# CARTILAGE

Cartilage belongs to the skeletal tissues and is a specialized form of connective tissue. Cartilage is composed of cells, **chondrocytes** (2-5% of the tissue volume only) located in **lacunae** surrounded by an intercellular **matrix**.

Cartilage is an **avascular tissue** with has no blood vessels of its own, though in some cases, such as in epiphyses of long bones, blood vessels traverse the tissue in cartilage canals to supply nutrients to other tissues. Cartilage is a tissue of very **low metabolic activity** and cell turnover (except in the embryo). Cartilage receives its nutrients from blood vessels from a surrounding dense connective tissue, the **perichondrium**. Nutrients and metabolites pass to and from the cells via the matrix by diffusion.

Nerves are not present in cartilage, but nerves and nerve ending are present in the perichondrium.

Cartilage is classified as:

- **Hyaline cartilage**
- **Elastic cartilage**
- **Fibrocartilage**

The difference between the different cartilage types depend on the different properties of the intercellular matrix, and in particular on the amount and type of the fibers embedded in the matrix.

## HYALINE CARTILAGE

Hyaline cartilage is the most common form of cartilage. Its name is derived from the Greek "*hyalos*" = glass. Fresh hyaline cartilage is a semi-transparent (translucent), milky-white tissue, that is both flexible and resilient to mechanical forces. In adults hyaline cartilage is found in the respiratory tract (nose, larynx, trachea, bronchi), the ventral part of ribs, and on articulating surfaces of long bones and joints (**articular cartilage**). Hyaline cartilage is much more common in the embryo, where it plays an important role in long bone development.

### Chondrogenesis

Like all connective tissue, cartilage is derived in the embryo from mesenchyme.

Mesenchyme cells grow and differentiate into young cartilage cells or **chondroblasts**, that are very active in secreting the surrounding matrix. The chondroblasts grow and develop in lacunae. These chondroblasts further differentiate into mature cartilage cells or **chondrocytes**.

There are two different types of chondrogenesis:

- **appositional growth**
- **interstitial growth**

## Appositional growth of cartilage

Appositional growth describes the addition of new cartilage cells from the surrounding perichondrium.
Flattened cells (**chondroprogenitor cells**) of the perichondrium divide and differentiate into elliptical **chondroblasts**. These chondroblasts, are active in secreting the intercellular matrix. The chondroblasts typically have basophilic cytoplasm. By transmission electron microscopy the cells are seen to have well-developed RER and Golgi bodies, typical of active secretory cells. The chondroblasts further differentiate into **chondrocytes**. The chondrocytes are less basophilic, more rounded and occupy more rounded lacunae. The amount of matrix surrounding the chondrocytes is greater than that of the chondroblasts.

## Interstitial growth of cartilage

Interstitial growth involves the addition of cartilage cells by the division of chondrocytes within specific lacunae deep in the tissue. As a consequence of this mitotic activity, lacunae may possess two, four, eight daughter chondrocytes. These are known as **isogenous** or **nest cells.** Interstitial growth is seen in histological preparations deeper in the older cartilage.

Chondrocytes may shrink during histological preparation and may not occupy the normal dimensions of the lacunae. This is a preparational artefact.

## Cartilage matrix

The most important component of cartilage and which provides the biomechanical characteristics of the tissue is the extracellular matrix. The matrix is composed of amorphous substance in which are embedded fibers.

The main components of hyaline cartilage (wet weight) are approximately:

- **Water 72-75%**
- **Proteoglycans 10%**
- **Collagen (type II) 16%**
- Other **glycoproteins** (e.g. chondronectin) 1.6%
- **Minerals 0.5%**

Hyaline cartilage matrix stains basophilic in regular H&E staining. It also stains positively with the PAS technique. The matrix is also **metachromatic** (after staining with e.g. toluidine blue, it is stained a purple color). The staining properties are the result of the molecular composition of the matrix.

The proteoglycans represent a complex of **protein** and **sulfated glycosaminoglycans** (GAG's), and in particular:

- **chondroitin-4-sulfate**
- **chondroitin-6-sulfate**
- **keratan sulfate**

These sulfated GAG's provide the basophilic staining characteristics.
In addition there are molecules of a **non-sulfated GAG**: **hyaluronic acid**.
The hyaluronic acid is a long thread-like molecule, to which are attached **link proteins** periodically along its length. **Proteoglycan monomers** (which resemble a test-tube brush) are attached to the link-proteins and consist of **core proteins** to which are connected the sulfated GAG's.

The network of macromolecules are held in place by the water, known as "**solvation water**". The solvation water is important for the diffusion of nutrients in the matrix of the tissue. The proteoglycans are important for maintaining the high osmotic pressure of the matrix and the resilient characteristics of the cartilage. **Type II collagen fibers** are embedded in the matrix and provide structural support (similar to that found in building materials such as the fibers embedded in resin in fiberglass). The type II collagen fibers constitute about 40% of the dry weight of cartilage. In normal histological preparations the collagen fibers are not seen as they have submicroscopic dimensions and their refractive index is similar to that of the amorphous matrix. By transmission electron microscopy, the collagen fibers are seen to have a 64nm banding and to be composed of regularly overlapping collagen fibrils.

The biomechanical properties of the cartilage allow it to function as a biomechanical spring or shock-absorber, to spread the load at joints and prevent too great pressures on bones. The capacity of the tissue for water-retention under load and resilience is an extremely important property of cartilage.

In histological sections the matrix surrounding the lacunae (nearest to the cells) is stained more intensely and is more basophilic (**capsular** or **territorial matrix**). Here the relative concentration of GAG's is greater than in the mass of the matrix, where the staining is less intense (**inter-territorial matrix**).

## ELASTIC CARTILAGE

Elastic cartilage is characterized by its great flexibility and elasticity owing to the large quantities of elastic fibers in the matrix. These elastic fibers provide the yellowish color in the fresh tissue. The elastic fibers in histological sections can be stained (e.g. with orcein). The elastic fibers are branched. The elastic fibers in the matrix near the perichondrium are less-densely packed (and easier to see) than those deeper in the tissue.

Elastic cartilage is found in the external ear, in the walls of the external auditory meatus and Eustachian tube and also in the epiglottis.

## FIBROCARTILAGE

Fibrocartilage is found in areas of the body subject to high mechanical stress or weightbearing. It lacks the flexibility of the other cartilage types.

Fibrocartilage is present in:

- intervertebral disks
- pubic symphysis
- temporo-mandibular joints
- at sites of connection of many ligaments to bones (e.g. *Ligamentum teres femoris*)
- tendon insertions.

Fibrocartilage is characterized by large numbers and concentrations of **collagen fibers** in the matrix. These collagen fibers are the dominant feature of the matrix and with relatively little amorphous matrix. The large amounts of collagen fibers result in the matrix appearing **acidophilic** in histological sections after H&E staining. Fibrocartilage is not surrounded by perichondrium.

The **intervertebral disks** consist of fibrocartilage plates between the vertebrae and act as mechanical shock absorbers. In sections they are seen to be formed of two components:

- **annulus fibrosus**, which is the outer region consisting of orderly concentric arrangements of cells and matrix dominated by type I collagen (as in tendons)
- **nucleus pulposus** (large vacuolated cells, that are vestiges of the embryonic notochord.

## FUNCTIONS OF CARTILAGE

Cartilage is important for:

- skeletal support in the embryo prior to the development of the bony skeleton.
- elongation of developing long bones (endochondral ossification).
- articulating joints (articular cartilage).
- flexible support in the ear and eartubes, and in the larger tubes of the respiratory tract (trachea, bronchi).

### Regeneration and repair

Despite the fact that cartilage is found in relatively few sites in the adult body, its functions are important for our well-being. Cartilage in adults has very little regenerative ability if damaged and is subject to tear and wear with aging. This is due to the dearth of cartilage cells, minimal mitosis, absence of an integral blood supply and overall low metabolic activity of the tissue. The clinical problems of damage or aging of the tissue (osteoarthritis) are substantial. With aging the cartilage matrix may develop calcified deposits (calcified cartilage).

### Secondary cartilage

This refers to cartilage that develops in association with specific bones formed by intramembranous ossification after the bones are already formed. This is the opposite of cartilage associated with endochondral ossification, where the cartilage precedes the bone formation. The cartilage of the temporomandibular joint is an example of a secondary cartilage.

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