

CONNECTIVE TISSUE

Connective tissue is responsible for providing structural support for the tissues and organs of the body. This mechanofunction is important in maintaining the form of the body, organs and tissues. The tissue derives its name from its function in connecting or binding cells and tissues.

Connective tissue is composed of:

- **cells**
- **extracellular matrix.**

The extracellular material of connective tissue, which plays a major role in the functioning of the tissue, is the dominant component of the tissue. The dominance of the extracellular material is a special feature that distinguishes connective tissue from the other tissues of the body.

The **extracellular matrix** is composed of :

- **protein fibers** (collagen fibers, reticular fibers, elastic fibers)
- **amorphous ground substance**
- **tissue fluid** (not preserved in histological preparations). The amount of tissue fluid is fairly constant and there is an equilibrium between the water entering and leaving the intercellular substance of the connective tissue. In pathological conditions (traumatic injury, inflammation) fluid may accumulate in the connective tissue, a condition known as edema.

Connective tissues are very heterogeneous in structure and function, however all have the three main structural components (cells, fibers and ground substance). The diverse composition and amount of these components in the various connective tissues can be correlated with the specific functional roles of the tissue.

FUNCTIONS OF CONNECTIVE TISSUE

- **Structural support**

The connective tissues serve several functions, of which the most prominent function is **structural support** to enable maintenance of anatomical form of organs and organ systems. Examples include the connective tissue capsules surrounding organs (such as the kidney, lymph nodes). The loose connective

tissue acts to fill the spaces between organs. The tendons (connecting muscles to bone) and the elastic ligaments (connecting bones to bones) are examples of specialized orderly forms of connective tissue. The skeletal tissues (cartilage and bone) are special forms of connective tissue.

- **Metabolic functions**

The connective tissues serve a **nutritive role**. All the metabolites from the blood pass from capillary beds and diffuse through the adjacent connective tissue to cells and tissues. Similarly **waste metabolites** from the cells and tissues diffuse through the loose connective tissue before returning to the blood capillaries.

The **adipose tissue** (especially that of the hypodermis) serves as an **energy store** and also provides **thermal insulation**. Surplus calories can be converted into lipid and stored in adipocytes.

- **Blood components and blood vessels**

The **hematopoietic tissues** (blood-forming tissues) are a further specialized form of connective tissue. These include the **myeloid tissue** (bone marrow) and the **lymphoid (lymphatic) tissue**. The lining of the blood and lymphatic vessels (**endothelial cells**) as well as the peripheral blood, are also specialized forms of connective tissue.

- **Defensive functions**

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. These all develop from monocytes and are grouped as part of the **Mononuclear Phagocyte System** of the body. Macrophages are important in tissue repair as well as defense against bacterial invasion. The fibroblasts of connective tissue proliferate in response to injury of organs and migrate to and deposit abundant new collagen fibers, resulting in the formation of **fibrous scar tissue**.

Cell type	Chief function
Mesenchyme	Embryonic source of all connective tissue cells

Fibroblasts Chondroblasts Osteoblasts	Structural support
Plasma cells Lymphocytes Neutrophils Eosinophils Basophils Mast cells Macrophages	Defense and immune
Adipocytes	Metabolic Energy storage Thermal insulation

Mesenchyme and the origin of connective tissue cells

All connective tissue cells are derived from mesenchymal cells. **Mesenchyme cells** are found in embryos and are for the most part derived from the middle germ layer of the embryo (mesoderm).

Several of the connective tissues of the head region are derived from the neural crest (ectodermal origin). Endothelial cells lining blood vessels are derived from mesenchyme and therefore are classified as connective tissue rather than epithelium. Epithelium, which can develop from all three embryonic germ layers, never develops from mesenchymal cells.

Mesenchymal cells are typically elongated cells, with relatively little cytoplasm. These cells have regular, oval nuclei with prominent nucleoli. The nuclei are often eccentric in position. Mesenchymal cells have several thin cytoplasmic processes. The spaces between the cell processes are filled in ground substance.

Mesenchyme cells are only found in embryos, however some mesenchyme-like cells persist in adult connective tissue. These mesenchyme-like cells retain their capacity to differentiate into other connective tissue cells in response to injury. Examples include the pericytes (perivascular cells) of blood capillaries.

Amorphous Ground Substance

The intercellular ground substance is an amorphous, transparent material composed mainly of glycoproteins and proteoglycans, with a fairly high water content.

The main proteoglycans consist of a core protein associated with sulfated glycosaminoglycans (GAGs). The main GAGs include : chondroitin-4-sulfate, chondroitin-6-sulfate, keratan sulfate, heparan sulfate) and the non-sulfated hyaluronic acid.

All substances passing to and from cells must pass through the ground substance.

CONNECTIVE TISSUE FIBERS

Connective tissue fibers are composed of structural proteins. The three main types of fibers are:

- **collagen fibers**
- **reticular fibers**
- **elastic fibers**

Collagen fibers

Collagen is the most abundant protein in the body (up to 30% dry weight). There are more than 12 different types of collagen, though the most common types are Types I to V.

Collagen type	Main sites	Special features
Type I	Bones, tendons, organ capsules, dentin	Most abundant, Typical collagen fibers (64nm banding)
Type II	Hyaline cartilage Elastic cartilage	Very thin fibrils
Type III	Reticular fibers	Often associated with Type I
Type IV	Basal lamina associated with	Amorphous (non-fibrous)

	epithelial and endothelial cells	
Type V	Basal lamina associated with muscle	Amorphous (non-fibrous)

Collagen is synthesized by a wide number of cell types (including: fibroblasts, osteoblasts, chondroblasts, odontoblasts, reticular cells, epithelial cells, endothelial cells, smooth muscle cells, Schwann cells).

The **main amino acids** of collagen are:

- glycine (33.5%)
- proline (12%)
- hydroxyproline (10%)

The amino acids, hydroxyproline and hydroxylysine are characteristic of collagen. Collagen is the only naturally occurring protein with both these amino-acids.

Tropocollagen molecules (280 nm long, 1.5 nm wide) form the basic unit, which polymerize to form collagen fibrils. The tropocollagen molecule consists of three linear twisted polypeptide chains (left-handed helices), which are further twisted to form a major right-handed helix. Two of the three polypeptide chains have similar amino acid composition, while the third is different.

At the ultrastructural level each collagen fibril shows a 64nm banding (periodicity), which is due to the stepwise overlapping arrangement of the rodlike tropocollagen subunits.

Collagen fibers consist of closely packed orderly fibrils and when seen in bundles (as in tendons, aponeuroses) appear white. In histological preparations after regular staining they are acidophilic (pink staining with eosin). Collagen fibers are flexible, but very inelastic with extremely high tensile strength.

Reticular fibers

Reticular fibers are very thin (diameters between 0.5 - 2 μ m) and are not visible in normal histological preparations after regular staining (H & E), however they can be visualized and stained black after impregnation with silver salts. This affinity for silver is called **argyrophilia**. Reticular fibers are also stained with the **PAS reaction** due to the high content of glycoproteins associated with the

fibers (6-12% hexoses as opposed to 1% in collagen fibers). It is now recognized that reticular fibers are a special form of collagen (Type III).

Reticular fibers form fine-meshed network around cells and cell groups

in diverse organs. They are abundant in lymphoid organs (lymph nodes, spleen), smooth muscle (in the sheath surrounding each myocyte), in endoneurium (connective tissue surrounding peripheral nerve fibers), and supporting epithelial cells of several glands (liver, endocrine glands).

Elastic fibers

Elastic fibers, as the name suggests, are highly elastic and stretch in response to tension. In particular they are formed from the protein **elastin**. The amino acid composition of elastin, similar to collagen, is rich in glycine and proline, but in addition has two unusual amino acids, **desmosine** and **isodesmosine**. Elastic fibers also have a high content of **valine**. Elastic fibers are very prominent in elastic tissues such as the elastic ligaments. When present in high concentration, the elastin imparts a yellow color to the tissue. The **elastic laminae of arterial blood vessel walls** are composed of a non-fibrillar form of elastin. Elastin can be stained in histological preparations using **orcein**.

CONNECTIVE TISSUE CELLS

Fibroblasts

Fibroblasts are the most common cell type found in connective tissue. 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. Abundant rough endoplasmic reticulum and active Golgi bodies are found in the cytoplasm.

Fibroblasts synthesize collagen, reticular and elastic fibers and the amorphous extracellular substance (including the glycosaminoglycans and glycoproteins).

Macrophages

Macrophages show pronounced **phagocytotic activity**. This can be demonstrated following injection of vital dyes such as trypan blue or Indian ink and the uptake of the particulate matter. Macrophages originate from

monocytes (from precursor cells in bone marrow), which migrate to connective tissue and differentiate into tissue macrophages. Today the various macrophages of the body are grouped in a common system called the **Mononuclear Phagocyte System (MPS)**. Today a wide range of macrophages are included in the MPS and include : **Kupffer cells** of the liver, **alveolar macrophages** of the lung, **osteoclasts**, **microglia** etc.

The main functions of macrophages are ingestion by **phagocytosis** of microorganisms (bacteria, viruses, fungi), parasites, particulate matter such as dust, 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).

Macrophages are normally long-lived and survive in the tissues for several months. In some cases where a foreign body (such as a small splinter) has penetrated the inner tissues of the body, several macrophages may fuse together to form multinuclear **foreign body giant cells**. These large cells accumulate at sites of invasion of the foreign body and sites of inflammation.

Mast cells

Mast cells are oval or round cells (20-30 μ m diameter) in connective tissue characterized by cytoplasm packed with large round **basophilic granules** (up to 2 μ m diameter). The **granules are stained metachromatically** (purple after toluidine blue staining). Two of the main components of mast cell granules are **histamine** and **heparin**. The granules of mast cells are released in inflammatory responses. Mast cells are abundant in loose connective tissue (especially adjacent to blood vessels), in the dermis, and in the lamina propria of the respiratory and digestive tracts.

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 (10-20 days) 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).

Leukocytes

The white blood corpuscles are commonly found in connective tissue. They migrate from the blood vessels to the connective tissue, especially to sites of injury or inflammation.

CLASSIFICATION OF CONNECTIVE TISSUE

The two main categories of connective tissue are:

- **Loose Connective Tissue**
- **Dense Connective Tissue**

Loose Connective Tissue

Loose connective tissue (**areolar tissue**) is the more common type. It fills the spaces between muscle fibers, surrounds blood and lymph vessels, is present in the serosal lining membranes (of the peritoneal, pleural and cardiac cavities), in the papillary layer of the dermis and in the lamina propria of the intestinal and respiratory tracts etc.

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 (such as in tendons) and relatively few cells.

Tendons

Tendons are the most common type of dense regular connective tissue.

Tendons connect skeletal muscles to bone. Owing to the dominance of the collagen fibers, the tendons have a white color (stains acidophilic in regular staining). The collagen bundles in tendons are arranged in bundles (primary bundles). Several primary bundles, each surrounded by loose connective tissue, are grouped into larger bundles (secondary bundles). The loose connective

tissue surrounding the primary and secondary bundles contains blood vessels and nerves. The whole tendon is surrounded by a denser connective tissue.

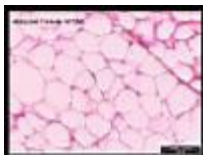
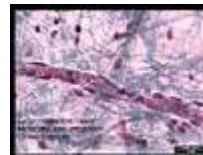
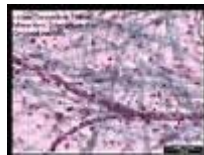
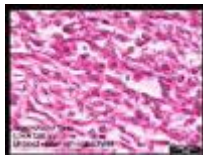
Each primary bundle has orderly-arranged rows of **fibrocytes**, when seen in longitudinal section. These fibrocytes have relatively little cytoplasm. Between the rows of fibrocytes, the collagen bundles are closely packed and arranged also in a longitudinal direction.

Ligaments

Ligaments are a special type of dense regular connective tissue that connects bones to bones. 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. The elastic fibers are stained a dark brown-red with orcein. Elastic fibers provide the ligament with remarkable elasticity (in contrast to tendons).

Mucous tissue

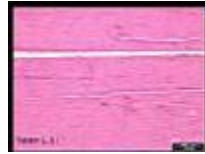
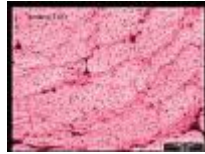
This is found in the umbilical cord (Wharton's jelly). It is a loose connective tissue composed of fibroblasts with several long cytoplasmic processes. The intercellular space is filled with a jelly-like amorphous ground substance, rich in hyaluronic acid and fibers.



Tissue
Mesenchymal Cells
Adipose Tissue-White

Loose Connective Tissue

Loose Connective

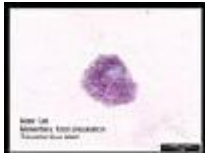
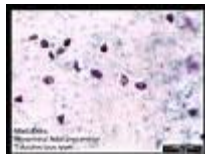


LS

Adipose Tissue-Brown
Ligamentum nuchae-TS

Tendon-TS

Tendon-

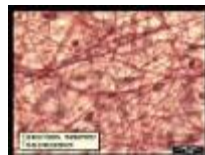


Cells

Ligamentum nuchae-LS
Mast Cells

Mast Cells

Mast



Mucous Connective Tissue

Adipose Cell

Elastic Fibers - Mesentery

Up 

 Back to lecture notes.



