

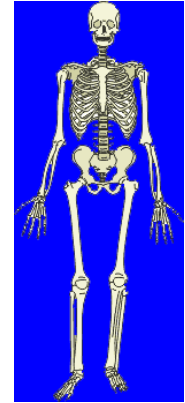
# Metabolic bone disease histopathology

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Department of Histopathology

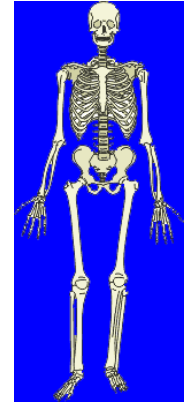
Charing Cross Hospital

# The function of bone



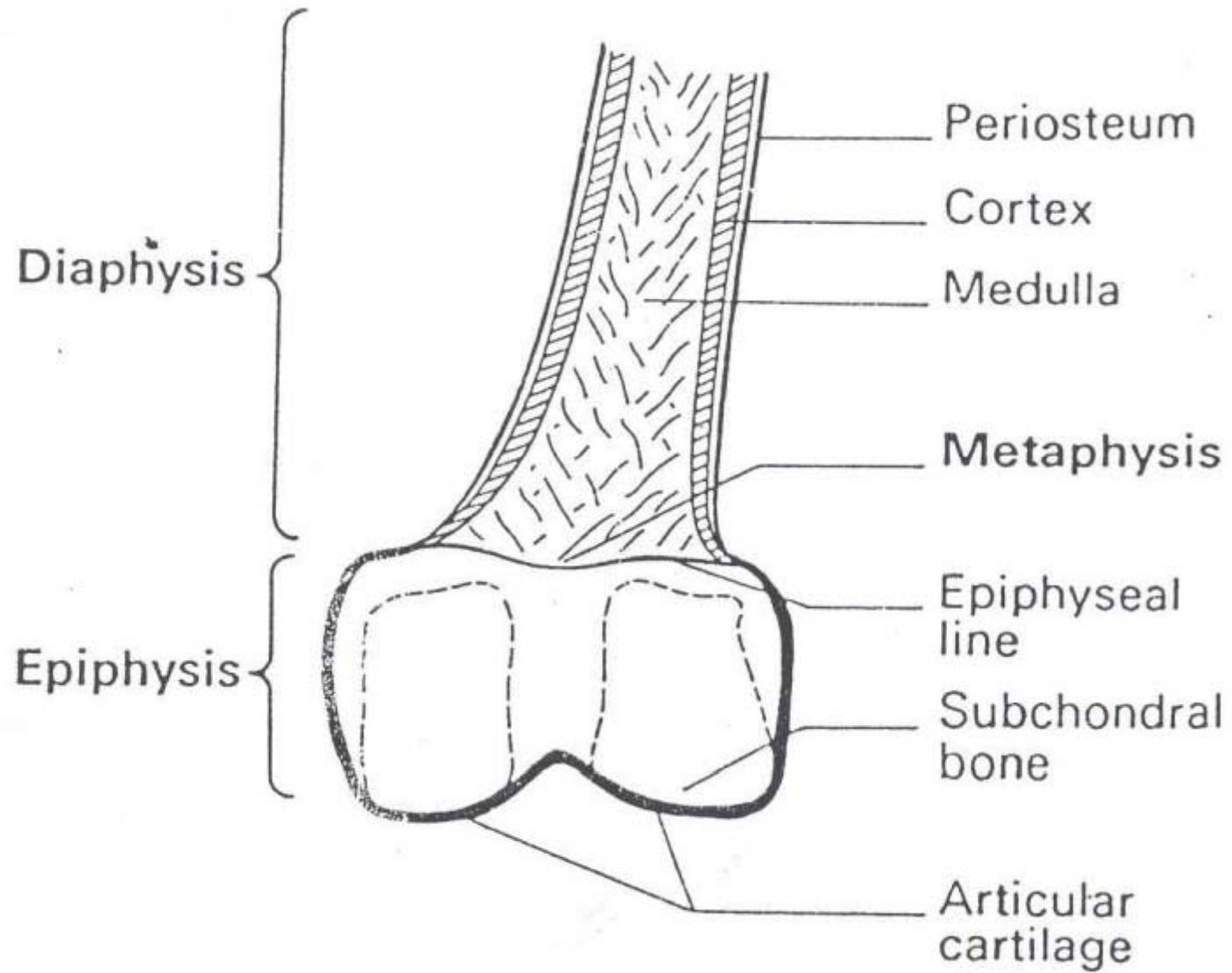
- MECHANICAL
  - support and site for muscle attachment
- PROTECTIVE
  - vital organs and bone marrow
- METABOLIC
  - reserve of calcium

# The composition of bone

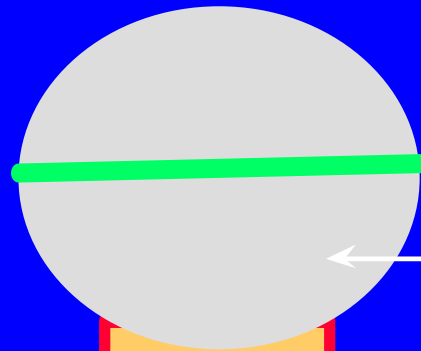


- **INORGANIC - 65%**
  - calcium hydroxyapatite ( $10\text{Ca } 6\text{PO}_4 \text{OH}_2$ )
  - is storehouse for 99% of Ca in the body
  - 85% of the phosphorous, 65% Na & Mg
- **ORGANIC - 35%**
  - bone cells and protein matrix

# Bone geography

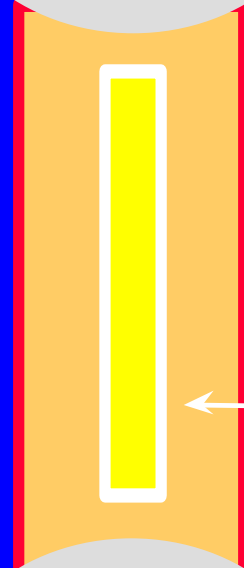


Epiphysis



Metaphysis

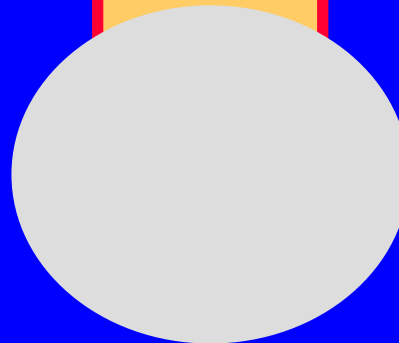
Diaphysis



periosteum

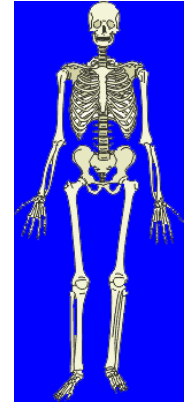
endosteum

Epiphysis



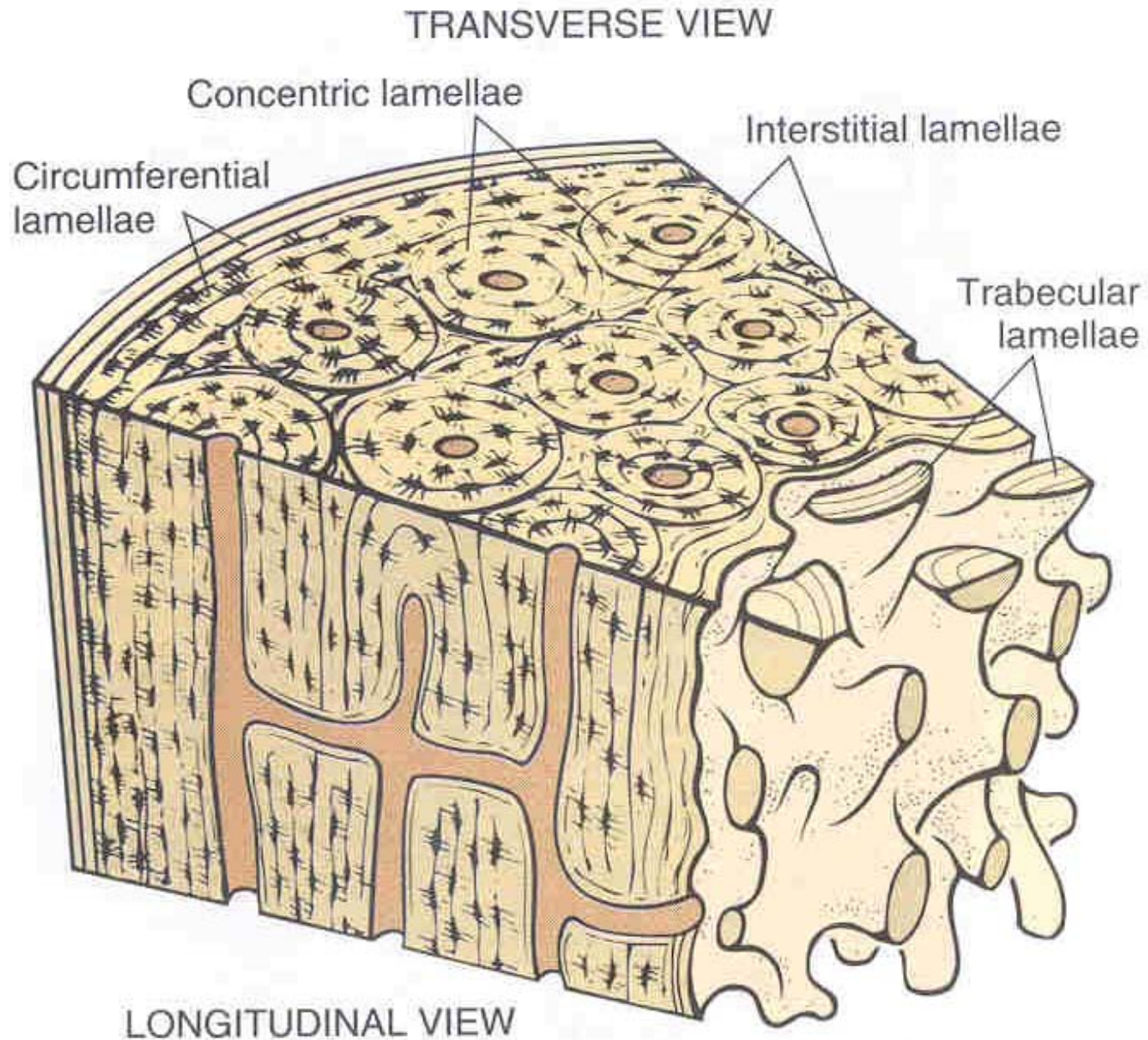


# Classification of bone



- **CORTICAL**
  - Long bones
  - 80% of skeleton
  - Appendicular
  - 80-90% calcified
  - mainly mechanical and protective
- **CANCELLOUS**
  - Vertebrae & pelvis
  - 20% of skeleton
  - Axial
  - 15-25% calcified
  - mainly metabolic
  - Large surface

# Cortical bone microanatomy





# Bone Biopsy

- Indications
- Evaluate bone pain or tenderness
- Investigate an abnormality seen on X-ray
- For bone tumour diagnosis (benign vs malignant)
- To determine the cause of an unexplained infection
- To evaluate therapy

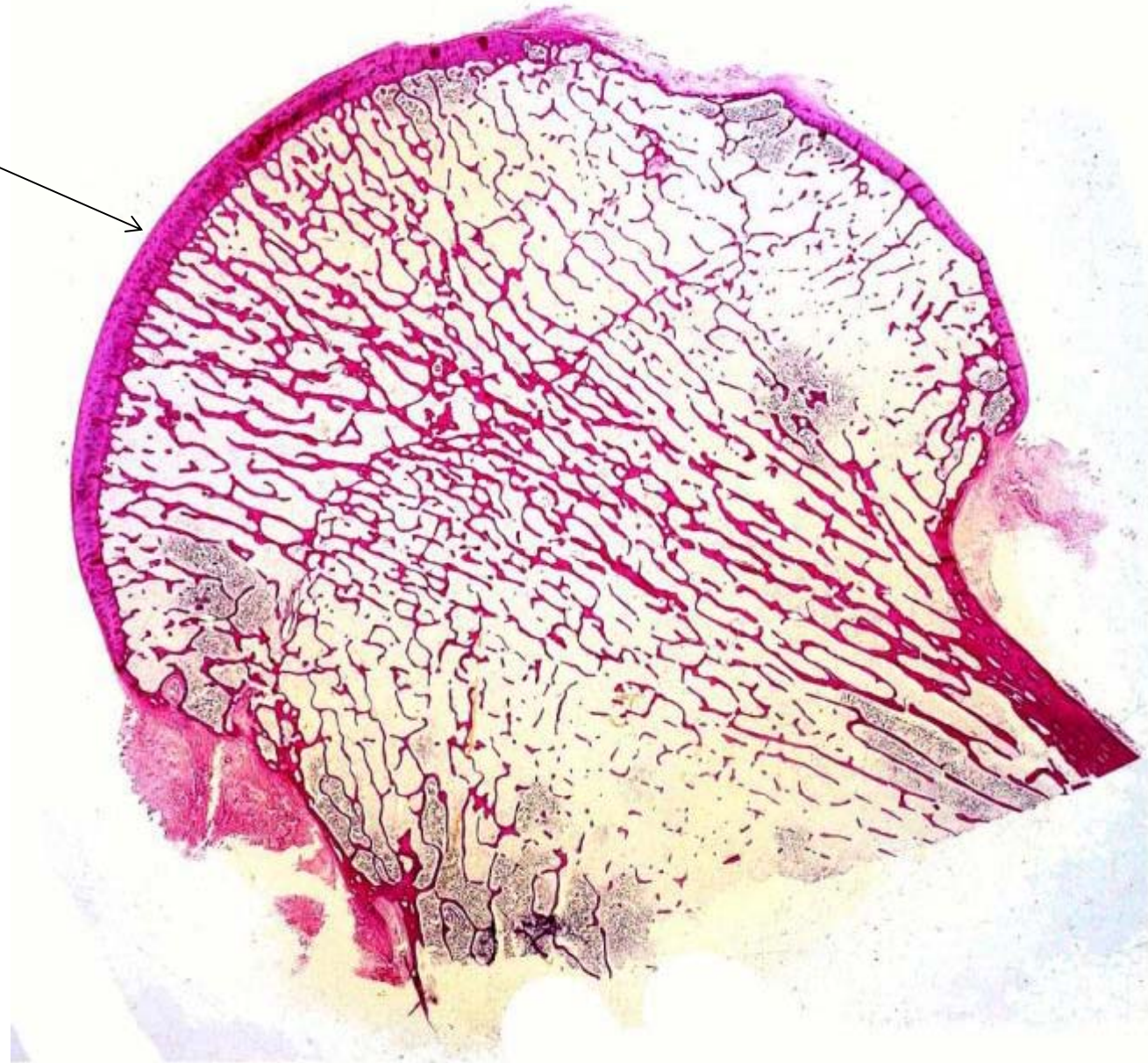
# Bone Biopsy

- Types
- Closed – needle - core biopsy (Jamshidi needle)

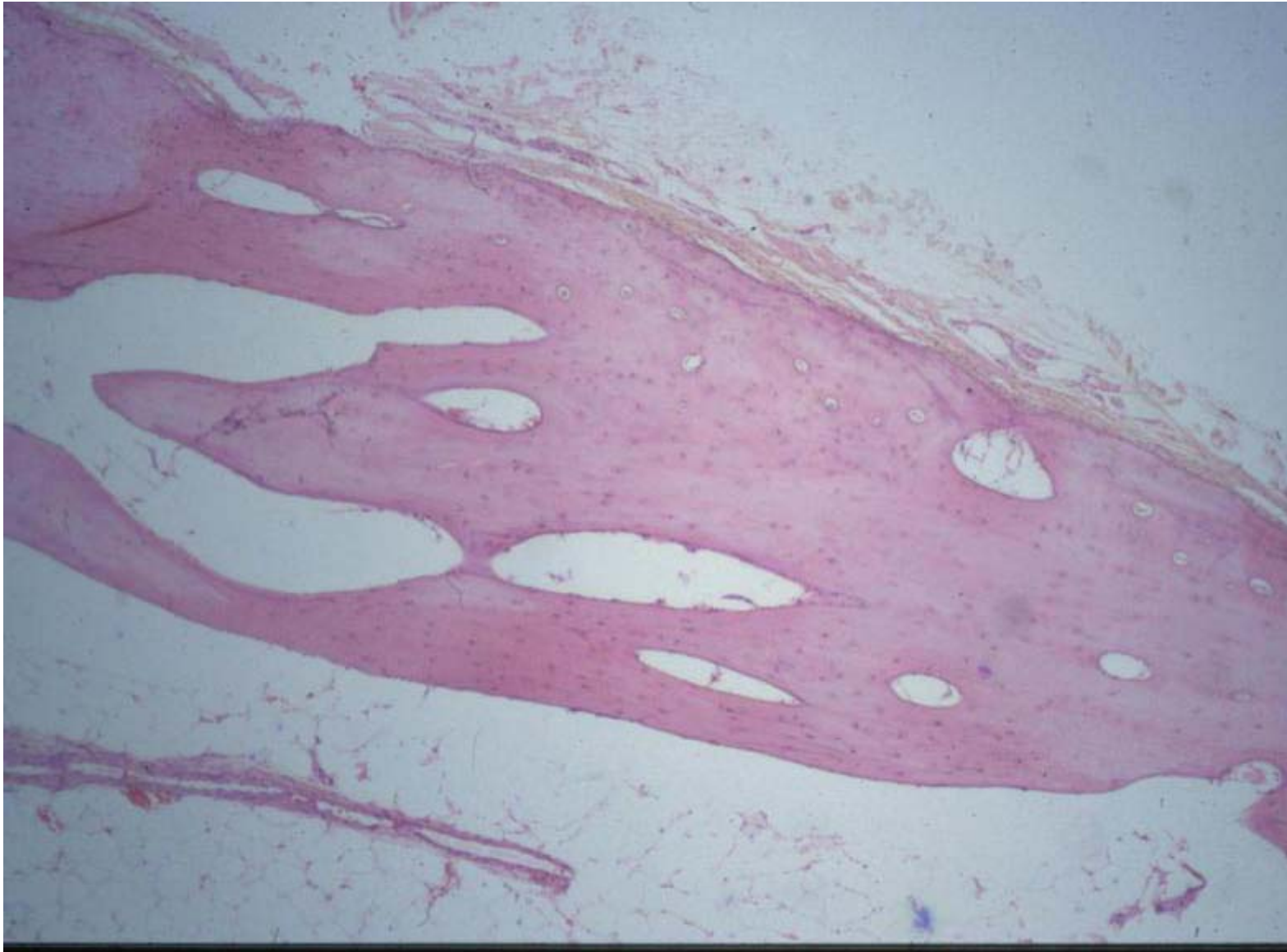


- Open – for sclerotic or inaccessible lesions

# Histology of bone – femoral head

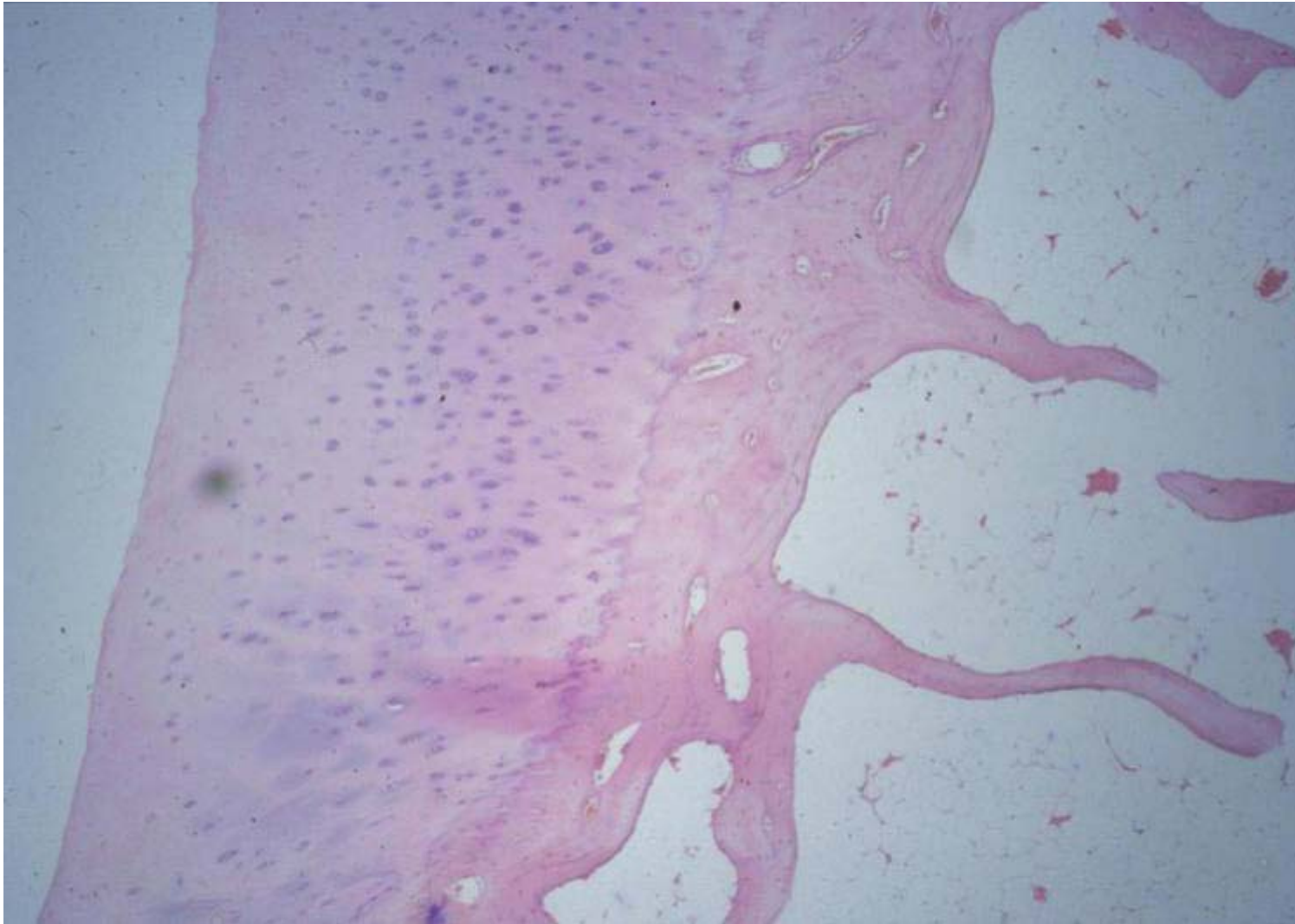


# Histology of shaft of long bone



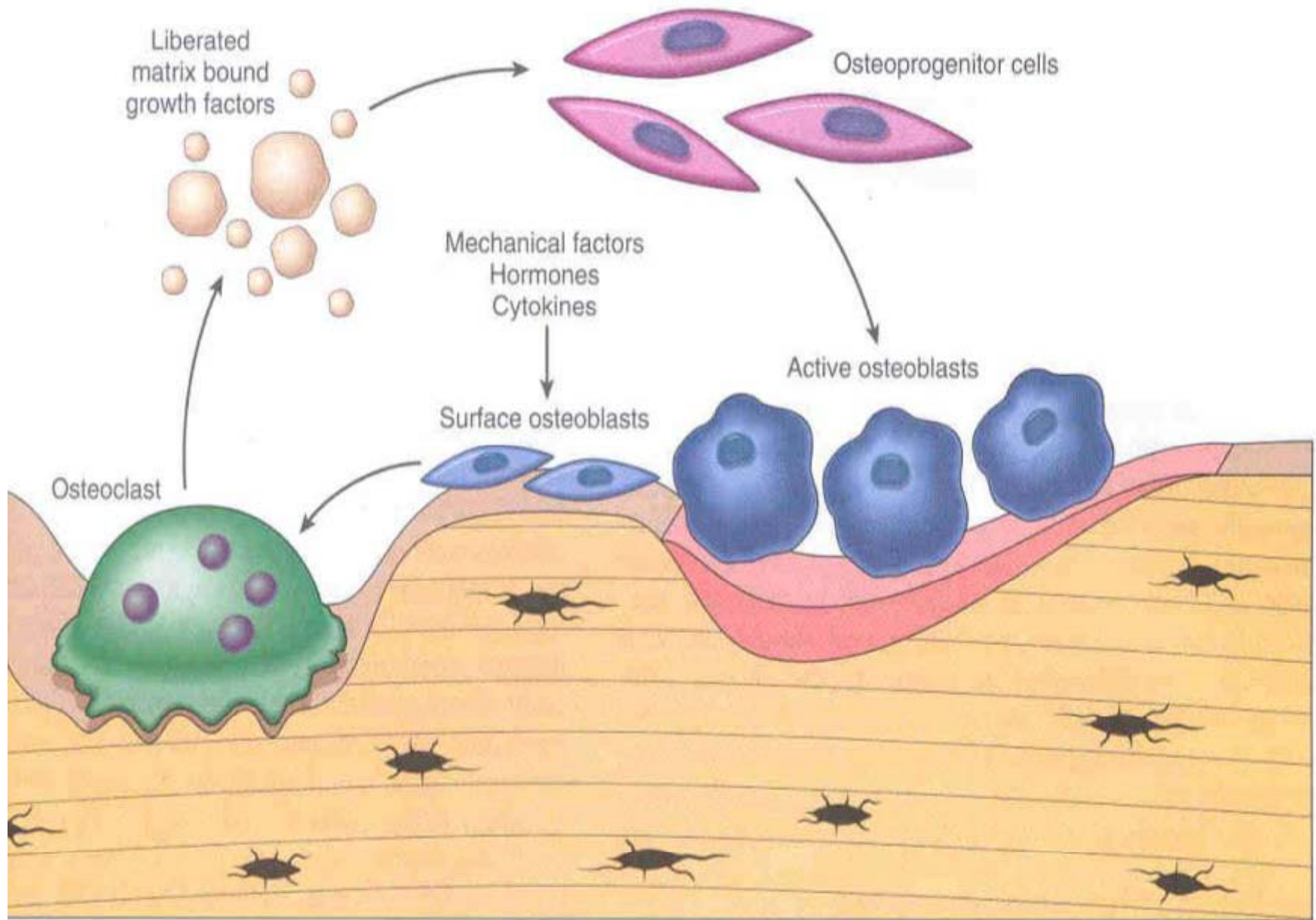


# Histology of the articular surface

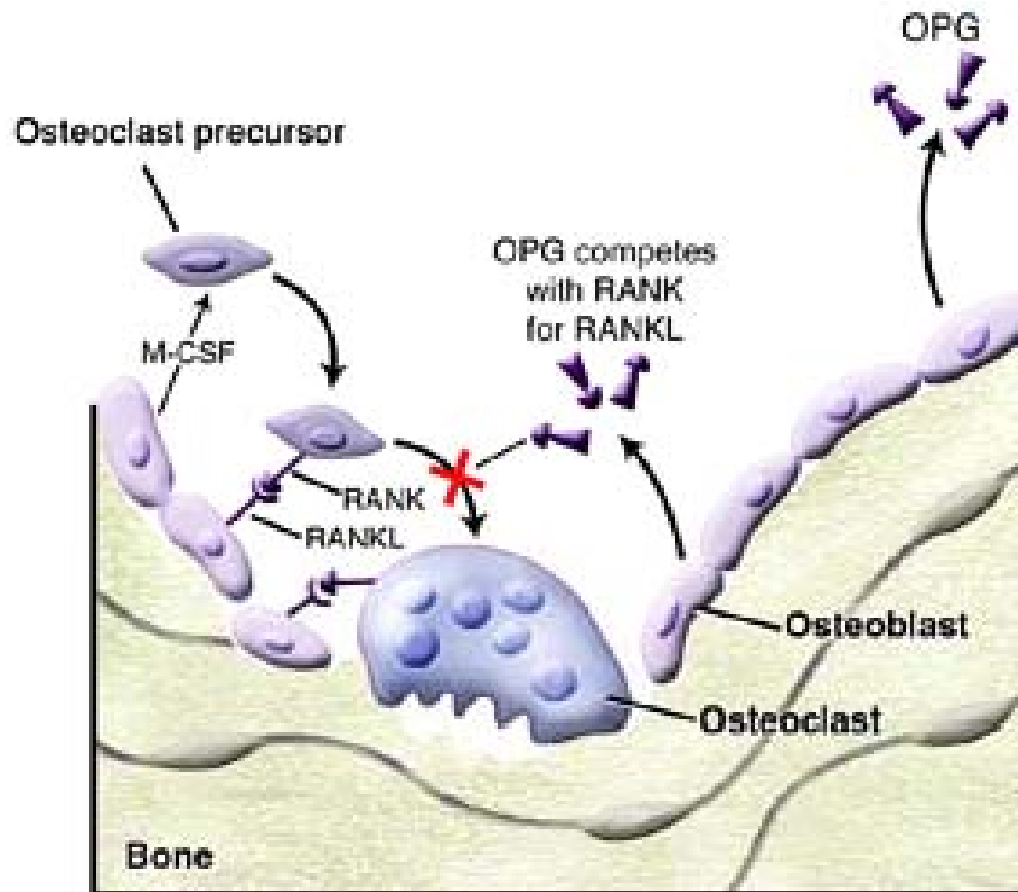


# Bone Cells

- Osteoblasts - build bone by laying down osteoid
- Osteoclasts - multinucleate cells of macrophage family resorb or chew bone
- Osteocytes - osteoblast like cells which sit in lacunae in bone



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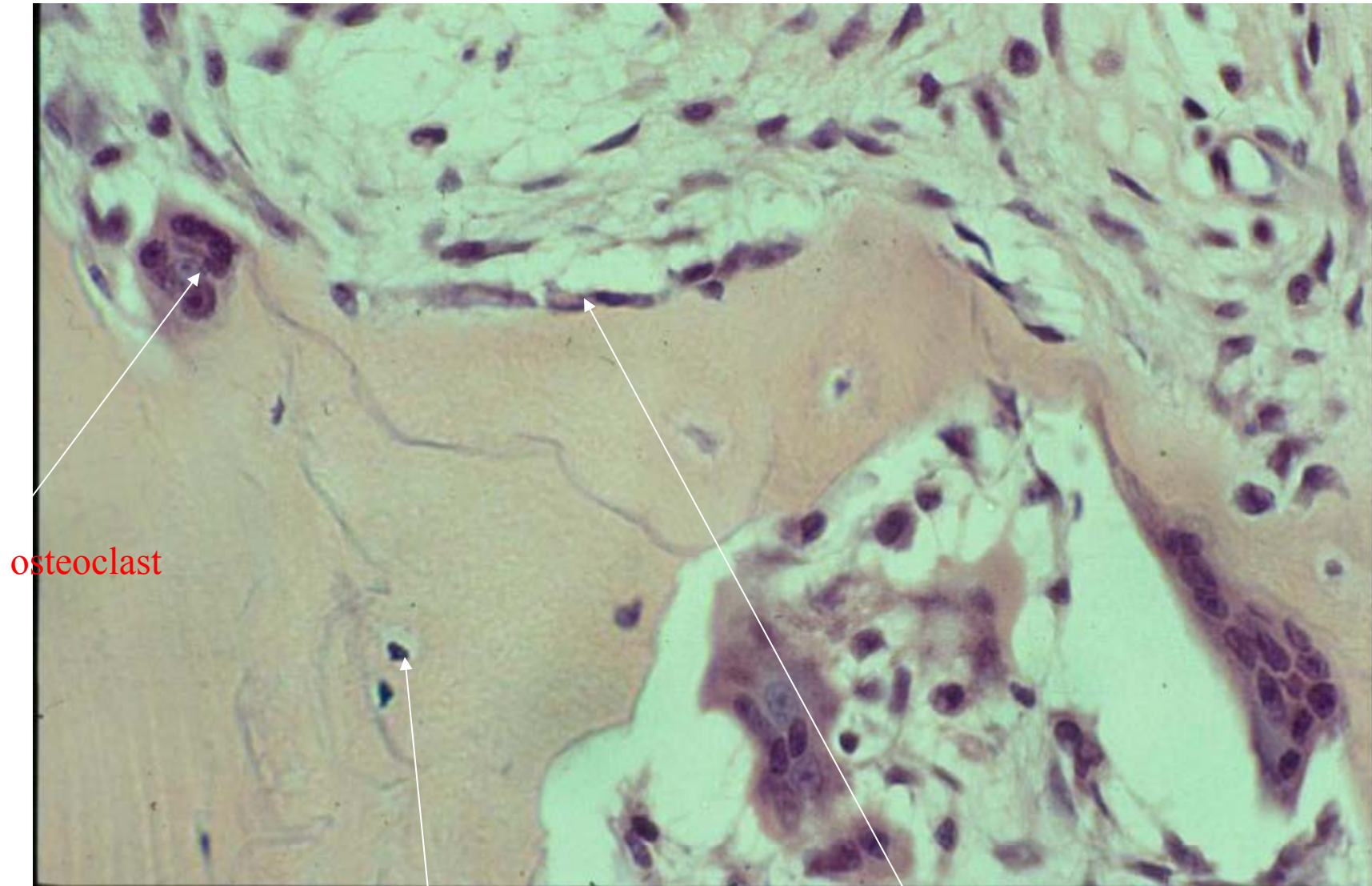


RANK = Receptor Activator for nuclear factor kB

OPG = Osteoprotegerin- inhibits RANK/RANKL binding and therefore inhibits osteoclastogenesis



# Bone Cells



osteoclast

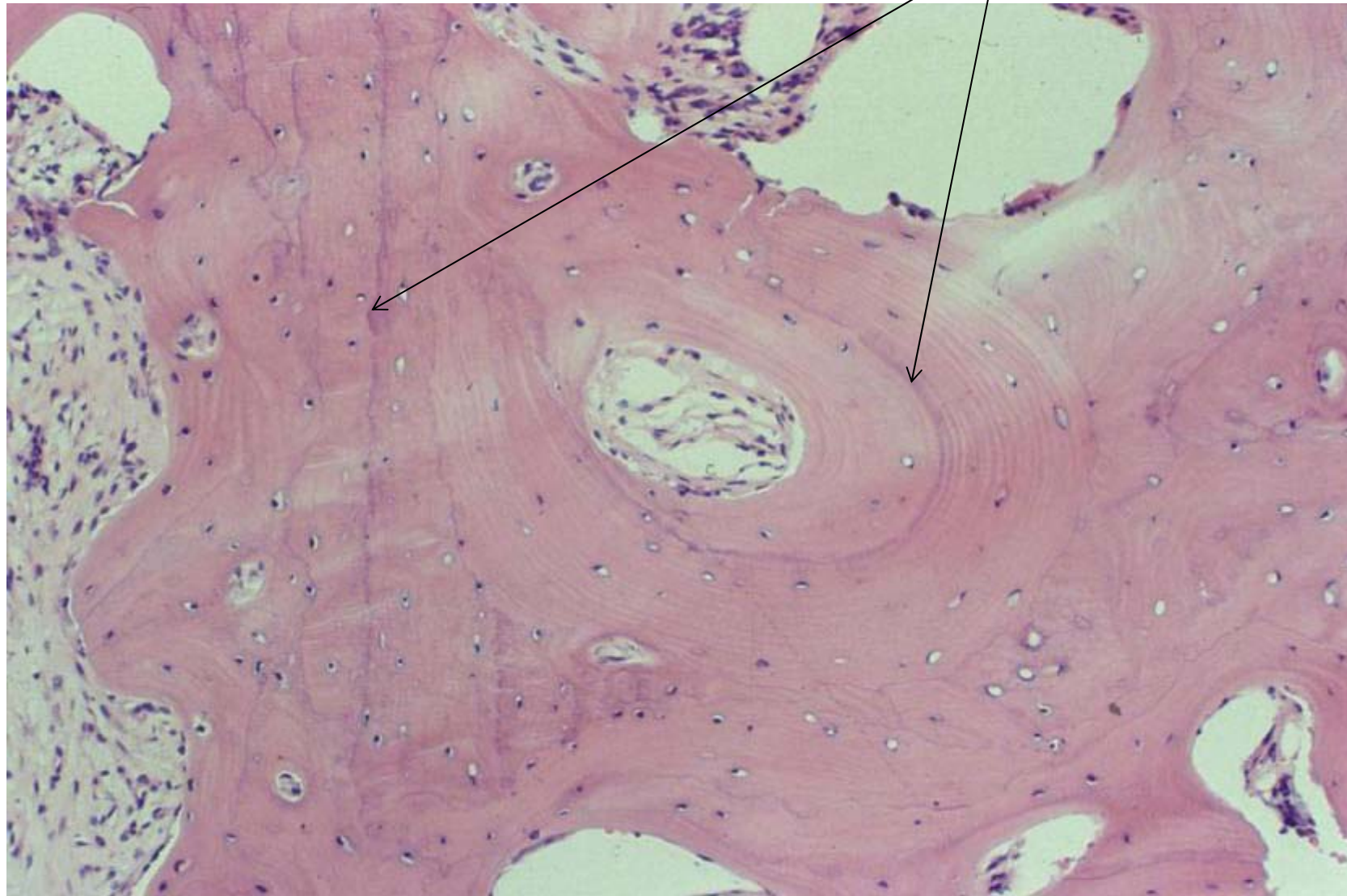
osteocyte

osteoblast

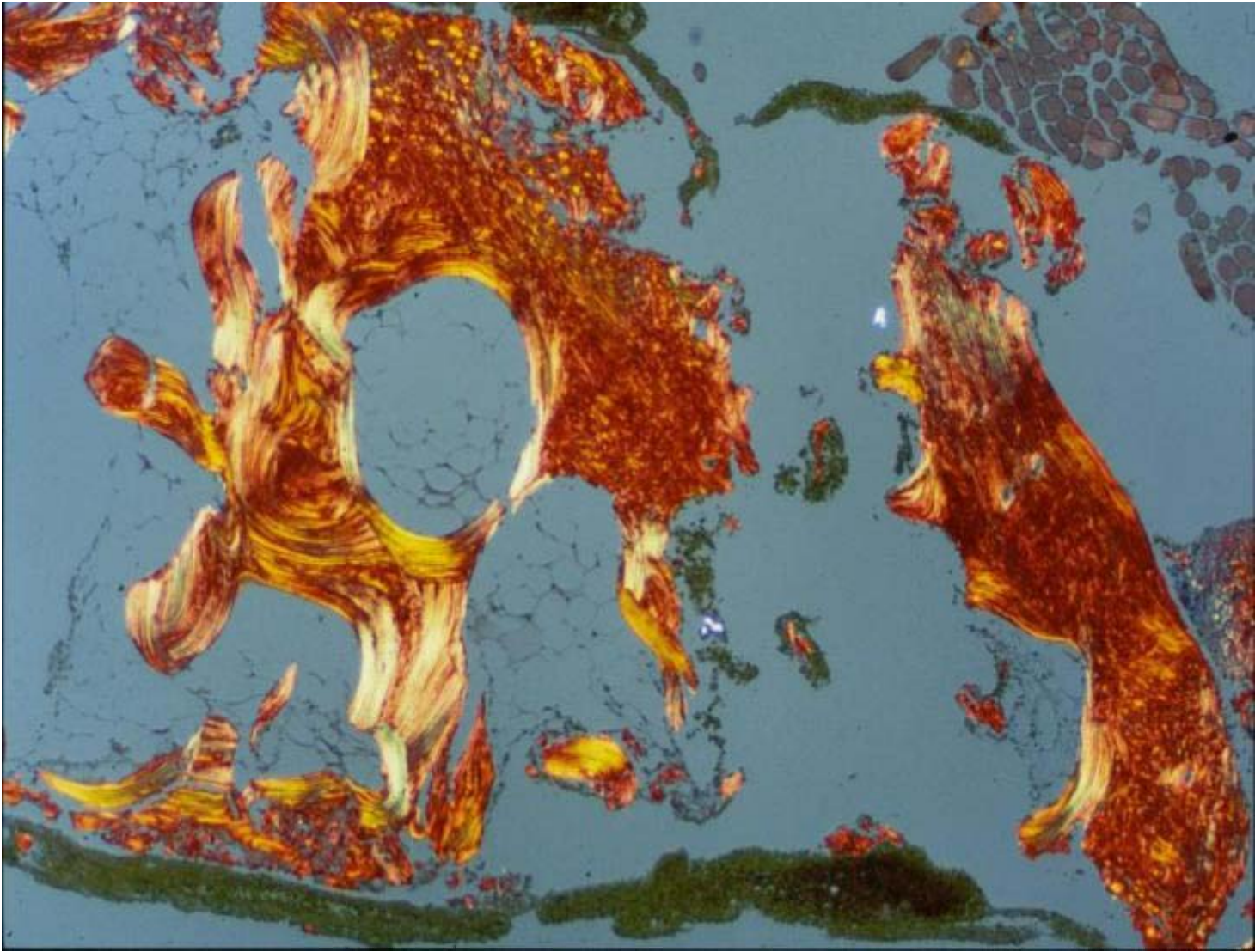
# Types/classifications

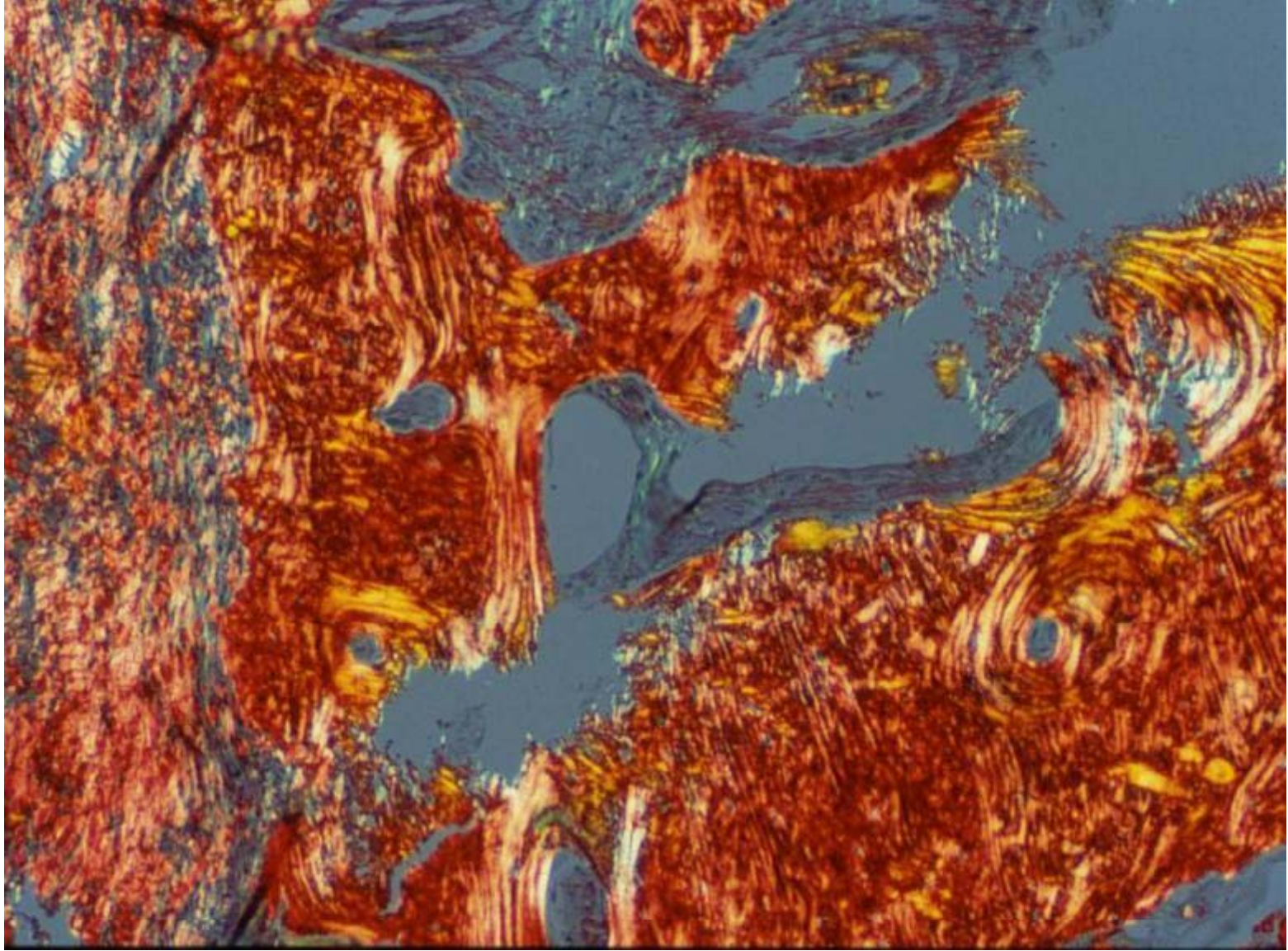
- Anatomically -Flat /long/cuboid bones
  - intramembranous ossification (flat) and endochondral ossification (long)
- Trabecular bone (cancellous)
- Compact bone (cortical)
- Woven bone (immature)
- Lamellar bone (mature)

# Trabecular lamellar bone with prominent 'reversal lines'



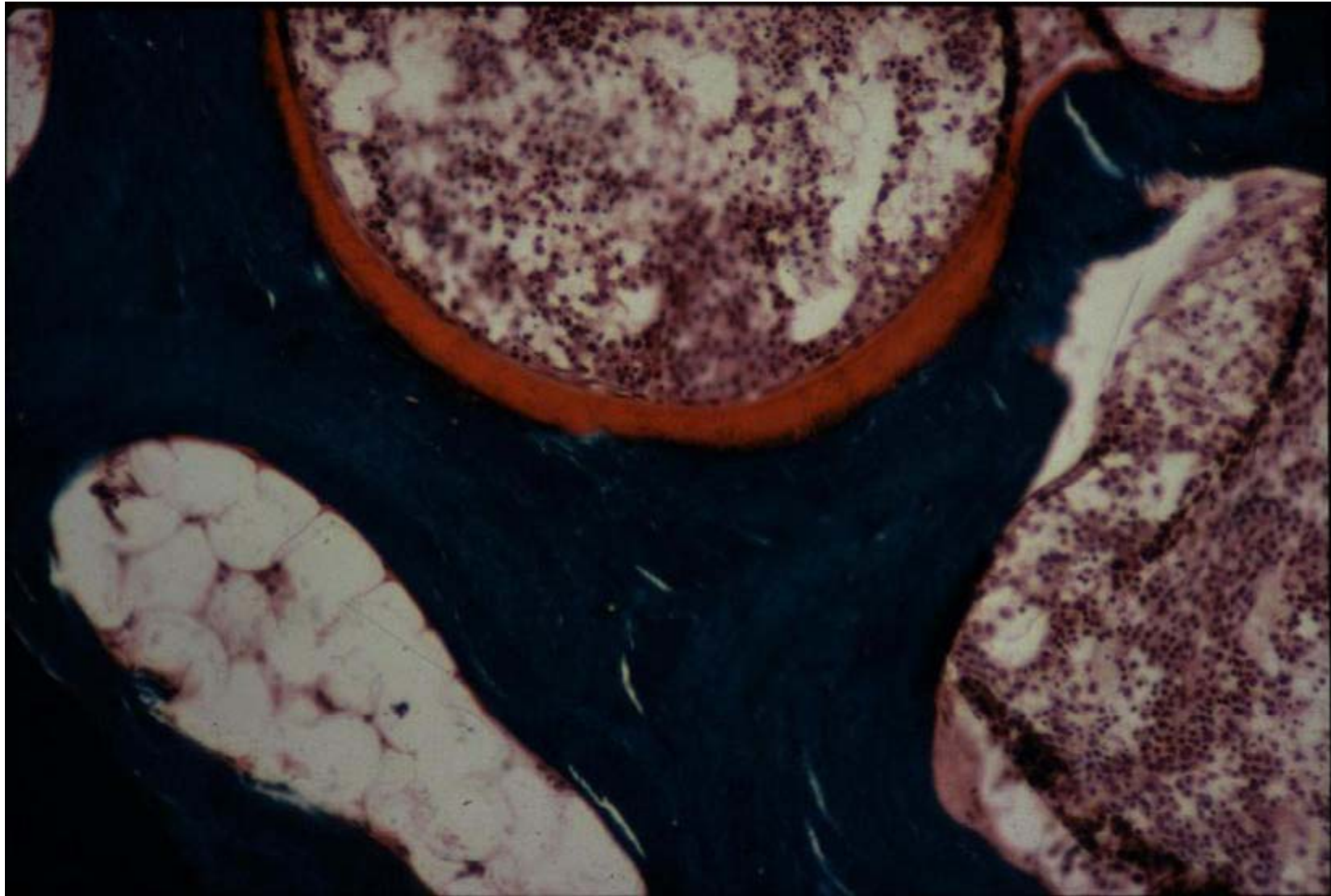








Special histological stain to show layer of osteoid on surface of normal trabecular bone



# Metabolic bone disease

- Disordered bone turnover due to imbalance of various chemicals in the body (vitamins, hormones, minerals etc)
- Overall effect is reduced bone mass (osteopaenia) often resulting in fractures with little or no trauma

# Metabolic bone disease

3 main categories of disease:-

1. Related to endocrine abnormality (Vit D; Parathyroid hormone)
2. Non-endocrine (e.g. age related osteoporosis)
3. Disuse osteopaenia

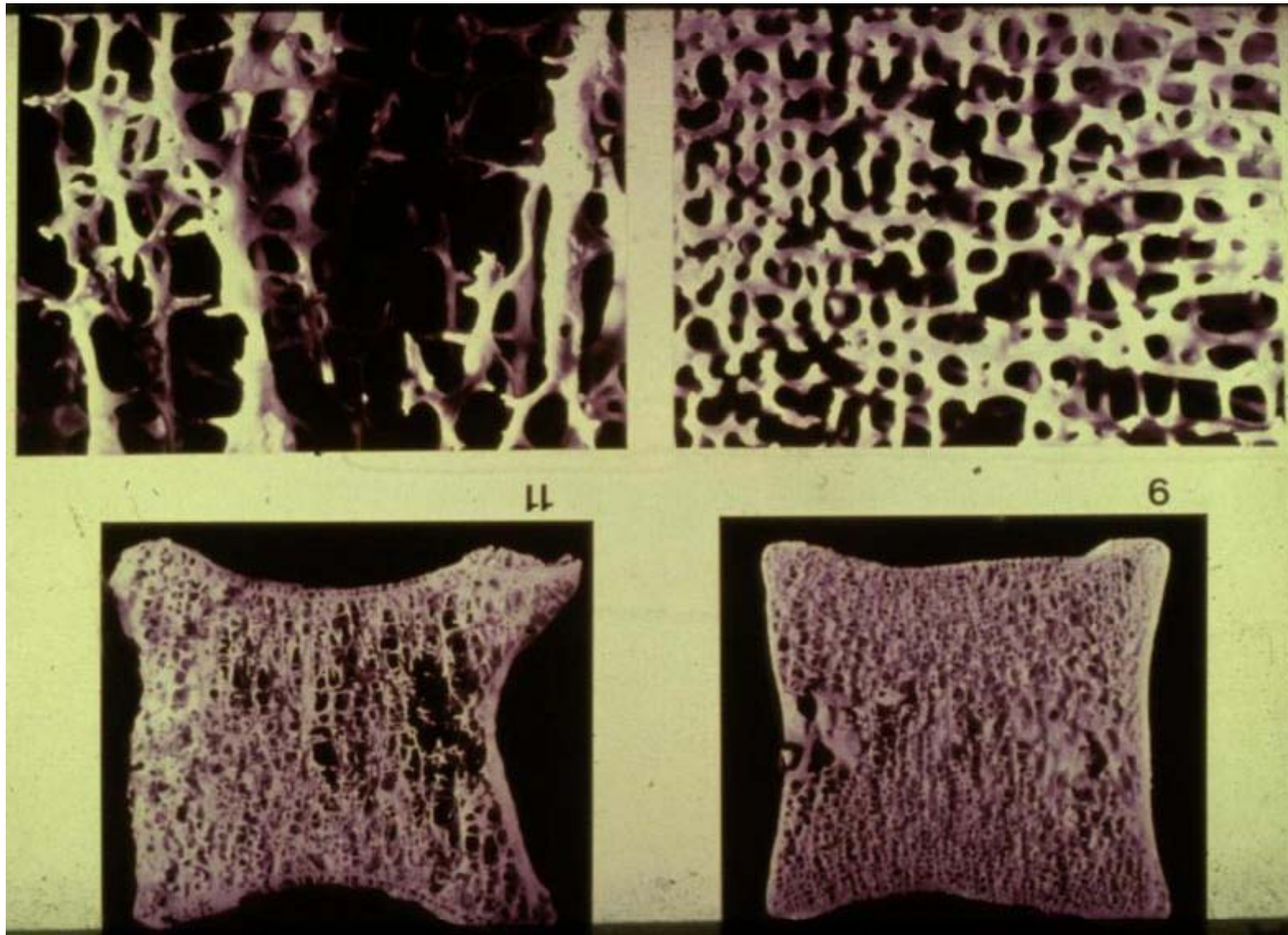


# Osteoporosis

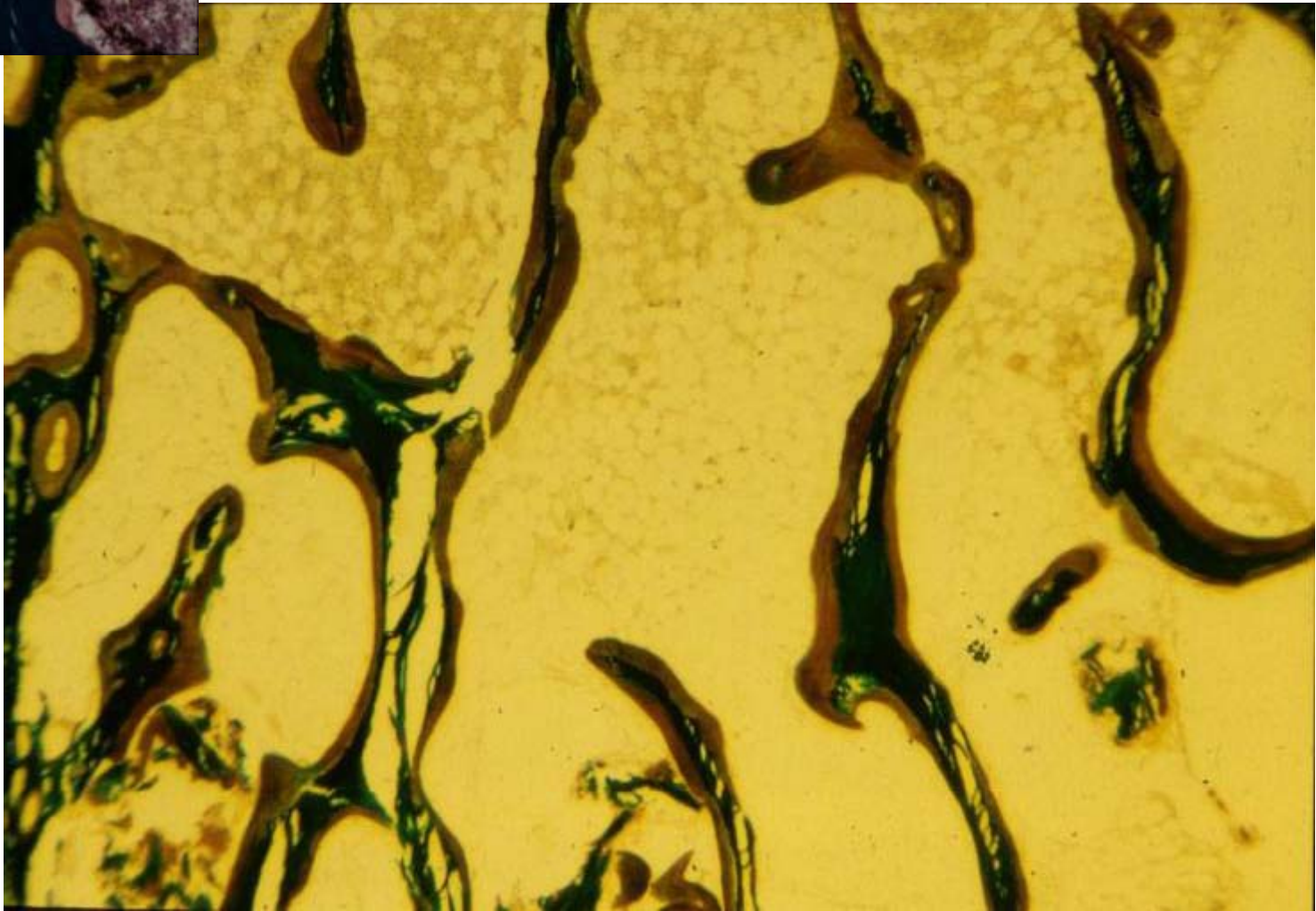
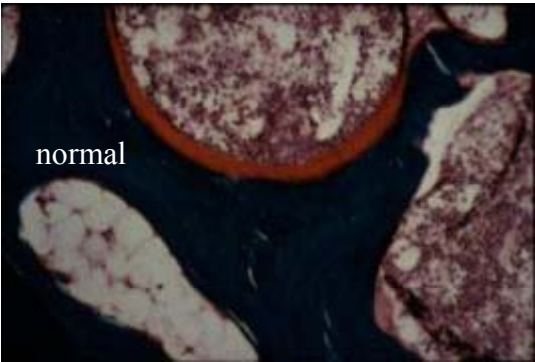
- Aetiology
  - 1° - age, post-menopause
  - 2° - drugs, systemic disease

Osteoporotic bone

Normal bone



# Osteoporotic bone



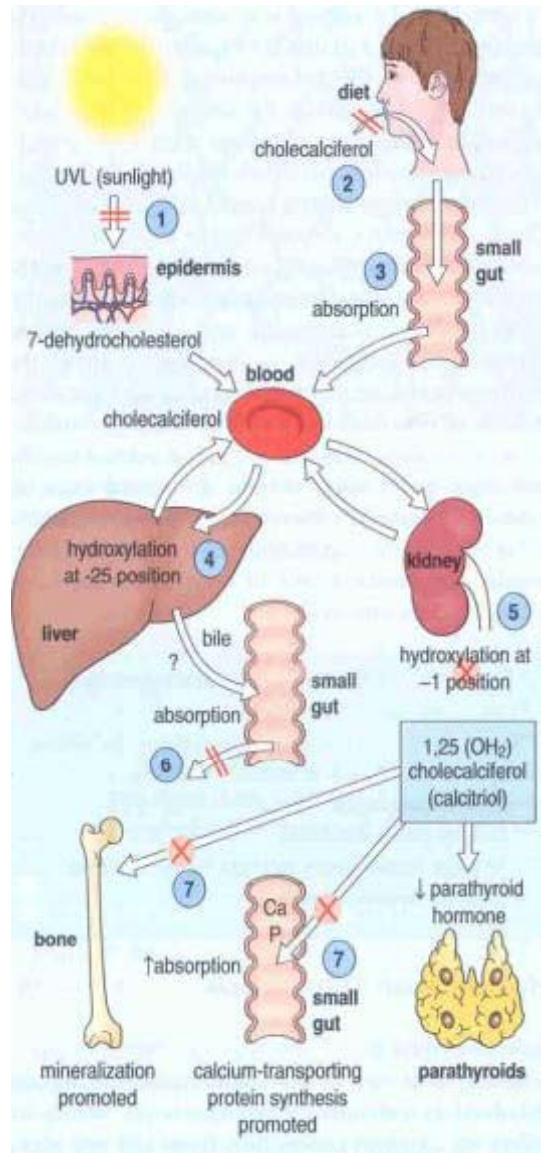
# Osteomalacia

- Defective bone mineralisation

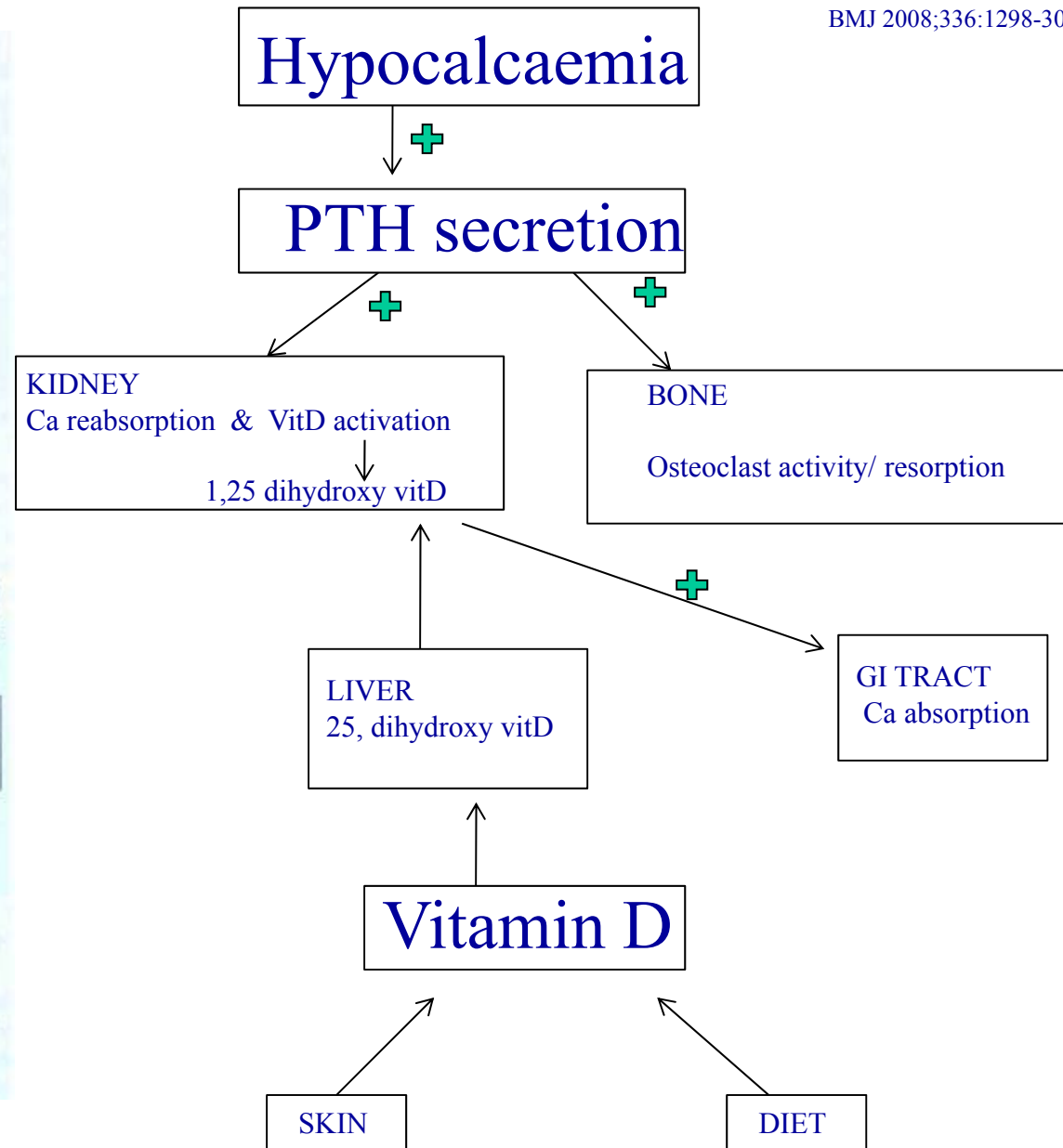
types effectively

- 1. Deficiency of vitamin D
- 2 Deficiency of  $\text{PO}_4$

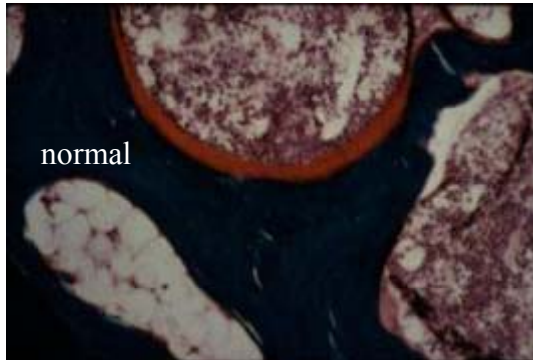




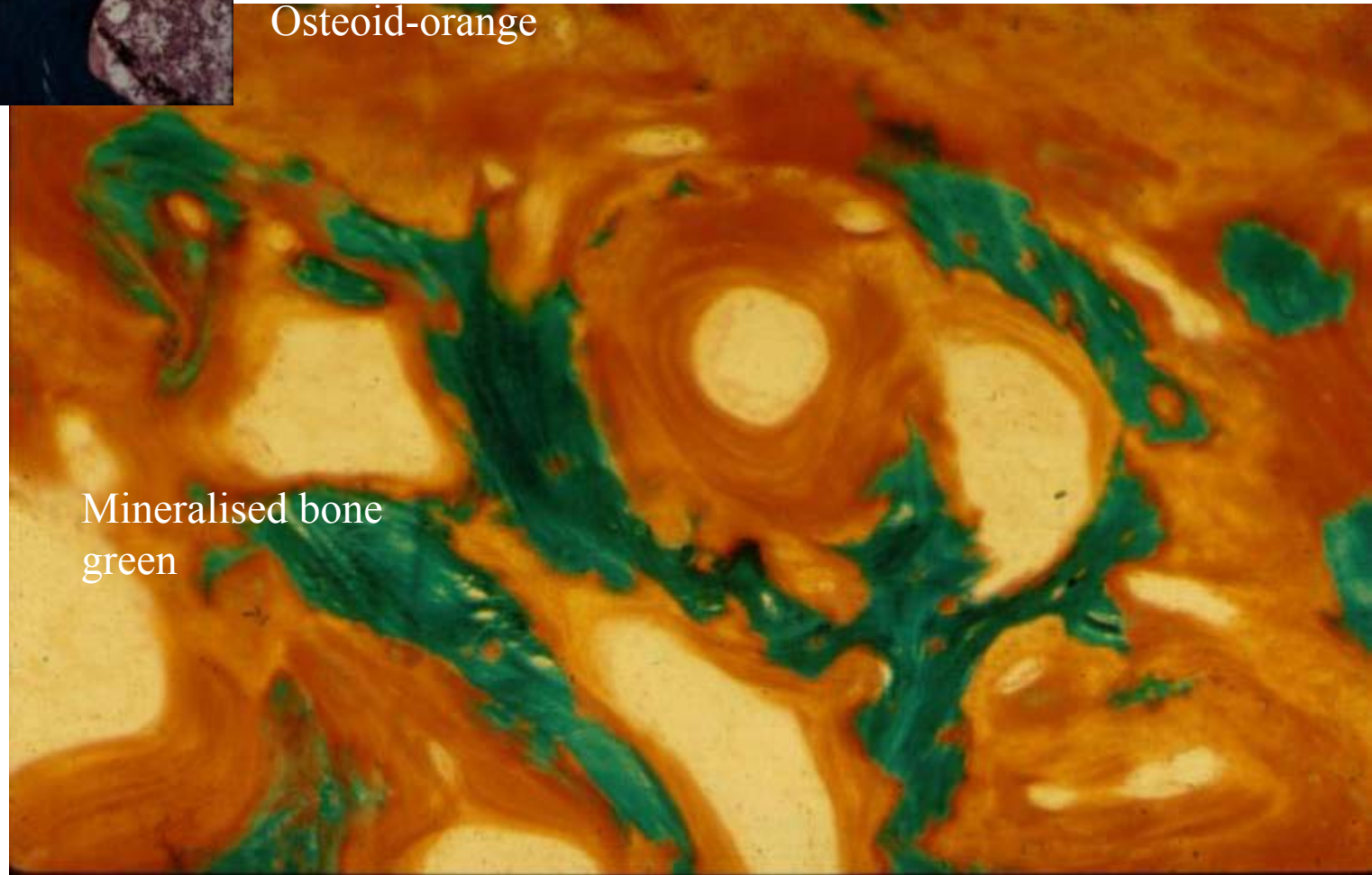
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# Bone in osteomalacia



Osteoid-orange



# Osteomalacia

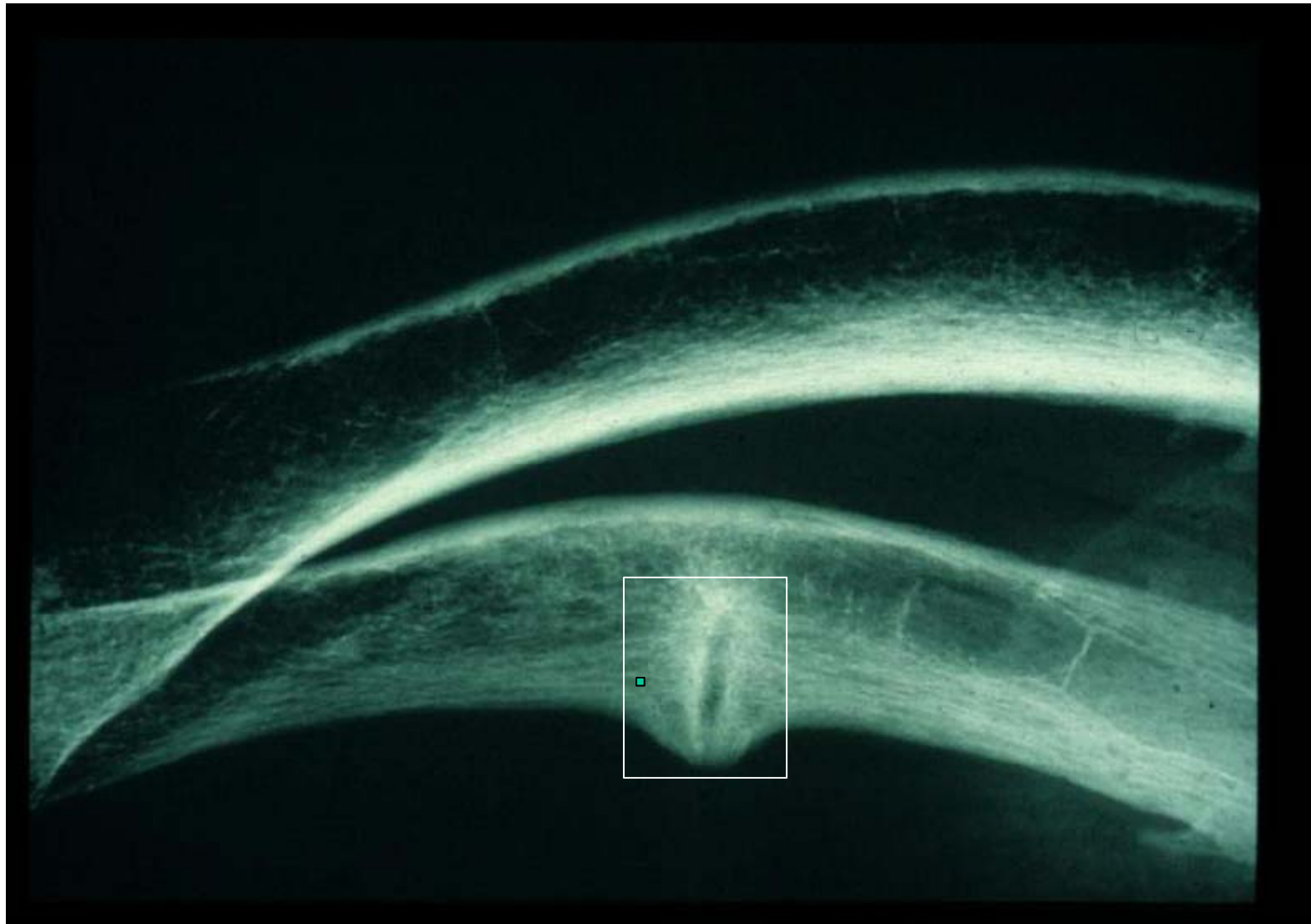
- Sequelae
- bone pain/tenderness
- fracture
- proximal weakness
- bone deformity

# Osteomalacia (rickets)





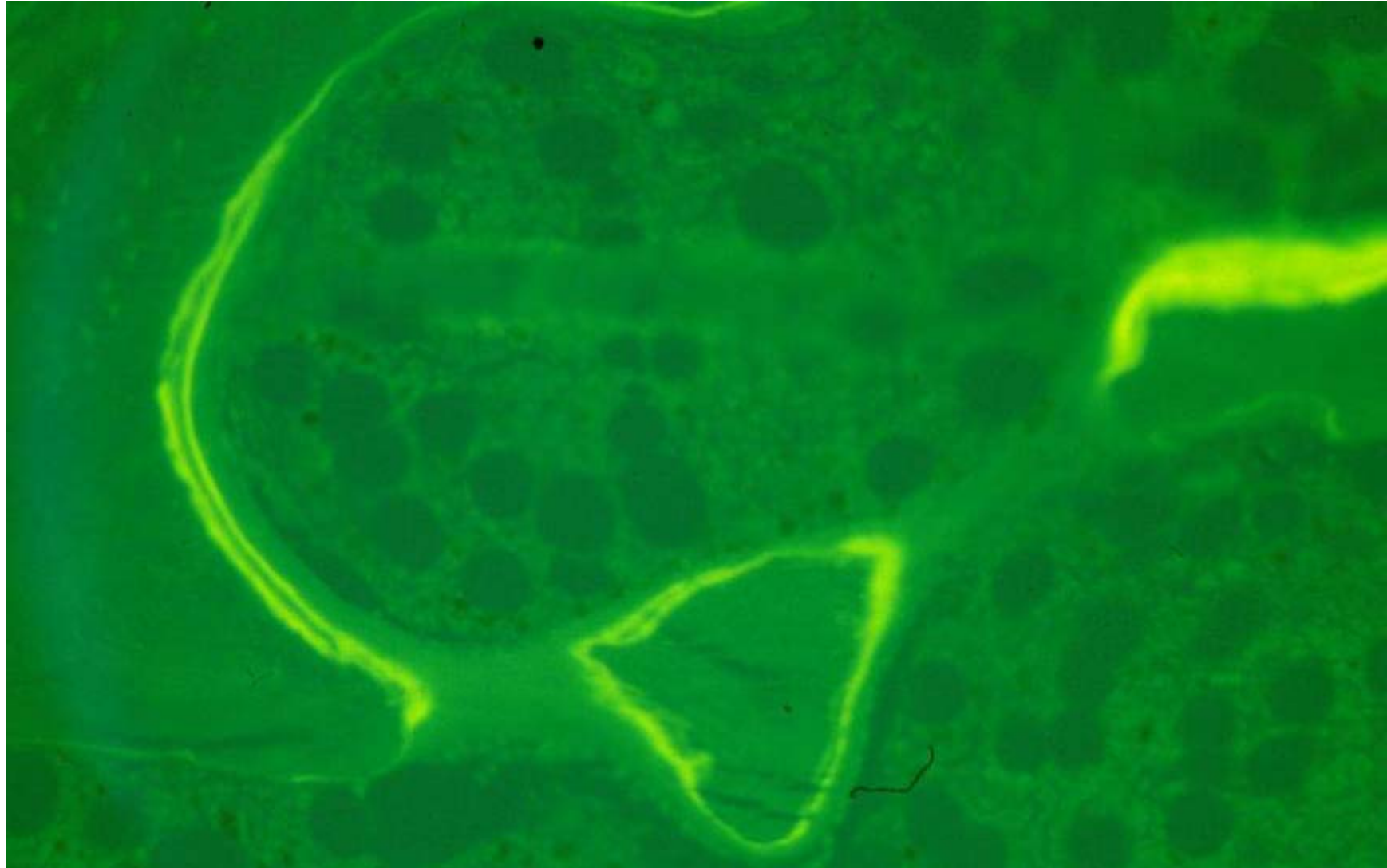
## Horizontal fracture in Looser's zone



## Horizontal fracture in Looser's zone



# Tetracycline labelling – normal bone



# Hyperparathyroidism

- Excess PTH
- increased Ca + PO<sub>4</sub> excretion in urine
- hypercalcaemia
- hypophosphataemia
- skeletal changes of osteitis fibrosa cystica

# Hyperparathyroidism

- 4 organs are directly or indirectly affected by PTH and between them control Ca metabolism
- Parathyroid glands
- Bones
- Kidneys
- Proximal small intestine

# Hyperparathyroidism

- 1° -
  - parathyroid adenoma (85-90%)
  - chief cell hyperplasia
- 2° -
  - chronic renal deficiency
  - vit D deficiency

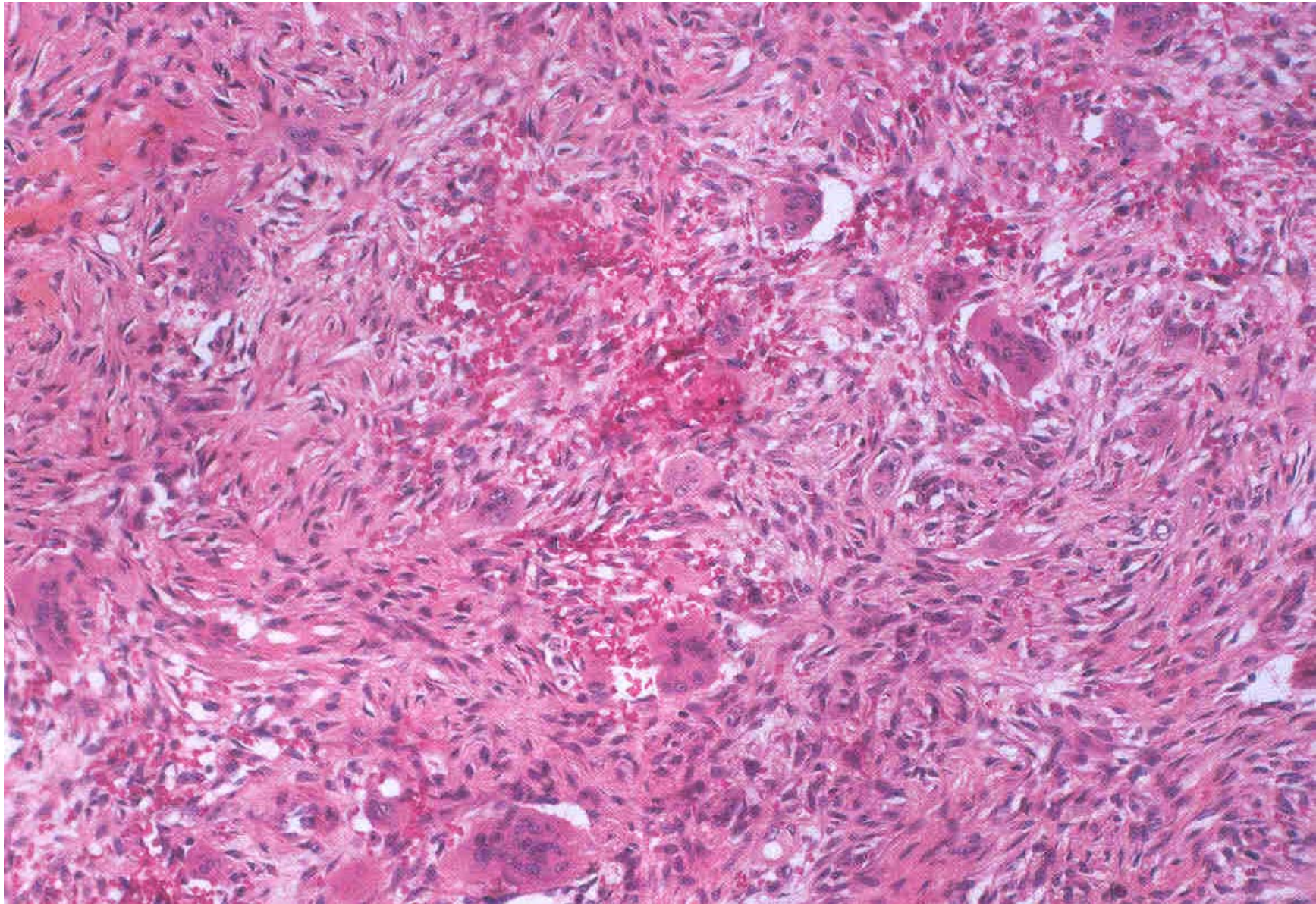
# Hyperparathyroidism

- Symptoms Mnemonic
- Stones (Ca oxalate renal stones)
- Bones (osteitis fibrosa cystica, bone resorption)
- Abdominal groans (acute pancreatitis)
- Psychic moans (psychosis & depression)





## Histology of brown cell tumour of Hyperparathyroidism



# Renal Osteodystrophy

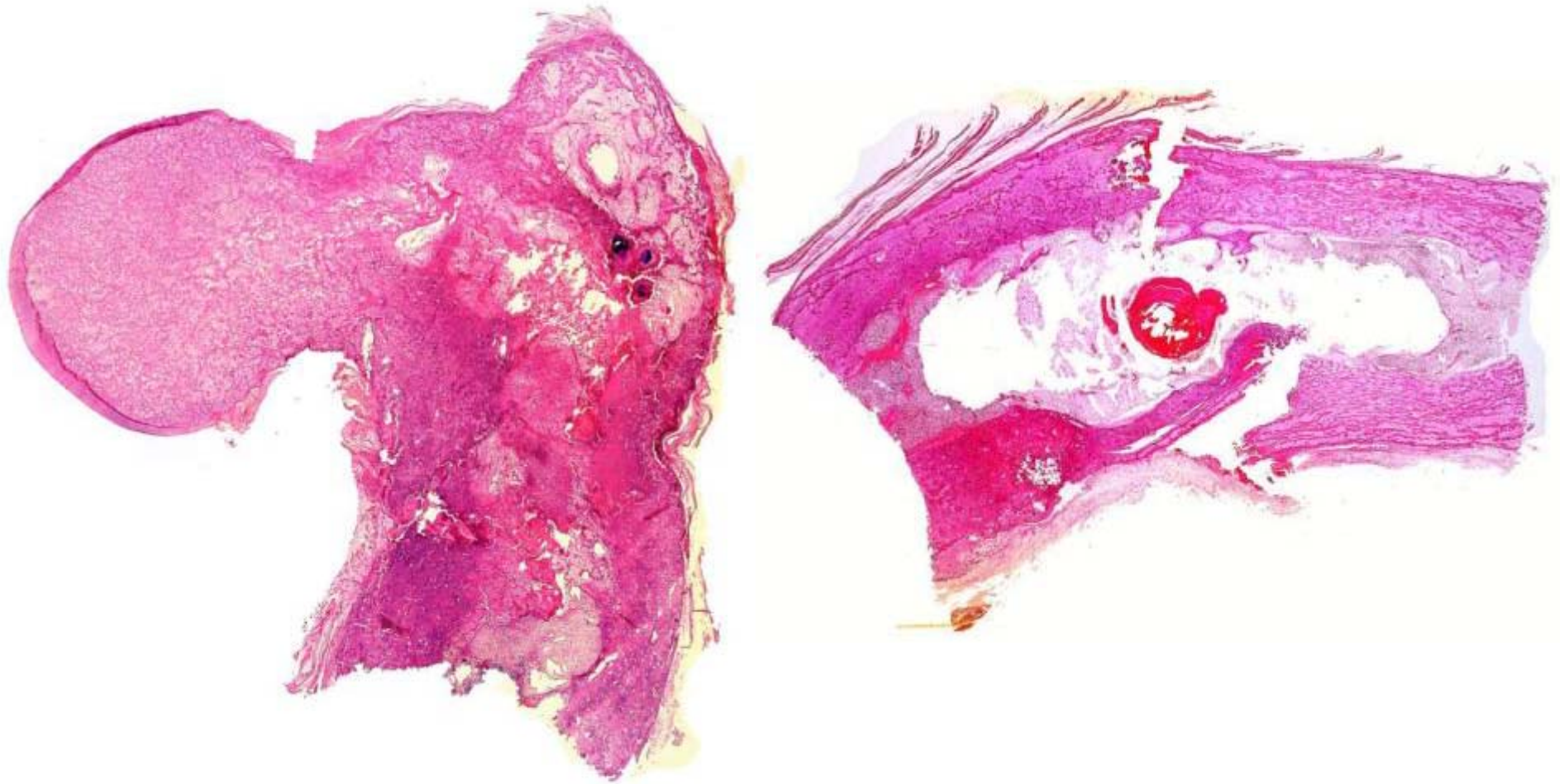
- Comprises all the skeletal changes of chronic renal disease:-
  1. Increased bone resorption (osteitis fibrosa cystica)
  2. Osteomalacia
  3. Osteosclerosis
  4. Growth retardation
  5. Osteoporosis



Xray showing features of osteitis fibrosa cystica affecting tibia



H&E stained sections show features of osteitis fibrosa cystica affecting femur



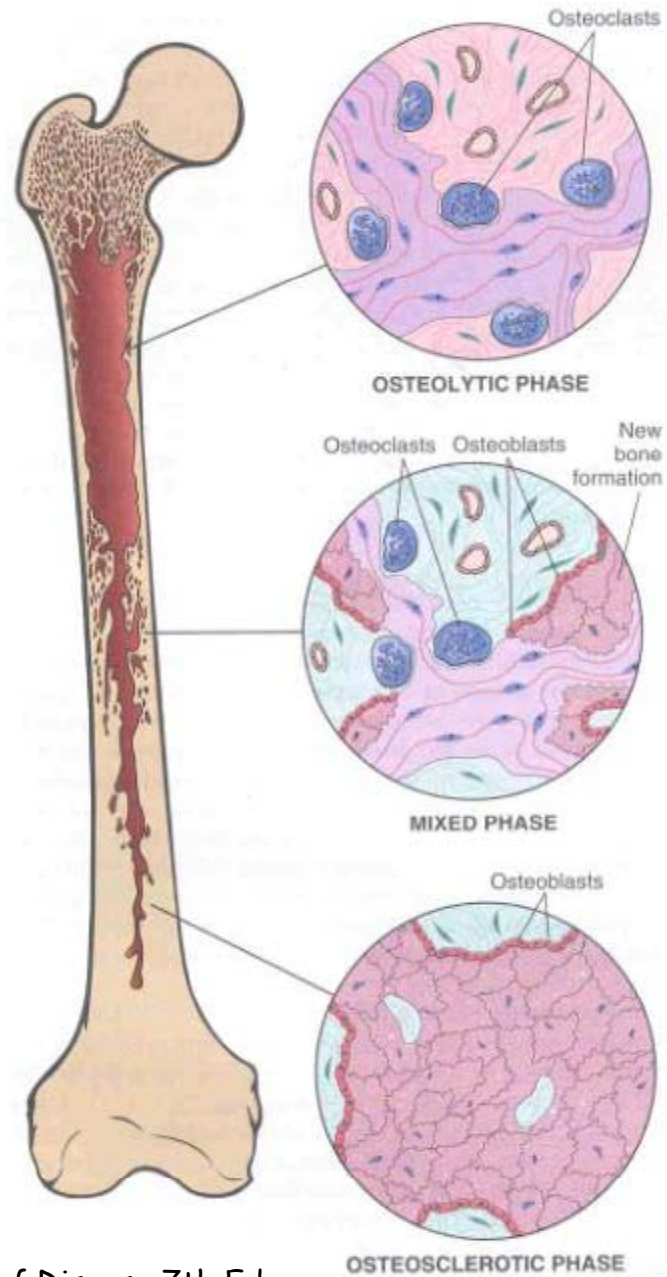
# Renal Osteodystrophy

- $\text{PO}_4$  retention – hyperphosphataemia
- Hypocalcaemia as a result of ↓vit D
- 2° hyperparathyroidism
- Metabolic acidosis
- Aluminium deposition



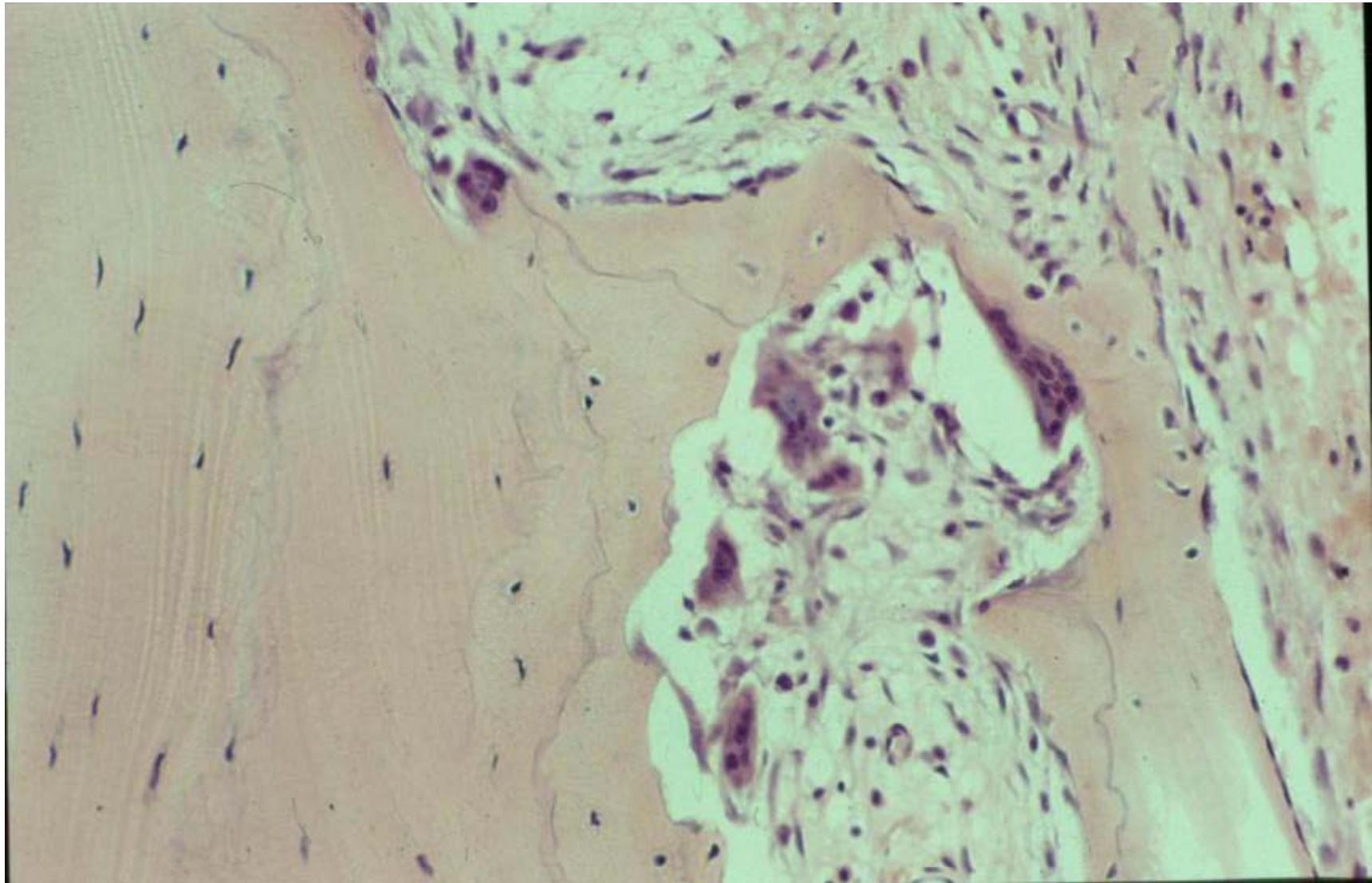
# Paget's disease

- Disorder of bone turnover
- Divided into 3 stages
- 1. Osteolytic
- 2. Osteolytic-osteosclerotic
- 3. Quiescent osteosclerotic



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# Histology of Paget's disease



# Paget's disease

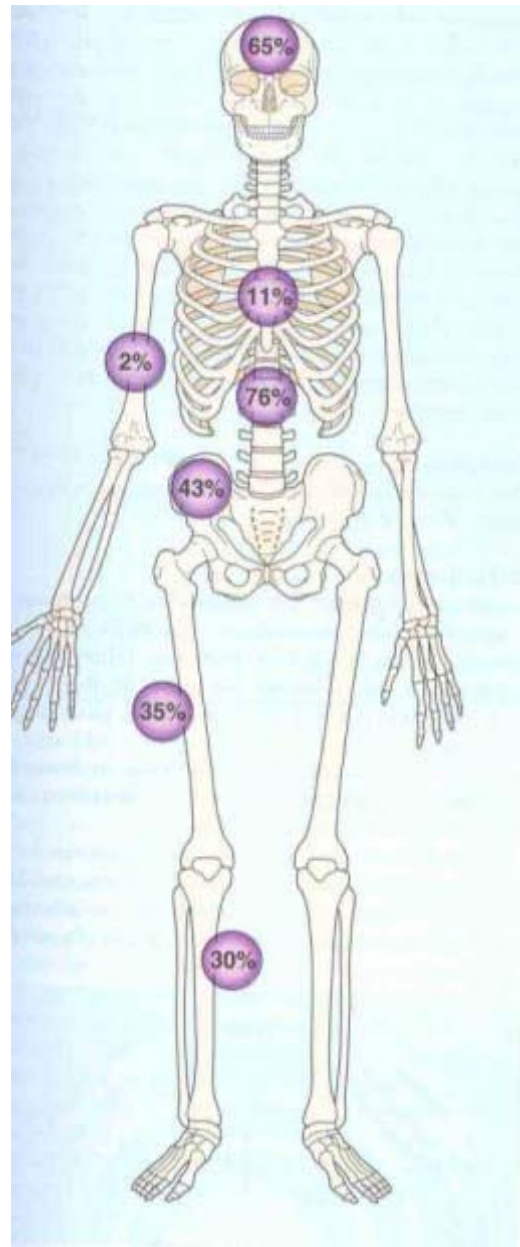
- Onset  $> 40y$  (affects 3% Caucasians  $> 55y$ )
- M=F
- Rare in Asians and Africans
- Mono-ostotic 15%
- Remainder polyostotic

# Paget's disease

- Aetiology is unknown
- Familial cases show autosomal pattern of inheritance with incomplete penetrance (mutation 5q35-qter - sequestosome 1 gene)
- Parvomyxovirus type particles have been seen on EM in Pagetic bone



# Site predilection in Paget's disease



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# Paget's disease

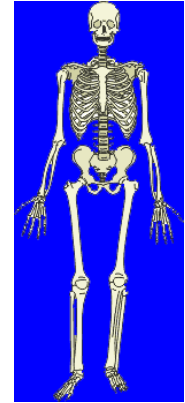
## Clinical symptoms:-

- pain
- microfractures
- nerve compression (incl. Spinal N and cord)
- skull changes may put medulla at risk
- deafness
- +/- haemodynamic changes, cardiac failure
- hypercalcaemia
- Development of sarcoma in area of involvement 1%

# Paget's disease affecting tibia



# Bone vocabulary



- Cortical
- trabecular
- lamellar
- haversian canal
- osteoblasts/osteoclasts/osteocytes
- canaliculae
- Howship's lacunae