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Lec. 2

Connective tissues:

The term **connective tissue** is applied to a tissue that fills the interstices between more specialised elements. Connective tissue serves to hold together, and to support, different elements within an organ. For this reason, such connective tissue is to be found in almost every part of the body. It is conspicuous in some regions and scanty in others. This kind of connective tissue is referred to as **general connective tissue** to distinguish it from more specialized connective tissues that we will consider separately. It is also called **fibro-collagenous tissue**. Connective tissues provide a matrix that supports and physically connects other tissues and cells together in organs. The interstitial fluid of connective tissue gives metabolic support to cells as the medium for diffusion of nutrients and waste products.

Components of connective tissue:

1. Cells,
2. Fibers, and
3. Ground substance.

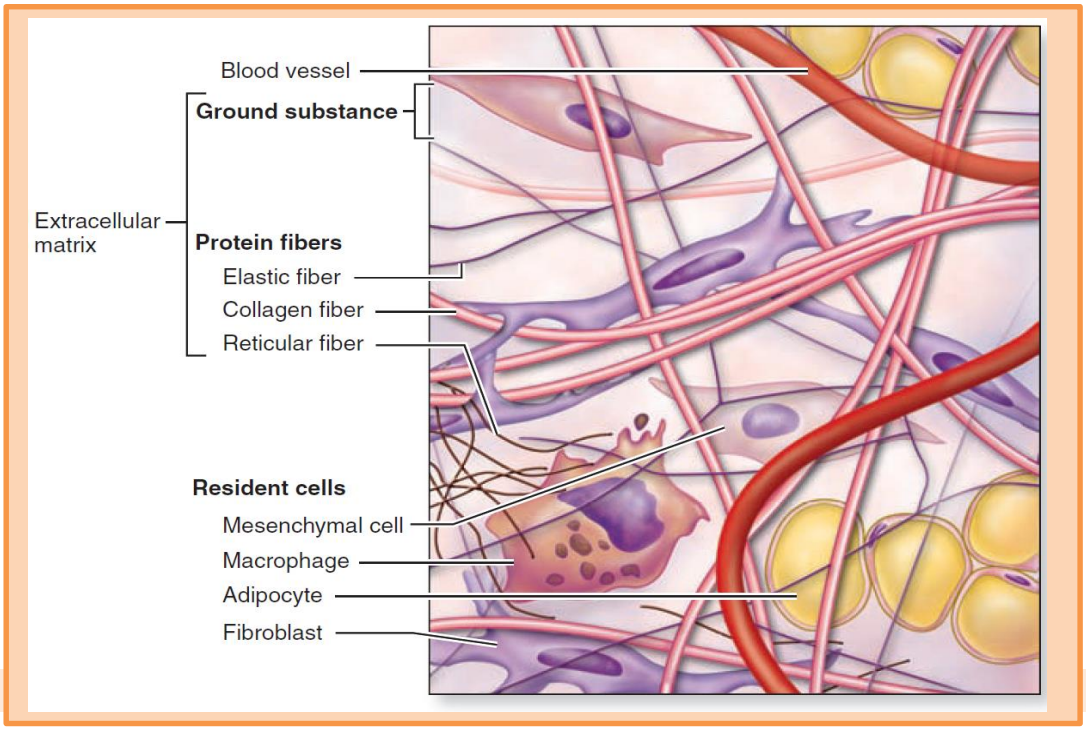


Figure 1: Cellular and extracellular components of connective tissue.

The major constituent is extracellular matrix consisting of different combinations of protein fibers (collagen, reticular and elastic) and ground substance. Variations in the amount of the three components of the connective tissue (cells, fibers and the ground substance) are responsible for the different types of tissues. The connective tissue originates from the mesenchyme developing mainly from the middle layer of the embryo (**mesoderm**). Mesodermal cells migrate from their site of origin, surrounding and penetrating developing organs.

The Cells: Various types of cells are present in connective tissue.

- **Fibroblasts**: Are the most common in connective tissues. Some histologists reserve the term "fibroblast" to denote the active cell and "fibrocyte" to denote the quiescent cell. The **active** fibroblast has more abundant and irregularly branched cytoplasm. Its nucleus is large, ovoid, euchromatic, and has a prominent nucleolus. The cytoplasm has much rough endoplasmic reticulum (RER) and a well-developed Golgi apparatus. The **quiescent** cell is smaller than the active fibroblast, is usually spindle-shaped with fewer processes and much less RER, and contains a darker, more heterochromatic nucleus. Fibroblasts synthesize and secrete collagen (the most abundant protein of the body) and elastin, which form large fibers …..etc.

- **Macrophages**: Cells of connective tissue are part of a large series of cells present in the body that have similar functions. These collectively form the **mononuclear phagocyte system**. Macrophage cells of connective tissue are also called **histiocytes** or **clasmatocytes.** They are characterized by their well-developed phagocytic ability and specialize in turnover of protein fibers and removal of dead cells, tissue debris, or other particulate material. Macrophages are derived from the marrow elements producing monocytes circulating in the blood. These cells cross the walls of venules and capillaries into connective tissues where they mature forming macrophages. In certain regions, macrophages have special names, e.g. **Kupffer cells** in the liver, **microglial cells** in the brain, **Langerhan's cells** in the skin and **osteoclasts** in the bone.

- **Mast Cells**: These are small round or oval cells (**mastocytes**, or **histaminocytes**). The nucleus is small and centrally placed. Irregular microvilli (filopodia) are present on the cell surface. Mast cells function in the localized release of many bioactive substances with roles in the local

inflammatory response, innate immunity, and tissue repair. There are **two** populations of mast cells: **1.** connective tissue mast cells found in the skin and peritoneal cavity. **2.** Mucosal mast cells present in intestinal mucosa and lungs. Mast cells originate from the bone marrow derived basophils.

- **Plasma Cells**: Plasma cells **or Plasmatocytes** are B-lymphocyte–derived, antibody-producing cells. Are large ovoid cells, have basophilic cytoplasm rich in RER. The nucleus is spherical and eccentrically placed, containing compact coarse heterochromatin alternating with lighter areas of equal size.

  There are few plasma cells in most connective tissues with a short average lives (10-20 days). They produce antibodies that may be discharged locally; may enter the circulation; or may be stored within the cell itself in the form of inclusions called **Russell's bodies**.

- **Leukocytes:** Besides macrophages and plasma cells, connective tissue normally contains other leukocytes derived from cells circulating in the blood. Leukocytes, or white blood cells, make up a population of wandering cells in connective tissue. They leave blood by migrating between the endothelial cells lining venules to enter connective tissue by a process called **diapedesis**. This process increases greatly during inflammation, which is a vascular and cellular defensive response to injury or foreign substances, including pathogenic bacteria or irritating chemical substances. The **lymphocytes** are derived from stem cells present in bone marrow. They are of two types. **B-lymphocytes** pass through blood to reach other tissues directly. Some B-lymphocytes mature into **plasma cells**. The second type of lymphocytes, called **T-lymphocytes**, travel (through blood) from bone marrow to the thymus. After undergoing a process of maturation in this organ they again enter the bloodstream to reach other tissues. Both B-lymphocytes and T-lymphocytes can be seen in connective tissue.
- **Other Leukocytes:** Apart from lymphocytes two other types of leukocytes may be seen in connective tissue. **Monocytes** are closely related in function to macrophages. **Eosinophils** (so called because of the presence of eosinophilic granules in the cytoplasm) are found in the connective tissue of many organs. They increase in number in allergic disorders.

- **Adipocytes:** Although some amount of fat (lipids) may be present in the cytoplasm of many cells, including fibroblasts, some cells store fat in large amounts and become distended with it. These are called **fat cells**, **adipocytes**, or **lipocytes**. Aggregations of fat cells constitute **adipose tissue.** The cytoplasm of the cell forms a thin layer just deep to the plasma membrane.

The nucleus is pushed against the plasma membrane and is flattened resembling a signet ring. Adipocytes are incapable of division.

- **Pigment cell (melanocytes):** Pigment cells are easily distinguished as they contain brown pigment (melanin) in their cytoplasm. They are most abundant in connective tissue of the skin, and in the choroid and iris of the eyeball. Of the many cells that contain pigment in their cytoplasm only a few are actually capable of synthesising melanin. Such cells, called **melanocytes**, are of neural crest origin. The remaining cells are those that have engulfed pigment released by other cells. Typically, such cells are star shaped (stellate) with long branching processes. In contrast to melanocytes such cells are called **chromatophores** or **melanophores**. They are probably modified fibroblasts.
- **Chondroblast.**
- **Osteoblasts.**

The fibers: The three main types of fibers include:

1. Collagen fibers.
2. Reticular fibers.
3. Elastic fibers.

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

Collagen fibers: Is most abundant type of connective tissue fibers. With the light microscope collagen fibers are seen in bundles. The bundles may be straight or wavy depending upon how much they are stretched. The bundles are made up of collections of individual collagen fibers which are 1-12μm in diameter. Collagen is not only synthesised by fibroblast but by other cells also, e.g., Chondroblasts in cartilage, osteoblast in bone and smooth muscle in blood vessel.

Reticular Fibers: Consists mainly of collagen III, they are formed by loosely-packed thin fibrils bound together by small interfibrillar bridges, composed of proteoglycans and glycoproteins. They are present with the smooth muscle of blood vessels, endoneurium and haematopoietic organs (spleen, lymph nodes and bone marrow), and around parenchymal organs (e.g. liver and endocrine glands). Reticular fibers produced by fibroblasts occur in the reticular lamina of basement membranes and typically also surround adipocytes, smooth muscle and nerve fibers, and small blood vessels.

Elastic Fibers (Elastin): Are also thinner than the type I collagen fibers and form sparse networks interspersed with collagen bundles in many organs, particularly those subject to much bending or stretching. **Proelastin** is a globular molecule produced by fibroblasts and smooth muscle cells in blood vessels, it polymerizes to form elastin. Elastin is resistant to boiling, acid and alkali extraction and digestion by usual proteases. It is easily hydrolyzed by pancreatic elastase. It contains two unusual amino acids: desmosine and isodesmosine.

The ground substance:

The interfibrillar transparent homogenous viscous solution is called **ground substance or matrix**. It fills the space between cells and fibers. Ground substance is a complex of anionic, hydrophilic proteoglycans, glycosaminoglycans, and multiadhesive glycoproteins (laminin, fibronectin, and others).

Functions of Ground Substance:

1. Fills the intercellular spaces.
2. Acts as a lubricant.
3. Acts as a barrier to penetration of invaders.
4. Facilitate adhesion between various elements of connective tissue.

Types of connective tissues:

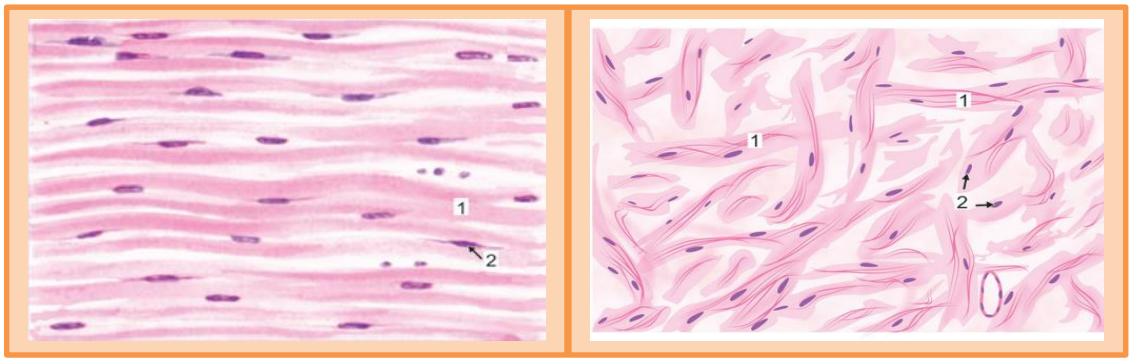
First: Connective tissue proper: In adults there are **two** general classes of connective tissue proper, **loose** and **dense**, terms that refer to amounts of collagen present.

A. **Loose connective tissue**: It fills spaces between groups of muscle cells, supports epithelial tissue and surrounds blood vessels, papillary layer of the dermis, serosal linings of peritoneal and pleural cavities, glands and mucous membranes. **Composition**: Fibroblasts, macrophages, collagen, reticular and elastic fibers. It includes:

1. Areolar connective tissue.
2. Adipose connective tissue.
3. Reticular connective tissue.
4. Mucous connective tissue.

B. **Dense connective tissue**: Contains fewer cells with predominance of collagen. Subdivided into:

1. **Dense irregular**: Collagen fibers arranged in bundles without orientation (e.g. dermis).
2. **Dense regular**: Collagen fibers are aligned with the linear orientation of fibroblasts in response to prolonged stress (e.g. tendons). Also elastic fibers may arrange in regular form as in ligaments.



A **B**

Figure 2: Dense Regular Collagenous Connective Tissue (Tendon, A), Dense Irregular Connective Tissue (Dermis of Skin, B), 1. Collagen fiber and 2. Nuclei of fibroblast.

Second: Special connective tissue: This type of tissues includes:

A- Skeletal connective tissue: that includes cartilage and bone.
B- Blood
C- Lymph
D- Haemopoietic tissue