Cartilage

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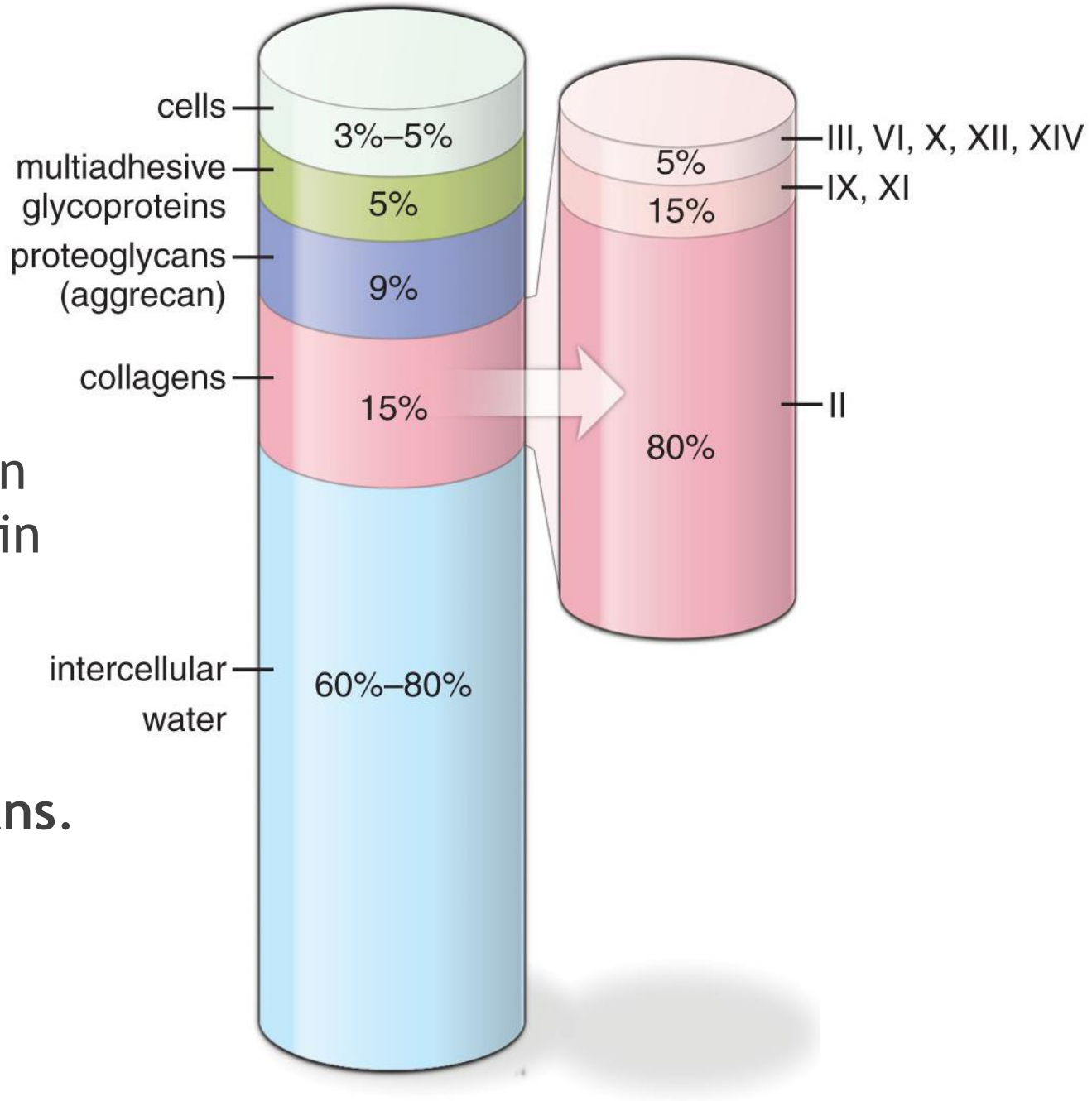
General Information

- **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 receive nutrients by diffusion from capillaries in surrounding connective tissue (the perichondrium).
- Cartilage also lacks nerves.

Composition

- Cartilage consists of cells called **chondrocytes** embedded in the ECM which contains no other cell types.
- Chondrocytes synthesize and maintain all ECM components and are located in matrix cavities called **lacunae**.
- ECM components are **type II collagen** fibrils, **hyaluronan**, and the sulfated GAGs on densely packed **proteoglycans**.

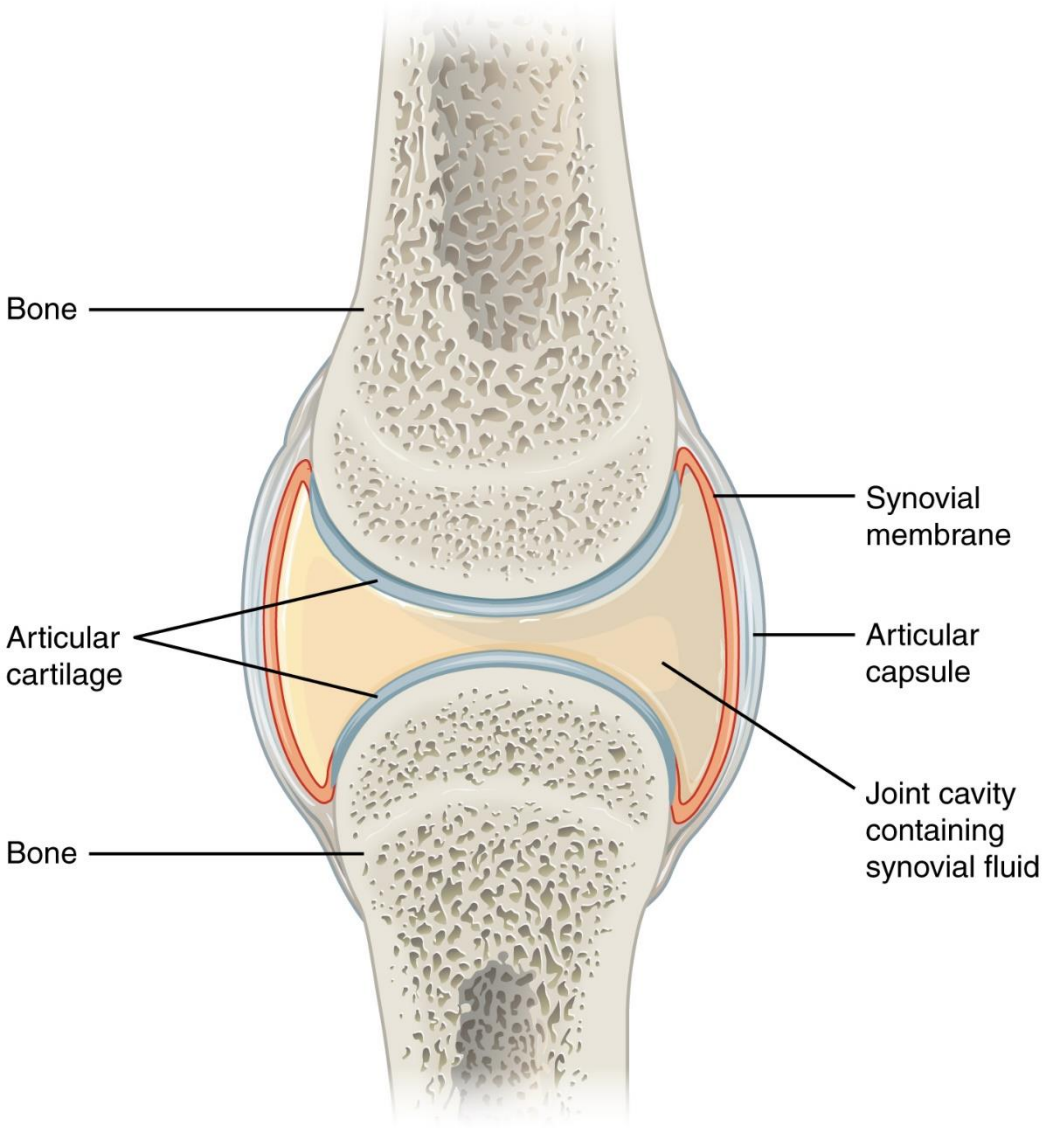


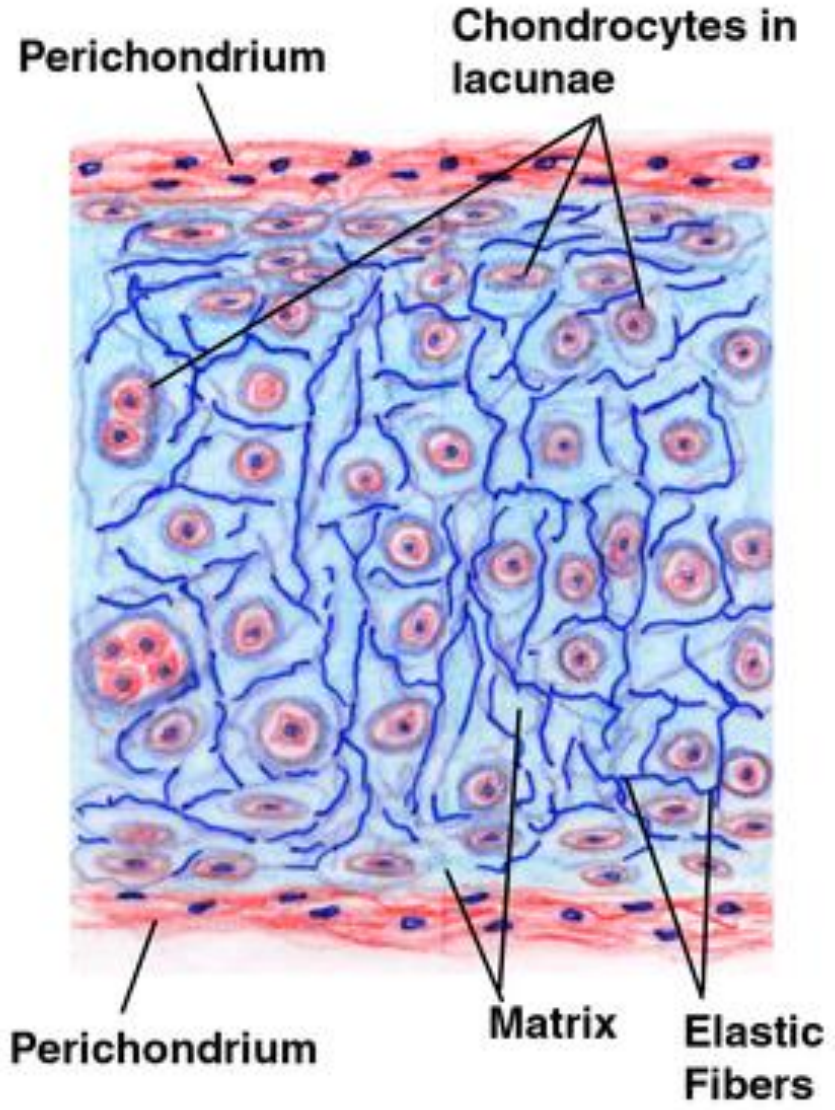
Medical Application

- Many genetic conditions in humans or mice that cause 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

- 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.


Bone
Articular cartilage
Bone
Synovial membrane
Articular capsule
Joint cavity containing synovial fluid


Perichondrium
Chondrocytes in lacunae
Perichondrium
Matrix
Elastic Fibers

Types

Three main types of cartilage:

- hyaline cartilage
- elastic cartilage
- fibrocartilage

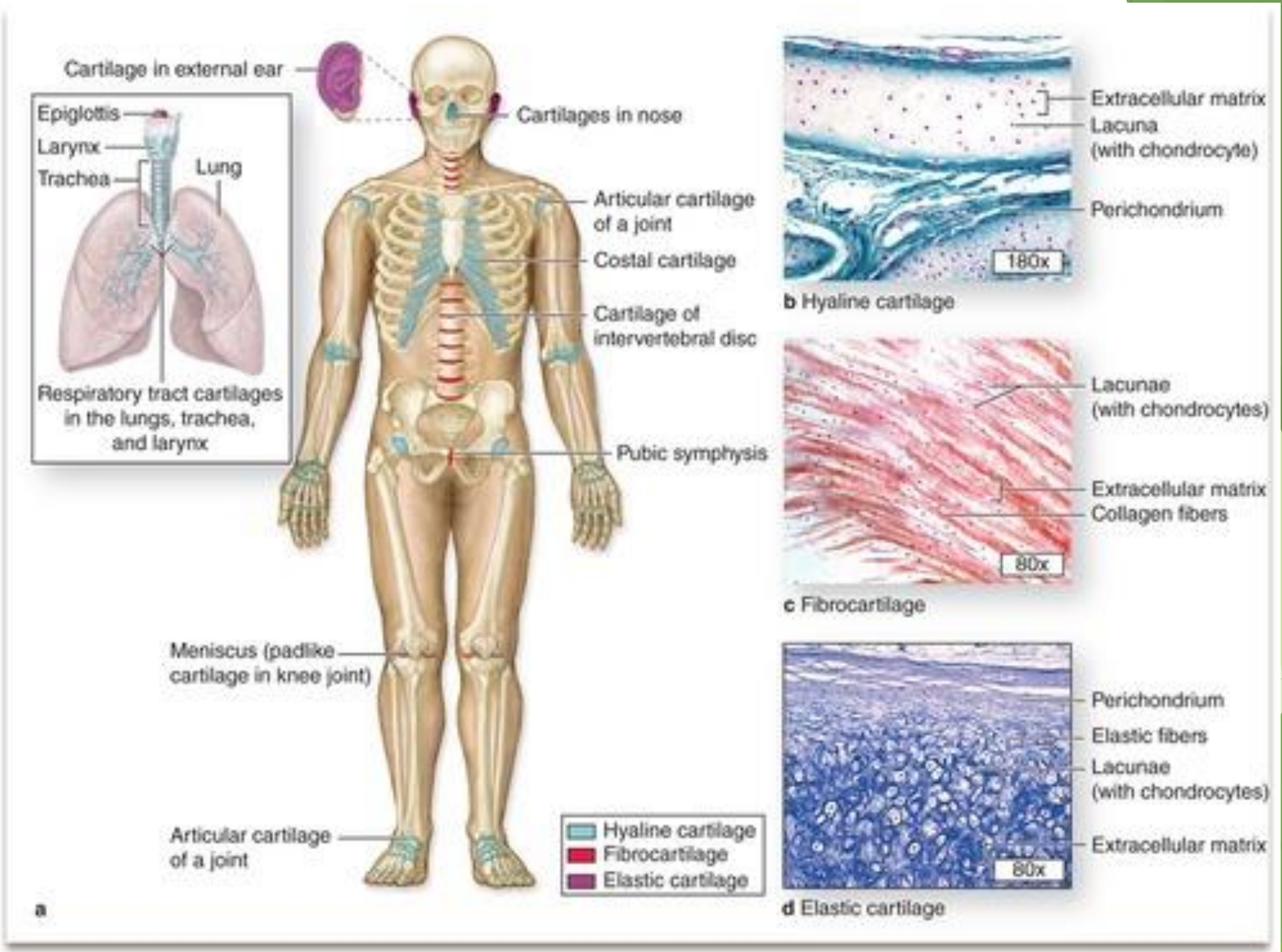

Cartilage in external ear
Epiglottis
Larynx
Trachea
Lung
Respiratory tract cartilages in the lungs, trachea, and larynx
Cartilages in nose
Articular cartilage of a joint
Costal cartilage
Cartilage of intervertebral disc
Pubic symphysis
Meniscus (padlike cartilage in knee joint)
Articular cartilage of a joint
Hyaline cartilage
Fibrocartilage
Elastic cartilage
a
Extracellular matrix
Lacuna (with chondrocyte)
Perichondrium
180x
b Hyaline cartilage
Lacunae (with chondrocytes)
Extracellular matrix
Collagen fibers
80x
c Fibrocartilage
Perichondrium
Elastic fibers
Lacunae (with chondrocytes)
Extracellular matrix
80x
d Elastic cartilage

TABLE 7–1 Important features of the major cartilage types.

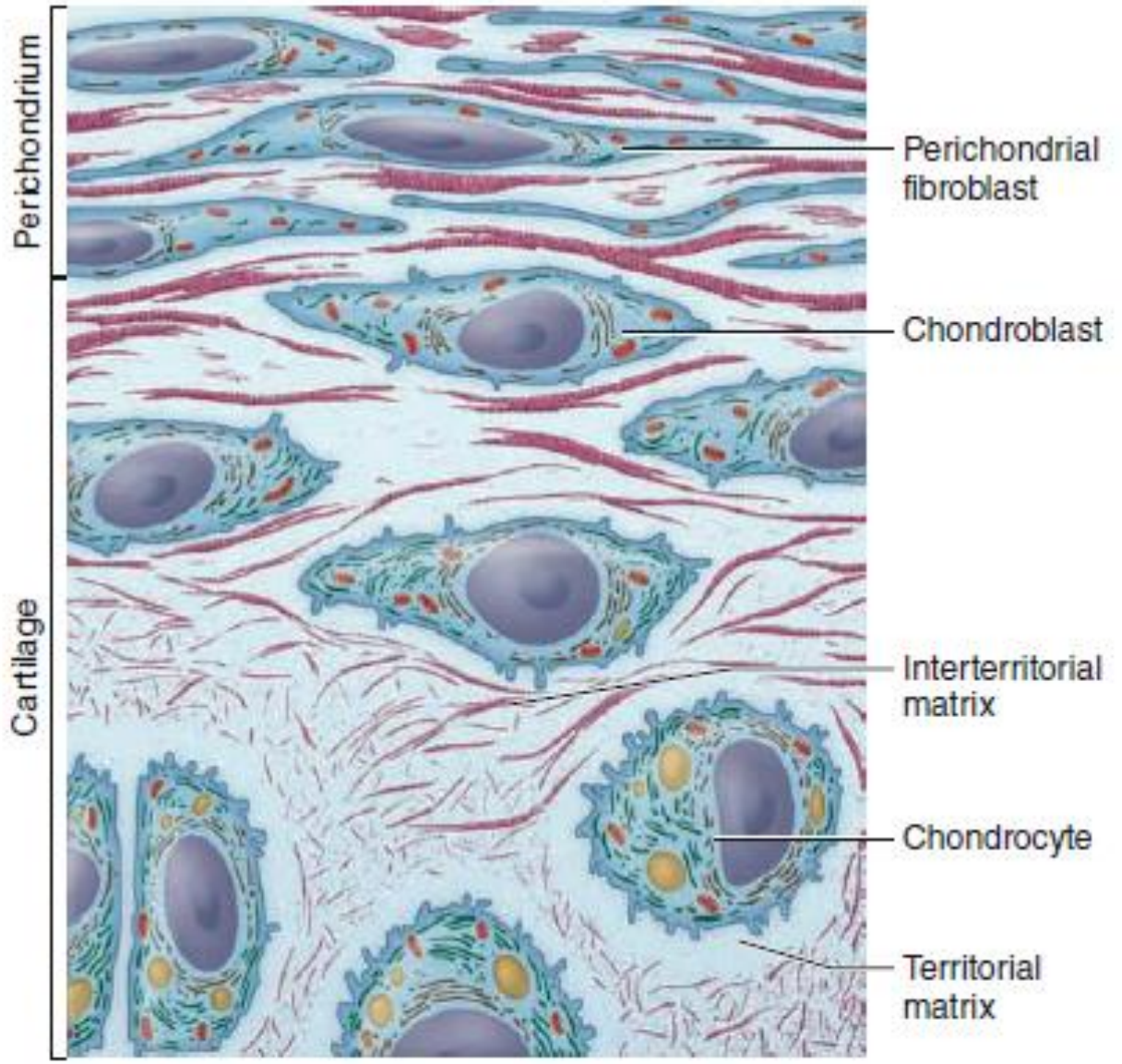
	Hyaline Cartilage	Elastic Cartilage	Fibrocartilage
Main features of the extracellular matrix	Homogeneous, with type II collagen and aggrecan	Type II collagen, aggrecan, and darker elastic fibers	Type II collagen and large areas of dense connective tissue with type I collagen
Major cells	Chondrocytes, 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

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
  - in the articular surfaces of movable joints
  - in the walls of larger respiratory passages (nose, larynx, trachea, bronchi)
  - in the ventral ends of ribs, where they articulate with the sternum
  - in the epiphyseal plates of long bones, where it makes possible longitudinal bone growth
- In the embryo, hyaline cartilage forms the temporary skeleton that is gradually replaced by bone.

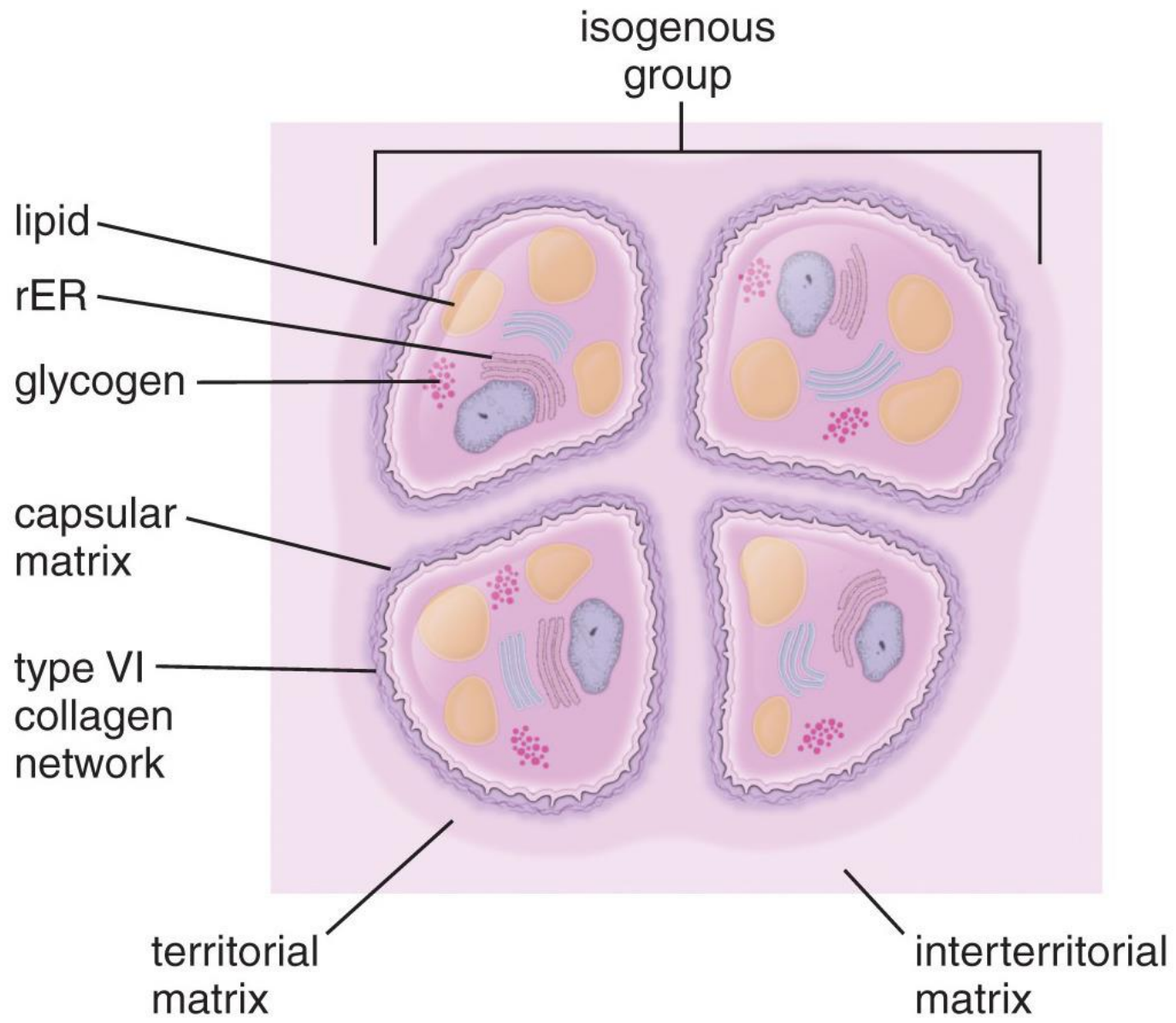
Chondroblasts and Chondrocytes

- 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.



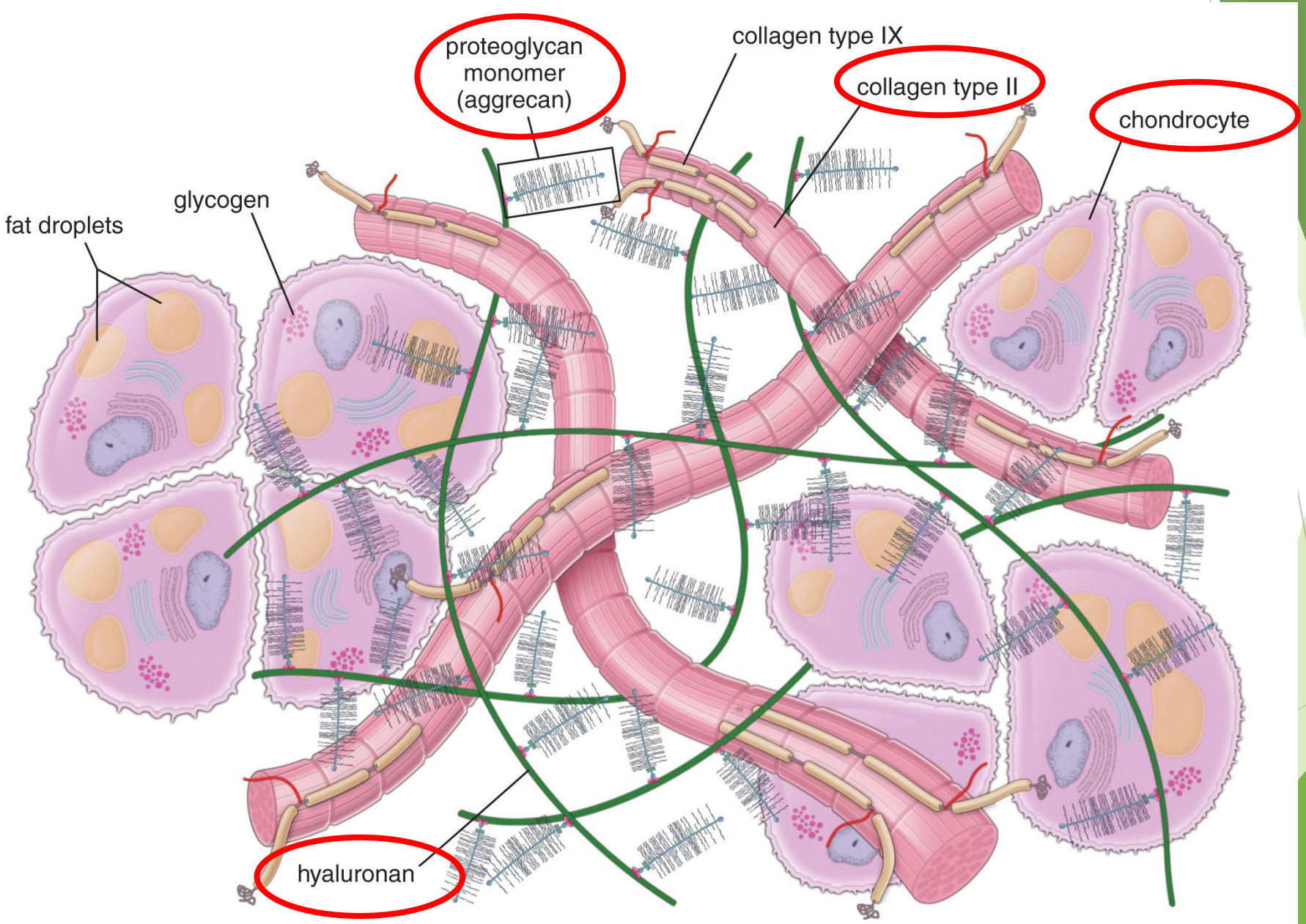
Chondrocytes

- 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.



Hylaine cartilage Matrix

- 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 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.

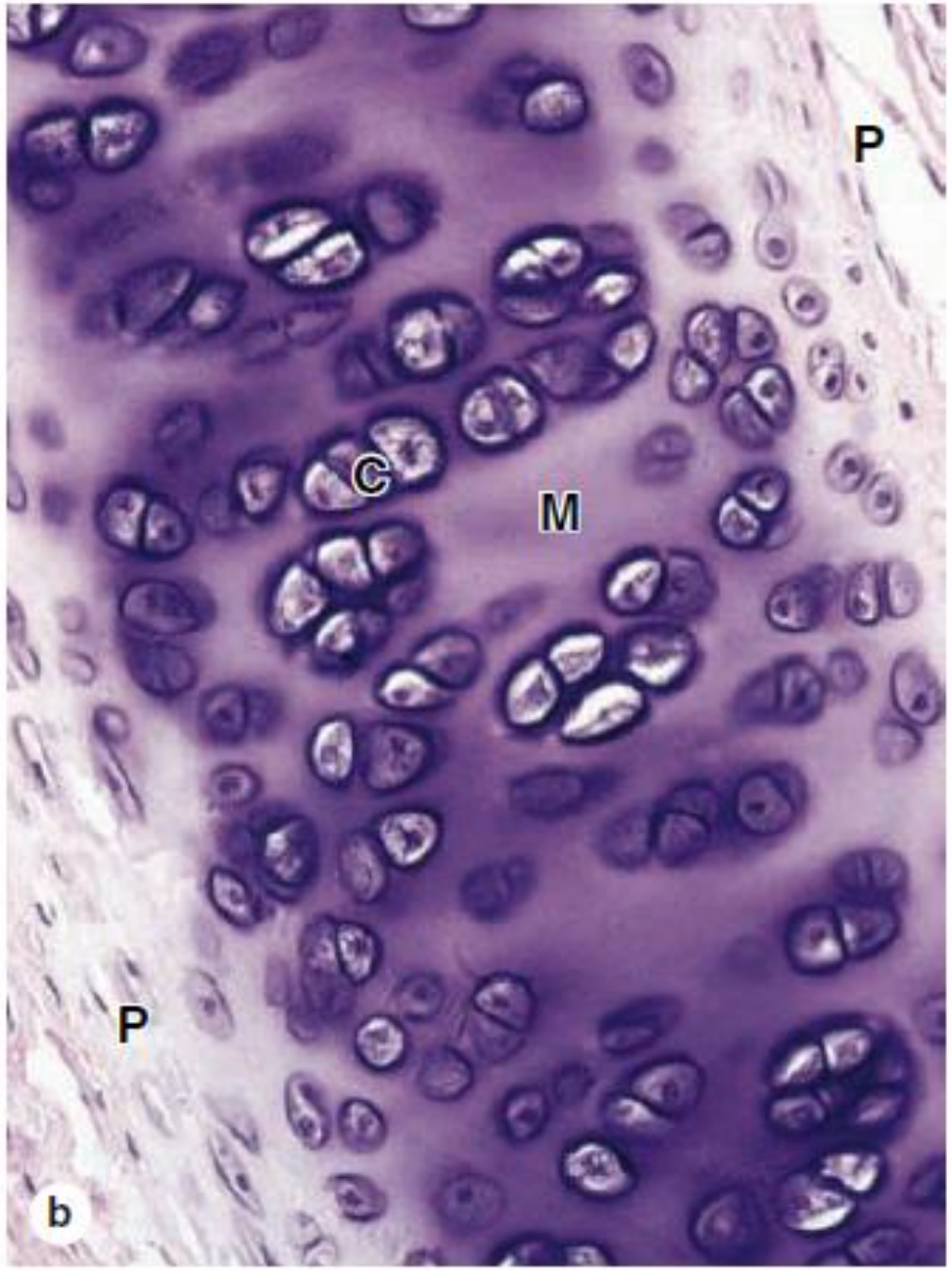


Territorial Vs Interterritorial matrix

- The ECM immediately around each lacuna is called the **territorial matrix.** It contains mostly proteoglycans and sparse collagen
- That ECM more distant from lacunae is called the **interterritorial matrix.** It is richer in collagen and may be less basophilic.

- 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.

- 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.



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.

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

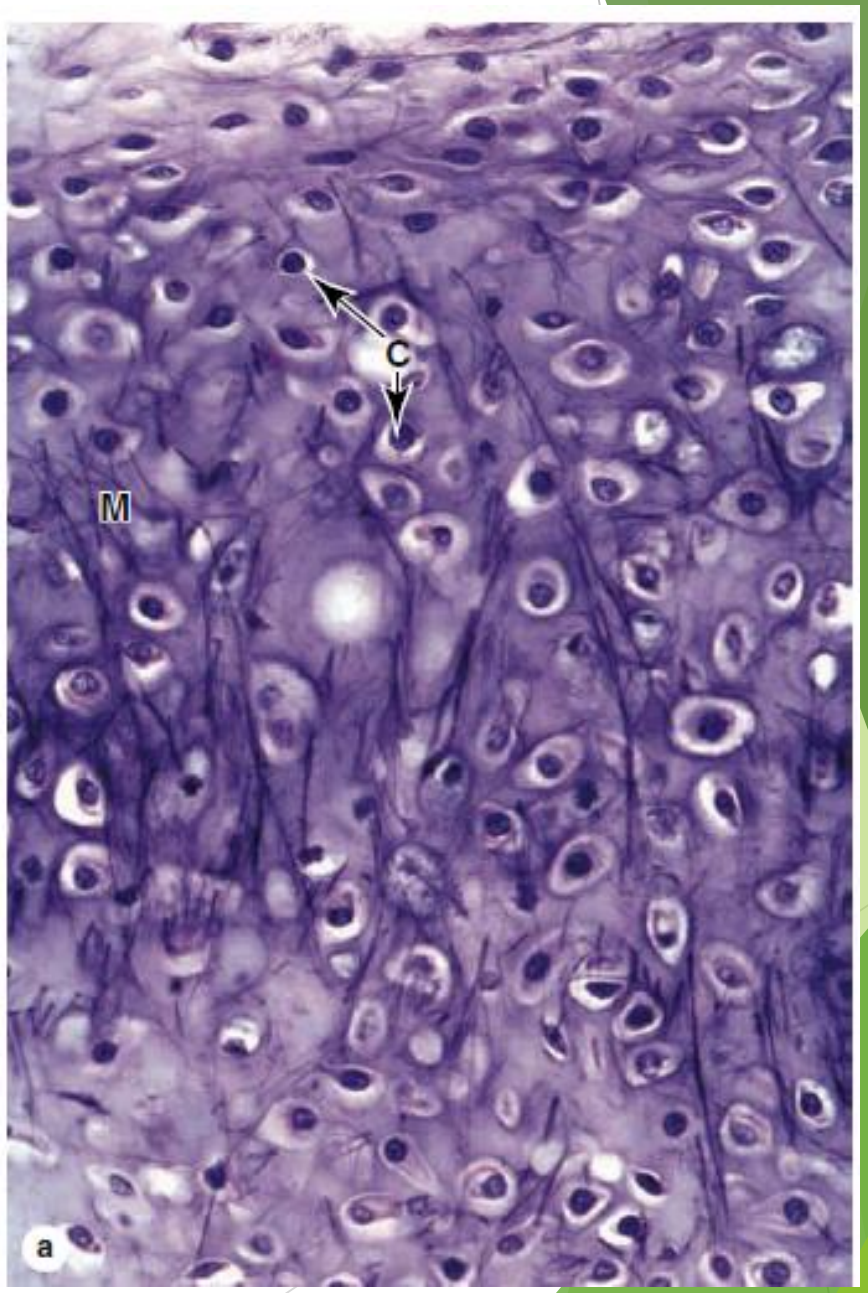
- Cells of cartilage can give rise to either benign (**chondroma**) or slow-growing, malignant (**chondrosarcoma**) tumors in which cells produce normal matrix components. Chondrosarcomas seldom metastasize and are generally removed surgically.

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

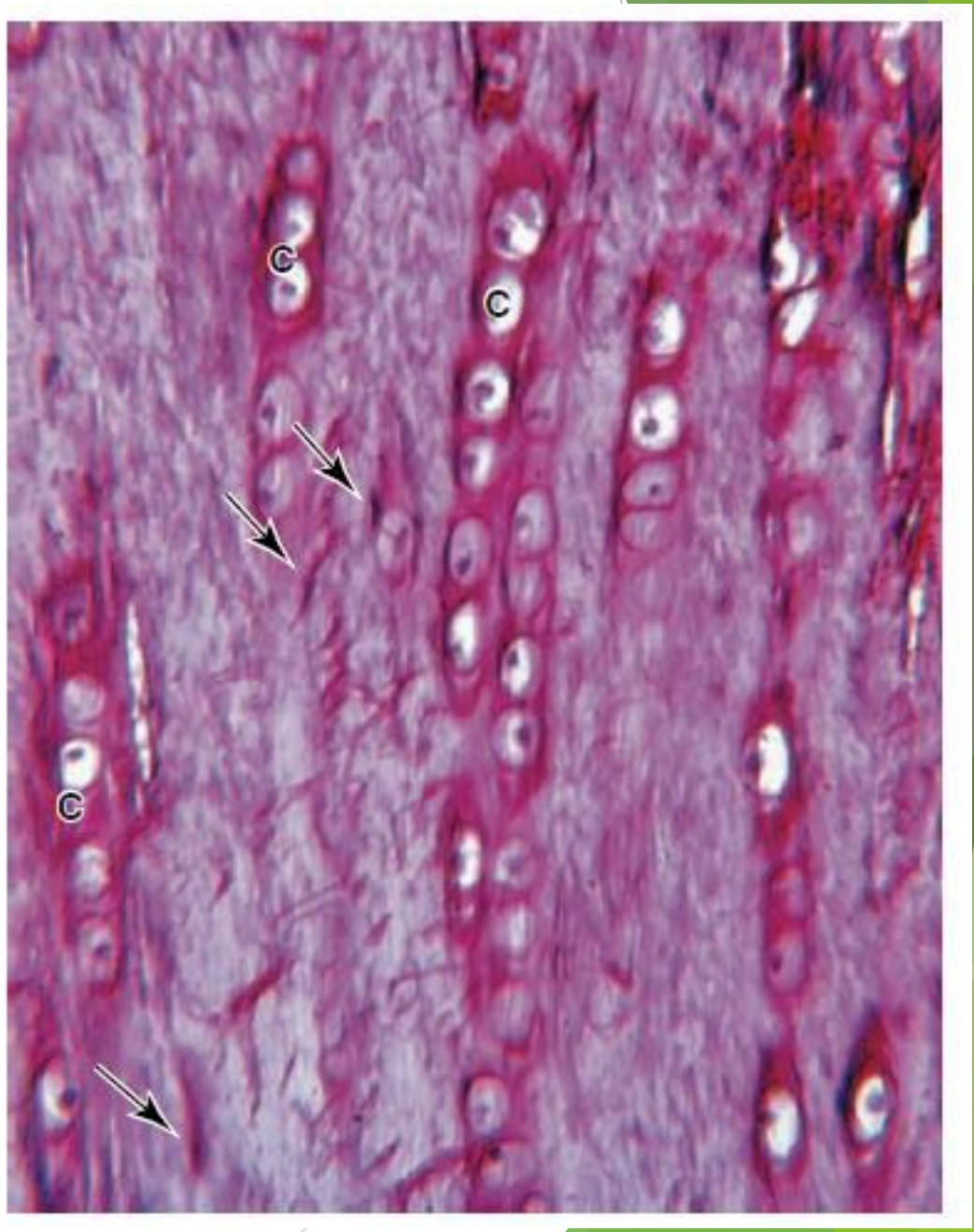
- The chondrocytes (**C**) and overall organization of elastic cartilage are similar to those of hyaline cartilage, but the matrix (**M**) also contains elastic fibers that can be seen as darker components (Stain: Hematoxylin & Orcein)



Fibrocartilage

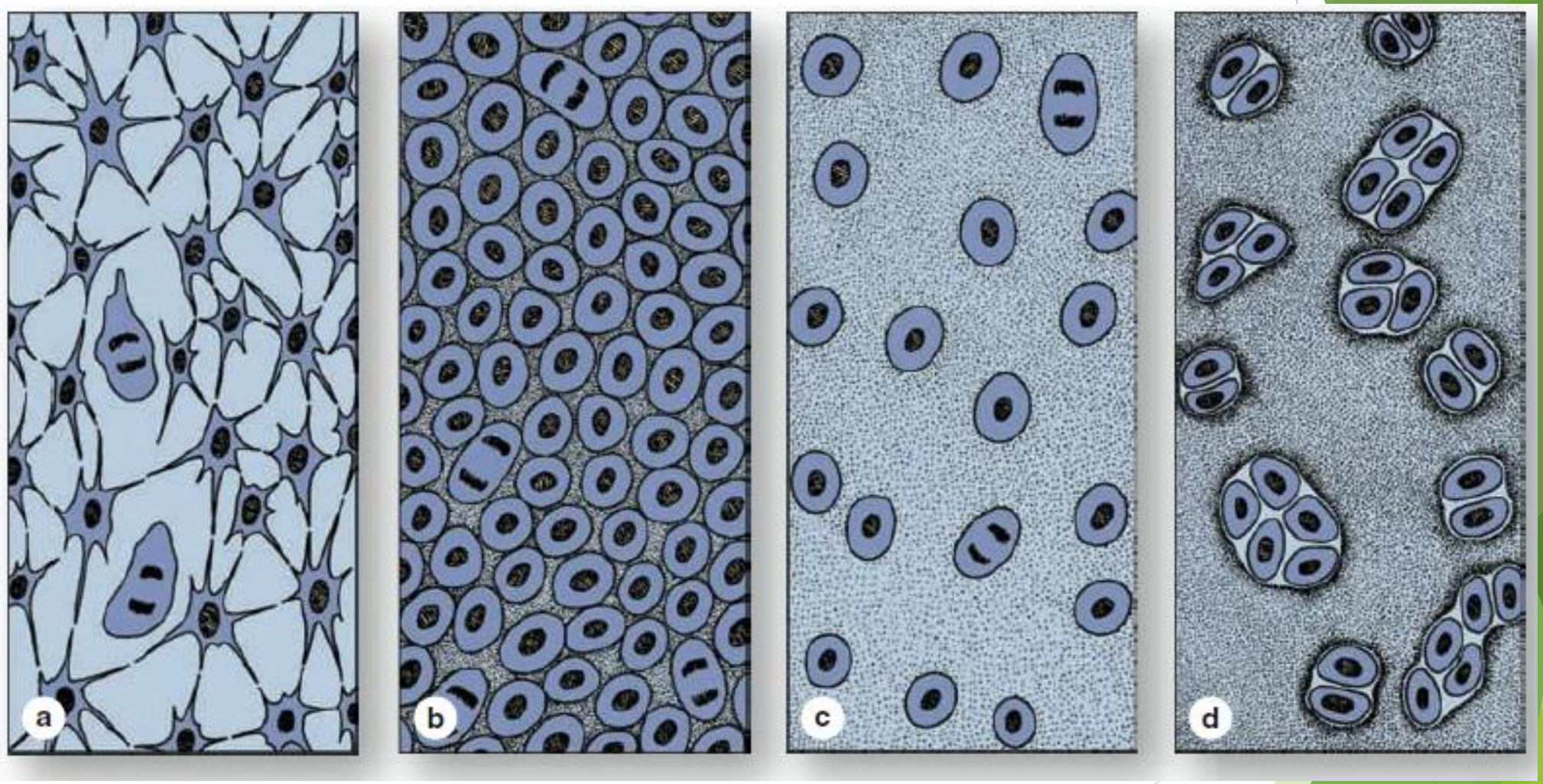
- **Fibrocartilage** is a mingling of hyaline cartilage and dense connective tissue
- It is found in intervertebral discs, in attachments of certain ligaments, and in the pubic symphysis
- It is very tough, and acts as a cushioning support tissue
- Chondrocytes of fibrocartilage occur singly
- Matrix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

- 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.


a
b
c
d

Cartilage growth

- Once formed, the cartilage tissue enlarges both by **interstitial growth** and **appositional growth**
- Interstitial growth involves mitotic division of preexisting chondrocytes
- Appositional growth involves chondroblast differentiation from progenitor cells in the perichondrium
- In both cases, the synthesis of matrix contributes greatly to the growth of the cartilage.
- Appositional growth of cartilage is more important during postnatal 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 in part to its avascularity and low metabolic rate.