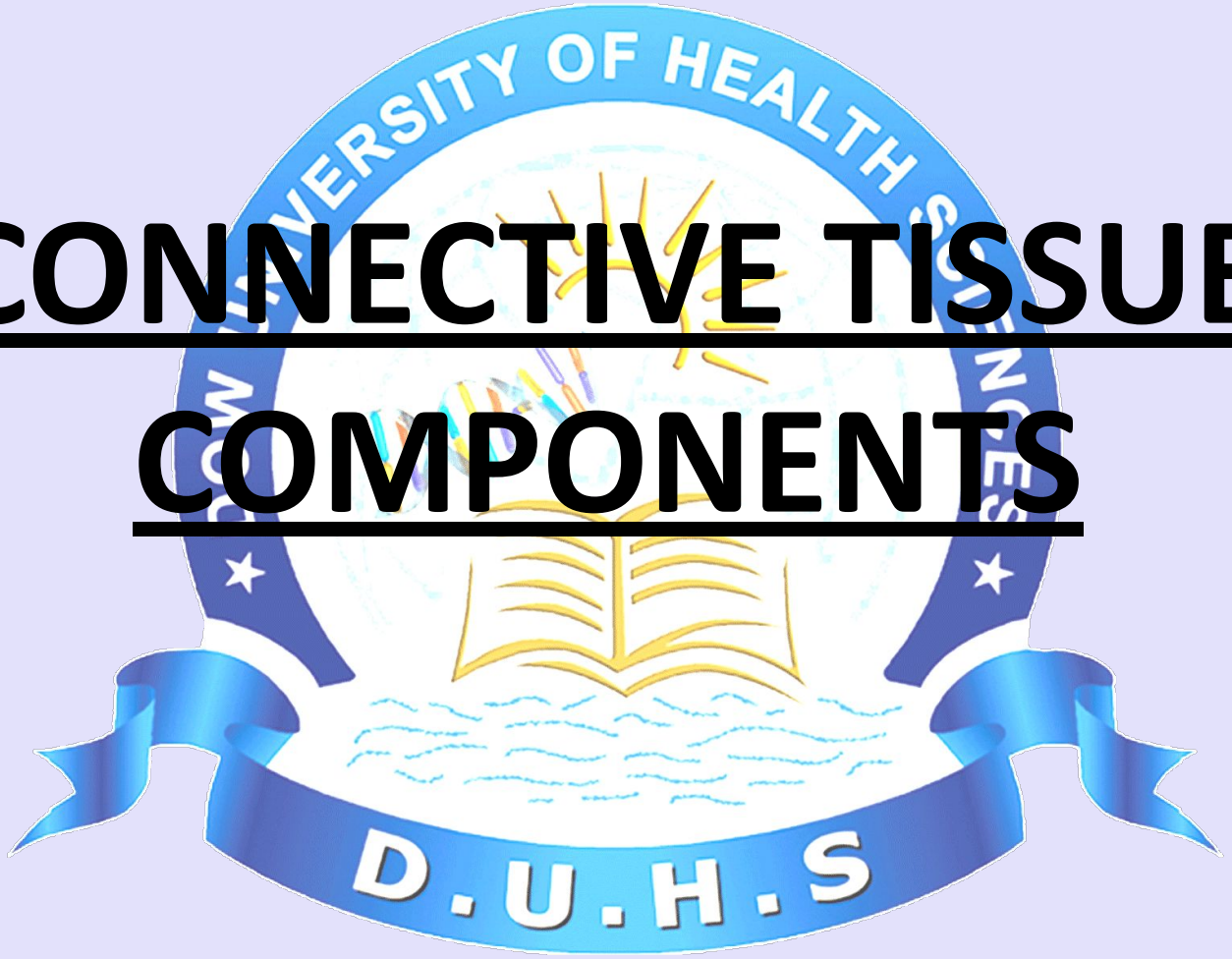
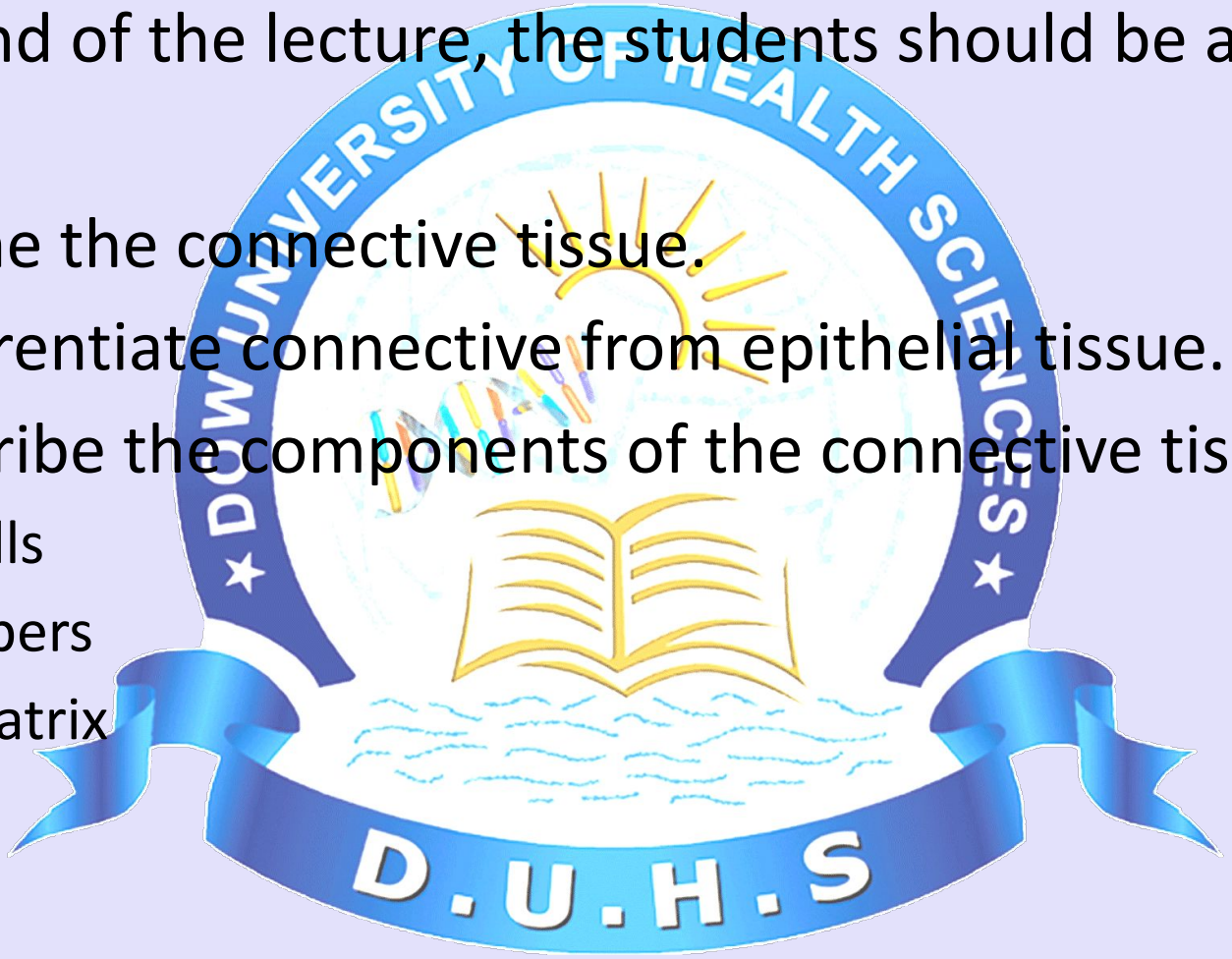
CONNECTIVE TISSUE COMPONENTS



LEARNING OBJECTIVES

At the end of the lecture, the students should be able to:

- Define the connective tissue.
- Differentiate connective from epithelial tissue.
- Describe the components of the connective tissue.
  - Cells
  - Fibers
  - Matrix



DEFINITION
CONNECTIVE TISSUE (CT)

A material made up of matrix, forming a framework and supports body tissues and organs.

- It is derived largely from embryonic mesoderm.
- It is characterized by the presence of relatively fewer cells and a large amount of intercellular substance, called "matrix."
- Matrix binds the cells & organs and ultimately gives mechanical support to the body.
- Unlike the other basic tissues (epithelium, muscle and nerve, which are formed mainly by the cells,) the major constituent of CT is **MATRIX**.

DIFFERENCE B/W CONNECTIVE AND EPITHELIAL TISSUE

- Epithelial tissues are tightly packed sheets of cells that are the covering/lining for every surface in the body.
- They protect the body (like skin), absorb nutrients and secrete fluids (ie. sweat, mucus, oil).
- They are not used to connect any part of the body to anything else.
- They also are the lining for many other organs.

- Connective tissues are used to connect tissues and organs to each other.
- Adipose, a connective tissue, connects the epidermis to the underlying tissues.
- They are not tightly packed.
- There are six different connective tissues: Blood, Bone, Adipose (Fat), Cartilage and loose connective tissue.

BASIC COMPONENTS of CONNECTIVE TISSUE

Basically all types of CT consist of 3 components:

A. Cells.
B. Fibers.
C. Matrix

Fibers and ground substance are collectively known as **MATRIX.**

GROUND SUBSTANCE: It is a colloidal gel-like material, in which cells & fibers are embedded. It is composed of proteoglycan, glycoprotein, water & salts.

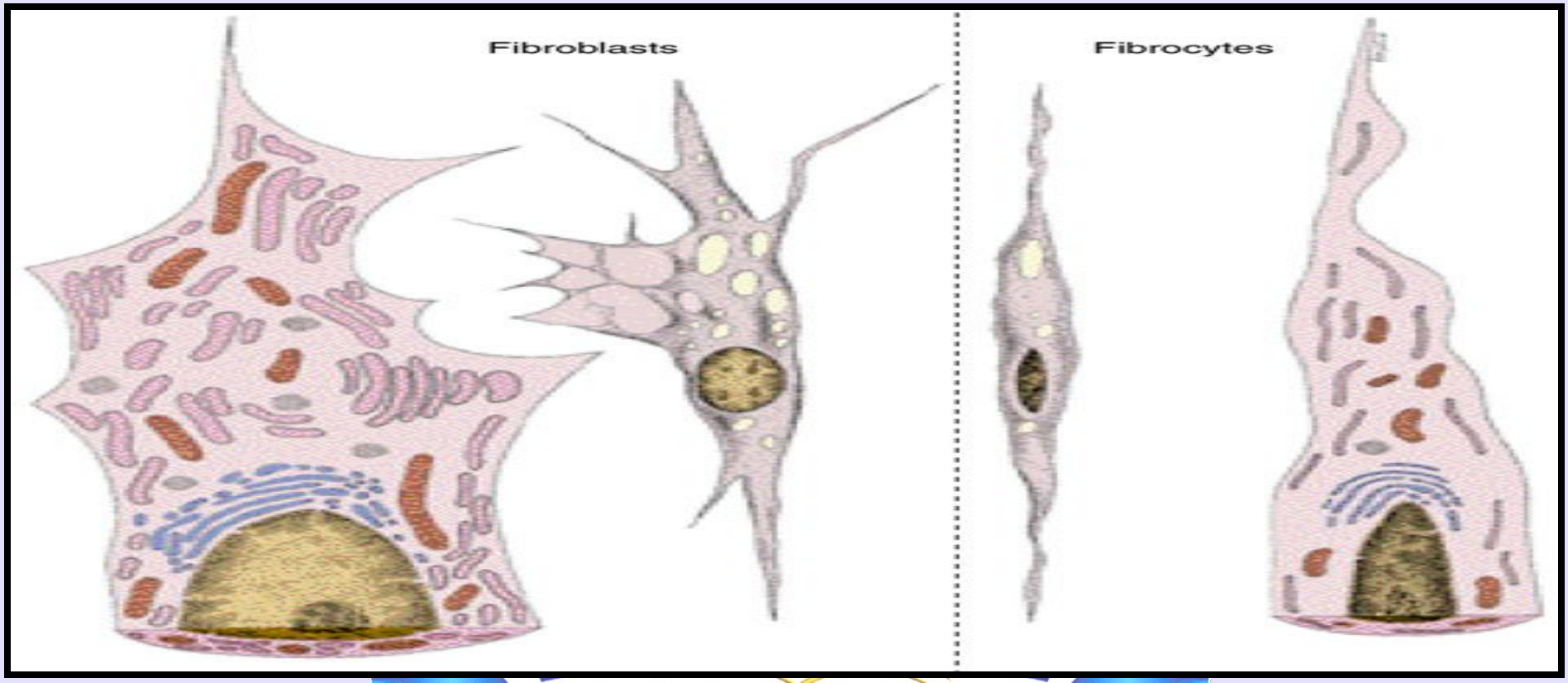
CELLS OF CONNECTIVE TISSUE

1. Fibroblasts.
2. Histiocytes (Macrophages).
3. Plasma cells.
4. Mast cells.
5. Fat cells.
6. Visitors or Wandering cells, (include Neutrophils, Eosinophils, Basophils, & Lymphocytes).

FIBROBLASTS

- Most abundant variety of CT cells.
- They produce CT fibers (hence the name fibroblast).
- Also secrete the ground substance of CT.
- Large, somewhat flattened, roughly ovoid cells with branching processes, but their appearance varies in relation to the functional state of the cell.
- Two stages of activity i.e.
- Inactive or quiescent cells are called "Fibrocytes".
- Active cells are called "Fibroblasts".

FIBROBLASTS



Active (left) and quiescent (right) fibroblasts.

Fibroblasts that are actively engaged in synthesis are richer in mitochondria, lipid droplets, Golgi complex, and rough endoplasmic reticulum than are quiescent fibroblasts (fibrocytes).

HISTIOCYTES (MACROPHAGES)

- They are characterized by an irregular surface with short & blunt processes.
- Cytoplasm appear filled with granules & vacuoles, containing ingested material.
- Usually have eccentric oval nuclei.
- Size range from 10 to 30 µm.
- They are long living cells, may survive for months.
- **FOUND** :in
- 1. Loose areolar CT.
- 2. Richly vascularized area of the body.
- 3. Most organs, and constitute "mononuclear phagocytes system".

HISTIOCYTES

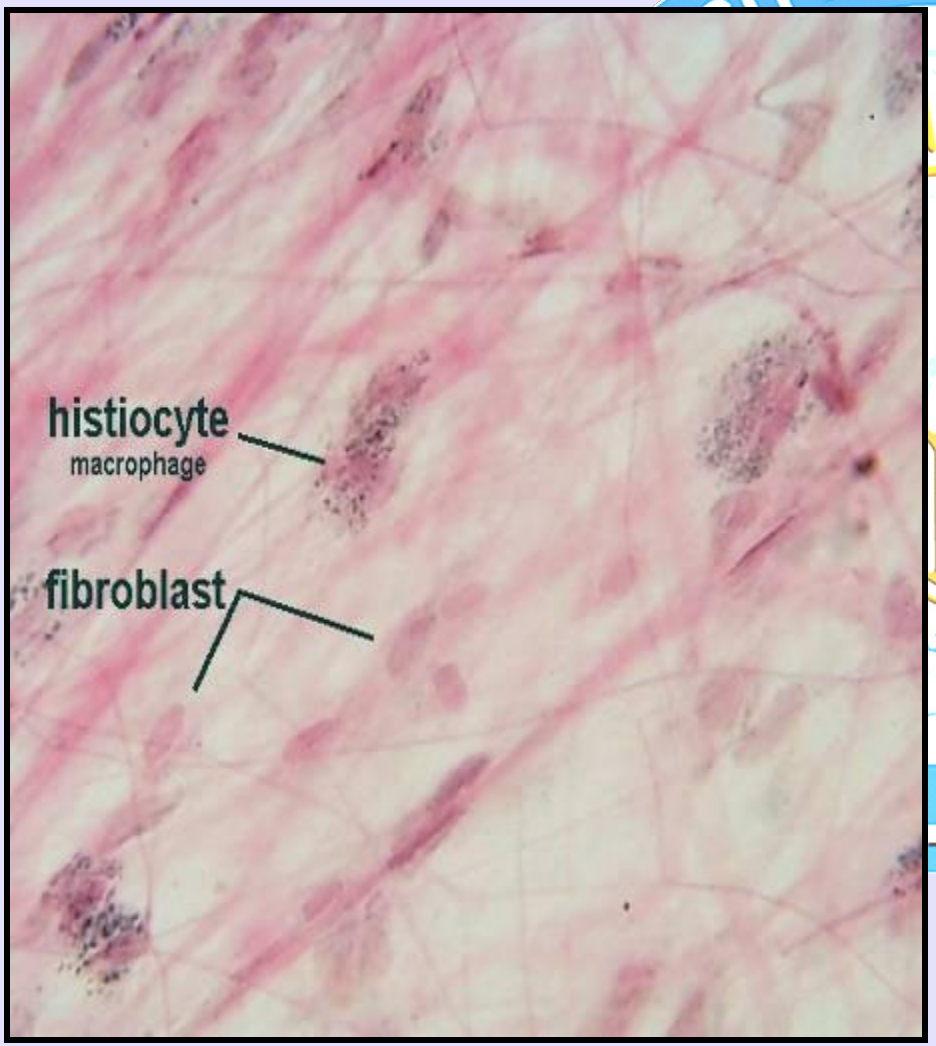
In certain regions of body, macrophages have special names, eg.

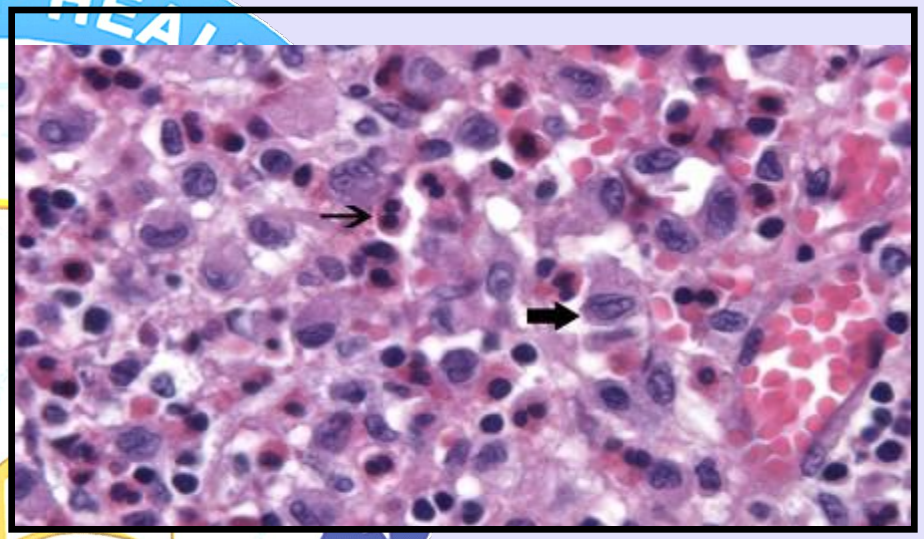
- 1. In Liver ------ Kupffer cells.
- 2. In CNS ------- Microglial cells.
- 3. In Bone ----- Osteoclasts.
- 4. In Lung ----- Alveolar macrophages.

ORIGIN:

- In bone-marrow, precursor cell divides to produce monocytes, circulates in the blood. When monocytes migrate into the CT, where they mature and called macrophages.

HISTIOCYTES (MACROPHAGES)





There are numerous large Histiocytes with folded nuclei and abundant cytoplasm (large arrow) associated with eosinophils (small arrow) infiltrating connective tissue.

FUNCTIONS (HISTIOCYTES)

- Important agents of defence.
- Engulf dead cells, extravasated blood cells, bacteria and foreign bodies.

PLASMA CELLS

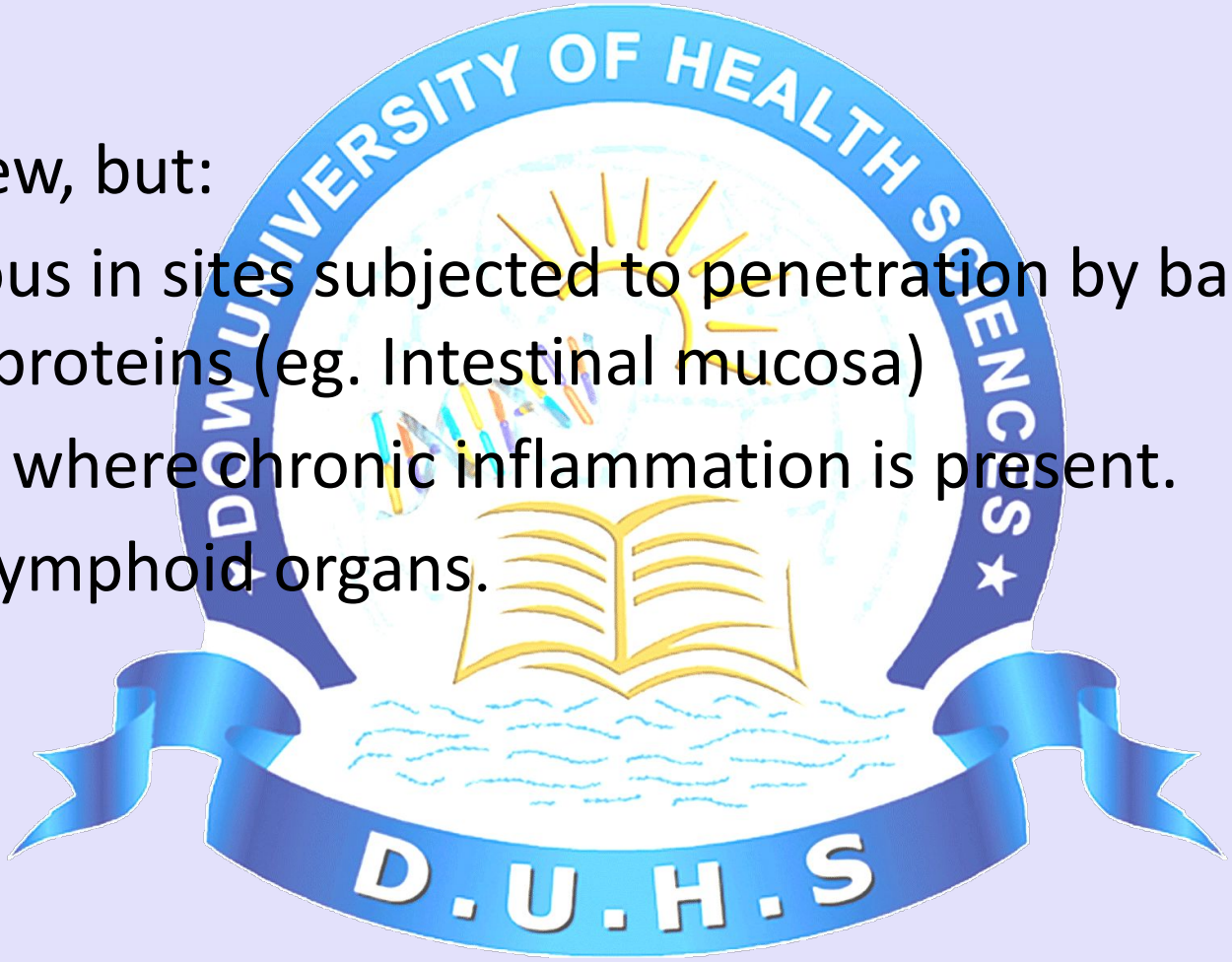
- They are large ovoid cells, having basophilic cytoplasm (due to abundant RER).
- In cytoplasm, a characteristic un-stained area near the nucleus.
- Nucleus is spherical & eccentric.
- Within the nucleus, granules of chromatin are arranged in a regular manner against the nuclear membrane. Due to which the nucleus said to exhibit a "cart-wheel appearance".
- **FUNCTION:**
- Principal function – production of antibodies.

PLASMA CELL

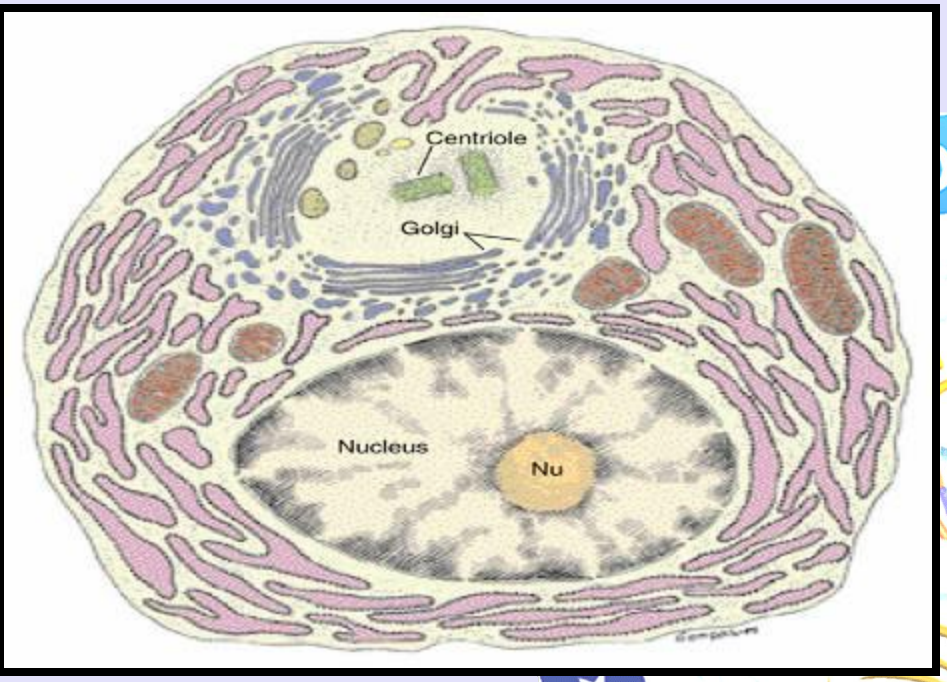
FOUND:

In CT few, but:

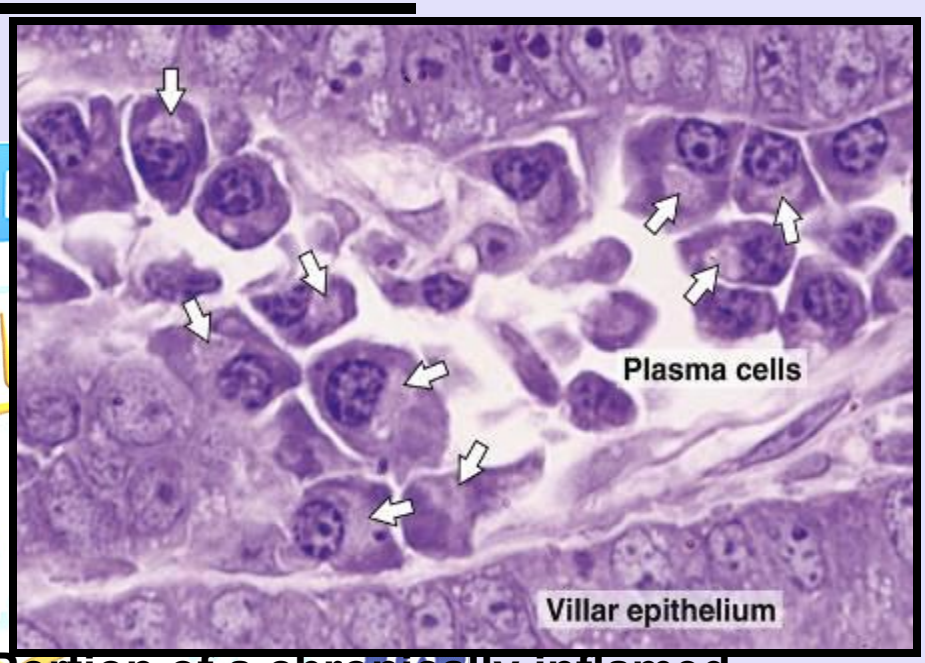
- Numerous in sites subjected to penetration by bacteria & foreign proteins (eg. Intestinal mucosa)
- In areas where chronic inflammation is present.
- Also in lymphoid organs.



PLASMA CELL



Ultrastructure of a plasma cell.
The cell contains a well-developed rough endoplasmic reticulum, with dilated cisternae containing immunoglobulins (antibodies).
In plasma cells, the secreted proteins do not aggregate into secretory granules. , nucleolus.



Portion of a chronically inflamed intestinal villus. The plasma cells are characterized by their size and abundant basophilic cytoplasm (rough endoplasmic reticulum) and are involved in the synthesis of antibodies. A large Golgi complex (arrows) is where the terminal glycosylation of the antibodies (glycoproteins) occurs. Plasma cells produce antibodies.

MAST CELLS

- (German word) Mast = well-fed.
- Oval or round cell with centrally placed spherical pale-staining nucleus.
- Cytoplasm is full of basophilic granules.
- Granules are soluble in aqueous fixatives.
- Granules are Metachromatic.

ORIGIN: From stem cells in the bone-marrow.

FOUND: widespread in the human body, but are particularly abundant in Dermis, Digestive & respiratory tracts, and around the blood vessels.

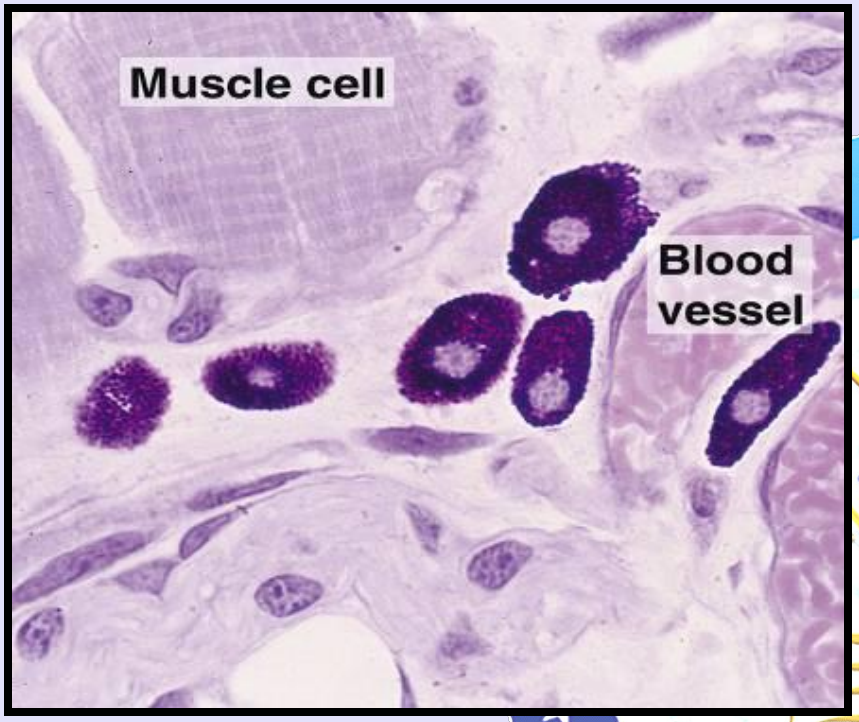
MAST CELLS (function)

- Principal function: storage of chemical mediators of inflammatory response.
- Release of chemical mediators promote the allergic reactions, which is known as "immediate hypersensitivity reaction".

They secrete:

- Histamine
- Heparin
- Leukotrienes

MAST CELLS



Several mast cells in the connective tissue surround muscle cells and blood vessels.

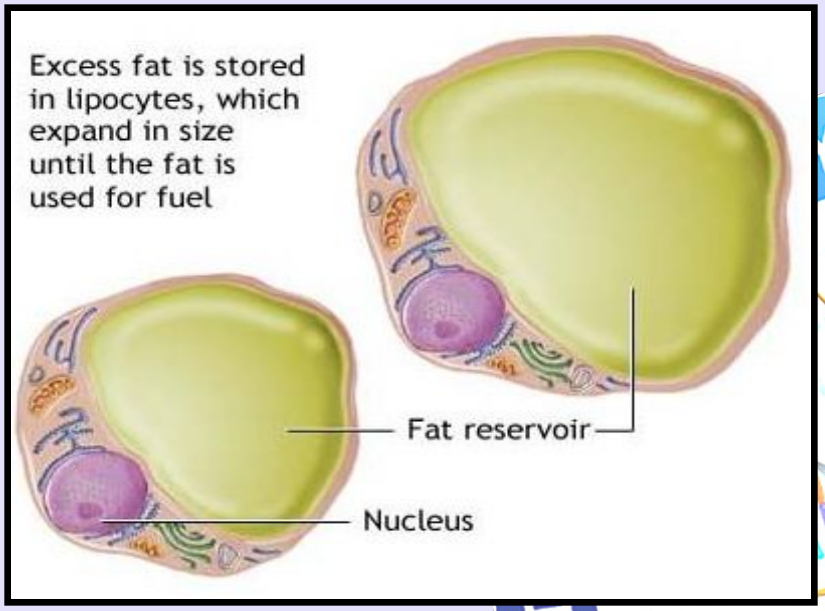
Electron micrograph of a human mast cell. The granules (G) contain heparin and histamine. Note the characteristic scroll-like structures within granules.
M, mitochondrion; C, collagen fibrils; E, elastic fibril; N, nucleus.
Inset: Higher magnification view of a mast cell granule. x44,600.

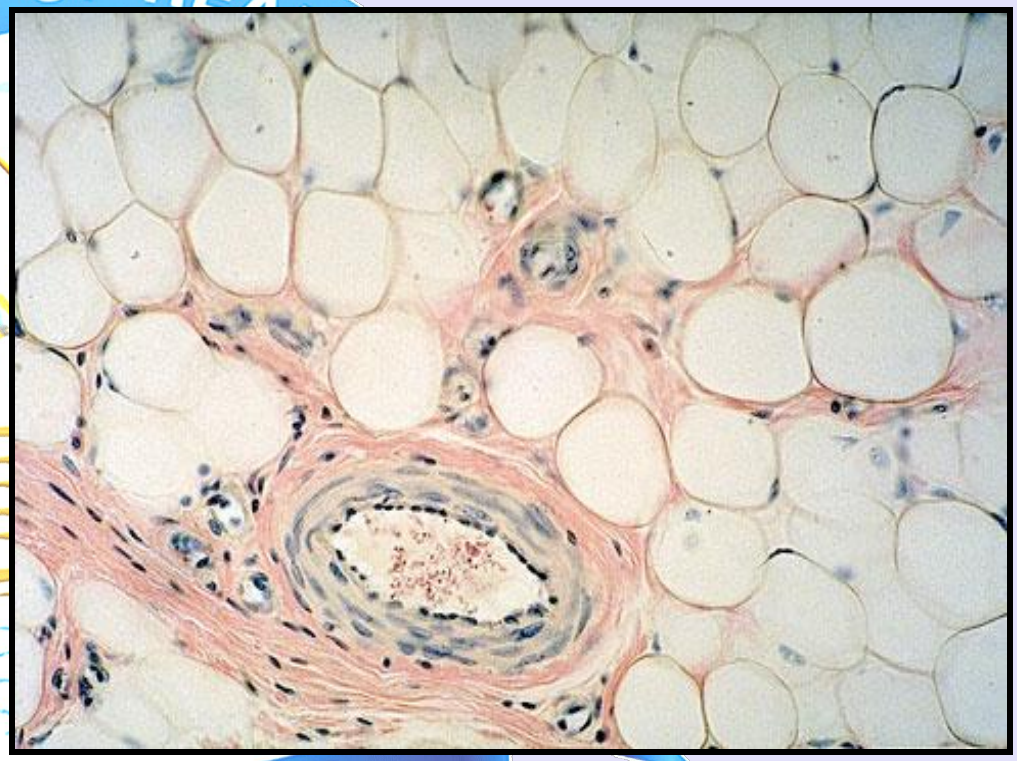
FAT CELLS (ADIPOCYTES)

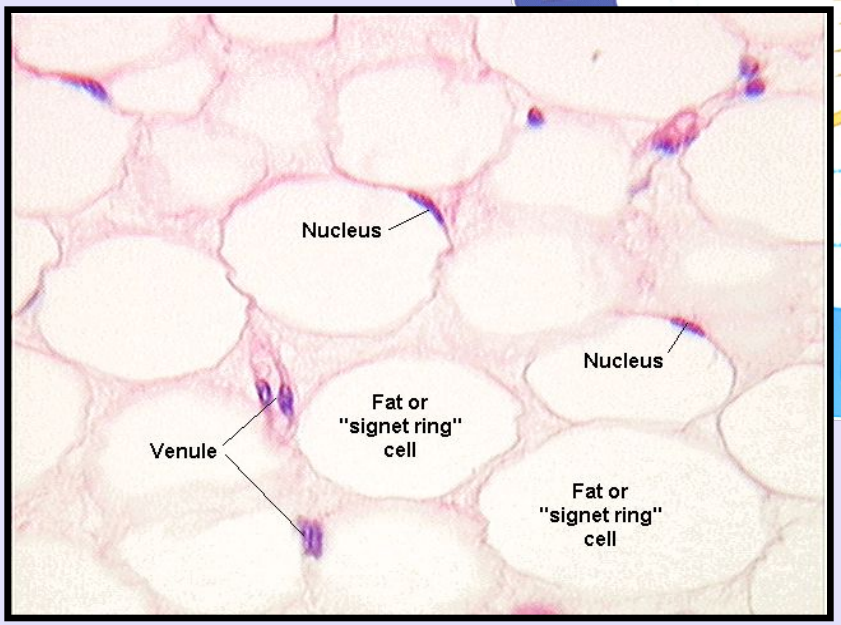
- Large ovoid or spherical cell.
- Nucleus & cytoplasm are displaced to periphery by a single fat droplet.
- Fat droplet is not membrane-bound.
- Nucleus is flattened and surrounded by a small amount of cytoplasm.

- **In Routine Preparation** fat droplet is dissolved out and is represent by a large empty vacuole. Thus after staining give a characteristic "signet-ring appearance."

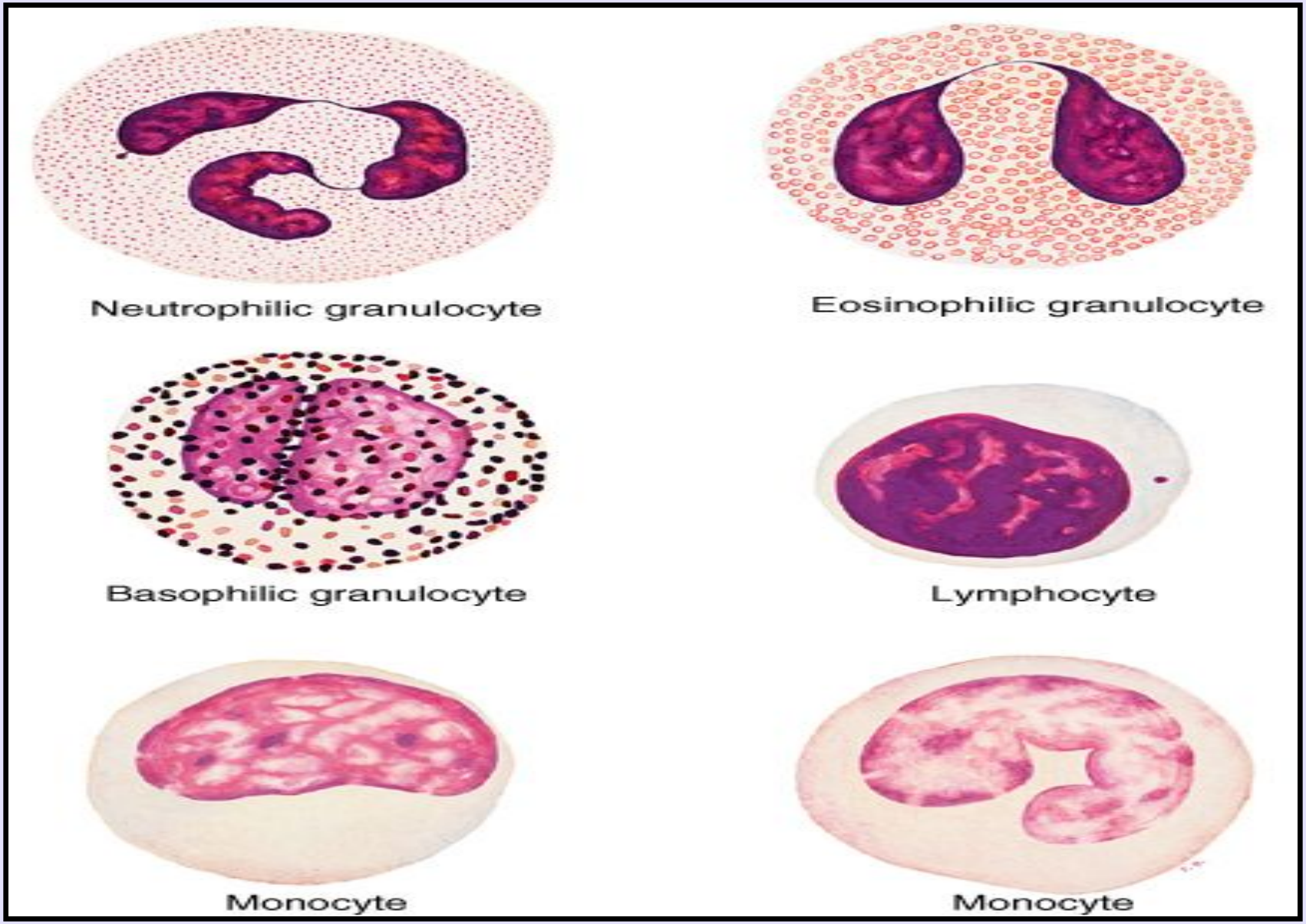
FAT CELLS


Excess fat is stored in lipocytes, which expand in size until the fat is used for fuel
Fat reservoir
Nucleus




Nucleus
Nucleus
Fat or "signet ring" cell
Venule
Fat or "signet ring" cell

Visitors or Wandering cells



FIBERS OF THE CT

They are formed by proteins that polymerize into elongated structures.

TYPES

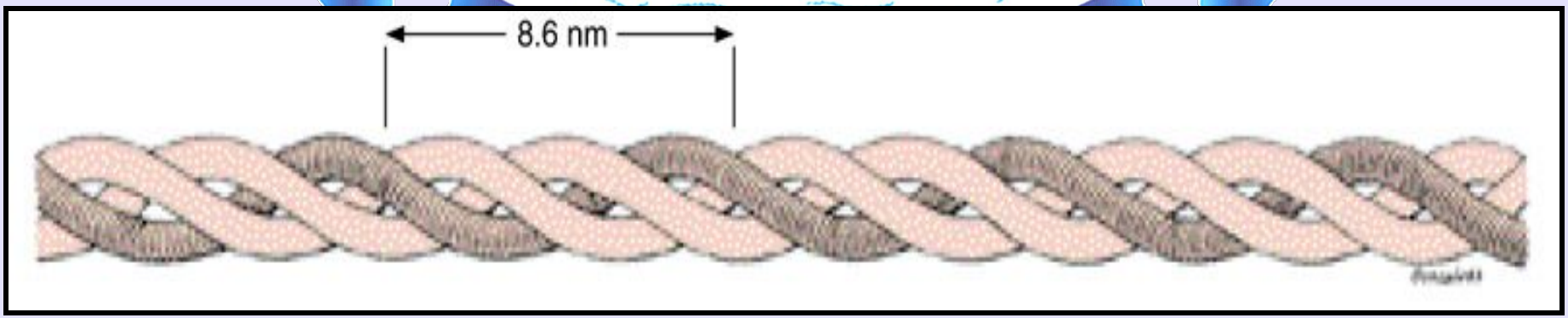
MAIN TYPES:-

A. Collagen fibers. (formed by protein collagen).
B. Reticular fibers. (formed by protein collagen).
C. Elastic fibers. (formed by protein elastin).

These fibers are distributed unequally among the different types of CT, but the predominant fiber type is responsible for giving specific properties on the tissue.

COLLAGEN PROTEIN

- It is the most abundant protein of the body, representing 30% of its dry weight.
- It is produced by several types of cells into extracellular matrix in the form of "**Tropocollagen**" molecules.
- Tropocollagen molecule consists of 3 polypeptide (alpha) chains, bound together to form a **triple helix**. It is 280 nm long and 1.5 nm in diameter.
- In extracellular matrix, Tropocollagen molecules polymerize to form "**collagen fibrils**."
- **Hydroxyproline & Hydroxylysin** are 2 characteristic aminoacids of collagen.



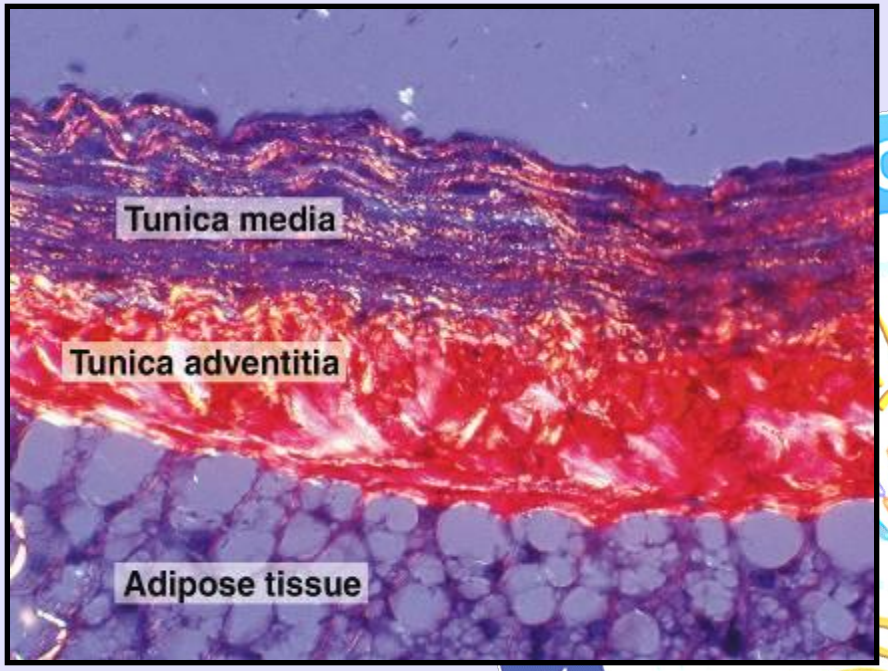
COLLAGEN PROTEIN

- On the basis of differences in the chemical structure of the polypeptide chains, more than 12 types of collagen have been described.
- The most common are type I, II, III, IV, & V.
- The tropocollagen molecules polymerize to form collagen fibrils.
- Collagen fibrils are thin elongated structure with diameter range from 20 t0 90 nm. They have transverse striations with a characteristic periodicity of 64 nm, due to overlapping arrangement of the tropocollagen molecules.
- In collagen types I & III, fibrils aggregate to form fibers.
- In collagen type I, fibers aggregate to form bundles.

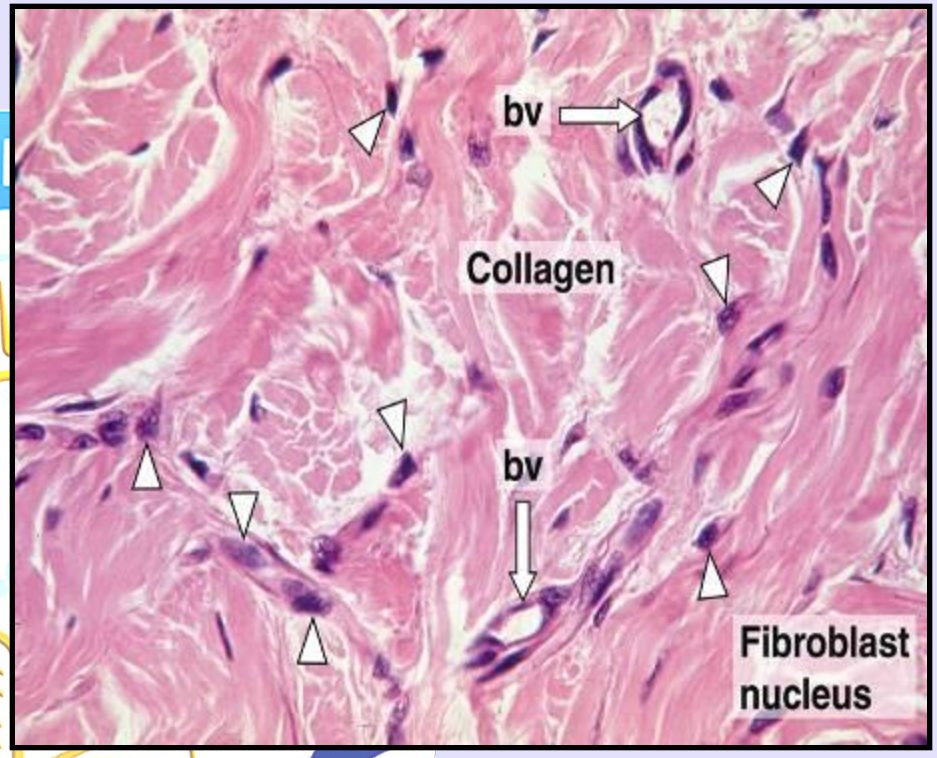
COLLAGEN FIBERS (WHITE FIBERS)

- Most numerous fibers found in CT.
- Fresh collagen fibers are colourless strands, but in bundles, they give white colour to the tissue in which they lie (eg. Tendon & aponeurosis).
- Individual fiber has diameter varies from 2 – 20 µm.
- They exhibit birefringence under polarized microscope.
- Bundles usually follow an irregular & wavy course.
- An individual fiber never branch.
- They are flexible but inelastic.
- They are extremely tough and can resist considerable strain without breaking.
- Thus they provide a unique combination of flexibility and strength to the tissue in which they are present.

COLLAGEN FIBERS



Section of a muscular artery stained with picro-sirius and observed with polarization optics. The upper tunica media (muscular layer) contains reticular fibers consisting mainly of collagen type III. The lower layer (tunica adventitia) contains thick fibers and bundles of collagen type I. Deficiencies of collagen type III may result in rupture of the arterial wall.



Dense irregular connective tissue from human dermis contains thick bundles of collagen fibers, fibroblast nuclei (arrowheads), and a few small blood vessels (bv).

RETICULAR FIBERS

- They are extremely thin **branching fibers.**
- Individual fiber has diameter varies from 0.5 to 2 µm.
- Usually form supporting framework or reticulum in certain organs.
- Not visible in H&E preparation, but easily stains black with silver salts. Because of their affinity for silver salts, they are called Argyrophilic fibers.
- Also stained intensely with periodic acid-Schiff (PAS) technique.
- Both PAS positive & argyrophilia are due to the high content of carbohydrate, associated with each fiber in the form of a surface coat.
- They are usually associated with type III collagen.

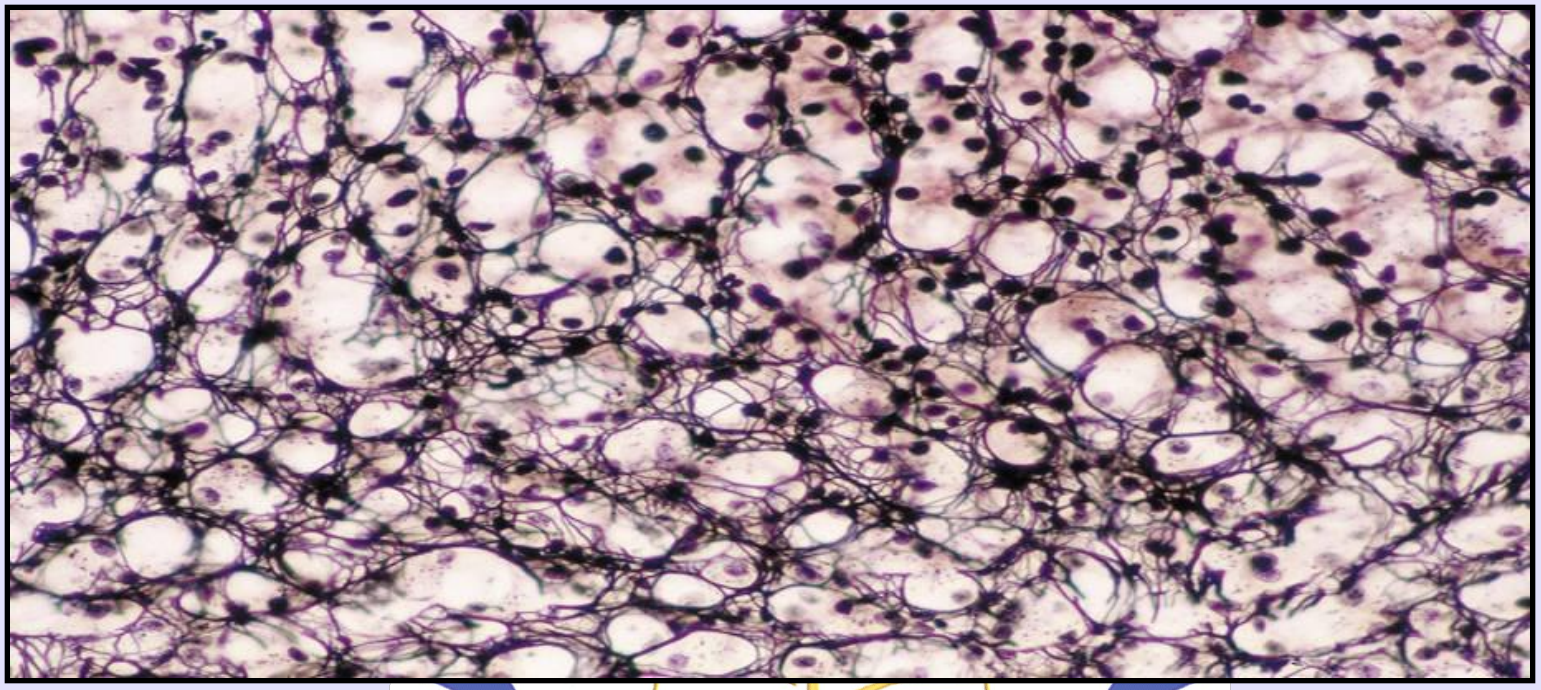
RETICULAR FIBERS CONT.

- Because of their small diameter, they have weak birefringence when stained with Sirius red dye, and observed under the polarized microscope. Under E/M, they also show characteristic 64 nm cross banding

  They particularly abundant in
  (a) Smooth muscle.
  (b) Endoneurium.
  (c) Framework of hemopoietic organs (eg. Spleen, Lymph nodes, red bone-marrow).
- Forms a network around the cells of parenchymal organs (eg. Liver, Kidney, Endocrine glands).

- With reference to the collagen fiber, the Reticular fiber are separated entities with characteristics biochemical, functional, morphological & pathological features.

RETICULAR FIBERS



Section of an adrenal cortex, silver stained to show reticular fibers. This is a thick section made to emphasize the networks formed by these fibers, which consist of collagen type III. Nuclei are black, and cytoplasm is unstained. Medium magnification.

ELASTIN PROTEIN

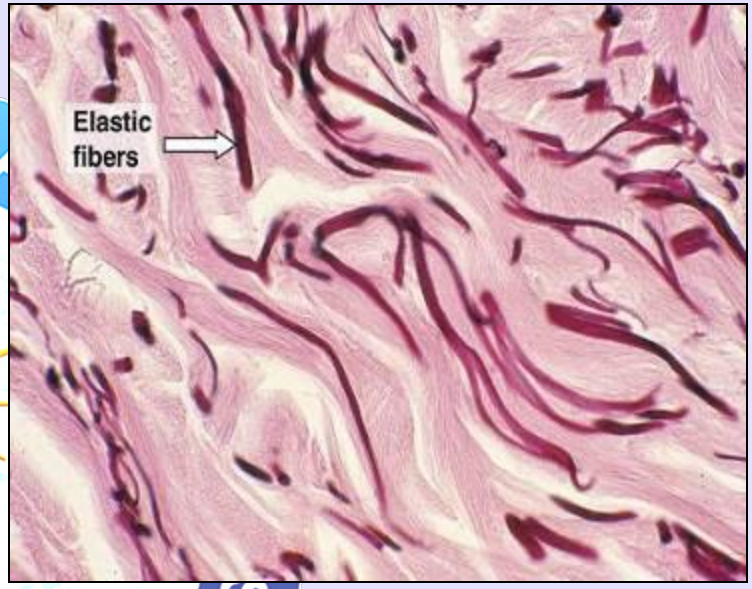
- It is resistant to boiling & acid & alkali extraction.
- It is secreted as "Proelastin" , which undergoes polymerization in the extra-cellular matrix as Elastin.
- It is easily hydrolyzed by pancreatic lactase.
- It is a rubber like material, which is arranged as fibers or discontinuous sheets in the extra cellular matrix particularly of skin, lung & blood vessels, where it confers the properties of stretching and elastic recoil.

It is synthesized by :-

- Fibroblasts in Skin & Tendon
- Smooth muscle cells in Large blood vessels.
- Desmosin & Isodcsmosin are 2 characteristic amino acids found in the elastin.

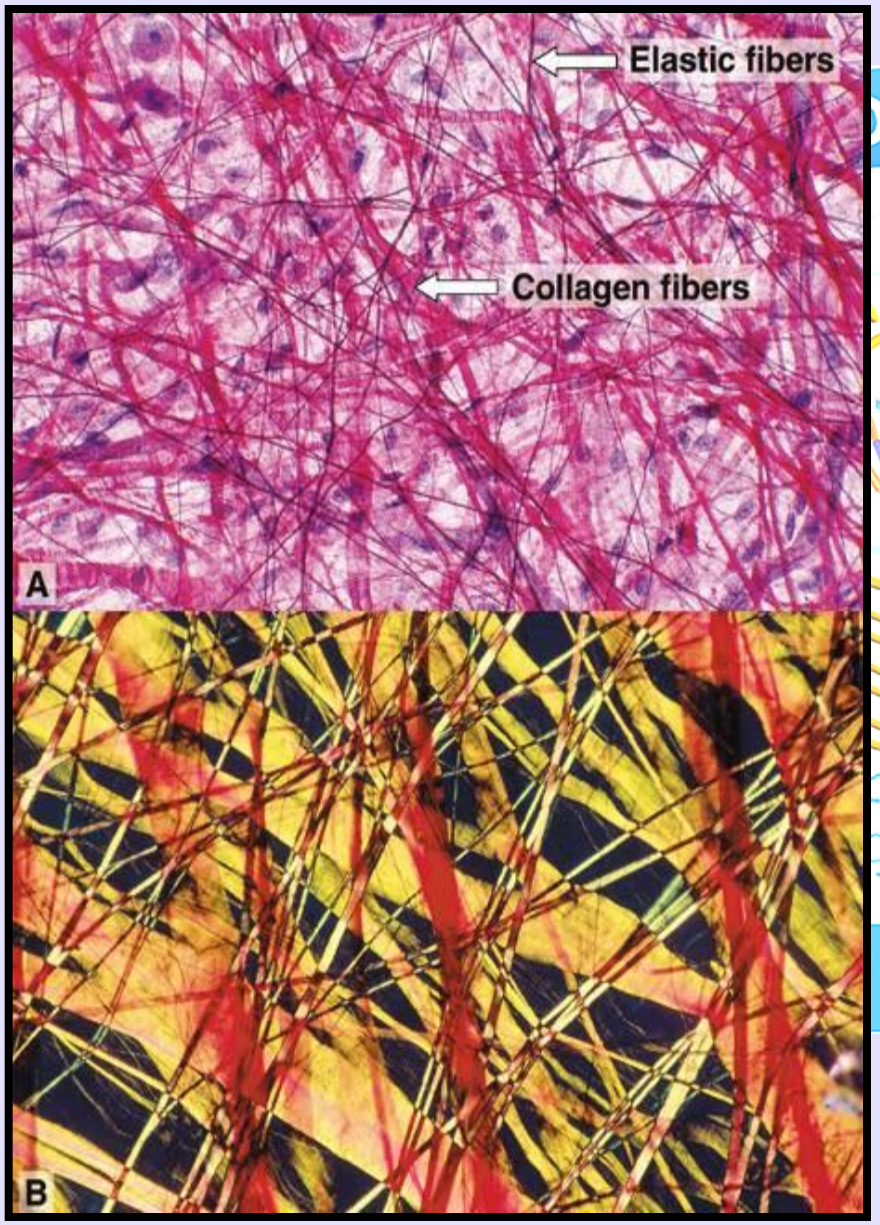
ELASTIC FIBERS

- They are fine, straight & highly refractile fibers, which occurs as cylindrical threads or flat ribbons.
- They generally 0.5 to 4 µm in diameter, but in certain elastic ligaments, eg. Ligamentum nuchae, they may reach a diameter of 10 to 12 µm.
- In fresh state, large mass of elastic fibers give a characteristic yellowish shade.
- They are capable of stretching to one & half of their original length
- They are Acidophilic in nature, but do not stain well with Eosin.
- They can be stained brown selectively with "orcein" dye by resorcin-fuchsin technique



Skin dermis, selectively stained for elastic fibers. Dark elastic fibers are interspersed with pale red collagen fibers. The elastic fibers are responsible for skin's elasticity.

COLLAGEN AND ELASTIC FIBERS

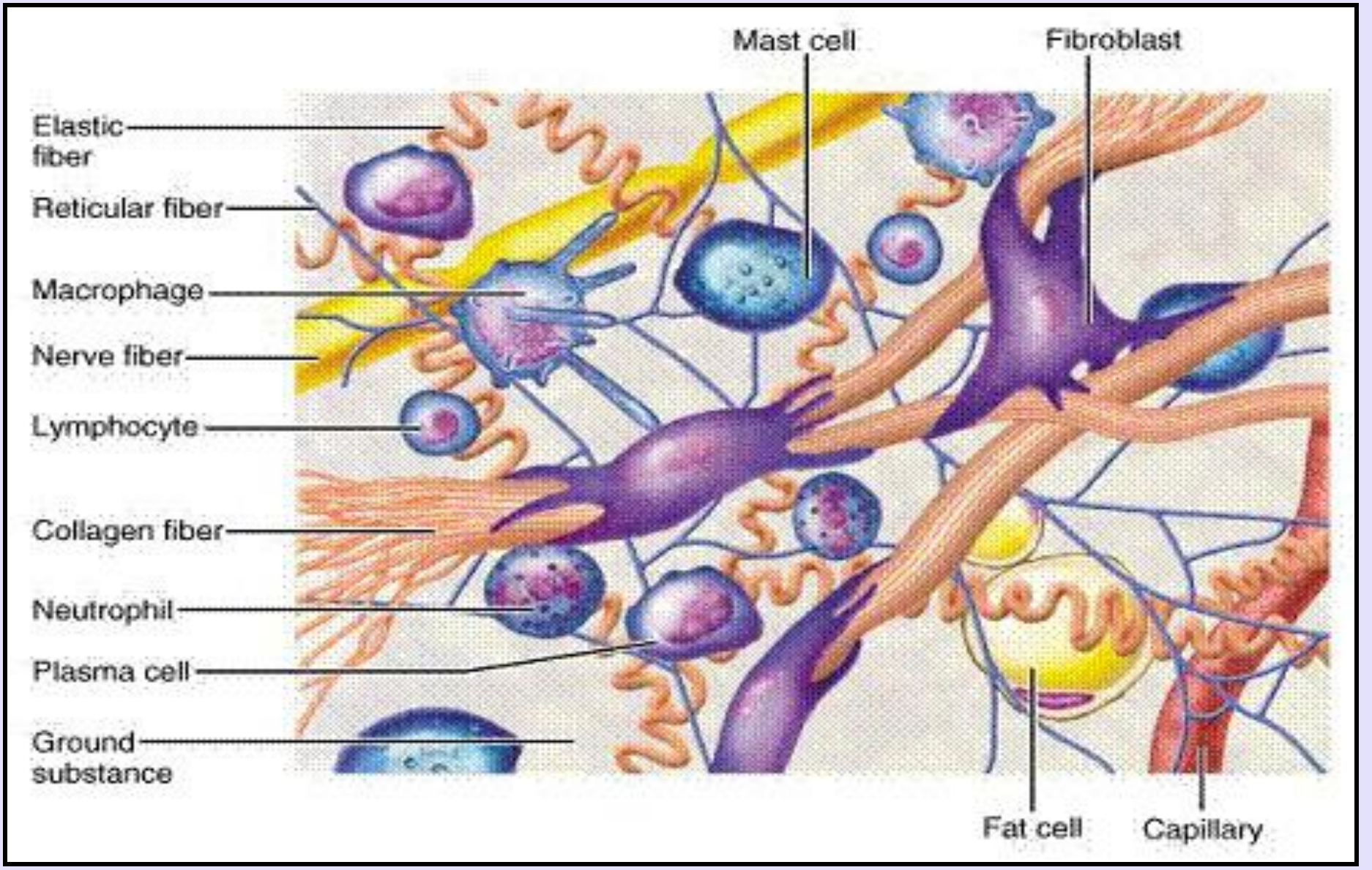


A: Young rat mesentery showing red picrosirius-stained nonanastomosing bundles of collagen fibers, while the elastic fibers appear as thin, dark anastomosing fibers stained by orcein.

Collagen and elastic fibers provide structure and elasticity, respectively, to the mesentery.

B: The same preparation observed with polarizing microscopy. Collagen bundles of various thicknesses are observed.
In the superimposed regions, the bundles of collagen are a dark color.

CONNECTIVE TISSUE



GROUND SUBSTANCE

- It is an amorphous substance in which the cells & fibers of the CT are embedded.
- It is a colorless, transparent & homogenous complex mixture of proteoglycan and glycoproteins.
- It is a colloidal gel-like material of variable viscosity, which binds varying amount of water.
- Bounded water serves a medium for diffusion of gases & metabolic substance b/w CT cells and blood vessels.
- Because of its high water content and amorphous appearance, it is difficult to study in both fresh & fixed states, due to 2 reasons:-
- It has same refractive index as water & isotonic saline solution.
- It is soluble in reagents generally used to prepare the tissue.

COMPOSITION OF GROUND SUBSTANCE

Mainly 2, in addition to water and salts.

1. Proteoglycans.
2. Glycoproteins.

PROTEOGLYCANS

- They are composed of a core protein associated with glycosaminoglycans.
- They consist of about 95% carbohydrates and 5% proteins.
- They are macromolecular protein polysaccharide complex.
- Glycosaminoglycans :- They are linear polysaccharides formed by characteristic repeating disaccharides units, usually composed of uronic acid & hexosamine.
- Glycosaminoglycans are of 2 types, i.e. non-sulfated & sulfated.

PROTEOGLYCANS Cont.

- Non-sulfated ------- Hyaluronic acid.
- Sulfated -------- Chondroitin sulfate, Dermatan sulfate, Heparan sulfate, and Keratan sulfate.

SYNTHESIS OF PROTEOGLYCANS

- Begins in RER with synthesis of its protein moiety.
- Glycosylation is initiated in RER and completed in Golgi complex.
- Sulfation also occur in GA.

GLYCOPROTEINS

- These are composed of proteins & carbohydrates, but in contrast to proteoglycans, the protein moiety is predominant.
- The carbohydrate moiety is frequently branched structure, instead of linear polysaccharides.
- Several glycoproteins have been isolated from various CT of the body, eg. Fibronectin, Chodronectin, Osteonectin, Laminin, Fibrillin,Tenascin.

REFERENCES

BASIC HISTOLOGY BY

JUNQUEIRA

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