Chapter 4
General Connective Tissues

Connective tissues are a diverse class of tissues including bone, blood, cartilage, adipose, and areolar Connective tissues. The types of connective tissues are classified based on the relative proportions of three components: ground substance, fibers, and cells. The ground substance and fibers are the extracellular components of the Connective tissues and make up the Matrix.

4.1. The Ground Substance of the Matrix

The ground substance functions as a molecular sieve. It facilitates the diffusion of metabolites between the blood and the tissues. It acts as a physical barrier to prevent the spread of large particles such as bacteria and other pathogens. Ground substance is an amorphous, viscous gel. It is produced primarily by a connective tissue cell called the Fibroblast. Fibroblasts are derived from embryonic mesenchyme (as are most c.t. cells).

4.1.1. Components of Ground Substance

1) water, 2) salts such as calcium phosphate and 3) glycosaminoglycans (GAGs). The particular type of GAGs present in a particular c.t vary in occurrence and proportion. Some types are: Hyaluronic Acid is the most common and largest type and Sulfated Proteoglycans is a class of GAG consisting of a sulfated gycosaminoglycan chain covalently bound to a core protein. There are four major classes: chondroitin sulfate, dermatin sulfate, keratin sulfate and heparin sulfate. GAGs have several functions:

1. They contribute to the viscosity of ground substance. This acts as a barrier to the spread of pathogens following tissue injuries.
2. They provide structural support to c.t.s
3. They act as a medium for the diffusion of nutrient and gases. They exert a direct influence on the surrounding cells. This is especially true during the development of cells.

A hyaluronic rich matrix is especially suitable for cell migration and proliferation. It may also prevent precocious differentiation. Specific interactions between the surface receptors of cells and GAGs may play a role in the regulation of cellular functions.

4.1.2. Structural Proteins

Structural proteins serve to bind the c.t. cells to the surrounding collagen fibers of the matrix. Some structural proteins are:

a] Fibronectin can be considered to be a cell matrix ligand since it promotes the attachment of c.t cells (especially fibroblasts) to collagen fibers. It also plays a role in other processes such as cell migration, cell differentiation, phagocytosis, and chemotaxis. It also directly influences the cytoskeletal organization of c.t. cells which can change their shapes and/or their functions.

b] Laminin is associated with the basement membrane where it is a specific

attachment protein for epithelial cells to the type IV collagen of the basement membrane.
c] Chondronectin promotes the attachment of cartilage cells to collagen.

4. 2. The Fibrous Component of the Matrix

Connective tissue fibers provide general support for other tissues. Ex; c.t. fibers form a dense supporting framework in the integument. In hollow organs and blood vessels which expand and contract c.t. fibers allow for flexibility. Three types of fibers are found in c.t.s: collagen, reticular, and elastic fibers. The density, proportion, arrangement, and occurrence of each type vary depending on the functional requirement of the tissue.

4.2.1. Collagen Fibers

Collagen fibers are the most abundant and strongest of the three classes.
Collagen is found in all types of c.t. in varying degrees. Collagen has a tensile strength greater than does a similar sized strand of steel. So it adds strength to the tissue and will decrease the effects of mechanical forces on the tissue. Collagen is a protein polymer composed of monomeric units of the protein Tropocollagen. Tropocollagen is produced by the fibroblasts typically. Although it is made by osteoblasts in bone and by chondroblasts in cartilage. Collagen gets it's strength from it's structural arrangement. Collagen is arranged into microfibrils. Microfibrils are arranged into fibrils. Fibrils are grouped into a fiber. Fibers are grouped into a collagen bundle. There are five identified molecular types of collagen:
1] Type I Collagen - is the most abundant and widespread type.
2] Type II Collagen - is found in cartilage and in certain tissues of the eye.
3] Type III Collagen - is found in the c.t. components of the skin, G.I. tract, cardiovascular system, and uterus. Type III collagen is often found in association with reticular fibers.
4] Type IV Collagen - is found in the basement membrane.
5) Type V Collagen - is found primarily in fetal tissues although vestigial amounts remain in the adult.

4.2.2. Reticular Fibers

Reticular fibers are actually thin collagen fibers arranged into delicate networks, not into bundles. They form a delicate supporting network around individual cells of many tissues and organs. Ex; hemopoietic organs. Reticular fibers also are a significant portion of the reticular lamina of the basement membrane.

4.2.3. Elastic Fibers

Elastic fibers are composed of the protein Elastin. Elastin gives these fibers the ability to stretch. However, elastic fibers are not as strong as are collagen fibers. Elastic fibers are fond in most fibrous c.t. but are most abundant in those tissues requiring flexibility. Ex; trachea, elastic arteries, skin. and uterus.

4.3. The Cells of the Connective Tissue Proper

The cells of the c.t. proper can be divided into two groups: permanent and transient cells. Permanent cells can be thought of as being involved with the long term maintenance of the c.t. They include: mesenchymal cell, fibroblasts, and adipocytes. Transient cells can be thought as being involved with short term events such as a reaction to an injury or to an invasion by pathogens. They include macrophages, mast cells, plasma cells and cells that invade from the blood stream such as neutrophils, eosinophils, monocytes, and

lymphocytes.

4.3.1. Permanent Cells

a) Fibroblasts and Fibrocytes

Fibroblasts are immature c.t. cells which will mature into fibrocytes. As is typical for immature connective tissue cells, fibroblasts are responsible for producing at least some of the organic component of the matrix. They produce all three fiber types as well as the ground substance. Fibroblasts are widely distributed cells. Their appearance may vary but overall they are long, tapered cells with thin, flat nuclei. They are often found in association with collagen bundles. Fibrocytes are mature fibroblasts. They are less active than are fibroblasts. They may help to maintain the c.t. by aiding in it's repair. They are similar in appearance to fibroblasts. One difference is that they have fewer cytoplasmic granules.

b) Mesenchymal Cells (aka; pericytes, perivascular cells)

Mesenchymal cells are less widely distributed than are fibroblasts. They are often found in association with blood vessels (hence the names pericytes and perivascular cells). Mesenchymal cells are not very differentiated. They retain the multipolarity of embryonic mesenchyme cells which can develop into other c.t. cell types during gestation. As a result, mesenchymal cells can develop into other cell types under the appropriate conditions. They can develop into a variety of c.t. cell types, including adipocytes and mast cells, and can even develop into smooth muscle cells. Mesenchymal cells are similar in appearance to fibroblast but they can easily be distinguished by their stellate shape.

c) Adipocytes

Adipocytes are specialized for the synthesis and storage of lipid. They may occur singly but more often in groups throughout loose connective tissues. Loose connective tissues having a high density of adipocytes are called Adipose Tissue. Adipocytes will alternately store fat and become depleted. Lipid deposition and mobilization is controlled by neuroendocrine secretions and by the organism's nutritional state. The pattern of lipid is storage differs between the two classes of adipose tissue. In white fat tissue the lipid is stored in a single, large droplet described as Unilocular. This gives the adipocyte it's classic "signet ring" appearance when full. In brown fat tissue the lipid is stored in several smaller vesicles. This pattern is termed Multilocular. Brown fat is a specialized type of adipose tissue. It is thermogenic in that it can convert stored energy (in the lipid) into heat. Brown fat is found in some mammal species (especially in hibernating species). It is found in humans only in the fetus and the neonate. The size of adipose tissue reflects the number of adipocytes present and their size. Adipose tissue demonstrates two patterns of growth: a} Hyperplastic Growth - adipocyte precursors proliferate for a limited period postnatally. b} Hypertrophic Growth - change in the size of adipocytes due to lipid accumulation. Hypertrophic growth, and it's reversal, can occur throughout an individual's lifetime. The result is that both the size and the number of adipocytes can be influenced during the postnatal period but influences occurring laterin life affect only cell size.

4.3.2. Some of the Transient Cells

a) Mast Cells

Mast cells are widely distributed throughout the connective tissues. They are usually

found in close association with blood vessels. They are particularly numerous in sites close to the outside of the body (i.e.; the dermis). Mast cells are very similar in appearance to basophils and share certain similar functions and products with these white blood cells. This is the reason why it was once incorrectly believed that mast cells were derived from basophils which had migrated into the c.t. from the blood stream. Mast cells are involved in the immune response mechanism of the body. In particular they play a role in the inflammation reaction and produce a variety of chemicals which promote it: a} histamine to increase vascular permeability
b} eosinophil chemotaxic factor to attract eosinophils which will phagocytosize certain pathogens and trigger the reverse of the inflammation response. c} prostaglandins to increase edema d} heparin which serves as an anticoagulant e} and a number of enzymes which degrade various c.t. components.

b) Lymphocytes

Lymphocytes are found in small numbers throughout the connective tissues where they perform much of their immunological functions. They are generally more abundant in the specialized loose connective tissues of the alimentary canal and respiratory tract called the Lamina Propria. In these passageways there is contact with the external environment and so a greater need for protection of the underlying tissues from pathogenic invasion. Lymphocytes will commonly penetrate the epithelium to perform their functions. Lymphocytes of the connective tissues are similar in appearance to what they look like in the blood stream: a cell having a prominent nucleus and little basophilic cytoplasm around it. It is very difficult to differentiate between B and T lymphocytes under the light microscope.

c) Plasma Cells

Plasma cells are actually antibody secreting B lymphocytes. Plasma cells are widely dispersed throughout the connective tissues. They are particularly abundant in the lamina propria of the alimentary canal and respiratory passageways. They are also found in the lymphoid organs. They are rarely found in the blood. Plasma cells are unlike other lymphocytes in appearance. They look more like basophilically staining fibroblasts being flat, tapered cells. The plasma cell nucleus is pinwheel shaped.

d) Macrophages

Macrophages are long-lived, highly mobile, phagocytic cells found throughout the c.t.s of the body. Macrophages are derived from the monocyte class of leucocyte which have migrated into the c.t. from circulation. Macrophages move about by means of a special type of ameboid movement called Diapedesis. This allows them to travel to the site of the infection. Macrophages are similar in appearance to mast cells in the both possess prominent cytoplasmic granules. They can be differentiated by staining and, when present, by pseudopodia which are found only in macrophages. The cytoplasmic granules of the macrophage contain a variety of substances: Some contain digestive enzymes to facilitate phagocytosis. These include lysosomes. Some produce immunoregulatory substances as well as a vast array of unrelated substances such as interferon, lysozyme, prostaglandins, peroxide, and growth factors.

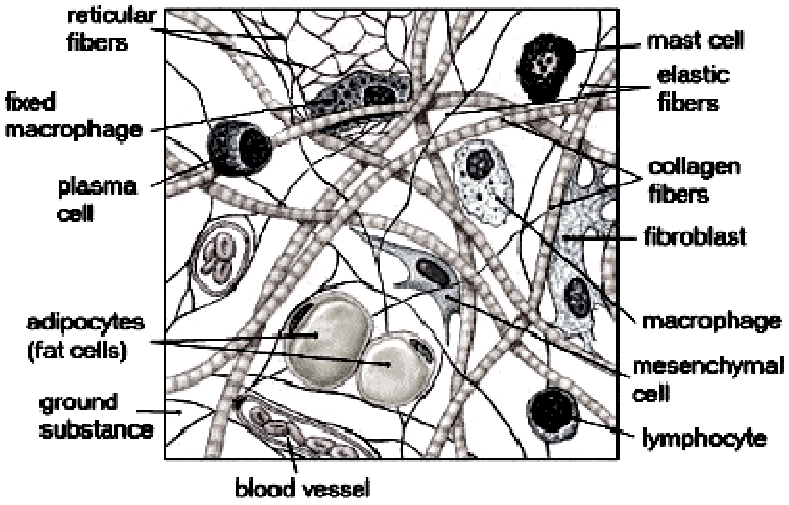

Fig.4.1. Connective Tissues

4.4. Classification of Connective Tissues

4.4.1. The Embryonic Connective Tissues

(a) Mesenchymal Connective Tissue

Mesenchyme fills the spaces between developing organs and is largely composed of mesenchymal cells and a fluid ground substance. Mesenchymal cells are stellate shaped and multipotent being able to give rise to all of the other connective tissue cell types. Mesenchyme will give rise to all of the adult connective tissue types. As development proceeds, the formation of various fibers, the formation of various cell types, and the formation of a relationship between fibers and cell types eventually yields an adult connective tissue.

(b) Mucus Connective Tissue

Mucus connective tissue is similar to mesenchymal connective tissue except that it contains collagen fibers and a more viscous ground substance. It develops from mesenchyme. Mucus connective tissue is typified by Wharton's Jelly of the umbilical cord. Mature connective tissues are classified based on: 1) relative density of fibers (i.e.: loose vs, dense c.t.s). 2) predominant cell type (ex; adipose tissue). 3) predominant fiber type if that is other than collagen (ex; elastic c.t.).

The Loose Connective Tissues - have a high cell content and a relatively low fiber content. Areolar connective tissue is widely distributed throughout the body. It is the most common type of loose c.t by far. It is the class of c.t. supporting the epithelia. It composes the stroma of various organs and glands. In certain organs and glands the areolar c.t. will also form septa which will divide the structure into lobes and/or lobules. It makes up some of the superficial fascia and dermis. These connective tissues Function in: 1] acting as a barrier to infection (up to a point). 2] cushioning the body (up to a point) and 3] allowing for the passage of nerves, blood vessels, and lymph vessels

4.4.2. Adipose Tissue

Adipose tissue is a loose c.t. with adipocytes as the predominant cell type. Adipose is found in a variety of places such as: 1] the hypodermis. 2] surrounding and protecting certain organs and 3] the medullary cavity of long bones. Adipose tissue Functions in: 1]

storing energy, 2] insulates the body form heat loss and 3] cushions the body and protects delicate organs (ex; the kidney) from mechanical trauma.

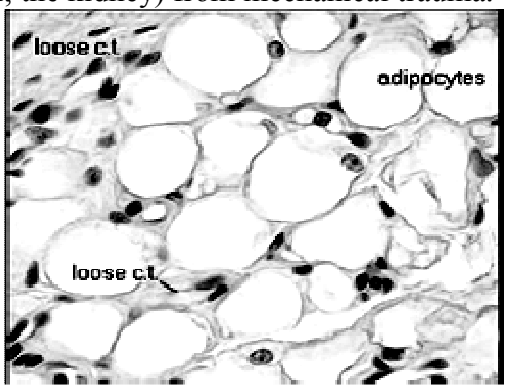

Fig.4.2. Adipose Tissue

4.4.3.Reticular Connective Tissue

Reticular is a loose c.t. where reticular fibers are the predominant fiber type. The reticular fibers form a delicate, supportive, framework. Associated with these reticular fibers are Reticular Cells/Reticulocytes which maintain the fibers and can also perform phagocytic functions. Reticular tissue is found in areas such as the inner stroma of many solid organs, the inner stroma of the lymphoid organs and the inner stroma of hemopoietic tissues such as red marrow

i) The Dense Connective Tissues - have a high fiber content and a relatively low cell content.

1) Irregular Dense/ Dense Irregular Connective Tissue

This class of dense connective tissue has a random weave of fibers and very few cells. Collagen makes up the vast bulk, or often all, of the fibers. Fibroblasts and fibrocytes are the most common cell types. Dense irregular connective tissue is found in areas such as: the sheaths of tendons and nerves, the capsules of organs, and the dermis. It is found in areas subject to stress from a number of directions or that need a protective barrier.

2) Regular Dense/ Dense Regular Connective Tissue

This class of dense connective tissue has a regular, repeating pattern of fibers and very few cells. Collagen also makes up the vast bulk, or often all, of the fibers. Fibroblasts and fibrocytes also are the most common cell types. Dense regular connective tissue is a flexible tissue with a great resistance to mechanical forces. The parallel arrangement of it's fibers gives a great deal of strength in one direction. So it is found in structures that must be able to resist a great deal of stress but primarily from one direction such as tendons and ligaments.

ii) Elastic Connective Tissue

Elastic tissue is a dense connective tissue where the predominant fiber type is the elastic fiber. It is found in areas that must be able to deal with a high degree of mechanical stress but also be highly resilient. Ex; elastic cartilage and elastic arteries.