BASIC Histology
B (206)

BY

Prof. Dr. Maha Khalil Ibrahim

Prof. Dr. Kareem H. Thamer

Lecture No. 1

EPITHELIAL TISSUE: INTRODUCTION

- Despite its complexity, the human body is composed of only four basic types of tissue: epithelial, connective, muscular, and nervous. These tissues, which are
- formed by cells and molecules of the extracellular matrix, exist not as isolated units but rather in association with one another and in variable proportions, forming
- different organs and systems of the body. The main characteristics of these basic types of tissue are shown in Table 4–1. Also of great functional importance are the
- free cells found in body fluids such as blood and lymph.

Table 4–1. Main characteristics of the four basic types of tissues.

Tissue	Cells	Extracellular Matrix	Functions
Nervous	elongated	None	Transmission of impulses
Epithelial	polyhedral cells	Small	protection , secretion
Muscle	Elongated cells	Moderate	movement
Connective	types of cells	Abundant	Support and protection

Organs can be divided into parenchyma, which is composed of the cells responsible for the main functions typical of the organ, and stroma, which is the supporting tissue. Except in the brain and spinal cord, the stroma is made of connective tissue.

Epithelial tissues are composed of closely aggregated polyhedral cells with very little extracellular substance. These cells have strong adhesion and form cellular sheets that cover the surface of the body and line its cavities.

The principal functions of tissues are:

1- Covering, lining, and protecting surfaces (eg, skin)
2- Absorption (e g, the intestines)
3- Secretion (eg, the epithelial cells of glands)
4- Contractility (eg, myoepithelial cells).

CHARACTERISTIC FEATURES OF EPITHELIAL CELLS:

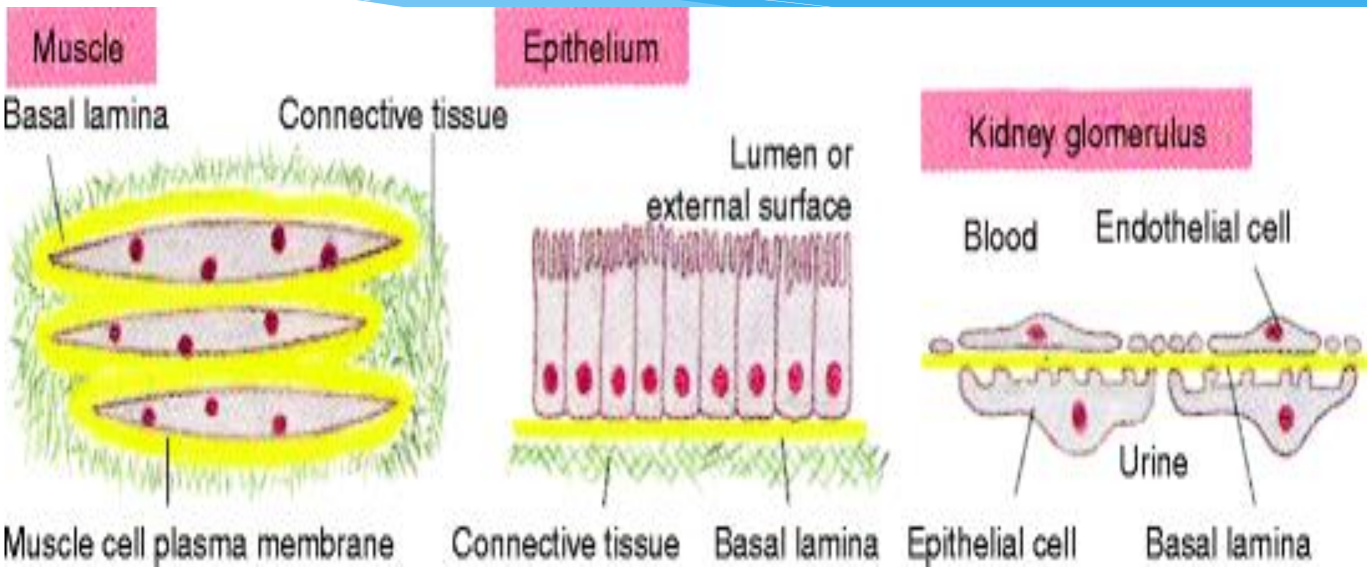
The forms and dimensions of epithelial cells range from high columnar to cuboidal to low squamous cells. Their common polyhedral form results from their close juxtaposition in cellular layers or masses.

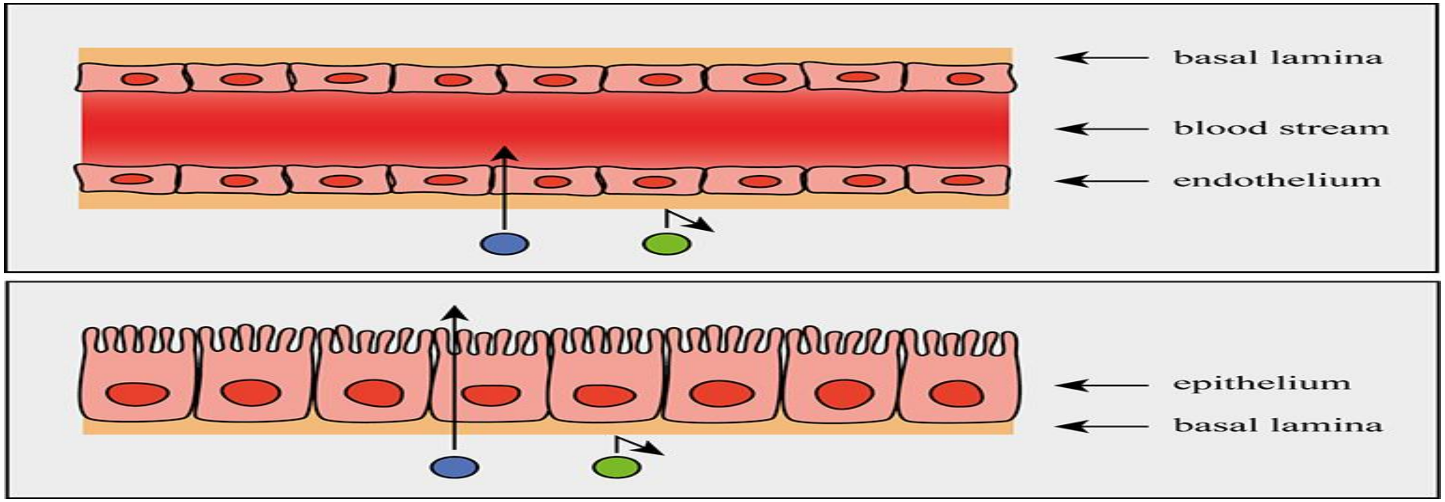
Epithelial cell nuclei have a distinctive shape, varying from spherical to elongated or elliptic. The nuclear form often corresponds roughly to the cell shape; thus, cuboidal cells have spherical nuclei, and squamous cells have flattened nuclei.

Most epithelia rest on connective tissue, this layer of connective tissue is often called the lamina propria. The lamina propria not only serves to support the epithelium but also provides nutrition and binds it to underlying structures.

- Epithelial cells generally show polarity, with organelles and membrane proteins distributed unevenly in different parts of the cell. The region of the cell that faces the connective tissue is called the basal pole, whereas the opposite pole, usually facing a space, is the apical pole and the intervening sides apposed in neighboring cells are the lateral surfaces. The membranes on the lateral surfaces of adjoining cells often have numerous infoldings to increase the area of that surface, increasing its functional capacity.

- **Basal Laminae & Basement Membranes**
- All epithelial cells in contact with subjacent connective tissue have at their basal surfaces a felt-like sheet of extracellular material called the basal lamina, this structure is visible only with the electron microscope, appears as an electron-dense layer, 20–100 nm thick, consisting of a network of fine fibrils, the dense layer or lamina densa ,and a layer called clear layers or laminae lucida(fig





- Fig (1) : Basal lamina

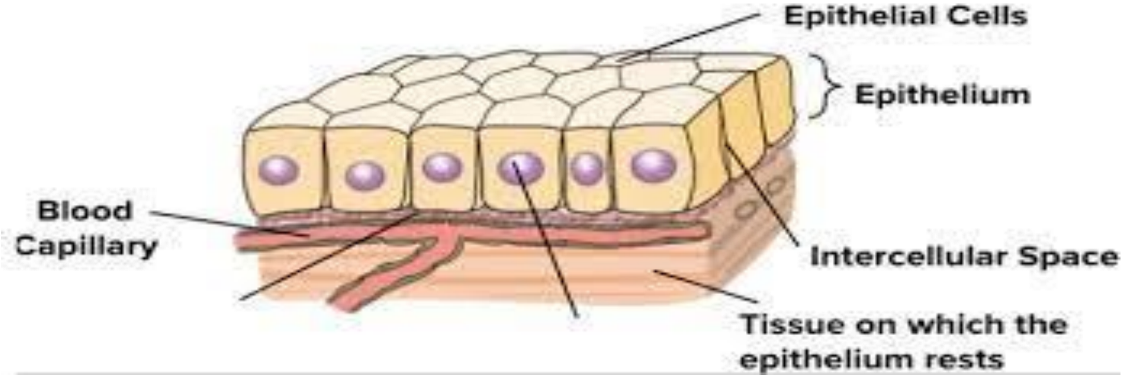
The macromolecular components of basal laminae include :

1- **Laminin:** These are large glycoprotein molecules that self-assemble to form a lace-like sheet immediately below the cells' basal poles.

2- **Type IV collagen:** Monomers of type IV collagen contain three polypeptide chains and self-assemble further to form a felt-like sheet associated with the laminin layer.

3- **Entactin (nidogen)**, a glycoprotein.

The term **basement membrane :** is used to specify a periodic acid–Schiff (PAS)-positive layer, visible with the light microscope beneath epithelia (Figure 2). Basement membrane is formed by the combination of a basal lamina and a reticular lamina and is therefore thicker. "Basement membrane" is used to denote the structures seen with the light microscope.



Intercellular Adhesion & Other Junctions

Several membrane-associated structures contribute to adhesion and communication between cells. They are present in most tissues but are particularly numerous and prominent in epithelia. Epithelial cells are extremely cohesive and relatively strong mechanical forces are necessary to separate them.

Intercellular adhesion is especially marked in epithelial tissues that are subjected to traction and pressure (eg, in the skin).

The **lateral membranes** of epithelial cells exhibit several specialized intercellular junctions. Various junctions serve to function as:

Seals to prevent the flow of materials between the cells (occluding junctions)

Sites of adhesion (adhesive or anchoring junctions)

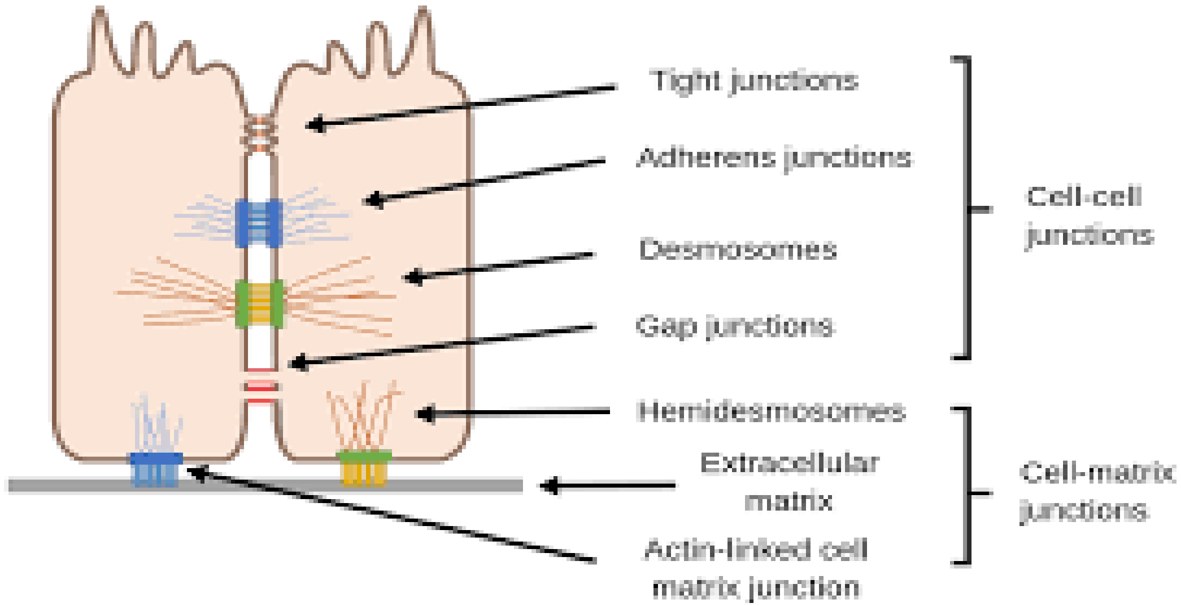
Channels for communication between adjacent cells (gap junctions).

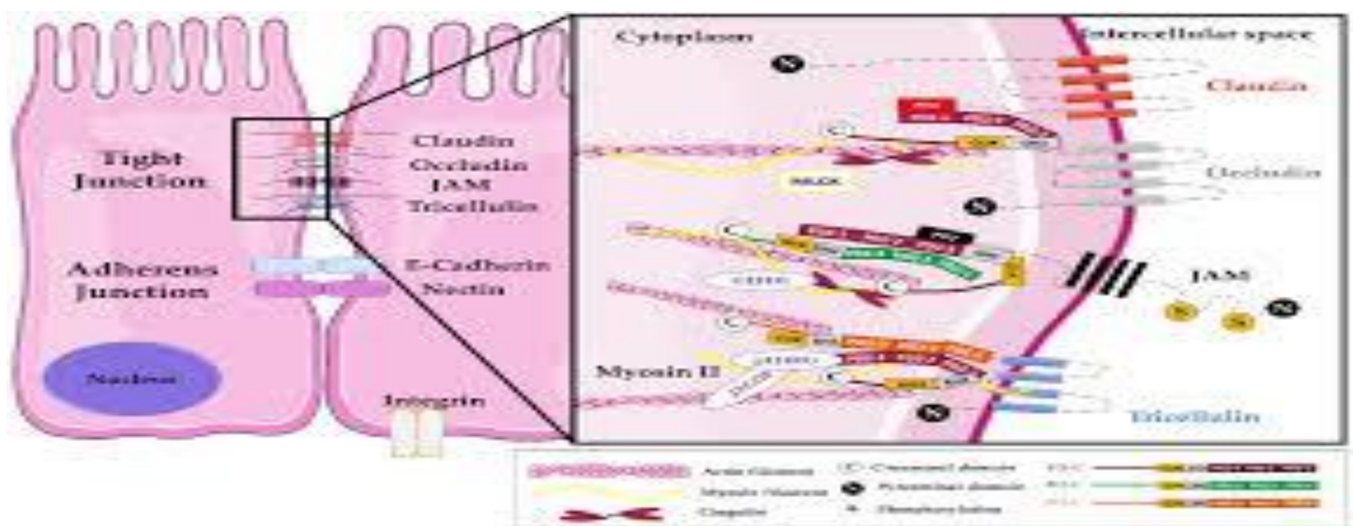
In several epithelia such junctions are present in a definite order from the apical to the basal ends of the cells:

Tight junctions, or zonulae occludens, are the most apical of the junctions. The Latin terminology gives important information about the geometry of the junction. "Zonula" indicates that the junctions form bands completely encircling each cell, and "occludens" refers to the membrane fusions that close off the space between the cells. The tight junction (zonula occludens) and adherent junction (zonula adherens) are typically close together and each forms a continuous ribbon around the cell's apical end. **occluding junctions** prevent passive flow of material between the cells, but are not very strong; the **adhering junctions** immediately below them serve to stabilize and strengthen these circular bands around the cells and help hold the layer of cells together.

Both desmosomes and gap junctions make spotlike plaques between two cells. Bound to intermediate filaments inside the cells, desmosomes form very strong attachment points which supplement the role of the zonulae adherens and play a major role to maintain the integrity of an epithelium. All of these junctional types are also found in certain other cell types besides epithelia.

Types of tight junctions





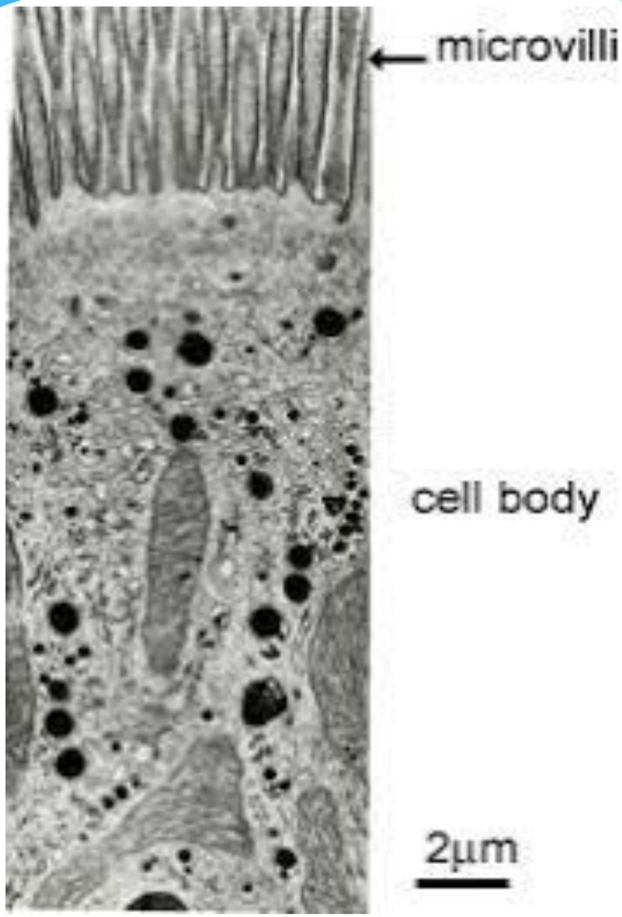
SPECIALIZATIONS OF THE APICALCELL SURFACE

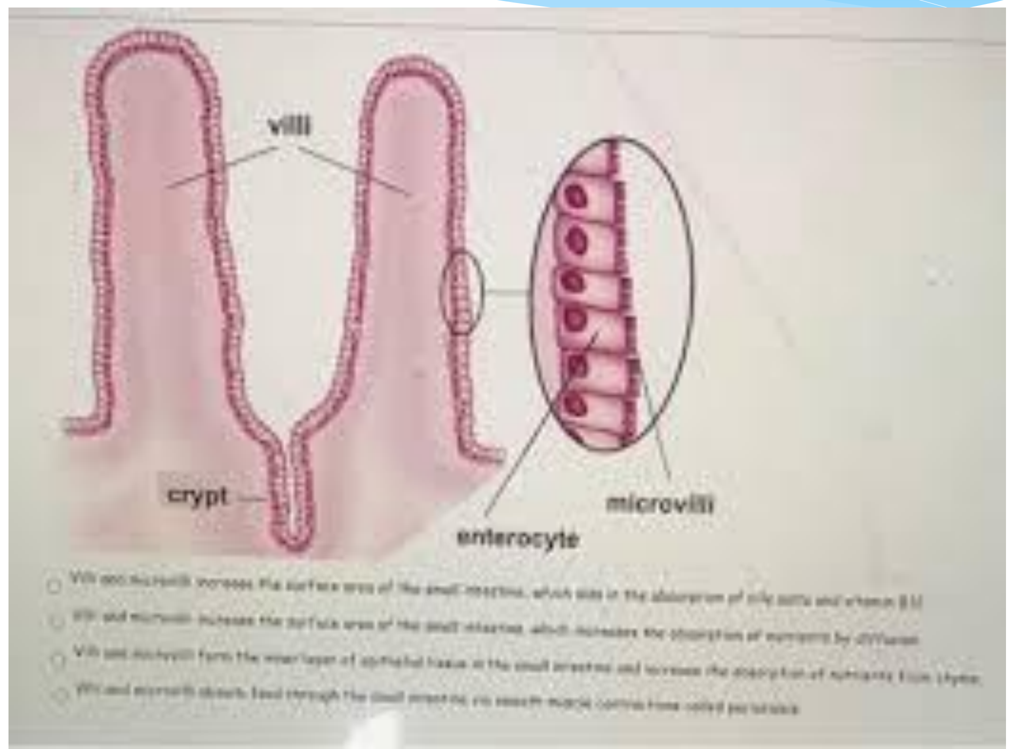
The free or apical surface of many types of epithelial cells has specialized structures to increase the **cell surface area** or to move substances or particles bound to the epithelium.

1-Microvilli

When viewed in the electron microscope, many cells are seen to have cytoplasmic projections, these projections may be short or long fingerlike extensions or folds and they range in number from a few to many, most are temporary, reflecting cytoplasmic movements and the activity of actin filaments.

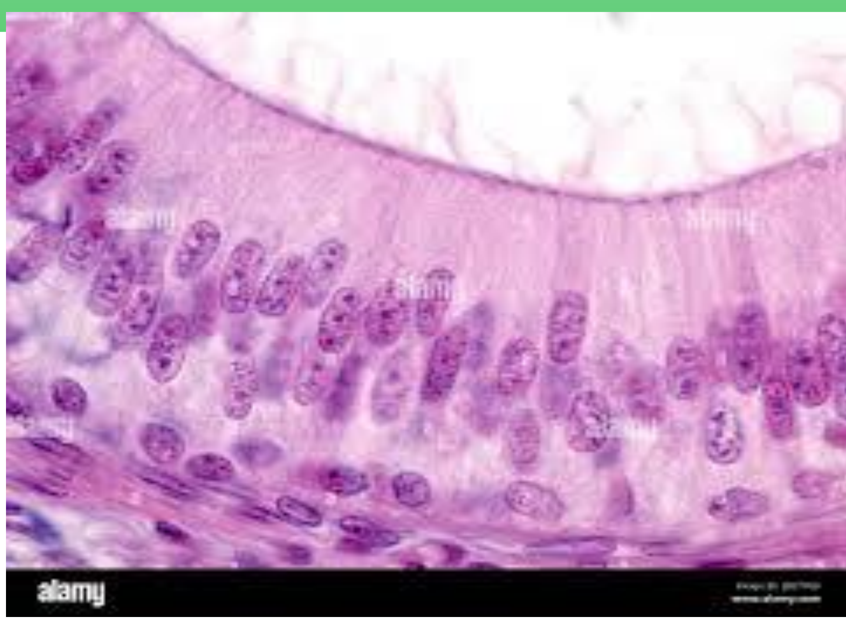
In absorptive cells, such as the lining epithelium of the small intestine, the apical surface presents orderly arrays of many hundreds of more permanent microvilli , the average microvillus is only about 1 μm high and 0.08 μm wide, but with hundreds or thousands present on the end of each absorptive cell, the total surface area can be increased as much as 20- or 30-fold. In these absorptive cells the glycocalyx is thicker than that of most cells and includes enzymes for the final stages of certain macromolecules' breakdown. The complex of microvilli and glycocalyx is easily seen in the light microscope and is called the brush or striated border.





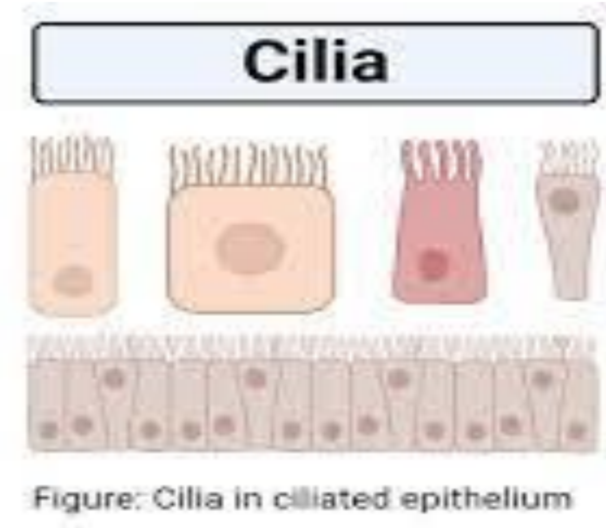
Small intestine microvilli

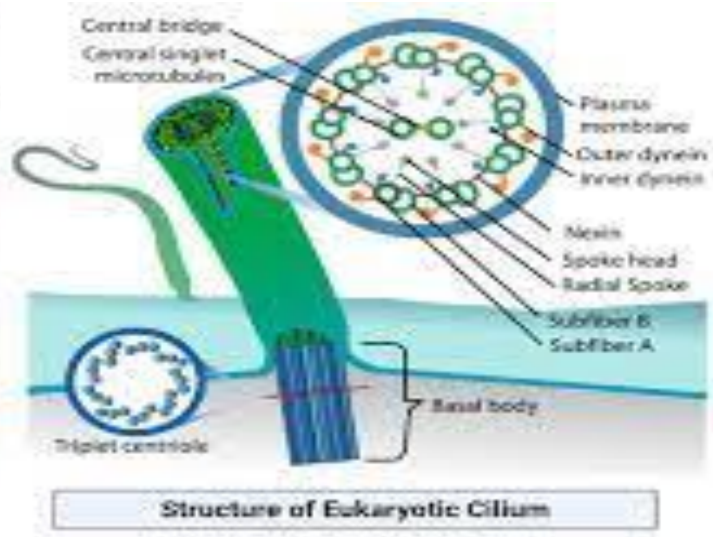
- 2- Stereocilia
- Stereocilia are long apical processes of cells in other absorptive epithelia such as that lining the epididymis and ductus deferens, these structures are much longer and less motile than microvilli, are branched, and should not be confused with true cilia, like microvilli, stereocilia also increase the cells' surface area, facilitating the movement of molecules into and out of the cell-.



3- Cilia

Cilia are elongated, highly motile structures on the surface of some epithelial cells, 5–10 µm long and 0.2 µm in diameter, which is much longer and two times wider than a typical microvillus. each cilium is bounded by the cell membrane and contains an axoneme with a central pair of microtubules surrounded by nine peripheral micro tubular pairs ,Cilia are inserted into basal bodies, which are electron-dense structures .





TYPES OF EPITHELIA

Epithelia can be divided into two main groups according to their **structure and function**:

1- covering (or lining) epithelia and

2- glandular epithelia.

This is an arbitrary division, for there are lining epithelia in which all the cells secrete (eg, the lining of the stomach) or in which glandular cells are distributed among the lining cells (eg, mucous cells in the small intestine or trachea).

Covering or Lining Epithelia

Covering epithelia are tissues in which the cells are organized in layers that cover the external surface or line the cavities of the body.

They are classified according to the number of cell layers and the morphologic features of the cells in the surface layer.

A- Simple epithelia contain only one layer of cells and

B- stratified epithelia contain more than one layer.

Common types of covering epithelia in the human body.

Number of Cell Layers	Cell Form	Examples of Distribution	Main Function
Simple (one layer)	Squamous	Lining of vessels (**endothelium**). Serous lining of cavities; pericardium, pleura, peritoneum (mesothelium).	Facilitates the movement , active transport, secretion of biologically active molecules .
	Cuboidal	Covering the ovary, thyroid	Covering, secretion
	Columnar	Lining of intestine, gallbladder.	Protection, lubrication, absorption, secretion.

	Pseudostratified (layers of cells with nuclei at different levels; not all cells reach surface but all adhere to basal lamina)	**Lining of trachea, bronchi, nasal cavity**	**Protection, secretion**
Stratified (two or more layers)	Squamous keratinized (dry)	Epidermis	Protection; prevents water loss.

Number of Cell Layers	Cell Form	Examples of Distribution	Main Function
	Squamous non-keratinized (moist)	Mouth, esophagus, larynx,	Protection, secretion; prevents water loss
	Transitional	Bladder, ureters, renal calyces.	Protection, distensibility
	Cuboidal	Sweat glands	Protection, secretion.

Based on cell shape, simple epithelia are classified as

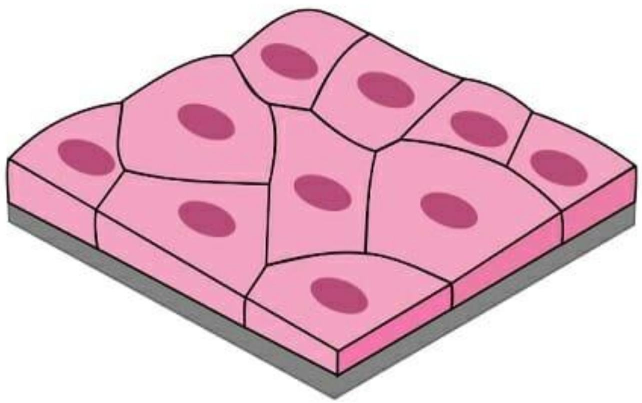
1- squamous (thin cells).

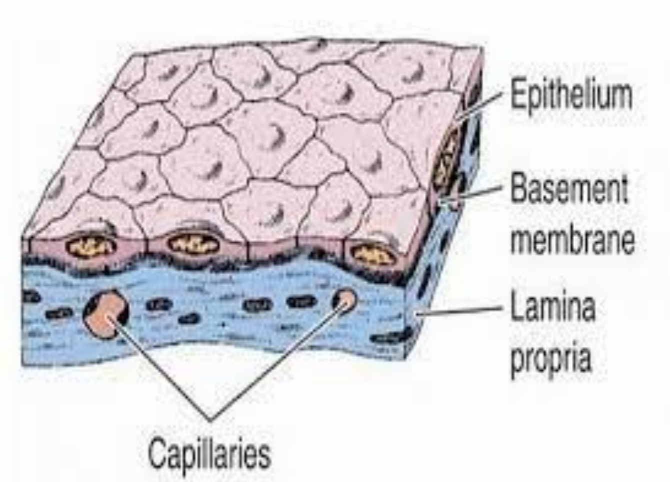
2- cuboidal (cells roughly as thick as they are wide) or

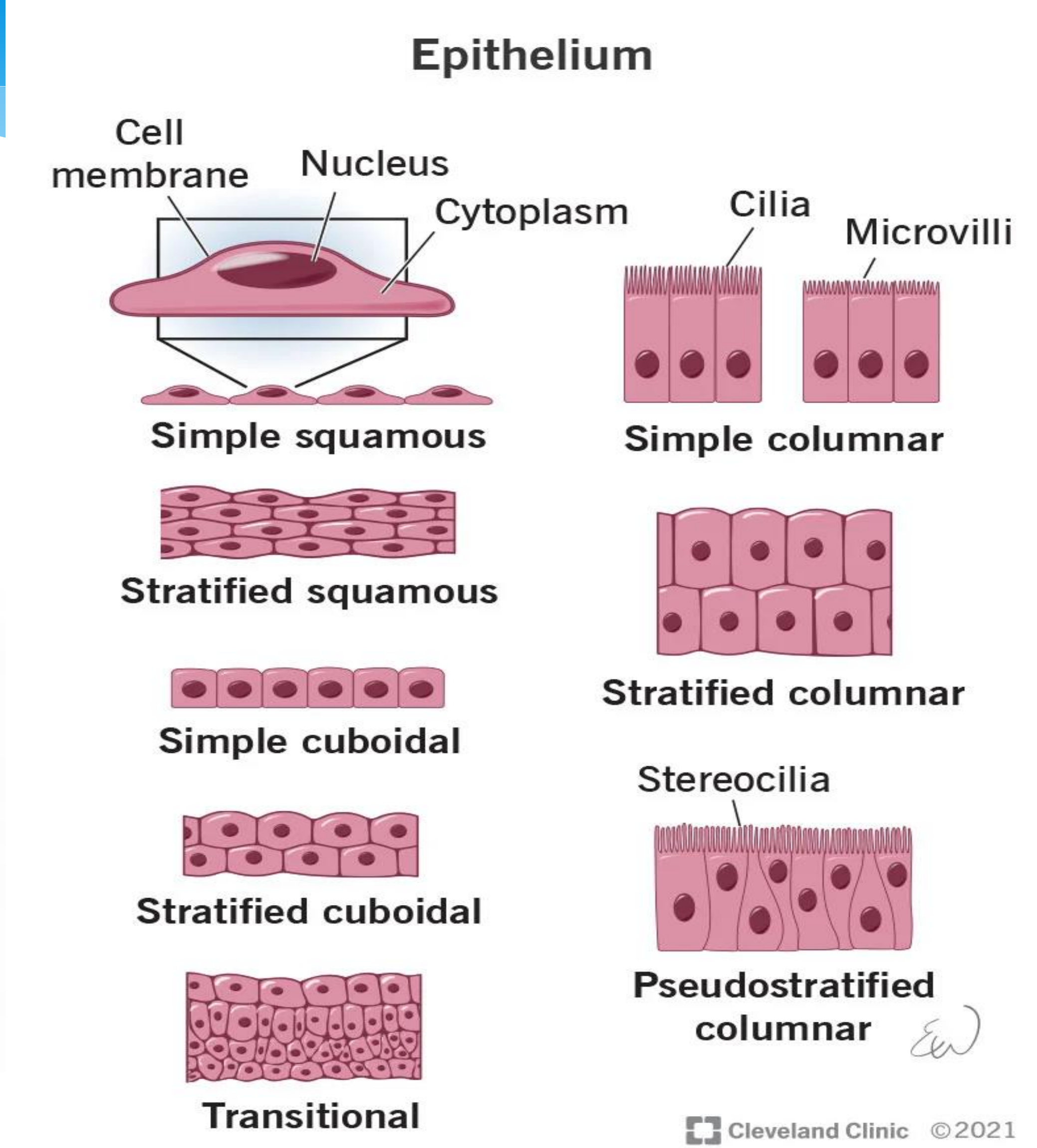
3- columnar (cells taller than they are wide).

Simple squamous epithelia.

In simple squamous epithelium, cells of the single layer are flat and usually very thin, with only the thicker cell nucleus appearing as a bulge to denote the cell. Simple epithelia are typically specialized as lining of vessels and cavities and regulate substances which can enter underlying tissue from the vessel or cavity. The thin cells often exhibit transcytosis. Examples shown here are those lining the renal loops of Henle, the mesothelium lining a mesentery, and the endothelium lining the inner surface of the cornea. Endothelium and mesothelium are nearly always simple squamous.



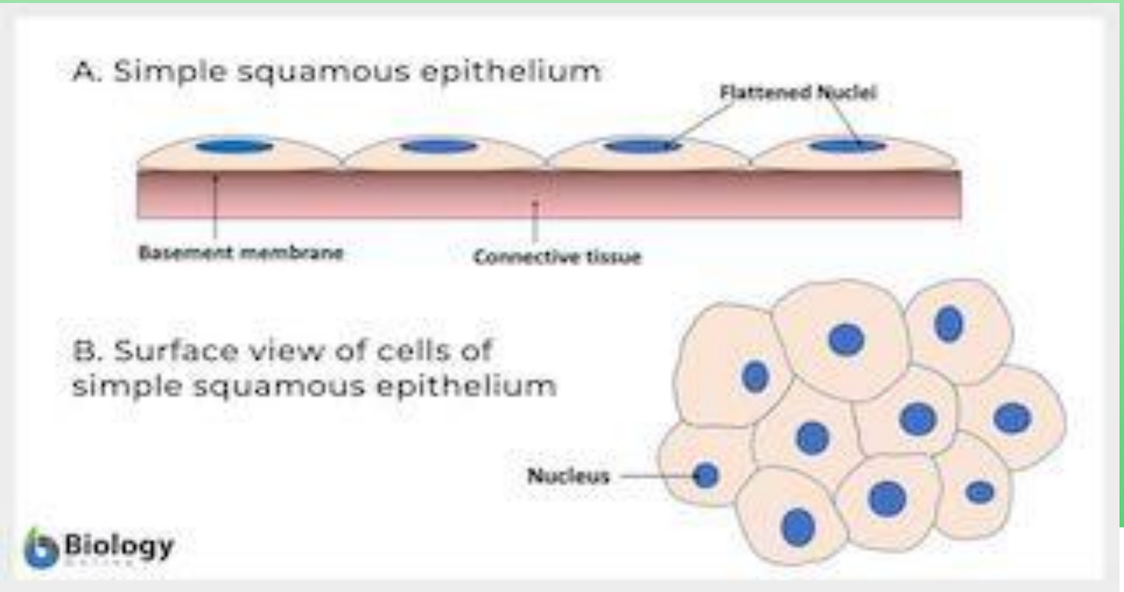




Types of epithelium/ simple squamous epithelium

. Squamous epithelium: Squamous epithelial cells are flat and sheet-like in appearance.

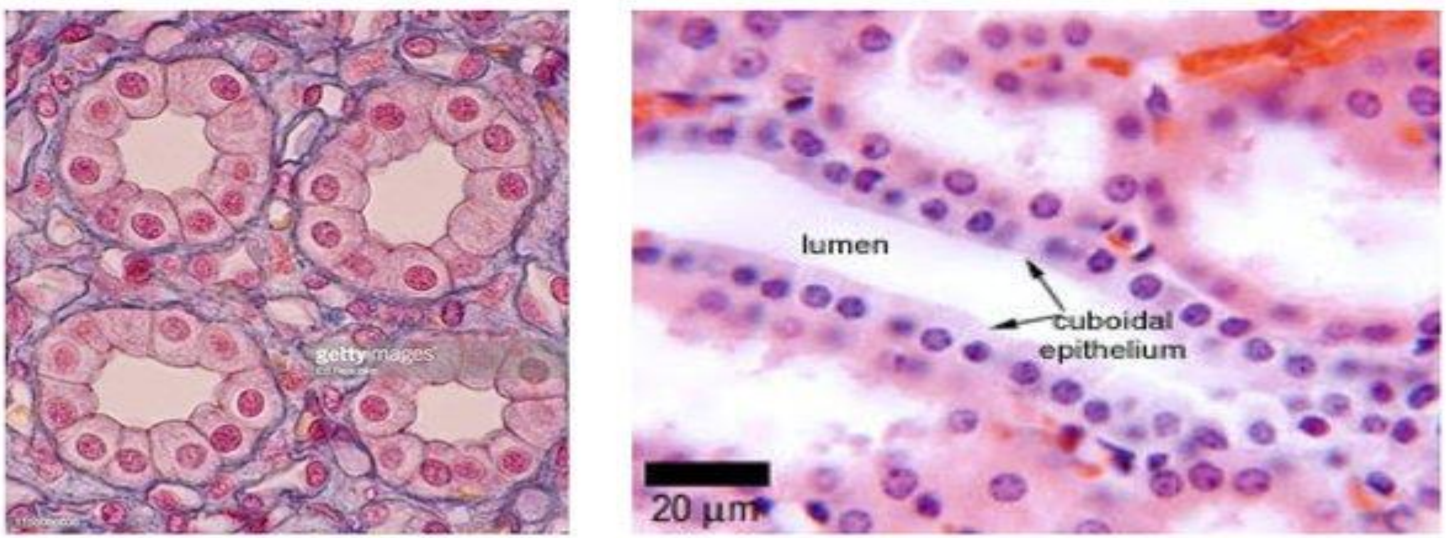
- Cuboidal epithelium: Cuboidal epithelial cells are cube-like in appearance, meaning they have equal width, height and depth.
- Columnar epithelium: Columnar epithelial cells are column-like in appearance, meaning they are taller than they are wide.



Simple cuboidal epithelium

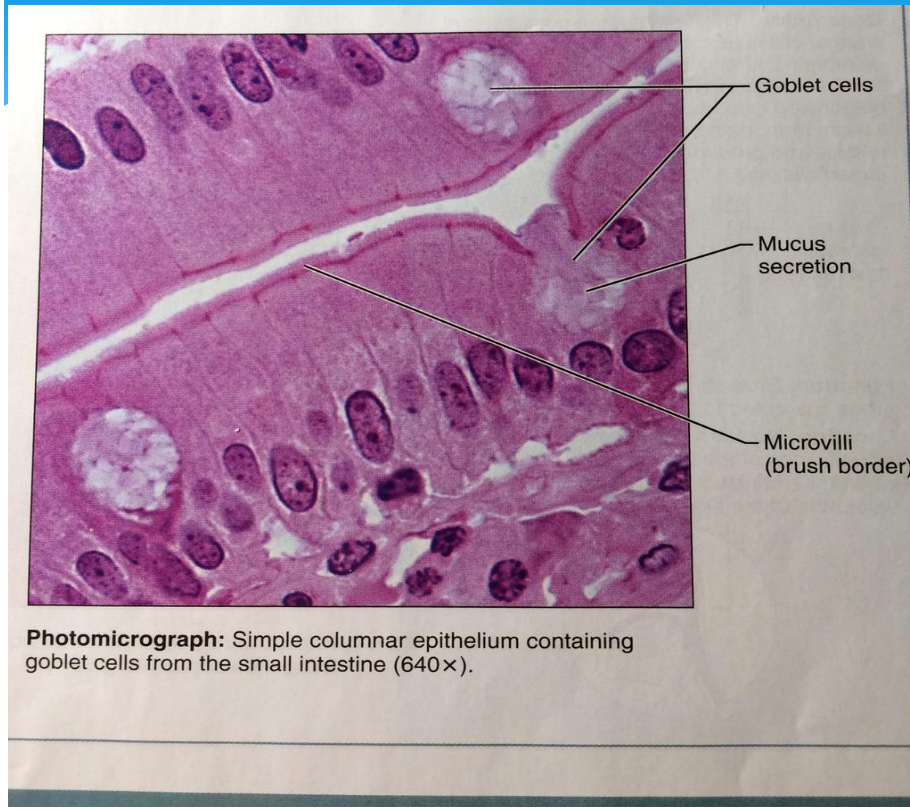
This epithelium is composed of cells which are roughly equal in height and breadth with spherical and centrally placed nuclei. The cytoplasm has more organelles like endoplasmic reticulum and mitochondria compared to simple squamous, which are responsible for several metabolic and functional activities.

Simple cuboidal epithelium



Four kidney tubules in cross section

Kidney tubule in longitudinal section



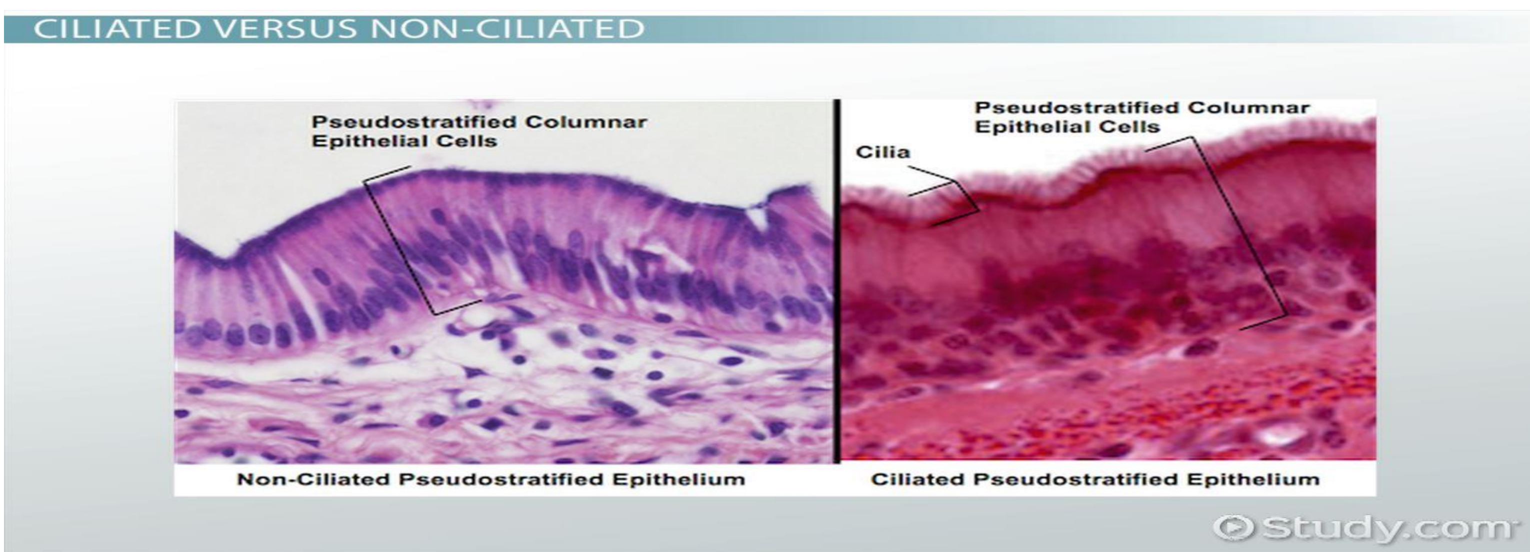
Simple columnar epithelium .

Cells of simple columnar epithelia are taller than they are wide. Such cells are usually highly specialized for absorption, with microvilli, and often have interspersed secretory cells or ciliated cells. Such epithelial cells always have tight and adherent junctional complexes at their apical ends.

pseudostratified columnar epithelia

special type of columnar epithelium composed of a single layer of columnar epithelial cells, which because of positioning and nuclei disposed at different levels appear to be stratified.

Cells of pseudo-stratified epithelia appear to be in layers, but the basal ends of the cells
thick in these are all in contact with the basement membrane, which is often very
epithelia. The best example of this epithelial type is the pseudostratified ciliated
columnar epithelium of the upper respiratory tract, which contains cell types with their
nuclei at different levels that give the false appearance of cellular stratification.

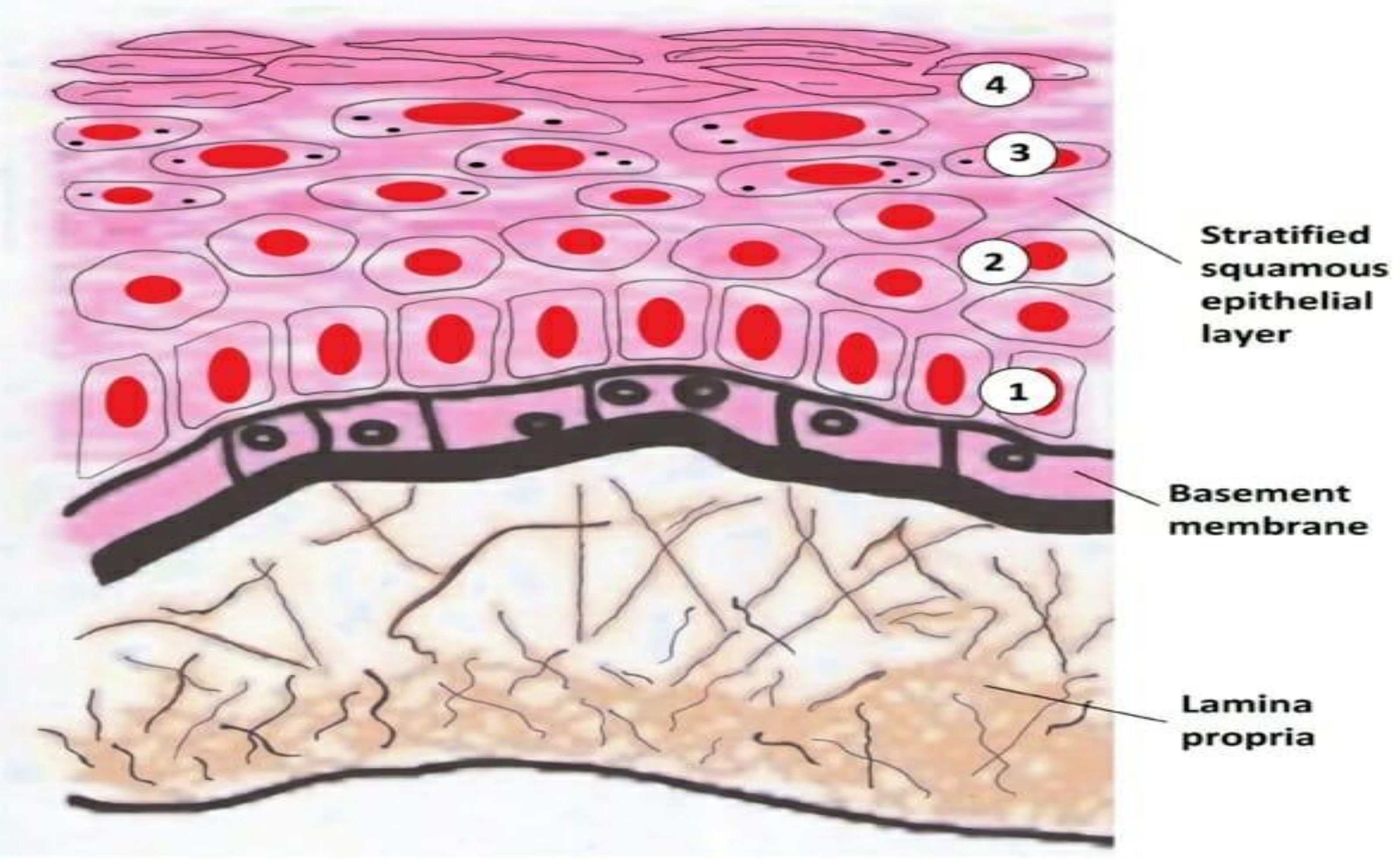


Stratified epithelia are classified according to the cell shape of the superficial layer(s):

squamous, cuboidal, columnar, and transitional.

The very thin surface cells of stratified squamous epithelia can be "keratinized" (rich in keratin intermediate filaments) or "nonkeratinized" (with relatively sparse the amounts of keratin). Stratified squamous keratinized epithelium is found mainly in epidermis of skin. Its cells form many layers, and the cells closer to the underlying connective tissue are usually cuboidal or low columnar. The cells become irregular in shape and flatten as they accumulate keratin in the process of keratinization and are moved progressively closer to the surface, where they become thin, metabolically inactive packets (squames) of keratin lacking nuclei. This surface layer of cells helps protect against water loss across this epithelium.

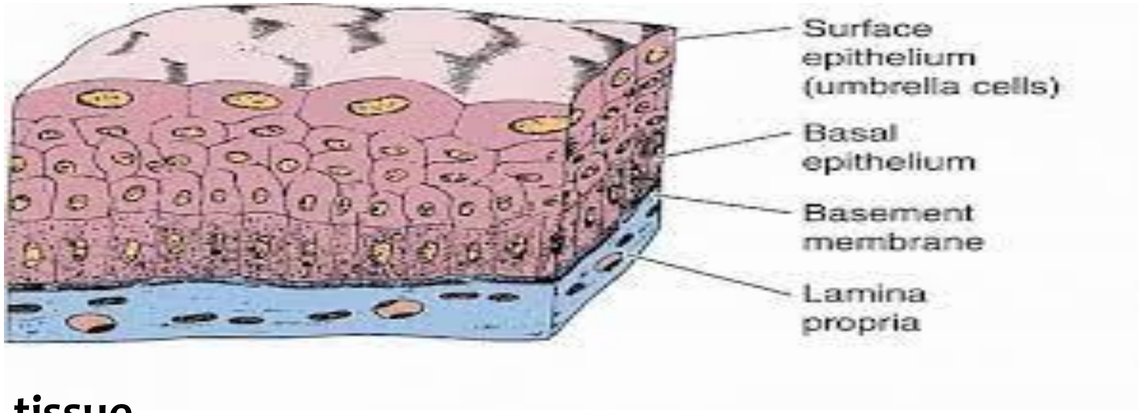
Stratified nonkeratinized epithelium lines wet cavities (eg, mouth, esophagus). In such where water loss is not a problem, the flattened cells, epithelial surface layer are living cells containing much less keratin and retaining their nuclei.



Stratified squamous keratinized epithelial

Transitional epithelium or **urothelium,** which lines only the urinary bladder, the ureter, and the upper part of the urethra, is characterized by a superficial layer of domelike cells that are neither squamous nor columnar ,these cells, sometimes called **umbrella cells**, are essentially protective against the hypertonic and potentially cytotoxic effects of urine. Importantly, the form of the surface cells changes according to the degree of distention of the bladder wall.

Stratified transitional epithelium lining the urinary bladder has rounded or dome-shaped superficial cells with two unusual features. The surface cells have specialized membranes and are able to withstand the hypertonic effects of urine and protect underlying cells from this toxic solution. Cells of transitional epithelium are also able to adjust their relationships with one another as the bladder fills and the wall is stretched, so that the transitional epithelium of a full, distended bladder seems to have fewer cell layers than that of an empty bladder.



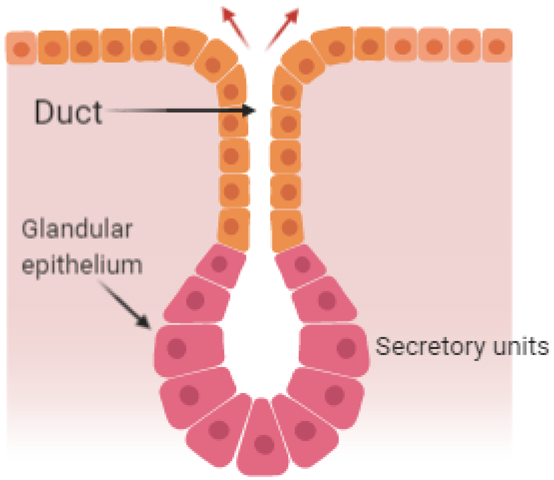
Transitional tissue

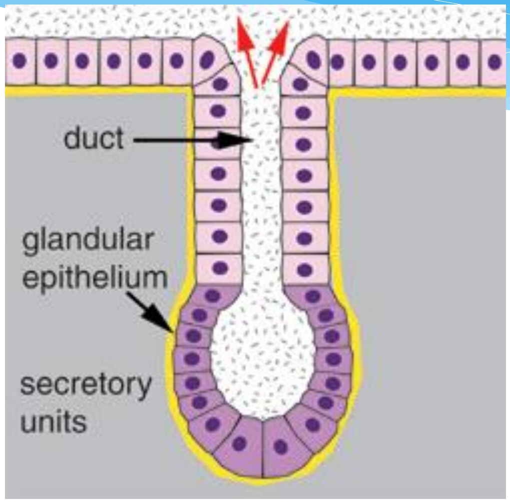
Lecture No. 2

Glandular Epithelia

Glandular epithelia are formed by cells specialized to secrete. The molecules to be secreted are generally stored in the cells in small membrane-bound vesicles called secretory granules.
Glandular epithelial cells may synthesize, store, and secrete proteins (eg, in the pancreas), lipids (eg, adrenal, sebaceous glands), or complexes of carbohydrates and proteins (eg, salivary glands). Mammary glands secrete all three substances. The cells of some glands have low synthetic activity (eg, sweat glands) and secrete mostly water and electrolytes transferred into the gland from the blood.

The epithelia that form glands can be classified according to various criteria.
1-Unicellular glands consist of large isolated secretory cells and
2-multicellular glands have clusters of cells. The classic unicellular gland is the goblet cell in the lining of the small intestine or respiratory tract. The term "gland," however, is
usually used to designate large aggregates of secretory epithelial cells, such as in the salivary glands and the pancreas.


Duct
Glandular
epithelium
Secretory units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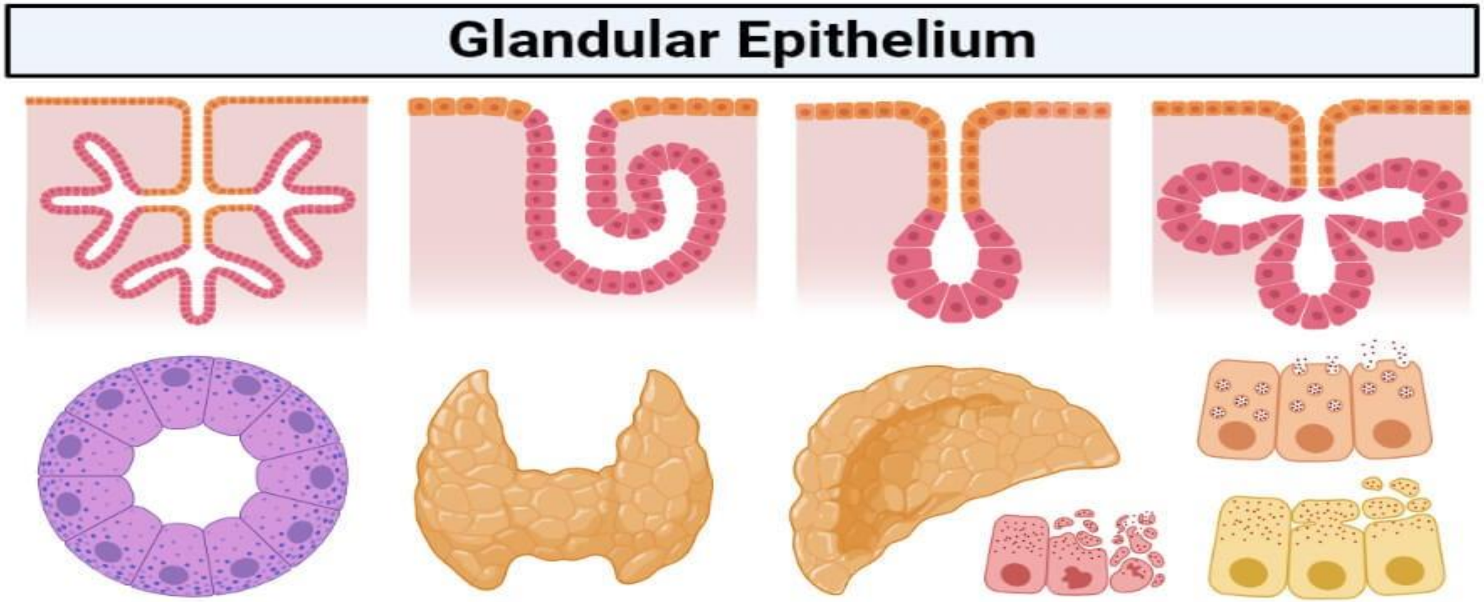

Glandular Epithelium

Unicellular Glands

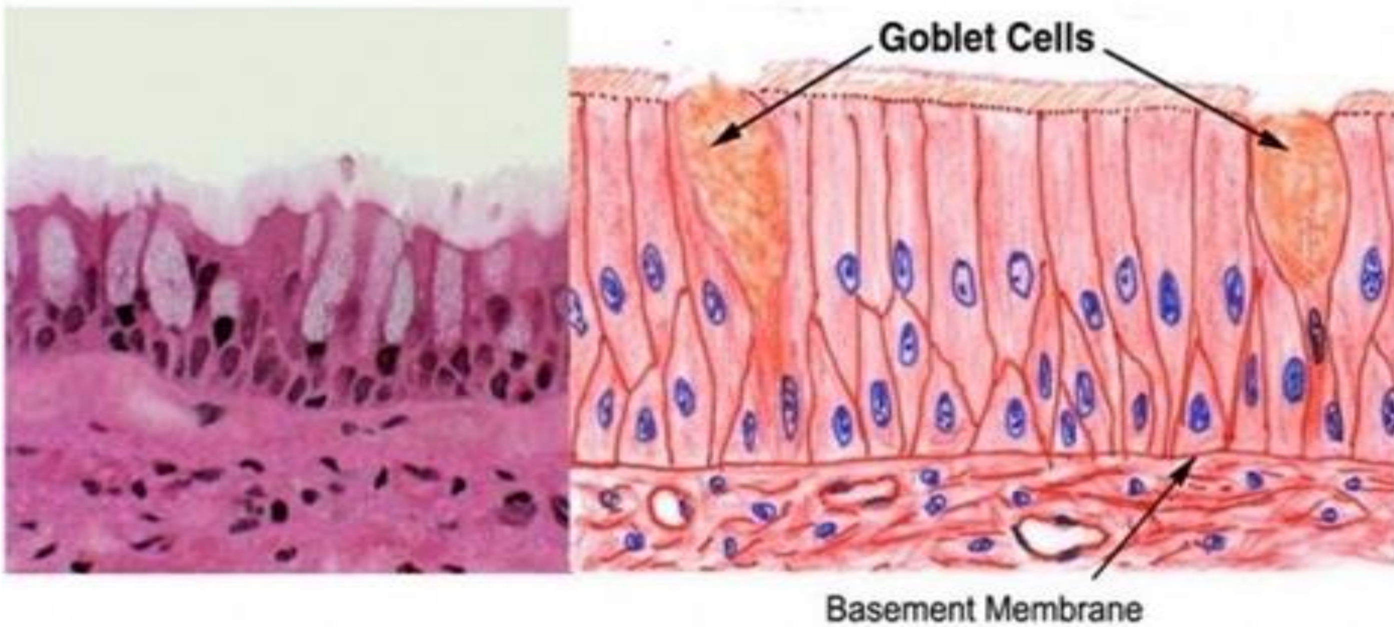
Made of only one glandular epithelium cell; called intraepithelial cells

Goblet cells are the only human example.

Multicellular Glands

Multiple cells make up one gland; called extra epithelial cells

Many examples, including secretory sheets in the human stomach.



The goblet cell is highly polarized with the nucleus and other organelles concentrated at the base of the cell. The remainder of the cell's cytoplasm is occupied by membrane- bound secretory granules containing mucin . .

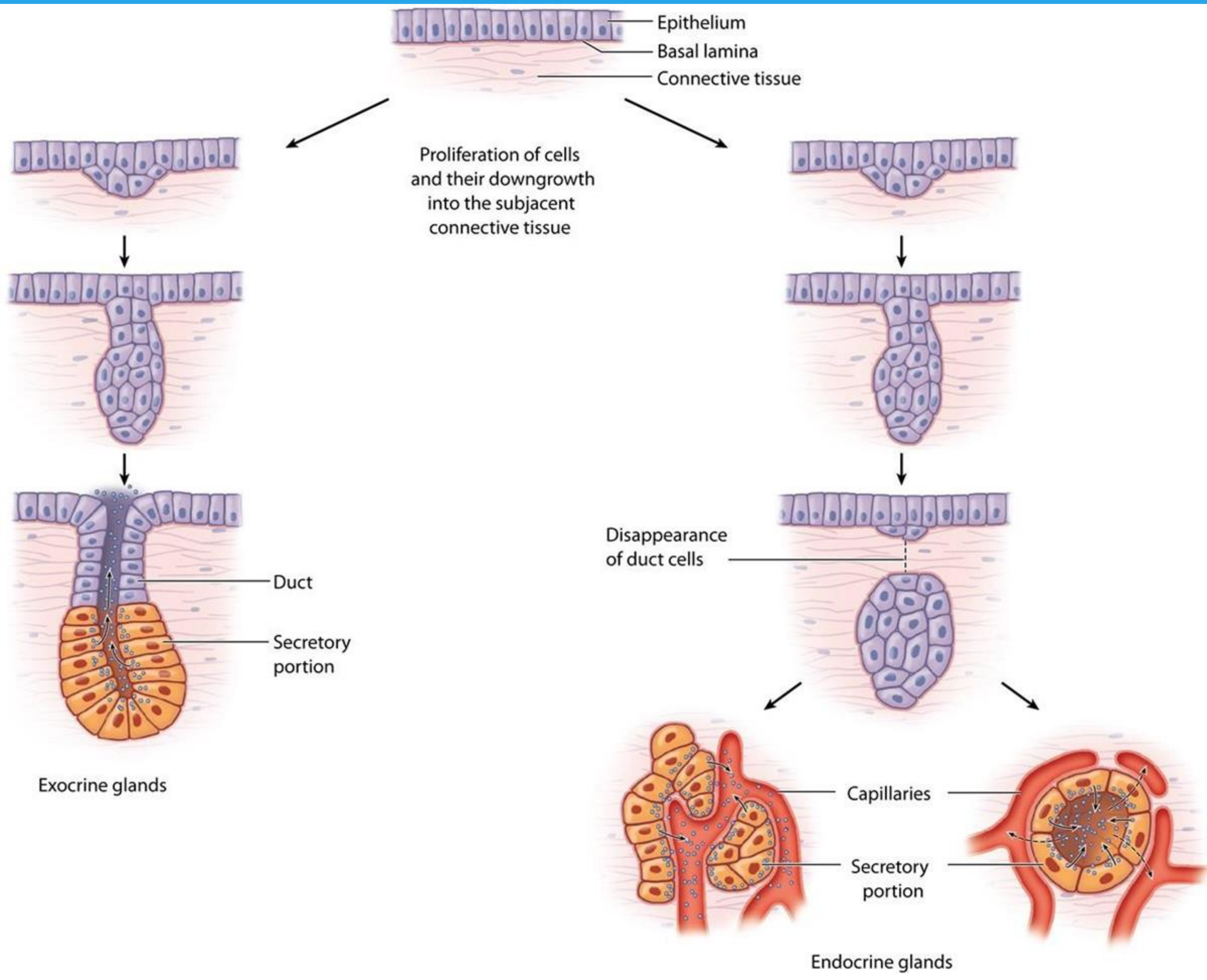
Glands development

Glands develop during fetal life from covering epithelia by means of cells proliferation and invasion of the subjacent connective tissue, followed by further differentiation into

1-Exocrine glands retain their connection with the surface epithelium, the connection taking the form of tubular ducts lined with epithelial cells through which the secretions pass to the surface.

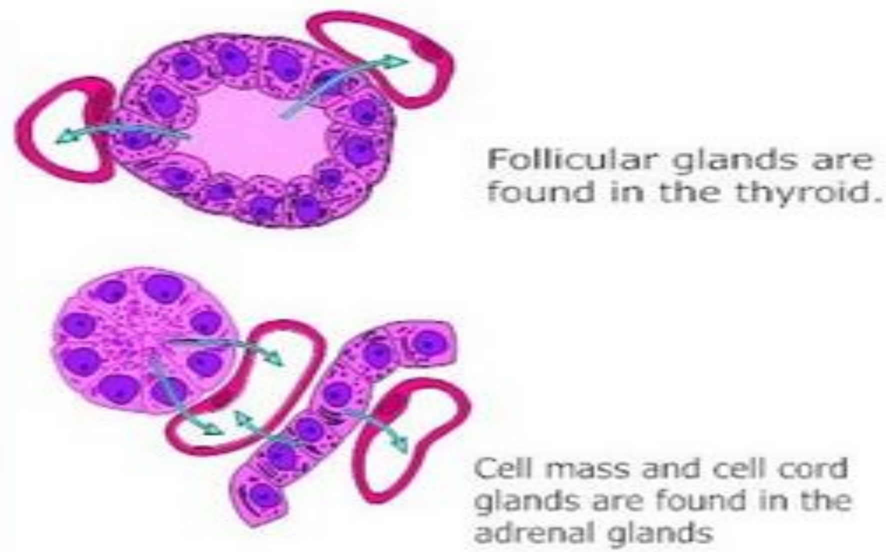
2- Endocrine glands have lost their connection to the surface from which they originated during development. These glands are therefore ductless and their secretions are picked up and transported to their sites of action by the bloodstream rather than by a duct system.

Multicellular glands, whether exocrine or endocrine, also have connective tissue in a surrounding capsule and in septa that divide the gland into lobules. These lobules then subdivide, and in this way the connective tissue separates and binds the glandular components together .


Epithelium
Basal lamina
Connective tissue
Proliferation of cells and their downgrowth into the subjacent connective tissue
Duct
Secretory portion
Exocrine glands
Disappearance of duct cells
Capillaries
Secretory portion
Endocrine glands

The cells of endocrine glands can be arranged in *cords* (e.g. adrenal, parathyroid, Ant pituitary) or in *follicles* .((e.g. thyroid

The lumens of the follicles accumulate large quantities of secretions; cells of the cords store only small quantities of secretions .in their cytoplasm



Exocrine glands are classified according to number of cells into:

A. Unicellular glands

e.g. Goblet cells which are present in • the lining epithelia of intestine and the respiratory tract

B. Multicellular glands

They form most of the glands of the body e.g. salivary gland

General structure of exocrine glands

Exocrine glands by definition have ducts that lead to an organ or body surface. Inside the gland the duct runs through connecting septa and branches repeatedly, until its smallest branches end in the secretory portions of the gland.

Exocrine glands have a secretory portion, which contains the cells specialized for secretion, and ducts, which transport the secretion out of the gland. The morphology of these components allows the glands to be classified as follows:

Ducts can be

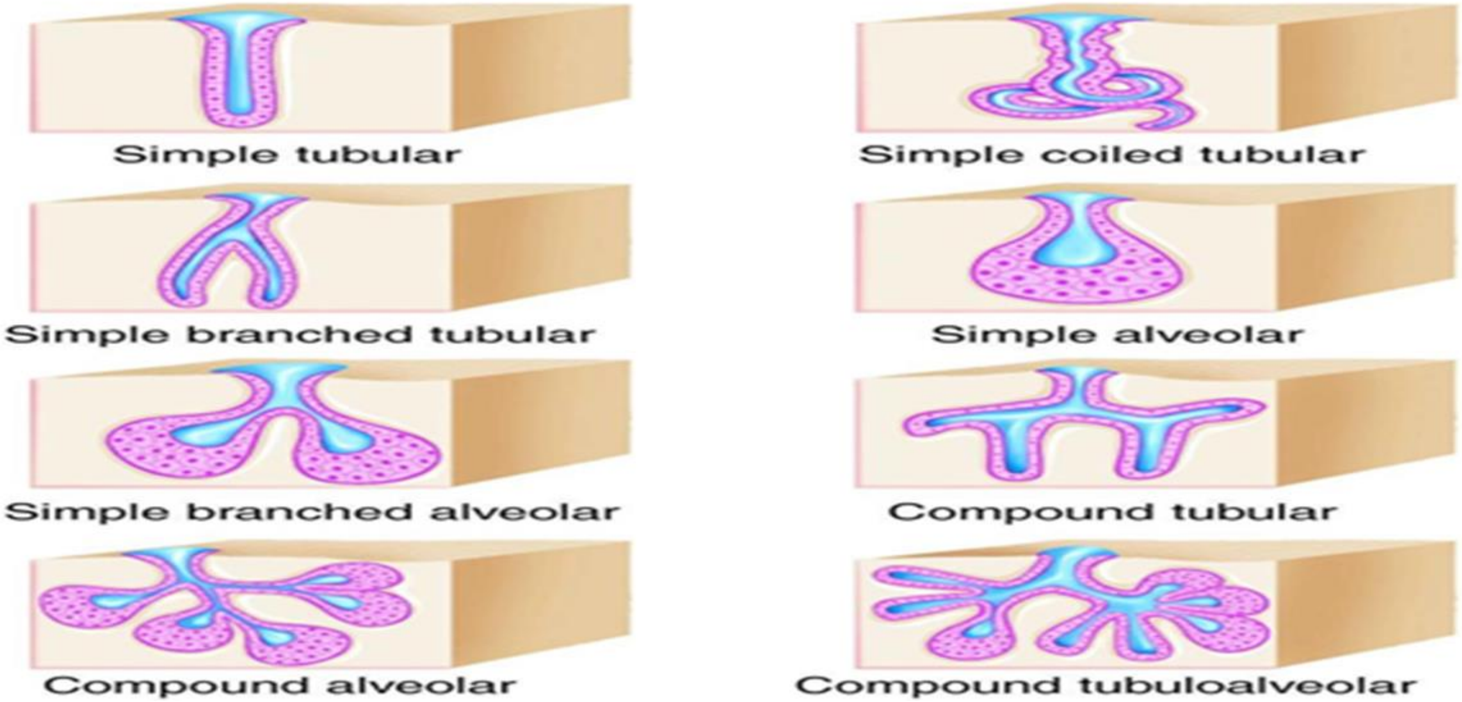
1-simple (unbranched) or

2-compound (with two or more branches).

Secretory portions can be tubular (either short or long and coiled) or acinar (round or globular).

Either type of secretory portion may be branched.

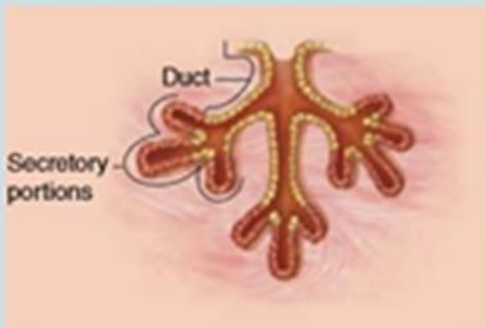
Compound glands can have tubular, acinar, or tubuloacinar secretory portions.


Simple tubular
Simple coiled tubular
Simple branched tubular
Simple alveolar
Simple branched alveolar
Compound tubular
Compound alveolar
Compound tubuloalveolar

SIMPLE Glands **(Ducts Do Not Branch)**

Class	Simple Tubular	Branched Tubular	Coiled Tubular	Acinar (or Alveolar)	Branched Acinar
Features	Elongated secretory portion; duct usually short or absent	Several long secretory parts joining to drain into 1 duct	Secretory portion is very long and coiled	Rounded, saclike secretory portion	Multiple saclike secretory parts entering the same duct
Examples	Mucous glands of colon; intestinal glands or crypts (of Lieberkühn)	Glands in the uterus and stomach	Sweat glands	Small mucous glands along the urethra	Sebaceous glands of the skin

COMPOUND Glands (Ducts from Several Secretory Units Converge into Larger Ducts)

Class	Tubular	Acinar (Alveolar)	Tubuloacinar
			
Features	Several *elongated* coiled secretory units and their ducts converge to form larger ducts	Several *saclike* secretory units with small ducts converge at a larger duct	Ducts of both tubular and acinar secretory units converge at larger ducts
Examples	Submucosal mucous glands (of Brunner) in the duodenum	Exocrine pancreas	Salivary glands

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Classification on the basis of the mode of secretion

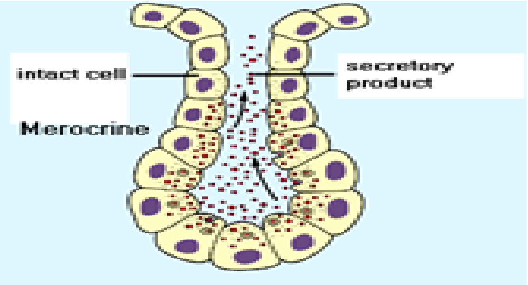
- Depending on their mode of secretion i.e; the manner in which the secretory product is elaborated, the exocrine glands are classified :into the following varieties

١. Merocrine glands
٢. Apocrine glands
٣. Holocrine glands

Merocrine glands

The secretory product is delivered in membrane-bounded vesicles to the apical surface of the cell. Here, vesicles fuse with the plasma membrane and extrude their contents by **exocytosis**

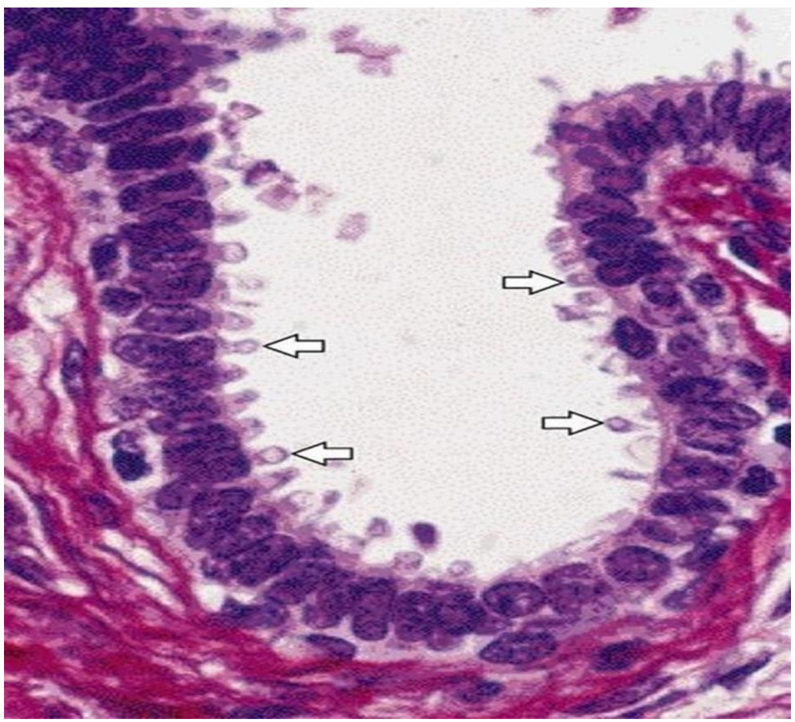
e.g; pancreas, salivary glands



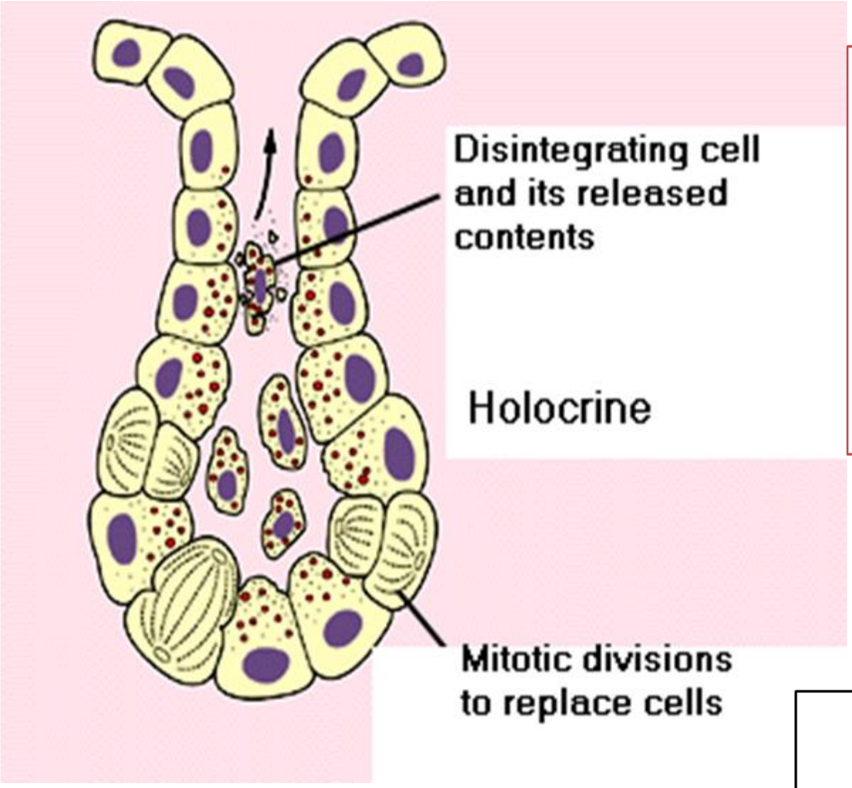
Apocrine glands

In these glands part of the apical cytoplasm is lost along with the secretory material .

e.g ; lactating mammary glands, special sweat glands located in axilla and perianal area and the ceremonious glands of the external auditory meatus.

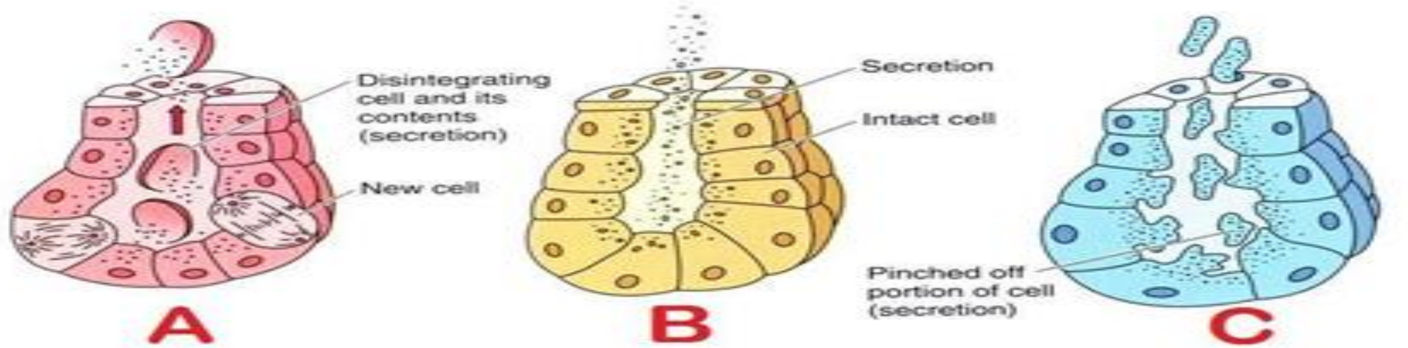


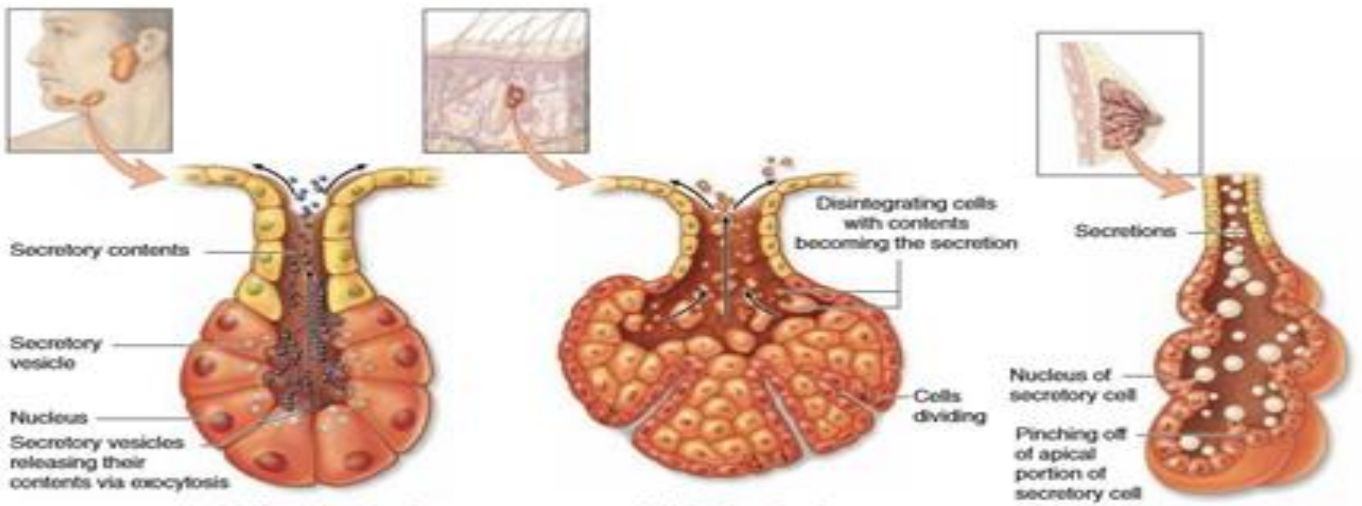
Holocrine glands



In these glands entire cells laden with secretory material disintegrate and all of the cellular contents are discharged from the gland as secretions

e.g; the sebaceous glands of skin





(a) **Merocrine gland** (b) **Holocrine gland** (c) **Apocrine gland**

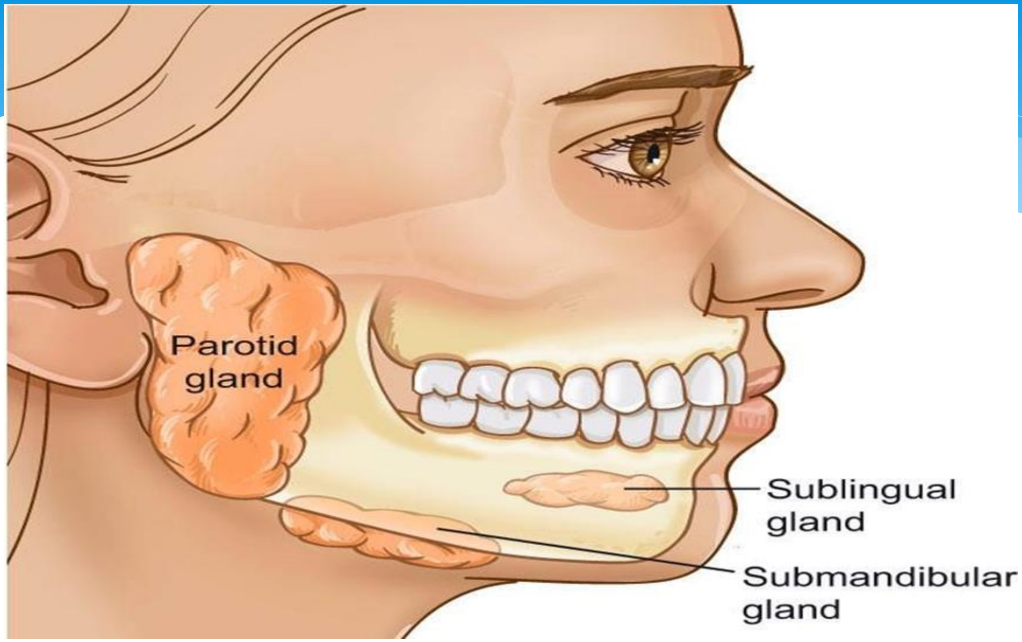
Classification on the basis of nature of secretory product:

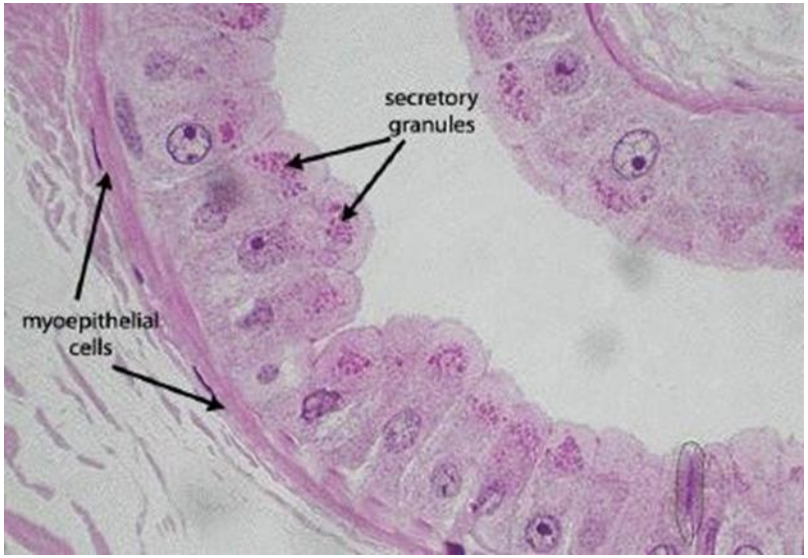
Exocrine glands with merocrine secretion can be further categorized as either serous or mucous according to the nature of the proteins or glycoproteins secreted and the resulting staining properties of the secretory cells. The acinar cells of the pancreas and parotid salivary glands are examples of the serous type which secrete digestive enzymes.

1-Mucous glands: these glands produce a viscid, slimy, carbohydrate-rich secretion which is called mucus, e.g; the goblet cells, some glands in digestive tube, respiratory tract and genital tract.

2-Serous glands: these glands produce a thin, watery, protein- rich secretions, often high in enzymatic activity e.g; the parotid salivary gland.

3-Mixed (seromucous) glands: these glands produce both mucous and serous secretions e.g; the sublingual and submandibular salivary glands.





Myoepithelial cells

Located between the secretory cells and the basement membrane

Rich in actin and myosin

Lecture No. 3

Connective tissue

contributes to numerous body functions, including supporting organs and cells, transporting nutrients and wastes, defending against pathogens, storing fat, and repairing damaged tissues. Connective tissue is composed primarily of an extracellular matrix and a limited number of cells . Extracellular matrices consist of different combinations of protein fibers (collagen, reticular, and elastic fibers) and ground substance.

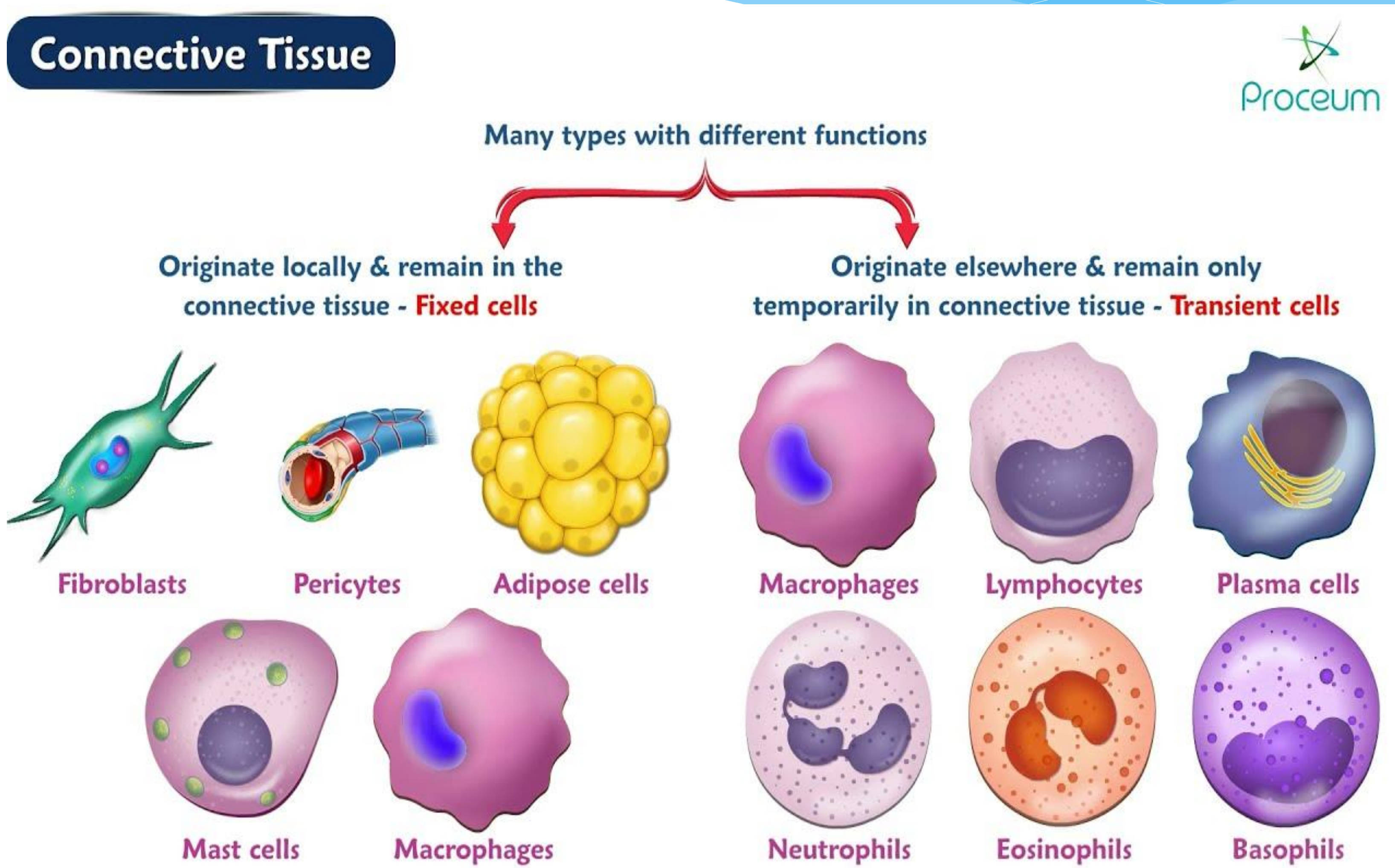
Ground substance is a highly hydrophilic, viscous complex of anionic macromolecules (glycosaminoglycans and proteoglycans) and multi adhesive glycoproteins (laminin, fibronectin, and others) that stabilizes the(ECM) by binding to receptor proteins (integrins) on the surface of cells and to the other matrix components. The connective tissues originate from the mesenchyme, an embryonic tissue formed by elongated undifferentiated cells, the mesenchymal cells.

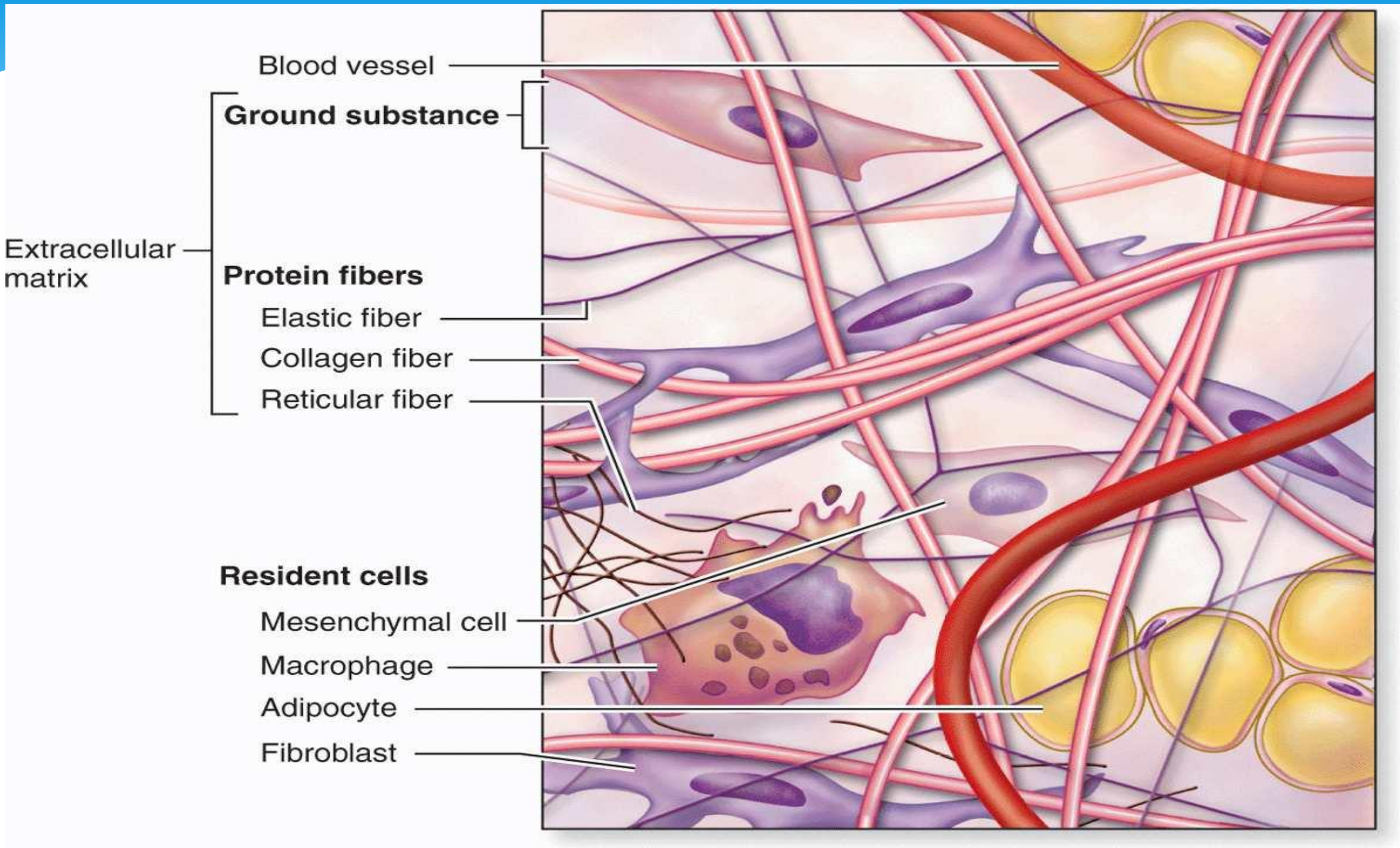
CELLS OF CONNECTIVE TISSUE

variety of cells with different origins and functions are present in connective tissue , Fibroblasts originate locally from undifferentiated mesenchymal cells and spend all their life in connective tissue,adipocyte and pericyte.

other cells such as mast cells, macrophages, and plasma cells originate from hematopoietic stem cells in bone marrow, circulate in the blood, and then move into connective tissue where they remain and execute their functions.

White blood cells (leukocytes) are transient cells of most connective tissues; they also originate in the bone marrow and move to the connective tissue where they reside for a few days, then usually die by apoptosis.


Connective Tissue
Proceum
Many types with different functions
Originate locally & remain in the connective tissue - Fixed cells
Originate elsewhere & remain only temporarily in connective tissue - Transient cells
Fibroblasts
Pericytes
Adipose cells
Macrophages
Lymphocytes
Plasma cells
Mast cells
Macrophages
Neutrophils
Eosinophils
Basophils



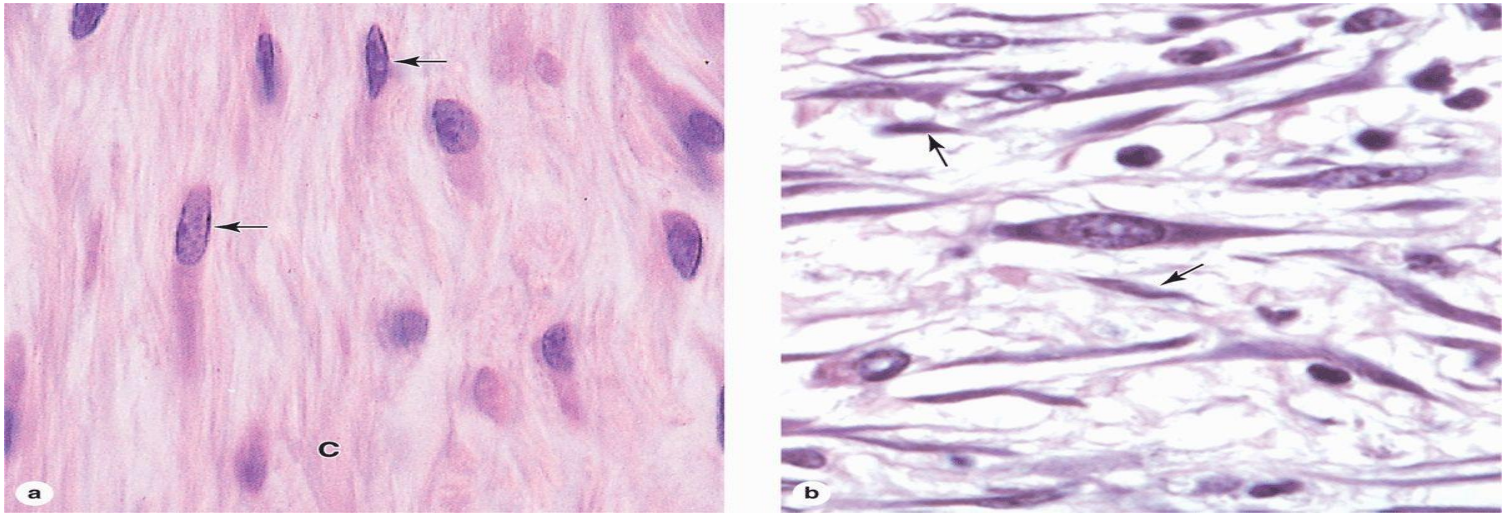
(Connective tissue components)

Cell Type	Major Product or Activity
Fibroblasts (fibrocytes)	Extracellular fibers and ground substance
Plasma cells	Antibodies
Lymphocytes (several types)	Various immune/defense functions
Eosinophilic leukocytes	Modulate allergic/vasoactive reactions and defense against parasites
Neutrophilic leukocytes	Phagocytosis of bacteria
Macrophages	Phagocytosis of ECM components and debris; antigen processing and presentation to immune cells; secretion of growth factors, cytokines, and other agents
Mast cells and basophilic leukocytes	Pharmacologically active molecules (eg, histamine)
Adipocytes	Storage of neutral fats

Fibroblasts

Fibroblasts synthesize collagen, elastin, glycosaminoglycans, proteoglycans and multi adhesive glycoproteins. Fibroblasts are the most common cells in connective tissue and are responsible for the synthesis of extracellular matrix components.

Two stages of activity—active and quiescent ,Cells with intense synthetic activity are morphologically distinct from the quiescent fibroblasts that are scattered within the matrix they have already synthesized. Some histologists reserve the term fibroblast to denote the active cell and fibrocyte to denote the quiescent cell.



(a) Fibroblasts typically have large active nuclei and tapers off in both directions along the axis of the nucleus, a morphology referred as "spindle-shaped." Nuclei (arrows) are clearly seen, but the eosinophilic cytoplasmic processes resemble the collagen bundles (C).

(b) Both active and quiescent fibroblasts may sometimes be distinguished, as in this section of dermis. Active fibroblasts have large, euchromatic nuclei and basophilic cytoplasm, while inactive fibroblasts (or fibrocytes) are smaller with more heterochromatic nuclei (arrows). The round, very basophilic round cells are in leukocytes.

Adipocytes

Adipocytes (L. adeps, fat + Gr. kytos, cell), or fat cells, are found in connective tissue of many organs. These large, mesenchymally derived cells are specialized for cytoplasmic storage of lipid as neutral fats, or less commonly for the production of heat. The large deposits of fat in the cells of adipose connective tissue also serve to cushion and insulate the skin and other organs.

Macrophages & the Mononuclear Phagocyte System

Macrophages are characterized by their well-developed phagocytic ability and specialize in turnover of protein fibers and removal of dead cells, tissue debris, or other particulate material. They have a wide spectrum of morphologic features corresponding to their state of functional activity and to the tissue they inhabit, has an eccentrically located, oval or kidney-shaped nucleus. Macrophages are present in the connective tissue of most organs and are often referred to by pathologists as “histiocytes.”

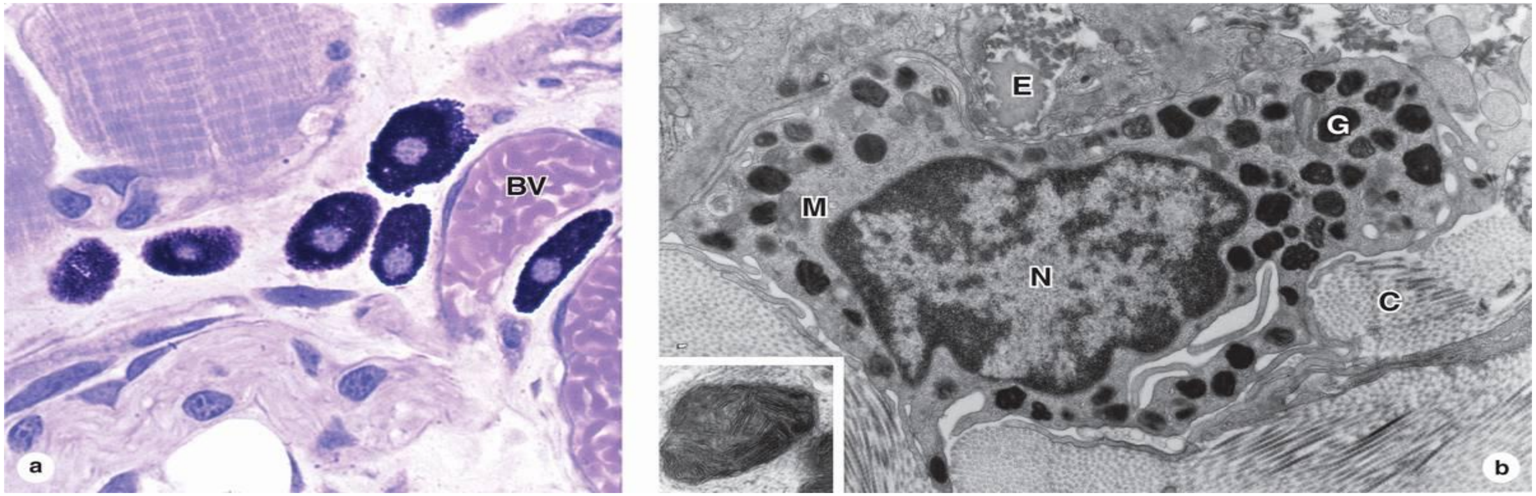
Macrophages derive from bone marrow precursor cells that divide, producing monocytes that circulate in the blood. These cells cross the epithelial wall of venules to penetrate connective tissue, where they differentiate further, mature, and acquire the morphologic features of phagocytic cells. Therefore, monocytes and macrophages are the same cell at different stages of maturation.

The macrophage-like cells have been given different names in different organs, for example Kupffer cells in the liver, microglial cells in the central nervous system, Langerhans cells in the skin, and osteoclasts in bone tissue. However, all are derived from monocytes. All are long-living cells and may survive for months in the tissues.

Cell Type	Major Locations	Main Function
Monocyte	Blood	Precursor of macrophages
Macrophage	Connective tissue, lymphoid organs, lungs, bone marrow, pleural and peritoneal cavities	Production of cytokines, chemotactic factors, and several other molecules that participate in inflammation (defense), antigen processing, and presentation
Kupffer cell	Liver (perisinusoidal)	Same as macrophages
Microglial cell	Central nervous system	Same as macrophages
Langerhans cell	Epidermis of skin	Antigen processing and presentation
Dendritic cell	Lymph nodes, spleen	Antigen processing and presentation
Osteoclast (from fusion of several macrophages)	Bone	Localized digestion of bone matrix
Multinuclear giant cell (several fused macrophages)	In connective tissue under various pathological conditions	Segregation and digestion of foreign bodies

Mast Cells

Mast cells are oval or irregularly shaped connective tissue cells, whose cytoplasm is filled with basophilic secretory granules. The nucleus is centrally situated and often obscured by abundant secretory granules , mast cell granules display metachromasia, which means that they can change the color of some basic dyes (eg, toluidine blue) from blue to purple or red. The granules are poorly preserved by common fixatives, so that mast cells are frequently difficult to identify.



Mast cells function in the localized release of many bioactive substances with roles in the local inflammatory response, innate immunity, and tissue repair, important of secretory granules includes the following :

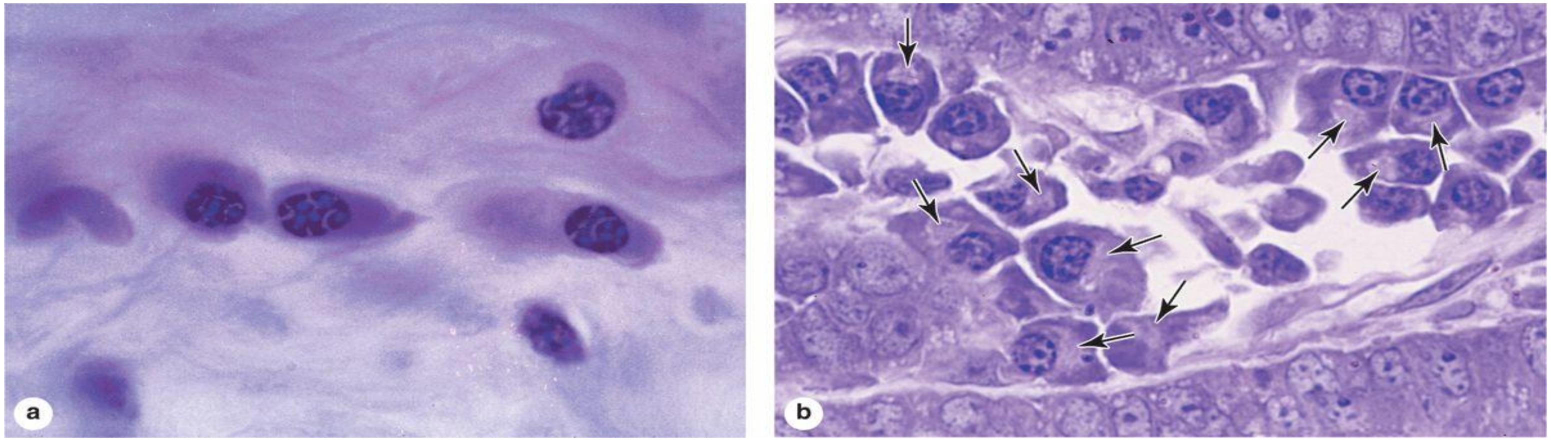
Heparin, a sulfated GAG that acts locally as an anticoagulant

Histamine, which promotes increased vascular permeability and smooth muscle contraction. Serine proteases, which activate various mediators of inflammation

Occurring in connective tissue of many organs, mast cells are especially numerous near small blood vessels in skin and mesenteries (perivascular mast cells) and in the tissue that lines digestive and respiratory tracts (mucosal mast cells); the granule content of the two populations differs somewhat.

Plasma Cells

Plasma cells are large, ovoid cells that have a basophilic cytoplasm due to their richness in rough ER. The juxtanuclear Golgi apparatus and the centrioles occupy a region that appears pale in regular histologic preparations.



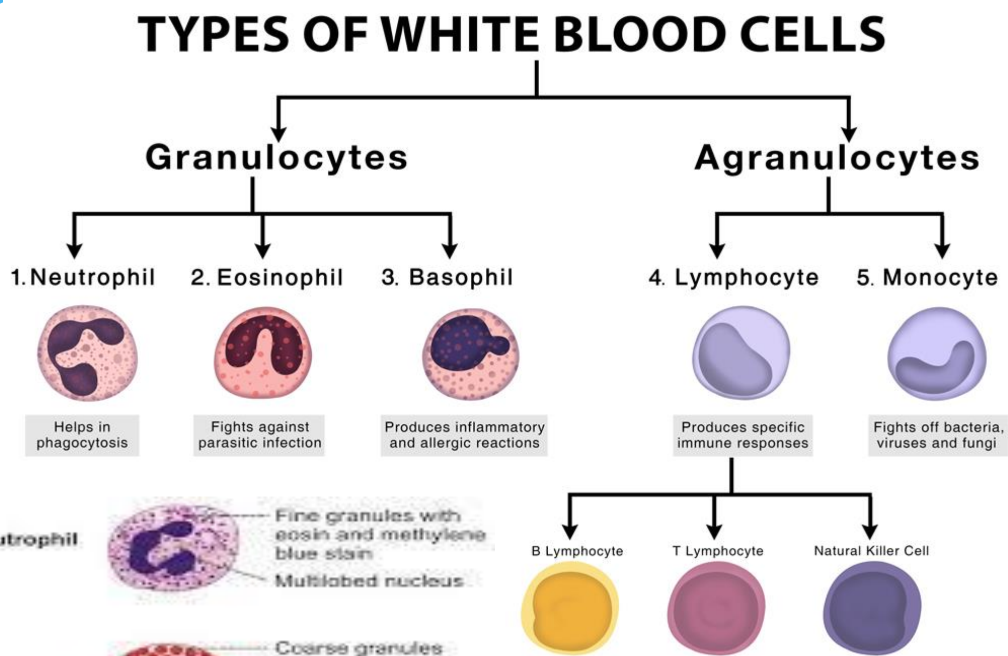
(a) Plasma cells are large, ovoid cells, with basophilic cytoplasm. The round nuclei frequently show peripheral clumps of heterochromatin, giving the structure a "clock-face" appearance.

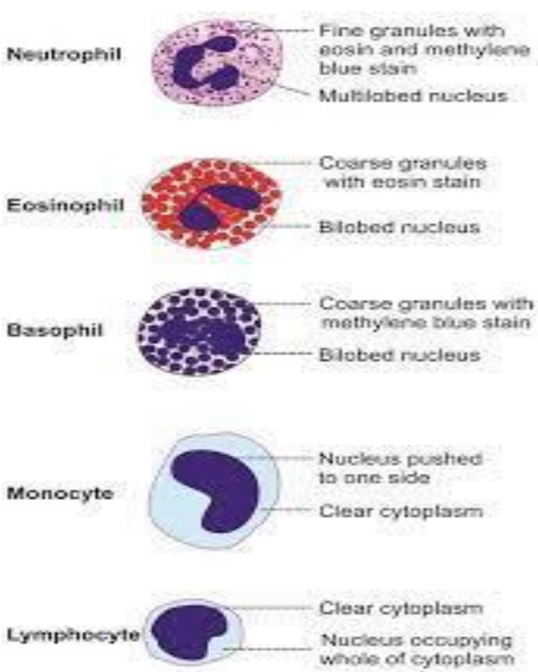
(b) Plasma cells are often more abundant in infected tissues.

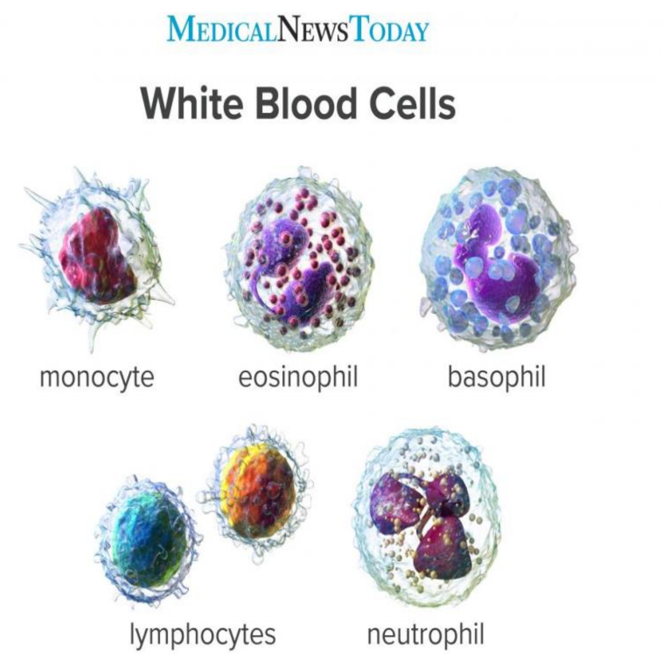
The nucleus of the plasma cell is generally spherical but eccentrically placed. Many of these nuclei contain compact, peripheral regions of heterochromatin alternating with lighter areas of euchromatin, a configuration that can give the nucleus of a plasma cell the appearance of a clock face. There are at least a few plasma cells in most connective tissues. Their average lifespan is only 10-20 days.

Leukocytes

Connective tissue normally contains leukocytes that migrate from the blood vessels by diapedesis. Leukocytes or white blood corpuscles, are the wandering cells of the connective tissue. They leave blood by migrating between the endothelial cells lining capillaries and venules to enter connective tissue by a process called diapedesis. This process increases greatly during inflammation, which is a vascular and cellular defensive reaction against foreign substances.







Granulocytes and a granulocytes are the two types of white blood cells or leukocytes.

Granulocytes contain granules or sacs in their cytoplasm and a granulocytes do not. The three types of granulocytes are neutrophils, eosinophils, and basophils.

The two types of agranulocytes are lymphocytes and monocytes.

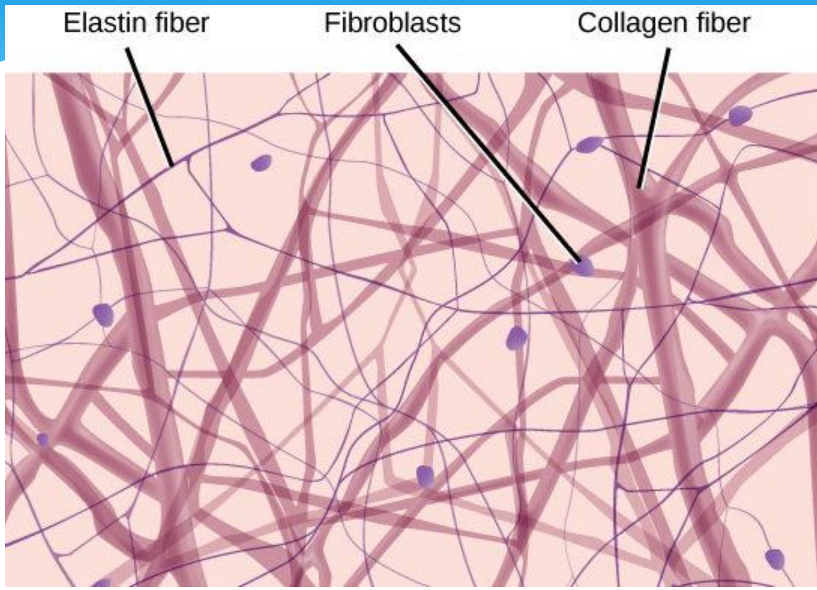
FIBERS

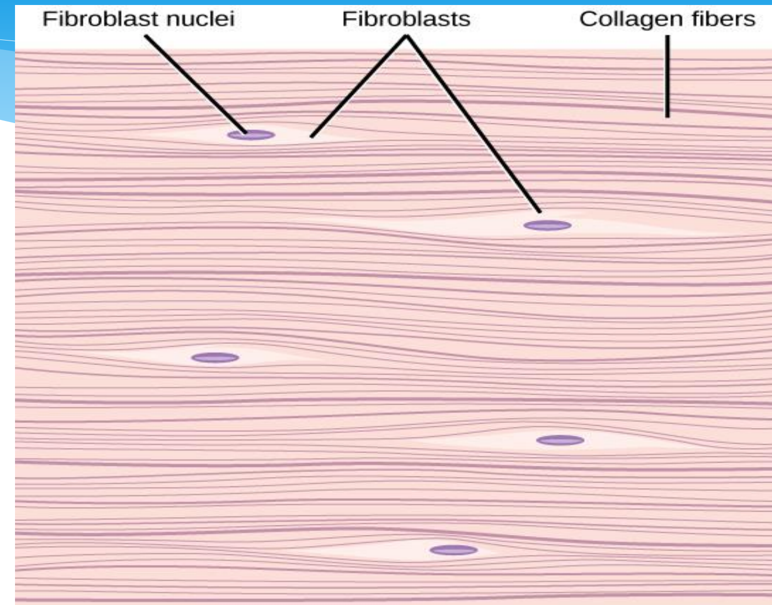
The connective tissue fibers are formed by proteins that polymerize into elongated structures. The three main types of connective tissue fibers are collagen, reticular, and elastic fibers. Collagen and reticular fibers are both formed by the protein collagen, and elastic fibers are composed mainly of the protein elastin. These fibers are distributed unequally among the types of connective tissue and the predominant fiber type is usually responsible for conferring specific properties on the tissue.

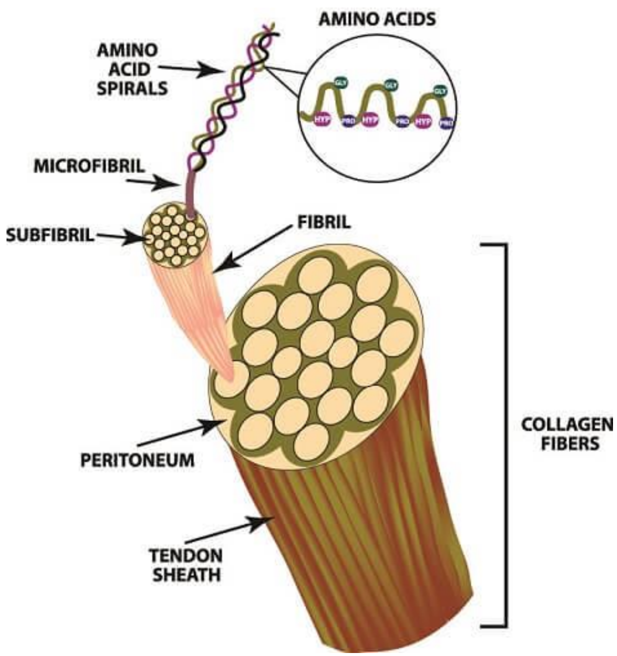
1- Collagen

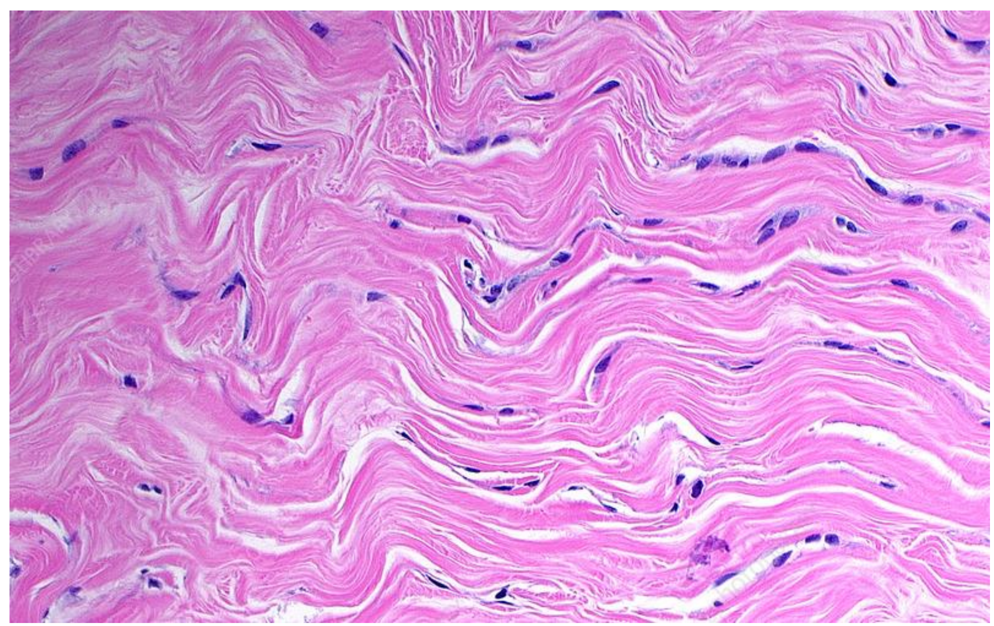
The collagens constitute a family of proteins selected during evolution for the execution of several (mainly structural) functions. These proteins are known collectively as collagen, and the chief examples among its various types are present in the skin, bone, cartilage, smooth muscle, and basal lamina.

Collagen fibers are the most abundant type of fibers in an extracellular matrix of connective tissue; this is also the case for connective tissue within a section of the peripheral nerve. Nowadays we know almost 30 types of collagen molecules, but 4 basic types are most represented.


Elastin fiber
Fibroblasts
Collagen fiber


Fibroblast nuclei
Fibroblasts
Collagen fibers


AMINO ACIDS
AMINO ACID SPIRALS
MICROFIBRIL
SUBFIBRIL
FIBRIL
COLLAGEN FIBERS
PERITONEUM
TENDON SHEATH



Types

Collagen I- found in bones, tendons, organs.

Collagen II- found mainly in cartilage.

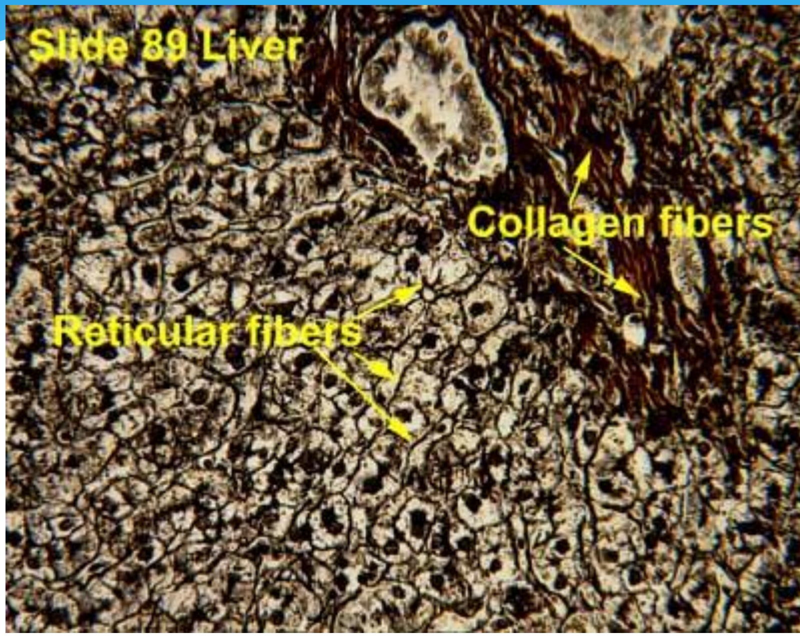
Collagen III- found mainly in reticular fibers (fine fibrous connective tissue occurring in networks to make up the supporting tissue of many organs).

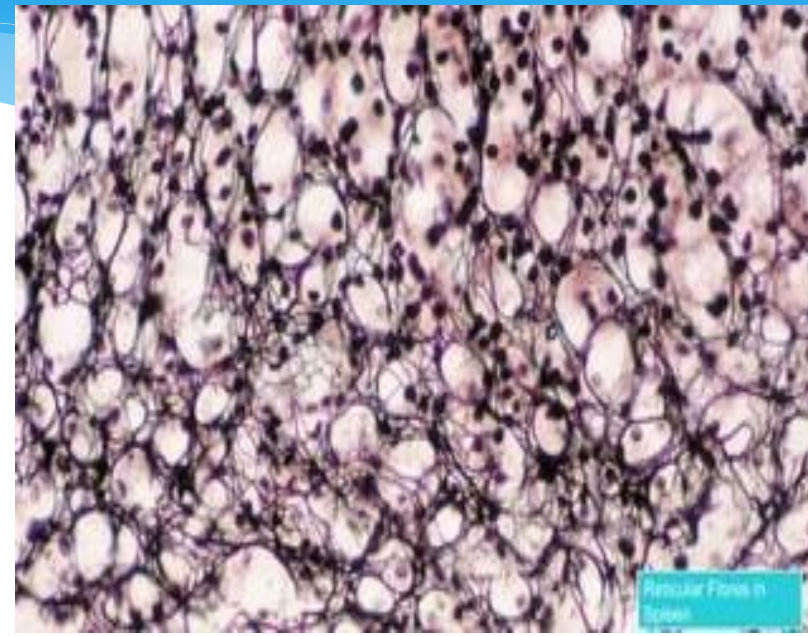
Collagen V Participates in type I collagen function

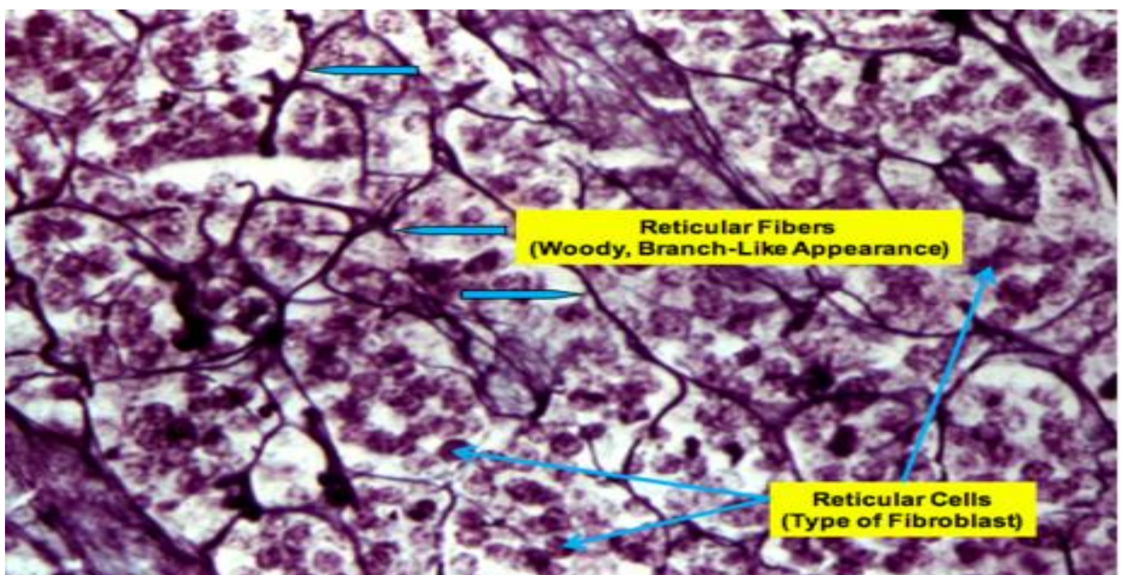
Collagen is the most abundant and has a widespread distribution. It occurs in tissues as structures that are classically designated as collagen fibers forming structures such as tendons, organ capsules, and dermis.

Reticular Fibers

of Uniquely distinct from collagen, reticular fibers are now known to consist mainly collagen type III, which forms extensive networks of extremely thin fibers in certain organs. They are not visible in hematoxylin-and-eosin (H&E) preparations but can be easily stained black by impregnation with silver salts. Because of their affinity for silver salts, these fibers are called argyrophilic .

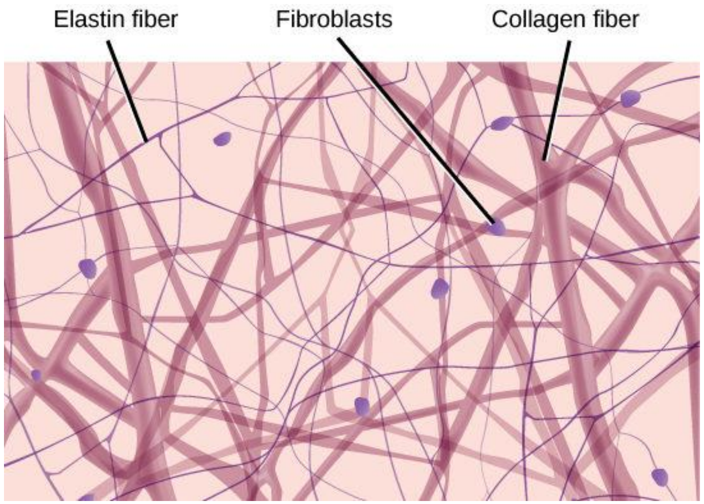

Slide 89 Liver
Collagen fibers
Reticular fibers

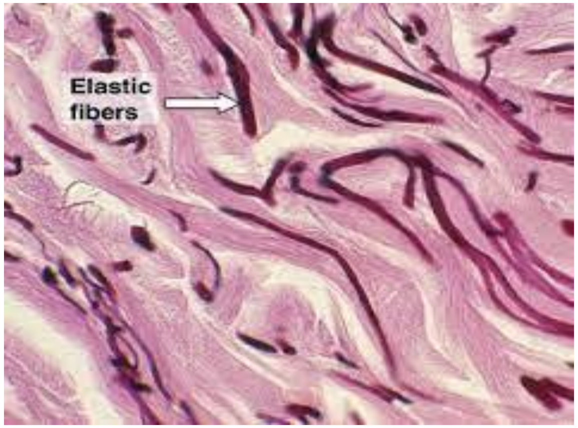



Reticular Fibers
(Woody, Branch-Like Appearance)
Reticular Cells
(Type of Fibroblast)

Elastic Fibers

Elastic fibers are also thinner than the average collagen fiber and form sparse networks interspersed with collagen bundles in many organs subject to much bending or stretching, such as the wall of large arteries. The name indicates the major functional property such fibers impart to these resilient organs .





Collagen Elastin vs Reticular Fibers

More Information Online WWW.DIFFERENCEBETWEEN.COM

	Collagen Fibers	Elastin Fibers	Reticular Fibers
	Collagen fibers are the strongest and thickest fibers	Elastin fibers are thinner fibers which can stretch and recoil	Reticular fibers are highly branched delicate fibers found in organs that have lots of mesh- like structures
ABUNDANCE IN EM	Collagen fibers are the most abundant type	Elastin fibers are less abundant compared to collagen fibers	Reticular fibers are less abundant than collagen fibers
PROTEIN	Collagen	Elastin	Collagen type III
FOUND IN	Various types of connective tissues such as cartilage, tendons, bones, and ligaments	Elastic tissues	Spleen and lymphoid organs
THICKNESS	Collagen fibers are the thickest fibers	Thin fibers	Thin fibers
STRENGTH	Collagen fibers are the strongest fibers	Less stronger than collagen fibers	Less stronger than collagen fibers

Ground Substance

The ground substance of the ECM is a highly hydrated, transparent, complex mixture of macromolecules, principally in three classes: glycosaminoglycans (or GAGs), proteoglycans, and multiadhesive glycoproteins. The complex molecular mixture of the ground substance is transparent and rich in bound water. It fills the space between cells and fibers of connective tissue and, because it is viscous, acts as both a lubricant and a barrier to the penetration of invaders.

GAGs (originally called mucopolysaccharides) are linear polysaccharides formed by repeating disaccharide units usually composed of a uronic acid and a hexosamine.

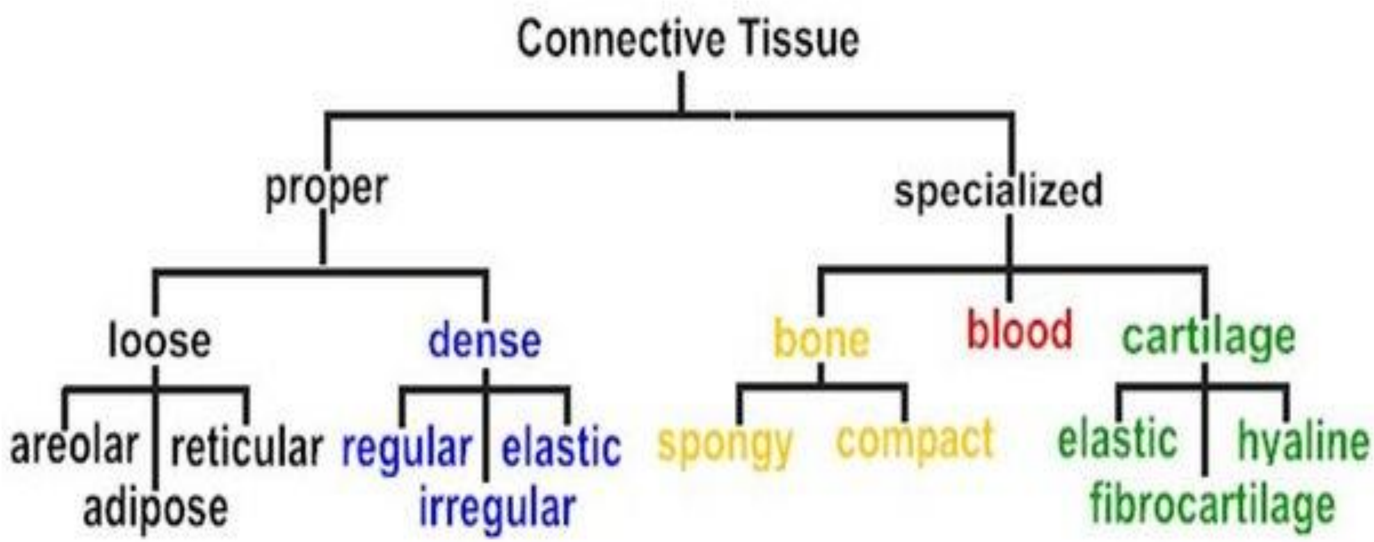
Proteoglycans are composed of a core protein to which are covalently attached various numbers and combinations of the sulfated GAGs just mentioned.

Multi adhesive glycoproteins have carbohydrates attached, but in contrast to proteoglycans the protein moiety usually predominates.

Lecture No. 4

TYPES OF CONNECTIVE TISSUE

Connective tissues composed of the cells, fibers, and ground substance components ,this has led to the classifications for various connective tissue types, denoting either the major component or a structural characteristic of the tissue.

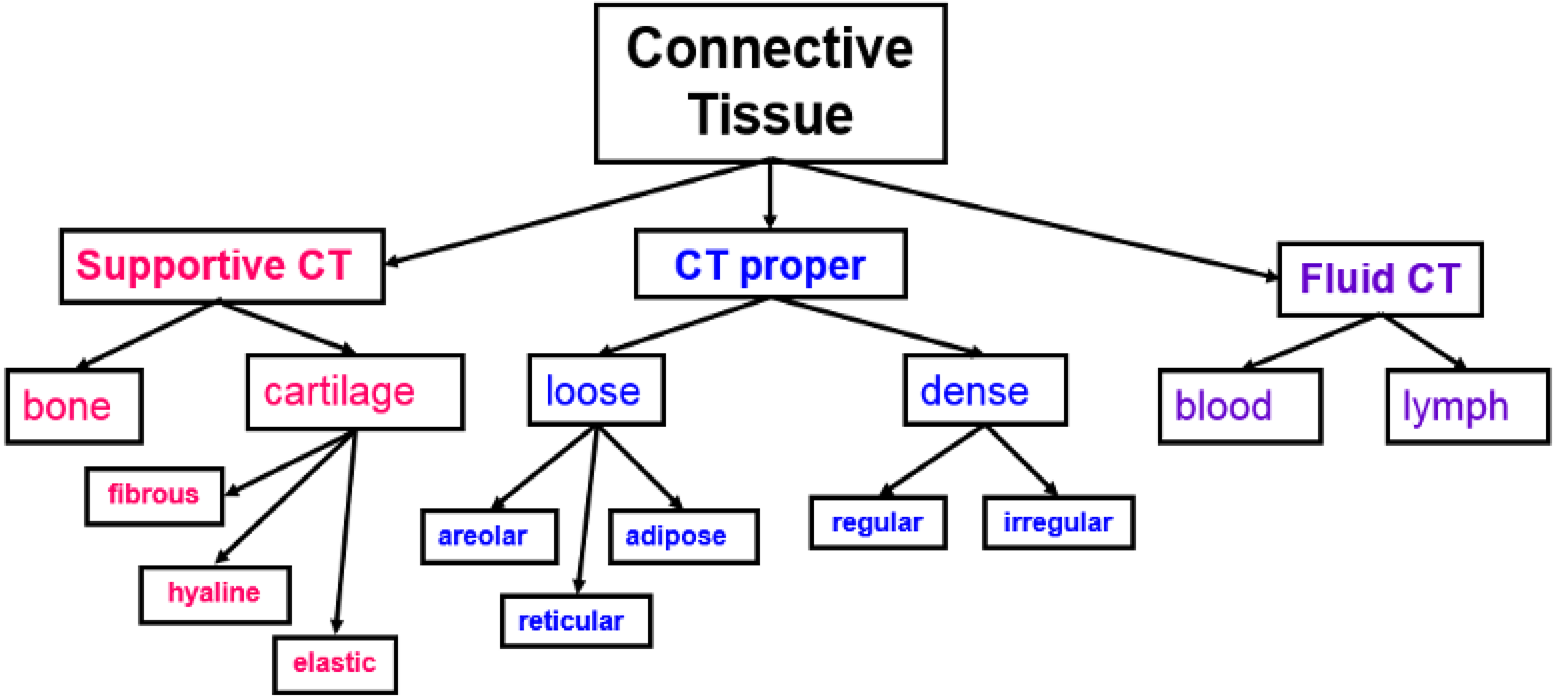


CONNECTIVE TISSUE

Types

- Connective tissue proper
  - Loose
    More matrix less fibre
    e.g., Areolar, Adipose
  - Dense
    More fibres less matrix
    e.g., Ligament, Tendon, White Fibrous, Yellow fibres, Connective Tissue
- Supportive connective tissue
  e.g., Bone, Cartilage
- Fluid Connective tissue
  e.g., Blood/Lymph

Classification of Connective Tissue



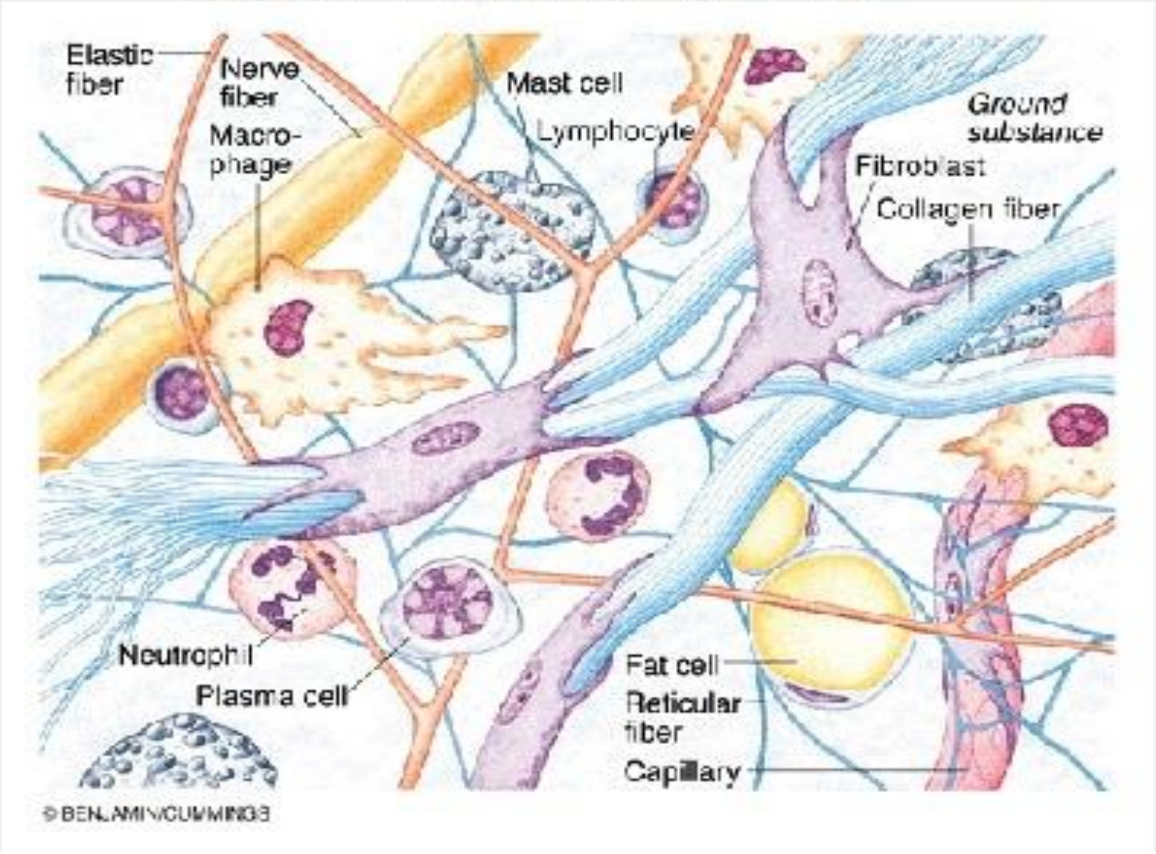
Loose connective tissue

is a very common type of connective tissue that supports many structures which are normally under some pressure and low friction.It usually supports epithelial tissue, forms a layer around small blood and lymphatic vessels, and fills the spaces between muscle and nerve fibers, also found in the papillary layer of the dermis, in the hypodermis, in the linings of the peritoneal and pleural cavities, in glands, and in the mucous membranes (wet membranes that line the hollow organs) supporting the epithelial cells.

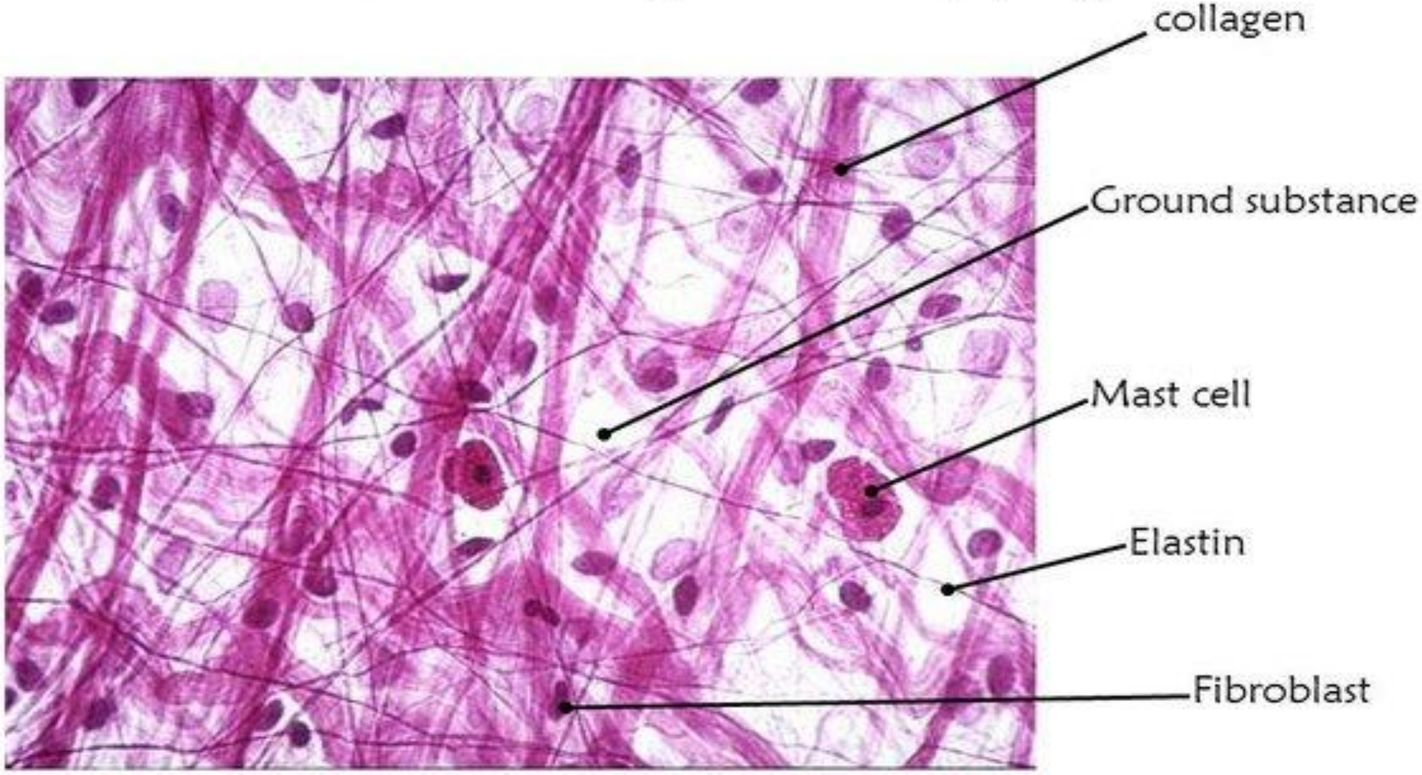
Loose connective tissue, sometimes called **areolar tissue**, has all the main components of connective tissue (cells, fibers, and ground substance) ,the most numerous cells are **fibroblasts** and **macrophages**, but other types of connective tissue cells are also present. **Collagen, elastic, and reticular fibers** also appear in this tissue.

Areolar Tissue

the Prototype Connective Tissue



Areolar (Prototype)

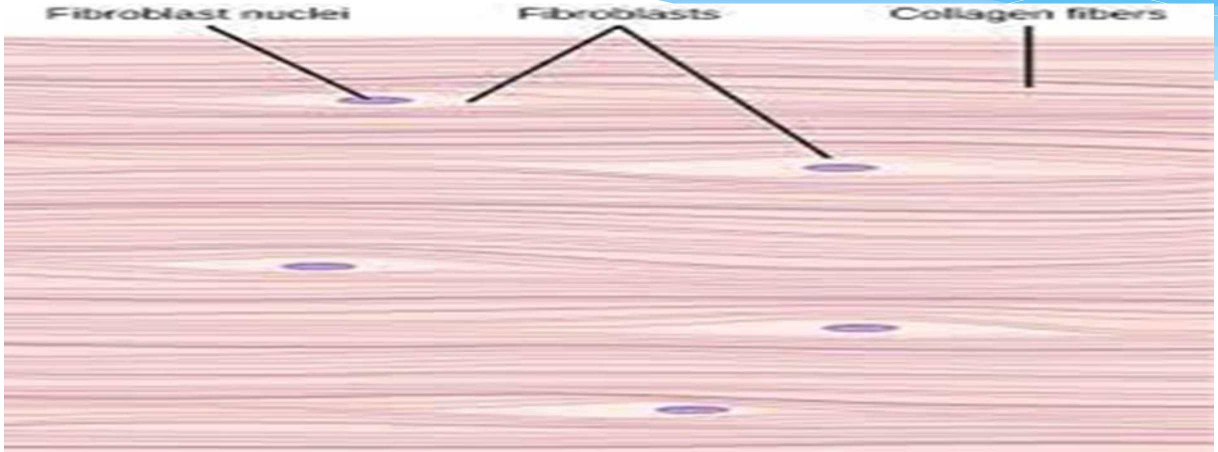


Dense connective tissue

Is adapted to offer resistance and protection. It has the same components found in loose connective tissue, but there are fewer cells and a clear predominance of collagen fibers over ground substance. Dense connective tissue is less flexible and far more resistant to stress than is loose connective tissue. It is known as **dense irregular connective** tissue when the collagen fibers are arranged in bundles without a definite orientation . The collagen fibers form a 3-dimensional network in dense irregular tissue, providing resistance to stress from all directions.

Dense irregular connective tissue is often found closely associated with loose connective tissue.

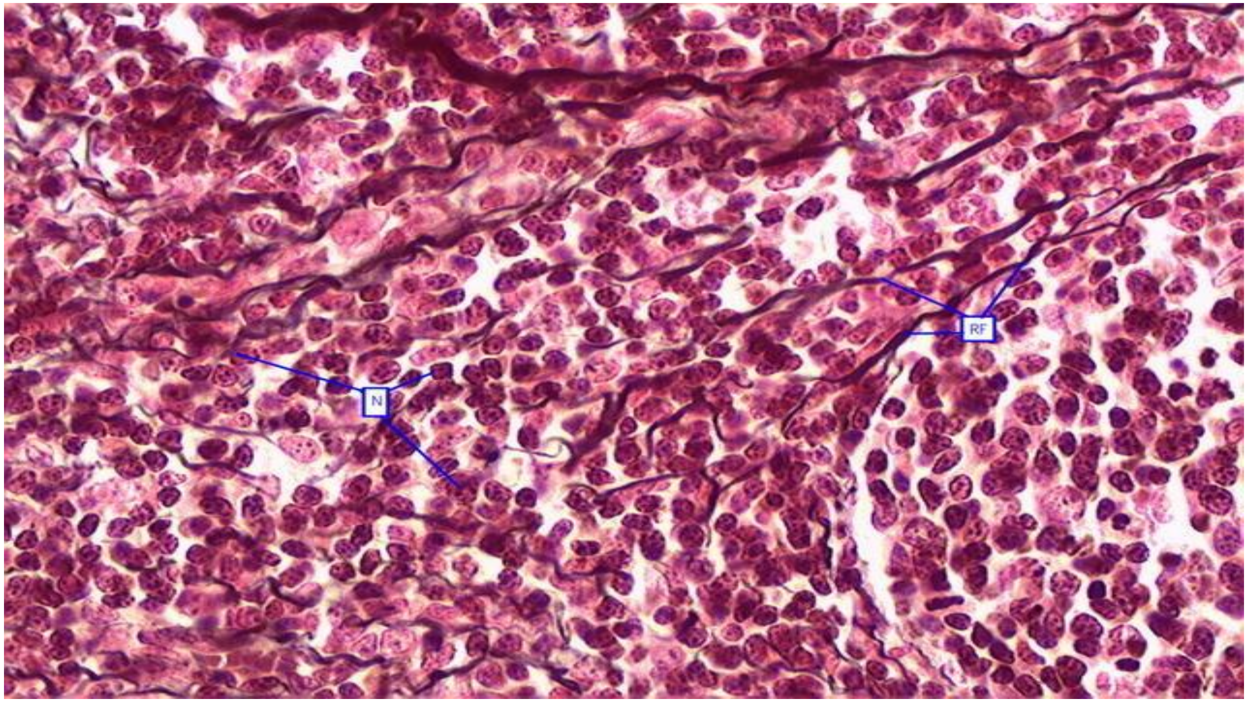
The collagen bundles of **dense regular connective tissue** are arranged according to a definite pattern, with collagen fibers aligned with the linear orientation of fibroblasts in response to prolonged stresses exerted in the same direction.


Fibroblast nuclei
Fibroblasts
Collagen fibers


Dense irregular connective tissue
Dense irregular connective tissue is a tissue with fibers that are not as organized as they are in the regular type.

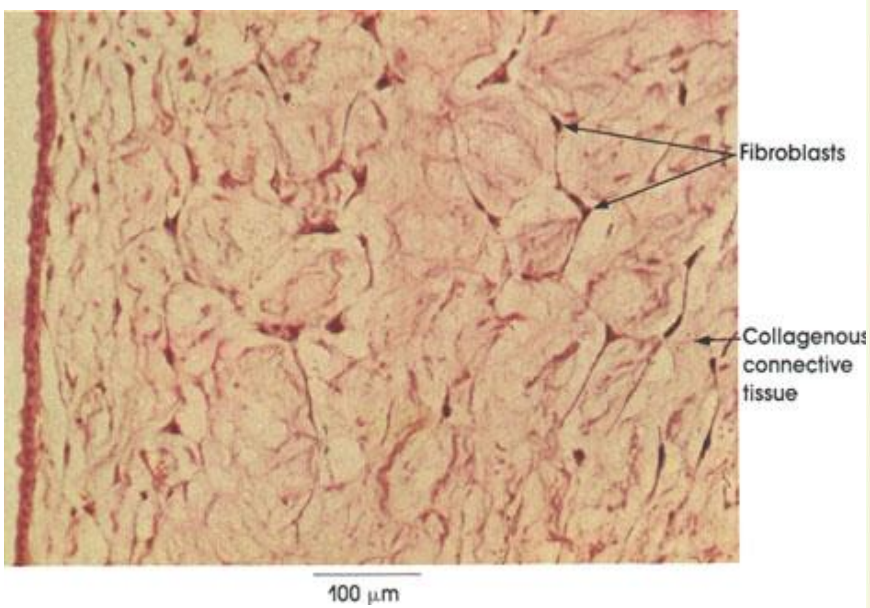
Reticular Tissue

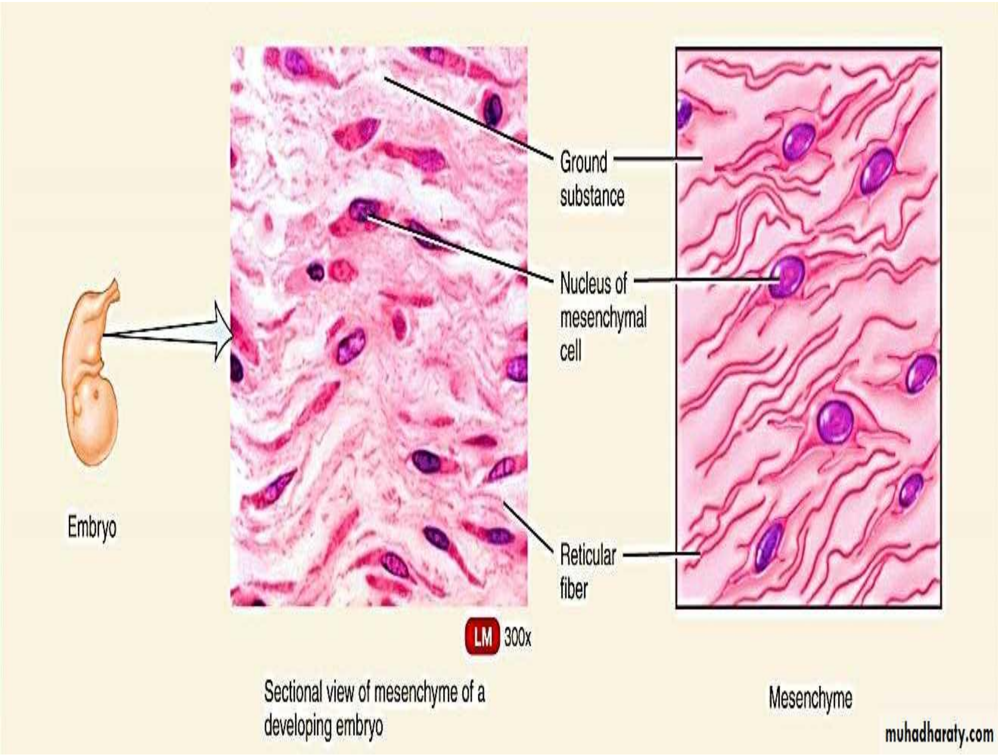
This specialized connective tissue consists of reticular fibers of type III collagen produced by specialized fibroblasts called reticular cells, reticular fibers provide the architectural framework that creates special microenvironments for hematopoietic organs and lymphoid organs (bone marrow, lymph nodes, and spleen). Reticular tissue is a special type of connective tissue that predominates in various locations that have a high cellular content. It has a branched and mesh-like pattern, often called reticulum, due to the arrangement of reticular fibers (reticulin).



Mucous tissue

is found mainly in the umbilical cord and fetal tissues. Mucous tissue has an abundance of ground substance composed chiefly of hyaluronic acid, making it a jellylike tissue containing very few collagen fibers with scattered fibroblasts , the principal component of the umbilical cord, where it is referred to **as Wharton's jelly**. A similar form of connective tissue is also found in the pulp cavity of young teeth.





ADIPOSE TISSUE:

Adipose tissue is a specialized type of connective tissue in which adipocytes or fat cells predominate. These cells can be found isolated or in groups within loose or irregular connective tissue, often in large aggregates where they are the major component of adipose tissue. Located in many areas throughout the body, adipose tissue represents 15–20% of the body weight in men of normal weight; in women of normal weight, 20–25% of body weight. Long considered little more than inert masses of energy stored as fat, adipocytes are now recognized as key regulators of the body's energy metabolism.

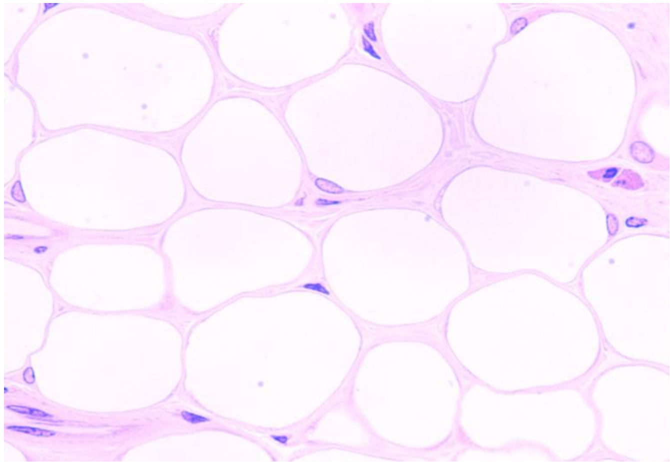
There are two types of adipose tissue with different locations, structures, colors, and pathologic characteristics.

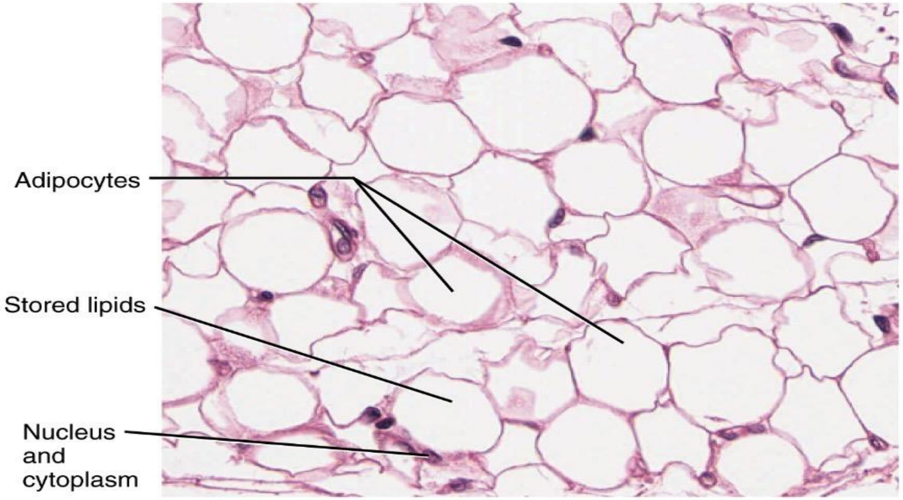
White adipose tissue, the more common type, is composed of cells that, when completely developed, contain one large central droplet of whitish yellow fat in their cytoplasm. **Brown adipose** tissue contains cells with multiple lipid droplets interspersed among **abundant mitochondria**, which give these cells the **darker** appearance. **Both types of adipose tissue have a rich blood supply.**

Adipose tissue is commonly known as body fat. It is found all over the body. It can be found under the skin (subcutaneous fat), packed around internal organs (visceral fat), between muscles, within bone marrow, and in breast tissue.

WHITE ADIPOSE TISSUE

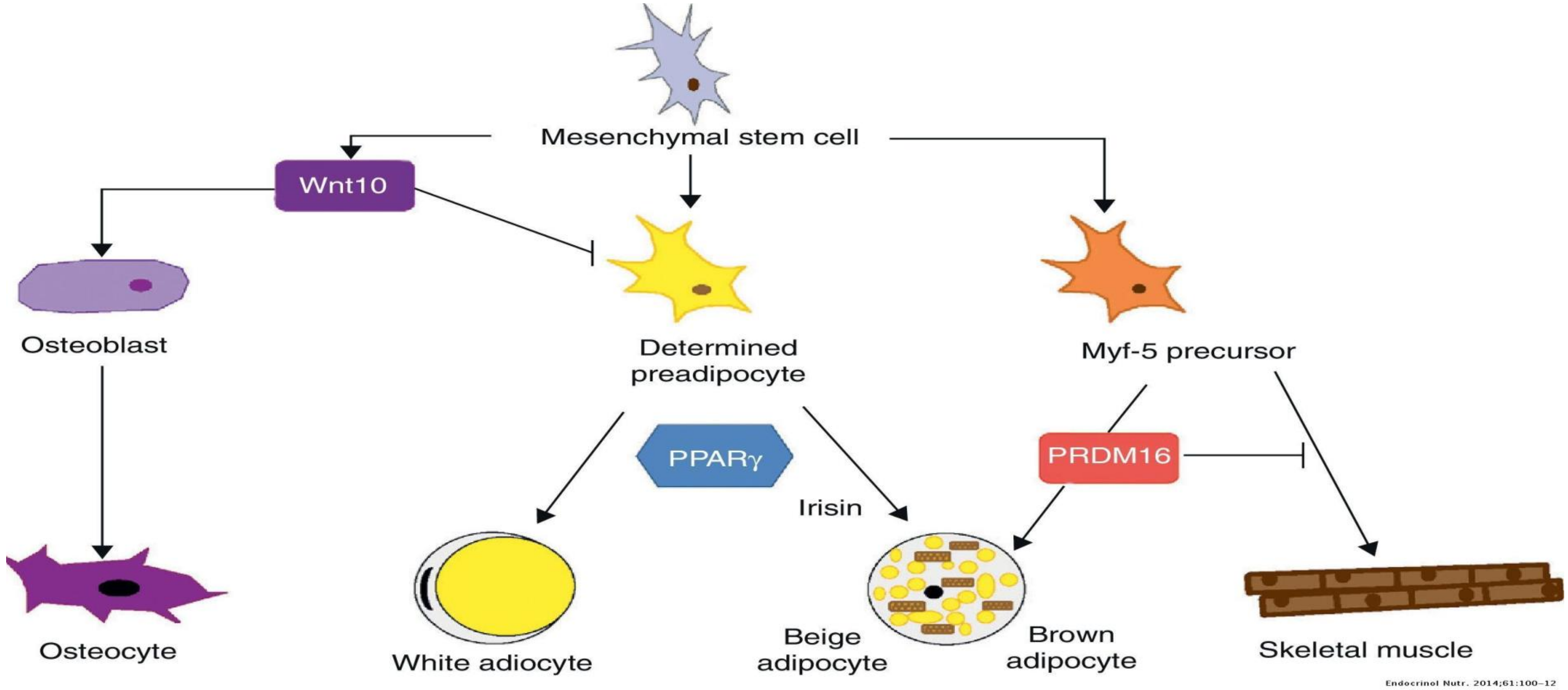
Specialized for long-term energy storage, white adipose cells are spherical when isolated but are polyhedral when closely packed in adipose tissue. White adipocytes are called unilocular because triglycerides are stored in a single locus. . Since lipid is removed from cells by the alcohol and xylene used in routine histological techniques, a unilocular adipocyte appears in microscope preparations as a thin ring of cytoplasm surrounding the empty vacuole left by the dissolved lipid droplet, sometimes referred to as the **signet ring cell**. The large droplet causes these cells to have eccentric and flattened nuclei.





Histogenesis of White Adipose Tissue

Like the fiber-producing cells of connective tissue, adipocytes undergo differentiation from embryonic **mesenchymal cell**s. Such differentiation is first seen with the appearance of **lipoblasts**. Early lipoblasts have the appearance of fibroblasts but are able to accumulate fat in their cytoplasm. Lipid accumulations are isolated from one another at first but soon fuse to form the single larger droplet that is characteristic of unilocular adipose tissue cells.

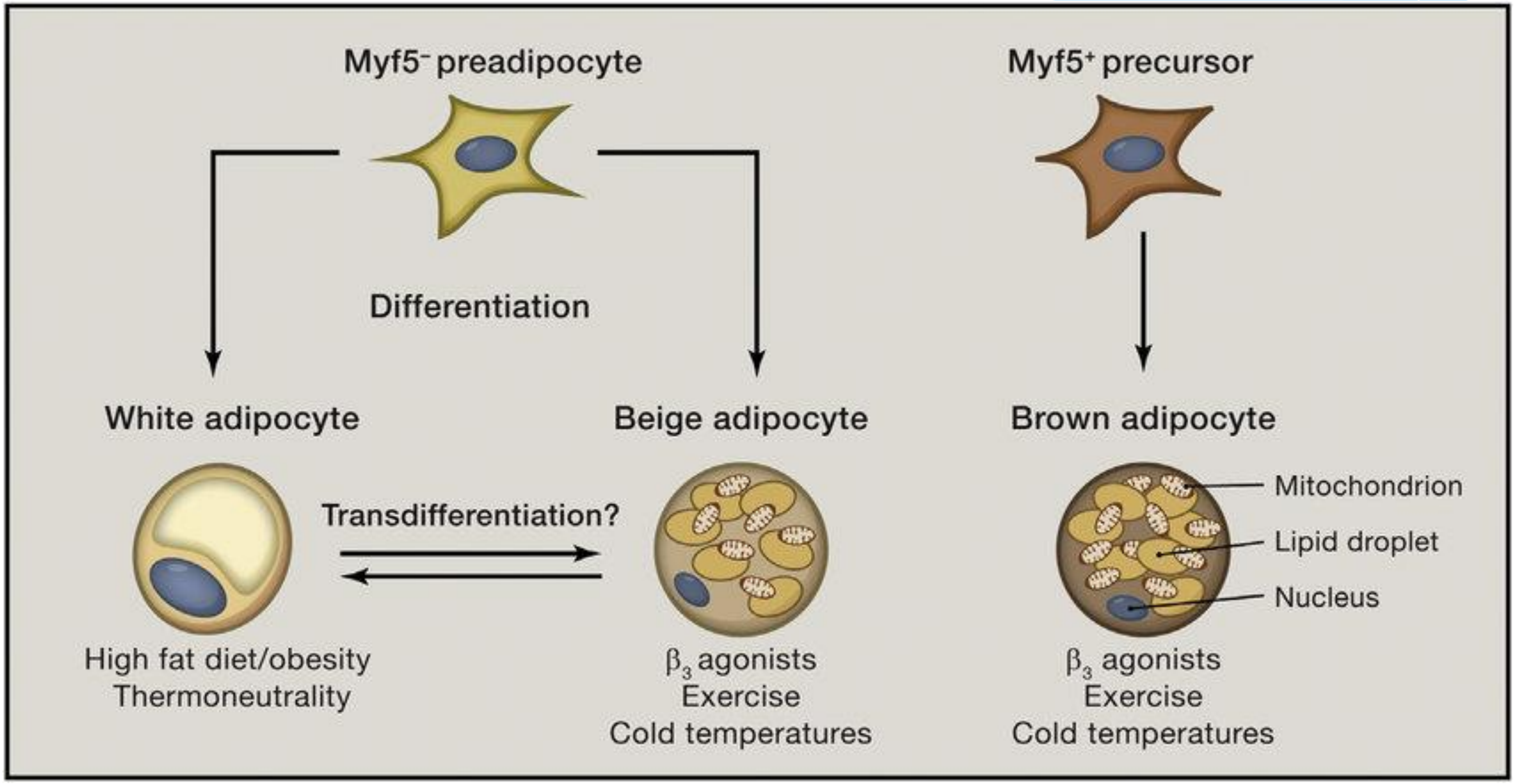


Development of white and brown fat cells.

Undifferentiated **mesenchymal cells** differentiate as **preadipocytes** and are transformed into **lipoblasts** as they accumulate fat and thus give rise to mature fat cells. The mature fat cell is larger than that shown here in relation to the other cell types. Undifferentiated mesenchymal cells also give rise to a variety of other cell types, including fibroblasts. When a large amount of lipid is mobilized by the body, mature unilocular fat cells may return to the lipoblast stage.

BROWN ADIPOSE TISSUE

The color of brown adipose tissue or brown fat is due to both the numerous mitochondria (containing colored cytochromes)scattered through the adipocytes and the large number of blood capillaries in this tissue. Adipocytes of brown fat contain many small lipid inclusions and are therefore called multilocular. The many small lipid droplets, abundant mitochondria, and rich vasculature all help mediate this tissue's principal function of heat production. In comparison with white adipose tissue, which is present throughout the body, brown adipose tissue has a much more limited distribution. Cells of brown adipose tissue cells are polygonal and generally smaller than cells of white adipose tissue but their cytoplasm contains a great number of lipid droplets of various sizes .These adipocytes have spherical and central nuclei and the numerous mitochondria .


Myf5⁻ preadipocyte
Myf5⁺ precursor
Differentiation
White adipocyte
Beige adipocyte
Brown adipocyte
Transdifferentiation?
Mitochondrion
Lipid droplet
Nucleus
High fat diet/obesity
Thermoneutrality
β_3 agonists
Exercise
Cold temperatures
β_3 agonists
Exercise
Cold temperatures

Lecture No. 5

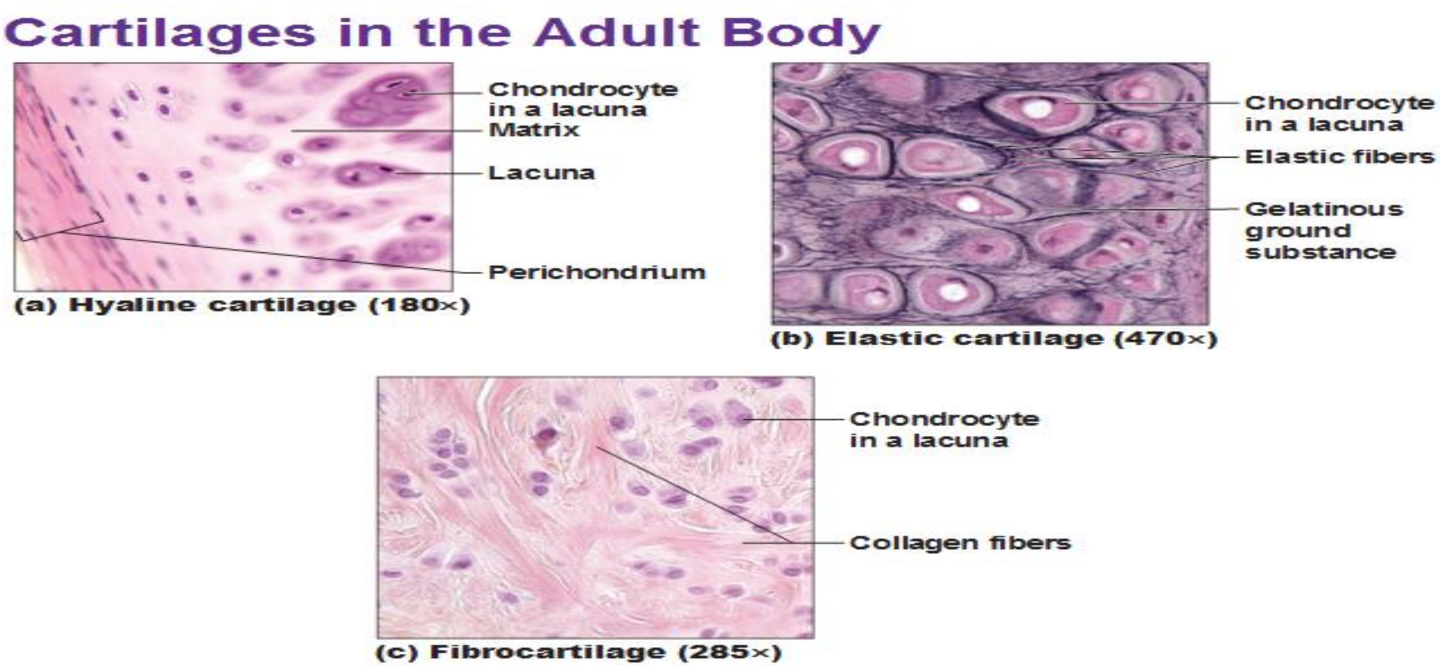
Cartilage tissue

Cartilage is characterized by an extracellular matrix (ECM) enriched with glycosaminoglycans and proteoglycans, macromolecules that interact with collagen and elastic fibers. Variations in the composition of these matrix components produce **three types of cartilage** adapted to local biomechanical needs.

Cartilage is a specialized form of connective tissue in which the firm consistency of the ECM allows the tissue to bear mechanical stresses without permanent distortion. In the respiratory system cartilage forms a framework supporting soft tissues. Because it is smooth-surfaced and resilient, cartilage provides a shock-absorbing and sliding area for joints and facilitates bone movements. Cartilage is also essential for the development and growth of long bones, both before and after birth .

Cartilage consists of cells called chondrocytes and an extensive extracellular matrix composed of **fibers** and **ground substance**. Chondrocytes synthesize and secrete the ECM and the cells themselves are located in matrix cavities called lacunae. Collagen, hyaluronic acid, proteoglycans, and small amounts of several glycoproteins are the principal macromolecules present in all types of cartilage matrix.

- Cartilage is a non-vascular type of supporting connective tissue that is found throughout the body . Cartilage is not innervated and therefore relies on diffusion to obtain nutrients. The main cell types in cartilage are chondrocytes, the ground substance is chondroitin sulfate, and the fibrous sheath is called perichondrium. There are three types of cartilage: **hyaline**, **fibrous**, and **elastic** cartilage



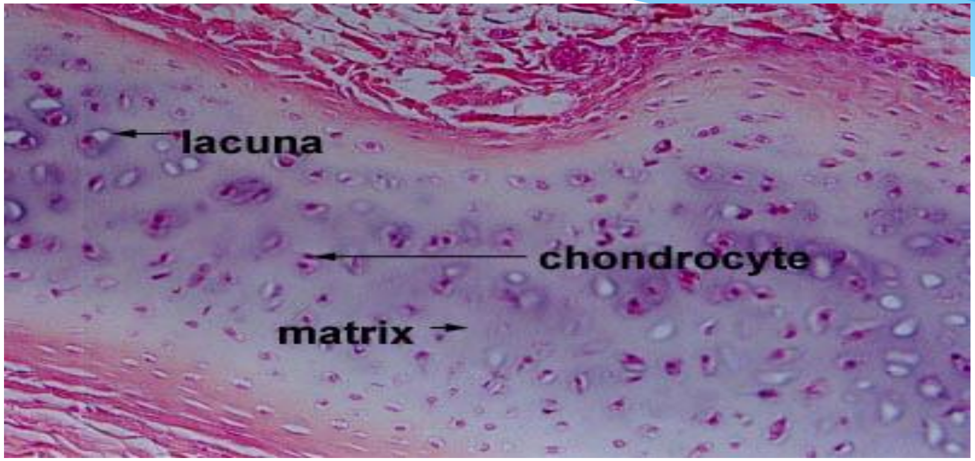
(a) Hyaline cartilage (180×)
(b) Elastic cartilage (470×)
(c) Fibrocartilage (285×)

In all three forms, cartilage is avascular and is nourished by the diffusion of nutrients from capillaries in adjacent connective tissue (perichondrium) or from synovial fluid in joint cavities. In some instances, large blood vessels traverse cartilage to nourish other tissues, but these vessels do not supply nutrients to the cartilage. As might be expected of cells in an avascular tissue, chondrocytes exhibit low metabolic activity. Cartilage also lacks lymphatic vessels and nerves.

The perichondrium is a sheath of dense connective tissue that surrounds cartilage in most places, forming an interface between the cartilage and the tissue supported by the cartilage. The perichondrium harbors the vascular supply for the avascular cartilage and also contains nerves and lymphatic vessels. **Articular cartilage**, which covers the surfaces of the bones in movable joints, is **devoid of perichondrium** and is sustained by the diffusion of oxygen and nutrients from the synovial fluid.

Hyaline cartilage

is the most common and best studied of the three forms. Fresh hyaline cartilage is bluish-white and translucent. In the embryo, it serves as a temporary skeleton until it is gradually replaced by bone.



Hyaline Cartilage has a smooth surface and is the most common of the three types of cartilage. It has a matrix that contains closely packed collagen fibers, making it tough but slightly flexible. It consists of a bluish-white, shiny ground elastic material, whose matrix contains many fine collagen fibrils and chrondrocytes. The chondrocytes are arranged in small groups within **cell nests** and the matrix is solid and smooth. Because of its smooth surfaces it allows tissues to slide/glide more easily, as well as providing flexibility and support. In adult mammals, hyaline cartilage is located in the articular surfaces of the movable joints, in the walls of larger respiratory passages (nose, larynx ,trachea, bronchi), in the ventral ends of ribs, and in the epiphyseal plate, where it is responsible for the longitudinal growth of bone .

- Chondrocytes
- At the periphery of hyaline cartilage, young chondrocytes have an elliptic shape, with the long axis parallel to the surface, they are round and may appear in groups of up to eight cells originating from mitotic divisions of a single chondrocyte. These groups are called isogenous aggregates. Chondrocytes synthesize collagens and the other matrix molecules. As matrix is produced, cells in the aggregates are moved apart and occupy separate lacunae.

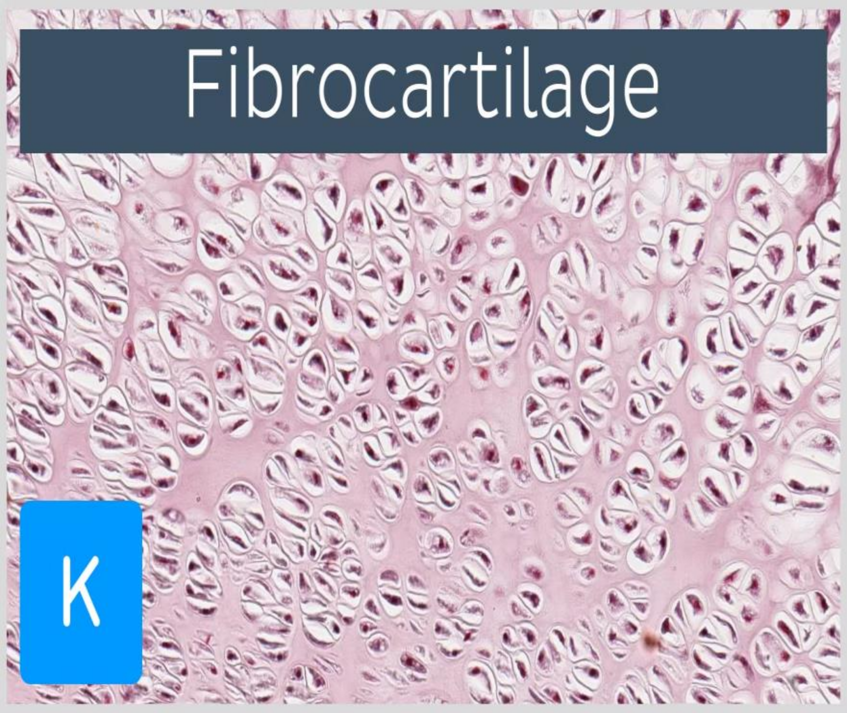
ELASTIC CARTILAGE

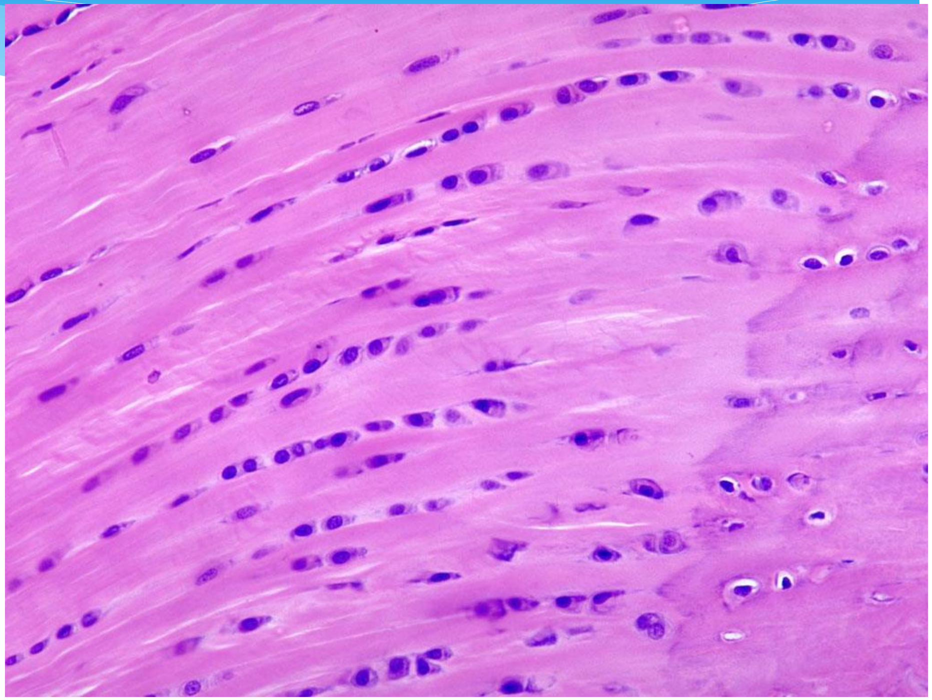
is essentially very similar to hyaline cartilage except that it contains an abundant network of fine elastic fibers in addition to collagen type II fibrils ,Fresh elastic cartilage has a yellowish color owing to the presence of elastin in the elastic fibers. Elastic cartilage is frequently found to be gradually continuous with **hyaline cartilage.** Like hyaline cartilage, elastic cartilage **possesses a perichondrium**. Elastic cartilage is found in the auricle of the ear, the walls of the external auditory canals, the auditory (eustachian) tubes, the epiglottis, and the cuneiform cartilage in the larynx.

Fibro cartilage: **is a tissue intermediate between dense connective tissue and hyaline cartilage. It is found in intervertebral disks, in attachments of certain ligaments, and in the pubic symphysis, is always associated with dense connective tissue and the border between these two tissues is not clear-cut, showing a gradual transition.**

Fibrocartilage contains chondrocytes, either singly or in isogenous aggregates, usually arranged axially, in long rows separated by coarse collagen type I fibers and less proteoglycans than other forms of cartilage.

Example : Intervertebral discs (between spinal vertebrae), the callus (formed at the ends of bones at the site of a fracture), between the Pubic Symphysis and at the junction where tendons insert into bone.

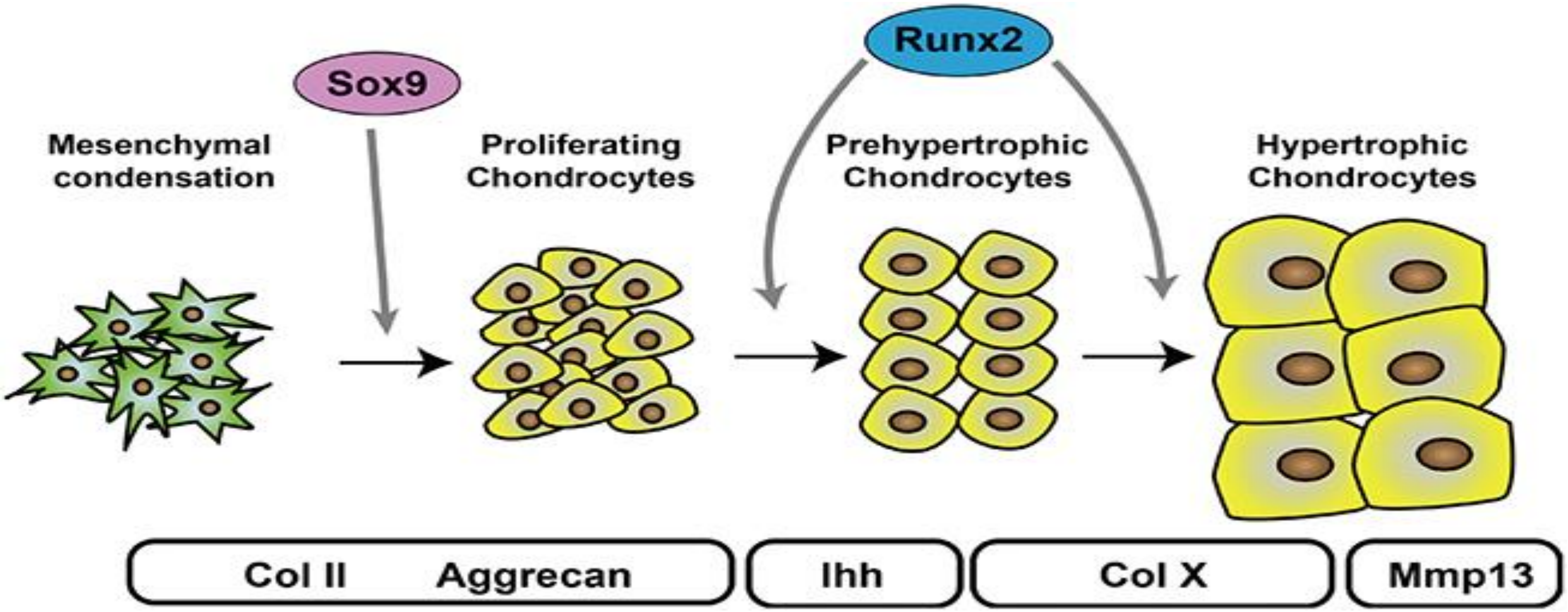




CARTILAGE FORMATION,GROWTH AND REPAIR

All cartilage derives from the embryonic **mesenchyme** in the process of chondrogenesis .The first indication of cell **differentiation** is the **rounding up** of the mesenchymal cells, which **retract their extensions**, **multiply rapidly**, and form cellular **condensations**. The cells formed by this direct differentiation of mesenchymal cells, now called **chondroblasts** , have a ribosome-rich basophilic cytoplasm.

- Synthesis and deposition of the matrix then begin to separate the chondroblasts from one another . During embryonic development, the differentiation of cartilage takes place primarily from the center outward; therefore, the more central cells have the characteristics of chondrocytes, whereas the peripheral cells are typical chondroblasts. The superficial mesenchyme develops into the perichondrium.



- BONE:

The main constituent of the adult skeleton, bone tissue supports fleshy structures, protects vital organs such as those in the cranial and thoracic cavities, and harbors the bone marrow, where blood cells are formed. Bone also serves as a reservoir of calcium, phosphate, and other ions that can be released or stored in a controlled fashion to maintain constant concentrations of these important ions in body fluids.

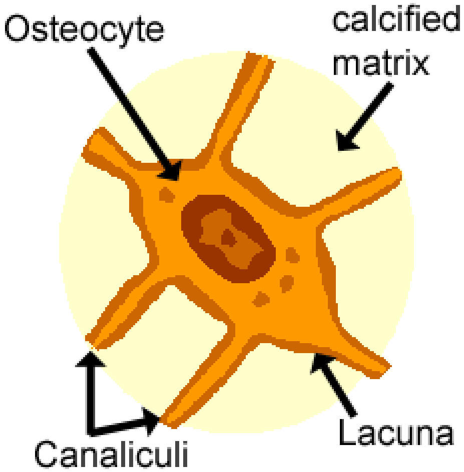
In addition, bones form a system of levers that multiply the forces generated during skeletal muscle contraction and transform them into bodily movements. This mineralized tissue therefore confers mechanical and metabolic functions to the skeleton.

Bone is a specialized connective tissue composed of calcified intercellular material, the bone matrix, and three cell types:

Osteocytes which are found in cavities (lacunae) between layers (lamellae) of bone matrix .

Osteoblasts which synthesize the organic components of the matrix.

Osteoclasts which are multi-nucleated giant cells involved in the resorption and remodeling of bone tissue.



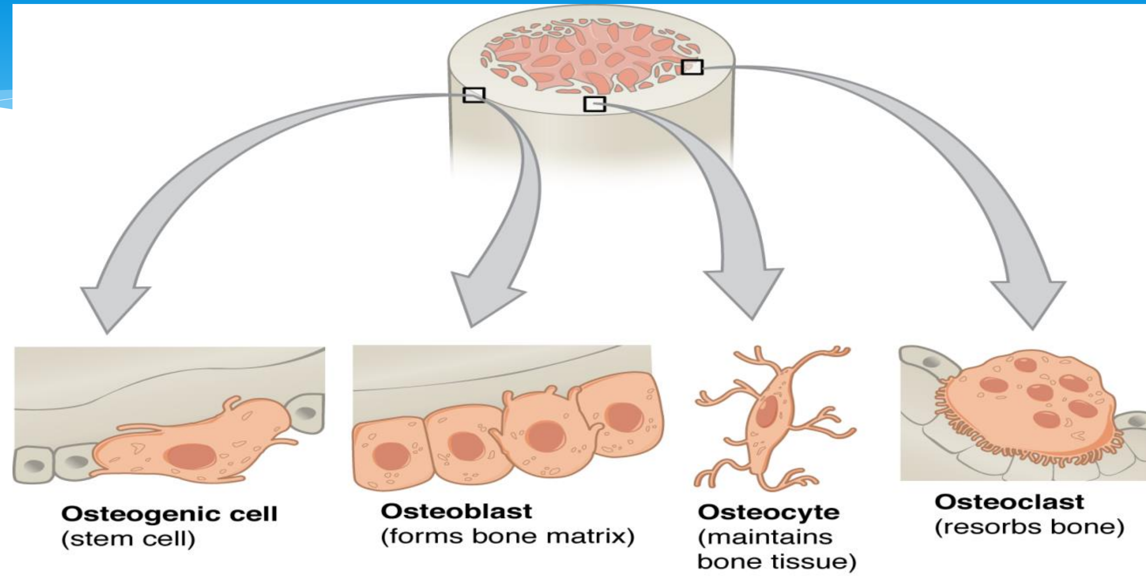
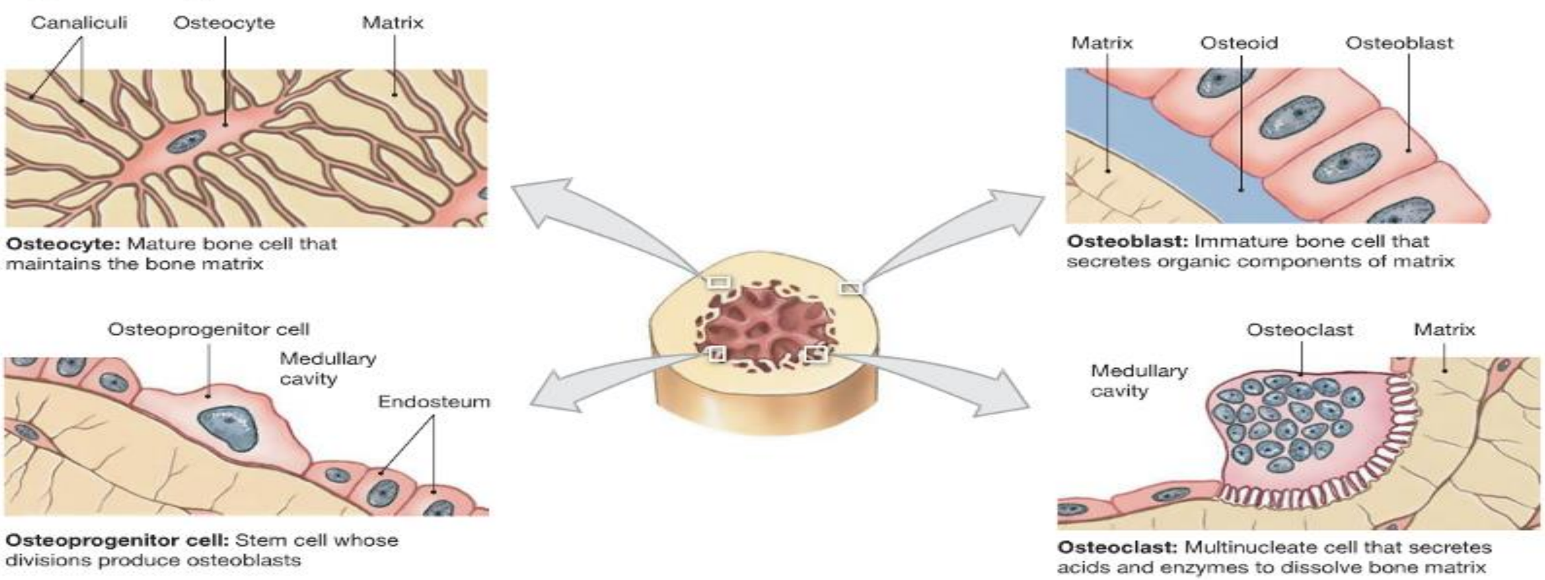


Figure 6–3 Types of Bone Cells.



The diagram shows an overview of the basic features of bone, including the three key cell types **osteocytes, osteoblasts**, and **osteoclasts;** their usual locations, **Osteoblasts secrete the matrix** which then hardens by calcification, trapping the differentiating cells now **called osteocytes** in individual lacunae. Osteocytes maintain the calcified matrix and receive nutrients from blood vessels via very small channels through the matrix **called canaliculi**.

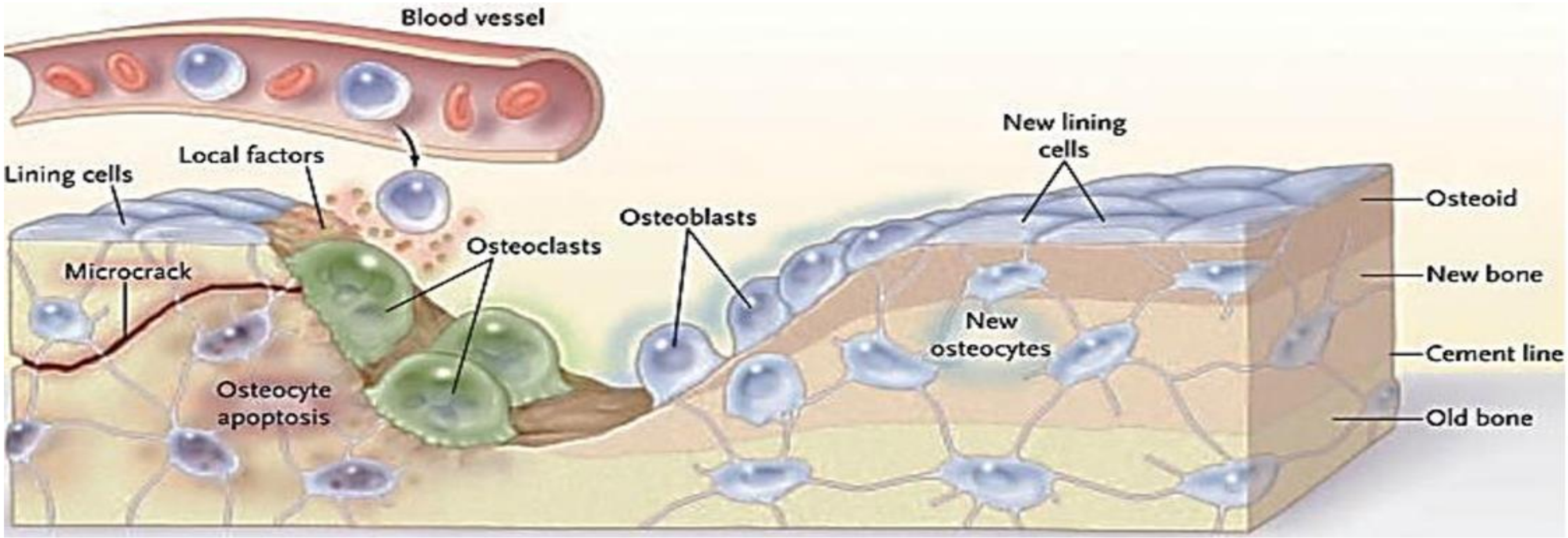
Osteoclasts are monocyte-derived cells in bone which are important in bone remodeling.

The **periosteum** consists of dense connective tissue, with a primarily fibrous layer covering a more cellular layer. Bone is **vascularized** by small vessels that penetrate the matrix from the periosteum

Osteoblasts

Osteoblasts are responsible for the synthesis of the organic components of bone matrix, consisting of type I collagen fibers, proteoglycans, and several glycoproteins including osteonectin. Deposition of the inorganic components of bone also depends on viable osteoblasts. Osteoblasts are **located exclusively at the surfaces of bone** matrix, usually side by side in a layer somewhat resembling a simple epithelium.

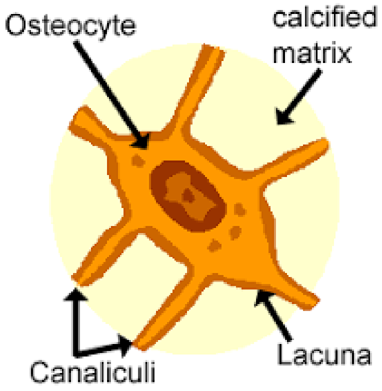
During matrix synthesis, osteoblasts have actively synthesizing proteins for secretion. Osteoblasts are polarized cells: matrix components are secreted at the cell surface in contact with older bone matrix, producing a layer of new material called **osteoid** between the osteoblast layer and the bone formed earlier. .



- **Osteocytes**
- Individual **osteoblasts** are gradually surrounded by their **own secretion** and become **osteocytes** enclosed singly within spaces called lacunae. In the transition from osteoblasts to osteocytes the cells **extend many long cytoplasmic processes,** which also become surrounded by calcifying matrix. An osteocyte and its processes occupy each lacuna and the canaliculi radiating from it .

Osteoclasts

Osteoclasts are very large, motile cells with multiple nuclei . The large size and multinucleated condition of osteoclasts is **due to their origin from the fusion of bone marrow-derived cells.** In areas of bone undergoing resorption, osteoclasts lie within enzymatically etched depressions or crypts in the matrix known as resorption bays (**formerly called Howship lacunae**).



BONE MATRIX

Inorganic material represents about **50%** of the dry weight of bone matrix. **Hydroxyapatite** is most abundant, but bicarbonate, citrate, magnesium, potassium, and sodium are also found. The surface ions of **hydroxyapatite** are **hydrated** and a layer of **water** and ions forms around this crystal. This layer, **the hydration shell**, **facilitates the exchange of ions between the crystal and the body fluids.**

PERIOSTEUM & ENDOSTEUM

External and internal surfaces of bone are covered by layers of bone-forming The periosteum consists of a dense fibrous outer layer of collagen bundles and fibroblasts. Bundles of periosteal collagen fibers, called **perforating** (**or Sharpey's) fibers**, penetrate the bone matrix, binding the periosteum to bone. The innermost cellular layer of the periosteum contains mesenchymal stem cells called osteoprogenitor cells, with the potential to divide by mitosis and differentiate into osteoblasts. Osteoprogenitor cells play a prominent role in **bone growth and repair**.

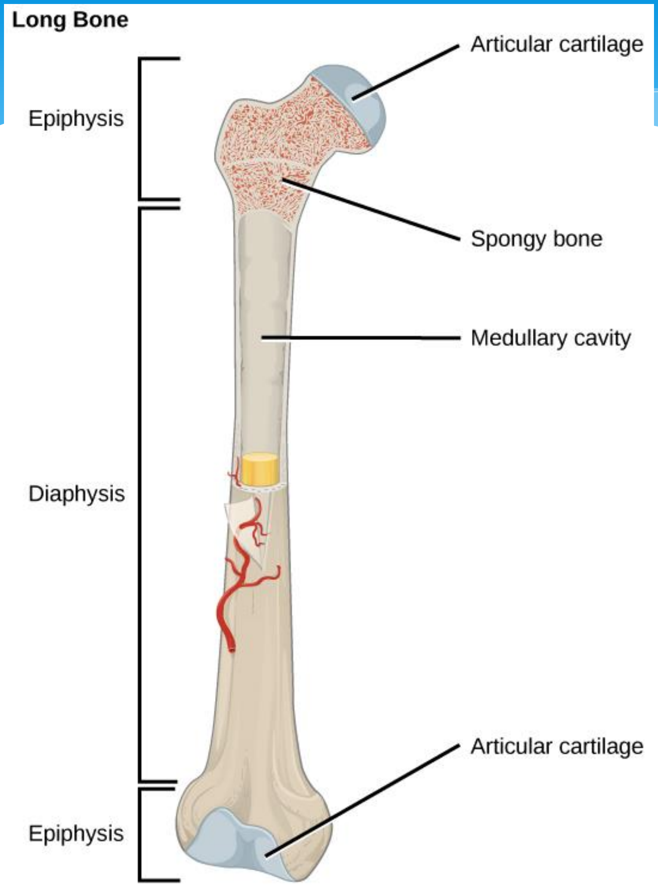
The large internal marrow cavities of bone are lined by endosteum. Endosteum is a single very thin layer of connective tissue, containing flattened osteoprogenitor cells and osteoblasts, which covers the small spicules or trabeculae of bone that project into these cavities. The endosteum is therefore considerably thinner than the periosteum.

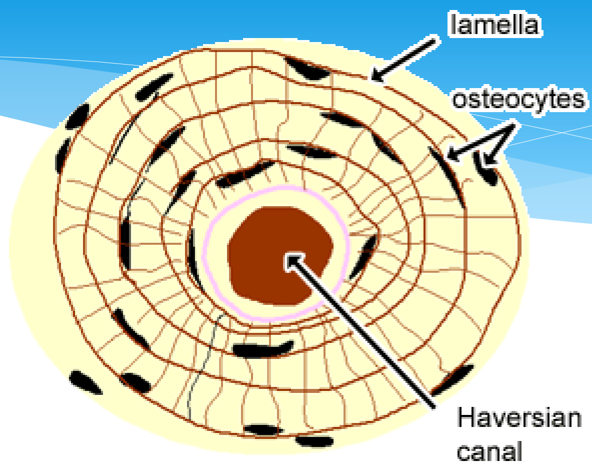
TYPES OF BONE

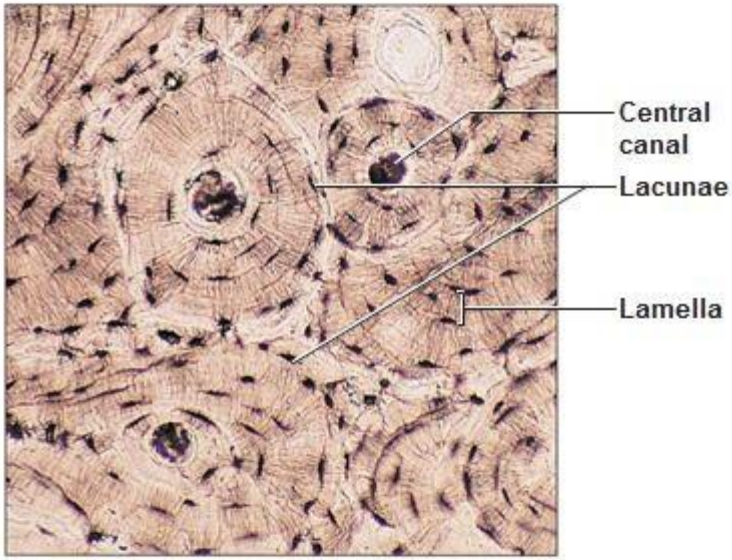
Gross observation of bone in cross section shows dense areas generally **without cavities**—corresponding to **compact bone**—and areas with **numerous interconnecting cavities**—corresponding to **cancellous (spongy) bone** . Under the microscope, however, both compact bone and the trabeculae separating the cavities of cancellous bone have the **same basic histologic structure**

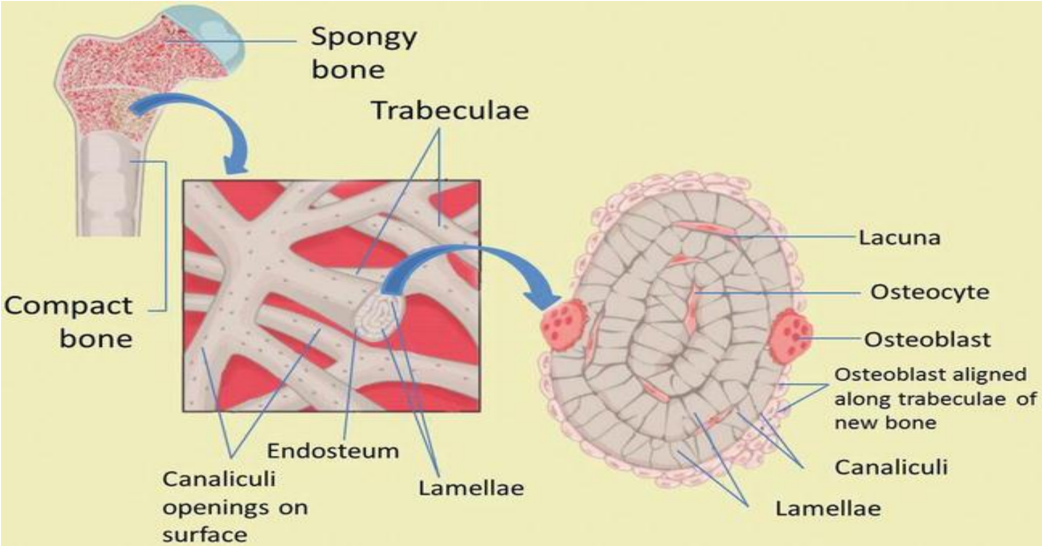
In long bones, the bulbous ends—called **epiphyses** are composed of **spongy bone** covered by a thin layer of compact bone. The cylindrical part—the diaphysis (Gr. diaphysis, a growing between)—is almost totally composed of **compact bone,** with a thin component of spongy bone on its inner surface around the bone marrow cavity. **Short bones** usually have a core of **spongy bone surrounded completely by compact bone. The flat bones that form the calvaria** (skullcap) have two layers of compact bone called plates separated by a thicker layer of spongy bone called the diploë.

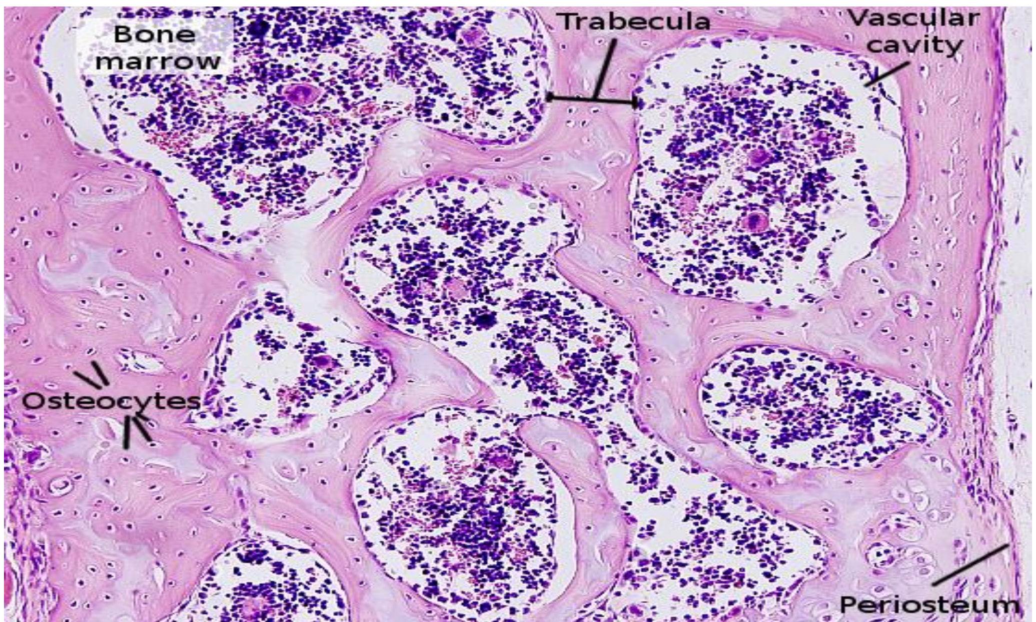
Microscopic examination of bone shows two types: **immature primary bone** and **mature secondary bone.**


Long Bone
Epiphysis
Articular cartilage
Spongy bone
Medullary cavity
Diaphysis
Articular cartilage
Epiphysis


lamella
osteocytes
Haversian canal


Central canal
Lacunae
Lamella





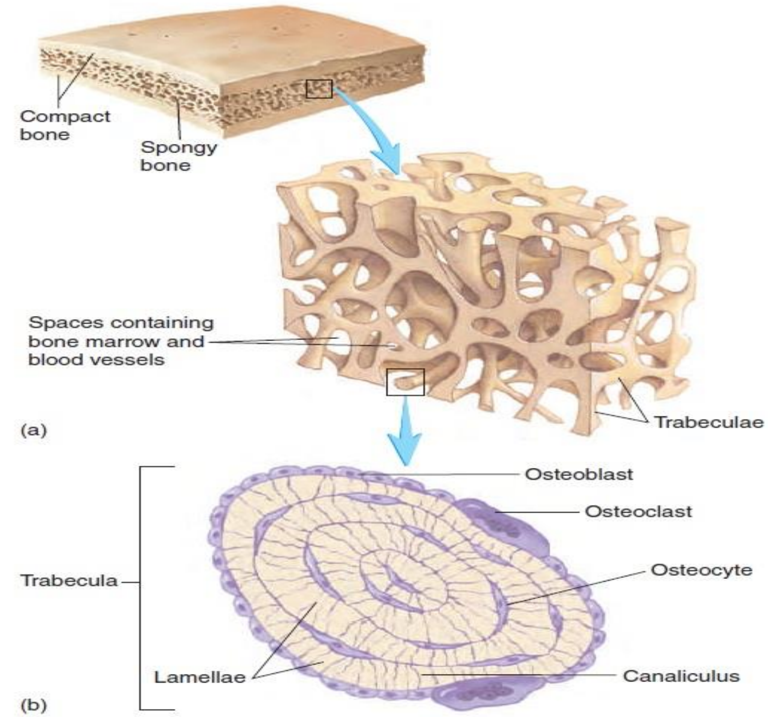


Figure 6.4 AP|R **Spongy Bone**
(*a*) Beams of bone, the trabeculae, surround spaces in the bone. In life, the spaces are filled with red or yellow bone marrow and with blood vessels. (*b*) Transverse section of a trabecula.

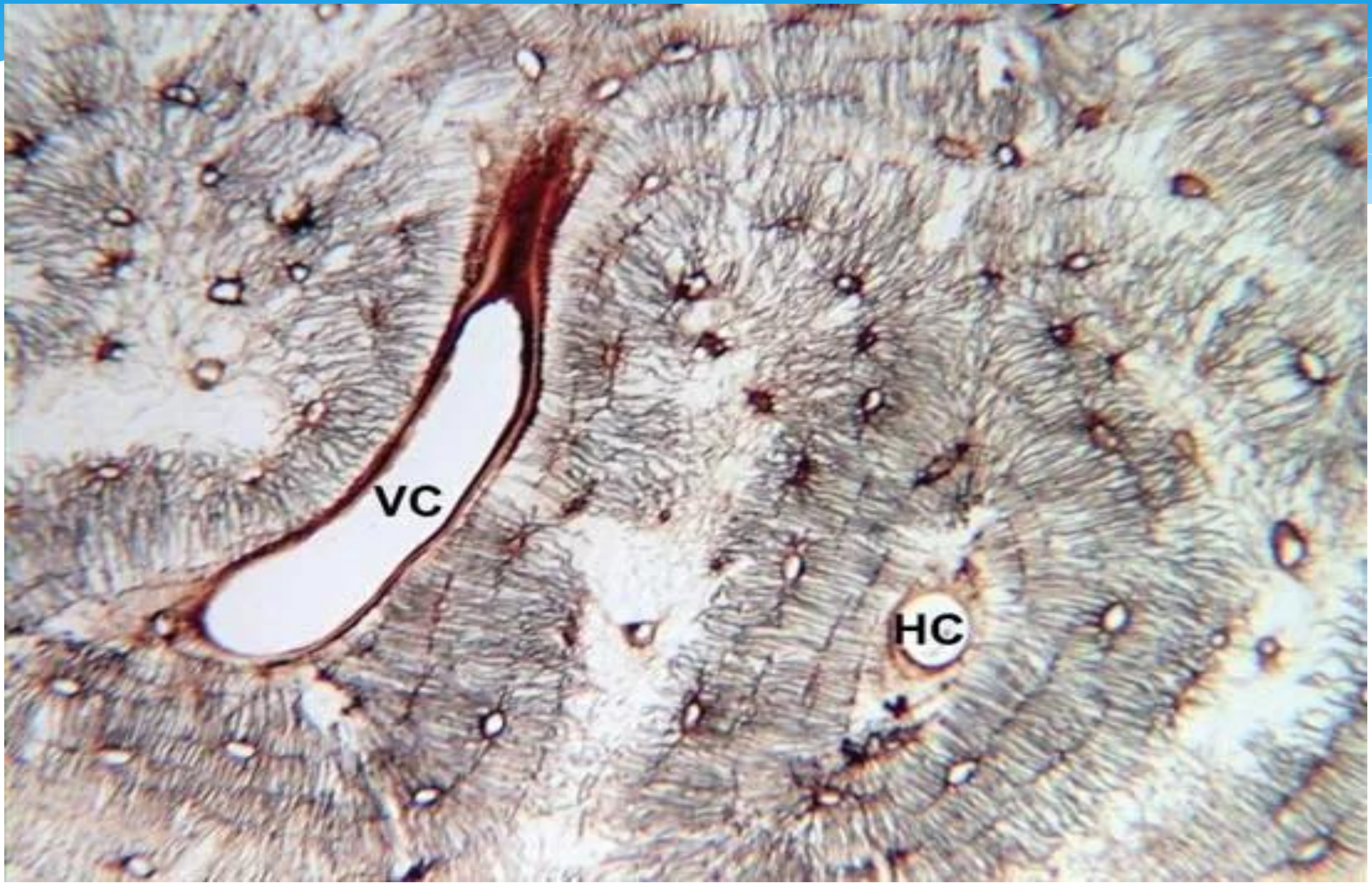
Primary Bone Tissue

Primary bone is the **first bone tissue** to appear in embryonic development and in fracture repair. It is characterized by random disposition of fine collagen fibers and is therefore often called **woven bone** . Usually **temporary** and is replaced in adults by **secondary bone** tissue except in a very few places in the body, eg , **near the sutures** of the calvaria, in **tooth sockets**, and in the **insertions of some tendons**.

In addition to the irregular array of collagen fibers, other characteristics of primary bone tissue are **a lower mineral content** (it is more easily penetrated by x-rays) and a higher proportion of osteocytes than that in secondary bones.

Secondary Bone Tissue

is the type usually found in adults. It characteristically shows multiple layers of calcified matrix and is often referred to as **lamellar bone.** The lamellae are quite organized, either parallel to each other or concentrically around a vascular canal. Each complex of concentric bony lamellae surrounding a small canal containing blood vessels, nerves, and loose connective tissue is called an **osteon** (formerly known as an **haversian system**) . Lacunae with osteocytes are found between the lamellae, interconnected by **canaliculi** which allow all cells to be in contact with the source of nutrients and oxygen in the **osteonic canal** . The central canals communicate with the marrow cavity and the periosteum and with one another through transverse or oblique **perforating canals** (formerly known as **Volkmann canals**) .



Transverse canal called Volkmann's canal

Osteogenesis

Bone can be formed initially by either of two ways:

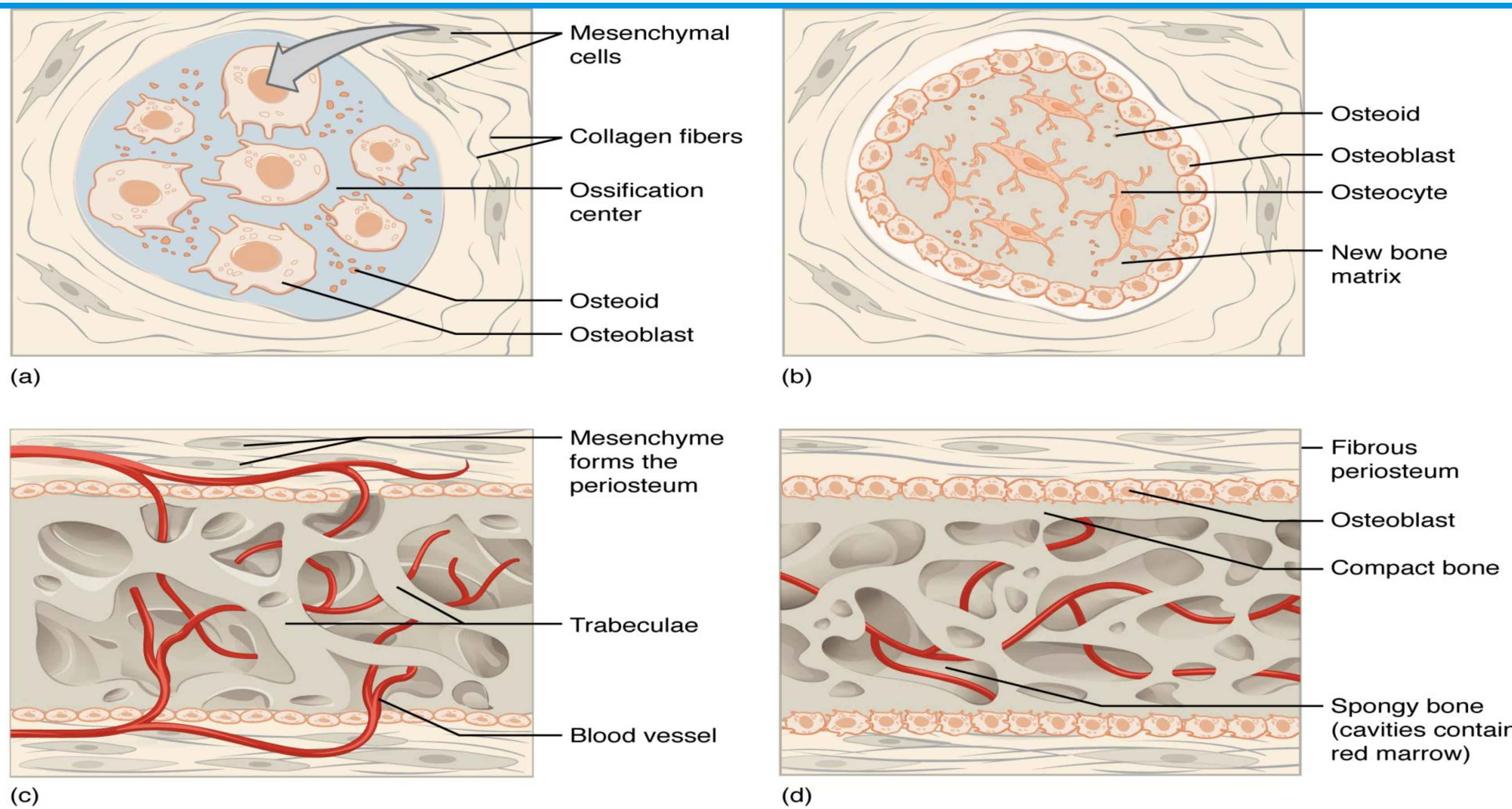
Intramembranous ossification, in which osteoblasts differentiate directly from mesenchyme and begin secreting osteoid.

Endochondral ossification, in which the matrix of preexisting hyaline cartilage is eroded and replaced by osteoblasts producing osteoid.

In **both processes**, the bone tissue that appears first is **primary or woven**. Primary bone is a **temporary** and is soon replaced by the **definitive secondary lamellar** bone. During bone growth, areas of primary bone, areas of resorption, and areas of secondary bone all appear side by side.

Intramembranous Ossification

by which most flat bones are produced, is so called because **it takes place within condensations of embryonic mesenchymal tissue.** The **frontal** and **parietal bones of the skul**l—as well as parts of the occipital and temporal bones and the **mandible and maxilla**—are formed by intramembranous Ossification.

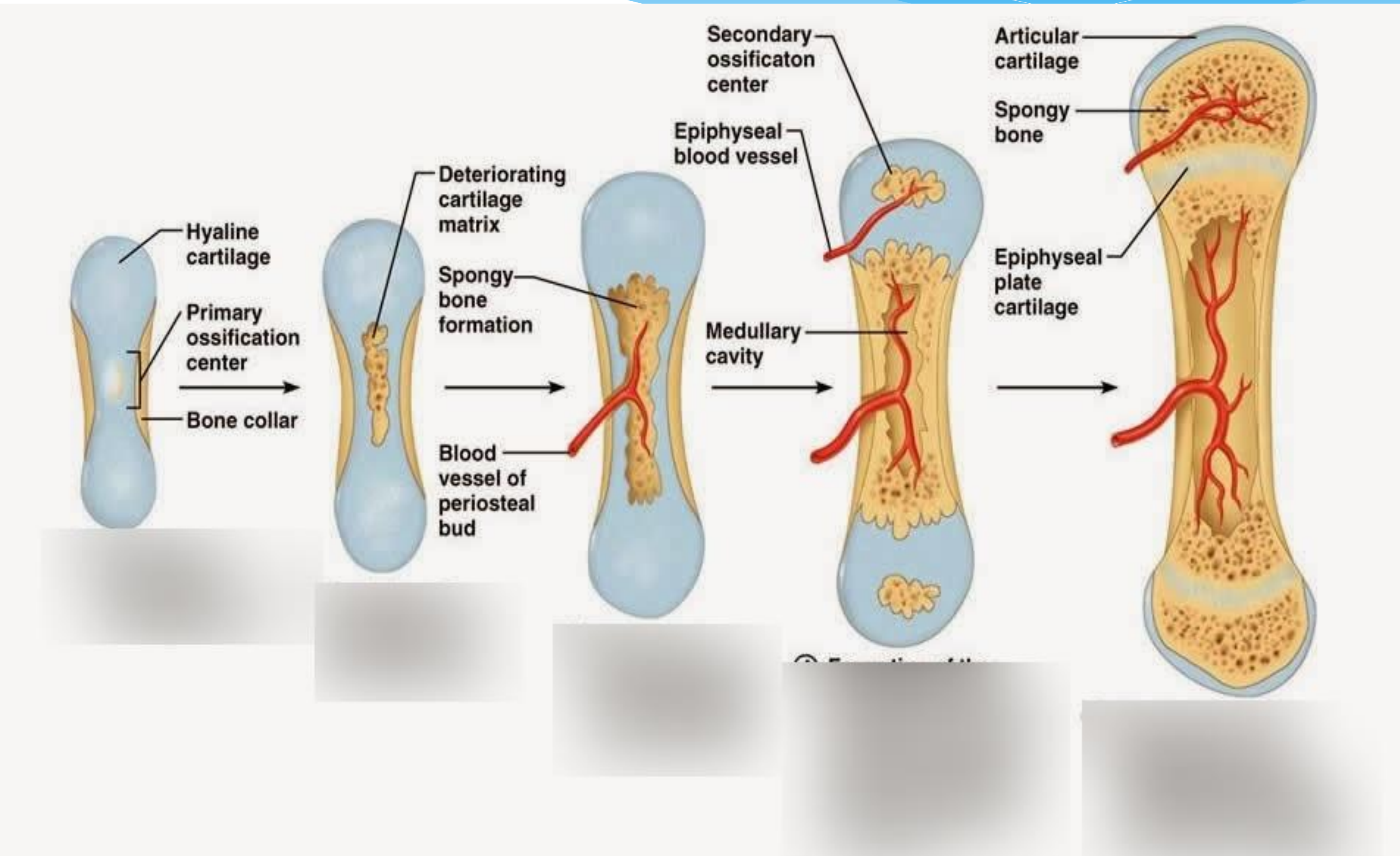


(a): Groups of mesenchymal cells in a "membrane" or sheet of this embryonic tissue, round up and differentiate as osteoblasts producing osteoid. (b): Cells trapped in the calcifying matrix differentiate as osteocytes. (c): **Woven bone** is produced in this manner, with vascularized internal spaces that will form the marrow cavity and surrounded on both sides by developing periosteum. (d):Remodeling of the woven bone produces the two layers of compact lamellar bone with **cancellous** bone in between, which is characteristic of these flat bones.

Endochondral Ossification

Endochondral (Gr. endon, within, + chondros, cartilage) ossification takes place within a **piece of hyaline cartilage** whose shape resembles a small version, or model, of the bone to be formed. This type of ossification is principally responsible for the formation of **short and long bones.**

Endochondral ossification of a long bone consists Initially, the first bone tissue appears **as a collar** surrounding the diaphysis of the **cartilage model**. This bone collar is produced by local osteoblast activity within the surrounding perichondrium. The collar now impedes diffusion of oxygen and nutrients into the underlying cartilage, promoting **degenerative changes** there. The **chondrocytes begin to swell up** (hypertrophy), enlarging their lacunae. These changes both compress the matrix **into narrower trabeculae** and lead to calcification in these structures. Blood vessels from the former perichondrium now the periosteum penetrate through the bone collar previously perforated by osteoclasts, bringing osteoprogenitor cells to the porous central region. Next, osteoblasts adhere to the calcified cartilage matrix and produce continuous layers of primary bone that surround the cartilaginous matrix remnants.



Hyaline cartilage
Primary ossification center
Bone collar
Deteriorating cartilage matrix
Spongy bone formation
Blood vessel of periosteal bud
Secondary ossificaton center
Epiphyseal blood vessel
Medullary cavity
Articular cartilage
Spongy bone
Epiphyseal plate cartilage

Lecture No. 6

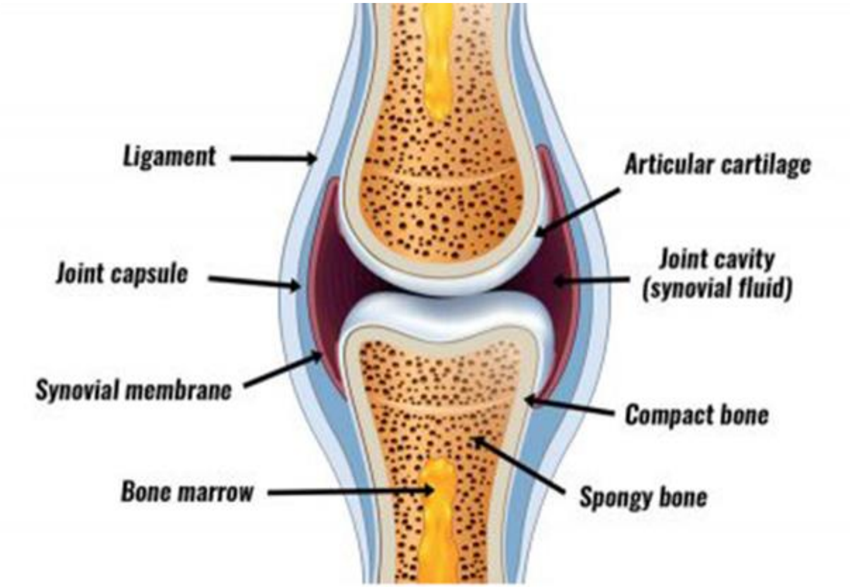
- **JOINTS**
- **Joints are regions where bones are capped and surrounded by connective tissues that firmly hold the bones together and determine the type and degree of movement between them. Joints may be classified as diarthroses, which permit free bone movement, and synarthroses (Gr. syn, together, + arthrosis, articulation), in which very limited or no movement occurs. There are three types of synarthroses, based on the type of tissue uniting the bone surfaces:**

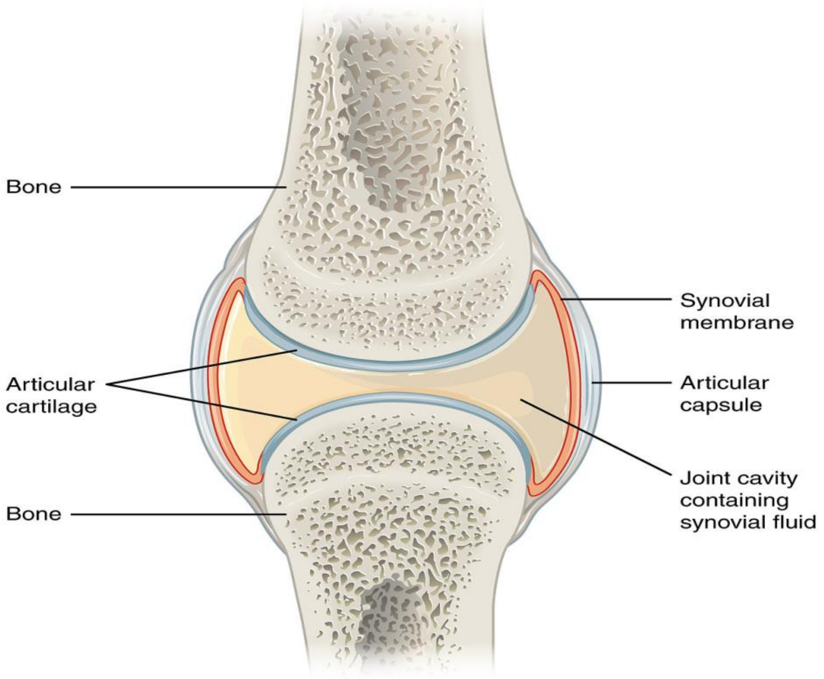
1- **Synostoses**, in which bones are united by bone tissue and no movement takes place. In older adults, synostoses unite the **skull bones**, which, in children and young adults, are united only by **dense connective tissue.**

2-**Synchondroses**, in which the bones are joined by **hyaline cartilage**. with little movement.

3-**Syndesmoses**, in which bones are joined by an interosseous ligament of dense connective tissue or fibrocartilage (eg, the pubic symphysis) with very limited movement.

Diarthroses are joints that generally **unite long bones and have great mobility**, such as the elbow and knee joints. In a diarthrosis, ligaments and a capsule of dense connective tissue maintain proper alignment of the bones. The capsule encloses a sealed joint cavity that contains **synovial fluid**, **a colorless, transparent, viscous fluid.** Synovial fluid is derived from blood plasma, but with a high concentration of hyaluronic acid produced by cells of the synovial membrane.





• Muscle Tissue

Muscle tissue is composed of cells differentiated for optimal use of the universal cell property termed contractility. Microfilaments and associated proteins together generate the forces necessary for cellular contraction, which drives **movement** within certain organs and the body as a whole. Nearly all muscle cells are of **mesodermal origin** and they differentiate mainly by a gradual process of cell lengthening with simultaneous synthesis of myofibrillar proteins.

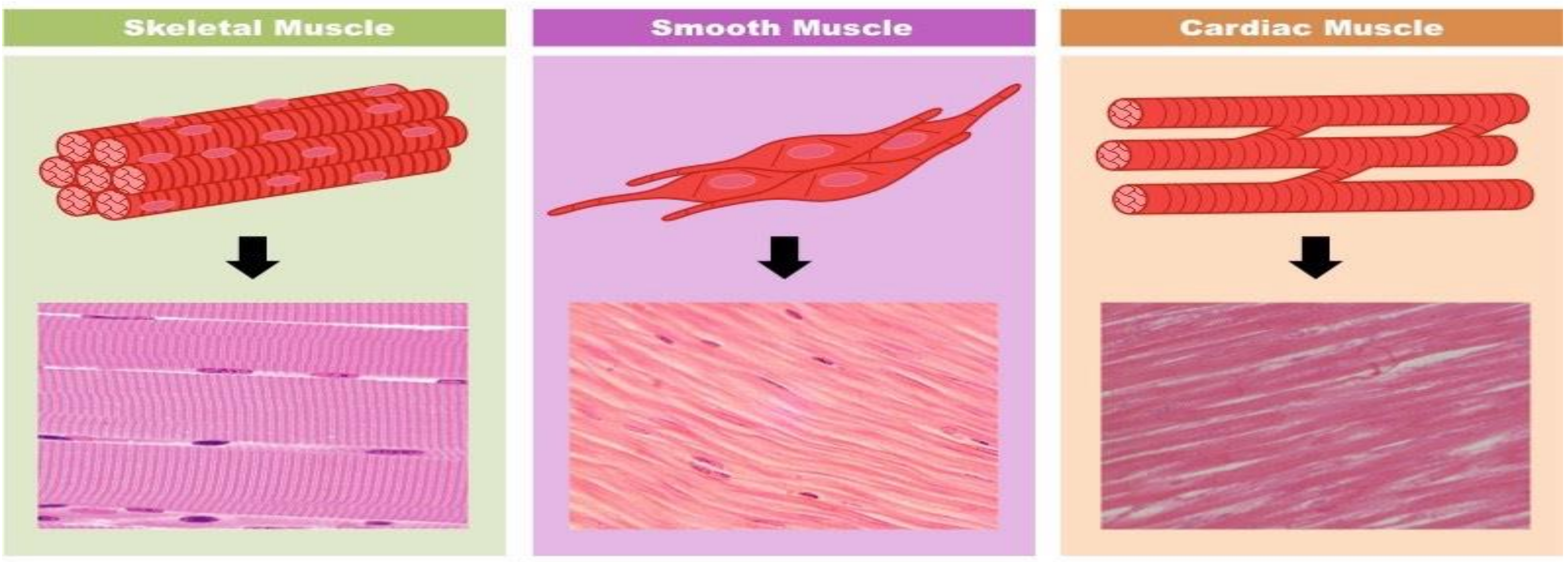
Three types of muscle tissue can be distinguished on the basis of morphologic and functional characteristics.

1- Skeletal muscle is composed of bundles of very long, cylindrical, multinucleated cells that show cross-striations. Their contraction is quick, forceful, and usually under voluntary control. It is caused by the interaction of thin actin filaments and thick myosin filaments whose molecular configuration allows them to slide upon one another.

- **2- Smooth muscle consists of collections of fusiform cells that do not show striations. Their contraction process is slow and not subject to voluntary control.**

3-Cardiac muscle

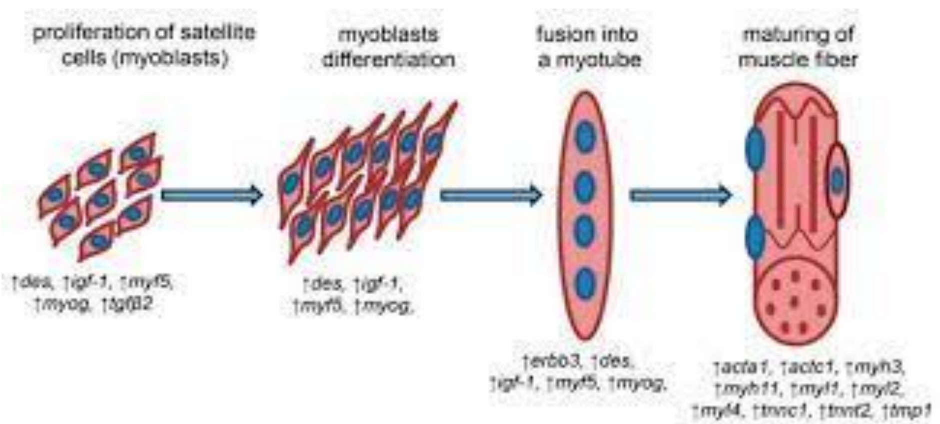
Has **cross-striations** and is composed of elongated, branched individual cells that lie parallel to each other. At sites of **end-to-end contact** are the **intercalated disks**, structures found only in cardiac muscle. Contraction of cardiac muscle is involuntary, vigorous, and rhythmic.

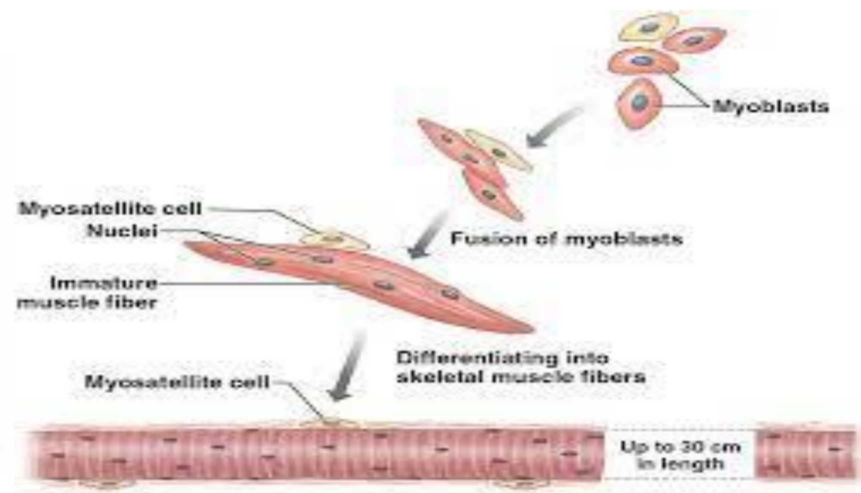


Some muscle cell organelles have names **that differ from their counterparts** in other cells. The **cytoplasm** of muscle cells is called **sarcoplasm** and the **smooth ER** is called **sarcoplasmic reticulum**. The **sarcolemma** is the cell membrane, or **plasmalemma**.

SKELETAL MUSCLE

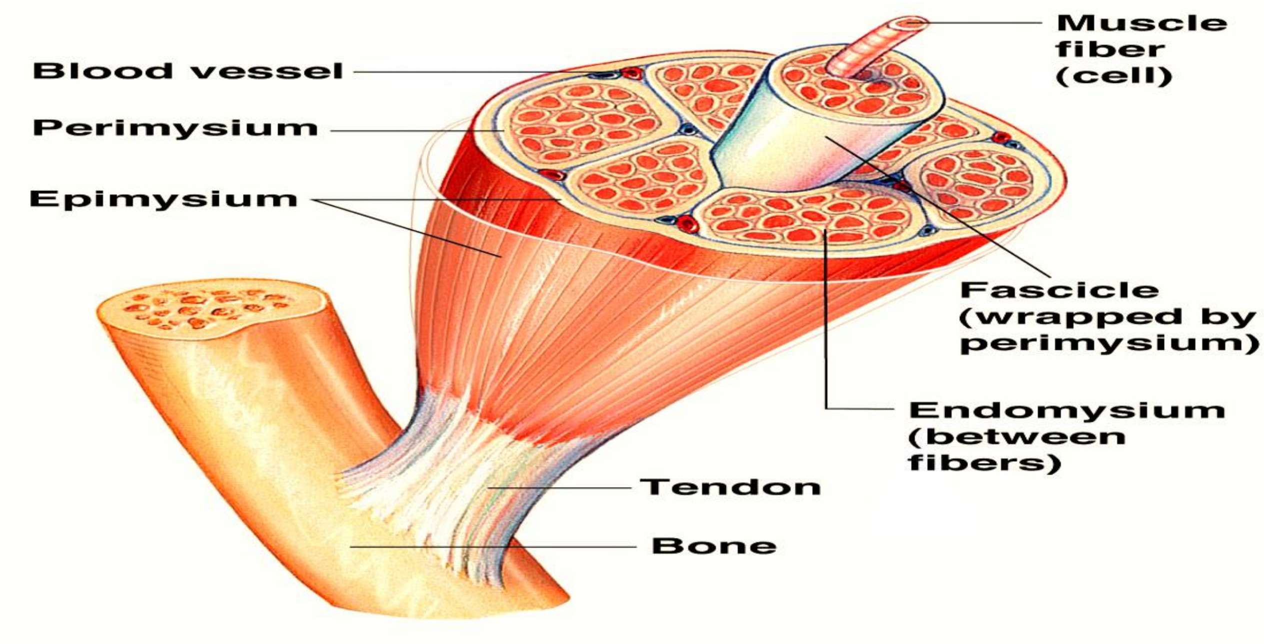
Skeletal muscle consists of muscle fibers, which are long, cylindrical multinucleated cells. **Multi nucleation** results from the fusion of embryonic mesenchymal cells called **myoblasts**. The long oval nuclei are usually found at the periphery of the cell **under the cell membrane** . This characteristic nuclear location is helpful in discriminating skeletal muscle from cardiac and smooth muscle, both of which have centrally located nuclei.





• Organization

The masses of fibers that make up the various types of muscle are arranged in **regular bundles** surrounded by the **epimysium**, **an external sheath of dense connective tissue surrounding the entire muscle** .From the epimysium, t**hin septa of connective tissue extend inward, surrounding the fascicles or bundles of fibers within a muscle** is called the **perimysium.** Each muscle fiber is itself surrounded by a more delicate connective tissue, the **endomysium**, **composed of a basal lamina synthesized by the multinucleated fibers themselves as well as reticular fibers and fibroblasts**. Within each fiber the nuclei are displaced **peripherally** against the sarcolemma.

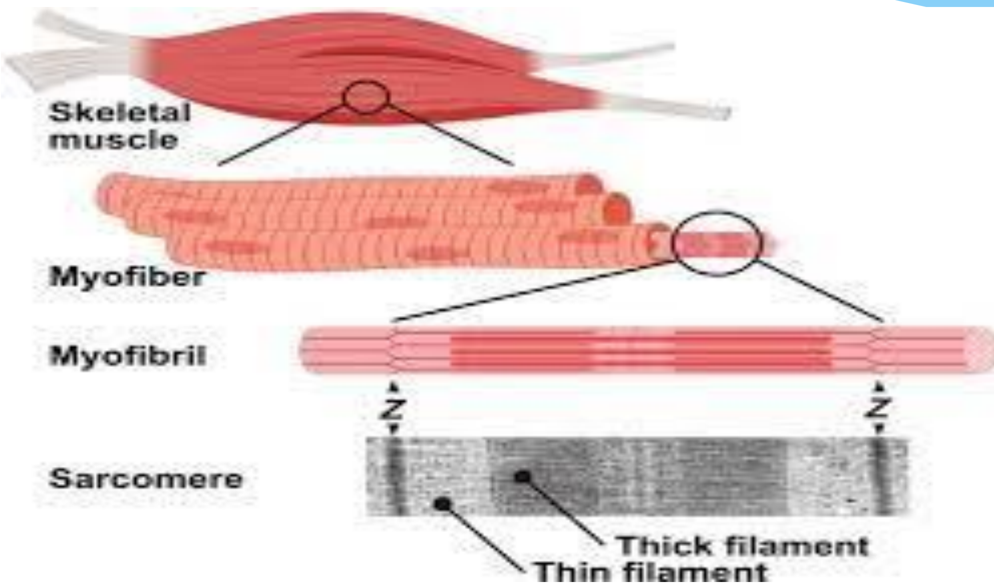


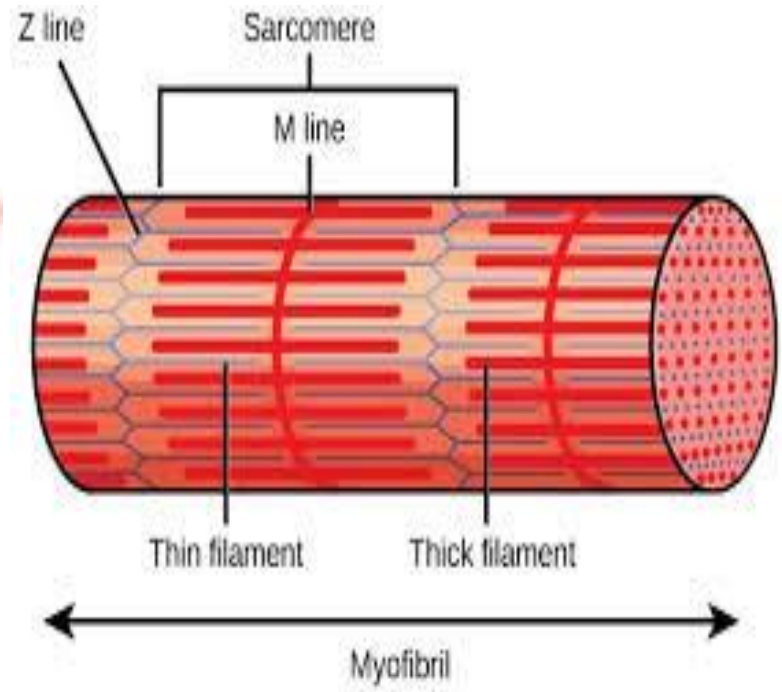
- One of the most important roles of this connective tissue is to transmit the mechanical forces generated by the contracting muscle cell/fibers because individual muscle cells extend from one end of a muscle to the other.
- Blood vessels penetrate the muscle within the connective tissue septa and form a rich capillary network in the endomysium . Lymphatic vessels and
- larger blood vessels are found in the other connective tissue layers.

Muscle Fibers

As observed with the light microscope, longitudinally sectioned skeletal muscle fibers show cross-striations of alternating light and dark bands .The **darker bands** are called **A bands** (anisotropic in polarized light); the **lighter bands** are called **I bands** (isotropic, do not alter polarized light). In the TEM each I band is seen to be **bisected by a dark transverse line**, the **Z line** (Ger. Zwischenscheibe, between the discs). **The repetitive functional subunit of the contractile apparatus**, **the sarcomere**, extends from Z line to Z line in resting muscle.

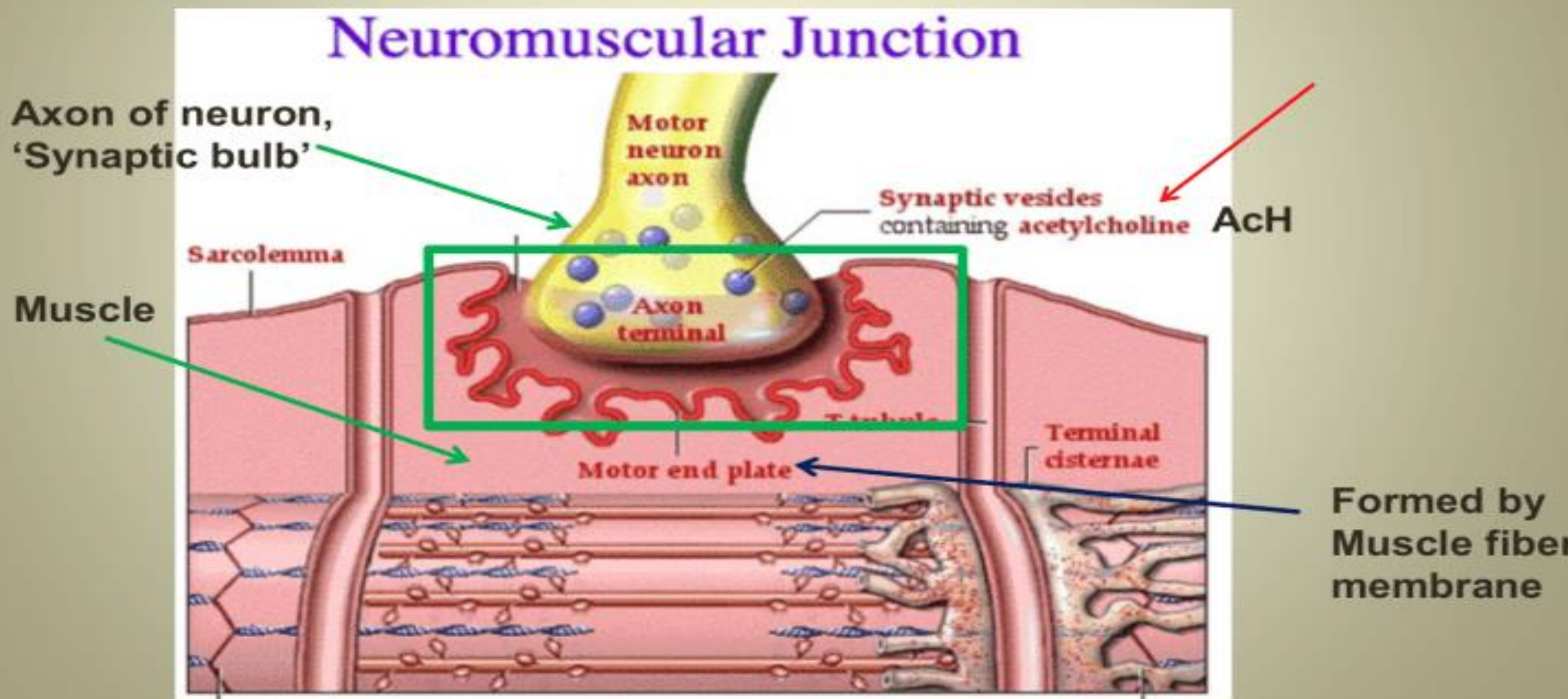
- Structure of muscle fiber





Skeletal Muscle Contraction

1. Neurotransmitter must stimulate muscle. This happens at the neuromuscular junction.

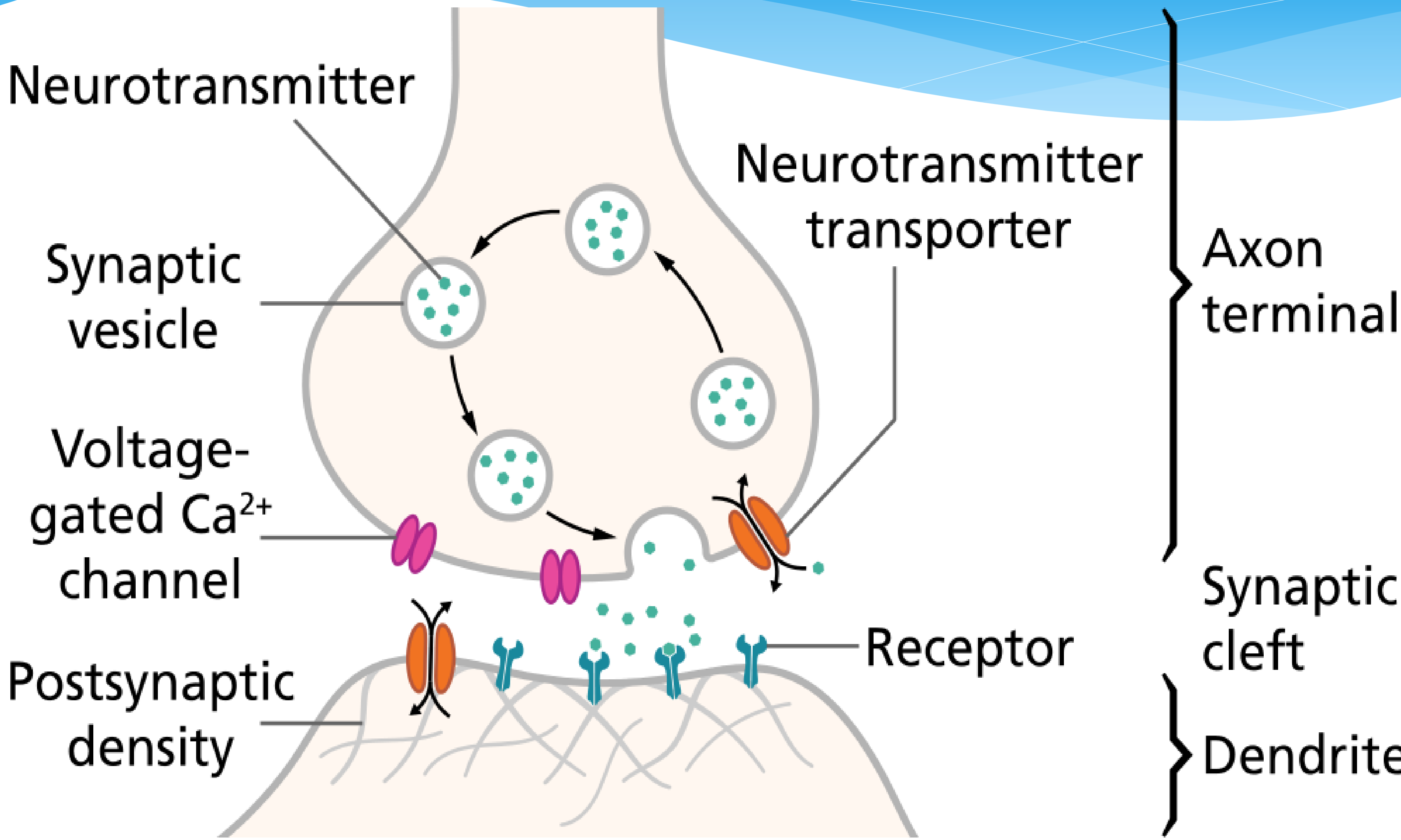


Structure of synapse

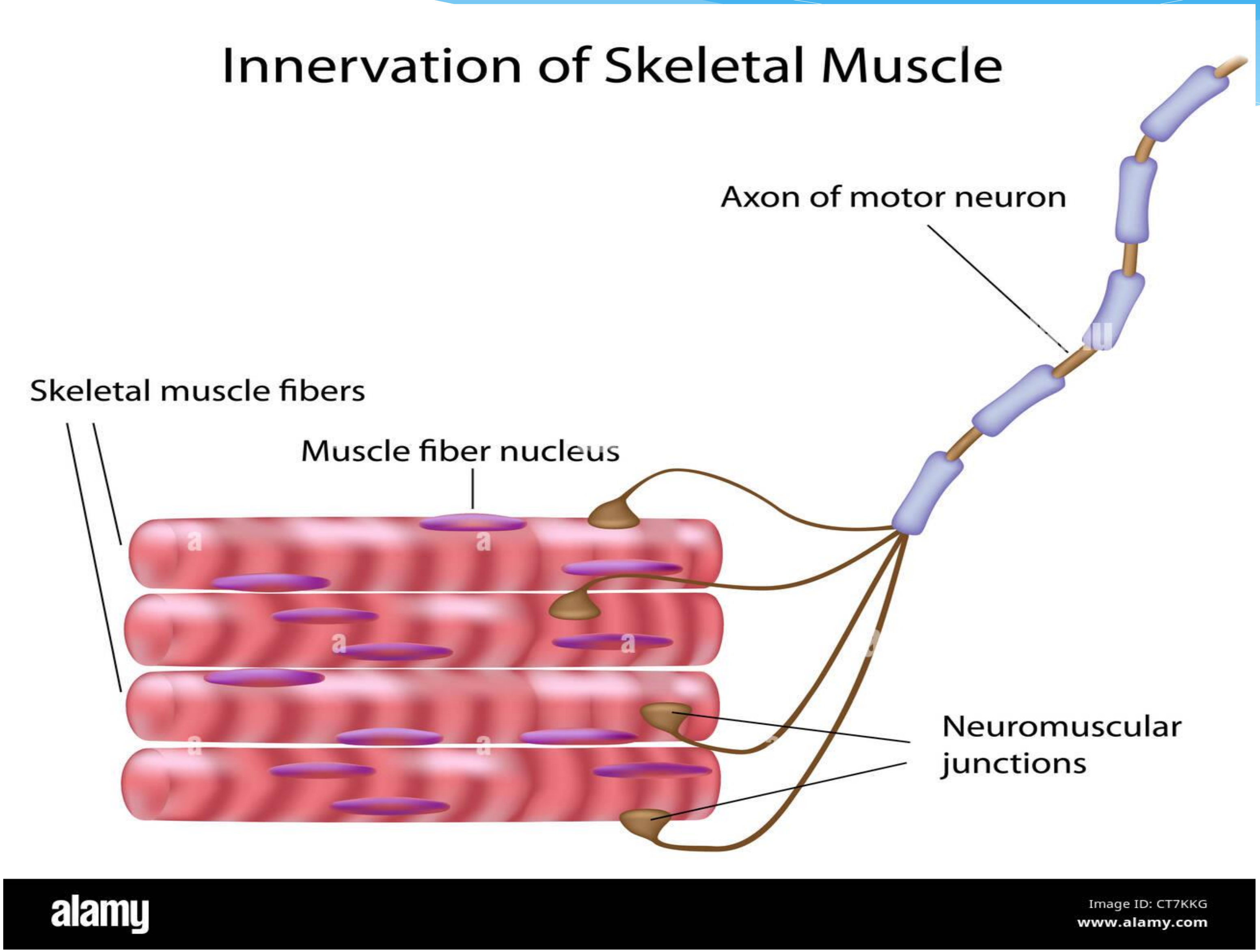
- **Mechanism of Contraction**
- 1-Resting sarcomeres consist of partially overlapping thick and thin filaments. During contraction, neither the thick nor thin filaments changes their length.
- 2-Contraction is the result of an increase in the amount of overlap between the filaments caused by the sliding of thin and thick filaments past one another.
- 3-Contraction is induced by an action potential produced at a synapse, the neuromuscular junction, between the muscle fiber and a terminus of a motor axon.

Innervation

Myelinated motor nerves branch out within the perimysium connective tissue, where each nerve gives rise to several terminal twigs. At the site of innervation, the **axon loses its myelin** sheath and forms a dilated termination situated within a trough on the muscle cell surface. This structure is called the **motor end-plate**, or the **neuromuscular junction** . At this site, within the axon terminal are numerous mitochondria and synaptic vesicles, the latter containing the **neurotransmitter acetylcholine**. Between the axon and the muscle is a space, the **synaptic cleft** . At the junction, the sarcolemma is thrown into numerous deep **junctional folds**, which provide for greater surface area. In the sarcoplasm below the folds lie several nuclei and numerous mitochondria, ribosomes, and glycogen granules.

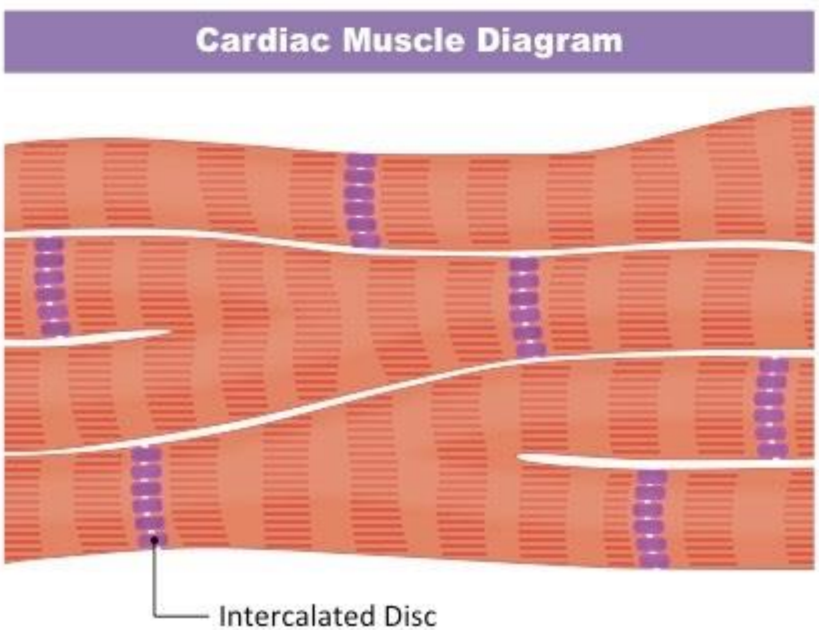


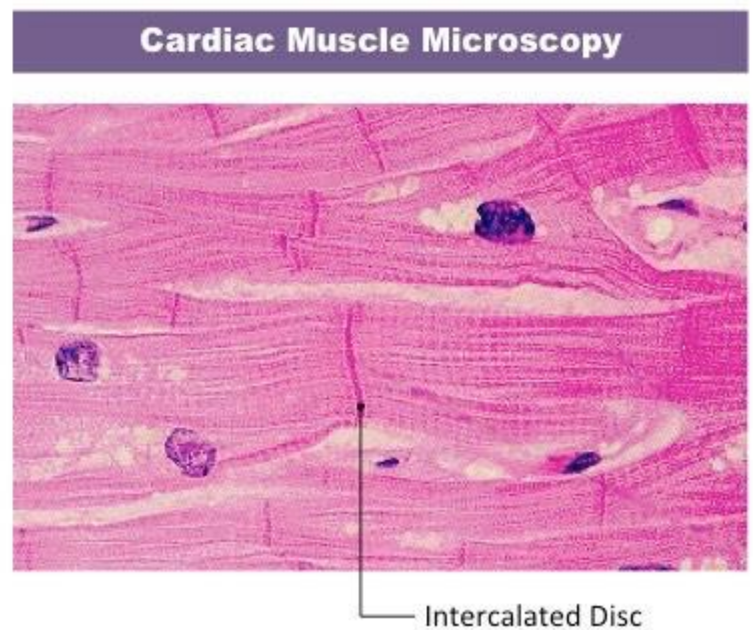
Structure of neuromuscular synapse


Innervation of Skeletal Muscle
Axon of motor neuron
Skeletal muscle fibers
Muscle fiber nucleus
Neuromuscular junctions
alamy
Image ID: CT7KKG
www.alamy.com

Cardiac muscle

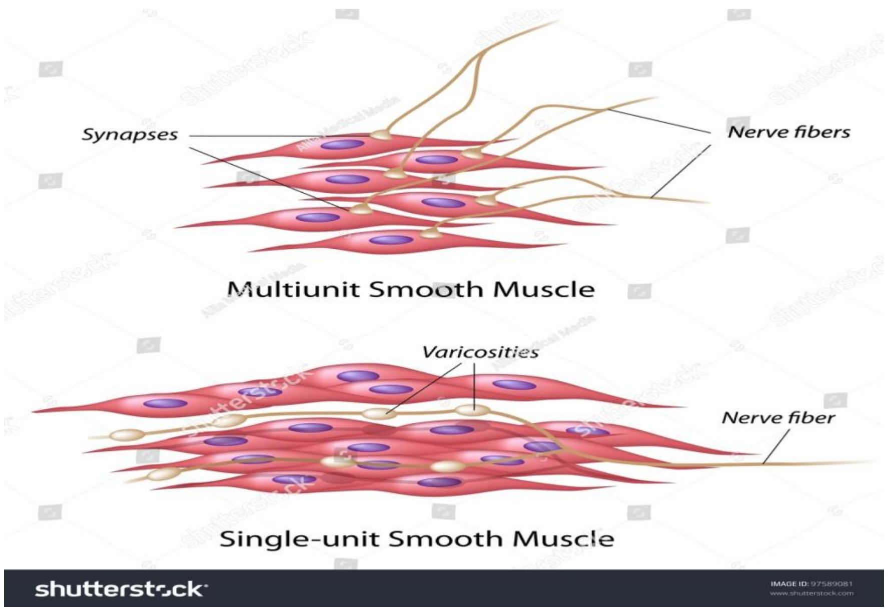
Cardiac muscle (or **myocardium**) makes up the thick middle layer of the heart. It is one of three types of muscle in the body, along with skeletal and smooth muscle. The myocardium is surrounded by a thin outer layer called the **epicardium** and an inner **endocardium.** The fibers consist of separate cells with interdigitating processes where they are held together. These regions of contact are called the **intercalated discs**. striated and have a **single, central nucleus**.

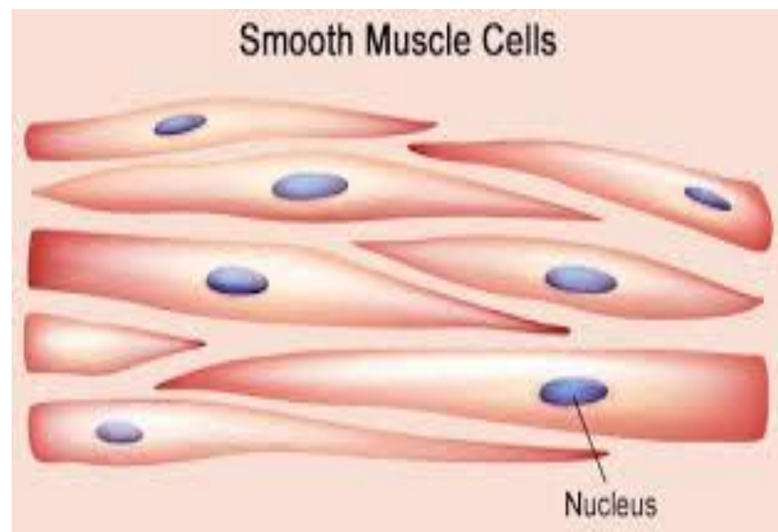


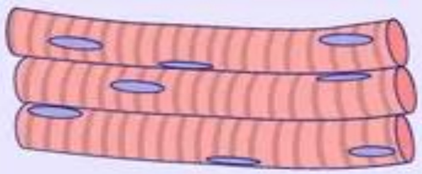
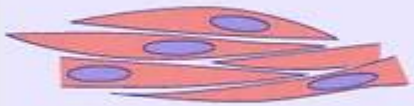
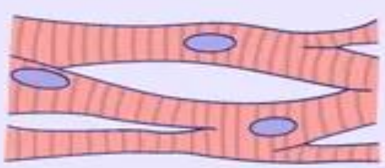


Smooth muscle

Smooth muscle fibers are elongated, tapering, and non striated cells, each of which is enclosed by a thin basal lamina and a fine network of reticular fibers. The connective tissues serve to combine the forces generated by each smooth muscle fiber into a concerted action, eg, peristalsis in the intestine. Each cell has **a single nucleus** located in the center of the cell's **broadest part**. Smooth muscle is present throughout the body, where it serves a variety of functions. It is in the stomach and intestines, where it helps with digestion and nutrient collection.





	Main features	Histology
Skeletal muscle	• Fibers: striated, tubular and multi nucleated • Voluntary • Usually attached to skeleton	
Smooth muscle	• Fibers: non-striated, spindle-shaped, and uninucleated • Involuntary • Usually covering wall of internal organs	
Cardiac muscle	• Fibers: striated, branched and uninucleated • Involuntary • Only covering walls of the heart	

Comparison among types of muscles

Lecture No. 7

Nerve tissue & Nervous system

The human nervous system is the most complex system in the body formed by a network of many billion nerve cells **(neurons),** all assisted by many more supporting **glial cells**. Each neuron has hundreds of interconnections with other neurons, forming a very complex system for processing information and generating responses. **Anatomists divide the nervous system into** :

1-Central nervous system (CNS), consisting of the brain and spinal cord

2-Peripheral nervous system (PNS), composed of the **cranial, spinal, and peripheral nerves** conducting impulses **to and from the CNS** (motor and sensory nerves respectively) and **ganglia** which are small groups of nerve cells outside the CNS.

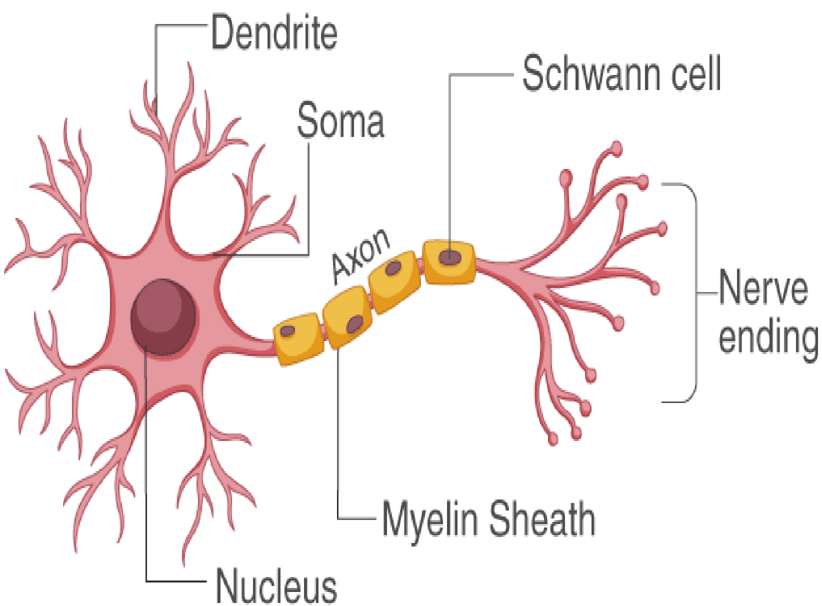
Both central and peripheral nerve tissue consists of two cell types: nerve cells, or **neurons**, which usually show numerous long processes; and **various glial cells** (**Gr. glia, glue**), which have **short processes**, **support and protect neurons**, and **participate in neural activity, neural nutrition, and defense of cells in the central nervous system**.

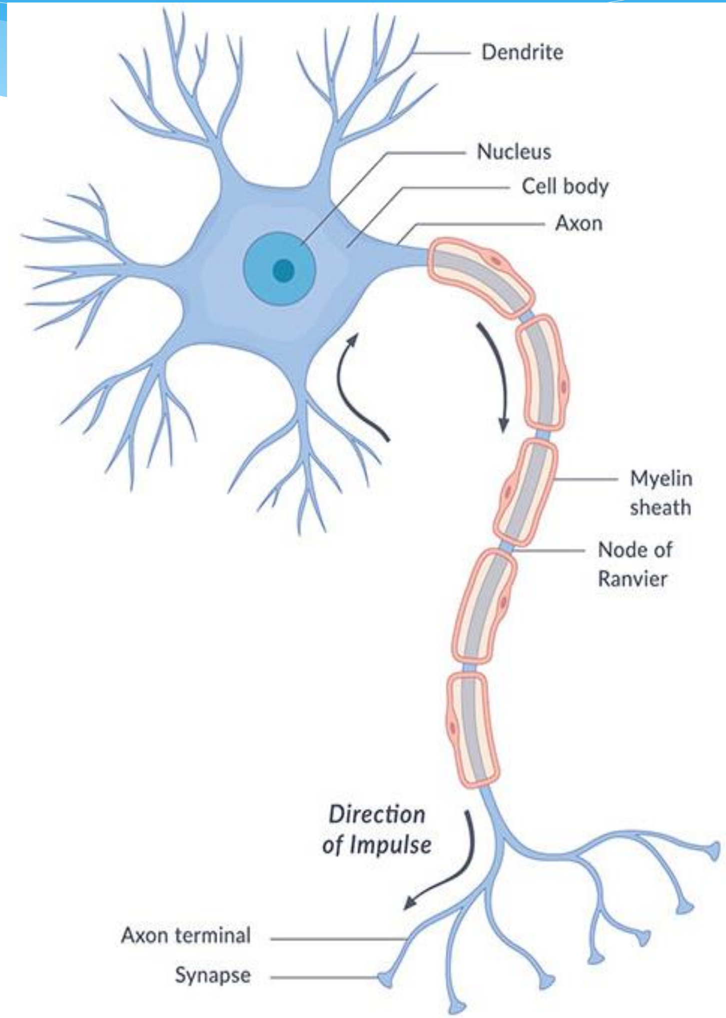
- **NEURONS**

The functional unit in both the CNS and PNS is the neuron or nerve cell. Most neurons consist of three parts ,the cell body**, or perikaryon,** **which is the synthetic or trophic center for the entire nerve cell and is receptive to stimuli**; **the dendrites**, many **elongated processes specialized to receive stimuli from the environment, sensory epithelial cells, or other neurons**; and the **axon (Gr. axon, axis**), which **is a single process specialized in generating and conducting nerve impulses to other cells (nerve, muscle, and gland cells).**

The distal portion of the axon is usually branched as the terminal **arborization.** Each branch terminates on the next cell in dilatations called end **bulbs** (boutons), which interact with other neurons or non nerve cells at structures called **synapses**. **Synapses initiate impulses in the next cell of the circuit**.

STRUCTURE OF NEURON

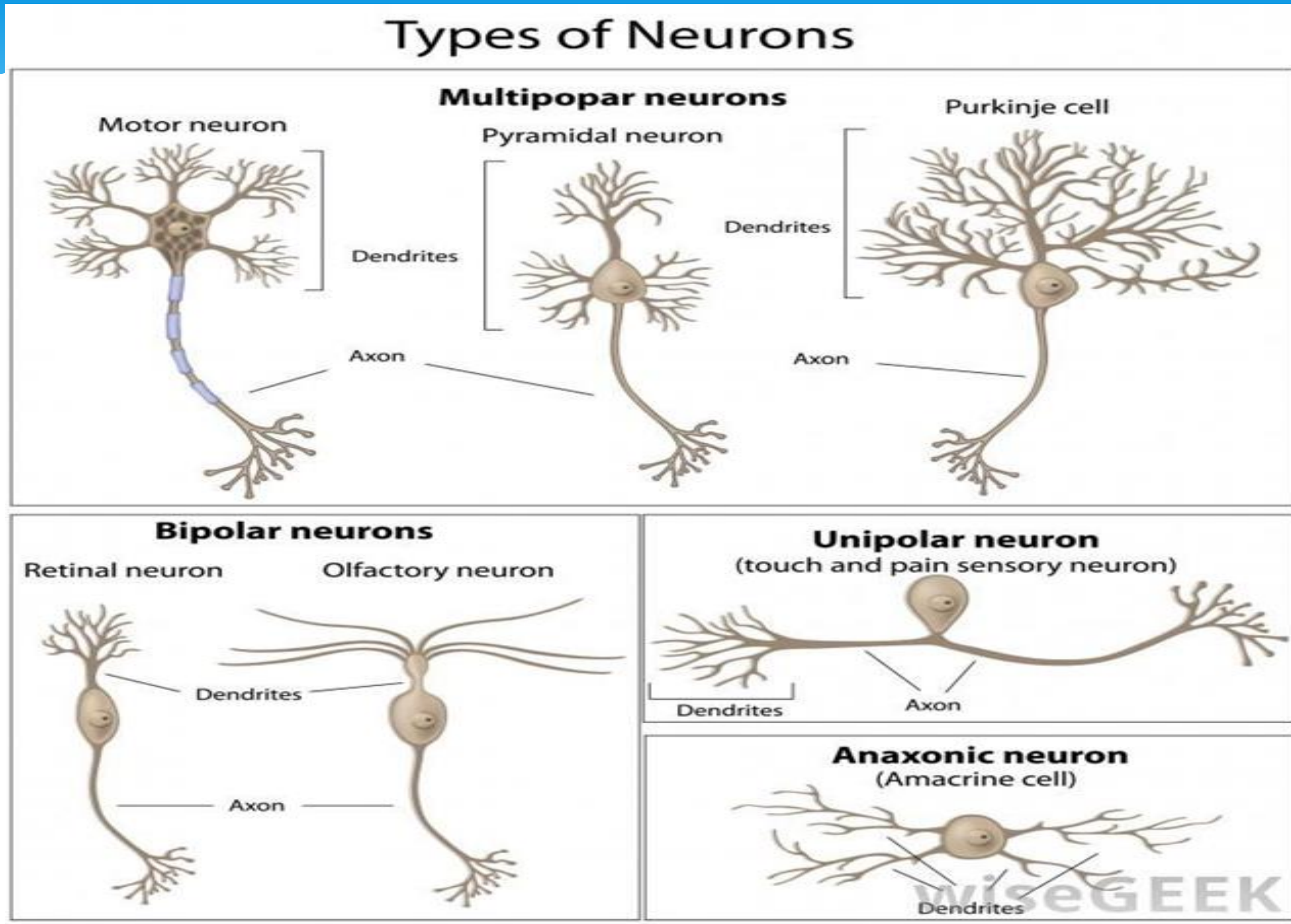




- **Neurons can be classified according to the number of processes extending from the cell body :**
- **Multipolar neurons, which have one axon and two or many dendrites.**
- **Bipolar neurons, with one dendrite and one axon.**
- **Unipolar or pseudo unipolar neurons, which have a single process that bifurcates close to the perikaryon, with the longer branch extending to a peripheral ending and the other toward the CNS.**

Neurons and their processes are extremely variable in size and shape. Cell bodies can be very large, Other cells are among the smallest cells in the body; for example, the cell bodies of granule cells of the.

Neurons **can also be subdivided according to their functional** roles . **Motor (efferent)** neurons control effector organs such as muscle fibers and exocrine and endocrine glands. **Sensory (afferent)** neurons are involved in the reception of sensory stimuli from the environment and from within the body.


Types of Neurons
Multipopar neurons
Motor neuron
Pyramidal neuron
Purkinje cell
Dendrites
Dendrites
Axon
Axon
Bipolar neurons
Retinal neuron
Olfactory neuron
Dendrites
Axon
Unipolar neuron
(touch and pain sensory neuron)
Dendrites
Axon
Anaxonic neuron
(Amacrine cell)
Dendrites
wiseGEEK

Cell Body (Perikaryon)

The cell body, or perikaryon (soma) , is the part of the neuron that contains the **nucleus** and surrounding **cytoplasm**, exclusive of **the cell processes**. It is primarily a **trophic** center, although most neurons perikarya also receive a great number of nerve endings that **convey excitatory or inhibitory stimuli** generated in other nerve cells. When appropriate stains are used, RER and free ribosomes appear under the light microscope as clumps of **basophilic material called chromatophilic substance** (often called **Nissl bodies).**

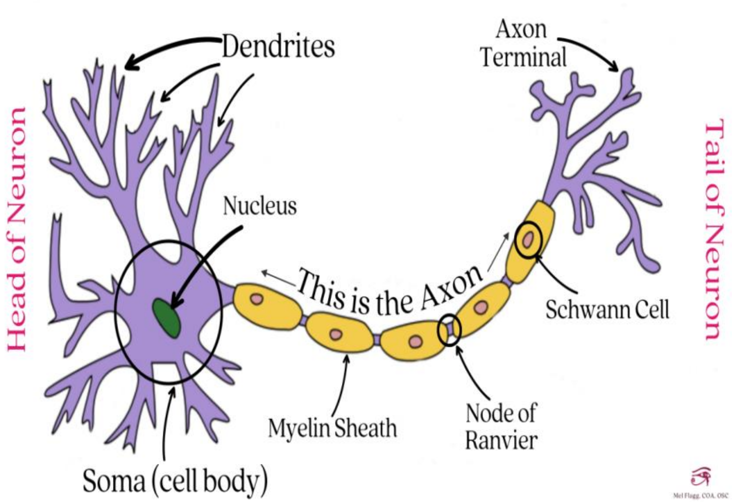
The amount of chromatophilic substance varies according to the type and functional state of the neuron and is particularly abundant in large nerve cells such as motor Neurons.

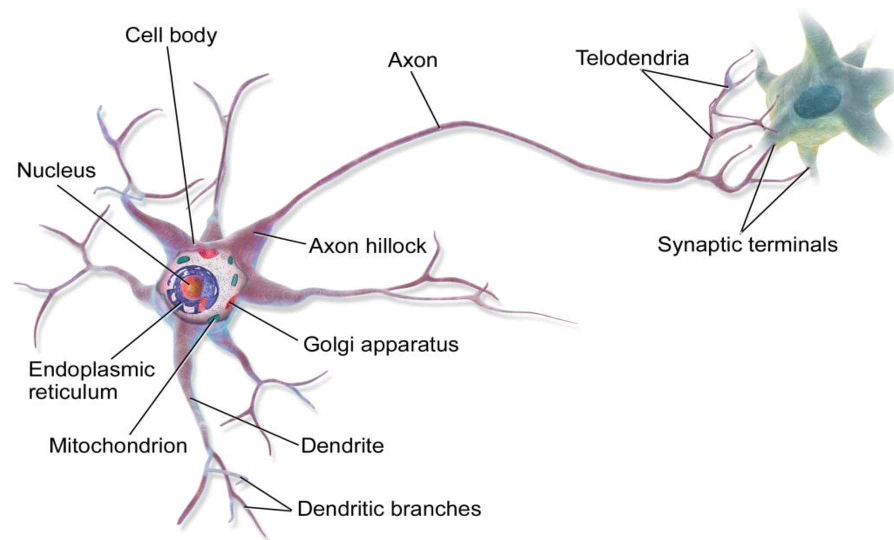
Dendrites

Dendrites (Gr. dendron, tree) are usually short and divide **like the branches of a tree .** They are often covered with many synapses and are the principal signal reception and processing sites on neurons. Most nerve cells have numerous dendrites, which considerably increase the receptive area of the cell. The **arborization** of dendrites makes it possible for **one neuron to receive and integrate a great number of axon terminals** from other nerve cells.

• Axons

Most neurons have **only one axon,** a cylindrical process that varies in length and diameter according to the type of neuron. Axons are usually very long processes. For example, axons of the motor cells of the spinal cord that innervate the foot muscles may have a length of **up to 100 cm** . All axons originate from **a pyramid-shaped region**, **the axon hillock,** arising from the perikaryon . The plasma membrane of the axon is often called the **axolemma** and its contents are known as **axoplasm.** Just beyond the axon hillock, at **an area called** the **initial segment, is the site where various excitatory and inhibitory stimuli impinging on the neuron.**





• Synaptic Communication

The synapse (Gr. synapsis, **union**) **is responsible for the transmission of nerve impulses from neuron to another cell and insures that transmission is unidirectional.** Synapses are sites of **functional contact** between neurons or between neurons and other effector cells. The function of the synapse is to **convert an electrical signal (impulse)** from the **presynaptic cell** into a **chemical signal** that acts on the **postsynaptic cells**. Most synapses transmit information by releasing **neurotransmitters .** Neurotransmitters **are chemicals that bind specific receptor proteins to either open or closed ion channels or initiate second-messenger cascades.**

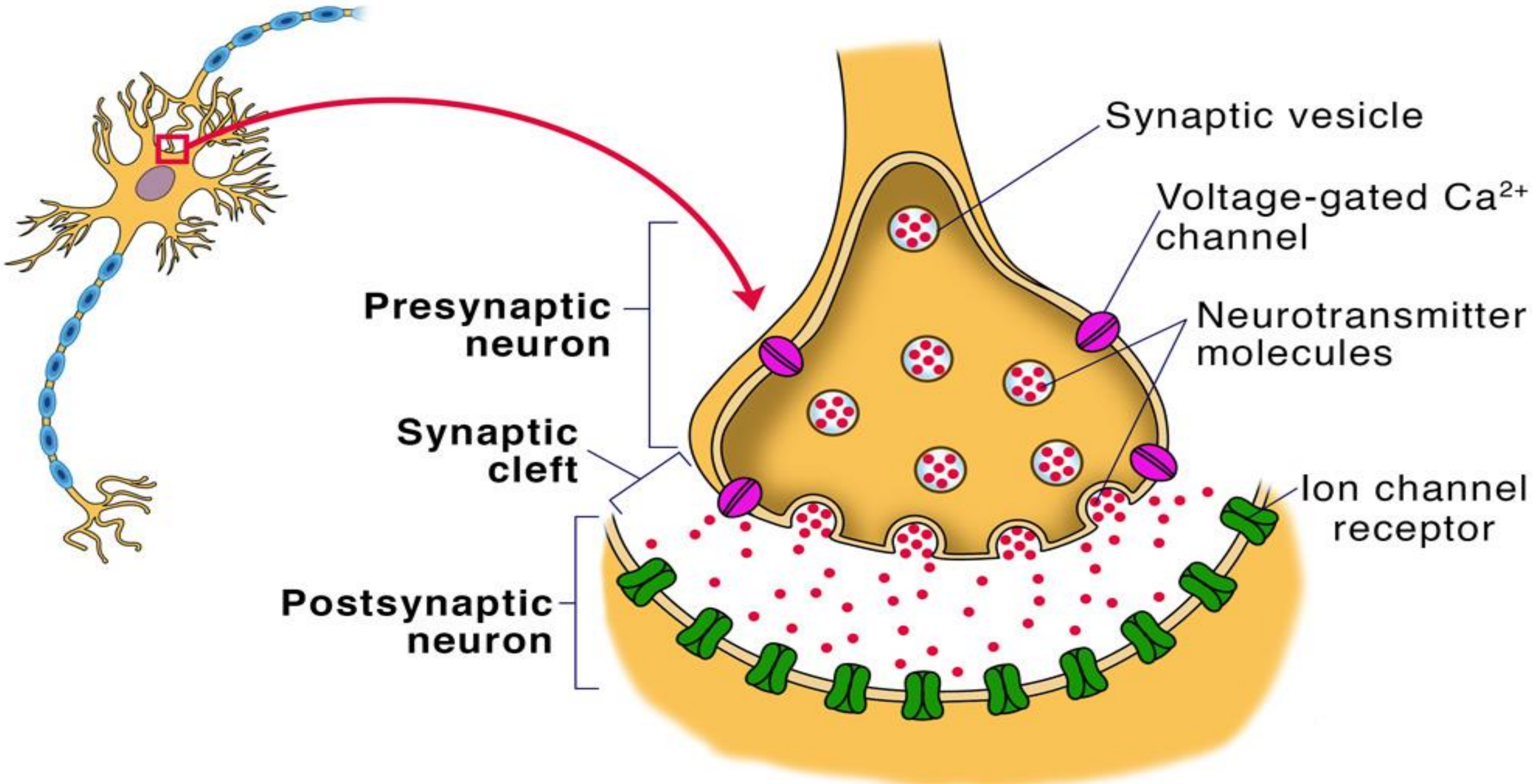
A synapse has the following structure:

1-Presynaptic axon terminal (terminal bouton) from which neurotransmitter is released.

2-Postsynaptic cell membrane with receptors for the transmitter and ion channels or other mechanisms to initiate a new impulse.

3-Synaptic cleft (20–30 nm) wide intercellular space separating the presynaptic and postsynaptic membranes.

Synapse

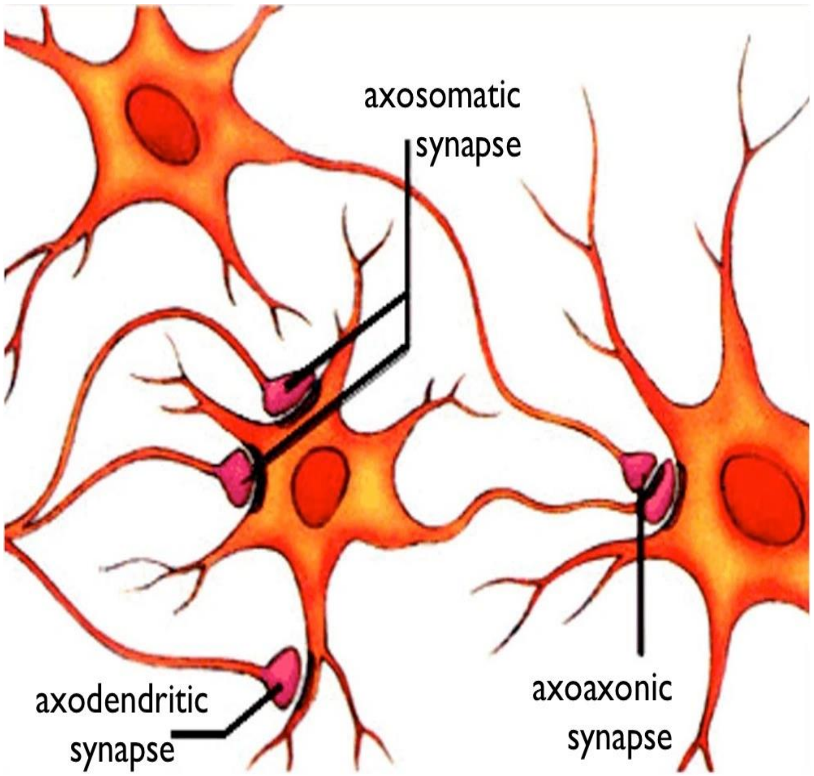

ScienceFacts.net
Synaptic vesicle
Voltage-gated Ca^{2+} channel
Neurotransmitter molecules
Presynaptic neuron
Synaptic cleft
Ion channel receptor
Postsynaptic neuron

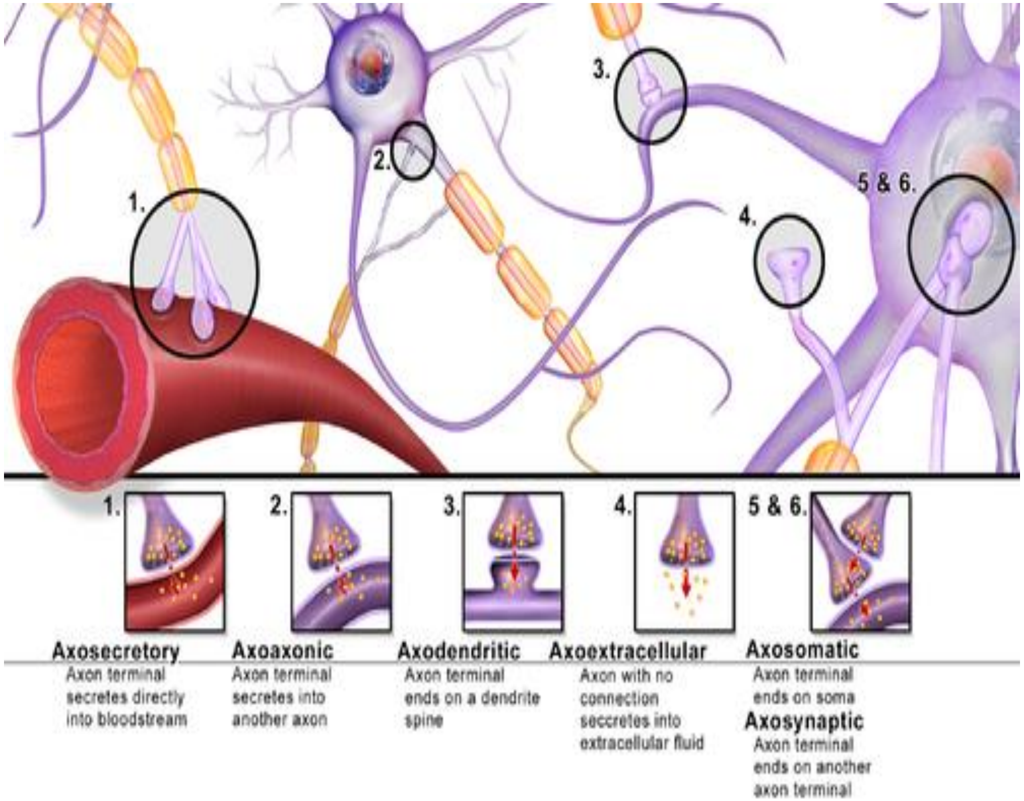
Morphologically, various types of synapses are seen between neurons.

1-If an axon forms a synapse with a cell body, it is called an **axosomatic synapse**.

2- with adendrite, axodendritic; or

3-with an axon, axoaxonic .The axoaxonic synapse is **less common** and is used to modulate synaptic activity.



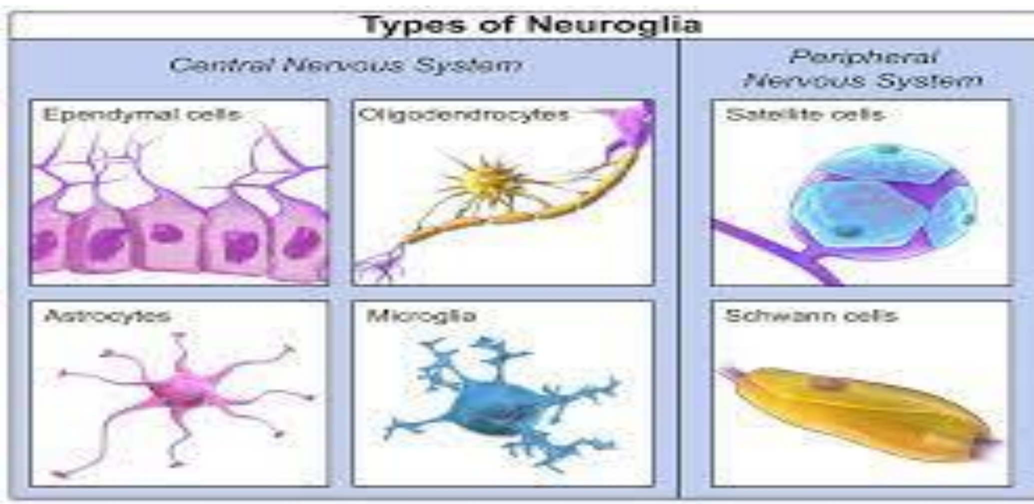


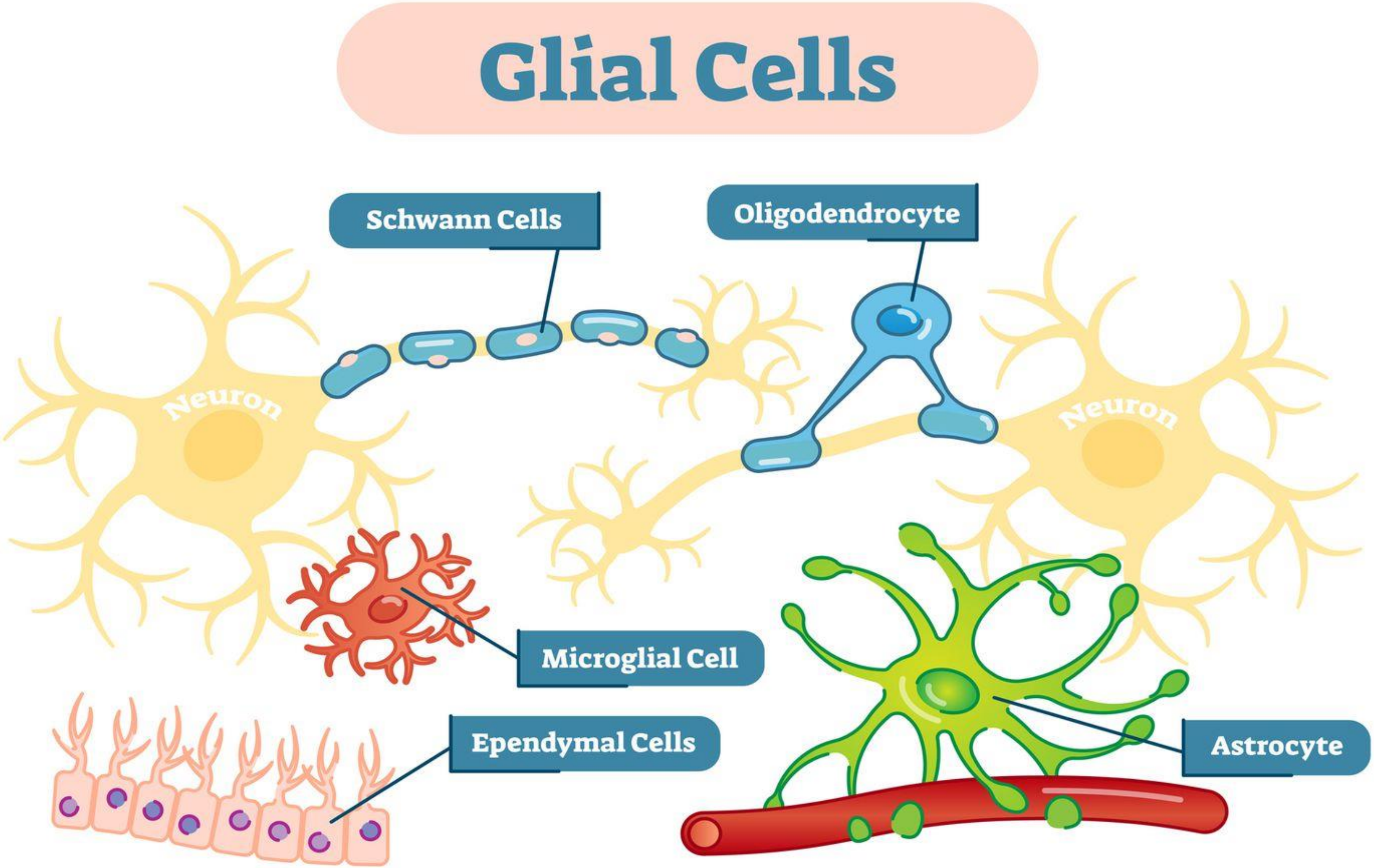
GLIAL CELLS

Glial cells are 10 times **more abundant in the mammalian brain than neurons**. In the CNS glial cells surround most of the neuronal cell bodies, which are usually much larger than glial cells, and the processes of axons and dendrites that occupy the spaces between neurons. Except around the larger blood vessels, the CNS has only a **very small amount of connective tissue or ECM.**

Glial cells furnish a microenvironment ideal for neuronal activity. A dense network of fibers from processes of both neurons and glial cells fills the inter neuronal space of the CNS and is called the **neuropil.**

Glial cells exist in **the both central nervous system (CNS) and the peripheral nervous system (PNS). T**he most glial cells include **oligodendrocytes** , **astrocytes, microglia**, and **ependymal cells in the CNS** and **schwann cells**, **satellite cells, and enteric glial cells in the PNS.**




Glial Cells
Schwann Cells
Oligodendrocyte
Neuron
Neuron
Microglial Cell
Ependymal Cells
Astrocyte

Oligodendrocytes

Oligodendrocytes (Gr. oligos, small, few + dendron, tree + kytos, cell) produce the **myelin sheath** that provides the electrical insulation for neurons in the CNS. Oligodendrocytes extend **processes that wrap around parts of several axons,** producing **a myelin shea**th .They are the **predominant** glial cell in **CNS** white matter.

Astrocytes

Astrocytes (Gr. astron, star, + kytos) have a **large number** of radiating processes and are unique to the **CNS**. Astrocytes with relatively few long processes are called **fibrous astrocytes** and are located in the **white matter**; **protoplasmic astrocytes**, with many short, branched processes, are found in the **gray matter**.

Ependymal Cells

Are low columnar or cuboidal cells that line the ventricles of the brain and central canal of the spinal cord .In some CNS locations, **the apical ends of ependymal cells** have **cilia**, which facilitate the movement of **cerebrospinal fluid (CSF**), or long microvilli, which are likely involved in **absorption.**

Microglia

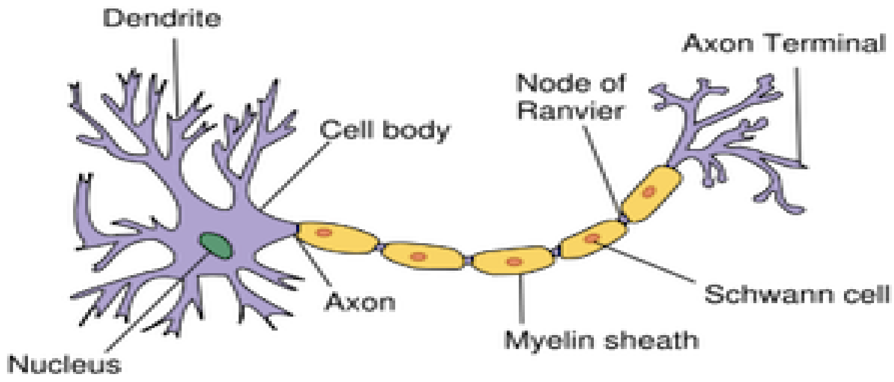
Somewhat **less numerous than** oligodendrocytes or astrocytes but more evenly distributed throughout **gray and white matter**, microglia are **small cells** with short irregular processes .Unlike other glial cells microglia migrate through the neuropil, analyzing the tissue for damaged cells and **invading microorganisms**.

Schwann Cells (Neurolemmocytes)

Also called **neurolemmocytes,** are found only in the PNS and have trophic interactions with axons and allow for their myelination like the oligodendrocytes of the CNS. One neurolemmocyte forms myelin around a segment of one axon, in contrast to the ability of oligodendrocytes to branch and sheath parts of more than one axon.

Satellite Cells

Closely associated with the neurons, the satellite cells exert a trophic or supportive role.

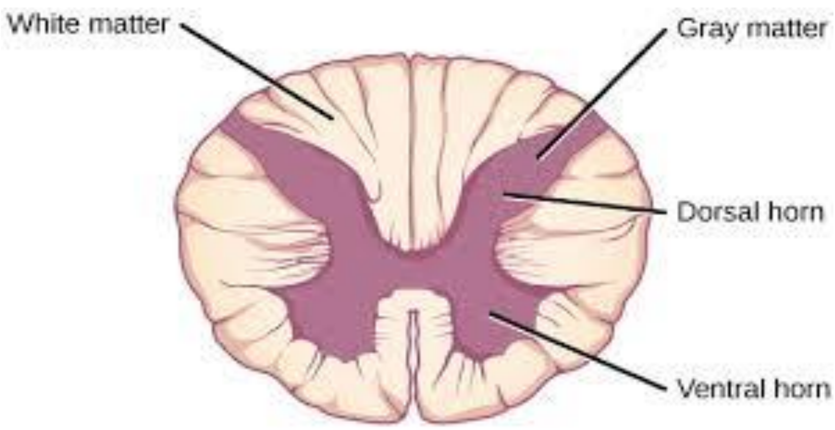


Central nervous system

The principal structures of the CNS are the **cerebrum, cerebellum,** and **spinal cord**. It has virtually **no connective tissue** and is therefore a relatively soft, gel-like organ.

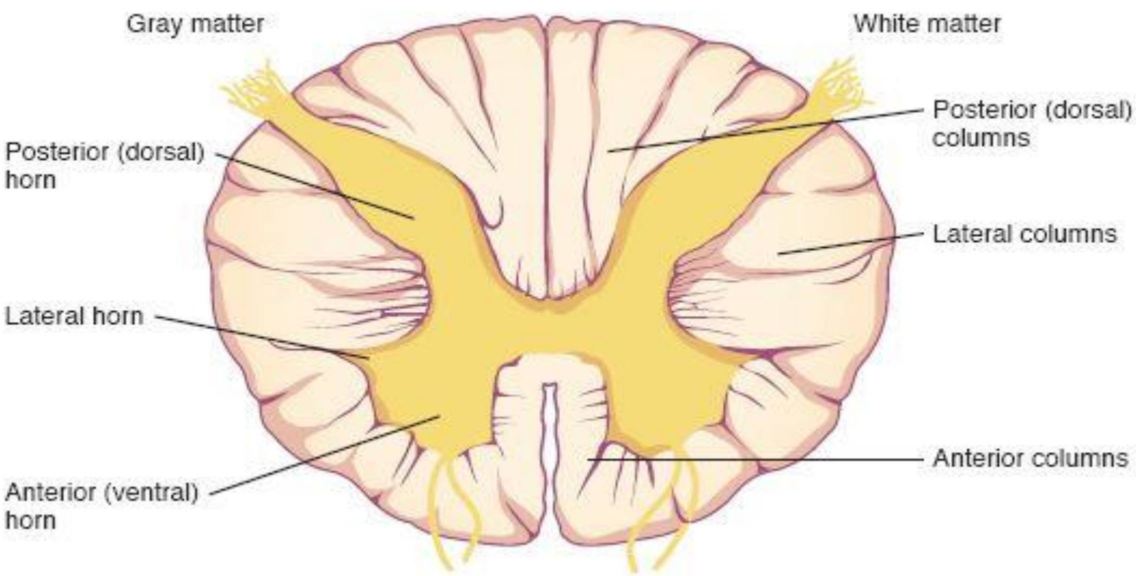
When sectioned, the cerebrum, cerebellum, and spinal cord show regions of **white** (**white matter**) and **gray** (**gray matter**), differences caused by the differential distribution of myelin. The main components of white matter are myelinated axons and the myelin-producing oligodendrocytes. White matter **does not contain neuronal cell bodies**, but microglia are present.

Gray matter contains abundant neuronal cell bodies , dendrites , the initial un myelinated portions of axons, astrocytes, and microglial cells.



Section in spinal cord

In cross sections of the spinal cord, white matter is **peripheral** and gray matter is **internal** and has the general shape of an **H** . In the center is an opening, the **central canal**, the gray matter forms the anterior horns, which contain motor neurons whose axons make up the ventral roots of spinal nerves, and the posterior horns, which receive sensory fibers from neurons in the spinal ganglia (dorsal roots). Spinal cord neurons are large and multipolar, especially the motor neurons in the anterior horns.



Meninges

The skull and the vertebral column protect the CNS. Between the bone and nervous tissue are membranes of connective tissue called the meninges .Three meningial layers are distinguished:

Dura mater

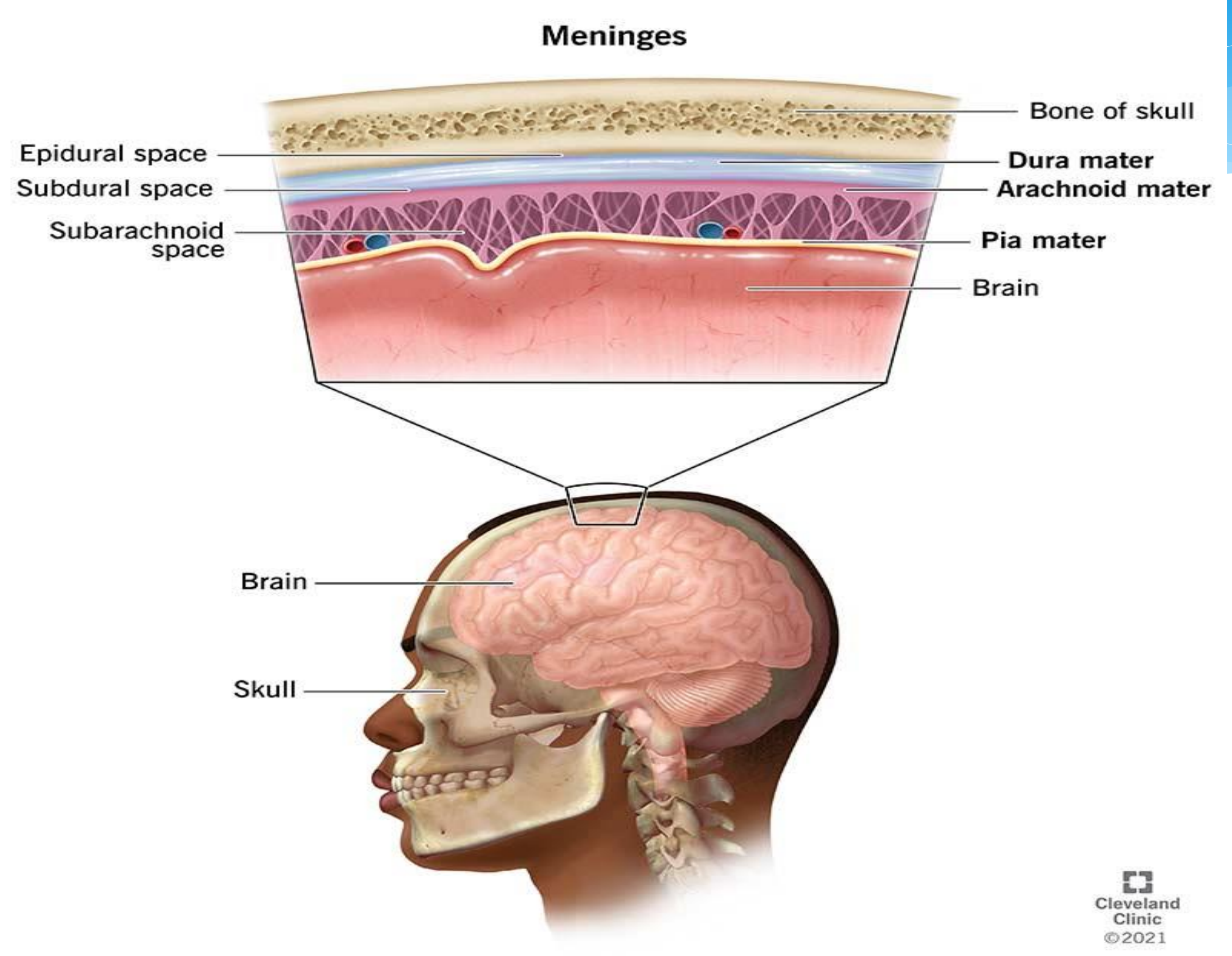
The dura mater is the **thick external layer consisting of den**se, fibroelastic connective tissue continuous with the periosteum of the skull.

Arachnoid

The arachnoid (Gr. arachnoeides, spider weblike) has two components: **(1) a** sheet of connective tissue in contact with the dura mater and **(2)** a system of loosely arranged trabeculae containing fibroblasts and collagen.

Pia mater

The innermost pia mater is lined internally by flattened, mesenchymally derived cells closely applied to the entire surface of the CNS tissue.


Meninges
Bone of skull
Epidural space
Dura mater
Subdural space
Arachnoid mater
Subarachnoid space
Pia mater
Brain
Brain
Skull
Cleveland Clinic
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PERIPHERAL NERVOUS SYSTEM

The main components of the peripheral nervous system are the nerves, ganglia, and nerve endings. Nerves are bundles of nerve fibers (axons) surrounded by glial cells and connective tissue.

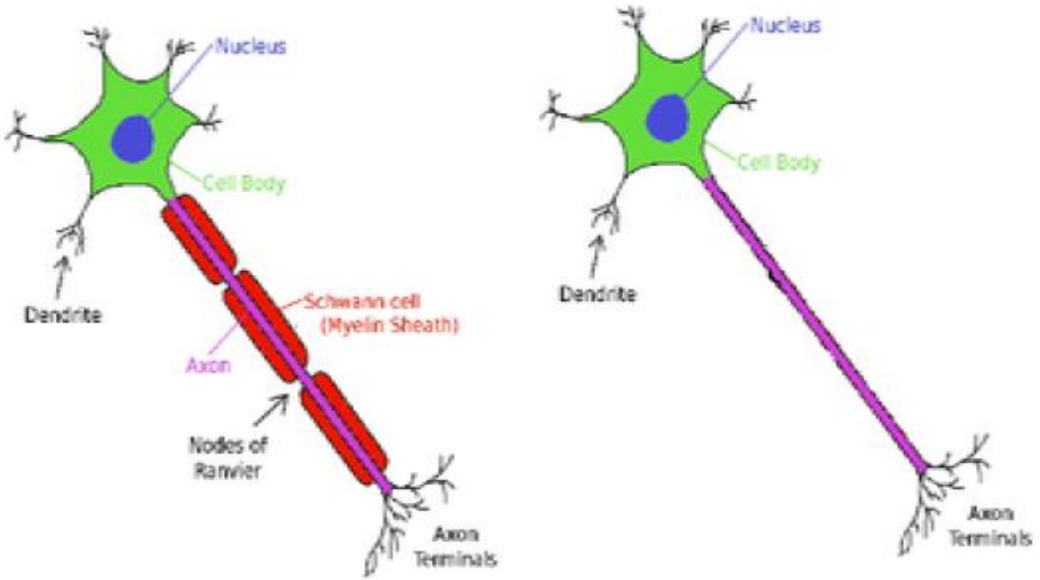
Nerve Fibers

Nerve fibers consist of **axons** enclosed within a **special sheath of cells**, peripheral nerves contain groups of nerve fibers. In peripheral nerve fibers, axons are **sheathed by Schwann cells,** also called **neurolemmocytes .**The sheath may or may not form myelin around the axons, depending on their diameter.

Axons of **small diameter** are usually **un-myelinated** nerve fibers .Progressively **thicker axons** are generally sheathed by increasingly numerous **concentric wrappings of the enveloping cell**, forming the myelin sheaths. These fibers are known as **myelinated** nerve fibers.

Unmyelinated nerve fibers

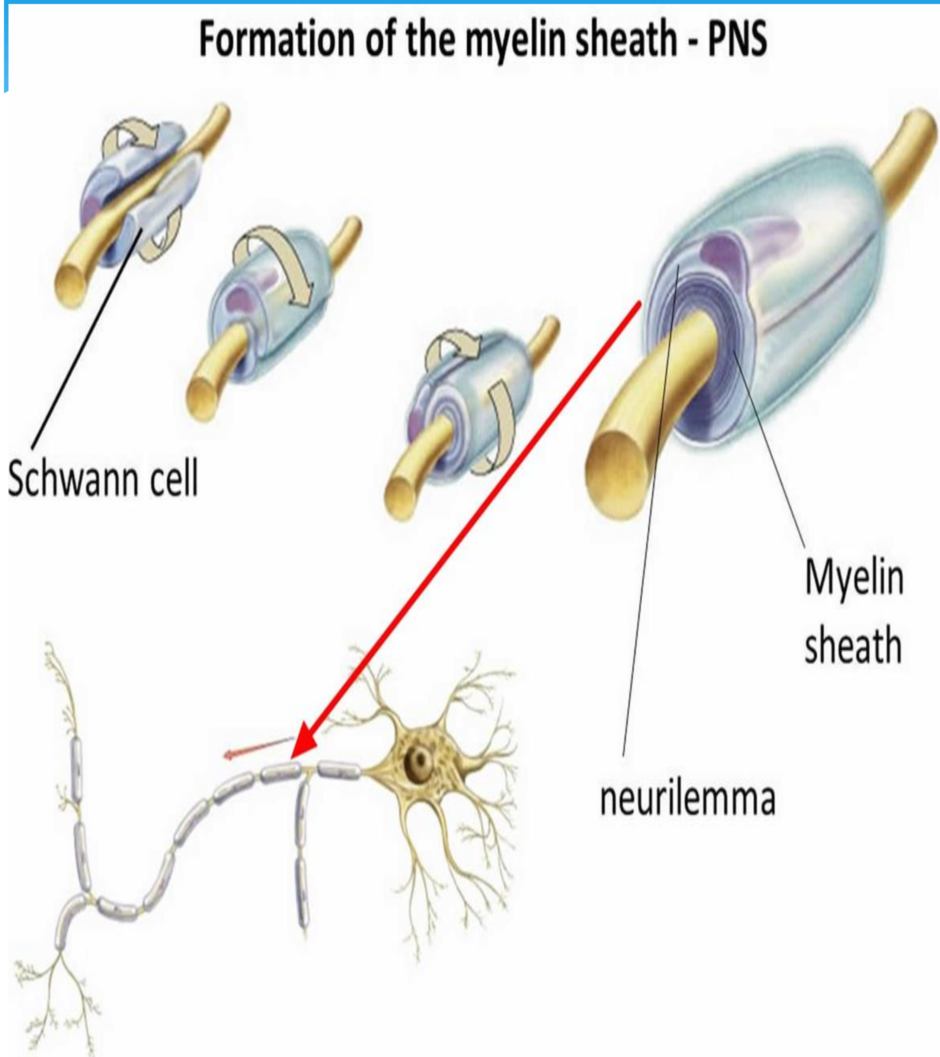
The CNS is rich in un-myelinated axons which are not sheathed at all but run free among the other neuronal and glial processes. However in the PNS, even all Un-myelinated axons are enveloped within simple folds of Schwann cells . In this situation the glial cell **does not form multiple wrapping** of itself as myelin. Unlike their association with individual myelinated axons, each Schwann cell can **enclose portions of many un-myelinated axons** with small diameters. Adjacent Schwann cells along un-myelinated nerve fibers do not form nodes of Ranvier.

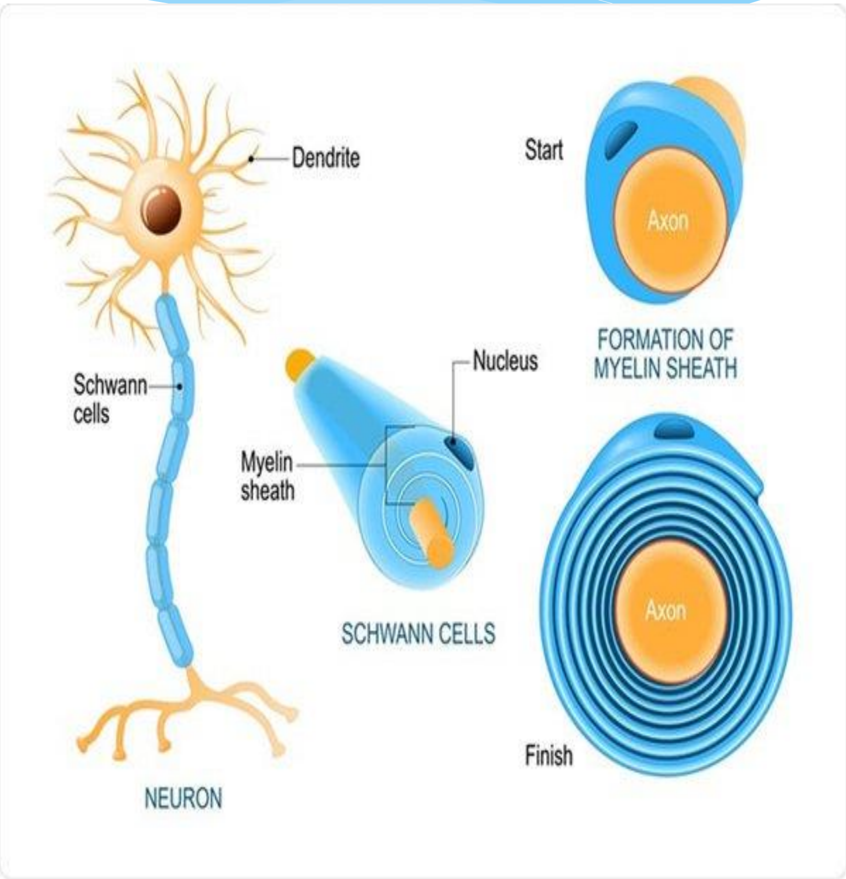


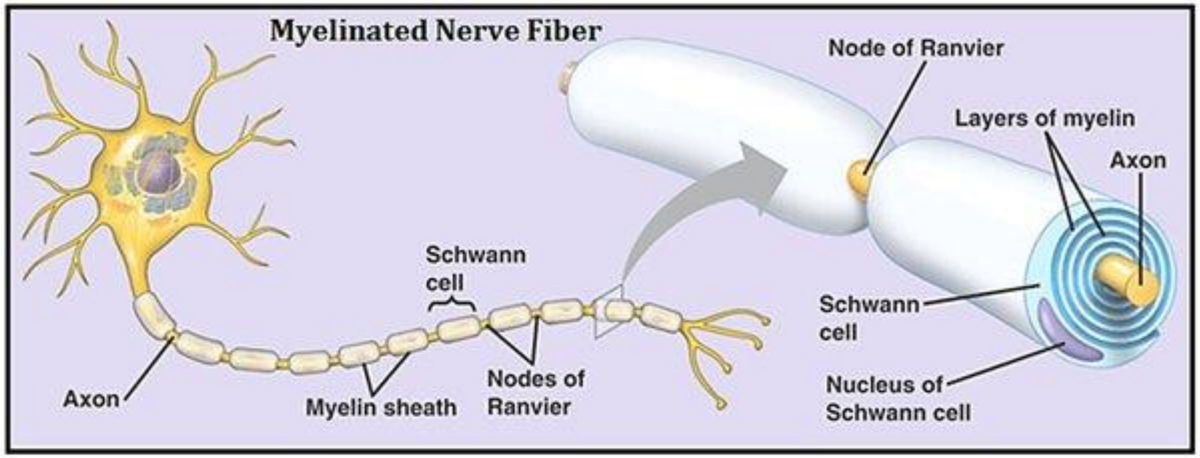
Myelinated fibers

As axons of **large diameter** grow in the PNS, they are engulfed along their length by many undifferentiated **neurolemmocytes** and become myelinated nerve fibers. The plasma membrane of the covering neurolemmocyte (Schwann cell) fuses around the axon and **becomes wrapped around** the nerve fiber as the glial cell body moves around and around the axon many times . The multiple layers of Schwann cell membrane unite as a layer **myelin, a whitish lipoprotein complex whose abundant lipid component .**

Membranes of Schwann cells have a **higher proportion of lipids** than do other cell membranes and the myelin sheath serves to protect axons and maintain a constant ionic microenvironment required for action potentials. Between adjacent Schwann cells the myelin sheath shows small nodal gaps along the axon, also called **nodes of Ranvier** .Interdigitating processes of Schwann cells partially cover each node . The length of axon covered by one Schwann cell is called the **internodal segment** and may be more than 1 millimeter. Unlike oligodendrocytes of the CNS, Schwann cells only form myelin around a portion of one axon.

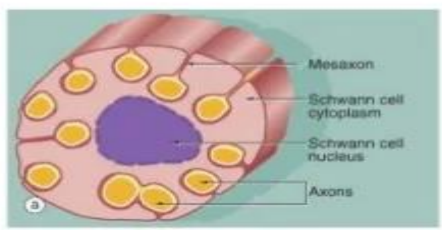

Formation of the myelin sheath - PNS
Schwann cell
Myelin sheath
neurilemma

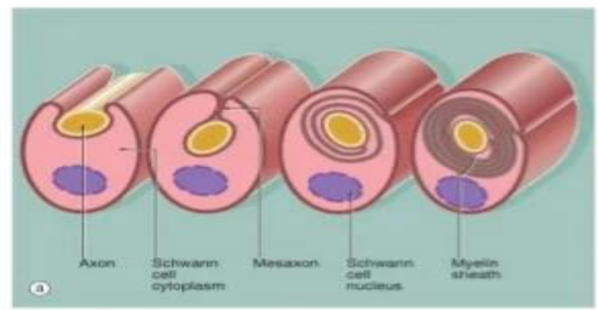

Dendrite
Schwann cells
NEURON
Nucleus
Myelin sheath
SCHWANN CELLS
Start
Axon
FORMATION OF MYELIN SHEATH
Axon
Finish



Myelinated and non myelinated nerve fibers

PNS:- schwann cell
CNS:- oligodendrocytes.





Non myelinated:-
- Small diameter axon
- simple envolop by the cytoplasm

Myelinated fibers:-
- large diameter fiber ,
- concentric layers .

Nerves

In the **PNS** , **nerve fibers are grouped into bundles to form nerves.** Except for very thin nerves containing only unmyelinated fibers, nerves have a whitish, glistening appearance because of their myelin and collagen content. Axons and Schwann cells of nerves are enclosed within connective tissue layers.

Externally is a dense, irregular fibrous coat called **epineurium**, which continues more deeply to also fill the space between bundles of nerve fibers. **Each such bundle** is surrounded by the **perineurium**, **a sleeve of specialized connective tissue formed by layers of flattened epithelial-like cells**. The perineurium a barrier to the passage of most macromolecules and has the important function of protecting the nerve fibers and helping maintain the internal microenvironment.

Within the perineurial sheath run the **Schwann cell–covered axons** and their **enveloping connective tissue** , **the endoneurium** , the endoneurium consists of a **sparse** layer of loose connective tissue that merges with type IV collagen, laminin, and other proteins produced by the Schwann cells.

The nerves establish communication between centers in the brain and spinal cord and the sense organs and effectors (muscles, glands, etc). They generally contain both **afferent and efferent** fibers. **Afferent fibers carry information from the interior of the body and the environment to the CNS**.

Efferent fibers carry impulses from the CNS to effector organs commanded by these centers.

Nerves possessing **only sensory fibers are called sensory nerves**; those composed only of **fibers carrying impulses to the effectors are called motor nerves**. Most nerves have **both sensory and motor fibers** and are called **mixed nerves** which usually have both myelinated and un-myelinated axons.

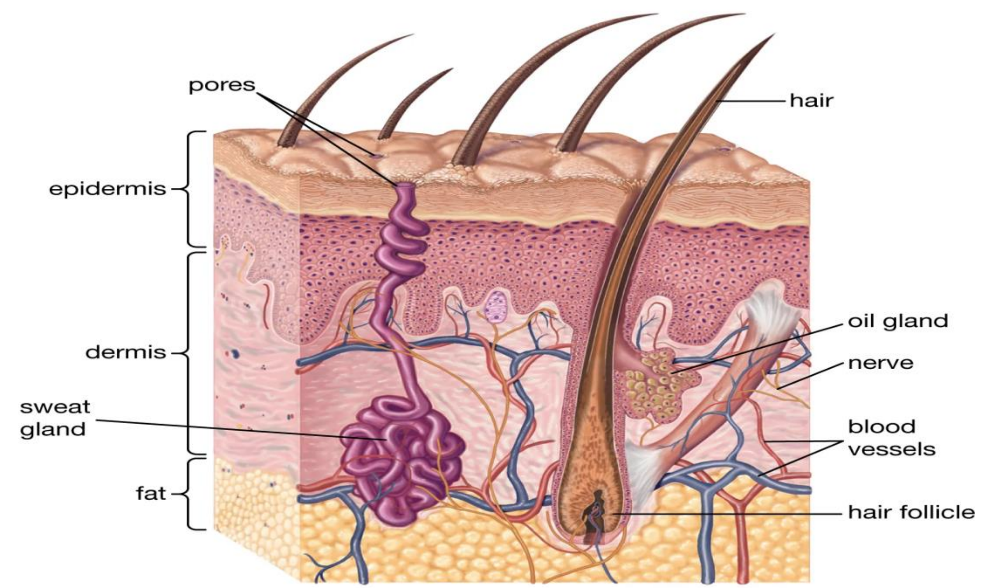
Ganglia

Are typically ovoid structures containing neuronal cell bodies and glial cells supported by connective tissue. Because they serve as relay stations to transmit nerve impulses, one nerve enters and another exits from each ganglion. The **direction of the nerve impulse** determines whether the ganglion will be a **sensory** or an **autonomic ganglion**. **Sensory ganglia receive afferent impulses that go to the CNS**, **Autonomic nerves effect the activity of smooth muscle, secretion of some glands, modulate cardiac rhythm and other involuntary activities by which the body maintains a constant internal environment (homeostasis).**

Lecture No. 8

SKIN

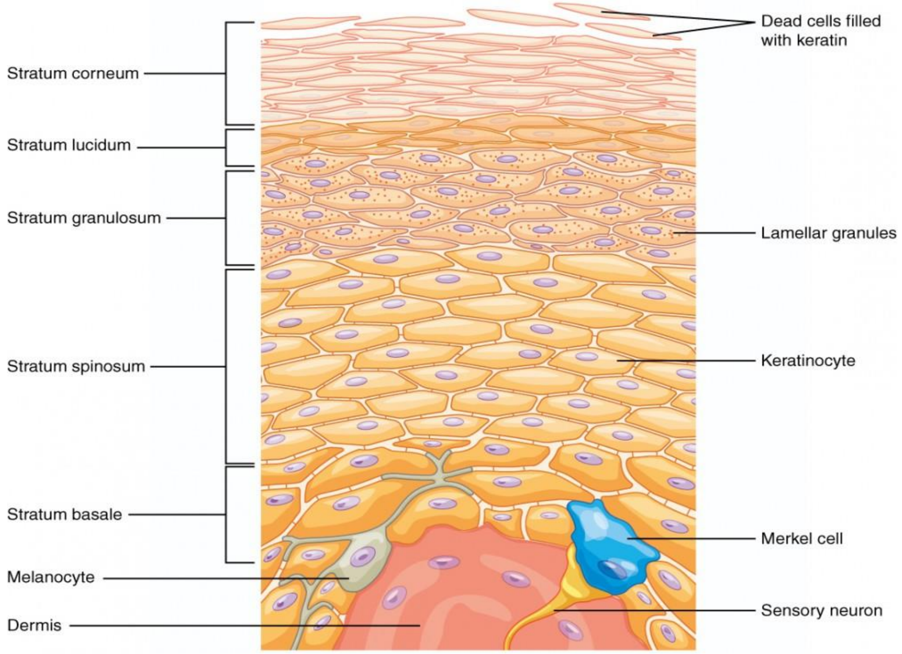
The skin is **the largest single organ of the body,** typically accounting for 15–20% of total body weight , also known as the **integument** (covering) or cutaneous layer, the skin is composed of the **epidermis,** and the **dermis** , a layer of mesodermal connective tissue . The junction of dermis and epidermis is irregular, and projections of the dermis called **papillae interdigitate with evaginations** of the epidermis known as **epidermal ridges**. **Epidermal derivatives** include **hairs, nails,** and **sebaceous and sweat glands.** Beneath the dermis lies the **subcutaneous tissue** or **hypodermis** (Gr. hypo, under, + derma, skin), **a loose connective tissue that may contain pads of adipocytes**. The subcutaneous tissue binds skin loosely to the underlying tissues.



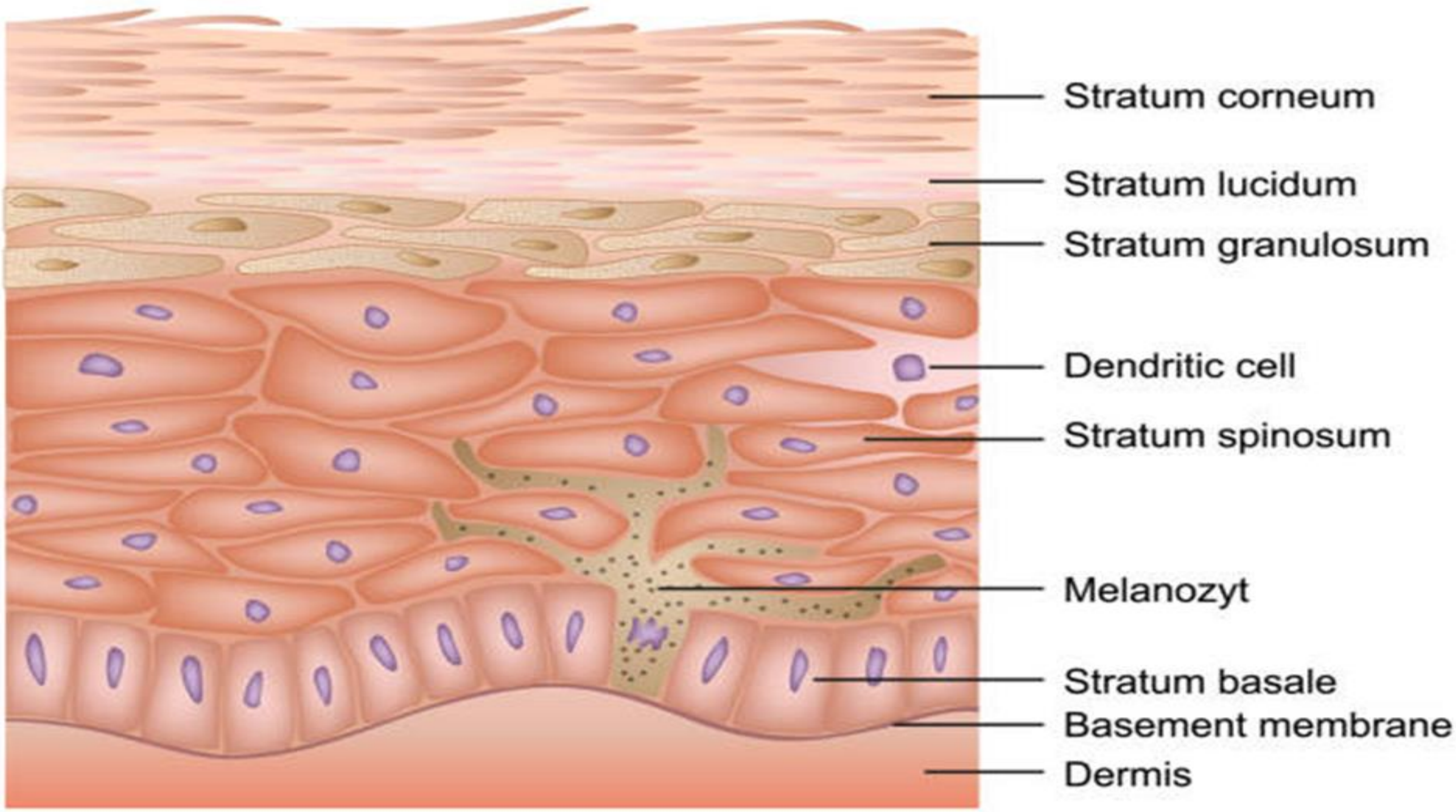
- The specific functions of the skin:
- Protective -Sensory - Thermoregulatory - Metabolic

EPIDERMIS

consists mainly of a **stratified squamous keratinized epithelium** composed of cells called **keratinocytes**. Three less abundant **epidermal cell types** are also present: pigment-producing melanocytes, antigen-presenting Langerhans cells, and tactile epithelial cells or Merkel cells.



Structure of the Epidermis



The **epidermis** forms the major distinction between **thick skin** ,found on the palms and soles, and **thin skin** found elsewhere on the body. The designations "thick" and "thin" refer to the thickness of the epidermal layer. Total skin thickness (epidermis plus dermis) also varies **according to site**. For example, skin on the back is about 4 mm thick, whereas that of the scalp is about 1.5 mm thick.

From the dermis outward, the epidermis consists of **four layers** of keratinocytes, **five layers** in thick skin :

1- The basal layer (stratum basale) is a single layer of basophilic columnar or cuboidal cells on the basement membrane at the dermal-epidermal junction.

2-The spinous layer (stratum spinosum), normally the thickest epidermal layer ,consists of polyhedral or slightly flattened cells having central nuclei with nucleoli and cytoplasm actively synthesizing keratin filaments.

3-The granular layer (stratum granulosum) consists of **3–5 layers of flattened** polygonal cells undergoing terminal differentiation. Their cytoplasm is filled with intensely basophilic masses called **keratohyaline** granules.

4-The stratum lucidum is **only seen in thick skin**, where it consists of a **thin, translucent laye**r of extremely flattened eosinophilic cells. The nuclei and organelles have been lost and the cytoplasm consists almost only of densely packed keratin filaments embedded in an electron-dense matrix.

5-The stratum corneum consists of 15–20 layers of flattened**, non nucleated keratinized cells** whose cytoplasm is filled with birefringent filamentous keratins. After **keratinization**, the cells contain only fibrillar and amorphous proteins with thickened plasma membranes and are called **squames** or **horny, cornified cells**. These cells are **continuously shed** at the surface of the stratum corneum.

- **Melanocytes** : The **color of the skin is the result of several factors**, the most important of which are the keratinocytes' content of **melanin** and **carotene** and the **number of blood vessels in the dermis**.
- **Dendritic (Langerhans) Cells**
- **Tactile (Merkel) Cells : Epithelial tactile cells (commonly called Merkel cells) are mechanoreceptors.**

DERMIS:

is the connective tissue that supports the epidermis and binds it to the subcutaneous tissue (hypodermis). The thickness of the dermis varies according to the region of the body, and reaches its maximum of 4 mm on the back.

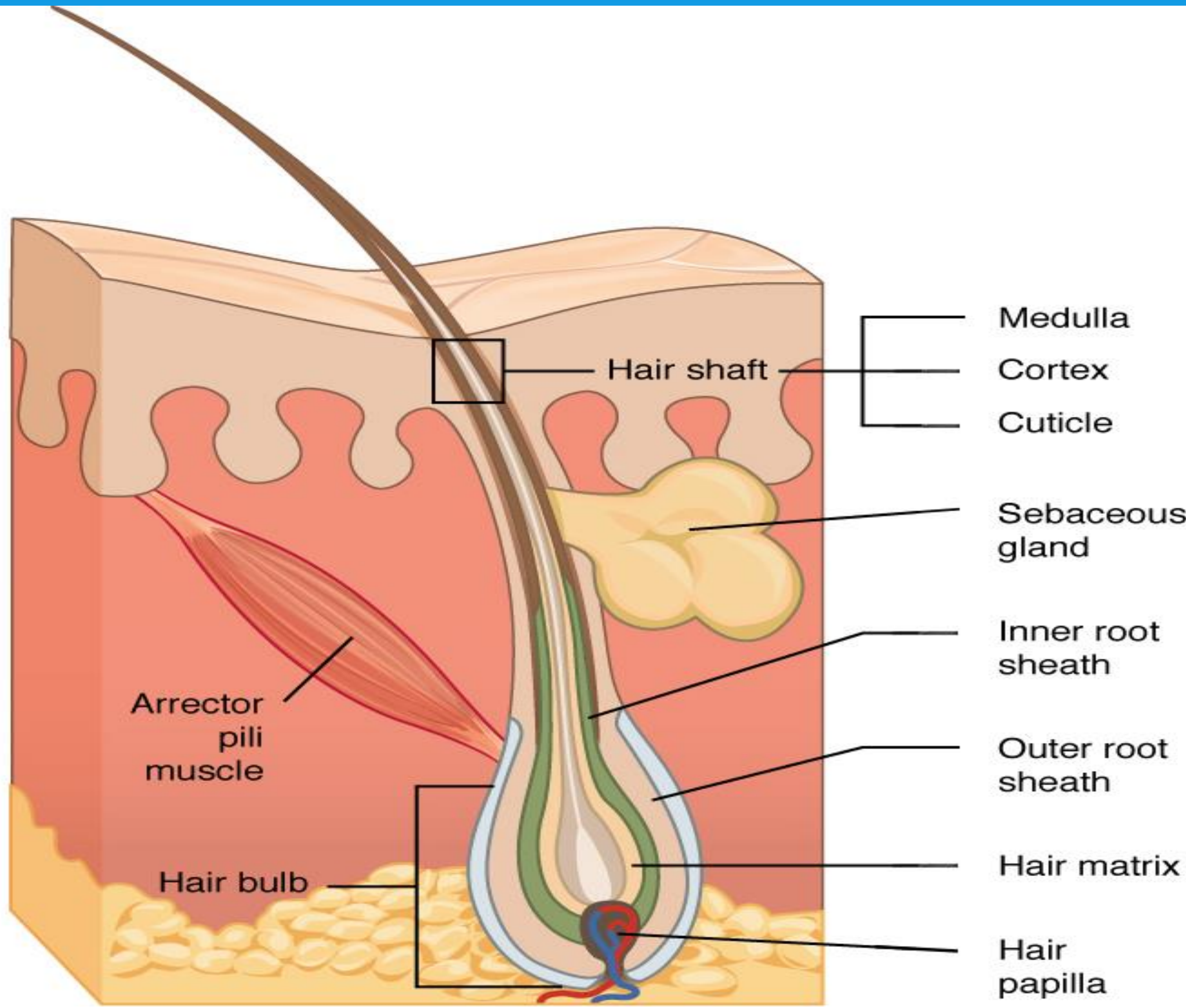
- The dermis contains **two layers** with rather indistinct boundaries—the outermost **papillary layer** and the **deeper reticular layer** . **The thin** papillary layer ,which constitutes the major part of the dermal papillae, is composed of loose connective tissue, with fibroblasts and other connective tissue cells, such as mast cells and macrophages. The **reticular layer is thicker**, composed of irregular dense connective tissue (mainly bundles of type I collagen), and has more fibers and fewer cells than the papillary layer. A network of elastic fibers is also present.

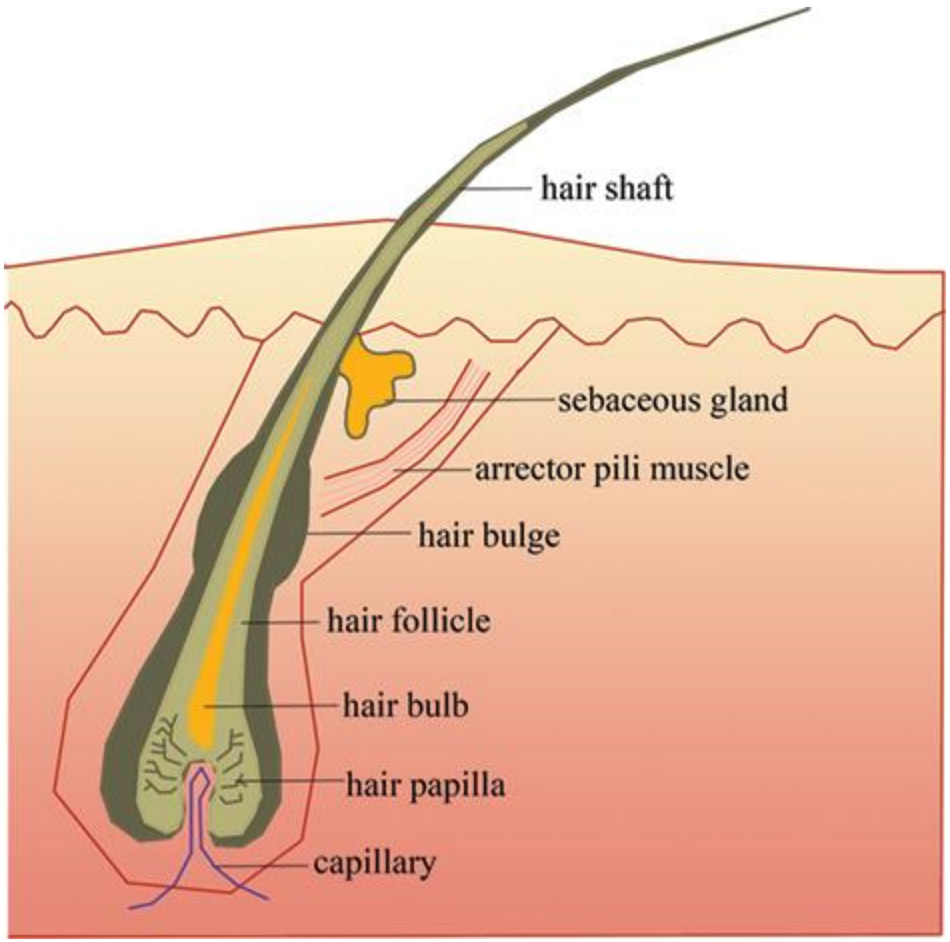
Subcutaneous layer

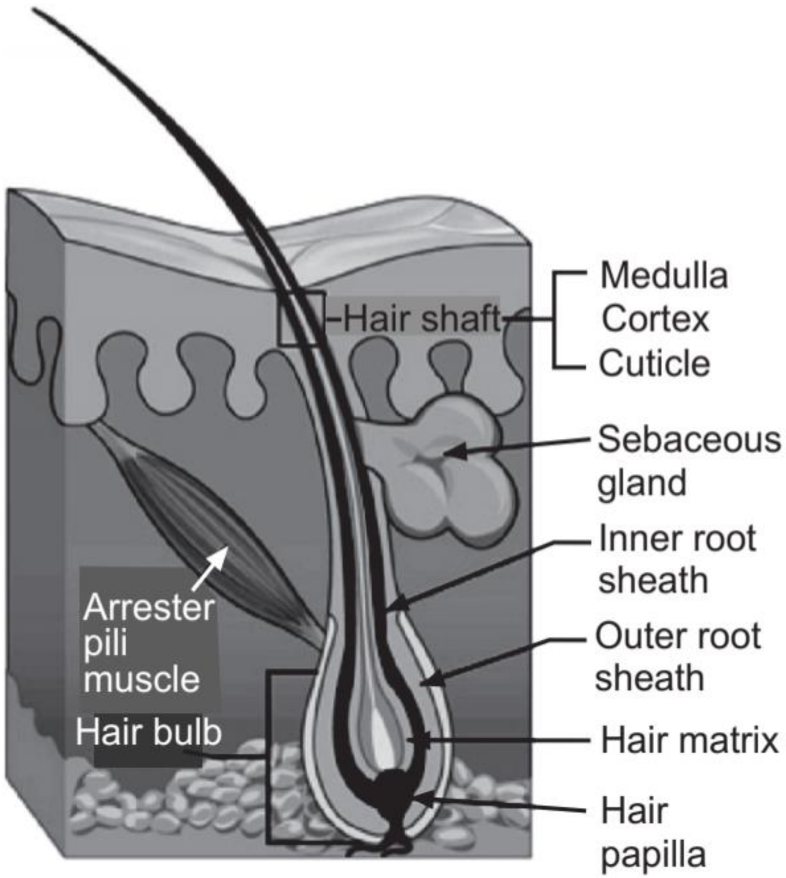
consists of **loose connective tissue** that binds the skin loosely to the subjacent organs, making it possible for the skin to **slide over them.**

Hair

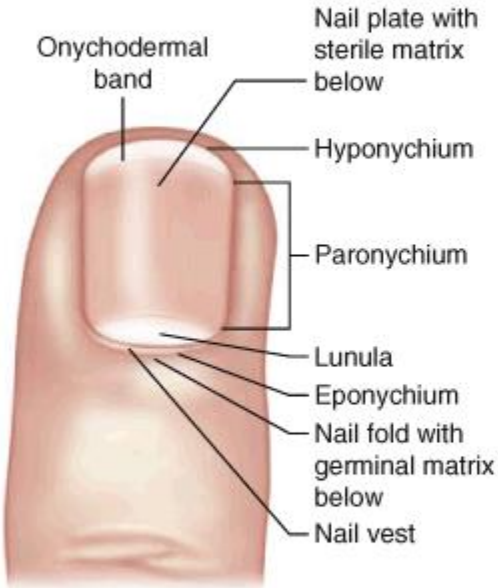
Hairs are elongated keratinized structures derived from invaginations of the epidermal epithelium called hair follicles .The color, size, shape and texture of hairs vary according to **age**, **genetic background**, and **region of the body**. All skin has at least minimal hair except that of the **palms, soles, lips**. The hair follicle has a terminal **dilatation called a hair bulb** . A **dermal papilla** inserts into the base of the hair bulb and contains a capillary network required to sustain the hair follicle. The epidermal cells covering this dermal papilla form the **hair root** that produces and is continuous with the **hair shaft** protruding beyond the skin surface. **The internal root sheath** completely surrounds the initial part of the hair shaft and **the external root sheath** covers the internal sheath and extends all the way to the epidermis.


Medulla
Hair shaft
Cortex
Cuticle
Sebaceous gland
Inner root sheath
Arrector pili muscle
Outer root sheath
Hair matrix
Hair bulb
Hair papilla

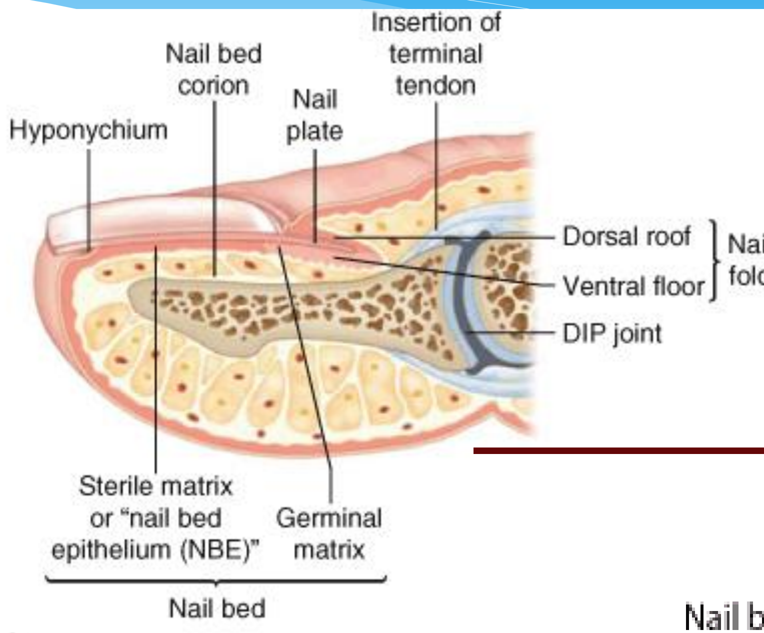

hair shaft
sebaceous gland
arrector pili muscle
hair bulge
hair follicle
hair bulb
hair papilla
capillary


Hair shaft
Medulla
Cortex
Cuticle
Sebaceous gland
Inner root sheath
Outer root sheath
Hair matrix
Hair papilla
Arrester pili muscle
Hair bulb

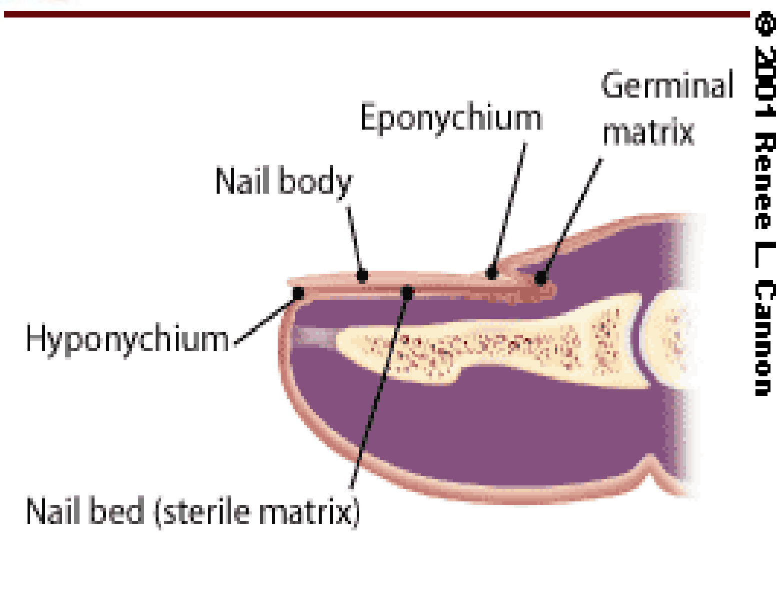
- **Hard, flexible plates of keratin on the dorsal surface of each distal phalanx .The proximal part of the nail is the nail root and is covered by the proximal skin fold which is thin and lacks both hair and glands. The epidermal stratum corneum extending from eponychium. The keratinized nail plate is bound to a bed of epidermis called the nail bed, The nail plate arises from the nail matrix, which extends from the nail root. The distal end of the plate becomes free of the nail bed at the epidermal fold called the hyponychium**


Onychodermal band
Nail plate with sterile matrix below
Hyponychium
Paronychium
Lunula
Eponychium
Nail fold with germinal matrix below
Nail vest

a


Insertion of terminal tendon
Nail bed corion
Nail plate
Hyponychium
Dorsal roof
Ventral floor
Nail fold
DIP joint
Sterile matrix or "nail bed epithelium (NBE)"
Germinal matrix
Nail bed

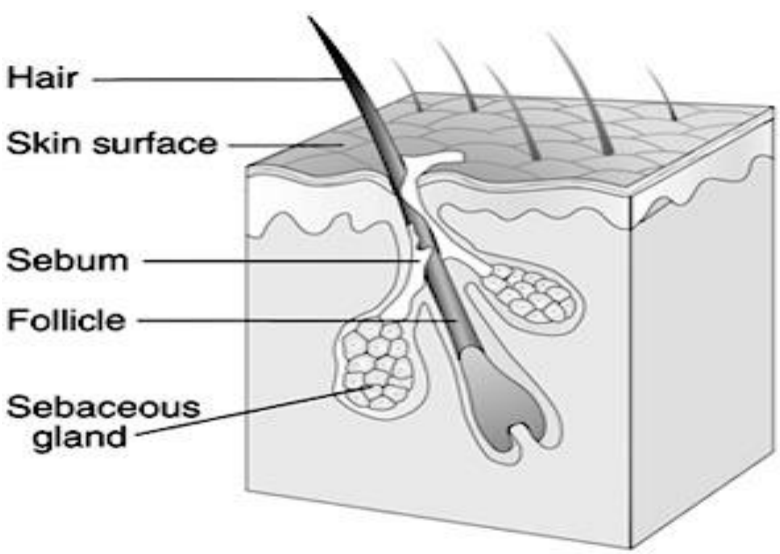
b

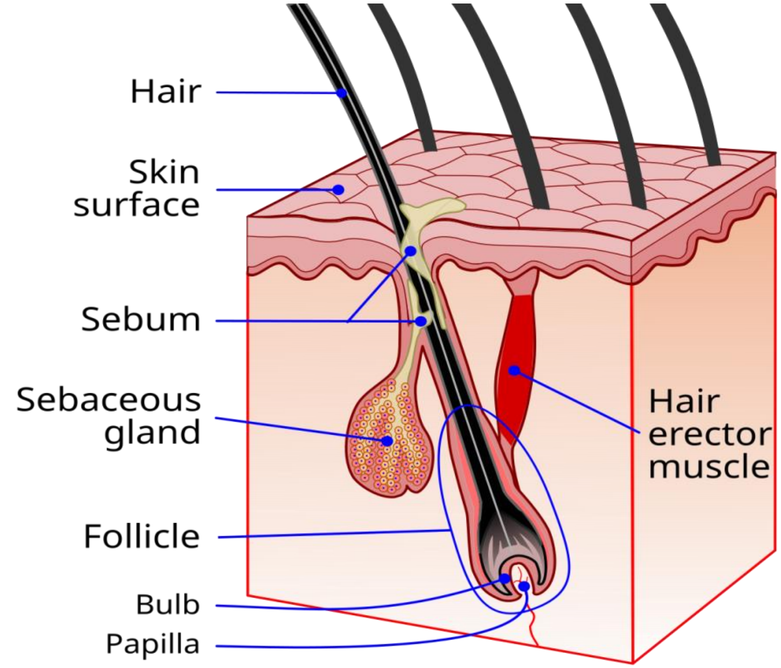

Germinal matrix
Eponychium
Nail body
Hyponychium
Nail bed (sterile matrix)
© 2001 Renee L. Cannon

GLANDS OF THE SKIN

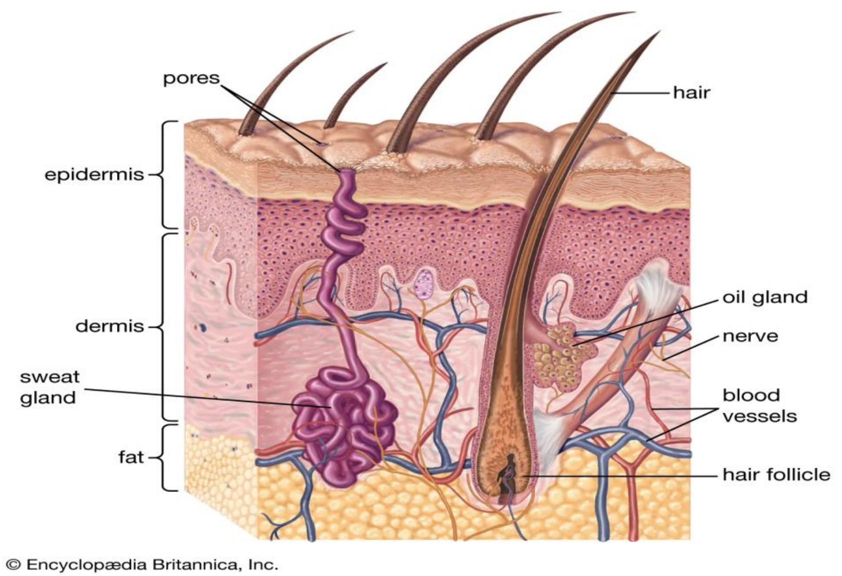
Sebaceous Glands

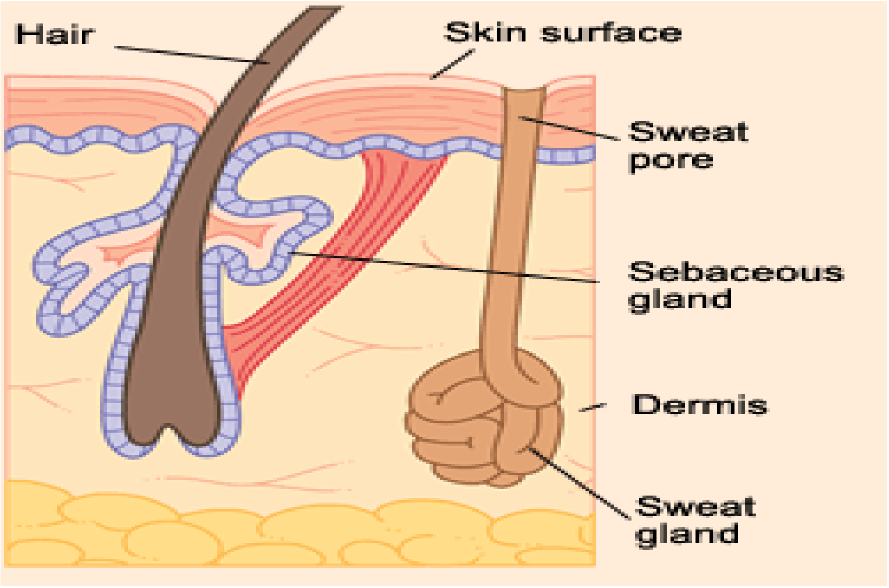
Sebaceous glands are embedded in the dermis over most of the body surface, except the thick, hairless (glabrous) skin of the palms and sole are branched acinar glands with several acini converging at a short duct which usually empties into the upper portion of a hair follicle, The product of this process is sebum, which is gradually moved to the surface of the skin along the hair follicle or duct.





- **Sweat Glands**
- Are epithelial derivatives embedded in the dermis which open to the skin surface or into hair follicles. **Eccrine sweat glands and apocrine sweat glands** have different distributions, functions, and structural details. **Sweating** is the physiological response to increased body temperature during physical exercise or thermal stress and in humans the most effective means of temperature regulation.





THE CIRCULATORY SYSTEM

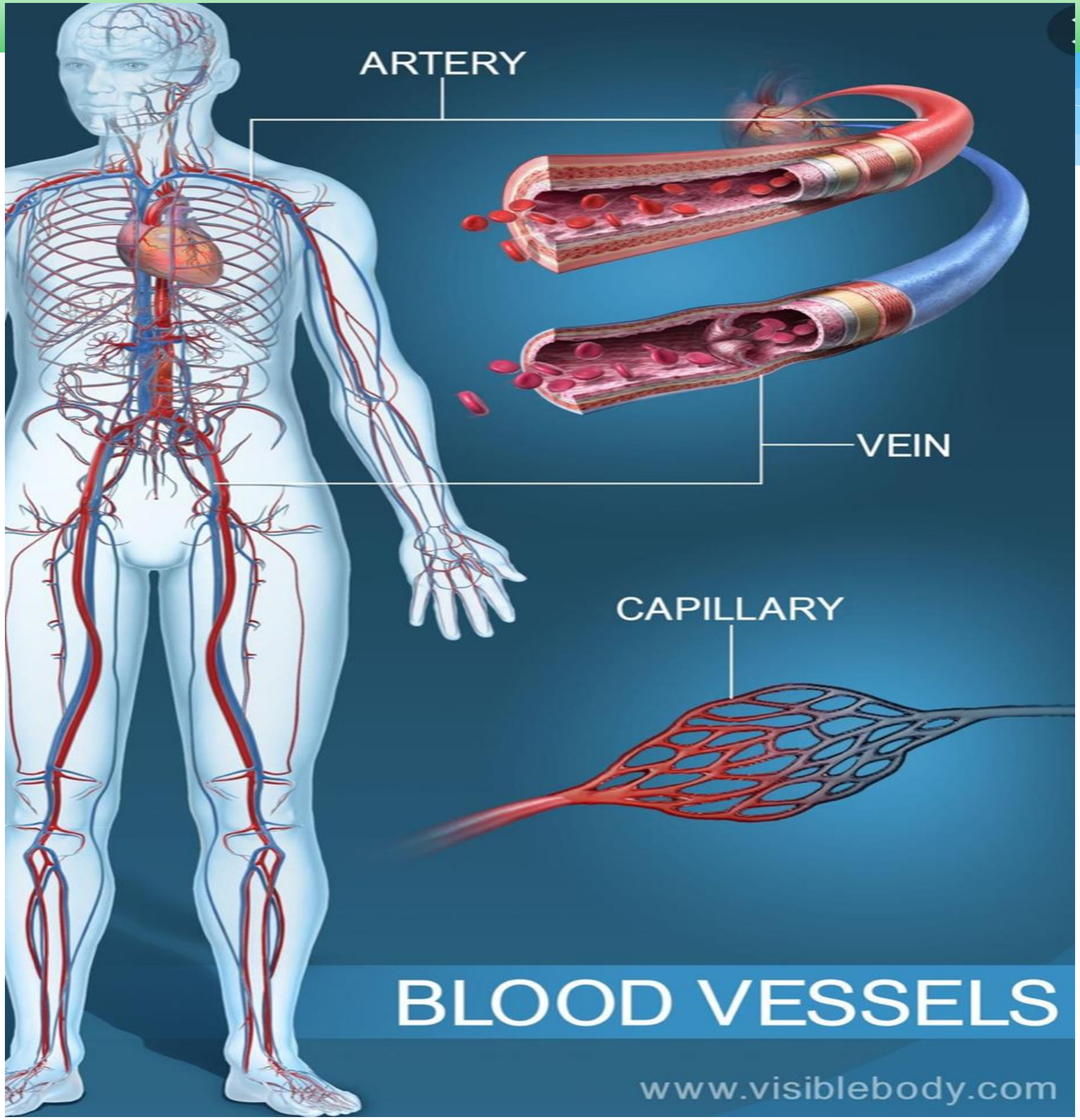
The circulatory system includes **both the blood and lymphatic vascular** systems. The blood vascular system is composed of the following structures:

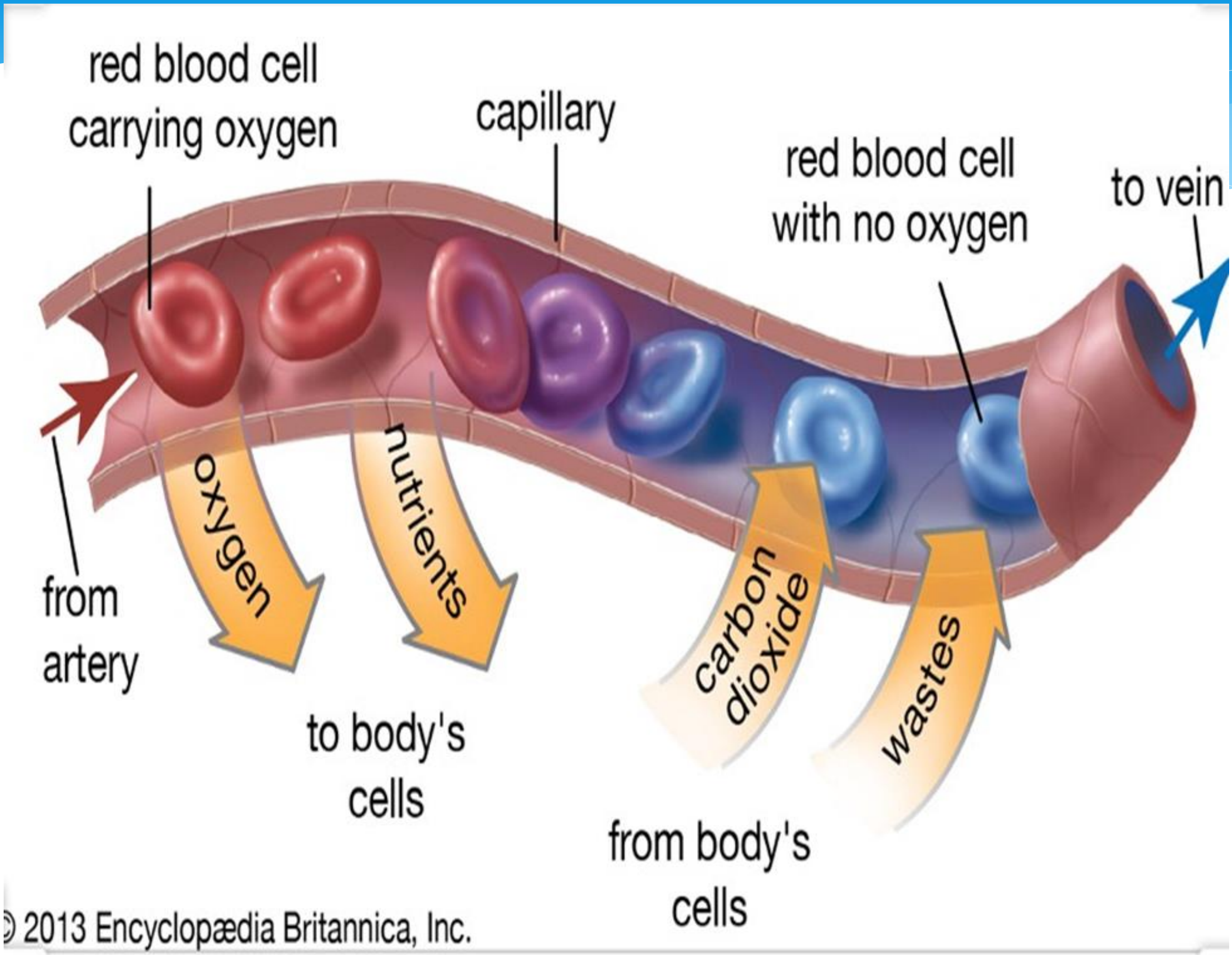
1-The heart, an organ whose function is to pump the blood.

2-**The arteries**, a series of **efferent vessels** that become smaller as they branch, and whose function is to carry the blood, with its nutrients and oxygen, to the tissues.

3-The capillaries, the **smallest blood vessels**, constituting a complex network of thin tubules that branch profusely in almost every organ and through whose walls the interchange between blood and tissues takes place.

4-The veins, which result from the convergence of capillaries into a system of larger channels that continue enlarging as they approach the heart, toward which they convey the blood to be pumped again.


ARTERY
VEIN
CAPILLARY
BLOOD VESSELS
www.visiblebody.com


red blood cell
carrying oxygen
capillary
red blood cell
with no oxygen
to vein
from
artery
oxygen
nutrients
to body's
cells
carbon
dioxide
wastes
from body's
cells
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The lymphatic vascular system, i begins with the lymphatic capillaries, which are closed-ended tubules that merge to form vessels of steadily increasing size; these vessels terminate in the blood vascular system emptying into the large veins near the heart. One of the functions of the **lymphatic system is to return the fluid of the tissue spaces to the blood**. The internal surface of all components of the blood and lymphatic systems is lined by a single layer of a **squamous epithelium, called endothelium**.

HEART

The heart is a muscular organ that contracts rhythmically, pumping the blood through the circulatory system , the right and left ventricles pump blood to the lungs and the rest of the body respectively; right and left atria receive blood from the body and the pulmonary veins respectively. The **walls of all four heart chambers** consist of three major layers : the **internal endocardium**; the **middle myocardium**; and the **external epicardium.**

The **endocardium** consists of a single layer of **squamous endothelial cells** on a thin layer of loose connective tissue containing elastic and collagen fibers as well as some smooth muscle cells.

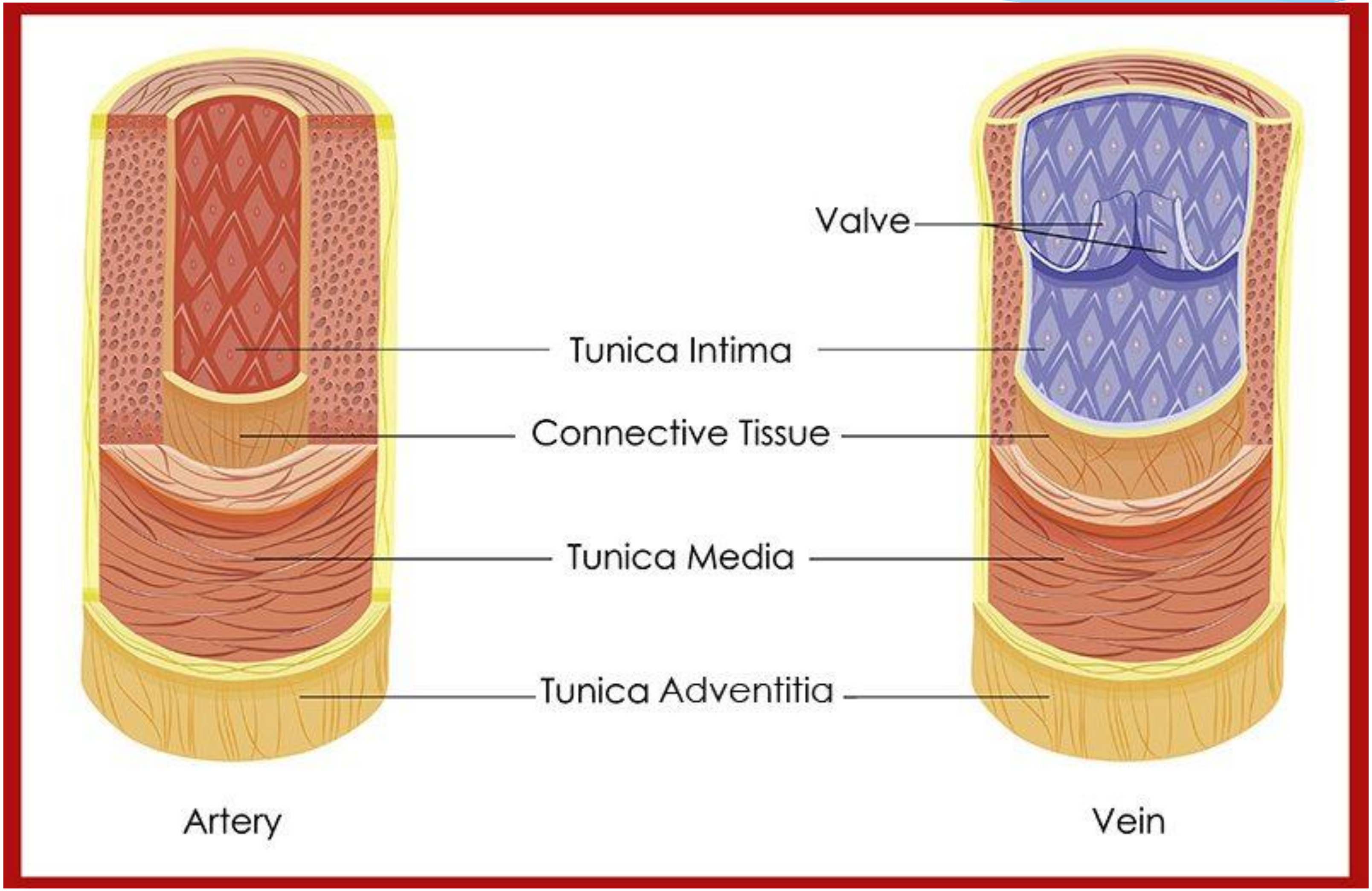
STRUCTURAL PLAN OF BLOOD VESSELS:

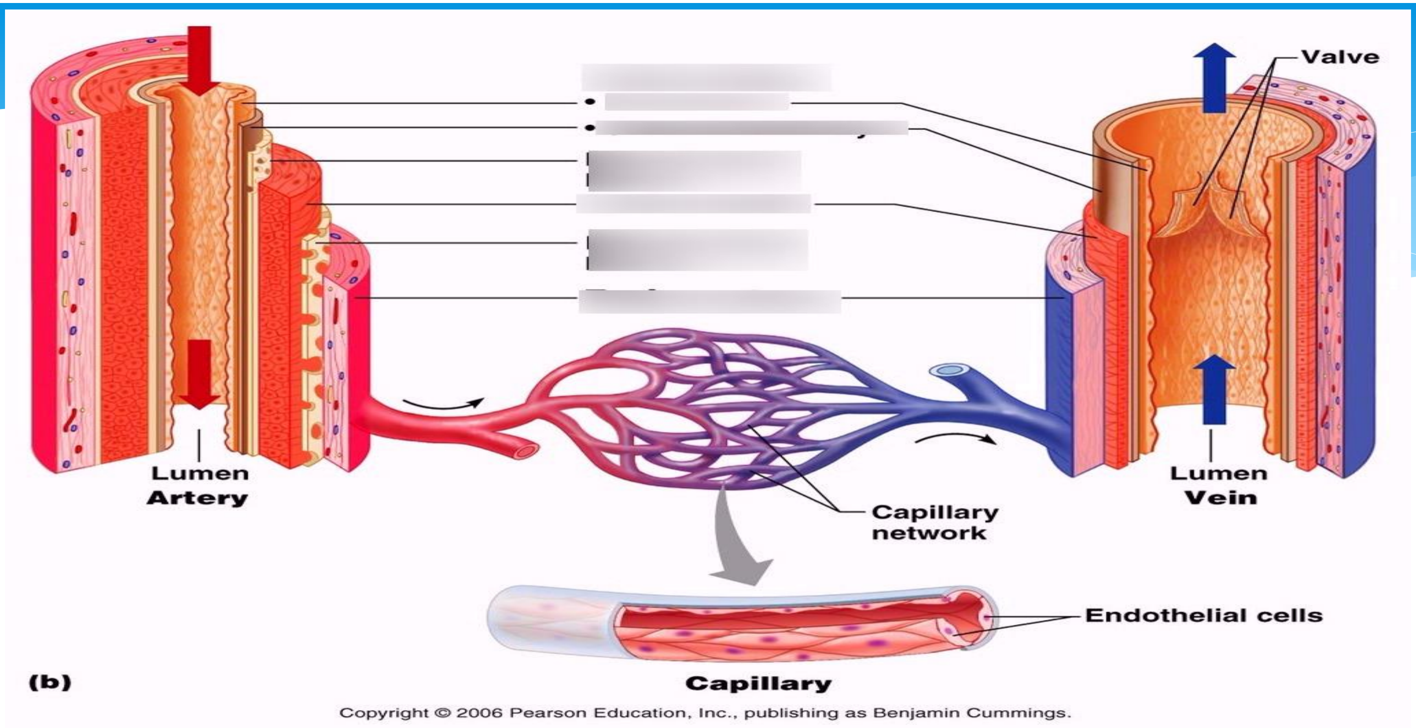
All blood vessels greater than a certain diameter have many structural features in common and present a similar plan of construction. The distinction between different types of vessels often is not clear-cut because the transition from one type to another is gradual. Blood vessels are usually composed of the following layers, or tunics:

1-The tunica intima has one layer of endothelial cells supported by a thin sub endothelial layer of loose connective tissue with occasional smooth muscle cells. In arteries, the intima is separated from the media by an internal elastic lamina, the most external component of the intima. This lamina, composed of elastin, has holes (fenestrae) that allow the diffusion of substances to nourish cells deep in the vessel wall.

3-The tunica media, the middle layer, consists chiefly of concentric layers of helically arranged smooth muscle cells .Interposed among the smooth muscle cells are variable amounts of elastic fibers and lamellae, reticular fibers and glycoproteins, all of which is produced by these cells. In arteries, the media has a thinner external elastic lamina, which separates it from the tunica adventitia.

3-The tunica adventitia or tunica externa consists principally of type I collagen and elastic fibers This adventitial layer is gradually continuous with the stromal connective tissue of the organ through which the blood vessel runs.


Valve
Tunica Intima
Connective Tissue
Tunica Media
Tunica Adventitia
Artery
Vein



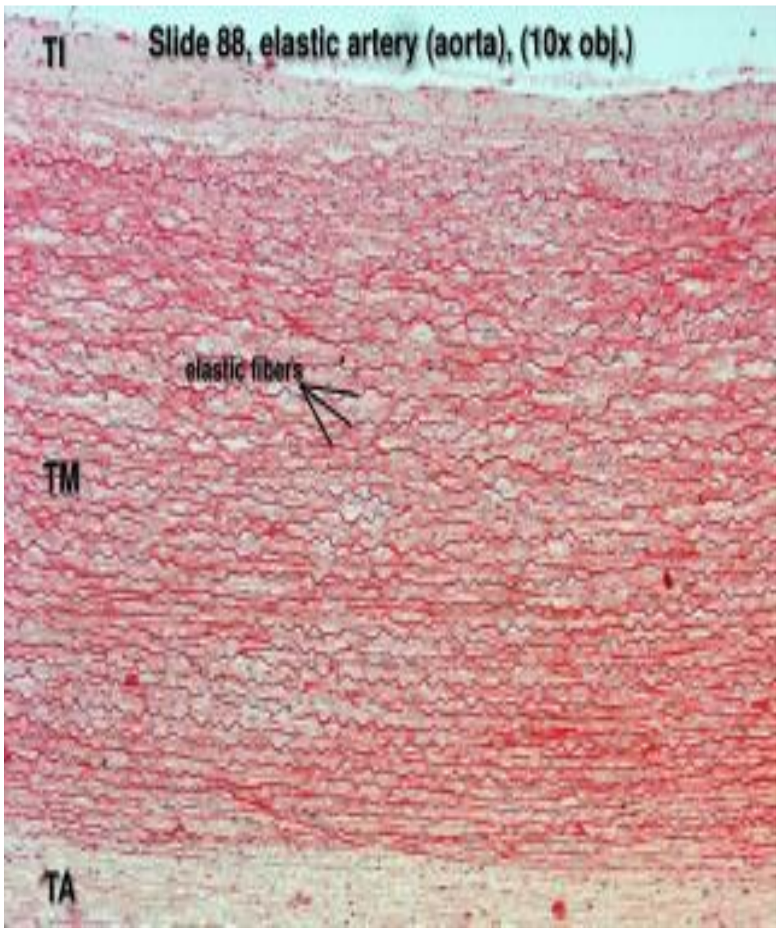
Walls of **both** arteries and veins have **a tunica intima, tunica media, and tunica externa (or adventitia)** . An **artery** has **a thicker tunica media** and relatively **narrow lumen.** A vein has a larger lumen and its tunica externa is the thickest layer. The tunica **intima** of veins is often folded to form **valves.** Capillaries have only an endothelium, with **no** subendothelial layer or other tunics.

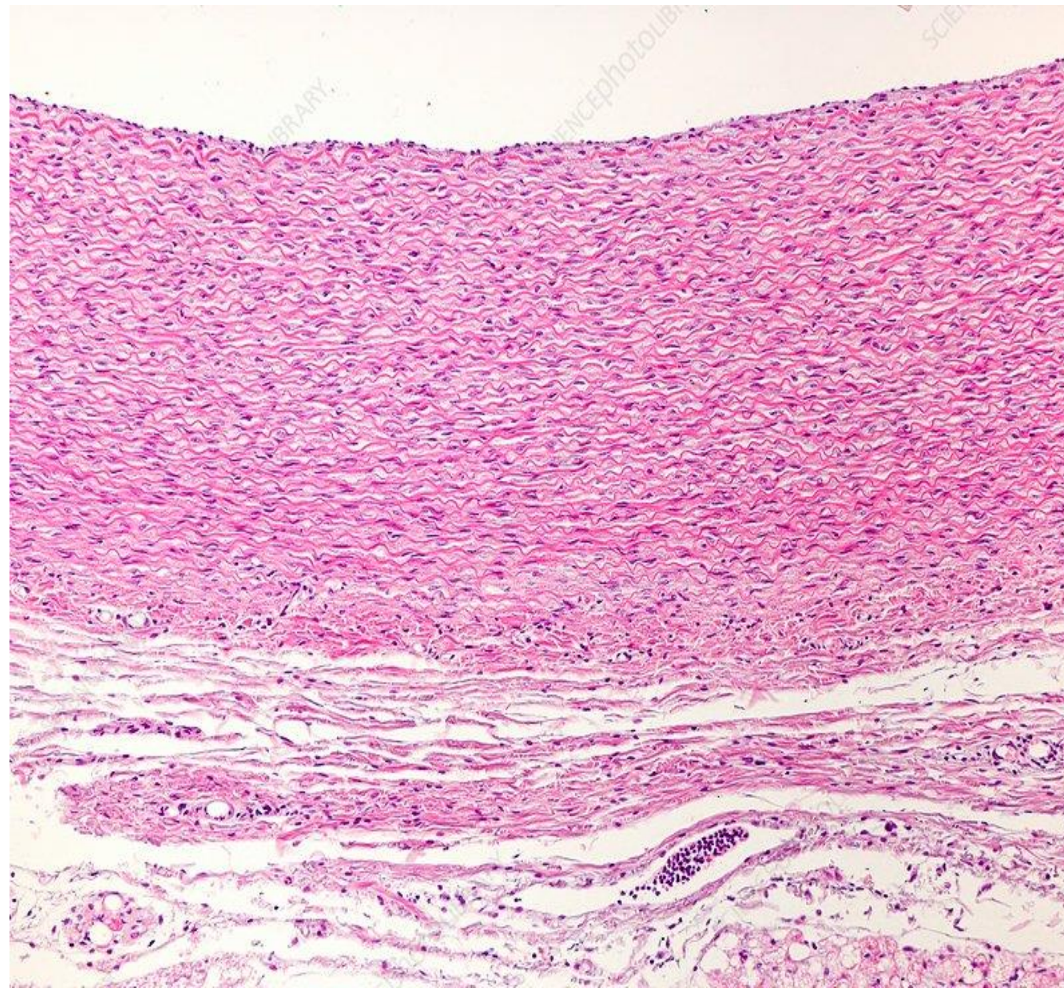
Large vessels usually have **vasa vasorum** ("vessels of the vessel"), which consist of arterioles, capillaries, and venules in the **tunica adventitia** and the outer part of the media .The vasa vasorum provide metabolites to cells of those layers, since in larger vessels the wall is too thick to be nourished solely by diffusion from the blood in the lumen. Luminal blood alone does provide nutrients and oxygen for cells of the tunica intima. Since they carry deoxygenated blood, **large veins typically have more vasa vasorum than arteries**.

Vasculature

vessels of the **macro vasculature** are classified as the types indicated in the following.

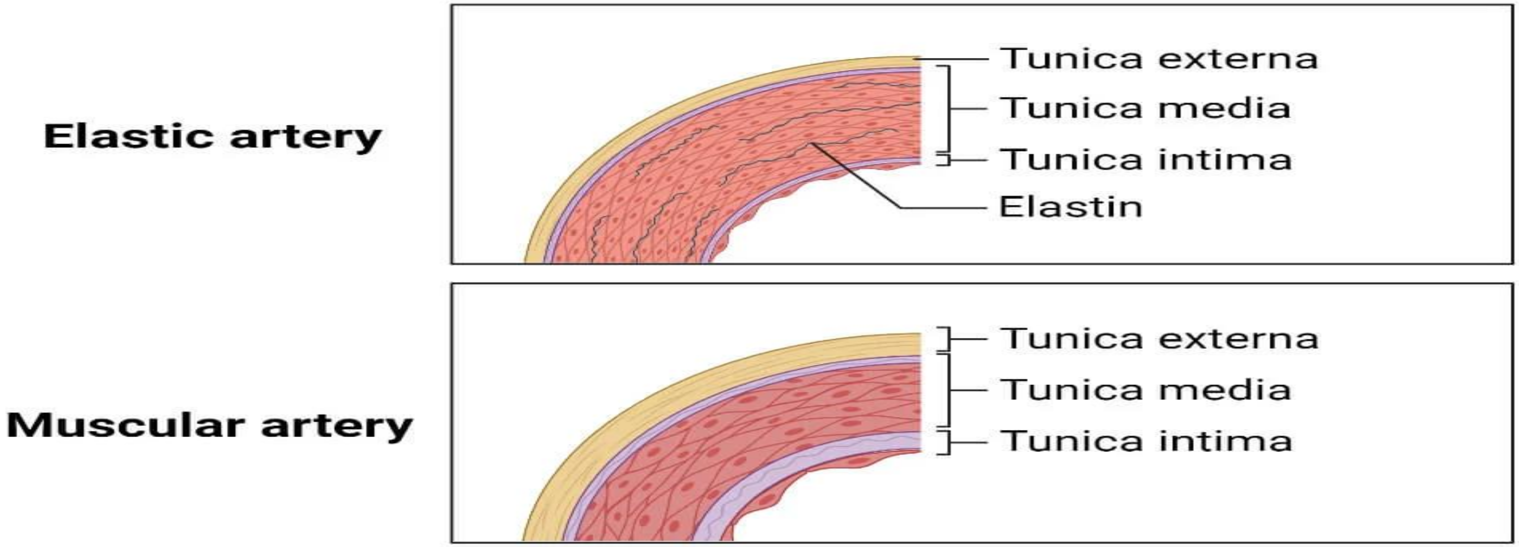
1-Large Elastic Arteries : stabilize the blood flow,include the aorta and its large branches, Freshly dissected, they have a **yellowish** color from the **elastin** in the media. The intima is **thicker than the corresponding tunic of a muscular artery**. An internal elastic lamina, although present, may **not be easily discerned**, since it is similar to the elastic laminae of the next layer .The media consists of **elastic fibers and a series of concentrically arranged**, whose number increases with age (there are about 40 in the newborn, 70 in the adult). The tunica adventitia is relatively underdeveloped.

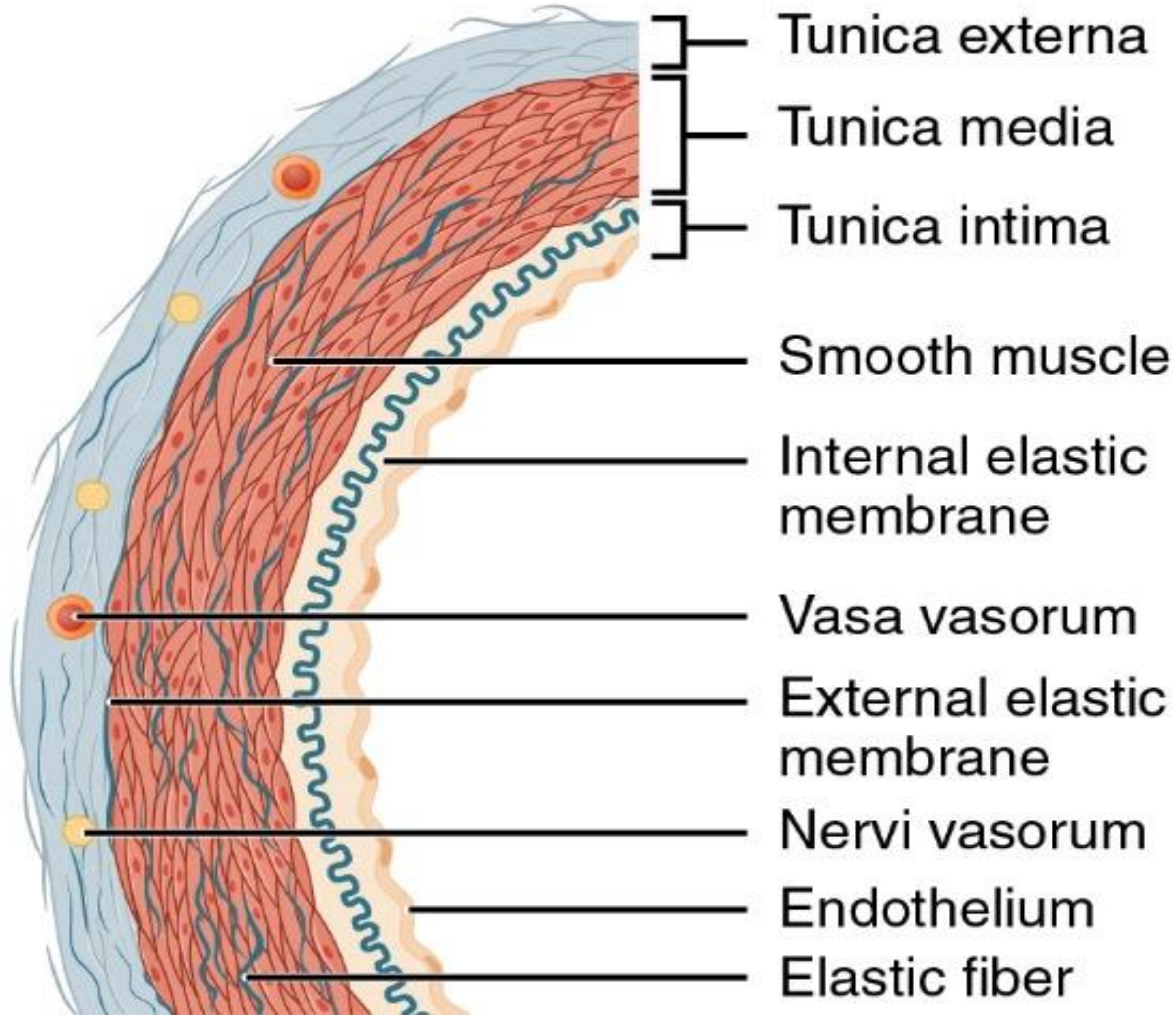

TI
Slide 88, elastic artery (aorta), (10x obj.)
elastic fibers
TM
TA



Muscular Arteries

The muscular arteries can control blood flow to organs by contracting or relaxing the smooth muscle cells of the tunica media**. The intima** has a very thin subendothelial layer and the internal elastic lamina, the most external component of the intima, is prominent . The **tunica media** may contain up to **40 layers** of more prominent smooth muscle cells which are intermingled with a variable number of elastic lamellae (depending on the size of the vessel) **An external elastic lamina, the last component of the media, is present only in the larger muscular arteries**. **The adventitia** consists of connective tissue. Lymphatic capillaries, vasa vasorum, and nerves are also found in the adventitia .




Tunica externa
Tunica media
Tunica intima
Smooth muscle
Internal elastic membrane
Vasa vasorum
External elastic membrane
Nervi vasorum
Endothelium
Elastic fiber

Arterioles

Muscular arteries branch repeatedly into smaller and smaller arteries, until reaching a size with only two or three medial layers of muscle. The smallest arteries branch as arterioles, which have one or two smooth muscle layers and indicate the beginning of an organ's microvasculature ,where exchanges between blood and tissue fluid occur. Arterioles are generally less than 0.5 mm in diameter. The sub endothelial layer is very thin, the elastic laminae are absent and the media is generally composed of circularly arranged smooth muscle cells. In both small arteries and arterioles, the tunica adventitia is very thin and inconspicuous.

Capillaries-:

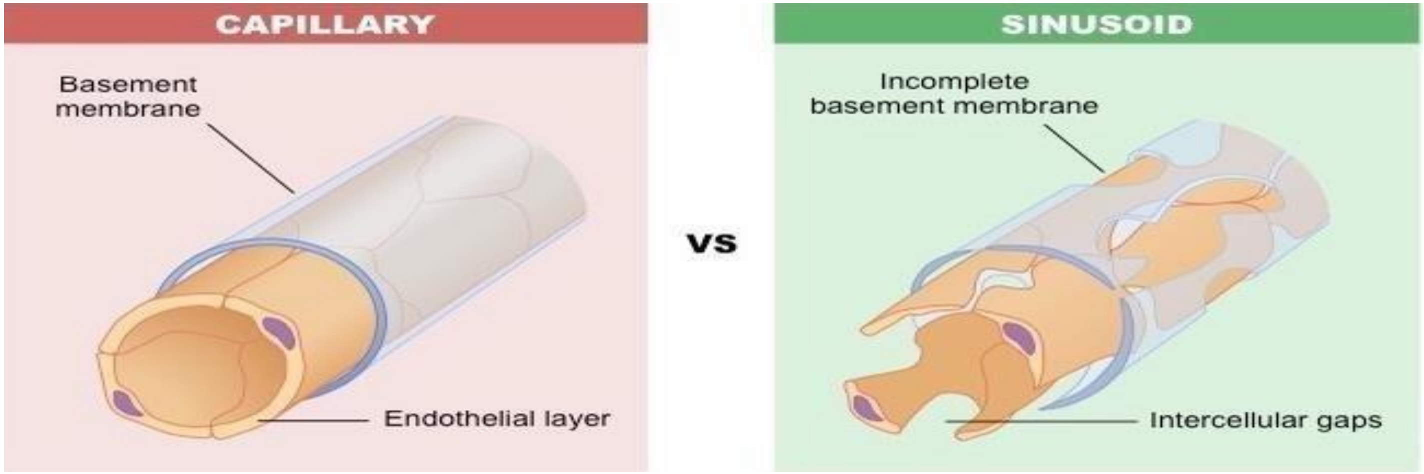
Capillaries permit different levels of metabolic exchange between blood and surrounding tissues. They are composed of **a single layer of endothelial cells** rolled up in the **form of a tube**.

Because of their thin walls and slow blood flow, capillaries are a favorable place for the exchange of water, solutes, and macromolecules between blood and tissues. Capillaries have structural variations which permit different levels of metabolic exchange between blood and surrounding tissue. They can be grouped into **three types**, **depending on the continuity of the endothelial cells and the external lamina:**

1-The continuous capillary ,allows regulated exchange of material and is characterized by the distinct continuity of the endothelial cells in its wall. This is the most common type **of capillary and is found in all kinds of** muscle tissue, connective tissue, exocrine gland.

2-The fenestrated capillary allows more extensive molecular exchange across the endothelium and is characterized by the **presence of small circular fenestrae**. Each fenestra is usually covered by a very thin diaphragm**. Fenestrated capillaries are found in tissues where rapid interchange of substances occurs between the tissues and the blood, as in the kidney, the intestine, the choroid plexus and the endocrine glands.**

3-The sinusoid or discontinuous capillary permits maximal exchange of macromolecules as well as cells between tissues and blood and has the following characteristics: endothelial cells have large fenestrae without diaphragms; the cells form a discontinuous layer and are separated from one another by wide spaces; the basal lamina is also discontinuous. Sinusoids are irregularly shaped and have diameters as large as 30–40 m, much greater than those of other capillaries, properties which further slow blood flow at this site. Sinusoidal capillaries are found in the liver, spleen, some endocrine organs, and bone marrow.



Capillaries

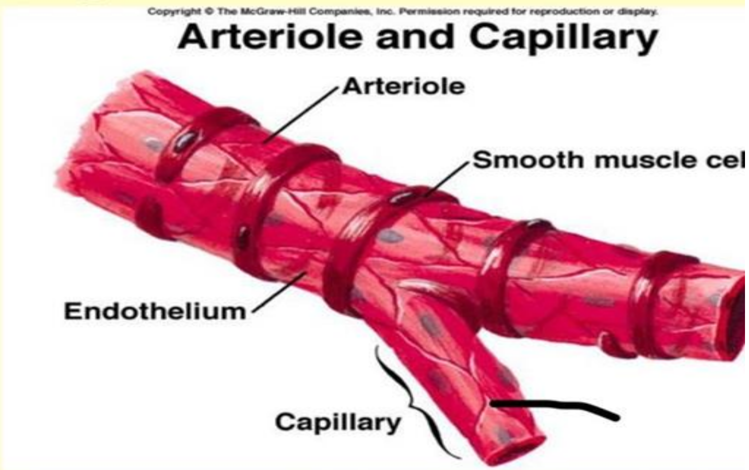
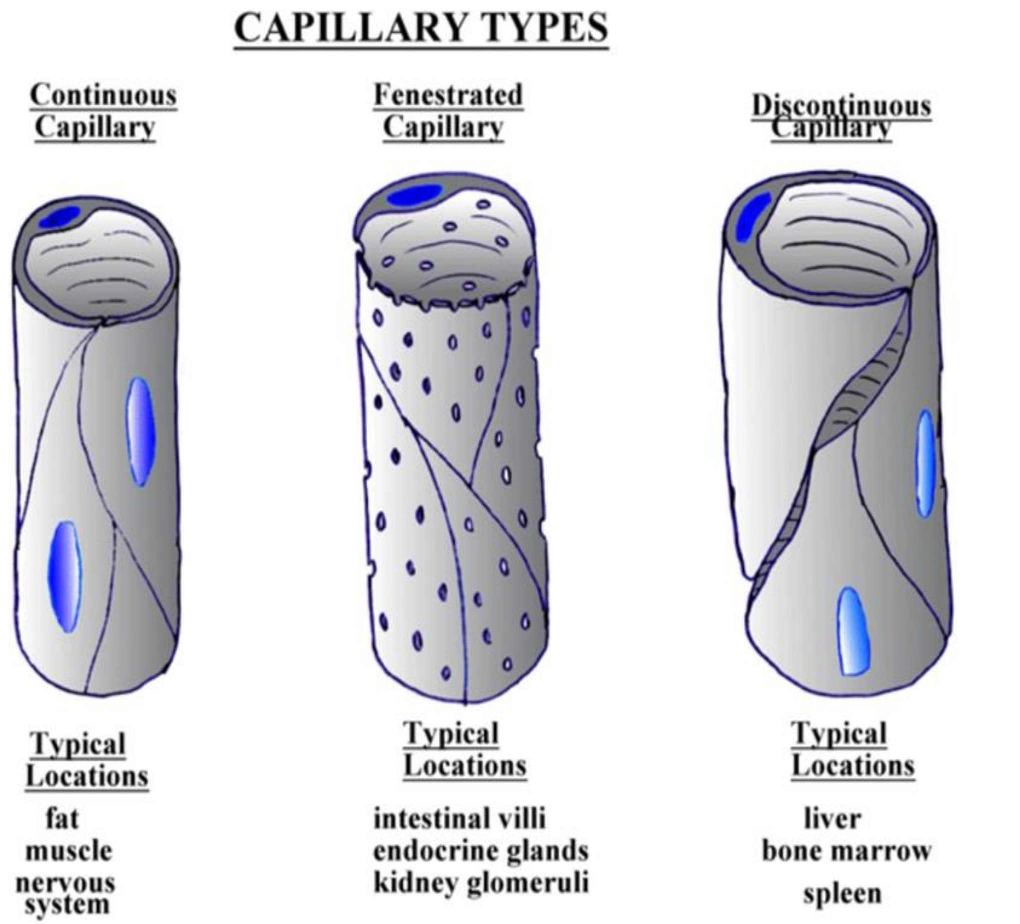


Figure 15.25



Venules

The transition from capillaries to venules occurs gradually.

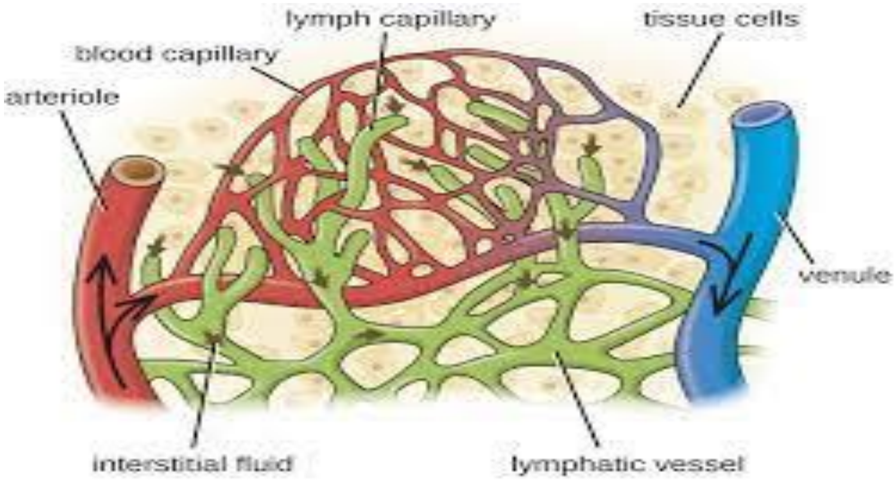
Veins

Blood entering veins is under **very low pressure** and moves toward the heart by contraction of the tunica media and external compressions from surrounding muscles and other organs. **Valves project from the tunica intima to prevent back-flow of blood.** Most veins are **small or medium** veins ,with diameters less than one centimeter. Such veins are usually located in parallel with corresponding muscular arteries. The intima usually has a thin Sub endothelial layer and the media consists of small bundles of smooth muscle cells intermixed with reticular fibers and a delicate network of elastic fibers. **The collagenous adventitial layer is well-developed.**

The big venous trunks, paired with elastic arteries close to the heart, are large veins . **Large veins have a well-developed tunica intima** , but the tunica media is relatively thin, with few layers of smooth muscle and abundant connective tissue.

LYMPHATIC VASCULAR SYSTEM

In addition to blood vessels, the body has a system of **thin-walled endothelial channels that collect excess interstitial fluid from the tissue spaces and return it to the blood.** This fluid is called **lymph; unlike the blood**, it flows in **only one direction, toward the heart.** The lymphatic capillaries originate in the various tissues **as thin, closed-ended vessels that consist of a single layer of endothelium and an incomplete basal lamina.** Lymphatic capillaries are held open by bundles of anchoring filaments of the elastic fiber system which also bind the vessels firmly to the surrounding connective tissue.



The thin lymphatic capillaries converge into larger lymphatic vessels. The larger lymphatics have a structure similar to that of veins except that they have thinner walls and lack a clear-cut separation between tunics. They also have more numerous internal valves.

Lymphatic vessels ultimately end up as two large trunks: **the thoracic duct** and the **right lymphatic duct,** which respectively empty lymph into the junction of the left internal jugular vein with the left sub clavian vein and into the confluence of the right sub clavian vein and the right internal jugular vein. The structure of these lymphatic ducts is similar to that of large veins.

Lymphatic vessels are tube-like structures that carry fluid (called lymph) away from the tissues to deliver it back into the blood's circulation. Unlike blood vessels that circulate blood in a continuous, closed-loop system, lymphatics carry fluid in one direction.

Lecture No. 9

• Lymphoid organs

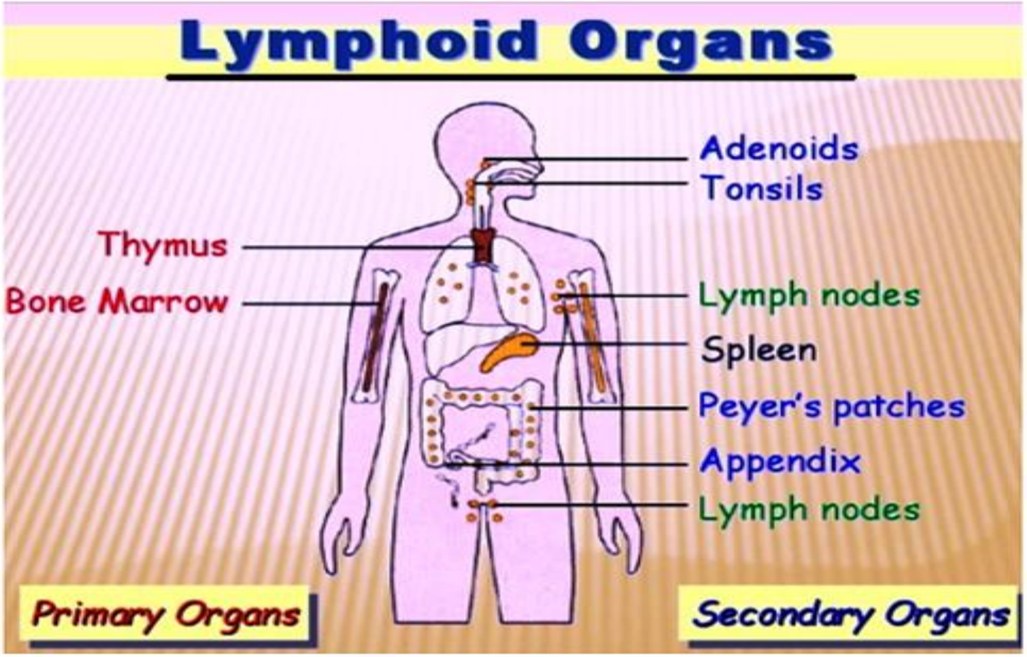
1- Primary lymphoid organs: These organs include the **bone marrow** and the **thymus.** They create special immune system cells called lymphocytes**.**

2- Secondary lymphoid organs: These organs include the **lymph nodes**, the **spleen, tonsils** and certain tissue in various **mucous membrane layers** in the body (for instance in the bowel.

The network of reticular fibers of the lymphoid tissue may be relatively dense and thus able to hold many free l**ymphocytes, macrophages**, and **plasma cells**. Areas of more loosely organized lymphoid tissue, with fewer and larger spaces, allow easy movement of these cells, In **nodular lymphoid tissue** groups of lymphocytes are arranged as spherical masses called lymphoid nodules or lymphoid follicles**,** containing primarily B lymphocytes. When lymphoid nodules become **activated** as a result of the arrival of antigencarrying APCs and recognition of the antigens by B lymphocytes, these lymphocytes proliferate in the central portion of the nodule, which then stains lighter and is called a germinal center.

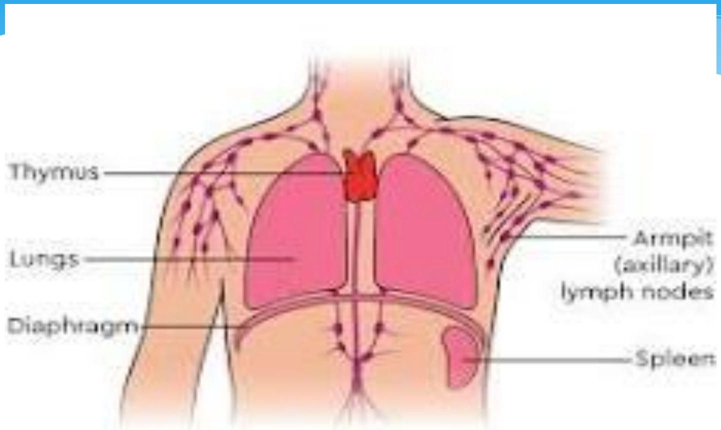
Lymphoid nodules vary widely in size, typically measuring a few hundred micrometers to one mm in diameter. They are found free in many connective tissues in the body and within lymph nodes, spleen, and tonsils, **but not in the thymus which contains only T cells**. Free lymphoid nodules are commonly present in the connective tissue of mucosal linings, where, together with free lymphocytes, they constitute the **mucosa-associated lymphoid tissue (MALT).**

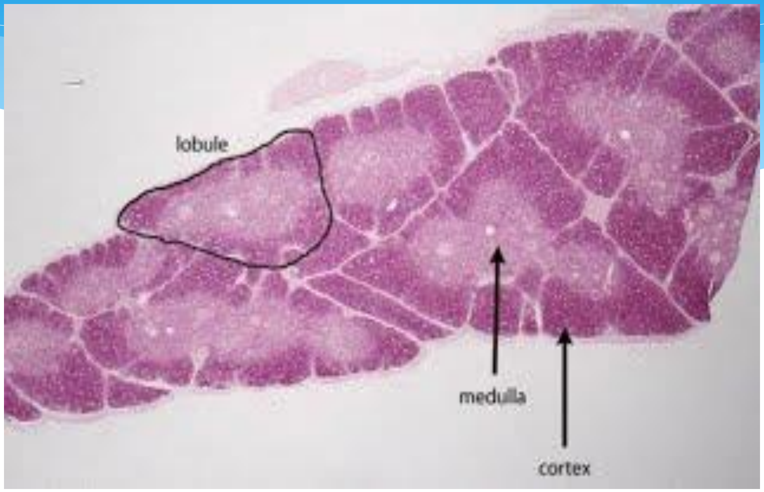
Individual lymphoid follicles are not encapsulated with connective tissue.

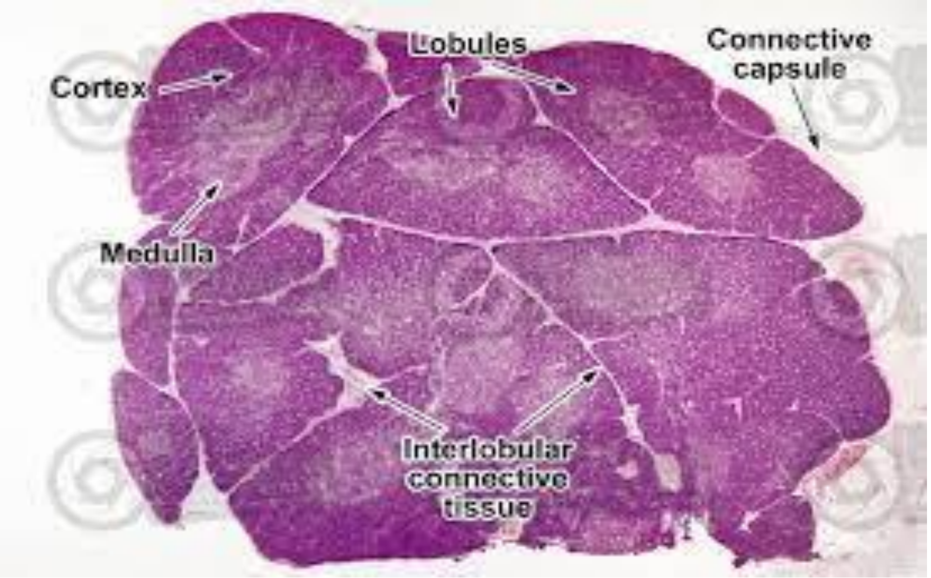


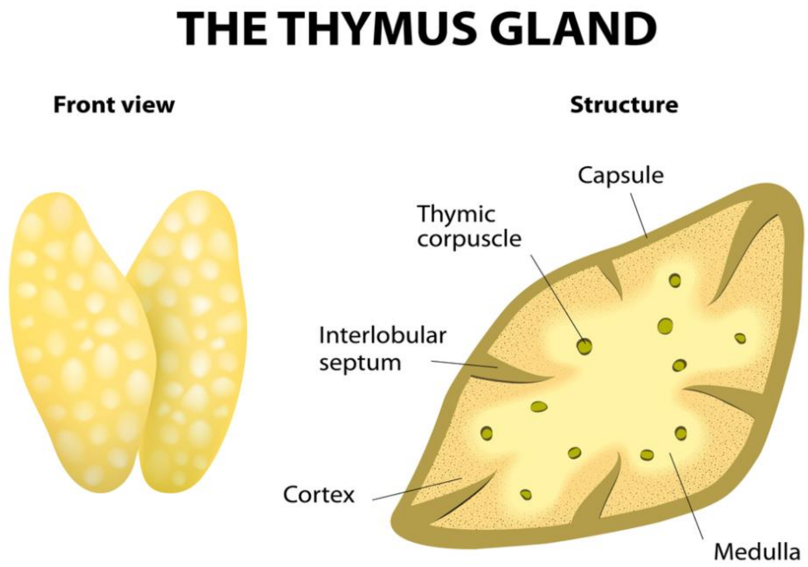
Thymus

The thymus is a bilateral organ located in the mediastinum; it attains its peak development during youth. Like bone marrow and B cells, the thymus is considered a central or **primary lymphoid** organ because T lymphocytes form there. Whereas all other lymphoid organs originate exclusively from mesoderm. The thymus has a connective tissue capsule that penetrates the parenchyma and divides it into incomplete lobules, with continuity between the **cortex and medulla** of adjoining lobules . Each lobule has a peripheral darkly stained zone known as the cortex and a central light zone called the medulla. The cortex is richer in small lymphocytes than the medulla and therefore it stains more darkly. The thymic cortex is composed of an extensive population of T lymphoblasts (also called thymocytes) and macrophages in a stroma of epithelial reticular cells. The thymic medulla also contains a cytoreticulum of epithelial reticular cells, many less densely packed differentiated T lymphocytes, and structures called thymic (Hassall's) corpuscles, which are characteristic of this region. Thymic corpuscles **consist of epithelial reticular cells arranged concentrically, filled with keratin filaments, and sometimes calcified**.


Thymus
Lungs
Diaphragm
Armpit
(axillary)
lymph nodes
Spleen


lobule
medulla
cortex


Lobules
Connective
capsule
Cortex
Medulla
Interlobular
connective
tissue

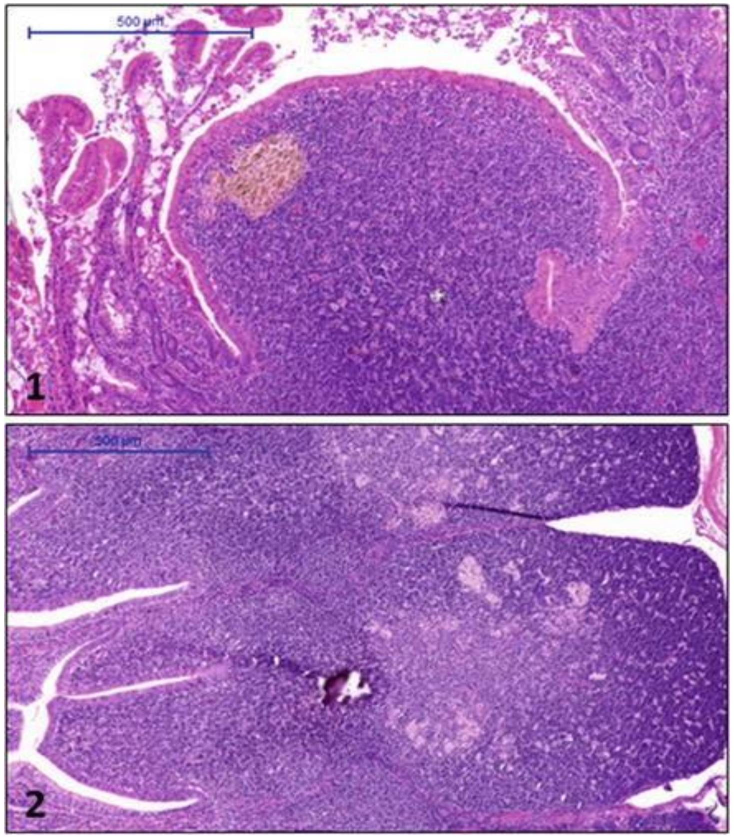

THE THYMUS GLAND
Front view
Structure
Capsule
Thymic
corpuscle
Interlobular
septum
Cortex
Medulla

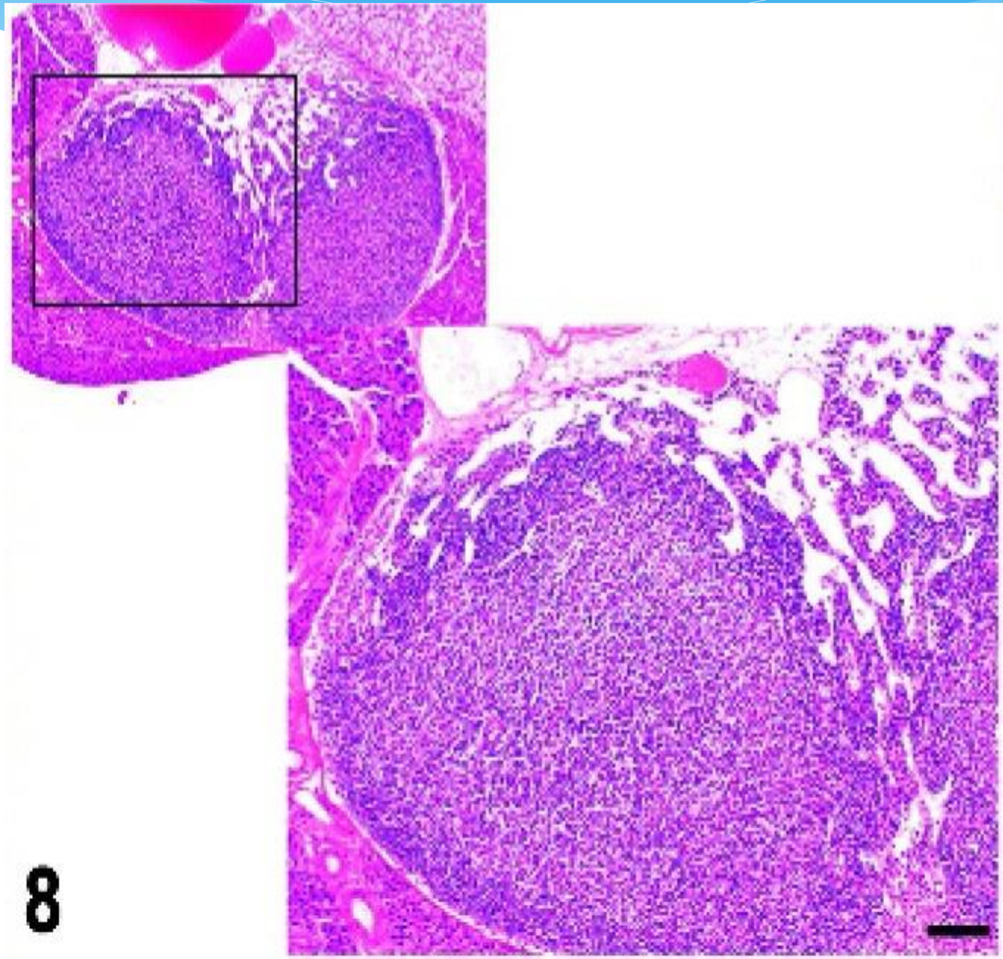
Mucosa -Associated Lymphoid Tissue (MALT)

The **digestive, respiratory, and genitourinary tracts are common sites of invasion by pathogens** because their lumens are open to the external environment. To protect the organism, the mucosal connective tissue of these tracts contains large and diffuse collections of dendritic cells, Lymphocytes and dendritic cells are also present within the epithelia lining the lumens.

In some places, these aggregates form large, conspicuous structures such as the tonsils and the Peyer patches in the ileum. Similar aggregates with lymphoid follicles are found in the appendix. Collectively the mucosa-associated lymphoid tissue (MALT) is one of the largest lymphoid organs, containing up to 70% of all the body's immune cells.

T**onsils are partially encapsulated lymphoid tissue lying beneath and in contact with the epithelium of the oral cavity and pharynx.** According to their location they are called **palatine**, **pharyngeal**, or **lingual tonsil**.

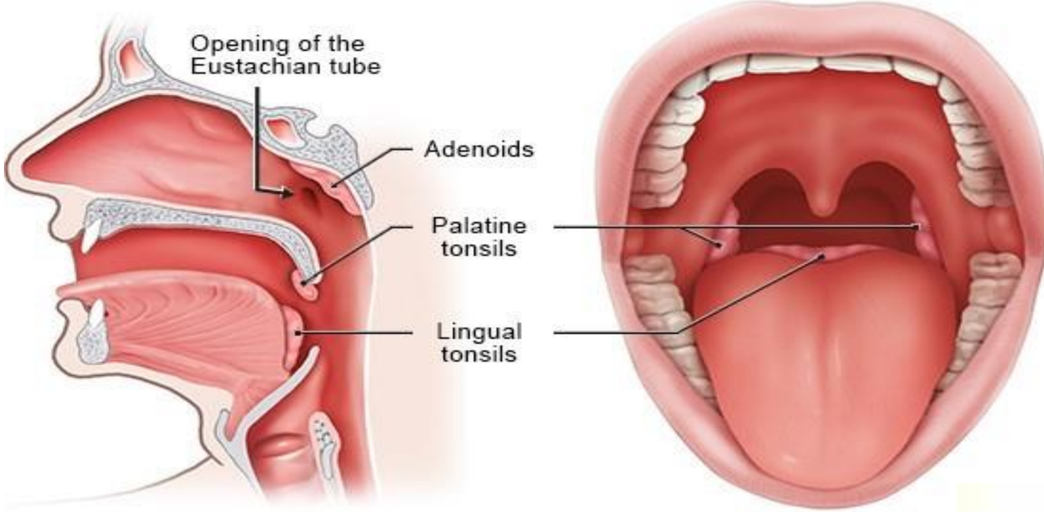


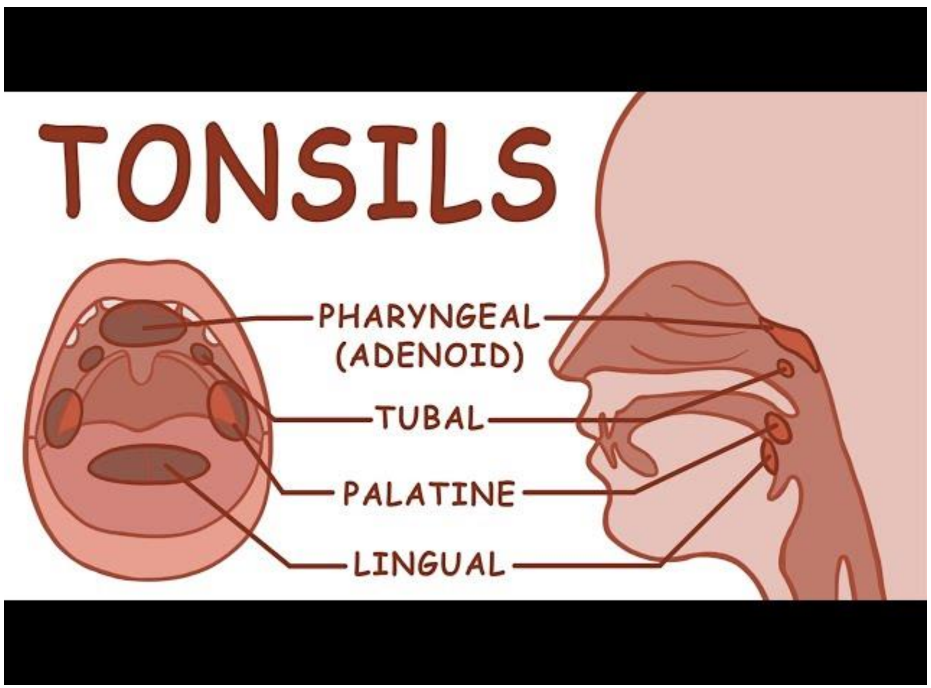


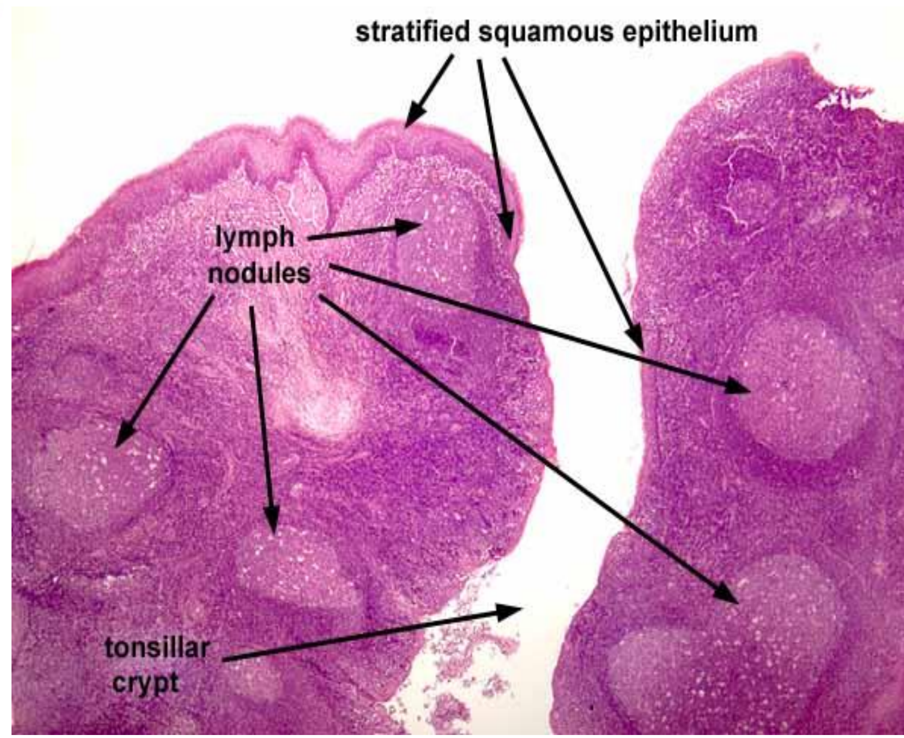
8

Masses of lymphoid nodules comprising the **tonsils** are collected in three general locations in the wall of the **pharynx.** **Palatine tonsils** are located in the posterior lateral walls of the oral cavity and **lingual tonsils** are situated along the surface of the posterior third of the tongue. Both are covered with stratified squamous epithelium. The **pharyngeal tonsil** is a **single tonsil** situated in the posterior wall of the nasopharynx. It is usually covered **by ciliated pseudostratified columnar epithelium**. Hypertrophied pharyngeal tonsils resulting from chronic inflammation are called **adenoids**.

Palatine tonsils, in the posterior parts of the soft palate, are covered by stratified squamous epithelium. Each has 10–20 epithelial invaginations that penetrate the tonsil deeply, forming crypts. The tonsils have many invaginations which form blind crypts. Below the epithelium, there are many lymphoid follicles beneath which have germinal centers like the lymph node. .

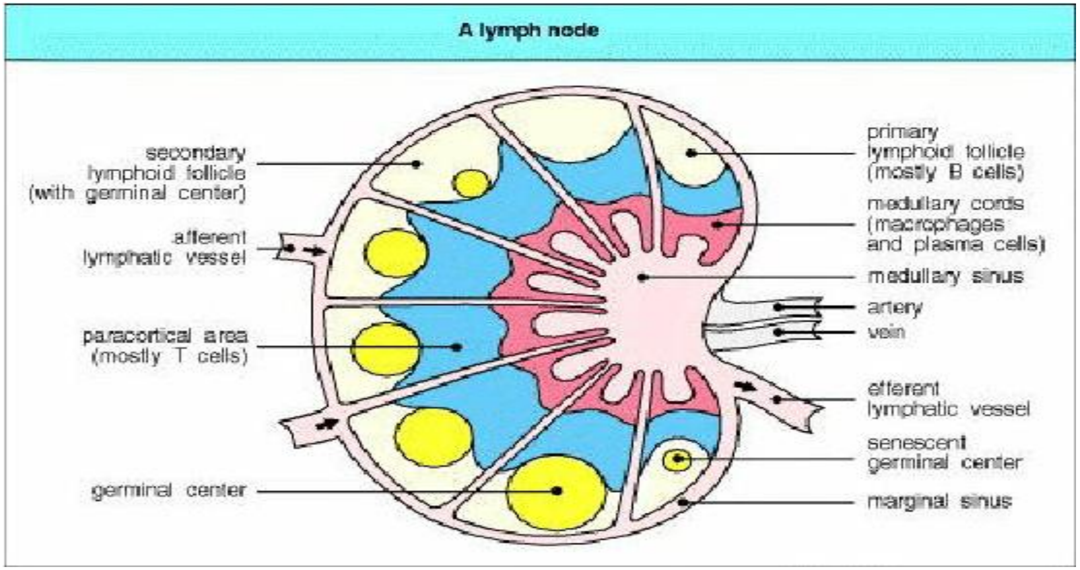

Opening of the Eustachian tube
Adenoids
Palatine tonsils
Lingual tonsils


TONSILS
PHARYNGEAL (ADENOID)
TUBAL
PALATINE
LINGUAL


stratified squamous epithelium
lymph nodules
tonsillar crypt

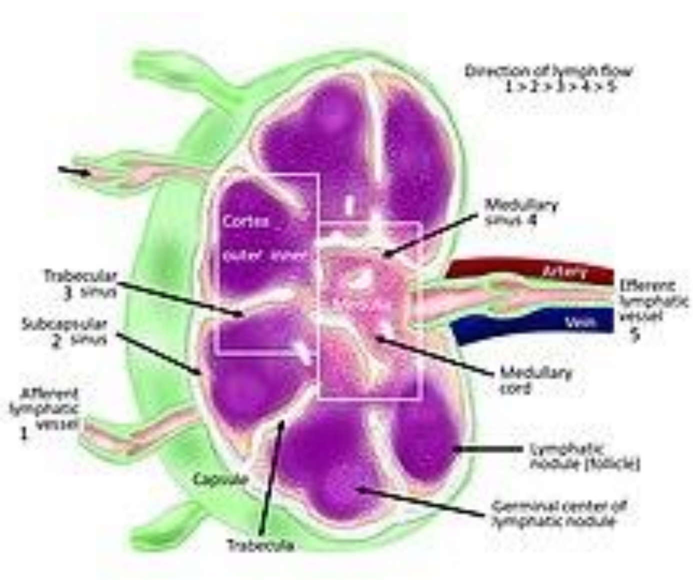
- LYMPH NODES

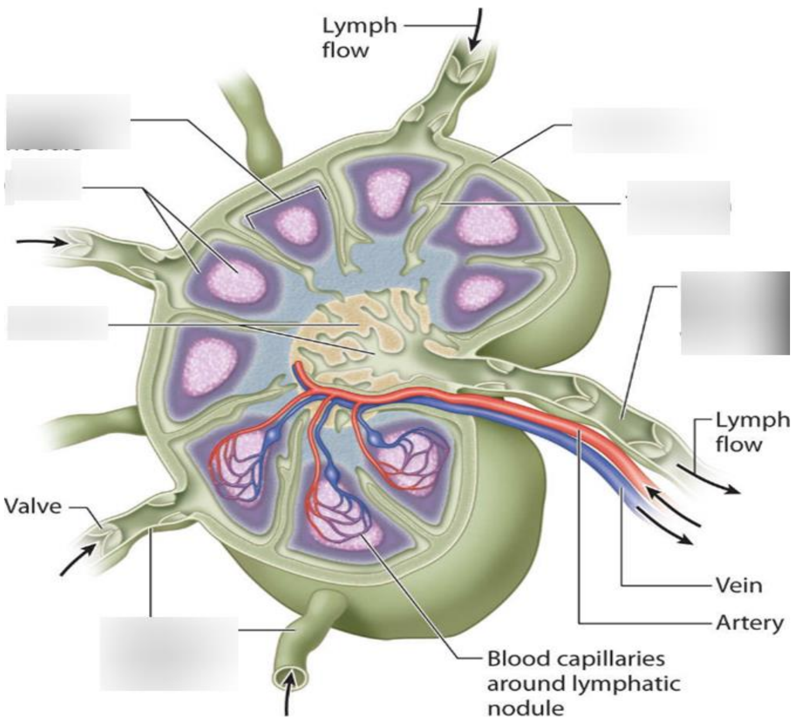
Lymph nodes are bean-shaped, encapsulated structures, generally 2–10 mm in diameter, distributed throughout the body along the course of the lymphatic vessels .The nodes are found in the axillae (armpits) and groin, along the great vessels of the neck, and in large numbers in the thorax and abdomen, especially in mesenteries. Lymph nodes constitute a series of in-line filters that are important in the body's defense against microorganisms. All this lymph, derived from tissue fluid, is filtered by at least one node before returning to the circulation. These **kidney-shaped organs** have a **convex surface** that is the entrance site of lymphatic vessels and a concave depression, **the hilum**, through which arteries and nerves enter and veins and lymphatic's leave the organ .A connective tissue **capsule** surrounds the lymph node, sending trabeculae into its interior.



The different arrangement of the cells and of the reticular fiber stroma supporting the cells creates a cortex, a medulla, and an intervening para cortex.

Afferent lymphatic vessels cross the capsule and pour lymph into the sub capsular sinus .From there, lymph passes through the cortical sinuses and then into the medullary sinuses. During this passage, the lymph infiltrates the cortex and the medullary cords and is filtered and modified by immune cells. The lymph is collected by efferent lymphatics at the hilum and valves in both lymphatics assure the unidirectional flow of lymph..





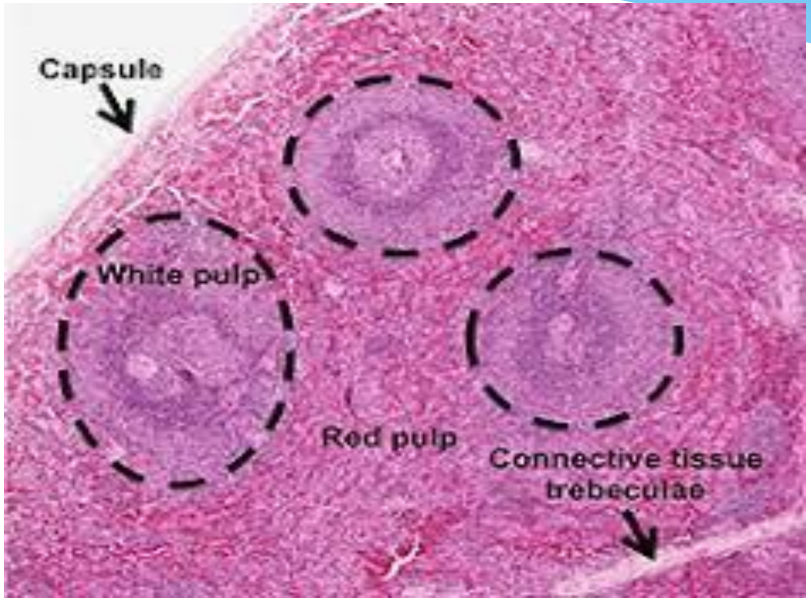
SPLEEN

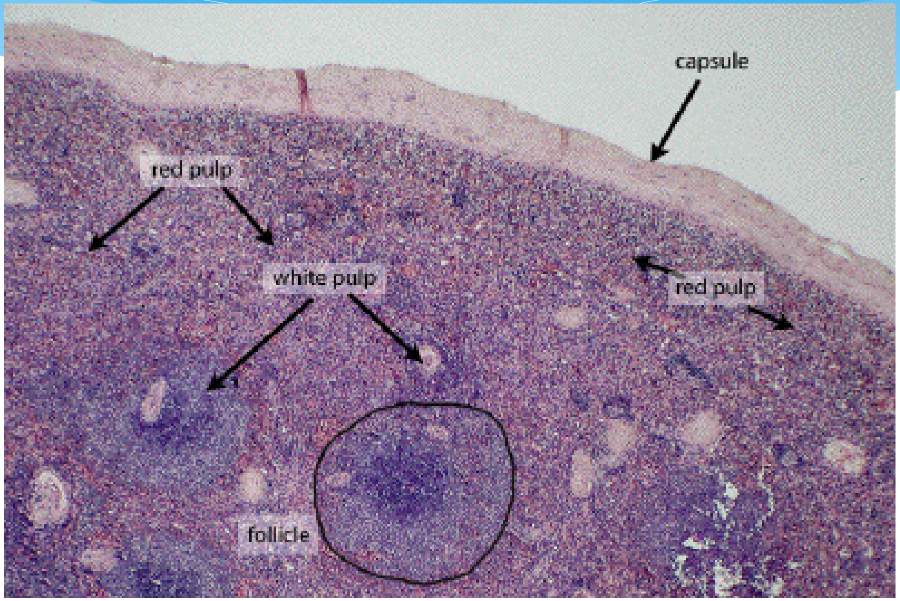
The spleen is the largest single accumulation of lymphoid tissue in the body and the only one involved in filtration of blood, making it an important organ in defense against blood-borne antigens. It is also the main site of destruction of aged erythrocytes.

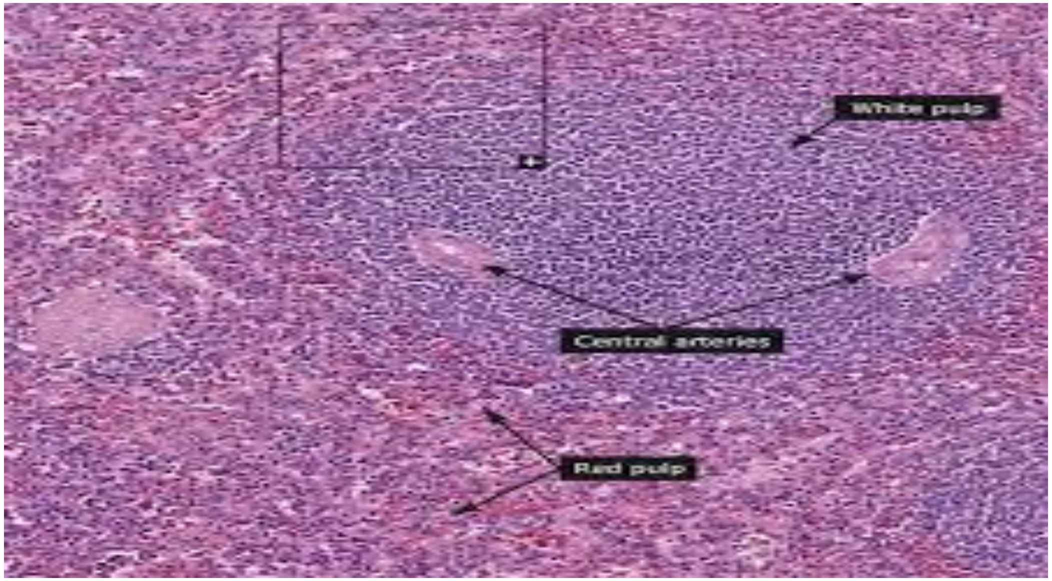
As is true of other secondary lymphoid organs, the spleen is a production site of antibodies and activated lymphocytes, which are delivered to the blood. The spleen is surrounded by a capsule of dense connective tissue from which emerge trabeculae, which partially subdivide the parenchyma or splenic. Large trabeculae originate at the hilum, these trabeculae carry nerves and arteries into the splenic pulp as well as veins that bring blood back into the circulation. Lymphatic vessels that arise in the splenic pulp also leave through the hilum via the trabeculae.

Splenic Pulp

The spleen is composed of reticular tissue containing reticular cells, many lymphocytes and other blood cells, macrophages, and APCs. The splenic pulp has **two components**, the **white pulp** and the **red pulp .The small masses of white pulp consist of lymphoid nodules** and the **periarteriolar lymphoid sheathes,** while the **red pulp consists of blood-filled sinusoids and splenic cords (of Bilroth). In these nodules the arteriole occupies an eccentric position but is still called the central arteriole.**


Capsule
White pulp
Red pulp
Connective tissue trebeculae


capsule
red pulp
white pulp
red pulp
follicle


White pulp
Central arteries
Red pulp

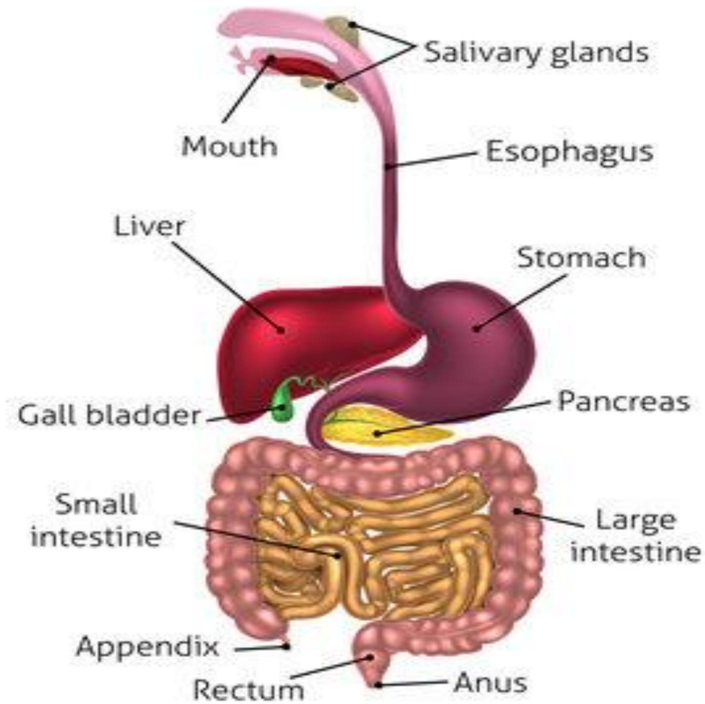
Lecture No. 10

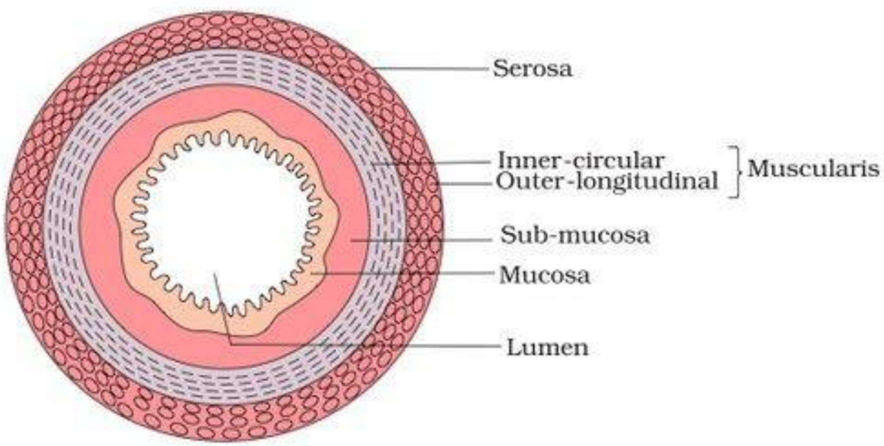
DIGESTIVE system

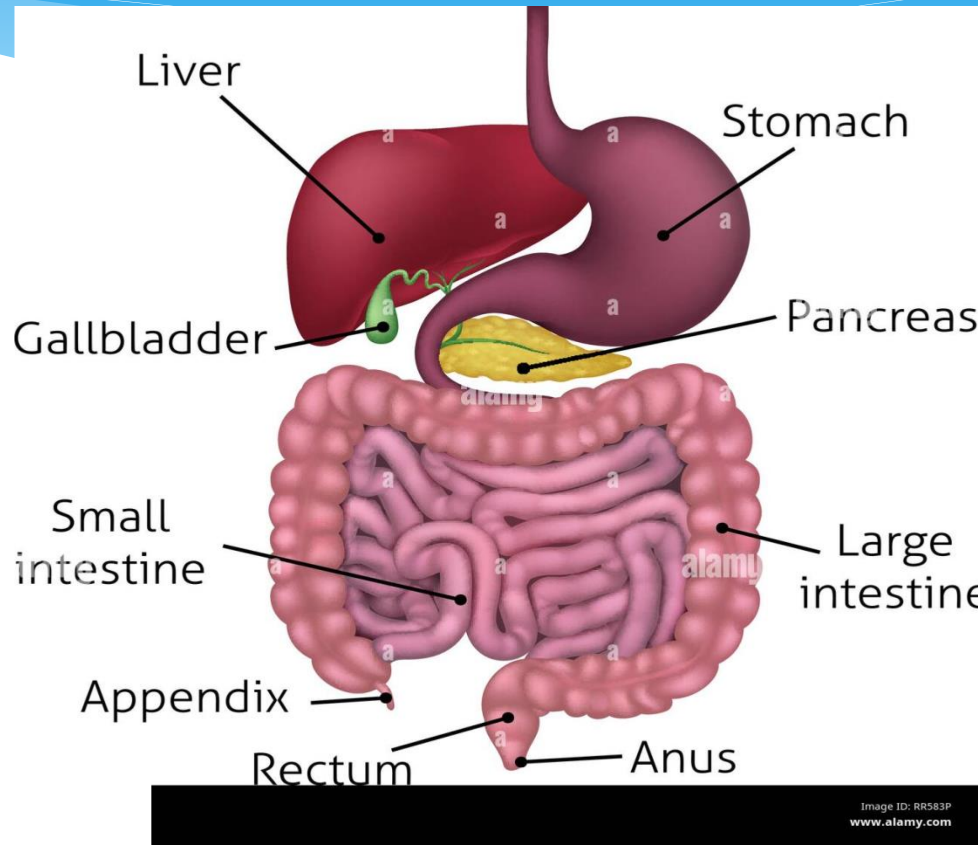
The digestive system consists of the **digestive tract—oral cavity, esophagus, stomach, small and large intestines, rectum, and anus—and its associated glands—salivary glands, liver, and pancreas .**Its **function** is to obtain from ingested food the molecules necessary for the maintenance, growth, and energy needs of the body. Macromolecules such as **proteins, fats, complex carbohydrates, and nucleic acids are broken down into small molecules that are more easily absorbed through the lining of the digestive tract, mostly in the small intestine.** Water, vitamins, and minerals from ingested food are also absorbed. In addition, the inner layer of the digestive tract is a protective barrier between the content of the tract's lumen and the internal milieu of the body.

GENERAL STRUCTURE OF THE DIGESTIVE TRACT

The entire gastrointestinal tract has certain common structural characteristics. It is a hollow tube with a lumen of variable diameter and a wall made up of four main layers: the mucosa, submucosa, muscularis, and serosa. The structure of these layers is summarized below:


Salivary glands
Mouth
Esophagus
Liver
Stomach
Gall bladder
Pancreas
Small intestine
Large intestine
Appendix
Rectum
Anus


Serosa
Inner-circular
Outer-longitudinal
Muscularis
Sub-mucosa
Mucosa
Lumen


Liver
Stomach
Gallbladder
Pancreas
Small intestine
Large intestine
Appendix
Rectum
Anus
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Major layers and organization of the digestive tract.

1- The **mucosa** comprises an epithelial lining; an underlying lamina propria of loose connective tissue rich in blood vessels, lymphatics, lymphocytes and smooth muscle cells, sometimes also containing glands; and a thin layer of smooth muscle called the **muscularis mucosae** usually separating mucosa from submucosa.

2-The **submucosa** contains denser connective tissue with many blood and lymph vessels and the submucosal plexus of autonomic nerves. It may also contain glands and lymphoid tissue.

3-The **thick muscularis** is composed of smooth muscle cells that are spirally oriented and divided into two sublayers. In the internal sub layer the orientation is generally **circular**; in the external sub layer, it is mostly **longitudinal**.

4-The serosa is a thin layer of loose connective tissue, rich in blood vessels, lymphatics, and adipose tissue, with a simple squamous covering epithelium (mesothelium). In the abdominal cavity, the serosa is continuous with the mesenteries (thin membranes covered by mesothelium on both sides), which support the intestines, and with the peritoneum, a serous membrane that lines the cavity. In places where the digestive tract is not suspended in a cavity but bound to other structures, such as in the esophagus, the serosa is replaced by **a thick adventitia**, consisting of connective tissue containing vessels and nerves, **lacking mesothelium**.

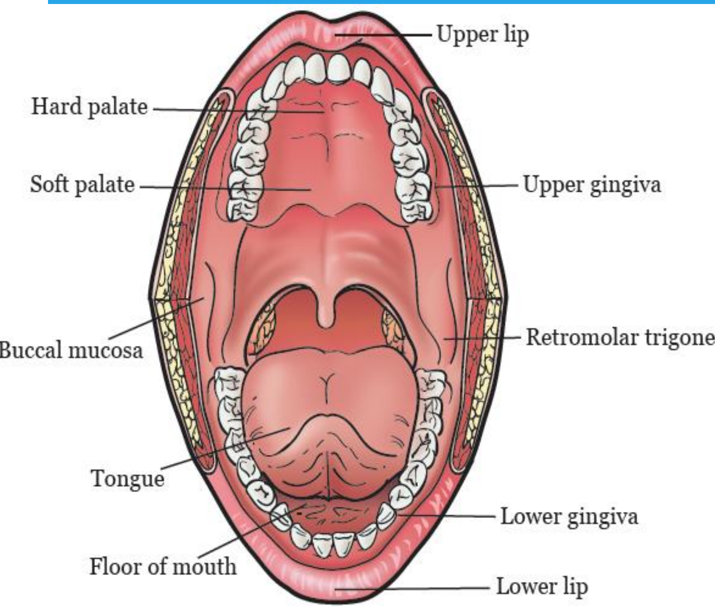
The main functions of the digestive tract's epithelial lining are to

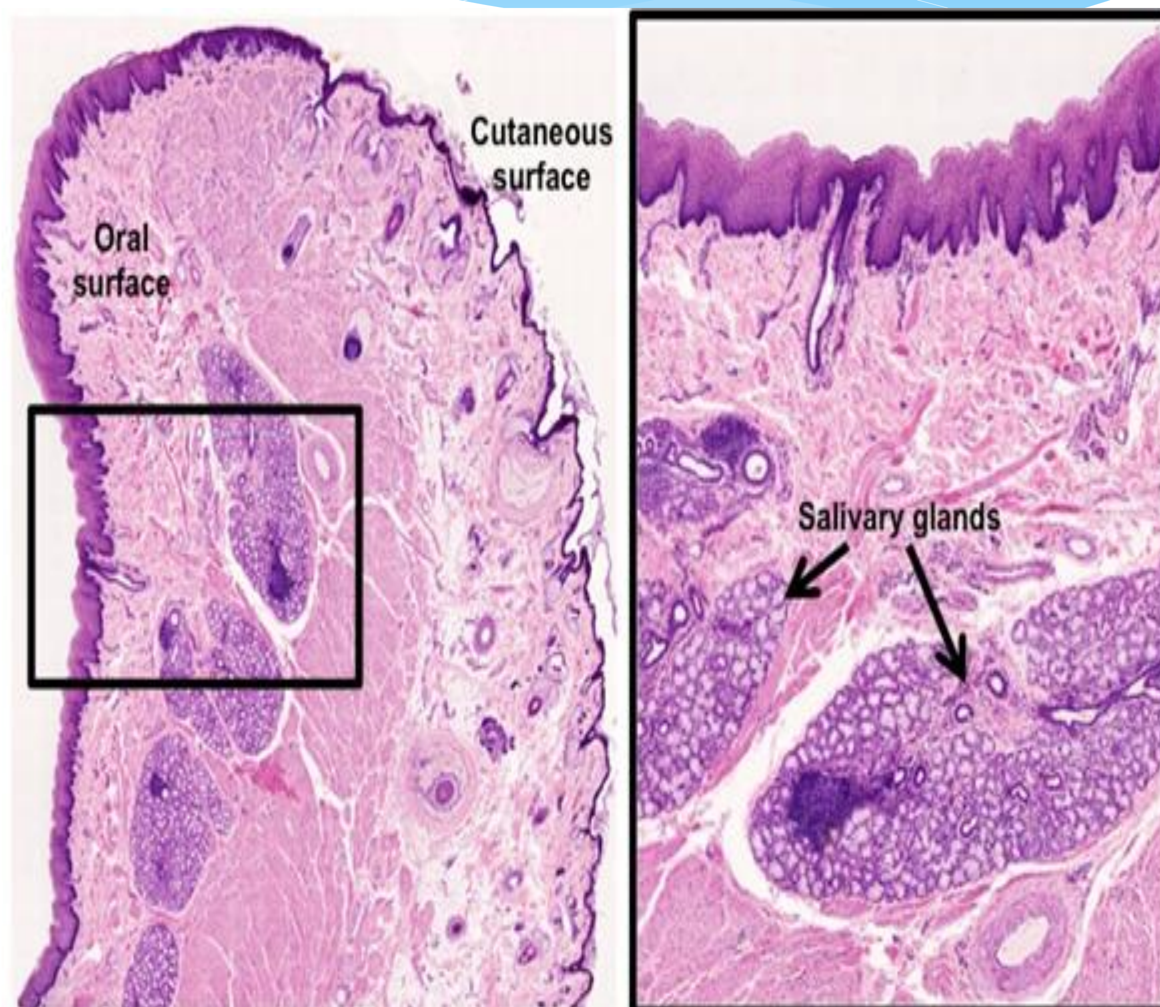
1- Provide a selectively permeable barrier between the contents of the tract and the tissues of the body.
2-Facilitate the transport and digestion of food.
3-Promote the absorption of the products of this digestion.
4-Produce hormones that affect the activity of the digestive system.
5-Produce mucus for lubrication and protection.

ORAL CAVITY

The oral cavity is lined with **stratified squamous epithelium, keratinized or nonkeratinized, depending on the region.** The keratin layer protects the oral mucosa from damage during masticatory function and is best developed on the gingiva (gum) and hard palate. The lamina propria in these regions has many papillae and rests directly on bony tissue. **Nonkeratinized squamous epithelium covers the soft palate, lips, cheeks, and the floor of the mouth.**

The lamina propria has papillae similar to those in the dermis of the skin and is continuous with a submucosa containing diffuse small salivary glands. The soft palate also has a core of skeletal muscle and lymphoid nodules. In **the lips,** there is also striated muscle and a transition from the oral nonkeratinized epithelium to the keratinized epithelium of the skin .


Upper lip
Hard palate
Soft palate
Upper gingiva
Buccal mucosa
Retromolar trigone
Tongue
Lower gingiva
Floor of mouth
Lower lip


Cutaneous surface
Oral surface
Salivary glands

Lip

Tongue

The tongue **is a mass of striated muscle covered by a mucous membrane whose structure varies according to the region.** The muscle fibers cross one another in three planes and are grouped in bundles separated by connective tissue. The mucous membrane **is smooth on the lower surface of the tongue**. The **tongue's dorsal surface is irregular, covered anteriorly by a great number of small eminences called papillae.** The posterior third of the tongue's dorsal surface is separated from the anterior two thirds **by a V-shaped groove**, the terminal sulcus. Behind this boundary is the root of the tongue, whose surface shows the many bulges of the lingual tonsils and smaller collections of lymphoid nodules .

The numerous papillae on the anterior portion of the tongue are elevations of the mucous membrane that assume various forms and functions. Four types are recognized:

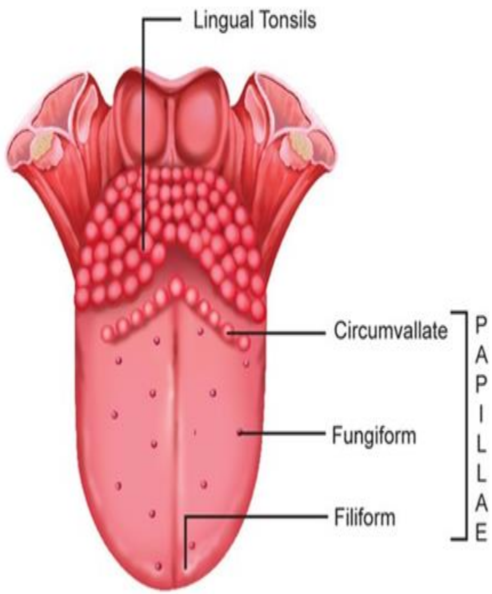
Taste buds are also present in other parts of the oral cavity, such as the soft palate, and are continuously flushed by numerous small salivary glands dispersed throughout the oral mucosa.

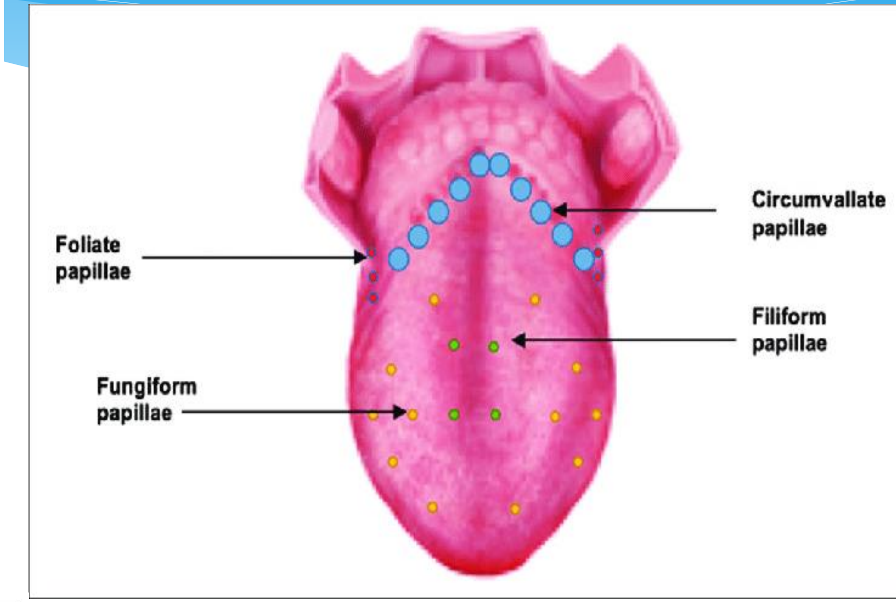
1- Filiform papillae are very numerous, have an elongated conical shape ,and are heavily keratinized, which gives their surface a gray or whitish appearance. Their epithelium lacks taste buds and their role is mechanical in providing a rough surface that facilitates food movement during chewing.

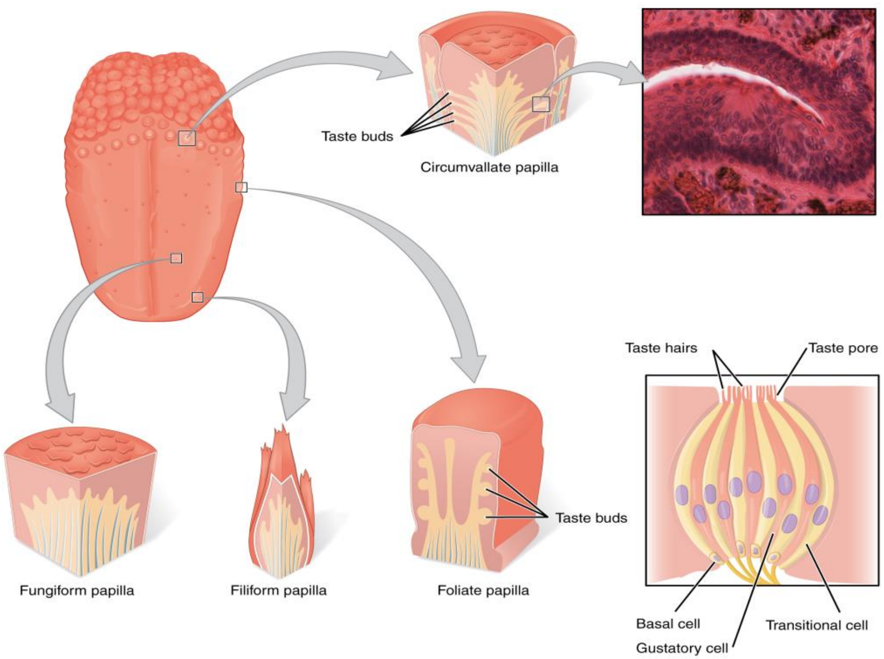
2-Fungiform papillae are less numerous, lightly keratinized, and mushroom-shaped with connective tissue cores and scattered taste buds on their upper surfaces. They are irregularly interspersed among the filiform papillae.

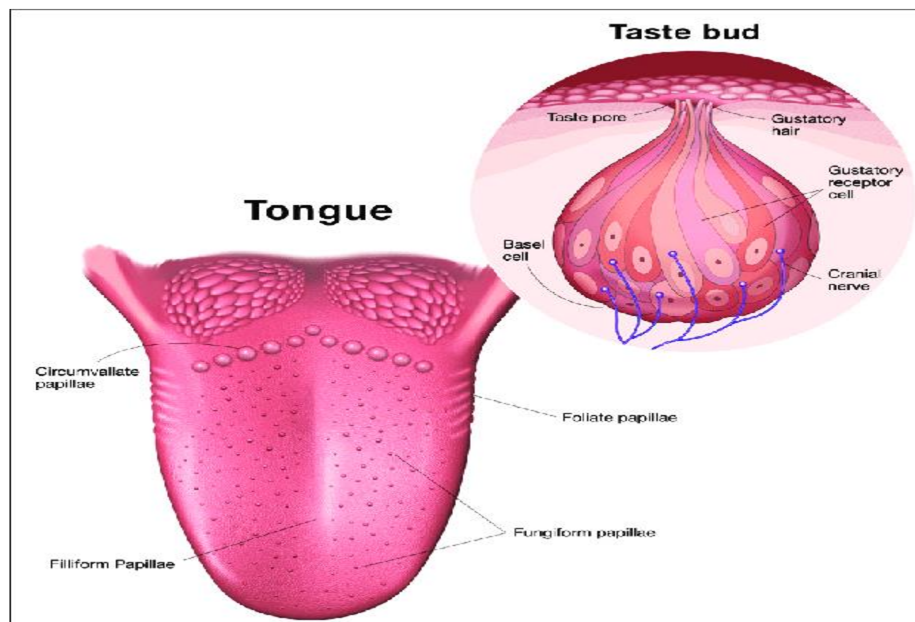
3- Foliate papillae are poorly developed in adults, but consist of parallel ridges and furrows on the sides of the tongue, with taste buds.

4-Vallate (or circumvallate) papillae are the **least numerous** and **largest** lingual papillae, and have over half the taste buds on the human tongue. circular vallate papillae normally form a V-shaped line just before the terminal sulcus. Ducts from several **serous salivary (von Ebner) glands** empty into the deep groove that surrounds each vallate papilla.

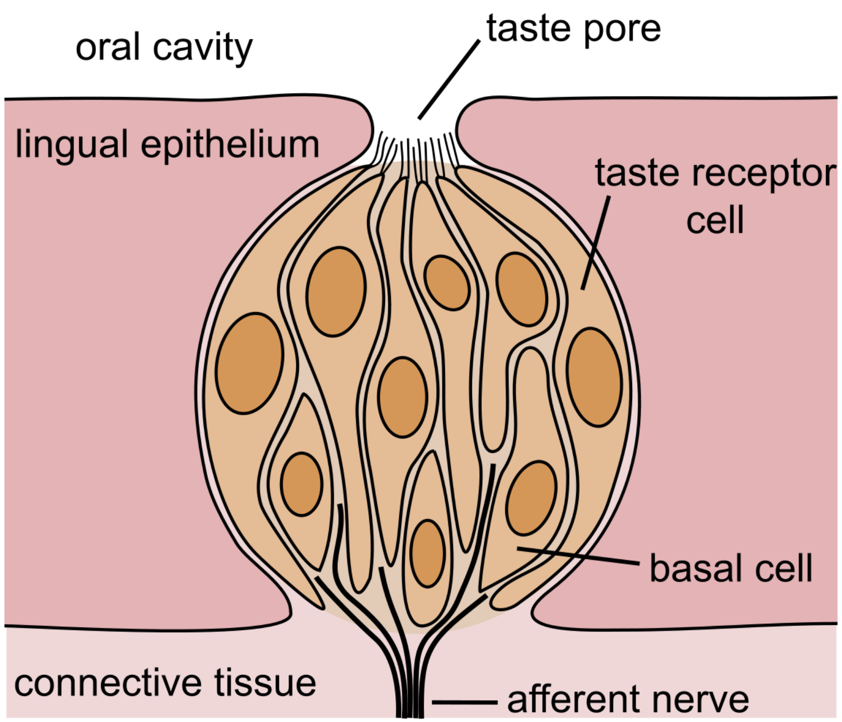

Lingual Tonsils
Circumvallate
Fungiform
Filiform
PAPILLAE

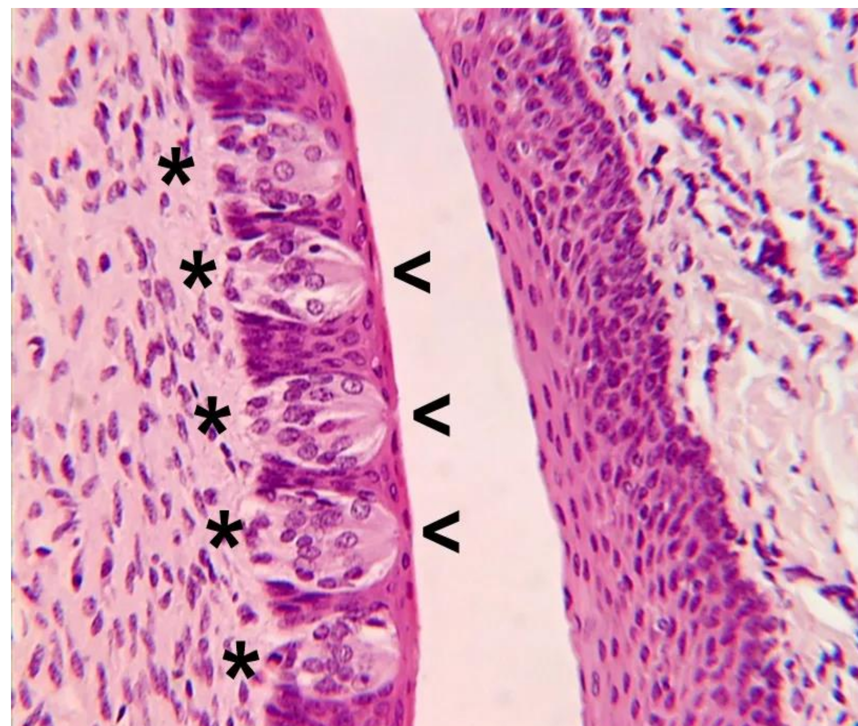

Circumvallate papillae
Foliate papillae
Filiform papillae
Fungiform papillae


Taste buds
Circumvallate papilla
Taste hairs
Taste pore
Taste buds
Fungiform papilla
Filiform papilla
Foliate papilla
Basal cell
Transitional cell
Gustatory cell


Taste bud
Taste pore
Gustatory hair
Gustatory receptor cell
Basel cell
Cranial nerve
Tongue
Circumvallate papillae
Foliate papillae
Fungiform papillae
Filliform Papillae

Taste buds are ovoid structures, each containing 50–75 cells, within the stratified epithelium of the tongue and the oral mucosa . About half the cells are elongated **gustatory (taste) cells** , which turn over with a 7- to 10-day life span. Other cells present are **slender supportive cells** immature cells, and **basal stem cells** which divide and give rise to the other two types. The base of each bud rests on the basal lamina and is entered by afferent sensory axons. At the apical ends of the gustatory cells microvilli project through an opening called the **taste pore**. Molecules (tastants) dissolved in saliva contact the microvilli through the pore and interact with cell surface taste receptors.





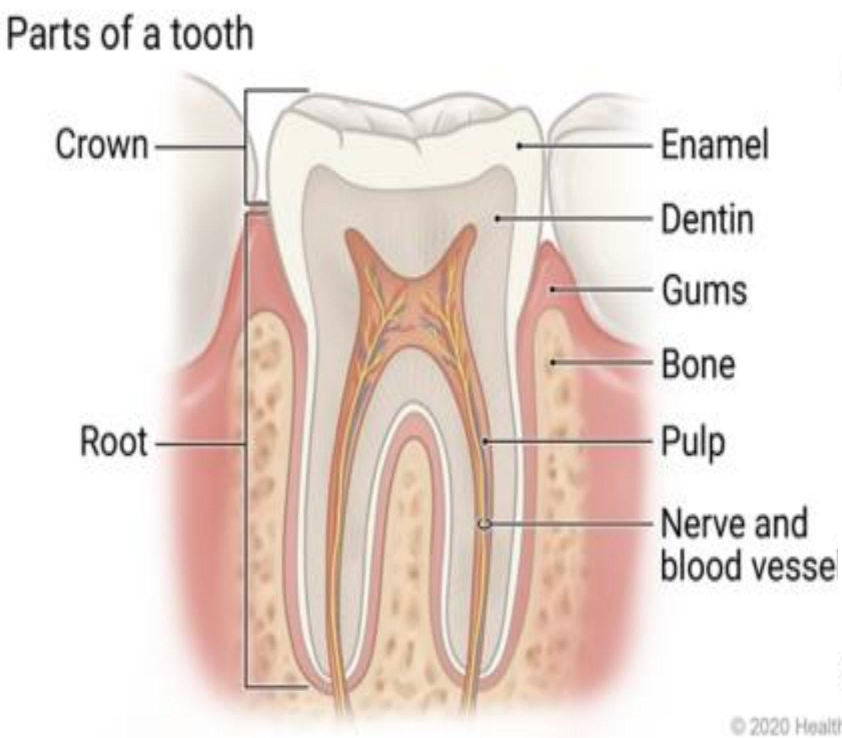
Teeth

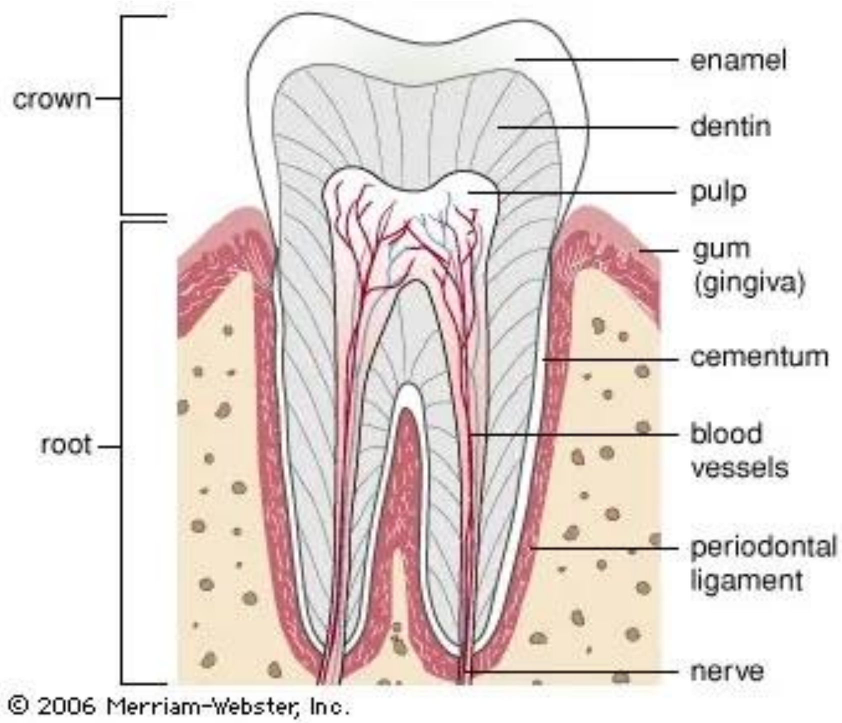
In the adult human there are normally **32 permanent teeth**, arranged in two bilaterally symmetric arches in the **maxillary and mandibular bones.** Each quadrant has eight teeth: two incisors, one canine, two premolars, and three permanent molars. Twenty of the permanent teeth are preceded by **deciduous (baby) teeth** which are shed; the others are permanent molars with no deciduous precursors. Each tooth has a crown exposed above the gingiva, a constricted neck at the gum, and one or more roots below the gingiva that hold the teeth in bony sockets called alveoli, one for each tooth.

The **crown** is covered by the extremely hard enamel and the roots by a bone-like tissue called cementum. These two coverings meet at **the neck** of the tooth. The bulk of a tooth is composed of another calcified material, dentin, which surrounds a soft connective tissue-filled space known as the pulp cavity. the tip of The pulp cavity narrows in the roots as the root canals, which extend to each root, where an opening (**apical foramen**) permits the entrance and exit of blood vessels, lymphatics , and nerves of the pulp cavity.

PULP

Tooth pulp consists of connective tissue resembling mesenchyme. Its main components are the layer of odontoblasts, many fibroblasts, thin collagen fibrils, and ground substance. Pulp is a highly innervated and vascularized tissue. Blood vessels and myelinated nerve fibers enter the apical foramen and divide into numerous branches. Some nerve fibers lose their myelin sheaths and extend into the dentinal tubules. Pulp fibers are sensitive to pain.





Esophagus

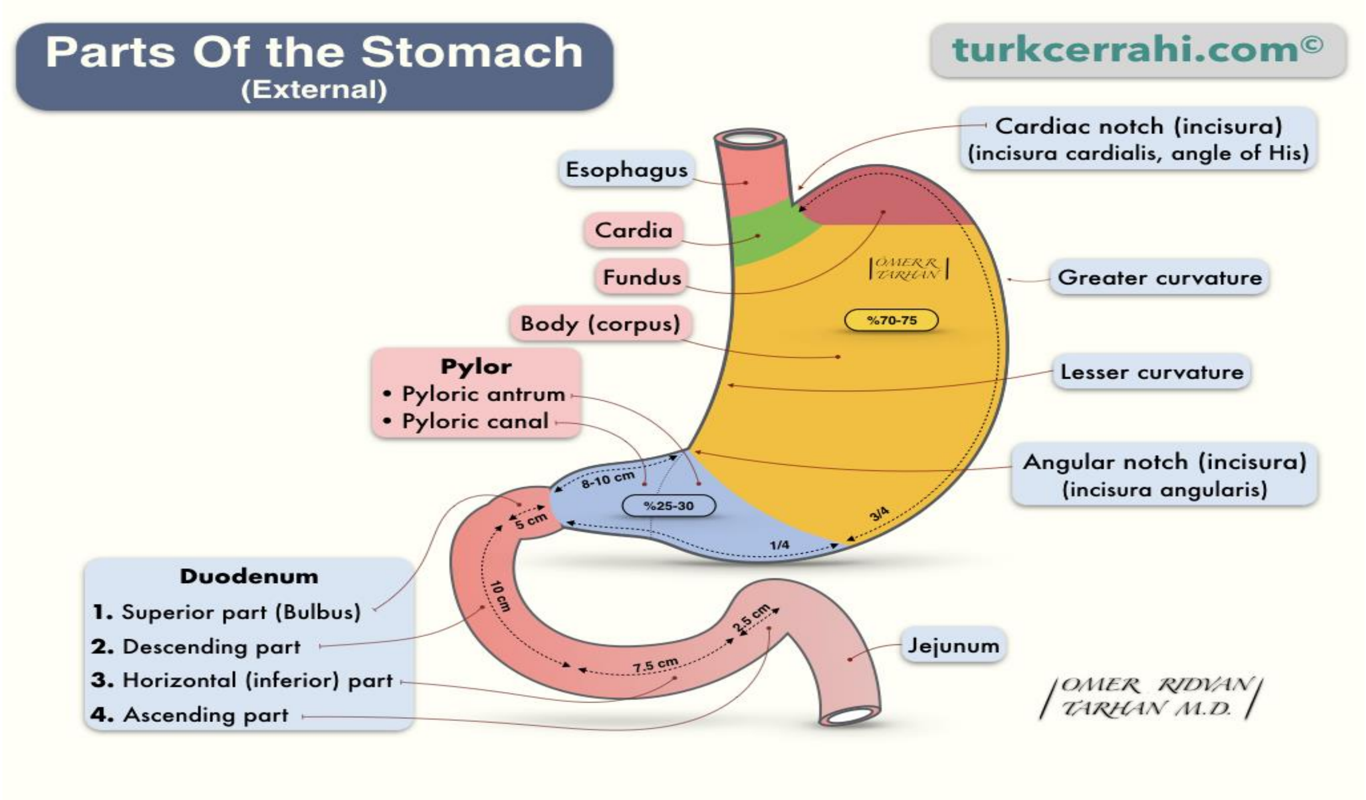
The part of the gastrointestinal tract called the esophagus is **a muscular tube** whose function is to transport food from the mouth to the stomach. It is lined by non keratinized stratified squamous epithelium with stem cells scattered throughout the basal layer. In the **submucosa** are groups of small mucus-secreting glands, the **esophageal glands**, secretions of which facilitate the transport of foodstuffs and protect the mucosa. In the **lamina propria** of the region near the stomach are groups of glands, **the esophageal cardiac glands**, which also secrete mucus.

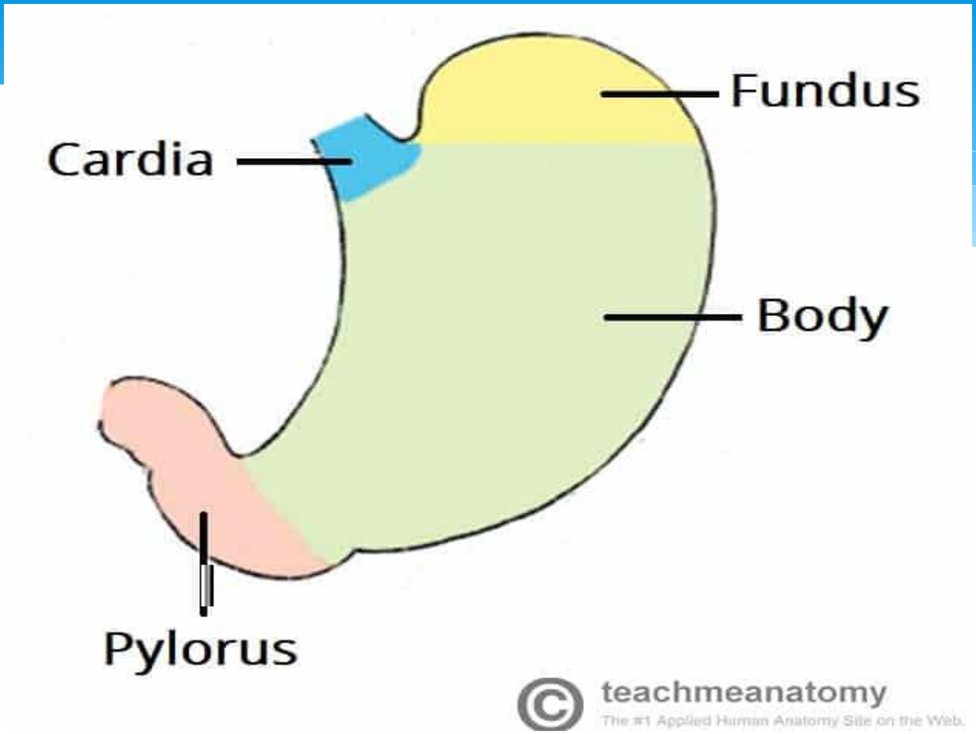
STOMACH

The stomach it is a dilated segment of the digestive tract whose main functions are to continue the digestion of carbohydrates initiated in the mouth, add an acidic fluid to the ingested food, transform it by muscular activity into **a viscous mass** (chyme), and promote the initial digestion of proteins with the enzyme pepsin. four regions: **cardia, fundus, body, and pylorus. The wall in all regions of the stomach is made up of all four major layers:**

Mucosa

Changing **abruptly at the esophago-gastric junction, the mucosa of the stomach consists of a simple columnar surface epithelium that invaginates into the lamina propria, forming gastric pits** .Emptying into the **gastric pits** are branched, tubular glands characteristic of the stomach region (**cardiac, gastric, and pyloric**). The vascularized lamina propria that surrounds and supports these pits and glands contains smooth muscle fibers and lymphoid cells. Separating the mucosa from the underlying sub mucosa is a layer of smooth muscle, the **muscularis mucosae**.





Mucosa

Changing abruptly at the esophago-gastric junction, the mucosa of the stomach consists of a simple columnar surface epithelium that invaginates into the lamina propria, forming gastric pits .Emptying into the gastric pits are branched, tubular glands characteristic of the stomach region (cardiac, gastric, and pyloric). Stem cells for the entire epithelial lining of the stomach are located in the upper regions of these glands near the gastric pits. The vascularized lamina propria that surrounds and supports these pits and glands contains smooth muscle fibers and lymphoid cells. Separating the mucosa from the underlying sub mucosa is a layer of smooth muscle, the muscularis mucosae.

In the fundus and body, the mucosa's lamina propria is filled with branched, tubular gastric glands, three to seven of which open into the bottom of each **gastric pit**. Each gastric gland has an **isthmus, a neck, and a base** .The isthmus, near the gastric pit, contains differentiating mucous cells that migrate and replace surface mucous cells, a few undifferentiated stem cells, and a few **parietal (oxyntic) cells**; the neck of the glands consists of stem cells, mucous neck cells (different from the isthmus mucous cells), and parietal cells ,the base of the glands contains **parietal cells and chief (zymogenic) cells**. Various enteroendocrine cells are dispersed in the neck and the base of the glands.

These cells of the gastric glands are as follows:

1-Mucous neck cells are present in clusters or as single cells between parietal cells in the necks of gastric glands .They are irregular in shape, with the nucleus at the base of the cell and the secretory granules near the apical surface. Their mucus secretion is less alkaline and quite different from that of the surface epithelial mucous cells.

2-Parietal cells are present mainly in the upper half of gastric glands, with fewer in the base. They are large rounded or pyramidal cells, each with one central spherical nucleus. Parietal cells **secrete both hydrochloric acid (HCl) and intrinsic factor**, **a glycoprotein required for uptake of vitamin B12 in the small intestine.**

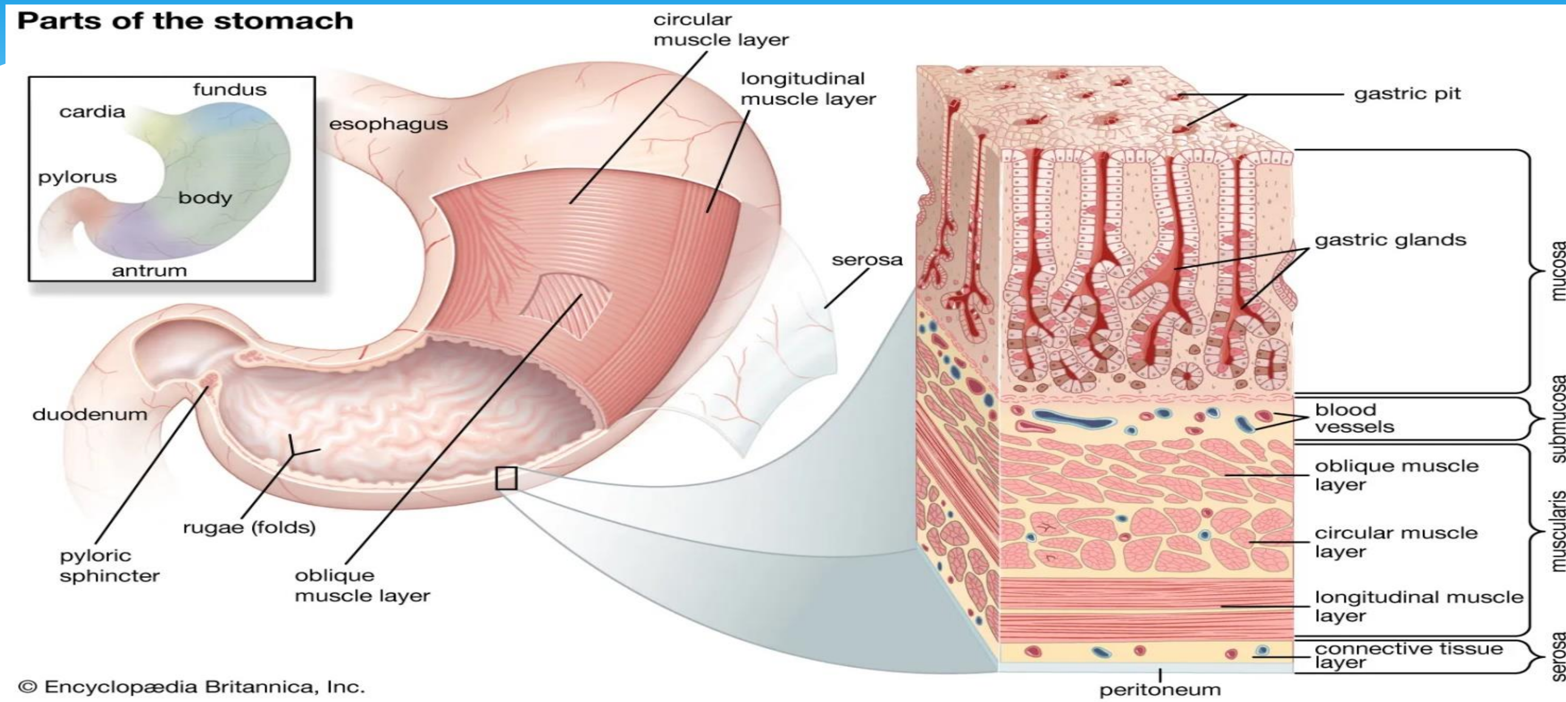
3-Chief (zymogenic) cells predominate in the lower region of the tubular glands and have all the characteristics of protein synthesizing exporting cells. The cytoplasmic granules contain the inactive enzyme **pepsinogen.** This precursor is rapidly converted into the highly active **proteolytic enzyme pepsin** after being released into the acid environment of the stomach.

4-Enteroendocrine cells.

5-Stem cells are few in number and found in the neck region of the glands.

Other Layers of the Stomach

The **submucosa** is composed of connective tissue containing blood and lymph vessels; it is infiltrated by lymphoid cells, macrophages, and mast cells. The **muscularis** is composed of smooth muscle fibers oriented in three main directions. The **external layer is longitudinal, the middle layer is circular, and the internal layer is oblique** . The stomach is covered by a thin **serosa.**


Parts of the stomach
fundus
cardia
pylorus
body
antrum
esophagus
circular muscle layer
longitudinal muscle layer
serosa
duodenum
pyloric sphincter
rugae (folds)
oblique muscle layer
gastric pit
gastric glands
blood vessels
oblique muscle layer
circular muscle layer
longitudinal muscle layer
connective tissue layer
peritoneum
mucosa
submucosa
muscularis
serosa
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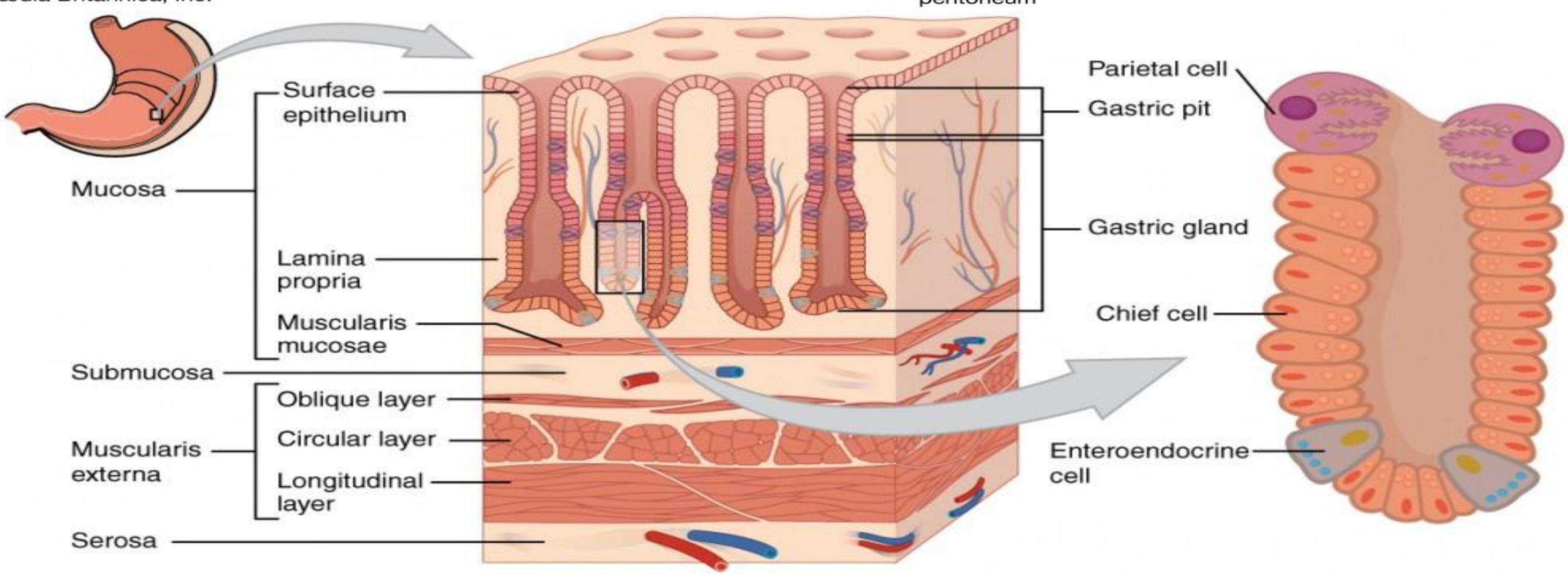
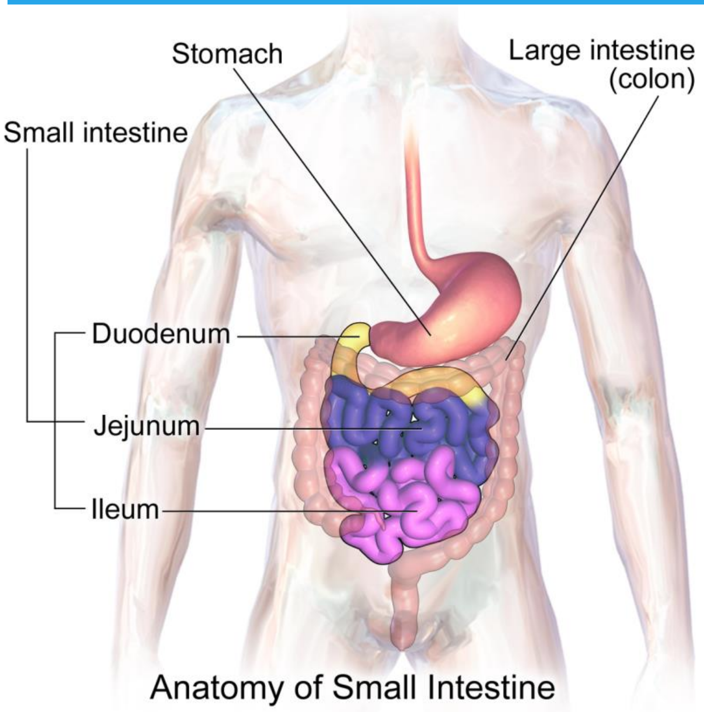

Surface epithelium
Mucosa
Lamina propria
Muscularis mucosae
Submucosa
Oblique layer
Circular layer
Muscularis externa
Longitudinal layer
Serosa
Parietal cell
Gastric pit
Gastric gland
Chief cell
Enteroendocrine cell

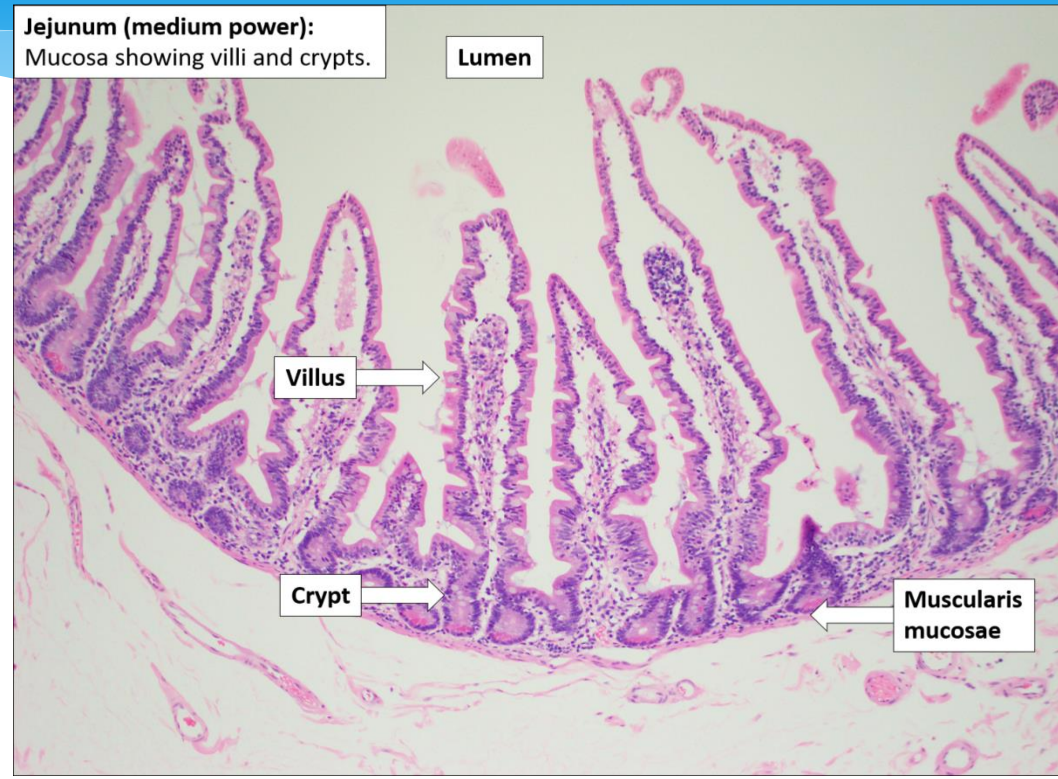
SMALL INTESTINE

The small intestine is the site of terminal food digestion, nutrient absorption, and endocrine secretion. The processes of digestion are completed in the small intestine, where the nutrients (products of digestion) are absorbed by cells of the epithelial lining. The small intestine is relatively long—approximately 5 m—and consists of three segments: **duodenum , jejunum, and ileum**.

The lining of the small intestine shows a series of permanent circular or semilunar folds (plicae circulares), consisting of mucosa and submucosa (Figures 15–25 and 15–26), which are best developed in the jejunum. Intestinal villi are 0.5- to 1.5-mm-long mucosal outgrowths (epithelium plus lamina propria) and project into the lumen . In the duodenum they are leaf-shaped, but gradually assume fingerlike shapes moving toward the ileum. Villi are covered by a simple columnar epithelium of **absorptive cells and goblet cells.**

Between the villi are small openings of short tubular glands called intestinal crypts or crypts of Lieberkühn . The epithelium of each villus is continuous with that of the intervening glands, which contain differentiating absorptive and goblet cells, Paneth cells, enteroendocrine cells, and stem cells that give rise to all these cell types.


Stomach
Large intestine (colon)
Small intestine
Duodenum
Jejunum
Ileum
Anatomy of Small Intestine


Jejunum (medium power):
Mucosa showing villi and crypts.
Lumen
Villus
Crypt
Muscularis mucosae

Enterocytes, the absorptive cells, are tall columnar cells, each with an oval nucleus in the basal half of the cell . At the apex of each cell is a homogeneous layer called the striated (or brush) border. When viewed with the electron microscope, the striated border is seen to be a layer of densely packed microvilli , each microvillus is a cylindrical protrusion of the apical cytoplasm approximately 1 m tall and 0.1 m in diameter containing actin filaments and enclosed by the cell membrane. Microvilli greatly increase the area of contact between the intestinal surface and the nutrients, a function also of the plicae and villi, which is an important feature in an organ specialized for absorption.

Goblet cells are interspersed between the absorptive cells . They are less abundant in the duodenum and more numerous in the ileum. These cells produce glycoprotein mucins that are hydrated and cross-linked to form mucus, whose main function is to protect and lubricate the lining of the intestine.

Paneth cells, located in the basal portion of the intestinal crypts below the stem cells, are exocrine cells with large, eosinophilic secretory granules in their apical cytoplasm .Paneth cell granules undergo exocytosis to release lysozyme, and hydrophobic peptides called **defensins**, all of which bind and breakdown membranes of microorganisms and bacterial walls. Paneth cells have an important role in innate immunity and in regulating the microenvironment of the intestinal crypts.

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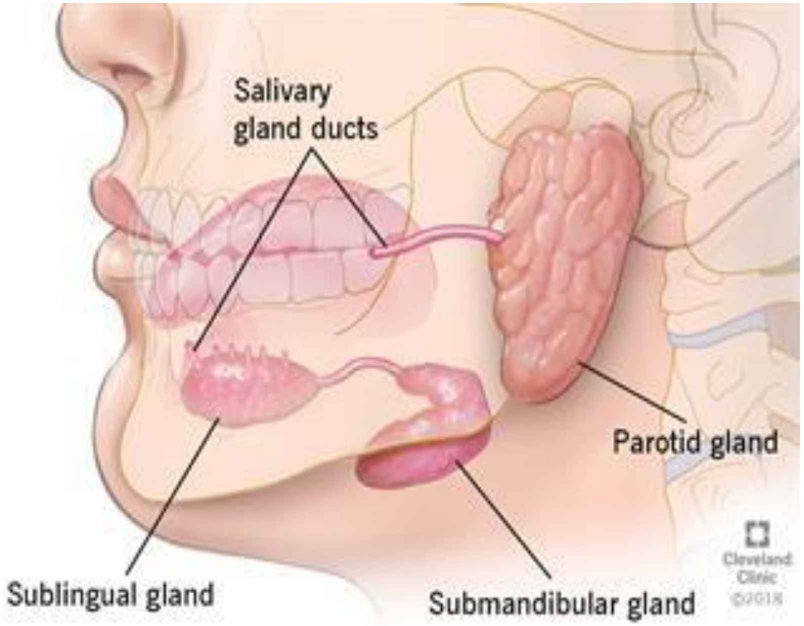
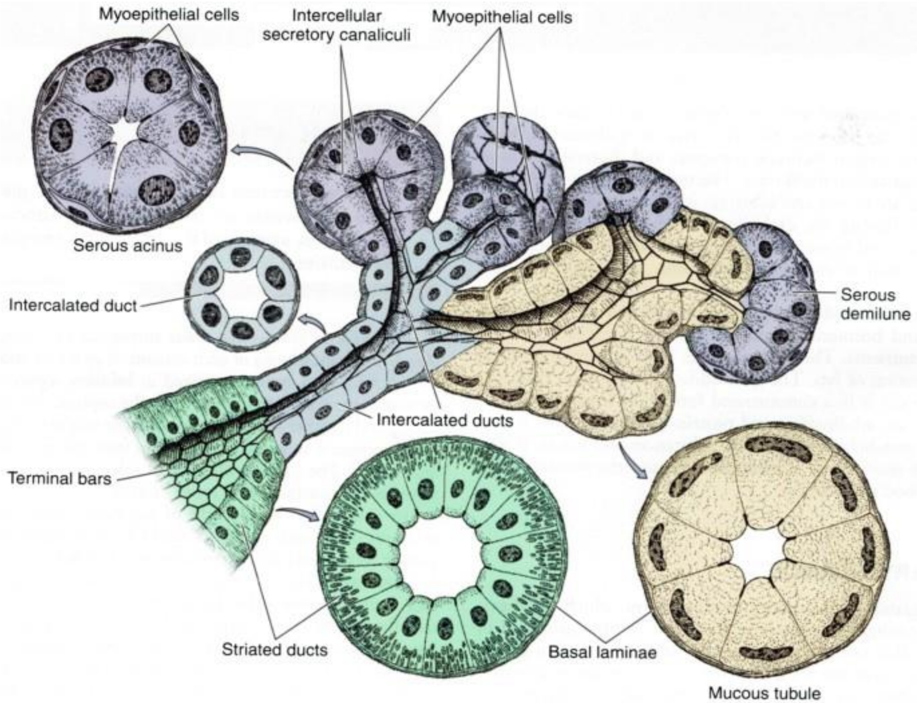
Lecture No. 11

Organs associated with the digestive tract

SALIVARY GLANDS

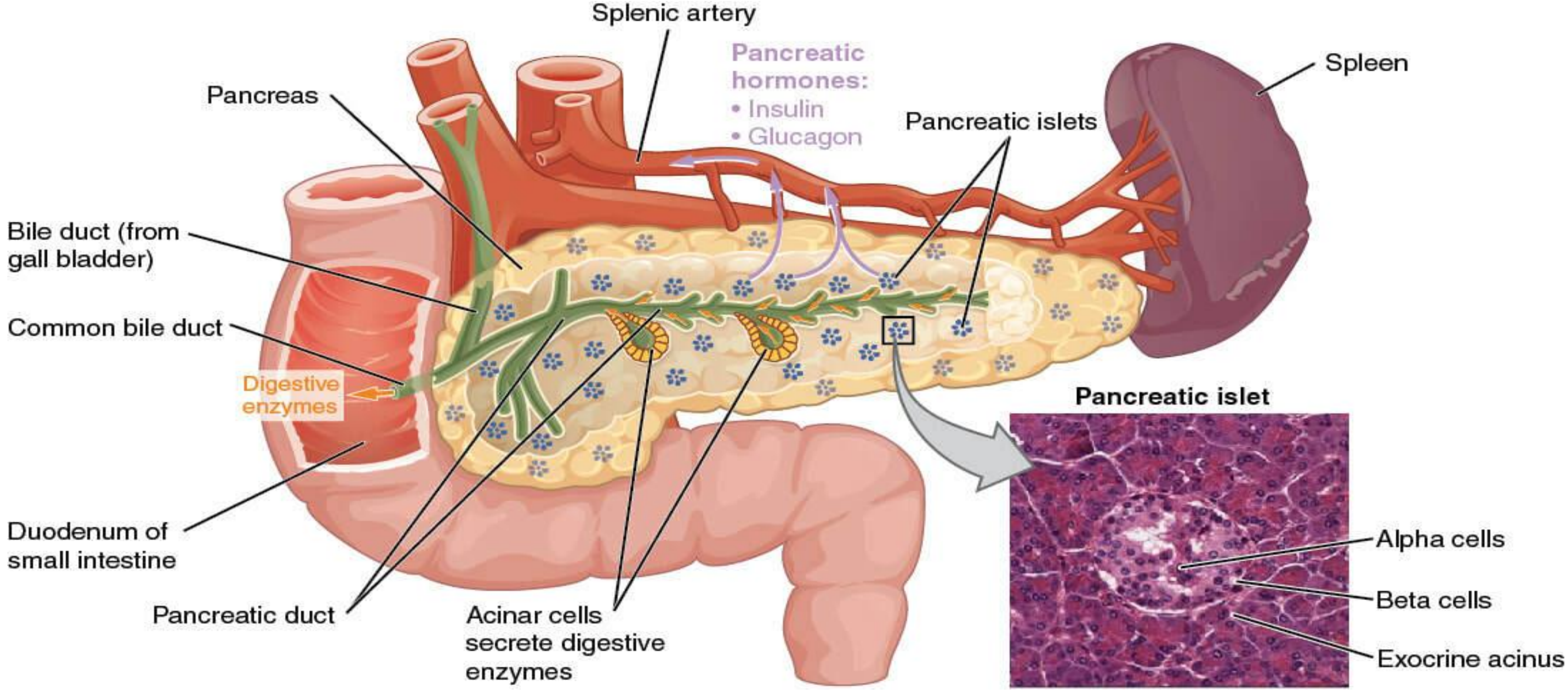
Exocrine glands in the mouth produce saliva, which has digestive, lubricating, and protective functions. With a usual pH of 6.5–6.9, saliva also has an important buffering function and in many nonhuman species is also very important for evaporative cooling. There are three pairs of large salivary glands: **the parotid, submandibular,** and **sublingual glands** , in addition to minor glands in mucosa and sub mucosa throughout the oral cavity which secrete 10% of the total volume of **saliva**.



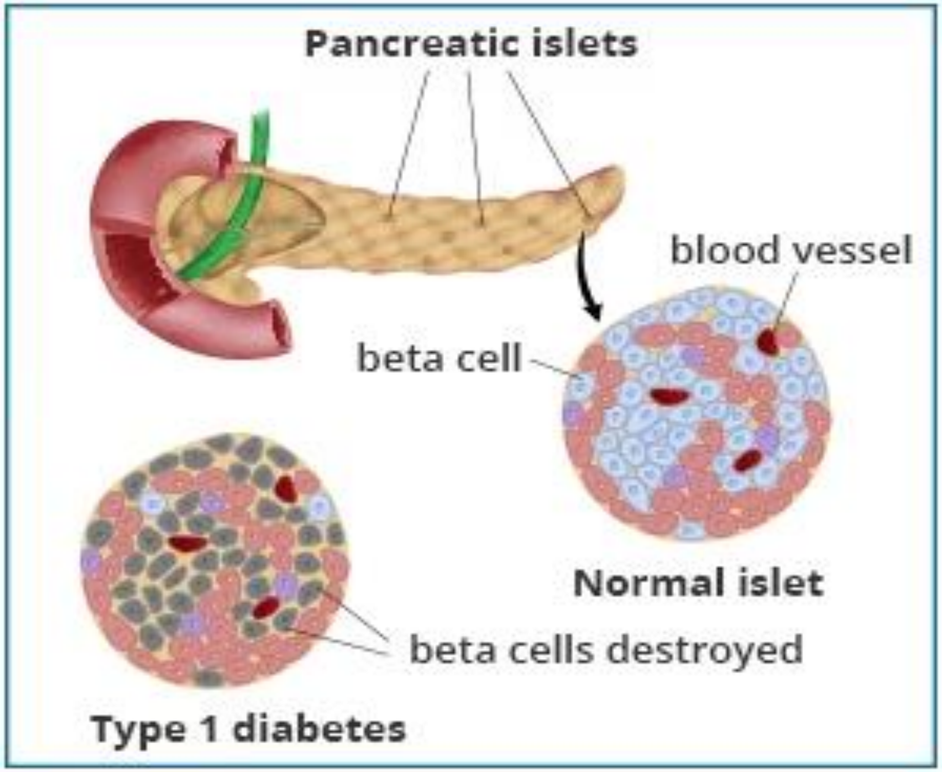


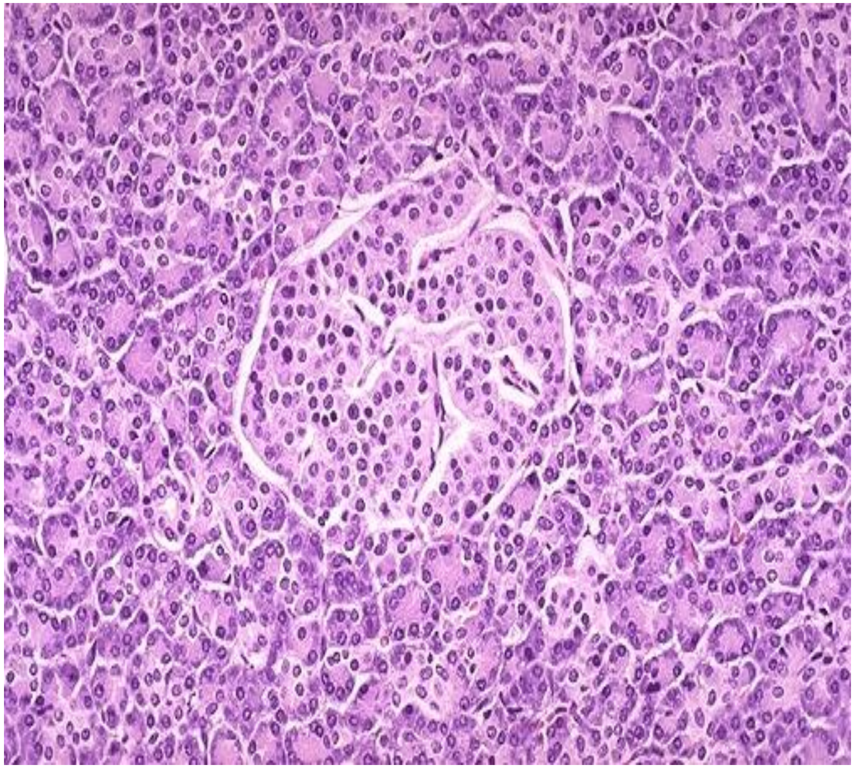
PANCREAS

The pancreas is a mixed exocrine-endocrine gland that produces both digestive enzymes and hormones . A thin capsule of connective tissue covers the pancreas and sends septa into it, separating the pancreatic lobules. The secretory acini are surrounded by a basal lamina that is supported by a delicate sheath of reticular fibers and a rich capillary network.



Islets of Langerhans are islands of endocrine cells scattered throughout the pancreas. A number of new studies have pointed to the potential for conversion of non-β islet cells in to insulin-producing β-cells to replenish β-cell mass as a means to treat diabetes.





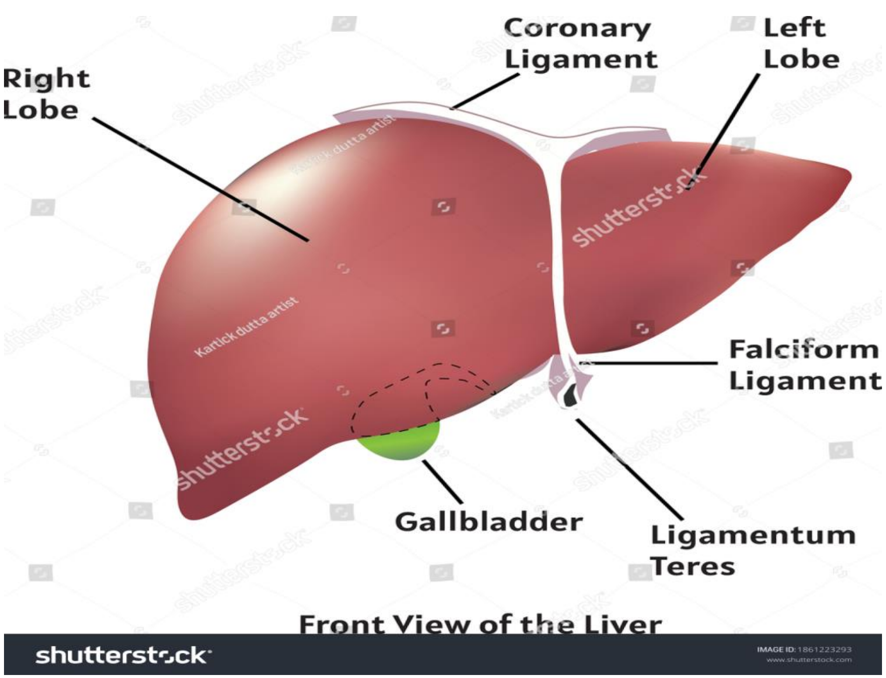
LIVER

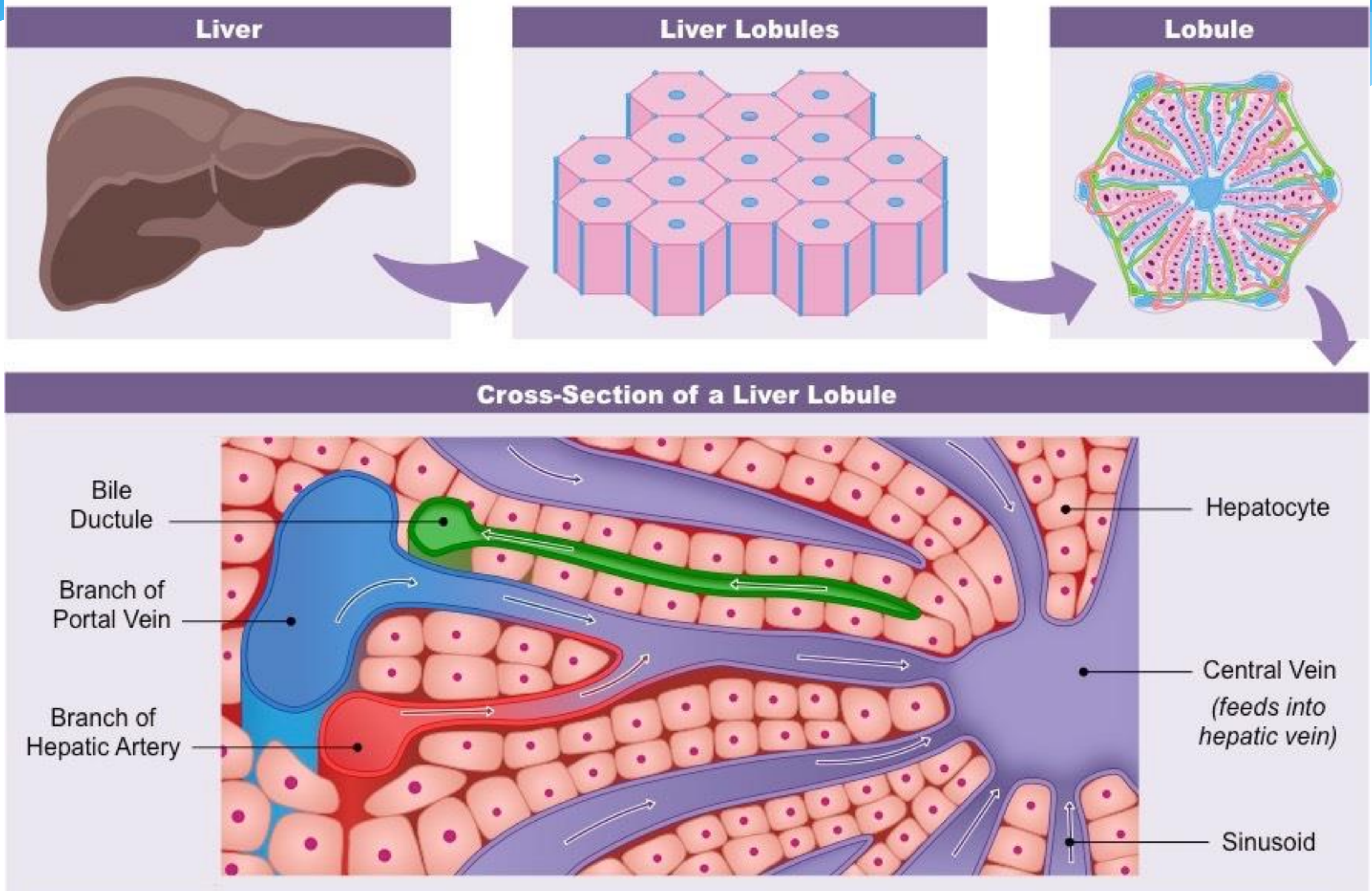
Except for the skin the liver is the body's biggest organ, weighing about 1.5 kg or about 2% of an adult's body weight. With a large right lobe and smaller left lobe, it is the largest gland and is situated in the abdominal cavity beneath the diaphragm. The position of the liver in the circulatory system is optimal for gathering, transforming, and accumulating metabolites from blood and for neutralizing and eliminating toxic substances in blood. The elimination occurs in the bile, an exocrine secretion of the liver that is important for lipid digestion in the gut. The liver also produces plasma proteins such as albumin, fibrinogen, and various carrier proteins.

The liver is covered by a thin fibrous **capsule** of connective tissue that becomes thicker at the **hilum**, where the portal vein and the hepatic artery enter the organ and where the right and left hepatic ducts and lymphatics exit. These vessels and ducts are surrounded by connective tissue all the way to their termination in the portal spaces between the **liver lobules**.

Hepatic Lobules

Liver cells or hepatocytes are epithelial cells grouped in interconnected plates. Hepatocytes are arranged into thousands of small polyhedral hepatic lobules which are the classic structural and functional units of the liver .Each lobule has three to six portal areas at its periphery and a venule called a **central vein** in its center, **Hepatocytes** make up each of the interconnected plates like the bricks of a wall and the plates are arranged radially around the central vein . From the periphery of the lobule to its center, the plates of hepatocytes branch and anastomose freely, forming a rather sponge-like structure . The spaces between these plates contain important micro vascular components, the liver sinusoids.





Liver
Liver Lobules
Lobule
Cross-Section of a Liver Lobule
Bile Ductule
Branch of Portal Vein
Branch of Hepatic Artery
Hepatocyte
Central Vein
(feeds into hepatic vein)
Sinusoid