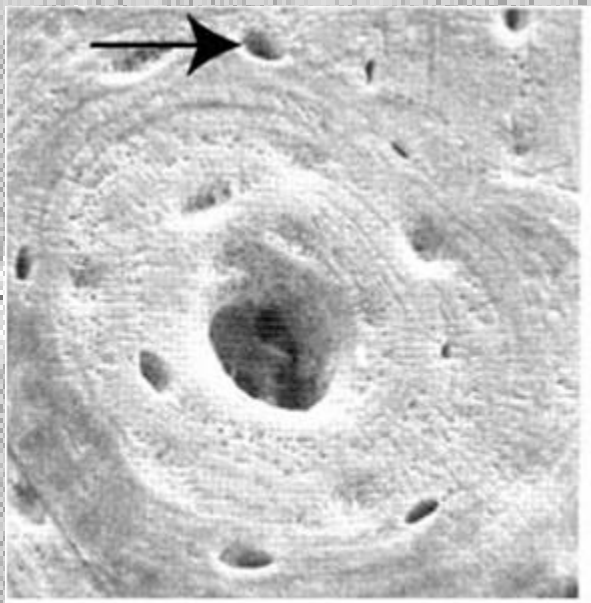
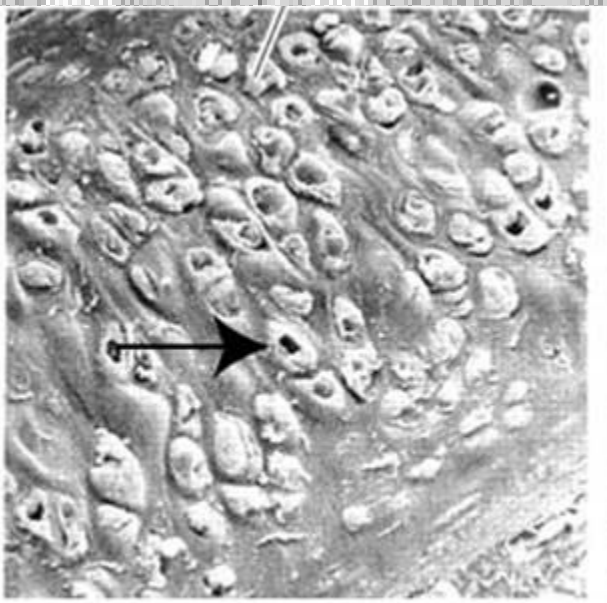
CARTILAGE and BONE



Bone Tissue



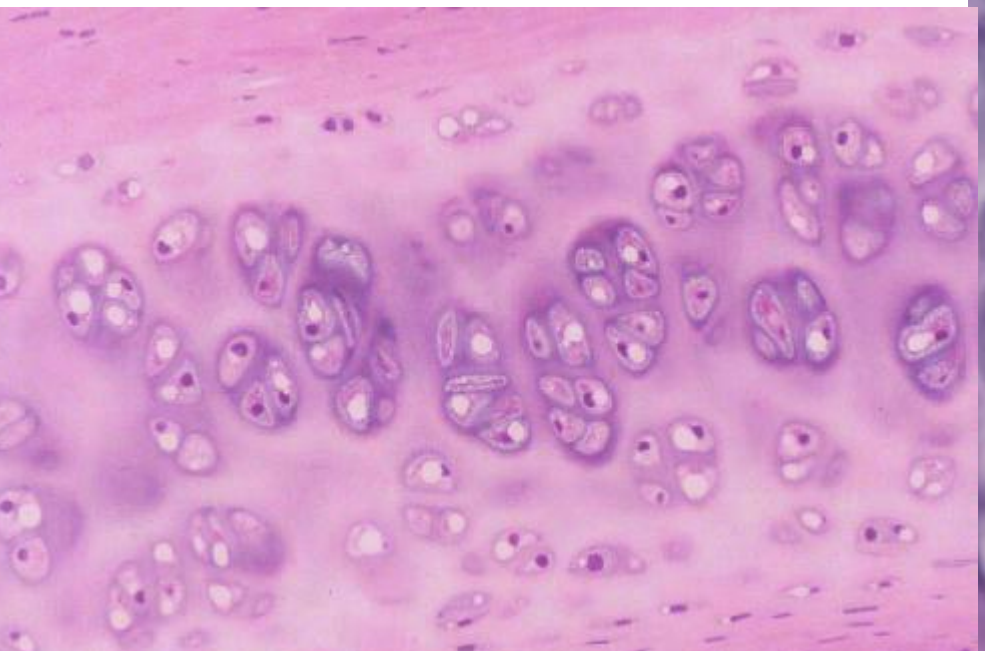
Cartilege

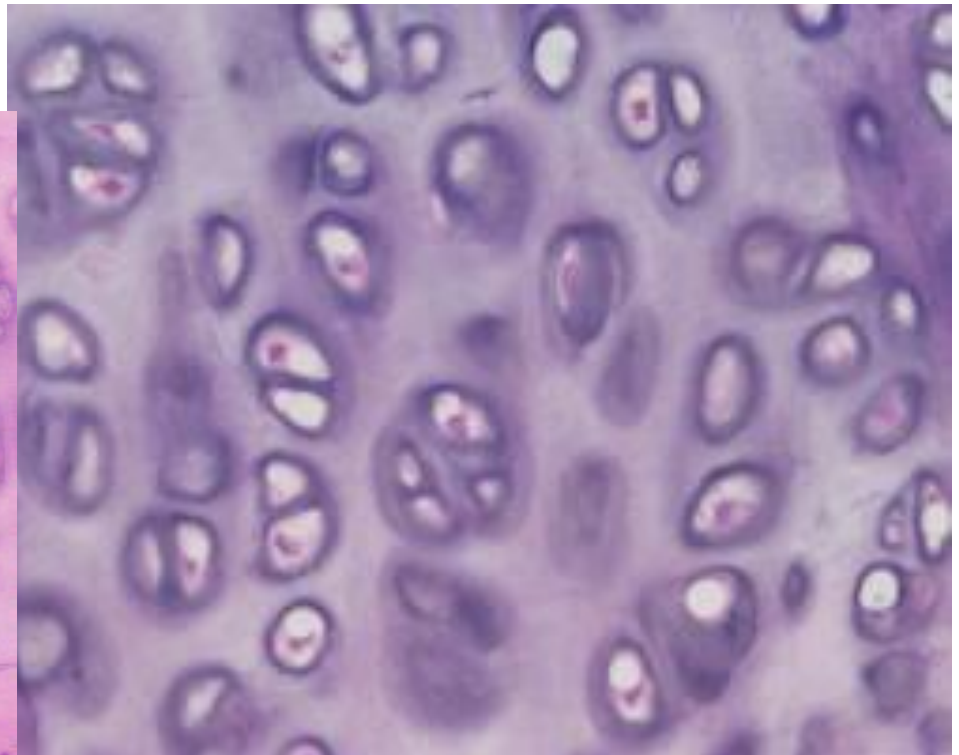
Connective Tissue

Structure of **cartilage**

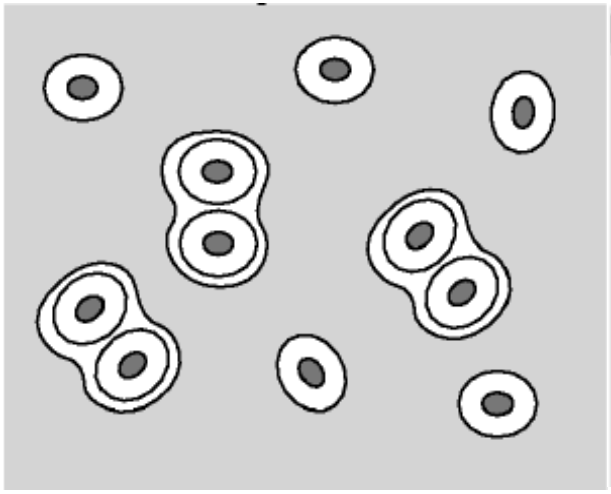
- cells – chondrocytes (in lacunae)
- extracellular matrix

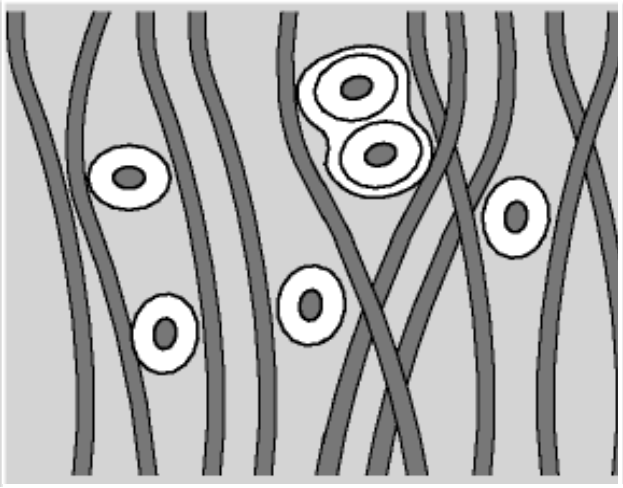
- absence of blood and lymphatic vessels
- lack of nerves

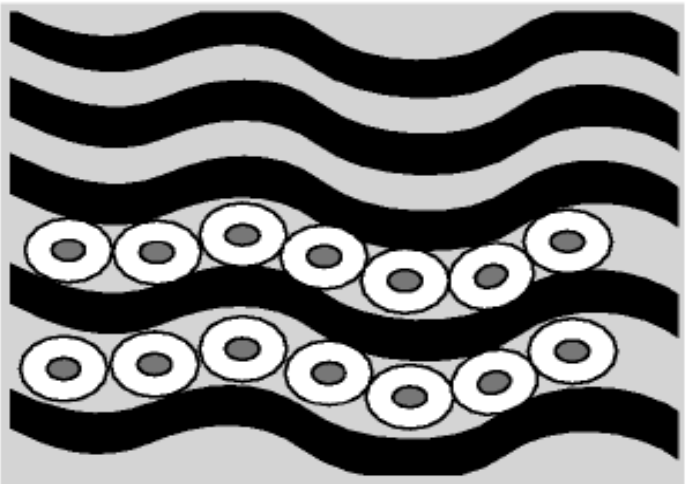




Types of cartilage







Hyaline cartilage

Type II collagen fibres

The most abundant cartilage in the body

Elastic cartilage

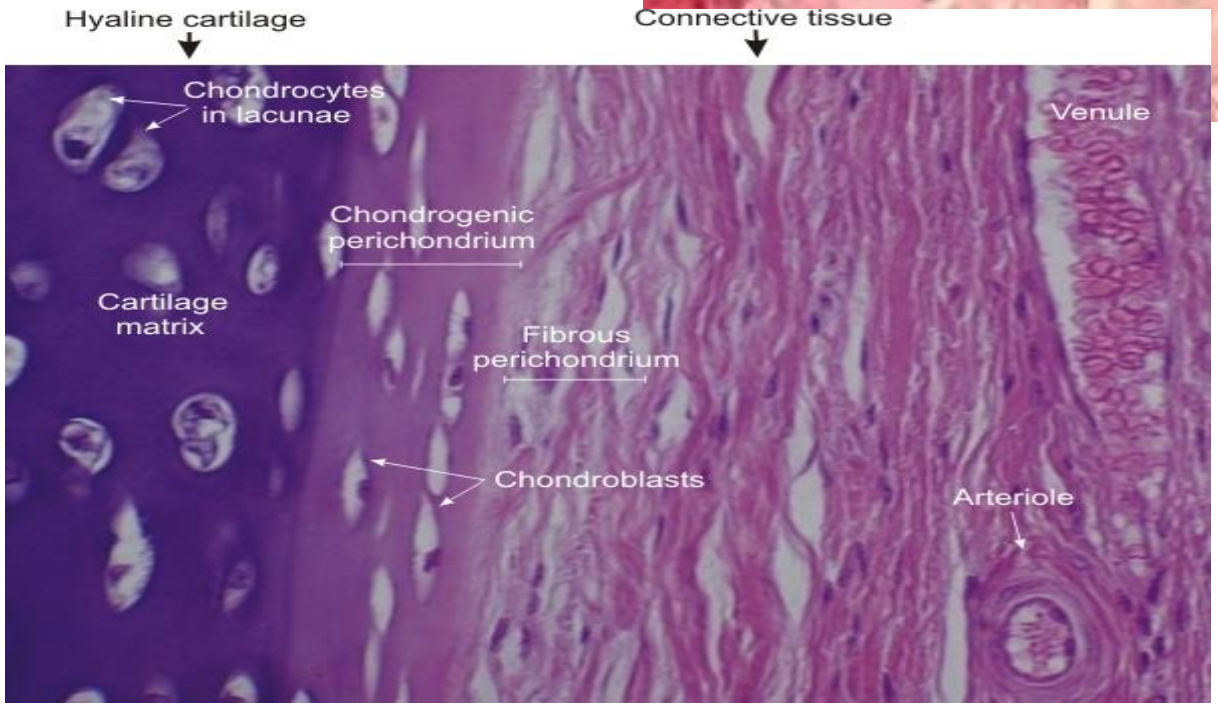
Type II collagen fibres + elastic fibres giving it more pliability

Fibrocartilage

Type I collagen fibres, allowing it to withstand strong tensile forces

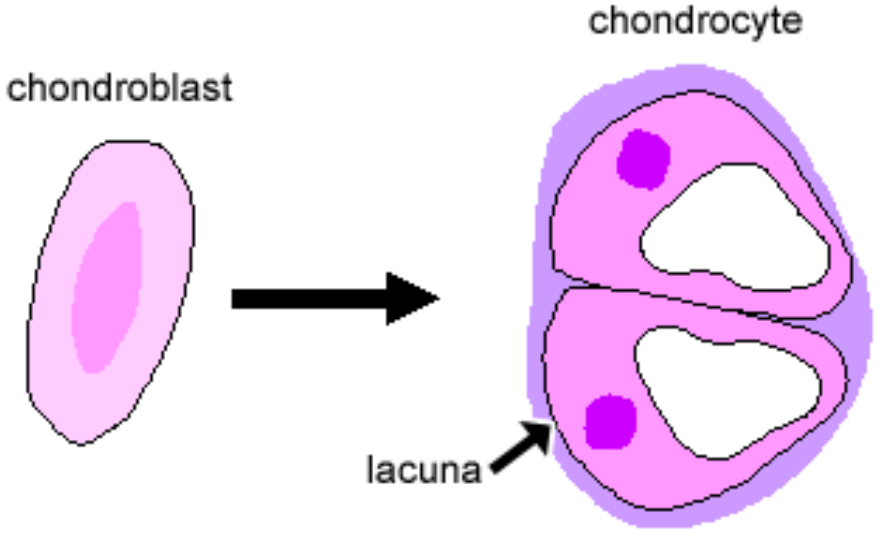
Perichondrium

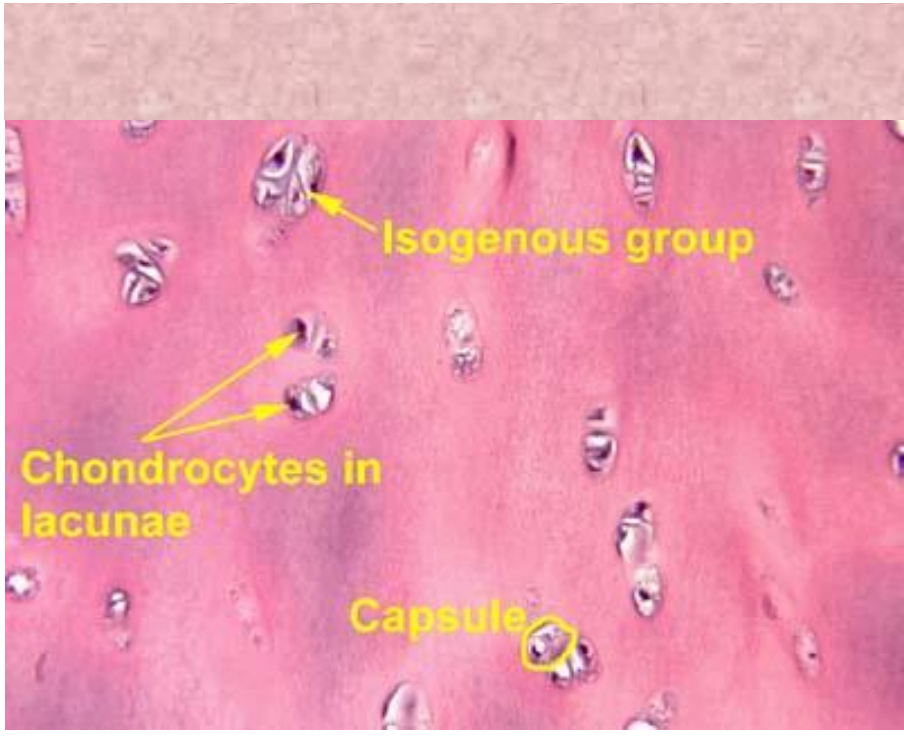
- is a connective tissue sheath covering cartilage
- absent in fibrocartilage



Cells of cartilage

1. Chondrogenic cells
2. Chondroblasts
3. Chondrocytes
    - rest in cartilage lacunae
    - form isogenous grups

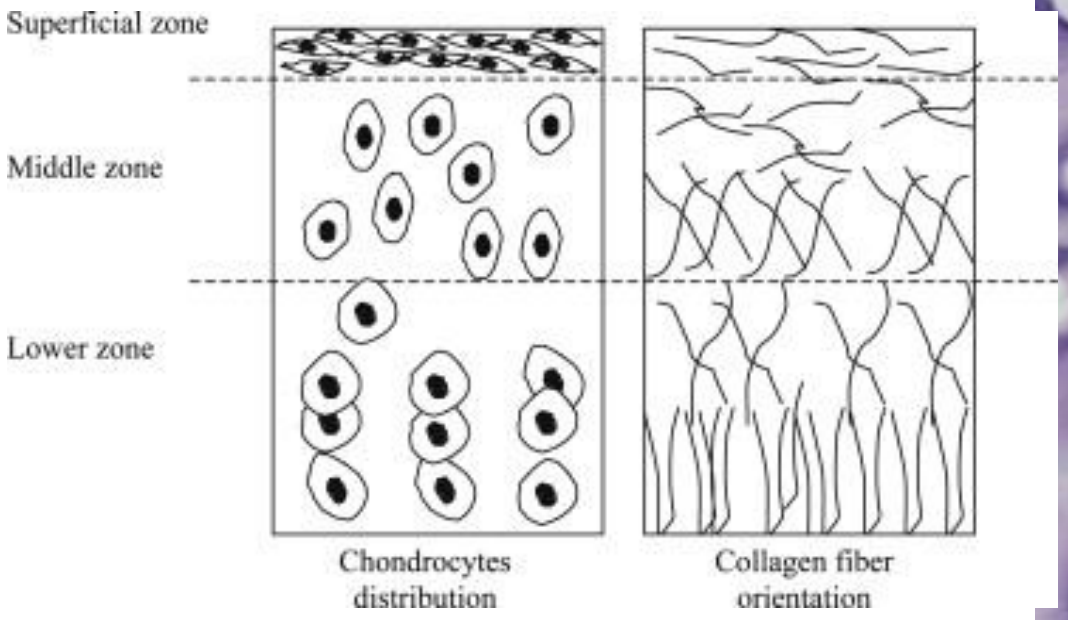


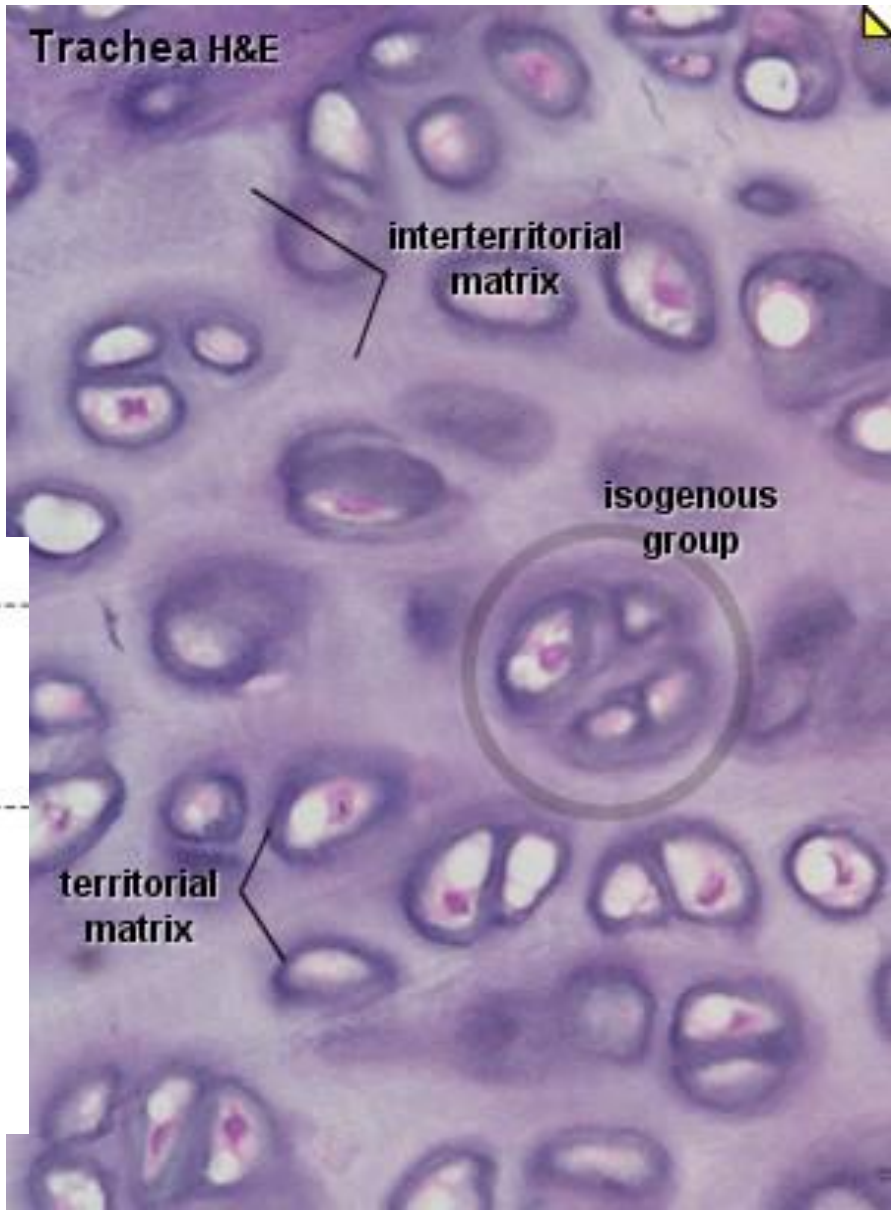


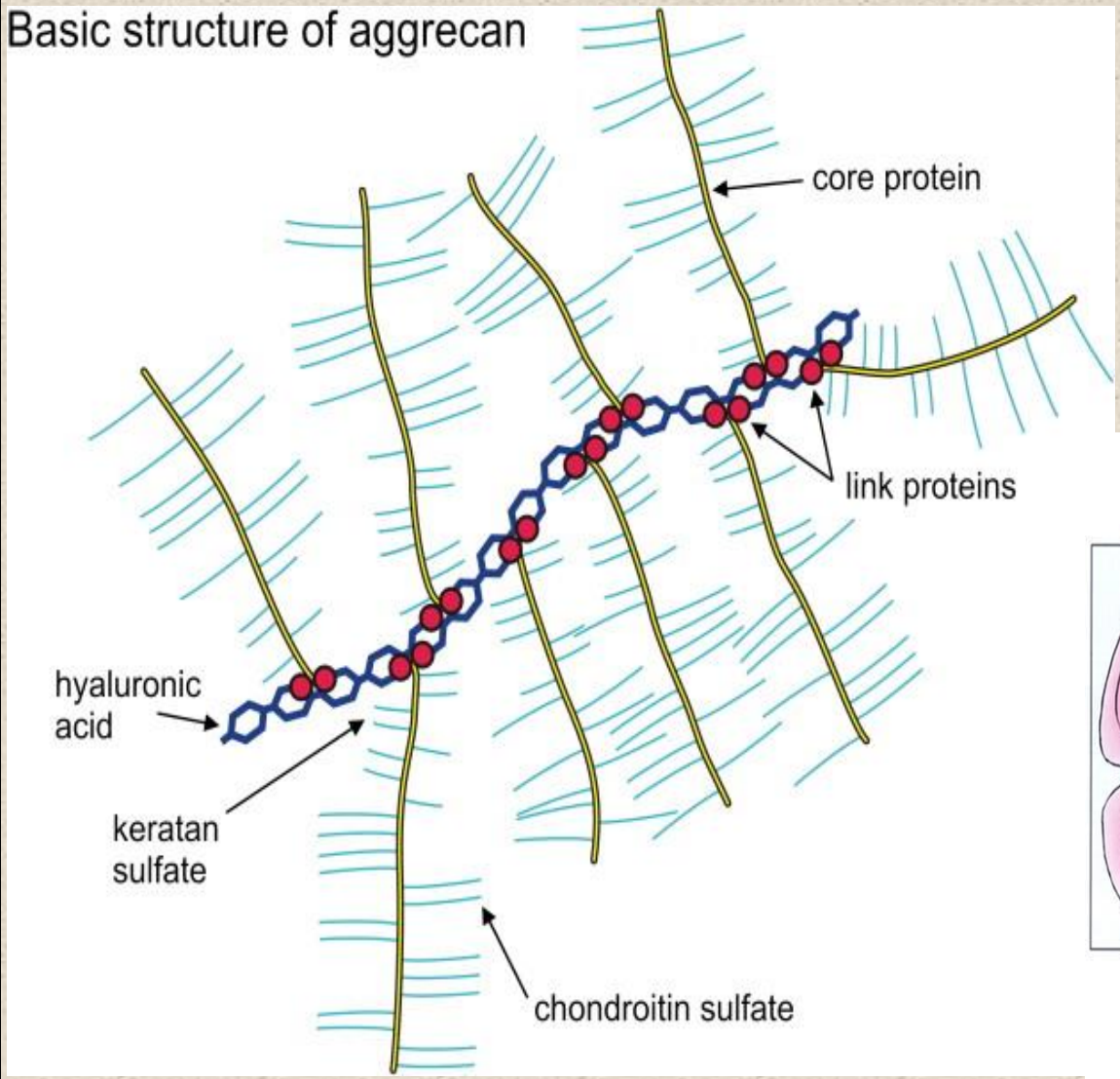
Matrix of hyaline cartilage

- type II collagen
- proteoglycans (**aggrecan**)

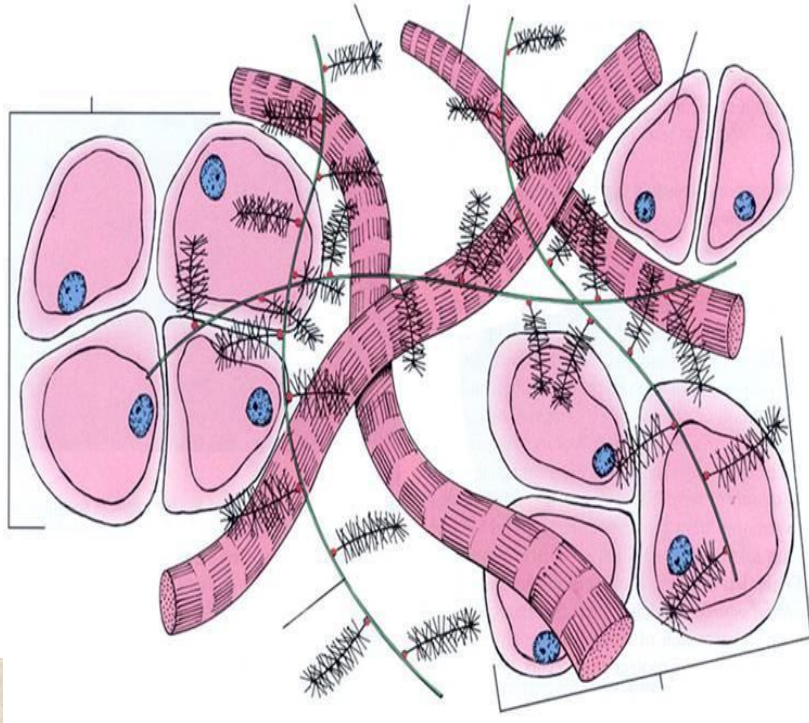
1. territorial matrix
2. interterritorial matrix

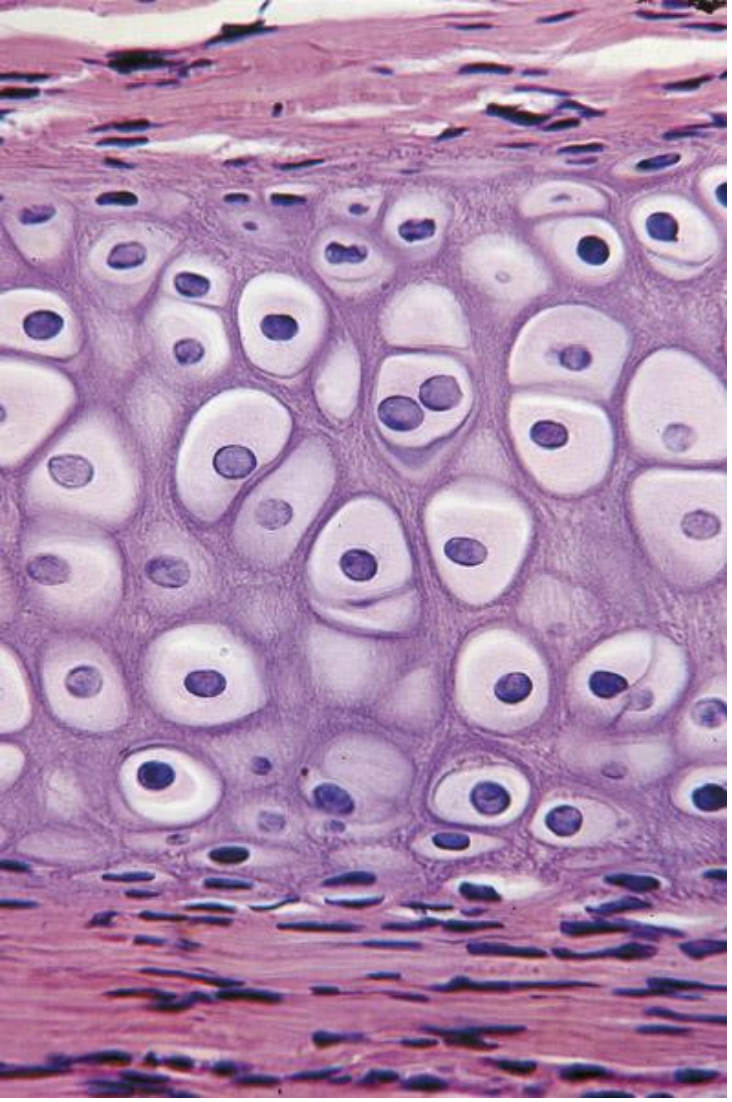






Chondronectin - has binding sites for type II collagen, aggrecan and integrins of chondrocytes





Perichondrium

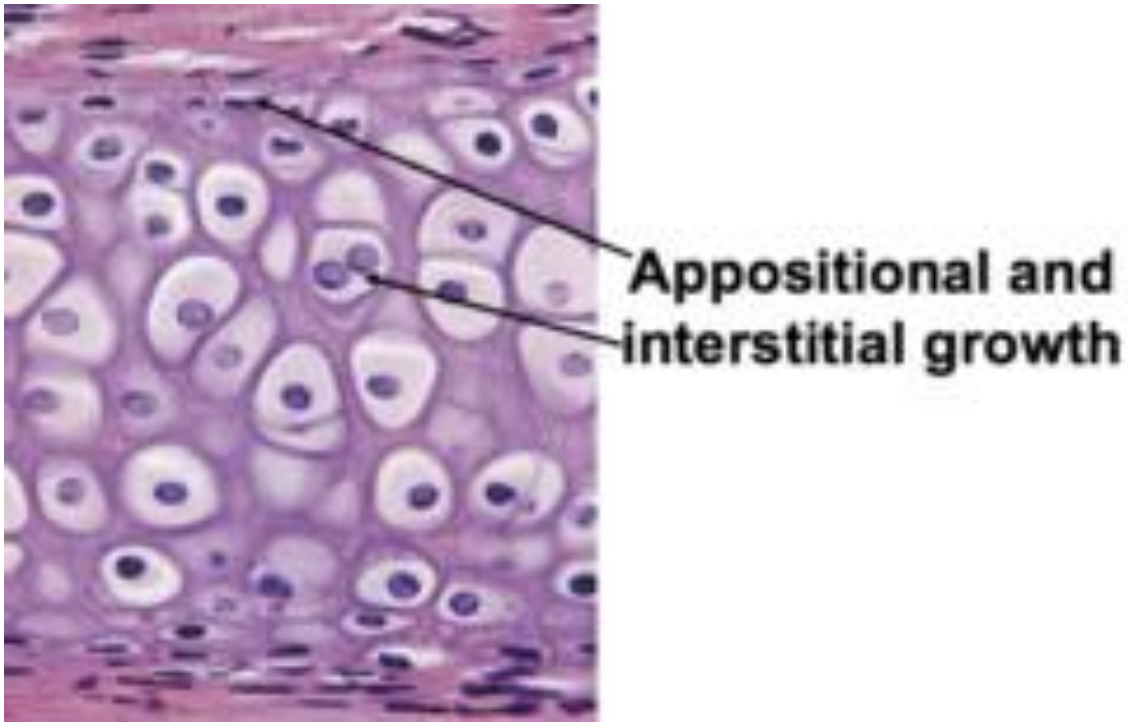
Hyaline cartilage

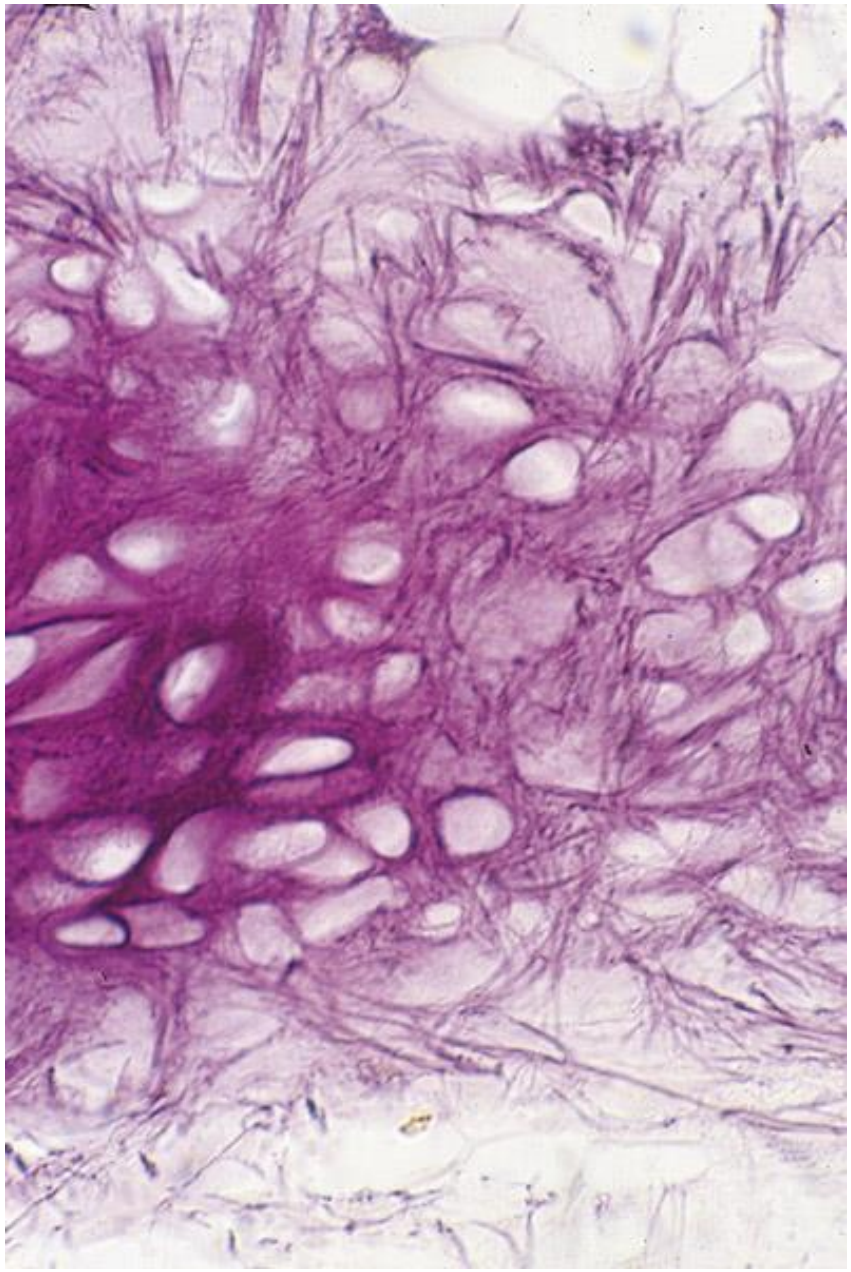
Nose
Larynx
Ventral ends of ribs
Trachea
Articular surface of joints

Types of growth of hyaline cartilage

- **Interstitial growth** – cells of isogenous groups manufacture matrix enlarging the cartilage from within

- **Appositional growth** – chondrogenic cells of inner layer of perichondrium undergo division and differentiate into chondroblasts which manufacture matrix Cartilage grows by adding to its periphery





Elastic cartilage

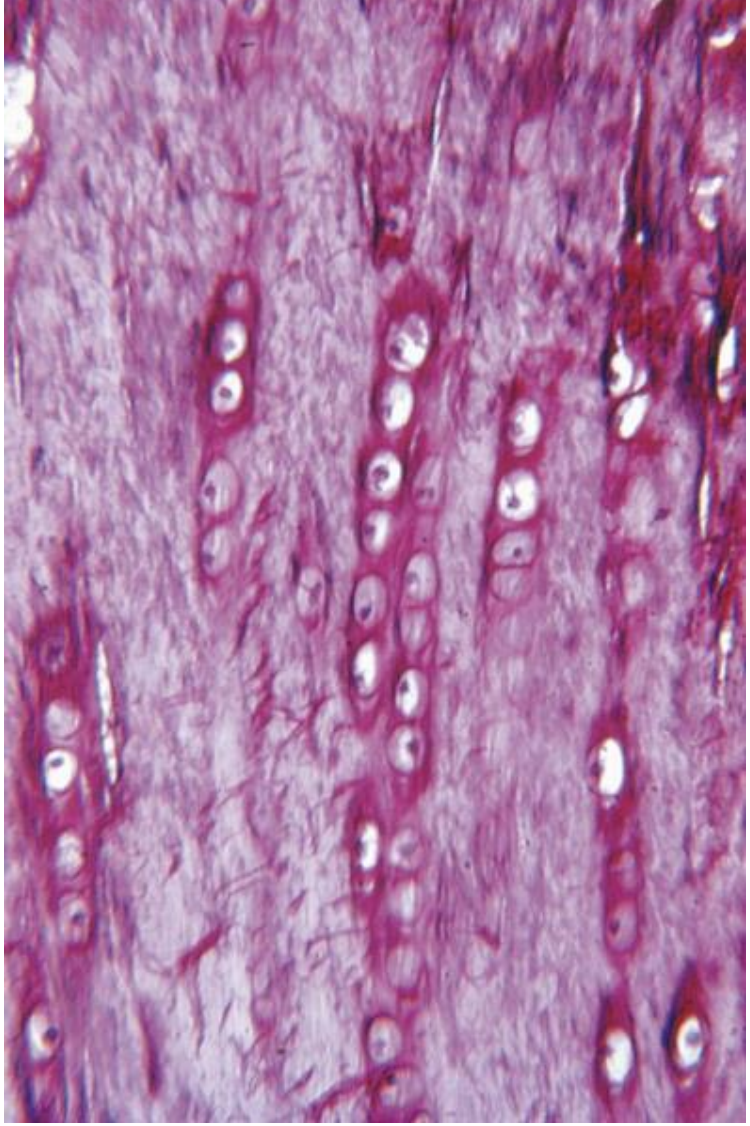
Located in:

the pinna of the ear,

the external and internal auditory tubes,

the epiglottis,

the larynx



Fibrocartilage

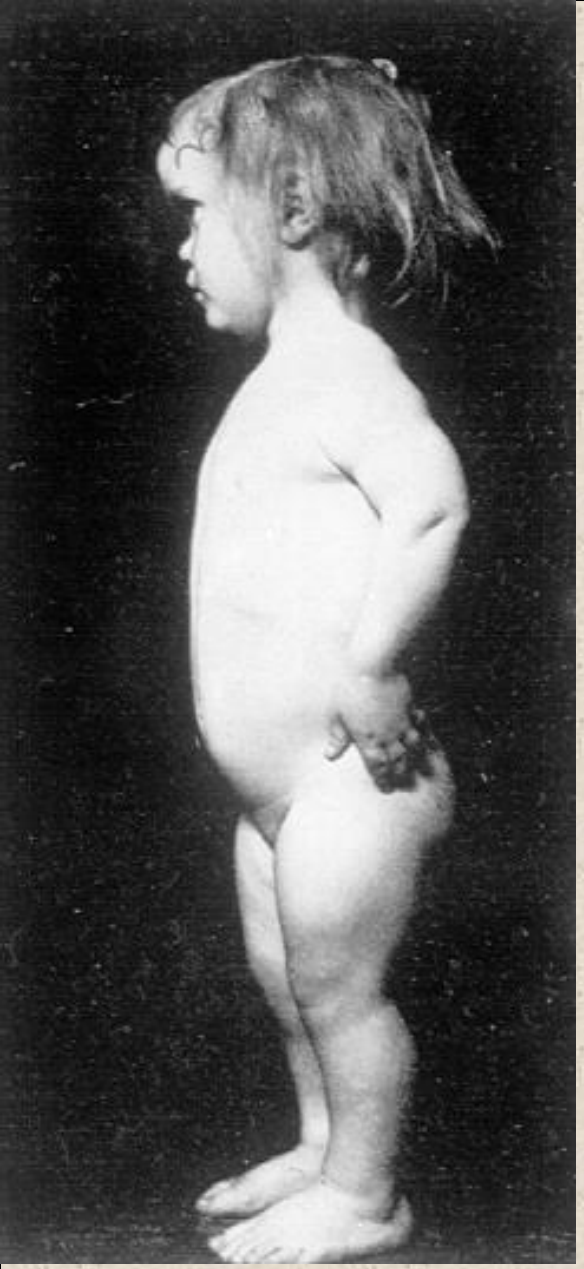
- type I collagen

Located in:

the intervertebral disks,

the pubic symphysis,

the articular disks



Achondroplasia.

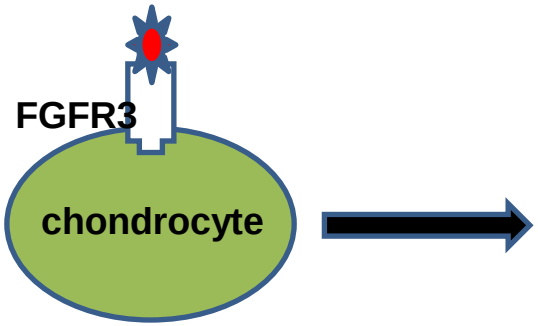
It is genetic disturbance of cartilage development. Leads to inhibition of growth and various deformities. It is characterised by dwarfism, with typical shortening of limbs, particularly in the proximal part, extensive lordosis in lumbar region and macrocephaly

Face of a child with achondroplasia

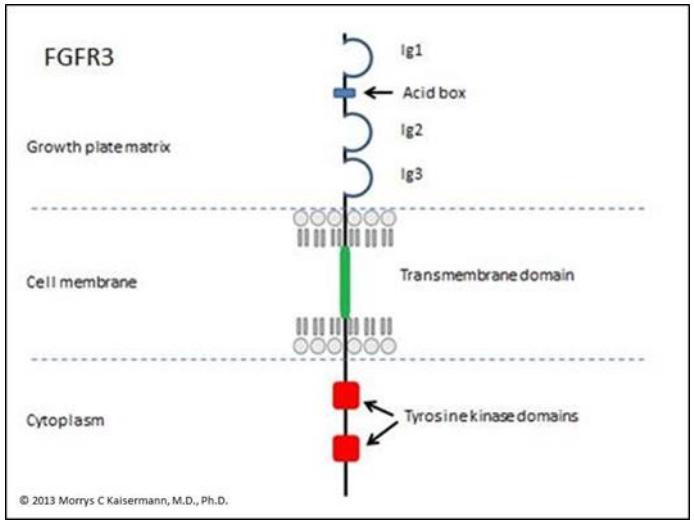
Large head, protruding forehead, collapsed nose and middle part of face.

i

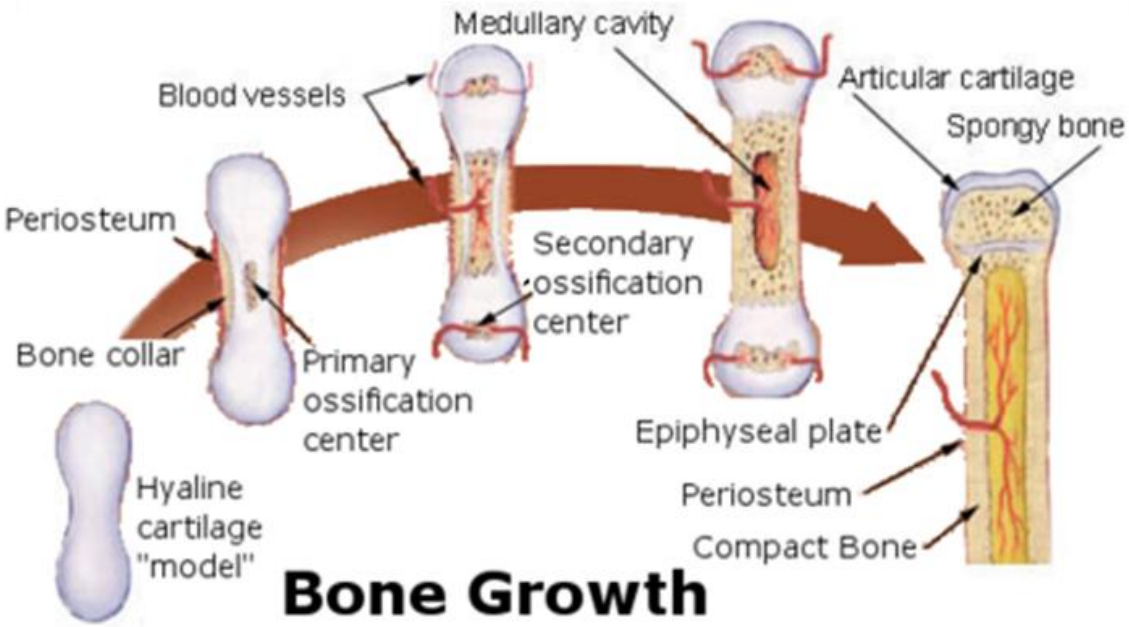
Achondroplasia is caused by a mutation in fibroblast growth factor receptor 3 (FGFR3).



Proliferation of chondrocytes



All long bones of the body are formed from hyaline cartilage models. Chondrocytes which form models must actively proliferate to the bone growth. In achondroplasia, the mutated form of the receptor leads to a significant shortening of of bones



BONE

- the hardest substance of the body
- dynamic tissue
- pressure – resorption
- tension – development of new bone

Bones:

- support and protect of the organs of the body
- serve as levers for the muscles attached to them
- are a reservoir mainly for calcium

BONE

collagen fibres – type I

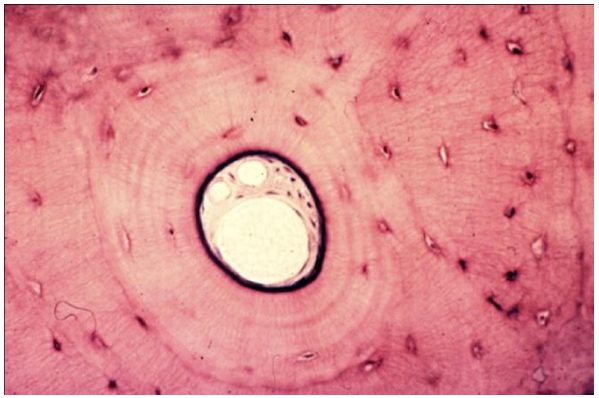
ground substance

hydroxyapatite

Outer layer of dense fibrous connective tissue

Inner cellular layer

endosteum – monolayer of osteoprogenitor cells and osteoblasts



Bone Matrix

Inorganic component

hydroxyapatite crystals

Organic component

Constitutes about 35% of its dry weight of bone

Collagen type I

Proteoglycans

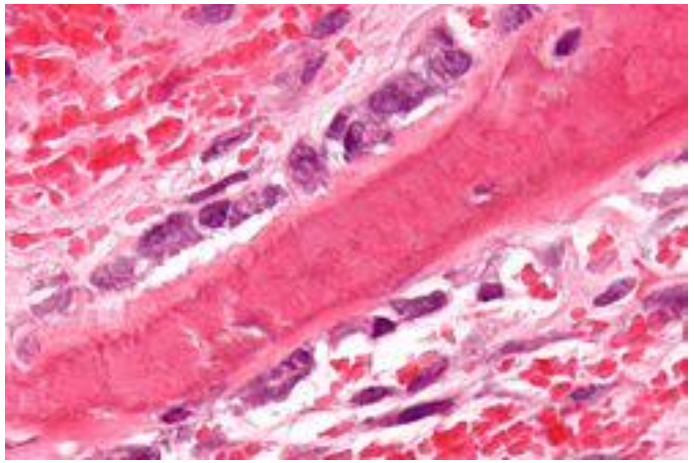
Glycoproteins:

osteocalcin

osteopondin

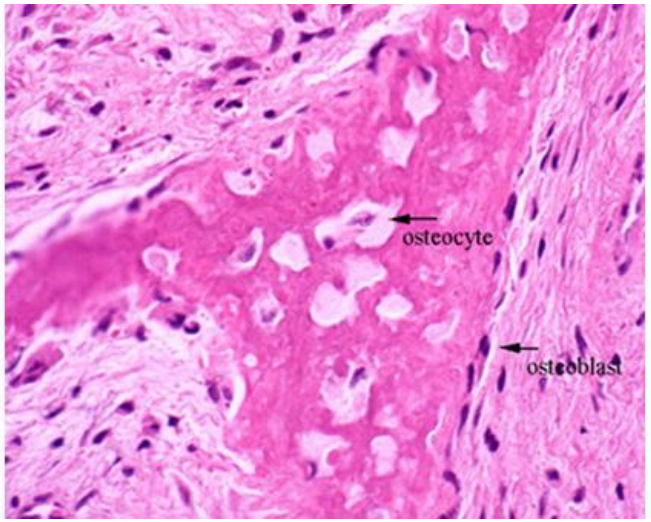
sialoprotein

Osteoprogenitor cells (or stem cells of bone)



Osteoblasts (or bone forming cells)

- synthesis of the organic components
- are located on the surface of the bone

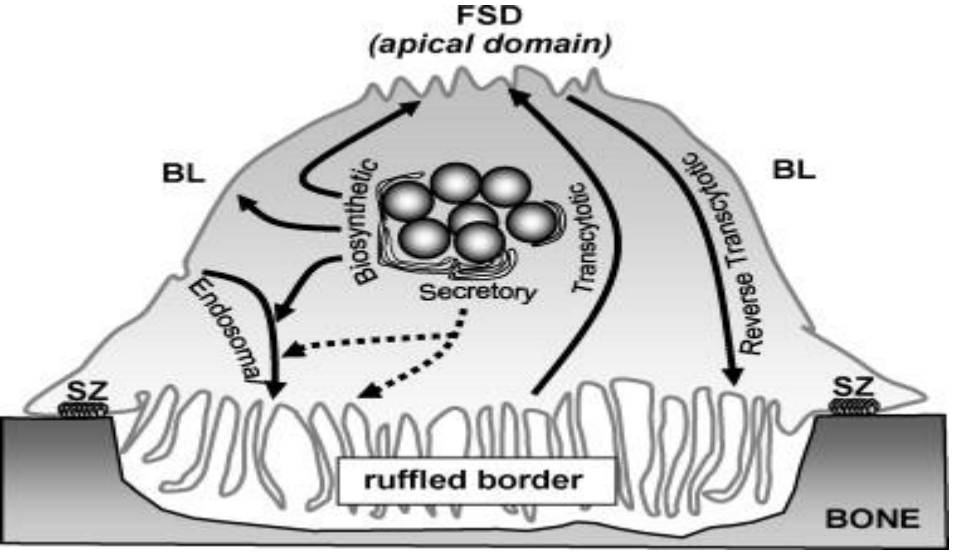


Osteocytes

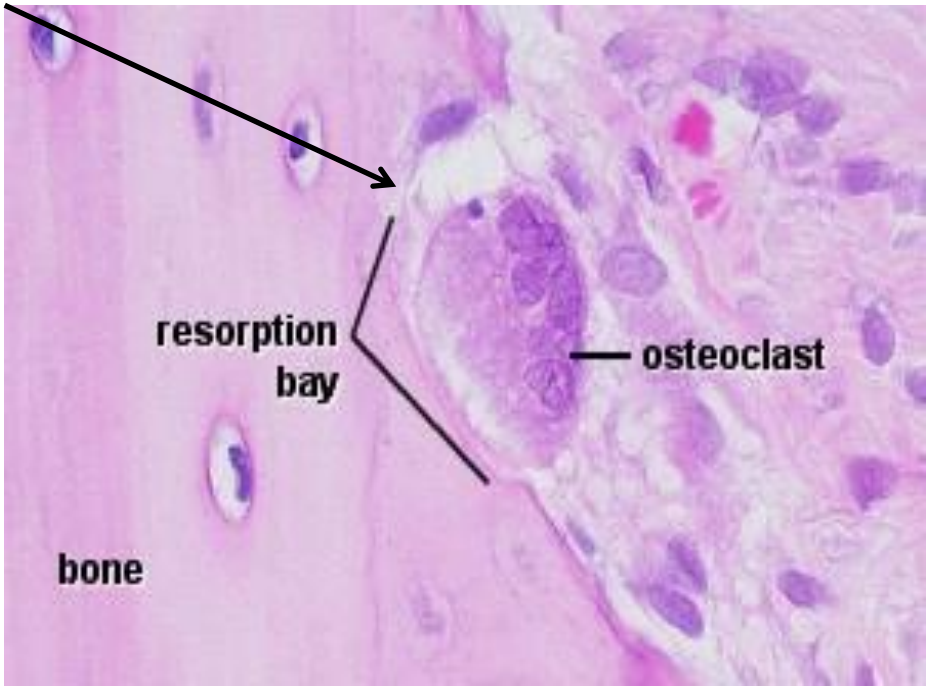
Osteoclasts

bone-resorbing cells

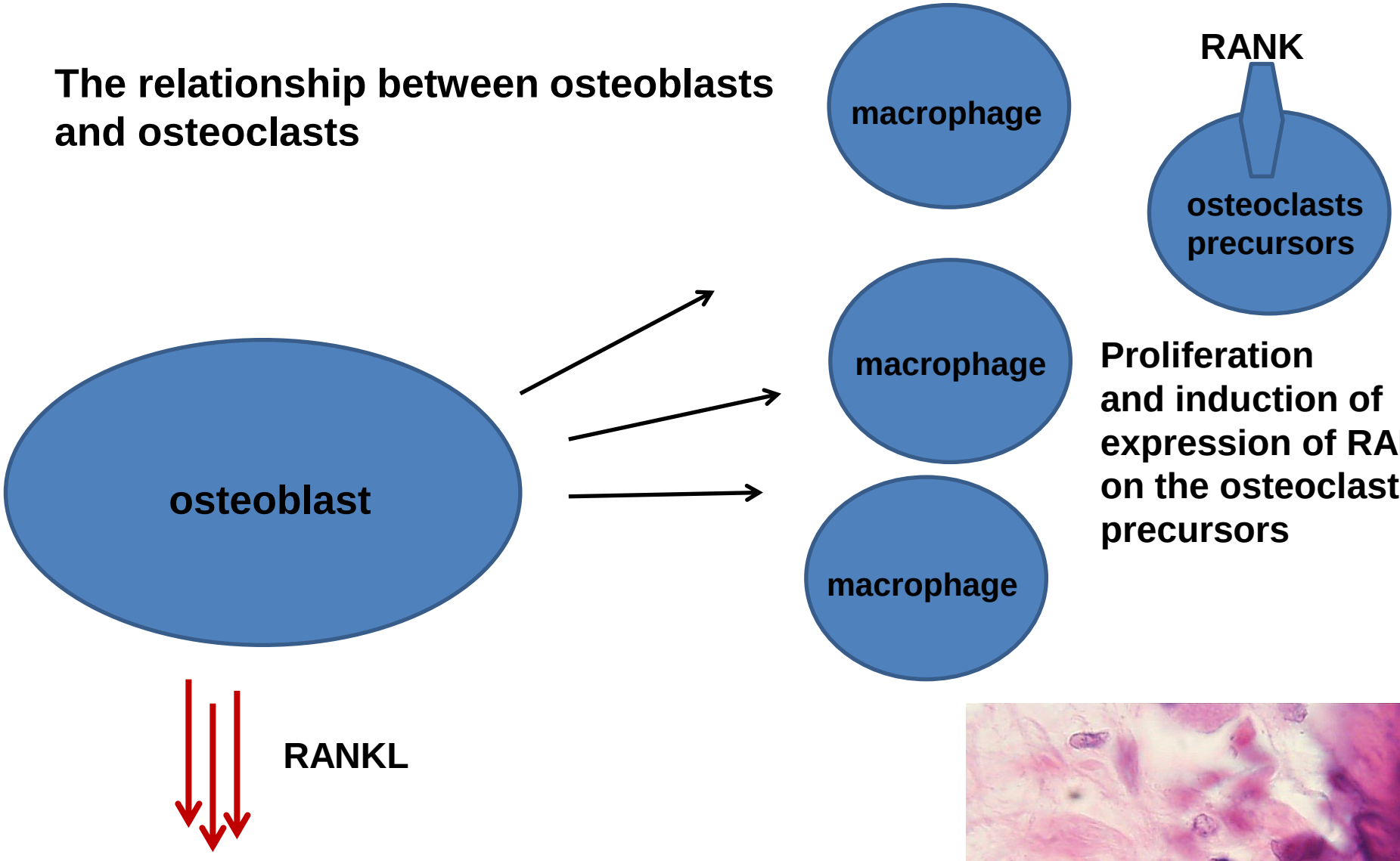
- are large, multinucleated cells
- occupy Howship's lacunae – regions of bone resorption
- ruffled border –a part of the cell directly involved in bone resorption (finger-like processes)
- activity of osteoclasts is stimulated by parathyroid hormone and inhibited by calcitonin



Howship's lacuna

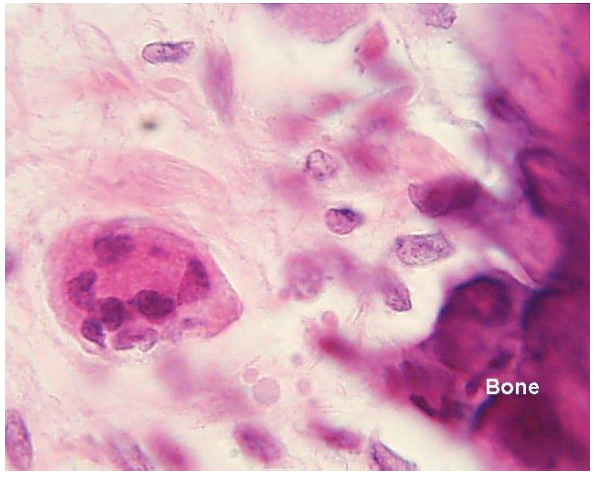


The relationship between osteoblasts and osteoclasts



Proliferation and induction of expression of RANK on the osteoclasts precursors

Osteoclasts precursors differentiate into the multinucleated osteoclasts



Bone Types

Primary bone

= immature bone

= woven bone

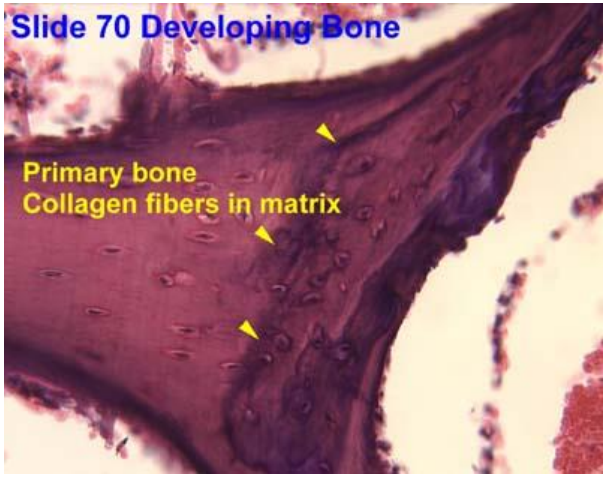
the first bone during fetal development and

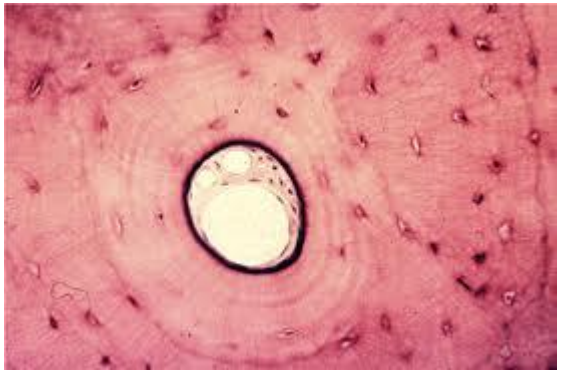
during bone repair

abundant osteocytes,

irregular bundles of collagen

low mineral content





Secondary bone

= mature bone

= lamellar bone

parallel or concentric bony lamellae,

osteocytes between lamellae

hight mineral content

Compact bone

spongy bone
= cancellous bone
= trabecular bone

Secondary bone

(Thick-walled tube of the shaft)

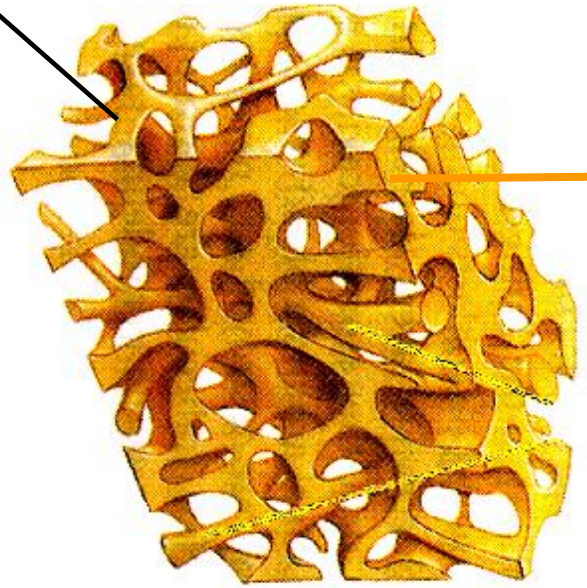
epiphysis

diaphysis

Compact bone

epiphysis

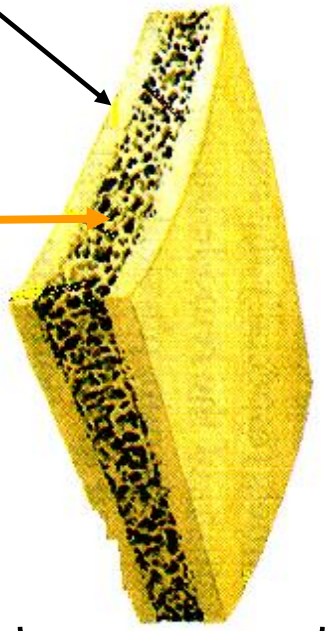
Long bone



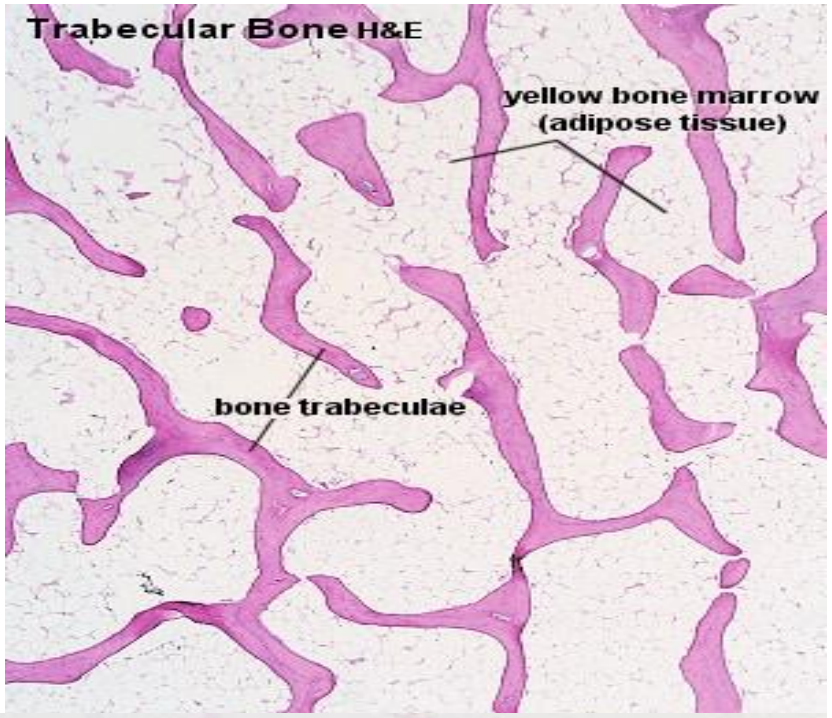
Spongy or cancellous bone

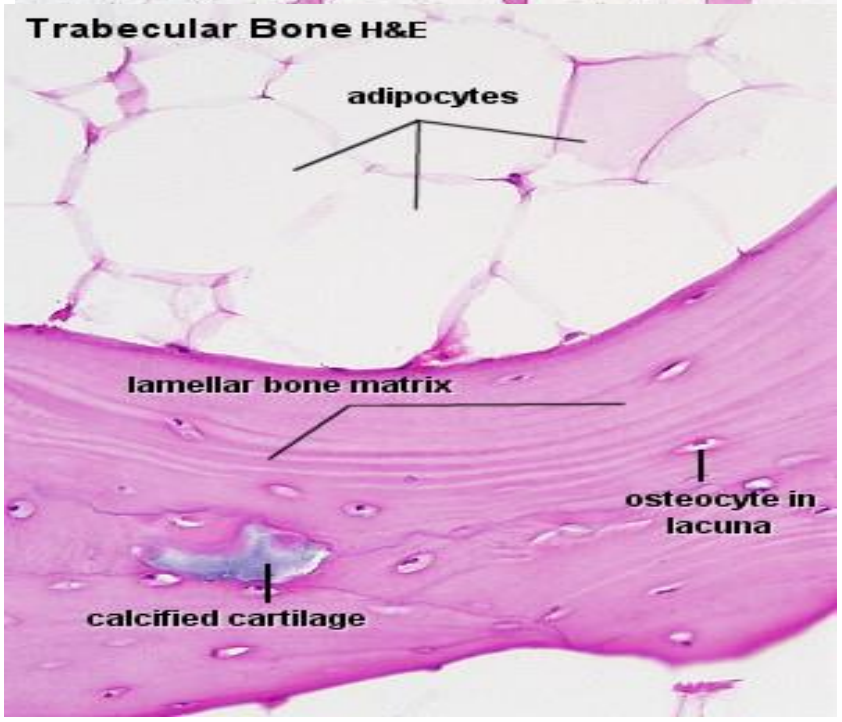
Compact bone

Inner and outer tables



Flat bone





SPONGY BONE

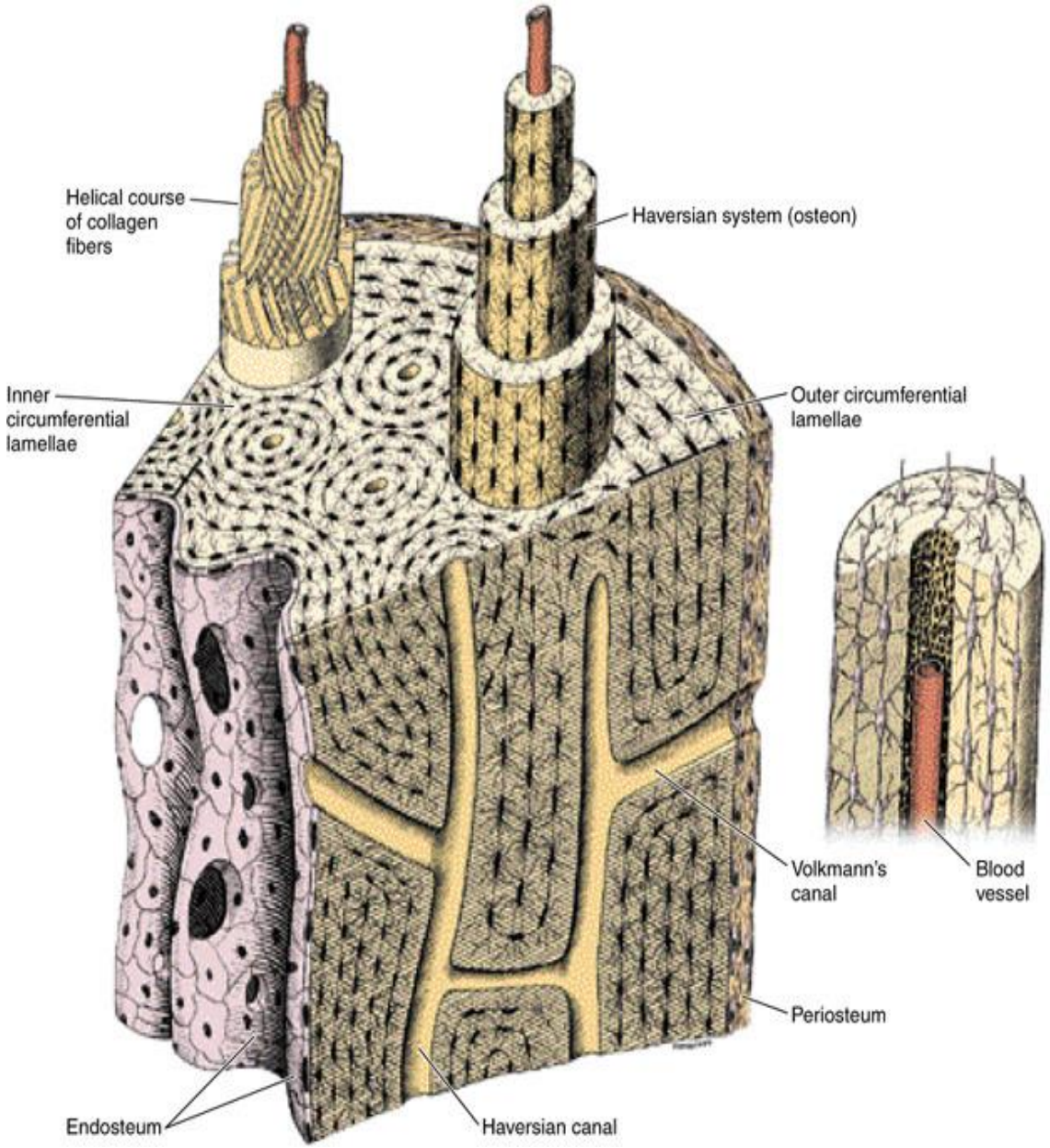
Low magnification
– interconnected meshwork of bony trabeculae
- spaces between the trabeculae are filled by red or yellow bone marrow.

High magnification
- elongated osteocytes in lacunae
- matrix of trabecular bone is formed by lamellae
- **Haversian systems are not present**

STRUCTURE OF COMPACT BONE

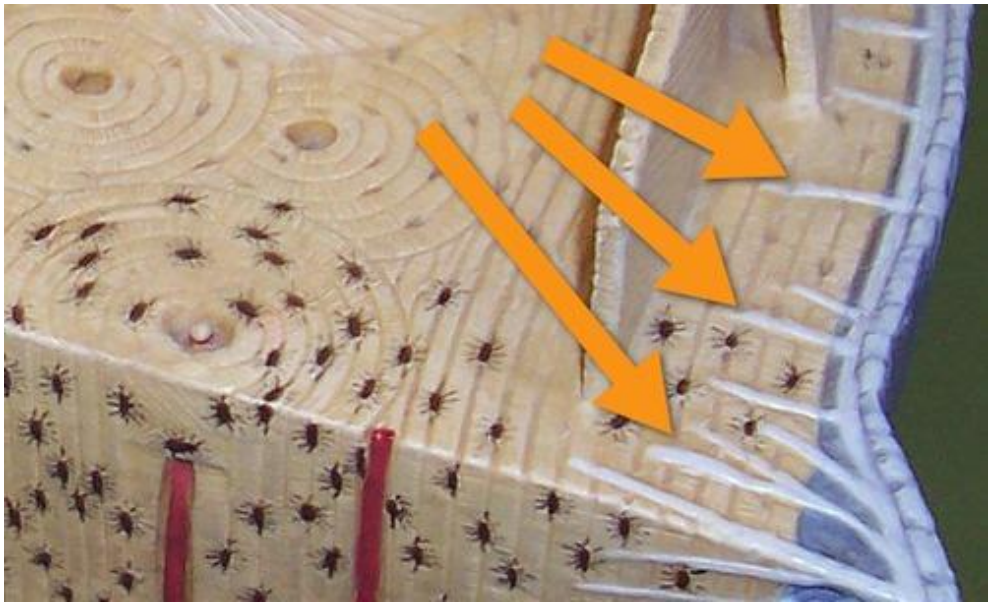
Four lamellar systems
of compact bone:

1. Outer circumferential lamellae
2. Inner circumferential lamellae
3. Osteons (Haversian systems)
4. Interstitial lamellae



Outer circumferential lamellae

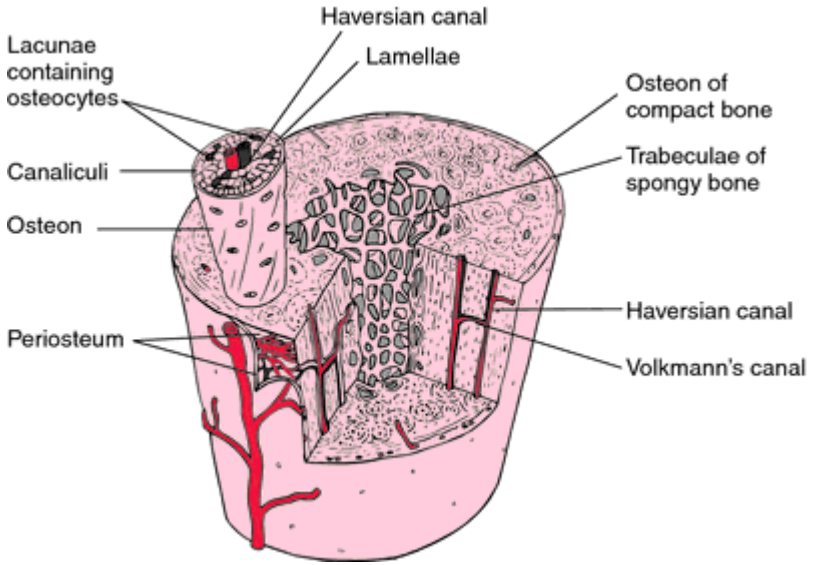
- **Sharpey's fibers**



Inner circumferential lamellae

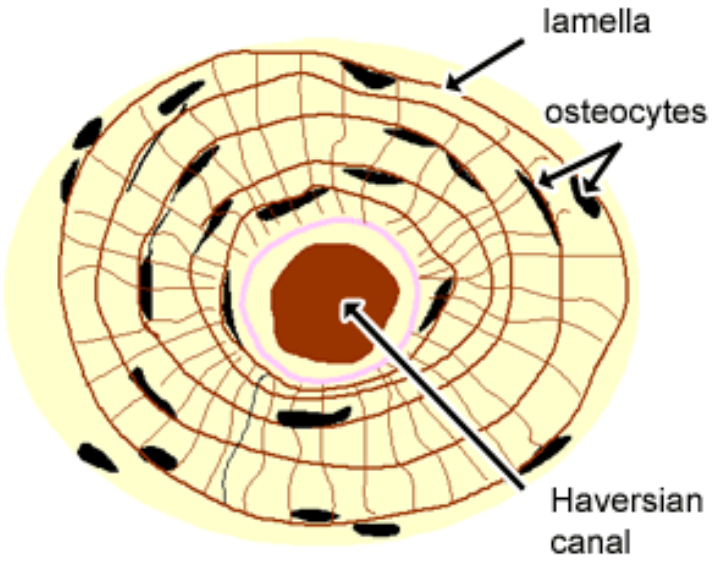
- completely encircle the marrow cavity

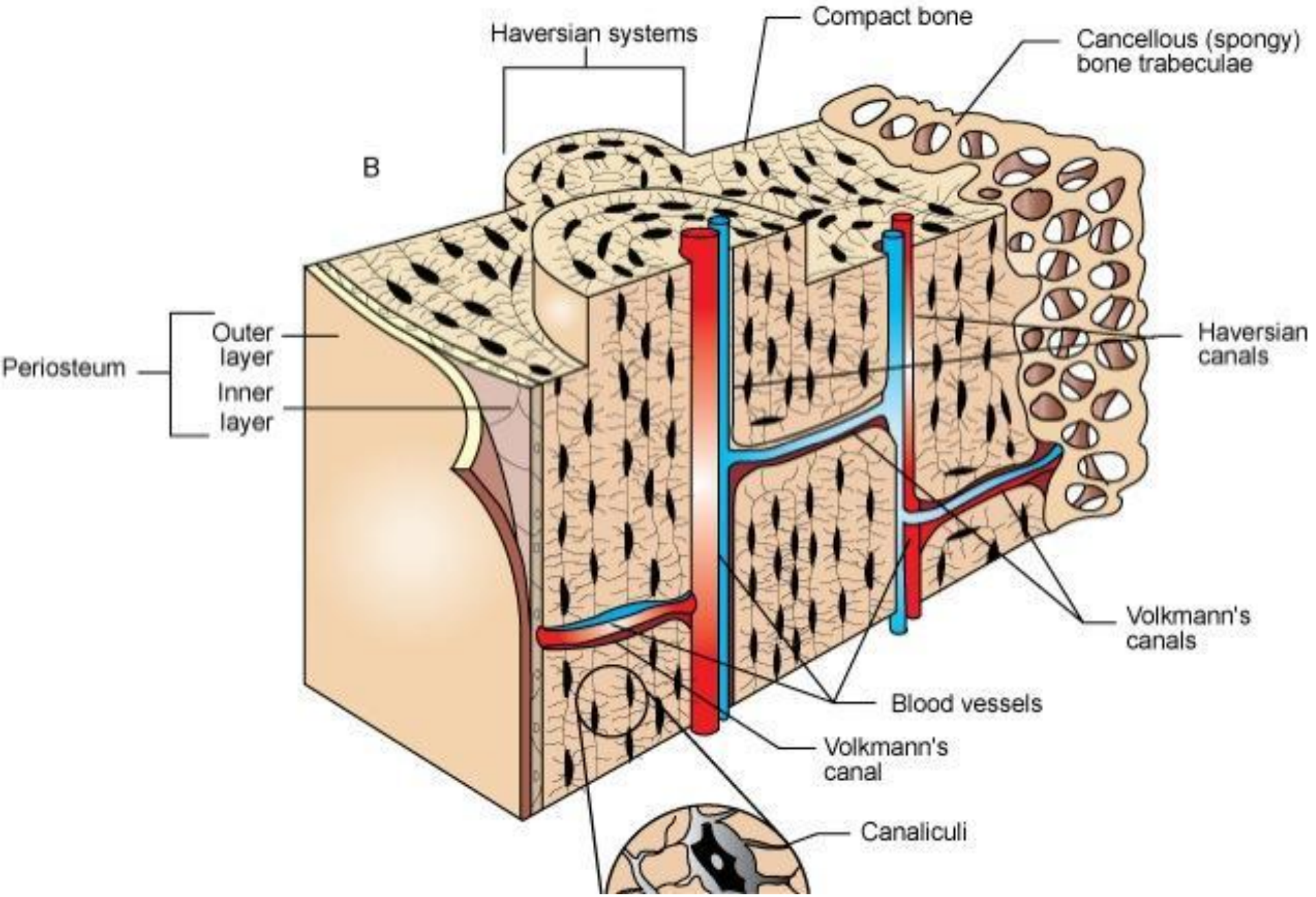
HAVERSIAN SYSTEMS (OSTEONS)



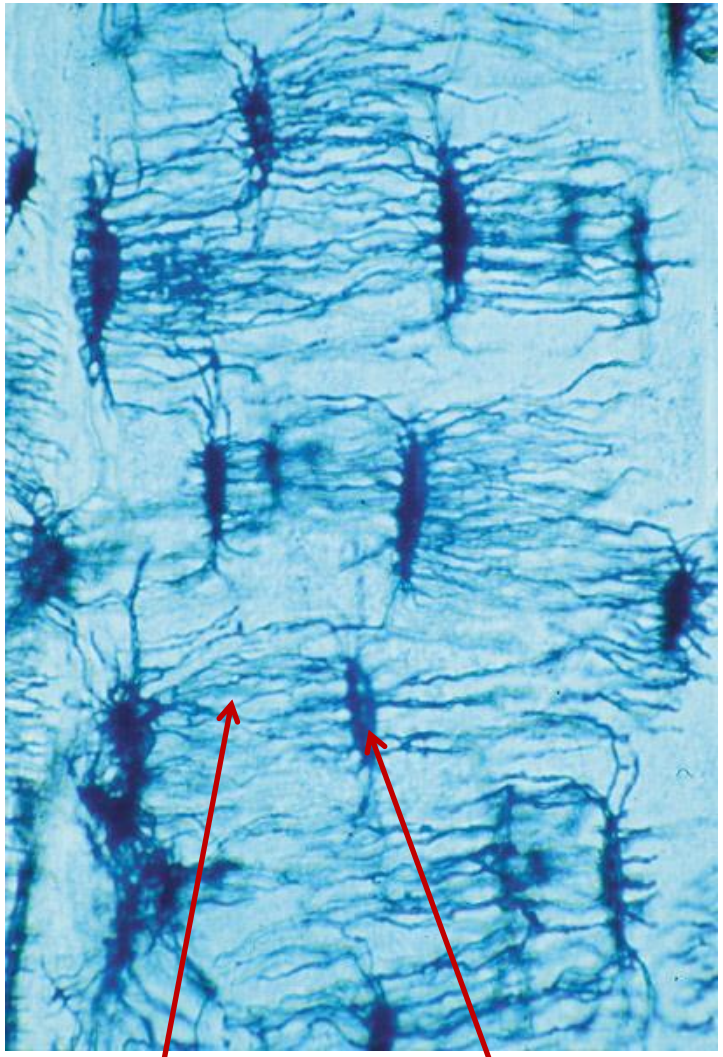
Haversian system

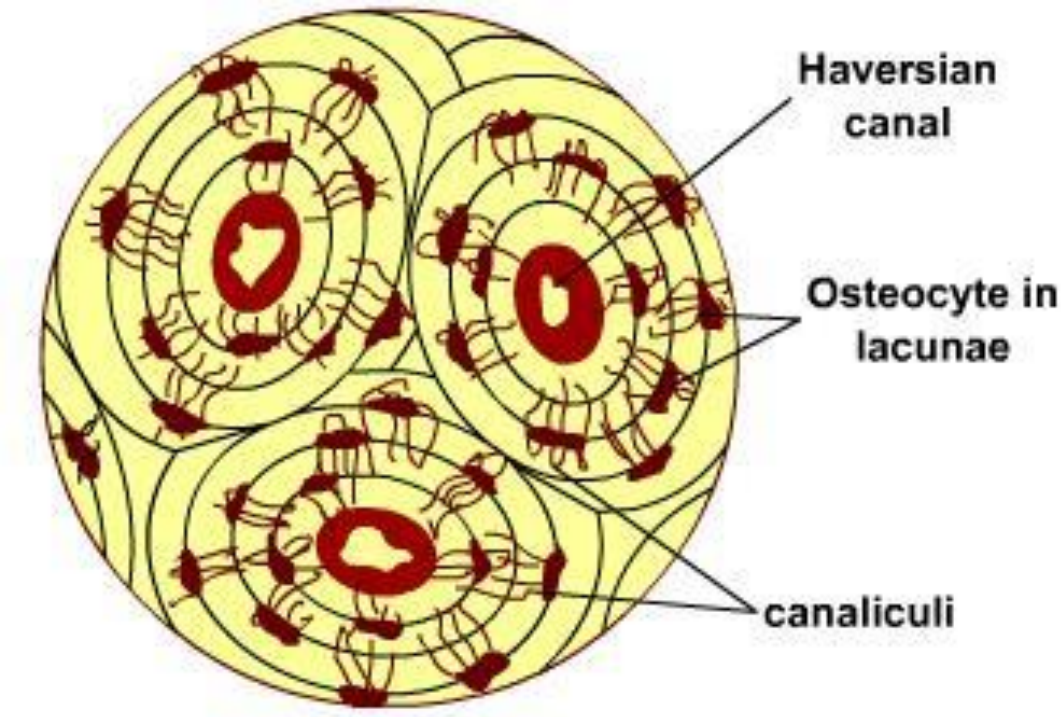
- Is composed od lamellae concentrically arranged around haversian canal



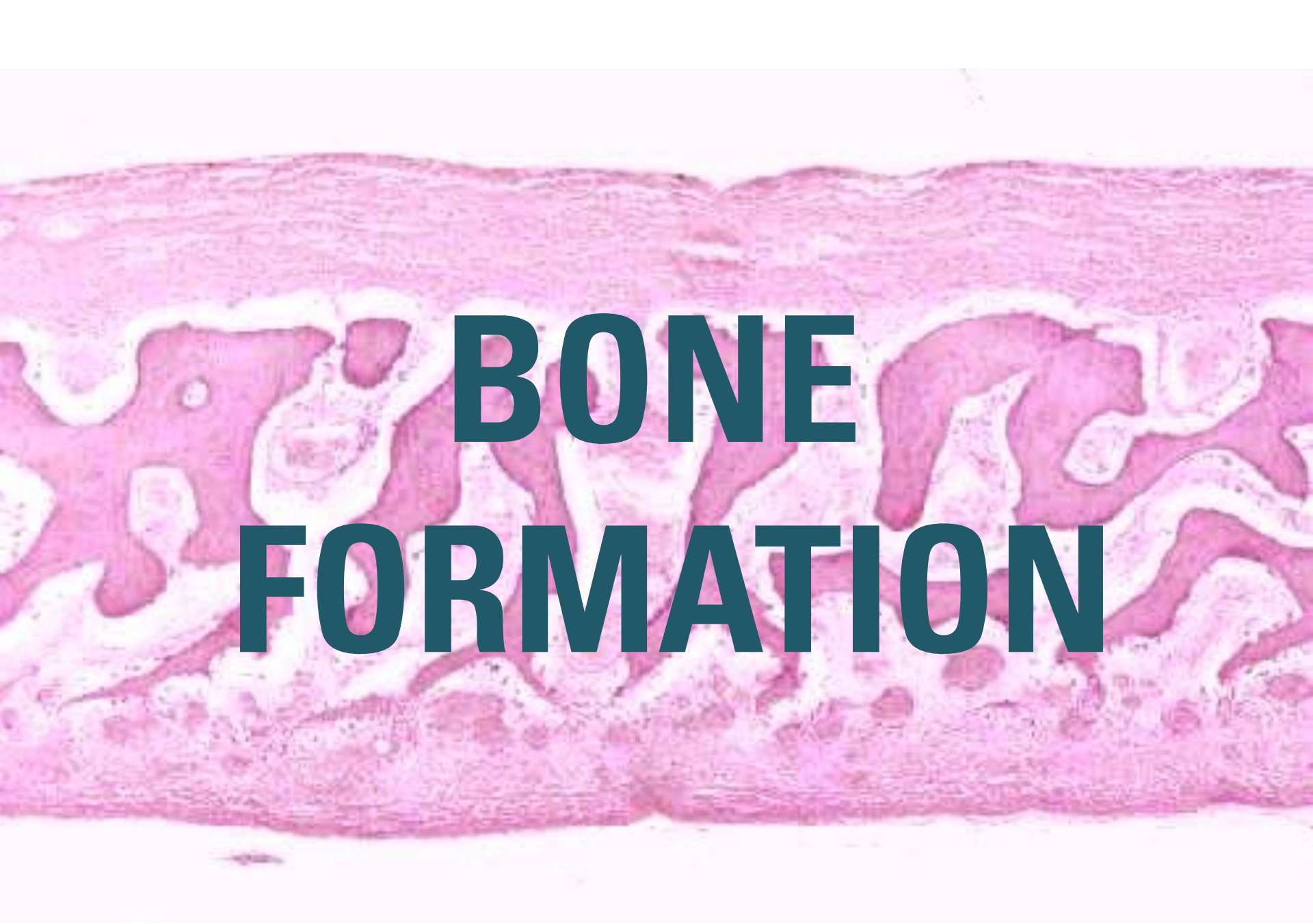

Haversian systems
Compact bone
Cancellous (spongy) bone trabeculae
B
Periosteum
Outer layer
Inner layer
Haversian canals
Volkmann's canals
Blood vessels
Volkmann's canal
Canaliculi

Osteocytes in bone lacunae





Osteocytes have cytoplasmic processes which make contact with similar processes of neighboring osteocytes, forming gap junctions, through ions and small molecules can move between the cells
Tunnel-like spaces (**canaliculi**) house these cytoplasmic processes


BONE
FORMATION

Bone formation

intramembranous

endochondral

Bone that is formed by either of the two methods is identical histologically

Flat bones
Occurs in a richly vascularized mesenchymal tissue

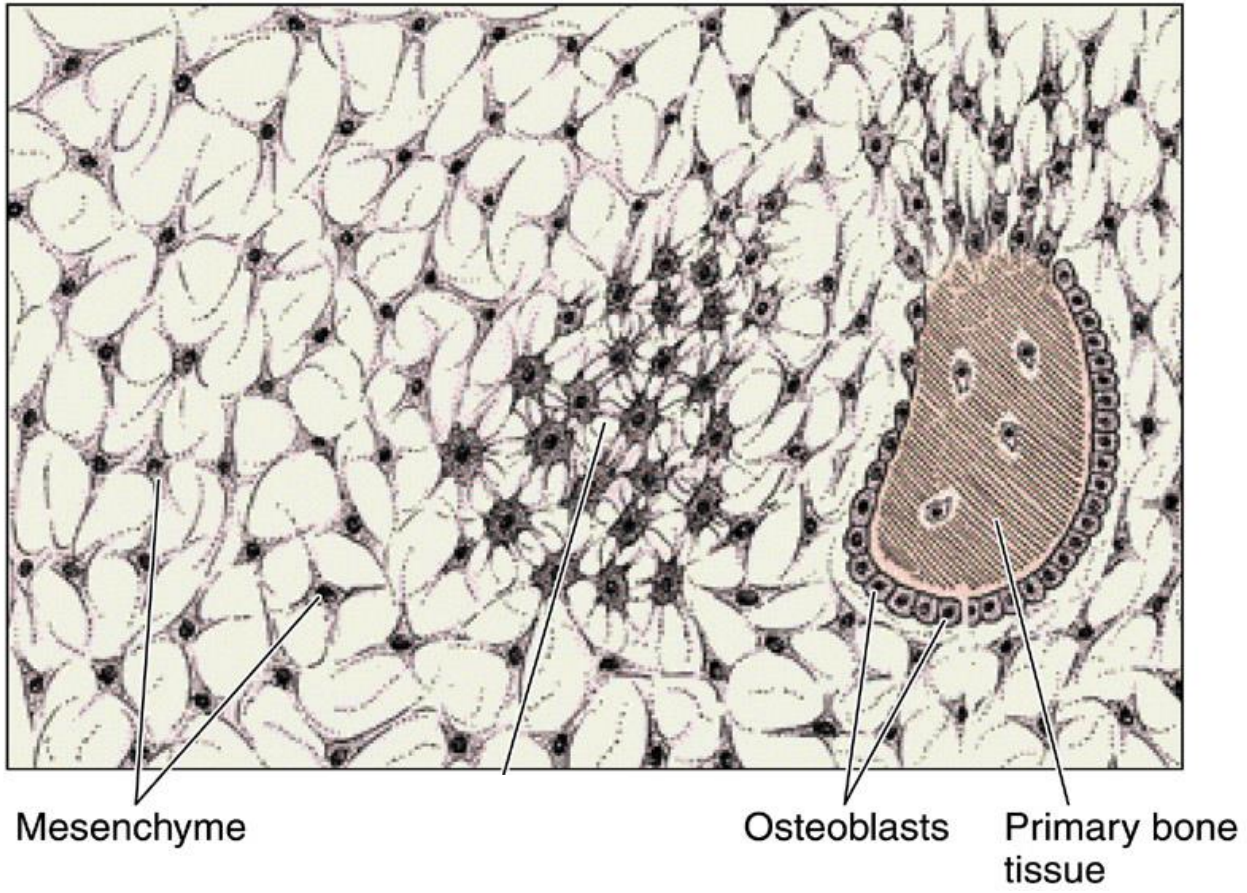
Long and short bones

Requires the formation of a

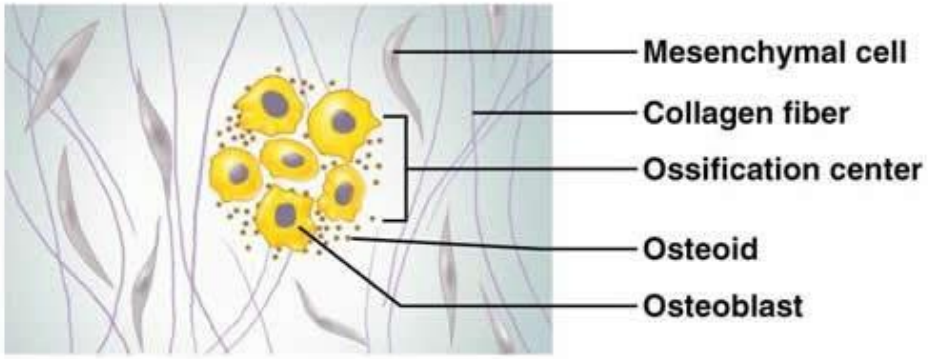
miniature hyaline cartilage model

The first bone – primary bone is being replaced by secondary bone.
Secondary bone is resorbed and replaced throughout the life.

Beginning of intramembranous ossification

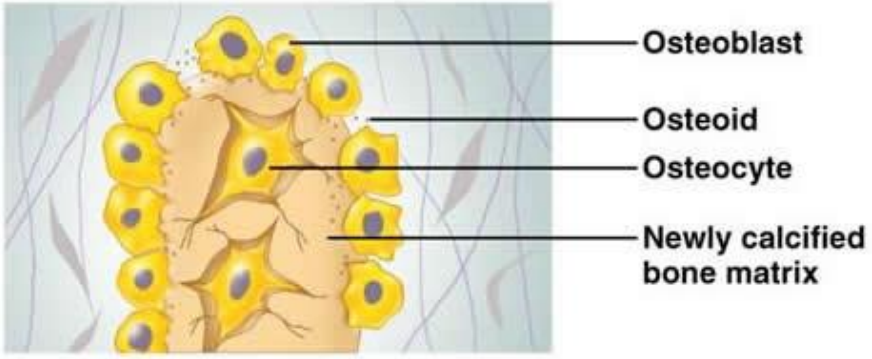


Intramembranous bone formation



① **An ossification center appears in the fibrous connective tissue membrane.**

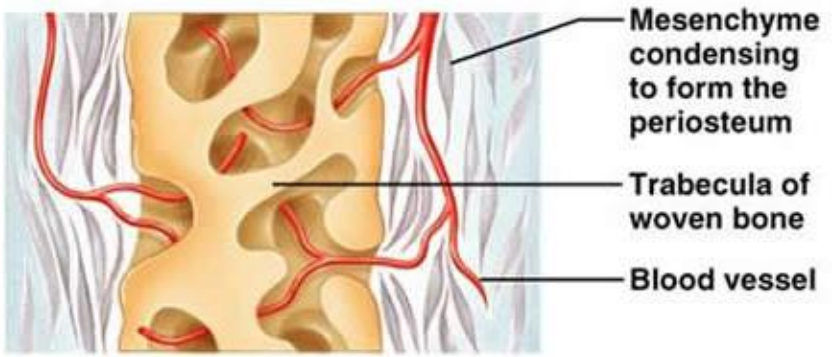
- Selected centrally located mesenchymal cells cluster and differentiate into osteoblasts, forming an ossification center.



② **Bone matrix (osteoid) is secreted within the fibrous membrane.**

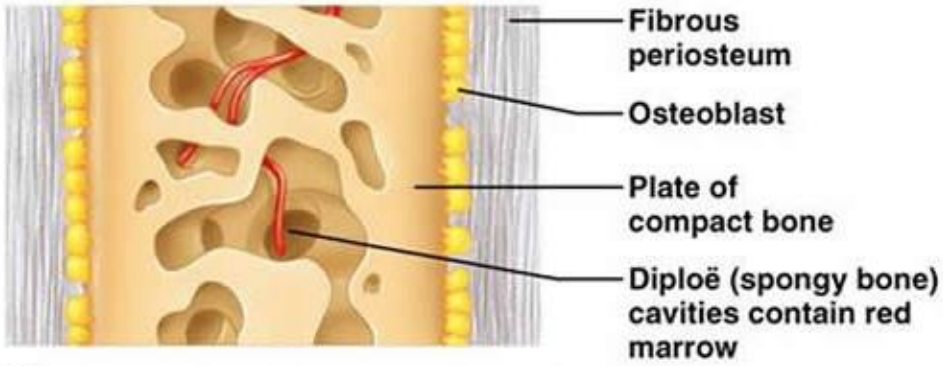
- Osteoblasts begin to secrete osteoid, which is mineralized within a few days.
- Trapped osteoblasts become osteocytes.

Intramembranous bone formation



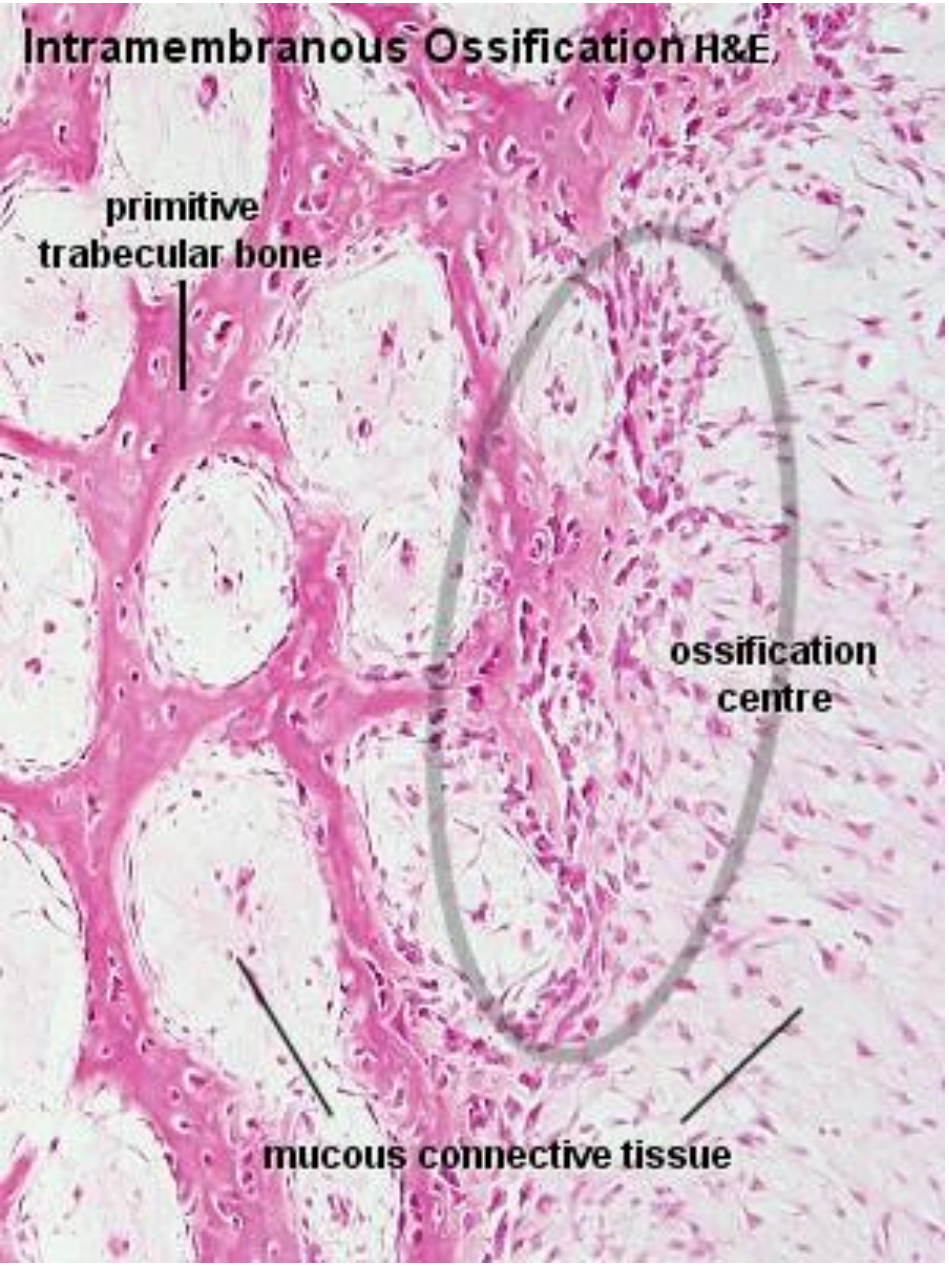
③ **Woven bone and periosteum form.**

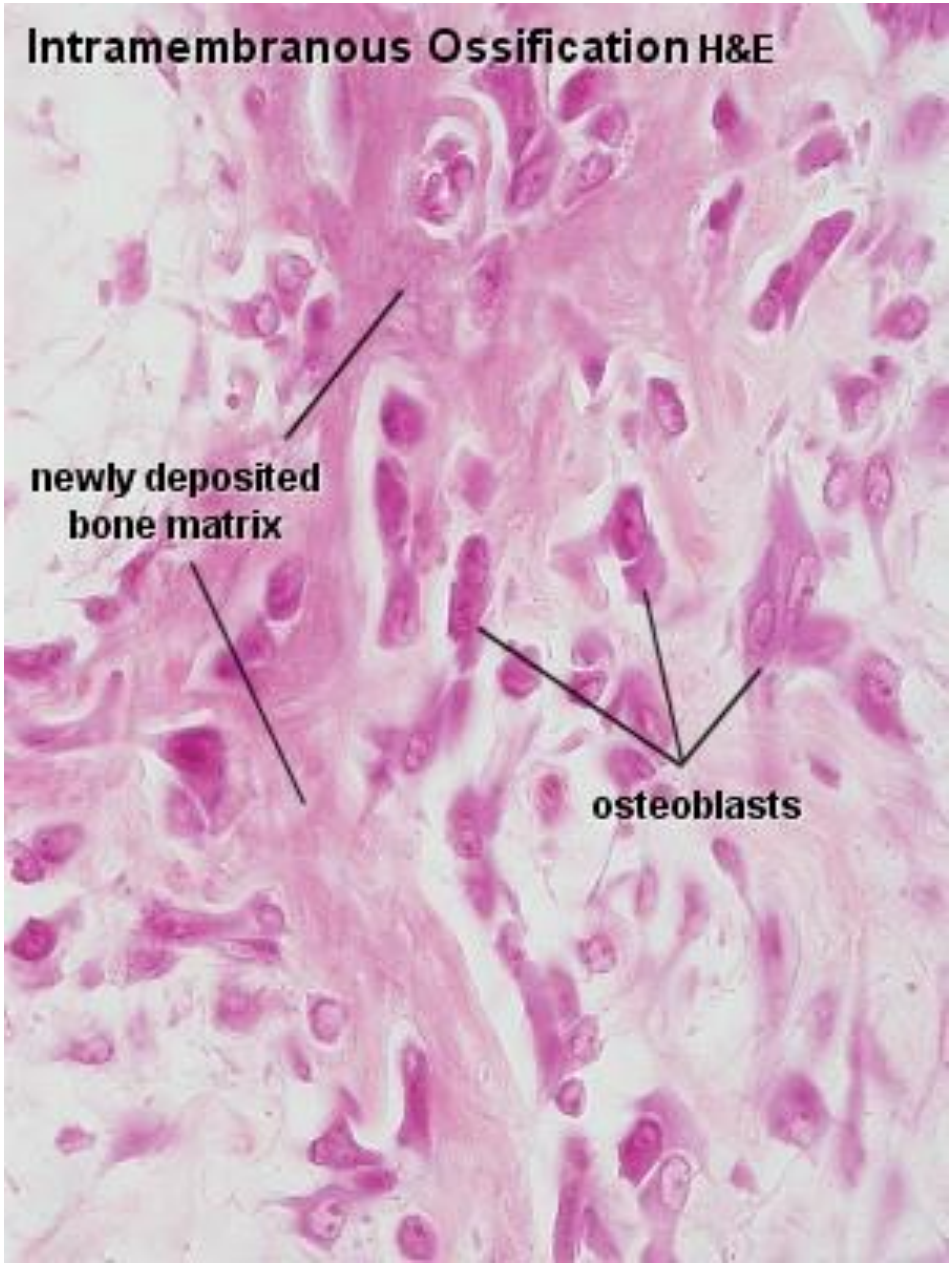
- Accumulating osteoid is laid down between embryonic blood vessels, which form a random network. The result is a network (instead of lamellae) of trabeculae.
- Vascularized mesenchyme condenses on the external face of the woven bone and becomes the periosteum.

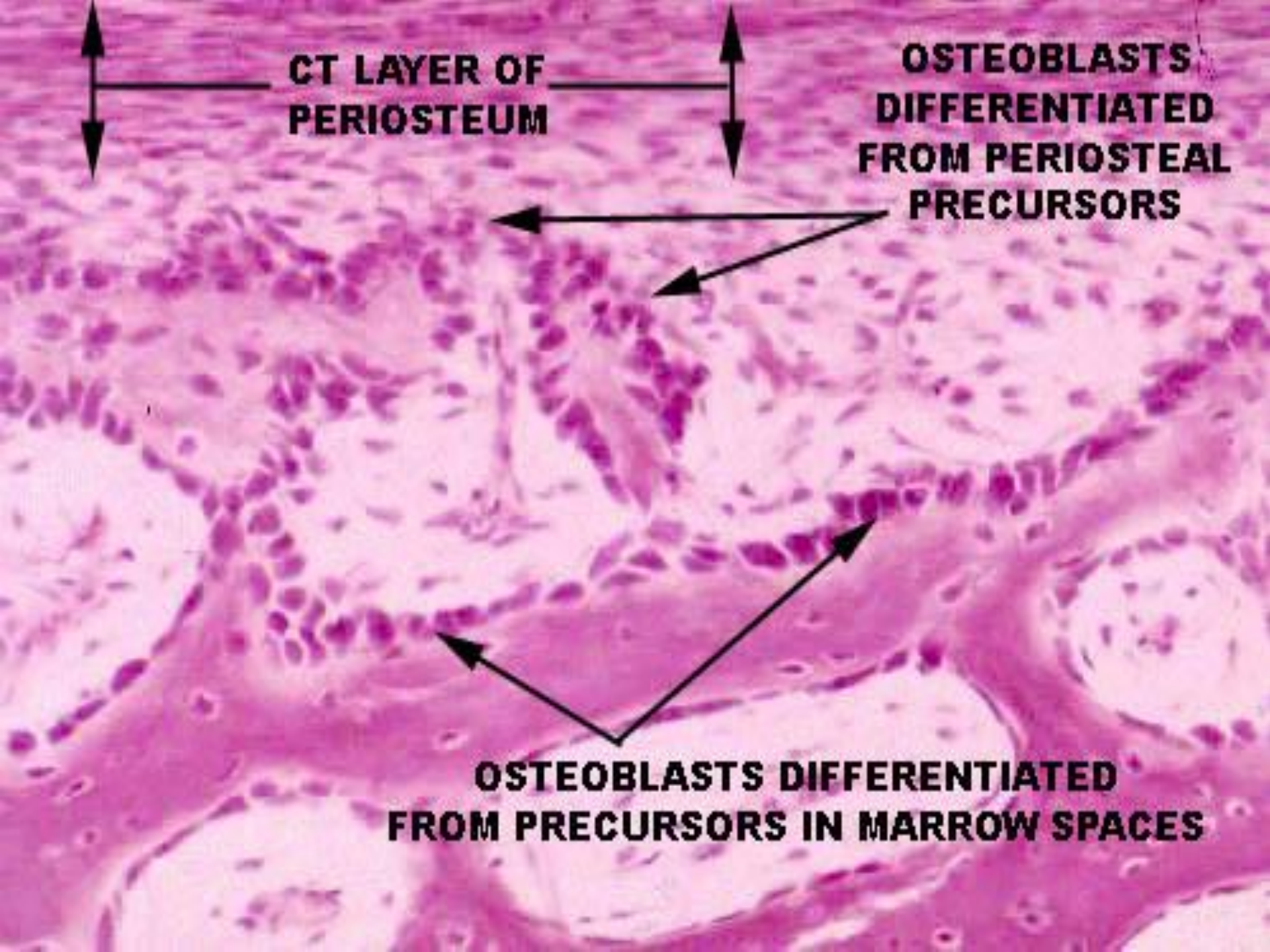


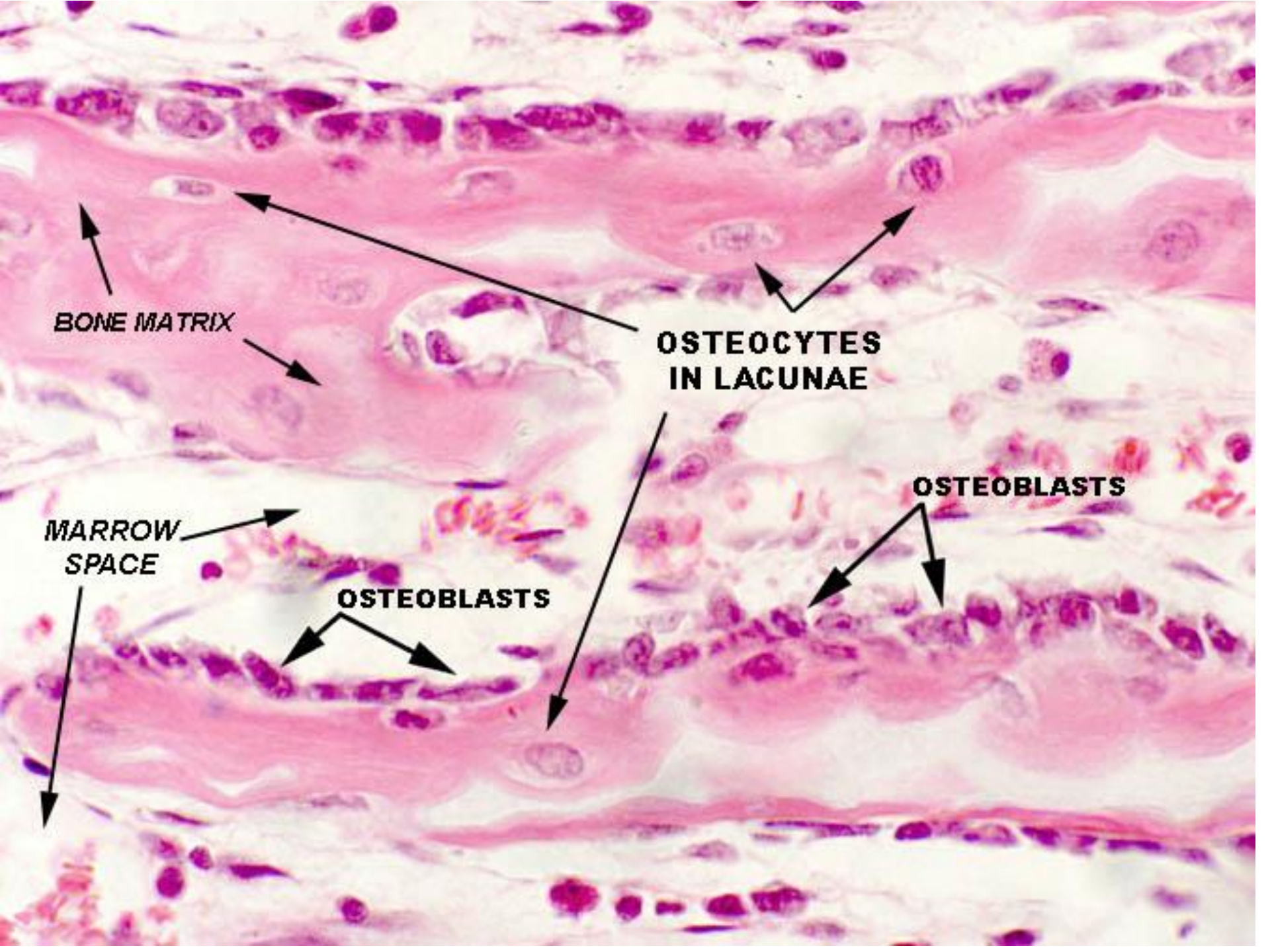
④ **Bone collar of compact bone forms and red marrow appears.**

- Trabeculae just deep to the periosteum thicken, forming a woven bone collar that is later replaced with mature lamellar bone.
- Spongy bone (diploë), consisting of distinct trabeculae, persists internally and its vascular tissue becomes red marrow.


Intramembranous Ossification H&E
primitive
trabecular bone
ossification
centre
mucous connective tissue

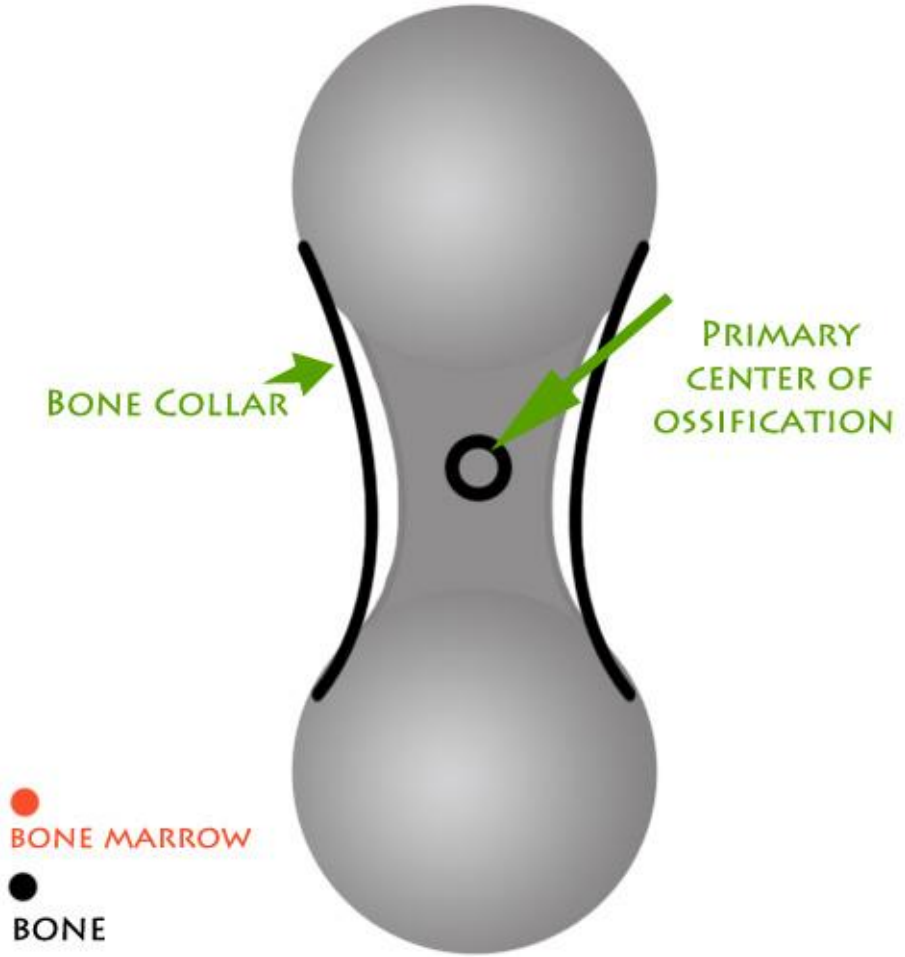

Intramembranous Ossification H&E
newly deposited
bone matrix
osteoblasts


CT LAYER OF PERIOSTEUM
OSTEOBLASTS DIFFERENTIATED FROM PERIOSTEAL PRECURSORS
OSTEOBLASTS DIFFERENTIATED FROM PRECURSORS IN MARROW SPACES


BONE MATRIX
OSTEOCYTES
IN LACUNAE
OSTEOBLASTS
MARROW
SPACE
OSTEOBLASTS

ENDOCHONDRAL BONE FORMATION

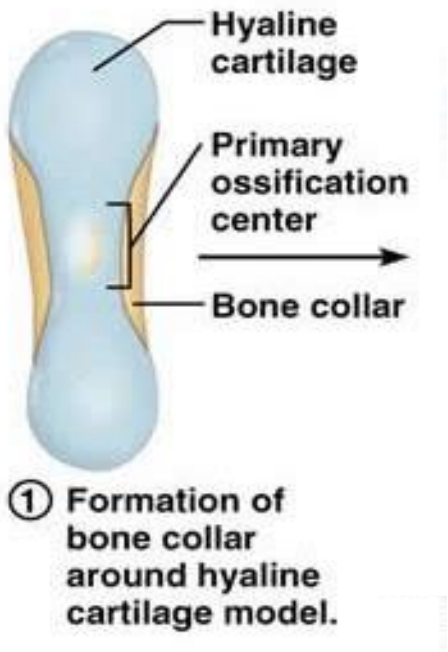
concurrently →



Vascularization of perichondrium at the midriff of diaphysis causes transformation of chondrogenic cells into osteoprogenitor cells, later osteoblasts, thus perichondrium becomes periosteum and newly formed osteoblasts secrete bone matrix – bone collar on the surface of the cartilage model by intramembranous bone formation – bone growth in width.

ENDOCHONDRAL BONE FORMATION

Fetus: first 2 months



Formation of miniature hyaline cartilage model

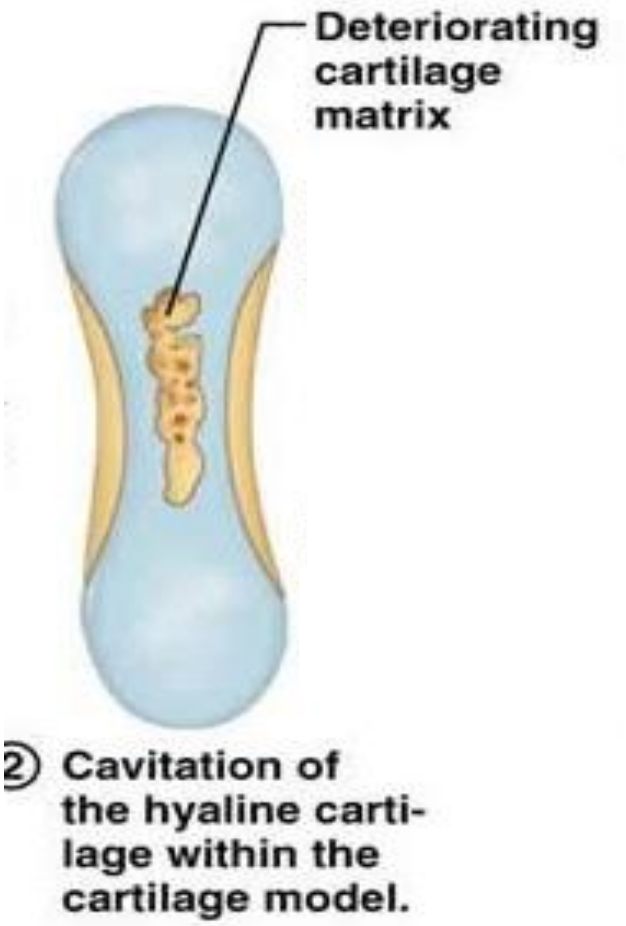
Appositional and interstitial growth of the model

Formation of the primary ossification center:

- Hypertrophy of chondrocytes in the center of the model
- Production of type X collagen and accumulation of glycogen by hypertrophied chondrocytes.
- Calcification cartilage matrix septae between hypertrophied chondrocytes.

ENDOCHONDRAL BONE FORMATION

Fetus: at 2–3 months

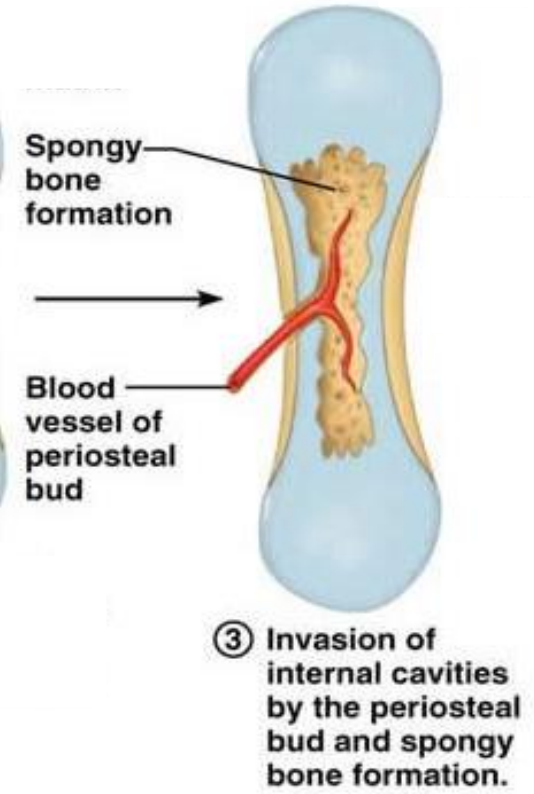


The diffusion of nutrients to hypertrophied chondrocytes is inhibited by the bone collar. These chondrocytes die.

New-formed empty lacunae connected to each other (concavities) form future marrow cavity.

ENDOCHONDRAL BONE FORMATION

Fetus



The osteoclasts etch holes in the bone collar. Periosteal bud - osteogenic bud (osteoprogenitor and hematopoietic cells and blood vessels) enters the concavities.

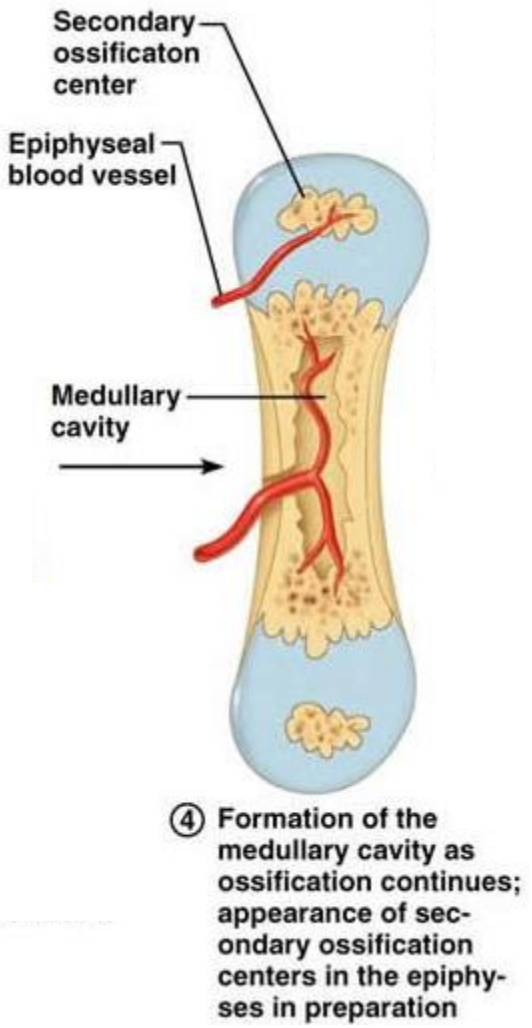
Osteoprogenitor cells divide and form osteoblasts which elaborate the bone matrix on the surface of the calcified cartilage matrix resulting in formation of a calcified cartilage/calcified bone complexes.

Bone collar becomes thicker.

Osteoclasts resorb the calcified cartilage/calcified bone complexes, bone marrow cavity enlarges. As the result of these processes the cartilage of diaphysis is replaced by bone except epiphyseal plate.

ENDOCHONDRAL BONE FORMATION

Fetus and childhood



Formation of secondary ossification centers at both epiphyses:

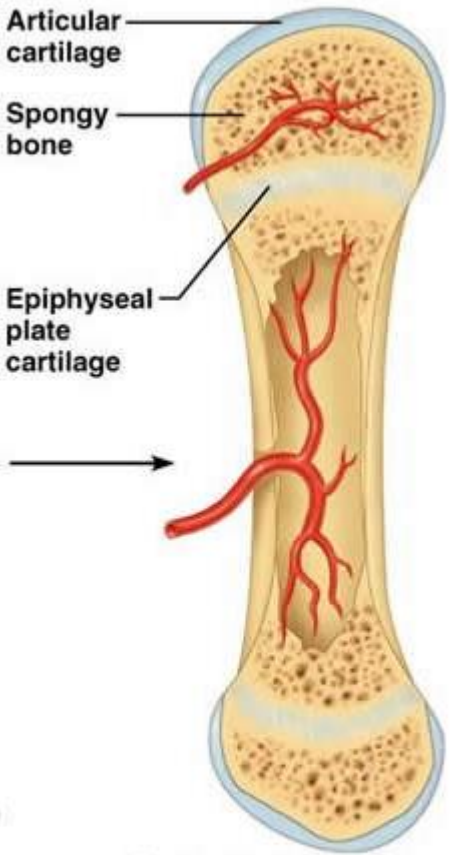
Osteoprogenitor cells invade the epiphysis, differentiate into osteoblasts

Osteoblasts secrete bone matrix on the cartilage scaffold

Bone collar is not formed.

ENDOCHONDRAL BONE FORMATION

Adolescence



⑤ Ossification of the epiphyses; when completed, hyaline cartilage remains only in the epiphyseal plates and articular cartilages.

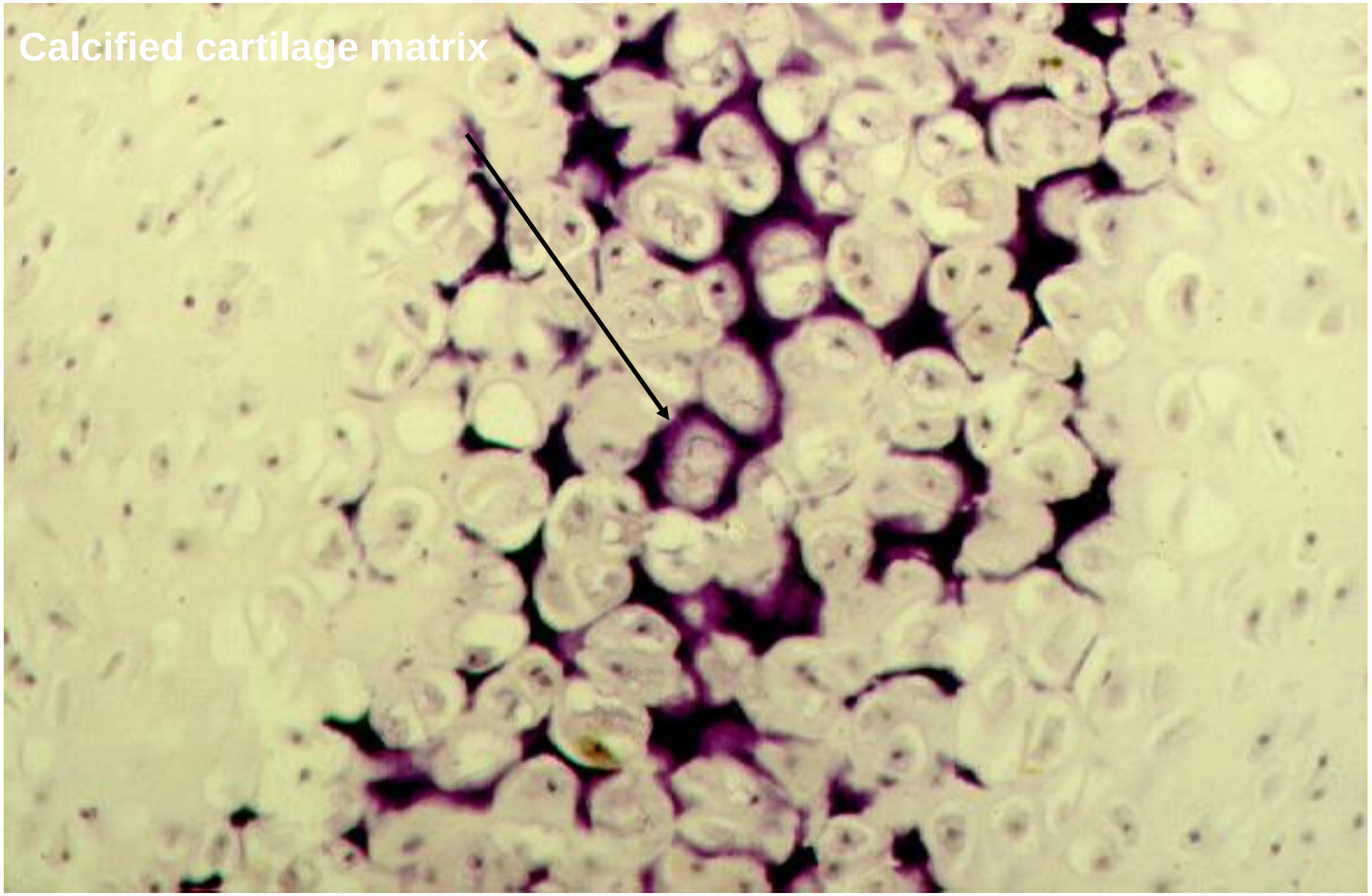
The cartilage of epiphyses and cartilage of diaphysis are replaced by bone except at the articular surface and at the epiphyseal plate.

At the same time bone is constantly being remodeled to meet the changing forces placed on it.

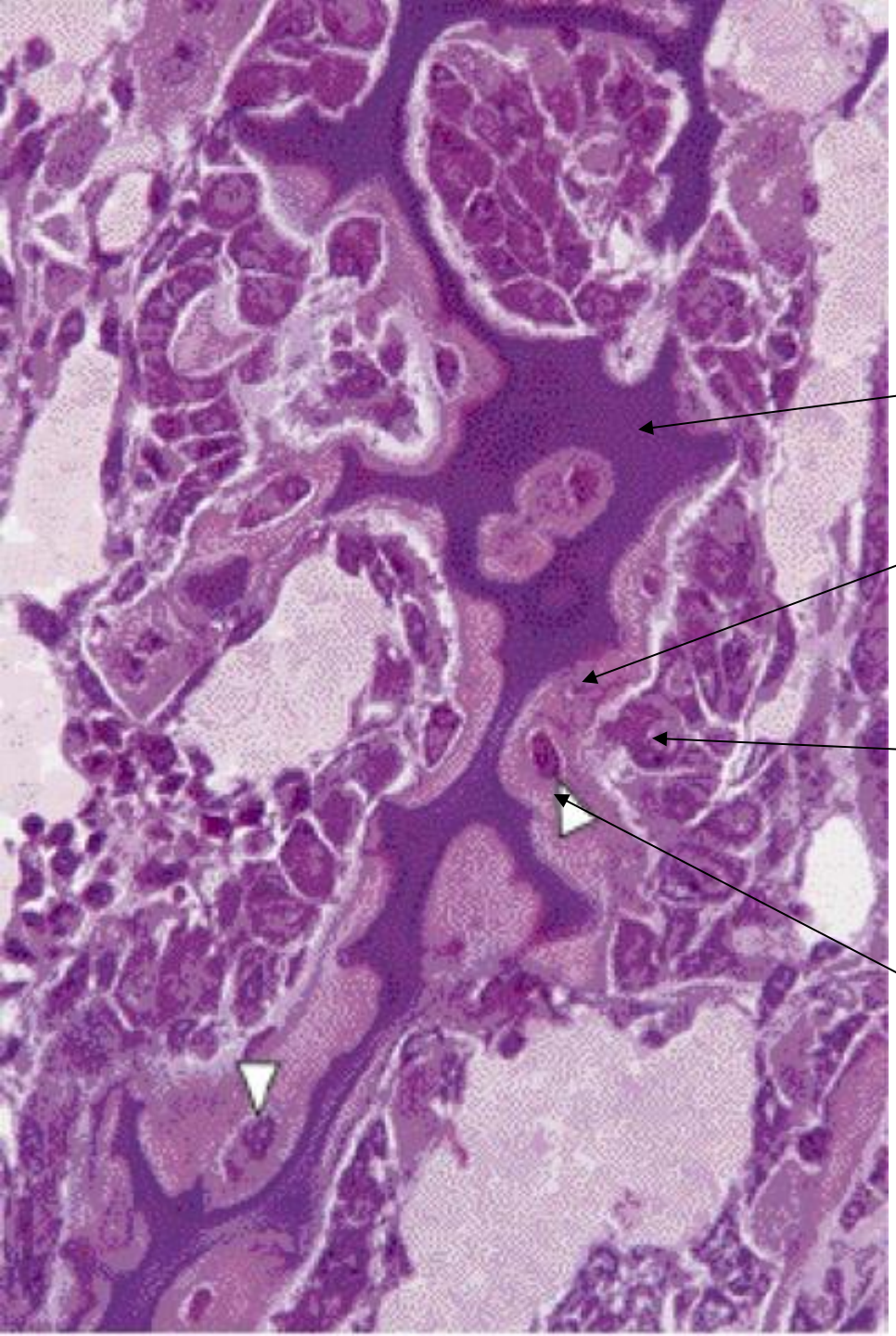

Ingrowth of periosteal (osteogenic) bud
Bone collar

X

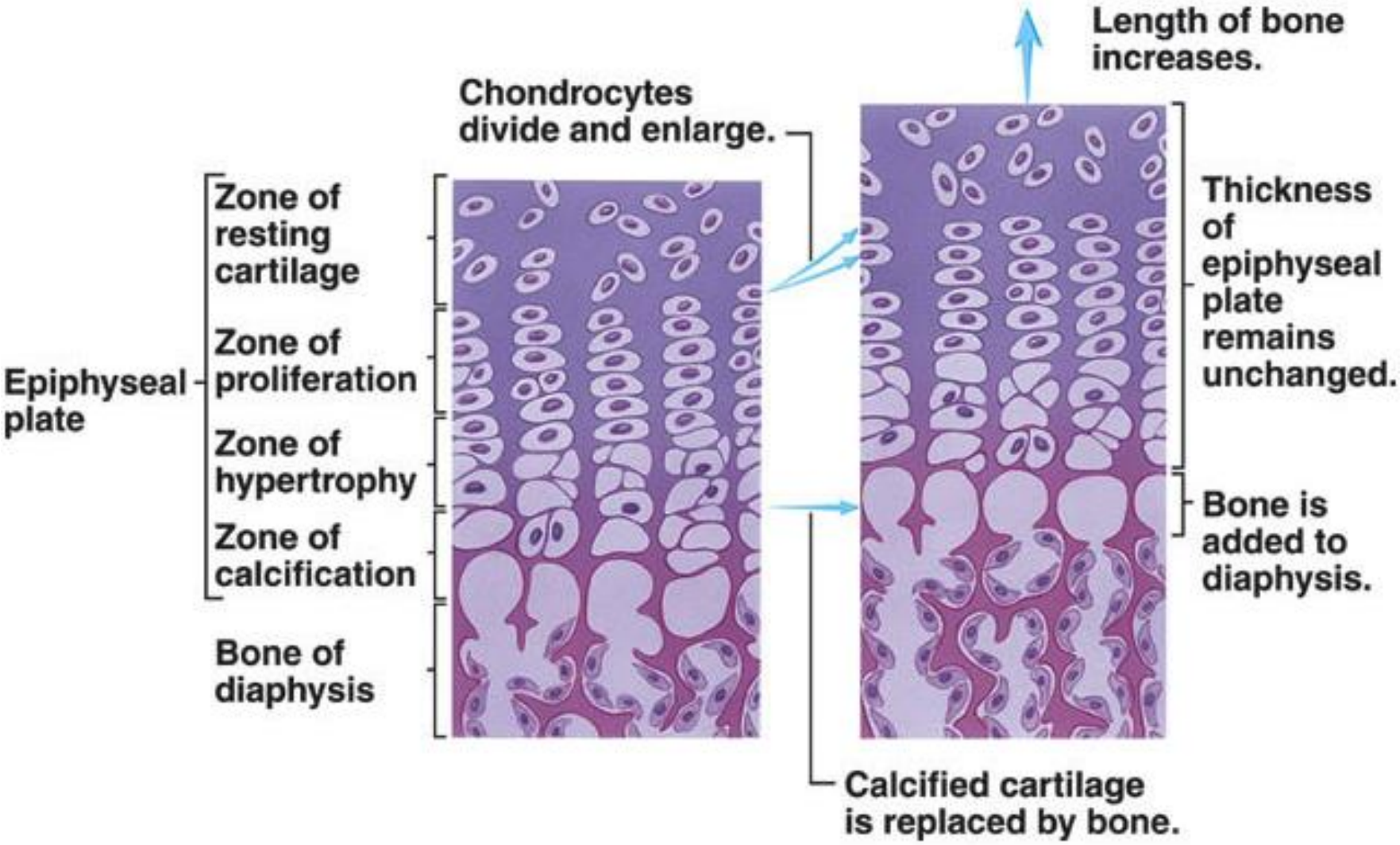
Primary ossification center



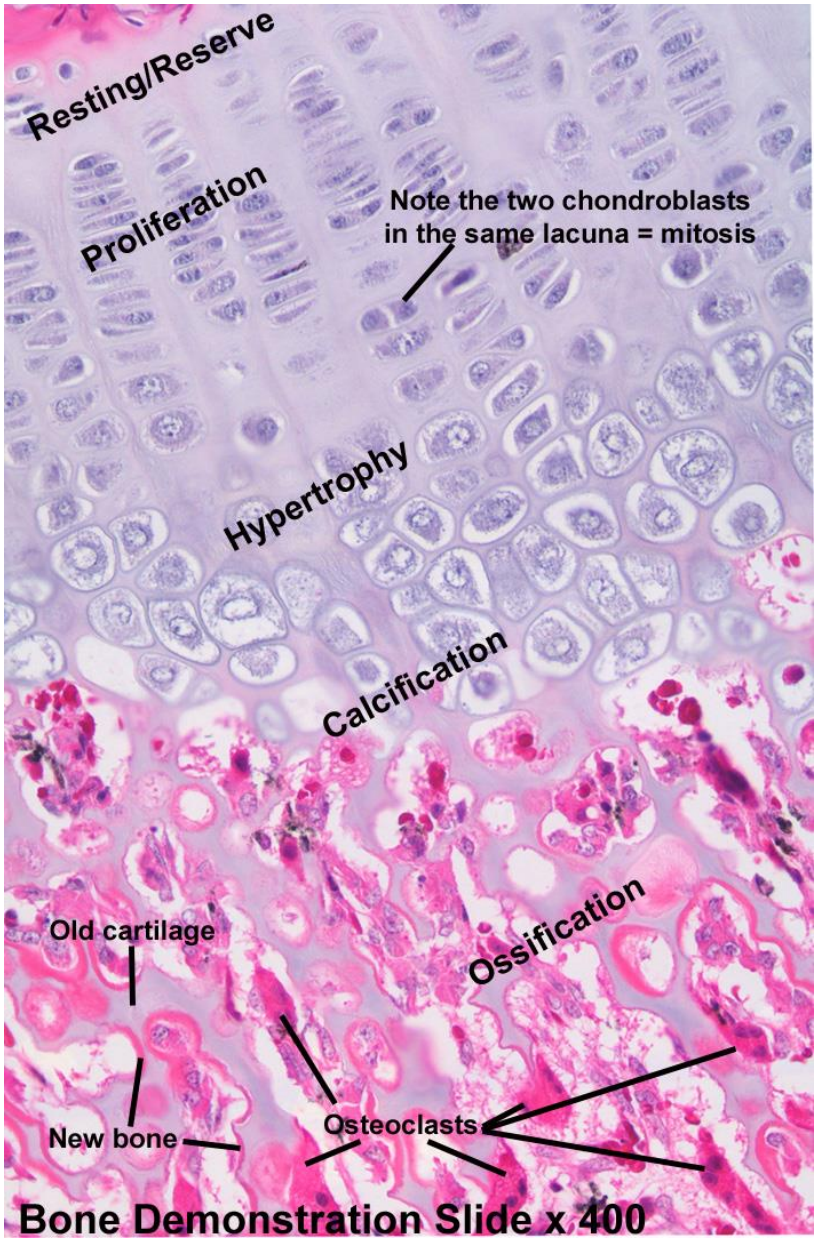
Early stage of endochondral ossification



The structure of growth plate



BONE GROWTH IN LENGHT



Reserve cartilage

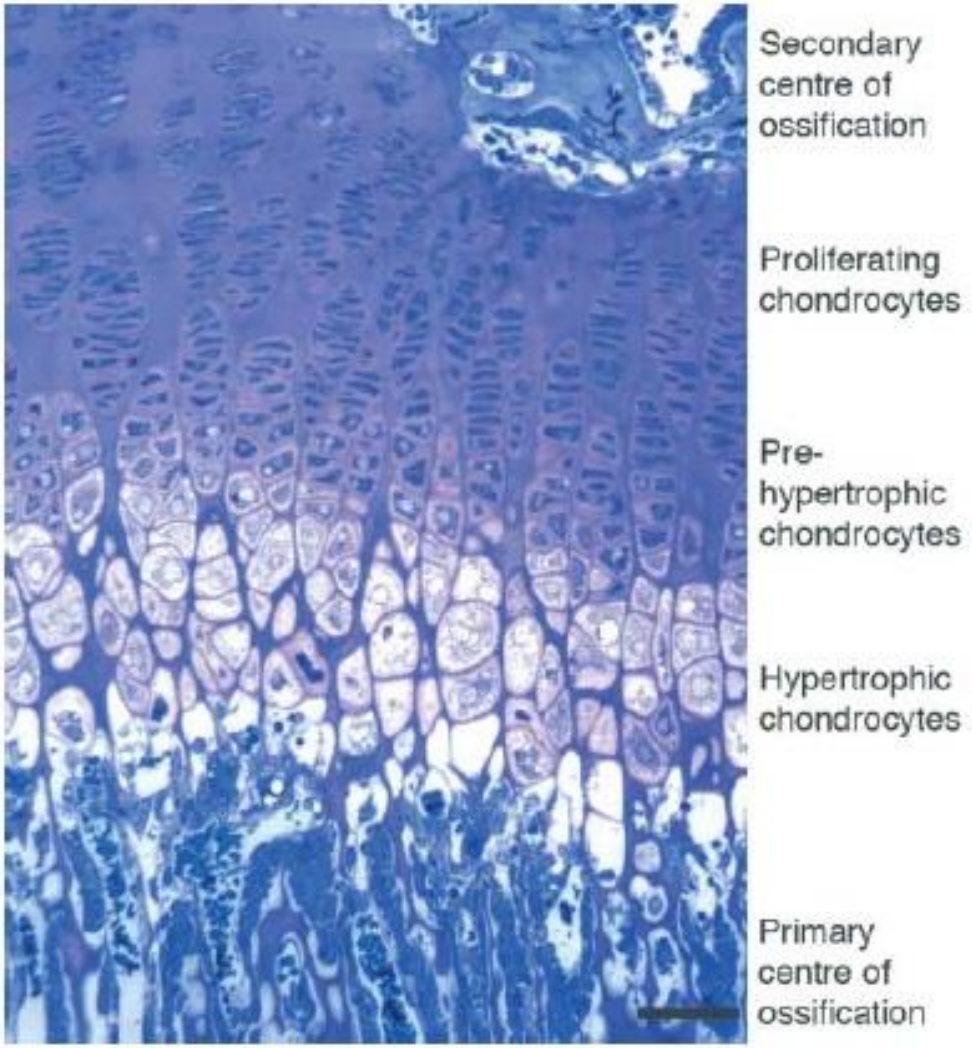
Proliferation

Maturation and hypertrophy

Calcification

Ossification

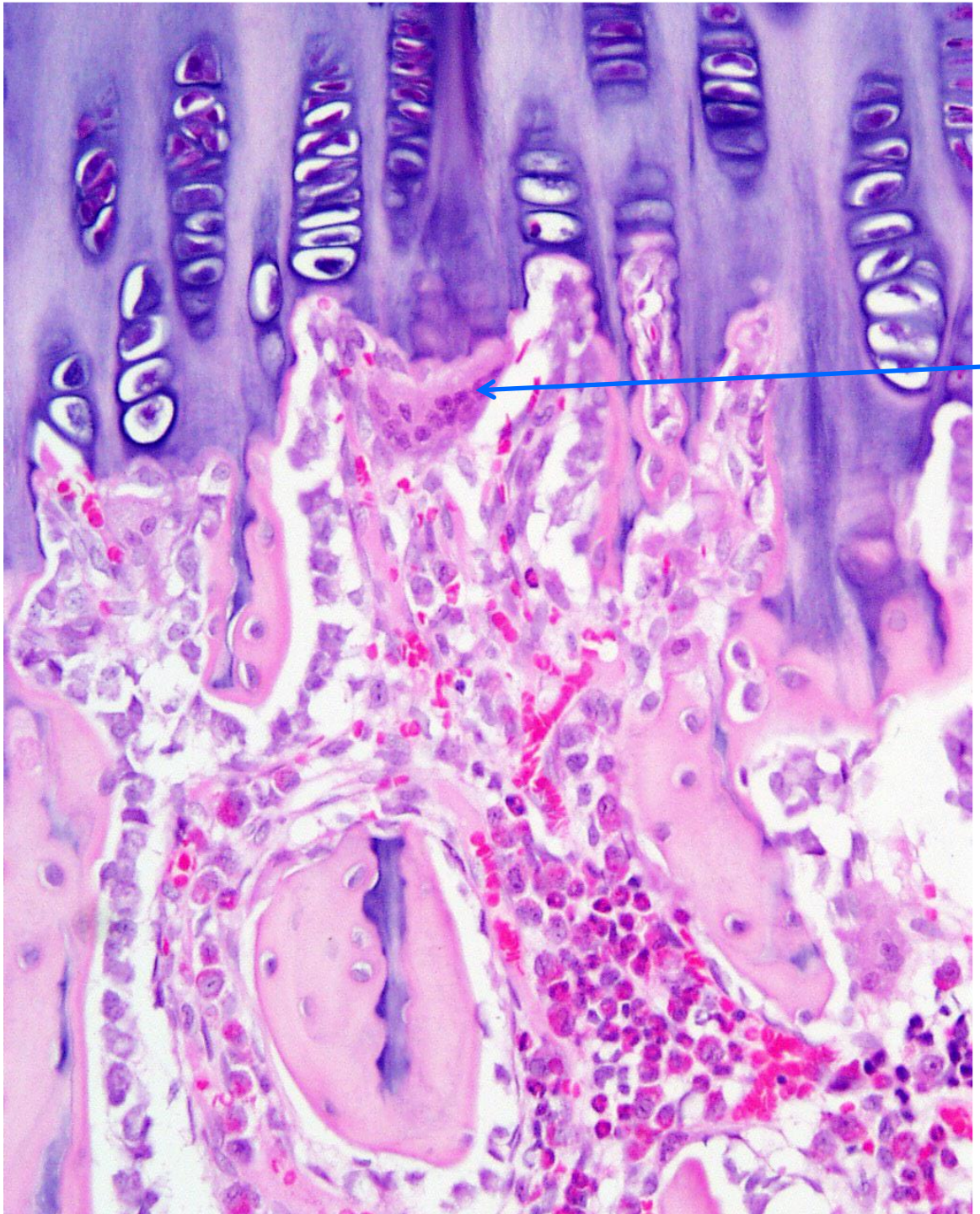
BONE GROWTH IN LENGHT



At about 20th year of age, the rate of mitosis decreases in the zone of proliferation and the zone of ossification overtakes the zones of proliferation.

Once the epiphyseal plate is resorbed and growth in length is no longer possible.

Somatotropin and testosteron stimulate the chondrocyte proliferation in growth plate


osteoclast

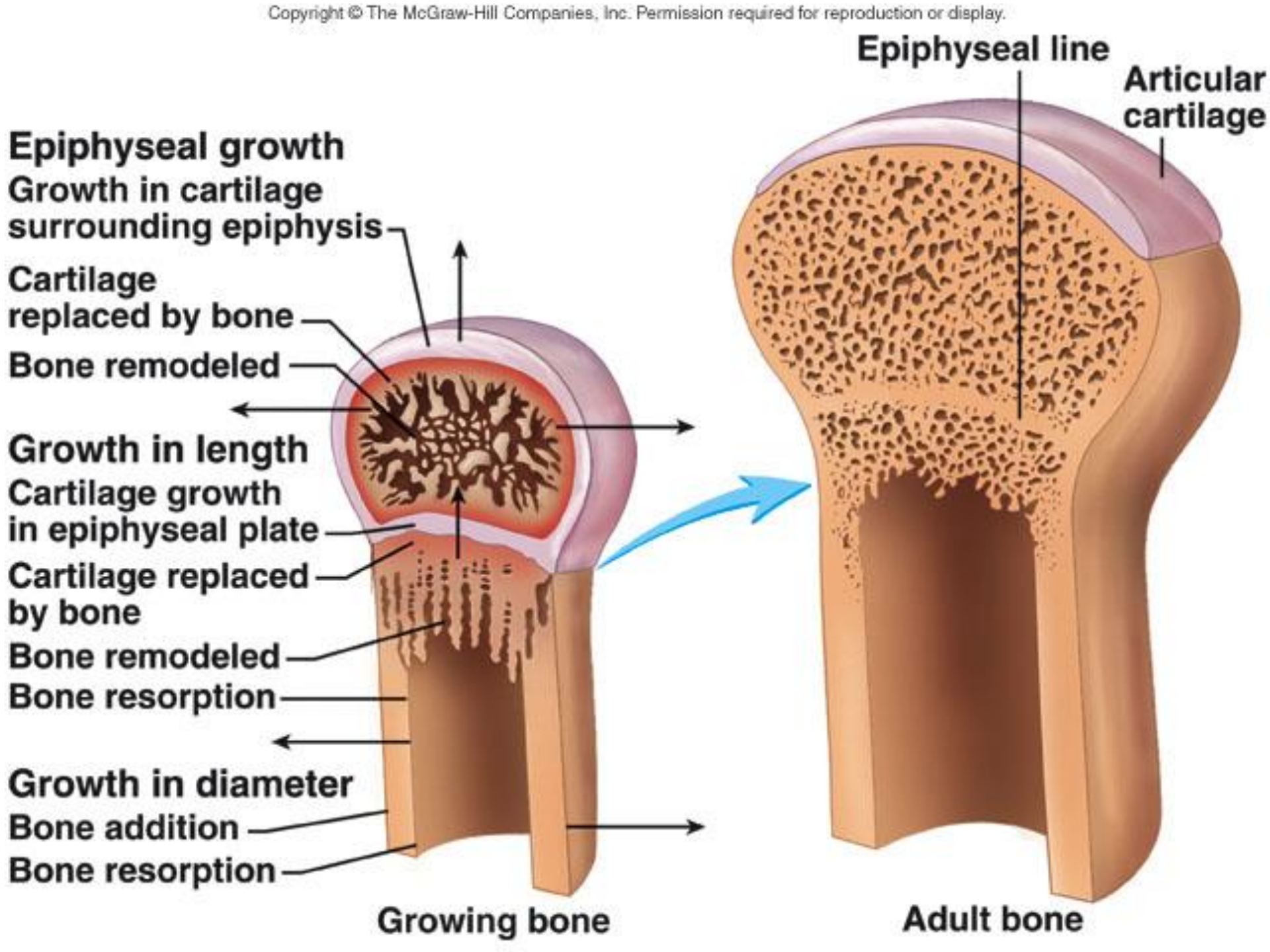


Table **HORMONES INVOLVED IN BONE GROWTH AND MAINTENANCE**

Growth hormone (anterior pituitary gland)	• Increases the rate of mitosis of chondrocytes and osteoblasts • Increases the rate of protein synthesis (collagen, cartilage matrix, and enzymes for cartilage and bone formation)
Thyroxine (thyroid gland)	• Increases the rate of protein synthesis • Increases energy production from all food types
Insulin (pancreas)	• Increases energy production from glucose
Parathyroid hormone (parathyroid glands)	• Increases the reabsorption of calcium from bones to the blood (raises blood calcium level) • Increases the absorption of calcium by the small intestine and kidneys (to the blood)
Calcitonin (thyroid gland)	• Decreases the reabsorption of calcium from bones (lowers blood calcium level)
Estrogen (ovaries) or	• Promotes closure of the epiphyses of long bones (growth stops)
Testosterone (testes)	• Helps retain calcium in bones to maintain a strong bone matrix

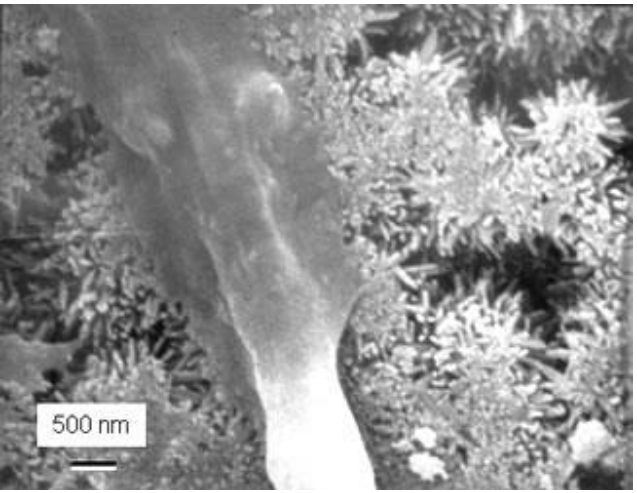
Minerals

- Large amounts of calcium and phosphorus and smaller amounts of magnesium, fluoride, and manganese are required for bone growth and remodeling

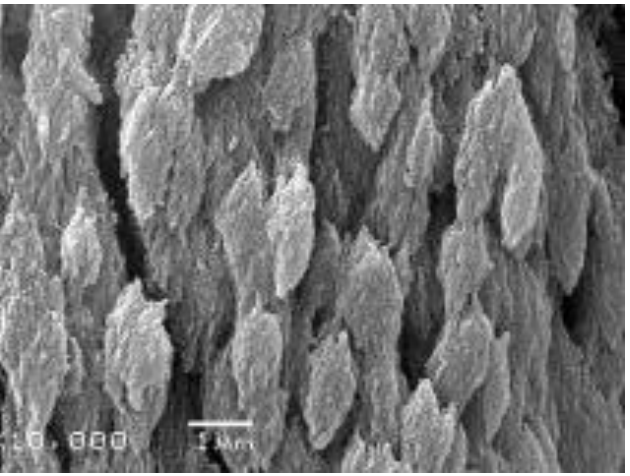
Vitamins

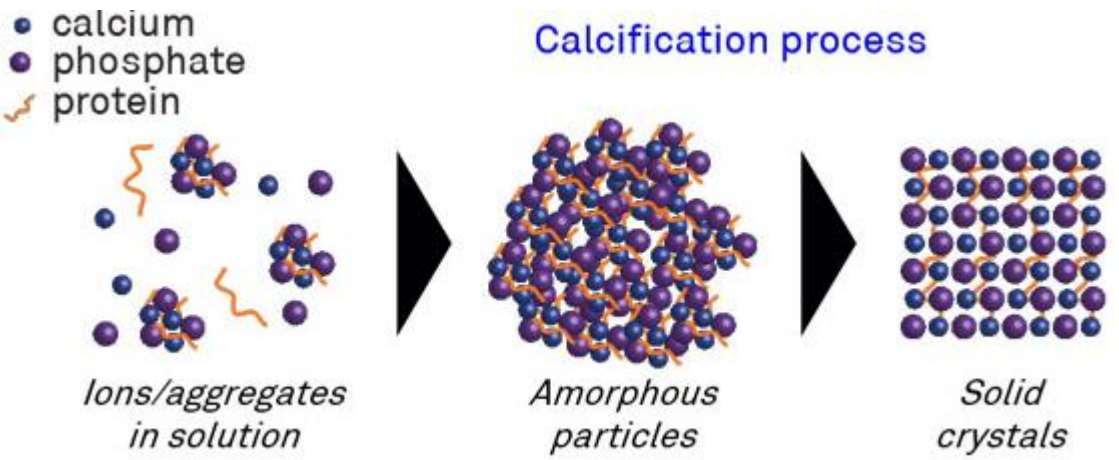
- Vitamin A stimulates activity of osteoblasts
- Vitamin C is needed for synthesis of collagen
- Vitamin D helps build bone by increasing the absorption of calcium from foods in the gastrointestinal tract into the blood
- Vitamins K and B12 are also needed for synthesis of bone proteins

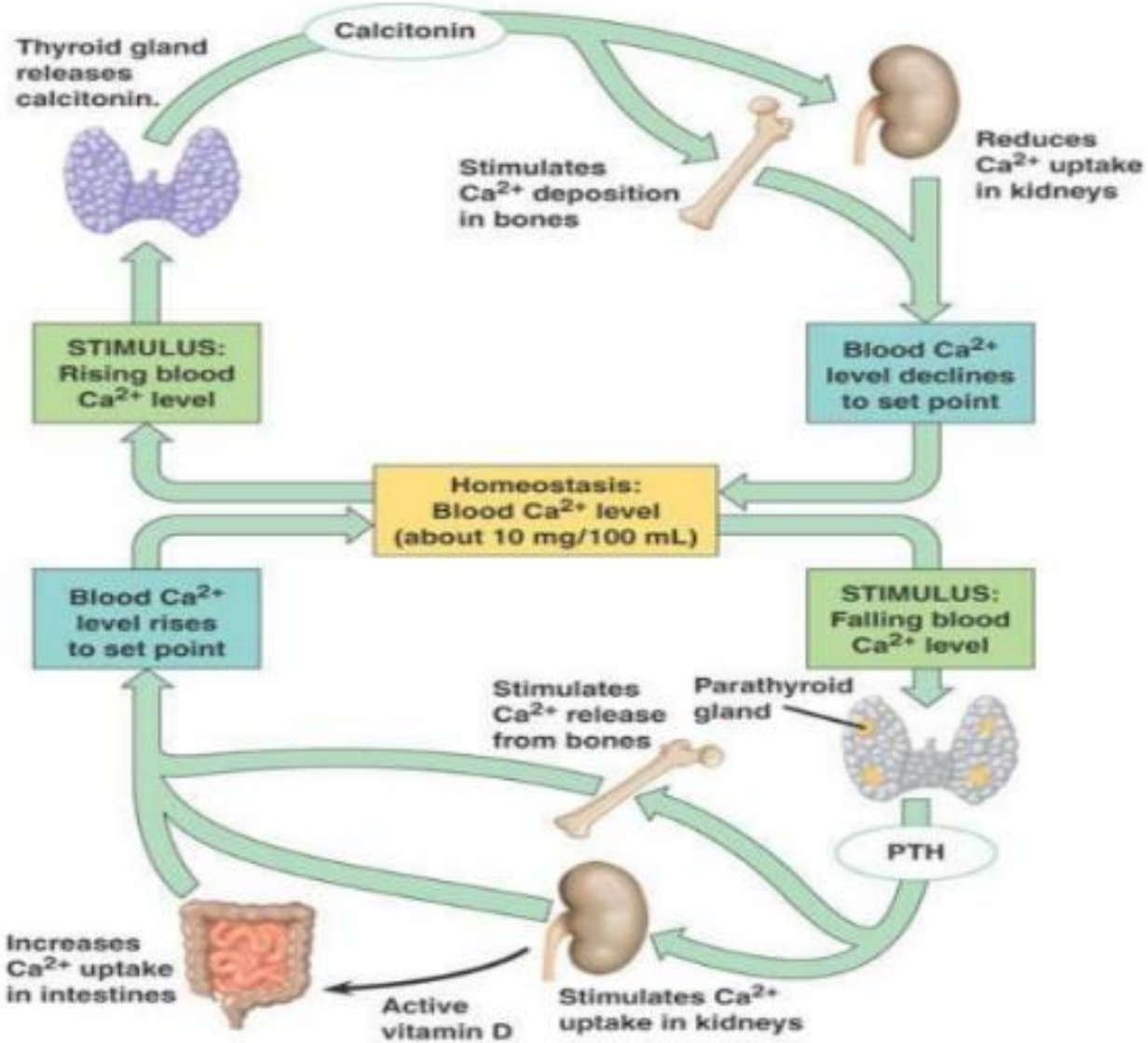
CALCIFICATION



Osteoblasts release **membrane-bounded matrix vesicles** which contain **calcium and phosphate ions**, cAMP, ATP, ATPase, alkaline phosphatase, pyrophosphatase and calcium binding proteins (**osteonectin**). These vesicles possess a lot of **calcium pumps** transporting calcium ions into the vesicle.

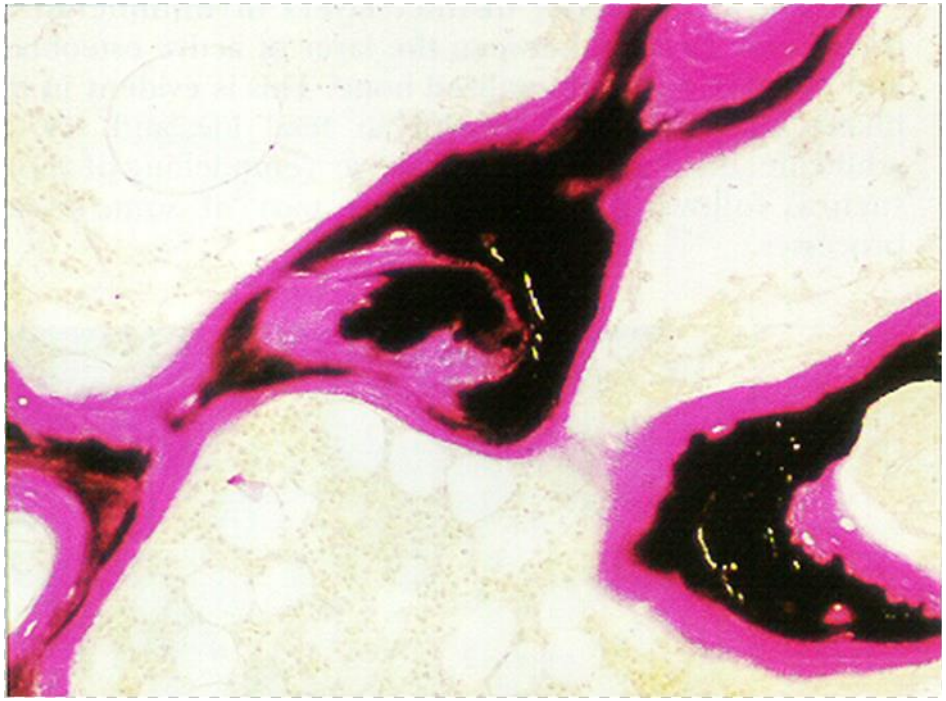





Calcitonin
Thyroid gland releases calcitonin.
Stimulates Ca^{2+} deposition in bones
Reduces Ca^{2+} uptake in kidneys
STIMULUS: Rising blood Ca^{2+} level
Blood Ca^{2+} level declines to set point
Homeostasis: Blood Ca^{2+} level (about 10 mg/100 mL)
Blood Ca^{2+} level rises to set point
STIMULUS: Falling blood Ca^{2+} level
Stimulates Ca^{2+} release from bones
Parathyroid gland
PTH
Increases Ca^{2+} uptake in intestines
Active vitamin D
Stimulates Ca^{2+} uptake in kidneys

Osteomalacia (failure of mineralization)

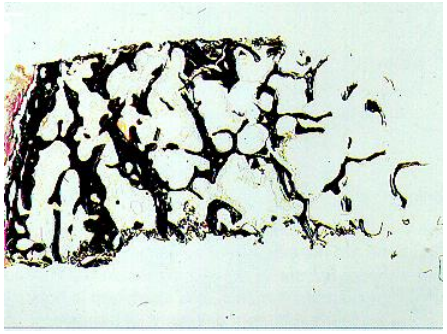
Mineralization of osteoid can take place only if there are sufficient Ca^{2+} and PO_4^{3-} ions. If the level of Ca^{2+} ions is low (inadequate dietary, lack of vitamin D or malabsorption resulting from small intestine disease) or if $PO4^{3-}$ level is low (excessive loss in the urine), then mineralization is impaired.



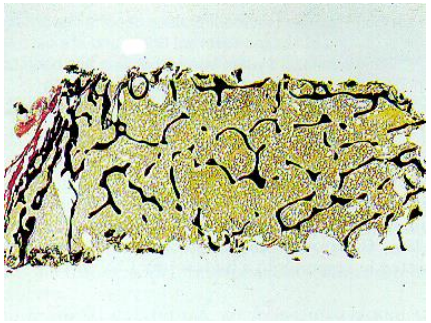
Iliac crest bone sectioned in plastic resin (without decalcification). Broad zone of unmineralized osteoid (magenta) and the central zone of mineralized bone (black) stained by the Von Kossa silver technique.

OSTEOPOROSIS

Osteoporosis (porous bones) is a progressive bone disease that is characterized by a decrease in bone mass and density which can lead to an increased risk of fracture. It can occur as a result of disuse (prolonged bed rest, limb paralysis) and also in otherwise healthy people, particularly post-menopausal women (decrease in estrogen level).

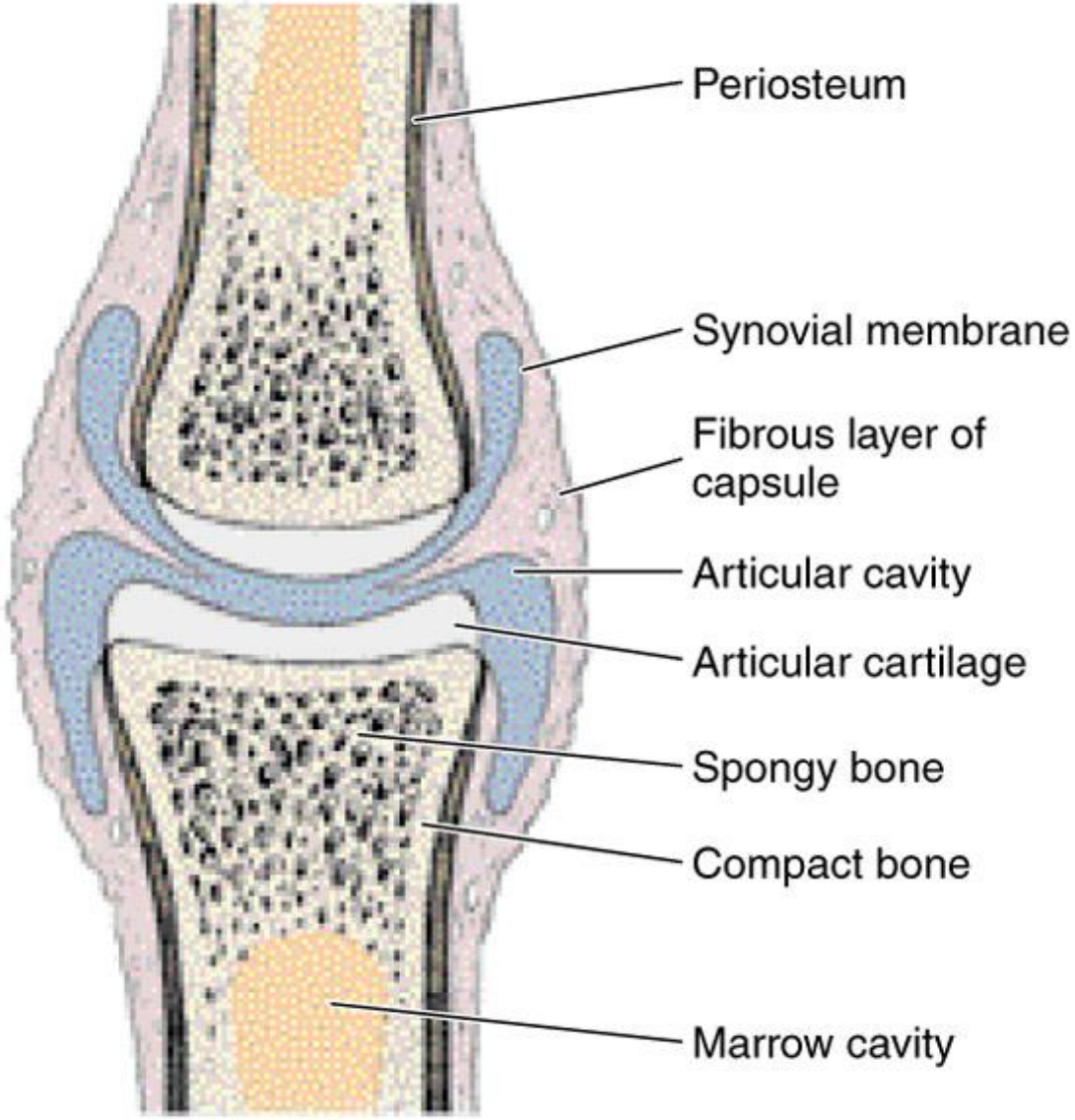


Bone biopsy from the iliac crest showing normal cortical and trabecular bone. Bone stained black by a silver method.



Bone from a patient with osteoporosis. Cortical zone is narrower and trabeculae are thinner and less numerous.

Structure of synovial joint



Types of joints:

1. **Diarthroses** (synovial joints, free movement)

2. **Synarthroses** (limited movement)

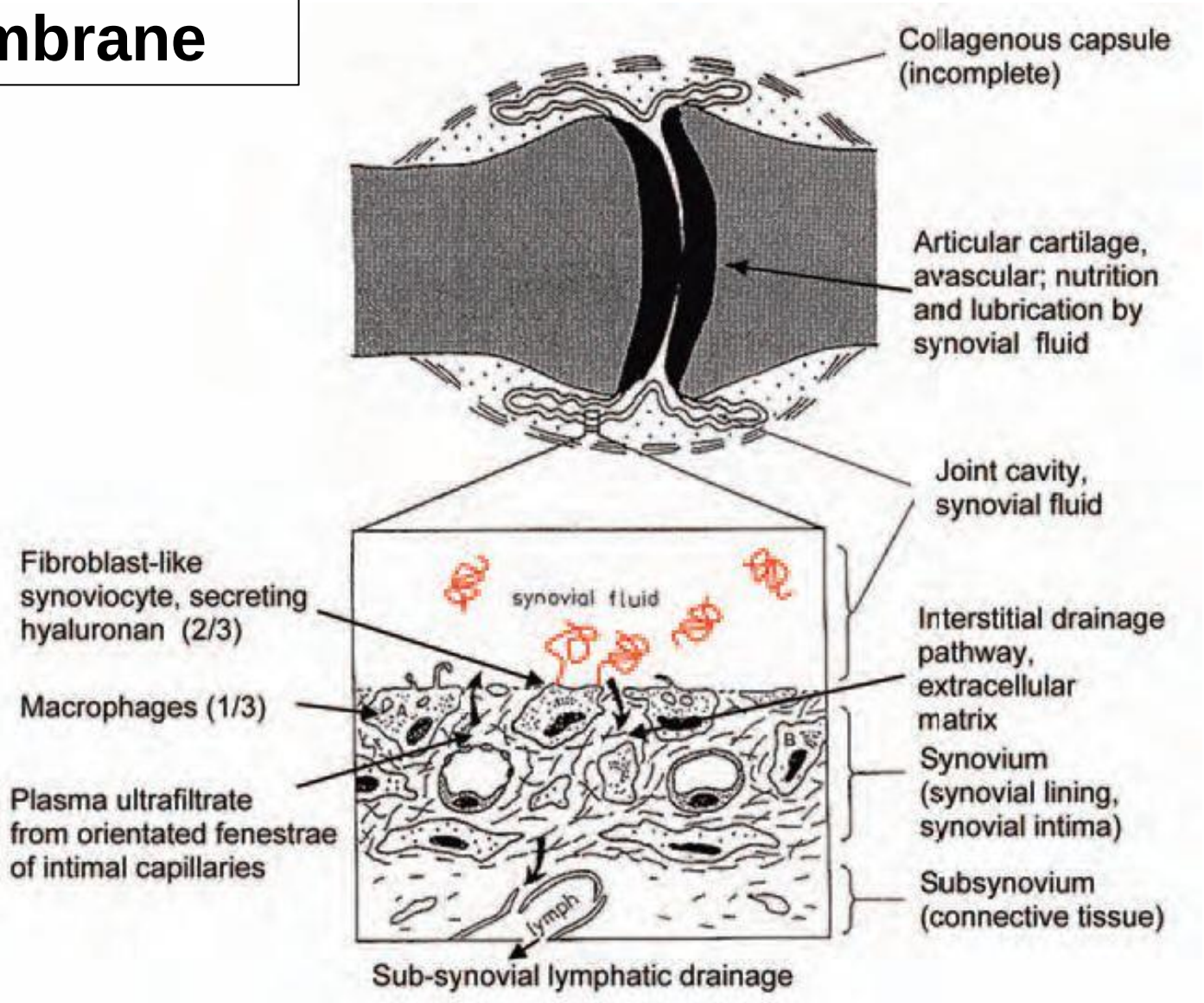
Synostosis – joint-uniting tissue is bone; skull bones in adults

Synchondrosis – joint-uniting tissue is hyaline cartilage; joint between first rib and sternum

Syndesmosis – bones joined by dense connective tissue; pubic symphysis.


ADO41 Demo Slide x 51
synovial membrane
joint cavity
meniscus
epiphyseal plate
articular cartilage

Synovial membrane



Rheumatoid arthritis