

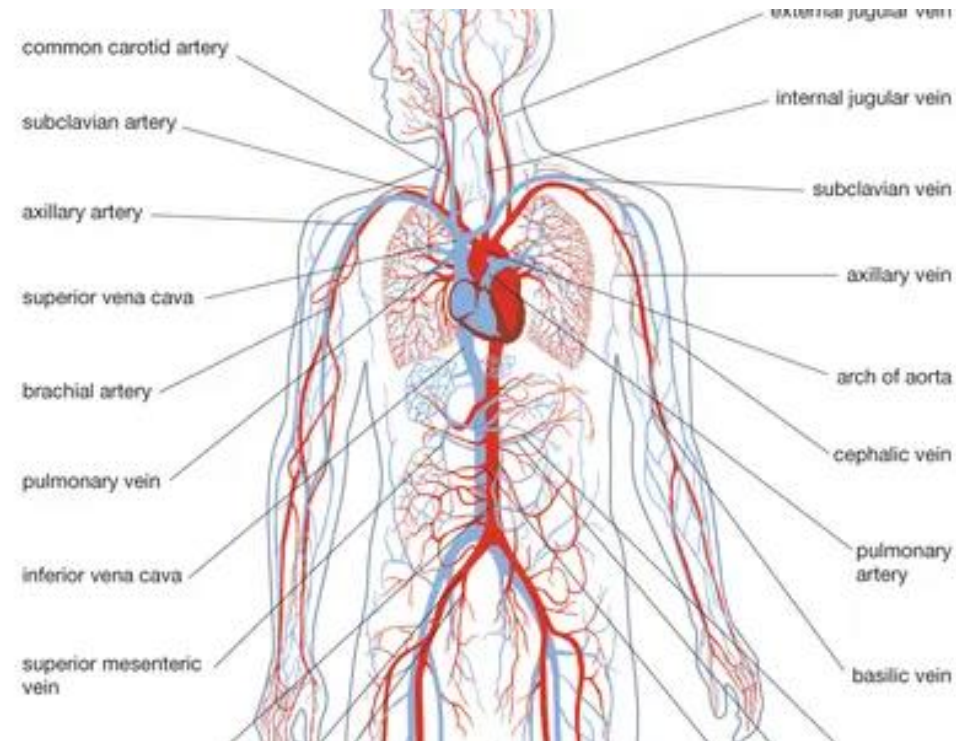


University of Kragujevac  
Faculty of Medical Sciences  
Integrated Academic Studies of Medicine  
Department of Histology and Embryology

# Circulatory system The Immune System & Lymphoid Organs

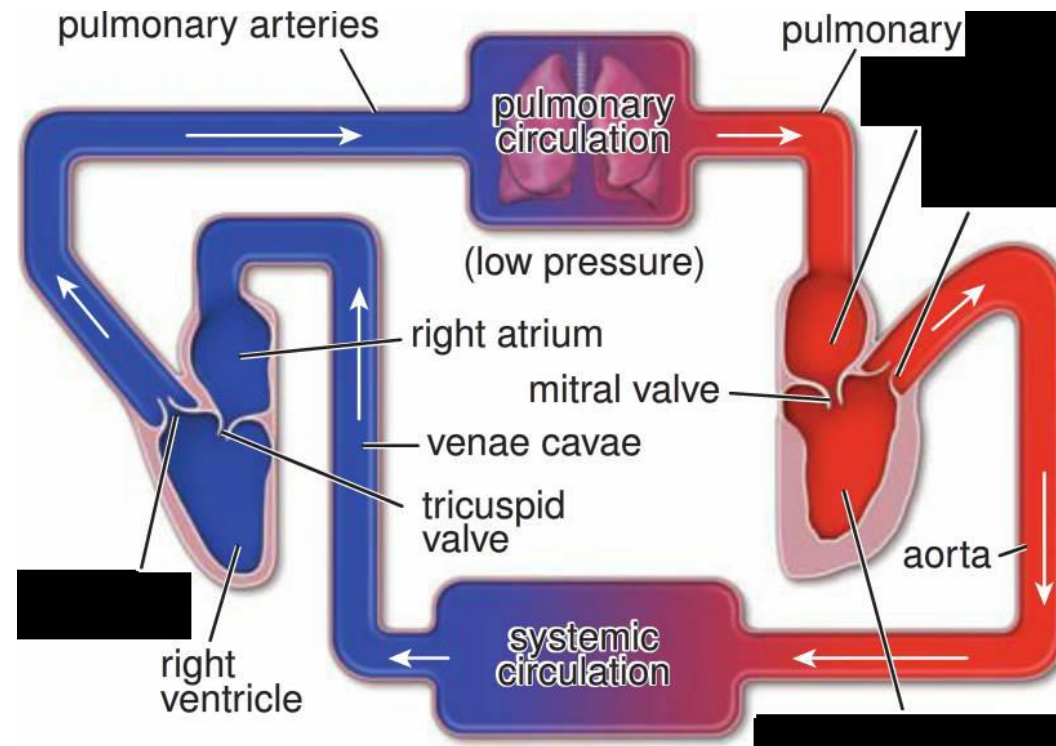
# **CIRCULATORY SYSTEM**

- ❖ Includes heart, blood vessels and lymphatic vessels.
- ❖ Main transport system that carries blood and lymph to and from the tissues of the body. The constitutive elements of these fluids include cells, nutrients, waste products, hormones, and antibodies.
- ❖ The circulatory system is also capable of regulating the temperature and coagulation of the blood.
- ❖ Consists of **cardiovascular** part and **lymphatic vessel** part



# Cardiovascular system - CVS

- Two pathways of circulation are formed by the blood vessels and the heart:
- **Pulmonary circulation** conveys blood from the heart to the lungs and from the lungs to the heart
- **Systemic circulation** conveys blood from the heart to other tissues of the body and from other tissues of the body to the heart



# Cardiovascular system - CVS

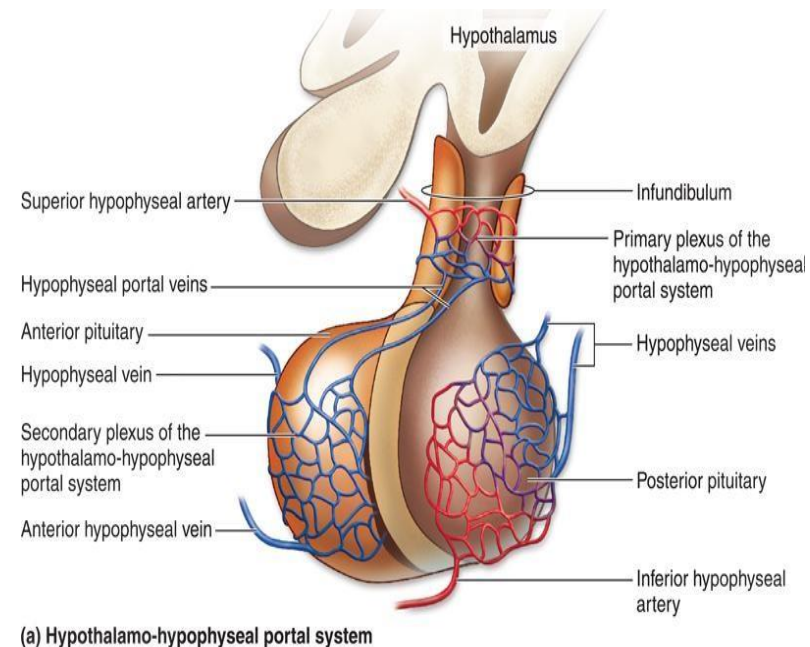
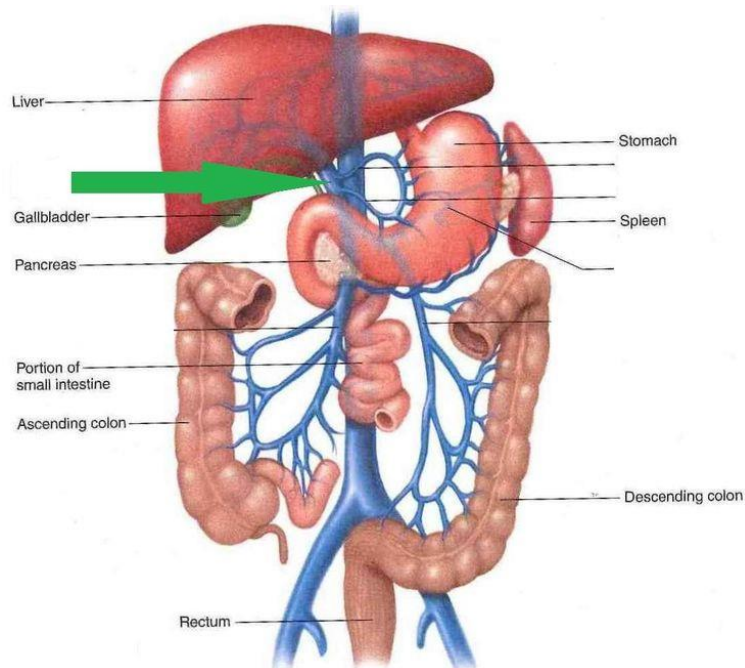
- ❖ The part of CVS that is located between the arterial and venous systems is composed of a network of the smallest blood vessels - **microcirculation**
- ❖ The microcirculation consists of **arterioles**, **capillaries** and **venules**.
- ❖ In capillaries and the smallest venules, oxygen and nutrients are exchanged between blood and tissues.
- ❖ Some blood cells can leave the blood stream through the walls of postcapillary venules.
- ❖ Other blood vessels are impermeable to blood plasma and blood cells, so they have the role of conducting channels.

In some organs, the capillary network does not connect the arterial and venous system, but the capillaries are inserted **between two veins** or **two arterioles**, forming the so-called **portal venous** and **portal arterial** systems.

Portal systems are specialized for absorption, transport and secretion of substances.

The largest portal system in the body is the **portal venous system of the liver**.

The smaller venous portal system is located in the pituitary gland hypothalamo-pituitary portal system, while arterial portal system located in Kidney glomerulus.

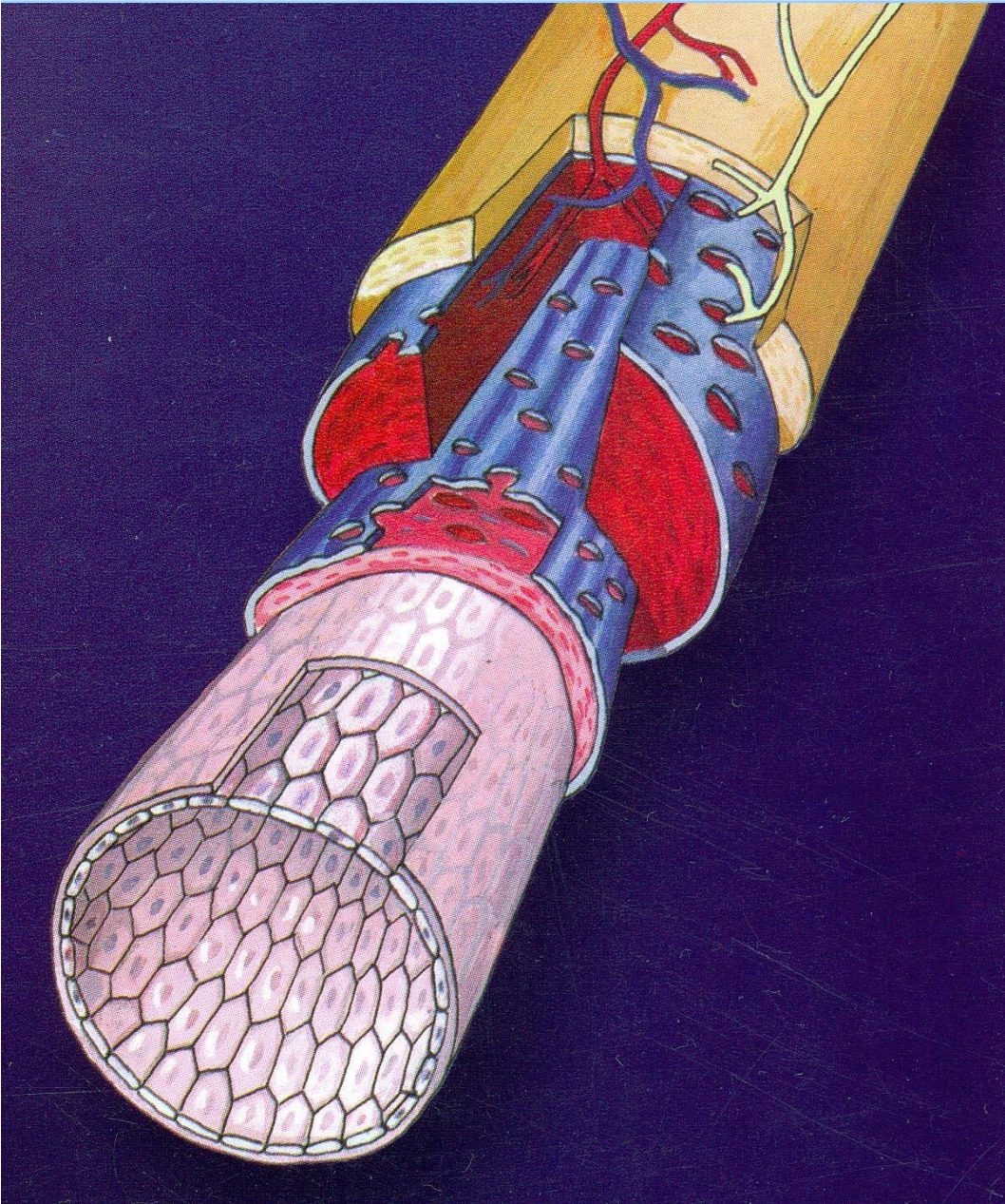


# Lymphatic vessels system

- ❖ Unlike blood vessels, lymphatic vessels are unidirectional, conveying fluid only **from** tissues.
- ❖ The smallest lymphatic vessels are called **lymphatic capillaries** with the function of returning the protein-rich tissue fluid (lymph) back to the circulation.
- ❖ Lymphatic capillaries converge into increasingly larger collecting vessels called **lymphatic vessels**. They ultimately unite to form two main channels that empty into the blood vascular system by draining into the large veins in the base of the neck.

# **Structure of the blood vessels**





### Tunica intima

- ❖ endothelium
- ❖ basement membrane
- ❖ subendothelial layer
- ❖ internal elastic membrane

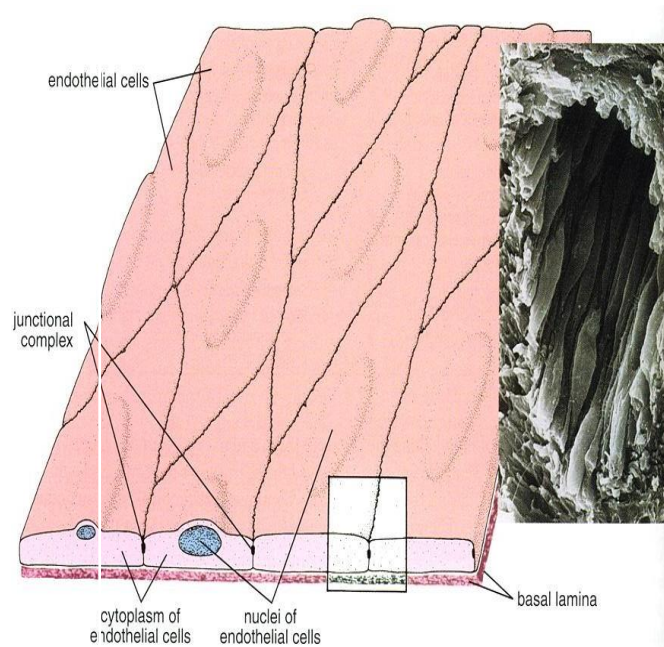
### Tunica media

- ❖ smooth muscle cells
- ❖ elastic fibers and lamellae
- ❖ collagen fibers

### Tunica adventitia

- ❖ external elastic membrane
- ❖ connective tissue
- ❖ vasa vasorum

# Tunica intima



**Endothelium**

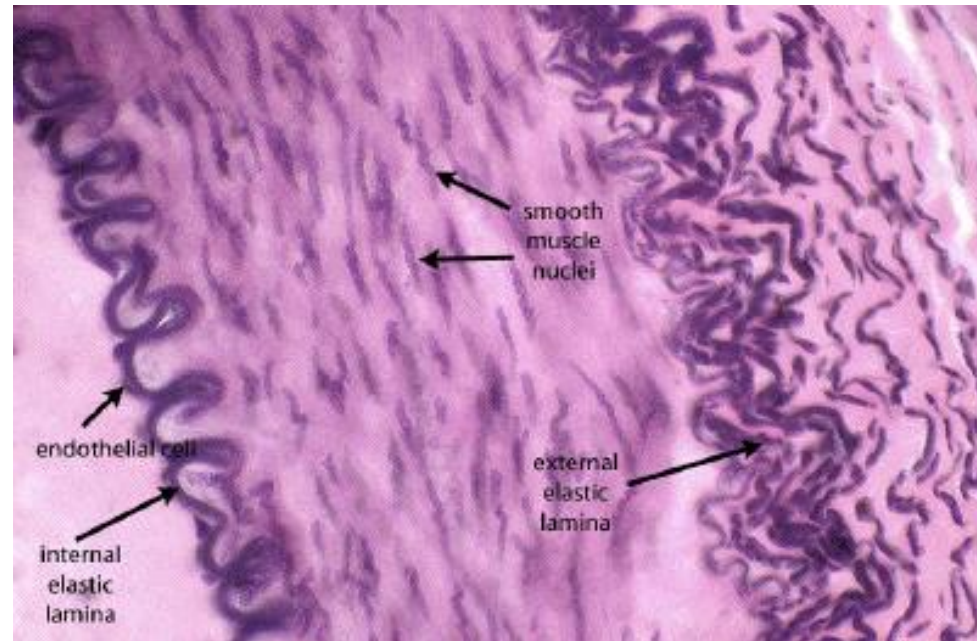
- ❖ In the **endothelial lining** with its **basal lamina** the cells are typically flat and elongated, with their long axes oriented parallel to the direction of blood flow in the artery.
- ❖ Endothelial cells possess rod-like inclusions called **Weibel-Palade bodies** that are present in the cytoplasm.

*Endothelial cells not only provide a physical barrier between the circulating blood and the subendothelial tissues but also produce*

*vasoactive agents.*



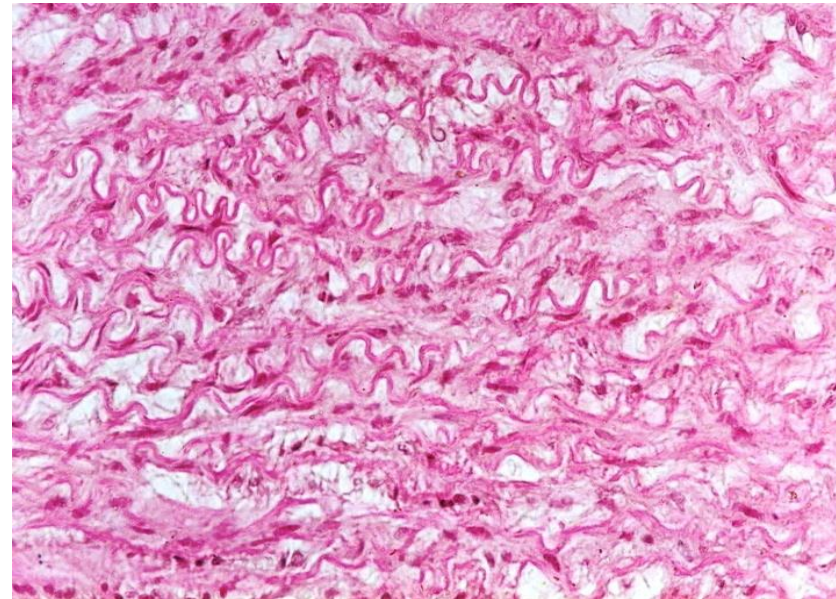
- ❖ **Subendothelial layer** of connective tissue in larger elastic arteries consists of connective tissue with both collagen and elastic fibers. The main cell type in this layer is the **smooth muscle cell**. It is contractile and **secretes extracellular ground substance** as well as collagen and elastic fibers.
- ❖ **Internal elastic membrane** built from elastic lamellae.



# Tunica media

Tunica media is the **thickest** of the three layers of elastic arteries and consists of:

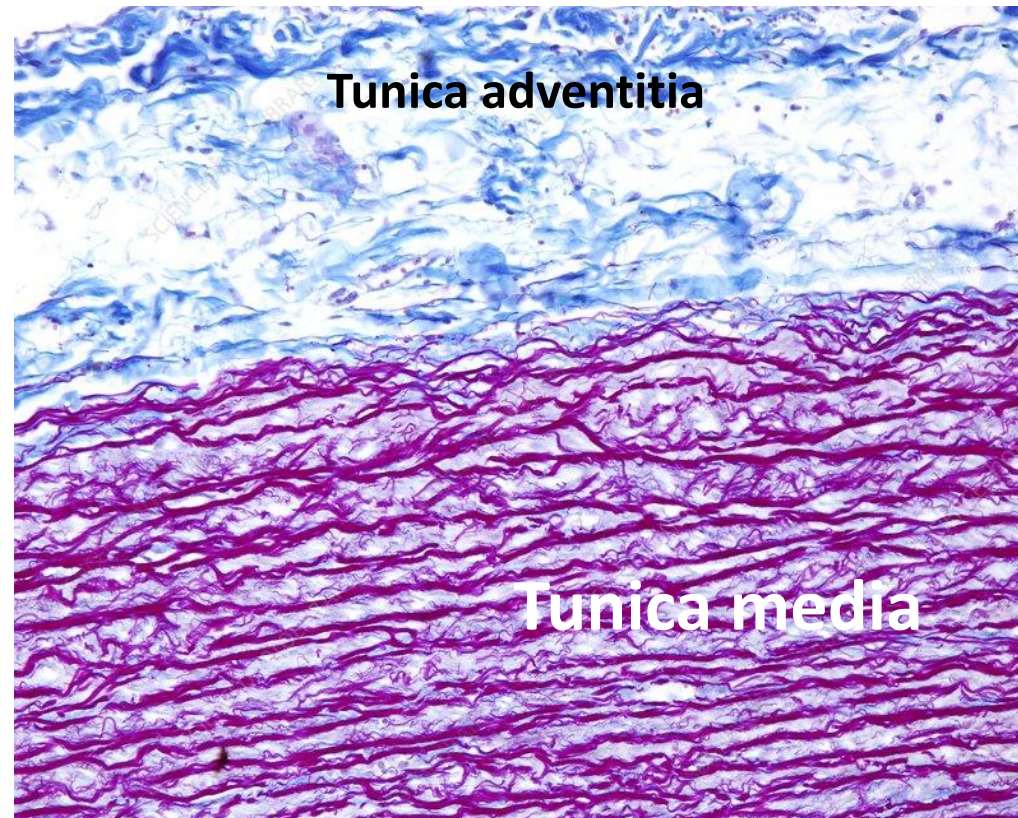
- ❖ **Elastin** in the form of **fenestrated sheets** or lamellae between the muscle cell layers. These lamellae are arranged in concentric layers.
- ❖ **Vascular smooth muscle cells** are arranged in layers. The smooth muscle cells are arranged in a low-pitch spiral. **Fibroblasts are not present in the tunica media.**
- ❖ **Collagen fibers** and **ground substance.**



# Tunica adventitia

Contains

- ❖ loose connective tissue
- ❖ *vasa vasorum*
- ❖ *nervi vasorum*
- ❖ lymphatic vessels



# Arteries

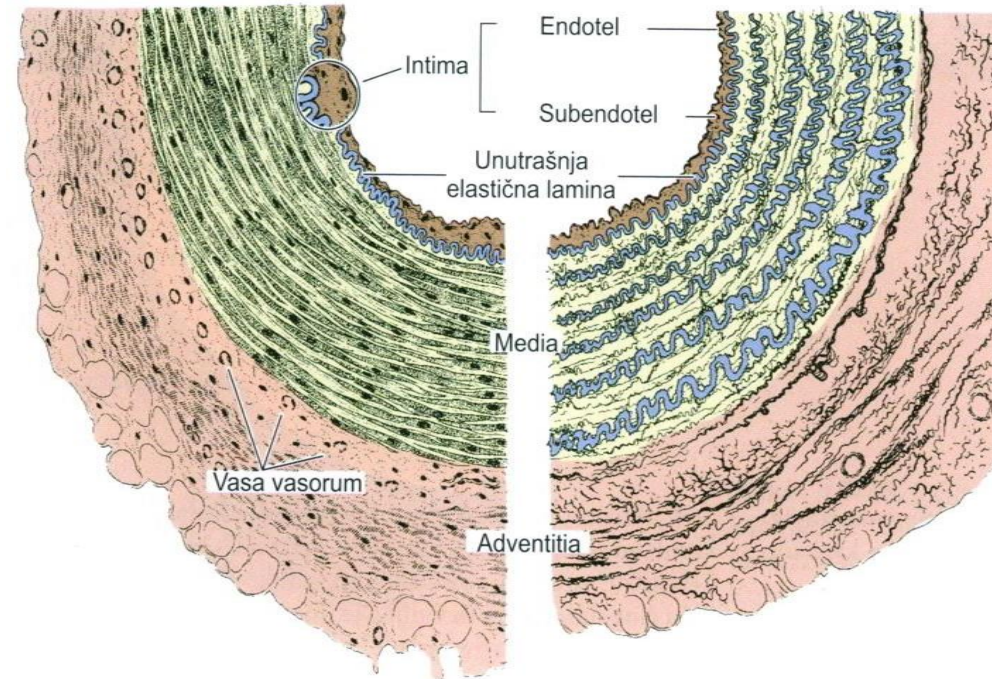
Based on its histological structure, arterial blood vessels are usually divided into 3 types:

- ❖ **Elastic arteries** (large arteries)
- ❖ **Muscular arteries** (smaller in diameter, formed by the branching of elastic arteries)
- ❖ **Arterioles** (smallest arteries including the metaarterioles)



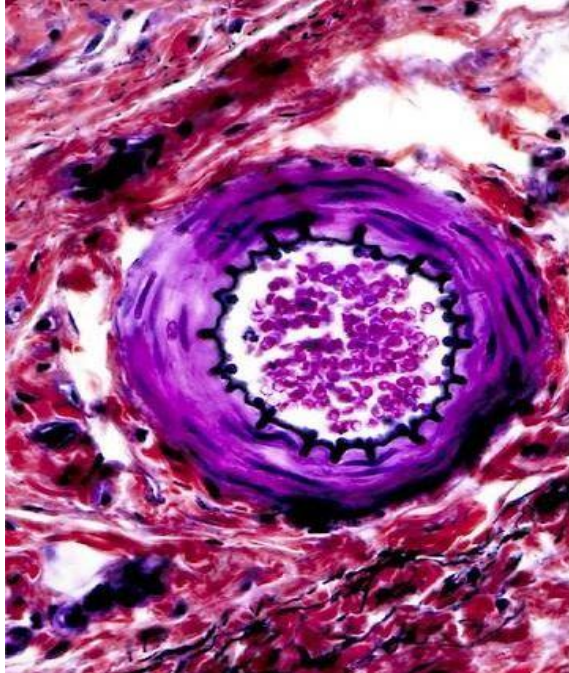
**Elastic arteries** serve primarily as conduction tubes. **Intima** of elastic arteries is relatively thick. **Media** is the thickest of the three layers and contains elastin in the form of 40-70 fenestrated lamellae. **Adventitia** is a relatively thin connective tissue layer.

**Muscular arteries** serve to distribute blood to the organs. **Intima** is thinner but with prominent **internal elastic membrane**. **Media** mainly consists of spirally arranged smooth muscle cells with marked external elastic membrane. **Adventitia** is composed from connective tissue.

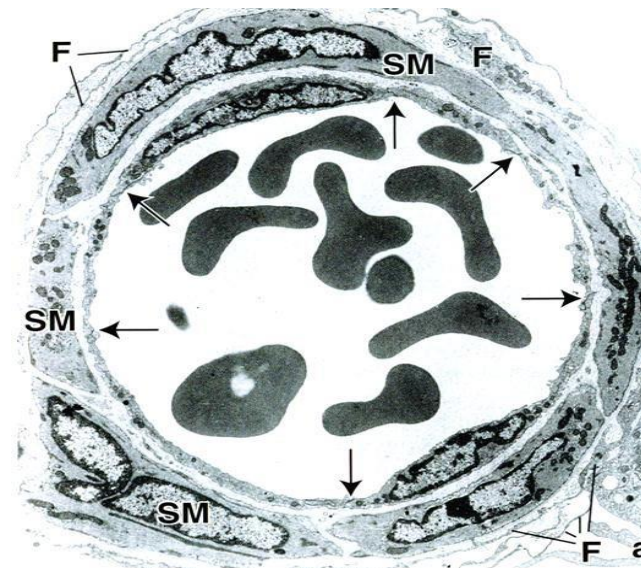


Muscular artery

Elastic artery



- ❖ Arterioles serve as flow regulators for the capillary beds.
- ❖ 10-100  $\mu\text{m}$  in diameter and with just a couple of smooth myocyte layer
- ❖ internal elastic membrane may or may not be present in the arteriole
- ❖ Marked myo-endothelial junctions.





# Capillaries

Capillaries are the **smallest blood vessels**, often smaller than the diameter of an erythrocyte with average length of 0,2-1 mm.

They connect metaarterioles with postcapillary venules.

They form blood vascular networks that allow fluids containing gases, metabolites, and waste products to move through their thin walls.

The capillary network is **rich** in the lungs, kidneys, liver, heart muscle, CNS, adipose tissue, and **scarce** in the bones, smooth musculature and dense connective tissue. Epithelia, cartilage, cornea, lens, enamel, dentin and cementum **do not have capillaries**.



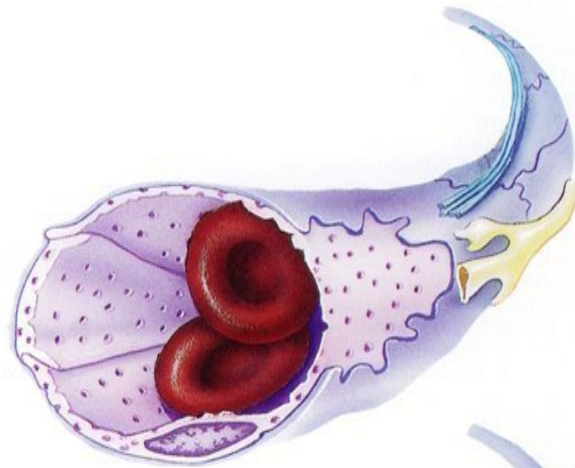
Capillary wall is composed from

- ❖ Endothelium
- ❖ Basal lamina
- ❖ Pericytes

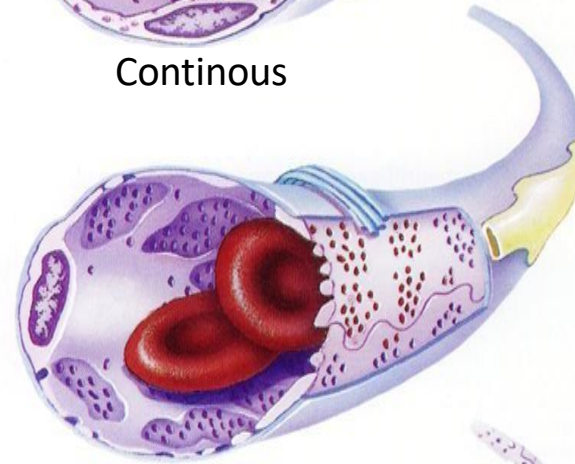
# Classification of capillaries

## Continuous capillaries

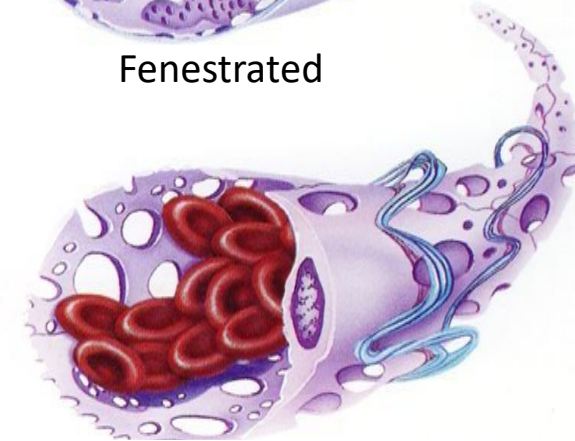
- ❖ Endothelial cells do not have fenestrae, and are connected by occludent, adherent and gap junctions. They are found in the testis, ovary, thymus, bones, CNS, muscles, exocrine glands.



Continuous



Fenestrated



Sinusoidal

## Fenestrated capillaries

### ❖ with a diaphragm

grouped fenestrae covered by a thin membrane. They are found in the endocrine glands, stomach, intestines, ciliary body, and most of the kidneys.

### ❖ without a diaphragm are present only in kidney glomeruli.

## Sinusoidal (discontinuous) capillaries

- ❖ Have larger diameter and endothelial cells with large openings in their cytoplasm. Furthermore, they are separated by wide, irregular, intercellular gaps that allow for passage of blood plasma proteins. The basal lamina is fragmented or completely missing, and the number of pericytes is lower than in other types of capillaries. They are found in the liver, spleen, bone marrow, adenohypophysis and cortex of the adrenal gland.

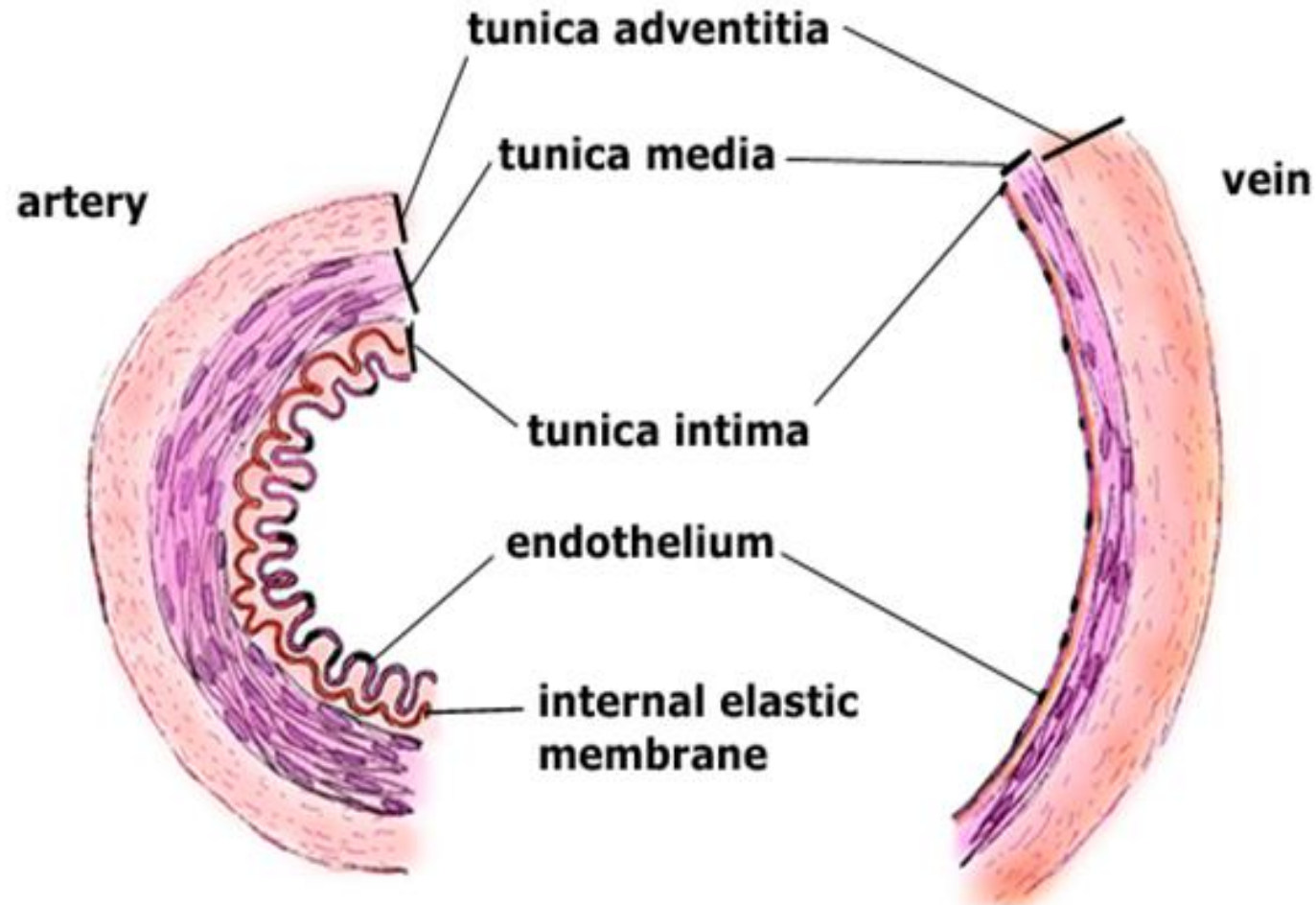
# Veins

Traditionally, veins are divided into four types on the basis of size.

- **Large veins** usually have a diameter greater than 10 mm.
- **Medium veins** represent most of the named veins in this category. They usually are accompanied by arteries and have a diameter up to 10 mm.  
*Large and medium veins of lower extremities possess small crescent-shaped flaps of intimal tissue, known as **valves**, that help prevent a backflow of blood.*
- **Small veins** are less than 1 mm in diameter.
- **Venules** are further subclassified as **postcapillary** and **muscular venules** which receive blood directly from capillaries and have a diameter as small as 0.1 mm.

Vein structure corresponds pretty much to a general blood vessel characteristics.

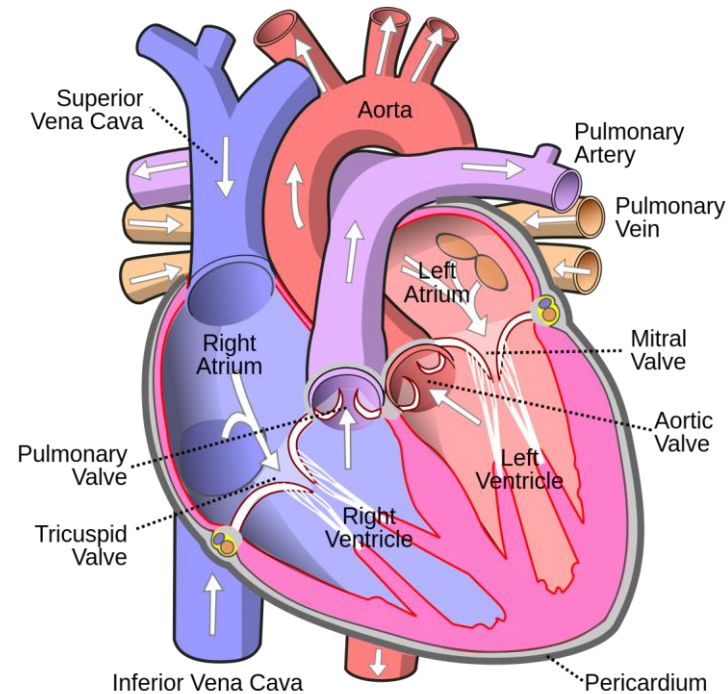
Generally, veins have **wider lumen and thinner wall** than accompanying arteries. Furthermore, their **thickest part of the wall is adventitia** opposed to media in arteries.



# Heart

**Heart** is a central part of the cardiovascular system.

The heart is a muscular pump that maintains unidirectional flow of blood from the veins to the arteries.



## Heart structure

- **Endocardium**
  - endothelium
  - basement membrane
  - Subendothelial layer
  - Subendocardial layer
- **Myocardium**
  - cardiac muscle cells
  - CT fibers
- **Epicardium**
  - mesothelium
  - loose CT
  - fat tissue

## Blood vessel structure

- **Tunica intima**
  - endothelium
  - basement membrane
  - Subendothelial layer
  - *membrana elastica interna*
- **Tunica media**
  - Elastic lamellae and/or
  - Smooth muscle cells
  - CT fibers
- **Tunica externa (adventitia)**
  - *membrana elastica externa*
  - loose CT
  - *vasa vasorum*

# Endocardium

Smooth and shiny membrane that covers the inner surface of the heart.

- endothelium
- basement membrane that is complete
- subendothelial and subendocardial connective tissue

# Myocardium

Consisting of cardiac muscle cells, is the principal component of the heart.

In the heart there are 3 types of myocytes

❖ contractile

❖ conducting

❖ Endocrine

And as a special type adrenergic cells



# Conducting myocytes

Specialized for initiation and propagation of rhythmic depolarizations, which results in rhythmic cardiac muscle contractions. Forms conducting system of the heart formed by modified cardiac muscle cells (Purkinje fibers),



# Endocrine myocytes

- In addition to contractile properties, they also have the ability to biosynthesize and secrete more hormonally active substances - cardiopeptides or natriuretic peptides
  - ANP - atrial natriuretic factor
  - BNP - B-type natriuretic peptide
- both causes** natriuresis and vasodilatation
- Synthesized cardiopeptides are deposited in specific perinuclear granules
  - They have an oval euchromatic nucleus, while the central part of the cell is devoid of myofibrils, and filled with well-developed organelles responsible for the biosynthetic and secretory activity of the cell.
  - Mostly localized in atriums.

# Adrenergic cells

- They synthesize adrenaline, noradrenaline and dopamine.
- They are located in groups, between blood vessels and myocytes.
- They are irregularly shaped and have a eccentrically placed euchromatic nucleus, with a pronounced nucleolus and numerous indentations.
- The cytoplasm is filled with electronically bright granules in which synthesized catecholamines are deposited (do not contain myofibrils).
- They do not have junctional complexes with the surrounding cardiomyocytes.

# Epicardium

The epicardium, also known as the visceral layer of serous pericardium , adheres to the outer surface of the heart. Made up of simple squamous epithelium (**mesothelium**) and thin **subepicardial layer**. Subepicardial layer consists of loose connective tissue containing CT fibers, blood and lymphatic vessels, nerve fibers and variable amounts of fatty tissue.

The epicardium represents the visceral sheet of the pericardial sac.

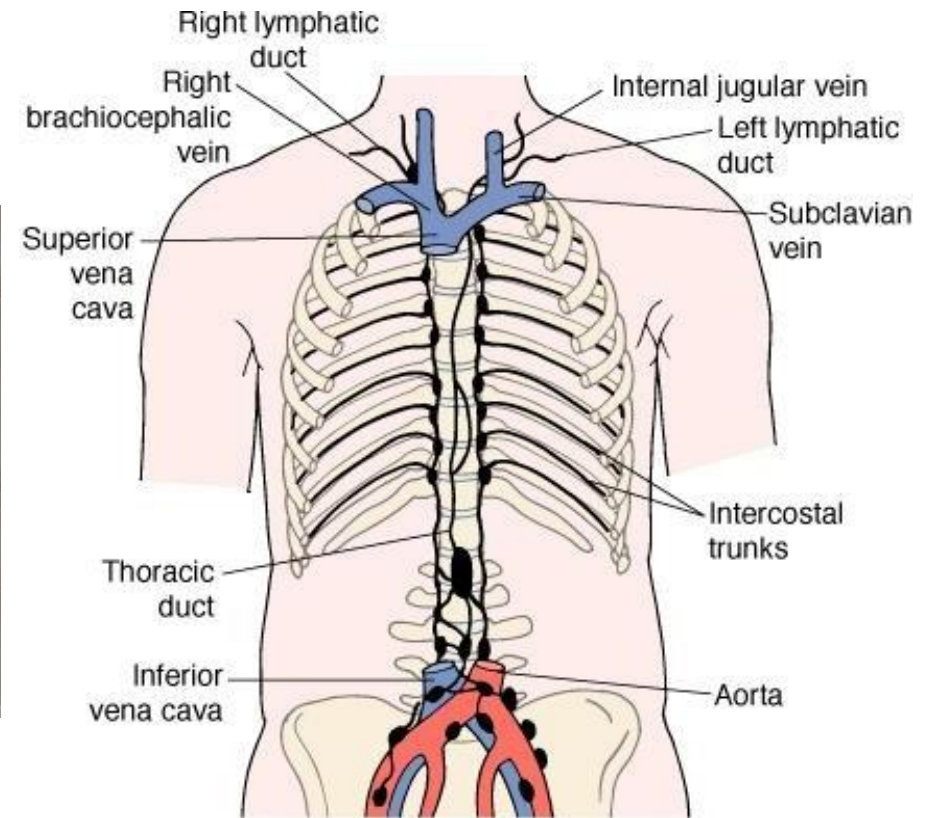
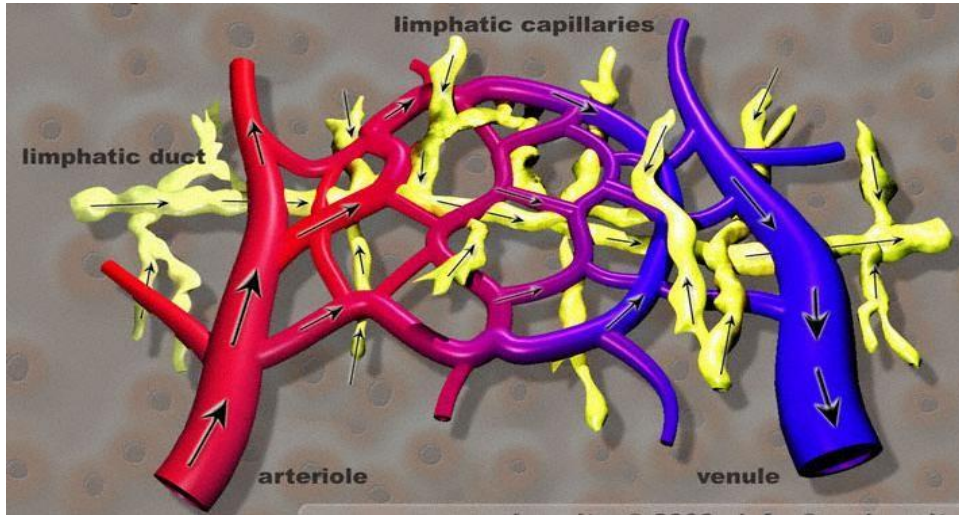
# Pericardium

Parietal layer of serous pericardium , which lines the inner surface of the pericardium that surrounds the heart and roots of great vessels. Thus, there is a potential space containing a minimal amount (**15 to 50 ml**) of **serous (pericardial) fluid** between the visceral and parietal layers of the serous pericardium. This space is known as the **pericardial cavity**; its lining consists of mesothelial cells

# **Lymphatic vessels**

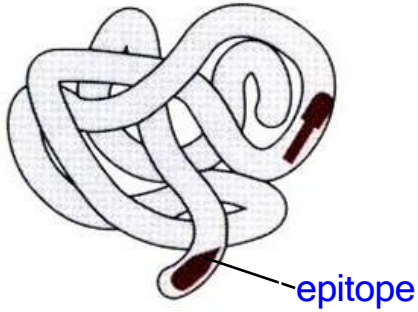


# Lymphatic vessels



- It drains 10% of the **blood filtrate** into the left and right venous corners.
- Lymphatic vessels are found everywhere in the body, except in the CNS, bone marrow, epithelia, cartilage, eye lens and cornea.
- The lymphatic vascular system consists of:
- lymphatic capillaries
- collecting lymphatic vessels
- large lymphatic vessels (d. thoracicus and d. lymphaticus dexter).

# **Lymphatic system**



System for defense and protection of the organism (lat. immunitas - protection from lawsuits)

It consists of groups of cells, tissues, and organs that monitor body surfaces and internal fluid compartments and react to the presence of potentially harmful substances (antigens).

An antigen is any molecule, foreign to the organism, which the cells of the immune system recognize and react against. Antigens can be soluble molecules (proteins, polysaccharides) or are integral parts of the cell (bacteria, protozoa, tumor cells, cells infected with viruses).

An antigenic determinant **or epitope** is a part (domain) of an antigen that is recognized by defense cells or their products (antibodies).

The reaction of the immune system to an antigen is called an **specific immune response**.



The body has two lines of defenses against foreign invaders and transformed cells: **nonspecific immunity (innate) and specific immunity.**

Innate immunity represents the of (1) **physical barriers** (e.g., the skin and mucous membranes) that prevent foreign organisms from invading the tissues, (2) **chemical defenses** (e.g., low pH) that destroy many invading microorganisms, (3) **various secretory substances** (e.g., saliva, lysozymes, interferons,) that neutralize foreign cells, (4) **phagocytic cells** (e.g., macrophages, neutrophils, and monocytes), and (5) **natural killer (NK) cells**.

With **specific (adaptive) immunity**, the immune system provides specific, or adaptive, defenses that target specific invaders. The initial contact with a specific antigen or foreign agent initiates a chain of reactions that involve effector cells of the immune system and frequently leads to a state of immune “memory.” During adaptive immune responses, specific ***B and T lymphocytes*** become activated to destroy invading organisms. Two types of specific defenses have been identified: **Humoral response** results in the production of proteins called **antibodies** that mark invaders for destruction by other immune cells, and the **cellular immune response** targets transformed and virus-infected cells for destruction by specific “killer” cells.

# Body tissues

**Tissues:** Groups of cells with similar structure and function

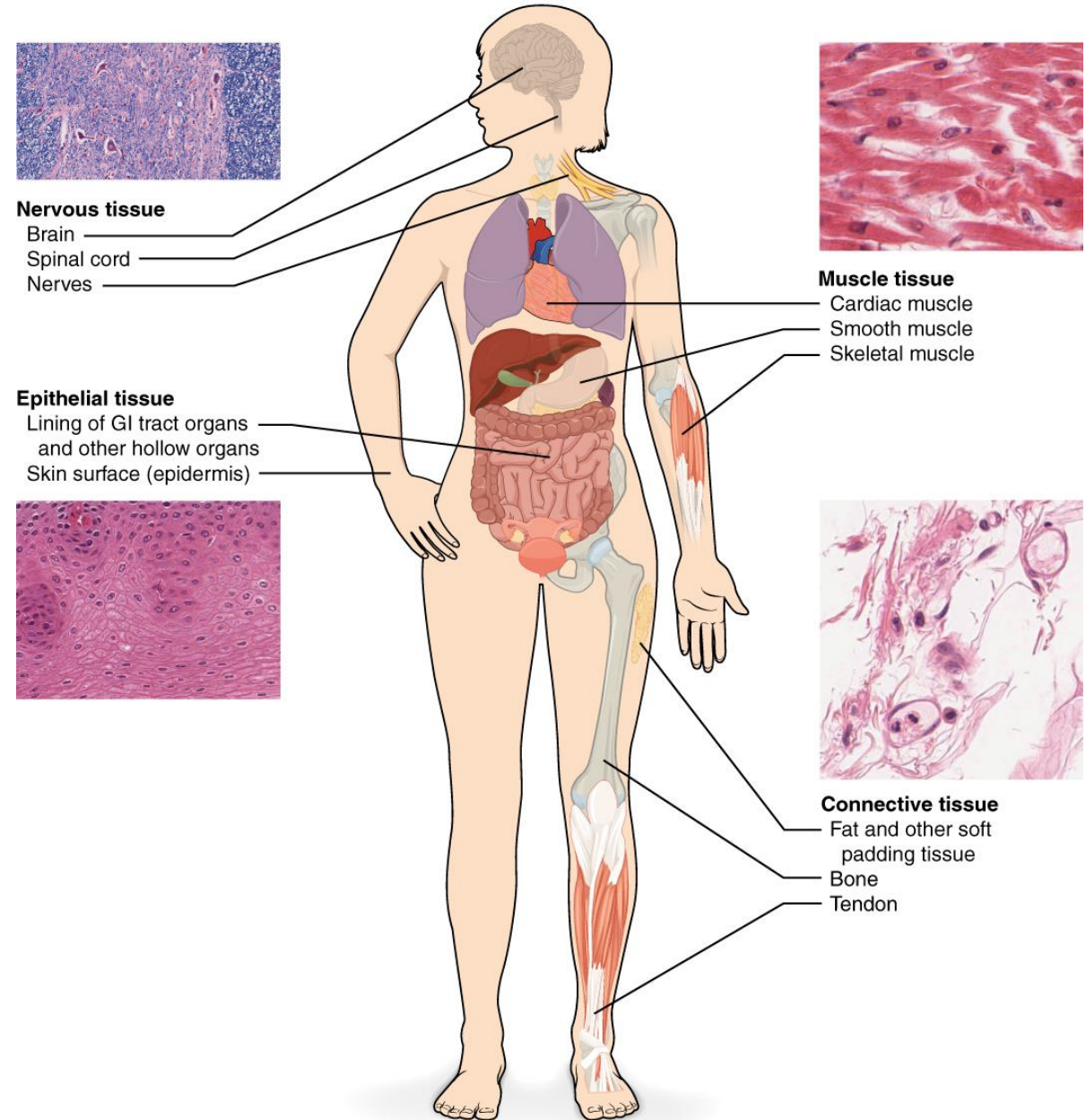
## Four primary types of tissues:

epithelial (**covering**)

connective (**support**)

muscle (**movement**)

nervous (**control**)



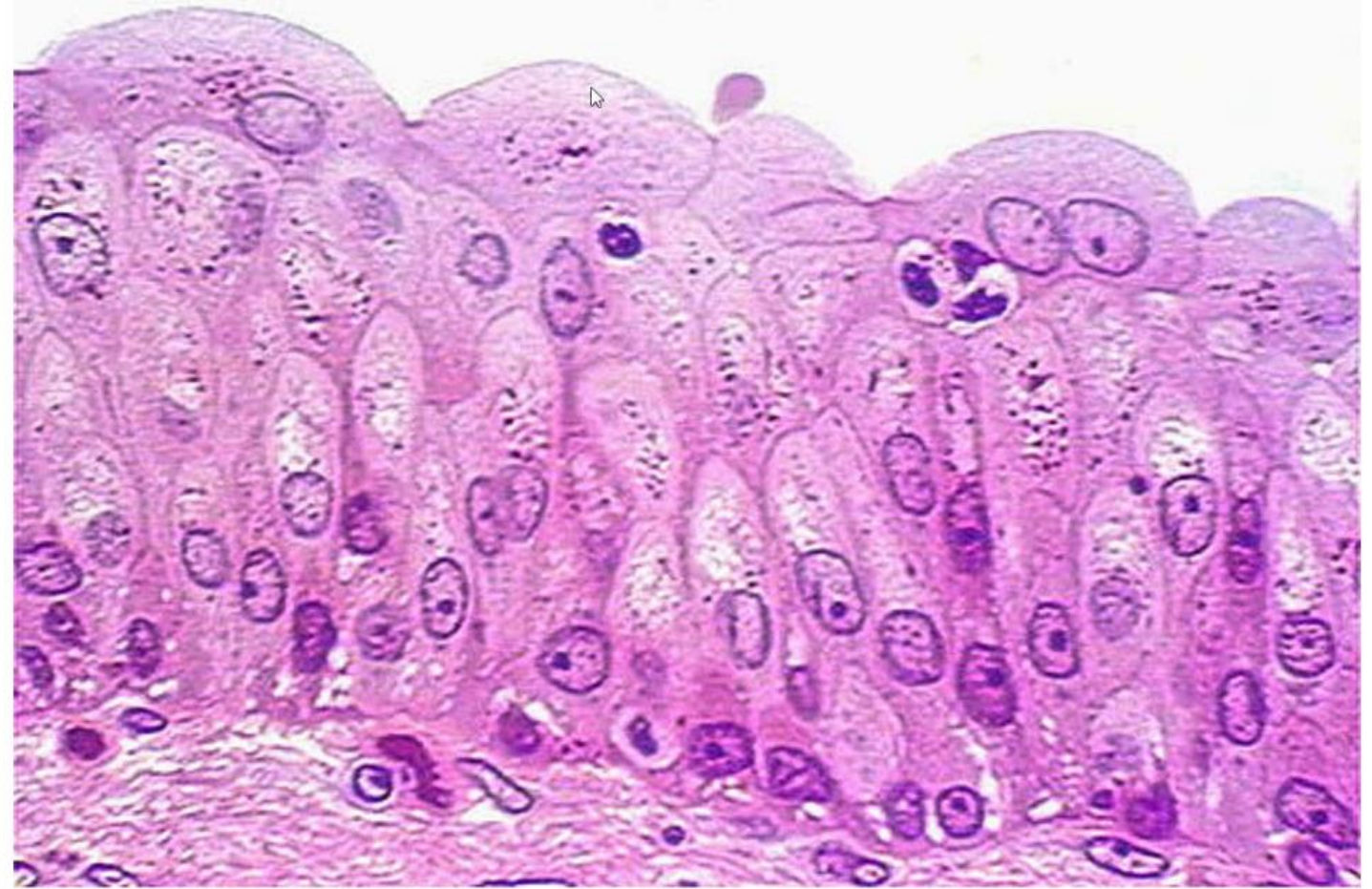
# Epithelial tissue

## Location:

- Body coverings
- Body linings
- Glandular tissue

## Function:

- Protection
- Absorption
- Filtration
- Secretion

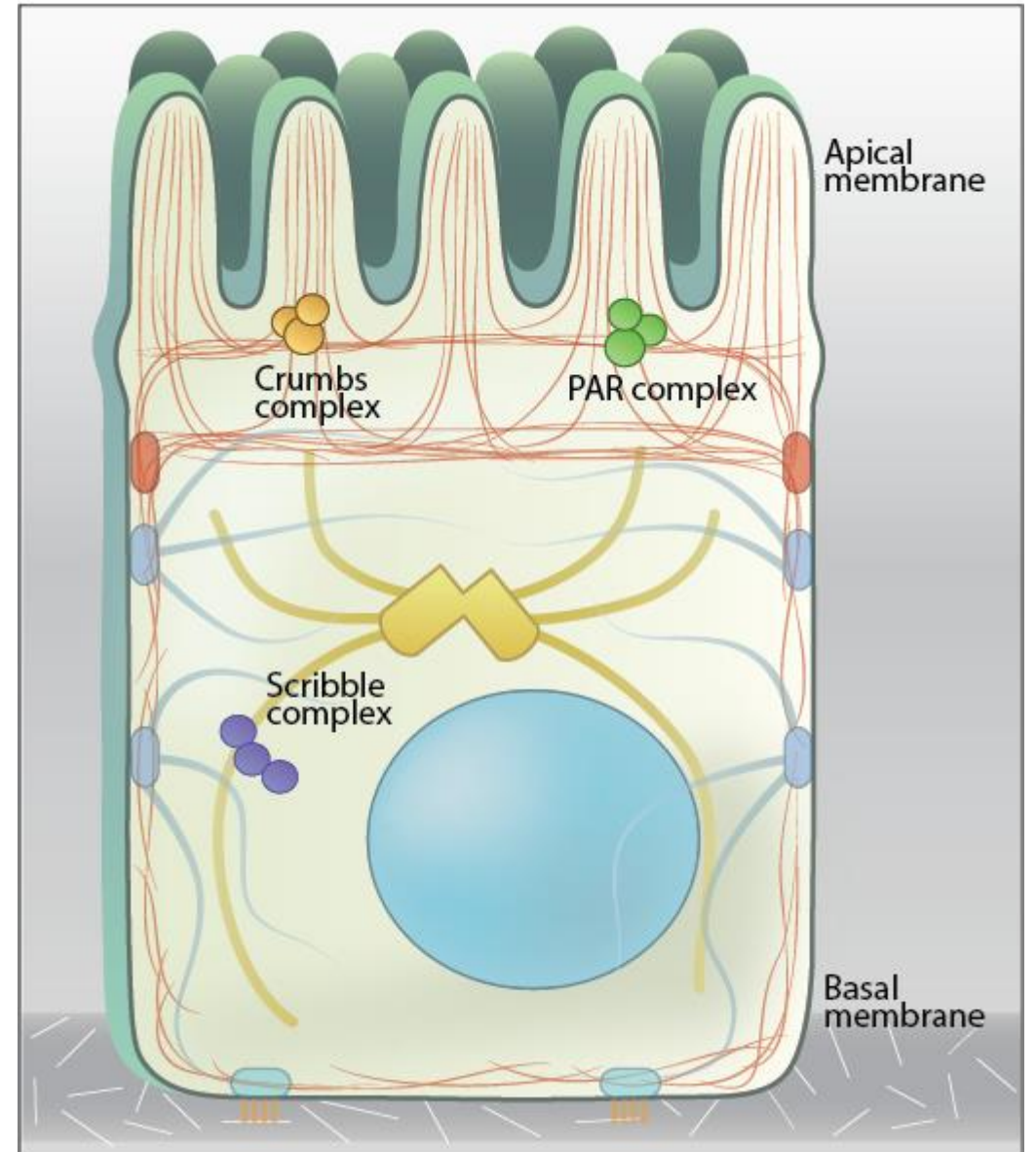




# Epithelial tissue

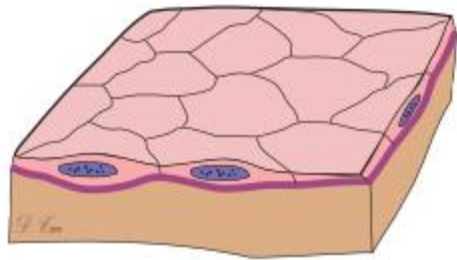
## Characteristics:

- Cover and line body surfaces
- Avascular
- Regenerates easily

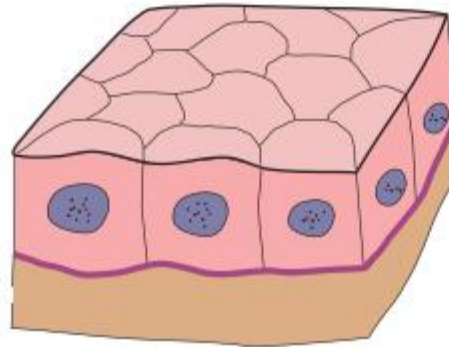
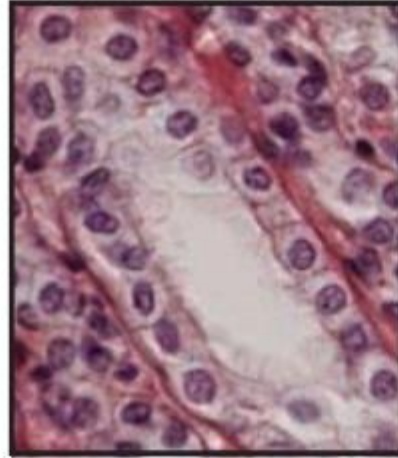


# Epithelial tissue

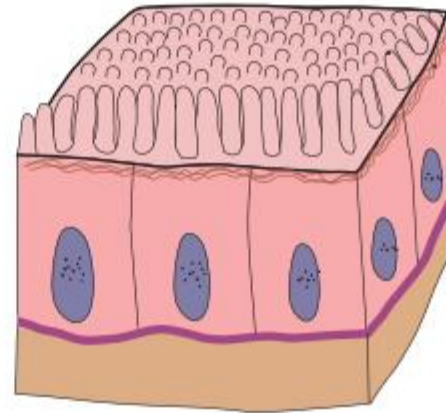
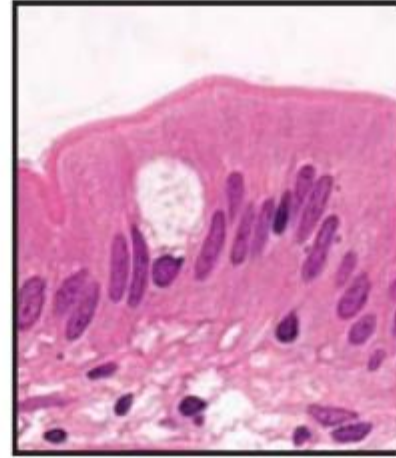
**Squamous  
epithelium**



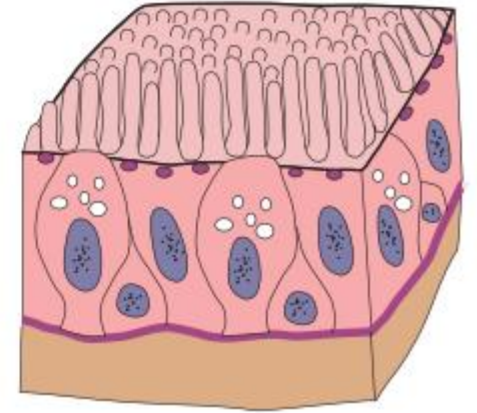
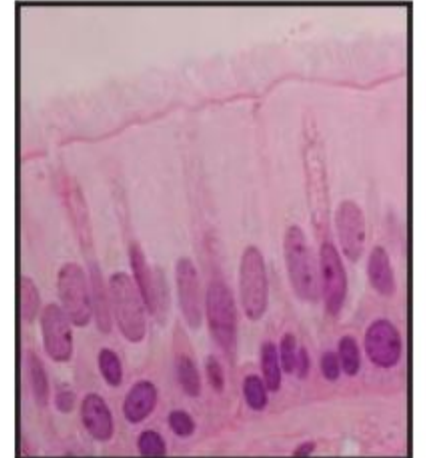
**Cuboidal  
epithelium**



**Columnar  
epithelium**



**Pseudostratified  
columnar epithelium**

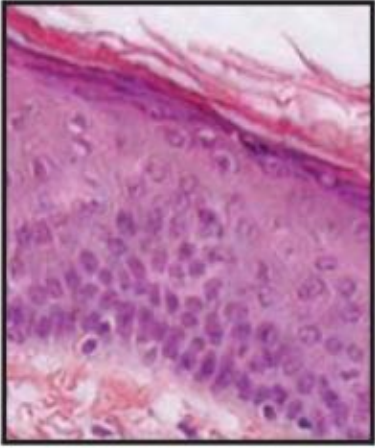


Simple epithelia (one layer of epithelial cells)

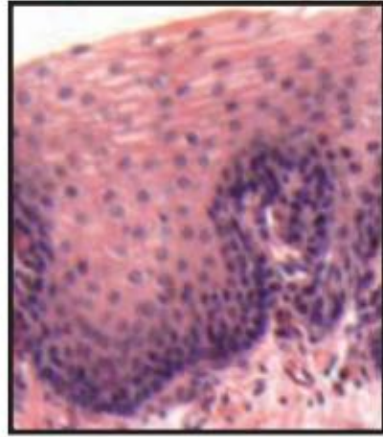


# Epithelial tissue

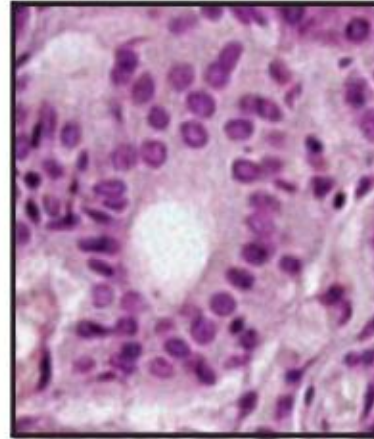
**Squamous  
epithelium  
(keratinized)**



**Squamous  
epithelium  
(nonkeratinized)**



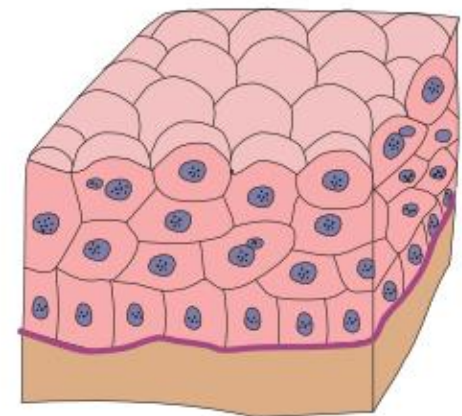
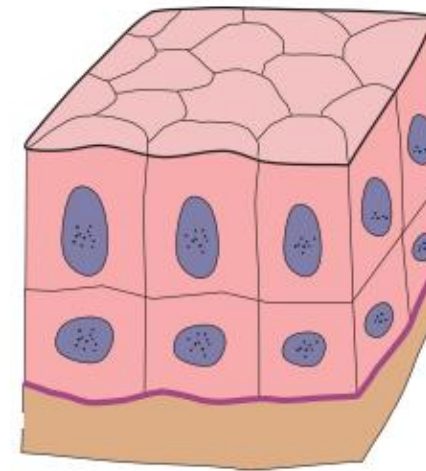
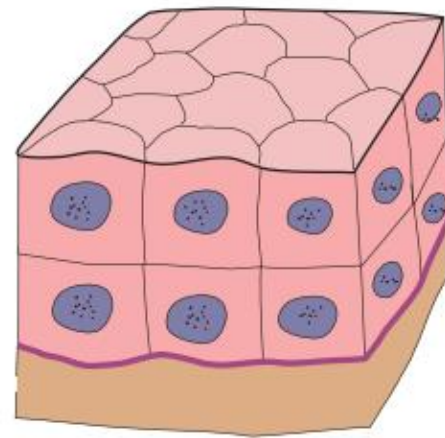
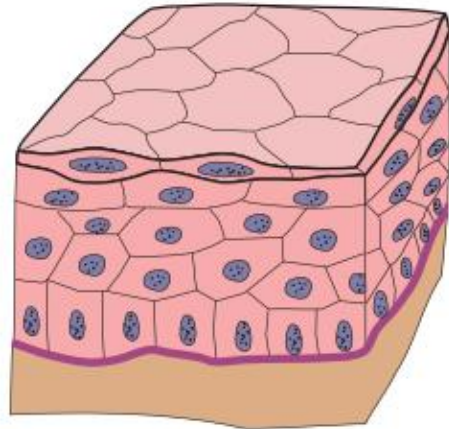
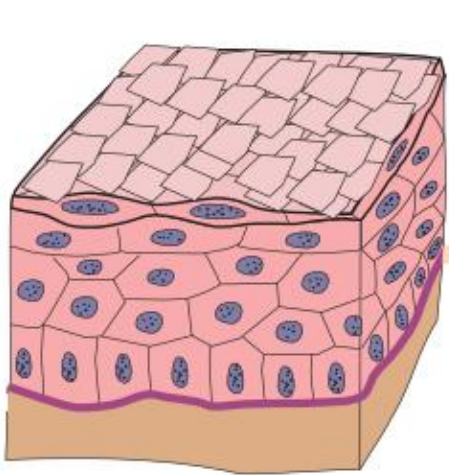
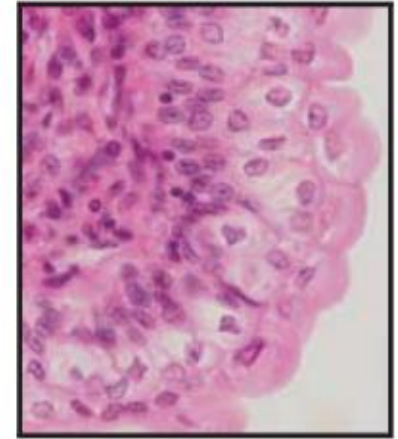
**Cuboidal  
epithelium**



**Columnar  
epithelium**



**Transitional  
epithelium  
(relaxed)**



Stratified epithelia (two or more layers of epithelial cells)

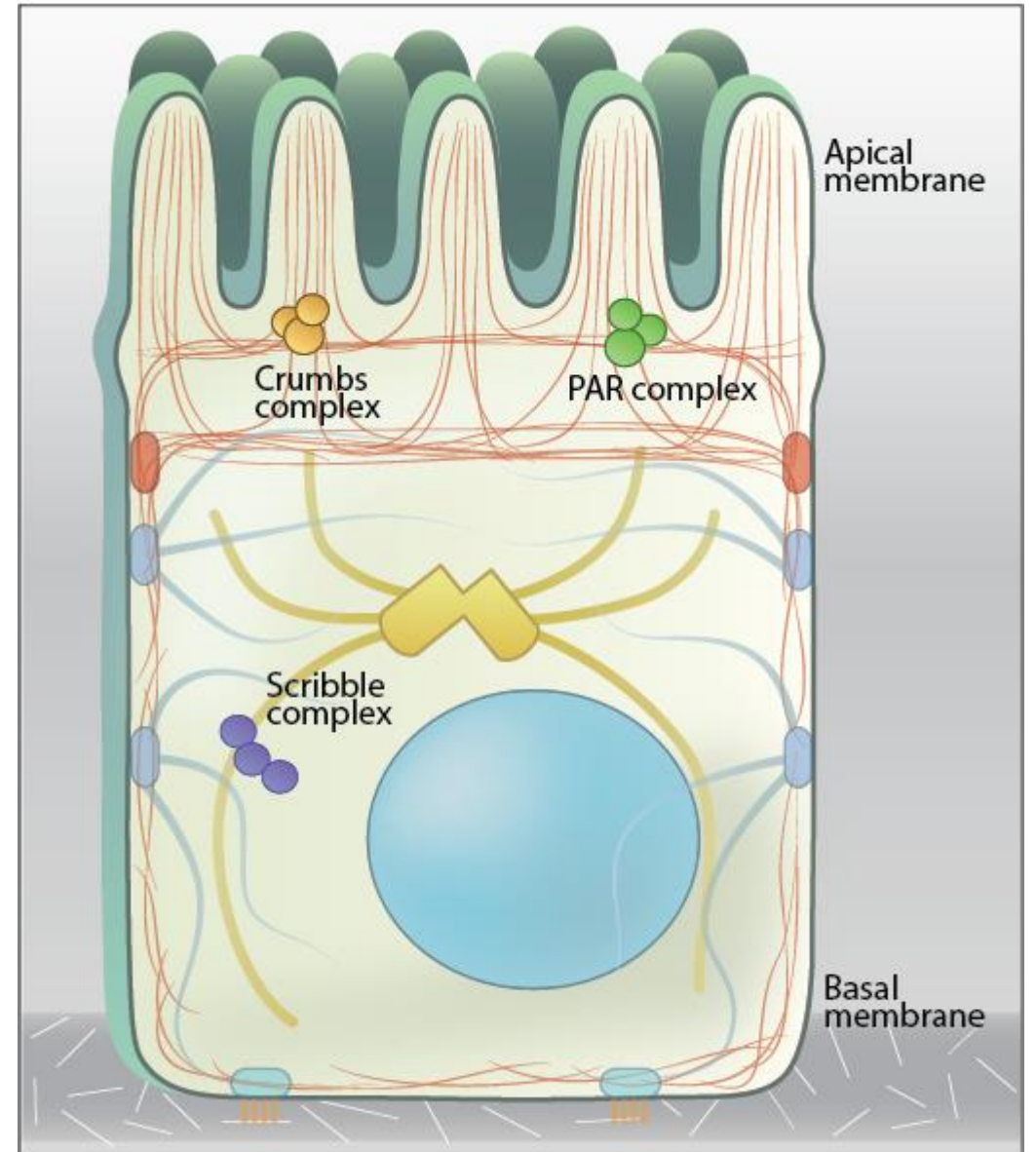
# Epithelial tissue - cells

## Polarised cells

**Apical** part of the cell

**Lateral** part of the cell

**Basal** part of the cell



central result differs external begins stems uses Insulin's patients ver varies island effects energy Porcine medically used composed fail human levels ellitus icose peptide version suffer weight example Da source metabolic depend vascular resistance metabolism

Which outer covering of the body has the largest surface area?

ho ab: spe adequa subcutane name L Langerhan anim strength use sources eventually take treat survival humans medications taken t d lov internally also blood lipids com several acid molecular cl especially variations structure longer transfer acids extensive functions pancreas stopping resistant require pig storing signal slightly glycogen forms



# Epithelial tissue - skin

**2<sup>nd</sup>**

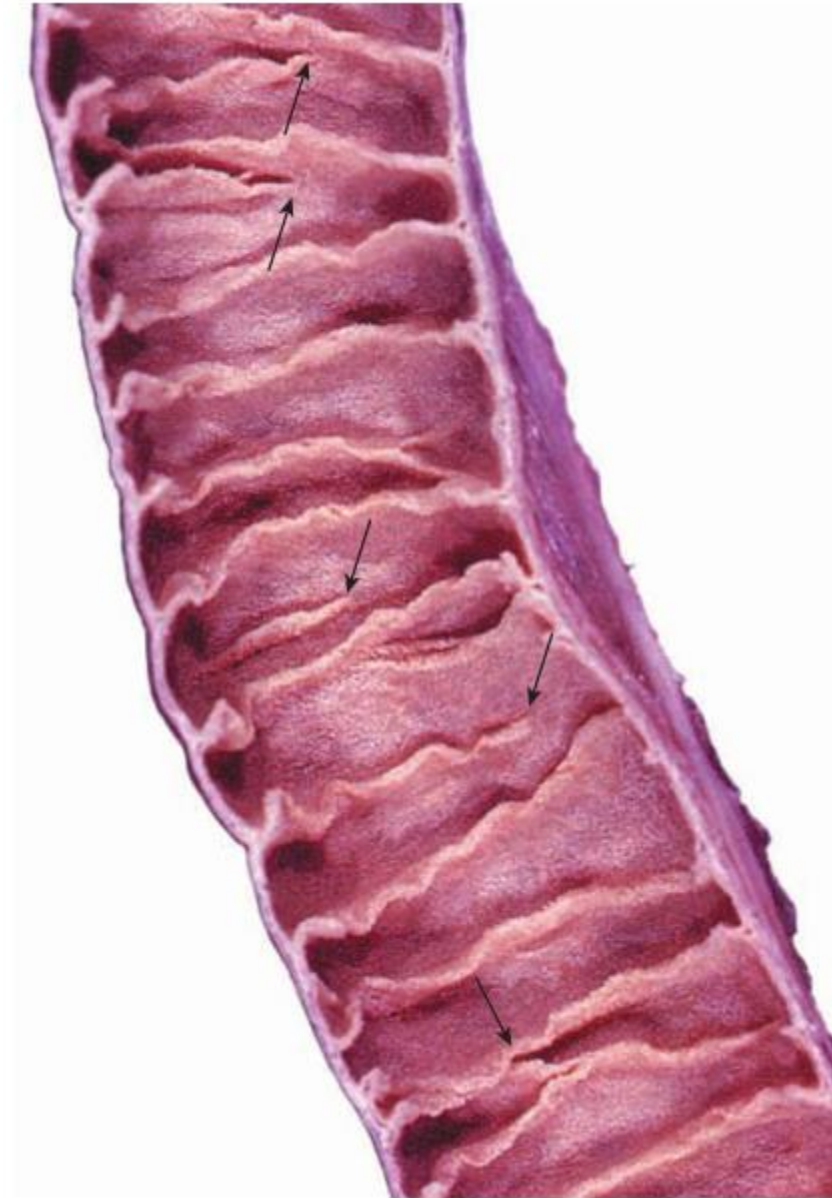
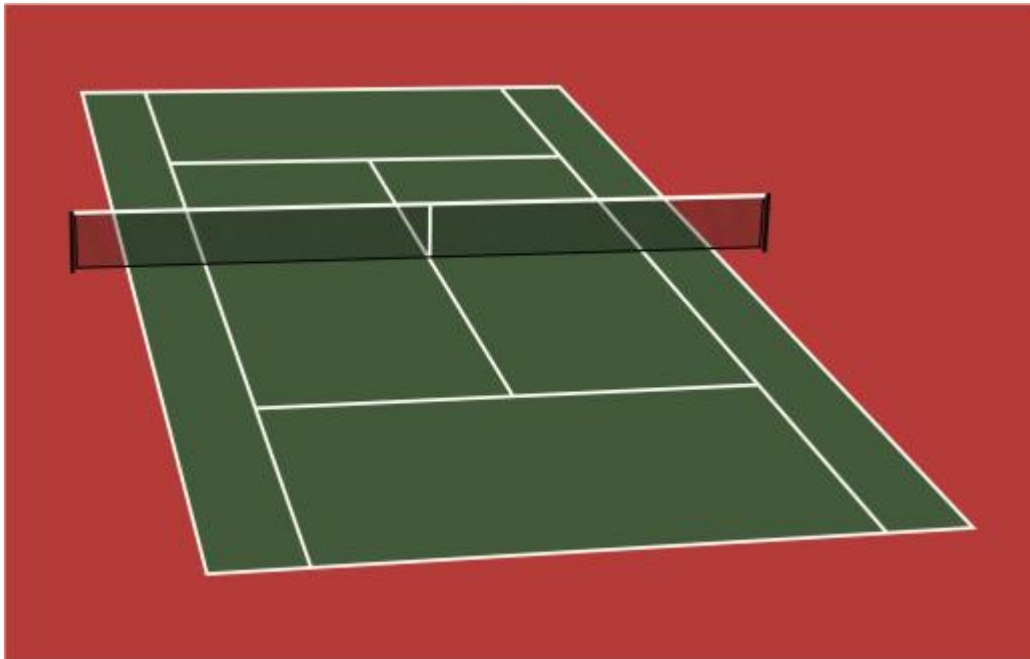
1.5-2.0 square metres



# Epithelial tissue – small intestine

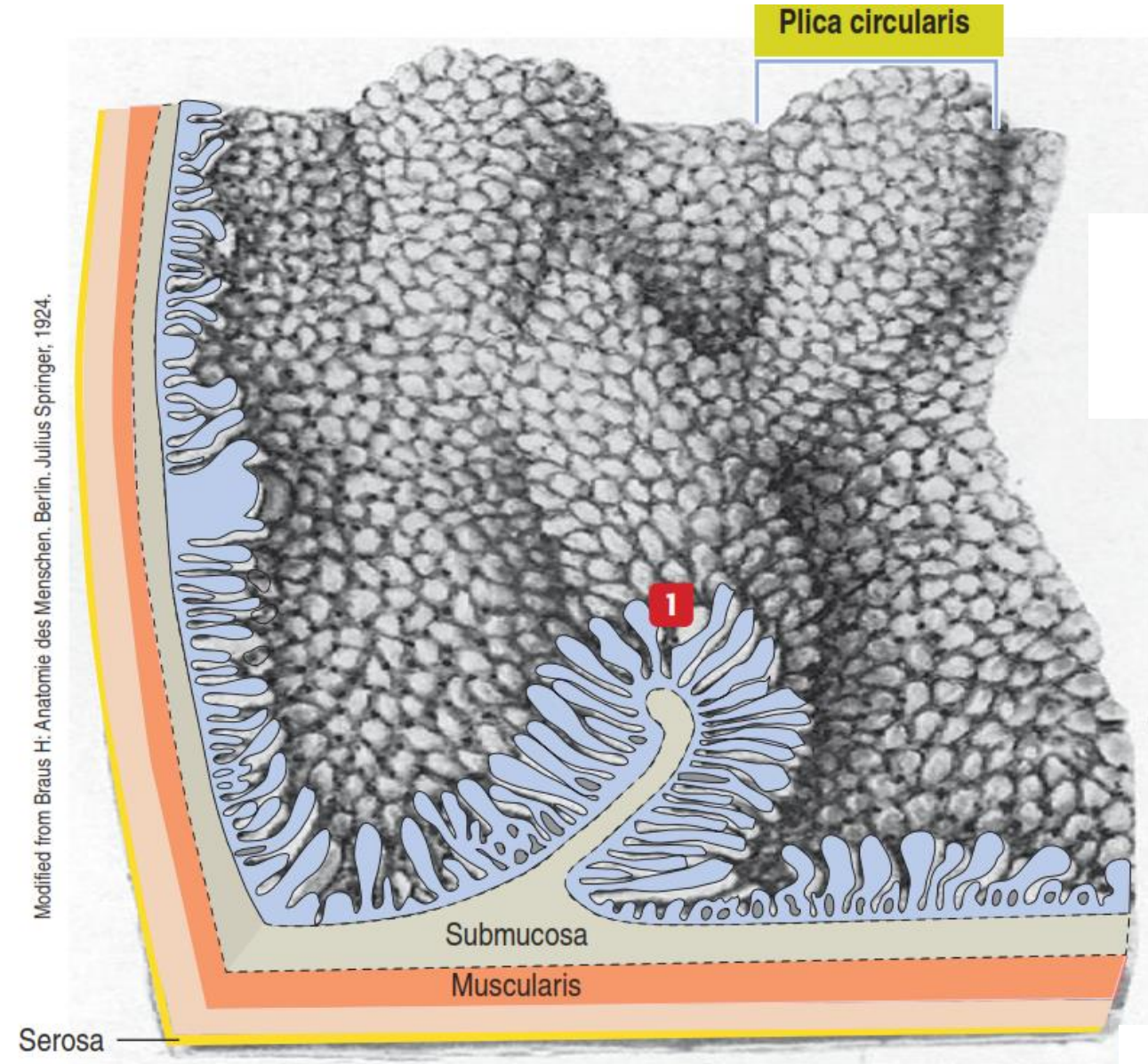
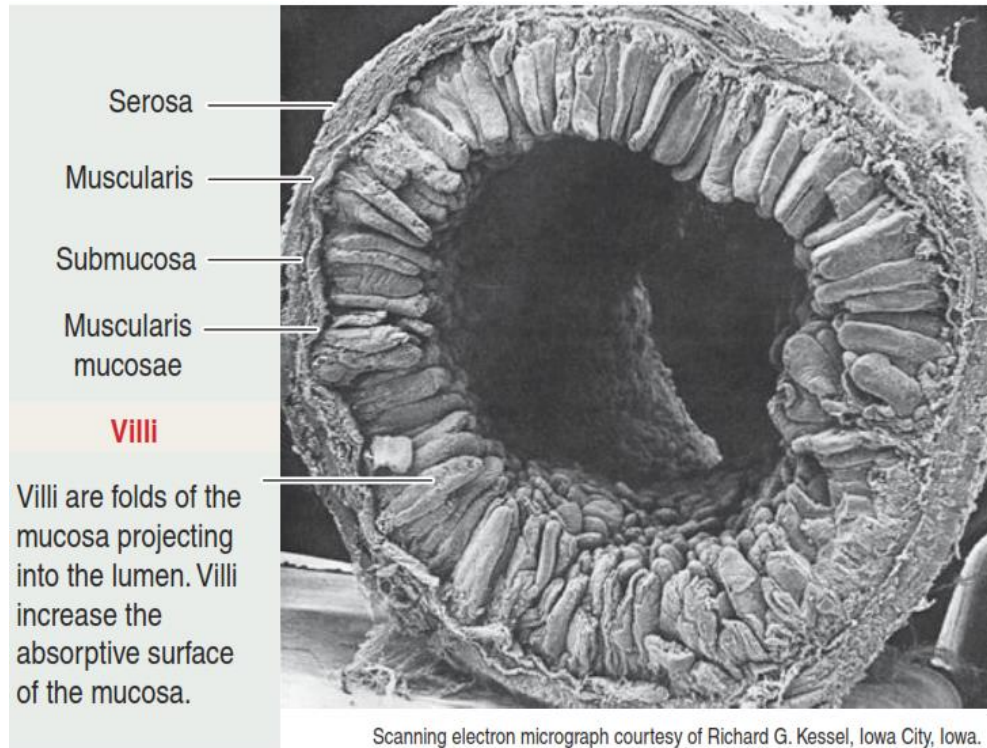
1<sup>nd</sup>

Small intestine surface is about 250 square meters –  
the size of a tennis court



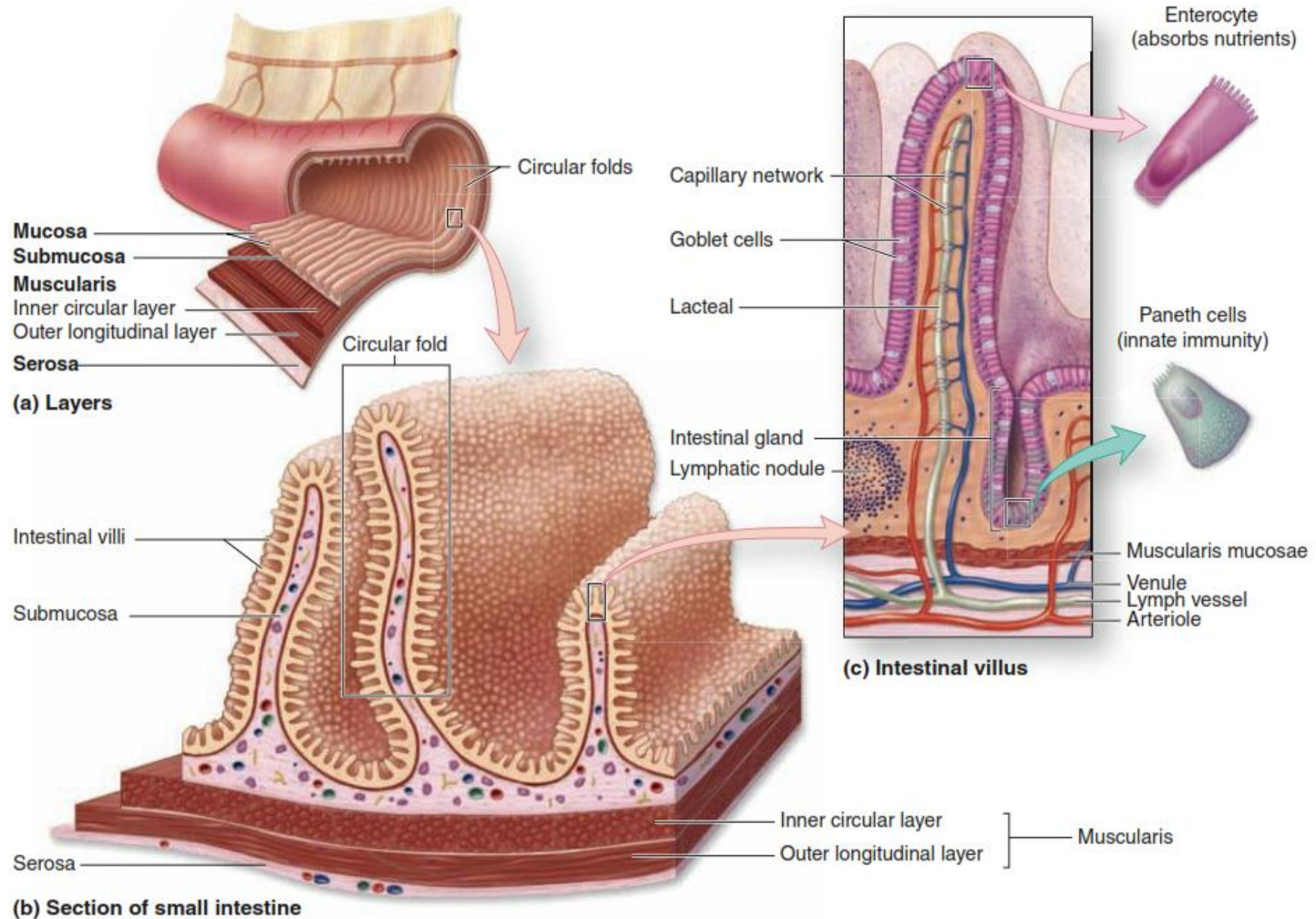


# Epithelial tissue – small intestine





# Epithelial tissue – small intestine



# Epithelial tissue – small intestine

**Enterocytes** are the most numerous and function primarily for nutrient absorption.

**Goblet cells** secrete the mucus layer that protects the epithelium from the luminal contents.

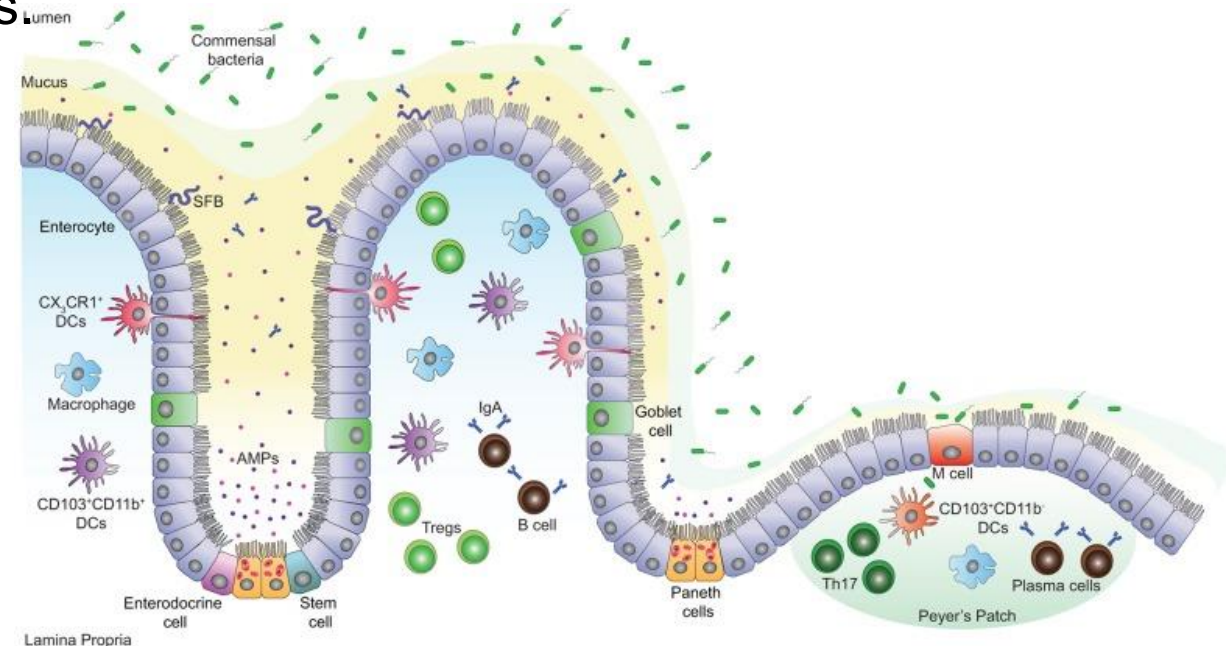
**Enteroendocrine cells** secrete various gastrointestinal hormones

**Paneth cells** produce antimicrobial peptides

**Microfold cells** associated with Peyer's patches

**Cup cells** no known function.

**Tuft cells** play a part in the immune response



# Epithelial tissue – small intestine

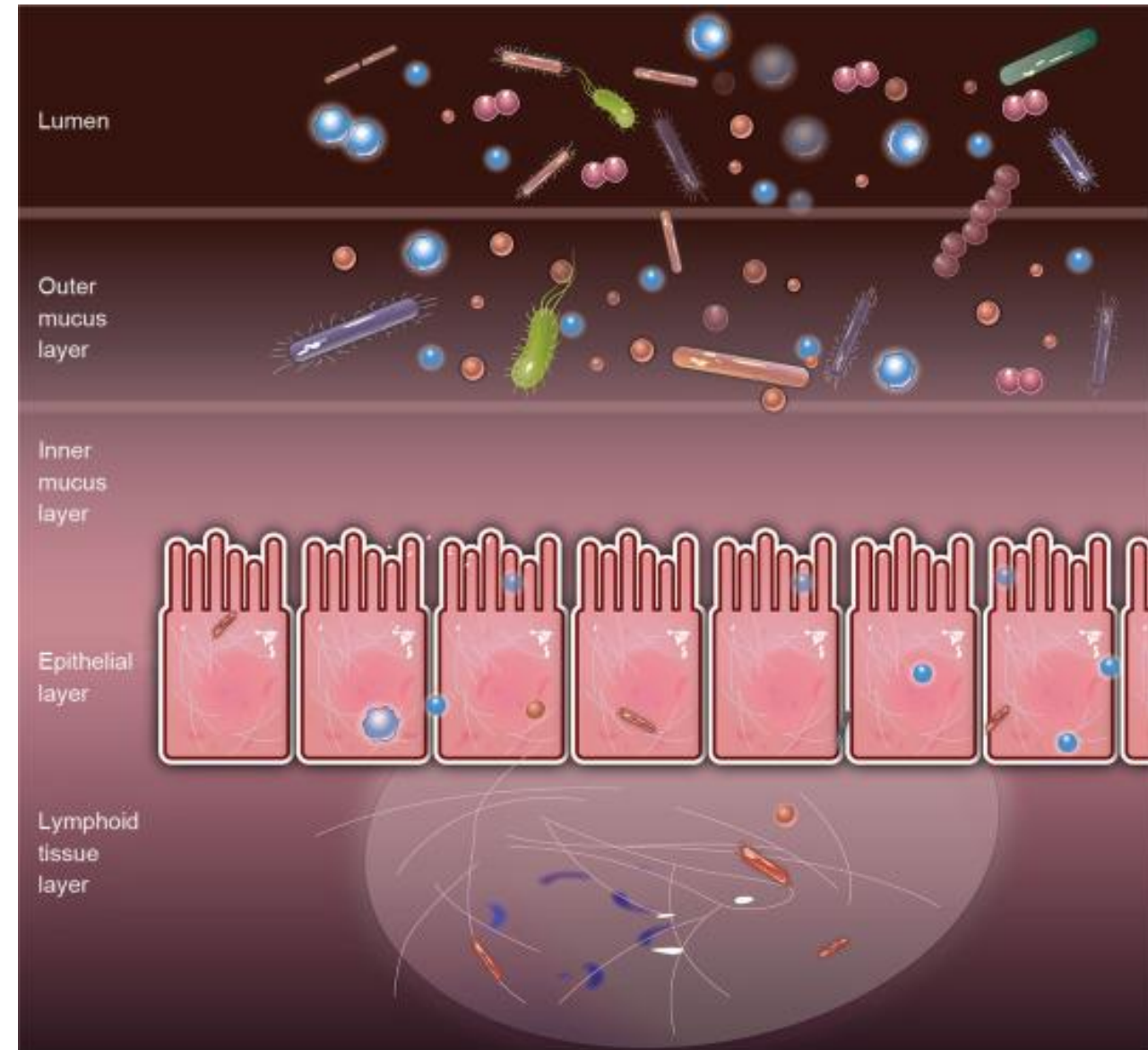
## Human gastrointestinal microbiota

**commensal** (a non-harmful coexistence)

commensal bacteria **can harm the host** if they extrude from the intestinal tract

**Translocation**, which occurs when bacteria leave the gut through its mucosal lining, can occur in a number of different diseases.

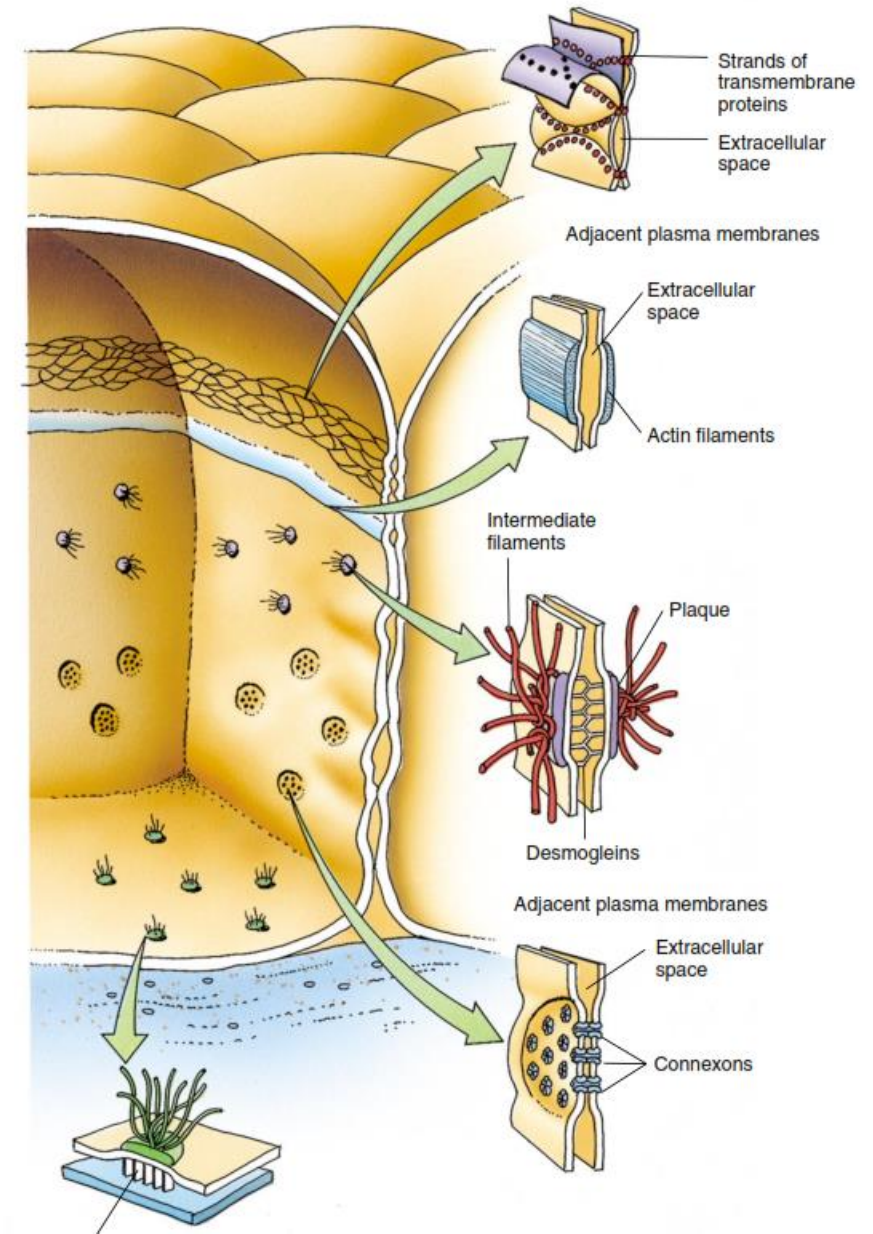
If the gut is perforated, bacteria invade the interstitium, causing a potentially **fatal infection**





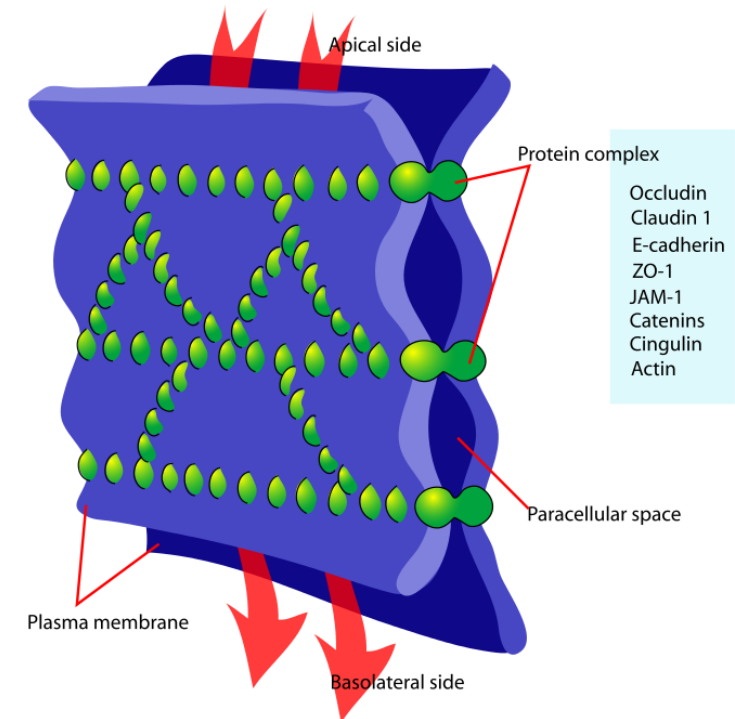
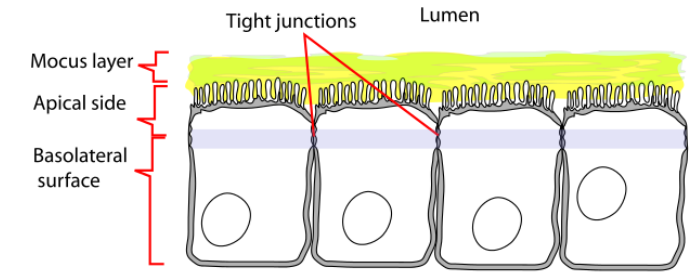
# Epithelial tissue – small intestine

Tight junctions, also known as occluding junctions or **zonulae occludentes** (singular, zonula occludens)



# Epithelial tissue – small intestine

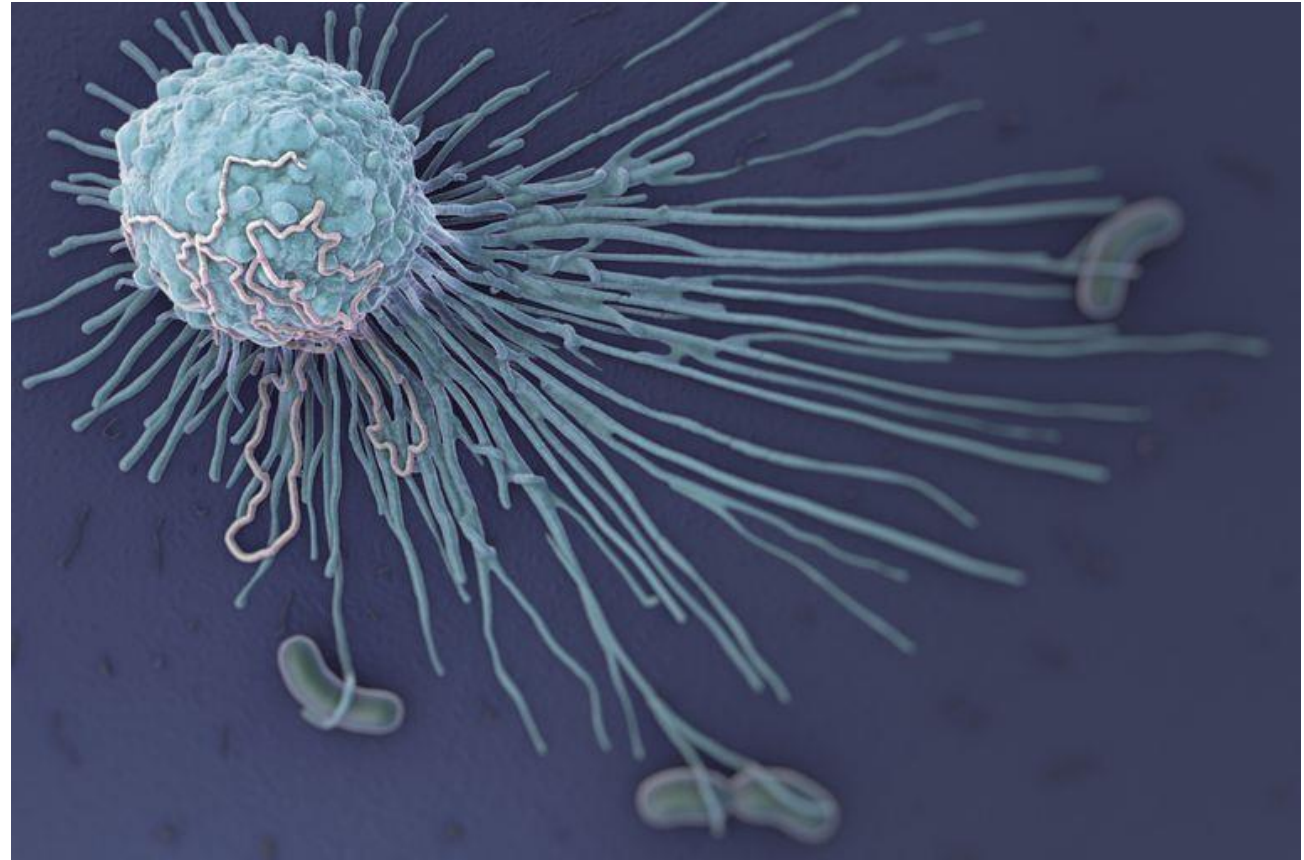
Tight junctions, also known as occluding junctions or **zonulae occludentes** (singular, zonula occludens)





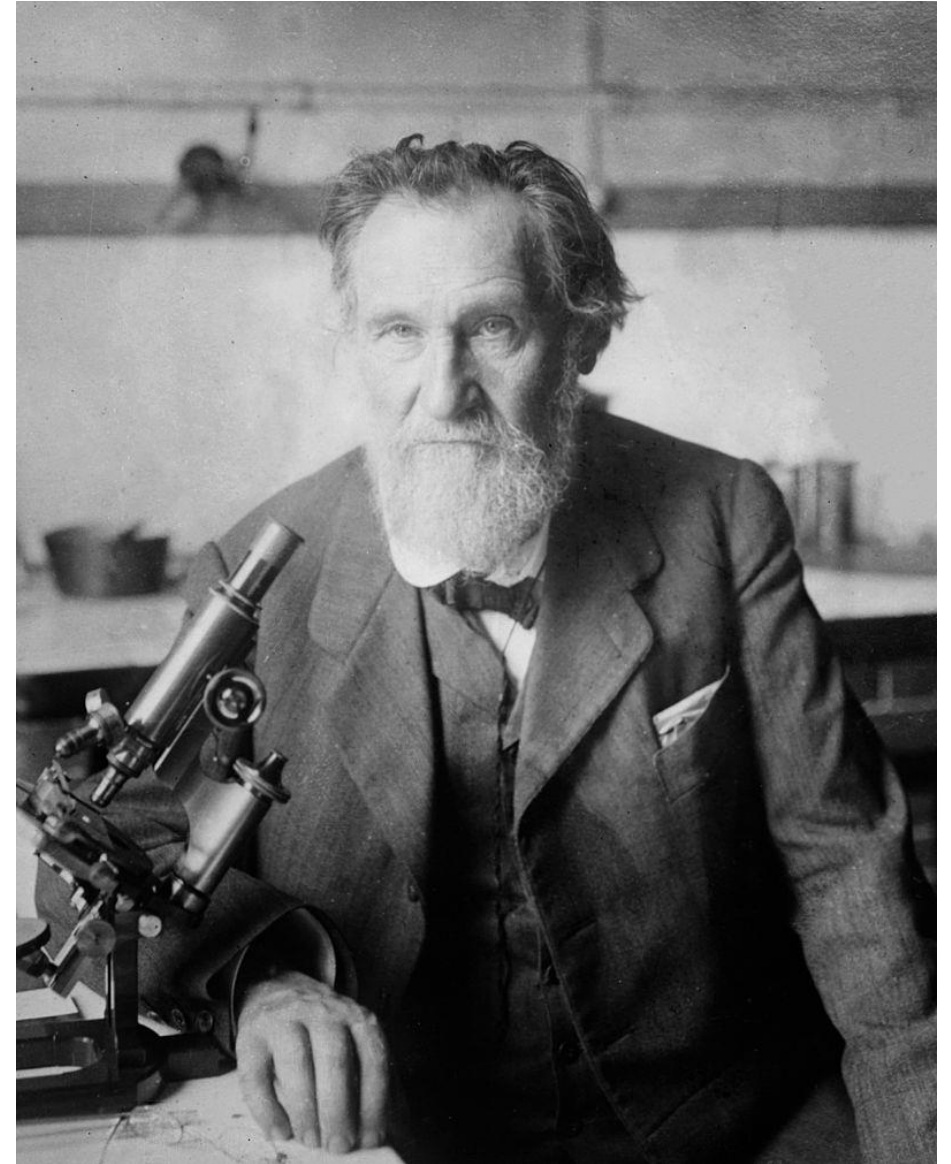
# Epithelial tissue – small intestine

**Macrophages** in lamina  
propria (connective tissue)  
Phagocytosis



# Ilya Ilyich Mechnikov

**Ilya Ilyich Mechnikov** (1845 –1916)  
Phagocytosis



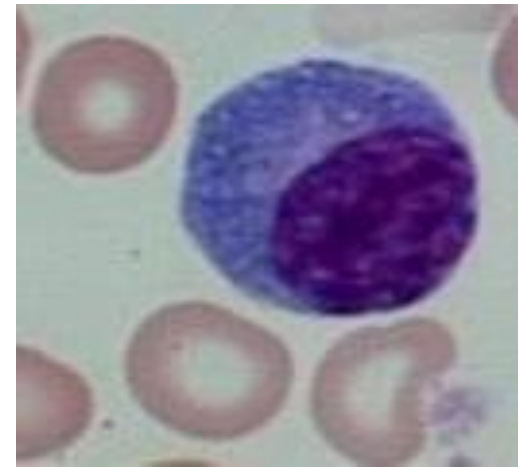
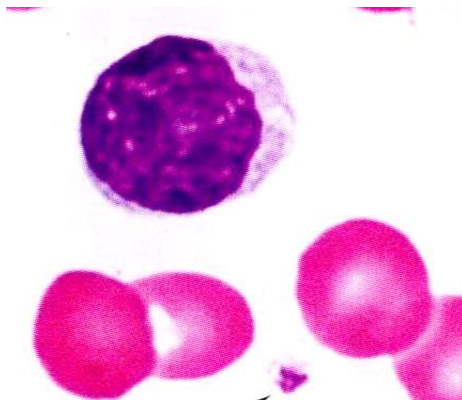
*He and Paul Ehrlich were jointly awarded the 1908 Nobel Prize in Physiology or Medicine "in recognition of their work on immunity"*



**Lymphocytes**

Lymphocytes are white blood cells responsible for defending the body against foreign agents.

They are scattered throughout the body, in the blood they make up 20-40% of white blood cells, while in the lymphatic tissue and lymphatic organs they are dominant cellular population.



**B-lymphocytes** are cells of **humoral immunity**.

They arise and mature in the bone marrow, and then, as naive lymphocytes, then migrate to the lymphatic follicles of the spleen, lymph nodes, tonsils and lymphatic tissue of the mucosa, which is why lymph follicles are designated as B-dependent zones.

**T lymphocytes** are effector cells of cellular immunity. They are created in bone marrow, undergo maturation in the thymus, and then migrate to the T-dependent zones of the peripheral lymphatic organs. They make up 60-80% of circulating lymphocytes.

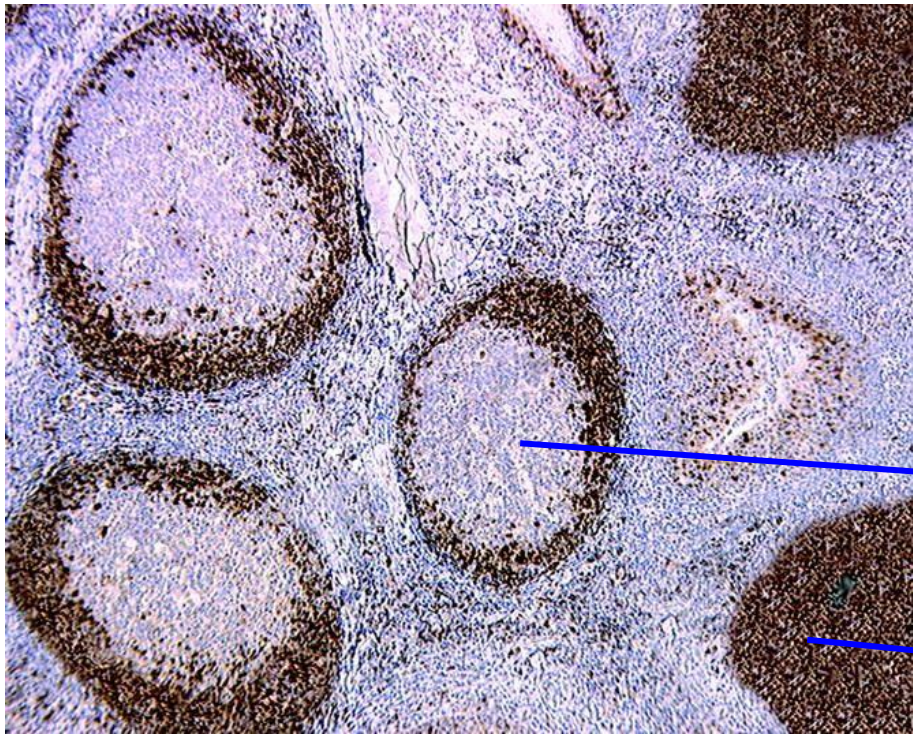
Antigen presenting cells have the ability to introduce, process and present antigens to T-lymphocytes.



# Lymphatic organs

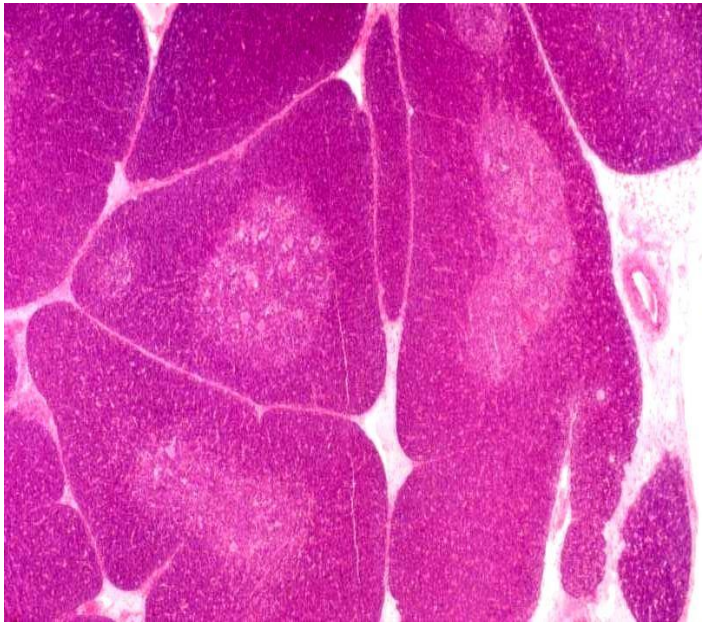
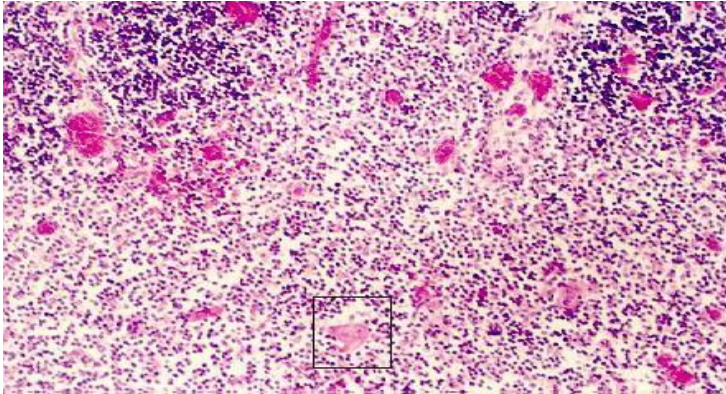
- These are organs made of lymphatic tissue (thymus, bone marrow, spleen, lymph nodes and tonsils).
- According to the stroma structure, lymphatic organs are divided into **lymphoepithelial** and **lymphoreticular**, and according to function into **primary** and **secondary**.
- The **lymphoepithelial** organ is the **thymus**, and the others are lymphoreticular.
- The **primary lymphatic** organs are the **bone marrow and thymus**, and the **secondary organs** are the **spleen, lymph nodes and tonsils**.
- In the primary lymphatic organs lymphocytes undergo maturation, and then migrate to secondary ones.

# Lymphatic nodule



- These are spherical or oval aggregates of lymphocytes.
- They are divided into primary ("resting") and secondary ("activated") lymphatics
- follicles.
- Unlike primary, secondary lymph follicles have **germinal center** and **corona**.

# Thymus



The central lymphatic organ in which T lymphocytes undergo maturation.

Made up of **stroma** and **parenchyma**

The stroma consists of a **capsule** and **trabeculae**, and the parenchyma is thymic tissue organized into lobules.

In the lobule, there are **cortex** and **medulla**.

## **cortex**

includes 85-90% of the parenchyma and is significantly darker than the medulla on histological preparations. It is dominated by densely packed immature lymphocytes of the thymus - thymocytes. In addition to thymocytes, the cortex contains epithelial cells and macrophages.

## **medulla**

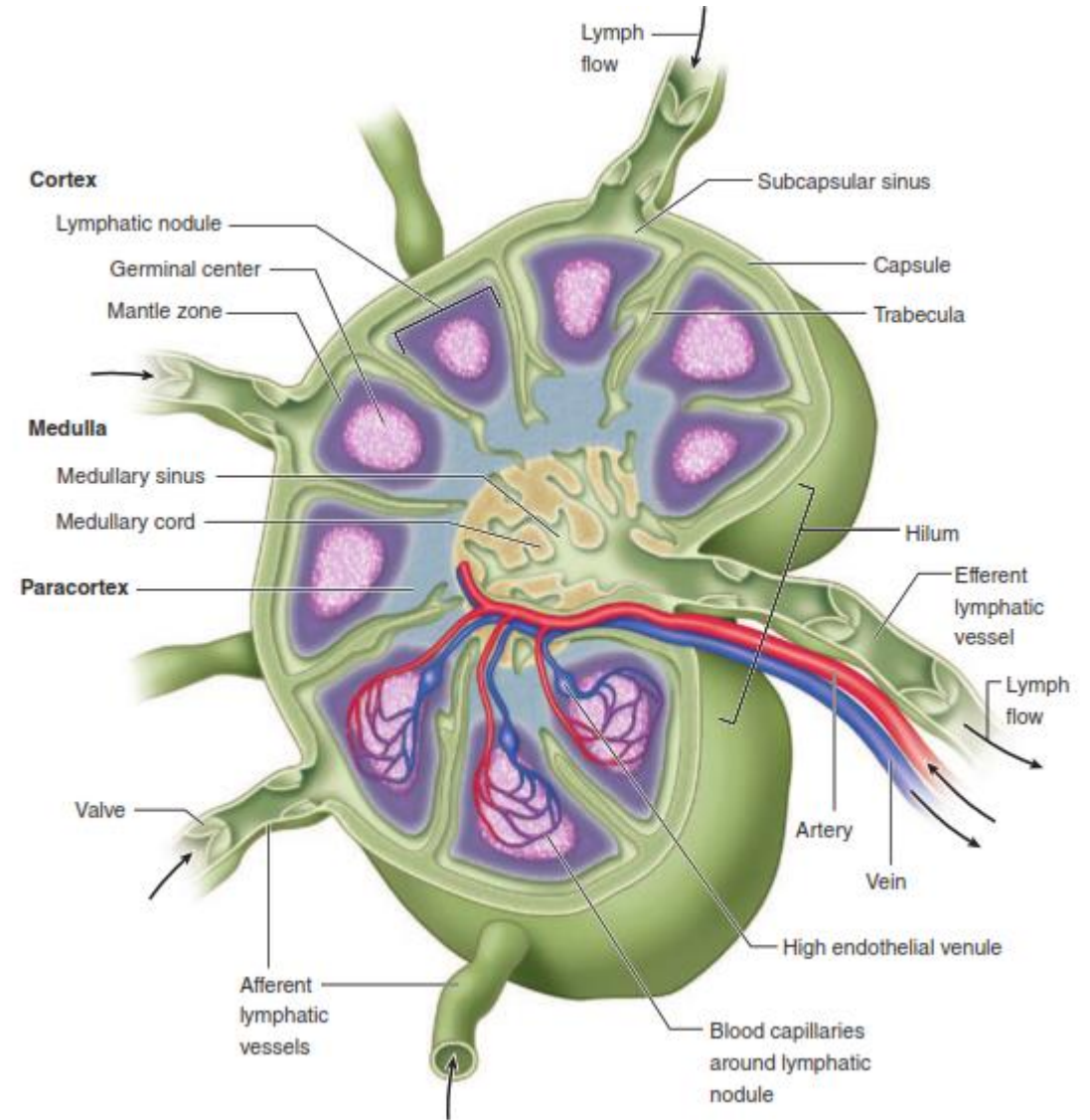
covers 10-15% of the parenchyma, contains significantly fewer thymocytes. In addition to them, epithelial cells, macrophages and dendritic cells are present. The most striking feature of the medulla are **thymic corpuscles** (Hassall's corpuscles) - round or oval agglomerates of thymus epithelial cells stacked in the form of concentric lamella.



# Lymph nodes

Posses stroma and parenchyme. Stroma consists of the capsule and septa, as well as reticular meshwork. The parenchyma has cortex and medulla. Cortex is divided into the **superficial** and **deep (paracortex)**.

The superficial cortex is a nodule filled B-dependent zone, while paracortex does not contain lymph nodules but densely and evenly scattered cells, mainly T-lymphocytes (Thymus-dependent zone). The medulla is built from the cords of lymphatic tissue separated by medullary sinuses as a labyrinthine system of lymphatic channels through which lymph is filtered.



# Spleen

The largest lymphatic organ, serves as a blood filter. Contains stroma and parenchyma. The stroma consists of a capsule and trabeculae as well as reticular meshwork, and the parenchyma is a lymphatic tissue, which is referred to as the **pulp**.

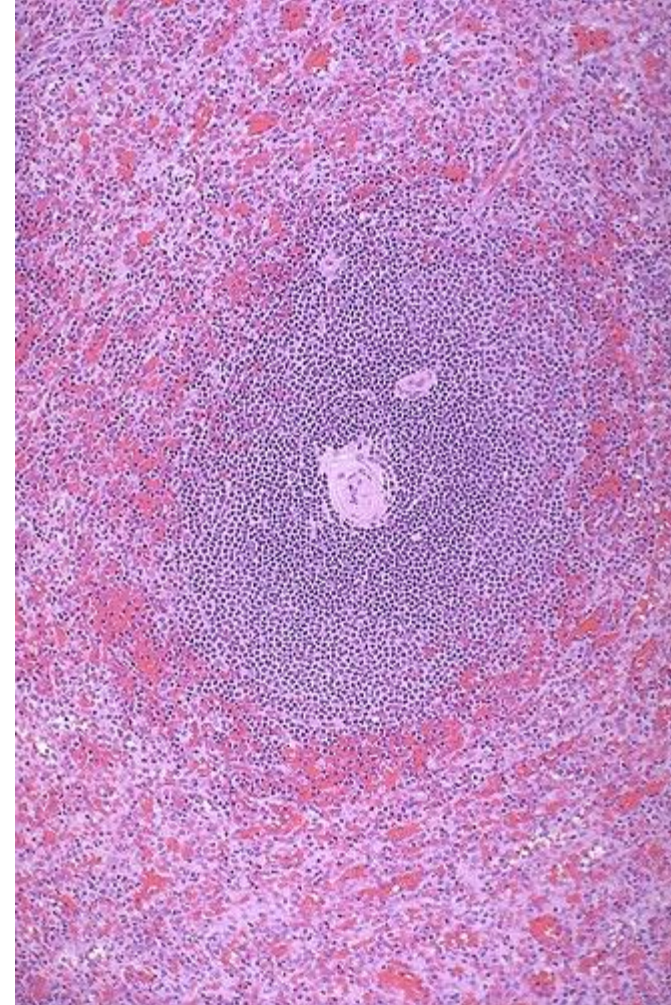
Splenic pulp is divided into two functionally and morphologically different regions: **white pulp and red pulp**.

**White pulp** (20-30% of spleen volume)

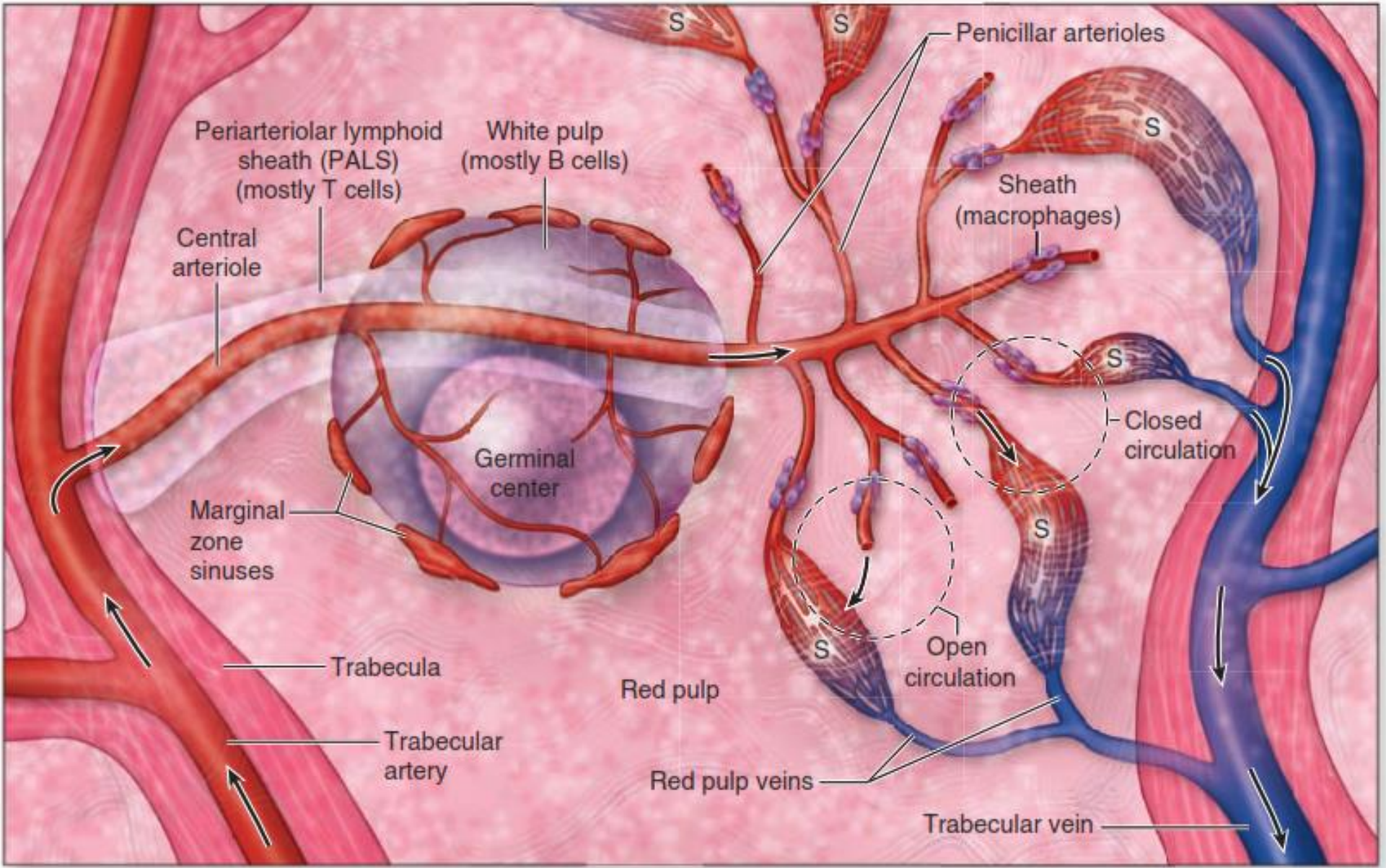
Contains **splenic nodules** and **PALS** (Periarterial Lymphatic Sheath). Splenic nodules contain central artery and are dominated by B-lymphocytes. T lymphocytes that surround the central artery constitute PALS.

**Red pulp** (70-80% of volume) contains venous sinuses and splenic cords.

Between red and white pulp there is a marginal zone, and the marginal sinuses are located in it.









# Mucosa associated lymph tissue

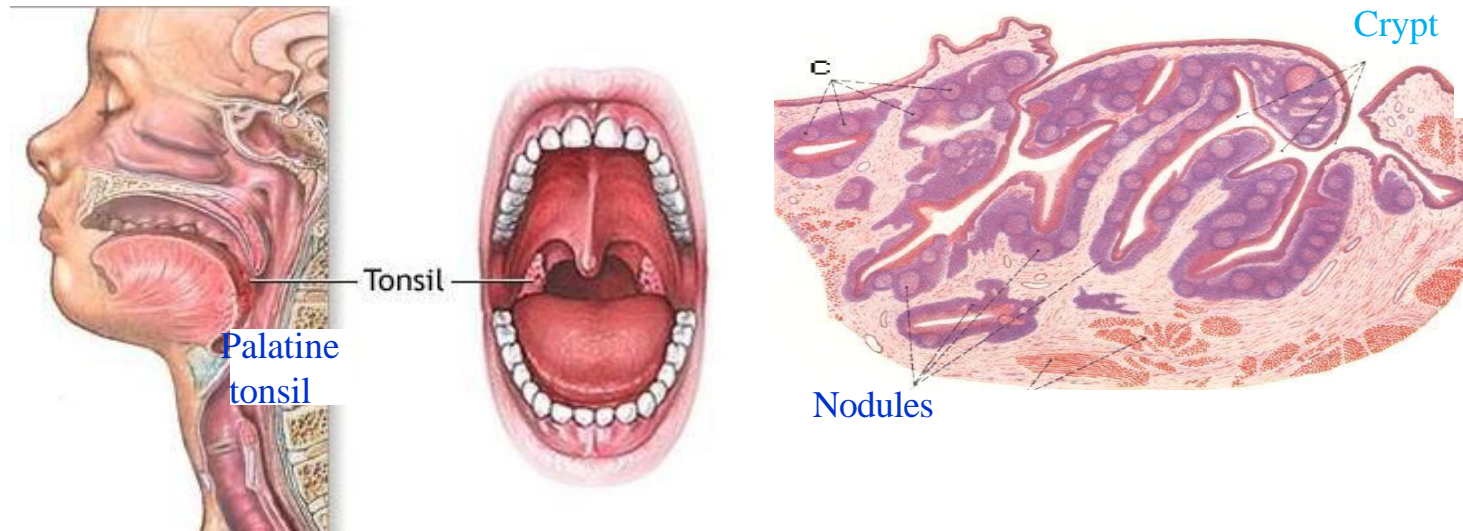


- **MALT** (**M**ucosa **A**ssociated **L**ymphoid **T**issue).
- Present in the mucous membranes of the digestive, respiratory and urogenital tracts.
- Lymphocytes distributed diffusely or in the form of nodules.

# Tonsils

- Tonsils are partially encapsulated lymph tissue aggregates arranged in the form of a protective ring at the entrance to the pharynx.
- Their superficial side is lined with epithelium and is in contact with antigens that can be found in the oral cavity and pharynx through food or air.
- At the bottom they have a connective-tissue semi-capsule.
- There are three types of tonsils that form Waldeyer's ring: palatine, lingual, and pharyngeal.

# Palatine tonsil



It contains 10-20 infoldings of mucosa separated by **tonsillar crypts** lined with squamous stratified epithelium without keratinization.

Cryptic epithelium shows a number of specificities: **microcrypts**, **leukocyte infiltration**, **presence of capillaries**.

Underneath the epithelium is a lamina propria made of lymphatic tissue.

Lymphatic follicles are the B-dependent zone of the tonsils. The interfollicular spaces are a T-dependent zone. In the germinal center of the follicle, plasma cells and memory B cells differentiate.