

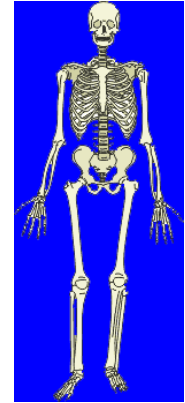
Metabolic bone disease histopathology

Dr Ann Sandison

Department of Histopathology

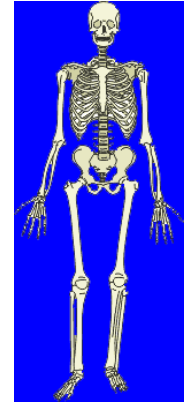
Charing Cross Hospital

The function of bone



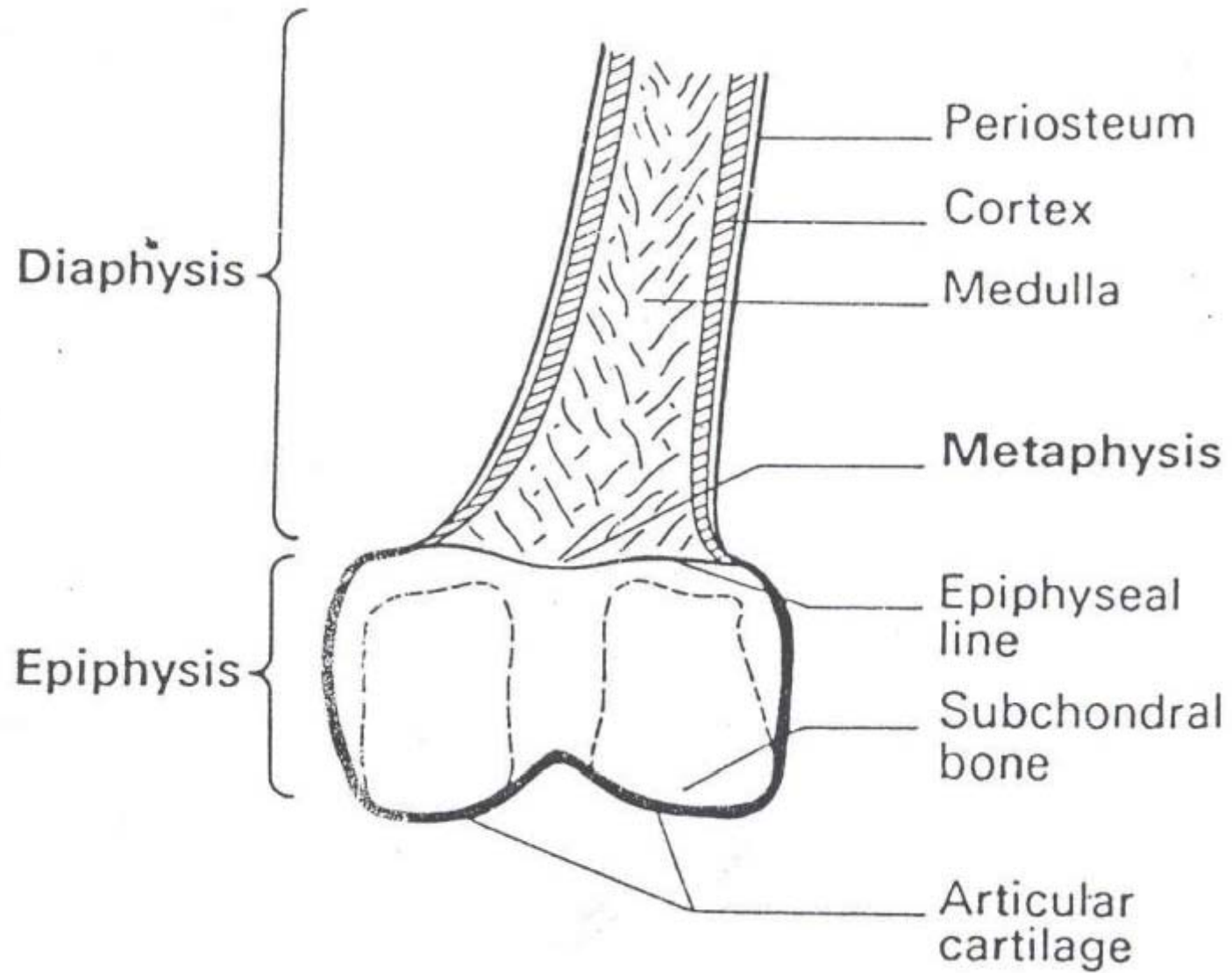
- MECHANICAL
 - support and site for muscle attachment
- PROTECTIVE
 - vital organs and bone marrow
- METABOLIC
 - reserve of calcium

The composition of bone

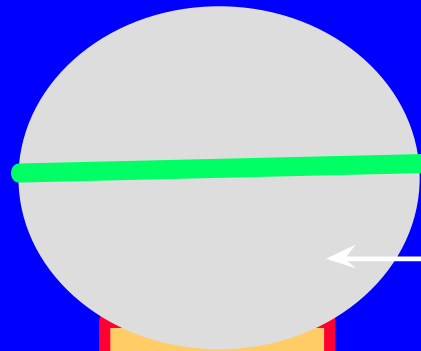


- **INORGANIC - 65%**
 - calcium hydroxyapatite ($10\text{Ca } 6\text{PO}_4 \text{OH}_2$)
 - is storehouse for 99% of Ca in the body
 - 85% of the phosphorous, 65% Na & Mg
- **ORGANIC - 35%**
 - bone cells and protein matrix

Bone geography



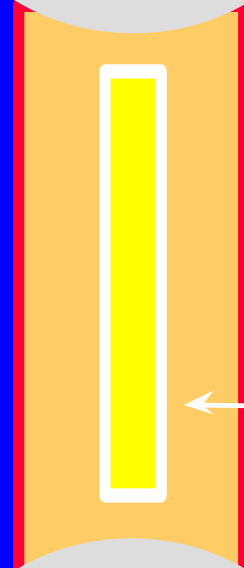
Epiphysis



Metaphysis



Diaphysis



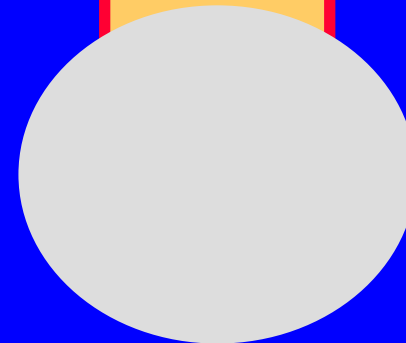
periosteum



endosteum

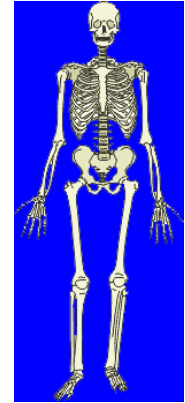


Epiphysis



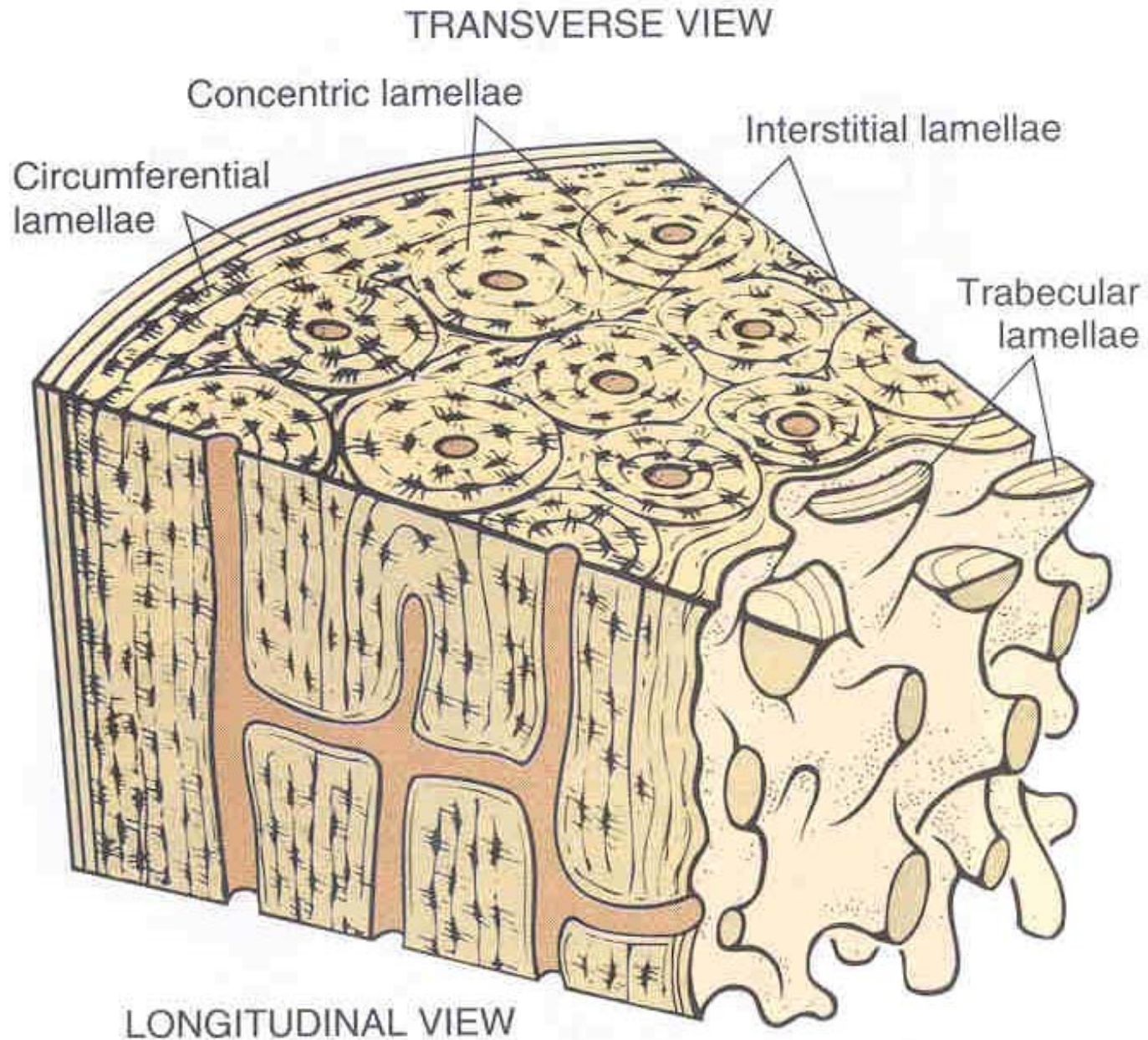


Classification of bone



- **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

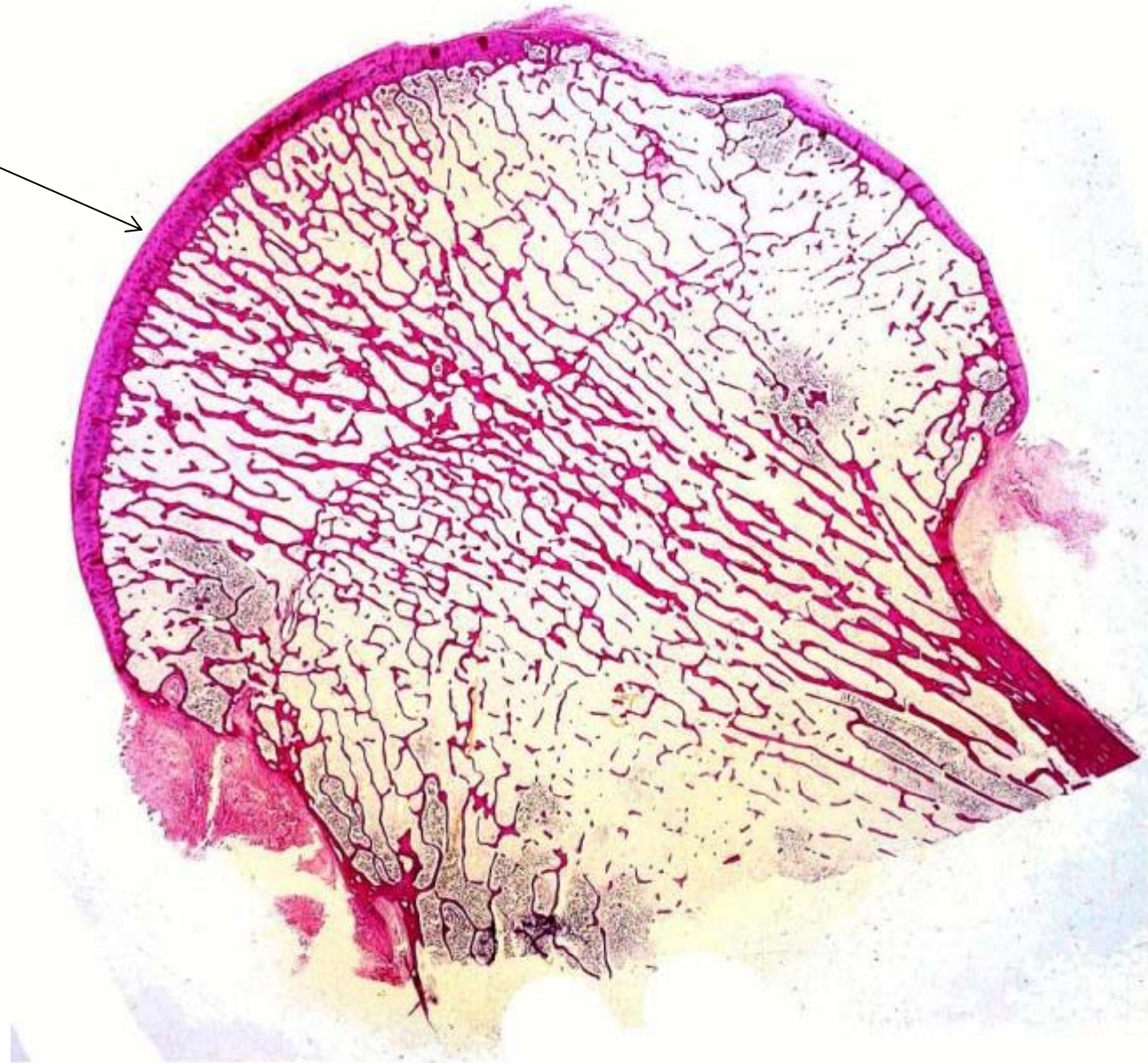
Bone Biopsy

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

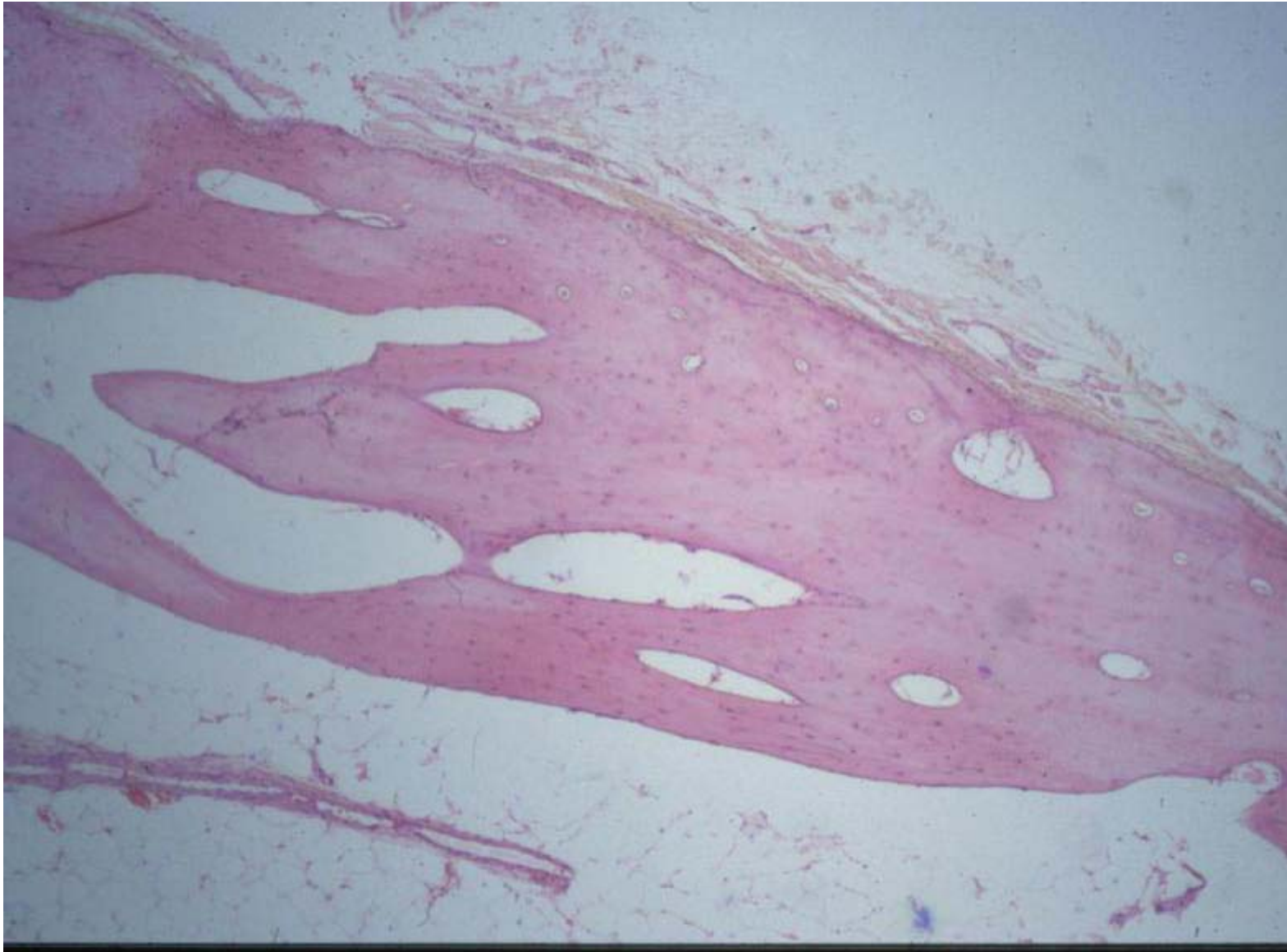


- Open – for sclerotic or inaccessible lesions

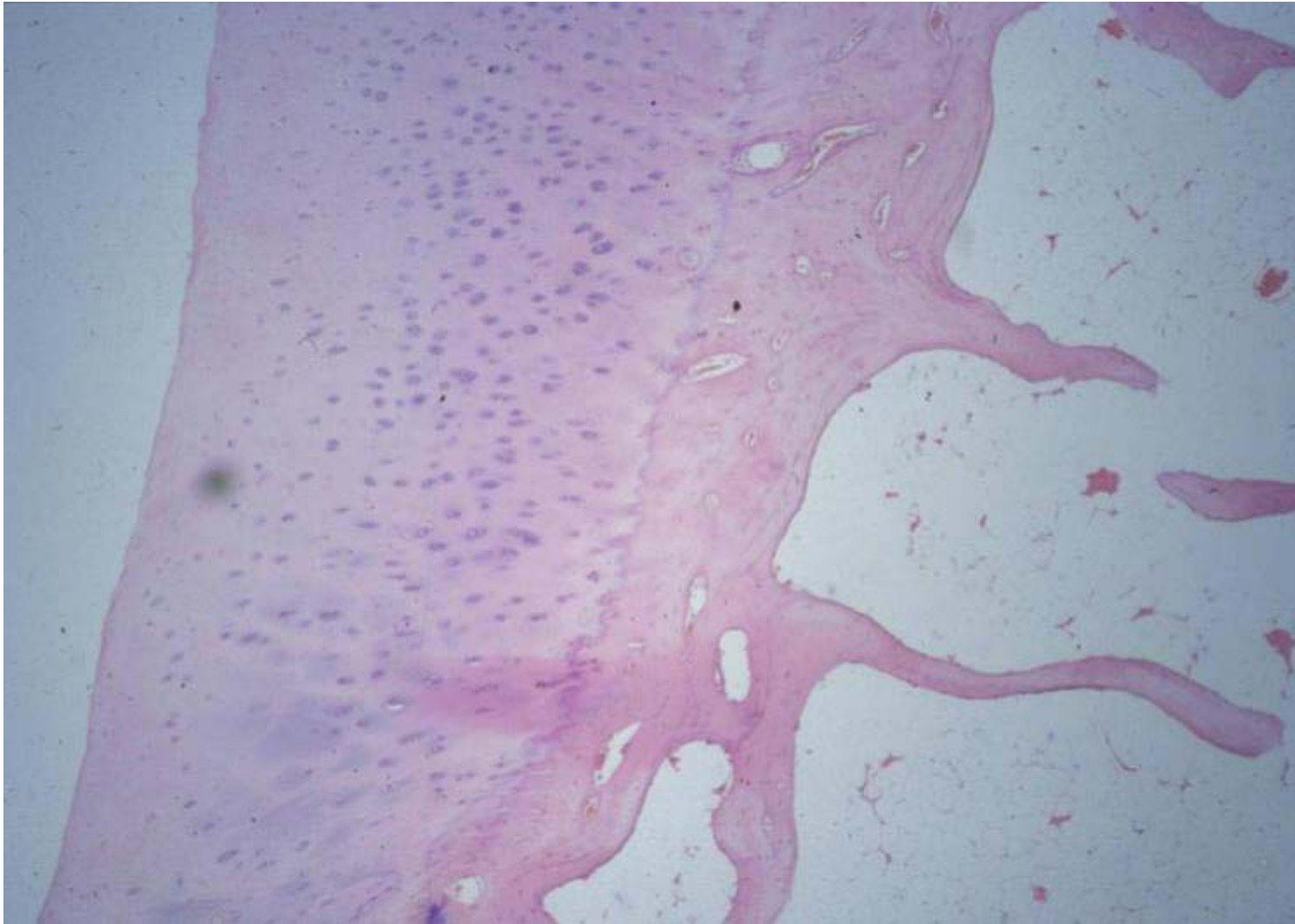
Histology of bone – femoral head



Histology of shaft of long bone

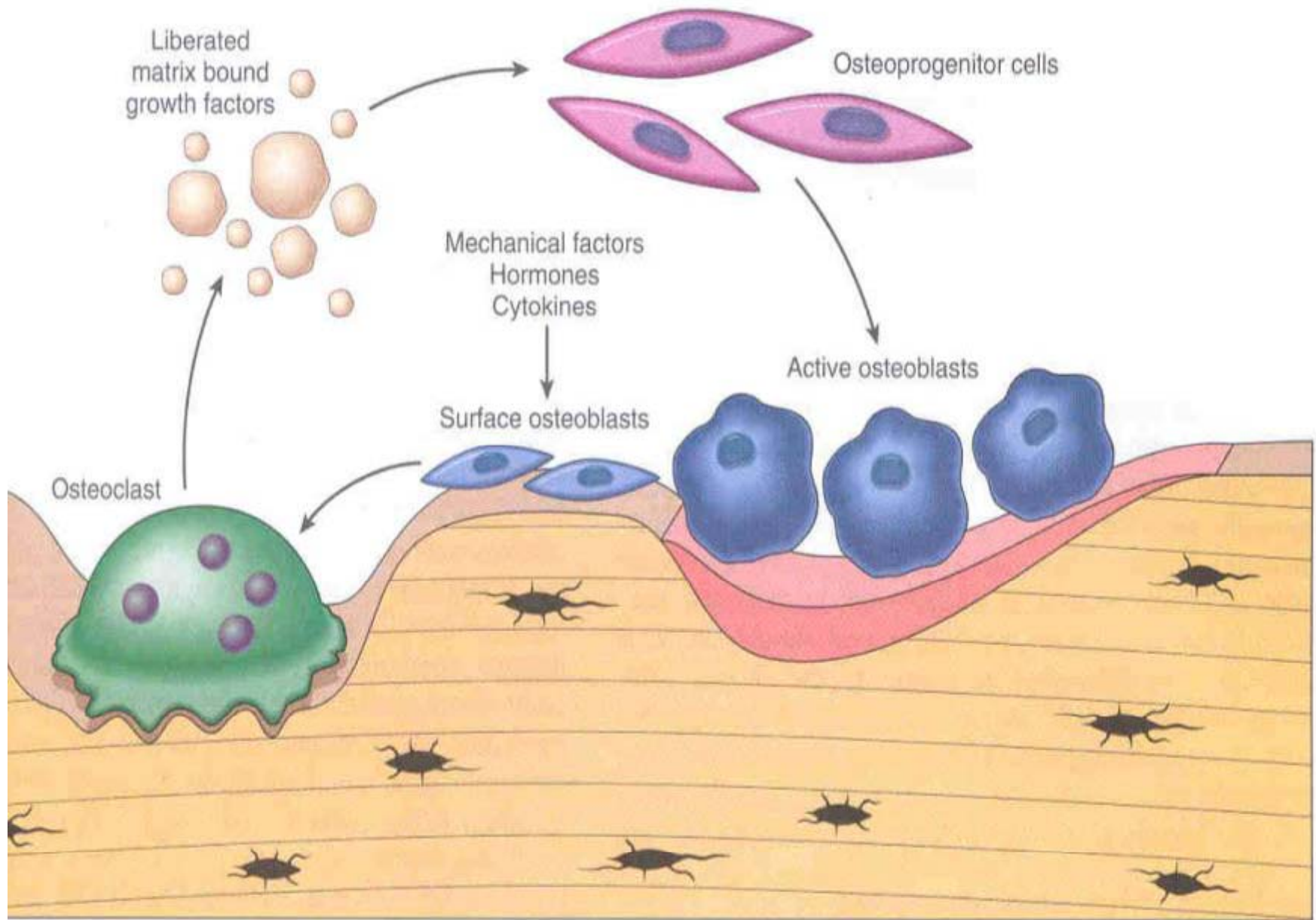


Histology of the articular surface

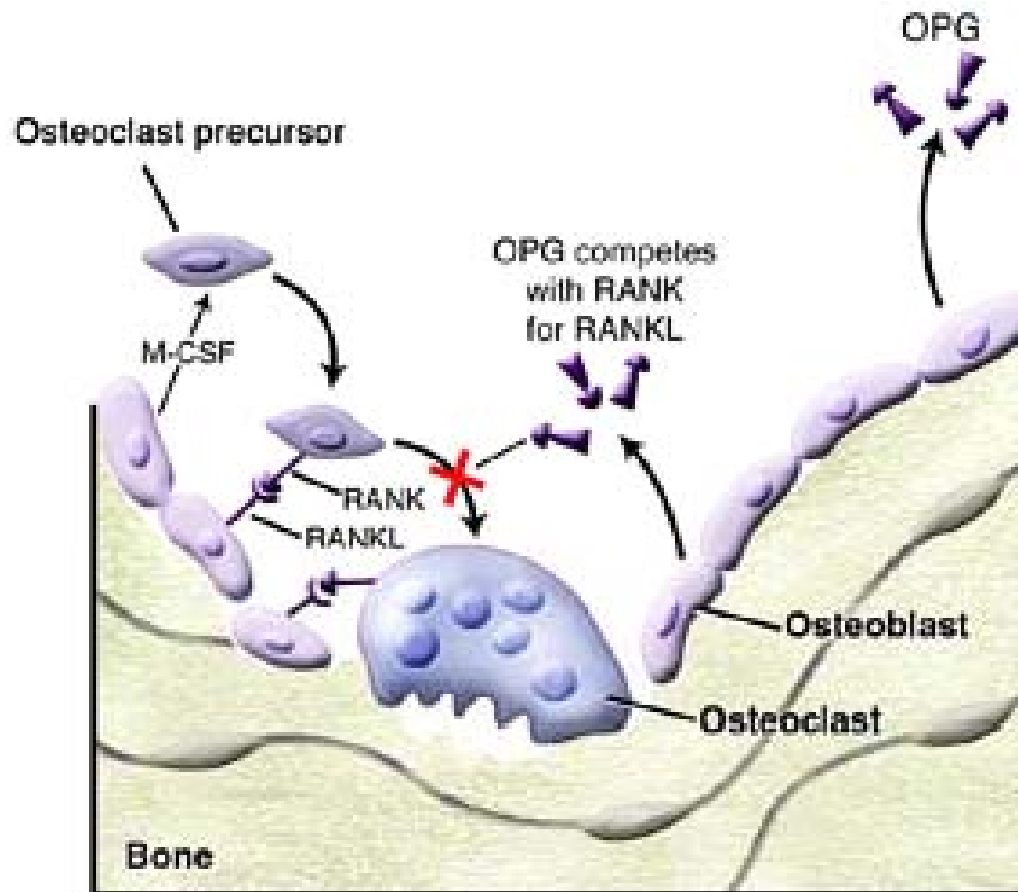


Bone Cells

- 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



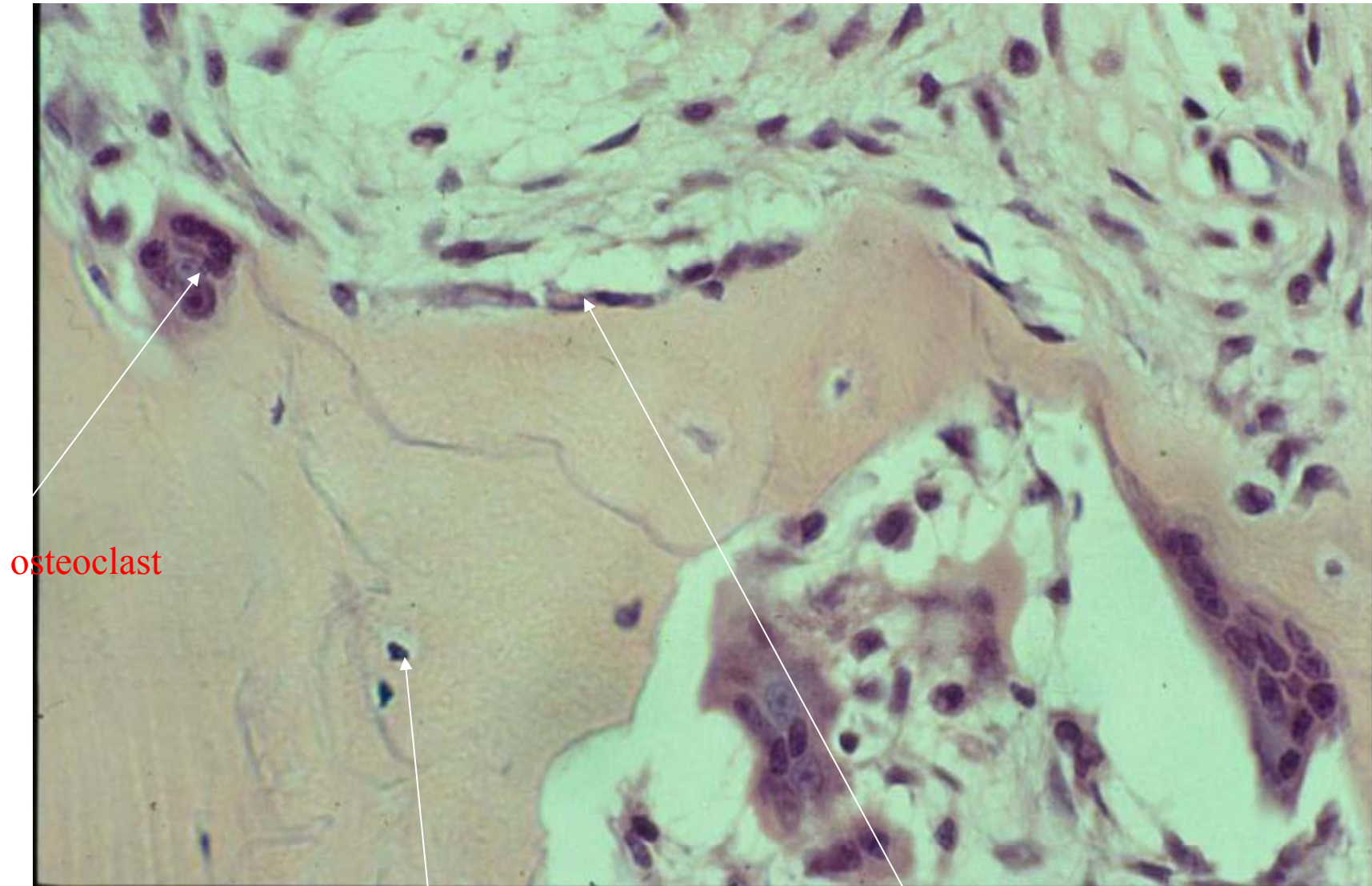
From Robbins & Cotran Pathologic Basis of Disease 7th Ed



RANK = Receptor Activator for nuclear factor κB

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

Bone Cells



osteoclast

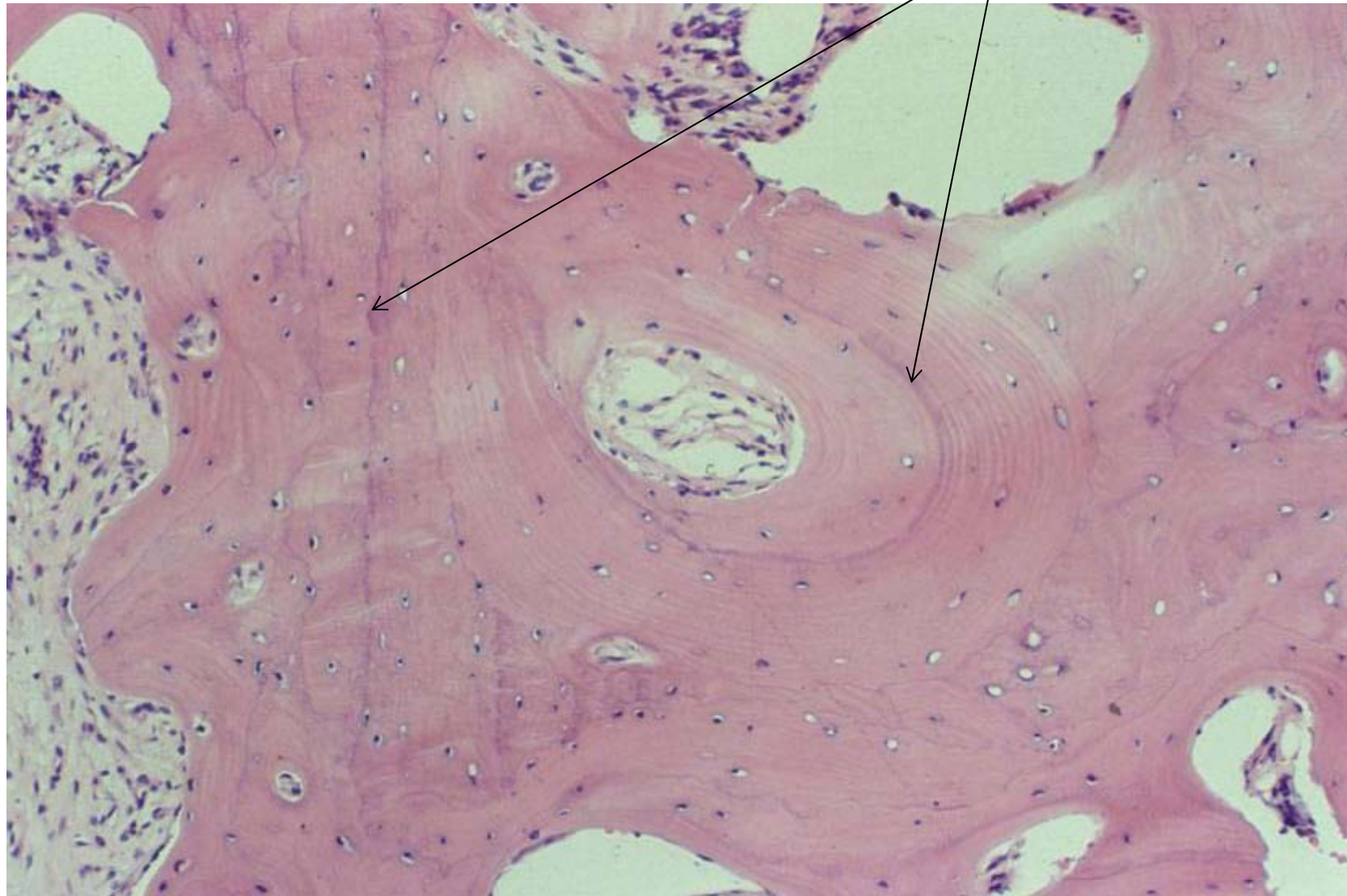
osteocyte

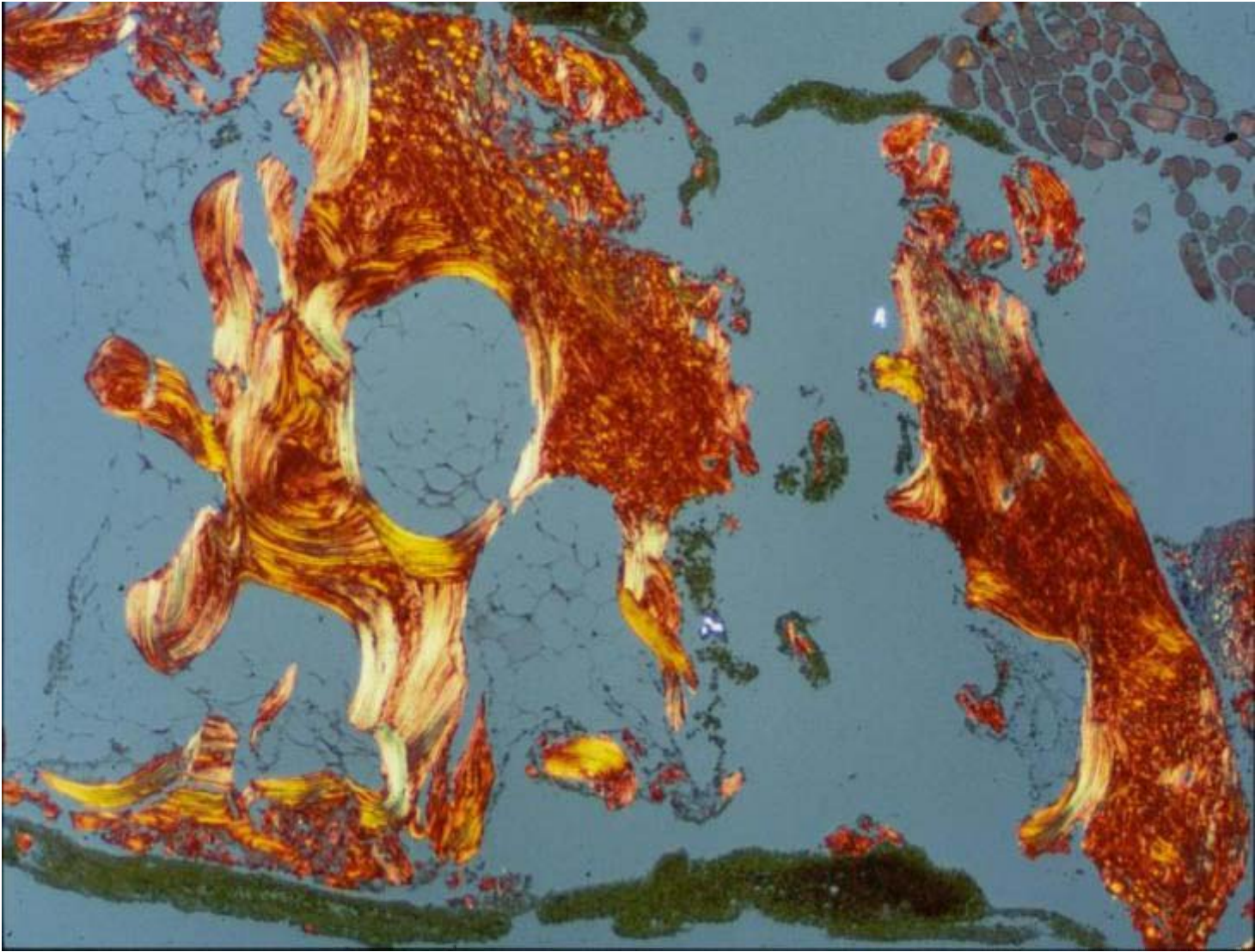
osteoblast

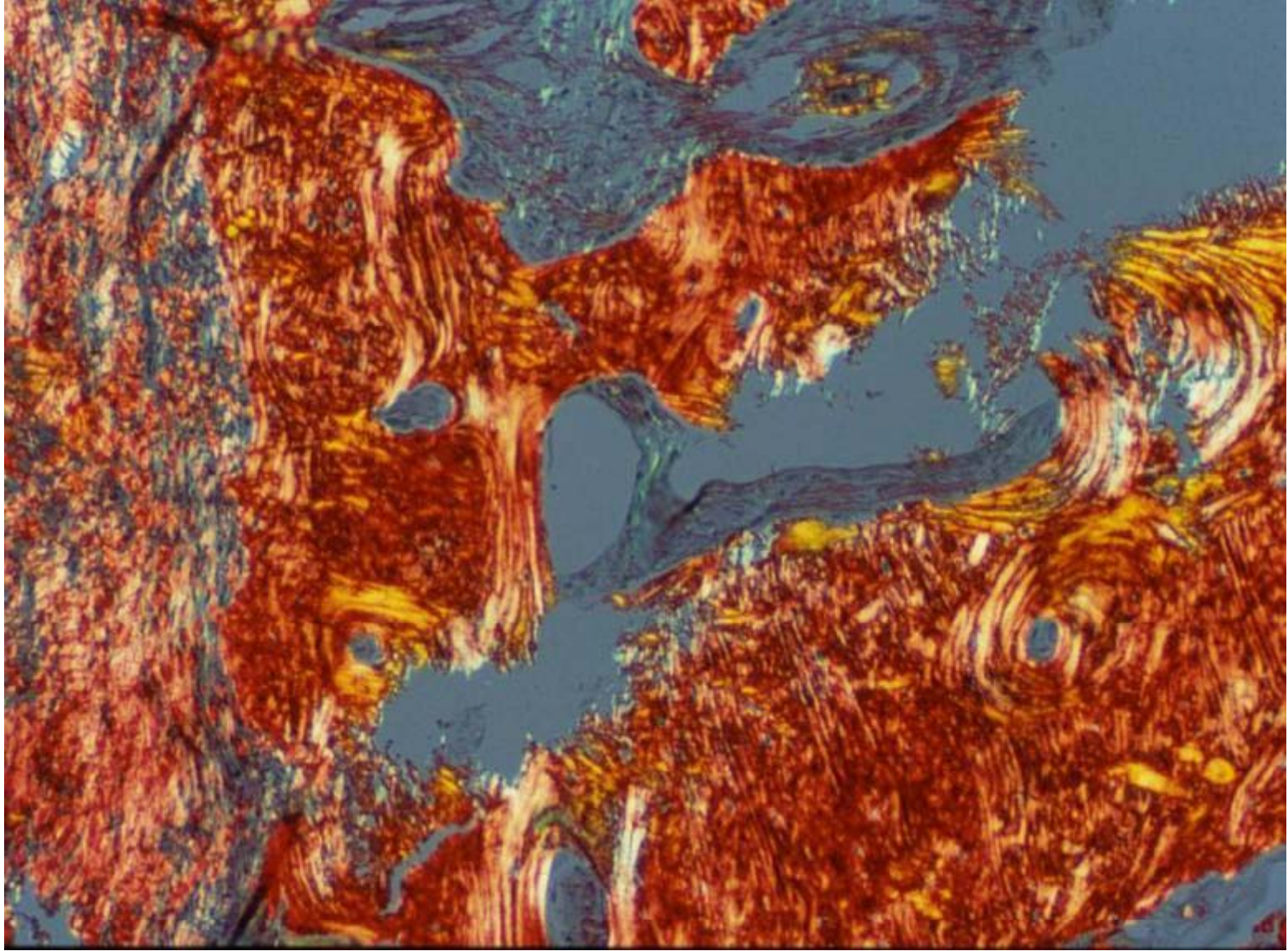
Types/classifications

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

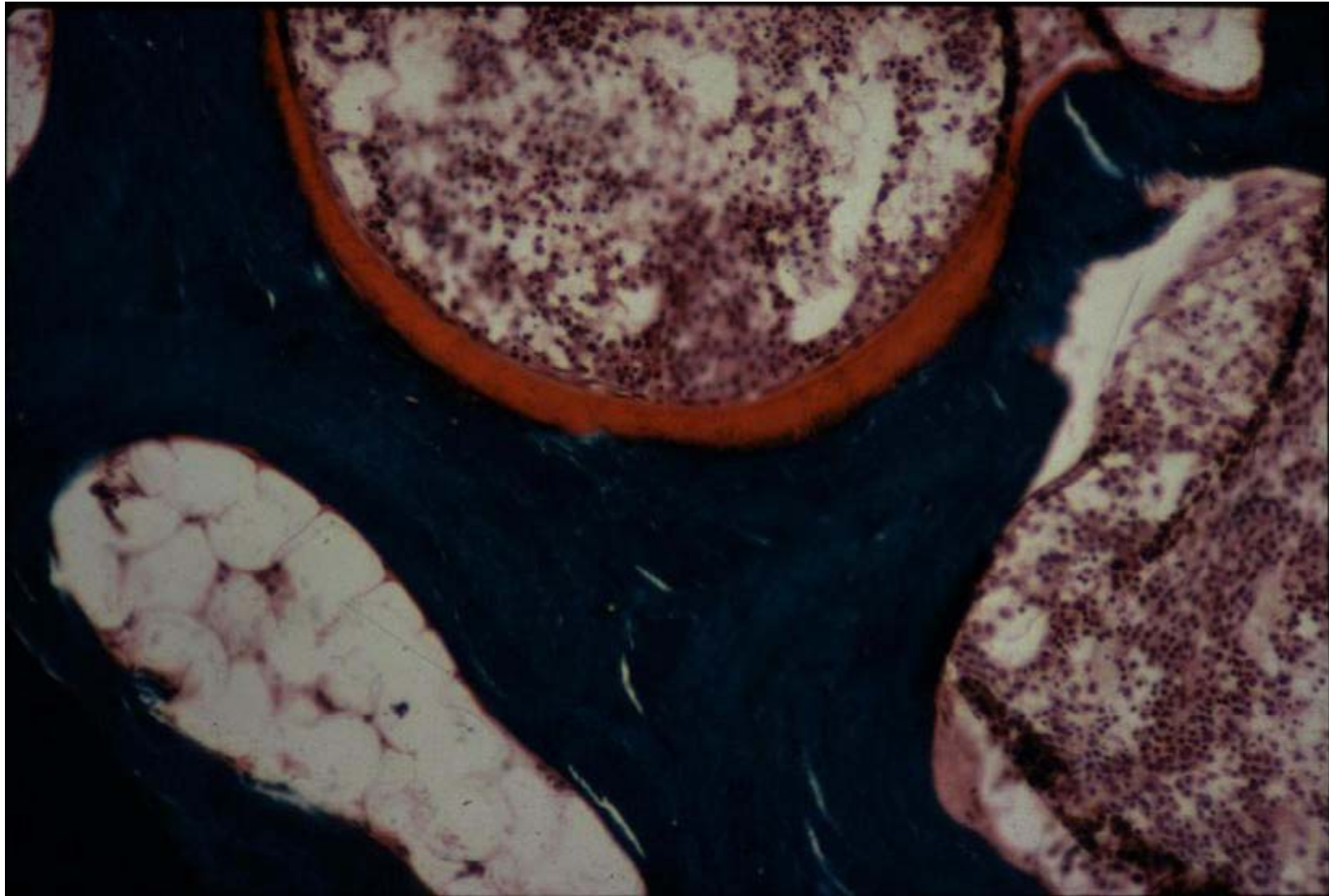
Trabecular lamellar bone with prominent 'reversal lines'







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:-

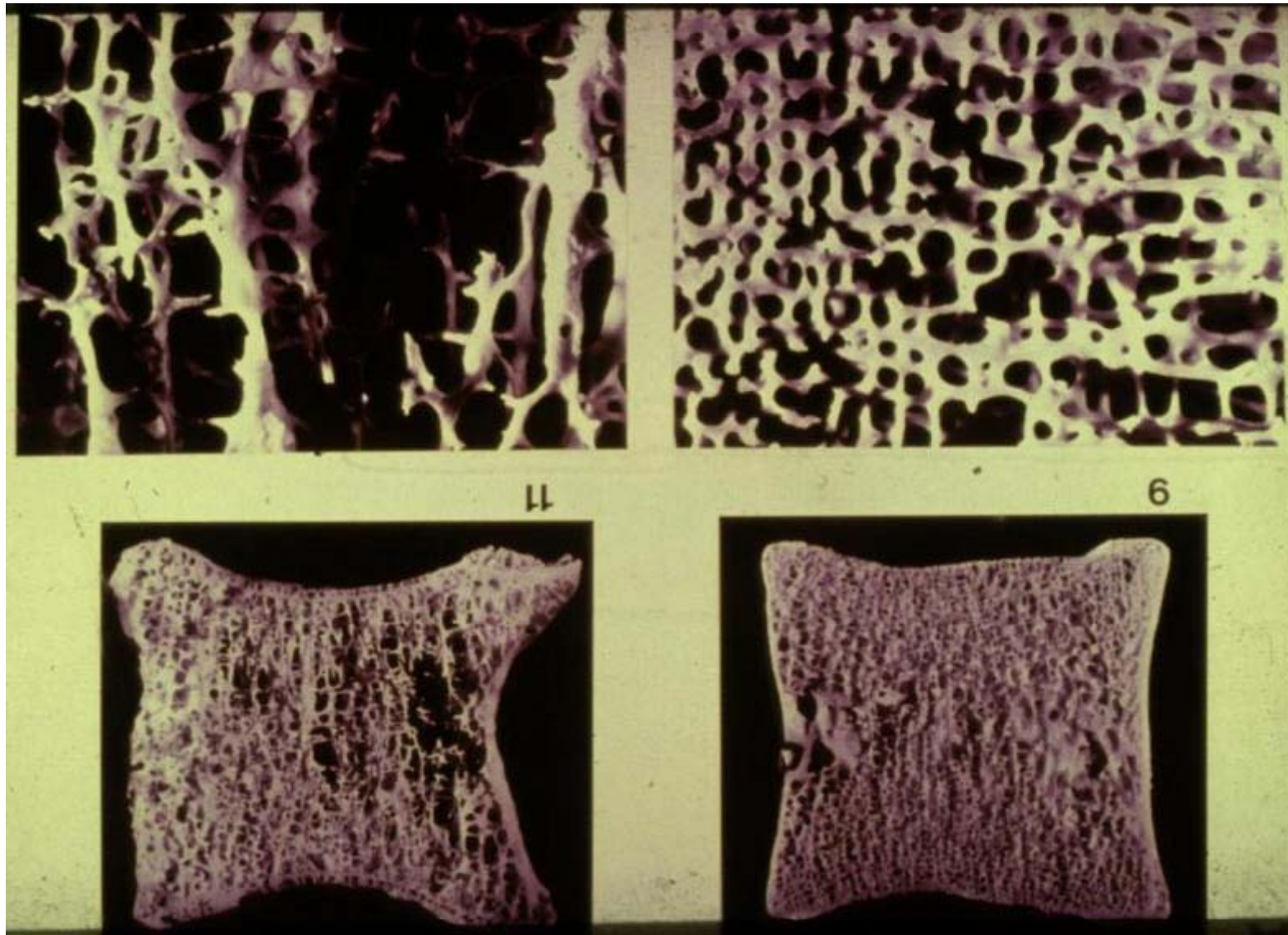
1. Related to endocrine abnormality (Vit D; Parathyroid hormone)
2. Non-endocrine (e.g. age related osteoporosis)
3. Disuse osteopaenia

Osteoporosis

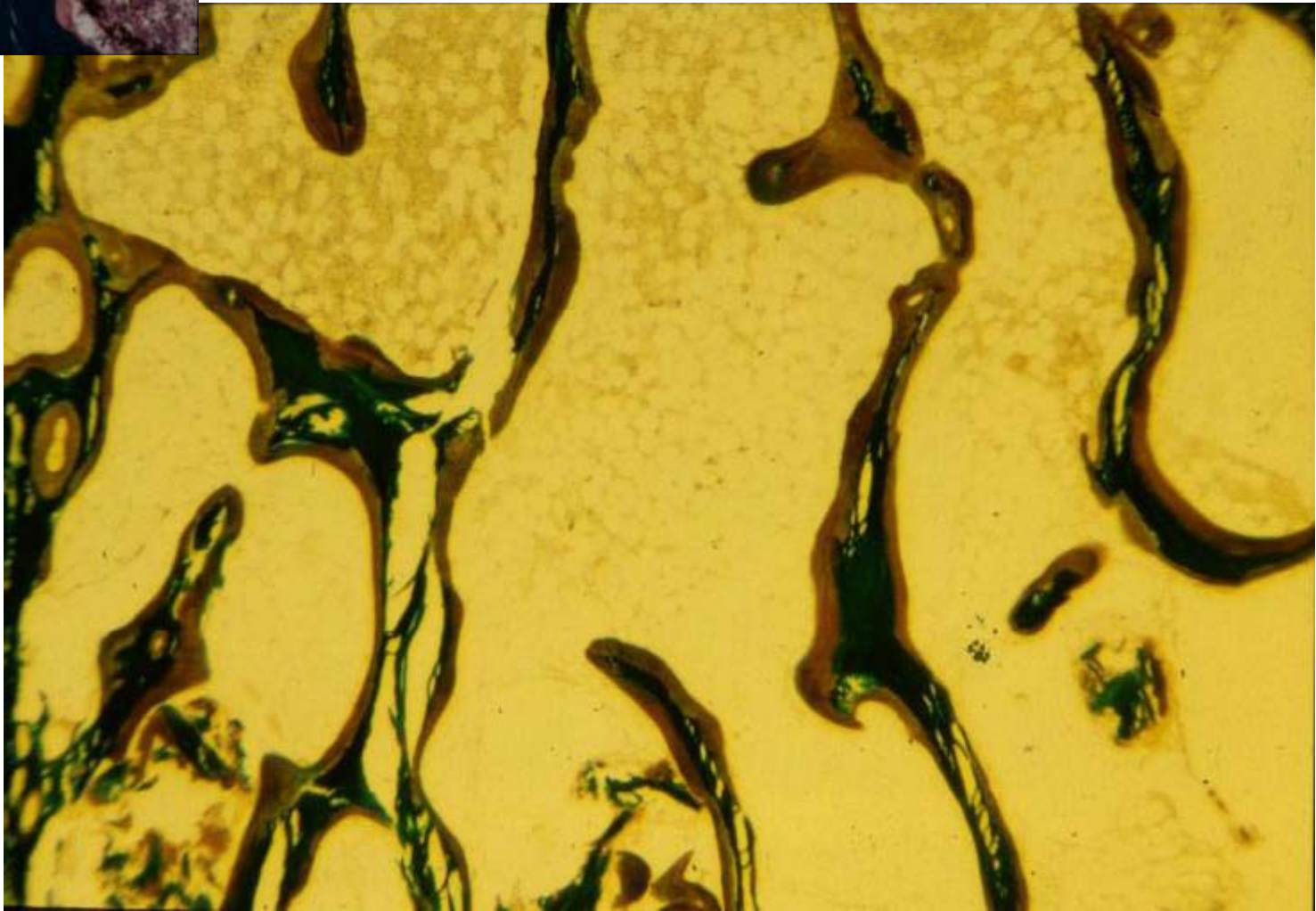
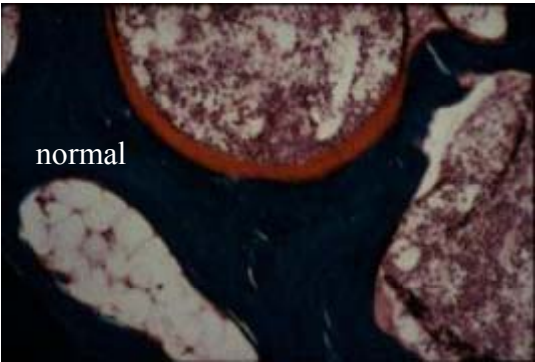
- Aetiology
 - 1° - age, post-menopause
 - 2° - drugs, systemic disease

Osteoporotic bone

Normal bone



Osteoporotic bone

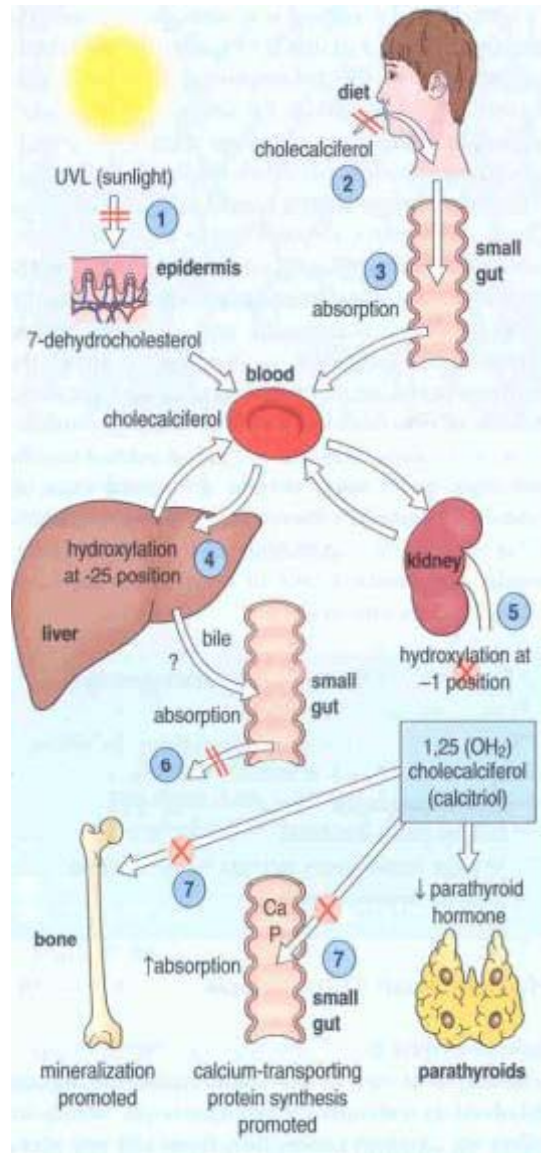


Osteomalacia

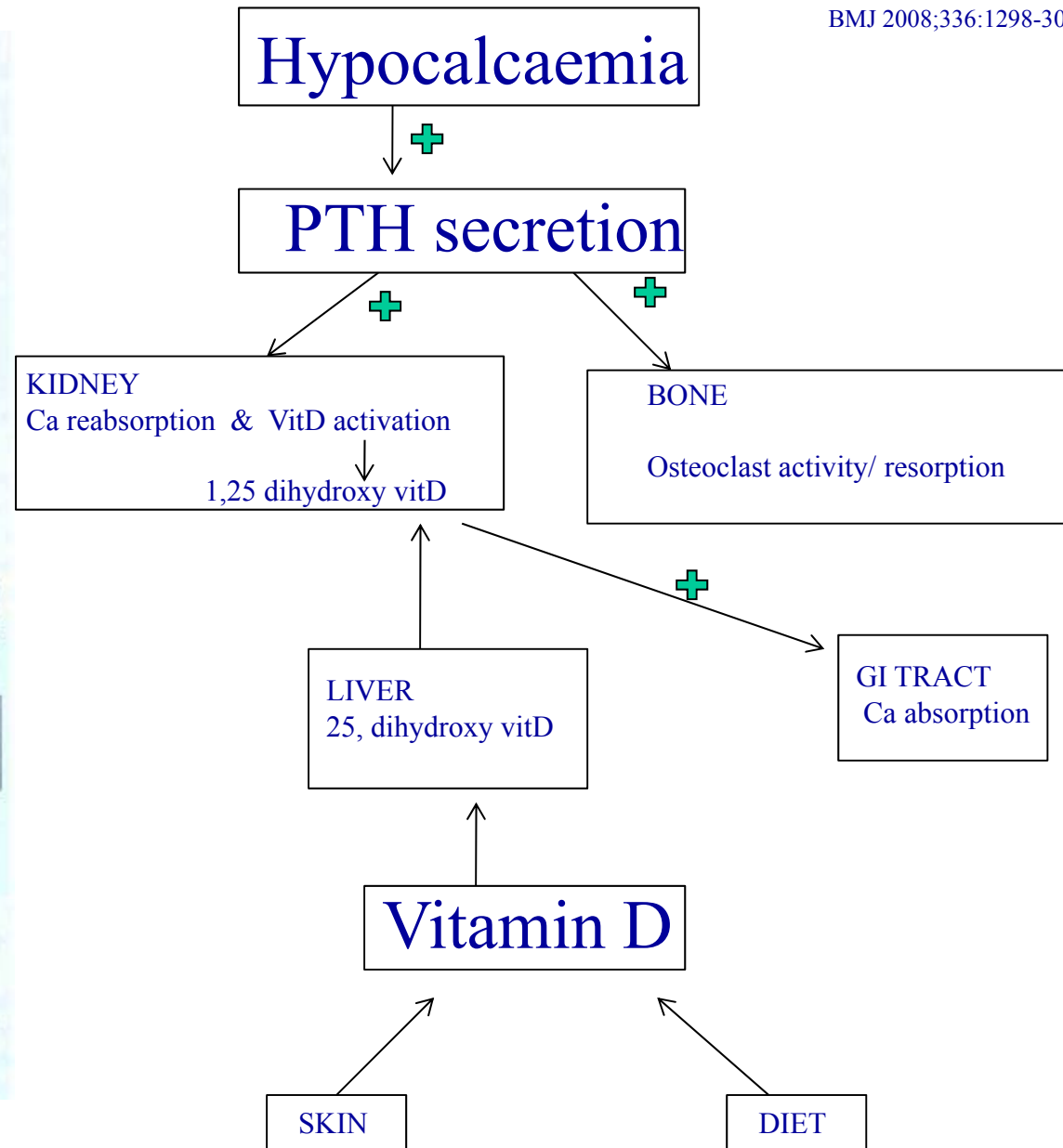
- Defective bone mineralisation

types effectively

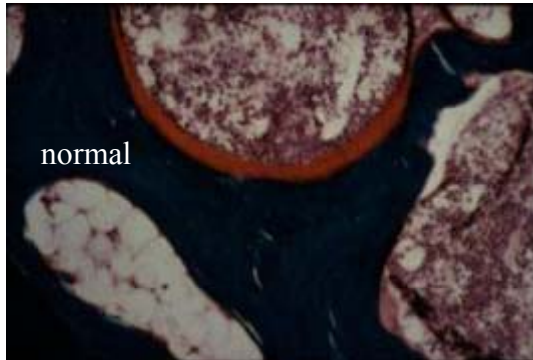
- 1. Deficiency of vitamin D
- 2 Deficiency of PO_4



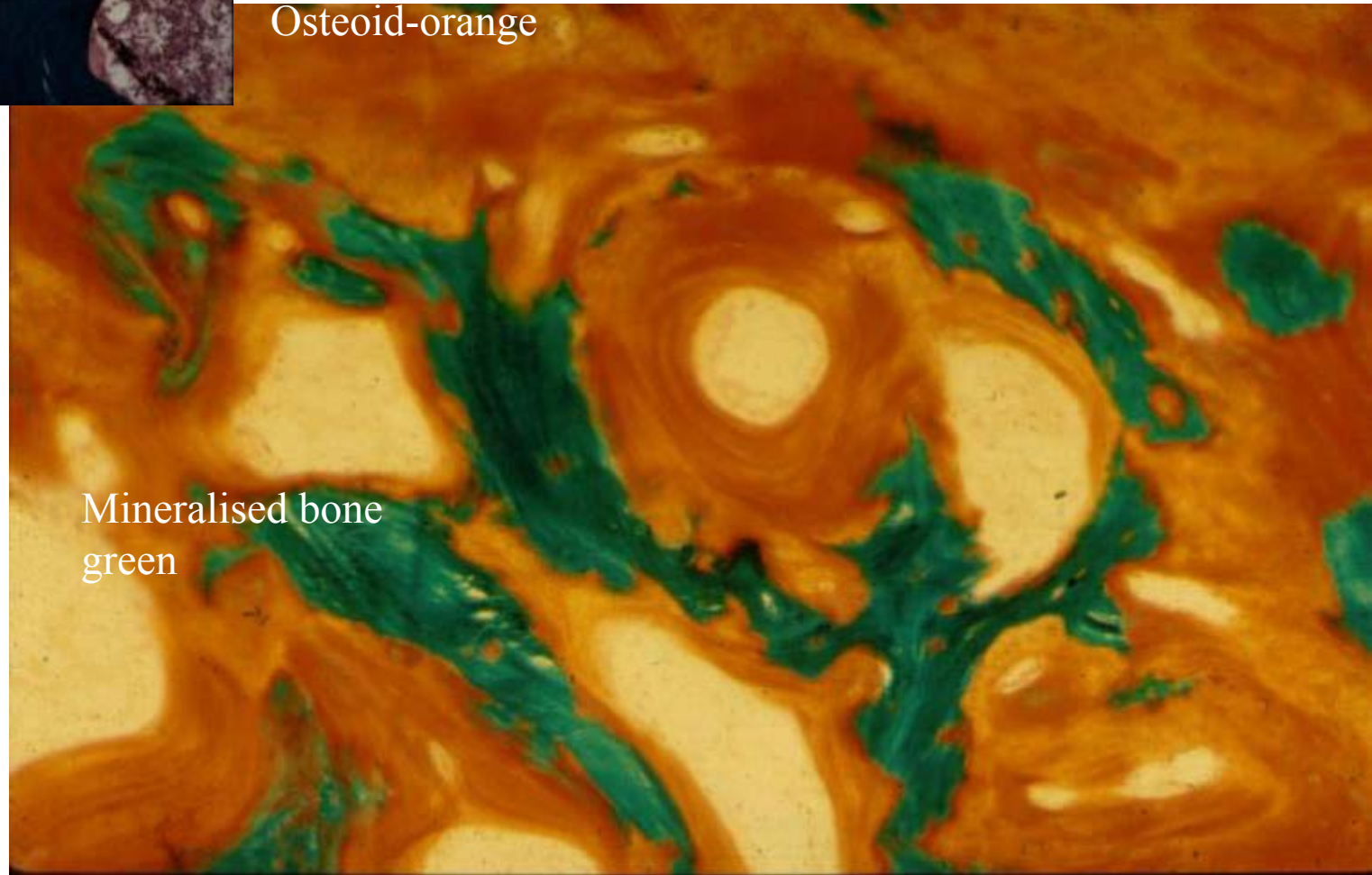
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Bone in osteomalacia



Osteoid-orange



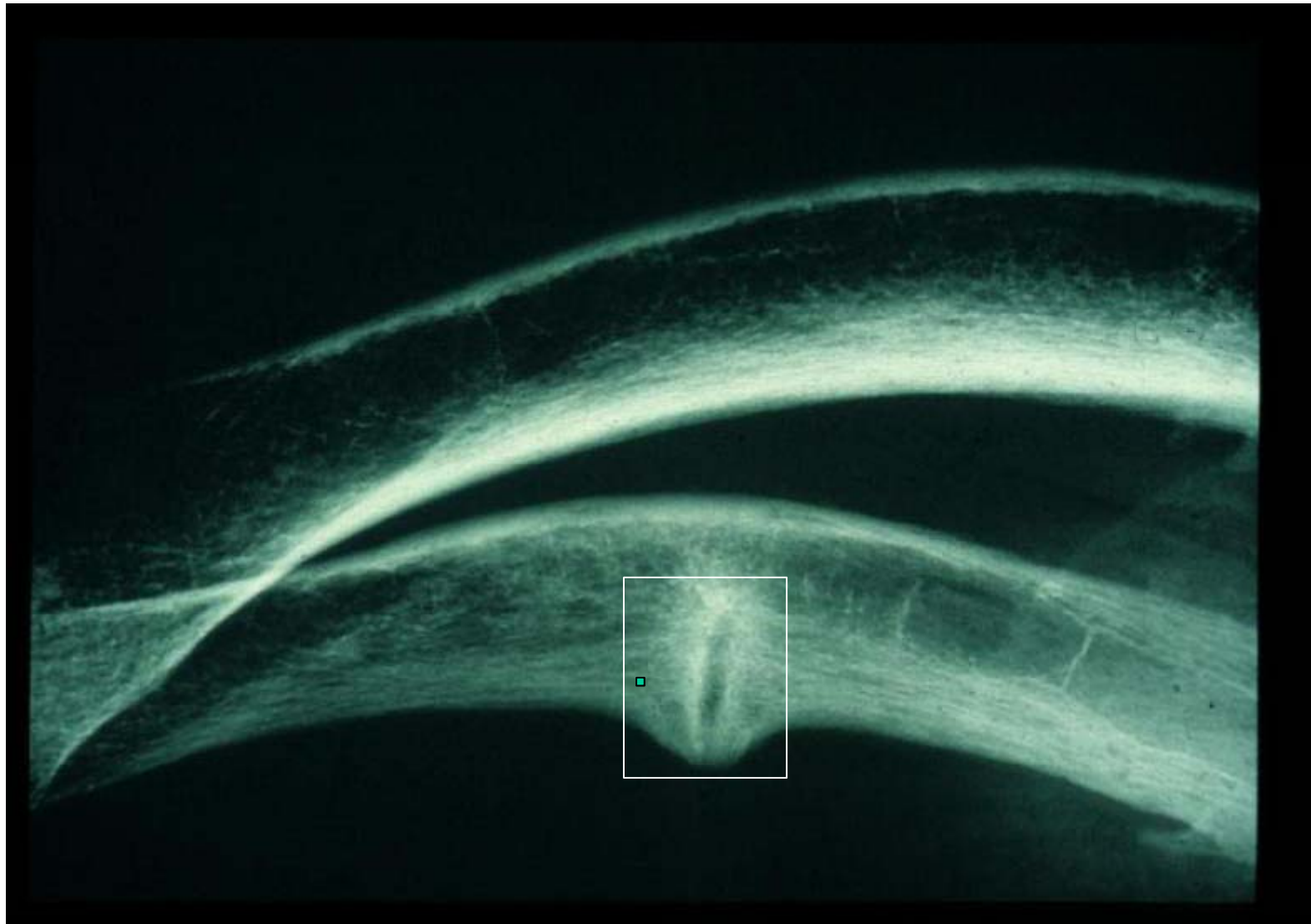
Osteomalacia

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

Osteomalacia (rickets)



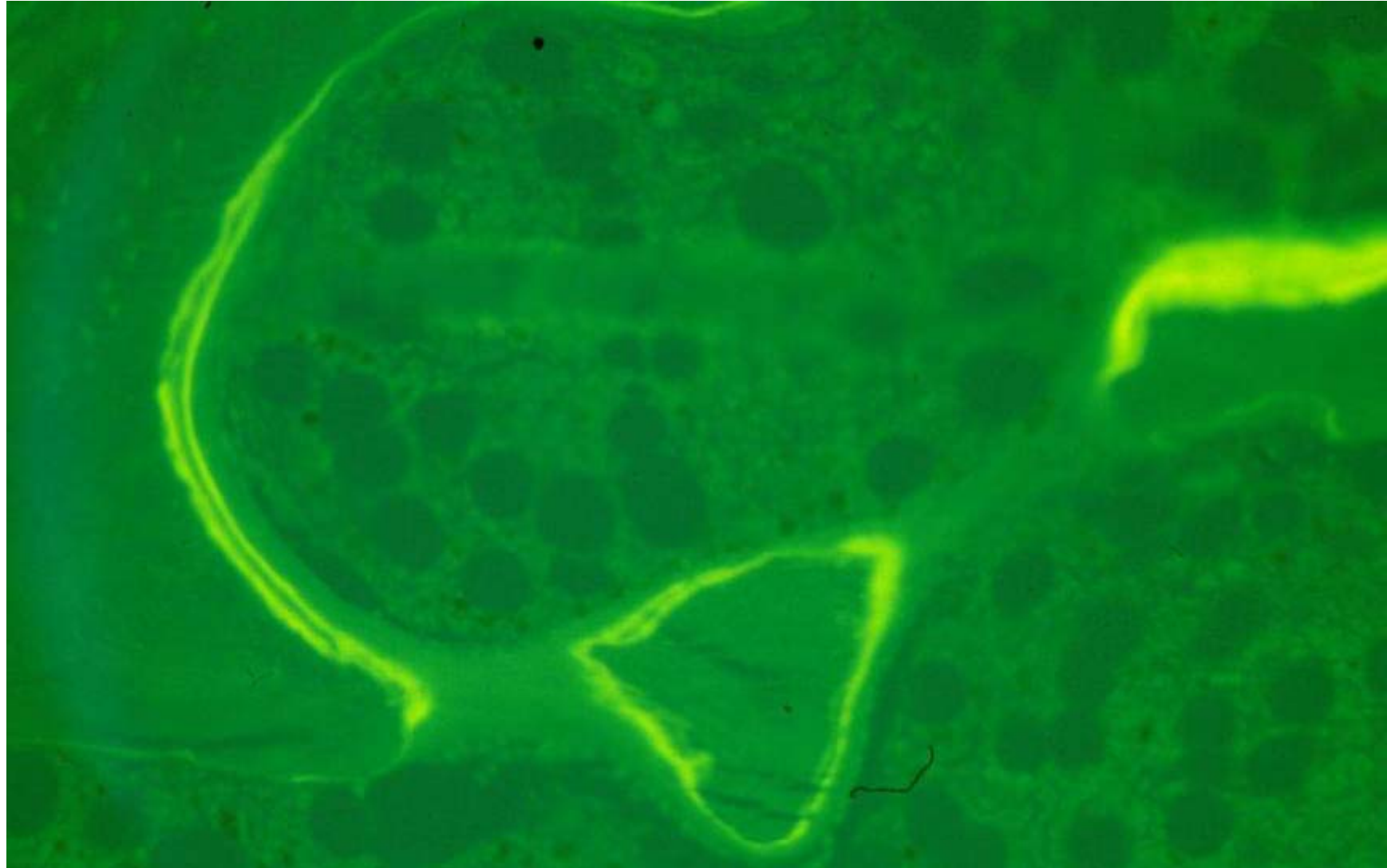
Horizontal fracture in Looser's zone



Horizontal fracture in Looser's zone



Tetracycline labelling – normal bone



Hyperparathyroidism

- Excess PTH
- increased Ca + PO₄ 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

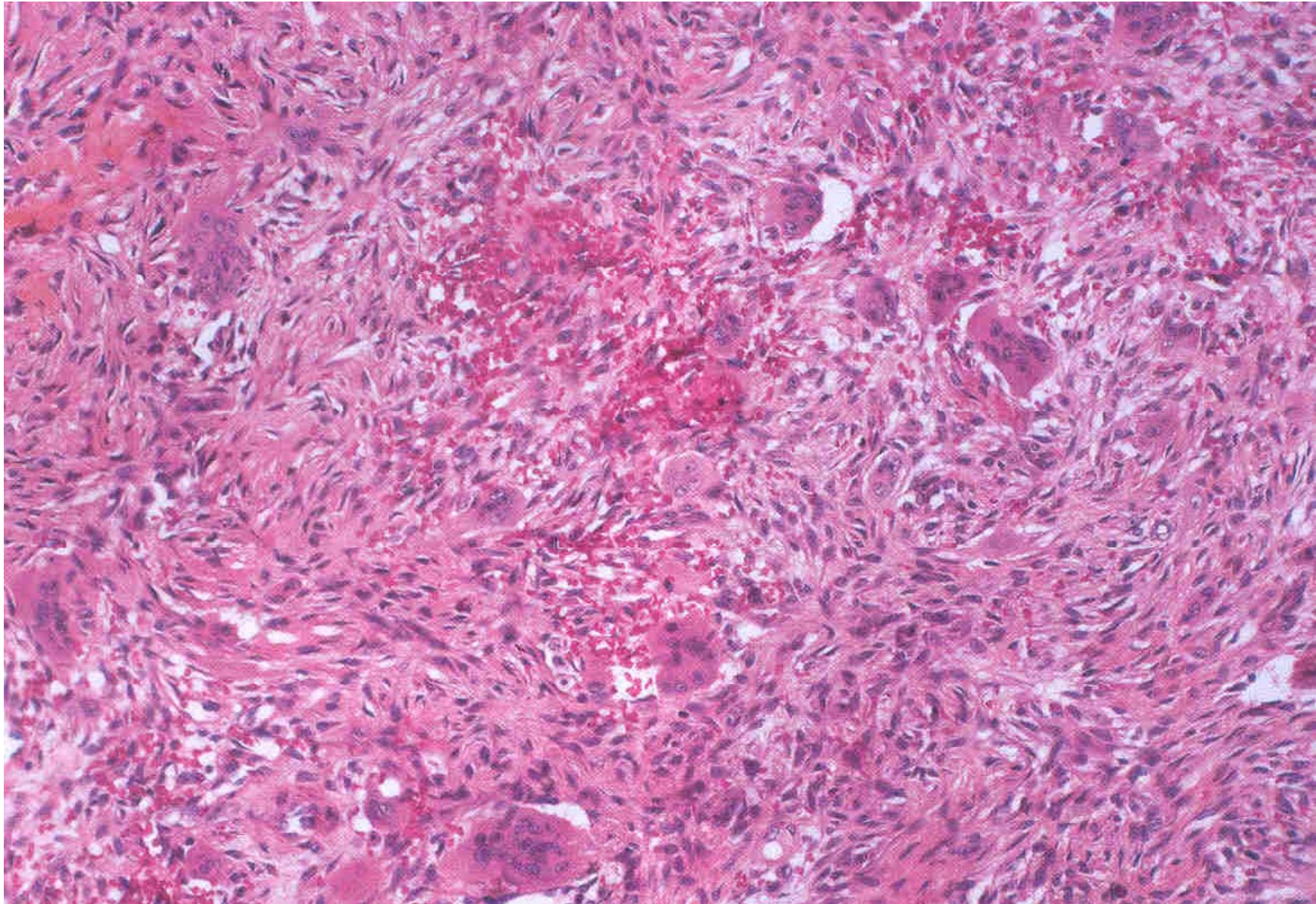
- 1° -
 - parathyroid adenoma (85-90%)
 - chief cell hyperplasia
- 2° -
 - chronic renal deficiency
 - vit D deficiency

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



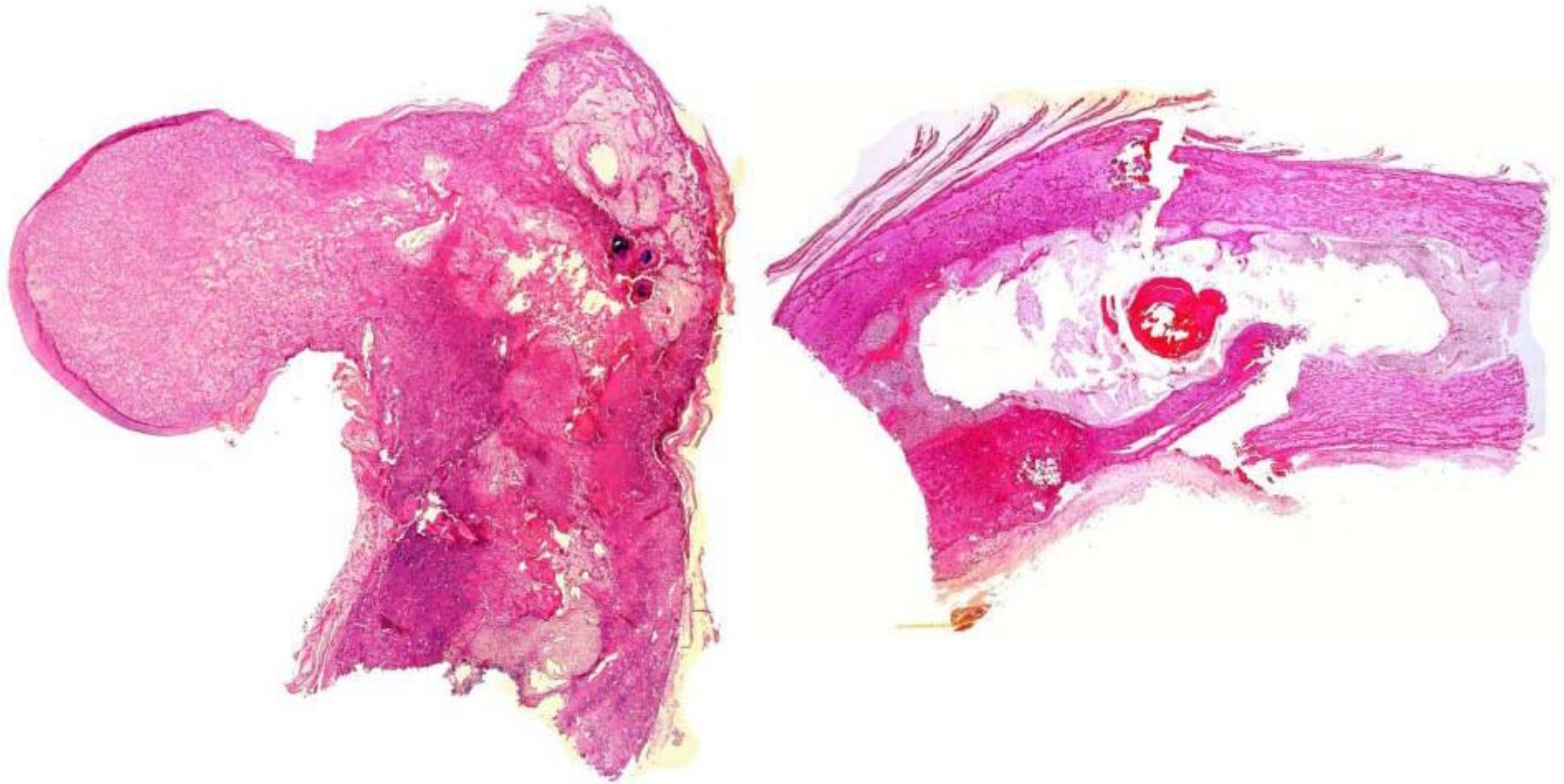
Renal Osteodystrophy

- 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

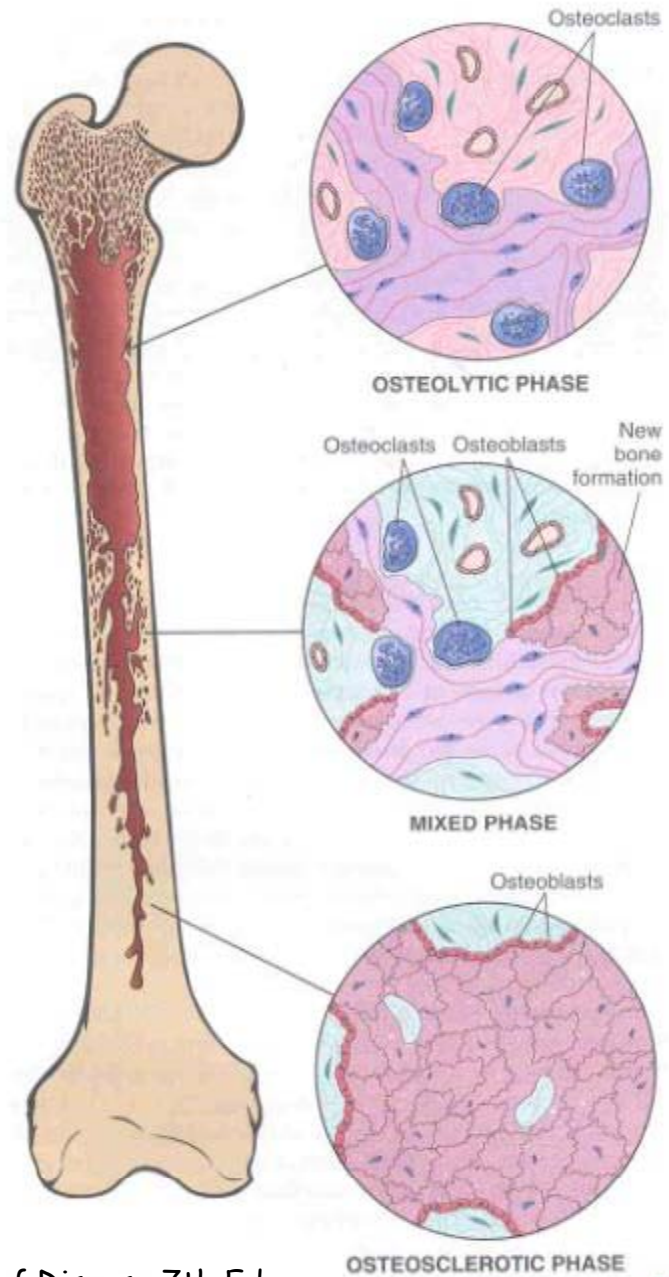


Renal Osteodystrophy

- PO_4 retention – hyperphosphataemia
- Hypocalcaemia as a result of ↓vit D
- 2° hyperparathyroidism
- Metabolic acidosis
- Aluminium deposition

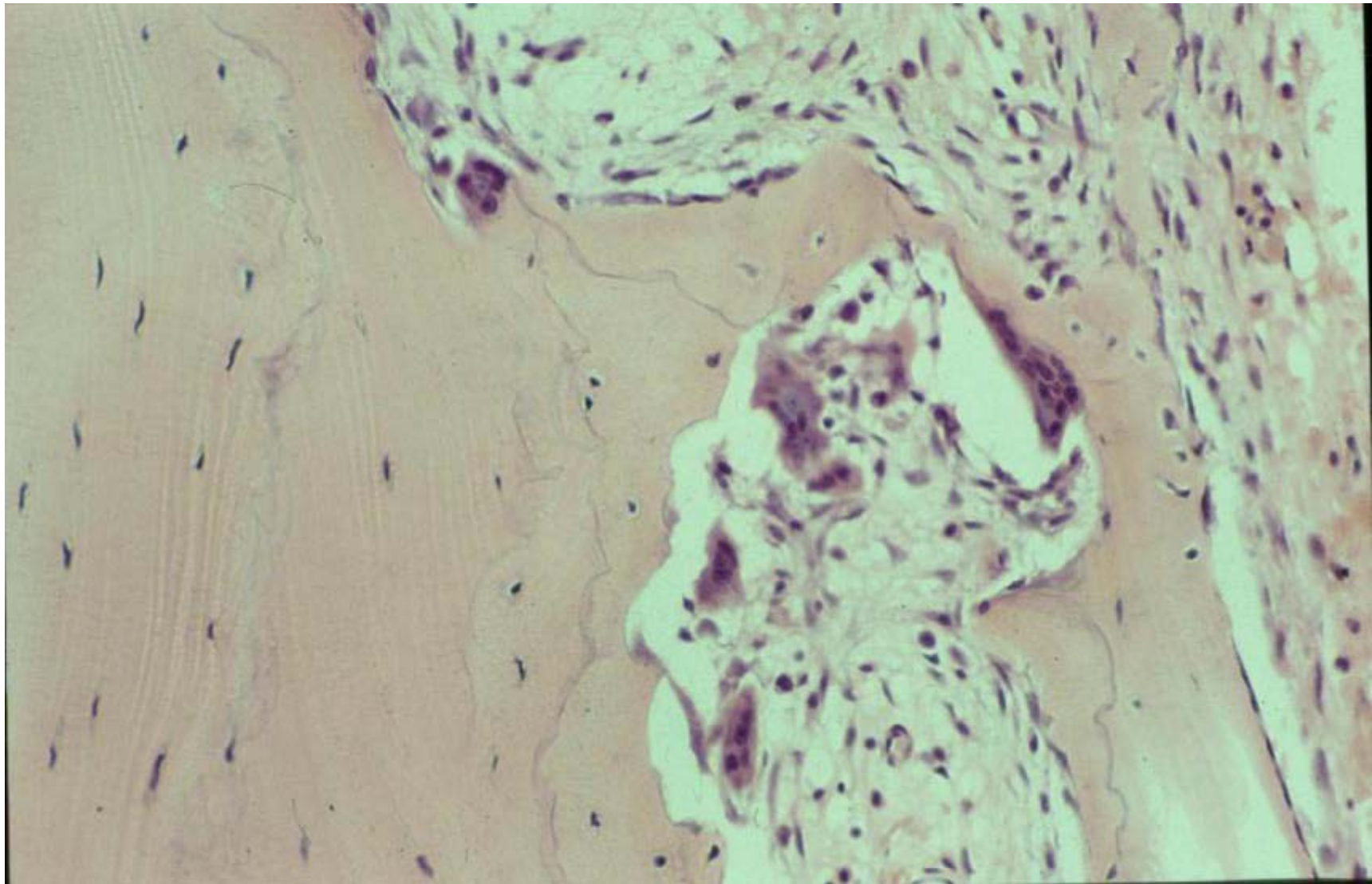
Paget's disease

- 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



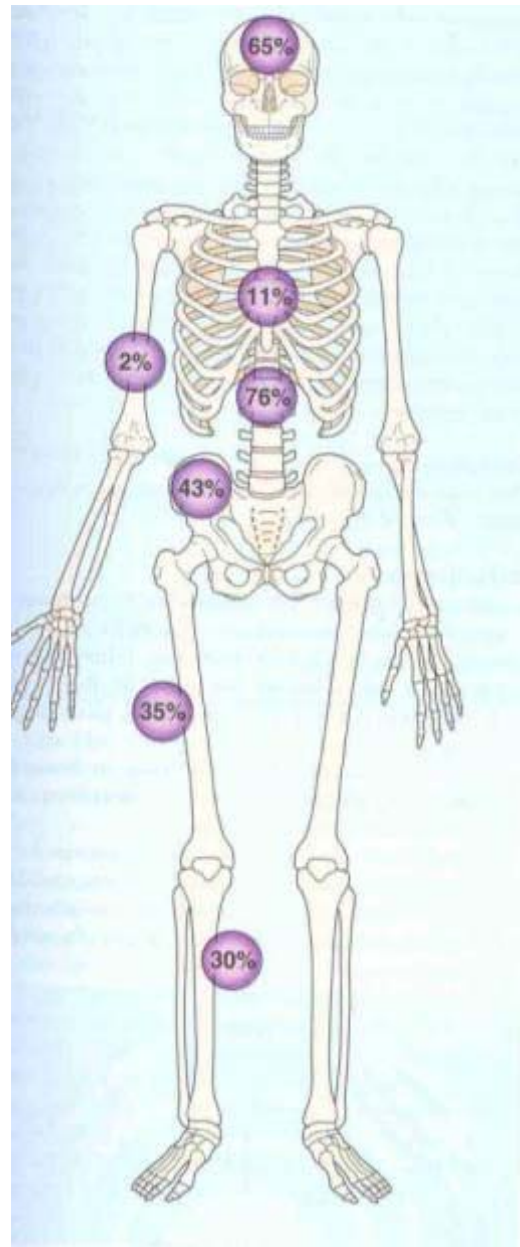
Paget's disease

- 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

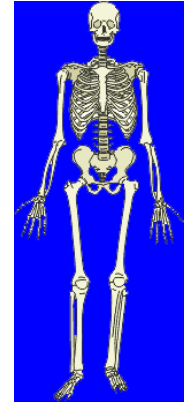
Clinical symptoms:-

- 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