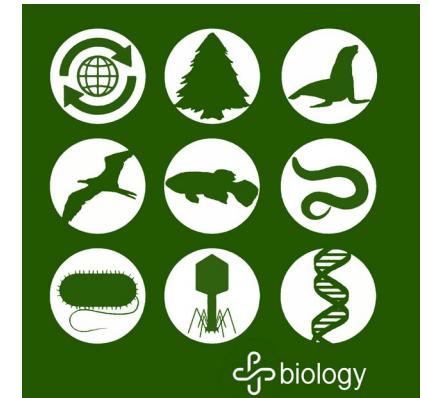


The Circulatory System, Blood, Hemopoiesis

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# BI 455 CHAPTER 11-13



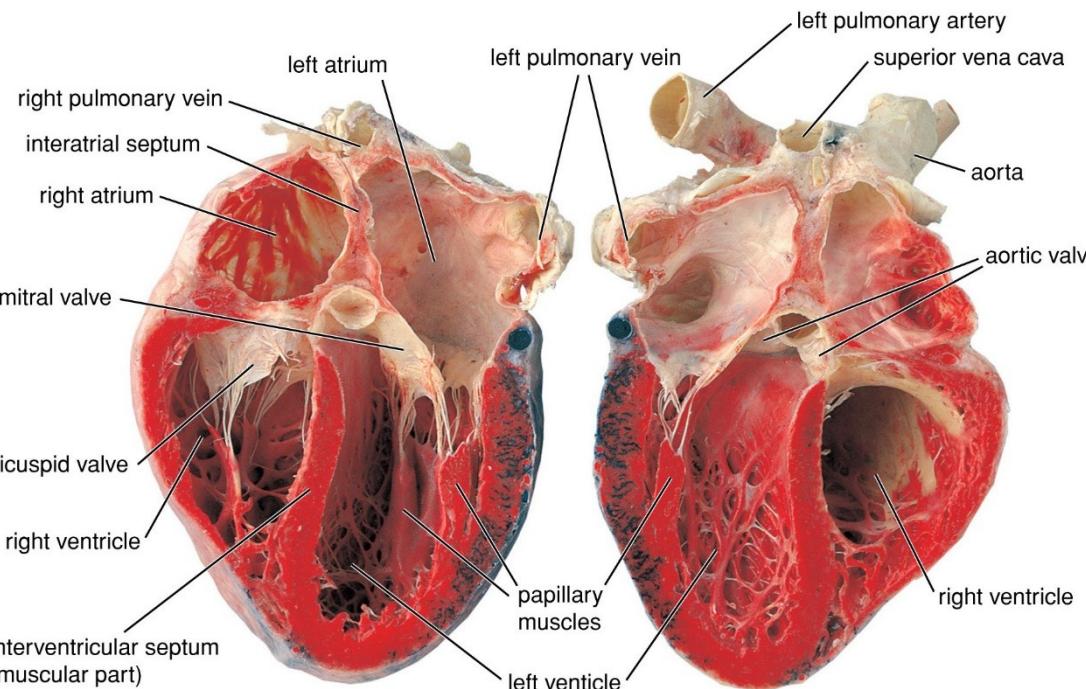
# Chapter 11 Circulatory System

## Key Points

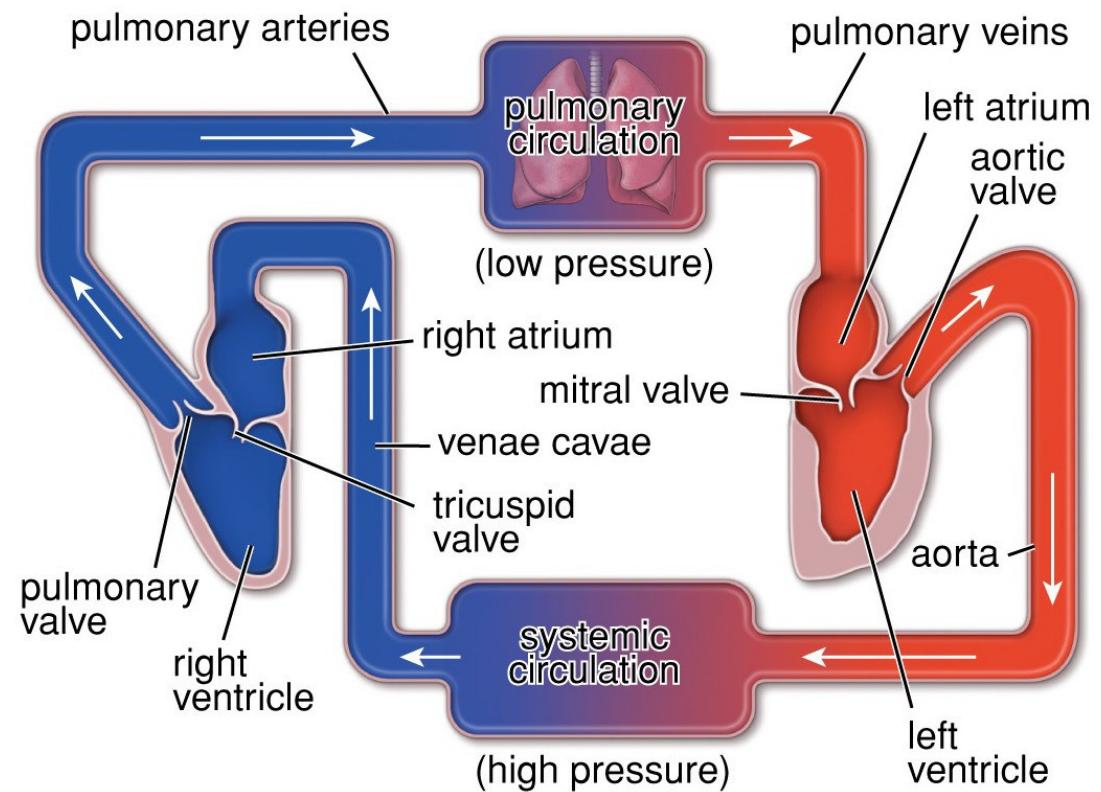
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1. The cardiovascular system includes the heart, blood vessels, and lymphatic vessels. It carries blood and lymph to and from various tissues of the body.
2. The heart is characterized by epicardium, myocardium, endocardium.
3. The conducting system autorhythmically generates heart muscle contractions
4. Arteries are classified based on size and thickness of their tunica media: large arteries (elastic arteries), medium arteries (muscular arteries), and small arteries (including arterioles)
5. Capillaries regulate substance exchange with tissues
6. Veins are divided into four types based on their size: venules, small veins, medium veins, and large veins
7. Lymphatic vessels convey interstitial fluids from tissues to the bloodstream

# The heart is a muscular pump that maintains unidirectional flow of blood



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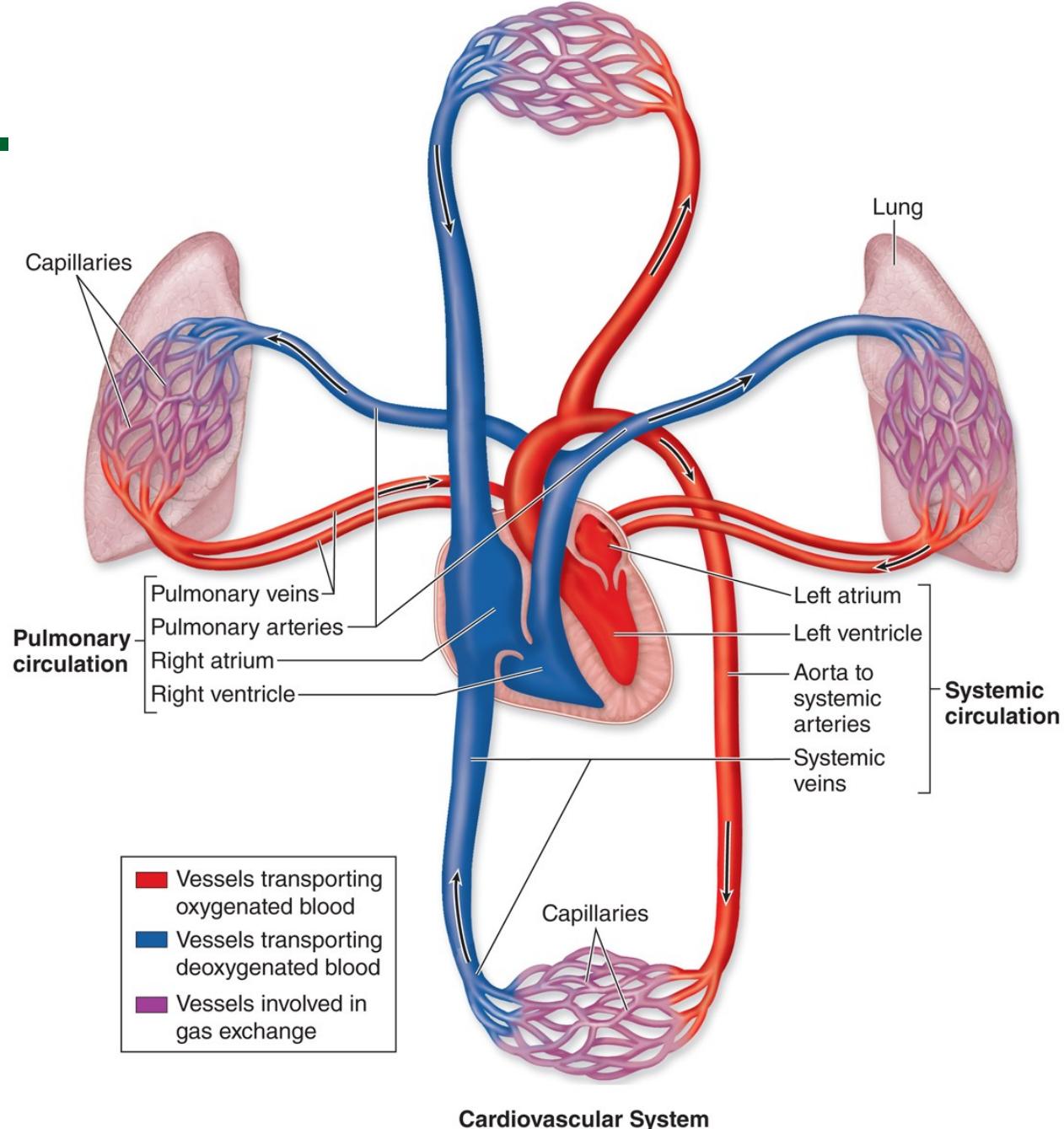


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# Circulation

**Systemic circuit:** tissues → superior and inferior vena cavae → right atrium → right AV valve → right ventricle → pulmonary valve → pulmonary trunk

**Pulmonary Circuit:** Lungs → four pulmonary veins → left atrium → left AV valve → left ventricle → aortic valve → ascending aorta



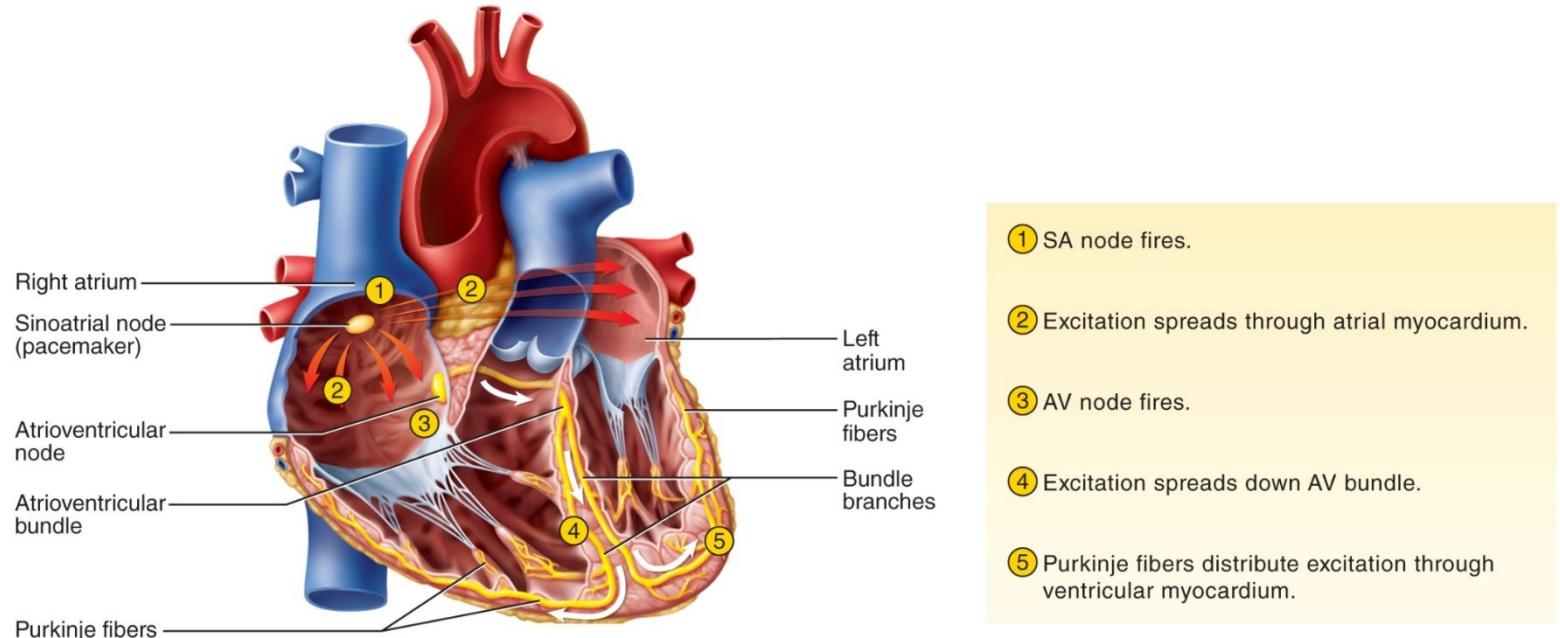
# Autorhythmic heart: Beats without stimuli from nervous system

Heart rhythm cessation: dysfunction in the conducting system → cardiac arrest → no circulation.

Sudden cardiac arrest is a medical emergency; first-aid treatment such as cardiopulmonary resuscitation (CPR) and defibrillation (electrical resetting of the heart)

Sinoatrial node(SA) fires automatically → Internodal conduction → Atrioventricular (AV) node → Atrioventricular (AV) bundle (bundle of His) → Purkinje fibers

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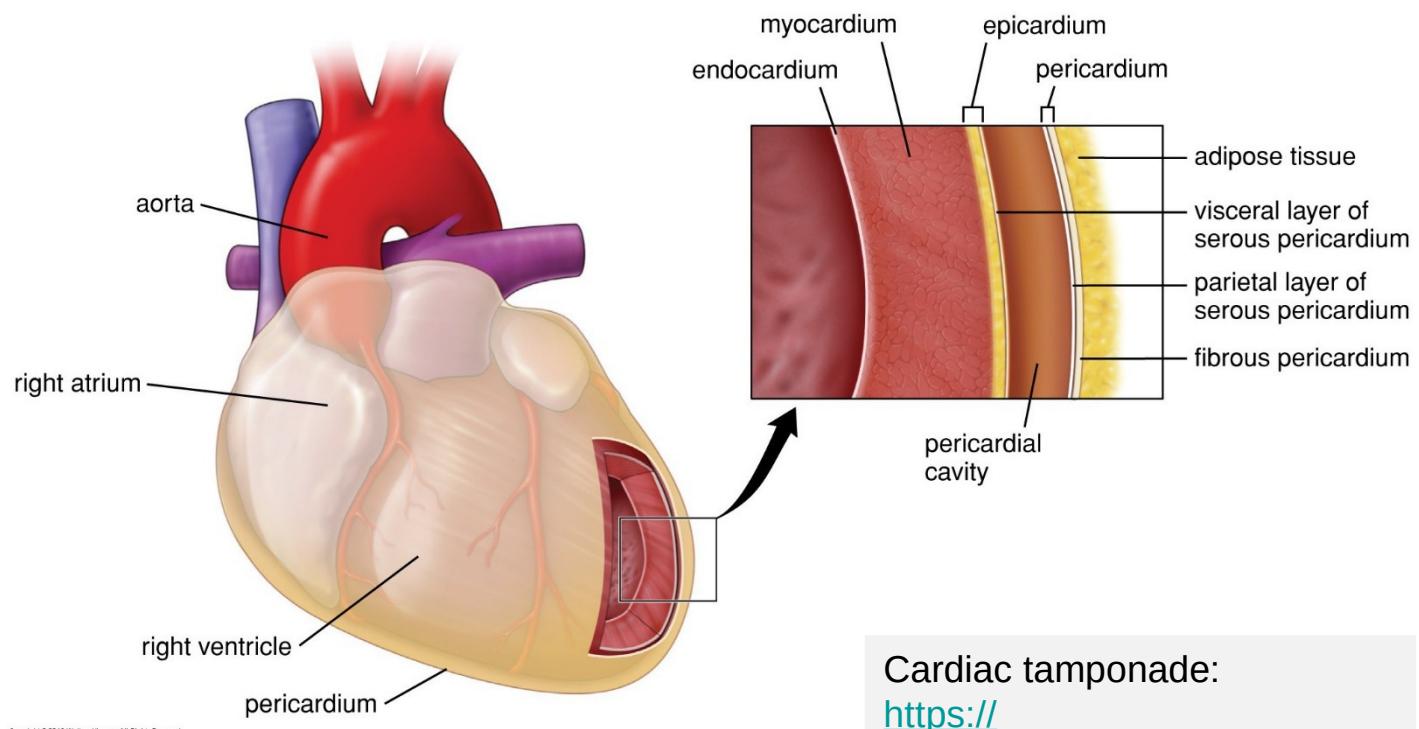


# Wall of the heart has three layers: epicardium, myocardium, and endocardium.

- **Epicardium (Visceral Serous Pericardium):** Thin layer covering surface of heart
- **Myocardium:** Most of heart mass. Composed of cardiac muscle. Does contractile work of heart, thickness varies according to workload
- **Endocardium:** Lines interior of heart chambers, Covers valve surfaces. Continuous with inner lining of blood vessels

**Outside the heart wall:** Pericardial cavity, parietal serous pericardium, Fibrous pericardium, adipose tissue

**Cardiac tamponade:** Fluid accumulation on pericardial cavity compresses heart. Caused by chest injury or pericarditis (inflammation of pericardium)

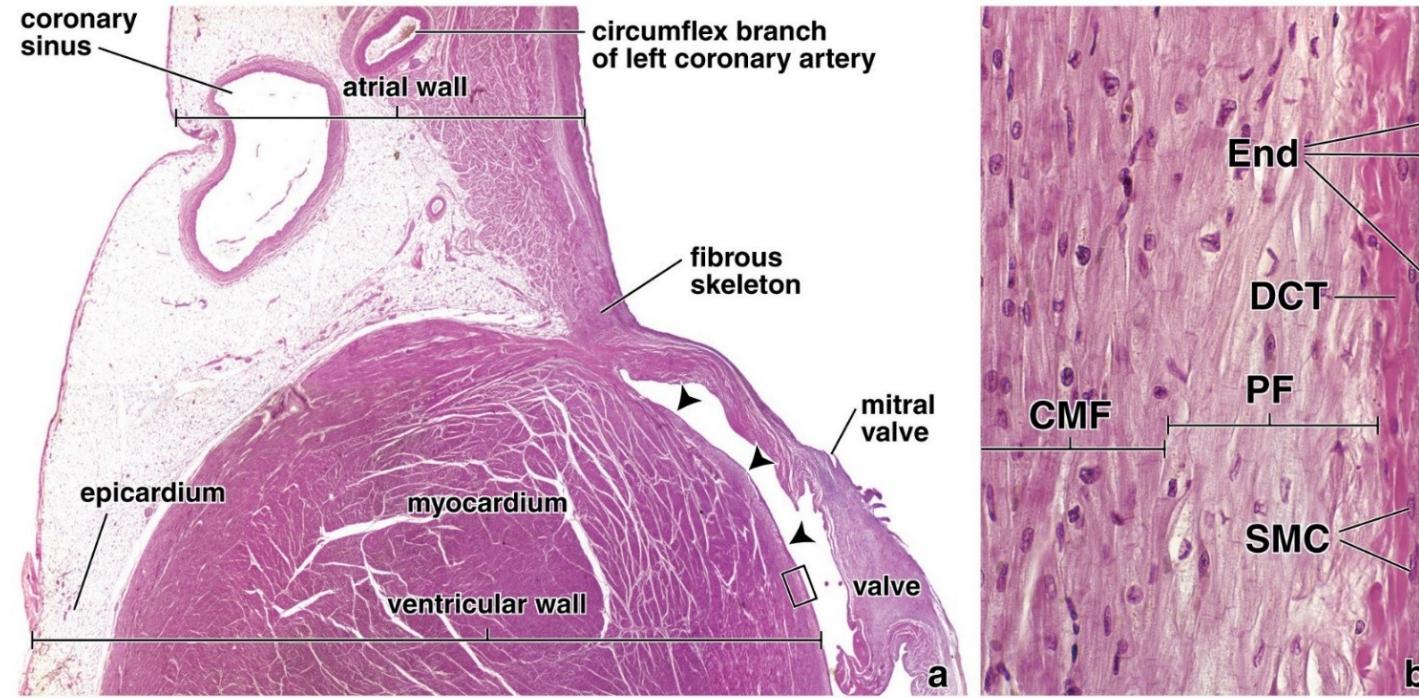


Cardiac tamponade:

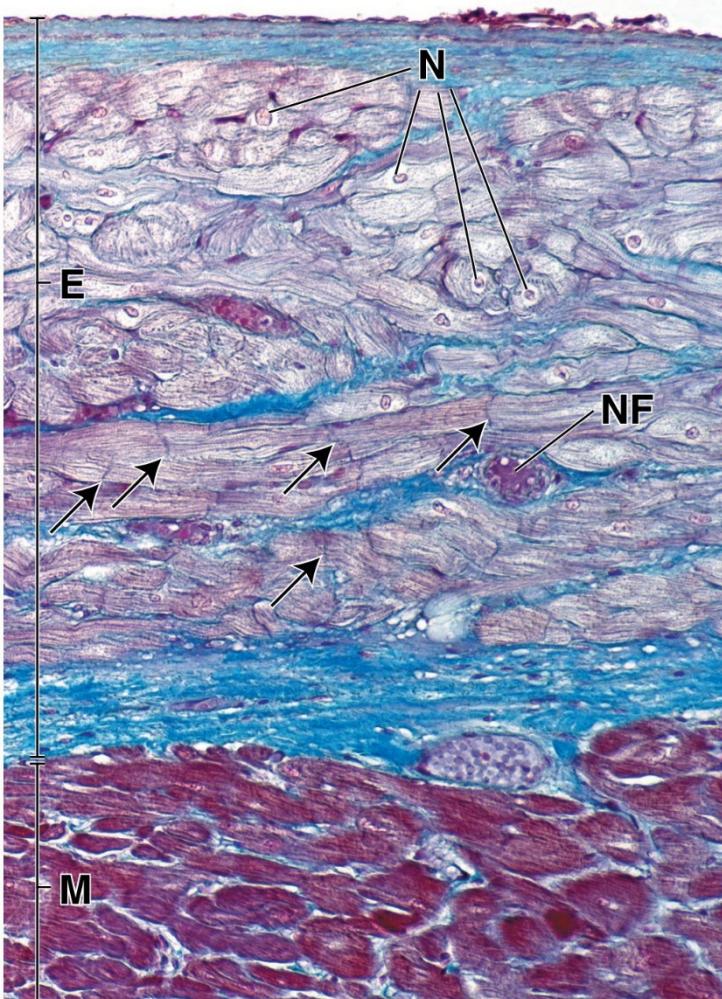
<https://www.youtube.com/watch?v=QwafuDegC5Y>

# The conducting system of the heart

Sagittal section of the posterior wall of left atrium and left ventricle: blood vessels of epicardium are surrounded by adipose tissue. Rectangle: Endocardium is squamous inner layer of endothelium (End), middle layer subendothelial dense connective tissue (DCT) containing smooth muscle cells (SMC), deep subendocardial layer of Purkinje fibers (PF). Myocardium: cardiac muscle fibers (CMF).

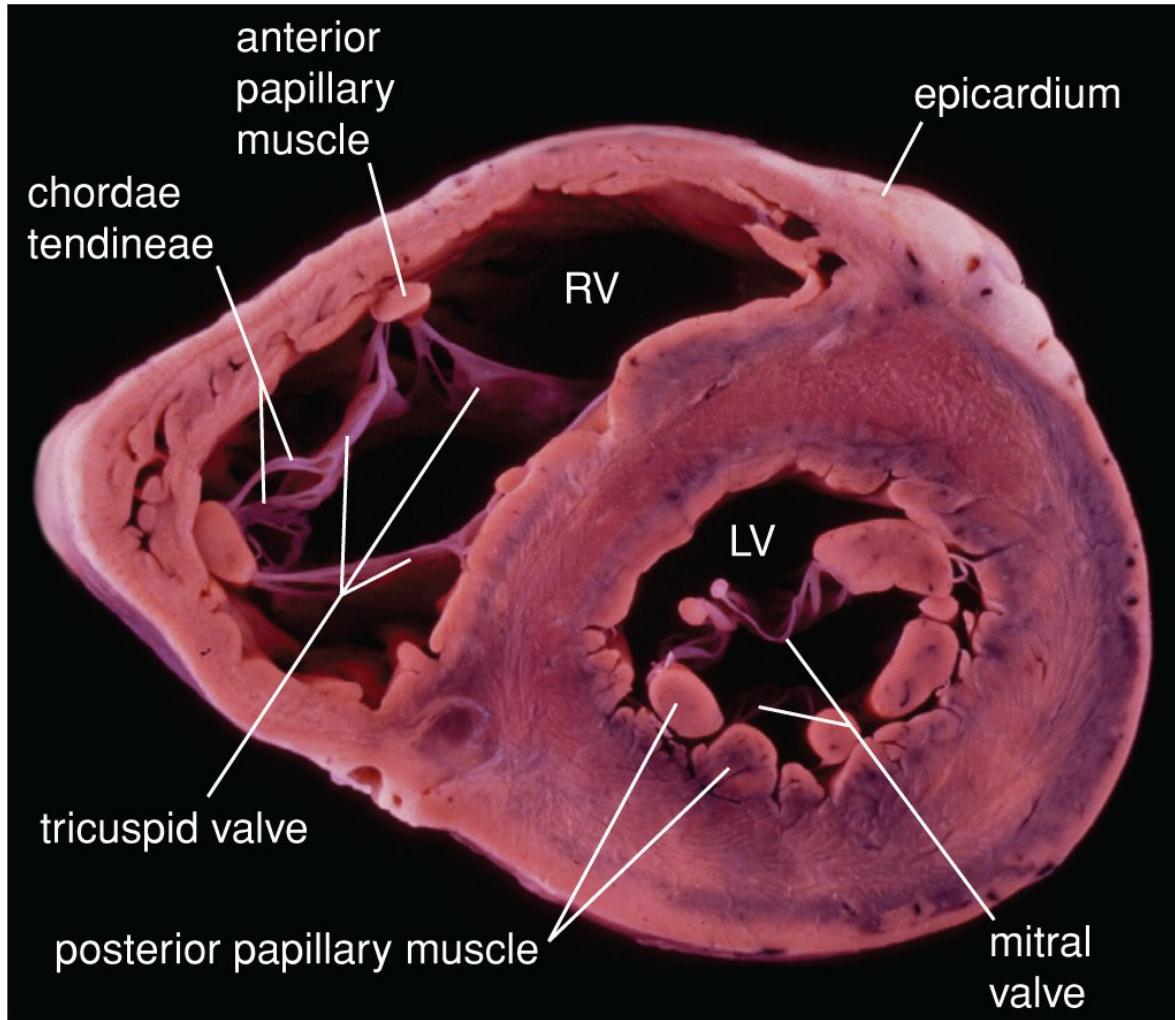


# Conducting system as seen in the ventricular wall



- **Endocardium (E):** The free luminal surface of the ventricle (top) is covered by endothelium and an underlying layer of subendothelial connective tissue (stained blue).
- **Intercalated discs** in the fibers (arrows).
- **Purkinje fibers:** large amounts of glycogen, pale-staining occupying center portion of the cell surrounded by the myofibrils. Among the Purkinje fibers are course nerves (NF) that belong to the autonomic nervous system
- Nuclei (N) are round and are larger than the nuclei of the cardiac muscle cells in the **myocardium (M)**.

# The heart wall in cross section



- Atria myocardium is thinner than ventricles
- Atria deliver blood to ventricles, while ventricles deliver to pulmonary and systemic circulations.
- Left ventricle delivers to systemic circulation, which requires more force.

Live Beating Heart and Heart Surgery:  
[https://www.youtube.com/watch?v=uR4t\\_\\_B-Zwg](https://www.youtube.com/watch?v=uR4t__B-Zwg)

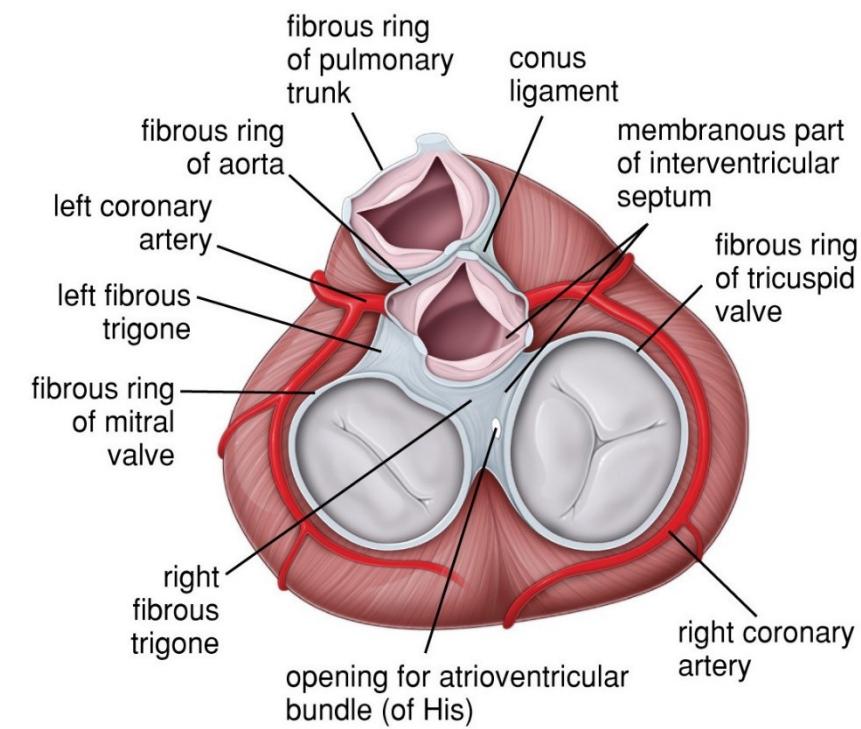
# Fibrous skeleton

This fibrous network (indicated in blue) serves for the attachment of cardiac muscle and cuspid valves between the atria and ventricles and for the semilunar valves of the aorta and the pulmonary artery.

» » **MEDICAL APPLICATION** Heart valve defects can be produced by developmental defects, scarring after certain infections, or hypertension.

If valves don't close tightly, backflow of blood produces heart murmur (sound), heart struggles to circulate blood.

Repaired by artificial or large animal donor valve, which lack endothelial covering. Requires exogenous anticoagulant agents to prevent thrombus formation.

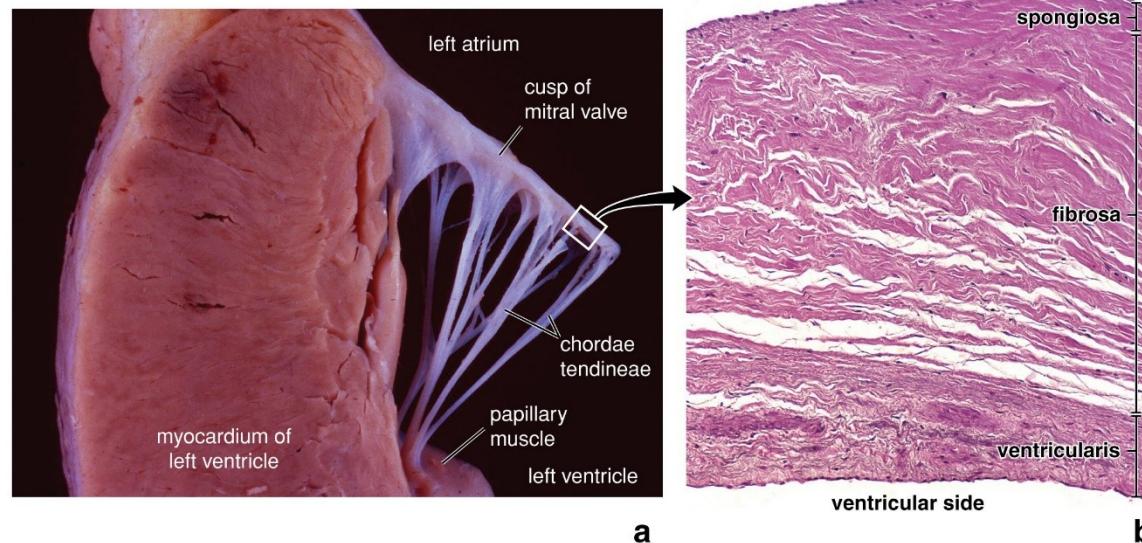


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# Heart Valve: Connective tissue with overlying endocardium

Valve cusps are normally avascular, but cusps are thin enough to allow nutrient diffusion from chamber blood.

**Valvular heart disease:** Inflammation of the heart valves (valvulitis) induces **angiogenesis** (blood vessel formation) in the valve and vascularization. This can lead to progressive replacement of elastic tissue by irregular masses of collagen fibers, causing the valve to thicken and then become rigid and inflexible



## Arteries

Vessel	Diameter	Tunica intima (inner layer)	Tunica media (middle layer)	Tunica adventitia (outer layer)
Large artery (elastic artery)	>10 mm	Endothelium Connective tissue Smooth muscle	Smooth muscle Elastic lamellae	Connective tissue Elastic fibers Thinner than tunica media
Medium artery (muscular artery)	2–10 mm	Endothelium Connective tissue Smooth muscle Prominent internal elastic membrane	Smooth muscle Collagen fibers Relatively little elastic tissue	Connective tissue Some elastic fibers Thinner than tunica media
Small artery	0.1–2 mm	Endothelium Connective tissue Smooth muscle Internal elastic membrane	Smooth muscle (8–10 cell layers) Collagen fibers	Connective tissue Some elastic fibers Thinner than tunica media
Arteriole	10–100 $\mu\text{m}$	Endothelium Connective tissue Smooth muscle	Smooth muscle (1–2 cell layers)	Thin, ill-defined sheath of connective tissue
Capillary	4–10 $\mu\text{m}$	Endothelium	None	None

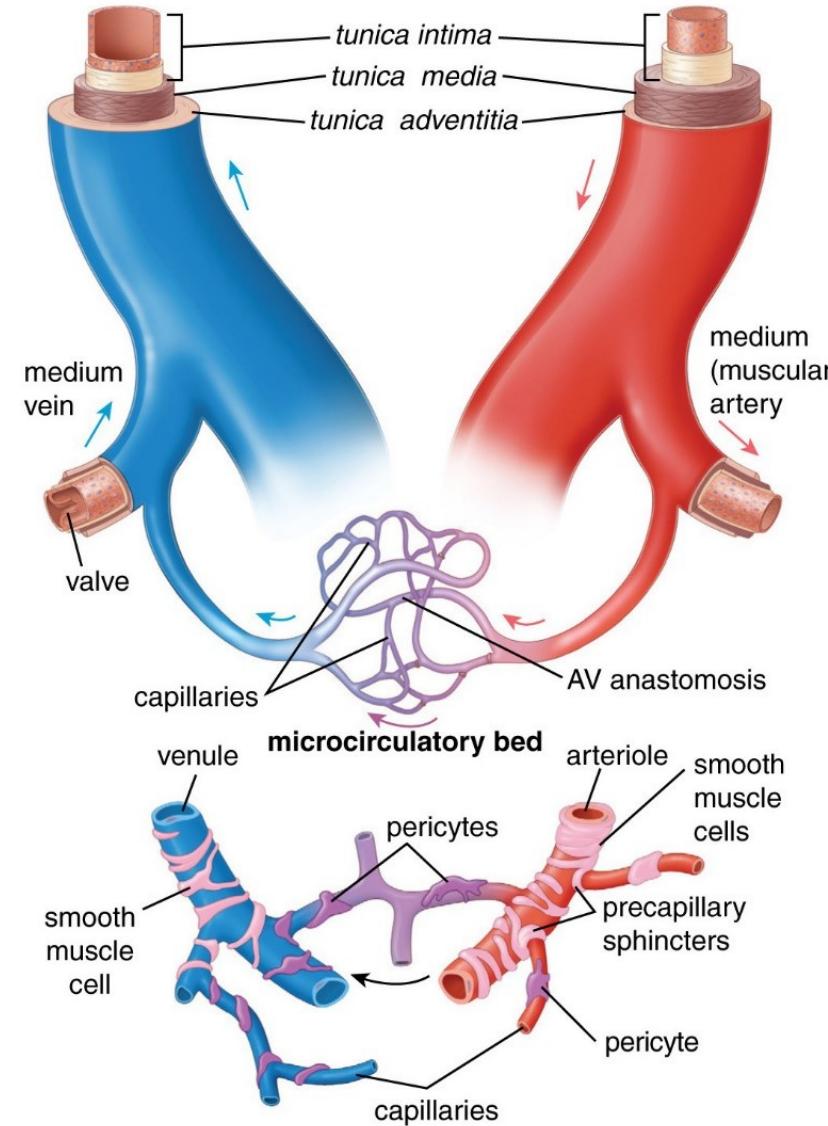
## VEINS

large vein



## ARTERIES

large (elastic) artery

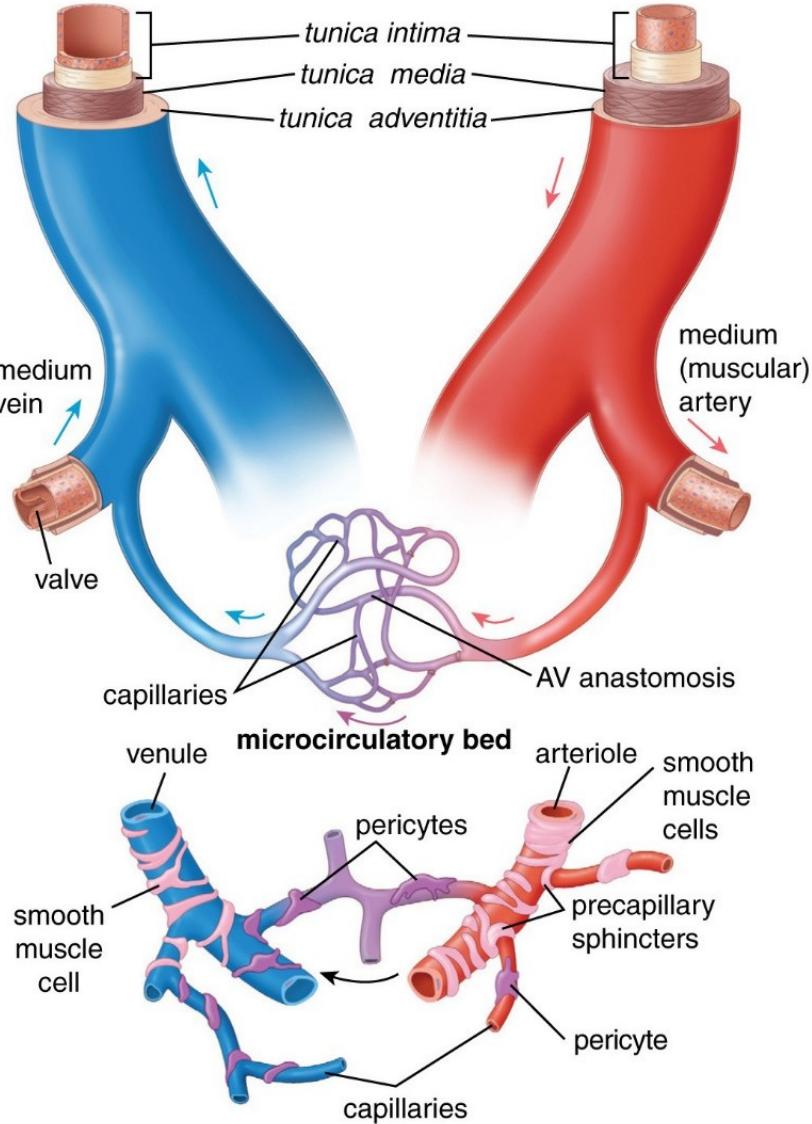


## Veins

Vessel	Diameter	Tunica intima (inner layer)	Tunica media (middle layer)	Tunica adventitia (outer layer)
Postcapillary venule	10–50 $\mu\text{m}$	Endothelium Pericytes	None	None
Muscular venule	50–100 $\mu\text{m}$	Endothelium	Smooth muscle (1–2 cell layers)	Connective tissue Some elastic fibers Thicker than tunica media
Small vein	0.1–1 mm	Endothelium Connective tissue Smooth muscle (2–3 layers)	Smooth muscle (2–3 layers continuous with tunica intima)	Connective tissue Some elastic fibers Thicker than tunica media
Medium vein	1–10 mm	Endothelium Connective tissue Smooth muscle Internal elastic membrane in some cases	Smooth muscle Collagen fibers	Connective tissue Some elastic fibers Thicker than tunica media
Large vein	>10 mm	Endothelium Connective tissue Smooth muscle	Smooth muscle (2–15 layers) Cardiac muscle near heart Collagen fibers	Connective tissue Some elastic fibers, longitudinal smooth muscles Much thicker than tunica media

## VEINS

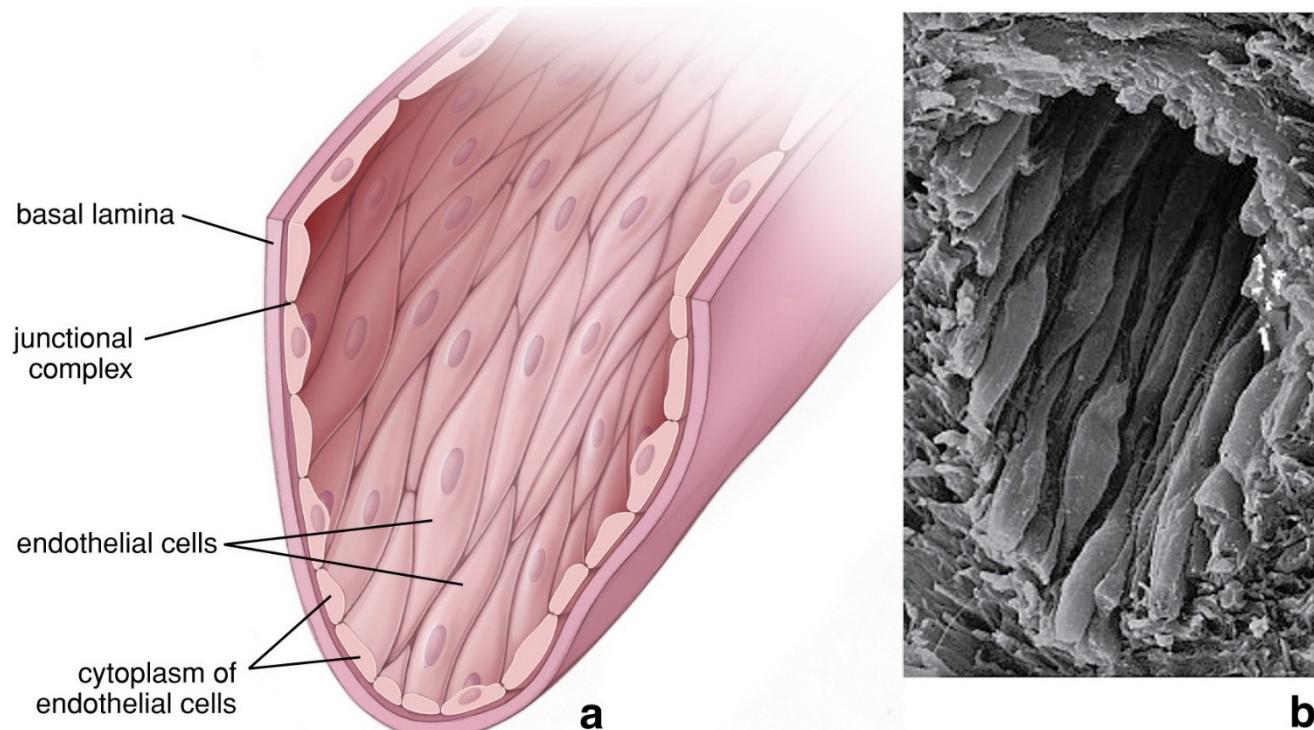
large vein



## ARTERIES

large (elastic) artery

# In the adult human body, a circulatory system consists of about 60,000 miles of different-sized vessels lined with vascular endothelium



- a. The cells are elongated with their long axis parallel to the direction of blood flow. Nuclei of endothelial cells are also elongated in the direction of blood flow.
- b. Scanning electron micrograph of a small vein, showing the cells of the endothelial lining. Note the spindle shape with the long axis of the cells running parallel to the vessel.

# Vascular endothelium: continuous layer of flattened, elongated, cells aligned with their long axes in the direction of the blood flow.

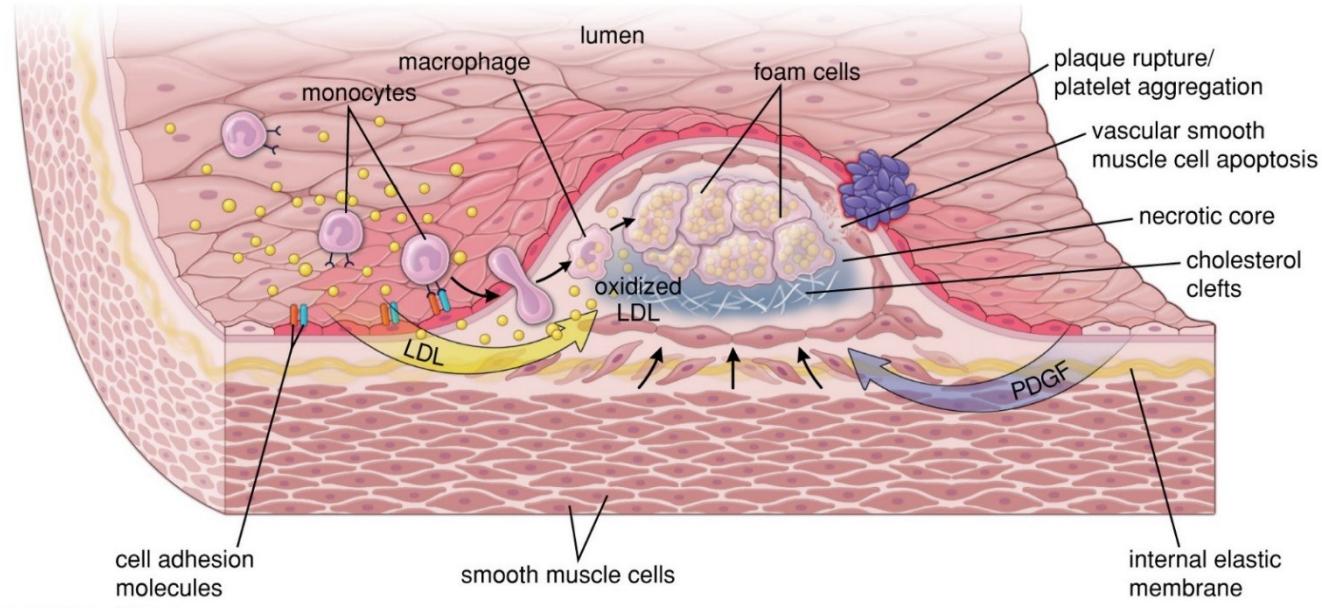
Endothelial surface adhesion molecules: Low-density lipoprotein [LDL], insulin, and histamine receptors

Endothelial activation: cells produce new surface that control blood coagulation.

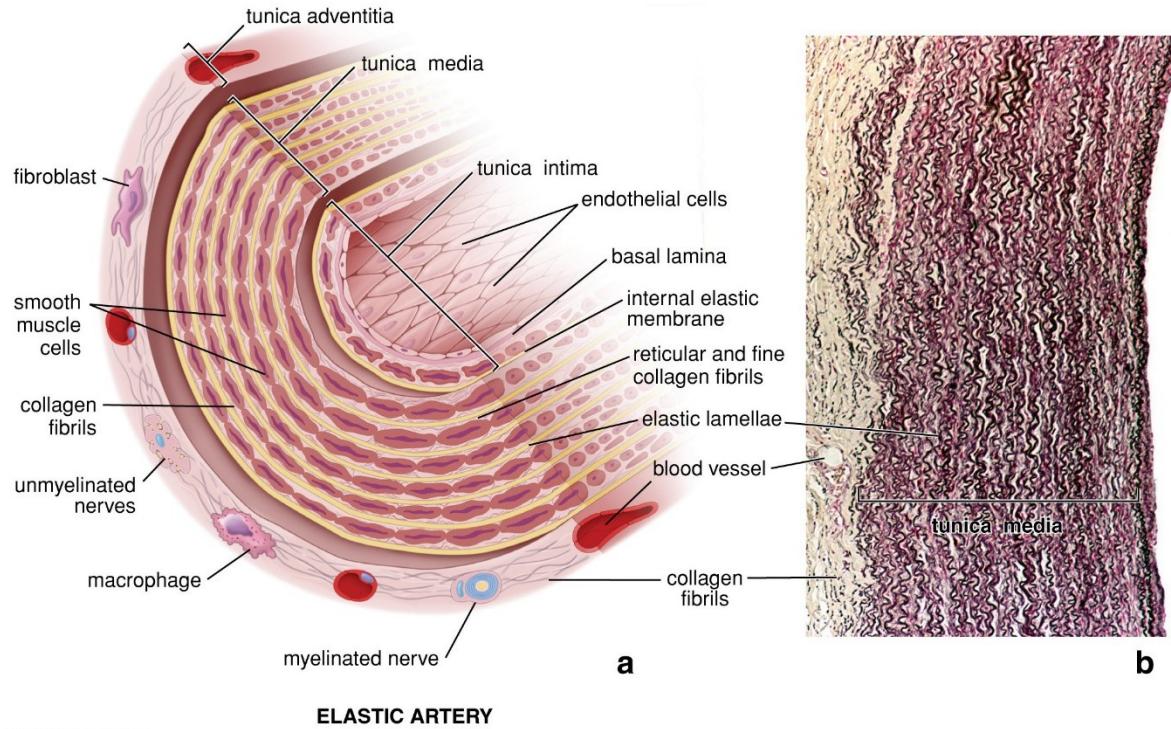
» » MEDICAL APPLICATION: Tissue injury → platelet aggregation → clotting.

**Embolii** (clots) may detach and obstruct distant vessels.

Myocardial infarct, stroke, or pulmonary embolism, are treated intravenously with tissue plasminogen activator, which breaks down fibrin and quickly dissolves the clot.



# Elastic (large) arteries: Arteries that distend after systole, then recoil to propel blood into circuit



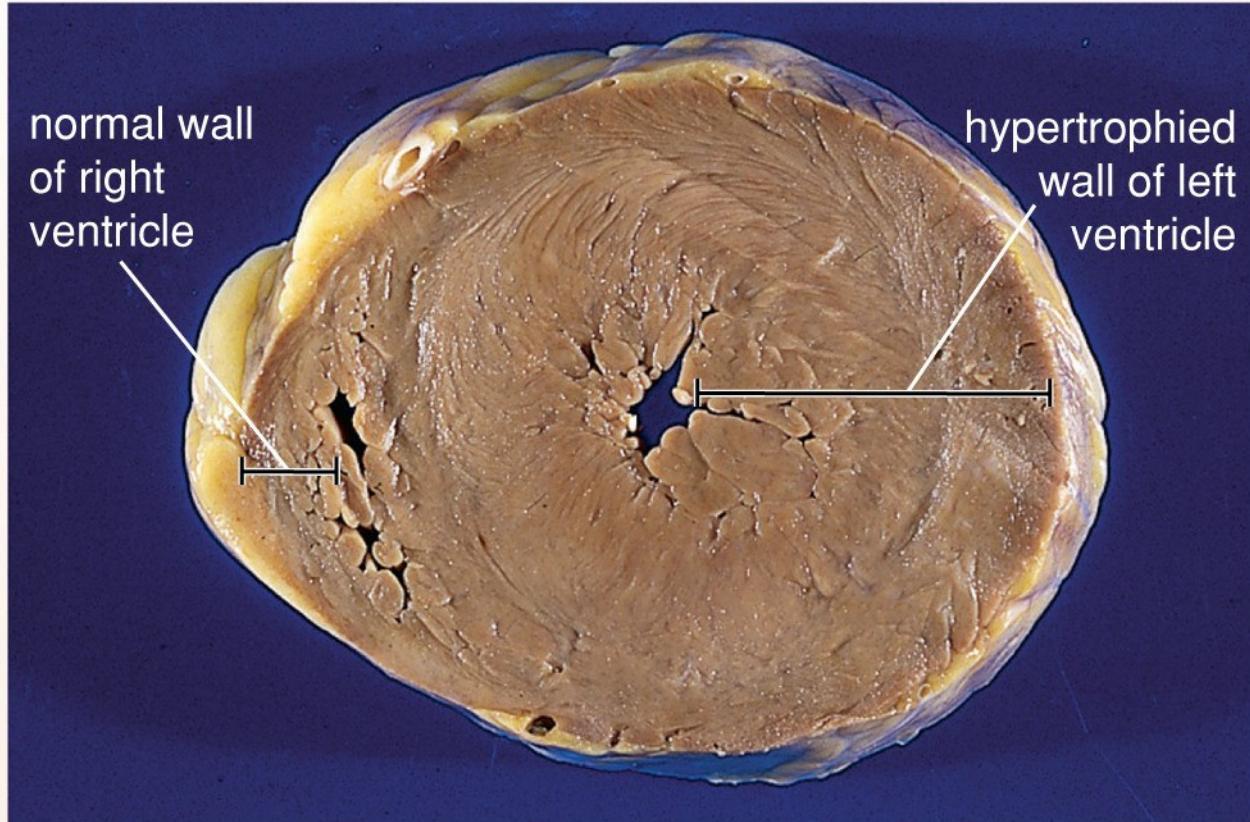
## »» MEDICAL APPLICATION

Atherosclerosis (Gr. *athero*, gruel or porridge, and *scleros*, hardening) may play a role in nearly half of all deaths in developed parts of the world. Poor LDL oxidation in the tunica intima induces monocytes/macrophages to remove the LDL. Lipid-filled macrophages (called foam cells) accumulate and produce plaques.

Predisposing factors include dyslipidemia (>3:1 ratios of LDL to HDL [high-density lipoprotein]), hyperglycemia of diabetes, hypertension, and the presence of toxins introduced by smoking.

In elastic arteries, this causes weakening and aneurysms that can rupture. In muscular arteries this can occlude blood flow to downstream vessels, leading to ischemic heart disease.

# Hypertension

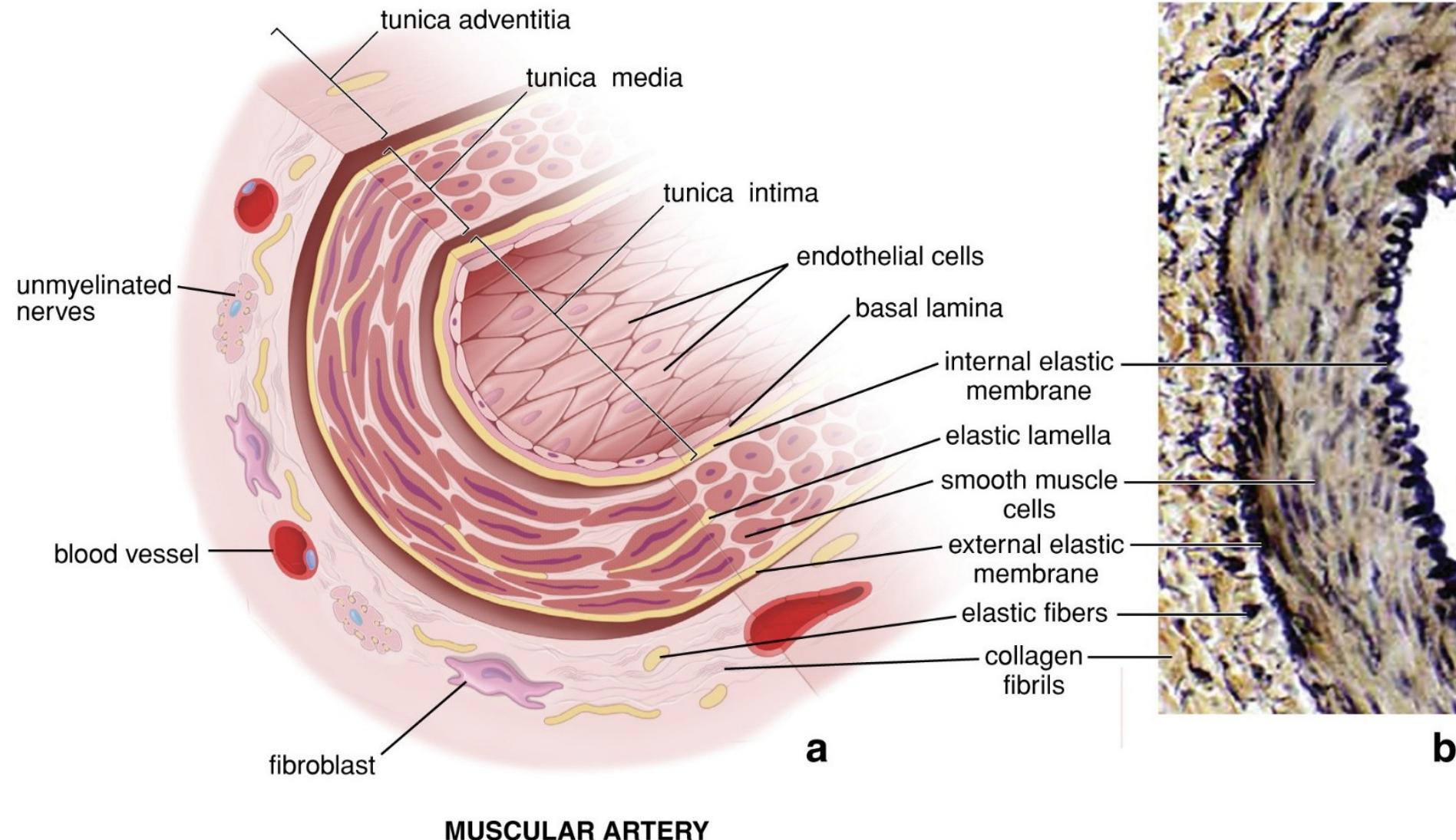


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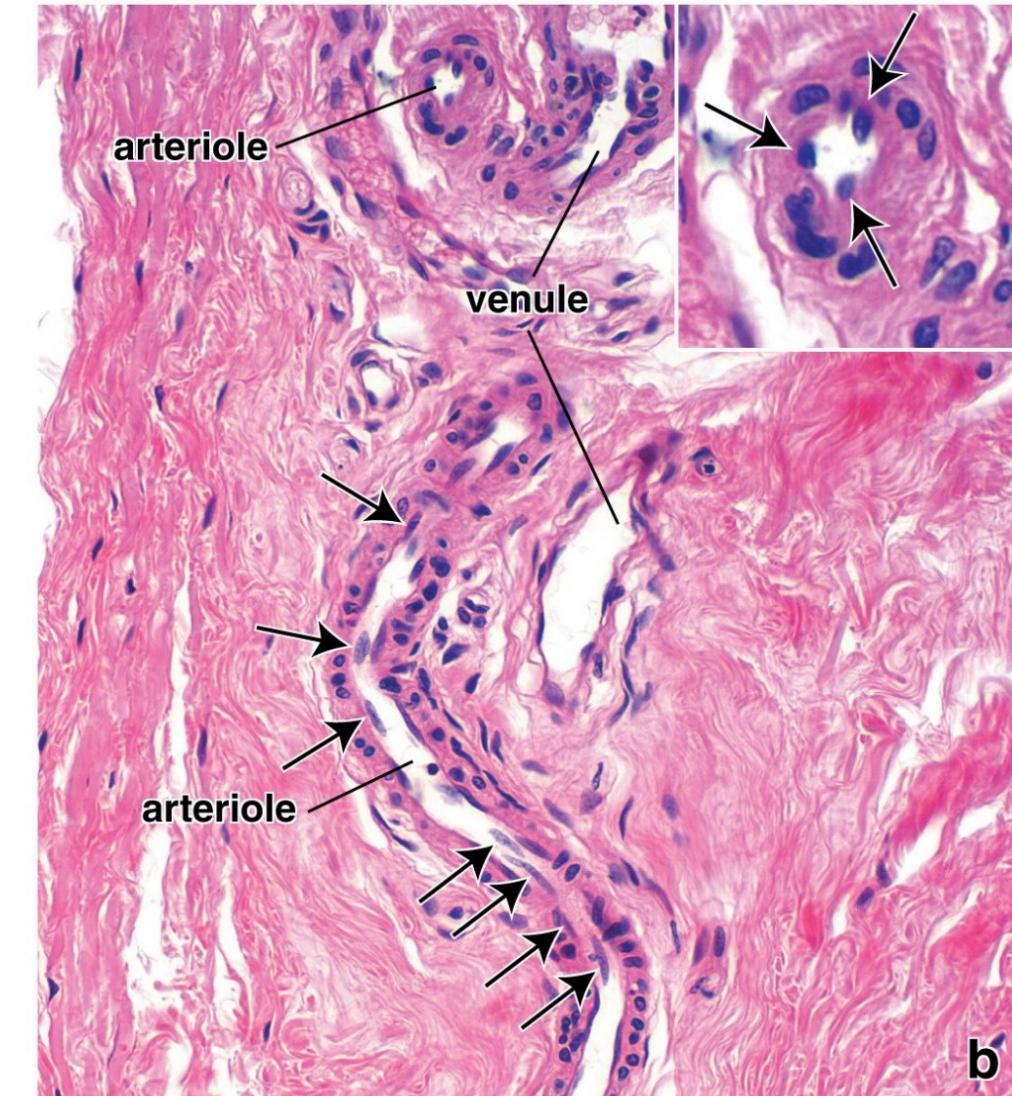
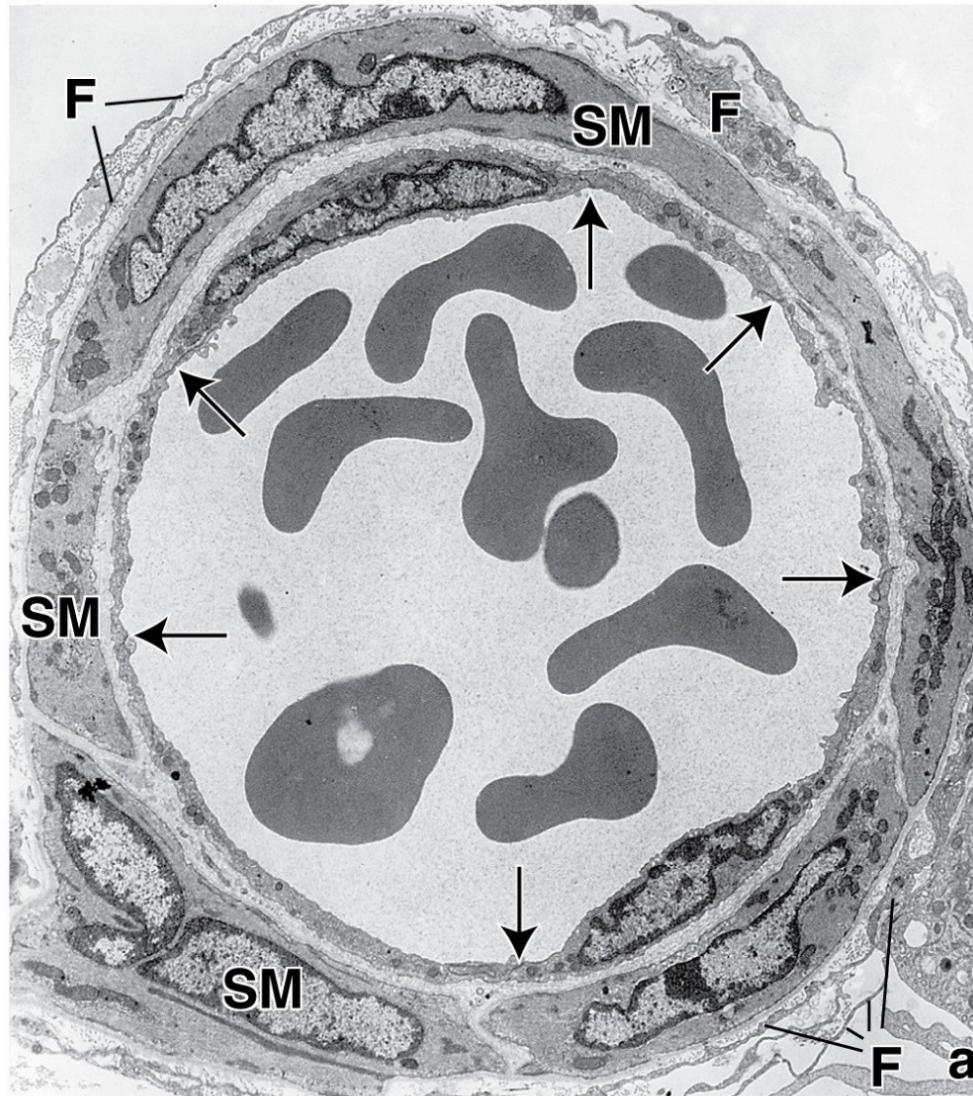
Atherosclerosis reduces diameter of small muscular arteries and arterioles is reduced, which leads to increased vascular resistance.

This causes compensatory left ventricular hypertrophy. Ventricular hypertrophy in this condition is caused by an increased diameter (not length) of cardiac muscle cells with characteristic enlarged and rectangular nuclei. Left ventricular hypertrophy is a common manifestation of **hypertensive heart disease**

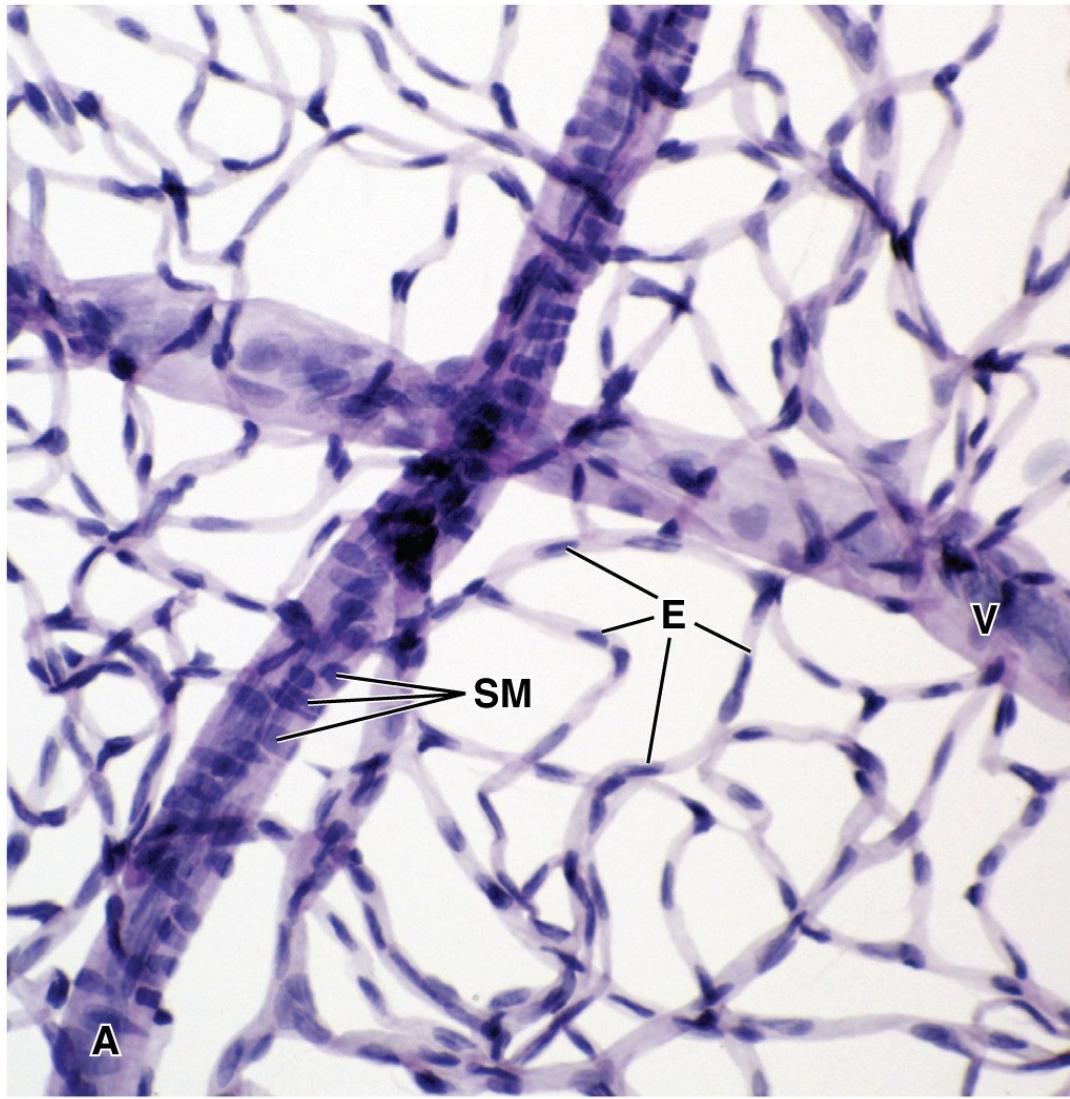
# Medium (muscular) arteries: more smooth muscle and less elastin in tunica media



# Small arteries (8 muscle cell layers) and arterioles (1-2 muscle cell layers)



# Capillaries: smallest diameter blood vessels, often smaller than the diameter of an erythrocyte



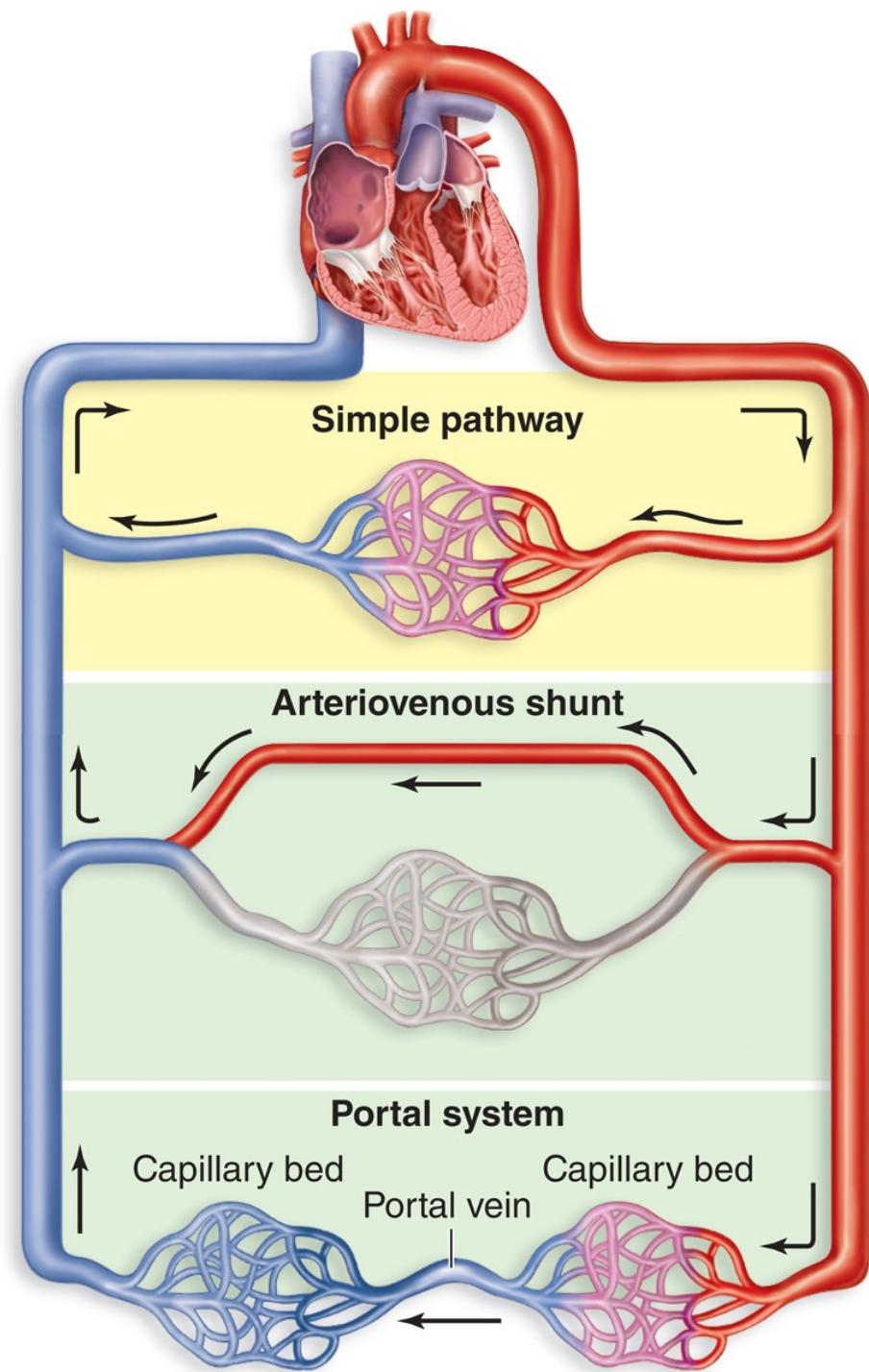
Capillaries allow fluids containing gases, metabolites, and waste products to move through their thin walls.

The human body contains approximately 50,000 miles of capillaries. Each consists of a single layer of endothelial cells and their basal lamina. The endothelial cells form a tube just large enough to allow the passage of red blood cells one at a time. In many capillaries, the lumen is so narrow that the RBCs fold to pass through.

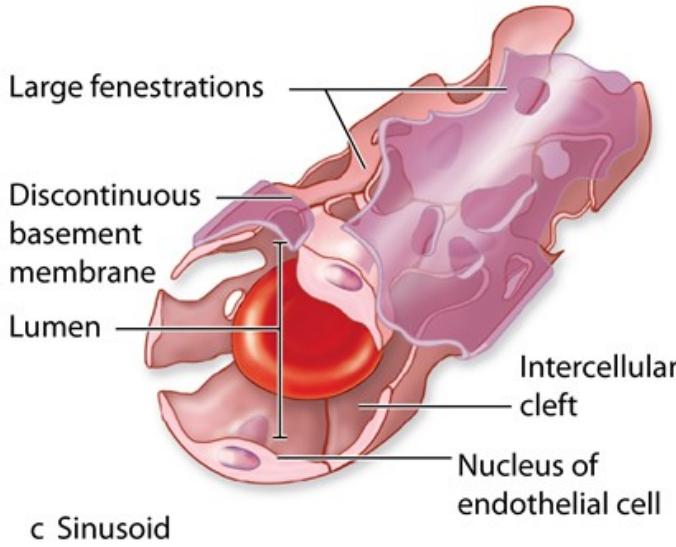
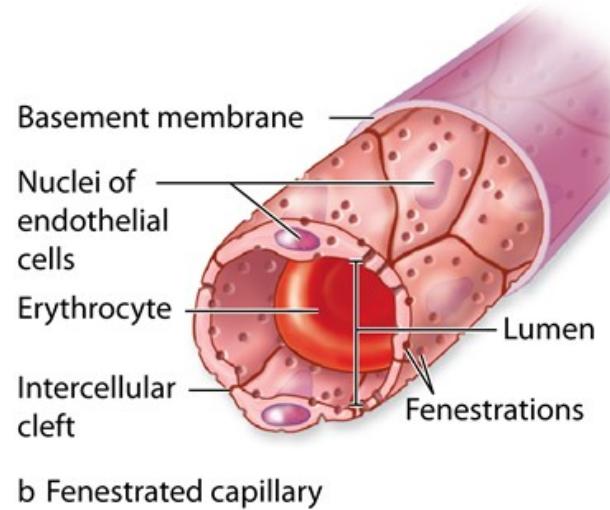
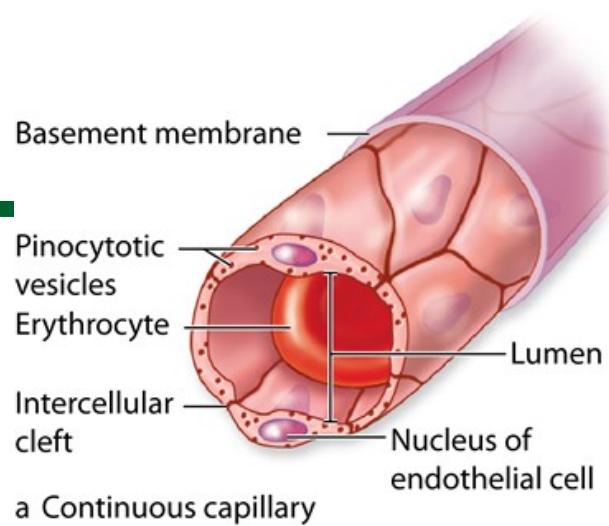
# Microvascular pathways

**Arteriovenous (AV) shunts (anastomoses):**  
Connect the arterial and venous systems and temporarily bypass capillaries. Common in skin to prevent heat loss.

**Venous portal systems:** allows molecules entering the blood in the first set of capillaries to be delivered quickly and at high concentrations to surrounding tissues at the second capillary bed, which is important in the anterior pituitary gland and liver.



# 3 Types of capillaries

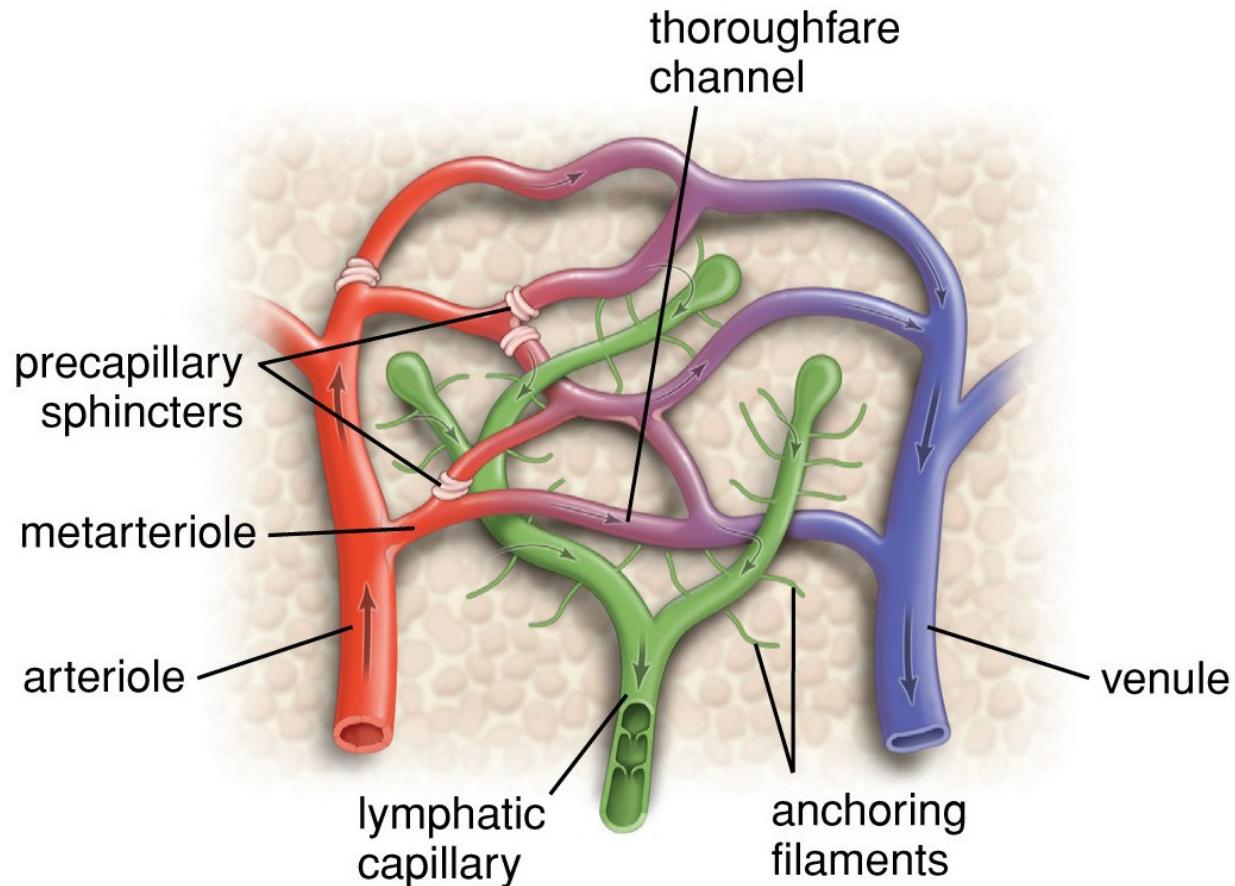


**(a) Continuous capillaries**, the most common type, have tight, occluding junctions sealing the intercellular clefts between all the endothelial cells to produce minimal fluid leakage. All molecules exchanged across the endothelium must cross the cells by diffusion or transcytosis.

**(b) Fenestrated capillaries** also have tight junctions, but perforations (fenestrations) through the endothelial cells allow greater exchange across the endothelium. The basement membrane is continuous in both these capillary types. Fenestrated capillaries are found in organs where molecular exchange with the blood is important, such as endocrine organs, intestinal walls, and choroid plexus.

**(c) Sinusoids**, or discontinuous capillaries, usually have a wider diameter than the other types and have discontinuities between the endothelial cells, large fenestrations through the cells, and a partial, discontinuous basement membrane. Sinusoids are found in organs where exchange of macromolecules and cells occurs readily between tissue and blood, such as in bone marrow, liver, and spleen.

# Venules and small veins



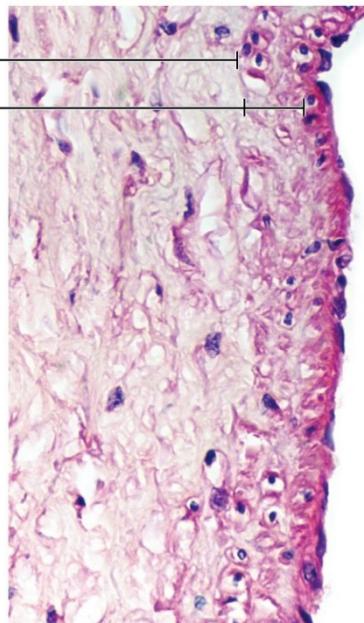
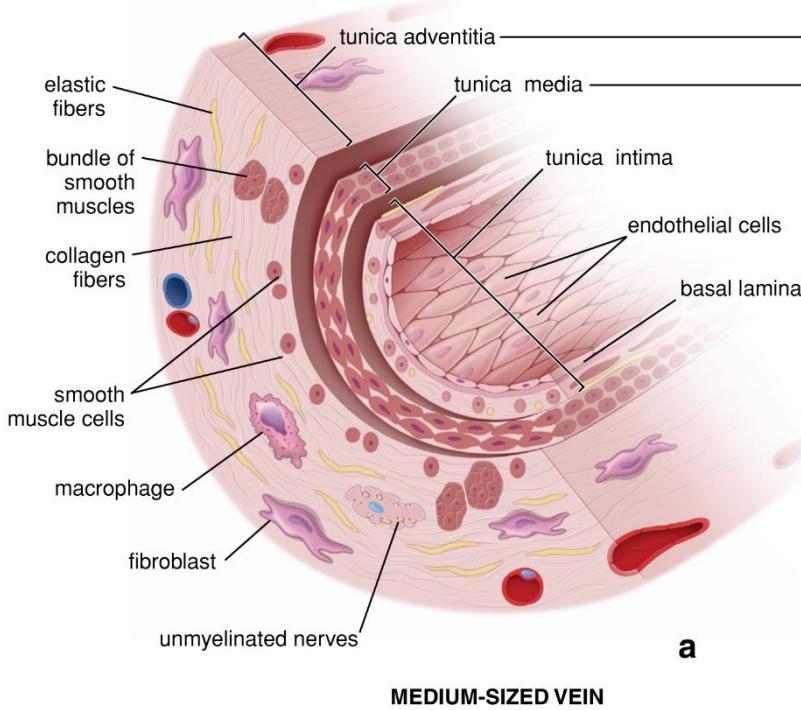
## >> MEDICAL APPLICATION

The hyperglycemia (excessive blood sugar) can lead to diabetic microangiopathy, a diffuse thickening of capillary basal laminae and concomitant decrease in metabolic exchange at these vessels, particularly in the kidneys, retina, skeletal muscle, and skin.

## >> MEDICAL APPLICATION

Junctions between endothelial cells of postcapillary can clog with leukocytes during inflammation. Loss of fluid here during the inflammatory response leads to tissue edema.

# Medium Veins



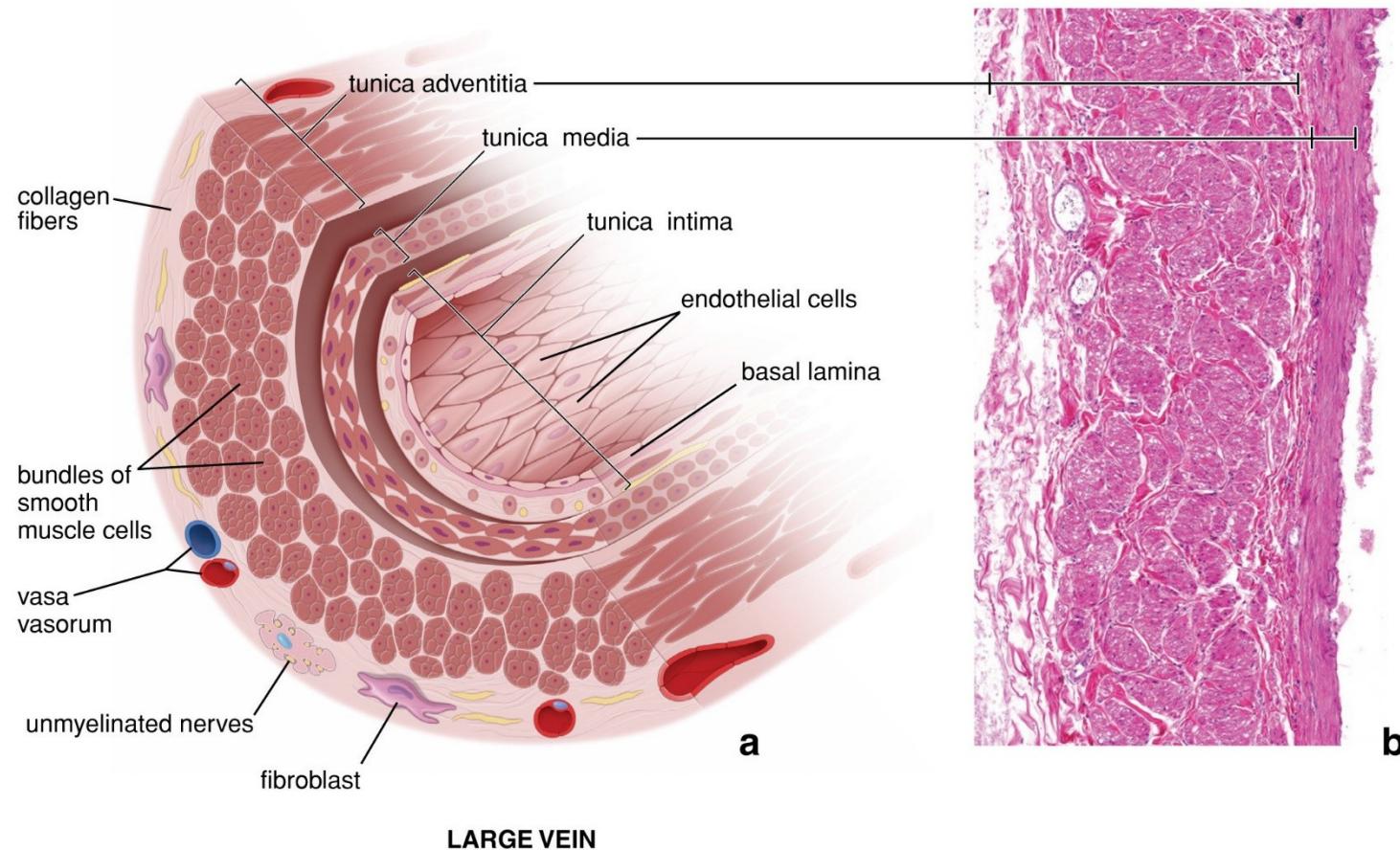
**Tunica media:** less smooth muscle than similar sized arteries, as flow back to heart is largely passive

**Skeletal muscle pump:** activity of limb muscles promote flow through one-way valves in medium veins, which prevent blood from flowing back

**Low venous return shock:** not enough blood returning to heart e.g., from hemorrhage

**Venus pooling:** Blood accumulated in lower body E.g., immune reactions causing vasodilation. E.g., standing too long so skeletal pump is not working may lead to fainting

# Large veins: Thin tunica media, thick tunica adventitia



Thick layer of smooth muscle cells in vessels nearest to heart may participate in initiating atrial fibrillation.

# Coronary Circulation: Receives disproportionate amount of blood supply which increases dramatically during exercise

## Left coronary artery (LCA)

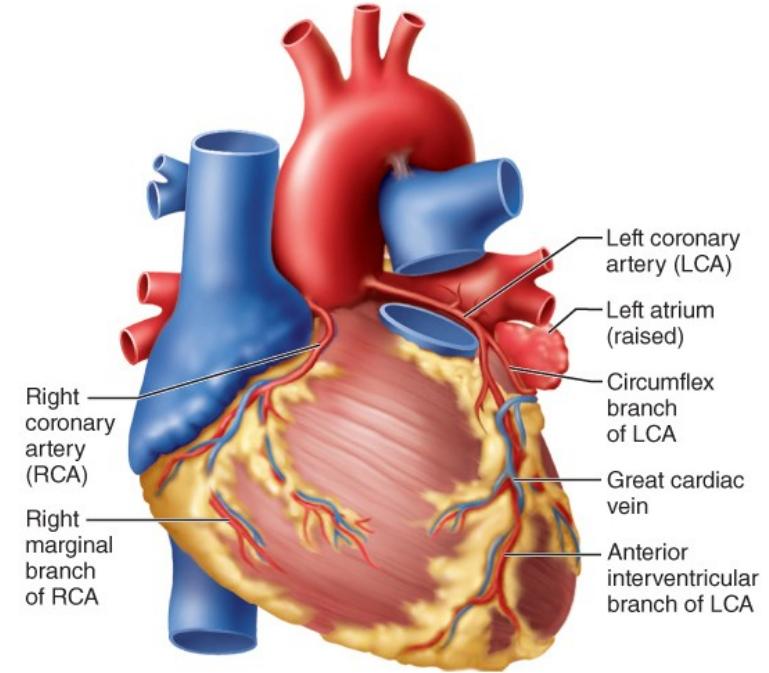
- Anterior interventricular branch (left anterior descending)
- Circumflex branch

## Right coronary artery (RCA)

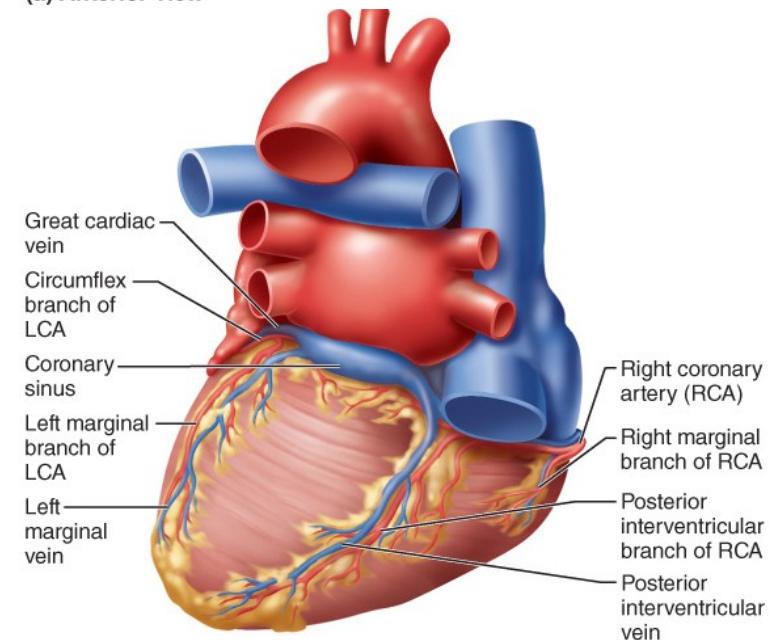
- Right marginal branch
- Posterior interventricular branch

## Venous drainage of heart: Coronary sinus

- Posterior interventricular vein
- Left marginal vein
- Great cardiac vein

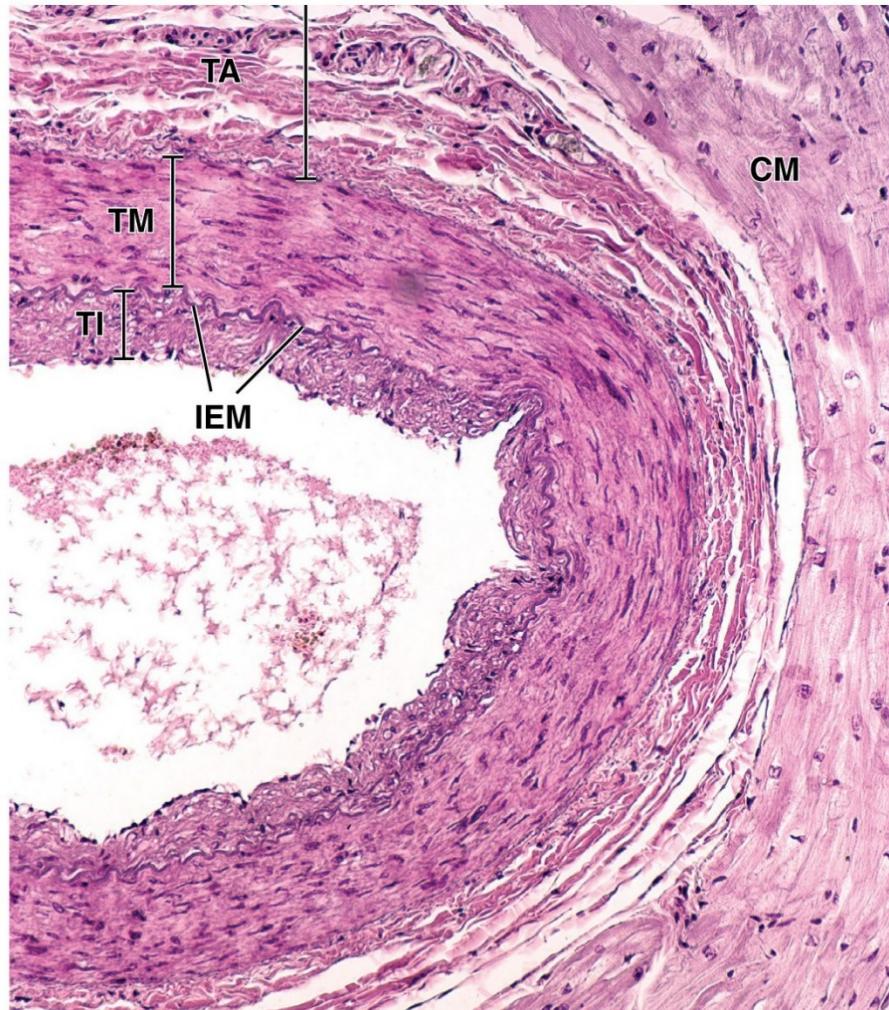


(a) Anterior view



(b) Posterior view

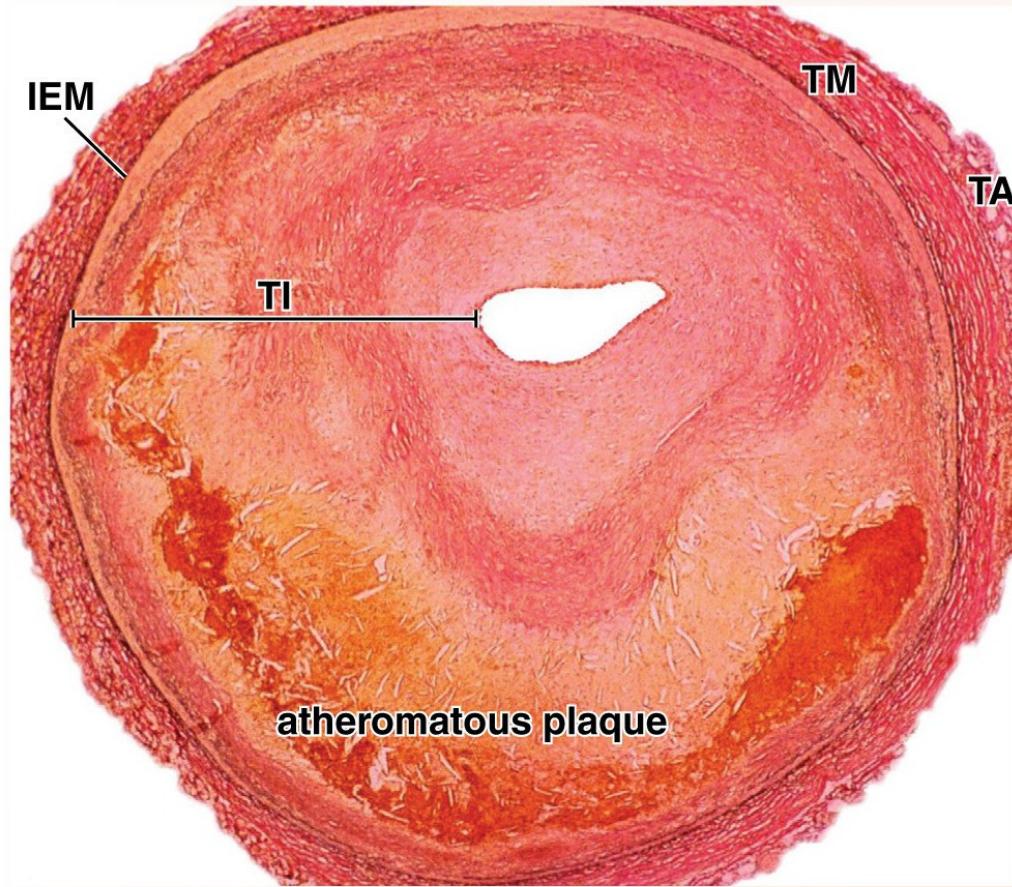
# The Coronary artery: medium muscular arteries



**tunica media:** large amounts of circular smooth muscle **tunica intima:** of younger people is inconspicuous, but it progressively thickens by increasing amounts of smooth muscle cell and fibroelastic tissue with aging

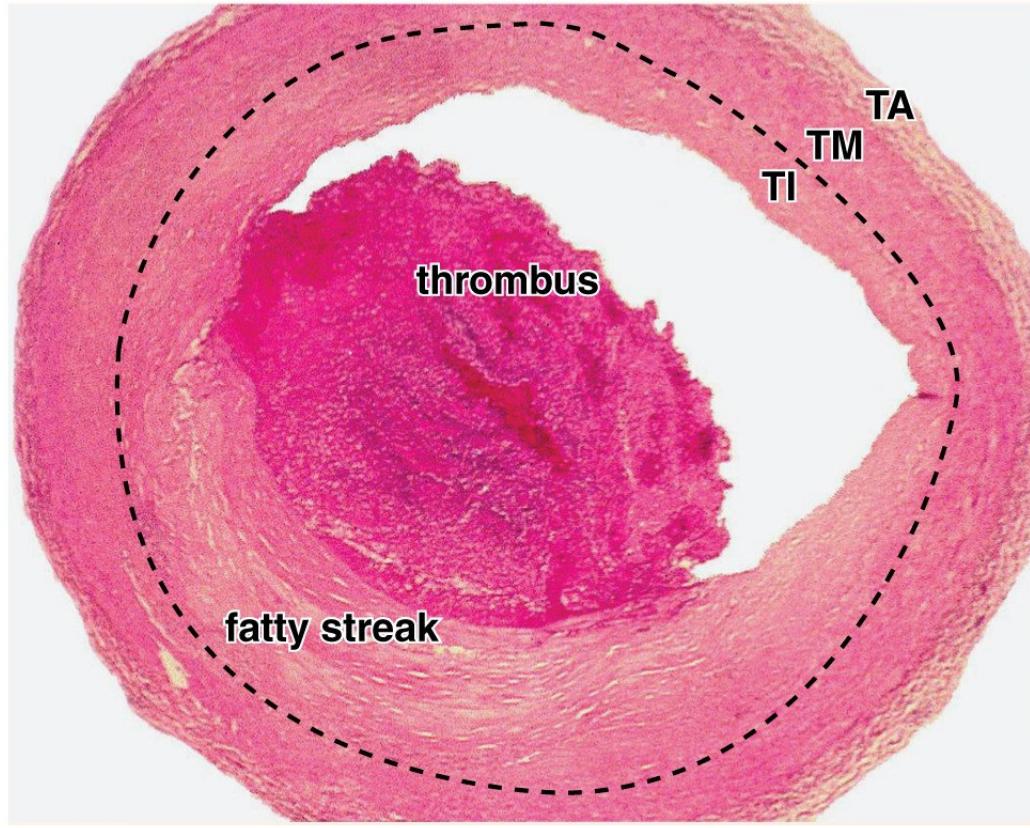
Atherosclerotic changes in coronary arteries that restrict blood flow and oxygen supply to cardiac muscle leads to **ischemic heart disease**

# A plaque in the coronary artery



Plaques are formed by intracellular and extracellular lipid deposition, smooth muscle proliferation, and increased synthesis of proteoglycans and collagen within the intima of the vessel wall.

# Thrombus (blood clot) in the coronary artery



Blood flow becomes critical when it is reduced by 90% or more. Sudden occlusion of the narrowed lumen by a thrombus (blood clot) released from the surface of an plaque precipitates an acute ischemic event.

Ischemic events are characterized by anginal pain associated with loss of oxygenated blood flow to the region of the heart supplied by the affected coronary vessel. **Coronary artery thrombosis** usually precedes and precipitates a **myocardial infarct** (insufficiency of blood causing muscle cell death). **Mural thrombus** may develop and is usually associated with dysfunctional or ruptured endothelium overlying plaque.

# Chapter 12 & 13 Blood and Hemopoiesis

## Key Points

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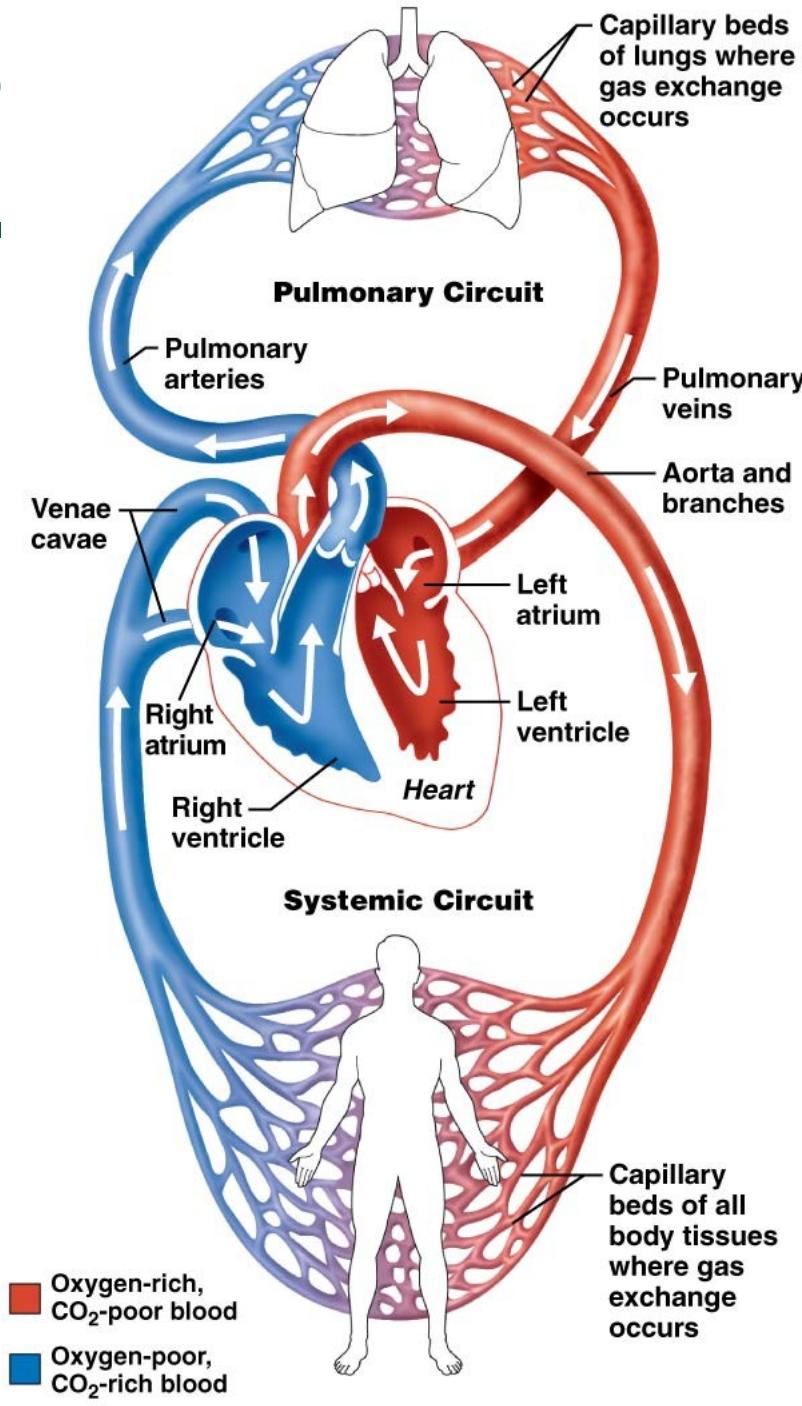
1. Blood is a fluid connective tissue that circulates through the cardiovascular system. It consists of protein-rich liquid extracellular matrix called **plasma** and **formed elements** (white blood cells, red blood cells, and platelets).
2. Plasma proteins consist of plasma proteins are secreted by the liver and serum
3. **Leukocytes** are subclassified into two groups based on the presence or absence of specific granules in the cytoplasm: **granulocytes (neutrophils, eosinophils, basophils)** or **granulocytes (lymphocytes, monocytes)**.
4. **Erythrocytes** are anucleate, biconcave discs (7.8  $\mu\text{m}$  in diameter) that are packed with hemoglobin and are designed to withstand shear forces experienced during circulation.
5. **Thrombocytes** are small, membrane-bounded, anucleate cytoplasmic fragments derived from megakaryocytes
6. **Hemopoiesis (hematopoiesis)** is initiated in early embryonic development and includes erythropoiesis (development of red blood cells), leukopoiesis (development of white blood cells), and thrombopoiesis (development of platelets).

# Circulatory system consists of the heart, blood vessels, and blood

## Functions of circulatory system

- **Transport:** O<sub>2</sub>, CO<sub>2</sub>, nutrients, wastes, hormones, and stem cells
  - **Protection:** Inflammation, limit spread of infection, destroy microorganisms and cancer cells, neutralize toxins, and initiate clotting
  - **Regulation:** Fluid balance, stabilizes pH of ECF, and temperature control
- 
- **Cardiovascular system** refers only to the heart and blood vessels
  - **Hematology:** the study of blood

<http://ed.ted.com/lessons/oxygen-s-surprisingly-complex-journey-through-your-body-enda-butler>



# Components and General Properties of Blood

Adults have 4 to 6 L of blood

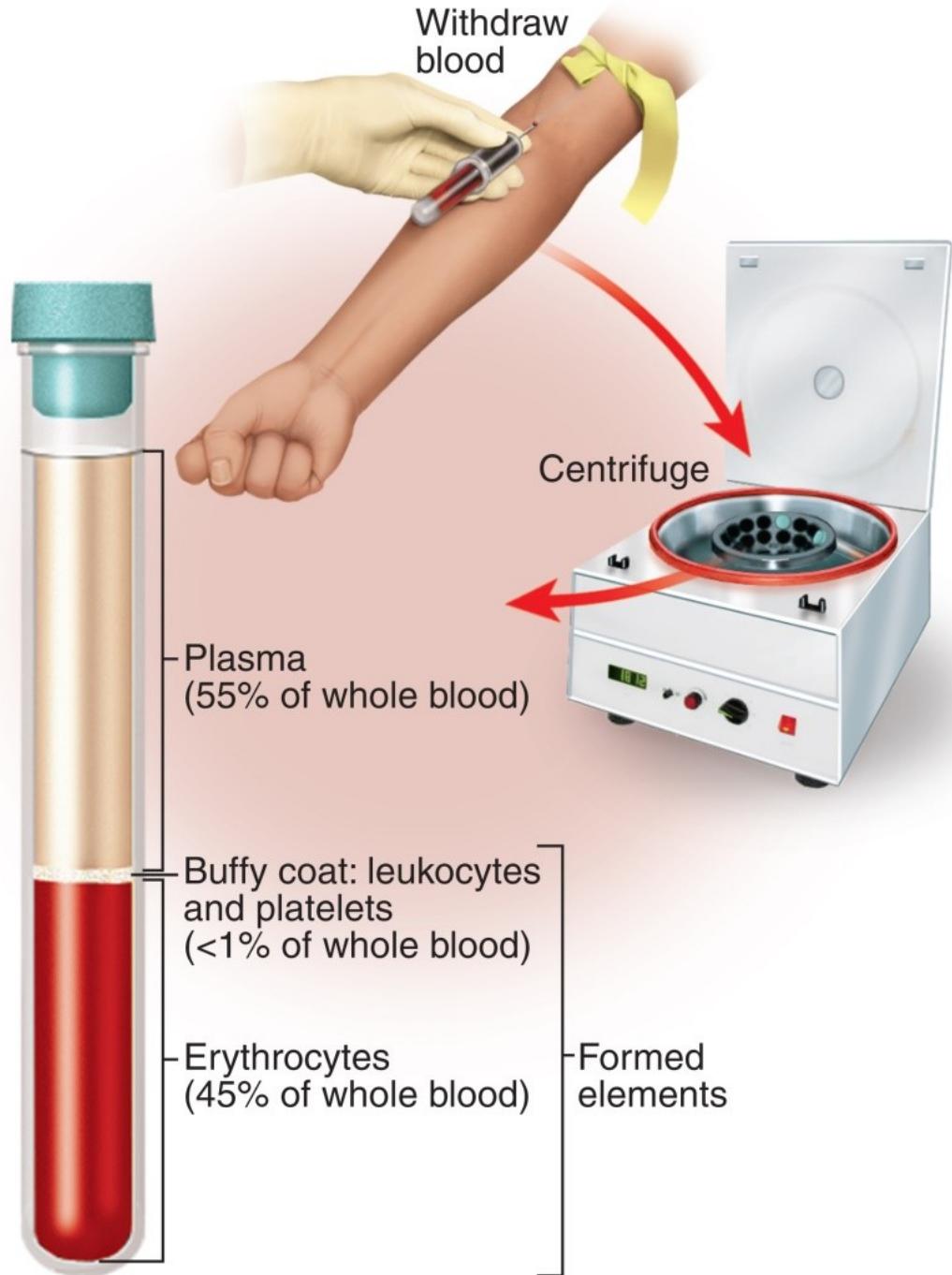
Blood is a liquid connective tissue consisting of cells and extracellular matrix

- **Plasma:** matrix of blood. Clear, light yellow fluid

- **Formed elements:** blood cells and cell fragments

Red blood cells, white blood cells, and platelets

**Hematocrit (packed cell volume):** percentage of whole blood volume composed of RBCs



# Seven kinds of formed elements

1) **Erythrocytes:** red blood cells (RBCs)

2) **Platelets:** Cell fragments from special cell in bone marrow

3) **Leukocytes:** white blood cells (WBCs)

Five leukocyte types divided into two categories

Granulocytes (with granules)

1) Neutrophils

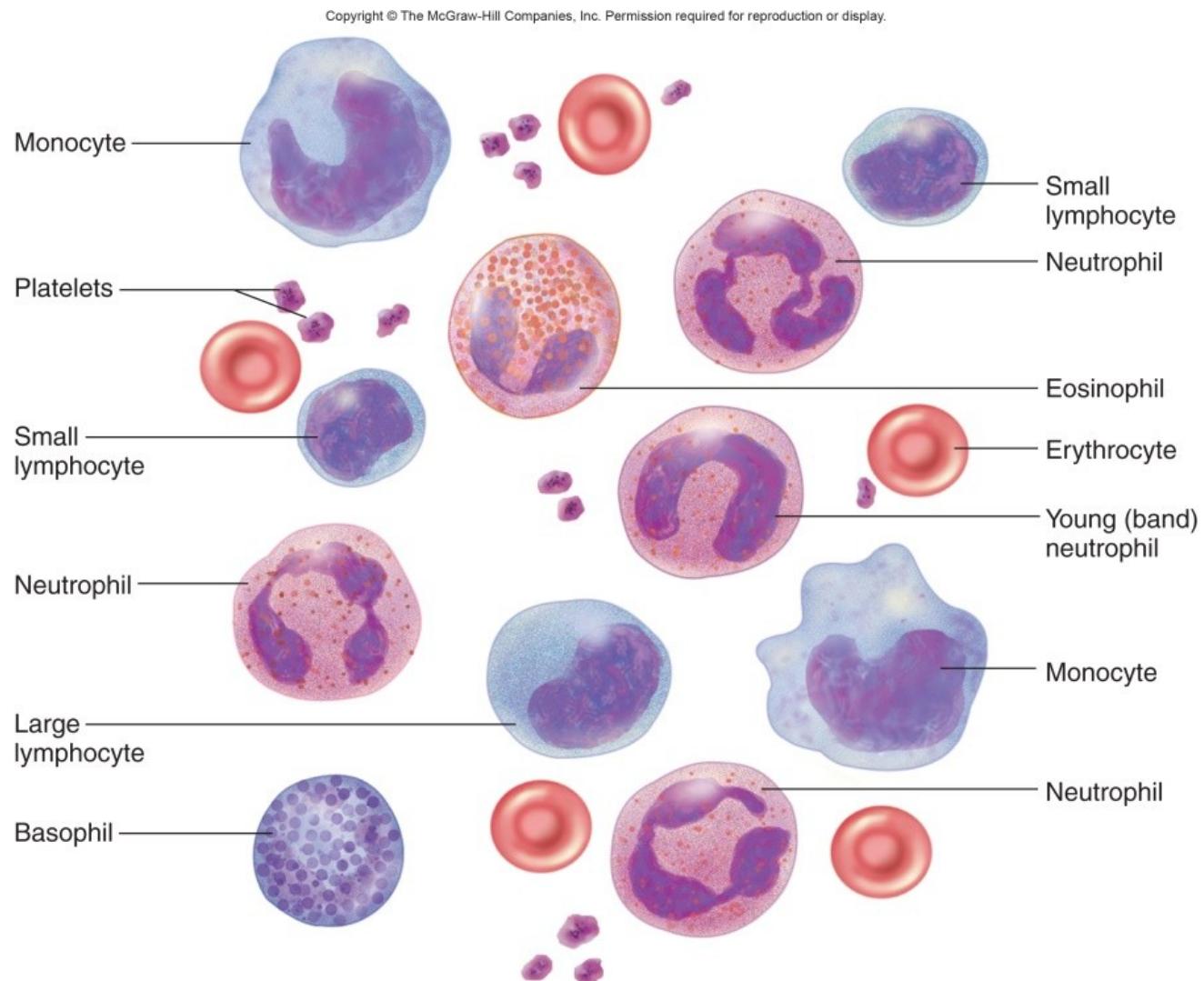
2) Eosinophils

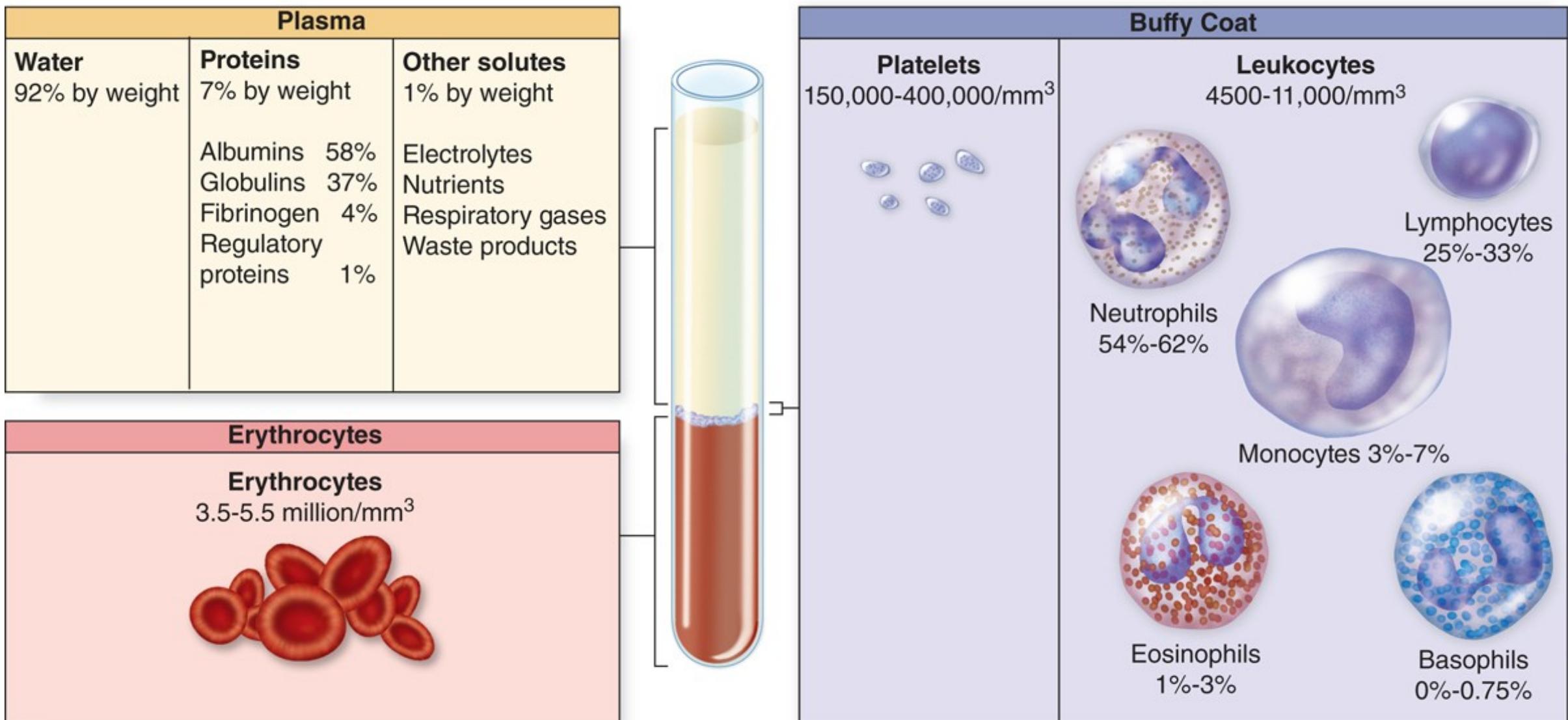
3) Basophils

Agranulocytes (without granules)

4) Lymphocytes

5) Monocytes





# Blood Plasma

**Plasma:** liquid portion of blood

- **Serum:** remaining fluid when blood clots and the solids are removed  
Identical to plasma except for the absence of fibrinogen

Three major categories of plasma proteins

**1) Albumins:** smallest and most abundant,  
Contribute to viscosity and osmolarity; influence blood pressure, flow, and fluid balance

**2) Globulins (antibodies):** Provide immune system functions

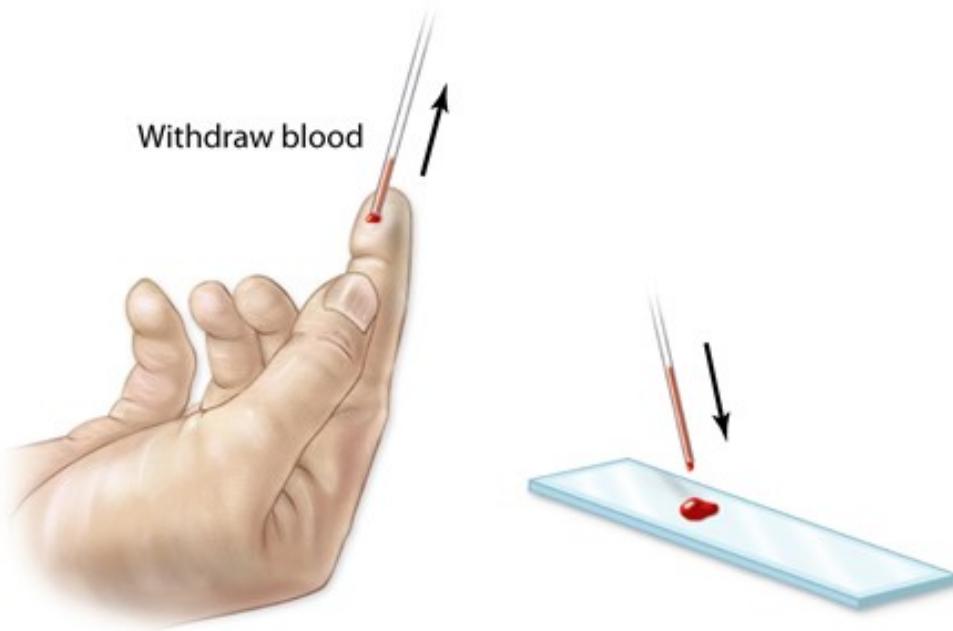
Alpha, beta, and gamma globulins

**3) Fibrinogen:** Precursor of fibrin threads that help form blood clots

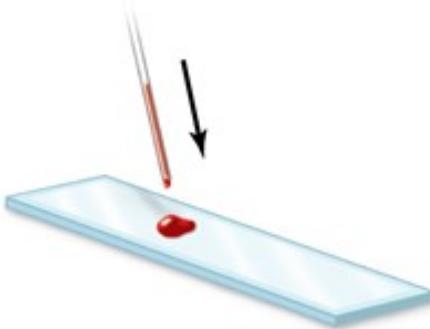
**TABLE 10.2 Composition of Blood Plasma**

Component	%
Water	91–92
Protein (albumin, globulins, fibrinogen)	7–8
Other solutes:	1–2
Electrolytes ( $\text{Na}^+$ , $\text{K}^+$ , $\text{Ca}^{2+}$ , $\text{Mg}^{2+}$ , $\text{Cl}^-$ , $\text{HCO}_3^{3-}$ , $\text{PO}_4^{3-}$ , $\text{SO}_4^{2-}$ )	
Nonprotein nitrogen substances (urea, uric acid, creatine, creatinine, ammonium salts)	
Nutrients (glucose, lipids, amino acids)	
Blood gases (oxygen, carbon dioxide, nitrogen)	
Regulatory substances (hormones, enzymes)	

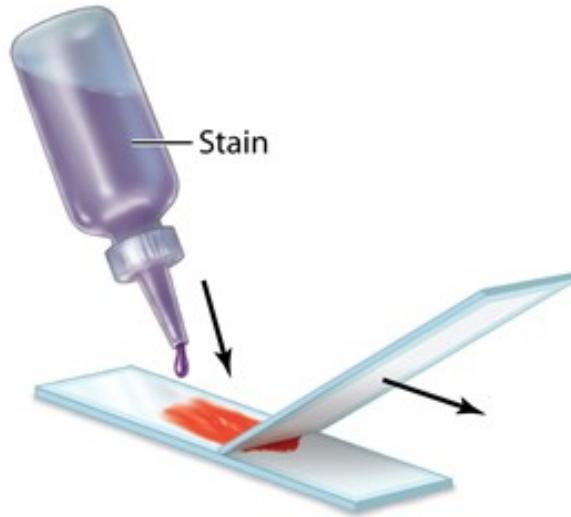
# Examination of blood cells requires special preparation and staining.



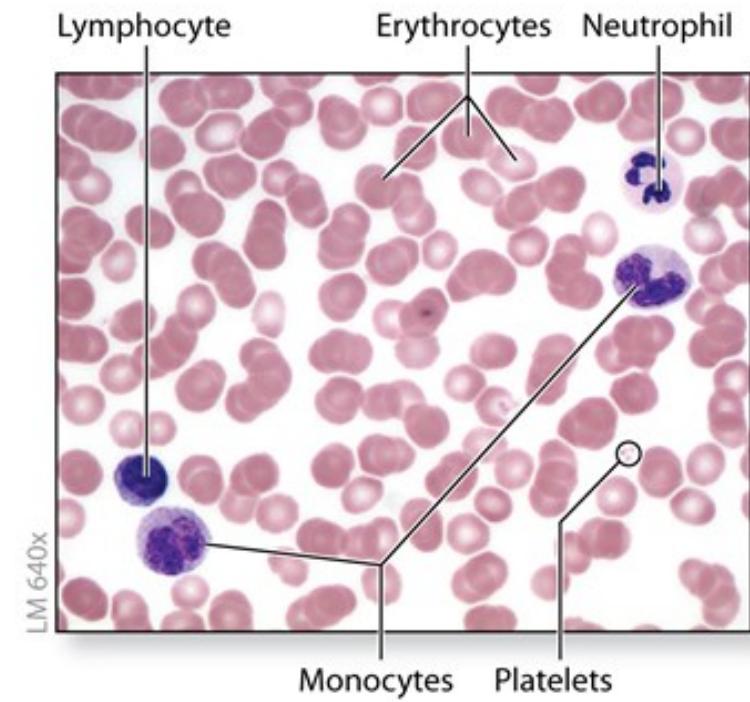
- ① Prick finger and collect a small amount of blood using a micropipette.



- ② Place a drop of blood on a slide.



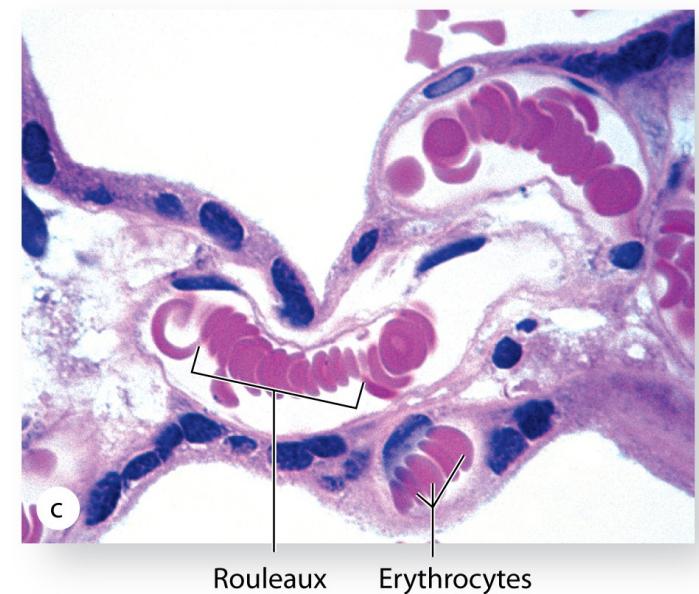
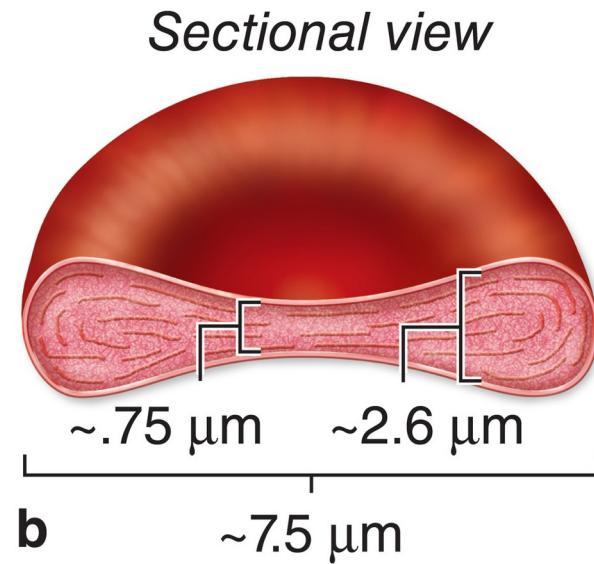
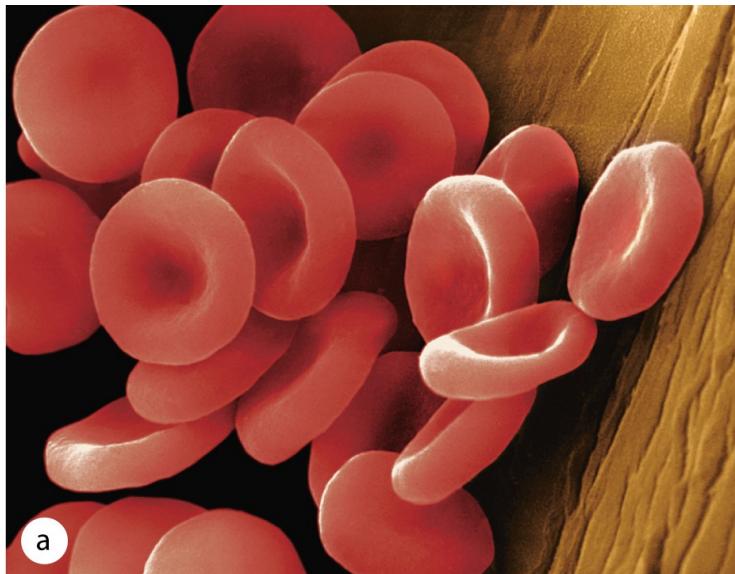
- ③a) Using a second slide, pull the drop of blood across the first slide's surface, leaving a thin layer of blood on the slide.  
③b) After the blood dries, apply a stain briefly and rinse. Place a coverslip on top.



- ④ When viewed under the microscope, blood smear reveals the components of the formed elements.

# Erythrocytes

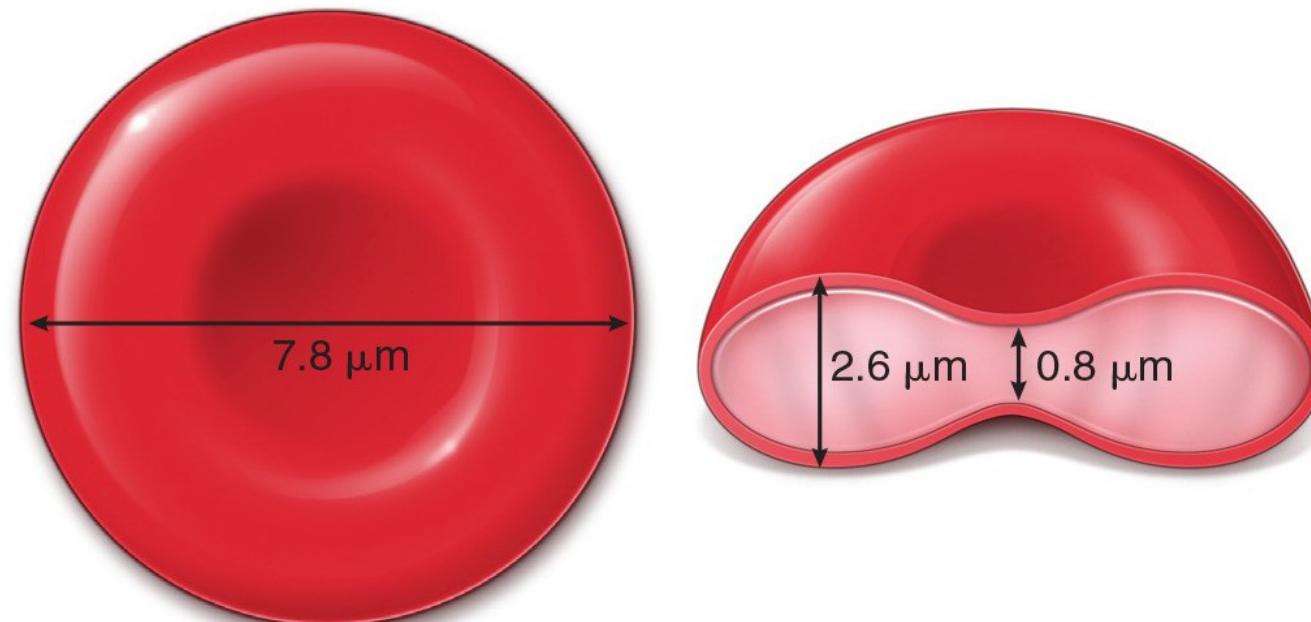
- Two principal functions
  - Carry oxygen from lungs to cell tissues
  - Pick up  $\text{CO}_2$  from tissues and bring to lungs
- Insufficient RBCs may kill in minutes due to lack of oxygen to tissues



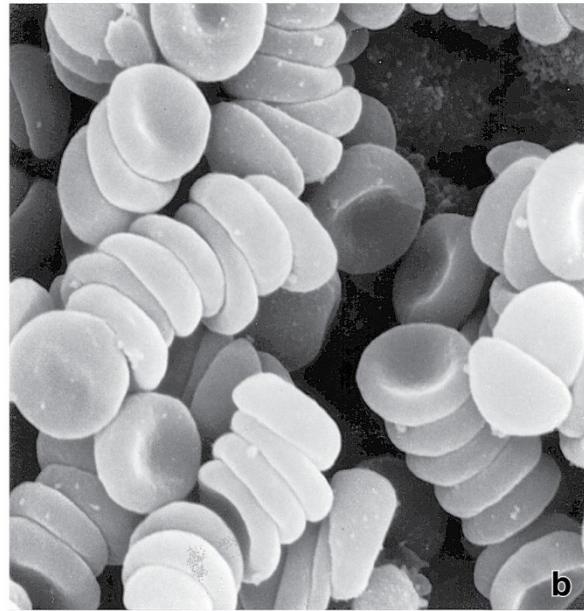
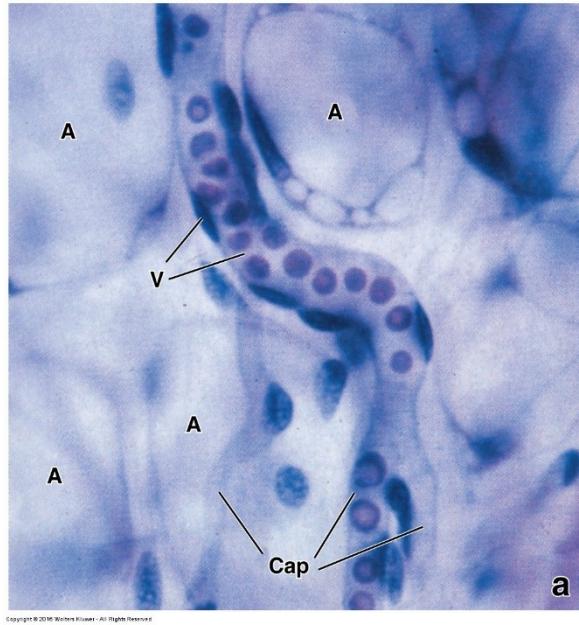
# Form and Function

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- Disc-shaped cell with thick rim
  - 7.8  $\mu\text{m}$  diameter and 2.0  $\mu\text{m}$  thick at rim
  - Lose nearly all organelles during development
  - Lack mitochondria, use anaerobic fermentation to produce ATP
  - Lack of nucleus and DNA, no protein synthesis or mitosis



# Erythrocyte Morphology



Hypoxia "Reading between the genes":  
<https://www.youtube.com/watch?v=djpTeVtMO-M>

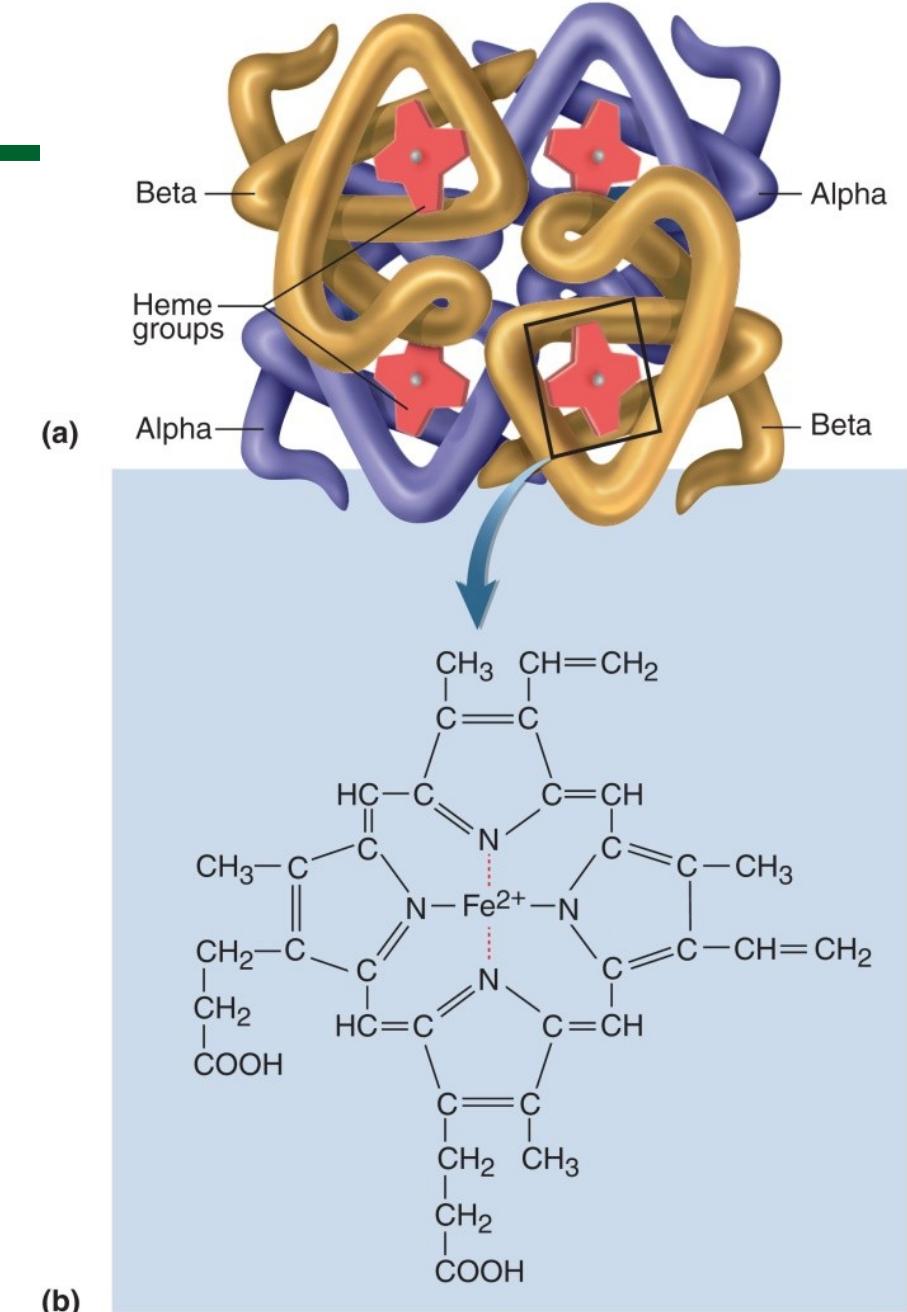
## >> MEDICAL APPLICATION

Anemia is the condition of having a concentration of erythrocytes below the normal range. With fewer RBCs per milliliter of blood, tissues are unable to receive adequate O<sub>2</sub>. Symptoms of anemia include lethargy, shortness of breath, fatigue, skin pallor, and heart palpitations. Anemia may result from insufficient red cell production, due, for example, to iron deficiency, or from blood loss with a stomach ulcer or excessive menses.

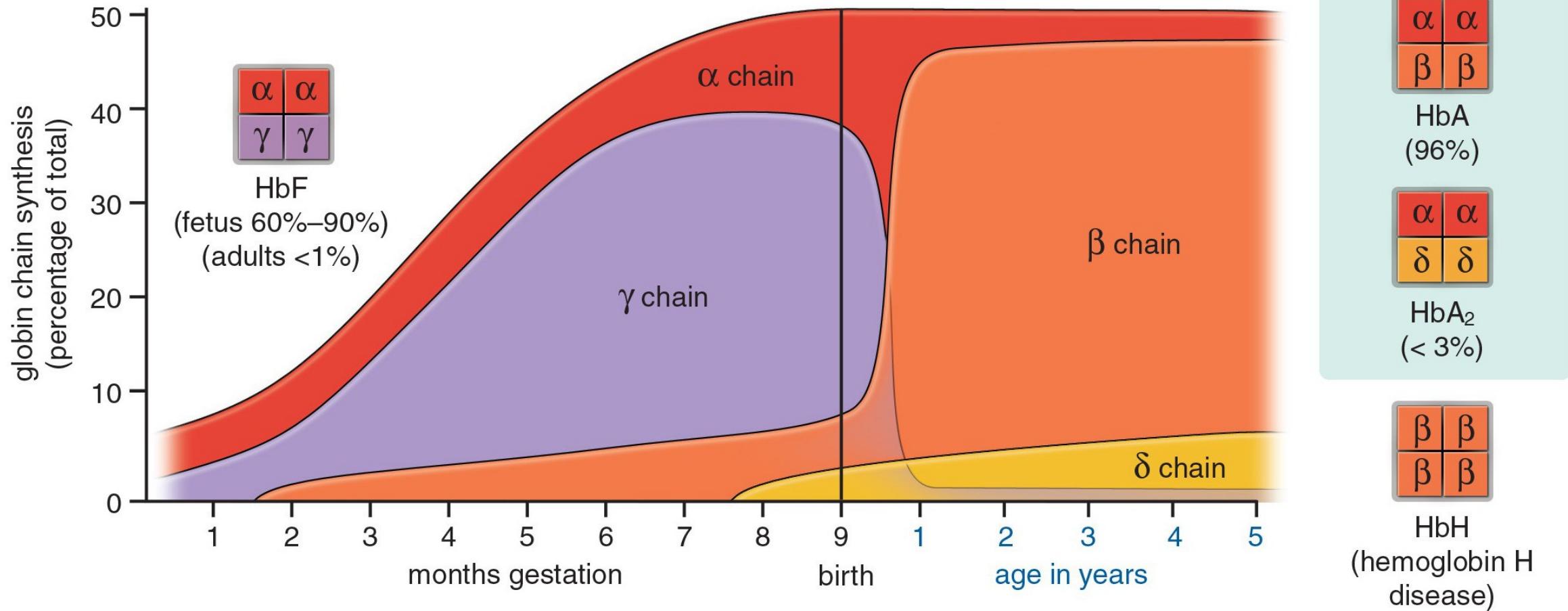
An increased concentration of erythrocytes in blood (**erythrocytosis**, or **polycythemia**) may be a physiologic Adaptation found, for example, in individuals who live at high altitudes, where O<sub>2</sub> is low. Elevated hematocrit increases blood viscosity, putting strain on the heart, and, if severe, can impair circulation through the capillaries.

# Hemoglobin

- Each Hb molecule consists of:
  - Four protein chains—globins
  - Four heme groups
  
- Heme groups
  - Nonprotein moiety that binds O<sub>2</sub> to ferrous ion (Fe<sup>2+</sup>) at its center
  
- RBC count and hemoglobin concentration indicate amount of O<sub>2</sub> blood can carry
  - **Hematocrit (packed cell volume):** percentage of whole blood volume composed of RBCs



# Major globin chain synthesis and hemoglobin composition in prenatal and postnatal periods.





## Sickle cell erythrocyte

A single nucleotide substitute in the hemoglobin gene produces a version of the protein that polymerizes to form rigid aggregates, leading to greatly misshapen cells with reduced flexibility. In individuals homozygous for the mutated *HbS* gene, this can lead to greater blood viscosity, and poor microvascular circulation, both features of sickle cell disease

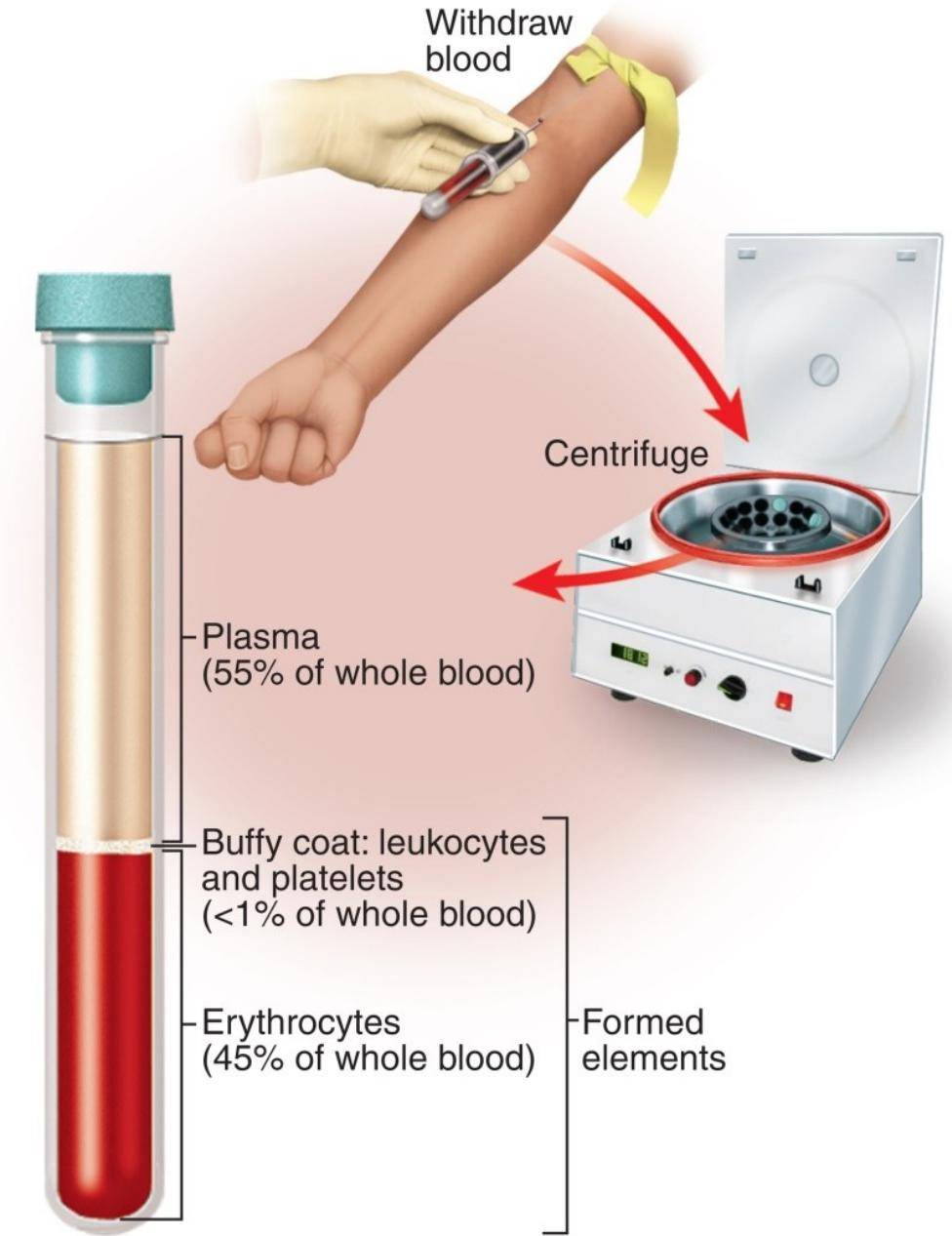
# Leukocytes

## Leukocytes (white blood cells, WBCs)

- Protect us from pathogens
- Spend only few hours in bloodstream
  - migrate through capillaries
  - spend rest of lives in connective tissue

## Leukocyte characteristics

- Vary in form and function
- Retain organelles throughout life
  - include instruments of protein synthesis
  - proteins needed for wide variety of function
  - e.g., digestive enzymes enabling pathogen digestion

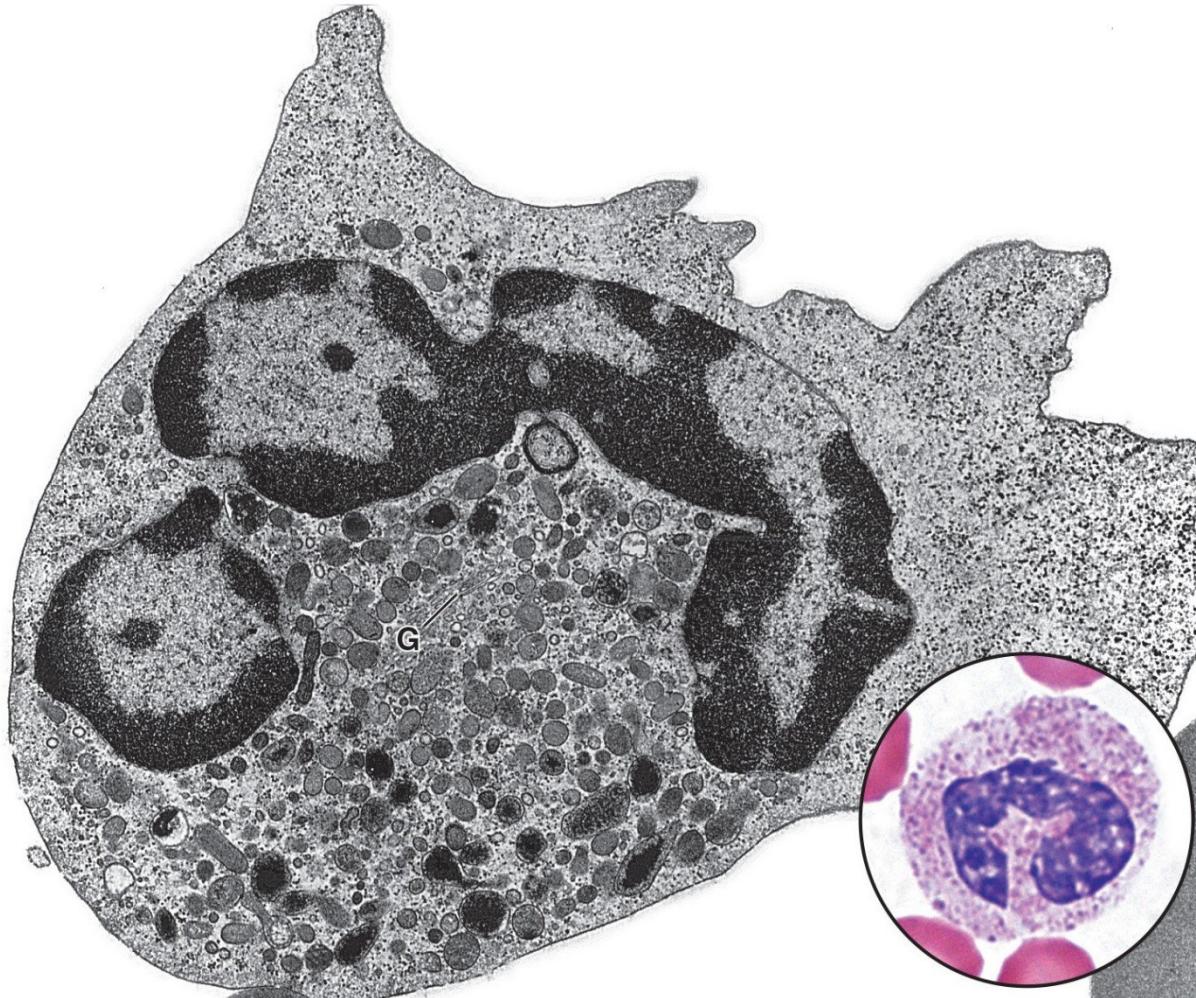


**Table 29.1** Summary of Formed Elements of the Blood

Cell type	Illustration	Description*	Cells/mm <sup>3</sup> (µl) of blood	Duration of development (D) and life span (LS)	Function
Erythrocytes (red blood cells, RBCs)		Biconcave, anucleate disc; salmon-colored; diameter 7–8 µm	4–6 million	D: about 15 days LS: 100–120 days	Transport oxygen and carbon dioxide
Leukocytes (white blood cells, WBCs)		Spherical, nucleated cells	4800–10,800		
Granulocytes					
Neutrophil		Nucleus multilobed; inconspicuous cytoplasmic granules; diameter 10–12 µm	3000–7000	D: about 14 days LS: 6 hours to a few days	Phagocytize bacteria
Eosinophil		Nucleus bilobed; red cytoplasmic granules; diameter 10–14 µm	100–400	D: about 14 days LS: about 5 days	Kill parasitic worms; complex role in allergy and asthma
Basophil		Nucleus lobed; large blue-purple cytoplasmic granules; diameter 10–14 µm	20–50	D: 1–7 days LS: a few hours to a few days	Release histamine and other mediators of inflammation; contain heparin, an anticoagulant
Agranulocytes					
Lymphocyte		Nucleus spherical or indented; pale blue cytoplasm; diameter 5–17 µm	1500–3000	D: days to weeks LS: hours to years	Mount immune response by direct cell attack or via antibodies
Monocyte		Nucleus U- or kidney-shaped; gray-blue cytoplasm; diameter 14–24 µm	100–700	D: 2–3 days LS: months	Phagocytosis; develop into macrophages in tissues
Platelets		Discoid cytoplasmic fragments containing granules; stain deep purple; diameter 2–4 µm	150,000–400,000	D: 4–5 days LS: 5–10 days	Seal small tears in blood vessels; instrumental in blood clotting

\*Appearance when stained with Wright's stain.

# Electron micrograph of a human mature neutrophil.



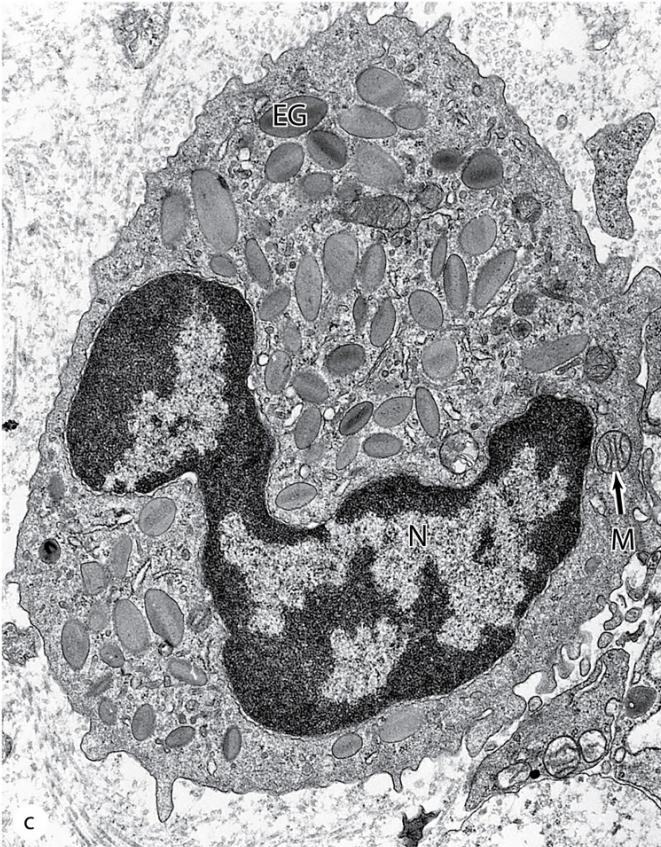
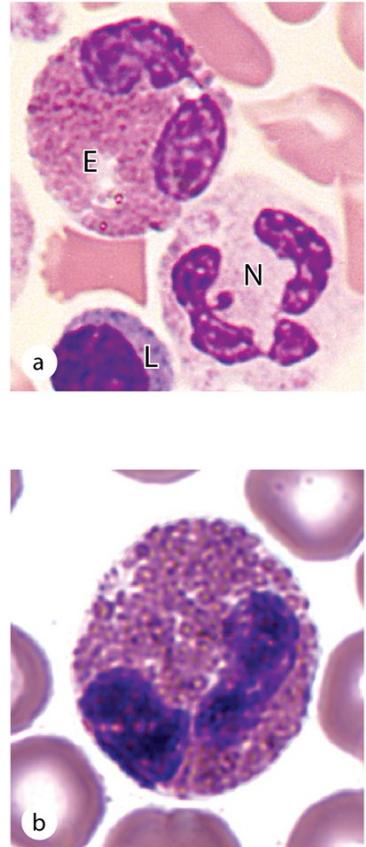
The nucleus shows the typical multilobed configuration with the heterochromatin at the periphery and the euchromatin more centrally located.

Granules contain lysosomes and enzymes

- Motile cells that leave circulation and migrate to their site of action in the connective tissue.
- Active phagocytes that utilize a variety of surface receptors to recognize bacteria and other infectious agents at the site of inflammation

# Eosinophils are about the same size as neutrophils but have bilobed nuclei and more abundant coarse cytoplasmic granules

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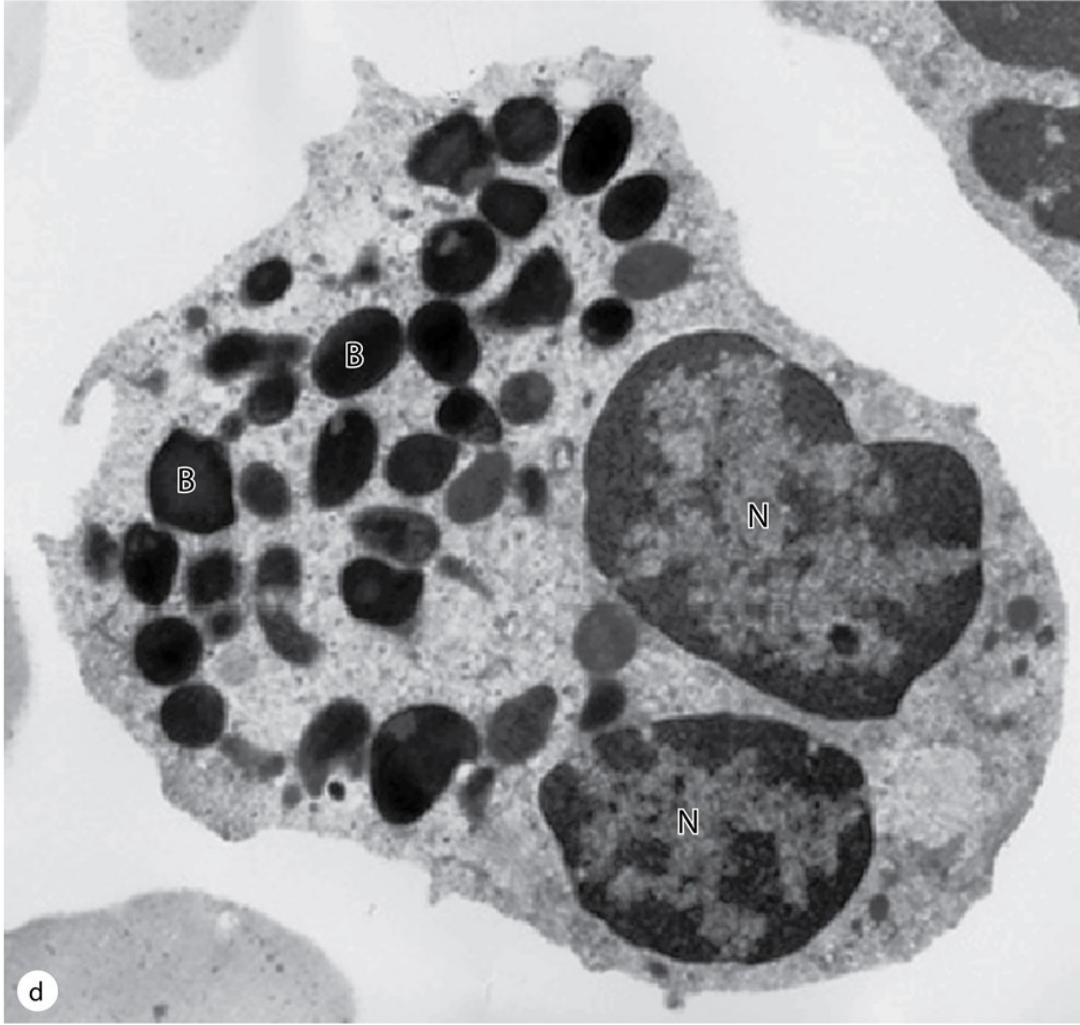
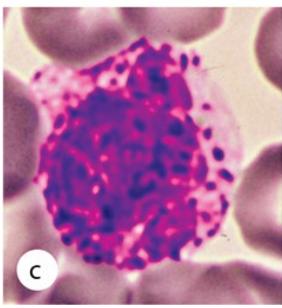
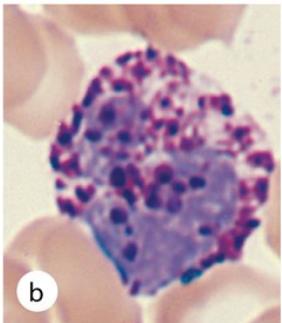
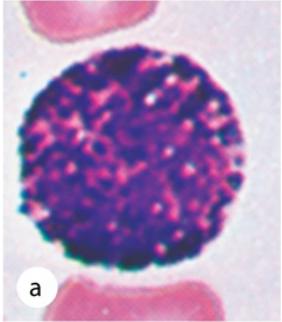


Eosinophils are associated with allergic reactions, parasitic infections, and chronic inflammation.

## »» MEDICAL APPLICATION

An increase in the number of eosinophils in blood (eosinophilia) is associated with allergic reactions and helminth parasitic infections. In patients with such conditions, eosinophils are found in the connective tissues underlying epithelia of the bronchi, gastrointestinal tract, uterus, and vagina, and surrounding any parasitic worms present.

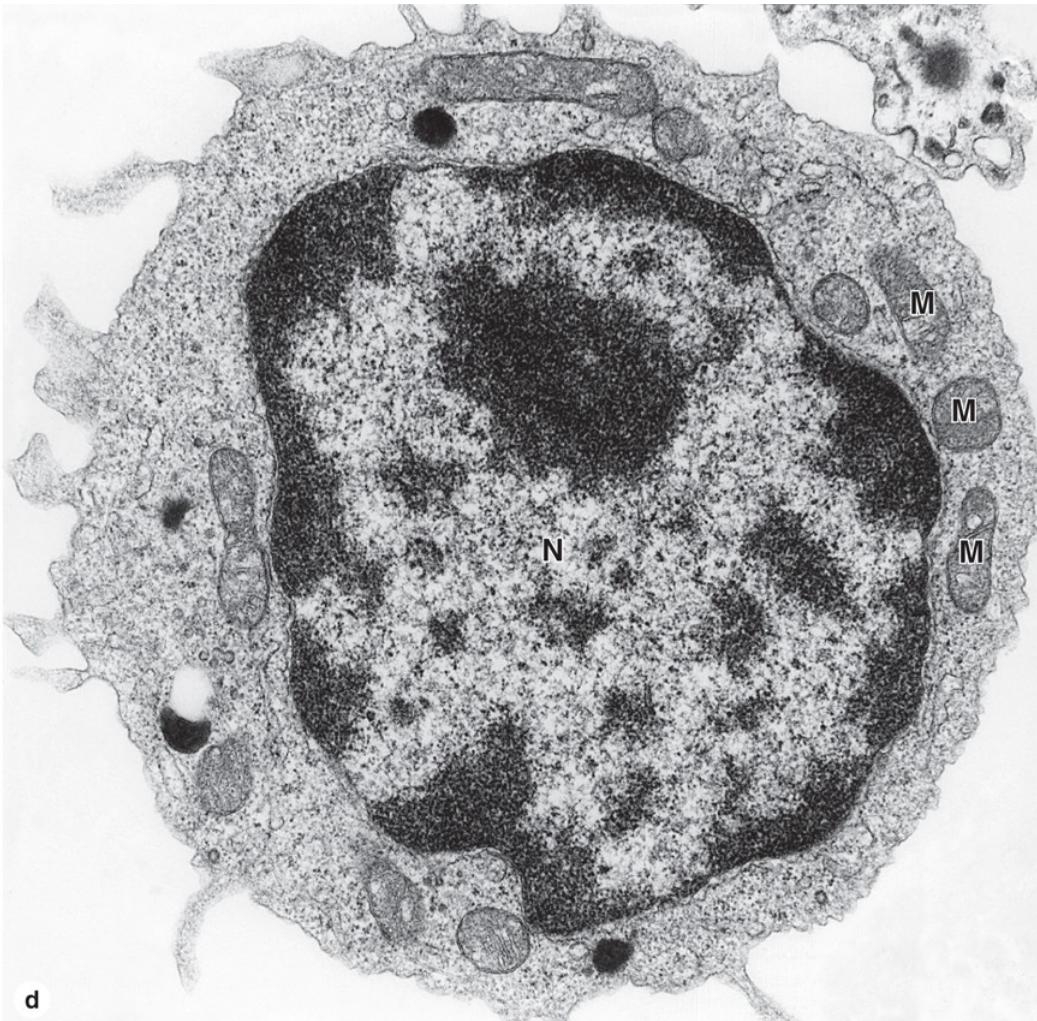
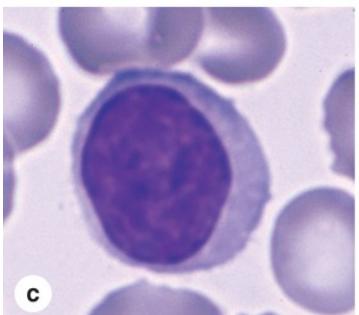
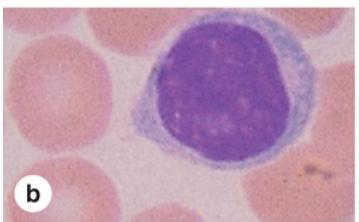
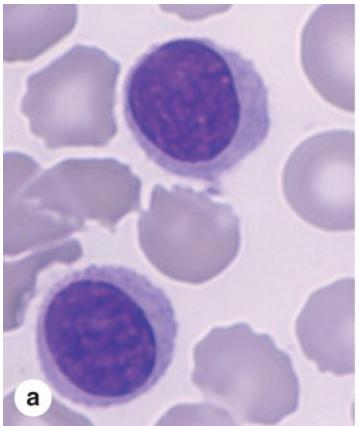
# Basophils are also approximately the same size as neutrophils and eosinophils



**Basophils** have large, strongly basophilic specific granules that usually obstruct the appearance of the nucleus which usually has two large irregular lobes

A TEM of a sectioned basophil reveals the single bilobed nucleus (**N**) and the large, electron-dense specific basophilic granules (**B**). Basophils exert many activities modulating the immune response and inflammation and have many functional similarities with mast cells, which are normal, longer-term residents of connective tissue.

# Lymphocytes are agranulocytes and lack the specific granules characteristic of granulocytes

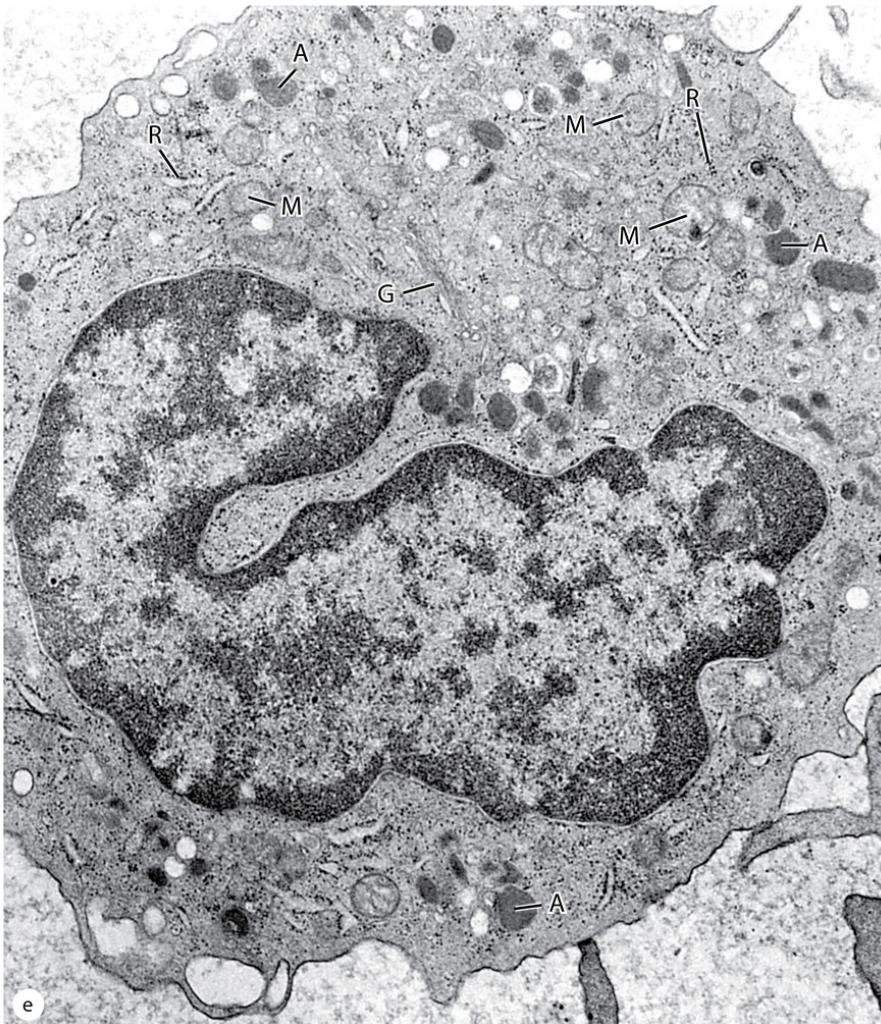
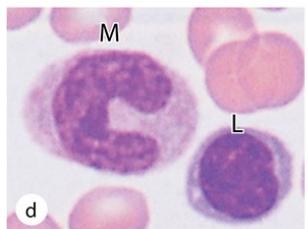
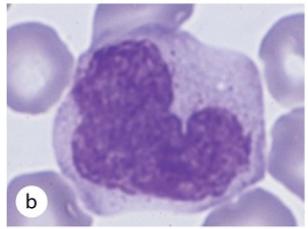
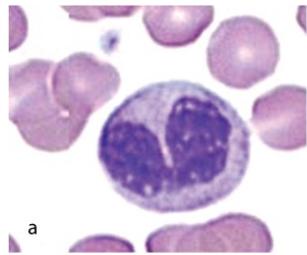


Lymphocytes circulating in blood generally range in size from 6 to 15  $\mu\text{m}$  in diameter

## »» MEDICAL APPLICATION

Lymphomas are a group of disorders involving neoplastic proliferation of lymphocytes or the failure of these cells to undergo apoptosis. Although often slow-growing, all lymphomas are considered malignant because they can very easily become widely spread throughout the body.

# Monocytes are large agranulocytes with diameters from 12 to 20 $\mu\text{m}$ that circulate as precursors to macrophages

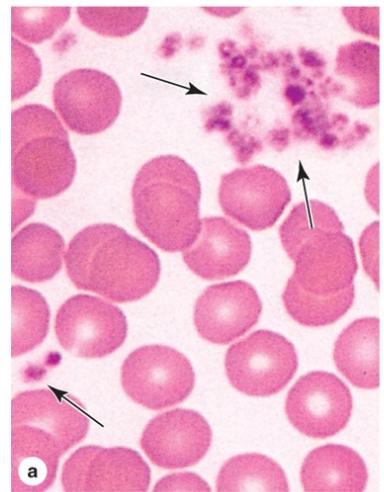


Monocytes have distinctive nuclei which are indented, kidney-shaped, or C-shaped

## »» MEDICAL APPLICATION

Accumulation of immigrating monocytes occurs in the early phase of inflammation following tissue injury. Acute inflammation is usually short-lived as macrophages undergo apoptosis or leave the site, but chronic inflammation usually involves the continued recruitment of monocytes. The resulting continuous presence of macrophages can lead to excessive tissue damage that is typical of chronic inflammation.

# Platelets (Thrombocytes) are cell fragments 2-4 $\mu\text{m}$ in diameter derived from megakaryocytes of bone marrow

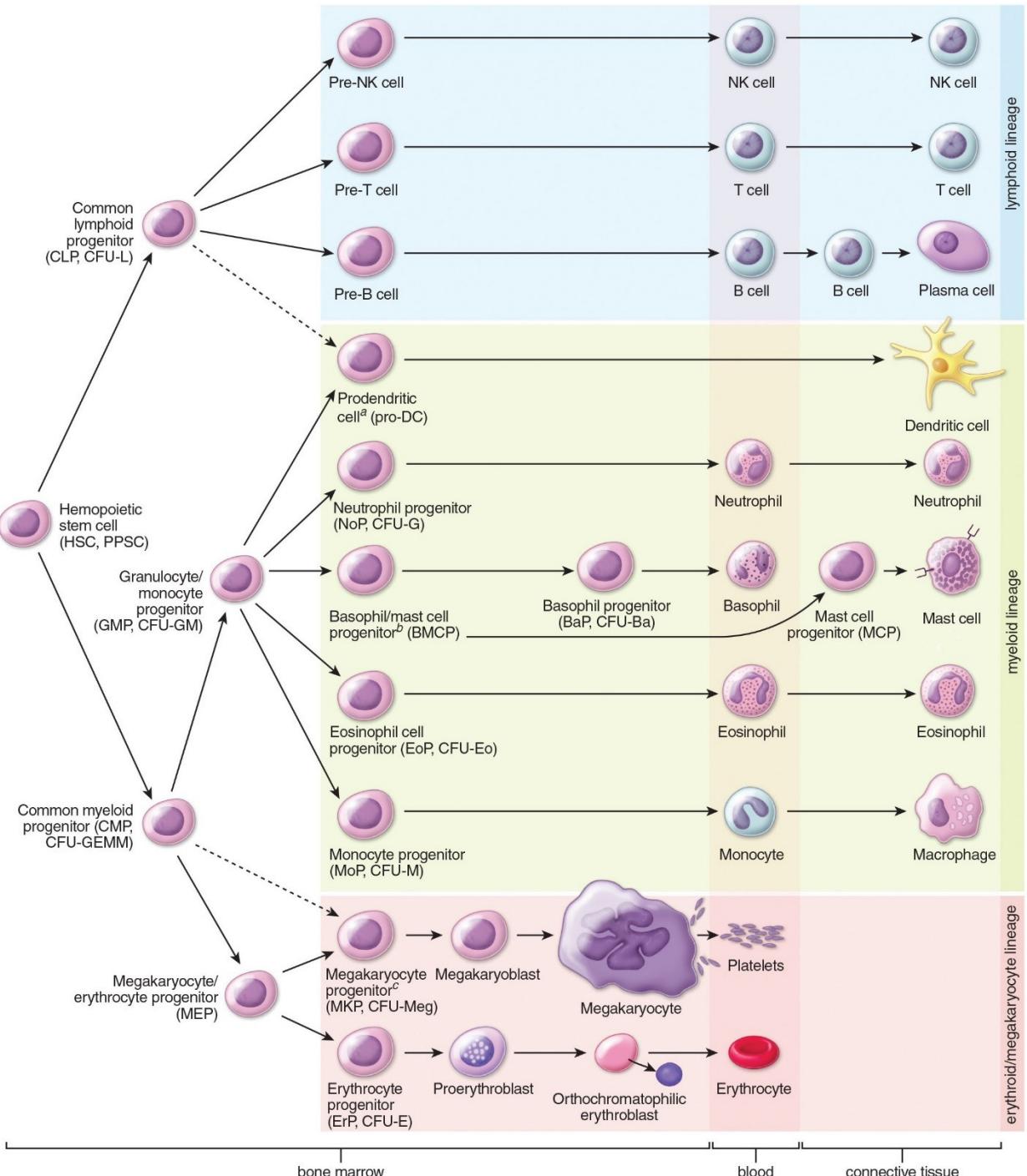


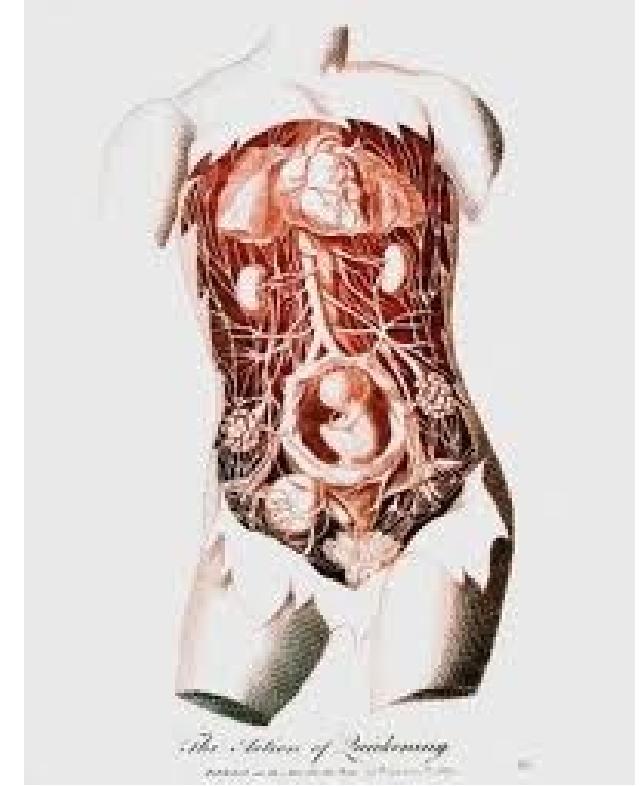
**Platelets:** release the content of their granules upon contact with collagen (or other materials outside of the endothelium) to begin the process of clot formation and reduce blood loss from the vasculature.

»» MEDICAL APPLICATION  
Aspirin and other nonsteroidal anti-inflammatory agents have an inhibitory effect on platelet function and blood coagulation because they block the local prostaglandin synthesis that is needed for platelet aggregation, contraction, and exocytosis at sites of injury. Bleeding disorders result from abnormally slow blood clotting.

# How Blood is Produced

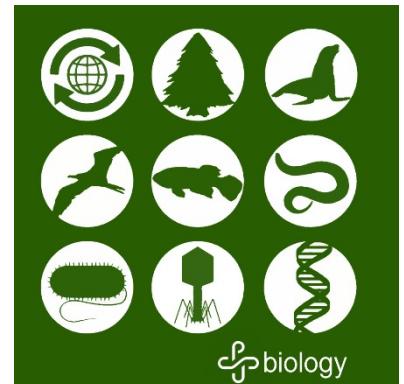
**Hemopoiesis** (hematopoiesis) is initiated in early embryonic development and includes **erythropoiesis** (development of red blood cells), **leukopoiesis** (development of white blood cells), and **thrombopoiesis** (development of platelets).





## Lymphatic, Digestive, and Associated Organs of the Digestive System

# BI 455 CHAPTER 14-16

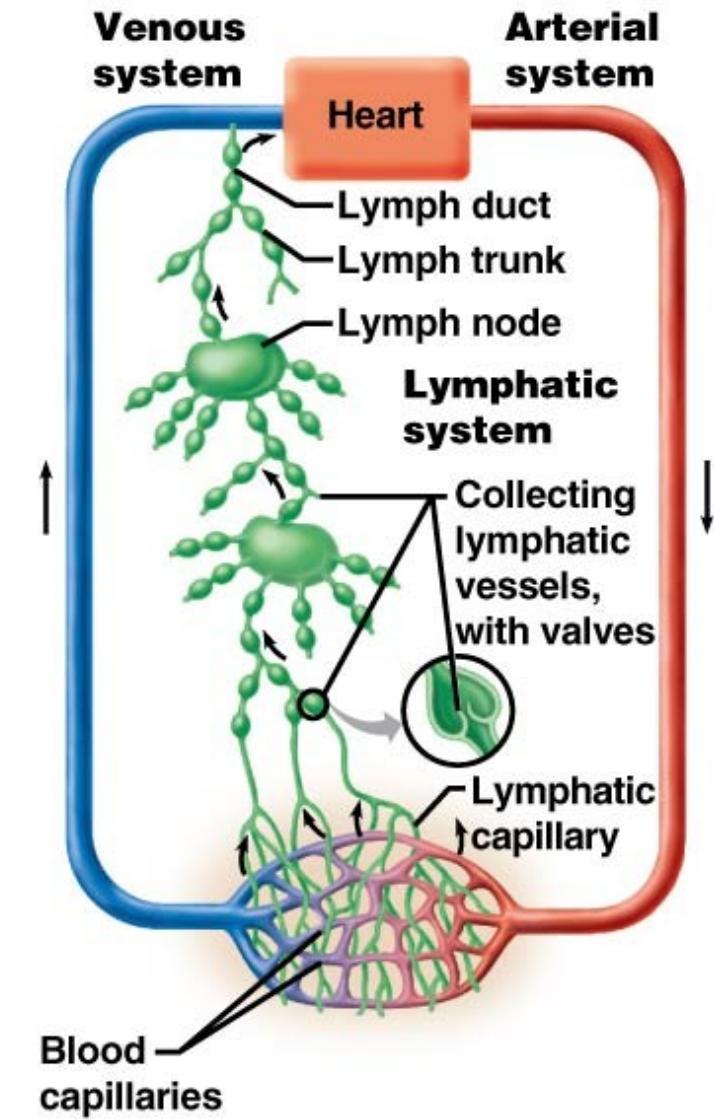


# Chapter 14: The Immune System and Lymphatic Organs

**Immune system:** Cell populations defending body from disease which are especially concentrated in lymphatic system

Fluid continually filters from the blood capillaries into the tissue spaces

- Blood capillaries reabsorb 85%
- lymphatic system absorbs 15% (2 to 4 L/day) of the water and about half of the plasma proteins enter the and then are returned to the blood



(a)

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# Mechanisms of Immune Defense

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Defenses against pathogens (environmental agents capable of producing disease such as Infectious organisms, toxic chemicals, and radiation)

**Innate (Nonspecific) Immunity:** does not depend on prior exposure

**1<sup>st</sup> defense:** External barriers, skin, and mucous membranes

**2<sup>nd</sup> defense:** Leukocytes and macrophages, antimicrobial proteins (interferons, complement system), immune surveillance, inflammation, and fever

**Adaptive (Specific) Immunity**

**3<sup>rd</sup> defense:** Relies on prior exposure of memory of pathogen, enabling faster defense in the future

Humoral: antibody marks invaders for other immune cells

Cellular: infected cells are destroyed by “killer” cells

Overview of Immune System: <http://www.youtube.com/watch?v=lWMJIMzsEMg>

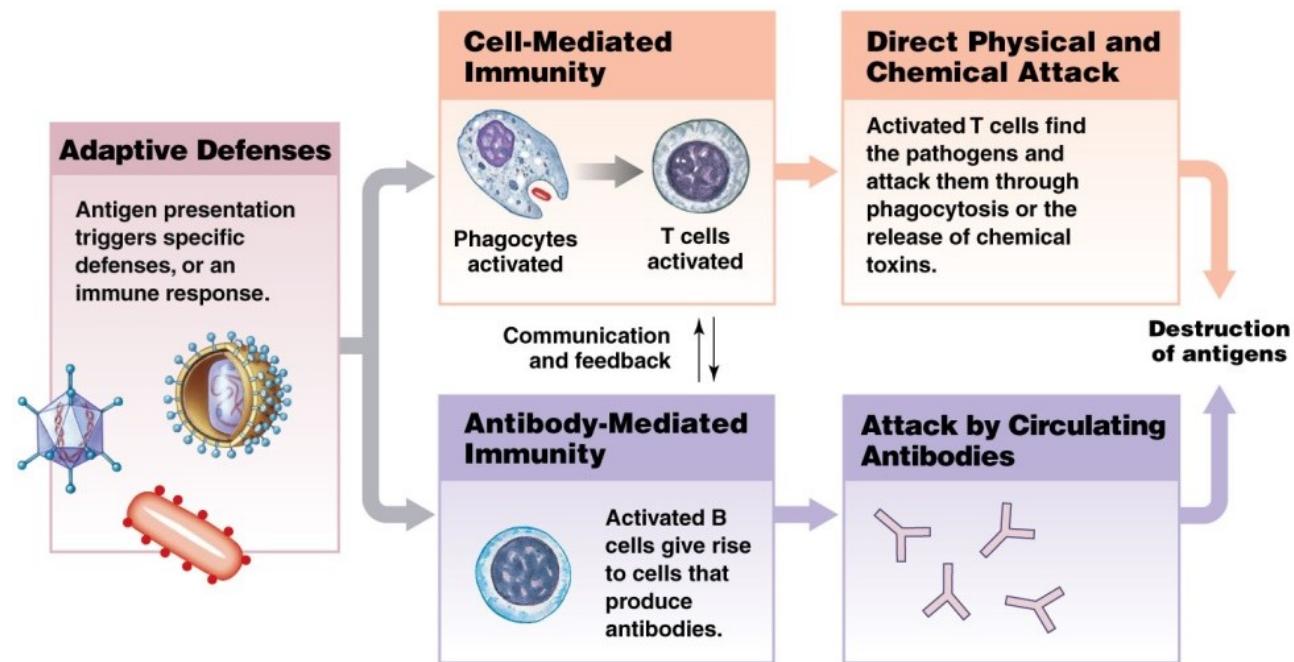
Crash Course The Immune System (long):

<https://www.khanacademy.org/partner-content/crash-course1/crash-course-biology/v/crash-course-biology-131>

# Functional classes of Adaptive Immunity

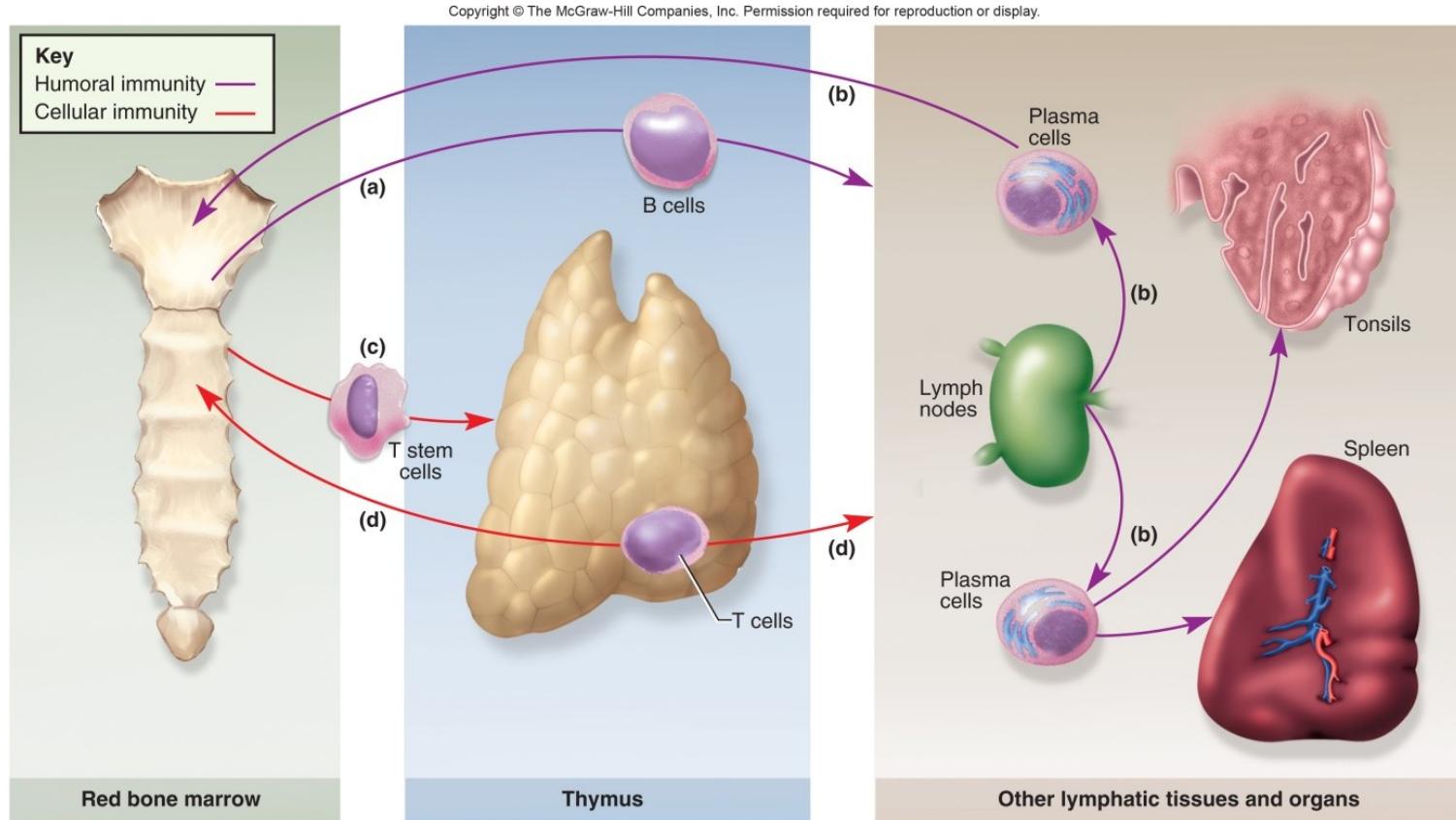
**Cellular (cell-mediated) immunity:** T cells respond to intracellular pathogens which are inaccessible to antibodies, and kill cells that harbor them

**Humoral (antibody-mediated) immunity:** B cells produce antibodies, which assault extracellular pathogens “Humoral”: relating to body fluids



# T Lymphocytes (T Cells) are “born” in the red bone marrow, but mature in thymus

- Reticuloendothelial (RE) cells secrete hormones which stimulate production of surface antigen receptors in T-cells
- Thymus “teaches T-cells to distinguish “self” from “non-self”



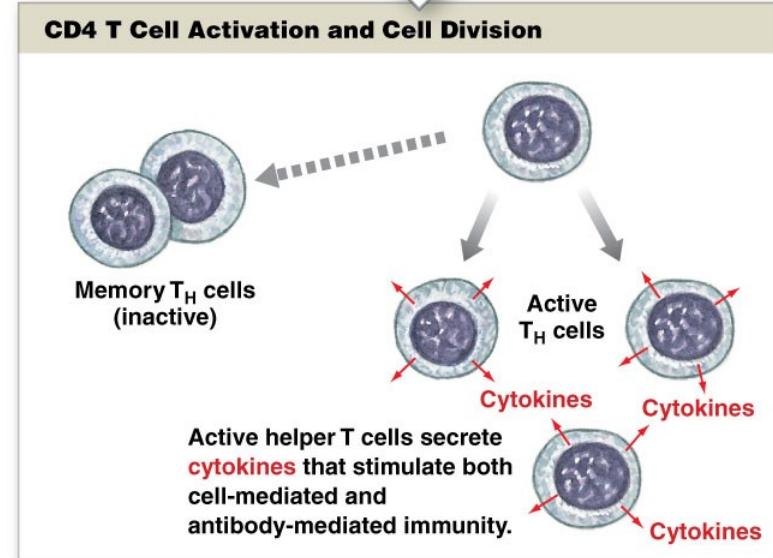
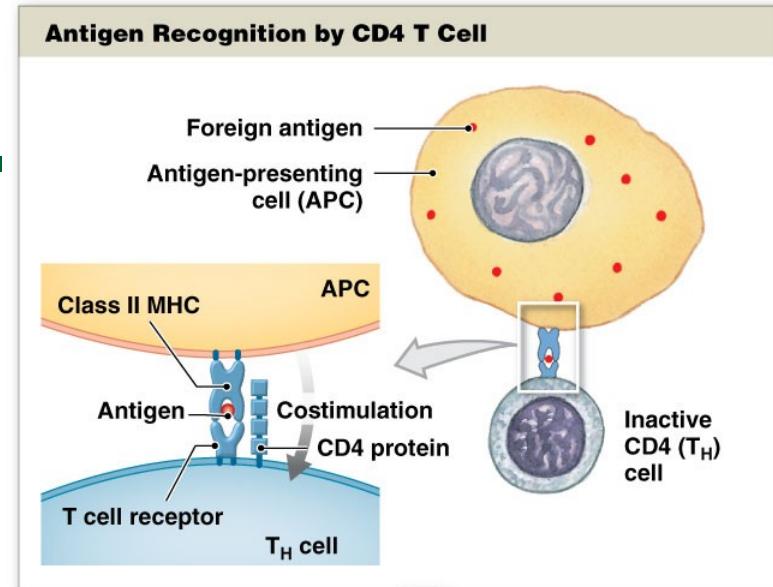
# Memory

Some  $T_c$  and  $T_h$  cells become **memory cells**

- respond more rapidly than naïve T cells
- Upon re-exposure to same pathogen later in life, memory cells launch a quick attack so that no noticeable illness occurs
- The person is immune to the disease

## » MEDICAL APPLICATION

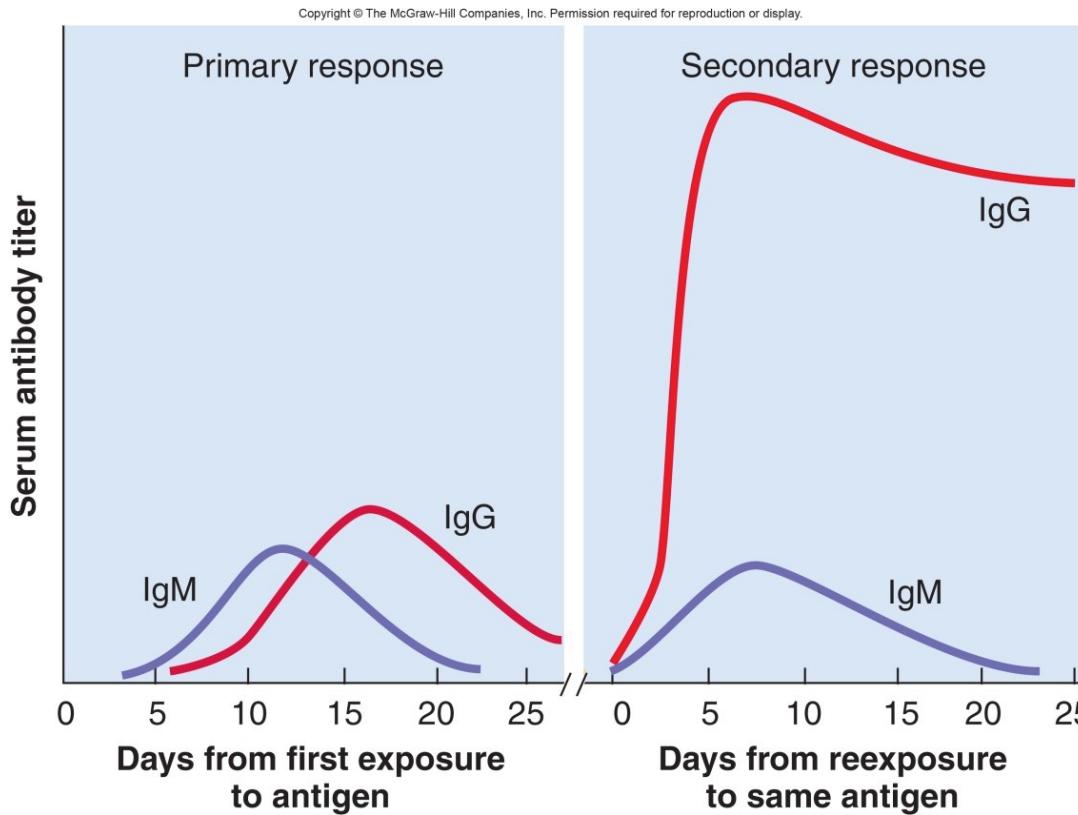
The retrovirus that produces acquired immunodeficiency syndrome (AIDS) infects and rapidly kills helper T cells, crippling the immune system rendering them susceptible to other infections.



# Memory

**Primary immune response:** antibody production upon first exposure to an antigen, 3 to 6 days

**Secondary (anamnestic) response:** Plasma cells form from Memory B cells within hours and no illness results

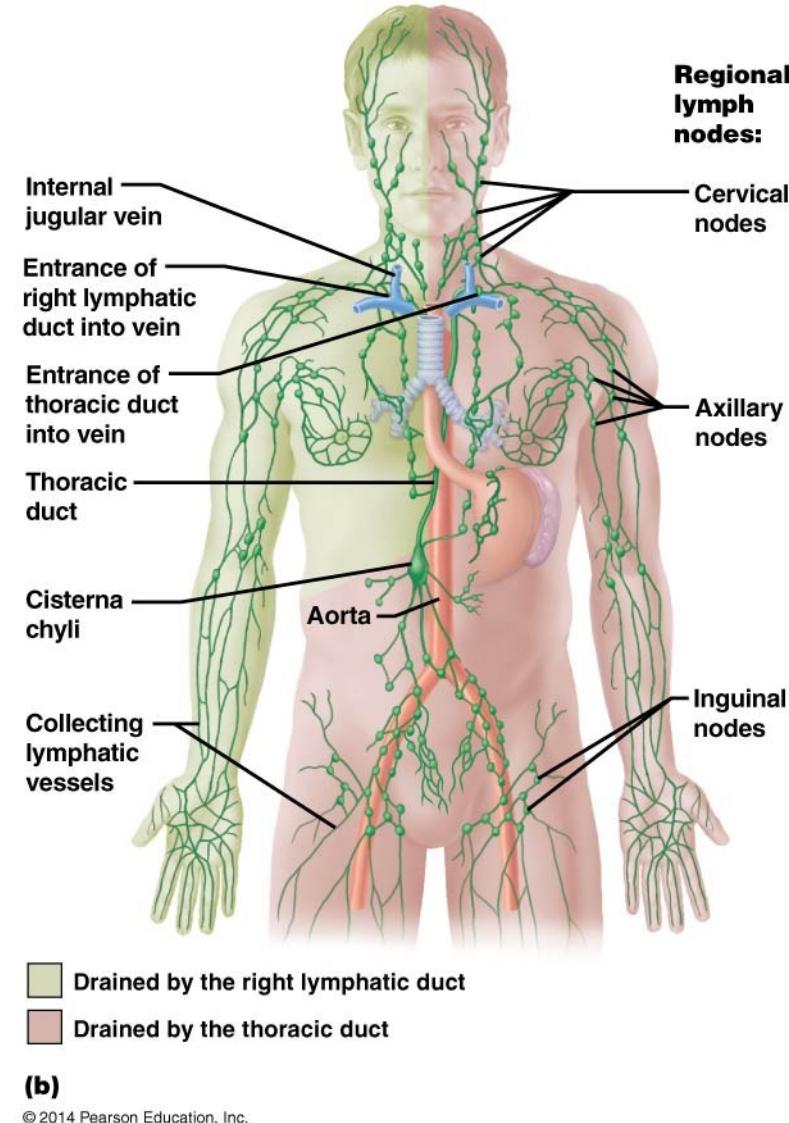


The immune response animation: [http://highered.mheducation.com/sites/0072495855/student\\_view/chapter24/animation\\_the\\_immune\\_response.html](http://highered.mheducation.com/sites/0072495855/student_view/chapter24/animation_the_immune_response.html)

# The Lymphatic System

Excess filtered fluid picks up foreign cells and chemicals from the tissues. This fluid passes through lymph nodes where **immune cells** “clean” it

- 1. Lymph:** Extracellular clear, colorless fluid, similar to plasma, but much less protein.
- 2. Lymphatic vessels:** Transport the lymph
- 3. Lymphatic tissues:** lymphocyte and macrophage rich aggregates
- 4. Lymphatic organs:** organs with concentrated populations of lymphatic cells



# Lymphatic Tissues

**Diffuse lymphatic tissue:** simplest form

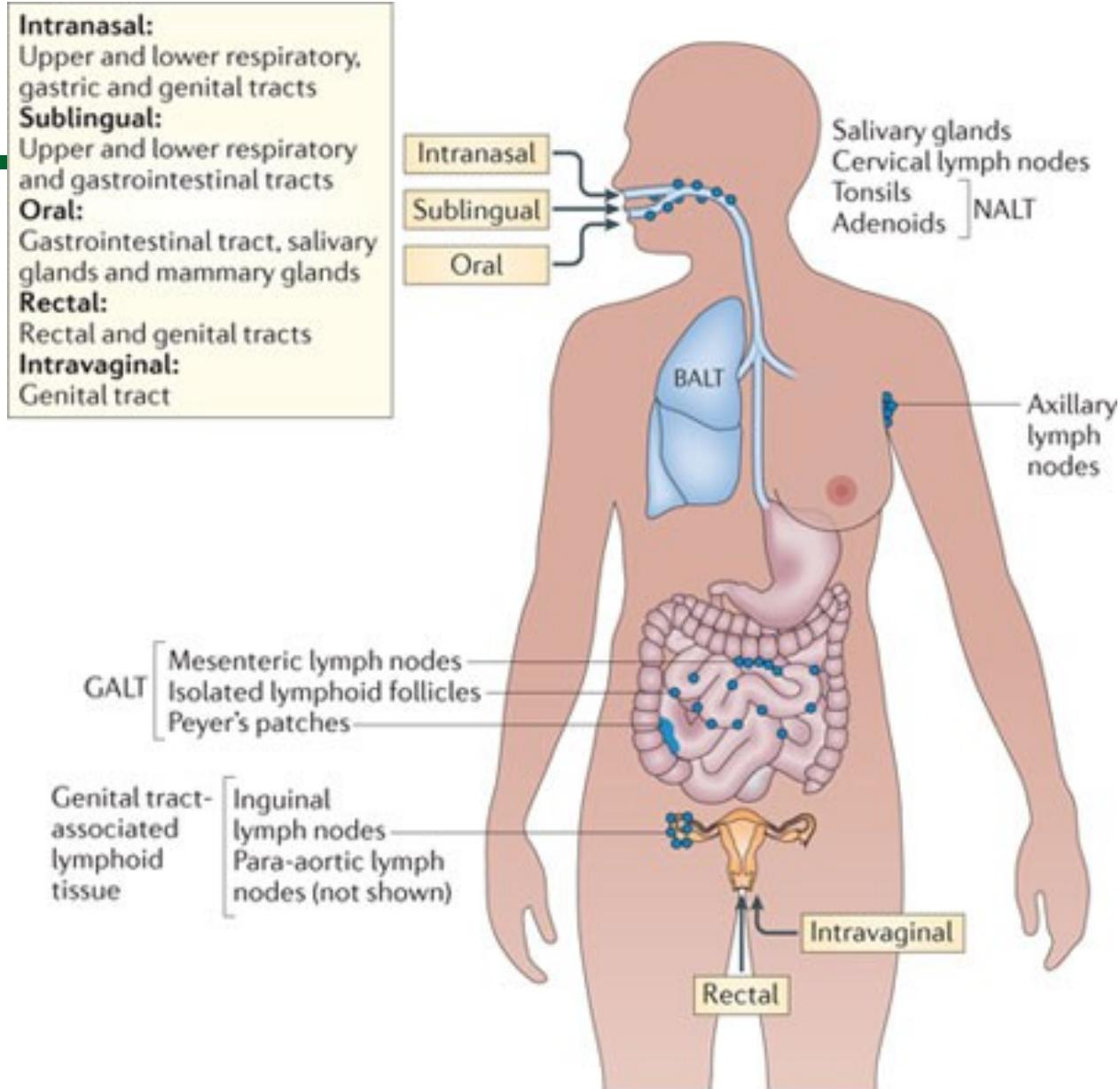
scattered lymphocytes are, body passages open to the exterior

**Ex Mucosa-associated lymphatic tissue (MALT):** Respiratory, digestive, urinary, and reproductive tracts

**Lymphatic nodules (follicles):** Dense congregate of lymphocytes

**Peyer patches:** lymph node clusters in small intestine

<b>Intranasal:</b> Upper and lower respiratory, gastric and genital tracts
<b>Sublingual:</b> Upper and lower respiratory and gastrointestinal tracts
<b>Oral:</b> Gastrointestinal tract, salivary glands and mammary glands
<b>Rectal:</b> Rectal and genital tracts
<b>Intravaginal:</b> Genital tract



# Lymphatic Organs

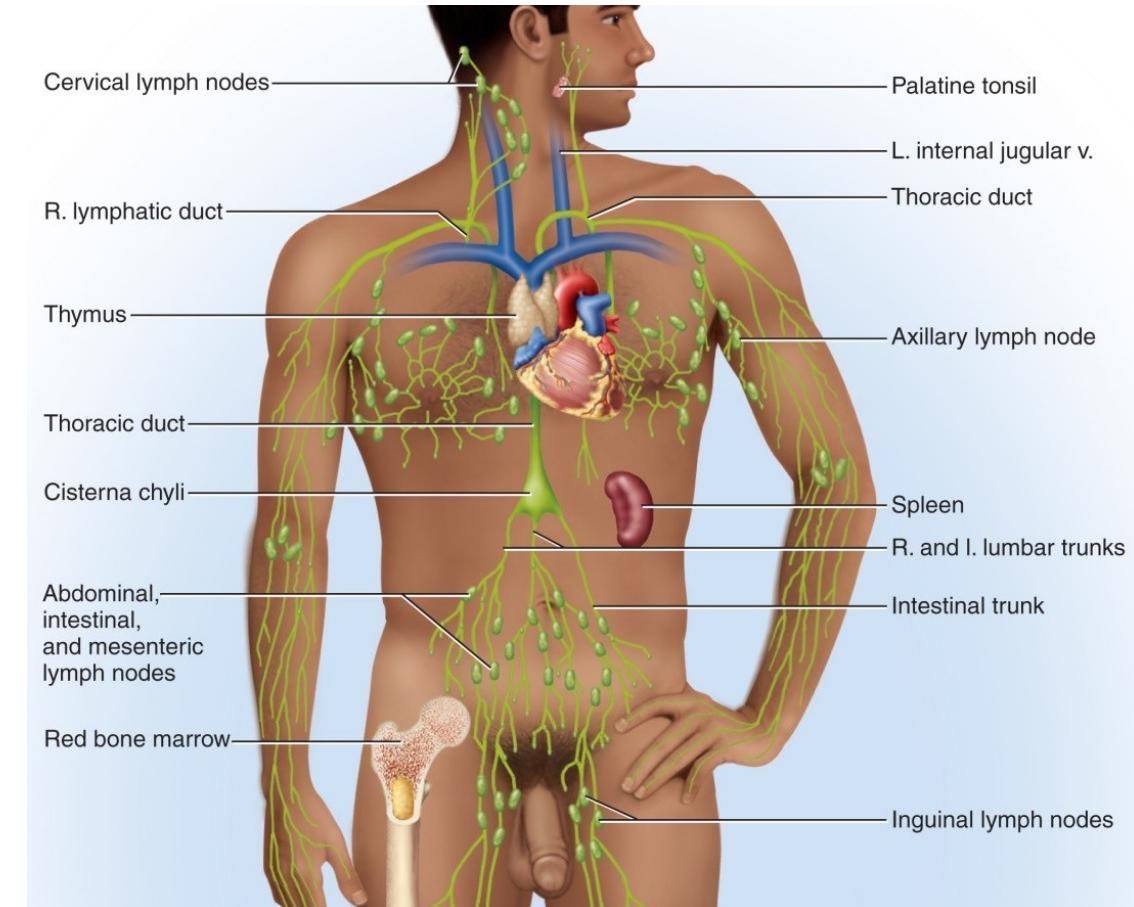
**Lymphatic organs** are surrounded by connective tissue capsule, separating them from neighboring tissues

**Primary lymphatic organs:** Site where T and B cells become immunocompetent (able to recognize and respond to antigens)

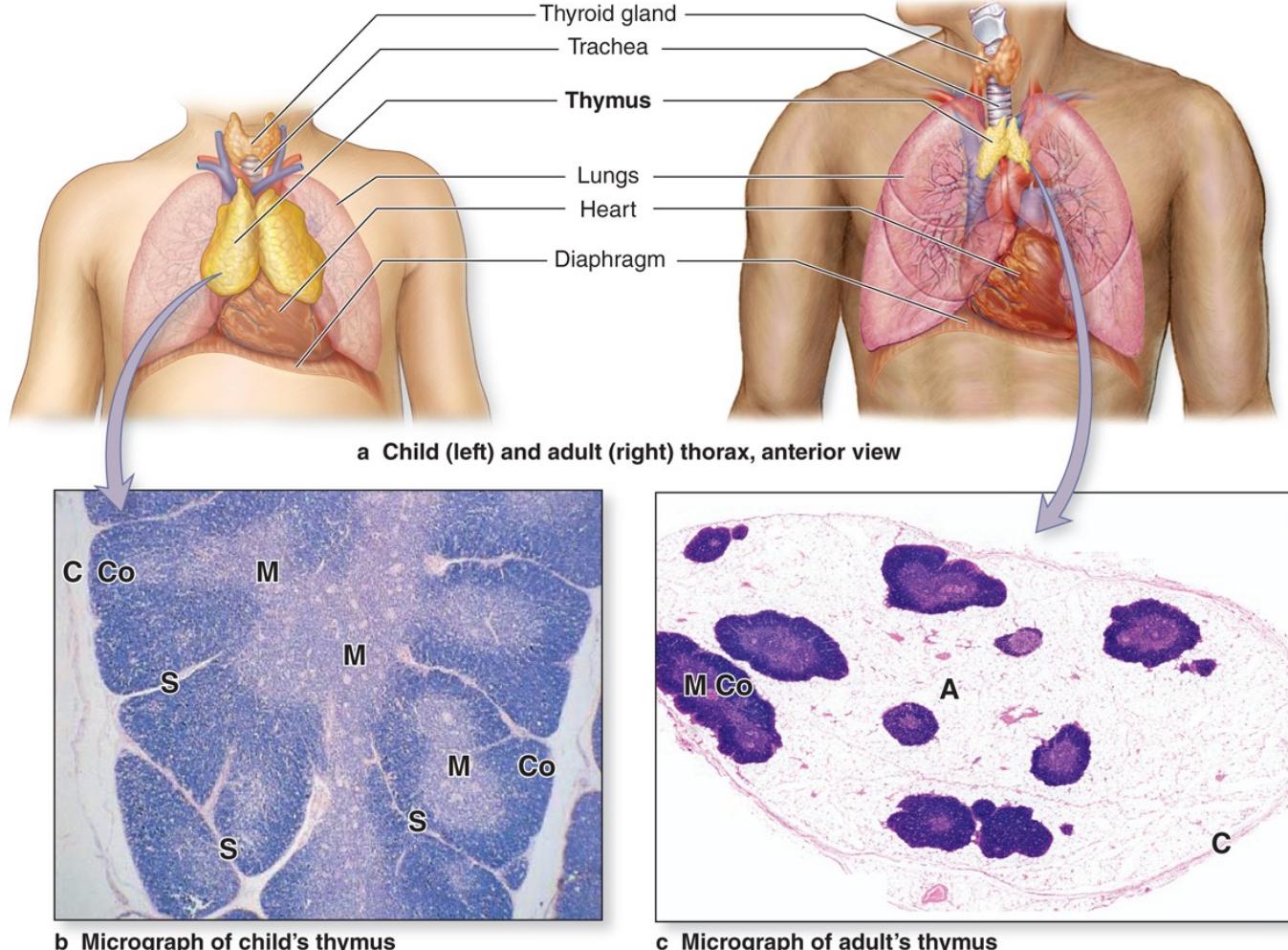
1. Red bone marrow
2. Thymus

**Secondary lymphatic organs:** populated by Immunocompetent cells

3. Lymph nodes
4. Tonsils
5. Spleen



**The thymus is a bilobed organ in the mediastinum that is most active and prominent before puberty and undergoes involution with less activity in the adult.**

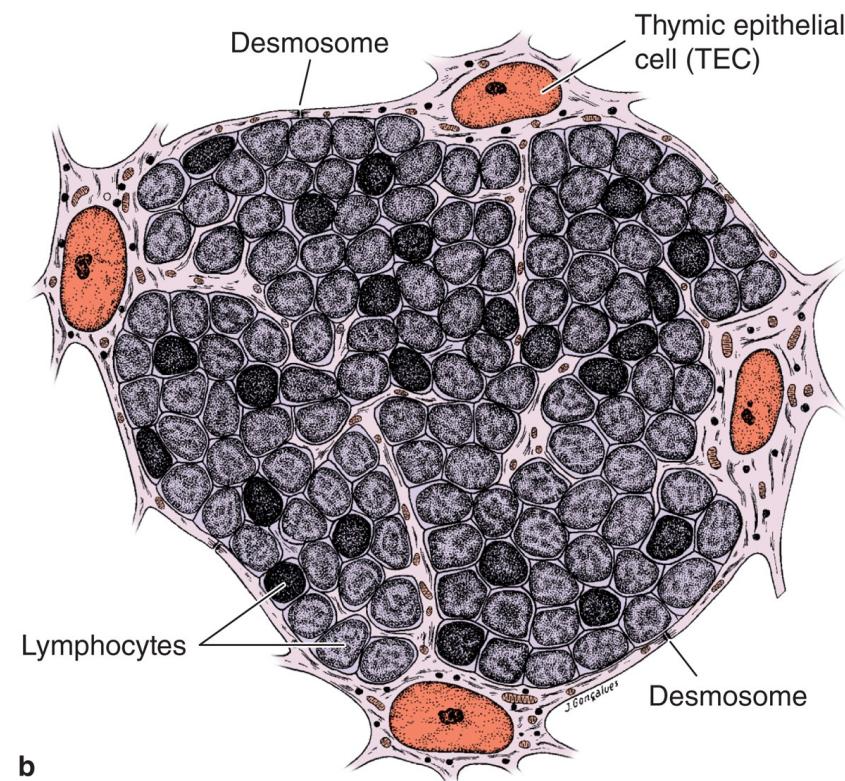
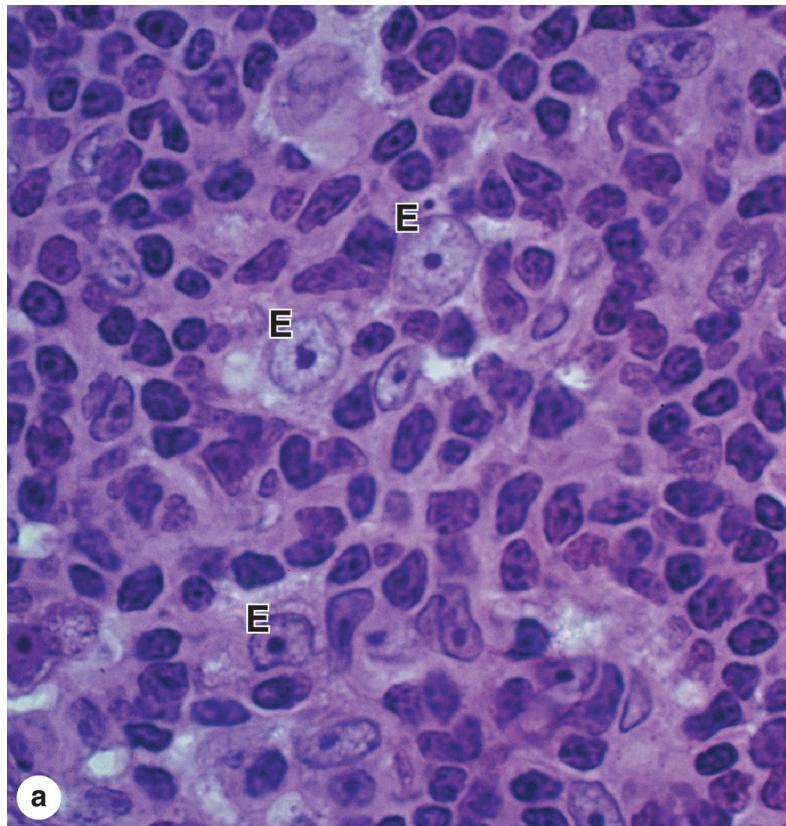


**(b) A child's thymus**, showing connective tissue of the capsule (**C**) and septa (**S**) -between thymic lobules, each having an outer cortex (**Co**) and -incompletely separated medulla (**M**) of lymphoid tissue.

**(c)** After- involution the thymus shows only small regions of lymphoid tissue, here still with cortex (**Co**) and medulla (**M**), and these are embedded in adipose tissue

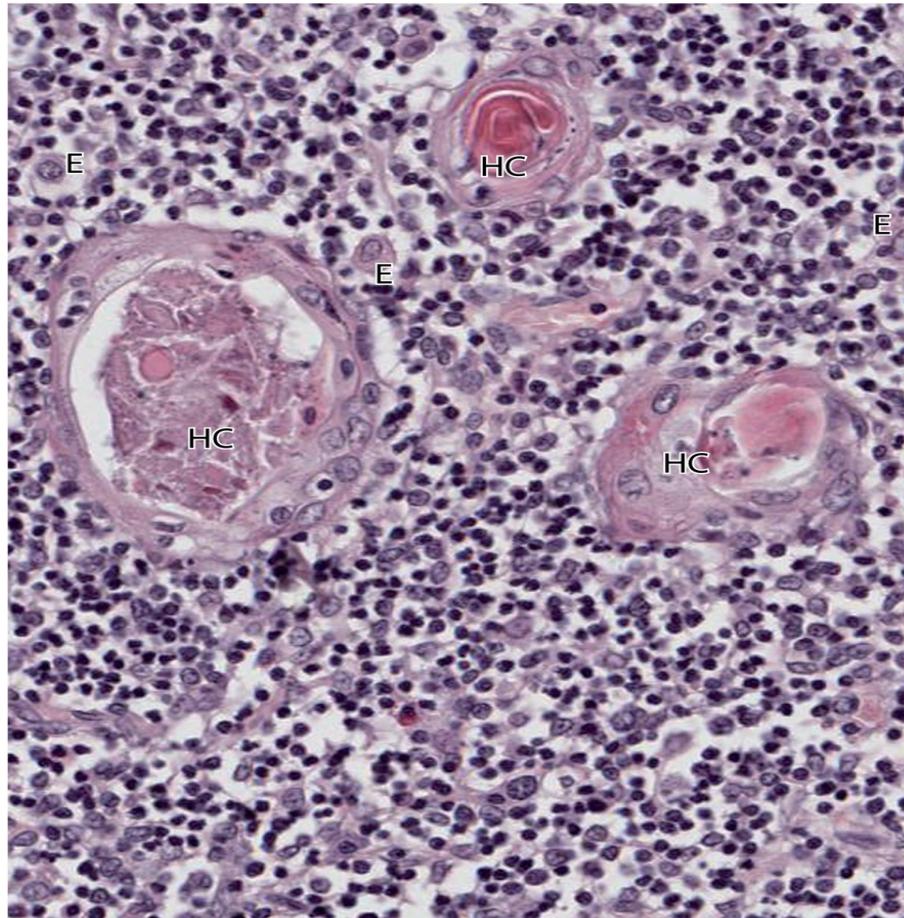
## Thymic Cortex: early T cell development

- (a) The cortical zone of an active thymus is packed with small **lymphoblasts**, and epithelial cells (**E**).
- (b) The epithelial reticular cells throughout the cortex secrete cytokines that promote T-cell maturation.



# Thymic (Hassall's) Corporcles are a distinguishing feature of the thymic medulla

---



The most characteristic feature of the medulla in humans is the presence of thymic (Hassall) corpuscles (H).

These are of variable size and contain aggregates of thymic epithelial cells releasing many cytokines important for the later differentiation of regulatory T cells.

# Structure of a lymph node.

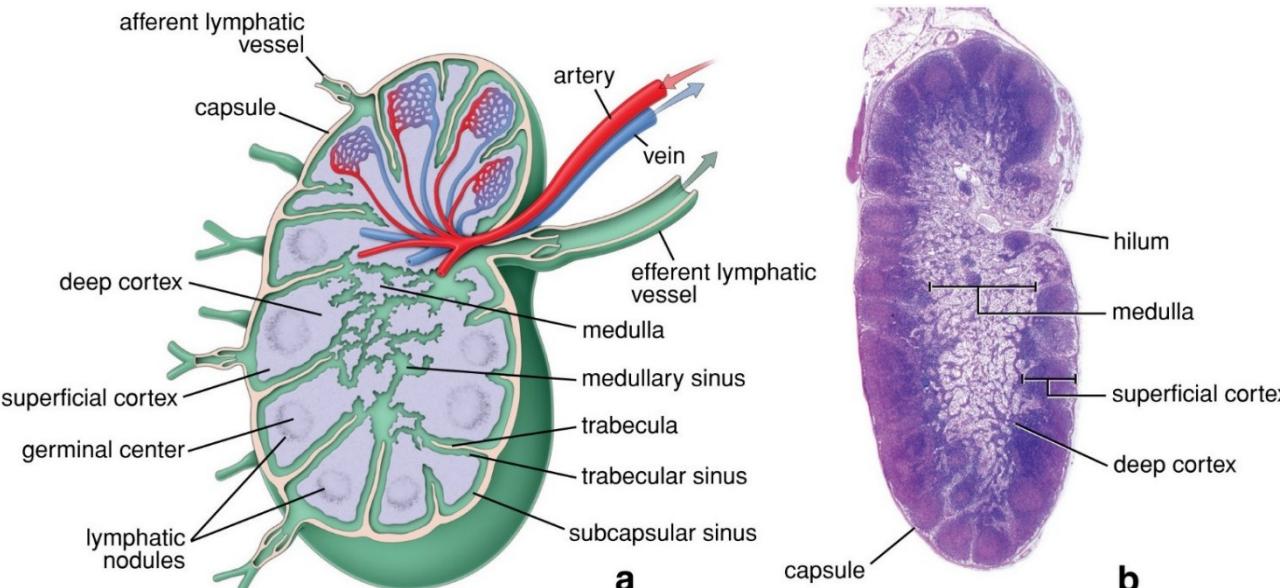
**Cortex:** contains lymphatic nodules with aggregates of lymphocytes.

**Germinal center:** region in nodule where lymphocytes are activated

**Medulla:** lymphatic tissue separated by lymphatic medullary sinuses.

**Capsule:** dense connective tissue from which trabeculae extend into the substance of the node.

**Flow of lymph:** afferent lymphatic vessels → subcapsular sinus. → trabecular sinus → medullary sinuses.

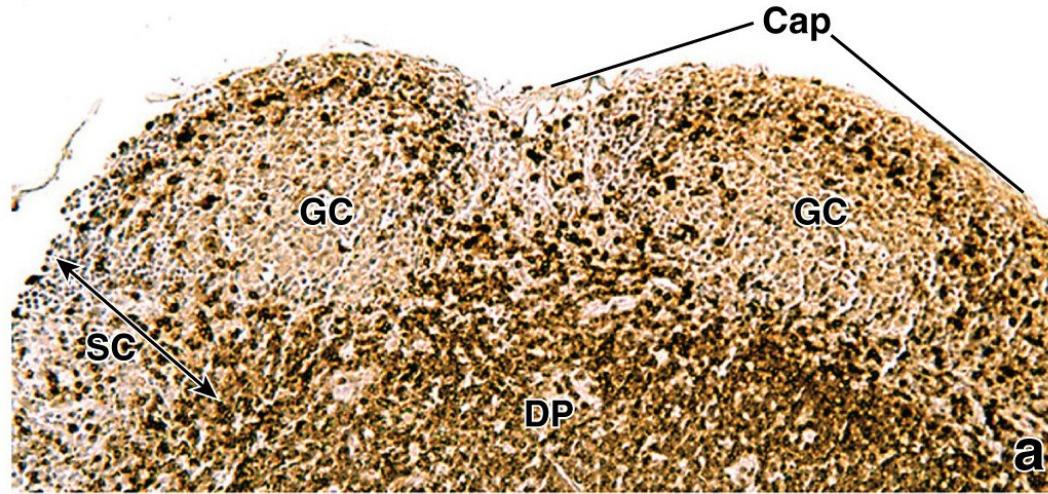


## »» MEDICAL APPLICATION

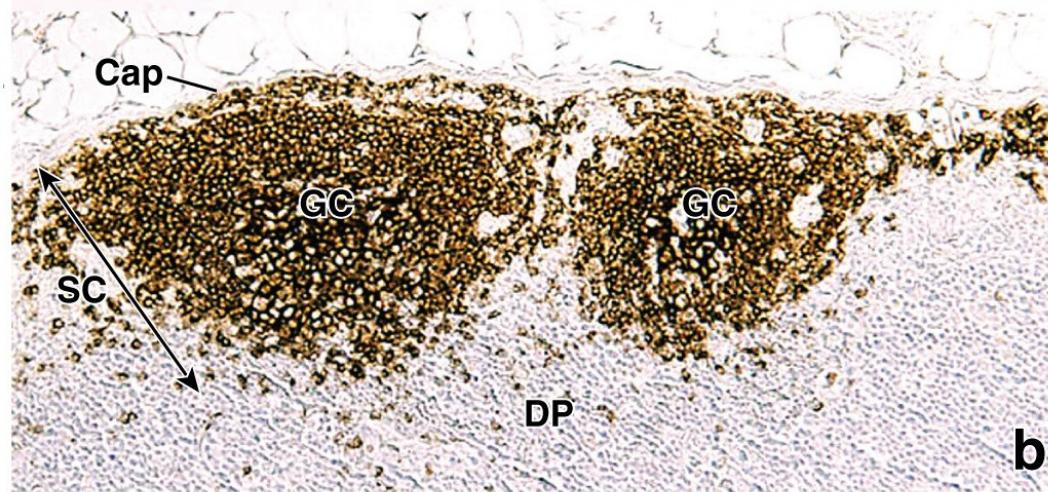
Metastatic cancer cells can be carried to nearby lymph nodes. The sentinel lymph node (first one downstream of tumor) is examined by pathologists for the presence of cancer cells.

Sentinel Lymph Node Biopsy: <https://www.youtube.com/watch?v=Cdl2JhhTfYc>

# B and T Lymphocytes in the Superficial Cortex of a Marmoset Monkey Lymph Node



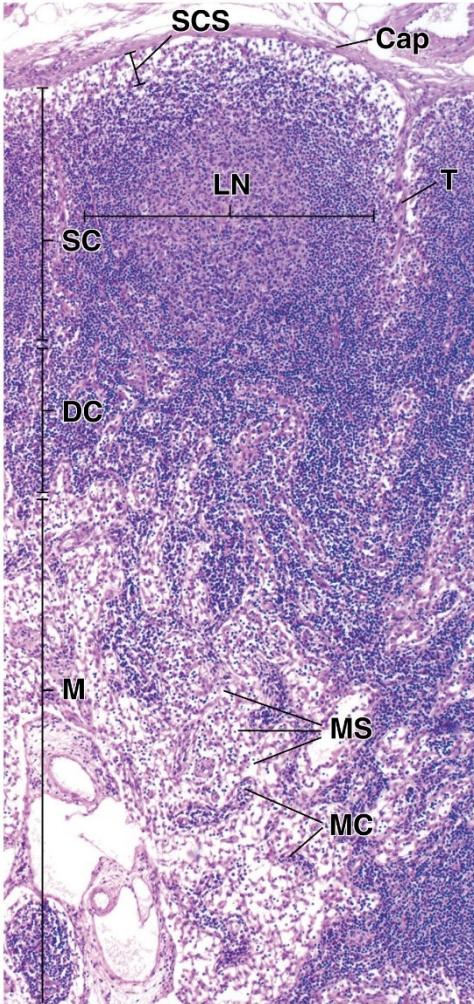
a: Anti CD3 (**T lymphocytes marker**) stain: Note that the majority of T cells are distributed within the deep cortex (DP); a small number of T cells are present in the superficial cortex (SC ), mainly around germinal centers (GC).



b: anti CD20 (**B lymphocytes marker**) stain: B cells accumulate in germinal centers (GC) of the superficial cortex (SC)

# H & E of a lymph node

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**Capsule (Cap):** dense connective tissue from which trabeculae (T) penetrate into the organ

**Subcapsular sinus (SCS):** receives lymph from afferent lymphatic vessels that penetrate the capsule.

**trabecular sinuses (T)**

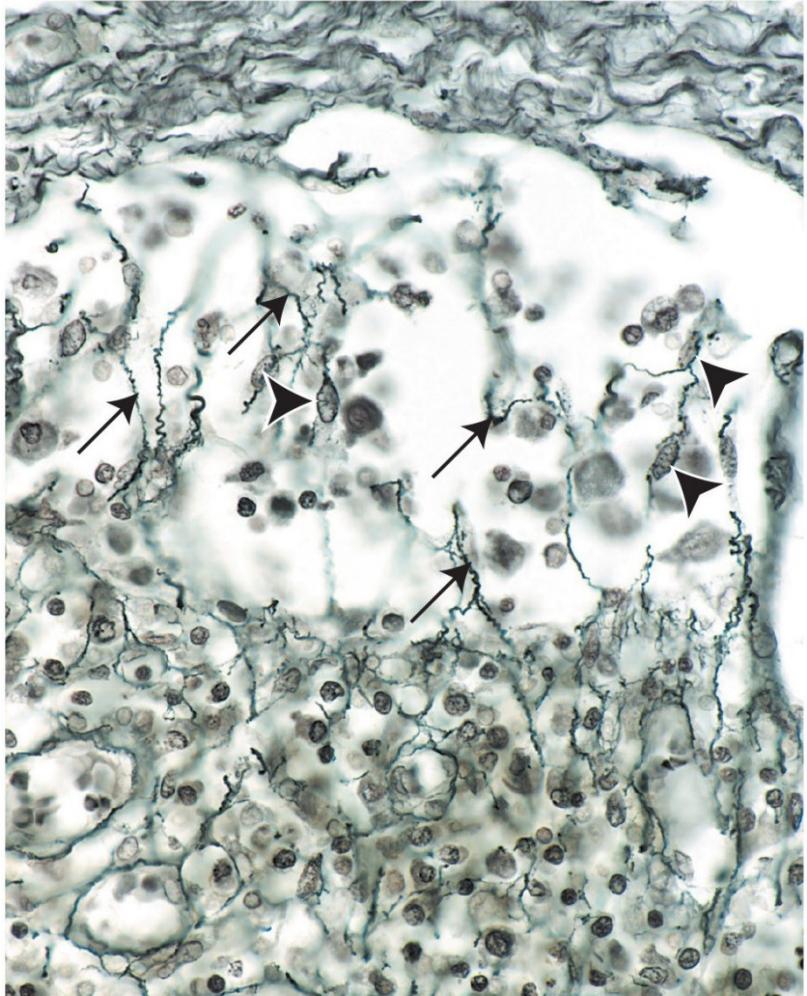
The **superficial cortex (SC)** contains the lymphatic nodules (LN)

**Deep cortex (DC)** is nodule-free: contains densely packed lymphocytes

**Medulla (M):** contains medullary cords (MC), which are separated by light-appearing spaces, the medullary sinuses (MS). The medullary sinuses receive lymph from the trabecular sinuses as well as lymph that has filtered through the cortical tissue.

# Silver Stain of a Lymph Node

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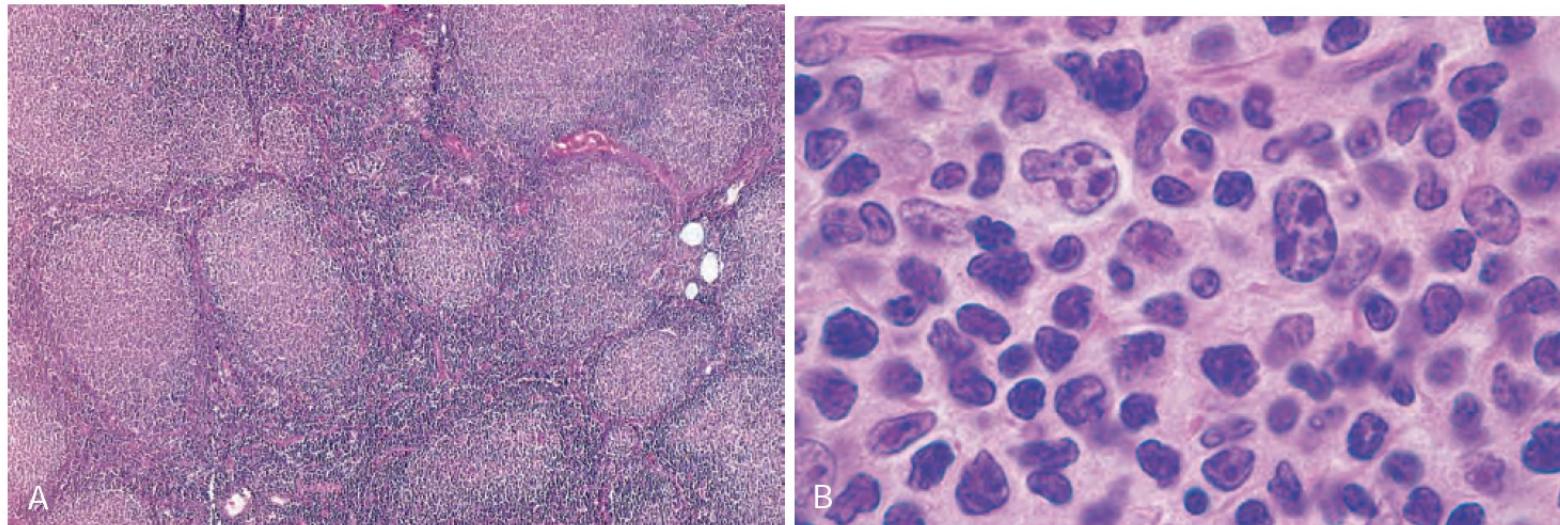


**Connective tissue capsule** (at the top)  
Subcapsular sinus, and the superficial cortex of the lymph node (at the bottom).

The reticular fibers (arrows) form an irregular anastomosing network throughout the stroma of the lymph node. Note elongated oval nuclei of reticular cells (arrow-heads), which are in intimate contact with reticular fibers in the sinus.

# Lymphoma

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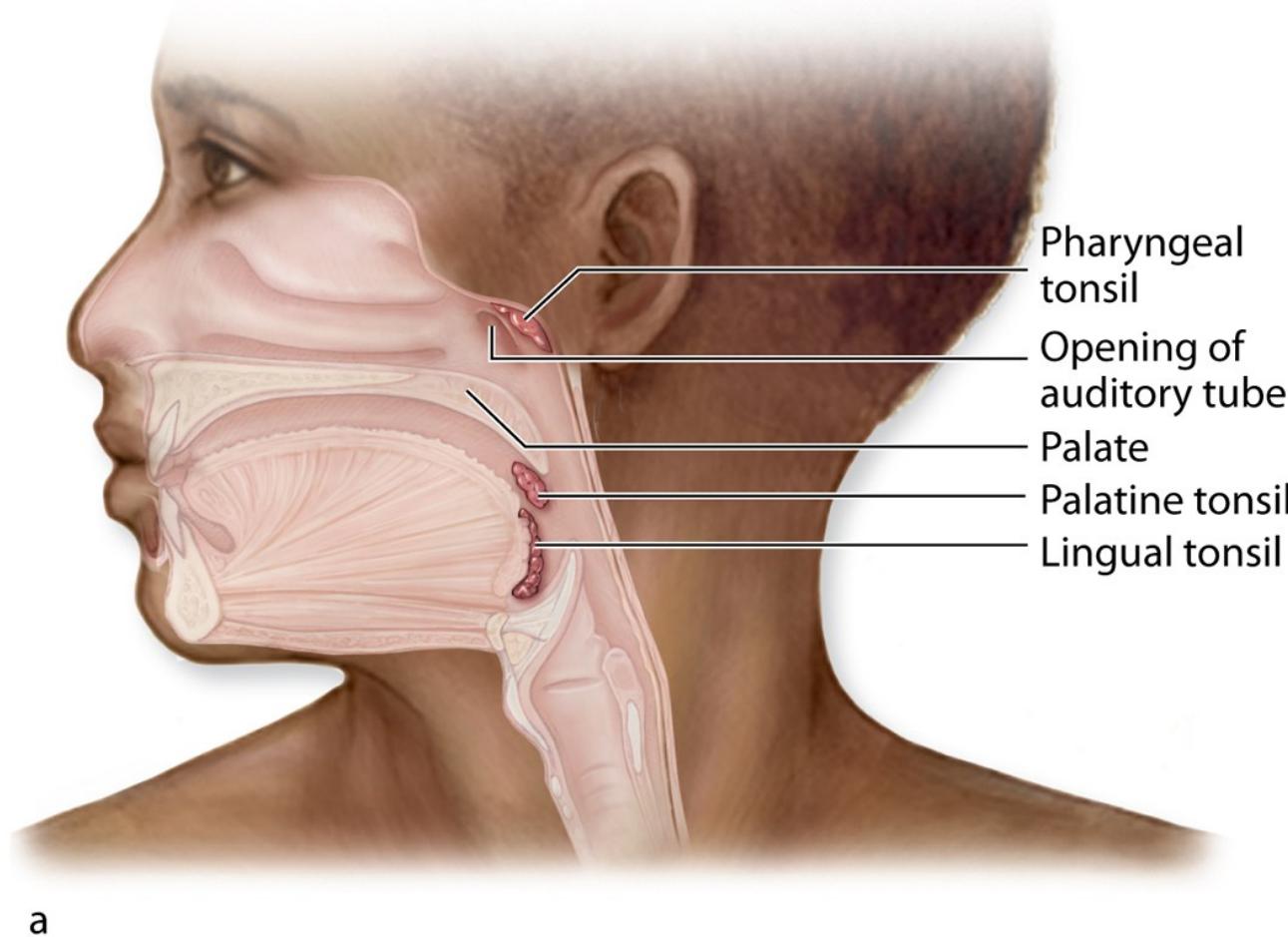


## >> MEDICAL APPLICATION

Neoplastic proliferation of lymphocytes can completely change the normal architecture of the node to a structure filled with lymphocytes, a condition called lymphadenopathy.

- A. Nodular aggregates of lymphoma cells are present throughout lymph node.
- B. At high magnification, small lymphoid cells with condensed chromatin and irregular or cleaved nuclear outlines are mixed with a population of larger cells with nucleoli.

# Masses of lymphoid nodules comprising tonsils are collected in three general locations in the wall of the pharynx.



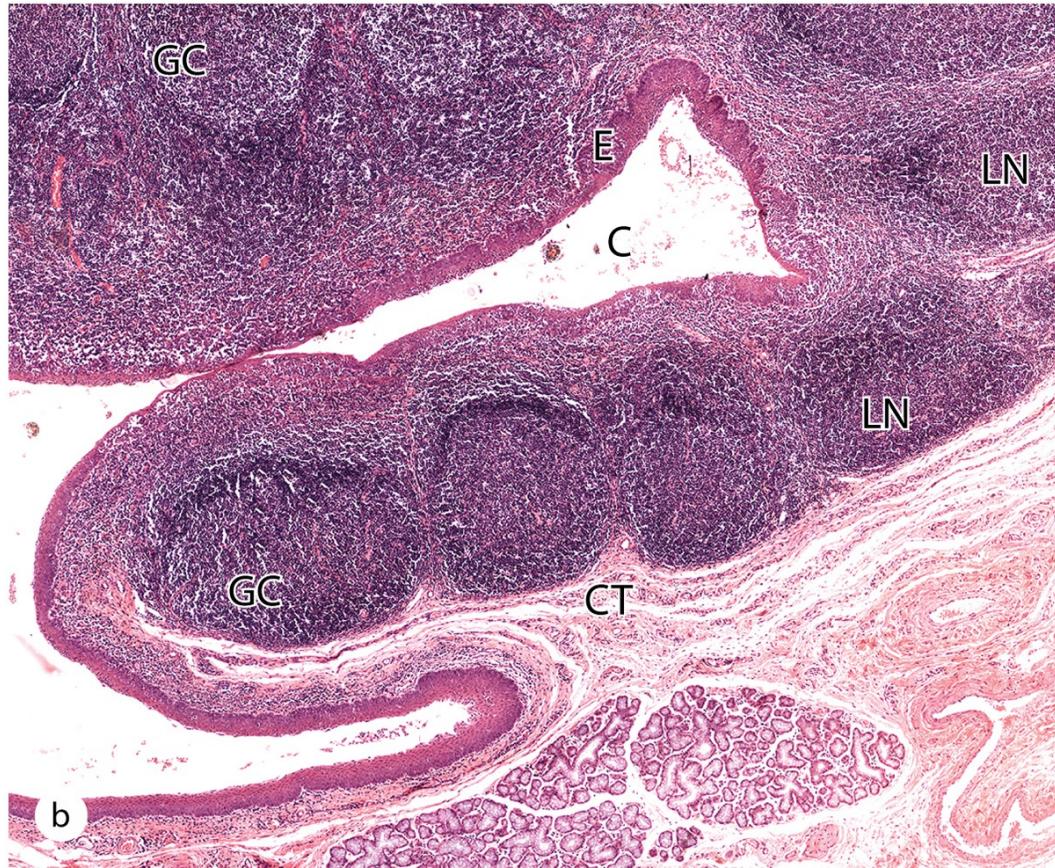
**Palatine tonsils:** posterior

**Lingual tonsils:** posterior third of the tongue. Both are covered with stratified squamous epithelium.

**Pharyngeal tonsil:** single medial mass situated in the posterior wall of the nasopharynx. It is usually covered by ciliated pseudostratified columnar epithelium,

Hypertrophied regions of pharyngeal tonsils resulting from chronic inflammation are called **adenoids**.

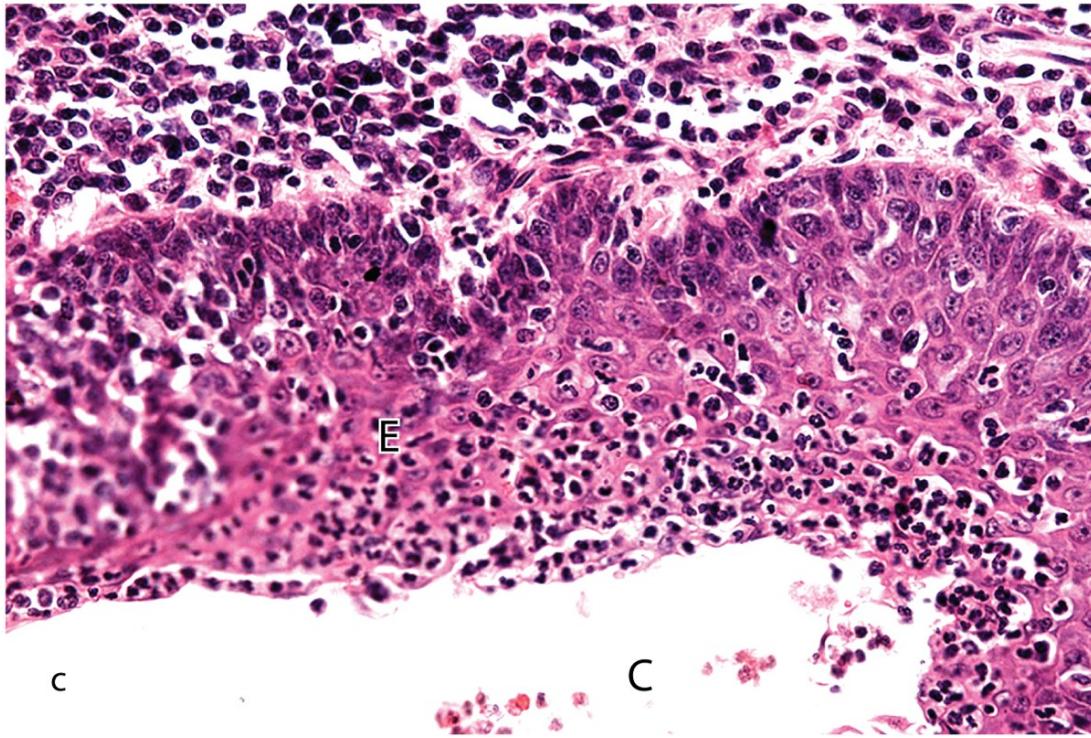
# Lymphoid Nodules of the Tonsils



lymphoid nodules (**LN**), -collectively covered by stratified squamous epithelium (**E**) on one side and a connective tissue capsule (**CT**) on the other.

Some nodules show lighter staining germinal centers (**GC**). Infoldings of the mucosa in some tonsils form **crypts** (**C**), along which nodules are especially numerous. Lumens of crypts contain desquamated epithelial cells, live and dead lymphocytes, and bacteria.

# Epithelium surrounding tonsillar crypts



Epithelium (**E**) surrounding tonsillar crypts (**C**) often becomes infiltrated with lymphocytes and other leukocytes and can become difficult to recognize histologically. Adjacent connective tissue at the top of the photo also contains numerous lymphocytes.

» » **MEDICAL APPLICATION** Chronic inflammation of the pharyngeal lymphoid tissue and tonsils of children often produces hyperplasia and enlargement of the tonsils to form “adenoids,” which can obstruct the eustachian tube and lead to middle ear infections.

# Spleen: body's largest lymphatic organ, highly vascular and vulnerable to trauma and infection

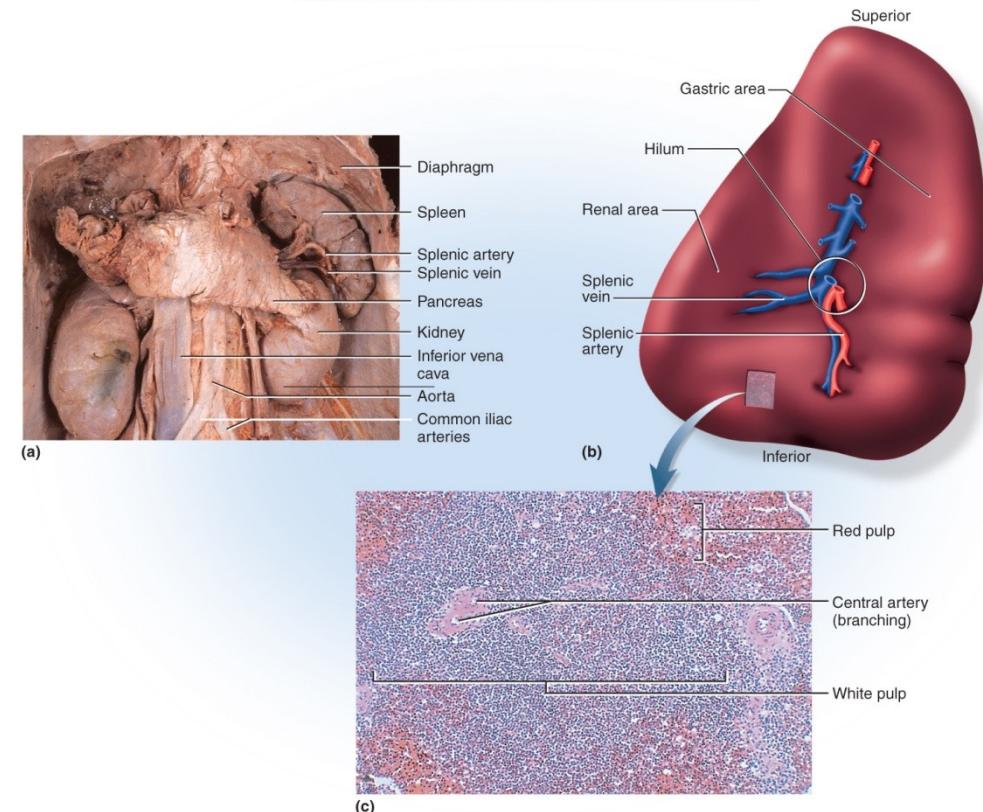
Ruptured spleen requires splenectomy

**Red pulp:** sinuses filled with erythrocytes

- Blood reservoir
- RBC disposal
- Blood production in fetus

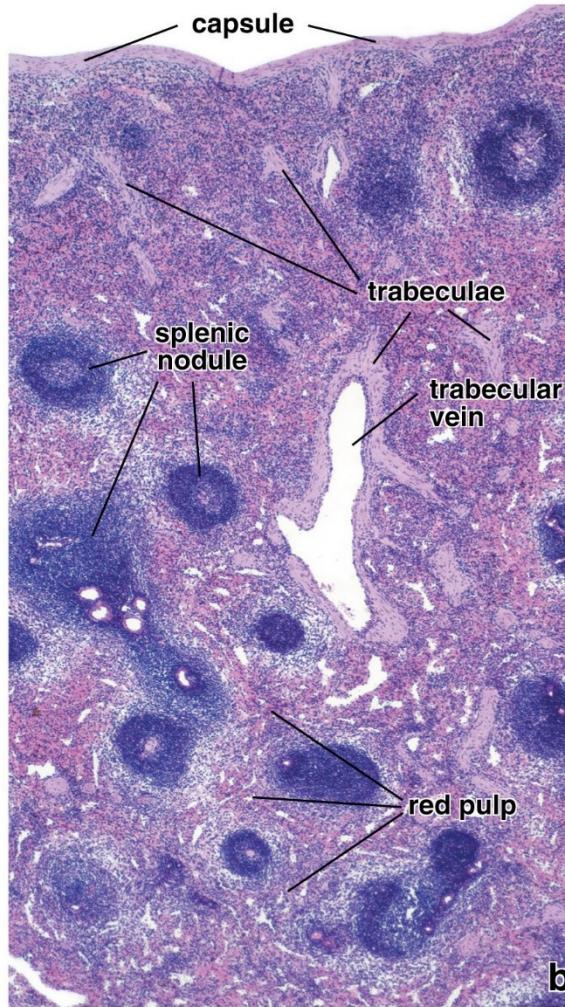
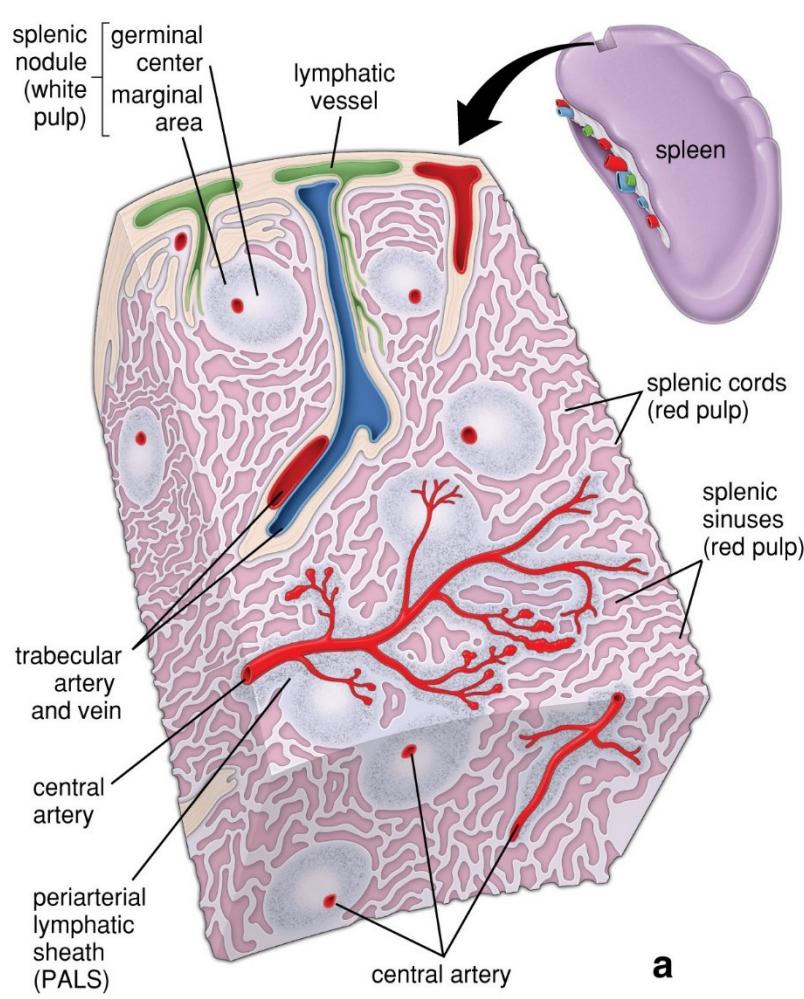
**White pulp:** lymphocytes, macrophages surrounding small branches of splenic artery, monitors blood for foreign antigens

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a: © The McGraw-Hill Companies, Inc./Dennis Strete, photographer; c: © The McGraw-Hill Companies, Inc./Photo by Dr. Alvin Telser

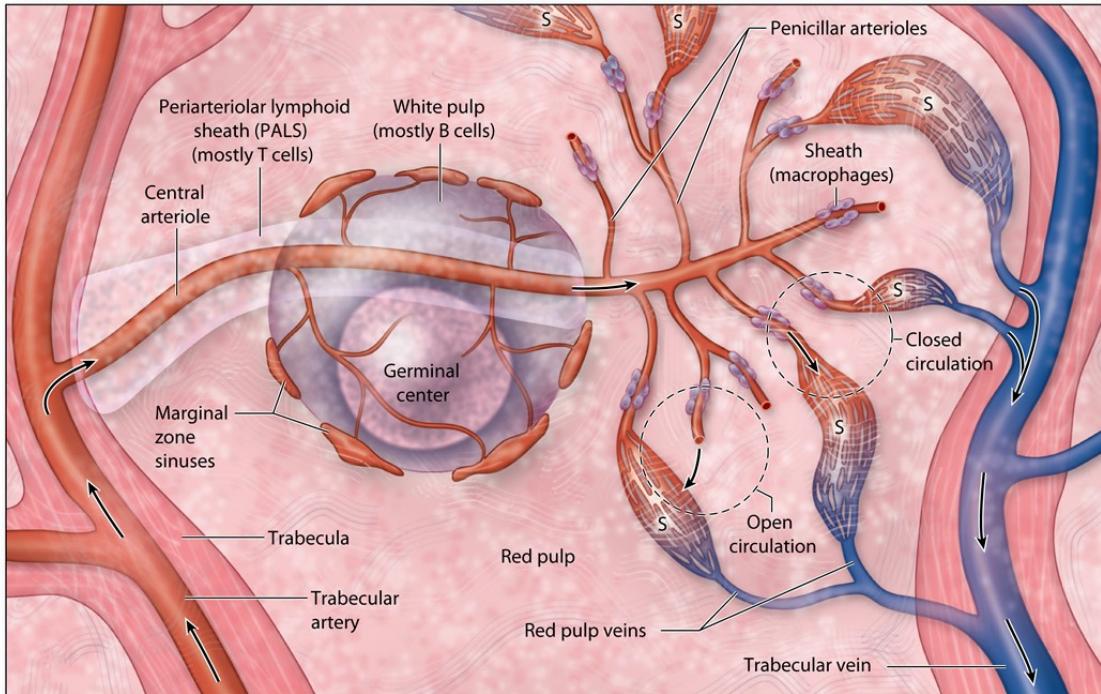
# Splenic Structure



**White pulp:** mass of lymphocytes. Expansion of the white pulp creates the **splenic nodules**.

**Red pulp:** splenic sinuses surrounded by splenic cords (cords of Billroth). Blood vessels traverse the capsule and trabeculae before and after passage within the substance of the spleen.

# Blood circulation and the structure of the spleen: trabecular artery to the trabecular vein



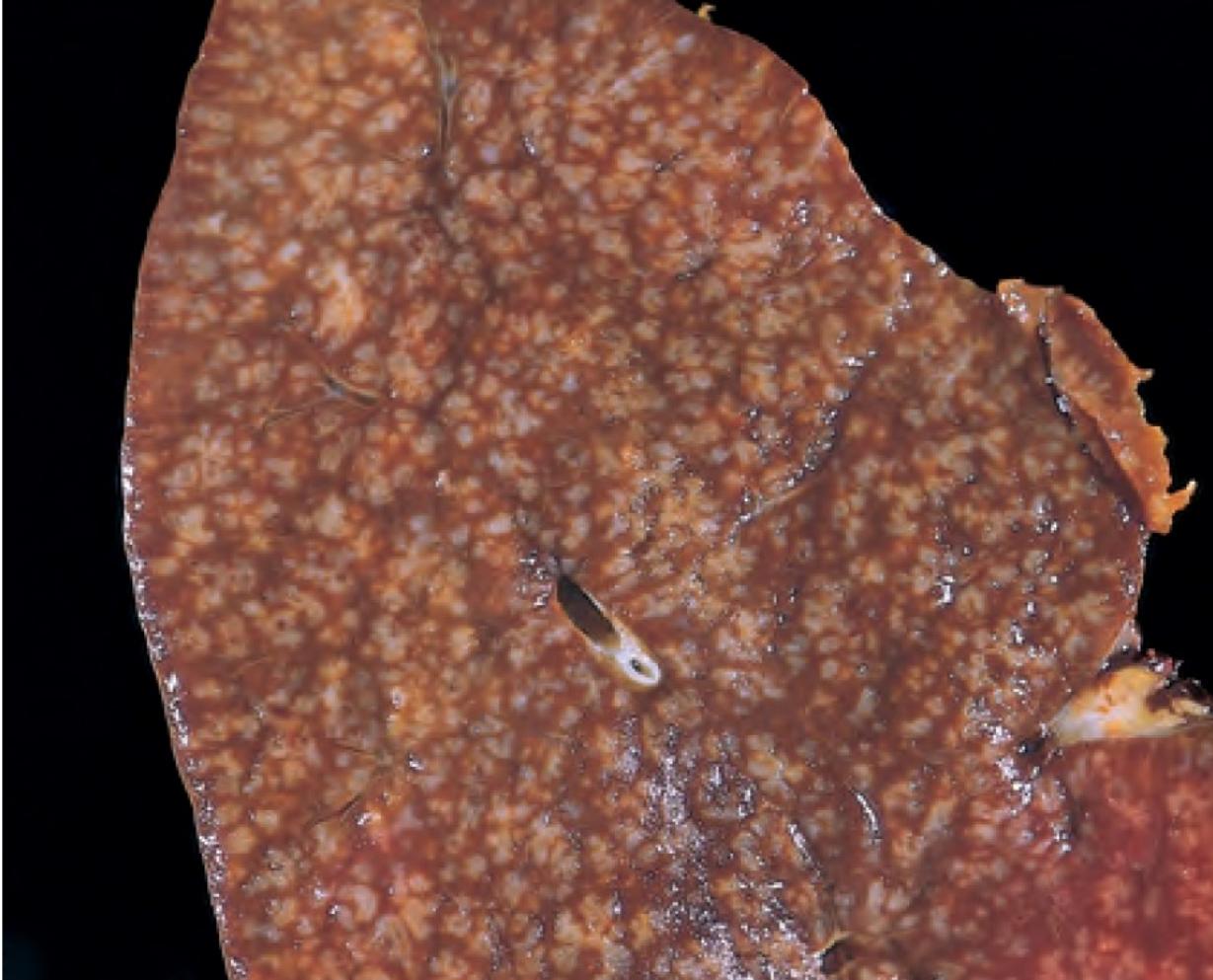
**central arterioles** are enclosed by lymphoid cell rich **periarteriolar lymphoid sheath (PALS)**, in white pulp.

B cells in these sheaths can form nodules as the largest masses of white pulp

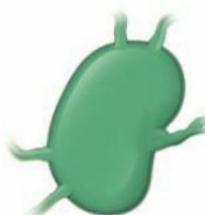
Blood flows into either a **closed circulation** passing directly into splenic sinuses (**S**) or an **open circulation**, being dumped from the vasculature into the lymphoid tissue of the red pulp's splenic cords. From there viable blood cells reenter the vasculature through the walls of the sinuses.

## Follicular lymphoma (spleen).

---



Prominent nodules represent white pulp follicles expanded by follicular lymphoma cells. Other indolent B-cell lymphomas (small lymphocytic lymphoma, mantle cell lymphoma, marginal zone lymphoma) can produce an identical pattern of involvement.

Features	(BALT, GALT, MALT)	Lymph Nodes	Thymus	Spleen
				
<b>Major function</b>	Immune surveillance of mucosal membranes	Filter lymph Generate immune responses to antigens in the lymph	Develops immunocompetent T lymphocytes	Filters blood Eliminates senescent erythrocytes Generates immune responses to circulating antigens
<b>Connective tissue capsule</b>	No	Yes	Yes	Yes; contains myofibroblasts
<b>Cortex</b>	No	Yes	Yes	No
<b>Medulla</b>	No	Yes	Yes	No
<b>Lymph nodules</b>	Yes	Yes; in the superficial cortex only	No	Yes; in white pulp only
<b>Afferent lymphatic vessels</b>	No	Yes; passing through the capsule	No	No
<b>Efferent lymphatic vessels</b>	Yes	Yes; leaving the node at the hilum	Yes (few); originate in connective tissue septa and capsule	Yes; inconspicuous, originate in white pulp near trabeculae
<b>High endothelial venules (HEVs)</b>	Yes; in well-established lymph nodules (i.e., tonsils, appendix, Peyer's patches)	Yes; associated with deep cortex	No	No
<b>Characteristic features</b>	Diffuse lymphatic tissue with randomly distributed lymphatic nodules underlying epithelial surface	Presence of lymphatic sinuses (subcapsular, trabecular, and medullary) Reticular meshwork	Thymic lobules Meshwork of epithelioreticular cells Hassall's corpuscles in medulla only	White pulp with PALS splenic nodules containing central artery Red pulp containing splenic sinuses, penicillar arteries, sheathed capillaries, and splenic cords

BALT, bronchus-associated lymphatic tissue; GALT, gut-associated lymphatic tissue; MALT, mucosa-associated lymphatic tissue; PALS, periarterial lymphatic sheath.

1) http://

ed.ted.com/lessons/you-are-your-microbes-jessica-green-and-karen-guillemin

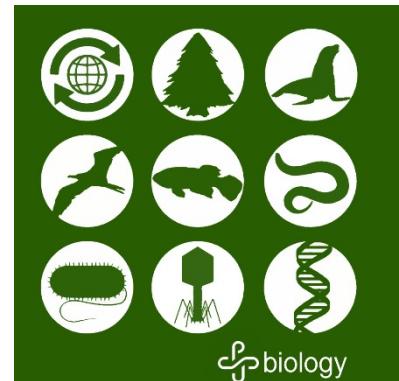
2) http://www.bozemanscience.com/digestive-system/

3) https://

www.khanacademy.org/partner-content/crash-course1/partner-topic-crash-course-bio-ecology/crash-course-biology/v/crash-course-biology-127

## Digestive Tract

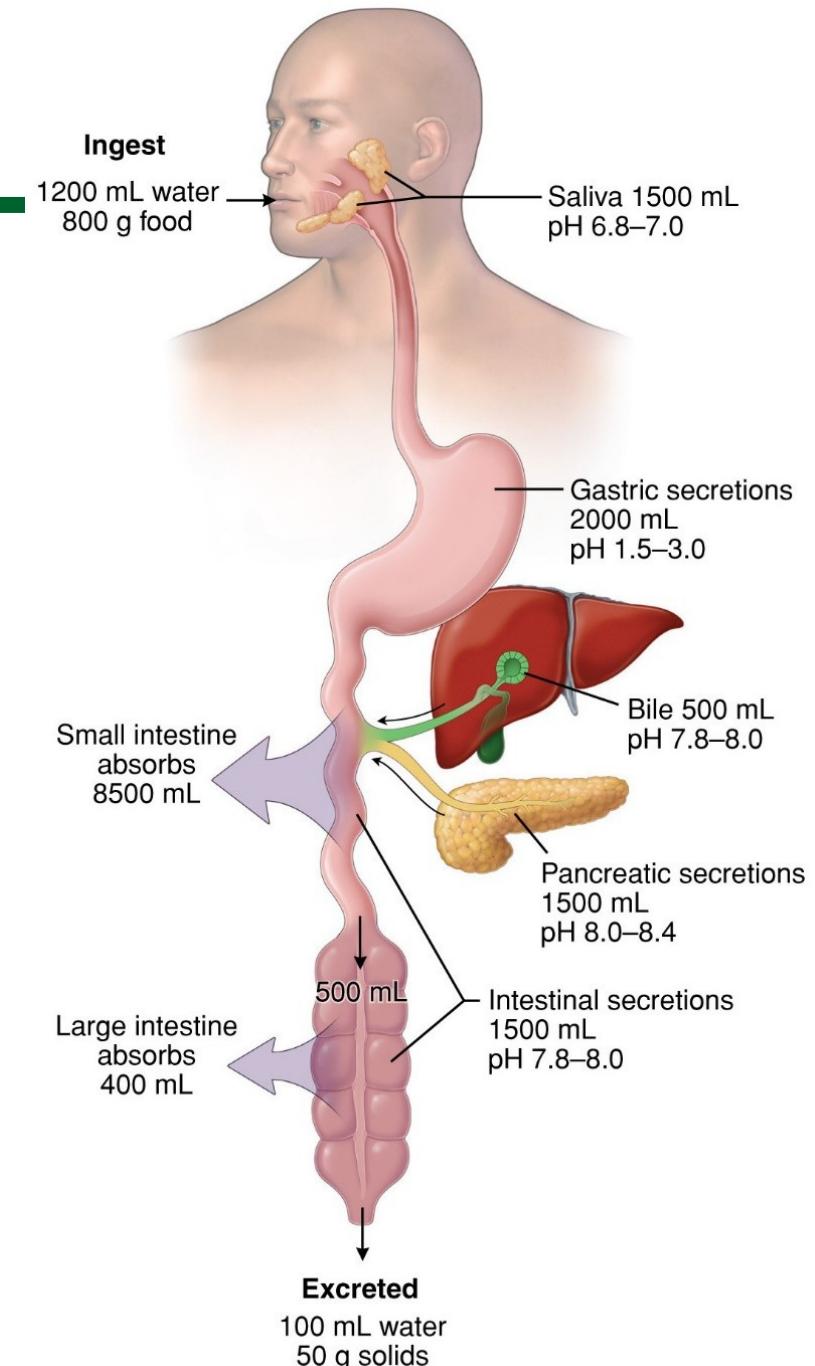
# BI 455 CHAPTER 15



# Digestive system has two anatomical subdivisions

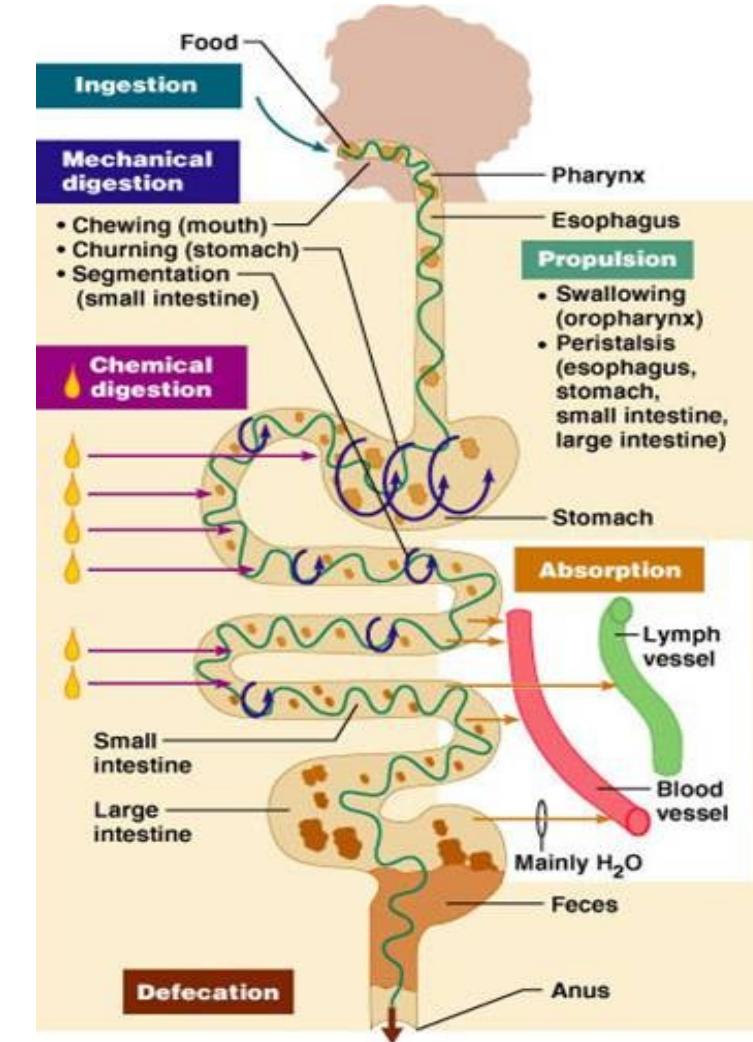
1. **Digestive tract (alimentary canal):** 30 ft long muscular tube extending from mouth to anus including mouth, pharynx, esophagus, stomach, small intestine, and large intestine
2. **Gastrointestinal (GI) tract:** stomach and intestines

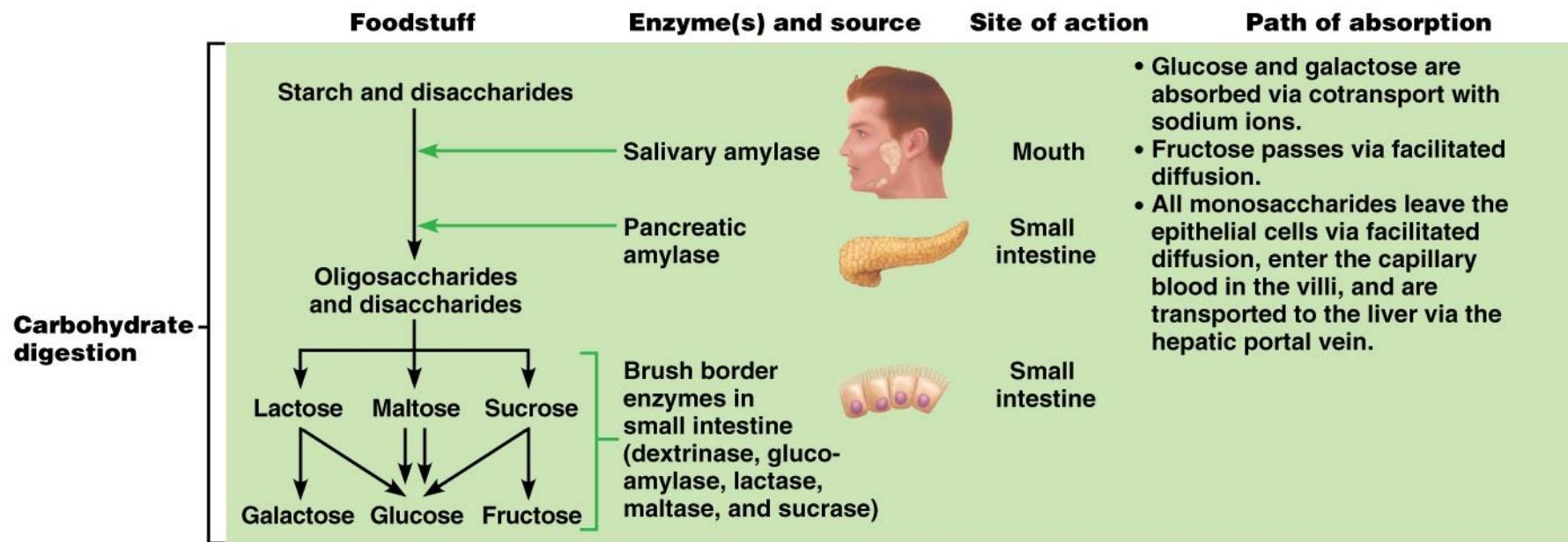
Accessory organs: Teeth, tongue, salivary glands, liver, gallbladder, and pancreas



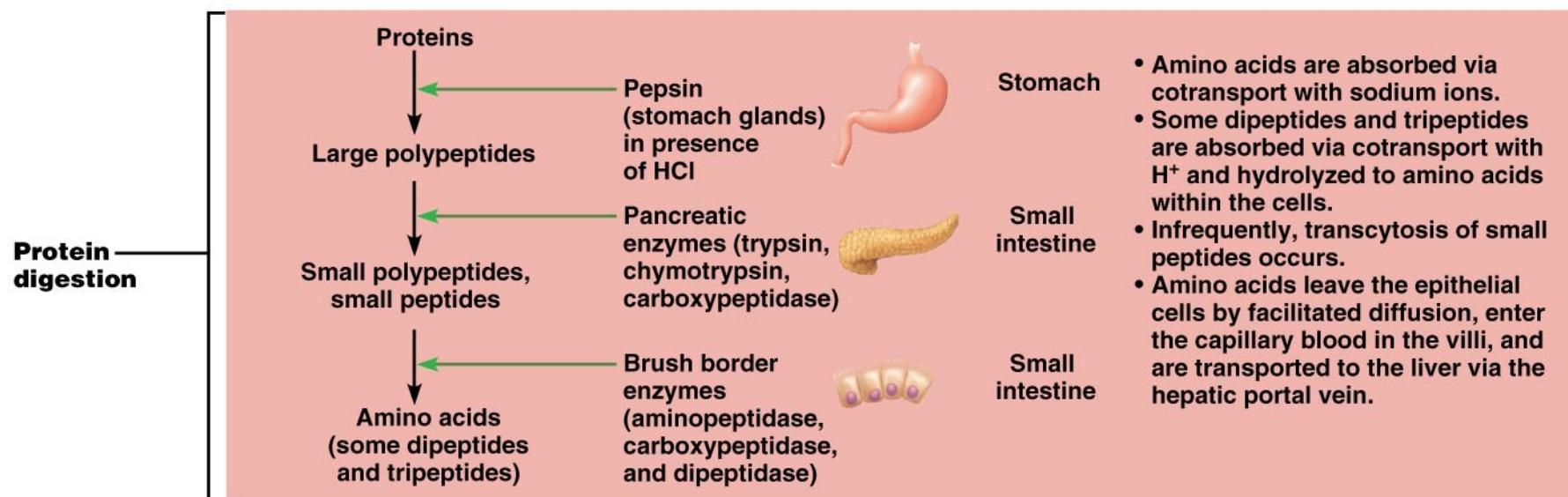
# Five stages of digestion

- 1. Ingestion:** selective intake of food
- 2. Digestion:** mechanical and chemical breakdown of food into a form usable by the body
- 3. Absorption:** uptake of nutrient molecules into the epithelial cells of the digestive tract and then into the blood and lymph
- 4. Compaction:** absorbing water and consolidating the indigestible residue into feces
- 5. Defecation:** elimination of feces

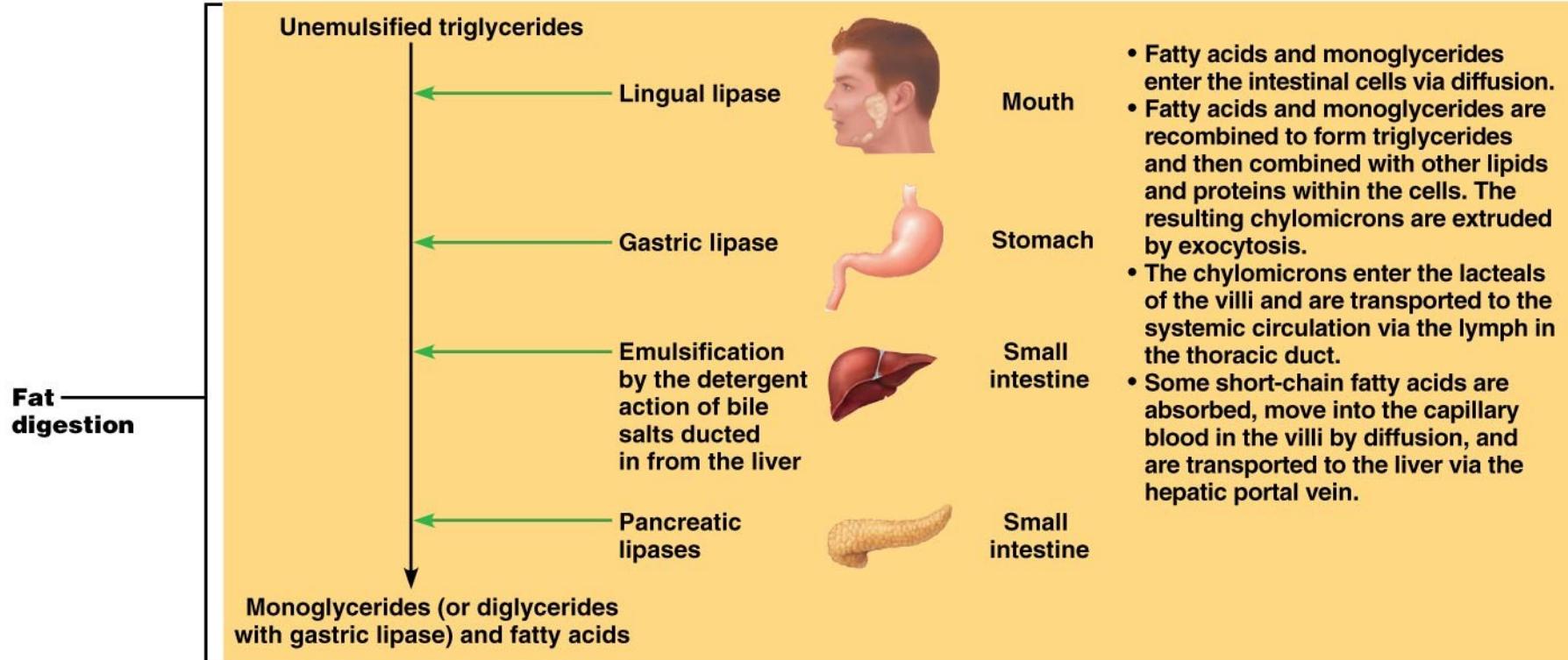




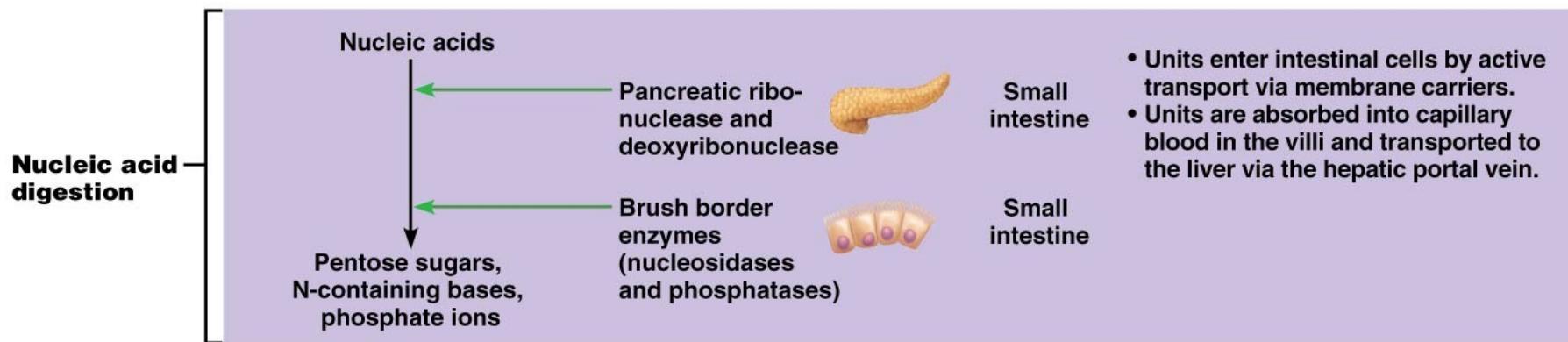
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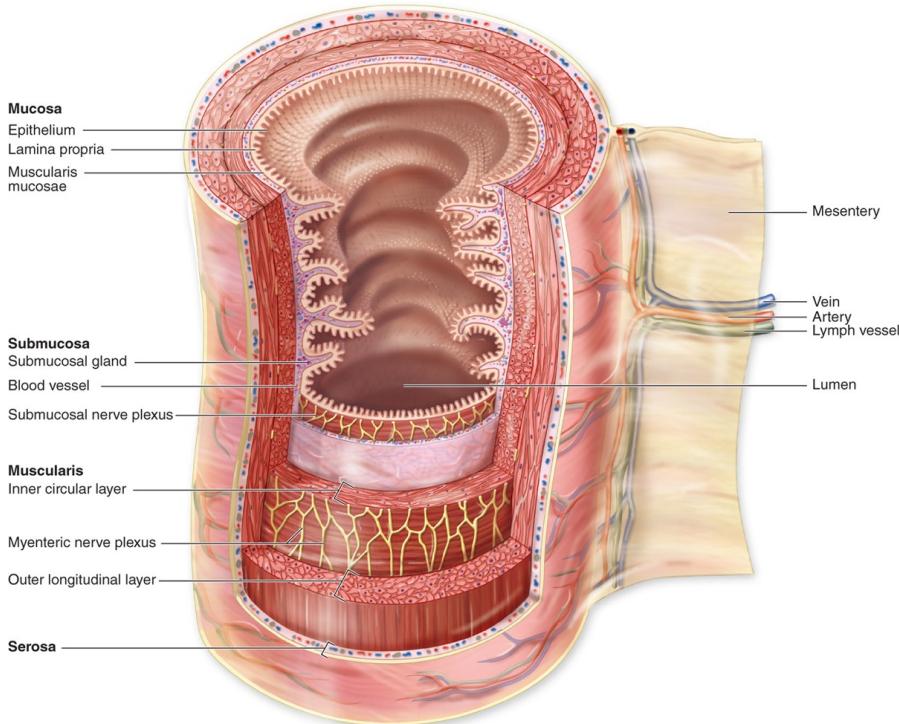
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- Fatty acids and monoglycerides enter the intestinal cells via diffusion.
- Fatty acids and monoglycerides are recombined to form triglycerides and then combined with other lipids and proteins within the cells. The resulting chylomicrons are extruded by exocytosis.
- The chylomicrons enter the lacteals of the villi and are transported to the systemic circulation via the lymph in the thoracic duct.
- Some short-chain fatty acids are absorbed, move into the capillary blood in the villi by diffusion, and are transported to the liver via the hepatic portal vein.

# Basic structural plan of digestive tract wall



## Mucosa:

- Epithelium
- Lamina propria (sometimes with MALT)
- Muscularis mucosae (smooth muscle)

**Submucosa:** blood vessels, lymphatic vessels, a nerve plexus, glands

## Muscularis externa

Inner circular layer: valves (sphincters)  
Outer longitudinal layer: propels food and residue through the tract

## Serosa (sometimes adventitia)

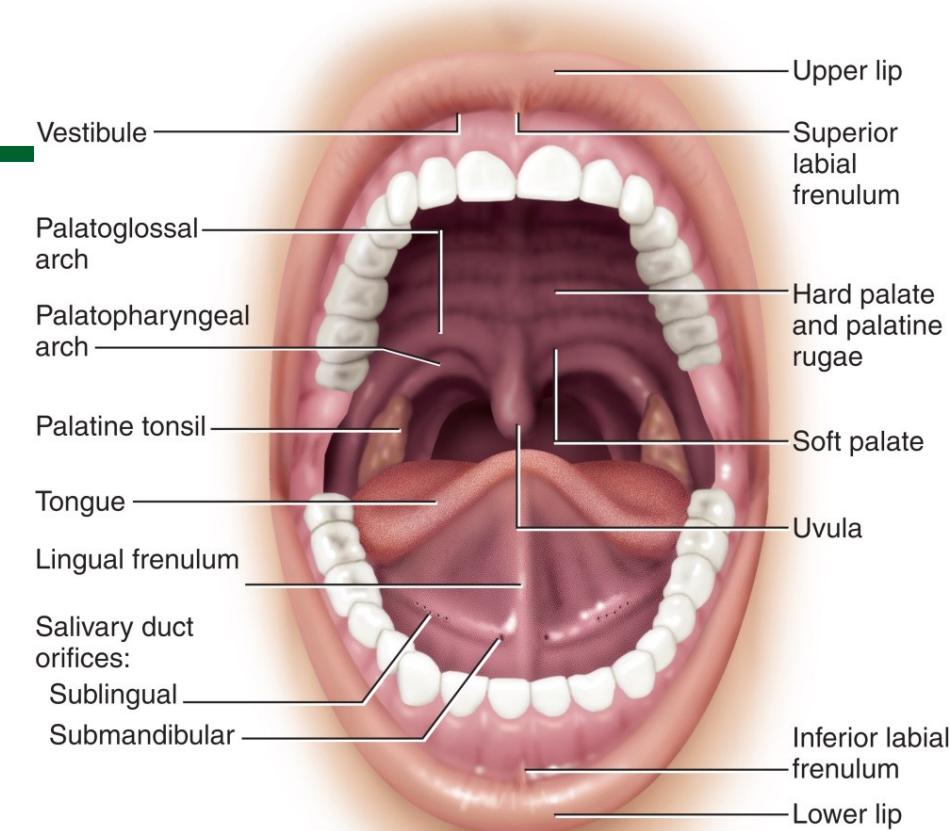
**>> MEDICAL APPLICATION** Infection disturbs plexuses in the digestive tract's enteric nervous system which then digestive tract motility and produces dilations in some areas. The rich autonomic innervation of the enteric nervous system also provides an anatomic explanation of the well-known actions of emotional stress on the stomach and other regions of the GI tract.

# The Mouth (oral or buccal cavity)

**Functions:** Ingestion (food intake), sensory responses to food (chewing and chemical digestion), swallowing, speech, and respiration

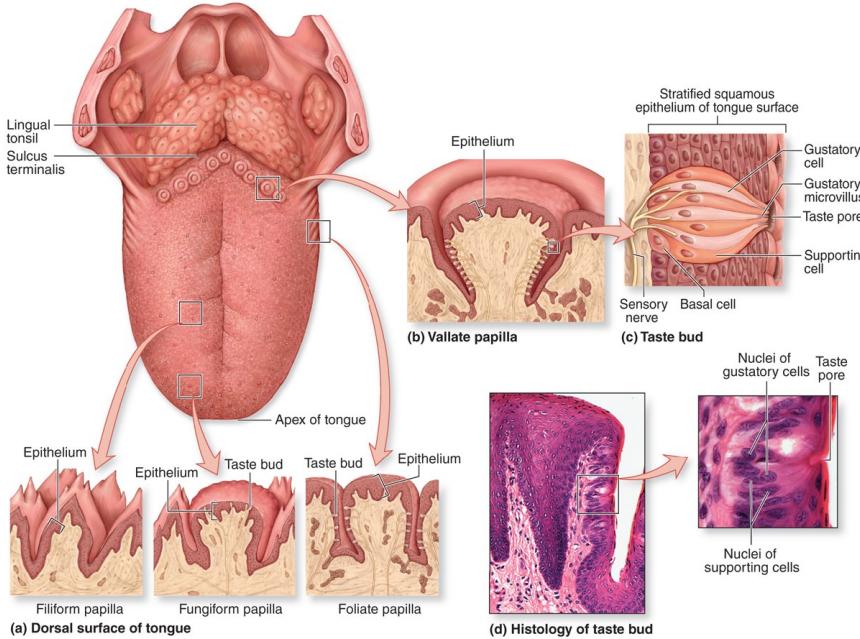
## Stratified squamous epithelium lining

- **Keratinized** in areas subject to food abrasion: gums and hard palate
- **Nonkeratinized** in other areas: floor of mouth, soft palate, and insides of cheeks and lips



» **MEDICAL APPLICATION** Viral infections with herpes simplex 1 cause death of infected epithelial cells that can lead to vesicular or ulcerating lesions of the oral mucosa or skin near the mouth. Such lesions, often painful and clustered, occur when the immune defenses are weakened by emotional stress, fever, illness, or local skin damage, allowing the virus, present in the local nerves, to move into the epithelial cells.

# Tongue, lingual papillae, and taste buds.



**Filiform papillae** provide friction to help move food during chewing.

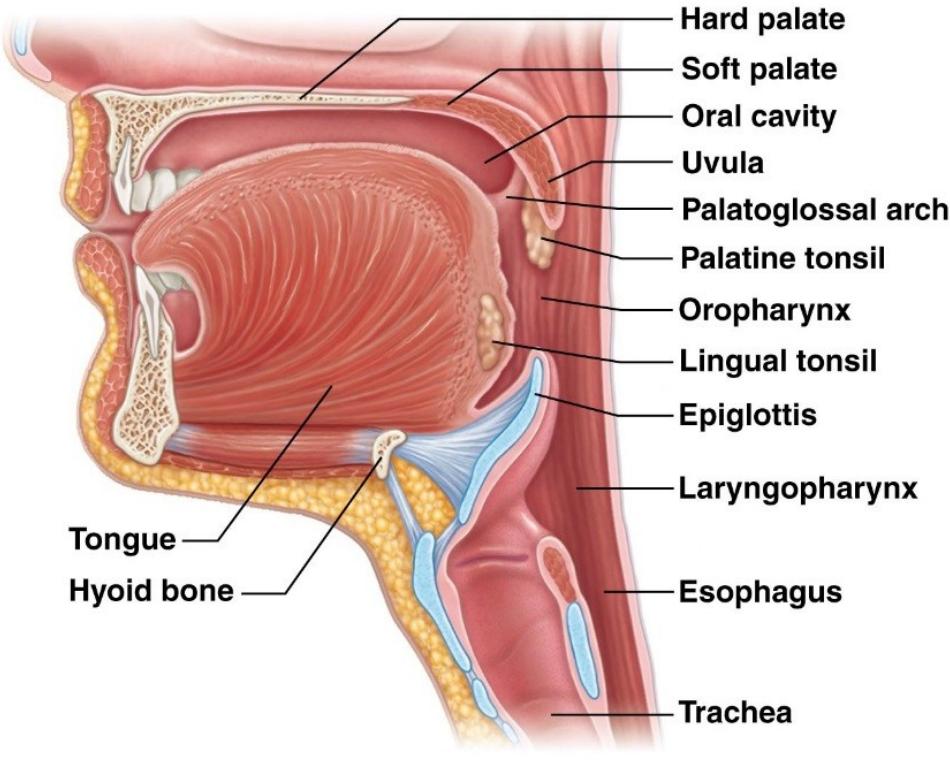
**Foliate papillae**: sides of the tongue, best developed in young children

**Fungiform papillae**: dorsal surface,

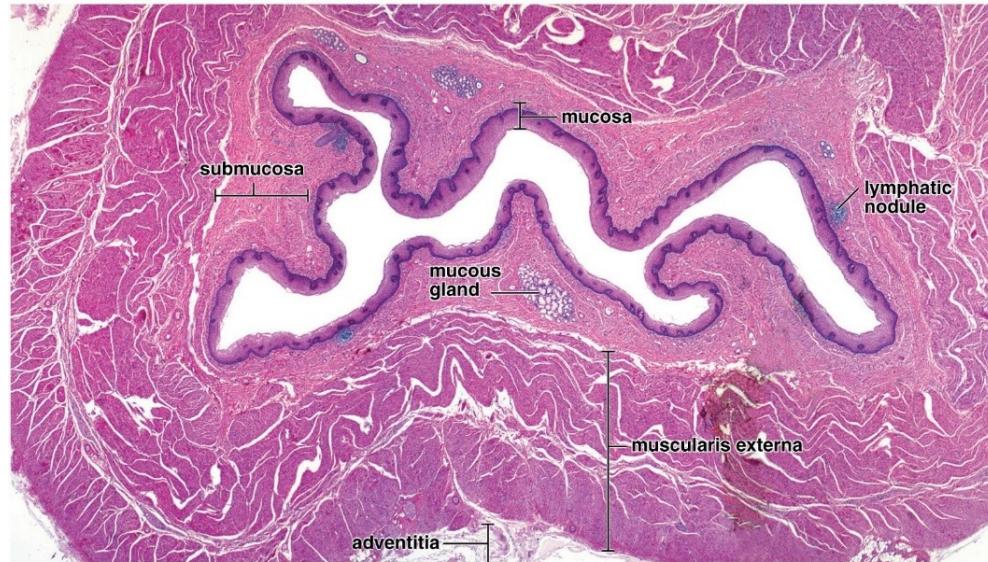
**Vallate papillae**: V-shaped line near the terminal sulcus.

**Taste buds** are present on fungiform and foliate papillae but are much more abundant on vallate papillae.

**Gustatory (taste) cells**: Microvilli at the ends of the gustatory cells project through an opening in the epithelium, the **taste pore**. Afferent sensory axons enter the basal end of taste buds and synapse with the gustatory cells.



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# The Esophagus

## Mucosa:

- thick stratified squamous epithelium,
- thin lamina propria containing occasional lymphatic nodules
- muscularis mucosae.

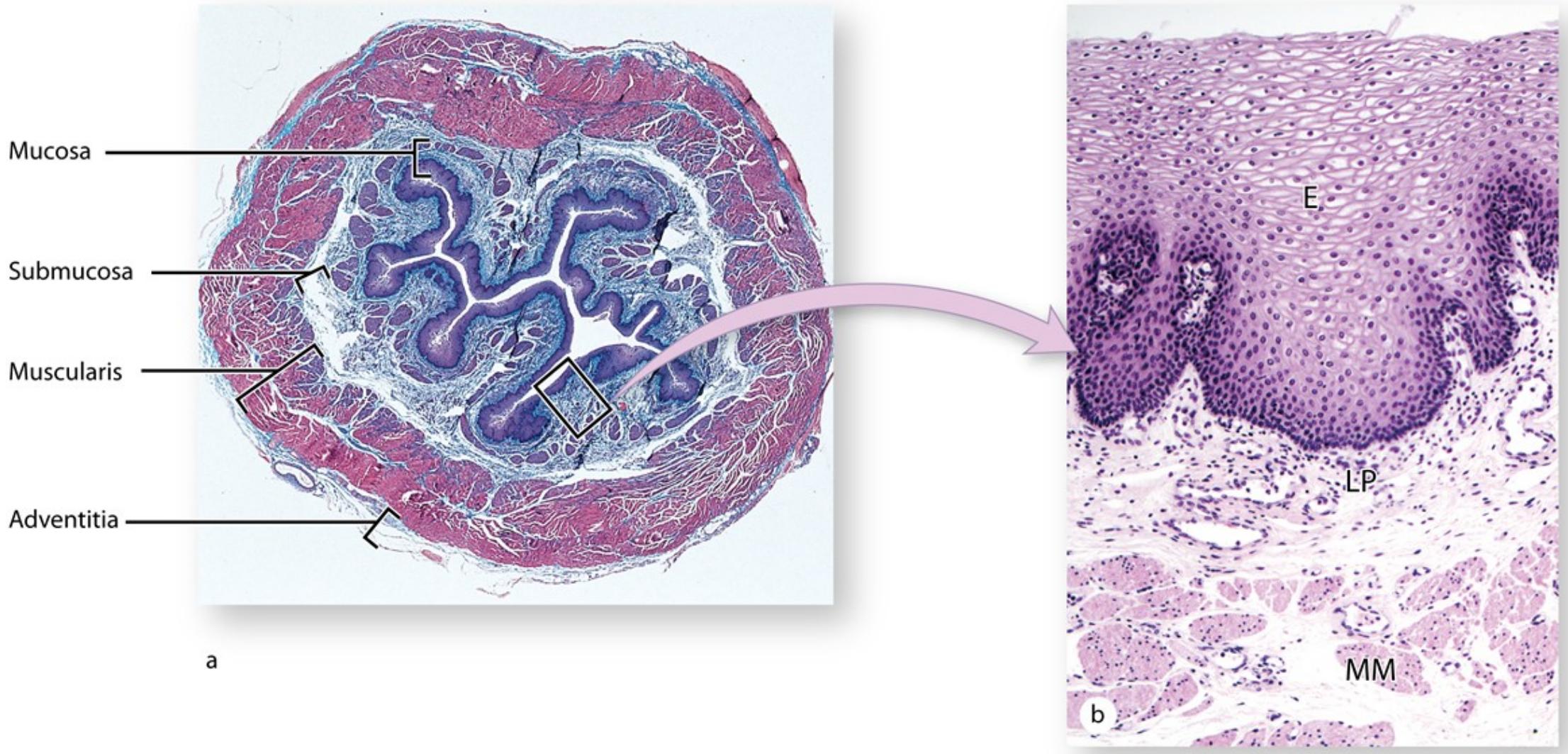
## Submucosa:

Mucous glands with ducts emptying into esophagus

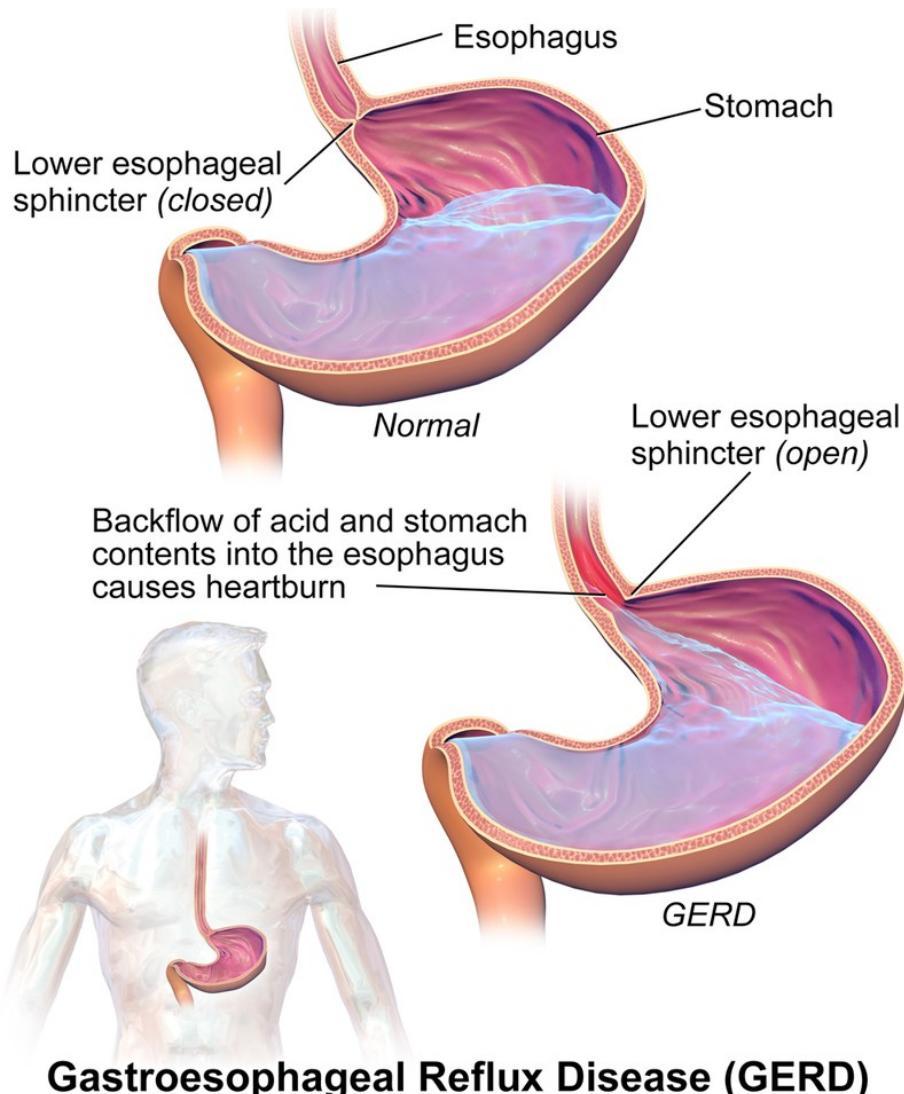
**Muscularis externa:** Thick inner layer circular smooth muscle outer layer longitudinal smooth muscle

## Adventitia

# The esophagus



# The esophagus transports swallowed material from the larynx to the stomach



## >> MEDICAL APPLICATION

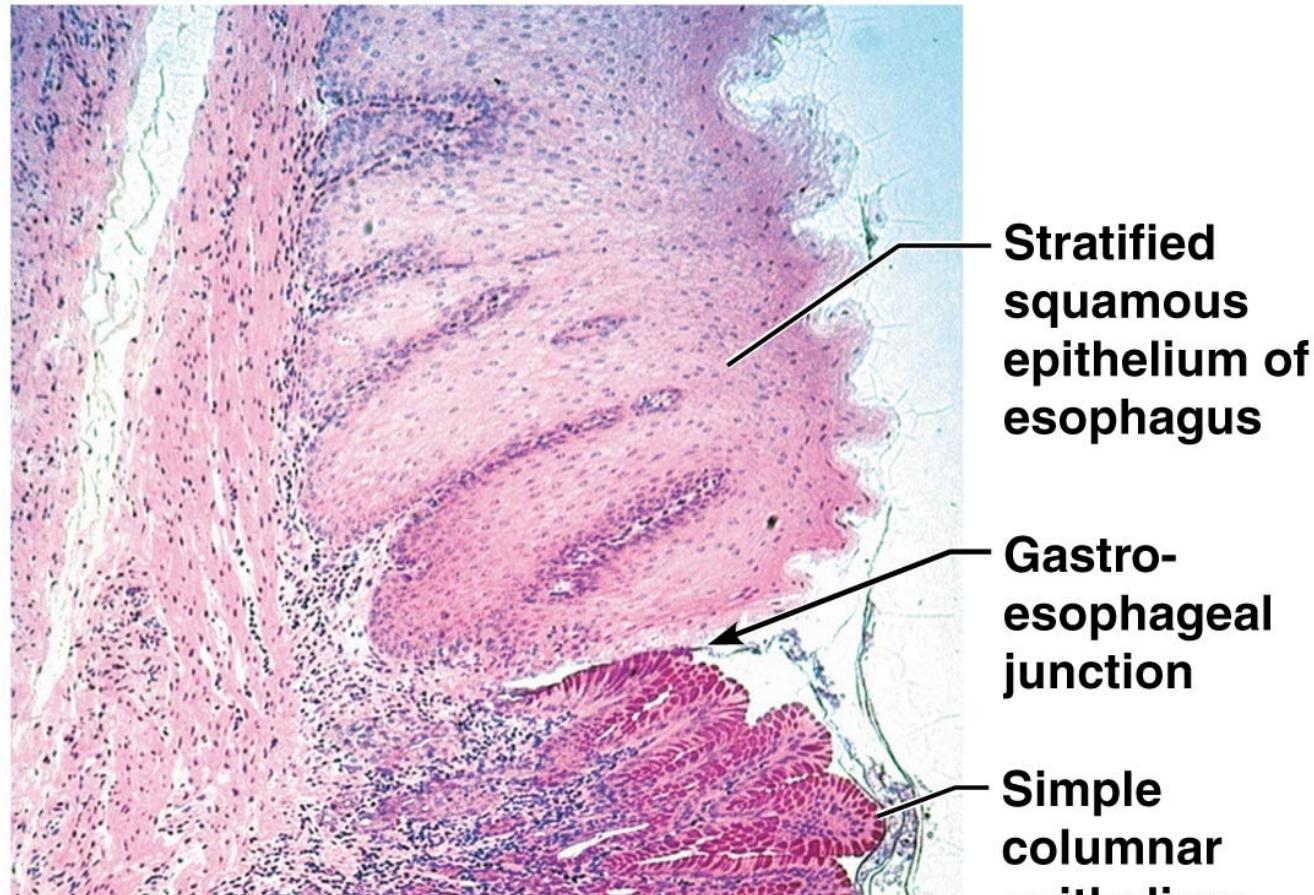
Those glands near the stomach tend to protect the esophagus from regurgitated gastric contents.

Under certain conditions they are not fully effective, and reflux results in pyrosis (heartburn).

This condition may progress to fully developed gastroesophageal reflux disease (GERD).

Understanding GERD (GERD #1): <https://www.youtube.com/watch?v=o8iShP84HP4>

# Esophogastric Junction



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Esophagus: **stratified squamous epithelium** (to handle abrasion)

Stomach: **simple columnar epithelium** (secretory & some absorptive functions), acid resistance

The main function of simple columnar epithelial cells are protection. The epithelium in the stomach and digestive tract provides an impermeable barrier against any bacteria that could be ingested but is permeable to any necessary ions.

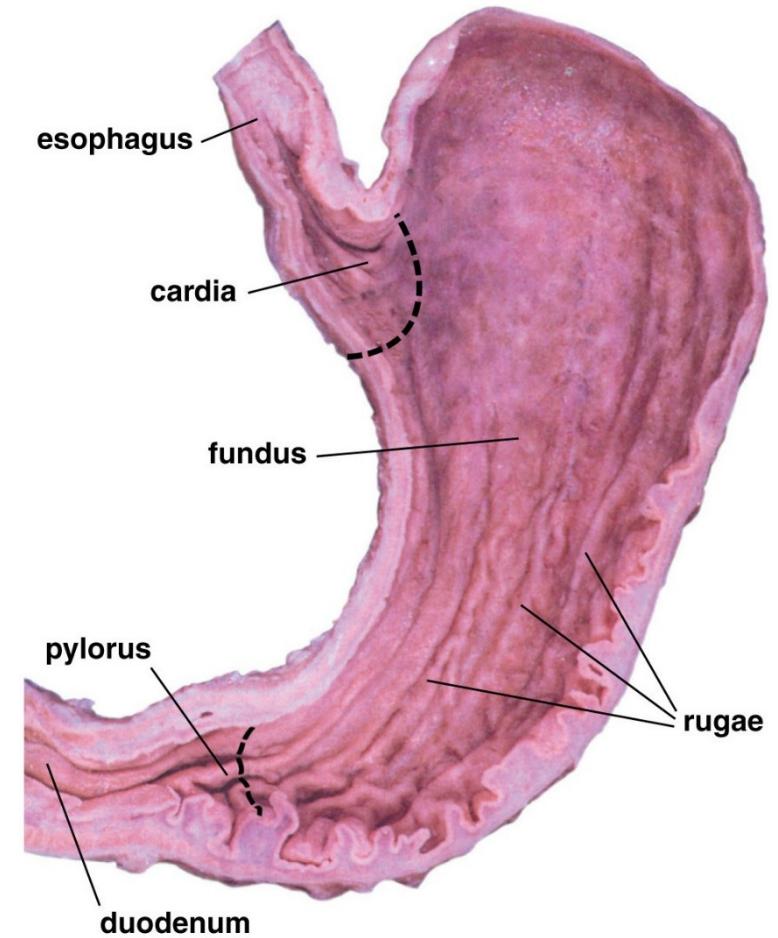
# The stomach is divided histologically into three regions based on the type of gland that each contains.

The stomach is a J shaped muscular sac which liquefies the food into **chyme**, and begins chemical digestion of protein and fat 50 mL (empty) to 4 L (full)

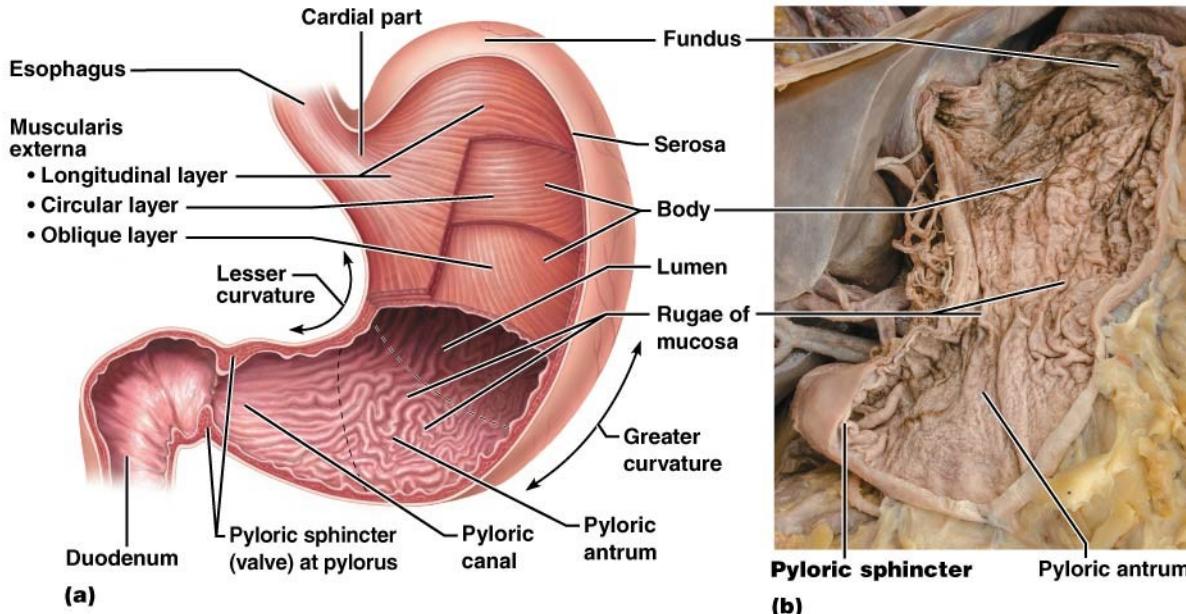
**Cardiac region (cardia):** near the esophageal orifice, contains the cardiac glands

**Pyloric region (pylorus):** proximal to the pyloric sphincter and contains the pyloric glands

**Fundic region (fundus):** situated between the cardia and pylorus and contains the fundic or gastric glands



# The major anatomical (as opposed to histological) stomach regions are the cardia, fundus, body, and pylorus



[http://highered.mheducation.com/sites/0072943696/student\\_view0/chapter16/animation\\_three\\_phases\\_of\\_gastric\\_secretion.html](http://highered.mheducation.com/sites/0072943696/student_view0/chapter16/animation_three_phases_of_gastric_secretion.html)

**Longitudinal gastric folds, or rugae:**  
Increase surface area

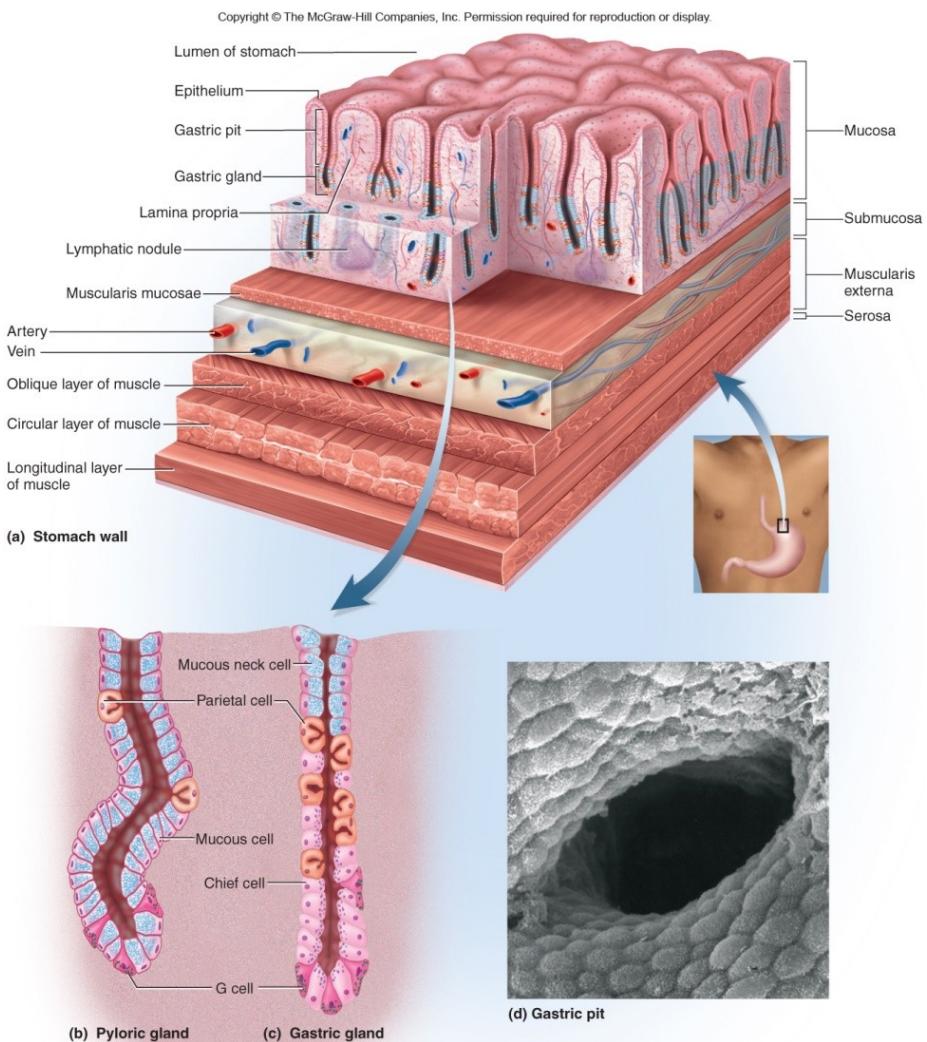
3 layers of **muscular externa** serves vigorous churning of food.

**Medical Application:**  
The stomach lining is not absorptive. However, some water, salts, and lipid-soluble drugs may be absorbed. For instance, alcohol and certain drugs such as aspirin or nonsteroidal anti-inflammatory drugs (NSAIDs) enter the lamina propria by damaging the surface epithelium.

# Mucosa: contains gastric pits that lead into gastric glands, lined by simple columnar epithelium containing five functional cell types.

Gastric pits: contain glands (gastric, pyloric, or cardiac)

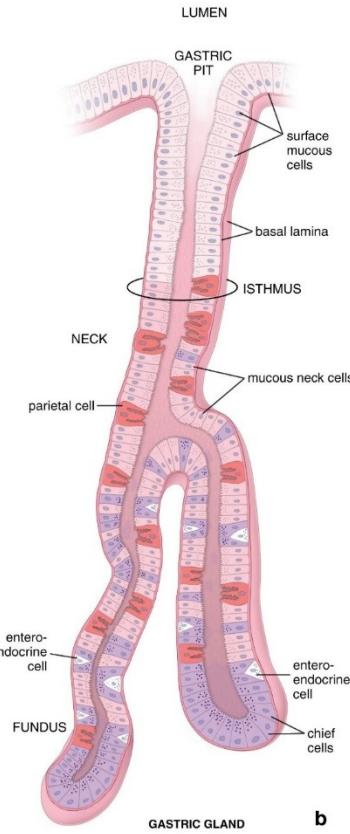
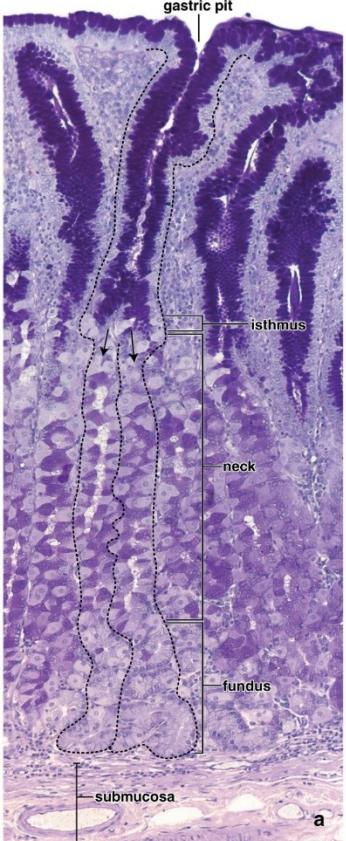
- **Mucous cells:** secrete mucus
- **Regenerative (stem) cells**
- **Parietal cells:** HCl, intrinsic factor (B12 absorption), ghrelin (hunger hormone)
- **Chief Cells:** produce gastric lipase (digests fats), pepsinogen (converted to pepsin, digests peptides)
- **Enteroendocrine (G) cells:** produces hormones, paracrine secretions, brain- gut peptides



**TABLE 25.1****Major Secretions of the Gastric Glands**

<b>Secretory Cells</b>	<b>Secretion</b>	<b>Function</b>
Mucous neck cells	Mucus	Protects mucosa from HCl and enzymes
Parietal cells	Hydrochloric acid	Activates pepsin and lingual lipase; helps liquefy food; reduces dietary iron to usable form ( $\text{Fe}^{2+}$ ); destroys ingested pathogens
	Intrinsic factor	Enables small intestine to absorb vitamin $\text{B}_{12}$
Chief cells	Pepsinogen	Converted to pepsin, which digests protein
	Gastric lipase	Digests fat
Enteroendocrine cells	Gastrin	Stimulates gastric glands to secrete HCl and enzymes; stimulates intestinal motility; relaxes ileocecal valve
	Serotonin	Stimulates gastric motility
	Histamine	Stimulates HCl secretion
	Somatostatin	Inhibits gastric secretion and motility; delays emptying of stomach; inhibits secretion by pancreas; inhibits gallbladder contraction and bile secretion; reduces blood circulation and nutrient absorption in small intestine
	Gut-brain peptides	Various roles in short- and long-term appetite regulation and energy balance

# Gastric Glands



**Medical Application:** Most of the bacteria entering the stomach are destroyed by HCl. However, some bacteria can adapt to the low pH of the gastric contents. ***Helicobacter pylori*** can create a protective basic “ammonia cloud” around itself, allowing it to survive. This bacteria degrades gastric epithelium, leading to 95% of all **Peptic Ulcer Disease (PUD)**.

**Medical Application: Intrinsic factor** complexes with **vitamin B12** in the stomach and duodenum, a step necessary for subsequent absorption of the vitamin in the ileum. Autoantibodies directed against intrinsic factor or parietal cells themselves lead to an intrinsic factor deficiency, resulting in malabsorption of vitamin B12 and **pernicious anemia** (loss of RBCs)

# **Small Intestine: most chemical digestion and nutrient absorption**

## **Duodenum:** pyloric valve to **duodenojejunal flexure**

- Receives stomach contents, pancreatic juice, and bile
- Neutralizes stomach acid is neutralized here
- Breaks down fats
- Pancreatic enzymes perform chemical digestion

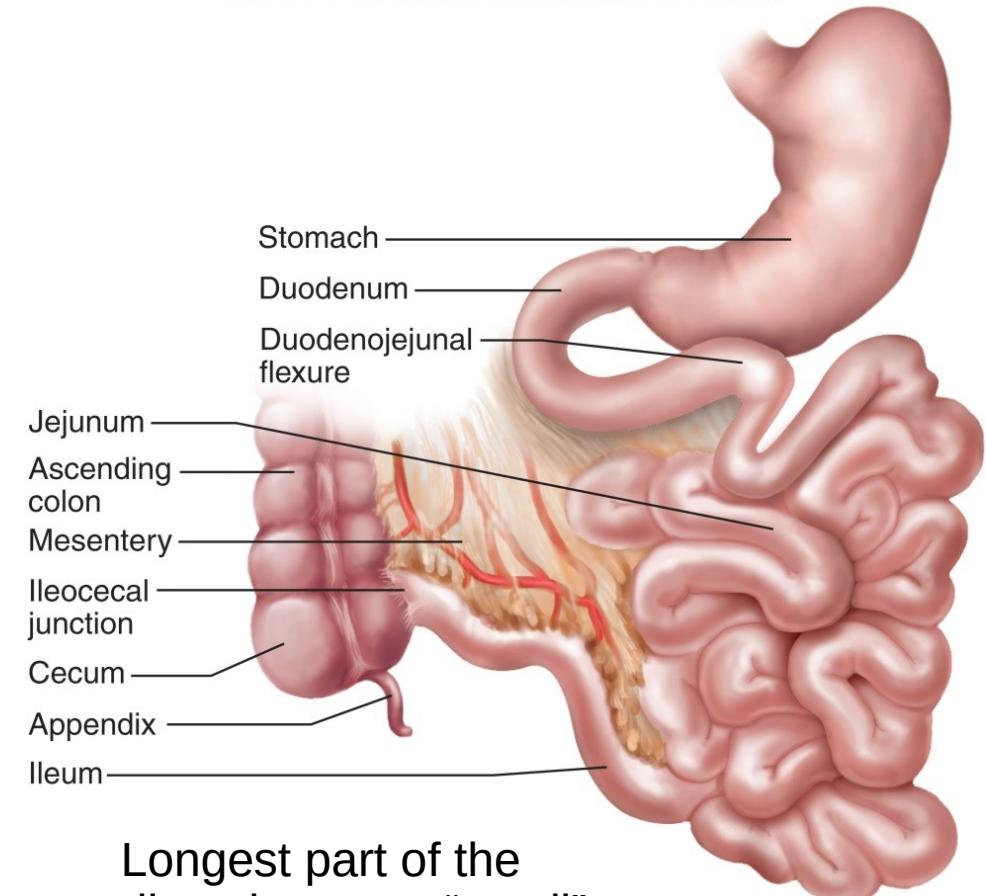
**Jejunum:** Most digestion and nutrient absorption, highly vascularized

**Ileum:** Peyer patches

**Ileocecal junction:** ileum to cecum

**Ileocecal valve:** sphincter, regulates food residue into large intestine

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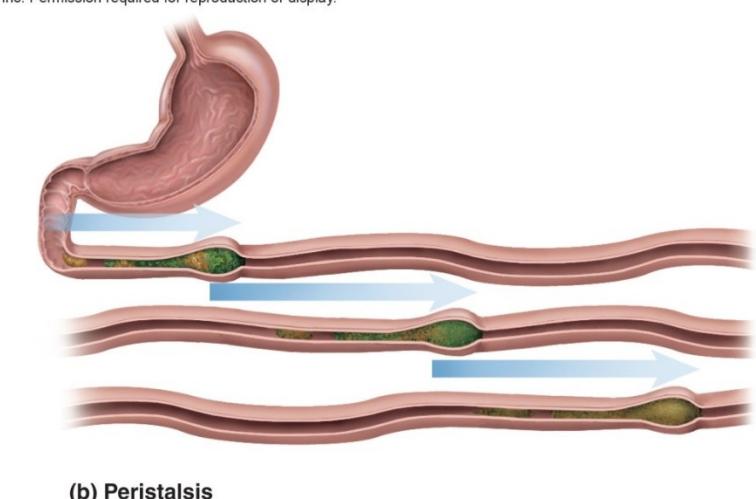
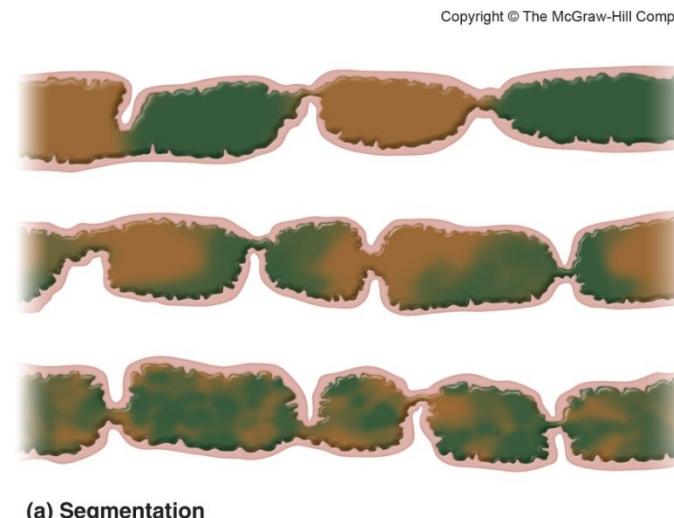
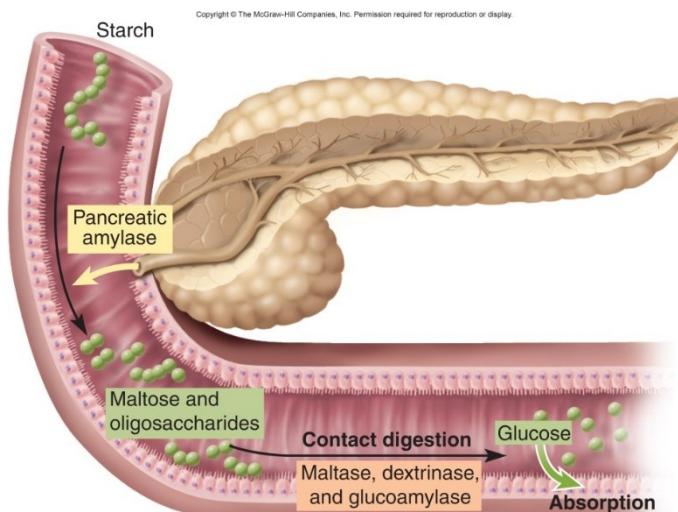
Longest part of the digestive tract, “small” refers to diameter

# Digestion Small Intestine

Pancreatic enzymes work together with brush border enzymes to accomplish chemical digestion

**Segmentation:** Pacemaker cells induce ring like constrictions which appear and disappear, allowing chyme to pass over microvilli for contact digestion

**Peristaltic wave** begins after segmentation, moving chyme toward colon over a period of 2 hours



Surface area for effective digestion and absorption increased by:

**Circular folds** (plicae circulares)

**Villi**

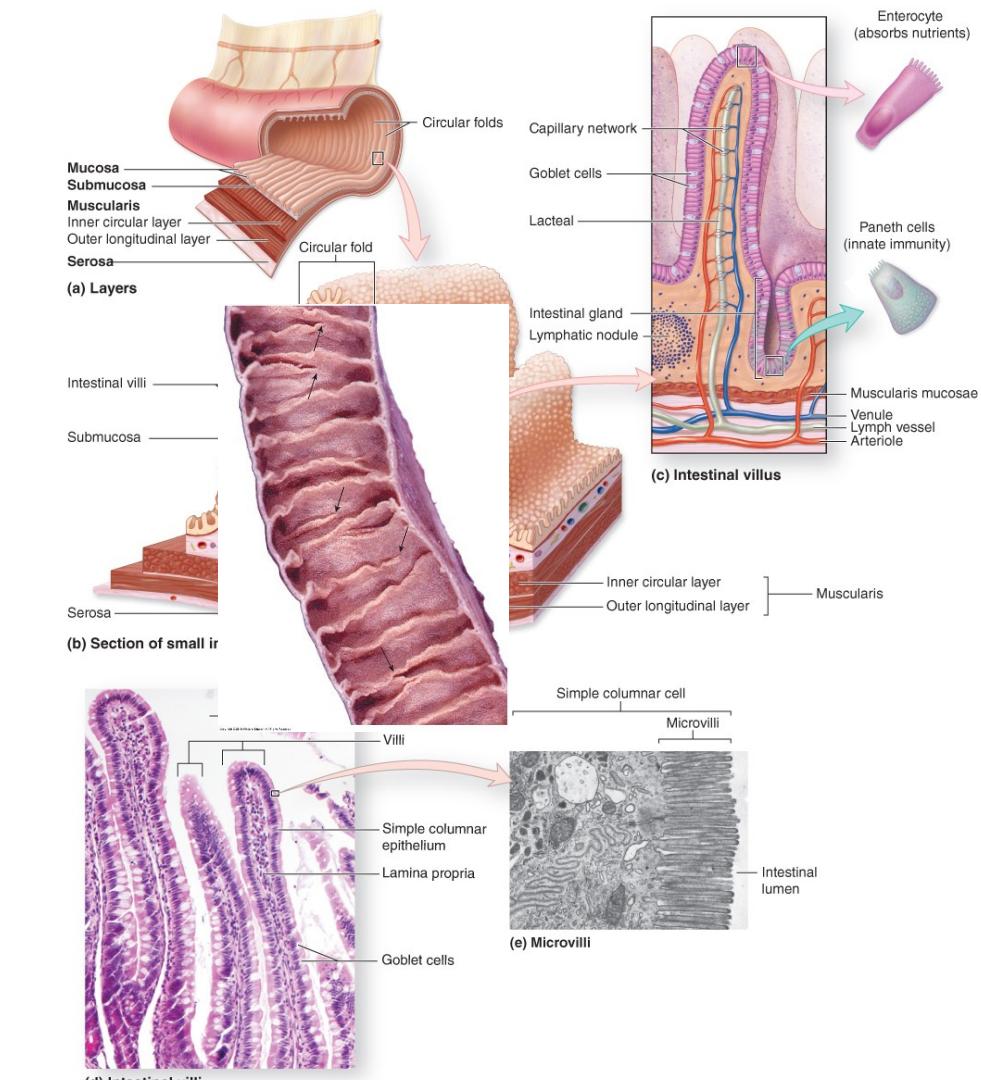
**Microvilli:** contain **brush border enzymes** for contact digestion (chyme must contact the brush border for digestion to occur)

Intestinal churning of chyme ensures contact with the mucosa

**Intestinal crypts** (crypts of Lieberkühn): dividing stem cells, and Paneth cells which secrete lysozyme, phospholipase, and defensins (resist bacterial invasion of the mucosa)

**Duodenal glands:** Neutralize stomach acid and shield the mucosa from its erosive effects

## Microscopic Anatomy of Small Intestine



# **Cells of the Intestinal Mucosal Epithelium**

**Enterocytes:** absorption

**Goblet cells:** unicellular mucin-secreting gland

**Paneth cells:** secrete antimicrobial substances

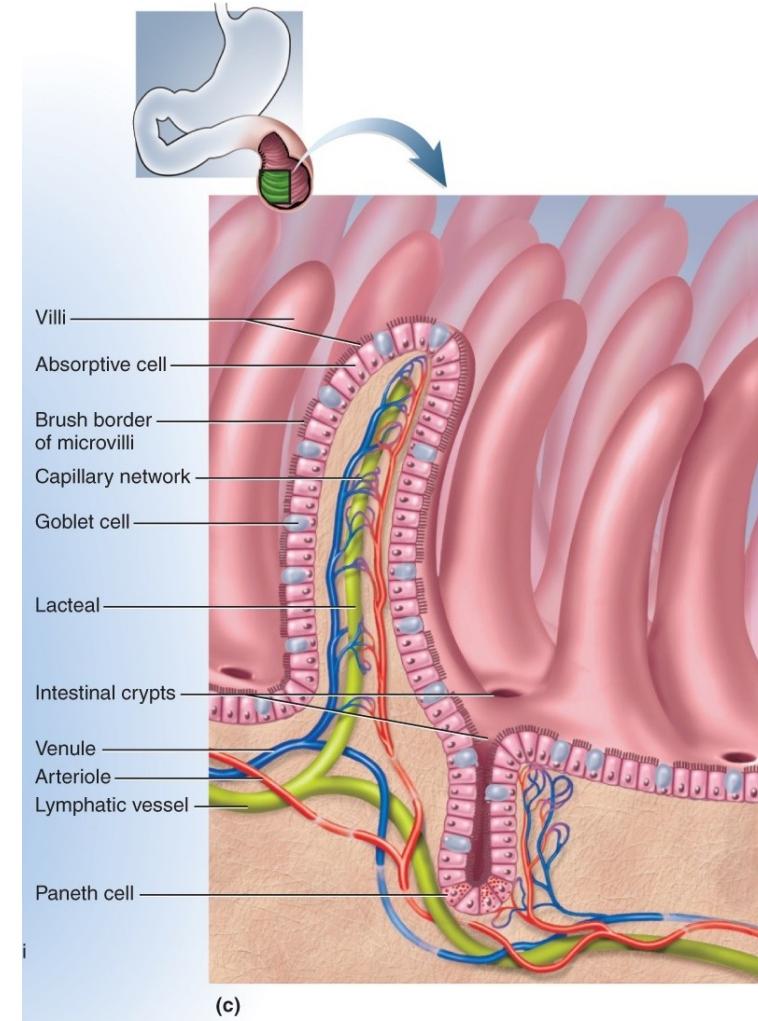
**Enteroendocrine cells:** produce endocrine hormones

**M cells (microfold cells):** specialized cells located in the epithelium that covers lymphatic nodules in the lamina propria

## **MEDICAL APPLICATION:**

Celiac disease (celiac sprue) is a disorder of the small intestine mucosa that causes malabsorption and can lead to damage or destruction of the villi. The cause of celiac disease is an immune reaction against gluten or other proteins in wheat and certain other types of grain. The resulting inflammation affects the enterocytes, leading to reduced nutrient absorption.

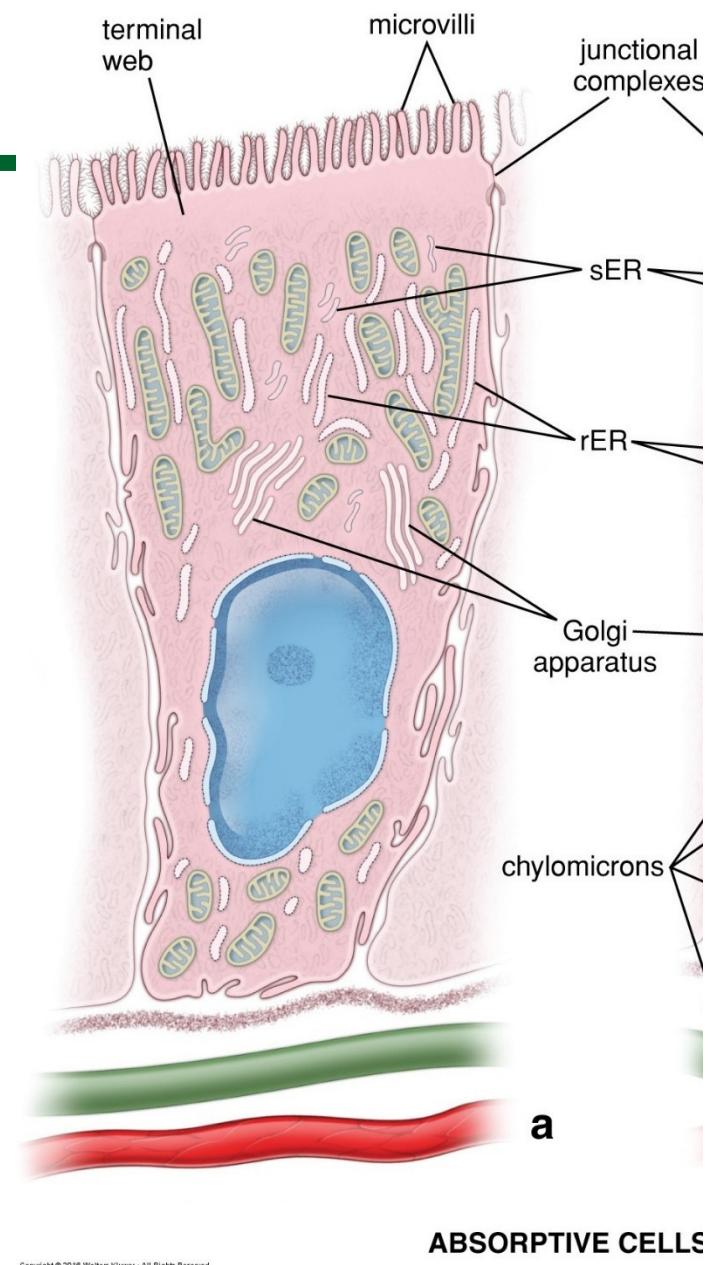
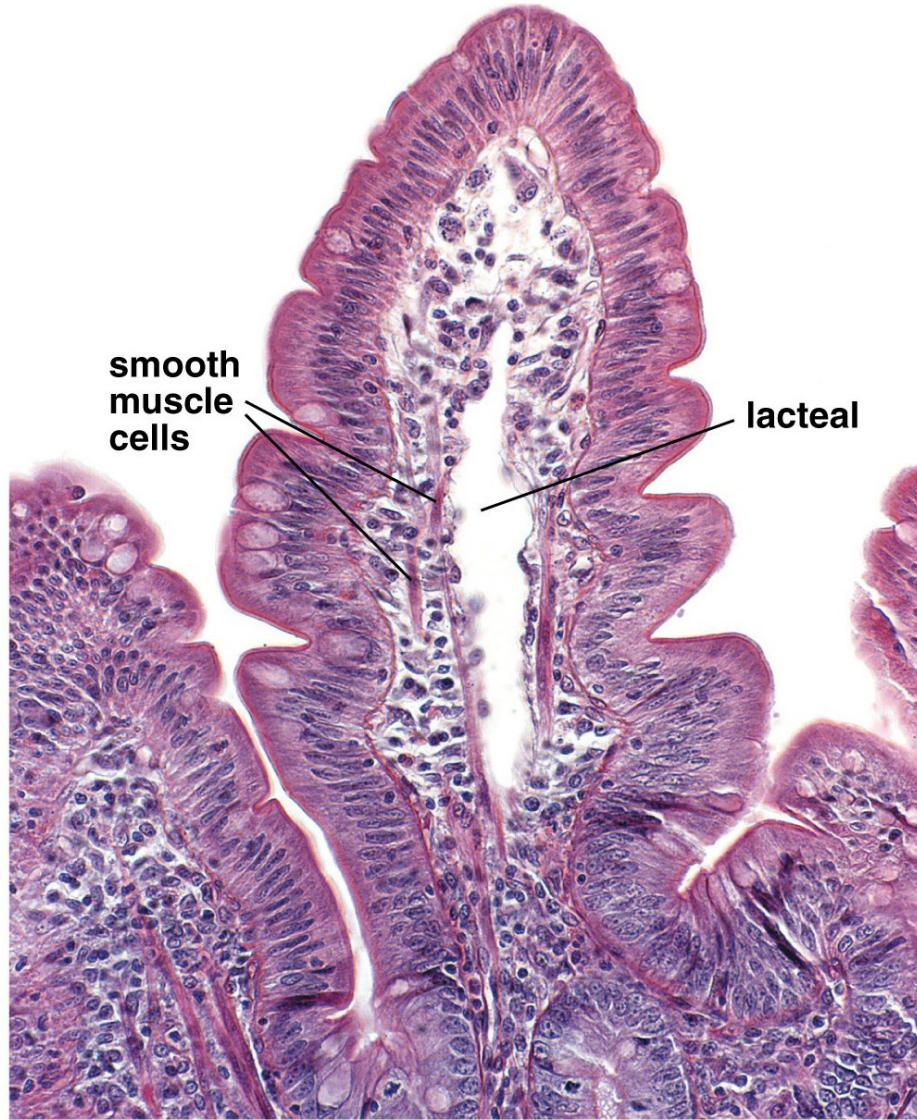
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# Enterocytes Absorb and Transport Substances to Circulation

**Tight junctions** establish a barrier between the intestinal lumen and the epithelial intercellular compartment.

**Enterocytes** are also secretory cells, producing enzymes needed for terminal digestion and absorption as well as secretion of water and electrolytes.



ABSORPTIVE CELLS

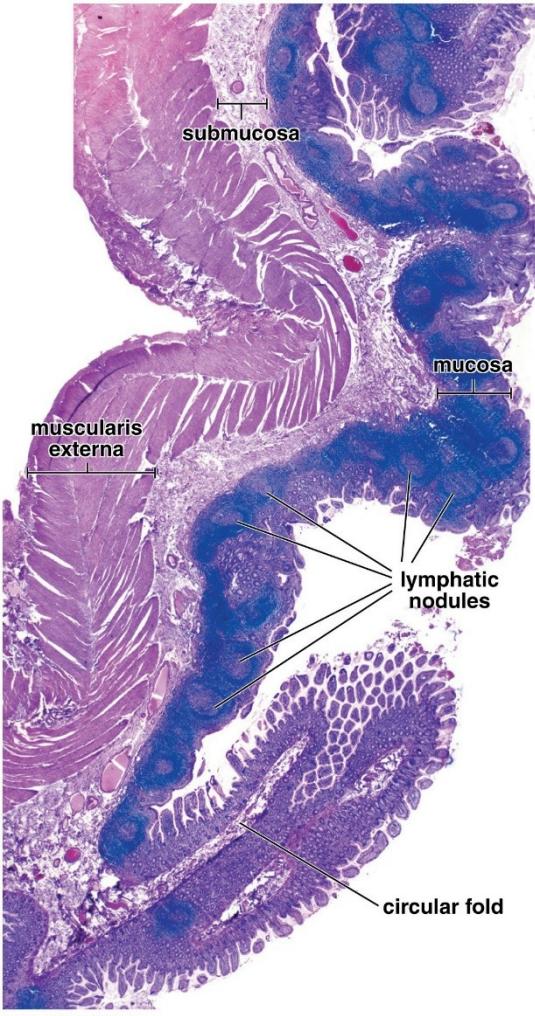
# Duodenal Brunner's Glands De-acidify Stomach Chyme



Submucosa (dense connective tissue) in duodenum contains Brunner's glands.

**Brunner's Glands** are branched, tubular glands with secretions of pH of 8.1 to 9.3 which protect the proximal small intestine by neutralizing the acid containing chime. It also brings the intestinal contents close to the optimal pH for the pancreatic enzymes that are also delivered to the duodenum.

# GALT in the Lamina Propria of the SI



Mucosal surface of the gut tube is constantly challenged by the presence of ingested microorganisms (i.e., viruses, bacteria, parasites) and toxins.

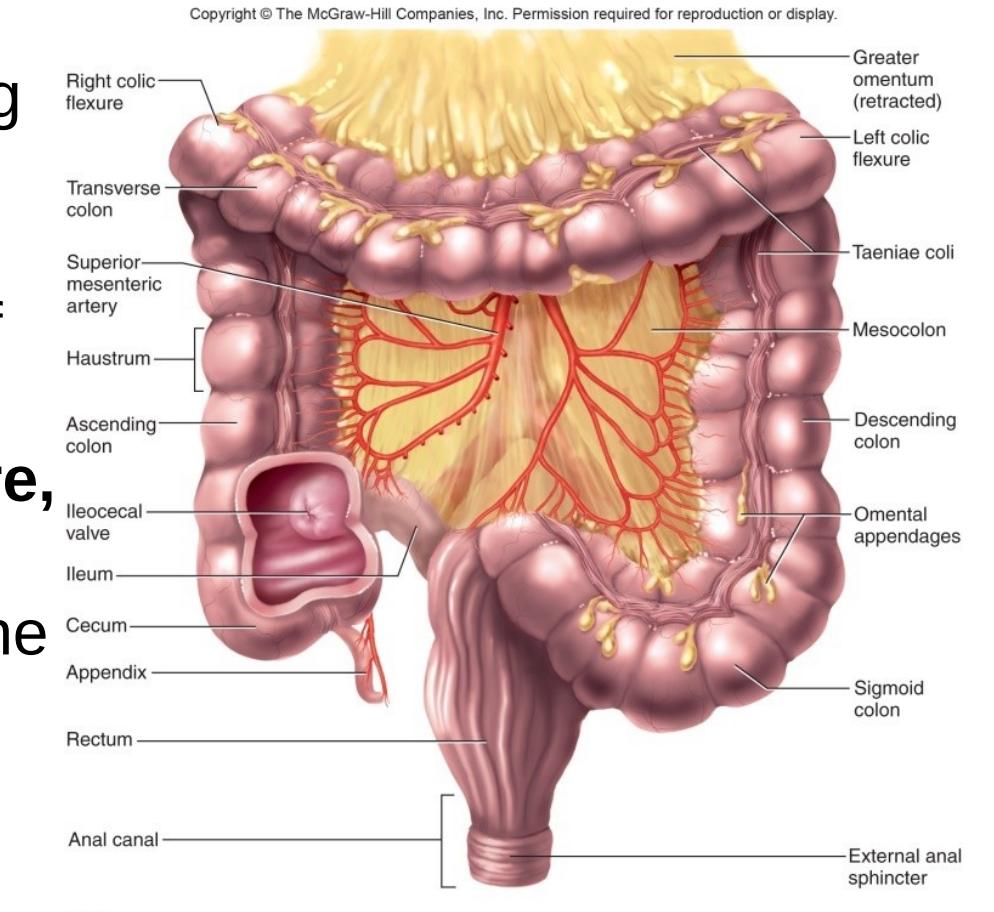
GALT serves as an immunologic barrier throughout the length of the gastrointestinal tract.

**MEDICAL APPLICATION:** Crohn's disease is a chronic inflammatory bowel disease that occurs most commonly in the ileum or colon, resulting from a poorly understood combination of immune, environmental, and genetic factors. Excessive lymphocytic activity and inflammation occur in any or all layers of the tract wall, producing pain, localized bleeding, malabsorption, and diarrhea.

# Large Intestine Receives Undigestible Residue

Large intestine receives about 500 mL/day, reduces it to about 150 mL of **feces** by absorbing water and salts. Eliminates feces by **defecation**

- **Cecum:** inferior to ileocecal valve
- **Vermiform appendix:** attached to lower end of cecum, densely populated with lymphocytes
- **Ascending colon, right colic (hepatic) flexure, transverse colon, left colic (splenic) flexure, and descending colon** frame the small intestine
- **Sigmoid colon** is S-shaped portion leading down into pelvis
- **Rectum:** portion ending at anal canal
- **Anal canal:** final 3 cm of the large intestine



**Taenia coli:** longitudinal fibers

**Haustra Coli:** pouches in the colon caused by the muscle tone of the taeniae coli

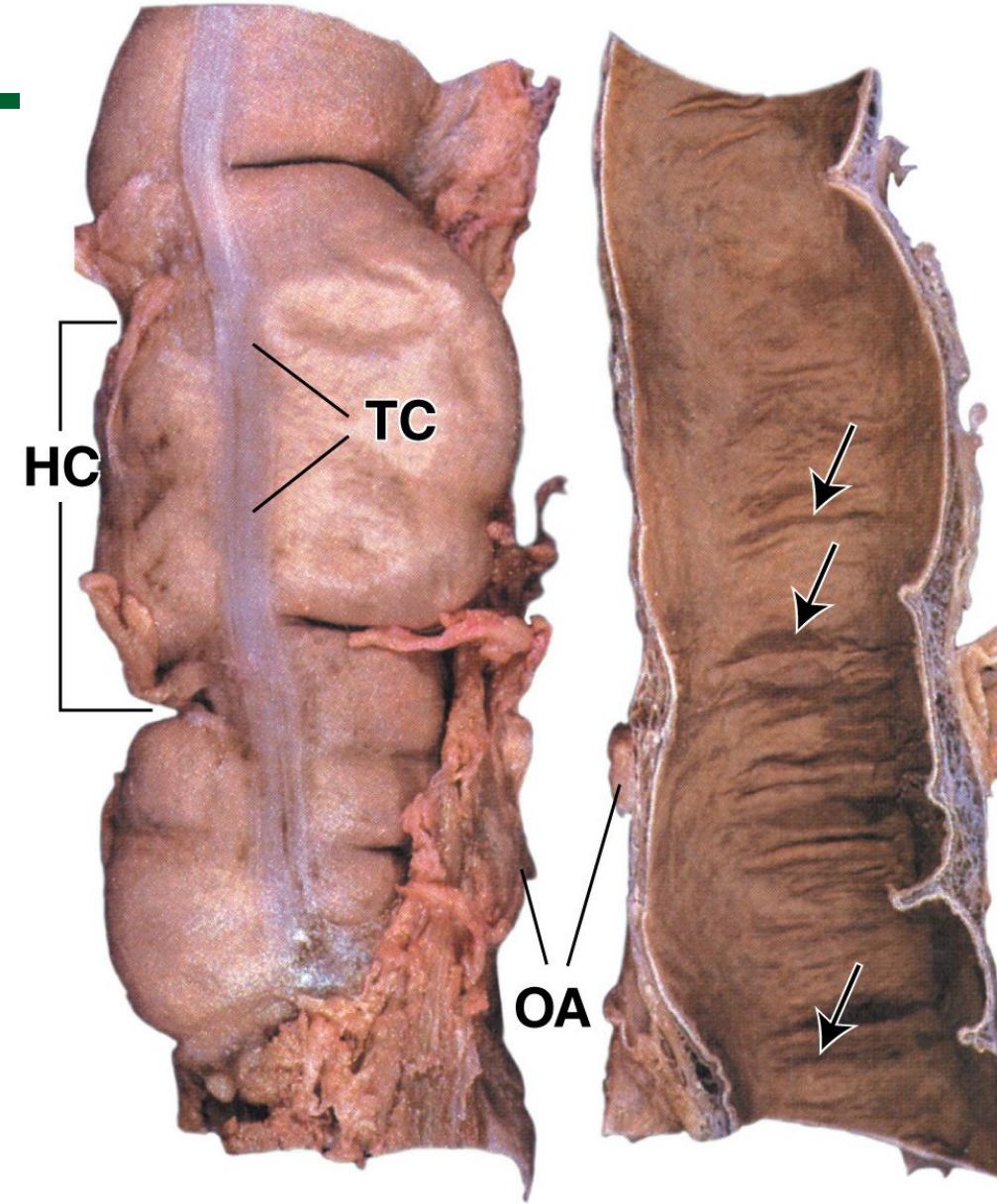
# Medical Applications

**Herniation:** outpocketing of the mucosa and submucosa of the colon can occur between the teniae coli resulting from structural defects in the colon wall or from high intraluminal pressure or constipation.

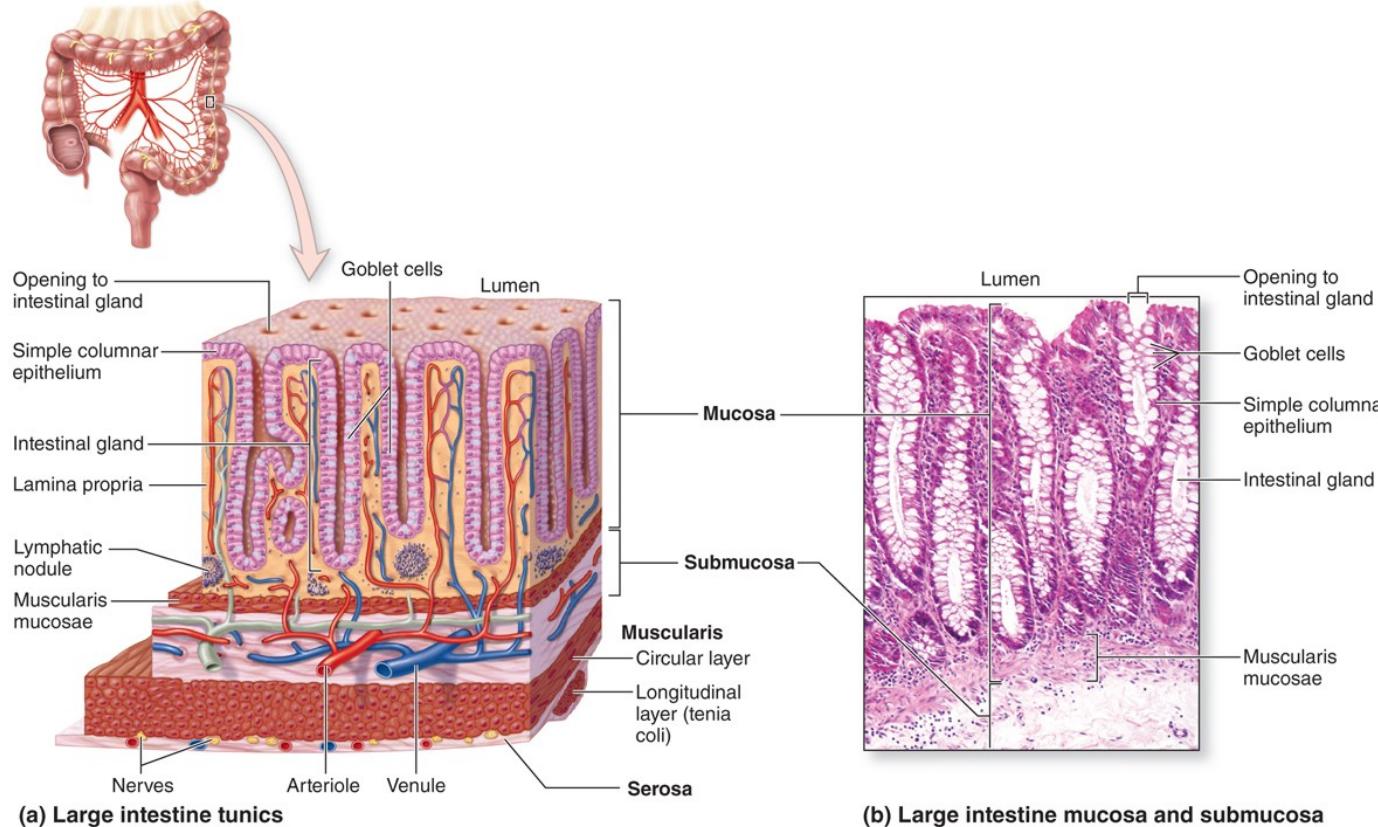
**Bacterial flora populate large intestine:** Digest cellulose and other undigested carbohydrates, help in synthesis of vitamins B and K. Fecal

**Flatus (intestinal gas):** Average person produces 500 mL per day (flatus) from 7 to 10 L of gas present but reabsorbed

Most is swallowed air, but hydrogen sulfide, indole, and skatole produce odor



# Wall of the Large Intestine

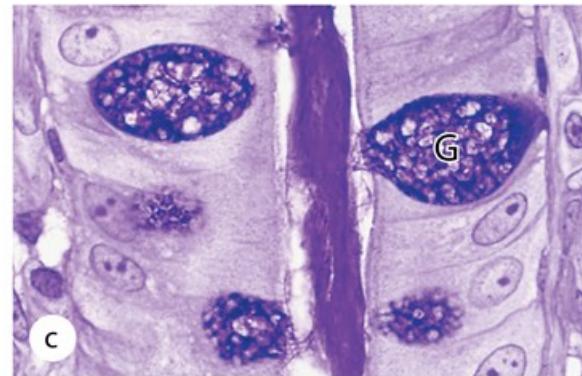
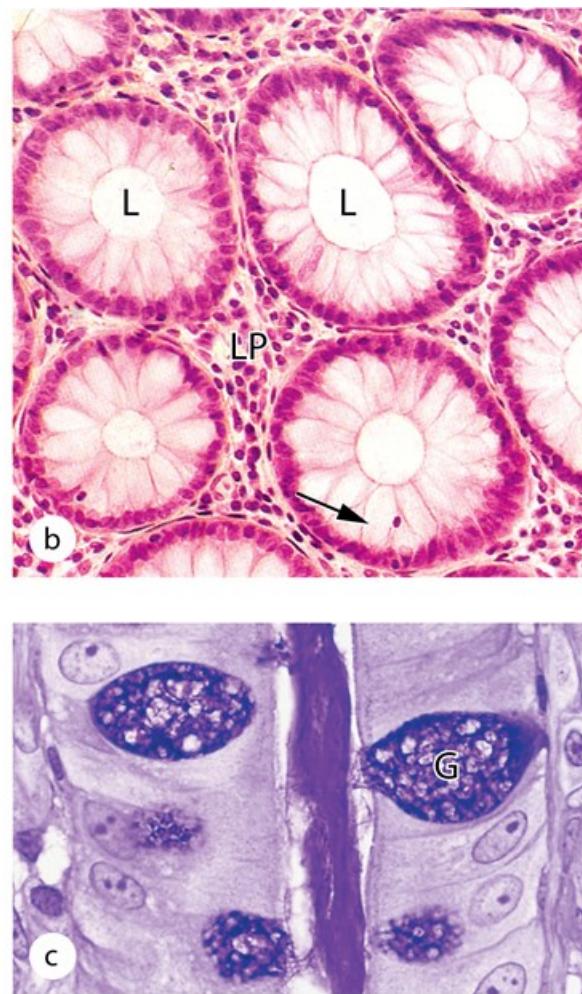


**Mucosa:** tubular **intestinal glands** extending as deep as the **muscularis mucosae** and by lamina propria rich in MALT

**Submucosa:** vascularized.

**Muscularis:** inner circular layer, outer longitudinal muscle: is only present in three equally spaced bands, the **teniae coli**.

# Colon mucosa



- (a) Transverse section of the colon shows the muscularis externa (**ME**), including a **tenia coli** cut transversely in the lower part of the figure, the submucosa (**S**), the mucosa (**M**) filled with **tubular intestinal glands**. Some of these glands are cut longitudinally, but most seen here are cut transversely.
- (b) Transversely cut glands are seen to consist of simple columnar epithelium surrounded by a tubular lumen (**L**) and embedded in lamina propria (**LP**) with many free lymphocytes. Lymphocytes can also be seen penetrating the epithelium (**arrow**).
- (c) Longitudinal section of one intestinal gland stained for glycoproteins shows **mucus** in the lumen and two major cell types in the epithelium: goblet cells (**G**) and the neighboring columnar cells specialized for water absorption.

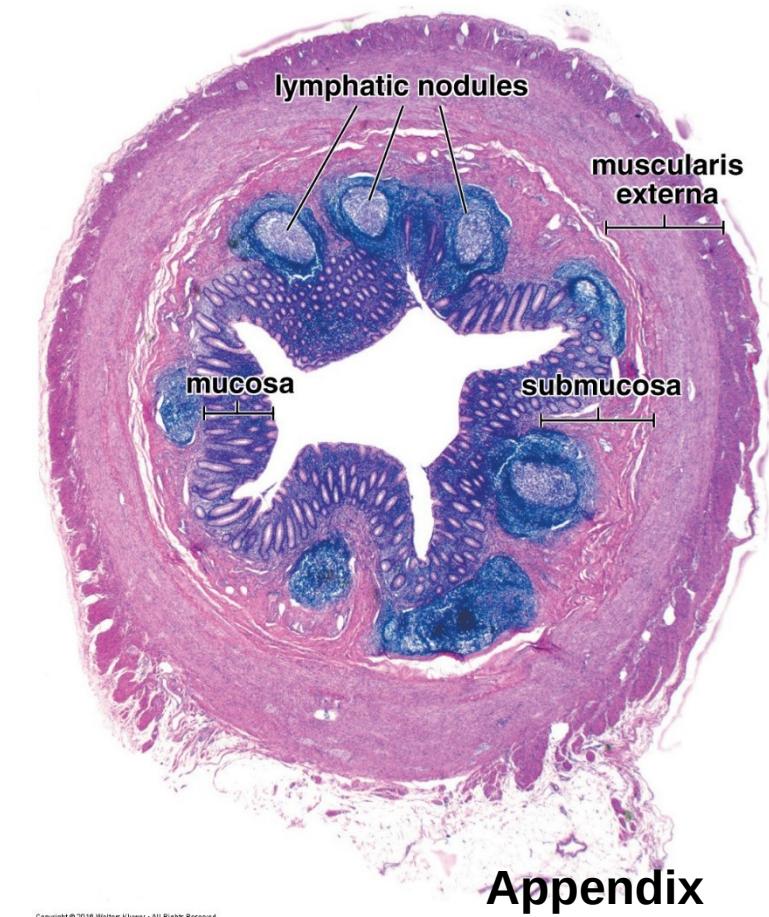
## Cecum and Appendix

**Cecum:** pouch distal to the ileocecal valve. The histology of the cecum closely resembles that of the rest of the colon.

**Appendix:** thin, finger-like extension of this cecum.

- uniform layer of longitudinal muscle in the muscularis externa
- large number of lymphatic nodules that extend into the submucosa.

**Medical Application:** Blockage of the opening between the appendix and the cecum, usually due to scarring, buildup of thick mucus, or stool that enters the lumen of the appendix from the cecum, may cause appendicitis.



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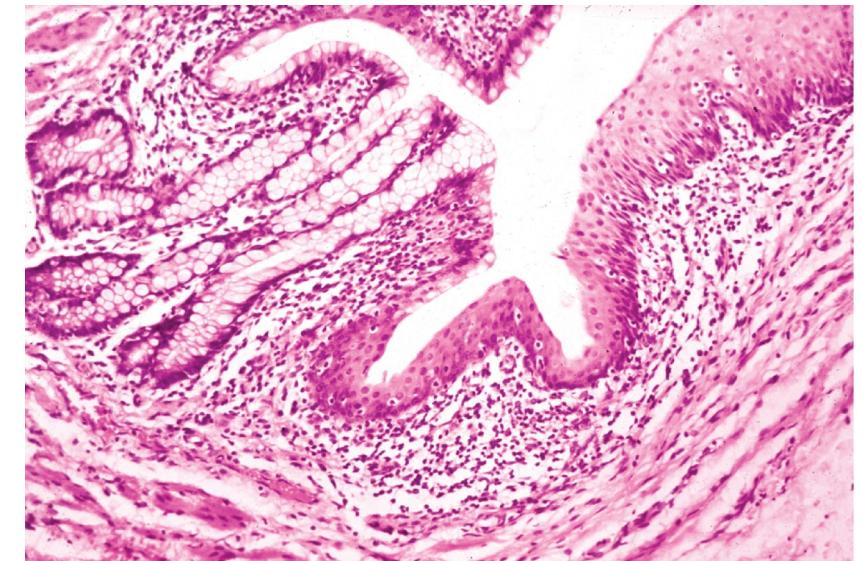
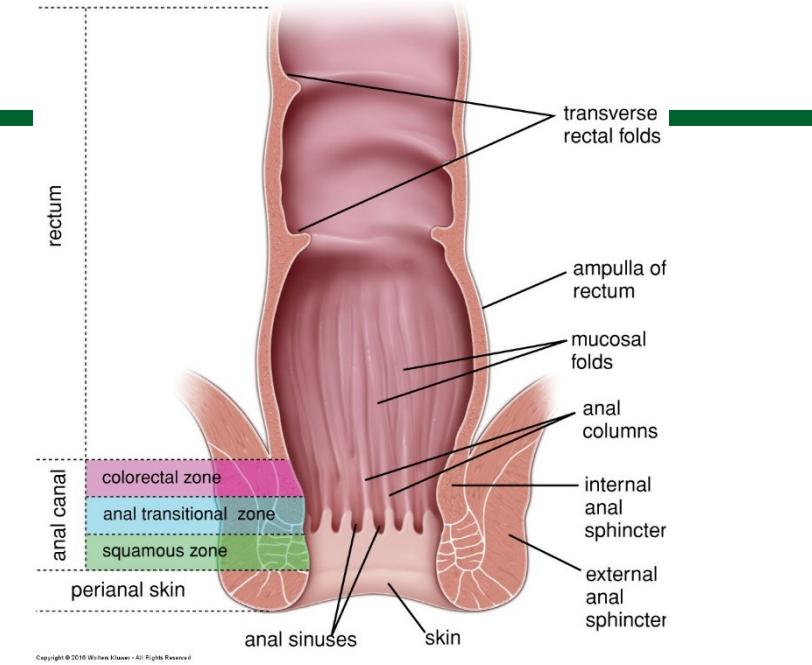
Appendix

# Rectum and Anal Canal

## Mucosa of the rectoanal junction.

The simple columnar epithelium with tubular **intestinal glands** in the rectum (left side of photo) changes abruptly to stratified squamous epithelium in the **anal canal** (right side of photo), as seen in this longitudinal section. The connective tissue of the lamina propria is seen to contain many free lymphocytes

**Hemorrhoids:** Swollen blood vessels in the mucosa or submucosa of the anal canal results from a low-fiber diet, constipation, prolonged sitting, or straining at defecation

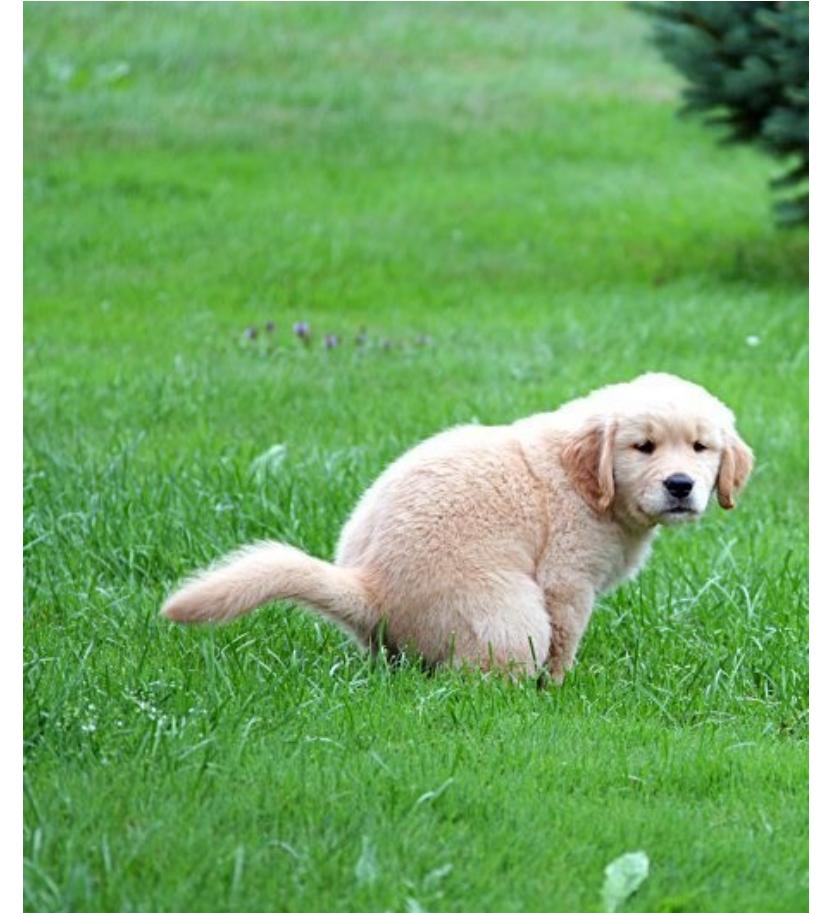


**Haustral contractions:** A form of segmentation, occurs every 30 minutes

- - This kind of colonic motility is segmentation
  - Distension of a haustrum stimulates it to contract
- Mass movements occur one to three times a day
- Stretching of rectum stimulates defecation reflexes, urge to **defecate** that is often felt soon after a meal
- Abdominal contractions (**Valsalva maneuver**) increase abdominal pressure as levator ani lifts anal canal upward
- Feces will fall away

## Defecation

---



[http://highered.mheducation.com/sites/0072943696/student\\_view/0/chapter16/animation\\_reflexes\\_in\\_the\\_colon.html](http://highered.mheducation.com/sites/0072943696/student_view/0/chapter16/animation_reflexes_in_the_colon.html)

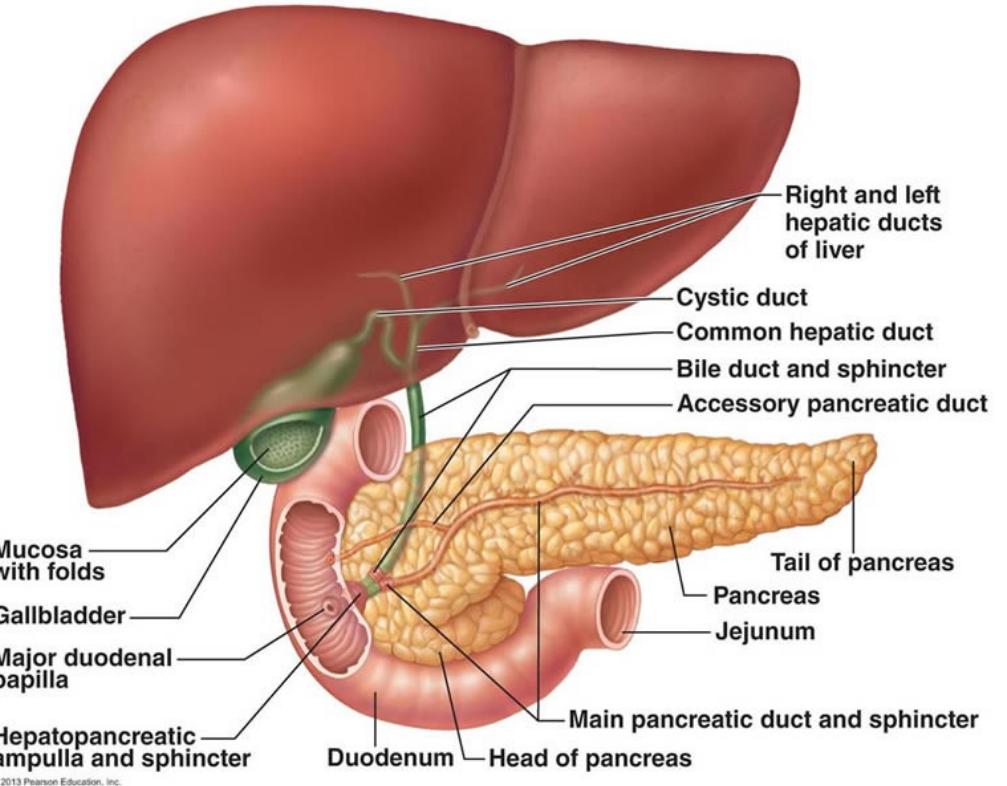
TABLE 15-2

## Summary of distinguishing digestive tract features, by region and layers.

Region and Subdivisions	Mucosa (Epithelium, Lamina Propria, Muscularis Mucosae)	Submucosa (with Submucosal Plexuses)	Muscularis (Inner Circular and Outer Longitudinal Layers, with Myenteric Plexuses Between Them)	Adventitia/Serosa
Esophagus (upper, middle, lower)	Nonkeratinized stratified squamous epithelium; cardiac glands at lower end	Small esophageal glands (mainly mucous)	Both layers striated muscle in upper region; both layers smooth muscle in lower region; smooth and striated muscle fascicles mingled in middle region	Adventitia, except at lower end with serosa
Stomach (cardia, fundus, body, pylorus)	Surface mucous cells and gastric pits leading to gastric glands with parietal and chief cells, (in the fundus and body) or to mucous cardiac glands and pyloric glands	No distinguishing features	Three indistinct layers of smooth muscle (inner oblique, middle circular, and outer longitudinal)	Serosa
Small intestine (duodenum, jejunum, ileum)	Plicae circulares; villi, with enterocytes and goblet cells, and crypts/glands with Paneth cells and stem cells; Peyer patches in ileum	Duodenal (Brunner) glands (entirely mucous); possible extensions of Peyer patches in ileum	No distinguishing features	Mainly serosa
Large intestine (cecum, colon, rectum)	Intestinal glands with goblet cells and absorptive cells	No distinguishing features	Outer longitudinal layer separated into three bands, the teniae coli	Mainly serosa, with adventitia at rectum
Anal canal	Stratified squamous epithelium; longitudinal anal columns	Venous sinuses	Inner circular layer thickened as internal sphincter	Adventitia

Organs Associated with the Digestive Tract  
Salivary Glands, Pancreas, Liver, Gallbladder, Pancreas

# BI 455 CHAPTER 16



# **Saliva and the Salivary Glands**

---

**Saliva:** starch and fat digestion, inhibits bacterial growth

**Salivary amylase:** starch digestion in the mouth

**Lingual lipase:** digests fat in stomach acid,

**Mucus:** lubricates food for swallowing

**Lysozyme:** kills bacteria

**Immunoglobulin A (IgA):** inhibits bacterial growth

**Electrolytes:**  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Cl}^-$ , phosphate, and bicarbonate



**»» MEDICAL APPLICATION** inadequate saliva production, leading to dry mouth or xerostomia, can be caused by various factors affecting the major salivary glands, such as mumps viral infection, radiation of the glands, or the normal side effect of drugs such as antihistamines .

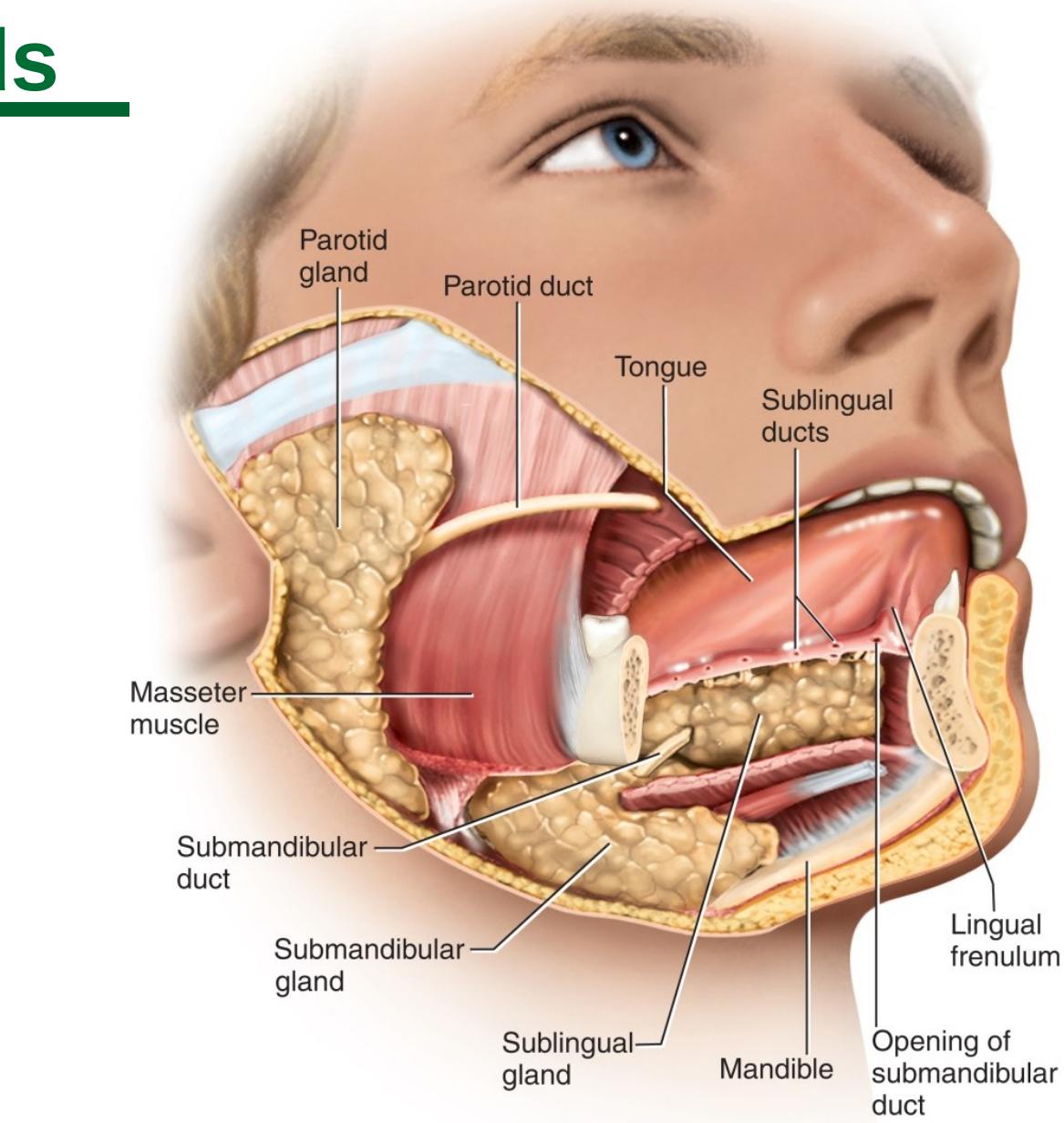
# Saliva and the Salivary Glands

**Extrinsic salivary glands:** connected to oral cavity by ducts. ~1 to 1.5 L of saliva per day

**Parotid:** Mumps is viral infection of parotid gland

**Submandibular gland:** empties near the lower central incisors

**Sublingual glands:** multiple ducts that empty posterior to submandibular duct



Compound **tubuloacinar glands** with branched ducts ending in acini

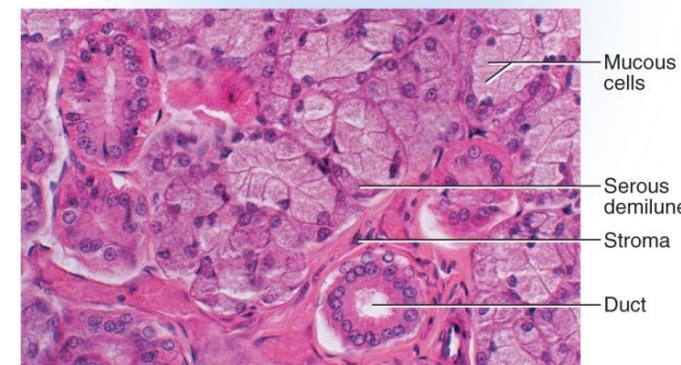
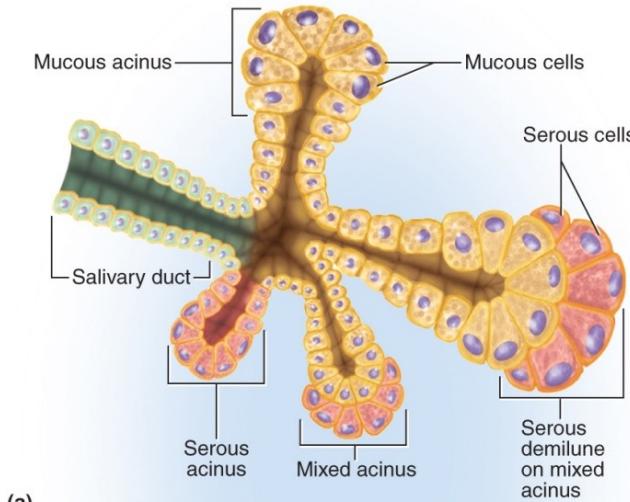
- Mucous (mucous) and serous cells (electrolytes & amylase)
- filter water and electrolytes from blood and add amylase, mucin, and lysozyme
- Salivary nuclei in the **medulla oblongata** and **pons** respond to signals generated by presence of food

### » MEDICAL APPLICATION

Excessive saliva production, or sialorrhea, is associated with the autonomic activity of nausea, inflammation within the oral cavity, and rabies viral infection.

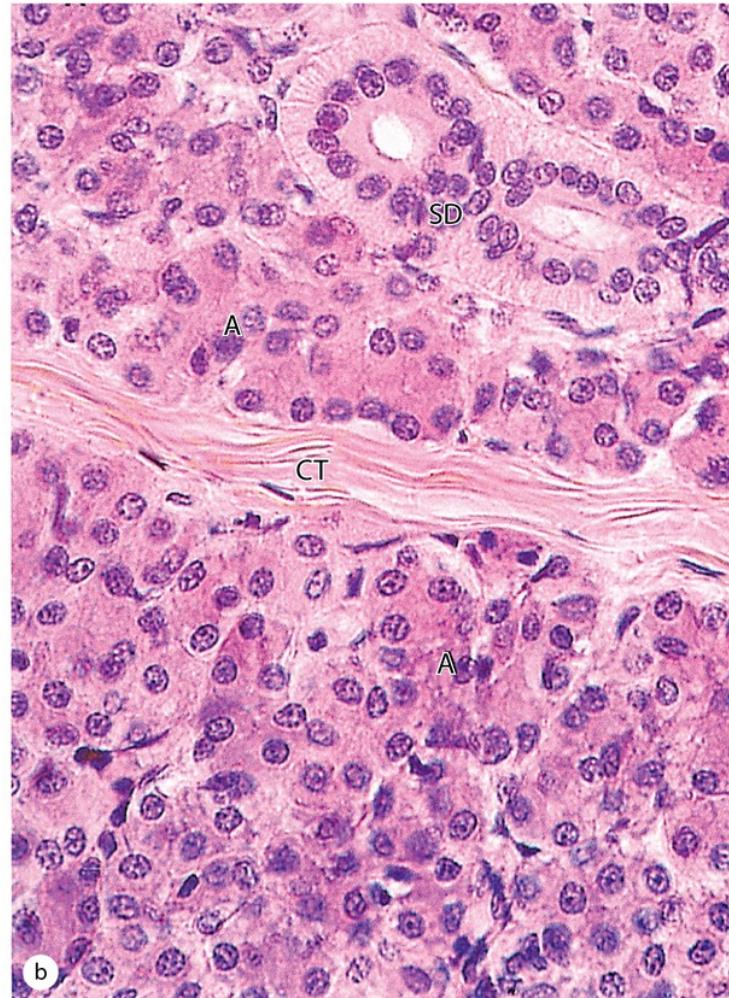
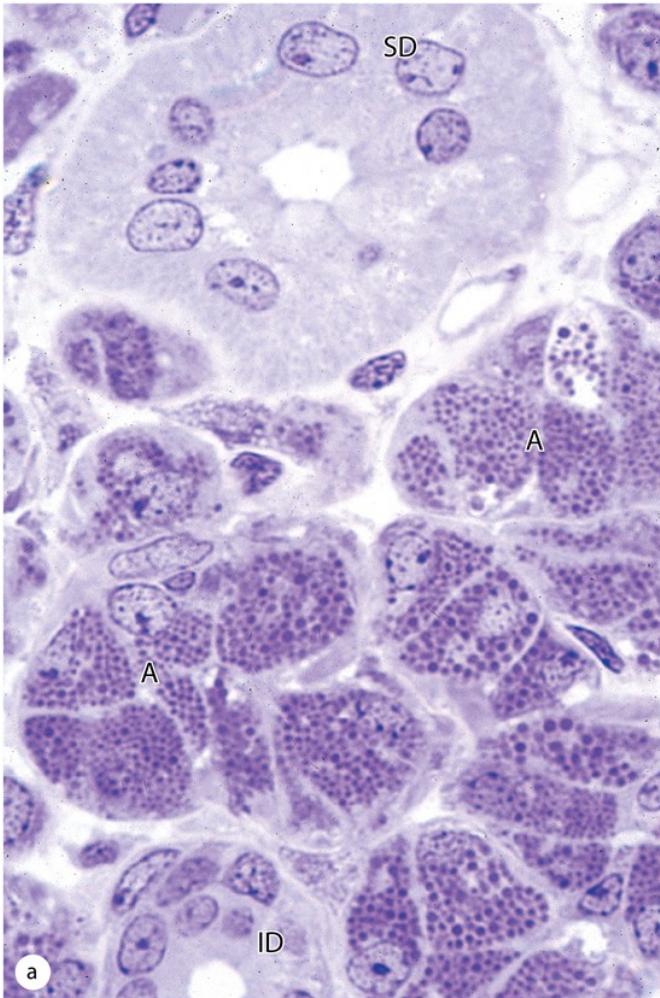
## Histology of Salivary Glands

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# Parotid gland



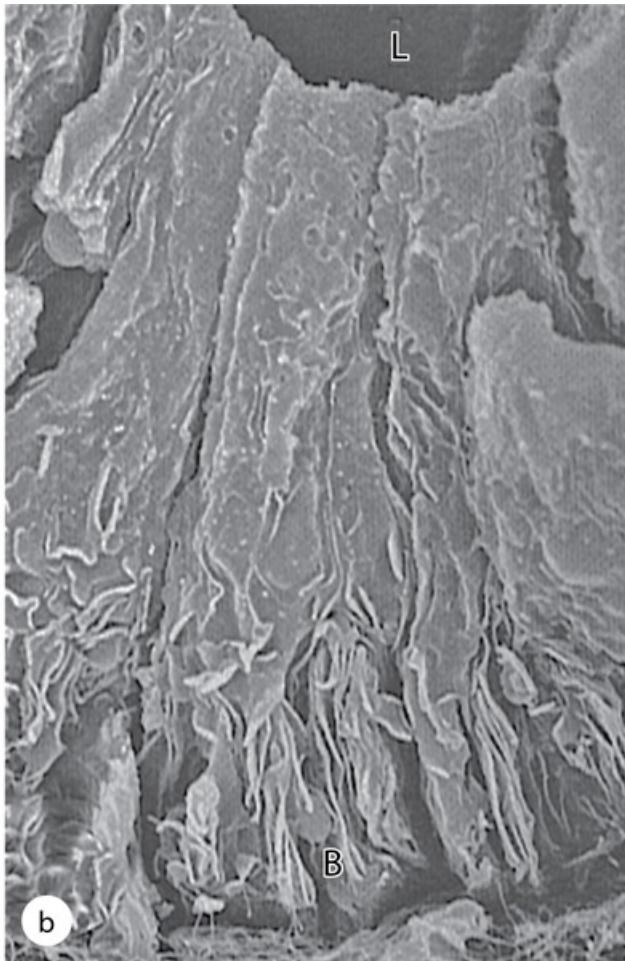
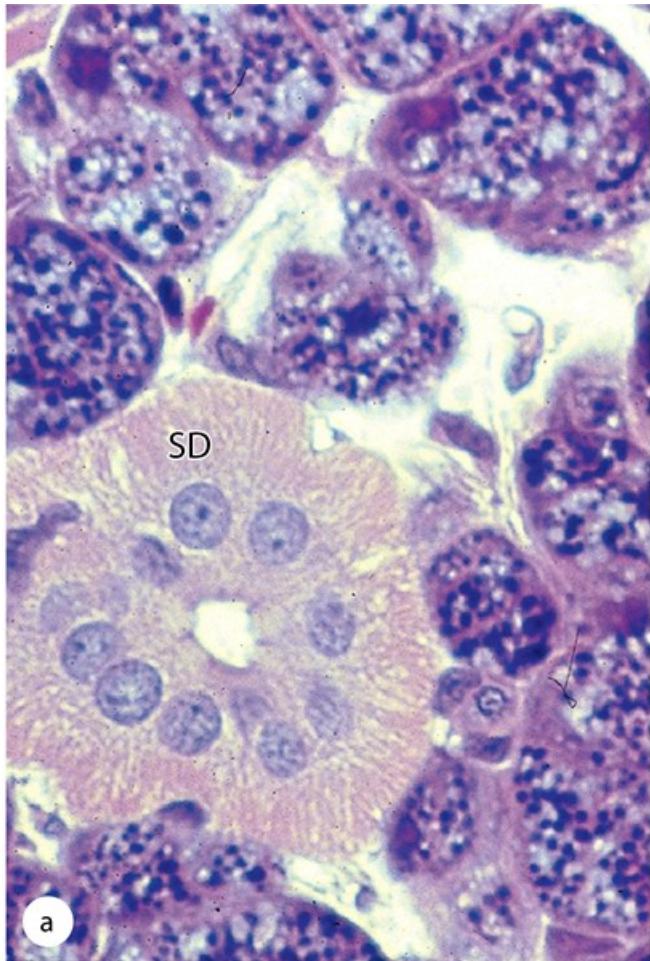
The large parotid gland consists entirely of serous acini with cells producing amylase and other proteins for storage in secretory granules.

**(a)** densely packed serous acini (**A**) with ducts show secretory granules

intercalated duct (**ID**) and striated duct (**SD**), both cut transversely.

**(b)** Striations of a duct (**SD**) are better seen here, along with a septum (**CT**) and numerous serous acini (**A**). The connective tissue often includes adipocytes.

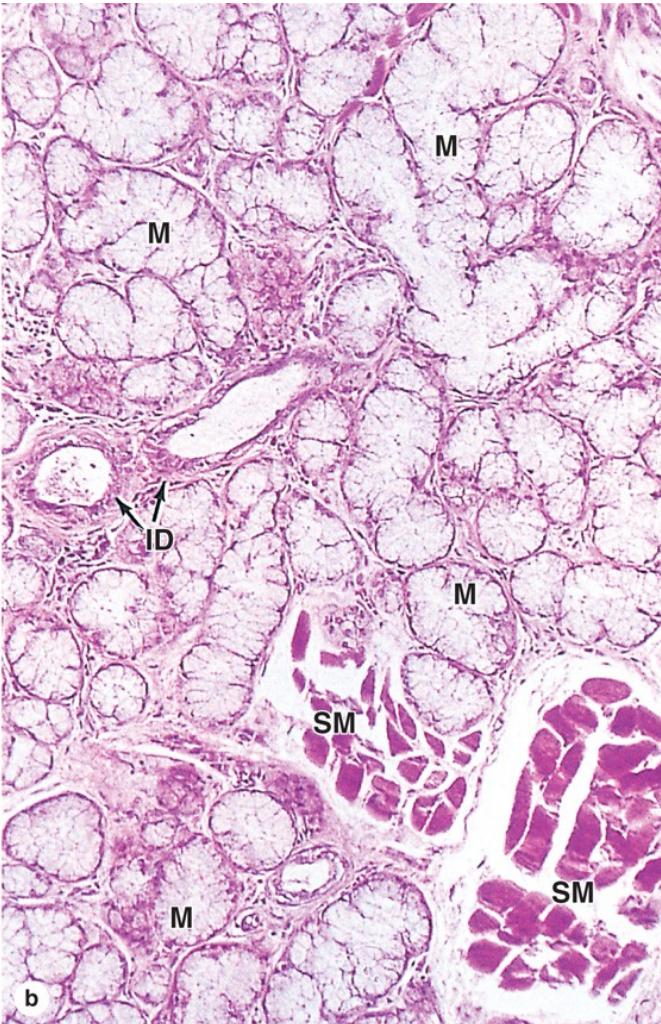
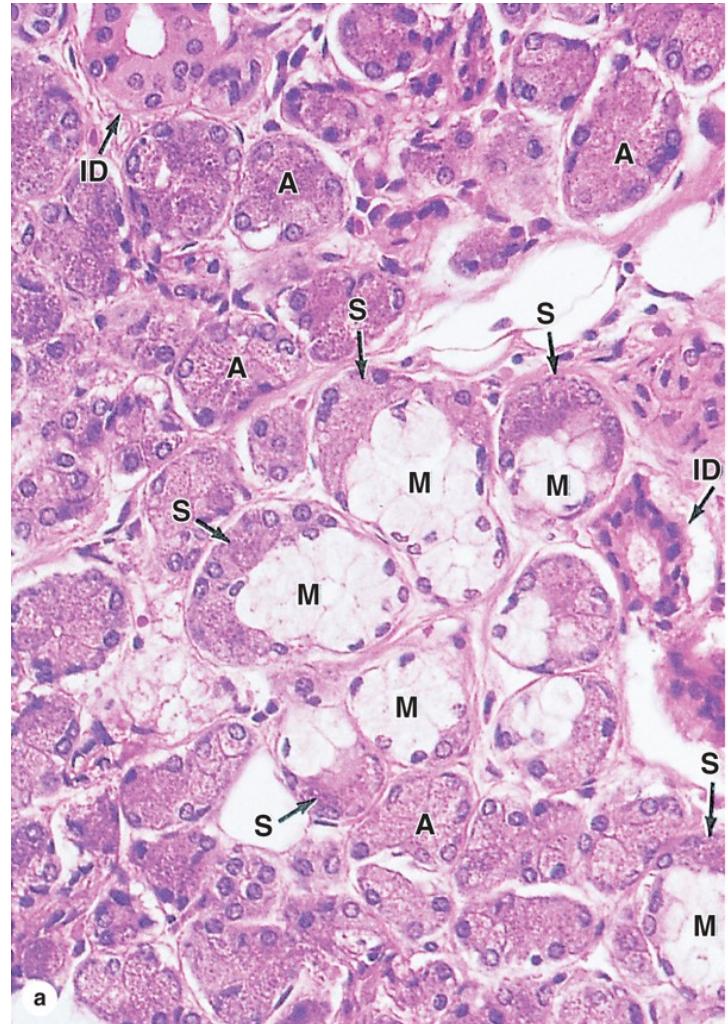
## Striated ducts



**(a)** A striated duct (**SD**) shows very faint striations in the basal half of the columnar cells, which represent mitochondria located in the folds of the lateral cell membrane.

**(b)** SEM indicates that the apical ends of the cells are joined together near the small lumen (**L**), with interdigitating folds of cell membrane best developed at the basal end (**B**).

# Submandibular gland and sublingual gland



(a) The **submandibular gland** is a mixed serous and mucous gland (serous cells predominate), and shows well-stained serous acini (A) and serous demilunes (S) and pale-staining mucous cells (M) grouped as tubules in this tubuloacinar gland. Small intralobular ducts (ID) drain each lobule.

(b) The **sublingual gland** is a mixed but largely mucous gland with a tubuloacinar arrangement of poorly stained mucous cells (M). Small intralobular ducts (ID) are seen in connective tissue, as well as small fascicles of lingual striated muscle

# The Liver Secretes Digestive Bile

## Functions

- Produces circulating plasma proteins (albumins,  $\beta$ -globulins, fibrinogen)
- Stores vitamins and iron
- Degrades drugs and toxins
- Secretes bile

**4 lobes:** right, left, quadrate, and caudate

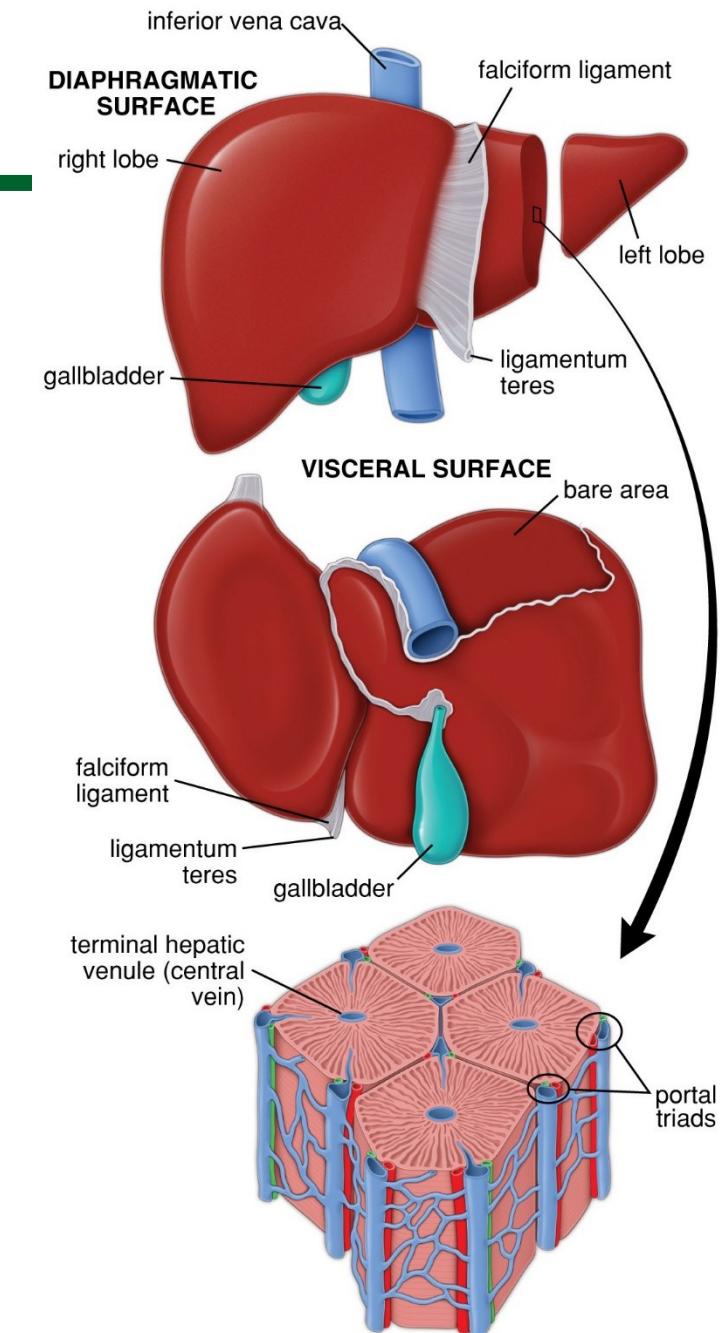
**Falciform ligament:** separates left and right lobes, suspends the liver from the diaphragm

**Round ligament (ligamentum teres):** remnant of umbilical vein, carrying blood to liver of the fetus

**Porta hepatis:** entry of hepatic portal vein and proper hepatic artery, exit of bile passages

**Gallbladder:** Stores bile

**Bile duct:** formed from union of cystic and common hepatic ducts.



# Microscopic Anatomy

**Hepatic lobules:** basic functional units

**Central vein:** passing down the core

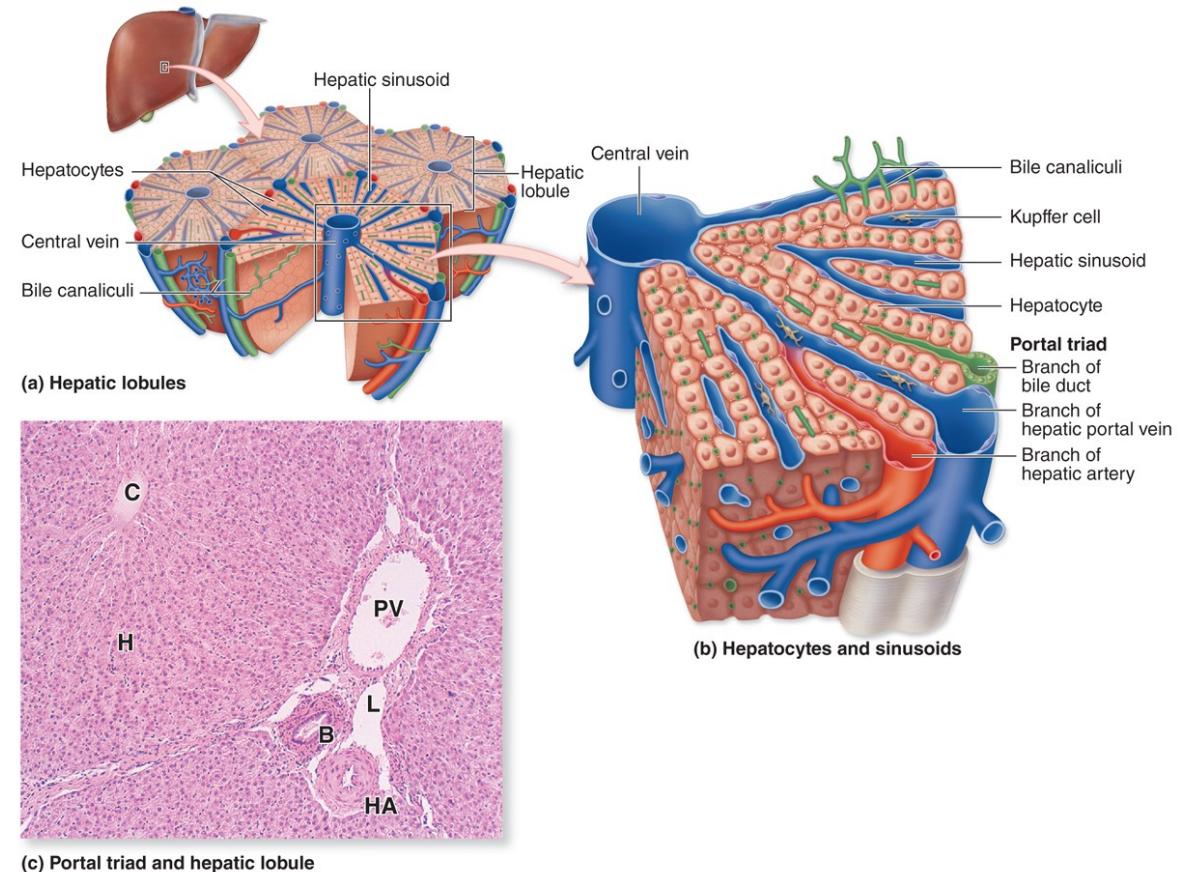
**Hepatocytes:** cuboidal cells, absorb nutrients from blood

**Hepatic sinusoids:** blood from stomach

**Hepatic macrophages (Kupffer cells):** phagocytets

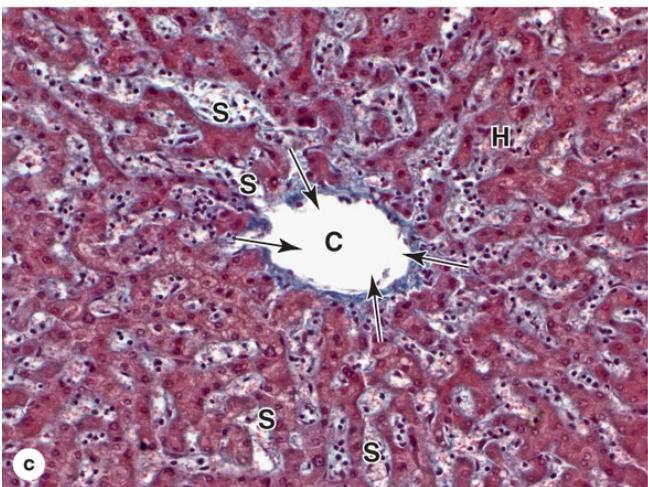
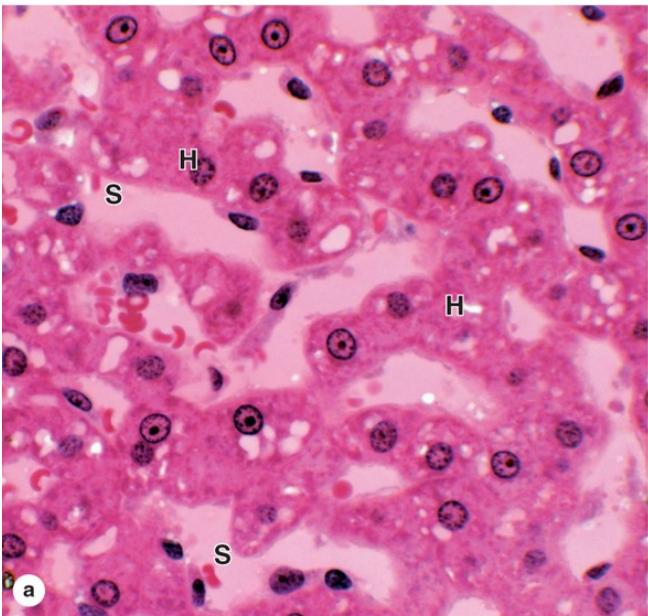
**Bile:** aids in digestion of lipids

**Bile canaliculi:** narrow channels into which the liver secretes bile



**(c)** Micrograph of a lobule shows the central vein (**C**), plates of hepatocytes (**H**), and in an adjacent portal area a small lymphatic (**L**) and components of the portal triad: a portal venule (**PV**), hepatic arteriole (**HA**), and bile ductile (**B**)

# Hepatic Lobule Microvasculature



(a) Hepatocytes (**H**) are polygonal epithelial cells, separated by venous sinusoids (**S**).

(c) hepatocytes (**H**), the central vein (**C**) of the lobule has more collagen than the smaller sinusoids (**S**) that drain into it from all directions (arrows). Mallory trichrome.

**MEDICAL APPLICATIONS:** **Cirrhosis** produces excess connective tissue that interferes with metabolic exchange between the hepatocytes and the sinusoids.

**Fatty liver disease** is a reversible condition in which large lipid droplets containing triglycerides accumulate abnormally in hepatocytes via the process called steatosis. This disorder has multiple causes, but it occurs most commonly in individuals with alcoholism or obesity. Accumulation of fat in hepatocytes may produce a progressive inflammation of the liver.

**Bile:** produced by liver

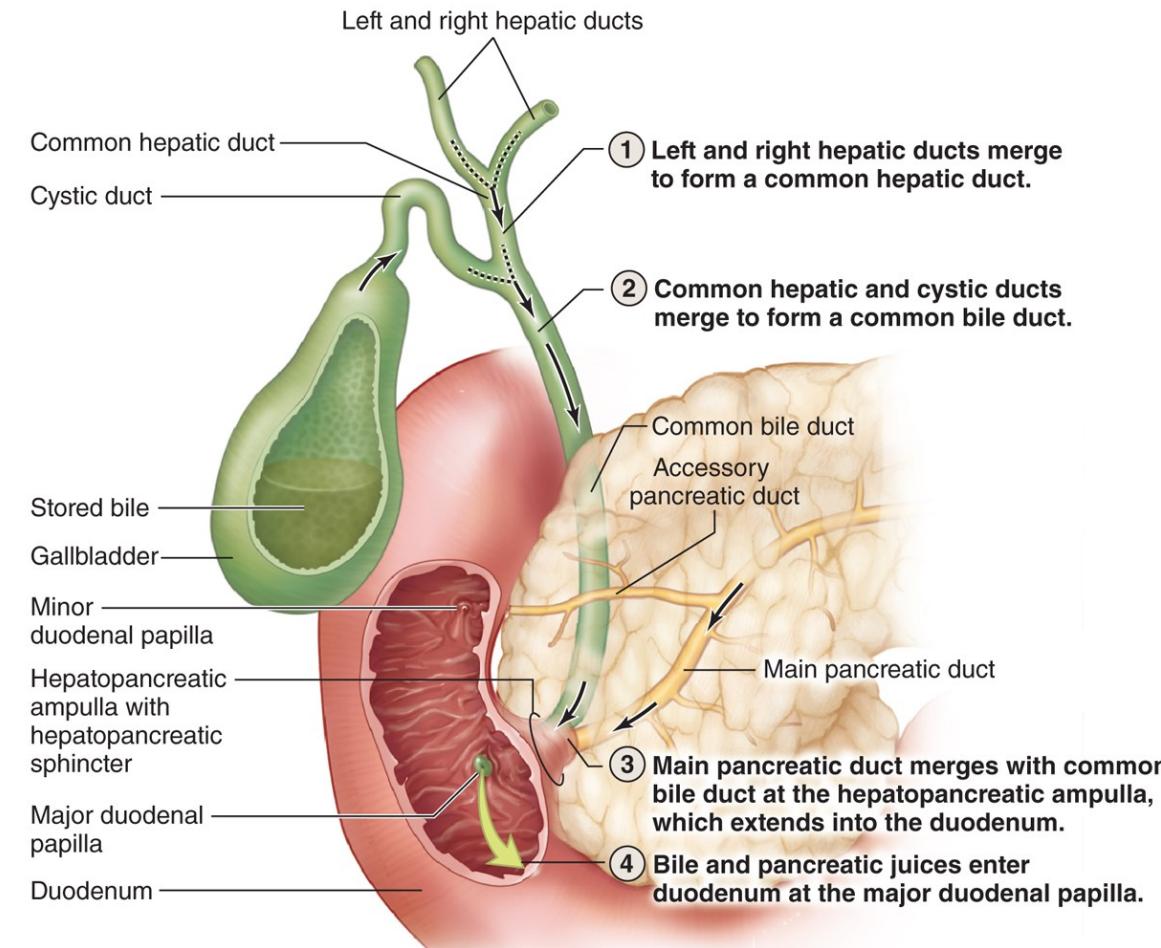
**Bile duct:** formed from union of hepatic ducts.

Bile and pancreatic juices are mixed before release into the duodenal lumen

**Medical Application:** Reabsorption of water from bile in the gallbladder is involved in the formation of **gallstones**. This disorder usually originates with bile that already contains excessive amounts of normal bile components.

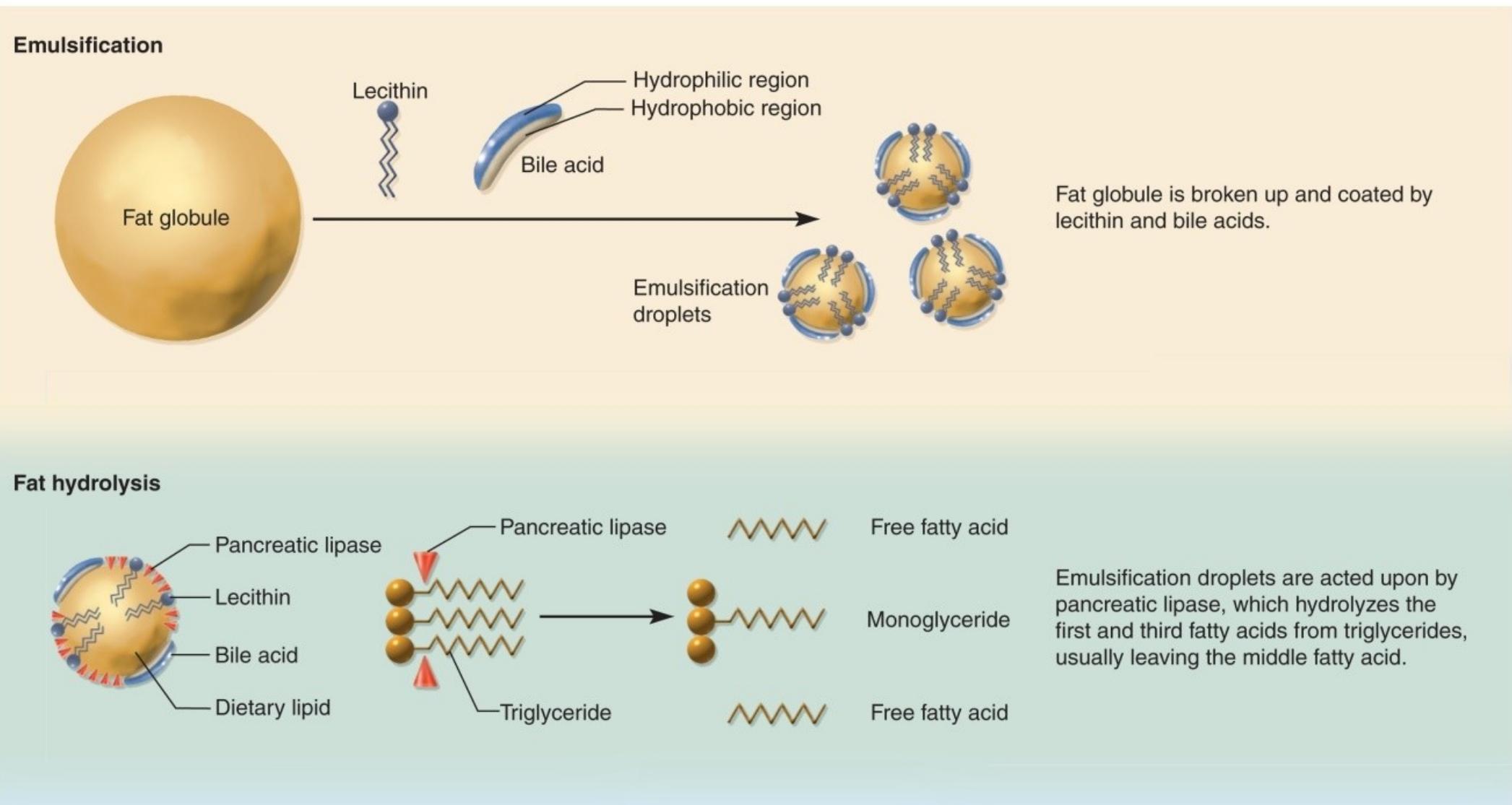
Supersaturation of cholesterol in bile can lead to the formation of cholesterol stones, the most common form.

## The Gallbladder Stores and Concentrates Bile

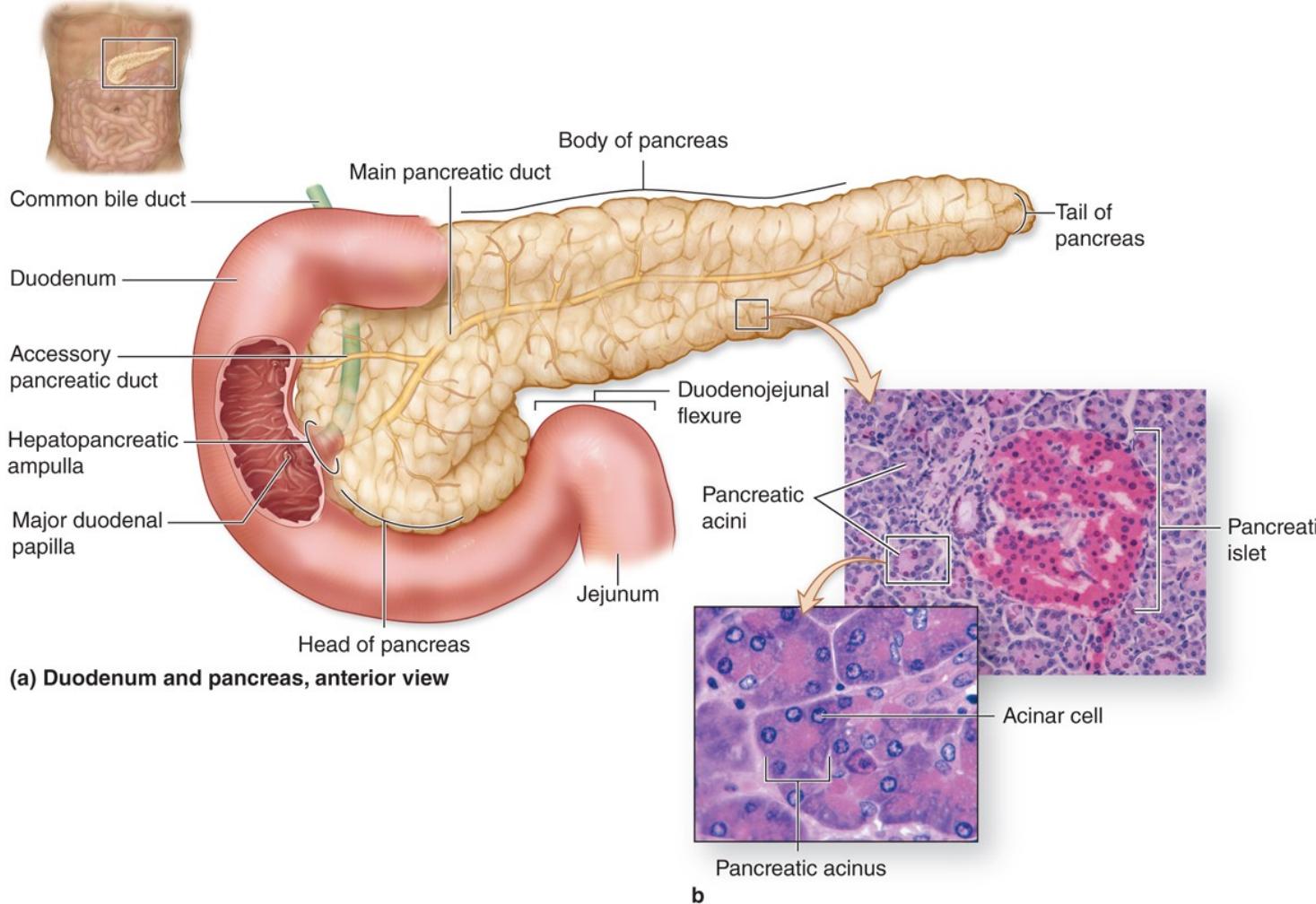


# Bile Acid Emulsifies Fat So Pancreatic Enzymes Can Access Their Substrate

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# Pancreas and duodenum



**(a)** The main regions of the pancreas are shown in relation to the two pancreatic ducts and the duodenum

**(b)** Micrographs show a pancreatic islet and several pancreatic acini

# The Pancreas is a Gland

**Endocrine:** pancreatic islets secrete insulin and glucagon

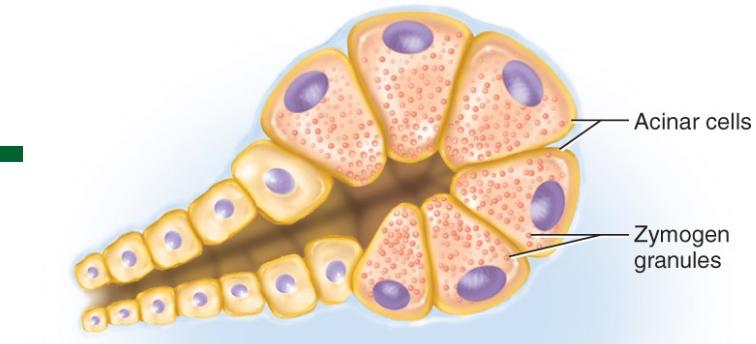
**Exocrine:** secretes 1,200 to 1,500 mL of pancreatic juice per day

**Pancreatic duct:** Joins the bile duct at the hepatopancreatic ampulla

**Hepatopancreatic sphincter:** releases bile and pancreatic juice into duodenum

**Accessory pancreatic duct:** Bypasses the sphincter allowing pancreatic juice(not bile) into duodenum

**Pancreatic juice:** alkaline mixture of water, enzymes, zymogens, sodium bicarbonate, and other electrolytes



(a)



(b)

**Trypsin:** peptide cleavage

**Trypsinogen:** Converted to trypsin by enterokinase

**Chymotrypsinogen:** converted to chymotrypsin by trypsin

**Procarboxypeptidase:** converted to carboxypeptidase by trypsin

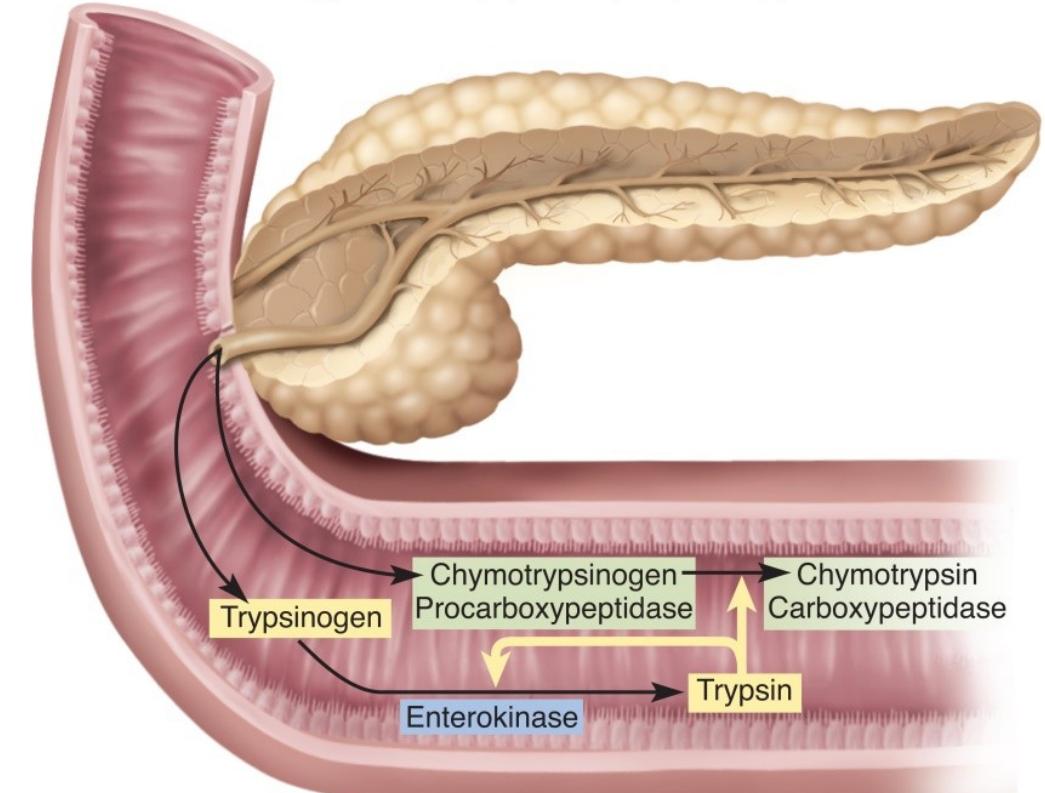
**Pancreatic amylase:** digests starch

**Pancreatic lipase:** digests fat

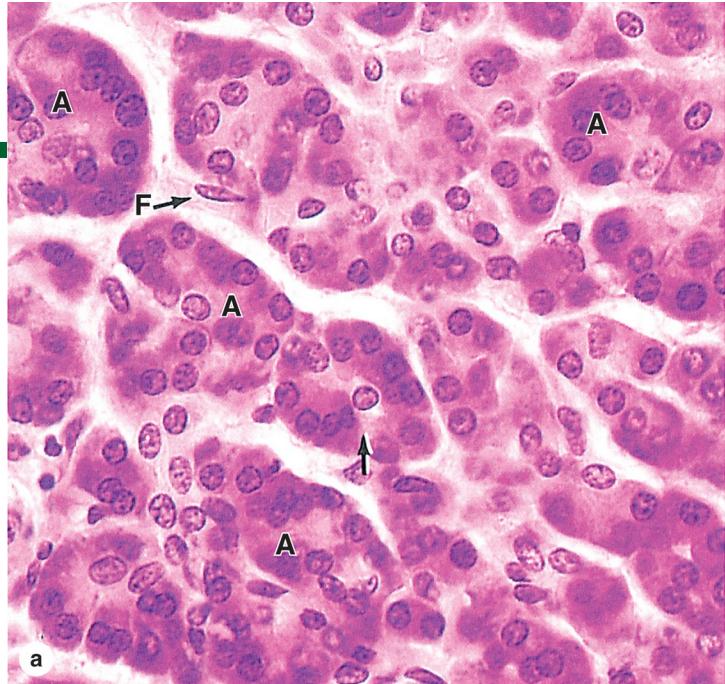
**Ribonuclease and deoxyribonuclease:** digest RNA and DNA  
Control of Release of pancreatic juice and bile

## Pancreatic Enzymes

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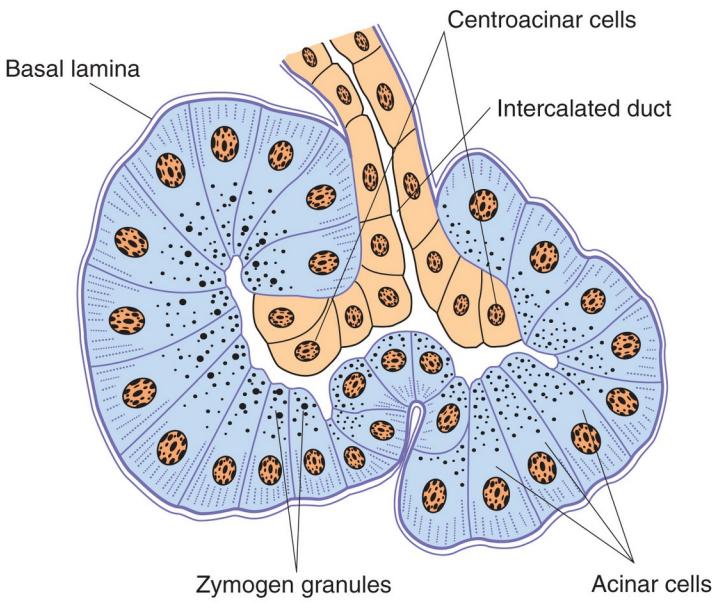


**MEDICAL APPLICATION:** In acute pancreatitis, the proenzymes may be activated and digest pancreatic tissues, leading to very serious complications. Possible causes include infection, gallstones, alcoholism, drugs, and trauma. Chronic pancreatitis can produce progressive fibrosis and loss of pancreatic function.

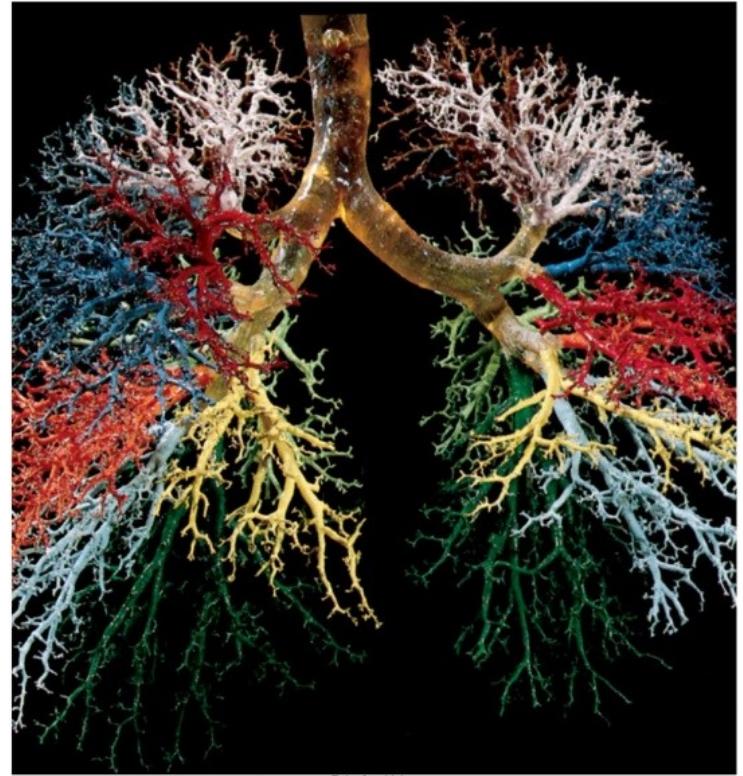


## Pancreatic acini

(a) Micrograph of exocrine pancreas shows the serous, enzyme-producing cells arranged in small acini (**A**) with very small lumens. Acini are surrounded by only small amounts of connective tissue with fibroblasts (**F**). Each acinus is drained by an intercalated duct with its initial cells, the centroacinar cells (**arrow**), inserted into the acinar lumen.



(b) The diagram shows the arrangement of cells more clearly. Under the influence of secretin, the **centroacinar** and **intercalated duct cells** secrete a copious  $\text{HCO}_3^-$ -rich fluid that hydrates, flushes, and alkalinizes the enzymatic secretion of the acini.



Peter Arnold, Inc.

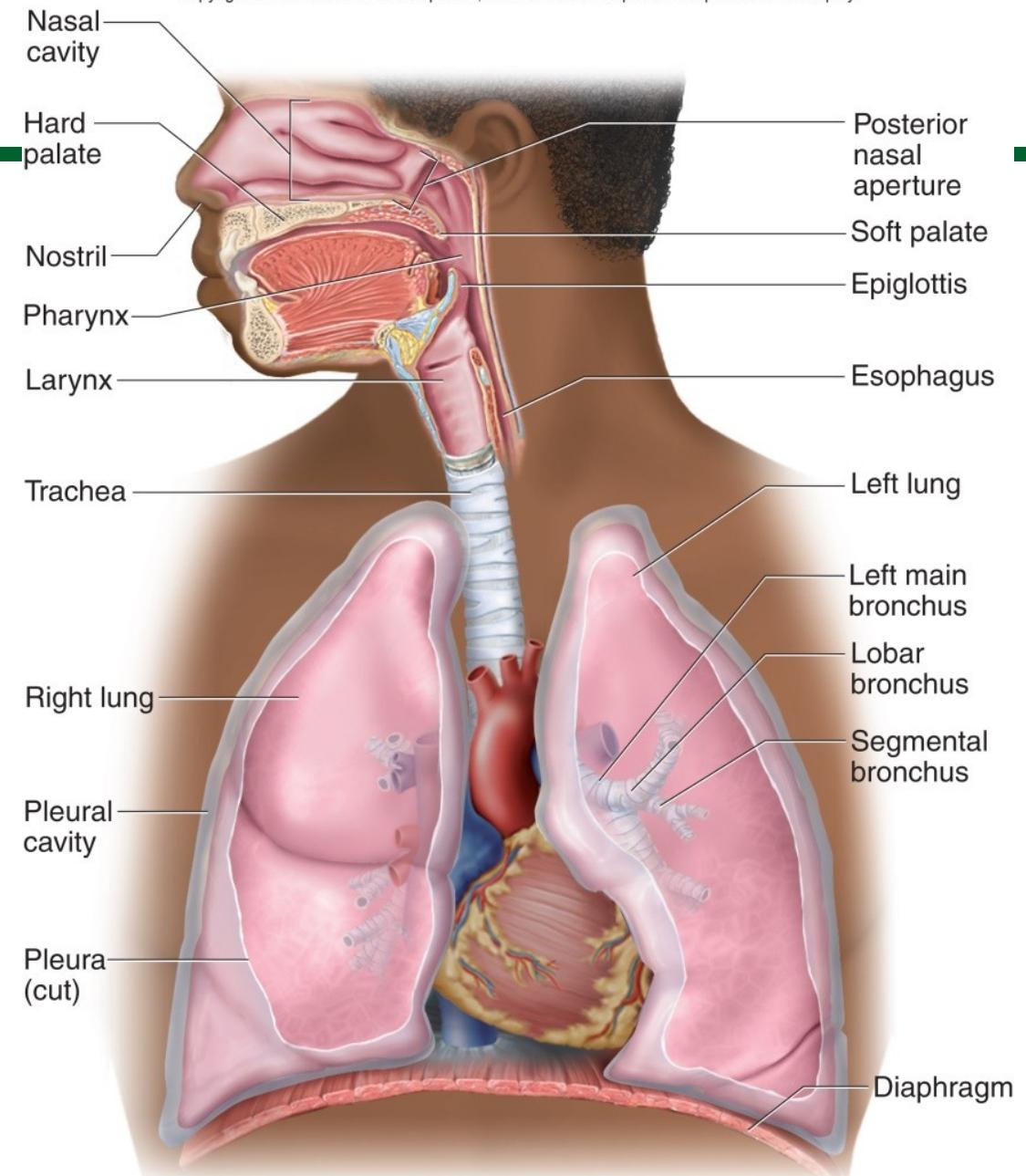
Respiratory

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# BI 455 CHAPTER 17

# What is respiration?

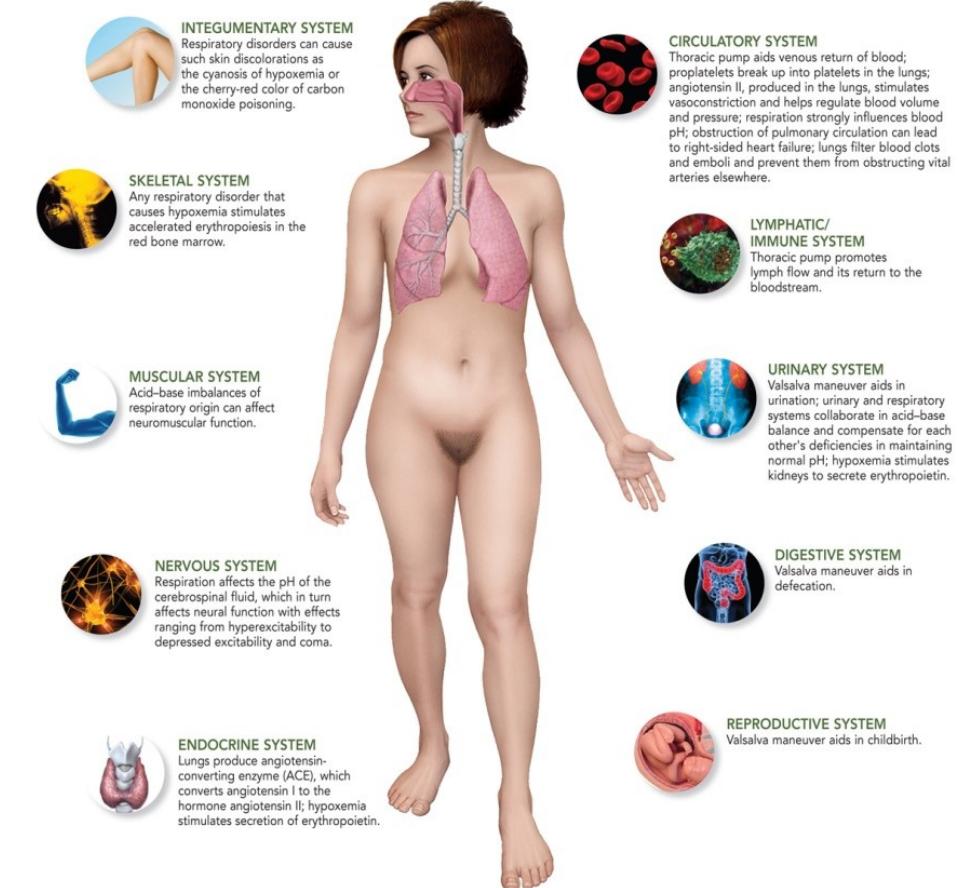
1. Ventilation of the lungs (breathing)
2. The exchange of gases between the air and blood, and between blood and the tissue fluid
3. The use of oxygen in cellular metabolism (ATP production)



# Functions of the Respiratory System

1. O<sub>2</sub> and CO<sub>2</sub> exchange between blood and air
2. Speech
3. Provides the sense of smell
4. Affects pH of body fluids by eliminating CO<sub>2</sub>
5. Affects blood pressure by synthesis of vasoconstrictor, angiotensin II
6. Breathing creates pressure gradients between thorax and abdomen that promote the flow of lymph and venous blood
7. Breath-holding helps expel abdominal contents during urination, defecation, and childbirth (Valsalva maneuver)

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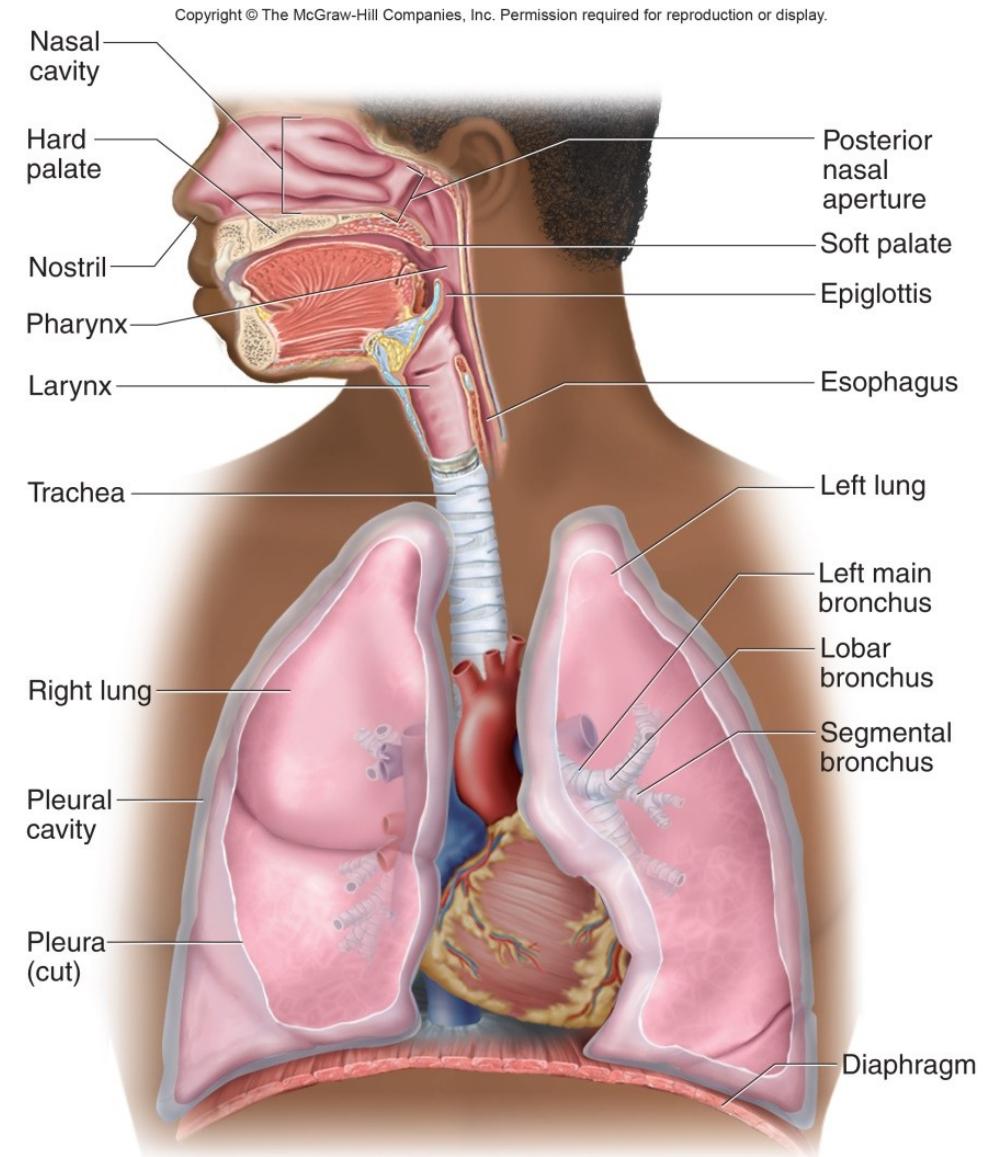


# Conducting Division of the Respiratory System

Nose, pharynx, larynx, trachea, bronchi, lungs

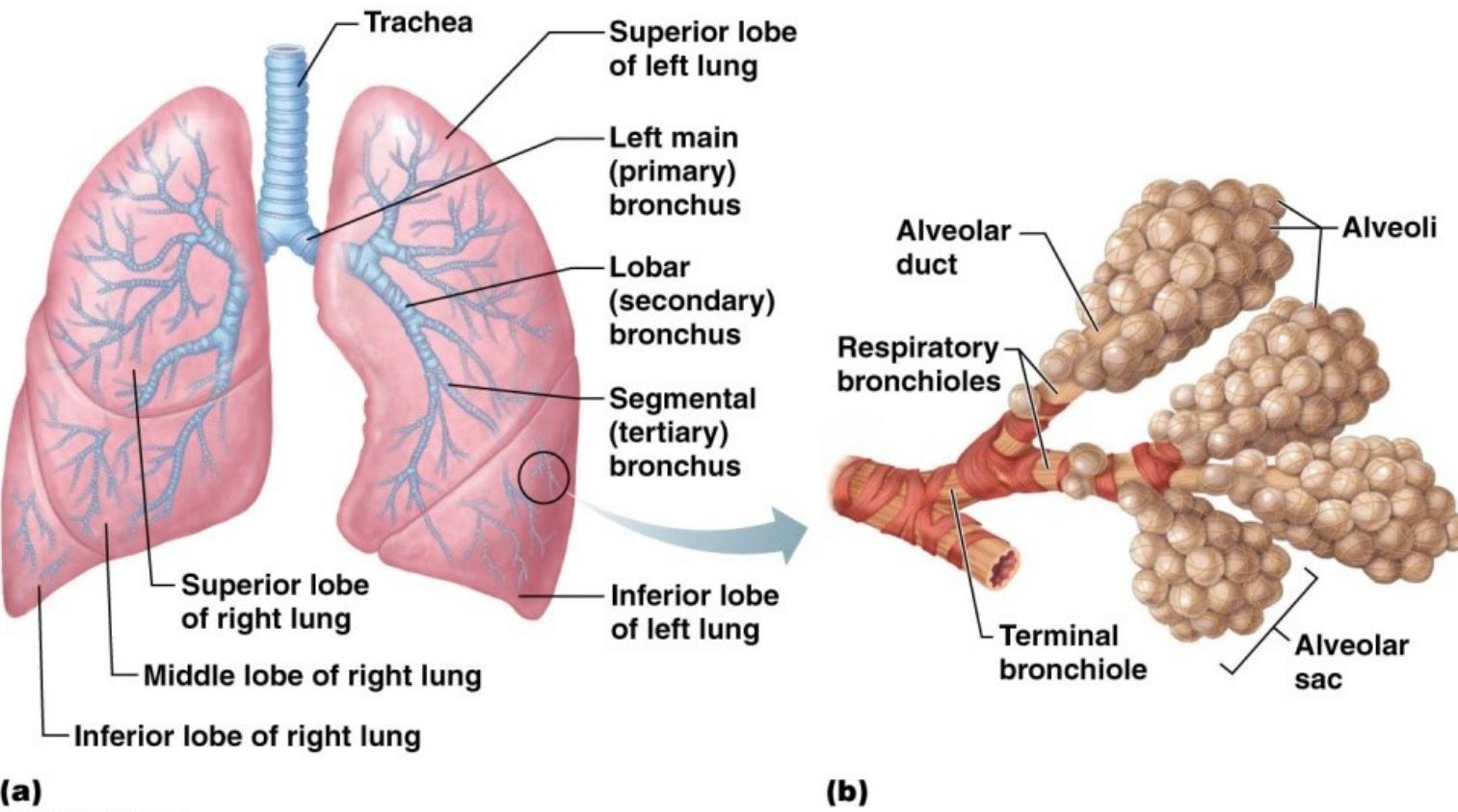
- Those passages that serve only for airflow
- No gas exchange
- Nostrils through major bronchioles
- **Upper respiratory tract:** Nose through larynx
- **Lower respiratory tract:** Trachea through lungs

Conducting division “conditions” air by warming, moistening, and removing particulate materials

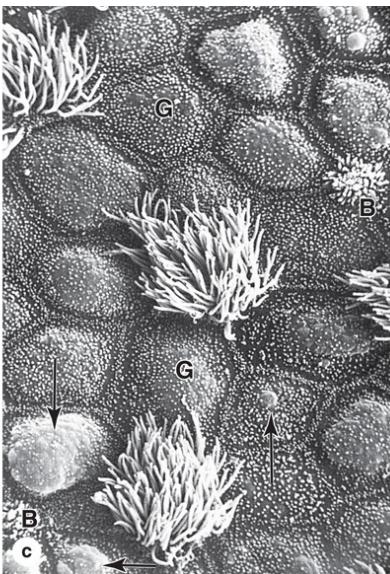
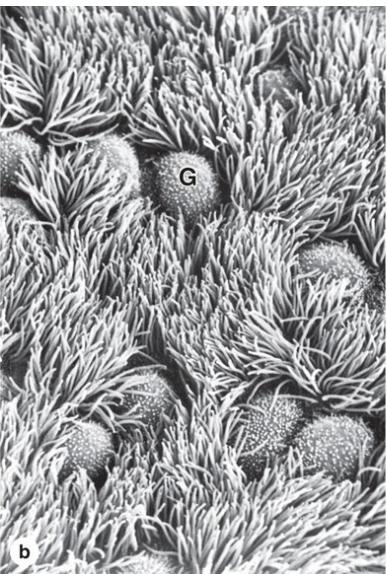
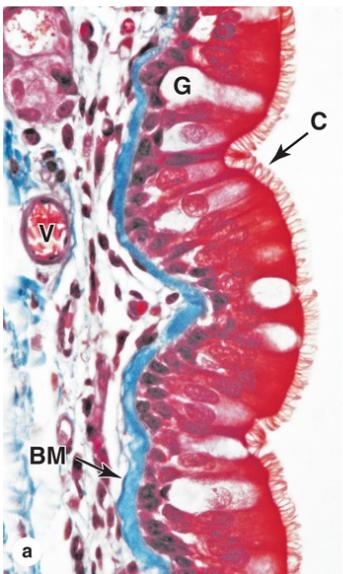


# Respiratory Division of the Respiratory System: respiratory bronchioles, alveolar ducts, alveolar sacs, alveoli

- Incoming air stops in the alveoli
- Millions of thin-walled, microscopic air sacs exchange gases with the bloodstream through the alveolar wall, and then flows back out



# Respiratory epithelium is the classic example of pseudostratified ciliated columnar epithelium.



## Respiratory mucosa cell types

**Ciliated cells (C):** tall columnar cells with cilia that project into the mucus covering the surface of the epithelium

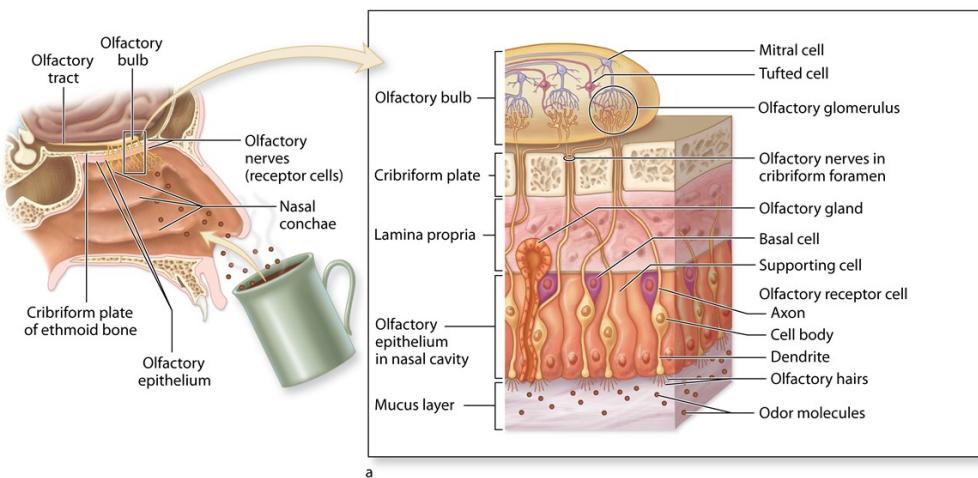
**Goblet cells (G):** synthesize and secrete mucus

**Brush cells (B):** a general name for those cells in the respiratory tract that bear short, blunt microvilli

**Small granule cells (Kulchitsky cells):** endocrine cells of the diffuse neuroendocrine system (DNES)

**Basal cells:** stem cells from which the other cell types arise (at base of columnar cells)

# Olfactory Region Sends Axons to the Brain



**MEDICAL APPLICATION:** The loss or reduction of the ability to smell, anosmia or hyposmia, respectively, can be caused by damage to the olfactory epithelium or nerve. Can be caused by intranasal drug use. The olfactory neurons are the best-known neurons to be replaced regularly because of regenerative activity of the epithelial stem cells from which they arise. For this reason, loss of the sense of smell due to toxic fumes or physical injury to the olfactory mucosa itself is usually temporary.

Aging and the loss of smell, taste:  
[https://www.youtube.com/watch?v=A\\_aevsFwlJA](https://www.youtube.com/watch?v=A_aevsFwlJA)

## Pseudostratified epithelium

(Only a thin basement membrane separates the olfactory basal cells (**B**) from the underlying lamina propria (**LP**). Nuclei of the bipolar olfactory neurons (**ON**) lie in the middle of the pseudostratified olfactory epithelium, with a zone of supporting cell (**S**) nuclei above it. At the apical end of the cells are the nonmotile cilia (**C**), or olfactory hairs, and a layer of mucus (**M**).

# The Larynx (voice box): cartilaginous chamber which keeps food and drink out of the airway

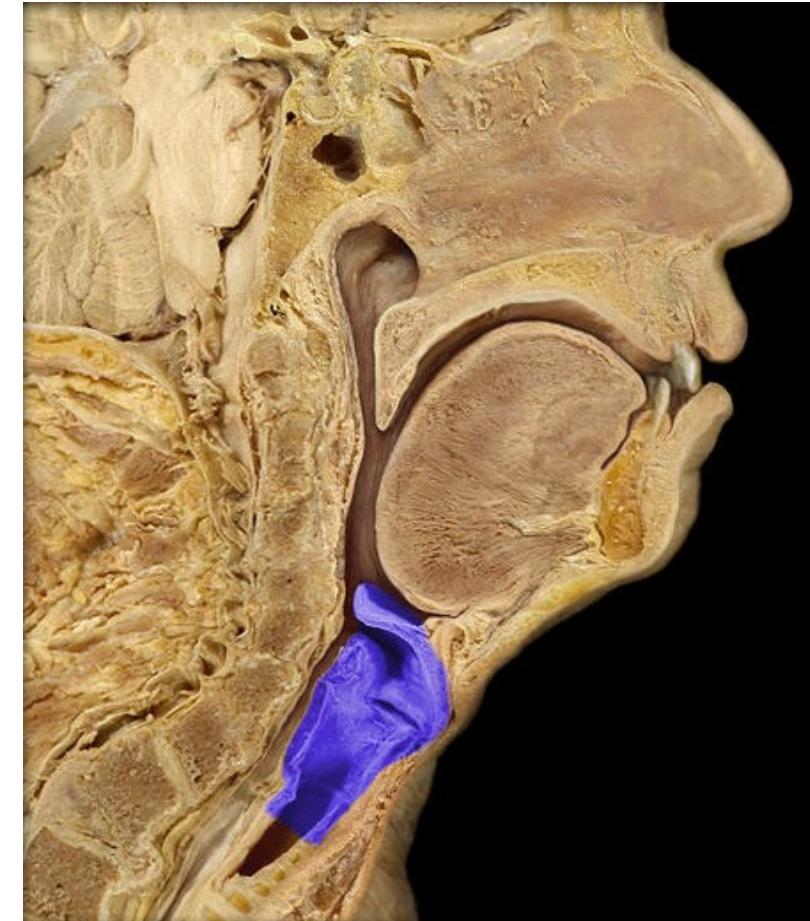
Has evolved role in production of sound

**Epiglottis:** flap of tissue that guards the superior opening of the larynx

- At rest, stands almost vertically
- Swallowing closes airway and directs food to esophagus behind it

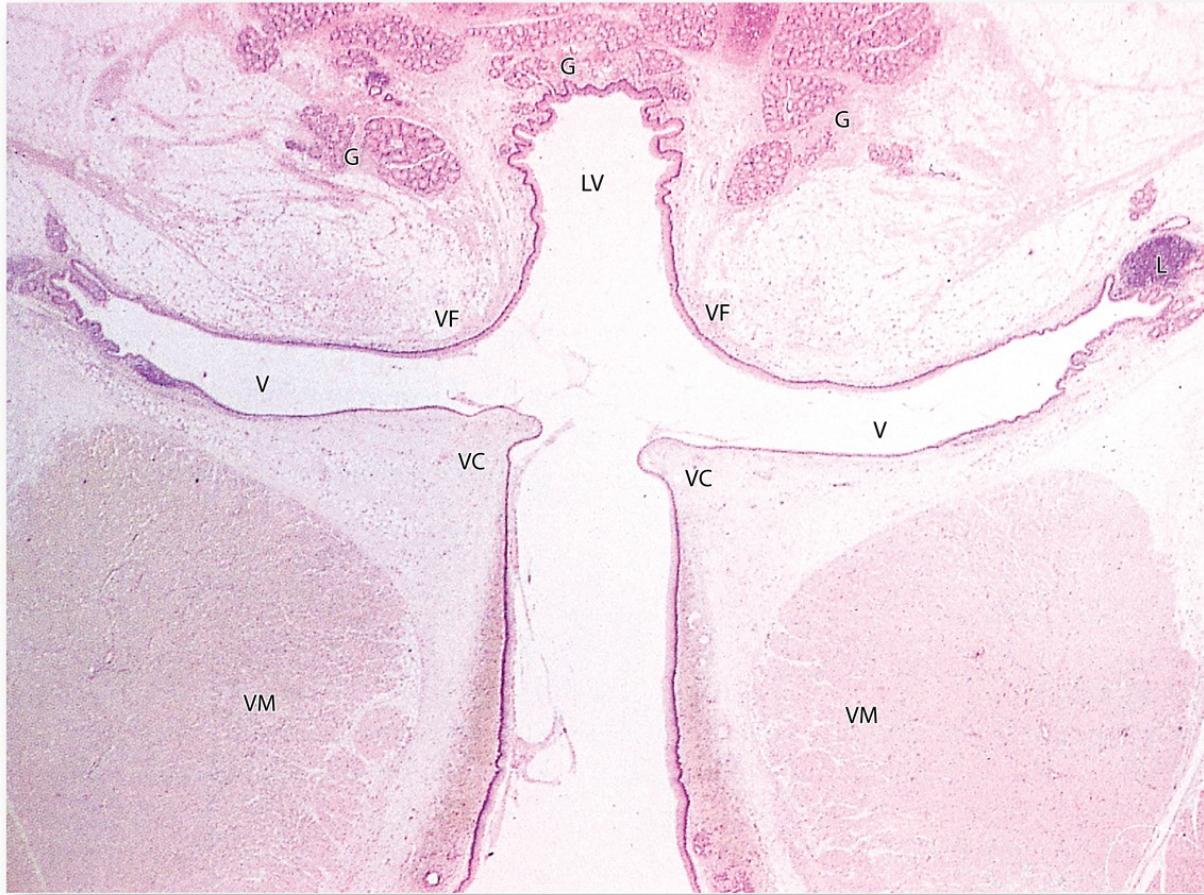
» » **MEDICAL APPLICATION:** Inflammation of the larynx, or laryngitis, changes the shape of the vocal folds or other parts of the larynx, producing loss of voice.

Benign reactive polyps, called singer's nodules, are frequent in the stratified squamous epithelium of the true vocal cords, affecting the voice



Laryngitis [https://www.youtube.com/watch?v=puqe3\\_HkDZA](https://www.youtube.com/watch?v=puqe3_HkDZA)

# Larynx: short air passage between the pharynx and trachea



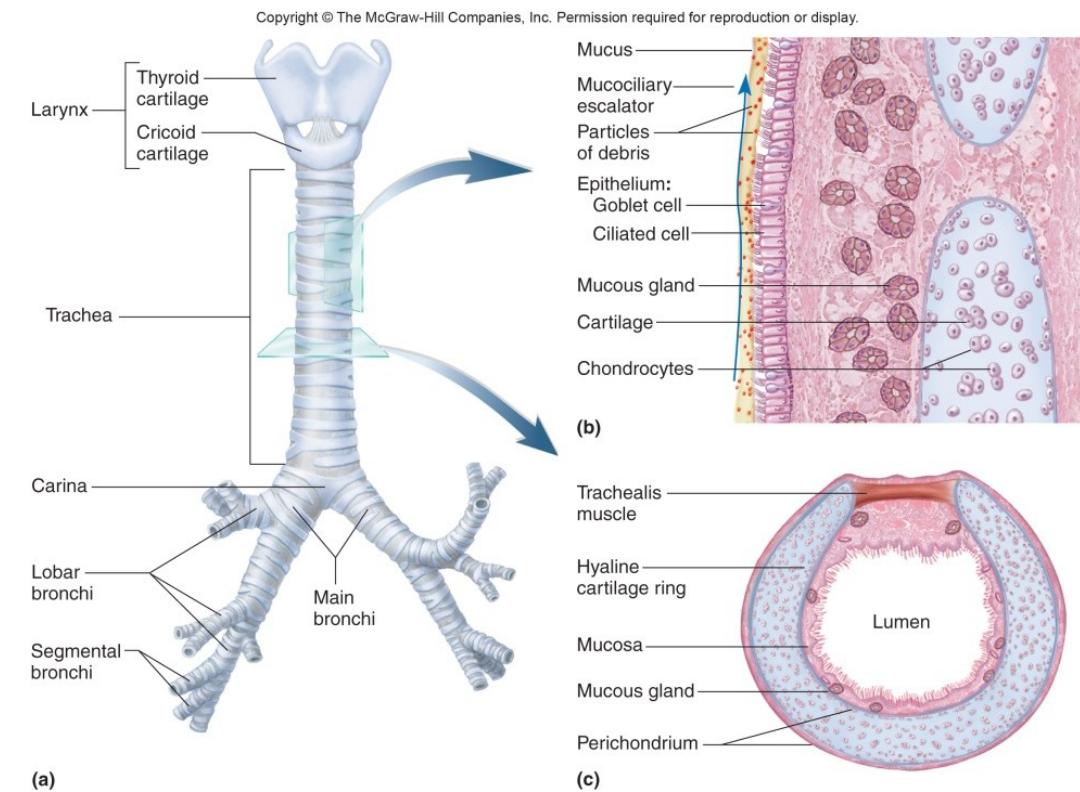
- laryngeal vestibule (**LV**)
- seromucous glands (**G**).
- vestibular folds (**VF**): Bulge of lateral walls, contain seromucous glands and areolar tissue with MALT, often with lymphoid nodules (**L**) and are largely covered by respiratory epithelium, with regions near the epiglottis having stratified squamous epithelium.
- ventricle (**V**)
- vocal folds or cords (**VC**): Lateral folds, covered by stratified squamous epithelium and contain a large striated vocalis muscle (**VM**). Variable tension of VM ligaments caused by the muscles produces different sounds as air is expelled across the vocal cords.

# The Trachea: 16 to 20 C-shaped rings of hyaline cartilage prevent collapse during inhalation

**Inner lining** : mucous secreting pseudostratified columnar epithelium

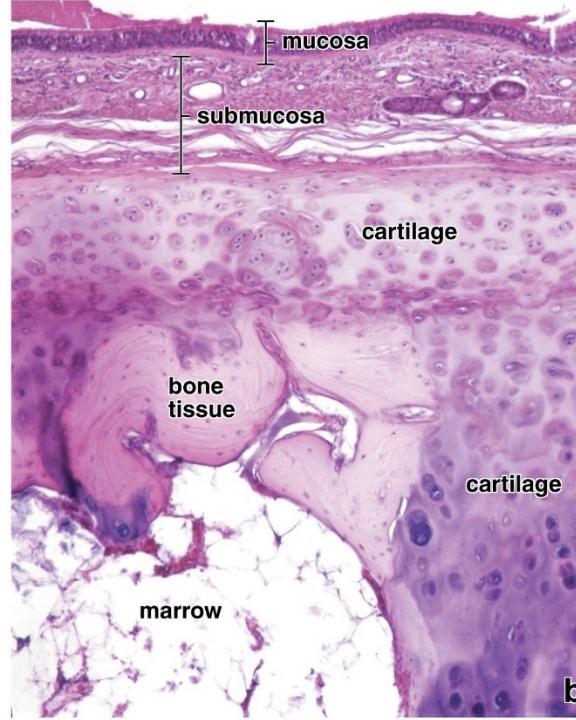
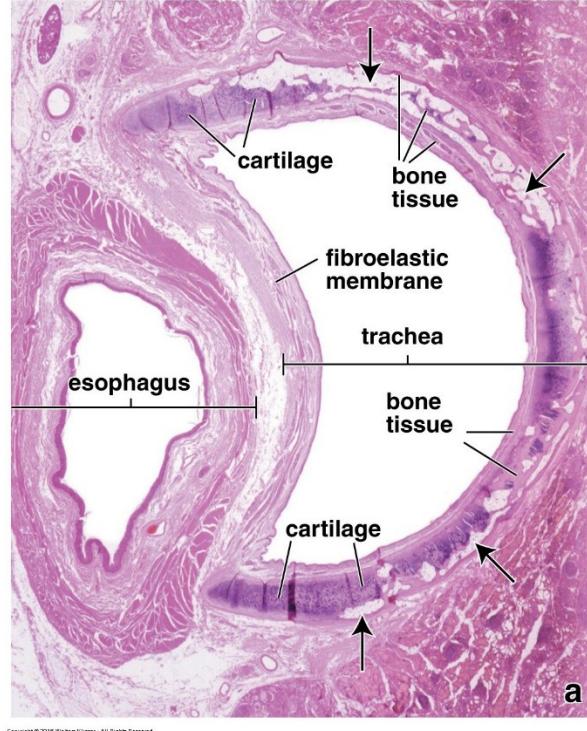
**Mucociliary escalator**: Mucus traps inhaled particles, upward beating cilia drives mucus toward pharynx where it is swallowed

**Middle tracheal layer**: connective tissue; contains lymphatic nodules, mucous and serous glands, and the tracheal cartilage.



**MEDICAL APPLICATION:** Coughing is a reflex action produced most often by viral infection or other irritation of the trachea or other region of the respiratory tract. A persistent dry cough, in which no mucus (phlegm) is produced, can be treated by cough suppressants that act on the brainstem and vagus nerve, while productive coughs are often treated with expectorants that help loosen mucus covering the re [Coughing: https://www.youtube.com/watch?v=usAqJoVYVSc](https://www.youtube.com/watch?v=usAqJoVYVSc)

# Relationship between the trachea and the esophagus at the base of the neck



Cartilaginous tracheal rings: keep the trachea patent, have a C-shaped appearance.

Cartilage gap: fibroelastic membrane that contains the trachealis muscle and numerous seromucous glands.

In this specimen, the tracheal ring has been transformed, in part, to bone, a process that occurs in aging.

TABLE 17-1

## Histologic features of the upper respiratory tract, larynx, and trachea.

Region	Epithelium	Glands	Musculoskeletal Support	Other Features and Major Functions
Vestibules of nasal cavities	Stratified squamous, keratinized to nonkeratinized	Sebaceous and sweat glands	Hyaline cartilage	Vibrissae (stiff hairs) and moisture both filter and humidify air
Most areas of nasal cavities	Respiratory	Seromucous glands	Bone and hyaline cartilage	Rich vasculature and glands warm, humidify, and clean air
Superior areas of nasal cavities	Olfactory, with bipolar neurons	Serous (Bowman) glands	Bone (ethmoid)	Solubilize and detect odorant molecules in air
Nasopharynx and posterior oropharynx	Respiratory and stratified squamous	Seromucous glands	Bone and skeletal muscle	Conduct air to larynx; pharyngeal and palatine tonsils
Larynx	Respiratory and stratified squamous	Mucous glands, smaller seromucous glands	Elastic and hyaline cartilage, ligaments, skeletal muscle	Site for phonation; epiglottis closes while swallowing
Trachea	Respiratory	Mainly mucous glands, some serous or mixed glands	C-shaped rings of hyaline cartilage, with smooth (trachealis) muscle in posterior opening of each	Conduct air to primary bronchi entering lungs; some MALT

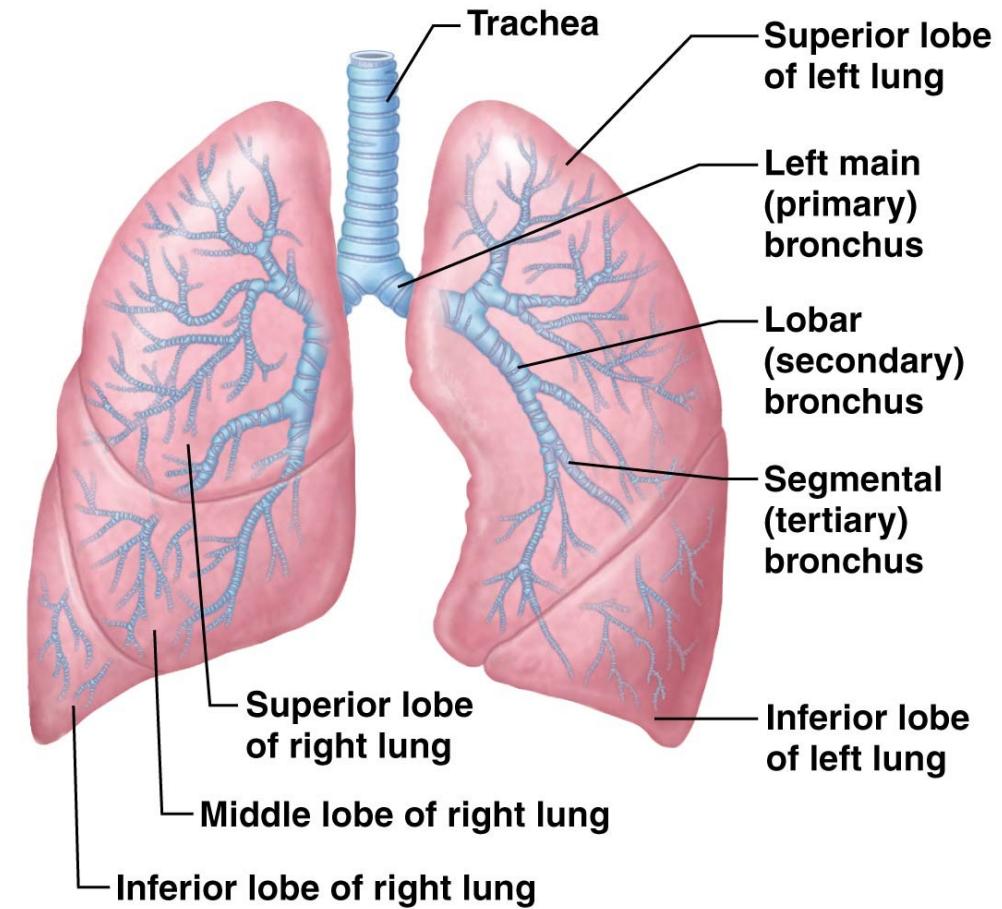
# Lungs are crowded by adjacent organs and are asymmetrical

**Right lung:** Shorter than left because the liver rises higher on the right

- three lobes: superior, middle, and inferior which are separated by **horizontal and oblique fissure**

**Left lung:** Taller and narrower because the heart tilts toward the left and occupies more space on this side of mediastinum

Cardiac impression: Indentation  
Two lobes: superior and inferior separated by a single oblique fissure



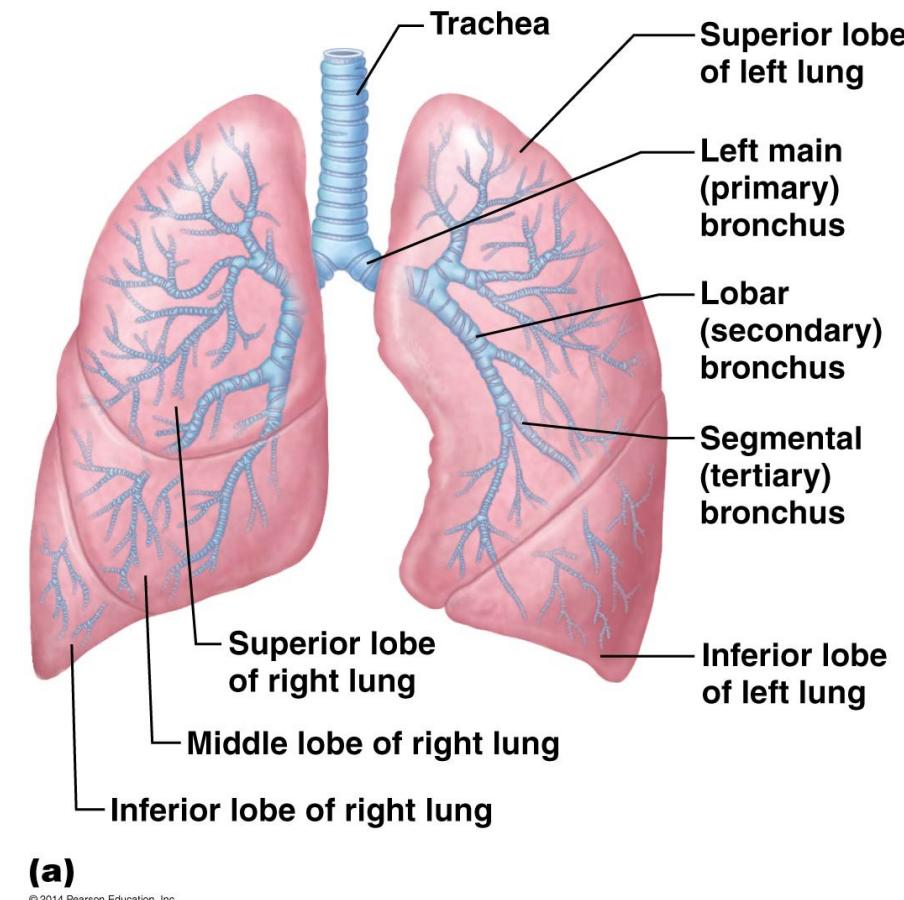
(a)

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# The Bronchial Tree: branching system of air tubes in each lung from main bronchus to 65,000 terminal bronchioles

Main (primary) bronchi: supported by C-shaped hyaline cartilage rings

- **Right main bronchus:** 2 to 3 cm long, arising from fork of trachea
  - slightly wider and more vertical than left
  - Aspirated (inhaled) foreign objects lodge right bronchus more often than the left
- **Left main bronchus:** about 5 cm long
  - Slightly narrower and more horizontal than the right



# The Bronchial Tree

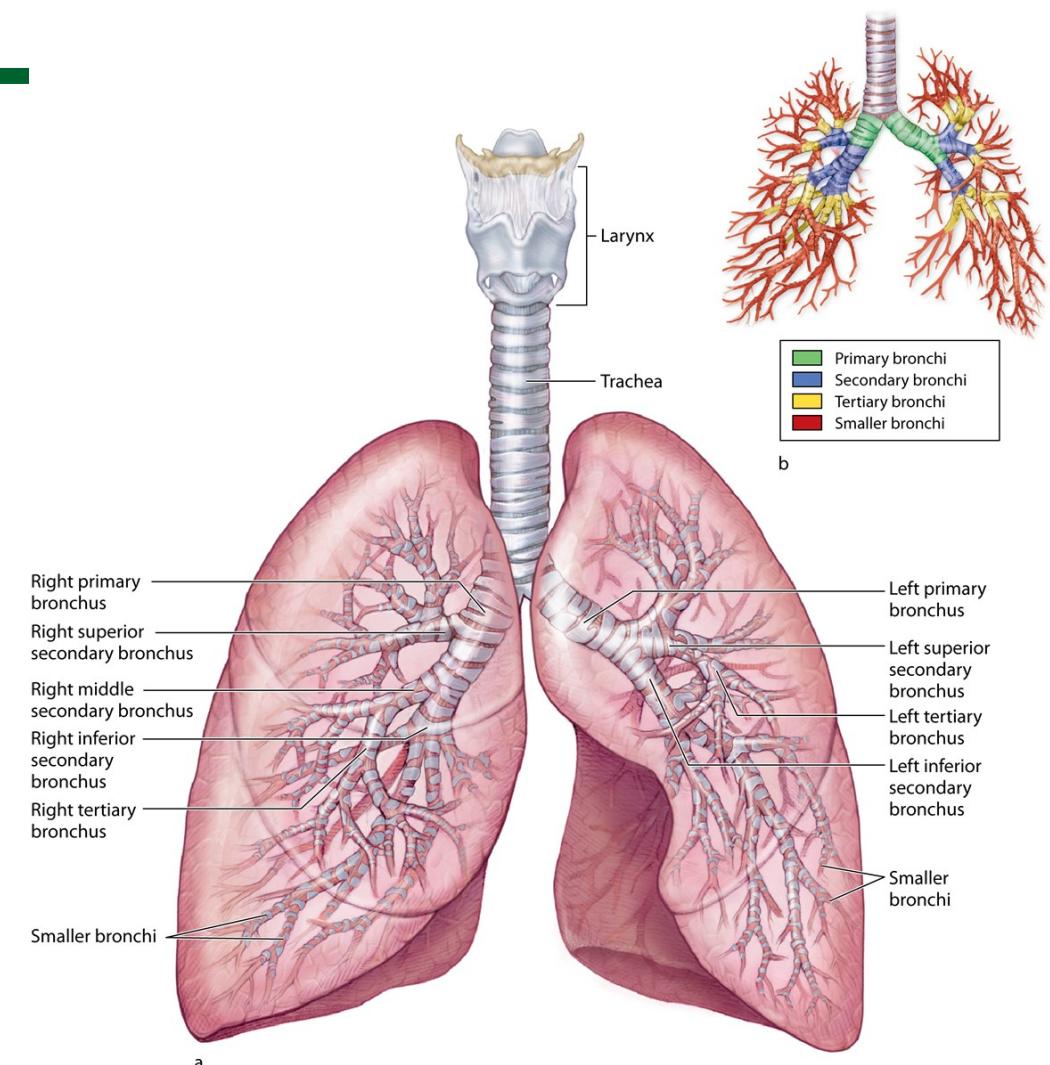
**Lobar (secondary) bronchi:** supported by crescent-shaped cartilage plates

- Three rt. lobar (secondary) bronchi
- Two lt. lobar bronchi

**Segmental (tertiary) bronchi:** supported by crescent-shaped cartilage plates

- 10 on right, 8 on left

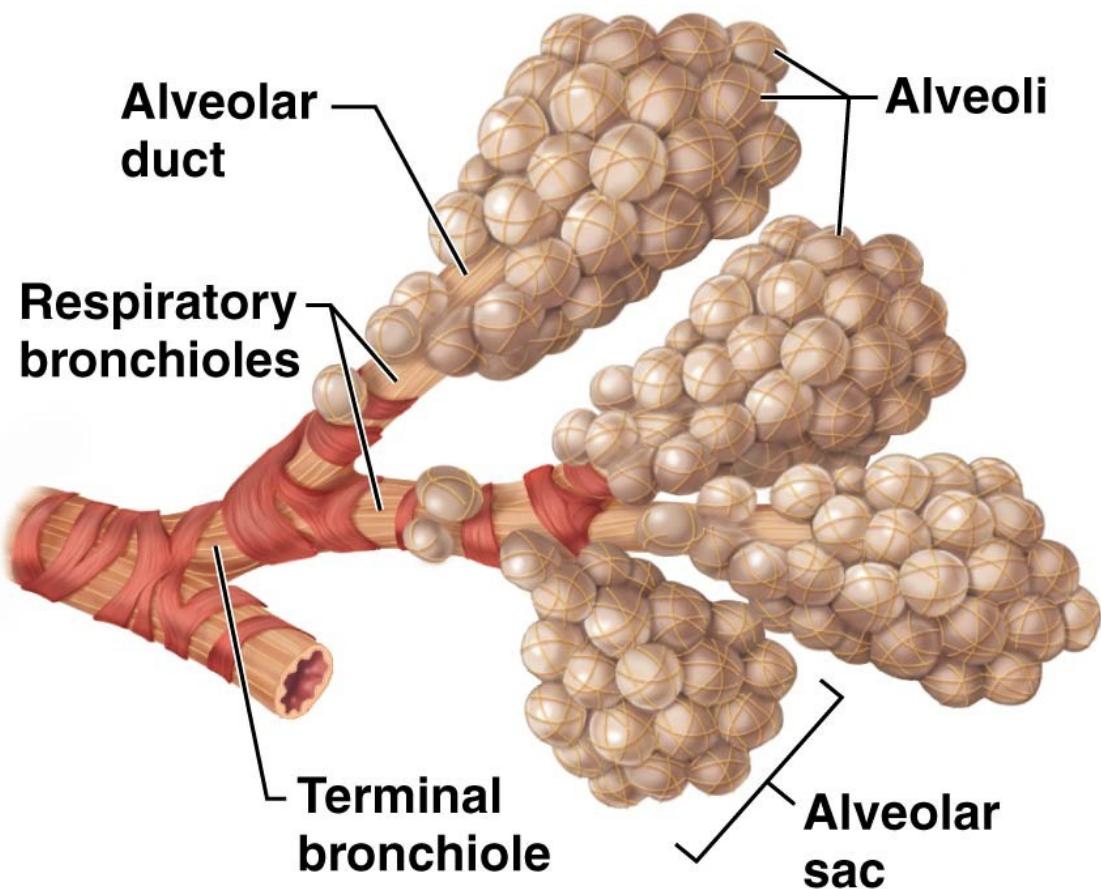
Primary → secondary → tertiary → bronchiole  
→ terminal bronchiole → respiratory  
bronchiole → alveolar duct → alveolar sac →  
alveoli



# Respiratory bronchioles

- Have **alveoli** budding from their walls
- Considered the beginning of the **respiratory division** since alveoli participate in gas exchange
- Divide into 2 to 10 **alveolar ducts**
- End in **alveolar sacs**: grapelike clusters of alveoli arrayed around a central space called the **atrium**

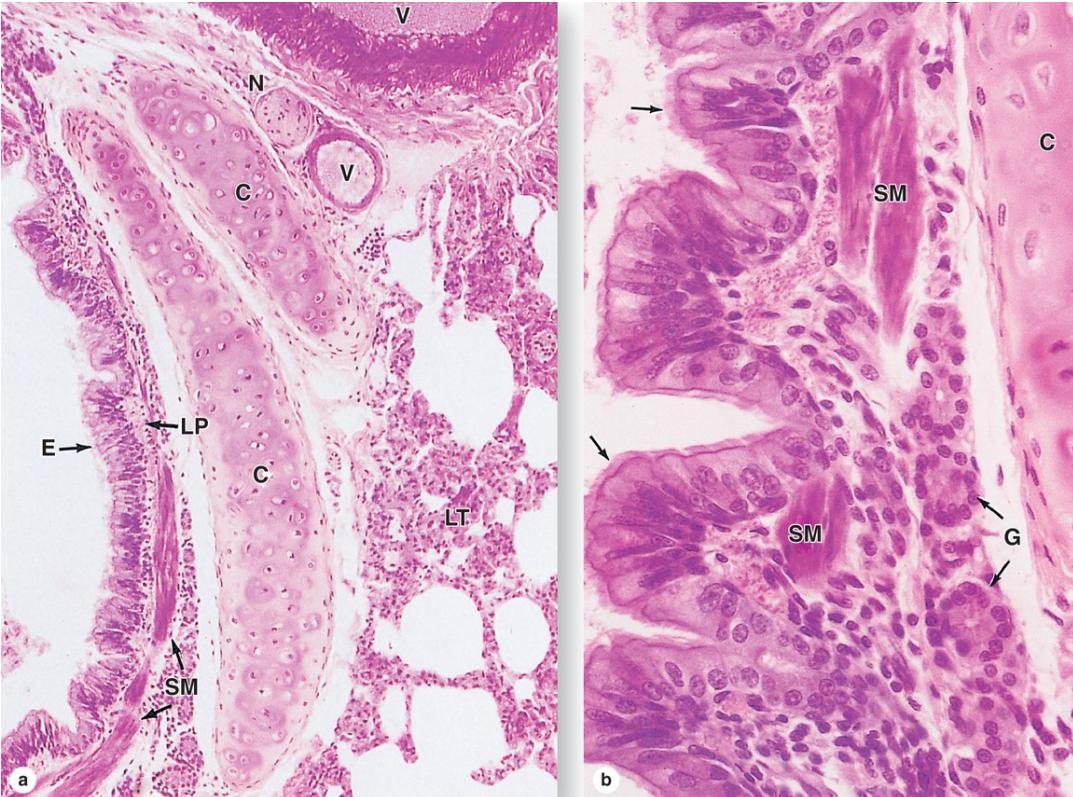
Primary → secondary → tertiary →  
bronchiole → terminal bronchiole →  
respiratory bronchiole → alveolar duct  
→ alveolar sac → alveoli



(b)

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# Bronchial tree is lined with ciliated pseudostratified columnar epithelium (E) to intercept inhaled pathogens



**Elastic connective tissue:** Contributes to the recoil that expels air from lungs

The lamina propria (**LP**) contains well-developed layer of smooth muscle (**SM**) which **contracts or relaxes to constrict or dilate the airway**, regulating airflow

The submucosa is the site of the supporting cartilage (**C**) and the adventitia includes blood vessels (**V**) and nerves (**N**). Lung tissue (**LT**) directly surrounds the adventitia of bronchi.

The lamina propria has both smooth muscle (**SM**) and small serous glands (**G**) near cartilage (**C**).

**MEDICAL APPLICATION:** Asthma is produced by chronic inflammation within the bronchial tree of the lungs. Sudden constrictions of the smooth muscle is caused by mast cells, resulting in difficulty in breathing.

Epinephrine and other sympathomimetic drugs relax the muscle and increase the bronchiole diameter by stimulating the sympathetic nervous system.

<https://ed.ted.com/lessons/how-does-asthma-work-christopher-e-gaw>

**MEDICAL APPLICATION:** **Squamous cell carcinoma**, which is closely correlated with a history of smoking, arises most often from epithelial cells of segmental bronchi.

**Adenocarcinoma**, the most common lung cancer in nonsmokers, usually arises from epithelial cells more peripherally, in bronchioles and alveoli. **Small cell carcinoma**, a less common but highly malignant form of lung cancer, develops after neoplastic transformation of small granule Kulchitsky cells in bronchial respiratory epithelium.

Clinical Features	Pathologic Changes	M
	Bronchus	Normal Epithelium/ Hyperplasia
	Bronchus	Squamous Dysplasia
	Bronchus	Angiogenetic Squamous Dysplasia
Smoking (with or without COPD)	Bronchus/ Bronchiole	Inflammatory Changes
	Small Bronchus/ Bronchiole	Normal Epithelium
	Alveoli	Adenomatous Alveolar Hyperplasia
Non-Smoking	Small Bronchus/ Bronchiole	Normal Epithelium

Dysplasia: The Progression of Cancer:

[https://www.youtube.com/watch?v=Gh\\_1PfLKqg4](https://www.youtube.com/watch?v=Gh_1PfLKqg4)

## Terminal bronchiole tissue lacks cartilage, has ciliated cuboidal epithelium and well developed layer of smooth muscle

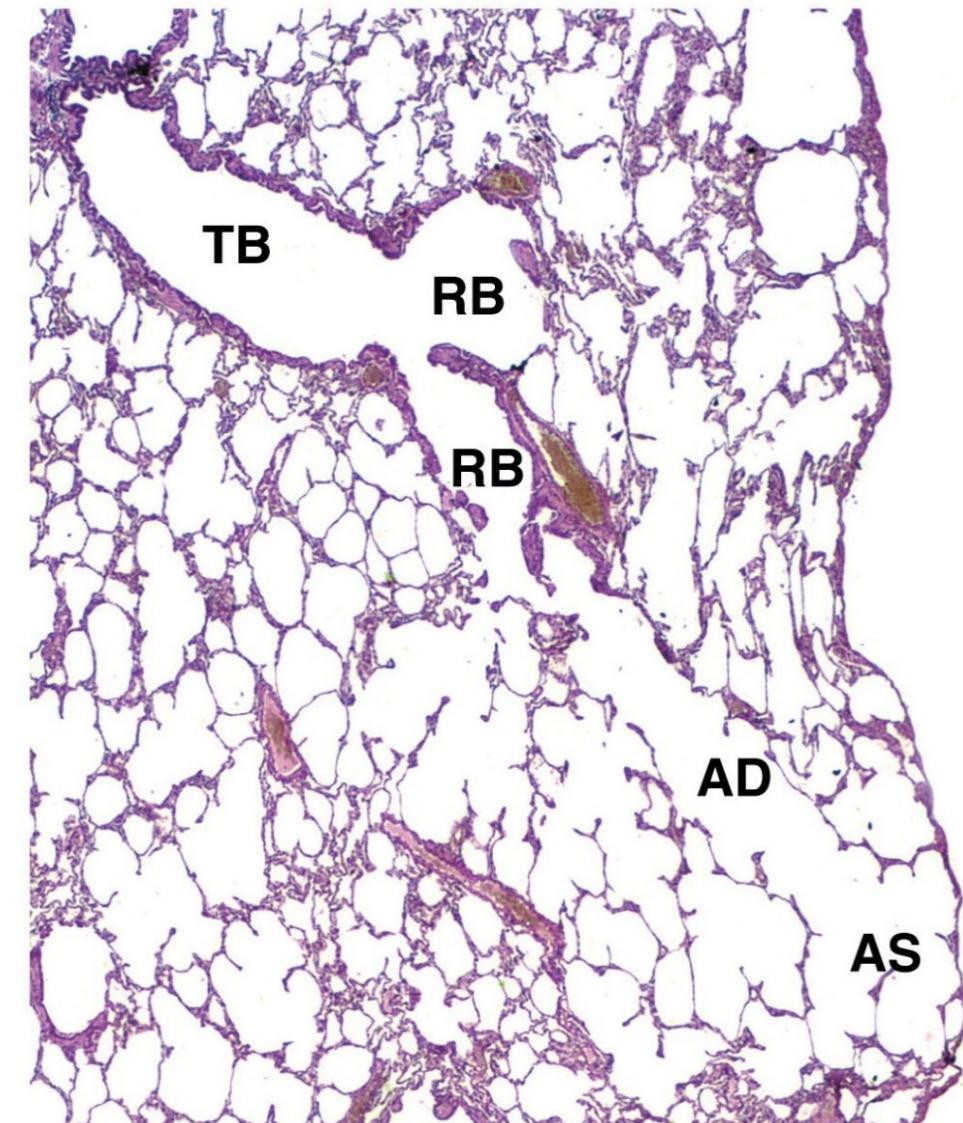
Each bronchiole divides into 50 to 80 **terminal bronchioles (TB)**, Final branches of conducting division

**Terminal bronchiole tissue:** no mucous glands or goblet cells, but have cilia that move mucus draining into them back by **mucociliary escalator**

Each terminal bronchiole gives off two or more smaller **respiratory bronchioles (RB)**

### Alveolar Ducts (AV) & Alveolar Sacs (AS)

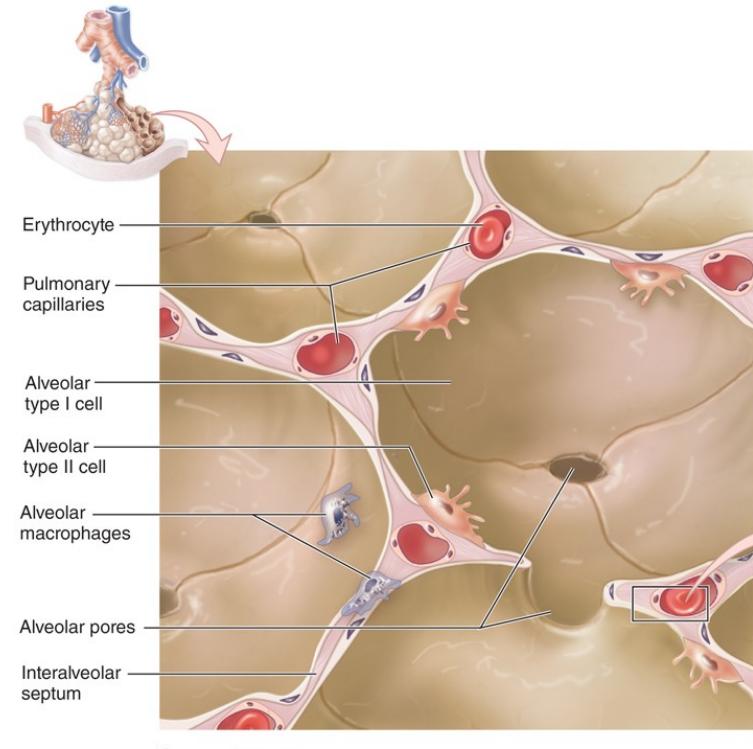
**MEDICAL APPLICATION** Bronchioles are affected by measles virus or adenovirus, both of which can cause bronchiolitis.



- **Squamous (type I) alveolar cells:** Thin, broad cells allowing **rapid gas exchange**, 95% of alveolus surface area
- **Great (type II) alveolar cells:** Round to cuboidal cells that repair the alveolar epithelium when the squamous (type I) cells are damaged
  - Secrete **pulmonary surfactant:** phospholipids and proteins that coat alveoli and prevents collapse during exhalation
- **Alveolar macrophages (dust cells):** keep alveoli free from debris by phagocytizing dust particles

**MEDICAL APPLICATION:** Infant respiratory distress syndrome, the leading cause of death in premature babies, is due to incomplete differentiation of type II alveolar cells and a resulting deficit of surfactant and difficulty in expanding the alveoli in breathing.

## Cells of the alveolus

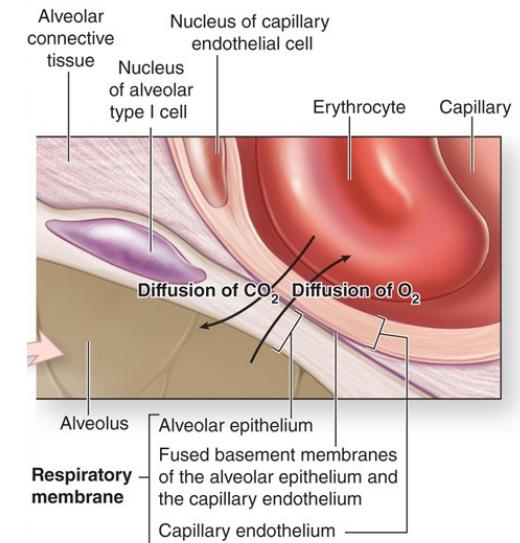
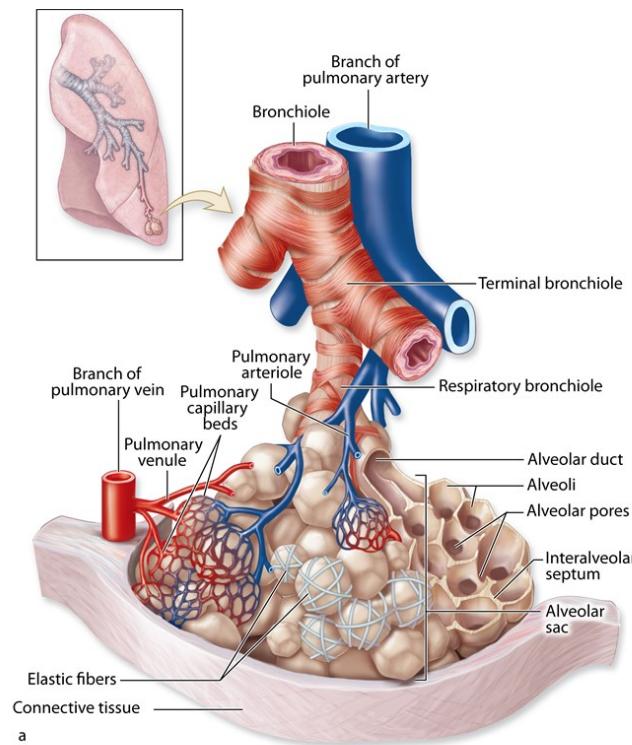


# Respiratory membrane: the barrier between the alveolar air and blood, prevents fluid from accumulating in alveoli

Each alveolus is surrounded by a basket of blood capillaries supplied by the pulmonary artery

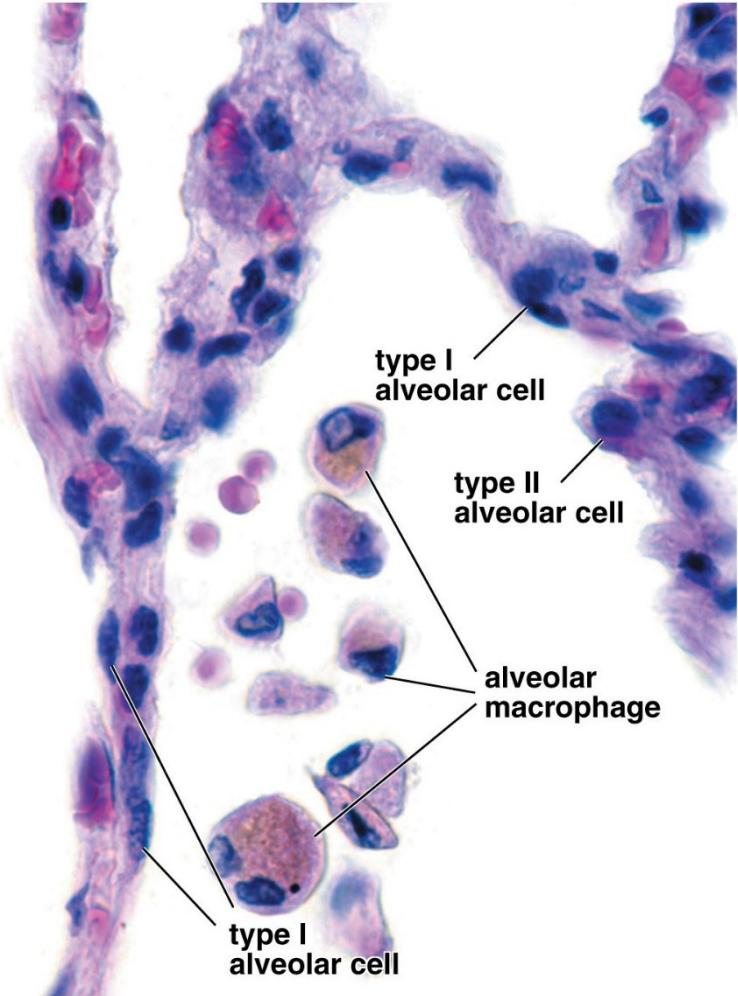
**MEDICAL APPLICATION:** Diffuse alveolar damage or adult respiratory distress syndrome can be produced by various types of injuries to the alveolar epithelial and the capillary endothelial cells. Common causes of such injuries include viral and bacterial respiratory tract infections or inhalation of toxic gases.

**MEDICAL APPLICATION** In congestive heart failure, the lungs become congested with blood, and erythrocytes pass into the alveoli, where they are phagocytized by alveolar macrophages.



# Alveoli and Alveolar Macrophages

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**MEDICAL APPLICATION:** Emphysema, a chronic lung disease most commonly caused by cigarette smoking, involves dilation and permanent enlargement of the bronchioles leading to pulmonary acini and accompanying loss of cells in the alveoli and other parts of the airway walls, leading to an irreversible loss of respiratory function.

**TABLE 17-2****Features of airways within the lungs.**

Region of Airway	Epithelium	Muscle and Skeletal Support	Other Features and Major Functions
Bronchi	Respiratory	Prominent spiral bands of smooth muscle; irregular hyaline cartilage plates	Repeated branching; conduct air deeper into lungs
Bronchioles	Simple ciliated cuboidal to columnar, with Clara cells	Prominent circular layer of smooth muscle; no cartilage	Conduct air; important in bronchoconstriction and bronchodilation
Terminal bronchioles	Simple cuboidal, ciliated and Clara cells	Thin, incomplete circular layer of smooth muscle; no cartilage	Conduct air to respiratory portions of lungs; Clara cells with several protective functions
Respiratory bronchioles	Simple cuboidal, ciliated and Clara cells, with scattered alveoli	Fewer smooth muscle fibers, mostly around alveolar openings	Conduct air deeper, with some gas exchange and protective Clara cells
Alveolar ducts and sacs	Simple cuboidal between many alveoli	Bands of smooth muscle around alveolar openings	Conduct air, with much gas exchange
Alveoli	Types I and II alveolar cells (pneumocytes)	None (but with network of elastic and reticular fibers)	Sites of all gas exchange; surfactant from type II pneumocytes; dust cells



Skin

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## BI 455 CHAPTER 18

# The Integumentary System: skin, hair, nails, and cutaneous glands

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## Functions

**Resistance to trauma and infection:** few organisms able to penetrate if intact

  cells packed with tough **keratin** and linked by strong desmosomes

  dryness of skin and protective acid layer helps keep organisms on skin in check

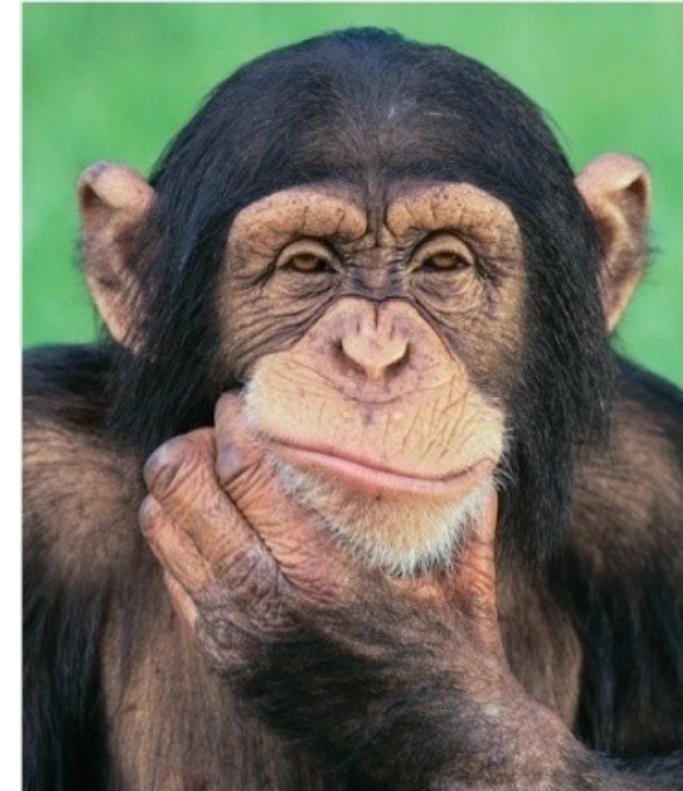
## **Water retention**

**Vitamin D synthesis:** important for  $\text{Ca}^{2+}$  absorption

**Sensation:** temperature, touch, and texture, pressure, vibration, and injury

## **Thermoregulation**

## **Nonverbal communication**



Intro to the integument:

<http://www.youtube.com/watch?v=BVIIgHyNRdl&feature=related>

(watch till 5:20)

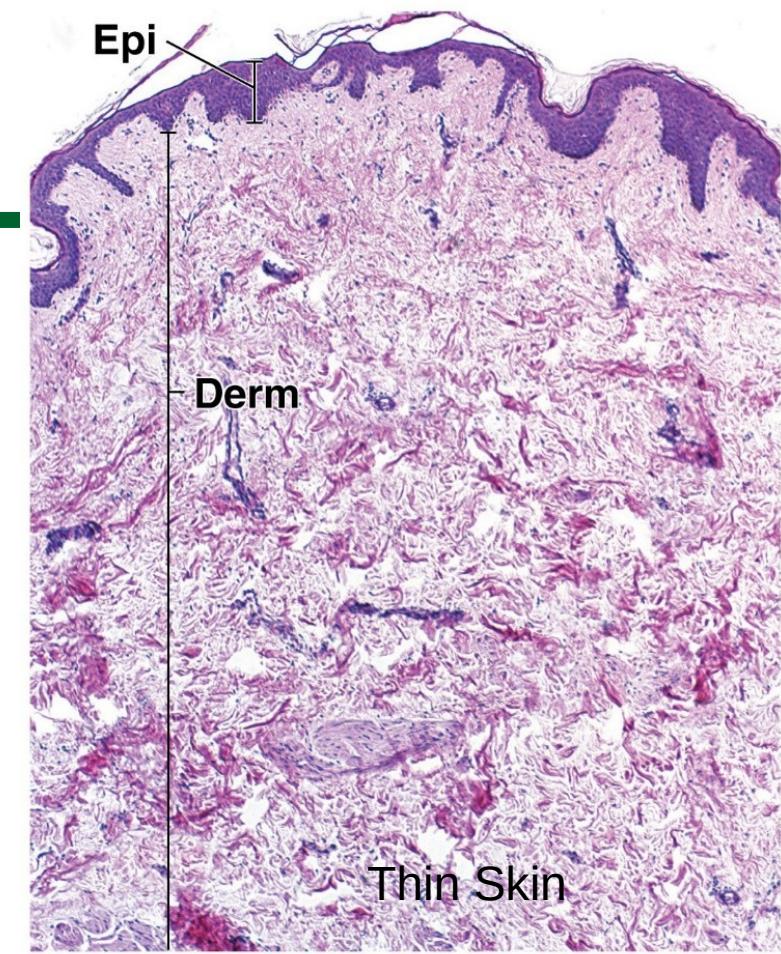
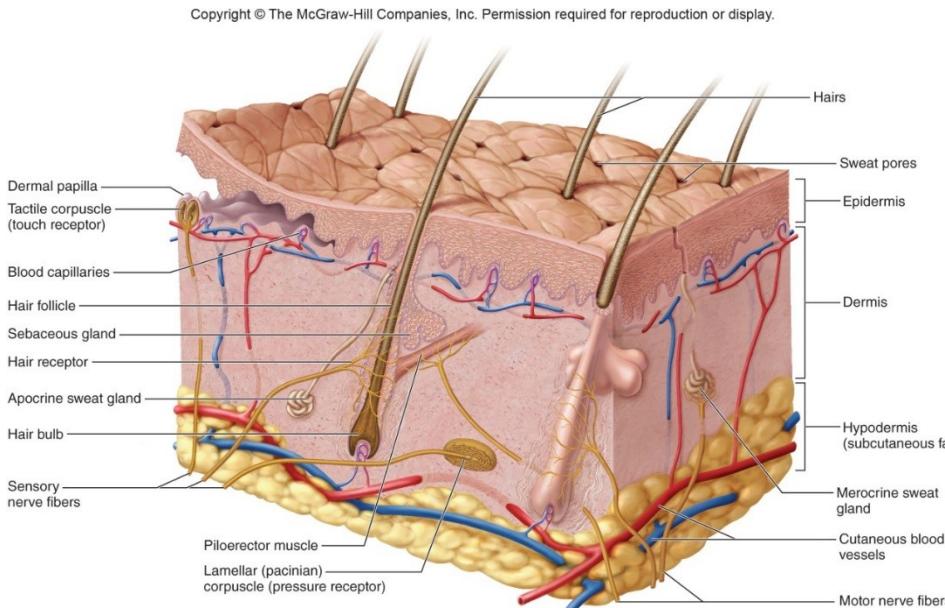
# The Skin and Subcutaneous Tissue

**Skin:** 2 layered membrane covering external surface of body

**Epidermis:** superficial epithelium

**Dermis:** deeper connective tissue

**Hypodermis:** loose connective tissue between skin and muscles



**>> MEDICAL APPLICATION:** Friction blisters are lymph-filled spaces created between the epidermis and dermis of thick skin by excessive rubbing, producing a protective thickening and hardening of the outer cornified epidermal layers, seen as corns and calluses.

# Characteristics of skin

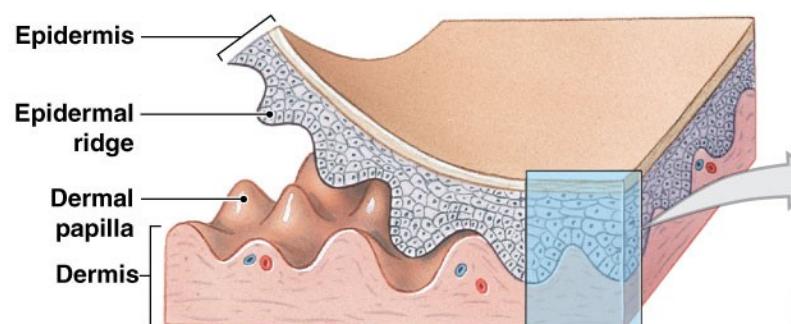
15% of body weight, ranges from 0.5mm to 6 mm, due mostly to variations in dermis

**Thick skin:** Epidermis about 0.5 mm thick, thick layer of dead cells, *stratum corneum*

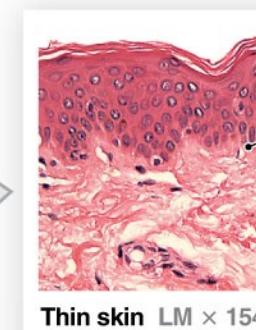
- Covers palms, soles, surfaces of fingers and toes, subject to greatest mechanical stress
- Has sweat glands, but no hair follicles or sebaceous glands

**Thin skin:** epidermis  
about 0.1 mm thick

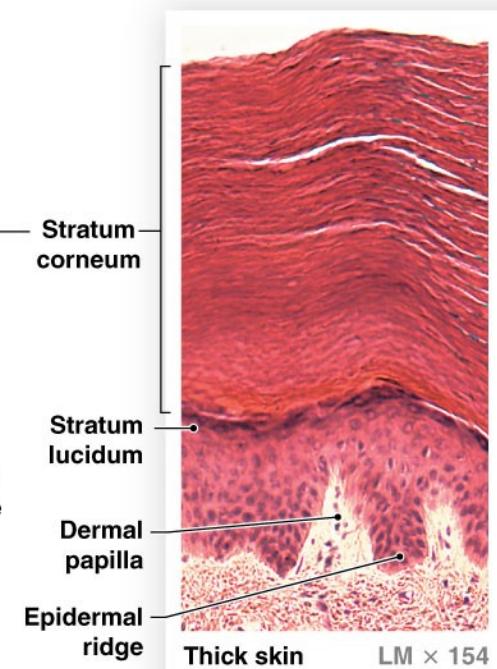
- Has hair follicles, sebaceous and sweat glands



**a** The structural relationship and interface between the epidermis and underlying dermis. The proportions of the various layers differ with the location sampled.



**b** A micrograph of thin skin, which covers most of the exposed body surface.



**c** A micrograph of thick skin, which covers the surface of the palms and the soles of the feet.

# Layers of skin

Layers of the skin:

<https://www.youtube.com/watch?v=oPzbwx8u7bU>

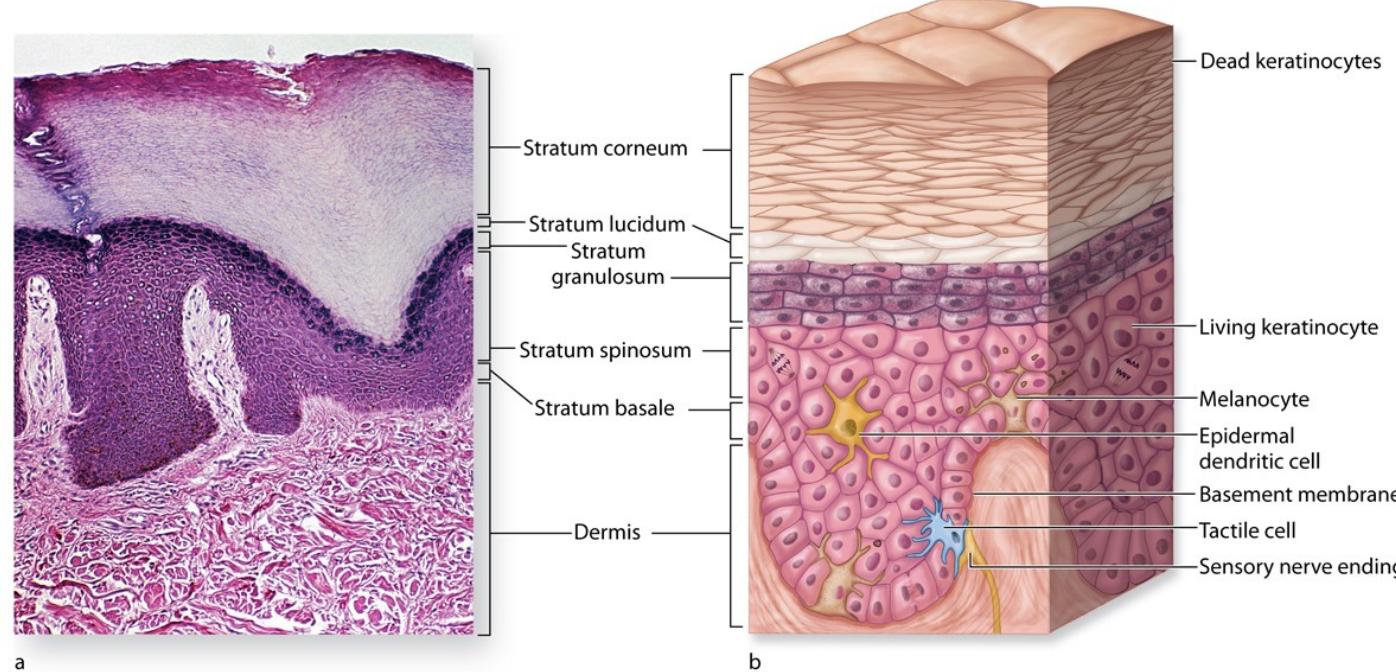
**Stratum basale:** single layer of stem cells, keratinocytes, melanocytes, and tactile cells

**Stratum spinosum:** keratinocytes that flatten as they produce keratin, and cease dividing as pushed upward). Also contain dendritic cells.

**Stratum granulosum:** three to five layers of flat dying keratinocytes. Keratin filaments in thick bundles produce water barrier

**Stratum lucidum** clear layer of dead cells present only in thick skin of palms and soles

**Stratum corneum:** up to 30 layers of dead anucleate squamous keratinocytes packed with keratin, gives skin toughness cells flaking off (exfoliate) are replaced by new cells 30 to 40 days from “birth” to exfoliation



# Cells of epidermis

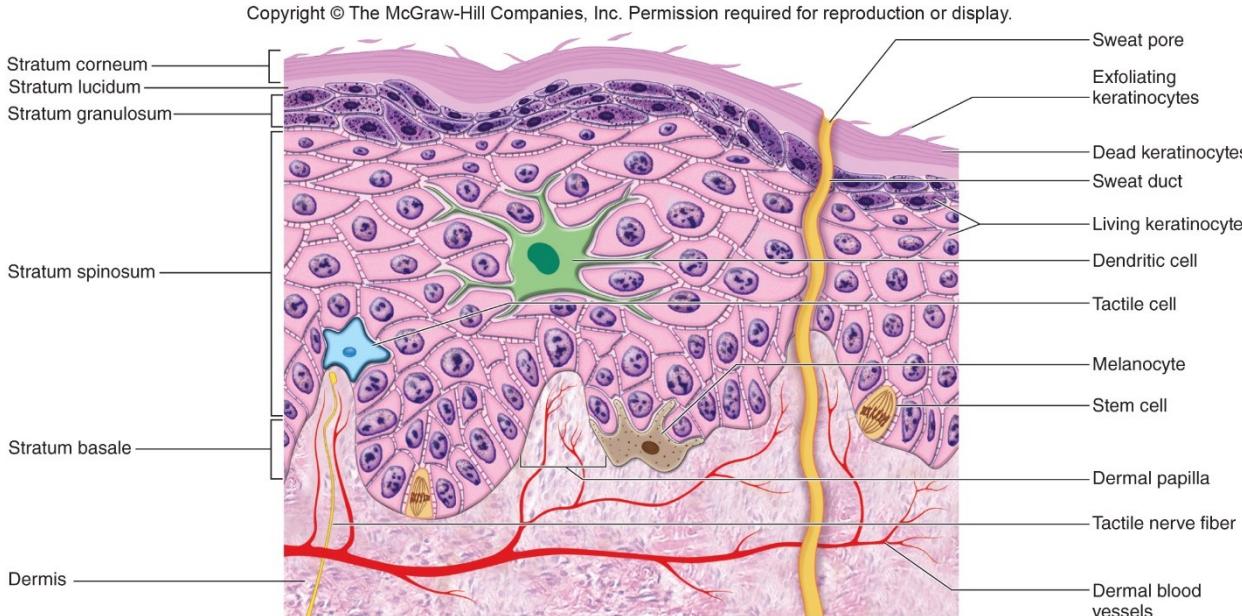
Keratinized stratified squamous epithelium is mostly **keratinocytes** packed with keratin

**Melanocytes:** pigment-producing cells

**Merkel's cells:** cells specialized for touch

**Stem cells:** divide and replace epidermal cells that die

**Dendritic Langerhans' cells:** Antigen Presenting Cells

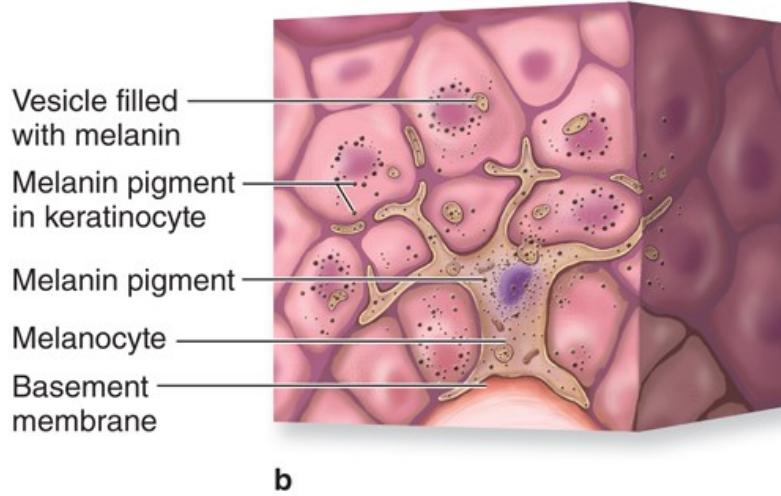
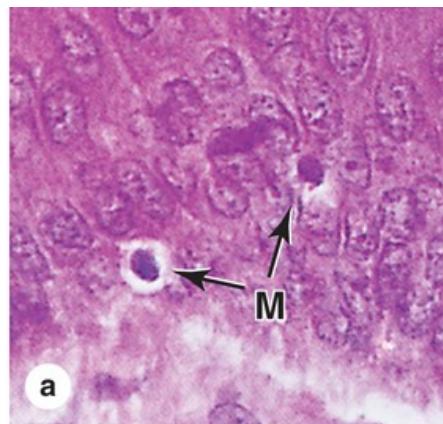
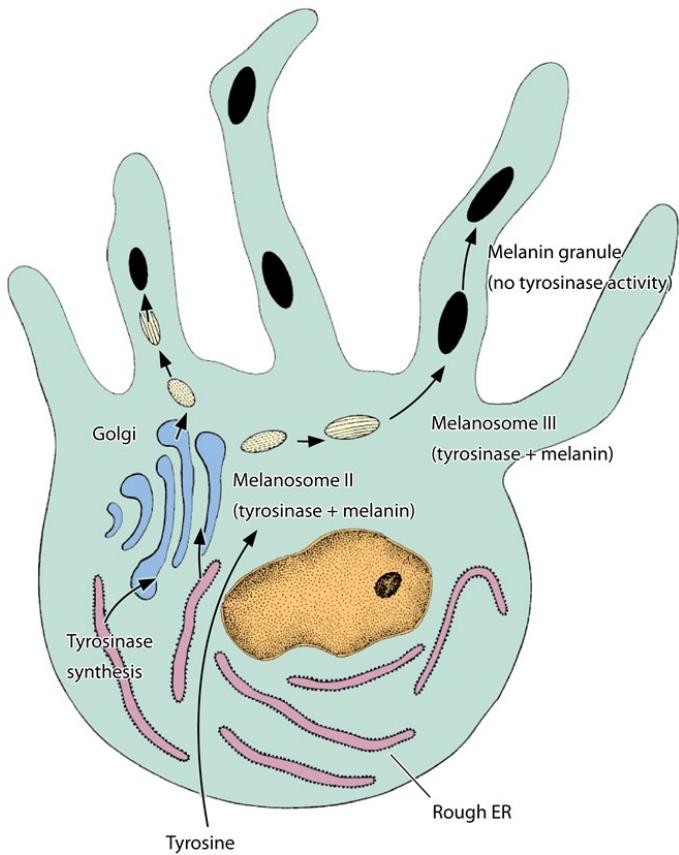


## »» MEDICAL APPLICATION

In psoriasis, keratinocytes are overproduced, causing at least slight thickening of the epidermal layers and increased keratinization and desquamation.

Psoriasis is caused by overactive T lymphocytes that trigger an autoimmune reaction in the skin, which can also lead to inflammation with redness, irritation, itching, and scaling, with a defective skin barrier.

# Melanocytes are scattered among the basal cells of the stratum basale



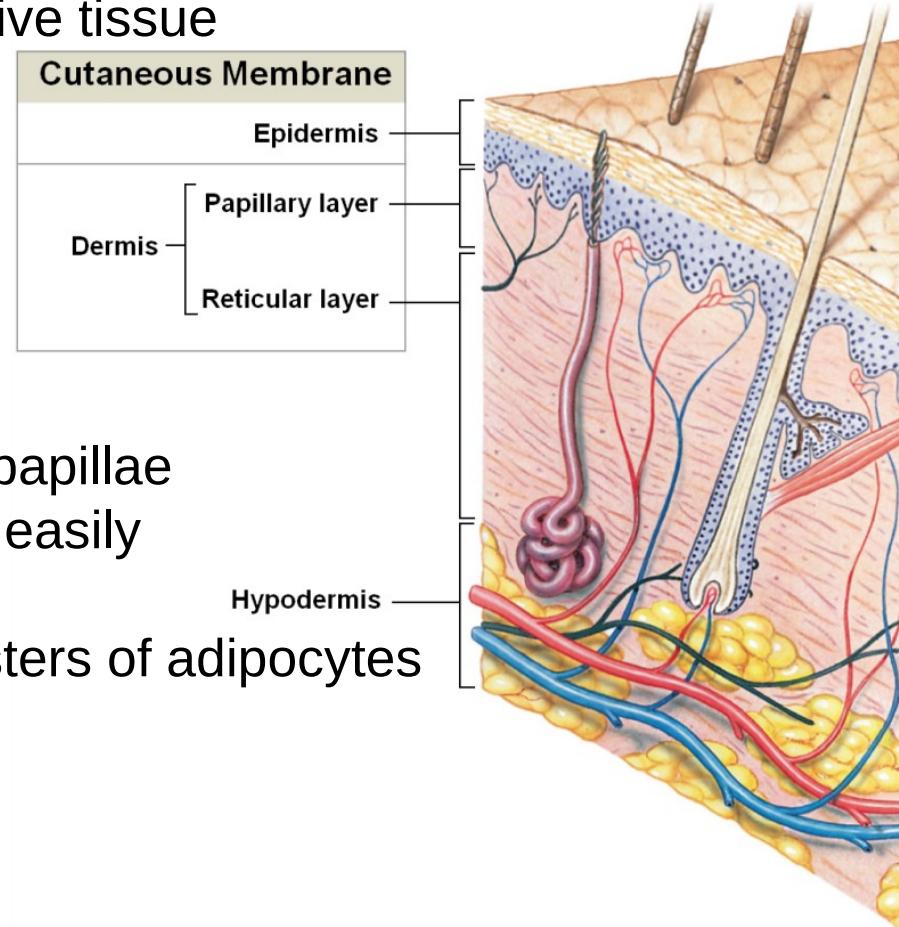
Melanocytes synthesize **melanin granules** and transfer them into neighboring **keratinocytes** of the basal and spinous layers. Typically melanocytes are pale-staining cells on the basement membrane, with lower total melanin content than the keratinocytes

A mature melanin granule is transported to the tips of the processes of melanocyte and transferred to the keratinocytes, where they accumulate as a supranuclear cap shading the DNA against the harmful effects of UV radiation.

**>> MEDICAL APPLICATION** In adults, one-third of all cancers originate in the skin. Most of these derive from cells of the basal or spinous layers, producing, respectively, basal cell carcinomas and squamous cell carcinomas.

## Dermis is mainly collagen

- From 0.2 mm to 6 mm
- Also has elastic and reticular fibers and cells of fibrous connective tissue
- Many blood vessels and nerve endings
- Sweat and sebaceous glands
- Hair or nails rooted here
- Where skeletal muscles attach on face



## Zones of Dermis

- **Papillary layer:** thin zone of areolar tissue in and near dermal papillae
  - loosely organized, which allows leukocytes to move around easily
- **Reticular layer:** four-fifths of dermis
  - thick bundles of collagen, elastic fibers, fibroblasts, and clusters of adipocytes
  - sweat glands, nail roots, and hair follicles

## Hypodermis (subcutaneous tissue) underlies dermis

- Looser connective tissue and more adipose tissue, Binds skin to muscles or other tissues
- Pads body
- Serves as an energy reservoir
- Provides thermal insulation
- Diffuses in thickness distribution

TABLE 18-1

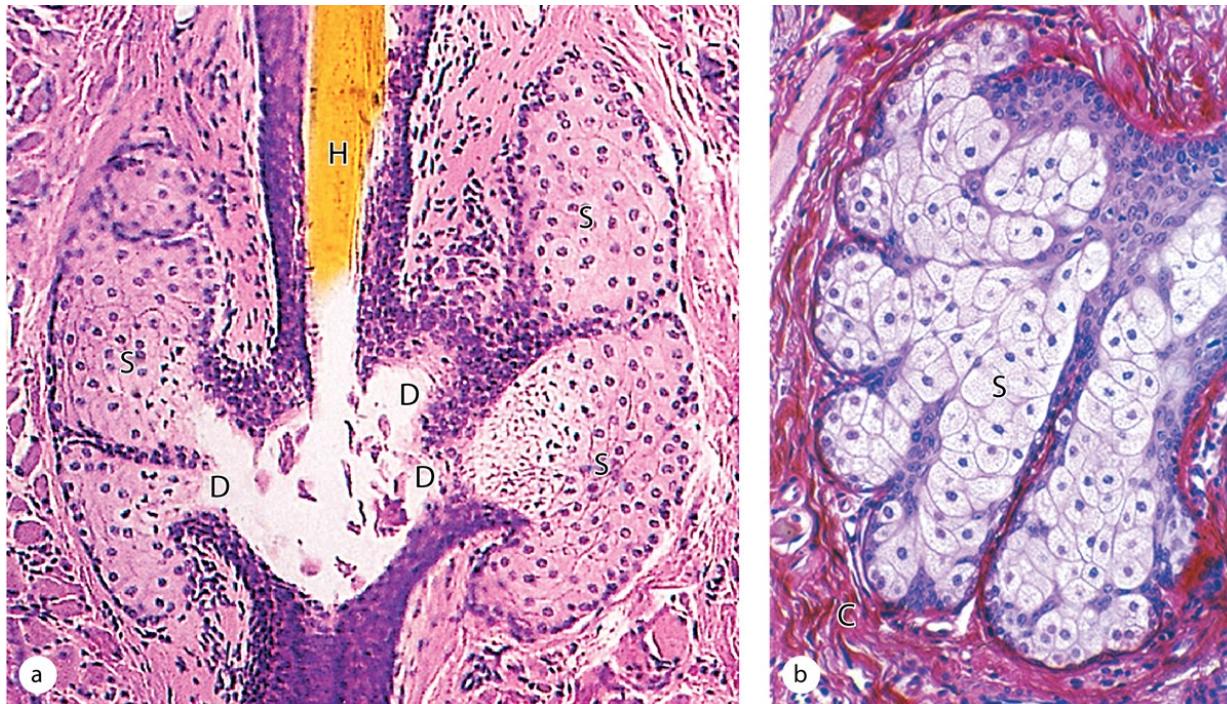
Skin layers and the subcutaneous layer.

Layer	Specific Layer	Description
Epidermis	Stratum corneum Stratum lucidum Stratum granulosum Stratum spinosum Stratum basale	Stratum corneum Most superficial layer; 20-30 layers of dead, flattened, anucleate, keratin-filled keratinocytes; protects against friction and water loss  Stratum lucidum 2-3 layers of anucleate, dead cells; seen only in thick skin  Stratum granulosum 3-5 layers of keratinocytes with distinct kerato-hyaline granules  Stratum spinosum Several layers of keratinocytes all joined by desmosomes; Langerhans cells present  Stratum basale Deepest, single layer of cuboidal to low columnar cells in contact with basement membrane; mitosis occurs here; melanocytes and Merkel cells also
Dermis	Papillary layer Reticular layer	Papillary layer More superficial layer of dermis; composed of areolar connective tissue; forms dermal papillae; contains subpapillary vascular plexus  Reticular layer Deeper layer of dermis; dense irregular connective tissue surrounding hair follicles, sebaceous glands and sweat glands, nerves, and deep plexus of blood vessels extending into subcutaneous layer
Subcutaneous layer	No specific layers	Not considered part of the integument; deep to dermis; composed of areolar and adipose connective tissue

## » MEDICAL APPLICATION

With age, collagen fibers thicken and collagen synthesis decreases. In old age, extensive cross-linking of collagen fibers and the loss of elastic fibers, especially after excessive exposure to the sun (solar elastosis), cause the skin to become more fragile, lose its suppleness, and develop wrinkles.

**Sebaceous glands secrete a complex, oily mixture of lipids called sebum into short ducts that in most areas open into hair follicles**

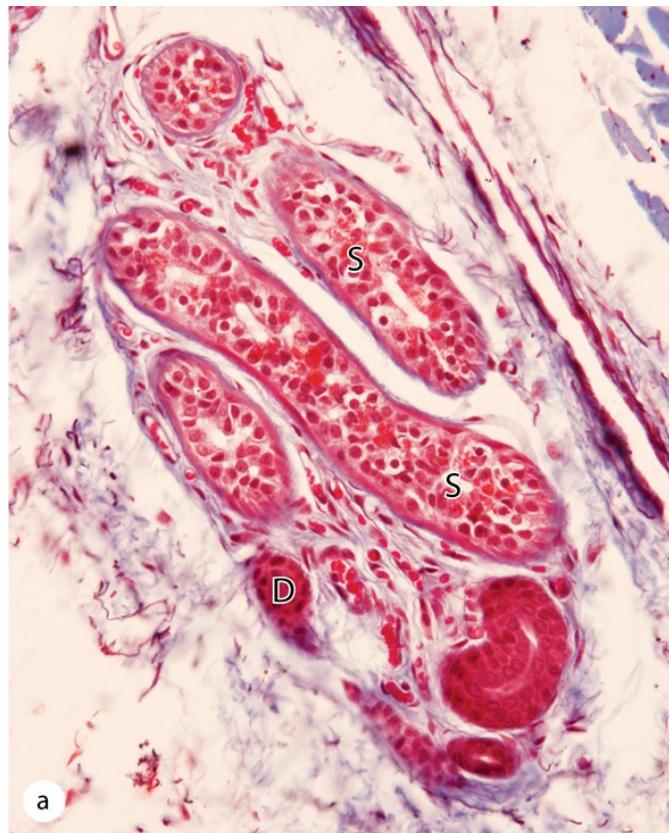


### Holocrine secretion

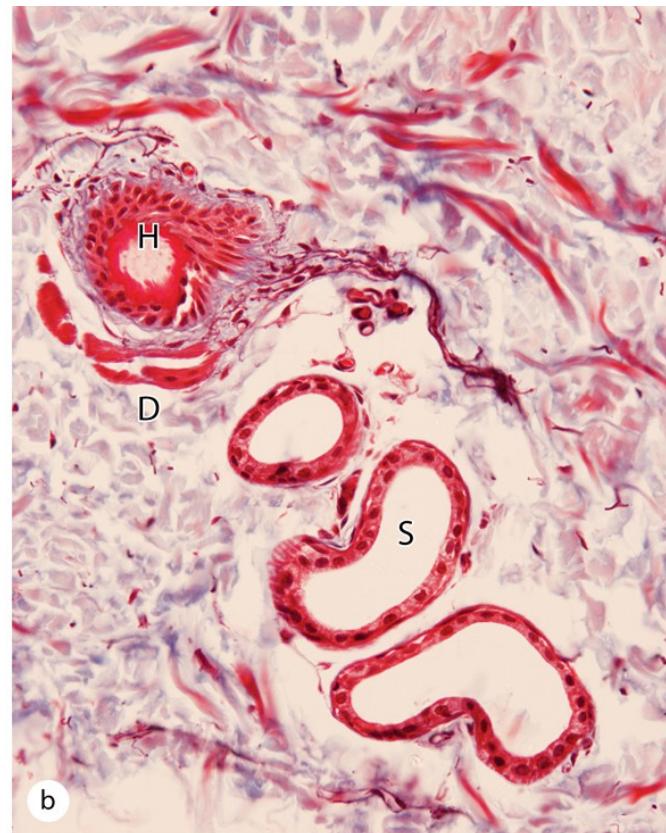
- (a) A section of a pilosebaceous unit shows acini composed of large sebocytes (**S**), which undergo terminal differentiation by filling with small lipid droplets and then disintegrating near the ducts (**D**) opening at the hair (**H**) shaft
- (b) The gland's capsule (**C**) and sebocytes (**S**) at higher magnification. Proliferation of the small progenitor cells just inside the capsule continuously forces sebum into the ducts

### »» MEDICAL APPLICATION

Acne vulgaris involves excessive keratinization within the pilosebaceous unit and excess sebum production. Blockage of ducts in the follicle allow anaerobic bacteria to grow in the accumulated sebum, leading to localized inflammation and neutrophil infiltration.



a



b

## Eccrine and apocrine sweat glands

(a) Eccrine glands have small lumens in the secretory components (**S**) and ducts (**D**), both of which have an irregular stratified cuboidal appearance. Both clear and acidophilic cells are seen in the stratified cuboidal epithelium of the secretory units.

(b) Apocrine sweat glands, which produce a more protein-rich secretion with pheromonal properties, are characterized by secretory portions (**S**) with lumens much larger than those of eccrine glands. Their ducts (**D**) open into hair follicles (**H**) rather than to the epidermal surface.

### » MEDICAL APPLICATION

The sweat of infants with cystic fibrosis (CF) is often salty and is commonly taken as indicative of this genetic disease. CF patients have defects in a transmembrane conductance regulator (CFTR) of epithelial cells that lead to disruptive accumulations of thick mucus in the respiratory and digestive tracts. Failure to remove salt from sweat is related to the same genetic defect.