# Malignant Bone tumors

Objective

Learn primary and secondary malignant bone tumors and tissue of origin

Appreciate pathology in clinical , imaging and tissue diagnosis

Diagnostic and treatment principles

# Epidemiology

- Bone tumors are rare
- Classification based on histo morphology
- Team work in making diagnosis from ( clinical features. Radiological and histo morphological
- Many tumors have characteristic features
- Immunohistochemistry and genetic needed for final classification
- Congenital, Hereditary and non hereditary raise the risk of bone tumors

# General considerations

- Bone Tumors can be divided into

  primary and secondary.
- Secondary tumors can be further subdivided into

  Metastatic tumors

  Tumors resulting from contiguous spread of adjacent soft tissue neoplasms

  Tumors representing malignant transformation of the pre-existing benign lesions

# RISK FACTORS FOR BONE CANCER

| Cancer | Risk factor |
|---|---|
| Osteosarcoma | P53& RB onco-gene mutation<br>History of radiation therapy<br>Paget disease<br>Implanted metal prostheses<br>Rothmund-Thomson syndrome |
| Ewing sarcoma | Translocation in chromosomes 11 and 22(95%), Xsome21 and 22(5-10%) |
| chondrosarcoma | Presence of benign cartilage tumors (enchondromas and osteochondromas) |

# Tissue of  source consideration

| Tissue | Sarcoma |
|---|---|
| bone | Osteosarcoma |
| cartilage | Chondrsarcoma |
| fibrous | Fibrosarcoma |
| haemopetic | Multiple myeloma/ leukemia/lymphoma |
| muscle | Leimyosarcoma |
| Fat | liposarcoma |
| varscular | agiosarcoma |
| others | chorndoma |

# Important features of bone tumors

1. The ability of some *to dedifferentiate*

eg., enchondroma or a low-grade chondrosarcoma transforming into a high-grade sarcoma

2.Tendency of high-grade sarcomas to *arise in damaged bone*,

at the sites of *bone infarcts, radiation osteitis and Paget's disease*

# CLINICAL FEATURES

- Pain
- Swelling
- Fracture
- Constitutional disturbance
- Cord compression and sensory motor deficit
- Others based on the origin of bone metastasis

# PAIN

- non-specific symptom, but useful differential diagnosis.
- benign non-growing lesions tend to be asymptomatic

Pain suggest:

locally aggressive lesions (eg., aggressive osteoblastoma and GCT), and malignant tumors

- Pathologic fracture complicating either benign or malignant tumor
- Significant local tissue inflammatory reaction to the tumor.
- Neurovascular infiltration- neurogenic pain

# Differential diagnosis

- Osteomyelitis
- Sickle
- Gout/metabolic syndrome
- brown tumor
- Neuropathic osteoarthropathy/charcot
- Hydatid cyst

# INVESTIGATION

- History and physical examination dictates the mode of investigation
- X-Ray
- CT-Scan
- MRI
- BONE SCAN/US
- Baseline heamatological/ biochemical test
- Biopsy

**X-RAY**

- Bone response and bone destruction
- Fractures
- Matrix
- Soft tissue involvement
- Metastasis to the lungs/bone

**CT-SCAN**

- High radiation test- justify
- Demonstrate calcification where MRI and X- ray fail
- Non contrast CT diagnose chest metastasis
- Whole body CT scan indicated in suspected metastasis
- Ct fluoroscopy guide biopsy and interventional procedure

# MRI

- Superior in diagnosis, staging ,monitoring treatment
- T1 evaluate bone marrow
- Fat suppression to demarcate tumor from normal tissue
- Gadolinium useful in detecting special characteristic, response to treatment, and recurrence
- Facilitate state of art care by combining features of bone lesion, morphology, anatomy and anatomical relationship
- Recognize MRI artifacts to make appropriate decision

# Nuclear medicine and US

- TmDP 99
- Non specific
- Detects bone metabolism
- Remains as a image of detecting bone tumor
- Viewed together with others

Detect sub periosteal tumor

- Accurately assess cartilage cap of osteochondroma
- Monitor soft tissue extension
- Diagnosis recurrence
- Guided biopsy
- ? Future assessment of treatment response

# Metastatic bone disease origin

| ***Most common malignancies producing skeletal metastases:*** | |
|---|---|
| ***Adults*** | More than 75% of skeletal metastases originate from carcinomas of the prostate, breast, kidney, and lung. Also common are metastases from thyroid and colon cancers. And do not forget melanoma. |
| ***Children*** | Neuroblastoma, rhabdomyosarcoma, and retinoblastoma |

# Metastatic Radiographic features

- Radiographic appearance of the metastatic tumors

Purely lytic (kidney, lung, colon, and melanoma)

Purely blastic (prostate and breast carcinoma)

Mixed lytic and blastic (most common appearance

# DECISION MAKING

| Criteria | Elements |
|---|---|
| Demographics | Age<br>Gender |
| Affected bone | Single or multiple<br>Long, short or flat |
| Localization in longitudinal axis | Epiphyseal<br>Metaphyseal<br>Diaphyseal |
| Localization in axial axis | Central<br>Eccentrical<br>Cortical<br>Yuxtacortical |
| Destruction pattern | Geographical (lytic, sclerotic or mixed)<br>Infiltrative (lytic, sclerotic or mixed)<br>Moth-eaten |
| Periosteal reaction | Sunburst<br>Hair-on-end<br>Codman's triangle<br>Onion-skin |
| Bone matrix | Osteoid<br>Cartilaginous<br>Amorphous |
| MRI signal | Fat<br>Fibrous/sclerotic<br>Myxoid<br>Hemorrhage<br>Edema (bone marrow or soft tissues)<br>Contrast enhancement |

# Interventional procedures in treatment

- Biopsy
- vascular embolization
- Vertebroplasty and kyphoplasty for spine metastasis
- Cementoplasty for pelvic pain control
- Palliative thermal ablation for MBD

# Six questions for appropriate differential diagnosis

1. What type of matrix is being made?

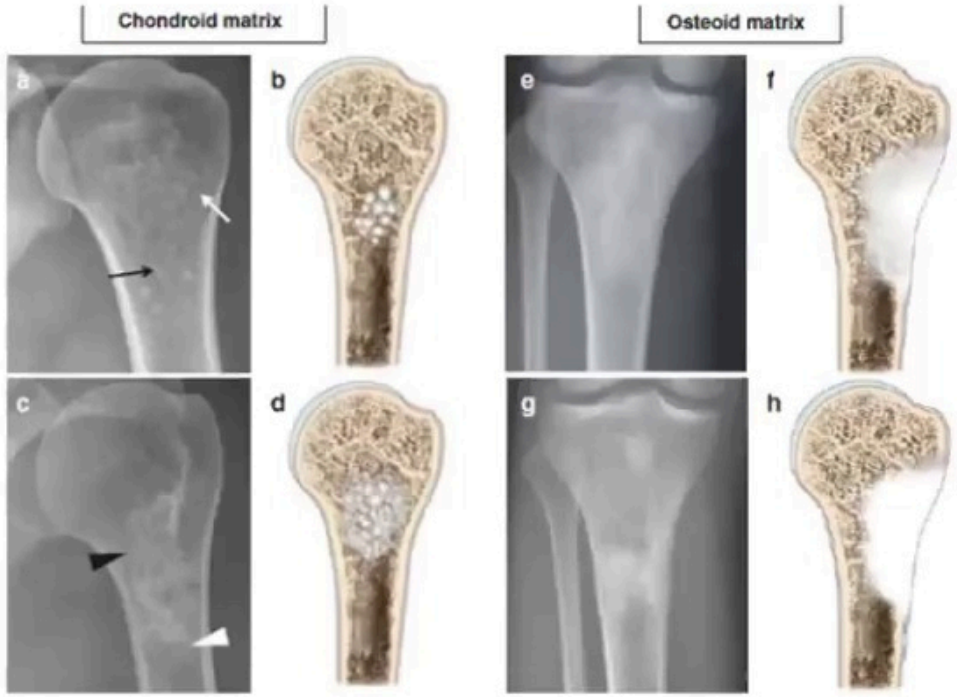
(a) Calcification

(b) Bone or osteoid (fluffy, cloud-like densities)

(c) Cartilage (arcs and rings, popcorn)

(d) Fibrous (ground-glass)

(e) Cystic (fallen-leaf)



2. If bone is being made, what type is it?

(a) Normal

(b) Reactive

(c) Tumor

3. What is the bone doing to the lesion and/or what is the lesion doing to the bone (morphology)?

(a) Border

(b) Pattern of destruction

(c) Periosteal reaction

(d) Matrix

(e) Soft tissue mass

4. What is the pattern of destruction?

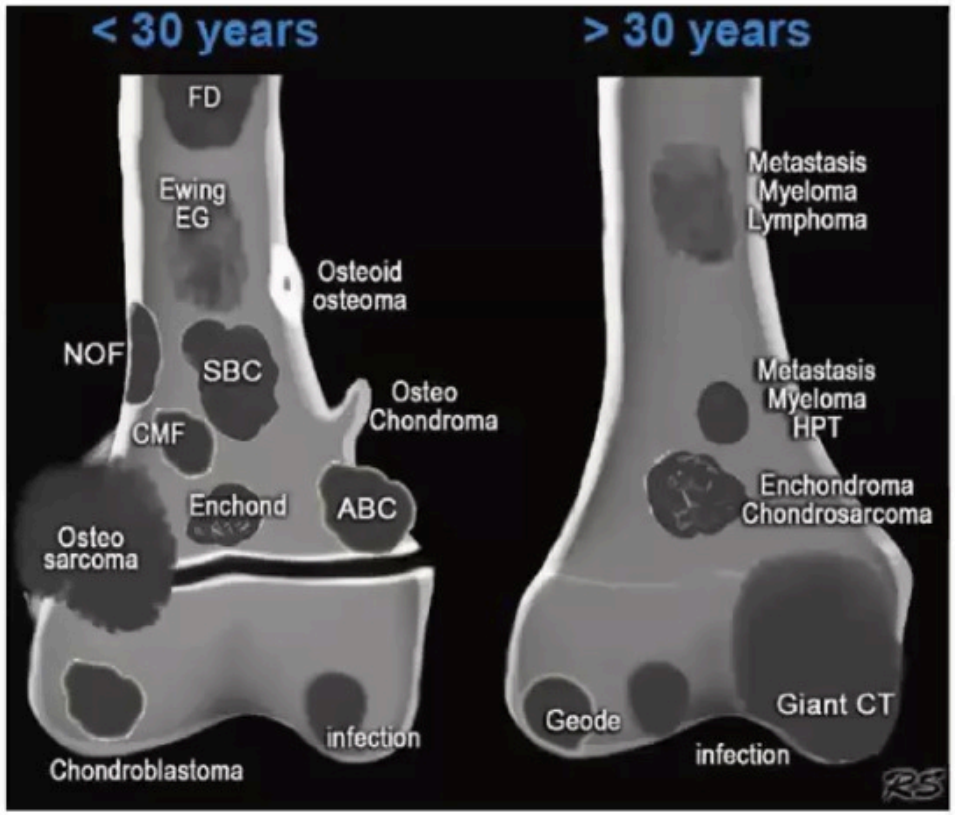
(a) Geographic

(b) Moth-eaten

(c) Permeate

5. What location in the bone is the lesion and which bone

- (a) Epiphyseal
- (b) Metaphyseal
- (c) Diaphyseal

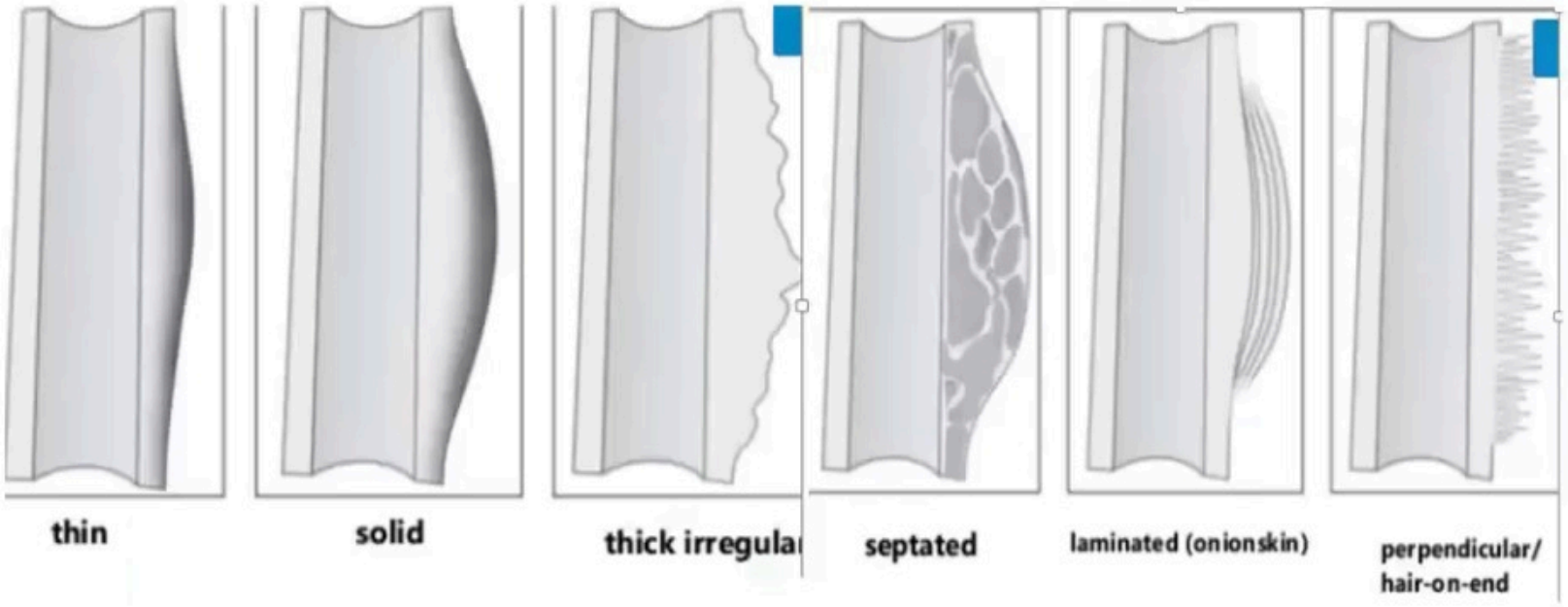


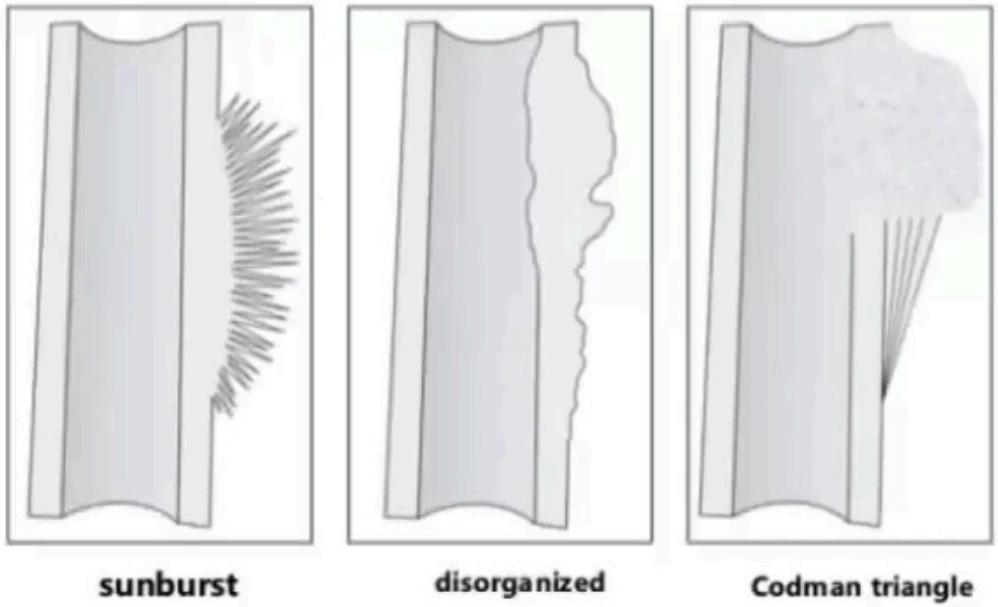
# 6. What is the age of patient?

| Age | Most common malignant tumor |
|---|---|
| 0- 10 | Ewing sarcoma,<br>leukemia,<br>neuroblastoma metastasis |
| 10 - 20 | Osteosarcoma<br>Ewing sarcoma<br>adentimanoma |
| 20- 40 | Chondrosarcoma<br>lymphoma |
| >40 | Metastasis<br>Multiple myeloma<br>lymphoma<br>Leukemia<br>MFH<br>Secondary osteosarcoma( pagets)<br>chondrosarcoma |

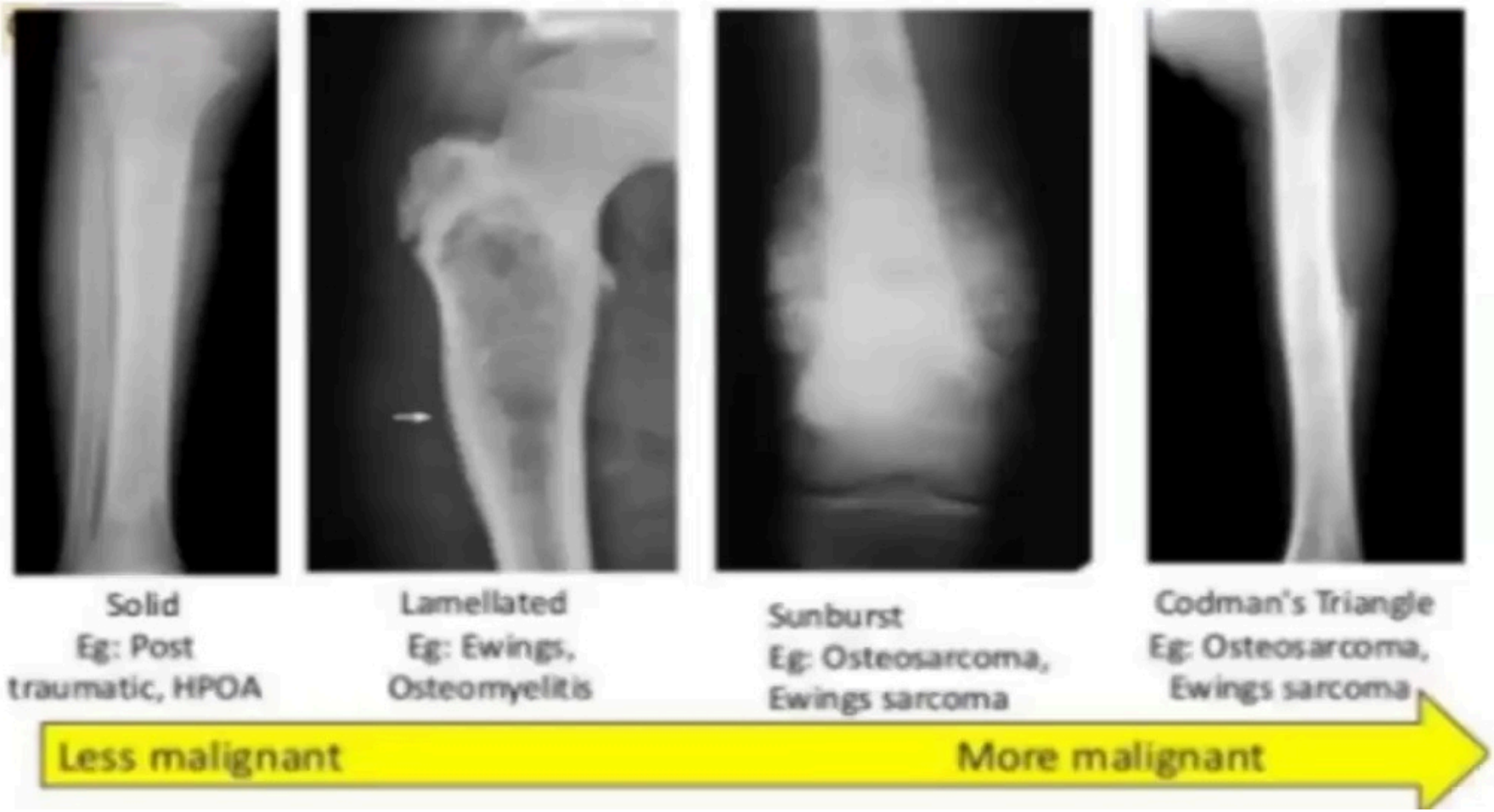
# Biological activity depiction by periosteal reaction

| Non aggressive | Solid type<br>Single layer lamellated |
| --- | --- |
| aggressive | Multilaminated( onion skin)<br>Spiculated<br>Hair on head<br>Sunburst<br>Codmans triangle |
| | |


thin
solid
thick irregular
septated
laminated (onionskin)
perpendicular/
hair-on-end


sunburst
disorganized
Codman triangle

# Biological activity of tumor



# Types of biopsy

- Frozen sections( intraoperative)
- FNA
- Trucut
- Curettage
- Resection and amputation
- Nb controlled decalcification of each specimen to avoid over decalcification
- Adjunctive diagnostic technique- histochemistry, immunohistochemistry, cyto genetic/molecular genetic, electron microscopy

# BIOPSY and Histological features of malignant bone tumors

Pattern of growth (eg., sheets of cells vs. lobular architecture)

Cytological characteristics of the cells

Presence of necrosis and/or hemorrhage and/or cystic change Matrix production

Relationship between the lesional tissue and the surrounding bone (eg., sharp border vs. infiltrative growth

# Enneckling staging of bone tumors

| Stage | Grade | Site (1) | Metastasis |
|---|---|---|---|
| IA | Low Grade | T1 - intracompartmental | M0 (none) |
| IB | Low Grade | T2 - extracompartmental | M0 (none) |
| IIA | High Grade | T1 - intracompartmental | M0 (none) |
| IIB | High Grade | T2 - extracompartmental | M0 (none) |
| III | Metastatic | T1 - intracompartmental | M1 (regional or distant) |
| III | Metastatic | T2 - extracompartmental | M1 (regional or distant) |

# Principles of treatment

- Multi disciplinary team approach
- History and physical examination( tailored to history)
- Biopsy- at tertiary Centre. Longitudinal incision, avoid tissue dissection, hemostasis
- Radiation
- Chemotherapy
- Operation; excision, amputation, limb salvage

# Treatment modalities

- Neoadjuvant is effective in Osteosarcoma and Ewing sarcoma
- Radiation used for lung metastasis in Ewing sarcoma
- Radiation is not effective in Both chondrosarcoma and osteosarcoma
- Surgery is used for any of bone sarcoma
- Limb salvage considered if clinically possible and clear surgical margin.

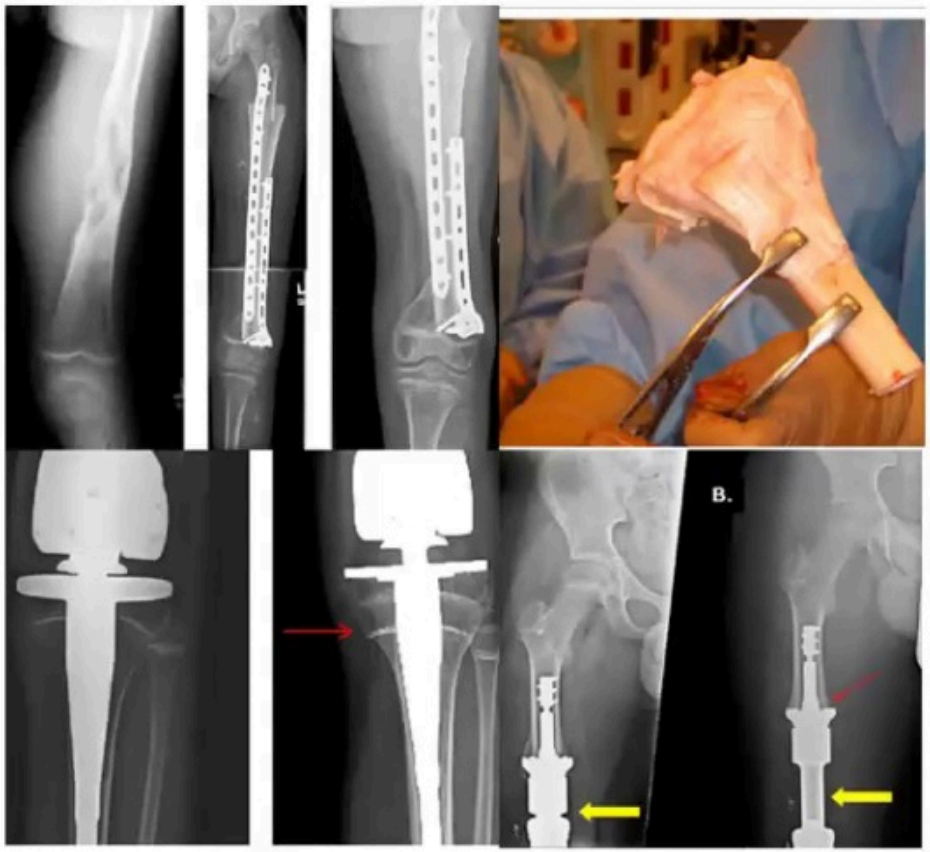
# Chemotherapy side effects

- Chemotherapy treatment can result in renal, cardiac, and hearing impairment.
- Patients undergoing chemotherapy must have baseline renal function testing
- cardiac function when anthracyclines are prescribed,
- audiogram in case of treatment with cisplatin.
- Sperm or oocyte cryopreservation should be offered prior to starting chemotherapy

# Prognostic factors for bone tumors

- Positive factors include: localized extremity disease, >90% tumor necrosis response to chemotherapt
- Negative factors : incomplete surgical reception, old age, presence metastases, size >8cm and axial skeleton localization
- Chondrosarcoma overall prognosis depends on histologic grade, worst in dedifferentiated.

# Limb salvage



# Follow up

- Physical examination, functional assessment, and possible complications of any reconstruction
- Radiological examination of primary tumor site: X-ray and/or MRI are the most used tools
- Chest X-ray/CT scans to detect early lung metastases
- Bone scintigraphy for bone metasisis
- Every 3 months for the first 2 years.
- Every 4–6 months from 2nd to 5th year.
- Every 12 months from 5th to 10th year

# HOMEWORK

Which is true about bone tumor?

A. Multiple myeloma is seen in more than 55 years age and above
B. Osteogenic sarcoma fourth decade
C. Chondrosarcoma first decade
D. Osteosarcoma fith decade

- The following tumors are benign except?

A. Chondroma
B. Chordoma
C. Osteochondroma
D. enchondroma

10 years old boy, LEAST common cause of proximal lytic lesion of head of femur is

A. Plasmacytoma
B. Metastasis
C. Histiocytosis
D. Bone tumor

Which of the following childhood tumors most frequently metastasizes of the bone?

A. Neuroblastoma
B. Gangliomeuroma
C. Wilms' tumor
D. Ewing's sarcoma

# THANK YOU