Lecture 19

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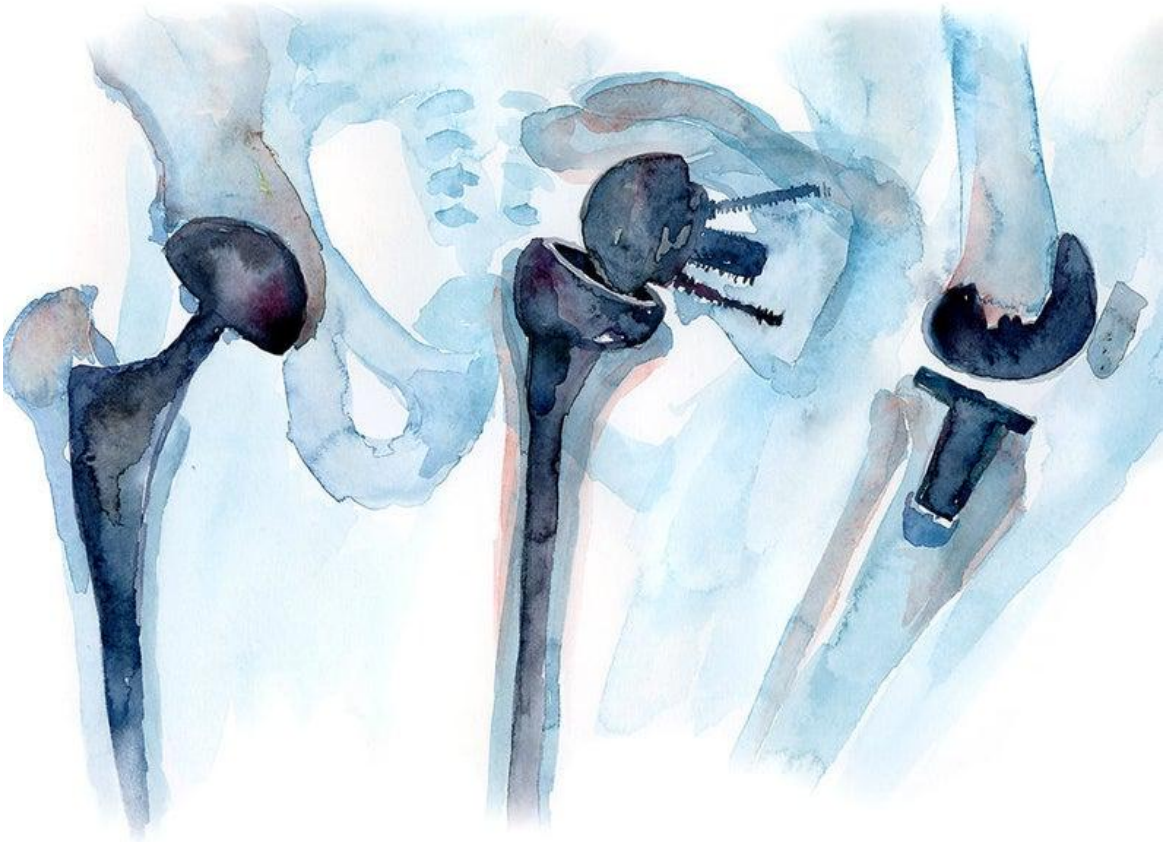


# MSK Tumors

Dr. Ibrahim Alshaygy

## Objectives:

- To be able to specify the symptoms and signs; outline the assessment and appropriate investigations; propose a limited differential diagnoses and; outline the principles of management of a patient with:
  - Metastatic bone disease
  - Primary bone lesions
  - Benign bone tumor: Osteoid osteoma, Bone Cysts (Unicameral bone cyst (UBC), Aneurysmal bone cyst (ABC) and Osteochondroma
  - Malignant tumors: Osteosarcoma and Ewing's Sarcoma
- Discuss presenting history and physical examination features of bone tumours
- Discuss imaging characteristics of bone tumours
- Discuss biopsy principles and techniques for biopsy.

## Color Index:

Original text | Doctor's notes | Text book
Important | Golden notes | Extra

# MSK Bone Tumors:

## Classification of bone tumors

- **Benign** [1]
- **Malignant** [2]
  - **Primary**
  - **Secondary**
    Malignant transformation of benign process
  - **Metastatic**

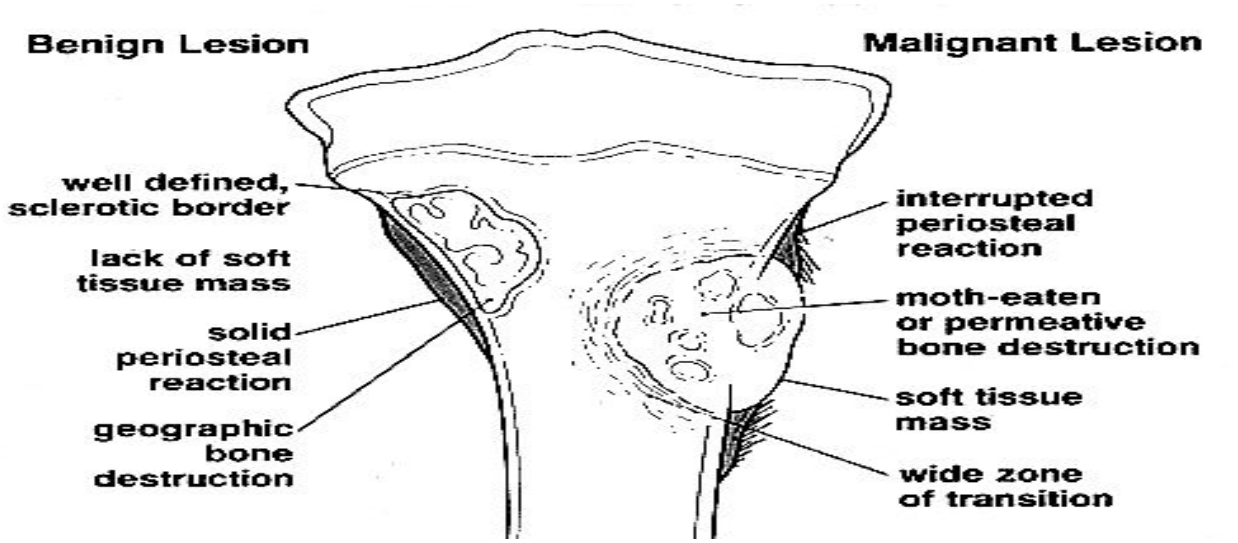



**Table 25. Distinguishing Benign from Malignant Bone Lesions on X-Ray**

| Benign | Malignant |
|---|---|
| No periosteal reaction or benign appearing reaction (e.g. uniform smooth periosteal thickening as seen in a healing fracture) | Acute periosteal reaction<br>• Codman's triangle<br>• "Onion skin"<br>• "Sunburst" |
| Sharp, well-demarcated borders, narrow zone of transition (between lesion and normal bone, suggesting slow-growing lesion) | Poorly defined borders, with a wide zone of transition, or infiltrative (suggesting fast-growing lesion) |
| Well-developed bone formation<br>Intraosseous and even calcification | Varied bone formation<br>Extraosseous and irregular calcification |
| No soft tissue mass | Soft tissue mass present |
| No cortical destruction or uniform cortical destruction in some low grade and locally aggressive benign lesions | Aggressive cortical destruction or tumour infiltration without cortical destruction |

Adapted from: Buckholtz RW, Heckman JD. Rockwood and Green's Fractures in Adults. Volume 1. Philadelphia: Lippincott Williams & Wilkins, 2001. p558

1-Most bone tumors are benign. Common in pediatrics.
2-Most malignant tumors are metastatic. Primary is very rare.

# MSK Bone Tumors:

| Classification of Tumors and Tumor Like Lesions by Tissue of Origin | | |
|---|---|---|
| **Histologic type** | **Benign** | **Malignant** |
| **Bone marrow Hematopoietic and lymphatic** | Giant cell tumor (osteoclastoma), Eosinophilic granuloma, Lymphangioma | Myeloma (plasmacytoma), Malignant giant cell tumor, Histiocytic lymphoma, Ewing's sarcoma, Leukemia |
| **Cartilage-forming Chondrogenic** | Enchondroma (chondroma), Periosteal (juxtacortical) chondroma, Enchondromatosis (Oiller's disease), Osteochondroma (osteocartilaginous exostosis, single or multiple) Chondroblastoma, Chondromyxoid fibroma | Chondrosarcoma (central), Conventional, Mesenchymal, Clear cell, Dedifferentiated, Chondrosarcoma (peripheral), Periosteal (juxtacortical) |
| **Bone-forming Osteogenic** | Osteoma, Osteoid osteoma, Osteoblastoma | Osteosarcoma (and variants), Juxtacortical osteosarcoma (and variants) |
| **Histiocytic origin** | Fibrous histiocytoma | Malignant fibrous histiocytoma |
| **Fibrous and fibrohistiocytic Fibrogenic** | Fibrous cortical defect (metaphyseal fibrous defect), Nonossifying fibroma, Benign fibrous histiocytoma, Fibrous dysplasia (mono- and _polyostotic), Periosteal desmoid, Desmoplastic fibroma, Osteofibrous dysplasia (Kempson-Campanacci lesion), Ossifying fibroma (Sissons' lesion) | Fibrosarcoma, Malignant fibrous histiocytoma |
| **Neural Neurogenic** | Neurofibroma | Malignant schwannoma |
| **Vascular** | Hemangioma, Glomus tumor, Cystic angiomatosis | Hemangioendothelioma, angiosarcoma, Hemangiopericytoma |
| **Fat Lipogenic** | Lipoma | Liposarcoma |
| **Notochordal** | Neurilemmoma | Chordoma |
| **Unknown origin** | Simple bone cyst, aneurysmal bone cyst, Intraosseous ganglion | Adamantinoma |

★ **The diagnosis of tumors is made by History, physical examination, and investigations.**

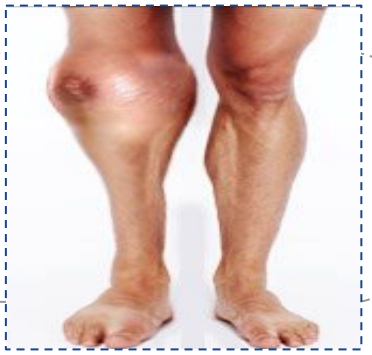
## History

**Key History Questions:**

- Onset of pain - traumatic vs. atraumatic
- Progressive pain
- Night pain, rest pain
- Relieving factors ( NSAIDS)
- Family history
- History of radiation, Paget's disease, other cancers, systemic diseases
- Constitutional symptoms (Weight loss, fever, night sweat, loss of appetite). not the primary presentation, as they present late (metastasis)
- DDx of any tumor is infection

## Clinical Features

1. Pain
2. Mass
3. Pathologic Fracture
4. Incidental finding on x-ray



## Physical Examination

**Lump** → 2Ts = tenderness, temperature, **3Ss = Site, size & shape.**

- Mass: fixed vs. mobile; [1]
  - ➔ Deep to fascia or superficial
  - ➔ Contract muscle group underneath – if deep to fascia then it becomes more fixed
- Estimate size of mass
- Lymphadenopathy
- Neurovascular examination

## Investigations

- **Lab**: CBC (infection or anemia), ESR, hematological investigations
- **Imaging**:
  1. Local: X-ray, MRI, CT.
  2. Systemic: chest CT, Bone scan.
- Biopsy: biopsy should be done by who will do the definitive surgery, ideally orthopedic oncologist or interventional radiologist who works with the orthopedic oncologist

1-

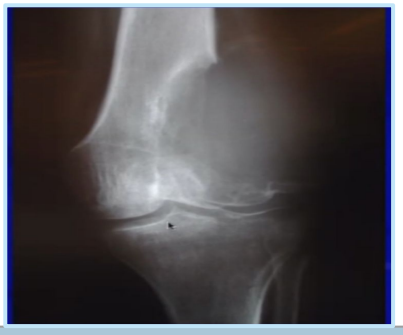
- Contraction and relaxation makes the mass fixed = fixed to the deep fascia
- Contraction fixes the mass while its mobile upon relaxation = mobile mass in the deep fascia
- Mass is mobile in both contraction and relaxation = mobile in the superficial fascia

# MSK Bone Tumors :

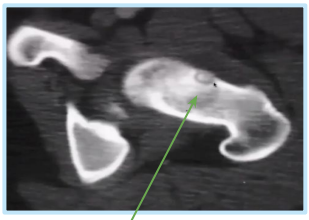
## Nine questions of Tumor Staging

### 1- Where is the lesion?

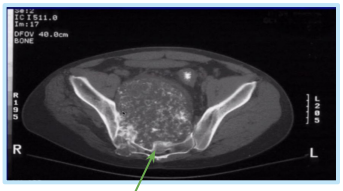
- Epiphyseal, metaphyseal, diaphyseal.
- Surface.
- Periarticular.
- Central or eccentric.
- A tumor in the epiphyseal, metaphyseal area - eccentric - periarticular- with cortical erosion - no periosteal reaction
- There is also a pathological fracture



### 2- How big is the lesion

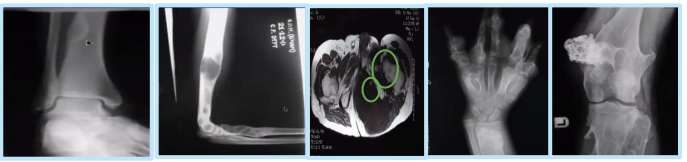


Neck lesion 1x0.5 cm



15x8 cm

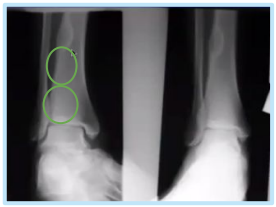
### 3-Is it solitary or multifocal?



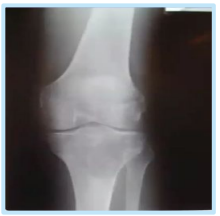
Solitary

Multifocal

### 4-What is the interface between the bone and the lesion? Sclerotic or Lytic or Mixed



Good demarcated sclerotic lesion



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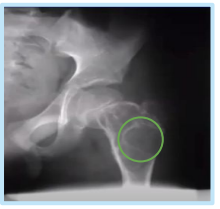
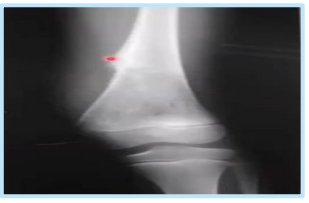
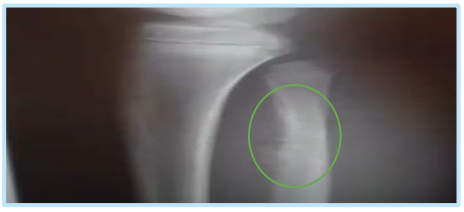


Well defined



Ill defined
Periosteal reaction (codman triangle) = bone try to form periosteal but مايلحق

### 5- Is there a periosteal reaction?

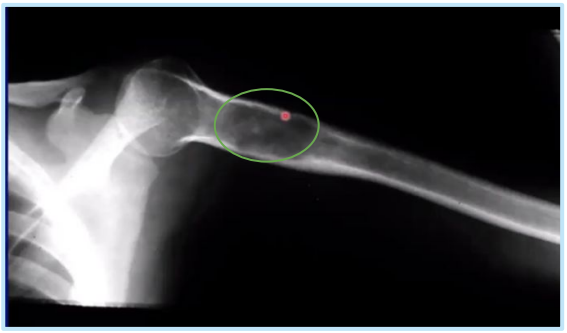


Sunburst usually in Ewing Sarcoma

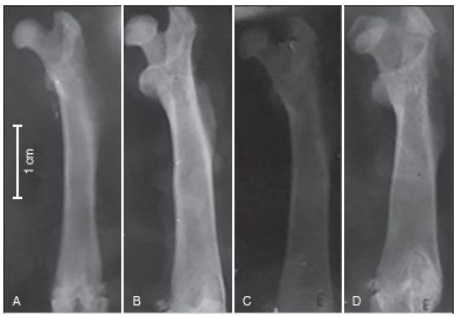
Codman triangle
(Commonly with osteosarcoma)

## Nine questions of Tumor Staging

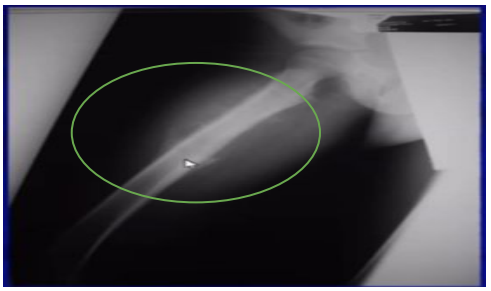
### 6- Is the cortex eroded?

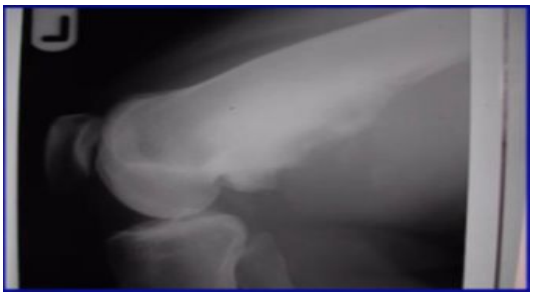


### 7-Is there bony remodeling?



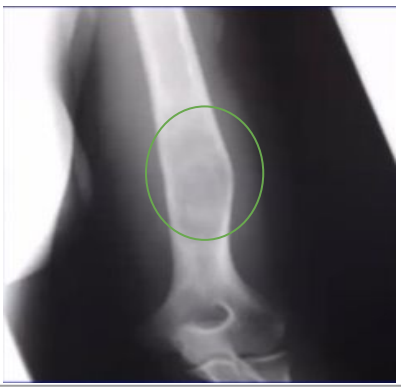
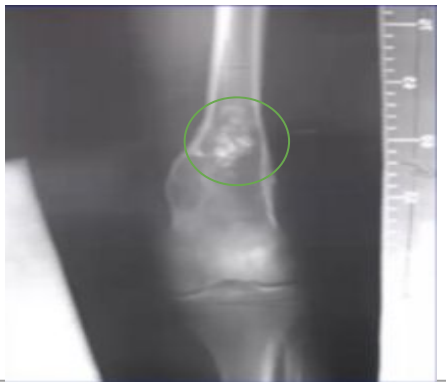
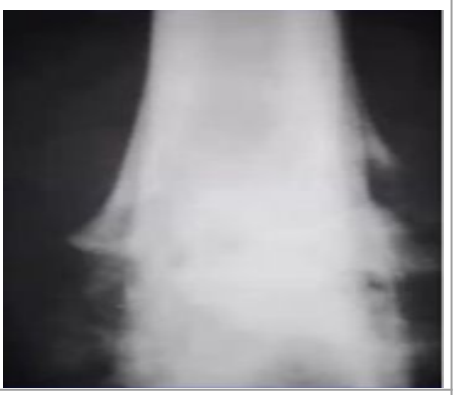

### 8-Is there a soft tissue mass?





Like codman triangle

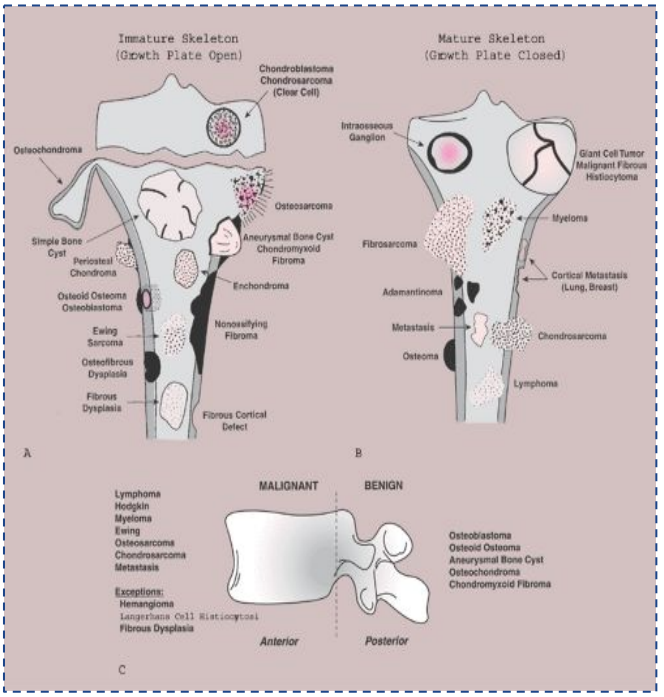
### 9- Is the cortex eroded?

| Types | Fibrous | Cartilaginous | Osseous bone |
|---|---|---|---|
| Picture |  |  |  |
| Features | Fibrous : ground glass | Cartilage : popcorn like appeaerance | Bone forming |

# X-Ray lesion description should include:

## 1 Number

- Is the lesion solitary or are there multiple lesions? [1]




## 2 Site

What bone is involved & where is the lesion in the bone?

1. Epiphysis,
2. Metaphysis (most common)
3. Diaphysis.
4. Centric (in the middle of the bone)
5. Eccentric (in the bone border)

Distribution of various lesions in a vertebra:

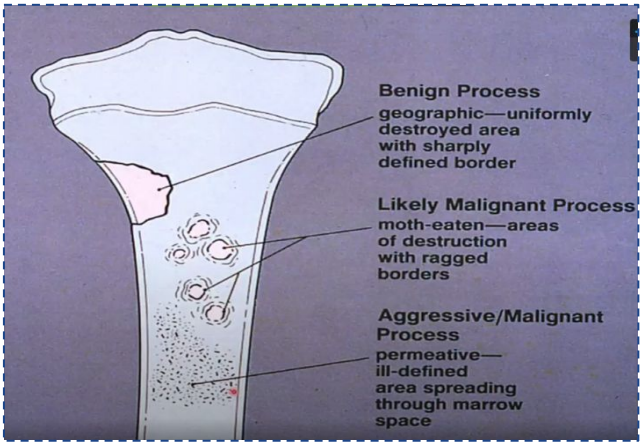
1- Malignant lesions are seen predominantly in its anterior part (body).

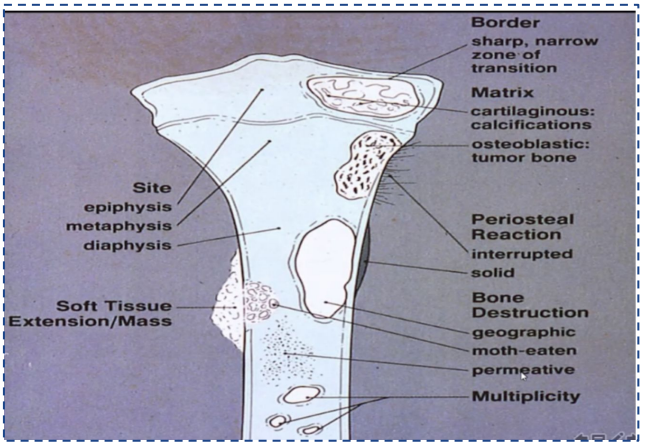
"Most likely" exceptions: hemangioma, Langerhans cells, fibrous dysplasia.

2- Benign lesions predominate in its posterior elements.

## 3 Types of bone destruction (morphology:Most important)

1. Geographic (Organized uniformly destroyed area with sharply defined border): benign.
2. Moth eaten كأنها ماكلتها العثة(areas of destruction with ragged/disorganized border): likely malignant.
3. Permeative "همجية" (ill-defined areas spreading through bone marrow): aggressive/malignant.




1- DDx for Multiplicity: metastases, myeloma, lymphoma, fibrous dysplasia, enchondromatosis

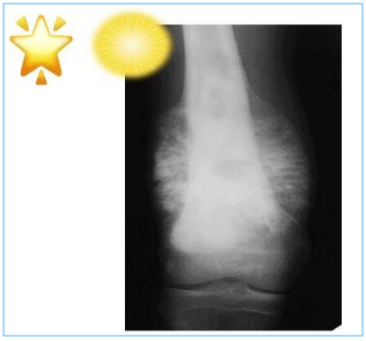
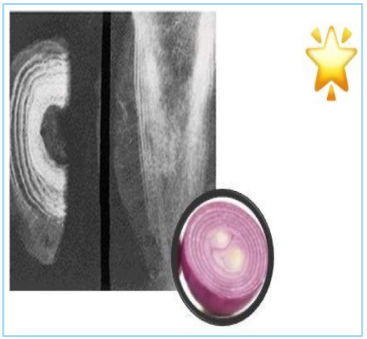
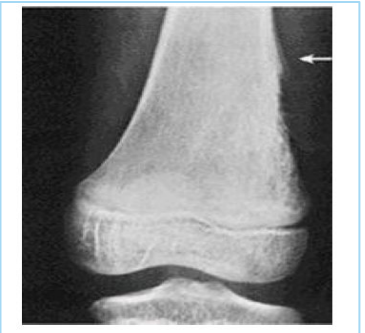
## 4 Border of the tumor or zone of transition:

A Well defined & sharp borders (either sharp sclerotic or sharp lytic), narrow zone of transition → benign (grow slowly > encapsulate by bone).

B Ill-defined borders, wide zone of transition → malignant tumors (fast, the bone didn't have the time to encapsulate it).

## 5 Periosteal reaction

- Uninterrupted periosteal reaction usually indicates a benign process (solid clear buttress).
- Interrupted / large (teeth like) reaction indicates a malignant or aggressive nonmalignant process:

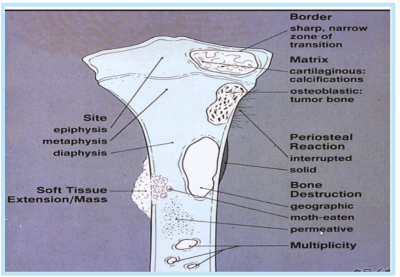
| Sunburst pattern[1] in osteosarcoma and in Ewing Sarcoma | Lamellated or onion-skin type in Ewing Sarcoma | Codman triangle (arrow) in Ewing Sarcoma and usually appears in Osteosarcoma |
|---|---|---|
|  |  |  |

## 6 Matrix of the tumor

- **Sclerotic**: it means bone forming (osseous). So, on X-ray → opaque/white.
- **Lytic**: it means forming tissue other than bone "fluid" (it may be cartilage, fibrous tissue, or cystic), on X-ray → translucent/ black (e.g. popcorn calcification = chondroid).

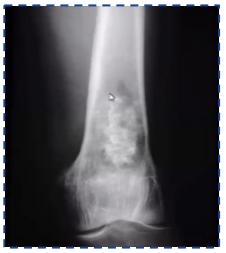
## 7 Soft tissue extension(swelling/shadow

- Mostly with malignant tumors (MRI is ideally used) .




1-when the periosteum does not have enough time to lay down a new layer and instead the Sharpey's fibres stretch perpendicular to the periosteum

# The Spectrum :

| Types | characteristics |
|---|---|
| **Benign latent** | • Asymptomatic<br>• Well defined<br>• Narrow zone of transition (geographic)<br>• No soft tissue mass<br>• No periosteal reaction<br>• No fracture<br>• May or may not have matrix<br>• eg's- enchondroma, non-ossifying fibroma |
| **Benign Active** | • **Symptomatic**<br>• Geographic<br>• Well-ordered periosteal reaction<br>• No soft tissue mass<br>• May or may not have matrix<br>• eg's - osteoid osteoma, UBC, eosinophilic granuloma, fibrous dysplasia, osteochondroma |
| **Benign Aggressive** | • Symptomatic<br>• Geographic or permeative<br>• Usually lytic, cortical erosion<br>• May have soft tissue mass<br>• Periosteal neocorticalization<br>• eg's-GCT, ABC, osteoblastoma, chondroblastoma, chondromyxoid fibroma, periosteal chondroma |
| **Low Grade Malignant** | • Usually permeative<br>• May have matrix<br>• Cortical erosion<br>• May have soft tissue mass in continuity with cortical erosion.<br>• Low-grade CSA, Adamantinoma, Parosteal OSA, Chordoma<br>• Image shows suspicious lytic lesions with popcorn like matrix<br>  |
| **High Grade Malignant** | • Permeative<br>• Usually has soft tissue mass<br>• Cortex usually intact (tumor penetrates the cortex)<br>• Malignant periosteal reaction (onion skinning, sunburst, codman's triangle)<br>• May or may not have matrix<br>• Osteosarcoma, Ewing's sarcoma, high grade chondrosarcoma, non-osteogenic spindle cell sarcoma (eg. MFH) |

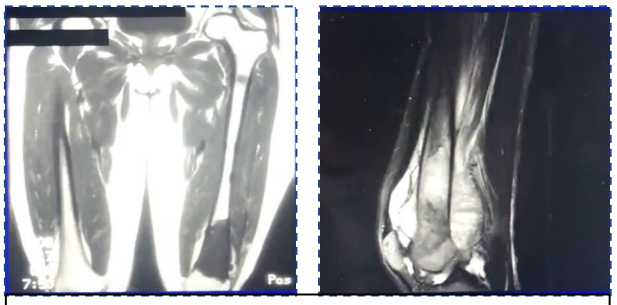
# What is Next? Staging

## What's next?

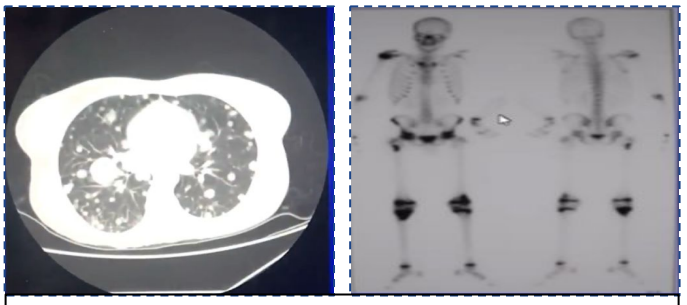
- If lesion is **benign** latent, no further investigation is usually necessary, may follow up after 6m.
- If **benign active or aggressive**, requires further local imaging, perhaps systemic staging.
- If **malignant**, requires further investigation including local and systemic staging.

## Local and Systemic Staging

- Blood Work – CBC, ESR, CRP, serum calcium, **Alkaline phosphatase , LDH (latter 2 are prognostic in sarcoma)**
- **Local x-ray =** whole bone, chest x-ray (To rule out lung metastasis)
- MRI of local site: must cover entire bone (full length MRI) may find lesions in proximal which is called skip lesions (occasionally CT = if there is soft tissue)
- CT chest to rule out metastasis.
- Total body bone scan for other lesions.
- For Ewing sarcoma we should order a gallium scan
- ★ We should take a bone marrow aspiration for lymphoma, ewing sarcoma and MM



Skip lesions (Full length MRI )



Systematic staging

## What if it's metastatic?

>40 = metastasis | <40 = primary tumor

- Bloodwork – same bloodwork plus PSA prostate surface antigen, serum immunoelectrophoresis (in case of lymphoma and multiple myeloma for M band)
- CT chest and abdomen to look for the source
- Mammogram
- Bone scan other area are involved

## How to stage tumors?

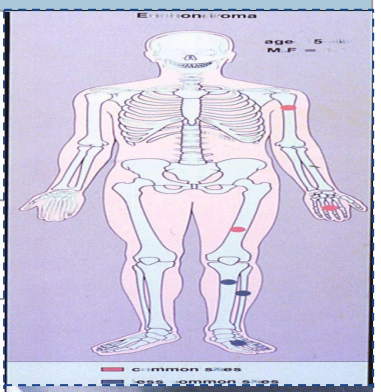
- Benign Latent/Active: Local - X ray +/- CT/MRI +/- TBBS = total body bone scan.
- Benign Aggressive: Local - X Ray/CT/MRI /Systemic - TBBS, CXR.
- Malignant: Systemic - CT Chest (<40) and bone scan , TBBS.
- Special: Gallium scan, CT Abd + Pelvis, Bone marrow biopsy.

# Primary Benign Bone Tumors:

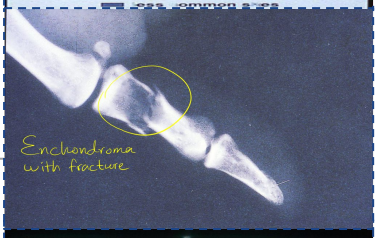
## Benign Latent Tumors

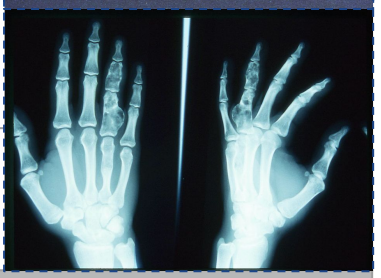
### (1) Enchondroma

- Middle aged patients (15-50 age group)
- It is composed of translucent hyaline cartilage (chondroid)
- **Mostly found in the fingers**



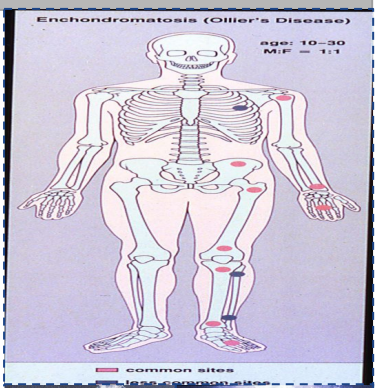
| | |
|---|---|
| Site | Mainly small bone e.g. phalanges in hand & foot...etc. |
| Presentation | • **Asymptomatic**: Usually found incidentally<br>• Rings may become tight due to the swelling<br>• Pathological fracture which may cause pain, affect one side and prolonged healing |
| Radiographic features | • **Popcorn matrix is characteristic for cartilaginous content**<br>• Benign features<br>• Can be seen on CT |
| Treatment | • If symptomatic (pain, bulky, fracture)<br>→ Curettage + bone graft ± fixation |



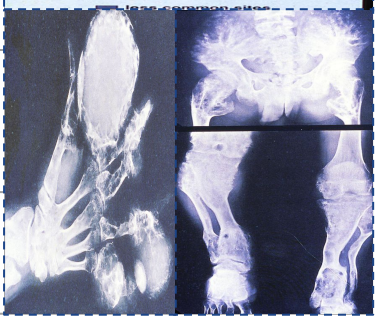



### Enchondromatosis (Ollier's Disease)

- Multiple sites of enchondroma in the body most common sites are proximal humerus/tibia , which are premalignant.
- Autosomal recessive
- Benign, **affects both sides,** Usually seen in children. Rare.
- The <u>difference</u> between single enchondroma and multiple enchondromatosis is the <u>high risk of malignant transformation</u> (10-15% transforms into **chondrosarcoma,** which is chemo- and radio- resistant).



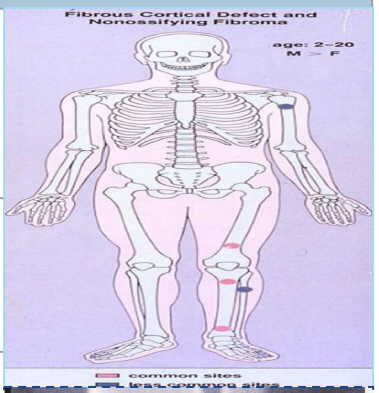

| | |
|---|---|
| Presentation | • Not painful<br>• Very disabling deformity → restricts movement |
| Treatment | • Only remove painful lesions |

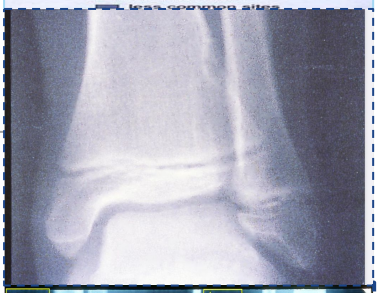


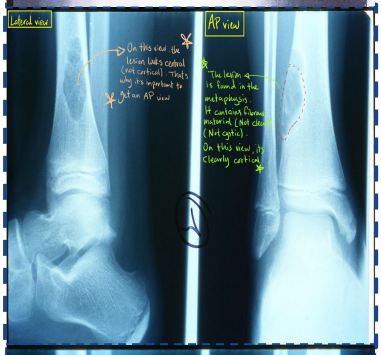
# Primary Benign Bone Tumors:

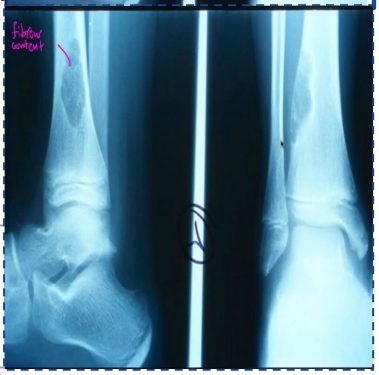
## (2) Fibrous Cortical Defect and Non-ossifying Fibroma

- A benign incidental finding, it is benign latent (never transfers to malignant)
- Found in children and it's usually an incidental finding






| | |
|---|---|
| Site | • Around the knee (lower femur and proximal tibia)<br>• Lower tibia<br>• May appear on proximal humerus |
| Presentation | • **Asymptomatic** |
| Radiographic features | • On x-ray, always found on the cortex (eccentric). Contains fibers and not clear material (ground glass appearance)<br>• **FIBROUS COMPONENT!!!**<br>• Metaphyseal Mixed lesion (cystic + sclerotic components)<br>• Lesion that appears to be 'central' is actually adjacent to or within the cortex, cortex intact, hence the alternative name 'fibrous cortical defect'.<br>• Benign features: No periosteal reaction, No Soft tissue swelling<br>• Well-defined, sclerotic margin.<br><br>X ray description: (bottom image)<br>- X ray of a child, growth palate is seen.<br>- Cloud shaped ,defect in the metaphyseal area, geographic shape and fibrous material.<br>- This xray shouldn't be worrisome and could be observed with no Tx. |
| Treatment | • **Self-limited (Reassurance)**<br>• If large or fractured → curettage + bone graft |

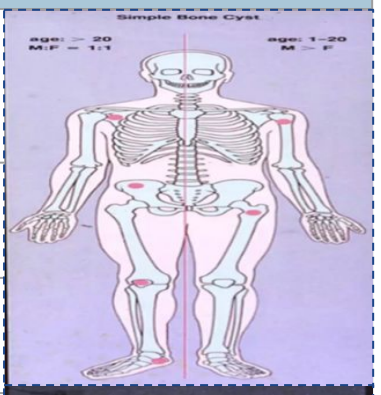
*We are not half-way done*

# Primary Benign Bone Tumors:

## Benign Active Tumors

### (1) Simple Cyst or Unicameral Bone Cyst (UBC)

- A common benign tumor, it is benign latent except if it ruptures
- Usually seen in young patients.
- Less than 20 year olds

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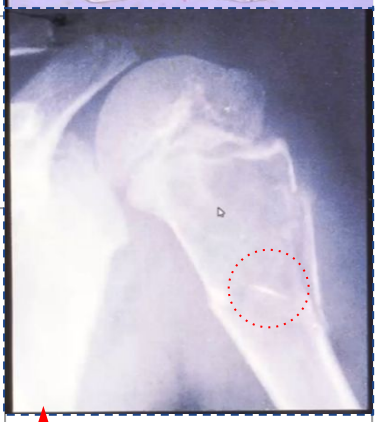
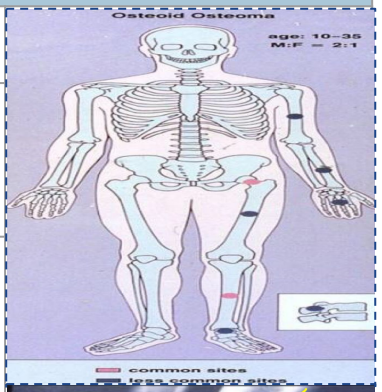
|---|---|
| Site | • Pelvis, calcaneus, scapula and around the knee<br>• Proximal part of long bones (e.g. proximal humerus, femur...) |
| Presentation | • Most commonly as incidental finding (asymptomatic) or pathological fracture |
| Radiographic features | • **Metaphysic lytic lesion** (it contains fluid like suntop juice)<br>• Well defined sharp border<br>• No periosteal reaction<br>• Fallen leaf sign indicates intra-cystic fracture |
| Treatment | • Observation unless there's a stress fracture<br>• Often supportive, lesions will regress following skeletal maturity<br>• Curettage and bone grafting may be required in areas at risk of fracture |



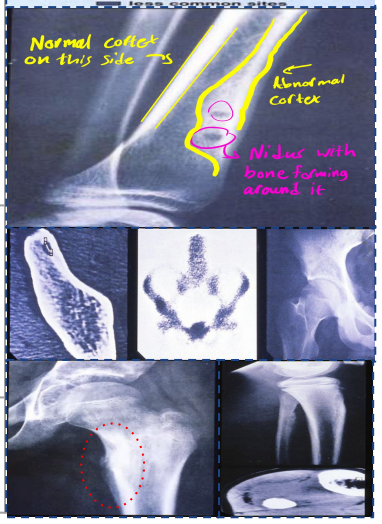
★ Fallen Leaf Sign

### (2) Osteoid Osteoma

- Bone forming bone



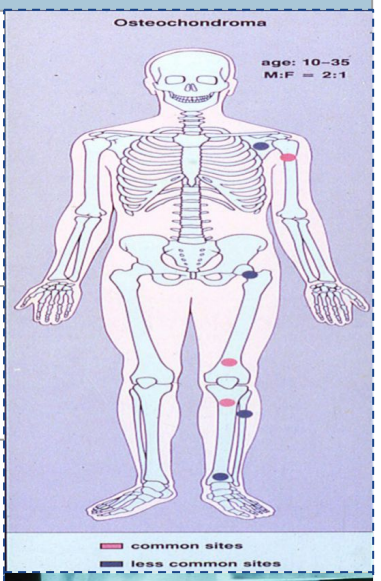

| | |
|---|---|
| Site | • Found in the diaphysis and neck of the femur, tibia, humerus and posterior element of the spine<br>• May arise in the cortex of long bones and rarely in the talus |
| Presentation | • Main presentation with **pain**<br>• Well localized pain (in the back or groin area)<br>• Worse at night and <u>prevents patient from sleep.</u><br>➔ Because of prostaglandin release.<br>• Responds well to NSAIDs, leading to complete resolution<br>• Painful scoliosis if affecting the spine. While idiopathic scoliosis is painless.<br>• Nothing on physical exam |
| Radiographic features | • Lytic lesion (central nidus), surrounded by a reactive zone of dense sclerotic new bone formation<br>• Fine cut CT scan → nidus (modality of choice)<br>• Cortical thickening on X ray |
| Treatment | • NSAIDs challenge (aspirin)<br>• **Radiofrequency ablation** |



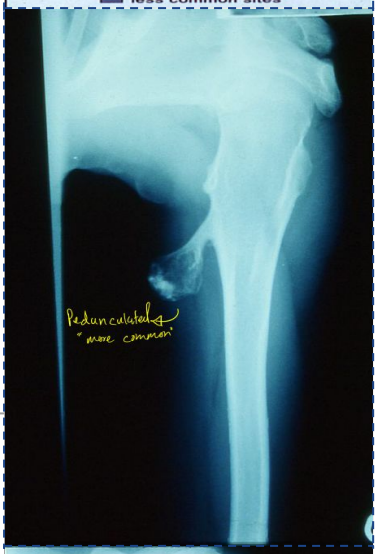
# Primary Benign Bone Tumors:

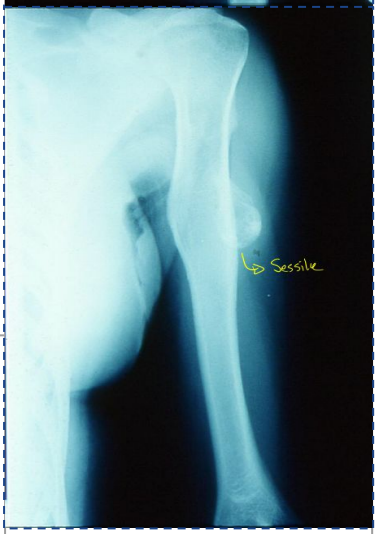
## (3) Osteochondroma

- Exostosis
- The only surface tumor (outside the bone)
- It is a combination of both bone & cartilage.
- Starts from the growth plate and Stops growing when patient stops to grow usually at 18 yrs
- > 2 cm masses have a risk of malignant transformation




| | |
|---|---|
| Site | • The commonest are around the knee (**distal femur** & proximal tibia)<br>• Proximal humerus, scapula and neck of femur |
| Presentation | • Patients usually present for cosmetic purposes or pain<br>• Painless progressive swelling<br>• Painful in children due to growth plate compression and pressure effects<br>• On adjacent nerve or vascular structures (obese patients won't notice it)<br>Complications:<br>1. Pressure symptoms:<br>- Pseudoaneurysm → artery<br>- Hypoesthesia/ paresthesia → nerve<br>- Limited ROM → tendon<br>- Formation of an overlying bursa due to friction<br>2. Fractures especially in the pedunculated type |
| Radiographic features | • Exostosis (fungated): mushroom-like stalk of the bony tumor (connected to the bone)<br>• Benign features.<br>• Metaphyseal lesion.<br>• MRI: cartilaginous cap<br>• **A distinctive feature is the continuity of the medullary canal content with tumor**<br>• According to the shape of the neck, we divide it into:<br>A. **Pedunculated type** (more common): long & thin neck. Directed away from the bone.<br>B. **Sessile type**: has short & thick neck. |
| Treatment | • We usually resect the lesion even if it's benign<br>• Surgery is indicated for: **(NEVER for cosmetic reasons)**<br>1. If the lesion is obstructing a nerve, vessel or tendon.<br>2. If the lesion limits movement.<br>3. If the lesion is quickly increasing in size |



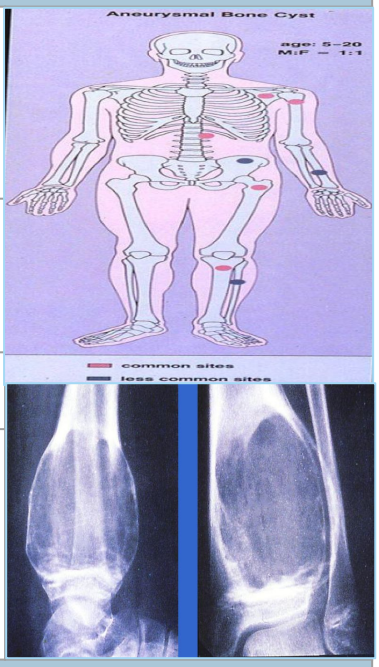



# Primary Benign Bone Tumors:

## Benign Aggressive Tumors

### (1) Aneurysmal Bone Cyst (ABC)

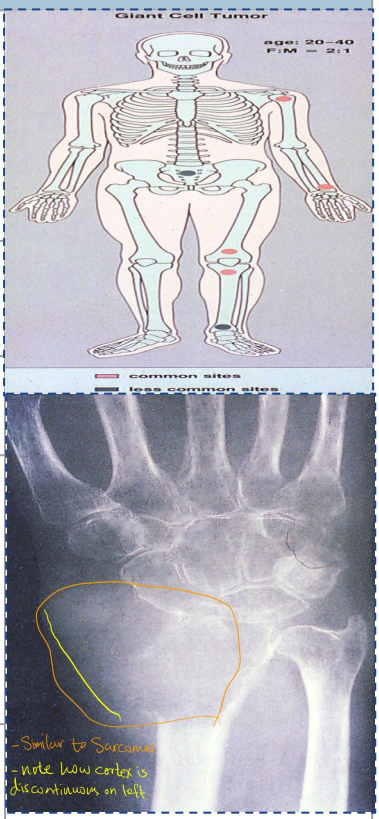
- They can recur and may transfer to osteosarcoma
- Blood-filled cystic spaces, bigger than simple cysts
- Simple cyst is not wider than the growth plate and has fallen leaf sign, aneurysm bone cyst is wider than growth plate




| | |
|---|---|
| Site | • Around joints: upper humerus, femur, and tibia<br>• Spine (neural arch: lamina and pedicle)<br>• Flat bones: scapula and pelvis |
| Presentation | • Asymptomatic |
| Radiographic features | • **Balloon like lesion** no periosteal and soft tissue swelling<br>• Metaphyseal, septated lytic lesion<br>• Well defined and sclerotic border<br>• Expansile with thinned cortex (egg-shell) →<br>• MRI shows fluid fluid level |

### (2) Giant Cell Tumor (GCT) very high recurrence rate (18%)

- Benign but very aggressive tumor (most aggressive benign one)
- The only benign that can metastasize (to the lung → get chest x-ray)
- GCTs can occasionally be seen with Paget's disease of bone and can arise in association with focal dermal hypoplasia (Goltz syndrome).
- In middle age group, In 20-40 years

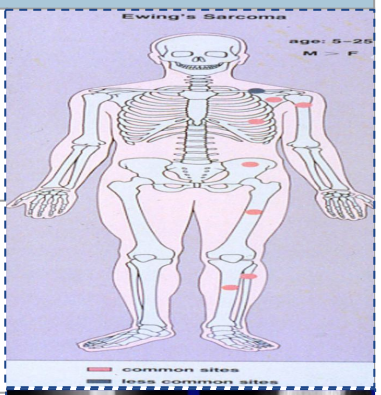


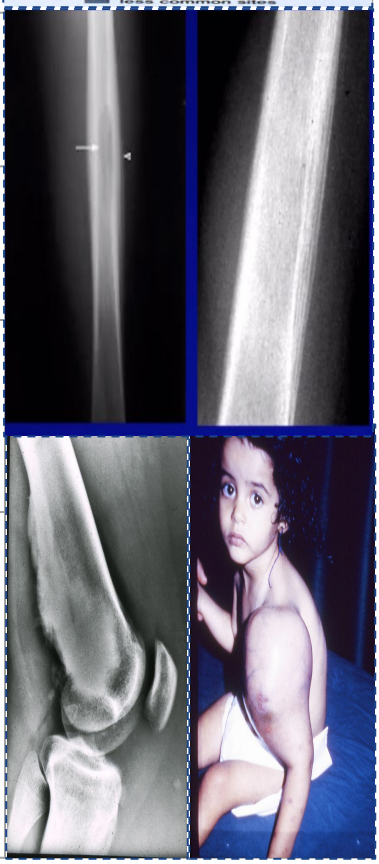

AP x-ray with a lesion on metaphysis or epiphysis with involvement of soft tissue with cortical destruction

Either aggressive benign or malignant.

| | |
|---|---|
| Site | • Proximal humerus, distal femur, proximal tibia (juxta articular)<br>• Most common: distal radius |
| Presentation | • Presents with: pain, swelling & later pathological fracture |
| Radiographic features | • Aggressive features:<br>- Permeative destruction<br>- Ill defined borders<br>- Huge soft tissue component<br>• No new bone formation because this tumor is made up of osteoclasts (little or no periosteal reaction) |
| Investigation | • Soft tissue extension → MRI<br>• Joint extension: the articular surface prevents extension<br>• Bone extension → CT scan<br>• Bone scan → metastasis<br>• Biopsy → rule out malignant transformation |
| Treatment | • No place for conservative treatment.<br>• Excision (Curettage) followed by either bone graft or prosthesis depending on the site of the tumor. |

# Primary Malignant Bone Tumors:

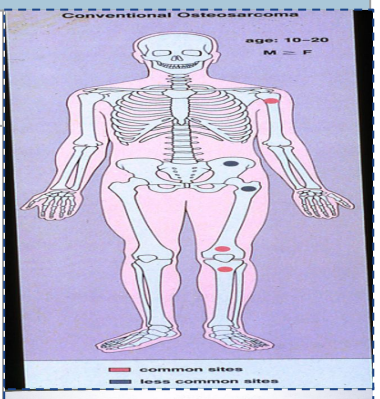
| Malignant Tumors | |
|---|---|
| **(1) Ewing Sarcoma** | |
| • **One** of the most common tumors in **children** (3-5y)<br>• Most Ewing's sarcomas are misdiagnosed as acute osteomyelitis because of systemic symptoms, elevated ESR, elevated CRP, high WBCs. Even with biopsy some **pus** comes out |  |
| Site | • Around the growth plate → femur (most common), tibia, and humerus.<br>• It is the only bone tumor which takes origin from **diaphysis**, Iliac flat bone, and ribs. |
| Presentation | • Pain<br>• Huge Swelling<br>• Lump with constitutional symptoms |
| Radiographic features | • Onion-skin periosteal reaction.<br>• Very significant soft tissue component (characteristic of Ewing sarcoma) |
| Investigation | • MRI and biopsy make definitive diagnosis<br>• N.B. you can't differentiate from osteosarcoma unless in biopsy. But hints are age group, radiological location (diaphysis in Ewing and metaphysis in osteosarcoma) |
| Treatment | For both Ewing and osteosarcoma:<br>• Neoadjuvant chemotherapy followed by tumor excision and reconstruction.<br>Why do we give neoadjuvant chemotherapy prior to surgical resection?<br>1. To shrink the tumor for easier removal<br>2. To kill micrometastasis<br>3. Hints on post surgical chemotherapeutic agent |

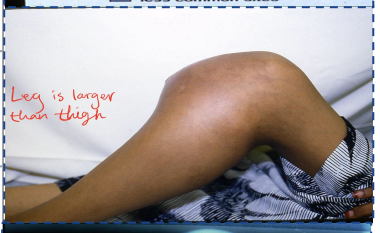


*Water break, stay hydrated :)*

# Primary Malignant Bone Tumors:

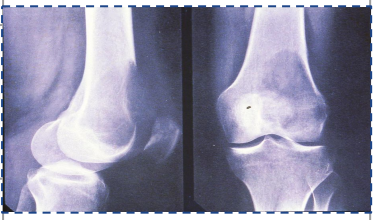
| Malignant Tumors | |
|---|---|
| **(2) Osteosarcoma** | |
| • More common than Ewing's sarcoma. **(age 10-20)**<br>• **History of radiation and paget's disease.** | |
| Types | 1. Primary (conventional, low-grade central, telangiectatic, multicentric (multifocal), juxtacortical; no need to know types of primary sarcoma)<br>2. Secondary (malignant transformation of benign process):<br>A. Paget's disease → Paget's sarcoma<br>B. Post radiation sarcoma<br>3. Metastatic from breast, lungs or bones. |
| Site | • Around the growth plate → around the shoulder, knee.<br>• Distal femur, proximal tibia/Humerus |
| Presentation | • Pain, pathological fracture (typical presentation of malignant tumor)<br>• Swelling (palpable mass in the site of the tumor "metaphysis commonly" but not as huge as Ewing's)<br>• There might be prominent veins overlying the skin over the swelling<br>• Overlying skin is warm due to high vascularity<br>• The patient may look cachectic (in late and advanced cases) |
| Radiographic features | • Codman triangle<br>• Irregular medullary and cortical destruction of metaphysis<br>• Cortex is intact |
| Investigation | • CT scan → bone extension, lung metastasis.<br>• MRI → soft tissue extension, neurovascular bundle involvement<br>• Bone scan → metastasis to other bones *characteristic feature*.<br>• Fever, elevated alkaline phosphatase (ALP) and lactate dehydrogenase (LDH)<br>• Definite diagnosis made by **biopsy** |
| Treatment | • Similar to Ewing's Sarcoma |



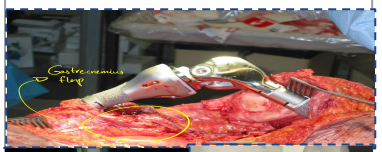



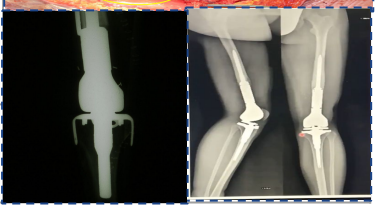


Bone producing, cortex is intact



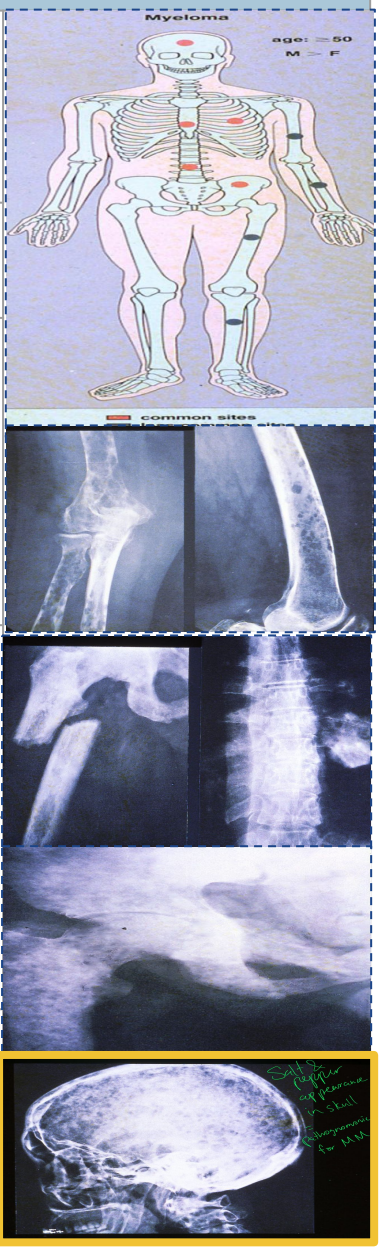
Juxtacortical metaphyseal-epiphyseal





# Primary Malignant Bone Tumors:

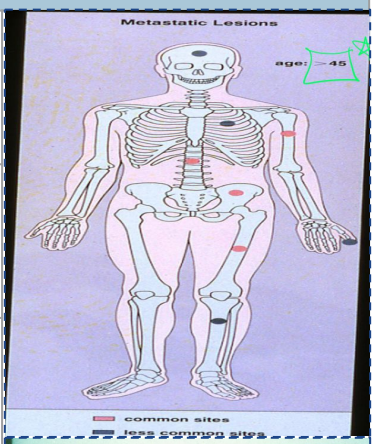
| Malignant Tumors | |
|---|---|
| **(3) Multiple Myeloma** | |
| • Systemic disease.<br>• Arise from plasma cells in the bone marrow.<br>• The most common primary malignant tumor in elderly > 50<br>• Some consider it a bone tumor, and some consider it hematological | |
| Site | • Central bones (axial skeleton): skull, ribs, pelvic girdle. & spine |
| Presentation | • Pain, spinal cord compression, Osteoporosis, Pathological fractures.<br>• Medical complications include anaemia, hypercalcaemia, hyperviscosity,<br>• Immunosuppression and renal dysfunction.<br>• CRAB: **C = Calcium** (elevated), **R = Renal failure, A = Anemia, B = Bone lesions** (bone pain) |
| Radiographic features | • Radiological features: Multiple Lytic or sclerotic lesions. "Moth-eaten appearance"<br>• In skull, there will be pepper (lytic) & salt (sclerotic) appearance (pepper-pot). You have to do skull x-ray. |
| Investigation | • Bence jones proteins test found in 24h urine collection (highly suggestive)(protein electrophoresis) ( urine & serum electrophoresis) UPEP and SPEP<br>• Only definitive diagnosis is by bone marrow aspiration |
| Treatment | • Radiotherapy, Chemotherapy (mainly medical)<br>• Bone marrow transplant: Success rate is 30% and it costs millions<br>• The role of orthopedic surgeon is only fix pathological fractures, do internal fixation. |

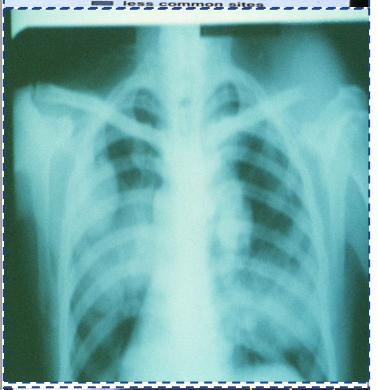


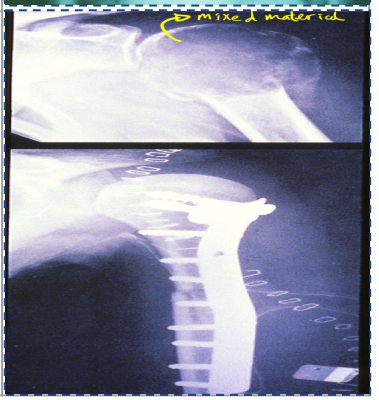


*Just get a break*

# Secondary Metastatic Bone Tumors:

| Malignant Tumors | |
|---|---|
| **Metastasis** | |
| • More common than all primary tumors. Common in adults (>45 y)<br>• The most common tumors are: thyroid, lung, breast, colorectal, prostate and kidney |  |
| Site | • Usually metastasis occurs in the **highly vascular bones** e.g. vertebral body, hip, ribs, pelvis, upper end of femur, and humerus |
| Presentation | • Patient may present with known primary tumor.<br>• May present with secondary metastasis. So, we must identify the primary sit and treat it |
| Radiographic features | • X-ray shows lytic lesions (bone eaten away) with thinning of the cortex.<br>• Resembles bone cysts but the **age group** directs the diagnosis |
| Investigation | • CT scan of the chest.<br>• Take biopsy to know where is the primary.<br>• You can do bone scan to check metastasis in other areas |
| Treatment | • Palliative chemotherapy (not surgical).<br>• The new trend is to downgrade the tumor then allograft it<br>Surgery indications:<br>❖ Severe pain<br>❖ Mechanical instability: pain in the spine with neurological symptoms (spinal cord compression)<br>❖ Prophylactic (preventive fixation): in weight bearing bones with involvement of >60% of the cortex<br>❖ Fixate a fracture (curettage, grafts and plates) |





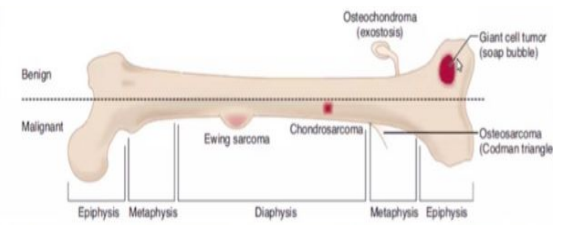

## ❖ Tumors Locations

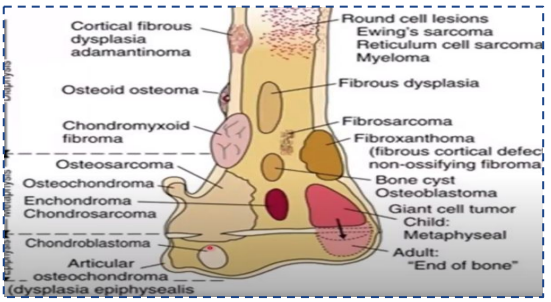
### Important Locations

Tumors usually have a common site (not necessary)

**Common sites of tumor in bones:**

- **Chondroblastoma**: epiphysis
- **Giant cell tumor**: cross metaphysis and epiphysis
- **Osteosarcoma**: cross **metaphysis** and epiphysis
- **Ewing sarcoma**: **diaphysis**
- **Osteoid osteoma**: cortex



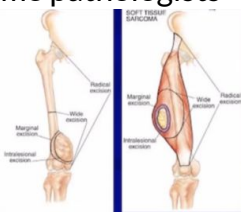
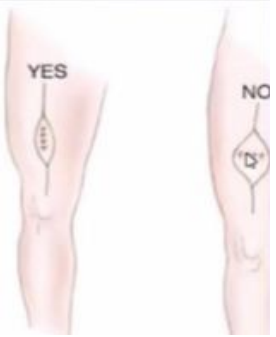
# What is Next? Biopsy

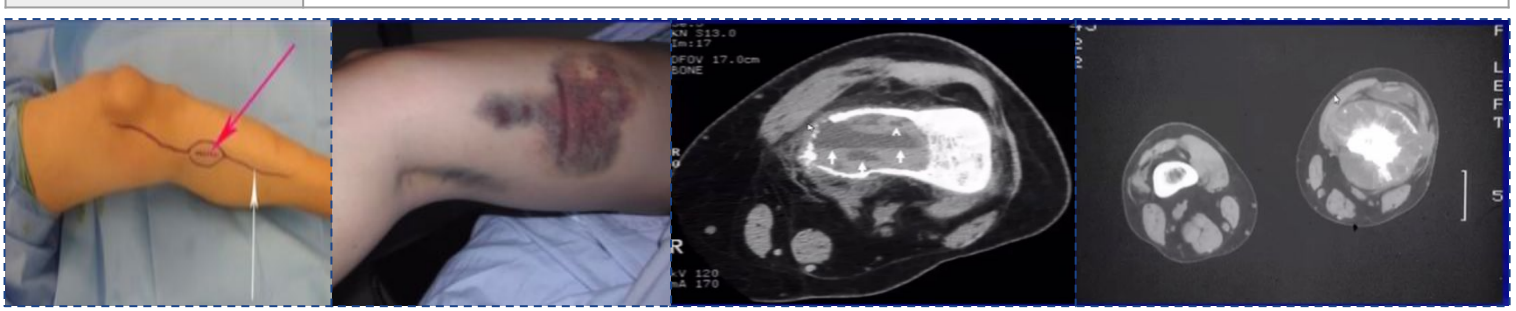
## Biopsies

- Is not a substitute for thorough history, physical examination and investigations.
- Serves to confirm diagnosis suspected from above
- If you don't know what it is before the biopsy you won't know what it is after.

**Every lesion doesn't need a biopsy!**

- An asymptomatic (latent) or symptomatic bone lesion (active) that appears entirely benign on imaging doesn't need a biopsy
- A soft tissue lesion that appears entirely benign on MRI ( lipoma, hemangioma) does not need a biopsy
- When in Doubt, it is safer to do a biopsy

| | |
|---|---|
| Indications for Biopsy<br>**V. Important** | • Aggressive or malignant appearing bone or soft tissue lesions.<br>• For soft tissue lesions > 5 cm, deep to fascia, bone or neurovascular structures.<br>• Unclear diagnosis in symptomatic patient<br>• Special situation - solitary bone lesion in a patient with a history of carcinoma |
| Prerequisites for Biopsy | • CBC, platelets, coagulation screen<br>• Cross sectional imaging- depicts local anatomy , solid areas of tumor<br>• Experienced musculoskeletal pathologist available |
| Biopsy Technique | • Fine needle aspirate - gives cytologic specimen (adequate for some pathologists experienced with this technique)<br>• Core biopsy (tru-cut) allows for ultrastructural examination<br>• Incisional biopsy<br>• Excisional biopsy (remove whole mass)<br>• Selected indications (small < 5c ,superficial soft tissue masses)<br>  |
| Principles of Open Biopsy | • Extensile incision – longitudinal in extremities.<br>• Avoid developing planes (cut only one time)<br>• Use involved compartment<br>• Do not expose neurovascular structures.<br>• Meticulous hemostasis<br>• Release tourniquet prior to wound closure.<br>• If using drain, bring out in line with incision.<br>  |
| General Recommendations | • For benign aggressive tumours without soft tissue mass, plan biopsy through area of maximal cortical weakening based on CT or MRI.<br>• For malignant tumours or benign aggressive with soft tissue mass, biopsy soft tissue rather than creating hole in bone. |



# Extra: 435

| Summary | | | | | | |
|---|---|---|---|---|---|---|
| Bone tumor | nature | age | site | symptoms | X-ray | treatment |
| **1) Simple bone cyst (unicameral cyst):** | benign | young < 20 | pelvis, scapula, etc. | Asymptomatic & pathological fracture. | lytic | No need for treatment, If symptomatic > curettage + bone graft |
| **2) Aneurysmal bone cyst:** | | | around joints | | lytic "**ballon like**" | |
| **3) Fibrous Cortical Defect (Non-Ossifying Fibroma):** | | | around knee | | Mixed (cystic + sclerotic) | |
| **4) Osteoid osteoma:** | | 10 - 35 | cortex of long bones | **PAIN** (at night, painful scoliosis) | Lytic nidus within sclerotic bone. | NSAIDs + burn the of nidus |
| **5) Enchondroma:** | | Around 40 | **phalanges** | Asymptomatic & pathological fracture. | Popcorn matrix (cartilaginous). | No need for treatment, If symptomatic > curettage + bone graft / prosthesis |
| **6) Multiple Enchondromatosis (AR):** | benign, with High risk of malignant transformation | 10-30 | | disabling deformity | multiple aggressive lesions | |
| **7) Osteochondroma:** | benign | 10-35 | around the knee | swelling | Exostosis. Benign features. | |
| **8) Giant cell tumor (GCT):** | benign but aggressive | 20-40 | | Pain, swelling, & pathological fracture | Aggressive features lytic, Permeative destruction | |
| **9) Ewing's sarcoma:** | malignant | 5-25 | | | Sclerotic. onion-skin periosteal reaction. | chemo & surgery (limb salvage or amputation) |
| **10) Osteosarcoma:**[14] | | 5-20 | | | Sclerotic. **sunburst** periosteal reaction | |
| **11) Multiple myeloma** | | > 50 | spine or femur | pain, osteoporosis, pathological # | lytic or sclerotic | chemo |
| **12) Metastasis:** | | > 35 | | | | |

# Extra:

## Bone Tumours

- primary bone tumours are rare after 3rd decade
- metastases to bone are relatively common after 3rd decade

### Clinical Features

- malignant (primary or metastasis): local pain and swelling (weeks to months), worse on exertion and at night, ± soft tissue mass
- minor trauma often initiating event that calls attention to lesion

**Table 25. Distinguishing Benign from Malignant Bone Lesions on X-Ray**

| Benign | Malignant |
|---|---|
| No periosteal reaction or benign appearing reaction (e.g. uniform smooth periosteal thickening as seen in a healing fracture) | Acute periosteal reaction<br>• Codman's triangle<br>• "Onion skin"<br>• "Sunburst" |
| Sharp, well-demarcated borders, narrow zone of transition (between lesion and normal bone, suggesting slow-growing lesion) | Poorly defined borders, with a wide zone of transition, or infiltrative (suggesting fast-growing lesion) |
| Well-developed bone formation<br>Intraosseous and even calcification | Varied bone formation<br>Extraosseous and irregular calcification |
| No soft tissue mass | Soft tissue mass present |
| No cortical destruction or uniform cortical destruction in some low grade and locally aggressive benign lesions | Aggressive cortical destruction or tumour infiltration without cortical destruction |

Adapted from: Buckholtz RW, Heckman JD. Rockwood and Green's Fractures in Adults. Volume 1. Philadelphia: Lippincott Williams & Wilkins, 2001. p558

### Diagnosis

- malignancy is suggested by rapid growth, warmth, tenderness, aggressive features on imaging
- staging should include:
  - blood work (with liver function assays, inflammatory markers, bone profile)
  - serum electrophoresis for older patients ± Bence Jones protein
  - CT chest /abdo/pelvis
  - biopsy
    - should be referred to specialized centre prior to biopsy
    - classified into benign, benign aggressive, and malignant
  - MRI of affected bone

**Red Flags**

- Persistent skeletal pain
- Localized tenderness
- Spontaneous fracture
- Enlarging mass/soft tissue swelling

**X-ray Findings**

- Lytic, lucent, sclerotic bone
- Involvement of cortex, medulla, soft tissue
- Radiolucent, radiopaque, or calcified matrix
- Periosteal reaction
- Permeative margins
- Pathological fracture
- Soft tissue swelling

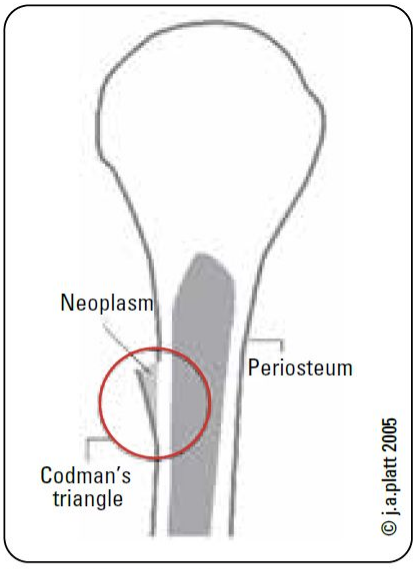



**Figure 56. Codman's triangle**
A radiographic finding in malignancy, where the partially ossified periosteum is lifted off the cortex by neoplastic tissue

## Benign Active Bone Tumours

### BONE-FORMING TUMOURS

#### Osteoid Osteoma

- benign bone tumour arising from osteoblasts; not known to metastasize
- peak incidence in 2nd and 3rd decades, M:F = 2-3:1
- proximal femur >tibia diaphysis most common locations, spine (can cause painful scoliosis)
- radiographic findings: small, round radiolucent nidus (<1.5 cm) surrounded by dense sclerotic bone ("bull's-eye")
- symptoms: constant and progressive pain from prostaglandin secretion and COX1/2 expression
  - pain worse at night (diurnal prostaglandin production); characteristically relieved by NSAIDs
- treatment: NSAIDs are first-line; percutaneous radiofrequency ablation, surgical resection

### FIBROUS LESIONS

#### Fibrous Cortical Defect (i.e. non-ossifying fibroma, fibrous bone lesion)

- developmental defect in which areas that normally ossify are filled with fibrous connective tissue
- most common benign bone tumour in children, typically asymptomatic and an incidental finding
- occur in as many as 35% of children, peak incidence between 2-25 yr old
- distal femur > distal tibia > proximal tibia most common locations
- radiographic findings: diagnostic, metaphyseal eccentric 'bubbly' lytic lesion near physis; thin, smooth/lobulated, well-defined sclerotic margin
  - multiple lesions can be present; large lesions may be associated with pathologic fractures
- treatment: most lesions resolve spontaneously; curettage and bone grafting for symptomatic lesions or to prevent pathologic fractures in larger lesions

#### Osteochondroma

- cartilage capped bony lesion arising on the external surface of a bone
- 2nd and 3rd decades, M>F
- most common benign bone tumour (~30%); true incidence unknown as many asymptomatic
- 2 types: sessile (broad based and increased risk of malignant degeneration) vs. pedunculated (narrow stalk)

# Extra:

- metaphysis of long bone near tendon attachment sites (distal femur, proximal tibia, or proximal humerus)
- radiographic findings: cartilage-capped bony spur on surface of bone ("mushroom" on x-ray)
- may be multiple (hereditary, autosomal dominant form) – higher risk of malignant change
- generally very slow growing and asymptomatic unless impinging on neurovascular structure ('painless mass')
  - growth usually ceases when skeletal maturity is reached
- malignant degeneration occurs in 1-2% (becomes painful or rapidly grows)
- treatment: observation; surgical excision if symptomatic or concern for malignant transformation

### Enchondroma

- benign hyaline cartilage growth; abnormality of chondroblasts, develops in medullary cavity
  - single/multiple enlarged rarefied areas in tubular bones
  - lytic lesion with sharp margination and irregular central calcification (stippled/punctate/popcorn appearance)
- majority asymptomatic, presenting as incidental finding or pathological fracture
- 2nd and 3rd decades
- 60% occur in the small tubular bones of the hand and foot; others in femur (20% - Figure 57), humerus, ribs
- radiographic findings: well-defined, lucent, central medullary lesions that calcify over time
- malignant degeneration to chondrosarcoma occurs in 1-2% (rest/nocturnal pain in absence of pathologic fracture is an important clue
- treatment: observation with serial x-rays; surgical curettage if symptomatic or lesion grows

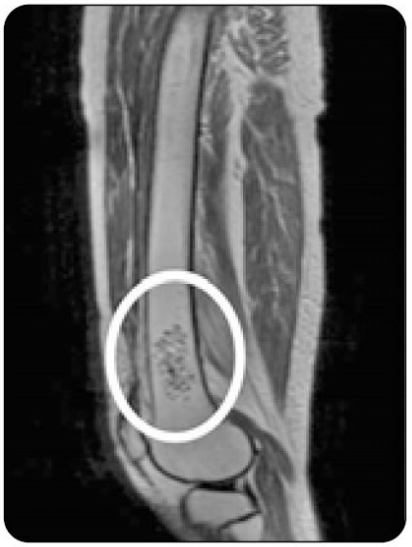


**Figure 57. T1 MRI of femoral enchondroma**

### CYSTIC LESIONS

### Unicameral/Solitary Bone Cyst

- most common cystic lesion; serous fluid-filled lesion with fibrous lining
- children and young adults, peak incidence during first 2 decades
- proximal humerus and femur most common
- symptoms: asymptomatic, or local pain; complete pathological fracture (50% of presentations) or incidental detection
- radiographic findings: lytic translucent area on metaphyseal side of growth plate, cortex thinned/expanded; well-defined lesion
- treatment: observation with serial radiography 4-6 mo; if needed, aspiration followed by steroid injection; curettage ± bone graft indicated if structural integrity of bone is compromised

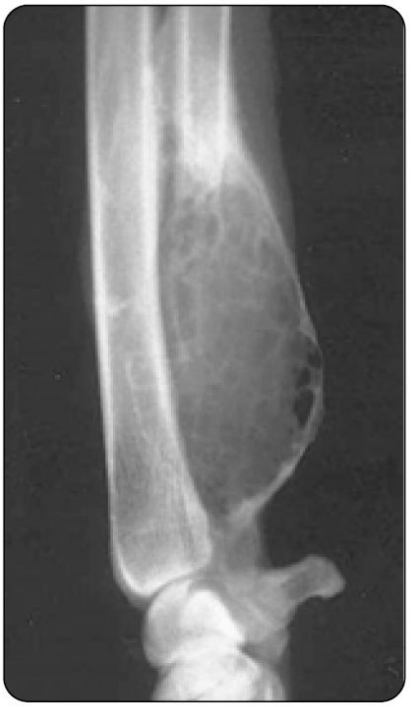


**Figure 58. X-ray of aneurysmal bone cyst**
Note the aggressive destruction of bone

## Benign Aggressive Bone Tumours

### Giant Cell Tumours/Aneurysmal Bone Cyst/Osteoblastoma

- affects patients of skeletal maturity, peak 3rd decade
- osteoblastoma: most commonly found in posterior elements of spine
- giant cell tumour: pulmonary metastases in 3%
- aneurysmal bone cysts: either solid with fibrous/granular tissue, or blood-filled
- radiographic findings
  - giant cell tumour: eccentric lytic lesions in epiphyses adjacent to subchondral bone; may break through cortex; T2 MRI enhances fluid within lesion (hyper-intense signal)
  - aneurysmal bone cyst: expansile, eccentric, and lytic lesion with bony septae ("bubbly appearance")
  - osteoblastoma: often nonspecific; calcified central nidus (>2 cm) with radiolucent halo and sclerosis
- symptoms: local tenderness and swelling, pain may be progressive (giant cell tumours), ± symptoms of nerve root compression (osteoblastoma)

### Treatment

- intralesional curettage + bone graft or cement
- wide local excision of expendable bones
- recurrence rates of up to 20%

## Malignant Bone Tumours

**Table 26. Most Common Malignant Tumour Types for Age**

| Age | Tumour |
|---|---|
| <1 | Neuroblastoma |
| 1-10 | Ewing's of tubular bones |
| 10-30 | Osteosarcoma, Ewing's of flat bones |
| 30-40 | Reticulum cell sarcoma, fibrosarcoma, periosteal osteosarcoma, malignant giant cell tumour, lymphoma |
| >40 | Metastatic carcinoma, multiple myeloma, chondrosarcoma |

# Extra:

### Osteosarcoma
- malignant bone tumour
- 2nd most common primary malignancy in adults after myeloma
- majority occur in 2nd decade of life, second peak in elderly patients with history of Paget's disease
- predilection for sites of rapid growth: distal femur (45% - Figure 59, OR49), proximal tibia (20%), and proximal humerus (15%)
  - invasive, variable histology; frequent metastases without treatment (lung most common)
- painful symptoms: progressive pain, night pain, poorly defined swelling, decreased ROM
  - radiographic findings: characteristic blastic and destructive lesion ("sunburst" pattern), periosteal reaction (Codman's triangle), soft tissue mass with maintenance of bone cortices; destructive lesion in metaphysis may cross epiphyseal plate
  - bone scan – rule out skeletal metastases; CT chest – rule out pulmonary metastases
- treatment: neo-adjuvant chemo + limb salvage resection (rarely amputation)
- prognosis: 90% survival for low-grade; 70% survival for high-grade

### Chondrosarcoma
- malignant chondrogenic tumour
- primary (2/3 cases)
  - previous normal bone, patient >40 yr; expands into cortex to cause pain, pathological fracture
- secondary (1/3 cases)
  - malignant degeneration of pre-existing cartilage tumour such as enchondroma or osteochondroma
  - age range 25-45 yr, better prognosis than primary chondrosarcoma
- symptoms: progressive pain, uncommonly palpable mass, pathologic fracture
- radiographic findings: in medullary cavity, irregular "popcorn" calcification
- treatment: generally resistant to chemotherapy and radiation,; treat with aggressive surgical resection + reconstruction; regular follow-up x-rays of resection site and chest
- prognosis: 90% survival for low-grade (10 yr survival); 29-55% survival for high-grade

### Ewing's Sarcoma
- malignant, small round cell sarcoma; metastases frequent without treatment
- most occur between ages 5-25 yr
- florid periosteal reaction in metaphysis of long bone with diaphyseal extension
- signs/symptoms: presents with pain, fever, erythema, and swelling; anemia, increased WBC, ESR, LDH (mimics an infection)
- radiographic findings: destructive lesion with moth-eaten appearance and periosteal lamellated pattern ("onion-skinning")
- treatment: resection + chemotherapy ± radiation
- prognosis: 70% survival; distant metastases significantly lower survival (<30%)

### Multiple Myeloma
- proliferation of neoplastic plasma cells
- most common primary bone malignancy
- 90% occur in people >40 yr; M:F=2:1; twice as common in individuals of African decent
- signs/symptoms: localized bone pain (cardinal early symptom), compression/pathological fractures, renal failure, nephritis, high incidence of infections (e.g. pyelonephritis/pneumonia), systemic (weakness, weight loss, anorexia)
- labs: anemia, thrombocytopenia, increased ESR, hypercalcemia, increased Cr
- radiographic findings: multiple, "punched-out" well-demarcated lesions, no surrounding sclerosis, marked bone expansion
- diagnosis
  - serum/urine immunoelectrophoresis (monoclonal gammopathy)
  - CT-guided biopsy of lytic lesions at multiple bony sites
- treatment
  - multiagent chemotherapy ± stem cell transplantation ± bisphosphonates
  - surgery for impending fractures: debulking, internal fixation
- prognosis: 5 yr survival 52%, prognosis increases with decreasing age
- see Hematology, H50

### Bone Metastases
- most common cause of bone lesions in adults; typically age >40
- majority arise from breast or prostate; some arise from lung, thyroid and kidney primary malignancies
- usually osteolytic lesions; prostate occasionally osteoblastic
- may present with mechanical pain and/or night pain, pathological fracture, hypercalcemia
- bone scan for MSK involvement; MRI if suspected spinal involvement
- treatment: pain control, bisphosphonates, stabilization of impending fractures if Mirel's Critera >8 (ORIF, IM rod, bone cement)

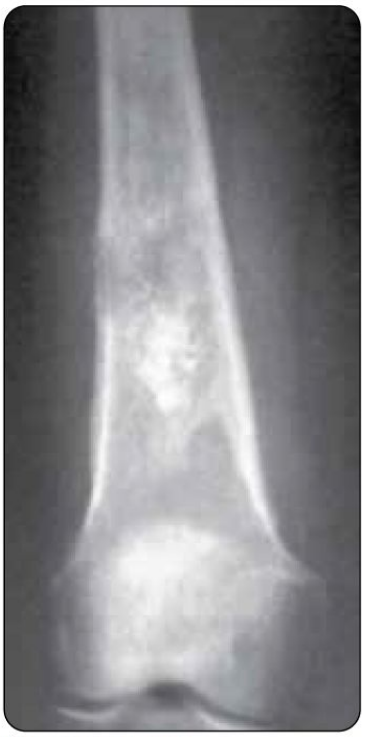
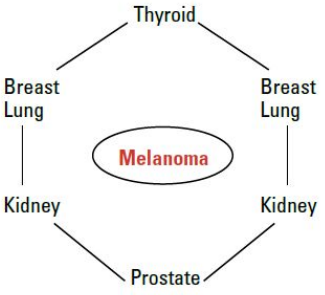


**Figure 60. X-ray of femur chondrosarcoma**

**Signs of Hypercalcemia**
**"Bones, Stones, Moans, Groans, Psychiatric overtones"**
**CNS**: headache, confusion, irritability, blurred vision
**GI**: N/V, abdominal pain, constipation, weight loss
**MSK**: fatigue, weakness, unsteady gait, bone and joint pain
**GU**: nocturia, polydipsia, polyuria, UTIs

**Most Common Tumours Metastatic to Bone**




**BLT with a Kosher Pickle**
**B**reast
**L**ung
**T**hyroid
**K**idney
**P**rostate

# Quiz

## MCQ

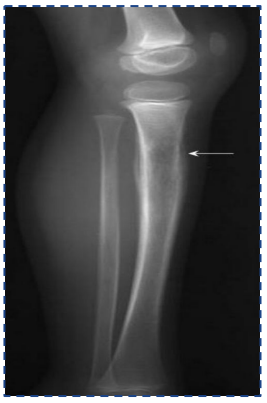
Q1: A 13-year old boy comes to the clinic because of a 6-week history of pain in his right shoulder. His pain is aggravated by the recent start of football practice and associated increased activity, but it persists after practice as well. He has no prior history of trauma. He denies fevers, weight loss and night sweats. His temperature is 37.1°C (98.8°F), pulse is 70/min, respirations are 16/min, and blood pressure is 120/82 mm Hg. Physical examination shows a hard immobile mass on the right proximal humerus which is slightly tender. His range of motion in the shoulder is minimally restricted. A radiograph obtained of his right upper extremity shows a sunburst pattern. Which of the following is the most likely diagnosis?

A. Osteosarcoma
B. Ewing Sarcoma
C. Giant Cell Tumor
D. Metastasis

Q2: A 15-year-old man comes to his pediatrician's office because of pain in his right humerus for the past 3 months. He also reports a recent low grade fever. Further examination reveals midshaft swelling on his right humerus. The patient denies any recent history of trauma. Genetic analysis shows an 11;22 translocation. An x-ray of his right arm is taken. Which of the following answer choices will most likely show up on imaging for this patient?

A. Onion-skin appearance
B. Punched-out lytic lesions
C. Necrosis surrounded by sclerotic bone
D. Central nidus with hyperactive cortex

Q3: A 10-year-old boy is brought to his pediatrician's office by his parents because of worsening pain over his left lower leg for the past 2 months. He denies any recent trauma to his leg within the past year and has been generally healthy. Physical examination shows a discrete, hard, and exquisitely tender mass over the anterior aspect of the right tibia about 3 inches below the knee. ESR today is 20mm/hr. An X-ray of this patient's left leg is shown . What is the most likely diagnosis?



A. Osteosarcoma
B. Ewing Sarcoma
C. Giant Cell Tumor
D. Osteoid osteoma

Q4: A 17 year old with swelling and pain at the right knee for the last 6 months, lost 7 kg, no history of trauma or infection, blood work done and was normal besides high alkaline phosphatase. X-ray was done which showed highly suspicious tumor most likely to be an osteosarcoma. What is the confirmatory diagnosis test?

A. MRI the knee
B. CT scan the knee
C. Bone scan
D. Biopsy

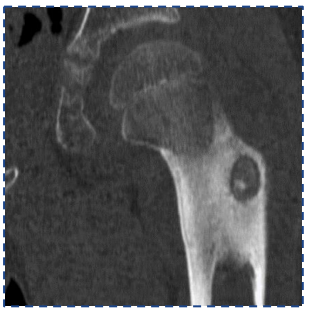
## Answers

| Q1 | Q2 | Q3 | Q4 |
|---|---|---|---|
| A | A | B | D |

# Quiz

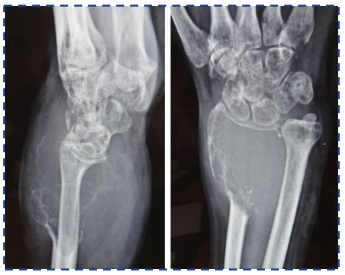
## MCQ

Q5: A 12-year-old boy comes to the clinic with his mother because of severe pain in his right leg for the past month. He says that the pain is mostly located in his thigh and that it was initially mild but now the pain is so bad that he cannot walk on his leg. His mother says that aspirin relieves his pain temporarily. Physical examination shows some localized pain over the area of the proximal femur. There is no palpable joint deformity, redness or swelling. He also walks with a visible limp. Neither increasing nor decreasing activity alleviates the pain, which tends to be worse at night. He has not had any recent trauma to the leg. An MRI of the leg shows a 1cm lesion within the femur (shown below). Which of the following is the most likely explanation for this patient's symptoms?



A. Aneurysmal bone cyst
B. Non-Ossifying Fibroma
C. Osteochondroma
D. Osteoid osteoma

Q6: A 23-year-old man comes to the emergency department because of a 10-month history of gradual painful swelling of his wrist. His temperature is 37.9°C (100.2°F), pulse is 82/min, respirations are 16/min, and blood pressure is 120/77 mm Hg. An X-ray is obtained and is shown below. Which of the following is the most likely diagnosis?



A. Osteoid osteoma
B. Osteosarcoma
C. Ewing sarcoma
D. Giant cell tumor

Q7: Which of the following is the most aggressively benign tumor?

A. Osteoid osteoma
B. Enchondroma
C. Giant cell tumor
D. Simple bone cyst

## SAQs

List three bone tumors that require bone marrow aspiration

1- Multiple Myeloma
2- Ewing Sarcoma
3- Lymphoma

What are 3 prerequisites to biopsy a highly suspicious bone tumor?

1- CBC, platelets, coagulation screen
2- Cross sectional imaging to depict local anatomy and solid areas of the tumor
3- Experienced musculoskeletal pathologist available

## Answers

| Q5 | Q6 | Q7 |
|---|---|---|
| D | D | C |

# THANK YOU

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