بِسْمِ اللَّهِ الرَّحْمَٰنِ الرَّحِيمِ

HISTOLOGY

وَلَقَدْ خَلَقْنَا الْإِنسَانَ وَنَعْلَمُ مَا تُوَسْوِسُ بِهِ نَفْسُهُ ۖ وَنَحْنُ أَقْرَبُ إِلَيْهِ مِنْ حَبْلِ الْوَرِيدِ

Final | Lecture # 3

Cartilage Pt.1

Written by : Rand Alkhateeb
Dareen Alhababseh

Reviewed by : Amal Al-khatib

Color coding used in the modified:

- *Black: the original slides*
- *Maroon: the doctor's explanation/words*
- *Gray: additional information and explanation*
- *Red: important information*

Cartilage

Cartilage

- Cartilage is a tough and durable CT

- Rich extracellular matrix (ECM) with high concentrations of **glycoproteins**, GAGs (specifically the sulfated types) and proteoglycans which Provide the thick gelatinous feature

- Contains collagen *type II mainly* and elastic fibers (making up a subtype called elastic cartilage).

Which is Good so they won't get damaged with the movement

- **Avascular** (low metabolic activity, don't divide ,unlike bones).

- **Lacks nerves** (not innervated).

Perichondrium

- Is a sheath of dense connective tissue that surrounds cartilage
- Forms an interface between the cartilage and the tissues supported by the cartilage.

Chondrogenic cells at the inner layer of perichondrium –> chondroblast –> chondrocyte

- Contains blood supply (vascular, nutrients diffuse to the Cartilage from it) and a small neural component.
- **Articular cartilage** (covers the ends of bones in movable joints) lacks perichondrium (diffusion of oxygen and nutrients from the synovial fluid)

You should move your joints to help the diffusing of the nutrients

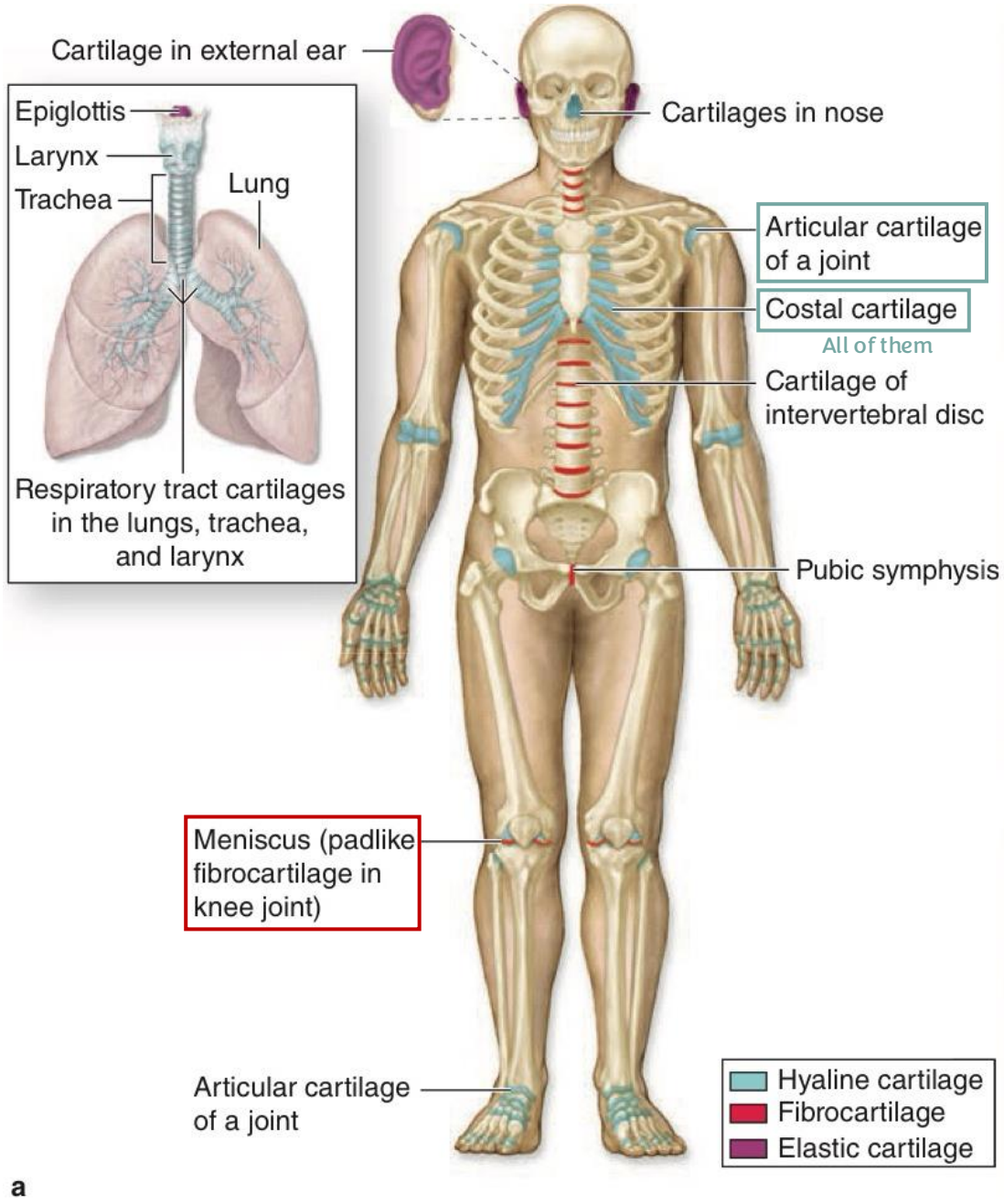
Features

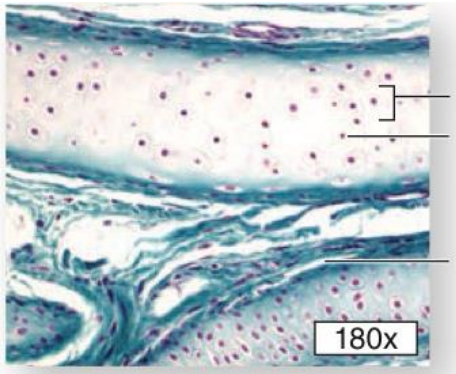
- *Its semi-rigid consistency is attributable to water bound to the negatively charged hyaluronan and GAG chains extending from proteoglycan core proteins, which in turn are enclosed within a dense meshwork of thin type II collagen fibrils*---**shock absorber**.

- *The physical properties of cartilage depend on electrostatic bonds between type II collagen fibrils, hyaluronan, and the sulfated GAGs on densely packed proteoglycans*

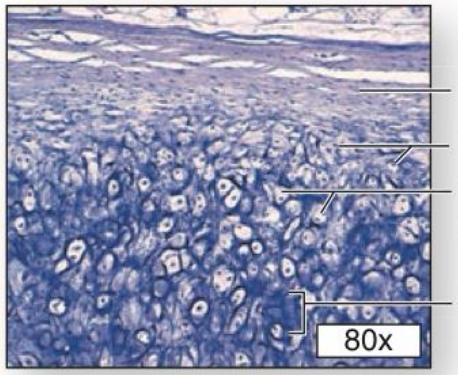
Types of cartilage

- Hyaline — Basic type
- Elastic
- Fibrocartilage

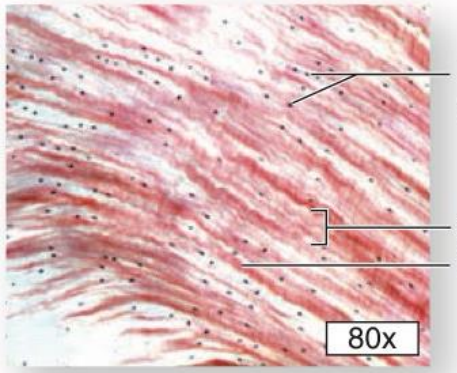




b Hyaline cartilage



c Elastic cartilage



d Fibrocartilage

Structure Hyaline

Cells

- Consists of only chondrocytes

embedded in the ECM

- Chondrocytes synthesize and maintain all ECM
- Located in matrix cavities called lacunae.

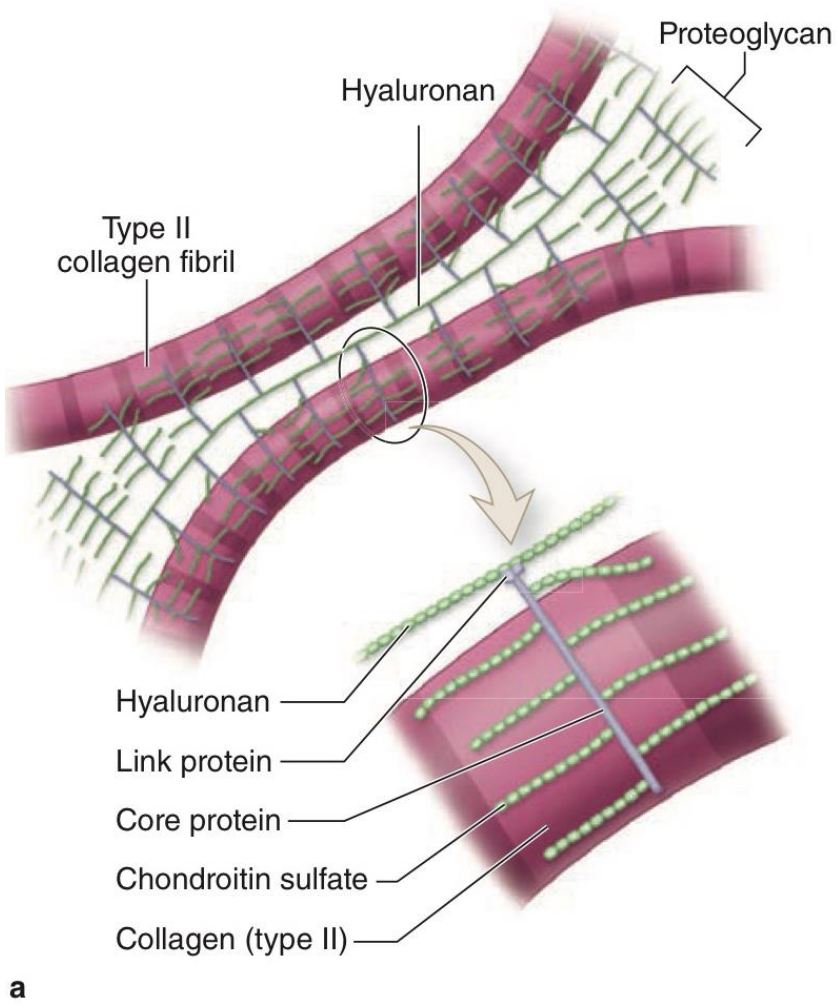
ECM

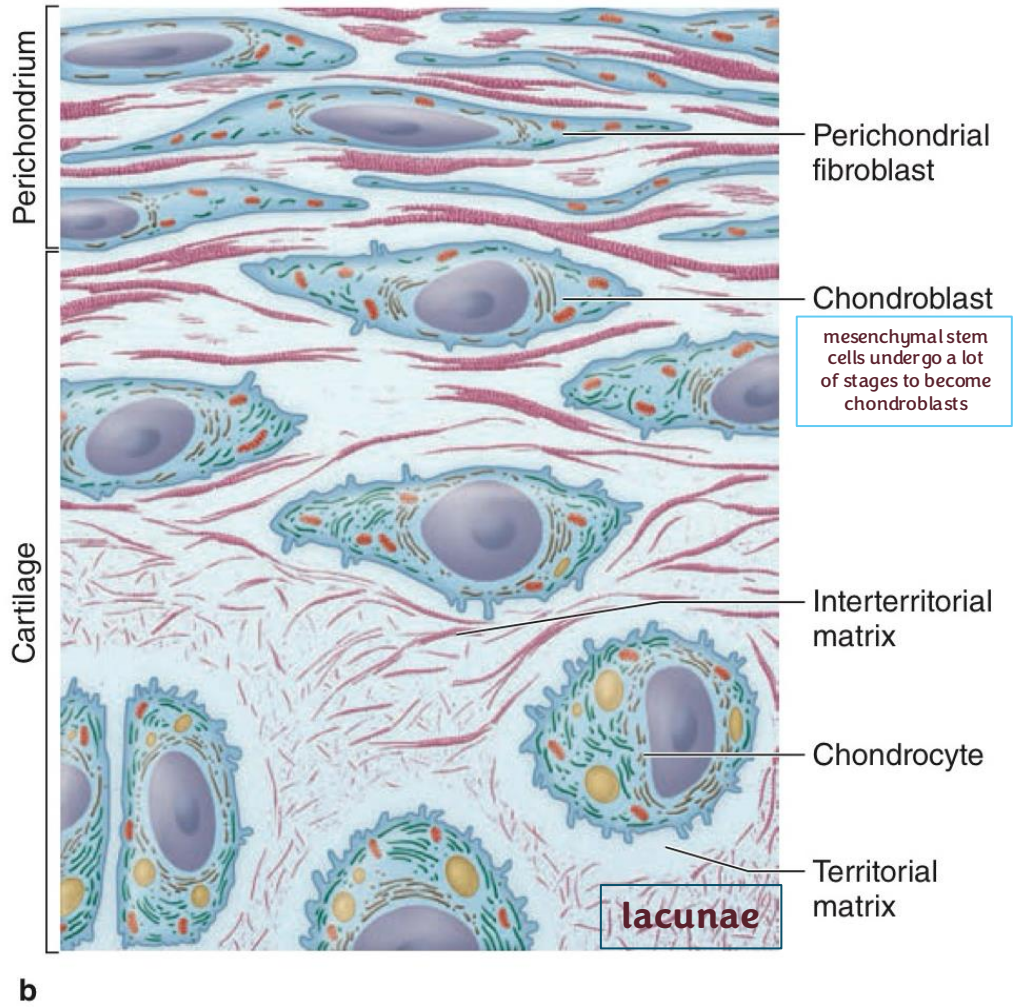
- Type II Collagen Fibrils
- Hyaluronan
- Sulfated GAGs
- Proteoglycans

- If we add elastic fibers we will get elastic cartilage
- If we add collagen type I we will get fibrocartilage

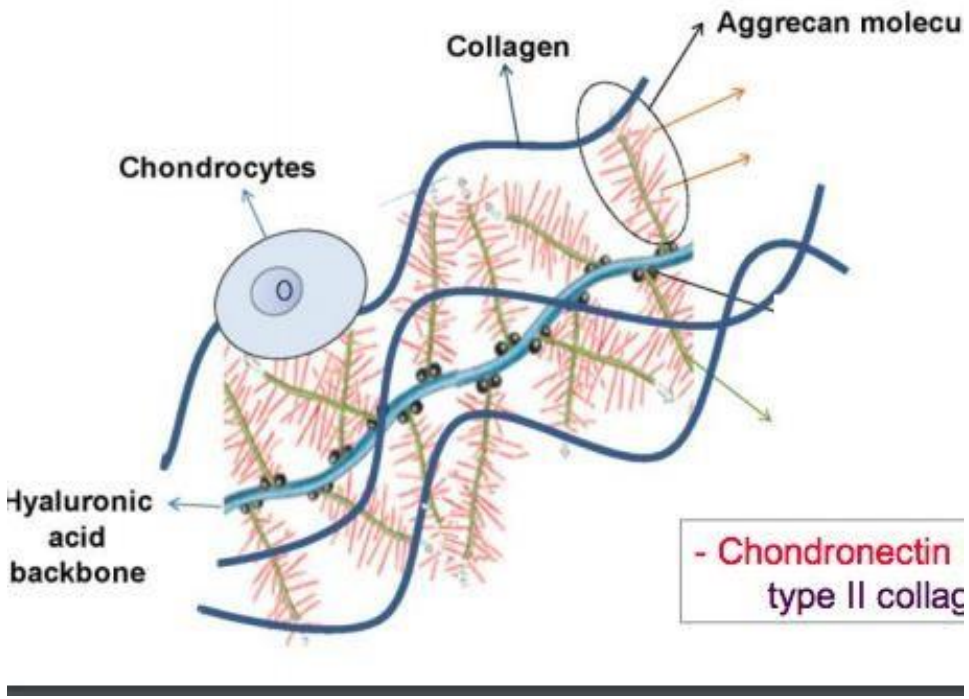
ECM

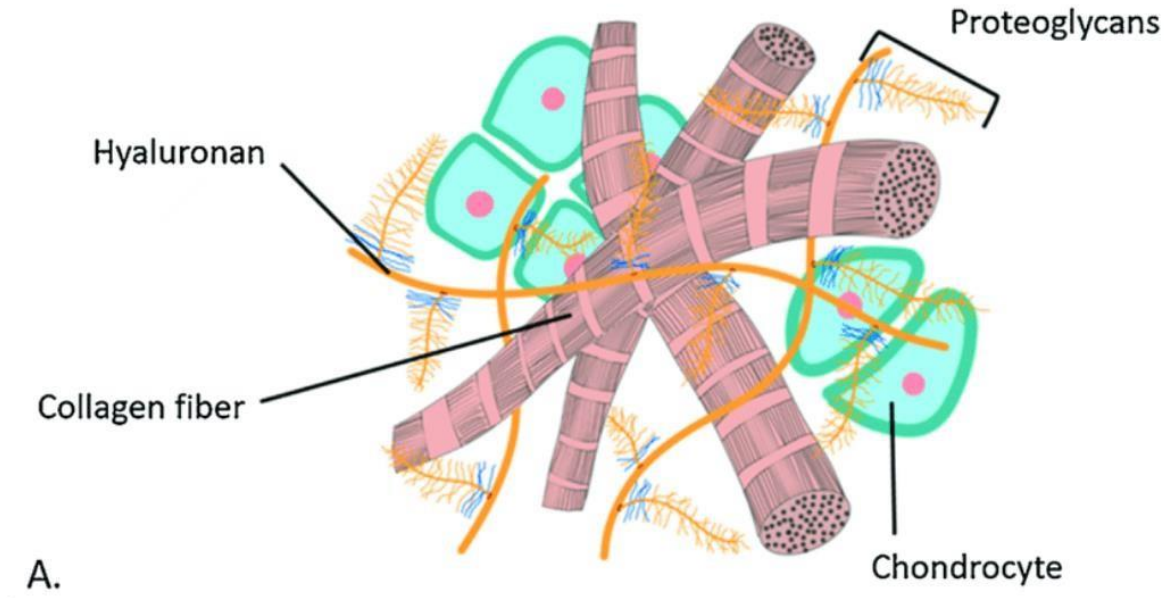
- Type II Collagen
- Hyaluronan
- Sulfated GAGs
- Proteoglycans

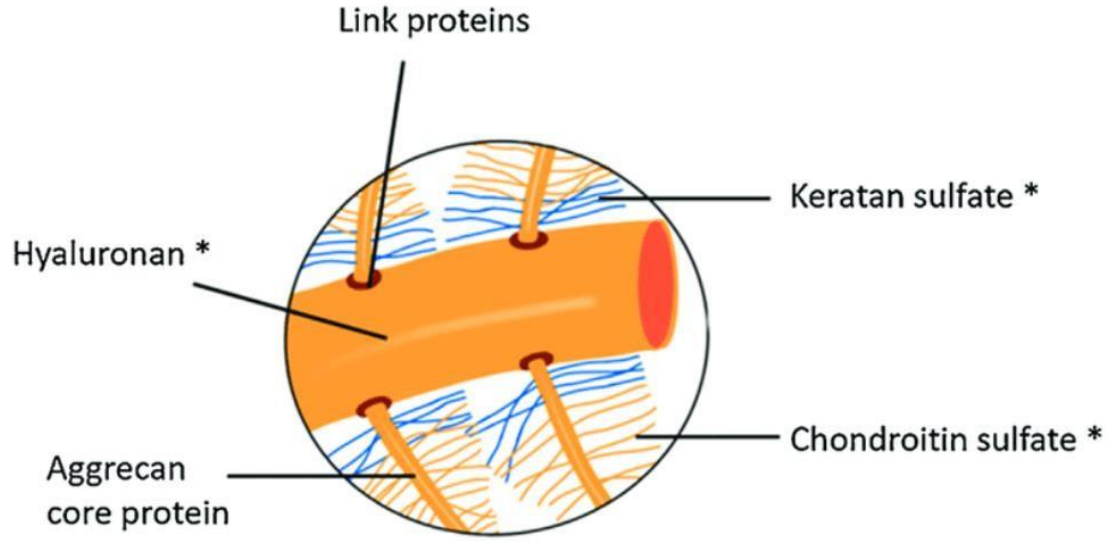




Hyaline Cartilage







Hyaline Cartilage

- Most common of the three types.
- Is homogeneous and semitransparent in the fresh state.
- 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, and in the epiphyseal plates of long bones.
- In embryoS, hyaline cartilage forms the temporary skeleton that is gradually replaced by bone.

The bone and cartilage are both connective tissue derived from the mesoderm. The mesoderm will differentiate into mesenchymal stem cells, and these mesenchymal stem cells can give rise to many types of tissues. But here we are focusing specifically on bone and cartilage.

For example, the sternum is a flat bone, while the humerus is a long bone. So of course, in the embryo they do not form in exactly the same way.
The sternum, before it becomes sternum, starts as mesenchyme in that region. This mesenchyme will represent the future sternum. In this case, the mesenchymal cells differentiate directly into osteoblasts. These osteoblasts start producing bone matrix, and then they become trapped inside it. Once trapped, they are located in lacunae, and all surrounding cells undergo the same process. So we can imagine that mesenchymal cells in the future sternum region differentiate into osteoblasts, which secrete matrix and gradually build up the bone until it forms the sternum.

On the other hand, the humerus develops differently. The mesenchyme in the future humerus region does not directly become bone. Instead, the mesenchymal cells first differentiate into chondroblasts, which produce cartilage (specifically hyaline cartilage). So initially, we get a small model of the humerus made of cartilage.
This is what happens in the embryo, but it does not remain like this permanently. There is a specific time point where this cartilage acts as a temporary structure. It starts as cartilage and then gradually undergoes ossification because it needs to be replaced by bone. This cartilage is considered a transitional structure.
Subsequently, ossification begins, and we can see primary ossification centers, which may appear as whitish areas under the microscope. After birth and during development, cartilage is gradually removed and replaced by bone over time.

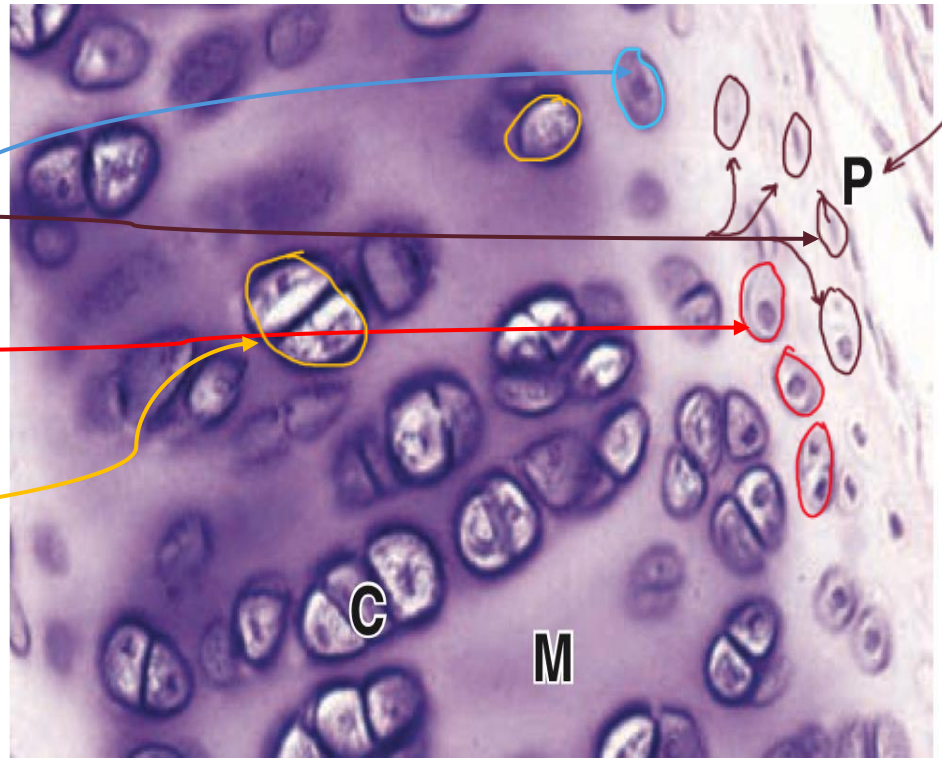
However, there are two important exceptions where hyaline cartilage remains:
-The epiphyseal (growth) plates, which are essential for bone length growth.
-The articular cartilage at joint surfaces, which must remain to provide smooth movement and reduce friction.

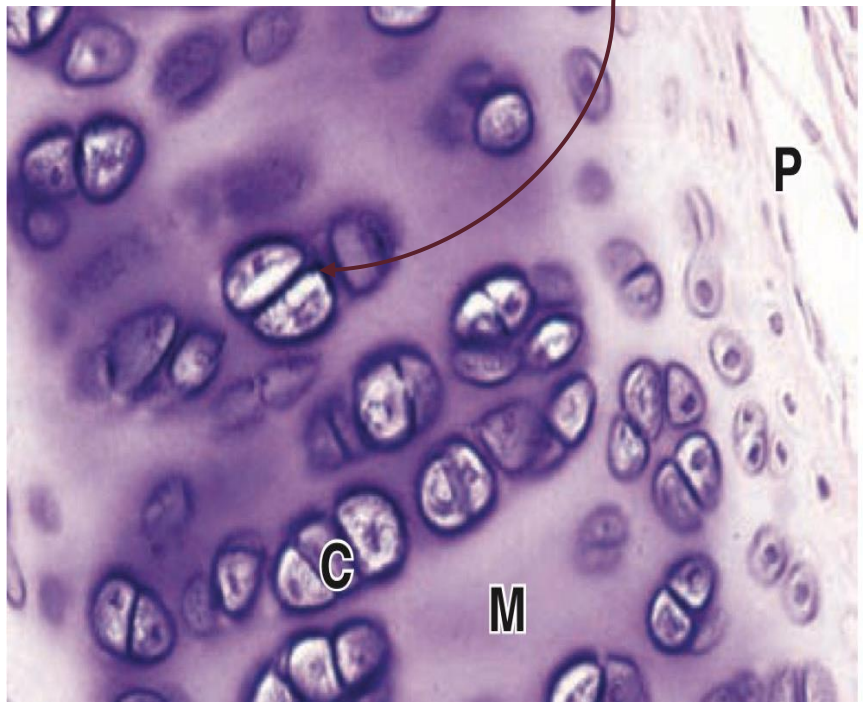
The epiphyseal plates eventually close after puberty, usually around 18, meaning most of the cartilage in those regions is replaced by bone. After that, the long bones stop growing in length, while articular cartilage remains throughout life.

Hyaline Cartilage / Structure

- Collagen is embedded in a firm, hydrated gel of proteoglycans and structural glycoproteins.
- Proteoglycans --matrix basophilic and the collagen fibrils are barely discernible.
- Most of the collagen is type II (small amounts of minor collagens are present).
- **Aggrecan** (150 GAGs--chondroitin sulfate and keratan sulfate) is the most abundant proteoglycan of hyaline c.
- Water bound to GAGs in the constitutes to 60%-80% of the weight.
- **Chondronectin:** structural multiadhesive glycoprotein, binds specifically to GAGs, collagen, and integrins, mediating the adherence of chondrocytes to the ECM.

Here in this image we have two distinctive zones, one on the right and one on the left: one lighter in color and one darker, one relatively eosinophilic and one more basophilic.
The region that is close to the surface of the cartilage is more eosinophilic. Now, these cells are chondrogenic cells, which are very similar to chondroblasts.
As we get closer to the surface, we can see slightly elongated cells – these are the chondroblasts. This cell is a bit away from the very outer surface because is has already started producing matrix. However, it is not fully embedded yet.
Then, the fully differentiated cells, which are completely surrounded by matrix, are the chondrocytes.
So:
-At the interface: chondroblast cells.
-Close to the surface: chondrogenic.





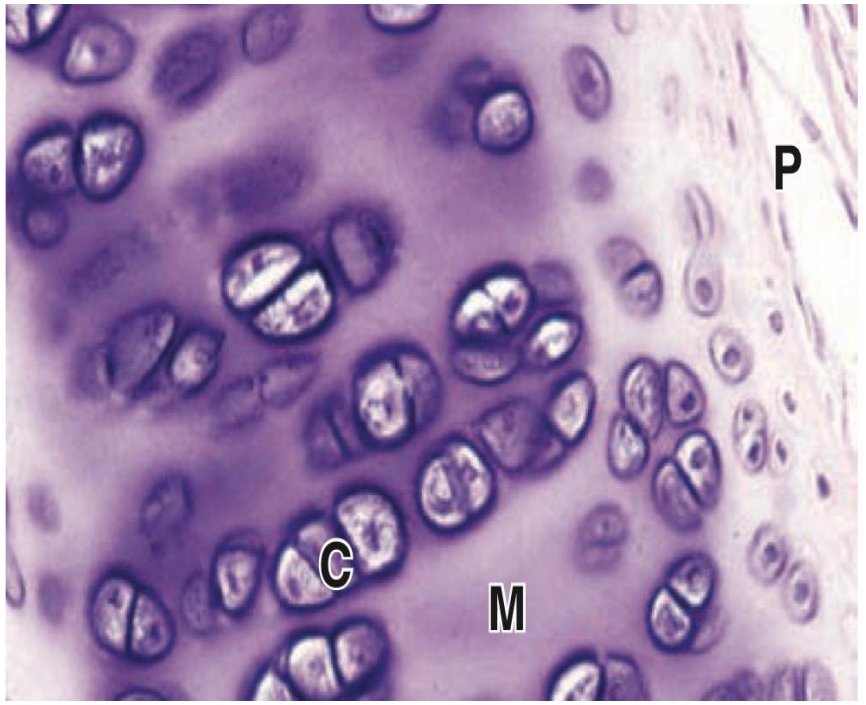
H&E staining

These are chondrocytes in lacunae. The line we can see between them indicates that there are two cells within closely related lacunae.
What is happening here? While these cells are producing matrix, some of them undergo mitosis. This means they divide while still being within the same lacunar space or very close to each other. As a result, we may see two cells, four cells, or even up to six cells grouped together. This is called an isogenous group.
We do not usually see this in bone because osteocytes do not undergo this type of division after being trapped in the matrix.
Each cell is located within its own lacuna, surrounded by extracellular matrix.

Around the lacunae, the matrix appears significantly darker compared to the areas in between. This difference is due to staining properties and matrix composition. When we talk about H&E staining, it is related to charge interactions: positively charged components have high affinity to acidic dyes (eosin), while negatively charged components have high affinity to basic dyes (hematoxylin).
So, the areas around the lacunae are more negatively charged because they contain a higher concentration of GAGs. These attract basic dyes more strongly.
We call the matrix around the lacunae the territorial matrix, which is richer in GAGs and proteoglycans and therefore stains more darkly.
Between these regions, we have the interterritorial matrix, which contains relatively more collagen fibers and a lower concentration of GAGs and proteoglycans. However, it still contains both components—just in different proportions.
So:
Territorial matrix (around lacunae): more GAGs + proteoglycans → darker staining
Interterritorial matrix (between lacunae): more collagen, fewer GAGs → lighter staining
Importantly, collagen is present in both regions, but the difference in staining is mainly due to the variation in GAG concentration, which explains the histological appearance.

Matrix

- **Territorial matrix**: immediately surrounding each chondrocyte, the ECM is relatively richer in gags than collagen, causing these areas of to stain more basophilic. Contains mostly proteoglycans and sparse collagen
- **Interterritorial matrix**: more distant from lacunae, richer in collagen and may be less basophilic.



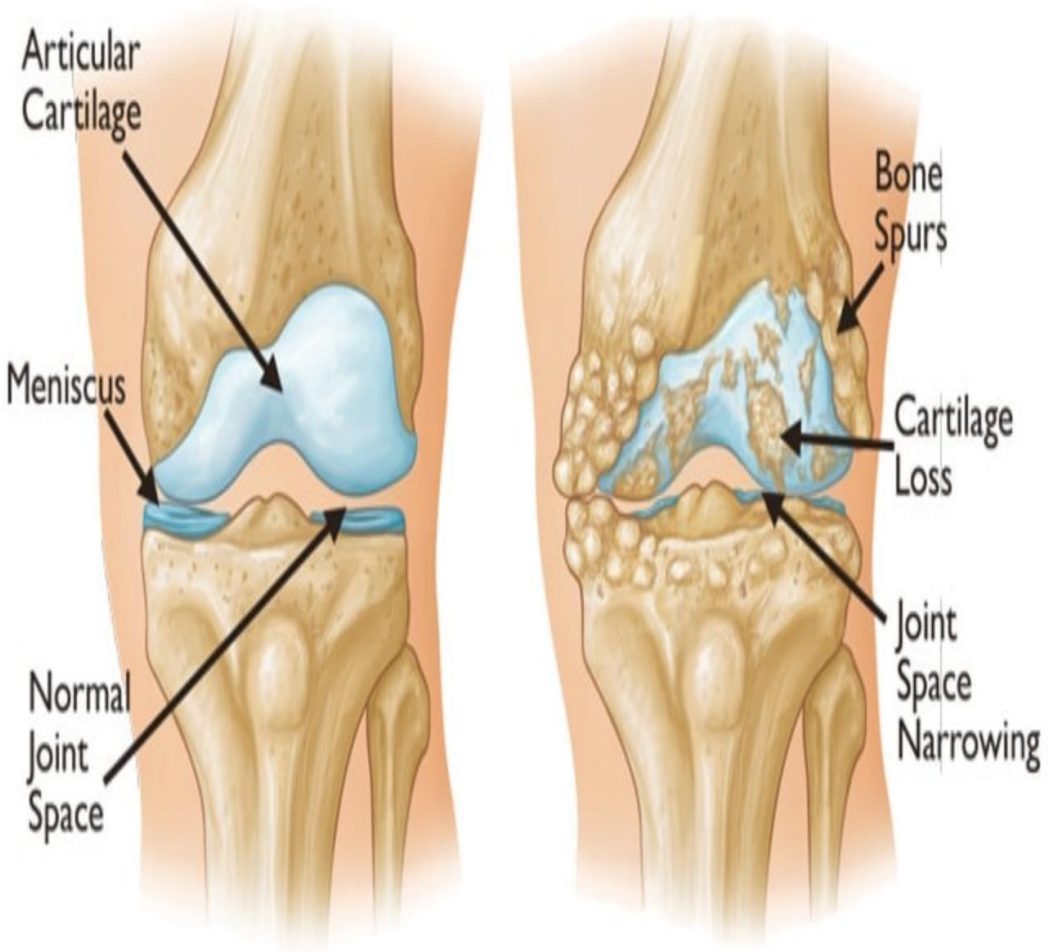
Osteoarthritis

Difference between the left and right images:
Left image:
-The **cartilage is intact** (normal appearance).
-The articular surface is smooth and continuous.
Right image:
-There is **erosion of the cartilage**.
-The joint has **lost cartilage in multiple areas**.
As a result, the **underlying bone becomes exposed and visible**.

Why are the ends of bones covered by hyaline cartilage?
There is a clear functional reason for this:
-Compressive resistance:
Hyaline cartilage helps absorb forces and resist compression.
-Not innervated:
It **does not contain nerves**, which reduces pain during normal movement.
-Slippery surface:
It provides a **smooth, low-friction surface** that allows easy movement.

What increases the "slipperiness" between joint surfaces?
The presence of **synovial fluid** plays a major role:
It lubricates the joint surfaces.
Enhances smooth gliding between the two bones.

Because of:
the **smooth hyaline cartilage**, and
the **synovial fluid**,
the movement becomes:
Passive
Sliding (gliding) movement, where the two surfaces move smoothly over each other.



Osteoarthritis

It is a degenerative disease of the joints that primarily affects the articular (hyaline) cartilage.

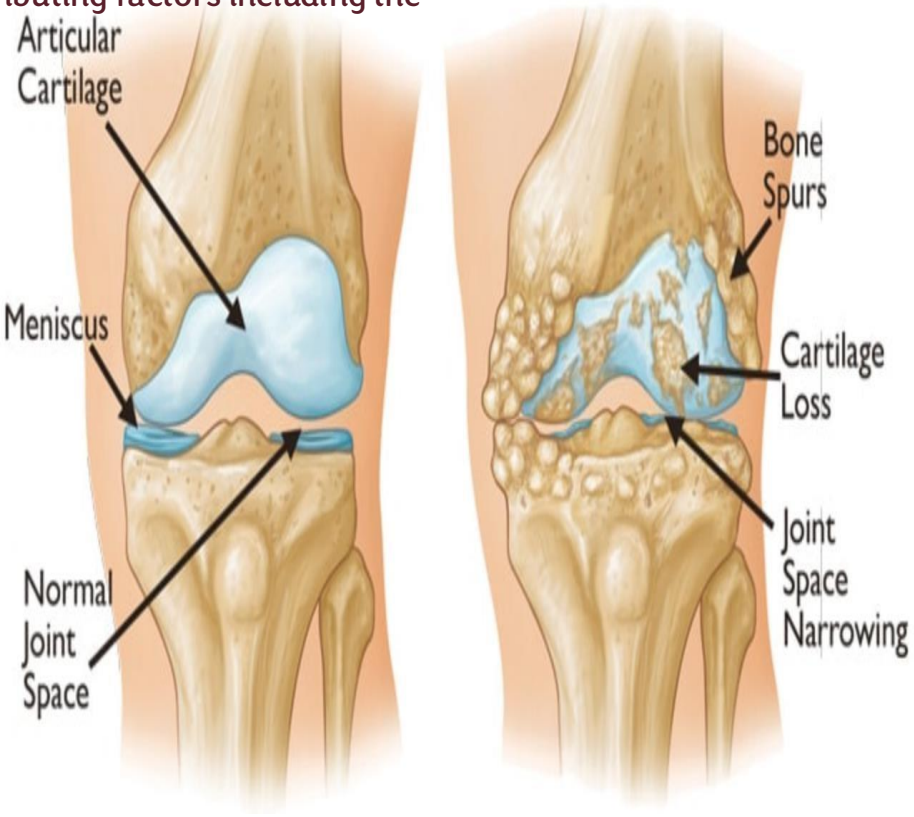
- A chronic condition that commonly occurs during aging.

It is basically an aging-related issue, meaning that its effects usually appear in older age. Genes have a big role in this condition, and physical activity also plays an important part. In general, you cannot isolate any disease—especially aging-related ones—from both genetic factors and lifestyle. For example, two brothers may have different lifestyles, and you might find that one have the problem while the other does not. In addition, the environment is also considered one of the contributing factors including the diet.

- Involves the gradual loss or changed physical properties of the articular cartilages.
- Weight-bearing Joints (knees, hips) or heavily used (wrist, fingers) are most prone to cartilage degeneration.

And ankle joint

The most commonly affected



It may start at a younger age especially in the joints of the hands. These joints are small (tiny) and are among the most frequently and extensively used joints in the body.
For example, certain professions such as dentists, anesthesia providers, and piano players use their finger joints much more than others, sometimes with very high repetitive movements compared to the average person.
Therefore, anyone who uses their small joints extensively and repeatedly may be more prone to developing Osteoarthritis.

Aging and disease progression:
When we say "aging", we do not mean that the cartilage suddenly disappears. There are gradual changes that precede this process.
-It begins with changes in the **synovial fluid**, where:
Its **quality decreases**
Its **quantity may decrease**
-This results in **reduced lubrication (slipperiness)** over the cartilage.

Effect on cartilage:
-Cartilage **depends on synovial fluid** for nutrition and hydration.
-With reduced synovial support:
The cartilage becomes **less hydrated**
Friction between surfaces **increases**
-Over time: The cartilage undergoes **degeneration and erosion**
Parts of it are lost . Eventually, the underlying bone becomes exposed → **bone-on-bone contact**

Symptoms progression:
-Early stage:
Discomfort with movement (e.g., walking, climbing stairs)
-Later stage:
Pain during movement
-Advanced stage:
Severe pain and discomfort
The patient may **avoid using the joint**
At this stage:
Medical intervention is required
This may include treatments such as **joint replacement**

Stem cell therapy:
Many studies have explored the use of **stem cells** in treatment and have shown some benefits.
However, all treatments have **limitations and cause side effects**.
They may help by:
Supporting tissue repair
Differentiating into **chondroblasts**, which contribute to cartilage formation

Calcification

Calcification in cartilage:
-**Calcification** is the extra deposition of calcium ions in the matrix.
-It is **not the same as ossification**, but it is **similar to some aspects of ossification**, especially what happens during development in **growing tissues (e.g., in children)**.

Process and effect on cartilage:
-In calcification, calcium is progressively deposited until:
The **matrix surrounding the chondrocytes becomes calcified**
-As a result:
Chondrocytes lose their **viability (lose vitality)** and eventually die.

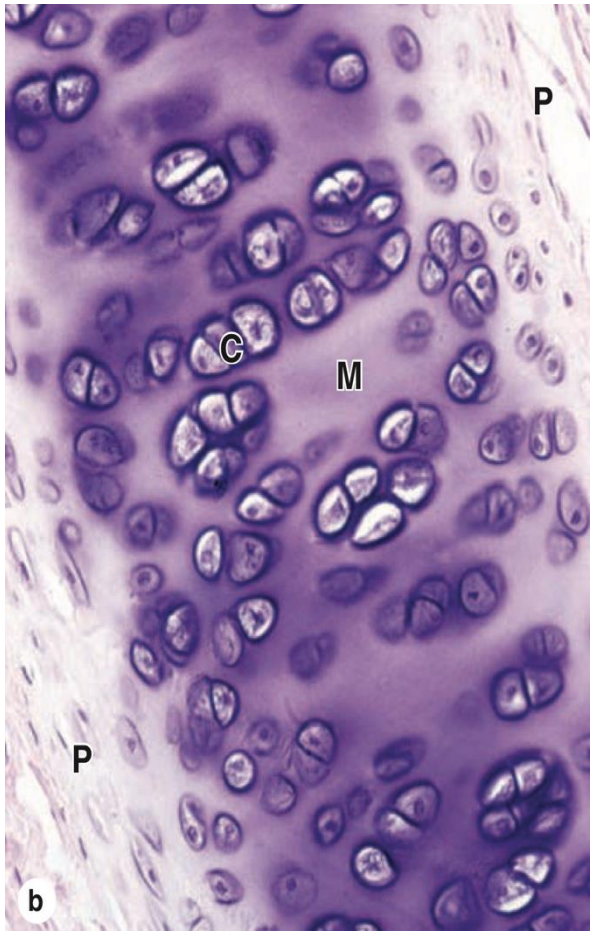
Why this leads to degeneration:
-Normally, cartilage matrix contains: **GAGs (glycosaminoglycans) , proteoglycans** and **type II collagen.**
These components allow **diffusion of nutrients and gases** because cartilage is **avascular**.
However, when calcification occurs:
The matrix becomes **hard and impermeable**
This blocks diffusion of nutrients and gases to chondrocytes

As a result:
Chondrocytes undergo **degeneration and death**
Since they are essential for maintaining the matrix, their loss leads to **further cartilage deterioration**

Calcification

- 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

Hyaline cartilage



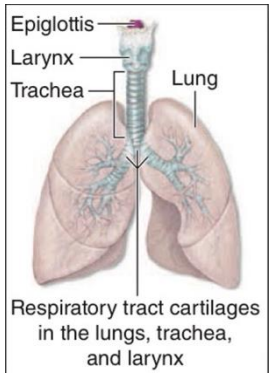
	Hyaline Cartilage
Main features of the extracellular matrix	Homogeneous, with type II collagen and aggrecan
Major cells	Chondrocytes, chondroblasts
Typical arrangement of chondrocytes	Isolated or in small isogenous groups Cells usually do not exist alone; it is rare to see a cell alone.
Presence of perichondrium	Yes (except at epiphyses and articular cartilage)
Main locations or examples	Many components of upper respiratory tract; articular ends and epiphyseal plates of long bones; fetal skeleton
Main functions	Provides smooth, low-friction surfaces in joints; structural support for respiratory tract

Is mainly due to hydration and the composition of the matrix, which contains a high amount of GAGs.

Elastic Cartilage

An important point is that hyaline cartilage can undergo calcification. Imagine if the ear were composed of hyaline cartilage—one day you might wake up and find your ear has become rigid and brittle, even prone to snapping.

- Similar to hyaline cartilage except that it contains an abundant network of **elastic fibers** in addition to a meshwork of collagen type II fibrils.
- The abundant elastic fibers provide greater flexibility to this type of cartilage.
- More flexible than hyaline cartilage,
- 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.
- Includes a perichondrium.

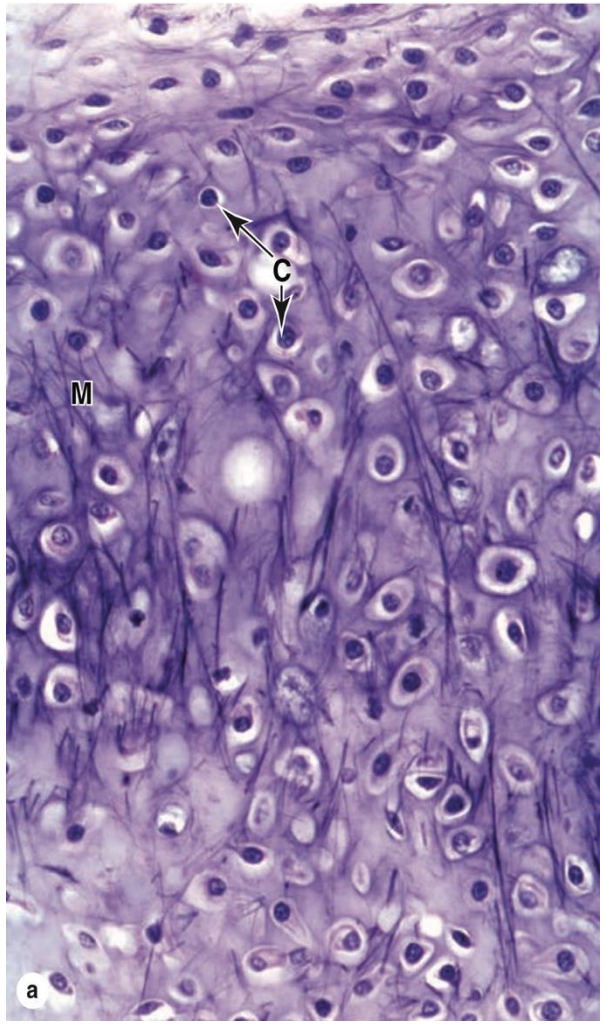


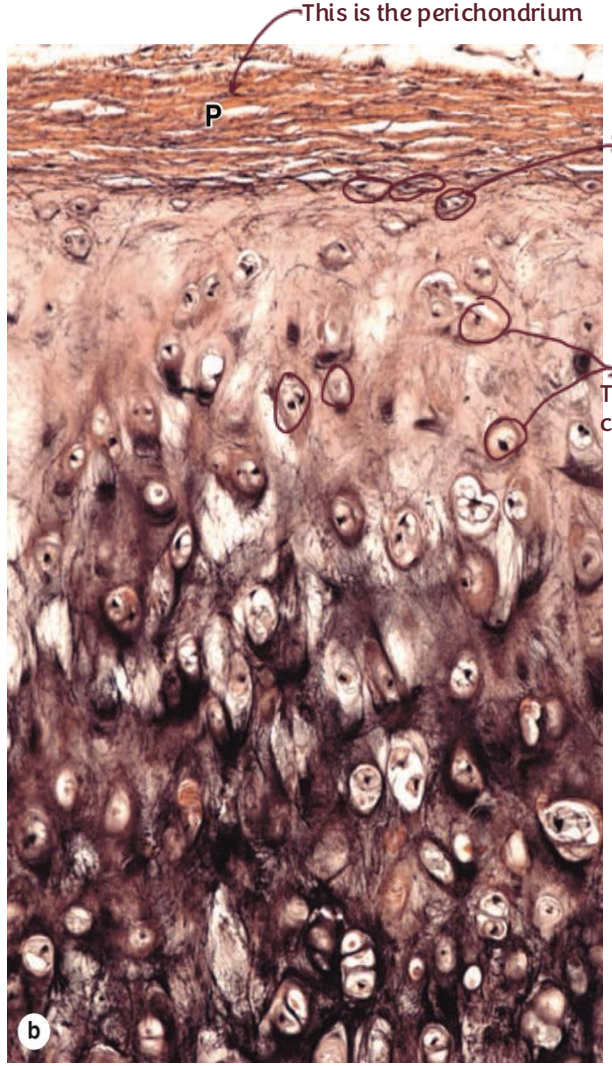
Respiratory tract cartilages in the lungs, trachea, and larynx

The epiglottis is part of the laryngeal cartilages. Some of these cartilages are large and form a structural framework, while others are smaller and are involved in the movement of the vocal cords.
Functionally, we have two passageways:
-The airway (larynx → trachea) anteriorly
-The digestive tract (oral cavity/pharynx → esophagus) posteriorly
During swallowing, these two pathways are very close to each other, so there is a risk that food could enter the larynx instead of the esophagus. This is prevented by the epiglottis, which is located posterior to the tongue (its anterior surface lies behind the tongue).
When we swallow, the epiglottis folds down to cover the laryngeal inlet, directing food toward the esophagus and preventing entry into the airway.
Breathing then resumes as the epiglottis returns to its position and the larynx reopens for air passage.
If this structure were made of rigid tissue like calcified cartilage, it would lose its flexibility and would not function properly in this rapid opening and closing mechanism.

If there is a perichondrium, we can find chondroblasts. If there is no perichondrium, chondroblasts are not present because chondrogenic cells arise from the perichondrium. So, no perichondrium means no chondrogenic layer and therefore no chondroblasts. This applies in adults.

Elastic Cartilage





	Elastic Cartilage
Main features of the extracellular matrix	Type II collagen, aggrecan, and darker elastic fibers (some / A lot of)
Major cells	Chondrocytes, chondroblasts
Typical arrangement of chondrocytes	Usually in small isogenous groups
Presence of perichondrium	Yes
Main locations or examples	External ear, external acoustic meatus, auditory tube; epiglottis and certain other laryngeal cartilages
Main functions	Provides flexible shape and support of soft tissues

Tap Picture to Test yourself

For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1	Slide 24 (The circles that represents the chondroblasts and chondrogenic)		
V1 → V2			

رسالة من الفريق العلمي:

"اللهم لا سهلاً إلا ما جعلته سهلاً، وأنت تجعل الحزن إذا شئت سهلاً"