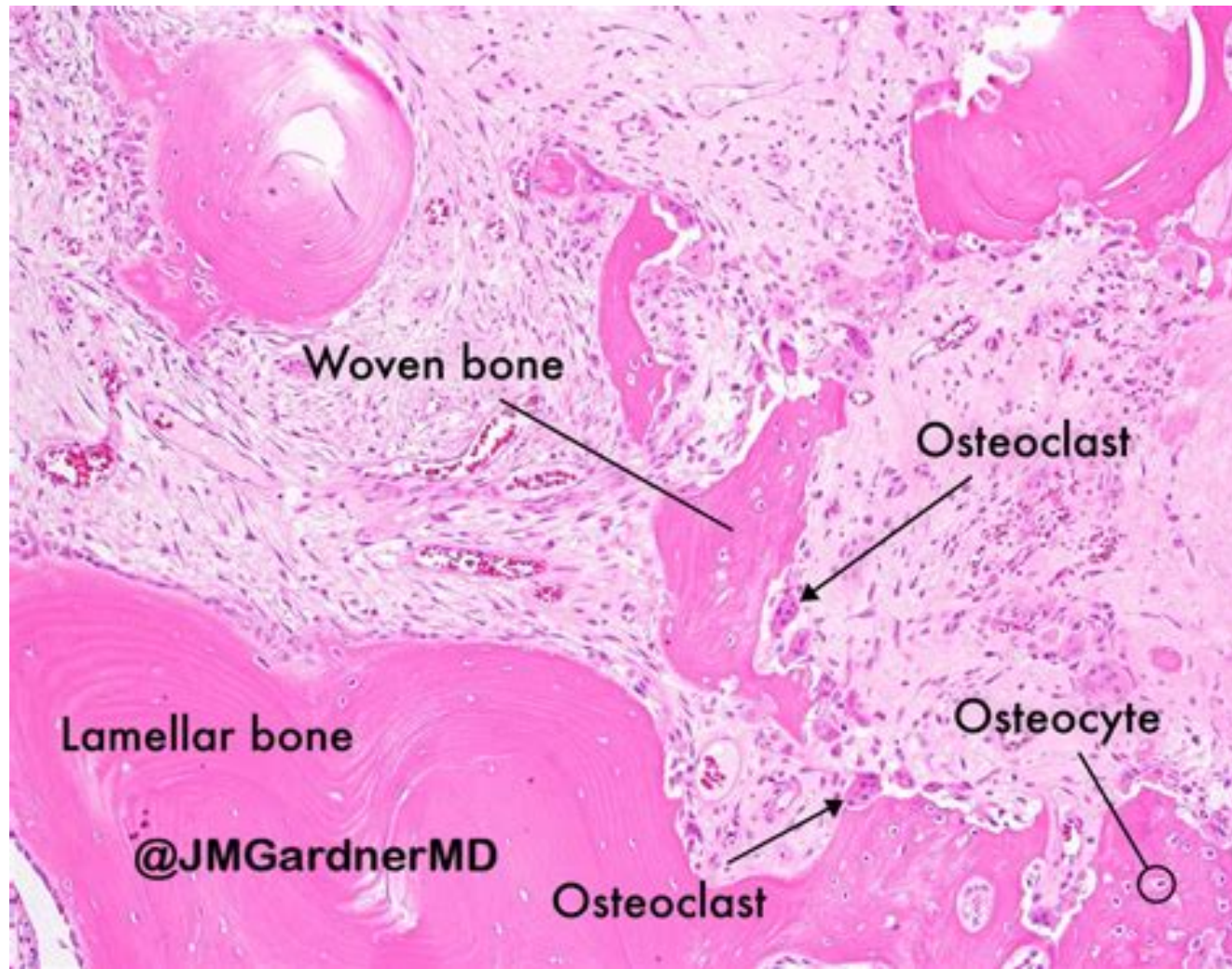


Bone Pathology

Dr. Raghad Hanoon

Normal histology



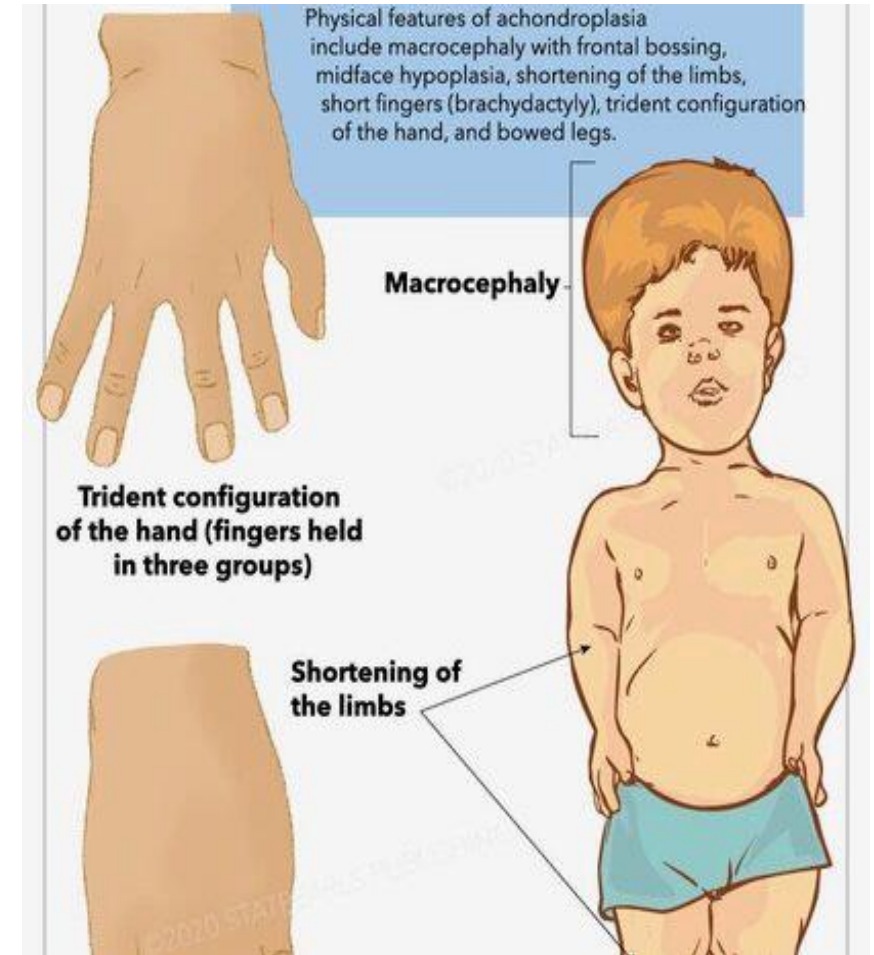
❖ **Main categories of bone diseases are;**

1. Congenital bone diseases.
2. Metabolic bone diseases.
3. Inflammatory diseases
4. Tumors of the bone.

❖ Congenital bone diseases

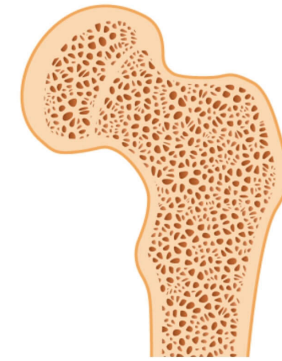
Achondroplasia .1

- Most common form of inherited dwarfism.
- It is an **autosomal dominant disorder**, characterized by impaired maturation of cartilage in developing growth plate.
- The disease is caused by gain-of-function mutations in fibroblast growth factor receptor 3 (**FGFR3**).
- Affected individuals **have shortened proximal extremities, a trunk of relatively normal length, and an enlarged head with bulging forehead and conspicuous depression of the root of the nose.**
- The skeletal abnormalities are usually **not associated** with changes in long life, intelligence, or reproductive status.

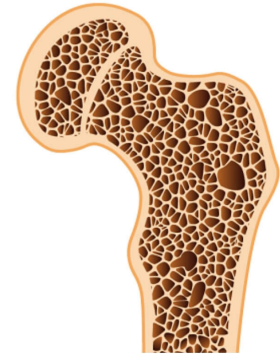


2. Osteogenesis Imperfecta

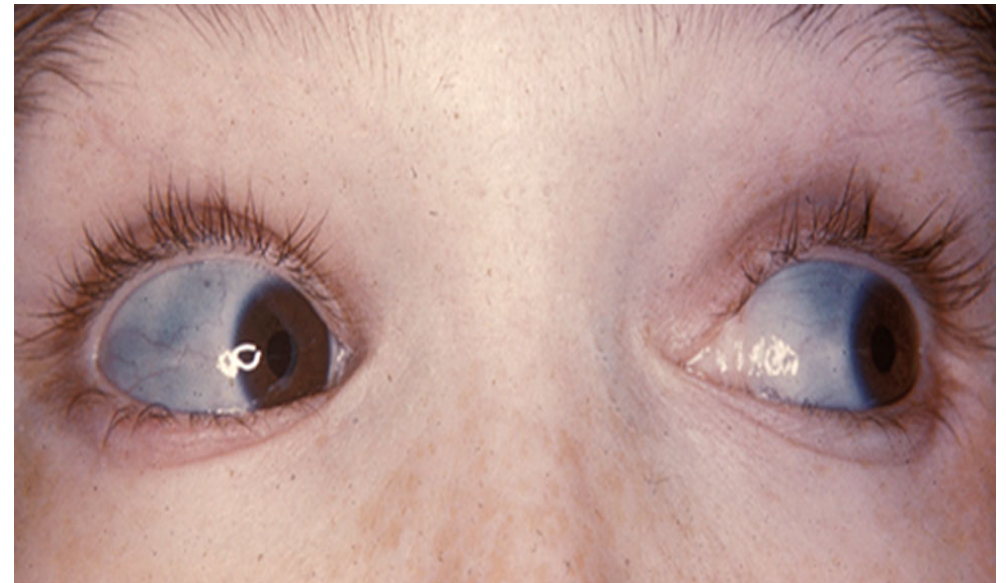
- Also called **brittle bone diseases**.
- Disorders caused by **qualitatively or quantitatively abnormal type I collagen** synthesis. It usually results from **autosomal dominant mutations** in the genes that encode the $\alpha 1$ and $\alpha 2$ chains of type I collagen.
- Result in **generalized bone fragility, blue sclera, hearing loss; dental imperfections** are due to dentin deficiency.



Healthy Bone Density



Osteogenesis Imperfecta

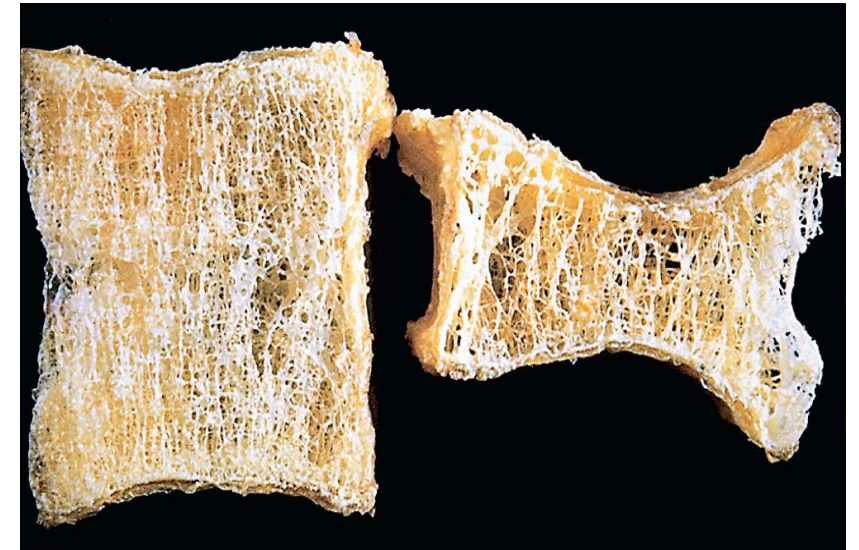




Metabolic bone diseases

□ Osteoporosis

- Characterized by **porous bones and reduced bone mass**, that predispose to fracture
- **Types of Osteoporosis;**
 1. **Localized;** Like in disuse osteoporosis.
 2. **Generalized;** This is either primary or secondary.
- **Causes of primary osteoporosis:**
 1. Estrogen deficiency- Postmenopausal osteoporosis. (Commonest)
 2. Senile osteoporosis.
 3. Lack of exercise
- **Causes of secondary osteoporosis:**
 1. Endocrine disorders (hyper & hypothyroidism, Cushing syndrome).
 2. Neoplasia (Multiple Myeloma)
 3. GIT causes like malabsorption, hepatic insufficiency.
 4. Drugs like, steroid.



Osteoporotic vertebral body (right) shortened by compression fractures compared with a normal vertebral body (left)

□ Pathogenesis of osteoporosis

- Normally there is equilibrium between bone formation (osteoblastic activity) & bone resorption (osteoclastic activity).
- In osteoporosis there is loss of this equilibrium with **more bone resorption** (increase osteoclastic activity) averaging a 0.7% deficit from bone each year regardless of gender.
- **Age related decrease in bone density.** Occur in all individuals & in both sexes (after thirty).
- **Site: spine, distal radius & femoral neck** (commonest sites of fractures).
- **Decrease physical activity accelerates bone loss**
- In postmenopausal women, decreased estrogen levels promote increased osteoclastic activity.

□ Morphology of osteoporosis.

- **Gross;** Loss of bone mass (mainly trabecular bone, become thinner & more widely separated than usual, that result in increase susceptibility to fractures).
- **Mic.;** Thinning of trabeculae. Prominent osteoclasts.

❖ Inflammatory disorders of bones (Osteomyelitis)

- Inflammation of bone & marrow cavity.
- May be acute or chronic.
- Most common organisms are pyogenic bacteria & tuberculosis.

□ Pyogenic Osteomyelitis

- **Routes of infection are;**

- ****Hematogenous** dissemination, (most common route)

- ****Direct extension** from a focus of acute infection in the adjacent joint or soft tissue.

- ****Traumatic** implantation after compound fractures or orthopedics surgery.

- **Causative organism:** Staphylococcus aureus (most common organisms).

- In 50% of cases of pyogenic osteomyelitis, the causative organisms cannot be isolated because of previous antibiotic treatment, inadequate sampling for culture, or suboptimal methods of culture.

- **Clinical features:**

- Fever and leukocytosis

- Localized pain, erythema, and swelling.

◆ Morphology

- Morphologic changes are dependent on the chronicity and location of the infection.

□ Acute phase (first 48 hrs):

- Bacteria cause **neutrophilic inflammation**, Entrapped bone undergoes necrosis (**sequestrum**). Infection spreads to periosteum. large **subperiosteal abscess** forms, lifting periosteum which further compromises vascular supply and worsen necrosis. If periosteum ruptures, lead to a **soft-tissue abscess and a draining sinus**.

□ Chronic phase (after 1 week):

- Chronic inflammatory infiltrates **stimulate osteoclastic bone resorption**, ingrowth of fibrous connective tissue, and deposition of reactive bone (**involucrum**) around dead bone.
- **Histology:** Marrow fibrosis, sequestrum and an inflammatory infiltrate of lymphocytes and plasma cells.

□ Clinical Course:

- Antibiotics and surgical drainage are usually curative, although 5% to 25% of cases persist as chronic infections (usually due to extensive bone necrosis, inadequate therapy, or immunocompromise).

□ Complications include;

- Pathologic fracture, secondary amyloidosis, endocarditis, and development of squamous cell carcinoma in the sinus tract or sarcoma in the infected bone.

Tuberculous osteomyelitis.

- More in **immunocompromised** patients like AIDS.
- Usually **as a complication** of pulmonary T.B.
- Typical site of infection is the **synovium** (because of high concentration of O₂ at this area).

□ **Route of infection** is mainly by blood stream .

□ **Sites** thoracic and lumbar vertebrae (**Pott disease**) or long bones

□ **Complications** are

- Vertebral deformity.
- Cold abscess in psoas muscle.

□ **Mic.** granulomatous inflammatory reaction, with caseous necrosis.

❖ **Paget Disease (Osteitis Deformans)**

- **Paget disease is a condition of focal increase in bone mass, the excess bone is disordered and structurally unsound.**
- Uncommon under 40 years.
- Paget disease progresses through three stages:
 1. Osteolytic bone resorption
 2. Mixed osteolytic and osteoblastic activity
 3. Burnt-out, quiescent osteosclerosis

□ **Pathogenesis:**

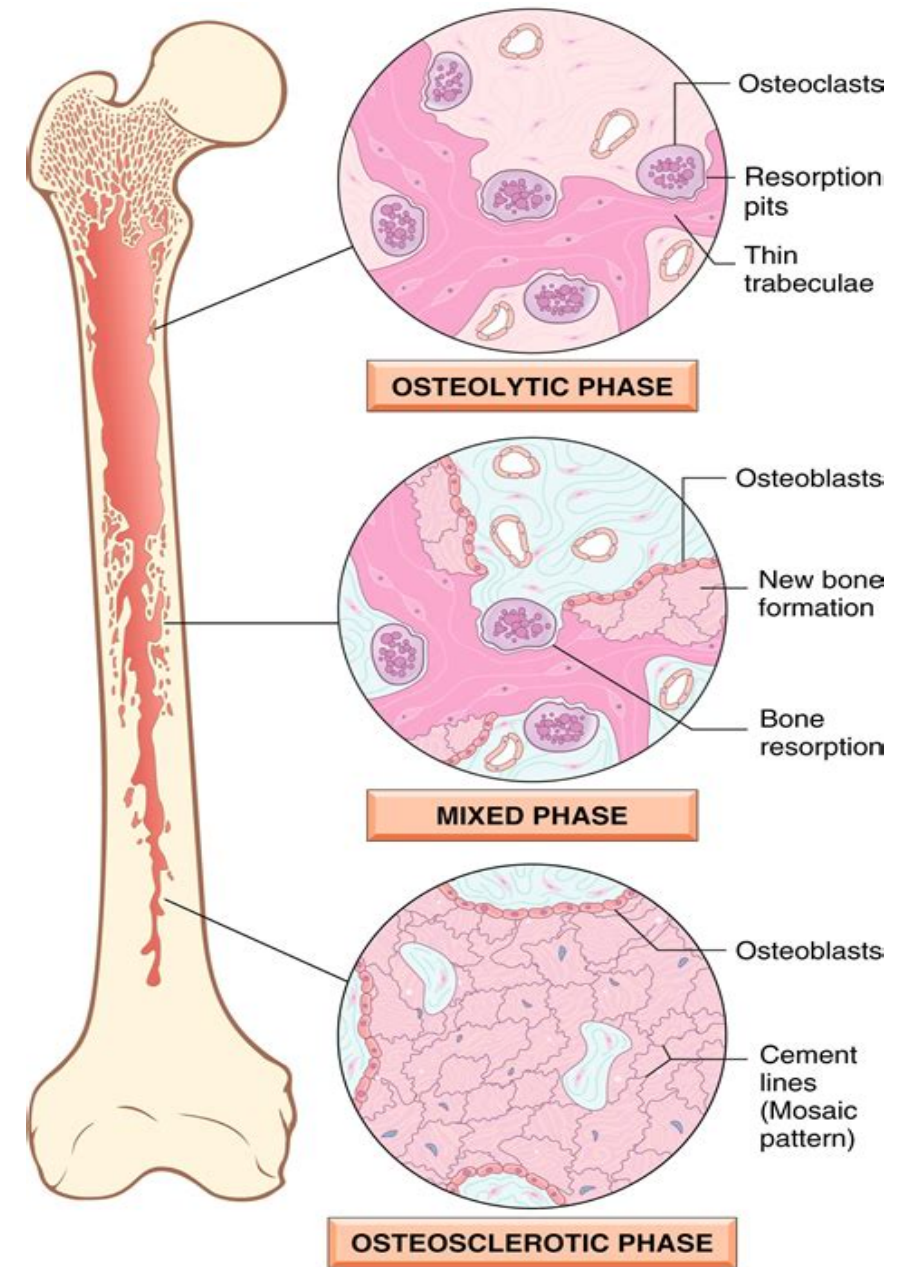
- Both environmental and genetic factors are implicated; mutations in the **SQSTM1 gene** are present in 50% of familial cases and 10% of sporadic cases.
- Cell culture studies have shown that **infection of osteoclast precursors** with viruses such as **Measles or other RNA viruses** can lead to increased bone resorption.

□ Morphology of Paget disease.

- The **initial lytic phase** is characterized by numerous large osteoclasts and resorption pits.
- **Mixed phase**; Osteoclasts persist but many of the bone surfaces are also lined by prominent osteoblasts.
- **The hallmark, seen in the sclerotic phase, is a mosaic pattern of lamellar bone.** The jigsaw puzzle–like appearance is produced by **prominent cement lines**, which join haphazardly oriented units of lamellar bone.

□ Complications:

1. Bone deformity (enlargement of head, kyphosis, scoliosis...).
2. Backache is due to involvement of vertebrae (vertebral fractures & nerve root compression).
3. Chalkstick fracture of long bones.
4. Osteosarcoma in less than 1% of cases.
5. High cardiac output failure in extensive cases





Tumors of bones

- Either **benign or malignant tumors**.
- **Malignant** tumors are **either primary or secondary** (metastatic tumors).
- **Metastatic tumors are much more common than primary malignancy of the bone.**
- The most common originating sites for bone metastases are (prostate, breast, lung, kidney, GIT (colon & thyroid)).
- **Most metastases are present as osteolytic lesions**; sometimes both **osteolytic & osteoblastic** lesions are seen in same metastases, other like metastases from prostate are mainly **osteoblastic lesions**.

□ **Classification of bone tumors:**

1. Bone forming tumors (like osteoma, osteosarcoma...).
2. Cartilaginous tumors. (chondromas, chondrosarcoma...).
3. Miscellaneous (Ewing sarcoma.....)

□ Osteoid Osteoma and Osteoblastoma

- Are benign bone producing tumors that have similar histologic features but differ clinically and radiographically.
- Male >female -ages between 10 and 30 years

□ Osteoid osteomas

- Are small (less than 2 cm)
- Involve the extremities- femur or tibia.
- They classically manifest with **nocturnal pain relieved by aspirin.** and other nonsteroidal anti-inflammatory agents.

□ Osteoblastomas

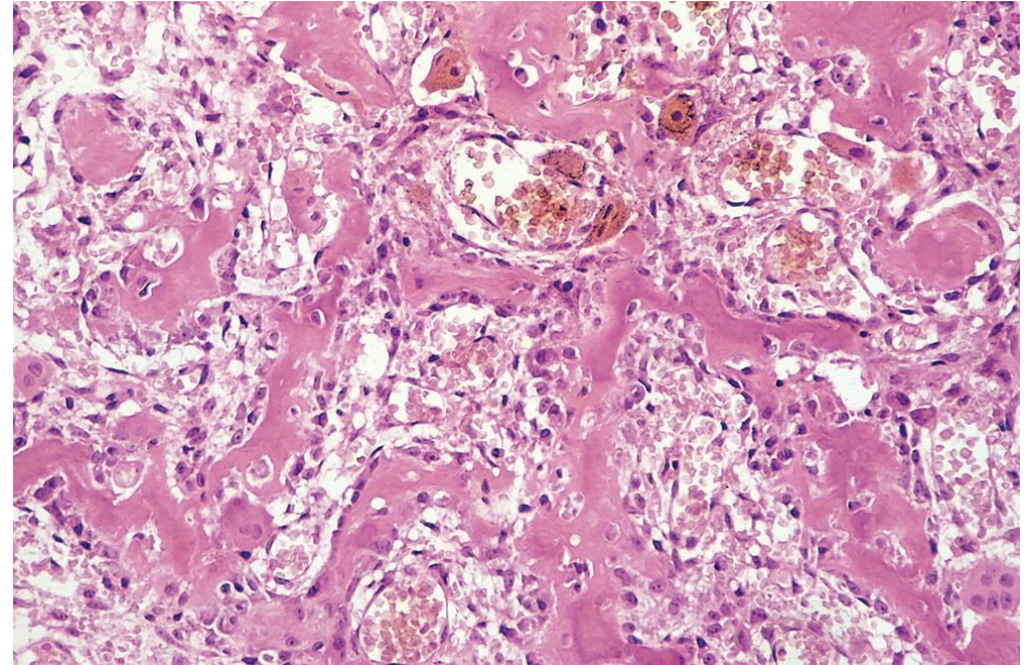
- Are longer than 2 cm,
- Involve the spine
- **The pain that is unresponsive to aspirin.**

Osteoid Osteoma and Osteoblastoma



Radiograph shows: central radiolucency surrounded by sclerotic rim.

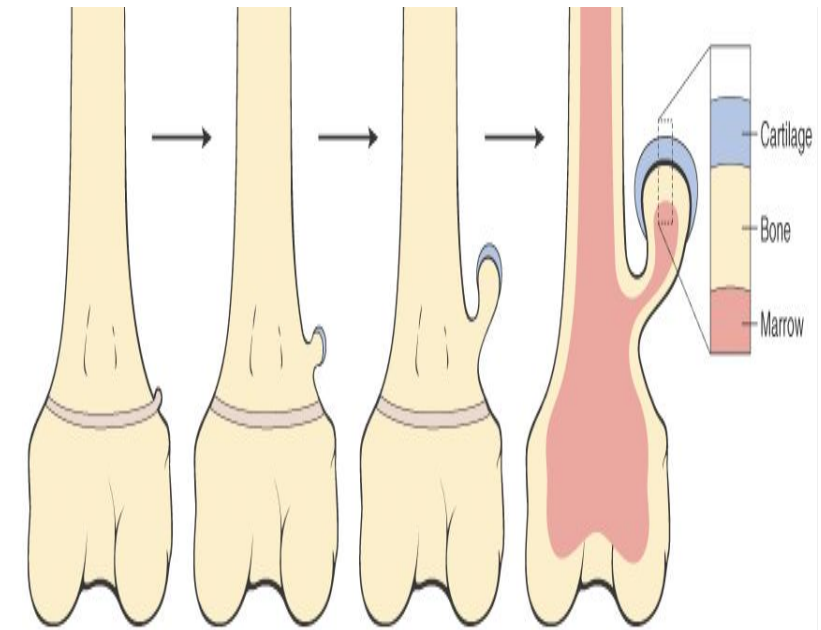
Gross: round-to-oval masses of hemorrhagic gritty tan tissue.



Mic.: Composed of haphazardly interconnecting trabeculae of woven bone that are rimmed by prominent osteoblasts. The intertrabecular spaces are filled by vascularized loose connective tissue.

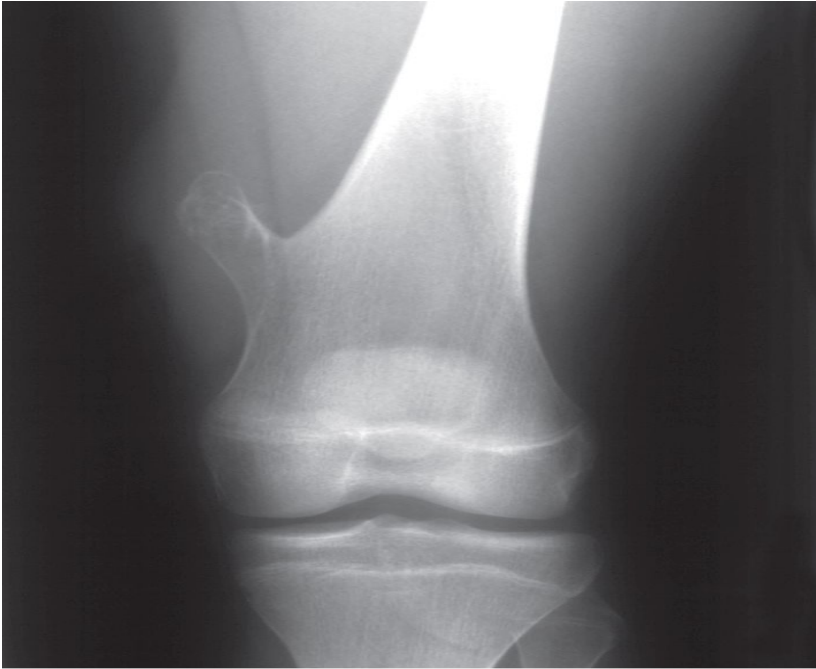
□ Osteochondroma (exostosis)

- Is a **benign cartilage-capped tumor** that is attached to the underlying skeleton by a bony stalk.
- **Male** to female ratio is 3:1
- Commonly develop in the metaphyseal region of long bones, especially near the knee.
- **Clinical feature:** present as slow-growing lesions that can be painful if they impinge on nerves or the stalk is fractured
- They rarely give rise to chondrosarcomas.
- **Grossly:** lesions are mushroom-shaped surface protrusions 1 to 20 cm in size.

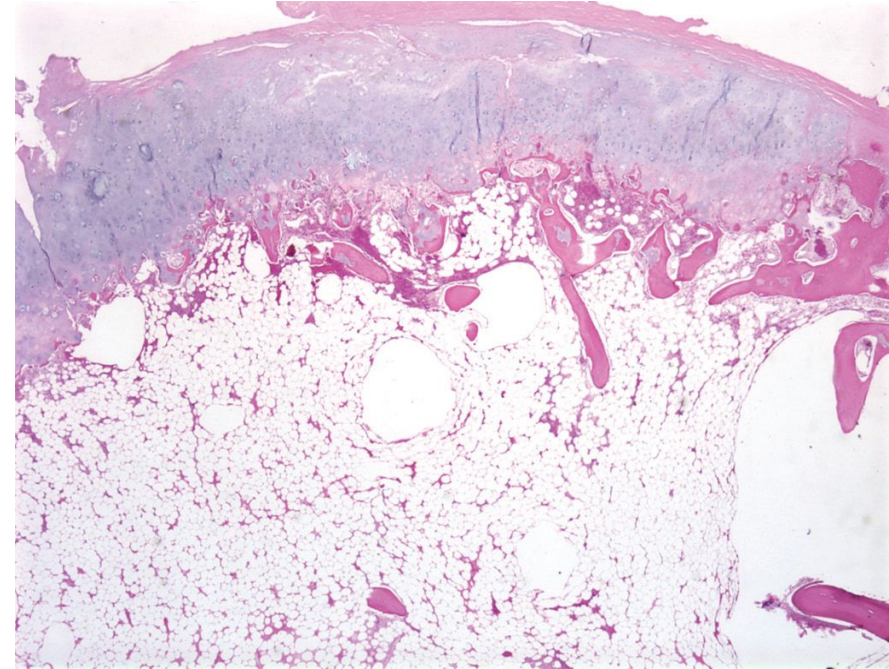


The development of an osteochondroma, beginning with an outgrowth from the epiphyseal cartilage.

Osteochondroma (exostosis)



Radiograph: an osteochondroma arising from the distal femur



Mic.: The cartilage cap (disorganized growth plate–like cartilage) with new bone forming the inner portion of the head and stalk. The cortex of the stalk merges with the cortex of the host bone resulting in continuity between the medulla of the osteochondroma and the host bone.

❖ Malignant bone tumors

□ Osteosarcomas (osteogenic sarcomas)

- **Is a malignant tumor that produces osteoid matrix or mineralized bone.**
- Most **common primary malignant** bone tumor after multiple myeloma.
- **Age:** 75% occur **before age 20 years**, with most of the remainder developing in **older** patients with known **risk factors** (e.g., Paget disease, bone infarct and radiation). Overall, **men** are more commonly affected than women (1.6:1).
- **Pathogenesis:** Approximately 70% of osteosarcomas have acquired genetic abnormalities; **p53 or RB** mutations; genetic abnormalities of **p16** (cell cycle regulator) and **p14** (aids p53 function) are also associated.
- **Sites:** metaphysis of long bones (distal femur, proximal tibia, & proximal humerus).
- **Clinical feature:** Present as painful, progressively enlarging masses. Sometimes a pathologic fracture is the first indication.
- **Sites of metastasis:** **lung (98%)**, other bones, rarely to lymph nodes, GI tract, liver, & brain.

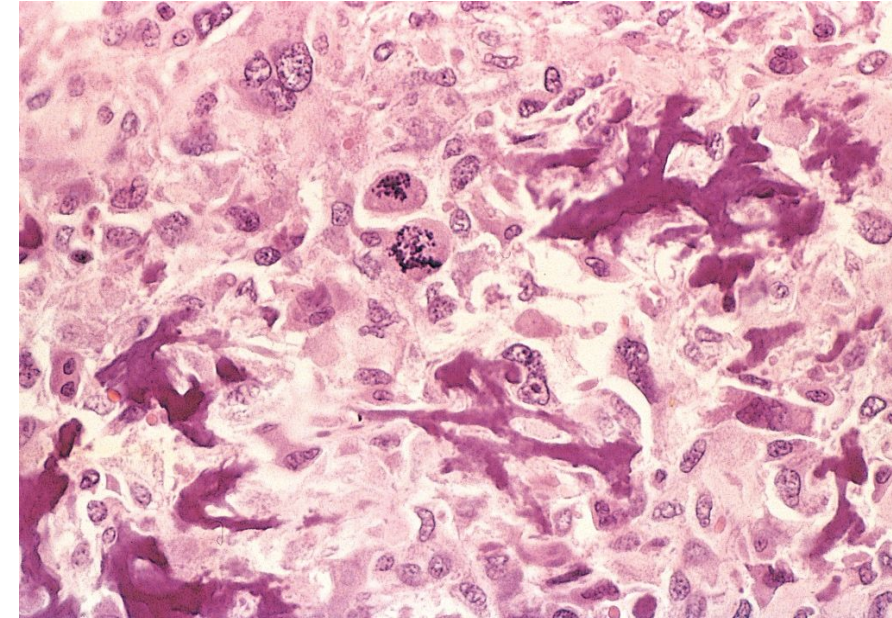
Osteosarcomas



Radiographs; show a large, destructive, mixed lytic and sclerotic mass with infiltrative margins. Codman triangle (periosteal elevation caused by tumor breaking through cortex). formation of new bone in a typical "sunburst" pattern.



Gross; bulky, gritty, tan-white tumor with areas of hemorrhage and cystic degeneration, fills the medullary cavity and destroy the surrounding cortices and produce soft tissue masses.

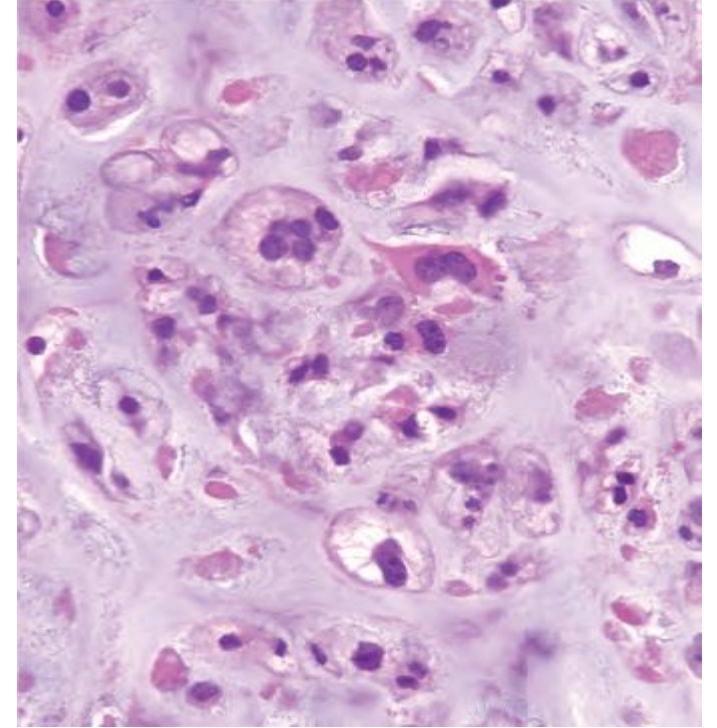
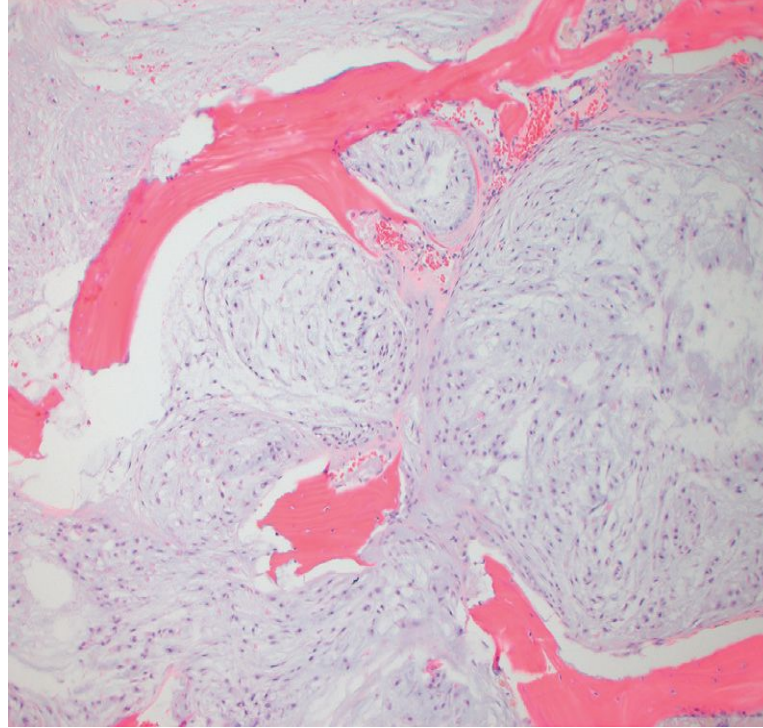


Mic.; Fine, lacelike pattern of neoplastic bone produced by anaplastic malignant tumor cells (pleomorphic, large hyperchromatic nuclei). Bizarre tumor giant cells and abnormal mitotic figure.

□ Chondrosarcomas

- **Chondrosarcomas are malignant cartilage-producing tumors.**
- **Age:** usually in 40s or older, and men are affected twice as frequently as women;
- **Sites:** arise in the axial skeleton, especially the pelvis, shoulder, and ribs.
- **Clinical features:** present as painful, progressively enlarging masses. The histologic grade correlates directly with biologic behavior.

Chondrosarcomas



- **Gross:** Nodules of hyaline and myxoid cartilage permeate the medullary cavity, grow through the cortex, and form a relatively well-circumscribed soft tissue mass.
- **Mic.:** The tumors vary in **cellularity**, **cytologic atypia**, and **mitotic activity** and are assigned a **grade from 1 to 3**. **Grade 1** tumors have relatively low cellularity, and the chondrocytes have plump vesicular nuclei with small nucleoli. By contrast, **grade 3** chondrosarcomas are characterized by high cellularity, extreme pleomorphism with bizarre tumor giant cells, and mitoses.

□ Ewing's sarcoma

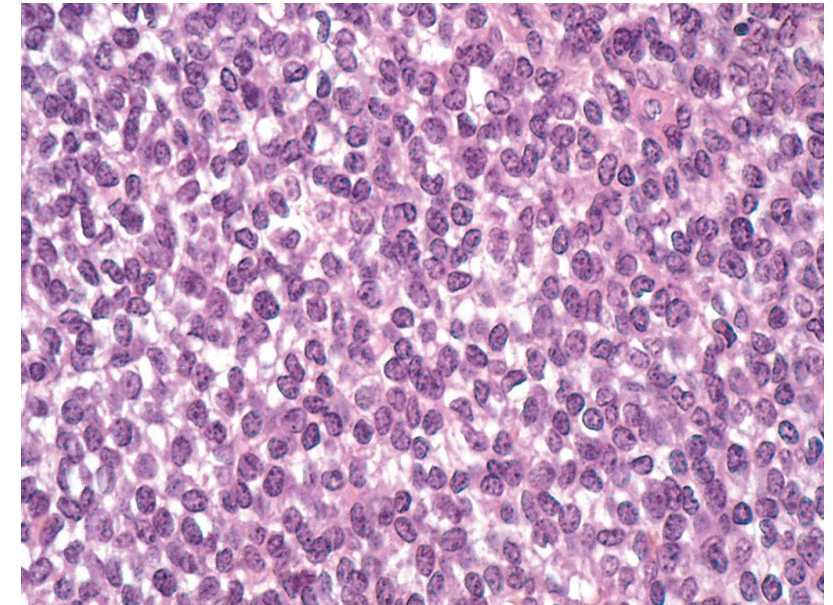
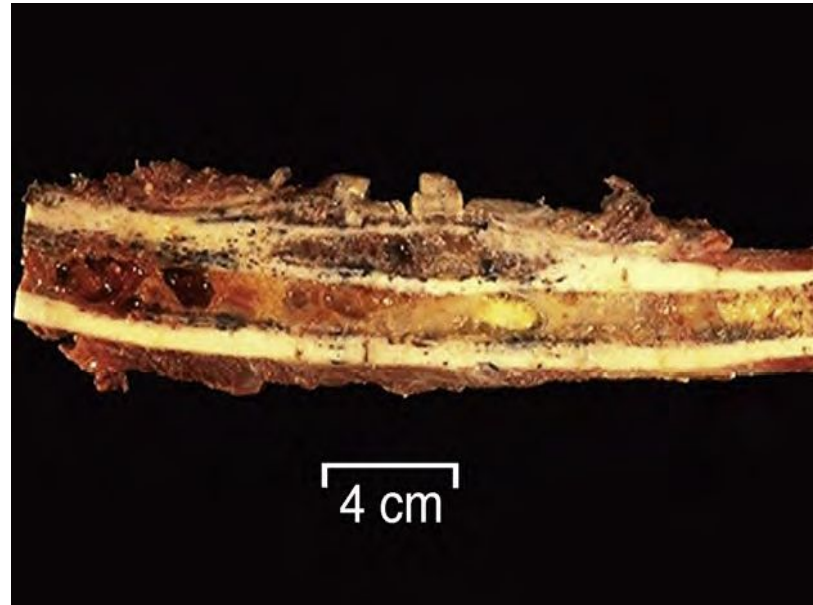
- It is a malignant bone tumor characterized by primitive round cells without obvious differentiation.
- **The second most common** bone tumors in children following the osteosarcoma.
- **Pathogenesis:** Greater than 90% of Ewing sarcomas contain a balanced translocation **t (11; 22)** which produces **EWS-FLI1 fusion gene**, that drive aberrant cell proliferation and survival.
- **Age:** Approximately 80% of patients are **younger than 20 years** of age. **Boys** are affected slightly more often than girls.
- **Sites:** **diaphysis** of long tubular bones, especially the femur and the flat bones of the pelvis.
- **Clinical features:** The affected site is frequently **tender, warm, and swollen**, and there may be systemic findings that mimic infection, including fever, elevated sedimentation rate, anemia, and leukocytosis.

Ewing's sarcoma

Ewing's Sarcoma



Onion Peel Appearance.



□ **Radiographs show;** destructive, lytic tumor with reactive periosteal bone resembling onion skin.

□ **Gross:** arises in the medullary cavity and invades the cortex, periosteum, and soft tissue. The tumor is soft, tan-white, and frequently contains areas of hemorrhage and necrosis

□ **Mic.:** Sheets of small, round, uniform cells with scant clear cytoplasm. **Homer-Wright pseudorosettes** (tumor cells arrayed in a circle about a central fibrillary space) may be present indicate neuroectodermal differentiation.

Thanks