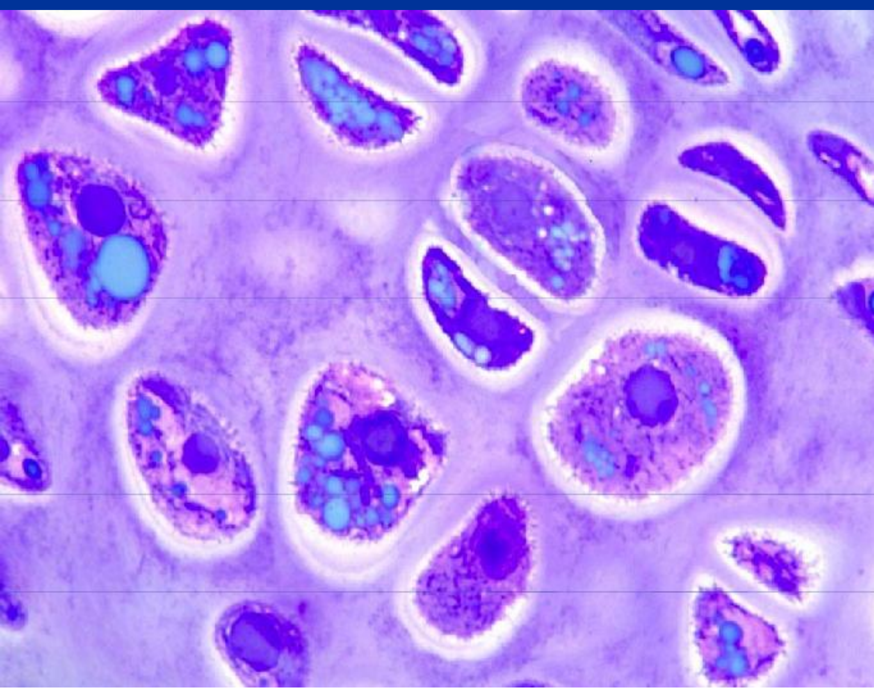
# Cartilage
## DANIL HAMMOUDI.MD

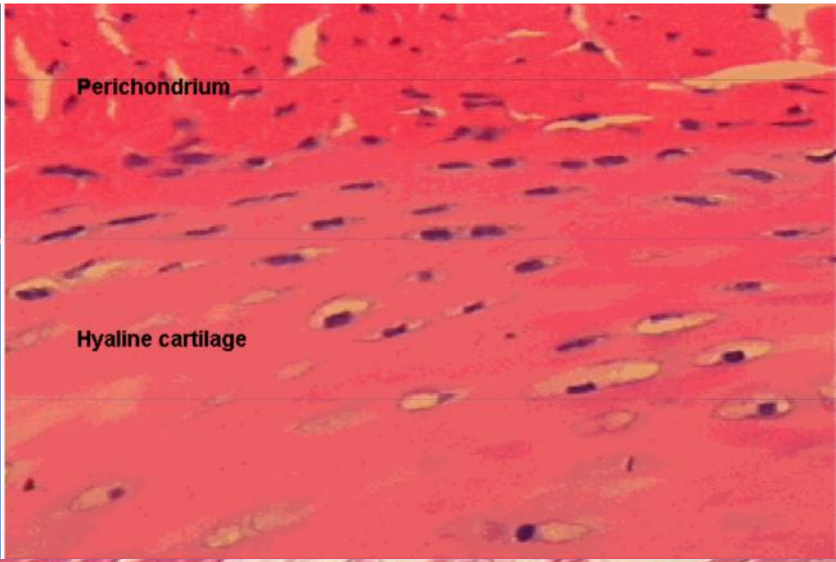
**Chrondrocyte**

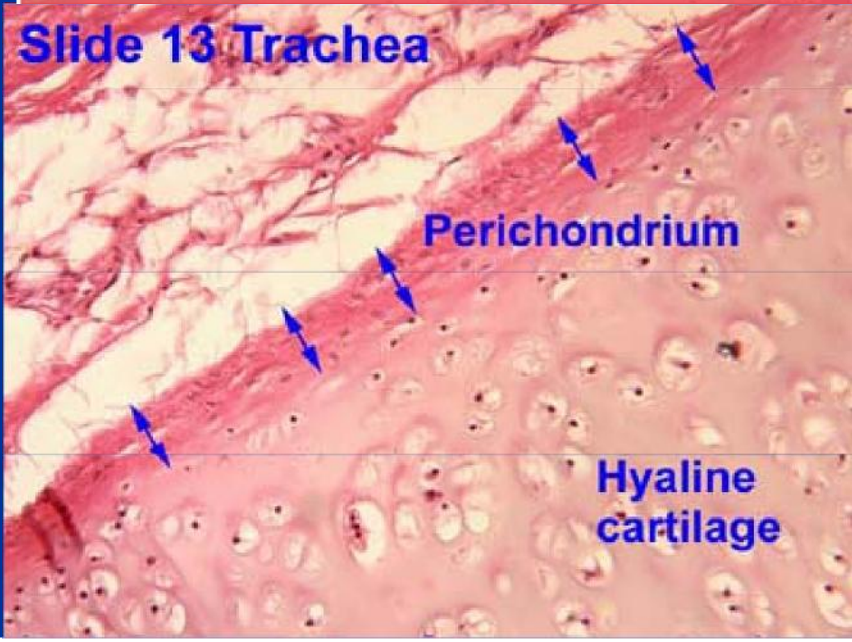
- are the only cells found in healthy cartilage.
- They produce and maintain the cartilaginous matrix, which consists mainly of collagen and proteoglycans.



# Skeletal Cartilage

- Contains **no blood vessels or nerves**
- **Surrounded by the perichondrium** (dense irregular connective tissue) that resists outward expansion
- **Three types –**
  - **hyaline**
  - **elastic**
  - **fibrocartilage**



# Types of Cartilage

- Hyaline
  - **<u>Smooth</u>** (but not totally flat!), bluish color
  - **<u>Articular cartilage</u>** and Cartilaginous Endplate
  - Larynx, trachea, bronchi, ribes, articular surface of bones
  - – Epiphyseal plate

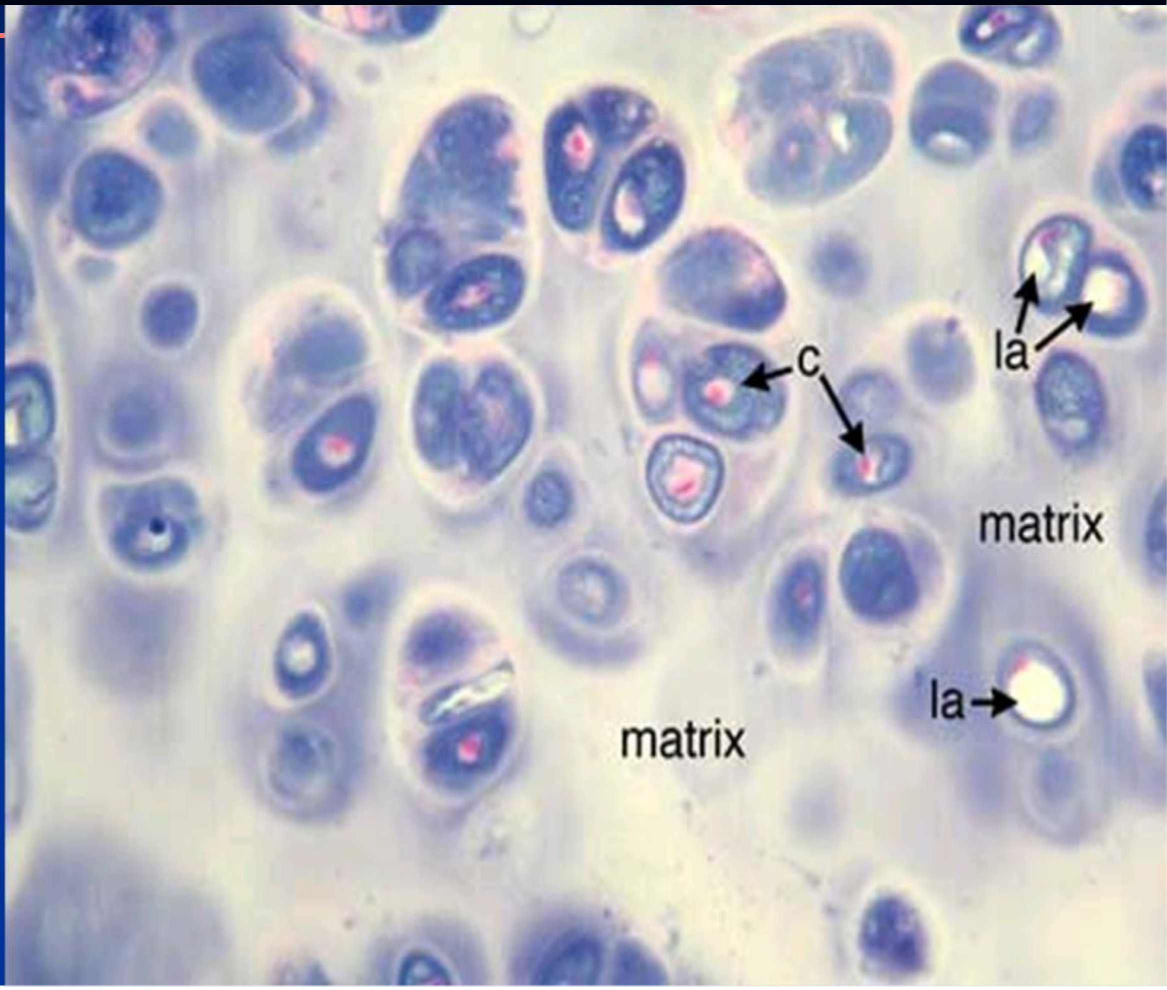
- Elastic
  - More flexible than hyaline
  - Epiglottis, external ear
  - Elastic fibers for resiliency

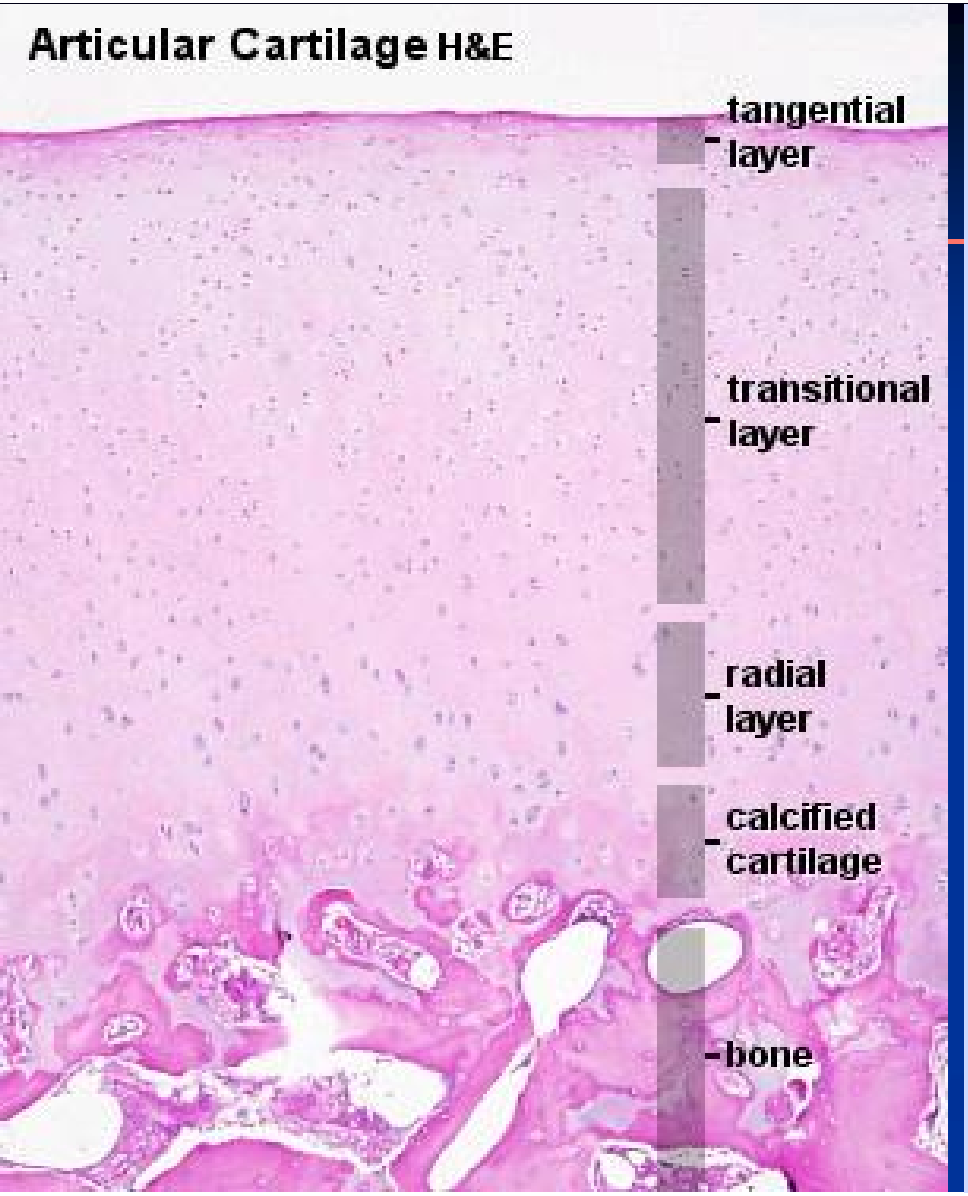
- Fibrocartilage
  - Fibrous tissues
  - Annulus Fibrosus (intervertebral discs), Meniscus, pubic symphysis
  - Type I collagen fibers for tensile strength, frictional forces
  - Between cartilage and connective tissue –,

# Hyaline Cartilage

- Provides support, flexibility, and resilience
- Is the most abundant skeletal cartilage
- Is present in these cartilages:
  - **Articular** – covers the ends of long bones
  - **Costal** – connects the ribs to the sternum
  - **Respiratory** – makes up larynx, reinforces air passages
  - **Nasal** – supports the nose

la = lacuna (chondrocytes shrunken or lost as artifact of slide preparation)
c = chondrocyte



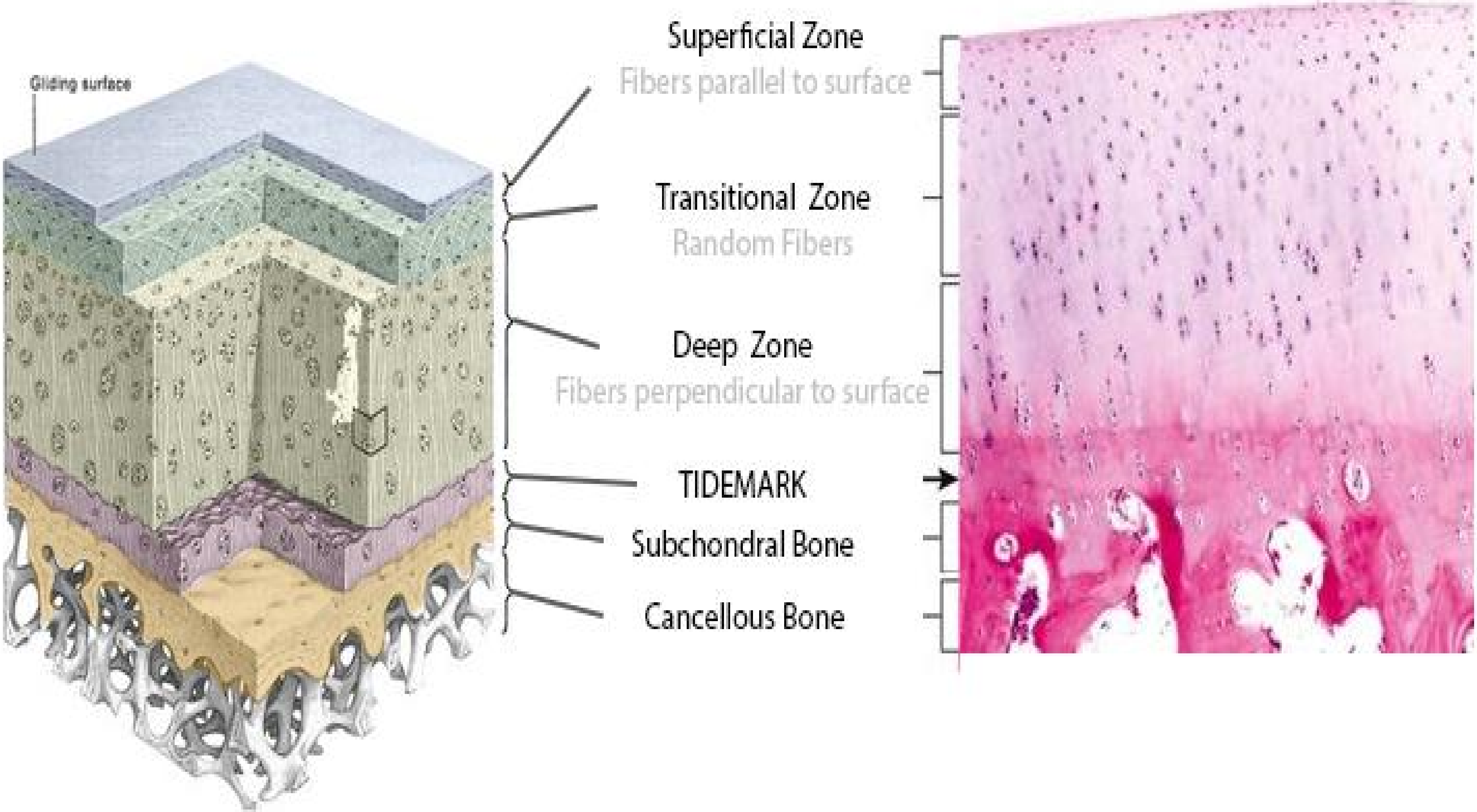


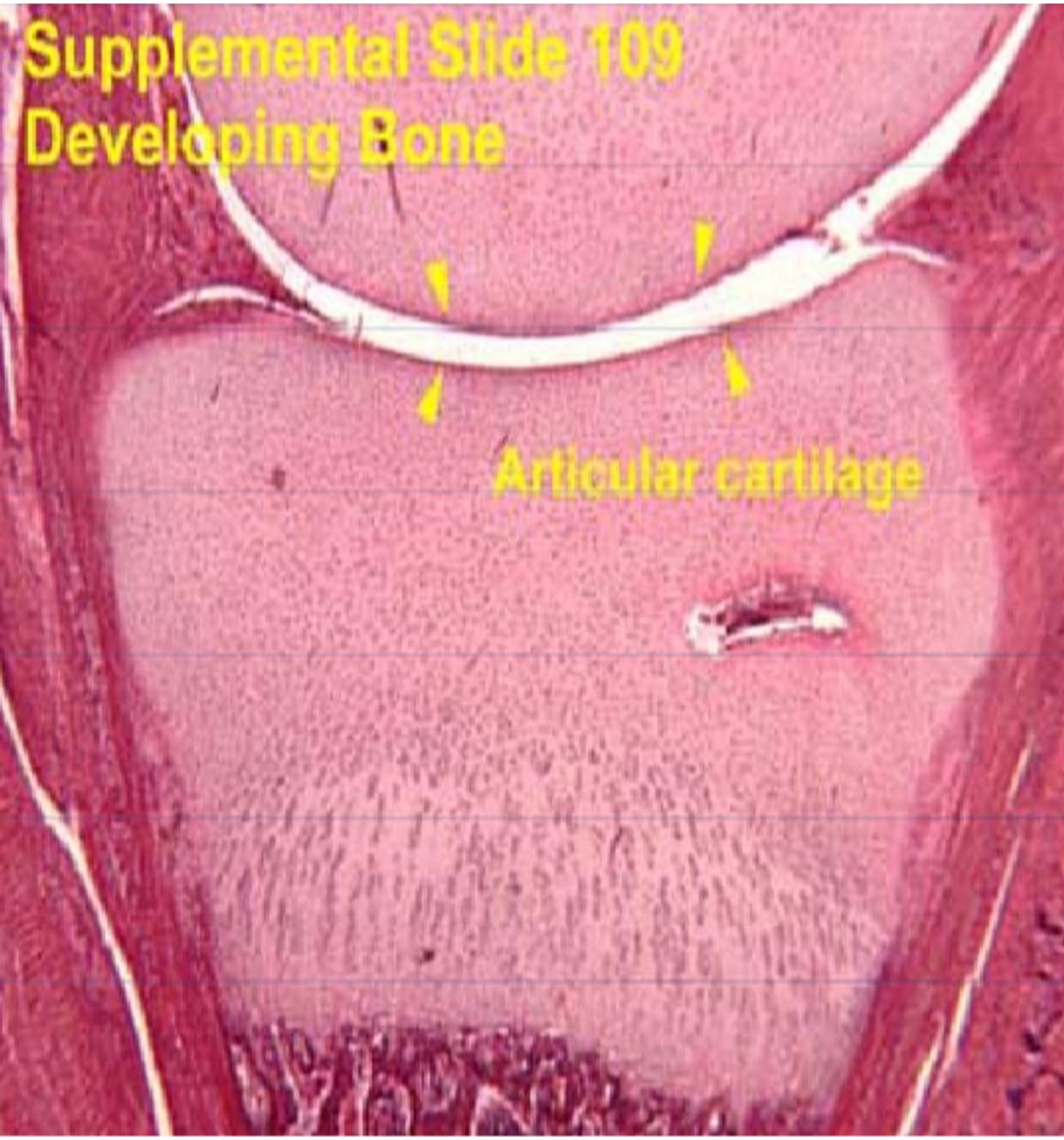

- **Articular Cartilage**

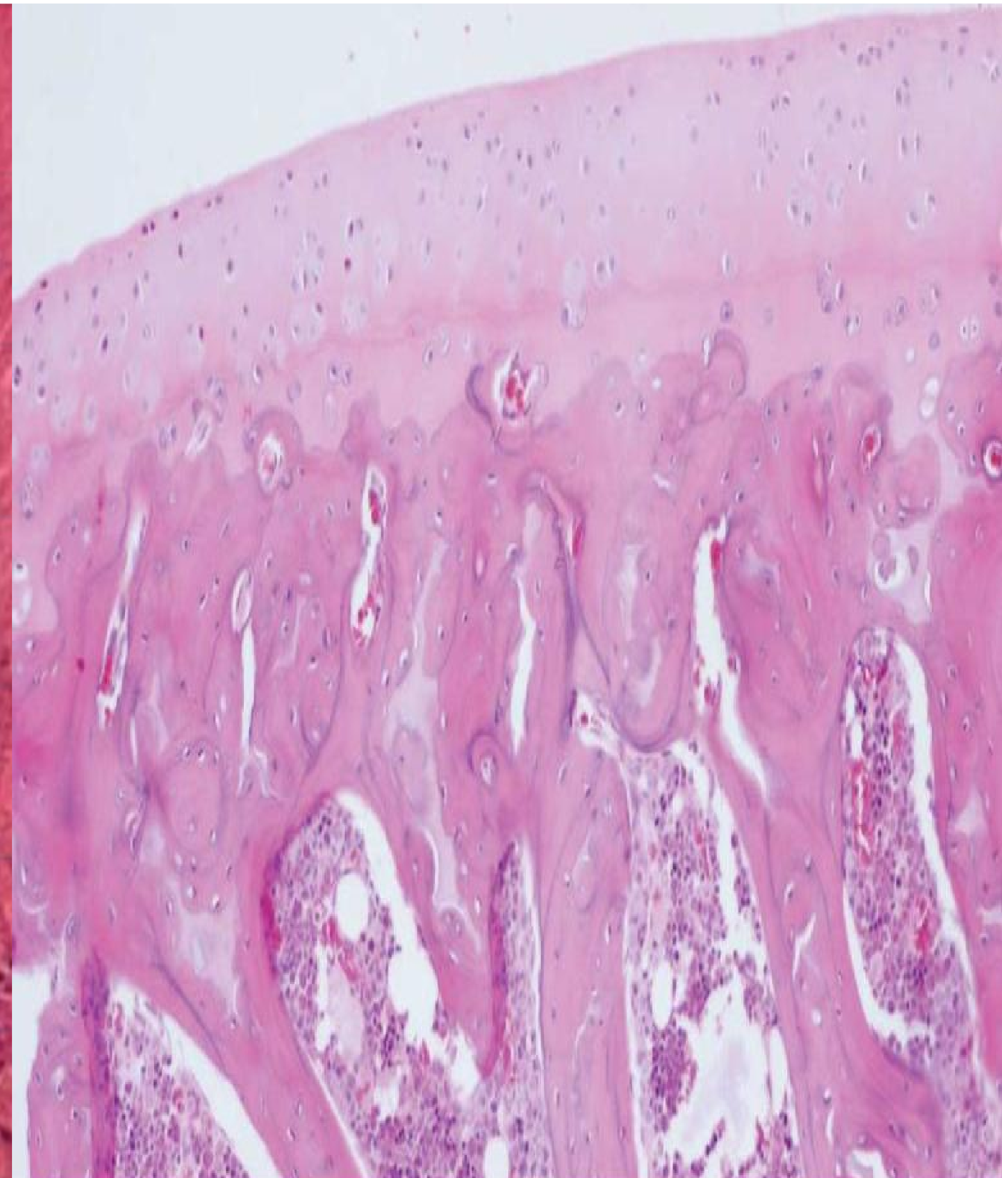
**is a specialised form of hyaline cartilage.**

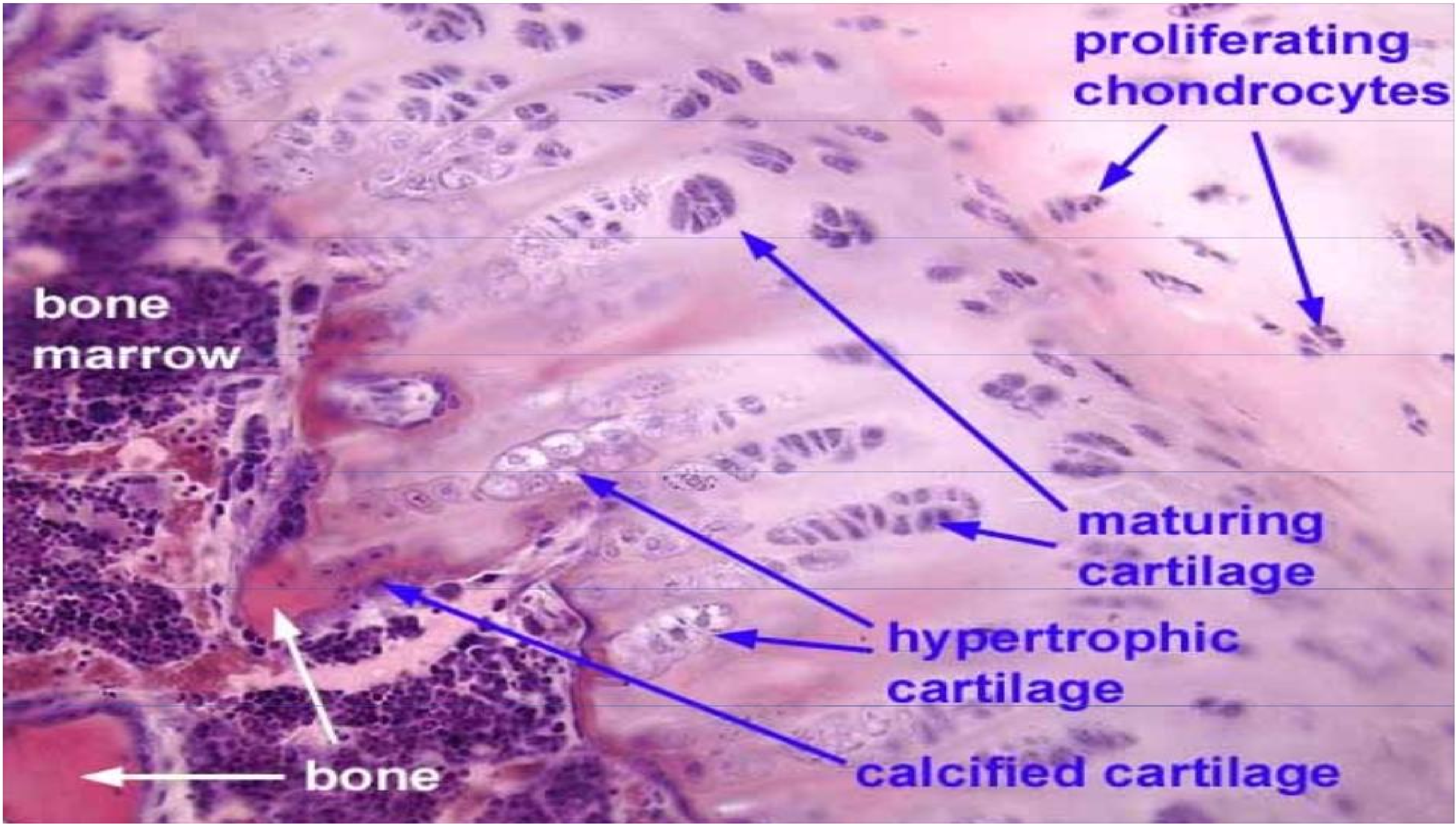
**transforms the articulating ends of the bones into lubricated, wear-proof, slightly compressible surfaces, which exhibit very little friction.**

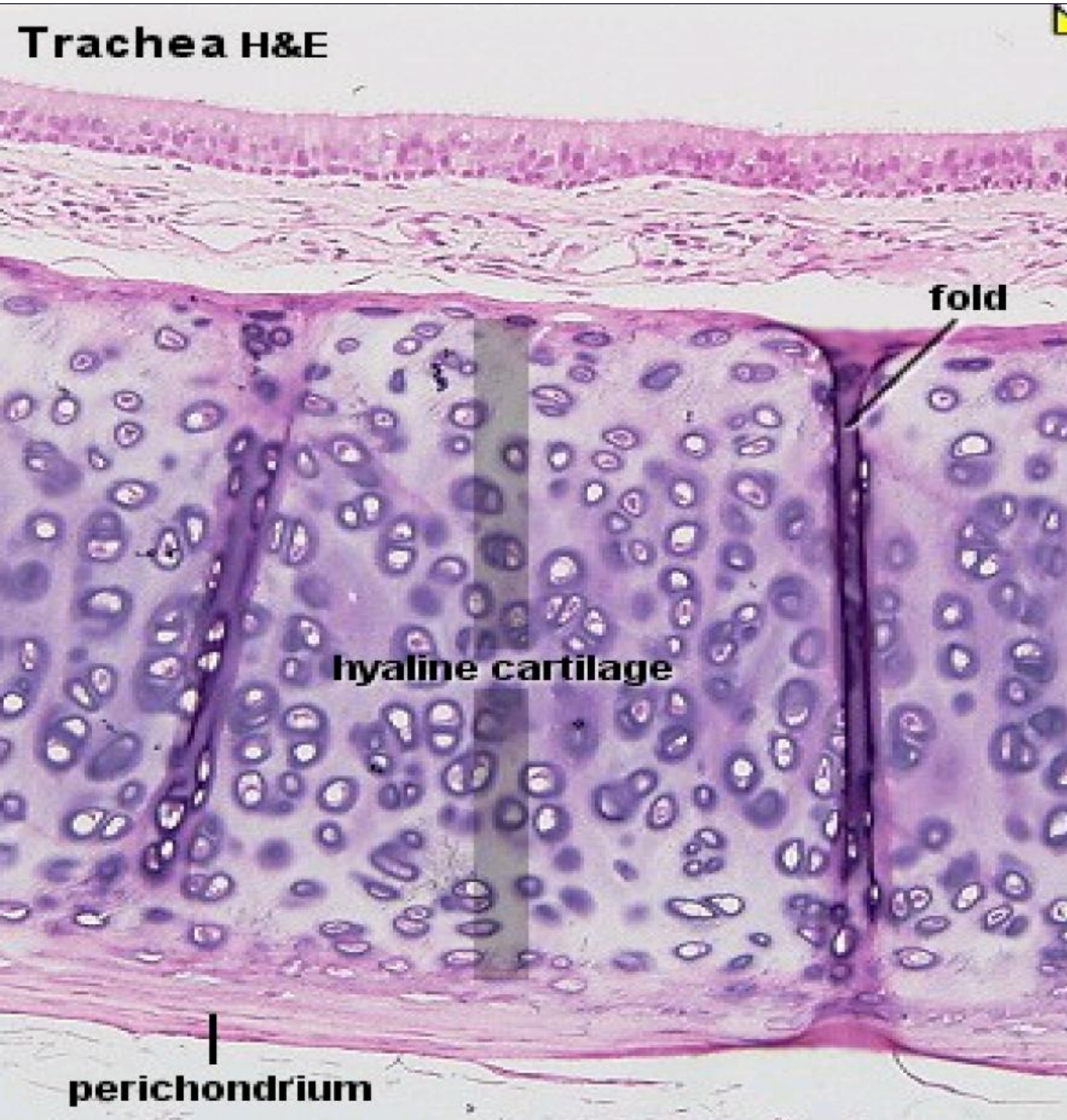
**is not surrounded by a perichondrium and is partly vascularised.**
**is, depending on the arrangement of chondrocytes and collagenous fibres, divided into several zones:**

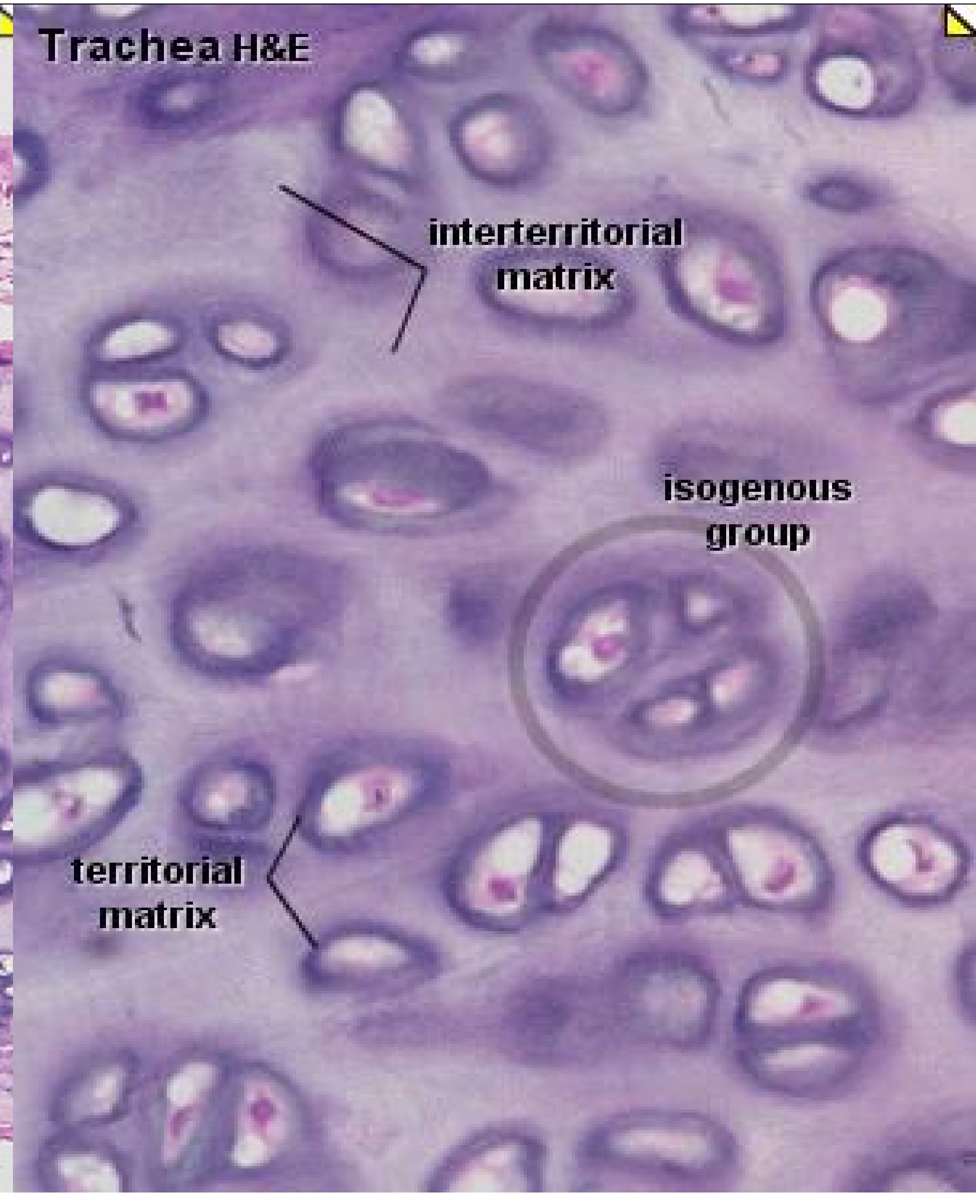

Gliding surface
Superficial Zone
Fibers parallel to surface
Transitional Zone
Random Fibers
Deep Zone
Fibers perpendicular to surface
TIDEMARK
Subchondral Bone
Cancellous Bone

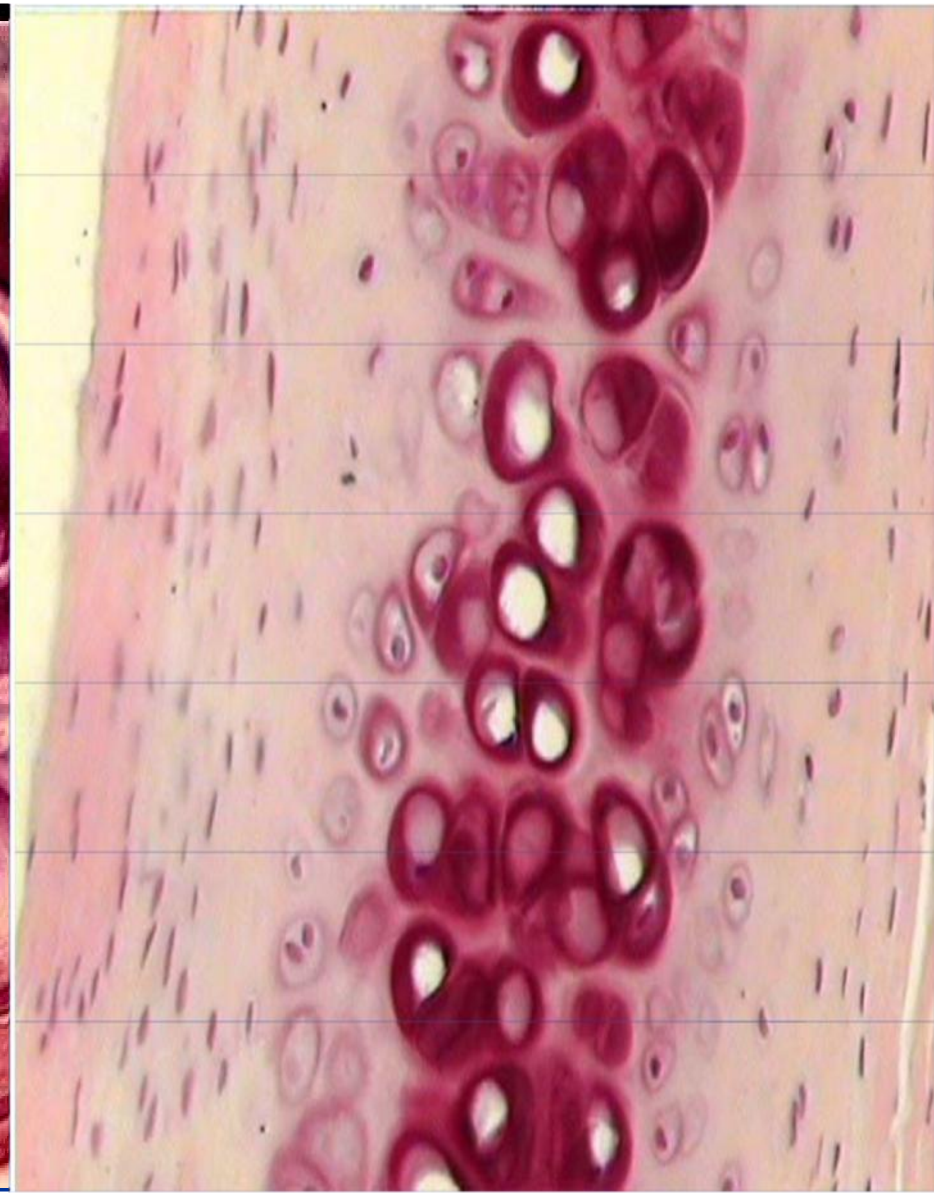

Supplemental Slide 109
Developing Bone
Articular cartilage




proliferating chondrocytes
bone marrow
maturing cartilage
hypertrophic cartilage
bone
calcified cartilage
bone


Trachea H&E
fold
hyaline cartilage
perichondrium


Trachea H&E
interterritorial
matrix
isogenous
group
territorial
matrix

# Hyaline Cartilage

**Matrix** (amorphous & glassy)

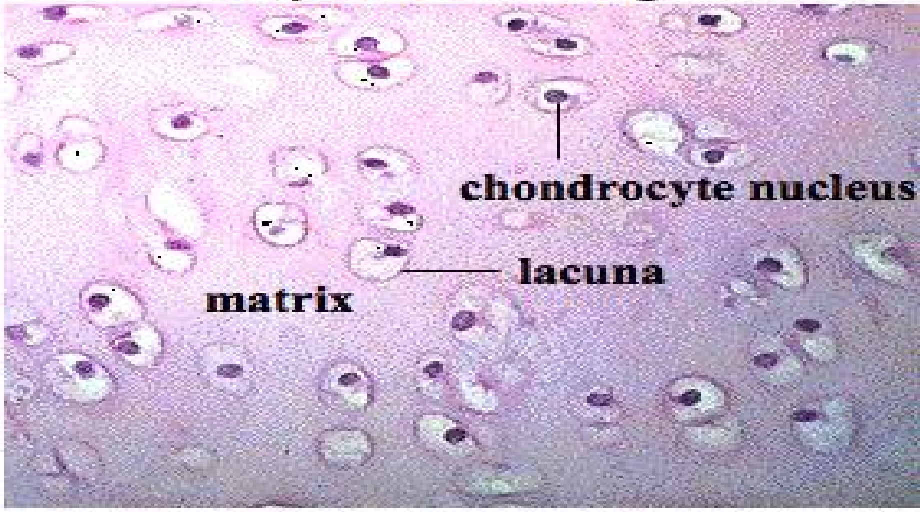
- hyaluronic acid
- chondroitin sulfate
- keratin sulfate
- $H_2O$ (60-78%)

**Fibers-** collagenous
(invisible due to same refractive index as matrix)

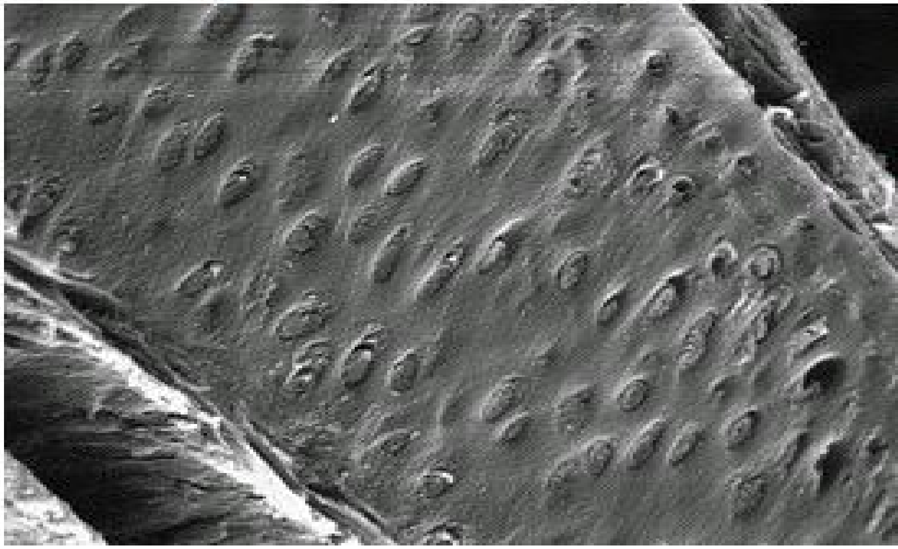
**Typical Locations**

- intercostals (connect ribs to the sternum)
- wall of trachea & bronchii
- articular cartilage of bone
- epiphyseal plate
- fetal axial skeleton

Hyaline Cartilage

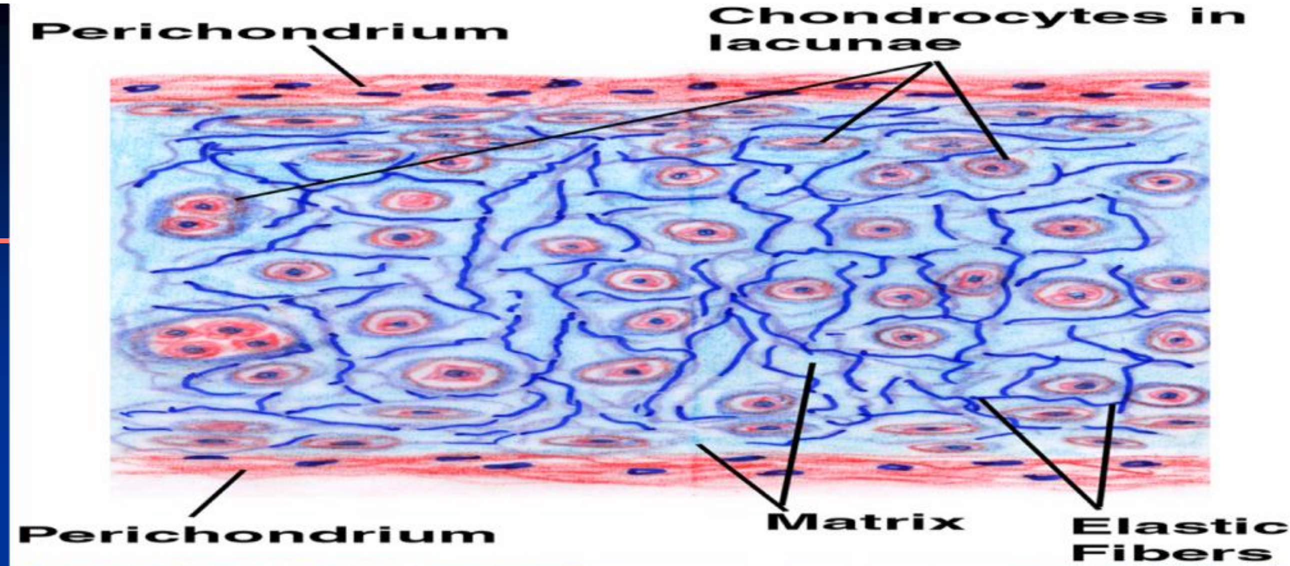


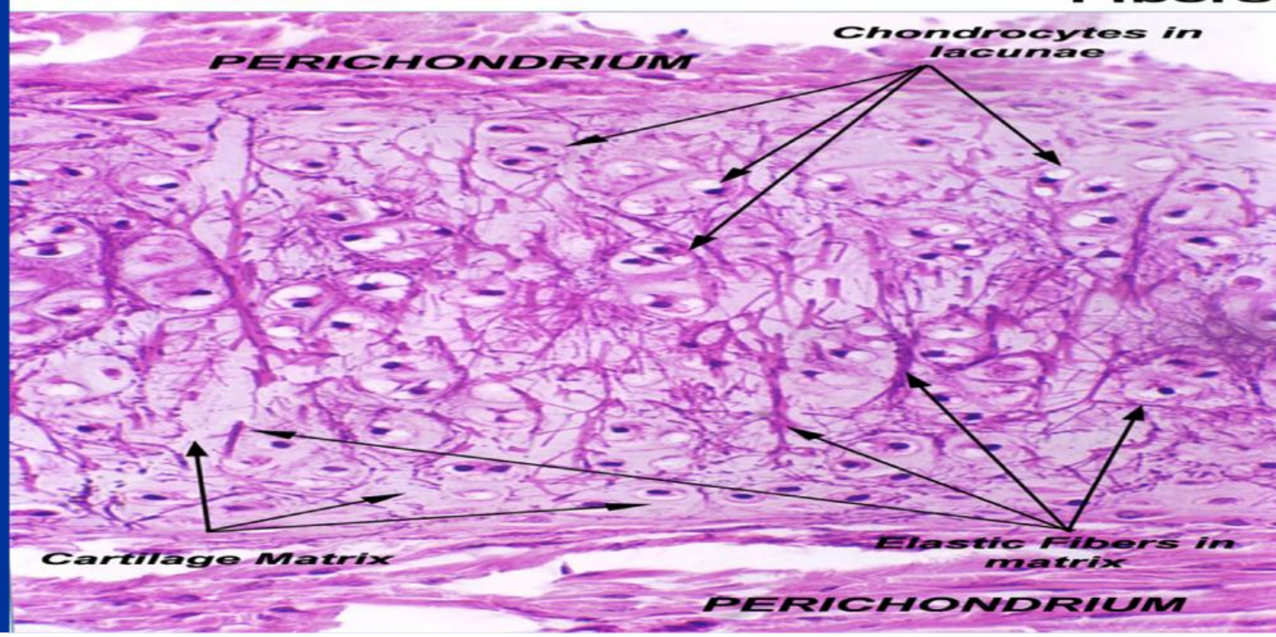

Hyaline Cartilage (SEM)

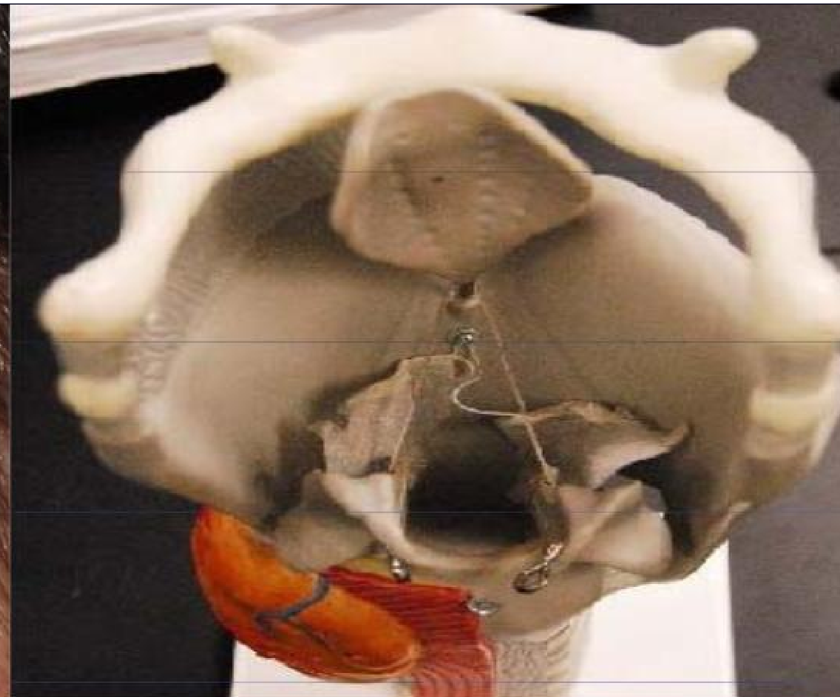


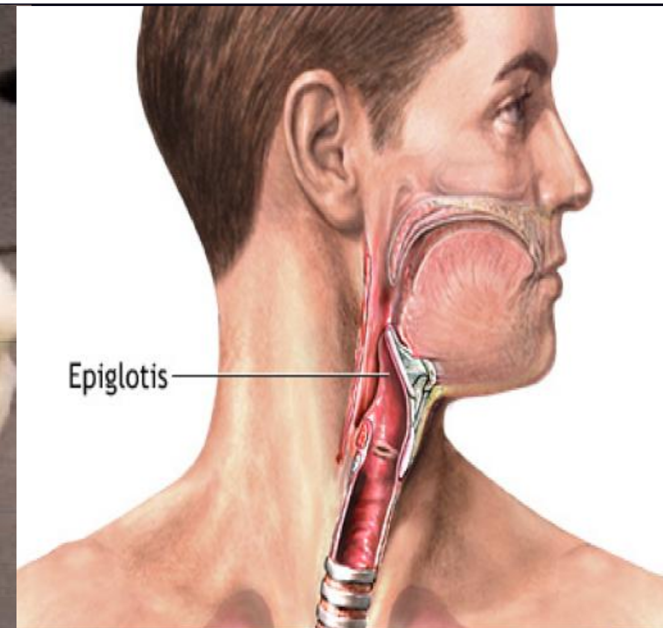
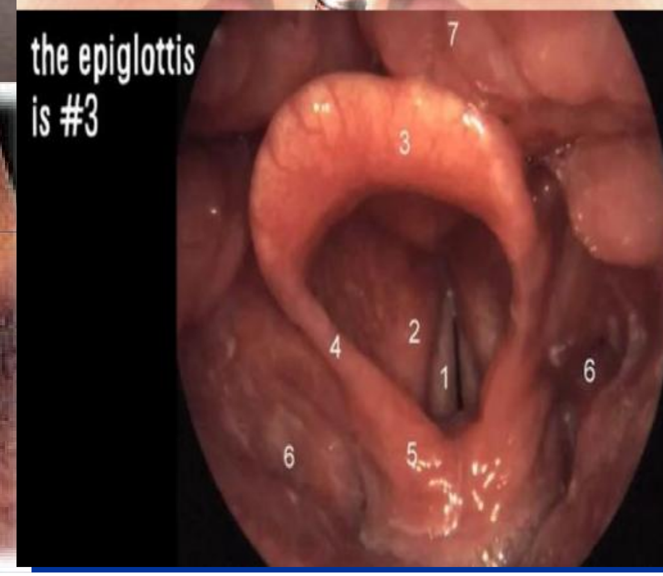
# Elastic Cartilage

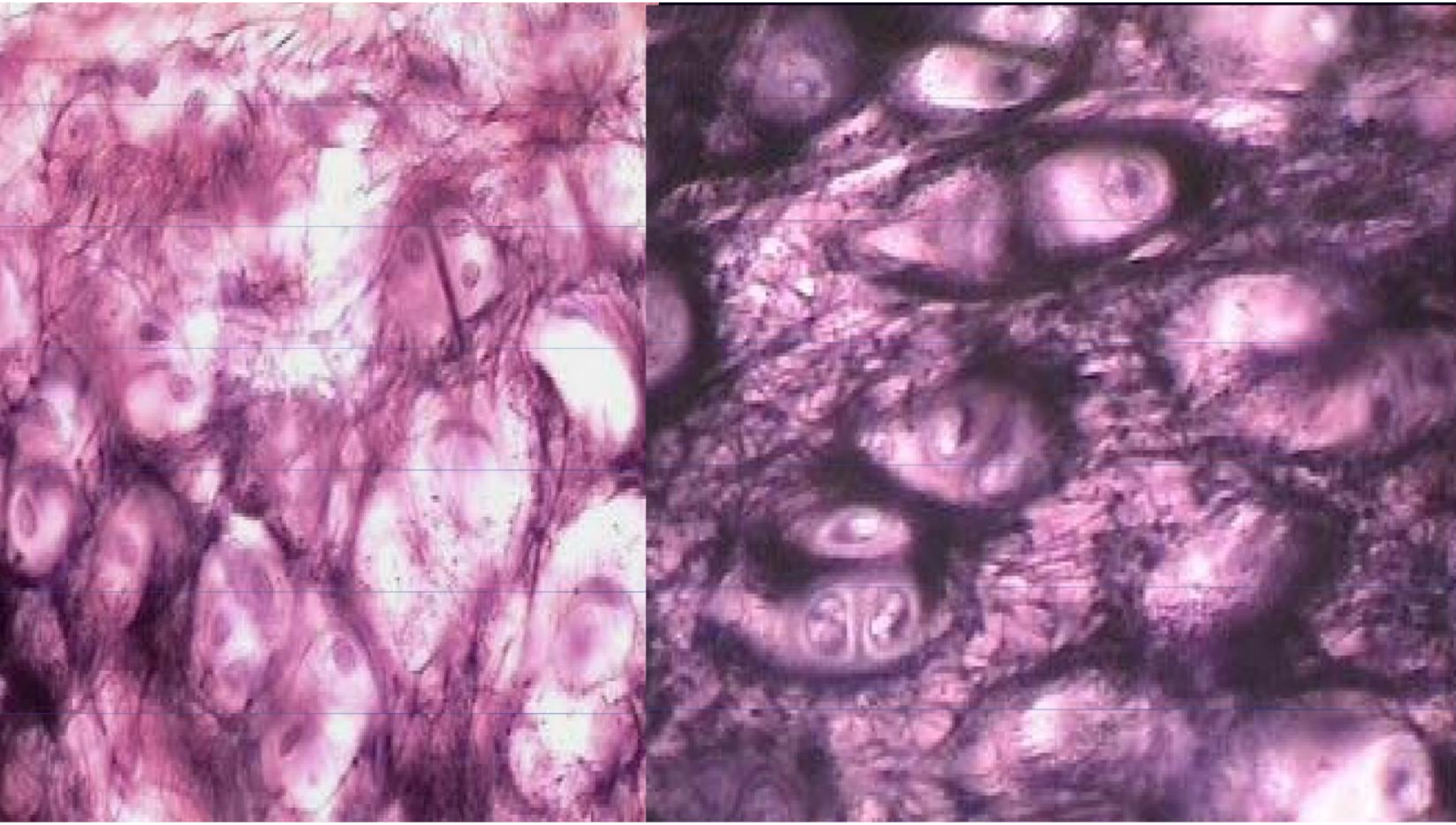
- Similar to hyaline cartilage, but contains elastic fibers
- Found in the external ear and the epiglottis




Epiglotis

the epiglottis is #3
7
3
2
4
1
6
6
5



# Elastic Cartilage

**Matrix**

hyaluronic acid
chondroitin sulfate
kertatin sulfate

**Fibers**

elastic (elastin)

**Typical Locations**

external ear

walls of external auditory canal and eustachian tubes

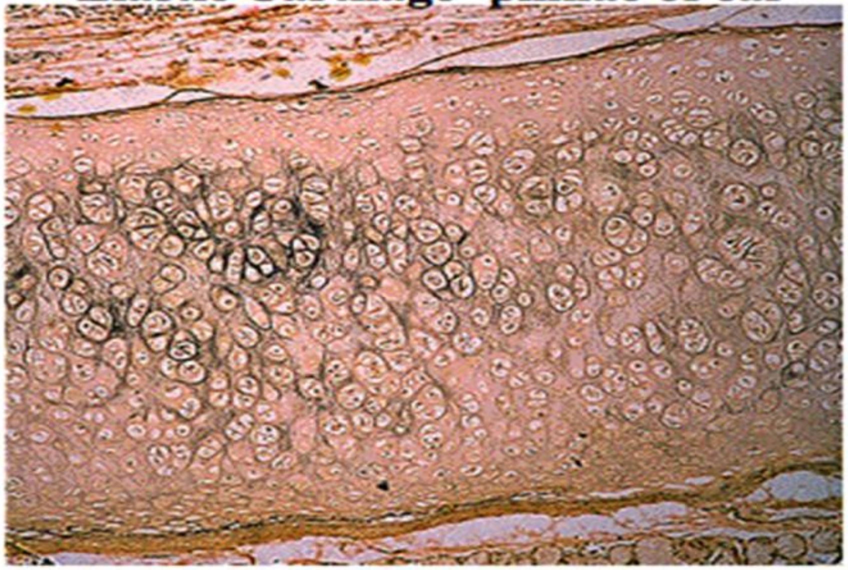
epiglottis & larynx

bridge of nose

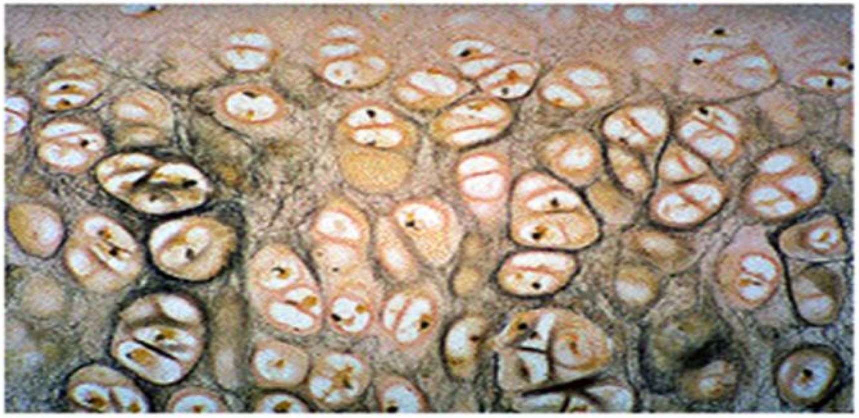
**Properties**

resiliency and pliability

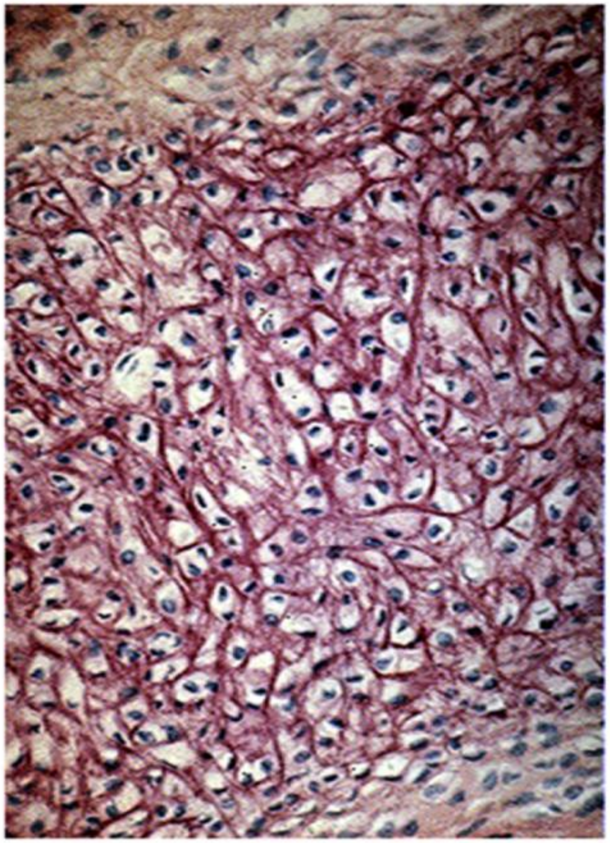
Elastic Cartilage- pinnae of ear



Elastic Fibers- silver stain



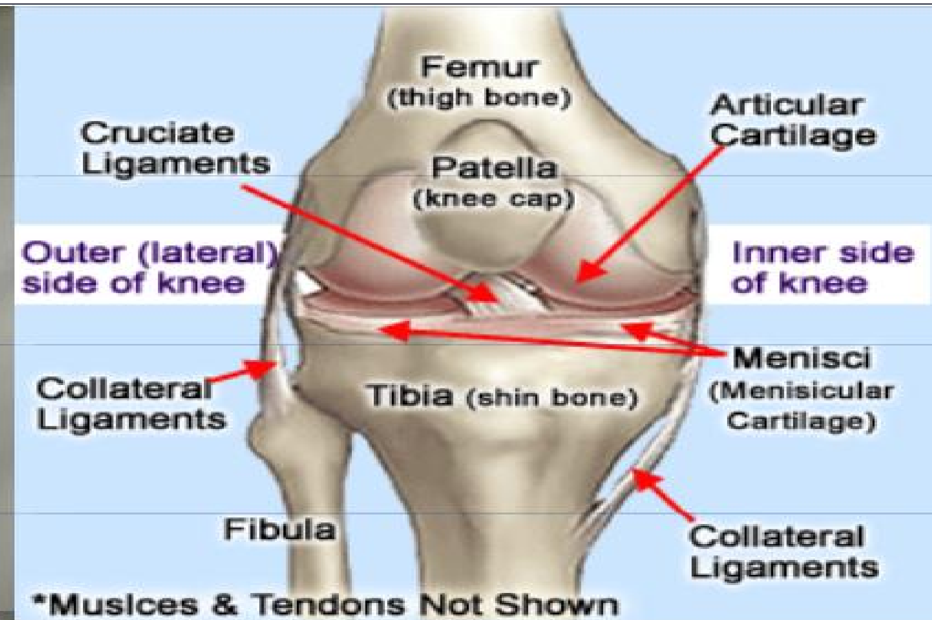
Elastic Fibers (resorcin-fuchsin stain)

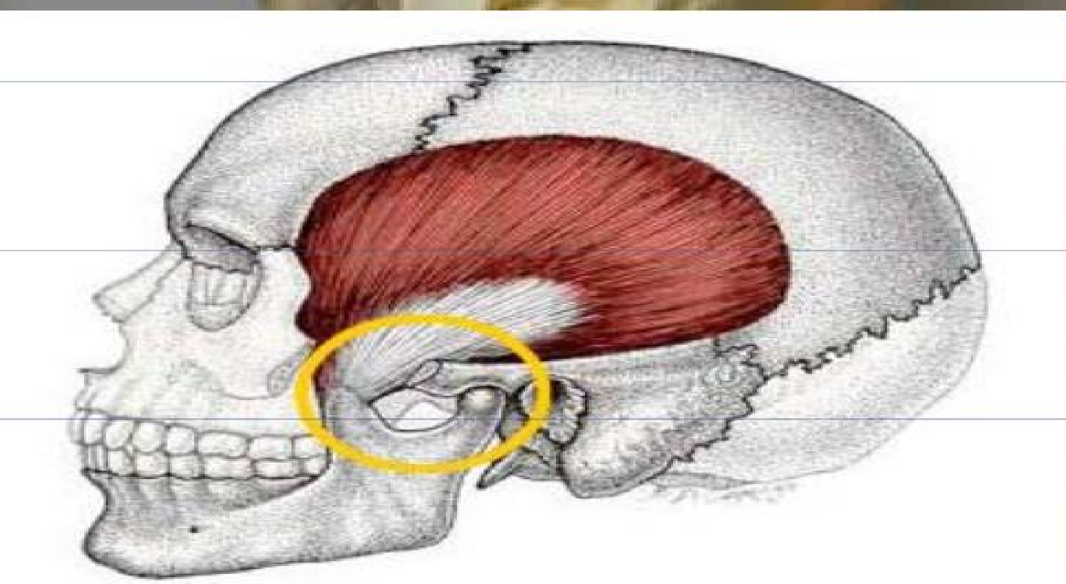


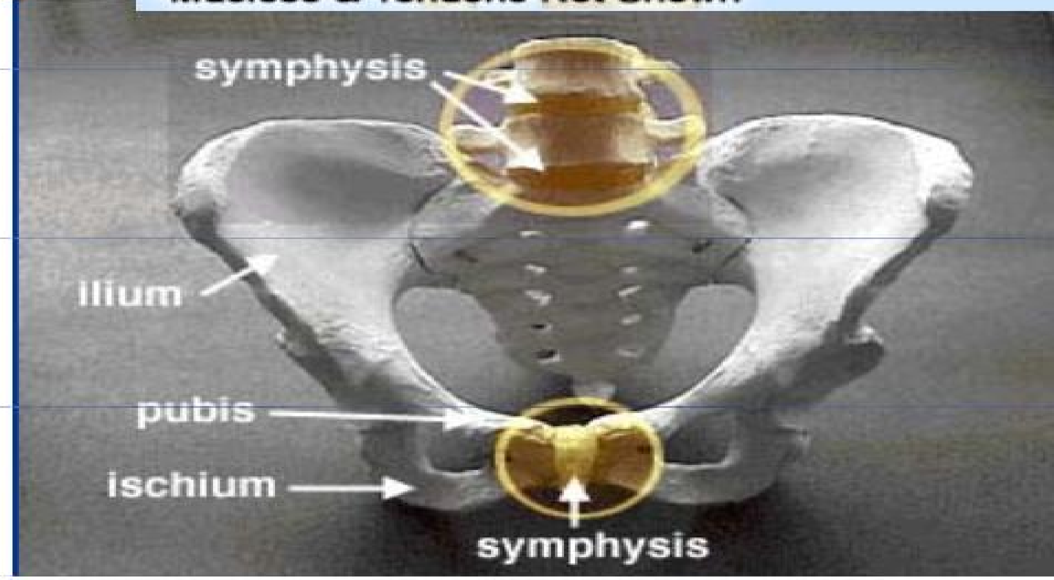
# Fibrocartilage

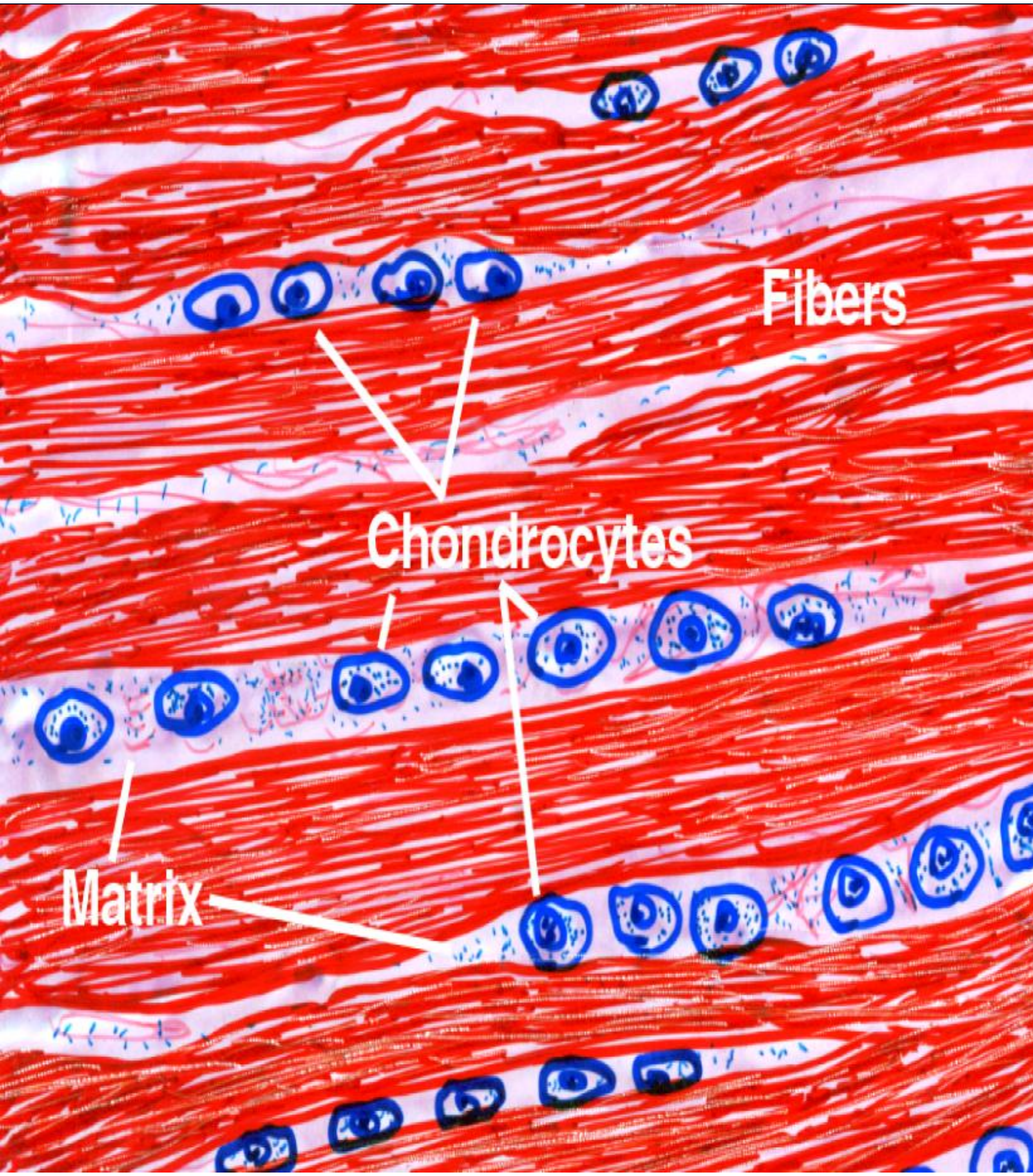
- Highly compressed with great tensile strength
- Contains collagen fibers type I in addition to type II
- Found in menisci of the knee and in intervertebral discs, TMJ,Pubic symphysis

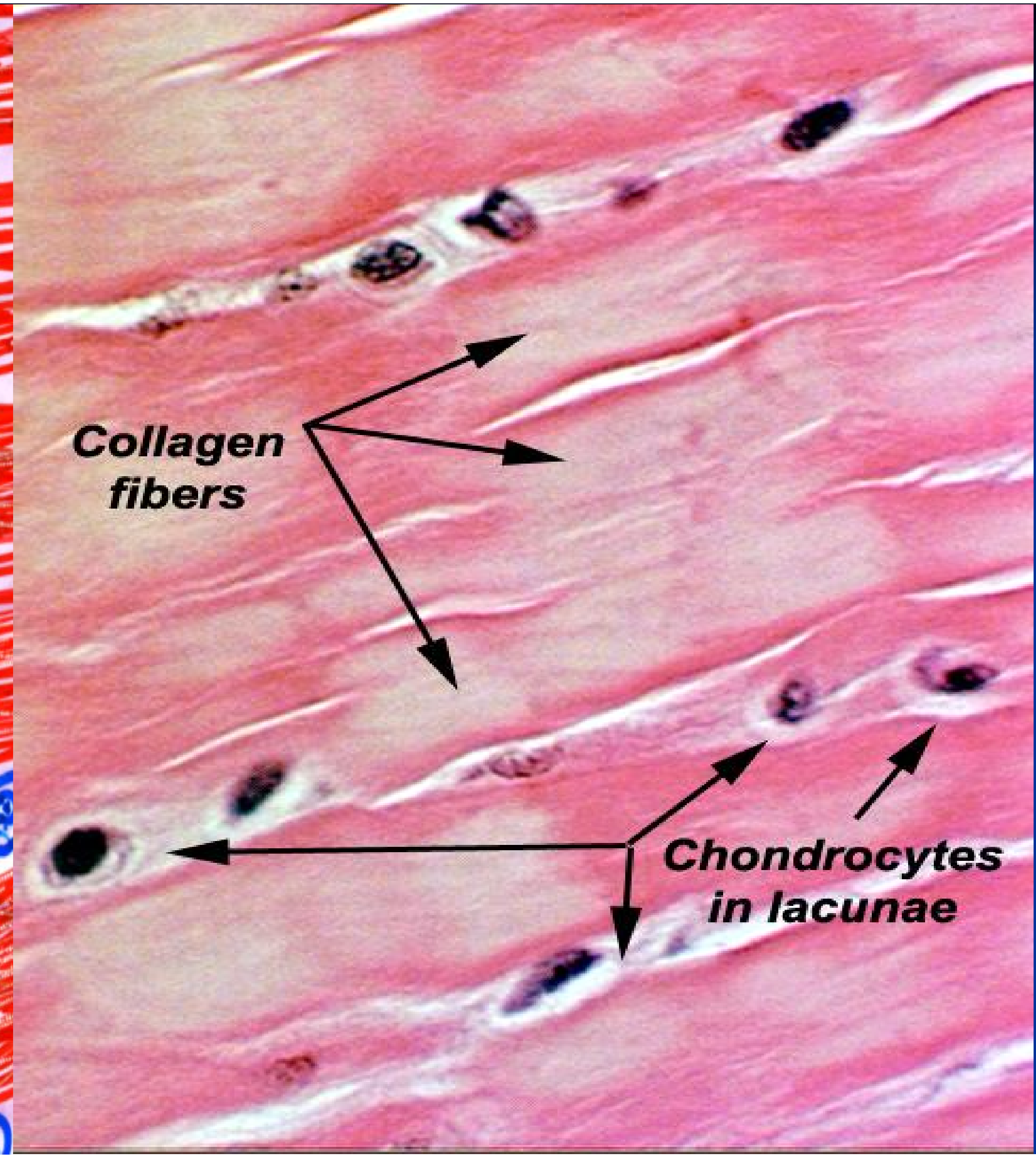

Lateral Meniscus
Medial Meniscus

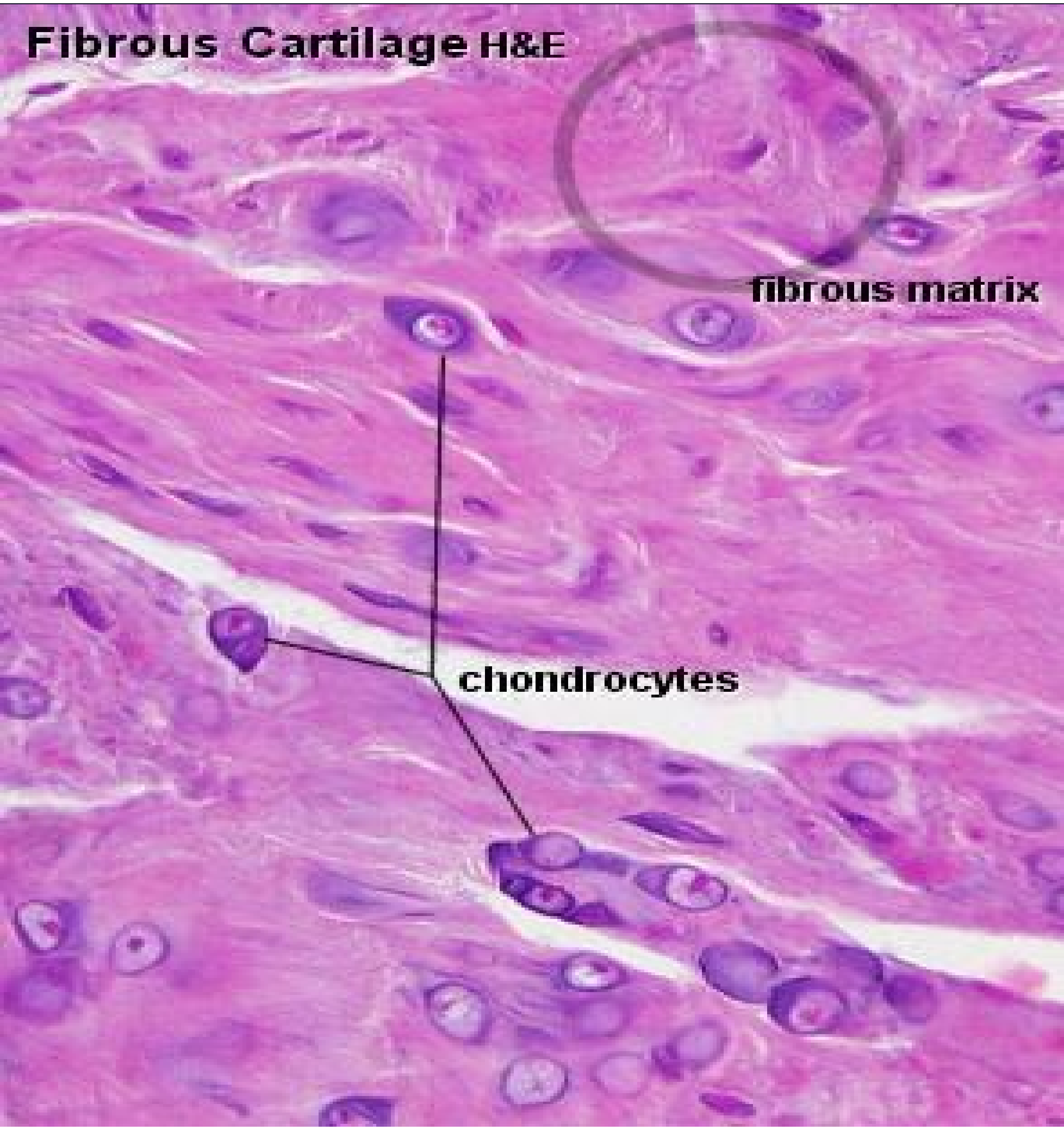

Femur
(thigh bone)
Articular Cartilage
Cruciate Ligaments
Patella
(knee cap)
Outer (lateral) side of knee
Inner side of knee
Menisci
(Menisicular Cartilage)
Collateral Ligaments
Tibia (shin bone)
Fibula
Collateral Ligaments
*Muslces & Tendons Not Shown

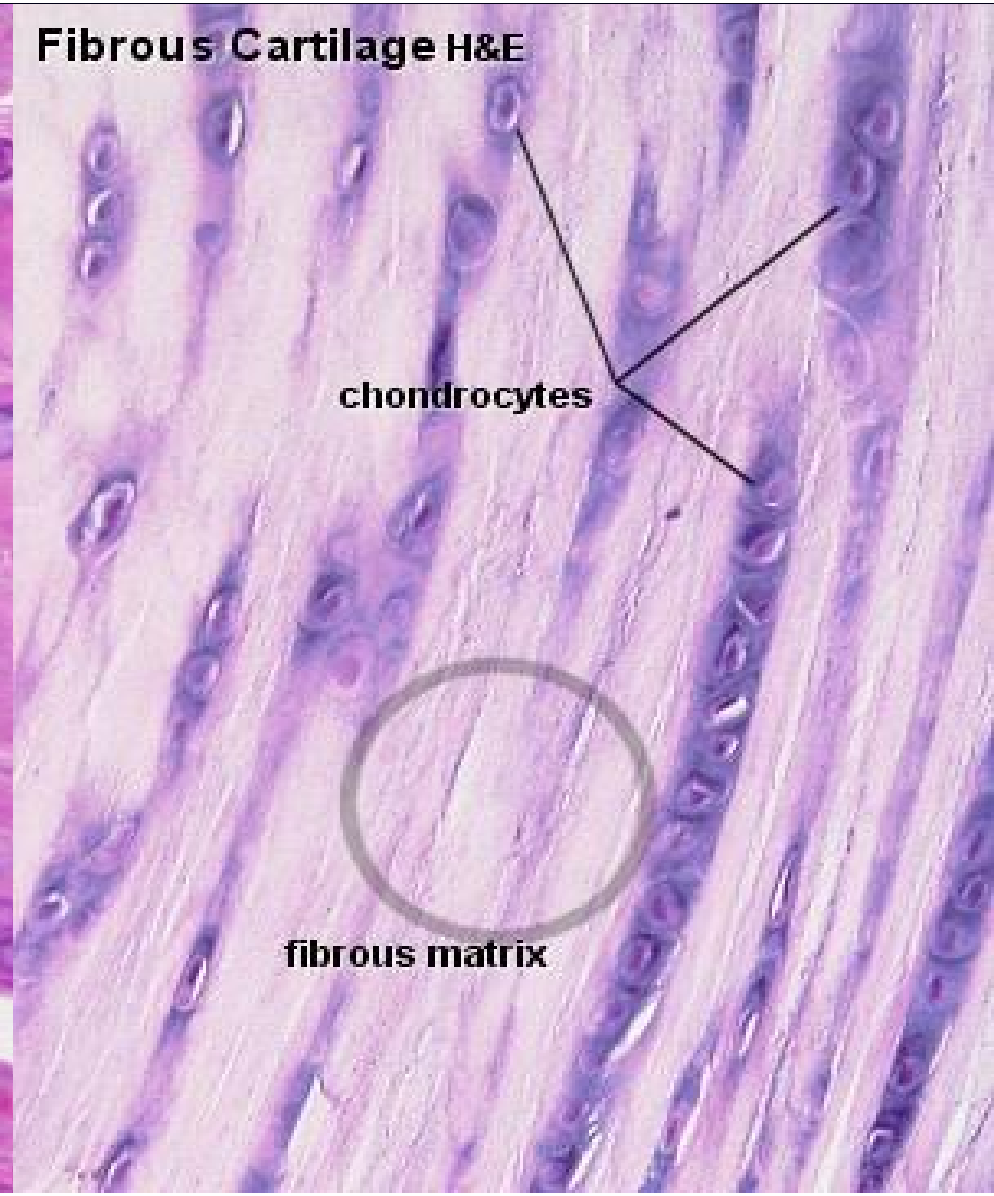


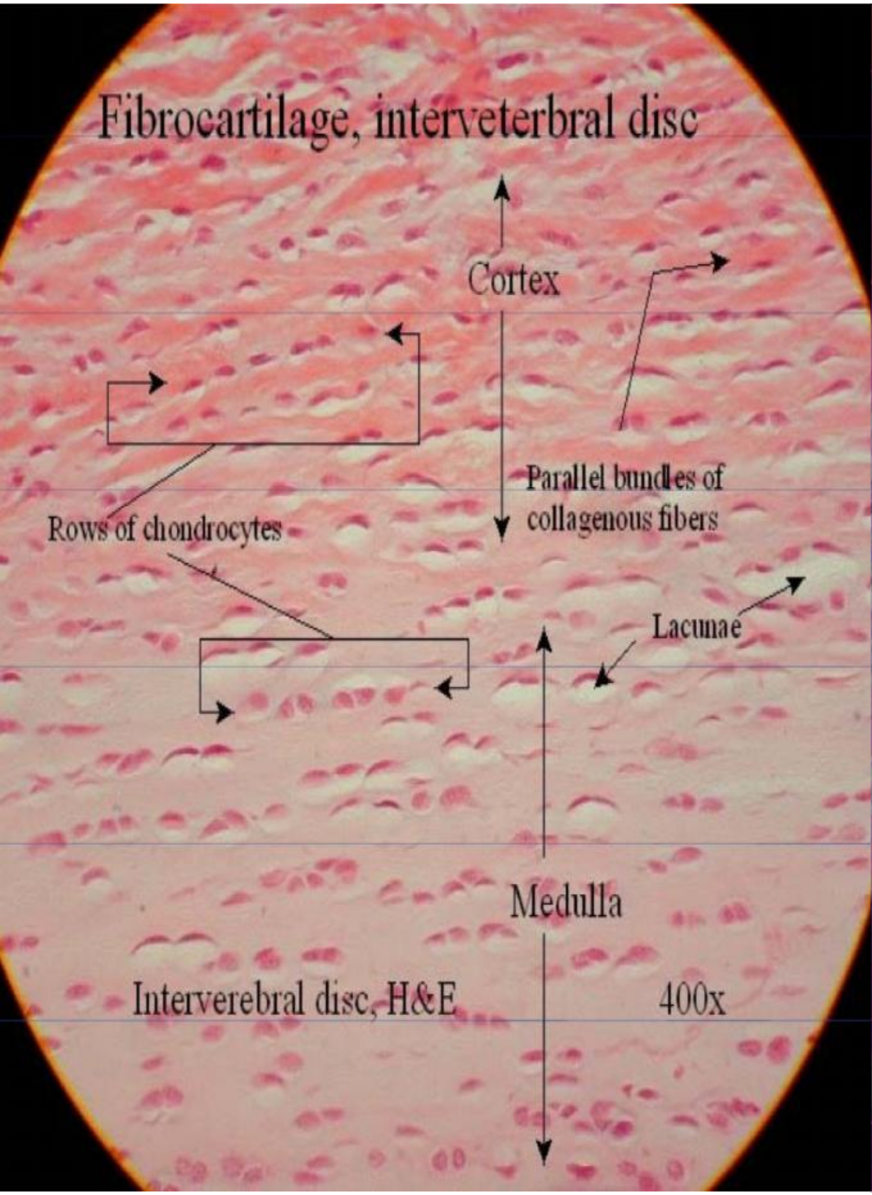

symphysis
ilium
pubis
ischium
symphysis

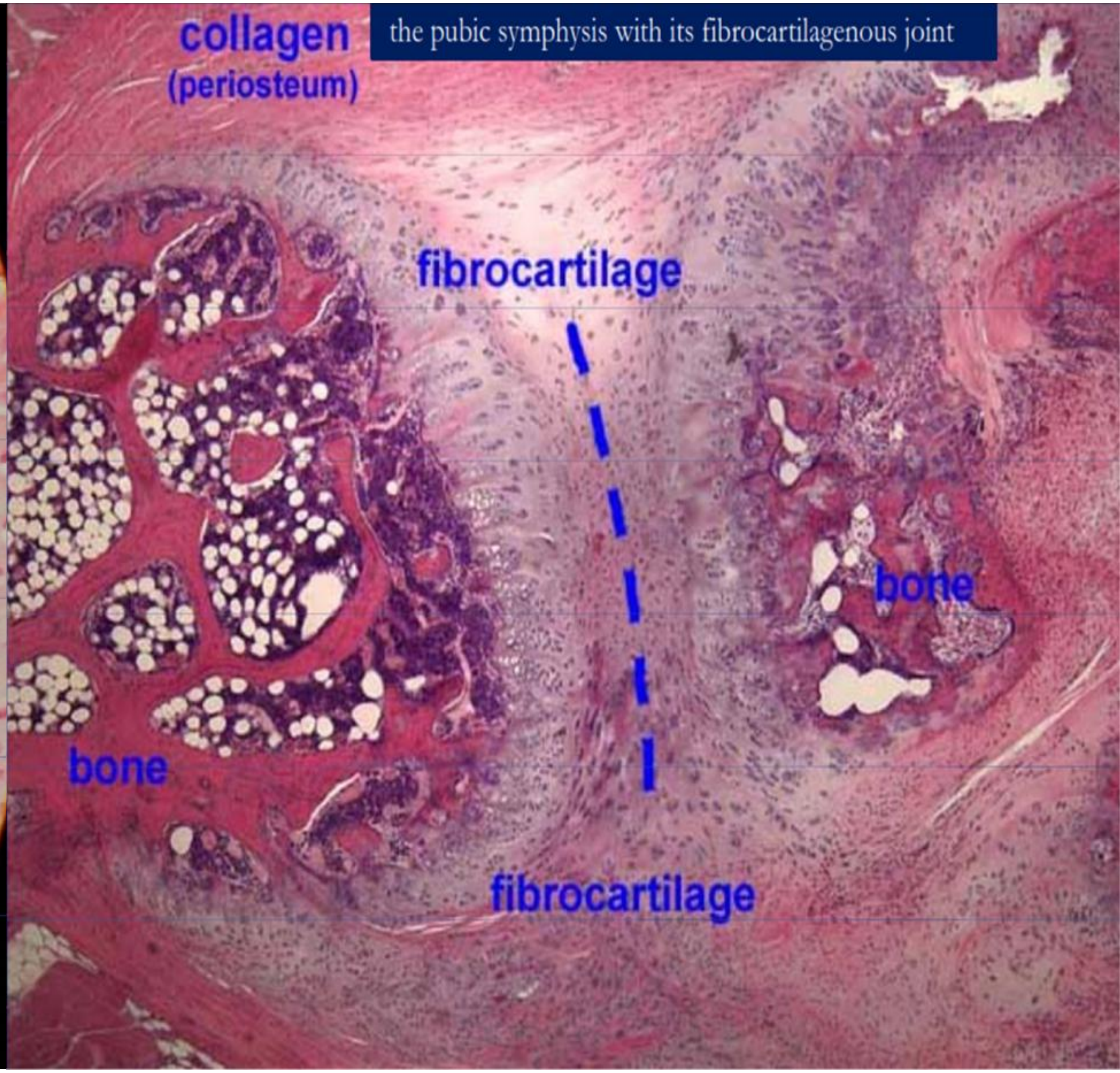

Fibers
Chondrocytes
Matrix

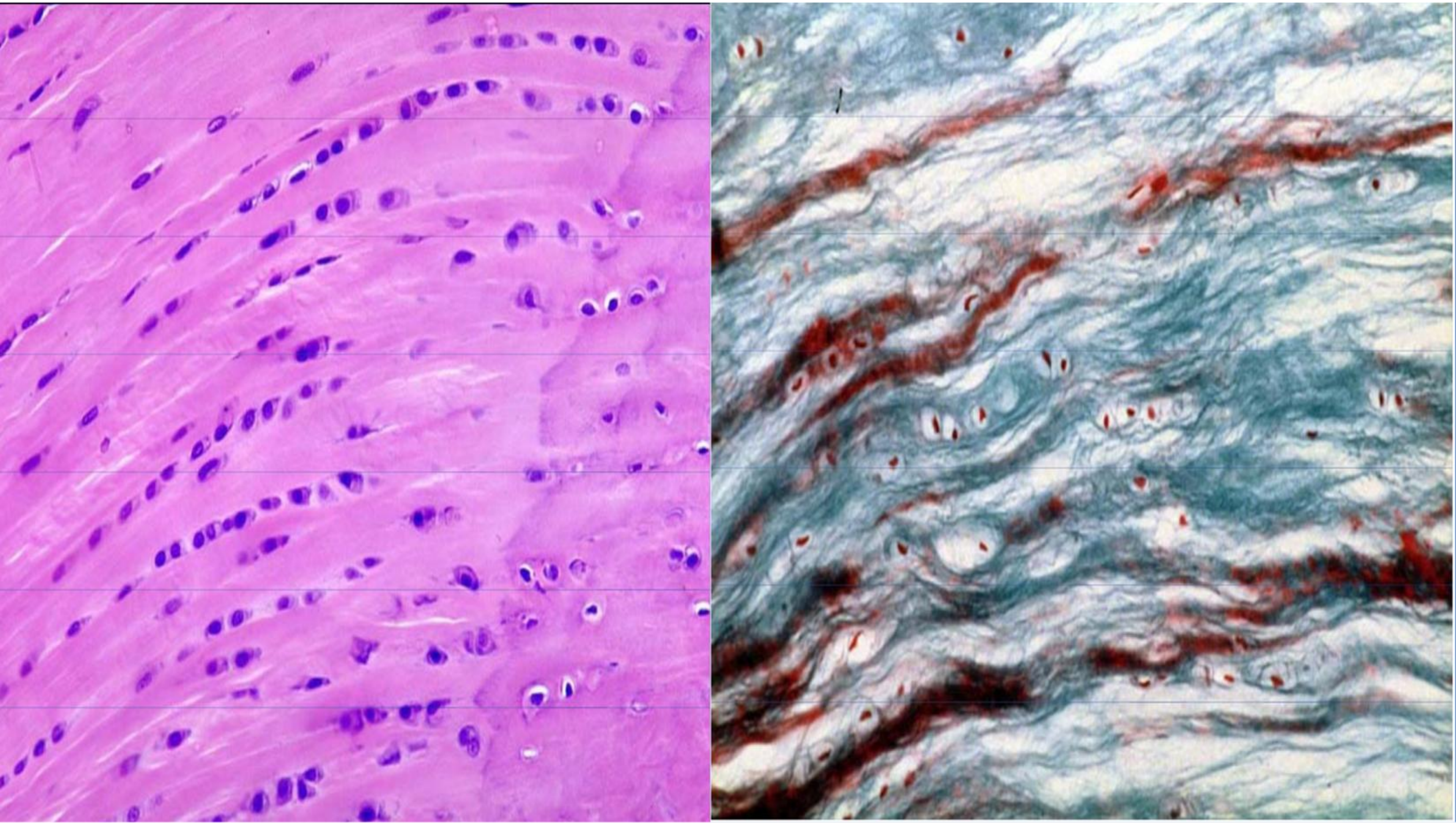

Collagen fibers
Chondrocytes in lacunae


Fibrous Cartilage H&E
fibrous matrix
chondrocytes


Fibrous Cartilage H&E
chondrocytes
fibrous matrix


Fibrocartilage, interveterbral disc
Cortex
Parallel bundles of collagenous fibers
Rows of chondrocytes
Lacunae
Medulla
Interverebral disc, H&E
400x


the pubic symphysis with its fibrocartilagenous joint
collagen
(periosteum)
fibrocartilage
bone
bone
fibrocartilage



# Fibrocartilage

## Matrix

hyaluronic acid
chondroitin sulfate
keratin sulfate

## Fibers

dense collagenous bundles

## Typical Locations

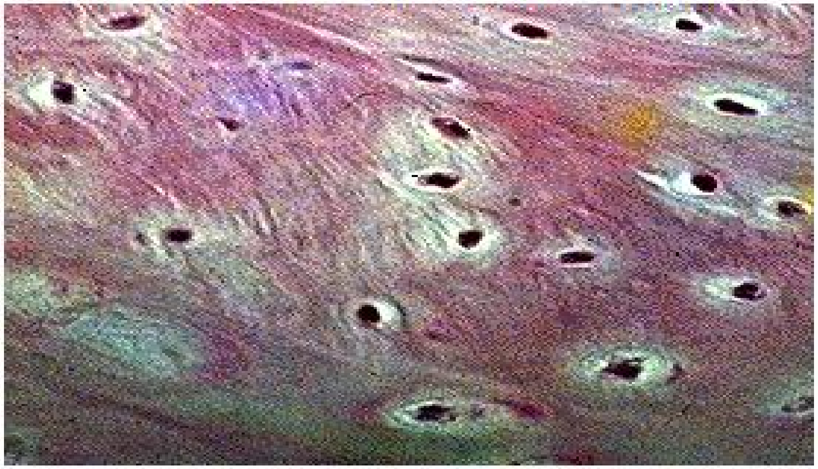
intervertebral discs
pubic symphysis
meniscus of knee joint
attach tendons to bone

## Properties

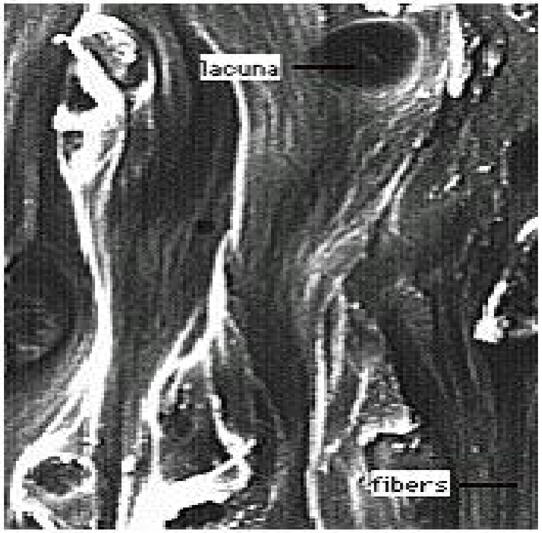
resistance to compression and shear forces

Fibrocartilage- longitudinal section

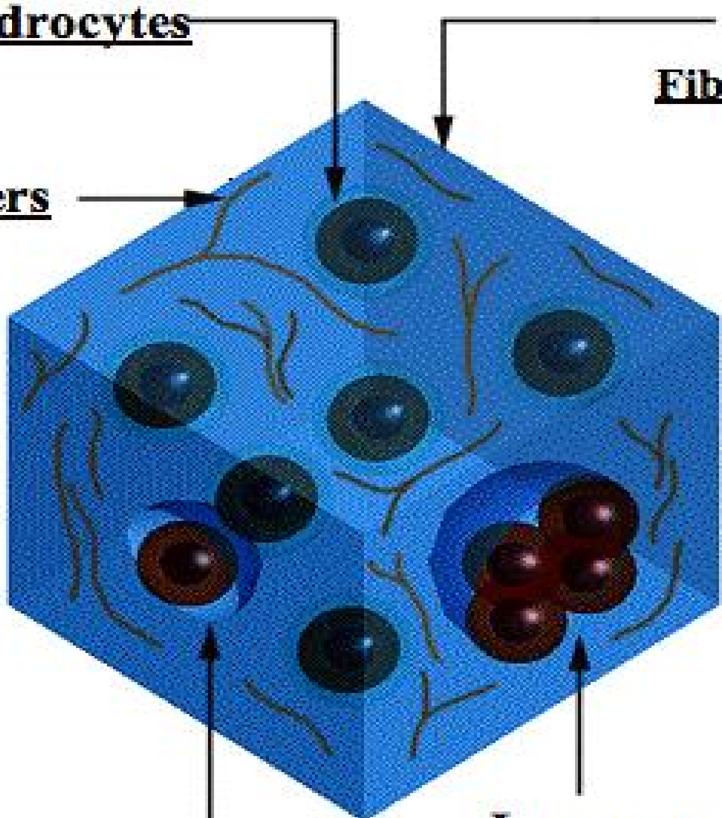

Fibrocartilage- transverse section



Fibrocartilage- SEM



# Cartilage




**Fibers**
(collagen Type II, elastic)

**Ground Substance**
(hyaluronic acid, chondroitin sulfate, keritin sulfate, 60-70% $H_2O$)

## Properties of Cartilage

1. Avascular
2. Permeable
   (conducts nutrients and water)
3. Flexible but Weight-Bearing
   (resistance to compression)
4. Elasticity and Resiliency
5. Resistance to Shear Forces
6. Slippery
   (low friction at articular joints)
7. Poor Regenerative Capacity

# Bones and Cartilages of the Human Body

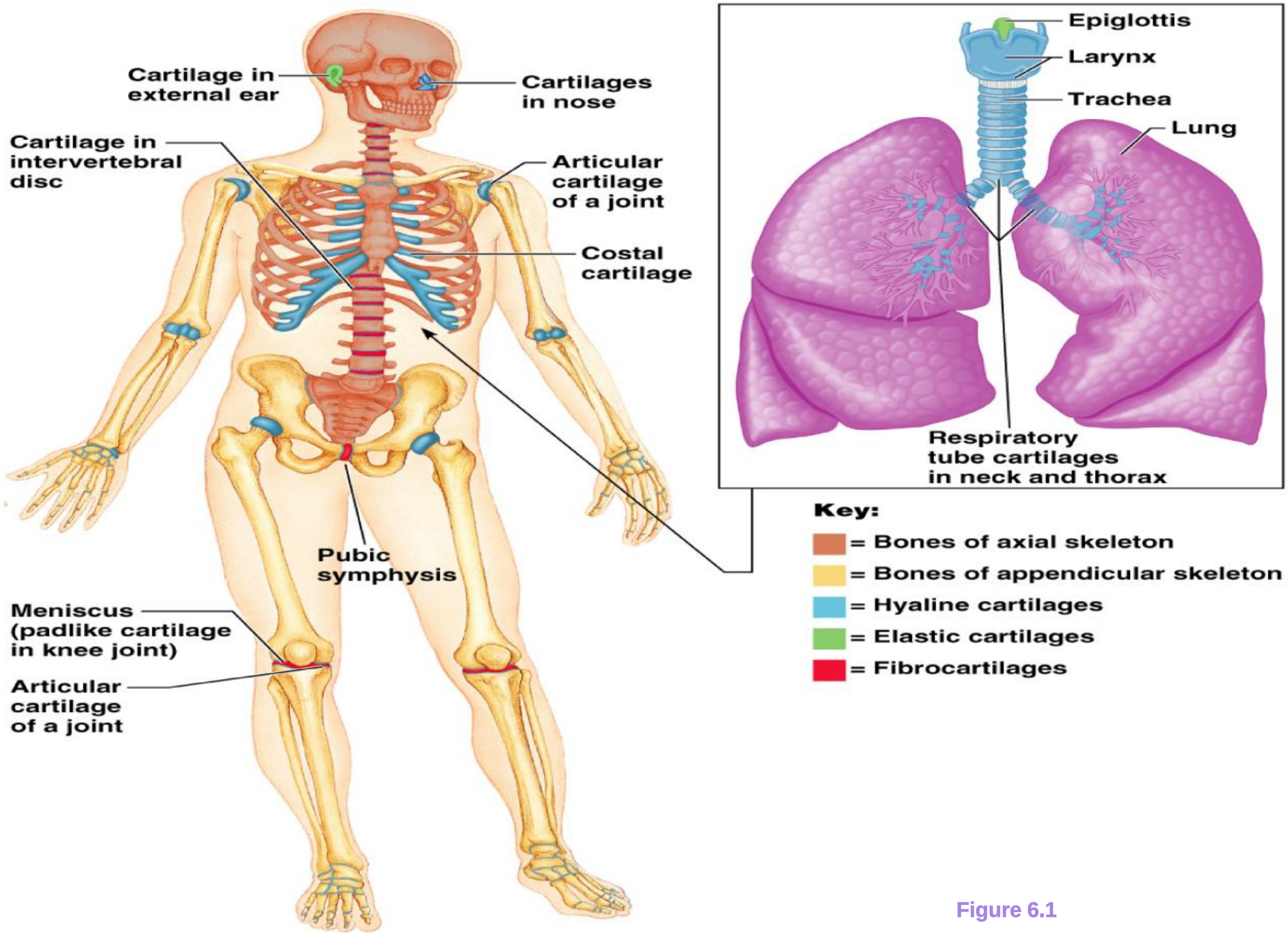



Figure 6.1

# Distribution of The Various Types Of Cartilage

**Hyaline Cartilage**

- Most bones of the embryonic skeleton
- Articular cartilage (synovial jt)
- Epiphyseal Plate
- Costal Cartilage
- Xiphoid process
- Nasal Cartilages
- Most Laryngeal Cartilages
- Tracheal Ring Cartilages
- Cartilage plates in large
- and medium bronchi

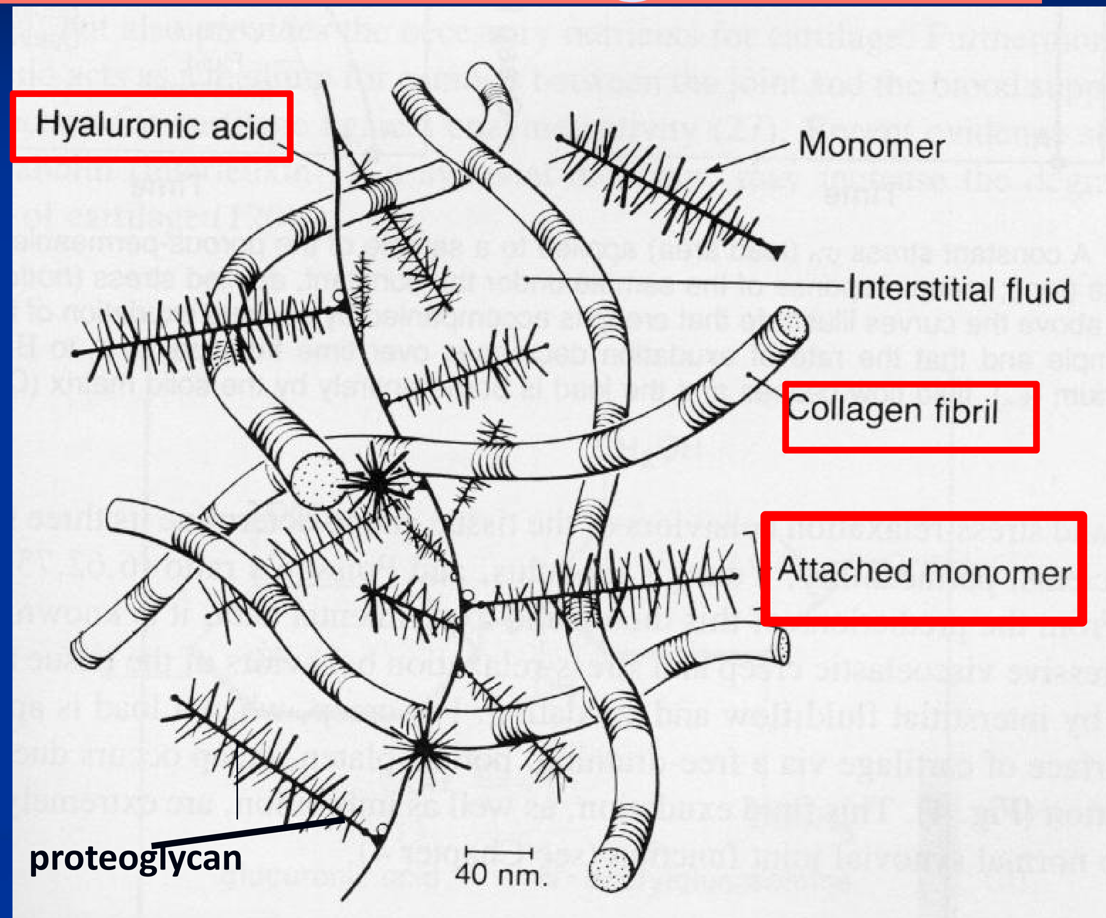
- **Elastic Cartilage**
  - Pinna
  - External Auditory tube
  - Eustachian Tube
  - Epiglottis
  - Laryngeal Cartilages (2)
  - Cartilage plates in small
  - bronchi
- **Fibrocartilage**
  - Symphyses
  - - Intervertebral disks
  - - Pubic symphysis
  - Menisci

# GENERAL CHARACTERISTICS OF CARTILAGE

- • Growth: appositional and interstitial
- • Perichondrium
- – Two layers:
- • Outer fibrous (type 1 collagen)
- • Inner chondrogenic (appositional growth)
- – Not found in articular cartilage and fibrocartilage
- • Cells = chondrogenic cells, chondroblasts, and chondrocytes
- • Matrix (ground substance and collagen)
- – Territorial matrix, rich in GAG's= basophilic, surrounds
- lacunae (also called "capsular" matrix)
- – Interterritorial matrix, less basophilic
- – Matrix binds water (negatively charged GAG's attract Na+, H20
- follows); resistant to compression
- • Avascular (nourished by diffusion)

# Components of Cartilage

- Water
  - 70%
- Collagen Type II, IX, XI
  - 10-20%
  - Tensile strength
  - Shear strength
- Proteoglycans
  - 5-10%
  - Compressive strength
- Chondrocytes
  - Cells ~5%
  - Maintenance of tissue



# Collagen Types

**TABLE 2. Some Types of Collagen and their Characteristics**

| Collagen Type | Molecular Structure* | Tissues | Function |
|---|---|---|---|
| Type I | $[\alpha1(I)]_2\ \alpha2(I)$ | Bone, tendon, ligament, | Support tensile loads |
| Type II | $[\alpha1(II)]_3$ | Cartilage | Support tensile loads; primary collagenous constituent of articular cartilage |
| Type VI | $\alpha1(VI)\ \alpha2(VI)\ \alpha3(VI)$ | Cartilage | Pericellular adhesion molecule |
| Type IX | $\alpha1(IX)\ \alpha2(IX)\ \alpha3(IX)$ | Cartilage | Fibril association; stabilizes Type II |
| Type X | $[\alpha1(X)]_3$ | Cartilage | Hypertrophic zone of growth plate; role in calcification postulated |
| Type XI | $\alpha1(XI)\ \alpha2(XI)\ \alpha1(II)$ | Cartilage | Core of Type II; controls fibril growth |

(Martin 1998)

Major type of collagen in articular cartilage (~80%)

**Stabilizes and forms core of the collagen type II fibril**

| | Water | | Proteoglycans |
|---|---|---|---|
| Articular Cartilage | 68-85% | 10-20% (type I) | 5-10% |
| Meniscus | 60-70% | 15-25% (type II) | 1-2% |

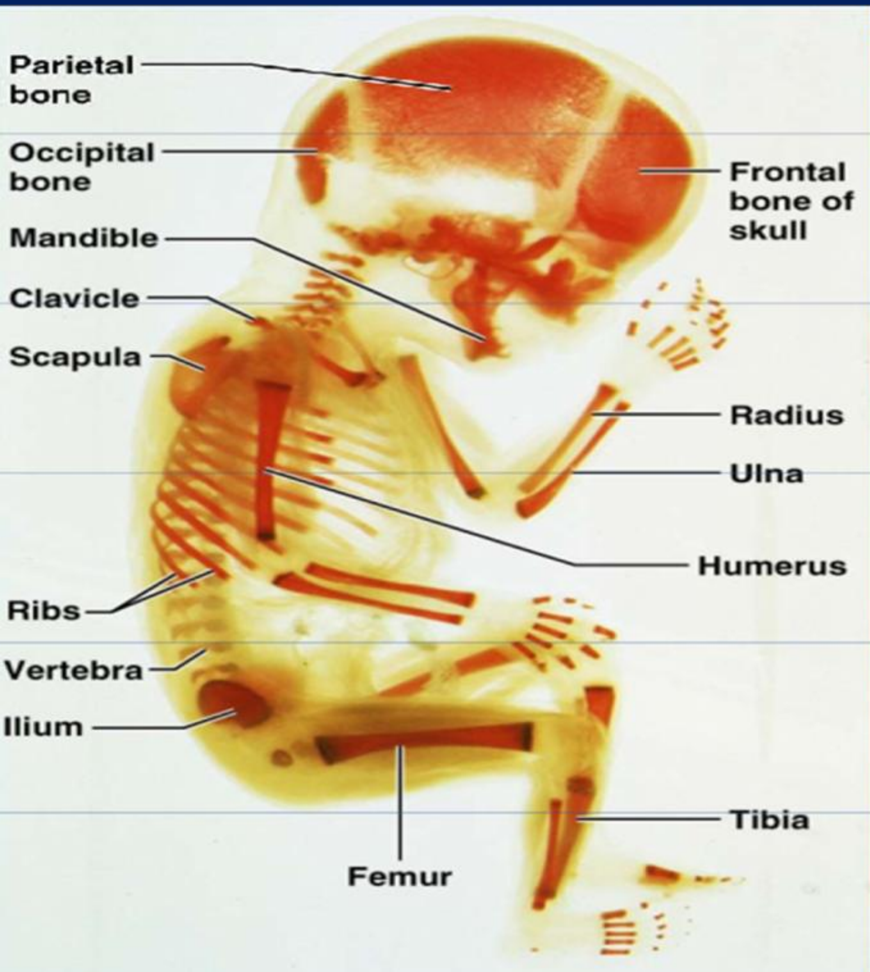
# Purpose of Cartilage

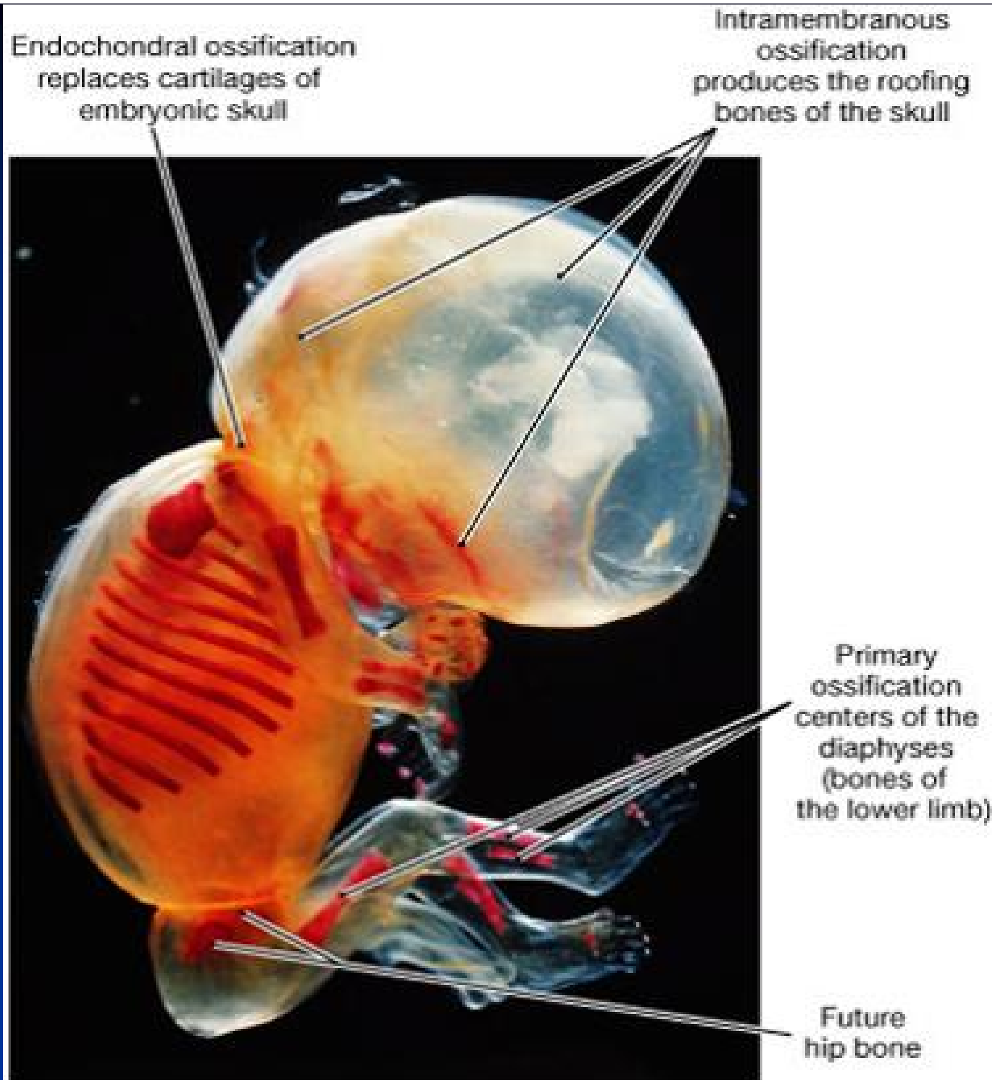
- Connective tissue
  - Transmit load from one bone to another
    - Load bearing surface about 2-3mm thick
  - Allows bones to articulate – or move with respect to one another
    - Friction

# Bone Development

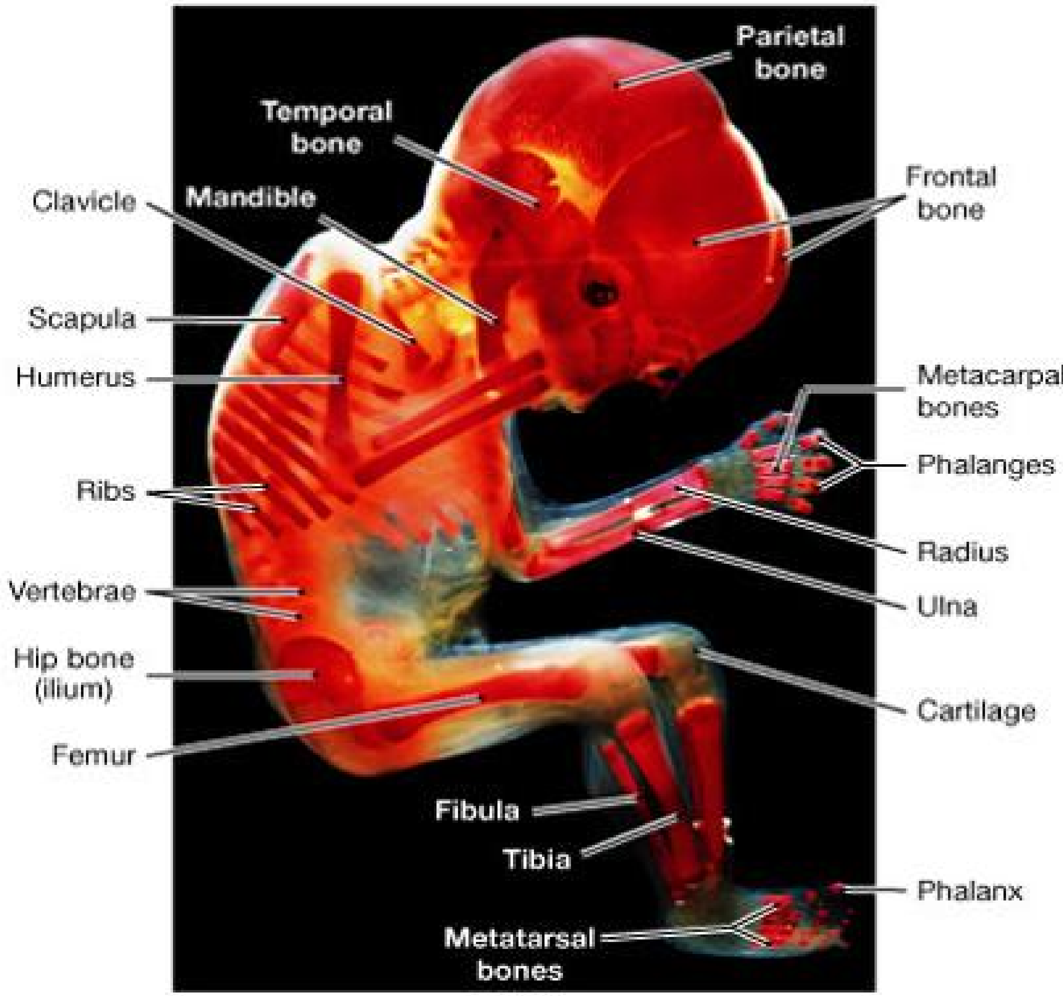
- **Osteogenesis and ossification** –
  - the process of bone tissue formation, which leads to:
    - **The formation of the bony skeleton in embryos**
    - **Bone growth until early adulthood**
    - **Bone thickness, remodeling, and repair**

# Fetal Primary Ossification Centers

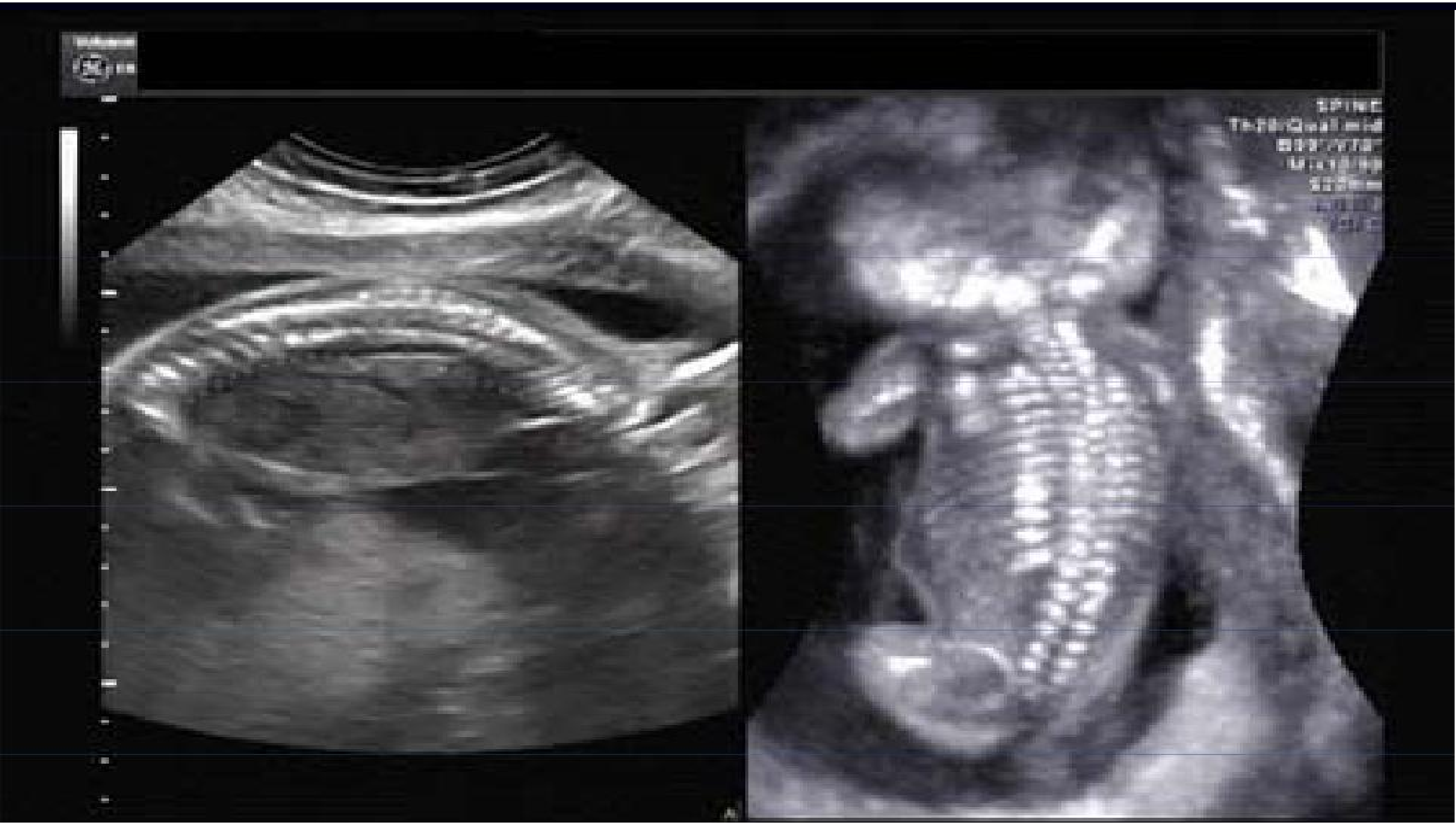




Endochondral ossification replaces cartilages of embryonic skull
Intramembranous ossification produces the roofing bones of the skull
Primary ossification centers of the diaphyses (bones of the lower limb)
Future hip bone

(a)

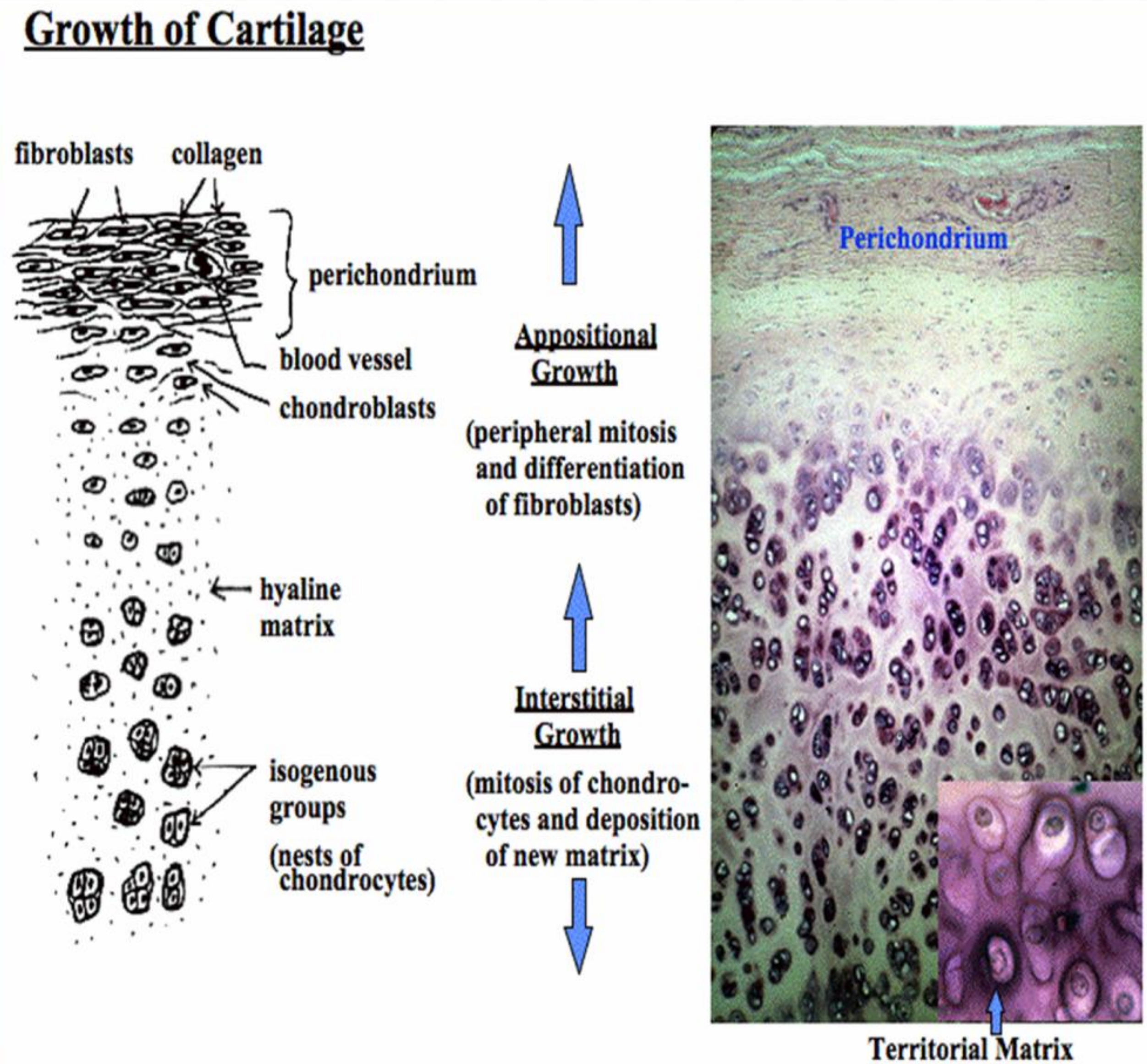

Parietal bone
Temporal bone
Frontal bone
Clavicle
Mandible
Scapula
Humerus
Metacarpal bones
Phalanges
Ribs
Radius
Vertebrae
Ulna
Hip bone (ilium)
Cartilage
Femur
Fibula
Tibia
Phalanx
Metatarsal bones

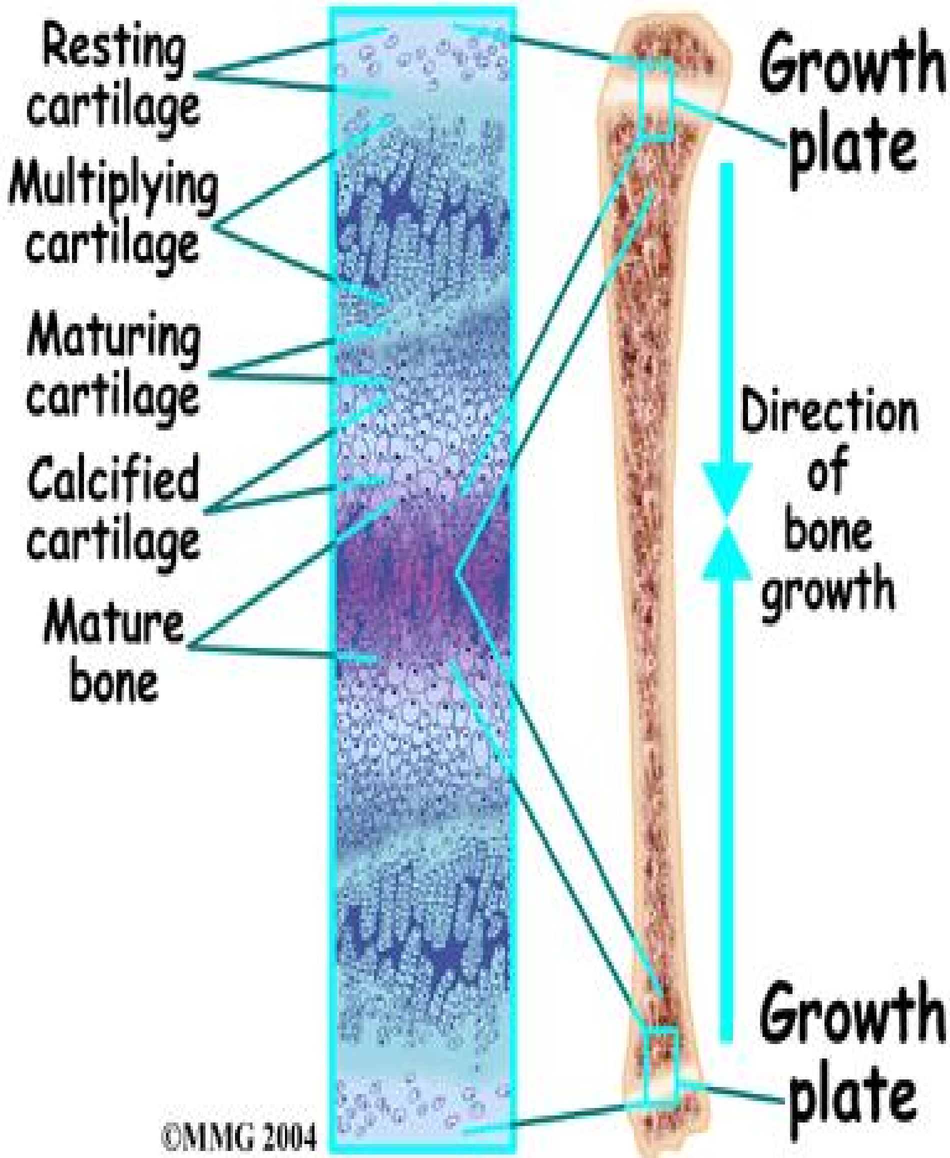
(b)

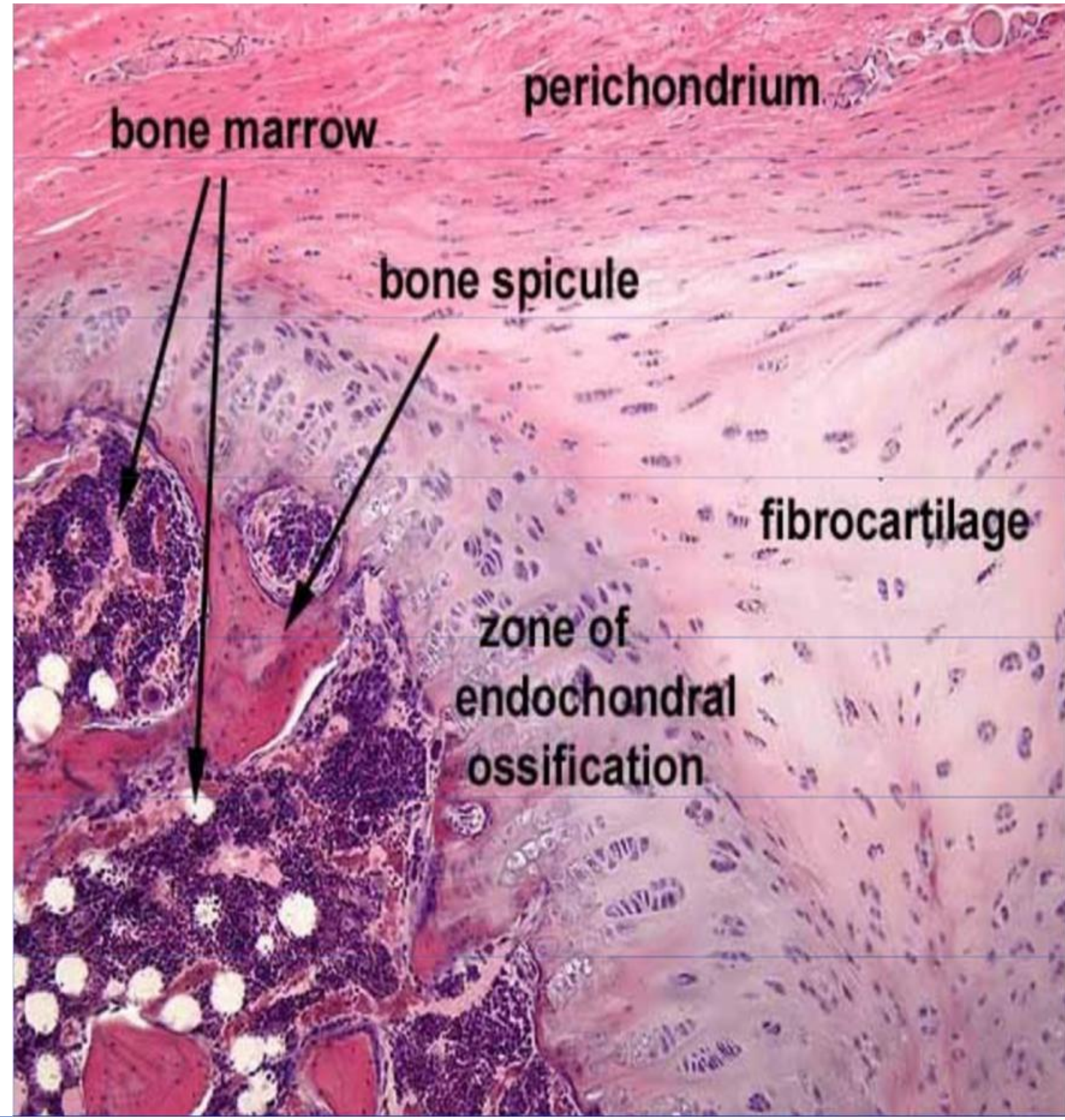

SPINE

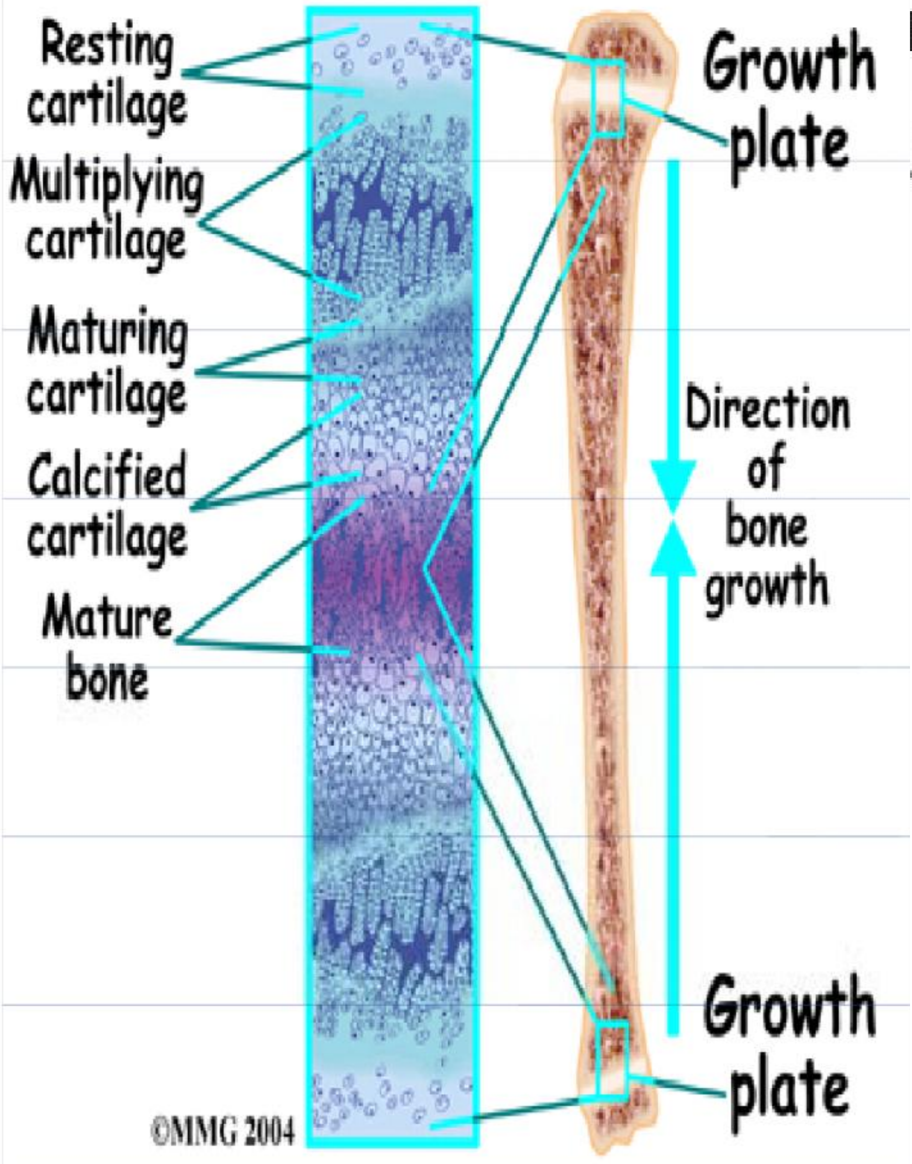
# Growth of Cartilage

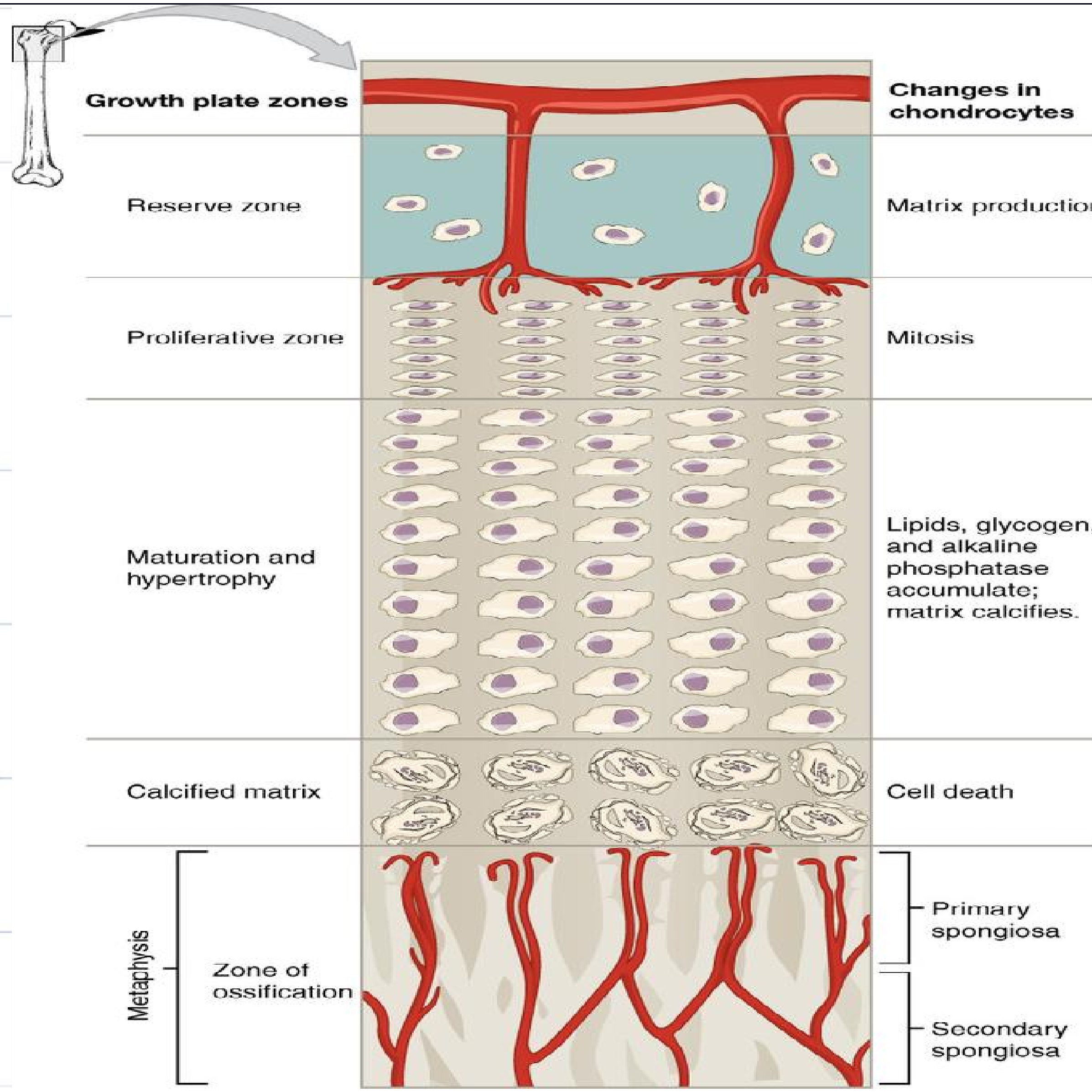
- **Appositional** – cells in the perichondrium secrete matrix against the external face of existing cartilage
- **Interstitial** – lacunae-bound chondrocytes inside the cartilage divide and secrete new matrix, expanding the cartilage from within
- Calcification of cartilage occurs
  - During normal bone growth
  - During old age

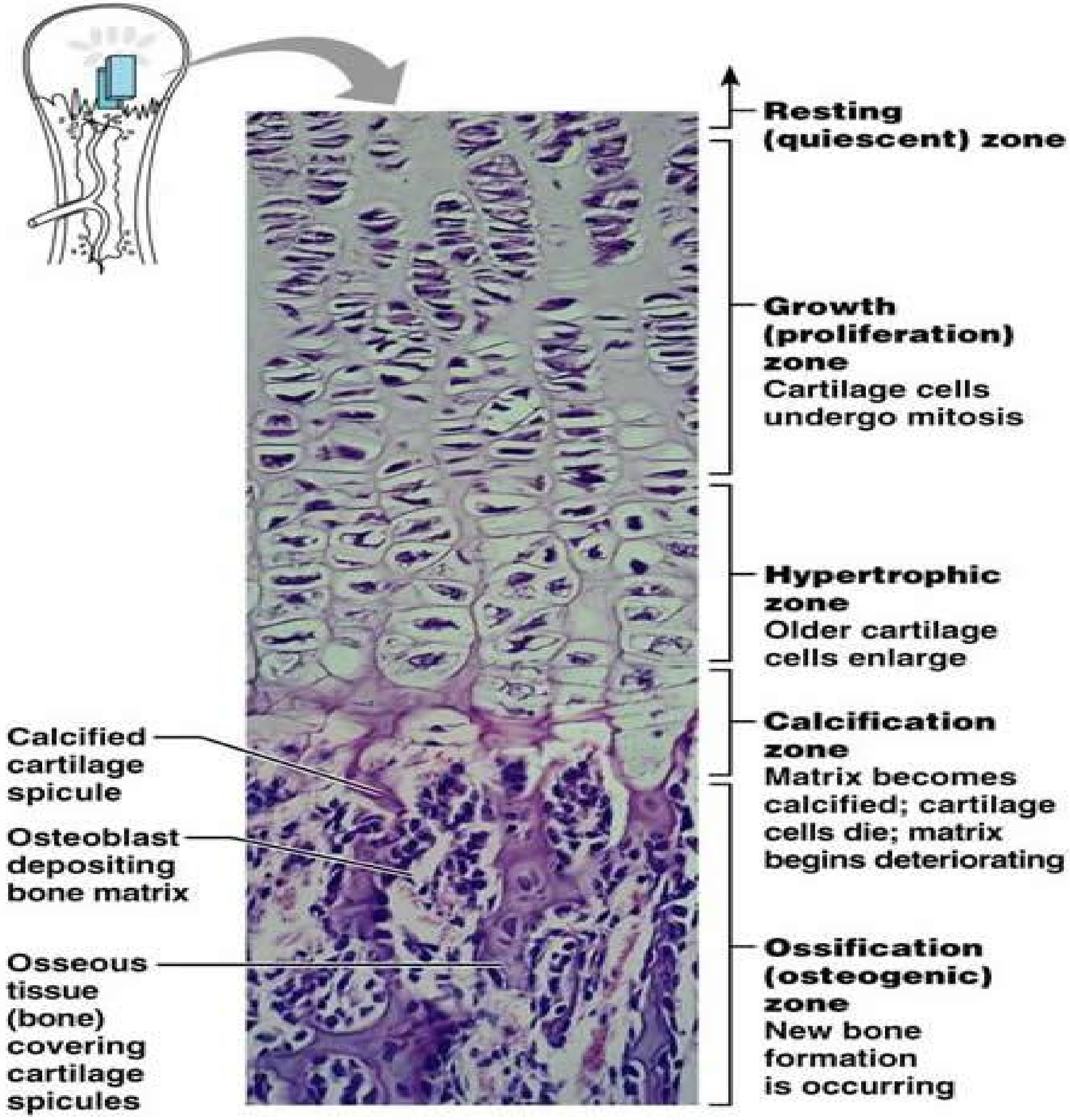



Resting cartilage
Multiplying cartilage
Maturing cartilage
Calcified cartilage
Mature bone
Growth plate
Direction of bone growth
Growth plate
©MMG 2004


perichondrium
bone marrow
bone spicule
fibrocartilage
zone of endochondral ossification


Resting cartilage
Multiplying cartilage
Maturing cartilage
Calcified cartilage
Mature bone
©MMG 2004
Growth plate
Direction of bone growth
Growth plate


Growth plate zones
Changes in chondrocytes
Reserve zone
Matrix production
Proliferative zone
Mitosis
Maturation and hypertrophy
Lipids, glycogen, and alkaline phosphatase accumulate; matrix calcifies.
Calcified matrix
Cell death
Metaphysis
Zone of ossification
Primary spongiosa
Secondary spongiosa




# Cartilage grows by appositional and interstitial growth



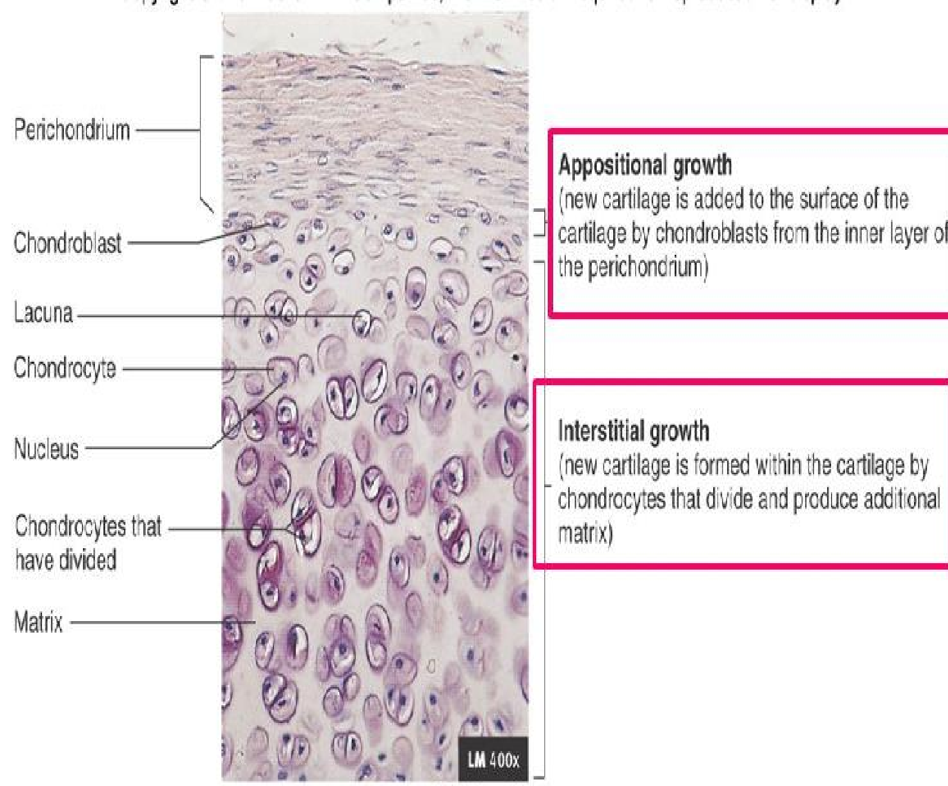
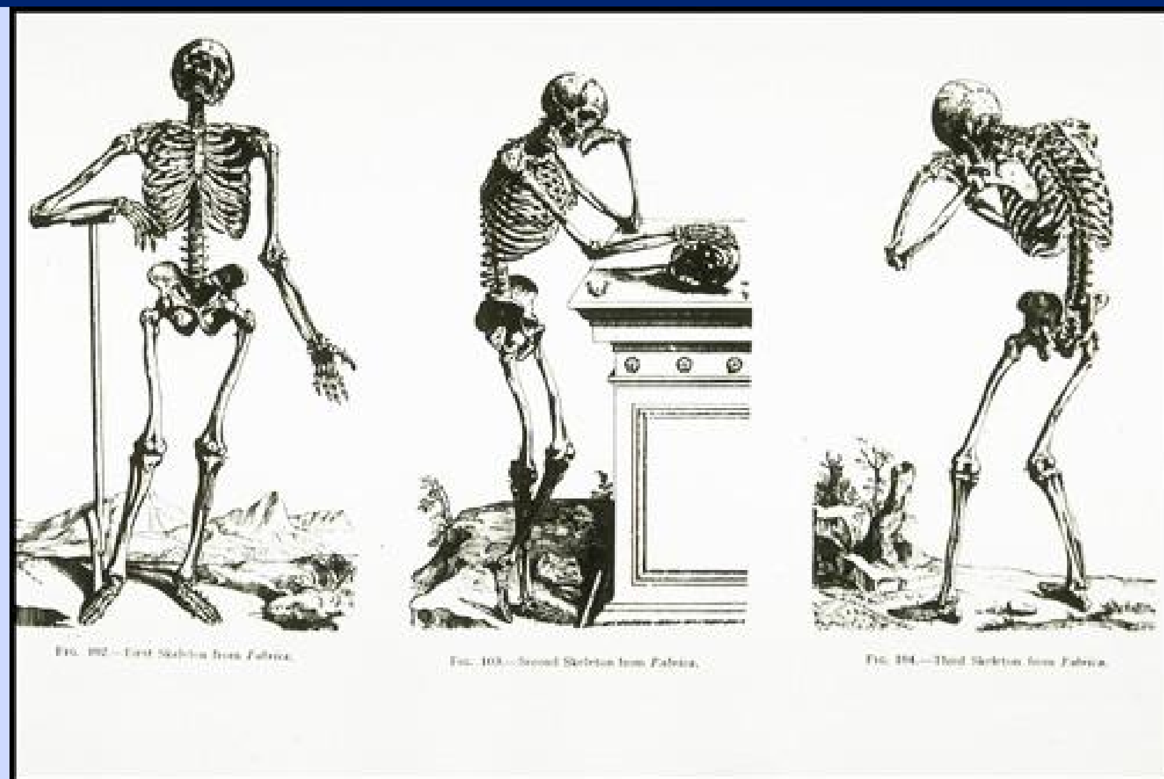





Fig. 6.1

# Bone Development

- **Osteogenesis** (a.k.a. ossification) is the process of bone tissue formation.
- **In embryos this leads to the formation of the bony skeleton**.
- **In children and young adults, ossification occurs as part of bone growth.**
- **In adults, it occurs as part of bone remodeling and bone repair.**



# Formation of the Bony Skeleton

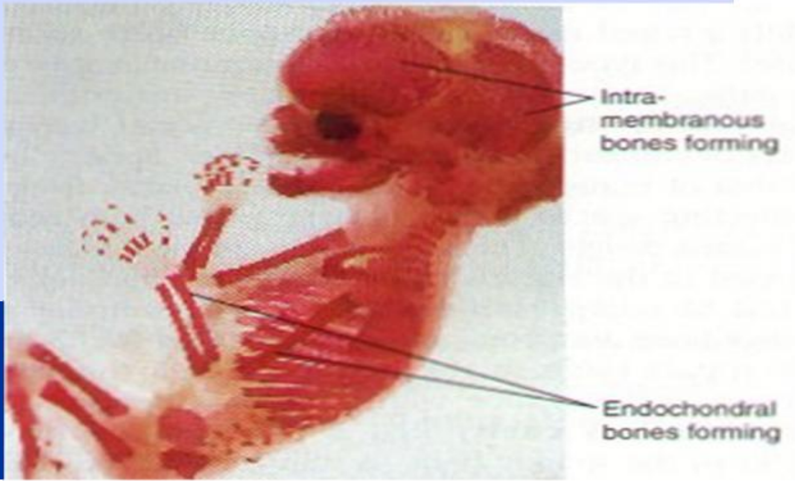
- **Begins at week 8 of embryo development**

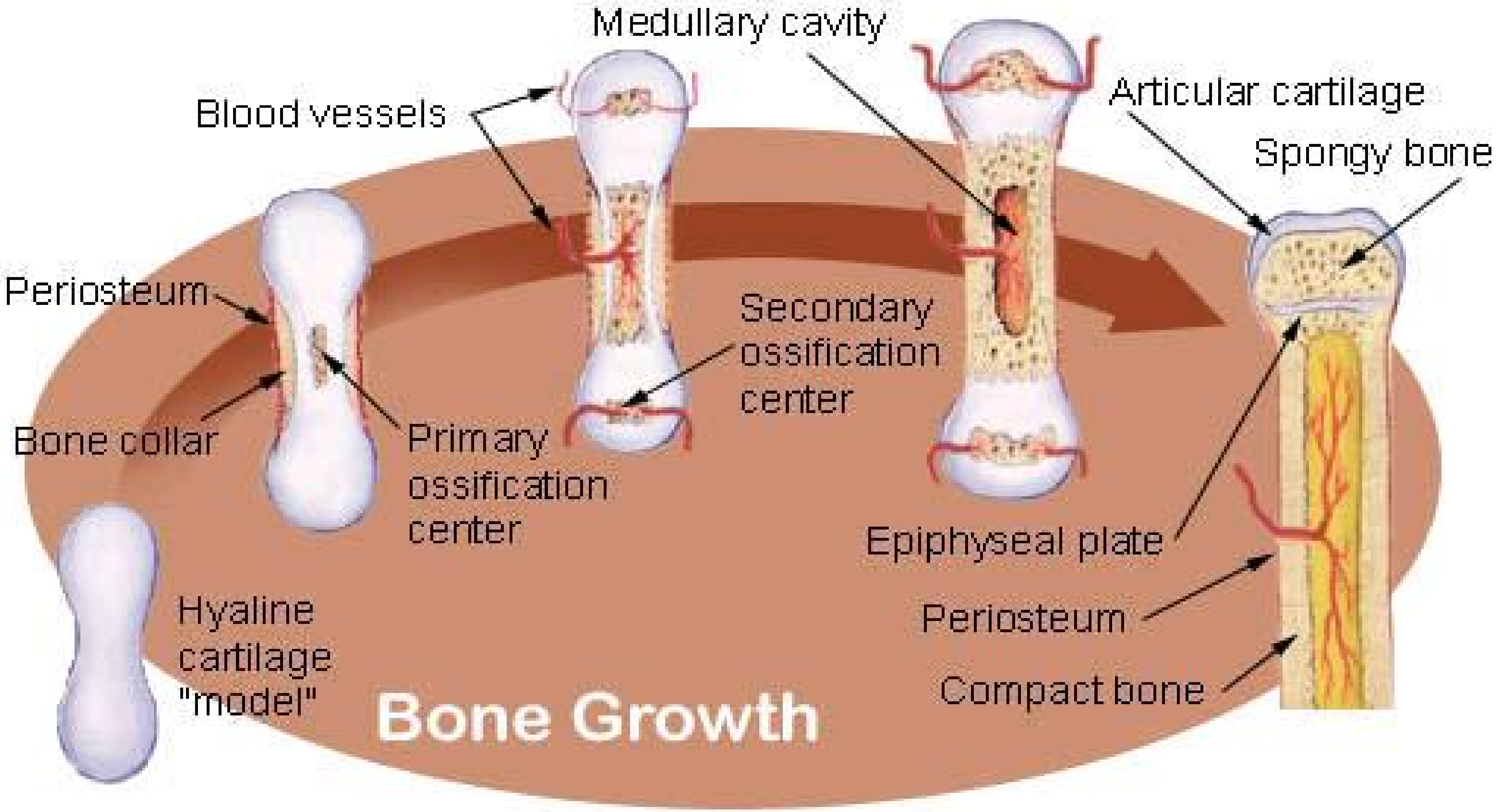
- **Intramembranous ossification** – bone develops from a fibrous membrane
  - **Formation of most of the flat bones of the skull and the clavicles**
  - **Fibrous connective tissue membranes are formed by mesenchymal cells**

- **Endochondral ossification** – bone forms by **replacing hyaline cartilage**
- **By age 25, nearly all bones are completely ossified**
- In old age, bone resorption predominates
- A single gene that codes for vitamin D docking determines both the tendency to accumulate bone mass early in life, and the risk for osteoporosis later in life

# Developmental Aspects of Bones

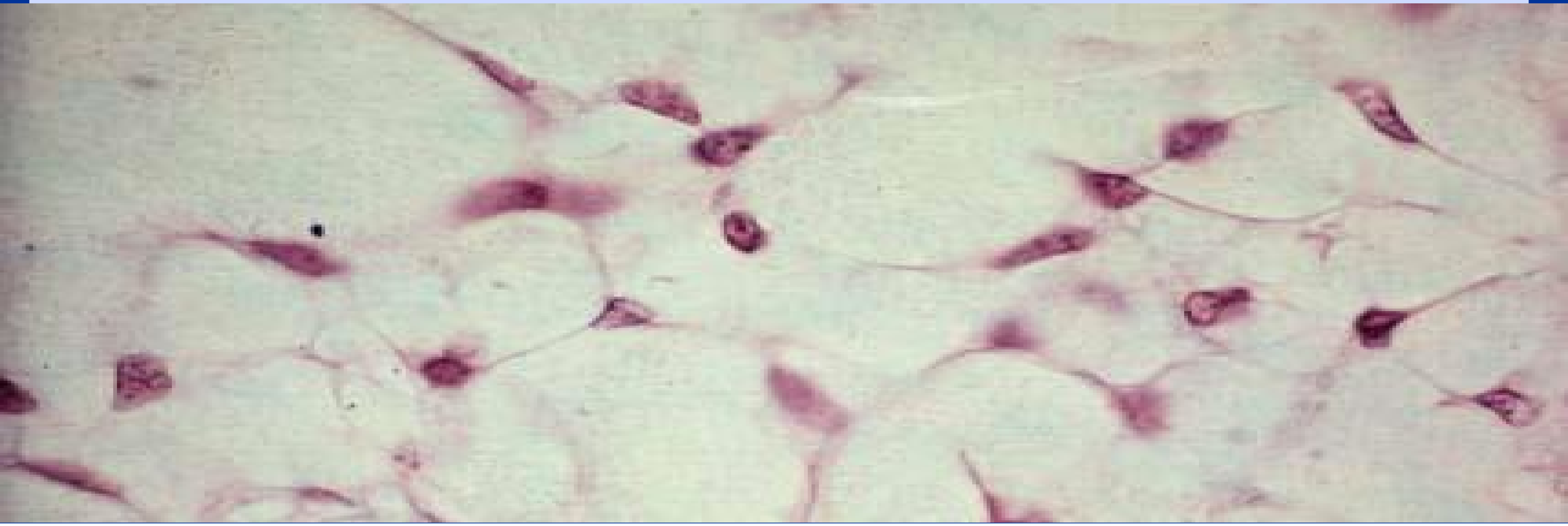
- Mesoderm gives rise to embryonic mesenchymal cells, which produce membranes and cartilages that form the embryonic skeleton
- The embryonic skeleton ossifies in a predictable timetable that allows fetal age to be easily determined from sonograms
- **At birth, most long bones are well ossified (except for their epiphyses)**



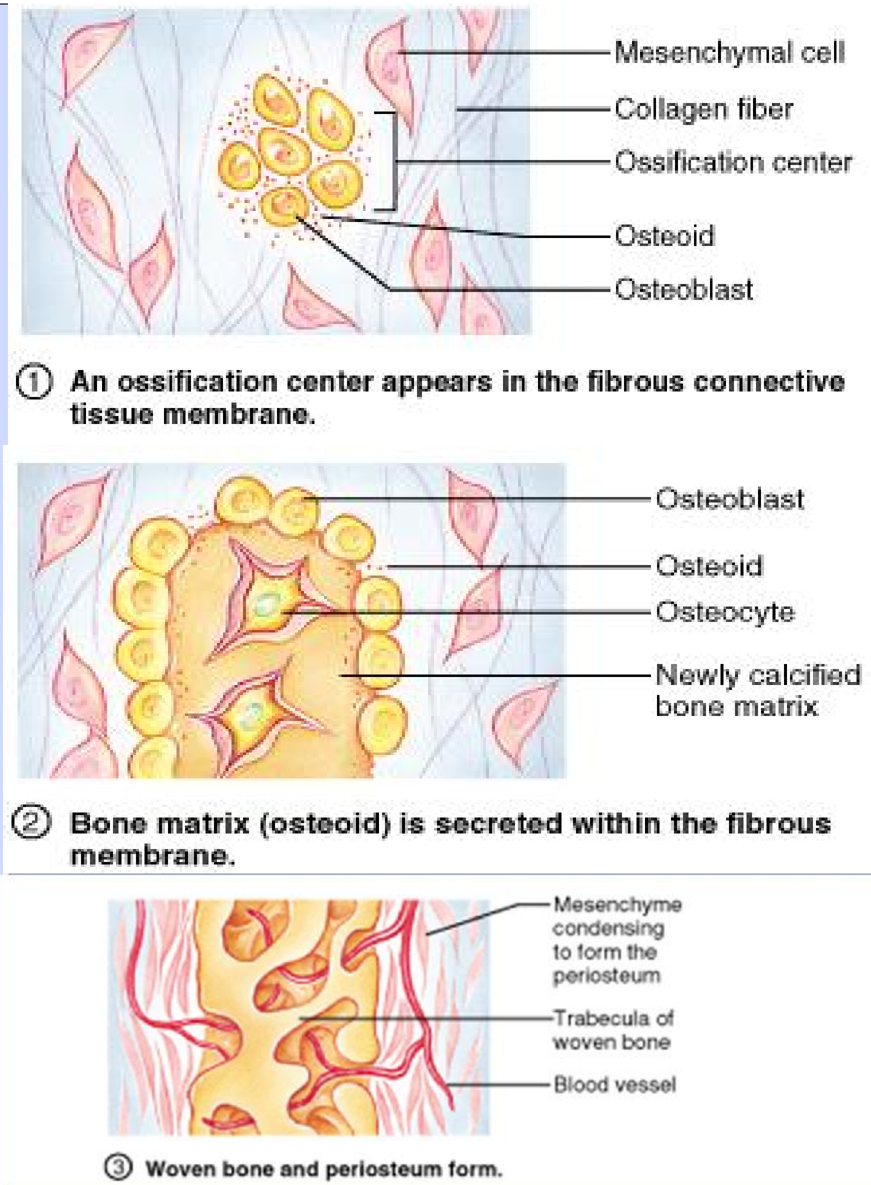


Medullary cavity
Blood vessels
Articular cartilage
Spongy bone
Periosteum
Secondary
ossification
center
Bone collar
Primary
ossification
center
Epiphyseal plate
Hyaline
cartilage
"model"
Periosteum
Compact bone
Bone Growth

# Intramembranous Ossification

- Some bones of the skull (frontal, parietal, temporal, and occipital bones), the facial bones, the clavicles, the pelvis, the scapulae, and part of the mandible are formed by intramembranous ossification
- Prior to ossification, these structures exist as fibrous membranes made of embryonic connective tissue known as **mesenchyme**.



- Mesenchymal cells first cluster together and start to secrete the organic components of bone matrix which then becomes mineralized through the crystallization of calcium salts. As calcification occurs, the mesenchymal cells differentiate into osteoblasts.
- The location in the tissue where ossification begins is known as an ossification center.
- Some osteoblasts are trapped w/i bony pockets. These cells differentiate into osteocytes.




- The developing bone grows outward from the ossification center in small struts called spicules.
- Mesenchymal cell divisions provide additional osteoblasts.
- The osteoblasts require a reliable source of oxygen and nutrients. Blood vessels trapped among the spicules meet these demands and additional vessels branch into the area.
- These vessels will eventually become entrapped within the growing bone.

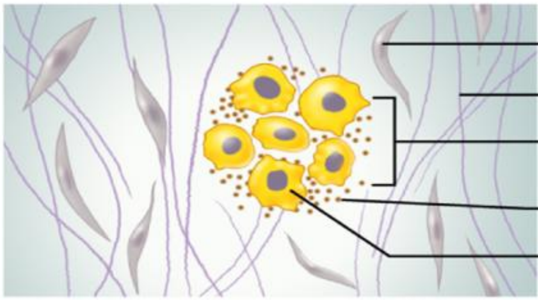
# Intramembranous Ossification

- Formation of most of the flat bones of the skull and the clavicles
- Fibrous connective tissue membranes are formed by mesenchymal cells

# Stages of Intramembranous Ossification

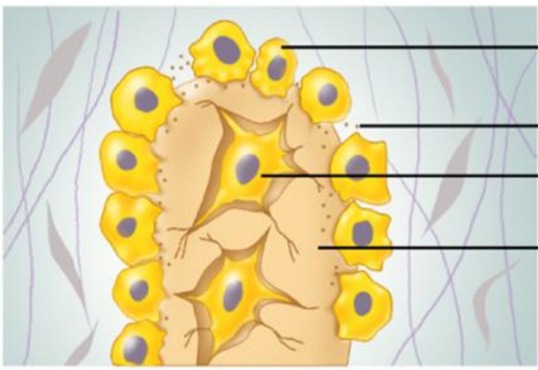
- An ossification center appears in the fibrous connective tissue membrane
- Bone matrix is secreted within the fibrous membrane
- Woven bone and periosteum form
- Bone collar of compact bone forms, and red marrow appears

# Stages of Intramembranous Ossification



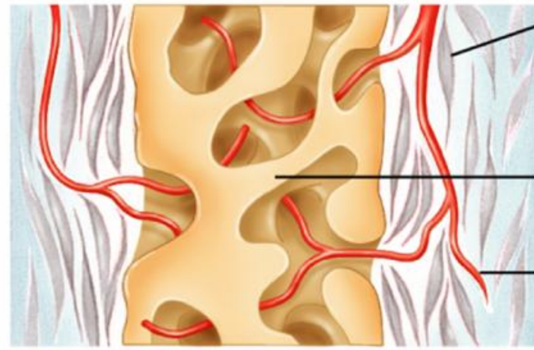

① **An ossification center appears in the fibrous connective tissue membrane.**

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



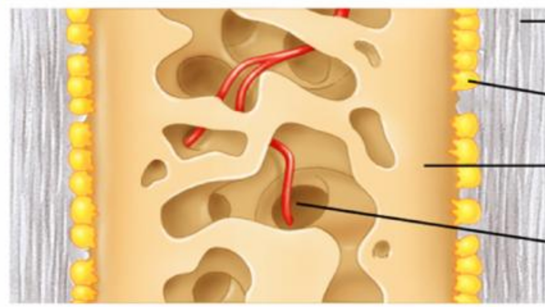

② **Bone matrix (osteoid) is secreted within the fibrous membrane.**

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




③ **Woven bone and periosteum form.**

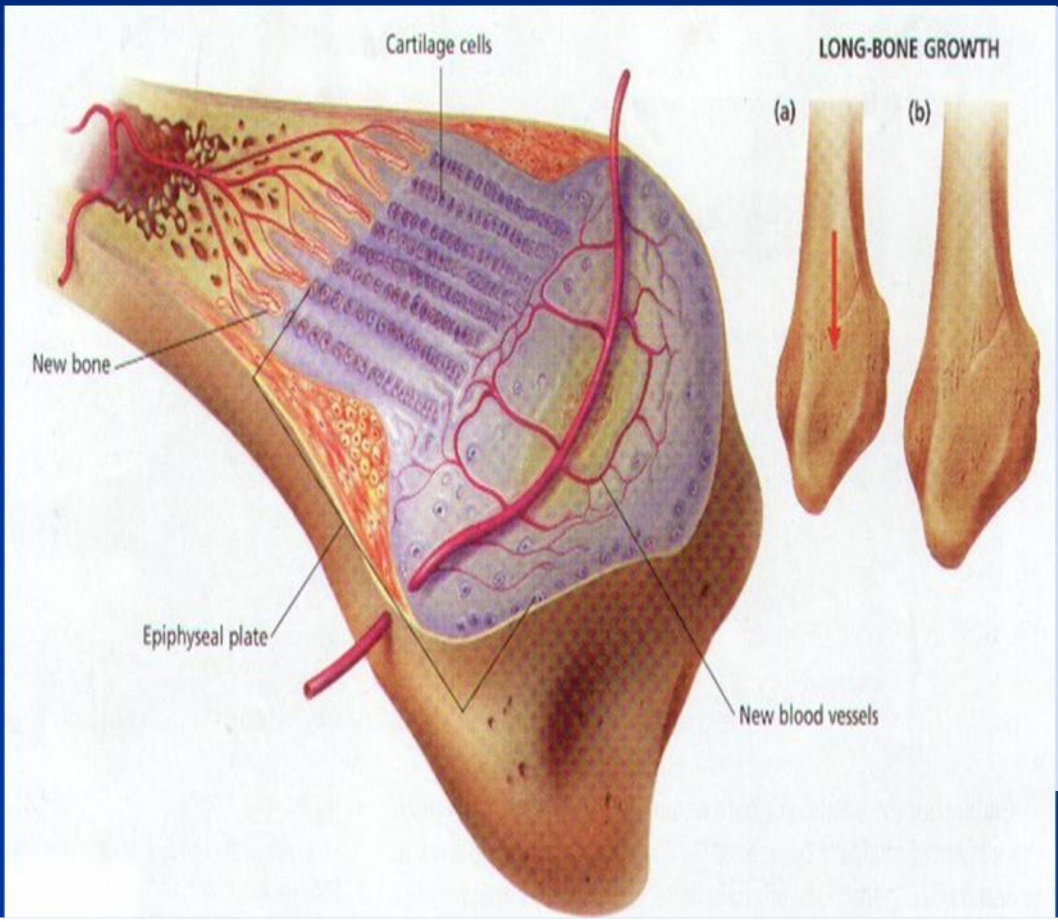
- Accumulating osteoid is laid down between embryonic blood vessels, which form a random network. The result is a network (instead of lamellae) of trabeculae.
- Vascularized mesenchyme condenses on the external face of the woven bone and becomes the periosteum.




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.

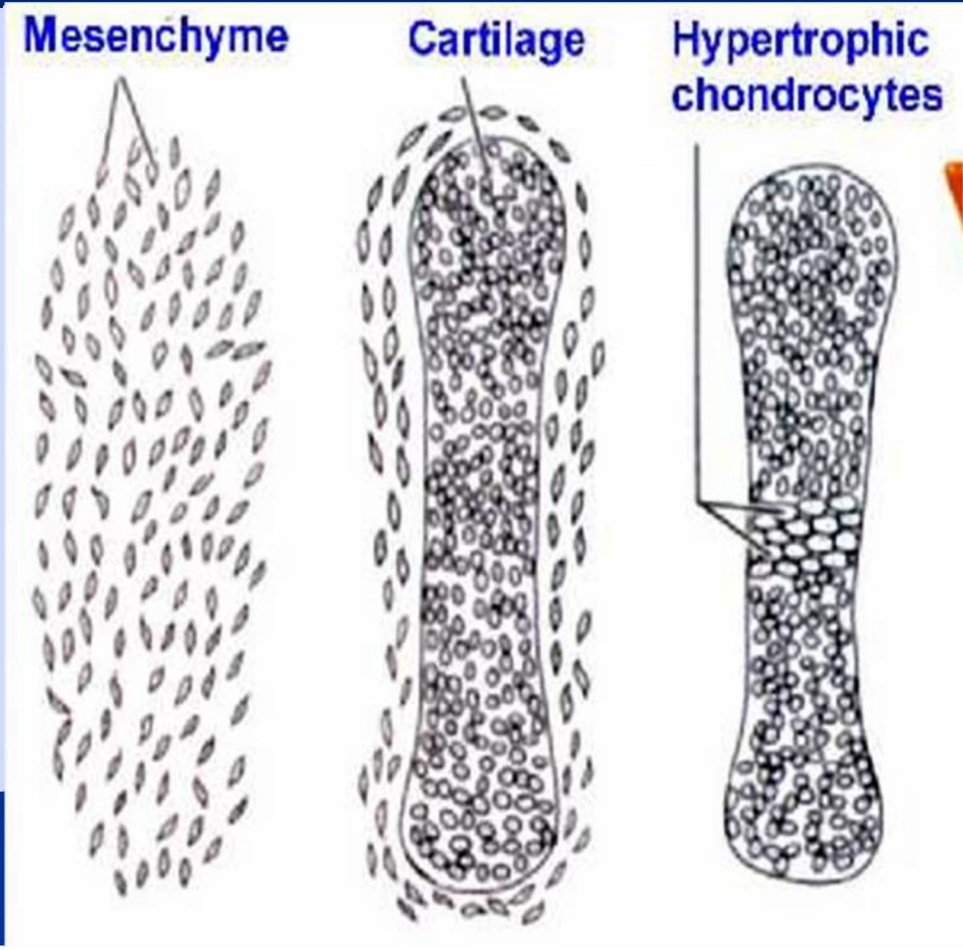
# Endochondral Ossification



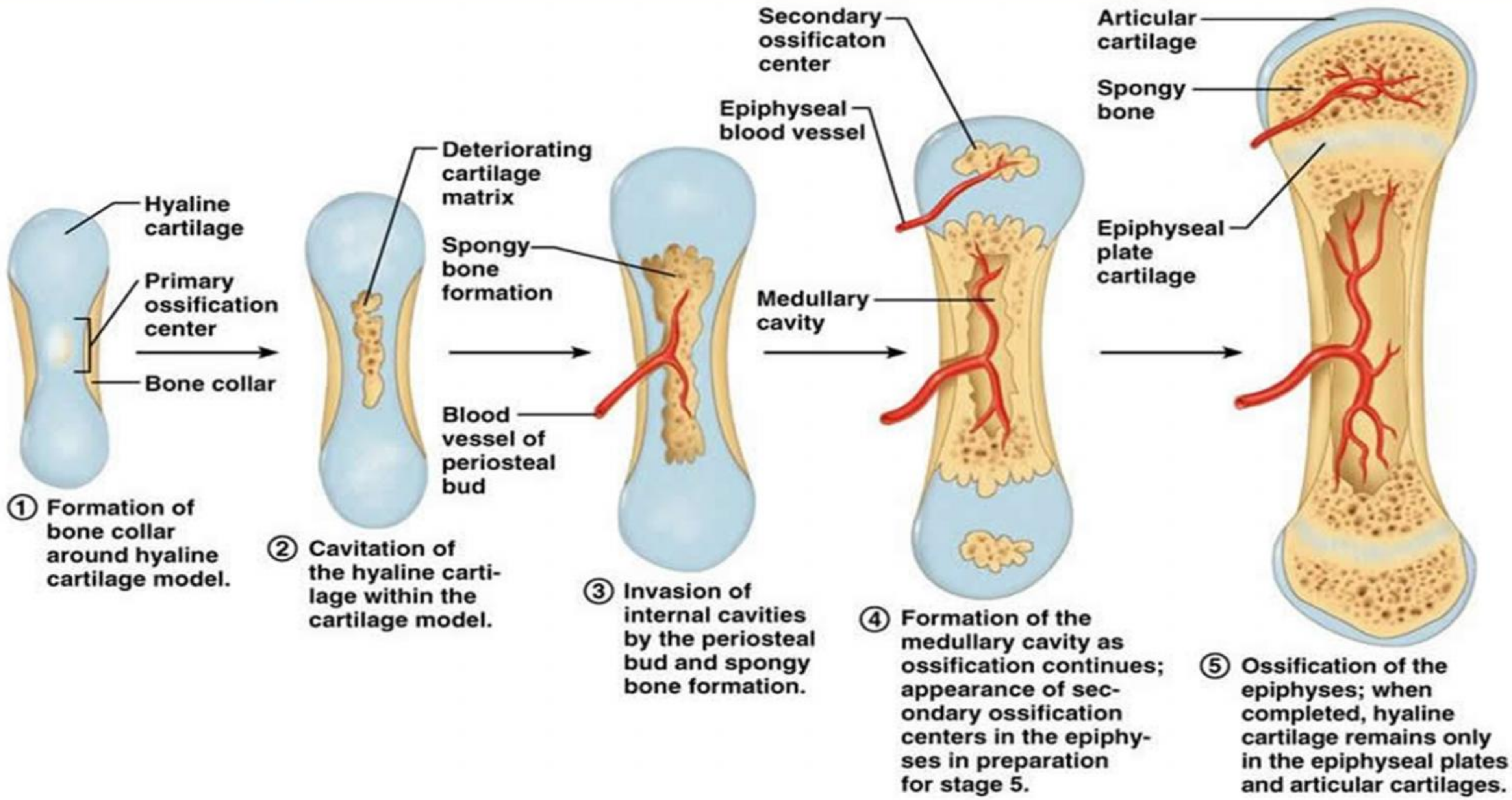

- **Begins in the second month of development**
- Uses hyaline cartilage "bones" as models for bone construction
- Requires breakdown of hyaline cartilage prior to ossification

# Stages of Endochondral Ossification

- Formation of bone collar
- Cavitation of the hyaline cartilage
- Invasion of internal cavities by the periosteal bud, and spongy bone formation
- Formation of the medullary cavity; appearance of secondary ossification centers in the epiphyses
- Ossification of the epiphyses, with hyaline cartilage remaining only in the epiphyseal plates

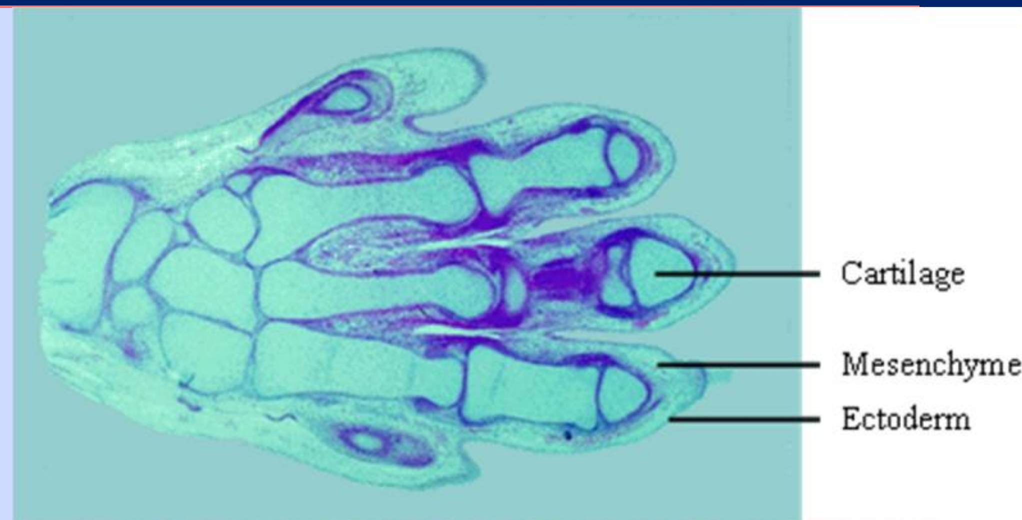


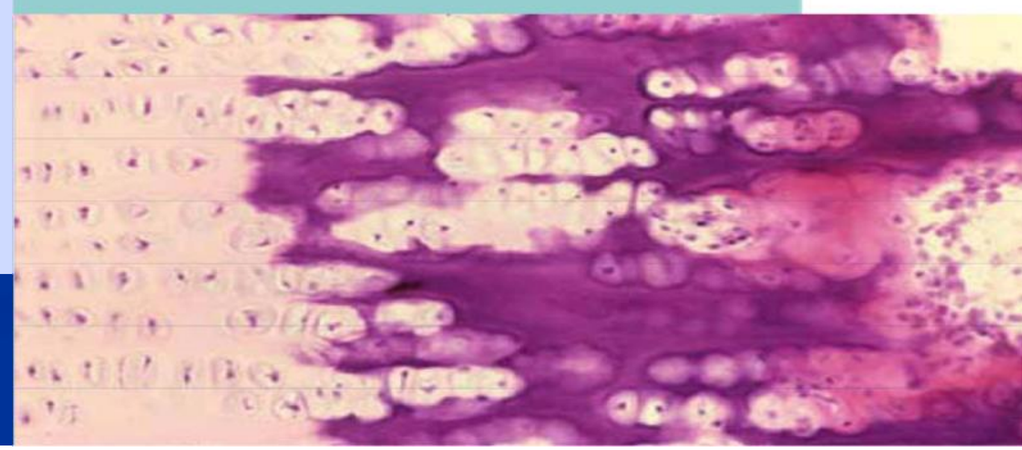
# Stages of Endochondral Ossification



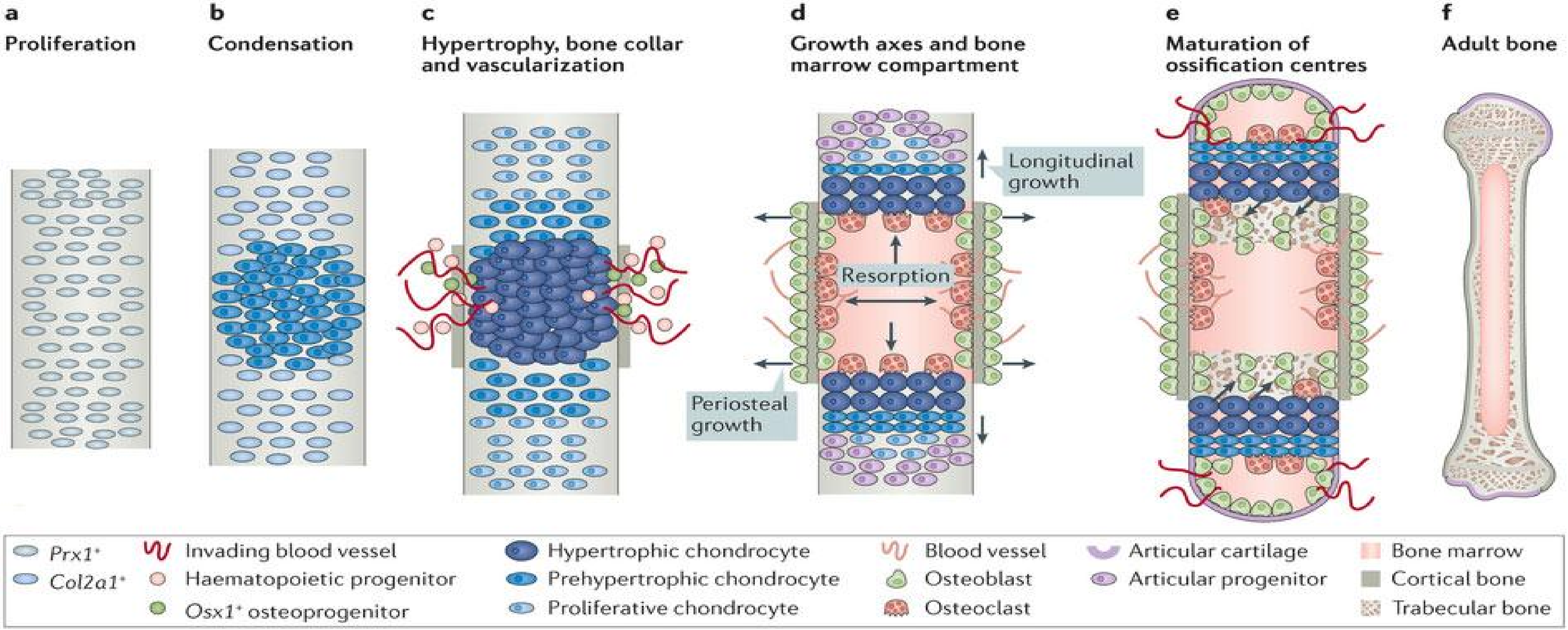
# Endochondral Ossification

- Begins with the formation of a hyaline cartilage model which will later be replaced by bone.
- Most bones in the body develop via this model.
- More complicated than intramembranous because the hyaline cartilage must be broken down as ossification proceeds.
- We'll follow limb bone development as an example.



# Endochondral Ossification

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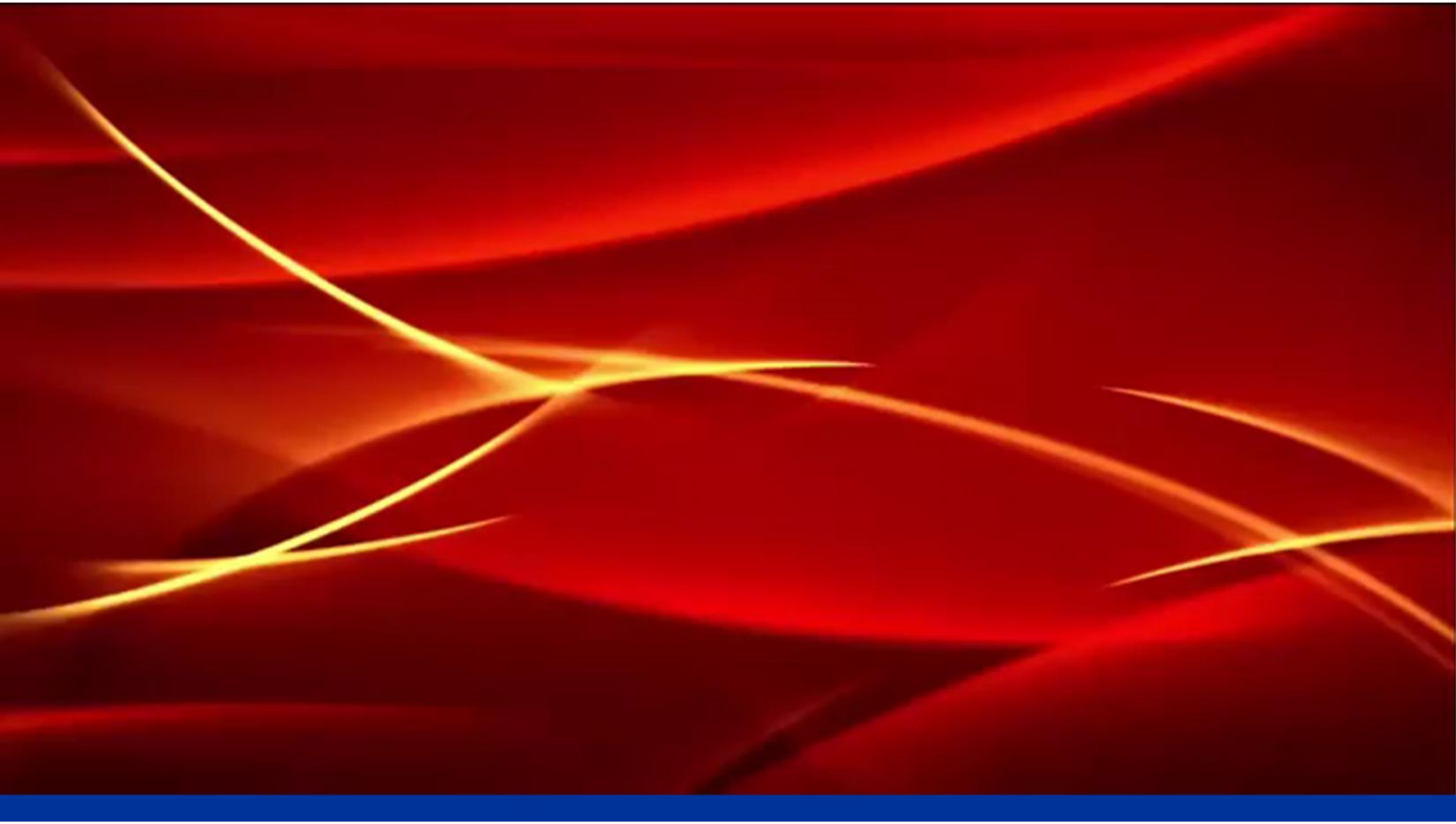
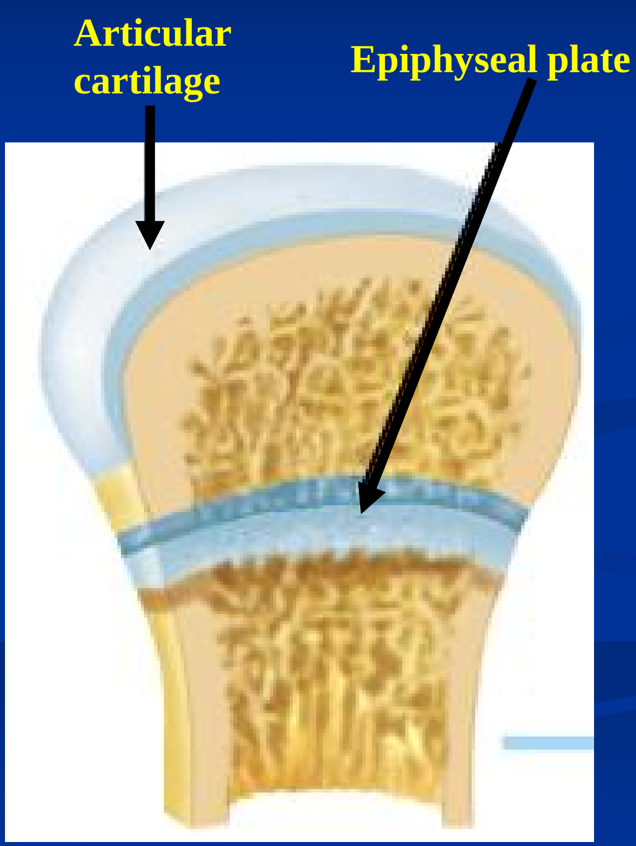
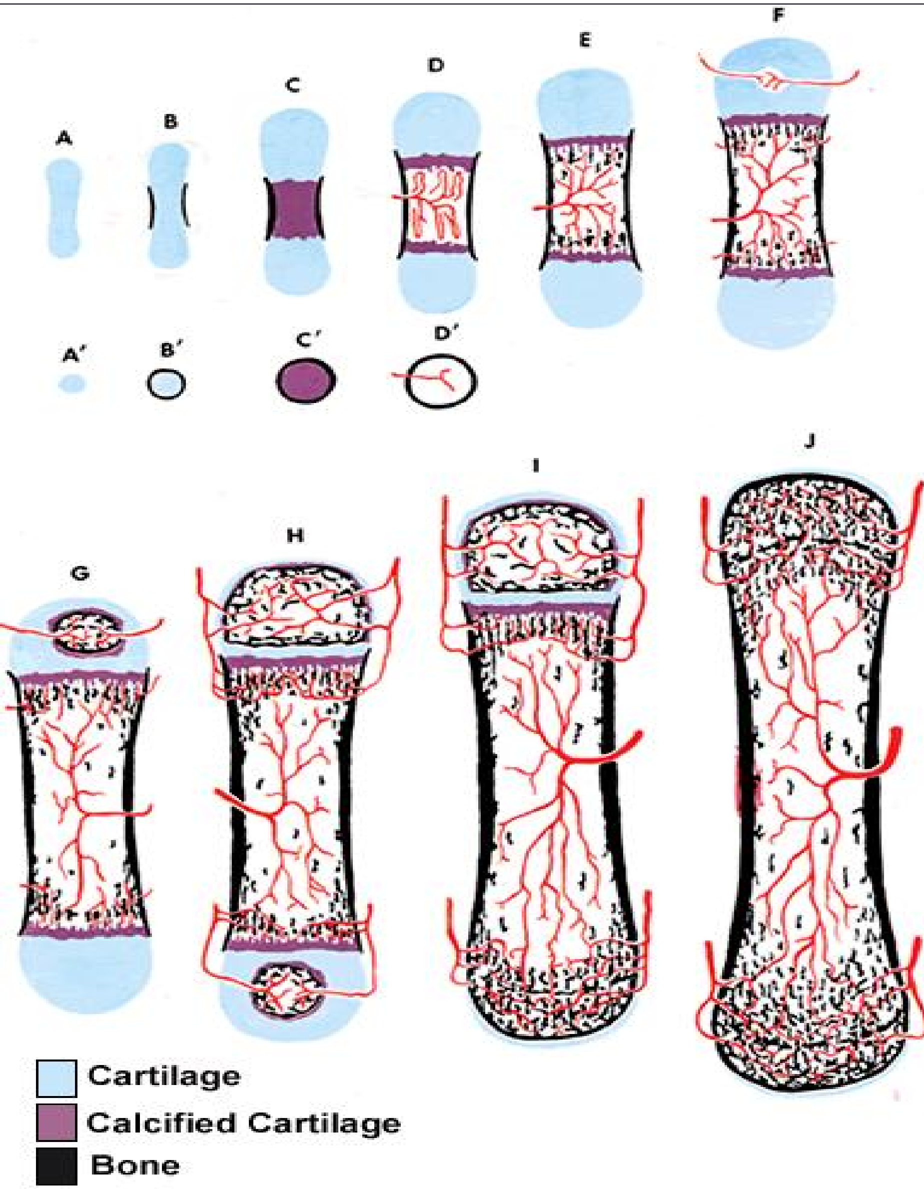


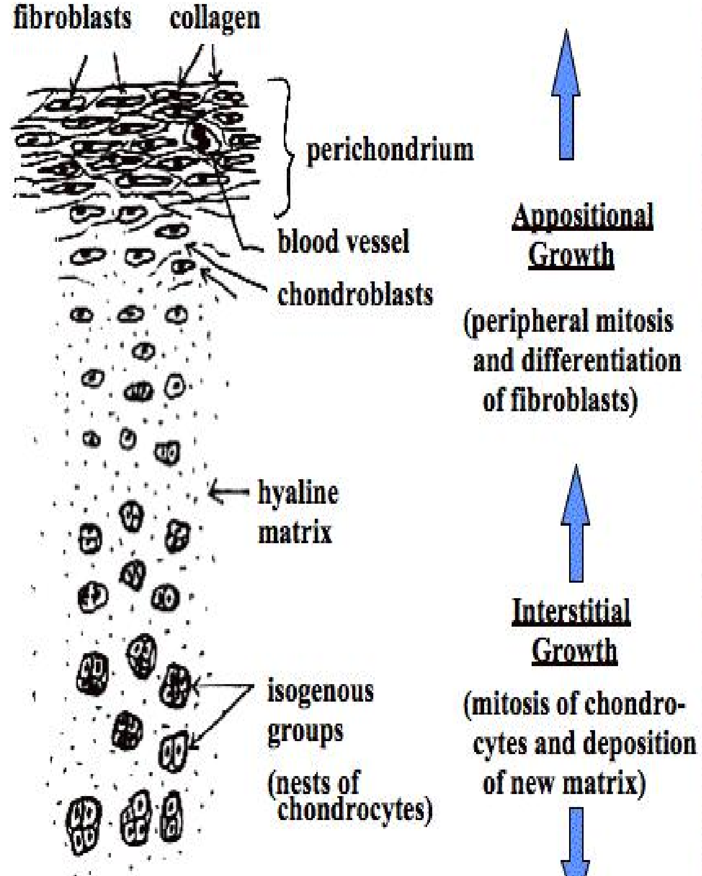
# Endochondral Ossification – Step 5

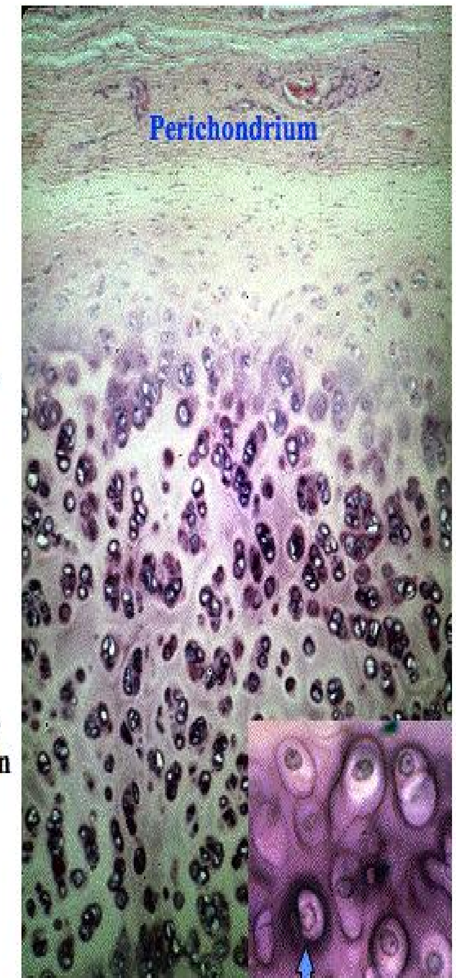
- **Around birth, most long bones have a bony diaphysis surrounding remnants of spongy bone**, a widening medullary cavity, and 2 cartilaginous epiphyses.
- At this time, capillaries and osteoblasts will migrate into the epiphyses and create secondary ossification centers.
- The epiphysis will be transformed into spongy bone.
- However, a small cartilaginous plate, known as the epiphyseal plate, will remain at the juncture between the epiphysis and the diaphysis.



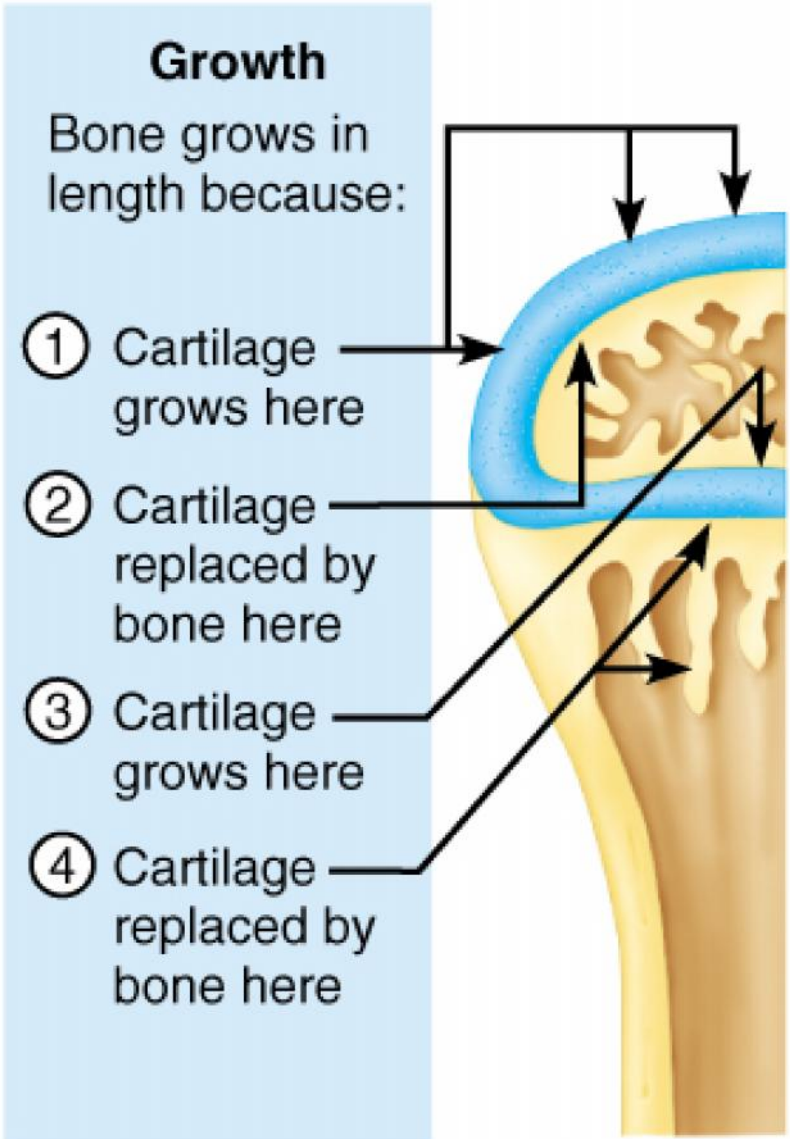



# Growth of Cartilage



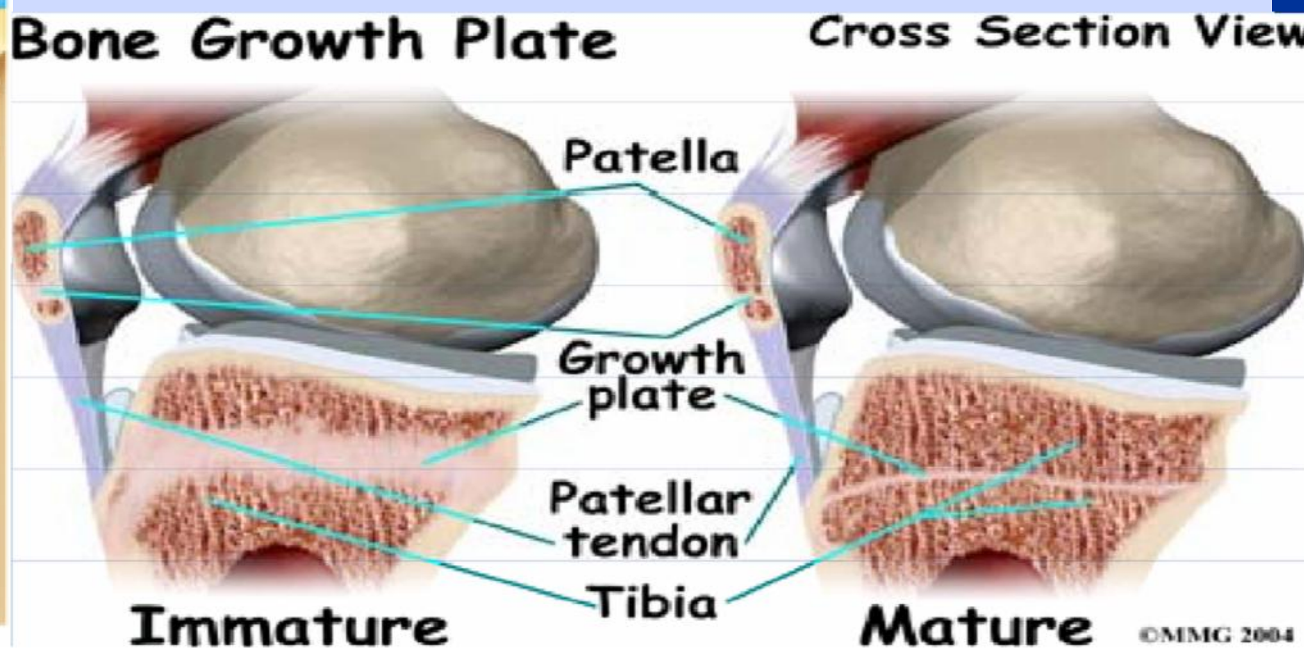




Territorial Matrix



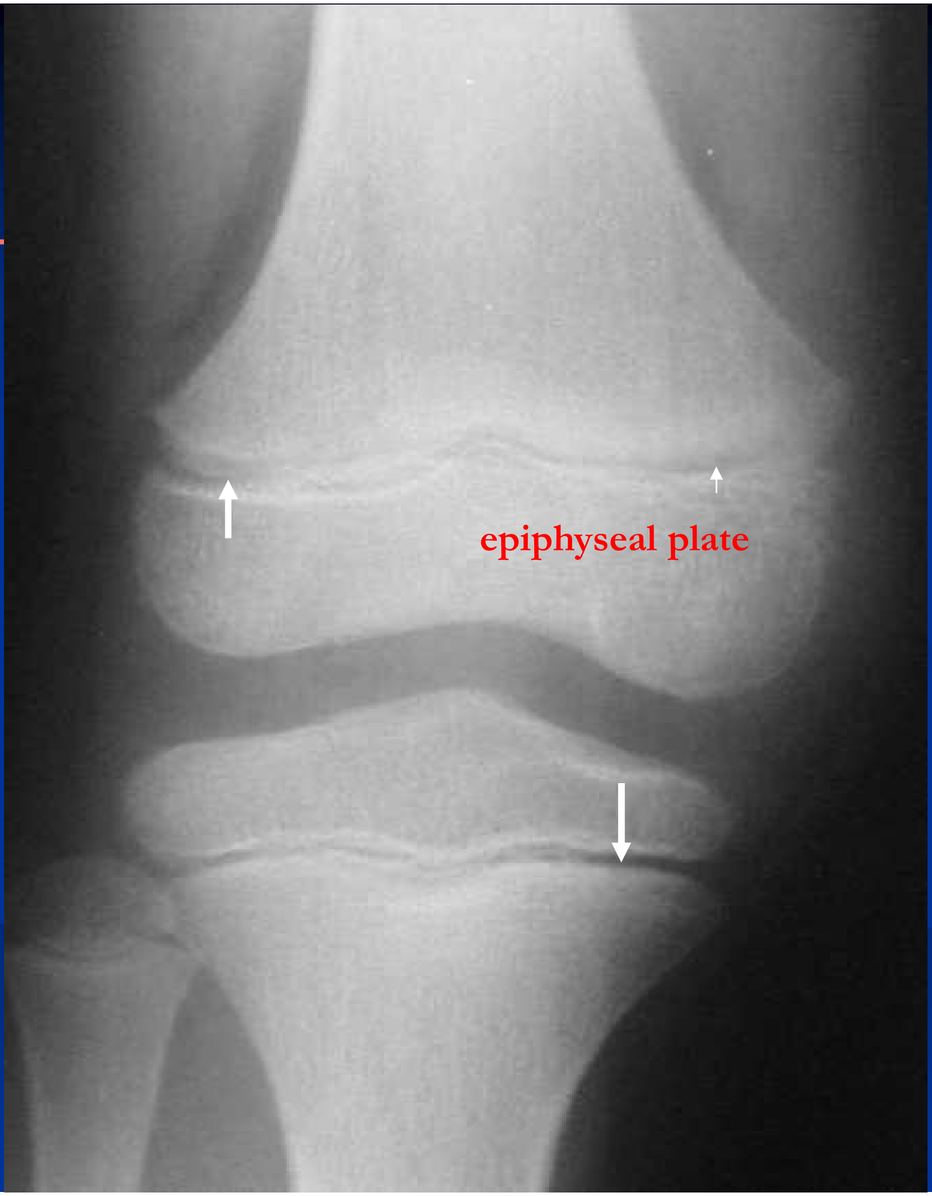

# Growth in Bone Length

- Epiphyseal cartilage (close to the epiphysis) of the epiphyseal plate divides to create more cartilage, while the diaphyseal cartilage (close to the diaphysis) of the epiphyseal plate is transformed into bone.
- This increases the length of the shaft.

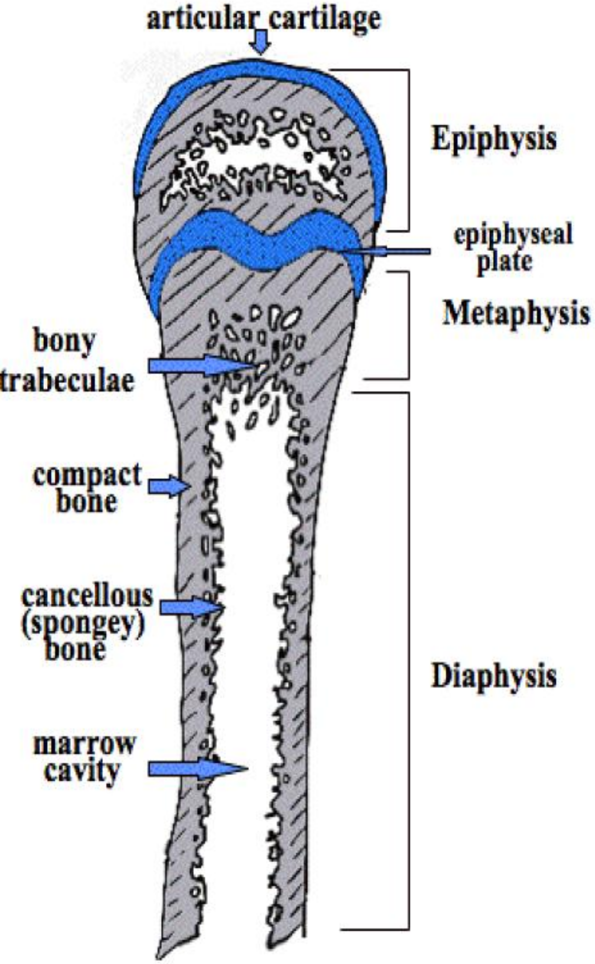


**At puberty, growth in bone length is increased dramatically by the combined activities of growth hormone, thyroid hormone, and the sex hormones.**

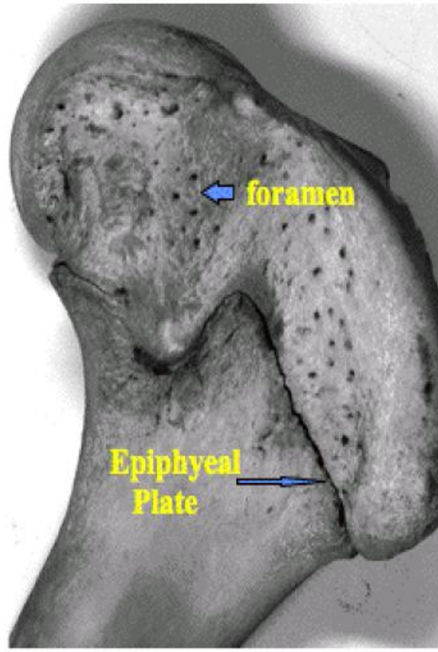
•As a result osteoblasts begin producing bone faster than the rate of epiphyseal cartilage expansion. Thus the bone grows while the epiphyseal plate gets narrower and narrower and ultimately disappears. A remnant **(epiphyseal line for adult)** is visible on X-rays *(do you see them in the adjacent femur, tibia, and fibula?)*

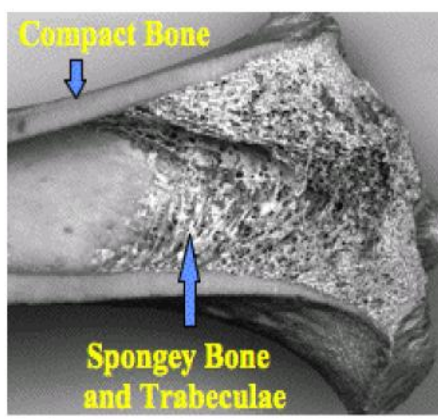


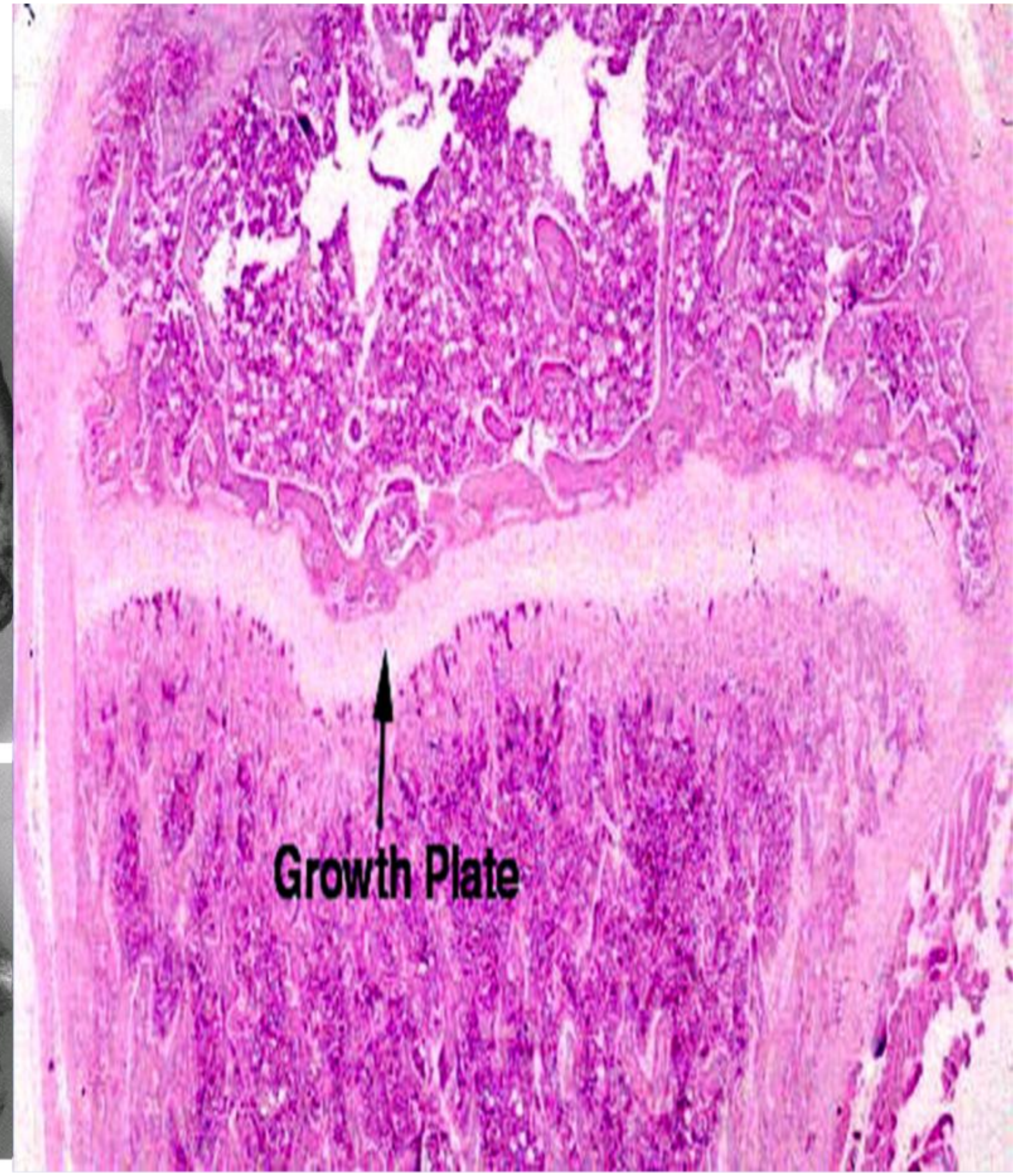
# BONE ANATOMY

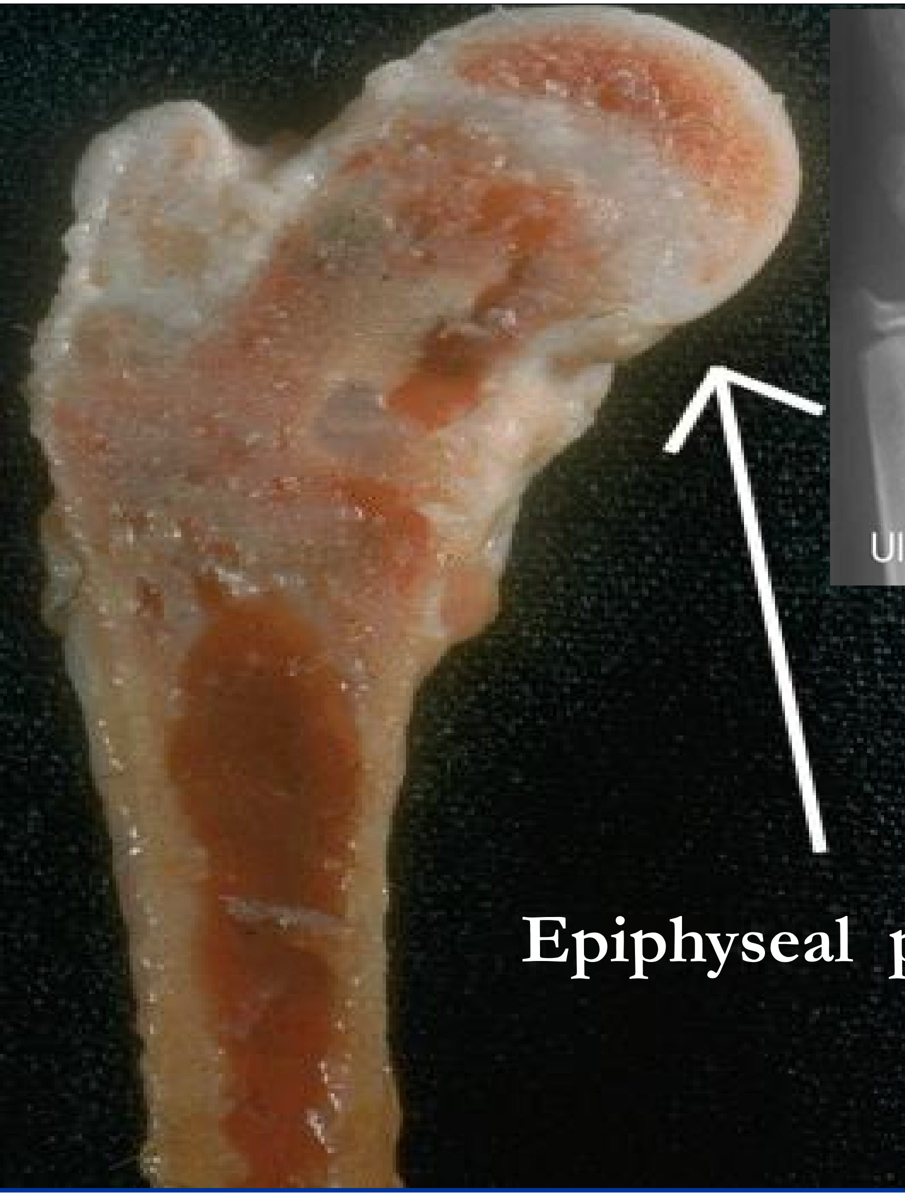


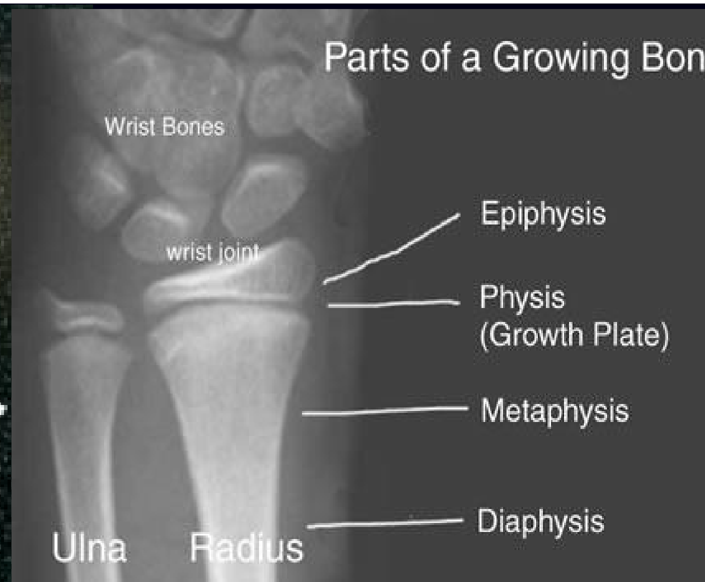

**Epiphysis and Metaphysis**

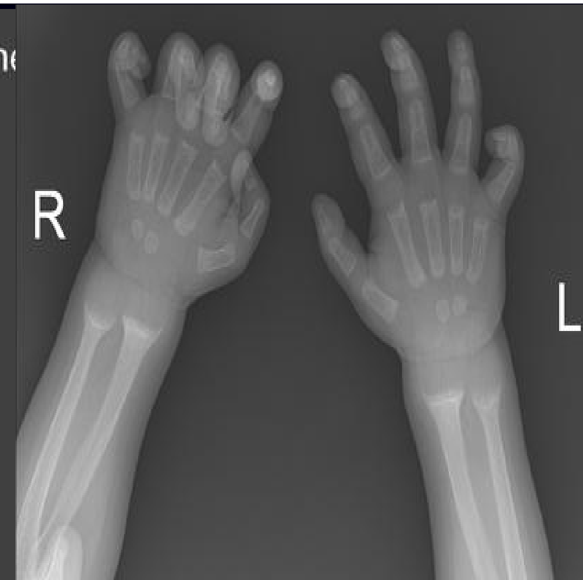


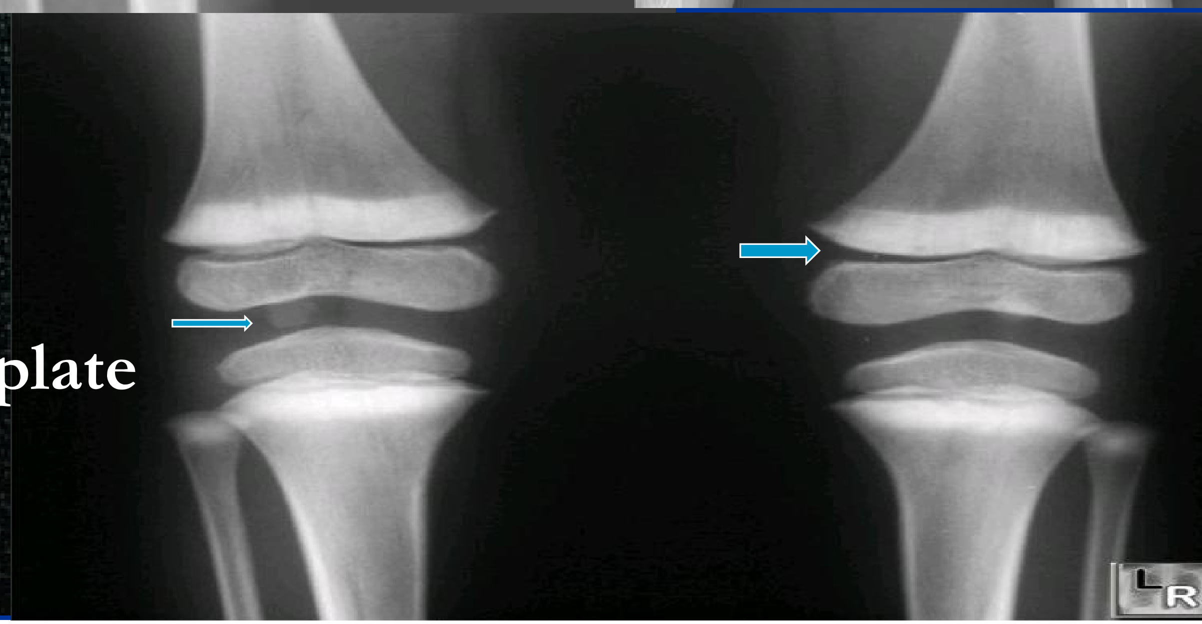



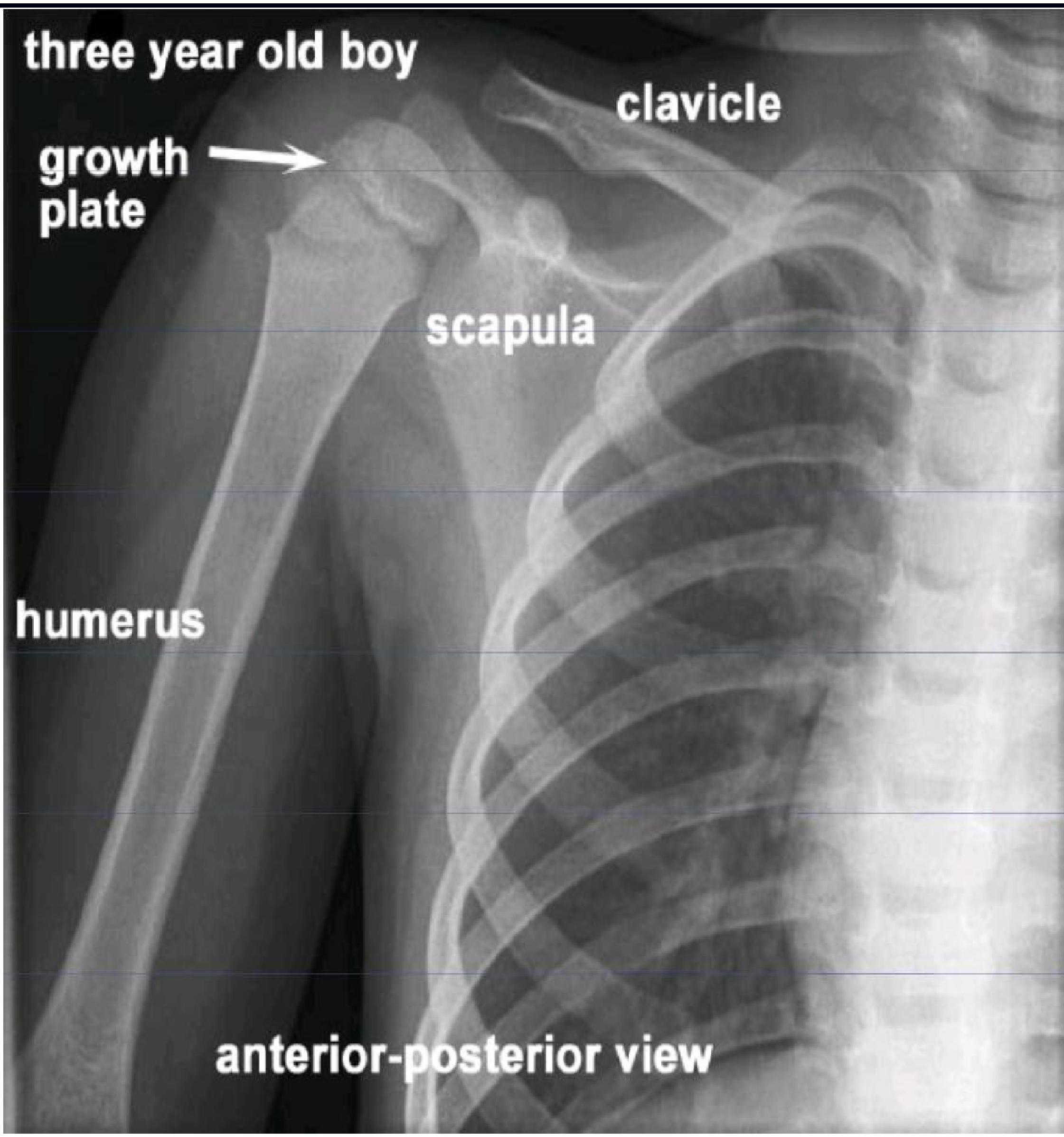




Epiphyseal plate

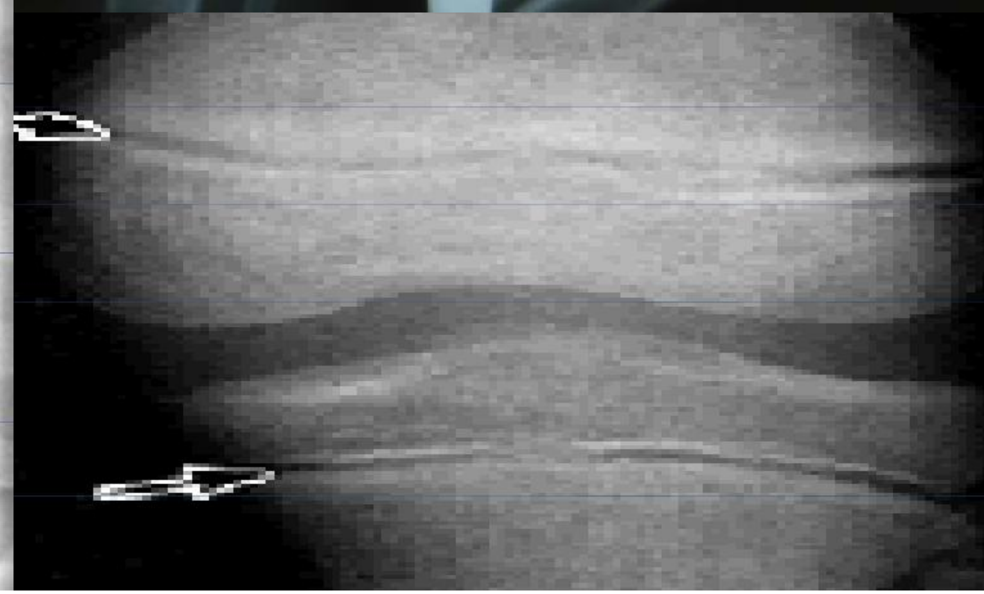

Parts of a Growing Bon
Wrist Bones
wrist joint
Epiphysis
Physis
(Growth Plate)
Metaphysis
Diaphysis
Ulna
Radius

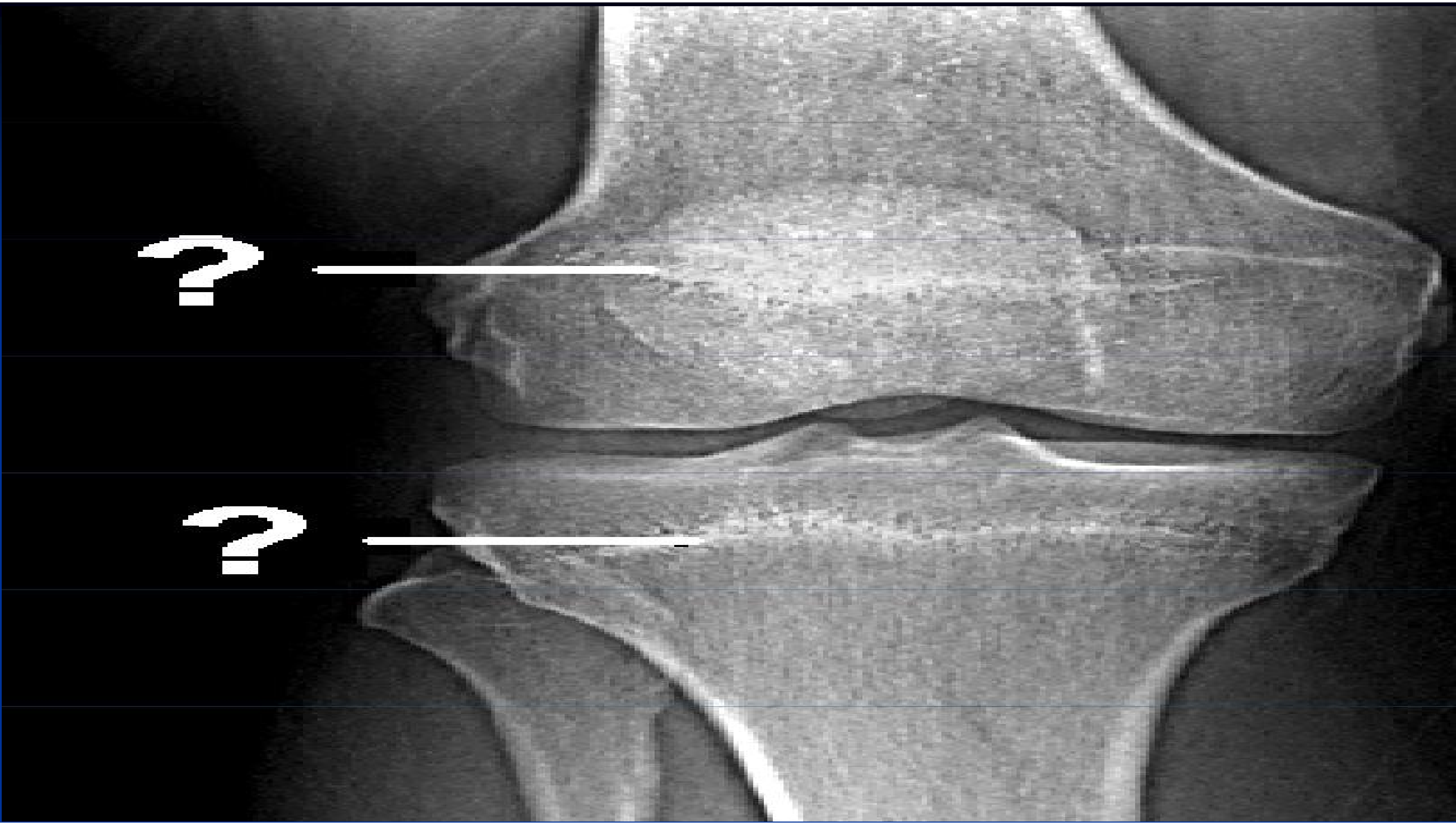

R
L




three year old boy
clavicle
growth plate
scapula
humerus
anterior-posterior view

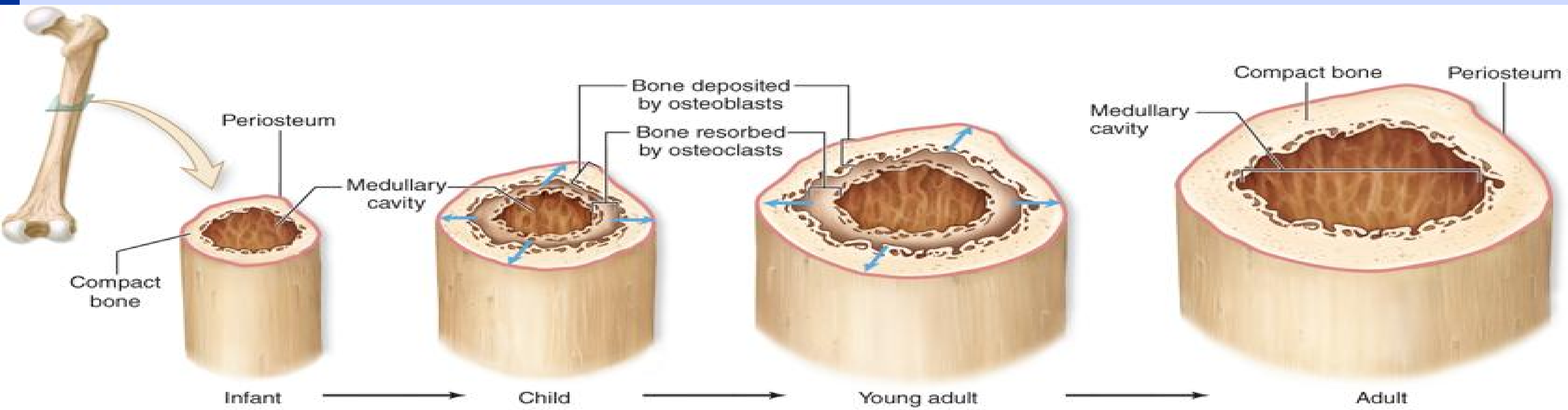

Medulla
Cortex





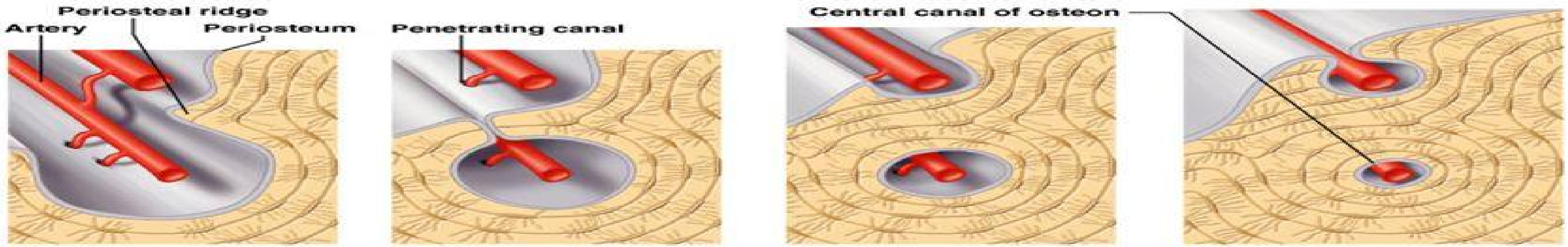
# Growth in Bone Thickness

- **Osteoblasts beneath the periosteum secrete bone matrix on the external surface of the bone. This obviously makes the bone thicker**.
- At the same time, osteoclasts on the endosteum break down bone and thus widen the medullary cavity.
- This results in an increase in shaft diameter even though the actual amount of bone in the shaft is relatively unchanged.




Source: Anthony L. Mescher: Junqueira's Basic Histology, 14th Edition.
www.accessmedicine.com

# Growth in Width (Thickness)




① Osteoblasts beneath the periosteum secrete bone matrix, forming ridges that follow the course of periosteal blood vessels.

② As the bony ridges enlarge and meet, the groove containing the blood vessel becomes a tunnel.

③ The periosteum lining the tunnel is transformed into an endosteum and the osteoblasts just deep to the tunnel endosteum secrete bone matrix, narrowing the canal.

④ As the osteoblasts beneath the endosteum form new lamellae, a new osteon is created. Meanwhile new circumferential lamellae are elaborated beneath the periosteum and the process is repeated, continuing to enlarge bone diameter.



- Growing bones widen as they lengthen
- ***<u>Increases in thickness by appositional growth</u>***

# Postnatal Bone Growth

- **Growth in length of long bones**
  - Cartilage on the side of the **epiphyseal plate closest to the epiphysis is relatively inactive**
  - Cartilage abutting the shaft of the bone organizes into a pattern that allows fast, efficient growth
  - Cells of the epiphyseal plate proximal to the resting cartilage form three functionally different zones: growth, transformation, and osteogenic

# Functional Zones in Long Bone Growth

- **Growth zone** – cartilage cells undergo mitosis, pushing the epiphysis away from the diaphysis
- **Transformation zone** – older cells enlarge, the matrix becomes calcified, cartilage cells die, and the matrix begins to deteriorate
- **Osteogenic zone** – new bone formation occurs

# Long Bone Growth and Remodeling

- **Growth in length** – cartilage continually grows and is replaced by bone as shown
- **Remodeling** – bone is resorbed and added by appositional growth as shown

# Growth in Length of Long Bone

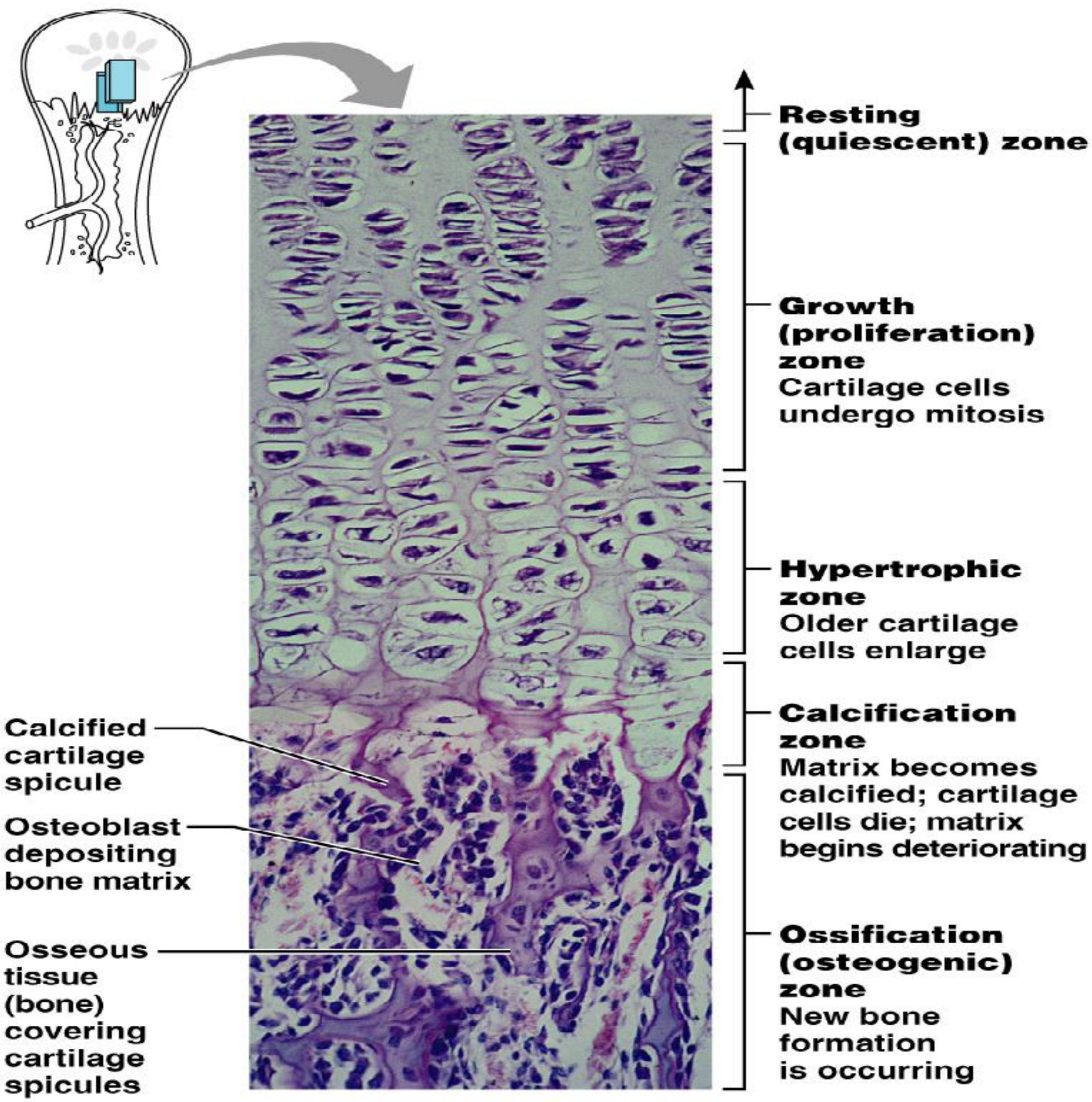
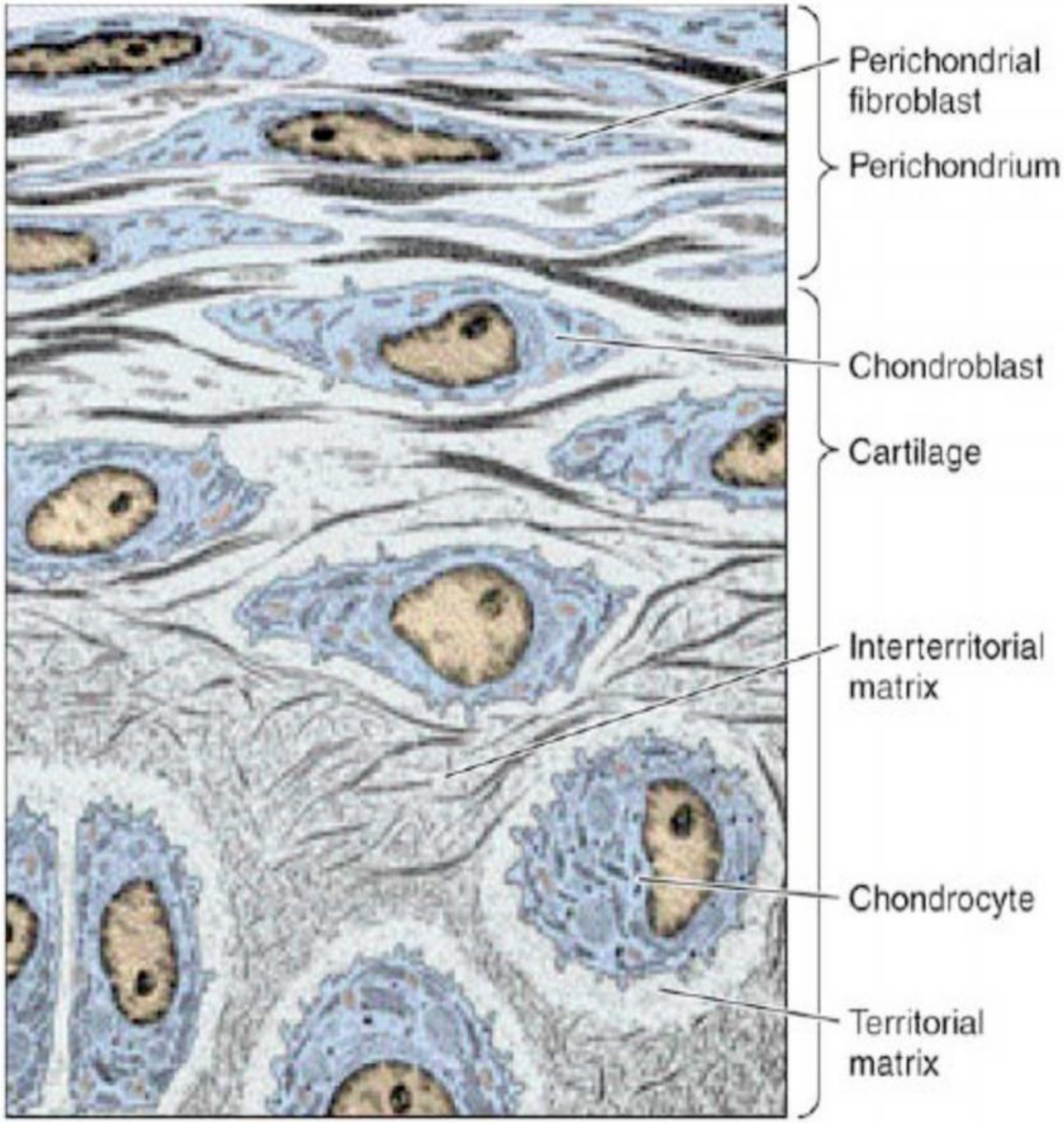
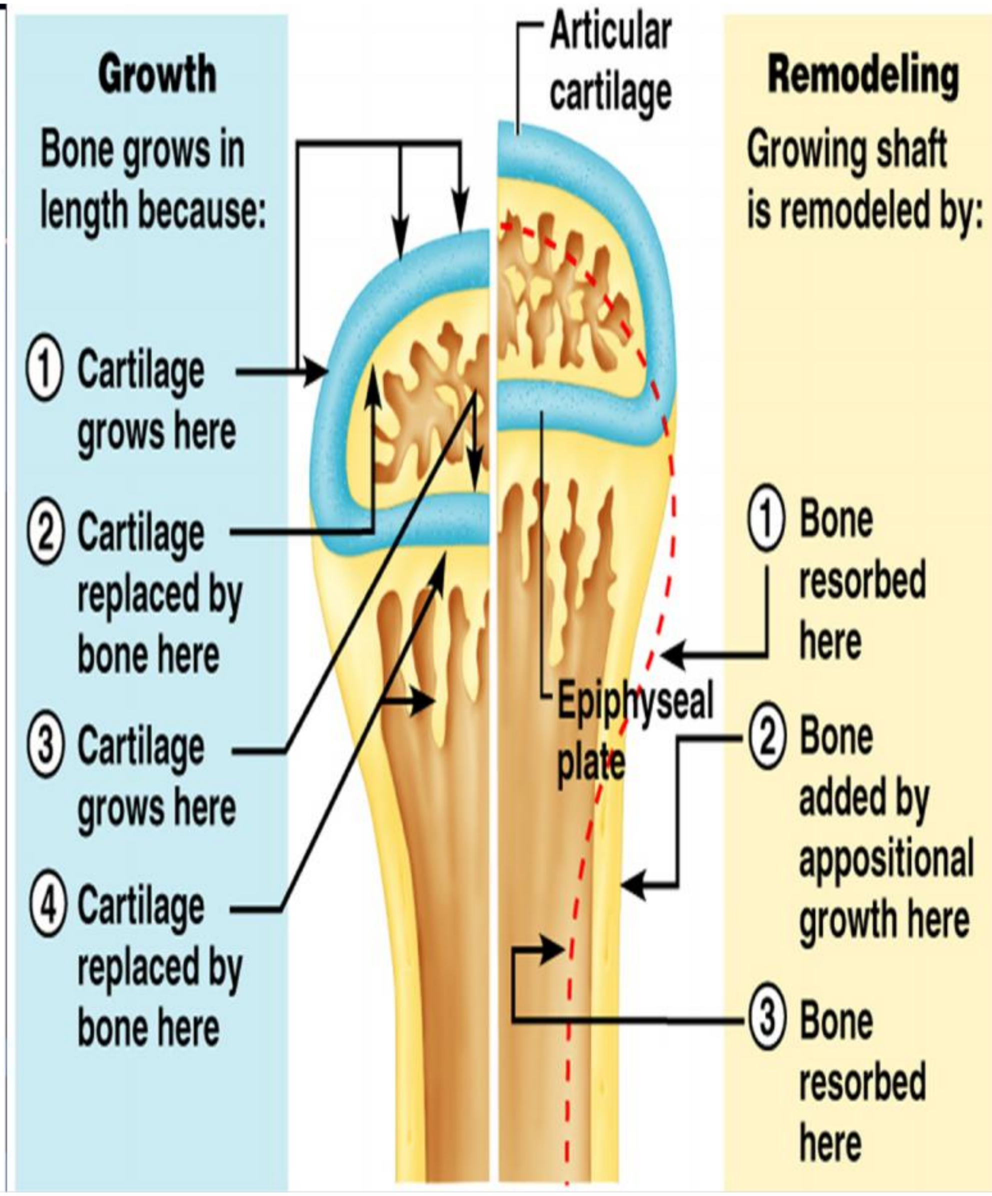



Figure 6.9


Perichondrial fibroblast
Perichondrium
Chondroblast
Cartilage
Interterritorial matrix
Chondrocyte
Territorial matrix

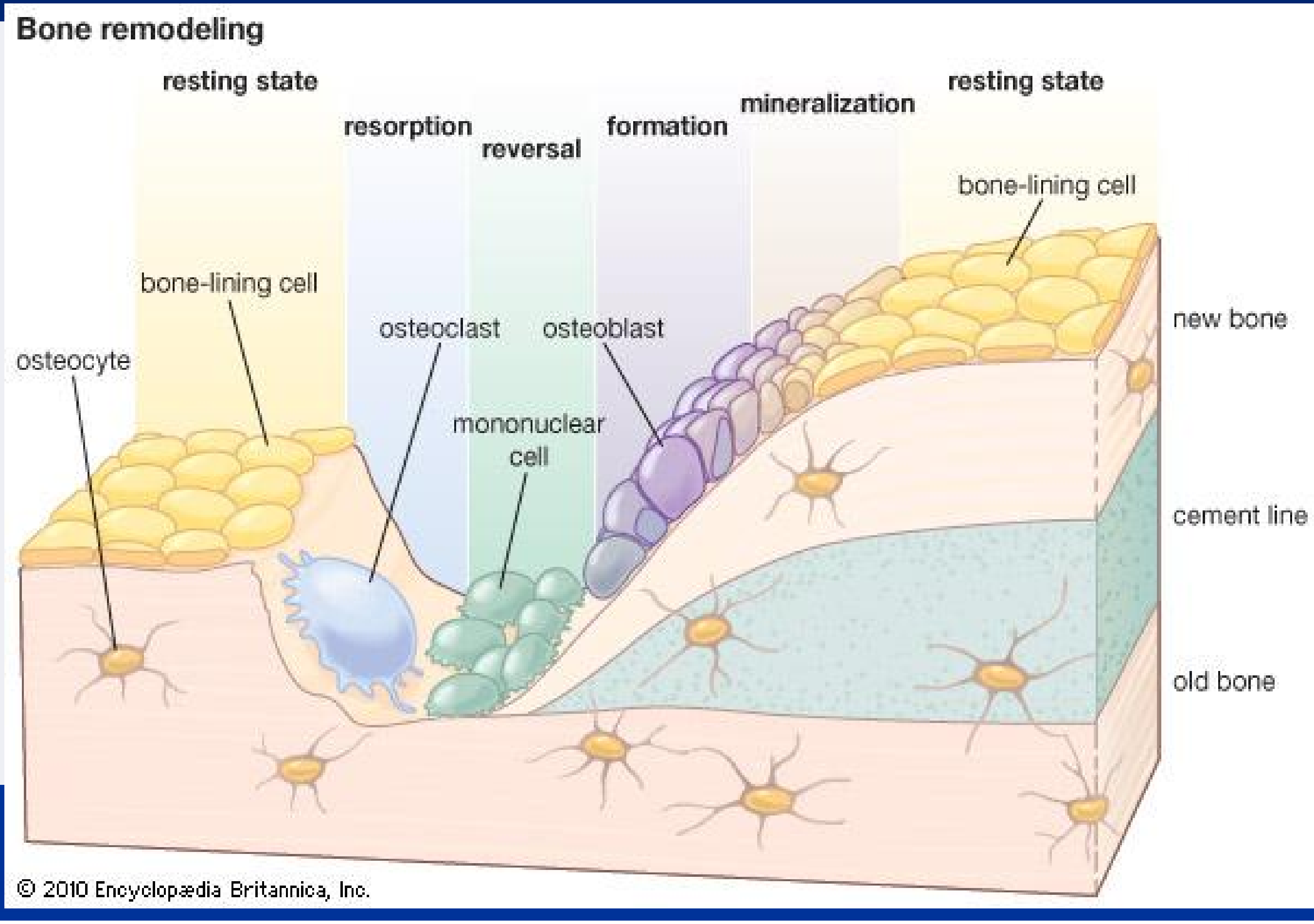

Growth
Bone grows in length because:
1 Cartilage grows here
2 Cartilage replaced by bone here
3 Cartilage grows here
4 Cartilage replaced by bone here
Articular cartilage
Epiphyseal plate
Remodeling
Growing shaft is remodeled by:
1 Bone resorbed here
2 Bone added by appositional growth here
3 Bone resorbed here

# Hormonal Regulation of Bone Growth During Youth

- During infancy and childhood, epiphyseal plate activity is stimulated by **growth hormone**
- **During puberty, testosterone and estrogens:**
  - Initially promote adolescent growth spurts
  - Cause masculinization and feminization of specific parts of the skeleton
  - **Later induce epiphyseal plate closure, ending longitudinal bone growth**

# Bone Remodeling

- **Remodeling units** – adjacent osteoblasts and osteoclasts deposit and resorb bone at periosteal and endosteal surfaces



# Bone Deposition

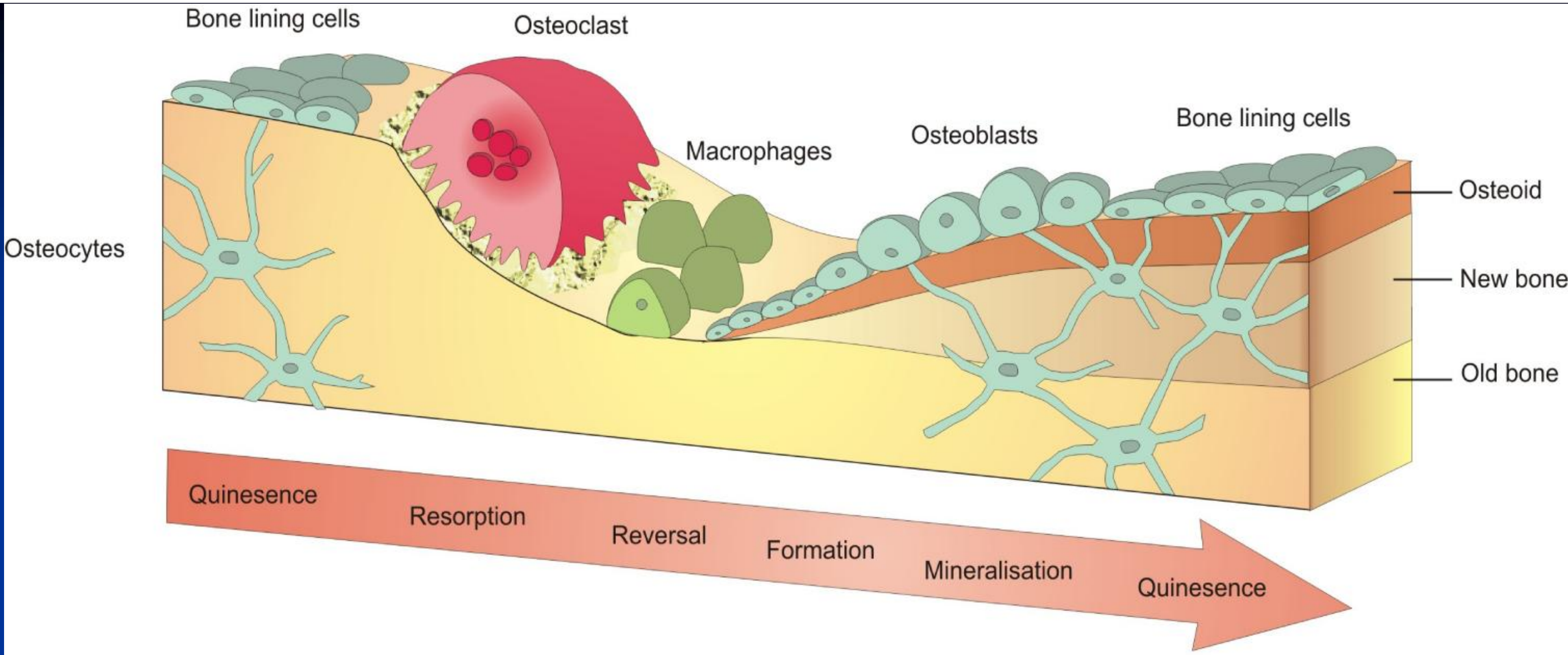
- Occurs where bone is injured or added strength is needed
- Requires a diet rich in protein, vitamins C, D, and A, calcium, phosphorus, magnesium, and manganese
- Alkaline phosphatase is essential for mineralization of bone

- Sites of new matrix deposition are revealed by the:
  - **Osteoid seam – unmineralized band of bone matrix**
  - Calcification front – abrupt transition zone between the osteoid seam and the older mineralized bone

# Bone Resorption

- **Accomplished by osteoclasts**
- Resorption bays – grooves formed by osteoclasts as they break down bone matrix
- **Resorption involves osteoclast secretion of:**
  - **Lysosomal enzymes that digest organic matrix**
  - **Acids that convert calcium salts into soluble forms**

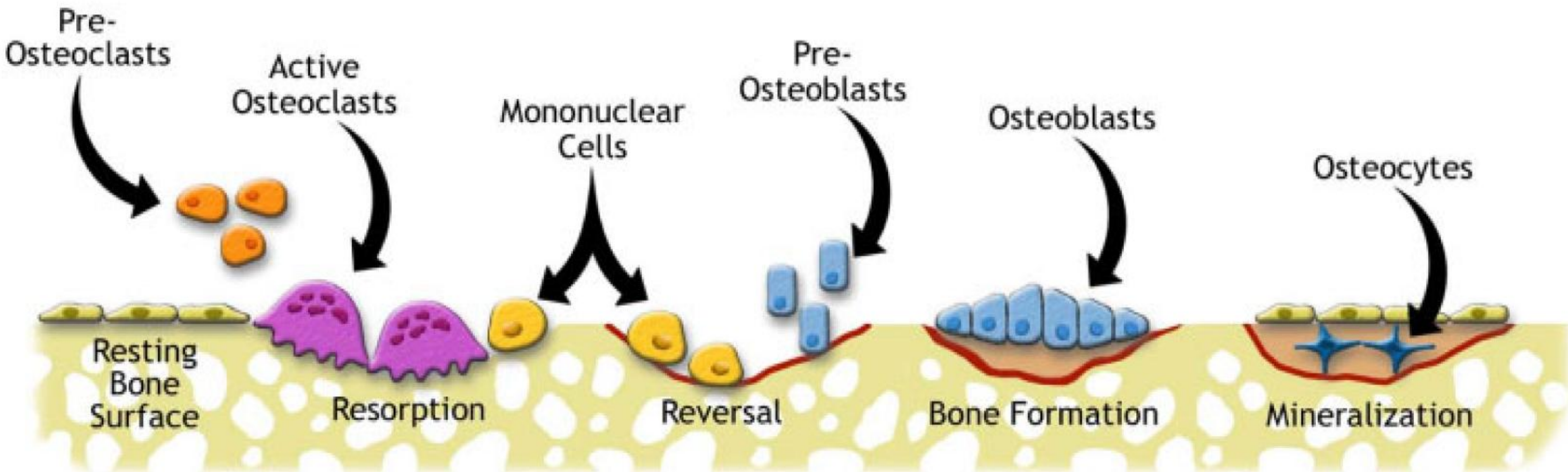
- Dissolved matrix is transcytosed across the osteoclast's cell where it is secreted into the interstitial fluid and then into the blood




**The bone remodelling process.**

Bone is continuously remodelled at discrete sites in the skeleton in order to maintain the integrity of the tissue. During this process, old bone is resorbed by osteoclasts and replaced with new osteoid, secreted by osteoblasts. First osteoclasts are activated, and the resorption phase takes approximately 10 days. Following resorption, unclassified macrophage-like cells are found at the remodelling site in the intermediate, or reversal phase. Osteoblast precursors are then recruited , which proliferate and differentiate into mature osteoblasts, before secreting new bone matrix. The matrix then mineralises to generate new bone and this completes the remodelling process. Copyright BTR©

# Bone Remodeling Cycle

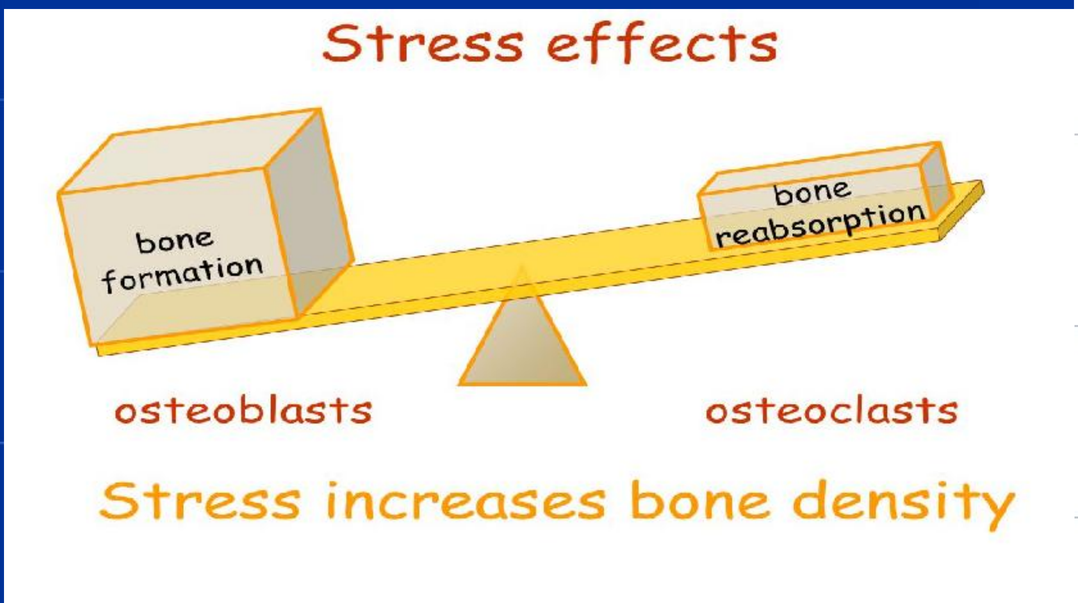



AMGEN

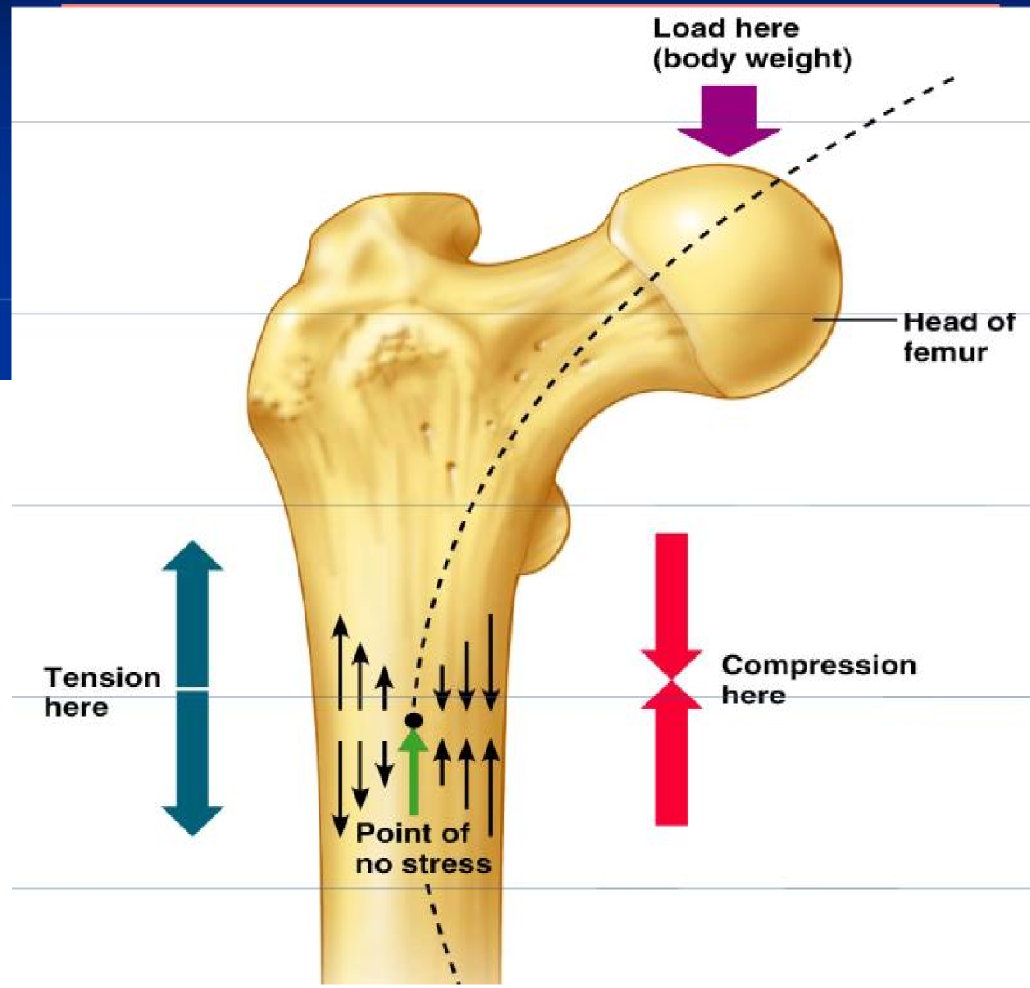

AMGEN

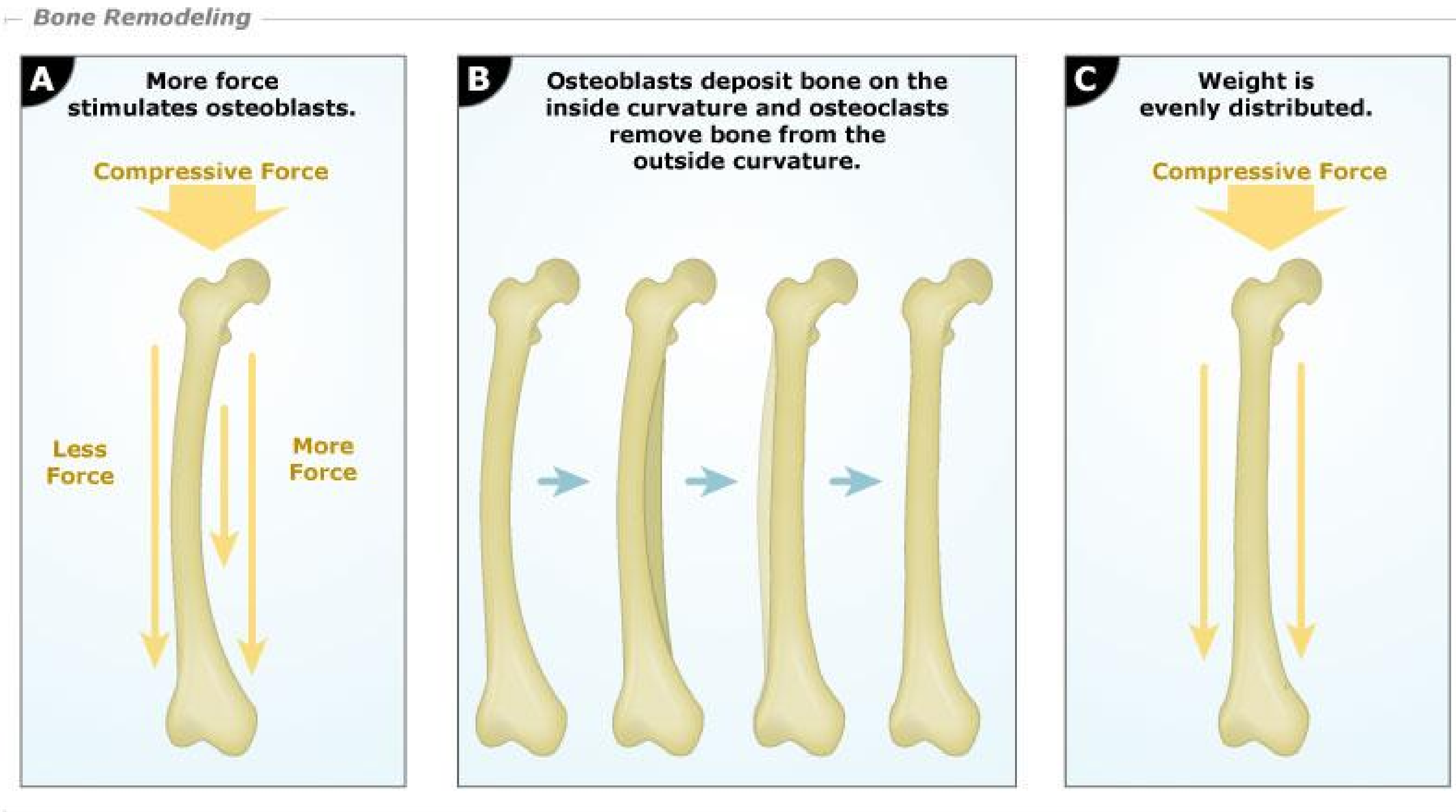
# Response to Mechanical Stress

- <u>Trabeculae form along lines of stress</u>
- Large, bony projections occur where heavy, active muscles attach

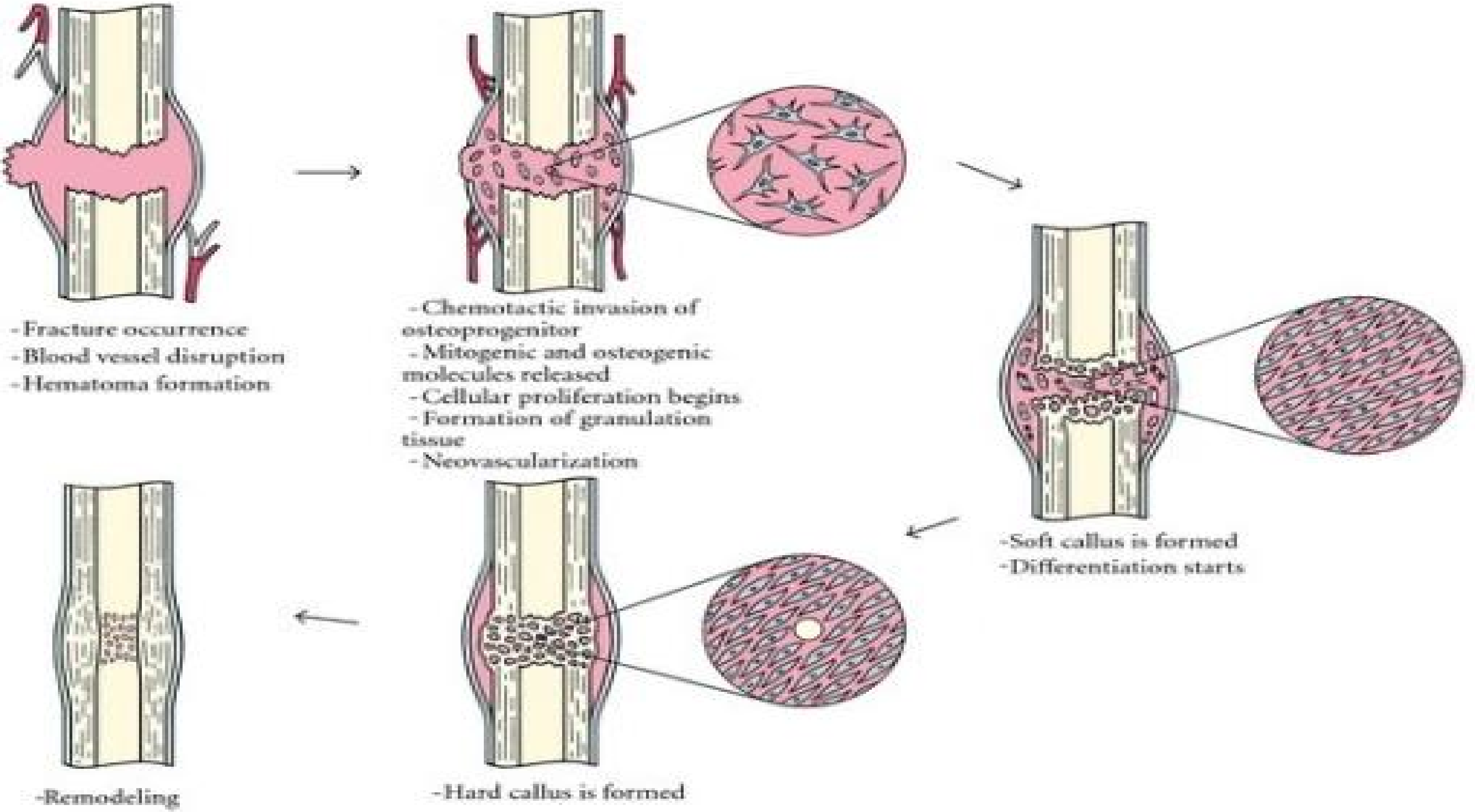


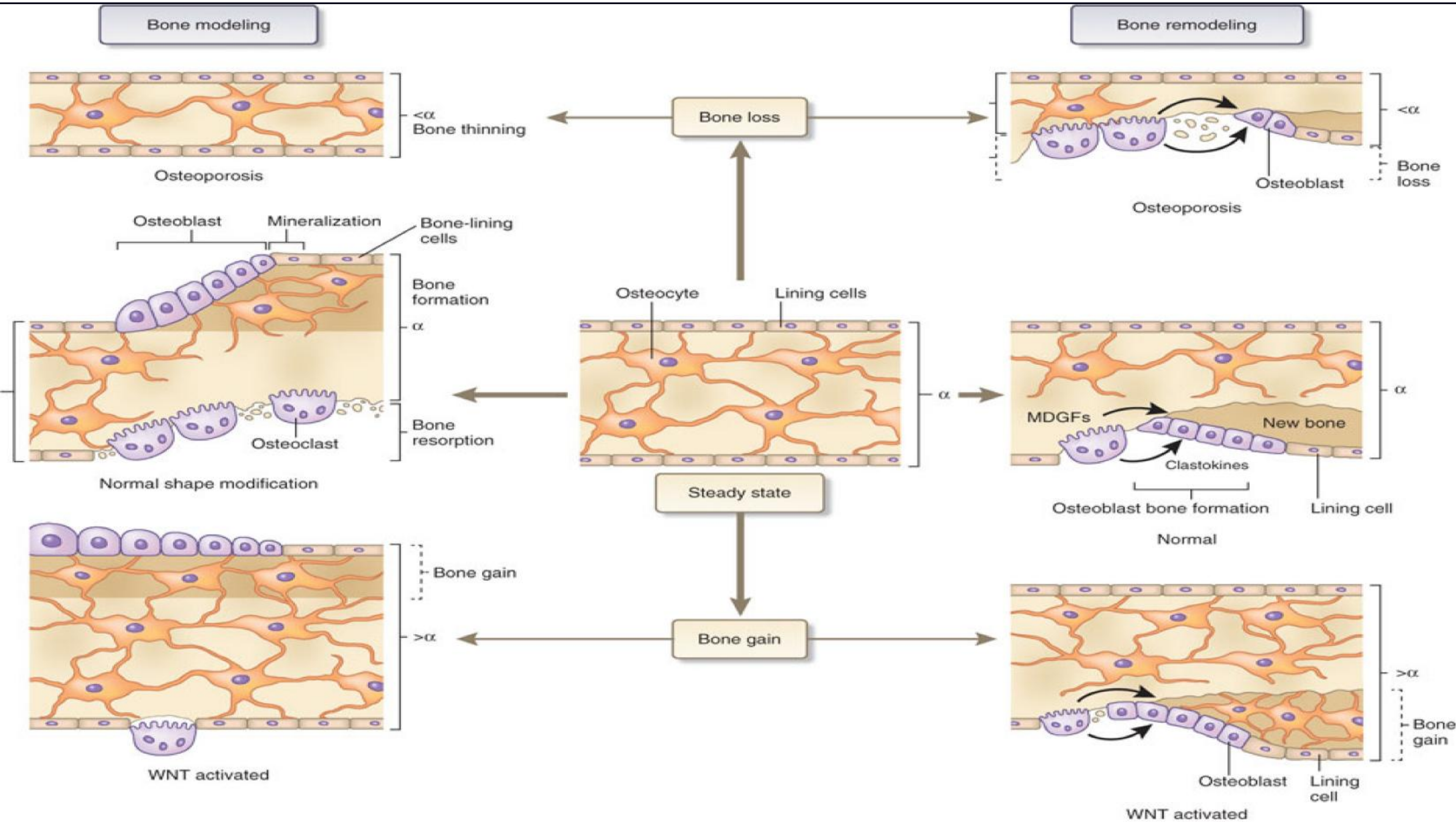

# Response to Mechanical Stress





Bone Remodeling
A
More force stimulates osteoblasts.
Compressive Force
Less Force
More Force
B
Osteoblasts deposit bone on the inside curvature and osteoclasts remove bone from the outside curvature.
C
Weight is evenly distributed.
Compressive Force


-Fracture occurrence
-Blood vessel disruption
-Hematoma formation
- Chemotactic invasion of osteoprogenitor
- Mitogenic and osteogenic molecules released
- Cellular proliferation begins
- Formation of granulation tissue
- Neovascularization
-Soft callus is formed
-Differentiation starts
-Hard callus is formed
-Remodeling



Bone modeling
Bone remodeling
<α
Bone thinning
Osteoporosis
Bone loss
Osteoblast
Osteoporosis
Osteoblast
Mineralization
Bone-lining cells
Bone formation
α
Osteoclast
Bone resorption
Normal shape modification
Osteocyte
Lining cells
Steady state
α
MDGFs
New bone
Clastokines
Osteoblast bone formation
Lining cell
Normal
Bone gain
>α
WNT activated
Osteoblast
Lining cell
WNT activated