APPROVED

Bone and Joint Part 2

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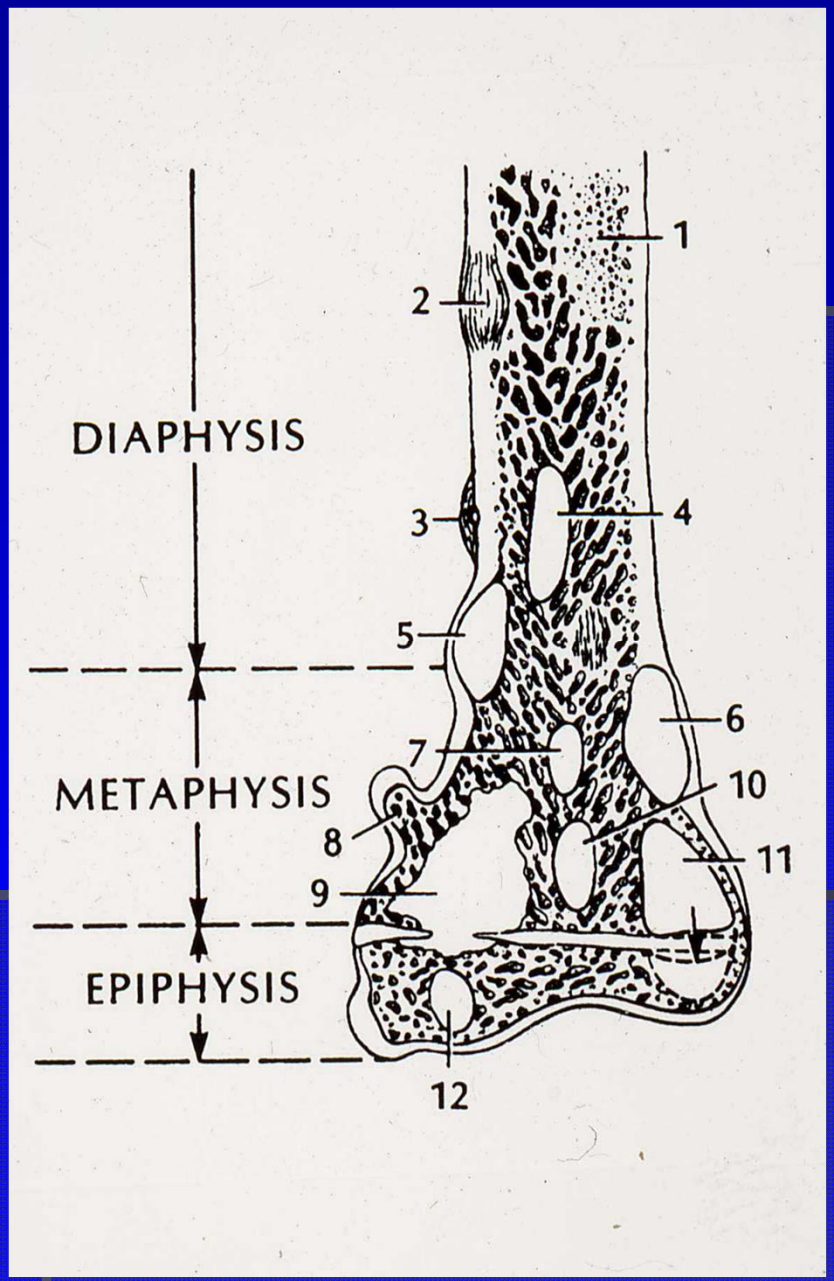
Relative rates of cancer

- Sarcomas are relatively uncommon tumors
  New cancer cases 2007

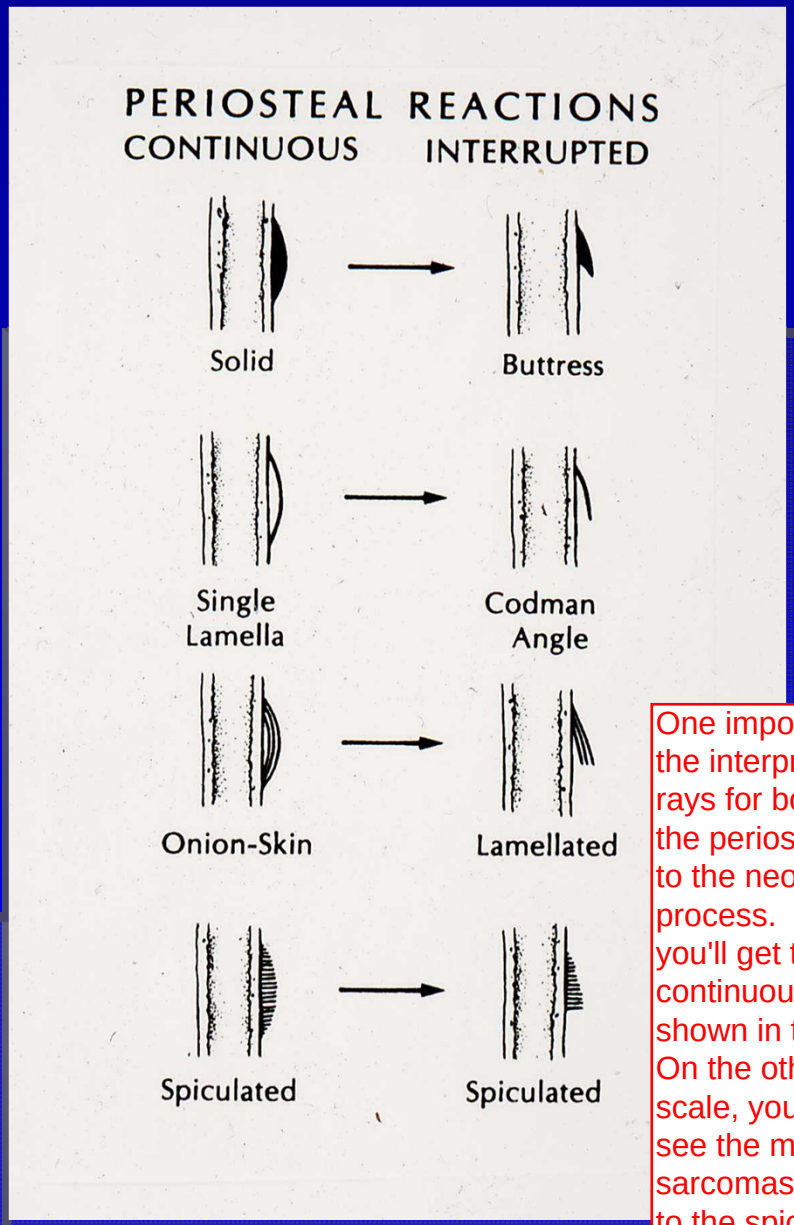
All sites	1.4 million
prostate	218,890
lung	213,380
breast	180,510
Soft tissue	**9,220**
Bone	**2,370**

It's important to remember that sarcomas/bone tumors are not that prevalent.

Jenal A, Siegel R, Ward E et al. Cancer Statistics, 2007. CA Cancer J Clin 2007:57:43-66



Metaphysis is the site for most of the sarcomas that we see. The reason for this is that there is active proliferation of cells here (where your pluripotent cells are)...amenable for bone tumor formation.



You never interpret the histology of a bone tumor without looking at the x-ray first. That's because x-rays can tell you so much in this case. As you will see later, it may be the only factor that helps you distinguish one tumor from another/non-neoplastic disease.

This triangular shadow here is called Codman's triangle...one of the cardinal signs of osteosarcomas.

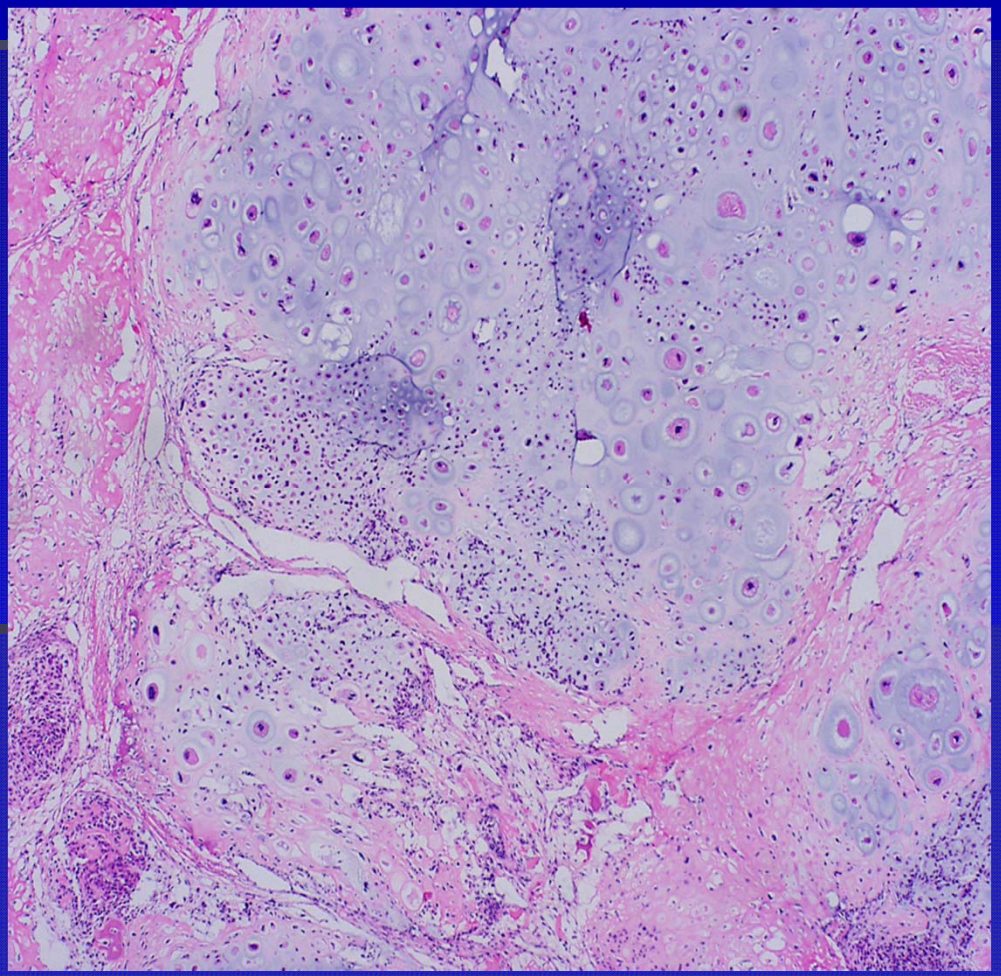
there are also spicules here.. (need a radiology view box to see them - Dr. H)

One important clue for the interpretation of x-rays for bone tumors is the periosteal reaction to the neoplastic process. In infections, you'll get the solid, continuous process shown in the upper left. On the other end of the scale, you'll more likely see the more agressive sarcomas that give rise to the spiculated reactions at the bottom of the figure.

In adults, if you see a bone tumor, think metastasis...primary bone tumors are RARE.
In children, the opposite is true.

Bone tumor classification

- Osseous lesions
  - benign
  - malignant
- Cartilage forming lesions
  - benign
  - malignant
- Other
  - Fibrous
  - Cyst
  - Giant cell tumor
  - Round cell
- Metastases

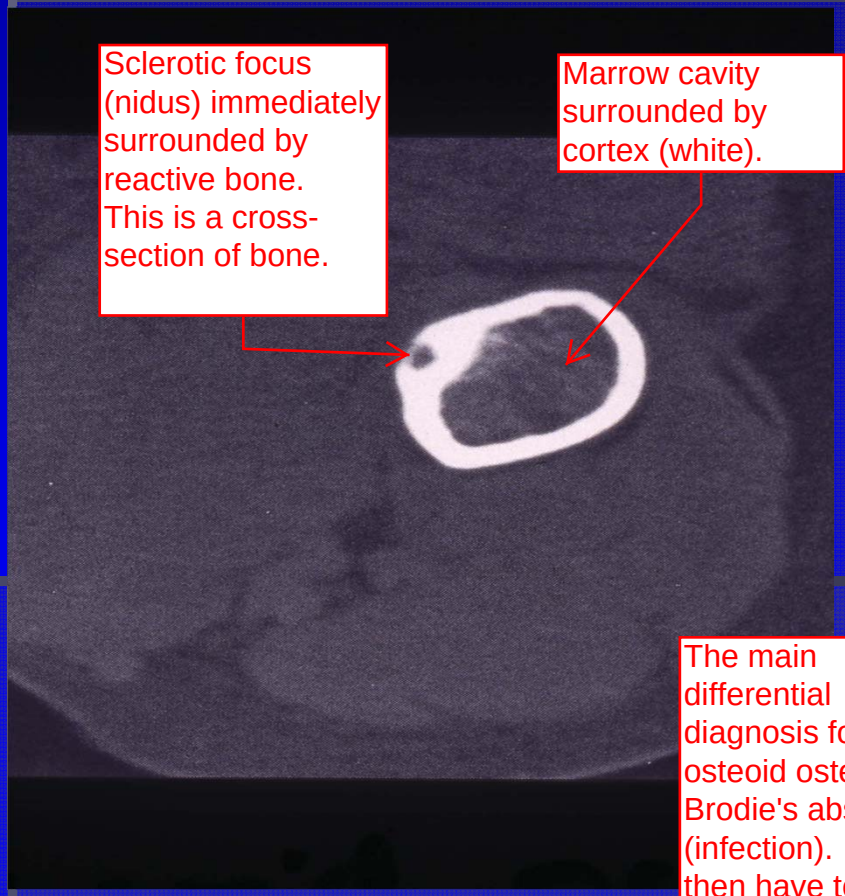


Osteoid Osteoma

One of the more prevalent bone tumors.
This is diagnosed clinically:
1)The children who have this will be able to pinpoint the site of pain.
2)The pain can be relieved by NSAIDs.
3)The pain is worse at night.
X-rays are a little more difficult...

- Clinical:
  - Pain of increasing severity; worse at night and relieved by aspirin
  - referred pain to joints; scoliosis, muscle atrophy and neurological disorder
  - Diaphysis/metaphysis of long bones and appendicular skeleton

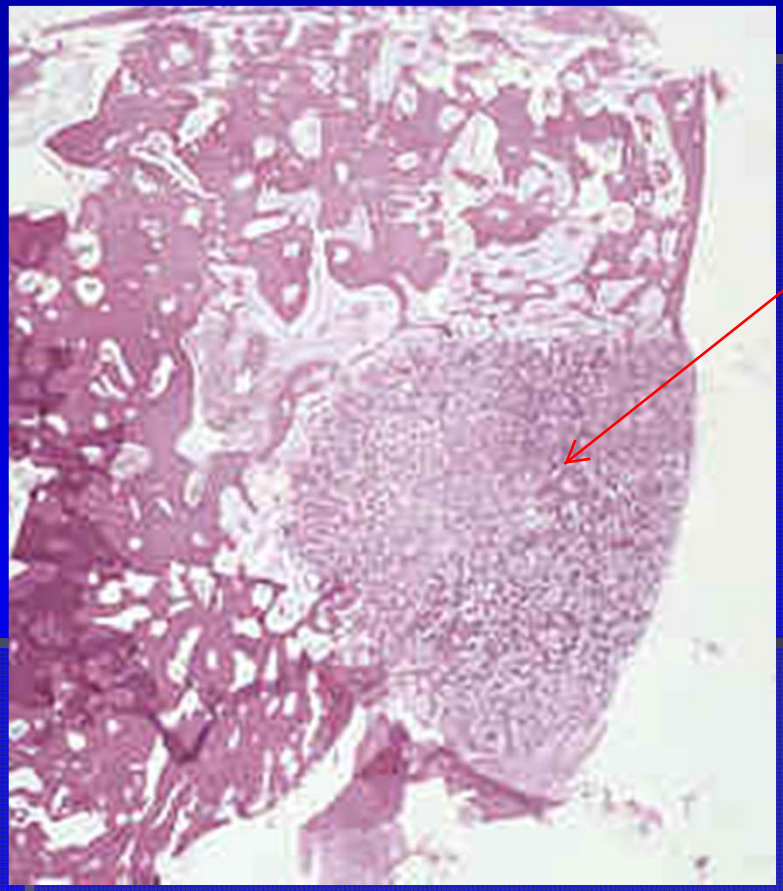
Osteoid Osteoma



- Radiology:
  - small lucency, surrounded by sclerosis and cortical reaction
  - At center of lucency is a nidus---small area of ossification
  - lesion is easily missed on conventional exam; may require tomo or CT
  - Ddx: Brodie’s abscess, stress fracture or osteoblastoma

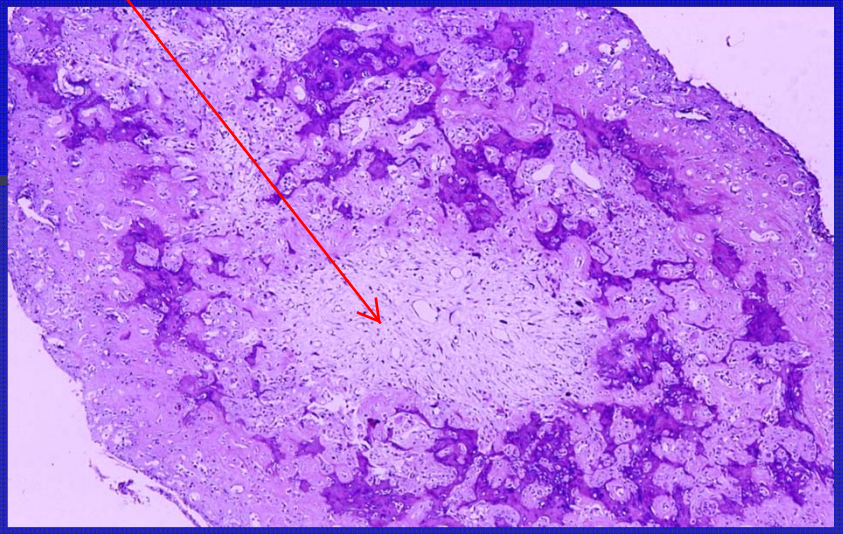
Osteoid osteoma

Tx: NSAIDs
If these don't work, then radioablation is used.
Could also go in the old fashioned way and cut it out.

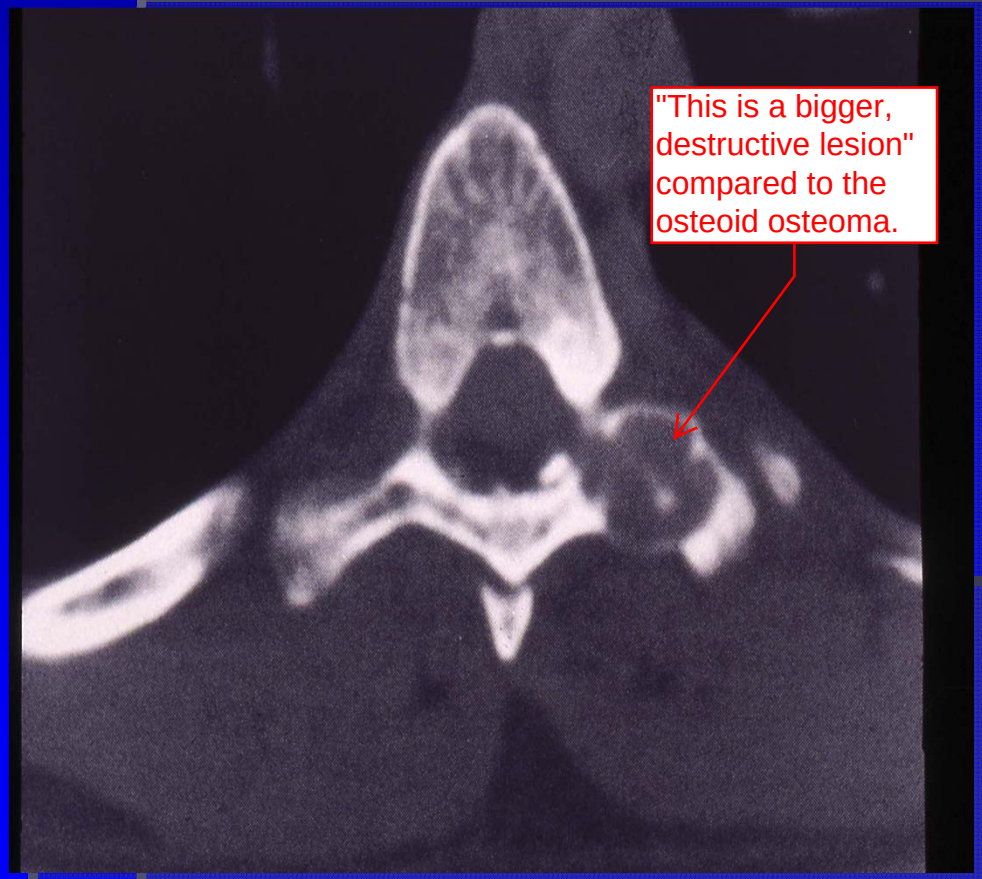


Nidus with surrounding reactive, sclerotic bone.

- Peripheral bone sclerotic
- Inner nidus

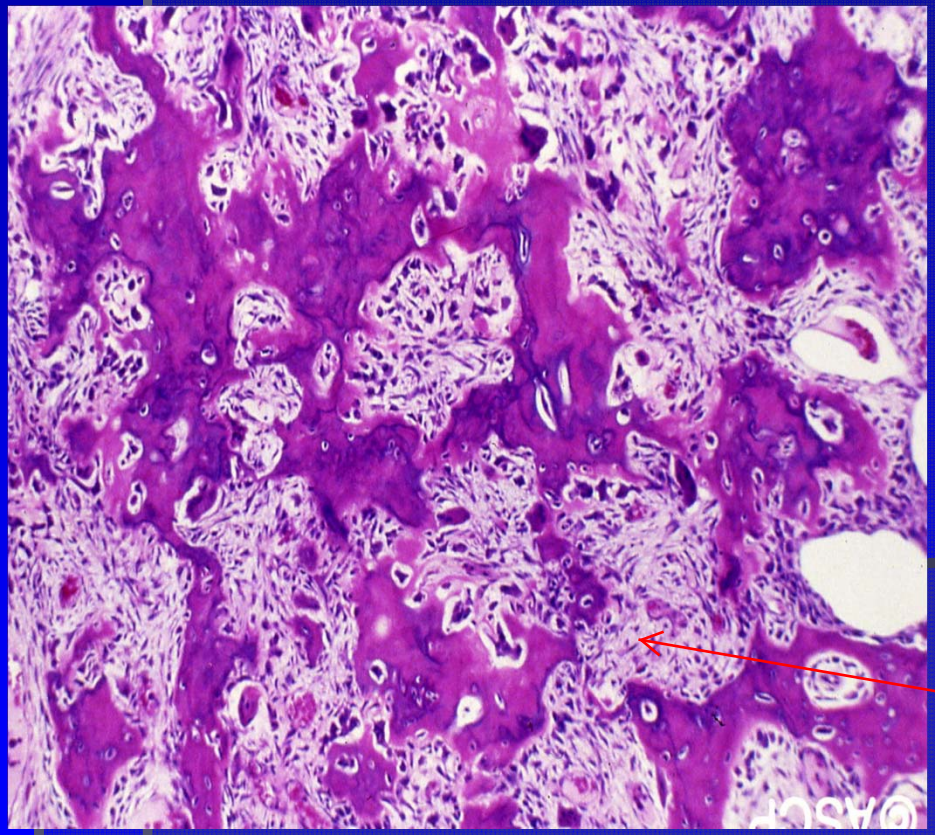


Osteoblastoma



- Radiology:
  - may simulate osteoid osteoma but can be highly variable in appearance
  - Can be destructive and confused for malignant process
  - Central ossification is common

Osteoblastoma



- Histopathology:
  - Similar to osteoid osteoma although not as well organized
  - Tends to be highly vascular in central portion

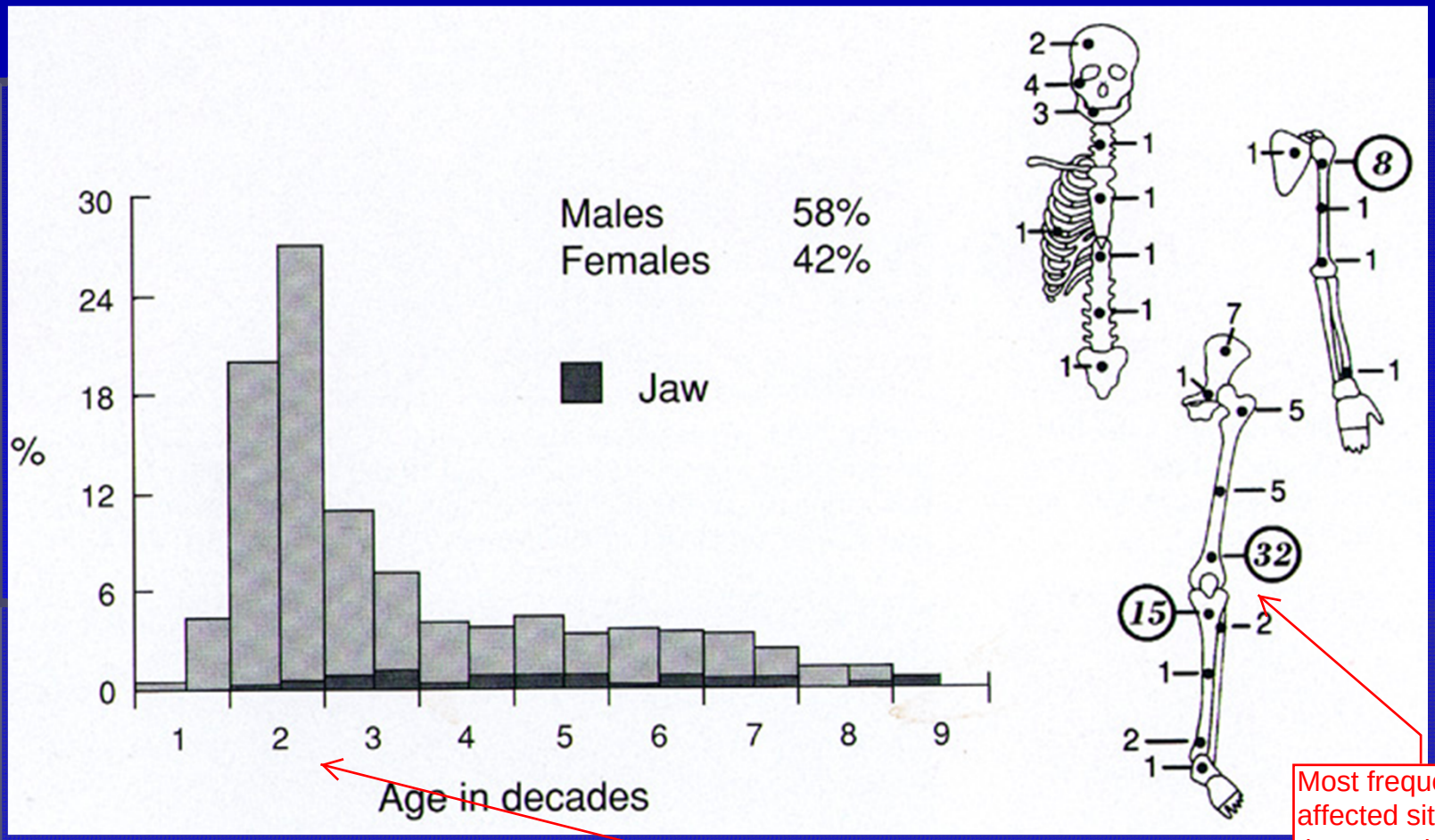
Loose, cellular stroma that is highly vascularized. Tx: is surgical excision.

Osteosarcoma

One of the more common bone tumors...especially in children.
This tumor tends to metastasize early and to the lungs.

- Clinical:
  - Pain and tender mass of relatively short duration
  - Knee is most common site
  - **Aggressive treatment approach with neoadjuvant chemotherapy and limb salvage
  - Early development of pulmonary mets
  - Predisposing conditions: Pagets' and Radiation

Also those that have the Retinoblasoma mutation and Li Fraumeni syndrome.



Large peak in children/young adults.
Small peak in later years.

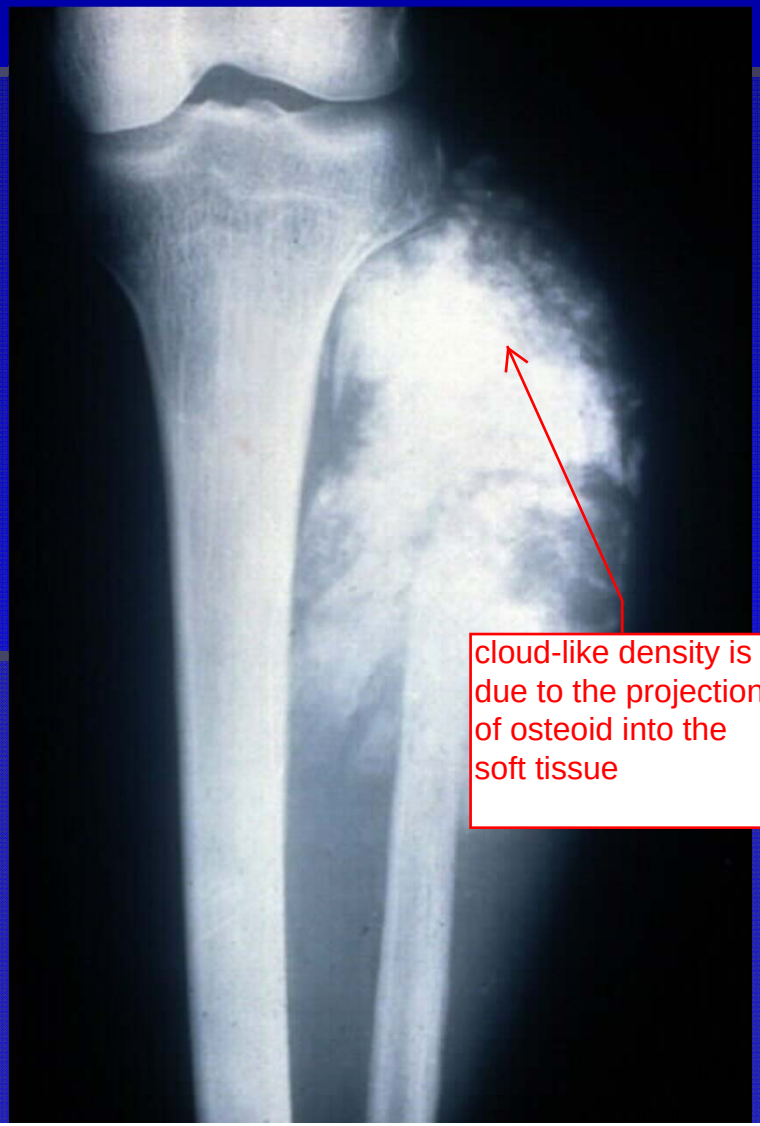
Most frequently affected site is in the metaphysial area in long bones, but can happen elsewhere.

Osteosarcoma

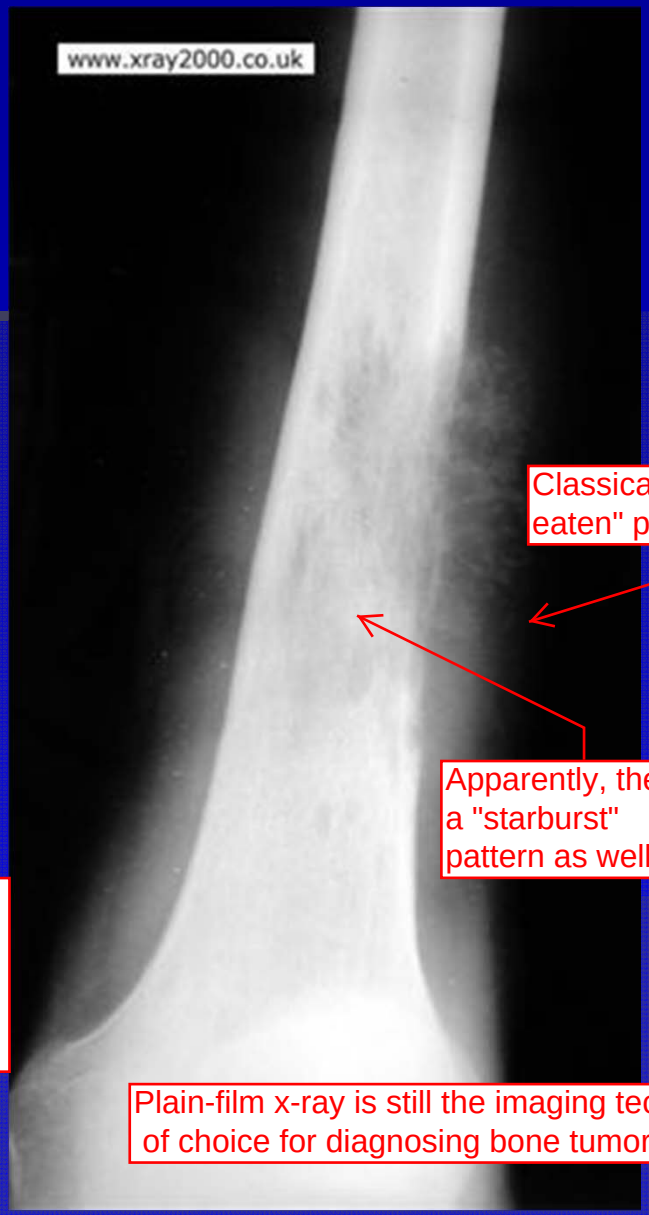
Very destructive looking lesion: spiculated, necrotic, Codman's triangle

- Radiology:
  - metaphyseal lesion which can be mixed lytic and blastic
  - Poorly delineated; cortical destruction with soft tissue extension
  - Spiculation and Codman’s triangle
  - MRI/CT to define extent of intramedullary spread

Osteosarcoma



cloud-like density is due to the projection of osteoid into the soft tissue



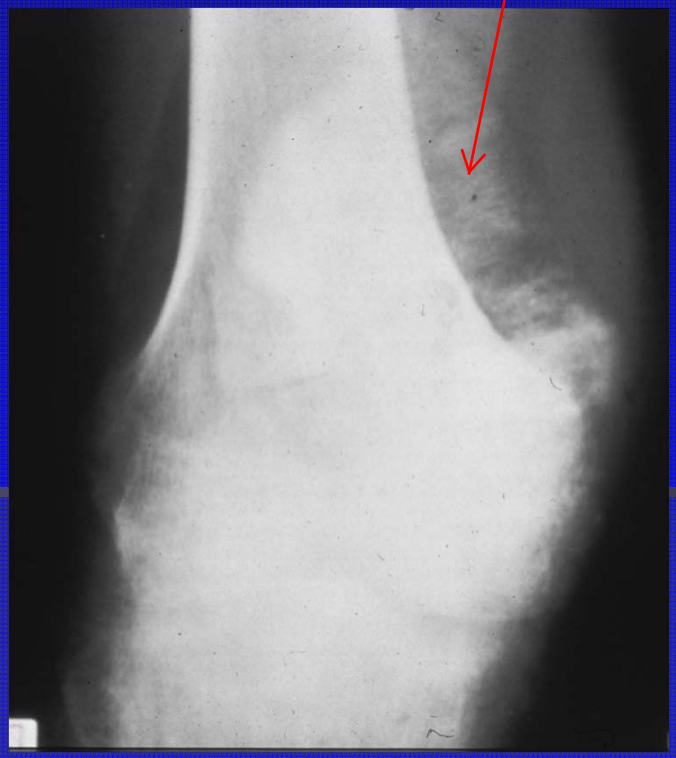
Classical, "moth-eaten" pattern.

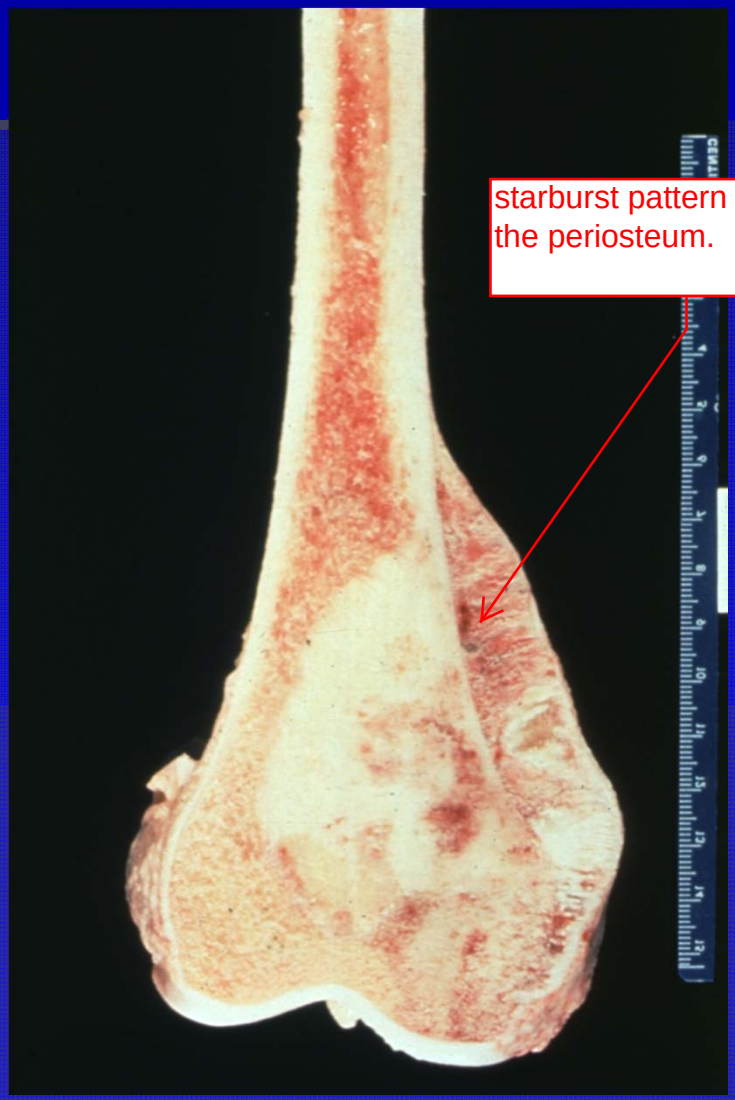
Apparently, there's a "starburst" pattern as well.

Plain-film x-ray is still the imaging technique of choice for diagnosing bone tumors

Osteosarcoma

This is a matching x-ray and specimen.



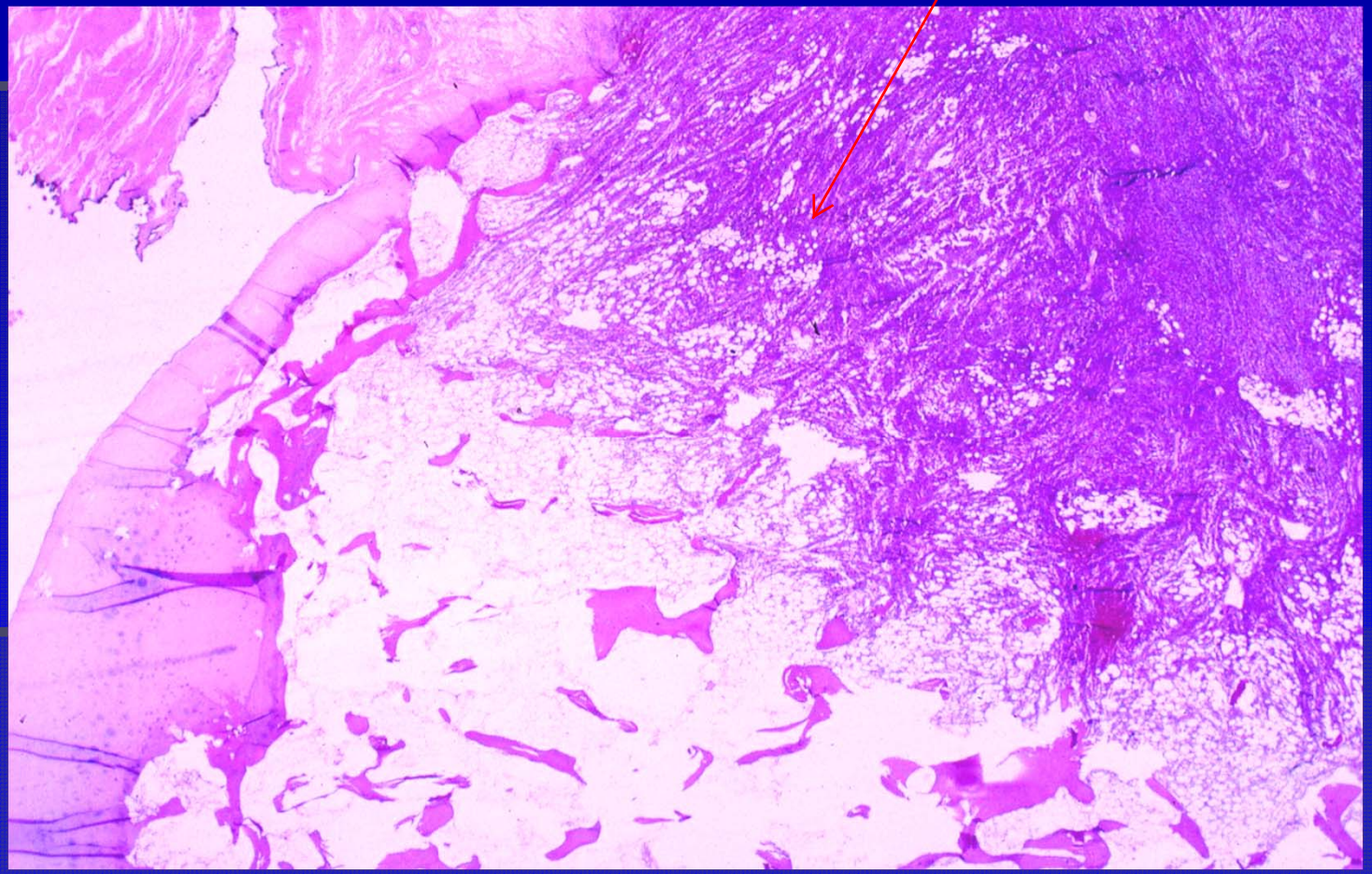


starburst pattern under the periosteum.

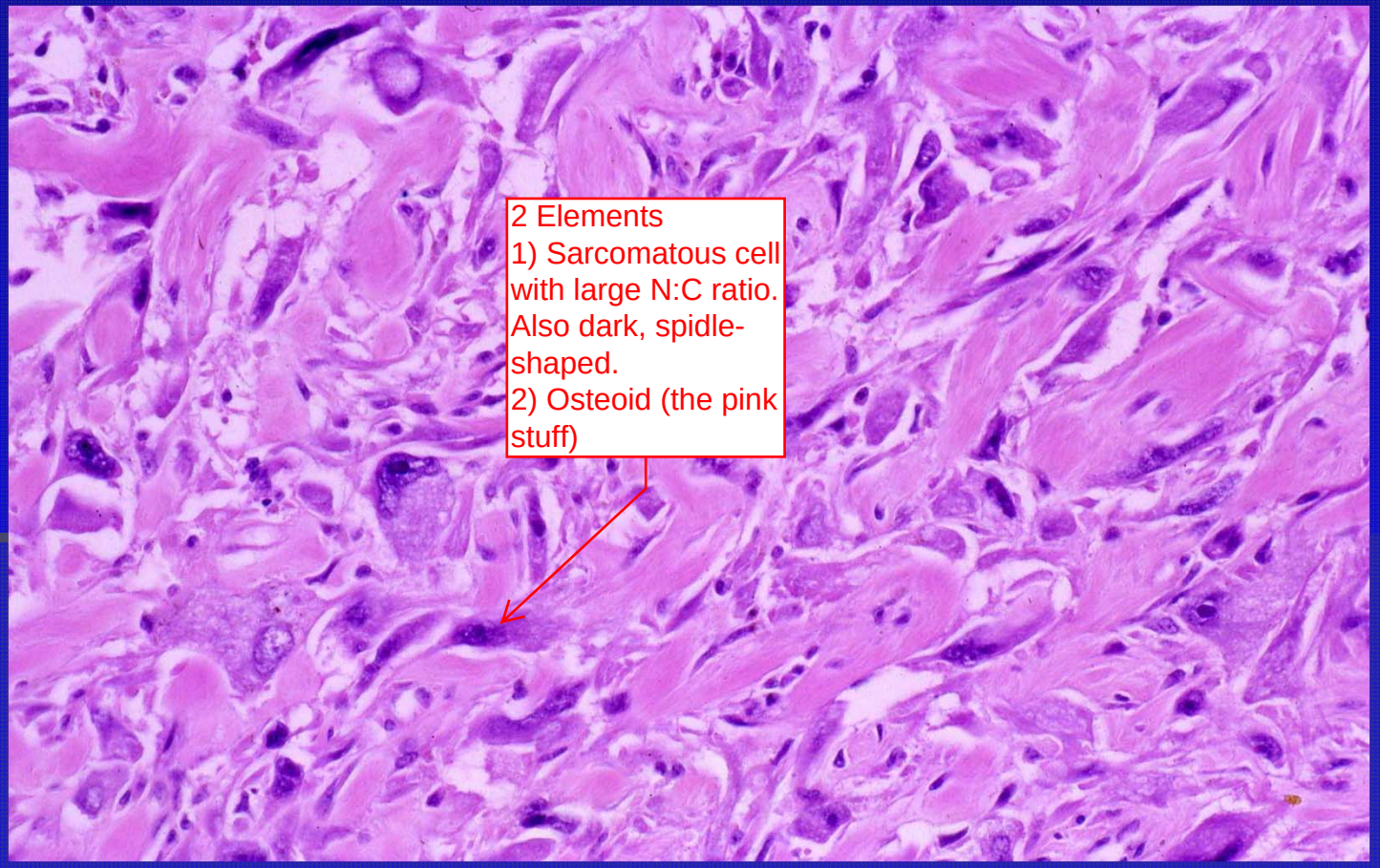
Osteosarcoma

All osteosarcomas have:
1)Malignant-appearing cells. Ex. High N;C ratio, very blue, etc.
2)Presence of Malignant Osteoid (meaning not in either the trabecular or lamellar arrangement).

- Histopathology:
  - Highly variable with osteoid, chondroid or fibrous matrix predominant
  - All have in common the production of tumor osteoid and malignant osteoblasts
  - Spindled sarcomatous stromal element with anaplasia and mitotic figures
  - Foci of degeneration, infarction or heavy osteoid formation with sclerosis
  - Lace-like osteoid pattern is common

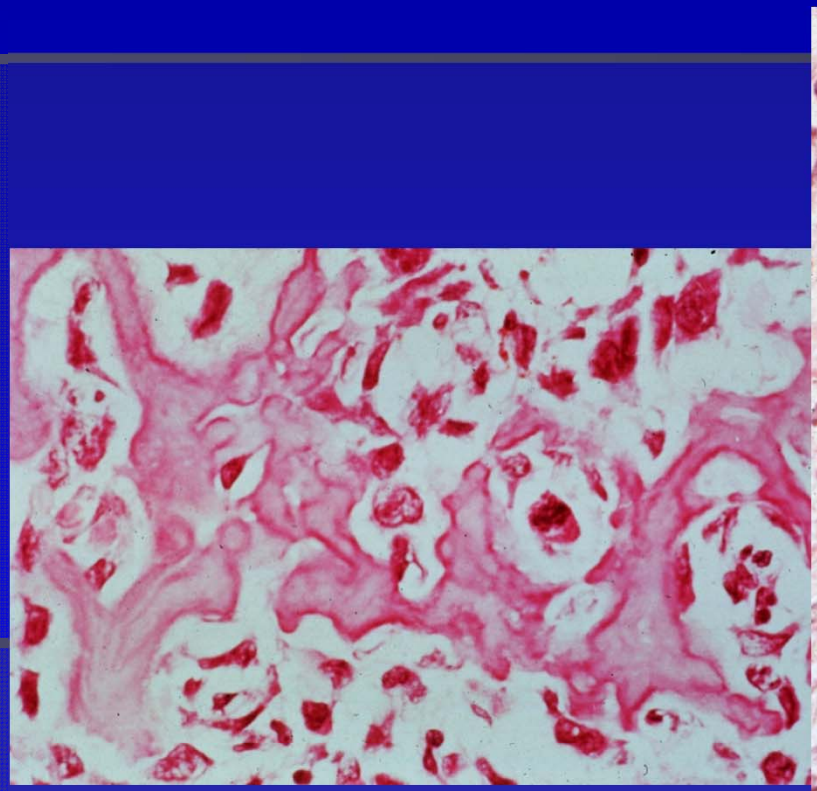

Tumor that is invading and destroying trabecular network.

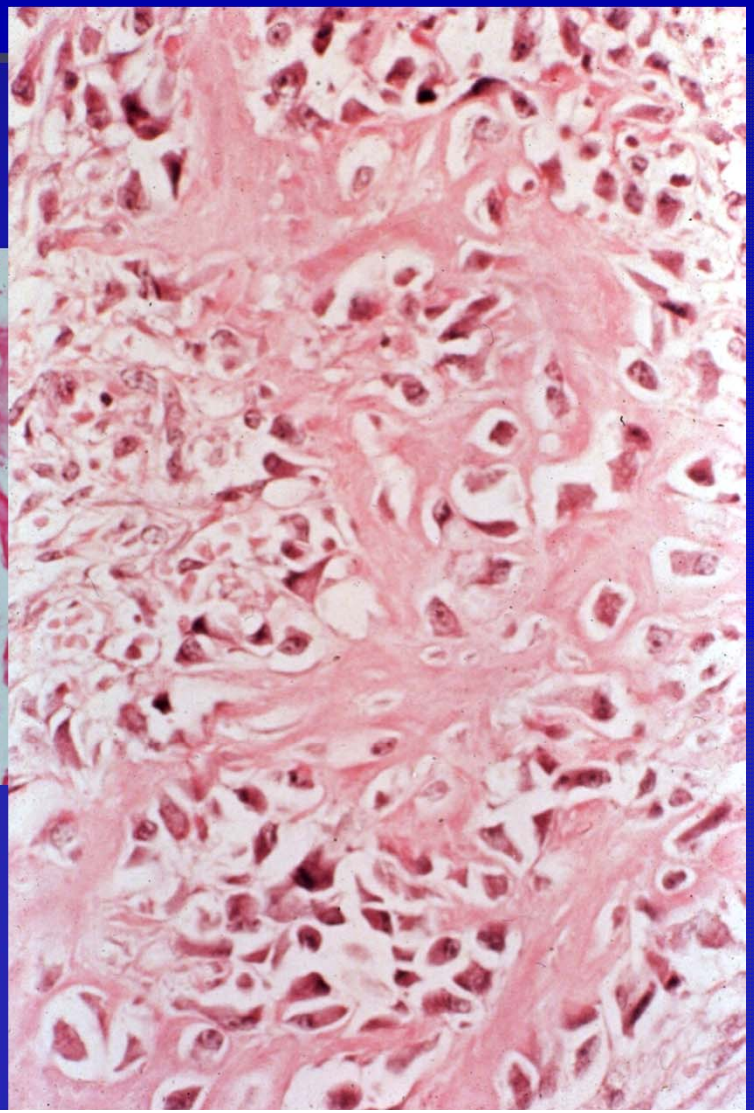
Osteosarcoma---conventional



Osteoid

not functional, not structural



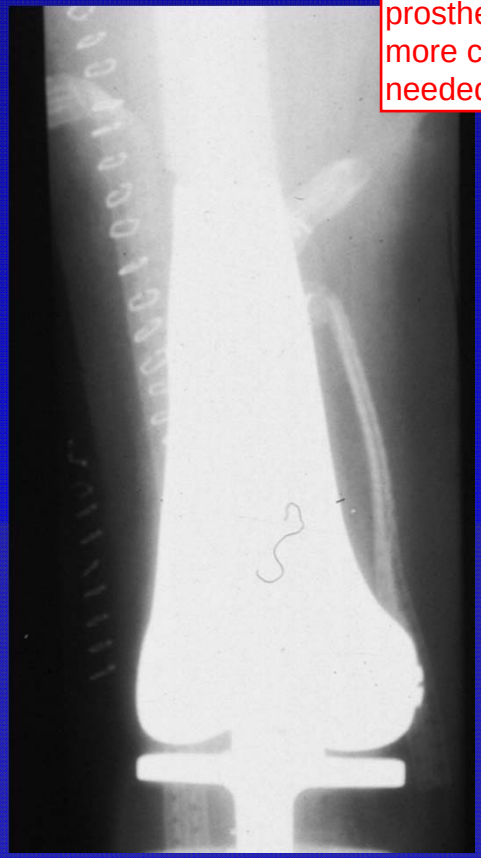


Treatment

Prior to the development of modern chemo/ radiotherapy procedures, sarcomas were uniformly fatal.

Limb-salvage surgery:
1)Neo-adjuvant therapy with chemotherapy or radiation.
2) Resection of tumor (usually doesn't cross joints)
3)Implant prosthesis/give more chemo if needed

- Amputation produced 20% 5 yr DFS
- Neo-adjuvant chemotherapy plus surgery results in 60-65% 5 yr DFS
- Limb salvage surgery appropriate in 80% of cases



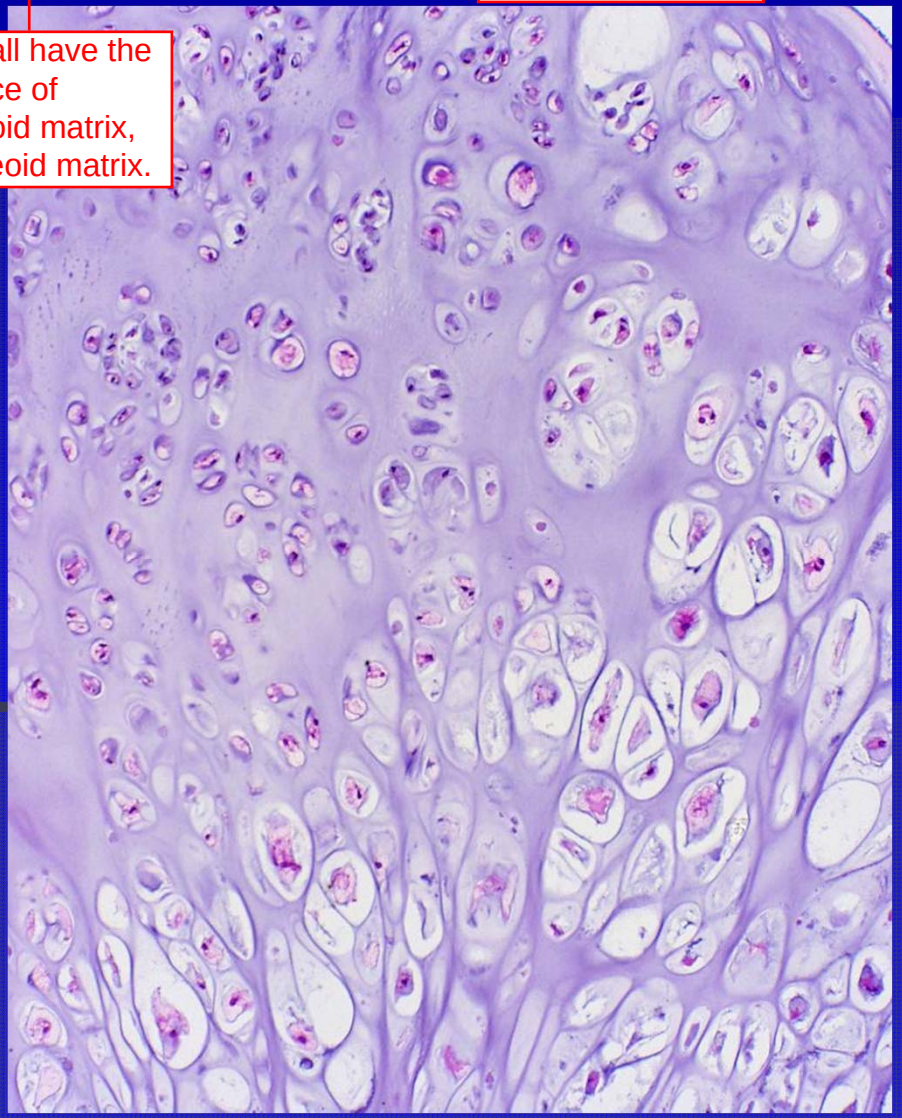
Chondroid tumors

Large group of tumors...we'll go through them quickly. Yes, I was hoping so...

These all have the presence of chondroid matrix, not osteoid matrix.

- Osteochondroma
- Enchondroma
- Chondroblastoma
- Chondromyxoid fibroma
- Chondrosarcoma

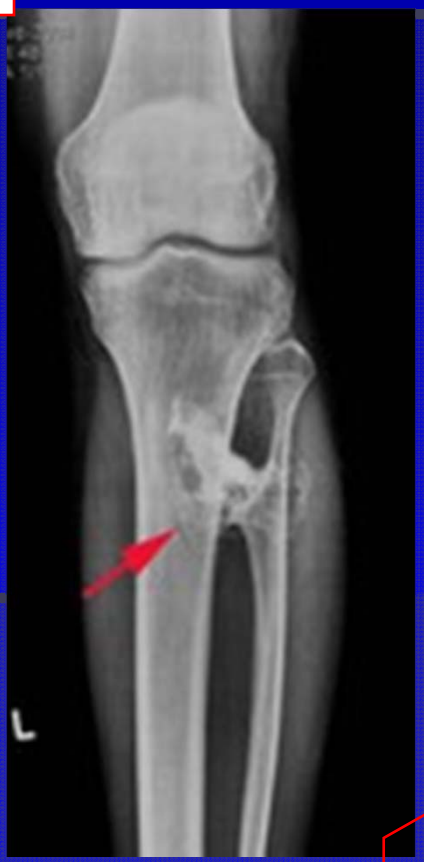
Only malignant tumor in this list.

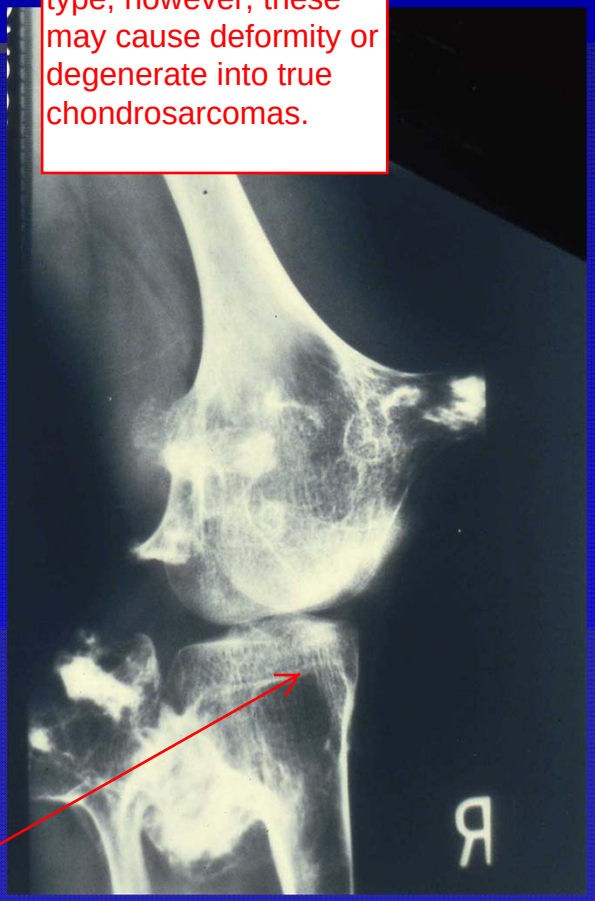


Osteochondroma

- Clinical:
  - Obvious mass lesion; often of long duration
  - Not painful unless impinges on a structure (bursa)
  - Risk of chondrosarcomatous degeneration
  - Hereditary multiple exostoses syndrome

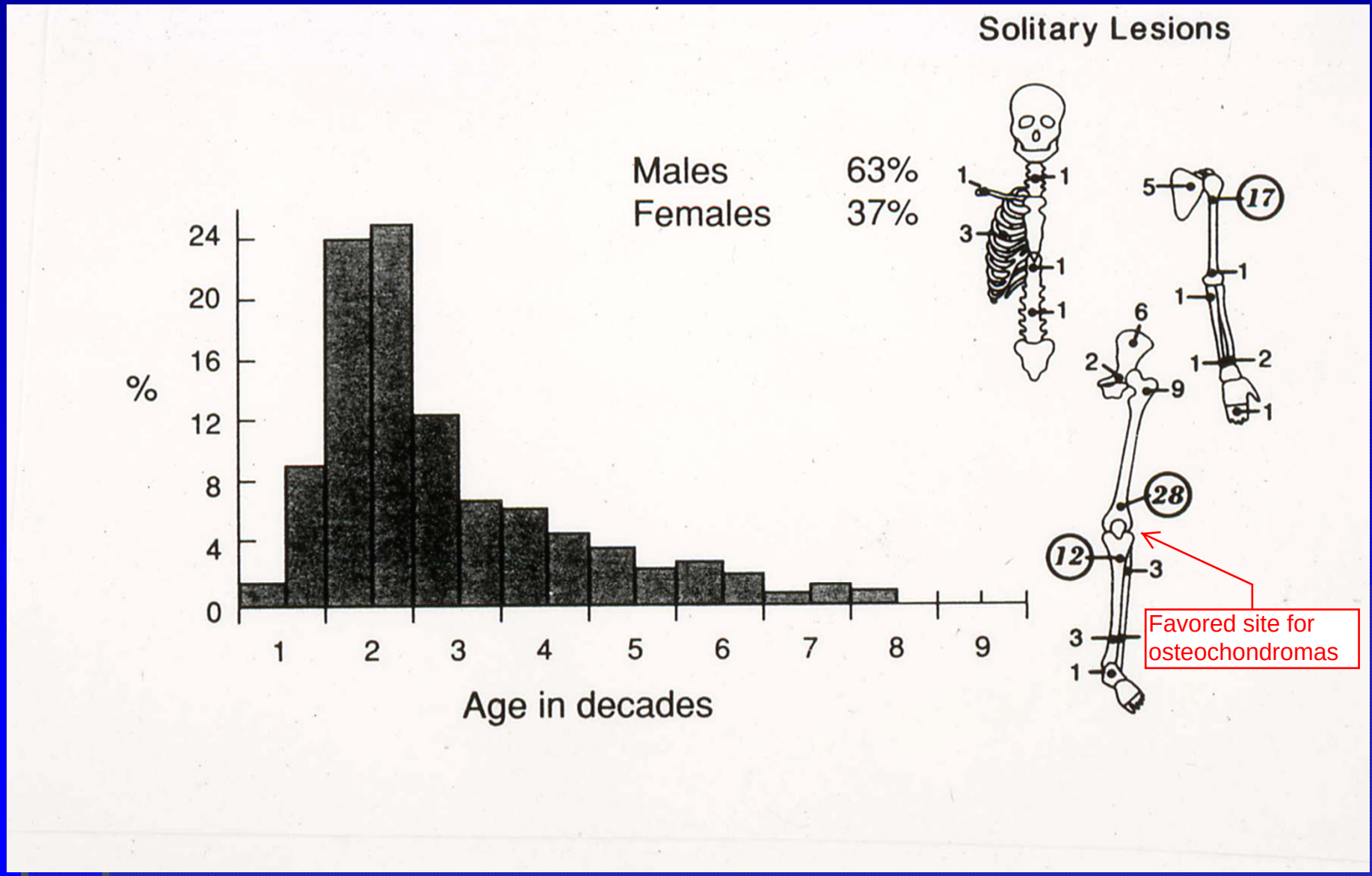
aka exostosis/ exostoses



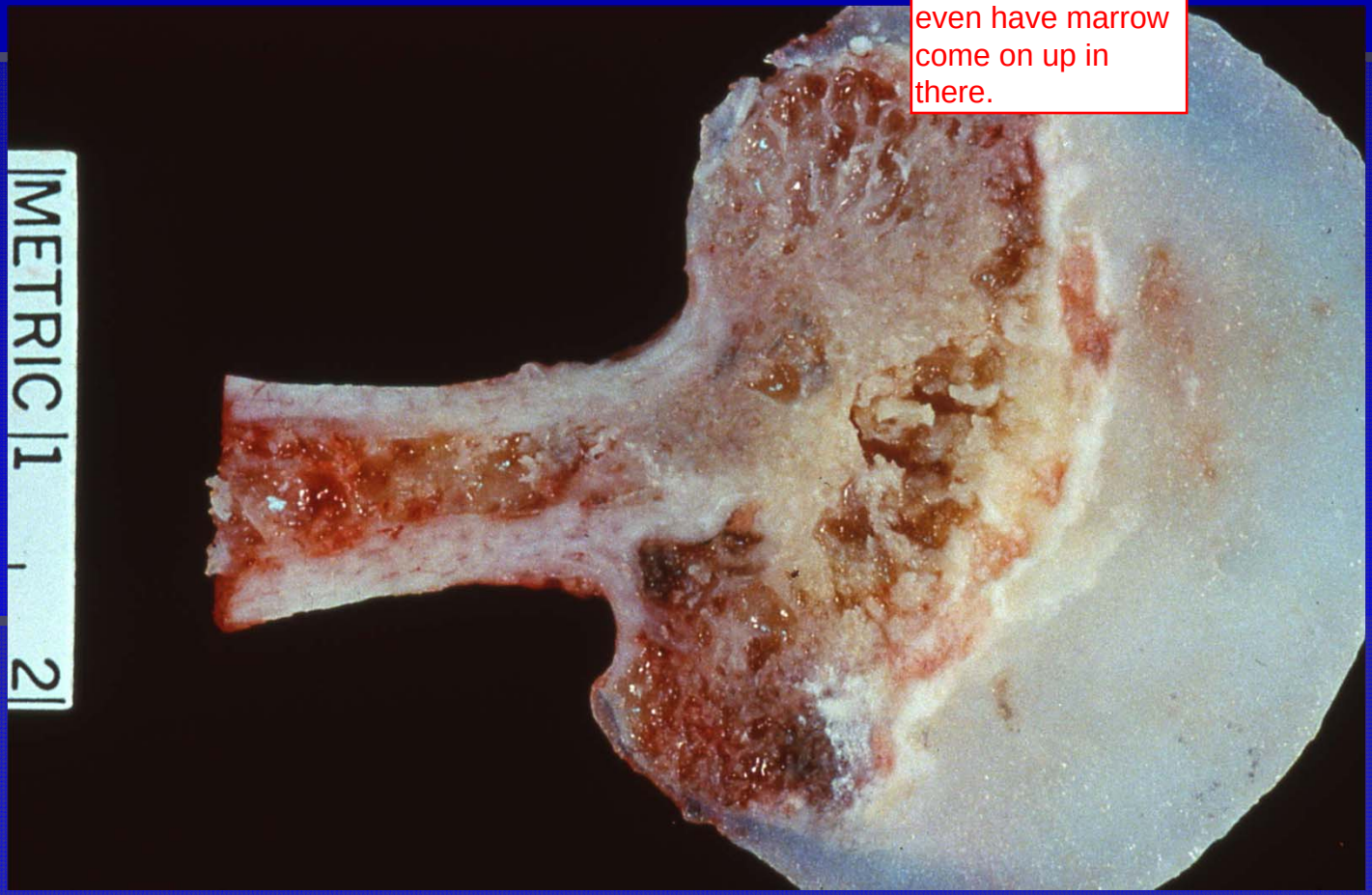


Think of these as tiny hamartomas that come off of the normal (host) bone.
Don't cause any symptoms unless they impinge on something.
In the multiple lesion type, however, these may cause deformity or degenerate into true chondrosarcomas.

Heriditary syndrome with multiple exostoses.


Solitary Lesions
Males 63%
Females 37%
%
24
20
16
12
8
4
0
1 2 3 4 5 6 7 8 9
Age in decades
1
1
3
1
1
5
17
1
1
1
2
1
6
2
9
28
12
3
3
1
Favored site for osteochondromas

The tumor burgeons out and is covered by cartilage...can even have marrow come on up in there.



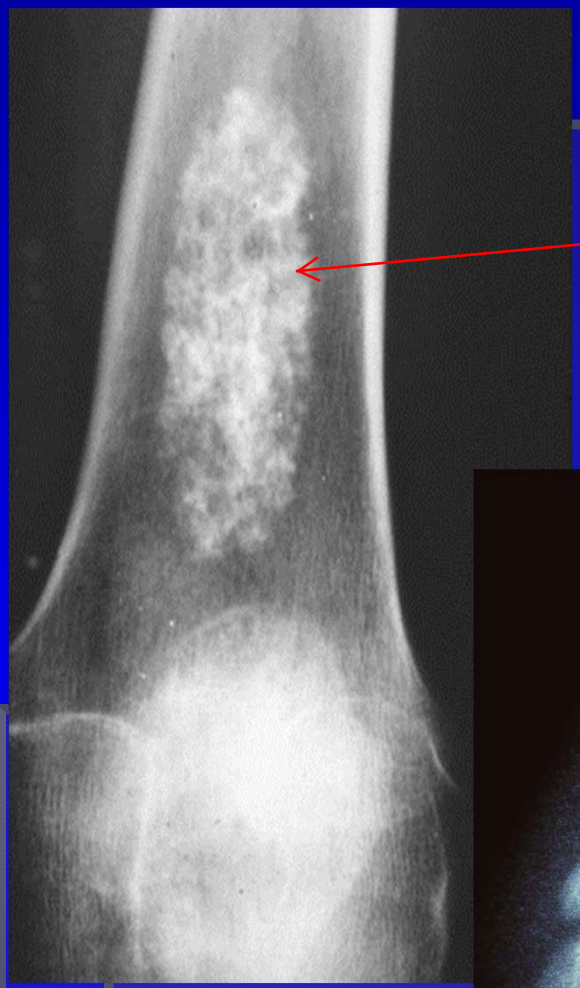
Enchondroma

More common in adults...in the hands/feet. Benign. Only when you have multiple lesions that these become a problem

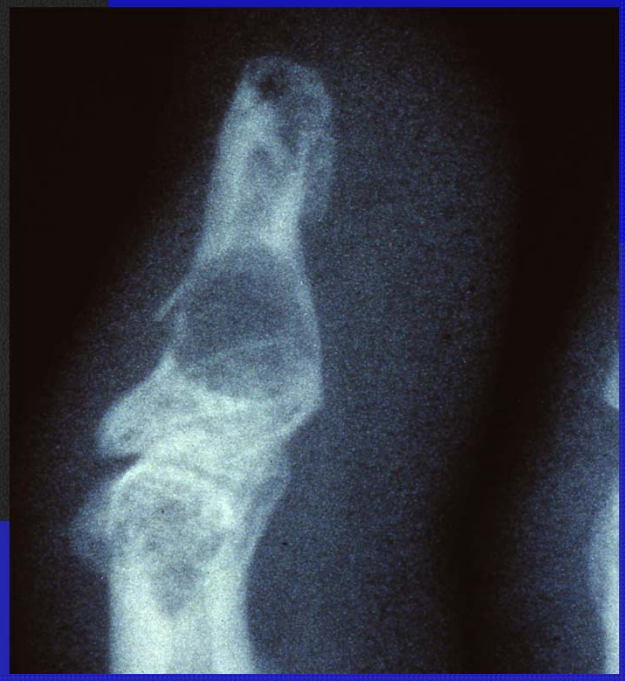
- Clinical:
  - Common benign lesion; asymptomatic, painless and incidentally discovered
  - Grow up to 3 cm; mass lesion in hands and feet
  - Peripheral skeleton is common (Vs. central for chondrosarcoma)
  - Up to 10% of all bone tumors
  - Multiple enchondromas associated with Ollier's and Maffuci's syndromes

Look for pics of these two sydromes later

Enchondroma-Radiology



"Ring and arcs pattern" is the buzzphrase for dx. These rings and arcs correspond to cartilage lobules. Well-circumscribed lesion.



- Variable intralesional calcification
  - Rings and arcs pattern
- in long bone have metaphyseal location and can simulate a bone infarct

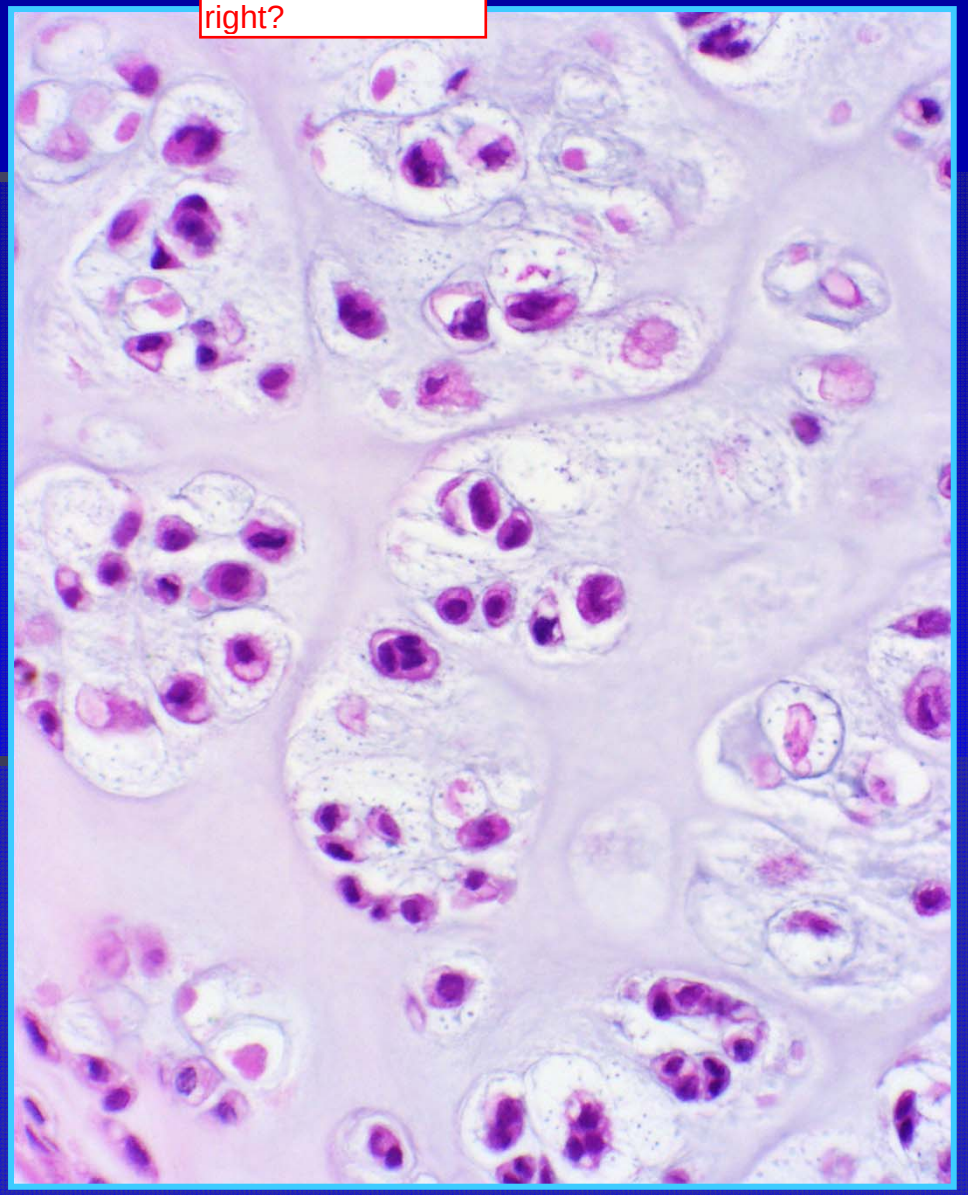
Enchondroma

- Histopathology:
  - Circumscribed, lobulated lesion comprised of lobules of cartilage separated by thin septae
  - micro appearance of benign cartilage

Enchondroma

- Peripheral concentration of chondrocytes
- Minimal cytologic atypia (digits); may have bi-nucleate chondrocytes
- Focal calcification and enchondral ossification

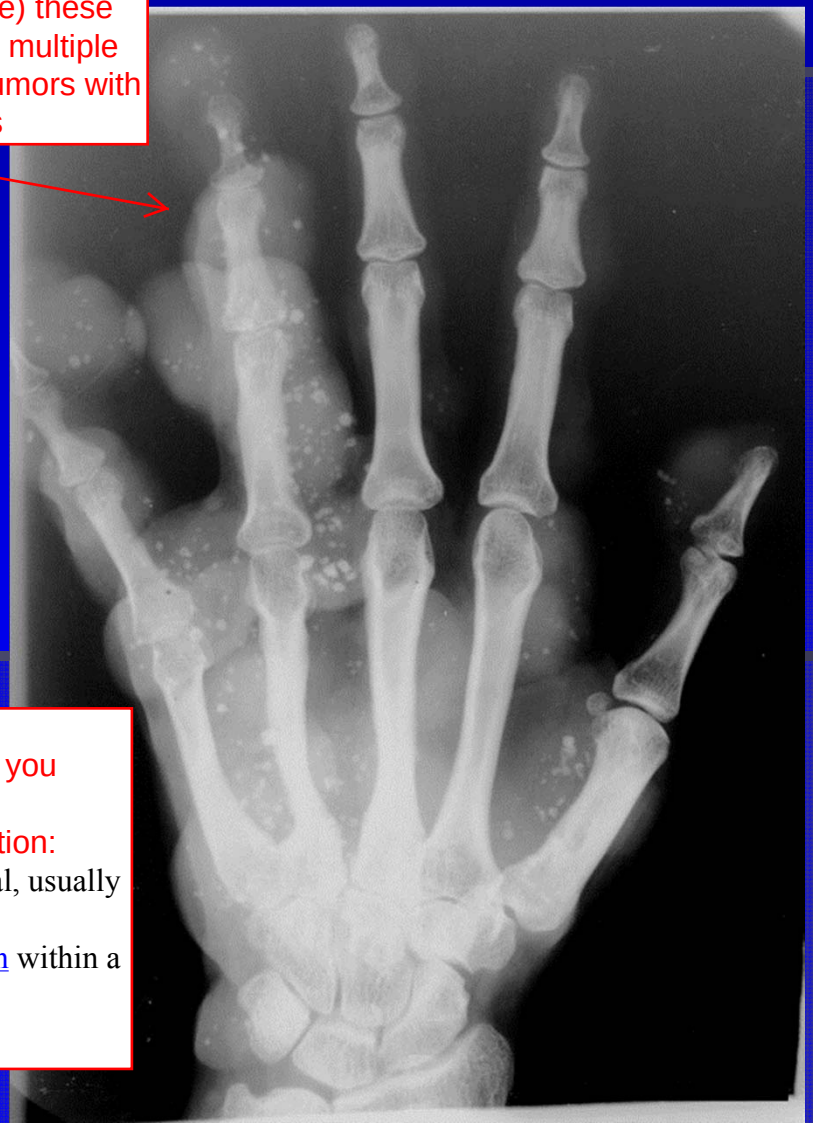
"Almost looks like normal cartilage", but we wouldn't be learning about it if it were normal right?



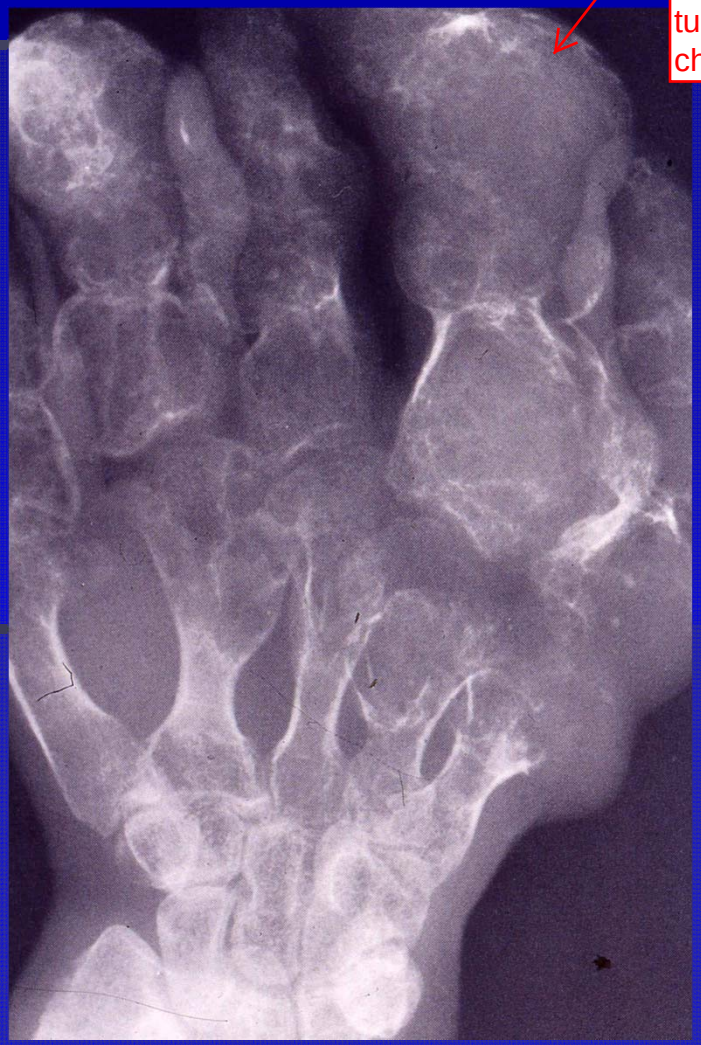
There they are...what did I tell you?

Multiple enchondromas- er's and Maffucci's

Maffucci's Syndrome: in addition to the multiple enchondromas (not shown here) these people get multiple vascular tumors with phleboliths



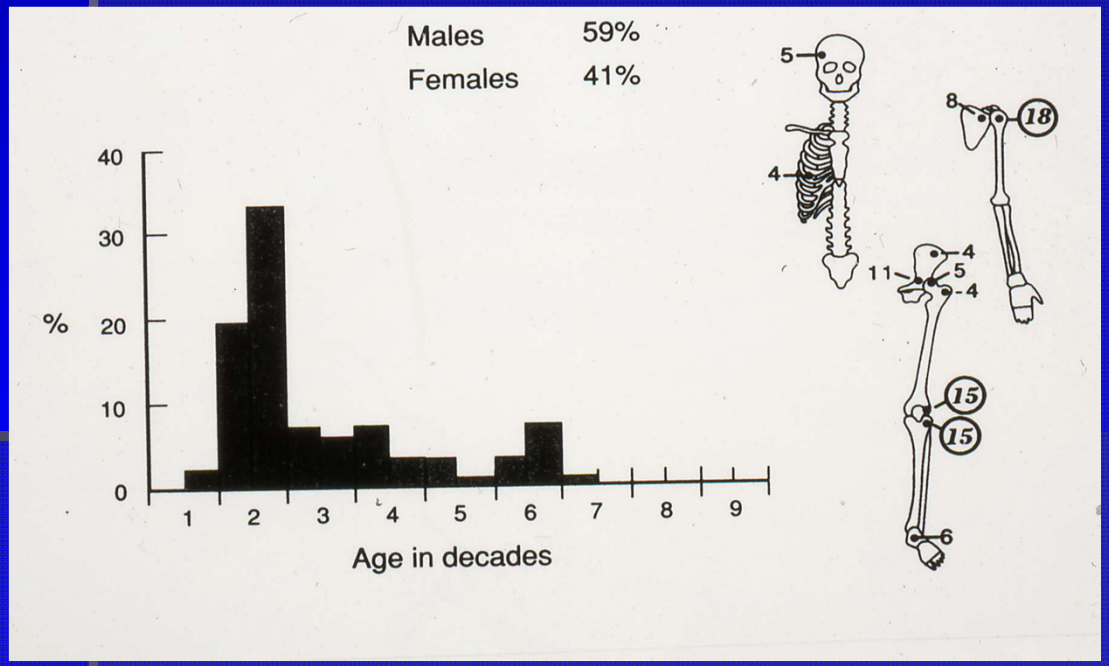
Ollier's syndrome: the more of these you have, the more chance you have that one will turn into a chondrosarcoma.



What is a phlebolith, you ask?
Wiki definition:
a small local, usually rounded, calcification within a vein.

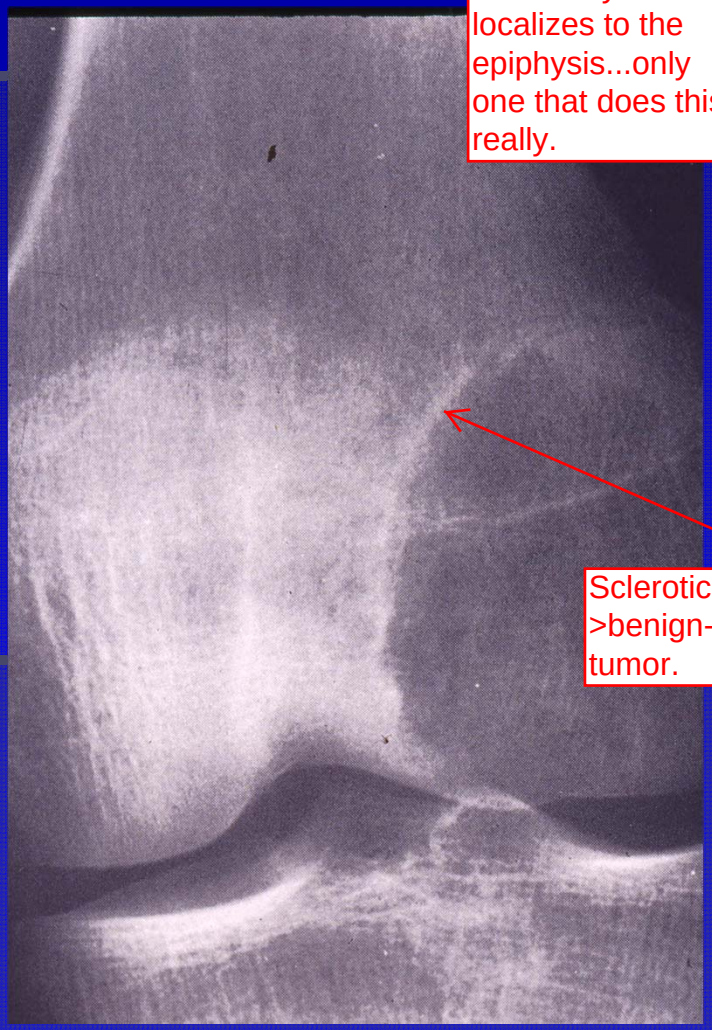
Chondroblastoma

Unusual in that it occurs in a weird location...the epiphysis.



- Clinical:
  - Less than 1% of all bone tumors
  - In young individuals with open epiphyses
  - Pain in affected region
  - May have corresponding joint effusion
  - Most common site is distal femur/proximal tibia

Chondroblastoma

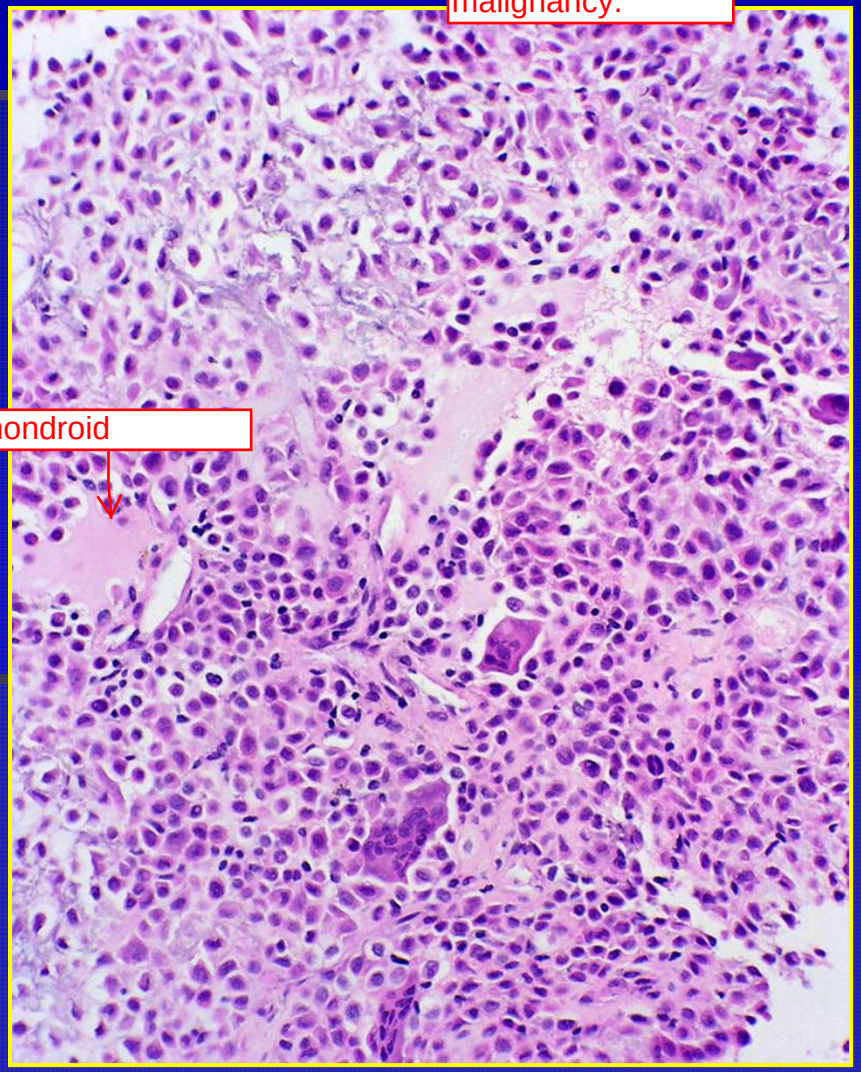


- Radiologic:
  - Located in epiphyses of long bones in skeletally immature individuals
  - Sharply demarcated oval/round lesion surrounded by sclerotic bone
  - Typically does not alter bone contour unless accompanied by ABC (20%)
  - May have fine to course intralesional calcification

Chondroblastoma

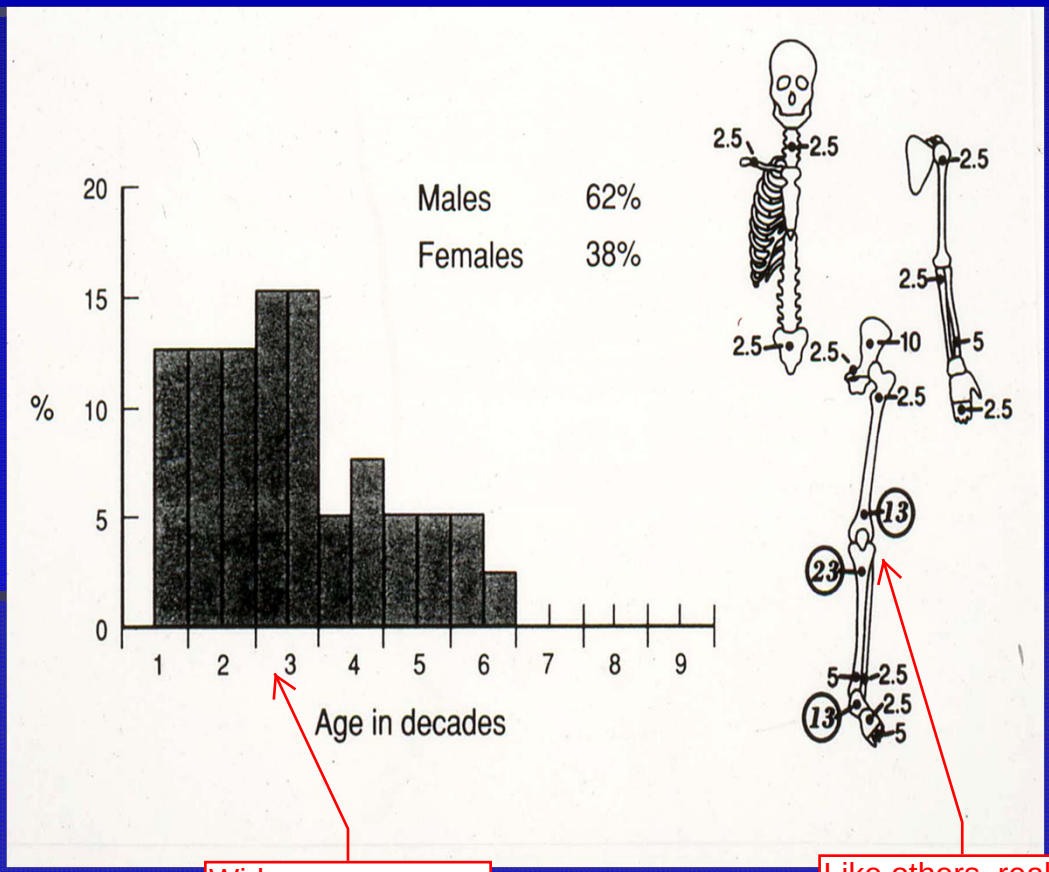
Name: unlike the other tumors that contain the "blastoma" name, this is NOT a malignant tumor. Otherwise, blasts are associated with malignancy.

- Histopathology:
  - Chondroblasts, characterized by small cells with high N/C ratio and clefted nuclei
  - Variable mature or immature cartilaginous matrix
  - “Chicken-wire” calcification pattern associated with blastic foci
  - Few multinucleate giant cells



Chondromyxoid fibroma

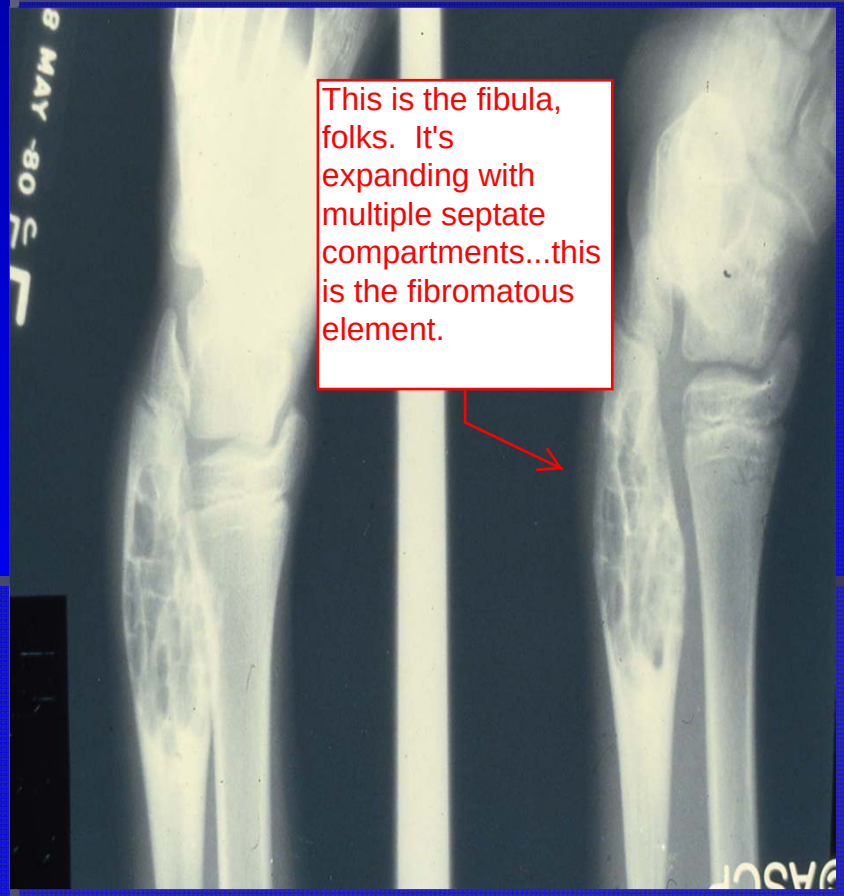
- Extremely rare lesion (< 1%) with wide age range
- Most common location is knee; proximal tibia accounts for 25% of all
- may present with tenderness or swelling but is often an incidental finding



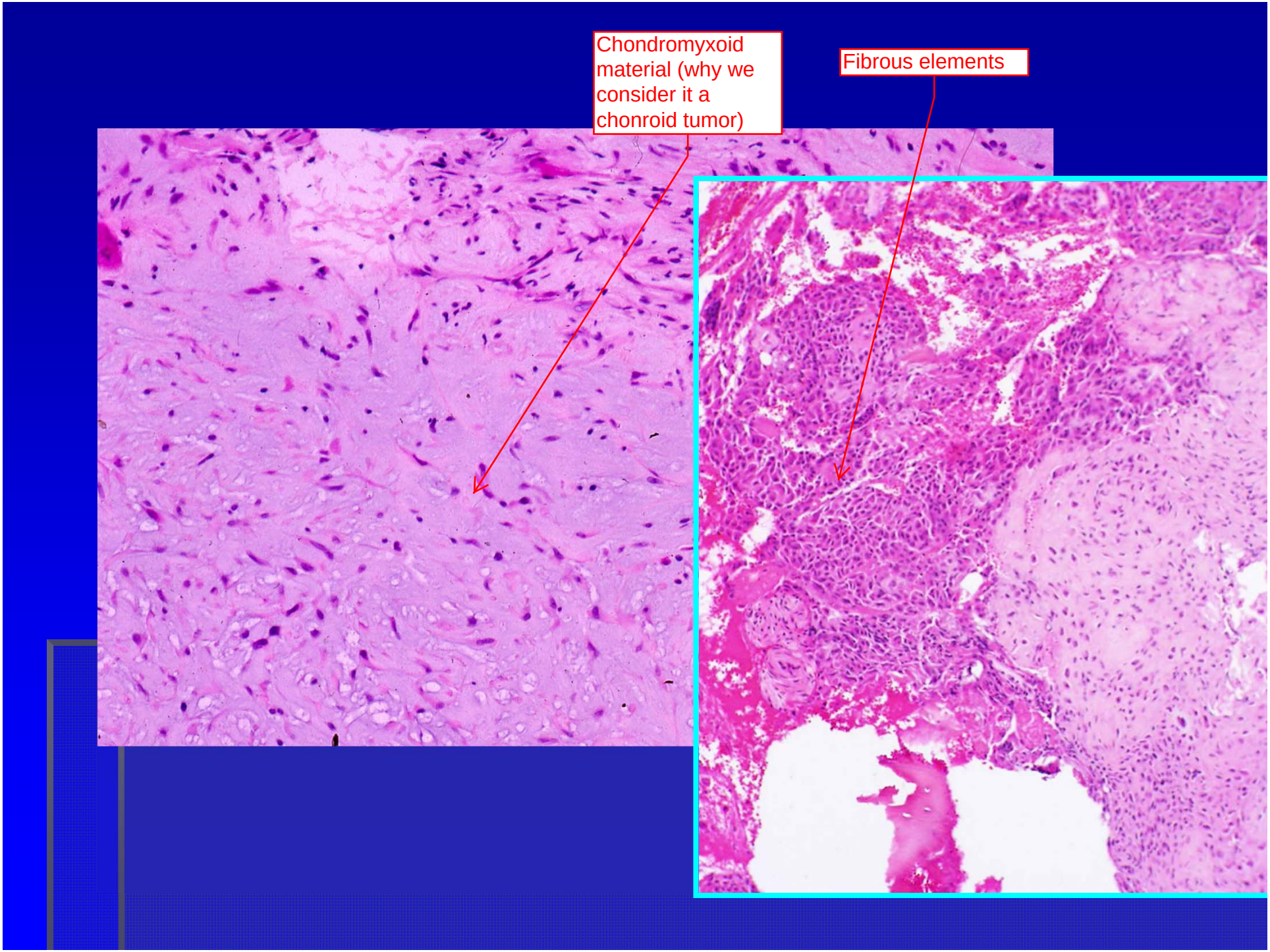
Wider age distribution than some others.

Like others, really likes the knee.

Chondromyxoid fibroma



- Radiologic:
  - Eccentric, metaphyseal lytic defect
  - Long axis of lesion parallels long axis of affected bone
  - Sharp, sclerotic and scalloped margins; may be lobulated or septated
  - Typically lacks intralesional calcification


Chondromyxoid material (why we consider it a chonroid tumor)
Fibrous elements

Chondrosarcoma

Malignant. Unusual in that it primarily affects older individuals (rather than children). Also occurs in "weird" places like the pelvis, ribs, and axial skeleton in addition to the long bones.

- Clinical:
  - Wide age range; tumor in adults is most common; predisposing factors
  - Appendicular skeleton and proximal extremities are most common sites
  - presents with pain and local tenderness; often of long duration
  - Palpable firm mass

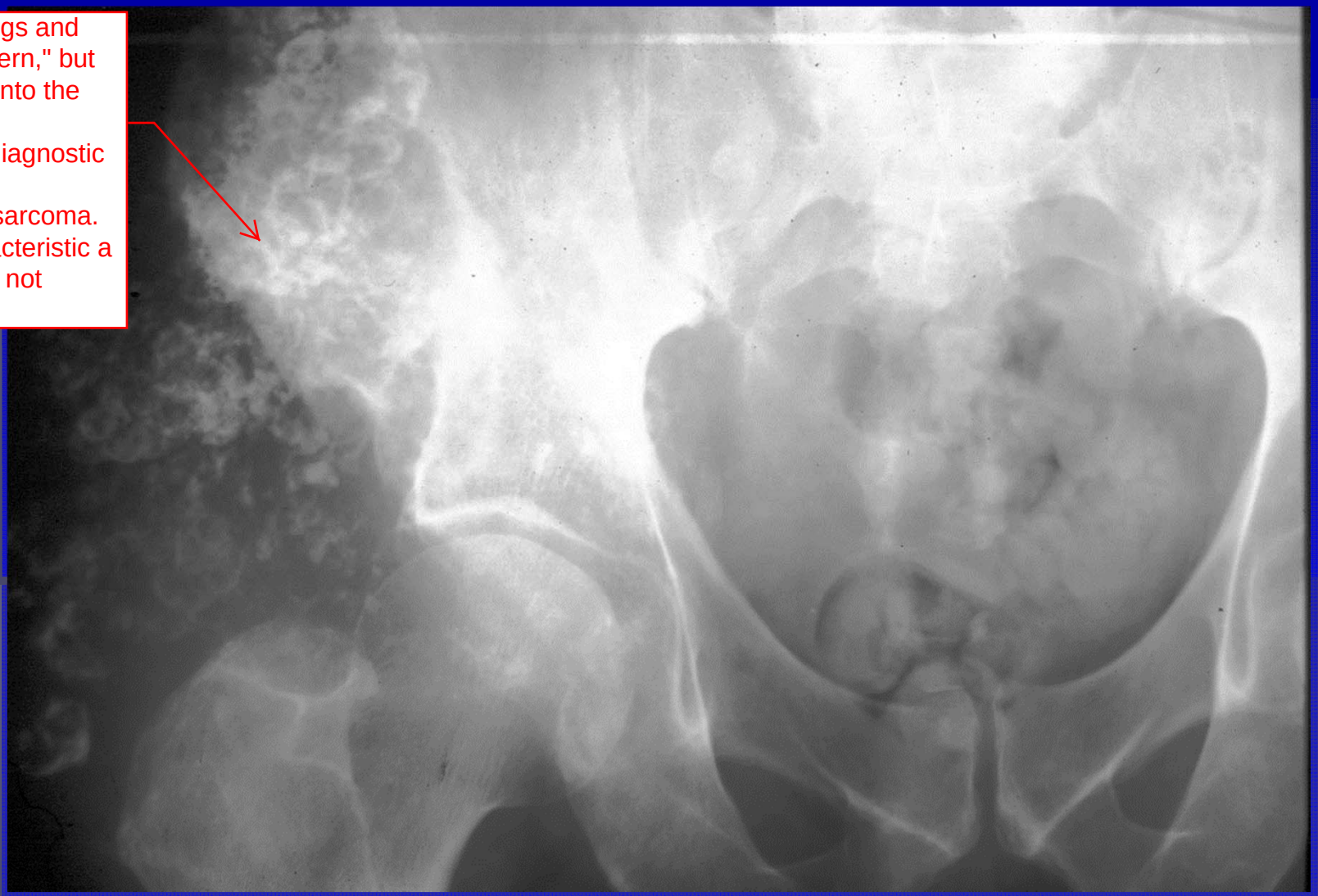
Chondrosarcoma

- Radiographic:
  - Predilection for central skeleton; acetabulum or metaphysis/diaphysis of long bones
  - Intralesional calcification classically in form or rings and arcs (65%)
  - Cortical destruction; soft tissue extension with large lesions

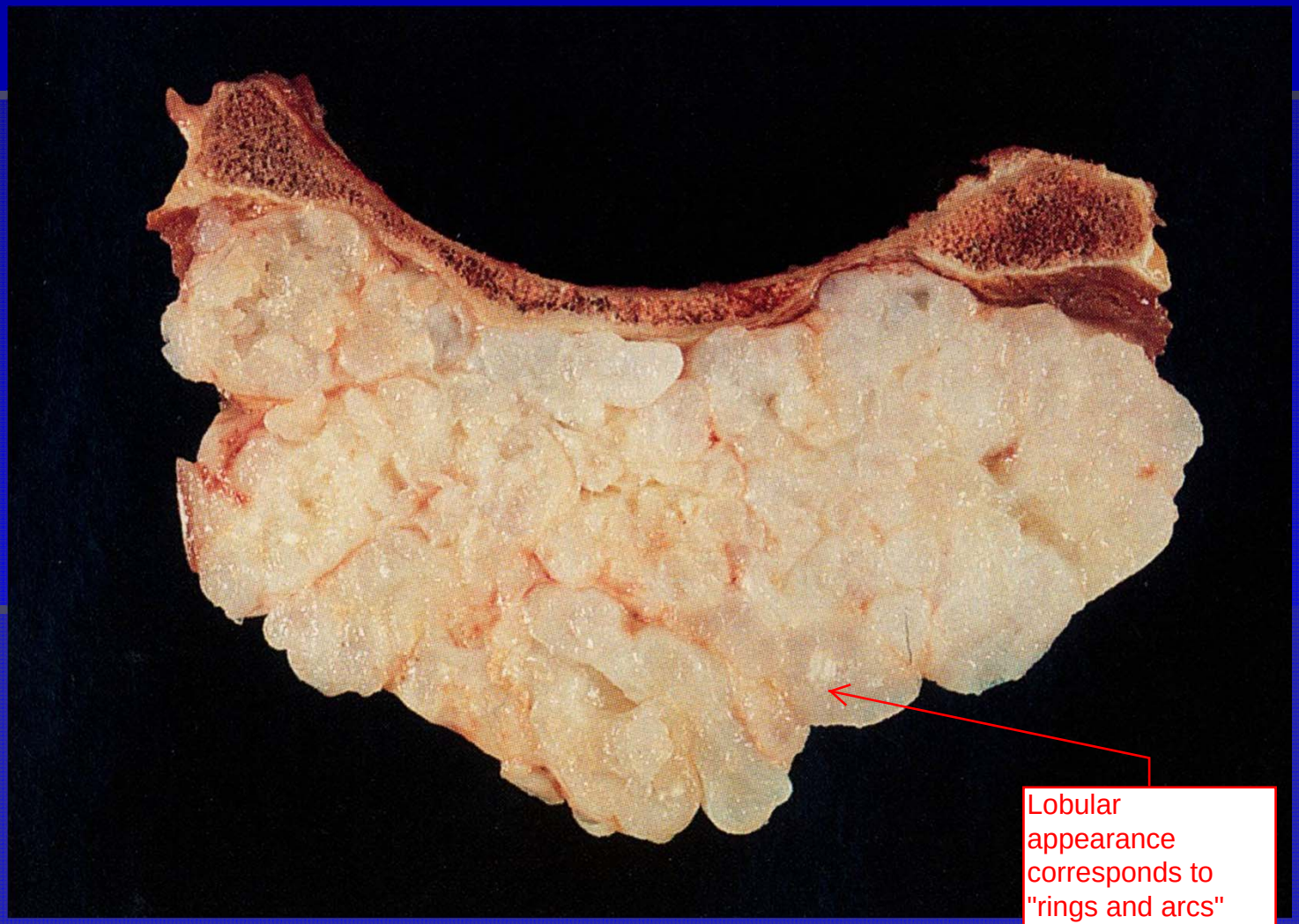
Here we are again.

Chondrosarcoma

Also, "rings and arcs pattern," but way out into the soft tissue...diagnostic of chondrosarcoma. So characteristic a biopsy is not needed.

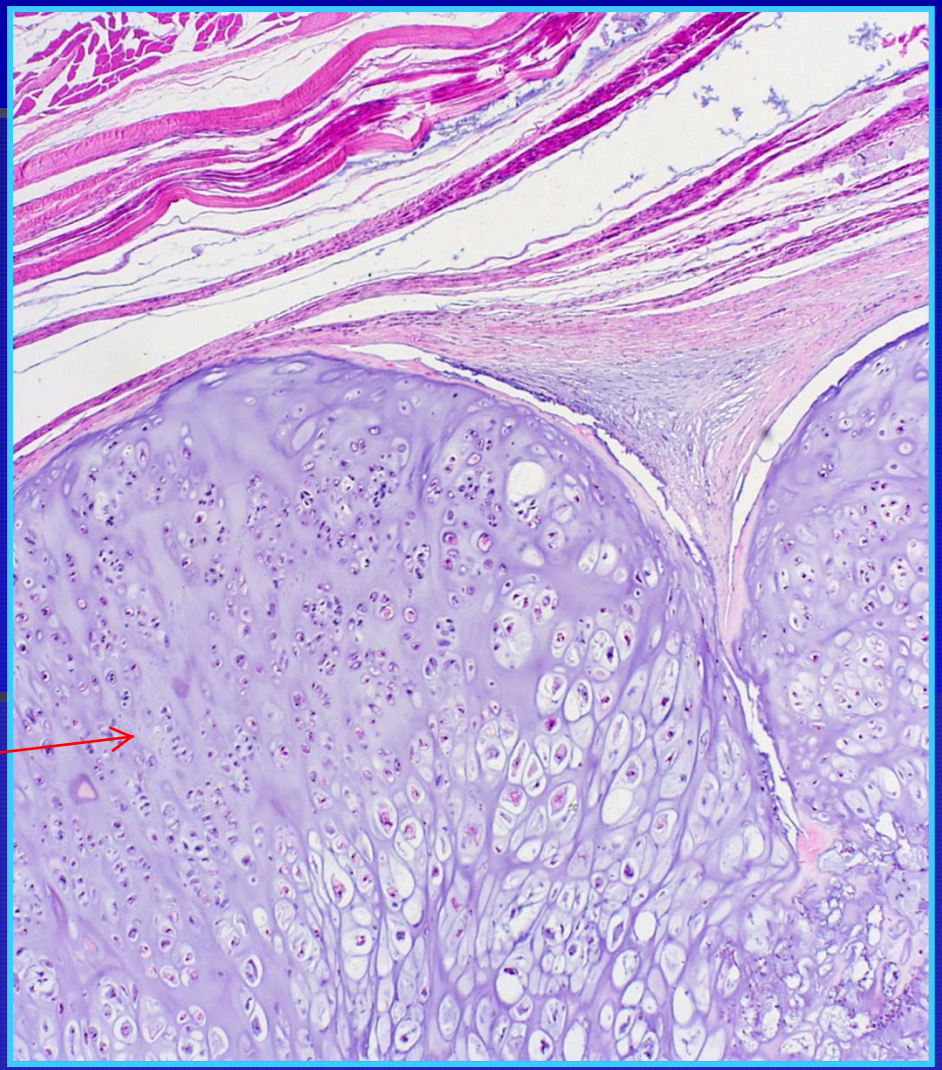


Chondrosarcoma



Chondrosarcoma

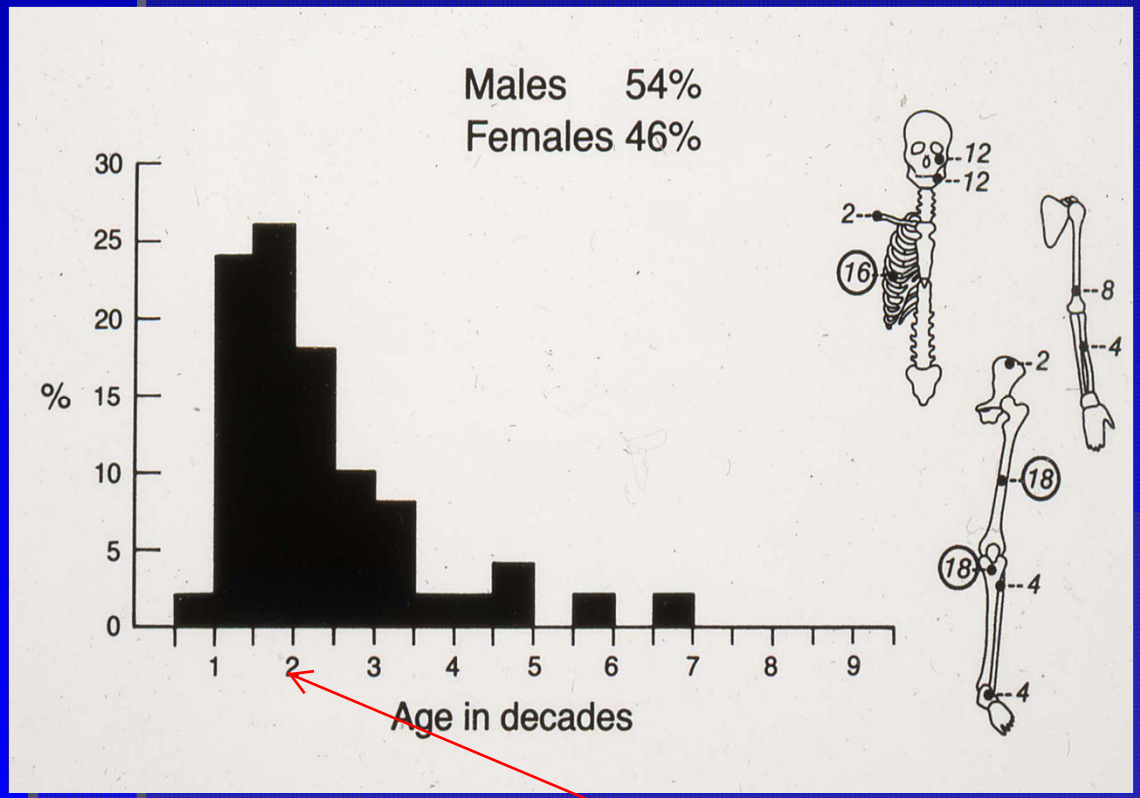
- Binucleation and myxoid change of cartilage are helpful but not absolute indicators of malignancy
- Lack of osteoid (conventional)



These are now the "other" disorders

Fibrous dysplasia

Probably not a tumor, but included because it forms solid lesions in the bone. Differential for this will include bone tumors.



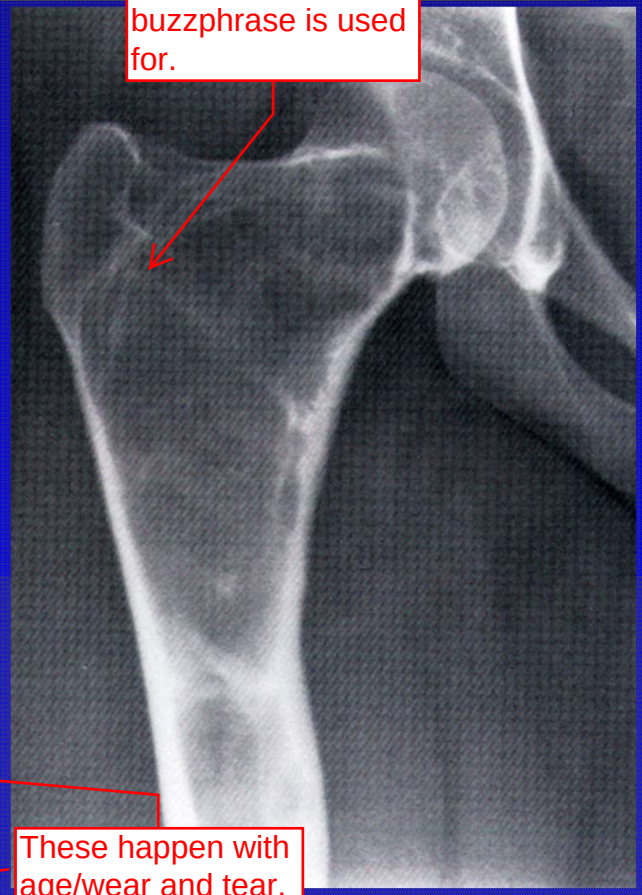
Once again, back to the children.

Clinical:

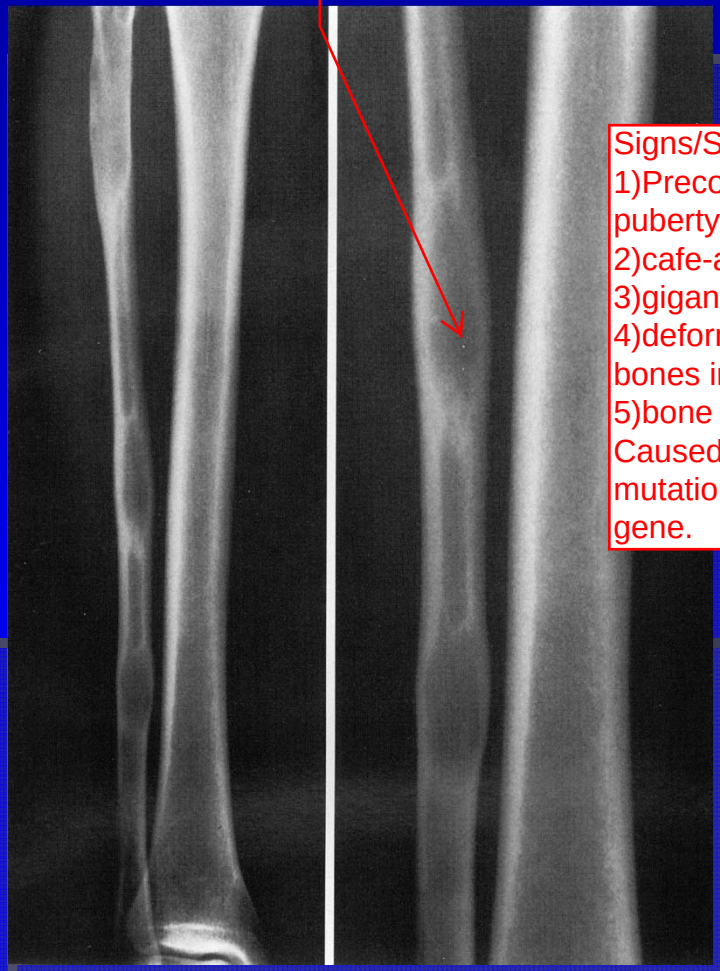
- Often asymptomatic; incidental finding or bone growth deformity
- Solitary (monostotic) or multiple bones involved (polyostotic)

Fibrous dysplasia

- Radiologic:
  - Metaphyseal or diaphyseal based lesion
  - Lytic or ground glass appearance
  - Bowing and pathologic fracture (shepherd's crook deformity)
  - Cystic degeneration is common



Fibrous dysplasia



Signs/Sx:
1)Precocious puberty
2)cafe-au-lait spots
3)gigantism
4)deformities of bones in the face
5)bone fractures
Caused by mutation in GNAS1 gene.

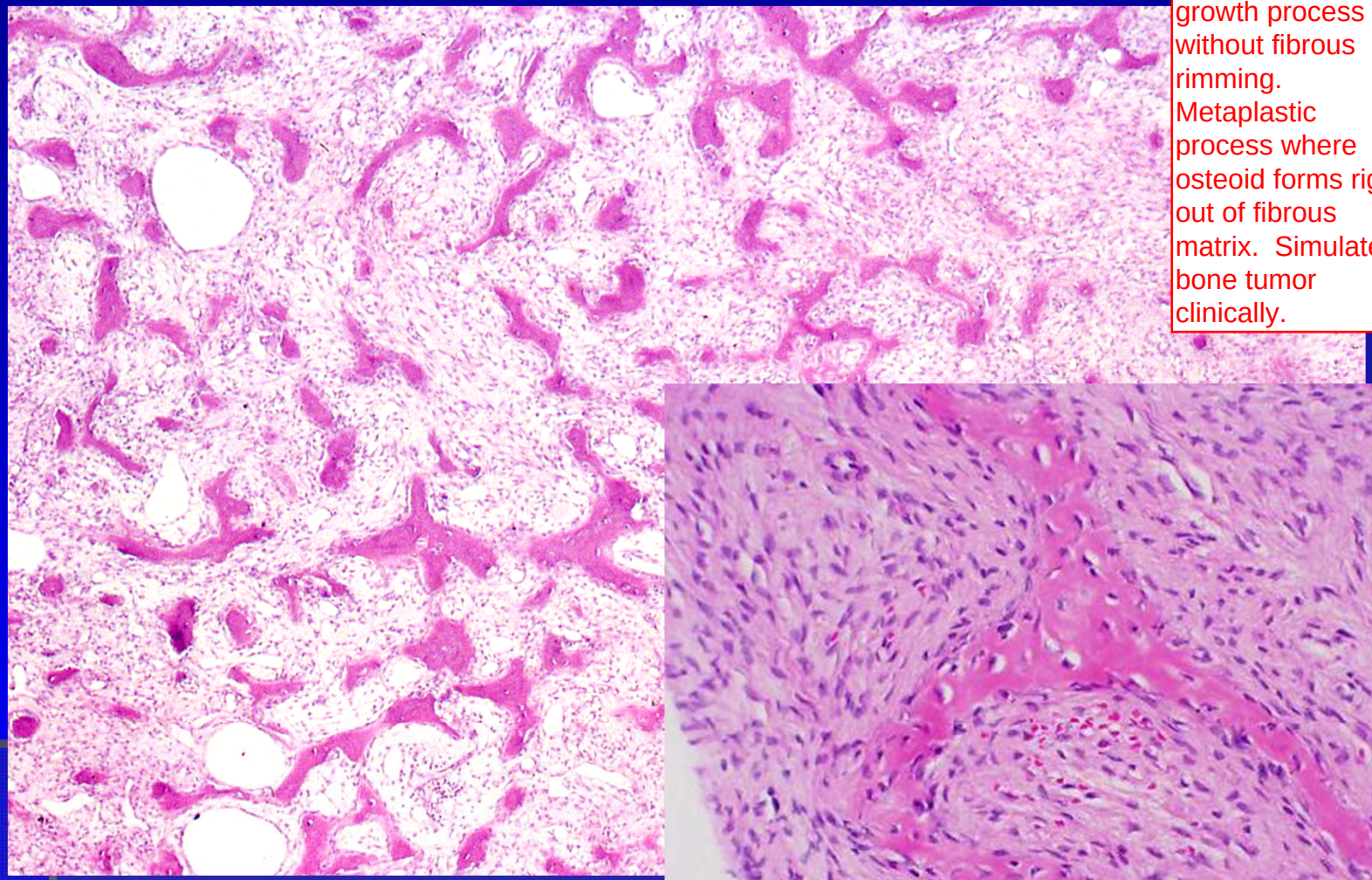
- Can be uni- or multifocal (polyostotic)
- Multifocal FD seen in Albright-McCune and Mazabraud's syndromes

Multiple myxomas and fibrous dysplasias

Fibrous dysplasia

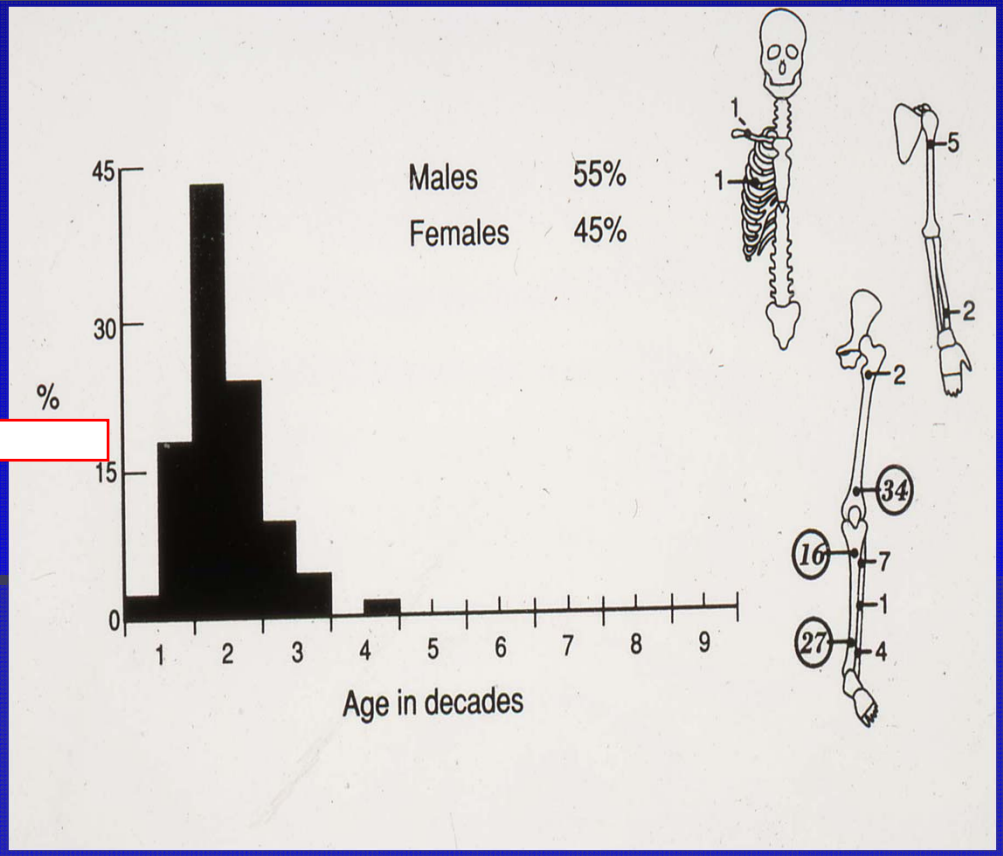
- Histopathology:
  - Fibrous stroma of variable density; small bland spindled cells
  - Osteoid trabeculae of unusual shapes; “alphabet soup” or psammoma bodies
  - Lack of osteoid rimming
  - Foci of cartilaginous metaplasia, lipid laden macrophages and cystic degeneration
  - Rare multinucleated giant cells

This resembles a membranous growth process without fibrous rimming. Metaplastic process where osteoid forms right out of fibrous matrix. Simulates bone tumor clinically.

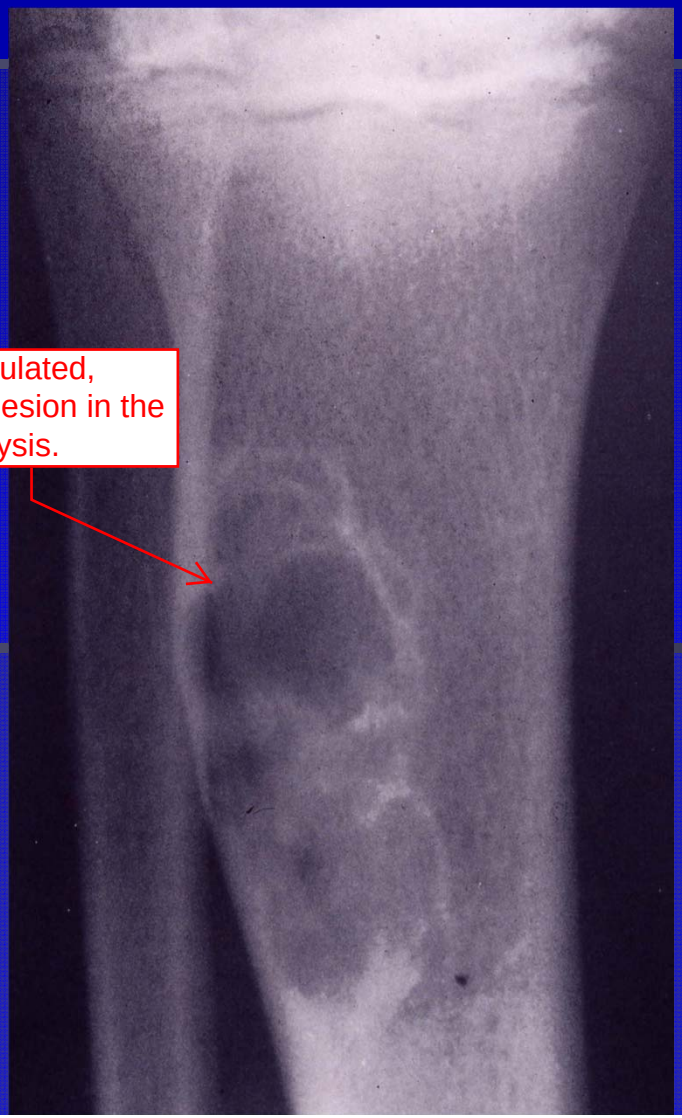


Fibroma

- Also known as fibrous metaphyseal defect, **non-ossifying fibroma**
- Peak incidence in adolescents and young adults
- May be discovered incidentally or present with pathologic fracture
- Metaphyseally centered lesion, lower extremity is most common location

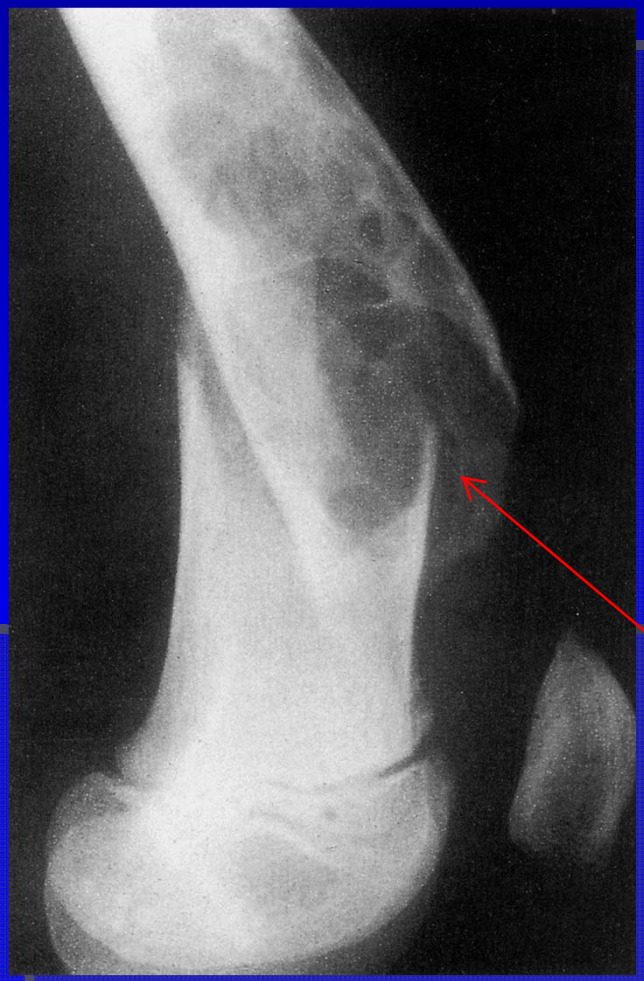


Fibroma/NOF



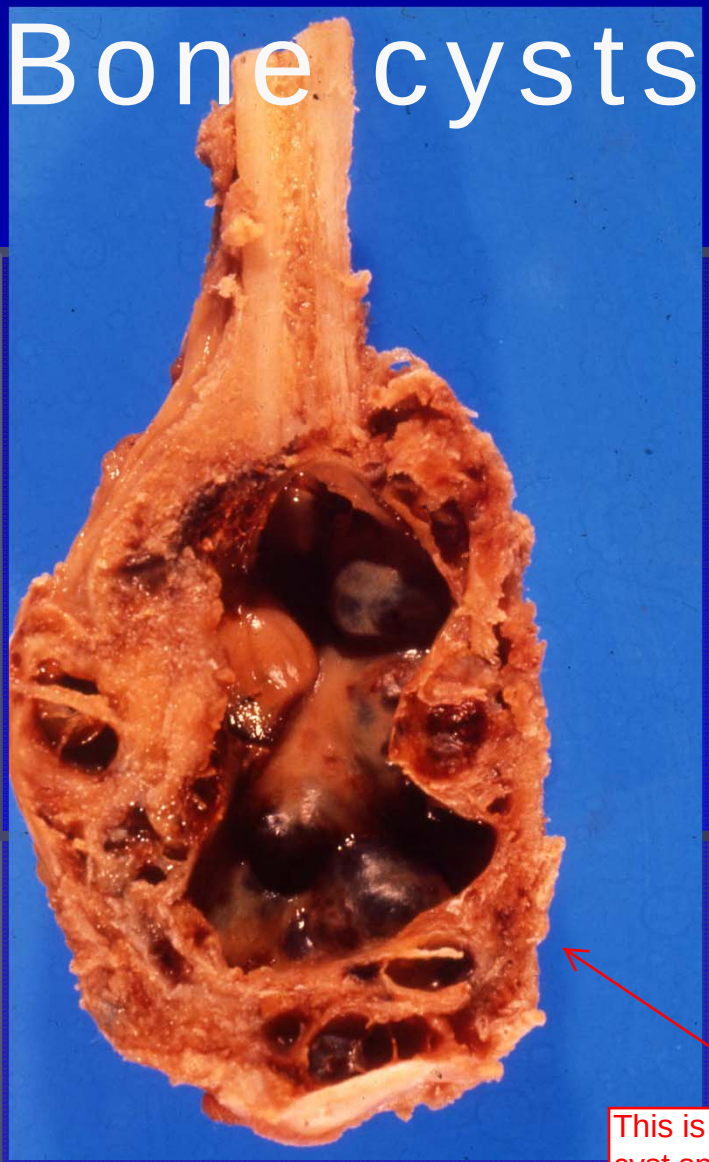
- Rad: sharply demarcated, expansile lesion of the cortex; metaphyseal
- Lesion is parallel to long axis of affected bone

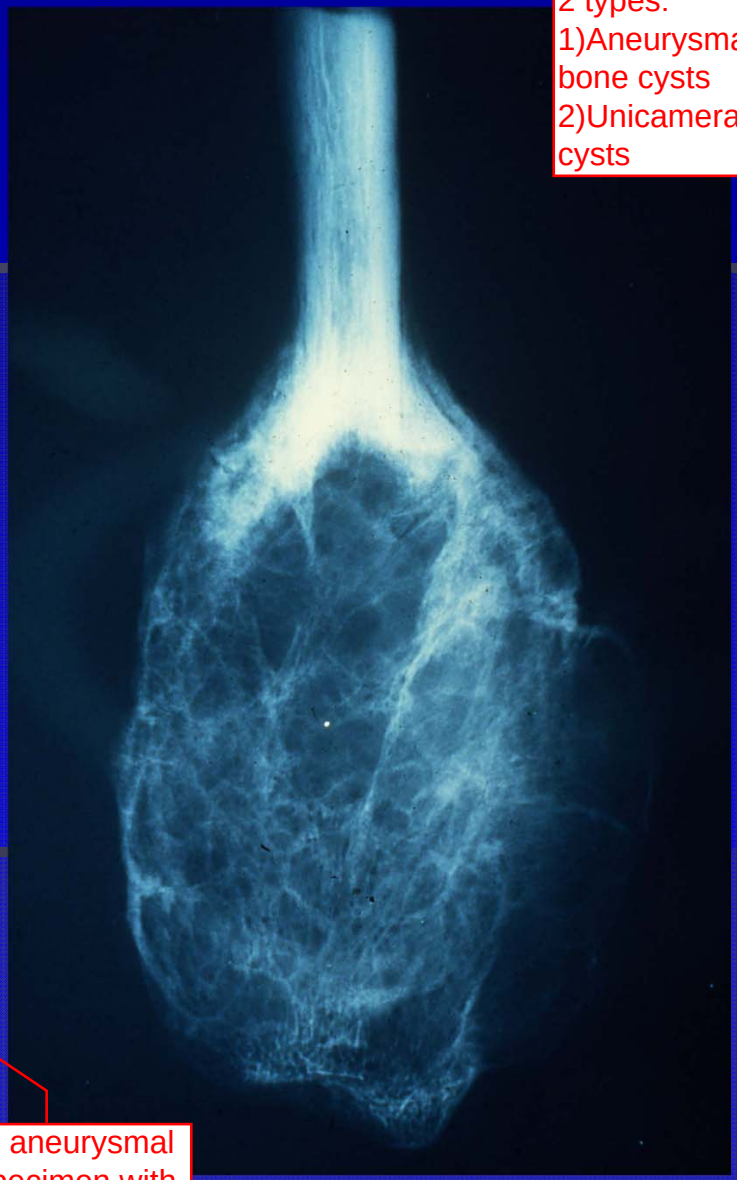
Fibroma/ NOF



- Because of pathognomonic appearance and tendency for spontaneous resolution, seldom encountered in SP

Bone cysts



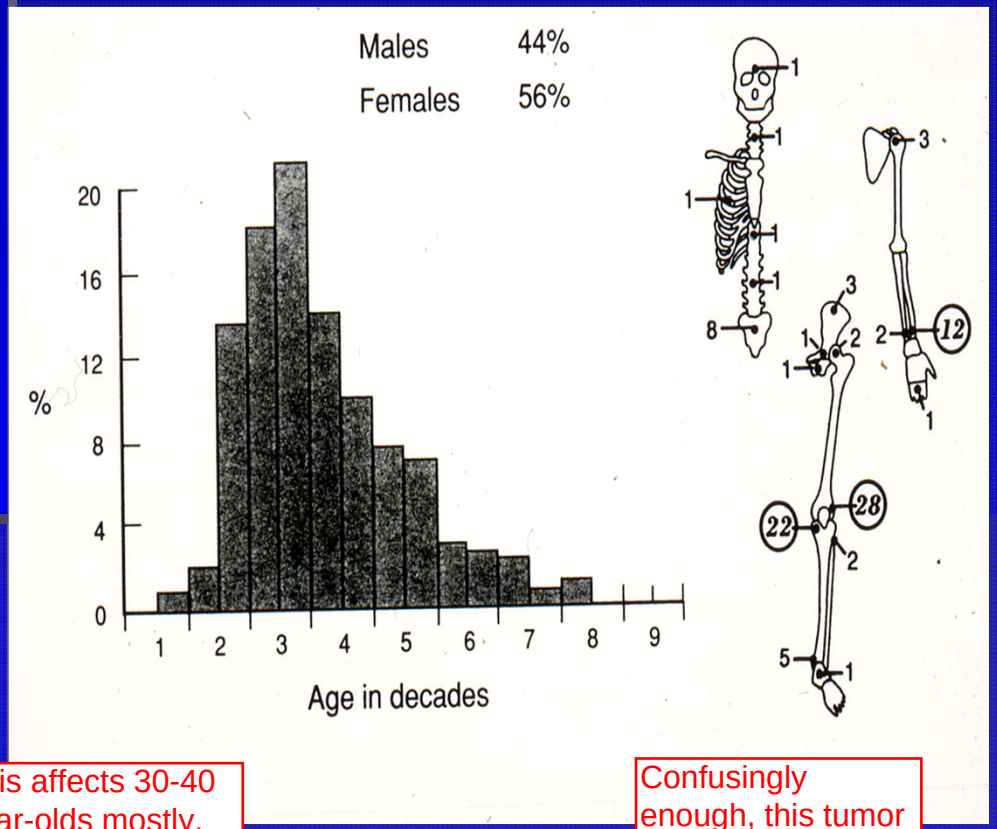


2 types:
1)Aneurysmal bone cysts
2)Unicameral bone cysts

This is aneurysmal cyst specimen with corresponding x-ray. Once again, a problem only with fracture or infection.

Giant cell tumor

This looks exactly like Brown's tumor of hyperparathyroidism. The way you can determine which is which is the location. Giant cell tumors are found almost exclusively in the epiphysis.
If you see the tumor elsewhere, think hyperparathyroidism.

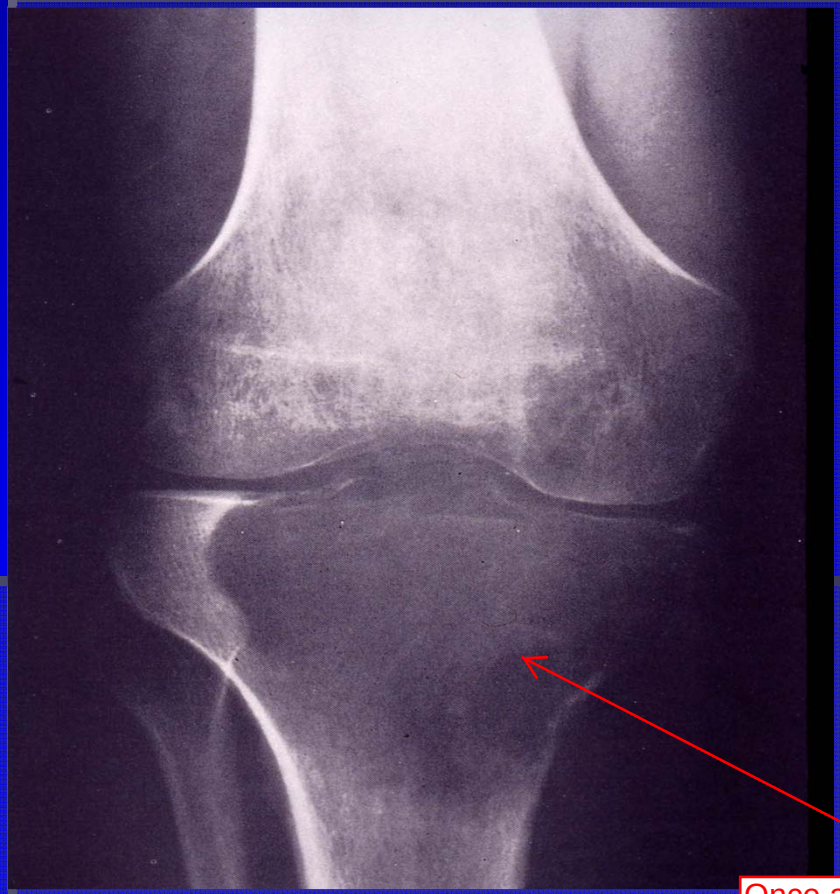


- Most often in skeletally mature individuals (third decade)
- Most common location = knee, distal radius, sacrum
- Pain, swelling and pathologic fracture
- Classically epiphyseal

This affects 30-40 year-olds mostly. This can be a nasty tumor with multiple recurrences. Benign but can recur.

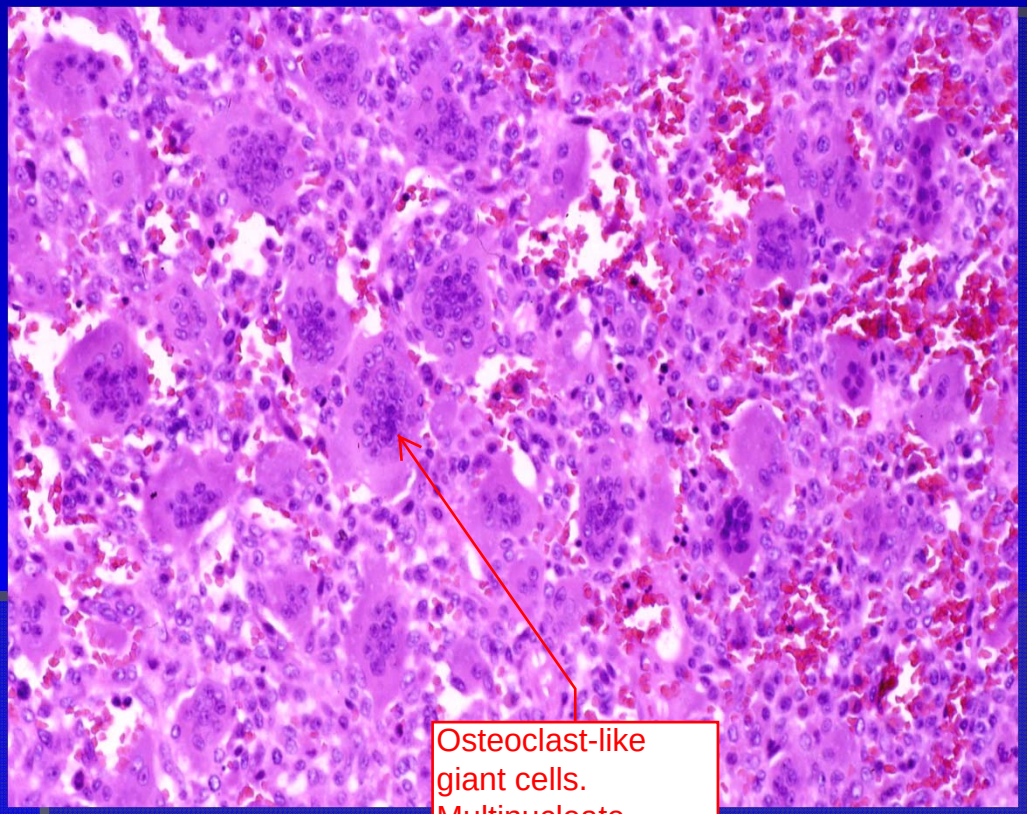
Confusingly enough, this tumor can get in the bloodstream and go to the lungs. NOT a metastasis though...figure that out.

Giant cell tumor



- Radiology:
  - Epiphyseal centered; extends to articular surface
  - lytic lesion lacking significant sclerosis or periosteal reaction
  - Confined to bone or break through cortex into soft tissue
  - Radiologically simulates malignancy: osteosarcoma

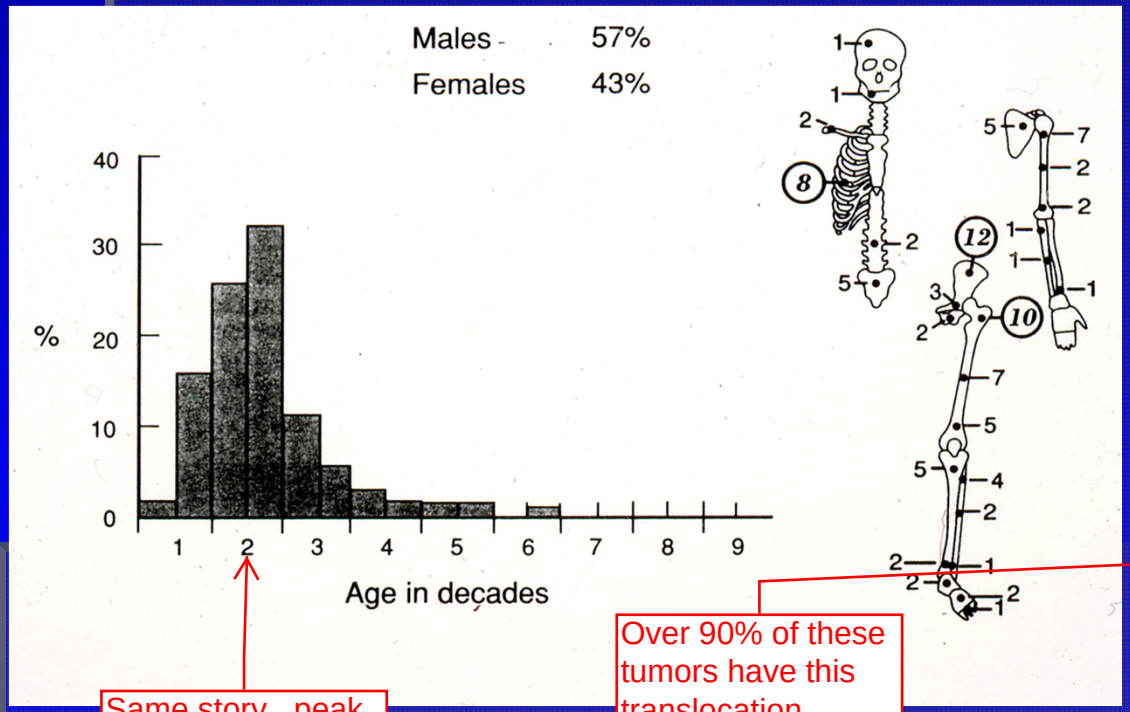
Giant cell tumor



- Histopathology:
  - May have necrosis or secondary cyst formation
  - Uniform pattern of growth with numerous giant cells
  - Background of round /oval mononuclear cells--same as multinucleate cells; no cytologic atypia

Ewings Sarcoma

Genetic. Ewing's sarcoma can show up anywhere in the skeleton.



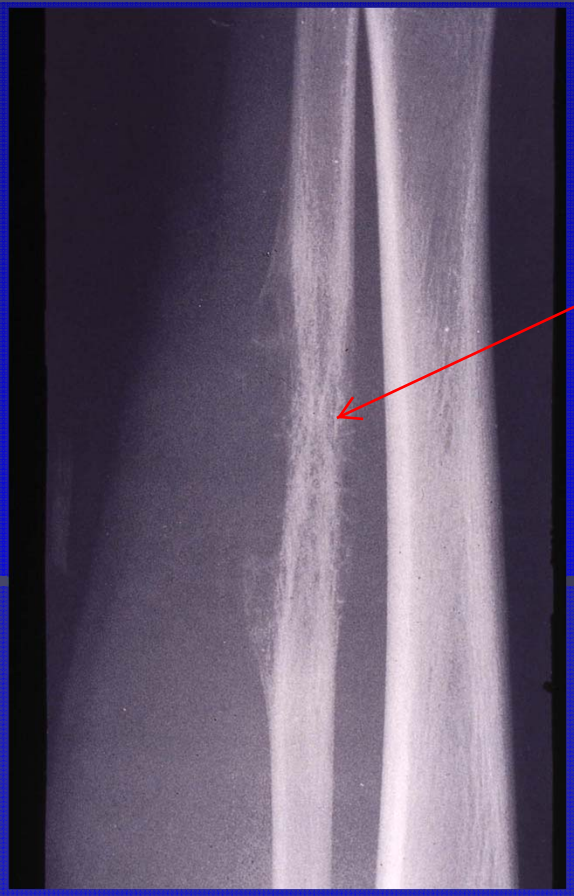
Same story...peak incidence in chldren/young adults.

Over 90% of these tumors have this translocation. Translocation of Ewings sarcoma gene to another partner gene (which can vary) to form an oncogene.

- Clinical:
  - Lesion of adolescents and young adults
  - Presents with local pain and swelling; may have fever and simulate infection
  - **Rx'd with radiation and adjuvant chemotherapy
  - t (11;22); related cytogenetically to PNET and DSRCT, Askins

Ewing Sarcoma

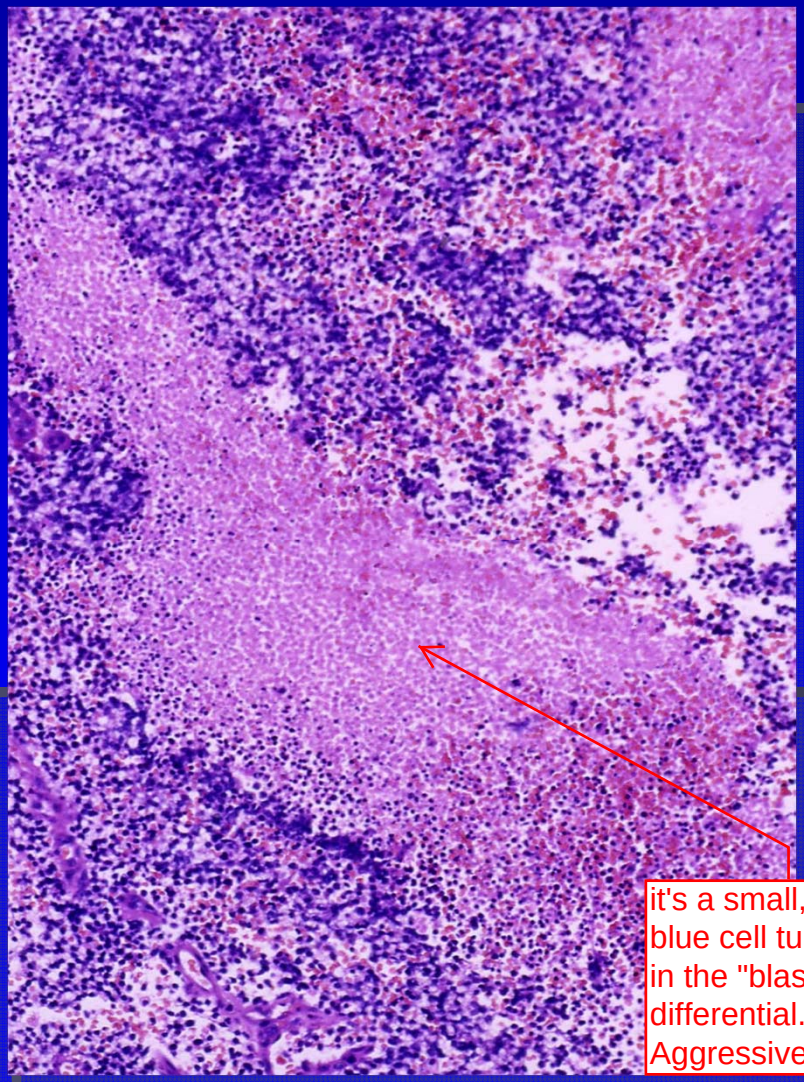
"moth-eaten" Starburst appearance. Very creative. This is in the diaphysis...unusual for other bone tumors.



- Radiologic:
  - Extensive, poorly marginated diaphyseal lesion
  - Periosteal new bone formation and soft tissue mass
  - May be lytic and /or sclerotic
  - Ddx: lymphoma and osteomyelitis

Ewing Sarcoma

Tx has really evolved in past 20 years. Now we treat with neo-adjuvant chemo/ radiotherapy with limb-salvage surgery.



it's a small, round blue cell tumor. It's in the "blast" differential. Aggressive tumors.

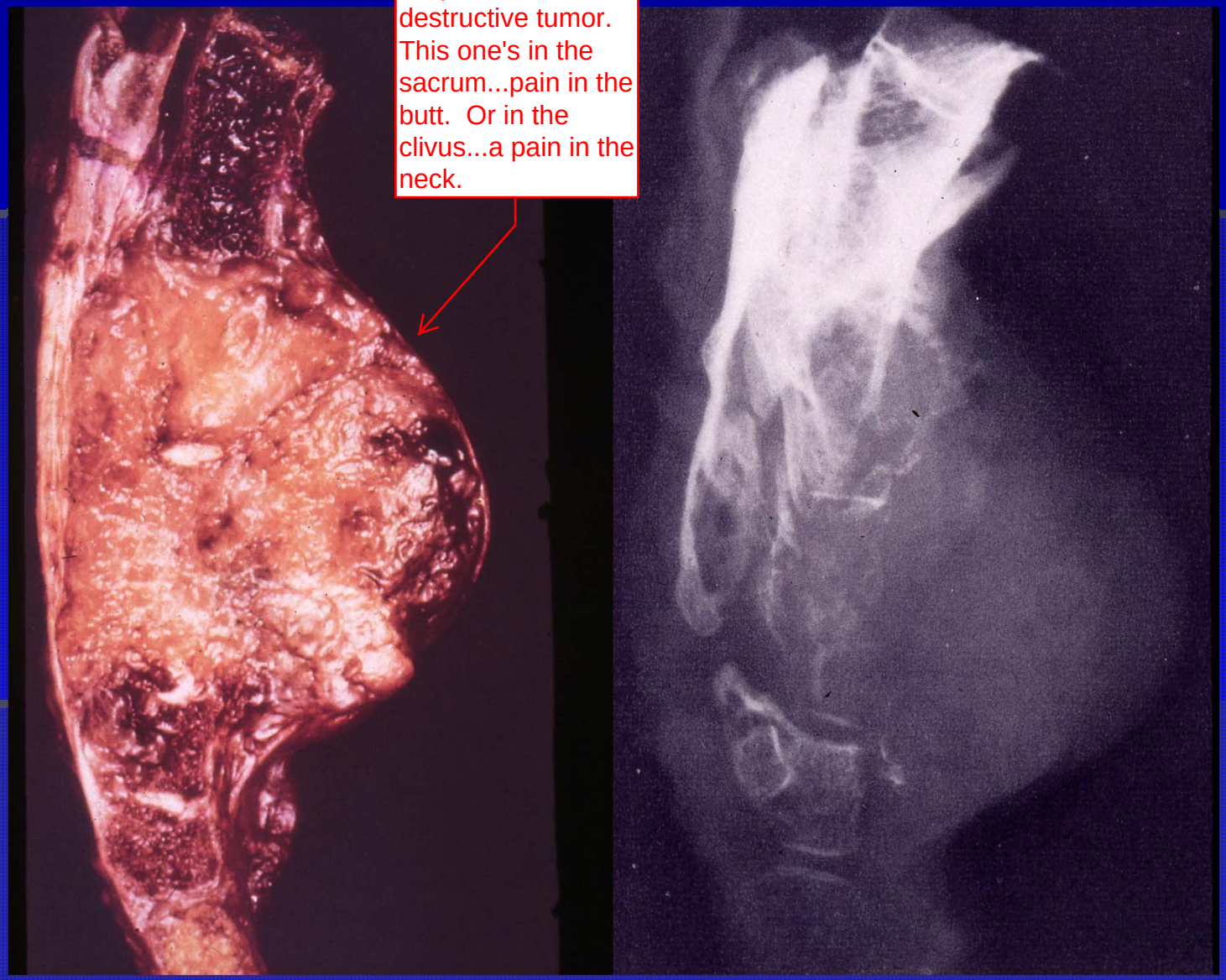
- Histopathology:
  - "Small round blue cell tumor"
  - Pas +/diastase-intracytoplasmic glycogen
  - may show extensive necrosis and crush artifact

Limb-salvage procedure can also be used to treat this tumor.

Chordoma

Very characteristic tumor that only appears in the sacrum or the clivus (base of the skull).

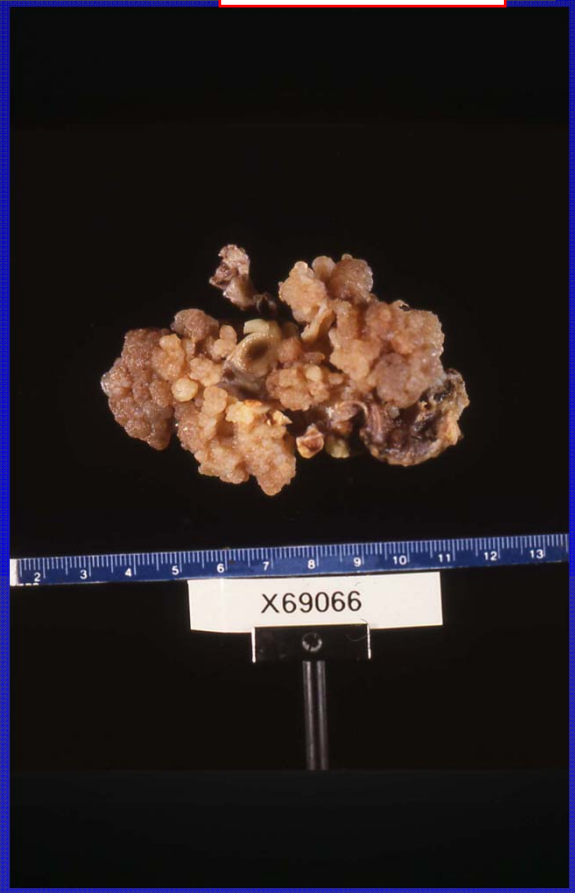
- Clinical:
  - Associated with wide age range
  - majority of lesions of sacrum or clivus
  - pain but also nerve/spinal cord compression, change in bowel, cranial nerve dysfunction or nasopharyngeal mass


Very localized and destructive tumor. This one's in the sacrum...pain in the butt. Or in the clivus...a pain in the neck.

Pigmented villonodular synovitis PVNS

Pseudoneoplasm of the joints, you'll frequently hear about this on the wards.

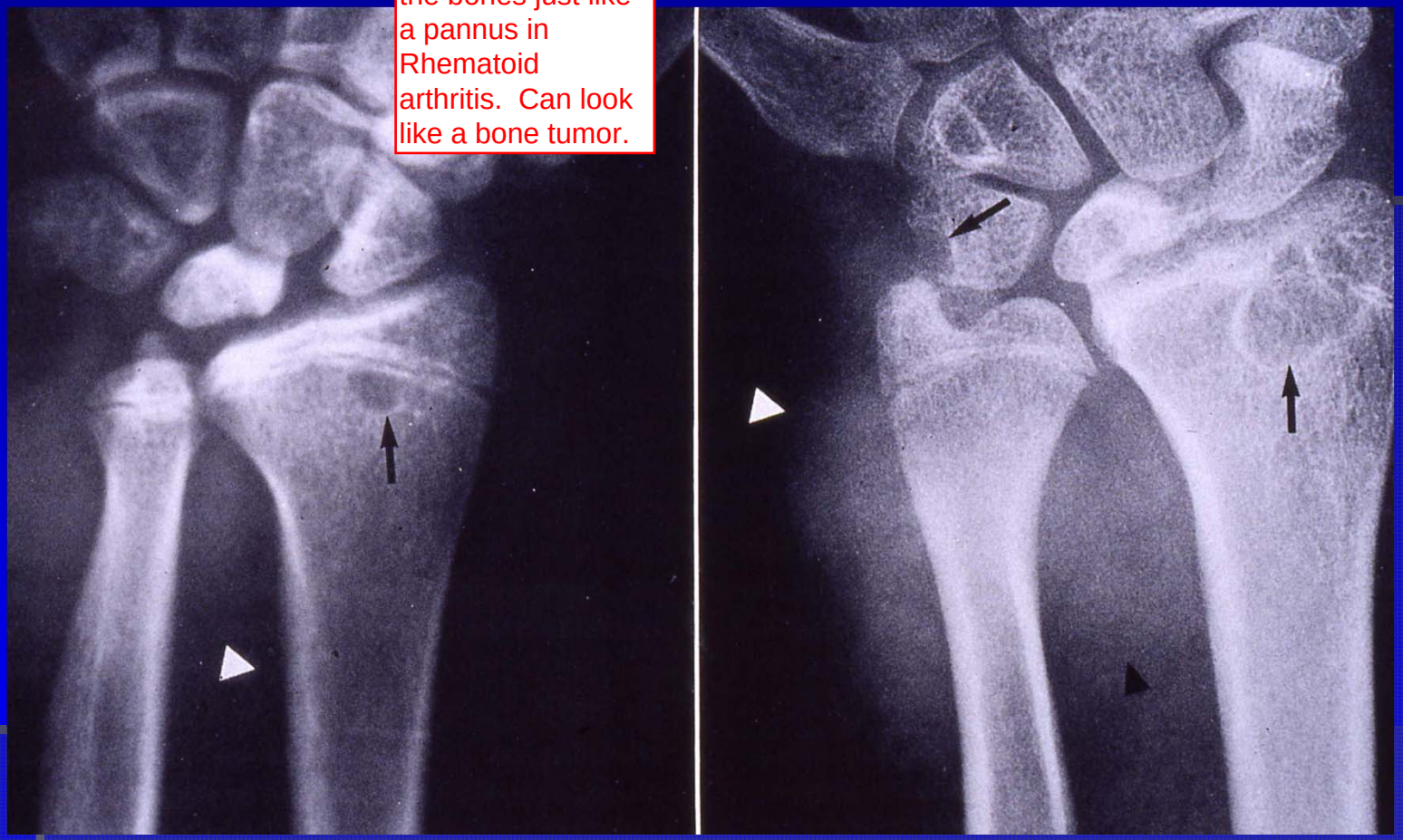
- Common proliferative/neoplastic lesions of joints; progressive discomfort
- nodular, villous thickening of the synovium with hemosiderin deposition



PVNS

PVNS can invade the bones just like a pannus in Rhematoid arthritis. Can look like a bone tumor.

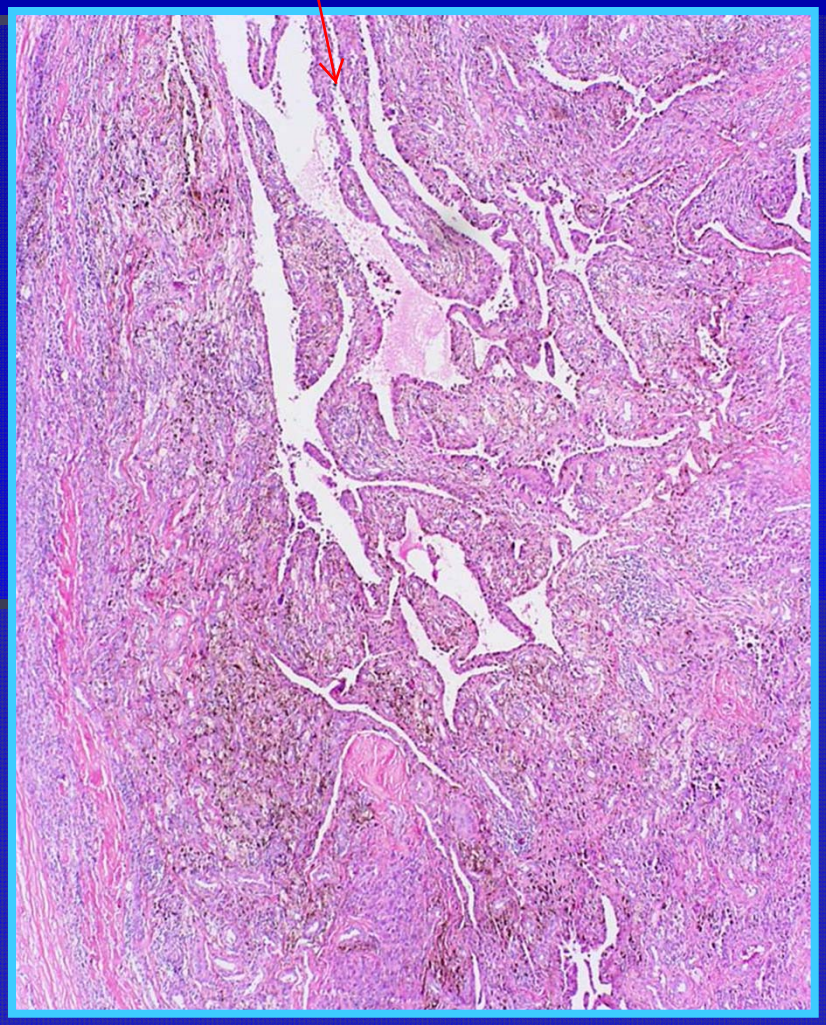
Tx: surgery



- Periarticular soft tissue swelling and mass effect
- Extensive bone destruction (simulating aggressive disease) can be present
- Hemosiderin identified on MRI

PVNS

- Large villi filled with dense infiltrate of fibrohistiocytic mononuclear cells, hemosiderin laden macrophages and giant cells.
- Numerous mitoses may be identified; NOT an indicator of “aggressive” potential



Soft tissue tumor/ Sarcoma

malignant

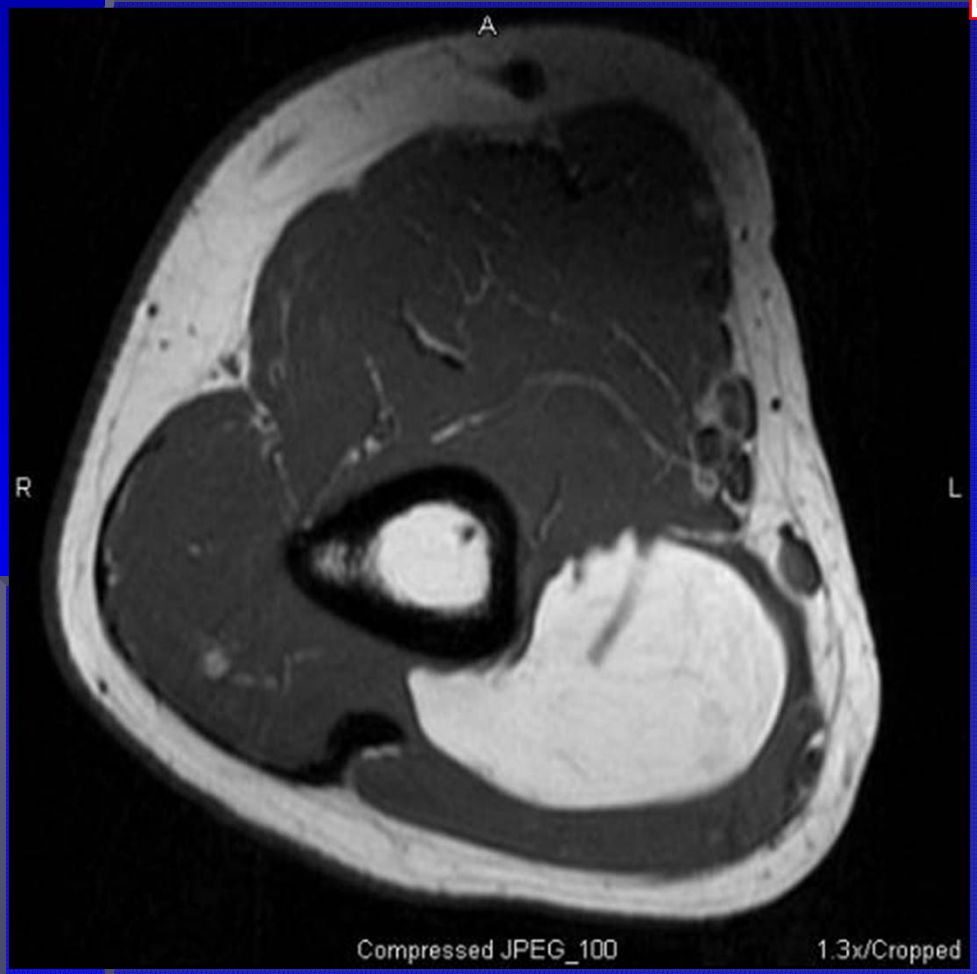
benign

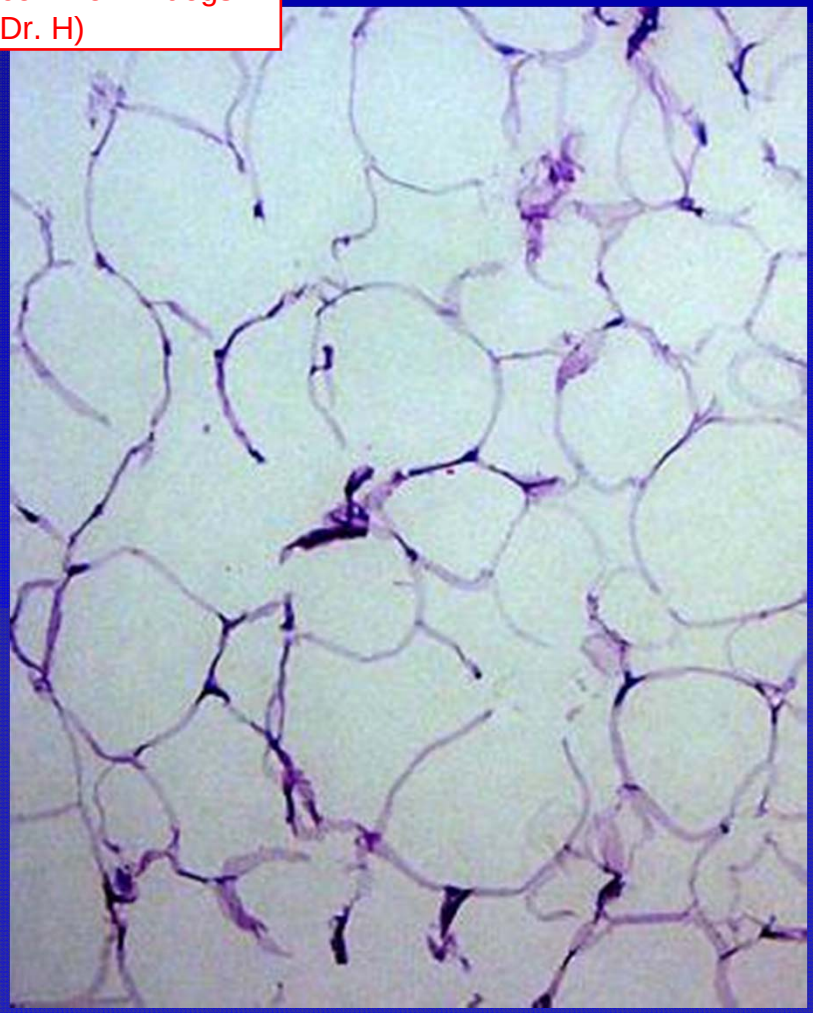
The number of soft tissue lesions is over 100! Thankfully, we're only going to talk about a few.
These are organized/named by the type of tissue that they affect.

- Lesions of adipose tissue: Lipoma/Liposarcoma
- Lesions of skeletal muscle: Rhabdomysarcoma
- Lesions of primitive/progenitor/multipotential cell: Malignant fibrous histiocytoma (MFH)
- Lesion of ? Tissue/cell: Synovial sarcoma

Lipoma

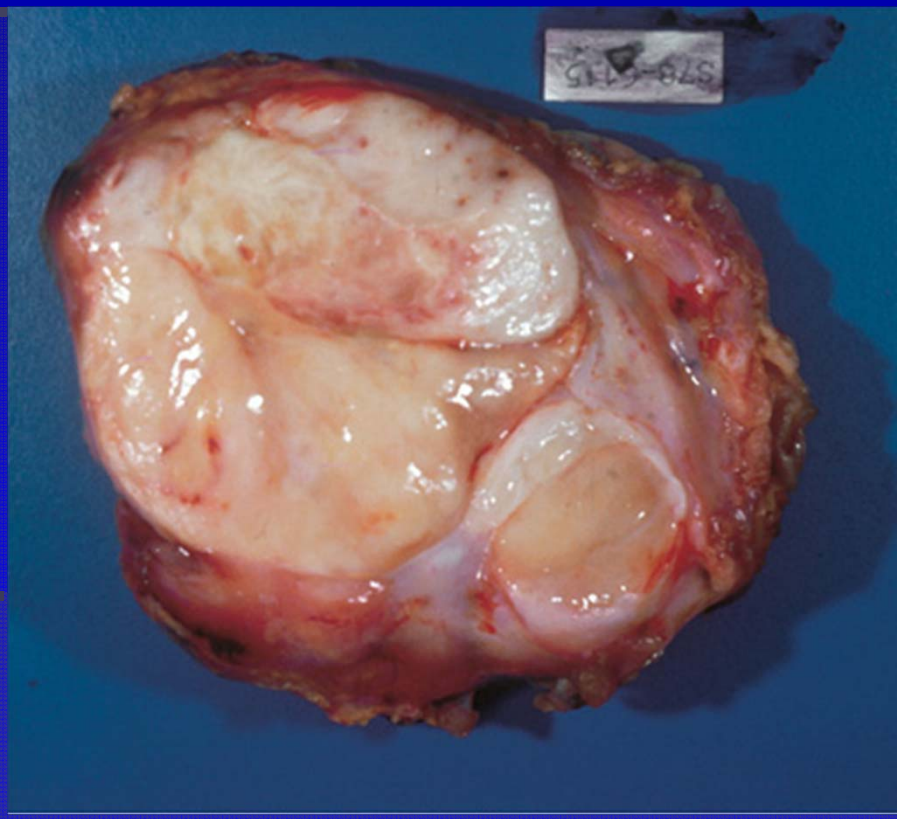
Happens in older people (Student- although I have one.) Fairly ubiquitous. (For dog lovers like me this is also common in dogs- Dr. H)





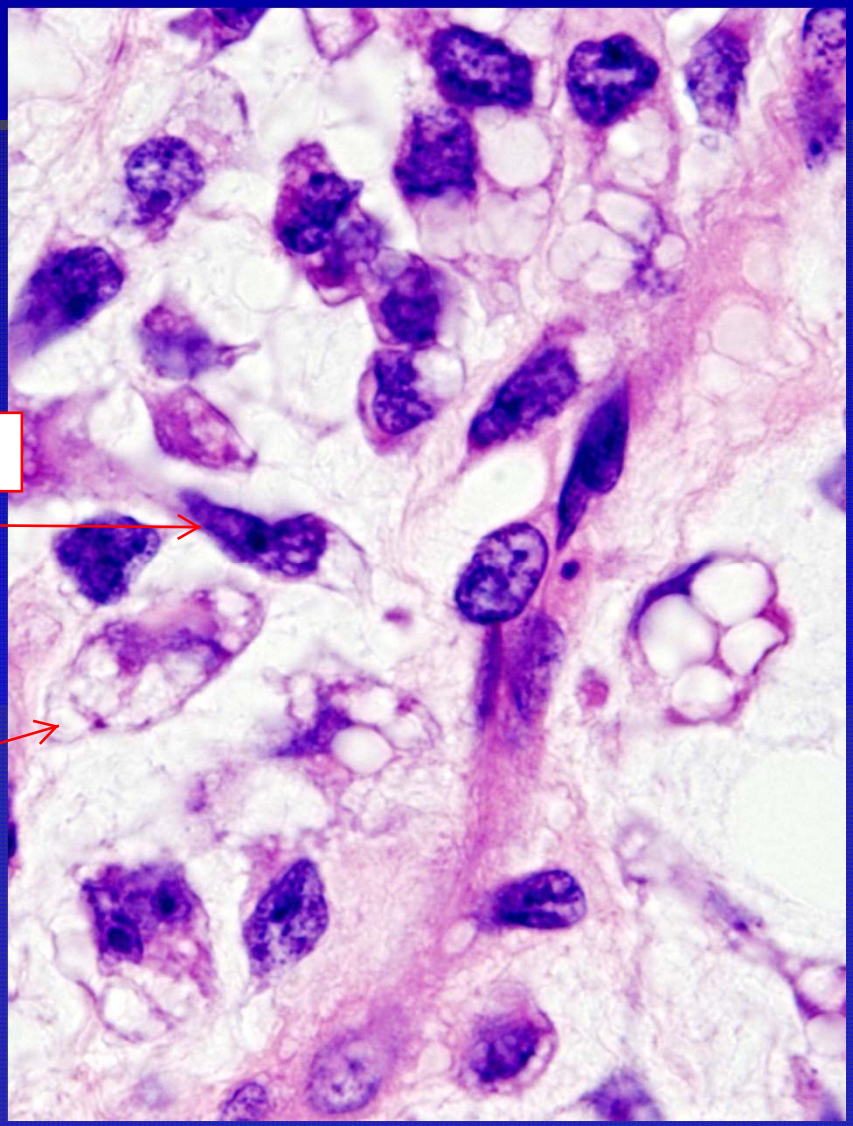
Liposarcoma

- One of the more common sarcomas
- Develop in the deep soft tissue; thigh and retroperitoneum
- Treatment is surgical; prognosis is dependent on grade, size, location



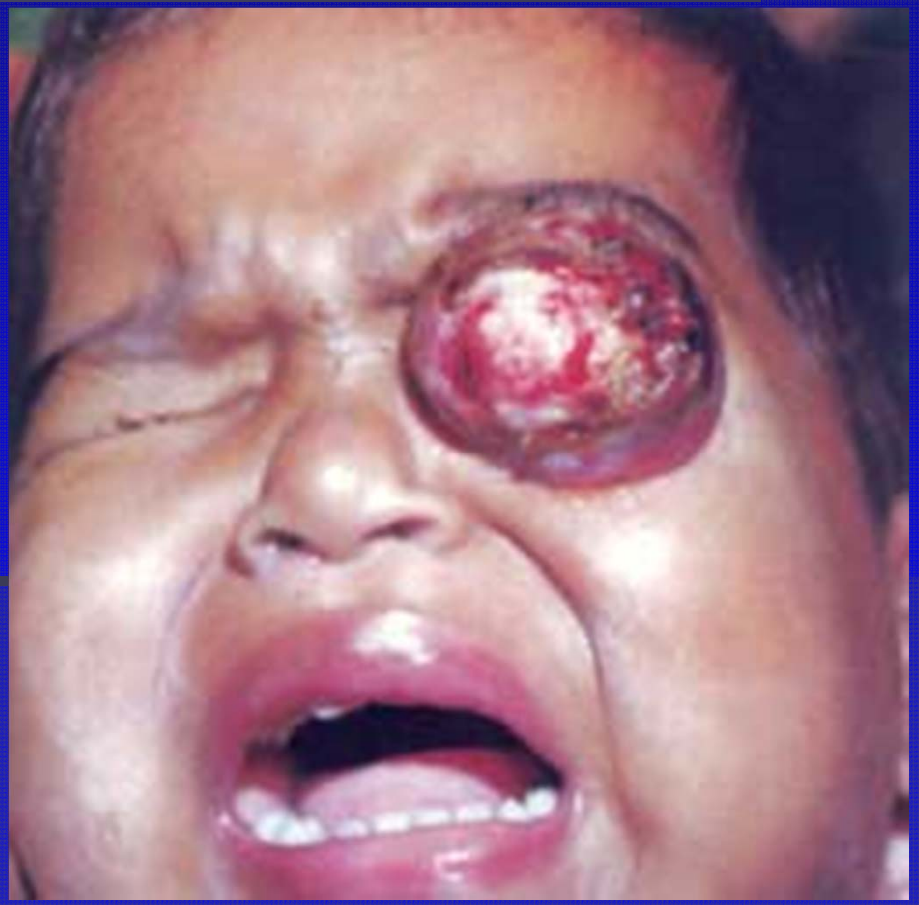
Liposarcoma

- Different variants with prognostic significance: well differentiated, myxoid/round cell and pleomorphic
- Histology = Lipoblasts



Rhabdomyosarcoma

- One of the more common tumors of children
- Occurs in unusual sites: head and neck, orbit, urogenital region



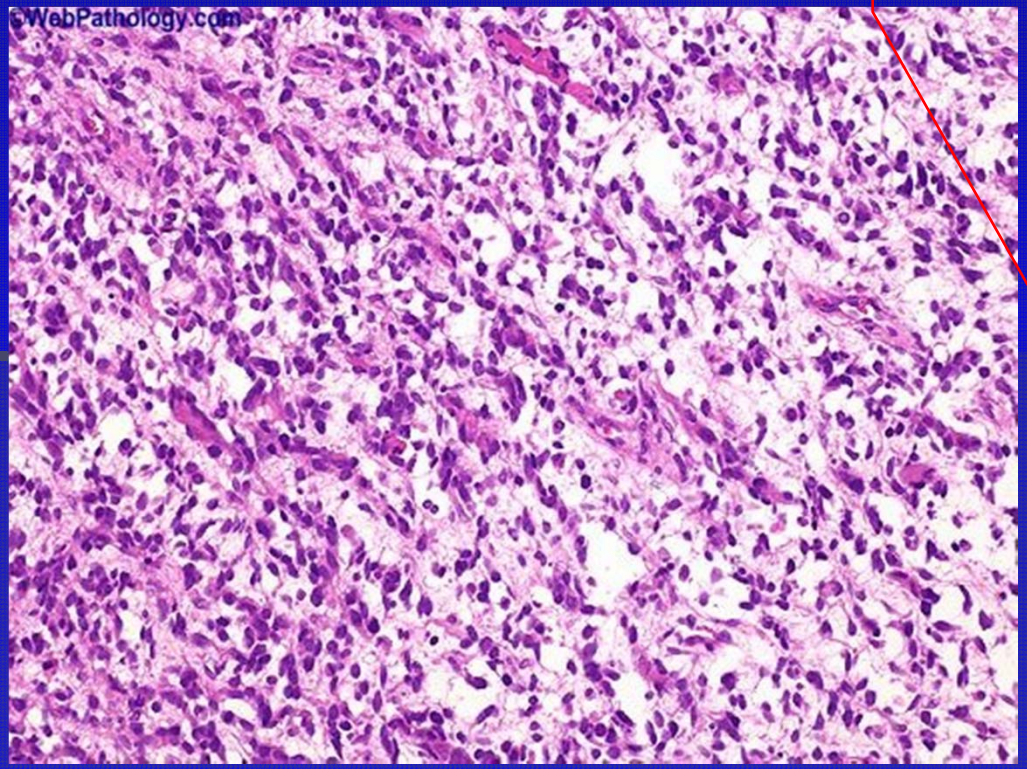
Rhabdomyosarcoma

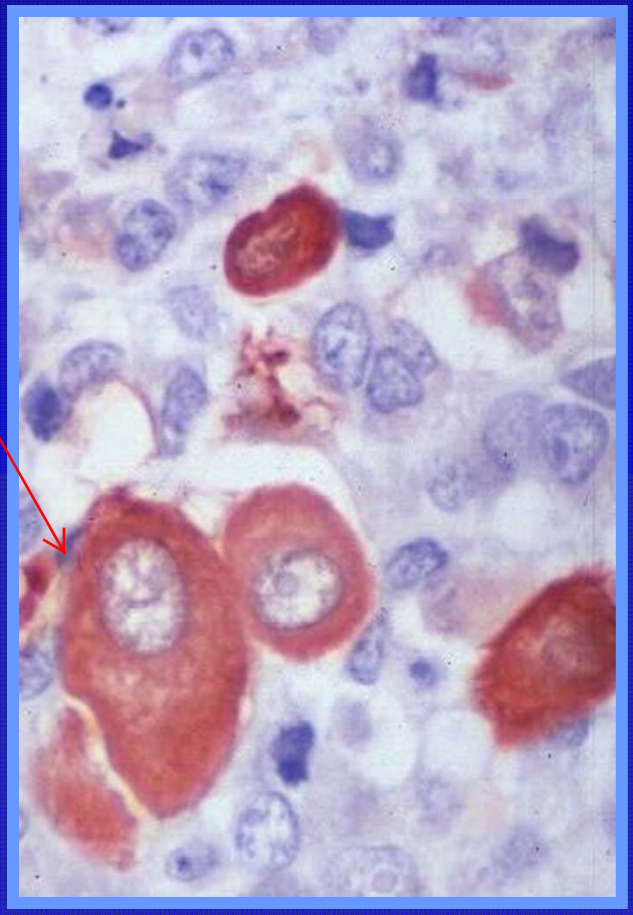
- Key to Dx is recognition of rhabdomyoblast

also contains a translocation, but not a big part of dx yet.

Fortunately this tumor responds very well to chemotherapy.

rhabdomyoblast: key to diagnosis

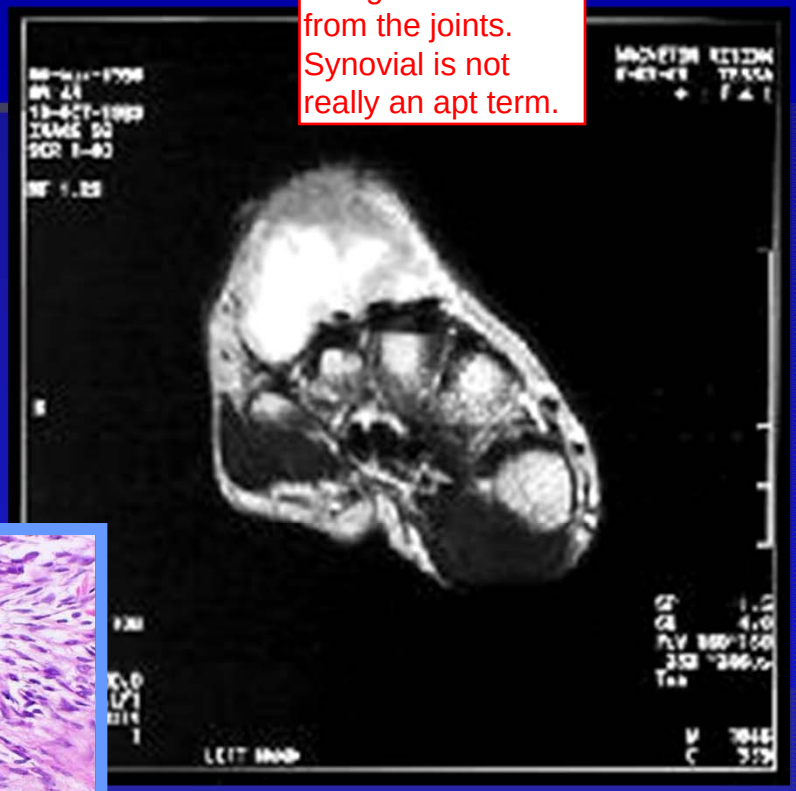


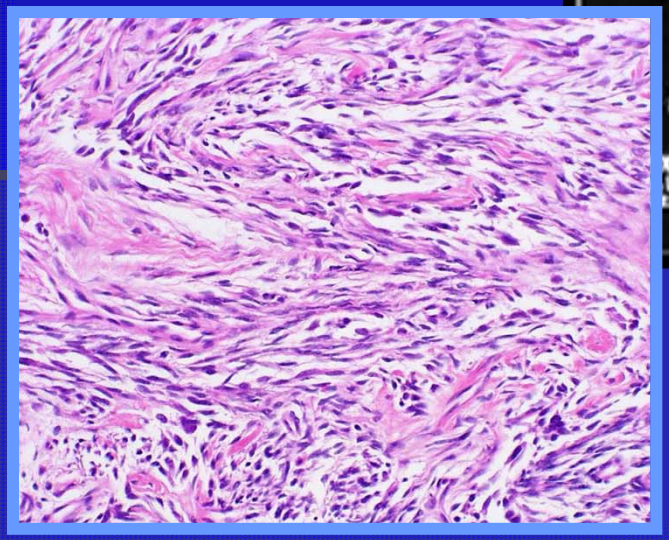


Synovial sarcoma

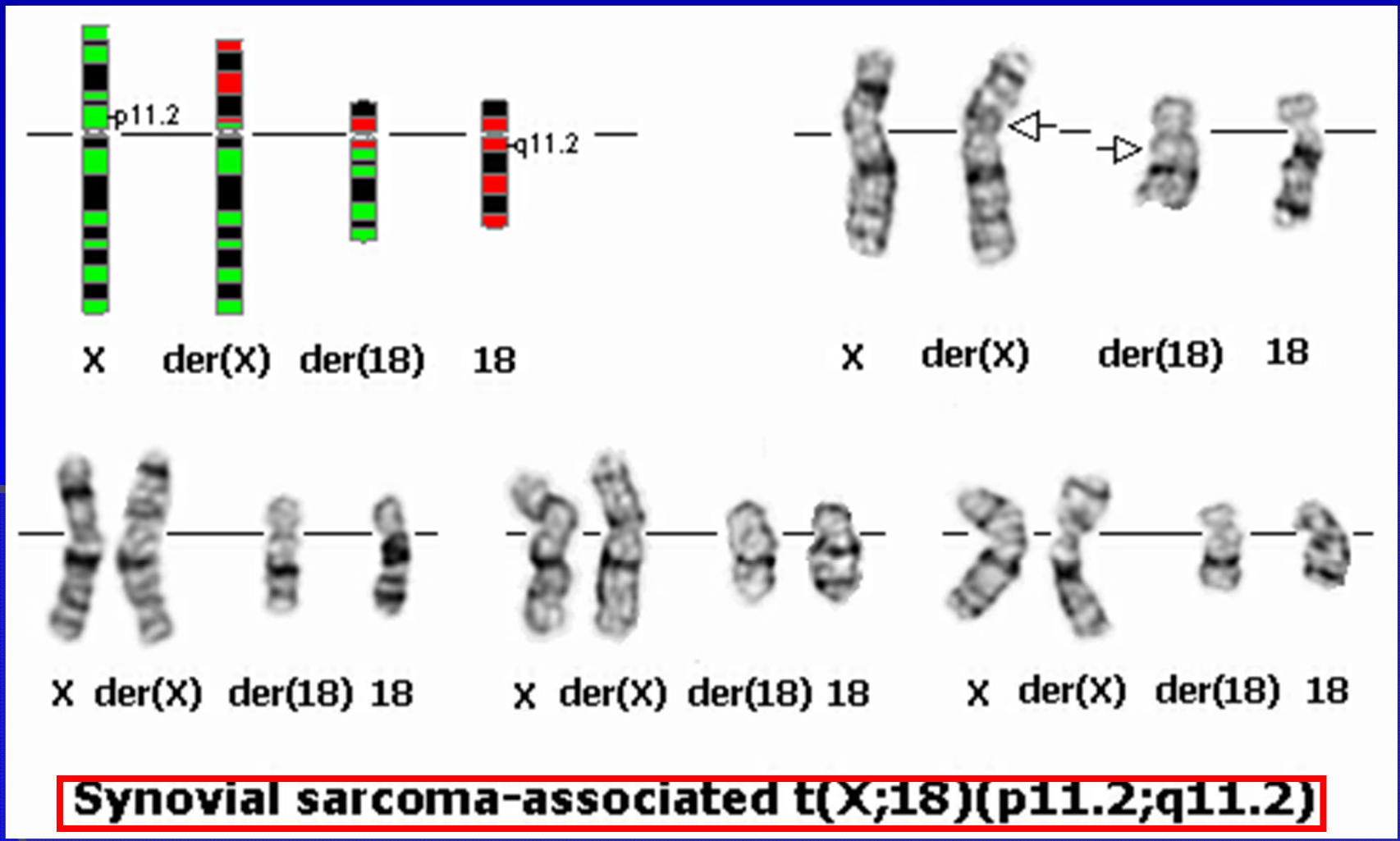
common soft tissue tumor that affects children/young adults.
Called synovial sarcoma because it was originally thought to evolve from the joints. Synovial is not really an apt term.

- Commonly arises near joints/extremities
- Histologically bi-phasic
- t(X;18)

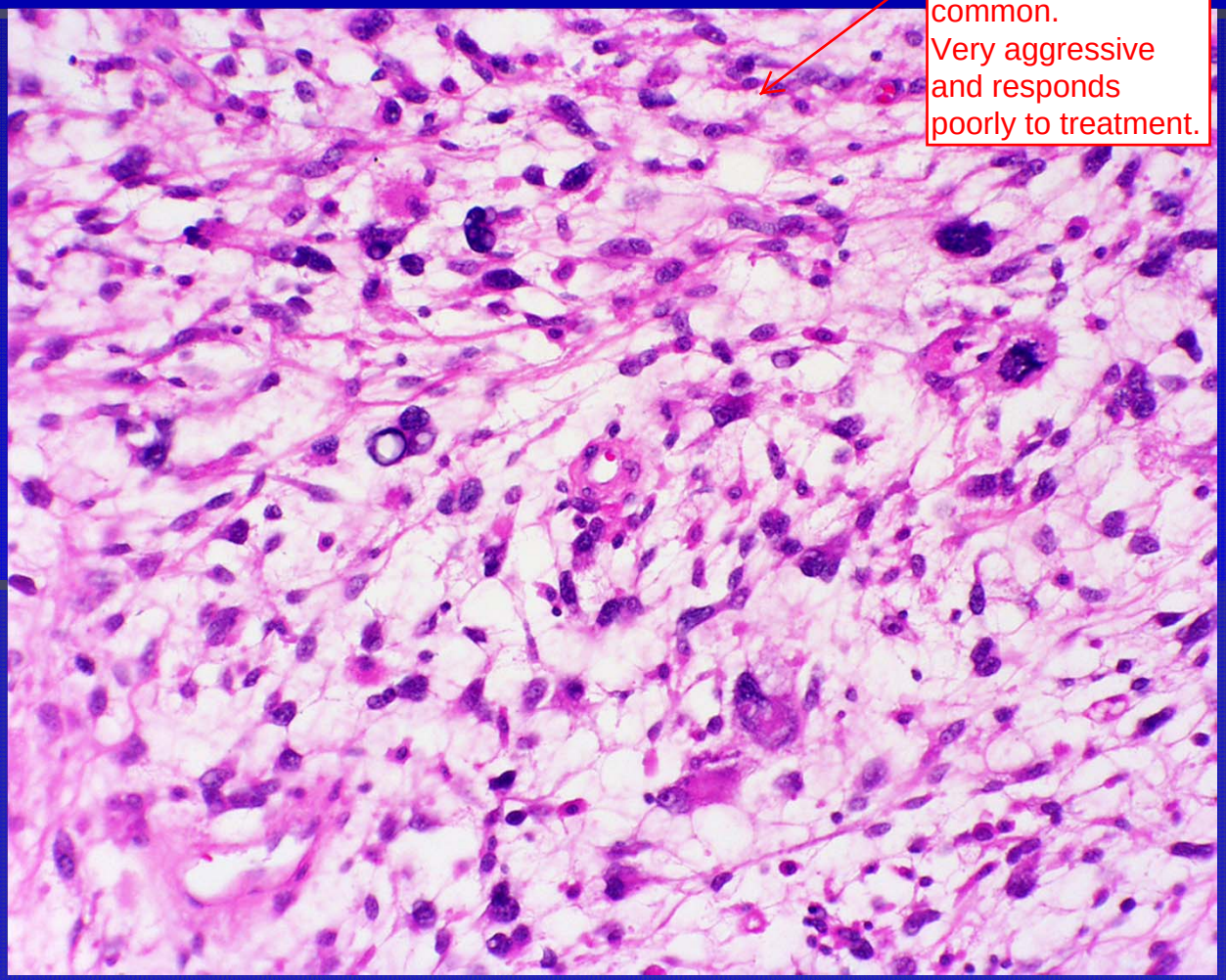




Chromosomal abnormalities in Soft tissue sarcoma



Malignant fibrous histiocytoma



High-grade undifferentiated sarcoma.
Relatively more common.
Very aggressive and responds poorly to treatment.