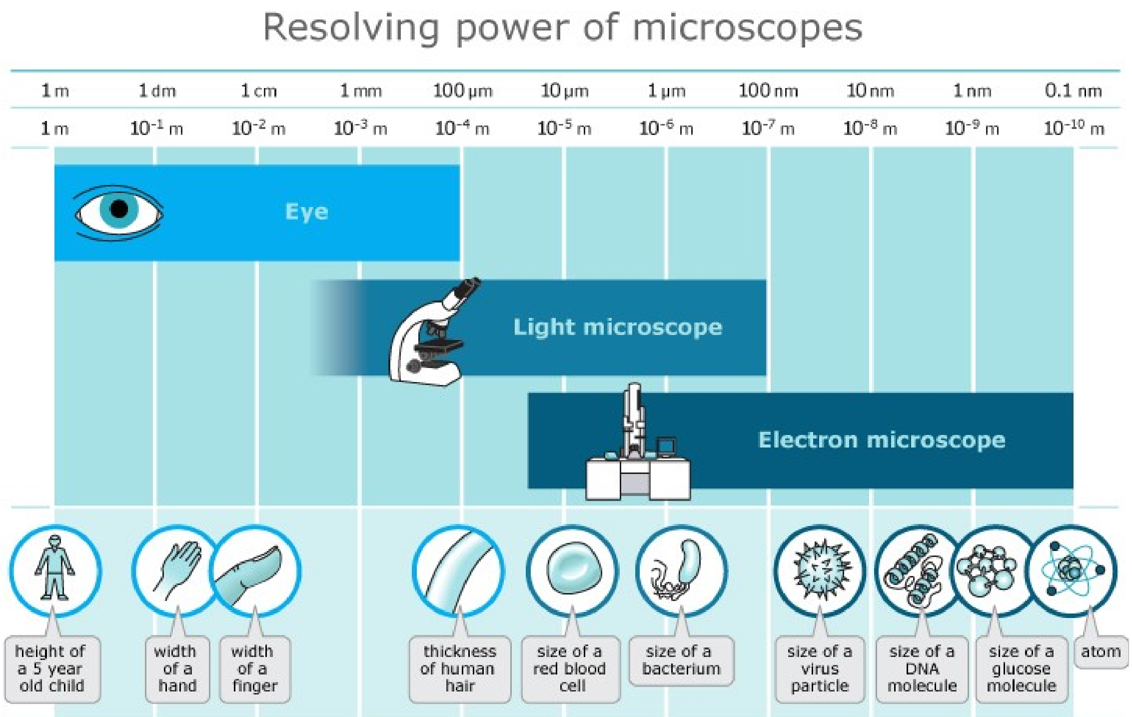
The microscope is one of the cell biologists most important tools. The vast majority of living organisms are too small to be seen in any detail with the human eye, and cells and their organelles can only be seen with the aid of a microscope. The most important features of a microscope are **Magnification** and **Resolution.**

- ✓ **Magnification** is how much bigger a sample appears to be under the microscope than it is in real life .
- ✓ **Resolution** is the ability to distinguish between two points on an image i.e. the amount of detail.

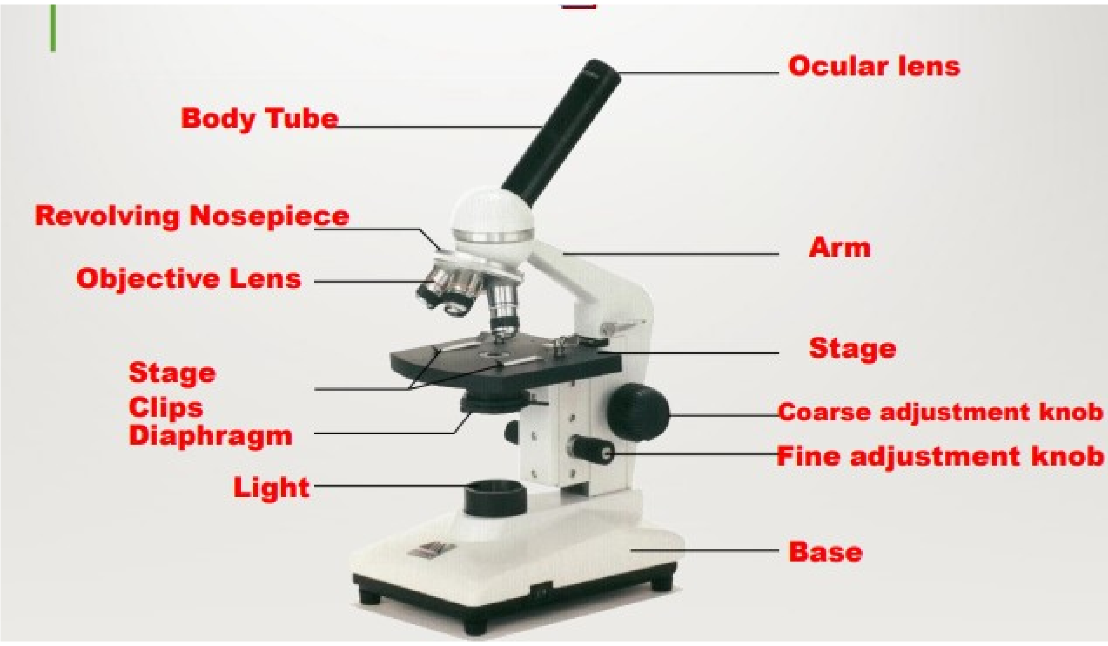
The resolution of an image is limited by the wavelength of radiation used to view the sample. This is because when objects in the specimen are much smaller than the wavelength of the radiation being used, they do not interrupt the waves, and so are not detected. The wavelength of light is much larger than the wavelength of electrons, so the resolution of the light microscope is a lot lower. Using a microscope with a more powerful magnification will not increase this resolution any further. It will increase the size of the image, but objects closer than 200nm will still only be seen as one point.



Types of microscopes

- Light Microscope
- •Dissection Microscope
- •Scanning Electron Microscope (SEM(
- •Transmission Electron Microscope (TEM)

Microscope Parts



Making histological sections for the light microscope.

Techniques

For light microscopy, three techniques can be used: the **paraffin technique**, **frozen sections**, and **semithin sections**.

The **paraffin technique** is the most commonly used. Once the sections are prepared, they are usually stained, to help distinguish the components of the tissue. Unstained, it's hard to make out much detail, because the optical density of the different tissue components is very similar.Section are prepared for the electron microscope using a method similar to that for semithin sections.

What is the paraffin technique?

In this technique, tissues are fixed, and embedded in wax. This makes the tissue hard, and much easier to cut sections from. The sections are then stained, and examined with the light microscope.

1. Fixation:

Square tissue blocks (about 1cm in each dimension), or whole organs, are fixed by chemical fixation:

The chemical added binds to and cross-links some proteins, and denatures other proteins through dehydration. This hardens the tissue, and inactivates enzymes that might otherwise degrade the tissue. Fixation also kills bacteria etc. It can also enhance tissue staining. The fixative most commonly used is a 4% of formaldehyde, (= 10% formalin) at neutral pH.

2. Dehydration and clearing:

To cut sections, the tissue has to be embedded in paraffin wax, but wax is not soluble in water or alcohol. However, it is soluble in a paraffin solvent called 'xylene'. Therefore, the water in the tissue needs to be replaced with xylene. To do this, first the tissue has to be dehydrated, by gradually replacing water in the sample with alcohol. This is achieved by passing the tissue through increasing concentrations of ethyl alcohol (from 0 to 100%). Finally, once the water has been replaced by 100% alcohol, the alcohol is replaced with xylene, which is miscible with alcohol. This final step is called 'clearing'.

3. Embedding:

The tissue is placed in warm paraffin wax, and the melted wax fills the spaces that used to have water in them. After cooling, the tissue hardens, and can be used to cut slices (sectioned).

4. Sectioning:

The tissue is trimmed, and mounted on a cutting device called a microtome (shown in the picture). Thin sections are cut, which can be stained and mounted on a microscope slide.

5. Staining and Mounting:

Unfortunately, most staining solutions are aqueous, so to stain the sections, the wax has to be dissolved and replaced with water (rehydration). This is essentially step 2 in reverse. The sections are passed through xylene, and then decreasing strengths of alcohol (100% to 0%) and finally water. Once stained, the section is then dehydrated once again, and placed in xylene. It is then mounted on the microscope slide in mounting medium dissolved in xylene. A coverslip is placed on top, to protect the sample. Evaporation of xylene around the edges of the coverslip, dries the mounting medium and bonds the coverlips firmly to the slide.

Are there any other ways of making sections for the light microscope?

There are two further ways that are sometimes used:

Frozen sections:

Tissues are frozen rapidly in liquid nitrogen, and then cut in a refrigerated cabinet (a cryostat) with a cold knife, then stained and observed in the microscope. This procedure is faster, and can preserve some tissue details that may be lost by the paraffin technique. Sections are 5 - 10 µm thick.

Semithin sections:

It is sometimes hard to see detail in thick sections. To get around this, sections can be embedded in epoxy or acrylic resin, which enable thinner sections (less than 2 µm) to be cut.

Kinds of histological stains

Most cells are colourless and transparent, and therefore histological sections have to be stained in some way to make the cells visible. The techniques used can either be non-specific, staining most of the cells in much the same way, or specific, selectively staining particular chemical groupings or molecules within cells or tissues. Staining usually works by using a dye, that stains some of the cells components a bright colour, together with a counterstain that stains the rest of the cell a different colour.

Basophilic and acidophilic staining.

Acidic dyes react with cationic or basic components in cells. Proteins and other components in the cytoplasm are basic, and will bind to acidic dyes. *Basic dyes* react with anionic or acidic components in cells. Nucleic acids are acidic, and therefore bind to basic dyes .

H&E staining

The most commonly used staining system is called H&E (Haemotoxylin and Eosin). H&E contains the two dyes haemotoxylin and eosin. Eosin is an acidic dye: it is negatively charged. It stains basic (or acidophilic) structures red or pink. This is also sometimes termed 'eosinophilic'. Haematoxylin can be considered as a basic dye: it is positively charged. It is used to stain acidic (or basophilic) structures a purplish blue.

This means that the nucleus, and parts of the cytoplasm that contain RNA stain up in one colour (purple), and the rest of the cytoplasm stains up a different colour (pink)

What structures are stained purple (basophilic)

DNA (heterochromatin and the nucleolus) in the nucleus, and RNA in ribosomes and in the rough endoplasmic reticulum are both acidic, and so haemotoxylin binds to them and stains them purple. Some extracellular materials (i.e. carbohydrates in cartilage) are also basophilic.

What structures are stained pink (eosinophilic or acidophilic)

Most proteins in the cytoplasm are basic, and so eosin binds to these proteins and stains them pink. This includes cytoplasmic filaments in muscle cells, intracellular membranes, and extracellular fibres

Histological Stains other than H&E

1. Periodic acid-Schiff reaction (PAS)
2. Masson's trichrome.
3. Alcian blue
4. van Gieson
5. Reticulin Stain
6. Azan
7. Giemsa.
8. Toluidine blue.
9. Silver and gold methods.
10. Chrome alum/haemotoxylin.
11. Isamin blue/eosin
12. Nissl and methylene blue
13. Sudan Black and osmium.

Hemostasis

Hemostasis is a sequence of responses that stops bleeding. When blood vessels are damaged or ruptured, the hemostatic response must be quick, localized to the region of damage, and carefully controlled in order to be effective. Three mechanisms reduce blood loss: (1) vascular spasm, (2) platelet plug formation, and (3) blood clotting (coagulation). When successful, hemostasis prevents hemorrhage, (hemorrhage means the loss of a large amount of blood from the vessels). Hemostatic mechanisms can prevent hemorrhage from smaller blood vessels, but extensive hemorrhage from larger vessels usually requires medical intervention.

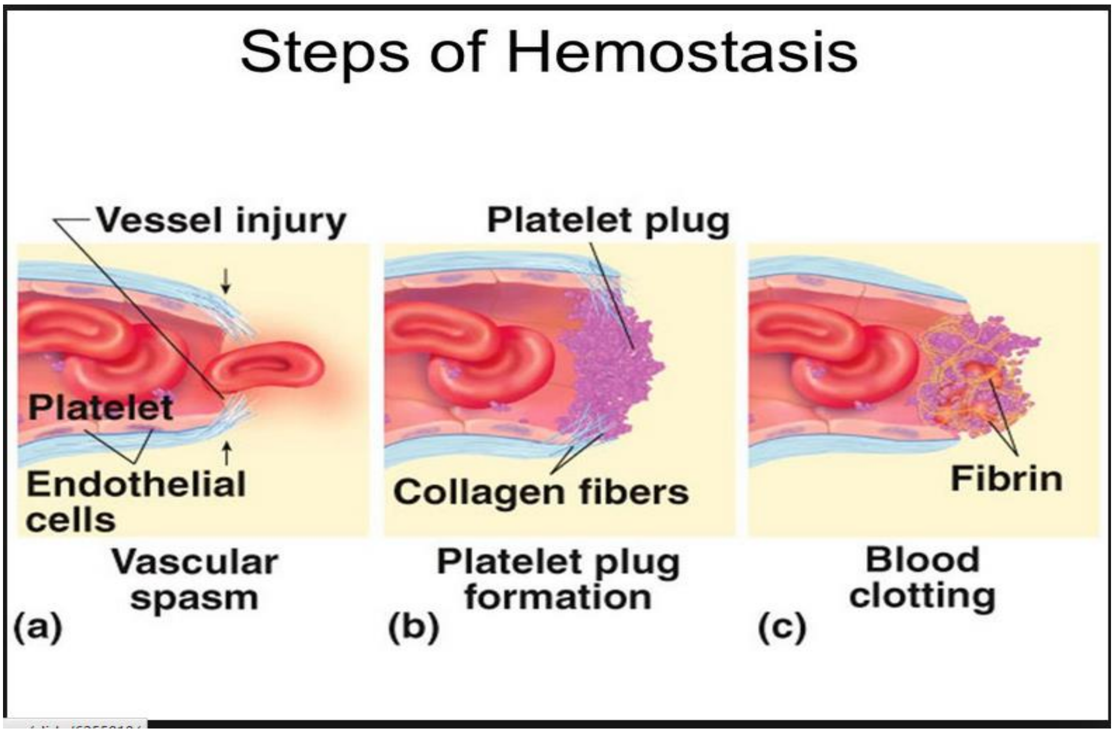
1. **Vascular spasm**

When arteries or arterioles are damaged, the circularly arranged smooth muscle in their walls contracts immediately, a reaction called vascular spasm. This reduces blood loss for several minutes to several hours, during which time the other hemostatic mechanisms go into operation.

This response is triggered by factors such as a direct injury to vascular smooth muscle, chemicals released by endothelial cells and platelets, and reflexes initiated by local pain receptors. The spasm response becomes more effective as the amount of damage is increased.

2. **Platelet plug formation** – Platelets adhere to damaged endothelium to form platelet plug (*primary hemostasis*) and then degranulate. This process is regulated through thromboregulation. Platelets play one of the biggest factors in the hemostatic process. Being the second step in the sequence they stick together (aggregation) to form a plug that temporarily seals the break in the vessel wall. As platelets adhere to the collagen fibers of a wound they become spiked and much stickier. They then release chemical messengers such as adenosine diphosphate (ADP), serotonin and thromboxane A2. These chemicals are released to cause more platelets to stick to the area and release their contents and enhance vascular spasms. As more chemicals are released more platelets stick and release their chemicals.. Platelets alone are responsible for stopping the bleeding of unnoticed wear and tear of our skin on a daily basis.

3. **Blood coagulation** – Clots form upon the conversion of fibrinogen to fibrin, and its addition to the platelet plug (*secondary hemostasis*). Coagulation: The third and final step in this rapid response reinforces the platelet plug. Coagulation or blood clotting uses fibrin threads that act as a glue for the sticky platelets. As the fibrin mesh begins to form the blood is also transformed from a liquid to a gel like substance through involvement of clotting factors and pro-coagulants. The coagulation process is useful in closing up and maintaining the platelet plug on larger wounds. The release of Prothrombin also plays an essential part in the coagulation process because it allows for the formation of a thrombus, or clot, to form. This final step forces blood cells and platelets to stay trapped in the wounded area. Though this is often a good step for wound healing, it has the ability to cause severe health problems if the thrombus becomes detached from the vessel wall and travels through the circulatory system; If it reaches the brain, heart or lungs it could lead to stroke, heart attack, or pulmonary embolism respectively. However, without this process the healing of a wound would not be possible.



Epithelial tissue, or epithelium, has the following general characteristics:

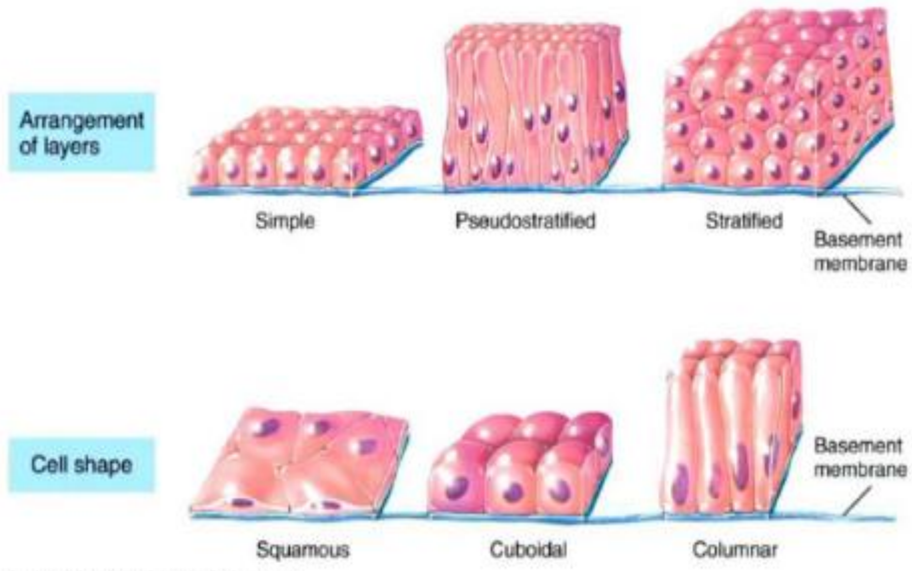
- Epithelium consists of closely packed, flattened cells that make up the inside or outside lining of body areas. There is little intercellular material.
- The tissue is **avascular,** meaning without blood vessels. Nutrient and waste exchange occurs through neighboring connective tissues by diffusion.
- The upper surface of epithelium is free, or exposed to the outside of the body or to an internal body cavity. The basal surface rests on connective tissue. A thin, extracellular layer called the *basement membrane* forms between the epithelial and connective tissue.

<u>There are two kinds of epithelial tissues:</u>

A. *Covering and lining epithelium* covers the outside surfaces of the body and lines internal organs.
B. *Glandular epithelium* secretes hormones or other products.

A .Epithelium that covers or lines

Epithelial tissues that cover or line surfaces are classified by cell shape and by the number of cell layers. The following terms are used to describe these features.



Cell shape:

- *Squamous cells* are flat. The nucleus, located near the upper surface.
- *Cuboidal cells* are cube- or hexagon-shaped with a central, round nucleus. These cells produce secretions (sweat, for example) or absorb substances such as digested food.
- *Columnar cells* are tall with an oval nucleus near the basement membrane. These thick cells serve to protect underlying tissues or may function to absorb substances. Some have microvilli, minute surface extensions, to increase surface area for absorbing substances, while others may have cilia that help move substances over their surface (such as mucus through the respiratory tract).
- *Transitional cells* range from flat to tall cells that can extend or compress in response to body movement.

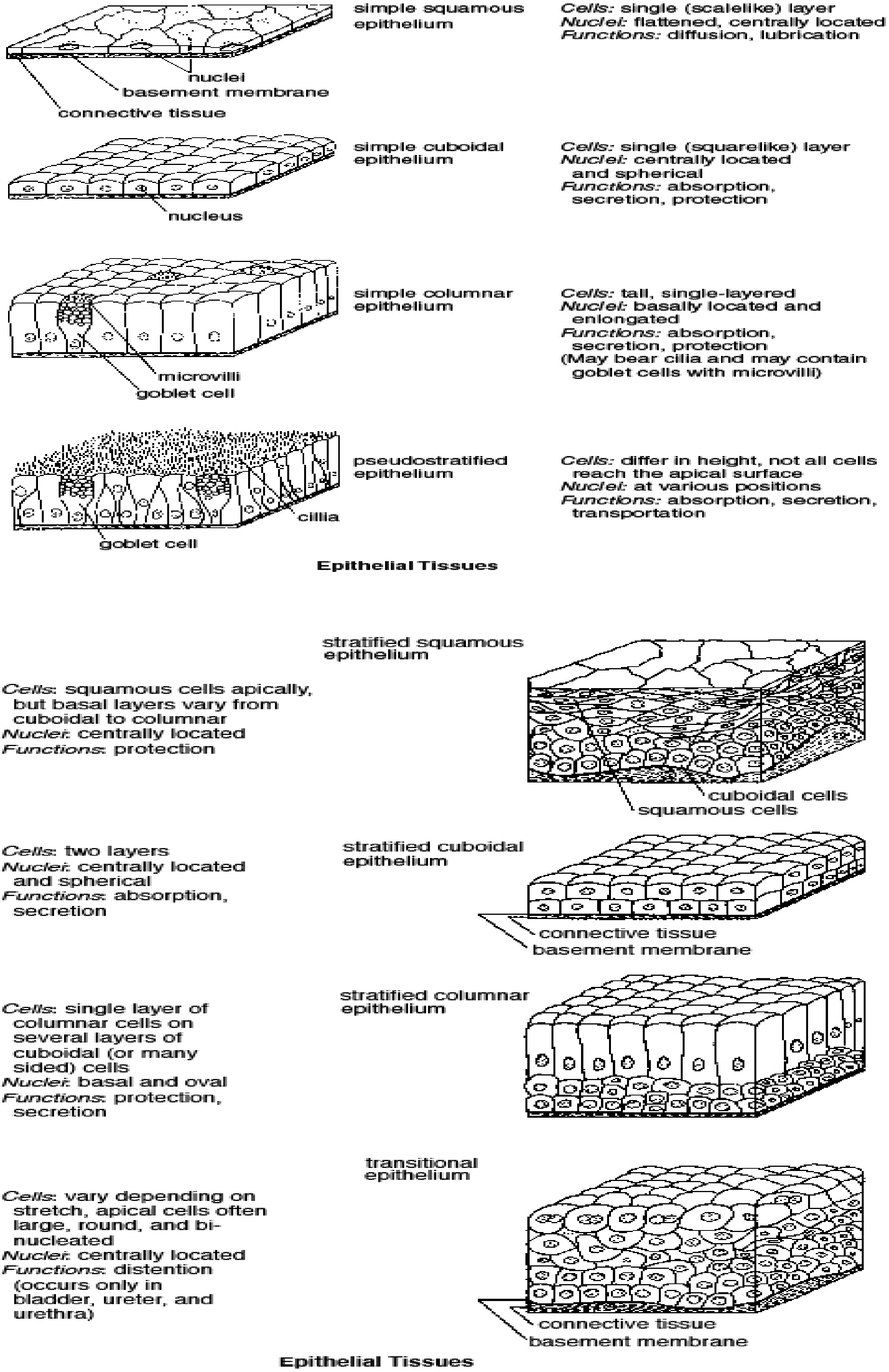
Number of cell layers:

- *Simple epithelium* describes a single layer of cells.
- *Stratified epithelium* describes epithelium consisting of multiple layers.
- *Pseudostratified epithelium* describes a single layer of cells of different sizes, giving the appearance of being multilayered.

Names of epithelial tissues include a description of both their shape and their number of cell layers. The presence of cilia may also be identified in their names. For example, simple squamous describes epithelium consisting of a single layer of flat cells. Pseudostratified columnar ciliated epithelium describes a single layer of tall, ciliated cells of more than one size. Stratified epithelium is named after the shape of the outermost cell layer. Thus, stratified squamous epithelium has outermost layers of squamous cells, even though some inner layers consist of cuboidal or columnar cells.

These and other epithelial tissues are illustrated in Figure 1.

Figure 1. Types of epithelial tissues.



B. Glandular epithelium

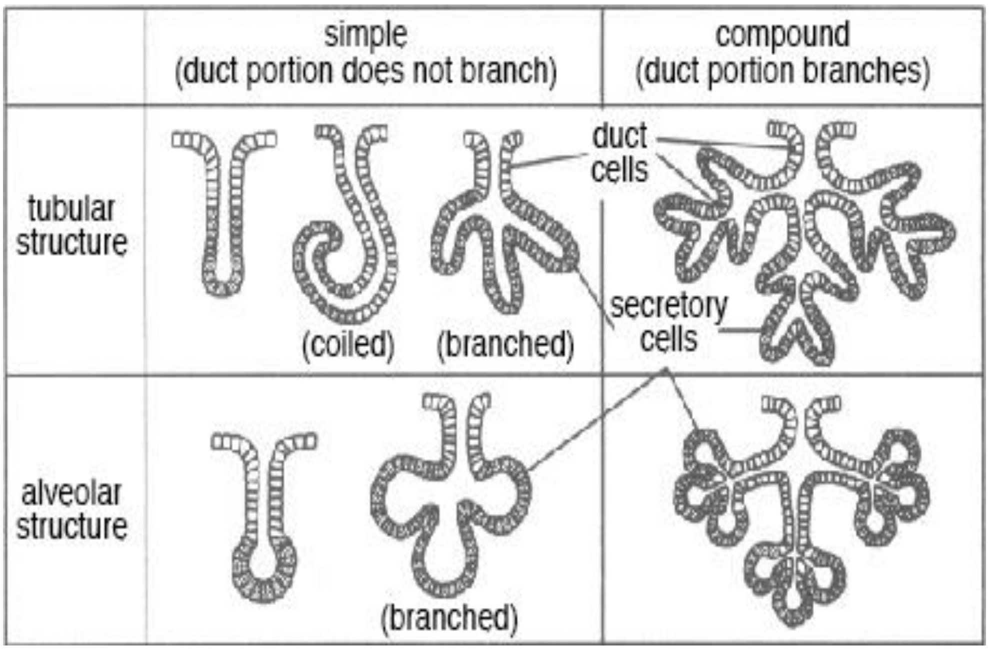
Glandular epithelium forms two kinds of glands:

- *Endocrine glands* secrete **hormones** directly into the bloodstream. For example, the thyroid gland secretes the hormone thyroxin into the bloodstream, where it is distributed throughout the body, stimulating an increase in the metabolic rate of body cells.
- *Exocrine glands* secrete their substances into tubes, or ducts, which carry the secretions to the epithelial surface. Examples of secretions include sweat, saliva, milk, stomach acid, and digestive enzymes.

Exocrine glands are classified according to their structure (see Figure 2):

- Unicellular or multicellular describes a single-celled gland or a gland made of many cells, respectively. A multicellular gland consists of a group of secretory cells and a duct through which the secretions pass as they exit the gland.
- Branched refers to the branching arrangement of secretory cells in the gland.
- Simple or compound refers to whether the duct of the gland (not the secretory portion) does or does not branch, respectively.
- Tubular describes a gland whose secretory cells form a tube, while alveolar (or acinar) describes secretory cells that form a bulblike sac.

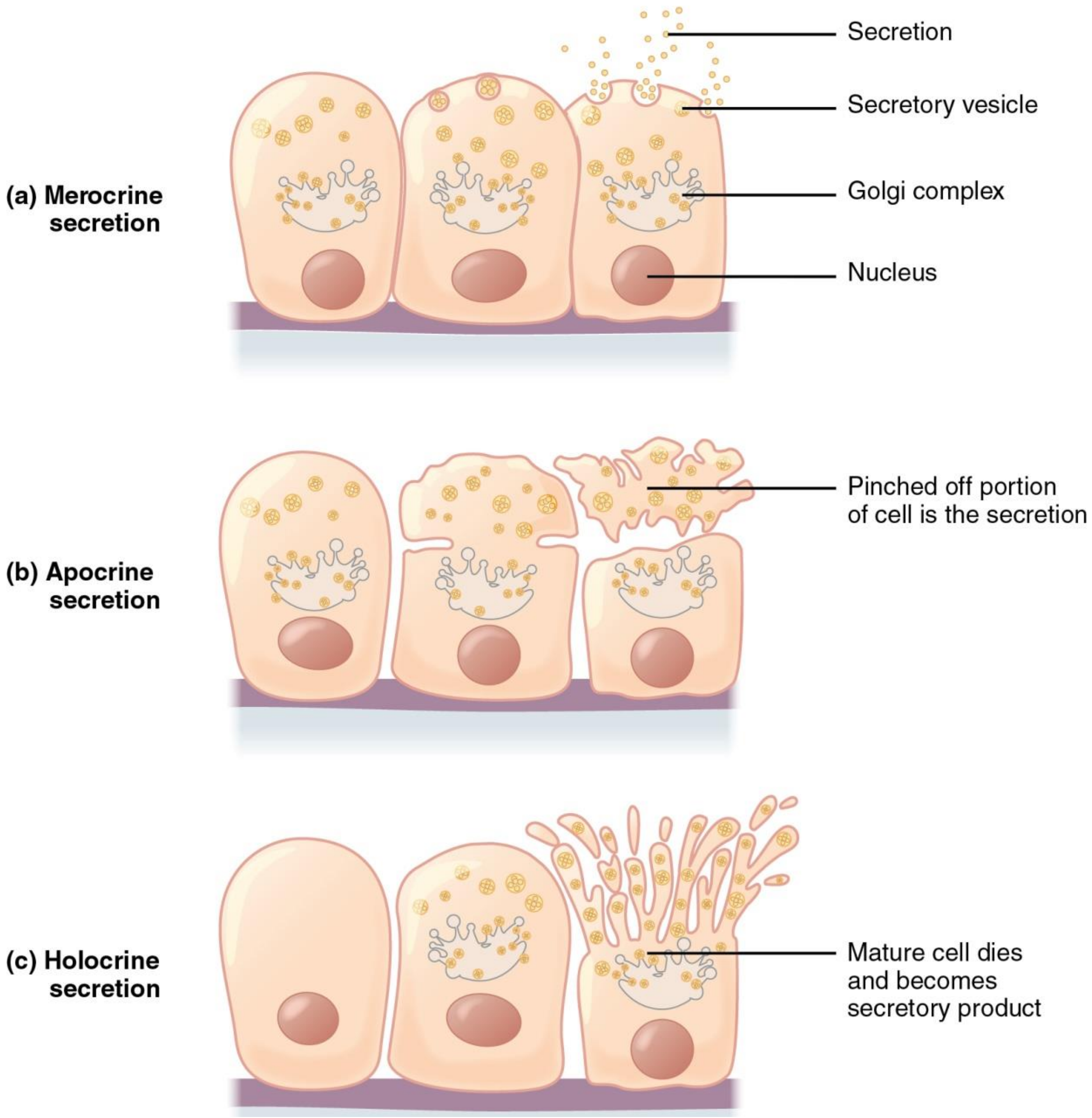
Figure 2. Exocrine glands can be classified as simple or compound with either a tubular or alveolar structure.



Exocrine glands are also classified according to their function (see Figure 3):

- In merocrine glands, secretions pass through the cell membranes of the secretory cells (exocytosis). For example, goblet cells of the trachea release mucus via exocytosis.
- In apocrine glands, a portion of the cell containing secretions is released as it separates from the rest of the cell. For example, the apical portion of lactiferous glands release milk in this manner.
- In holocrine glands, entire secretory cells disintegrate and are released along with their contents. For example, sebaceous glands release sebum to lubricate the skin in this manner.

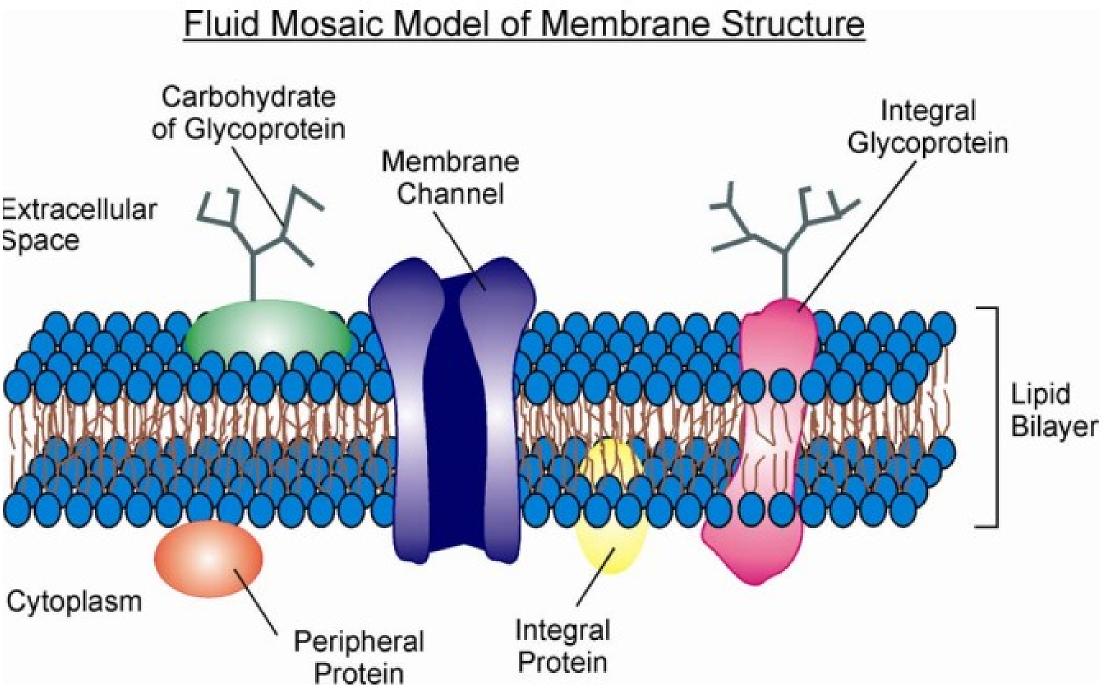
Figure 3. Exocrine glands can be classified according to their function.



The cell membrane (plasma membrane) is a thin semi-permeable membrane that surrounds the cytoplasm of a cell. It controls how substances can move in and out of the cell and is responsible for many other properties of the cell as well. The membranes that surround the nucleus and other organelles are almost identical to the cell membrane.

▪ Cell Membrane Structure

The most widely accepted model of plasma membrane structure is the **fluid mosaic model** of Singer & Nicolson (1972).The fluid mosaic model indicates that the cell membrane is not solid. It is flexible and has a similar consistency to vegetable oil, so all the individual molecules are just floating in a fluid medium, and they are all capable of moving sideways within the cell membrane. Mosaic refers to something that contains many different parts. The plasma membrane is a mosaic of phospholipids, cholesterol molecules, proteins and carbohydrates.



The molecular composition of cell membrane includes mainly 3 components**:**

A. Cell Membrane Lipid

B. Cell Membrane Protein

C. Cell Membrane Carbohydrate

Cell Membrane proteins

Proteins constituting 25 to 75% of the mass the of various membranes of the cells .These proteins are divided into two general classes , based on the nature of their association with the membrane :

1. **Integral membrane proteins** , They are partially embedded in lipid bilayer or formed of transmembrane proteins ,they are exposed on both sides of the membrane.

2. **Peripheral membrane proteins** They are located on inner or outer surfaces of lipid bilayer and attached to the integral membrane proteins or the phospholipid molecules.

Proteins found in plasma membrane serve different functions:

1. **Channel Proteins** - form small openings for molecules to diffuse through the membrane.
2. **Carrier Proteins**- binding site on protein surface "grabs" certain molecules and pulls them into the cell.
3. **Receptor Proteins** - molecular triggers that set off cell responses (such as release of hormones or opening of channel proteins)
4. **Cell Recognition Proteins**, to identify cells to the body's immune system.
5. **Enzymatic Proteins** - carry out metabolic reaction.

▪ Function of Cell Membrane

1. Isolate the cytoplasm from the external environment.
2. Regulate the exchange of substance.
3. Communicate with other cells.
4. Identification.
5. The cell membrane also plays a role in anchoring the cytoskeleton to provide shape to the cell.

▪ Cell Membrane Specialization.

➢ **lateral modification of plasma membrane:**
The lateral parts of the cell membrane can show , several specialization that form "intercellular junctions"

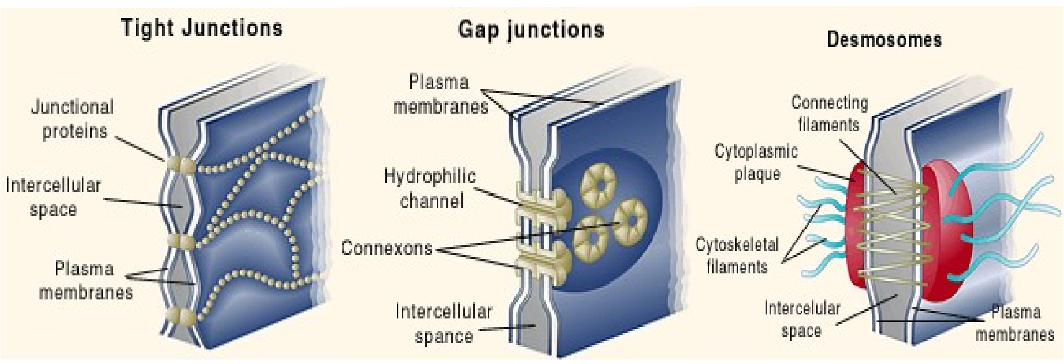
Functions of these junctions:
1-They are the sites of adhesion between adjacent cell.
2-They prevent the flow of materials through the intercellular.
3- They help in the cellular communication.

There are three types of lateral junctions :

a) **Tight Junction** : Seal membranes of adjacent animal cells together, preventing substances from moving through the spaces between the cells; in the intestine the digestive juices stay out of the body, and the kidneys the urine stay within the kidney tubules.

b) **Gap junctions:** Are proteins complexes form channels in membranes, allowing communication between cytoplasm of adjacent animal cells by channel is lined by six plasma membrane proteins; in heart muscle & smooth muscle, because they permit a flow of ions that is required for the cells to contract muscle and smooth muscle because they permit a flow of ions that is required for the cells to contact.

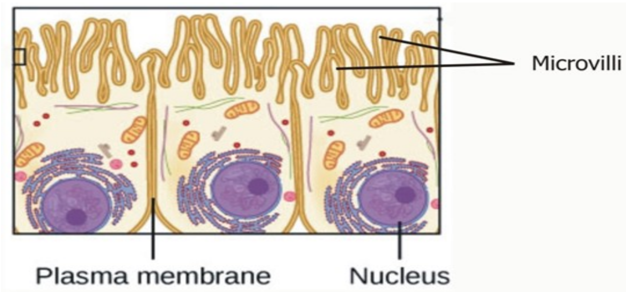
c) **Adhesion junctions (desmosomes) :** Desmosomes links adjacent animal cells together .It found in heart , stomach & bladder .



➢ Apical modification of plasma membrane:

a) Microvilli:

Fingers like extensions of plasma membrane that are particularly abundant on the surface of the cells, involved in the absorption, such as the epithelial cells lining the intestine.

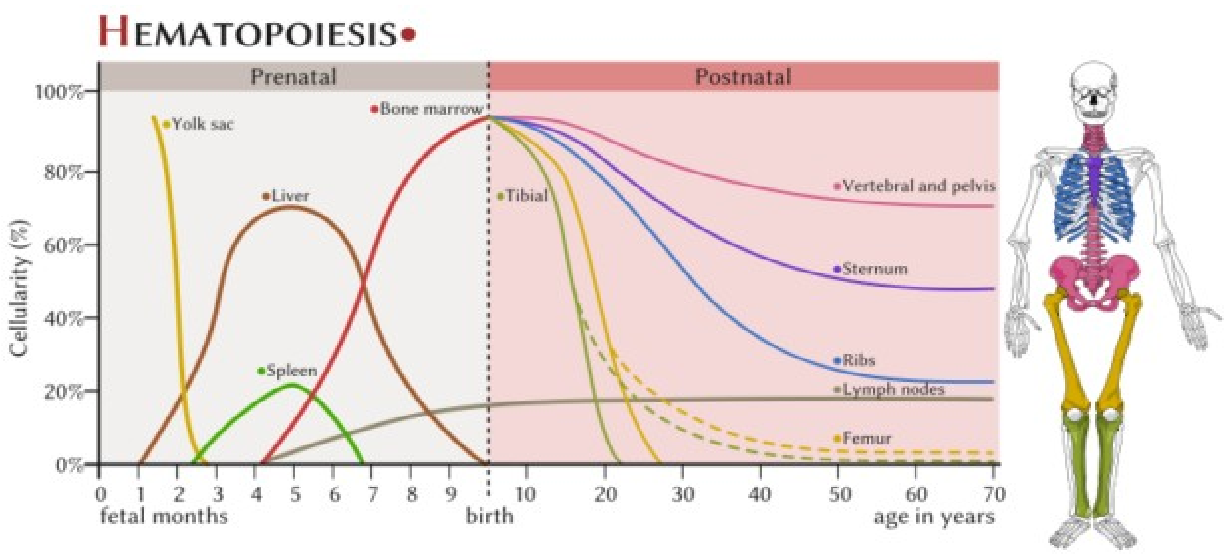


b) Stereocilia:

Specialized form of microvilli. The stereocilia of auditory hair cells, are responsible for hearing by detecting sound vibrations.

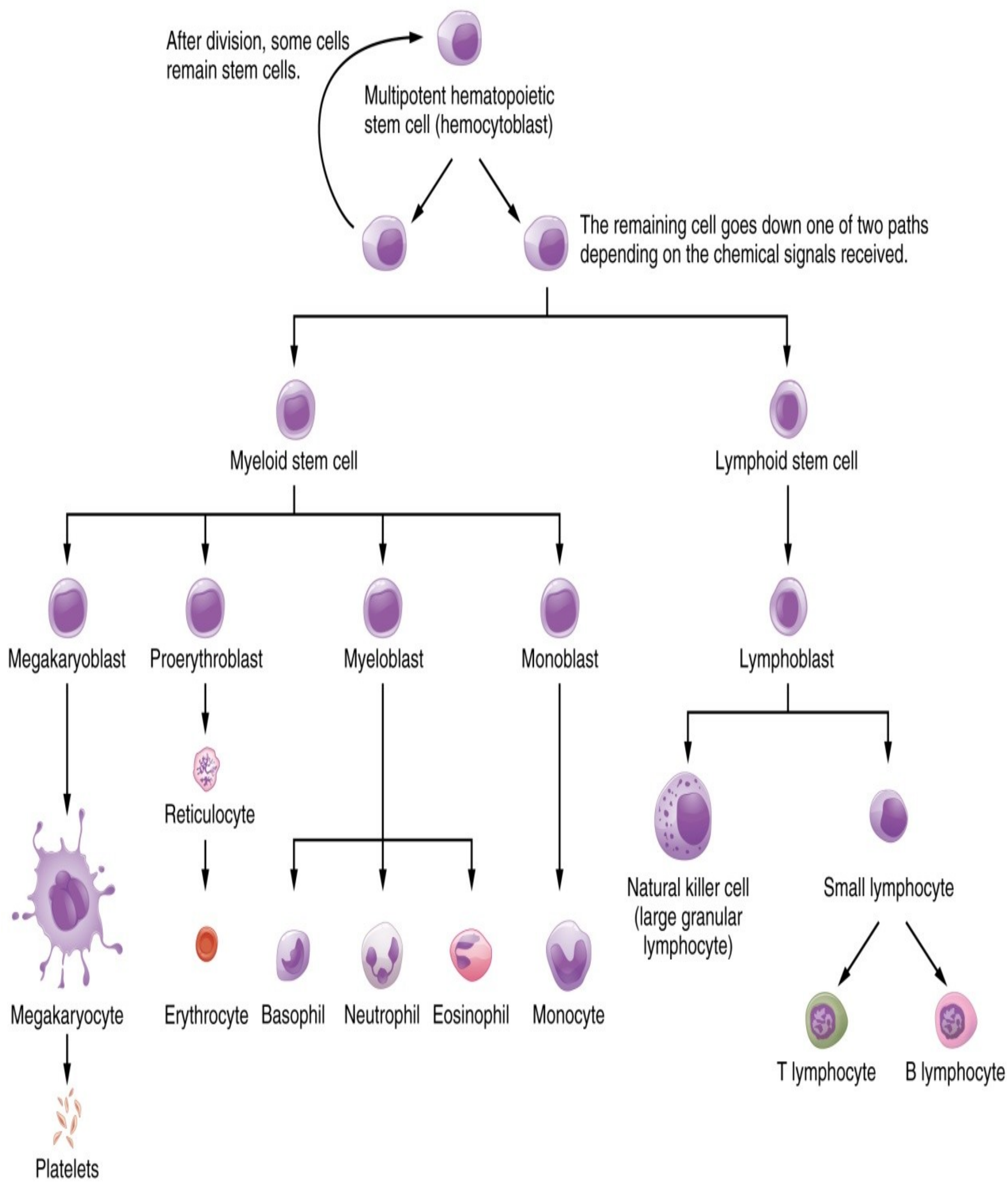
Mature blood cells have a relatively short life span and must be continuously replaced with new cells from precursors developing during hemopoiesis. In the early embryo these blood cells arise in the yolk sac. In the second trimester, hemopoiesis (also called **hematopoiesis**) occurs primarily in the developing liver, with the spleen playing a minor role . Skeletal elements begin to ossify and bone marrow develops in their medullary cavities, so in the third-trimester marrow of specific bones becomes the major hemopoietic organ. Throughout childhood and adult life, erythrocytes, granulocytes, monocytes, and platelets continue to form from stem cells located in bone marrow.

Still, the maturation, activation and some proliferation of the lymphoid cells occur in the spleen, thymus and lymph nodes later in life. In children, this process occurs in the long bones, such as the femur and tibia, while in adults it occurs in the pelvis, cranium, vertebrae, and sternum. In some cases, the extra-medullary sites also start the process of hematopoiesis at a later point in life. This process is called **extra-medullary hematopoiesis**.



All blood cells arise from a single type of multipotent hemopoietic stem cell in the bone marrow that can give rise to all the blood cell types . These stem cells give rise to two major lineages of progenitor cells committed to produce specific blood cells: one for lymphoid cells and another for myeloid cells , which develop in bone marrow.

Myeloid cells include granulocytes, monocytes, erythrocytes, and megakaryocytes., The lymphoid progenitor cells migrate from the bone marrow to the thymus or the lymph nodes, spleen, and other lymphoid structures, where they proliferate and differentiate.

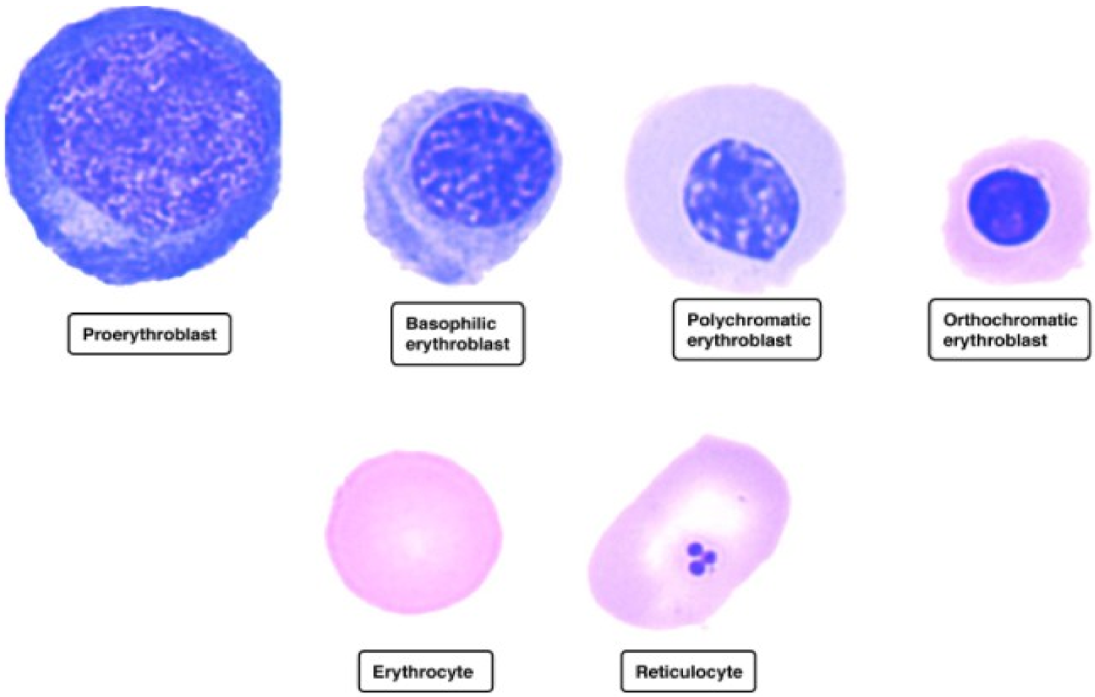


General scheme for blood cell formation (hematopoiesis).

Erythropoiesis

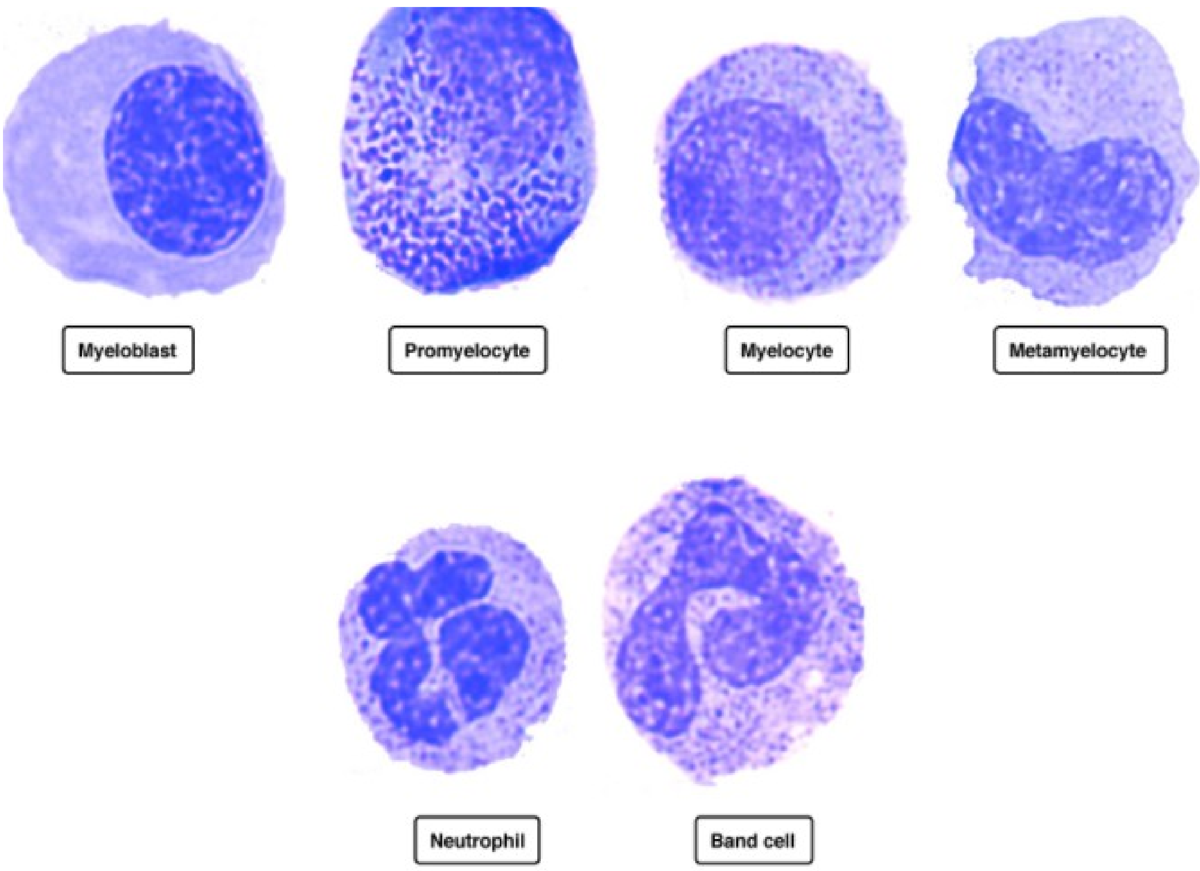
Erythropoiesis is the process by which red blood cells, also known as erythrocytes, are made and are stimulated by decreased levels of oxygen in the blood, which sets into motion the secretion of erythropoietin, a hormone central to the formation of red blood cells . The process of red blood cell formation takes on average 2 days to be completed from unipotential hematopoietic cell to mature red blood cell.. Hematopoietic cells committed to becoming red blood cells usually get smaller and more condensed as they mature until there is eventually loss of their nuclei.

The unipotential cell becomes what is known as a proerythroblast, which has a nucleus that is not condensed and takes up most of the cell with basophilic or blue cytoplasm. The cell then becomes a basophilic erythroblast, which is followed by a polychromatophilic erythroblast stage, where the nucleus is more condensed than the latter two stages and the cytoplasm becomes reduced. In the subsequent orthochromatophilic erythroblast stage, the nucleus is much smaller than that of the previous stages with a pinker cytoplasm. In the reticulocyte stage the red blood cell has no nucleus, but still stains somewhat blue due to the remnants of polyribosomes within the cell. Finally, the erythrocyte is the mature red blood cell, which has no nucleus and no polyribosome remnants and a s a result stains pink.



Granulopoiesis

Granulopoiesis is the formation of granulocytes, which are white blood cells with multi-lobular nuclei and cytoplasmic granules. The unipotential hematopoietic cell that becomes a myeloblast is large and has a cytoplasm that stains blue with a large nucleus. This cell evolves into a promyelocyte that contains azurophilic granules, and then becomes a myelocyte, which has a non-indented still rather large nucleus. This cell then becomes a metamyelocyte, which is similar in size to a mature granulocyte and the nucleus begins to become indented. Following this stage is the band cell stage, where the nucleus has definitive indentation and resembles a horseshoe. Finally, there is the mature granulocyte, which has a lobed nucleus and cytoplasmic granules. The entire process happens over a period of 2 weeks.



Monopoiesis, Lymphopoiesis and Thrombopoiesis

Monopoiesis is the process by which monocytes are formed. The committed progenitor cell, the monoblast, is found only in the bone marrow and has a basophilic cytoplasm without granules. These evolve into promonocytes, which are smaller with nuclei that become slightly indented, before becoming monocytes, which have kidney-shaped nuclei and can develop into dendritic cells or macrophages.

Lymphopoiesis is the formation of lymphocytes, which start from their first committed progenitor cells, lymphoblasts. These cells go on to mature into lymphocytes that are capable of differentiating into either B, T or natural killer cells.

Thrombopoiesis is the formation of platelets, which come from extremely large cells within the bone marrow called megakaryocytes. The creation of individual platelets occurs when the plasma membranes of megakaryocytes are fragmented, thereby generating platelets containing many granules.

The Respiratory System (R.S.)

The R.S. provides for exchange of O_2 and co_2 to and from the blood, with external environment .

R.S. include the lungs and a branching system of bronchial tubes . Functionally the system has two components :

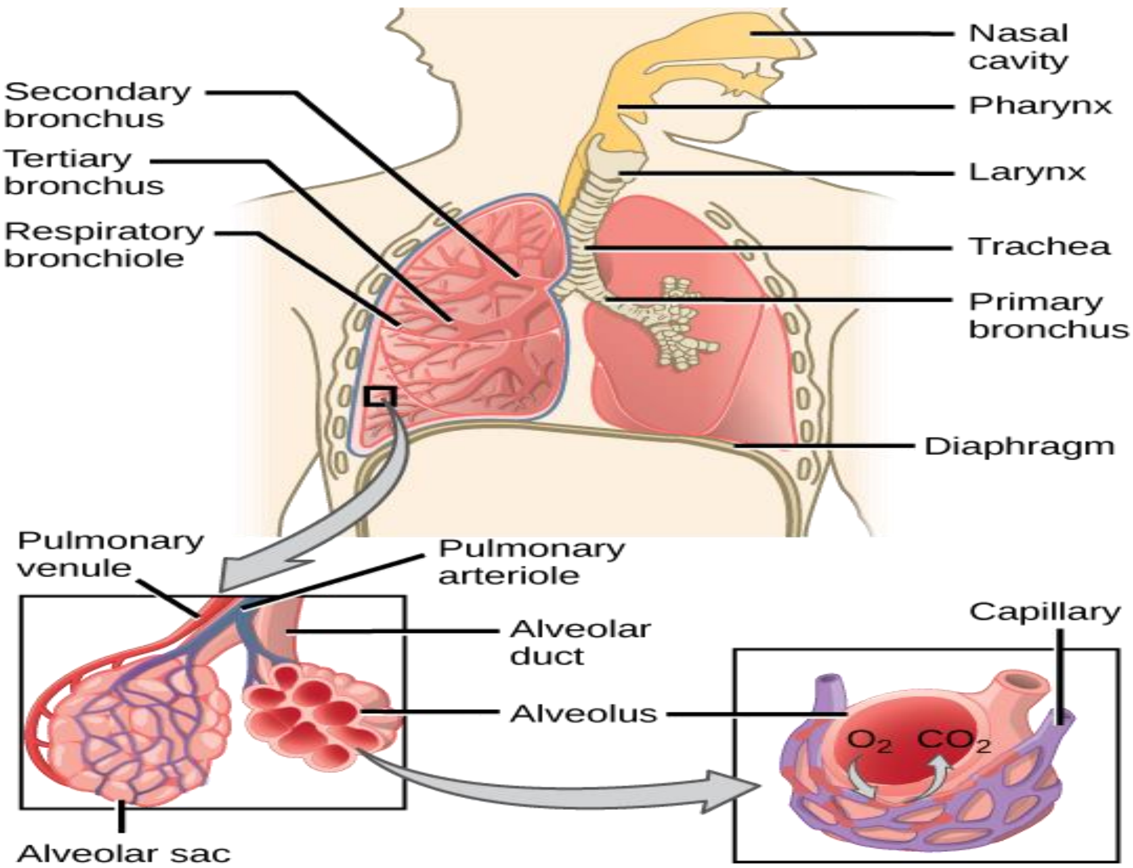
1- The conducting portion , which consists of the nasal cavities , pharynx

, larynx, trachea , bronchi (windpipe), bronchioles , and terminal bronchioles .

2- The respiratory portion, where gas exchange

exchange occurs , consisting of respiratory bronchioles ,alveolar ducts , alveolar sac , and terminal alveoli

Alveoli , are small , air – fired , saclike structures , it's the sites of O_2 and CO_2 exchange between inspired air and blood .



(Part 1)

Upper Respiratory system

Nasal Cavity (nasal passages):

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

A. vestibules:

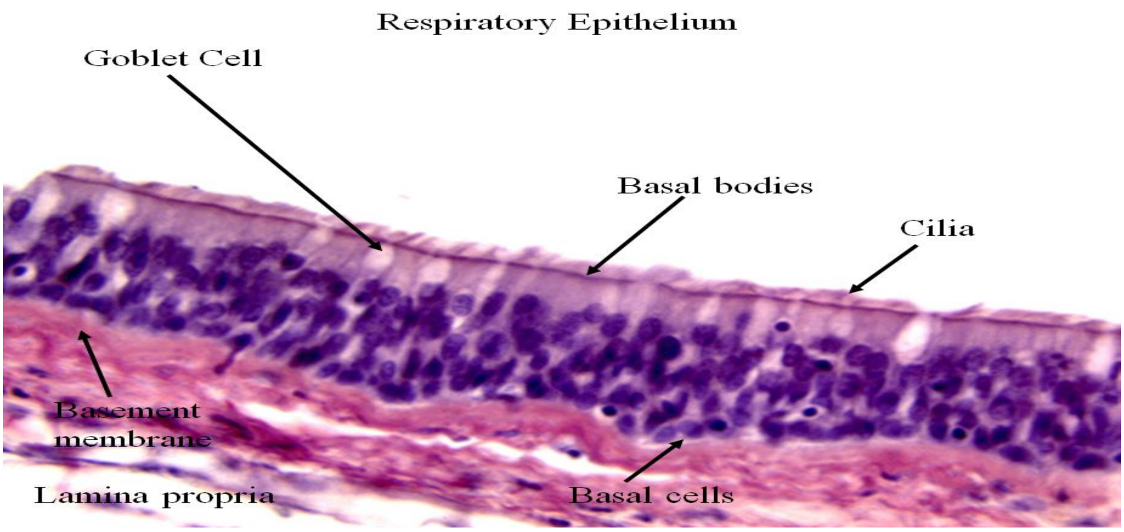
Lined by stratified and continuous that of adjacent epidermis, the underlying stroma is very cellular and there are large sebaceous gland, the heir is long.

- The vestibules (the first 1.5 cm of the conductive portion following the nostrils) are lined with a keratinized stratified squamous epithelium.
- Hairs, which filter large particulate matter out of the airstream, and sebaceous glands are also present .

B. Nasal cavity

1. The respiratory region.

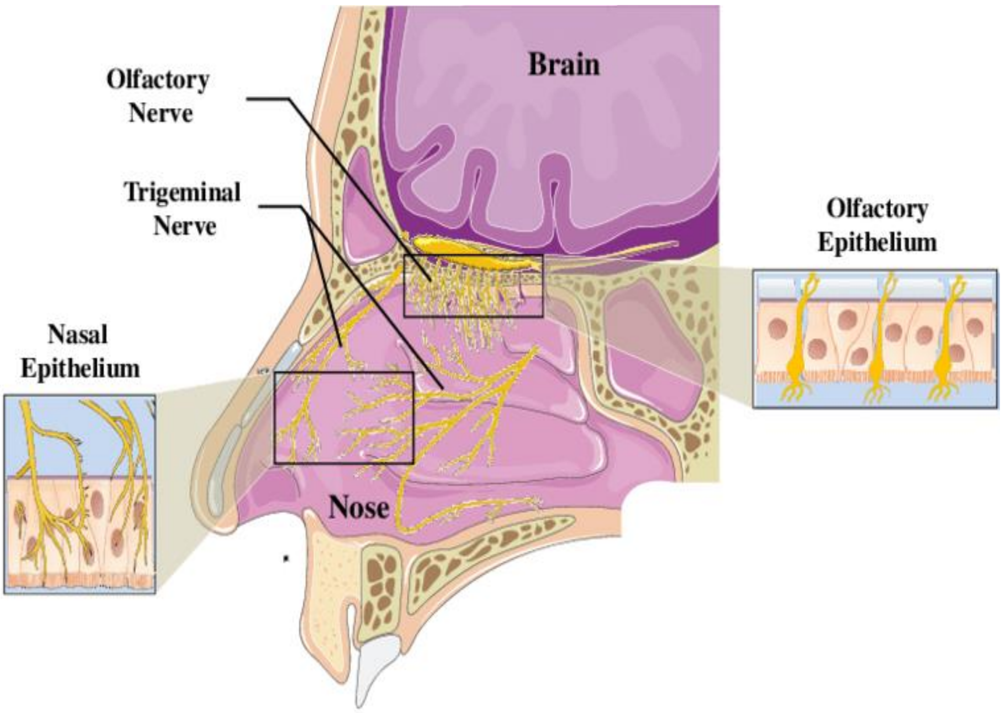
- At the transition from the vestibule to the respiratory region of the nasal cavity the epithelium becomes first stratified squamous and then pseudo stratified columnar and ciliated. This type of epithelium is characteristic for all conductive passages dedicated to the respiratory, system and therefore also called respiratory epithelium . Mucus producing goblet cells are present in the epithelium.



The surface of the lateral parts of the nasal cavity is found into folds by bony projections called conchae .These folds increase the surface area of the nasal cavity and create turbulence in the stream of passing air, both. of which facilitate the conditioning (warming, cooling and filtration) of the air.

2- Olfactory regions:

- Tissues on the superior concha and the nasal septum form the Olfactory regions 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 odour -producing substances, odorants, dissolved in the serous covering the epithelium.
- The olfactory epithelium is thick and of the pseudo stratified columnar type.



There are three kinds of cells in olfactory epithelium:

1. *Supporting cell*:

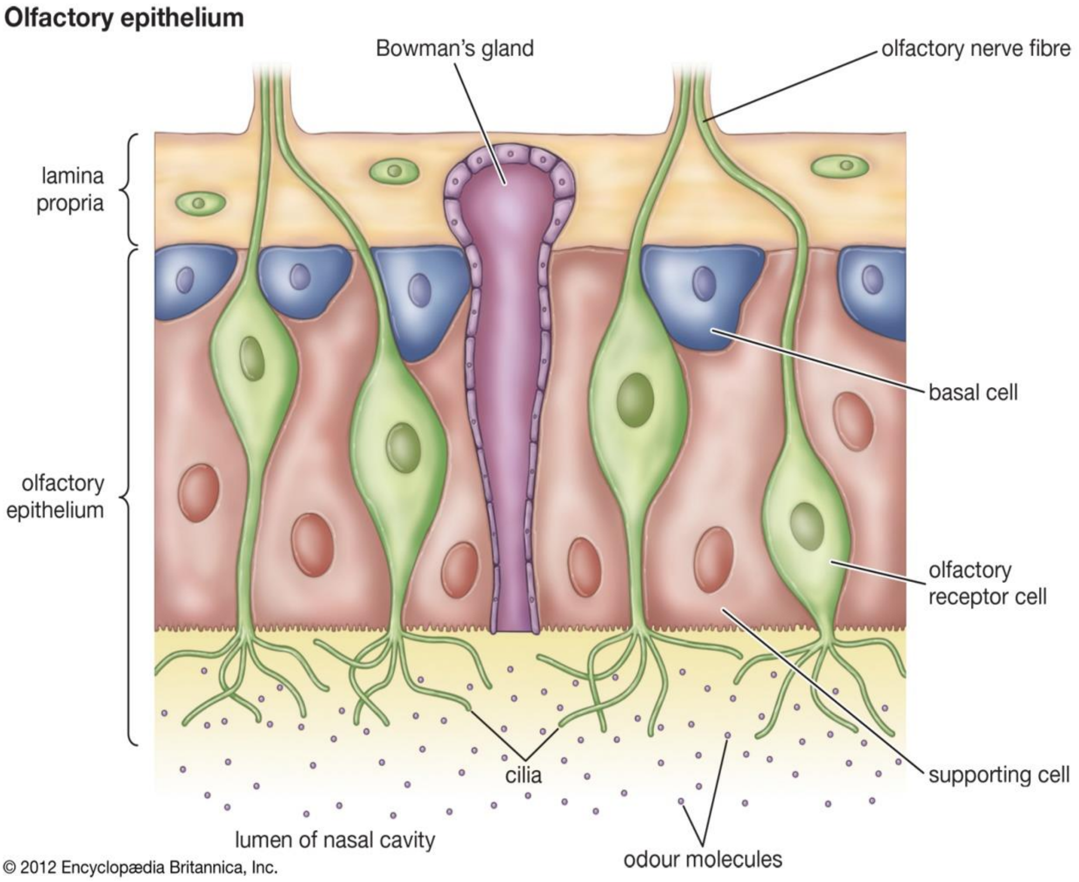
there are cylindrical granular cells with oval nuclei
the secretion of the serous glands contain lipofuscin granules, which give a yellow brown colour to the surface the olfactory region.

2. *Olfactory cells:*

There are bipolar fusiform nerve cell with rounded nuclei.

3. *Basal cells*: These lie between the basses of other cells and usually conical and darkly lining

In the lamina propria, **Bowman's glands** (also called olfactory glands) produce serous secretions that dissolve odiferous particles so that they can interact with the **olfactory cilia**. The olfactory cilia are short hair-like projections that extend into the mucous lining to detect and transmit odors through the olfactory nerve cells

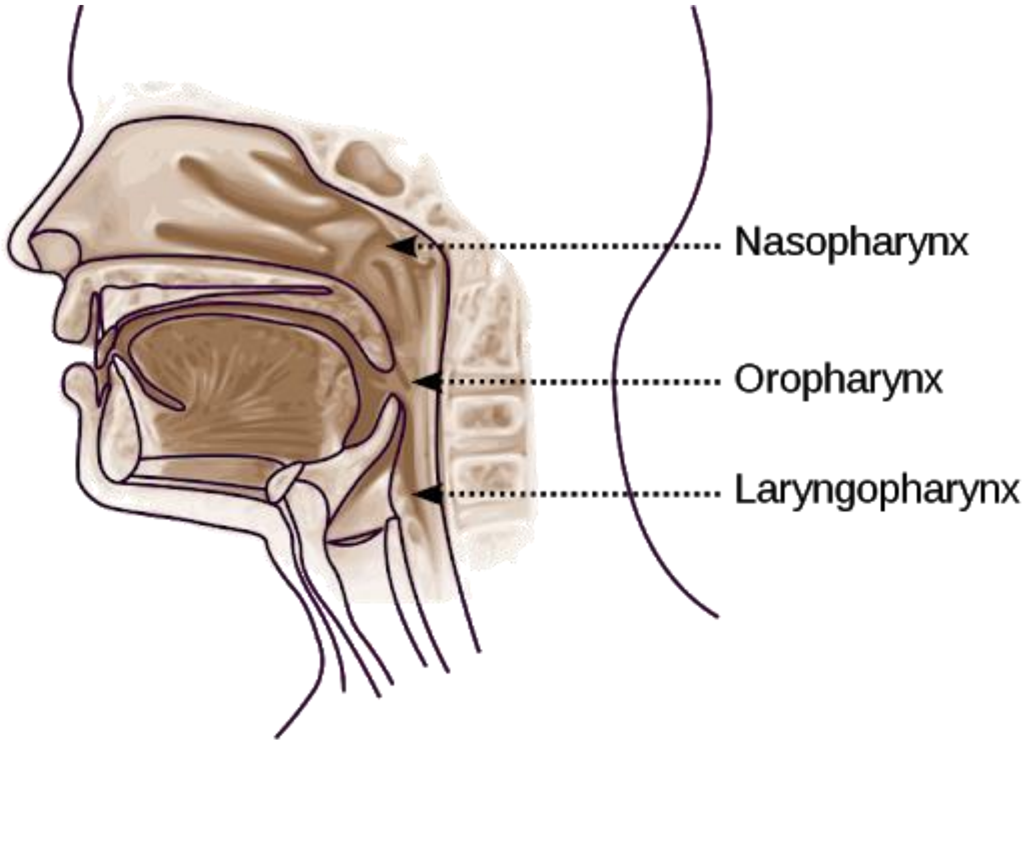


pharynx

Pharynx, (Greek: “throat”) cone-shaped passageway leading from the oral and nasal cavities in the head to the esophagus and larynx. The pharynx chamber serves both respiratory and digestive functions. Thick fibres of muscle and connective tissue attach the pharynx to the base of the skull and surrounding structures. Both circular and longitudinal muscles occur in the walls of the pharynx; the circular muscles form constrictions that help push food to the esophagus and prevent air from being swallowed, while the longitudinal fibres lift the walls of the pharynx during swallowing.

The pharynx consists of three main divisions:

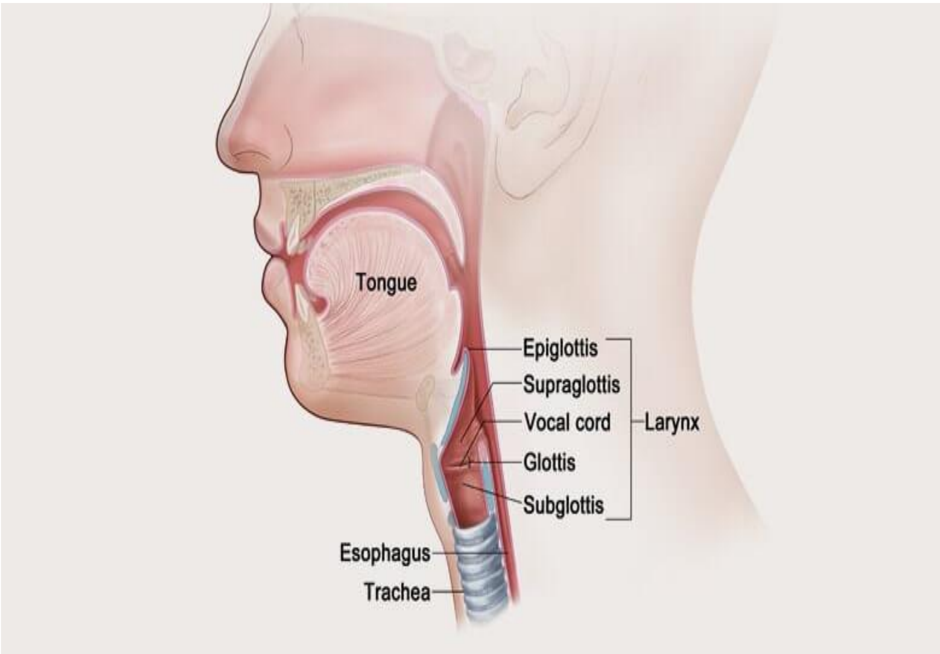
The **first region** is the nasopharynx, the back section of the nasal cavity. The nasal pharynx connects to the **second region**, the oropharynx. The oral pharynx begins at the back of the mouth cavity and continues down the throat to the epiglottis, a flap of tissue that covers the air passage to the lungs and channels food to the esophagus.The **third region** is the laryngopharynx, which begins at the epiglottis and leads down to the lung.



Larynx

- The larynx connects the pharynx and trachea.
- The larynx consist of framework of cartilages joined by fibrous bands
- Besides acting as a part of air passages, the larynx is modified in structure to enable it to perform the special function of voice.
- It situated in the mid-line of the neck between the pharynx above and trachea below and the tube which is formed composed of following layers:

- The epithelium is the pseudo stratified columnar ciliated type and goblet cells.
- Some parts of the larynx are lined by stratified squamous epithelium.
- The lamina propria composed of connective tissue contains muco-serous glands.
- A very thin sub mucosa of fibrous connective tissue.
- Intrinsic laryngeal muscles of skeletal type .
- The laryngeal cartilage mainly hyaline cartilage and some cartilage are elastic.
- The extrinsic skeletal muscle layer.
- A connective tissue adventitia continuous with surrounding connective tissue.

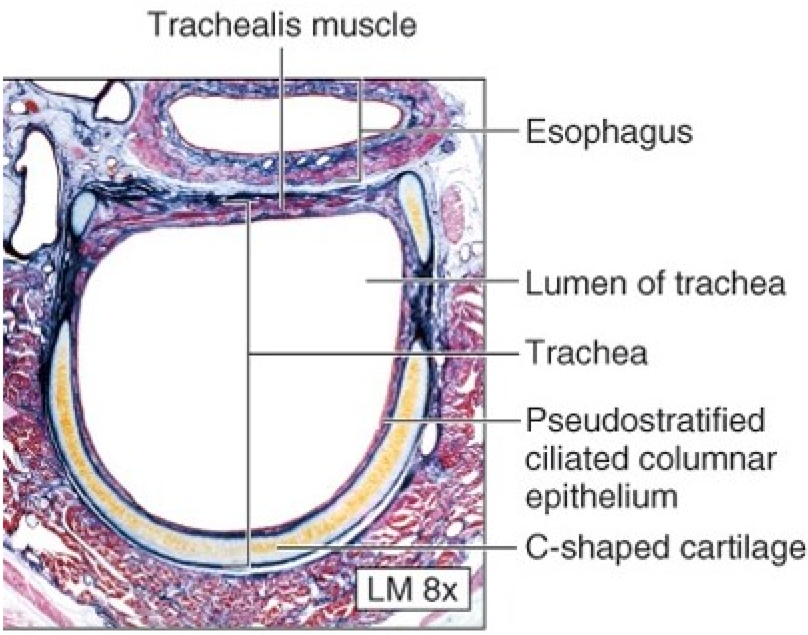


(Part 2)

Lower Respiratory system

Trachea

- The trachea a short tube (10-12 cm) with a diameter of ~ 2.5 cm.
- Its upper half is situated in the mid-line of the neck. It lies in front of the is esophagus.
- The wall formed of the following layers: is Epithelium, Mucosa and Sub mucosa layers .
- 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 increase goblet cell number. Prolonged intense irritation of the epithelium may lead to its transformation to a stratified epithelium (squamous metaplasia)
- 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), Surfactant-producing cells (or Clara cells), and serous cells.



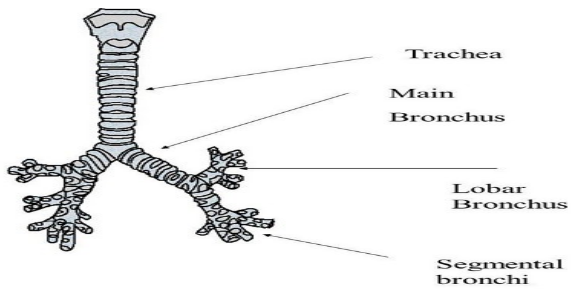
(b) Cross section

- 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) that produce a more fluid mucus. The submucosa ends with the perichondrium of the trachea 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. Longitudinal collagenous and elastic connective tissue fibers (annular ligaments) link the individual cartilages and allow both the lengthening and shortening of the trachea for example during swallowing or movements of the neck. They are inseparable from the fibers of the perichondrium.

Bronchi

- In the lungs we find the last segments of the conductive portion of the respiratory system .
- The main bronchi divide into lobar (secondary) bronchi which in turn give rise to segmental (tertiary) bronchi.
- Bronchial branches are accompanied by branches of the pulmonary artery, nerves and lymph vessels.



- Bronchi are characterized by the presence of glands and supporting cartilage. The cartilage supporting the bronchi is typically found in several small pieces.
- The histological structure of the epithelium and the underlying connective tissue of the bronchi corresponds largely to that of the trachea and the main bronchi.
- In addition, bronchi are surrounded by a layer of smooth muscle, which located between the cartilage and epithelium.

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.
- Bronchioles divide into *respiratory bronchioles*, which are the first structures that belong to the respiratory portion of the respiratory system. Small out pouching 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 alveoli

Histological Structure of Alveoli (or air sac).

- The wall of the alveoli is formed by a thin sheet of tissue separating two neighboring 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 find a dense, anastomosing network of pulmonary capillaries. The wall of the capillaries are in direct contact with the epithelial lining of the alveoli. The basal laminae of the epi- and endothelium may actually fuse.
- Neighboring alveoli may be connected to each other by small alveolar pores.

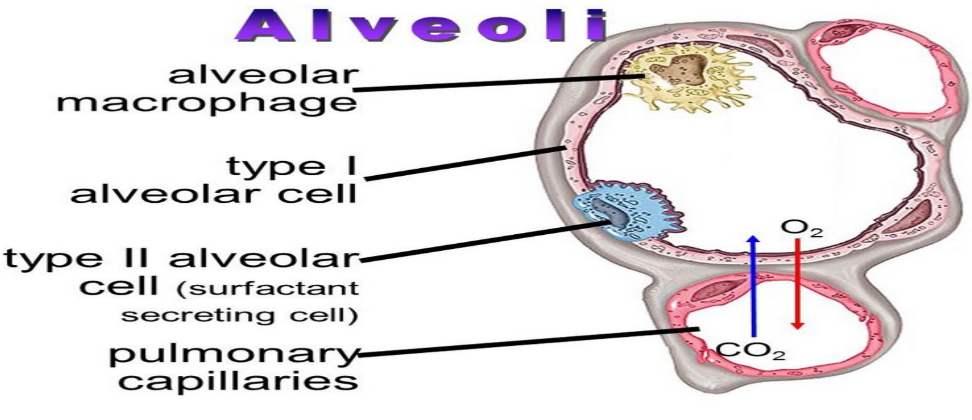
The epithelium of the alveoli is formed by two cell types:

Alveolar type I cells (small alveolar cells or type I pneumocytes).

- Are extremely flattened and form the bulk (95%) the surface alveolar walls actually form part .
- Their functions include providing physical structural support for the **alveoli** and facilitating the fast exchange of gases.
-

Alveolar type II cells (large alveolar cells or type II pneumocytes)

- Are irregularly (sometimes cuboid shaped. T)
- May form small bulges on the alveolar walls.
- Type II alveolar cells contain a large number of granules called cytosomes (or multilamellar bodies), which consist of precursors to which keep surface pulmonary surfactant (the mixture of phospholipids tension in the alveoli low).



Cilia are absent from the alveolar epithelium and cannot help to remove particulate matter which continuously enters the alveoli with the inspired air. Alveolar macrophages take care of this job. They migrate freely over the alveolar epithelium and ingest particulate matter .

Histology of urinary system

Composed of two kidneys, two ureters, the urinary bladder, and the urethra, the urinary system plays a critical role in:

1- Blood filtration,(filtration of cellular wastes from blood).

2- Maintenance of fluid homeostasis

3 Regulation of blood pressure

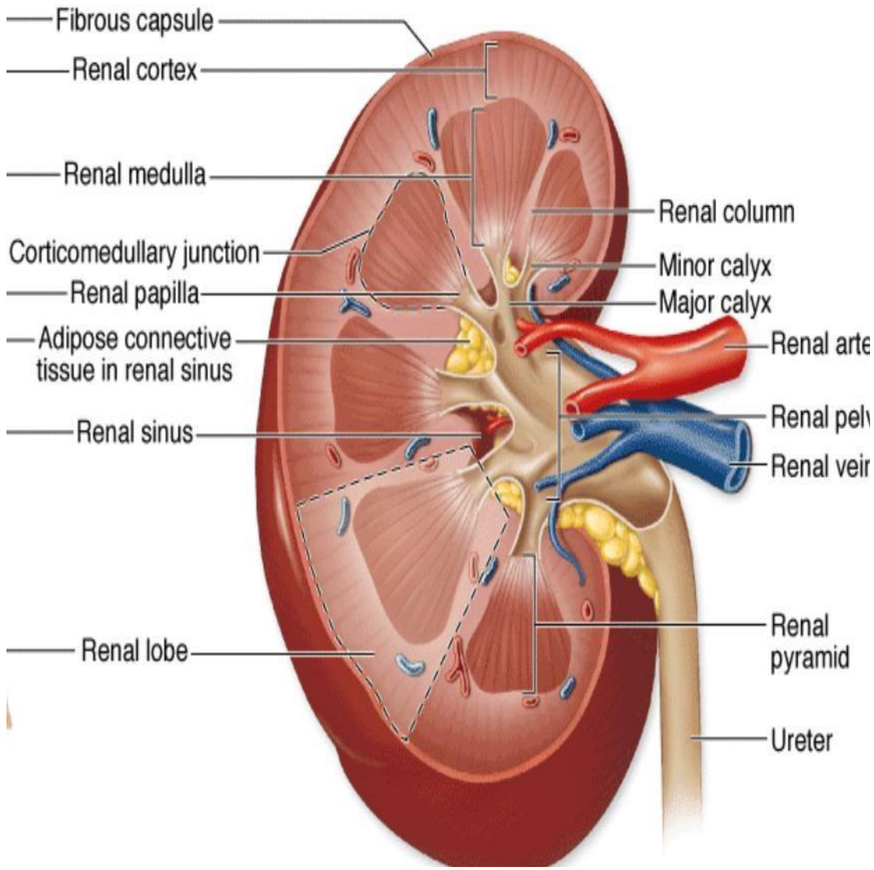
4-Erythrocyte formation

5- Vitamin D conversion to an active form.

Functionally, the urinary system is subdivided into the:

- Excretory portion (nephrons), responsible for blood filtration and production of urine.
- The collecting portion (collecting ducts, calyces, ureter, bladder, and urethra), which receives, transports, and temporarily stores formed urine until excretion

Kidneys



The **hilum**—where nerves enter, the ureter exits, blood and lymph vessels enter and exit. Both kidneys covered by a thin fibrous capsule , dense connective tissues .

The expanded upper end of the ureter, called the **renal pelvis,** divides into two or three **major calyces.** Smaller branches, the **minor calyces,** arise from each major calyx. The area surrounding the calyces, called the **renal sinus,** usually contains considerable adipose tissue.

The kidney has an outer **cortex** and an inner **medulla** . The renal medulla consists of conical structures called **renal pyramids**, which are separated by cortical extensions called **renal columns**. Each medullary pyramid plus the cortical tissue at its base and along its sides constitutes a **renal lobe**.

Each kidney contains 1–1.4 million functional units called **nephrons** .

Nephron: Structural and functional unit of the kidney composed of the following segments :

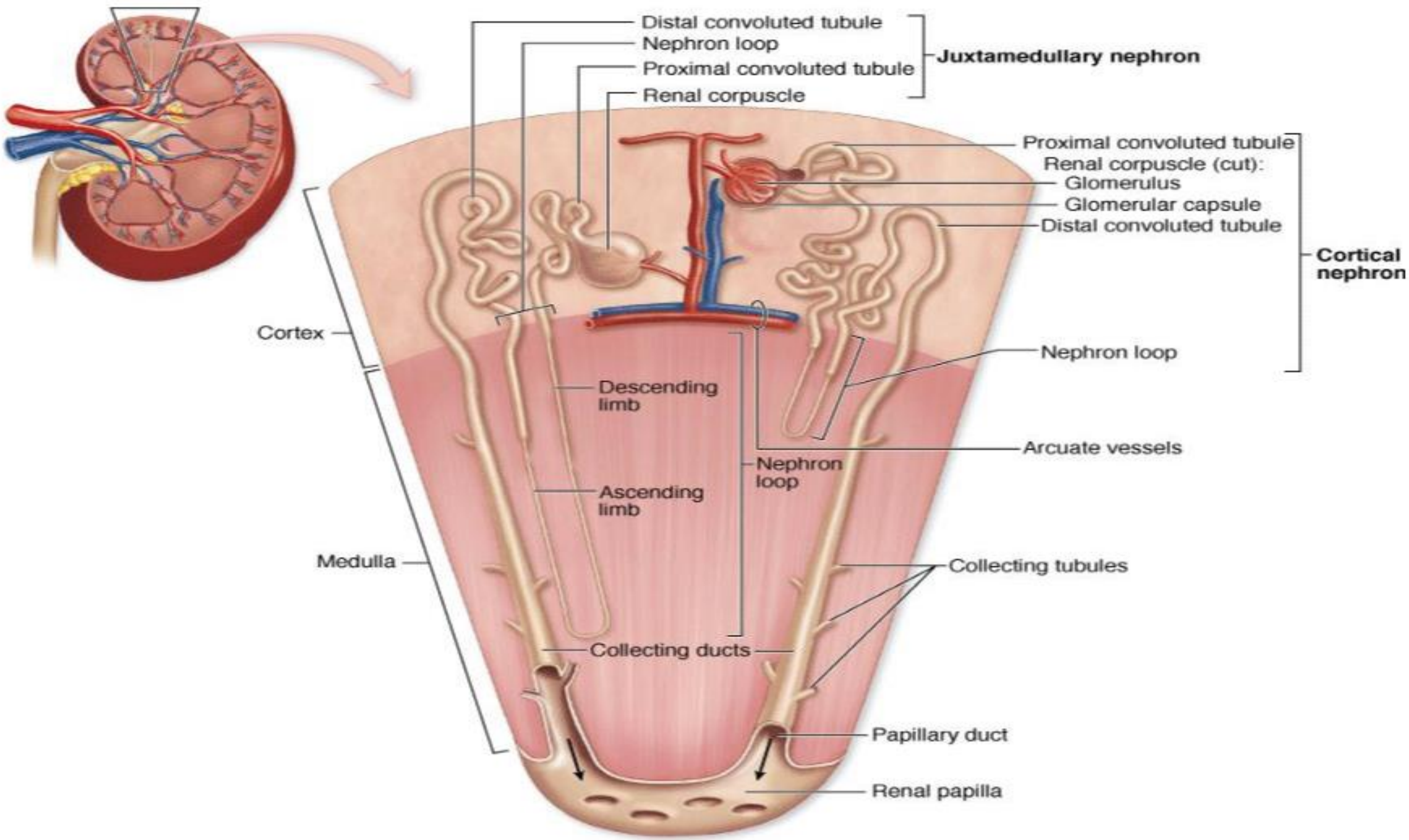
- **Renal corpuscle:** an initial dilated portion in cortex, Spherical structure made of glomerulus surrounded by a double-layered Bowman capsule .
- **Proximal convoluted tubule:** located in the cortex.
- **Loop of Henle:** thin and thick limbs , Where concentration of urine takes place.
- **Distal convoluted tubule:** Where resorption, acid-base balance occurs.
- **Collecting tubules and ducts:** They belong to the collecting portion of the urinary system.

- **Juxtaglomerular apparatus:** Composed of macula densa of the Distal convoluted tubule, Juxtaglomerular cells (also called granular cells) which secrete renin, and lacis cells (also called extraglomerular mesangial cells). It's main function is to regulate blood pressure and the filtration rate of the glomerulus.

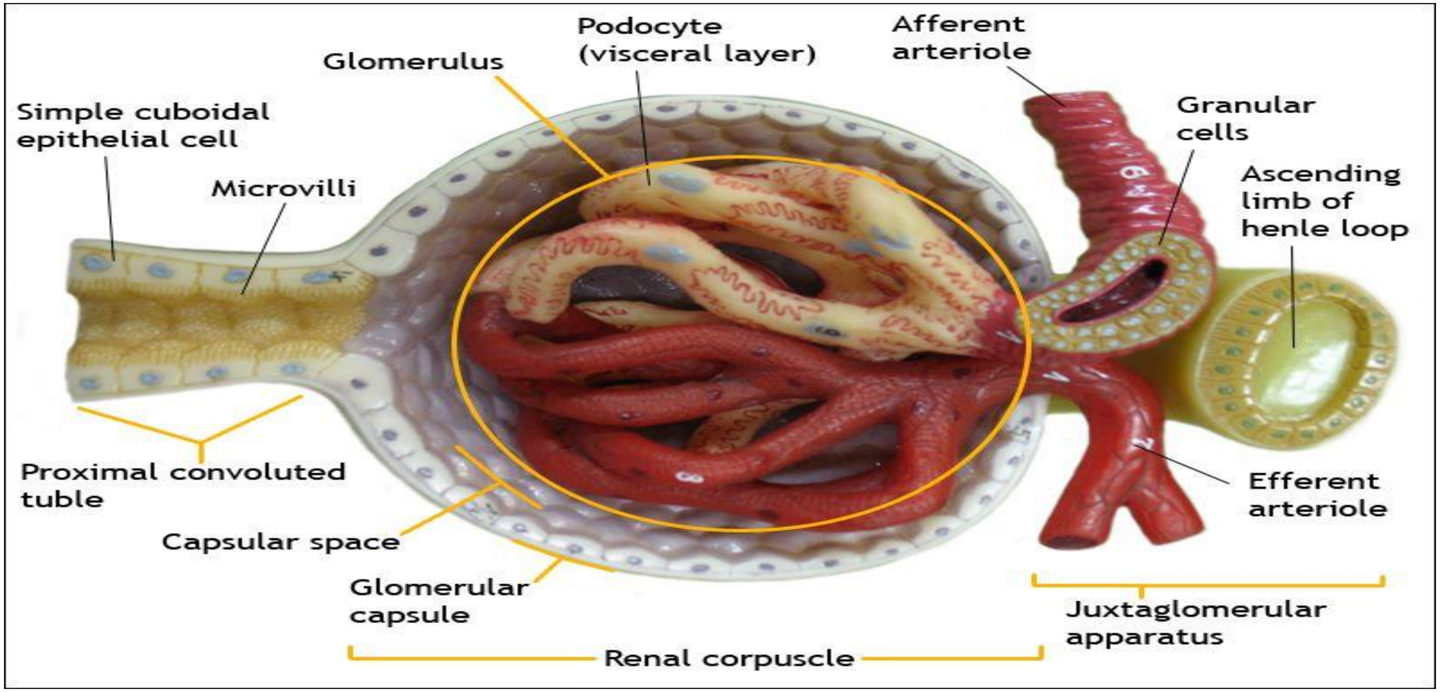
- **Glomerular filtration barrier:** Layers through which blood filtrate passes to enter the urinary space. Composed of glomerular endothelium, basement membrane, and podocyte filtration slits of the visceral layer of the Bowman capsule. The basement membrane in particular plays a critical role in restricting the movement of large proteins and molecules

- **Cortical nephrons:** Positioned closer to the capsule with the loop of Henle traveling only a short distance into the medulla. Hence, urine produced is not as heavily concentrated.

- **Juxtamedullary nephrons:** Positioned closer to the medulla with the loop of Henle traveling deep into the medulla. Hence, urine produced is more concentrated.



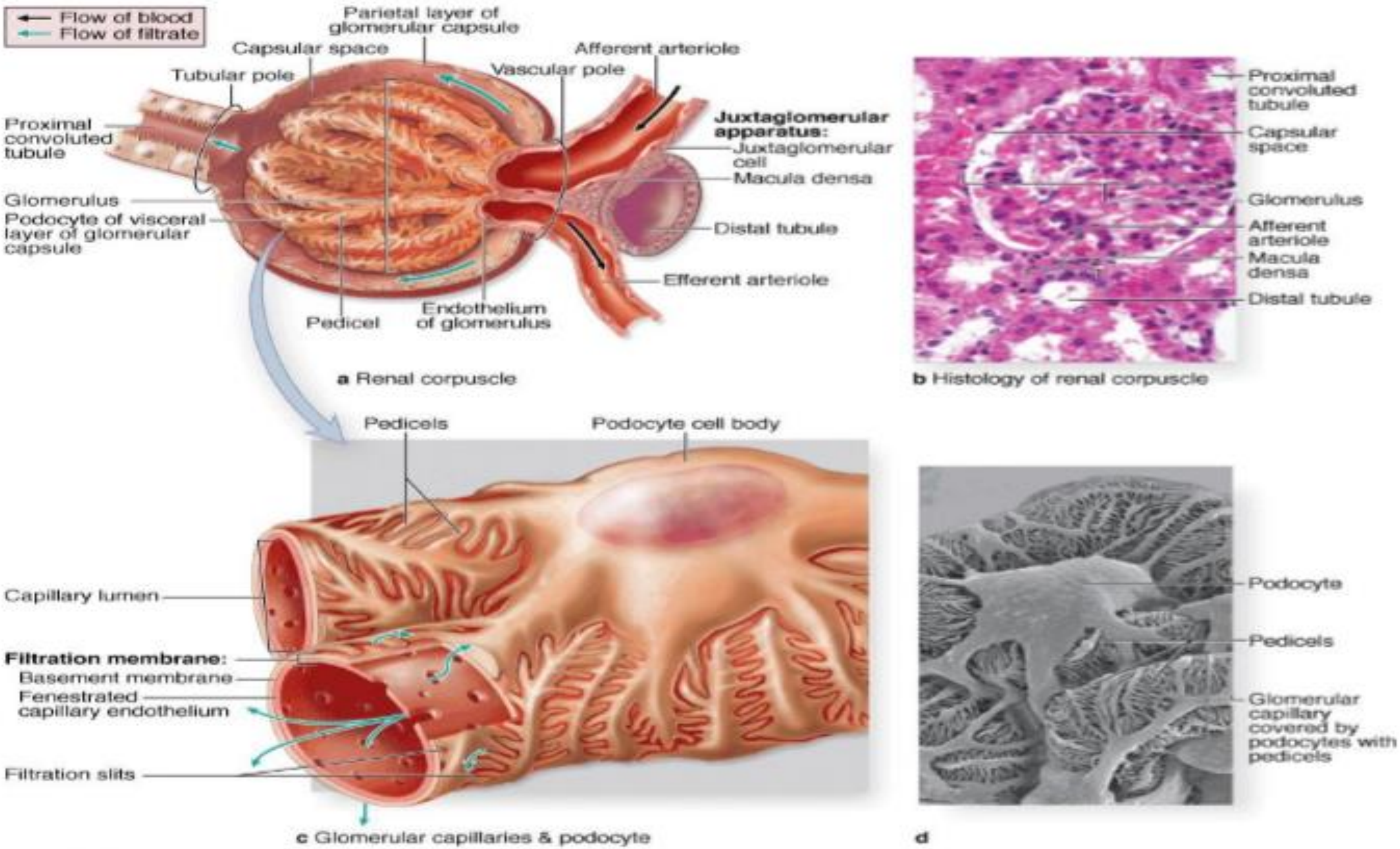
Source: Mescher AL: *Junqueira's Basic Histology: Text and Atlas,*



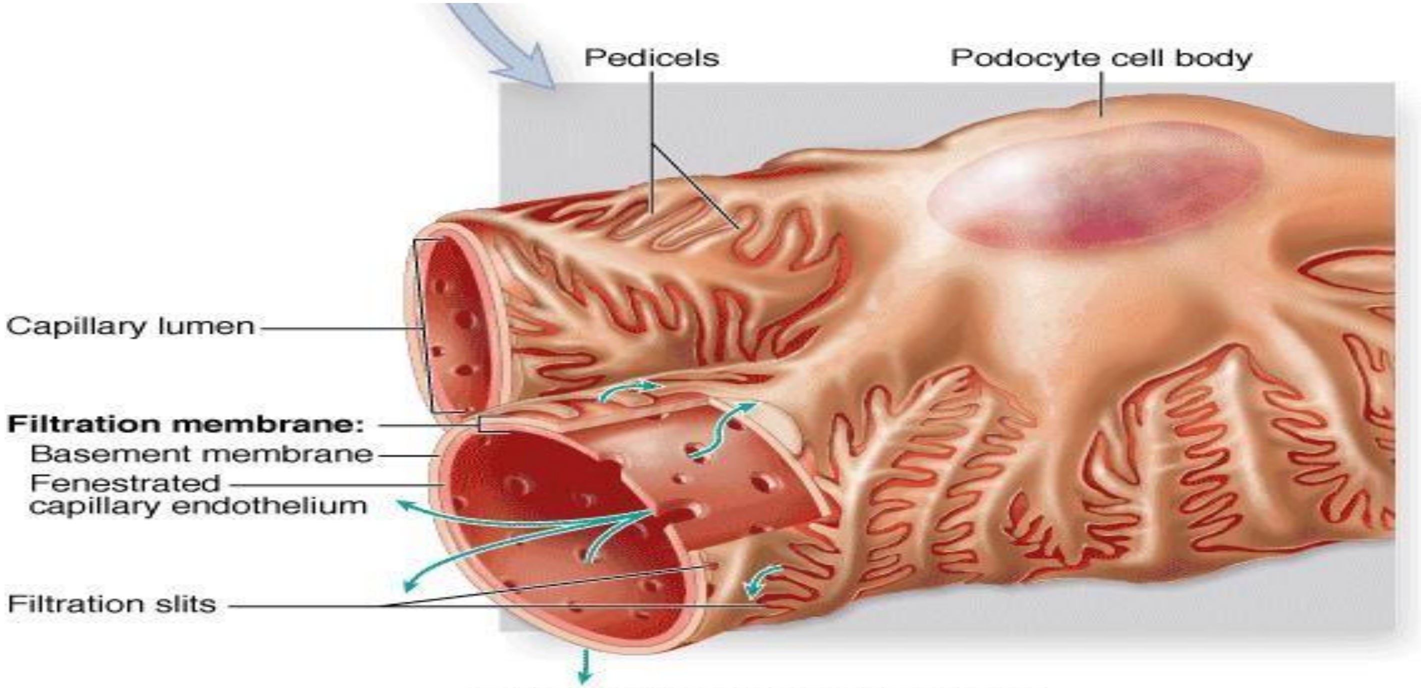
At the beginning of each nephron is a renal corpuscle, containing a loose knot of

capillaries, the glomerulus, surrounded by a double-walled epithelial capsule called the glomerular (Bowman's) capsule. The internal layer (visceral layer) of the capsule closely envelops the glomerular capillaries . The external parietal layer forms the outer surface of the capsule.

Between the two capsular layers is the urinary or capsular space, which receives the fluid filtered through the capillary wall and the visceral layer



Source: Mescher AL: *Junqueira's Basic Histology: Text and Atlas, 12th Edition*: http://www.accessmedicine.com

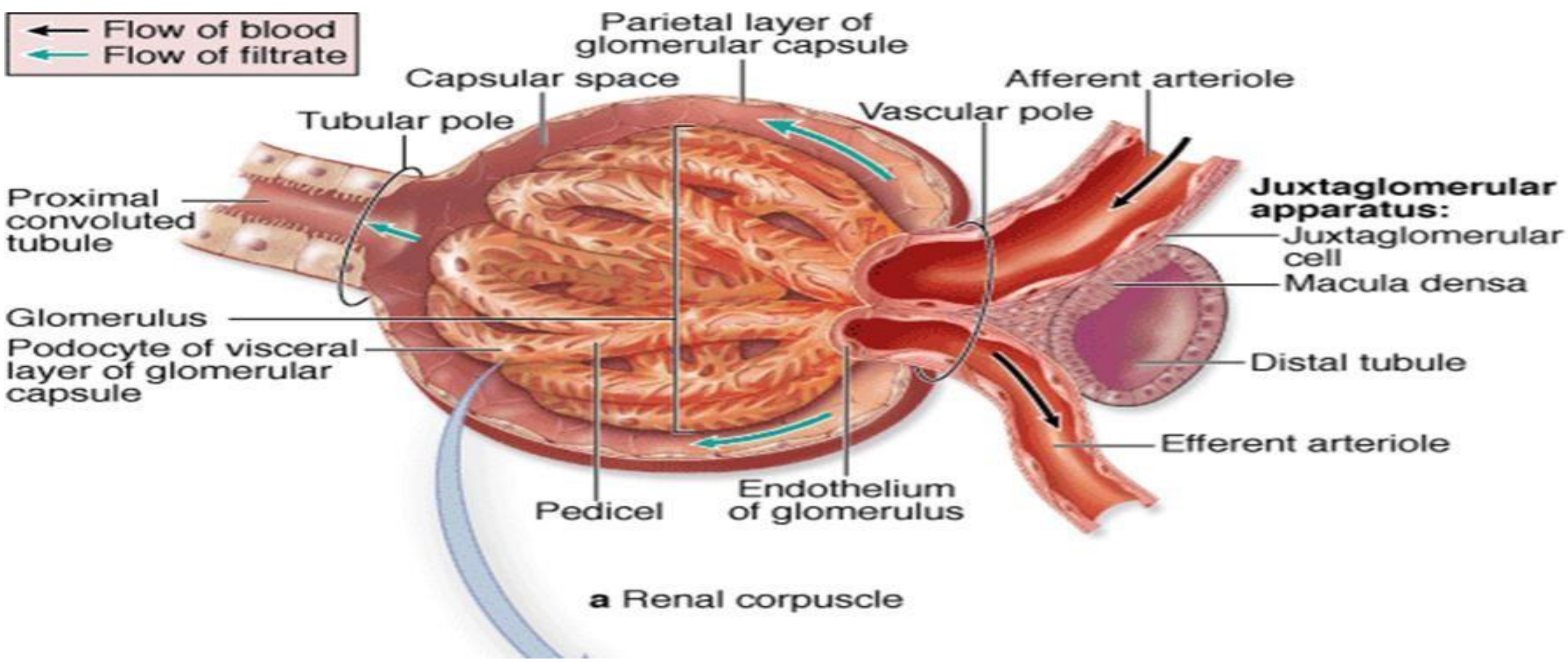


c Glomerular capillaries & podocyte

The cells of this layer, the **podocytes** , have a cell body from which arise several primary processes. Each primary process gives rise to numerous secondary (foot) processes or pedicels that embrace a portion of one glomerular capillary . The cell bodies of podocytes do not contact the basement membrane of the capillary, but each pedicel is in direct contact with this structure .

Each renal corpuscle has a vascular pole, where the afferent arteriole enters and the efferent arteriole leaves, and a urinary or tubular pole, where the proximal convoluted tubule begins .

The parietal layer of a glomerular capsule consists of a simple squamous epithelium supported externally by a basal lamina and a thin layer of reticular fibers. At the tubular pole, this epithelium changes to the simple cuboidal epithelium characteristic of the proximal tubule .

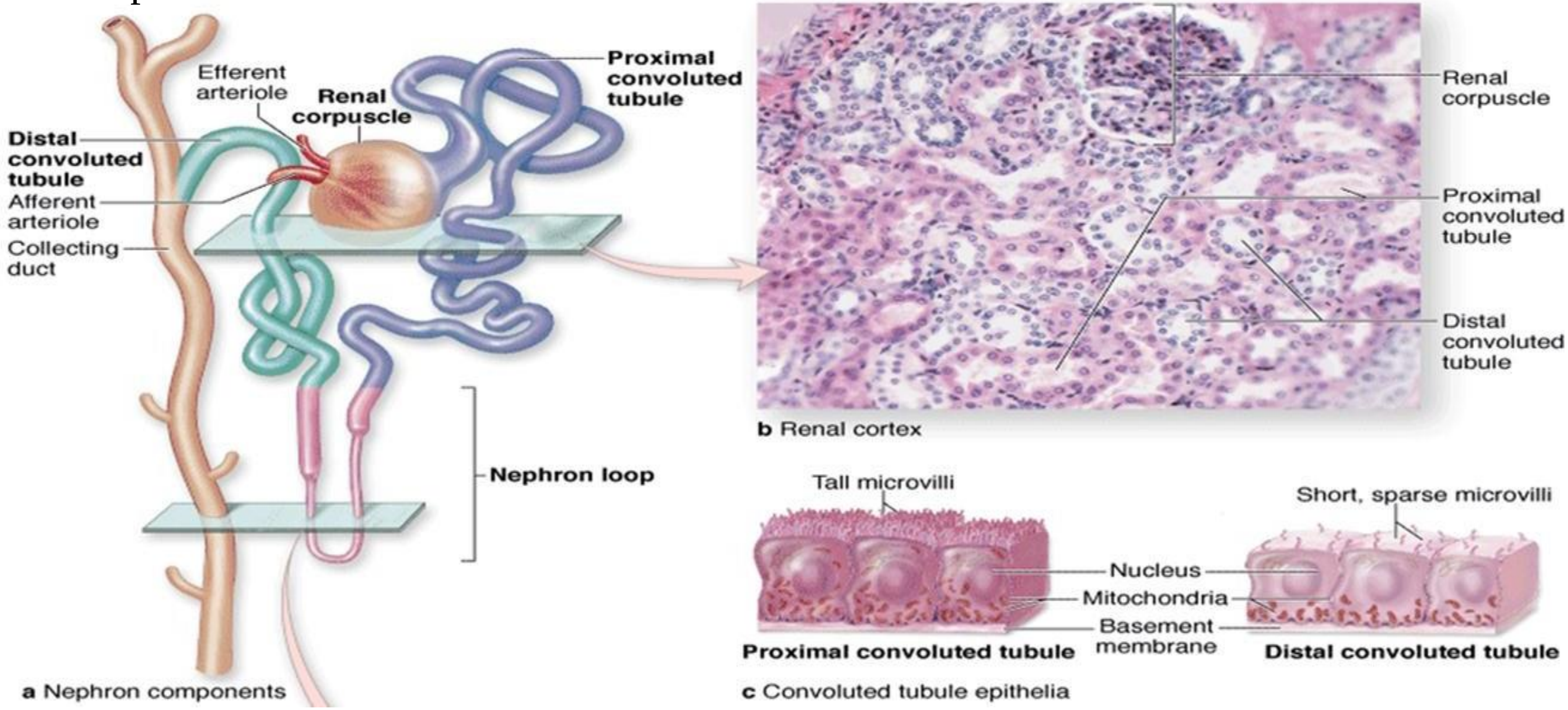


a Renal corpuscle

Proximal Convoluted Tubule

At the tubular pole of the renal corpuscle, the squamous epithelium of the capsule's parietal layer is continuous with the cuboidal epithelium of the proximal convoluted tubule . This very tortuous tubule is longer than the distal convoluted tubule

The cell apex has abundant long microvilli which form a prominent brush border for reabsorption .



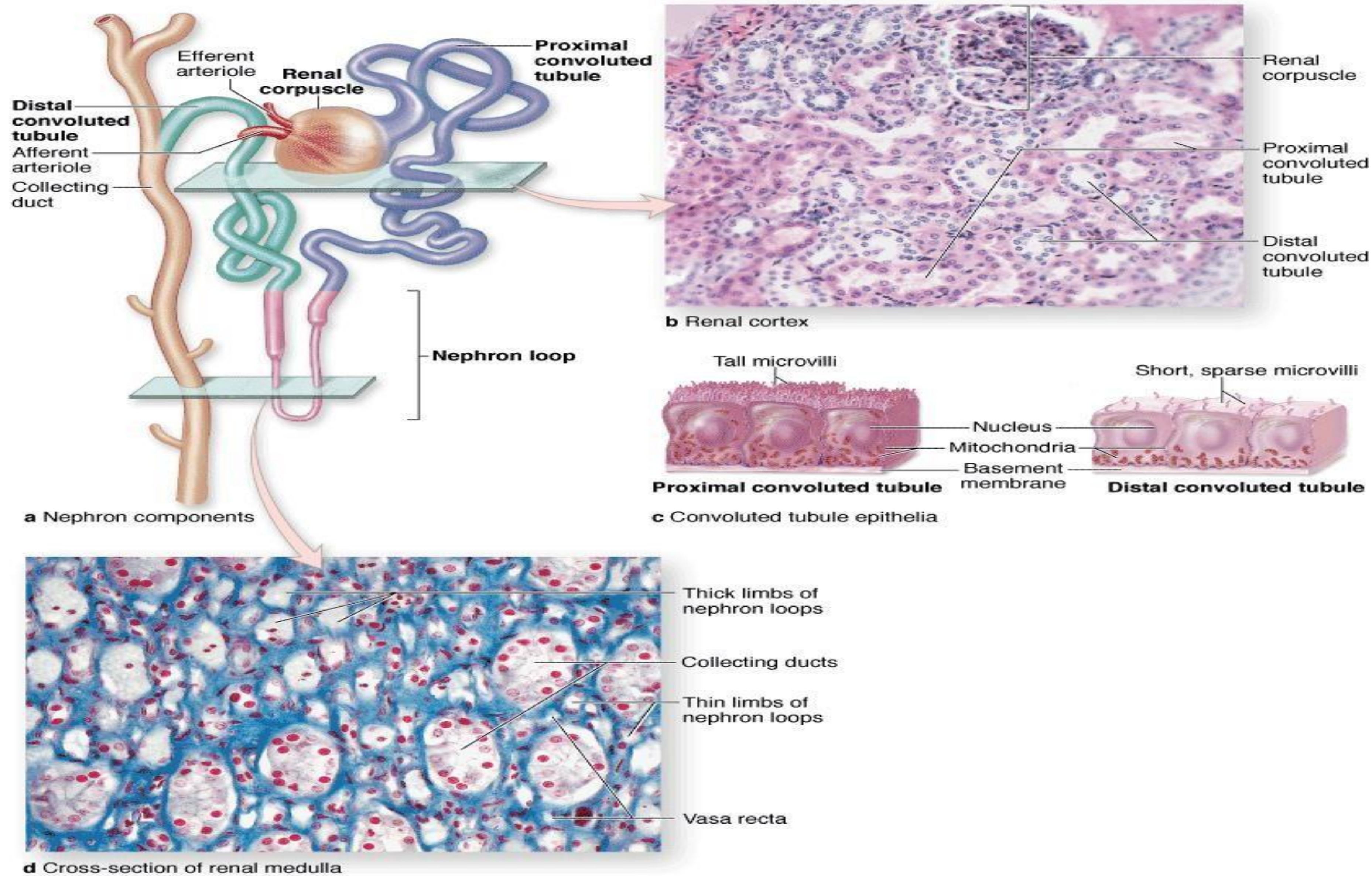
a Nephron components
b Renal cortex
c Convoluted tubule epithelia

Nephron Loop (of Henle):

- This is a U-shaped structure with a descending limb and an ascending limb, both composed of simple epithelia, cuboidal near the cortex, but squamous deeper in the medulla .
- Thick descending limb : Simple Cuboidal epithelium, permeable to water, impermeable to salt .
- Thin descending limb: Simple squamous epithelium. permeable to water, impermeable to NaCl.
- Thin ascending limb : Simple squamous epithelium. Resorb NaCl ,impermeable to water .
- Thick ascending limb : Simple cuboidal epithelium, permeable to NaCl, impermeable to water.

Distal Convoluted Tubule& Juxtaglomerular Apparatus

The thick ascending limb of the nephron loop is straight as it enters the cortex, and then becomes tortuous as the distal convoluted tubule . The simple cuboidal cells of these tubules differ from those of the proximal convoluted tubules in being smaller and having no brush border . The rate of Na^+ absorption and K^+ secretion by the sodium pumps is regulated by aldosterone from the adrenal glands and is important for the body's water-salt balance.



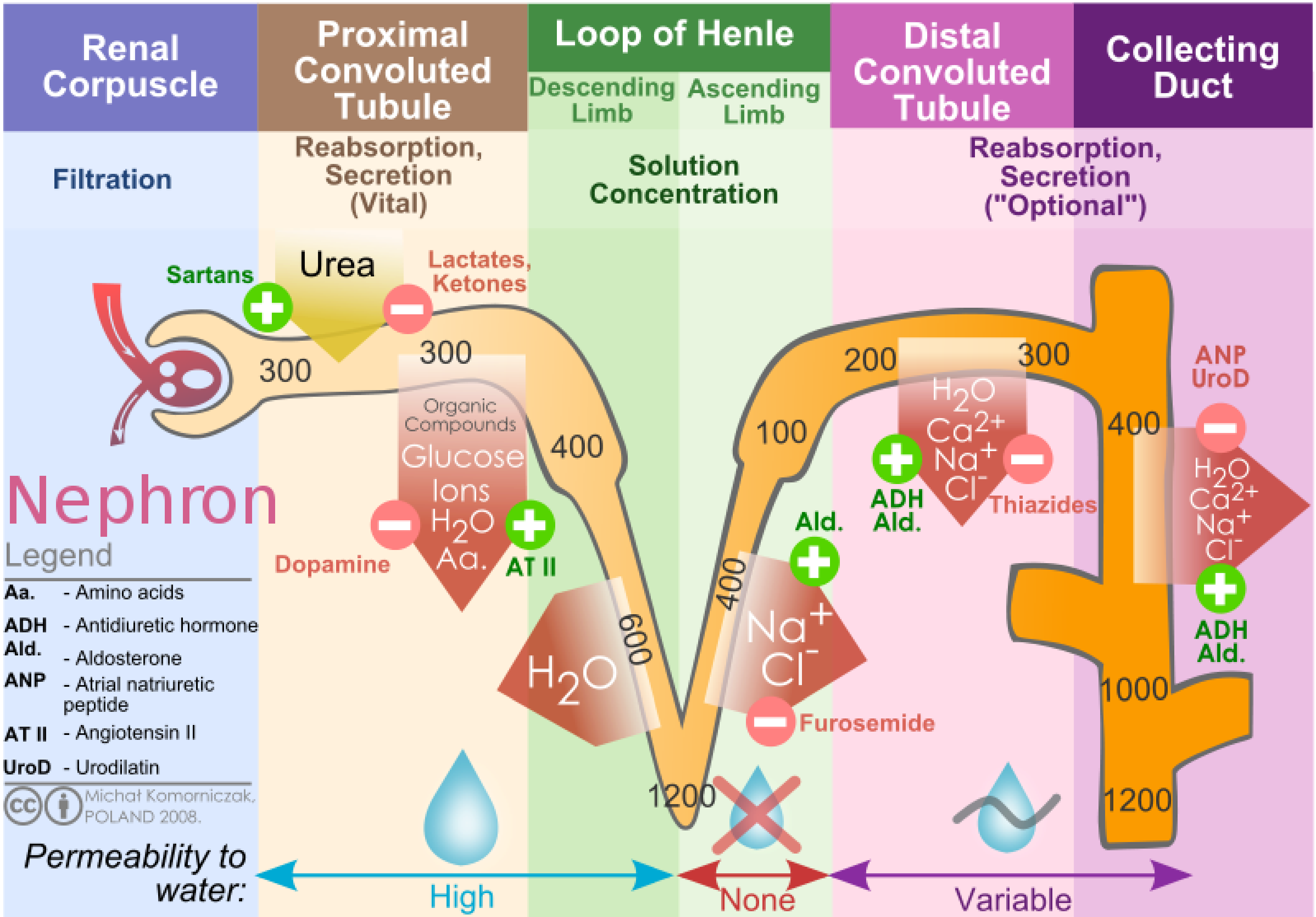
a Nephron components
b Renal cortex
c Convoluted tubule epithelia
d Cross-section of renal medulla

Source: Mescher AL: *Junqueira's Basic Histology: Text and Atlas, 12th Edition*: http://www.accessmedicine.com

Collecting Tubules & Ducts

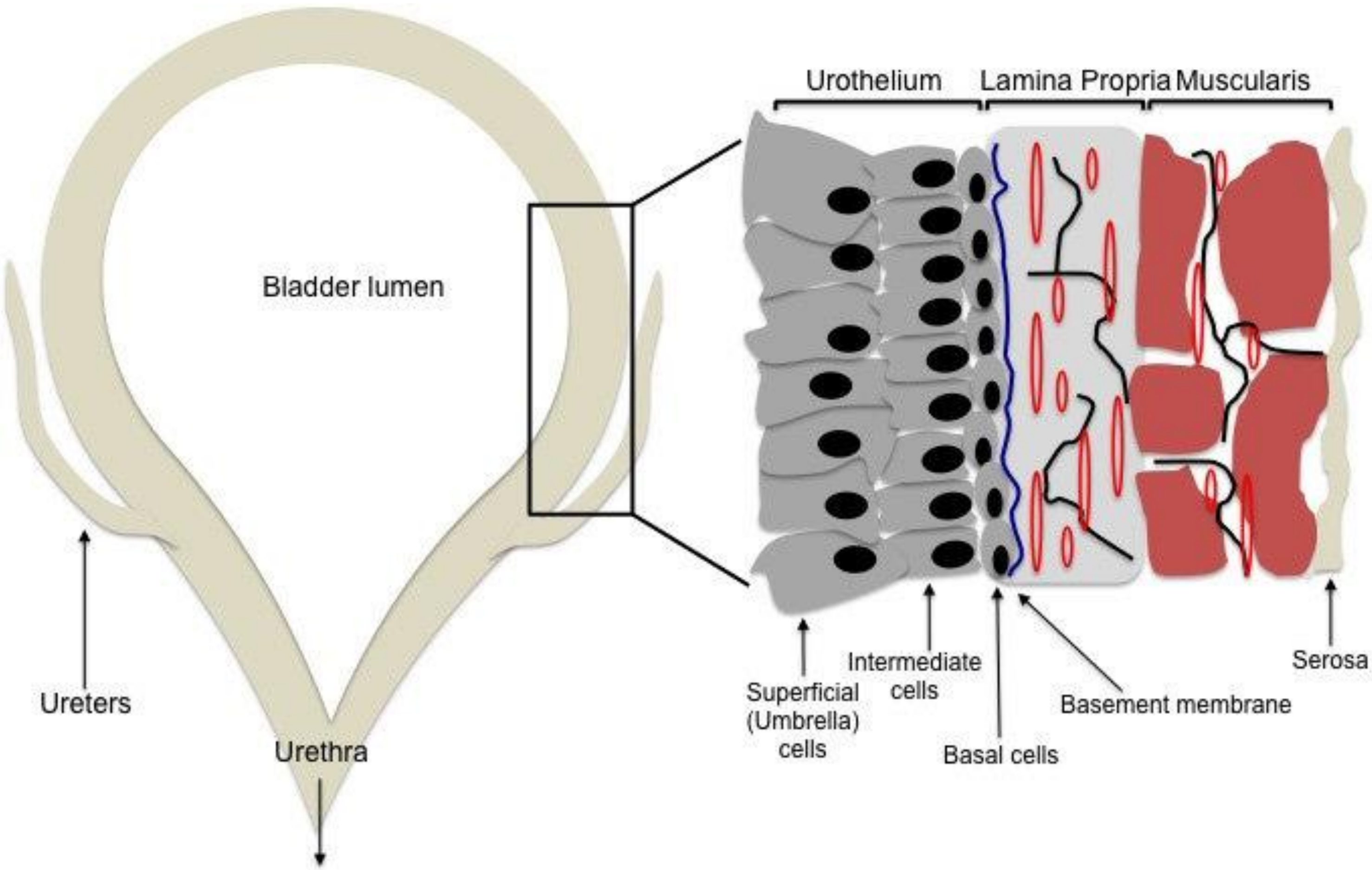
Urine passes from the distal convoluted tubules to **collecting tubules**, the last part of each nephron, which join each other to form larger, straight **collecting ducts** that run to the tips of the medullary pyramids and empty into the minor calyces . The collecting tubules are lined with cuboidal epithelium .

Along their entire extent, collecting tubules and ducts are composed mainly of weakly staining **principal cells** with few organelles and scanty microvilli . In the medulla, collecting ducts are a major component of the urine-concentrating mechanism. Cells of collecting ducts are particularly rich in **aquaporins**, integral proteins found in most cell membranes that function as selective pores for passage of water molecules.


Renal Corpuscle
Proximal Convoluted Tubule
Loop of Henle
Descending Limb
Ascending Limb
Distal Convoluted Tubule
Collecting Duct
Filtration
Reabsorption, Secretion (Vital)
Solution Concentration
Reabsorption, Secretion ("Optional")
Sartans
Urea
Lactates, Ketones
300
300
Organic Compounds
Glucose
Ions
H2O
Aa.
Dopamine
AT II
400
600
H2O
1200
400
Na+
Cl-
Ald.
Furosemide
100
200
300
H2O
Ca2+
Na+
Cl-
ADH
Ald.
Thiazides
ANP
UroD
400
H2O
Ca2+
Na+
Cl-
ADH
Ald.
1000
1200
Nephron
Legend
Aa. - Amino acids
ADH - Antidiuretic hormone
Ald. - Aldosterone
ANP - Atrial natriuretic peptide
AT II - Angiotensin II
UroD - Urodilatin
Michał Komorniczak, POLAND 2008.
Permeability to water:
High
None
Variable

Ureters, Bladder, & Urethra

Ureter, and bladder have the same basic histologic structure, with the walls becoming gradually thicker closer to the bladder. The mucosa of these organs is lined by unique stratified **transitional epithelium** or urothelium . This is surrounded by a folded lamina propria and submucosa, followed by a dense sheath of interwoven smooth muscle layers and adventitia . Urine moves from the renal pelvises to the bladder by peristaltic contractions.


Bladder lumen
Ureters
Urethra
Urothelium
Lamina Propria
Muscularis
Superficial (Umbrella) cells
Intermediate cells
Basal cells
Basement membrane
Serosa

The urothelium is composed of the following three layers:

1 - a single layer of small basal cells resting on a very thin basement membrane,

2 - an intermediate region containing from one to several layers of more columnar cells,

3 - a superficial layer of very large, polyhedral or bulbous cells called **umbrella cells** which are bi- or multinucleated and are highly differentiated to protect underlying cells.

The **urethra**

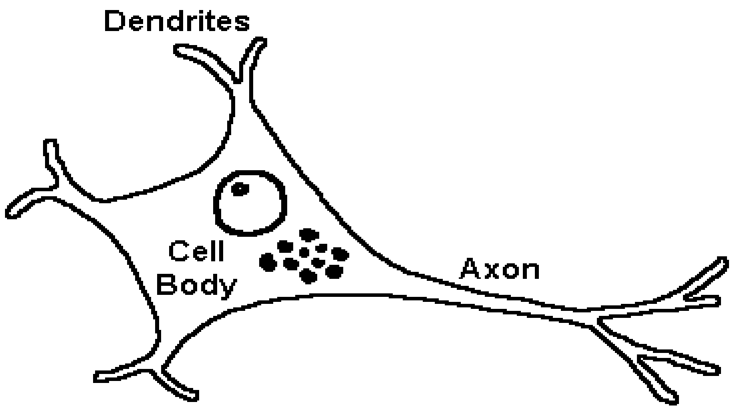
The epithelium of the urethra starts off as transitional cells as it exits the bladder. Further along the urethra there are pseudostratified columnar and stratified columnar epithelia, then stratified squamous cells near the external urethral orifice

The two major divisions of the nervous system are the central nervous system (CNS), consisting of the brain and spinal cord, and the peripheral nervous system (PNS) consisting of the peripheral nerves, nerve receptor endings, and ganglia distributed throughout the body. Embryologically, the central nervous system is derived from the neural plate which closes to form the neural tube. From the anterior neural tube additional folding and development produces the complex regions of the brain. The neural crest cells migrate to give rise to most of the peripheral nervous system.

Cells of the Nervous System

1. Neurons

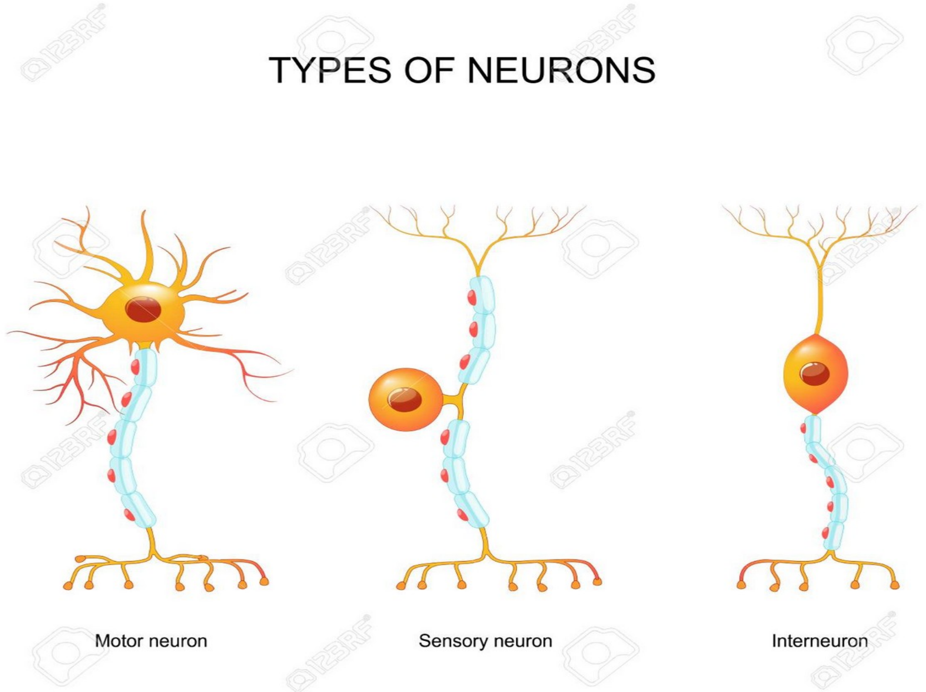
The major function of the nervous system is provided by neurons. Neurons come in a variety of shapes and sizes. In general, they have the following components:



- **Cell body**: the nucleus and cytoplasm containing organelles are contained here. The cytoplasm contains rough endoplasmic reticulum grouped to form the Nissl substance. There are neurofilaments that can occur singly or in clusters.
- **Dendrites:** these small arborizing processes receive almost all of the input (nerver impulses). They contain some organelles and many neurofilaments.
- **Axon:** a long process that conducts impulses (action potentials) away from the cell body. Most neurons have a single axon, though some can have more than one. At the distal end there is a terminal arborization with synapses to other neurons. Axons contain organelles and neurofilaments. Some axons are covered in a sheath of myelin.

Neurons can be subdivided into:

1. **Sensory neurons** carry signals from the outer parts of your body (periphery) into the central nervous system.
2. **Motor neurons** (motoneurons) carry signals from the central nervous system to the outer parts of your body.
3. **Interneurons** connect various neurons within the brain and spinal cord.



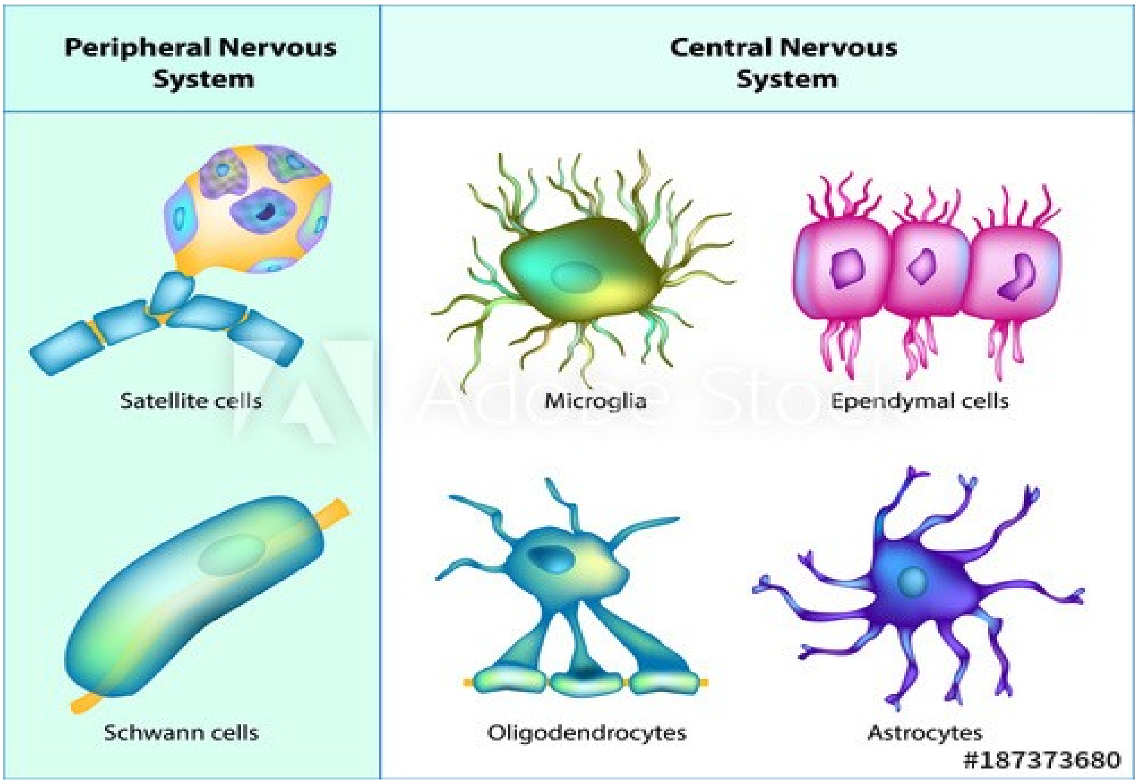
2. Glial Cells (supportive cells)

There are a variety of cells which support neuronal function. These include:

1. **Astrocytes:** these cells in the brain have a small, round nucleus and many very thin **processes** that radiate from them. The processes extend between neurons. At least one process either extends to and surrounds a capillary or extends to the overlying pia of the brain. The cytoplasm of astrocytes contains intermediate filaments that are composed of glial fibrillary acidic protein (GFAP) that serves to identify these cells.
2. **Oligodendroglia**: the oligodendroglial cells are small round cells that are most prominent in white matter. They produce the myelin that surrounds the axons of myelinated neurons of the CNS. A single oligodendrocyte can provide myelin for as many as 40 neurons.

3. **Microglia**: these cells are part of the mononuclear phagocyte system of fixed macrophages in tissues. They are ordinarly not numerous. However, when injury occurs, they become more numerous.
4. **Ependymal cells** are a specialized type of epithelial **cells** that line the ventricular system of the brain and play a key role in the production of cerebrospinal fluid.

These four types supporting cells are found within the central nervous system. Within the peripheral nervous system the supporting cells called **schwann cells** and **satellite cells.**

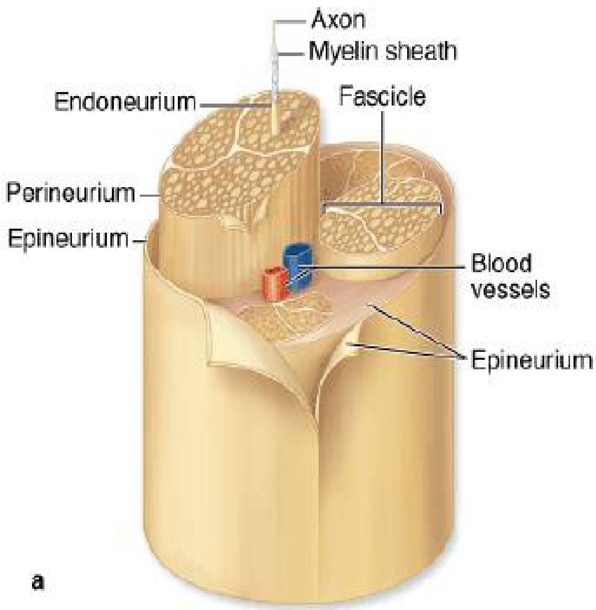


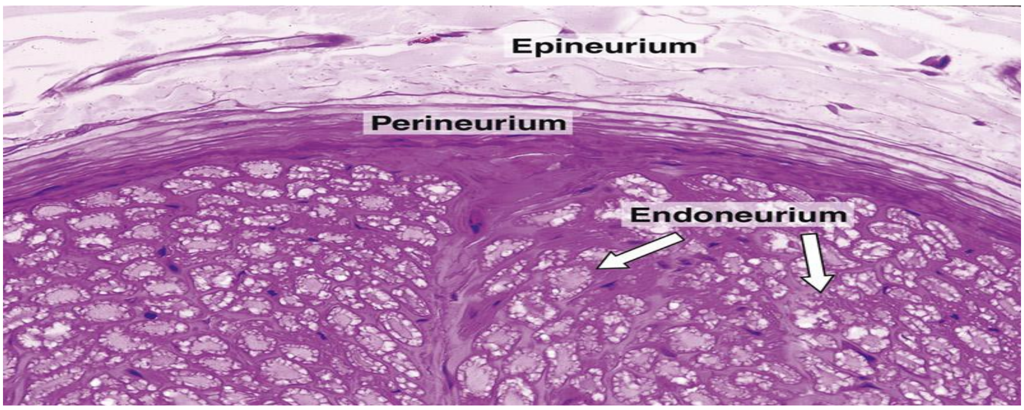
Structure of nerves

Is a bundle of nerve fibers surrounded by a series of connective tissue sheaths.

Each nerve has three types of support tissue:

1. **Epineurium**: an external fibrous coat of dense C.T. ,
2. **Perineurium**: consists of 7-8 concentric layers of epithelial like flattened cells.
3. **Endoneurium**: consists of longitudinally oriented reticular fibers, extracellular matrix, with few fibroblasts and mast cells.

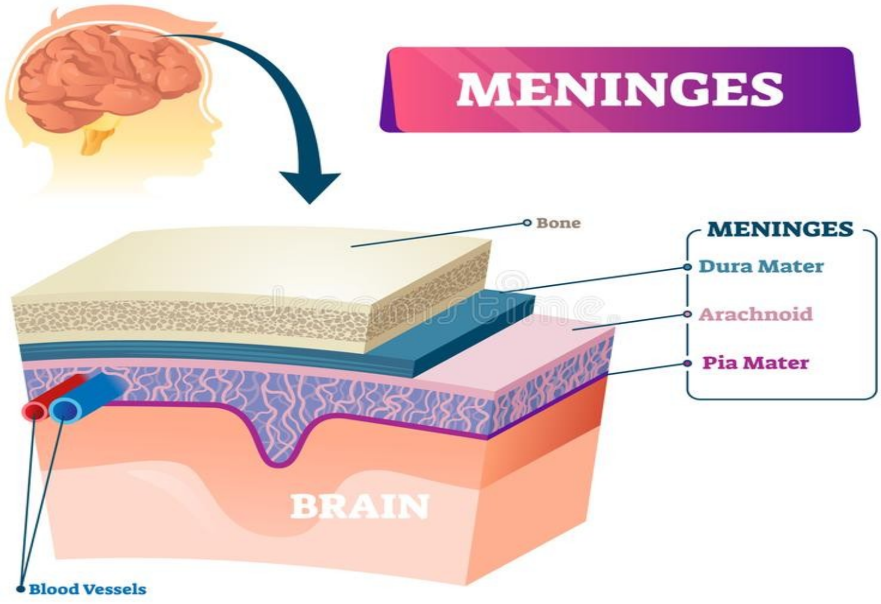




Meninges

The central nervous system is covered by specialized connective tissues that are divided into ***three*** layers:

1. **Dura mater**: the outer covering of the brain just inside the cranial cavity is a very tough layer of connective tissue--the dura. The potential space outside the dura next to the skull is known as the *epidural space* and separated from the arachnoid by the thin , *subdural space*.
2. **Arachnoid:** this thin avascular connective tissue layer has irregular channels below it comprising the subarachnoid space, though which the cerebrospinal fluid accumulates.
3. **Pia**: this thin layer of loose connective tissue highly vascular is directly adjacent to the CNS. The pia and arachnoid are so close and so similar in structure that they are often called the pia-arachnoid, better known as the leptomeninges.



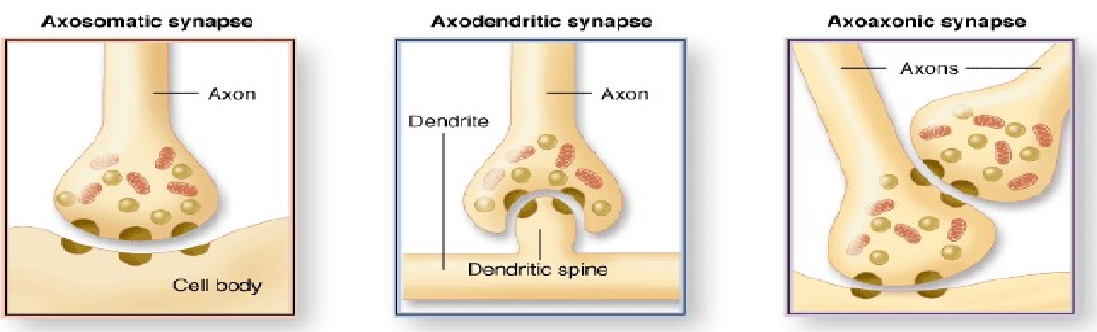
Synapses :

It is a unidirectional area of nerve impulse transmission through a contact between neurons, or between neurons and effector cells (muscle or gland).

The Parts of the Synapse

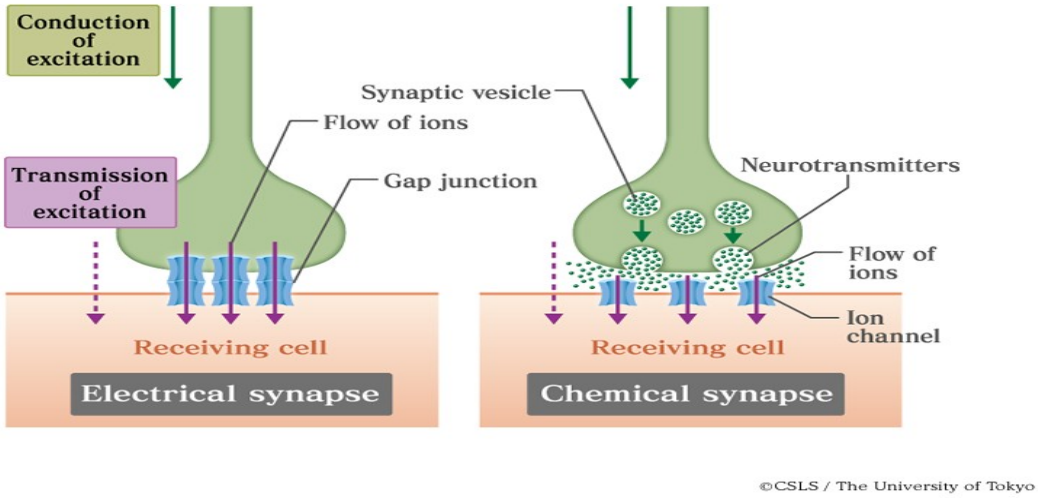
Synapses are composed of three main parts:

1- **Axo-somatic.**
2- **Axo- dendritic.**
3- **Axo-axonic.**



There are two main types of synapses:

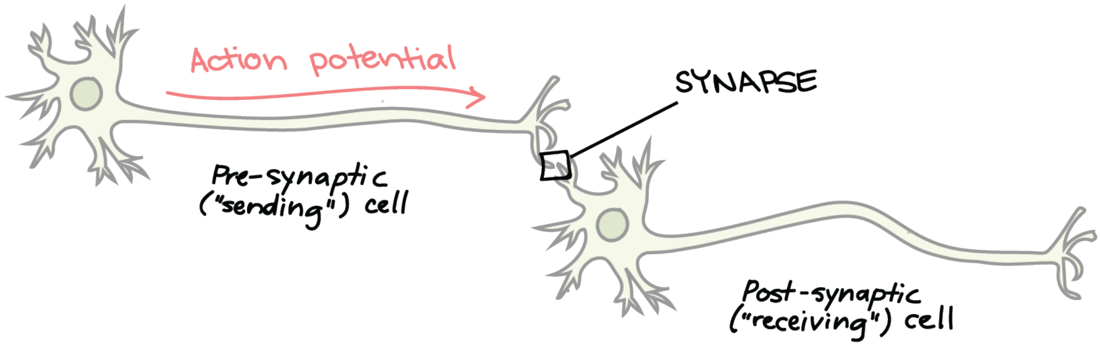
1. **Chemical synapse**: where the transmission of impulse is through a neurotransmitter.
2. **Electrical synapse:** the transmission of impulse is through gap junctions, where ions can freely pass, and the impulse is directly conducted.



Structure of synapse:

The synapse lies at the axon terminal, which is the swollen terminal end of the axon that is closely applied to the target cell. The synapse consists of the following structure:

1. **Presynaptic terminal (membrane):** lies at the axon terminal, slightly thickened, contains special membrane proteins. It is rich in mitochondria, microtubules, neurofillaments, and a membrane-bound vesicles is called neurosecretory vesicle. Each vesicle is small, round, with clear center, or dense-core vesicle. These vesicles contain the neurotransmitter which is synthesized in the cell body.
2. **Synaptic cleft**: a small gap between pre and post synaptic membranes. Sometimes, there are bridges at this cleft.
3. **Post synaptic terminal (membrane):** slightly thickened membrane at the target cells, which contains receptor sites with which the neurotransmitter interacts.



Cerebrum :

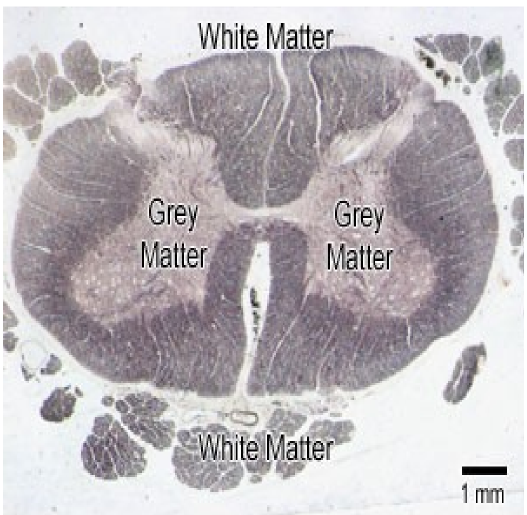
The cerebral cortex , the gray matter presents six layers of cells with different forms and size. The outer layer of gray matter consists of dendrites and axons of neurons from underlying layers.

Cerebellum:

The cerebellum cortex has three layers , an outer molecular layer, a central layer of large purkinje cells, and inner granular layer. The granular layer formed by very small neuron.

Spinal cord:

In cross section of the spinal cord , the white matter is peripheral and gray matter is central formed the shape of an H. the H shape have two anterior horns. These contain motor neurons whose make up the ventral roots of the spinal nerve. Two posterior horns which receive sensory fibers from neurons in the spinal ganglia.



Digestive System :

The digestive system is a tube extending from the mouth to the anus, and its associated accessory organs, primarily glands, which secrete fluids into the digestive tract. The digestive tract is also called the alimentary tract, or alimentary canal. The term gastrointestinal only refers to the stomach and intestines but is often used as a synonym for the digestive tract.

The regions of digestive tract include:

- **Oral cavity**: Lips and Tongue.
- **Digestive tract:** Pharynx, Esophagus, stomach, small intestine, large intestine, rectum, anus .
- **Accessory glands of digestive system:** salivary glands, pancreas, and liver.

A) Oral cavity:

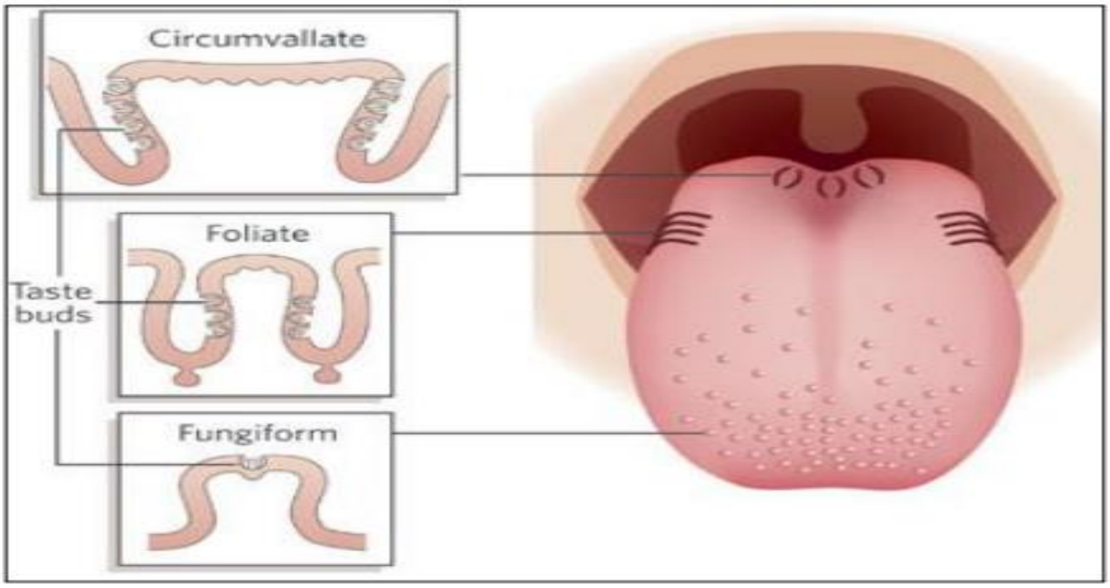
Tongue: is a muscular organ, covered by Stratified Squamous Epithelium resting on basement membrane; and lamina propria (binds epithelium to underlying muscle) that contains serous glands**. Tongue papillae (4 types):**

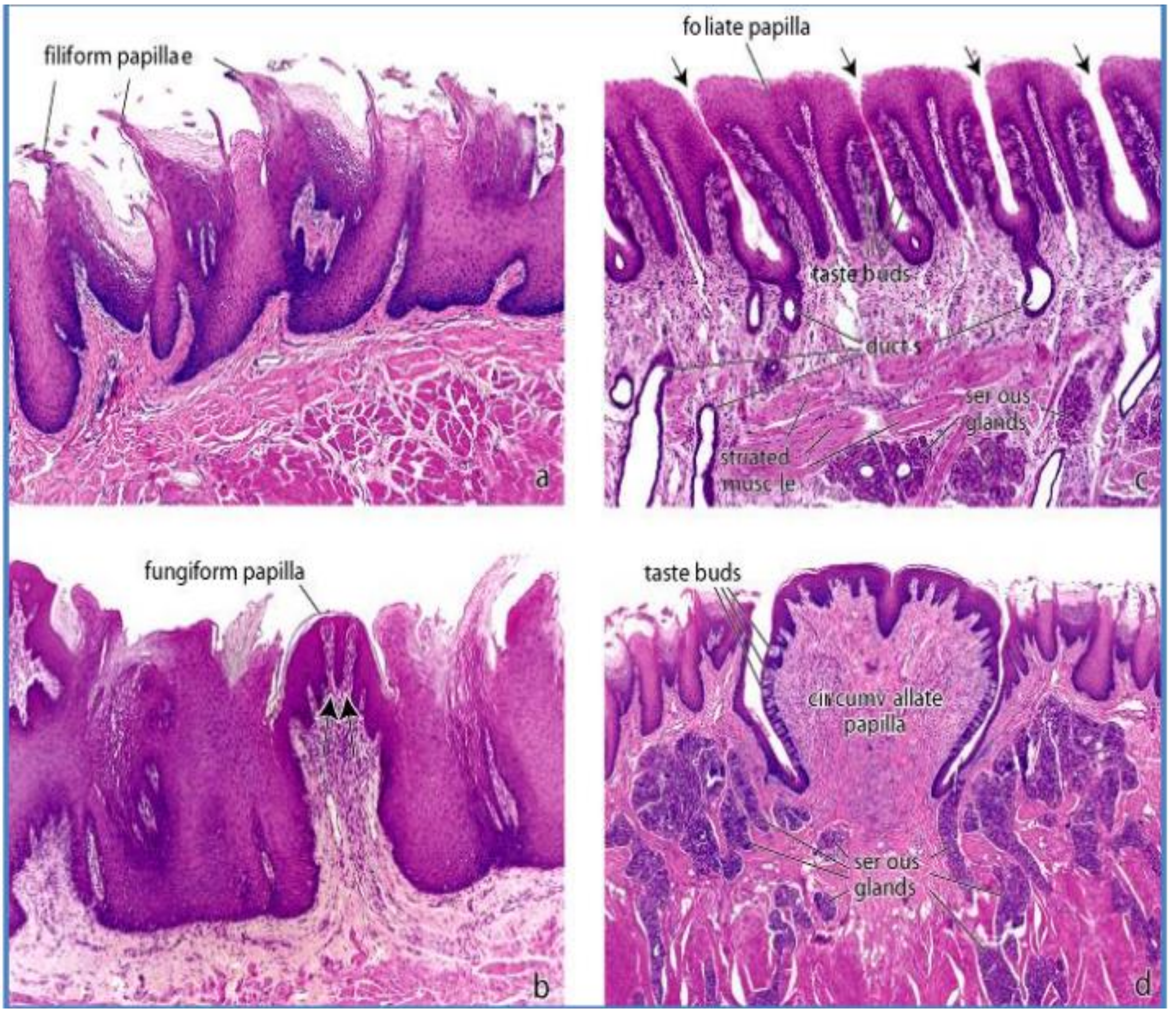
1. ***Filiform (leaf-like):*** along side of tongue; have no taste buds, and covered by keratinized epithelium.

2. **Fungiform:** globular; contain taste buds and covered by nonkerat. epith.

3. **Circumvallate:** contains taste buds, serous glands and covered by non-keratinized epithelium

4. Foliate papillae: are not well developed in humans and may be absent in aged individuals. They contain taste buds and covered by non-kerat. epith


Circumvallate
Foliate
Taste
buds
Fungiform


filiform papillae
a
fungiform papilla
b
foliate papilla
taste buds
ducts
serous
glands
striated
muscle
c
taste buds
circumvallate
papilla
serous
glands
d

.

B) Digestive canal:

In their general histological structure the wall of digestive canal is formed of 4 layers, or tunics. These tunics are present in all areas of the digestive tract from the esophagus to the anus :

1. The innermost tunic, the **Mucosa** consists of three sub-layers:

   A. the inner mucous ***epithelium***, which is moist stratified squamous epithelium in the mouth, oropharynx, esophagus, and anal canal and simple columnar epithelium in the remainder of the digestive tract;
   B. a loose connective tissue called the ***lamina propria*** and
   C. an outer thin smooth muscle layer, the ***muscularis mucosa.***

2. **Submucosa**

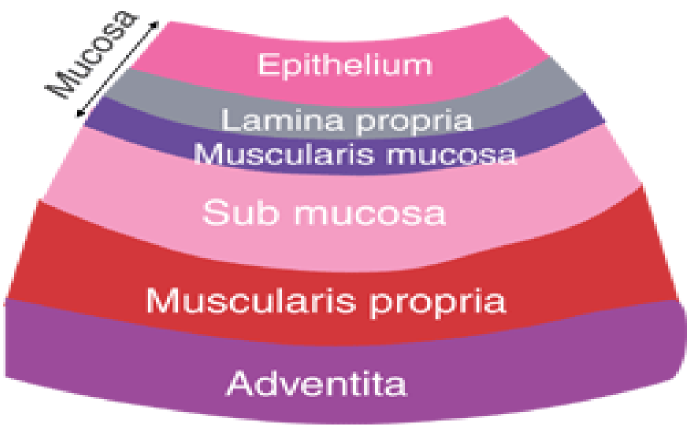
Is a thick connective tissue layer containing nerves, blood vessels, and small glands that lies beneath the mucosa.

3. **Muscularis**:

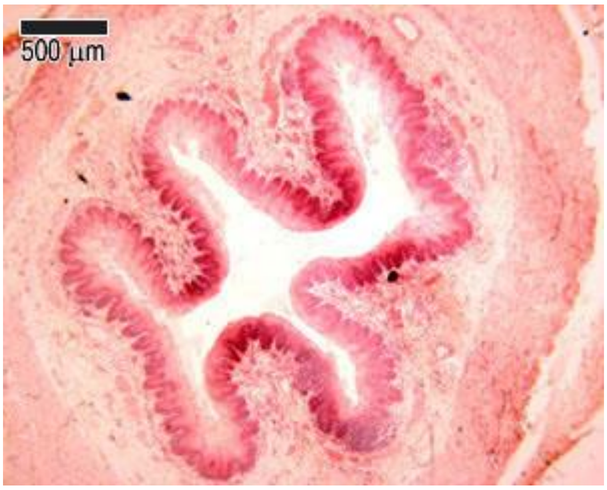
This consists of an inner layer of circular smooth muscle and an outer layer of longitudinal smooth muscle. *Two exceptions* are the upper esophagus, where the muscles are striated, and the stomach, which has three layers of smooth muscle.

4. **Adventia layer (or serosa)**

Outermost layer of loose connective tissue - covered by the visceral peritoneum. Contains blood vessels, lymphatics and nerves.



❖ **The oesophagus** : a muscular tube that transports food from mouth to stomach. Lining same as much of the oral cavity, that is a non-keratinized stratified squamous epithelium. Layers same as general digestive tract as outlined above.



❖ **Specializations of esophageal tissues:**

1. Small mucus secreting glands called esophageal glands proper are present in the submucosa. Their ducts extend to the esophageal lumen.
2. Near region of stomach esophageal cardiac glands are found in the lamina propria. These are branched mucous glands.
3. The muscular layer of the esophagus changes from striated muscle near mouth, to smooth muscle near stomach.

Stomach: Food starts to be digested and absorbed in the stomach, although absorption is mostly limited to water, alcohol and some drugs. The stomach is an expandable, muscular bag, and it keeps swallowed food inside it by contracting the muscular pyloric sphincter. Food is broken down *chemically*, by **gastric juice**, and *mechanically*, by contraction of the three layers of **smooth muscle** in the muscular externa layer. The broken up food at the end of this process is called **chyme**.

When the stomach is empty, and not distended, the lining mucosa and submucosa of the stomach are thrown up into folds called **rugae**. After eating, these folds flatten, and the stomach is able to distend greatly.

The stomach has three anatomical regions:

1. cardiac, which contains mucous secreting glands (called cardiac glands) and is closest to the oesophagus
2. fundus, the body or largest part of the stomach which contain the gastric (fundic) glands
3. pyloric, which secretes two types of mucus, and the hormone gastrin.

Layers of the stomach:

The stomach composed of four layers

A- Mucosa :

- *Epithelium* : consist of simple columnar epithelium, forming gastric pits .
- *Lamina propria* : contain numerous gastric glands (cardiac, fundic and pyloric glands) , slender blood vessels and various connective tissue with smooth muscle and lymphoid cells .
- *Muscularis mucosa*: is composed of the inner circular and an outer longitudinal smooth muscle .

B- Submucosa: Its composed of dense connective tissue containing blood and lymph vessels and no gland. It is infiltrated by lymphoid cells , macrophages and mast cells .

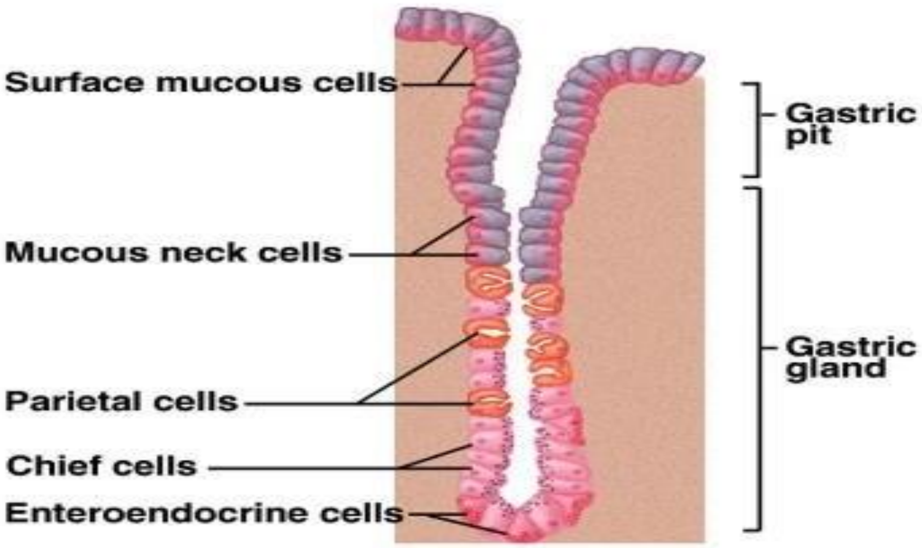
C- Muscularis externa : is composed of smooth muscle fibers oriented in *three* main directions . The external layer is longitudinal , the middle layer is circular , and the internal layer is oblique .

D- Serosa : The stomach is covered by a thin connective tissue coat enveloped in visceral peritoneum .

Cells of gastric glands:

- **Mucous neck cells** :, *mucous secreting cells* protect stomach cells from corrosive nature of gastric acid.
- **Chief cells** (zymogene cells) produces pepsin, rennin, and lipase (digestive enzymes).
- **Parietal (oxyntic) cells**: secret *hydrochloric acid* and *intrinsic factor* (glycoprotein binds vitamine B12).
- – **Gastric enteroendocrine cells**; produce hormones.

Gastric Pit and Gastric Gland



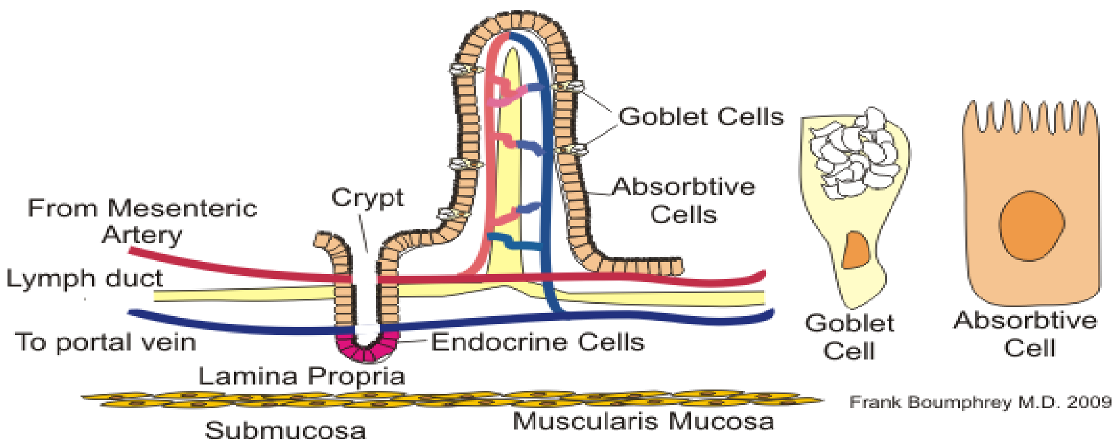
❖ **Small Intestine:** has three distinct regions – the duodenum, jejunum, and ileum.

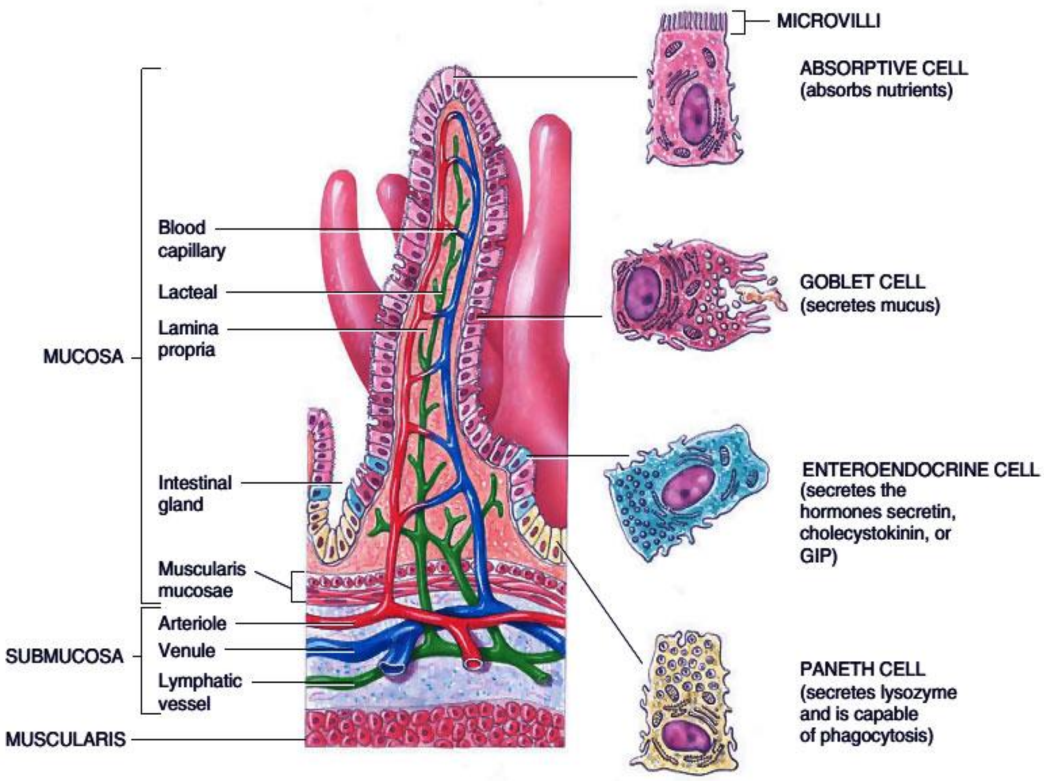
Duodenum

The surface of the duodenum has several modifications that increase its surface area about 600-fold to allow for more efficient digestion and absorption of food. The mucosa and submucosa form a series of folds called the circular folds, or plicae circulares, which run perpendicular to the long axis of the digestive tract. Tiny fingerlike projections of the mucosa form numerous villi.

Each villus is covered by simple columnar epithelium and contains a blood capillary network and a lymphatic capillary called a lacteal. Regulations and Maintenance cytoplasmic extensions called microvilli, which further increase the surface area. The combined microvilli on the entire epithelial surface form the brush border. These various modifications greatly increase the surface area of the small intestine and, as a result, greatly enhance absorption. The mucosa of the duodenum is simple columnar epithelium with ***four*** major cell types:

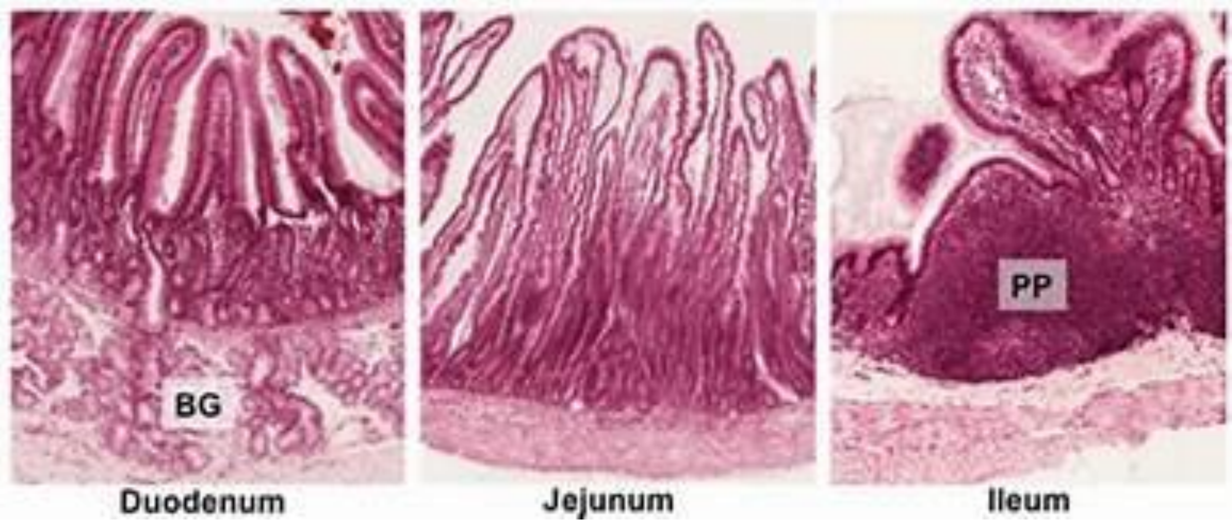
1. **Absorptive cells** are cells with microvilli, which produce digestive enzymes and absorb digested food.
2. **Goblet cells,** which produce a protective mucus
3. **Granular cells (Paneth's cells),** which may help protect the intestinal epithelium from bacteria.
4. **Endocrine cells,** which produce regulatory hormones. The epithelial cells are produced within tubular invaginations of the mucosa, called intestinal glands (crypts of Lieberkühn), at the base of the villi.





Jejunum and Ileum:

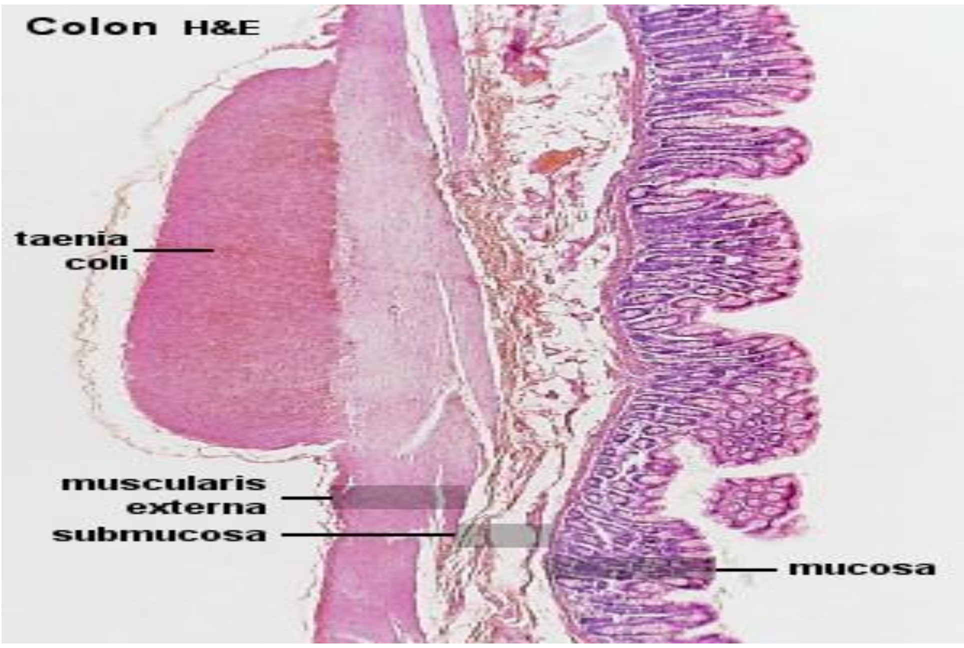
The jejunum and ileum are similar in structure to the duodenum, except that a gradual decrease occurs in the diameter of the small intestine, the thickness of the intestinal wall, the number of circular folds, and the number of villi as one progresses through the small intestine. The duodenum and jejunum are the major sites of nutrient absorption, although some absorption occurs in the ileum. Lymph nodules called Peyer's patches are numerous in the mucosa and submucosa of the ileum.

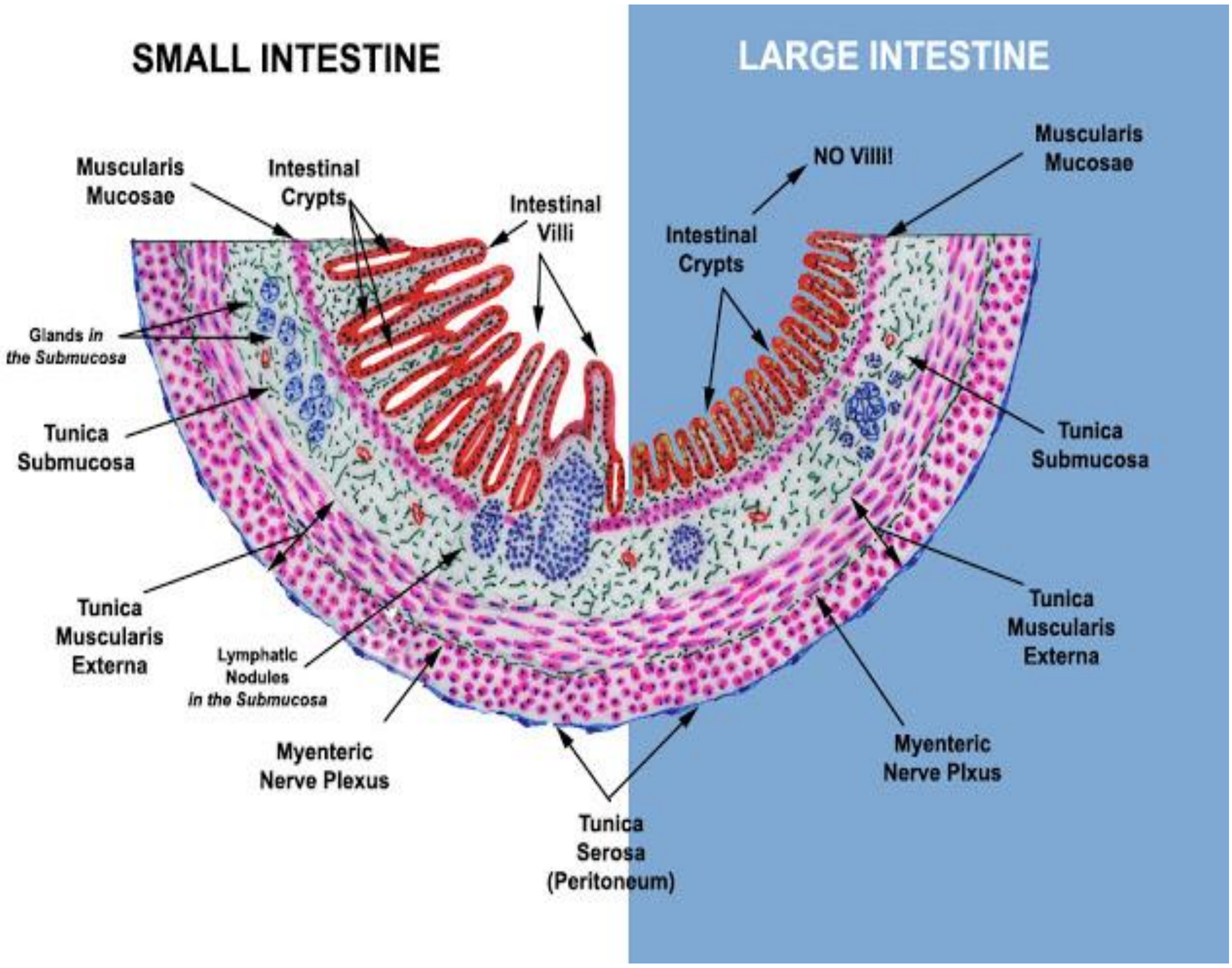


❖ Large Intestine:

The divide region: cecum, colon, rectum, and anal canal.

- The large intestine completes absorption, and retrieves water and sodium , remove are fecal residue. It secretes large amounts of mucus, and some hormones, but no digestive enzymes.
- The thick **mucosa** has deep **crypts,** but there are no villi. The epithelium is formed of **columnar absorptive cells** with a striated border, many goblet cells, endocrine cells and basal stem cells, but no Paneth cells. The surface epithelial cells are sloughed into the lumen, and have to be replaced around every 6 days.
- The **lamina propria** and **submucosa** are similar to the small intestine.
- The **longitudinal smooth muscle** in the **muscularis externa** is arranged in three longitudinal bands called **taenia coli**. At the anus, the circular muscle forms the internal **anal sphincter.**

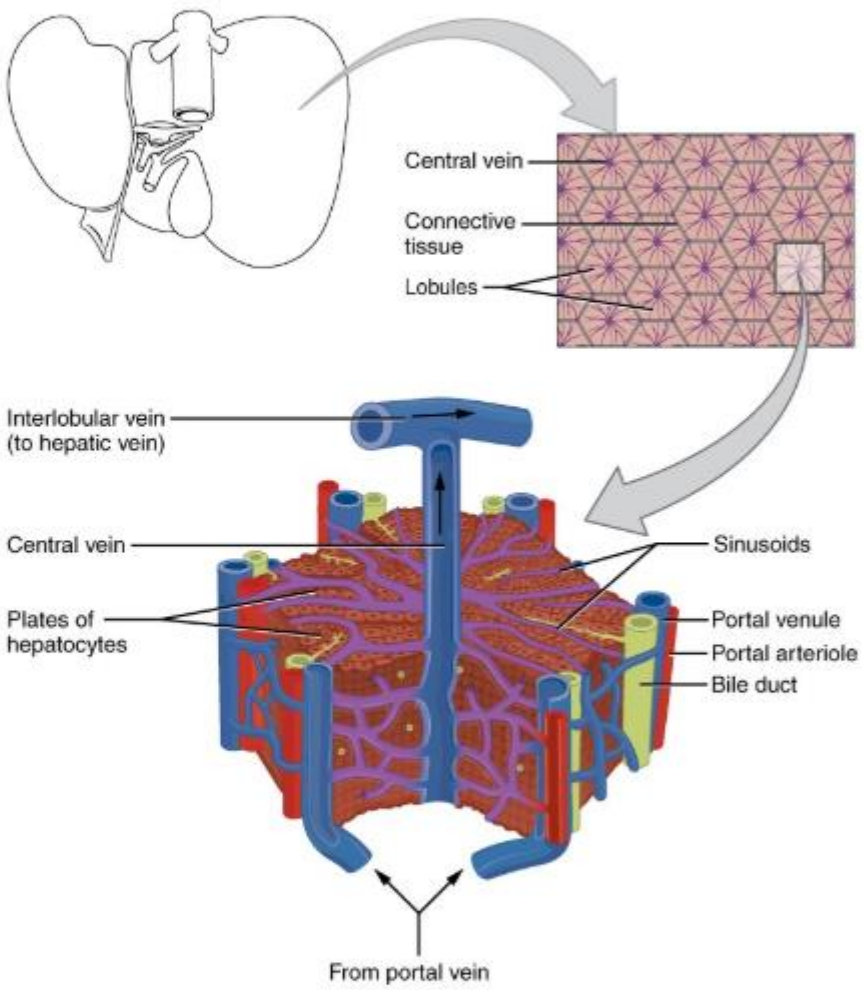

Colon H&E
taenia coli
muscularis externa
submucosa
mucosa


SMALL INTESTINE
LARGE INTESTINE
Muscularis Mucosae
Intestinal Crypts
Intestinal Villi
Glands in the Submucosa
Tunica Submucosa
Tunica Muscularis Externa
Lymphatic Nodules in the Submucosa
Myenteric Nerve Plexus
Tunica Serosa (Peritoneum)
NO Villi!
Intestinal Crypts
Muscularis Mucosae
Tunica Submucosa
Tunica Muscularis Externa
Myenteric Nerve Plxus

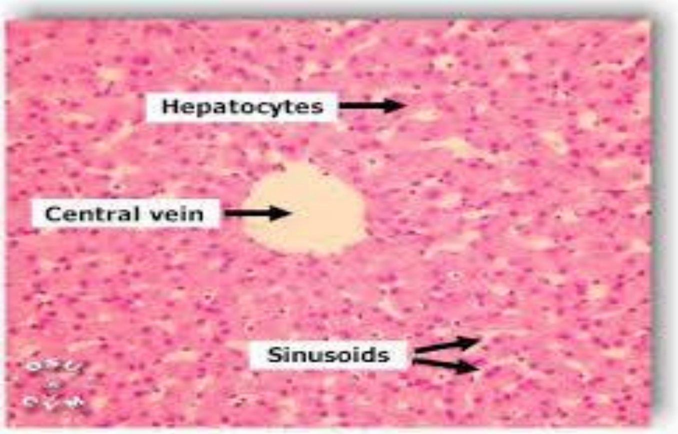
The salivary glands, liver, gallbladder, and pancreas are all accessory digestive organs that support the digestive system. Their histological composition will be discussed in this lecture.

Liver

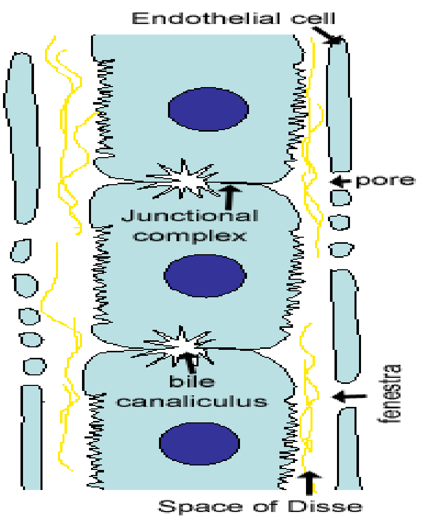
The liver is the largest organ in the human body. It is able to filter and process nutrient rich blood from the digestive tract because of its intricate histological arrangement. Its fibrous capsule infiltrates the substance of the organ and divides it into lobules that are almost hexagonal. Each lobule typically has three to six portal areas/canals (also known as the portal triad) – each of which is usually located at the apices of the lobule. Each portal canal contains a branch of the hepatic portal vein, hepatic artery, lymphatic vessels and a bile duct.

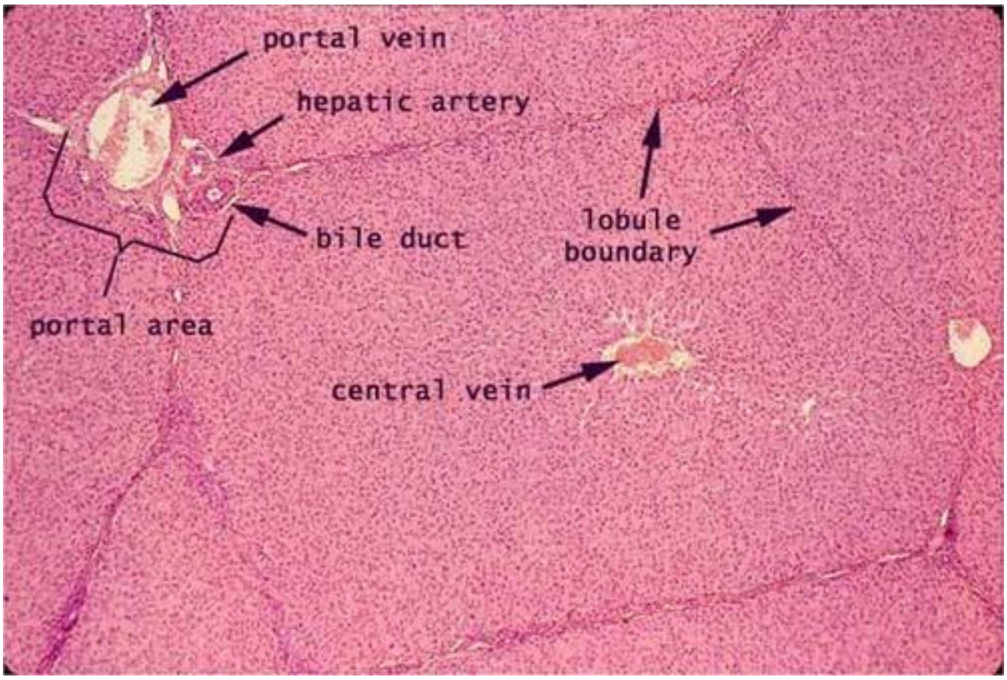


Liver cells (hepatocytes) appear as cords of cells from the center of the lobule and travels towards its periphery. In between the cords are fenestrated capillaries known as sinusoids. The perisinusoidal space of Disse provides some degree of separation between the hepatocytes and the sinusoids. It's by way of the fenestrations of the sinusoids that mixed blood from both the hepatic portal vein and the hepatic artery gains access to the hepatocytes where they are processed. Additionally, the nutrient rich blood also encounters macrophagic Kupffer cells that degrade worn out cellular structures. The sinusoids travel a convoluted pathway towards the center of the lobule where it drains into the central vein, which then drains to larger hepatic veins that drain directly to the inferior vena cava.



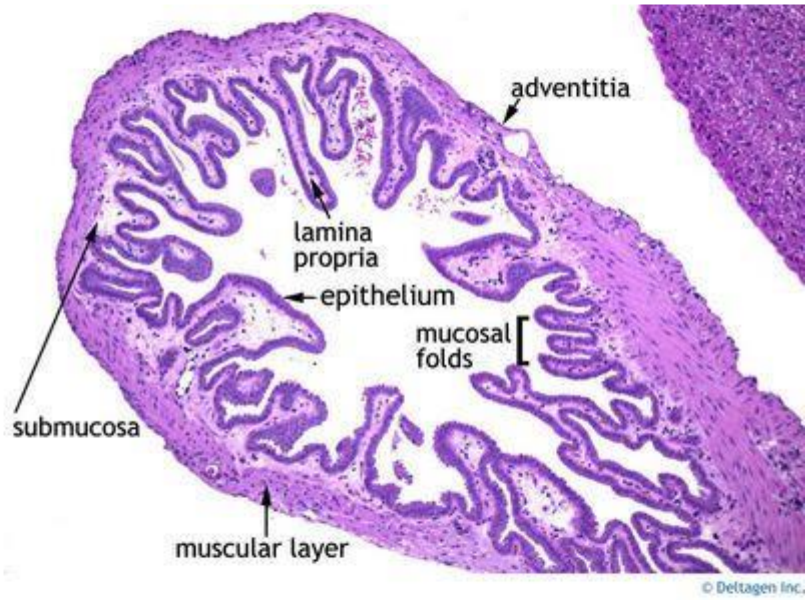
Finally, bile produced by the hepatocytes is released into bile canaliculi, which are adjacent to individual liver cells. The canaliculi then merge at the edge of the lobules to form bile duct in the portal triad. Therefore blood travels centrally to the central vein of the lobule, while bile travels peripherally to the portal triad; thus preventing any mixture of the two substances.





Gallbladder

Although the gallbladder is not a true gland (because it doesn't produce any secretions), it stores and concentrates bile for subsequent release upon hormonal signalling.
The muscular sac's histological layout is similar to that of the gastrointestinal tract. It has a mucosa, muscular layer and an outer serosa. The epithelium of the mucosa is lined with simple columnar cells attached to a lamina propria that is made up of loose connective tissue and vasculature. The smooth muscle fibers of the muscularis layer surround the lamina propria. These muscle fibers aid in the ejection of bile from the gallbladder.

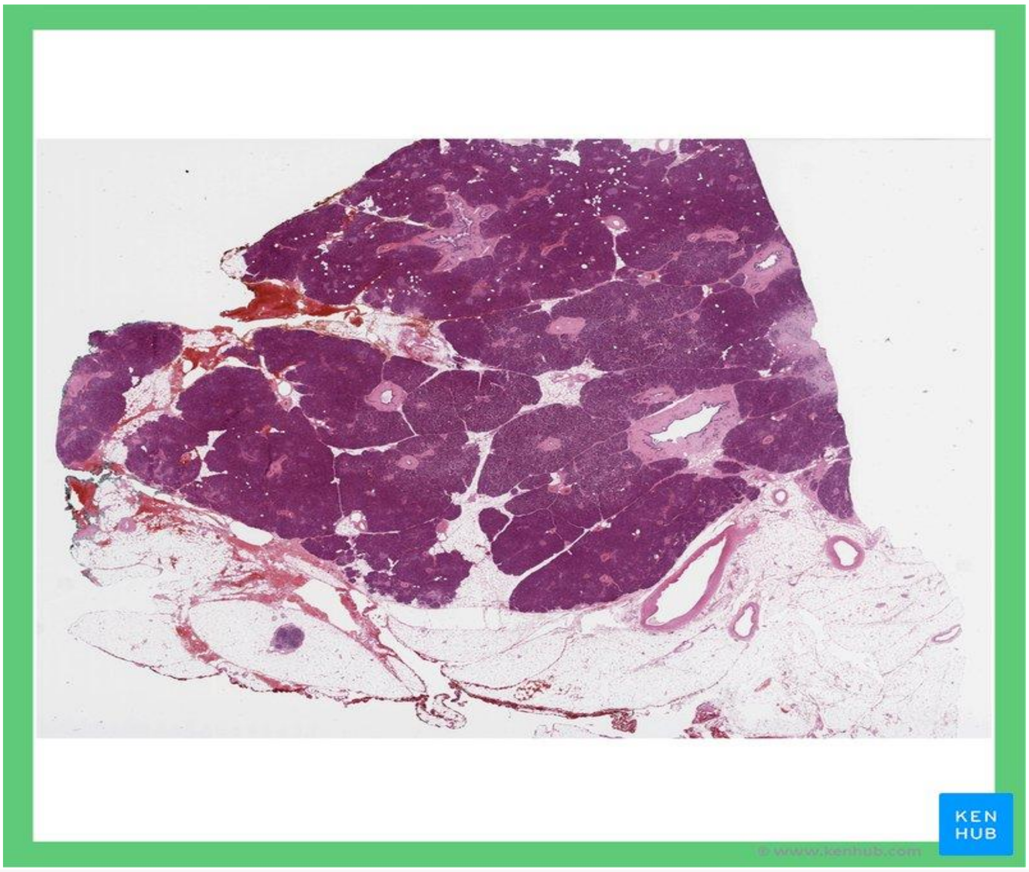


Gallbladder (histological slide)

When the gallbladder is empty, it has numerous temporary mucosal folds. In this state, the histological appearance of the gallbladder is similar to that of the small intestines. External to the smooth muscle layer is thick, dense connective tissue – in which large neurovascular and lymphatic structures are embedded. The serosa +covers the aspect of the gallbladder that is not attached to the inferior surface of the liver.

Pancreas

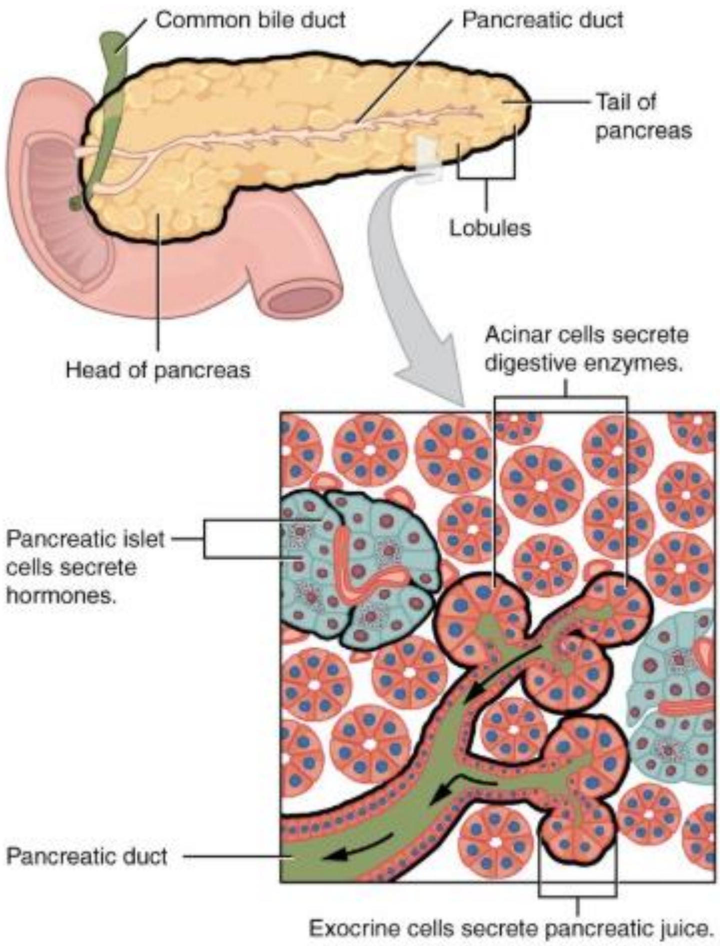
The pancreas is functionally and histologically divided into exocrine and endocrine components. In the exocrine component, there are zymogenic cells that are pyramidal and form the serous acini. The gland is also lobulated by fibrous septae that contains general neurovascular structures as well as specialized nerves called Pacinian corpuscles. The Pacinian corpuscle provides specialized sensory perception to the gland. Because the exocrine portion is made up of serous glands that are similar to those found in the parotid glands, one can be easily mistaken for the other. However, the presence of paler staining, isolated clusters of cells (islets of Langerhans) in the pancreas should safeguard the observer from such an error. The absence of myoepitheilal cells in the pancreatic acini is also another good indication to the observer that the specimen being reviewed is the pancreas and not the parotid gland.



Body of pancreas (histological slide)

Centroacinar cells form the initial segment of the duct system for the pancreatic serous acini. They continue with the simple cuboidal epithelium of the intercalated ducts that drain the acini to their interlobular ducts (also covered by simple cuboidal epithelium), which terminate in the pancreatic ducts.

The endocrine component of the gland is formed by the islets of Langerhans. The highly vascular islets are surrounded by a connective tissue capsule. The endocrine unit is made up of alpha cells that produce glucagon, beta cells that are responsible for the secretion of insulin, somatostatin-secreting delta cells and pancreatic polypeptide cells that inhibit the secretion of alkaline solutions and the production of pancreatic enzymes.

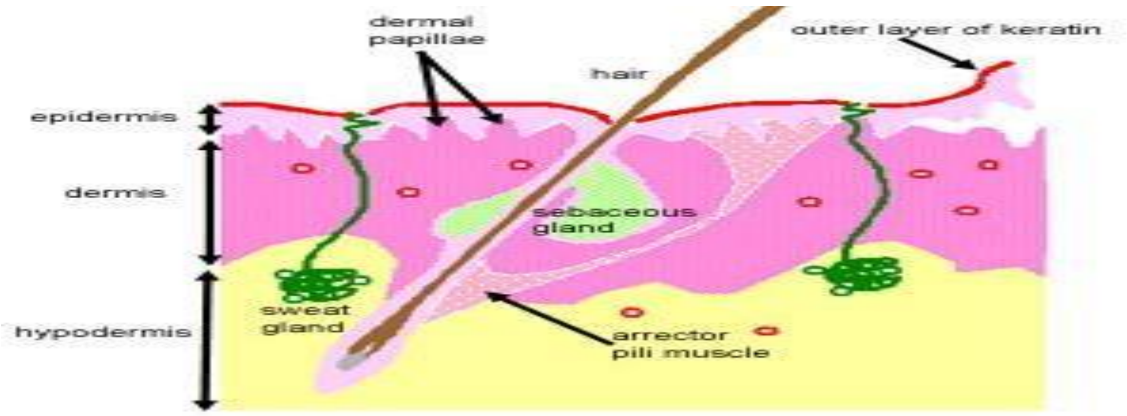

Common bile duct
Pancreatic duct
Tail of pancreas
Lobules
Head of pancreas
Acinar cells secrete digestive enzymes.
Pancreatic islet cells secrete hormones.
Pancreatic duct
Exocrine cells secrete pancreatic juice.

Skin

The layer covers the body, and is the major external barrier between the outside world and the body. It has important protective functions, and is constantly renewing itself.

Functions of skin

1. **Protection**: it protects against UV light, mechanical, thermal and chemical stresses, dehydration and invasion by micro-organisms.
2. **Sensation**: skin has receptors that sense touch, pressure, pain and temperature.
3. **Thermoregulation**: various features of the skin are involved in regulating temperature of the body. For example sweat glands, hair, and adipose tissue.
4. **Metabolic functions**: subcutaneous adipose tissue is involved in production of vitamin D, and triglycerides.

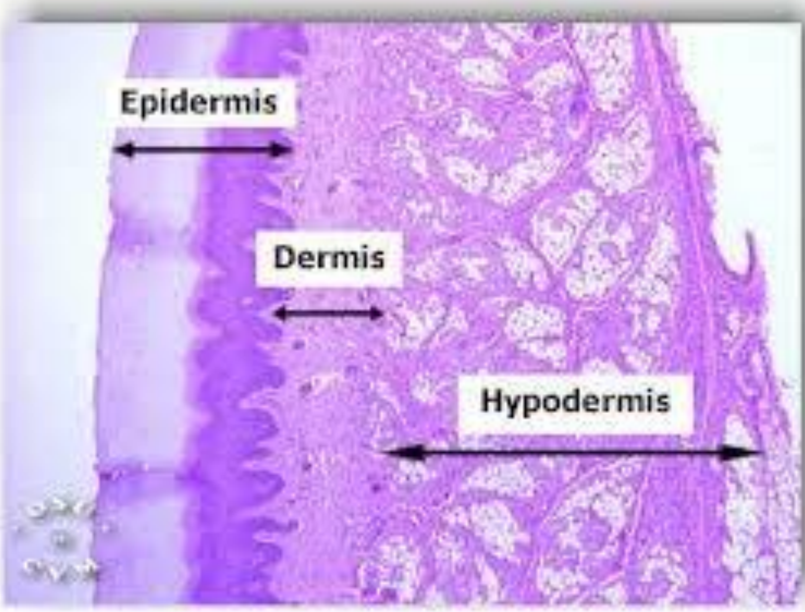


This diagram shows the layers found in skin. There are three main layers: the **epidermis**, **dermis** and **hypodermis**. There are also sweat glands, and hairs, which have sebaceous glands, and a smooth muscle called the arrector pili muscle, associated with them.

Hairs are only found in thin skin, and not in the thick skin present on the fingertips, palms and soles of your feet.

Three layers of skin:

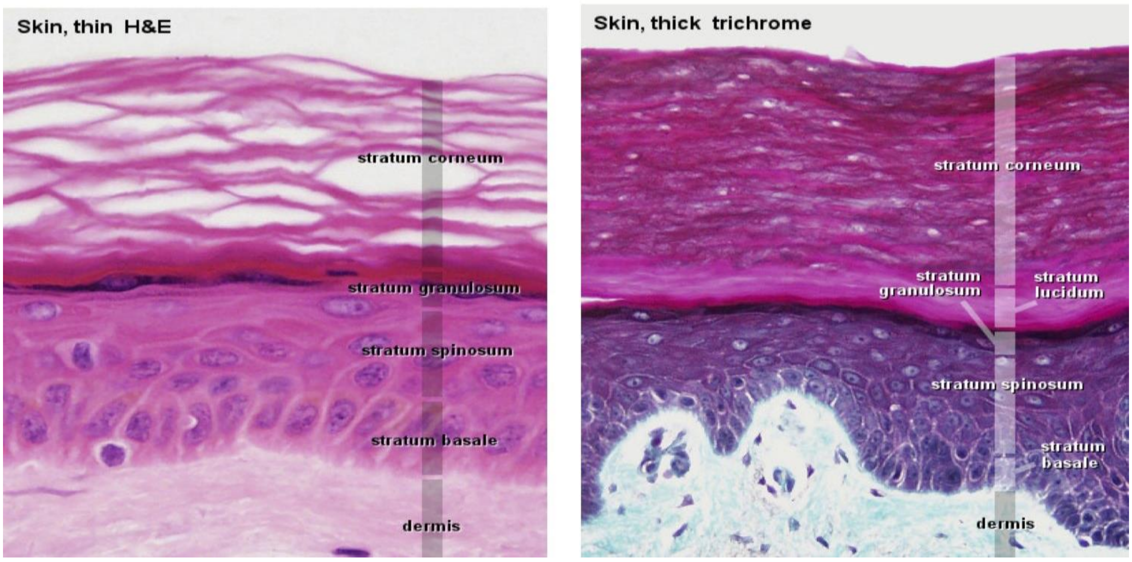
- The **epidermis**: a thin outer portion, that is the keratinized stratified squamous epithelium of skin. The epidermis is important for the protective function of skin. The basal layers of this epithelium are folded to form dermal papillae.
- The **dermis:** a thicker inner portion. This is the connective tissue layer of skin. It is important for sensation, protection and thermoregulation. It contains nerves, the blood supply, fibroblasts, etc., as well as sweat glands, which open out onto the surface of the skin, and in some regions, hair. The apical layers of the dermis are folded, to form dermal papillae.
- The **hypodermis**. This layer is underneath the dermis, and merges with it. It mainly contains adipose tissue and sweat glands. The adipose tissue has metabolic functions: it is responsible for production of vitamin D, and triglycerides.



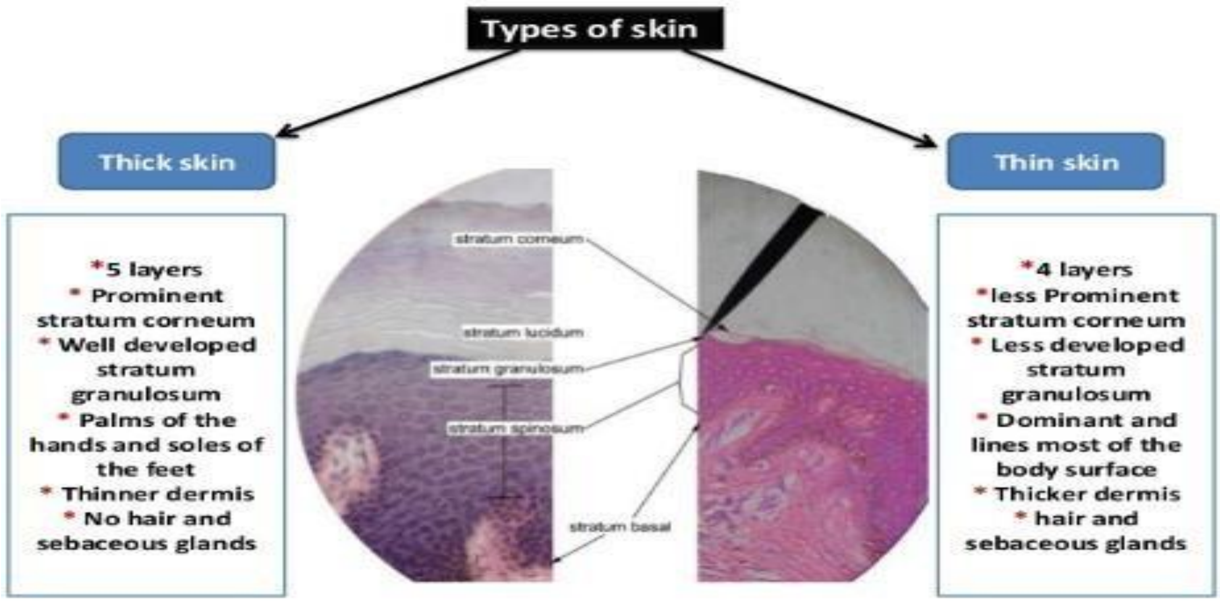
Layers in the Epidermis

- The basal cell layer (**stratum basale**, or stratum germinosum), is a single layer of cells, closest to the dermis. It is usually only in this layer that cells divide. Some of the dividing cells move up to the next layer.
- The prickle cell layer (**stratum spinosum**) is the next layer (8-10 layers of cells). The cells in these layers have lots of desmosomes, which anchor the cells to each other.
- The granule cell layer (**stratum granulosum**) is the next layer (3-5 layers of cells). As the cells move up into this layer, they start to lose their nuclei and cytoplasmic organelles, and turn into the keratinized squames of the next layer.
- (**stratum lucidum**) is sometimes identified - between the stratum granulosum and stratum corneum layer. It is a thin transparent layer, difficult to recognize in routine histological sections.
- The keratinised squames layer (**stratum corneum**) is the final layer. These are layers of dead cells, reduced to flattened scales, or squames, filled with densely packed keratin.

Thin vs. Thick Skin Epidermis



The differences between thick and thin skin :



Cell types

The epidermis is made up a variety of cell types. Cell that contain keratin are known as **keratinocytes.** These are stratified squamous epithelial cells that are shed from the surface of the skin daily. They are the progeny of cells in the basal layer.

There are also mature non-keratinocytes that exist in the epidermis. These include the **melanocytes** (which are derived from embryonic neural crest), and lymphocytes and Langerhans cells that arise from bone marrow dendritic cells. As stated earlier, melanocytes synthesize and store melanin, which not only contributes to the color of the skin and hair, but also provides protection against ultraviolet radiation. They appear as clear cells in the basal layer with large, round, euchromatic nuclei. It is possible for a single melanocyte to provide melanin for approximately 30 keratinocytes via its dendritic arborisation.

The **Langerhans cells** serve as antigen presenting cells. They are distributed throughout the strata spinosum and basale, sparing only the sweat glands. These cells can be readily identified by a hallmark tennis racket-like discoid Birbeck granule, in addition to its euchromatic cytoplasm and Golgi complex.

There are also mechanoreceptors within the epidermis that facilitate sensory perception. The **Merkel cells** are clear, ovoid and may occur singly or in clusters in the stratum basale. Free nerve endings in the form of expanded discs are present at the base of these cells. Merkel cells may act as a sensory mechanoreceptors and are also thought to function as neuroendocrine sensory receptors.

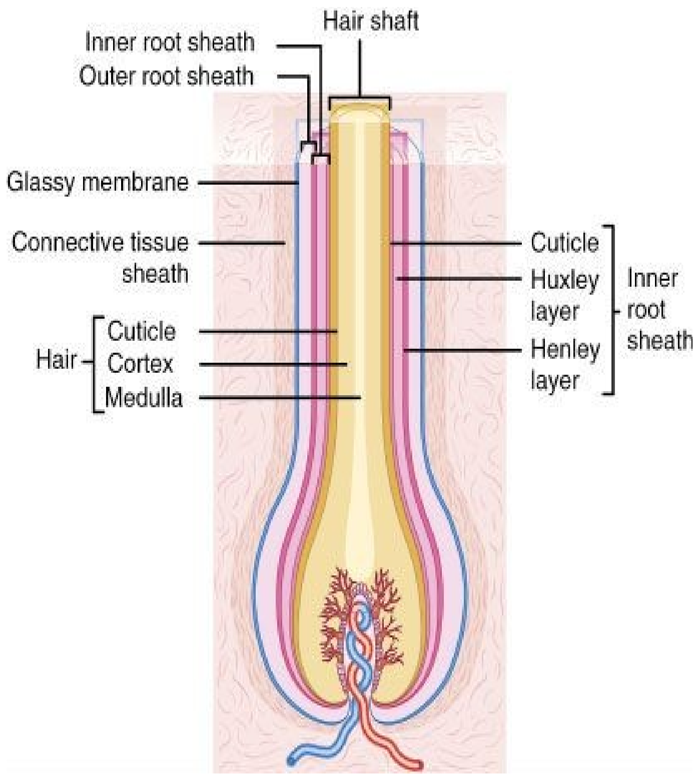
Skin Appendage:

1. Hair

In simple terms, hair strands are filaments that have been keratinized that extend from the cutaneous surface at an angle. The distribution of hair over the body, as well as its morphology (colour, texture, curl pattern etc.) is genetically predetermined. There are areas of the body that are devoid of hair. These include glabrous skin of the palm and sole, as well as in another thin skin .

Hair strands exist in conjunction with several other structures (including sebaceous and apocrine glands) that form a pilosebaceous unit. From outside in, there is:

- ***A connective tissue sheath***
- ***A glassy membrane*** - homogenous modified basement membrane
- ***An outer root sheath*** starts as a single or double layer at the upper bulb. The cells here are undifferentiated and filled with glycogen granules. Subsequently, they become stratified and differentiate into interfollicular epidermal cells and form the walls of the opening of sebaceous duct.



An inner root sheath with three layers, from superficial to deep

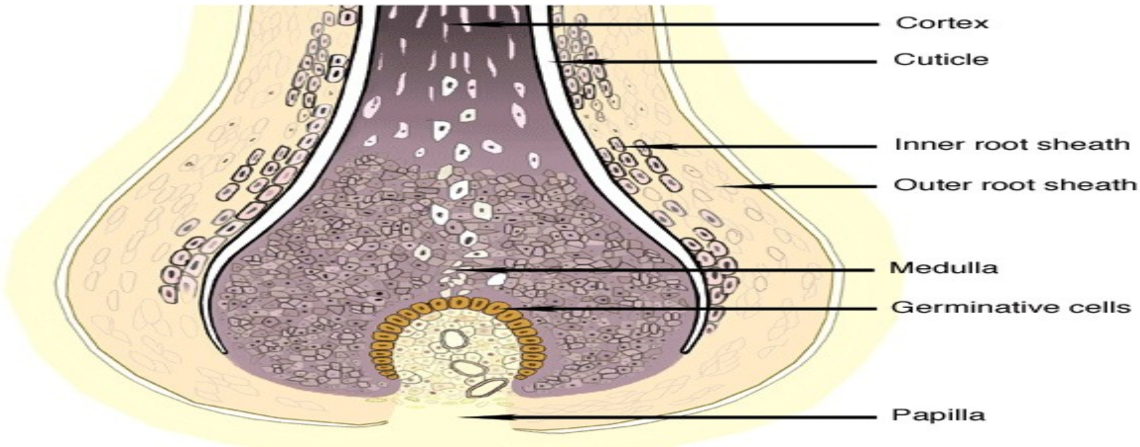
- ***Henle's layer*** is a thickened keratinized envelope that contains keratin filaments in a matrix and clear cells of squamous to cuboidal variety. It becomes keratinized at the level of the upper bulb.
- ***Huxley's layer*** has a similar composition to Henle's layer. It becomes cornified from the mid inferior follicle and beyond. The flattened keratinized cells contain keratohyalin granules known as trichohyalin granules.
- ***Cuticle of the inner root sheath*** becomes interlocked with the hair shaft during cornification up to where the inner root sheath starts to fragment at above the isthmus at the level of the sebaceous duct opening
- Note that prior to cornification of Henle's and Huxley's layers of the inner root sheath, these structures contain dense, irregular arrangements of keratohyalin.

And finally, the *hair shaft*; which has three layers listed from superficial to deep

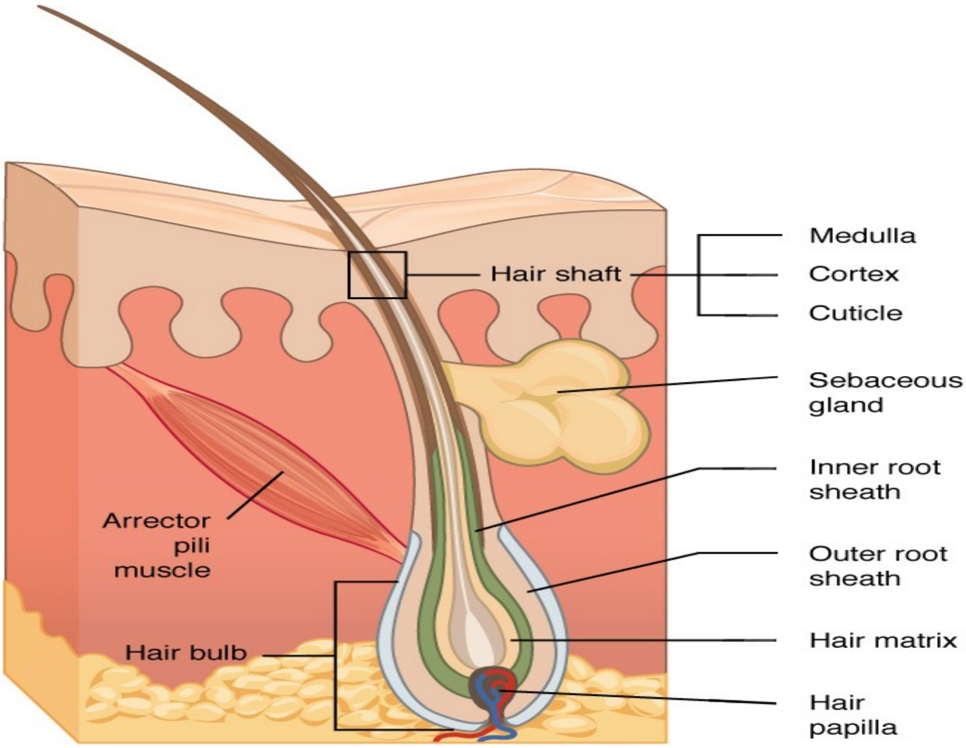
- ***Cuticle*** of the hair shaft is a layer of stratified keratinized squames that encircles the cortex.
- ***Cortex*** is a multitude of elongated, densely packed squames that surrounds the medulla.
- ***Medulla*** is absent in hair shaft of fine hairs.

It should be noted that the proximal swollen part of the unit known as the hair bulb also contains melanocytes, as well as a dermal hair papilla that carries neurovascular structures to the hair matrix. The dermal papilla also has the necessary mesenchymal cells that are needed for cyclical hair growth during adulthood.

The hair bulb can be subdivided into the germinal matrix inferiorly, and the upper bulb superiorly. In addition to Langerhans cells and melanocytes, the germinal matrix also has pluripotent keratinocytes that are actively dividing. In the upper bulb, the cells move toward the apex as they differentiate to form the three layers of the shaft



The relationship of individual hair strands to the surface of the skin is under neuro-hormonal regulation. This action is mitigated by the arrector pili muscle. This is a typical smooth muscle structure with intervening collagen fibres and unmyelinated sympathetic nerve fibres. The muscle bundle forms an oblique angle with the hair follicle at its insertion into the bulge of the follicle, where elastin fibres facilitate their attachment above the level of the sebaceous gland. In addition to piloerection, arrector pili muscles also aid in expelling the contents of sebaceous gland into the hair canal. Of note, there are no arrector pili fibres in the face and axillar .



2. Nails

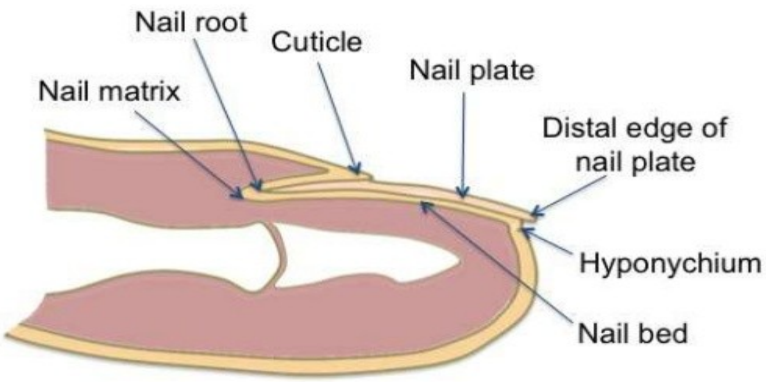
The fingernail is an important structure made of keratin. The fingernail generally serve two purposes. It serves as a protective plate and enhances sensation of the fingertip. The protection function of the fingernail is commonly known, but the sensation function is equally important. The fingertip has many nerve endings in it allowing us to receive volumes of information about objects we touch. The nail acts as a counterforce to the fingertip providing even more sensory input when an object is touched.

Nail Structure

The structure of the nail is divided into six specific parts: the root, nail bed, nail plate, eponychium (cuticle), perionychium, and hyponychium.

1. **Root** (nail matrix) The root of the fingernail is also known as the germinal matrix. This portion of the nail is actually beneath the skin behind the fingernail and extends several millimeters into the finger. The fingernail root produces most of the volume of the nail and the nail bed. This portion of the nail does not have any melanocytes, or melanin producing cells. The edge of the germinal matrix is seen as a white, crescent shaped structure called the lunula.
2. **Nail Bed** is part of the nail matrix called the sterile matrix. It extends from the edge of the germinal matrix, or lunula, to the hyponychium. The nail bed contains the blood vessels, nerves, and melanocytes, or melanin-producing cells. As the nail is produced by the root, it streams down along the nail bed, which adds material to the undersurface of the nail making it thicker.

3. **Nail Plate** is the actual fingernail, made of translucent keratin. The pink appearance of the nail comes from the blood vessels underneath the nail. The underneath surface of the nail plate has grooves along the length of the nail that help anchor it to the nail bed.
4. **Eponychium** of the fingernail is also called the eponychium. The cuticle is situated between the skin of the finger and the nail plate fusing these structures together and providing a waterproof barrier.
5. **Perionychium** is the skin that overlies the nail plate on its sides. It is also known as the paronychial edge.
6. **Hyponychium** is the area between the nail plate and the fingertip. It is the junction between the free edge of the nail and the skin of the fingertip, also providing a waterproof barrier.



1. Sweat Glands

Two types of sweat glands are present in humans. They are distinguished by their secretory mechanism into *merocrine (~eccrine)* and *apocrine sweat glands*. In addition, they differ in their detailed histological appearance and in the composition of the sweat they secrete.

- **Merocrine sweat glands** are of critical importance for the regulation of body temperature. The skin contains ~3,000,000 sweat gland which are found all over the body - with the exception of, parts of the external genitalia.

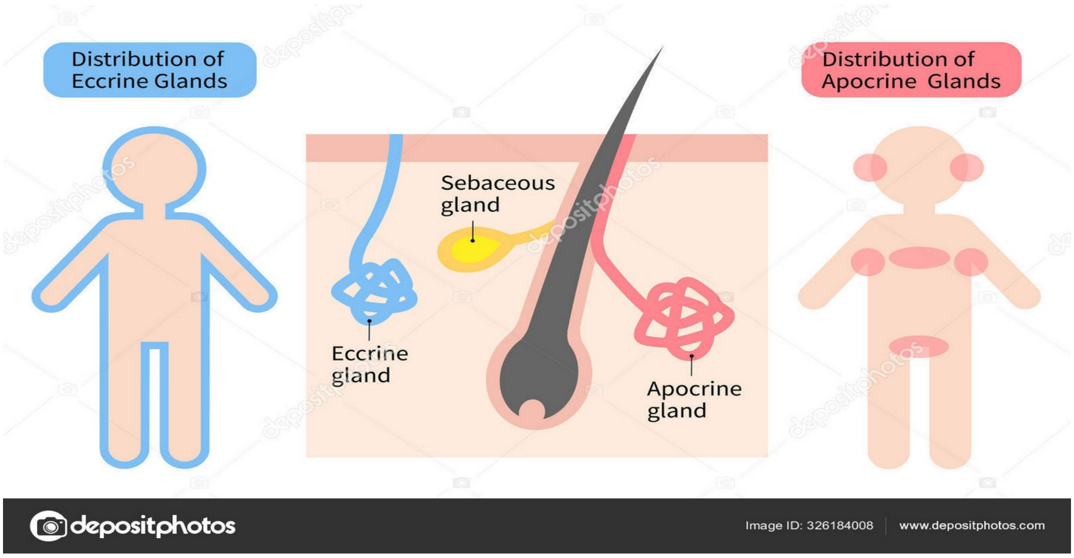
- Sweat glands are *simple tubular glands*. The secretory tubulus and the initial part of the excretory duct are coiled into a roughly spherical ball at the border between the dermis and hypodermis.
- The secretory epithelium is cuboidal or low columnar. Two types of cells may be distinguished: a light type, which secretes the watery eccrine sweat, and a dark type, which may produce a mucin-like secretion. The cells have slightly different shapes and, as a result of the different shapes, the epithelium may appear pseudostratified.
- A layer of *myoepithelial cells* is found between the secretory cells of the epithelium and the basement membrane.
- The excretory duct has a stratified cuboidal epithelium (two layers of cells).

The excretory ducts of merocrine sweat glands empty directly onto the surface of the skin.

- **Apocrine sweat glands** occur in, for example, the axilla. They are stimulated by sexual hormones and are not fully developed or functional before puberty. Apocrine sweat is a milky, proteinaceous and odourless secretion. The odour is a result of bacterial decomposition and is, at least in mammals other than humans, of importance for sexual attraction.

The histological structure of apocrine sweat glands is similar to that of merocrine sweat glands, but the lumen of the secretory tubulus is much larger and the secretory epithelium consists of only one major cell type, which looks cuboidal or low columnar. Apocrine sweat glands as such are also much larger than merocrine sweat glands.

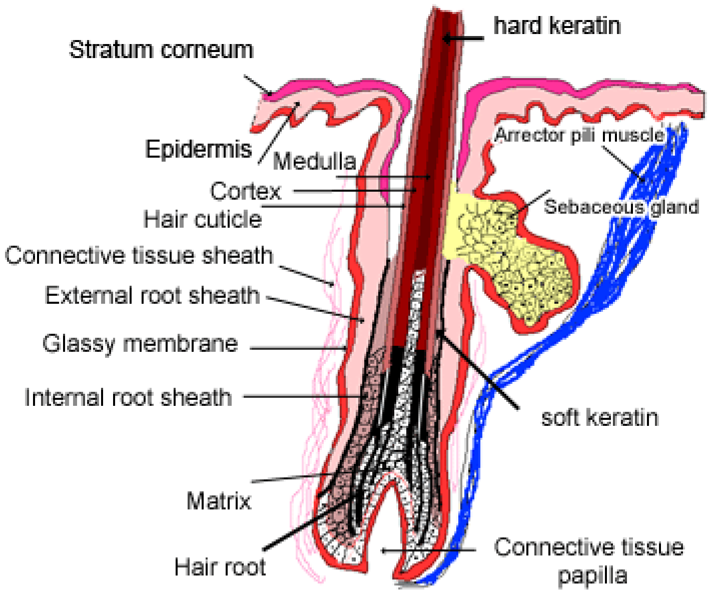
The excretory duct of apocrine sweat glands does **not** open directly onto the surface of the skin. Instead, *the excretory duct empties the sweat into the upper part of the hair follicle*. Apocrine sweat glands are therefore part of the pilosebaceous unit.

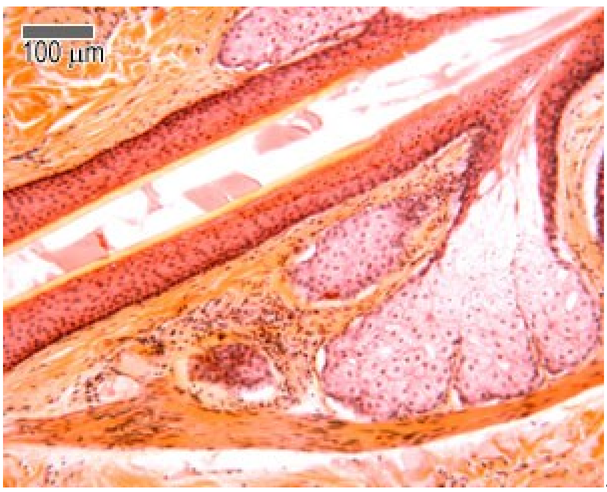


2. Sebaceous Glands

Sebaceous glands are branched acinar (spherical) glands which make an oily substance called **sebum**. The rounded cells are filled with lipid filled vacuoles, and towards the end of the duct, the cells degenerate to release their contents into the duct - HOLOCRINE secretion. This oil coats hair and the surface of thin skin to help keep it soft, supple and waterproof.

At puberty, the size of the sebaceous glands, and their secretory activity increase, in response to increasing levels of androgens. If the gland become blocked, the sebum can be forced out into the dermis, where it elicits an inflammatory response. This can cause **acne**.





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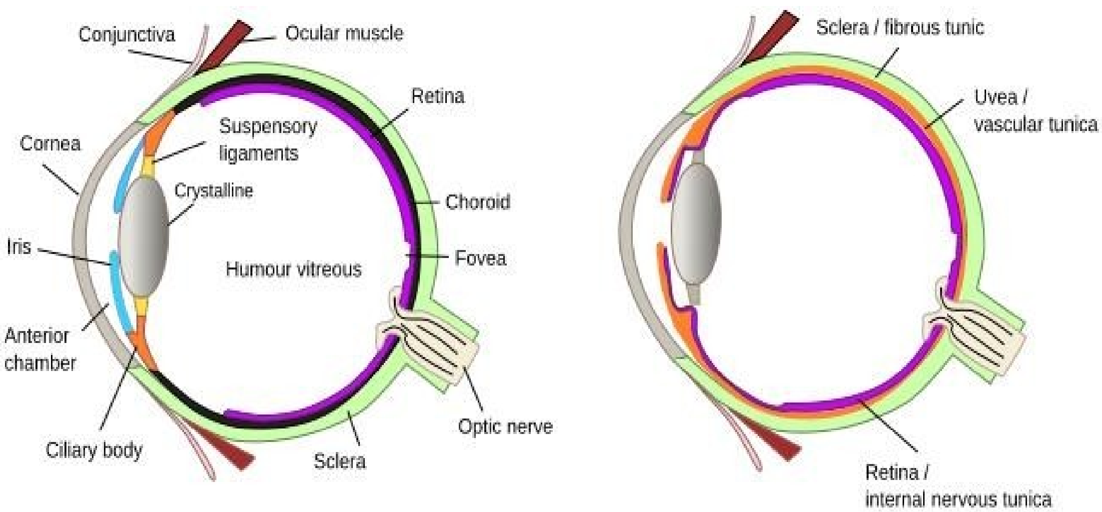
Sense Organ bnmn:

Definition of sense organ: a bodily structure that receives a stimulus and is affected in such a manner as to initiate excitation of associated sensory nerve fibers which convey specific impulses to the central nervous system .

❖Eye

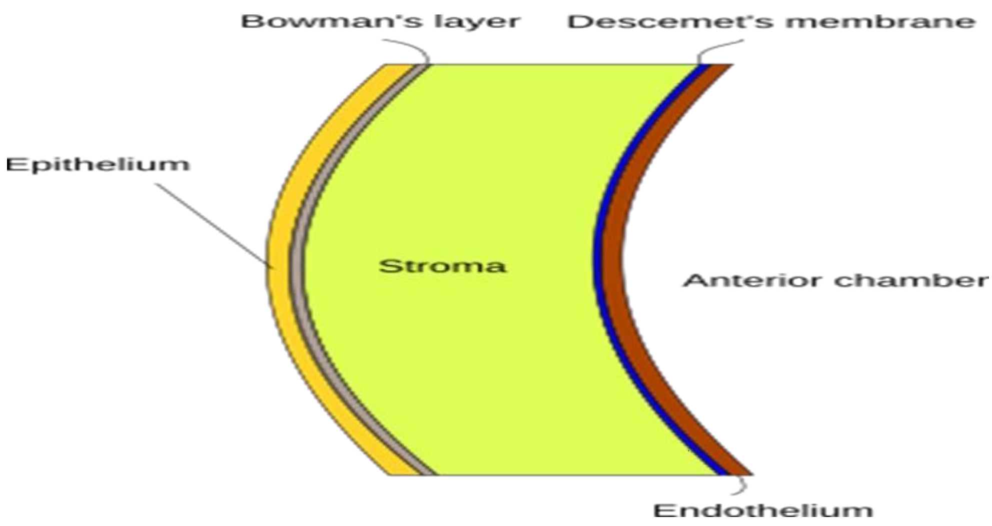
Eyes are structures that detect the light reflected by objects, transduce it into electrical information that, after a local processing, is sent to other parts of the encephalon for combining with other neuronal information that altogether eventually change the animal behavior.



Main components of the eye of mammals.

- **Cornea** is the most external part of the eye so it is in contact with the air. It is a transparent structure that focuses the light and protects the eye surface.

The cornea is a sheet of tissue made up of five layers: corneal epithelium, Bowman's layer, stroma, Descemet's membrane, and endothelium. Corneal epithelium is the most outer layer, it is stratified squamous epithelium, contains many nervous fibers, and can be easily auto-repaired. Corneal epithelium is laterally continuous with the epithelium of the conjunctiva.



Layers of the cornea

- The **ciliary body** is found behind the iris and performs main **function**: changing the shape of the crystalline to focus the light on the retina.
- The **iris** is the structure or the eye that separates the anterior chamber from the posterior chamber, and is attached to the ciliary body through its periphery part. In the central area of the iris, there is an opening, known as pupil, through which the light can reach the crystalline lens. The iris is mostly highly vascularized loose connective tissue. No matter the diameter, blood vessels show the same organization. They do not contain muscle layer.
- The **crystalline lens** is located behind the pupil and shows a transparent biconvex body Covering the crystalline.
- The **vitreous body** fills the cavity between the crystalline lens and the retina. It is a gelatinous substance with similar transparency to crystal glass and composed of an aqueous solution with abundant type II and XI collagen, and hyaluronan.

- The **retina** is the light-sensitive structure of the eye and the most internal tunica of the eye. It results from an evagination of the central nervous system during the embryo development. This evagination folds to get a cup-shape morphology with **two layers**: a pigmented external one and a nervous internal one.