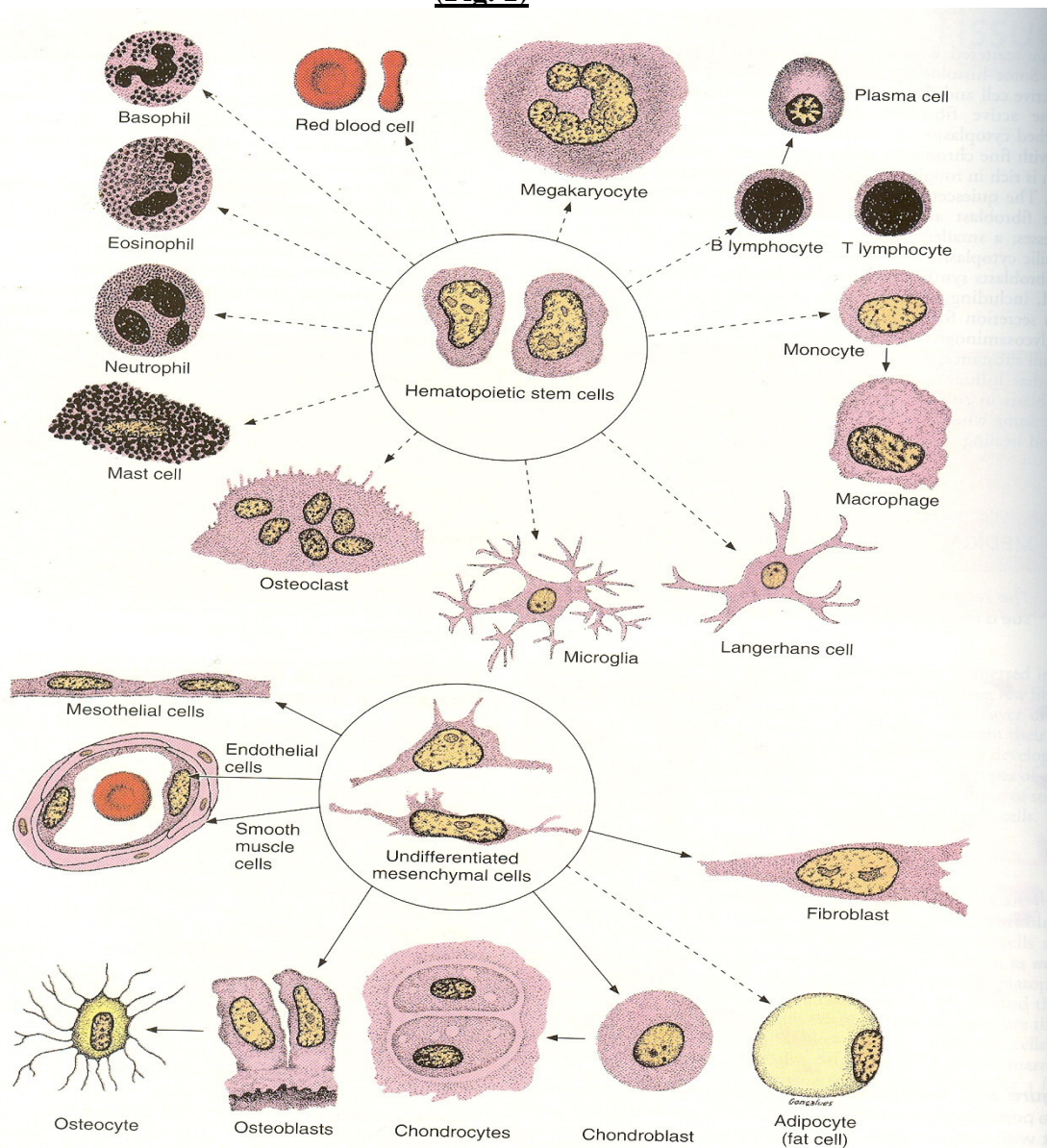


The Connective/Supporting Tissue

The connective tissue is an assemblage of specialized supportive cells in a gel-like extracellular matrix of organic material and fibres in which the extracellular materials predominate. It is mesenchymal in origin. Its principal function is provision of structural and metabolic support for other body tissues and organs. It also facilitates exchange of materials including nutrients and wastes between these body component parts. The connective tissue is also implicated in storage, defense, packaging, maintenance of shape of organs, regulation of body temperature and repair of damaged tissues.

(Fig. 1)



Lineages of connective tissue cells. This simplified representation of the connective tissue cell lineage include cells from the multipotential embryonic **mesenchyme cells** and **hematopoietic stem cells** of bone marrow. Dotted arrows indicate that one or more intermediate cell types exist between the examples illustrated. The cells are not drawn in proportion to actual sizes, eg, adipocyte, megakaryocyte, and osteoclast cells are significantly larger than the other cells illustrated.

CELLS OF THE CONNECTIVE TISSUE (Fig. 1)

Most cells of the connective tissue are mesenchymal in origin. Others are derived from the hematopoietic stem cell. These cells are divided into several types based on their functions and localization in the body.

The commonest and most widely distributed cell of the connective tissue is the **Fibroblast (Fibrocyte)**. Other cell types include:

- Adipocytes of the adipose (Fat) tissue
- Reticular cell of the parenchyma of organs
- Osteocytes of the bone
- Chondrocyte of the cartilage
- Myofibroblast of the muscle
- Mast cells, Plasma cells, Leucocytes and Macrophages of the defense and immune system.

Ground Substance

This is the amorphous, transparent, gel-like material of the connective tissue. It serves as the medium through which materials are exchanged within the connective tissue and with the circulatory system. It is composed of a mixture of complex linear polysaccharide molecules (Formed from repeated disaccharide units) called **Glucosaminoglycan**, the most abundant of which is **Hyaluronic acid**. This is also the only GAG which has no sulphate side group.

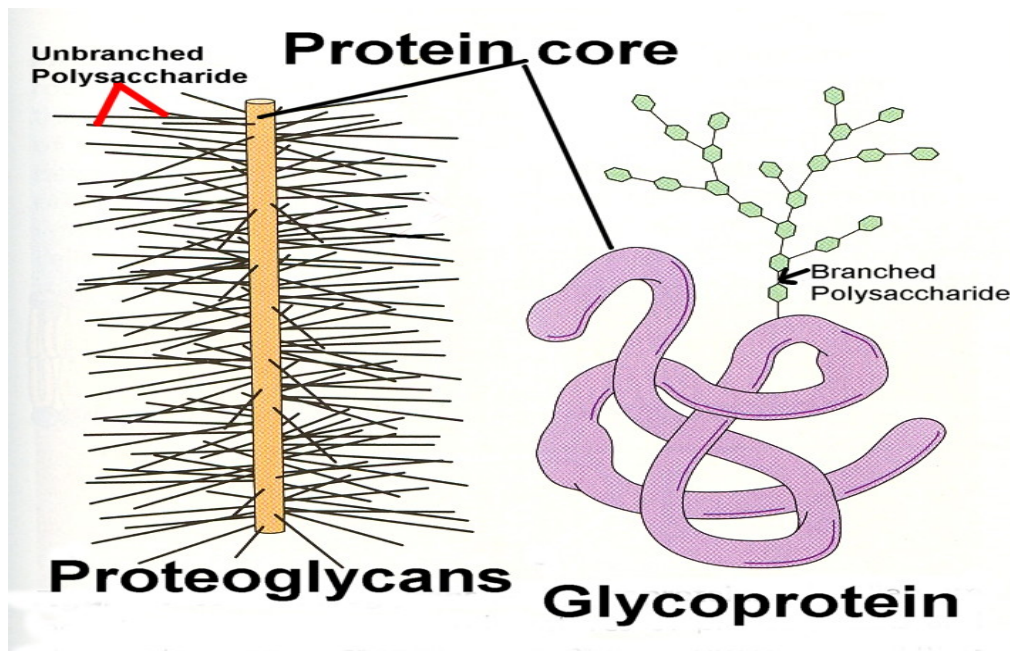
GAG with sulphate side groups include:

- Chondroitin-4-sulphate
- Chondroitin-6-sulphate
- Dermatan sulphate
- Heparin sulphate
- Heparan sulphate and
- Keratan sulphate

GAGs are all acidophilic and hydrophilic hence highly attracted to positive ions, such as sodium and water in the extracellular space.

Proteoglycans are another component part of the ground substance. These are formed by covalent bonding of proteins to the sulphate side groups of GAGs (Protein + GAG). The mechanical properties of the ground substance are further reinforced by structural **Glycoproteins** which are also found in the ground substance. Glycoproteins are formed by the binding of proteins to branched polysaccharide molecules.

In view of its high viscosity, the ground substance also serves as lubricants and barrier to the penetration of invaders.



Fibres of the Ground Substance

The fibre components of the supportive tissue are formed from polymerized elongated proteins and confer tensile strength and resilience on the tissue. Two main types of fibres are encountered in the connective tissue, viz. collagen and elastic fibres.

Collagen Fibres

Collagen is further subdivided into collagen and reticular fibres based on the morphology and organization of the fibres.

Collagen fibres are the commonest and most widely distributed fibres of the connective tissue. Collagen is formed from a precursor molecule called tropocollagen (3 polypeptide chain molecule) and consists of 27 different types. Five of these which are commonly encountered are:

- Type I: The fibrils of this type are often organized into thick bundles. They are found in: Dermis of the skin, Bone, Tendons and Ligaments
- Type II: This consist of fine fibrils and are confined to the cartilage
- Type III: This is the reticular fibre and is distributed in the highly cellular organs such as the liver, spleen, lymphoid tissue and bone marrow. It is secreted by reticular cells
- Type IV: This is often arranged in a meshwork and is found in the basement membrane.
- Type VII: This forms the anchoring fibres linking up the basement membrane to the surrounding connective tissue.

Clinical Correlates

Diseases associated with collagen fibres include:

- Ehler-Danlos Type IV, which is associated with Type III fibres and could lead to aortic/intestinal rupture
- Ehler-Danlos Type VI, which is associated with faulty lysine hydroxylation and affects the skin and eyeballs
- Ehler-Danlos Type VII, which is associated with collagen fibres and often lead to joint dislocation.
- Osteogenesis Imperfecta, which is linked to collagen type I and might lead to spontaneous bone fracture and cardiac insufficiency.

Elastic Fibres

Elastic fibre is synthesized principally from microfibril of the glycoprotein **Fibrillin** and the protein **Elastin**. Its fibres are thinner than collagen fibres and are organized in sparse network interspersed with collagen bundles. Elastic fibres are mainly distributed into highly resilient organs which are subject to bending and stretching. Elastic fibres are also organized into fenestrated sheet in the walls of large blood vessels.

Clinical Correlates

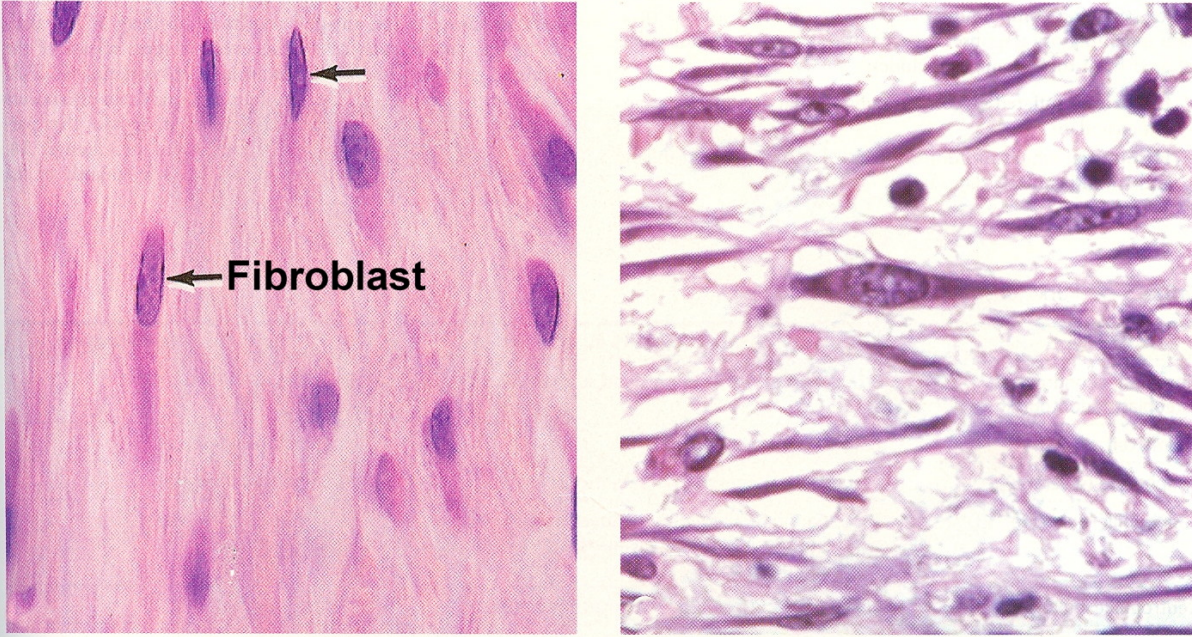
Marfan syndrome is an elastic fibres disease characterized by loss of arterial wall resistance resulting in arterial rupture affecting large vessels

TYPES OF CONNECTIVE TISSUES

The connective tissue occurs in various forms in the human body. Its distribution within the body is based on its major component, characteristic features and functional requirement of the location where it is found; Connective tissue types include:

1. **Loose Connective Tissue (Areolar Tissue):** This tissue contains all the component parts of connective in almost equal amounts. It has a delicate consistency, highly flexible and vascularised and offers minimum resistance to stress. It is extensively distributed around most organs and structures of the body.
2. **Dense Connective Tissue:** This tissue type is densely packed with much fewer cells than loose connective tissue. There is also a predominance of collagen fibres over ground substance. It is also more resistant to stress and less flexible than loose connective tissue. Dense connective tissue is classified into two types viz. **Dense Regular** connective tissue in which the collagen bundle are organized in linear orientation to the long axis of the elongated fibroblasts (as in Tendons and Ligaments) and **Dense Irregular** connective tissue which is devoid of definite pattern of orientation of collagen fibres (Haphazard arrangement). Irregular dense connective tissue is commonly found in association with loose connective tissue

Dense Regular Connective Tissue Loose Connective Tissue



OTHER TYPES OF CONNECTIVE TISSUES

BONE TISSUE

Bone is specialized connective tissue composed of mineralized matrix called bone matrix and three different cell types viz.

- Osteocytes – These are involved in bone formation and nutrition. They are located in the lacunae within the matrix.
- Osteoblast – Matrix (Osteoid) forming and mineralizing cell.
- Osteoclast – This is a giant multinucleated cell that is involved in resorption and modeling of bone. It is a derivative of the haemopoietic cell line.

In view of the high viscosity of bone matrix, metabolites are transported to the lacunae through canaliculi connected to the lacunae. Bone also serves as a storage site for calcium, phosphate and other ions such as magnesium, potassium and sodium. Apart from these functions, bone also:

- Forms the skeletal framework of the human body
- Forms attachment sites for muscle.
- Facilitates locomotion
- Protects several body organs

CARTILAGE TISSUE

Cartilage is a highly specialized connective tissue which is adapted to bear mechanical stress without permanent distortion of its structure. Its ground substance is heavily laden with Proteoglycans and Glucosaminoglycan molecules mingled with collagen and elastic fibres in varying proportions based on local biomechanical needs of the organs in which it is located. Interactions between these molecules in the matrix

confer a firm, gel-like consistency on cartilage tissue. Small amounts of glycoproteins are also accommodated in cartilage matrix. Within the matrix are lacunae which accommodate cartilage cells called **Chondrocytes**. These cells are derived from **Chondroblasts** which are responsible for synthesis and deposition of cartilage matrix. Chondroblasts are found in the **Perichondrium** of matured cartilage.

Classification of Cartilage:

Cartilage is classified based on the proportions in which the compositions of its matrix are present in the cartilage and on functional requirements in the location of the cartilage. Thus we have:

1. Hyaline cartilage in which type II collagen is the prominent fibre. (articular heads of bones)
2. Elastic cartilage with abundance of elastic fibre. (lower respiratory passage)
3. Fibrocartilage with an abundance of type I collagen. (intervertebral discs)

Cartilage is an avascular connective tissue receiving its blood supply by diffusion from the Perichondrium and Synovial fluid of the joint space. It is also devoid of lymphatic and nerve supplies.

Cartilage Functions include:

- Provision of support for soft tissues of the body
- Facilitates joint mobility
- Facilitates locomotion
- Involved in development and growth of long bones

MUCOUS TISSUE

This is composed principally of ground substance in which Hyaluronic acid predominates. It also contains very few collagen fibres and scattered fibroblasts. Its distribution is limited to the umbilical cord (Wharton's jelly), embryonic tissue and the pulp cavity of young teeth.

ADIPOSE TISSUE

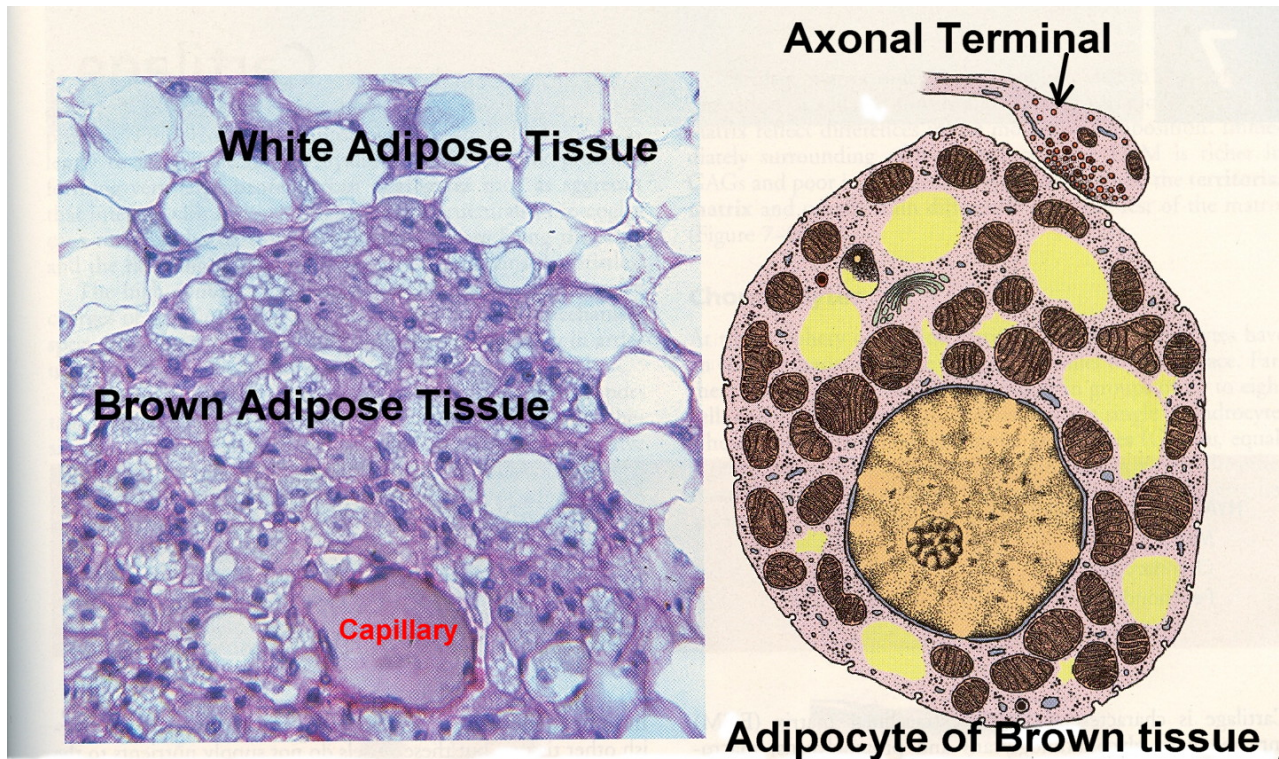
Adipose tissue is composed mainly of adipocytes and loose connective tissue. The adipocytes of adipose tissue synthesizes triglycerides from glucose and receives triglycerides from the liver and chylomicron from the blood stream. Adipocyte also secretes several proteins called **adipocytokines** which are implicated in endocrine functions. Adipose tissue is widely distributed in the body where it serves the following functions:

- Padding and insulation of tissues and organs
- Thermoregulation
- Shock absorption beneath the skin
- Determining shape and form of body parts and the body as a whole
- Energy storage
- Modulation of body metabolism
- Endocrine function

Based on location, structure, color and pathological characteristics, adipose tissue is classified into two types. These are:

1. White adipose tissue in which the developed adipocyte contain a large central droplet of whitish yellow fat and
2. Brown Adipose tissue (Brown Fat) in which the mature adipocyte contains several droplet of fat amidst a part of mitochondria. The cytochrome content of mitochondria is responsible for the color of

the tissue. The main function of this tissue is heat production. Adipocytes of this tissue receives direct sympathetic innervation



Clinical Correlates

- Obesity is excessive accumulation of white adipose tissue
- The chronic mild inflammation associated with obesity has been linked to the proinflammatory cytokines secreted by adipocytes of white adipose tissue
- The proinflammatory cytokine may also be responsible for the diabetes and heart diseases associated with obesity.
- Adipose tissue account for 15-20% of total body weight in the male and 20-25% in the female
- Triglycerides which are of lower density compared to glycogen yield more calories than glycogen (9.3kcal/g – 4.1kcal/g). This makes fat a more efficient energy storage molecule than carbohydrate.