

# Pathology of Musculoskeletal System “Practical”

Green: Males doctor notes.  
Grey: Females doctor notes.  
Red: Important.  
Purple: Key word for the cases.

Editing File



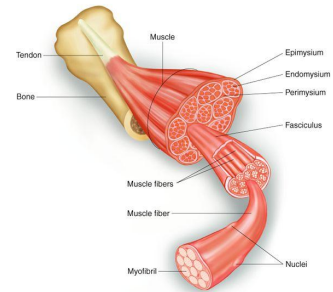
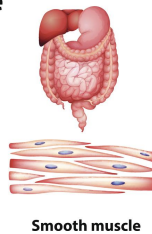
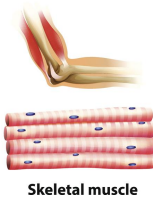
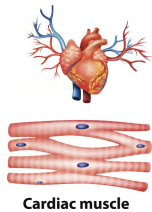
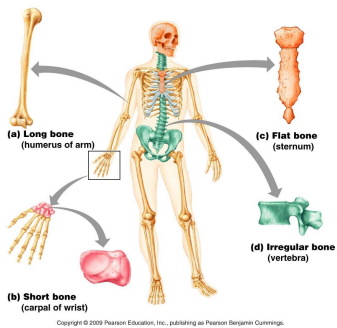
# Objectives

- Describe the normal structure of the musculoskeletal system.
- Identify the morphological features (gross and microscopic) of bone and joints' diseases and muscular dystrophies.

## Contents

- the anatomical and histological structure of bones and muscles.
- the gross and histopathological features of the following disorders through case discussion:
  - Duchenne Muscular Dystrophy.
  - Dermatomyositis
  - Myasthenia Gravis.
  - Myotonic Dystrophy.
  - Osteoporosis.
  - Osteoarthritis.
  - Rheumatoid arthritis.
  - Gout.
  - Osteomyelitis.
  - Pott's disease.
  - Osteochondroma.
  - Osteosarcoma.

## Types of Muscle



Types of muscles

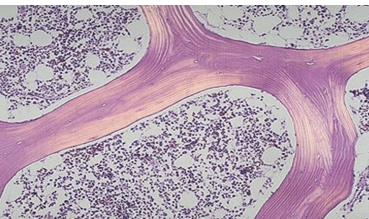
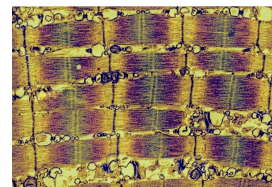
Components of skeletal muscle

Body Skeleton

Normal Cancellous bone -LPF

Sarcomere within a myofibril - HPF

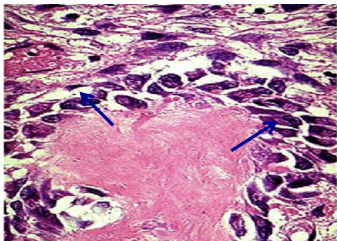
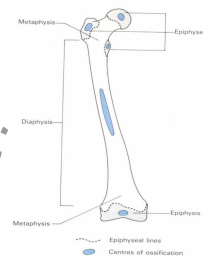
# Normal anatomy and histology



Normal cancellous bone as seen under polarized light microscopy, which highlights the lamellar structure. The bony spicules are even, with occasional lacunae containing osteocytes. Cellular marrow is seen between the spicules of bone.

Bone structure - HPF

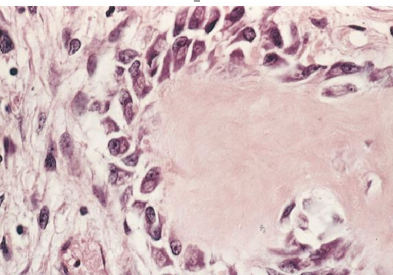
Long bone structure



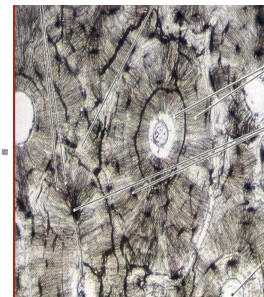
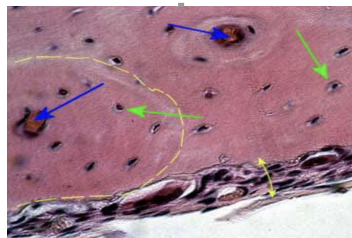
Active osteoblasts synthesizing bone matrix. The surrounding spindle cells represent osteoprogenitor cells.

Bone structure - HPF

Thin section of a compact bone



Bone structure - LPF



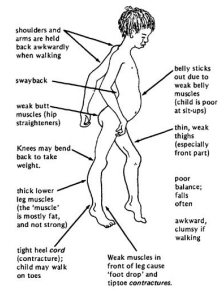
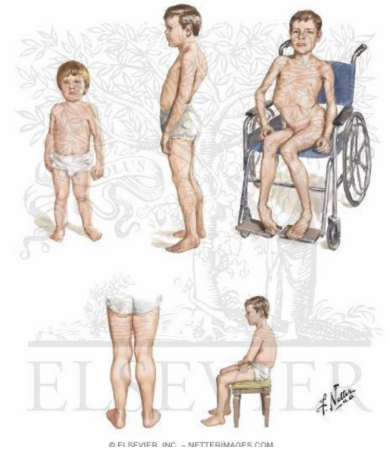
# Duchenne Muscular Dystrophy (DMD)

Key words:

- Western blot
- Fatigue unstable gait
- ABSENT dystrophin

## Case 1

- A 3 - year- old boy presented to his pediatrician with complaint of his parents from:
  - 1- difficulty in walking.
  - 2- poor balance.
  - 3- frequent falls.
- Laboratory investigation shows:
  - 1- **elevated** creatine kinase.
- Muscle biopsy shows:
  - 1- **absence of dystrophin** by western blot analysis

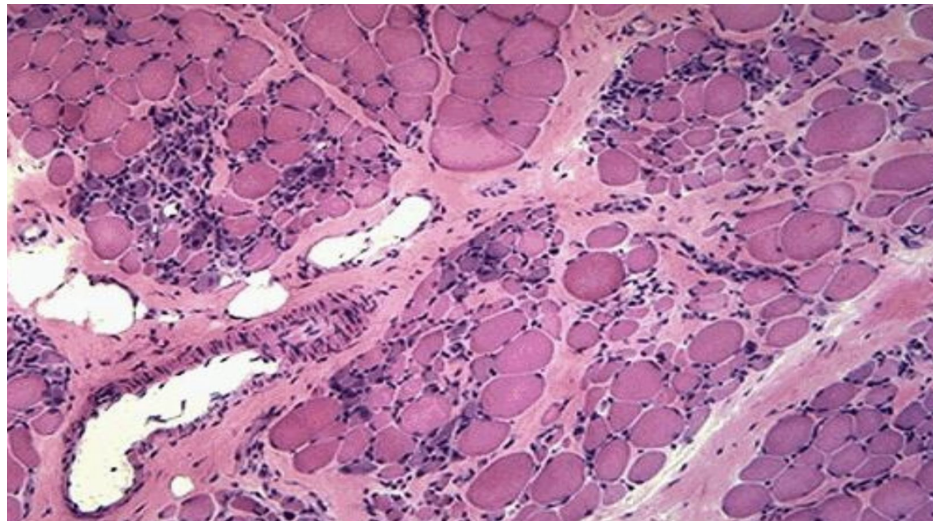


## What is your provisional diagnosis?

- DMD is the most severe and common type of muscular dystrophy.
- DMD is characterized by the wasting away of muscles.
- DMD affects mostly males at a rate of 1 in 3,500 births.
- Diagnosis in boys usually occurs between 16 months and 8 years.
- Death from DMD usually occurs by age of 30.

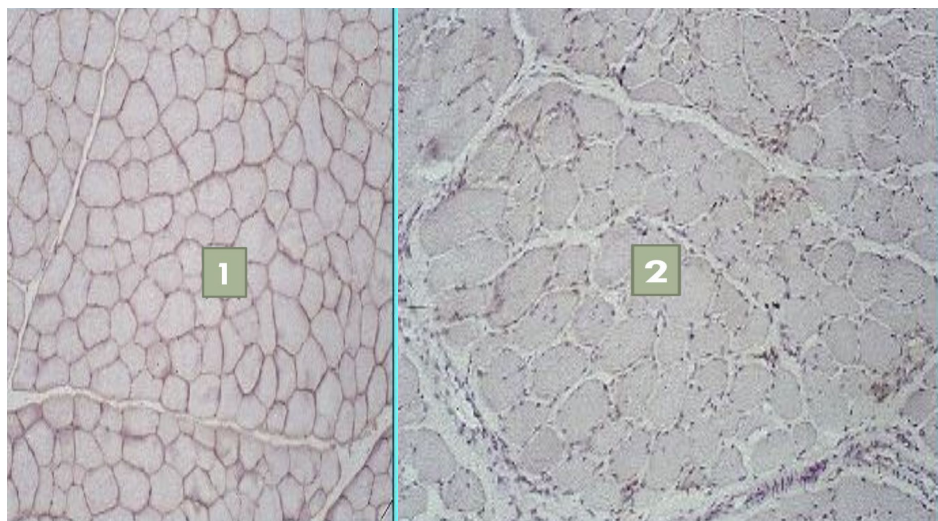
## DMD showing:

- 1- variations in muscle fiber size.
- 2- increased endomysial connective tissue.
- 3- regenerating fibers (blue tint) / (hyaline fibres).



In DMD : **Dystrophin**, an intracellular protein, forms:

- 1- an interface between the cytoskeletal proteins.
- 2- A group of transmembrane proteins.



- 1- Normal muscle
- 2- DMD

# Dermatomyositis

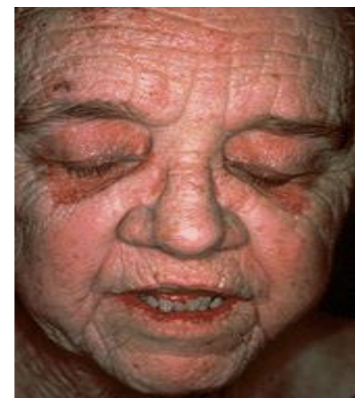
## Key words:

- Muscle weakness
- Skin rash
- Skin lesion
- Discoloration
- Elevated creatine kinase (muscle death)

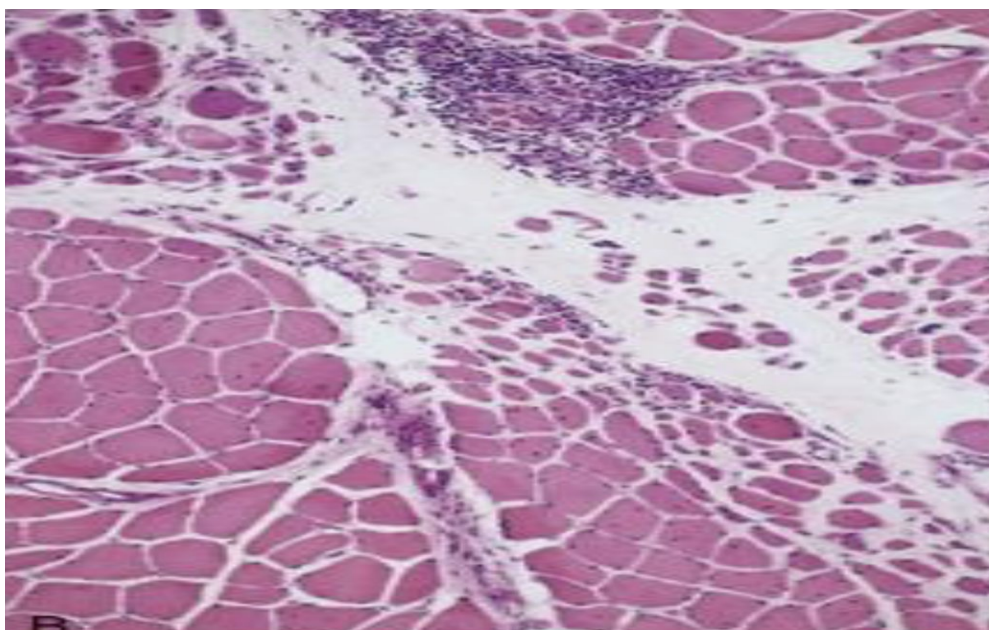
## Case 2

- A 52-year-old woman presents with:
  - 1- 6-month history of progressive muscle weakness
  - 2- skin rash.
- Physical examination is remarkable for:
  - 1- a diffuse purple/red discoloration of the skin over her cheeks, nose, and eyelids.
- Examination confirms
  - 1- proximal muscle weakness.
- Laboratory findings show:
  - 1- an **increase** in creatine kinase (10 times the normal).

- **Dermatomyositis** is an inflammatory myopathy characterized by:
  - 1- Inflammation of muscle tissue.
  - 2- Skin rash.
- Can occur in any individual with peak age patterns at: 5-15 years of age 40-60 years of age.
- Occurs more frequently in women.
- Purple/violet colored upper eyelids Purple-red skin rash.



Skin rash under the eyes



## Histology:

The histologic appearance of muscle shows:

- 1- **perifascicular atrophy** of muscle fibers.
- 2- **inflammation**.

# Myasthenia Gravis

## Key words:

- Antibodies
- Ptosis
- Fatigue
- Enlarged thymus (MIGHT be mentioned)

(creatine kinase might be elevated)

## Types of Myasthenia Gravis:

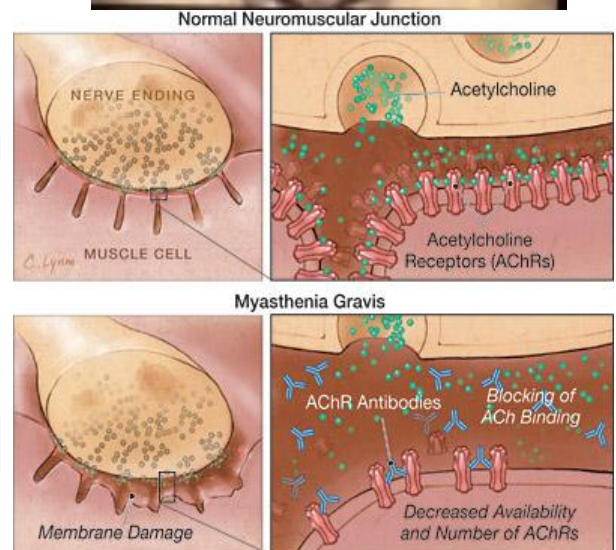
- **Neonatal Myasthenia Gravis:** A transient condition in 10% to 15% of infants born to mothers with MG.
- **Congenital Myasthenia.**
- **Juvenile Myasthenia:** Onset is around 10 years of age.
- **Ocular Myasthenia.**
- **Generalized Autoimmune Myasthenia.**

## Acquired autoimmune disorder:

- fundamental defect is a **decrease in the number of available AChRs at the postsynaptic muscle membrane.**
- simplification of the postsynaptic folds and widening of the synaptic cleft.

## Clinically characterized by:

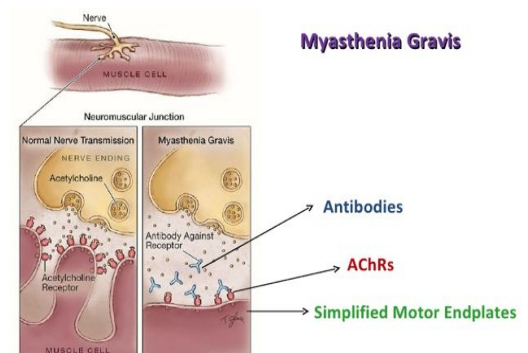
- Weakness of skeletal muscles
- Fatigability on exertion.



- Surface is flattened
- Less receptors

## Pathology of Myasthenia Gravis:

- The neuromuscular abnormalities in MG are brought about by an **autoimmune response** mediated by specific **anti-AChR antibodies**
- These antibodies reduce the available AChR's at neuromuscular junctions
- the **thymus is abnormal** in approximately 75% of patients with MG
- In 65% of patients the **thymus is hyperplastic**

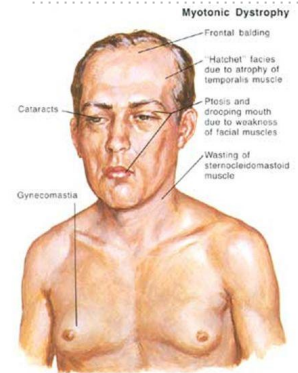


# Myotonic dystrophy

How do you know this is myotonic dystrophy?

- **Dystrophy**
- **Dystrophin is present** (will not be mentioned but this is how you differentiate between it and DMD)

- Also known as *dystrophia myotonica*
- Composed of 2 clinical disorders with overlapping phenotypes & distinct molecular genetic defects:
  1. **DM1**- the classic disease
  2. **DM2**- proximal myotonic myopathy
- **Autosomal dominant disease**

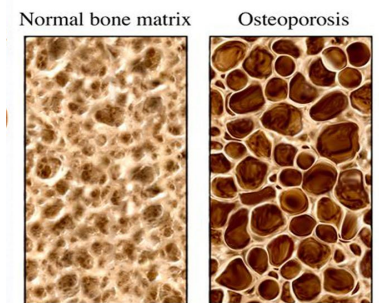


# OSTEOPOROSIS

Key words:

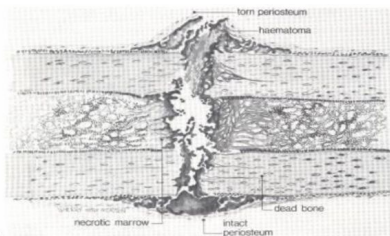
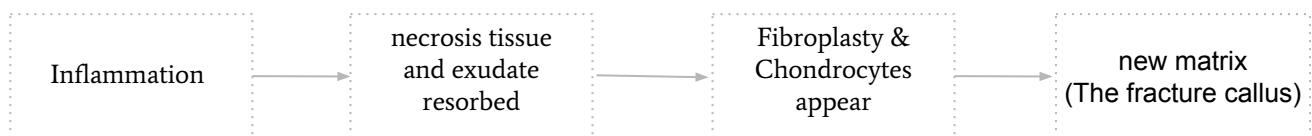
- **Old women**
- **Minor fall**
- **Hormonal replacement therapy** (or something along the line)

- A disease **characterized by:**
  - 1- low bone mass.
  - 2- microarchitectural deterioration of the bone tissue.
- **Leading to:**
  - 1- enhanced bone fragility.
  - 2- increase in fracture risk.

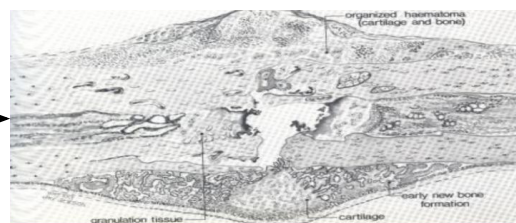


Inflammation → necrosis tissue and exudate resorbed → Fibroplasty & Chondrocytes appear → new matrix (The fracture callus)

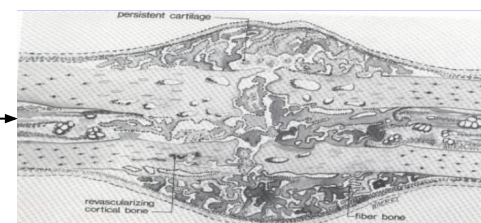
## STAGES OF FRACTURE HEALING



Inflammation



Bone Healing



Repair

# Osteoarthritis

Key words:

- Overweight person (OBESE)
- Long term difficulty in moving
- Hip replacement
- Pain

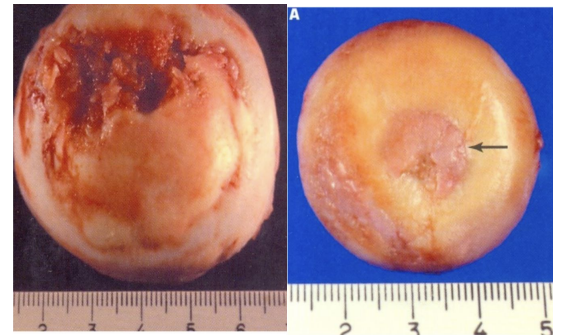
## Case 3

An obese 56-year-old woman presented with:  
1- bilateral localized pain to her knees and hands  
2- difficulty in walking .



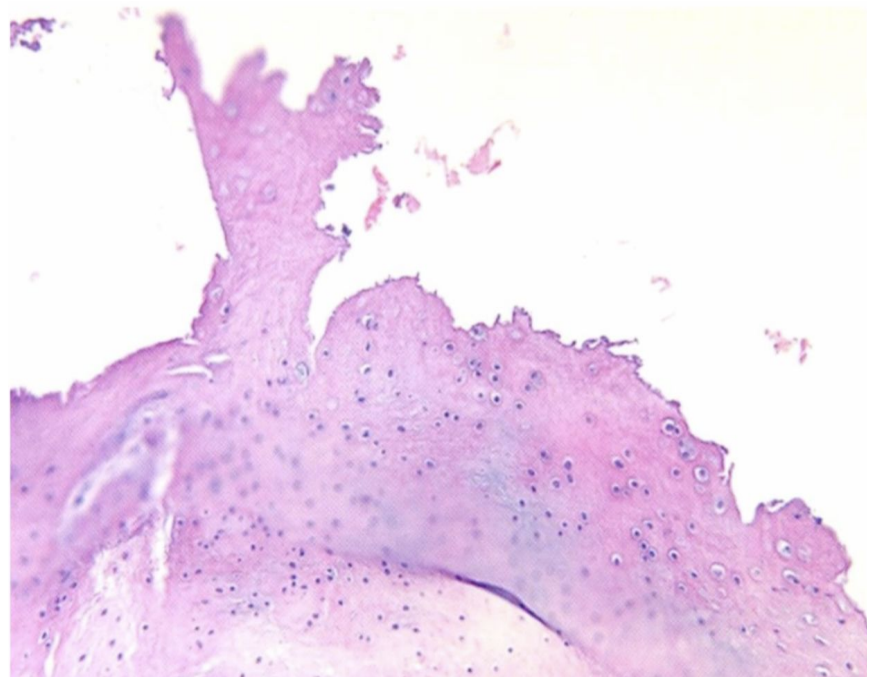
## Osteoarthritis - Gross

- 1- Progressive erosion of articular cartilage
- 2- eburnated articular surface
- 3- subchondral cyst
- 4- residual articular cartilage (Osteoarthritis)

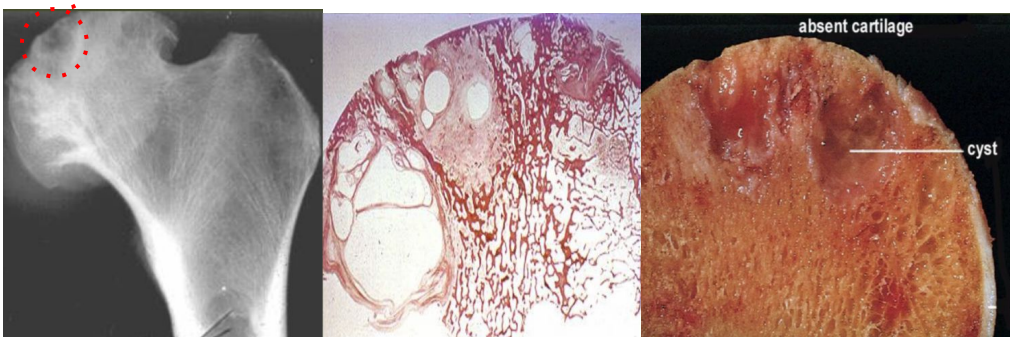


## Osteoarthritis - LPF

- 1- **Mushroom-shaped osteophytes** (bony outgrowths ) develop at the margins of the articular surface and are capped by fibrocartilage and hyaline cartilage that gradually ossify.
- 2- Note the **ABSENCE of inflammation**.



Cyst





# Rheumatoid Arthritis

Key words:

- Women
- Morning stiffness

## Case 4

A 45-year-old woman **complains of:**

- 1- Low grade fever.
- 2- Malaise.
- 3- Stiffness in her joints each morning.

- Ulnar deviation of fingers
- Radial deviation of wrist

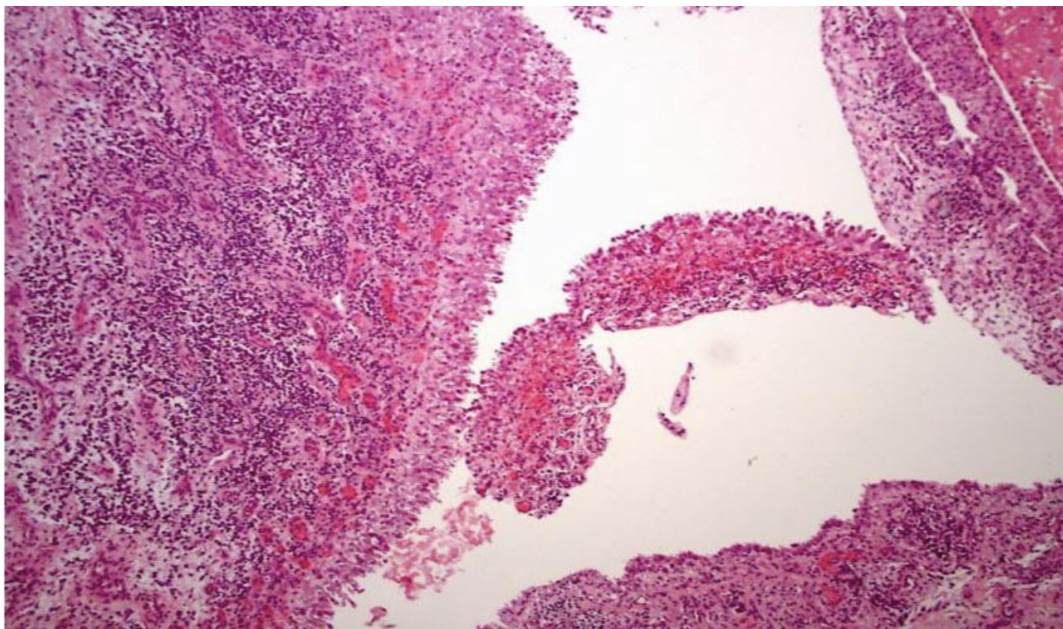
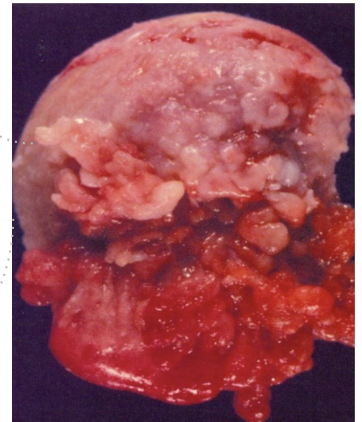


## Rheumatoid Arthritis - Gross

- Affecting the **head of the femur**.
- The **synovium** becomes:
  - 1- edematous
  - 2- thickened
  - 3- hyperplastic
  - 4- transforming its smooth contour to one covered by delicate and bulbous fronds .

Diagnosis? RA  
in the the of  
the femur

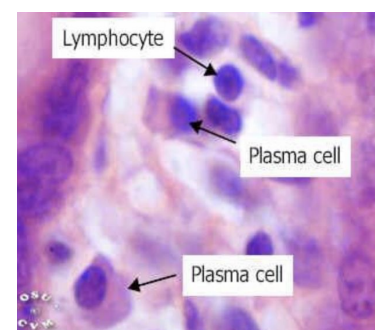
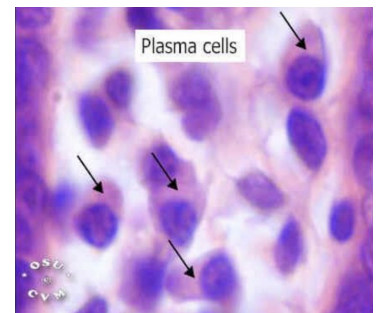
Also: - Edema  
- Redness  
- finger-like projections



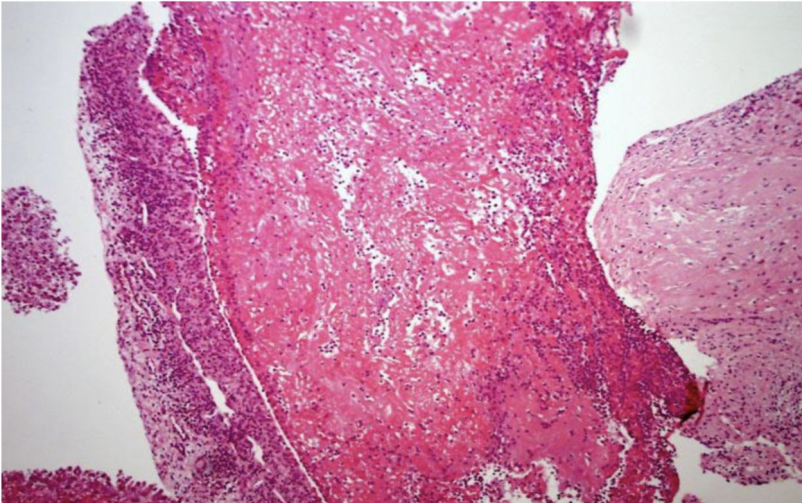
### Hyperplastic Synovium - LPF

**Hyperplastic synovial lining** with:

- 1- villous-like (finger-like) projections.
- 2- underlying dense **lymphocytic** infiltration
- 3- vascular congestion (congested RBCs) Cells: lymphocytes and plasma cells

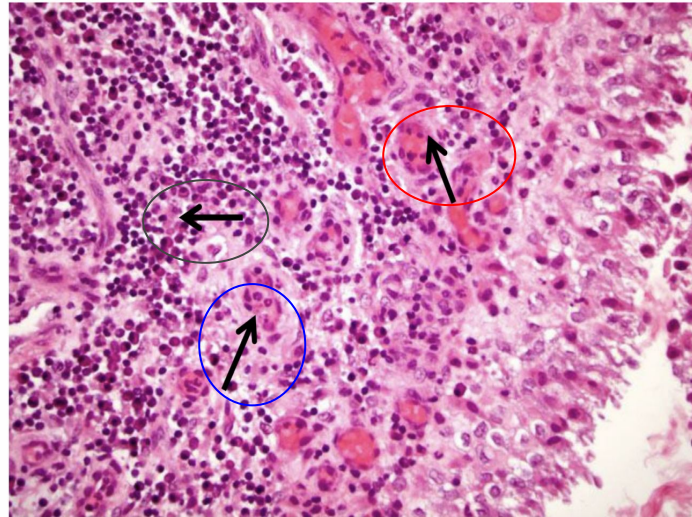


# Rheumatoid Arthritis Cont'



## Hyperplastic Synovium - LPP

Section shows a **pannus** (the middle red area) consisting of:  
 1- fibrinous inflammatory exudates  
 2- underlying markedly inflamed synovium.  
 Later on, the pannus may fill the joint space and undergo:  
 1- fibrosis  
 2- calcification  
 causing permanent ankylosis adhesions



## Hyperplastic Synovium - HPF

**Hyperplastic synovium** with:  
 1- underlying plasma cells  
 2- lymphocytes  
 3- many congested blood vessels

Upper arrow: plasma cells  
 Middle arrow: Vascular congested blood vessels  
 Lower arrow: lymphocytes

# GOUT

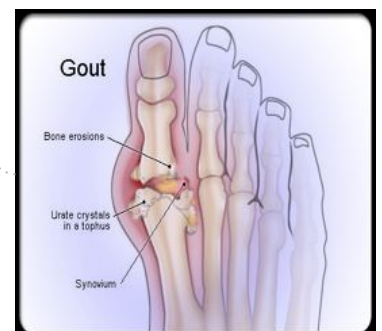
**Key words:**

- High meat consumption
- Tests for uric acid
- Inflammation in the big toe

Most common site: first metatarsophalangeal joint

**Gout:** a syndrome caused by the inflammatory response to tissue deposition of **monosodium urate crystals (MSU)**

Remember: in pseudogout the crystals are calcium-biphosphate crystals



**Acute gouty arthritis** on the big toe of an elderly man.



# GOUT Cont'

- **Severe gout** in the fingers resulting in:
  - large, hard deposits of crystals of uric acid called **Tophi**



**Needle-shaped urate crystals** diagnostic of gout from an acutely inflamed joint (left) as seen under polarized microscopy and unpolarized microscopy (right)



## Osteomyelitis

### Case 5

A 22- year- old male presented with:

- localized pain above his right knee joint.
- recurrent fever.
- Later, he had a discharging sinuses from the skin overlying the right knee.

Hint: fever means it is an infection or inflammation

#### Key words:

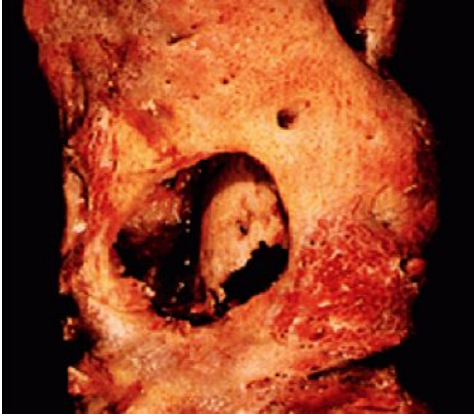
- Bacteria in pus from **sinus**
- Recent travel

What is the most likely diagnosis ?

#### What is osteomyelitis?

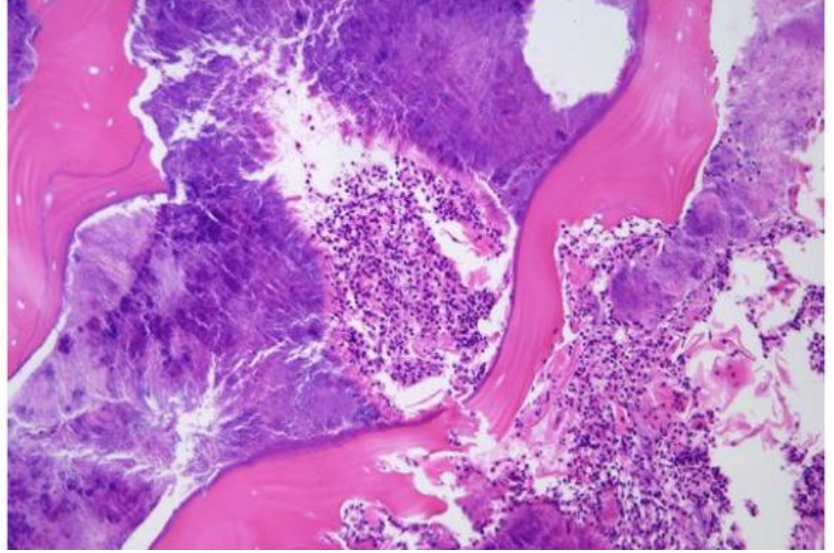
- Direct infection of bone
- Bacterial most often
  - Staphylococcus
  - Salmonella (Sickle Cell Disease)
  - Tuberculosis (Spine first)
  - Syphilis (Periosteum)

# Osteomyelitis Cont'



## Osteomyelitis - gross

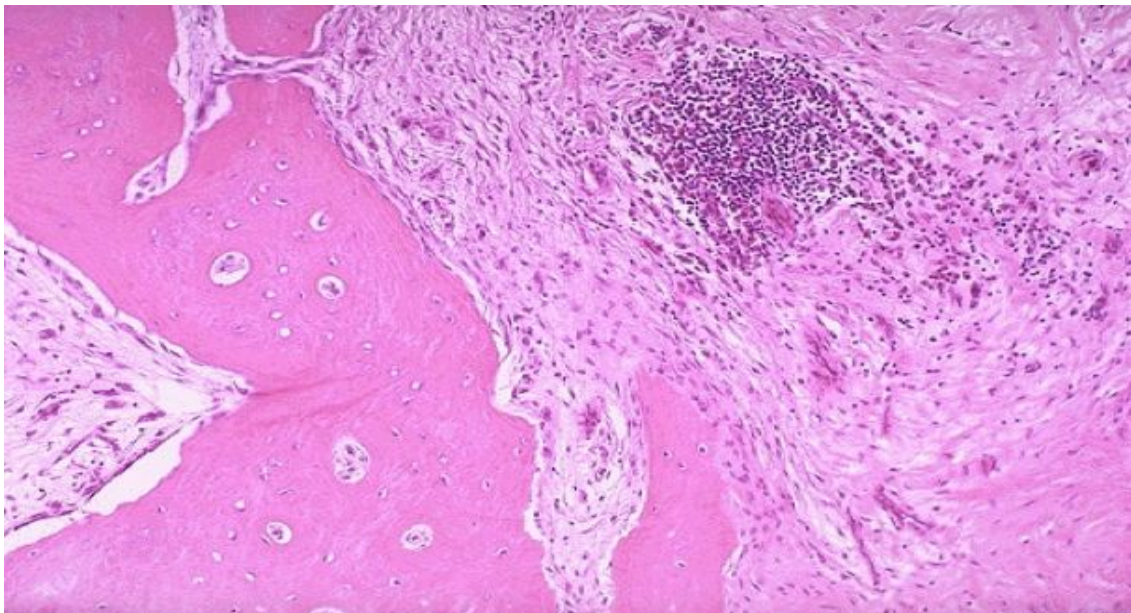
Resected femur in a patient with **draining osteomyelitis**. The drainage tract in the subosteal shell of viable **new bone (involucrum)** reveals the inner native **necrotic cortex (sequestrum)**



## Osteomyelitis - LPF

### Acute Osteomyelitis:

- 1- Bony sequestrae
- surrounded by:
- 2- colonies of bacteria as well as
  - 3- purulent infiltrate.



## Osteomyelitis - LPF

### Chronic Osteomyelitis:

- 1- fibrosis of the marrow space
- 2- chronic inflammatory cells. There can be bone destruction with remodeling.

How do you know it is chronic? There is fibrous tissue

# Spinal TB – Pott’s Disease (Tuberculous Osteomyelitis)

Key words:

- Blood coughing
- Kyphosis
- Scoliosis
- Spine

## Case 6

A 30 -year-old debilitated man presented to the orthopedic clinic with:

- back pain.
- low grade fever.
- marked elevation of sedimentation rate.
- recent kyphosis and scoliosis .

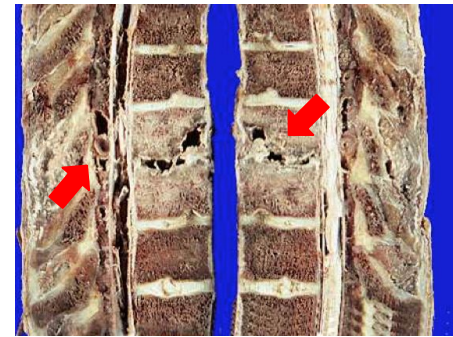
The patient has a history of:

- Coughing up blood.
- Fever.
- Chills
- night sweats
- Weight loss
- pallor
- Tendency to fatigue very easily

### T.B. Osteomyelitis of the vertebral spines (Pott’s Disease) - Gross



Granulomatous necrosis of vertebral column

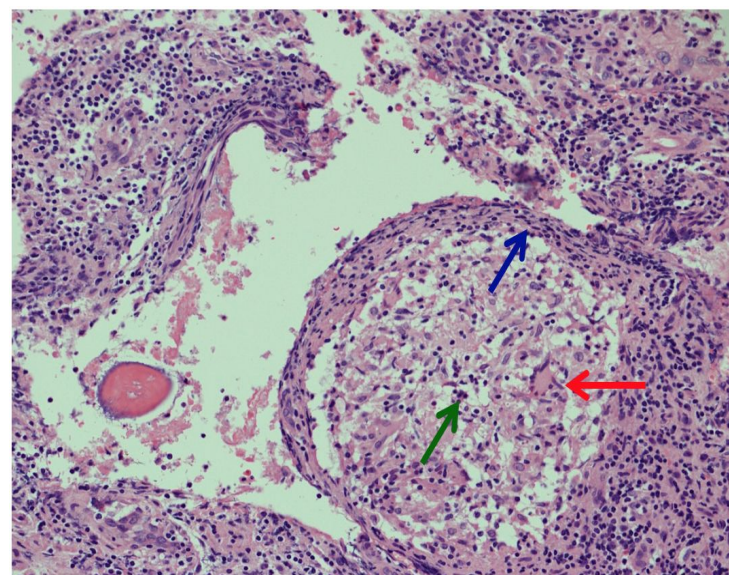
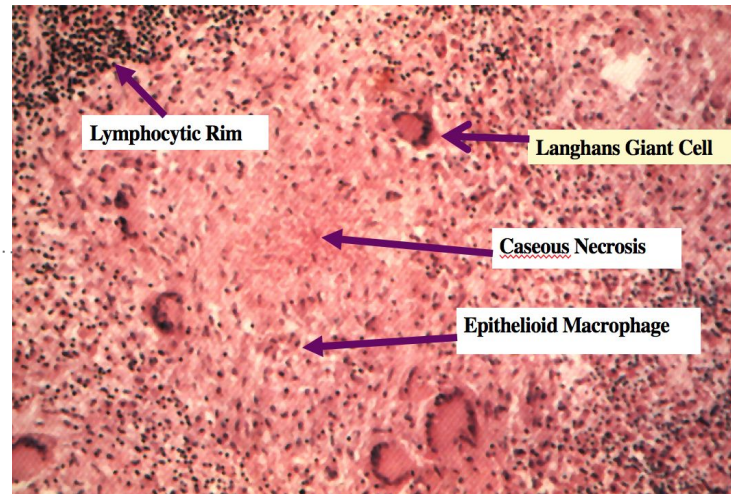


Necrotizing granuloma (very common in TB)

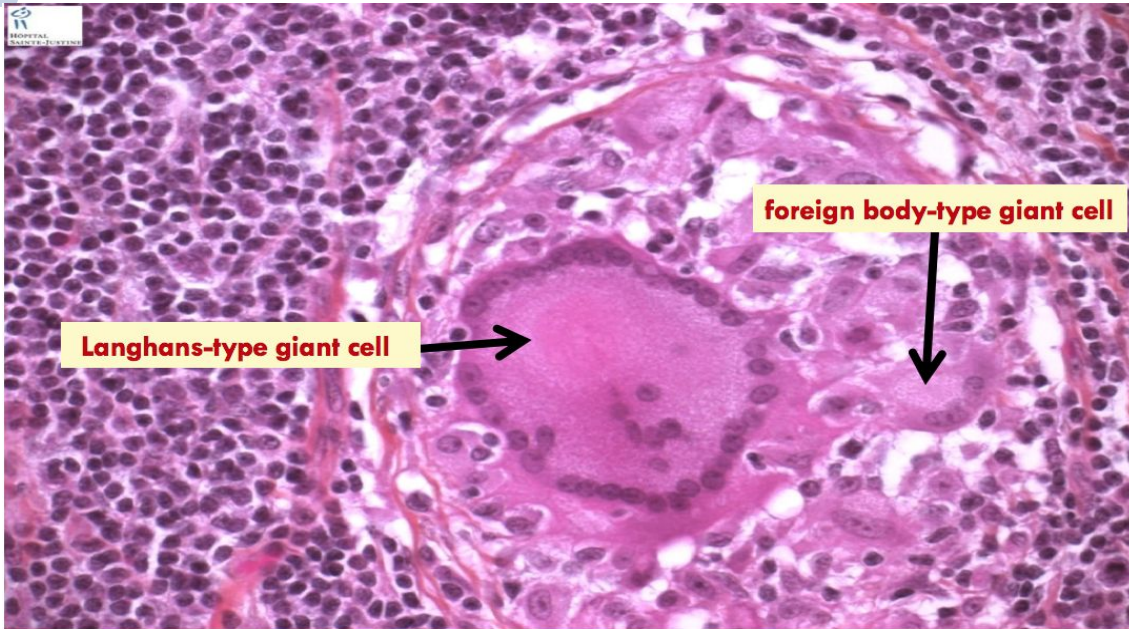
Section of bone shows **granuloma formation** with:

- epithelioid like cells.
- langhans-type giant cells.
- rim of lymphocy.

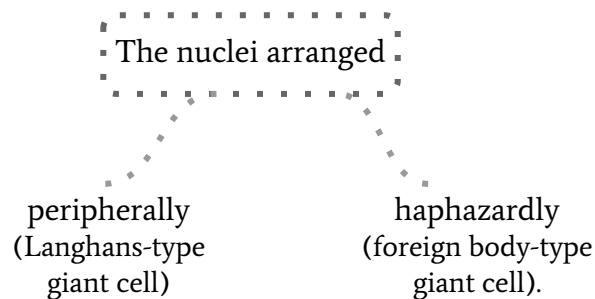
Coloring based on the arrows on the second picture



# Spinal TB – Pott's Disease (Tuberculous Osteomyelitis) Cont'



Bone section shows **Epithelioid cells** fuse to form giant cells containing 20 or more nuclei.



These giant cells can be found either at the periphery or the center of the granuloma.



# Bone Tumors

- Doctors recommended reading this part from Robbin's (Pages in Robbins 10th edition: 809-811)
- Questions on this part may come as practical (picture identification) or theoretical.

# Osteochondroma (osteochondroma exostosis)

Key words:

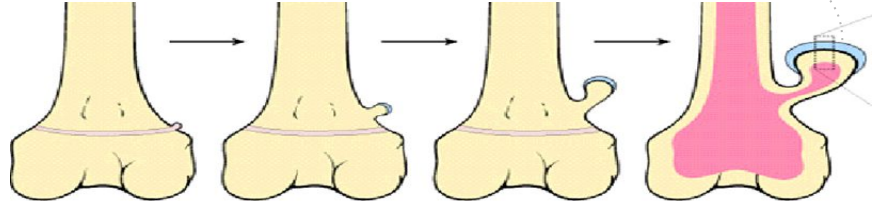
- YOUNG person
- Slowly developed pain in the joints
- Asymmetry in lesion

BENIGN

Cartilage & bone

The solitary osteochondroma is the most common benign bone tumors

- Seen in patients aged from 10-30 years
- Arise during skeletal growth
- Equally in males and females
- Etiology is unknown



## Case 7

A 16-year-old male was found to have a small swelling protruding from upper part of his leg with local pain.

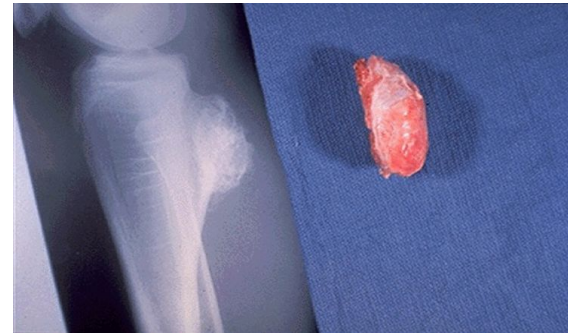
### Osteochondroma: Gross & X-ray

benign lesion appears as a bony projection (**exostosis**).

Most are solitary, incidental lesions that may be **excised if they cause local pain**.

There is a **rare** condition of **multiple osteochondromatosis** marked by:

- 1- bone deformity
- 2- a greater propensity for development of chondrosarcoma.



Osteochondroma: X-ray

Outgrowth in the lower end of a femur consisting of cartilage and bone



MRI picture showing two osteochondromatous exostosis which are arising from the upper third of fibula .



Multiple Cartilaginous Exostoses  
- Gross

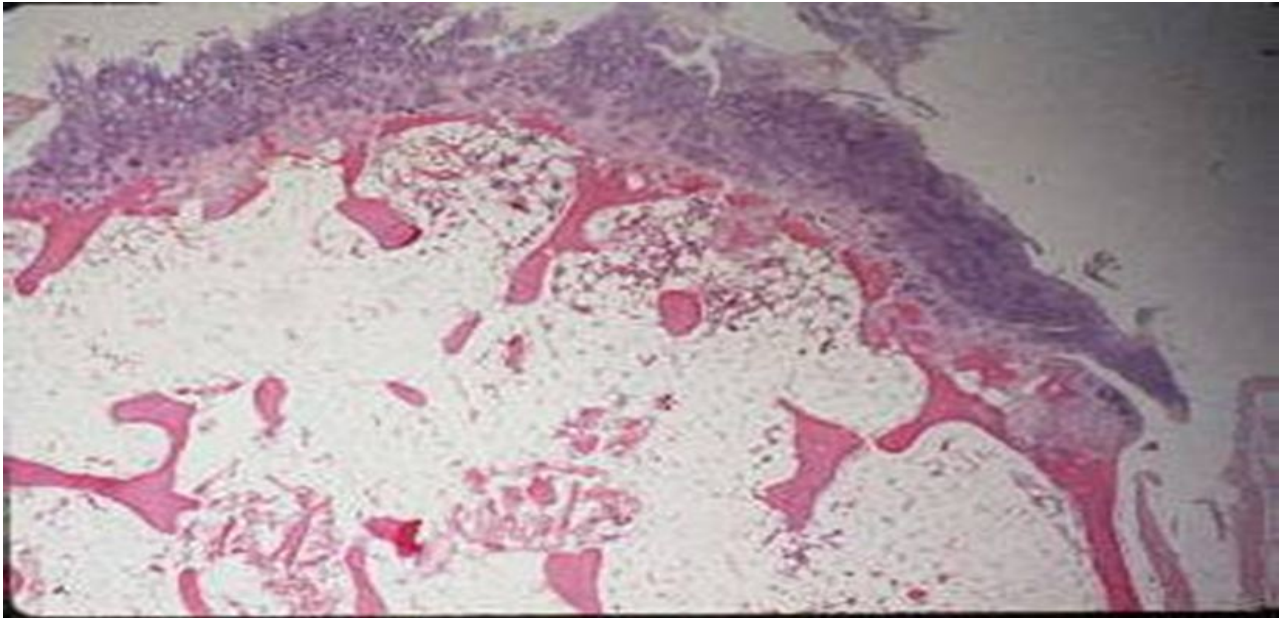


Layer 1: fibroscap  
Layer 2: hyaline cartilage  
Layer 3: bone & bone marrow

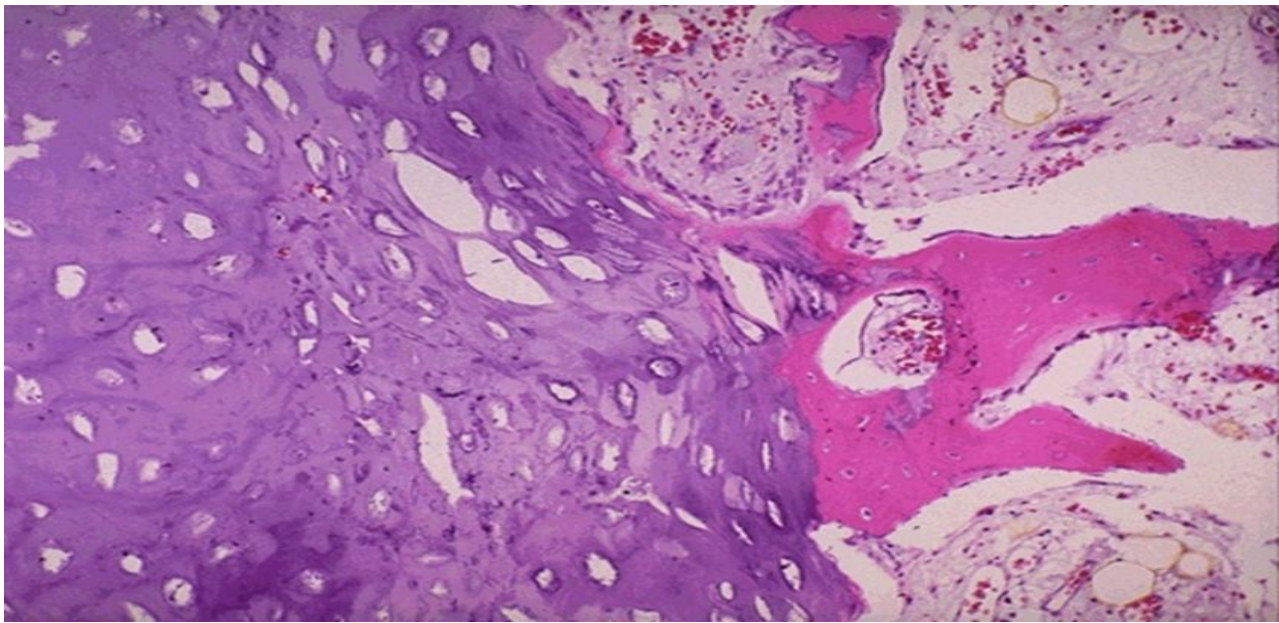
Solitary osteochondroma, Gross osteochondroma specimen at the time of resection.  
Bone stalk and overlying membrane on cartilage cap.



# Osteochondroma (osteochondroma exostosis) **Cont.**



Osteochondroma - LPP



Osteochondroma - HPF

The microscopic appearance of an osteochondroma displays

- 1- the **benign cartilaginous** cap at the upper
- 2- the bony cortex at the left lower.

This bone growth, though benign, can sometimes cause problems of **pain** and **irritation** that leads to **removal surgically**.

# Osteosarcoma

Based on scans and histopathology

Key words:

- Multiple exostomas
- Pain

## Primary Malignancy

- Osteoblast is malignant cell.
- Weight bearing Long bones.
- **Young people**, Osteosarcoma has a bimodal age distribution; 75% of osteosarcomas occur in persons younger than 20 years of age.
- Genetics of tumor being unraveled.

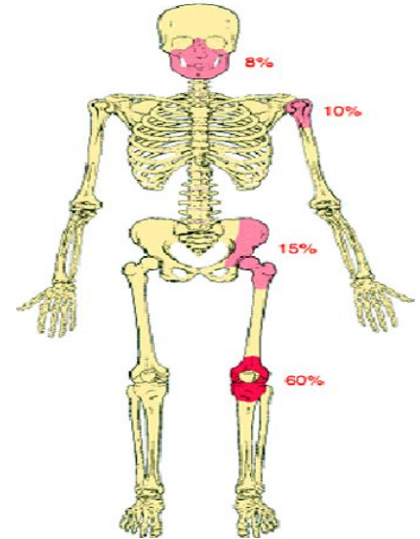
The smaller second peak occurs in older adults, who frequently suffer from conditions known to predispose to osteosarcoma, such as:

- Paget disease
- bone infarcts
- previous radiation.

These are referred to as **secondary osteosarcomas**.

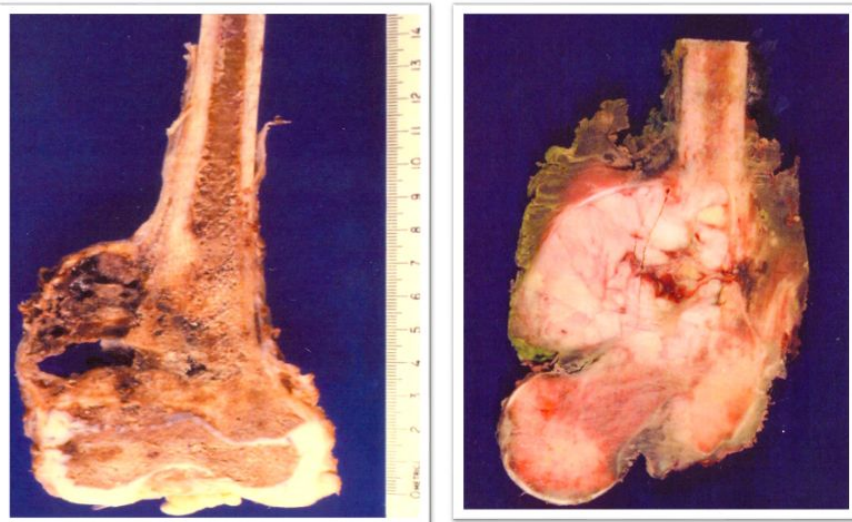
- 2nd most common primary bone tumor.
- Malignant tumor of mesenchymal origin

DISTRIBUTION OF OSTEOSARCOMA

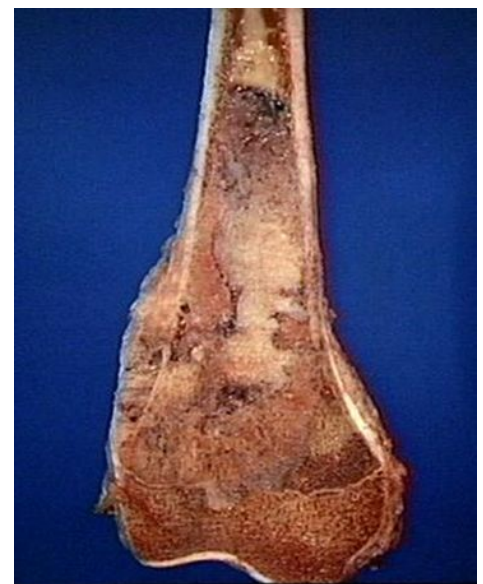


## Case 8

An 18-year-old female presented to the rheumatology clinic with 2 months history of pain and swelling in her upper thigh with weight loss.



- Mixture of:
- 1- osteoid
  - 2- fibrous
  - 3- cartilaginous
  - 4- necrotic
  - 5- hemorrhagic
  - 6- cystic areas



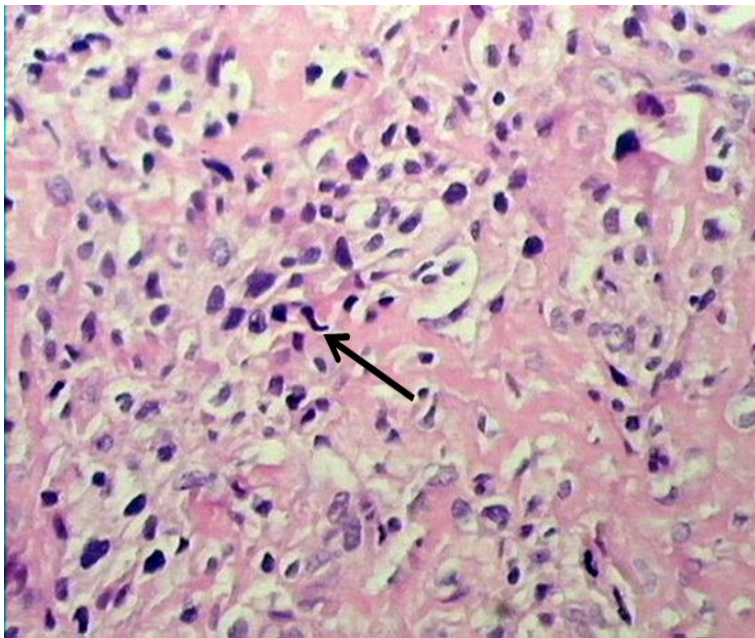
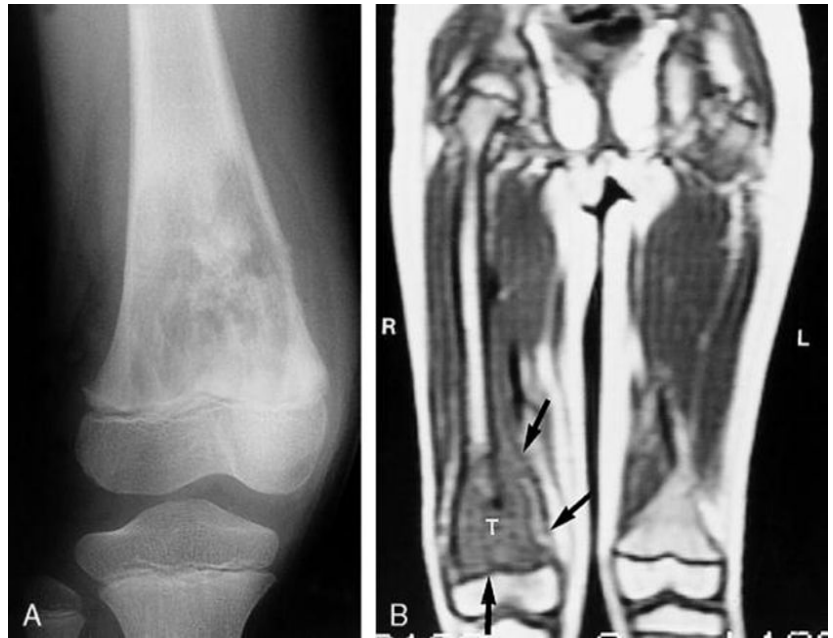
**Osteosarcoma of the upper end of the tibia.** The tan-white tumor fills most of the medullary cavity of the metaphysis and proximal diaphysis. It has infiltrated through the cortex, lifted the periosteum, and formed soft tissue masses on both sides of the bone.

# Osteosarcoma Cont.

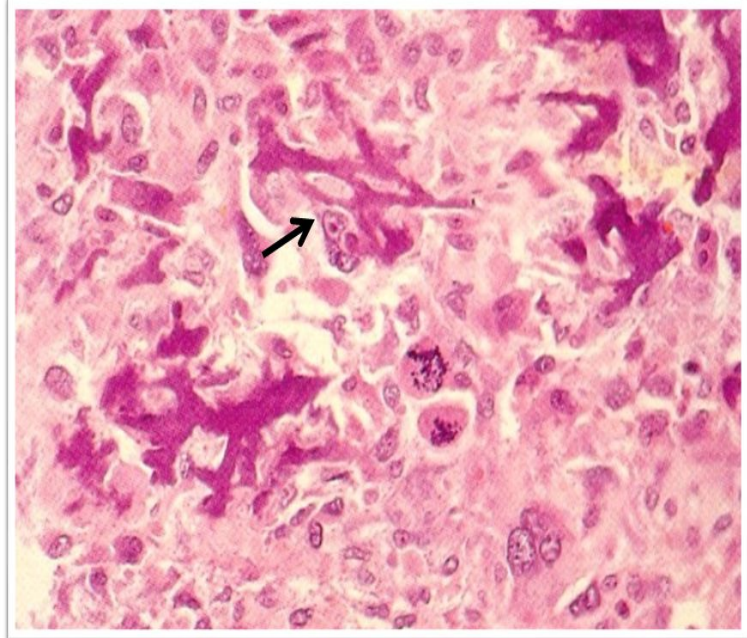
## Central Osteosarcoma

A: destructive lesion is seen in the metaphysis on this anteroposterior view of the knee in a **young teenager** with pain.

B: magnetic resonance scan of both legs shows soft tissue extent of the tumor (arrows).



Osteosarcoma - HPF



Osteosarcoma - LPF

- Spindle shaped cells producing osteoid (the arrows: abnormal osteoblasts).
- Mitotic figures

This lecture was done by ★

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# Thank you

