The objectives

1- Be able to identify connective tissue

2. What is the function of the connective tissue.

3. Explain the main component of C.T?

4. Describe the components of the extracellular matrix

5-Numerate the types of cells which are found in C.T.?

6. What are the fibers? Classify it?

7- Be able to recognize between the three types of fibers

Connective Tissue: Introduction

Connective tissue are responsible for providing and maintaining the form of organs throughout the body. Functioning in a mechanical role, they provide a matrix that connects and binds other tissues and cells in organs and gives metabolic support to cells as the medium for diffusion of nutrients and waste products.

Structurally, connective tissue is formed by **three classes of components: cells, fibers, and ground substance**. Unlike the other tissue types (epithelium, muscle, and nerve), which consist mainly of cells, the major constituent of connective tissue is the **extracellular matrix (ECM).** Extracellular matrices consist of different combinations of **protein fibers** (collagen, reticular, and elastic fibers) and **ground substance.** In addition to its major structural role, molecules of connective tissue serve other important biological functions, such as forming a reservoir of factors controlling cell growth and differentiation. The hydrated nature of much connective tissue provides the medium

through which nutrients and metabolic wastes are exchanged between cells and their blood supply.

1- Cells of Connective Tissue

A variety of cells with different origins and functions are present in connective tissue. **Fibroblasts** originate locally from undifferentiated mesenchymal cells and spend all their life in connective tissue; other cells such as **mast cells**, **macrophages**, and **plasma cells** originate from hematopoietic stem cells in bone marrow, circulate in the blood, and then move into connective tissue where they remain and execute their functions. White blood cells (leukocytes) are transient cells of most connective tissues; they also originate in the bone marrow and move to the connective tissue where they reside for a few days, then usually die by apoptosis.

FIBROBLASTS are the most common cells in connective tissue. Their nuclei are ovoid or spindle shaped and can be large or small in size depending on their stage of cellular activity. They have pale-staining cytoplasm and contain well- developed rough endoplasmic reticulum (RER) and rich Golgi complexes. With routine H&E staining, only the very thin, elongated nuclei of the cells are clearly visible. They are responsible for the synthesis of all components of the extracellular matrix (fibers and ground substance) of connective tissue

MACROPHAGES, also called tissue histiocytes, are highly phagocytic cells that are derived from blood monocytes. With conventional staining, macrophages are very difficult to identify unless they show visible ingested material inside their cytoplasm. Macrophages may be named differently in certain organs. For example, they are called Kupffer cells

in the liver, osteoclasts in bone, and microglial cells in the central nervous system.

MAST CELLS: are of bone marrow origin and are distributed chiefly around small blood vessels. They are oval to round in shape, with a centrally placed nucleus. With toluidine blue stain, large basophilic purple staining granules are visible in their cytoplasm. These granules contain and release heparin, histamines, and various chemotactic mediators, which are involved in inflammatory responses. Mast cells contain Fc membrane receptors, which bind to immunoglobulin (Ig) E antibodies, an important cellular interaction involved in anaphylactic shock

PLASMA CELLS are derived from B-lymphocytes. They are oval shaped and have the ability to secrete antibodies that are antigen specifi c. Their histological features include an eccentrically placed nucleus, a cartwheel pattern of chromatin in the nucleus, and basophilic-staining cytoplasm due to the presence of abundant RER and a small, clear area near the nucleus. This cytoplasmic clear area (Golgi zone [GZ]) marks the position of the Golgi apparatus

LEUKOCYTES, white blood cells, are considered the transient cells of connective tissue. They migrate from the blood vessels into connective tissue by the process of diapedesis. This process increases greatly during various inflammatory conditions. After entering connective tissue, leukocytes, with the exception of lymphocytes, do not return to the blood. The following leukocytes are commonly found in connective tissue:

(1) Lymphocytes: These cells have a round or bean-shaped nucleus and are often located in the subepithelial connective tissue.

(2) Neutrophils (polymorphs): Each cell has a multilobed nucleus and functions in the defense against infection.

(3) Eosinophils: Each cell has a bilobed nucleus and reddish granules in the cytoplasm. They have antiparasitic activity and moderate the allergic reaction function.

(4) Basophils: These cells are not easy to find in normal tissues. Their primary function is similar to that of mast cells.

ADIPOCYTES (FAT CELLS) arise from undifferentiated mesenchymal cells of connective tissue. They gradually accumulate cytoplasmic fat, which results in a significant flattening of the nucleus in the periphery of the cell. Adipocytes are found throughout the body, particularly in loose connective tissue. Their function is to store energy in the form of triglycerides and to synthesize hormones such as leptin.

2- **Ground substance** is a highly hydrophilic, viscous complex of an ionic macromolecules (glycosaminoglycan and proteoglycans) and multiadhesive glycoproteins (laminin, fibronectin, and others) that stabilizes the ECM by binding to receptor proteins (**integrins**) on the surface of cells and to the other matrix components. It is a colorless, transparent, gel-like material in which the cells and fibers of connective tissue are embedded. Ground substance serves as a lubricant, helps prevent invasion of tissues by foreign agents, and resists forces of compression.

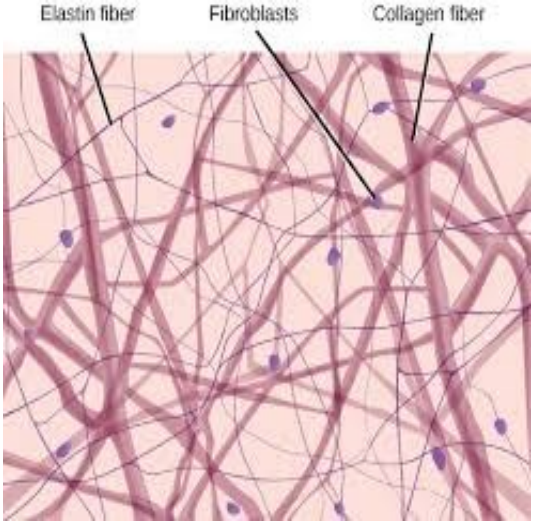
3- **Fibers**: are long, slender protein polymers present in different proportions in different types of connective tissue. The three main

types of connective tissue fibers are **collagen, reticular,** and **elastic fibers.** Collagen and reticular fibers are both formed by the protein **collagen,** and elastic fibers are composed mainly of the protein **elastin.** These fibers are distributed unequally among the types of connective tissue and the predominant fiber type is usually responsible for conferring specific properties on the tissue.

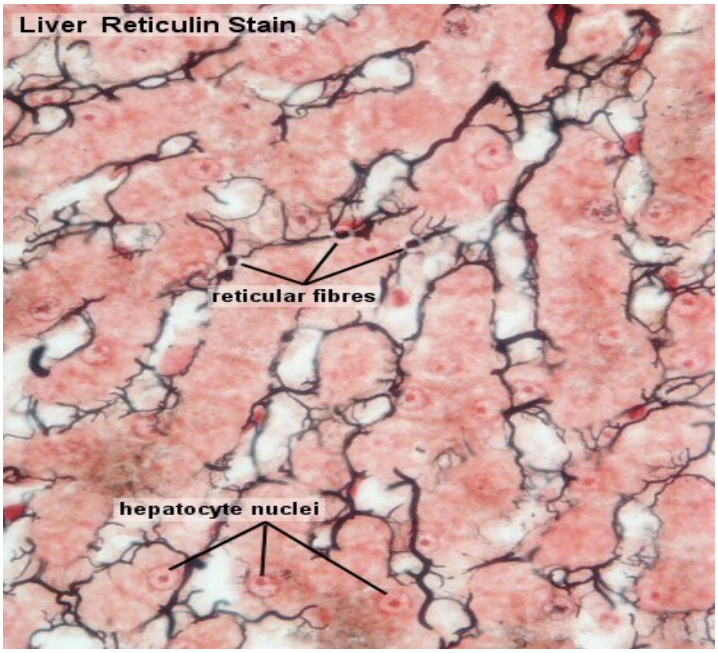
1- Collagen fibers

Collagen fibers are the most common and widespread fibers in connective tissue and are composed primarily of type I collagen. The collagen molecule (tropocollagen) is a product of the fibroblast. Each collagen molecule is 300 nm in length and consists of three polypeptide amino acid chains (alpha chains) wrapped in a right-handed triple helix. The molecules are arranged head to tail in overlapping parallel, longitudinal rows with a gap between the molecules within each row to form a collagen fibril. The parallel array of fibrils forms crosslinks to one another to form the collagen fiber. Collagen fibers stain readily with acidic and some basic dyes. When stained with H&E and viewed with the light microscope, they appear as pink, wavy fibers of different sizes. When stained with osmium tetroxide for EM study, the fibers have a transverse banded pattern (light–dark) that repeats every 68 μm along the fiber. The banded pattern is a reflection of the arrangement of collagen molecules within the fibrils of the collagen fiber. Collagen fibers are the dominant fiber type in most connective tissues. The primary function of collagen fibers is to add strength to the connective tissue. The thickness of the fibers varies from ~ 1 to 10 μm. Longitudinal striations may be visible in thicker fibers. These striations reveal that the fibers are composed of thinner collagen fibrils (0.2 to 0.5 μm in diameter). Each of these

fibrils is composed of microfibrils, which are only visible using electron microscopy.

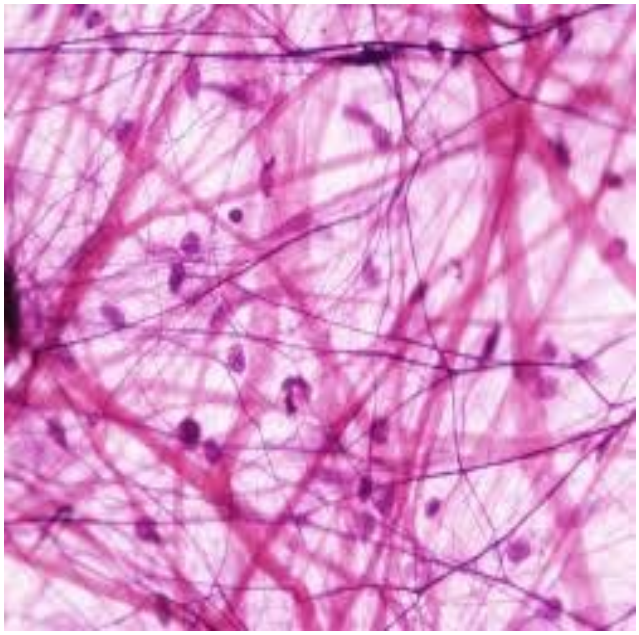


2- **Reticular fibers**: Reticular fibers are very delicate and form fine networks instead of thick bundles. It is small diameter fibers that can only be adequately visualized with silver stains; they are called argyrophilic fibers because they appear black after exposure to silver salts. They are produced by modified fibroblasts (reticular cells) and are composed of type III collagen. These small, dark-staining fibers form a supportive, meshlike framework for organs that are composed mostly of cells (such as the liver, spleen, pancreas, lymphatic tissue, etc.). Reticular fibers give support to individual cells, for example, in muscle and adipose tissue.



3- Elastic fibers

Elastic fibers are colored in fresh tissues they are light yellow - but this coloration is only visible if large amounts of elastic fibers are present in the tissue, for example, in the elastic ligaments of the vertebral column. Special stains are necessary to show elastic fibers in tissue sections. Elastic fibers have a very resilient nature (stretch and recoil), which is important in areas like the lungs, aorta, and skin. They are composed of two proteins, elastin and fibrillin, and do not have a banding pattern. These fibers are primarily produced by the fibroblasts but can also be produced by smooth muscle cells and chondrocytes.



MDICAL APPLICATION

The regenerative capacity of connective tissue is clearly observed in organs damaged by ischemia, inflammation, or traumatic injury. Spaces left after such injuries, especially in tissues whose cells divide poorly or not at all (eg, cardiac muscle), are filled by connective tissue, forming dense irregular scar tissue. The healing of surgical incisions and other wounds depends on the reparative capacity of connective tissue, particularly on activity and growth of fibroblasts. In some rapidly closing wounds, a cell called the myofibroblast, with features of both fibroblasts and smooth muscle cells, is also observed. These cells have most of the morphologic characteristics of fibroblasts but contain increased amounts of actin microfilaments and myosin and behave much like smooth muscle cells. Their activity is important for the phase of tissue repair called wound contraction.