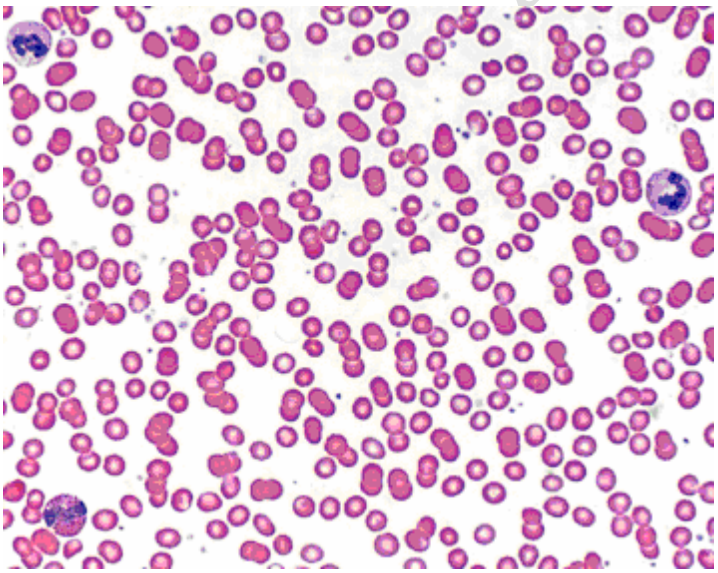
# Blood

**Blood** is a viscous fluid formed of cellular element suspended in plasma.

- The **cellular element** composed of: Erythrocytes (red blood cells), Leucocytes (white blood cells), and Platelets.

- **Plasma** is a viscous, translucent, yellowish fluid composed of water (90%), proteins (7%), organic salts (1%), and organic compound (2%) such as amino acids, lipids, and vitamins. The total blood volume in human is about 5 L (depending on body size). Outside the blood vessels, blood undergoes a complex reaction called coagulation or clot formation, which plays an important role in repairing damaged blood vessels and preventing blood loss.

- Erythrocytes and blood platelets perform their functions inside the blood vessels, whereas leukocytes reside temporarily in the blood vessels and then leave the blood stream through the capillary walls and venules to enter either the connective tissues or lymphoid tissues. - The ratio of erythrocytes to the total blood volume is about 43% and is known as haematocrit.



**Composition Of Plasma**

**A. Water:** constitutes 90% of plasma volume.

**B. Solutes:** constitutes 10% of plasma. and include plasma proteins and other organic compounds as well as inorganic salts.

**1. Plasma proteins.** Plasma contains a rich variety of soluble proteins, 7% by volume. Important examples include:

**a. Albumin.** This is the most abundant plasma protein (3.5-5 g/dL of blood) and is mainly responsible for maintaining the osmotic pressure of blood.

**b. Globulins (**Alpha, beta, and gamma globulins) are globular proteins dissolved in the plasma. The gamma globulins include the antibodies, or immunoglobulins, synthesized by plasma cells.

**c. Blood coagulation proteins**: such as prothrombin, fibrinogen which is converted into fibrin during clot formation. Fibrinogen is synthesized and secreted by the liver.

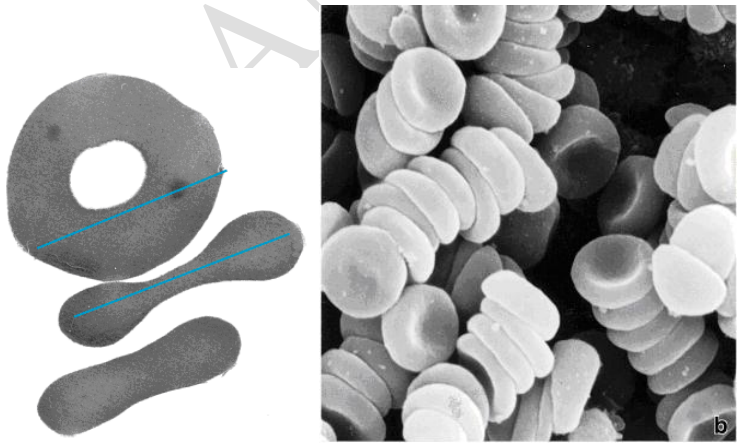
**2. Organic compounds.** They include nutrients such as amino acids and glucose, vitamins, and a variety of regulatory peptides, steroid hormones, and lipids.

**3. Inorganic salts.** They constitutes 0.9% of plasma volume, include blood electrolytes such as sodium, potassium, and calcium salts.

**The cellular or formed elements of blood**

**A- Erythrocytes (RBC)**

RBCs are structurally and functionally specialized to transport oxygen from the lungs to other tissues. Their cytoplasm contains the oxygen binding protein hemoglobin. Mature RBCs lack nuclei and cytoplasmic organelles, which they lose during differentiation. Mature erythrocytes therefore have a limited lifespan (120 days) in the circulation before they are removed by macrophages in the spleen and bone marrow.



Erythrocytes (RBC) are anucleated corpuscles (nucleated in embryonic and fetal mammals and in other vertebrates). They are biconcave disks about ~7µm in diameter, 2µm thick at its rim and less than 1µm at its center. They contain hemoglobin, which fills almost the entire cytoplasm. Erythrocytes are elastic and can withstand deformation. Their number is about 4.5-5 million/$mm^3$, the number is more in males than in females. The lifespan of an erythrocyte in the bloodstream is 100-120 days i.e. about $5\times10^{11}$ erythrocytes are formed/ destroyed each day.

 Erythron (census): whole mass of RBCs & their precursors in bone marrow.

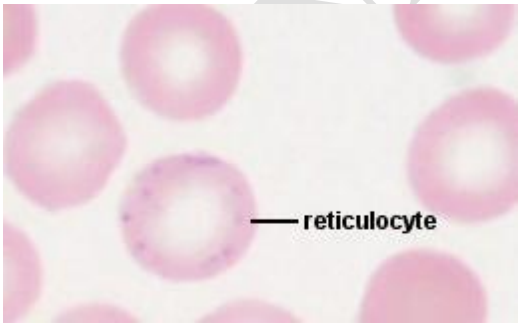
**Abnormalities of RBCs**: usually named as anemia that are due to changes in shape, number, or hemoglobin content.

**Anisocytosis**: refers to the presence of a high percentage of RBCs with great variations in size. Those larger than 9µm in diameter are termed **macrocytes**, and those smaller than 6µm are termed **microcytes**.

**Nuclear fragments:** in some diseases nuclear fragments or ***Howell-Joliy bodies*** remain in some mature RBCs. When these form circular filaments they are termed ***Cabot rings***.

**Reticulocytes** are immature RBCs released from bone marrow; normally estimated ~ 1% of circulating RBCs. Reticulocytes contain a small amount of residual RER and ribosomes.

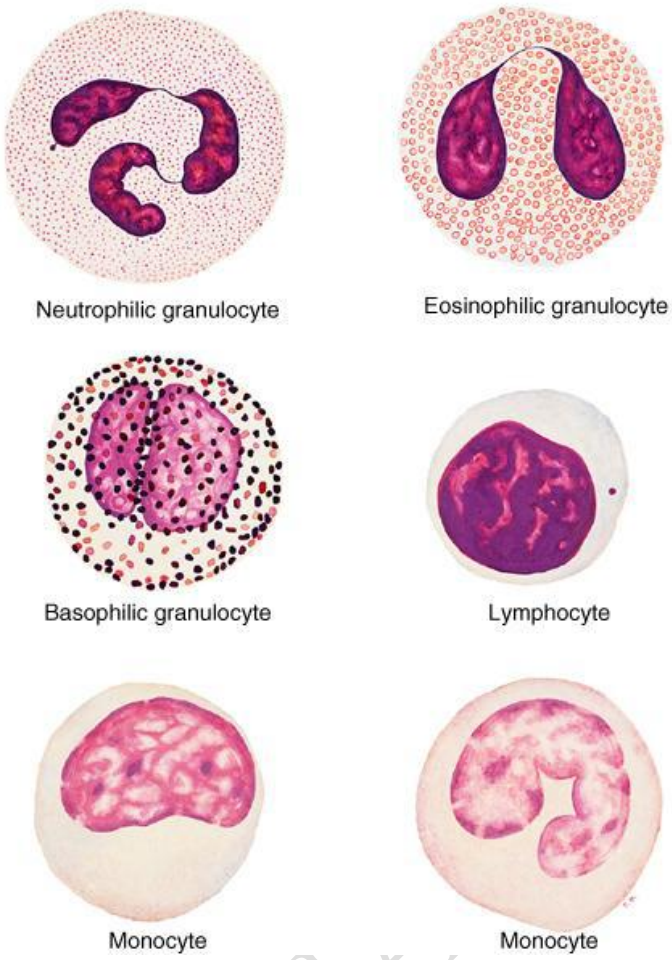
**Reticulocytosis** means increase reticulocyte count which indicate an increased demand for oxygen carrying capacity (eg, from loss of RBCs due to hemorrhage or anemia).




**B- White blood cells (WBC) or leucocytes**

- Leukocytes can be subdivided into granular leukocytes (neutrophils, basophils and eosiniphils) and non-granular leukocytes (monocytes and lymphocytes). In healthy individuals the total number of circulating leukocyte is about 4000- 10.000/$mm^3$. - Increase the leucocytes count above the upper range is called *leuocytosis*; which occurs in infection, inflammatory conditions, and in leukemia. - Whereas, decrease

the count below the lower range is called *leucopenia*; which occurs in excessive exposure to X-ray and after prolonged treatment with steroids.



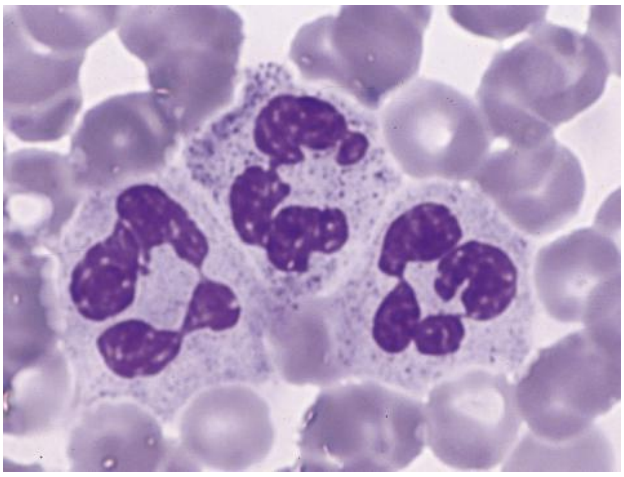

**Granular Leukocytes** - Granular leukocytes are all approximately the same size (12-15 μm in diameter). - Their nuclei are lobulated and nucleoli cannot be seen.

The number of nuclear lobes varies according to cell type. - All granulocytes are motile. - The term granulocyte refers to the presence of granules in the cytoplasm of these cells. - The granules correspond to secretory vesicles and lysosomes. - Specific granules are the granules which are only found in one particular type of granulocytes.

**1- Neutrophils**

 Neutrophils (polymorphonuclear granulocytes): one of granular leucocytes that have a very characteristic nucleus. It is divided into 3-5 lobes, which are connected together by thin strands of chromatin. The number of lobes increases with cell age. Up to 7 lobes can be found in very old neutrophils (hypersegmented cells).

Barr body is a drumstick chromosome or condensed chromatin visible in about 3% peripheral blood of females.



**Neutrophilia:** Means increased number of neutrophils in circulation as in acute bacterial infection, tissue injury and malignancy.

**Neutropenia:** Means decreased number of neutrophils in circulation as in viral infection, chronic bacterial infection such as typhoid fever and tuberculosis.

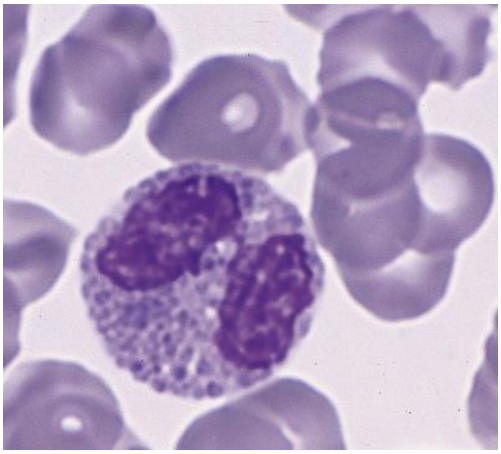
**Functions:**

- Their lifespan is only about one week inside blood vessels, and then pass to the connective tissue where they last for another 1-4 days. - Neutrophils play a central role in inflammatory processes. - Neutrophils are the first wave of cells invading infection sires.

- Receptors in their plasma membrane allow them to recognize foreign bodies, e.g. bacteria, and tissue debris, which begin to phagocytose and destroy. - The phagocytotic activity of neurophils is further stimulated if invading microorganisms are "tagged" with antibodies (or *opsonised*). - Dead neutrophils and tissue debris are the major components of pus.

**2- Eosinophils**

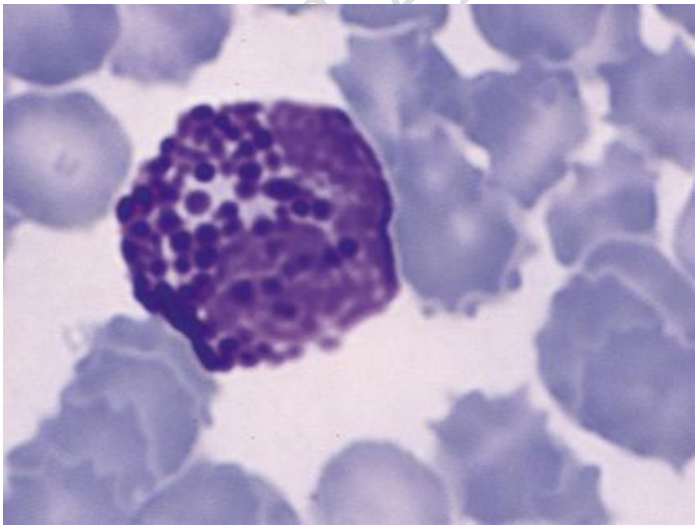
 Eosinophils are small 12-18μ in diameter, slightly larger than neutrophils. Eosinophils represent 1-6% of the total white cell count, and show diurnal variation (greatest in morning; least in afternoon). Their nuclei usually have two lobes that hidden by the numerous granules, which cover almost all of the cytoplasm. As the term "eosinophil" indicates, these granules are stained red or pink with eosin or other similar dyes.



Eosinophils contain some large rounded vesicles (~1 μm) in their cytoplasm. Life span: Eosinophils circulate in blood for 3 to 8 hours before migrating to connective tissue where they last for 10-12 days. Eosinophilia: Increase the number of eosinophils above the normal as in parasitic disease; and in allergic disorders.

**Functions**

- Contain receptors for IgE which stimulates the immune system. - Their granules contain histaminase and arylsufatase enzymes that break down histamine and leukotrienes. - Major Basic Protein, which can function as a cytotoxin, and involved in the response of the body against parasitic infections. - Produce eosinophil-derived-inhibitor, which inhibits mast cell degranulation.



Their specific granules (about 0.5 μm) appear quite dark in EM pictures. They contain heparin, histamine lysosomal enzymes and leukotrienes. Their cell

membrane contains receptors for IgE (produced in response to allergens); that triggers rapid exocytosis of granular contents (degranulation).

**Functions**

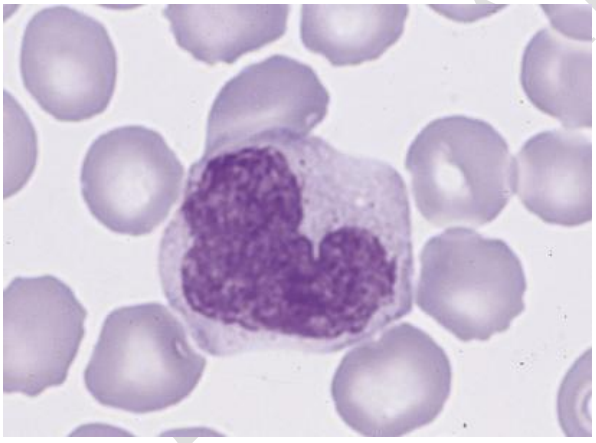
- Heparin and histamine are vasoactive substances, dilate the blood vessels, make vessel - walls more permeable and prevent blood coagulation. - They facilitate the access of lymphocytes and other antibodies to the site of infection.

**granular leukocytes**

**1- Monocytes**

 Monocytes are large cells, 12-18μm in diameter; represent 2-10 % of the differential cell count.

 Monocytes are highly motile and phagocytic cells; i.e. they are the precursor of tissue phagocytes that migrate into tissues. Their nucleus less dense than lymphocytes; deeply indented, kidney or C-shaped. Their cytoplasm is pale grayish blue with small pink to purple stained lysosomal granules, and contain cytoplasmic vacuoles (frosted glass).



**Functions**

- Once monocytes enter the connective tissue they differentiate into macrophages that phagocytose microorganisms, tissue debris and the dead neutrophils.

- Monocytes also give rise to mononuclear phagocytic system: which include histiocytes; multinucleate giant cells; hepatic macrophages (Kupffer ) cells; microglia of CNS; macrophages (Langerhans cells) of skin; antigen-presenting cells (APCs) of lymphoid organs; and osteoclasts of bone. - Monocytosis: increase numbers of

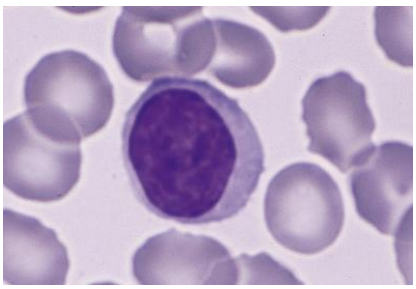
monocytes more than 8% as in lymphoma and monocytic leukemia; subacute bacterial endocarditis; some chronic infection and malaria.

**2- Lymphocytes**

Lymphocytes represent 20 to 40% of the differential white cell count. There are two structural types:

Small lymphocytes: ~5μm in diameter, and represent 3% of lymphocytes in peripheral blood. Most small lymphocytes in the blood stream belong to either the group of B-lymphocytes (~5%) or the group of T-lymphocytes (~90%).

Large lymphocytes: 9 to 15μm in diameter, possibly natural killer cells; possibly dividing lymphocytes.



Only blood lymphocyte capable of division outside the bone marrow.

**Functional types of lymphocytes:**

o B-lymphocytes: responsible for humoral immune response and produce antibodies.

o T- lymphocytes: responsible for cell mediated immune response.

o T- helper lymphocytes

o T- suppressor lymphocytes

o T- memory lymphocytes

o Cytotoxic T- lymphocytes (Killer cells)

o Natural killer lymphocytes

**Functions**

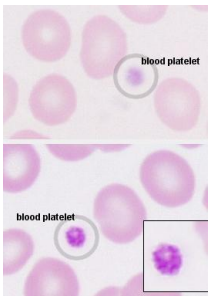
- Upon exposure to antigens B-lymphocytes differentiate into antibody producing plasma cells that produce antibodies which directed against foreign antigen. - T-

lymphocytes represent the "cellular arm" of the immune response (cytotoxic T cells) and may attack foreign cells, cancer cells and cells infected by e.g. a virus. - Lymphocytosis: increased numbers above the normal as in viral infection, chronic bacterial infection such as typhoid fever and tuberculosis; lymphoma and lymphocytic leukemia. - Lymphopenia: decrease the number of lymphocytes less than 20% as in AIDS, and in aplastic anemia.

### C- Blood Platelets (Thrombocytes)

Blood platelets or thromhacytes, are the smallest formed elements in the blood.

They are cytoplasmic fragments of very large thrombocyte (megakaryocytes) that are found in the bone marrow. Their number is 150,000 - 400,000/mm³, with a lifespan of about 8 days, and appear in clumps in blood smears.




They are rounded or oval, biconvex discs, 1.5 to 3.5µm in diameter.

 Platelets have an important physical role in plugging wounds, and they contribute to the cascade of molecular interactions among the various clotting factors dissolved in the plasma.

**The Clot and Serum:** Clotted blood consists of 2 parts:
of the clot, or thrombus, which includes the formed elements and some of the proteins dissolved in the plasma, of the serum, a clear yellow liquid that is similar to plasma except that it lacks fibrinogen and contains more serotonin.

**The Role of Platelets:**

 **Primary aggregation.** Platelets in the damaged region attach to collagen revealed by the discontinuity in the vessel wall, forming a platelet plug.

 **Secondary aggregation**. Platelets in the plug release the contents of their alpha and delta granules. This release of serotonin explains the higher concentration of

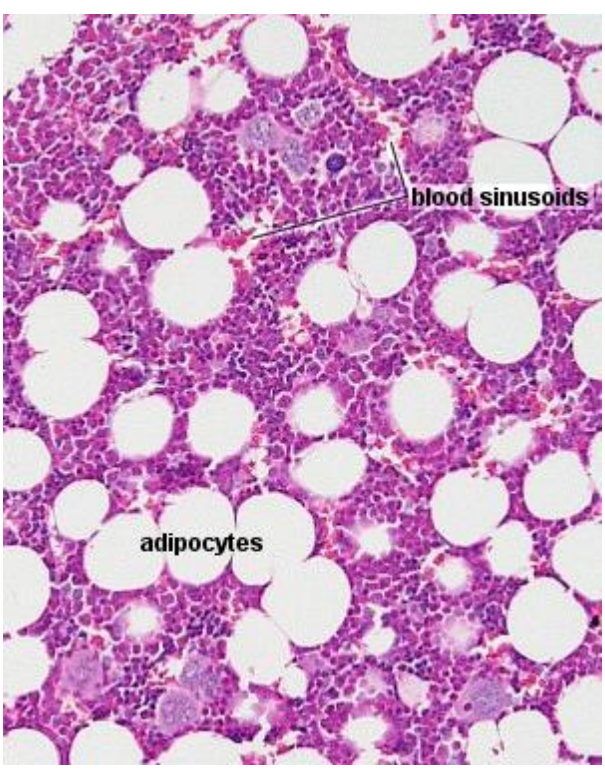
serotonin in serum than in plasma. Serotonin, a vasoconstrictor, restricts blood flow to the damaged area by causing contraction of vascular smooth muscle.

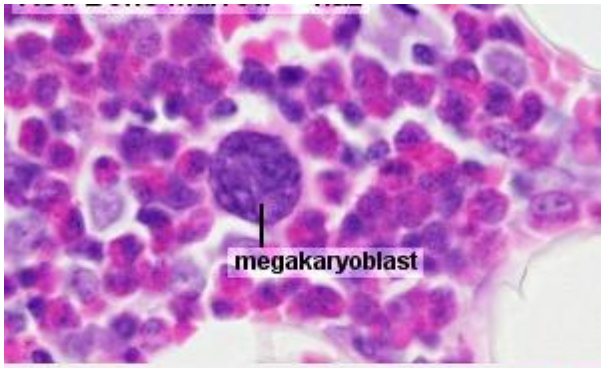
 **Blood coagulation.** Platelets release fibrinogen in addition to that normally found in the plasma. The fibrinogen is converted by the clotting factor cascade into fibrin, which forms a dense fibrous mat to which more platelets and other blood cells attach, forming a clot and plugging the opening in the blood vessel wall.

**Clot Retraction:** The clot (thrombus) initially bulges into the vessel lumen, but later it contracts and condenses through the interactions of thrombosthenin (a contractile protein) and platelet actin, myosin, and ATP. **Clot Removal:** As the vessel wall heals and the protection afforded by the clot is no longer needed, the clot is removed by the enzyme plasmin, Plasmin is formed by the action of plasminogen activators (from endothelial cells) on the plasma proenzyme plasminogen (from the liver). Enzymes released by the lambda granules (lysosomes) of the platelets also aid in clot digestion.

**Haemopoiesis:**
During foetal development, the formation of blood cells (*haemopoiesis*) commences in wall of the yolk sac. After the second month of foetal development, the liver, and the spleen become the dominant sites of haemopoiesis. From the 6th month, and dominating from the 7th month onwards, the formation of blood cells occurs in bone marrow, which is the major site of formation blood cells in normal adult man.

**Bone marrow:** Functionally and histologically, there are two types of bone marrow; yellow and red bone marrow. Yellow bone marrow, which harbours mainly adipocytes, dominates in the hollow of the diaphysis of adult long bones. Haemopoiesis occurs in red bone marrow, which is typically found between the trabeculae of spongy bone in the epiphysis of adult long bones. Both age and demands on haemopoiesis may affect the relative amounts of red and yellow bone marrow. Haemopoietic cells surround the vascular sinusoids and are supported by reticular connective tissue. In addition to the endothelial cells of the sinusoids and the reticulocytes of the connective tissue, macrophages are frequent in red bone marrow.


blood sinusoids
adipocytes


megakaryoblast


megakaryocyte

# Circulatory System

The circulatory system transports various substances, such as nutrients, gases and hormones, to various organs and tissues of the body and collects metabolic wastes from them.

## Components Of The Circulatory System

- The circulatory system is subdivided into two major components:

(a) The blood vascular system
(b) The lymph vascular system

- The components of the blood vascular system are blood vessels and heart, while the components of the lymph vascular system are lymphatic capillaries and ducts. Small vessels in the tissues and organs constitute microcirculation, which includes arterioles, venules, capillaries and lymphatic capillaries.

## Blood Vessels

- Blood vessels are classified into two groups: arterial and venous systems. The arterial system transports blood away from the heart to the various organs and tissues of the body. It includes arteries, arterioles and capillaries. The venous system returns blood to the heart from the various organs and tissues of the body. It includes venules and veins.

## Basic Structure Of Blood Vessels

- Histologically, the wall of the blood vessels is composed of three coats or tunics: tunica intima, tunica media and tunica adventitia ( from inside to outside) .
- The thickness of these walls, chief y of the media and adventitia, varies depending on the type of the blood vessel.

## Tunica Intima

- Tunica intima is the innermost layer. It consists of endothelium ( acing the lumen of the blood vessel), subendothelial connective tissue and internal elastic lamina . The endothelium consists of simple squamous epithelium; the endothelial cells (squamous cells) rest on a basal lamina.

## Tunica Media

●Tunica media is the middle layer .It consists of concentric layers of smooth muscles and elastic and collagen fibres. There are several layers of perforated sheets of elastin. In between these sheets, there are smooth muscles and collagen fibres.

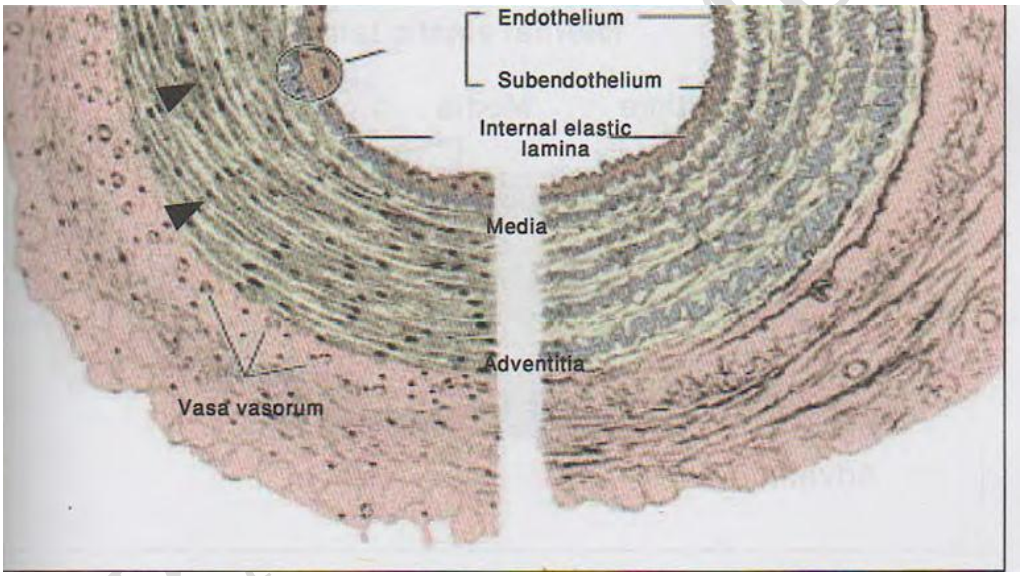
●Tunica media is thicker in arteries than in veins of similar size. In arteries, it has relatively more smooth muscle and elastic fibres than in a vein of comparable size.

● Contraction and relaxation of the smooth muscles is under the control of the autonomic nervous system. These smooth muscles communicate with each other through gap junctions.

● In the arteries, the media is separated from adventitia by external elastic lamina. External elastic lamina is similar to internal elastic lamina, except that the former is thinner than the latter.

## Tunica Adventitia

● Tunica adventitia is the outermost layer . It consists of connective tissue, chiefly collagen fibers. It also contains some elastic fibers.




## Arteries

● Arteries carry blood away from the heart to various tissues and organs.

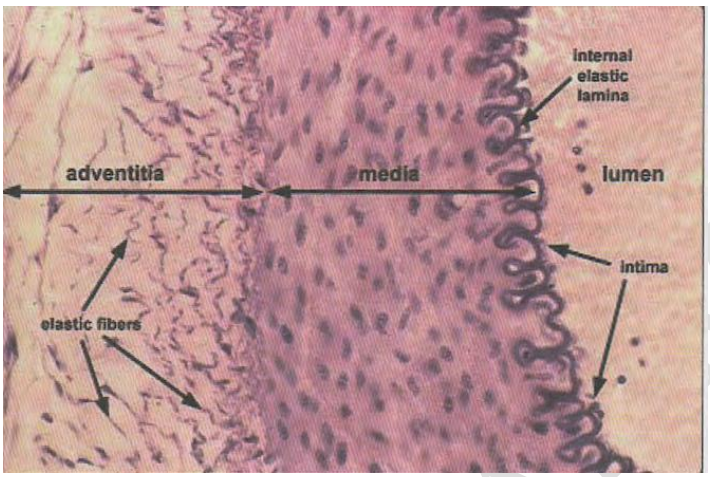
● As mentioned previously, tunica media of an artery is relatively more thick, having more smooth muscle and elastic fibers than a vein of comparable size. The arterial system consists of elastic and muscular arteries, arterioles and capillaries. Large arteries are elastic arteries, and tunica media of these arteries has more elastic fibers and less smooth muscles as compared to muscular arteries. Medium-sized arteries are muscular arteries with diameters of 0.5–10 mm. Tunica media of these arteries has more smooth muscles and less elastic fibers.

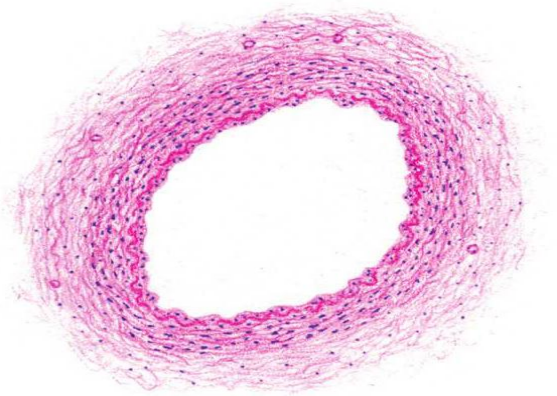
## Elastic Artery

● Elastic arteries are also called large arteries or conducting arteries. Their intimal layer consists of endothelium, subendothelial connective tissue and internal elastic lamina. However, the internal elastic lamina cannot be distinguished due to the presence of a large component of elastic tissue.

## Muscular Artery

● Muscular arteries are also called medium-sized arteries or distributing arteries as they arise from the large elastic arteries and distribute blood to various tissues and organs. The intima is thin; however, a well-distinguished internal elastic lamina is seen .Tunica media is thick and has relatively more layers of smooth muscles



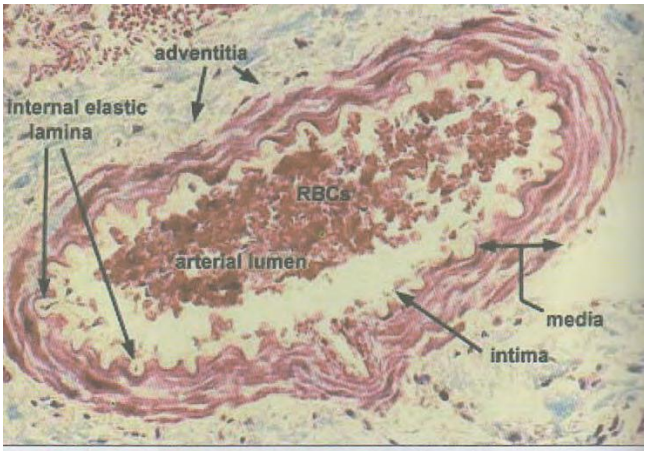



● . adventitia is also thin. Examples: Arteries of the limbs, brachial artery and femoral artery.

## Arteriole

● Arterioles arise from muscular arteries; these are thin-walled, small arteries with diameters of 20–500 μm. In arterioles, tunica intima is thin and subendothelial connective tissue is absent. Internal elastic lamina is thin and it gradually disappears. Tunica media consists of two or three layers of concentrically arranged smooth muscles. As arterioles branch, layers of smooth muscle cells progressively decrease. Tunica adventitia is very thin.

Arterioles are the main regulators of peripheral vascular resistance. Contraction and relaxation of the smooth muscles present in the walls o the arterioles can alter the peripheral vascular resistance or blood pressure and the blood flow.




## Capillaries

● Capillaries are the smallest blood vessels. They are thin-walled blood vessels which form a network. One end of the network is continuous with the smallest arterioles and another end with the smallest venules. Capillaries are the site or exchange of gases, nutrients and metabolic wastes between the tissue and blood as these substances can pass through the thin walls of the capillaries.

● The capillary wall is formed by a single layer of endothelial cells and basal lamina. Pericytes, the contractile cells wrapped around the capillaries outside the basal lamina, can be seen occasionally. According to the appearance of the wall of the capillaries under electron microscope, capillaries are of three types: continuous, fenestrated and sinusoidal.

● Continuous and fenestrated capillaries have diameters of 6–10 μm. Sinusoidal capillaries are larger than continuous and fenestrated capillaries; they have diameters of 30–40 μm.

## Continuous Capillaries

● Endothelial cells and basal lamina are continuous without any fenestrations. Such capillaries are present in muscles, nervous tissues, etc.

## Fenestrated Capillaries

● Endothelial cells have fenestrations, 70–90 nm in diameter, through which interstitial fluid or the components of blood can pass.

Fenestrations in endothelial cells are covered by a thin membrane known as diaphragm.

Basal lamina is continuous. These capillaries are present in endocrine glands, small intestine and glomeruli of kidneys. In glomeruli of kidneys, fenestrations in capillaries lack diaphragm.

## Sinusoidal Capillaries

● Sinusoidal capillaries are large capillaries with irregular shape. Endothelial cells are fenestrated. Basal lamina is discontinuous. These capillaries are present in large numbers in red bone marrow, liver and spleen.

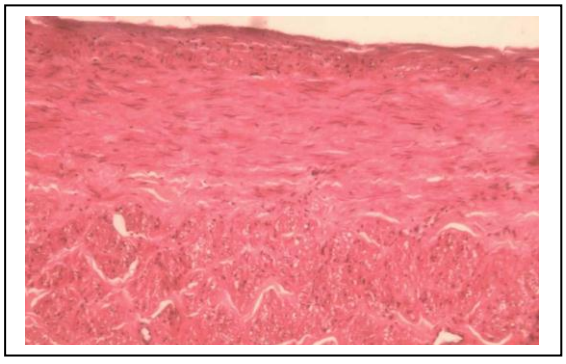
## Veins

● Veins carry blood from the capillaries to the heart. The venous system includes venules and small-, medium- and large-sized veins. The postcapillary venules begin at the venous end of the capillary plexus and drain into large muscular venules.

The large muscular venules drain into small-sized veins. The wall of a vein is thinner and has relatively less smooth muscle and elastic fibres than an artery of comparable size. Unlike arteries, in which tunica media is thick and most prominent, in veins tunica adventitia is thick and most prominent. The lumen of veins is collapsed. In general, veins have valves which help to maintain unidirectional f low of blood. Contraction of skeletal muscles surrounding the veins in the limbs and negative intrathoracic pressure created during inspiration help in venous circulation of the blood.

## Large-Sized Vein

● Veins with a diameter o 1 cm or more are large-sized veins. Internal elastic lamina is poorly defined

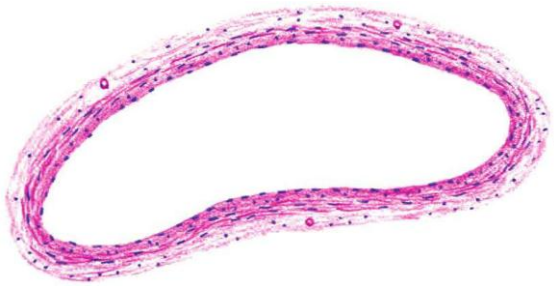


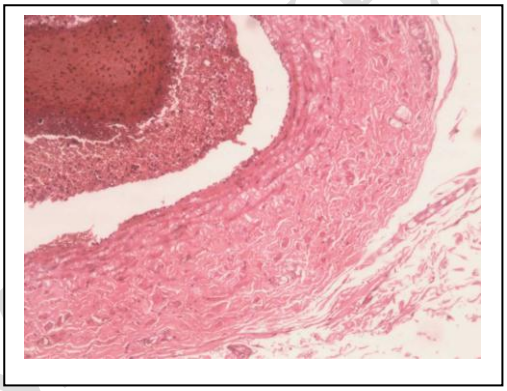
Tunica media is thin and has less smooth muscle. Tunica adventitia is well developed and is the thickest layer. Bundles of longitudinally arranged smooth muscles are present in tunica adventitia. Examples: Superior vena cava and in ferior vena cava.

## Medium-Sized Vein

Medium-sized veins have a diameter o 1–10 mm.

All three layers are thinner than the corresponding layers in a large vein. Internal elastic lamina is poorly defyned. Tunica media is less muscular .Tunica adventitia is well developed. Examples: Femoral vein and superior mesenteric vein.





## Small-Sized Vein

- Small-sized veins have a diameter o 0.1–1 mm. They are similar to medium-sized veins. Their wall is thin and diameter is small.

## Venules

- Capillaries drain into post capillary venules, and post capillary venules drain into large muscular venules. The diameter of post capillary venules is 10–40 μm and that of large muscular venules is 40–100 μm. Venules are important sites or exchange of metabolites. The smallest venules have tunica intima and adventitia. As the size of venules increases, smooth muscles appear and orm tunica media.

## Lymphatic Vascular System

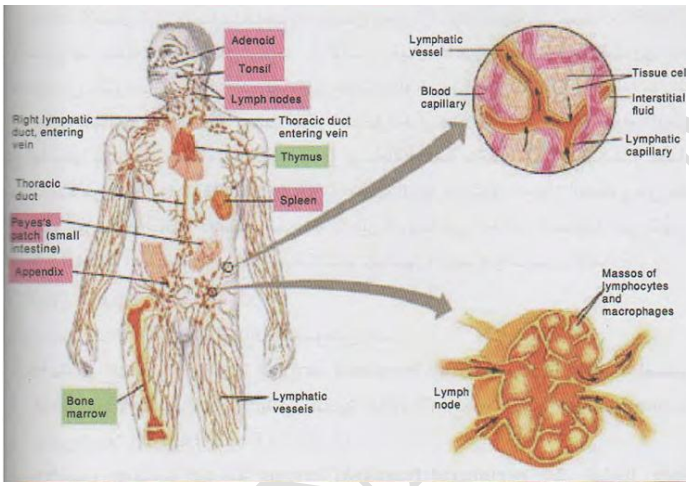
- In tissues, some plasma leaks out of the capillaries. A part of this is taken up at the venous end of the capillaries; the remaining fluid is called lymph, which is drained by lymphatic vessels. From lymphatic vessels, the lymph finally enters the systemic circulation through the thoracic duct.
- Lymph nodes are present along the course of lymphatic ducts to filter the lymph.
- Lymphatics are present in all the tissues of the body except the central nervous system and bone marrow. Basic structure of these vessels is similar to blood vessels.

*Theoretical Of Histology*

*Lecture …..3*

# The Lymphoid System

- The lymphatic system is vital to the defense mechanism against infectious agents. The cells which deal with these agents arose, developed, matured, and/or stored in lymphatic tissues. The lymphatic vessels and lymphoid organs are closely associated with the cardiovascular system. Lymph itself is a clear and slightly yellowish fluid derived from blood, and contains white blood cells (mainly lymphocytes). Lymph starts as blood fluid that passes through the tissue spaces and drained back by thin vein like lymphatic vessels, and then re-enter the venous circulation. There are lymphoid cells in most tissues of the body arranged either loosely as aggregations, formed into encapsulated structures such as lymph nodes, or freely mobile as individual




## Cells Of Lymphoid System

Lymphocytes are the principle cells of the immune system. Macrophages and reticular cells are also present.

### Lymphocytes

- All lymphocytes originate in the bone marrow. They are present in blood, lymph, tissue spaces and lymphoid tissues.
- There are three types of lymphocytes:

(a) T lymphocytes

(b) B lymphocytes

(c) Natural killer (NK) cells

*T Lymphocyte s (T Cells)*

● lymphocytes are responsible or cell-mediated immunity. They are produced in the bone marrow and mature in thymus . These cells have receptors ( cell receptor [ CR]) to recognise the specific antigen. Based on the types of receptor present, lymphocytes are classified into CR1 and CR2.

● These receptors recognise the antigen that is bound to the cell membrane proteins called major histocompatibility complex (MHC) molecules. Recognition of the antigen bound to MHC molecule on a cell by cells triggers the proliferation and differentiation of T cells into effectors and memory T cells.

(a) Effector T cells are of three subtypes: helper T cells, cytotoxic T cells and suppressor T cells.

(i) Helper T cells (TH cells): These cells are the key regulators, and they assist almost all the other cells in immunological processes, including maturation of B cells into plasma cells, other subtypes of T lymphocytes and macrophages.

(ii) Cytotoxic T cells (TC cells): They kill virally infected cells and tumour cells.

(iii) Suppressor T cells: These cells regulate the immune response by suppressing the helper cells.

(b) Memory T cells: These cells persist or a long time after an infection has cleared. If a similar infection occurs again, these cells proliferate more rapidly and mount a faster and stronger immune response.

*B Lymphocyt e s (B Ce lls)*

● B lymphocytes originate and mature in the bone marrow.

● They are responsible or humoral immunity. These cells also have antigen-specific receptors on their surface; these receptors are immunoglobulin D (IgD) and M (IgM).

● Once activated, these cells diferentiate into plasma cells, and a few cells become memory cells.

● Plasma cells synthesise and secrete antibodies.

● Memory cells help in aster immune response during subsequent exposure to the same antigen (secondary response).

*Natural Killer (NK) Cells*

● NK cells are another variety of lymphocytes. They are large lymphocytes with granular cytoplasm. They kill tumour cells and virus-infected cells. They destroy antibody-bound target cells, and this process is known as antibody-dependent cellular cytotoxicity (ADCC).

## Macrophages

● Macrophages are derived from monocytes. They function in humoral immunity as well as cellular immunity. These cells phagocytose the antigen, process them and present them to cells.

## Reticular Cells

● In spleen, lymph node and tonsils, the structural framework is made up of a three-dimensional network of reticular f ibres, which are produced by reticular cells. These networks of reticular f fibers support lymphocytes, macrophages and other cells of the lymphoid tissue. The reticular cells of spleen, lymph node and tonsils are derived from mesoderm, whereas the reticular cells of thymus (described under 'Thymus') are endodermal in origin.

## Lymphoid Nodules (Or Follicles)

● Lymphocytes are organised into spherical masses in all the lymphoid organs except thymus. These spherical masses are referred to as lymphoid nodules. The lymphoid nodule is clearly delineated from the surrounding tissue. There are two types of lymphoid nodules: primary and secondary.

## Primary Nodules

● Primary nodules are uniform in appearance. They are present before birth.

● Secondary nodules become secondary nodules after antigen exposure.

## Secondary Nodules

● Secondary nodules have a lightly stained central region, the germinal centre, surrounded by a peripheral dark region .

● The germinal centre is the site or proliferation of B lymphocytes.

● Secondary nodules appear after birth following antigen exposure.

## Lymphoid Organs

As mentioned earlier, large lymphoid aggregates form lymphoid organs. Lymph node, thymus, spleen and bone marrow are the lymphoid organs. Lymph node, thymus and spleen are covered with a capsule o dense connective tissue. Extensions of the capsule entering the substance of the organ are known as trabeculae. On histological examination, a lymphoid organ may show two distinct zones: a central zone known as the medulla and a peripheral zone known as the cortex; the cortex surrounds the medulla. However, spleen does not show this kind of arrangement; instead it has white and red pulp (described in 'Spleen').

● Lymphoid organs are classified as follows:

(a) Primary (or central)

(b) Secondary (or peripheral)

## Primary Lymphoid Organs

Thymus and bone marrow are the primary lymphoid organs . Primary lymphoid organs are the sites of lymphocyte proliferation and maturation. This proliferation and maturation does not depend on antigenic stimulation. Both T and B lymphocytes are produced in the bone marrow. lymphocytes leave the bone marrow and mature in the thymus. Lymphocytes produced in primary lymphoid organs migrate to secondarylymphoid organs.

## Secondary Lymphoid Organs

- Lymph node, spleen, Peyer's patches (in the small intestine), tonsils and appendix are the secondary lymphoid organs.

Numerous unencapsulated lymphoid Follicles in the mucous membranes (mucosa-associated lymphoid tissue [MAL ]), lining of the large intestines, in the upper airways and genital tract are also secondary lymphoid organs.

- Secondary lymphoid organs are the sites or interaction between mature lymphocytes and antigens to induce immune response.
- Lymphocytic proliferation in the secondary lymphoid organ is antigen dependent.

*Diffuse Lymphoid Tissue*

- Mucosa of gastrointestinal, respiratory and genitourinary tracts are constantly exposed to various antigens, and these surfaces are protected by the presence of unencapsulated collection of lymphocytes.

These lymphatic tissues constitute diffuse lymphoid tissue or MAL . In the gastrointestinal tract, they are called gut-associated lymphoid tissue (GAL ), and those in the respiratory tract are called bronchus-associated lymphoid tissue (BAL ). These lymphoid tissues are non-capsulated aggregations of lymphoid cells present underneath the epithelium in the lamina propria as lymphoid nodules. GAL includes Peyer's patches of ileum, adenoids, lingual tonsils
(present in the posterior one-third of the tongue) and palatine tonsils. Tonsils are aggregates of lymphoid tissue present underneath the mucosa of the oral cavity and pharynx.

**Lymph nodes** The lymph node is the most organized of the lymphatic organs and are found along larger lymphatic vessels. They are bean shaped, with a depression on one side (hilum). Blood vessels enter and leave the lymph node at the hilum, whereas lymphatic vessels enter at the periphery, and exit at the hilum. The lymph nodes act as "filters" for lymph as it passes through. Lymph is pushed through from the periphery of the node to its center, and then continues on its way back to join the venous circulation.

**Structure of lymph nodes:** lymph nodes are formed of stroma and parenchyma

- Lymph nodes have a discrete **CT stroma** in the form of capsule which sends **trabeculae** deep into the volume of the organ. The capsule acts as an overall envelope for the node, and is composed of dense irregular collagen with a few elastic fibers. Between the trabeculae, there is a network of reticular fibers and reticular cells that form the framework of the lymph node. The meshes of this network are filled with lymphocytes, plasma cells and macrophages.

- **Lymph sinuses** are lymph spaces found in the cortex and medulla and are divided into subcapsular, cortical, and medullary lymph sinuses.

- **Parenchyma** of lymph nodes are formed of cortex and medulla

- **Cortex:** The cortex is further divided into outer cortex and deep or medullary cortex.

o **The outer cortex is formed of**

**Primary lymphoid nodules which** contain B-lymphocytes

**Secondary lymphoid nodules** which contain germinal center.

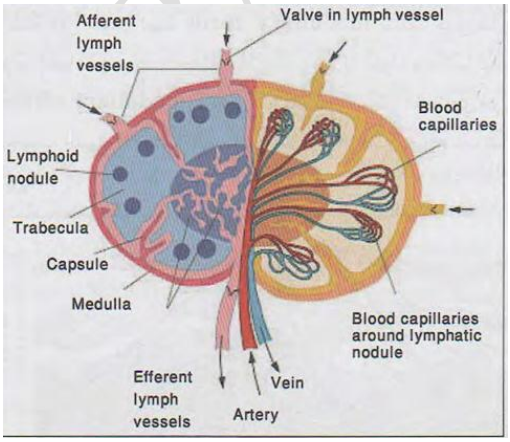
**Internodal lymphoid tissue** formed of diffuse lymphoid tissue.

o **The inner or deep cortex** which is formed of diffuse lymphoid tissue that extend towered the medulla to join medullary cords. The inner cortex is the site of T-lymphocytes and is called thymus dependent zone.

- **Medulla:** is formed of aggregation of lymphoid tissues that branch and anastomose to form medullary cords. These cords contain small lymphocytes, plasma cells, and macrophages.

**Function of lymph nodes:**

- Filtration of lymph ,Lymph nodes are the sites of antigen recognition.



**Spleen**

The spleen is a complex organ found in the abdominal cavity, carrying out filtration of particles and aged red cells from the blood, and responding to the presence of antigens. The spleen is really part of the circulatory system, but it is always described with the lymphatic organs because of the very large population of lymphocytes found in it. The spleen is a flaccid bag that serves as a storage site for blood.

**Structure of spleen:** Spleen is formed of stroma and parenchyma

- Spleen has a discrete **CT stroma** in the form of capsule which sends septa or trabeculae deep into the volume of the organ. The capsule is formed of collagen with some elastic fibers. - Between the trabeculae, there is a network of reticular fibers and reticular cells that form the framework of the spleen. The meshes of this network hold cells of splenic parenchyma.

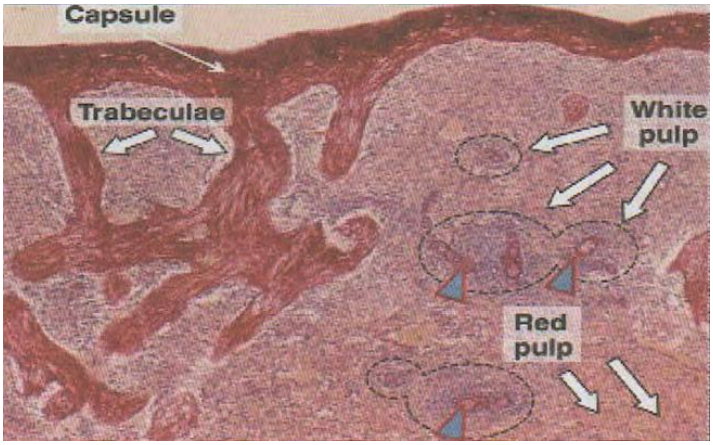
- **Parenchyma** of spleen is formed of splenic pulps (red pulps and white pulps).

o **Red pulp** consists of splenic cords separated by blood sinusoids. The red pulp is made up of a mesh of leaky sinusoids through which the red cells are squeezed. Many of the cells lining the sinusoids are phagocytic and are able to engulf debris from the blood or fragments of broken red cells.

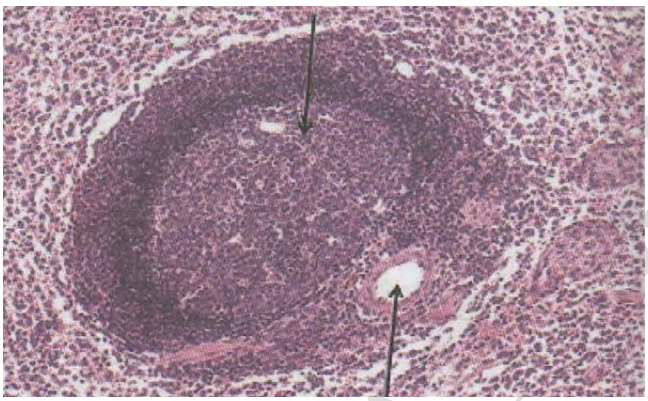
 **Splenic cords (Cords of Billroth):** Formed of loose meshwork of reticular fibers and reticular cells. The meshwork holds cellular elements of the parenchyma such as T-and B-lymphocytes, plasma cells, and blood cells.

 **Splenic sinusoids:** Vary in shape and size, and are lined by elongated endothelial cells. The sinusoidal wall is leaky, with incomplete basement membrane and lack muscular wall.

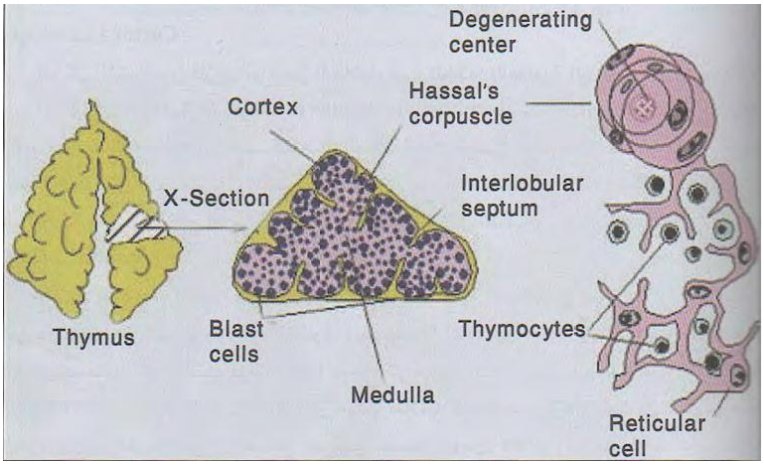
o **White pulp:** Splenic artery penetrates the hilum, branched to give trabecular arteries that leave the trabeculae and enter parenchyma, of spleen. The arteries then surrounded by sheath of lymphocytes called peri-arterial lymphatic sheath (PALS). The sheath contains mainly T-lymphocytes (thymus dependent zone), whereas the lymphoid follicles contain B-lymphocyts.




**Function of spleen:** - Filtration of blood from foreign materials. - Disposal of defective blood cells - Spleen is involved in recycling g of iron in the body. - Spleen acts as a reservoir of red blood cells. - Spleen acts as a hemopoietic organ during embryonic life. - Spleen has an immunological response; which contain large number of B- and T-lymphocytes that play an important role in defense mechanism.



**Thymus gland** The thymus is a primary lymphatic organ, present in the superior mediastinum and it is formed of two lobes. Its presence is required for the immune response to be fully established. The thymus gland reaches maturity during childhood and become rudimentary later on at puberty. Although the thymus is packed with lymphocytes, it does not filter lymph.




**Structure of thymus gland:** Thymus gland is formed of stroma and parenchyma

- Thymus is covered with thick connective tissue capsule that sends septa into the two lobes which dividing them into incomplete lobules. - Each lobule is divided into peripheral dark stained cortex and central pale stained medulla. The stroma is formed of reticuloepithelial network that hold lymphocytes.

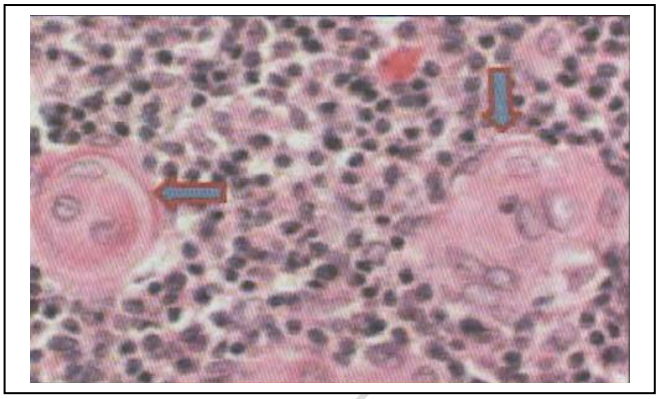
- **Cortex:**

 It is much darker than medulla because of the presence of large number of T-lymphocytes or thymocytes. Cortex is the site of T-lymphocytes maturation. The cortex contains also macrophage, and reticuloepithelial cells. Reticuloepithelium are stellate cells with pale nuclei and long cytoplasmic processes that join together and completely isolate the cortex from the medulla, and are divided into three types; type I, type II, and type III.

- **Medulla**

 It is much lighter than the cortex because of lymphocytes are lass abundant than the cortex, and contain large number of reticuloepithelial cells. It contains spherical acidophilic structure called thymic **or Hassell`s corpuscles**, which is found only in the medulla, and appears to be degenerating reticuloepithelial cells. It contains also non-fenestrated blood capillaries that form the thymic barriers.

The reticuloepithelial cells are responsible for the secretion of factors which promote the maturation of the T cells. As the cells mature they are pushed in towards the medulla, where they enter the blood vessels.

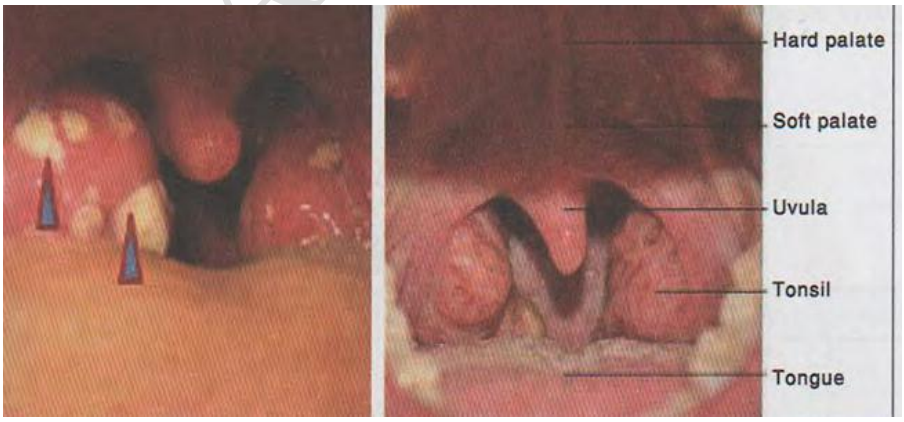


**Blood thymic barrier:** The blood thymus barrier, a continuous endothelium (non-fenestrated), prevents blood borne antigens from reaching the cortex. The capillaries of the medulla are fenestrated and allow T- cells to enter the circulation. **Function of the thymus gland:**

- Thymus gland is essential for T-lymphocyte maturation. Reticuloepithelial cells act as endocrine gland that secret different hormones required for T-cell maturation such as; thymosin, thymopoietin, thymolin, and thymic humoral factor.

**Diffuse lymphoid tissues Tonsils**

Tonsils are found in association with the oral cavity, and can easily be identified by their surface covering of folding mucous membrane (stratified squamous epithelium) with deep crypts between these folds, and lymphoid tissue filling the spaces between them. Tonsils are usually well encapsulated by CT on the side away from the oral cavity; germinal centers are normally present in the lymphoid follicles. Small mucus salivary glands are present below the lymphatic tissue and their ducts open onto the surface of the tonsil. The tonsils contain lymphocytes, macrophages and plasma cells.



**Aggregated Lymphatic Nodules of the Ileum and Appendix**

These structures are large enough to be visible with the naked eye as whitish areas on that side of the intestine opposite to its mesenteric attachment. These lymphoid follicles have germinal centers, the site of maturation and development of the B-lymphocytes.This cross section of the ileum nicely displays the aggregated lymphatic nodules (still universally called "Peyer's Patches" despite the official nomenclature rules against eponyms). These are the sites of maturation and development of B-lymphocytes. They're very prominent structures in most species. It's quite common to find germinal centers in them, though as the animal ages the number of germinal centers decreases. In cattle, for example, germinal centers are present at the time of birth and they decline relatively rapidly with age, as the pool of "memory" lymphocytes increases.

**The Concept of the GALT** Tonsils and Peyer's patches, along with all the diffuse lymphatic tissue in the gastrointestinal tract and respiratory system, collectively are labeled **G**ut **A**ssociated **L**ymphatic **T**issue (GALT) or **M**ucus **A**ssociated **L**ymphatic **T**issue (MALT).

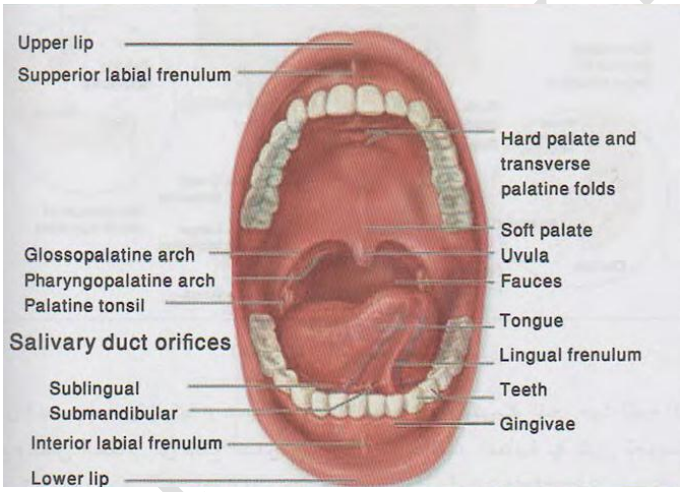
## The Digestive Tract

The gastrointestinal tract (GI ) is a long muscular tube. It begins with the oral cavity and ends in the anus.

- The parts o the GI are the oral cavity, the pharynx, the oesophagus, the stomach, the small intestine and the large intestine .
- The main function of the GI is digestion. Several glands help in bringing about this unction. These glands may be present either within the tract or outside it, but all o them open inside the tract.
- Different parts of the tract are specialised to perform different functions, and hence structural modicationsare seen in various parts of the GI .

**Oral cavity**

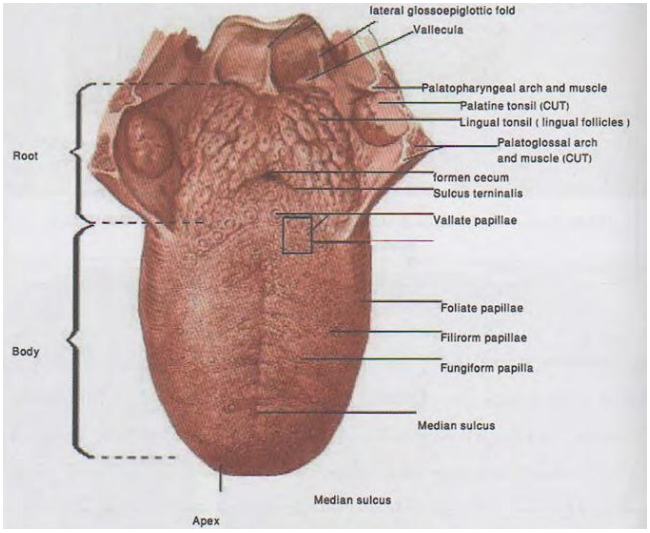
The oral cavity is formed in part by the lips and cheeks . In the oral cavity , this region lined by non -keratinized stratified squamous epithelial tissue.




Lips The core of the lips contain a large of striated muscles called orbicularis oris .In the upper part of the figure showed the thin skin epidermis and dermis {sweat glands, hair follicles with erector pili muscle (which is the smooth muscle attached to hair follicles ) and sebaceous glands .

The transition zone from the thin epidermis to the epithelium ,this zone characterized by rich blood vessels that giving the lip red color. In the lower part of the figure showed thick oral epithelium (nonkeratinized stratified epithelium ,the underling oral epithelium found loose connective tissue with numerous labial glands adipose tissue.

**Tongue**




The dorsal surface of the tongue is rough because of its characterized by numerous of mucosal projections called papillae in contrast the mucosa of the ventral surface is smooth . The core of the tongue concentrate of criss-crossing bundle of skeletal muscles in different directions (longitudinal , circular and oblique ).

Types of the tongue papillae:-

1- **Filiform papillae**: The most numerous and smallest papillae on the surface of the tongue

2- **Fungiform papillae**: Less numerous but larger and broader then the filiform papillae ,Mushroom like shape .

3- **Circuumvallate papillae**: are much larger than fungiform and filiform papillae and located in the posterior region of the tongue. Within the stratified of the lingual mucosa the taste buds embedded ,however they are distinguished by oval shape and elongated cells .

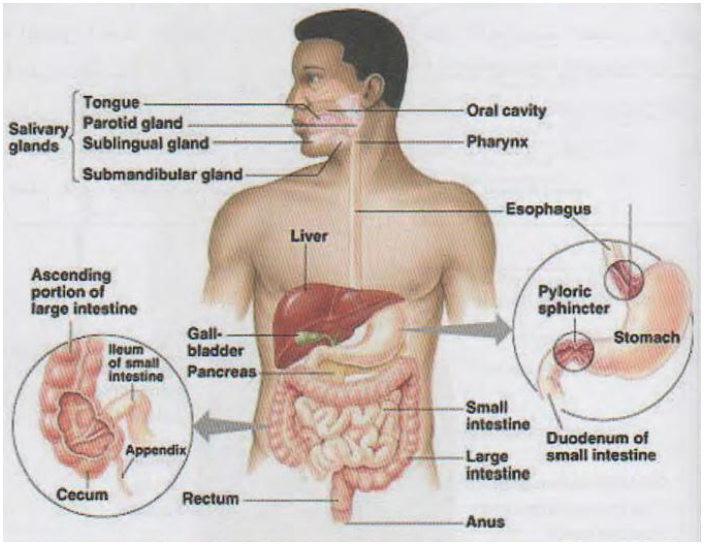
Taste buds :- Are barrel-shape structure ,located in the epithelium of the papillae with pore called taste pore several types of cells are found in the taste buds :-

a- **Sustentacular cells**: are elongated and exhibit a lighter cytoplasm with slender dark nucleus

b- **Taste (gustatory )cells** :-dark cytoplasm and more oval lighter nucleus

c- **basal cells** :- are located at the peripheral of the taste buds near the basement membrane .

**Gastrointestinal tract (Gut)**




The gastrointestinal tract is a long ,hollow tube that extends from the esophagus to the rectum . It includes the esophagus ,stomach ,small intestine (duodenum , jejunum and ileum) ,large intestine (colon) and rectum. The wall of the digestive tube exhibits four layers that show a basic histologic organization . these layers are the mucosa,Submucosa ,Muscularis externa and Serosa or adventitia. Because of the different functions of the digestive organs in the digestive process ,the morphology of these layers exhibits variations.

1- **Mucosa** :- Is the innermost layers of the digestive tube . It consists of the a covering epithelium and glands that extend into the underlying layer of loose connective tissue ,called the lamina propria . An inner circular and outer longitudinal layers of smooth muscles called the Muscularis mucosa ,from the outer boundary of the mucosa .

2- **Submucosa** :- Is located below the mucosa . It consists of dense irregular connective tissue . with numerous blood and lymph vessels and nerve plexus

3- **Muscularis externa** :- Is a thick ,smooth muscle layer that is located inferior to the Submucosa in circular and longitudinal
directions.

4- **Serosa or adventitia** :- Is a thin layer of loose connective tissuethat surrounded the visceral organs.

**Esophagus:**

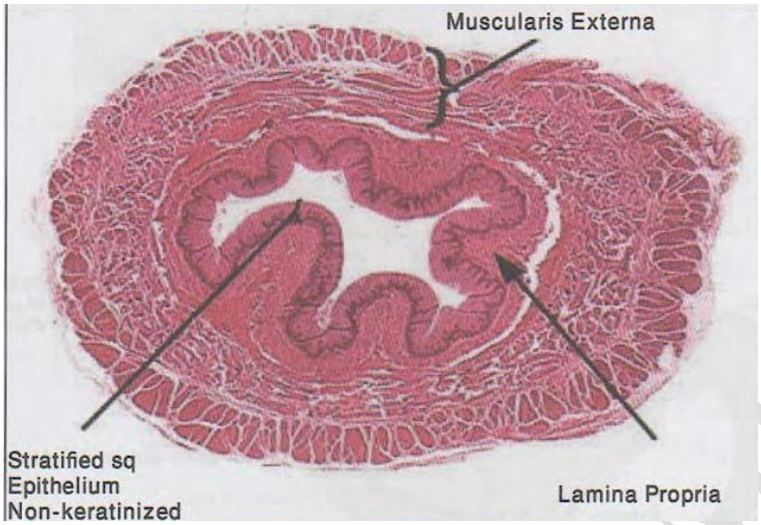
Four layers (mucosa ,Sub mucosa ,Muscularis externa and adventitia ) in the esophagus.

1- **Mucosa** :- Epithelium( Stratified squamous non keratinized epithelium). Lamina propria possesses esophageal cardiac glands that are mucus-secreting

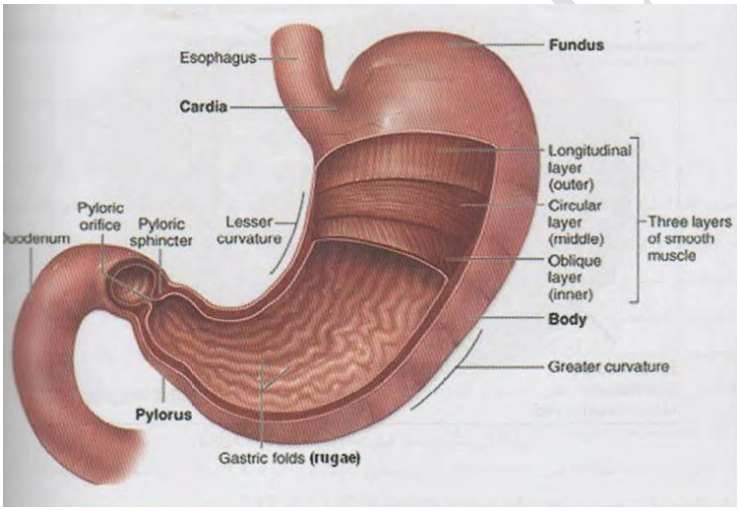
2- **Submucosa**

3- **Muscularis externa** is composed of striated muscle in the upper portion of the esophagus, skeletal, and smooth muscle in the middle portion, and smooth muscle in the lower portion.

4- **Adventitia**. Composed of loose connective tissue.




**Stomach**




**layers of the Stomach**

1- **Mucosa** :- Surface epithelium. Simple columnar epithelium facing the lumen is modified so that all cells secrete mucus, forming a sheet gland that protects , the stomach from its acidic environment.

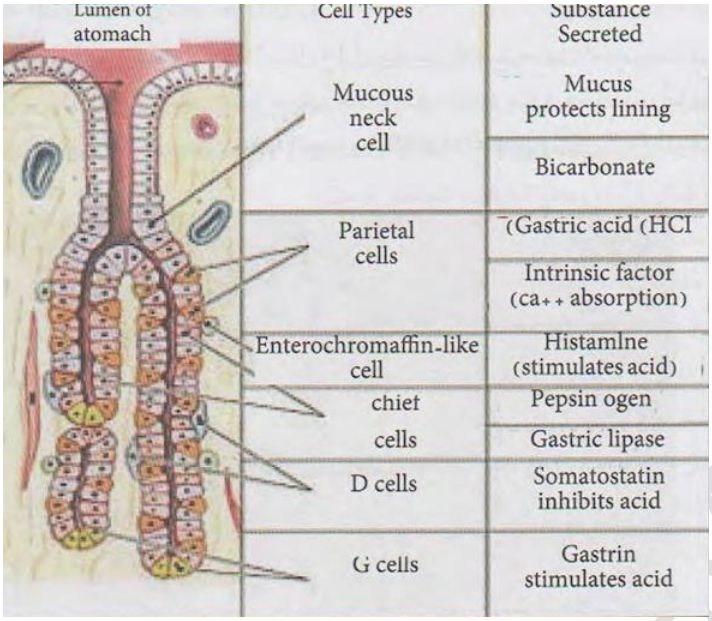
**Gastric pit**. A channel formed by the invagination of the surface epithelium into the underlying lamina propria;. Gastric glands:- Simple, branched tubular glands

2- **Submucasa**

3- **Muscularis externa**. Internal oblique layer. Middle circular layer .
Outer longitudinal layer

4- **Serosa**

Gastric glands of stomach




**The small intestine**

The small intestine is a large convoluted tube approximately 5-7 m in the length :- it is the largest section of the digestive tract . The small intestine extends from the junction with the stomach to join with the large intestine or colon . The small intestine divided into three parts :- the duodenum , jejunum and ileum

The mucosa of the small intestine exhibits specialized structural modifications that increase the cellular surface are for the absorption of nutrients and fluids the modifications includes:-

1. **The plicae** circulates are permanent , spiral folds or elevations
of the mucosa with Submucosa that extend into the intestinal
lumen

2**. Villi** are permanent ,finger –like projections of the lamina propria of the mucosa that extend into the intestinal lumen , they are covered by simple columnar epithelium , and contain lymphatic and blood capillaries and strand smooth muscles.

3. **Microvilli** are cytoplasmic extensions that cover the apices of the intestinal absorptive cells they are visible microscope as a striated (brush) bord

**Small intestine (dunenum)**

-Characterized by found numerous of duodenal glands in the Submucosa called (Bruuner s glands )and also in the lamina propria and in the Submucosa founds less numbers of lymphatic nodules .

- Muscularis externa characterized by the inner longitudinal and the outer circular smooth muscles.

**Small inteestine (jujenium)**

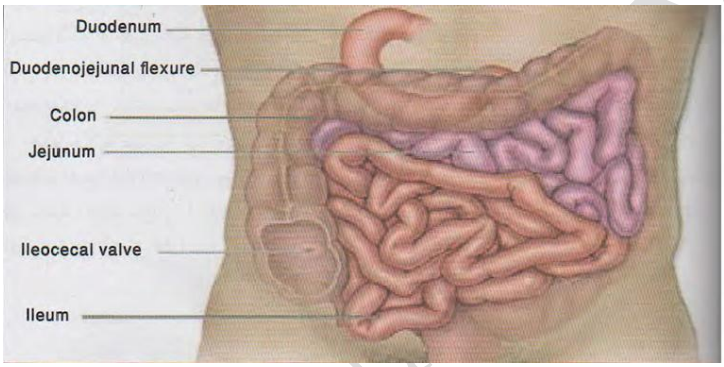
-Characterized by found the plica circularis (10), and few number of lymphatic nodules in the Submucosa(without duodenal glands ) .

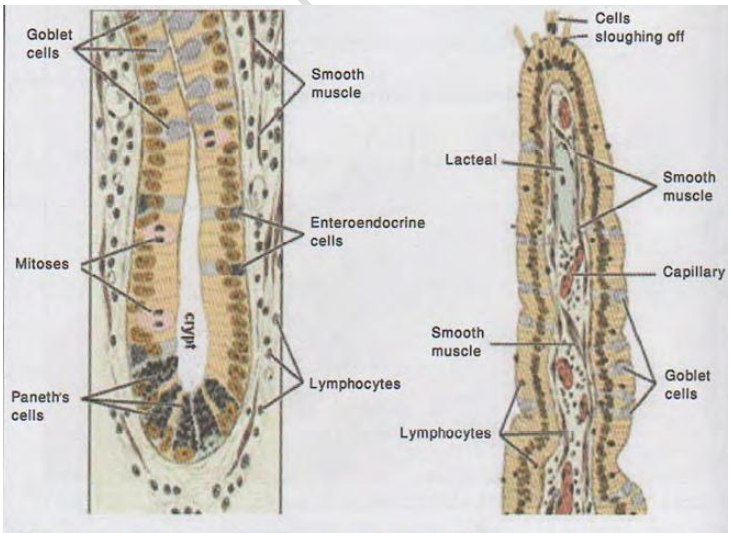
Muscularis externa characterized by inner circular and outer longitudinal smooth muscle.

**The small intestine (ileium)**

-Characterized by numerous of lymphoid nodules as a peyers patches in the Muscularis mucosa (Muscularis mucosa disrupted in the ileum

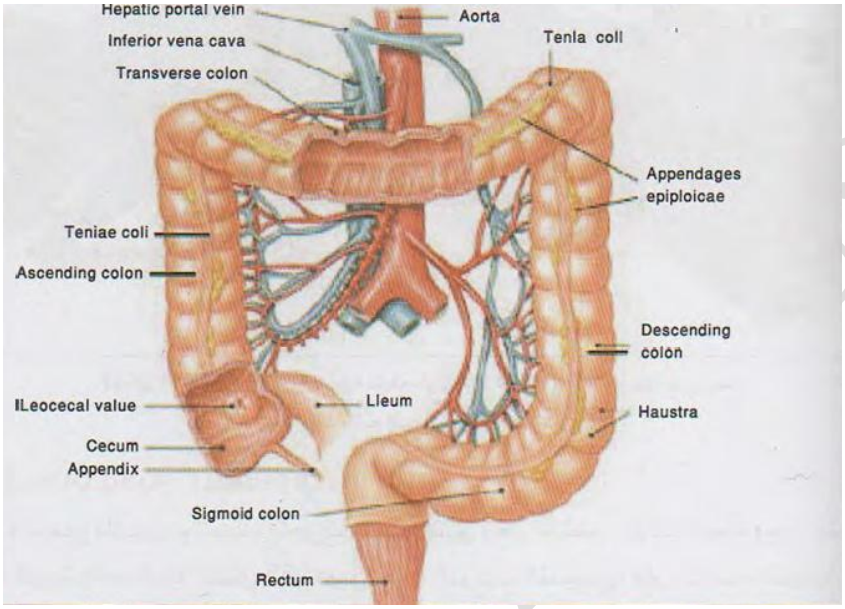
- Muscularis externa inner circular and the outer longitudinal smooth muscles.



**Large intestine(colon):-**

The colon dose not have Villi or plice circulares and found temporary folds .In the lamina propria and Submucosa of the colon are lymphatic nodules . The simple columnar epithelium contains are absorptive columnar cells and the mucous filled goblet cells , which increase in number toward the terminal end of the colon ..The lamina propria and Submucosa are filled with aggregation of the lymphoid cells and lymphatic nodules . Inner circular and outer longitudinal smooth muscles of the Muscularis externa



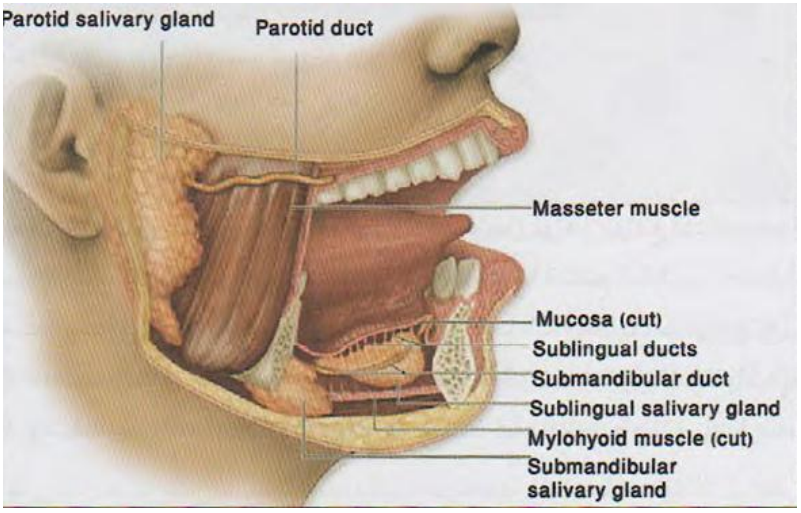

*Theortical of Histology*

*Lecture ….5*

## Organs Associated with The Digestive Tube

### Salivary Glands

Secretion of salivary glands is known as saliva; around 1 L of saliva is produced every day. Functions of saliva: These include lubricating the luminal surface of the upper aero digestive tract, moistening the food to help in deglutination and initiating digestion of carbohydrates by the enzyme salivary amylase present in it. Saliva also acts as a bactericidal due to the presence of lysozyme and immunoglobulin A.




## General Structure Of Major Salivary Glands

Basically, a salivary gland consists of stroma, parenchyma and a duct system which carries the secretions into the oral cavity.

### Stroma

The stroma consists of connective tissue capsule and septa. Numerous septa arise from the capsule and enter the parenchyma of the gland, dividing the gland into numerous lobules. These septa bring the blood vessels and nerves into the gland. Large ducts of the glands are also present in it.

### Parenchyma

Parenchyma has two components: the secretory part and myoepithelial cells.

*Secretory Part*

The secretory part consists of branched tubuloacinar glands, containing two types of acini (singular: acinus): mucous and serous .

A salivary gland may have only one type of acini or may have both. The salivary gland having both types of acini is known as mixed or seromucous gland.

**1. Serous acini**

- The lumen of these acini is small.
- The secretion of serous acini is watery.

**2. Mucous acini**

- Cells in these acini are tall with f at nuclei at their bases .
- The lumen of these acini is larger than that of serous acini.
- The secretion of mucous acini is thick.

## Major Salivary Glands

As mentioned earlier, there are three pairs of major salivary glands—the sublingual glands are located within the oral cavity, underneath the tongue, while the other two, parotid and submandibular, glands are situated outside the oral cavity.

## Parotid Gland

The parotid gland is a serous salivary gland .

## Sublingual Gland

The sublingual gland is a mucous salivary gland; however, it also has very few serous acini

## Submandibular Gland

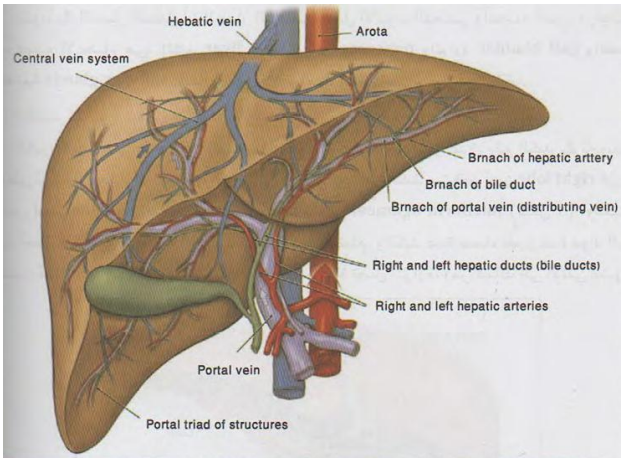
The submandibular gland is a mixed salivary gland, predominantly serous with a few mucous acini. Some of mucous acini are capped with serous cells arranged as a half moon; hence, they are called serous demilunes .

## Liver

The liver is the largest gland o the body. it consists of our lobes: right, le t, caudate and quadrate lobes. On the anterior surface right and le t lobes separated by aciform ligament can be seen, while on the posterior surf ace caudate and quadrate lobes are also present.

The hilum or porta hepatis is present between the caudate and quadrate lobes. Many structures pass (enter and leave the liver) through the hilum. Structures entering the liver are right and le t branches o the hepatic artery, portal vein and hepatic plexus o nerves, while structures leaving the liver are right and left hepatic ducts and lymphatics .

- Functions: These include synthesis of urea, formation and secretion of bile, detoxication of metabolic wastes as well as many drugs, storage of glycogen, metabolism of cholesterol and at, synthesis of plasma proteins and gluconeogenesis (i.e. conversion o lipids and amino acids into glucose)



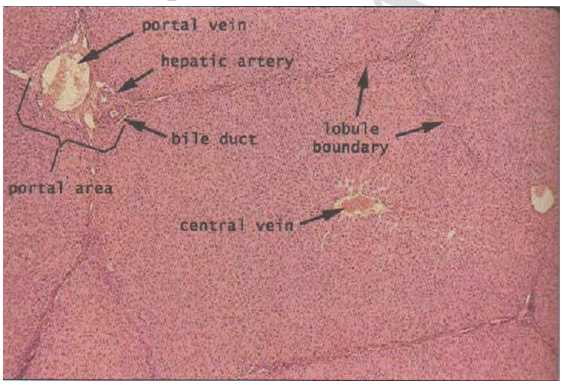

## Microscopic Structure

- The stroma of the liver consists of connective tissue capsule (Glisson's capsule).
- The parenchyma of the liver consists o chiefly the hepatocytes.

## Hepatic Sinusoids

As the blood passes through the sinusoids, which are present in between the plates, the hepatocytes exchange metabolites from the blood.

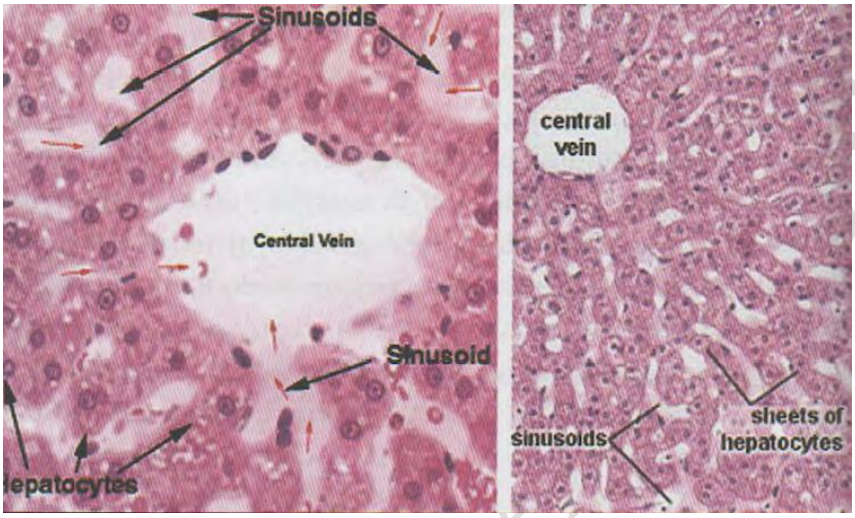
These sinusoids are lined by phagocytic cells, also called Kupffer cells, and endothelial cells These sinusoids are fenestrated. The lining endothelial cells are discontinuous and they lack basal lamina. There is a narrow space between the endothelial cells, lining the hepatic sinusoids, and the hepatocytes, and this space is called the space of Disse.




## Hepatic Acinus

- Hepatic acinus is another way of dividing the liver into parenchymal units. It is also the functional unit of the liver. of understand the concept o hepatic acinus, it is important to understand the blood supply of the liver. Blood supply of liver—this is as follows: –

The liver gets its blood supply from two sources—the hepatic artery and the portal vein. The hepatic artery brings oxygenated blood; it provides about 20–25% o the blood to the liver. The portal vein brings nutrient-rich blood from the intestine and breakdown products of haemoglobin from the spleen to the liver; it provides about 75–80% o the blood to the liver. – Both these vessels enter the liver through porta hepatis; lying within the connective tissue, they divide as the connective tissue divides in the liver parenchyma. – In the classical lobule, they are present at the angles of the lobule in the portal triad. – From the portal triad, blood is delivered into the hepatic sinusoids and from the sinusoids to the central vein .




## Pancreas

Pancreas is a retroperitoneal organ; it extends from the concavity of the duodenum to the hilum of the spleen. It consists of (from right to left) a head located within the concavity of the duodenum, a neck which is a constricted part, a body which forms the major bulk of the gland and a tail which is related to The pancreas has three components: stroma, parenchyma and a duct system. The parenchyma has exocrine and endocrine parts. The duct system carries the secretion of the exocrine part into the duodenum. the hilum of the spleen.

## Stroma

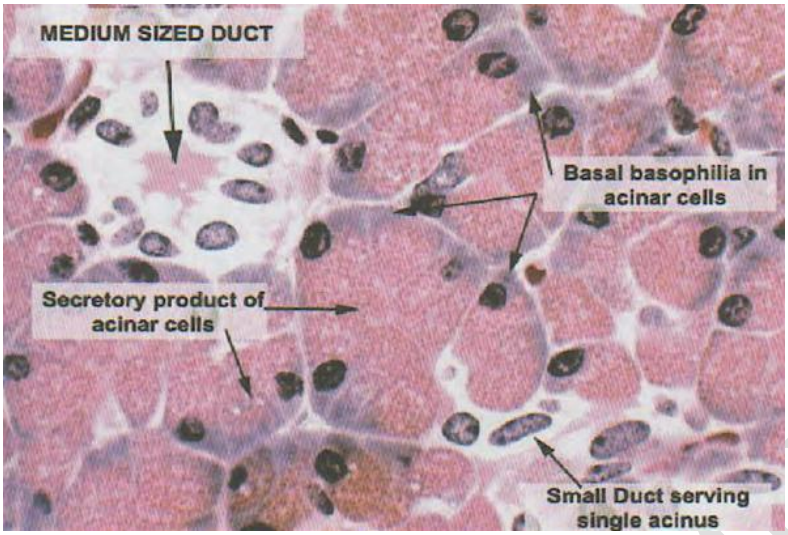
The gland is covered with a thin capsule of connective tissue. From this capsule numerous septa arise which divide the parenchyma of the gland into lobules

## Exocrine Part and Duct System

The exocrine part consists of compound acinar glands.

*Pancreatic Acini*

● The acini of pancreas resemble the acini of parotid glands and consist of a group of pyramid-shaped acinar cells arranged around a small lumen. Secretions of these cells drain into this lumen .




*Duct System*

The duct system begins within the acini; the initial part of the duct is known as intercalated duct. The part of the intercalated duct inside the acini is lined by centroacinar cells . These ducts drain into intercalated ducts which drain into intralobular ducts located within a lobule. Intralobular ducts drain into large interlobular ducts which are present in the connective tissue septum separating the adjacent lobules ,and finally, into the main pancreatic duct which opens into the second part of the duodenum along with the bile duct. Smaller ducts (intralobular) are lined by simple cuboidal epithelium and larger ducts (interlobular) by columnar epithelium.

**Endocrine Part**

● Islets of Langerhans constitute the endocrine part, and they are scattered throughout the exocrine part, most abundantly in the tail region. These islets consist of polyhedral cells, arranged in irregular cords .

In between the cords there are capillaries; secretions of the endocrine cells are drained into these capillaries. Islets of Langerhans have our types of cells: alpha, beta, delta and PP cells. Majority of the beta cells are located in the centre of the islets; alpha and delta cells are in the periphery and PP cells are found throughout the islets. These cells can be demonstrated by immunocytochemical method. (The microscopic structure of pancreas resembles parotid glands; look or islets of Langerhans.)

## Pancreatic Secretions

Secretions of both the exocrine and endocrine parts of pancreas are discussed below.

### Exocrine Part

The main components of the secretions of the exocrine part are fluid rich in bicarbonate ions and digestive enzymes. Bicarbonate ions make the secretions alkaline and they (along with bile juice) neutralise the acidic chyme. These secretions are under hormonal control, secretin and cholecystokinin being the principal hormones.

### Endocrine Part

Secretions of the endocrine part and their effects are mentioned in
Cell Types of Islets of Langerhans

## Gallbladder

The gallbladder is a blind sac, present at the inferior surface of the liver . The neck of the gallbladder is continuous with the cystic duct, which joins the common hepatic duct to form the common bile duct. The common bile duct opens into the second part of the duodenum. The gallbladder stores and concentrates bile.

### Microscopic Features

Microscopically, the wall of the gallbladder consists of three layers ( from lumen to outside):

(a) Mucosa
(b) Muscularis externa
(c) Adventitia and serosa

- There is no submucosa.

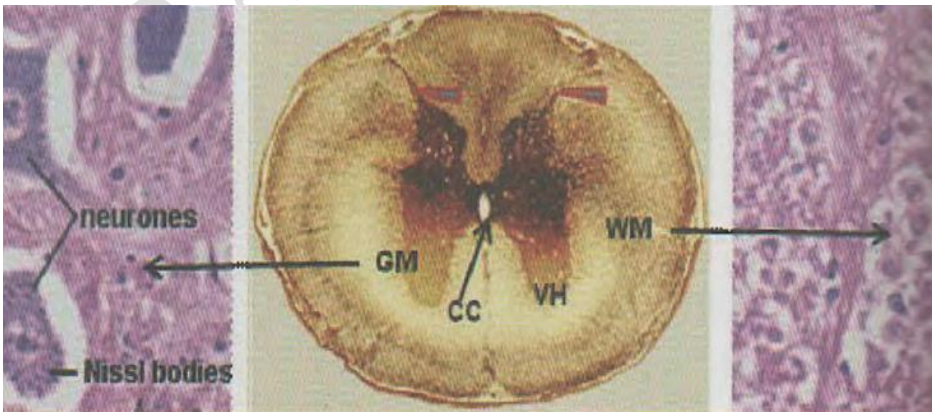
*Theortical of Histology*
*Lecture ….6*

# The Nervous System

- The central nervous system (CNS) consists of brain and spinal cord. The brain consists of (a) the cerebrum, which includes cerebral hemispheres and diencephalon, (b) the brain stem, which consists of medulla, pons and midbrain, and (c) the cerebellum.
- The entire CNS is surrounded by three membranes of connective tissue collectively known as the meninges ( from outside to inside)—dura mater, arachnoid mater and pia mater.
- Histologically, like peripheral nervous system, the CNS also consists of neurons and glial cells. On gross appearance, most o the CNS is composed of white matter and grey matter (posterior pituitary and pineal glands are part of CNS, but they lack white and grey matter. I a fresh specimen of brain or spinal cord is sliced, on the cut surface some parts appear white while some appear grey in colour; hence, they are known as white and grey matter respectively.
- White matter consists of axons of myelinated nerve fibres and glial cells. Afew unmyelinated axons are also present. It does not contain cell bodies of the neurons.
- Grey matter contains cell bodies of the neurons, dendrites and unmyelinated parts of the axons and glial cells.

## Spinal Cord

The spinal cord begins at the upper border of atlas vertebra, as a continuation of the medulla oblongata. It extends till the lower border of the first lumbar vertebra.



## Structural Organisation

● The spinal cord has a deep ventral median f]issure with a ventrolateral sulcus on both its sides. There is also a shallow dorsal median sulcus with a dorsolateral sulcus on both its sides. The dorsal roots of spinal nerves enter the spinal cord at the dorsolateral sulcus, while the ventral roots emerge through the ventrolateral sulcus.

● A cross-section of the spinal cord shows H-shaped grey matter in the centre, which is surrounded by white matter .

## Grey Matter

● The H-shaped grey matter consists of a pair of ventral and dorsal horns (or columns) and a central part which connects these horns. In thoracic segments of the spinal cord, a pair of lateral horns is also present. In the central part of the grey matter, there is a central canal lined by a single layer of columnar cell. T e central canal contains cerebrospinal fluid.

● Ventral horns of the grey matter are very prominent. They contain the cell bodies of the lower motor (multipolar) neurons ,and the axons of these neurons emerge from the ventrolateral sulcus and form the ventral roots of spinal nerves.

● Dorsal horns are thinner than ventral horns. They contain central fibres of the pseudounipolar cells of dorsal root ganglion and cell bodies of the second-order sensory neurons of pain and temperature pathway.

● Lateral horns are present only in thoracic segments. Cells of this region give rise to preganglionic fibres of the sympathetic nervous system.

## White Matter

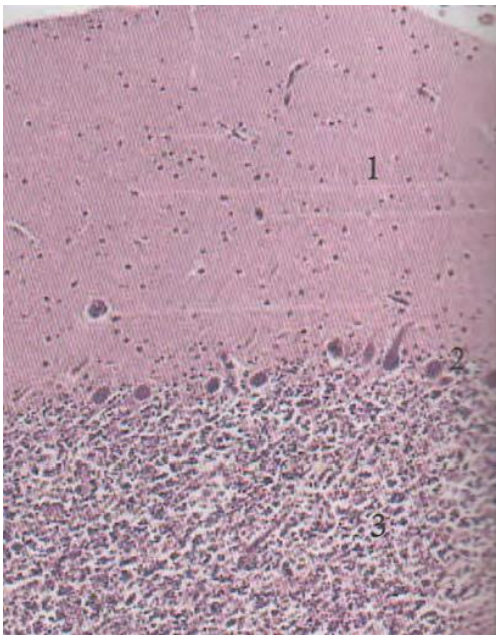
● The white matter consists of axons of ascending and descending tracts. It is subdivided into 3 pairs of columns—anterior, lateral and posterior columns . The anterior column lies between the ventral median ssure and the ventrolateral sulcus. The lateral column lies between the ventro lateral and dorsolateral sulci. The posterior column lies between the dorsal median sulcus and the dorso lateral sulcus.

## Coverings of Spinal Cord

● Coverings o spinal cord ( from outside to inside) are dura mater, arachnoid mater and pia mater.

## Cerebellum

● The cerebellum is a part of the hind brain, located in the in ratentorial compartment of the posterior cranial fossa. It plays an important role in coordination of voluntary movements and maintenance of the equilibrium and muscle tone.




## Neurons Of Cerebellar Cortex

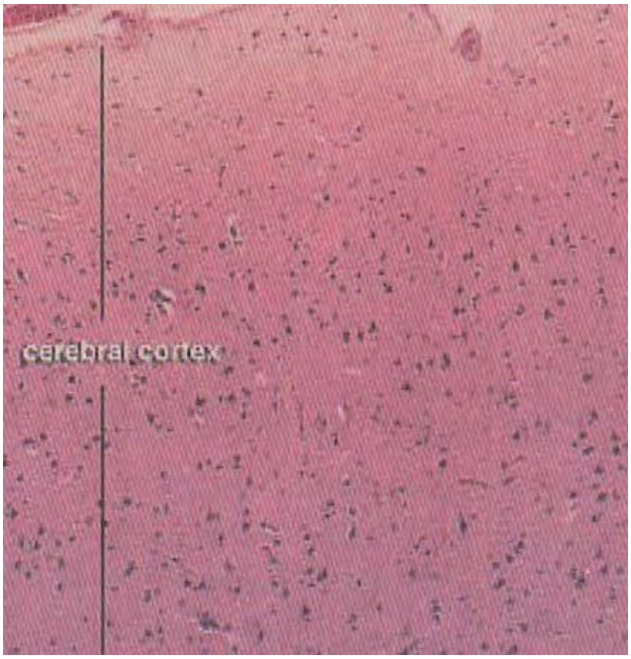
The cerebellar cortex has the following five types of neurons: stellate, basket, Purkinje, Golgi and granule cells. Purkinje cells are large neurons with flask-shaped cell bodies. The other cells of the cerebellar cortex are small-sized neurons. Except granule cells, which are excitatory, the rest of the neurons are all inhibitory. Silver-stained histological slides of the cerebellar cortex reveal morphological details of these neurons.

## Structural Organisation

Unlike the spinal cord, the cerebellum has a central core of white matter covered by grey matter. The cerebellar cortex shows numerous folds called folia .The cerebellar cortex consists of three layers: the outer molecular, middle Purkinje and inner granular layers .

## Cerebrum

- Cerebrum is the largest part of the brain. The two cerebral hemispheres are separated by a median longitudinal fissure. The surface of the cerebrum has numerous olds separated by fissures—the olds are called gyri and the fissures are called sulci. Each gyrus has a central core of white matter, which is covered by a thin layer of grey matter. This thin layer of grey matter is the cerebral cortex.




## Neurons Of The Cerebral Cortex

The cerebral cortex has the following five types of neurons: pyramidal cells, stellate cells, cells of Martinotti, horizontal cells of Cajal and fusiform cells. Morphological details of these neurons can be studied in silver-stained histological slides of the cerebral cortex.

## Structural Organisation

The cerebral cortex consists of six layers, and there are no sharp boundaries between these layers.

Six layers from superficial (towards the surface of the brain) to deep are as follows

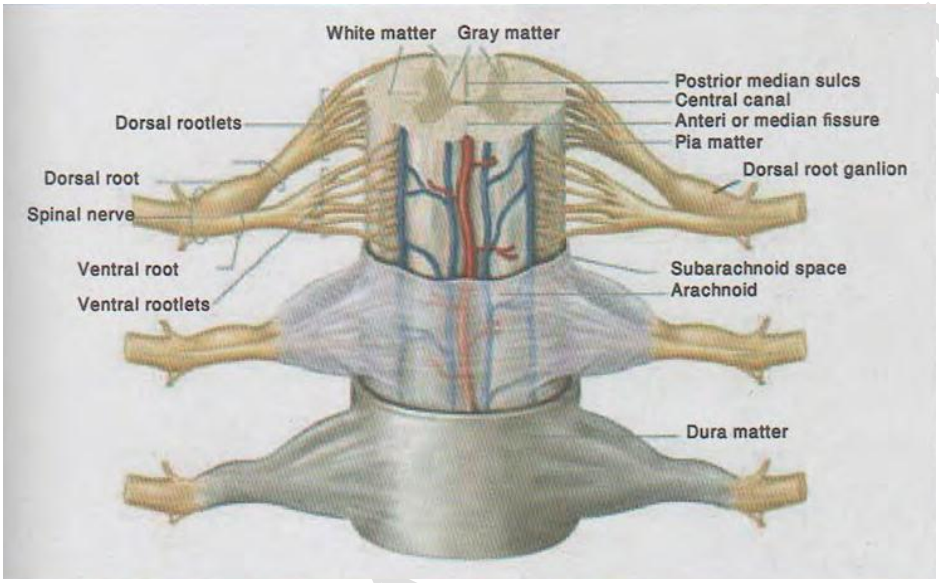
**1. Plexiform or molecular layer**
**2. Outer granular layer**
**3. Pyramidal cell layer**
**4. Inner granular layer**
**5. Ganglionic layer**
**6. Polymorphous or multiform cell layer**

## Meninges

- Meninges are three layers of connective tissue surrounding the CNS. From superff cial to deep, they are the dura mater, arachnoid mater and pia mater. Arachnoid mater and pia mater are collectively called leptomeninges . Between the dura mater and the arachnoid mater, there is a subdural space containing a small volume of serous fluid.
- Between the arachnoid mater and the pia mater, there is a cerebrospinal fluid–containing space, the subarachnoid space.

## Dura Mater

- The dura mater is composed of dense connective tissue .
- This is the outermost layer. In the brain, it further consists of two layers—outer endosteal and inner meningeal. The endosteal layer serves as the periosteum of the skull bones. As it continues down wards, this layer gets attached to the margin of oramen magnum and thus it does not form a covering around the spinal cord. The meningeal layer continues in the spinal cord. In the spinal cord, dura consists of the meningeal layer only. It is separated from the periosteum of the vertebral canal by epidural space.




## Arachnoid Mater

- The arachnoid mater is a layer of connective tissue consisting of bundles of collagen fibres and broblasts.
- Both surfaces of the arachnoid are lined by mesothelium.
- Fine laments arising from arachnoid mater extend between the arachnoid mater and the pia mater across the subarachnoid space.
- Arachnoid villi are small projections of arachnoid mater into the venous sinuses of brain; they pass through the dura mater. These villi act as one-way valves, and the cerebrospinal fluid present in subarachnoid space drains into the venous sinuses through these villi. Aggregations of these villi are called arachnoid granulations.

## Pia Mater

- The pia mater is the innermost layer of the meninges and it covers the CNS, lining each sulcus and ssure. It is a thin layer of vascular connective tissue containing collagen and elastic fibres and broblasts. It is lined by mesothelium.

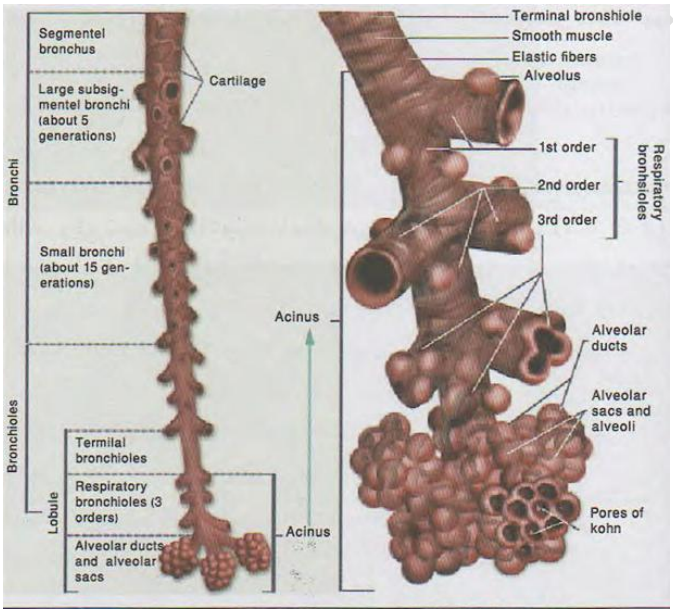
*Theortical of Histology*
*Lecture ….7*

# Respiratory System

**Respiratory system**

Mechanical respiration: process by which oxygen is absorbed from the atmosphere into the blood vascular system and carbon dioxide is excreted into the atmosphere occurs in respiratory system. Respiratory system composed of two compartments:- - Conducting system - Respiratory system **Alveoli:** blind-ended sacs; sites of gas exchange; constitute bulk of lung tissue; thin-walled structures enveloped by rich network of capillaries = **pulmonary capillaries**

**Upper Respiratory Tract** filtering, humidifying and adjusting temperature of inspired air; lined by pseudostratified columnar epithelium with numerous goblet cells (respiratory epithelium), supported by loose collagenous layer = **lamina propria** (with numerous glands)




**Nasal Cavity**

The Nasal cavity is divided into three structurally and functionally different parts.

1. The ***vestibules*** are lined with a keratinised stratified squamous epithelium. Hairs, which filter large particulate matter out of the airstream, and sebaceous glands, are also present.

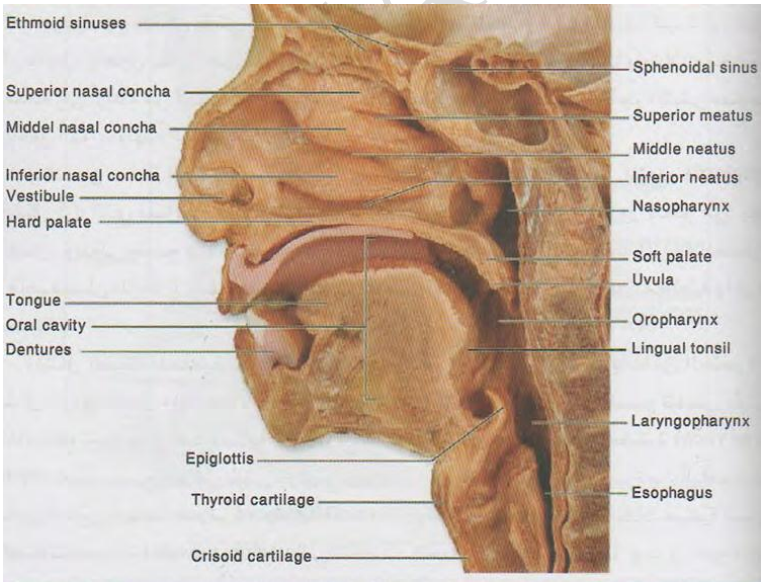
2. At the transition from the vestibule to the ***respiratory region*** of the nasal cavity the epithelium becomes first stratified squamous and then *pseudostratified columnar and*

*ciliated*. The surface of the lateral parts of the nasal cavity is thrown into folds by bony projections

3. called *conchae*. Mucous and serous glands in the connective tissue underlying the epithelium, the ***lamina propria***, supplement the secretion of the goblet cells. Veins in the lamina propria form thin-walled, cavernous sinusoids, also called *cavernous bodies*.

4. Tissues on the superior concha and the nasal septum form the ***olfactory region*** of the nasal cavity. Cilia in the epithelium of the olfactory region arise from *olfactory cells*.
The cell membrane covering the surface of the cilia contains olfactory receptors which respond to fodour-producing substances, *odorants*, dissolved in the serous covering the epithelium. The axons of the olfactory cells collect into bundles in the lamina propria.

5. The olfactory cells and their processes receive mechanical and metabolic support from *supporting cells* (or sustentacular cells). *Basal cells* can divide and differentiate into either olfactory or supporting cells. The supporting cells and the secretion of the serous glands contain lipofuscin granules, which give a yellow-brown colour to the surface of the olfactory region.



**Trachea**

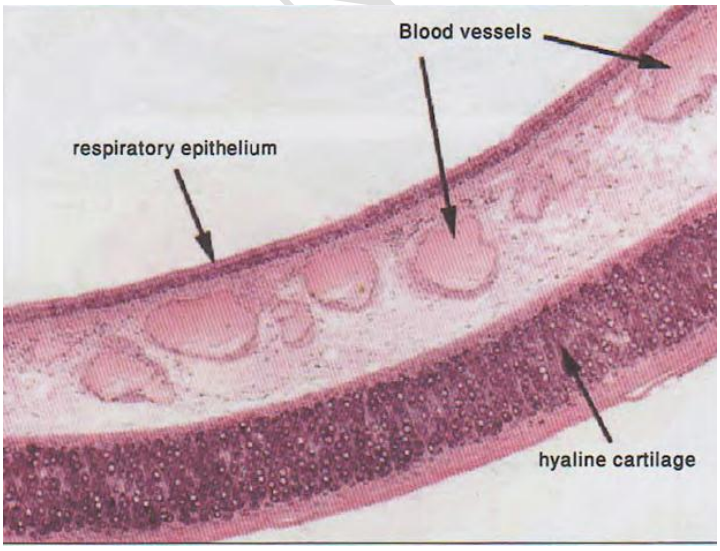
The trachea is a fairly short tube (10-12 cm) with a diameter of ~2 cm.

**Mucosa and Submucosa** The trachea is lined by respiratory epithelium. The number of goblet cells is variable and depends on physical or chemical irritation of the epithelium which increases goblet cell number. In addition to the staple of basal cells, ciliated cells and goblet cells, the respiratory epithelium also contains *brush cells*, *endocrine cells* (or small granule cells, function not clear), *surfactantproducing cells* (or Clara cells), and serous cells. Epithelium and underlying lamina propria are called the ***mucosa***. The lamina propria consists of loose connective tissue with many elastic fibers, which condense at the deep border of the lamina propria to form an elastic membrane.

This elastic membrane forms the border between the mucosa and the connective tissue below it, which is called the ***submucosa***. Muco-serous glands in the submucosa (*submucosal glands*) supplement the secretions of cells in the epithelium. The submucosa ends with the perichondrium of the tracheal cartilages.

**Tracheal cartilages**

The trachea is stabilized by 16-20 C-shaped cartilages (hyaline cartilage). The free dorsal ends of the cartilages are connected by bands of smooth muscle (**trachealis muscle**) and connective tissue fibers. The tracheal cartilages may ossify with age. The trachea bifurcates to give rise to the ***main bronchi***. Their histological structure corresponds largely to that of the trachea.



## Conductive Structures in the Lung

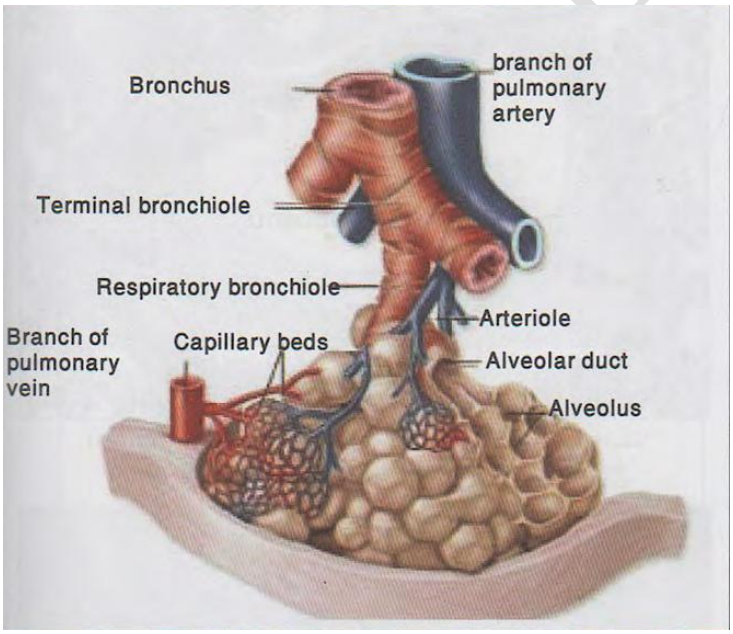
### Bronchi

In the lungs we find the last segments of the conductive portion of the respiratory system. The main bronchi divide into *lobar bronchi* which in turn give rise to *segmental bronchi*. The latter supply the *bronchopulmonary segments* of the lungs.

Bronchial branches are accompanied by branches of the pulmonary artery, nerves and lymph vessels. These structures usually travel in intersegmental and interlobar sheets of connective tissue. Conductive structures of a size down to ~1 mm are termed bronchi. Smaller ones are called *bronchioles*. Aside from their different sizes, *bronchi are characterized by the presence of glands and supporting cartilage*. The cartilage supporting the bronchi is typically found in several small pieces.

### Bronchioles

Bronchioles are the terminal segments of the conductive portion. At the transition from bronchi to bronchioles the epithelium changes to a *ciliated columnar epithelium*, but most of the cell types found in the epithelium of other parts of the conductive portion are still present. *Glands and cartilage are absent*. The layer of smooth muscle is relatively thicker than in the bronchi.



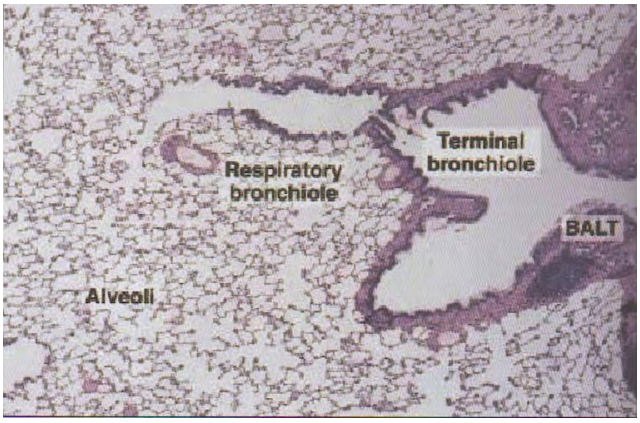
**Respiratory Structures in the Lung**

Bronchioles divide into *respiratory bronchioles*, which are the first structures that belong to the respiratory portion of the respiratory system. Small out pouchings of the walls of the respiratory bronchioles form ***alveoli***, the site of gas exchange. The number of alveoli increases as the respiratory bronchioles continue to divide. They terminate in *alveolar ducts*. The "walls" of alveolar ducts consists of entirely of alveoli.

**Histological Structure of Alveoli**

The wall of the alveoli is formed by a thin sheet (~2μm) of tissue separating two neighbouring alveoli. This sheet is formed by epithelial cells and intervening connective tissue. Collagenous (few and fine), reticular and elastic fibers are present. Between the connective tissue fibers we find a *dense, anastomosing network of pulmonary capillaries*. The wall of the capillaries is in direct contact with the epithelial lining of the alveoli. The basal laminae of the epi- and endothelium may actually fuse. Neighbouring alveoli may be connected to each other by small *alveolar pores*. The epithelium of the alveoli is formed by two cell types:

1. ***Alveolar type I cells*** (small alveolar cells or type I pneumocytes) are extremely flattened (the cell may be as thin as 0.05 μm) and form the bulk (95%) of the surface of the alveolar walls. The shape of the cells is very complex, and they may actually form part of the epithelium on both faces of the alveolar wall.
2. ***Alveolar type II cells*** (large alveolar cells or type II pneumocytes) are irregularly (sometimes cuboidal) shaped. They form small bulges on the alveolar walls. Type II alveolar cells contain are large number of granules called *cytosomes* (or multilamellar bodies), which consist of precursors to pulmonary surfactant (the mixture of phospholipids which keep surface tension in the alveoli low). There are just about as many type II cells as type I cells. Their small contribution to alveolar area is explained by their shape.




*Theortical of Histology*

*Lecture ….8*

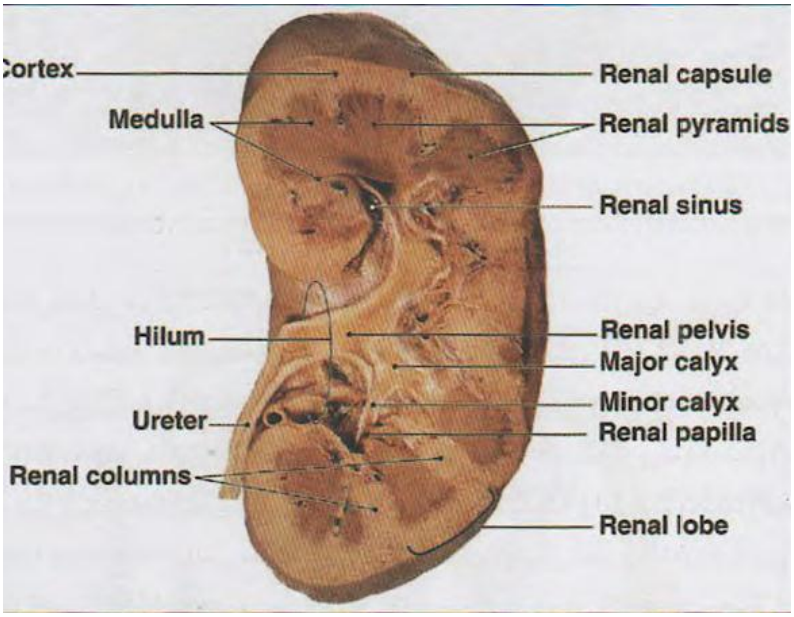
# Urinary System

The urinary system consists of a pair of kidneys and ureters, a urinary bladder and a urethra. The main function of the urinary system is to remove metabolic waste from the blood, and this is achieved by urine production and excretion. Kidneys also help in regulating fluid and electrolyte balance and produce renin and erythropoietin.

- The urine produced by kidneys is conveyed outside the body by excretory passages. These passages consist of the minor and major calyces, renal pelvis, ureter, urinary bladder and urethra. These are hollow tubes. Except in urethra, the walls of these tubes have similar organisation and consist of mucosa, muscular layer and adventitia. Most of the excretory passage (except some parts of urethra) is lined by transitional epithelium (the urothelium).

## Kidneys

- Kidneys are retroperitoneal organs located in the posterior abdominal wall. Each kidney is bean shaped and the medial border has central concavity known as hilum . Through the hilum, the renal artery enters and the renal vein and the ureter leave the kidney.



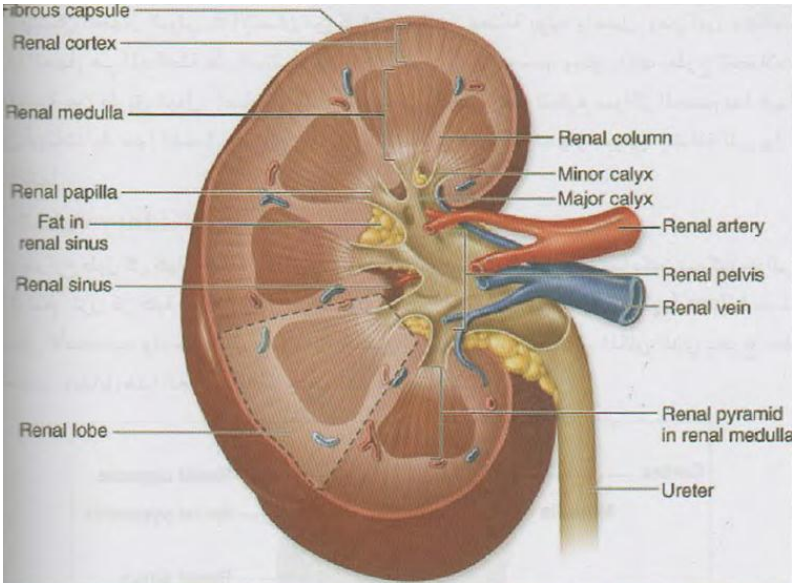



## Structural Organisation

● A longitudinal section of the kidney shows that it consists of a capsule which covers the surface of the kidney. Underneath the capsule are the outer cortex and the inner medulla. The medulla surrounds the renal sinus .Capsule is a layer of dense connective tissue that covers the kidney. It passes through the hilum and lines the renal sinus. Inside the renal sinus, it is continuous with the connective tissue of the walls of the calyces.

Medulla: Each kidney consists of 10–15 medullary pyramids. The base of each pyramid is directed towards the cortex ,and the apex projects into the renal sinus. The apex of the medullary pyramid is known as renal papilla .

The medullary pyramid contains the collecting ducts, loop of Henle, and vasa recta . Through the renal papilla, numerous collecting ducts pass, which are received by the funnel-shaped minor calyx . Cortex is present underneath the capsule surrounding the medulla .It contains the renal corpuscles, proximal and distal convoluted tubules, medullary rays and interlobular artery and veins. There are thin projections of medulla from the bases of medullary pyramids into the cortex, known as medullary rays .It has the collecting tubules and ducts, and the straight portion of nephrons. Renal sinus is a cavity inside the kidney. It is surrounded by medullary pyramids and it communicates outside through the hilum. It contains renal blood vessels, lymphatics, fat and minor calyces.




## Microscopic Structure

● Histologically, the kidney consists of three components: stroma, parenchyma and collecting system.

(a) Stroma includes the capsule and the connective tissue which support the parenchyma, the interstitium. (b) Parenchyma consists of nephrons.

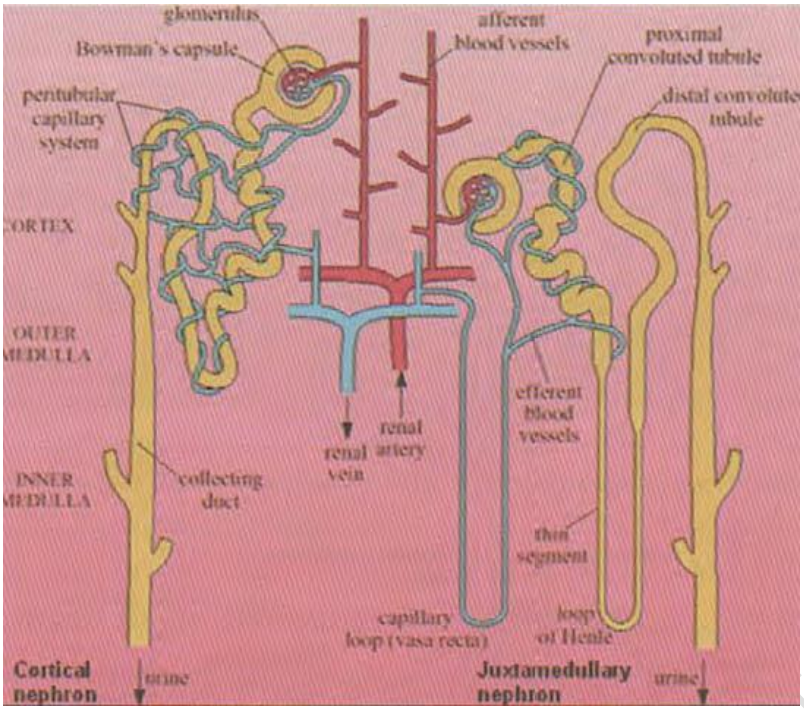
(c) Collecting system includes the collecting tubules and ducts.

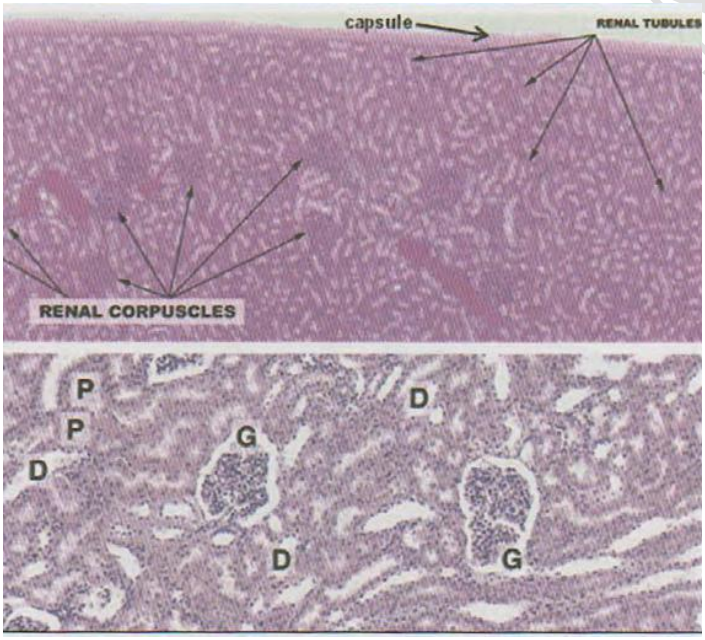
## Nephron

Nephron is the structural and functional unit of the kidney. Major part of a nephron is located in the cortex and part of it is present in the medulla. Each nephron consists of the following:

(a) Renal corpuscle: It consists of Bowman's capsule and glomerulus

(b) Tubule: The tubule consists of a proximal convoluted tubule (PC ), a loop of Henle and a distal convoluted tubule (DC ) .

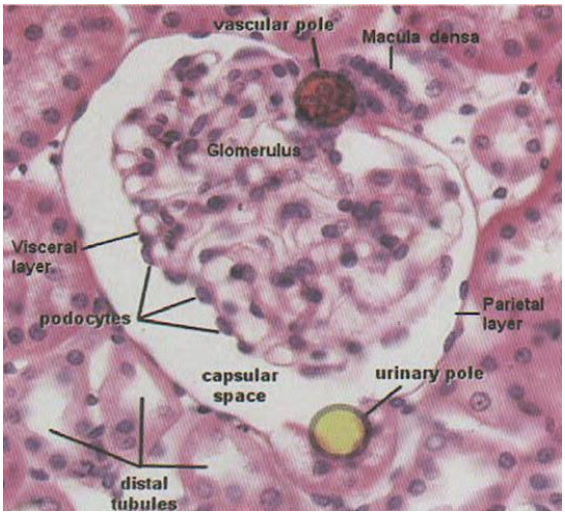



*Renal Corpuscle*

● This part of nephron is present in the cortex . The part of the corpuscle where the afferent arteriole enters and the efferent arteriole leaves is called vascular pole, and the part of the corpuscle opposite to the vascular pole, where the PC begins, is called urinary pole . The renal corpuscle consists of Bowman's capsule and glomerulus (plural: glomeruli).

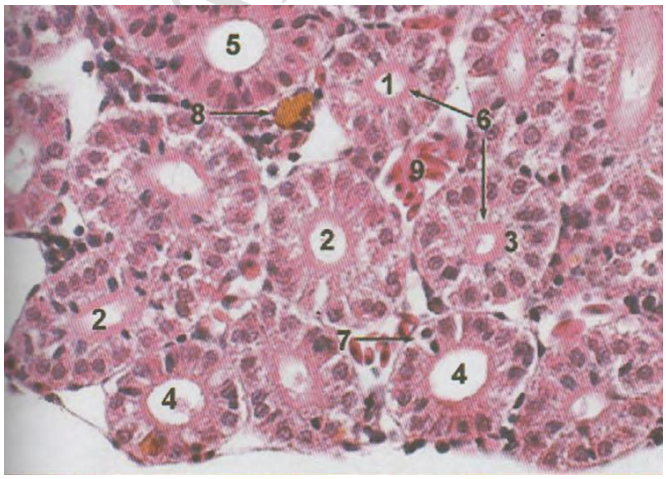
Bowman's capsule is the blind beginning of the nephron. It is invaginated by a tuft of capillaries, the glomerulus. The afferent arteriole enters the renal corpuscle through the vascular pole and divides into capillaries ( fenestrated); these capillaries join to form the efferent arteriole which leaves the glomerulus through the vascular pole.




*Tubule*

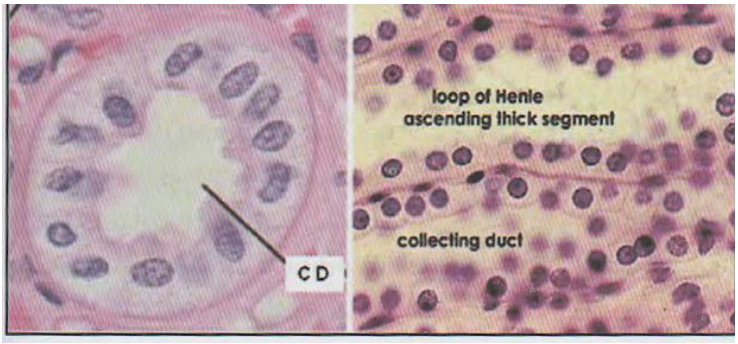
As mentioned earlier, the tubule of a nephron consists of a PC , a loop of Henle and a DC . The tubule consists of epithelial cells resting on a basement membrane. The basement membrane of the parietal layer of the Bowman's capsule is continuous with the basement membrane of the tubule. The epithelial cells lining a tubule vary in different parts of the tubule.

**1. Proximal convoluted tubule (PCT)**




**2. Loop of Henle**

### 3. Distal convoluted tubule (DCT)




## Collecting System

- The collecting system consists of the following:

(a) Collecting tubules (small ducts)
(b) Ducts

- The DC empties into the collecting tubules, which pass through the medullary ray and join with other collecting tubules to form larger ducts (duct of Bellini) . Larger ducts enter the medullary pyramid, pass through the renal papillae and open into the minor calyces. The collecting system is lined by simple epithelium which rests on a basement membrane. Tubules are lined by cuboidal cells and ducts are lined by columnar cells; these cells have pale-stained cytoplasm .

## Interstitium

Interstitium is the connective tissue present around the components of the renal parenchyma, that is it occupies the space between glomeruli, tubules, ducts, vessels and nerves.

## Types o f Nephrons

There are two types of nephrons: cortical and juxtamedullary . Majority of the nephrons are cortical nephrons, and their renal corpuscles are present in the renal cortex. The renal corpuscles of the juxtamedullary nephrons are located in the cortex,

close to the medulla. These nephrons have long loops of Henle extending deep into the medulla.

## Podocytes

● As described earlier, the visceral layer of Bowman's capsule is formed by podocytes . These cells give several extensions known as foot processes. The foot processes wrap around the capillary loops and inter digitate with the foot processes of the neighbouring podocytes . There are openings (30–40 nm wide) between the foot processes of the podocytes called ltration slits.

## Glomerular Filtration Barrier

● The glomerular ltration barrier consists of the structures present between the blood in the glomerular capillary and the urinary space .

These structures are as follows:

(a) Endothelium of the capillary, which is fenestrated

(b) GBM

(c) Podocytes

● This barrier acts as a selective barrier. The selectivity depends upon the size and the charge of the molecule. Small molecules pass through the ltration barrier and enter the urinary space; blood cells and large proteins are retained within the blood capillary.

## Juxtaglomerular Apparatus

● It is present at the vascular pole of the renal corpuscle, where the DC comes in contact with the afferent arteriole of the glomerulus. It is involved in regulation of blood pressure. It consists of macula densa, juxtaglomerular cells (JG cells) and lacis cells or extraglomerular mesangial cells .JG cells are present in the wall of afferent arterioles of the glomerulus. They are modifed smooth muscles and they secrete renin. Lacis cells are a group of cells present close to macula densa between aferent and eferent arterioles. The renin is released from the JG cells into the blood in response to reduced blood pressure or low sodium concentration in the fluid present in the distal tubule.

## Ureter

Ureters convey the urine from the renal pelvis to the urinary bladder.

## Microscopic Structure

The wall of the ureter consists of mucosa, muscular layer and adventitia

## Mucosa

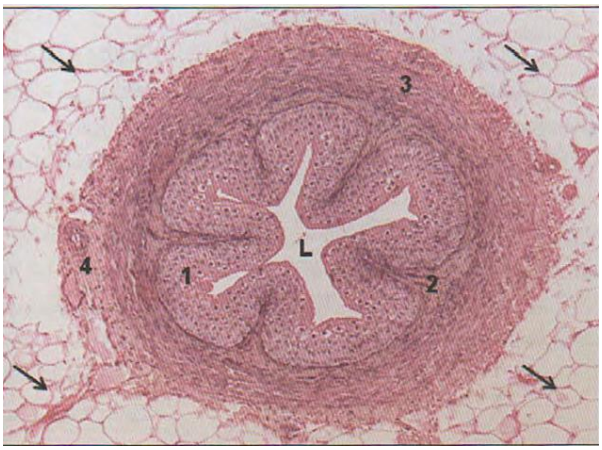
● The mucosa is folded; the lumen appears ‘star shaped’ in the transverse section. Lining epithelium is transitional epithelium, and it is our to five layers thick. Underneath the epithelium is lamina propria.

## Muscular Layer

● It consists of inner longitudinal and outer circular layers of smooth muscles (note that the arrangement of smooth muscles in the gastrointestinal tract is inner circular and outer longitudinal layers). Contractions of these muscles produce peristaltic movement which propels the urine into the urinary bladder.

## Adventitia

● It is the outermost layer.

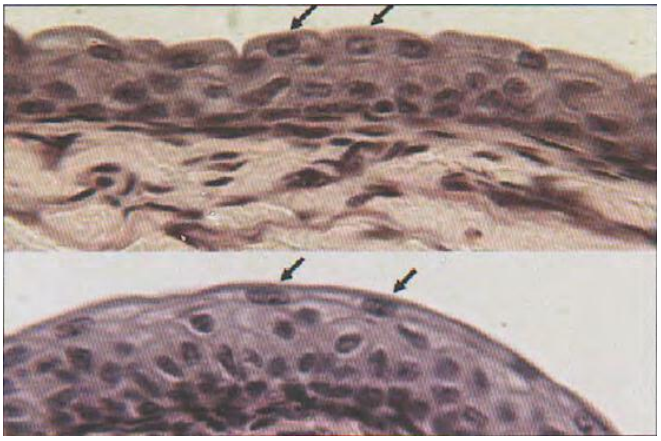



## Urinary Bladder

The urinary bladder is a distensible sac located in the pelvis. It stores urine temporarily.

## Microscopic Structure

● The structure of the wall of the urinary bladder is almost same as the lower one-third of the ureter. The bladder wall is thicker than the ureter. In the relaxed state, the mucosa is highly folded; the epithelium is five to six layers thick . The muscular layer forms the detrusor muscle. It consists of three layers of smooth muscles, as in the lower one-third of the ureter, i.e. middle circular, inner and outer longitudinal layers. Near the urethral opening of the urinary bladder, the smooth muscles are arranged circularly to form internal urethral sphincter; it is involuntary in function. Adventitia is the outermost layer except in the upper part of the bladder where the outermost layer is serosa (since it is covered by peritoneum).



## Urethra

- The urethra conveys the urine from the urinary bladder to the exterior.

## Microscopic Structure

- The wall of the urethra consists of epithelium, lamina propria and muscular layer. The type of epithelium varies within the urethra. Lamina propria has numerous mucus-secreting glands (glands of Littre). The muscular layer consists of an inner longitudinal and an outer circular layer of smooth muscles.

## Male Urethra

- It consists of three parts: prostatic part (in the prostate), membranous part (in the urogenital diaphragm) and penile part (in the corpus spongiosum of the penis) . The prostatic part of the urethra is lined by transitional epithelium.

Other parts of the male urethra are lined by pseudostratif ed or stratiffed columnar epithelium, except at the distal end where it changes to stratif ed squamous epithelium. The membranous part o the urethra is surrounded by skeletal muscles of the urogenital diaphragm to form the external urethral sphincter; it is voluntary in unction.

## Female Ure thra

- At the beginning (near the internal urethral orifice), it is lined by transitional epithelium; the remaining urethra is lined by stratiffed squamous epithelium.

*Theortical of Histology*

*Lecture ….9*

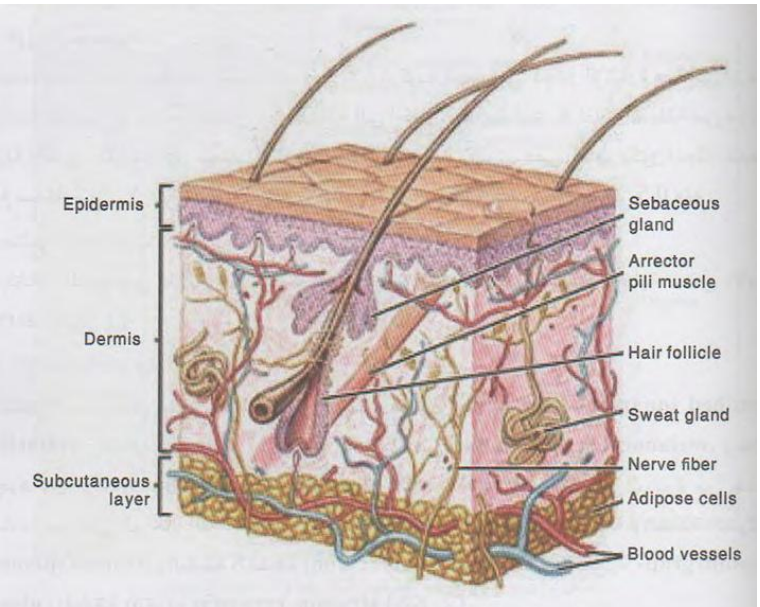
# Epithelial Tissues



* Skin is the heaviest single organ of the body.
* It is composed of :
- Epidermis; Epithelium of ectodermal origin
- Dermis; Layer of CT of mesodermal origin
- Hypodermis; Or subcutaneous tissue; it is not a component of the skin.

1. Epidermis is composed of stratified squamous keratinized epithelium, containing *keratinocytes* and *non-keratinocytes*.

2. Dermis is dense irregular CT rich in B.V., collagen and elastic fibers.




**Functions**

- It serves as a barrier against infection.
- It is impermeable prevents pass of fluids from the external environment.
- It is a hydrophobic layer prevents loss of body fluids.
- It regulates body temperature by regulating the blood flow through the capillary beds and by sweating.

**Types of Skin**

Two types based on the comparative thickness of the epidermis into; *thin* and *thick* skin.

- The epidermal layer of thin skin is about 75-150 μm, but it is about 400- 600μm in thick skin. Thick skin is smooth, non-hairy, and is found in the palms and soles.
- Thin skin is hairy, and is found elsewhere on the body.

1- Epidermis contains two types of cells

**A – Keratinocyts**

- They are keratin forming cells.
- They are organized into layers and become mature in about 4 weeks.
- Each layer represents a dynamic stage of cell division and cell maturation.
- Cell renewal (Mitosis).

Cell differentiation (Keratinization)

- Cell death
- Exfoliation (Sloughing off the dead cells OFF)

**B - Non-Keratinocytes:**

- Melanocytes
- Langerhans cells
- Merkel`s cells

**Layers of Epidermis**

- Stratum Basale
- Stratum spinosum
- Stratum Granulosum
- Stratum Lucidum
- Stratum Corneum

**1- Stratum Basale**

- Single layer of basophilic columnar or cuboidal cells resting on a basement membrane at the dermal -epidermal junction.

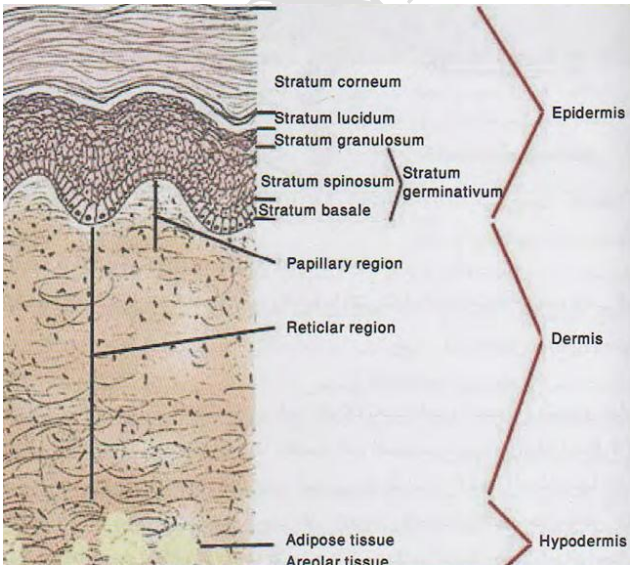
- They contain stem cells (*have intense mitotic activity*), which are responsible for renewal of epidermal cells.

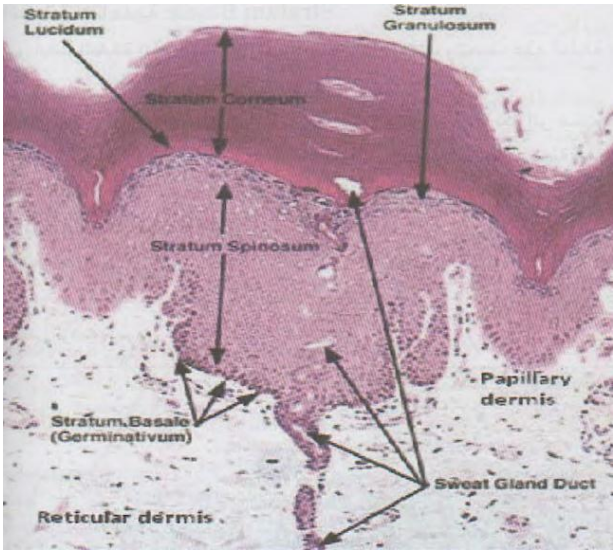
- All cells in stratum basale contain *intermediate keratin filaments*.

- As cells progress upward, the number of keratin filaments increases until they represent half the total proteins in the stratum corneum.

- Desmosomes bind cells of this layer in their lateral and upper surfaces.

- Hemidesmosomes bind cells to the basal lamina.

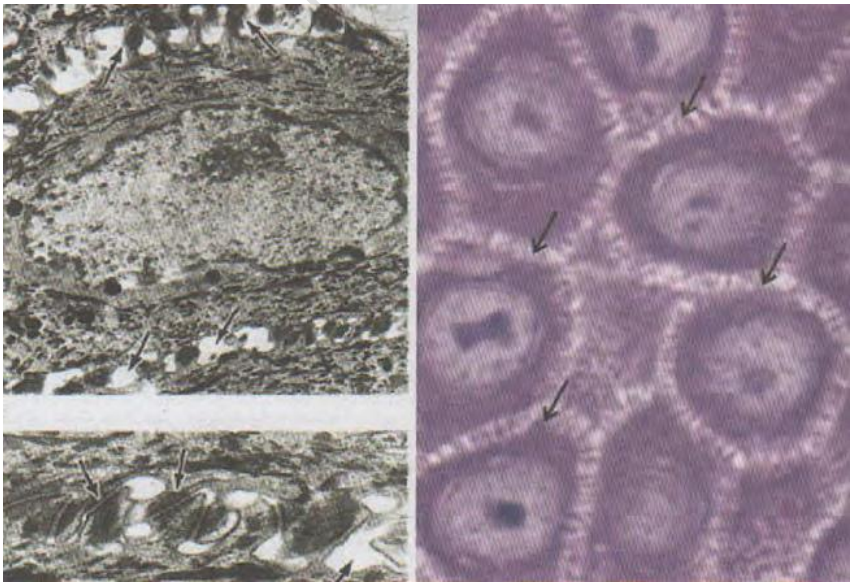





**2- Stratum Spinosum**

- It is composed of cuboidal or slightly flattened cells, with central nuclei.
- The cytoplasm filled with bundles of keratin . filaments (TONOFILAMENTS)
- These bundles end at and insert into the cytoplasmic densities of the desmosomes.
- Cells of this layer are firmly bound together by the filaments filled the cytoplasmic spines and desmosomes that punctate the cell surface, giving them spine-like appearance. - The first two layers are called *MALPIGIAN LAYER*, which show mitotic activity and contain stem cells.





**3- Stratum Granulosum**

- It is consisted of 3 -5 layers of flattened polygonal cells, whose cytoplasm is filled with non-membranous basophilic granules called *Keratohyalin Granules*.

- Another type of granules that can be seen by E/M are membranous *Lamellar granules*.

- The lamellar granules are 0.1 – 0.3 μm ovoid or rod-like structure containing Lamellar Disks of Lipid Bilayers.

- These granules fuse with the cell membrane and release their lipid content into the intercellular spaces forming a Sheet of Lipid Deposit.

- These sheet acts as a barrier sealing the skin.

**4- Stratum Lucidum**

- More common in thick skin, as a translucent thin layer of flattened eosinophilic cells.

- The cytoplasm and cell organoids are no longer present, but desmosomes are still present.

- The cytoplasm consists of densely packed Keratin Filamints embedded in electron dense matrix.

**5- Stratum Corneum**

- - It is consisted of 15-20 layers of flattened non-nucleated keratinized cells, whose cytoplasm is filled with Keratin. After keratinization, the *horny cells* contain only fibrillar and amorphous proteins and thickened plasma membrane.

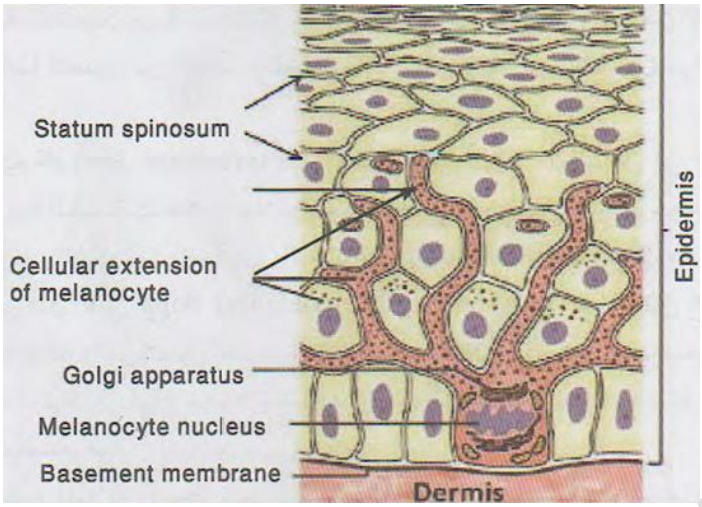
- During keratinization, the lysosomal hydrolytic enzymes play a role in disappearance of cytoplasmic organelles.

**Non- Keratinized Cells**

**1- Melanocytes**

- The color of skin is the result of several factors such as melanin, carotene and the hemoglobin in the dermal capillaries.
- There are two types of melanin:
- Eumelanin: dark brown pigment produced by melanocytes.
- Pheomelanin: reddish pigment present in red hair.
- Melanocytes have long cytoplasmic processes that branch into the epidermis, running between cells of stratum basale and spinosum.
- They are located beneath or between cells of stratum basale.

- They are ectodermal in origin, derived from the neural crest and migrate to the skin.
- We cannot see melanocytes in skin sections stained with Hx&E, but they can be seen if the sections are stained with DOPA REACTION (when fresh sections of skin are incubated with DOPA, the tyrosenase enzyme within the melanocytes converts DOPA into dark melanin pigment).




**Mechanism Of Melanin Formation**

Melanin synthesis starts in rER; then melanin is concentrated, accumulated and stored in Golgy bodies.

The pigments are found in secretory vesicles called Melanosomes.

Then the pigment granules leave melanocytes by exocytosis.

Lastly, the pigments are phagocytosed by keratinocytes.

**2- Langerhans Cells**

- They are phagocytic skin cells present mainly within the cells of Stratum Spinosum; and represent 2- 8% of the cells.
- They are mesodermal in origin.
- They are star shaped cells, with indented nucleus.
- The cytoplasm contain special granules called **BIRBECKS GRANULES**.
- They are demonstrated by **gold chloride impregnation**.

**3- Merkel's Cells**

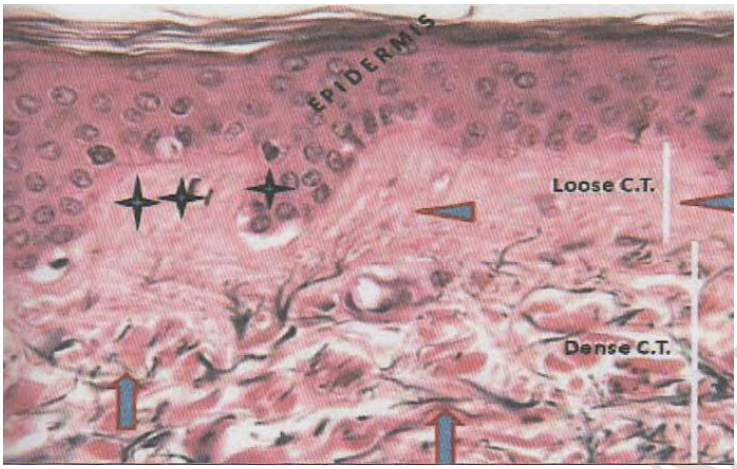
- Sensory skin cells.
- Located mainly in thick skin.
- Act as mechanoreceptors.

- Other evidence suggests that they have functions related diffuse neuro-endocrine cells.

**Dermis**

- It is a CT layer rich in BV, lymphatics, and CT cells.

- It is formed of two layers:-
- Papillary layer
- Reticular layer




**Papillary Layer**

- Vascular C.T. layer separated from the epidermis by basement membrane.
- It contains fine axonal connections of free sensory nerve endings (sensory receptors ) such as : - Superficial touch receptor or corpuscle of touch (Meissner's corpuscles).
- Lamellated corpuscle or deep pressure receptor (Pacinian corpuscle) .

**Dermal Papillary**

They are the junction of the dermis and epidermis. They are irregular projections of the dermis (papillae) interdigitate with evaginations of the epidermis ( epidermal ridges). They contain fine interlacing collagen and elastic fibers, BV, and lymphatics.

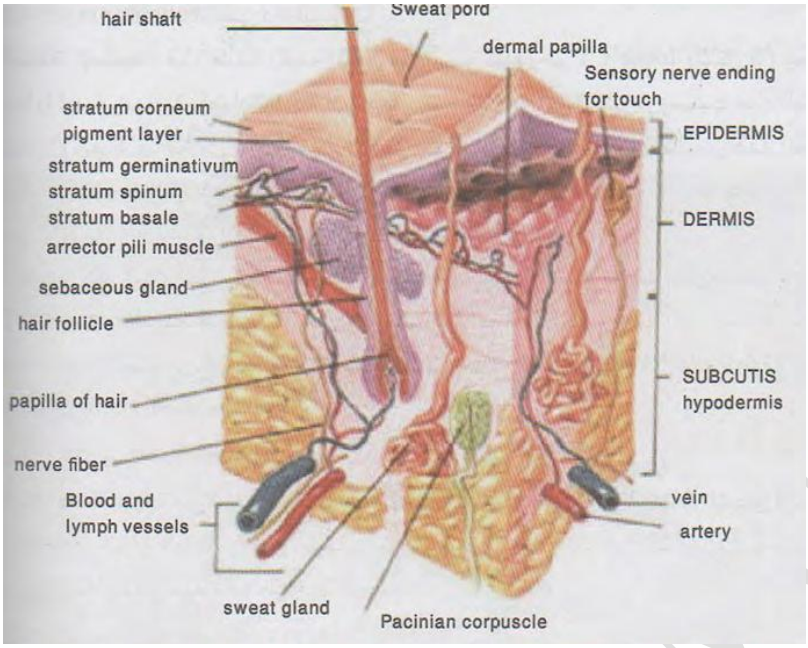
**Reticular layer**

- It is thicker than the papillary layer.
- It is formed of reticular, collagen and elastic fibers.
- It contains many sensory receptors like Pacinian Corpuscles.

**Skin association**

- Subcutaneous tissues
- Sensory receptors

- Hair follicles
- Nails
- Sweat glands
- Sebaceous glands






*Theortical of Histology*

*Lecture ….10*

# Endocrine System

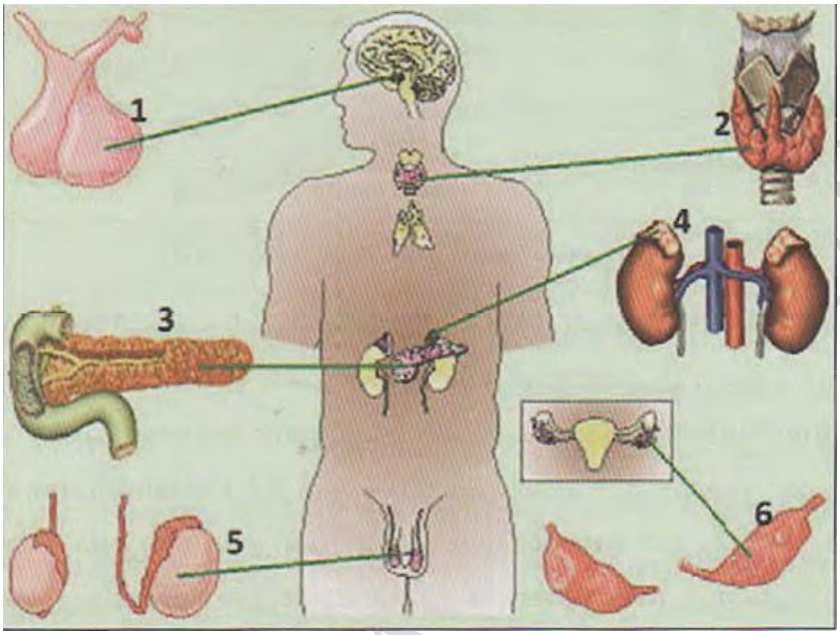
Endocrine glands are ductless glands. They develop as invaginations of surface epithelium; however they later get separated from the epithelium.

The secretory cells of endocrine glands are arranged as cords or clumps around capillaries or sinusoids. In some endocrine glands (such as thyroid), cells are arranged as follicles. Since these glands are ductless, the secretory cells release the hormones into the interstitial fluid. From the interstitial fluid, the hormones enter the

bloodstream and reach their target organs. This chapter deals with pituitary, thyroid, parathyroid and adrenal glands. Other endocrine glands have been described in their respective systems.

## Pituitary Gland

The pituitary gland or the hypophysis is an endocrine gland; it is about the size of a pea. It is located in the base of the skull inside the bony cavity of the sphenoid bone, known as sella turcica. It is connected to the hypothalamus by a pituitary stalk. The pituitary gland is considered the 'master gland' of the endocrine system as it secretes the hormones that regulate the other endocrine glands.






## Parts Of Pituitary

It consists of two parts: adenohypophysis and neurohypophysis.

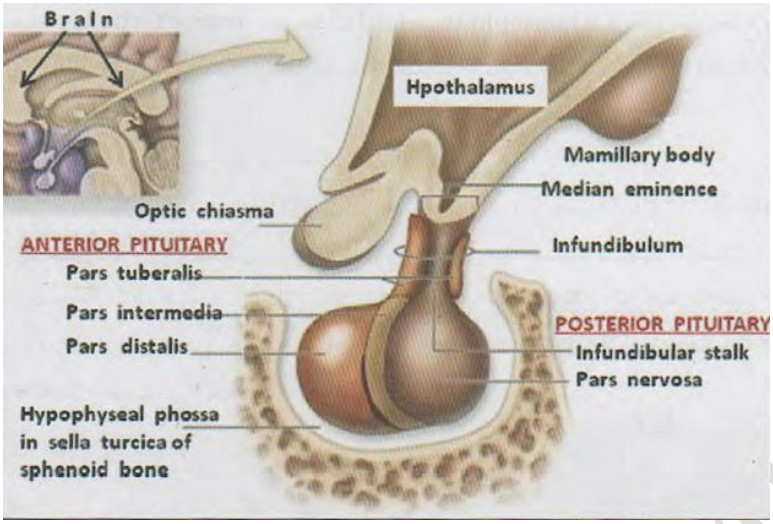
### Adenohypophysis (Anterior Pituitary)

● The anterior pituitary is further subdivided into following parts: pars distalis, pars tuberalis and pars Intermedi Pars distalis or pars anterior is the largest part. Pars tuberalis is the upward extension of pars distalis surrounding the pituitary stalk. Pars intermedia is the part of denohypophysis present as a thin band between the pars distalis and pars nervosa. Adenohypophysis develops from an outgrowth (Rathke's pouch) from the roof of the primitive oral cavity. The remnant of Rathke's pouch may persist as intraglandular cleft in anterior pituitary.

### Neurohypophysis (Poste rior Pituitary)

It develops from the downward growth of the hypothalamus. It consists of pars nervosa, infundibulum and median eminence. The major part of neurohypophysis is pars nervosa, which lies posterior to pars intermedia.

- Pars nervosa is connected to the hypothalamus by the pituitary stalk, also called infundibulum. Infundibulum is continuous with the median eminence.

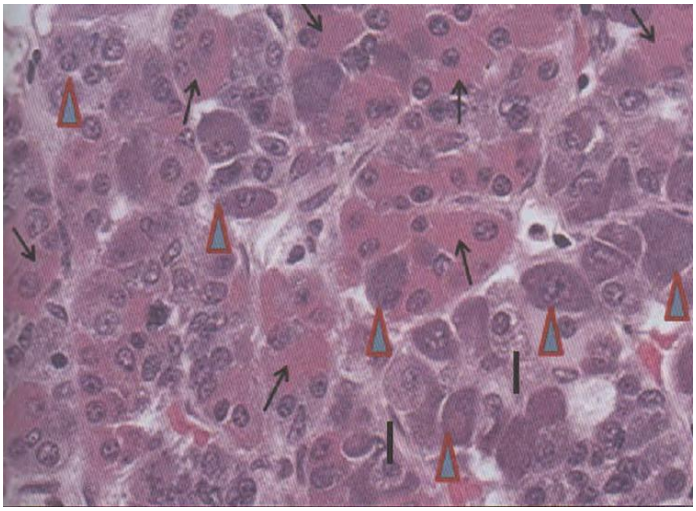



## Microscopic Features

The entire gland is covered by a connective tissue capsule. The microscopic features of pars distalis, tuberalis and intermedia and neurohypophysis are as follows.

## Pars Distalis

- It consists of cells that are arranged in clumps or irregular cords between networks of capillaries. These cells are supported by a network of reticular fibers. Based on their a finites or H&E stains, cells are classiffed as chromophobe and chromophil cells. Chromophil cells are further subdivided into acidophils and basophils.



## Pars Tuberalis

It is same as pars distalis.

## Pars Intermedia

Small cysts containing colloid, lined by cuboidal cells, can also be seen, and these cysts are remnants of Rathke's pouch. It contains basophilic cells arranged in irregular clumps and cords PT e cells of pars intermedia produce melanocyte-stimulating hormone (MSH).

## Neurohypophysis (Posterior Pituitary)

Neurohypophysis stores the hormones synthesised in the hypothalamus.

It contains the hypothalamo-hypophyseal tract, which consists of unmyelinated axons of neurosecretory cells. The cell bodies of these neurons are located in supraoptic and paraventricular hypothalamic nuclei of the hypothalamus. It also contains supporting cells called pituicytes .

Neurosecretory products (oxytocin and vasopressin) are produced by the cell bodies of the neurosecretory cells, in the hypothalamus. Two hormones, oxytocin and antidiuretic hormone (ADH) or vasopressin, pass through the axons of the hypothalamo-hypophyseal tract to the posterior pituitary where they are contained in axonal swellings called Herring bodies .The products are f nally released into the capillaries.



## Pituitary Hormones

The pituitary, the master gland of the endocrine system, produces several hormones which have vast efects on various systems of the body

## Anterior Pituitary Hormones

**1. Growth hormone (GH):** Somatotrophs produce growth hormone, which is important or body growth and development in children and adolescents. It stimulates production of somatomedin in the liver, and somatomedin then acts on epiphyseal cartilage and causes growth of long bones. In most of the cells in the body, it increases the rate of metabolism.

**2. Prolactin:** Mammotrophs produce prolactin, which promotes mammary gland development during pregnancy and maintains milk secretion during lactation.

**3. Thyroid-stimulating hormone ( SH):** Secreted by thyrotrophs, it acts on ollicular cells of thyroid and stimulates synthesis and release of thyroid hormones.

**4. Follicle-stimulating hormone (FSH):** Produced by gonadotrophs, it stimulates growth of ovarian ollicles and secretion of oestrogen in emales. In males, it acts on Sertoli cells o the semini erous tubules, which synthesise androgen-binding protein, and this protein stimulates spermatogenesis.

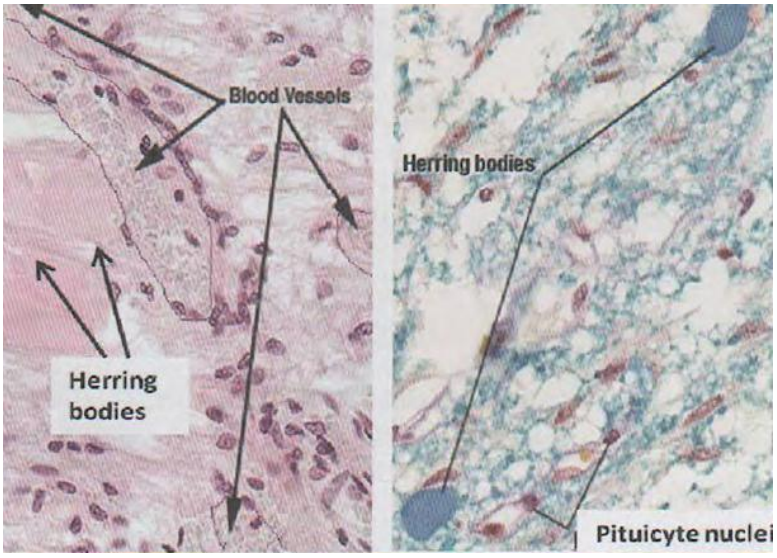
**5. Luteinising hormone (LH):** Produced by gonadotrophs, it induces ovulation, ormation of corpus luteum and secretion of progesterone in emales. In males, it stimulates production of testosterone by
the interstitial cells of the testis.

**6. Adrenocorticotropic hormone (AC H):** Produced by corticotrophs, it stimulates synthesis and secretion of glucocorticoids in zona asciculata and adrenal androgen in zona reticularis of the adrenal cortex.

## Posterior Pituitary Hormone s

1. **Oxytocin:** It is released in lactating women. The release of oxytocin is caused by a neuronal reflex that is initiated during suckling. Oxytocin causes contraction of myoepithelial cells around the secretory alveoli of the mammary gland and causes ejection of milk. Oxytocin causes contraction of smooth muscles in the uterus and allopian tube during copulation and acilitates sperm transport. Oxytocin also induces contraction of uterine smooth muscles during parturition.

**2. Antidiuretic hormone (ADH):** It helps in resorption of water in the kidney to produce concentrated urine. It increases the permeability of collecting tubules of the kidney to water, which results in concentration of urine and a decrease in its volume. In diabetes insipidus there is de ciency of ADH, the urine becomes hypotonic to plasma, and the urine volume is increased—all of these result in water loss.




## Control of Anterior Pituitary Secretion

● The adenohypophysis, which controls various endocrine organs, is itsel under the control of the hypothalamus. The neurosecretory cells of the hypothalamus secrete various stimulating and inhibitory hormones.

The axons of these neurosecretory cells terminate in median eminence and release the hormones.The hormones are transported from the median eminence to the adenohypophysis through hypophyseal portal veins and stimulate or inhibit the acidophils and basophils. The secretions of neurosecretory cells o hypothalamus are regulated by the level of hormones, by negative eedback mechanism. For example, the hypothalamus secretes corticotropin-releasing hormone (CRH), which stimulates corticotrophs of adenohypophysis to synthesise and secrete ACH, which in turn stimulates the adrenal cortex to synthesise and secrete glucocorticoids .Once glucocorticoids have been released into the blood in su cient amount, they inhibit the hypothalamus rom releasing CRH and the adenohypophysis rom releasing AC H, through negative eedback mechanism .



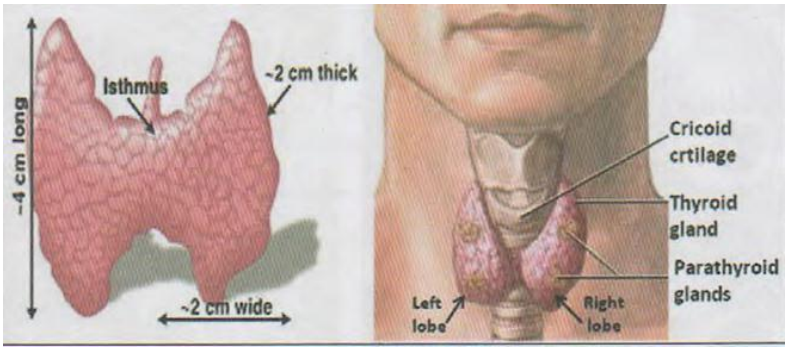
## Control of Posterior Pituitary Secretion

● ADH is stored in the Herring bodies of the secretory neurons in posterior pituitary, and it is released into the blood by the impulses in these neurons. Increase in plasma osmolality or a decrease in blood volume (or blood pressure) triggers the release of ADH into the blood. Like ADH, oxytocin is also stored in the Herring bodies. The

release of oxytocin is triggered by neuroendocrine ref ex, which is initiated by stimulation of touch receptors present on the nipple, while suckling.

## Thyroid Gland

Thyroid is a bilobed organ, located in the anterior aspect of the neck. The two lobes are connected to each other by the isthmus in front of the trachea.




## Microscopic Features

- It is covered by a thin connective tissue capsule. Many septa arise rom the capsule, and they convey blood vessels, nerves and lymphatics into the gland. The parenchyma consists of hollow, spheroidal structures called thyroid follicles and para follicular cells.

## Thyroid Follicle

- The wall of thyroid follicle consists of a single layer of cells called follicular cells. These cells rest on a basement membrane. The connective tissue between the follicles contains capillaries, nerves and lymphatic vessels. The lumen of the follicle is filled with a colloid material. Follicular cells are usually cuboidal, but the shape varies depending upon the functional status of the follicles. In actively secreting

follicles, the amount of colloid decreases and the cells lining the follicle become tall. In less active follicles, the amount of colloid is more and lining cells become fat. The colloid is formed by the follicular cell. Its main component is thyroglobulin, which is the inactive storage form of thyroid hormone. Thyroid is unique among endocrine glands as it stores its secretory product, colloid, extracellularly in the lumen of the follicle.

*Follicular Cells*

● Each follicular cell has a spherical nucleus containing one or two nucleoli. The lateral plasma membranes have junctional complexes towards the apex. The luminal surface of follicular cells has microvilli.

The basal cytoplasm has numerous rough endoplasmic reticulum. Golgi complexes and numerous colloid resorption droplets are present in apical cytoplasm.

**Parafollicular Cells**

● These cells are also called 'C' cells. They are present in clusters in the connective tissue in between the follicles. They are also present as single cells within the follicle .Within the follicle, they are located away from the colloid, adjacent to the basement membrane. They secrete calcitonin hormone which reduces the blood calcium level by reducing bone resorption by osteoclasts.



## Hormones Of Thyroid Gland

● Thyroid hormone increases the basal metabolic rate in most of the tissues. It is essential or normal body growth and development of the central nervous system. Calcitonin antagonises the action of parathyroid hormone by reducing the blood calcium levels and thus helps to maintain the blood calcium level.

### Synthesis of Thyroid Hormone

T is involves the following steps:

**1. Synthesis and storage:** Thyroglobulin is synthesised by rough endoplasmic reticulum and is then carried to Golgi complex, where it is packed into vesicles. These vesicles are transported to the apical surface of the cell where thyroglobulin is discharged into the lumen of the follicle by exocytosis.

**2. Iodide uptake:** Under the inf uence of SH, follicular cells take up iodine from the blood. Iodide is oxidised to iodine by enzyme thyroid peroxidase.

**3. Iodination of thyroglobulin:** Iodination o thyroglobulin occurs at the luminal sur ace of the ollicular cells. Triiodothyronine (T3) and tetraiodothyronine (T4, also known as thyroxine) are ormed.

**4. Release of thyroid hormones:** Stimulation of follicular cells by SH causes endocytosis of thyroglobulin Numerous colloid resorption droplets containing iodinated thyroglobulin are ormed. Lysosomes use with the colloid resorption droplets and release T4 and T3 hormones, which enter blood circulation

## Control of Thyroid Hormo ne

- Secretion of thyroid hormone is under the control of SH, produced by adenohypophysis, through negative feedback mechanism .

The hypothalamus secretes thyrotropin-releasing hormone RH , which stimulates thyrotrophs of adenohypophysis to synthesise and secrete SH, which in turn stimulates the ollicular cells of thyroid to synthesise and secrete 3 and 4. Once 3 and 4 have been released into the blood in suffcient amount, they inhibit the hypothalamus rom releasing RH and the adenohypophysis rom releasing SH, through negative feedback mechanism

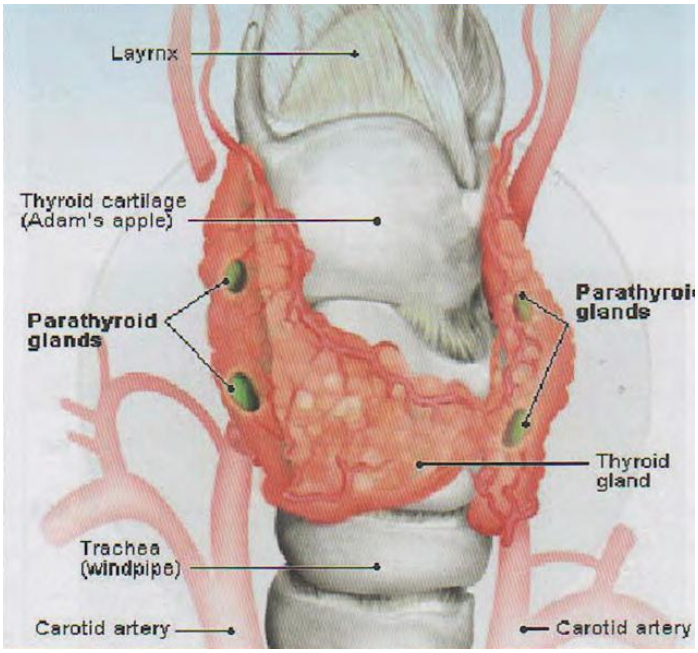


*Theortical of Histology*

*Lecture ….11*

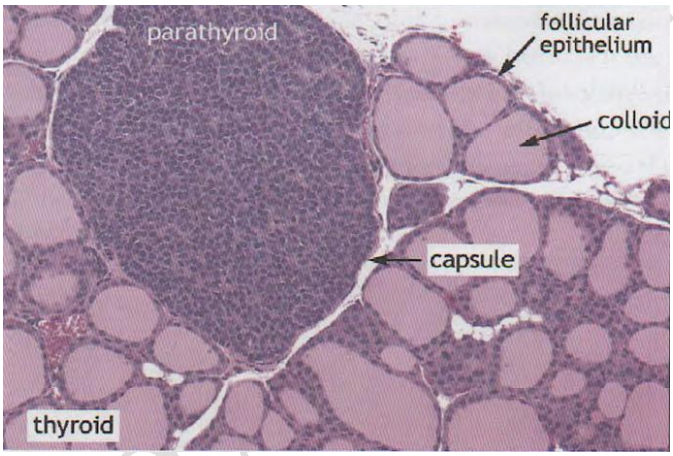
## Parathyroid Glands

There are two pairs of parathyroid glands. They are embedded in the capsule of thyroid on its posterior aspect .




## Microscopic Features

Parathyroid glands contain two types of cells: principal or chief cells and oxyphil cells.



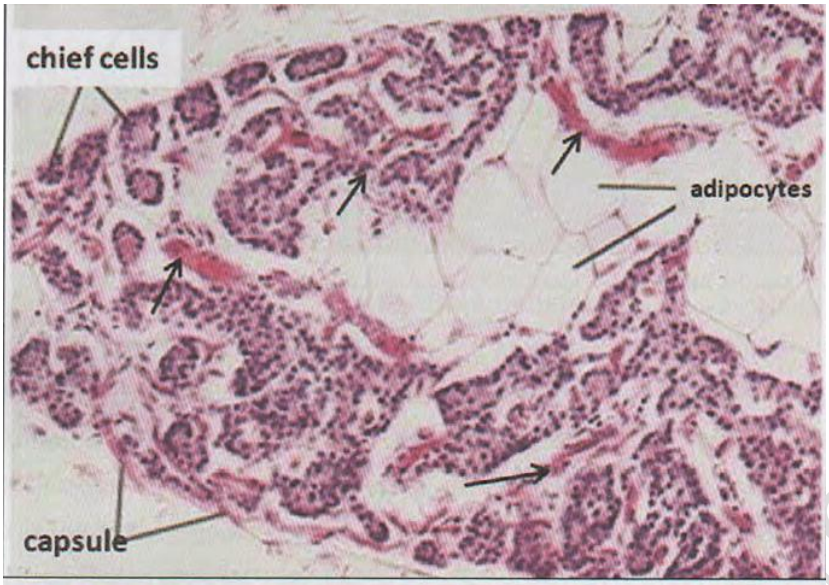

## Chief Cells

● Chief cells are the most numerous cells; they are polygonal in shape and are arranged in clumps or irregular cords.

The cytoplasm of the cells shows numerous secretory granules; each cell has a centrally located spherical nucleus. Large capillaries are present in between the cords and clumps. Chie cells secrete parathyroid hormone P H or parathormone .

## Oxyphil Cells

● These cells are larger in size but fewer in number than chief cells. They are arranged in clumps. Their function is not clear.




## Parathyroid Hormone

● P H is secreted by the chief cells. It raises the blood calcium level. P H acts on three different sites to increase the blood calcium level: bone, kidney and intestine . In the bone, P H acts on osteoclasts and increases the bone resorption. In kidney, P H decreases phosphate resorption in proximal tubules and increases calcium resorption in distal tubules. P H increases the absorption of calcium in the small intestine.

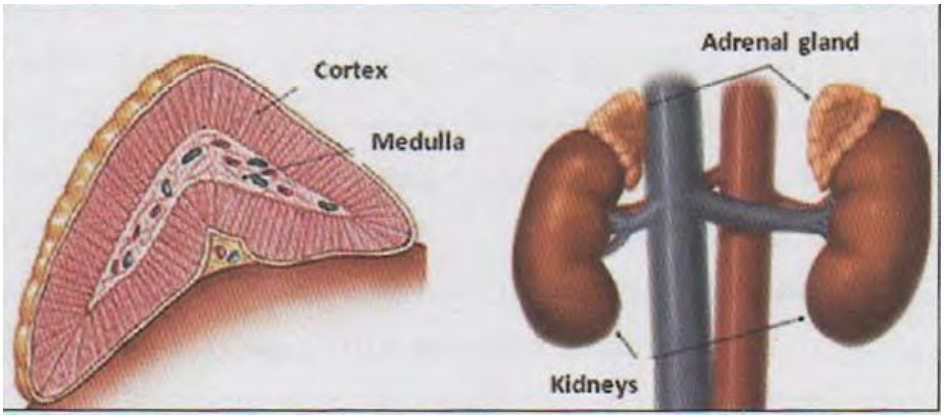
## Control o f Parathyroid Secretion

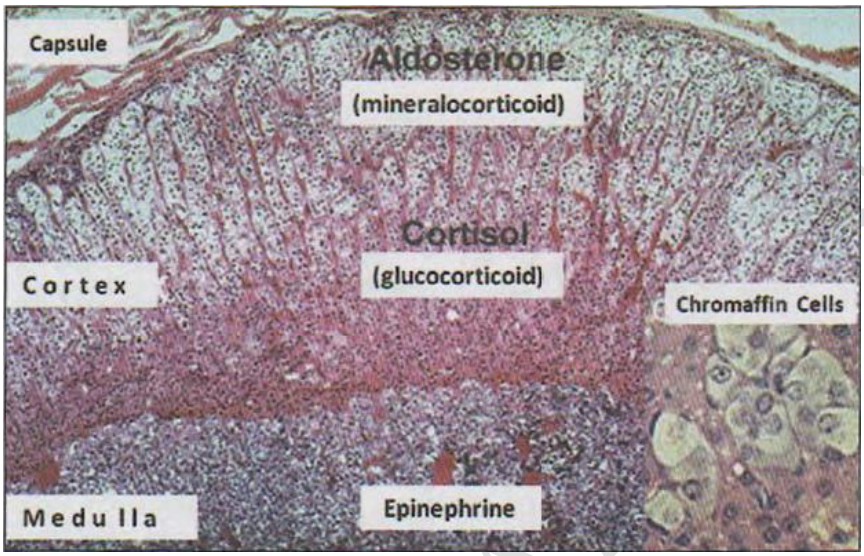
● The secretion of the parathyroid is regulated by the calcium level in blood, by negative feedback mechanism . The low blood calcium level stimulates the gland to produce and secrete P H. As described in the preceding text, P H acts on kidney, bone and small intestine and increases the blood calcium level. Increase in the blood calcium level inhibits the parathyroid gland.



## Adrenal Glands

● An adrenal gland is located at the upper pole of each kidney . Each gland has two components: cortex and medulla .Both components have different structural organisation, origin and functions.



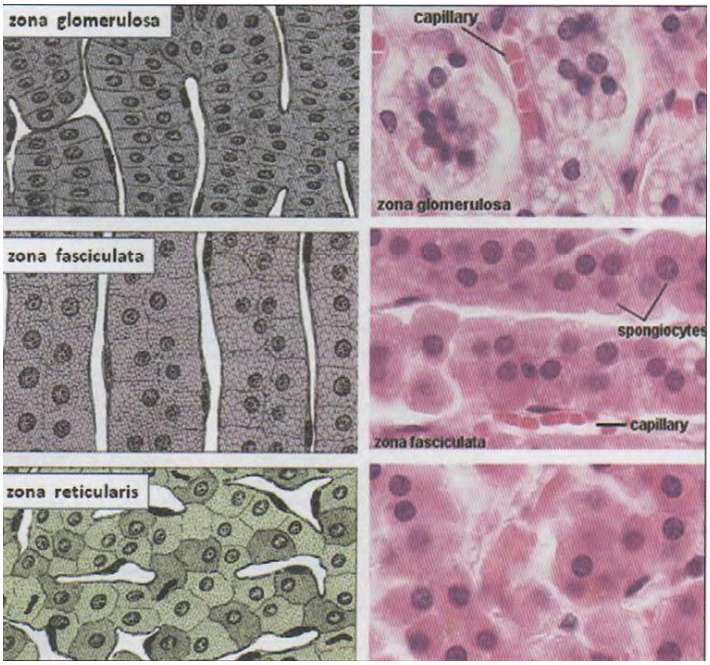



## Microscopic Features

- As mentioned earlier, the adrenal gland consists of two components: outer cortex and inner medulla. Each gland is enclosed in a connective tissue capsule. Connective tissue septa extend from the capsule towards the medulla, conveying the vessels and nerves.

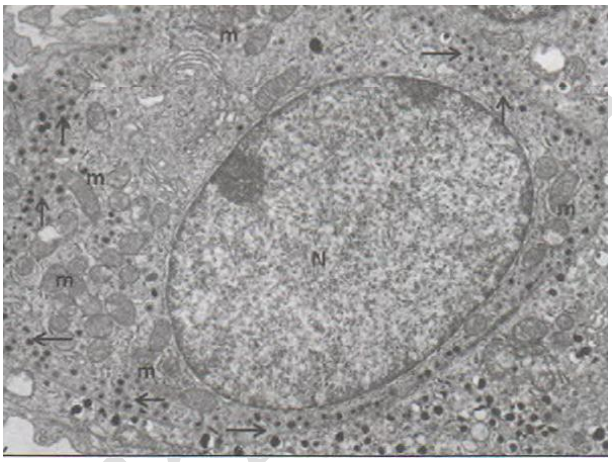
## Adrenal Cortex

- It develops from mesoderm. It consists of three layers: outermost zona glomerulosa, middle zona fasciculata and innermost zona reticularis .




## Adrenal Medulla

● It develops from neural crest cells. It consists of two types of cells: chromaf n cells and ganglion cells.




## Adrenal Hormones

● Adrenal cortex secretes three hormones: mineralocorticoids (aldosterone), glucocorticoids and adrenal androgens. Adrenal medulla secretes catecholamines.

(a) Aldosterone: It is secreted from zona glomerulosa of adrenal cortex. It regulates the resorption of sodium and excretion of potassium in the tubules of the kidney.

(b) Glucocorticoids: Glucocorticoids are secreted the from zona fasciculata.

They have various effects on protein, at and glucose metabolism. They increase the blood glucose level. They also decrease the cellular and humoral immunity.

(c) Adrenal androgen: Zona reticularis secretes the steroid sex hormone adrenal androgen. T e hormone is responsible or masculinising eatures. It also promotes bone growth and increases muscle mass.

(d) Catecholamines: Adrenal medulla secretes catecholamines. Catecholamines prepare the body for physical activity; they cause bronchial dilation, increased heart rate and cardiac output, and elevated blood glucose and lipolysis.

## Control o f Adrenal Secretions

Hormones of adrenal cortex are under the control of negative feedback mechanism, whereas adrenal medulla secretion is under the control of sympathetic stimulation.

### *Aldosterone*

- Secretion of aldosterone is under the control of negative feedback mechanism, which involves the renin–angiotensin system. A fall in the blood pressure or sodium ion concentration in the blood causes the release of renin from juxtaglomerular cells of the kidney and this converts angiotensinogen into angiotensin I. Angiotensin I is converted into angiotensin II which stimulates the cells of zona glomerulosa to secrete aldosterone. As the blood pressure and sodium ion concentration rise and become normal, the release of renin is inhibited from the juxtamedullary apparatus.

### *Glucocorticoid s and Adrenal Androgens*

- Secretions of zona fasciculata and reticularis are under the control of ACTH, produced by adenohypophysis, through negative feedback mechanism (described under ‘Control of Anterior Pituitary Secretion’).

### *Catecholamines*

- As described earlier, the chroma n cells of adrenal medulla are innervated by preganglionic sympathetic fibres, and they themselves correspond unctionally to postganglionic sympathetic neurons. During sympathetic stimulation, chroma n cells are stimulated by preganglionic sympathetic fibres and release the content of secretory granules by exocytosis.

## Capsular Capillaries

- Small branches of superior, middle and interior suprarenal arteries form a capillary plexus in the capsule.

## Pituitary Adenoma

● It is the benign tumour of the pituitary and is the most common cause of hyperpituitarism. Pituitary adenomas are classied on the basis of hormone produced by the tumour cells. The most common pituitary adenoma is prolactinoma, which secretes prolactin and causes galactorrhoea, hypogonadism and in ertility.
It is treated by surgical excision.

## Thyroiditis

● Inflammation of thyroid is called thyroiditis. Hashimoto thyroiditis is an autoimmune disorder causing hypothyroidism, characterised by invasion of the thyroid parenchyma by leucocytes.

## Goitre

● Enlargement of the thyroid gland is called goitre. There are various causes or goitre—neoplastic, inf ammatory, toxic (it has symptoms of hyperthyroidism) and simple goitre (gland is enlarged without any symptoms of hyperthyroidism or hypothyroidism).

## Hyperparathyroidism

● Hyperparathyroidism is commonly due to adenoma, a benign tumour of parathyroid gland. Hypoparathyroidism is less common than hyperparathyroidism, usually seen a ter thyroidectomy, as parathyroid also gets excised along with the thyroid gland during the surgery.

## Hyperadrenalism

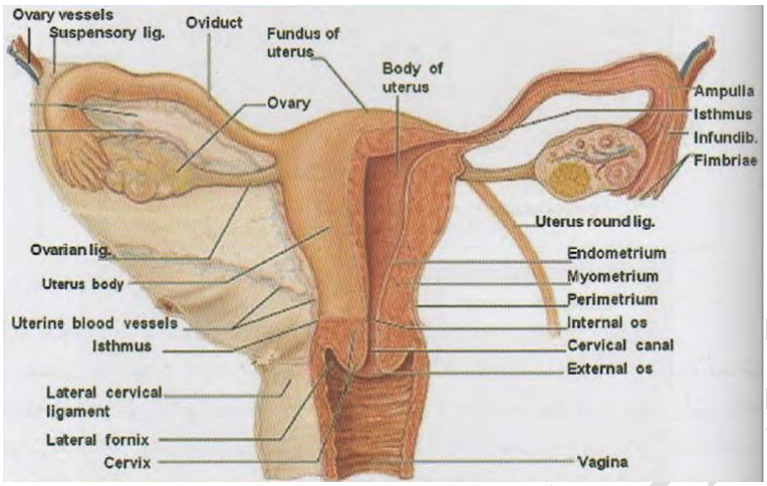
● Hyperplasia of adrenal cortex, the hormone-secreting tumour of the adrenal gland or the pituitary causes hyperadrenalism. Excess glucocorticoids level causes Cushing's syndrome and excess mineralocorticoid causes Conn's syndrome. Hypoadrenalism is caused by damage to the adrenal glands (autoimmune disease, congenital adrenal hypoplasia, tuberculosis, etc.), and it results in Addison's syndrome. Pheochromocytoma is the tumour of the chroma n cells which produce and secrete catecholamines. Hypertension is the most common symptom

*Theortical of Histology*

*Lecture ….12*

# The Female Reproductive System

The system is formed of **internal reproductive organs**: the ovaries, oviducts, uterus and vagina. The **external genitalia** include the labia minora and majora, clitoris and vestibule. Accessory reproductive gland: the mammary gland.




**The Ovaries**

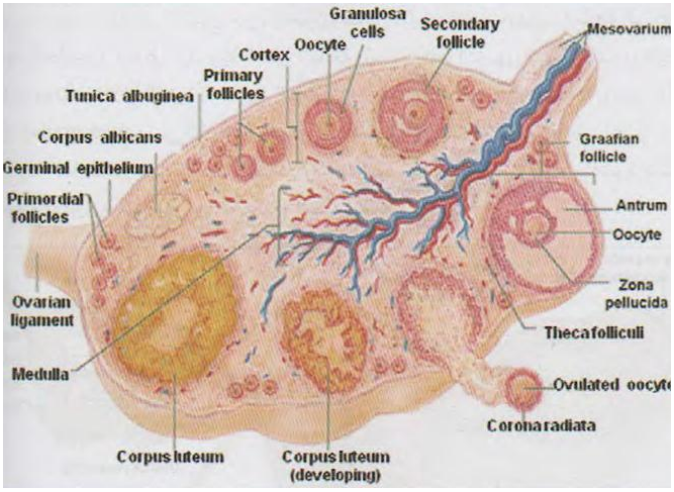
The functions:-

- Production of oocytes

- production and secretion of hormones.

The surface of the ovary is covered by a single layer of cuboidal epithelium called **germinal epithelium.** Fibrous connective tissue forms a thin capsule, the **tunica albuginea**, immediately beneath the epithelium.

The ovary is divided into an outer **cortex** and an inner **medulla**. The cortex consists of a very cellular connective tissue stroma in which the ovarian follicles are embedded. The medulla is composed of loose connective tissue, which contains blood vessels and nerves.




**Ovarian Follicles**

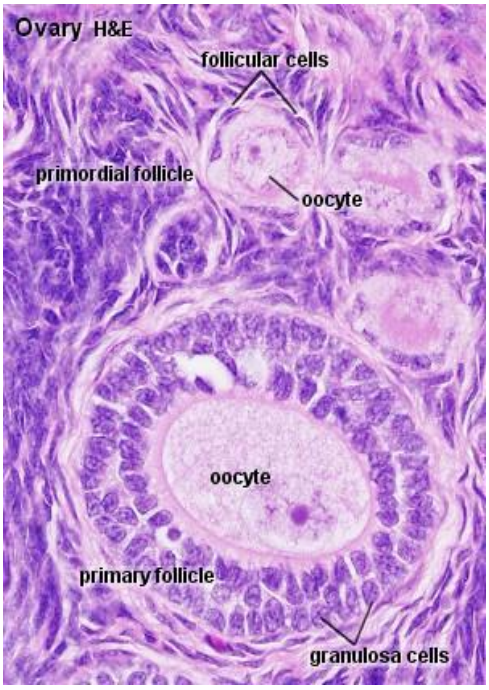
Ovarian follicles consist of one **oocyte** and surrounding **follicular cells**. Follicular development can be divided into :-

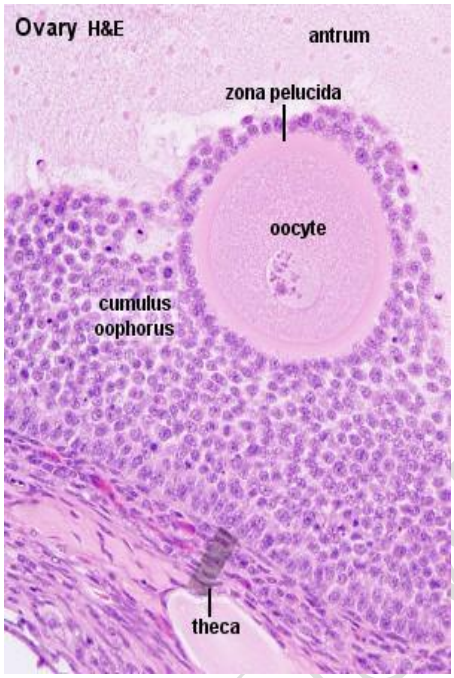
***1-*** **Primordial follicles**: are located in the cortex just beneath **tunica albuginea**. One layer of flattened follicular cells surround the oocyte (about 30 μm in diameter). The nucleus of the oocyte is positioned eccentric in the cell. It appears very light and contains a prominent nucleolus.

***2-*** **The primary follicle**: is the first morphological stage that marks the onset of follicular maturation. The previously flattened cell surrounding the oocyte now form a cuboidal or columnar epithelium surrounding the oocyte. Their cytoplasm may have a granular appearance, and they are for this reason also called **granulosa cells**.

***3-*** **Secondary follicle:** Small fluid-filled spaces become visible between the granulosa cells as the follicle reaches a diameter of about 400 μm. These spaces enlarge and fuse to form the *follicular antrum*, **which is the defining feature of the secondary follicle**. The oocyte is now located eccentric in the follicle in the *cumulus oophorus*, where it is surrounded by granulosa cells. The theca folliculi differentiates with the continued growth of the follicle into a *theca interna* and a *theca externa*.

***4- The mature or tertiary or preovulatory or Graafian follicle***: increases further in size (in particular in the last 12h before ovulation). The Graafian follicle forms a small "bump" on the surface of the ovary, the *stigma* (or macula pellucida). The stigma is characterised by a thinning of the capsule and a progressive restriction of the blood



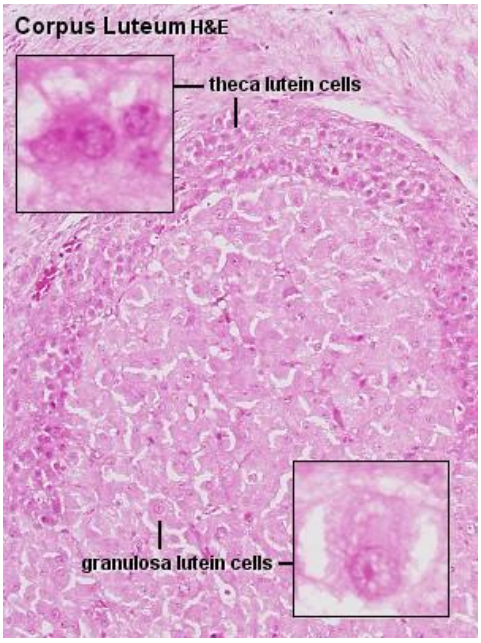



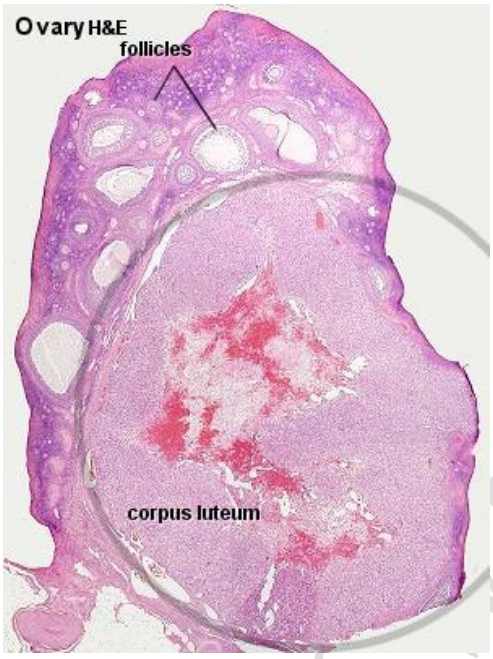



**Atresia**

Atresia is the name for the degenerative process by which oocytes (and follicles) perish without having been expelled by ovulation. Only about 400 oocytes ovulate - about 99.9 % of the oocytes that where present at the time of puberty undergo atresia. Atresia may effect oocytes at all stages of their "life" - both prenatally and postnatally. By the sixth month of gestation about 7 million oocytes and oogonia are present in the ovaries. By the time of birth this number is reduced to about 2 million. Of these only about 400.000 survive until puberty. Atresia is also the mode of destruction of follicles whose maturation is initiated during the cyclus (10-15) but which do not ovulate. Atresia is operating before puberty to remove follicles which begin to mature during this period (none of which are ovulated). Given that atresia affects follicles at various stages of their development it is obvious that the process may take on quite a variety of histological appearances.

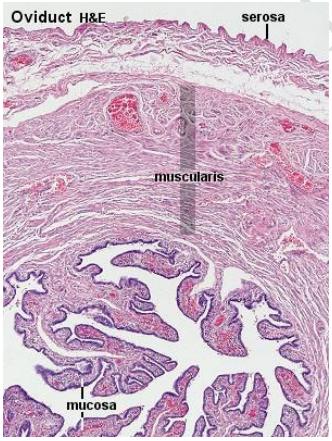
**The Corpus luteum**

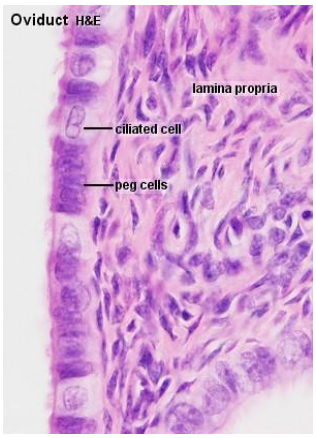



The corpus luteum *is formed by both* ***granulosa cells*** *and* ***thecal cells*** **after ovulation** has occurred. The wall of the follicle collapses into a folded structure, which is characteristic forthe corpus luteum. Vascularization increases and a connective tissue network is formed. Theca interna cells and granulosa cells triple in size and start accumulating lutein hormone within a few hours after ovulation. They are now called *granulosa lutein cells* and *theca lutein cells* and produce *progesterone* and *oestrogens*. Hormone secretion in the corpus luteum ceases within 14 days after ovulation if the oocyte is not fertilised. In this case, the corpus luteum degenerates into a **corpus albicans** - whitish scar tissue within the ovaries. Hormone secretion continues for 2-3 month after ovulation if fertilisation occurs.

## The Oviduct



Oviduct is a nice descriptive term, but not the only one there were other terms *such as Fallopian tubes* or *uterine tubes*. The oviduct functions as a conduit for the oocyte, from the ovaries to the uterus. Histologically, the oviduct consists of a *mucosa*, *muscularis* and serosa.

 ***The mucosa:*** is formed by a simple columnar ciliated and secretory epithelium resting on a lamina propria. The number of ciliated cells and secretory cells varies along the oviduct. Secretory activity varies during the menstrual cycle, and resting secretory cells are also referred to as *peg-cells*. Some of the secreted substances are thought to nourish the oocyte and the very early embryo.

 ***The muscularis***: consists of an inner circular muscle layer and an outer longitudinal layer. An inner longitudinal layer is present in the isthmus and the intramural part of the oviduct.

The oviduct is divided into four subdivisions :-

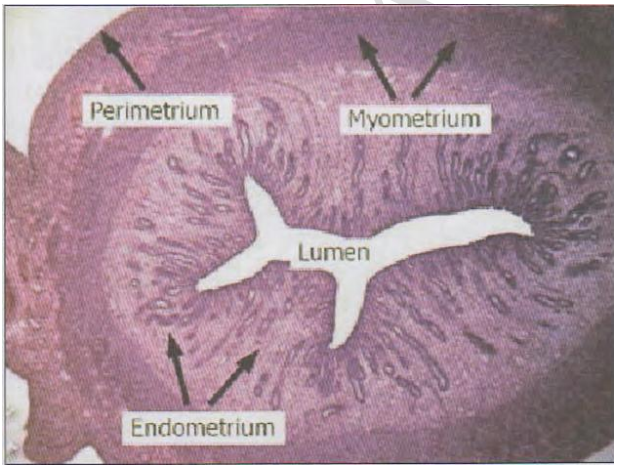
1. The **infundibulum**

2. the **ampulla**

3. The **isthmus**

4.**intramural** part of the oviduct, which penetrates the wall of the uterus.

**The Uterus** :The uterus is divided into *body* (upper two-thirds) and *cervix*. The walls of the uterus are composed of a mucosal layer, the *endometrium*, and a fibromuscular layer, the *myometrium*. The peritoneal surface of the uterus is covered by a serosa.



***Myometrium***: The muscle fibers of the uterus form layers with preferred orientations of fibers (actually 4), but this is very difficult to see in most preparations. The muscular tissue hypertrophies during pregnancy, and GAP-junctions between cells become more frequent.

***Endometrium***: The endometrium consists of a simple columnar epithelium (ciliated cells and secretory cells) and an underlying thick connective tissue stroma. The mucosa is invaginated to form many simple tubular **uterine glands**. The glands extend through the entire thickness of the stroma. The stromal cells of the endometrium are embedded in a network of reticular fibers. The endometrium is subject to cyclic changes that result in menstruation. Only the mucosa of the body of the uterus takes part in the menstrual cycle. The endometrium can be divided into two zones based on their involvement in the changes during the menstrual cycle: the *basalis* and the *functionalis*. The basalis is not sloughed off during menstruation but functions as a regenerative zone for the functionalis after its rejection.

**Vagina**

The vagina is a fibromuscular tube with a wall consisting of three layers: the mucosa, muscularis and adventitia of the vagina


 **Mucosa:** The stratified squamous epithelium (deep stratum basalis, intermediate stratum spinosum, superficial layers of flat eosinophilic cells which do not normally form a true horny layer) rests on a very cellular lamina propria (many leukocytes). Towards the muscularis some *vascular cavernous spaces* may be seen (typical erectile tissue).

 **Muscularis:** Inner circular and outer longitudinal layers of smooth muscle are present. Inferiorly, the striated, voluntary bulbospongiosus muscle forms a sphincter around the vagina.

 **Adventitia:** The part of the adventitia bordering the muscularis is fairly dense and contains many elastic fibers. Loose connective tissue with a prominent venous plexus forms the outer part of the adventitia.

**Female Accessory Reproductive Glands – Mammary Glands**



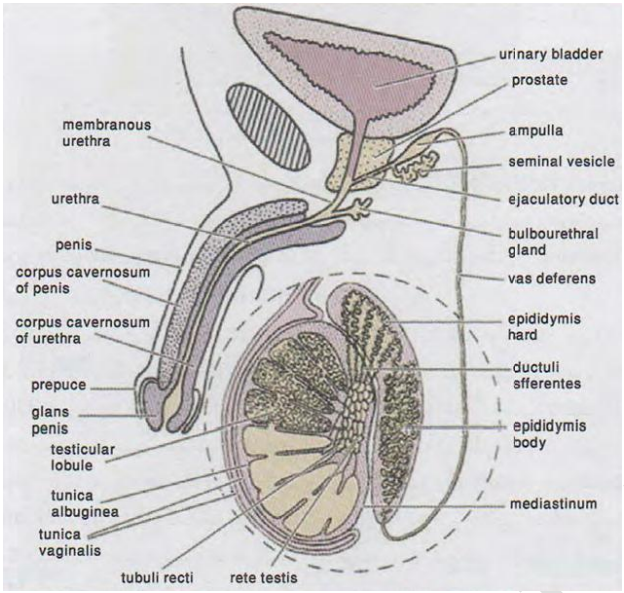
The mammary glands are modified glands of the skin. They are compound branched alveolar glands, which consist of 15-25 lobes separated by dense interlobar connective tissue and fat. Each lobe contains an individual gland. The excretory duct of each lobe, also called *lactiferous duct*, has its own opening on the nipple.

*Theortical of Histology*

*Lecture ….13*

# The Male Reproductive System

The internal male genitalia consist of the testes with the adjoining epididymis, the vas deferens and the accessory sex glands, namely the seminal vesicles, the prostrate and the bulbourethral glands; which sometimes included in the external genitalia.



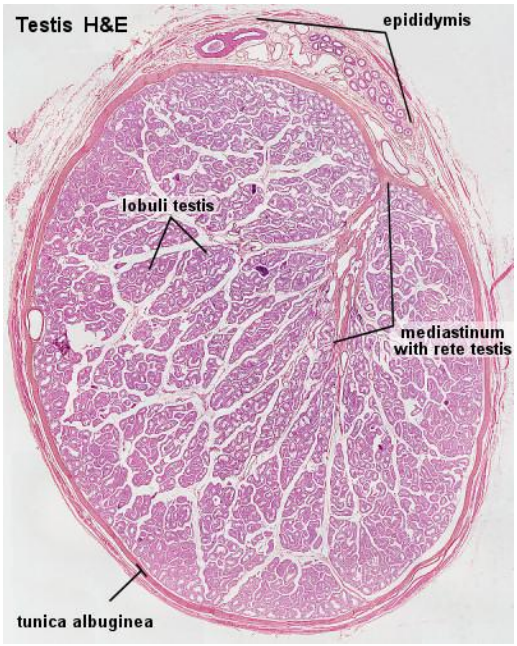

**Testes**

The testes have two functions: they *produce the male gametes or spermatozoa, and they produce male sexual hormone, testosterone*, which stimulates the accessory male sexual organs and causes the development of the masculine extragenital sex characteristics.

The testis is surrounded by a thick capsule, the **tunica albuginea**, from which a conical mass of connective tissue, the **mediastinum testis**, projects into the testis. The tunica albuginea is covered externally by a **serosa**.

From the mediastinum, delicate fibrous septa radiate towards the tunica albuginea and divide the parenchyma of the testis into about 300 **lobuli testis**, which communicate peripherally. Each lobule contains 1-4 **convoluted seminiferous tubules** (about 150-300 μm in diameter, 30-80 cm long). Interstitial tissue between the convoluted tubules is continuous with a layer of loose vascular connective tissue, the *tunica vasculosa testis*, which is found beneath the tunica albuginea.

Each seminiferous tubule continues near the mediastinum into a straight tubule, a *tubulus rectus*. The straight tubules continue into the *rete testis*, a labyrinthine system of cavities in the mediastinum.




**The Convoluted Seminiferous Tubules**

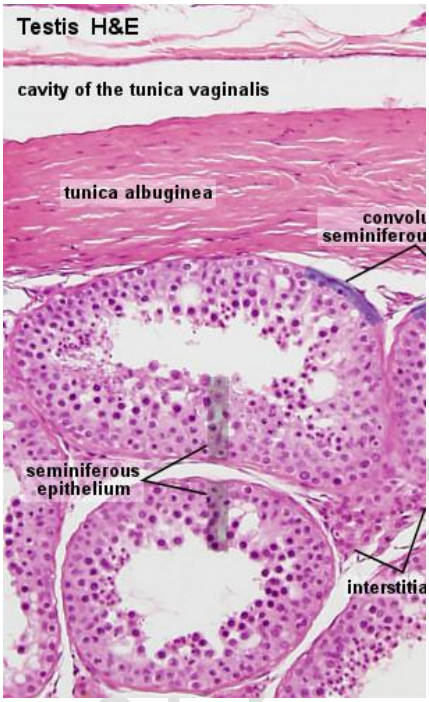
These tubules are enclosed by a thick basal lamina and surrounded by 3-4 layers of smooth muscle cells (or myoid cells). The insides of the tubules are lined with *seminiferous epithelium*, which consists of two general types of cells: *spermatogenic cells and Sertoli cells*.

**Spermatogenic cells**

- **Spermatogonia:** are the first cells of spermatogenesis. They originate in the 4th week of foetal development in the endodermal walls of the yolk sac and migrate to the primordium of the testis, where they differentiate into spermatogonia. Spermatogonia remain dormant until puberty. They are always in contact with the basal lamina of the tubule. Two types of spermatogonia can be distinguished in the human seminiferous epithelium: A,B

- **Primary spermatocytes:** which lie in the cell layer luminal to the spermatogonia. They appear larger than spermatogonia. They immediately enter the prophase of the first meiotic division, which is extremely prolonged (about 22 days!).

A large number of primary spermatocytes is always visible in cross-sections through seminiferous tubules. Cell divisions, from the formation of primary spermatocytes and onwards, to the production of the spermatocytes, are incomplete. The cells remain connected by bridges of cytoplasm. The completion of the first meiotic division results in the formation of - **Secondary spermatocytes:** which are smaller than primary spermatocytes. They rapidly enter and complete the second meiotic division and are therefore seldom seen in histological preparations. Their division results in the formation of - **Spermatids:** which lie in the luminal part of the seminiferous epithelium. They are small (about 10 μm in diameter) with an initially very light (often eccentric) nucleus. The chromatin condenses during the maturation of the spermatids into spermatozoa, and the nucleus becomes smaller and stains darker.

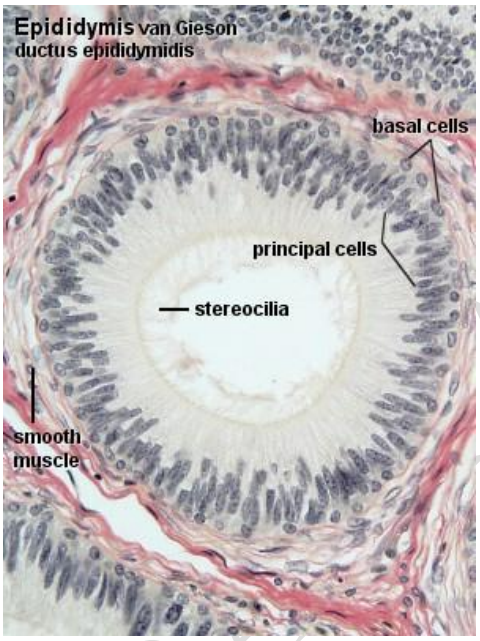



The terminal phase of *spermatogenesis* is called *spermiogenesis* and consists of the differentiation of the newly formed spermatids into **Spermatozoa:** The mature human spermatozoon is about 60 μm long and actively motile. It is divided into head, neck and tail. *It takes about 48 days from the time cells enter meiosis until morphologically mature spermatozoa are formed.*

*Depending on the length of reproduction of spermatogonia (which is not precisely determined) it takes approximately 64 days to complete spermatogenesis.*

Spermatogenesis is regulated by follicle stimulating hormone (FSH), which in males stimulates the spermatogenic epithelium, and luteinizing-hormone (LH), which in males stimulates testosterone production by Leydig cells in the interstitial tissue.
***Sertoli cells***: are far less numerous than the spermatogenic cells and are evenly distributed between them. Their shape is highly irregular - columnar is the best approximation. Sertoli cells extend from the basement membrane to the luminal surface of the seminiferous epithelium. Processes of the Sertoli cells extend in between the spermatogenic cells (cell limits are therefore not clearly visible in the LM).

The nucleus of Sertoli cells is ovoid or angular, large and lightly stained and often contains a large nucleolus. The long axis of the nucleus is oriented perpendicular to wall of the tubule. A fold in the nuclear membrane is characteristic for Sertoli cells but not always visible in the LM



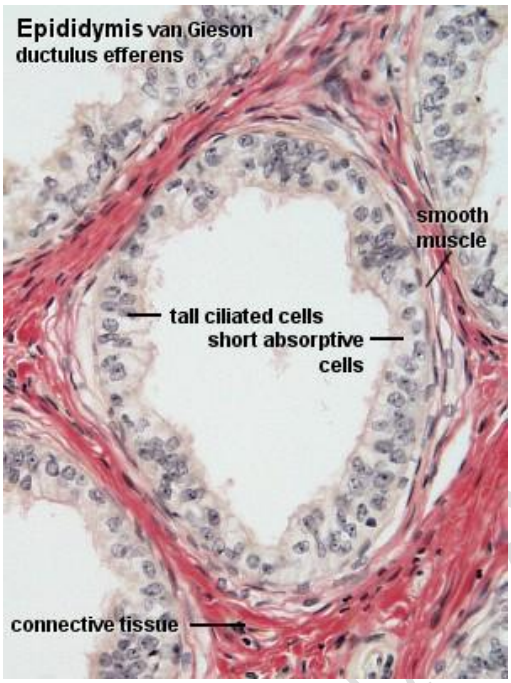

Sertoli cells provide mechanical and nutritive support for the spermatogenic cells. Sertoli cells also secrete two hormones - *inhibin* and *activin* - which provide positive and negative feedback on FSH secretion from the pituitary.

**Interstitial tissue**: *Leydig cells* (15-20 μm), located in the interstitial tissue between the convoluted seminiferous tubules, constitute the *endocrine component of the testis*. *They synthesise and secrete testosterone*. Ledig cells occur in clusters , which are

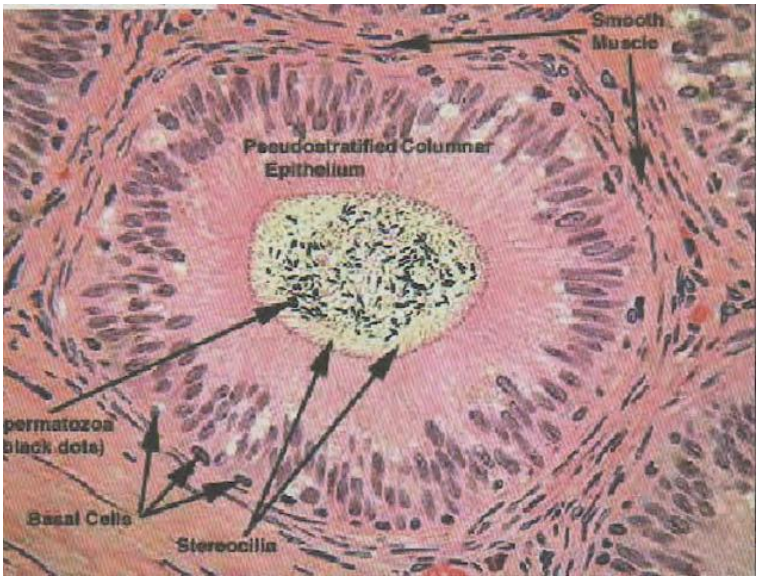
variable in size and richly supplied by capillaries. The cytoplasm is strongly acidophilic and finely granular. The nucleus is large, round and often located eccentric in the cell.

**Ducts of the Testis**

Spermatozoa pass via the *tubuli recti* (low columnar epithelium) and the *rete testis* (flattened or cuboidal epithelium) into numerous *ductuli efferentes*, which are lined by a columnar epithelium, which consists of both absorptive and ciliated cells. *The height of the two cells types which form the epithelium of the ductuli efferentes is variable which gives the lumen a characteristic wavy outline*.

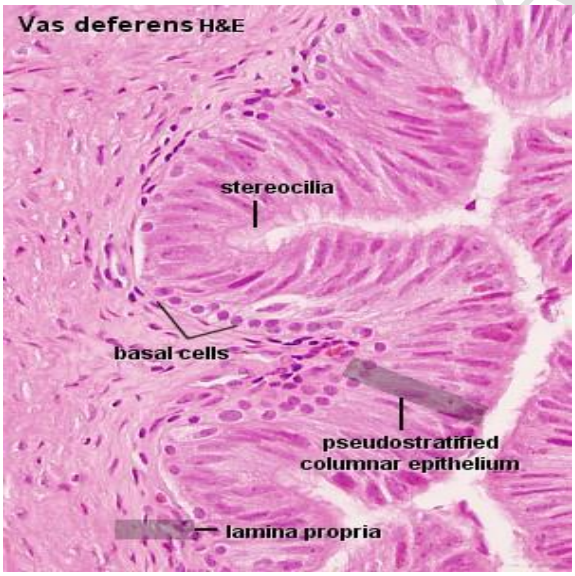



Peristaltic contractions of smooth muscle cells surrounding the ductus epididymidis move the spermatozoa towards the *middle segment of the duct, which is the site of final functional maturation of the spermatozoa* - now they are motile. *The terminal segment of the ductus epididymidis is the site of storage of the mature spermatozoa*. Smooth muscle fibres of the terminal part of the ductus epididymidis do not contract spontaneously. They contract during sexual stimulation concurrently with the contraction of the musculature of the duct into which it opens, the vas deferens.




**The Vas deferens (or ductus deferens)**

The *mucosa* of the vas deferens forms low longitudinal folds. It is lined by a pseudostratified columnar epithelium. Similar to the epididymis, cells have long stereocilia. The lamina propria is unusually rich in elastic fibres. The *muscularis* is well developed (up to 1.5 mm thick) and consists of a thick circular layer of smooth muscle between thinner inner and outer longitudinal layers. The muscularis is the structure which makes the vas deferens palpable in the spermatic cord. The vas deferens is surrounded by an adventitia, which is slightly denser than usual.




**Male Accessory Reproductive Glands**

The accessory (or secondary) male sex glands consist of the seminal vesicles, the prostrate and the bulbourethral glands.

**Prostate**

The prostate is the largest accessory sex gland in men (about 2 × 3 × 4 cm). It contains 30 - 50 tubuloalveolar glands, which empty into 15 - 25 independent excretory ducts. These ducts open into the urethra. The glands are embedded into a fibromuscular stroma, which mainly consists of smooth muscle separated by strands of connective tissue rich in collagenous and elastic fibres. The muscle forms a dense mass around the urethra and beneath the fairly thin capsule of the prostrate.

*The secretion of the prostate contains citric acid, the enzyme fibrinolysin (liquefies the semen), acid phosphatase, a number of other enzymes and lipids*. The secretion of the prostate is the first fraction of the ejaculate.

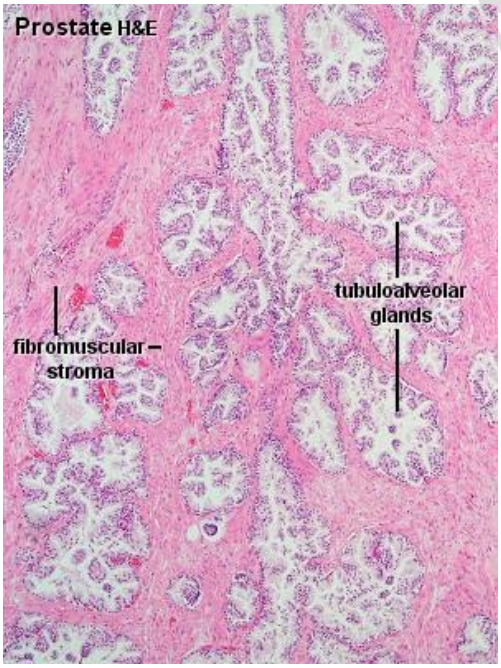
The secretory ducts of the prostate are lined by a simple columnar epithelium, which changes to a transitional epithelium near the openings of the ducts into the urethra.

In good histological sections it is possible to distinguish three concentric zones, which surround the prostatic part of the urethra.

 The peripheral zone contains large, so-called *main glands*, whose ducts run posteriorly to open into the urethra.

 The internal zone consists of the so-called *submucosal glands*, whereas

 the innermost zone contains *mucosal glands*.



**Seminal Vesicles**

The seminal vesicles develop from the vas deferens. Their histological organisation resembles to some extent that of the vas deferens. The **mucosa** shows thin, branched, anastomosing folds. The structure of the epithelium is variable appearing columnar or pseudostratified columnar (columnar cells and basal cells). The lamina propria of the mucosa is fairly thin and loose. The *muscularis* consists of inner circular and outer longitudinal layers of smooth muscle.

Seminal vesicles were thought to store semen - hence there name. This turned out to be wrong. They are glands, whose secretion constitutes 60-70 % of the ejaculate. The secretory product of the columnar cell, which may be seen in the lumen of the seminal vesicles, is strongly acidophilic. It contains large amounts of *fructose* which the spermatozoa utilise as a source of energy. Furthermore, the secretion contains prostaglandins, flavins (yellow fluorescing pigment - of use in forensic medicine to detect semen stains) and several other proteins and enzymes.

The cocktail of compounds which is released by the seminal vesicles in addition to fructose has three main functions:

1. the formation of the sperm coagulum,
2. the regulation of sperm motility and
3. the suppression of immune function in the female genital tract.

The secretion of the seminal vesicles is the third fraction of the ejaculate (the spermatozoa are released with the second fraction - the contents of the vas deferens).