Biology

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Connective Tissue

It is the most numerous tissues in the body, which connects the structures with each other, it characterized by:

1. binding and supporting the organs.
2. it is vascular except the cartilage.
3. it is derived from mesoderm layer.

Connective tissue is composed of:

- Cells
- Extracellular materials

The extracellular matrix is composed of:

- fibers (collagen fibers, reticular fibers, elastic fibers)
- ground substance is a highly hydrophilic viscous complex of anionic macromolecules.

Functions of connective tissue

1-Establishing a structural framework and Protecting delicate organs:

The most prominent function of connective tissue is structural support to enable maintenance of anatomical form of organs.

2-Transporting fluids and dissolved materials:

The connective tissues serve a nutritive role.

3-Storing energy reserves:

The adipose tissue serves as an energy store and also provides thermal insulation.

4-Defending the body from microorganisms:

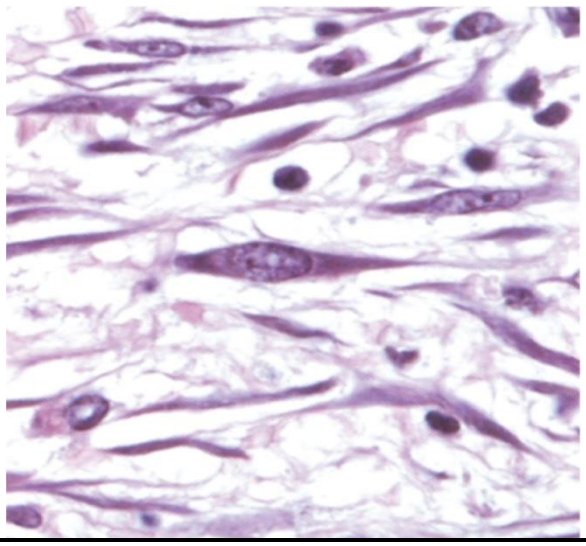
Various components of the connective tissue play roles in the defense or protection of the body including many of the components of the vascular and immune systems (plasma cells, lymphocytes, neutrophils, eosinophils, basophils, mast cells). The various macrophages of the body are also categorized as connective tissue cells.

Connective tissue component

1) Cells:

- **Fibroblasts:**

Fibroblasts are the most common cell type found in connective tissue. They are derived from undifferentiated mesenchymal cells. The term "fibroblast" is commonly used to describe the active cell type, whereas the more mature form, which shows less active synthetic activity, is commonly described as the "fibrocyte". **Fibroblasts** are elongated, spindle-shaped cells with many cell processes. They have oval, pale-staining, regular nuclei with prominent nucleoli. Fibroblasts synthesize collagen, reticular and elastic fibers and the amorphous extracellular substance.



The **fibrocytes** (inactive fibroblast) is smaller than active fibroblast. The nucleus is small elongated and more deeply stained.

MEDICAL APPLICATION

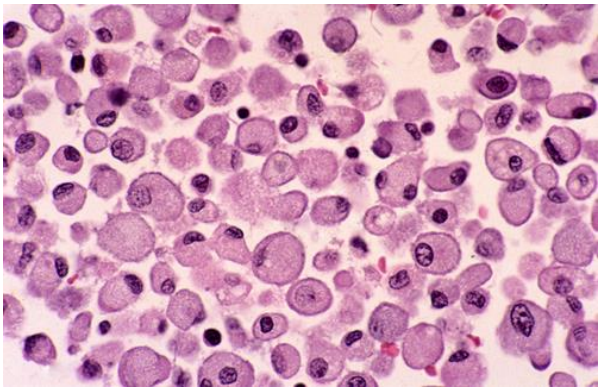
The regenerative capacity of the connective tissue is clearly observed when tissues are destroyed by inflammation or traumatic injury. In these cases, the spaces left after injury to tissues whose cells do not divide (eg, cardiac muscle) are filled by connective tissue, which forms a scar. The healing of surgical incisions depends on the reparative capacity of connective tissue. The main cell type involved in repair is the fibroblast.

When it is adequately stimulated, such as during wound healing, the fibrocyte reverts to the fibroblast state, and its synthetic activities are reactivated.

In such instances the cell reassumes the form and appearance of a fibroblast. The **myofibroblast**, a cell with features of both fibroblasts and smooth muscle cells, is also observed during wound healing. These cells have most of the morphological characteristics of fibroblasts but contain increased amounts of actin microfilaments and myosin and behave much like smooth muscle cells. Their activity is responsible for wound closure after tissue injury, a process called **wound contraction**.

- **Macrophages:**

Macrophages originate from monocytes, which migrate to connective tissue via blood and differentiate into tissue macrophages. There, exist different populations of macrophage. These include: Langerhans cells in skin, dendritic cells in lymph nodes, Kupffer cells in the liver, histiocytes in the connective tissue proper, osteoclasts in bone, and microglia in nervous system.

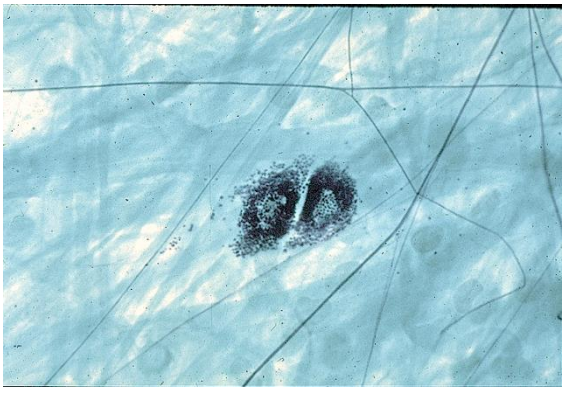


The main functions of macrophages are ingestion by phagocytosis of microorganisms, and they also participate in the breakdown of aged cells including erythrocytes. The intracellular digestion occurs as a result of fusion of lysosomes with the phagosome (ingested body). Other functions include: antigen presentation, removing cell debris e.g. during pregnancy, the increased uterus size is involuted immediately after delivery by action of macrophages. Macrophages also are secretory cells that secret enzymes and cytokines have defensive functions.

The macrophages usually appear round with slightly irregular cell outlines, the nucleus is small but stained darker than the nucleus of the fibroblast and it is eccentric.

- **Mast cells:**

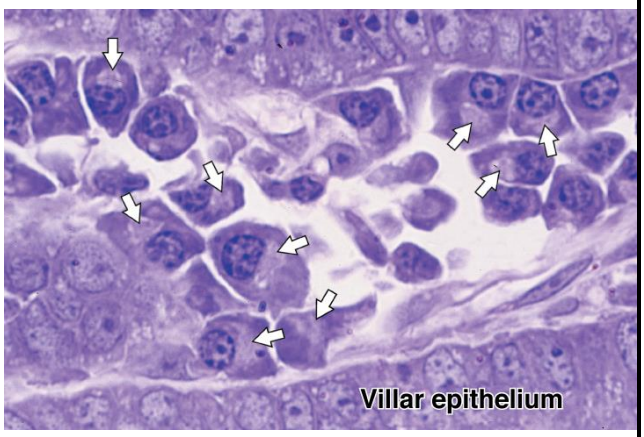
Mast cells are oval or round cells characterized by cytoplasm packed with large round basophilic granules. Two of the main components of mast cell granules are histamine (vasodilator) and heparin (anticoagulant). The granules of mast cells are released in inflammatory responses.



The surface of mast cell contains specific receptors for immunoglobulin E (IgE), a type of immunoglobulin produced by plasma cells. Most IgE molecules are bound to the surface of mast cells and blood basophile.

- **Plasma cells:**

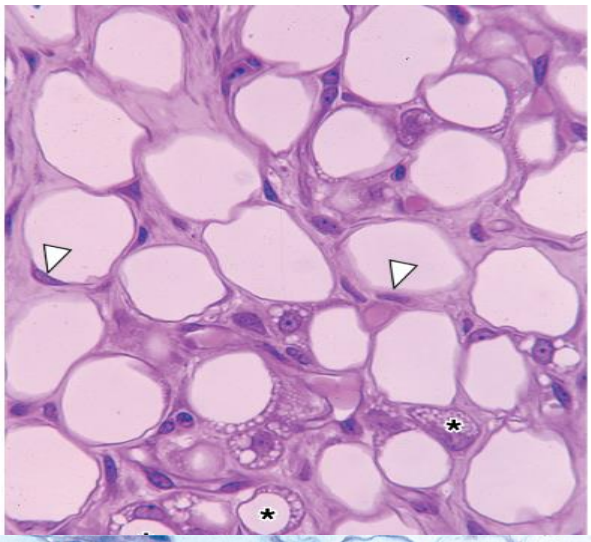
Plasma cells are responsible for antibody production. These large cells have eccentric nuclei, basophilic cytoplasm (much rough endoplasmic reticulum associated with protein synthesis) and well-developed Golgi bodies. Plasma cells are relatively short-lived and are found in sites of chronic inflammation or sites of high risk of invasion by bacteria or foreign proteins (such as the lamina propria of the intestinal and respiratory tracts). The plasma cell is easily recognized by its intensely stained cytoplasm (which is quite basophilic, since these cells are making antibodies at a great rate) and by its characteristic "clock face" pattern of chromatin distribution in the nucleus.



- **Adipose cells:**

Adipocytes are the cells that primarily compose adipose tissue, specialized in storing energy as fat, also act as an endocrine organ to secrete leptin hormone which regulate the appetite under normal condition and so regulate the amount of adipose tissue, defect in its secretion result in obesity.

There are two types of adipose tissue, white adipose tissue and brown adipose tissue.

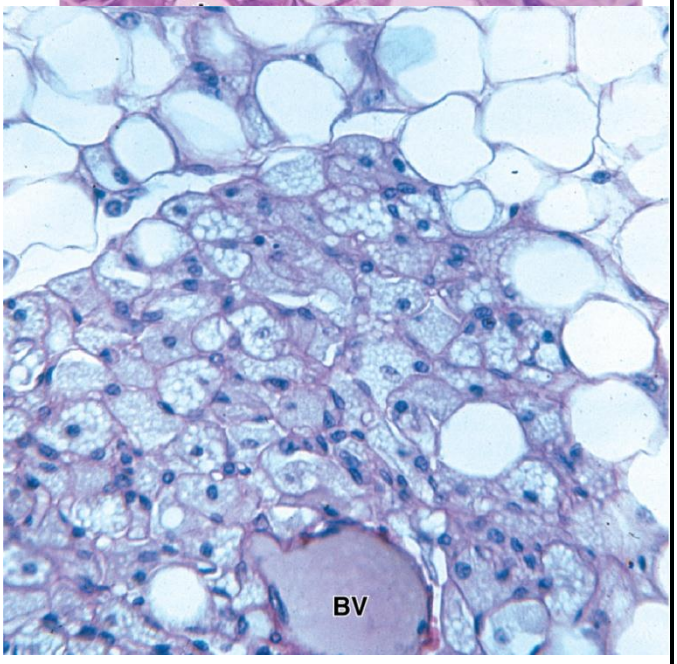


1.White fat cells (unilocular cells):

White fat cells contain a large lipid droplet surrounded by a ring of cytoplasm. The nucleus is flattened and located on the periphery.

2.Brown fat cells (multilocular cells):

It is especially abundant in newborns and in hibernating mammals. Its primary function is to generate body heat in animals or newborns that do not shiver. Brown adipocytes contain numerous smaller droplets and a much higher number of mitochondria (rich in iron) and make it brown. Brown fat also contains more capillaries than white fat, since it has a greater need for oxygen than most tissues.



- **Leukocytes:**

The white blood cells (lymphocytes, eosinophilis, and basophilis) are commonly found in connective tissue. They migrate from the blood vessels to the connective tissue, especially to sites of injury or inflammation.

- **Undifferentiated mesenchymal cells (cells of regeneration):**

These cells have ability to give rise any kind of cells, it form osteoblasts, chondrocytes, adipocytes, they are smaller than fibroblast but have the same appearance, so it characterized by small cell body, with few cytoplasmic processes, large round nucleus with a prominent nucleolus.

2) extracellular matrix:

I-Ground Substance:

Ground substance in connective tissue consists primarily of amorphous, transparent and colorless extracellular matrix, which has the properties of a semifluid gel and a high water content. It is binding cells to the fibers of connective tissue.

Ground substance composed of:

1. **glycoaminoglycans**.
2. **proteoglycans**.
3. **adhesive glycoproteins**.

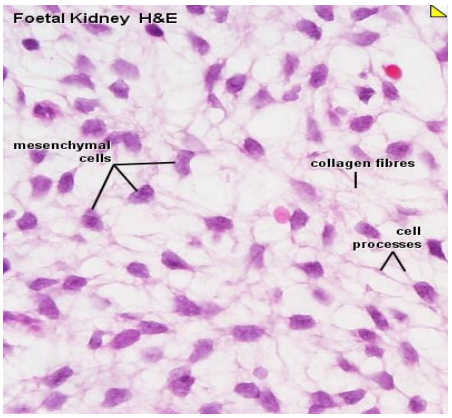
The **glycosaminoglycan** are unbranched polysaccharide molecules of 5 types:

1. Hyaluronan (or hyaluronic acid) is the dominant glycosaminoglycan in connective tissues.
2. The remaining 4 major glycosaminoglycans are chondroitin sulfate, dermatan sulfate, keratan sulfate and heparan sulfate.

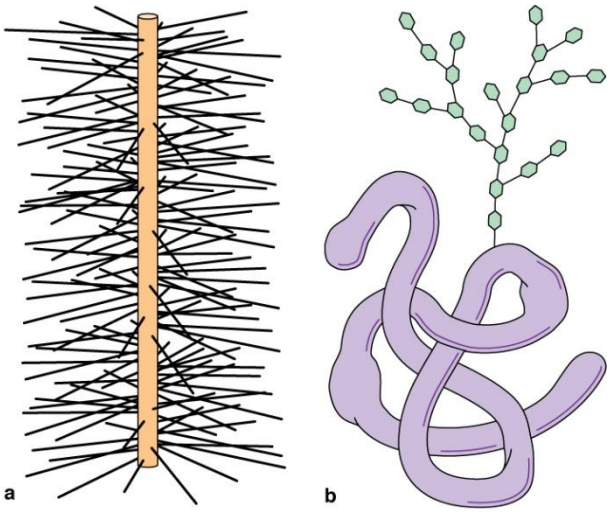
Except for hyaluronic acid, the other 4 glycosaminoglycans are bound to a core protein to form much larger molecules called **proteoglycan aggregates**. These proteoglycans attract large amounts of water, which forms the hydrated gel of the ground substance.

The third class of ground substance constituents is **adhesive glycoproteins** responsible for linking the components of the matrix both to one another and to the surfaces of cells. These includes:

- Fibronectin
- Laminin



Such laminin glycoprotein are the major structural components of the cell basement membrane. This protein binds epithelial cells to the basal lamina.



a proteoglycan b glycoprotein

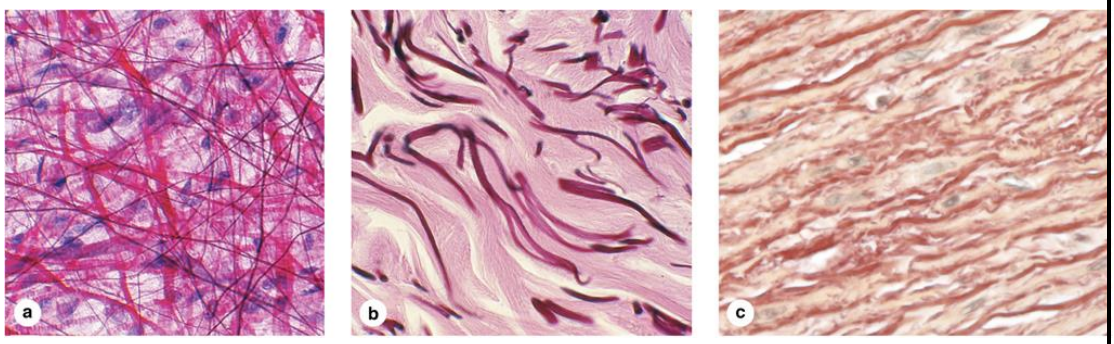
In addition to the hydrated ground substance, there is small quantity of free fluid called **interstitial** or **tissue fluid** that is similar to blood plasma in its content of ions and diffusible substances, tissue fluid contain small percentage of plasma proteins that pass through the

capillary walls as a result of the hydrostatic pressure of the blood. Edema result from accumulation of water in the extracellular space in many pathological conditions. Edema may result from venous or lymphatic obstruction or from a decrease in venous blood flow (e.g, congestive heart failure). It may also be caused by the obstruction of lymphatic vessels due to parasitic plugs or tumor cells and chronic starvation; protein deficiency results in a lack of plasma proteins and a decrease in colloid osmotic pressure. Water therefore accumulates in the connective tissue and is not drawn back into the capillaries.
Another possible cause of edema is increased permeability of the blood capillary endothelium resulting from chemical or mechanical injury or the release of certain substances produced in the body (eg, histamine).

II-Fibers:

Collagen fibers (white fibers):

They are the most numerous and strongest fibers in the body derived from connective tissue cells called fibroblasts. Fresh collagenous fibers are colorless and they give the tissue white color when grouped in great no. e.g. in tendon. These fibers are straight or wavy, unbranched consist of protein called collagen which is the major structural protein of the extracellular matrix and the single most abundant protein in human tissues. This protein characterized by the formation of triple helices in which 3 polypeptide chains are wound tightly around one another in a ropelike structure.



Collagen fibers always run parallel to each other forming bundles, which branched and anastomose.
There are several types of collagen fibers (currently named type I to XXI)

MEDICAL APPLICATION

Keloid is a local swelling caused by abnormal amounts of collagen that form in scars of the skin. Keloids, which occur most often in individuals of black African descent, can be a troublesome clinical problem to manage; not only can they be disfiguring, but excision is almost always followed by recurrence.
Vitamin C (ascorbic acid) deficiency leads to scurvy, a disease characterized by the degeneration of connective tissue. Without this vitamin, fibroblasts synthesize defective collagen, and the defective fibers are not replaced. This process leads to a general degeneration of connective tissue that becomes more pronounced in areas in which collagen renewal takes place at a faster rate. The periodontal ligament that holds teeth in their sockets has a relatively high collagen turnover; consequently, this ligament is markedly affected by scurvy, which leads to a loss of teeth.

Elastic fibers (yellow fibers):

Connective tissues also contain elastic fibers, which are particularly abundant in organs that regularly stretch and then return to their original shape.
Elastic fibers are composed principally of a protein called elastin.

They differ from collagen that they are thinner than the white fibers, they branched and unite with one another forming irregular network, when they present in great quantity they appear yellow, the fibers run individually and not in bundle.
They are not stained with heamatoxylin-eosin, but stain with special stain orcein, they are generally formed by fibroblasts.

Medical application:

Marfan syndrome, a disease characterized by a lack of resistance in the tissues rich in elastic fibers. Because the large arteries are rich in components of the elastic fibers and because the blood pressure is high in the aorta, patients with this disease often experience aortic swellings called aneurysms, a life-threatening condition.

Reticular fibers:

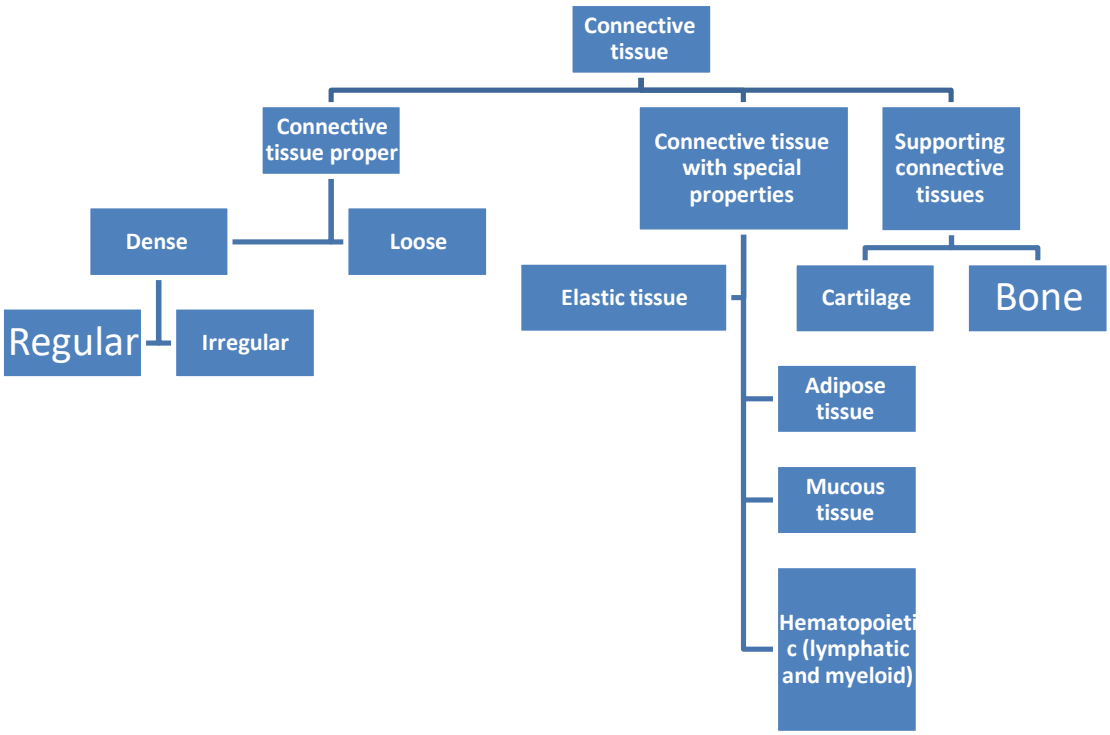
Reticular fibers are another form of collagen (Type III). They are arranged as a loose meshwork of thin fibers providing supportive scaffolding for the specialized cells of various organs as well as blood vessels.
They are formed from collagen, and they are not stained with heamatoxylin-eosin, but stained with silver stain and appear black, they are associated with special cells called reticular cells.

Clinical Correlation:

Sun Exposure and Molecular Changes in Photoaged Skin

Chronological aging of the skin is a complex process that is associated with functional and structural changes within the stratified squamous epithelium (epidermis) as well as the underlying connective tissue of the dermis. When these changes are intensified by prolonged exposure to solar or ultraviolet (UV) radiation, the process is referred to as **photoaging.**
Chronic sun exposure ages the skin at an accelerated rate, especially in exposed areas of the body such as the face, neck, dorsal surface of the hands, and forearms. Clinical signs associated with photoaging include dyspigmentation, freckles, deep wrinkles, increased laxity, and increased risk for cutaneous cancers.
The best strategies to prevent photodamage caused by solar and UV radiation is the use of physical and chemical sunscreens to prevent UV penetration into skin. Other methods are also used in treating damaged skin. These include reducing skin inflammatory reactions with anti-inflammatory medications.

Connective tissue classification



a-Loose Connective Tissue:

Loose connective tissue (areolar tissue) supports many structures that are normally under pressure and low friction. A very common type of connective tissue, Loose connective tissue comprises all the main component of connective tissue proper. There is no predominant element in this tissue. The most numerous cells are fibroblasts and macrophages but all the other types of connective tissue cells are present. A moderate amount of collagen, elastic, and reticular fibers.

b-Dense Connective Tissue:

Dense connective tissue is divided into two sub-categories:

- **dense irregular connective tissue**
- **dense regular connective tissue**

Dense connective tissue contains relatively few cells with much greater numbers of collagen fibers.

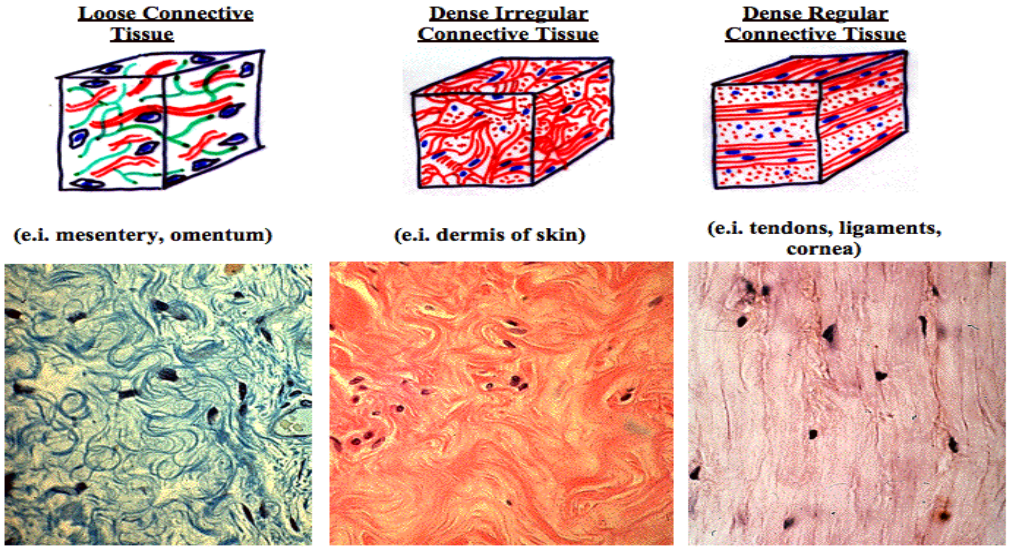
Dense irregular connective tissue has bundles of collagen fibers that appear to be fairly randomly orientated (as in the dermis).

Dense regular connective tissue has closely-packed densely-arranged fiber bundles with clear orientation (cord like structure or bands) and relatively few cells (such as in tendons). This type include:

1. white regular dense connective tissue e.g. tendons.

2. yellow elastic dense regular connective tissue e.g. ligaments: They have a similar structural arrangement to tendons, but differ in their yellow color, which is due to the abundance of elastic fibers in the tissue.

TYPES OF CONNECTIVE TISSUE



II- Connective tissue with special properties:

Elastic tissue:

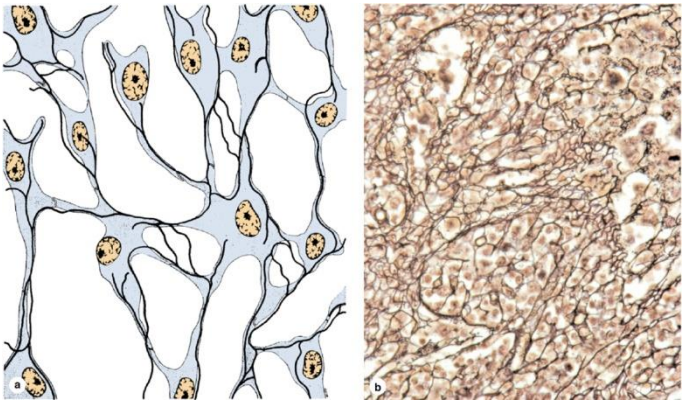
Elastic tissue is composed of bundles of thick, parallel elastic fibers.

Mucous tissue:

This is found in the umbilical cord (Wharton's jelly). It is a loose connective tissue composed of fibroblasts.

Reticular tissue:

Reticular tissue is a specialized loose connective tissue consisting of reticular fibers initially associated with specialized fibroblast called reticular cells. Reticular tissue provides the architectural framework that creates a special microenvironment for hematopiotic and lymphoid organs (bone marrow, lymph nodules, nodes and spleen).



Mesenchymal tissue:

Is the connective tissue of embryo, consists of mesenchymal cells in a gel like amorphous ground substance containing scattered reticular fibers.