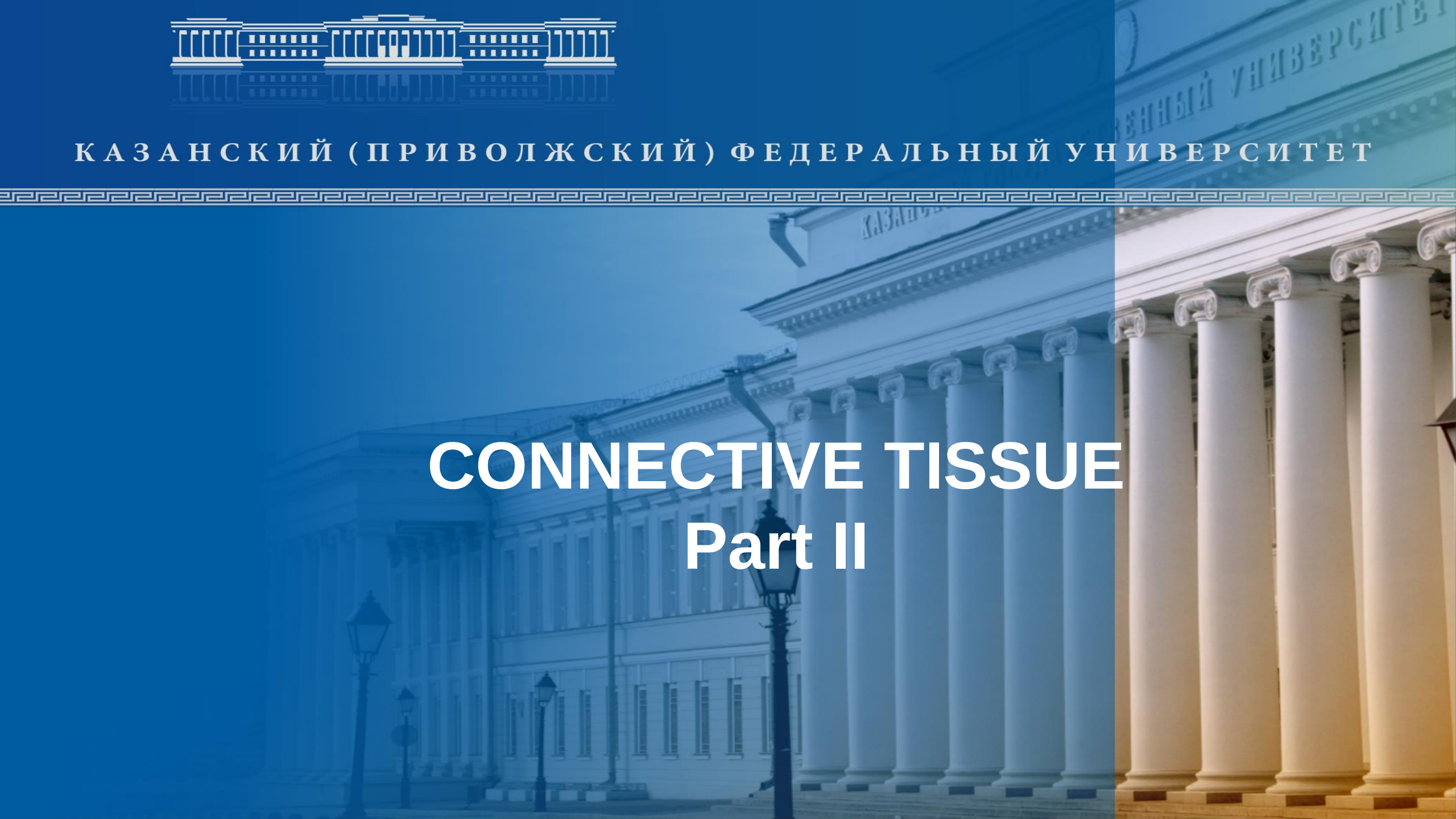
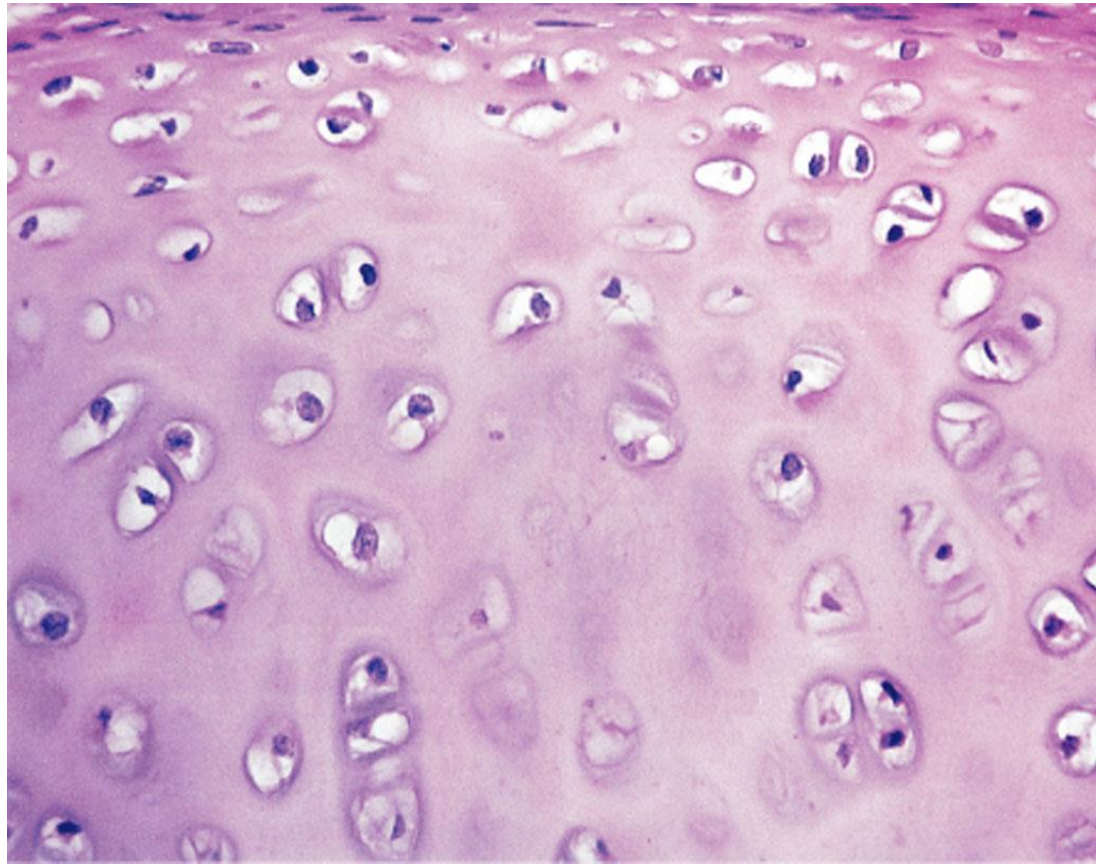


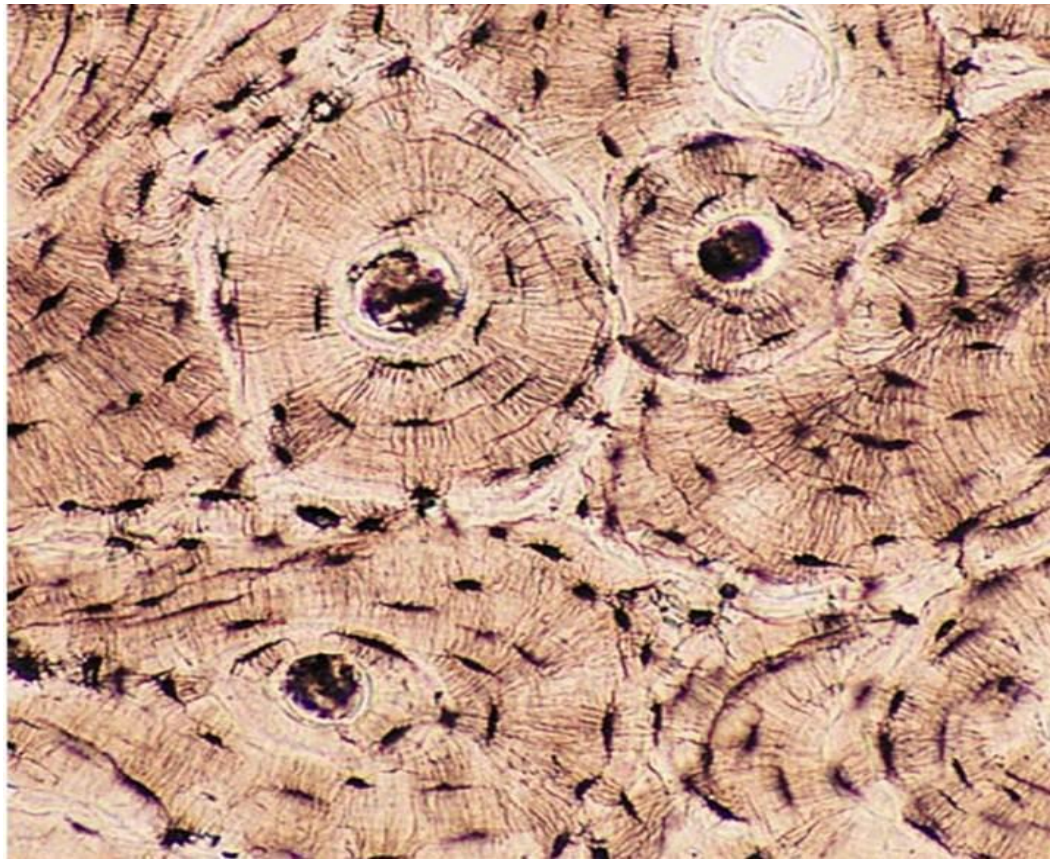
CONNECTIVE TISSUE
Part II

Skeletal Connective tissue:

- Cartilage



- Bone

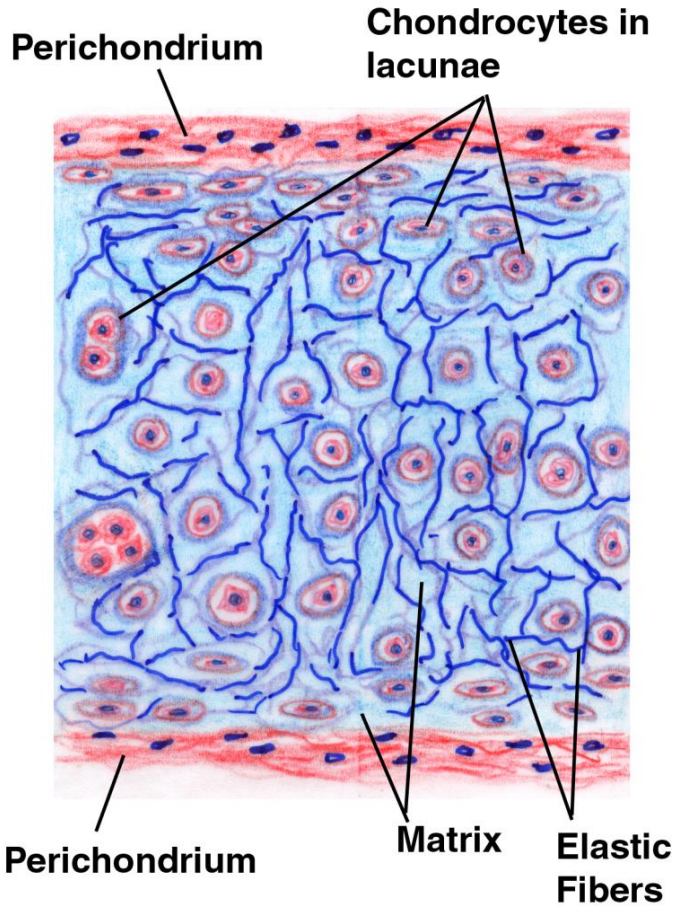


Cartilage

Specialized form of firm and resilient CT that can bear stresses without permanent distortion

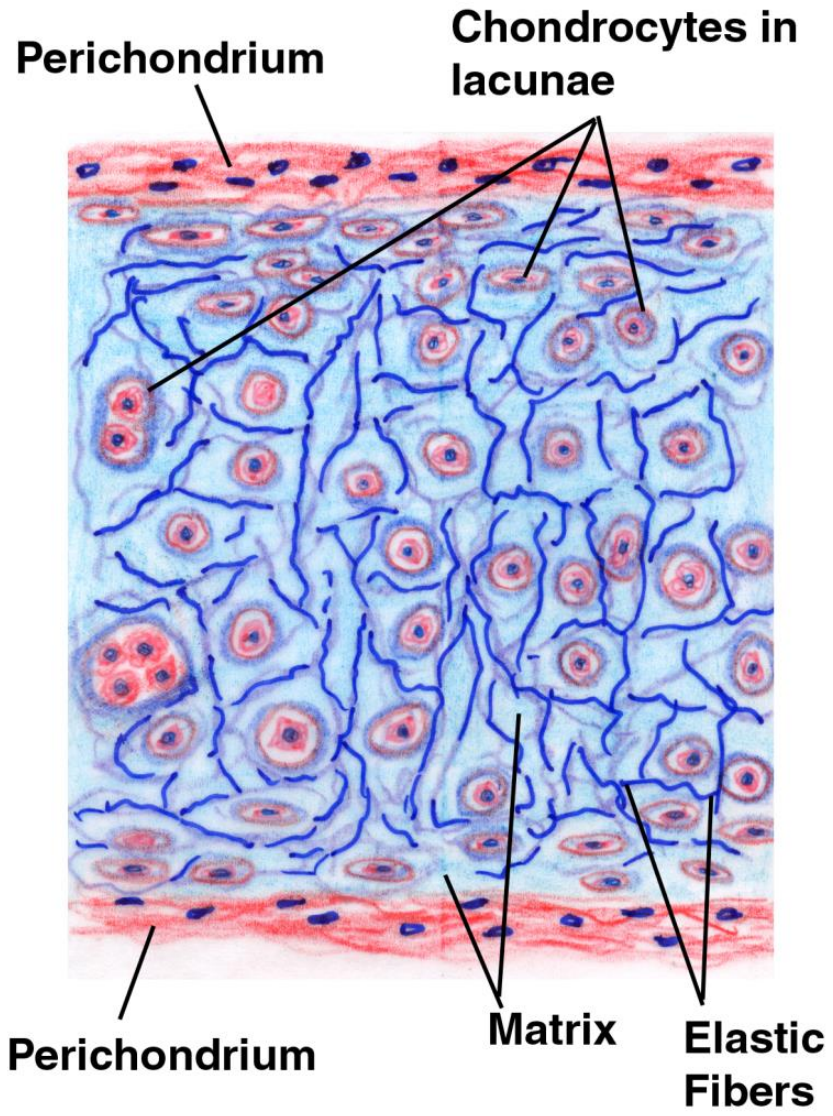
Functions

- Load bearing and shock absorbing tissue
- Participates in bone development and repair

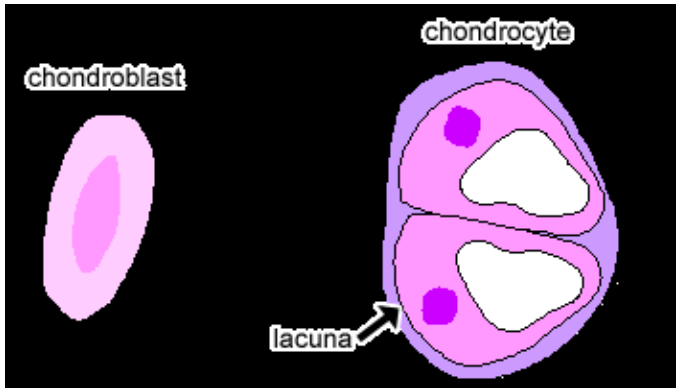


Cartilage

- Consists of **cells** and **extracellular matrix**
- Is an **avascular** tissue
- Is covered by **perichondrium**

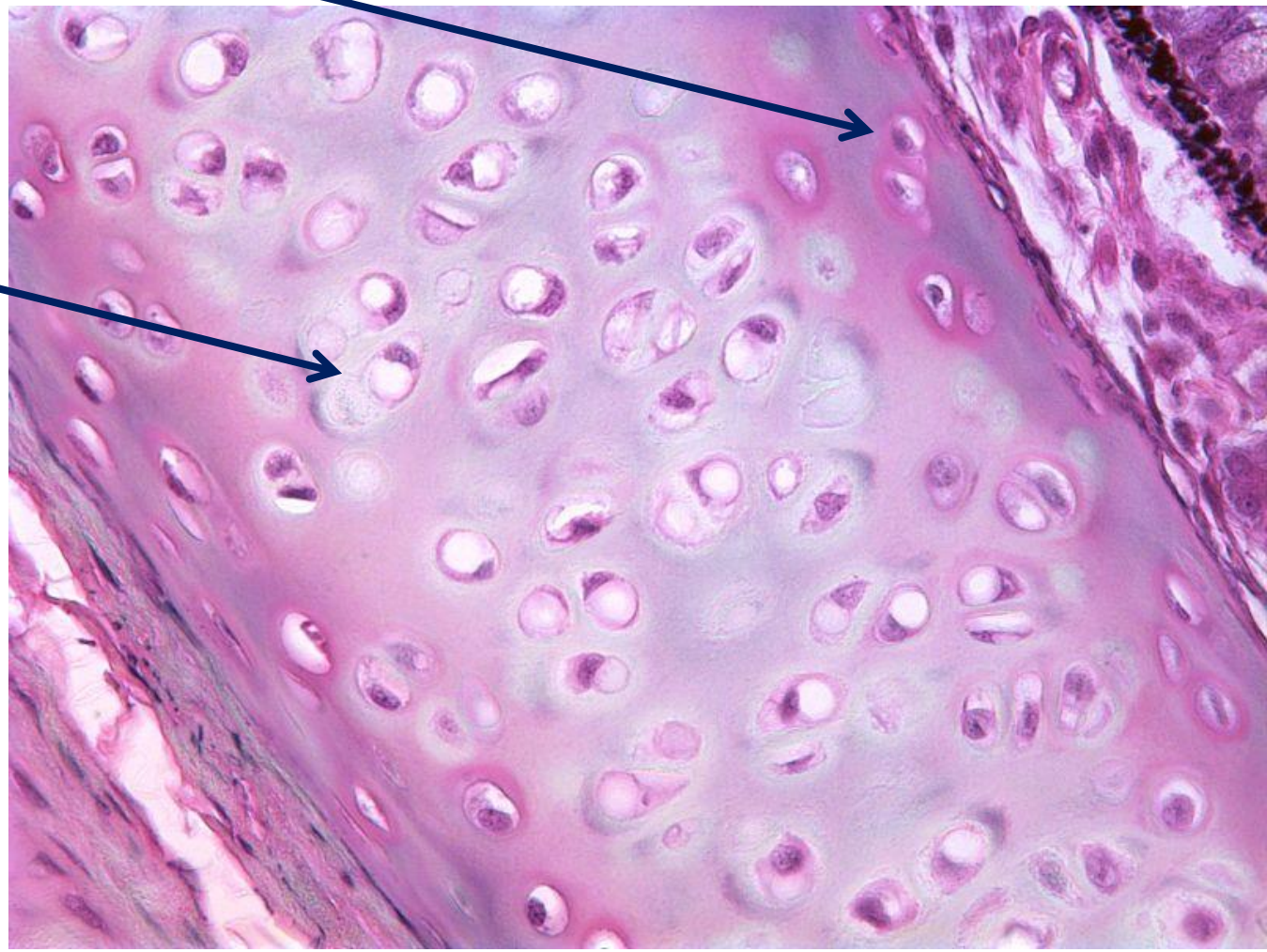


Cartilage Cells



- **chondroblasts** – *immature cells*
  - In the inner layer of the perichondrium and right under in the lacunae
  - Synthesize the matrix around themselves, thereby becoming chondrocytes

- **chondrocytes** – *differentiated chondroblasts that have surrounded themselves with matrix*
  - In the center of the cartilage in the lacunae
  - form **isogenous groups** (a cluster of chondrocytes, resulting from the proliferation of a single chondrocyte)
  - Synthesize cartilage matrix
  - Synthesize enzymes breaking down the matrix - collagenase, elastase, hyaluronidase

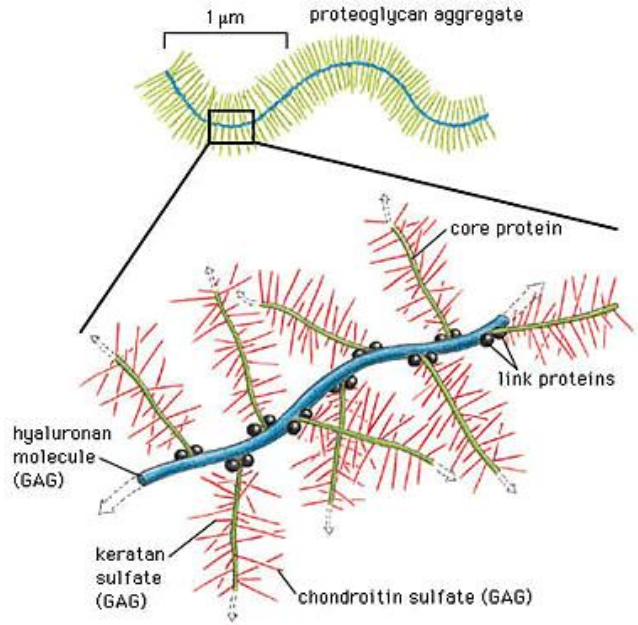


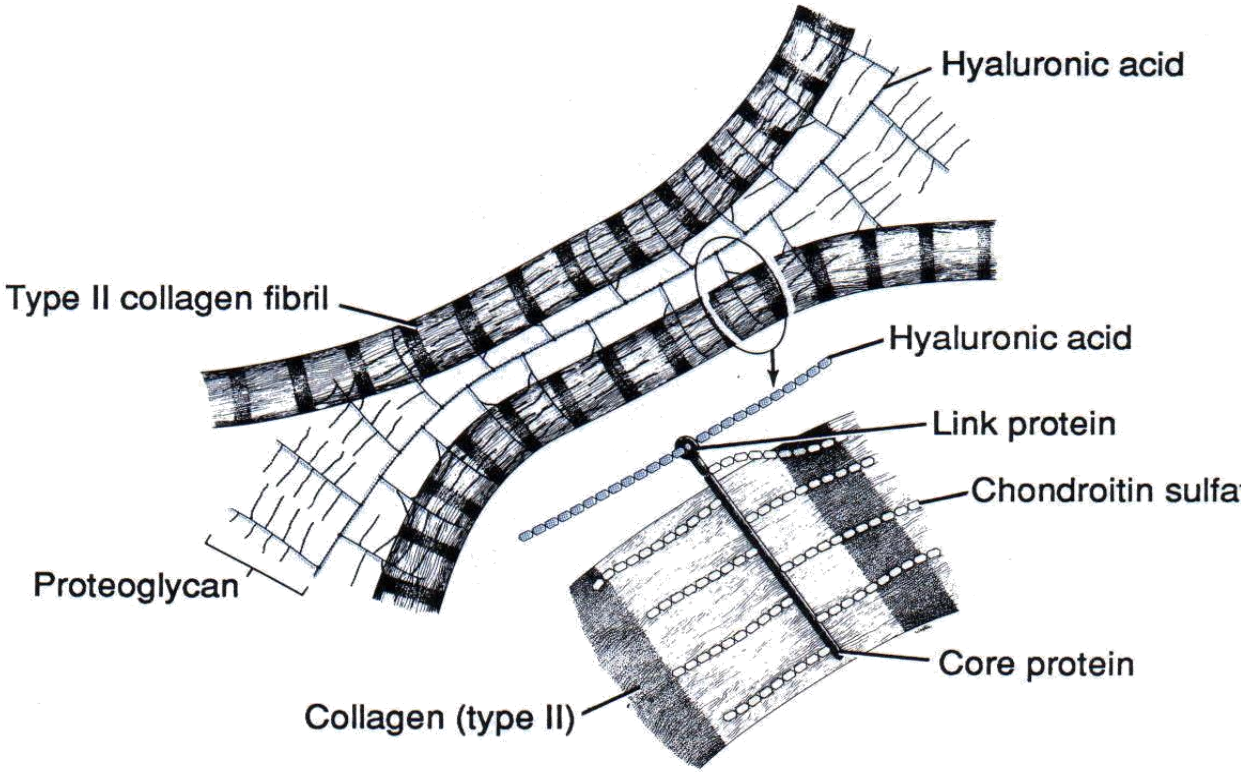
Cartilage matrix

(95% of cartilage volume)

Both flexible and non-compressible

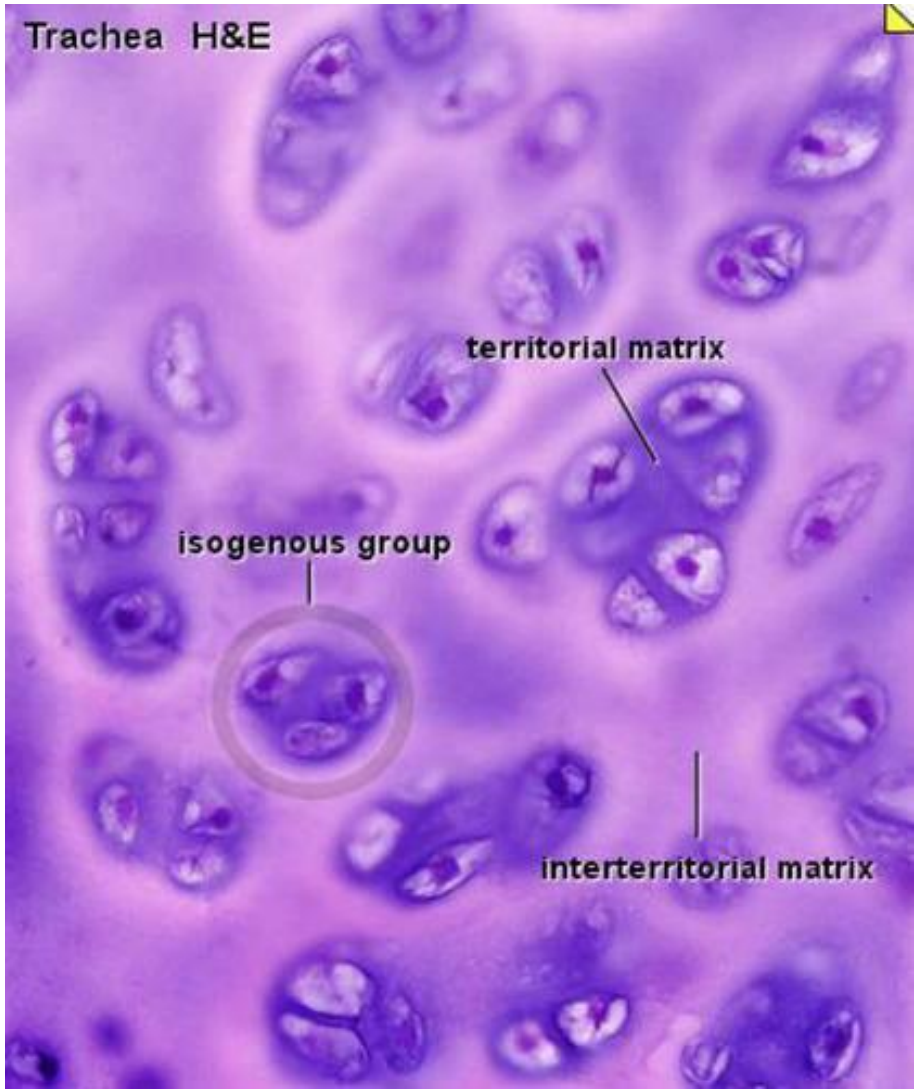
- Fibers (collagen type II)
- Ground substance:
  - Hyaluranan (hyaluronic acid)
  - Proteoglycans:
    - # Core protein
    - # GAGs:
      - * chondroitin sulfate
      - * keratan sulfate





- **Territorial matrix** immediately surrounds chondrocytes. This matrix stains more intensely with hematoxylin due to the high concentration of proteoglycans.

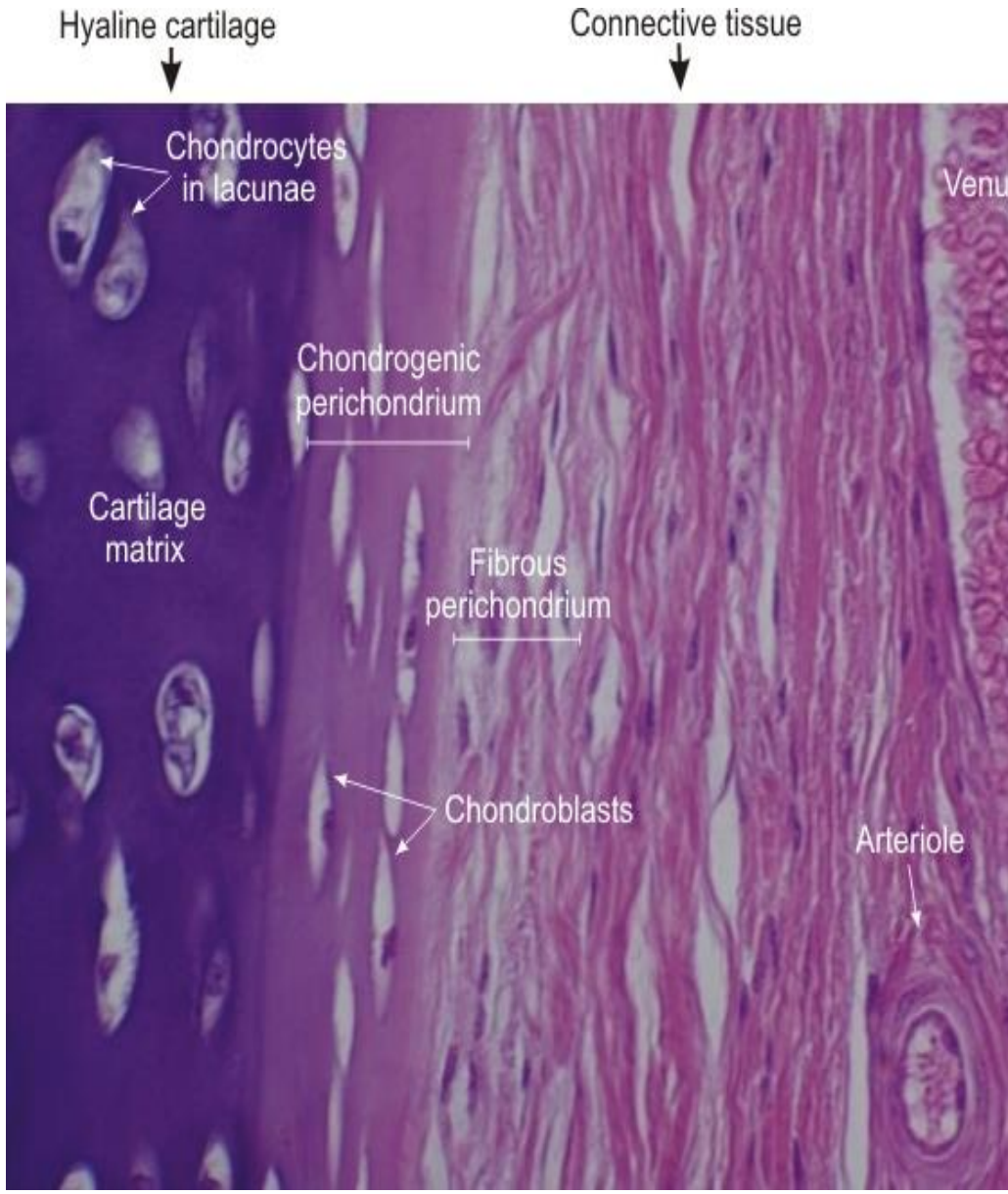
- **Interterritorial matrix** is the lighter-staining matrix outside the territorial matrix and between isogenous groups.



Perichondrium

- **2 layers:**
  - **Fibrous layer** – outer portion, composed of dense connective tissue, serves as a source of reserve cells for the chondrogenic layer
  - **Chondrogenic layer-** inner, more cellular portion contains chondroblasts and loose connective tissue

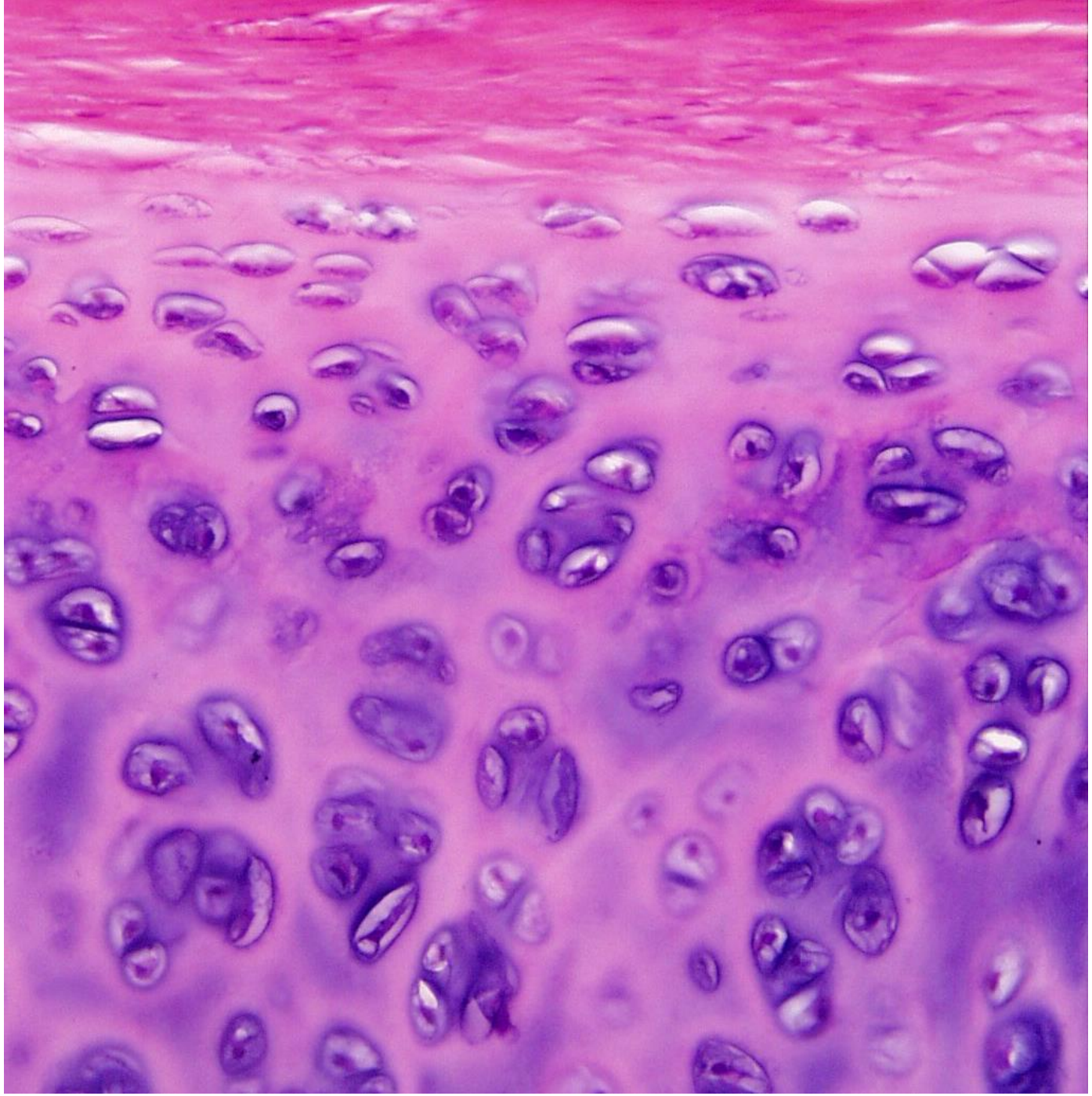
- **Function**: nutrition, appositional growth, repair



perichondrium

chondroblasts

chondrocytes



Growth of cartilage

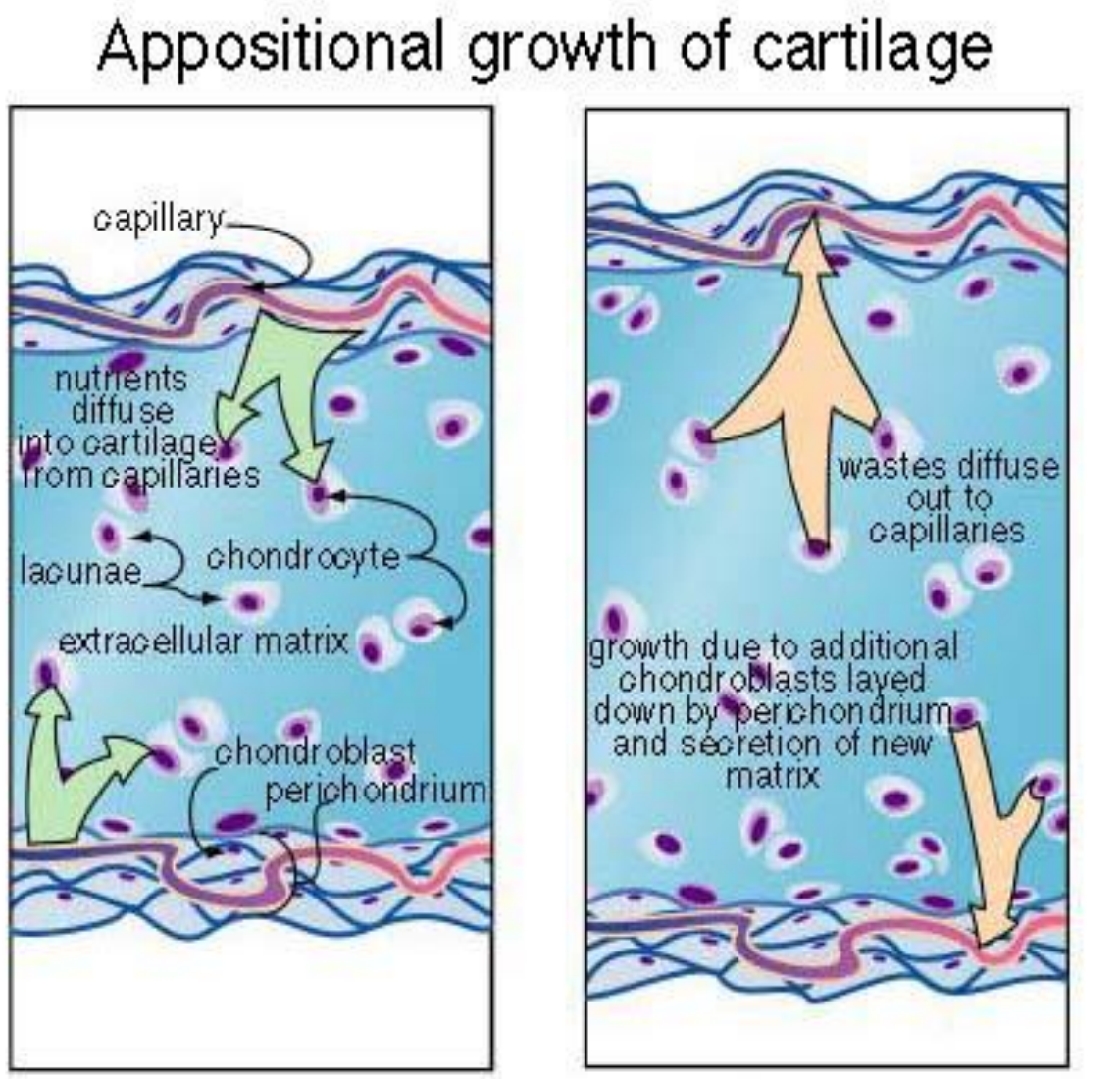
- Appositional growth

- formation of new cartilage on the surface of pre-existing cartilage

❖ Occurs within inner layer of perichondrium

❖ Differentiation of chondroblasts and chondrogenic cells into the chondrocytes

❖ Growth in girth

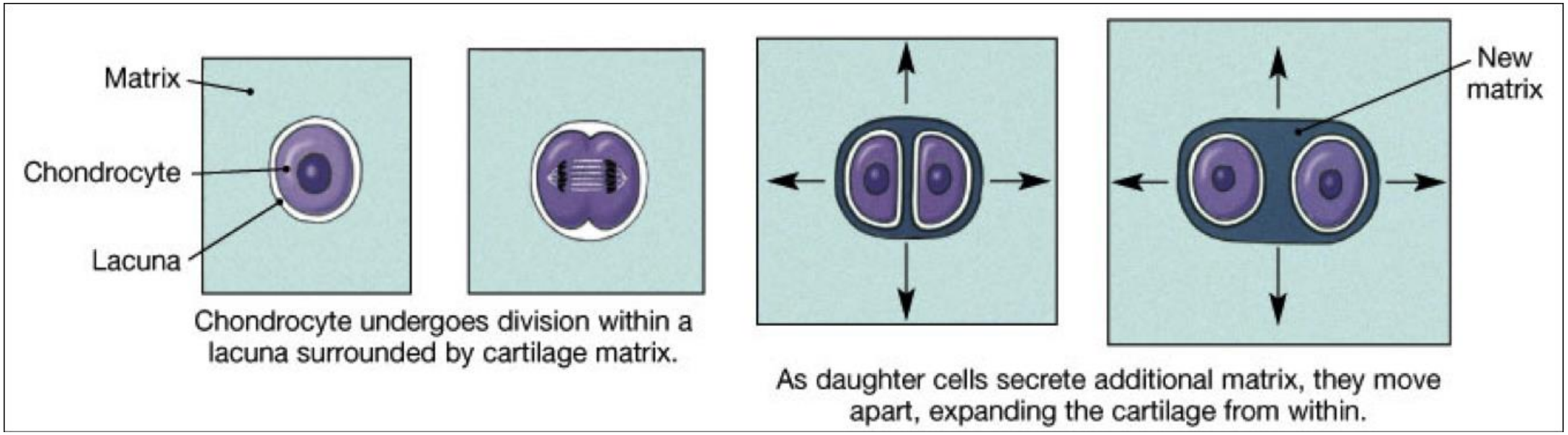


Growth of cartilage

- Interstitial growth

- formation of new cartilage from within cartilage tissue.
- existing chondrocytes divide within lacunae creating isogenous groups

❖ New chondrocytes secrete more matrix

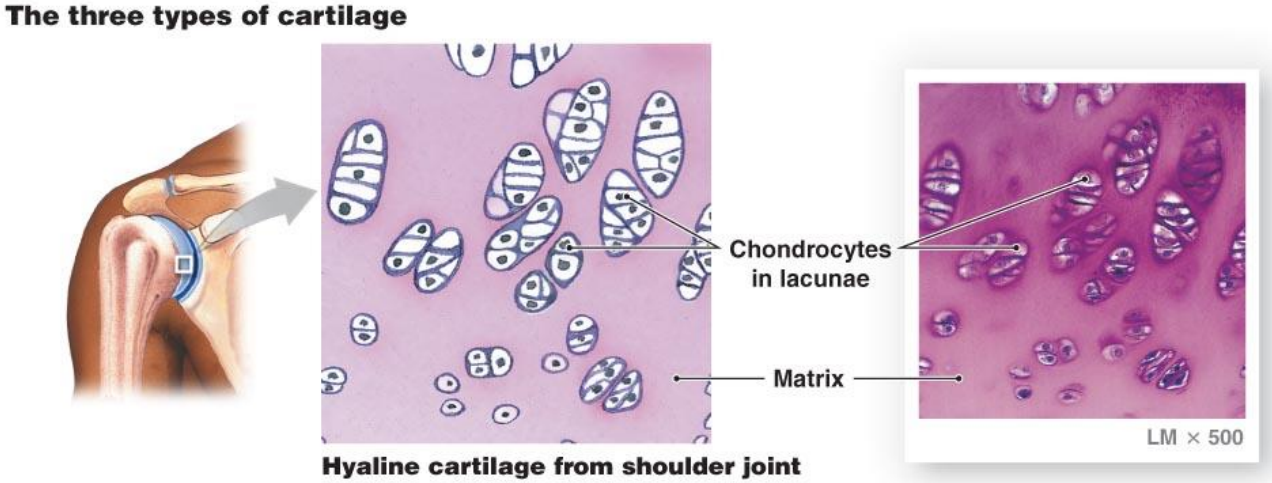


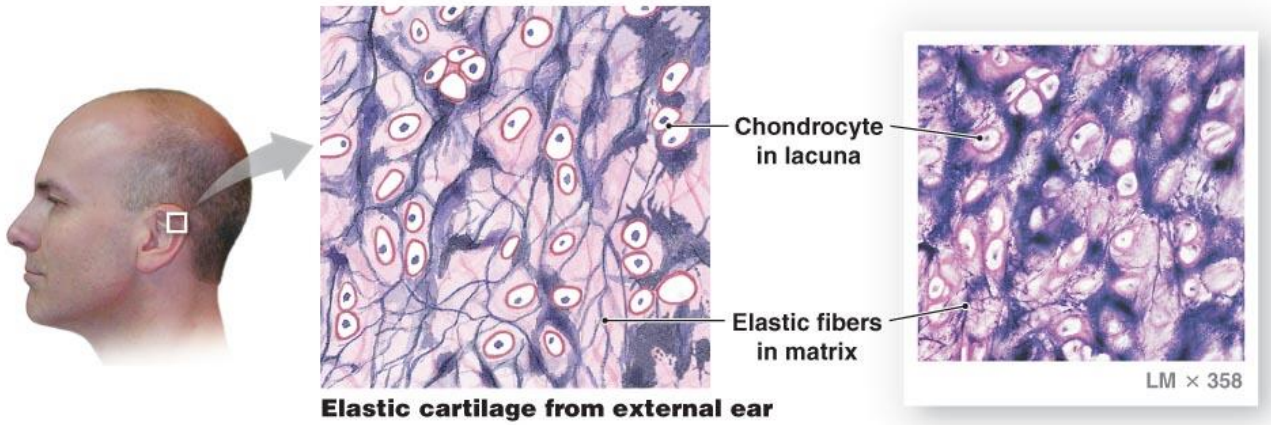
Types of cartilage

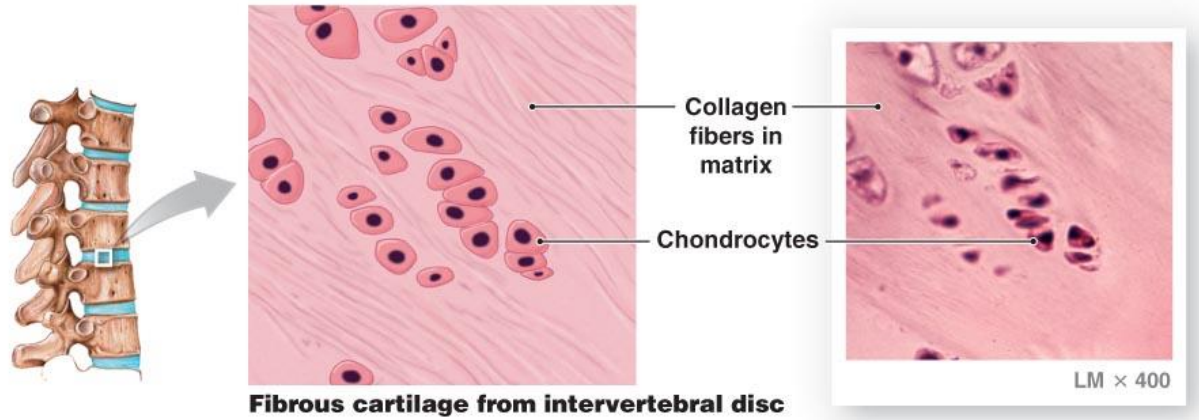
– HYALINE

– ELASTIC

– FIBROCARTILAGE

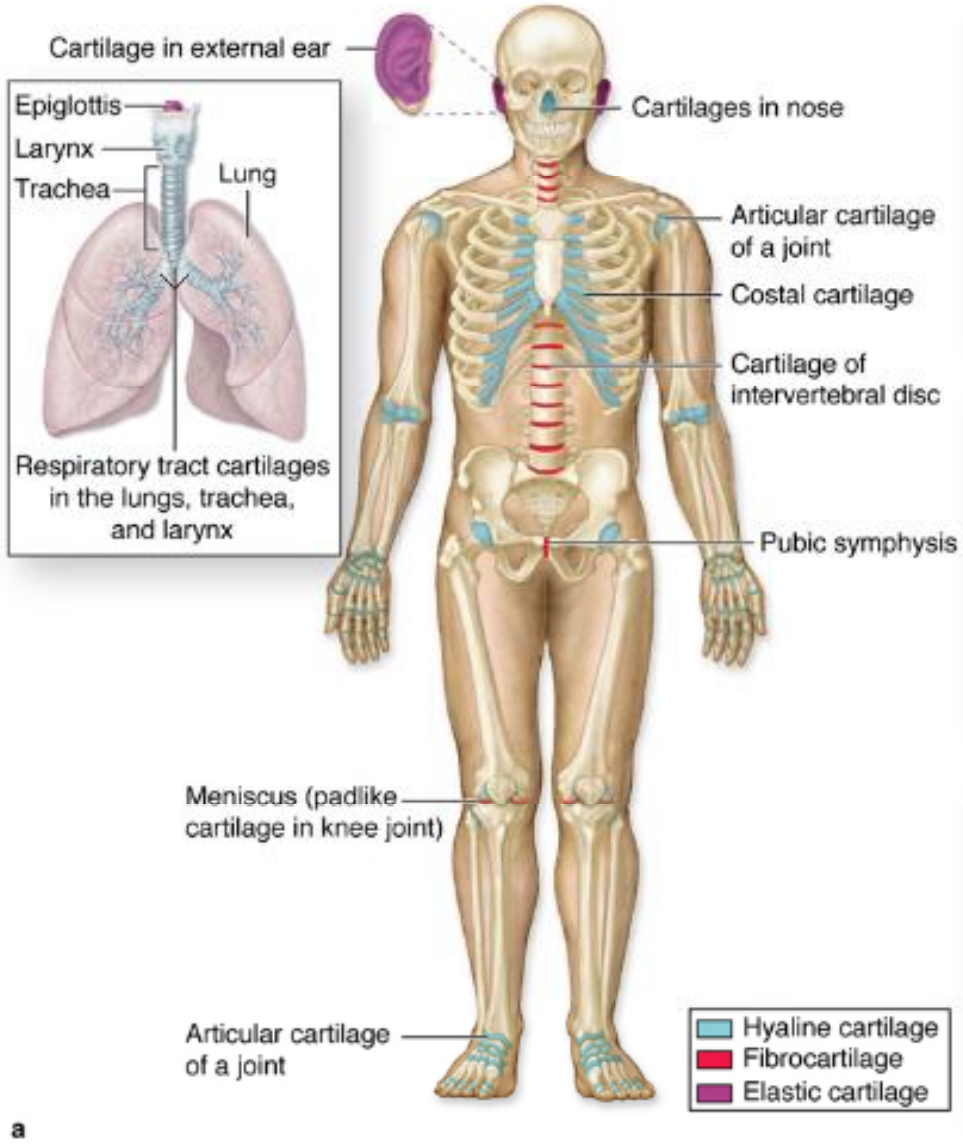






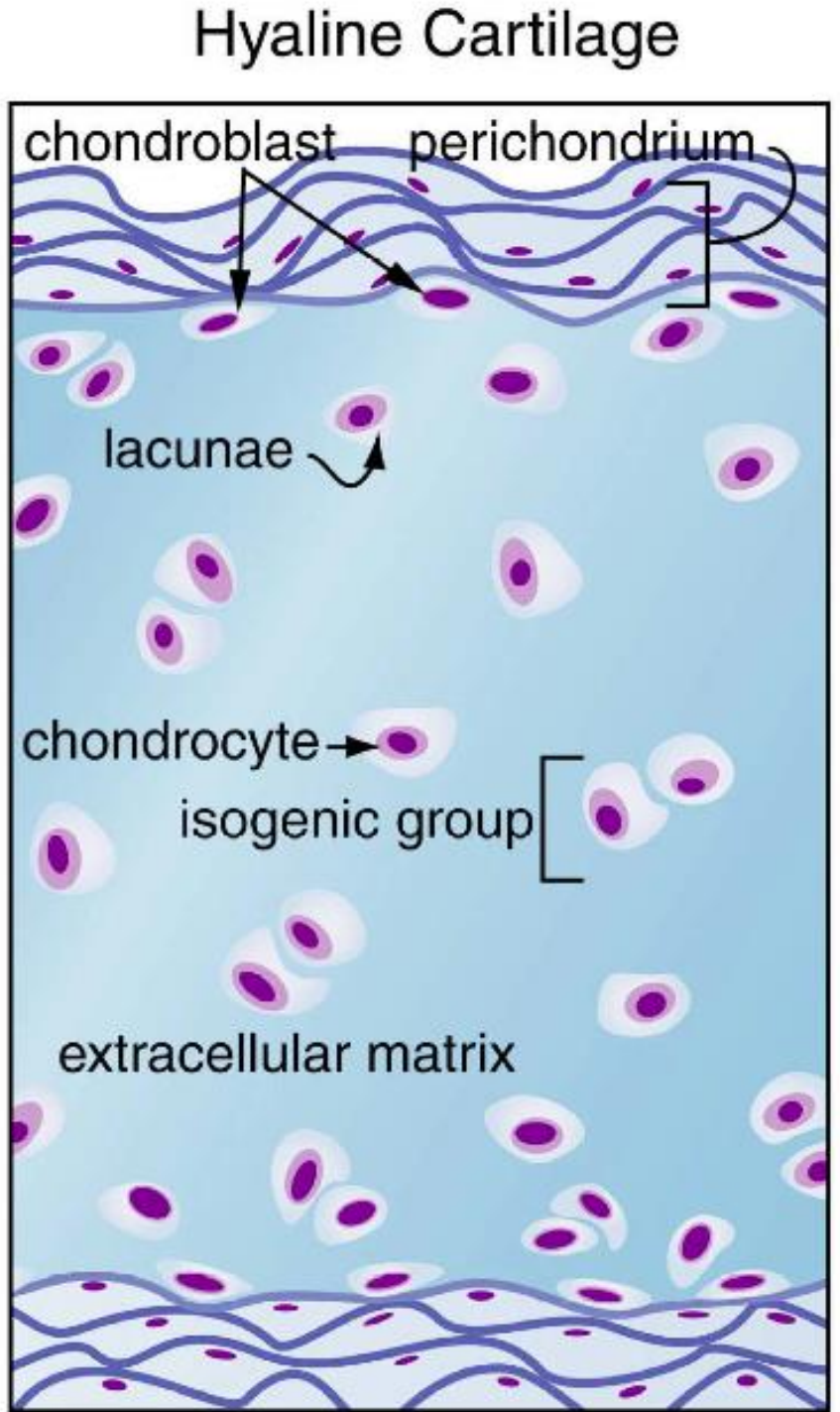
Hyaline cartilage

- The most abundant type of cartilage
- Provides support through resilience
- Found in: fetal skeleton, trachea, most of the laryngeal cartilages, articular cartilage, ends of ribs, external nose, epiphyseal plates

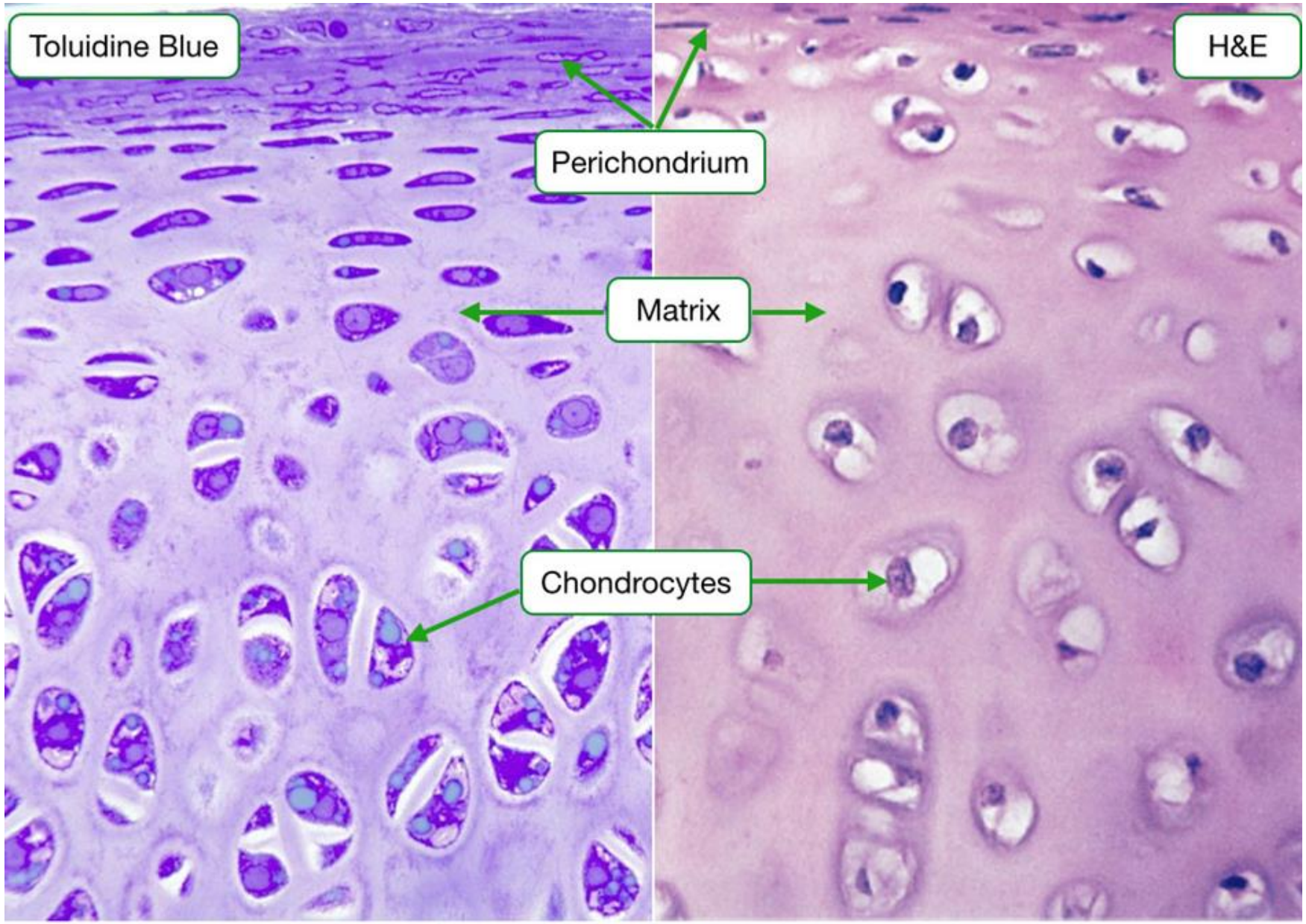


Hyaline cartilage

- Extracellular matrix looks translucent with no clearly visible collagen fibers (glassy appearance). Because of the small size of these fibrils and because they have the same refractive index as ground substance, they are not visible with the LM by conventional staining methods
- Numerous isogenous groups
- Mainly covered by perichondrium (except the articular cartilages!)

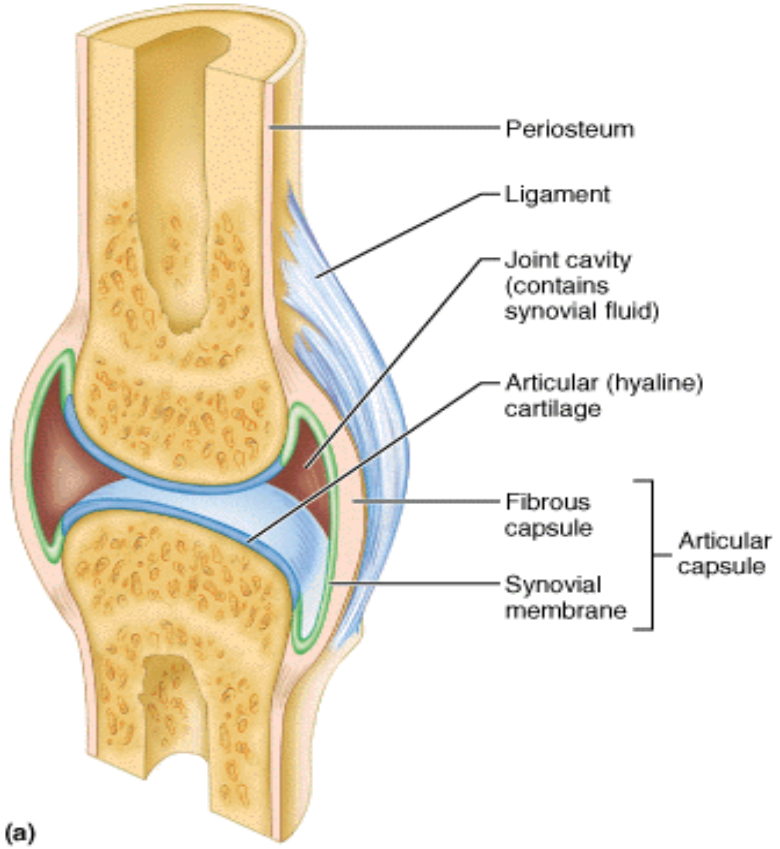


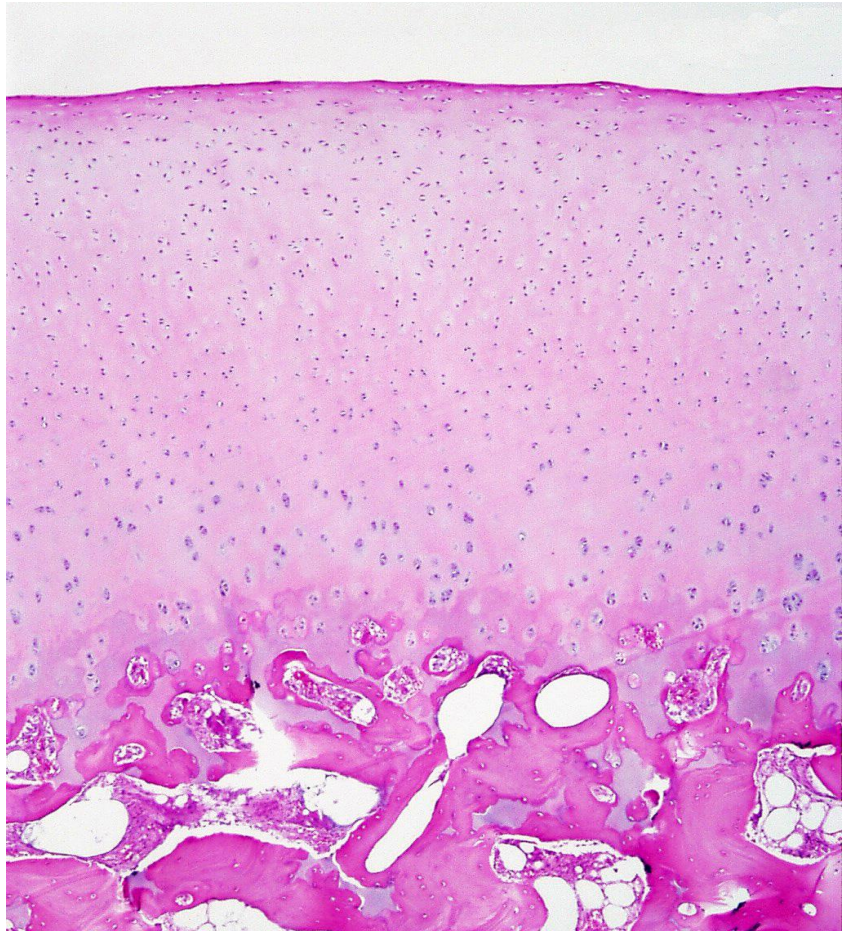
Hyaline cartilage



Articular cartilage (Hyaline cartilage)

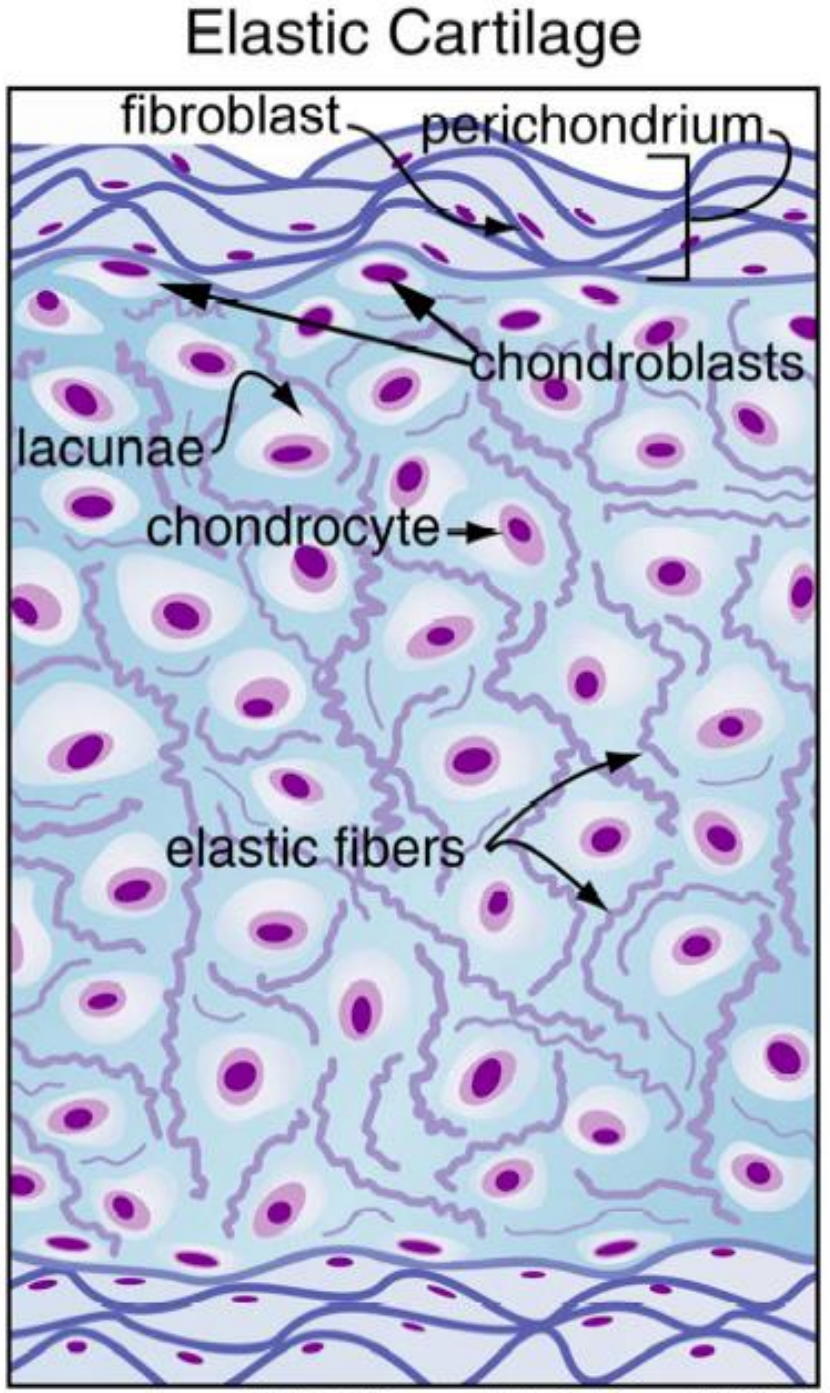
- Lines articular surfaces
- Does not have a perichondrium
- Cartilage calcifies and merges with bone tissue





Elastic cartilage

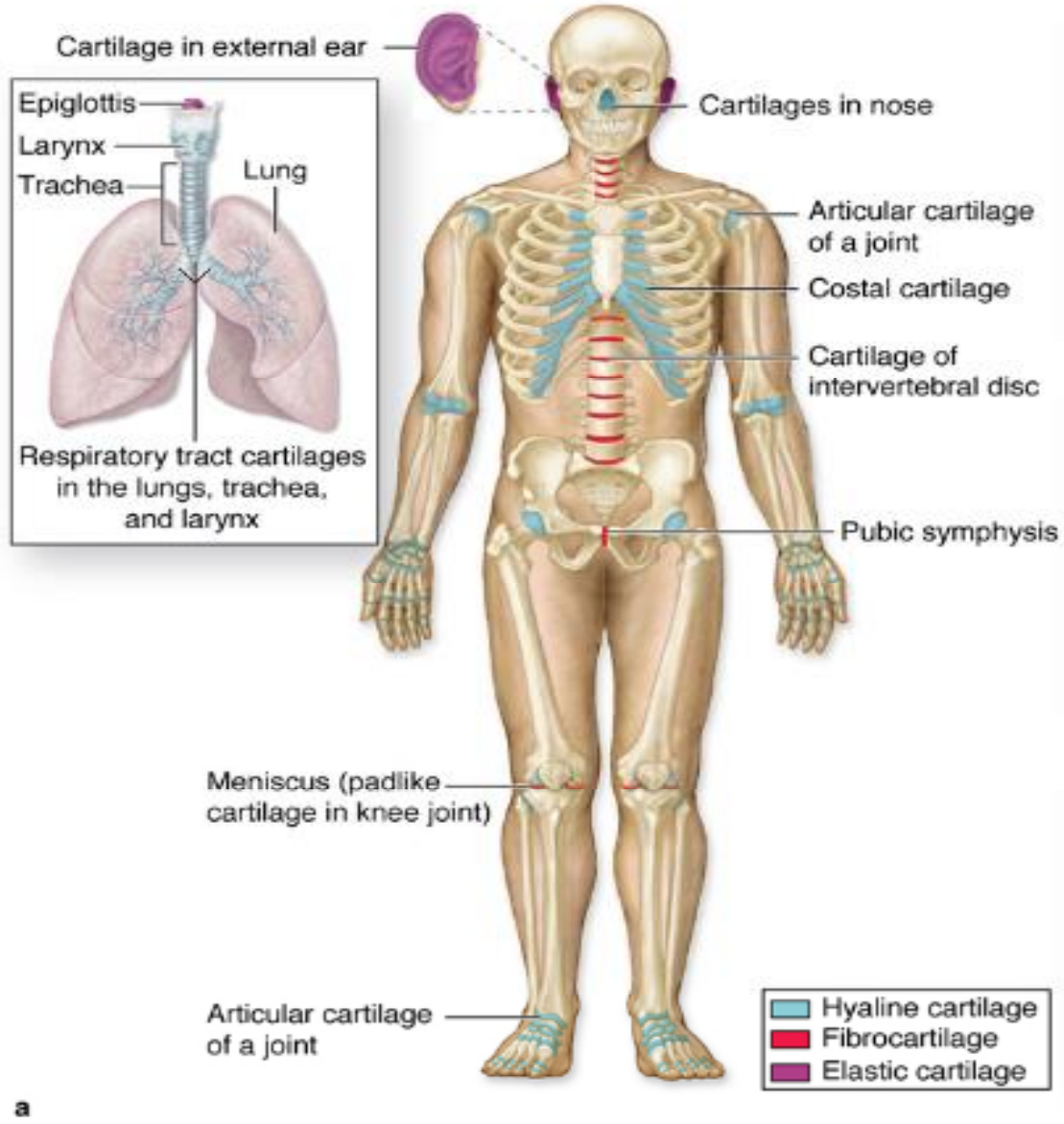
- Dense network of **elastic fibers** in addition to collagen fibers
- More fibers in the center of the cartilage
- Fewer isogenous groups than in hyaline cartilage
- Surrounded by a perichondrium
- Provides **flexible support** and maintains shape



Elastic cartilage

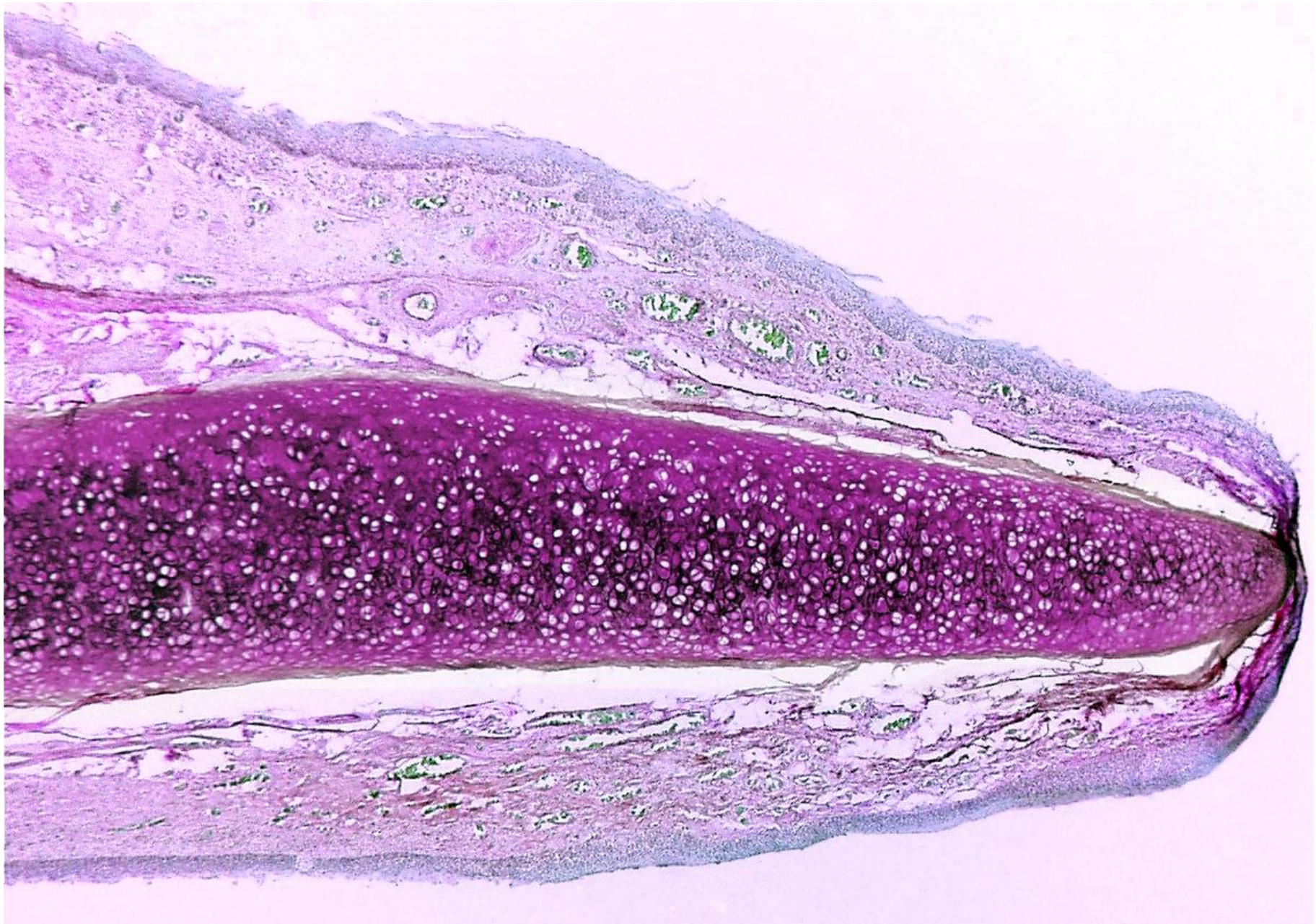
Found in:

- external ear,
- epiglottis,
- corniculate and cuneiform cartilages of the larynx



Elastic fibers stained by Weigert

Elastic cartilage – darker staining matrix



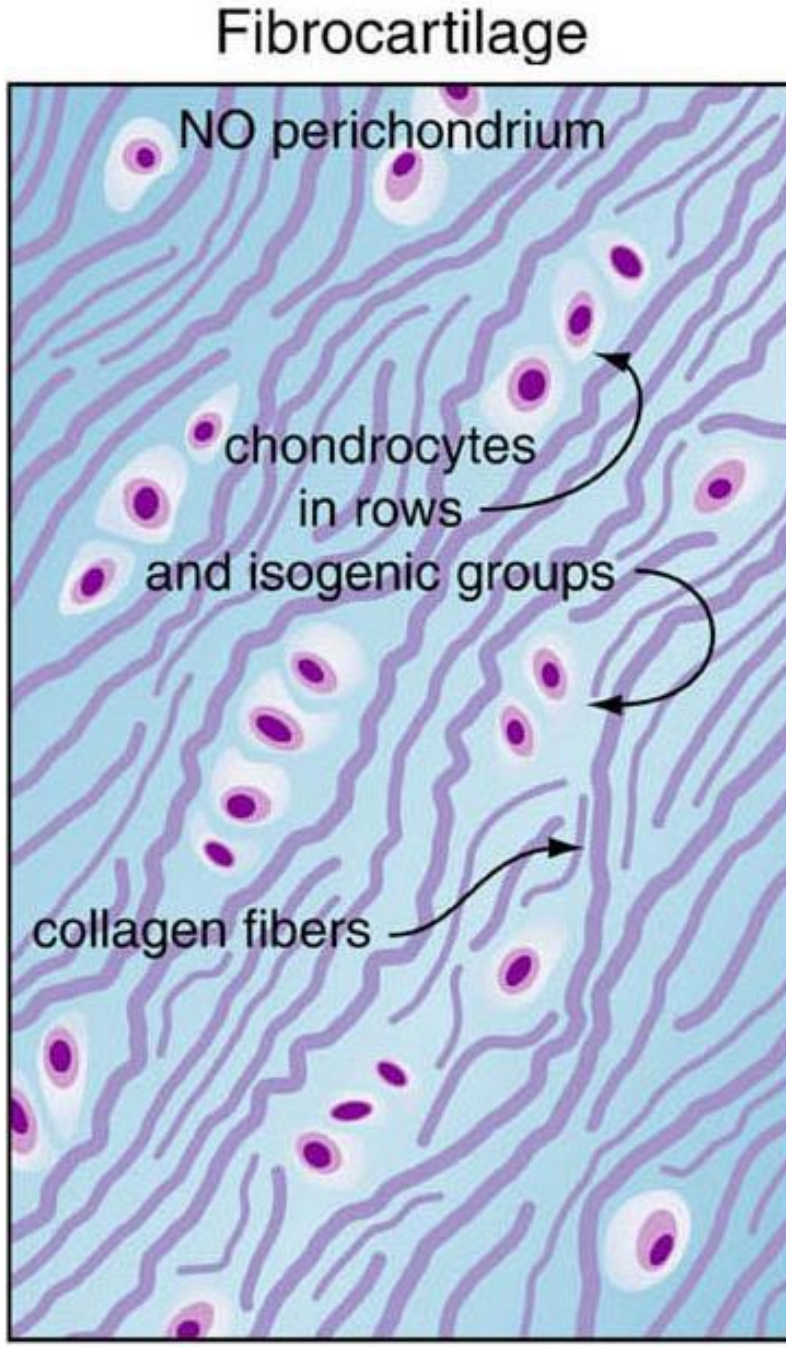
Fibrocartilage

- Is a functional and structural intermediate between hyaline cartilage and dense connective tissue

- Consists of chondrocytes and their matrix material
- Bundles of **type I collagen** in addition of type II
- Has minimal ground substance. The ground substance that is present is usually located immediately around the chondrocytes

- Chondrocytes are dispersed among the collagen fibers singularly, in rows, and in isogenous groups

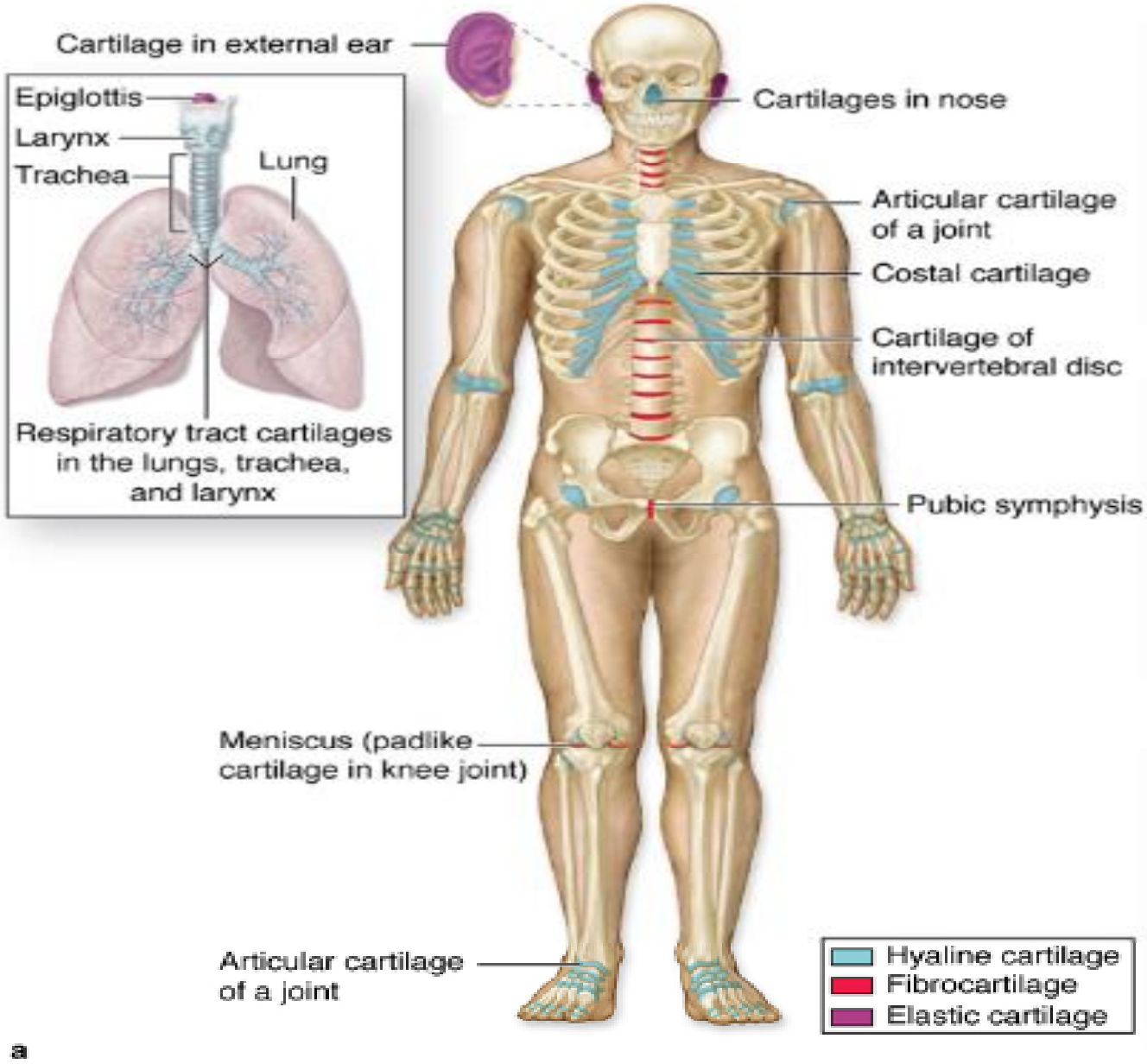
- Gives support and rigidity



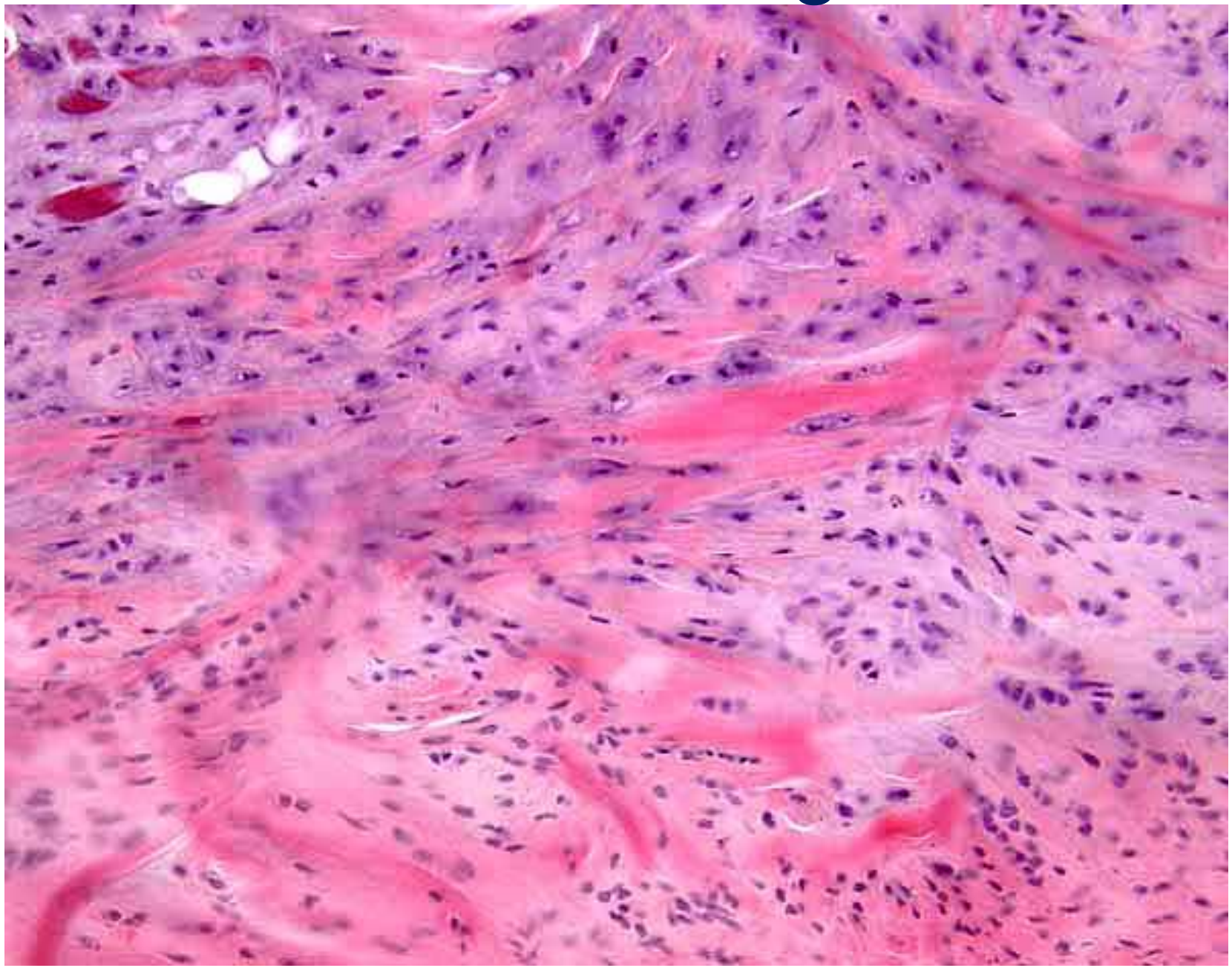
Fibrocartilage

Found in:

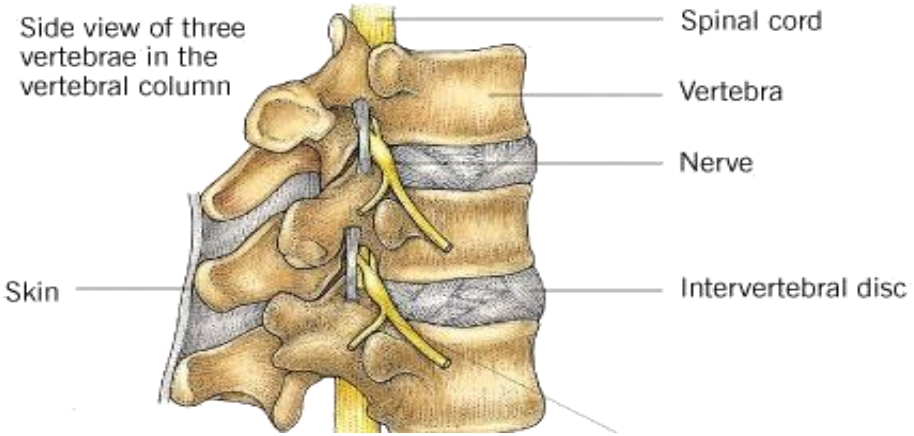
- pubic symphysis,
- annulus fibrosus of the intervertebral disk,
- menisci of the knee joint, some tendons insertions

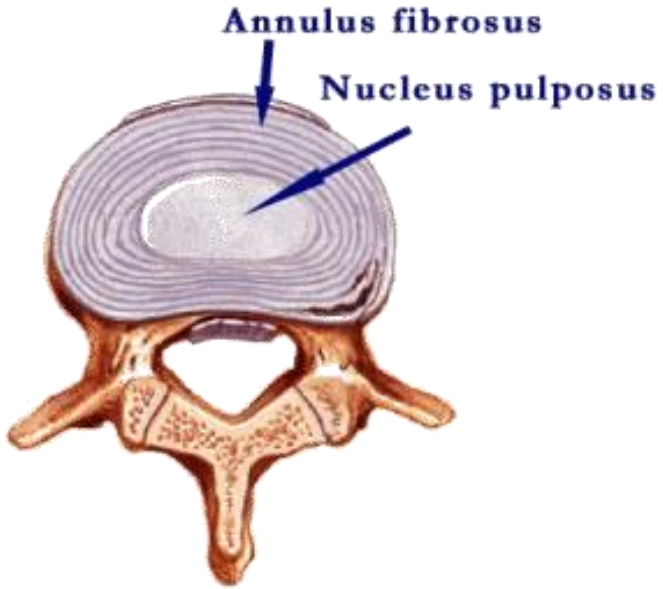


Fibrocartilage

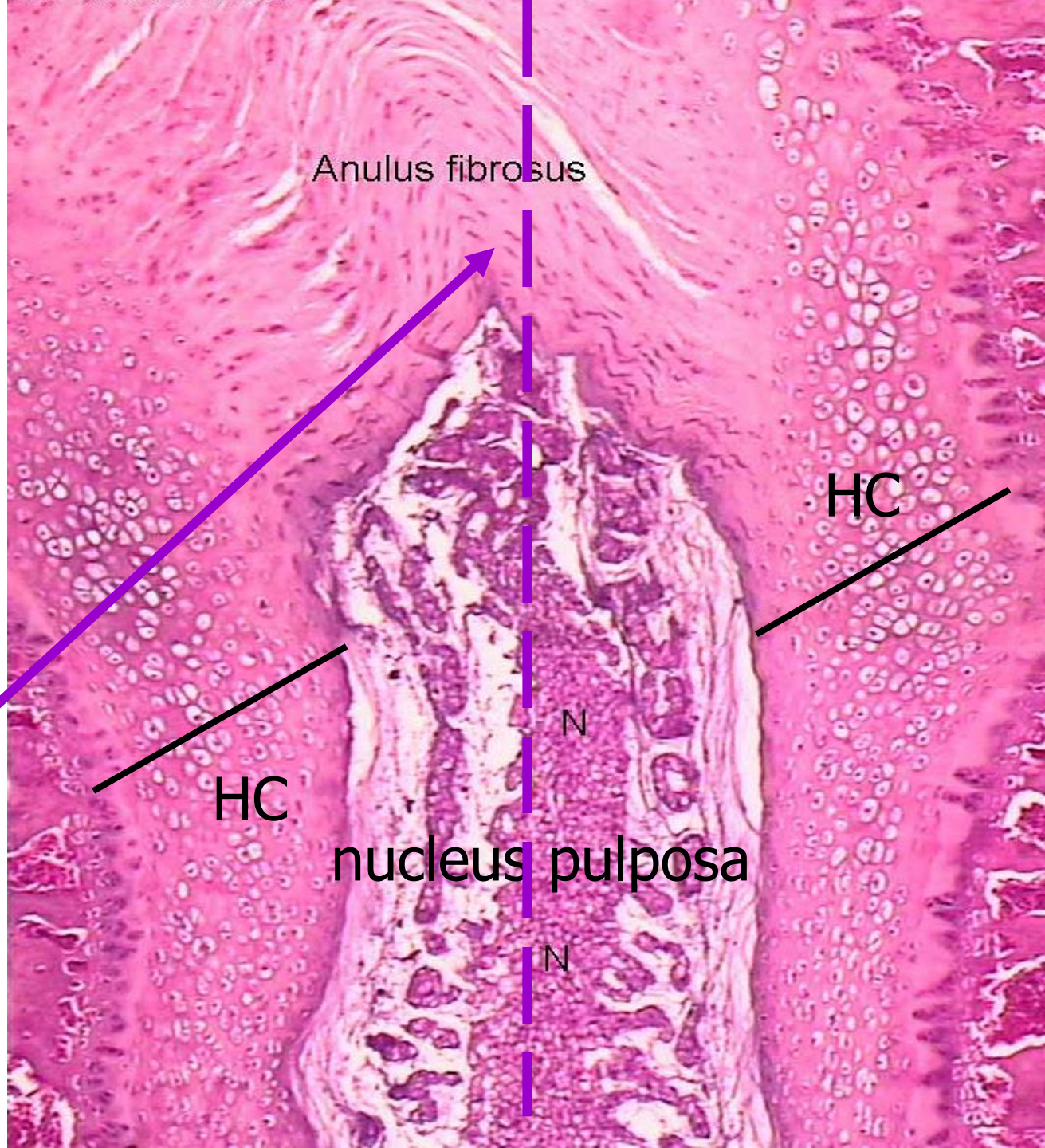


Fibrocartilage
(Intervertebral disc)





- Provides tensile and compressive strength

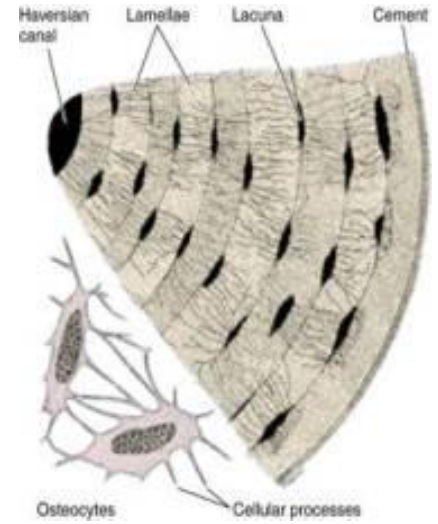


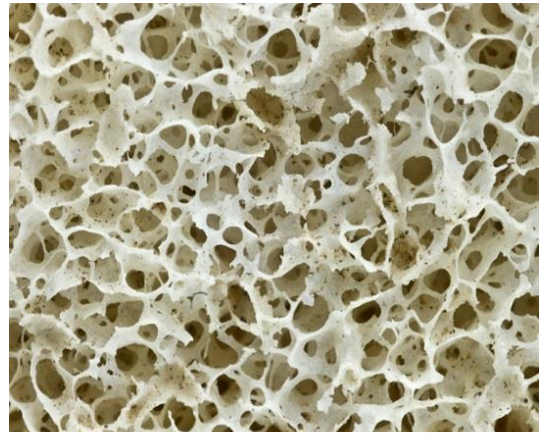
Cartilage

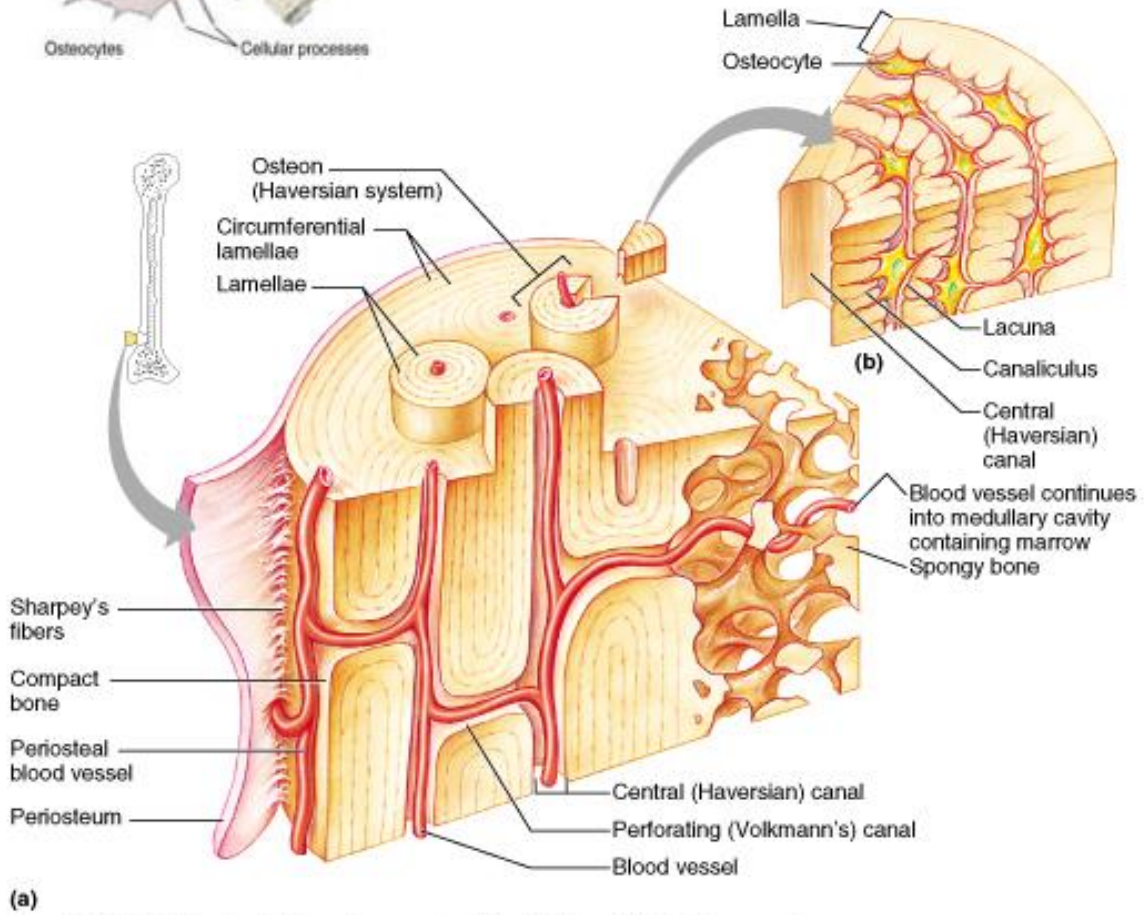
Type	Hyaline	Elastic	Fibro
Location	Fetal skeleton, trachea, most of the laryngeal cartilages, articular cartilage, ends of ribs, external nose, epiphyseal plates	External ear, epiglottis, corniculate and cuneiform cartilages of the larynx	Pubic symphysis, intervertebral disk, menisci of the knee joint, some tendons insertions
Function	Cushioning, lubricant, structural support, bone development and repair	Flexible structural support	Structural stability under stress
Perichondrium	Yes Not in articular cartilage and growth plate	Yes	No
Undergoes calcification?	Yes	No	Normally not, but may calcify during repair
Cell types	Chondroblasts, chondrocytes	Chondroblasts, chondrocytes	Chondrocytes, fibroblasts
ECM	Collagen 2 (and 6, 9, 10, 11), aggrecan	Collagen 2 and elastic fibers, aggrecan	Collagen 2 and Collagen1

Bone tissue

- Second to cartilage in ability to withstand compression and second to enamel in hardness
- Consists of **extracellular matrix** and **cells**
- Covered by **periosteum** from the outside
- Covered by **endosteum** from the inside







Functions of bone

- Major **support** of the body
- **Protection** for internal organs
- **Attachment** for muscle tendons, creating lever systems for body movement
- Harbors hematopoietic organs (**red bone marrow**)
- **Storage** for calcium and other essential minerals

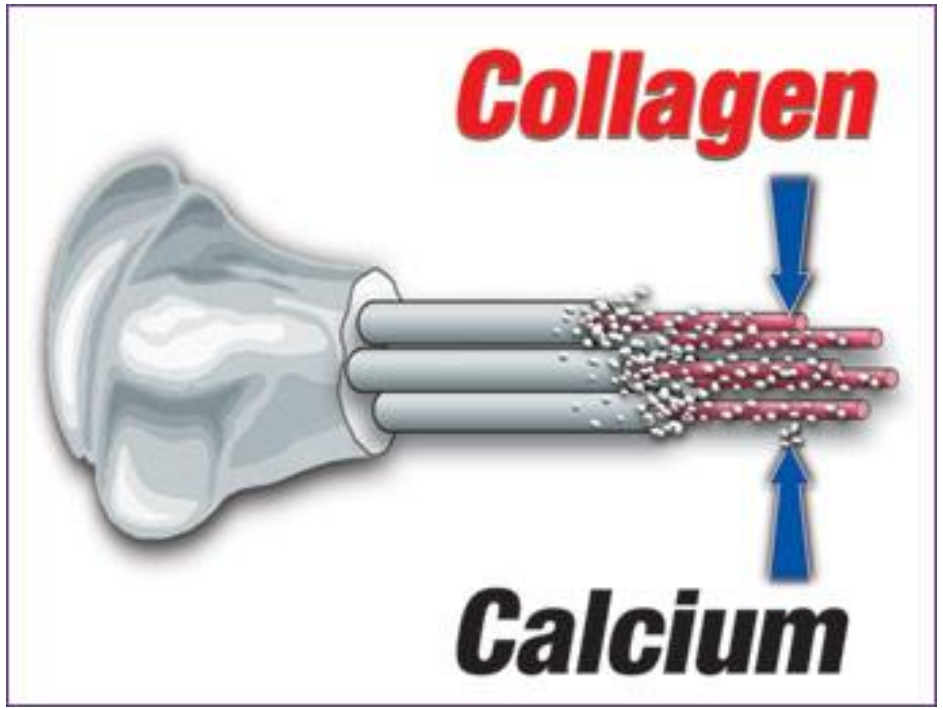
Bone matrix

- Organic part –

  50% of volume (25 % of weight)

- Inorganic part –

  50% of volume (75% of weight)

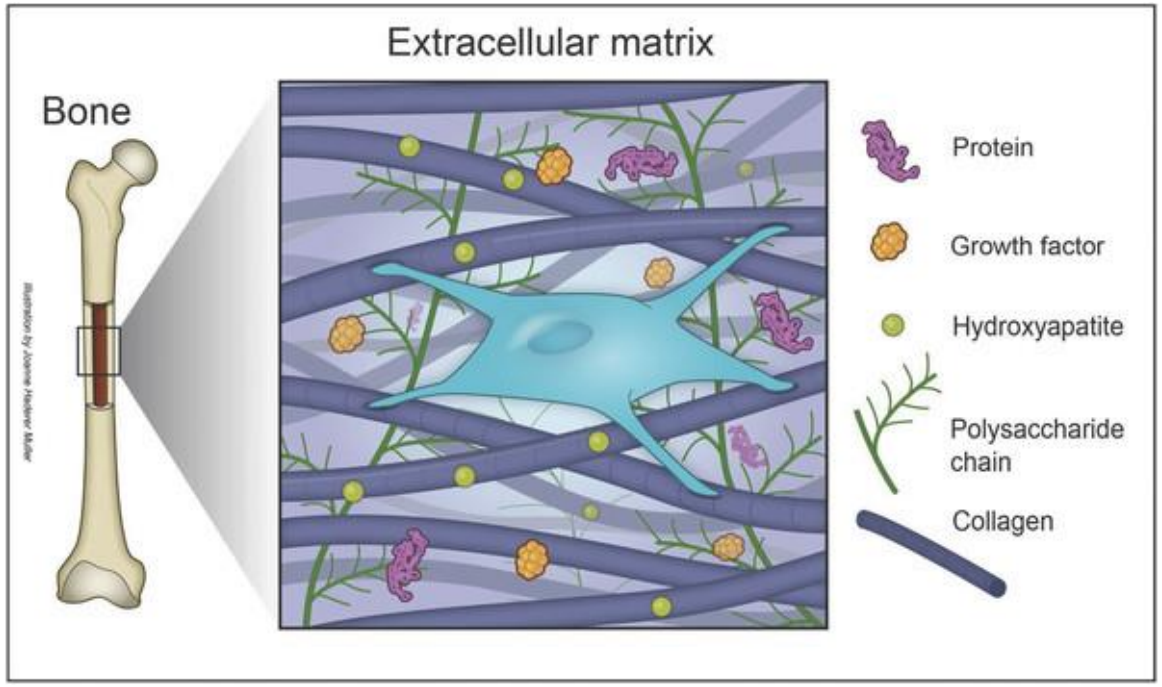


Organic portion (osteoid)

- Synthesized by osteoblasts

– Fibers: **Collagen type I** (90-95%)

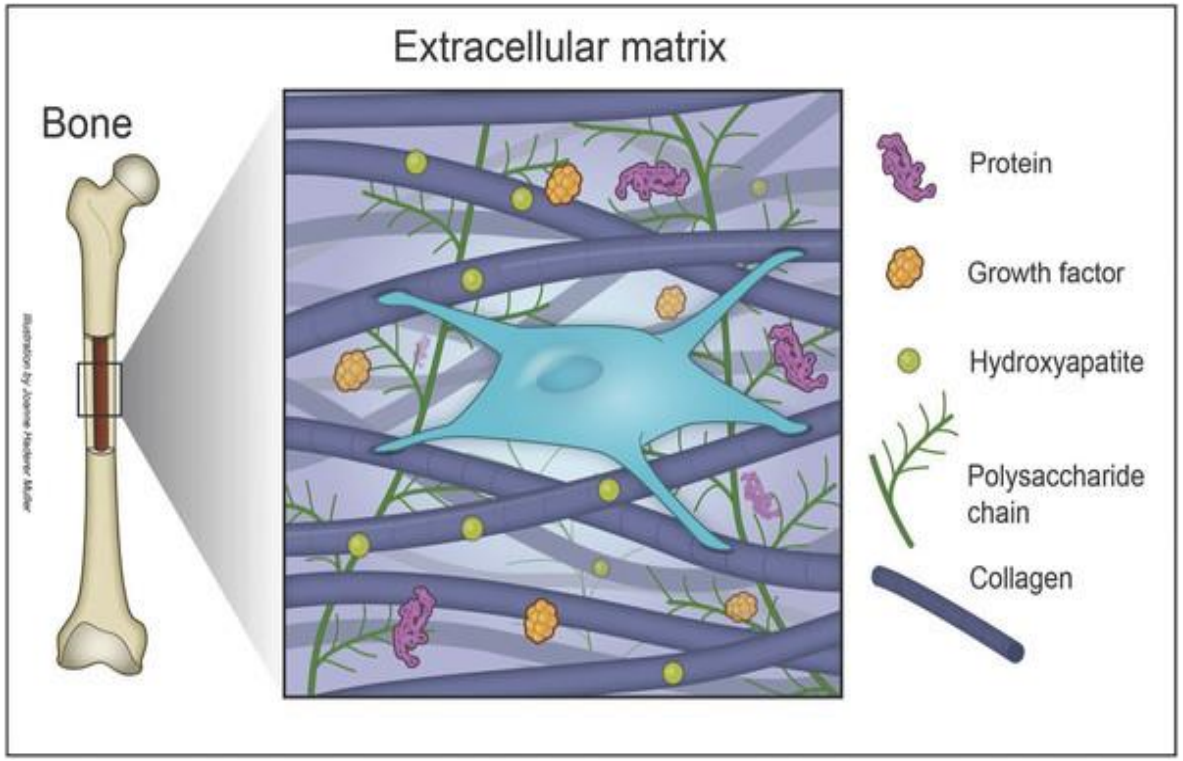
– Ground substance is minimal: **glycosaminoglycans** such as chondroitin sulfate, keratan sulfate, and some **glycoproteins** that bind calcium



Inorganic portion

- **Calcium** and **phosphate**, in the form of **hydroxyapatite crystals**, which make junctions with collagen

- Some bicarbonate, potassium, magnesium and citrate



Bone matrix

- It is like reinforced concrete where steel bars are collagen fibers and cement is hydroxyapatite

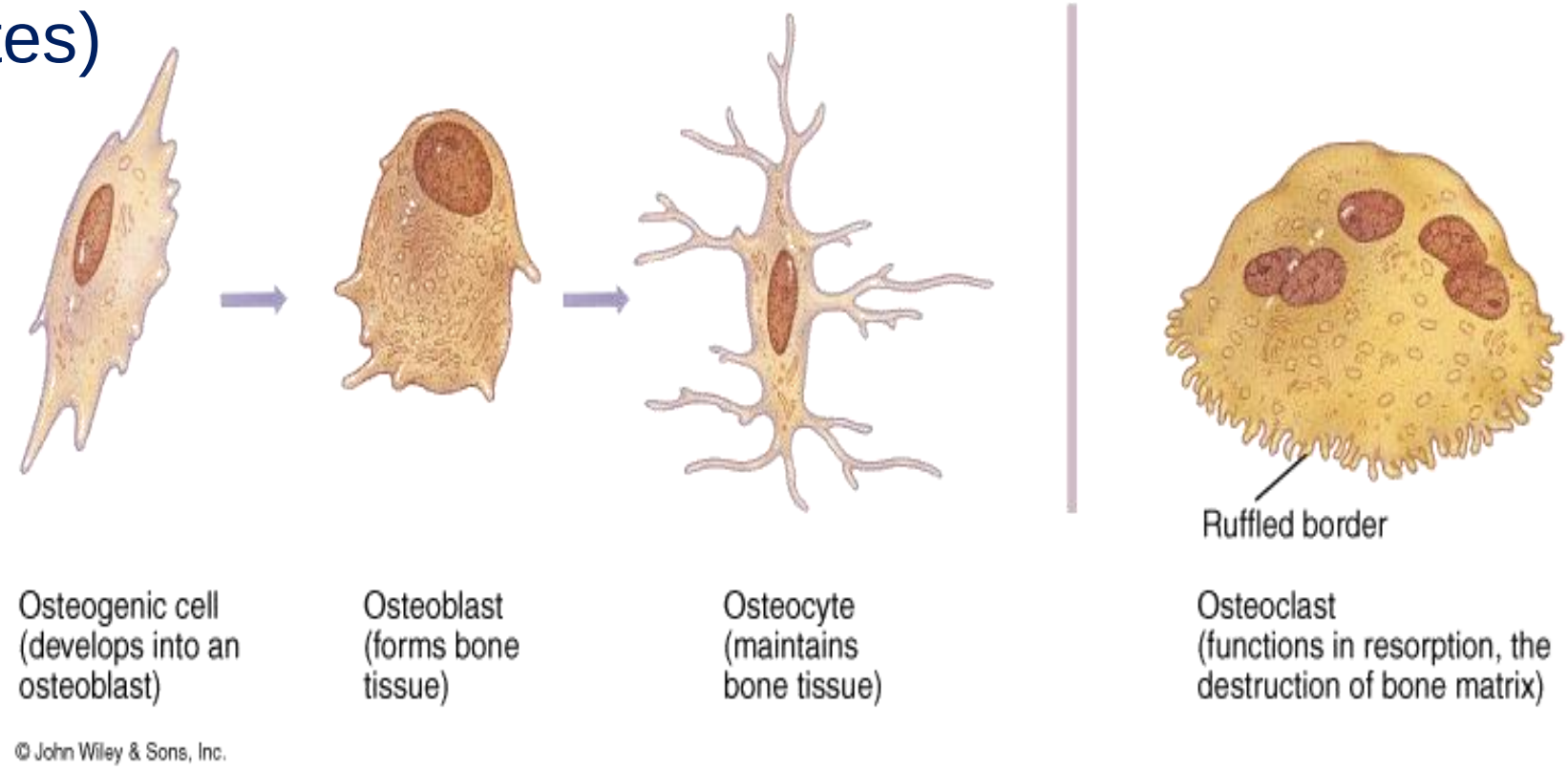
- Thus, it is responsible for major functional characteristic of the bone

- If the mineral is removed, bone is too flexible

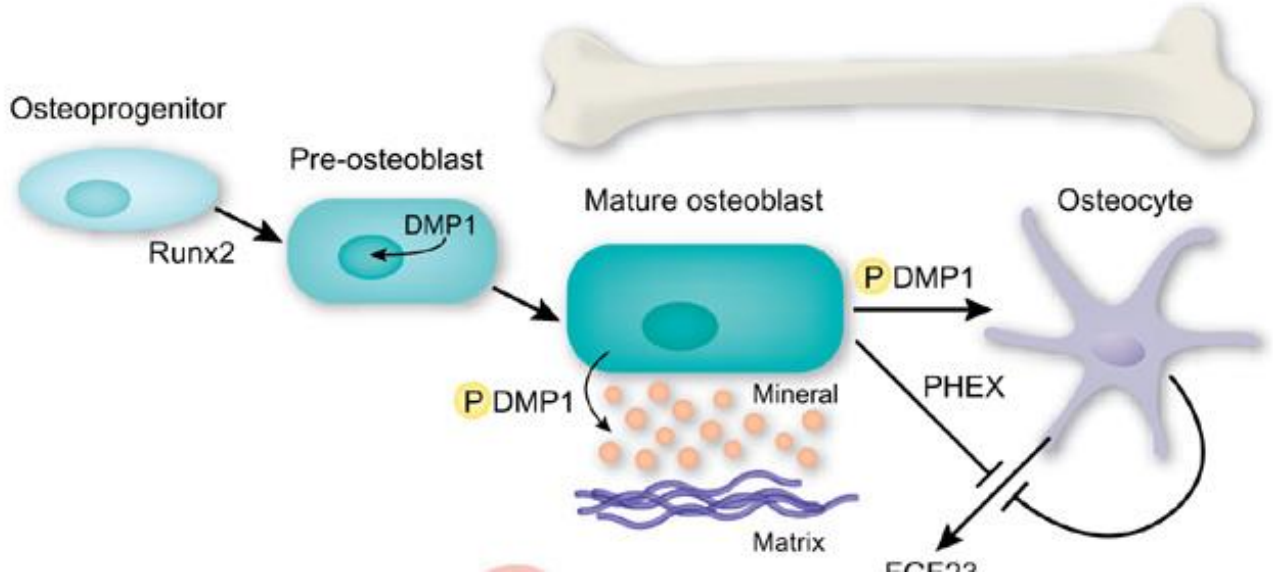
- If the collagen is removed, bone is too fragile

Bone Cells

- Osteoprogenitor cells (bone stem cells)
- Osteoblasts (matrix synthesis)
- Osteocytes (maintain matrix)
- Osteoclasts – bone macrophages, bone resorbtion (develop from blood monocytes)

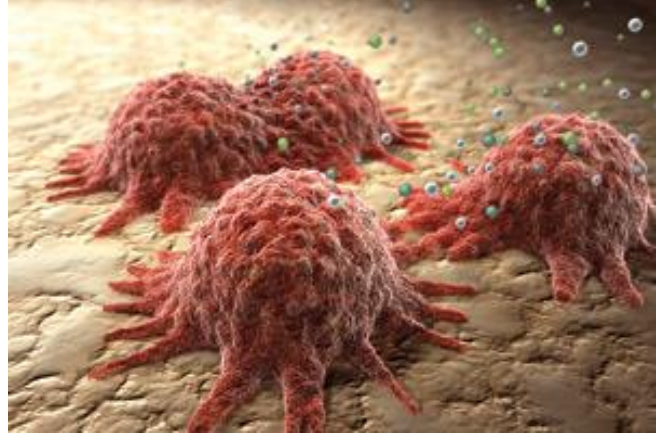


Osteoprogenitor cells



- Develop from undifferentiated mesenchyme cells
- Lay in the inner layer of periosteum
- **Function** – stem cells, they are osteoblasts precursors

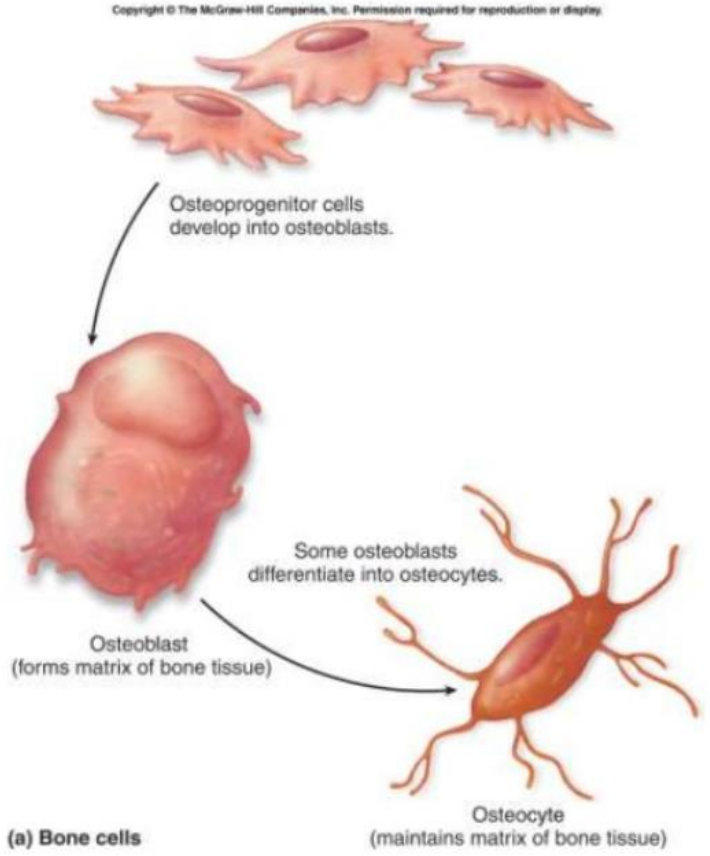
Osteoblasts

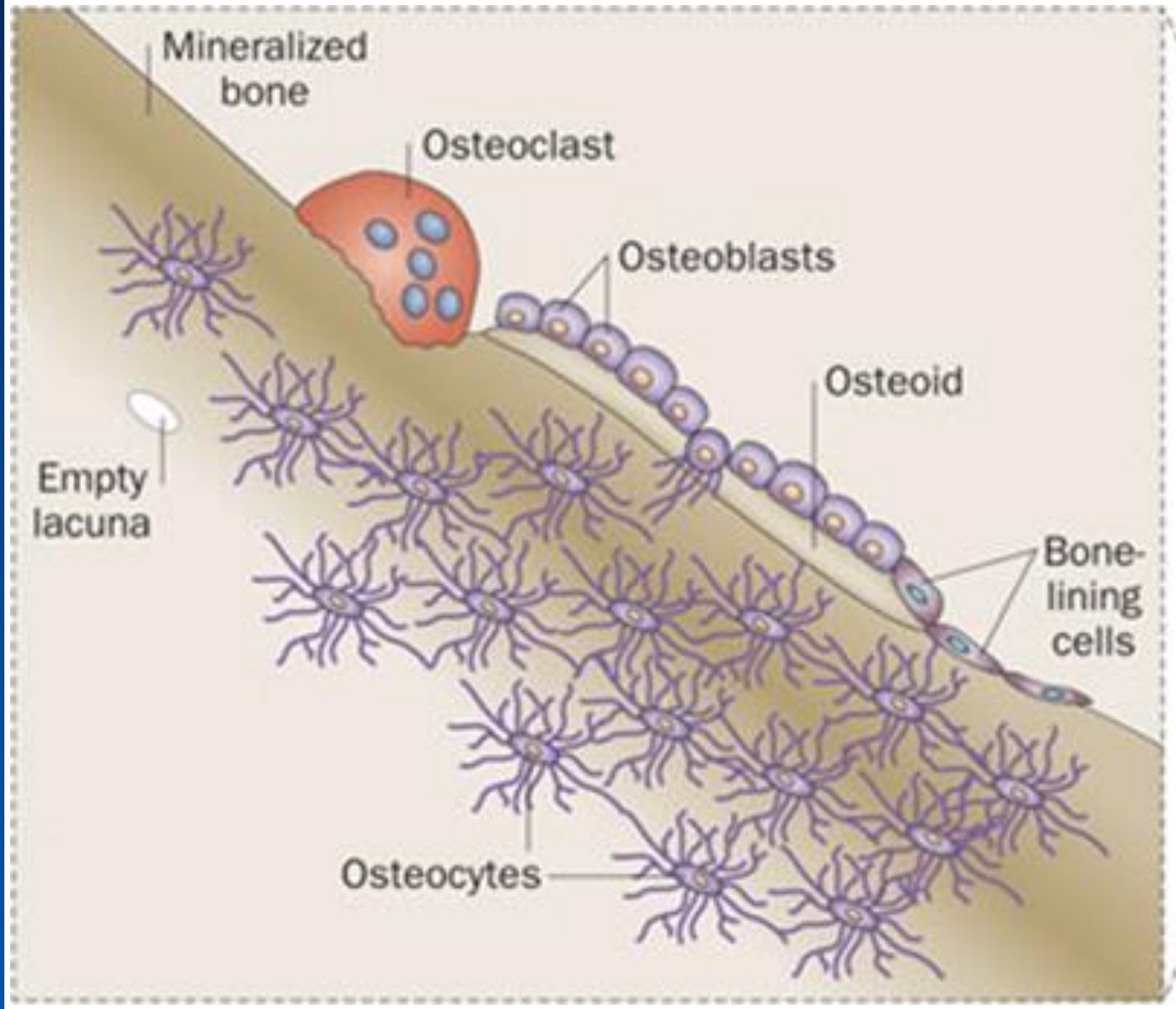


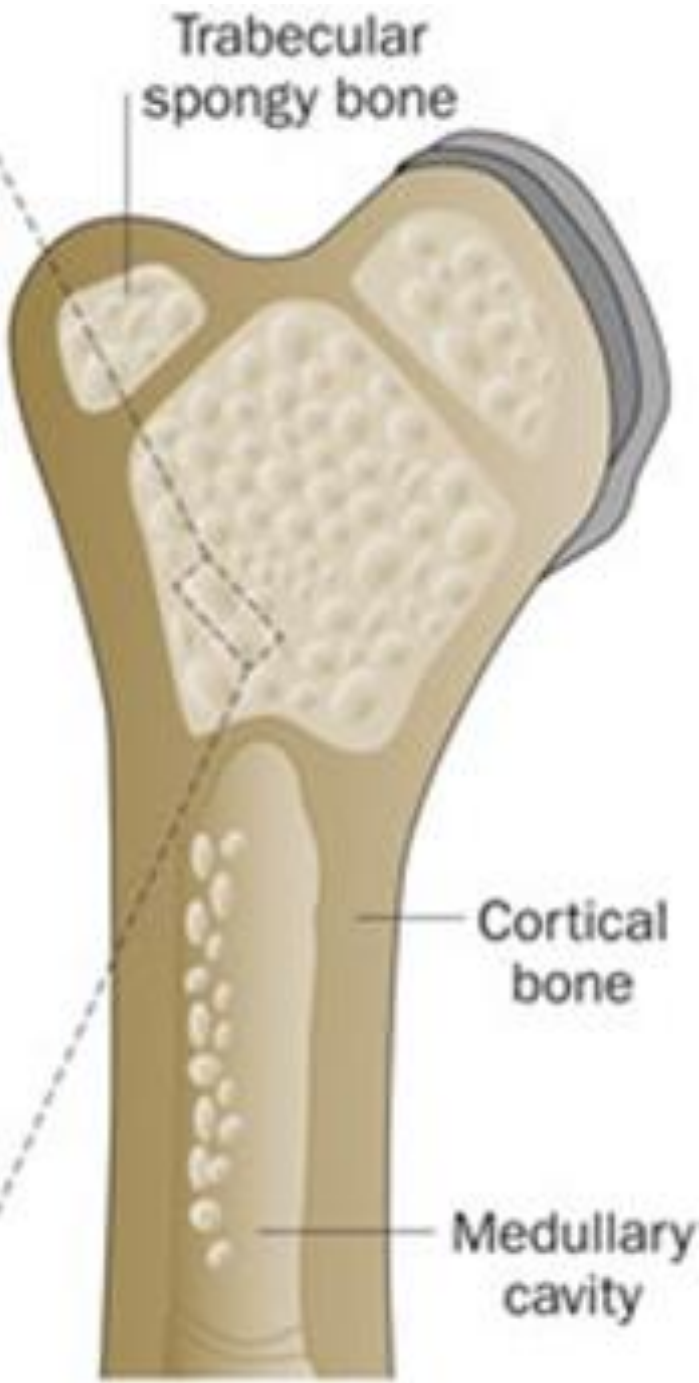
- Differentiate from osteoprogenitor cells
- Are on the surface of the bone and around blood vessels
- **Function** – bone matrix synthesis.

Secrete osteoid first. In the presence of alkaline phosphatase, osteoblasts facilitate the deposition of calcium phosphate, thus mineralizing the osteoid

- Once surrounded with secreted matrix, it is referred to as an osteocyte

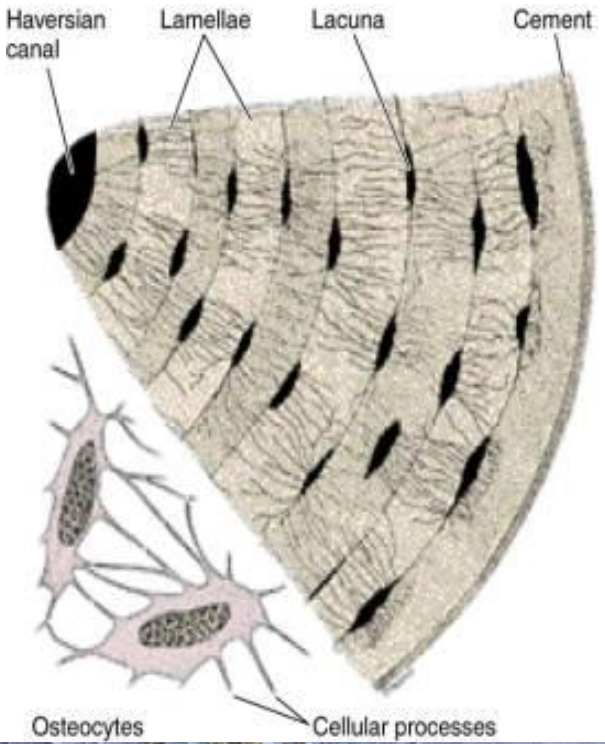


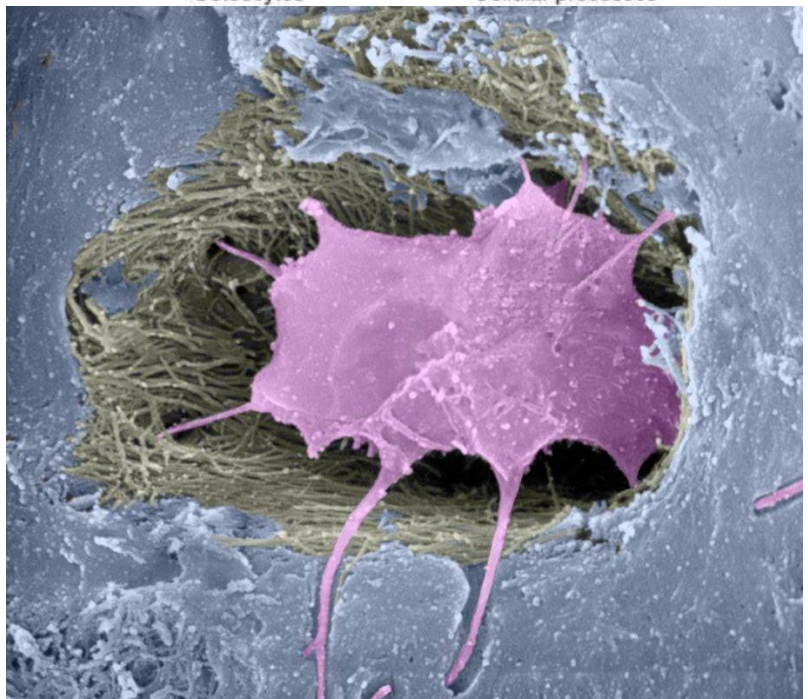

Mineralized bone
Osteoclast
Osteoblasts
Osteoid
Empty lacuna
Bone-lining cells
Osteocytes


Trabecular spongy bone
Cortical bone
Medullary cavity

Osteocytes

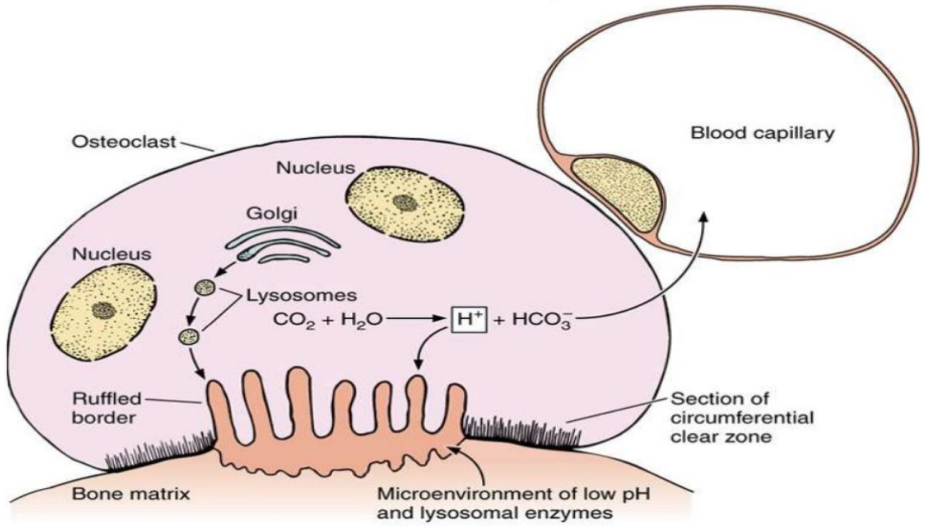
- Differentiate from osteoblasts
- Inactive cells lie in **lacunae** in the bone
- Extend long processes from the cell body– **philopodia** by means of which cells contact via gap junctions to exchange nutrients
- Cells lay in the lacunae, processes – in the canaliculi
- **Function** – bone matrix maintaining





Osteoclasts

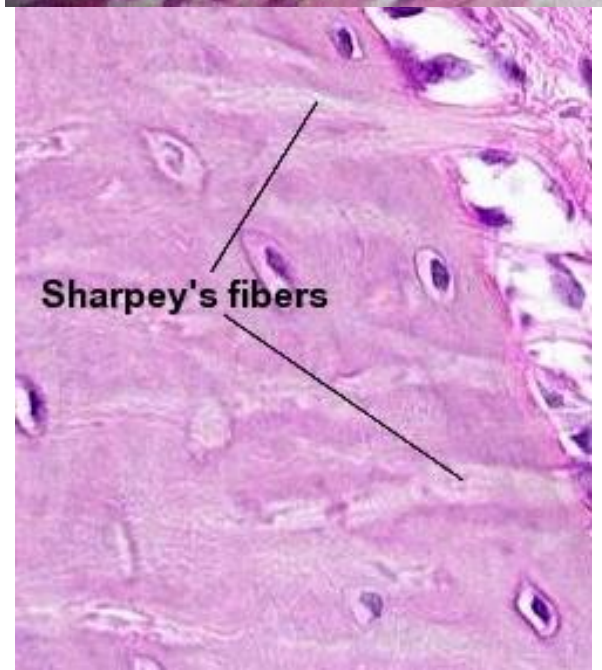
- Large multinucleated cells
- Lay in the Howship's lacunae
- **Ruffled border –** plasma-membrane infoldings on the side facing the matrix, forming many compartments where enzymes are released
- **Function** – bone matrix resorption

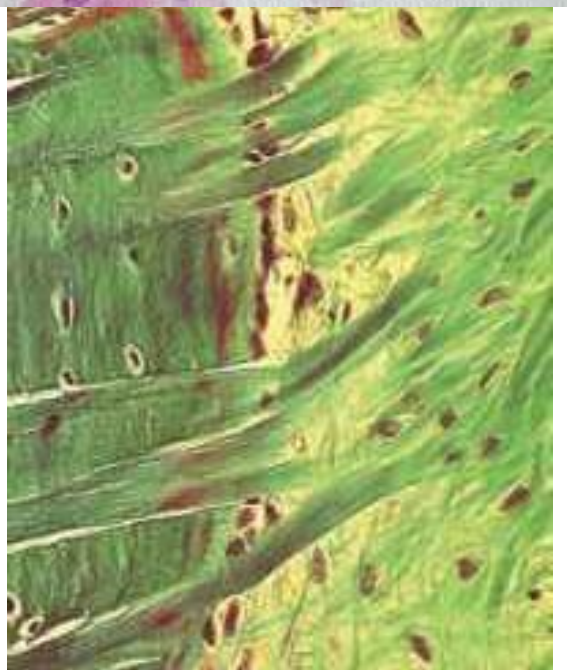


PERIOSTEUM

- 2 layers:
  - **Fibrous layer.** Outer layer of dense connective tissue that serves as a reserve-cell source for the osteogenic layer
  - **Osteogenic layer.** Inner, more cellular layer, contains osteoblasts, osteoclasts and osteoprogenitor cells. Site of bone deposition and resorption, respectively

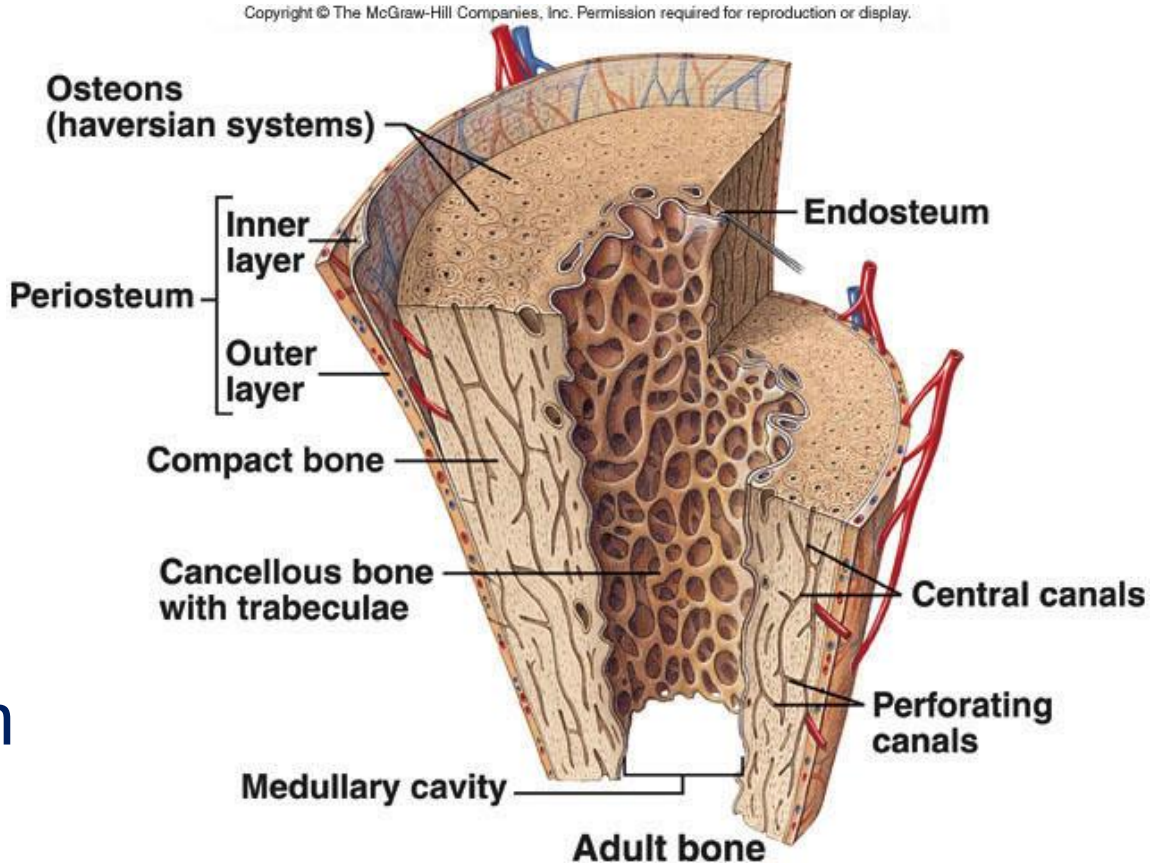
  Sharpey's fibers – collagen fibers that anchor periosteum to the bone
- **Functions**: nutrition, growth of bone in girth, repair





ENDOSTEUM

- Lines all interior surfaces of bone except for lacunae and canaliculi
- Structure resembles the inner layer of periosteum
- Contains bone and blood cell precursor
- Serves as a means of bone growth and/or resorption



Types of bones

I. MICROSCOPIC APPEARANCE OF BONE (RELATED TO THE AGE OF A BONE)

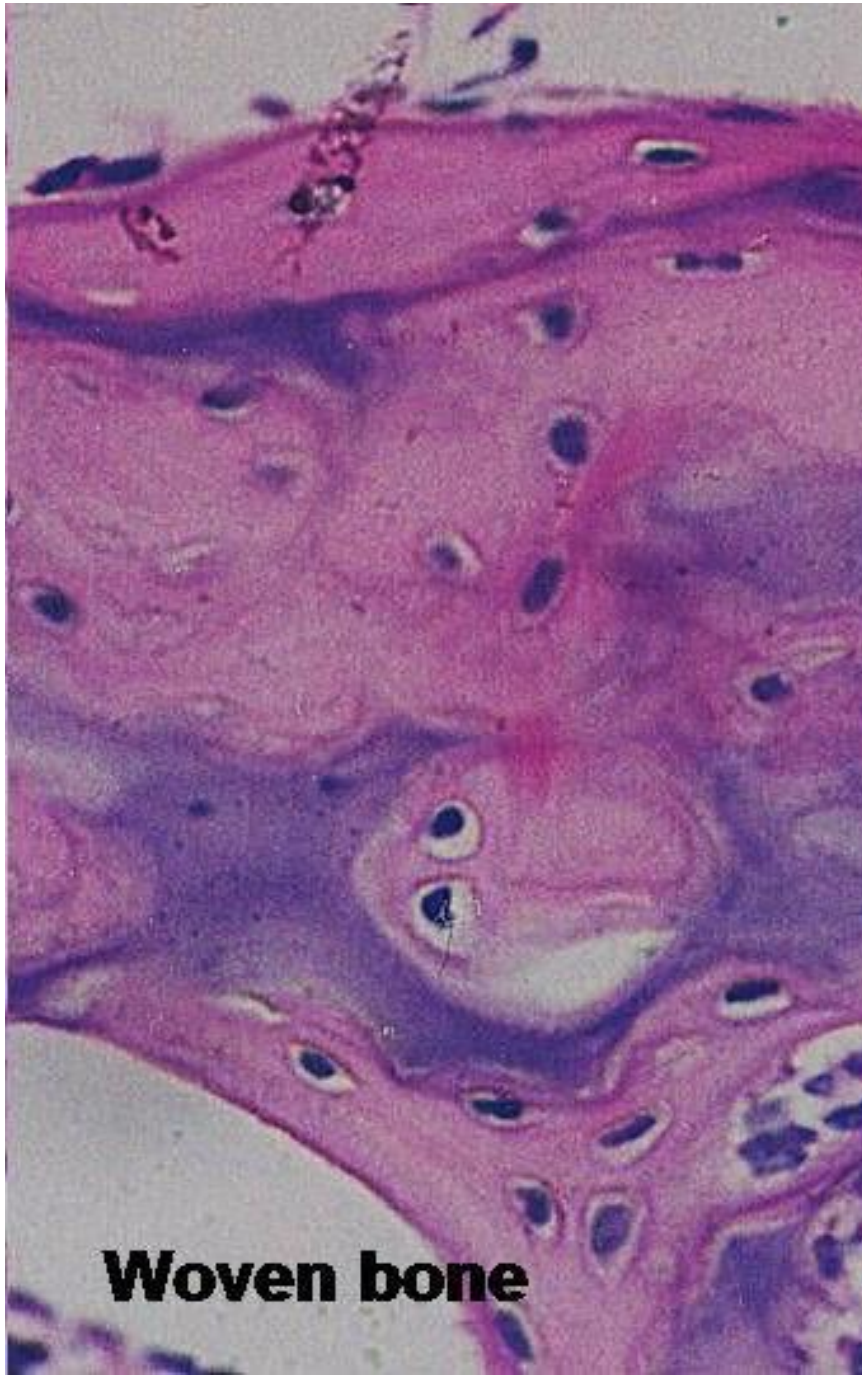
- Primary (woven) bone
- Secondary (lamellar) bone

II. GROSS APPEARANCE OF BONE, MACROSCOPIC STRUCTURE

- Spongy bone
- Compact bone

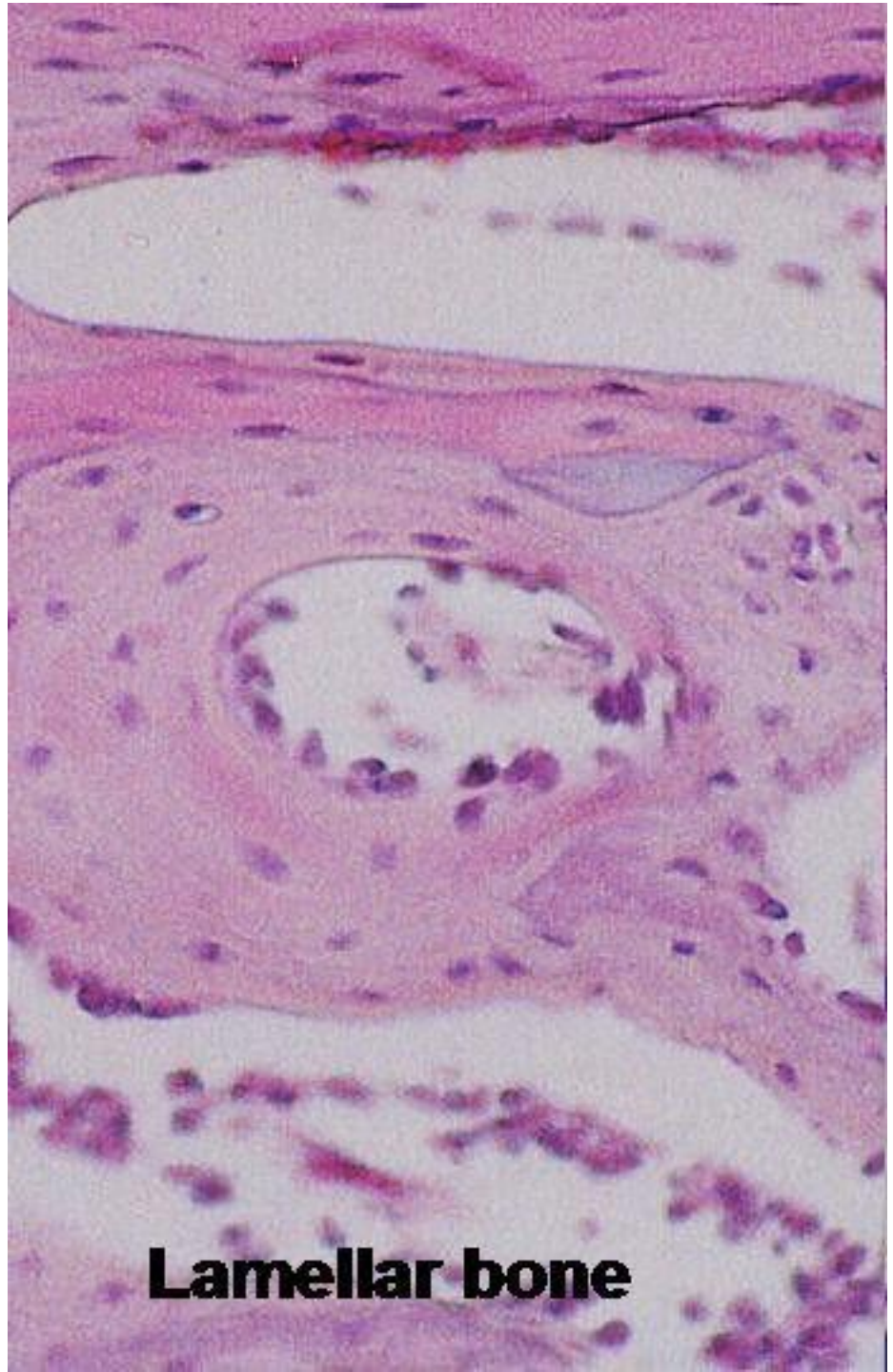
Primary (woven) bone

- First bone tissue that appears in embryonic development and fraction repair
- Collagen fibers are arranged in irregular arrays
- Many cells, less minerals
- Eventually replaced by secondary bone, except cranial sutures and alveolus of maxilla and mandible



Secondary (lamellar) bone

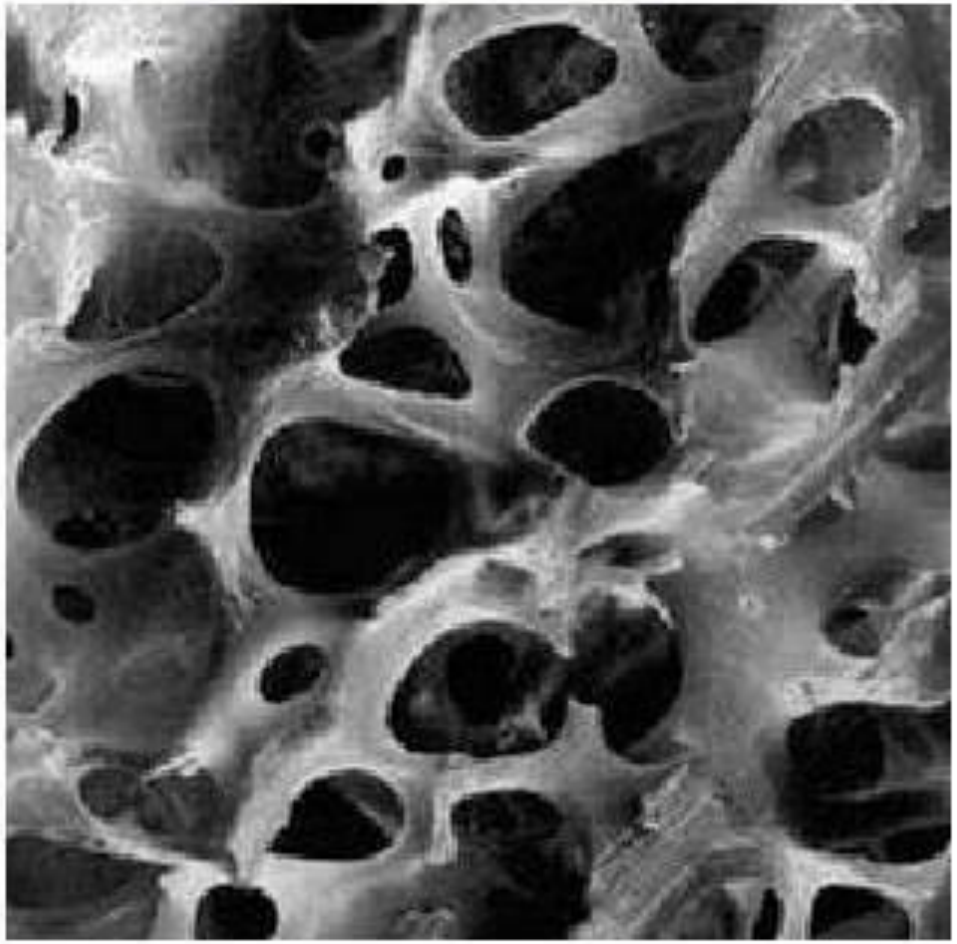
- Matrix is deposited in layers or **lamellae**
- Fibers are deposited in parallel array within a lamella
- Better mineralized than woven bone
- May be either spongy or compact



GROSS APPEARANCE OF BONE, MACROSCOPIC STRUCTURE

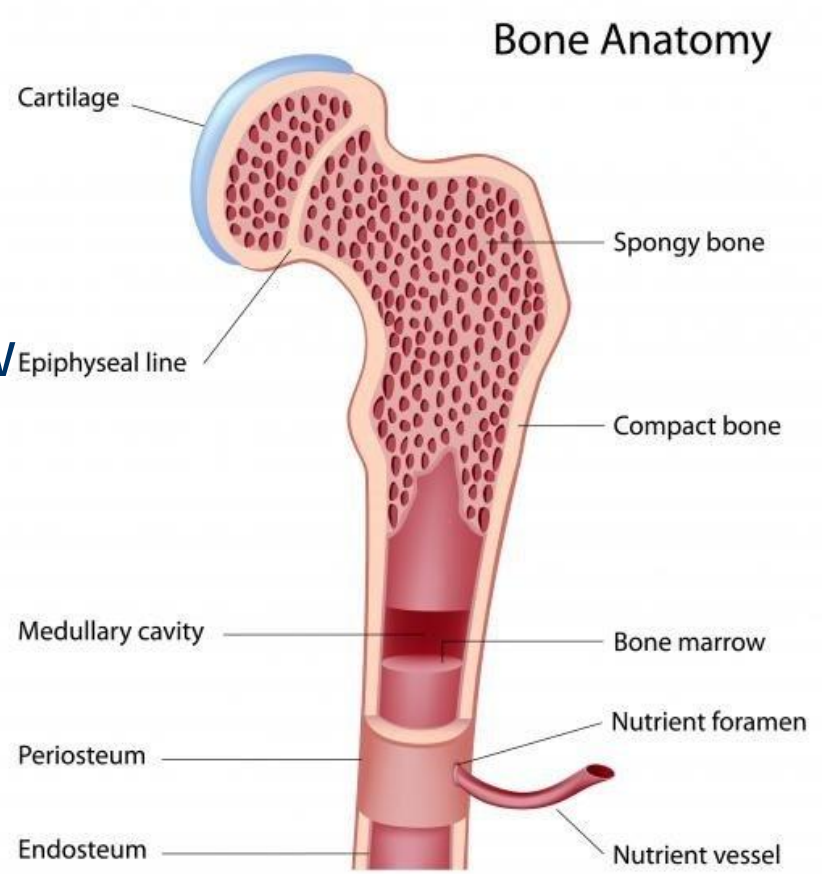
Compact bone

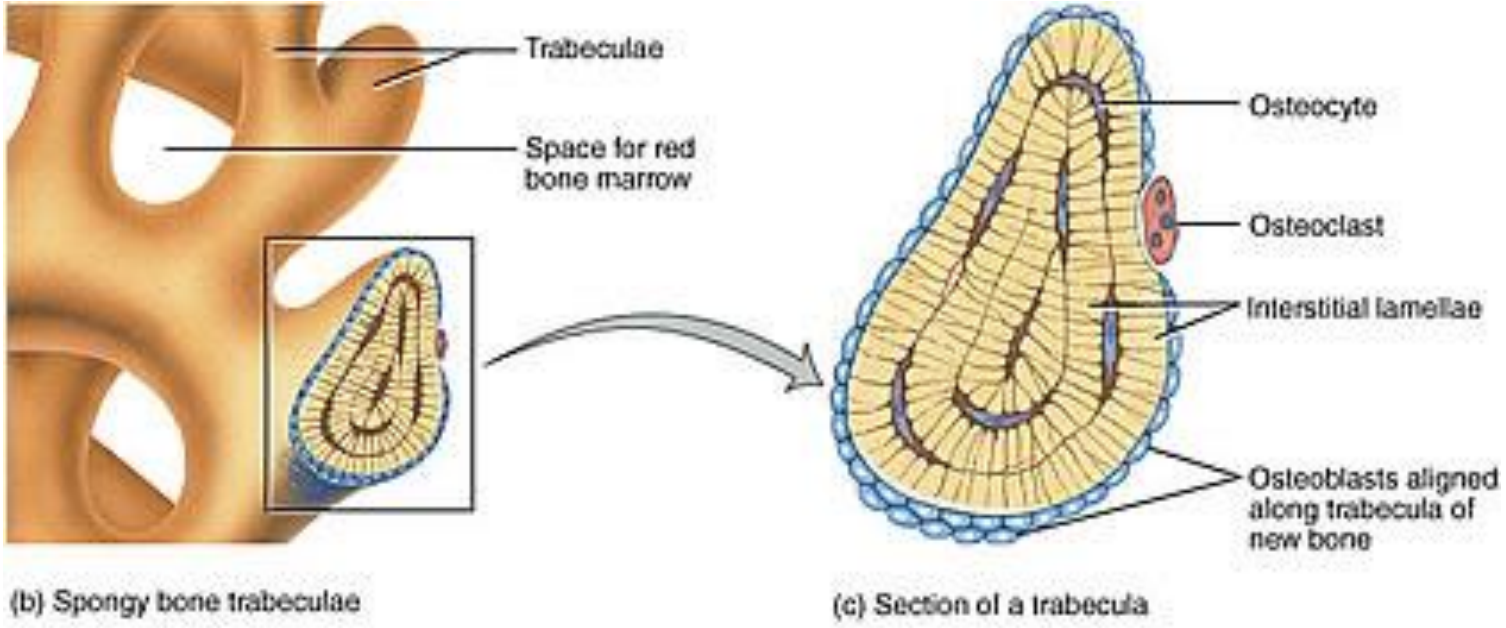
Spongy bone



Spongy bone

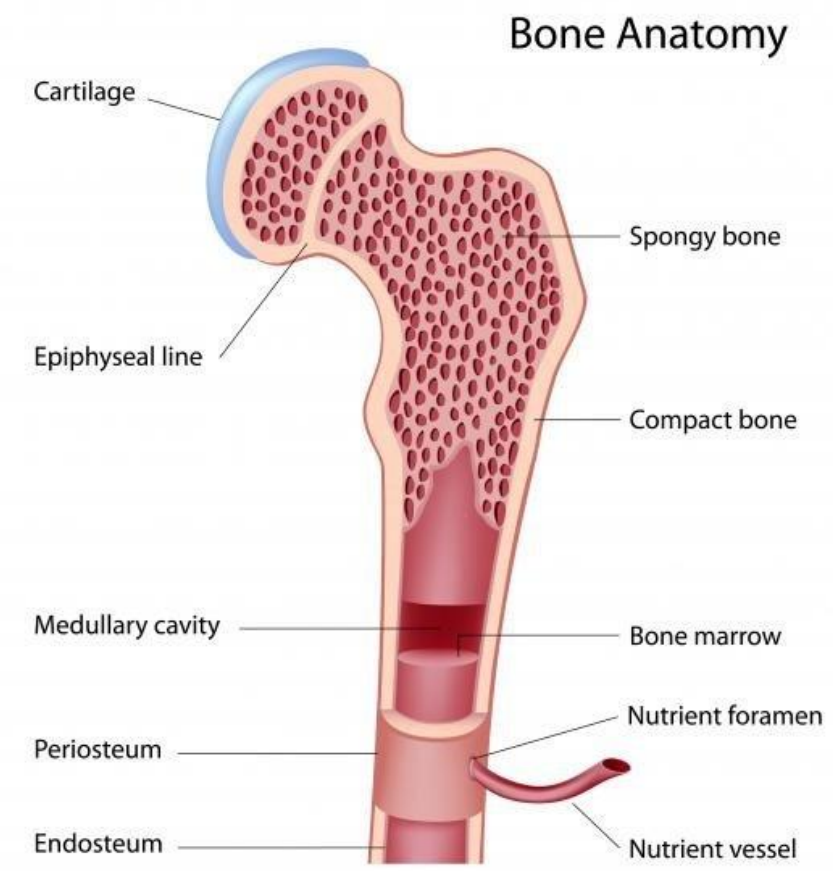
- Like a sponge, with a labyrinth of bony **spicules/trabecules** and intervening spaces that are filled with loose connective tissue or red marrow and blood vessels.
- Located in the interior of bones
- Trabeculae are composed of lamellae
- Trabeculae outside are covered with osteogenic cells, osteoblasts, osteoclasts





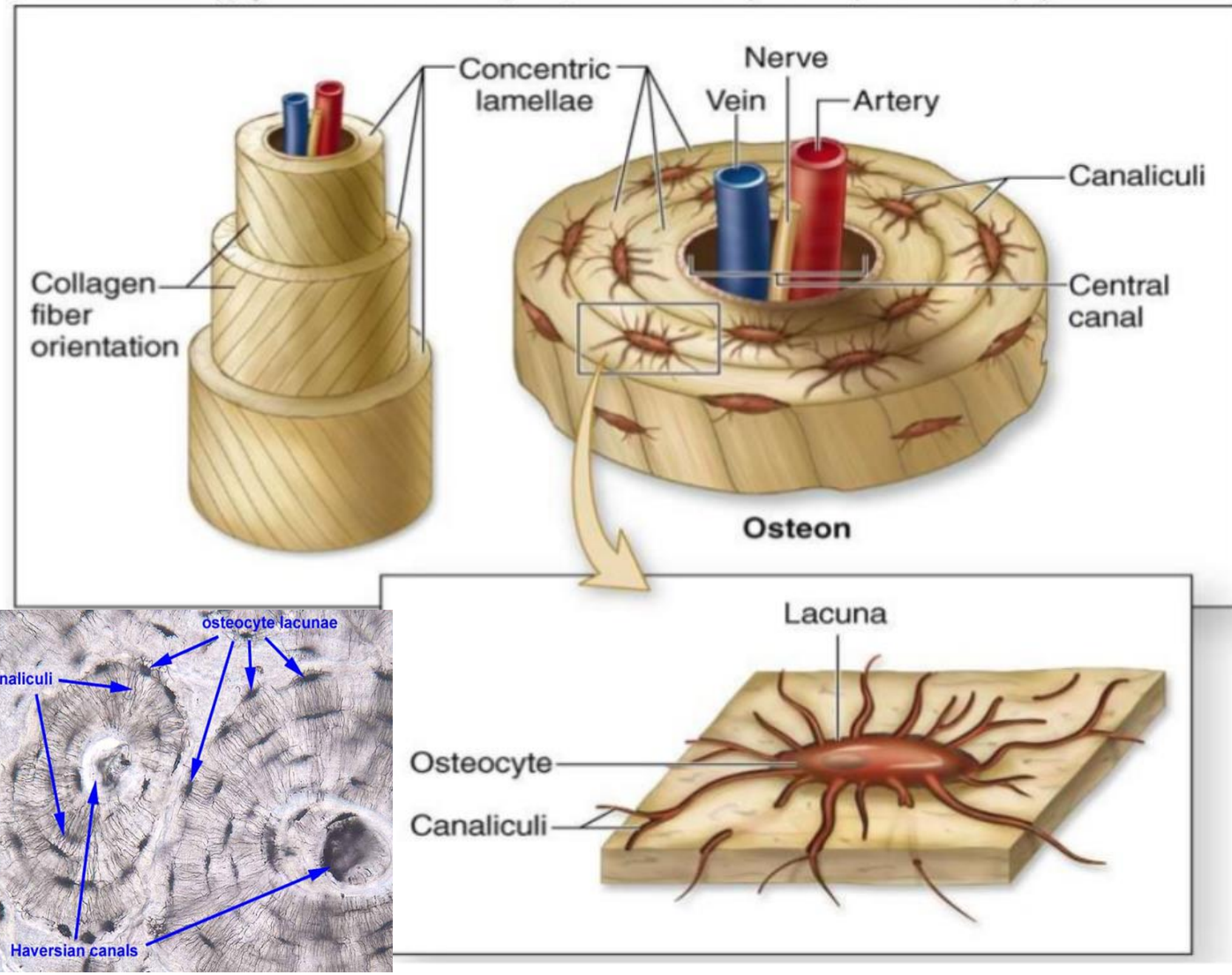
Compact bone

- Appears as a solid mass to the naked eye, covering the exterior of bones and forming the shaft of long bones.



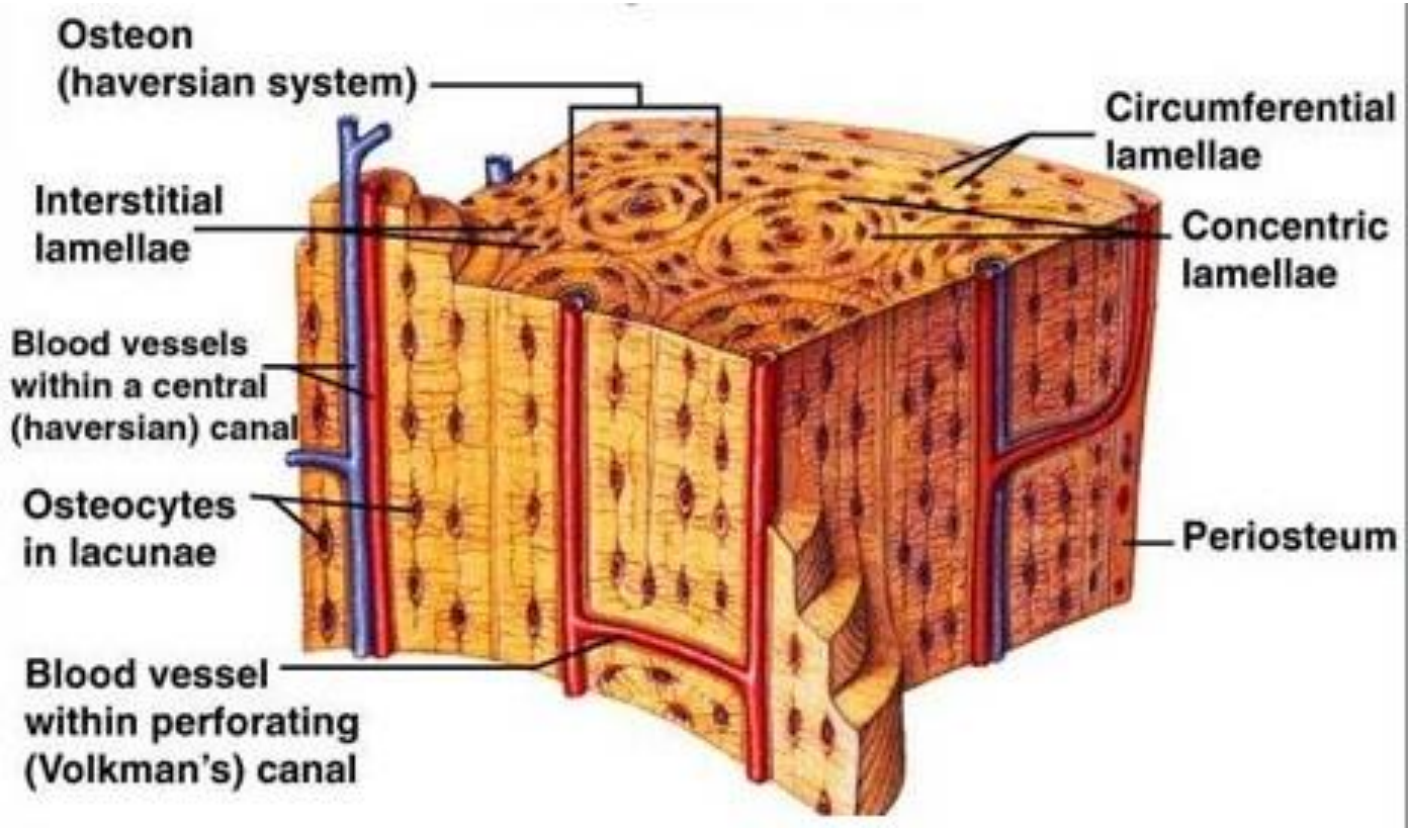
Compact bone

- Collagen fibers in one plate – parallel
- Collagen fibers in adjacent lamellae are perpendicular
- Osteocytes lie in the lacunae between the lamellae
- The lacunae are connected by the canaliculi in which the processes of osteocytes lie
- The tissue fluid circulates in the canaliculi , which feeds the osteocytes
- The canals are lined by endosteum with osteogenic cells, osteoblasts, osteoclasts

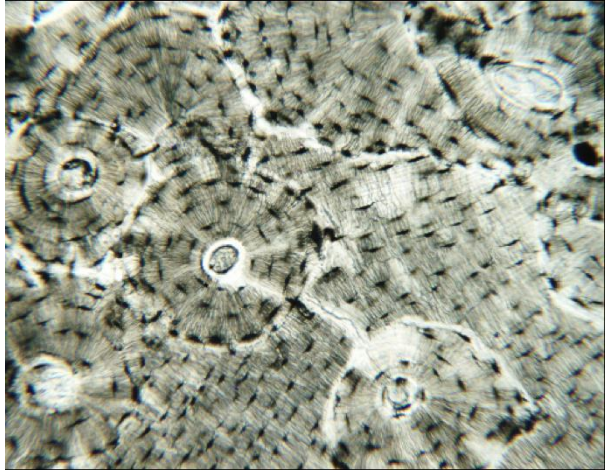


Haversian system (osteon)

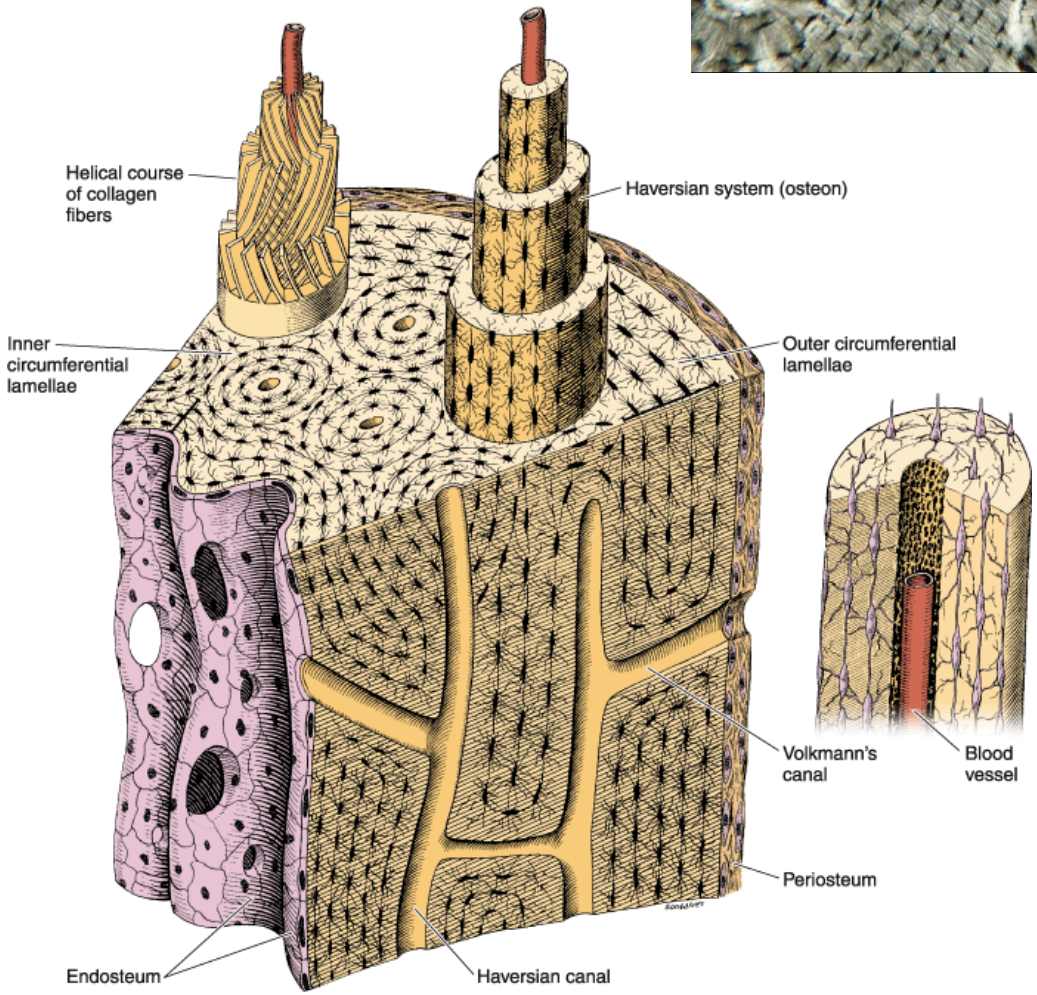
- ✓ Cylinders of concentric lamellae, deposited by endosteum, that run parallel to the long axis of a bone
- ✓ **Haversian canal** contains a blood vessel(s) and loose connective tissue, lined with an endosteum
- ✓ **Concentric lamellae** (4-20) surround the Haversian canal.
- ✓ Collagen fibers are in parallel alignment within a single lamella, wrapping helically around the Haversian canal



Haversian system (osteon)



- ✓ Provides great strength to a long bone
- ✓ An osteon is formed by the centripetal deposition of the concentric lamella
- ✓ Outer lamella is the oldest
- ✓ **Volkmann's canals** oriented perpendicularly between adjacent Haversian canals, contain blood vessels that transport blood from the surface of bone to blood vessels within Haversian canals.

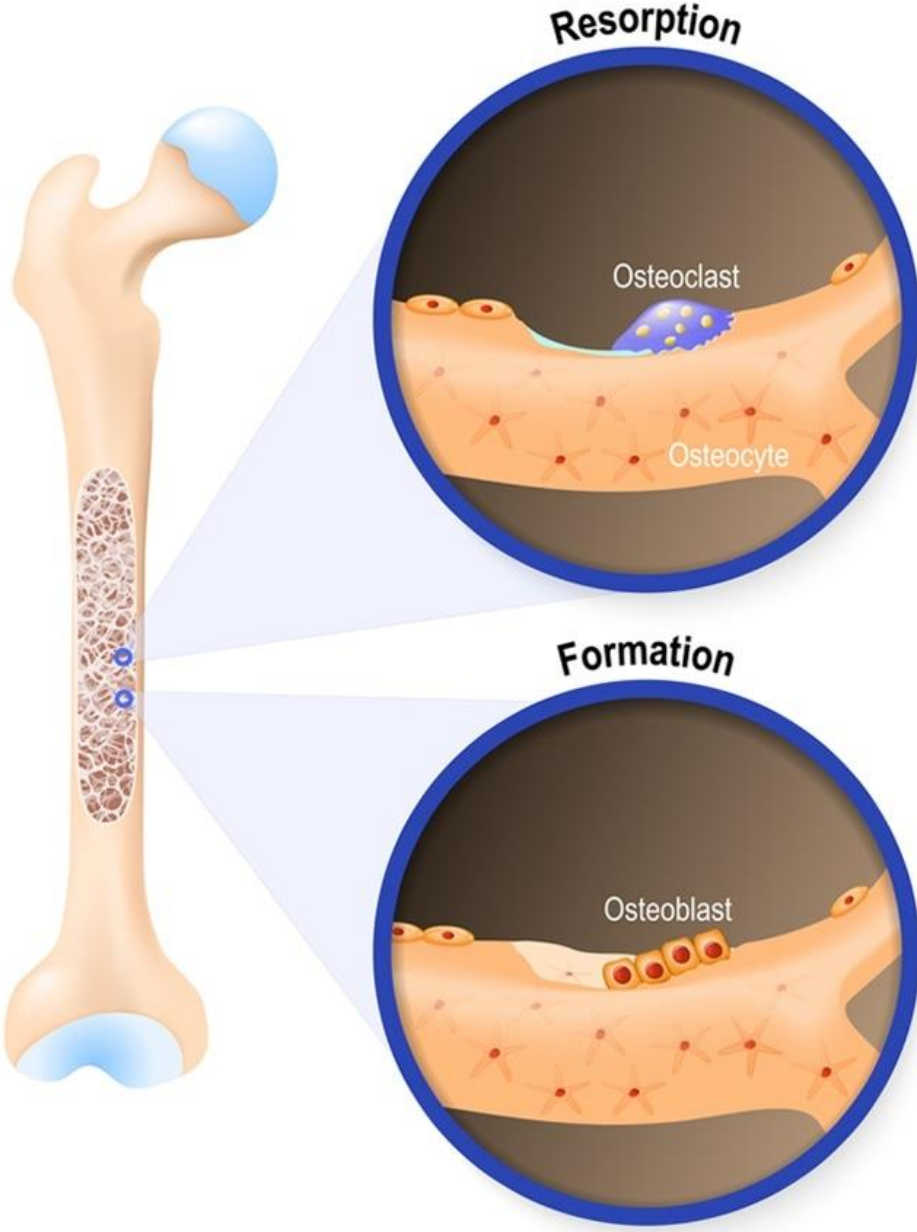


Bone growth

- In the adult, new bone is always laid down on preexisting bone or cartilage.
- Bone growth is always appositional, with either endosteum or periosteum laying down lamellae of bone.
- Interstitial growth is impossible in bone because its rigid, ossified matrix does not allow osteocytes to secrete additional matrix or to divide.

Bone resorption

- Removal of bone by osteoclasts for **remodeling** during growth and/or to mobilize calcium throughout life
- When resorption stops, osteoblasts begin filling in a resorption canal by centripetal (from outside to inside) deposition of new lamellae,forming a new osteon.



BONE FORMATION (OSSIFICATION)

2 types of prenatal ossification:

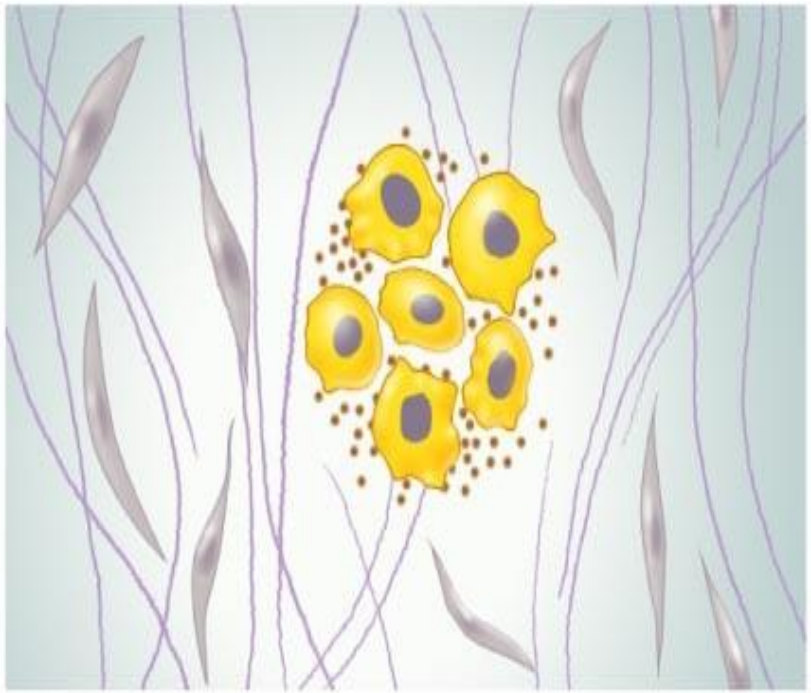
1. Intramembranous

- Bone develops from fibrous membrane
- Forms bones of skull and clavicle + all flat bones
- Begins at 8 weeks of development

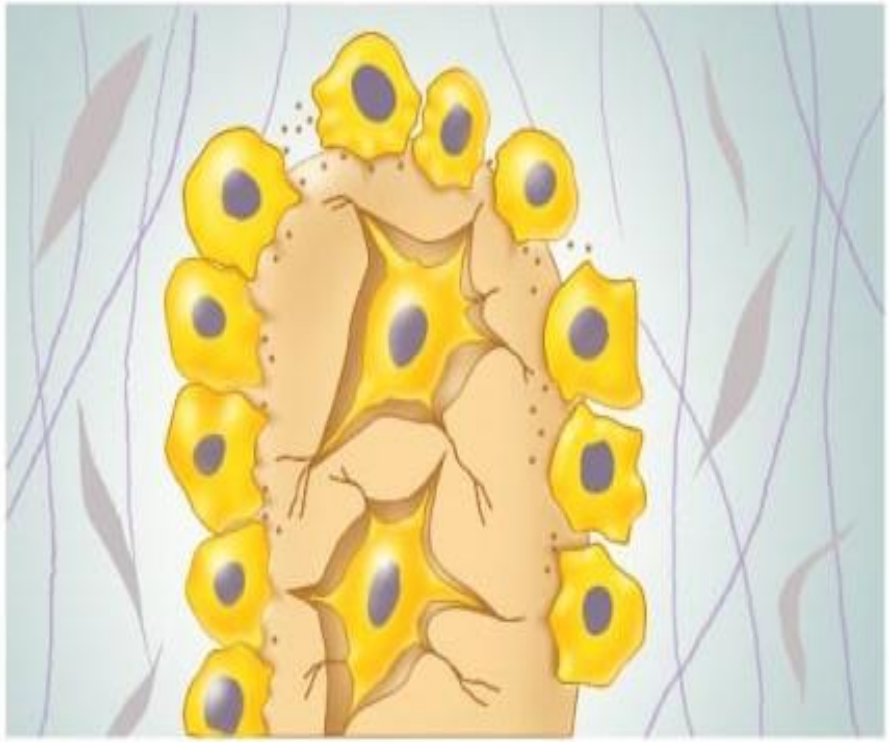
2. Endochondral

- Bone develops from hyaline cartilage
- Forms all long bones, bones at the base of the skull, vertebrae, pelvis, ribs
- Begins at ~5 weeks of development

INTRAMEMBRANOUS BONE FORMATION

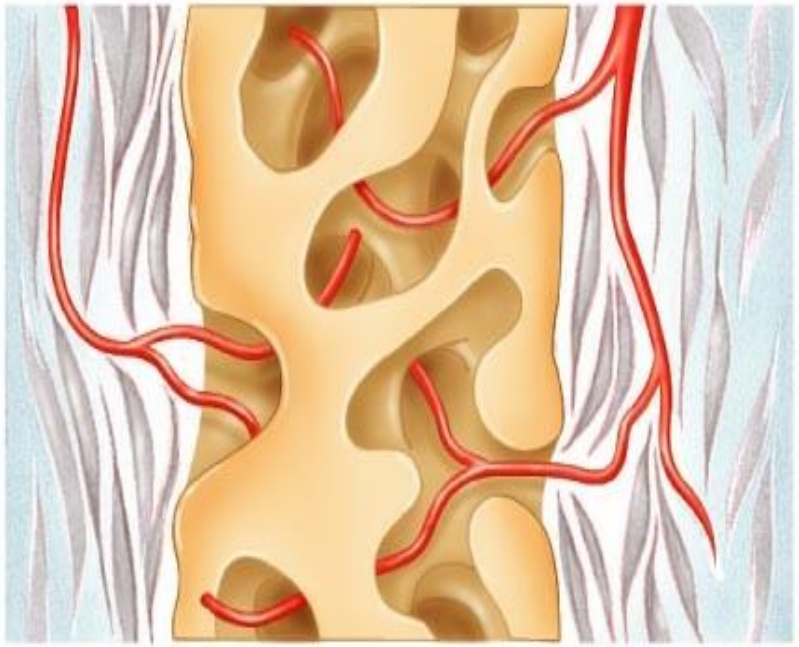


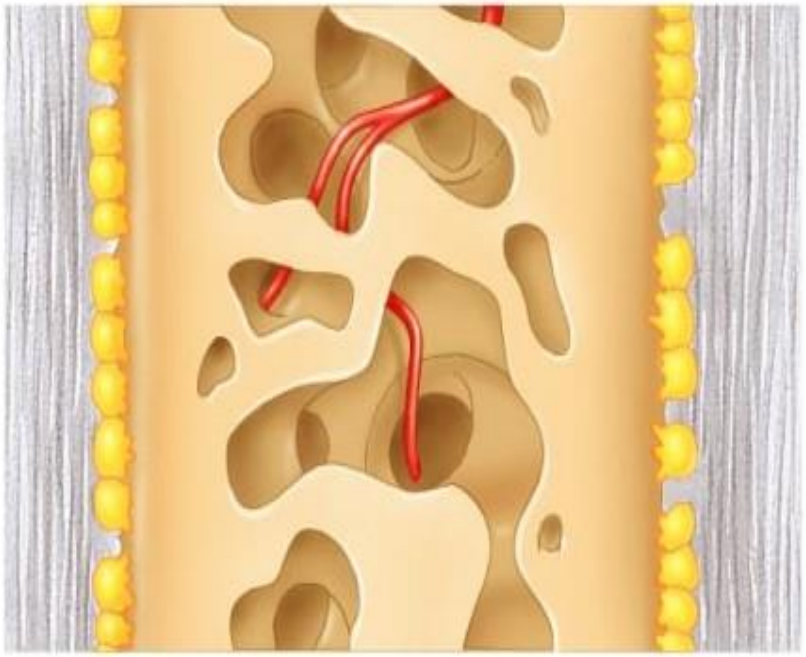
I Mesenchymal cells create fibrous CT framework for ossification
Some mesenchymal cells proliferate and differentiate into **osteoblasts** in an ossification center
Osteoblasts secrete bone matrix, **osteoid**



II Mineralization and calcification of osteoid
Trapped osteoblasts become **osteocytes**

INTRAMEMBRANOUS BONE FORMATION



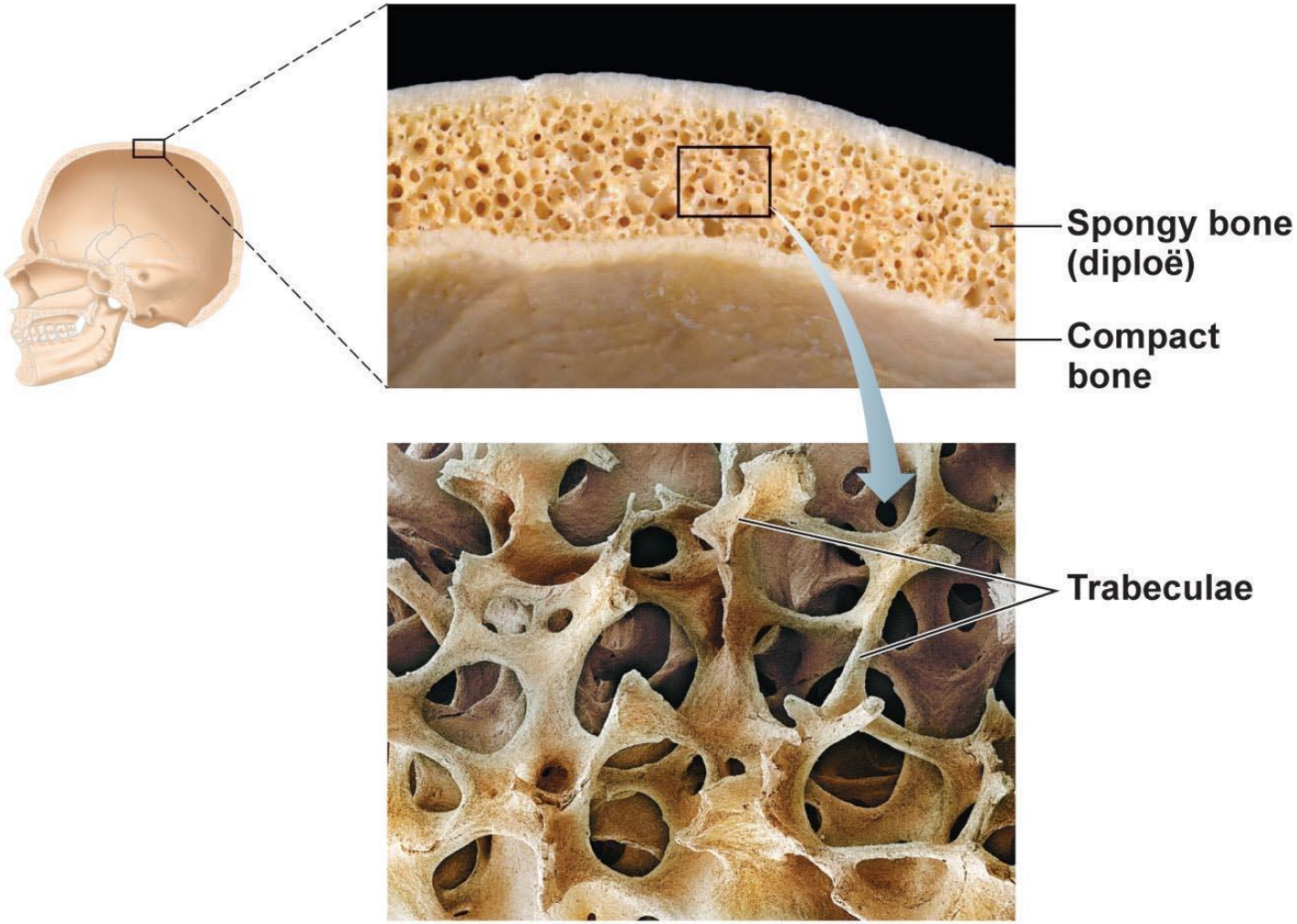


III Osteoid accumulates in between embryonic blood vessels, creating **trabeculae** of woven bone. Mesenchyme on bone surface condenses and differentiates into **periosteum**

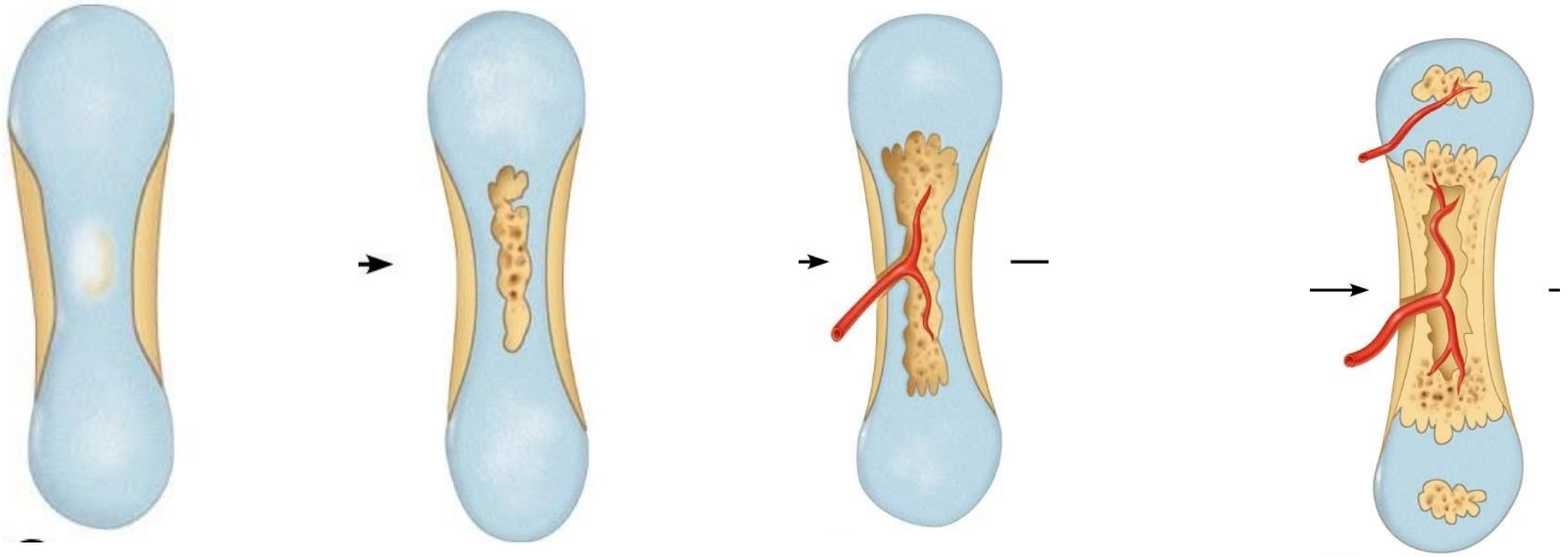
IV A bone collar of woven osteoid forms around trabeculae and ossifies into **compact bone**

Spongy bone (diploë) cavities made up of trabeculae fill with **red bone marrow** created from vessels (vascular tissue)

INTRAMEMBRANOUS BONE FORMATION



ENDOCHONDRAL BONE FORMATION



Bone collar formed around diaphysis by osteoblasts located on inner side of periosteum

This is formed by intramembranous ossification

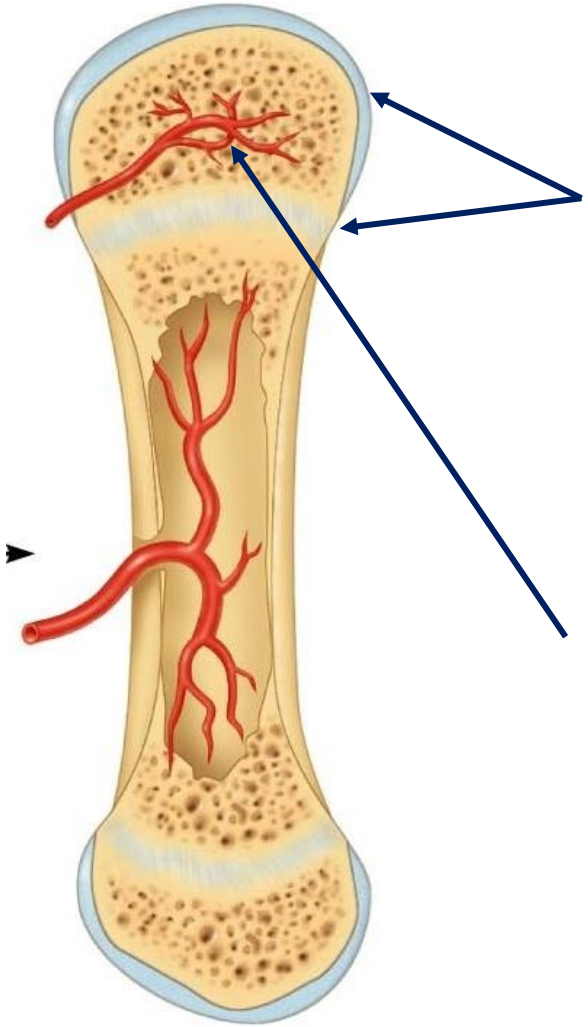
Cartilage in primary ossification center calcifies, then the cells die and cavities are formed

Periosteal bud (lymph, blood vessels, nerves, red marrow, osteoblasts and osteoclasts) enters cavity and builds spongy bone

Osteoclasts resorb spongy bone to create **medullary cavity**

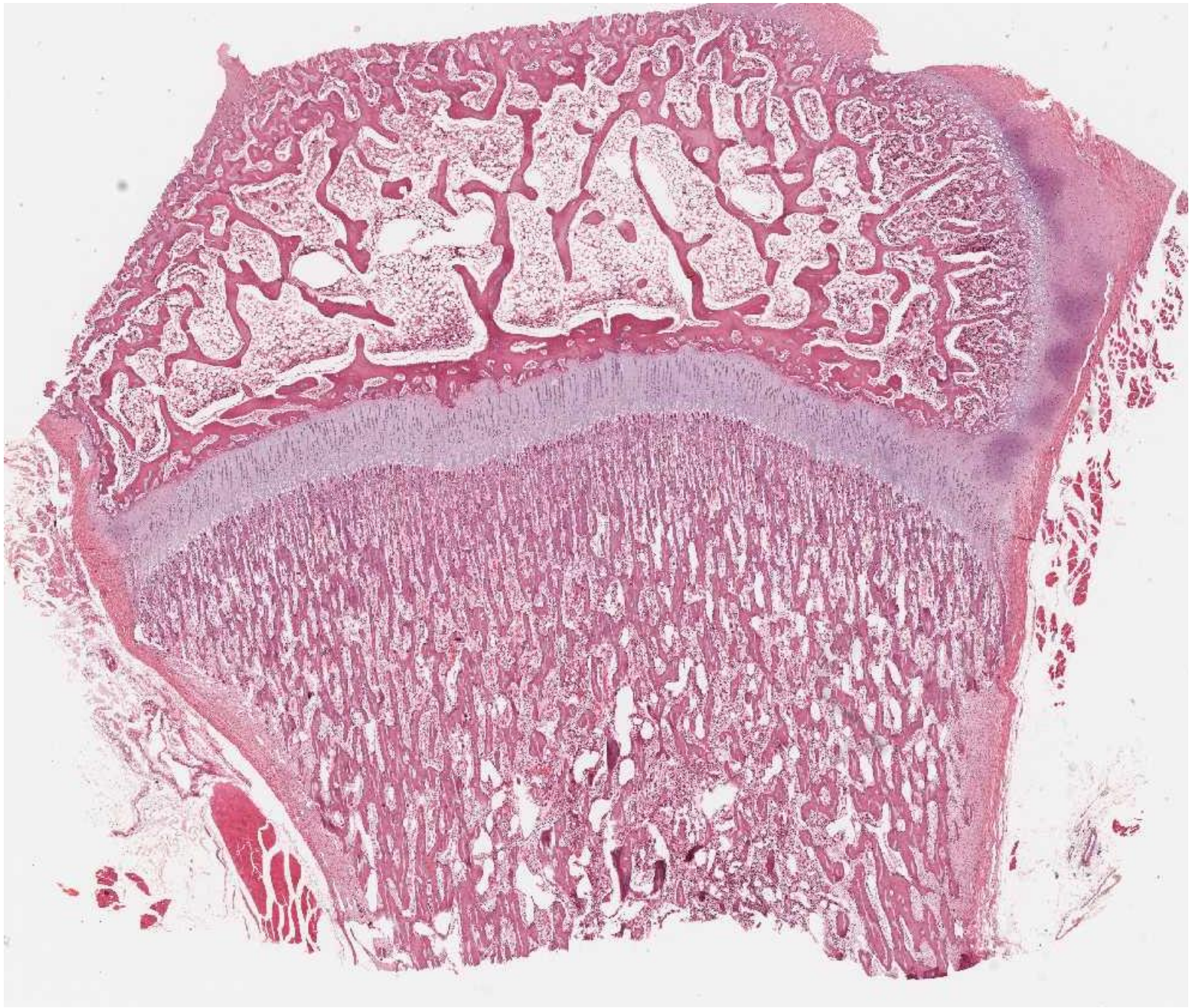
Secondary Ossification Center forms in epiphysis

ENDOCHONDRAL BONE FORMATION



Hyaline cartilage only remains on **epiphyseal surface** (articular cartilage) and at metaphysis and epiphysis junction, to form the **epiphyseal plates**.

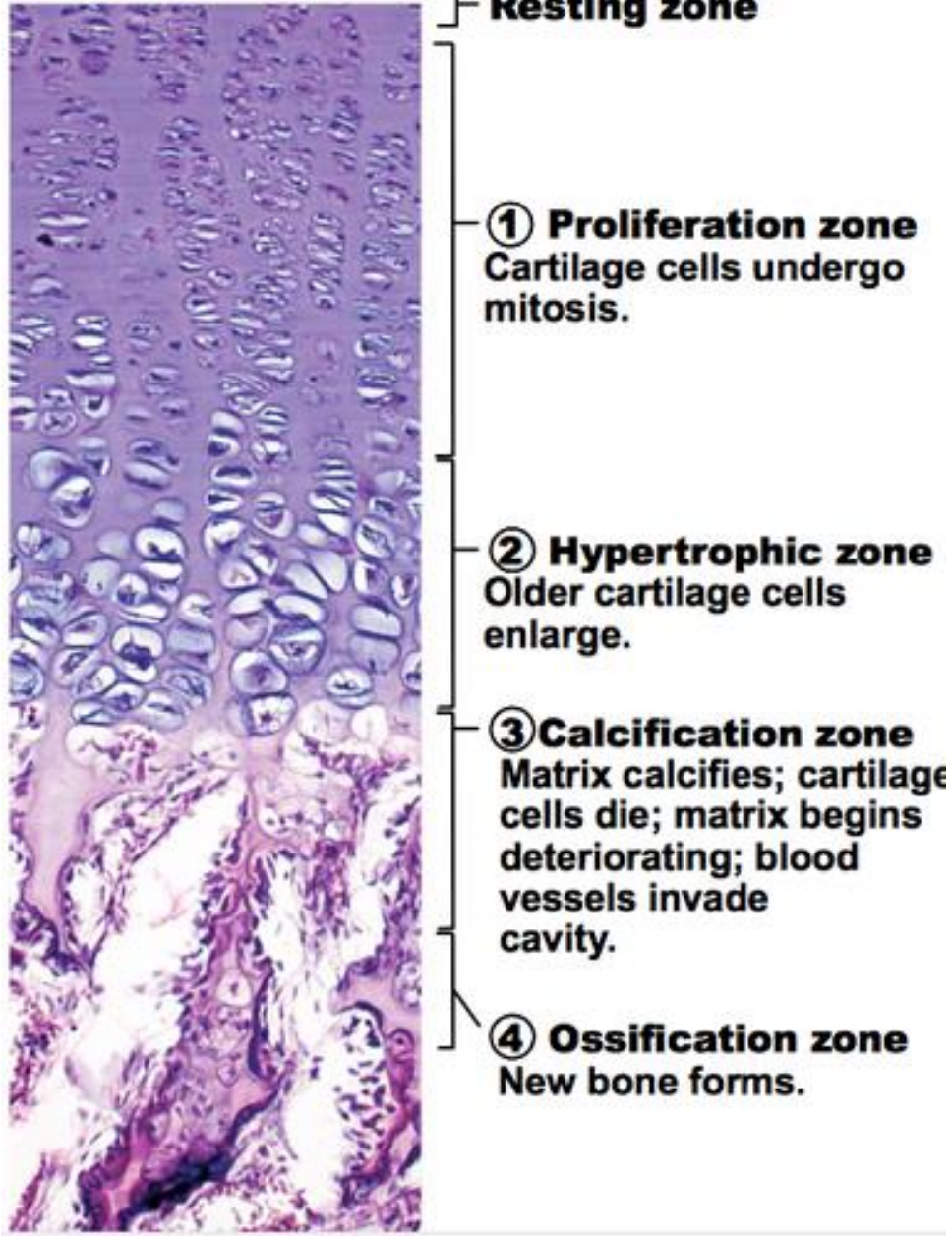
Secondary Ossification Center containing spongy bone occurs in each epiphysis.



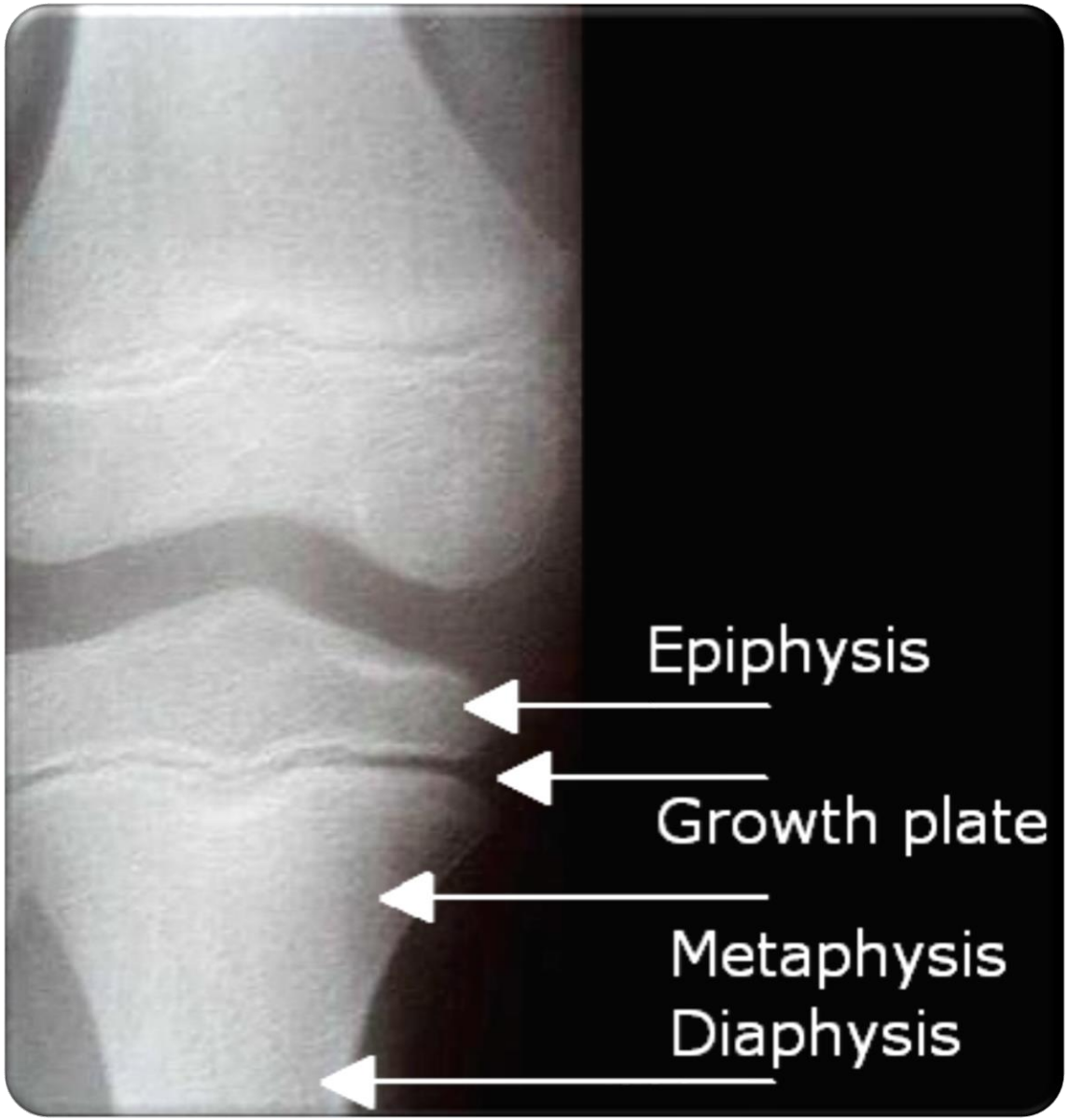
Bone growth in length

Occurs due to the epiphyseal plate

Resting zone of normal hyaline cartilage
Zone of proliferation where isogenous groups of chondrocytes actively divide, forming linear isogenous groups. This zone maintains cartilage thickness.
Zone of hypertrophy where chondrocytes mature, hypertrophy and produce alkaline phosphatase with the subsequent calcification of the cartilage matrix.
Zone of calcification where chondrocytes die, leaving empty lacunae surrounded by vertically oriented spicules of calcified cartilage
Zone of ossification where bone is deposited on the calcified cartilage spicules immediately adjacent to the bony diaphysis, thus increasing the length of that diaphysis.

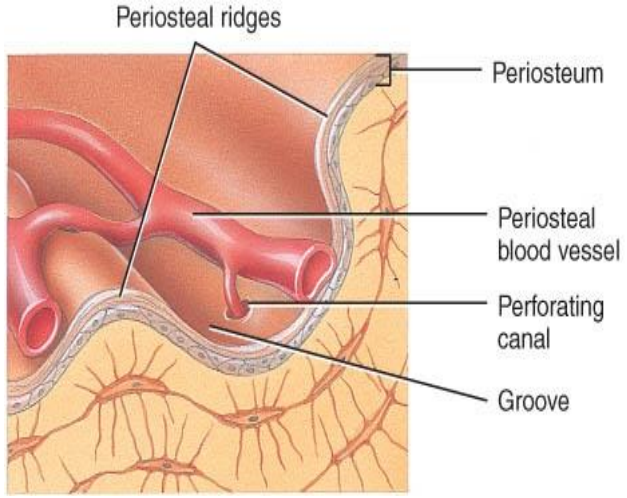


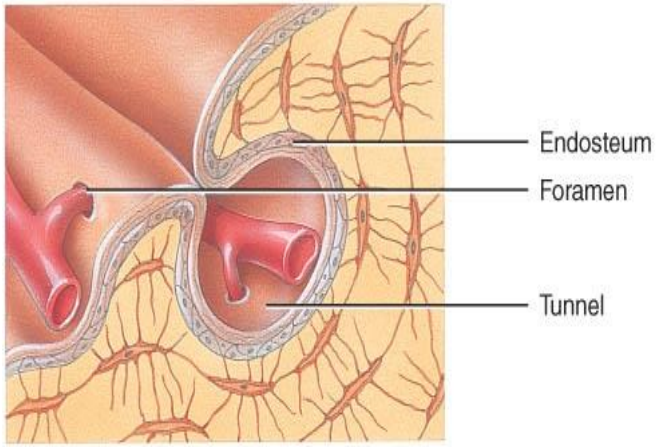
Spongy bone replaces the epiphyseal plate, leaving an epiphyseal line as its remnant. This process is referred to as closure of the epiphyseal plate.

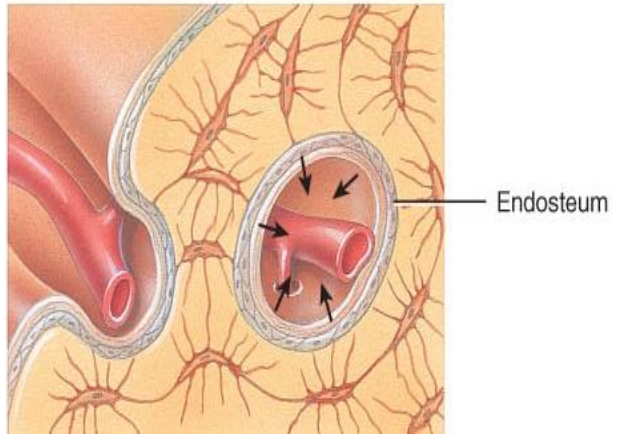

Epiphysis
Growth plate
Metaphysis
Diaphysis

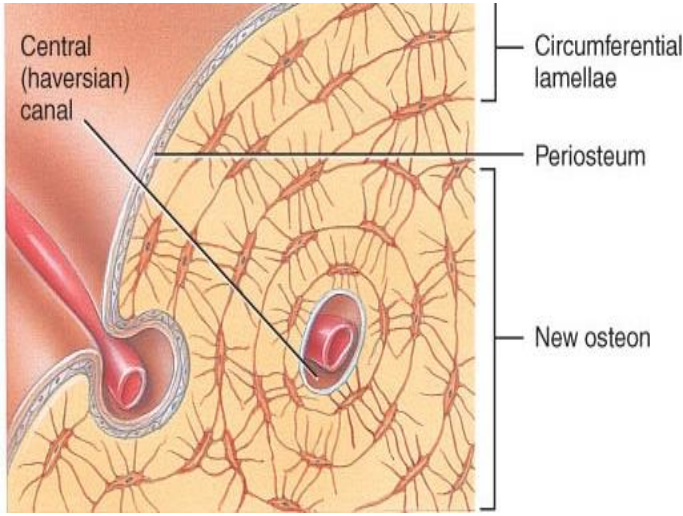
Bone growth in girth due to the periosteum

- Bone can grow in thickness or diameter only by *appositional growth* at the bone surface.
- This process corresponds to the intramembranous ossification model
- **The steps in these process are:**
  - Periosteal cells differentiate into osteoblasts which secrete collagen fibers and organic molecules to form the matrix.
  - Periosteal cells differentiate into osteoblasts and form bony ridges and then a tunnel around periosteal blood vessel.
  - Ridges fuse and the periosteum becomes the inner layer of a new osteonal canal.
  - New concentric lamellae fill in the tunnel to form an osteon.
  - Osteoblasts under the periosteum form new circumferential lamellae.



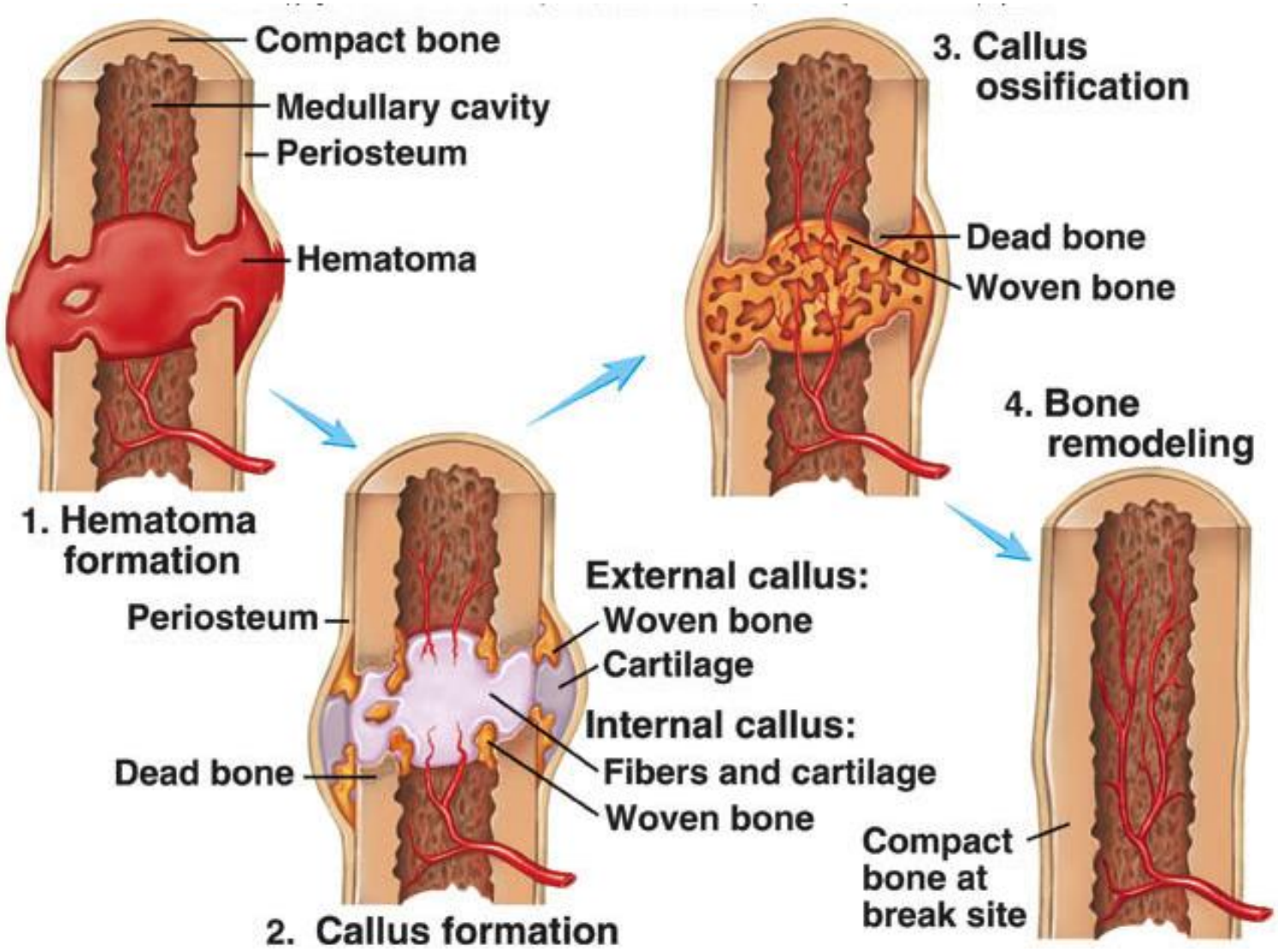






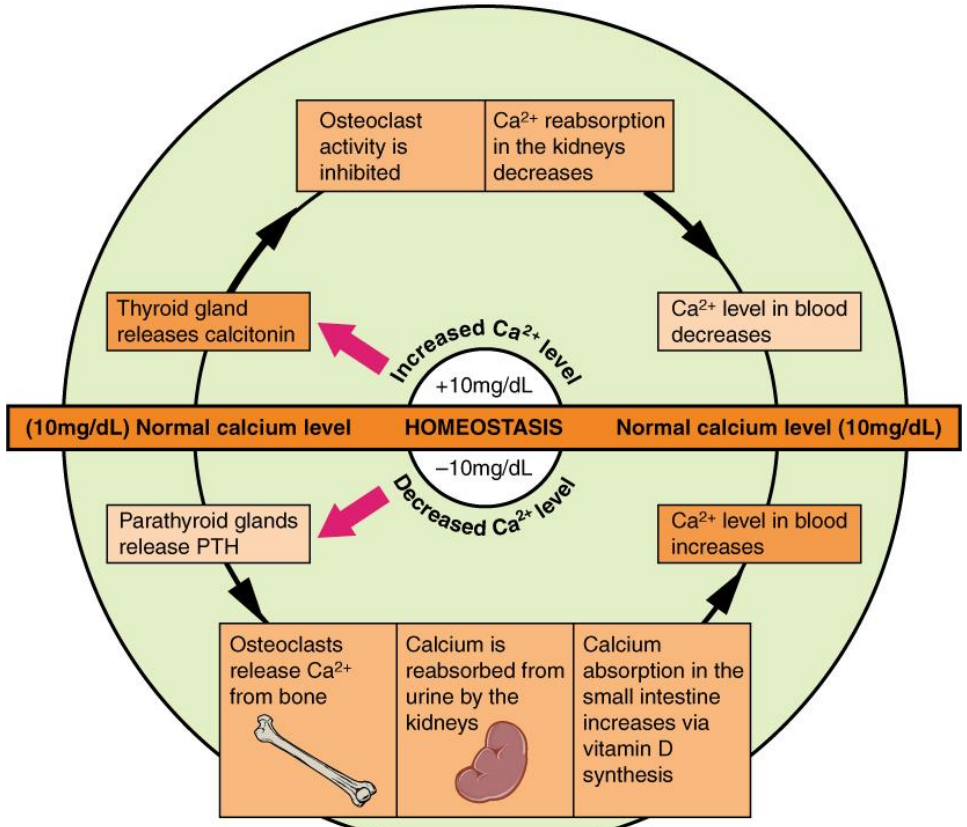
Bone fracture

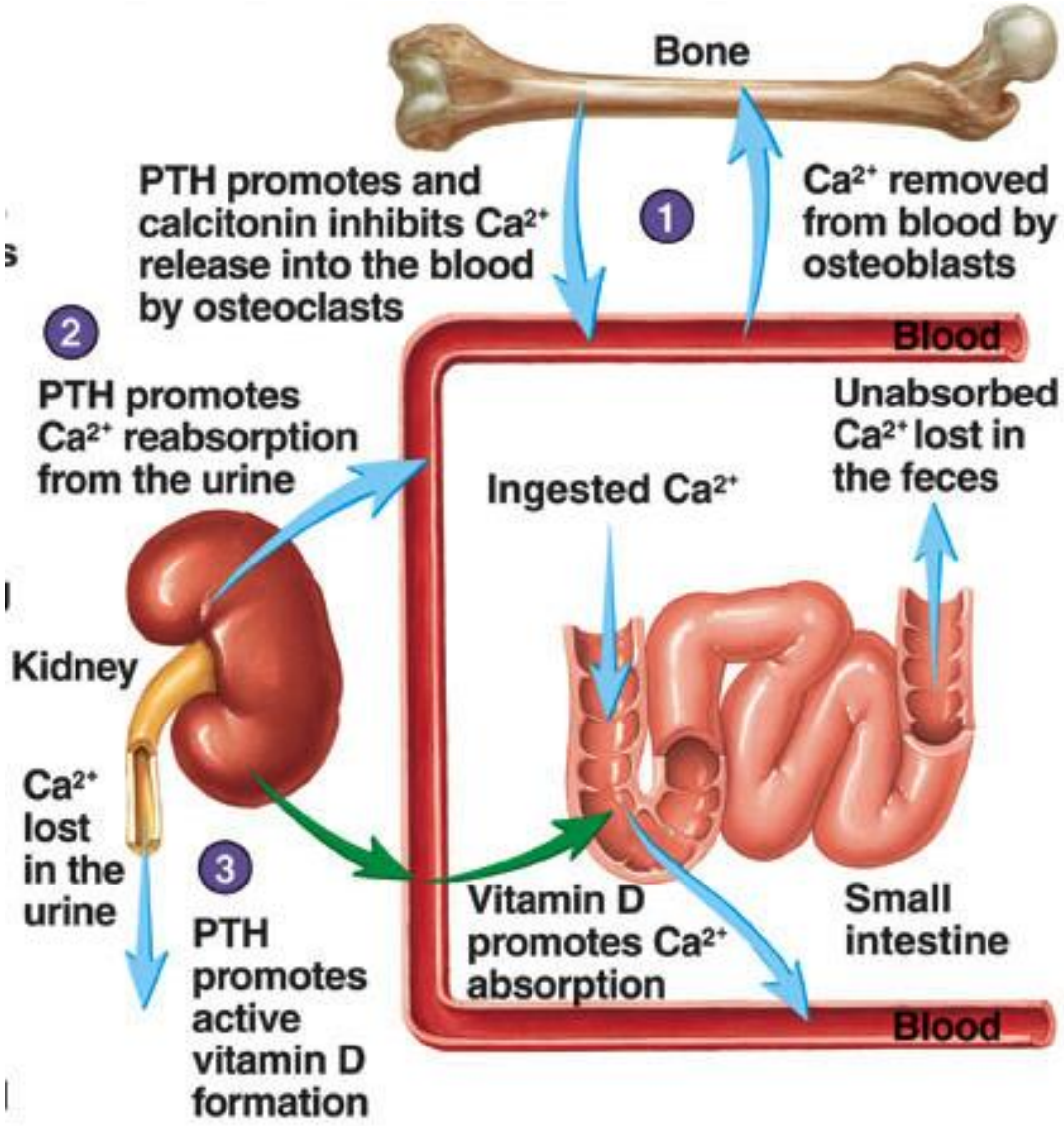
1. Formation of blood clot at the site of injury
2. Formation of the callus
   - Growth of blood vessels
   - Formation of primary bone
3. Ossification of callus
4. Callus remodeling, lamellar bone formation



Hormone regulation

- PTH and Vit D3 ↑ level of Ca in blood
- Calcitonin ↓ level of Ca in blood





Factors affecting bone tissue:

- Protein deficiency
- Ca deficiency (defect matrix calcification- rickets/osteomalacia)
- Vit D deficiency (Ca^{++} is not absorbed in the intestines)
- Vit A deficiency (defect synthesis of GAGs and bone growth)
- Vit A excess (early closure of epiphyseal plates)
- Vit C deficiency (defect collagen synthesis)

ENJOY YOUR CLASSES!