

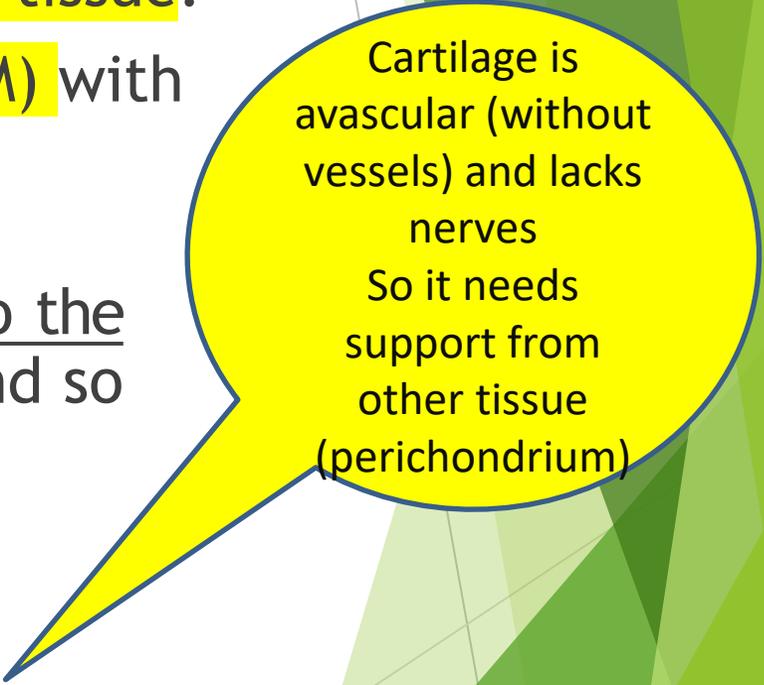
Cartilage

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General Information

- **Cartilage** is a tough form of supporting **connective tissue**.
- It is characterized by an **extracellular matrix (ECM)** with **high concentrations of GAGs and proteoglycans**, interacting with collagen and elastic fibers.
- Its **semi-rigid** consistency is due to water bound to the negatively charged hyaluronan and GAG chains, and so acts as a cushion.
- All types of cartilage **lack vascular supplies** and chondrocytes (**the type of cells in cartilage**) receive nutrients by diffusion from capillaries in surrounding connective tissue (**the perichondrium**). **peri means around**
- **Cartilage also lacks nerves.**



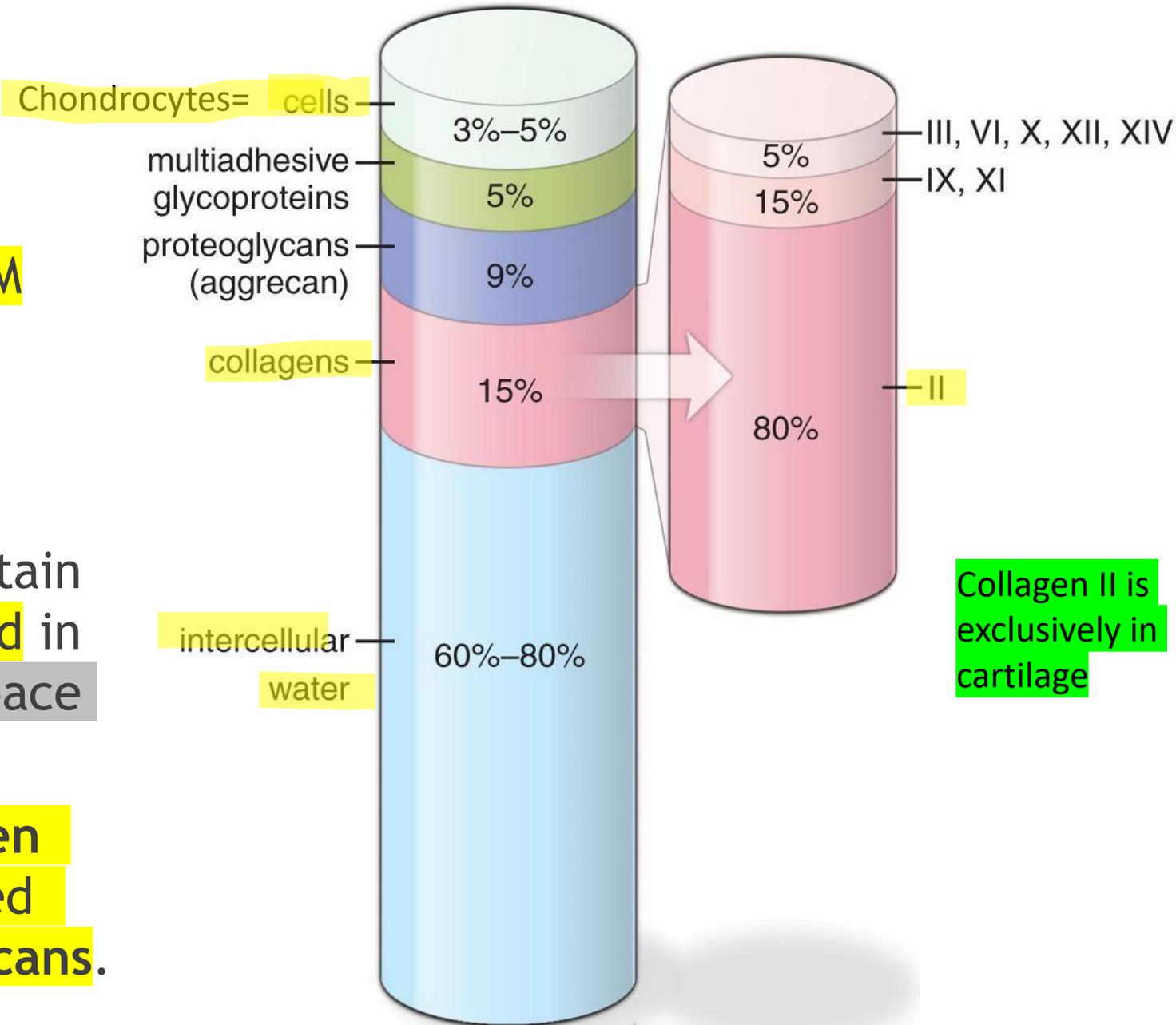
Cartilage is avascular (without vessels) and lacks nerves
So it needs support from other tissue (perichondrium)

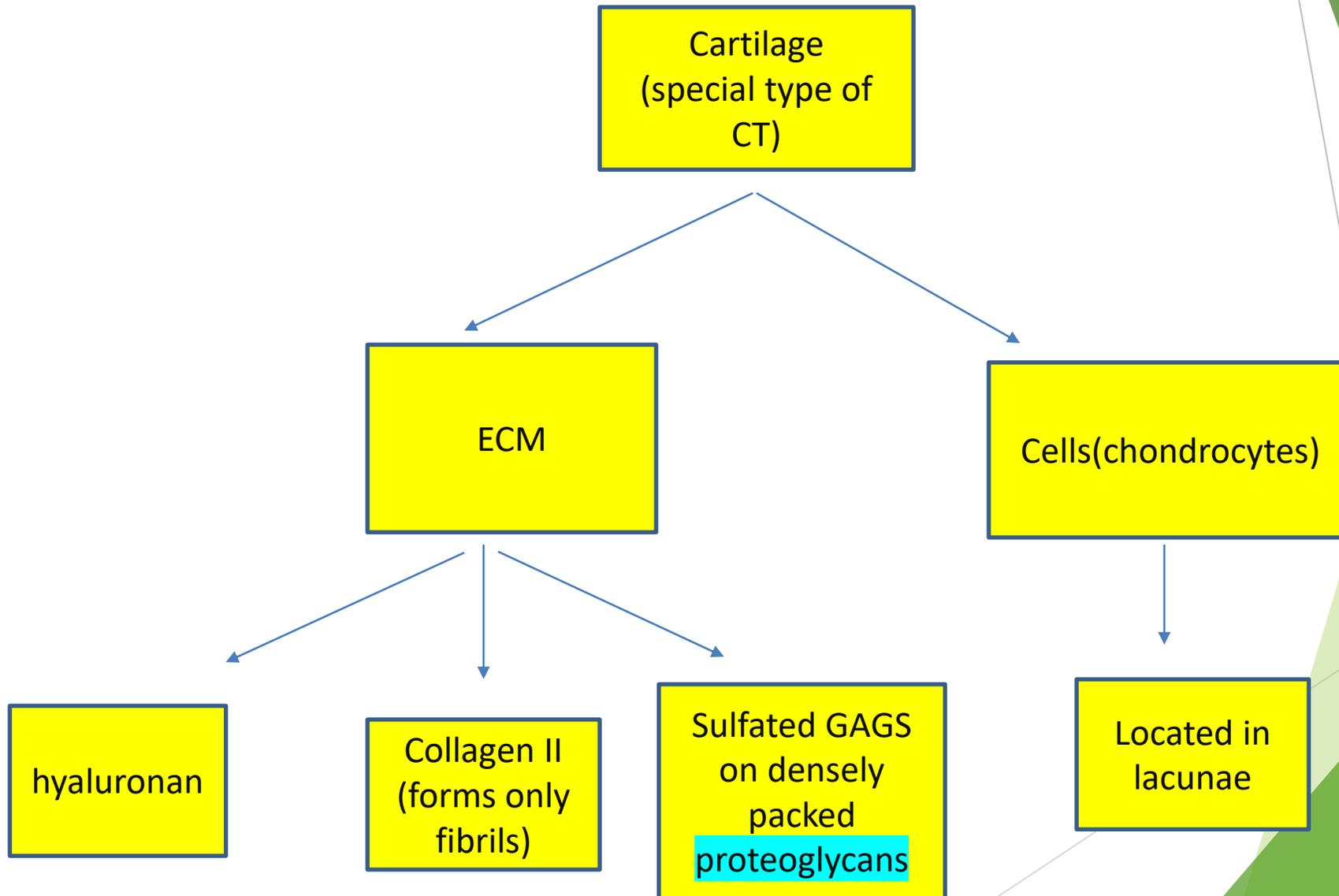
Composition

Cartilage consists of cells called **chondrocytes** embedded in the ECM which contains no other cell types. (the chondrocytes are originated from chondroblasts which are differentiated from mesenchymal cells)

Chondrocytes synthesize and maintain all ECM components and are located in matrix cavities called **lacunae**. (space that surround chondrocytes)

ECM components are **type II collagen** fibrils, **hyaluronan**, and the sulfated GAGs on densely packed **proteoglycans**.





Medical Application

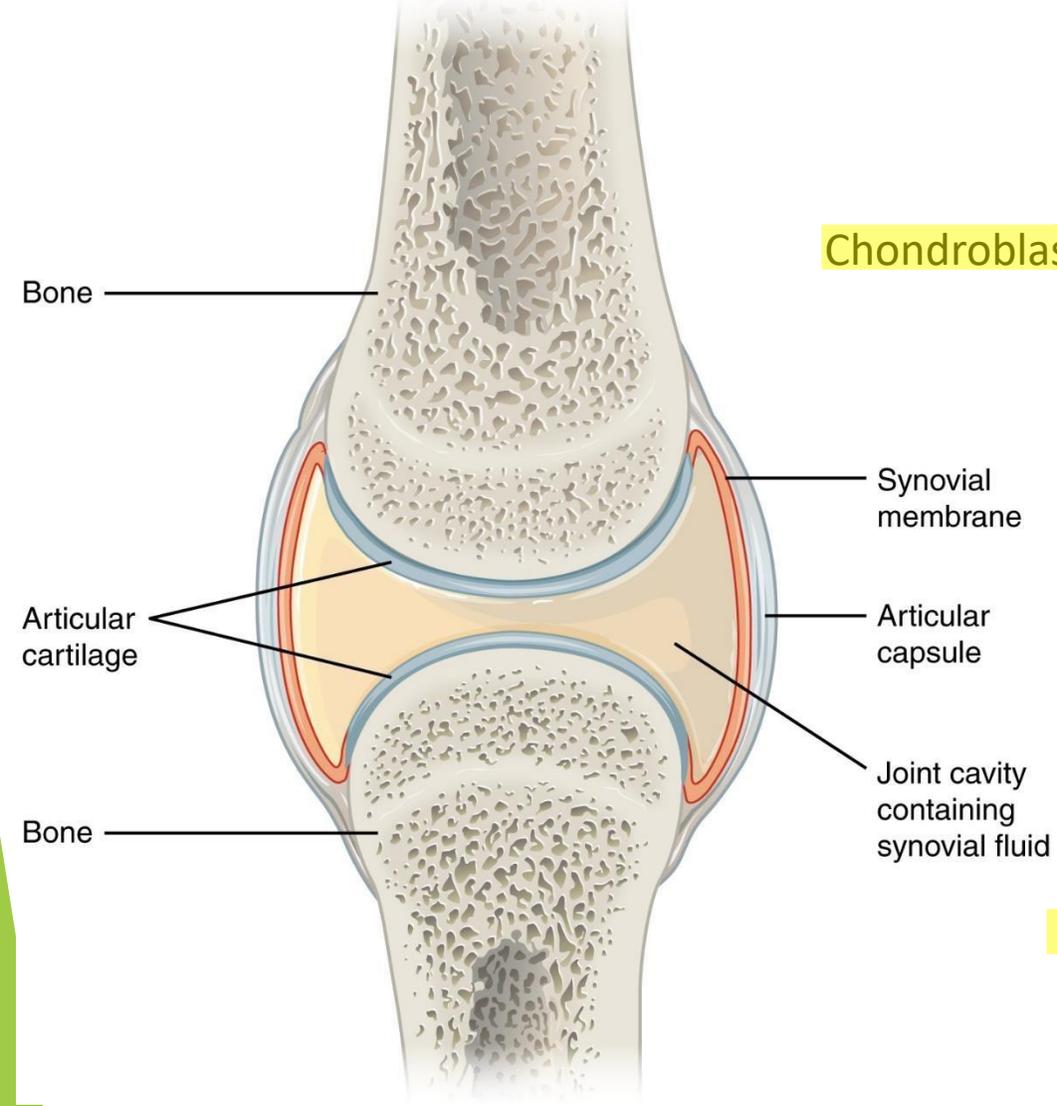
- Many genetic conditions in humans or mice that cause (mutations in coding cell division) defective cartilage, joint deformities, or short limbs are due to recessive mutations in genes for collagen type II, the aggrecan core protein, the sulfate transporter, and other proteins required for normal chondrocyte function.

Perichondrium

peri: around''chondrium: cartilage

Perichondrium cartilage=fibers
(collagen I)+cells(fibroblast)
It is vascular

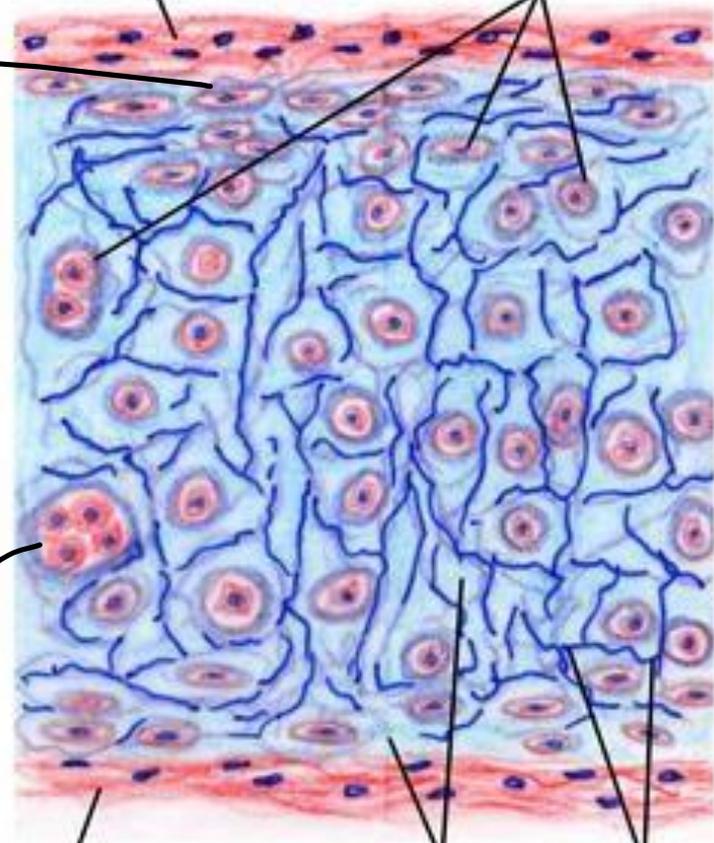
- The perichondrium is a sheath of dense connective tissue that surrounds cartilage, forming an interface between the cartilage and the tissues supported by the cartilage.
- The perichondrium harbors the blood supply serving the cartilage and a small neural component.
- ** Articular cartilage, which covers the ends of bones in movable joints, **lacks perichondrium** and **is sustained** by the diffusion of oxygen and nutrients from the **synovial fluid**.



Chondroblasts



Perichondrium
Chondrocytes in lacunae



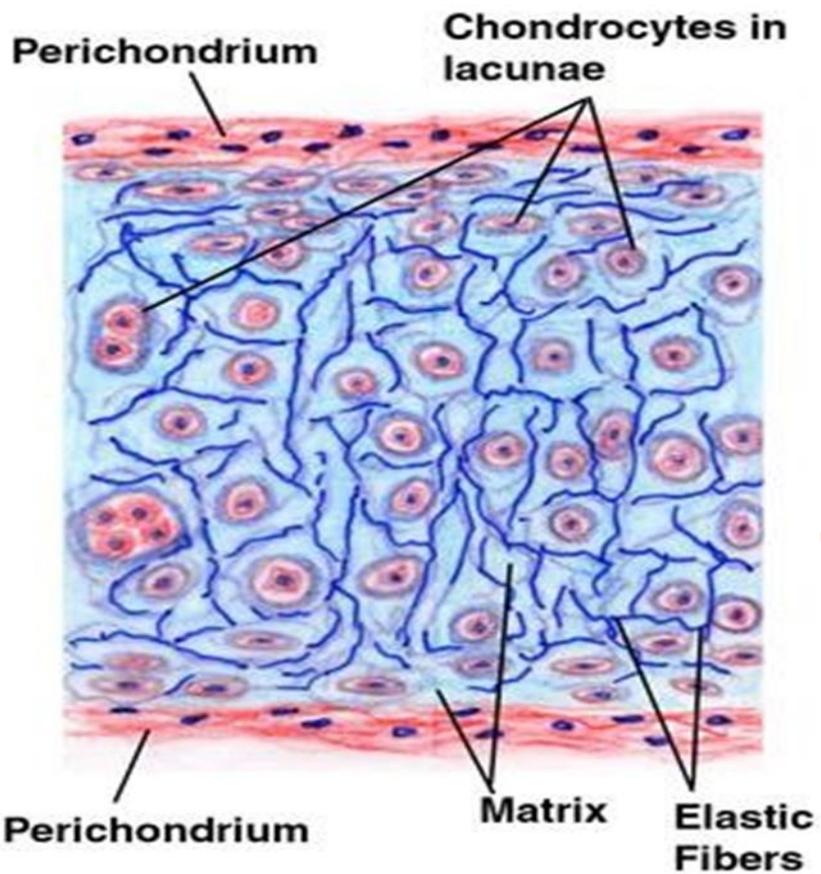
Isogenous group



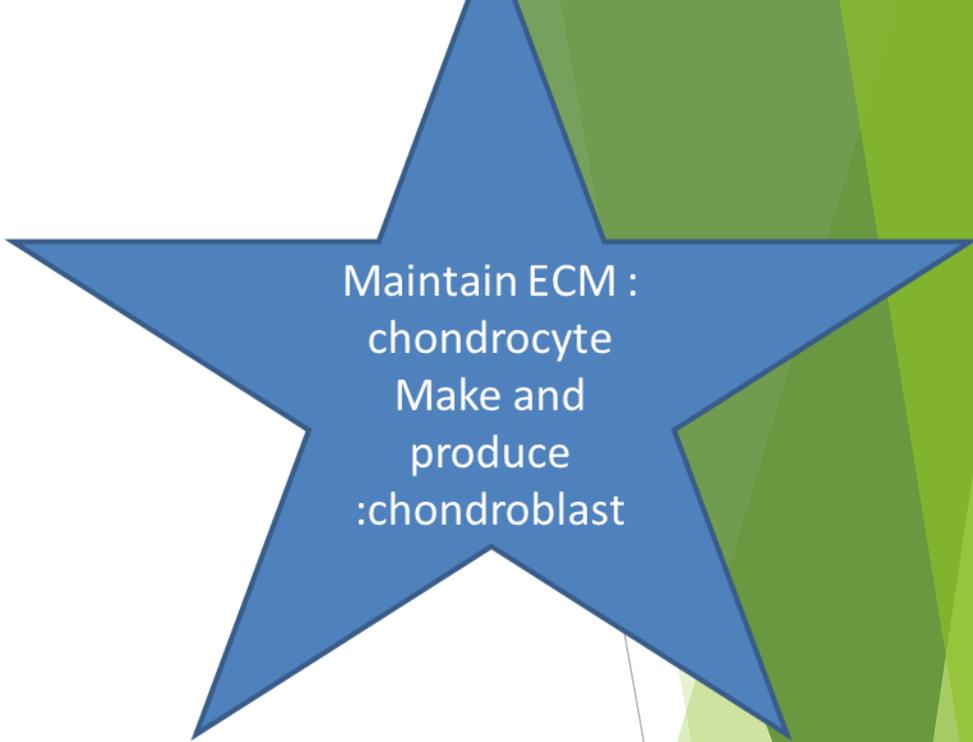
Perichondrium
Matrix
Elastic Fibers

Notice that:
Chondroblast is between perichondrium and chondrocytes

Articular cartilage is avascular and it does not have Perichondrium because it is a highly friction region so it gets nutrition by synovial fluid



*mesenchymal cells differentiate into chondroblasts
 *chondroblasts start to produce and make ECM until it becomes surrounded by ECM and located in small space (lacunae) "بتصير محشورة", so it will be inactive becoming chondrocytes

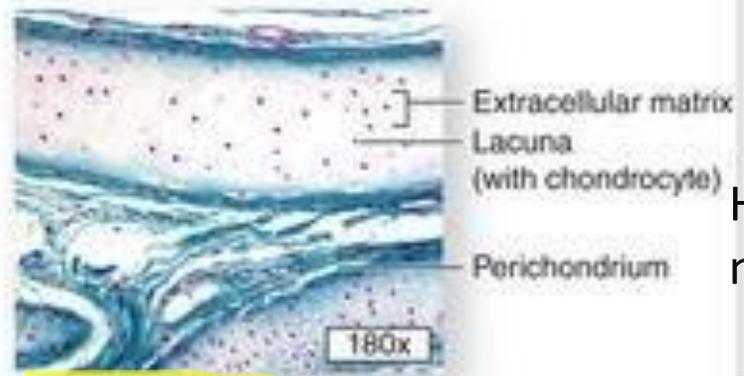
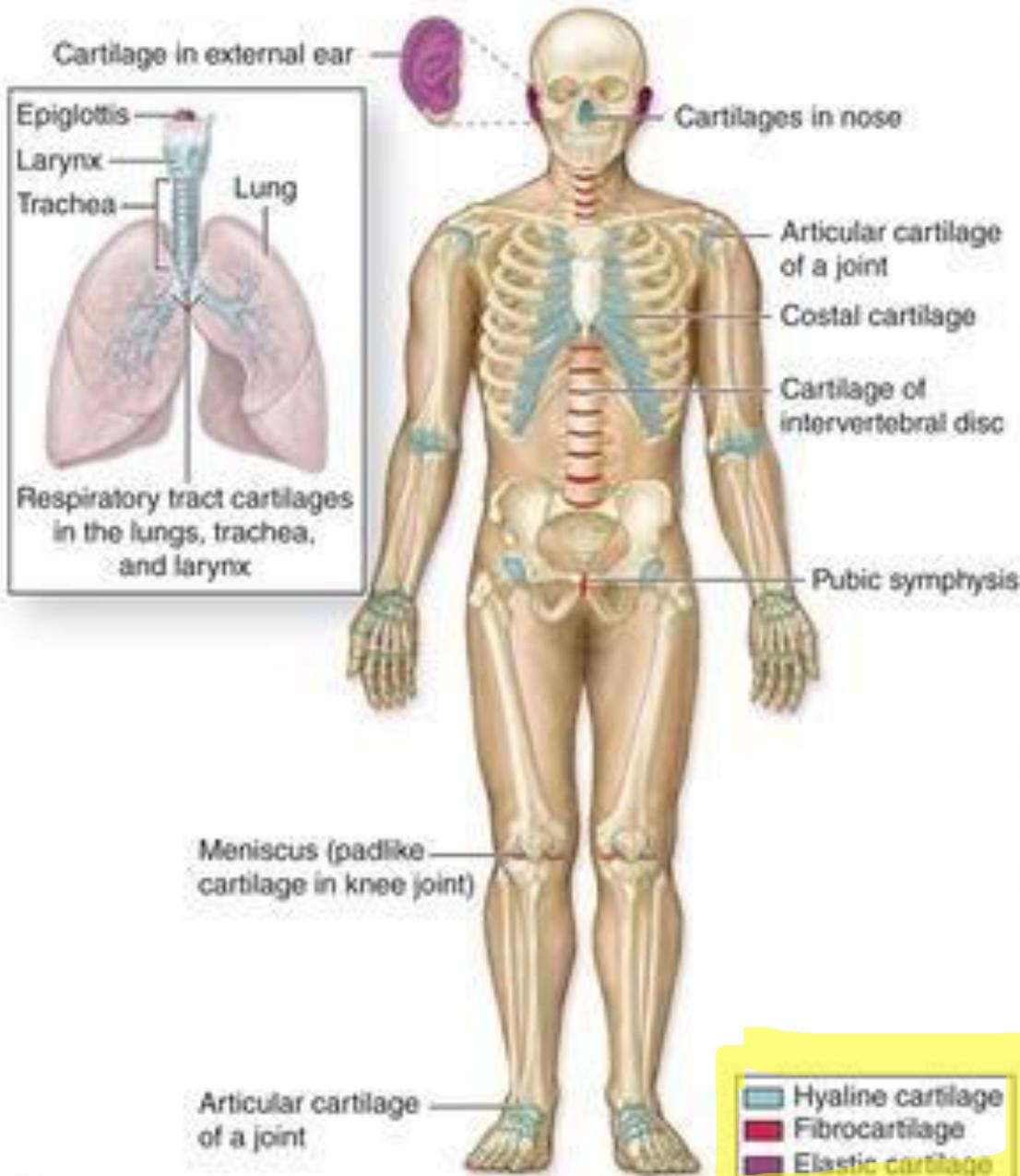


In some cases chondrocyte undergoes mitosis in its lacunae as a response to stimuli making *isogenous groups=aggregated*: similar cells

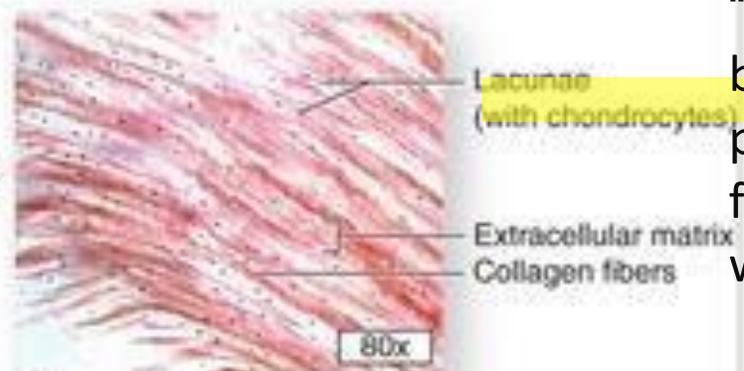
Types

Three main types of cartilage:

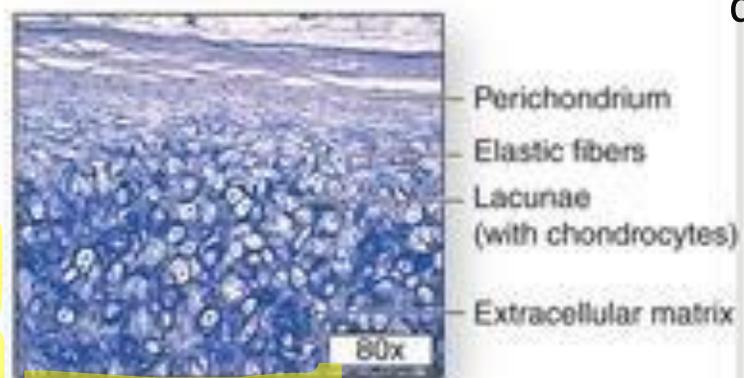
- hyaline cartilage:: glass like , semi transparent
- elastic cartilage : fibers have ability to stretch out and recoil
- fibrocartilage: chondrocytes +fibers(resist tension and stress)



b Hyaline cartilage



c Fibrocartilage



d Elastic cartilage

Hyaline cartilage locates in nose , ends of ribs

Elastic : ear, epiglottis “لسان المزمار” it needs elastic because its function is preventing the passage of food to respiratory tract while eating

Fibrocartilage : intervertebral disc , pubic symphysis

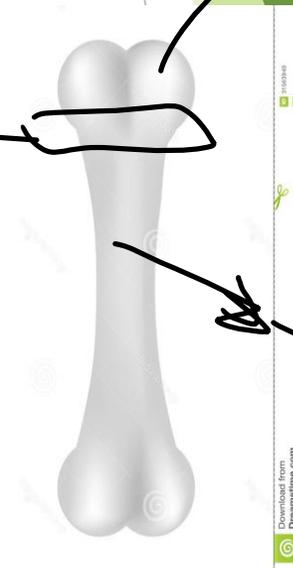
TABLE 7-1**Important features of the major cartilage types.**

	Hyaline Cartilage	Elastic Cartilage	Fibrocartilage
Main features of the extracellular matrix	Homogeneous, with type II collagen and aggrecan	Type II collagen, aggrecan, and darker elastic fibers	Type II collagen and large areas of dense connective tissue with type I collagen
Major cells	Chondrocytes, chondroblasts	Chondrocytes, chondroblasts	Chondrocytes, fibroblasts
Typical arrangement of chondrocytes	Isolated or in small isogenous groups	Usually in small isogenous groups	Isolated or in isogenous groups arranged axially
Presence of perichondrium	Yes (except at epiphyses and articular cartilage)	Yes	No
Main locations or examples	Many components of upper respiratory tract; articular ends and epiphyseal plates of long bones; fetal skeleton	External ear, external acoustic meatus, auditory tube; epiglottis and certain other laryngeal cartilages	Intervertebral discs, pubic symphysis, meniscus, and certain other joints; insertions of tendons
Main functions	Provides smooth, low-friction surfaces in joints; structural support for respiratory tract	Provides flexible shape and support of soft tissues	Provides cushioning, tensile strength, and resistance to tearing and compression

No chondroblast after differentiating in fibrocartilage because there is no perichondrium that facilitates differentiation of chondrocyte from -blast

Hyaline Cartilage

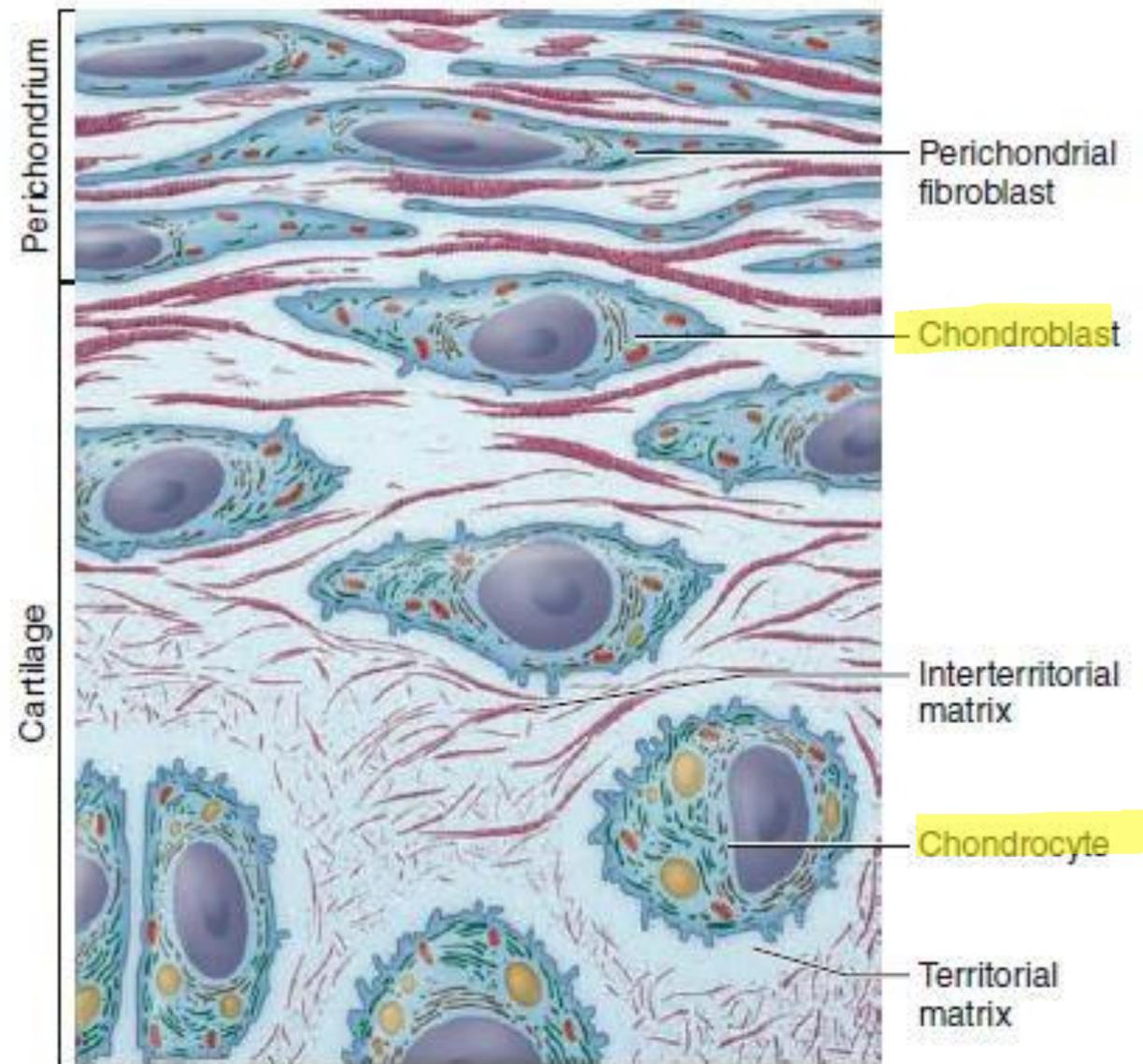
- Hyaline cartilage is the **most common** of the three types
- It is homogeneous and **semitransparent** in the fresh state
- **In adults** hyaline cartilage is located
 - 1 □ in the articular surfaces of movable joints
 - 2 □ in the walls of larger respiratory passages (nose, larynx, trachea, bronchi)
 - 3 □ in the ventral ends of ribs, where they articulate with the sternum
 - 4 □ in the **epiphyseal plates** of long bones, (**function:** where it makes possible longitudinal bone growth **النمو الطولي للعظم** (it is located in the confluence between epiphysis (the heads of long bones) with diaphysis (shaft of bone))
- **In the embryo**, hyaline cartilage forms the temporary skeleton that is gradually replaced by bone. (replace NOT convert to bone)



Chondroblasts and Chondrocytes

- Fibroblast-like progenitor (mesenchymal) cells in the perichondrium give rise to larger chondroblasts, which divide and differentiate as chondrocytes.
- These functional cells produce matrix components and exist in **lacunae** surrounded by the matrix.

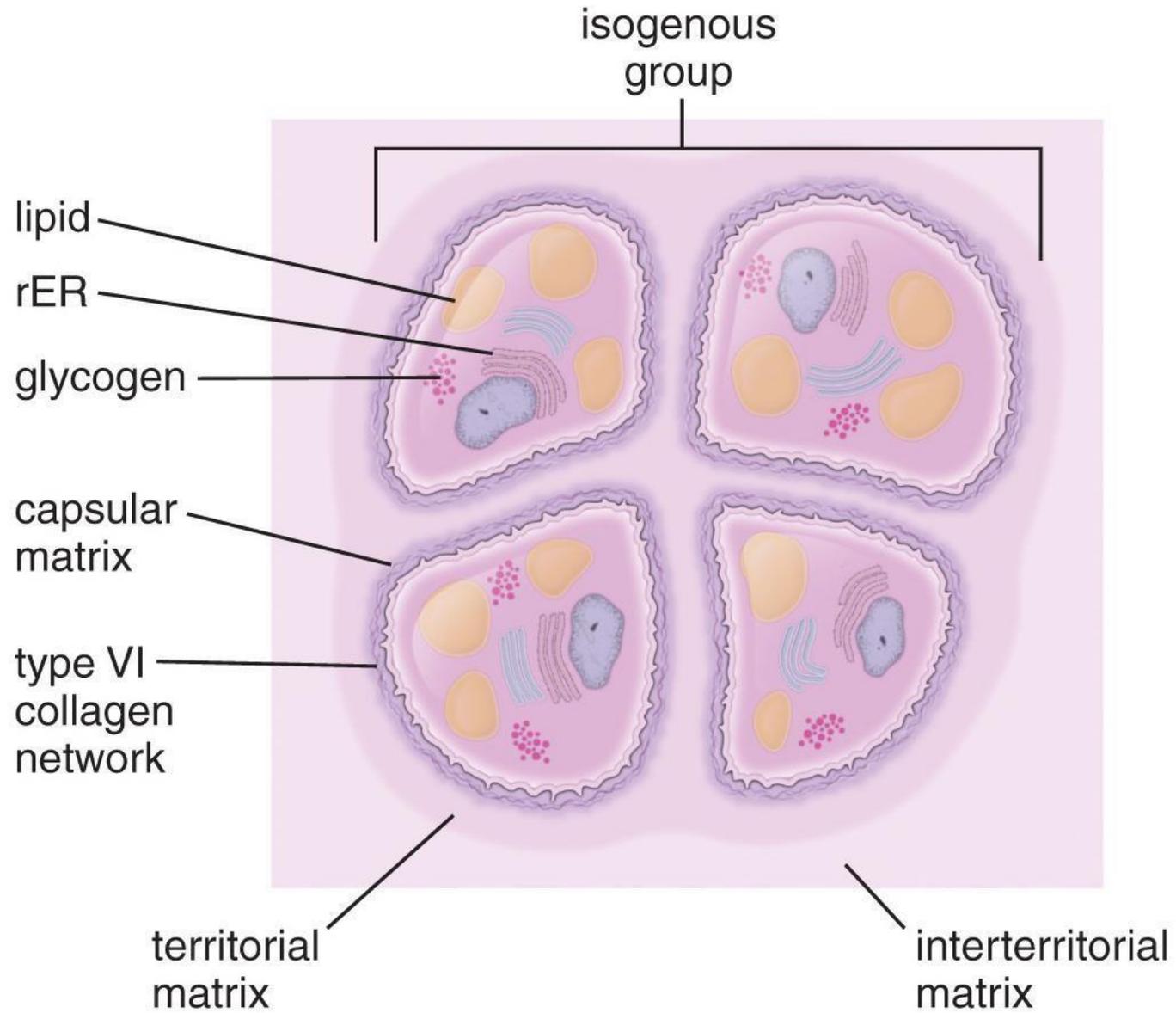
Active in maintaining ECM



Chondrocytes

: occupy 3-5% of cartilage weight

- Cells occupy relatively little of the hyaline cartilage mass.
- Deeper in the cartilage, cells may appear in groups of up to eight cells that originate from mitotic divisions of a single chondroblast and are called isogenous aggregates.
- As the chondrocytes become more active in secreting collagens and other ECM components, the aggregated cells are pushed apart and occupy separate lacunae.

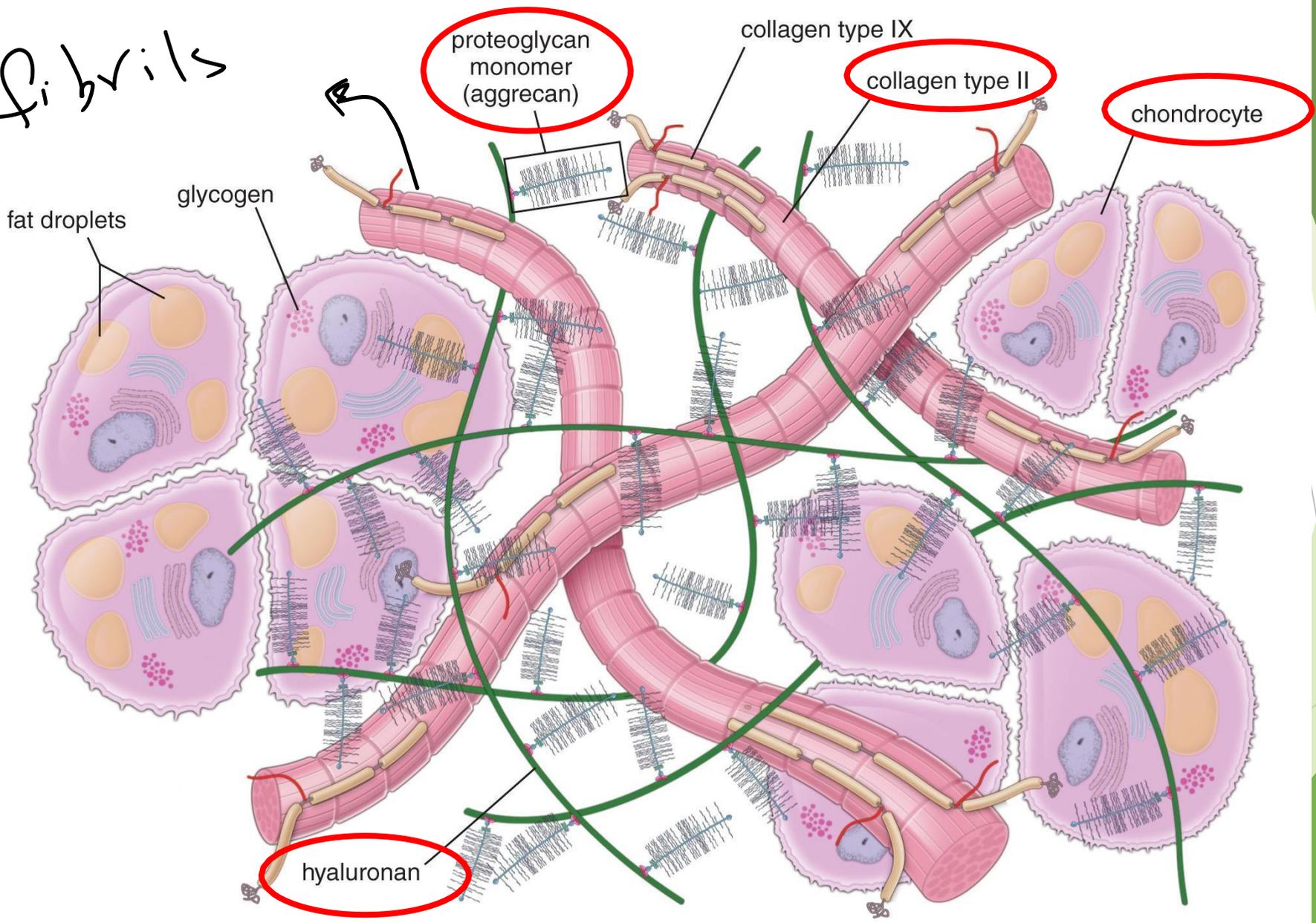


Hyaline cartilage Matrix

collagen type II+GAGS+holding to water

- The dry weight of hyaline cartilage is nearly 40% collagen embedded in a firm, hydrated gel of proteoglycans and structural glycoproteins.
- In routine histology preparations, the proteoglycans make the matrix generally basophilic (appears purple or blue) and the thin collagen fibrils are not visible. Most of the collagen in hyaline cartilage is type II, although small amounts of minor collagens are also present.
- Chondroitin sulfate and keratan sulfate are the most abundant proteoglycans of hyaline cartilage.
- Another important component of cartilage matrix is the structural multiadhesive glycoprotein chondronectin, which binds specifically to GAGs, collagen, and integrins, mediating the adherence of chondrocytes to the ECM.

fibrils



Territorial Vs Interterritorial matrix

- The ECM immediately **around each lacuna** is called the **territorial matrix**. It contains mostly **proteoglycans** and **sparse collagen** (**highly basophilic: it contains GAGS that are negatively charged**)
- That ECM more distant from lacunae is called the **interterritorial matrix**. (**between 2 adjacent chondrocytes**) It is richer in **collagen** and may be **less basophilic**. (**it has a lot of collagen II that is acidophilic but of course it has more GAGS so it is still baso but lighter**)

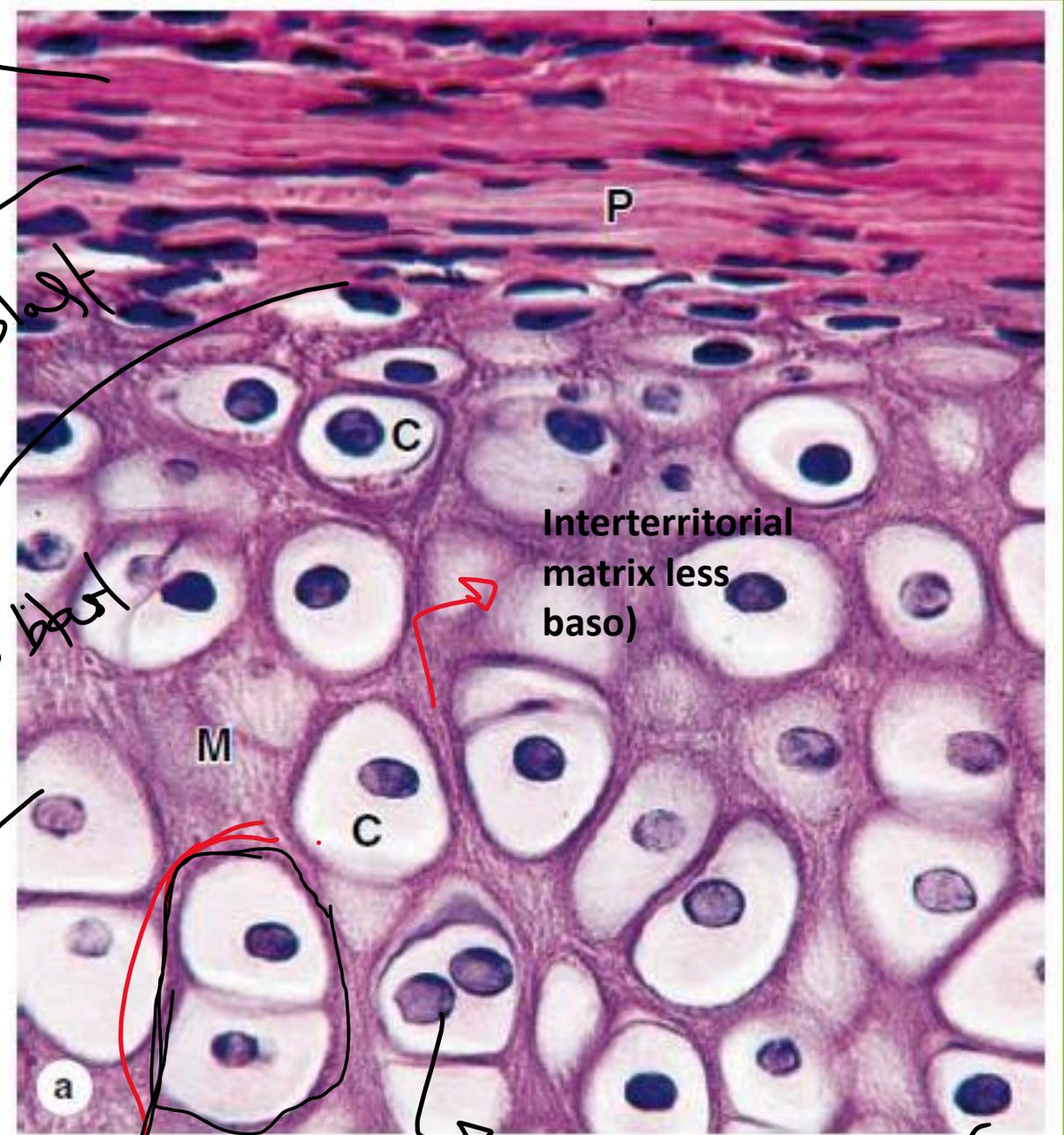
- The upper part of the photo shows the perichondrium (P), an example of dense connective tissue consisting largely of type I collagen.
- There is a gradual transition and differentiation of cells from the perichondrium to the cartilage, with some elongated fibroblast-like cells becoming larger and more rounded as chondroblasts and chondrocytes (C).
- These are located within lacunae surrounded by the matrix (M) which these cells secreted.

fibers

Fibroblast

Chondroblast

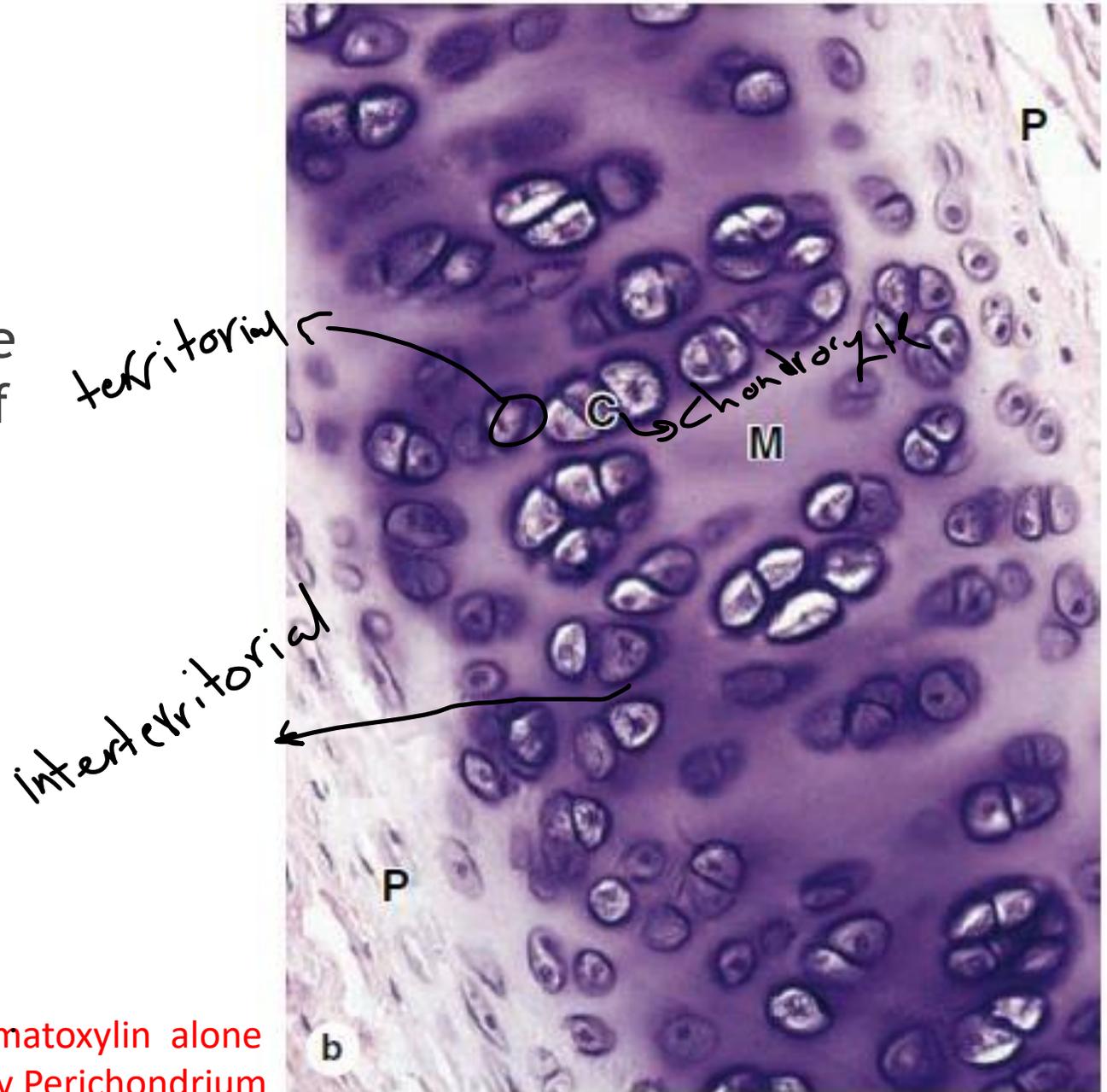
Chondrocyte



territorial matrix (highly basophilic)

isogenous group

- The thin region of hyaline cartilage shown here has perichondrium (P) on both sides and shows larger lacunae containing isogenous groups of chondrocytes (C) within the matrix (M).
- Territorial matrix immediately around the chondrocytes is more basophilic than interterritorial matrix farther from the cells.



This is Hematoxylin alone that is why Perichondrium looks unstained (it is acido)

Medical Application

- In contrast to other forms of cartilage and most other tissues, hyaline cartilage is susceptible to partial or isolated regions of **calcification** during aging, especially in the costal cartilage adjacent to the ribs. Calcification of the hyaline matrix, accompanied by degenerative changes in the chondrocytes, is a common part of the aging process and in many respects resembles endochondral ossification by which bone is formed. **(with aging cartilage becomes stiff so it is replaced with bones)**

Perichondrium of Hyaline Cartilage

- The perichondrium has two regions; an outer fibrous and inner cellular
- The outer region of the perichondrium consists largely of collagen type I fibers and fibroblasts
- The inner layer adjoining the cartilage matrix contains mesenchymal stem cells which provide a source for new chondroblasts that divide and differentiate into chondrocytes.

Medical Application

- Cells of cartilage can give rise to either **benign حميد** (**chondroma**) or slow-growing, **malignant** **خبيث (chondrosarcoma)** tumors in which cells produce normal matrix components. Chondrosarcomas seldom metastasize and are generally removed surgically.

Tumor is any strange growth
It doesn't mean cancer

Tumor that invaginates and metastasizes is malignant
In cartilage we call it chondrosarcoma

Tumor that is just divides it is benign (no spread) in cartilage we call it chondroma

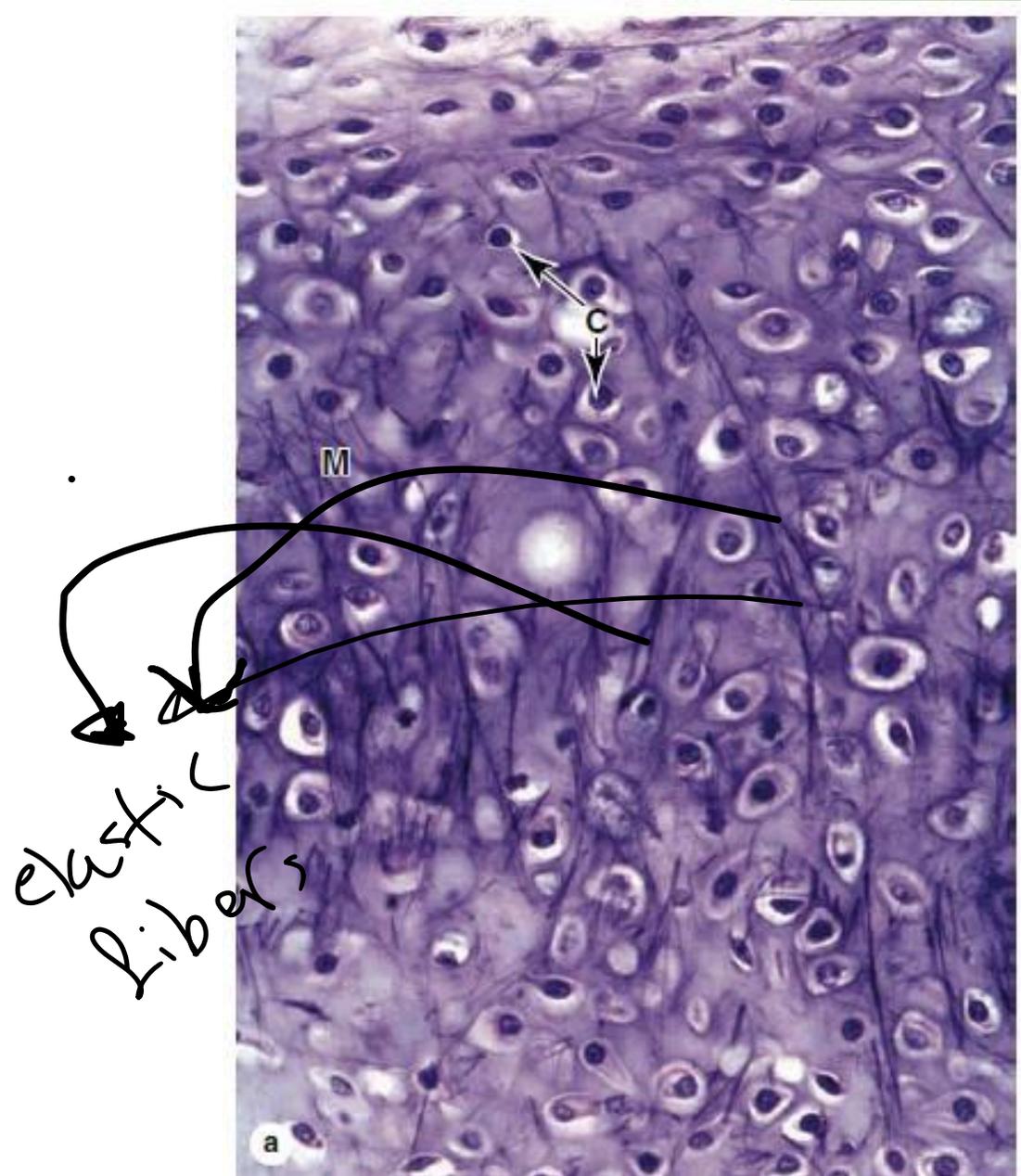
Elastic Cartilage

- **Elastic cartilage** is similar to hyaline cartilage except that it contains an abundant network of **elastic fibers** in addition to a meshwork **of collagen type II fibrils**
- It is more flexible than hyaline cartilage
- Elastic cartilage is found in the auricle of the ear, the walls of the external auditory canals, the auditory (Eustachian) tubes, the epiglottis, and the upper respiratory tract.
- Elastic cartilage in these locations includes a perichondrium similar to that of most hyaline cartilage.

Elastic Cartilage

- The chondrocytes (C) and overall organization of elastic cartilage are similar to those of hyaline cartilage, but the matrix (M) also contains elastic fibers that can be seen as darker components (Stain: Hematoxylin & Orcein)

The fibers are prominent in elastic and transparent in hyaline

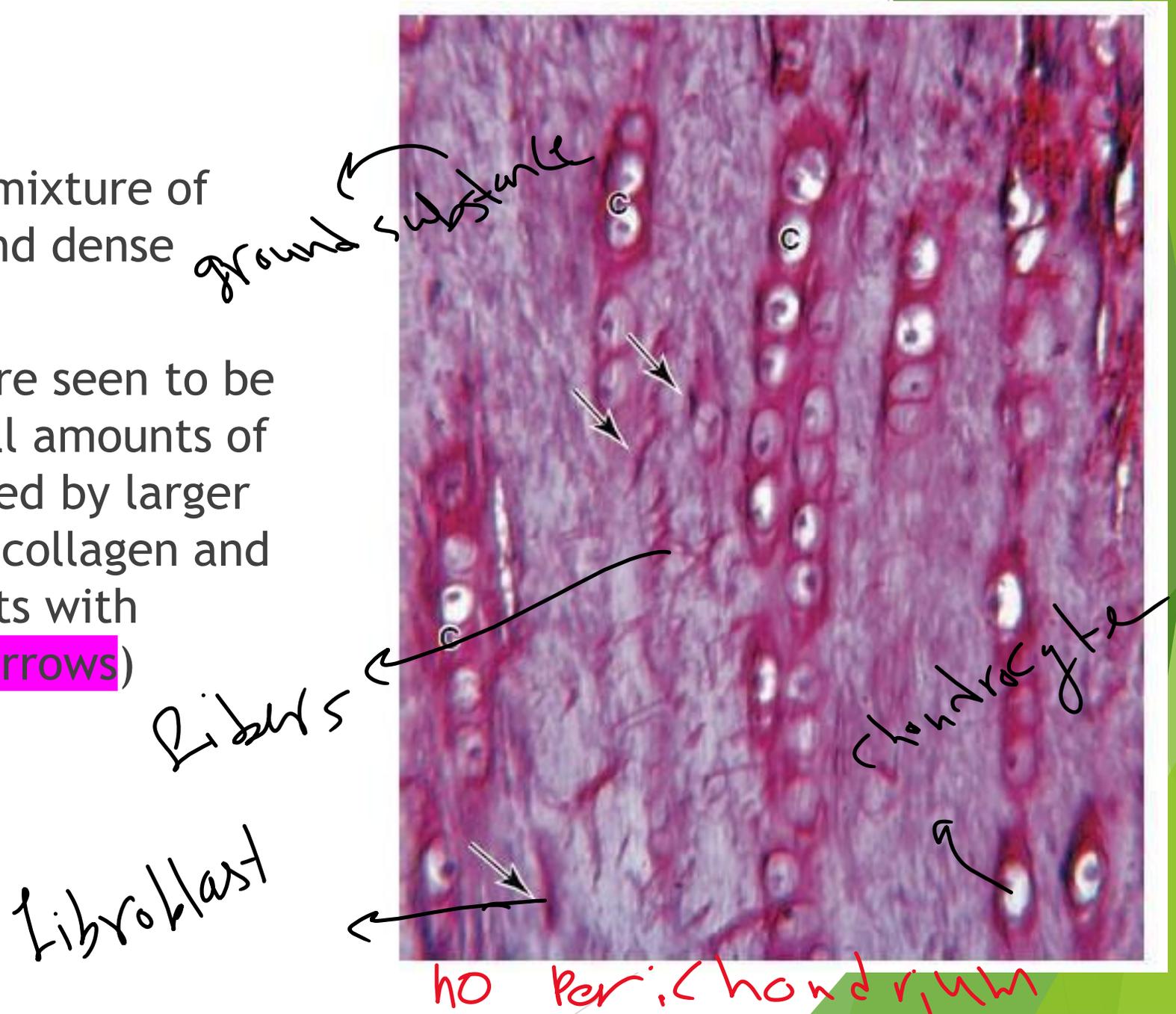


Fibrocartilage

collagen1 +chondrocyte + fibroblast

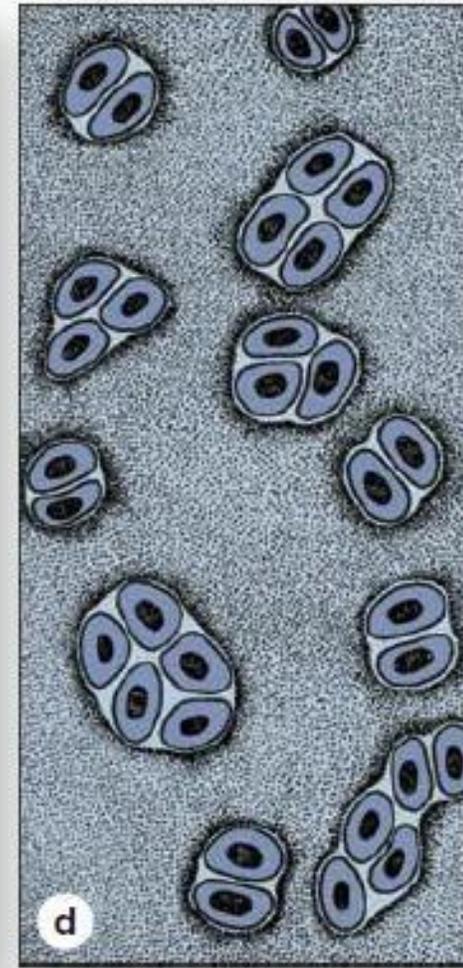
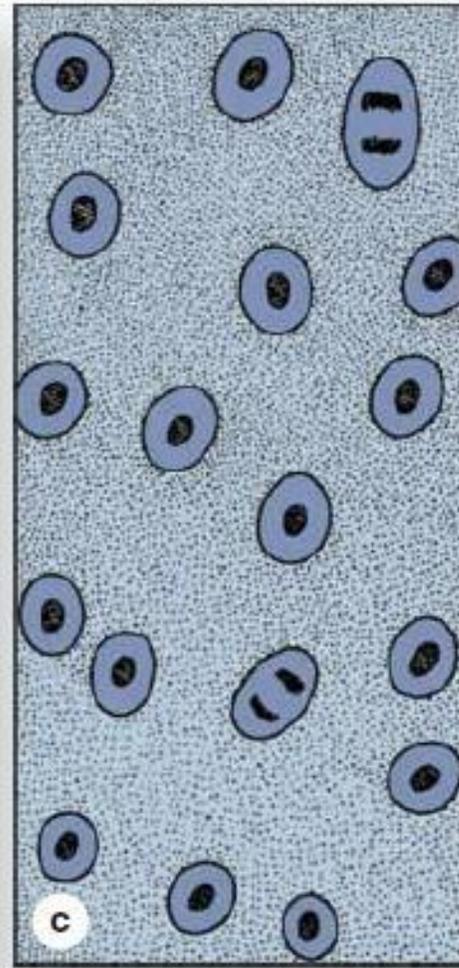
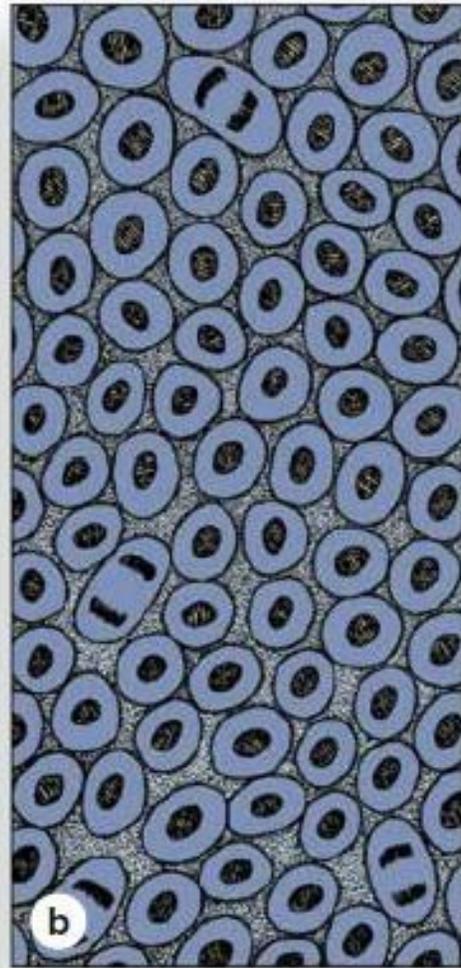
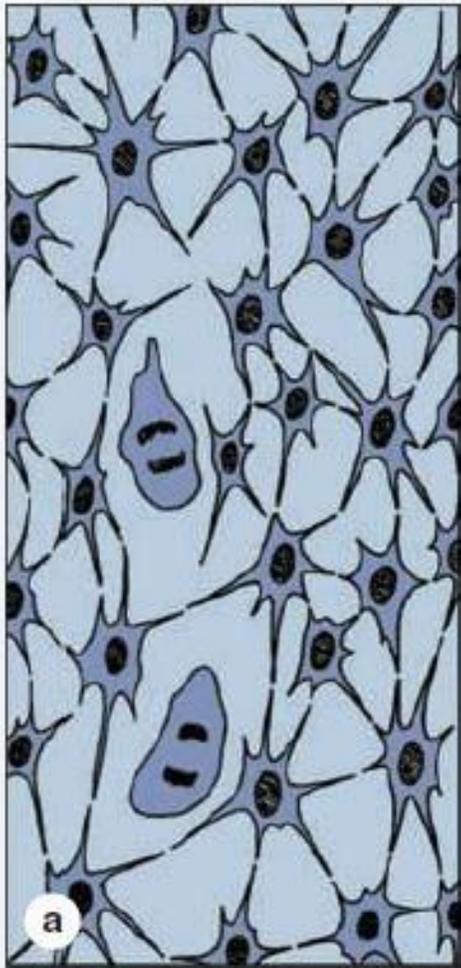
- **Fibrocartilage** is a mingling of hyaline cartilage and dense connective tissue
- It is found in intervertebral discs, in attachments of certain ligaments, and in the pubic symphysis
- It is very tough, and acts as **a cushioning support** tissue
- Chondrocytes of fibrocartilage occur singly
- **Matrix proteoglycans are less than in hyaline and elastic,** which makes **fibrocartilage matrix more acidophilic**
- There **is no** distinct surrounding perichondrium in fibrocartilage.**so there is no chondroblast if any injury happens , fibroblast will make scar**ندبة

- Fibrocartilage is a mixture of hyaline cartilage and dense connective tissue.
- Chondrocytes (C) are seen to be surrounded by small amounts of matrix and separated by larger regions with dense collagen and scattered fibroblasts with elongated nuclei (arrows)



Chondrogenesis

- All cartilage forms from embryonic mesenchyme in the process of chondrogenesis
- The first indication of cell differentiation is the rounding up of the mesenchymal cells, which retract their extensions, multiply rapidly, and become more densely packed together.
- Chondroblasts are cartilage cells during the period of rapid proliferation.
- Chondrocytes are cartilage cells after the period of rapid proliferation.
- At both stages the cells have basophilic cytoplasm rich in RER for collagen synthesis.
- Production of the ECM encloses the cells in their lacunae and then gradually separates chondroblasts from one another.
- During embryonic development, the cartilage differentiation takes place primarily from the center outward; therefore the more central cells have the characteristics of chondrocytes, whereas the peripheral cells are typical chondroblasts.
- The superficial mesenchyme develops as the perichondrium.



Chondroblast starts producing ECM then becomes in small space (lacunae) then becomes inactive chondrocyte...
.....in some cases isogenous group forms

The major stages of embryonic cartilage formation, or chondrogenesis, are shown here.

(a) Mesenchyme is the precursor for all types of cartilage. **(b)** Mitosis and initial cell differentiation produces a tissue with condensations of rounded cells called **chondroblasts**. **(c)** Chondroblasts are then separated from one another again by their production of the various matrix components, which collectively swell

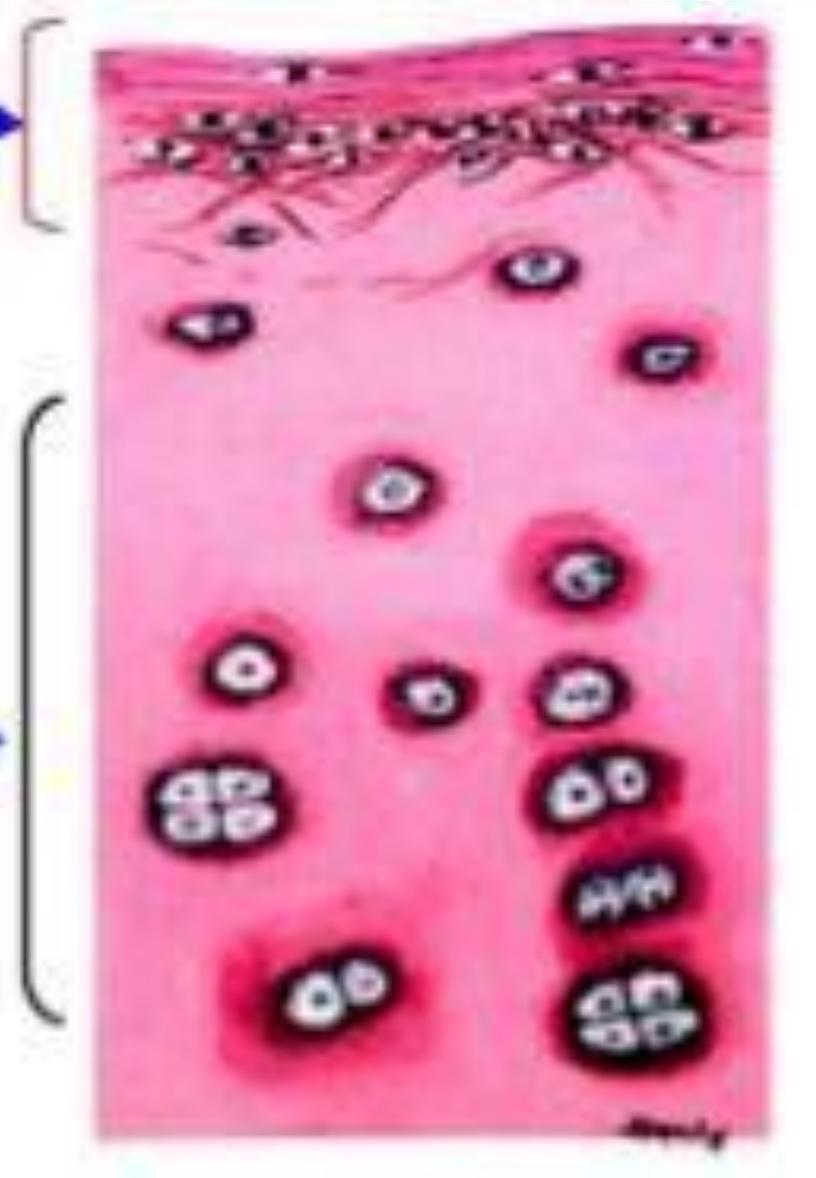
with water and form the very extensive ECM. **(d)** Multiplication of chondroblasts within the matrix gives rise to isogenous cell aggregates surrounded by a condensation of territorial matrix. In mature cartilage, this interstitial mitotic activity ceases and all chondrocytes typically become more widely separated by their production of matrix.

Cartilage growth

- Once formed, the cartilage tissue enlarges both by **interstitial growth** and **appositional growth**
- **Interstitial** growth involves mitotic division of preexisting chondrocytes(**inside cell**)/**increase width ...more space between chondrocytes**
- **Appositional** growth involves chondroblast differentiation from progenitor cells in the perichondrium(**from outside**)**increase in thickness**
- In both cases, the synthesis of matrix contributes greatly to the growth of the cartilage.
- **Appositional growth** of cartilage is more **important during postnatal** ولادة **development,**
- **Interstitial growth** in cartilaginous regions (epiphyseal plates) within long bones is important **in increasing the length** of these structures.

- **Appositional growth:** chondroblasts in perichondrium differentiate into chondrocytes, start producing matrix, and add to existing cartilage

- **Interstitial growth:** proliferation and hypertrophy of existing chondrocytes



Articular cartilage regeneration

- In articular cartilage, cells and matrix near the articulating surface are gradually worn away and must be replaced from within, because there is no perichondrium to add cells by appositional growth

Cartilage repair

- Except in young children, damaged cartilage undergoes slow and often incomplete repair, primarily dependent on cells in the perichondrium which invade the injured area and produce new cartilage.
- In damaged areas the perichondrium produces a scar of dense connective tissue instead of forming new cartilage.
- The poor capacity of cartilage for repair or regeneration is due to limited blood supply (its avascularity and low metabolic rate).

