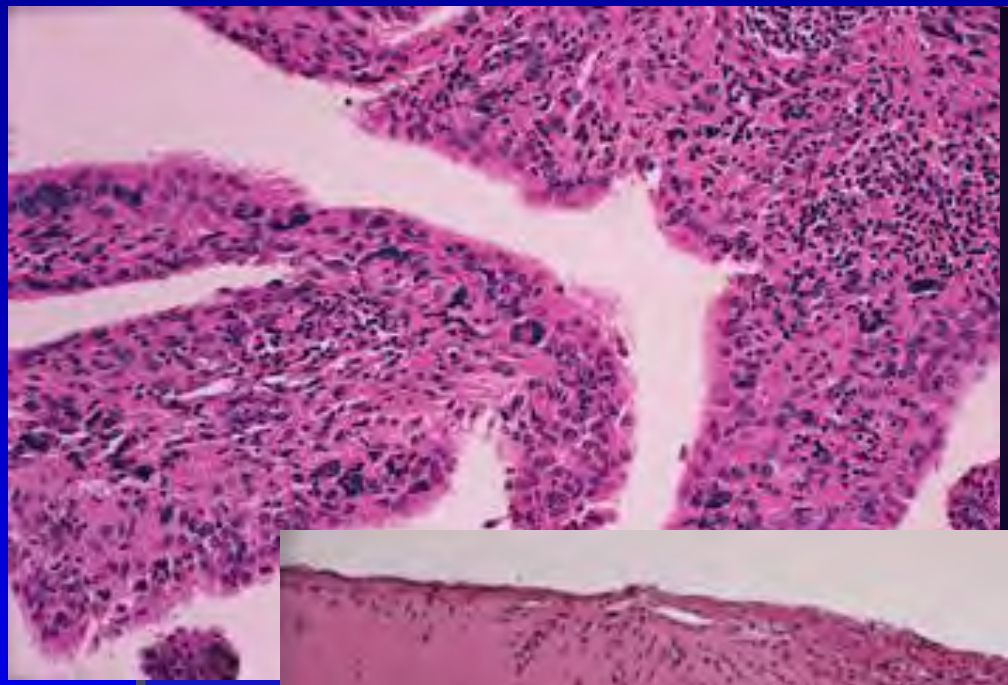
affects proximal joints of hands

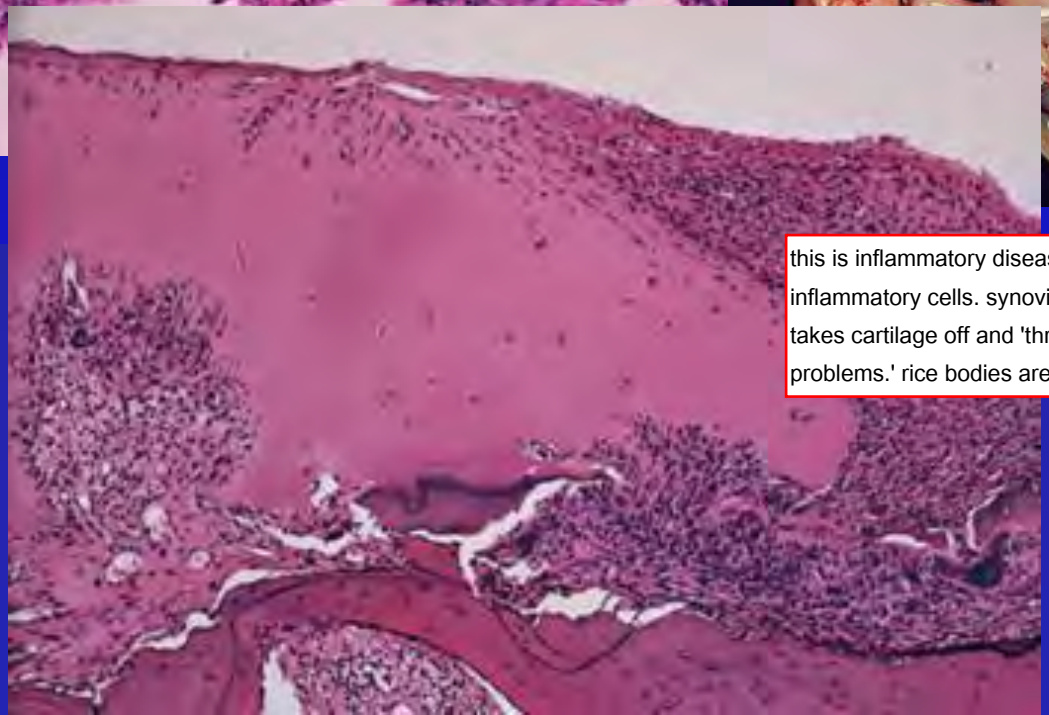
Rheumatoid arthritis

'ulnar deformity of the hands.' usually women b/c more susceptible. large joints get involved relatively late in the dz.

- Affects small joints before large joints
- Hands and feet ; later wrists, ankles, cervical spine
- More common in women than men; 40 to 70. Genetic susceptibility

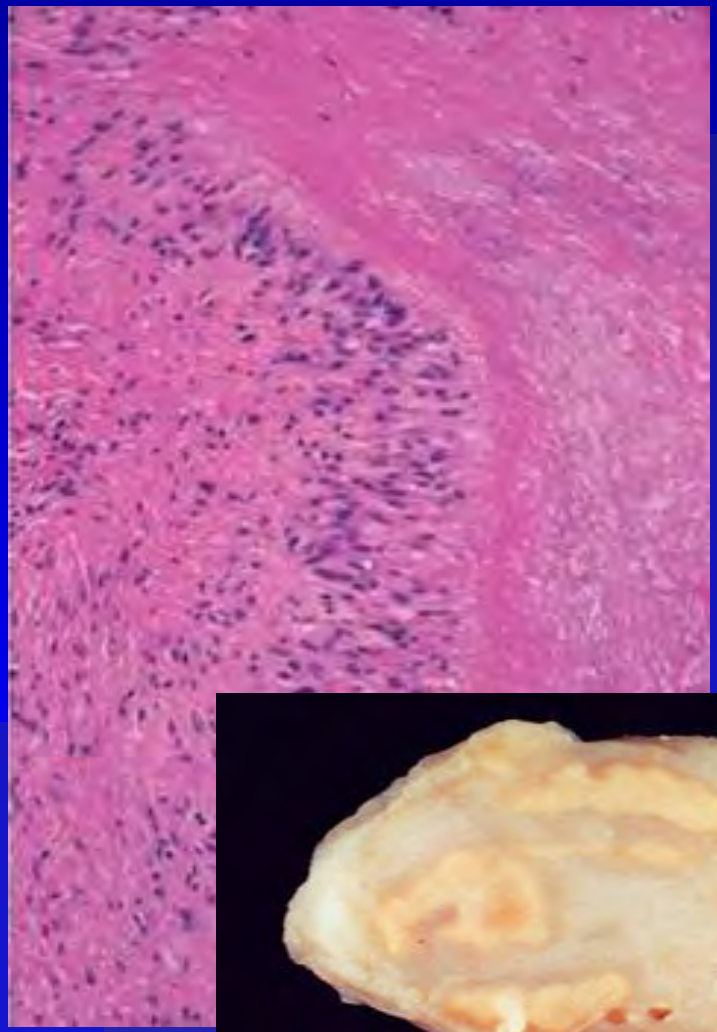
Rheumatoid arthritis





this is inflammatory disease. in synovium, which is hypertrophic, see influx of inflammatory cells. synovium makes pannus, pannus invades cartilage, which takes cartilage off and 'throws it' into the joint. 'rice bodies cause all kinds of problems.' rice bodies are made up of hypertrophic synovium that break off.

Rheumatoid arthritis



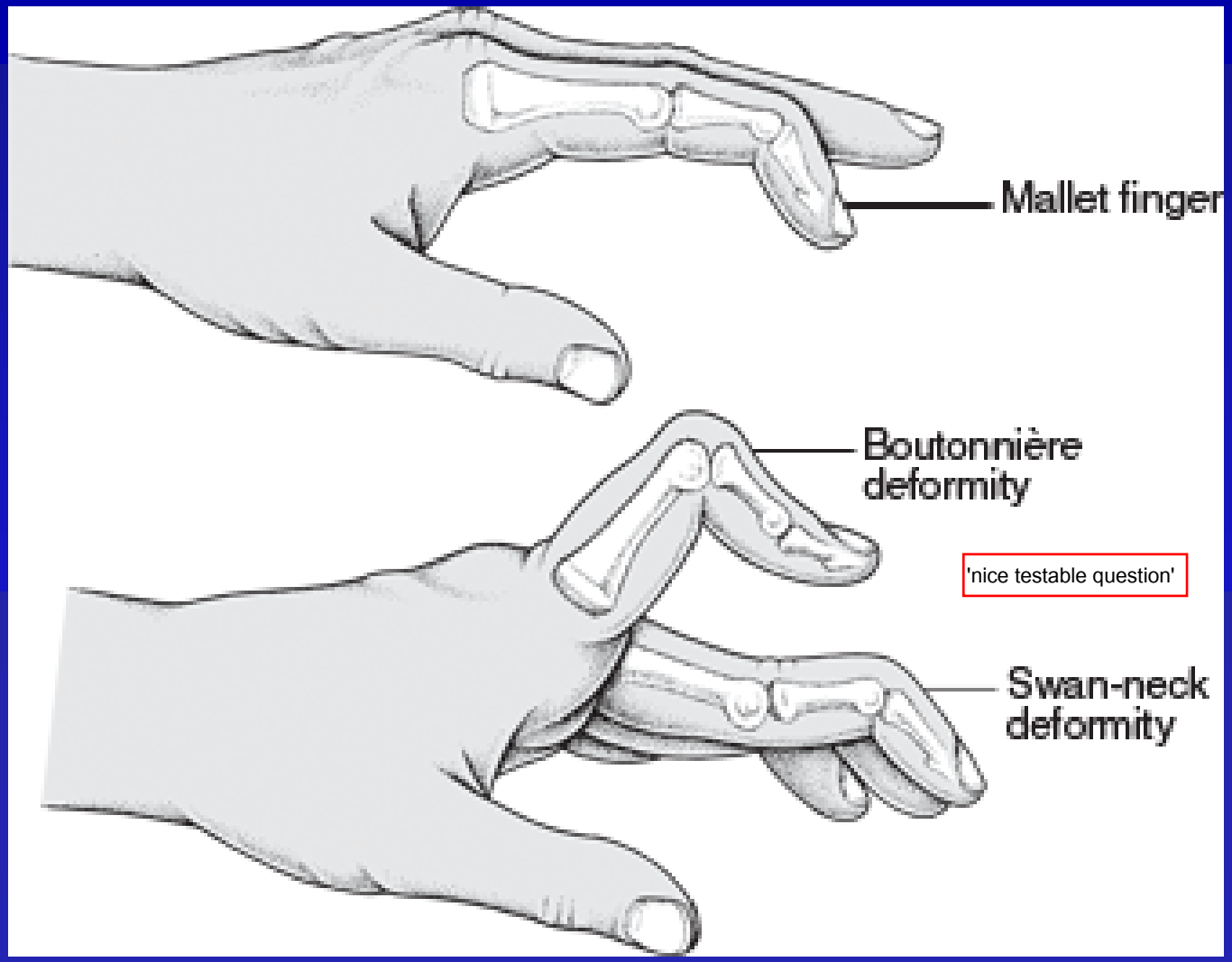
- Diagnosis on basis of multiple clinical and lab findings
- Other findings:
  - Rheumatoid nodule

foci of necrosis can occur on elbows, arms.

- Lab:
  - Serum Rheumatoid factor: IgM to Fc of IgG

Other common deformities

instead of ulnar, can get boutonniere ('button hole') and swan-neck deformity.



'nice testable question'

Juvenile Rheumatoid Arthritis

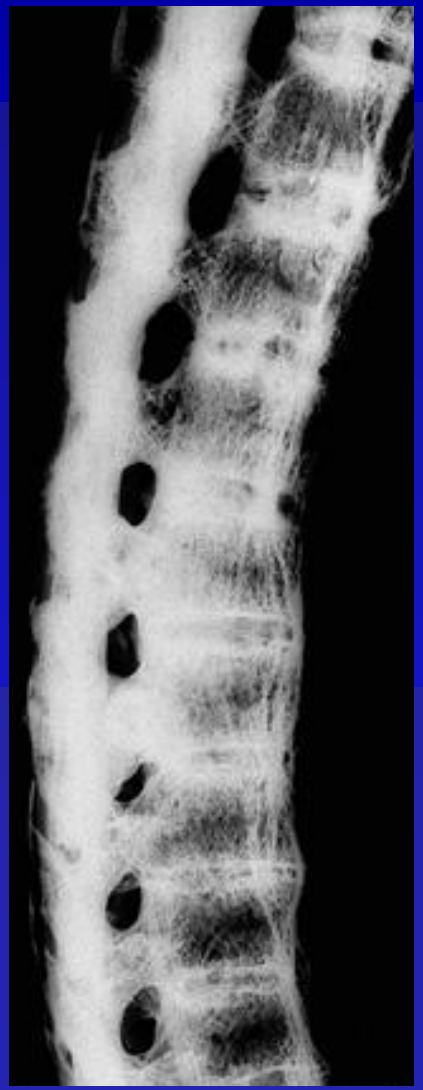
occurs in persons <18.
affects large joints.
histology is the same as RA, but dont have the RhF as seen in adults (usually 80% adults). instead have ANA+.

- Begins in large joints:
  - Knees, ankles, elbow
- Rheumatoid factor is negative
- ANA is positive

Rheumatoid variants

related in pathophys but have different etiologies; usually related to HLA-B27.
ankylosing spondylitis -- affects more men than women. path: isolated to spine -- get inflammation and ankylosis (complete fusion of elements of the spine). causes devastatingly limited mobility.

- AKA Seronegative spondyloarthopathies
- HLA-B27
- Ankylosing spondylitis, psoriatic arthritis, mixed connective tissue disease, others



'GOUT IN ONE MINUTE!'

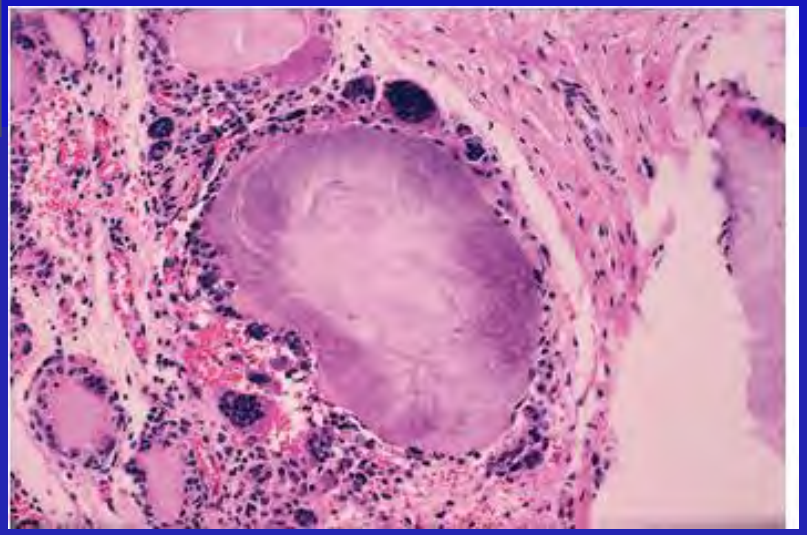
Gout

'the dz of kings.' usually have a very rich diet (meat, alcohol instead of just grains).
distinct clinical presentation -- pain in the toe!

- Intense pain in peripheral joints
- Usually occurs in adult men
- Diet and alcohol consumption
- Genetic predisposition

Gout

uric acid crystal is elevated in individuals; usually due to defect in urate metabolism enzyme. when urate is super-saturated, goes to the coldest place of the body (distal extremity) and crystalizes.
it is the inflammation that gets recruited to the cryrstaline deposits that causes the pain.



- Precipitation of sodium urate crystals in and around joints
- Predilection for small peripheral joints, particularly metatarsal phalangeal

Gout--Diagnosis

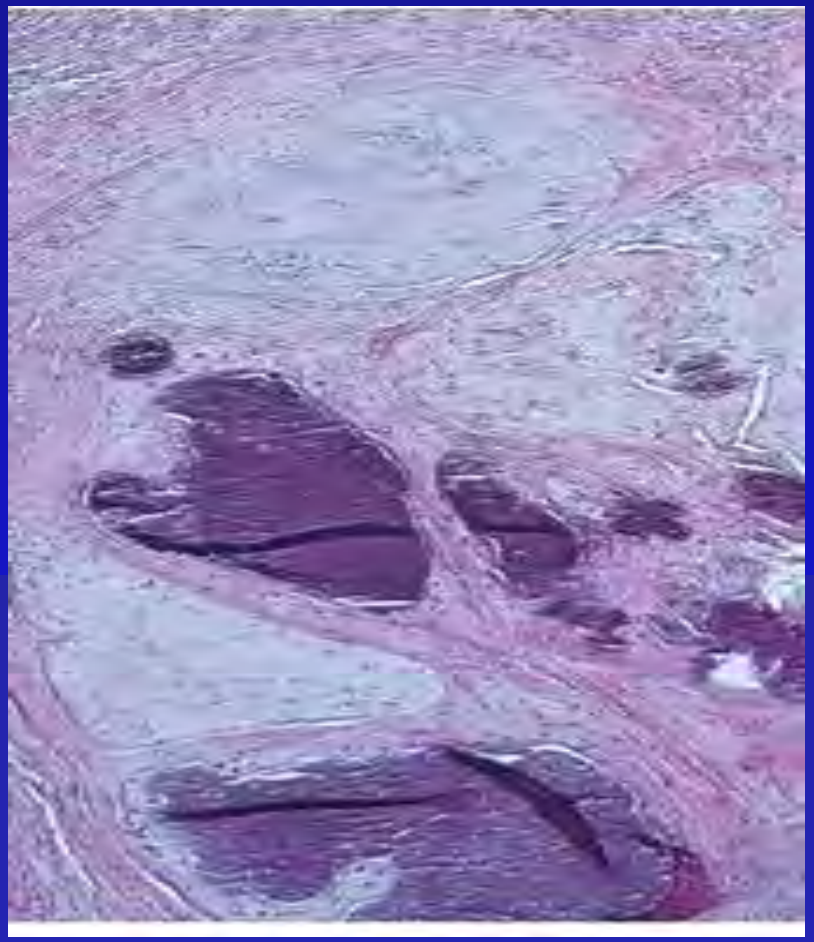
distinct clinical pres: elevated serum uric acid. if you aspirate, can see crystaline uric acid

- Demonstration of refractile needle shaped crystals in joint fluid and tissue
- elevated serum urate levels

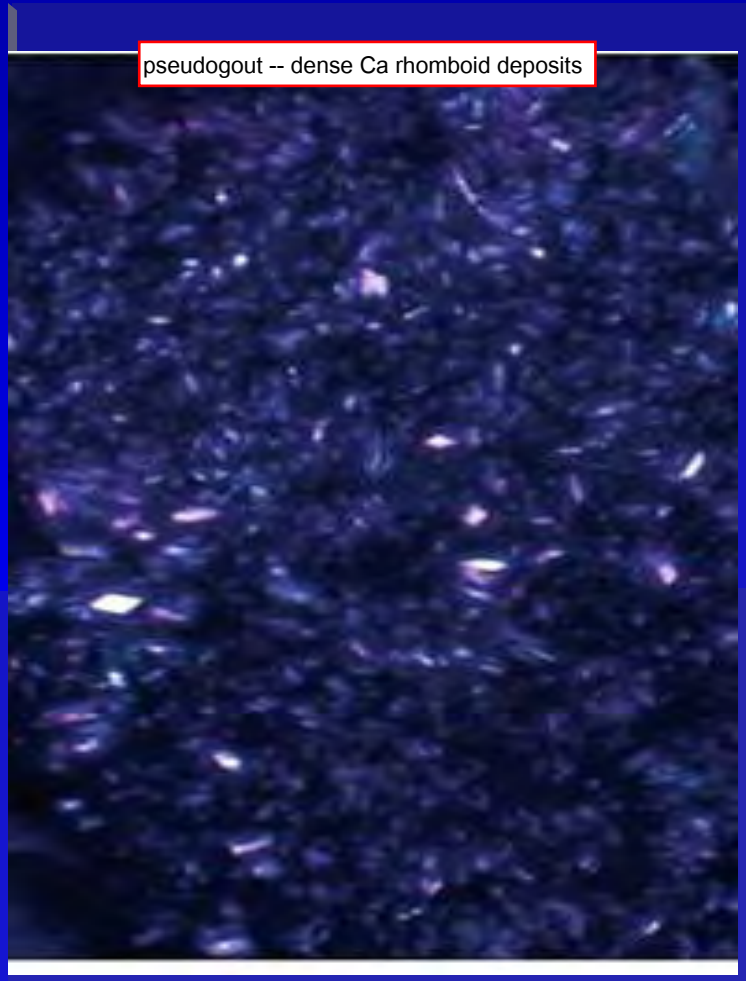
Gout vs Pseudogout

pseudogout can mimic gout. caused by Ca crystal. this dz has a lot of similarites but dont have elvated uric acid (or if is elevated, it is not the cause of arthropathy). usually ass'd with several other types of dzs, ie collagen and vascular dzs that increase with age

- Deposition of Calcium Pyrophosphate Dihydrate crystals (CPPD) in synovial fluid and tissue
- Simulates other diseases: Gout, DJD, RA
- Prevalence increases with age



Crystals gout vs pseudogout



Path – Bone metabolic disease

	Serum Calcium	Serum Phosphate	Alk Phos	PTH	Comments
Osteoporosis	-	-	-	-	C: Elderly, postmenopausal E: ↓ bone mass
Osteopetrosis (marble bone)	-	-	-	-	C: Failed normal bone resorption E: Thickened dense bones, anemia, infection-prone, etc.
Osteomalacia /Rickets	↓	↓	-	↑	C: Defective mineralization E: Bowing of legs, "Rosary chest"
Osteitis fibrosa cystica /"Von Reckl-inghausin's"	↑	↓	↑	↑	C: Hyperparathyroidism E: "Brown" tumors – cystic spaces lined by osteoclasts and full of stroma and sometimes blood
Paget's Disease	-	-	↑	-	C: Increased osteoblastic and osteoclastic actibity (~balanced) E: Mosaic bone pattern. Can lead to osteogenic sarcoma

Slide from MSIII USMLE Review!