Schedule: Week 1

1. TA Introduction: Rachel Wilson, Lindsay Holden
2. Welcome
3. Syllabus
4. Week 1 Lecture
   - Chapter 1: Histology and Its Methods of Study
   - Chapter 2: The Cytoplasm
   - Chapter 3: The Nucleus

Welcome

About me: Radhika Reddy

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- Ph.D Neuroscience Johns Hopkins University
- Post Doctoral Fellow New York University
- Peace Corp Volunteer
- Senior Research Associate Oregon Health & Science University
- Instructor PSU present

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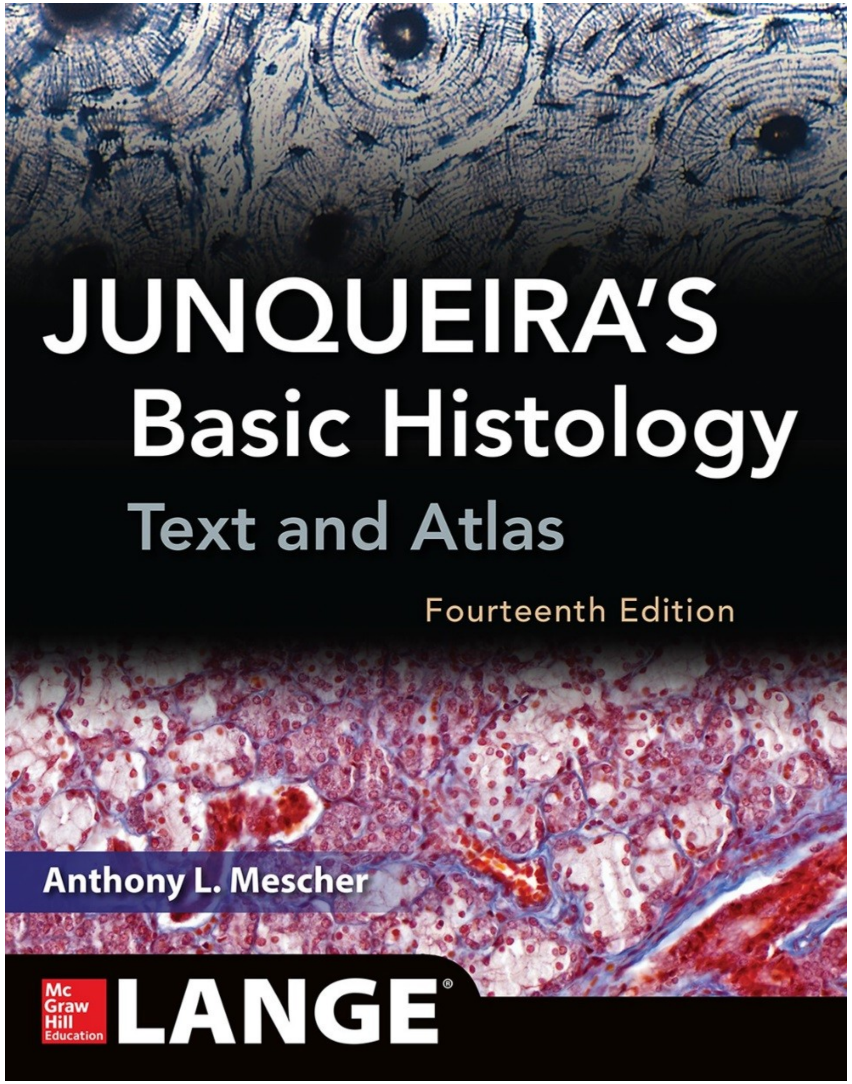
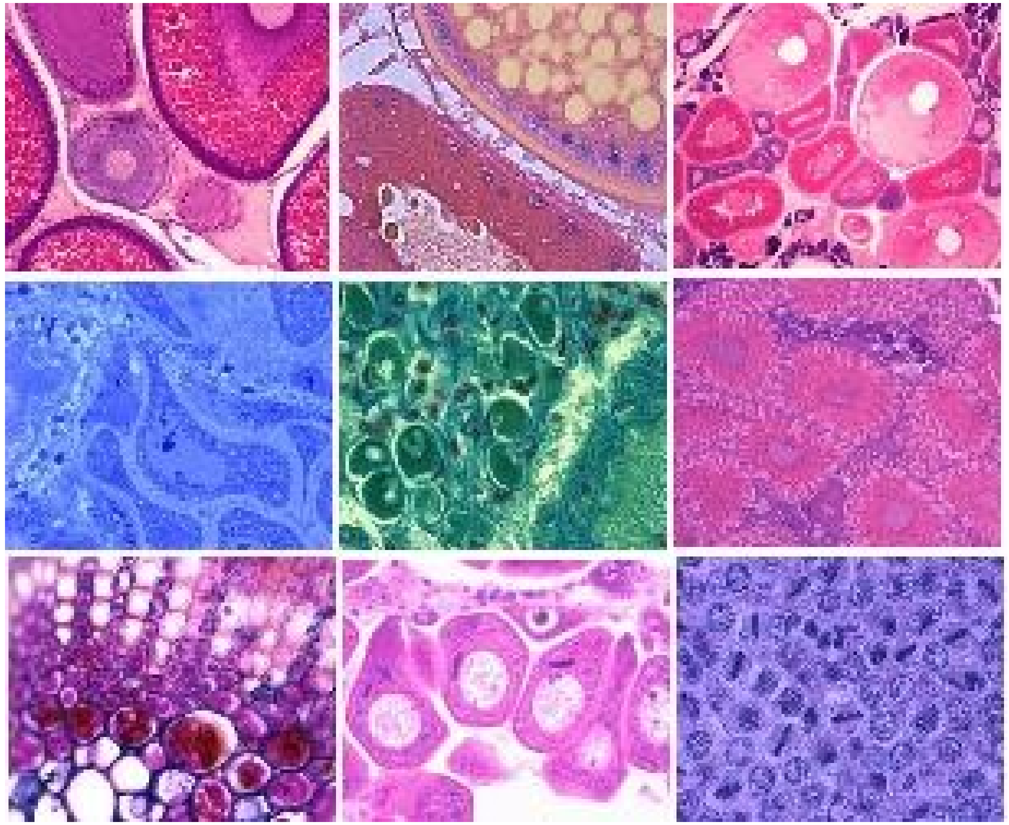
Syllabus

The course syllabus can be found on our D2L webpage. It is your ultimate resources for navigating this course

Week 1 Lab

- **Always bring the text book to lab!!!**
- Day 1: Complete the 1st 9 pages of the lab manual
- Day 2: Group cancer activity, complete remainder of lab.





Radhika Reddy, PhD

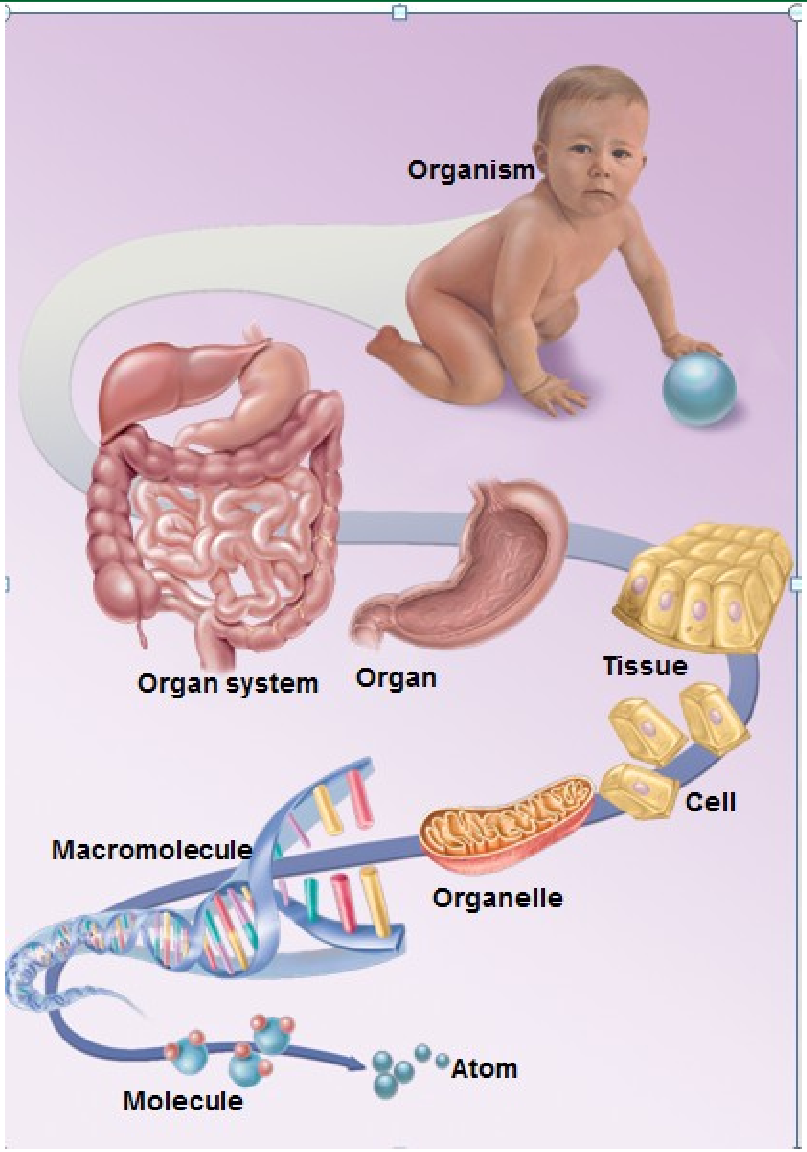
BI 455 CHAPTER 1- 3

Tissue Preparation, Staining, Microscopy

CHAPTER 1: HISTOLOGY AND ITS METHODS OF STUDY

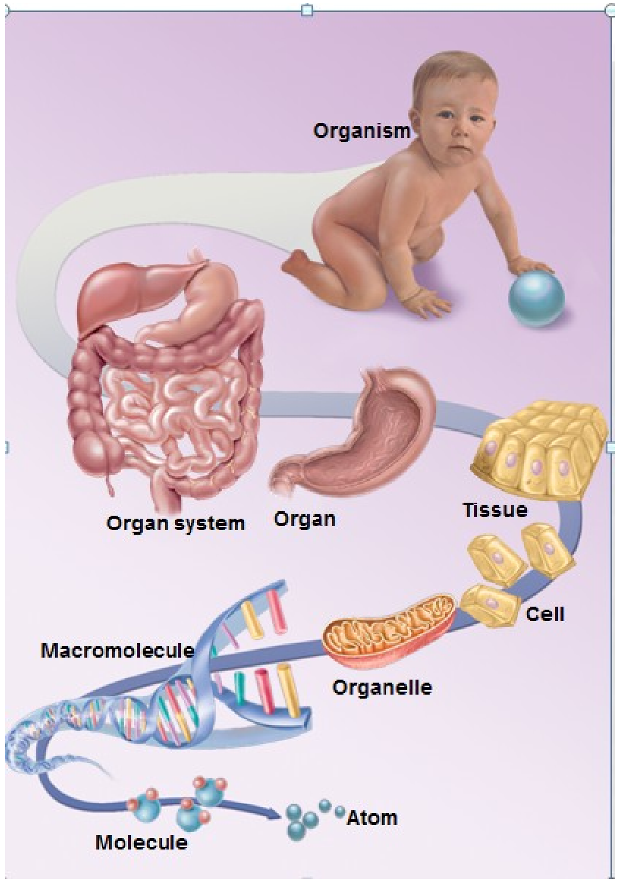
The Structural Basis of Human Function: The Anatomical Sciences

- **Organism** is composed of **organ systems**
- **Organ systems** composed of **organs**
- **Organs** composed of **tissues**
- **Tissues** composed of **cells**
- **Cells** composed of **organelles**
- **Organelles** composed of **molecules**
- **Molecules** composed of **atoms**



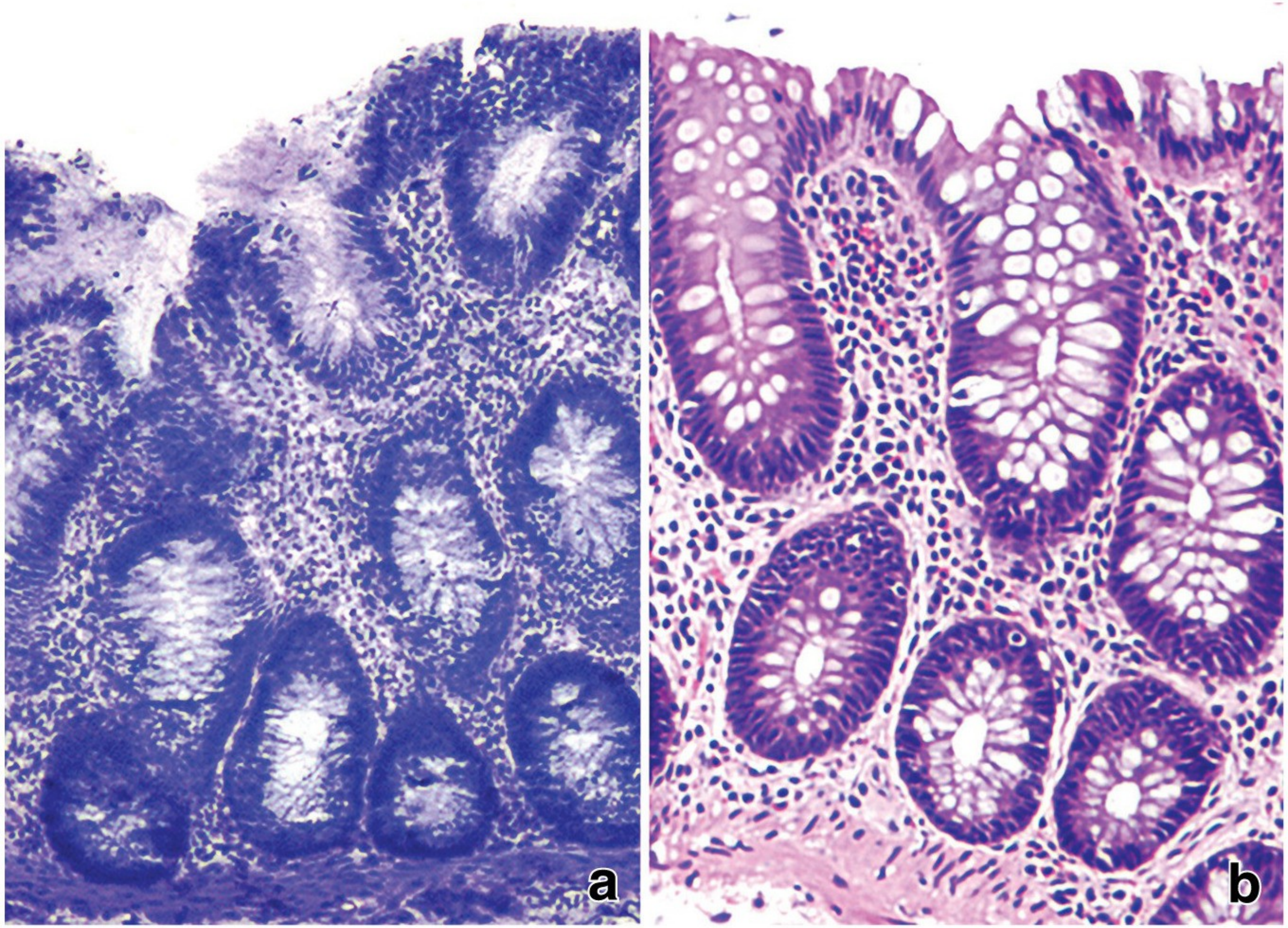
The Structural Basis of Human Function: The Anatomical Sciences

- **Gross anatomy**
  - Structure visible to the naked eye
  - by surface observation or dissection
- **Histology (microscopic anatomy)**
  - Tissue specimens thinly sliced and stained
  - Observed under a microscope
  - **Histopathology**: microscopic examination of tissues for disease
- **Surface anatomy**
  - External structure of the body
  - Important in conducting physical exam
- **Systemic anatomy**
  - Study of one organ system at a time



Histology at the University of Bristol: https://www.youtube.com/watch?v=PafHxS5bq9A&noredirect=1

Clinical Correlation: Frozen sections and stained tissue

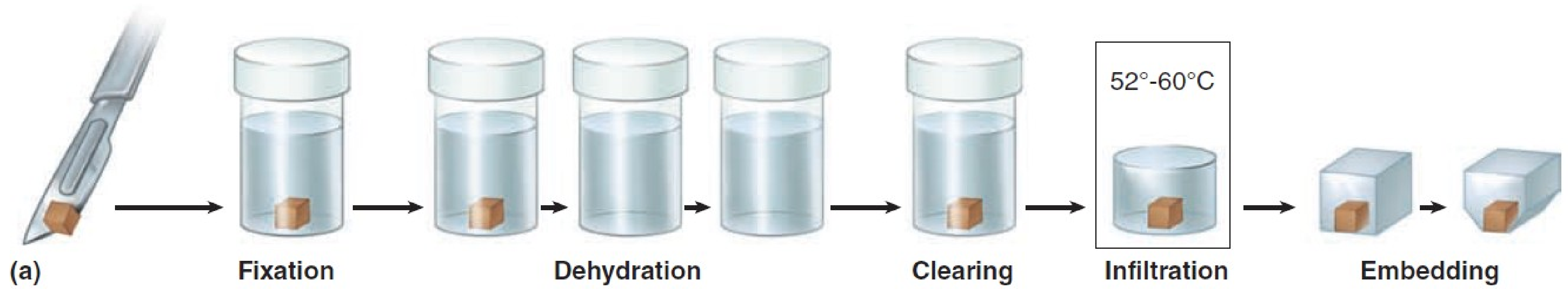


Evaluation of a specimen obtained during surgery by frozen-section technique.

a. This photomicrograph shows a specimen obtained from the large intestine that was prepared by frozen-section technique and stained with methylene blue.

b. Part of the specimen was fixed in formalin and processed as a routine H&E preparation. Examination of the frozen section revealed it to be normal. This diagnosis was later confirmed by examining the routinely prepared H&E specimen.

Most tissues studied histologically are prepared as shown, with this sequence of steps:



1. **Fixation**: Small pieces of tissue are placed in solutions of chemicals that preserve by cross-linking proteins and inactivating degradative enzymes.
2. **Dehydration**: The tissue is transferred through a series of increasingly concentrated alcohol solutions, ending in 100%, which removes all water.
3. **Clearing:** Alcohol is removed in toluene or other agents in which both alcohol and paraffin are miscible.
4. **Infiltration**: The tissue is then placed in melted paraffin until it becomes completely infiltrated with this substance.
5. **Embedding:** The paraffin-infiltrated tissue is placed in a small mold with melted paraffin and allowed to harden
6. The resulting paraffin block is trimmed to expose the tissue for sectioning (slicing) on a microtome.

A microtome is used for sectioning paraffin-embedded tissues for light microscopy

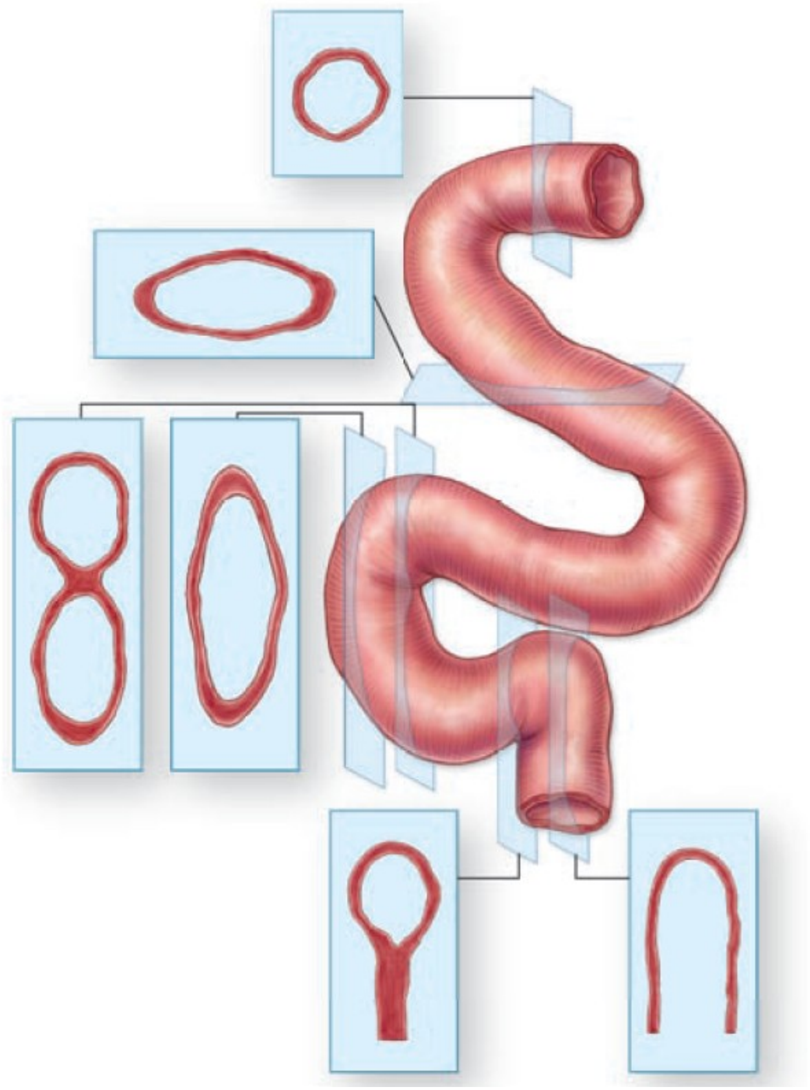
1. The trimmed tissue specimen is mounted in the paraffin block holder, and each turn of the drive wheel by the histologist advances the holder a controlled distance, generally between 1 and 10 μm.
2. After each forward move, the tissue block passes over the steel knife edge and a section is cut at a thickness equal to the distance the lock advanced.
3. The paraffin sections are placed on glass slides and allowed to adhere, deparaffinized, and stained for light microscope study.

Sectional Planes

- When a structure's three-dimensional volume is cut into very thin sections, the sections appear microscopically to have only two dimensions: length and width.

- When examining a section under the microscope, the viewer must always keep in mind that components are missing in front of and behind what is being seen because many tissue structures are thicker than the section.

FIGURE **1–14** **Interpretation of 3D structures in 2D sections.**



Staining

- Most cells and extracellular material are **completely colorless**, and to be studied microscopically sections must typically be **stained (dyed).**
- Methods of staining have been devised that not only make the various tissue components conspicuous but also permit distinctions to be made between them
- Dyes stain tissue components more or less selectively, with many behaving like acidic or basic compounds and forming electrostatic (salt) linkages with ionizable radicals of molecules in tissues

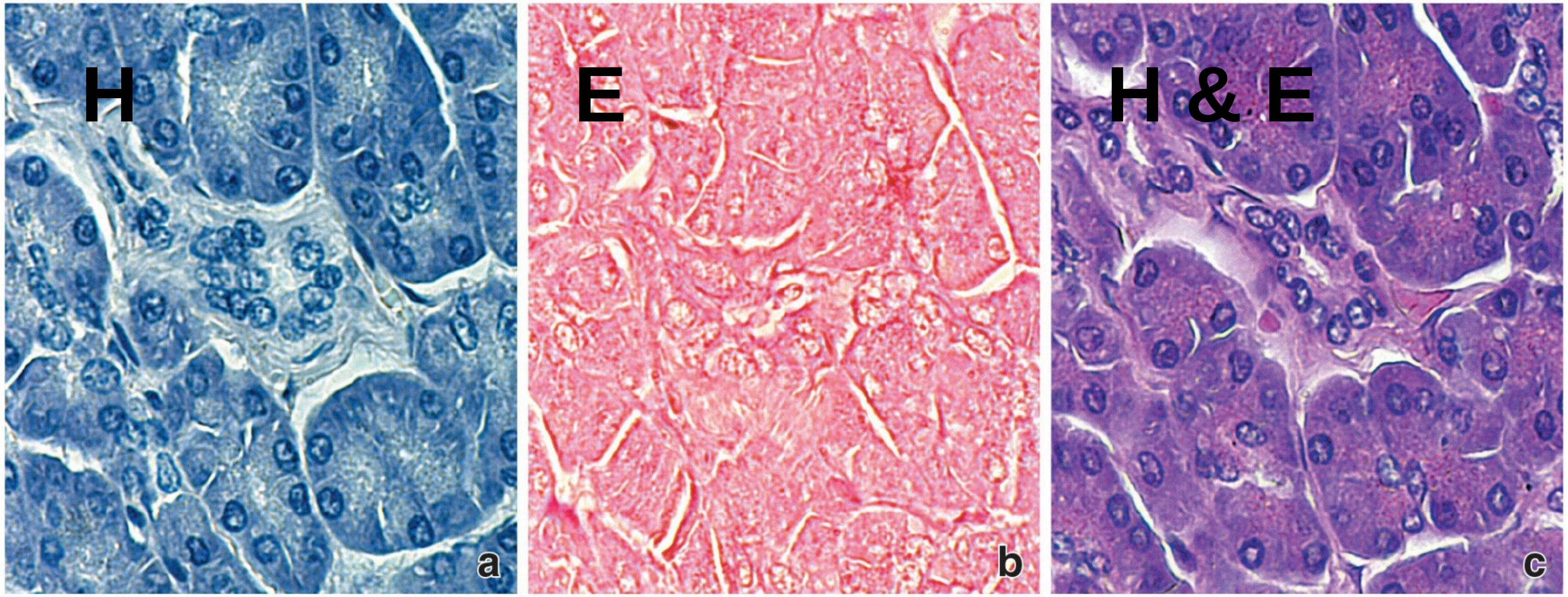
TABLE 1.2 Some Basic and Acidic Dyes

Dye	Color
Basic dyes	
Methyl green	Green
Methylene blue	Blue
Pyronin G	Red
Toluidine blue	Blue
Acidic dyes	
Acid fuchsin	Red
Aniline blue	Blue
Eosin	Red
Orange G	Orange

The Hematoxylin and Eosin (H&E) stain is used most commonly

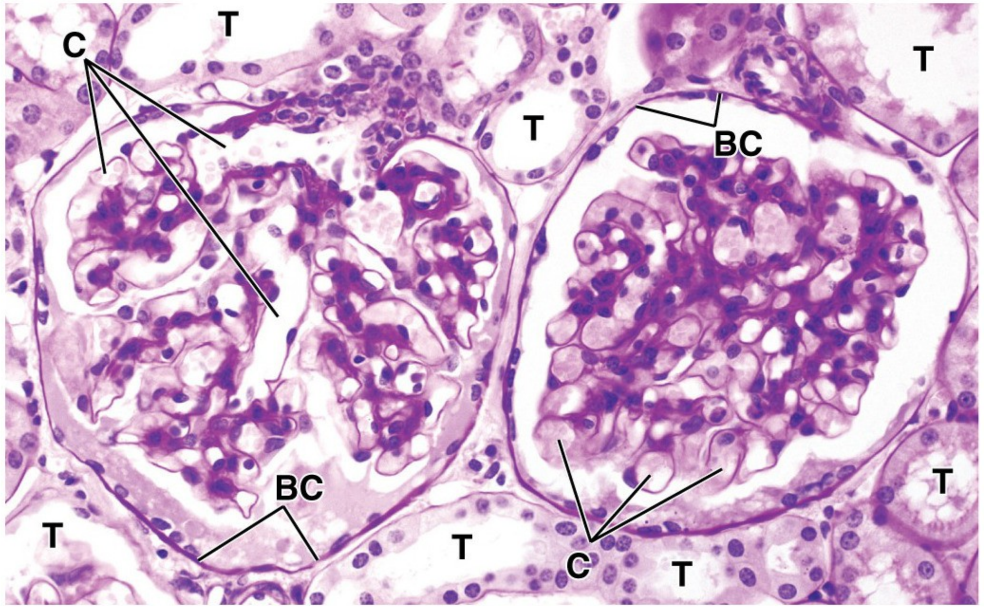
- **Hematoxylin** (almost basic) produces a dark blue or purple color, staining **DNA** in the cell nucleus and other acidic structures (such as **RNA-rich** portions of the cytoplasm and the **matrix of cartilage**).

- **Eosin** stains other **cytoplasmic components and collagen** pink



Periodic Acid-Schiff (PAS) reagent.

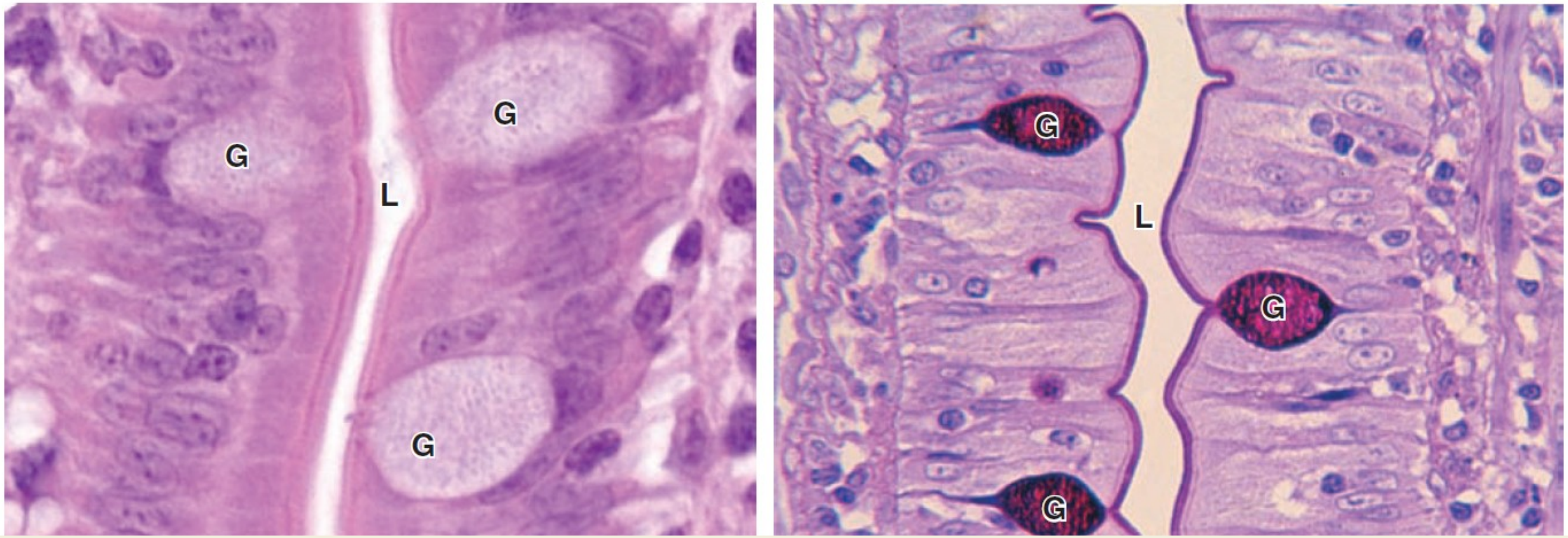
- The PAS reaction is based on the transformation of 1,2-glycol groups present in sugars into aldehyde residues, which then react with Schiff reagent to produce a purple or magenta color



This histochemical method demonstrates and localizes carbohydrates and carbohydrate-rich macromolecules.
The basement membranes in this kidney tissue are PAS positive as evidenced by the magenta staining of these sites. The kidney tubules (T) are sharply delineated by the stained basement membrane surrounding the tubules. The glomerular capillaries (C) and the epithelium of Bowman's capsule (BC) also show PAS-positive basement membranes.

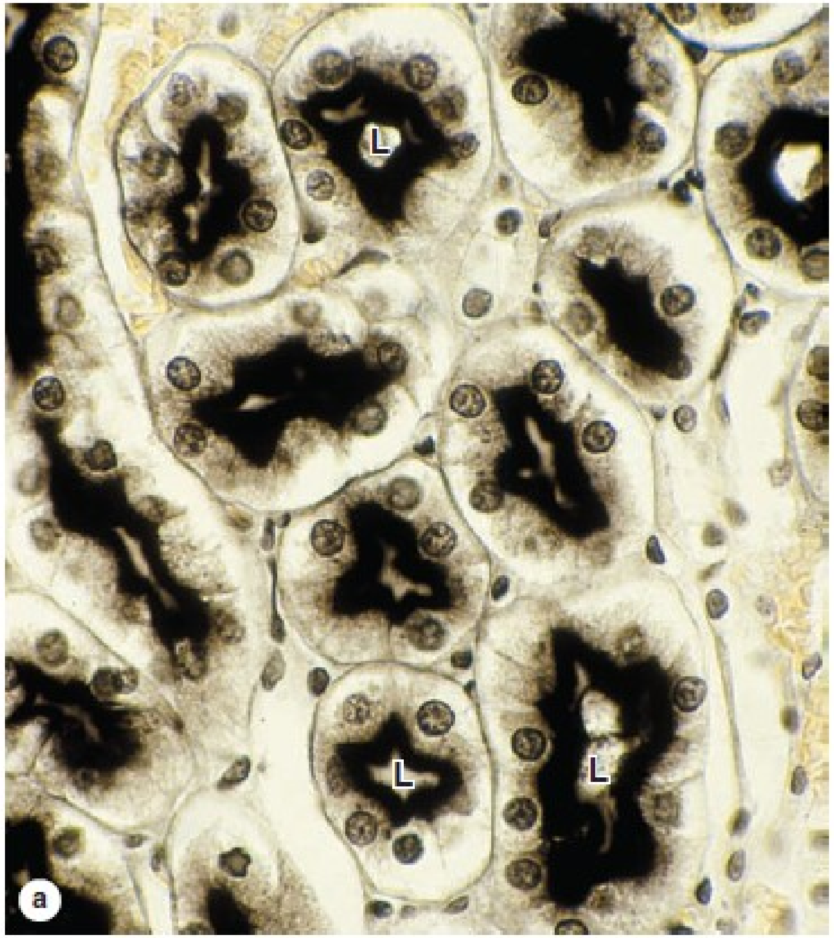
H & E vs PAS

FIGURE **1–2** **Hematoxylin and eosin (H&E) and periodic acid-Schiff (PAS) staining.**



Micrograph of epithelium lining the small intestine, **(a)** stained with H&E, and **(b)** stained with the PAS reaction for glycoproteins. With H&E, basophilic cell nuclei are stained purple while cytoplasm stains pink. Cell regions with abundant oligosaccharides on glycoproteins, such as the ends of the cells at the lumen (**L**) or the scattered mucus-secreting goblet cells (**G**), are poorly stained. With PAS, however, cell staining is most intense at the lumen, where projecting microvilli have a prominent layer of glycoproteins at the lumen (L) and in the mucin-rich secretory granules of goblet cells. Cell surface glycoproteins and mucin are PAS-positive because of their high content of oligosaccharides and polysaccharides respectively. The PAS-stained tissue was counterstained with hematoxylin to show the cell nuclei. Both X300.

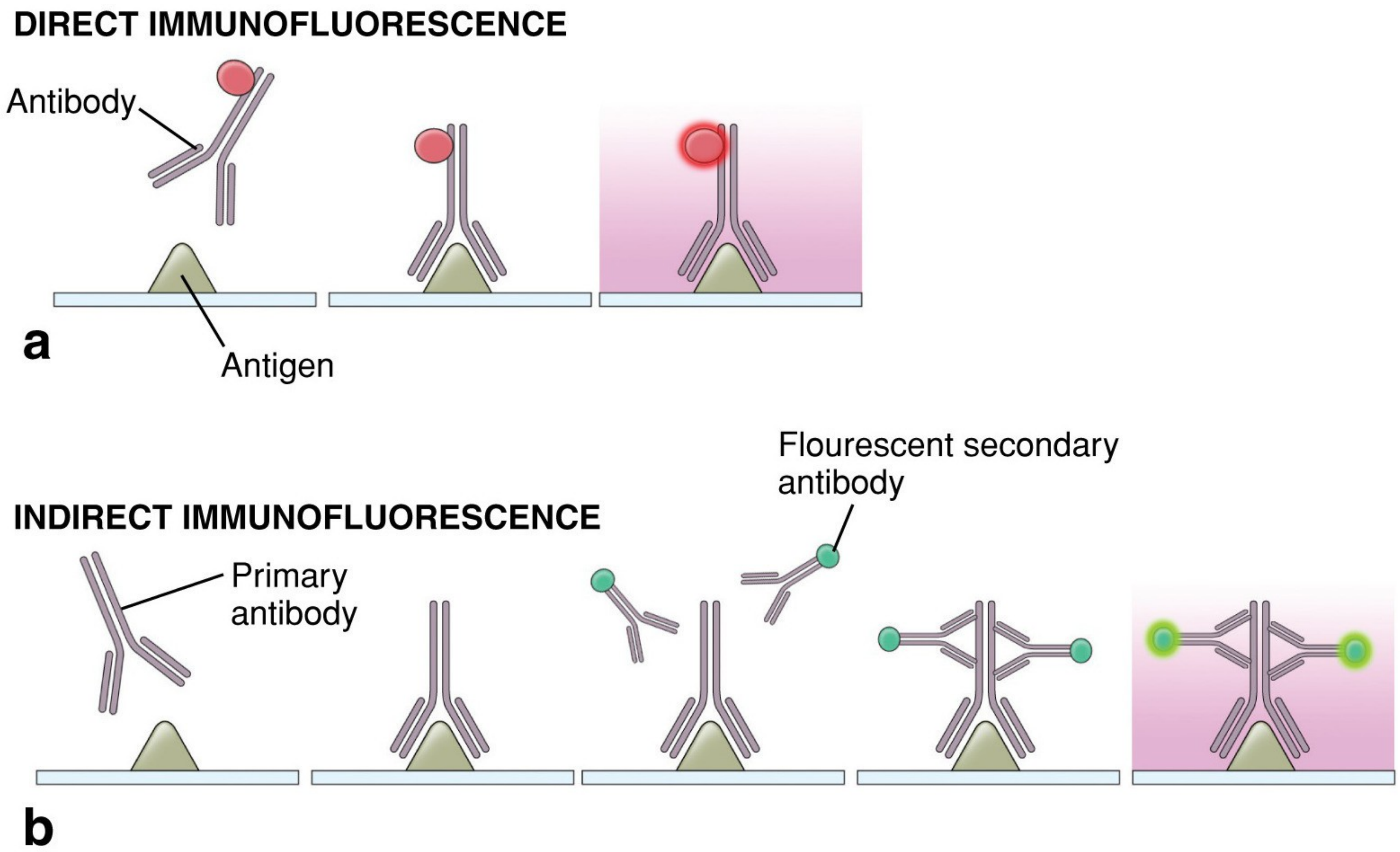
Enzyme histochemistry (cytochemistry): localizes cellular structures using a specific enzymatic activity present in those structures



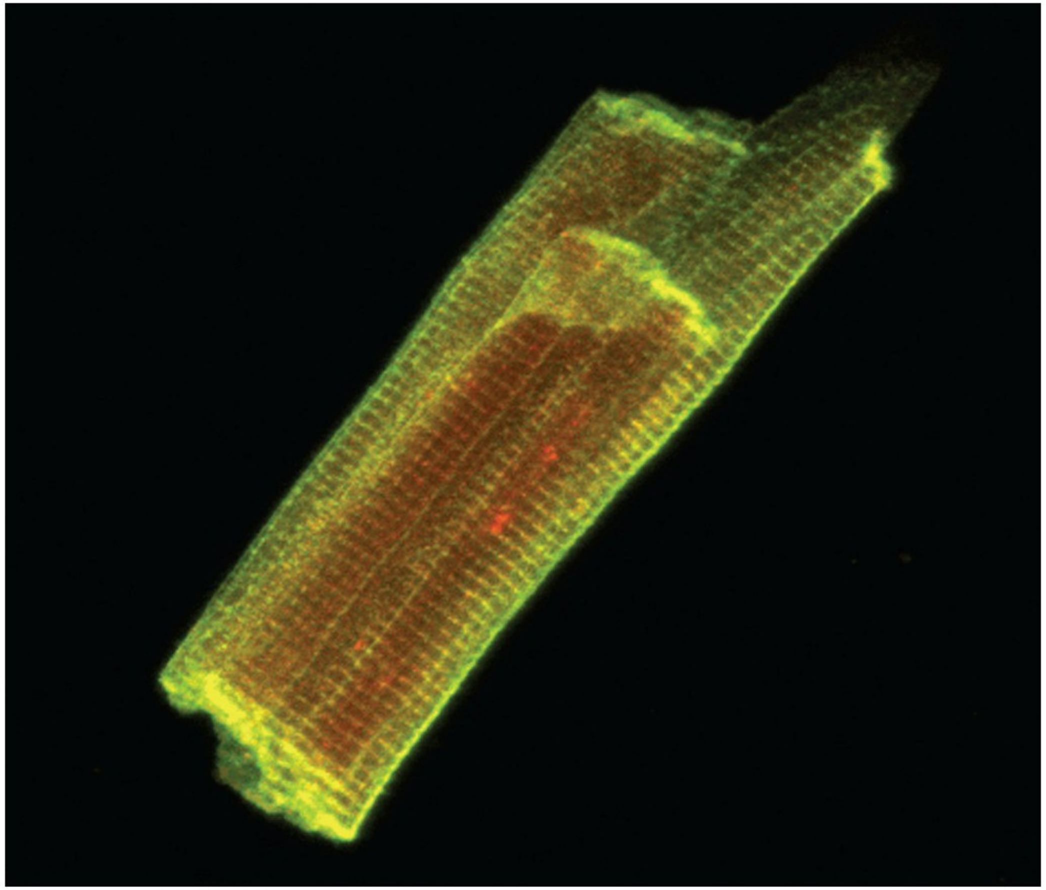
Micrograph of cross sections of kidney tubules treated histochemically to demonstrate alkaline phosphatases shows strong activity of this enzyme at the apical surfaces of the cells at the lumens (L) of the tubules.

(1) Tissue sections are immersed in a solution containing the substrate of the enzyme to be localized
(2) The enzyme is allowed to act on its substrate
(3) The section is put in contact with a marker compound that reacts with a product of the enzymatic action on the substrate
(4) The final product has color or electron density, and precipitates over the site of the enzymes causing contract between enzymatically active vs inactive areas

Immunocytochemistry: uses reaction between an antigen and an antibody to visualize proteins



Immunocytochemistry: uses reaction between an antigen and an antibody to visualize proteins



Rat Cardiac Muscle Cell:

RED: lactate transporter (MCT1) antibody is detected with a secondary antibody conjugated with rhodamine (red).

GREEN: transmembrane protein CD147 antibody is detected by a secondary antibody labeled with fluorescein (green).

YELLOW: secondary antibodies exactly co-localize within the cardiac muscle cell.

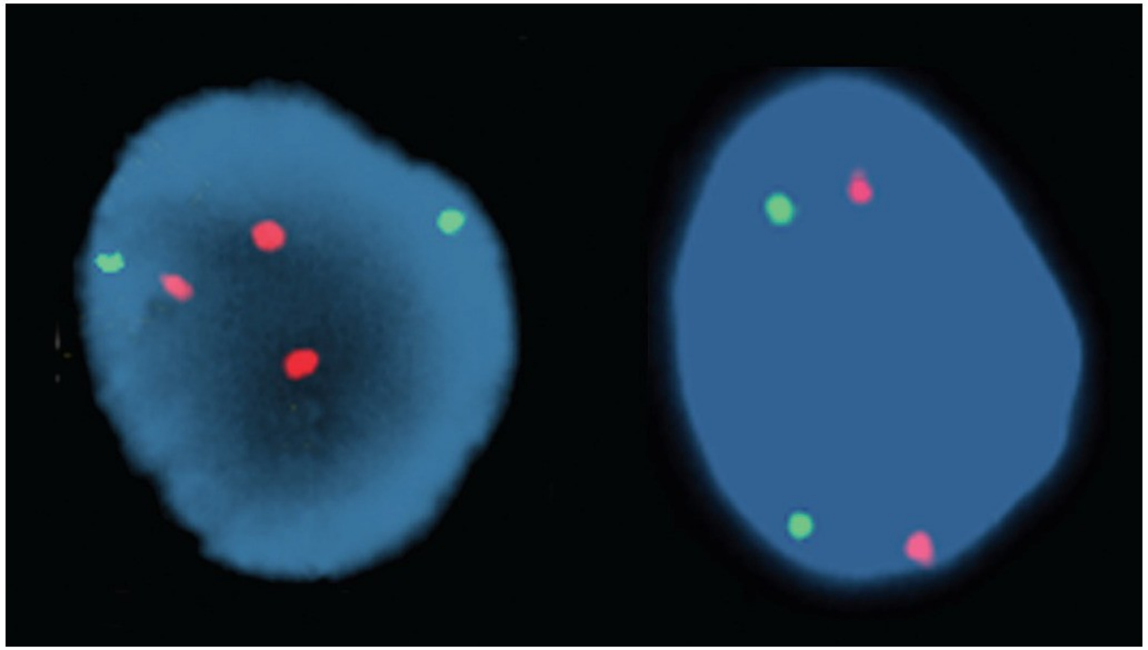
Hybridization: visualizing gene expression by hybridizing an added nucleotide probe to mRNA in the cell

Prenatal screening test. Interphase nuclei of cells obtained from amniotic fluid specimens were hybridized with two specific DNA probes.

ORANGE (LSI 21) chromosome 21 probe
GREEN (LSI 13) chromosome 13 probe

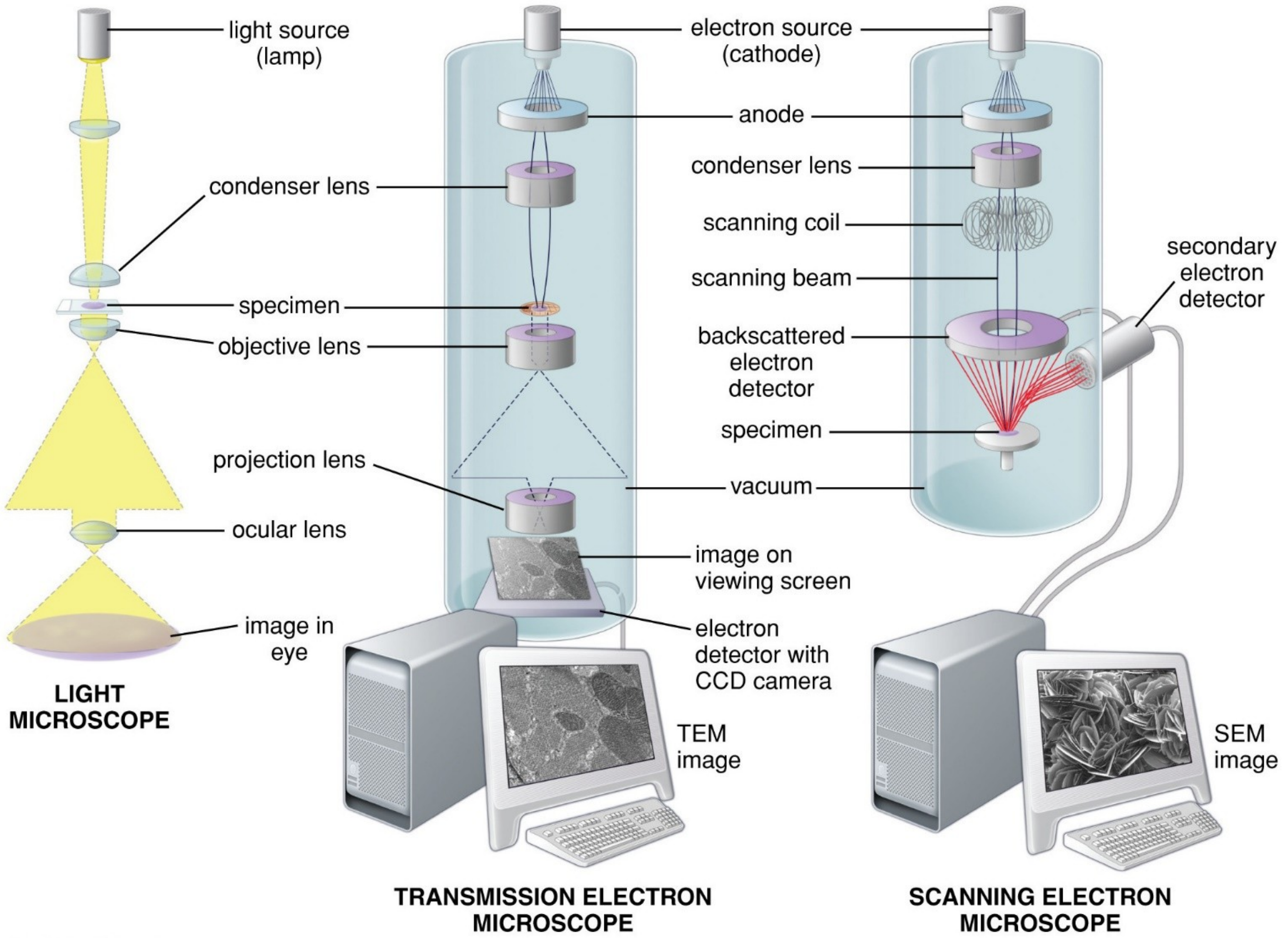
The right nucleus is from a normal Amniotic fluid specimen

The left nucleus has three orange signals, which indicate trisomy 21 (Down syndrome).



Microscopy

1. Light Microscopy
   a. Bright-field
   b. Phase Contrast
   c. Fluorescence
   d. Confocal
2. Electron Microscopy (EM)
3. Atomic Forces Microscopy
4. Virtual Microscopy



How to focus a microscope:
https://www.youtube.com/watch?v=scEhgAiazzU

Resolving Power

- The distance by which two objects must be separated to be seen as two objects

TABLE 1.3 Eye Versus Instrument Resolution

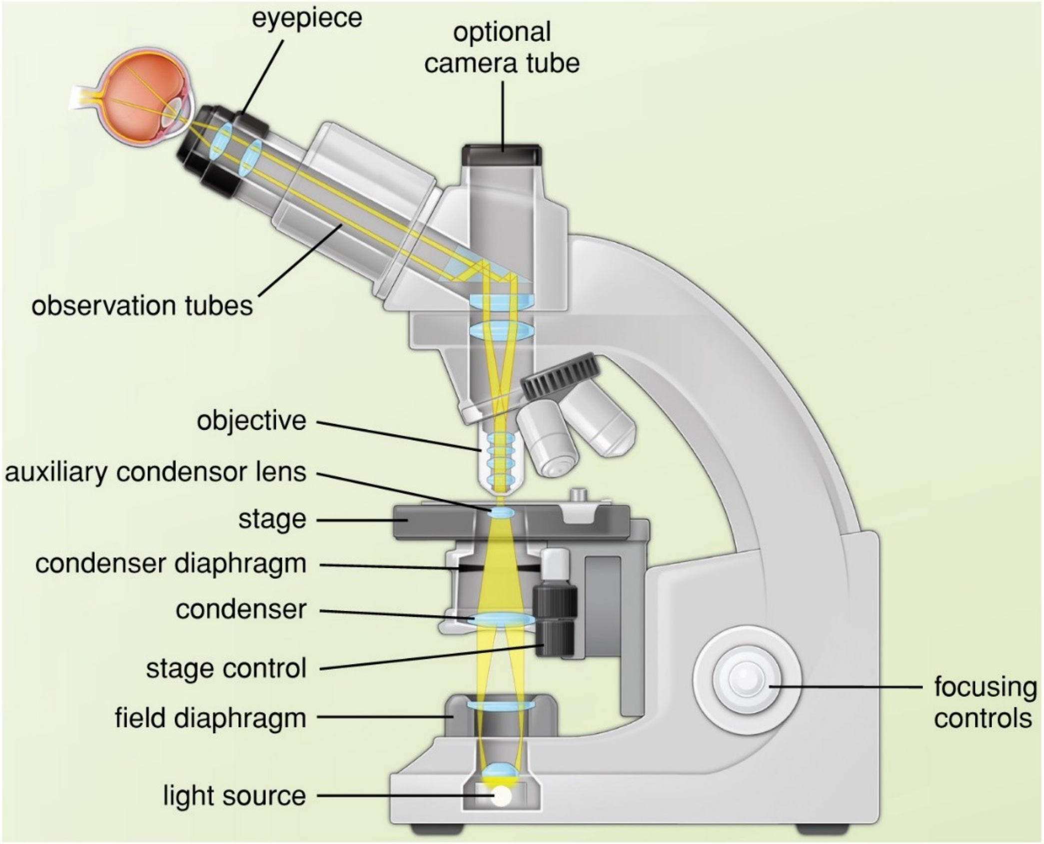
Distance Between Resolvable Points	
Human eye	0.2 mm
Bright-field microscope	0.2 µm
SEM	2.5 nm
TEM	
Theoretical	0.05 nm
Tissue section	1.0 nm

Light Microscopy: interaction of light with tissue components and are used to reveal and study tissue features in different ways

Bright-field microscopy (which we will use this term): stained preparations are examined as ordinary light passes through the specimen.

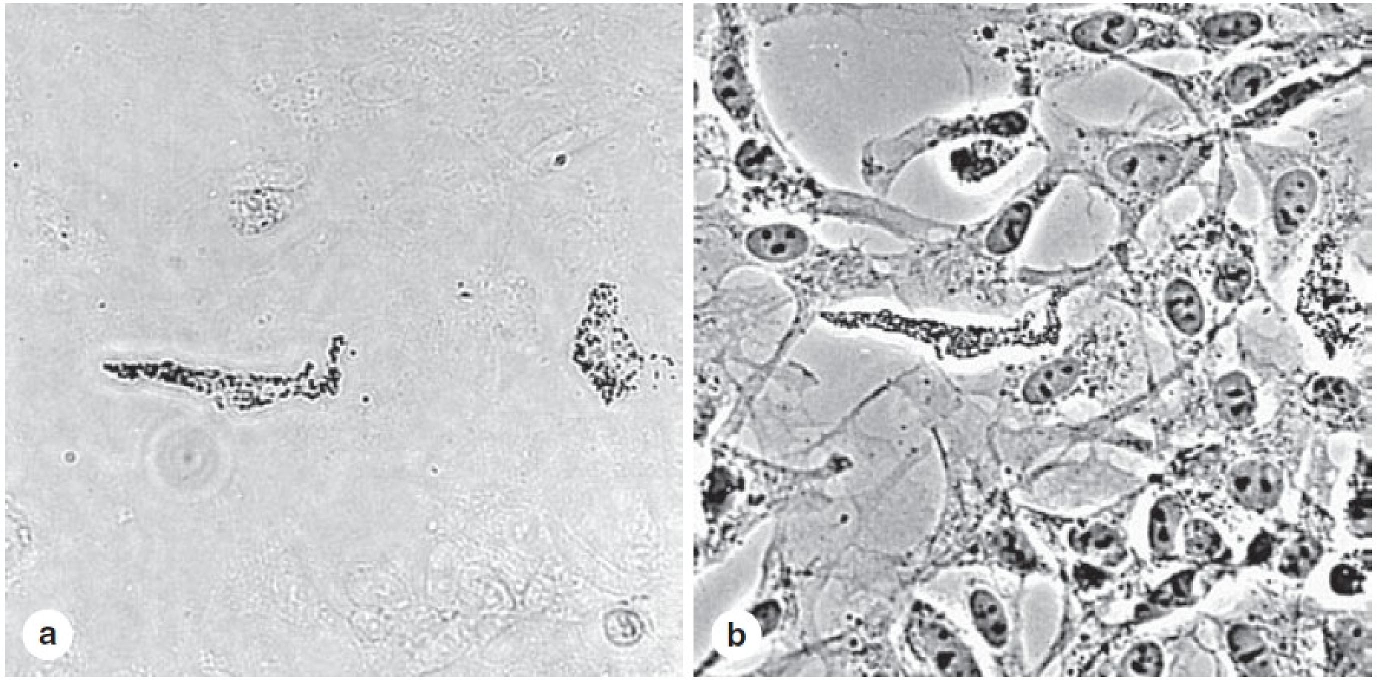
Optical Components:

- **condenser:** collects and focuses light
- **objective lens:** enlarges and projects the image of the object toward eyepiece.
- **ocular lens (eyepiece):** further magnifies image low light levels with a monitor and camera.
- **total magnification**: product of magnifying power of the objective and ocular lenses.



Other types of light microscopy

- **Phase-contrast microscopy** uses the differences in refractive index of various natural cell and tissue components to produce an image without staining, allowing observation of living cells.

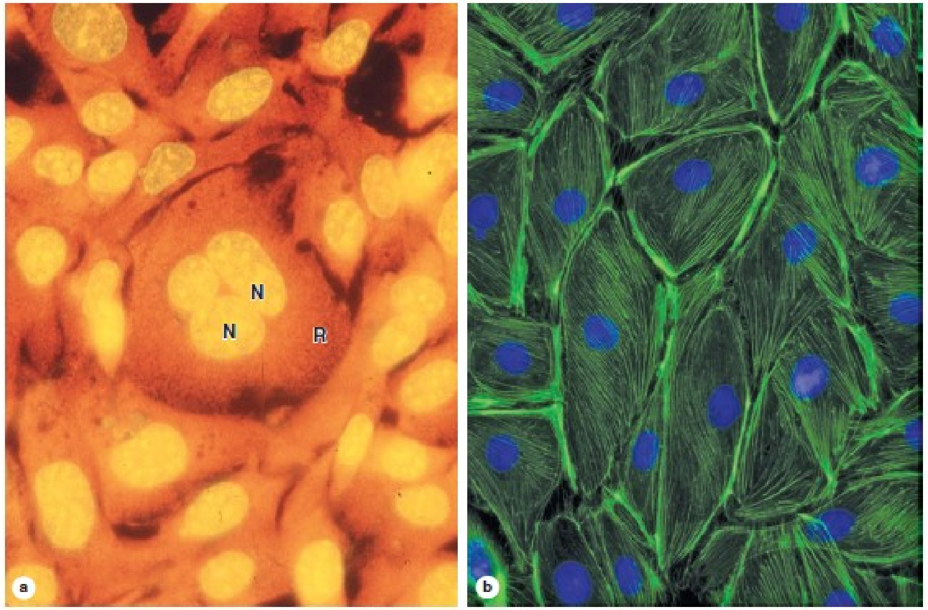


(a) Bright-field microscopy: Without fixation and staining, only the two pigment cells can be seen.

(b) Phase-contrast microscopy: Cell boundaries, nuclei, and cytoplasmic structures with different refractive indices affect in-phase light differently and produce an image of these features in *all* the cells.

Other types of light microscopy

- **Fluorescence microscopy** uses ultraviolet light, under which only fluorescent molecules are visible, allowing localization of fluorescent probes which can be much more specific than routine stains.



http://www.nature.com/nmeth/journal/v11/n5/fig_tab/nmeth.2888_SV2.html

Components of cells are often stained with compounds visible by fluorescence microscopy.

(a) Acridine orange binds nucleic acids and causes DNA in cell nuclei (**N**) to emit yellow light and the RNA-rich cytoplasm (**R**) to appear orange in these cells of a kidney tubule.

(b) Cultured cells stained with DAPI (4′,6-diamino-2-phenylindole) that binds DNA and with fluorescein-phalloidin that binds actin filaments show nuclei with blue fluorescence and actin filaments stained green. Important information such as the greater density of microfilaments at the cell periphery is readily apparent. Both X500.

(*Figure 1–4b, contributed with permission, from Drs Claire E. Walczak and Rania Risk, Indiana University School of Medicine, Bloomington.*)

Other types of light microscopy

- **Confocal microscopy** involves scanning the specimen at successive focal planes with a focused light beam, often from a laser, and produces a 3D reconstruction from the images.

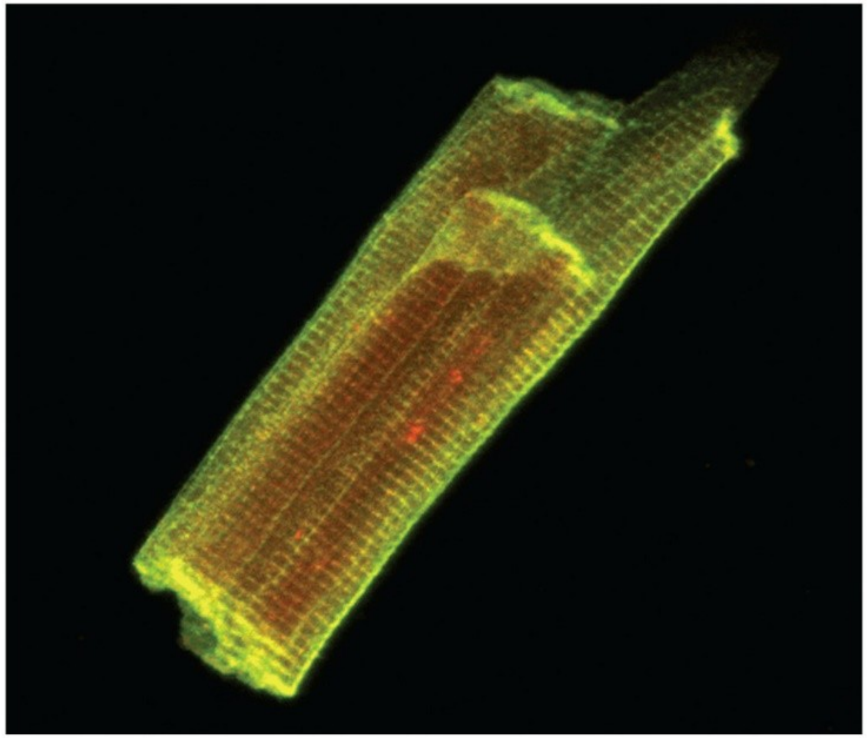
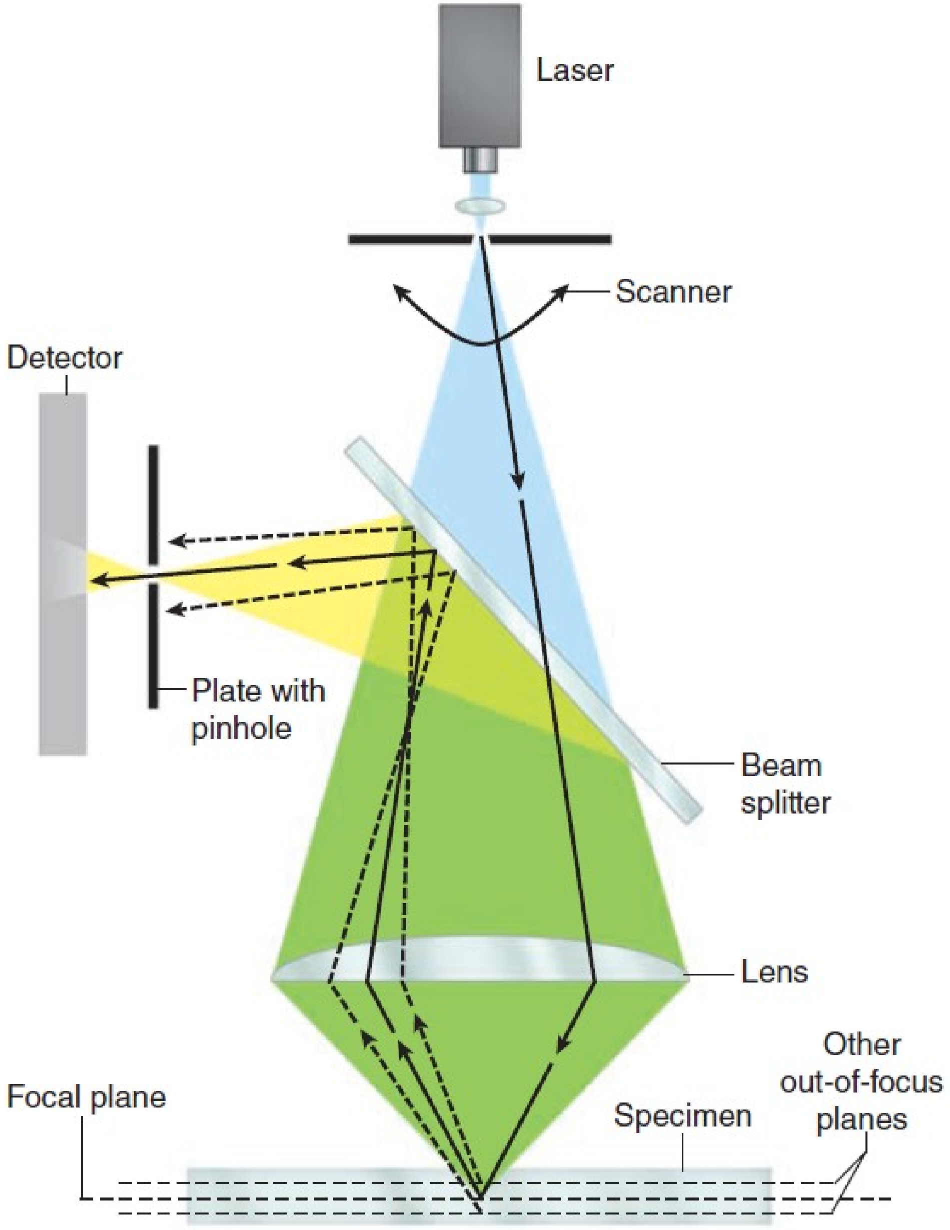


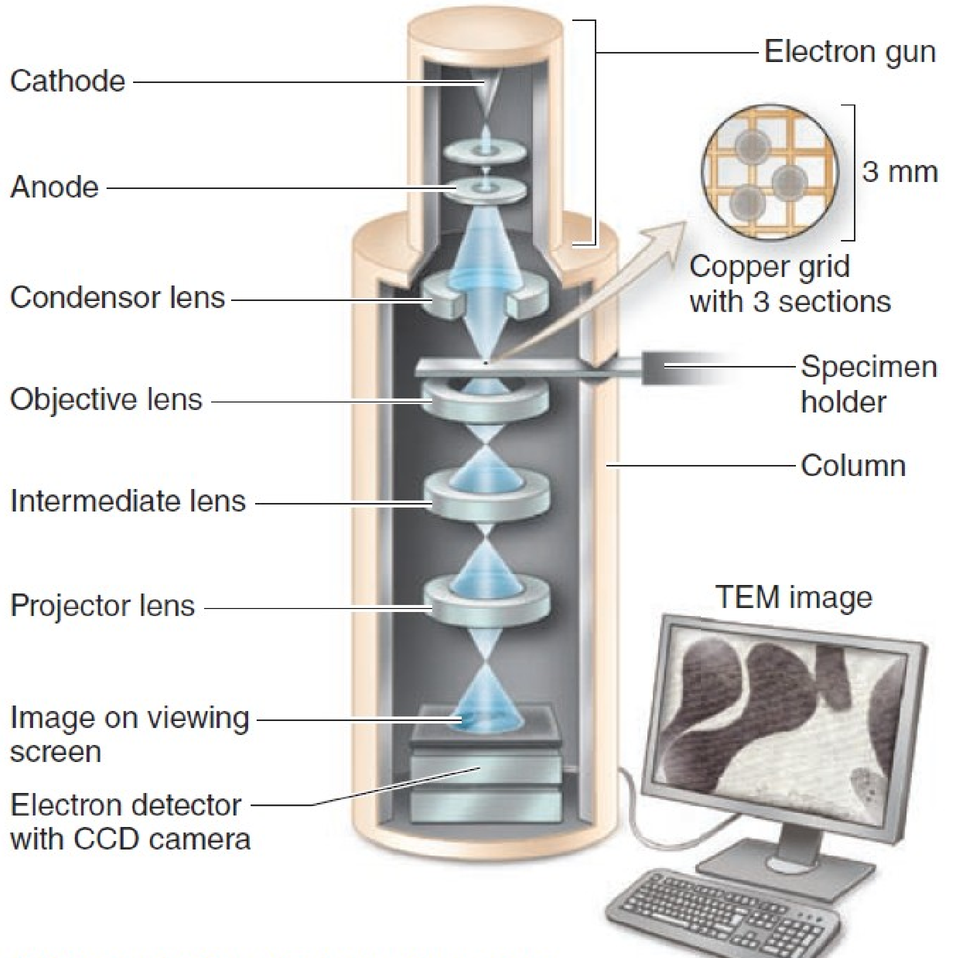
FIGURE 1–6 Principle of confocal microscopy.



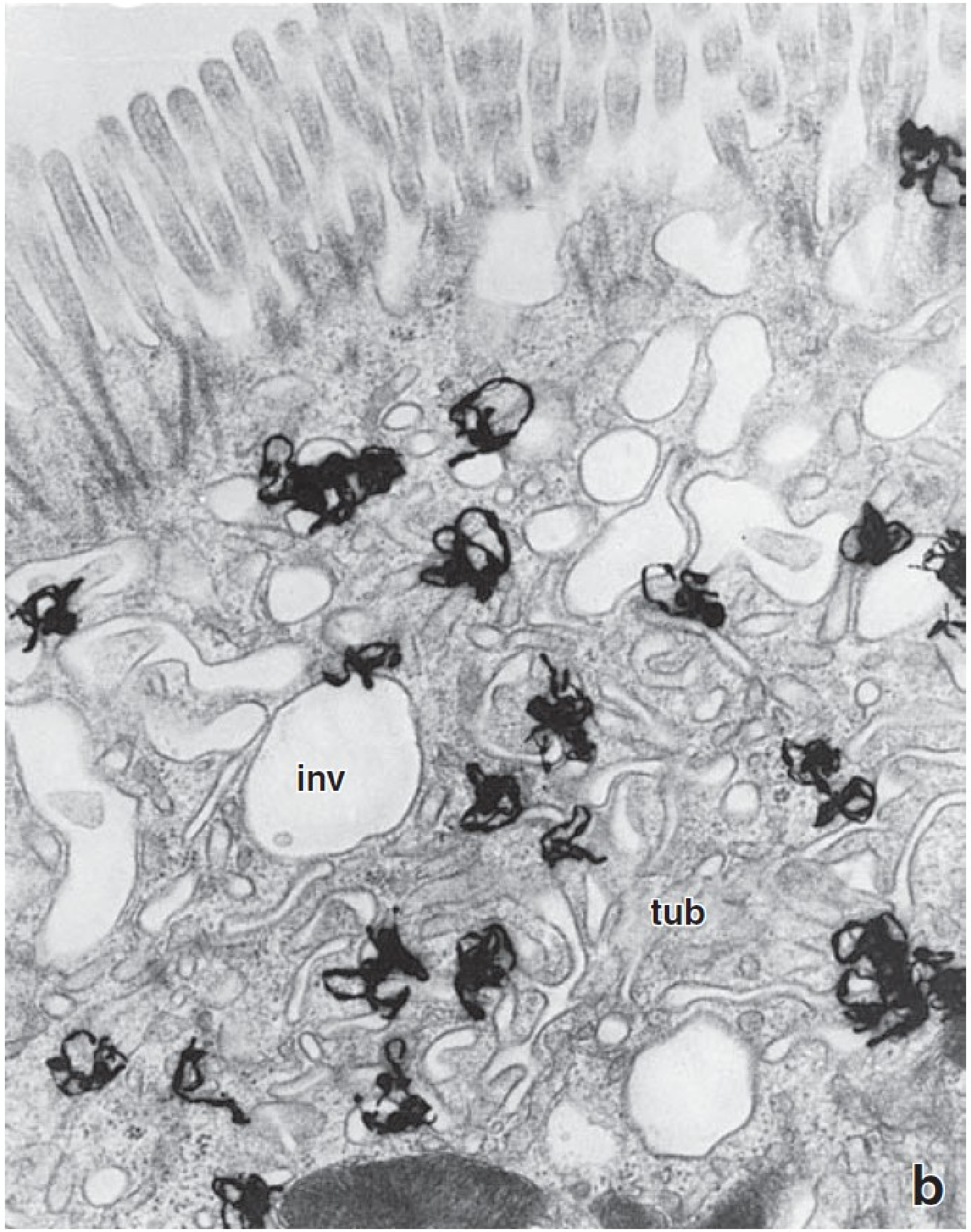
Electron Microscopy

- Transmission and scanning electron use beams of electrons rather than light. The wavelength in the electron beam is much shorter than that of light, allowing a 1000-fold increase in resolution.
- **Transmission EM** sends an electromagnetically focused beam of electrons at very high voltage through ultrathin sections of tissue.
- Tissue preparation for TEM involves adding **heavy metal ions** that associate at different electron densities with cell and tissue components, improving contrast in the resulting image

FIGURE 1–8 **Electron microscopes.**



(a) **Transmission electron microscope**

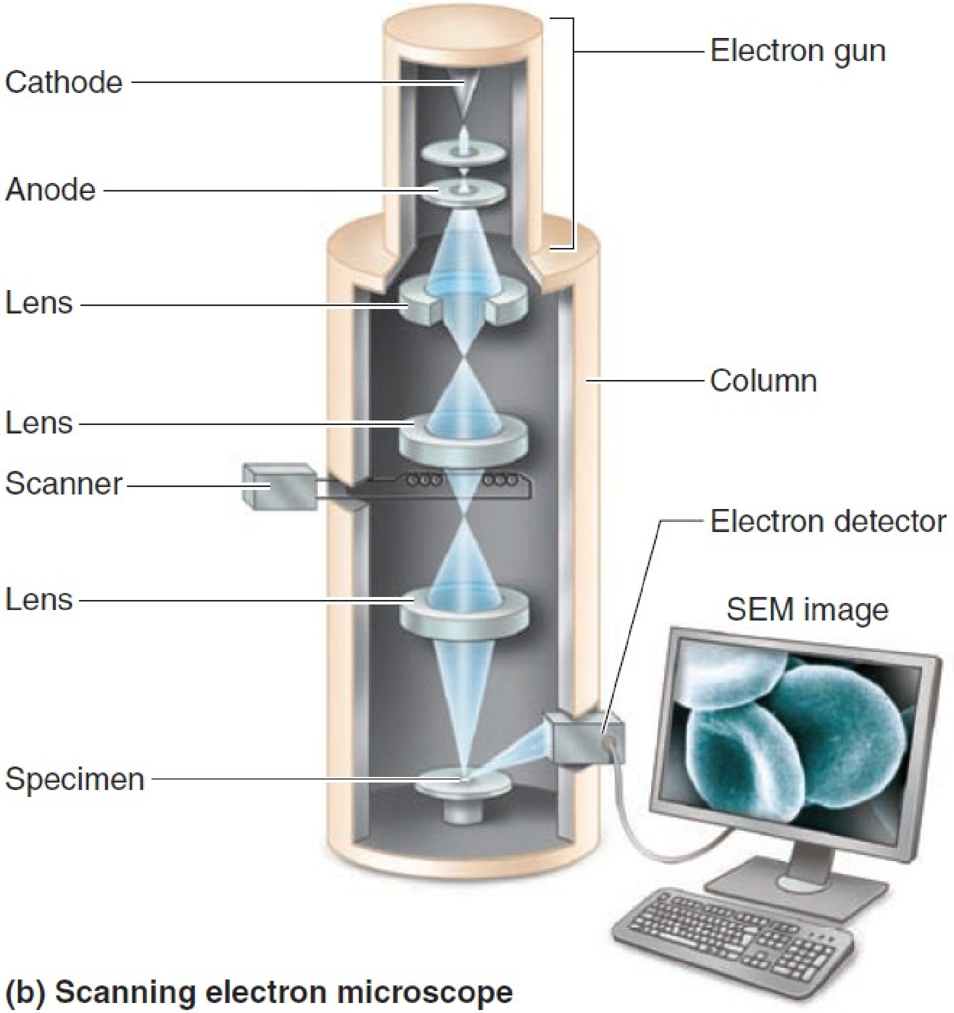


Electron microscopic autoradiograph of the apical region of an intestinal absorptive cell. In this specimen, ^{125}I bound to nerve growth factor (NGF) was injected into the animal, and the tissue was removed 1 hour later.

The specimen was prepared in a manner similar to that for light microscopy. The relatively small size of the silver grains aids precise localization of the ^{125}I–NGF complexes. Note that the silver grains are concentrated over apical invaginations (*inv*) and early endosomal tubular profiles (*tub*). 32,000.

Electron Microscopy

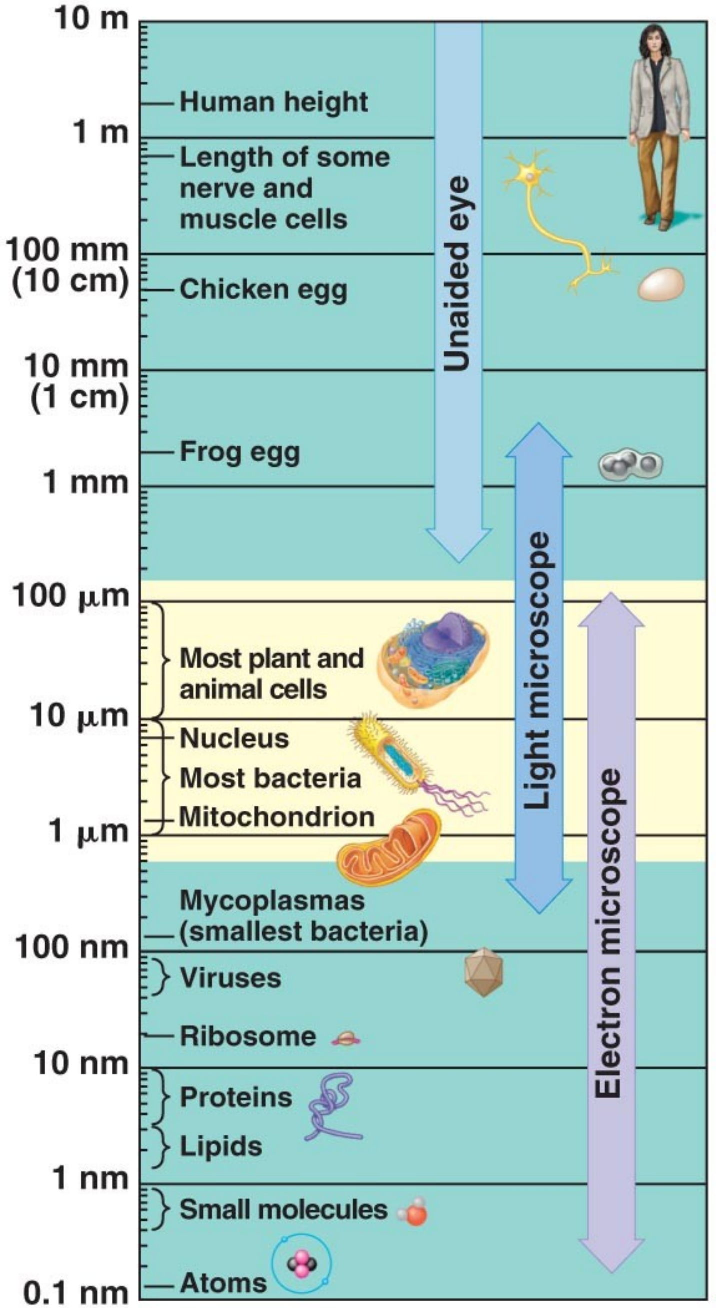
- **Scanning EM** scans an electron beam across a specimen coated with a thin layer of heavy metal; reflected and secondary electrons from the specimen are processed into a 3D ultrastructural image

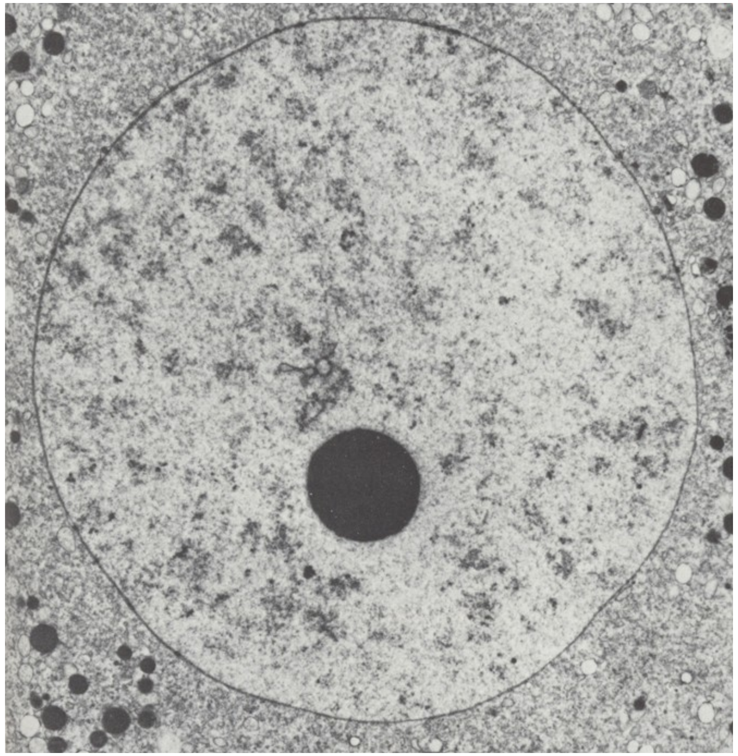


(b) Scanning electron microscope

Most cells are microscopic

- Most cells cannot be seen without a microscope
  - Bacteria are the smallest of all cells and require magnifications up to 1,000X
  - Plant and animal cells are 10 times larger than most bacteria





Membranous/Non-Membranous Organelles, Inclusions, Cytoplasmic Matrix

CHAPTER 2: CELL CYTOPLASM

An Introduction to Cells

The four major life processes in eukaryotic cells & their organelles

1. Manufacturing: nucleus, ribosomes, endoplasmic reticulum, and Golgi apparatus
2. Breakdown of molecules: lysosomes, vacuoles, and peroxisomes
3. Energy processing: mitochondria in animal cells and chloroplasts in plant cells
4. Structural support, movement, and communication: cytoskeleton, plasma membrane, and cell wall

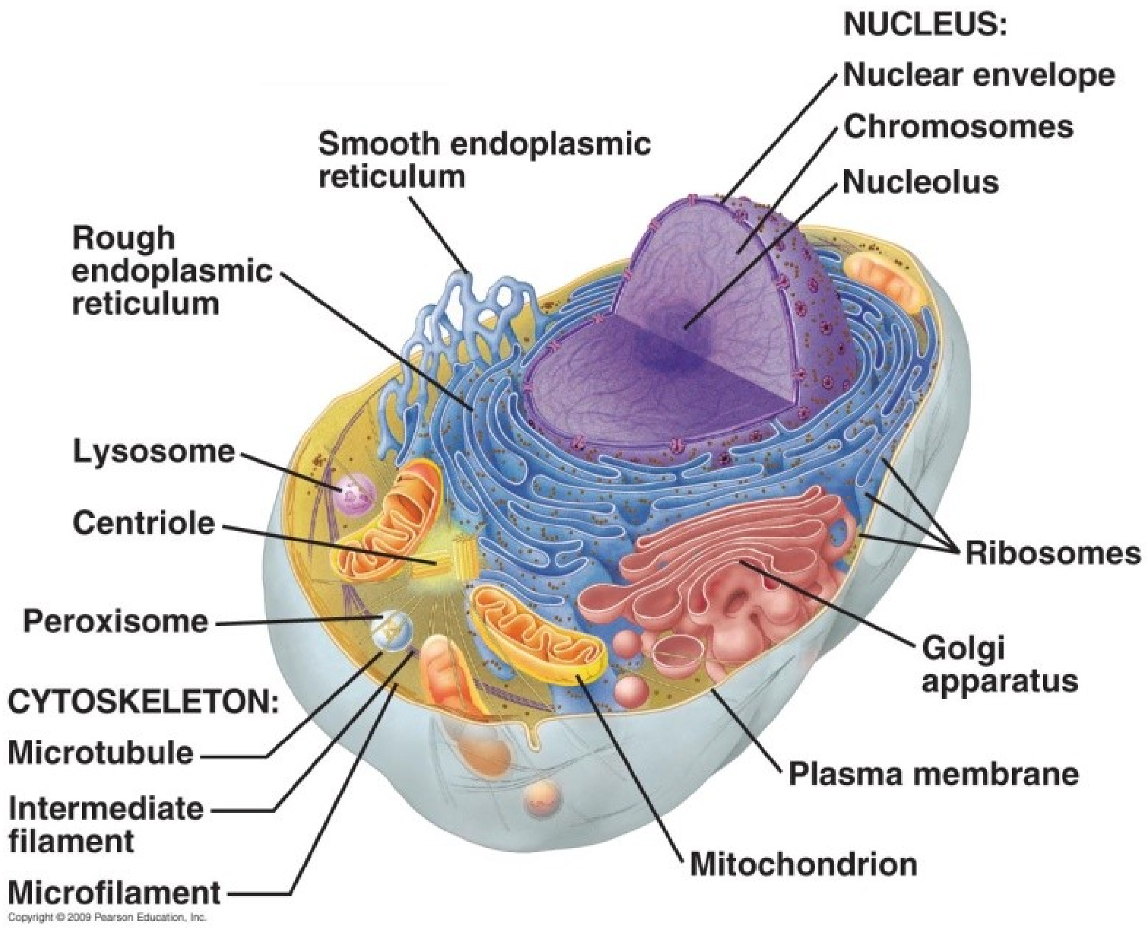
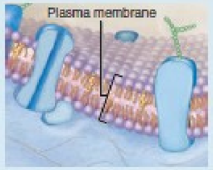
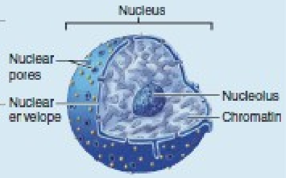
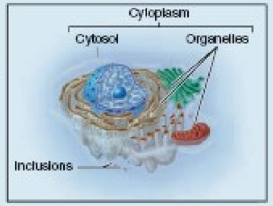


TABLE 2–6 **Summary of cellular structural components.**

Component	Structure	Major Function	Appearance
Plasma membrane	Phospholipid bilayer containing cholesterol and proteins (integral and peripheral) and some carbohydrates (externally); forms a selectively permeable boundary of the cell	Acts as a physical barrier to enclose cell contents; regulates material movement into and out of the cell; establishes and maintains an electrical charge difference across the plasma membrane; functions in cell communication	
Cilia	Short, numerous membrane extensions supported by microtubules, which occur on exposed membrane surfaces of some cells	Move substances (eg, mucus, and dissolved materials) over the cell surface	
Flagellum	Long, singular membrane extension supported by microtubules; present on sperm cells	Propels sperm	
Microvilli	Numerous thin membrane folds projecting from the free cell surface; supported by microfilaments	Increase membrane surface area for greater absorption	
Nucleus	Large structure enclosed within a double membrane; contains chromatin, nucleolus, and nucleoplasm	Houses the DNA that serves as the genetic material for directing protein synthesis	
Nuclear envelope	Double membrane boundary between cytoplasm and nuclear contents; continuous with rough endoplasmic reticulum	Separates nucleus from cytoplasm	
Nuclear pores	Openings through the nuclear envelope	Allow passage of materials between the cytoplasm and nucleoplasm, including ribonucleic acid (RNA), protein, ions, and small water-soluble molecules	
Nucleolus	Large, prominent structure within the nucleus	Functions in synthesis of ribosomes	
Cytoplasm	Contents of cells between the plasma membrane and nuclear envelope	Responsible for many cellular processes	
Cytosol	Viscous fluid medium with dissolved solutes (eg, ions, proteins, carbohydrates, lipids)	Provides support for organelles; serves as the viscous fluid medium through which diffusion occurs	
Organelles	Membrane-bound and non-membrane-bound structures	Carry out specific metabolic activities of the cell	
Rough endoplasmic reticulum (rough ER)	Extensive interconnected membrane network that varies in shape (eg, cisternae, tubules); ribosomes attached on cytoplasmic surface	Modifies, transports, and stores proteins produced by attached ribosomes; these proteins are secreted, become components of the plasma membrane, or serve as enzymes of lysosomes	
Smooth endoplasmic reticulum (smooth ER)	Extensive interconnected membrane network lacking ribosomes	Synthesizes, transports, and stores lipids (eg, steroids); metabolizes carbohydrates; detoxifies drugs, alcohol, and poisons; forms vesicles and peroxisomes	

(Continued)

An excellent summary of chapter 2

Crash Course Cells
https://www.khanacademy.org/partner-content/crash-course1/crash-course-biology/v/crash-course-biology-104

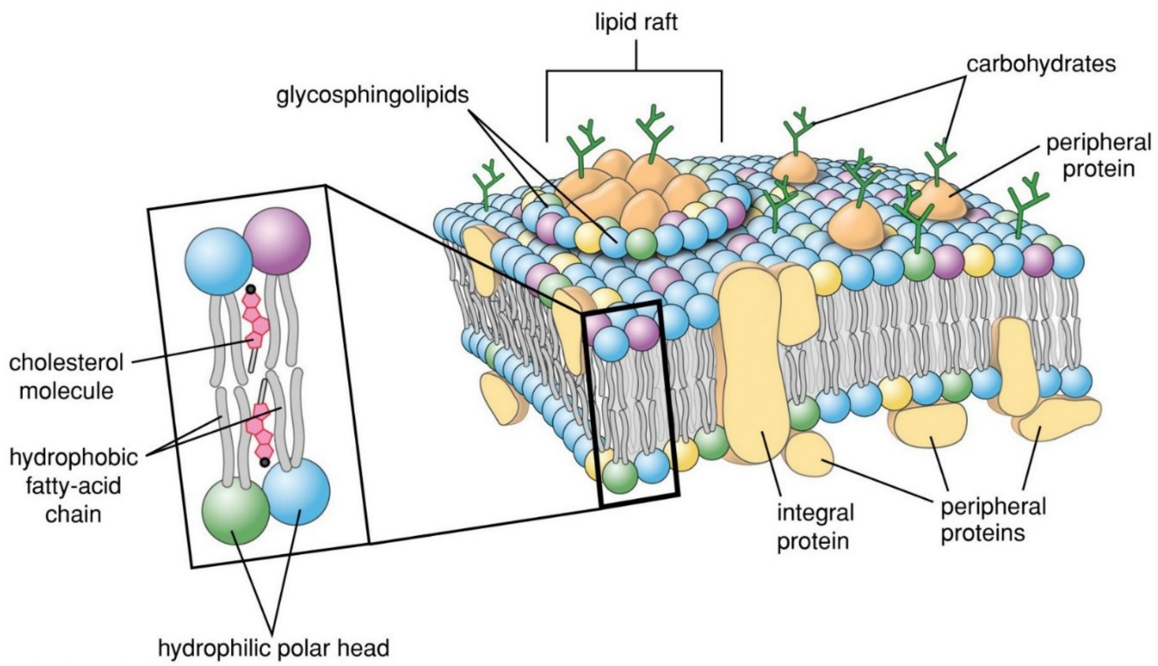
The membranous organelles: with plasma membranes that separate the internal environment of the organelle from the cytoplasm

- **plasma (cell) membrane**, a lipid bilayer that forms the cell boundary as well as the boundaries of many organelles within the cell;
- **rough-surfaced endoplasmic reticulum (rER)**, a region of endoplasmic reticulum associated with ribosomes and the site of protein synthesis and modification of newly synthesized proteins;
- **smooth-surfaced endoplasmic reticulum (sER)**, a region of endoplasmic reticulum involved in lipid and steroid synthesis but not associated with ribosomes;
- **Golgi apparatus**, a membranous organelle composed of multiple flattened cisternae responsible for modifying, sorting, and packaging proteins and lipids for intracellular or extracellular transport;

The membranous organelles: with plasma membranes that separate the internal environment of the organelle from the cytoplasm

- **Endosomes:** membrane-bounded compartments interposed within endocytotic pathways that have the major function of sorting proteins delivered to them via endocytotic vesicles and redirecting them to different cellular compartments for their final destination;
- **lysosomes**, small organelles containing digestive enzymes that are formed from endosomes by targeted delivery of unique lysosomal membrane proteins and lysosomal enzymes
- **transport vesicles** (**pinocytotic, endocytotic,** and **coated):** involved in both endocytosis and exocytosis and vary in shape and the material that they transport
- **mitochondria**, organelles that provide most of the energy to the cell by producing adenosine triphosphate (ATP) in the process of oxidative phosphorylation; and
- **peroxisomes**, small organelles involved in the production and degradation of H_2O_2 and degradation of fatty acids.

The Plasma Membrane

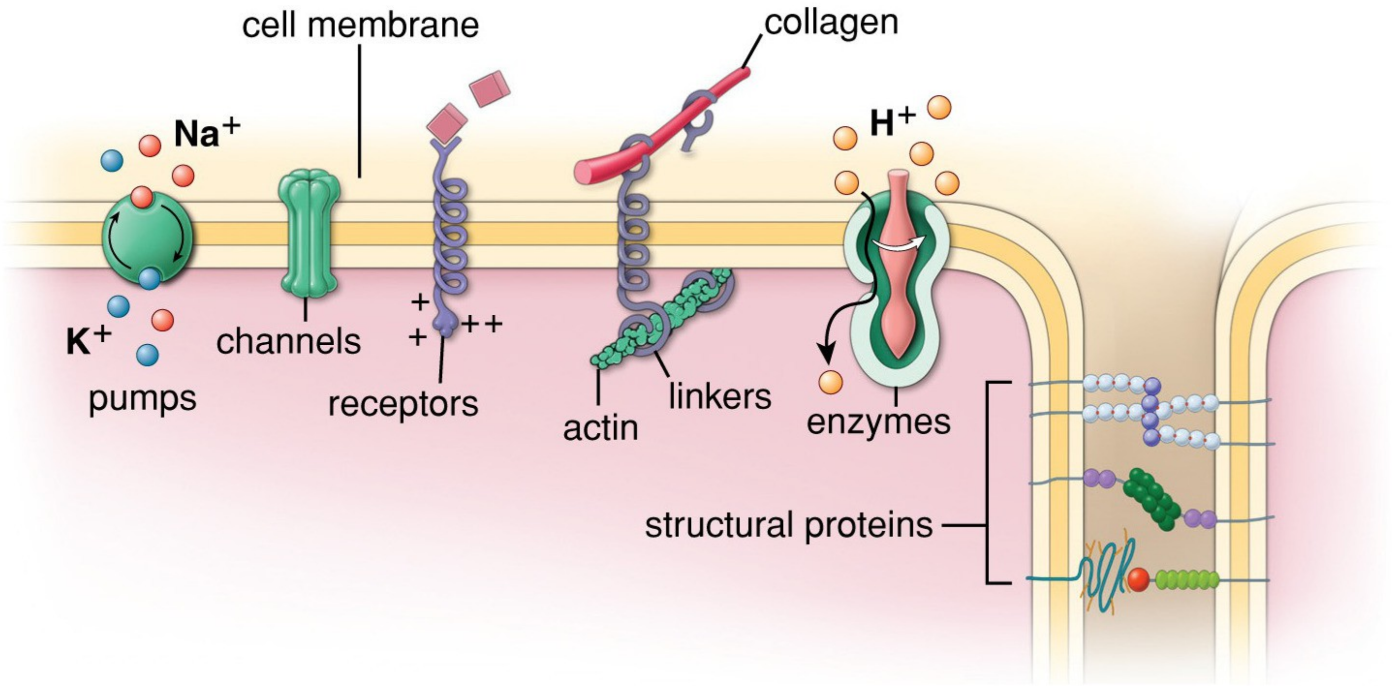


The plasma membrane is a **lipid bilayer** consisting primarily of phospholipid molecules, cholesterol, and protein molecules.

The **hydrophobic fatty-acid chains** of phospholipids face each other to form the inner portion of the membrane, whereas the **hydrophilic polar heads** of the phospholipids form the extracellular and intracellular surfaces of the membrane.

Cholesterol molecules are incorporated within the gaps between phospholipids equally on both sides of the membrane.

Integral Membrane Proteins



Different functions of integral membrane proteins. The six major categories of integral membrane proteins are shown in this diagram:

1. pumps
2. channels
3. receptors
4. linkers
5. enzymes
6. structural proteins.

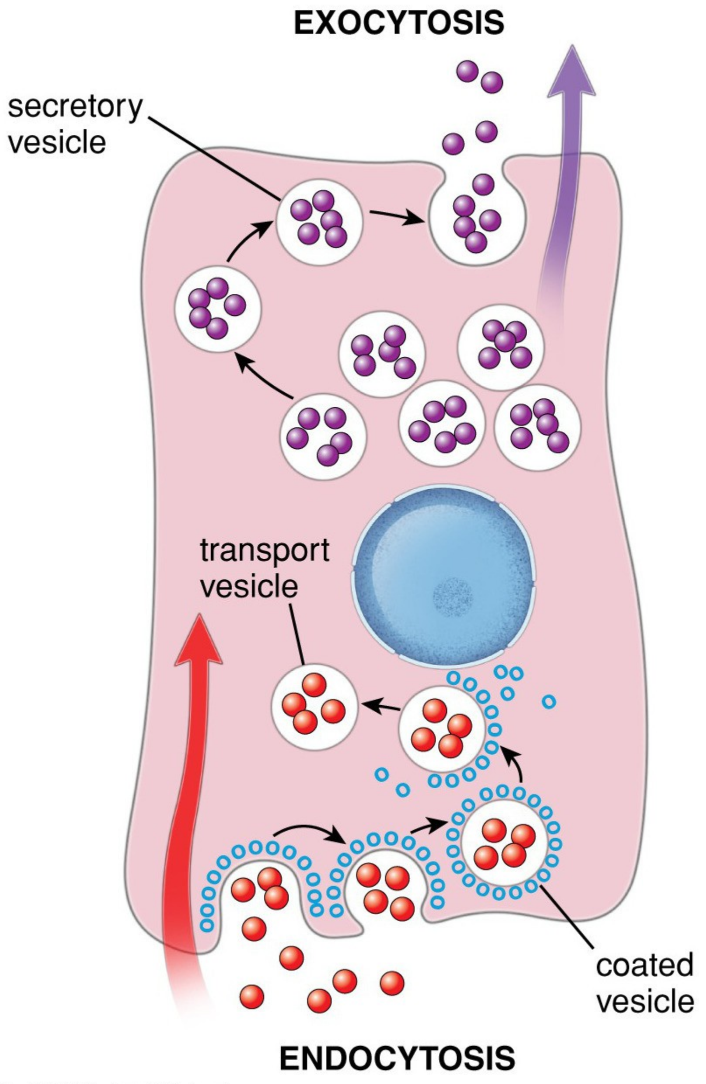
These categories are not mutually exclusive.

A structural membrane protein involved in cell-to-cell junctions might simultaneously serve as a receptor, enzyme, linker, or a combination of these functions.

Exocytosis and endocytosis transport large molecules across membranes

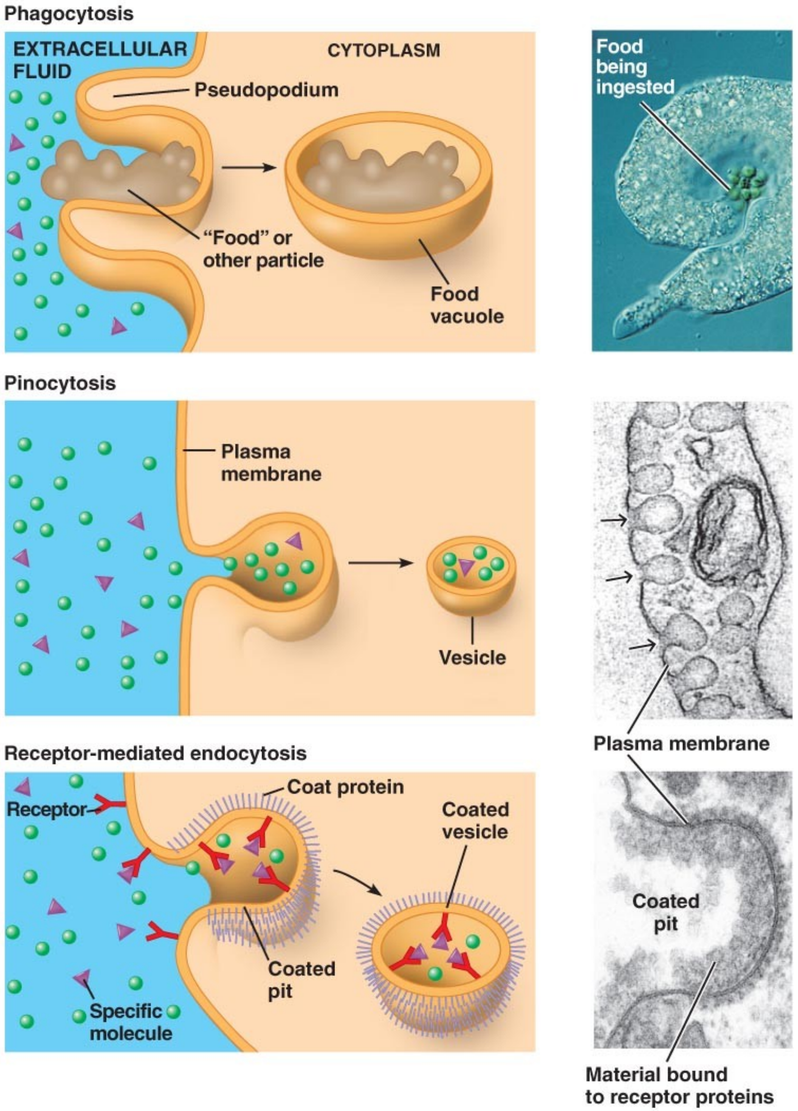
- A cell uses two mechanisms for moving large molecules across membranes
  - **Exocytosis** is used to export bulky molecules, such as proteins or polysaccharides
  - **Endocytosis** is used to import substances useful to the livelihood of the cell
- In both cases, material to be transported is packaged within a vesicle that fuses with the membrane

http://www.mhhe.com/biosci/ap/ap_prep/bioC8.html

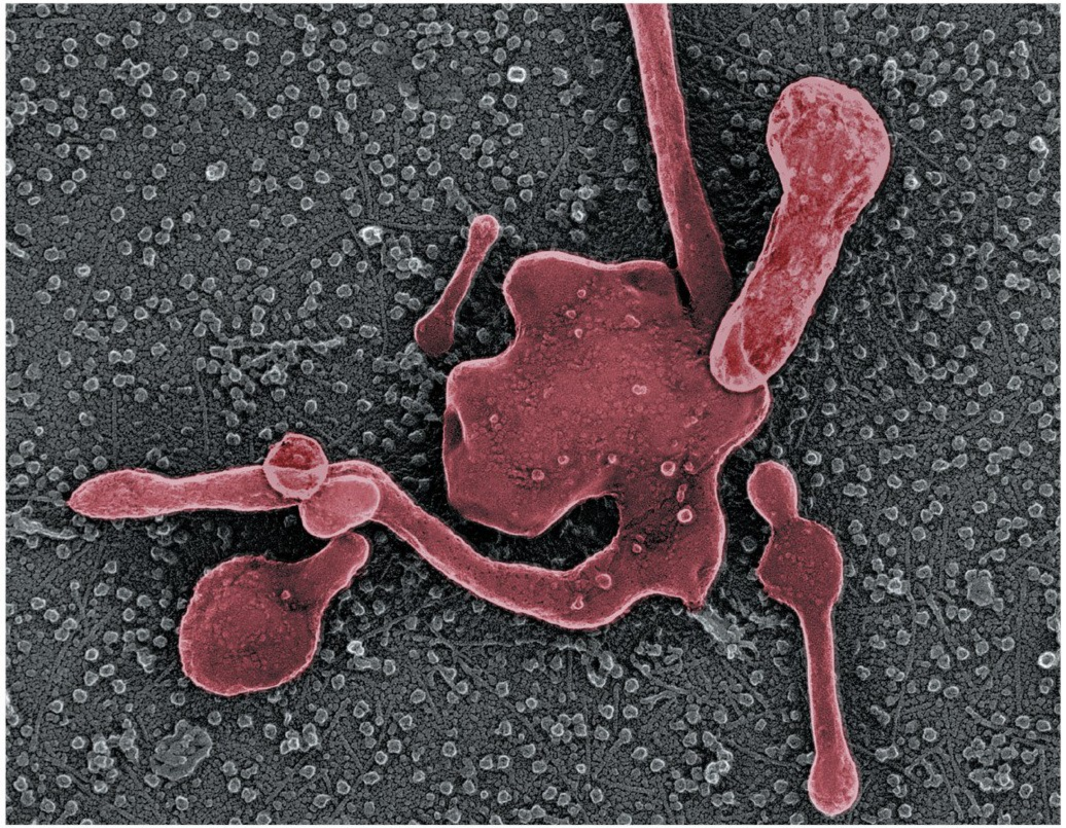


Exocytosis and endocytosis transport large molecules across membranes

- Three kinds of endocytosis
  - **Phagocytosis** is engulfment of a particle by wrapping cell membrane around it, forming a vacuole
  - **Pinocytosis** is the same thing except that fluids are taken into small vesicles
  - **Receptor-mediated endocytosis** is where receptors in a receptor-coated pit interact with a specific protein, initiating formation of a vesicle



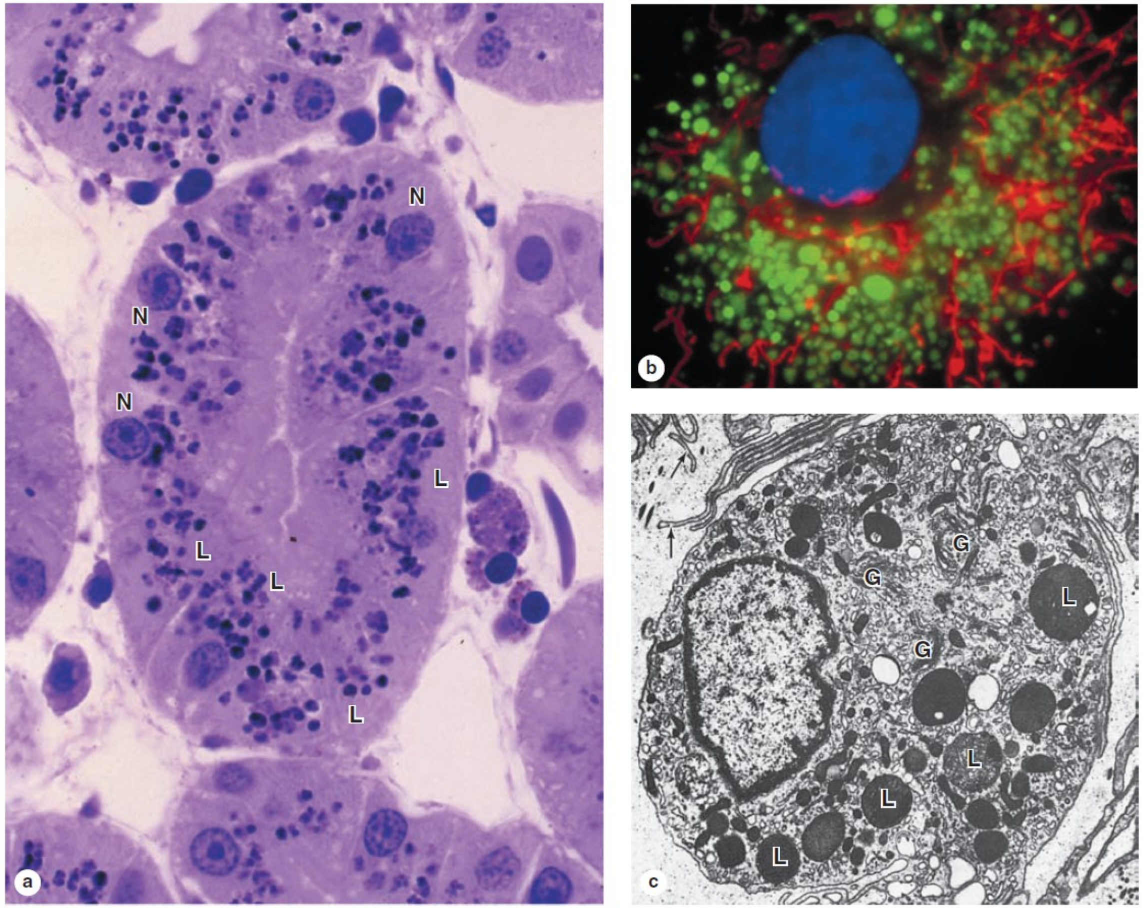
Endosomes can be viewed either as stable cytoplasmic organelles or as transient structures formed as the result of endocytosis.



The TEM reveals the presence in the cytoplasm of membrane enclosed compartments associated with all the endocytotic pathways described above (Fig. 2.15). These compartments, called **early endosomes**, are restricted to a portion of the cytoplasm near the cell membrane where vesicles originating from the cell membrane fuse. From here, many vesicles return to the plasma membrane.

However, large numbers of vesicles originating in early endosomes travel to deeper structures in the cytoplasm called **late endosomes**. The latter typically mature into **lysosomes**.

Lysosomes are spherical membrane-enclosed vesicles that function as sites of intracellular digestion and are particularly numerous in cells active after the various types of endocytosis.



Lysosomes are not well shown on H&E-stained cells but can be visualized by light microscopy after staining with toluidine blue.

(a) Cells in a kidney tubule show numerous purple lysosomes

(b) Lysosomes in cultured vascular endothelial cells can be specifically stained using fluorescent dyes: lysosomes (green), Mitochondria (red) are scattered among the lysosomes.

(c) In the TEM lysosomes (L) have a characteristic very electron-dense appearance and are shown here near groups of Golgi cisternae (G). The less electron-dense lysosomes represent heterolysosomes in which digestion of the contents is under way.

Lysosomal Storage Diseases, Lysosome Development: https://www.youtube.com/watch?v=-q8voqiXmF8

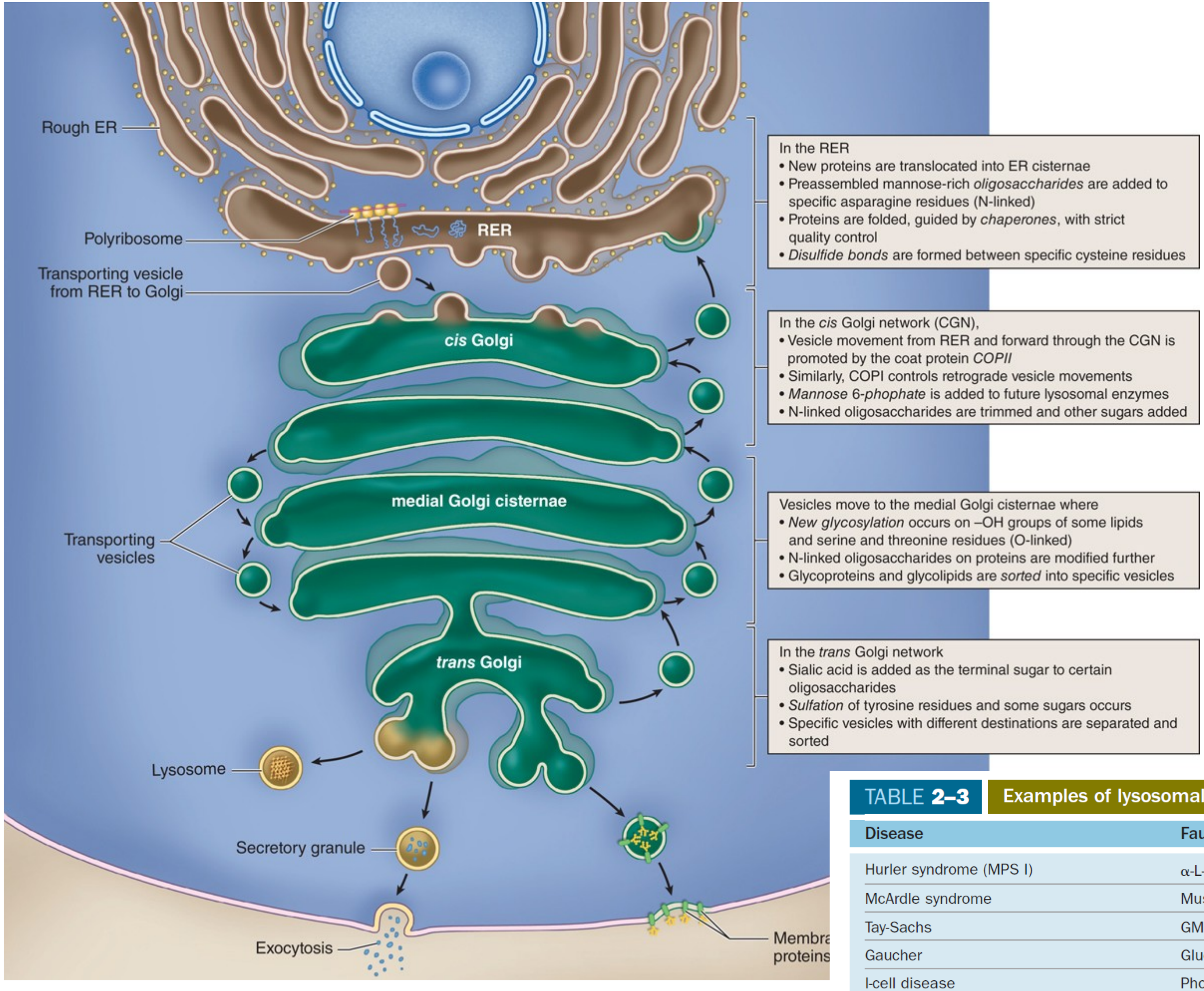
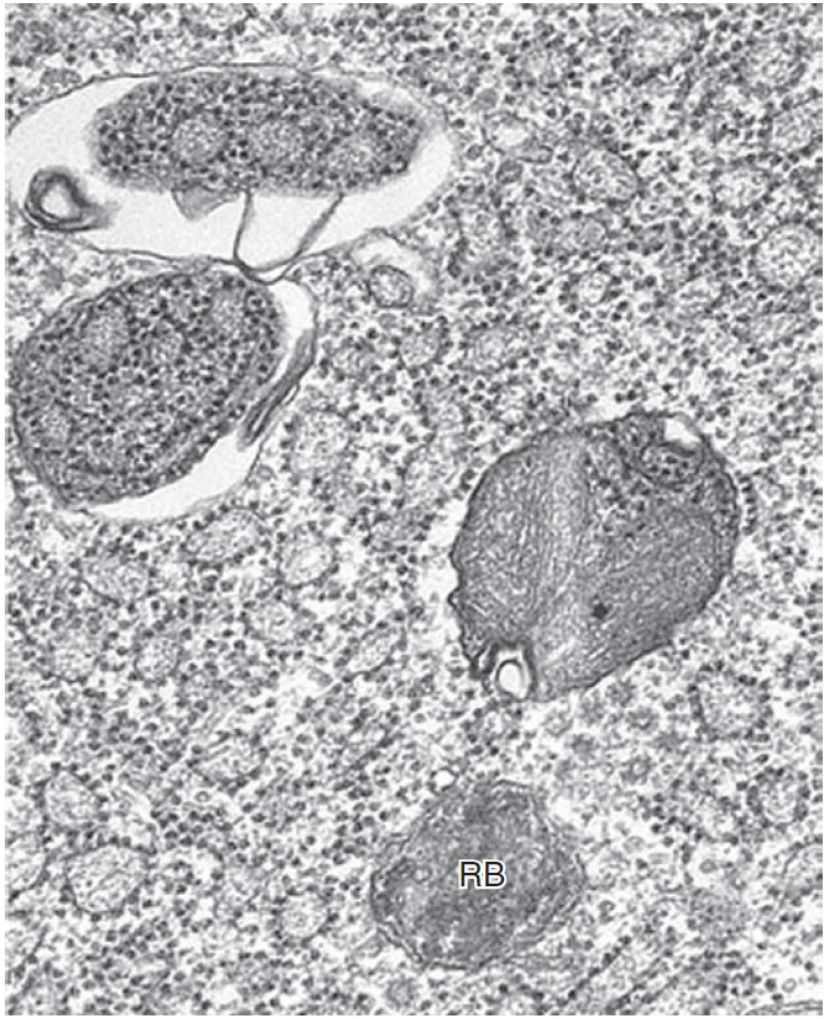


TABLE 2–3 Examples of lysosomal storage diseases caused by defective lysosomal enzymes.

Disease	Faulty Enzyme	Main Organs Affected
Hurler syndrome (MPS I)	α-L-Iduronidase	Skeleton and nervous system
McArdle syndrome	Muscle phosphorylase	Skeletal muscles
Tay-Sachs	GM_2-gangliosidase	Nervous system
Gaucher	Glucocerebrosidase	Liver and spleen
I-cell disease	Phosphotransferase for M6P formation	Skeleton and nervous system

Autophagy: proteins, organelles, and other cellular structures are degraded in the lysosomal compartment

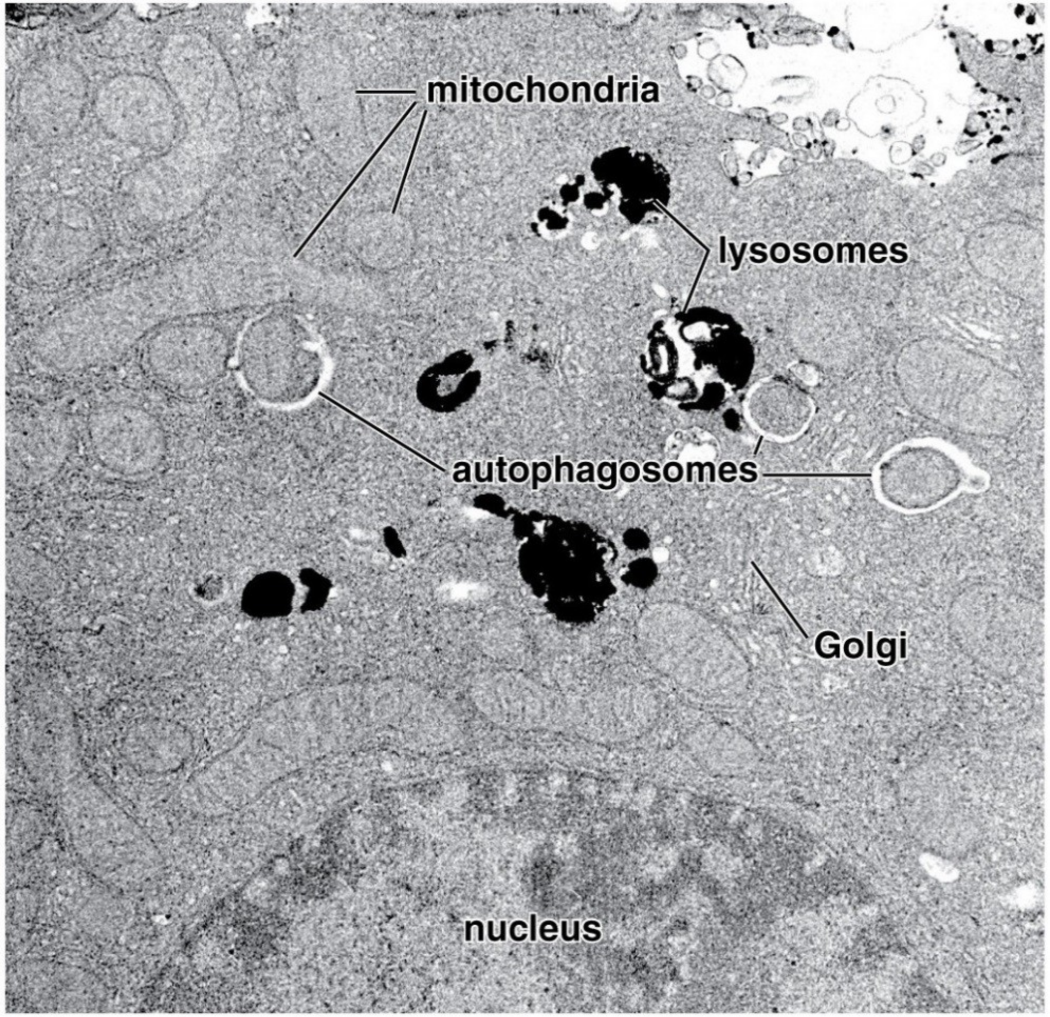


Autophagy is a process in which the cell uses lysosomes to dispose of excess or nonfunctioning organelles or membranes.

Membrane that appears to emerge from the SER encloses the organelles to be destroyed, forming an autophagosome that then fuses with a lysosome for digestion of the contents. In this TEM the two autophagosomes at the upper left contain portions of RER more electron dense than the neighboring normal RER and one near the center contains what may be mitochondrial membranes plus RER.

Also shown is a vesicle with features of a residual body
(RB).

Proteasomes are protein complexes that destroy proteins without involvement of lysosomes.



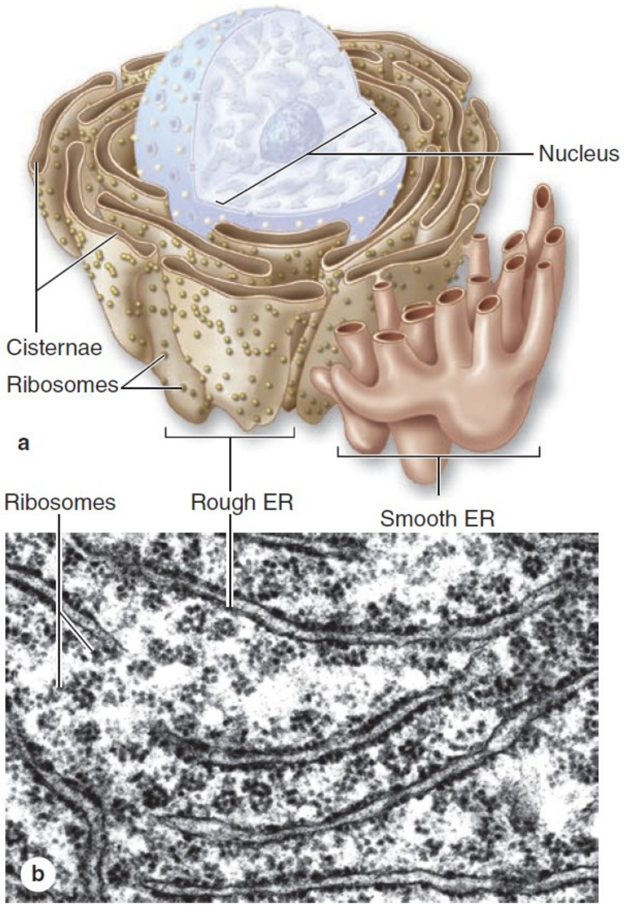
Electron micrograph of autophagosomes in a hepatocyte shows several autophagosomes containing degenerating mitochondria. Note the surrounding lysosomes that have been stained with acid phosphatase

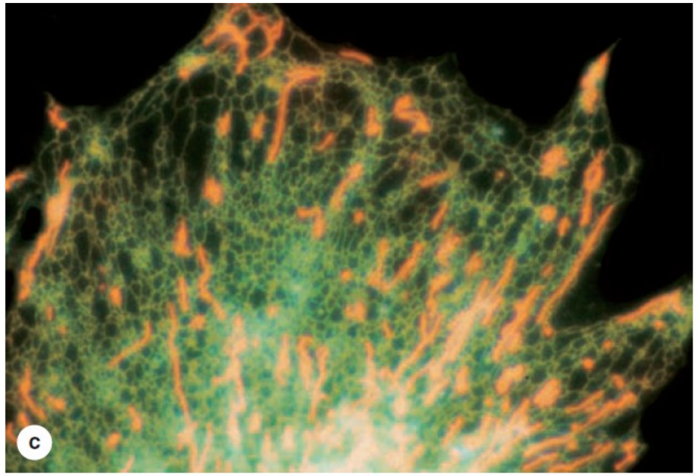
Rough ER manufactures proteins targeted for secretion or other organelles and membranes

Electron micrograph of the rER. This image of the rER in a chief cell of the stomach shows the membranous cisternae (*C*) closely packed in parallel arrays.

Polyribosomes are present on the cytoplasmic surface of the membrane surrounding the cisternae. The image of a ribosome-studded membrane is the origin of the term *rough endoplasmic reticulum.* A few ribosomes are free in the cytoplasm. *M,* mitochondrion.

Smooth ER lacks ribosomes and synthesizes lipids





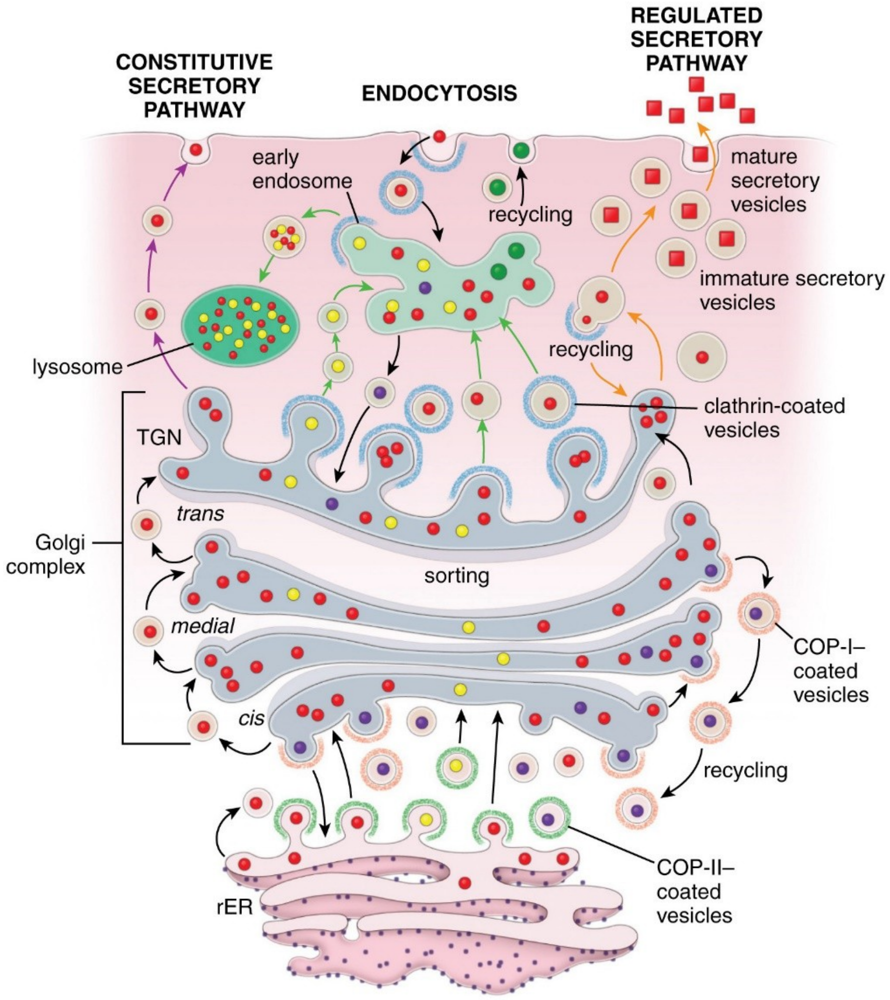
Functions of Endoplasmic Reticulum

1. **Synthesis:** Provides a place for chemical reactions
   a. Smooth ER is the site of lipid synthesis and carbohydrate metabolism
   b. Rough ER synthesizes proteins for secretion, incorporation into the plasma, membrane, and as enzymes within lysosomes
2. **Transport:** Moves molecules through cisternal space from one part of the cell to another, sequestered away from the cytoplasm
3. **Storage:** Stores newly synthesized molecules
4. **Detoxification:** Smooth ER detoxifies both drugs and alcohol

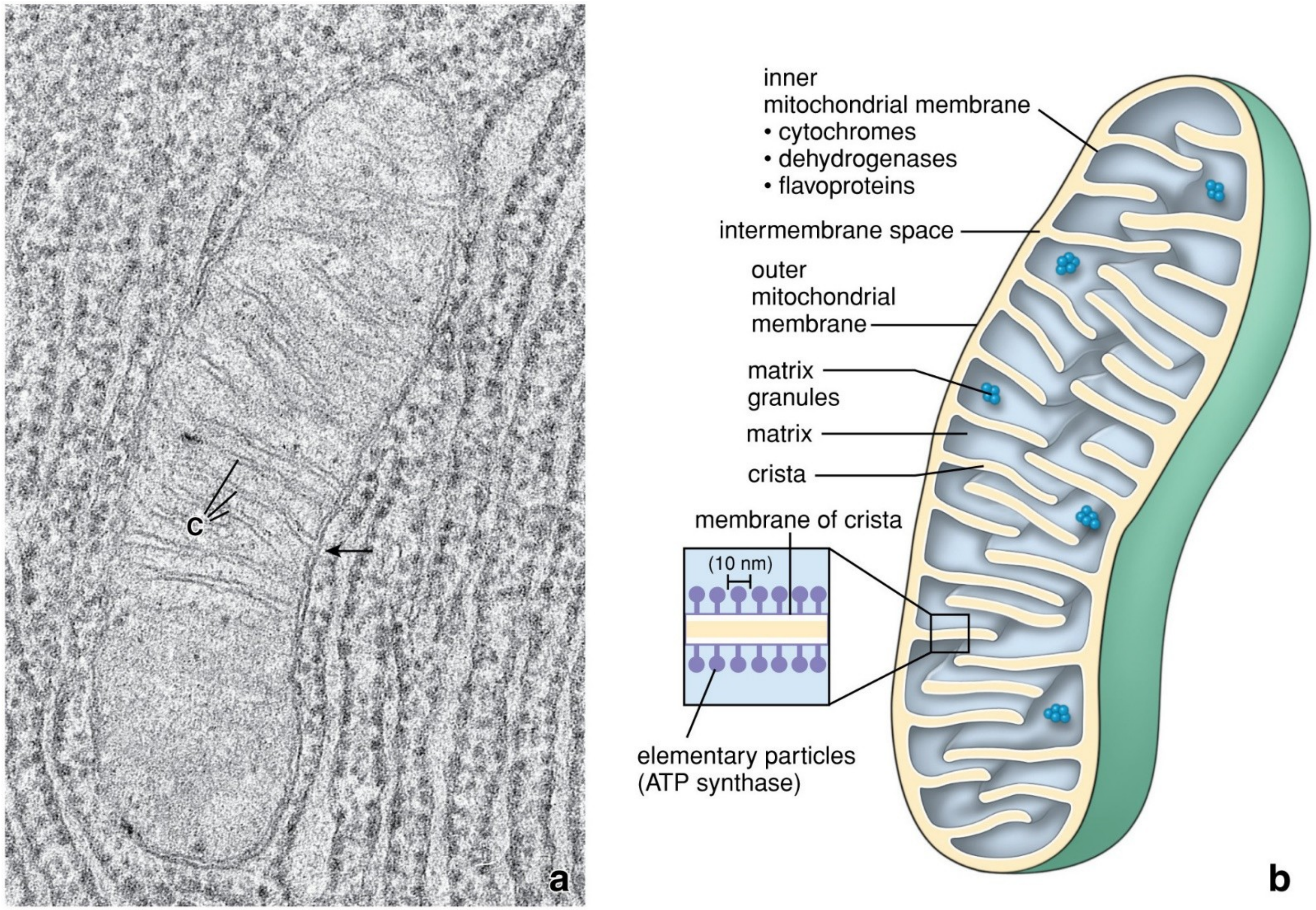
›› MEDICAL APPLICATION

Jaundice denotes a yellowish discoloration of the skin and is caused by accumulation in extracellular fluid of bilirubin and other pigmented compounds, which are normally metabolized by SER enzymes in cells of the liver and excreted as bile. A frequent cause of jaundice in newborn infants is an underdeveloped state of SER in liver cells, with failure of bilirubin to be converted to a form that can be readily excreted.

The Golgi Apparatus and vesicular trafficking



Mitochondria are abundant in cells that generate and expend large amounts of energy



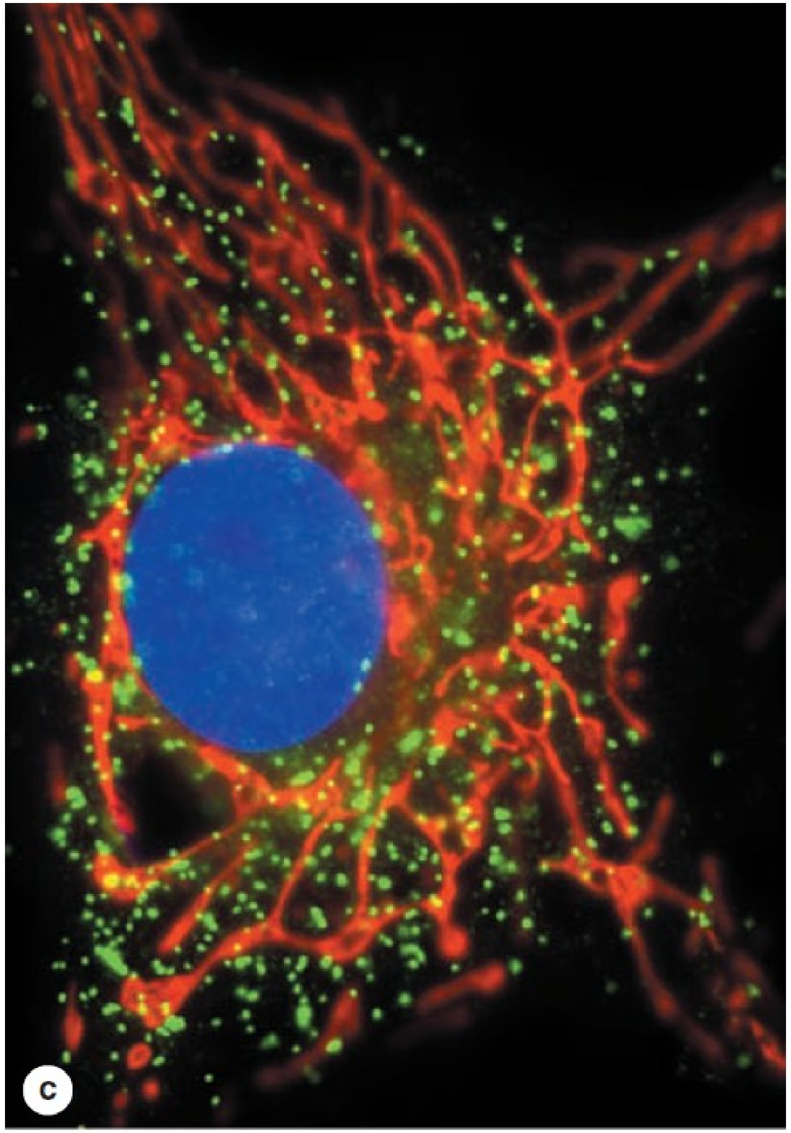
a. This electron micrograph shows a mitochondrion in a pancreatic acinar cell. Note that the inner mitochondrial membrane forms the cristae (*C*) through a series of infoldings, as is evident in the region of the *arrow.* The outer mitochondrial membrane is a smooth continuous envelope that is separate and distinct from the inner membrane.

b. Schematic diagram showing the components of a mitochondrion. Note the location of the elementary particles (inset), the shape
of which reflects the three-dimensional structure of ATP synthase.

Peroxisomes are spherical organelles enclosed by a single membrane

Peroxisomes produce and degrade hydrogen peroxide inactivate various potentially toxic molecules, including some prescription drugs, particularly in the large and abundant peroxisomes of liver and kidney cells

A cultured endothelial cell processed by immunocytochemistry shows many peroxisomes (green) distributed throughout the cytoplasm among the vitally stained elongate mitochondria (red) around the DAPI-stained nucleus (blue). Peroxisomes shown here were specifically stained using an antibody against the membrane protein PMP70.

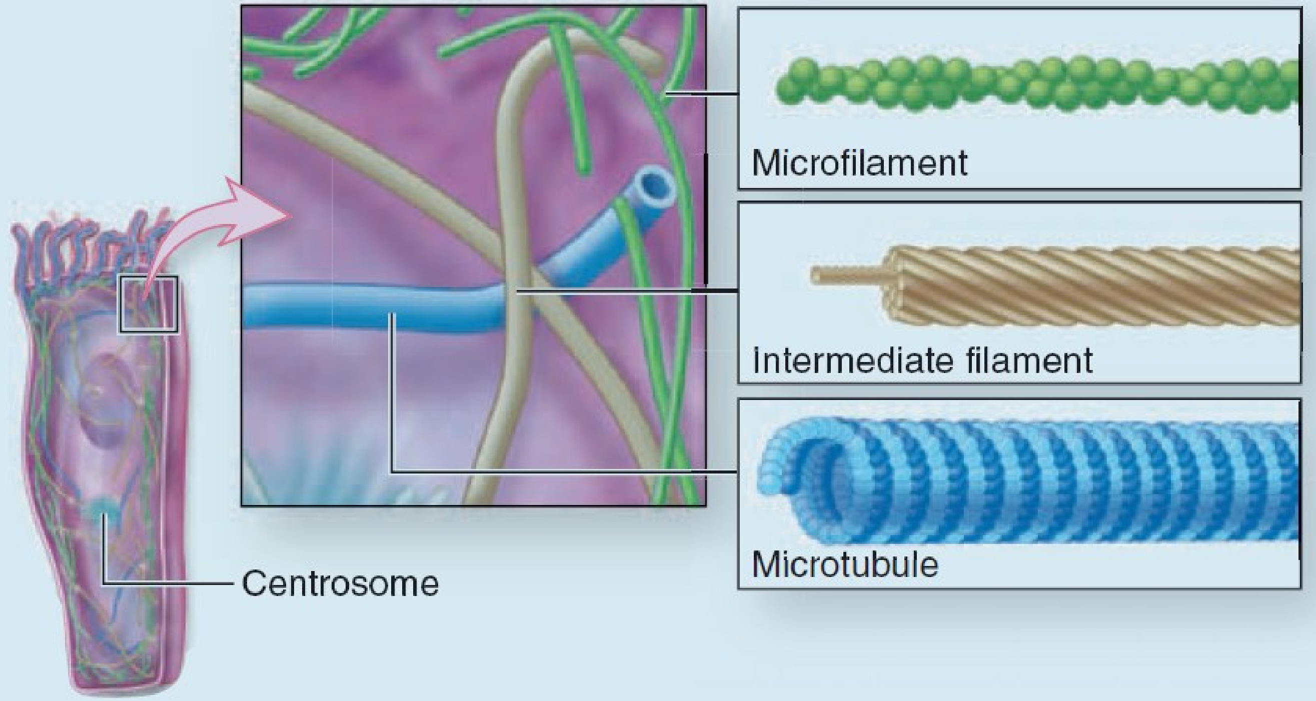


Non-membranous organelles

- **Microtubules**: form elements of the **cytoskeleton** and continuously elongate (by adding tubulin dimers) and shorten (by removing tubulin dimers), a property referred to as **dynamic instability**;
- **Filaments**, which are also part of the cytoskeleton
  - **actin filaments:** flexible chains of actin molecules,
  - **intermediate filaments:** which are ropelike fibers formed from a variety of proteins—both groups providing tensile strength to withstand tension and confer resistance to shearing forces;
- **Centrioles**, or short, paired cylindrical structures found in the center of the **microtubule-organizing center (MTOC)** or **centrosome** and whose derivatives give rise to basal bodies of cilia
- **Ribosomes**, structures essential for protein synthesis and composed of ribosomal RNA (rRNA) and ribosomal proteins (including proteins attached to membranes of the rER and proteins free in the cytoplasm).

Microtubules & Filaments

TABLE 2–4 Properties of cytoskeletal components (microtubules, microfilaments, and intermediate filaments).



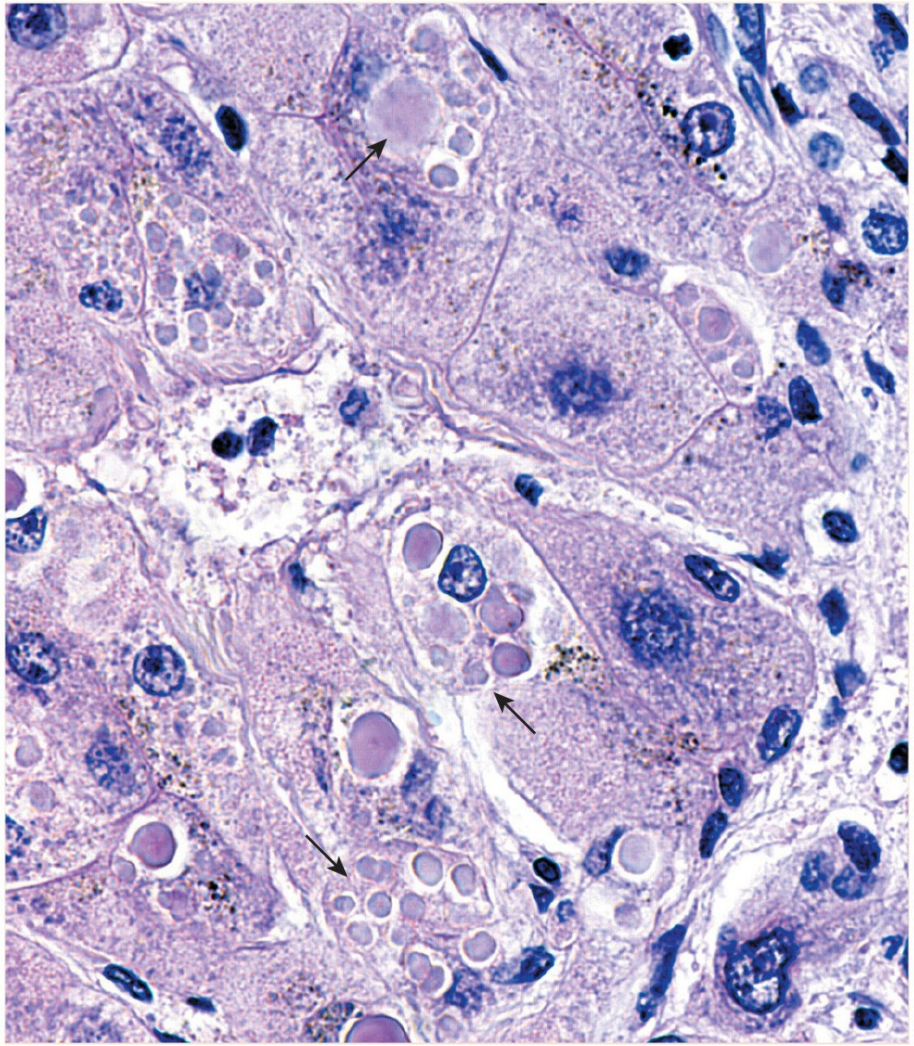
General Function of Cytoskeleton
1. **Structural:** Provides structural support to cell; stabilizes junctions between cells
2. **Movement:** Assists with cytosol streaming and cell motility; helps move organelles and materials throughout cell; helps move chromosomes during cell division

Abnormalities in microtubules and filaments

Photomicrograph of Mallory bodies. Accumulation of keratin intermediate filaments forming intercellular inclusions is frequently associated with specific cell injuries.

In **alcoholic liver cirrhosis**, hepatocytes exhibit such inclusions (*arrows*), which are known as Mallory bodies.

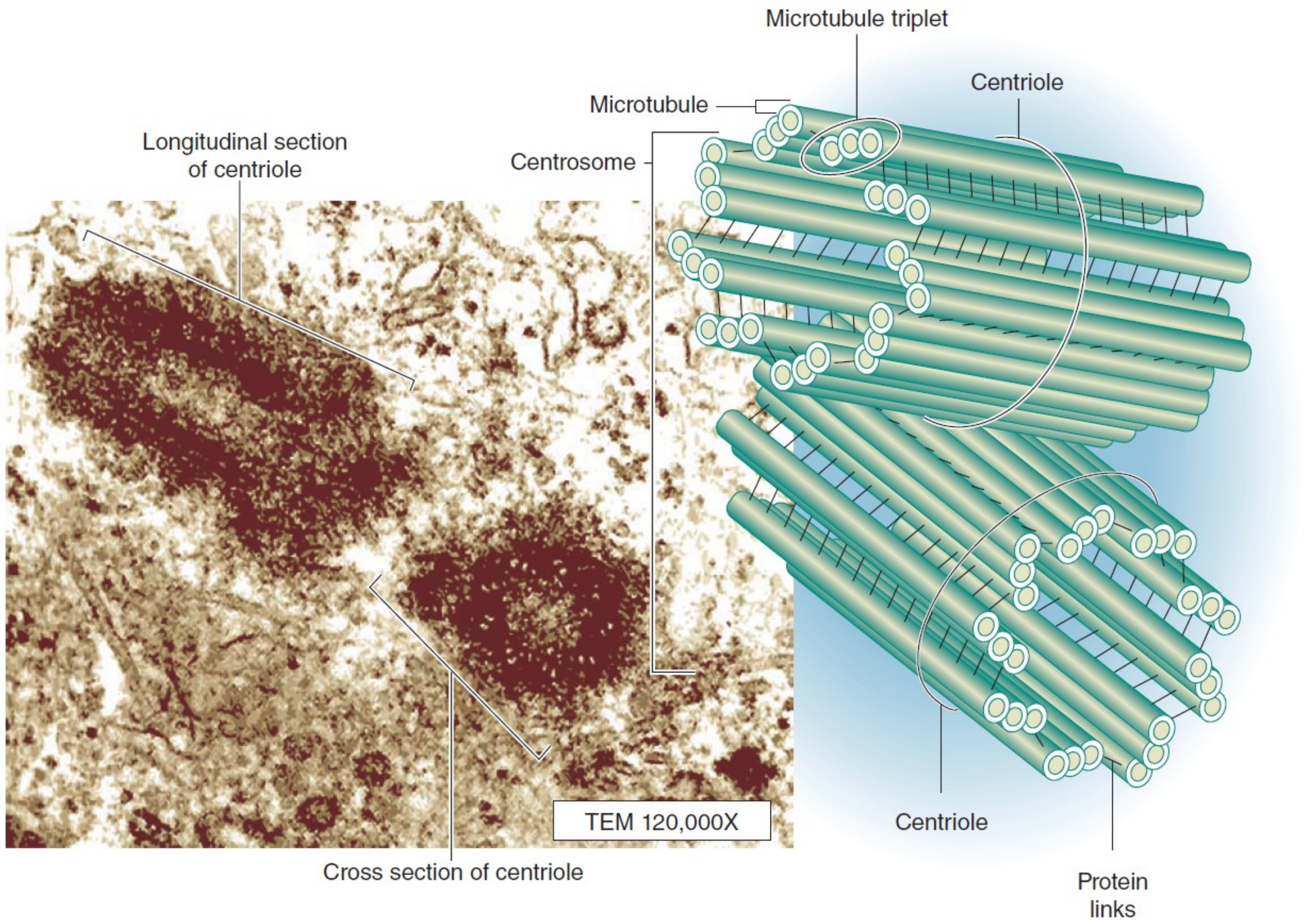
Lymphocytes and macrophages responsible for an intense inflammatory reaction surround cells containing Mallory bodies



Centrioles

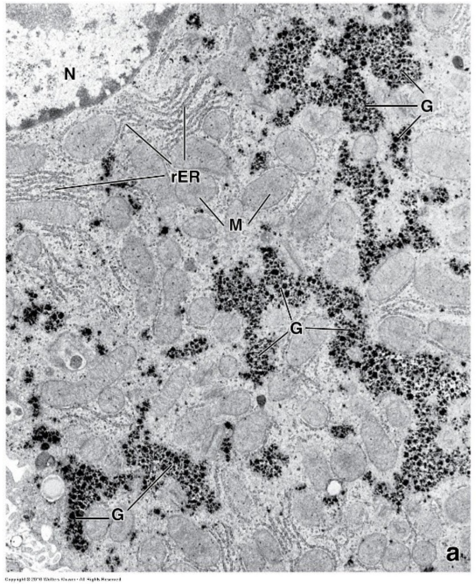
The centrosome is the microtubule-organizing center for the mitotic spindle and consists of paired centrioles. The TEM reveals that the two centrioles in a centrosome exist at right angles to each other in a dense matrix of free tubulin subunits and other proteins

FIGURE 2–24 **Centrosome.**



Inclusions contain accumulated metabolites or other substances not enclosed by membrane

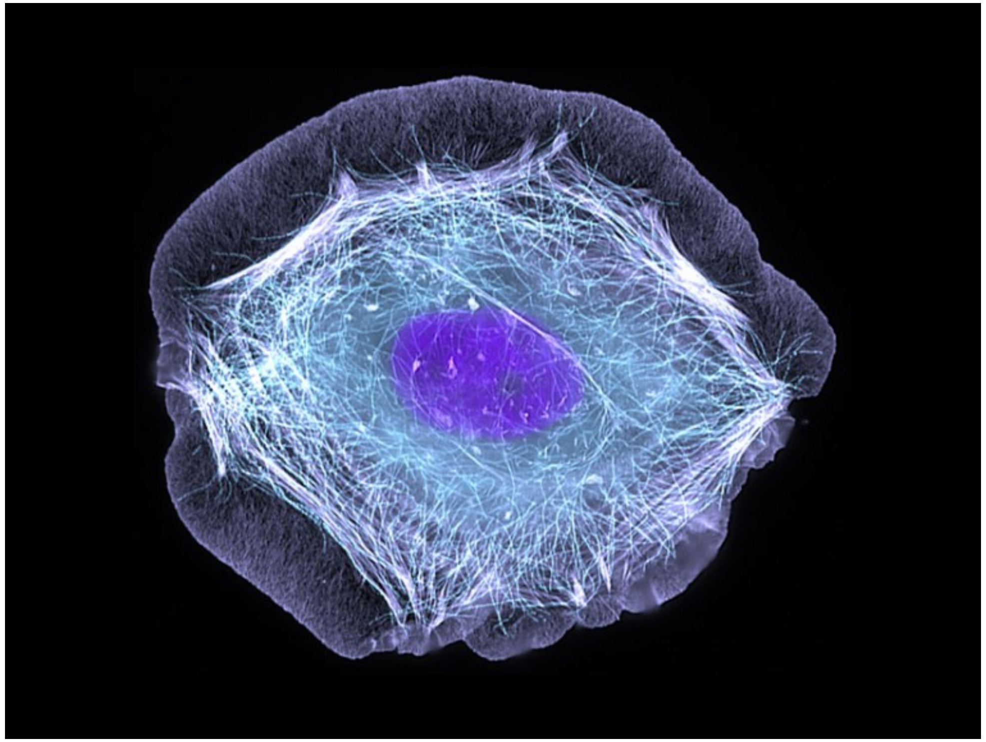
- **Fat droplets**: accumulations of lipid
- **Glycogen granules**: aggregates of glycogen mainly liver cells
- **Lipofuscin:** yellowish-brown pigment found in stable nondividing cells (eg, neurons, cardiac muscle).
- **Hemosiderin:** dense brown aggregate of denatured proteins bound to iron. Found in liver and spleen



Electron micrographs of a hepatocyte (liver cell) with glycogen inclusions.

- Nucleus (*N, upper left*).
- Glycogen (*G*) appears as irregular electron-dense masses.
- Profiles of rough endoplasmic reticulum (*rER*) and mitochondria (*M*) are also evident.

A Human Skin Cell. The purple in the center is the cell’s nucleus. Surrounding it are wispy blue and white microtubules and filaments that make up the cell’s cytoskeleton



Nuclear Components, Cell Renewal, Cell Cycle, Cell Death

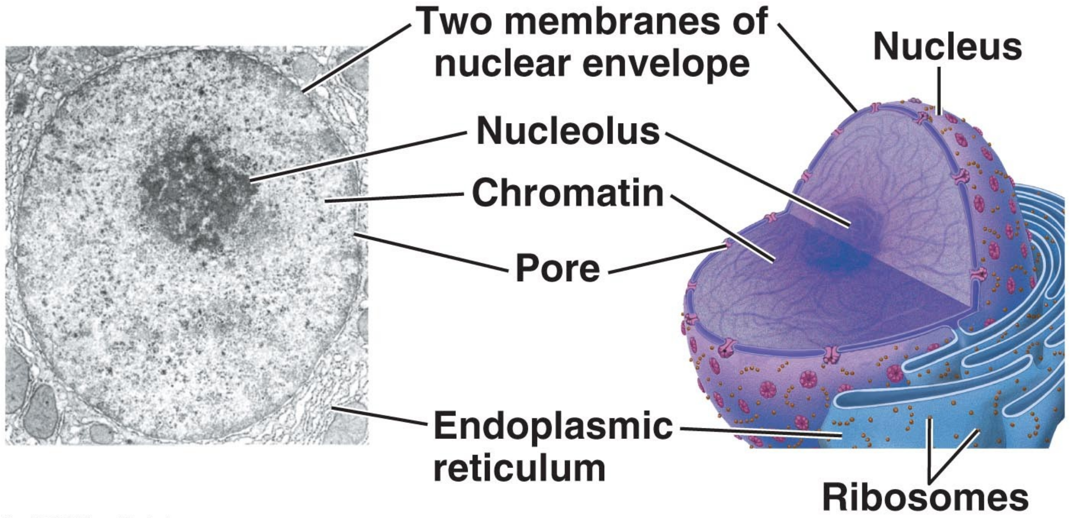
CHAPTER 3: THE NUCLEUS

The nucleus is the cell's genetic control center

- The **nucleus** controls the cell's activities and is responsible for inheritance
  - Inside is a complex of proteins and DNA called **chromatin**, which makes up the cell's chromosomes
- The **nuclear envelope** is a double membrane with pores that allow material to flow in and out of the nucleus

Nucleolus: contains DNA in the form of transcriptionally active ribosomal RNA (rRNA) genes, RNA, and proteins.

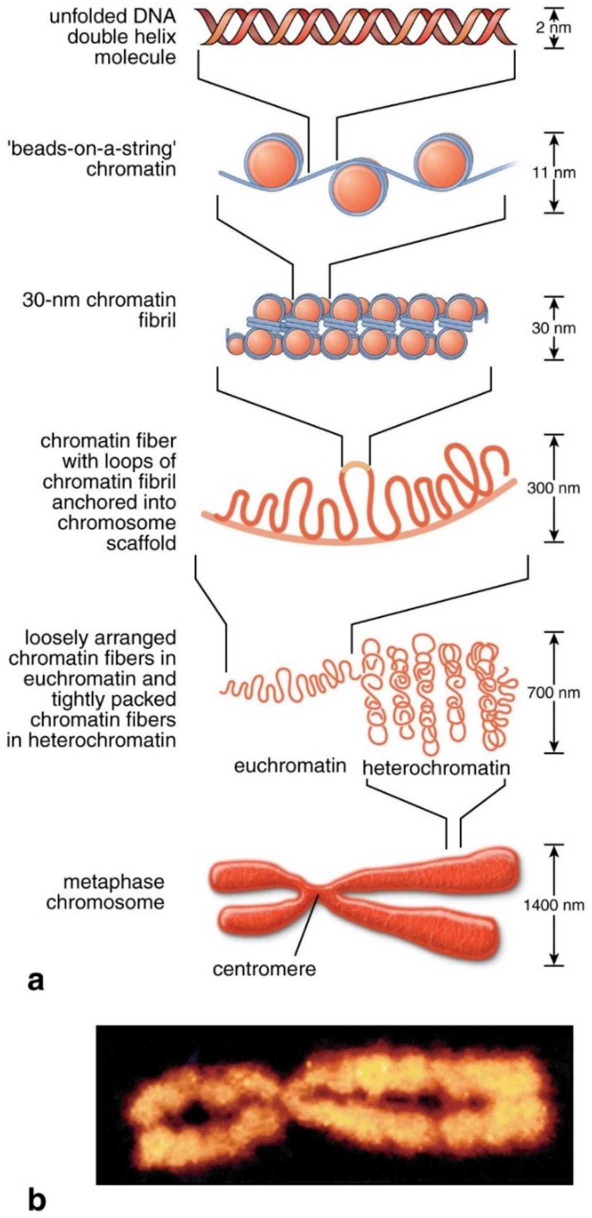
Nucleoplasm: nuclear content other than chromatin and nucleolus



Packaging of chromatin into the chromosomal structure

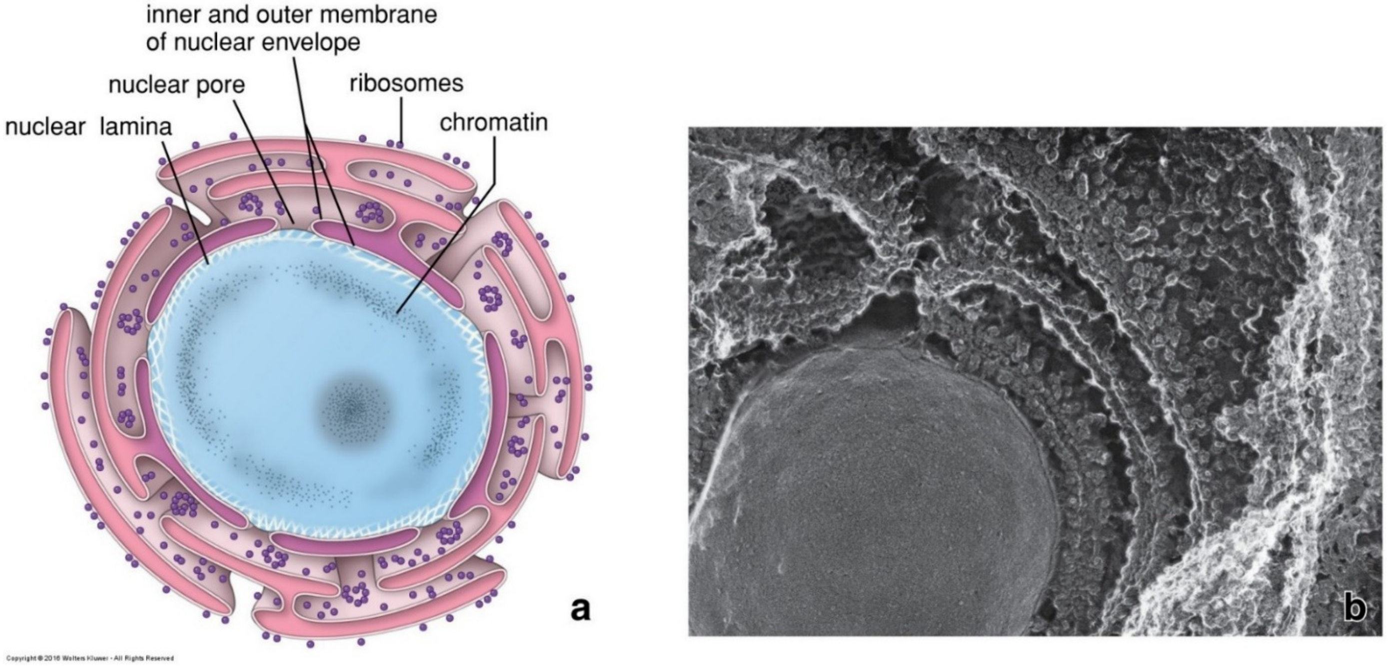
a. Sequential steps in the packaging of nuclear chromatin are shown in this diagram, beginning with the DNA double helix and ending with the highly condensed form found inchromosomes.

b. Structure of human metaphase chromosome 2 (Courtesy of Dr. Tatsuo Ushiki.)

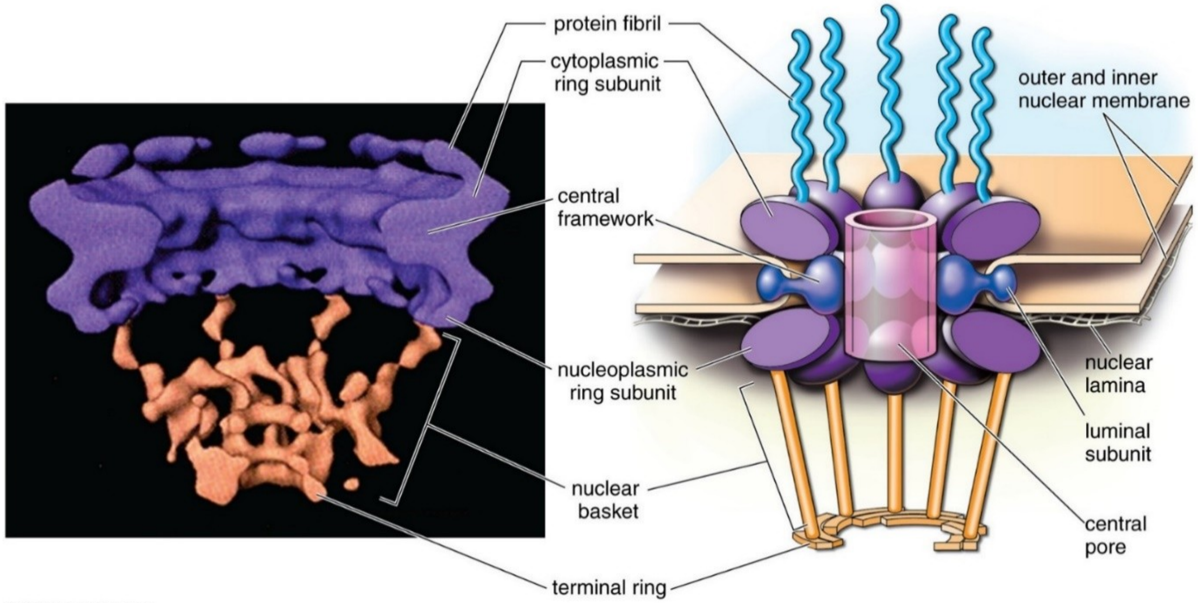


Structure of the nuclear envelope and its relationship to the rER

a. Double membrane envelope surrounds nucleus: outer membrane is continuous with the membranes of the rER; Perinuclear space communicates with the rER lumen. The inner membrane is adjacent to nuclear intermediate filaments that form the nuclear lamina.
b. Electron micrograph of nucleus surrounded by the nuclear envelope. Note that the outer membrane possesses ribosomes and is continuous with the rER.



Nuclear Pore Complex



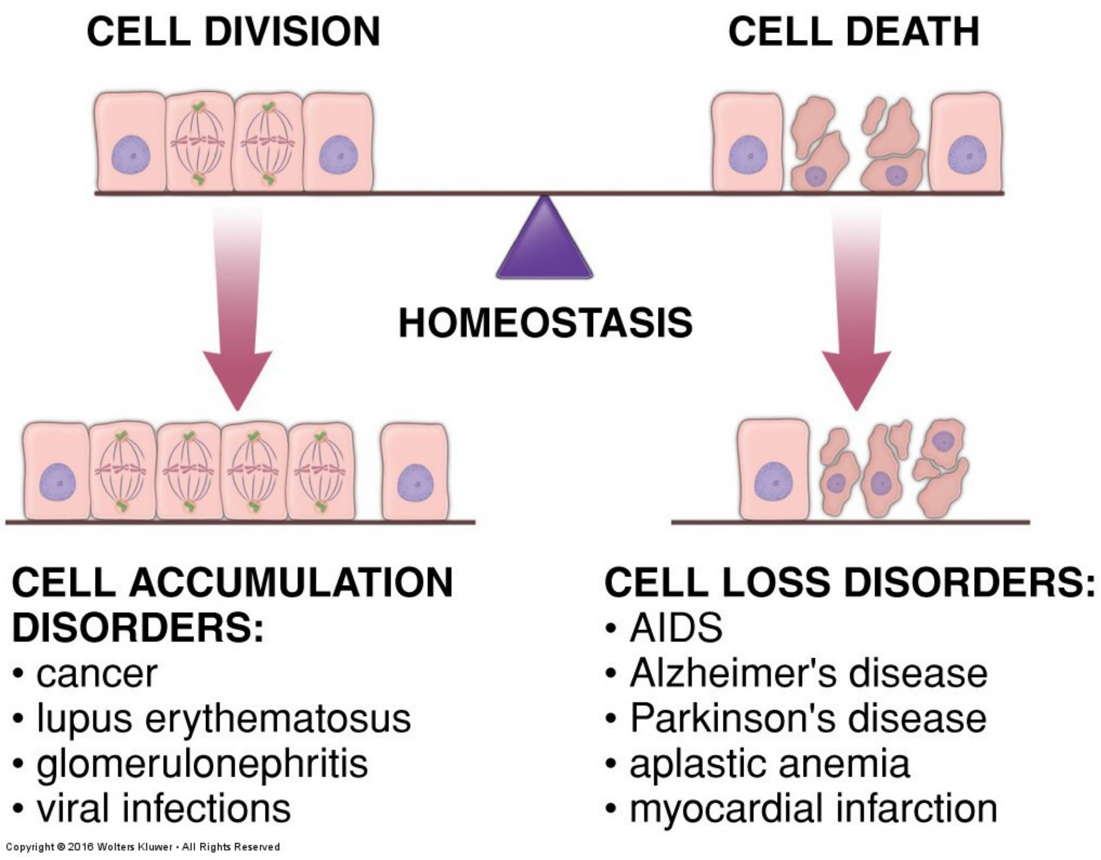
- Each pore contains eight protein subunits arranged in an octagonal central framework at the periphery of the pore.
- These subunits form a nuclear pore complex that is inserted between two cytoplasmic and nucleoplasmic rings
- The cylindrical central framework encircles the central pore, which acts as a close-fitting diaphragm.

Cell Division and Cell Death

- Under normal physiologic conditions (homeostasis), the rates of cell division and cell death are similar.

- If the rate of cell death is higher than that of cell division,then a net loss of cell number will occur. Such conditions are categorized as **cell loss disorders**.

- When the situation is reversed and the rate of cell division is higher than the rate of cell death, then the net gain in cell number will be prominent, leading to a variety of disorders of **cell accumulation.**



Cell Renewal and the Cell Cycle

Somatic cells in the adult organism may be classified according to their mitotic activity

Interphase:

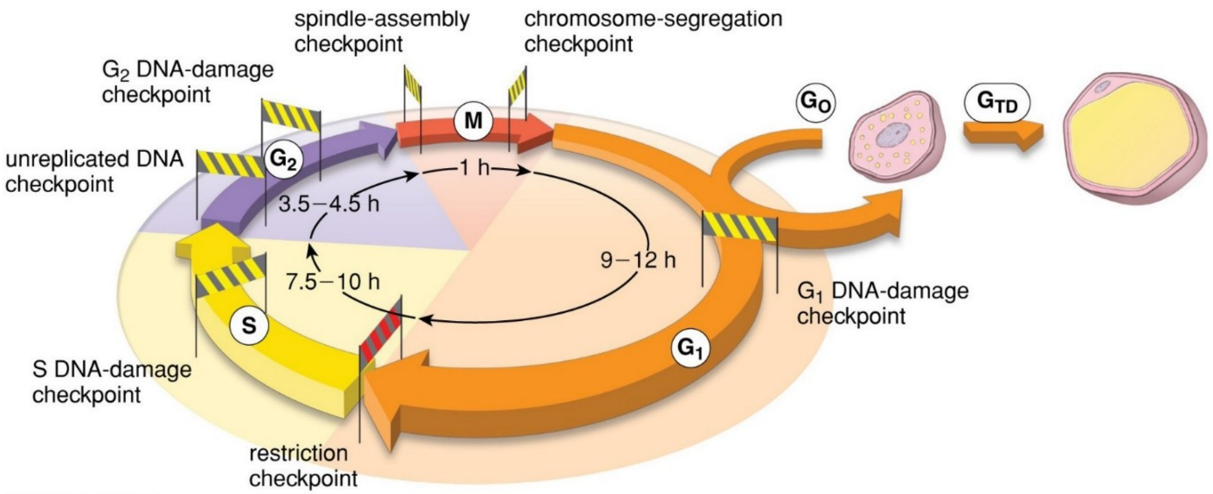
1. **G_1** (growth phase 1) acquisition of nutrients, growth
2. **S** (DNA synthesis): chromosome replication
3. **G_2** (growth phase 2) completion of cell growth, preparation for cell division

Cell division:

4. **Mitosis:** division of the nucleus
5. **Cytokinesis**: cytoplasmic division

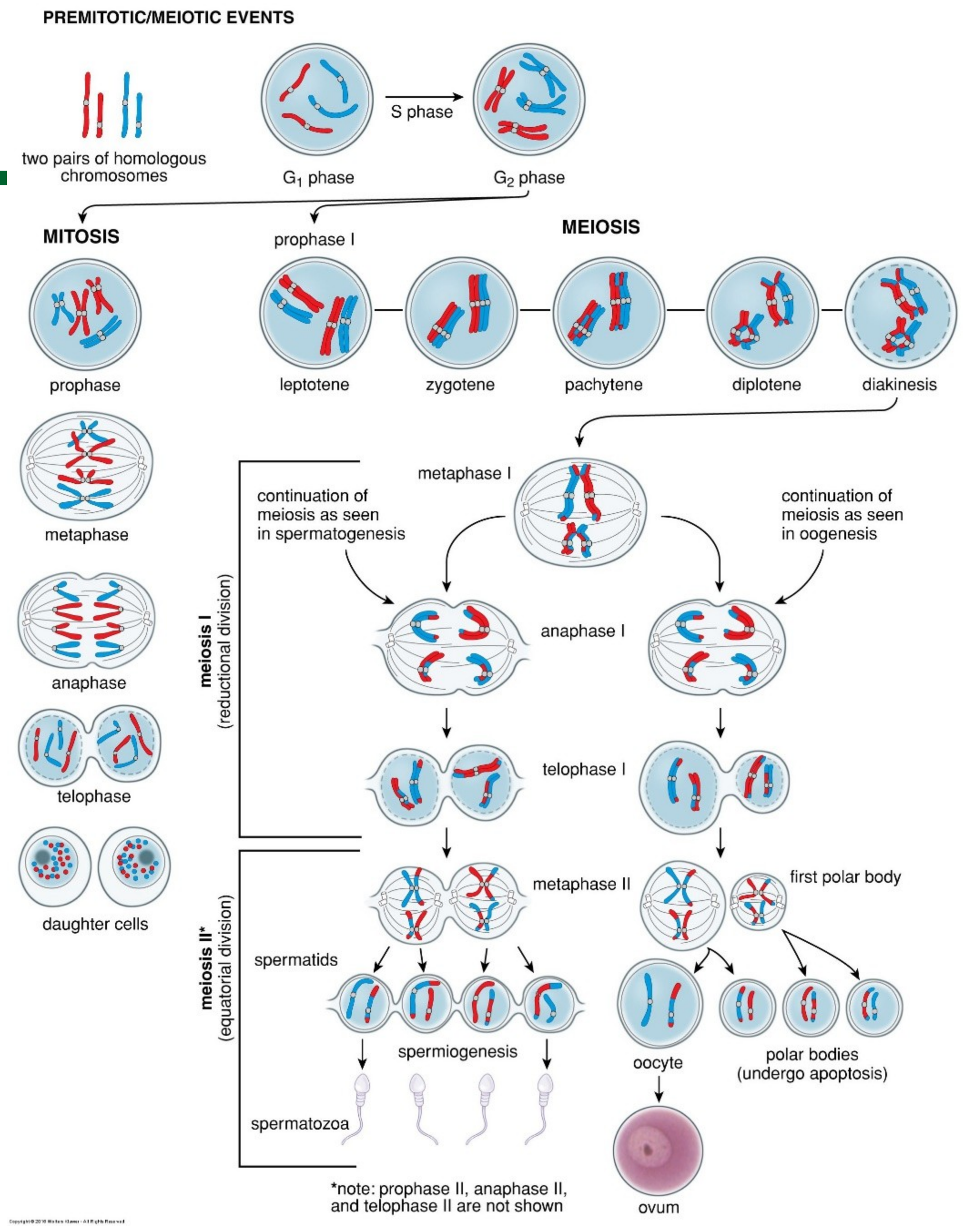
MEDICAL APPLICATION

Tissues with either stable or rapidly renewing cell populations can include cells that become transformed to grow at a higher rate and in an uncoordinated manner. Such **neoplastic proliferation** typically follows damage to the DNA of proto-oncogenes and failure of the cells to be eliminated. Neoplastic growth can be either benign (with slow growth and no invasiveness to neighboring organs) or malignant (with rapid growth and great capacity to invade other organs). **Cancer** is the common term for all malignant tumors.



The Stages of Mitosis

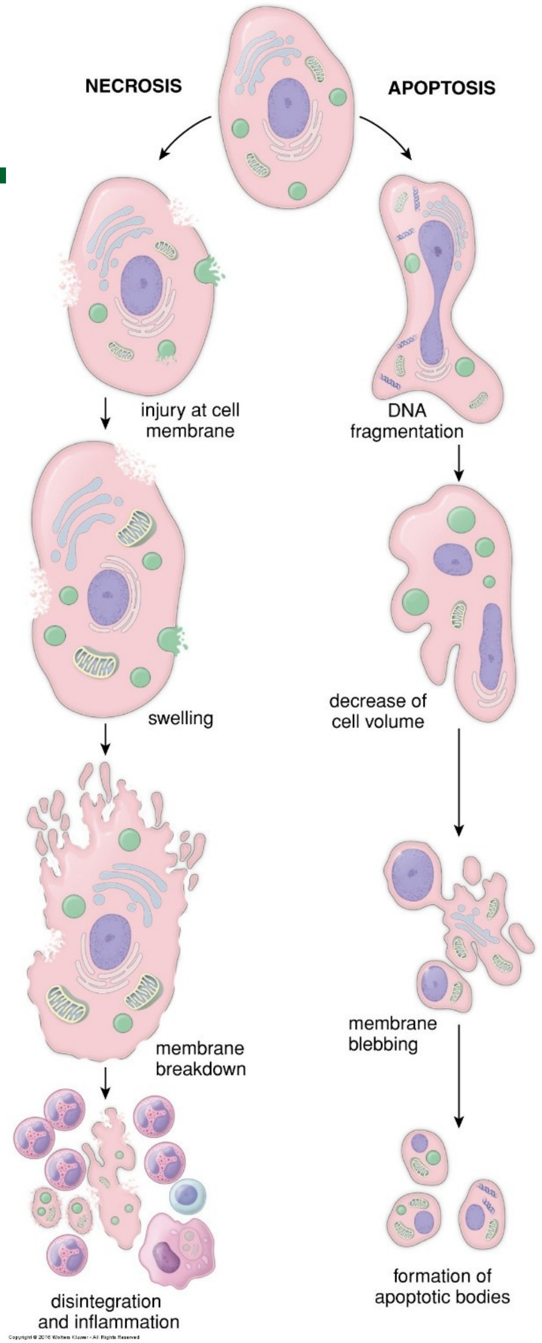
1. **Prophase**
2. **Metaphase**
3. **Anaphase**
4. **Telophase**



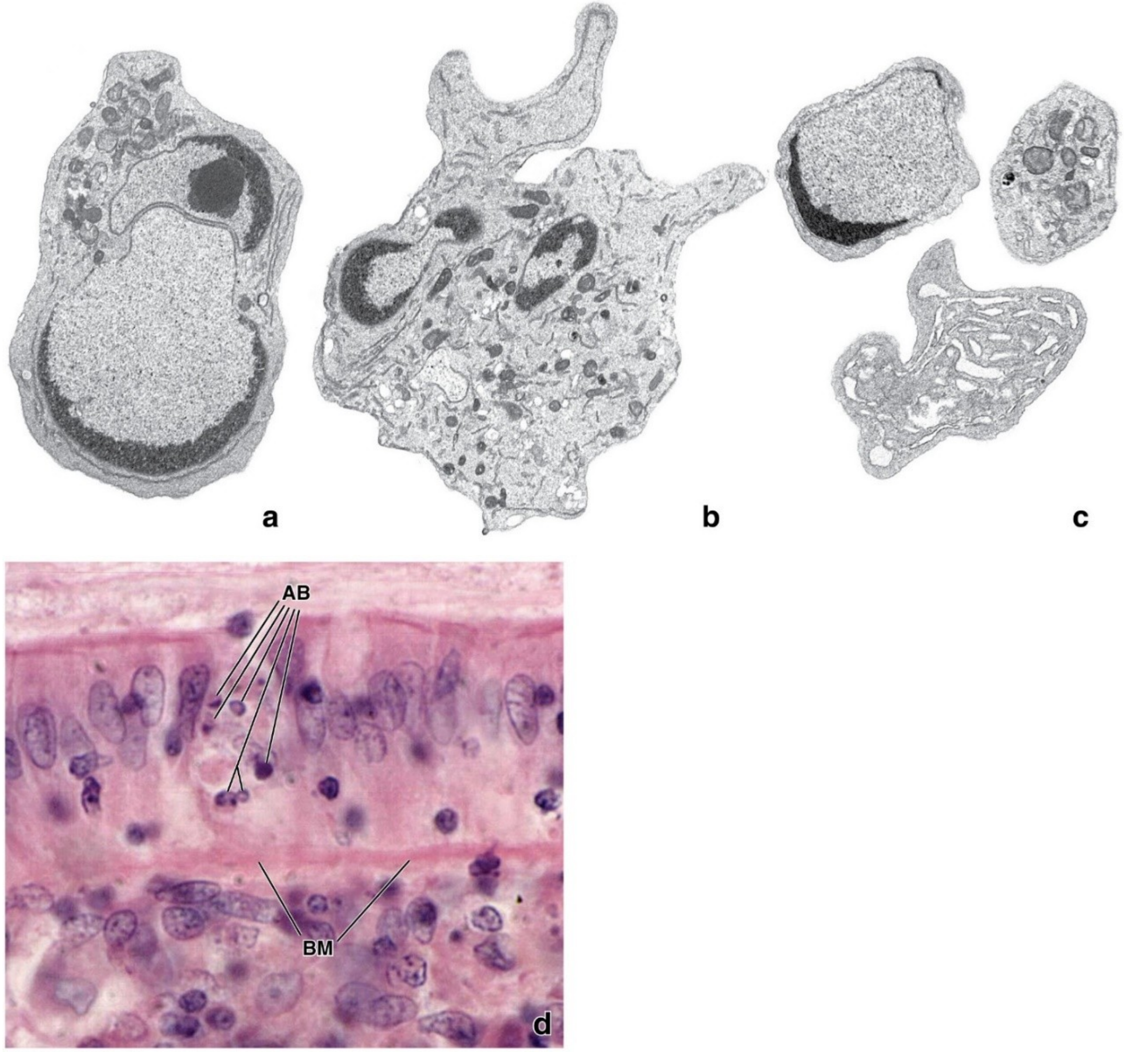
Apoptosis vs Necrosis

- In **necrosis** (*left side*), breakdown of the cell membrane results in an influx of water and extracellular ions, causing the organelles to undergo irreversible changes. Lysosomal enzymes are released into the extracellular space, causing damage to neighboring tissue and an intense inflammatory response.

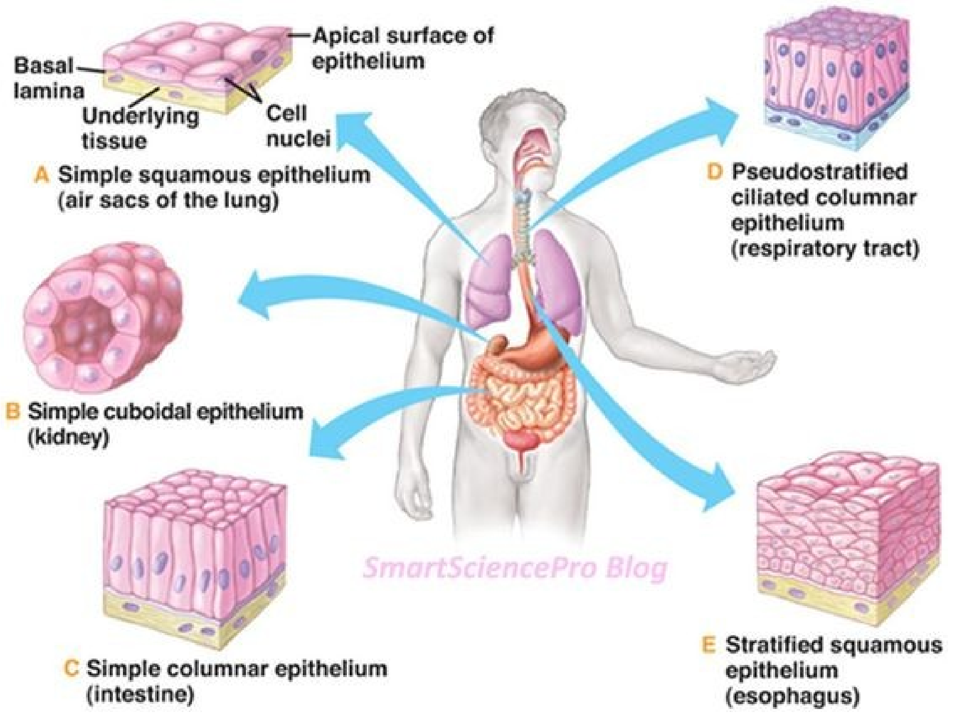
- In **apoptosis** (*right side*), the cell shows characteristic morphologic and biochemical features such as DNA fragmentation, decrease in cell volume, membrane blebbing without loss of membrane integrity, and formation of apoptotic bodies, causing cell breakage. Apoptotic bodies are later removed by phagocytotic cells without inflammatory reactions.



Electron micrographs of apoptotic cells



a. The nucleus is already fragmented, and the irreversible process of DNA fragmentation is turned on. Note the regions containing condensed heterochromatin adjacent to the nuclear envelope.
b. Further fragmentation of DNA.
c. Apoptotic bodies
d. This photomicrograph taken with light microscopy of intestinal epithelium from the human colon shows apoptotic bodies (*AB*) within a single layer of absorptive cells. *BM*, basement membrane



Radhika Reddy, PhD

CHAPTER 4-7: EPITHELIAL, CONNECTIVE, ADIPOSE, CARTILAGE

Tissues

Cells work together in functionally related groups called tissues

Types of tissues:

1. Epithelial – lining and covering
2. Connective – support
3. Muscle – movement
4. Nervous – control

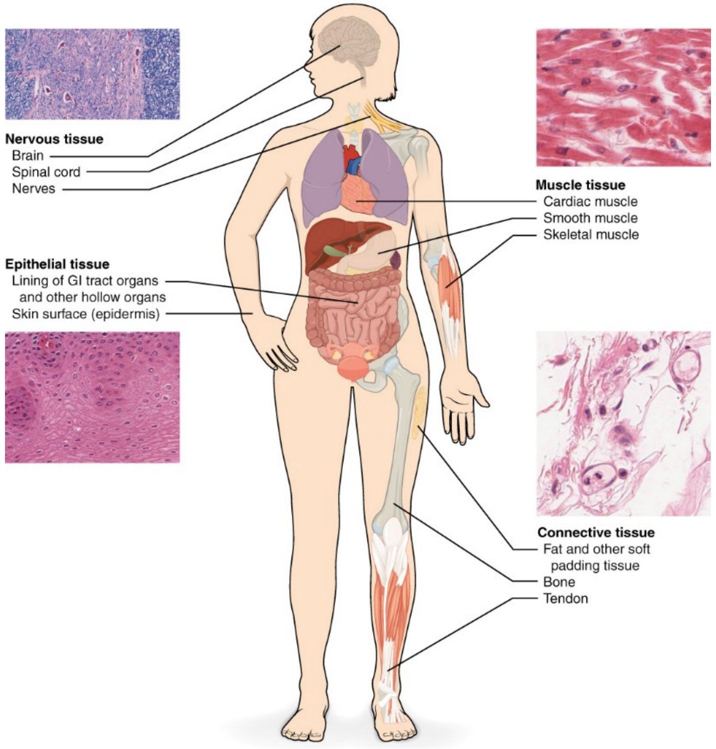
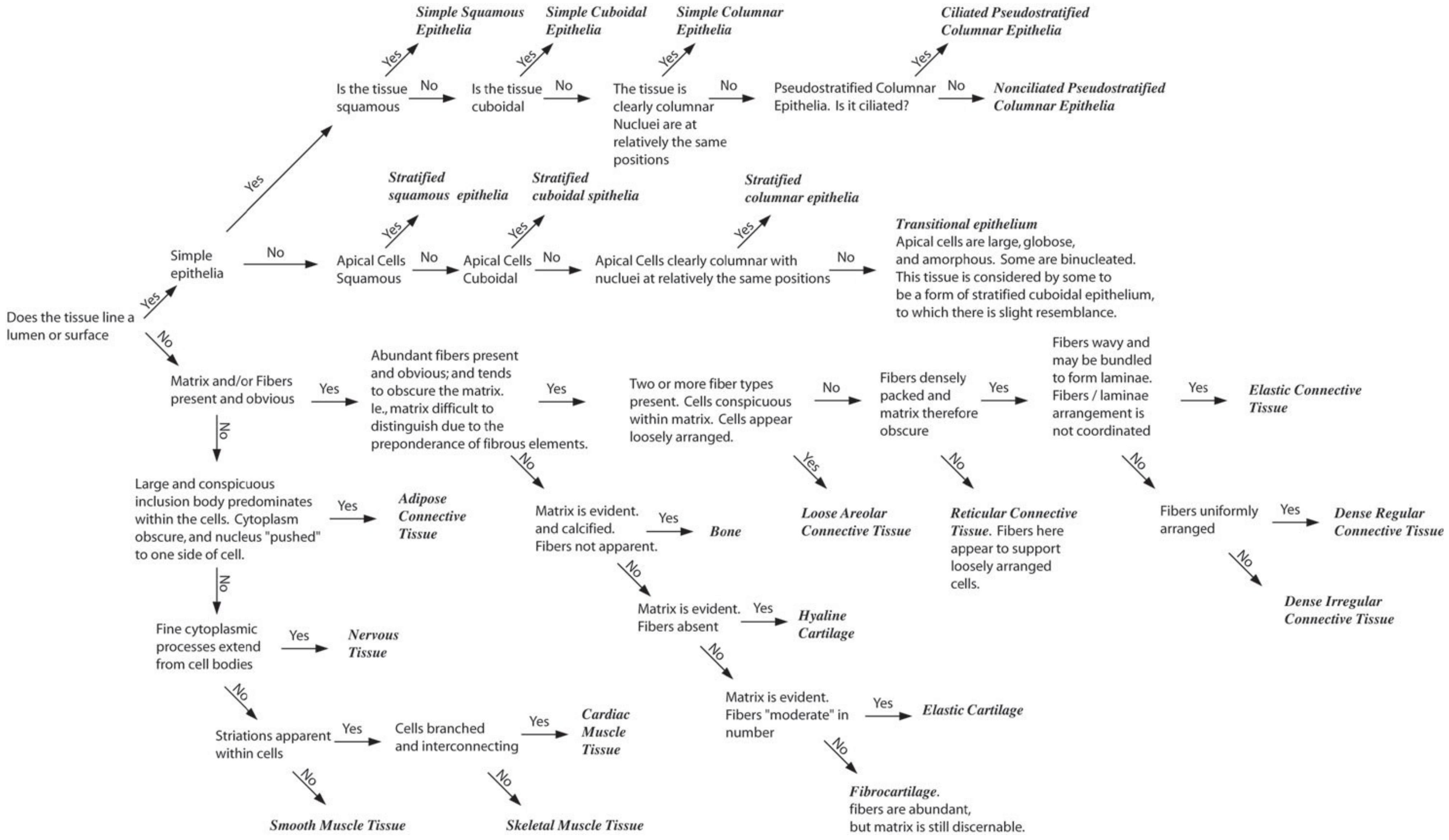


TABLE 4–1 Main characteristics of the four basic types of tissues.

Tissue	Cells	Extracellular Matrix	Main Functions
Nervous	Elongated cells with extremely fine processes	Very small amount	Transmission of nerve impulses
Epithelial	Aggregated polyhedral cells	Small amount	Lining of surface or body cavities; glandular secretion
Muscle	Elongated contractile cells	Moderate amount	Strong contraction; body movements
Connective	Several types of fixed and wandering cells	Abundant amount	Support and protection of tissues/ organs

http://www.bozemanscience.com/anatomy-and-physiology-introduction

Watch 3:25-9:25



Help with Histology: https://www.youtube.com/watch?v=ux9rvC5NvQ8

Chapter 4 Epithelial Tissues Objectives

1. General Characteristics of epithelium
2. Basal domain: basement membrane, basal lamina, focal adhesions, hemidesmosomes
3. Lateral Domain: cell junctions and adhesions
4. Apical domain: microvilli and cilia
5. Glands: exocrine and endocrine
6. Classification of epithelium based on shape and complexity

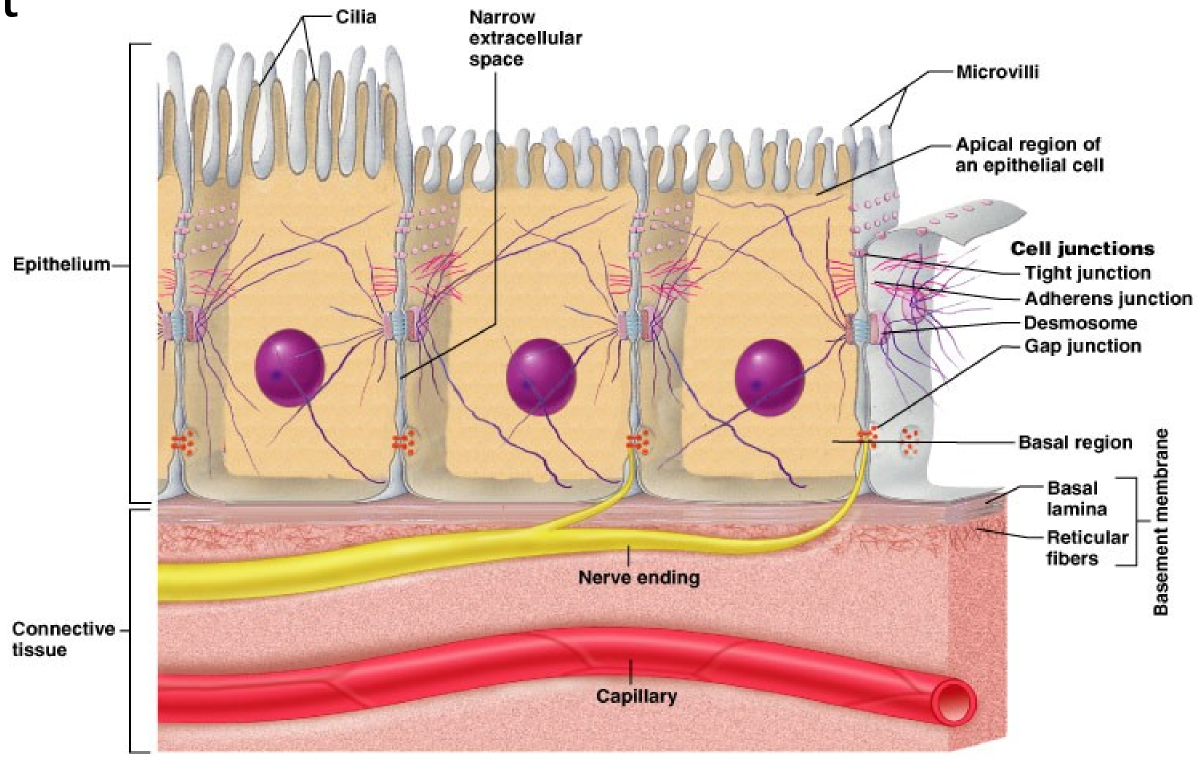
Epithelial Tissue: General Characteristics & Functions

Covers a body surface or lines a body cavity

Forms most glands

Functions of epithelium

1. Protection
2. Absorption, secretion, and ion transport
3. Filtration
4. Forms slippery surfaces



Special Characteristics of Epithelia

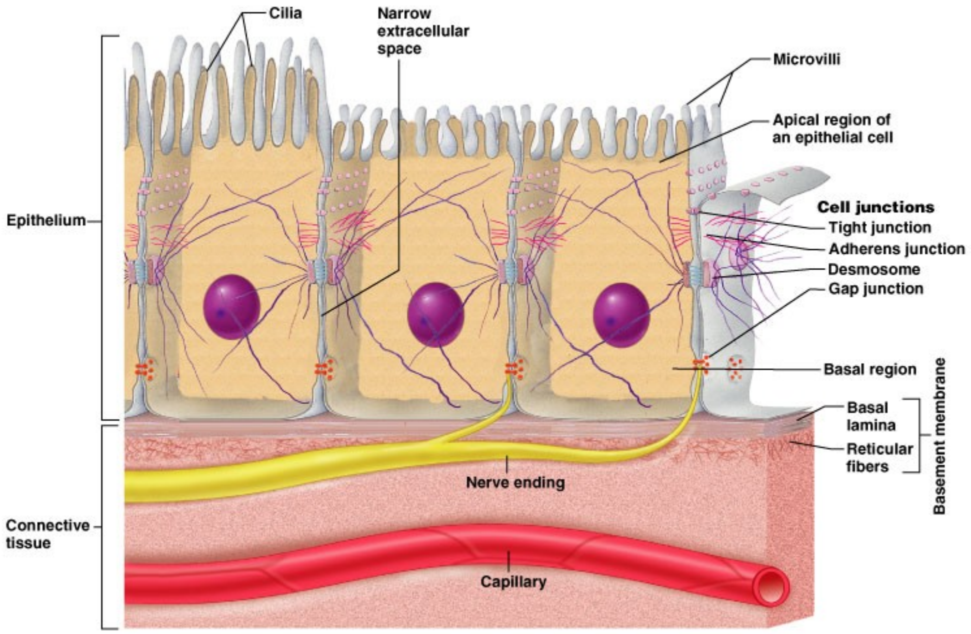
Cellularity: cells are in close contact with each other with little or no intercellular space between them
Specialized contacts: may have junctions for both attachment and communication
Polarity: epithelial tissues always have an **apical** and **basal surface**

Support by connective tissue: at the basal surface, both the epithelial tissue and the connective tissue contribute to the **basement membrane**

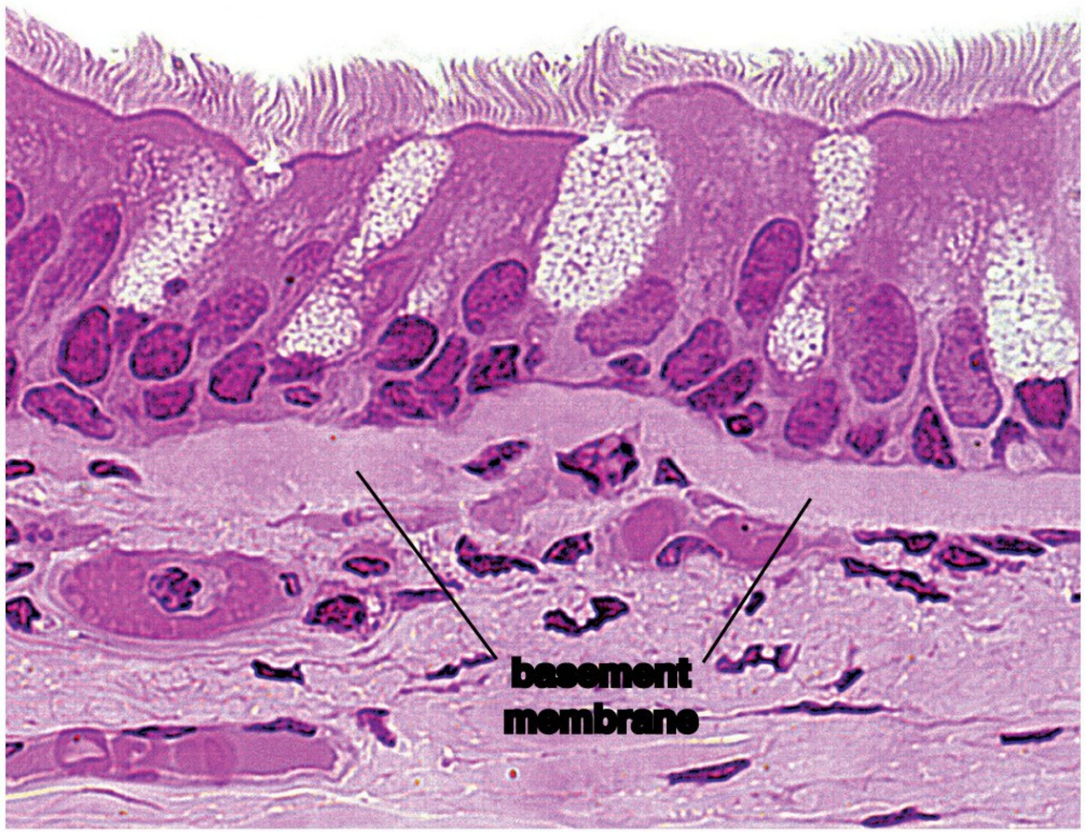
Avascular: nutrients must diffuse

Innervated

Regeneration: epithelial tissues have a high capacity for regeneration



The basal domain of epithelial cells



The **basement membrane** is a specialized structure located next to the basal domain of epithelial cells and the underlying connective tissue stroma.

Cell-to-extracellular matrix junctions anchor the cell to the extracellular matrix

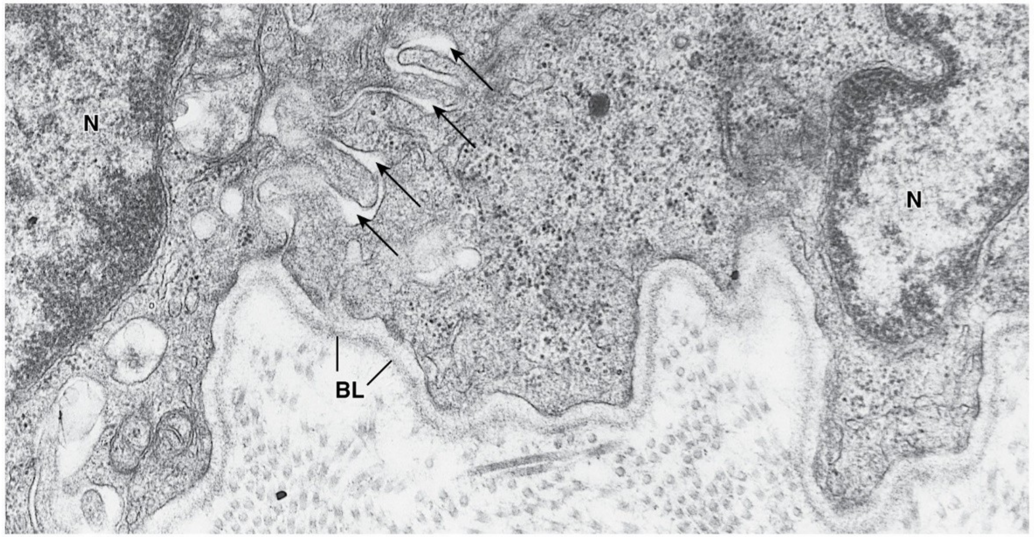
Basal cell membrane infoldings increase the cell surface area and facilitate morphologic interactions between adjacent cells and extracellular matrix proteins

Basement Membrane = basal lamina + reticular lamina

Basal lamina (also called **lamina densa**): discrete layer of electron-dense matrix material 40- to 60-nm thick between the epithelium and the adjacent connective tissue

Composed of **laminins**, a **type IV collagen molecule**, and various associated **proteoglycans** and **glycoproteins**.

Reticular lamina: below basal lamina, more diffuse and fibrous



Nutrient Absorption in Small Intestine: https://www.youtube.com/watch?v=P1sDOJM65Bc

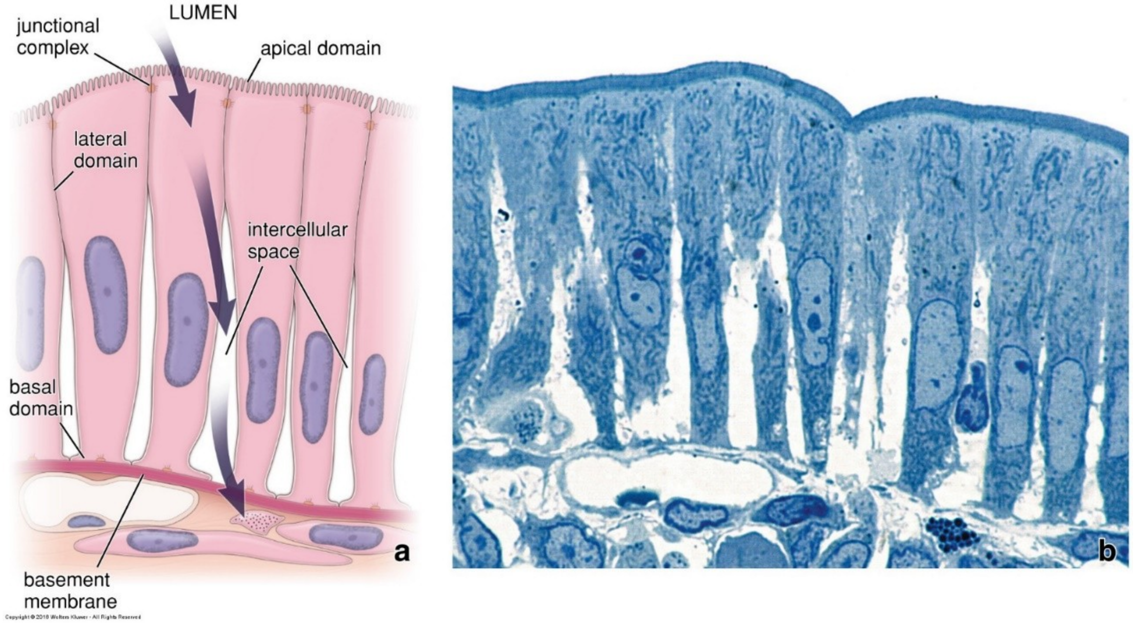
Cellular domains of epithelia

The **junctional complex** provides adhesion between adjoining cells and separates the luminal space from the intercellular space, limiting the movement of fluid between the lumen and the underlying connective tissue.

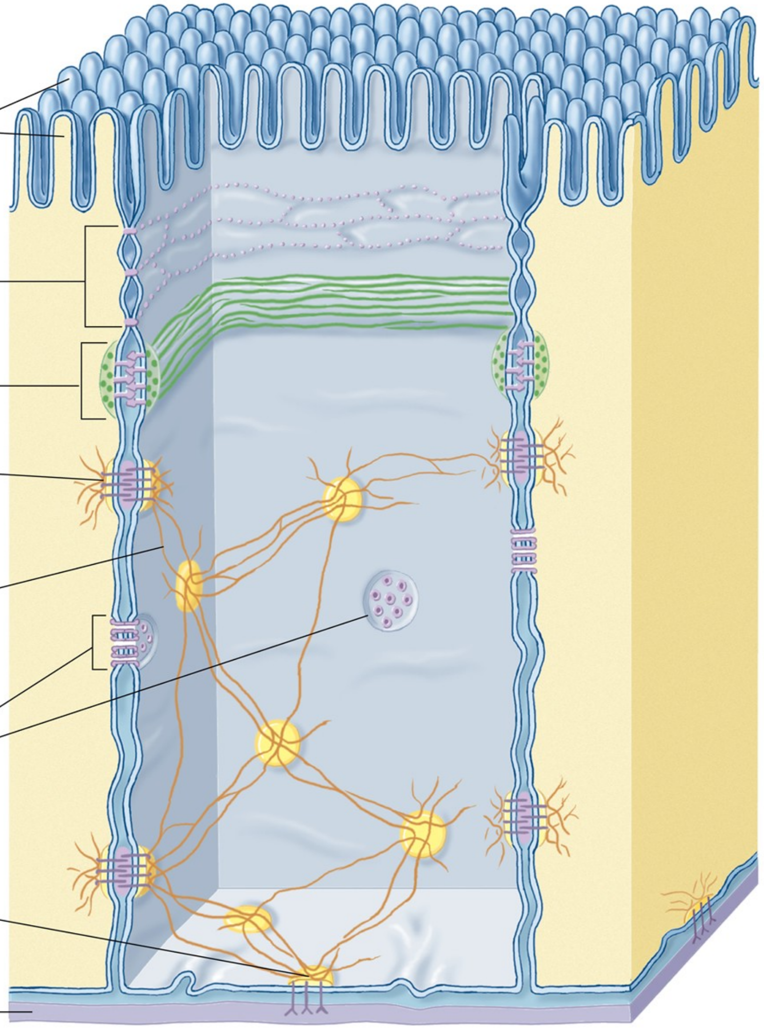
The **intracellular pathway** of fluid movement during absorption (*arrows*) is from the intestinal lumen into the cell, then across the lateral cell membrane into the intercellular space, and, finally, across the basement membrane to the connective tissue

❯❯ **MEDICAL APPLICATION**

The enterotoxin secreted by *Clostridium perfringens*, which causes “food poisoning prevents maintenance of tight junctions, and causes loss of tissue fluid into the intestinal lumen via the intracellular pathway.



Junctional complexes of epithelial cells.



Tight Junctions: prevent passive flow of material between the cells

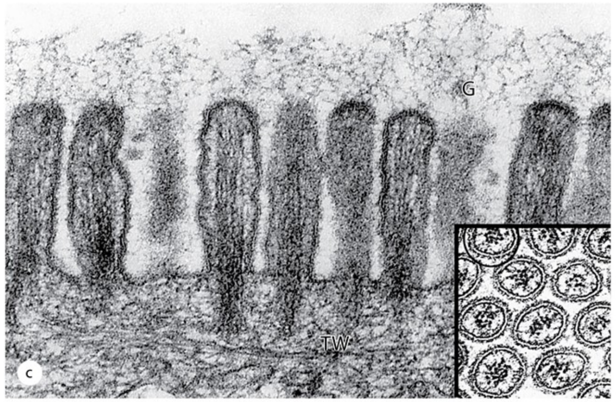
Adhering junctions: stabilize and strengthen the circular

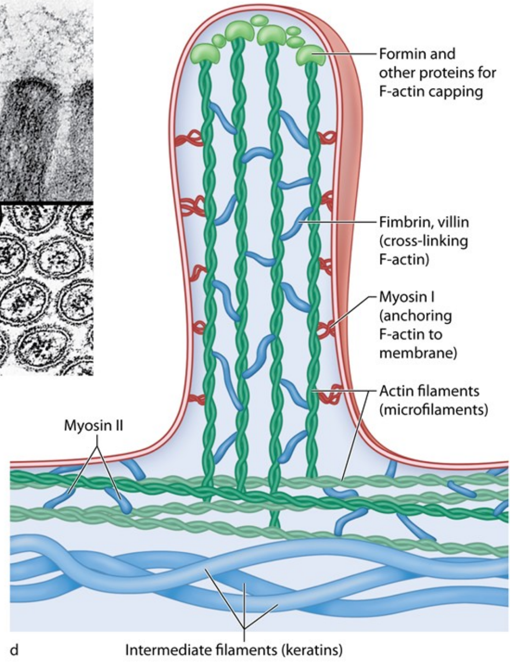
Desmosomes: form very strong attachment points, play a major role to maintain the integrity of an epithelium.

Gap junctions: patch of many **connexons**, serve as intercellular channels for flow of molecules.

Hemidesmosomes bind epithelial cells to the underlying basal lamina

Microvilli are fingerlike cytoplasmic projections on the apical surface of most epithelial cells.





The internal structure of microvilli contains a core of actin filaments that are cross-linked by several actin bundling proteins. Actin filaments (*arrows)*

Actin filament–bundling proteins: fimbrin, espin, and fascin

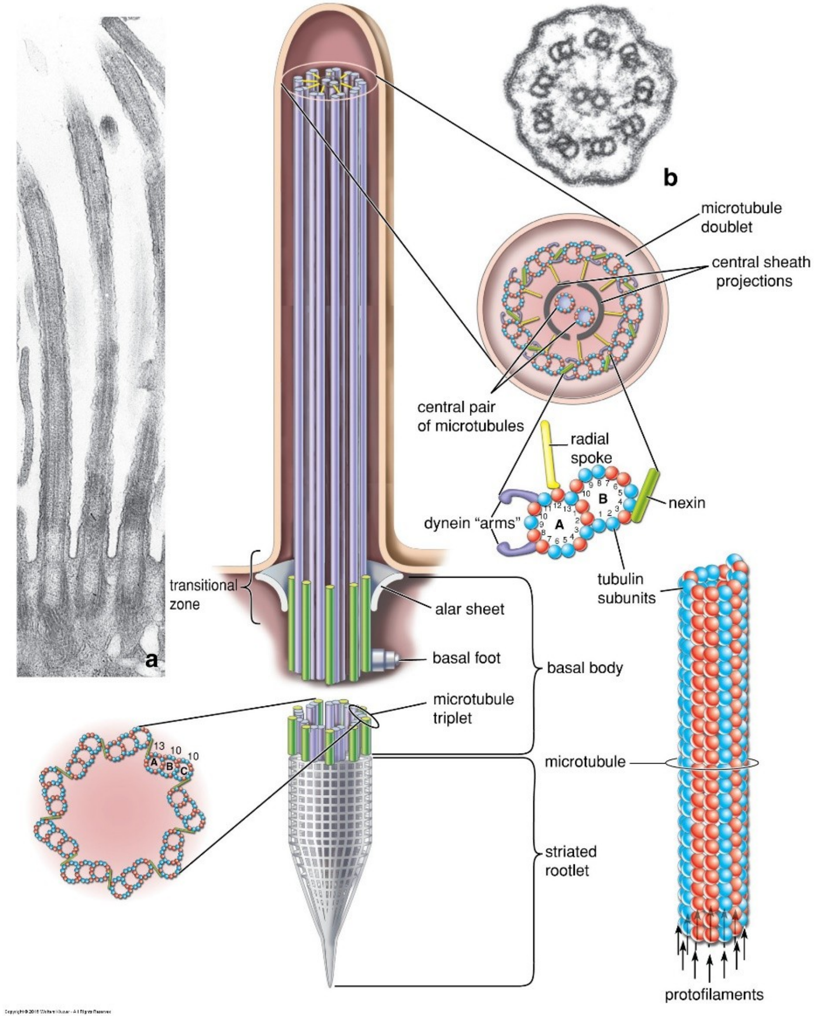
The spectrin molecules stabilize the actin filaments within the terminal web and anchor them into the apical plasma membrane.

Endoscopy of Celiac Disease (0-1:00): https://www.youtube.com/watch?v=WStdJSgf-LQ

❯❯ MEDICAL APPLICATION

Celiac disease: loss of microvilli in brush border of the absorptive cells of small intestine, caused by immune reaction against the wheat protein gluten during its digestion, which produces diffuse enteritis (intestinal inflammation), changes to the epithelial cells leading to malabsorption, and eventually to pathologic changes in the intestinal wall.

Cilia are long projecting structures, larger than microvilli, which contain internal arrays of microtubules



Epithelial cilia exhibit rapid beating patterns of movement
that propel a current of fluid and suspended matter in one
direction over the epithelium

Axoneme: The nine doublets form an array around two central microtubules; the 9 + 2 assembly of microtubules

Primary Ciliary Dyskinesia (Immotile Cilia Syndrome)

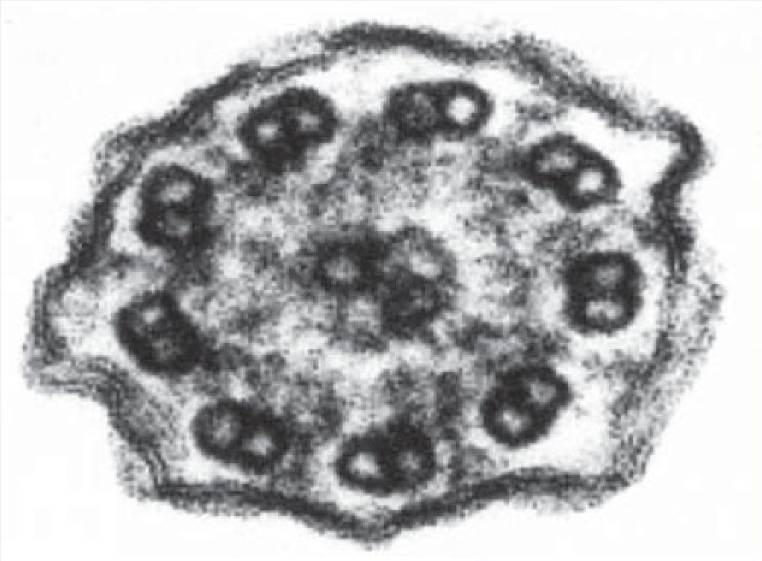
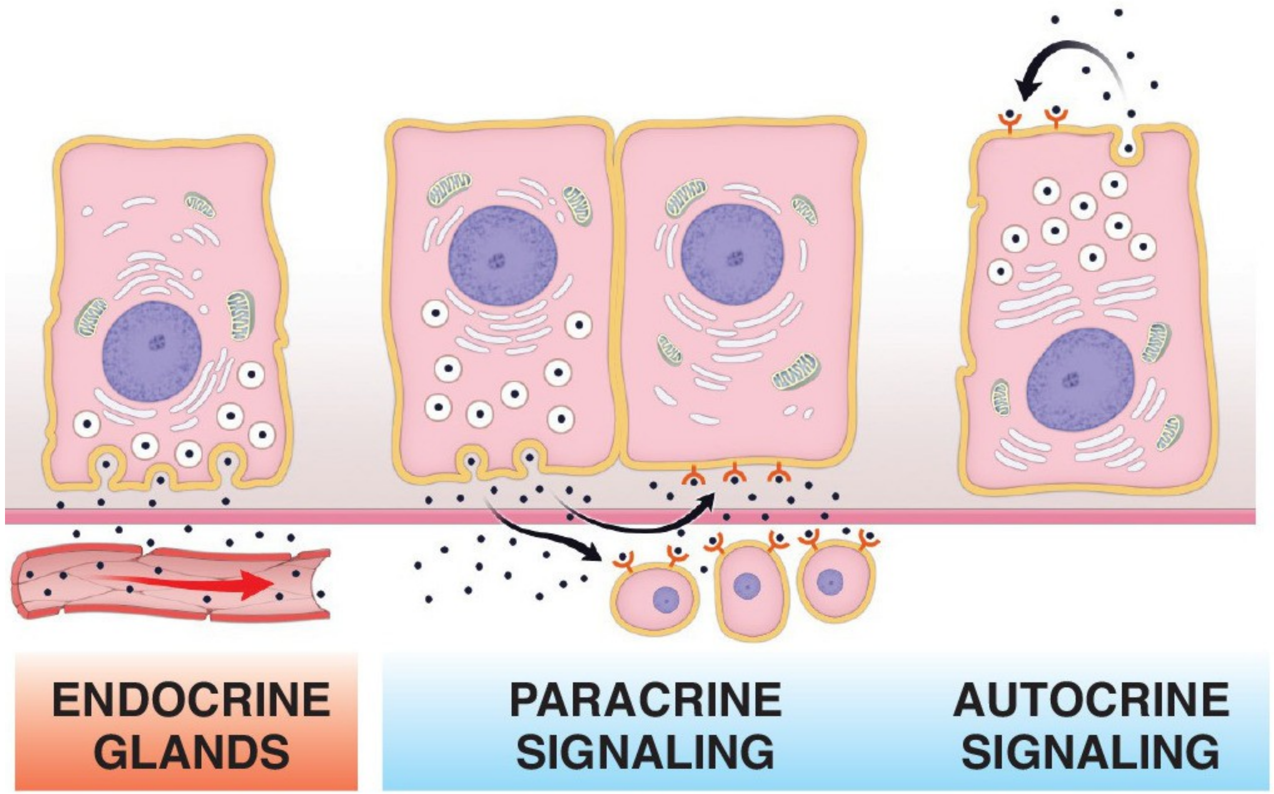


FIGURE F5.2.1 • **Electron micrograph of the cilium from an individual with primary cilary dyskinesia (PCD).** Note the absence of dynein arms on microtubule doublets. ×180,000. (Courtesy of Patrice Abell-Aleff.)

MEDICAL APPLICATION

Kartagener syndrome: muations in proteins of cilia, whose symptoms are chronic respiratory infections caused by the lack of the cleansing action of cilia in the respiratory tract and immotile spermatozoa, causing male infertility

Types of glands and their mechanism of secretion



Endocrine glands lack a duct system. They secrete their products into the connective tissue, from which they enter the bloodstream to reach their target cells. The products of endocrine glands are called **hormones**.

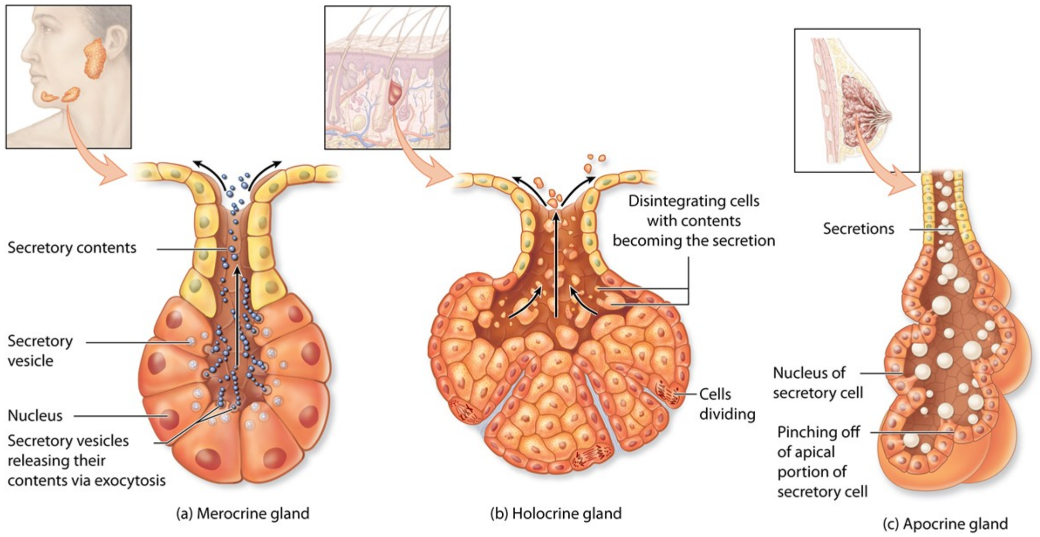
Types of glands and their mechanism of secretion

Exocrine glands secrete their products onto a surface directly or through epithelial ducts or tubes that are connected to a surface.

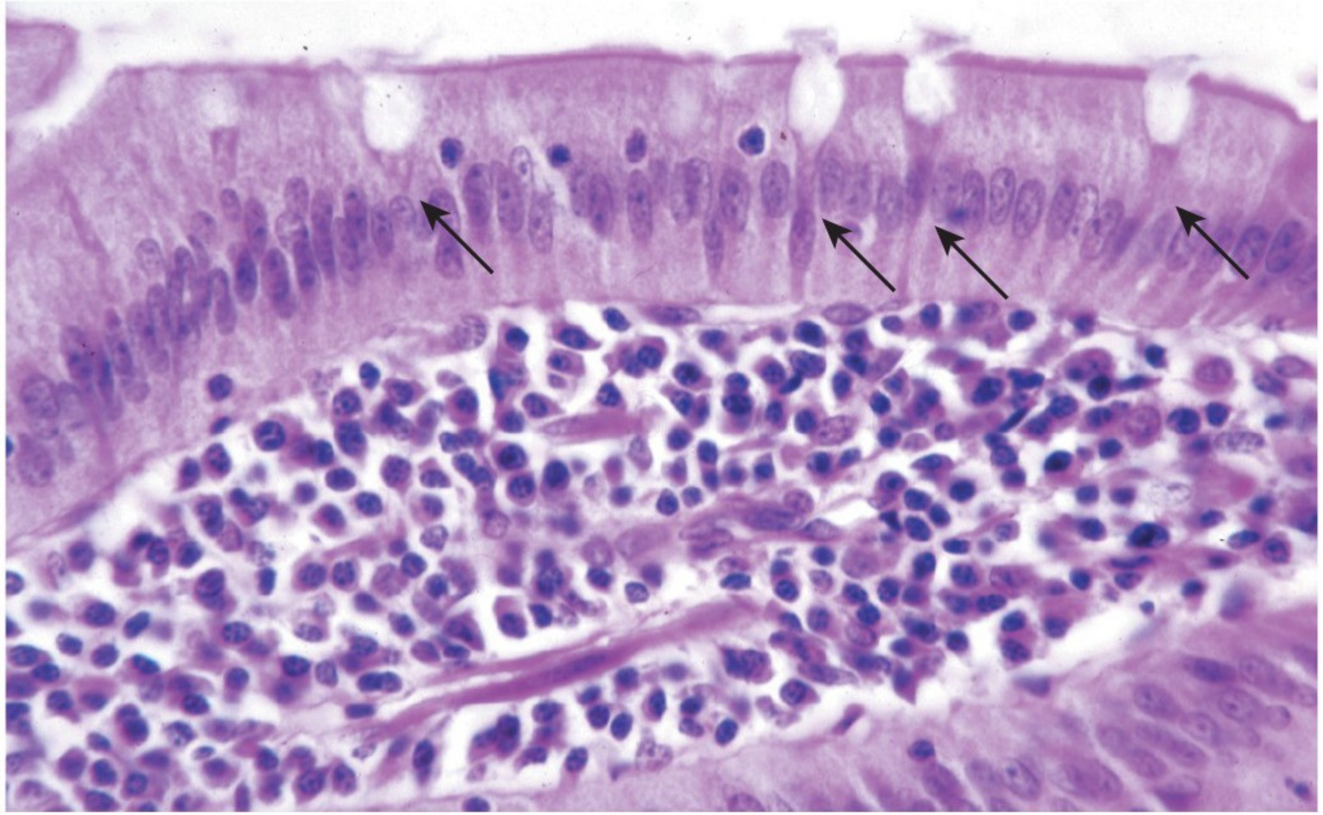
Merocrine secretion. This secretory product is delivered in **membrane-bounded vesicles** to the apical surface of the cell and extrude their contents by exocytosis.

Apocrine secretion. The secretory product is released in the apical portion of the cell, surrounded by a thin layer of cytoplasm within an envelope of plasma membrane. Ex **mammary gland**, where it is responsible for releasing large lipid droplets into the milk. It also occurs in the **apocrine glands** of skin, **ciliary (Moll's) glands** of the eyelid, and the **ceruminous glands** of the external auditory meatus.

Holocrine secretion. **Programmed cell death**. Both secretory products and cell debris are discharged into the lumen of the gland. This mechanism is found in sebaceous glands of skin and the tarsal (Meibomian) glands of the eyelid.



Unicellular glands



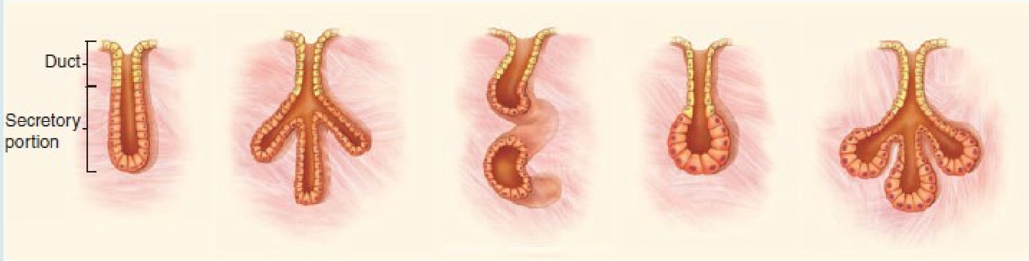
Unicellular glands. Photomicrograph of intestinal epithelium showing single goblet cells (*arrows*) dispersed among absorptive cells. Each goblet cell may be regarded as a unicellular gland—the simplest exocrine type gland.

❯❯ MEDICAL APPLICATION

In chronic bronchitis, common among habitual smokers, the number of goblet cells in the lining of airways in the lungs often increases greatly. This leads to excessive mucus production in areas where there are too few ciliated cells for its rapid removal and contributes to obstruction of the airways. The ciliated pseudostratified epithelium lining the bronchi of smokers can also be transformed into stratified squamous epithelium by metaplasia.

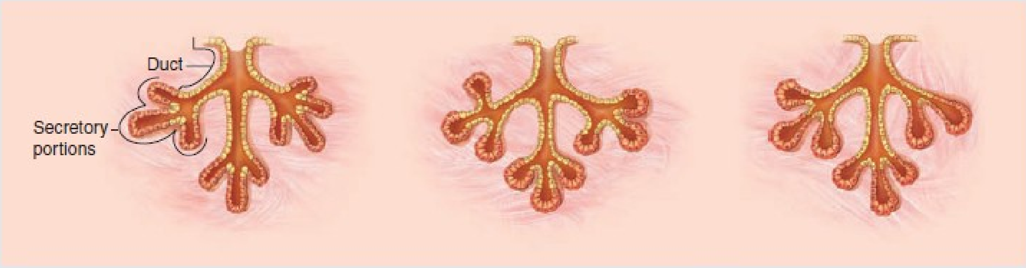
TABLE 4–4 Structural classes of exocrine glands, features of each class, and examples.

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



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

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



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

Multicellular glands subclassification according to the arrangement of the secretory cells (parenchyma) and the presence or absence of branching of the duct elements.

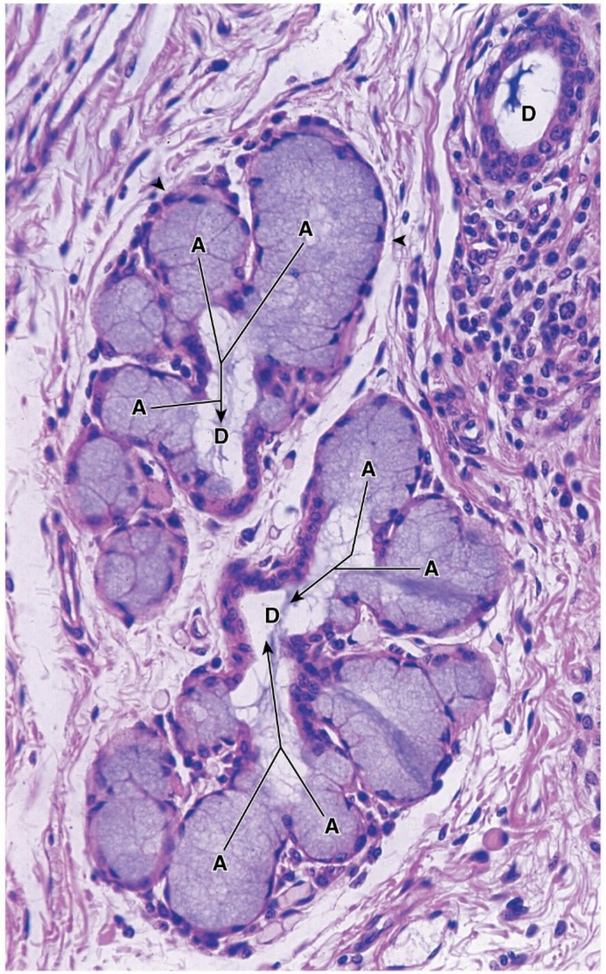
MEDICAL APPLICATION: Acne Excessive holocrine secretion of sebum and keratin triggered by the surge of the steroid hormone testosterone. Activity of the normal commensal skin bacterium *Propionibacterium acnes* within the blocked duct commonly produces localized inflammation.

Is There A Pimple Cure? https://www.youtube.com/watch?v=CGvx4gl3D7w

Mucus-secreting surface cells of stomach.

Mucus-secreting surface cells of stomach. Photomicrograph of stomach surface. The epithelial cells lining the surface are all mucus-secreting cells, as are the cells lining the gastric pits (*P*). The cells of the gastric pit form simple tubular glands.

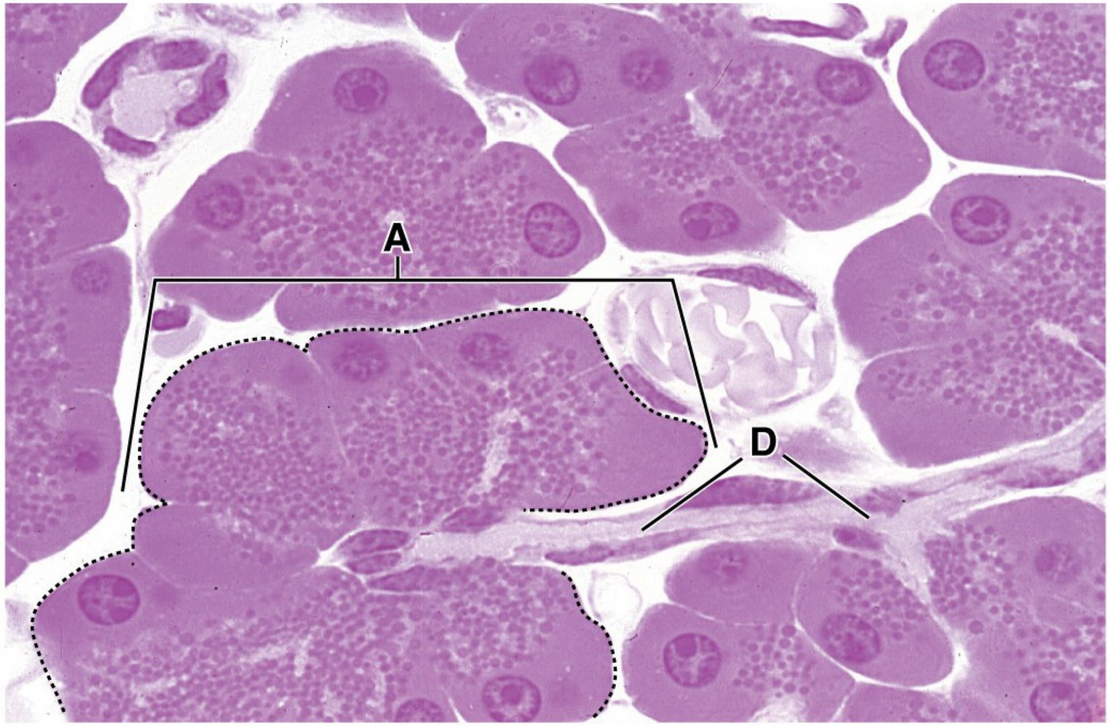
Mucus-secreting compound gland



Mucus-secreting compound gland. Photomicro - graph showing two small lobes of a mucus-secreting gland associated with the larynx. Each displays the beginning of a duct (*D*) into which mucin is secreted (*arrows*). The individual secretory cells that form the acinus (*A*) are difficult to define. Their nuclei (*arrowheads*) are flattened and located in the very basal portion of the cell, a feature typical of mucus-secreting glands.

The cytoplasm is filled with mucin that has been retained during preparation of the tissue and appears stained

Serous-secreting compound gland

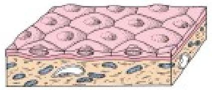
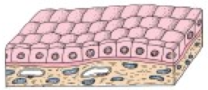
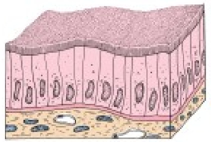
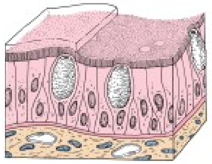
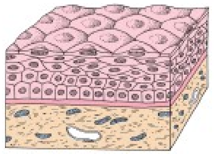
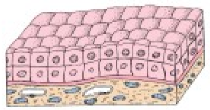
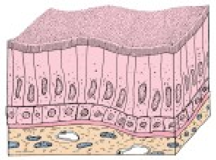
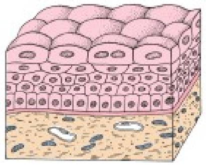


Serous-secreting compound gland. Photomicrograph of pancreatic acinus (*A;* outlined by the *dotted line*) with its duct (*D*). The small round objects within the acinar cells represent the zymogen granules, the stored secretory precursor material.

Classification

The traditional classification of epithelium is descriptive and based on two factors: the number of cell layers and the shape of the surface cells. The terminology, therefore, reflects only structure, not function.

TABLE 5.1 Types of Epithelium

	Classification	Some Typical Locations	Major Function
	Simple squamous	Vascular system (endothelium) Body cavities (mesothelium) Bowman's capsule (kidney) Respiratory spaces in lung	Exchange, barrier in central nervous system Exchange and lubrication Barrier Exchange
	Simple cuboidal	Small ducts of exocrine glands Surface of ovary (germinal epithelium) Kidney tubules Thyroid follicles	Absorption, conduit Barrier Absorption and secretion
	Simple columnar	Small intestine and colon Stomach lining and gastric glands Gallbladder	Absorption and secretion Secretion Absorption
	Pseudostratified	Trachea and bronchial tree Ductus deferens Efferent ductules of epididymis	Secretion, conduit Absorption, conduit
	Stratified squamous	Epidermis Oral cavity and esophagus Vagina	Barrier, protection
	Stratified cuboidal	Sweat gland ducts Large ducts of exocrine glands Anorectal junction	Barrier, conduit
	Stratified columnar	Largest ducts of exocrine glands Anorectal junction	Barrier, conduit
	Transitional (urothelium)	Renal calyces Ureters Bladder Urethra	Barrier, distensible property

Epithelial metaplasia is a reversible conversion of one mature epithelial cell type to another mature epithelial cell type.

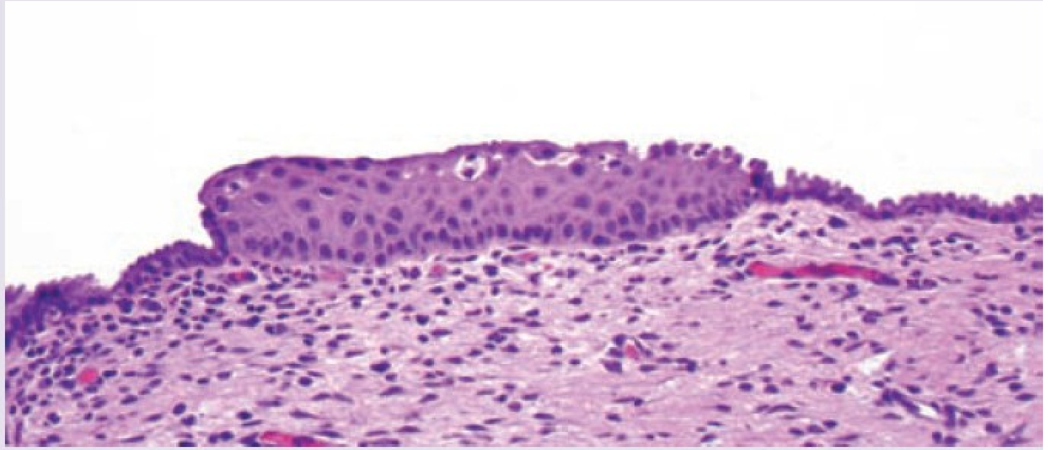


FIGURE F5.1.1 • **Squamous metaplasia of the uterine cervix.** Photomicrograph of a cervical canal lined by simple columnar epithelium. Note that the center of the image is occupied by an island containing squamous stratified epithelium. This metaplastic epithelium is surrounded on both sides by simple columnar epithelium. Since metaplasia is triggered by reprogramming of stem cells, metaplastic squamous cells have the same characteristics as normal stratified squamous epithelium. ×240. (Courtesy of Dr. Fabiola Medeiros.)

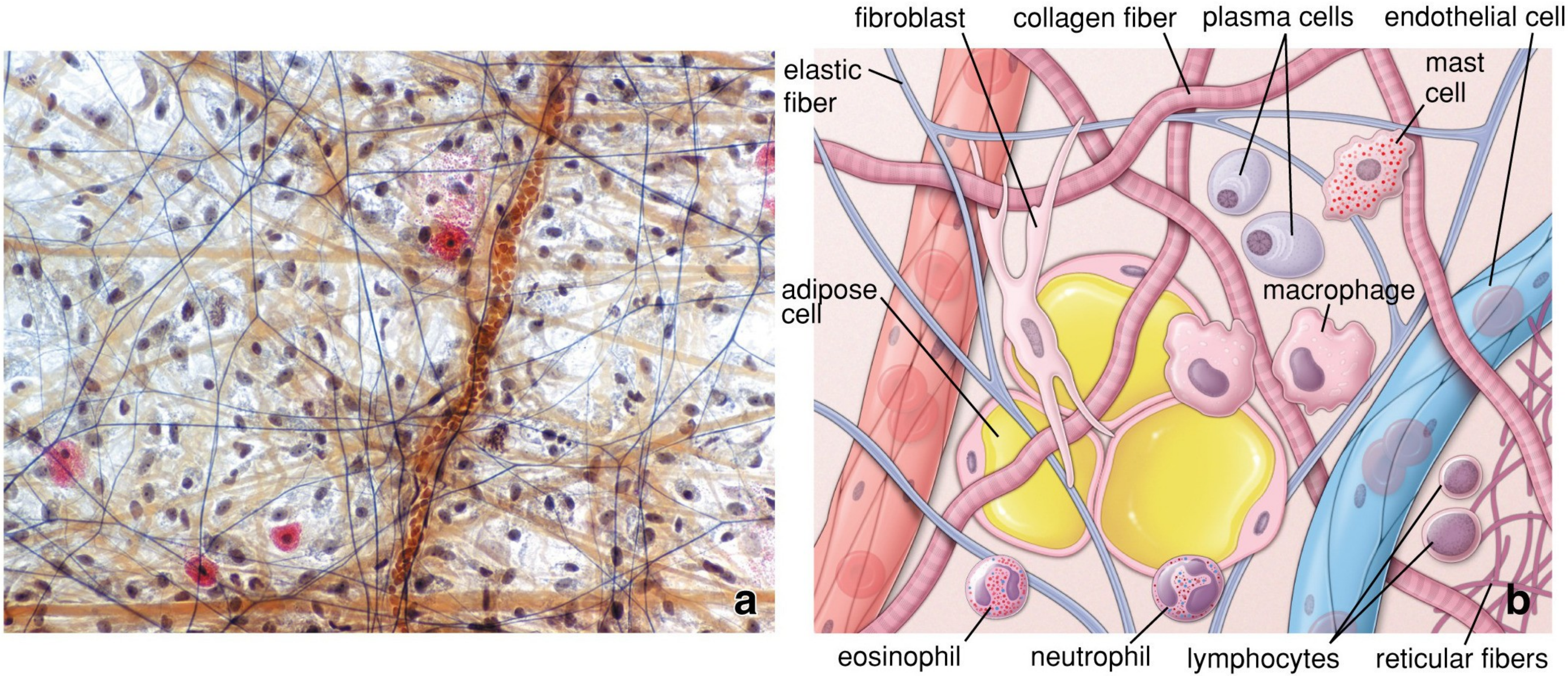
Cancers of the lung, cervix, and bladder often originate from squamous metaplastic epithelium. Squamous columnar epithelium may give rise to **glandular adenocarcinomas**.

When metaplasia is diagnosed, all efforts should be directed toward removing the pathogenic stimulus (i.e., cessation of smoking, eradication of infectious agents, etc.) and monitoring the metaplastic site to ensure that cancerous changes do not begin to develop.

Chapter 5 Connective Tissue Objectives

1. General properties of connective tissue: extracellular matrix, ground substance
2. Connective tissue cells: resident (fibroblasts, macrophages adipocytes, mast cells, stem cells) and wandering (lymphocytes, plasma cells, neutrophils, eosinophils, basophils, monocytes)
3. Connective tissue fibers: collagen, reticular, elastic
4. Extracellular matrix: proteoglycans, glycosaminoglycans, multiadhesive glycoproteins
5. Connective tissue proper: Loose, dense irregular, dense regular
6. Embryonic connective tissue: Mesenchyme, mucous connective tissue

Loose Connective Tissue: A prototype of cells, fibers, and ECM



Cells of Fibrous Connective Tissue

- **Fibroblasts** produce fibers and ground substance
- **Macrophages** phagocytize foreign material and activate immune system when they sense foreign matter (antigen)
  - Arise from white blood cells called monocytes
- **Leukocytes**, or white blood cells
  - Neutrophils wander about attacking bacteria
  - Lymphocytes react against bacteria, toxins, and other foreign material
- **Plasma cells** synthesize disease-fighting antibodies
  - Arise from lymphocytes
- **Mast cells** are found alongside blood vessels
  - Secrete heparin to inhibit clotting
  - Secrete histamine to dilate blood vessels
- **Adipocytes** store triglycerides (fat molecules)

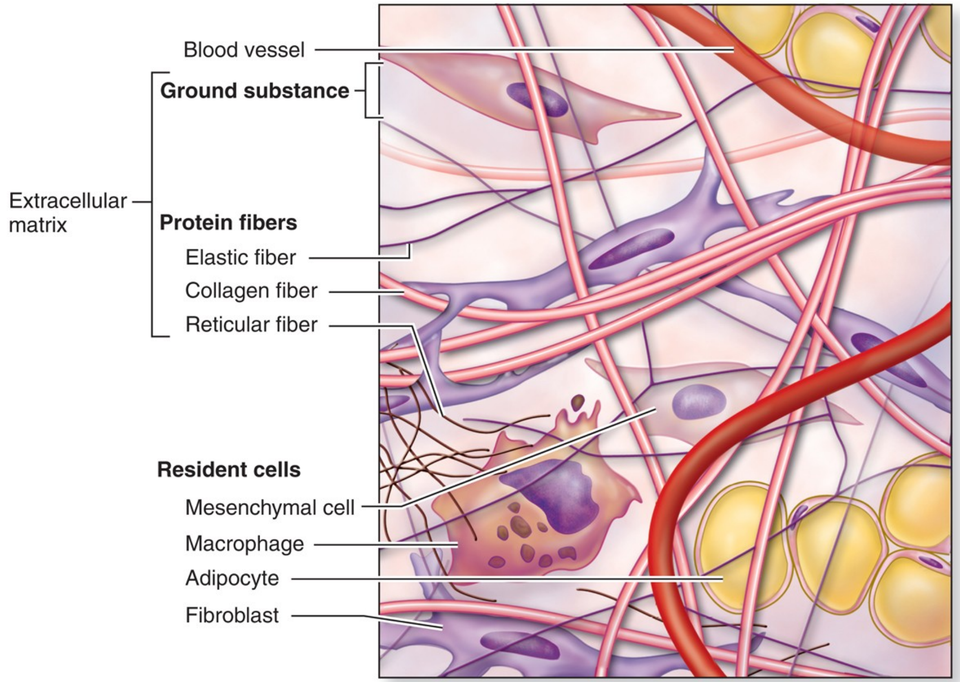
Connective tissue cells can be resident or wandering.

Resident cell population are relatively stable; they typically exhibit little movement and can be regarded as permanent residents of the tissue.

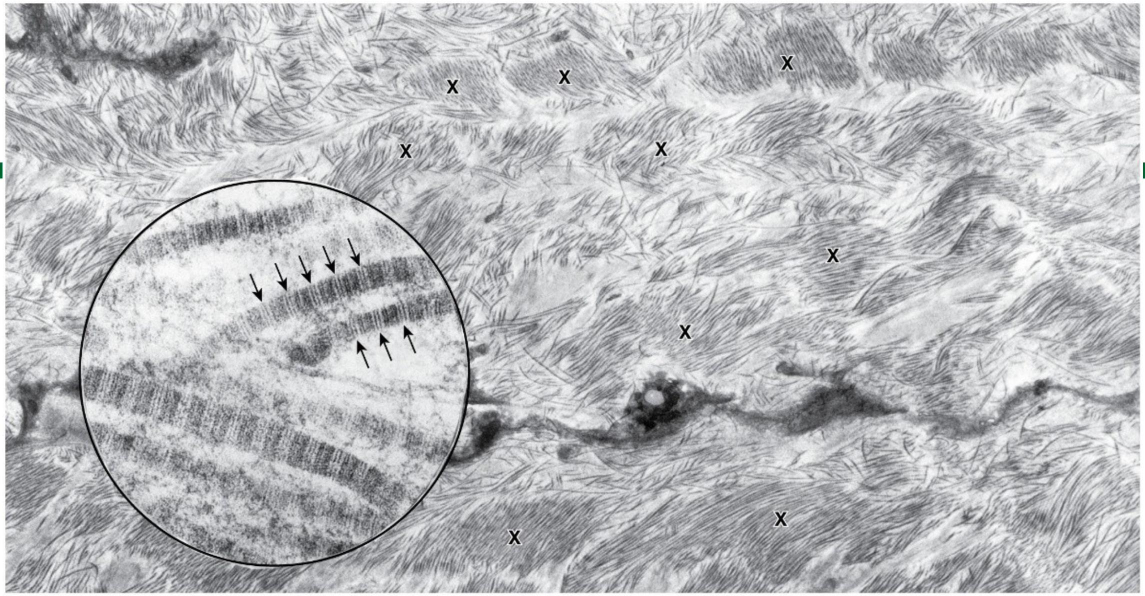
- **fibroblasts** and a closely related cell type, the **myofibroblast**
- **macrophages**
- **adipocytes**
- **mast cells**
- **adult stem cells**.

Wandering cell population or **transient cell population:** cells that have migrated into the tissue from the blood in response to specific stimuli.

- **lymphocytes**
- **plasma cells**
- **neutrophils**
- **eosinophils**
- **basophils**



Connective Tissue Fibers



Electron micrograph of dense irregular connective tissue from the capsule of the testis of a young male. The threadlike collagen fibrils are aggregated in some areas (*X*) to form relatively thick bundles; in other areas, the fibrils are more dispersed

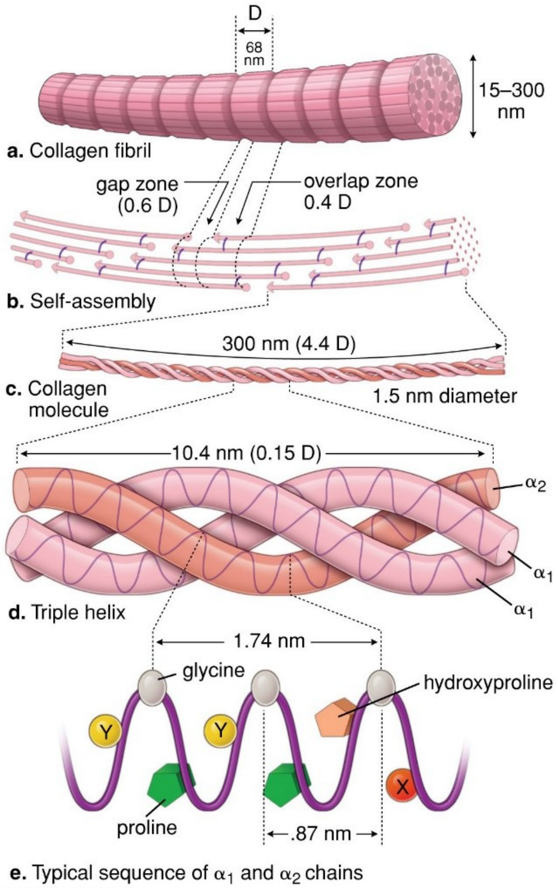
Inset. A longitudinal array of collagen fibrils from the same specimen seen at higher magnification. Note the banding pattern. The spacing of the arrows indicates the 68-nm repeat pattern.

- Connective tissue fibers are present in varying amounts, depending on the structural needs or function of the connective tissue.
- Produced by fibroblasts
- Composed of protein consisting of long peptide chains.
    - **Collagen fibers**
    - **Reticular fibers**
    - **Elastic fibers**

Fibers Fibrous Connective Tissue

- **Collagenous fibers**
  - Most abundant of the body's proteins—25%
  - Tough, flexible, and resist stretching
  - Tendons, ligaments, and deep layer of the skin are mostly collagen
  - Less visible in matrix of cartilage and bone
- **Reticular fibers**
  - Thin collagen fibers coated with glycoprotein
  - Form framework of such organs as spleen and lymph nodes
- **Elastic fibers**
  - Thinner than collagenous fibers
  - Branch and rejoin each other
  - Made of protein called elastin
  - Allows stretch and recoil
  - Yellow fibers—fresh elastic fibers

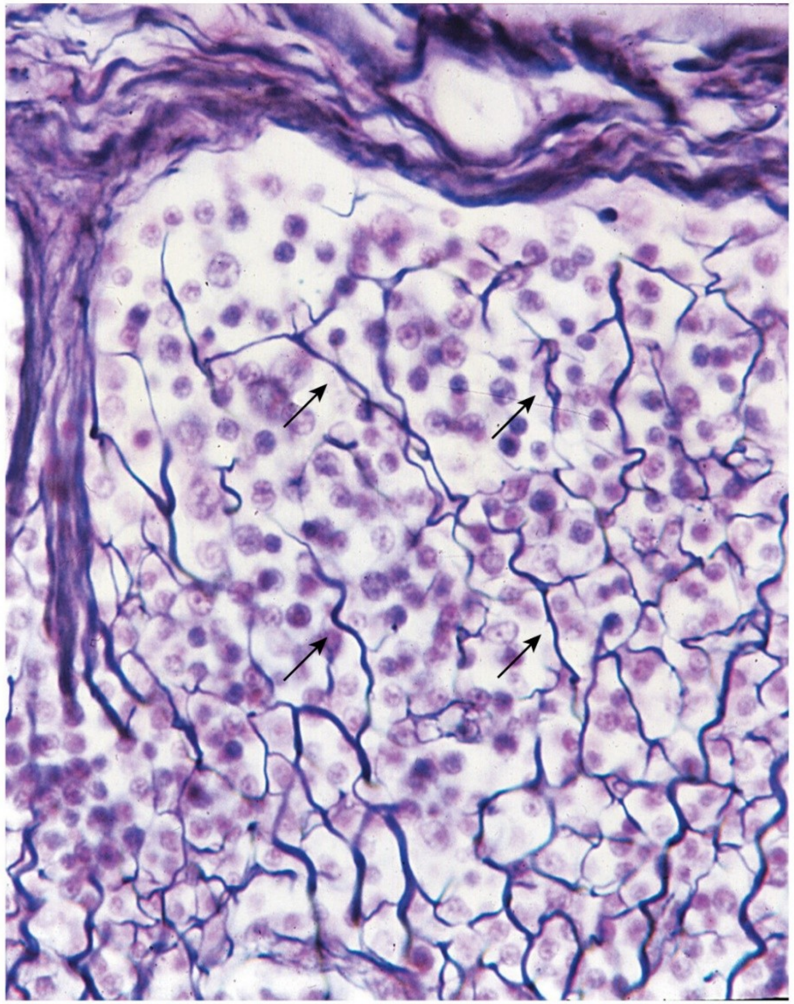
Collagen Fibrils in Dense Irregular CT



MEDICAL APPLICATION
A keloid is a local swelling caused by abnormally large amounts of collagen that form in scars of the skin.
Stretch marks

MEDICAL APPLICATION
Scurvy Lack of vitamin C, a required cofactor for collagen synthesis results in ulceration of gums, hemorrhages

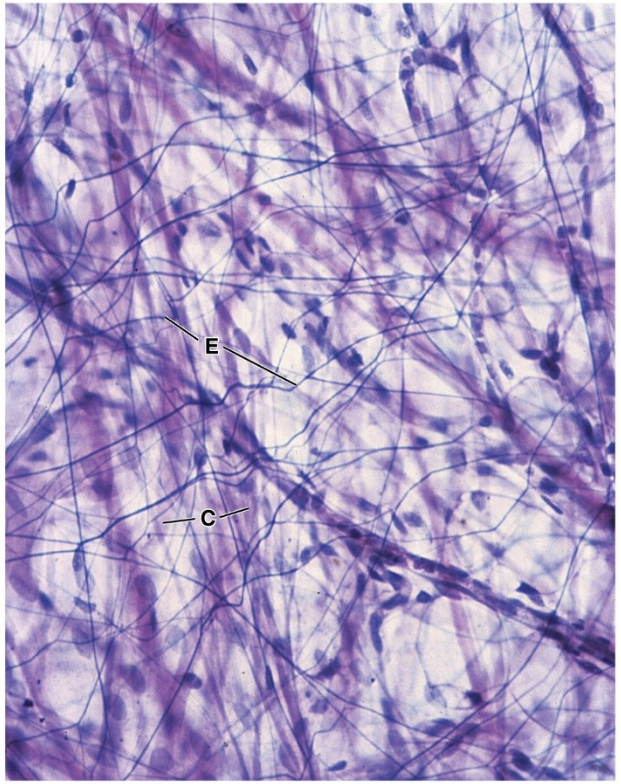
Reticular Fibers in the Lymph Node

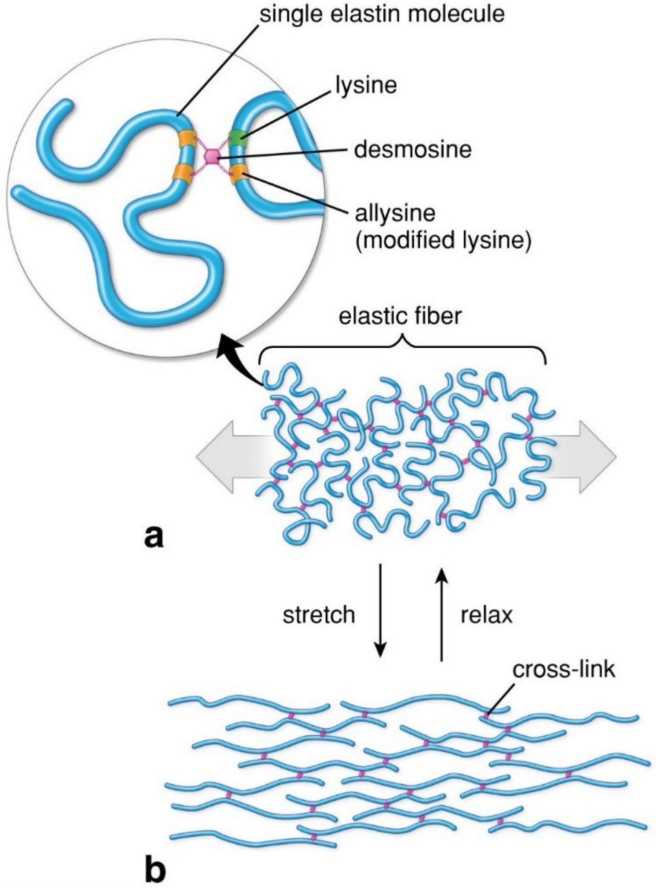


Reticular fibers exhibit a branching pattern, and typically do not bundle to form thick fibers

Photomicrograph of a lymph node silver preparation showing the connective tissue capsule at the top and a trabecula extending from it at the left. The reticular fibers (*arrows*) form an irregular anastomosing (connection of branching structures) network.

Elastic Fibers





Elastic fibers are typically thinner than collagen fibers, branching pattern. The fibers are interwoven with collagen fibers to limit the distensibility of the tissue and prevent tearing from excessive stretching

MEDICAL APPLICATION:
Mutations in the fibrillin genes result in **Marfan syndrome**, a disease characterized by a lack of resistance in tissues rich in elastic fibers. Because the walls of large arteries are rich in elastic components and because the blood pressure is high in the aorta, patients with this disease often experience aortic swellings called aneurysms, which are life-threatening conditions.

What Lincoln had: http://www.nature.com/news/2007/071130/full/news.2007.226.html

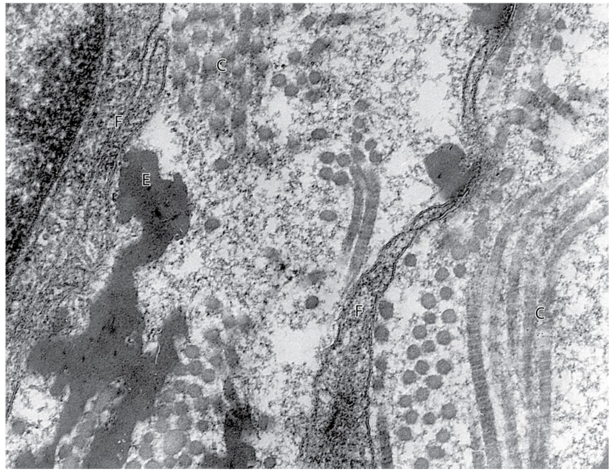
Clinical Correlation: Sun Exposure and Molecular Changes in Photoaged Skin

Chronological aging: changes in stratified squamous epithelium (epidermis) and connective tissue of the dermis.

Photoaging: Chronic sun exposure leads to decreased production of type I and type III collagen fibers

- Altered crosslinking that occurs between collagen molecules resulting in abnormal stability and decreased resistance to enzymatic degradation.
- number of abnormally thick and nonfunctional elastic fibers increases

Extracellular Matrix (ECM)



Ultrastructure of the extracellular matrix (ECM). TEM of the connective tissue ECM reveals ground substance as either empty or containing fine granular material that fills spaces between the collagen (**C**) and elastic (**E**) fibers and surrounds fibroblast cells and processes (**F**).

The **extracellular matrix (ECM)** structural network that surrounds and supports cells within the connective tissue.

ground substance:

- **proteoglycans** (e.g., aggrecan, syndecan)
- **multiadhesive glycoproteins** (such as fibronectin and laminin)
- **glycosaminoglycans** (e.g., dermatan sulfate, keratan sulfate, hyaluronan).

MEDICAL APPLICATION Edema is the excessive accumulation of water in the extracellular spaces of connective tissue. This water comes from the blood, passing through the capillary walls that become more permeable during inflammation

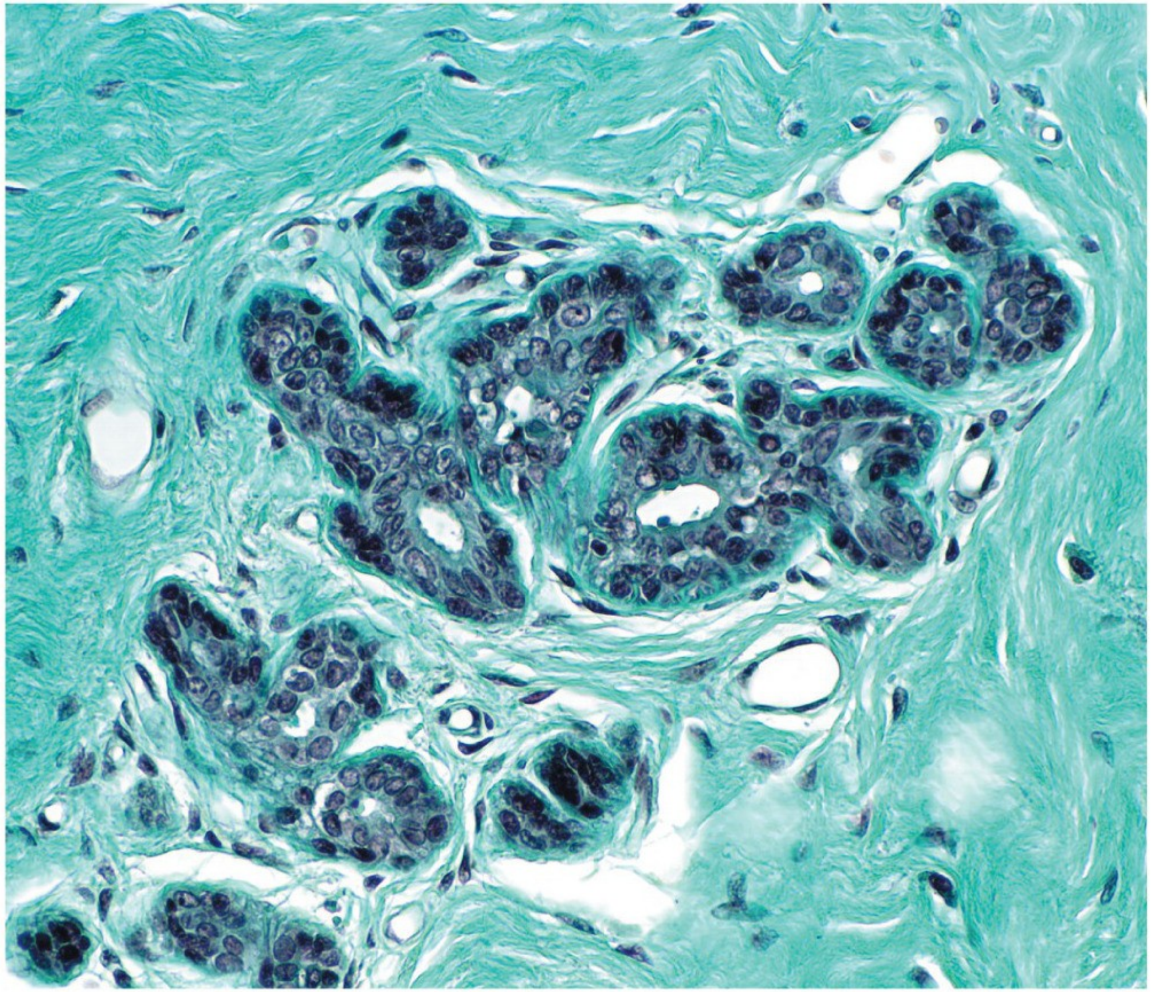
Classification of Connective Tissue

TABLE 5–6 Classification of connective or supporting tissues.

	General Organization	Major Functions	Examples
Connective Tissue Proper			
Loose (areolar) connective tissue	Much ground substance; many cells and little collagen, randomly distributed	Supports microvasculature, nerves, and immune defense cells	Lamina propria beneath epithelial lining of digestive tract
Dense irregular connective tissue	Little ground substance; few cells (mostly fibroblasts); much collagen in randomly arranged fibers	Protects and supports organs; resists tearing	Dermis of skin, organ capsules, submucosa layer of digestive tract
Dense regular connective tissue	Almost completely filled with parallel bundles of collagen; few fibroblasts, aligned with collagen	Provide strong connections within musculoskeletal system; strong resistance to force	Ligaments, tendons, aponeuroses, corneal stroma
Embryonic Connective Tissues			
Mesenchyme	Sparse, undifferentiated cells, uniformly distributed in matrix with sparse collagen fibers	Contains stem/progenitor cells for all adult connective tissue cells	Mesodermal layer of early embryo
Mucoid (mucous) connective tissue	Random fibroblasts and collagen fibers in viscous matrix	Supports and cushions large blood vessels	Matrix of the fetal umbilical cord
Specialized Connective Tissues			
Reticular connective tissue (see Chapter 14)	Delicate network of reticulin/collagen III with attached fibroblasts (reticular cells)	Supports blood-forming cells, many secretory cells, and lymphocytes in most lymphoid organs	Bone marrow, liver, pancreas, adrenal glands, all lymphoid organs except the thymus
Adipose Tissue (Chapter 6)			
Cartilage (Chapter 7)			
Bone (Chapter 8)			
Blood (Chapter 12)			

Connective Tissue: Types, Functions & Disorders: https://www.youtube.com/watch?v=eJ7snAlCaCg

Loose and Dense Irregular CT



Dense irregular connective tissue

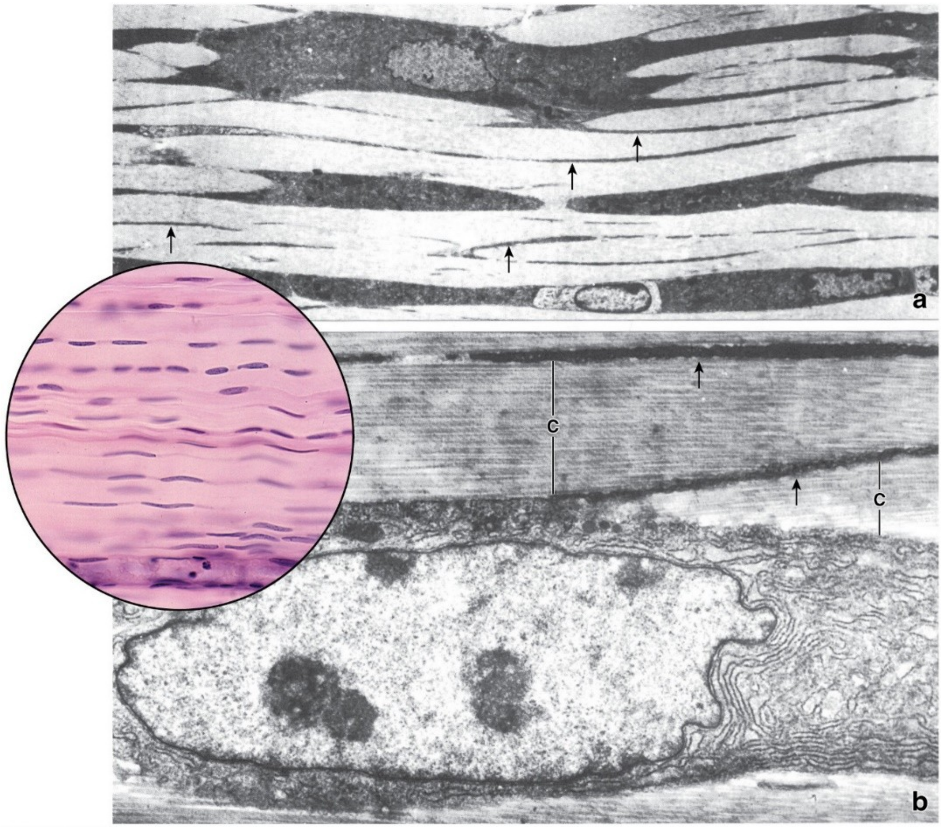
- contains mostly collagen fibers.
- Cells are sparse fibroblasts.
- contains relatively little ground substance

Mammary gland stained with Masson's trichrome:

- Center: loose connective tissue surrounds the glandular epithelium. Note wispy arrangement of collagen fibers with many cells.
- upper left: dense irregular connective tissue. few nuclei, collagen is considerably more abundant and is composed of very thick fibers

Skin contains dense irregular connective tissue called the **reticular layer** of the dermis, which provides resistance to tearing from stretching forces from different directions

Dense Regular CT



Dense regular connective tissue

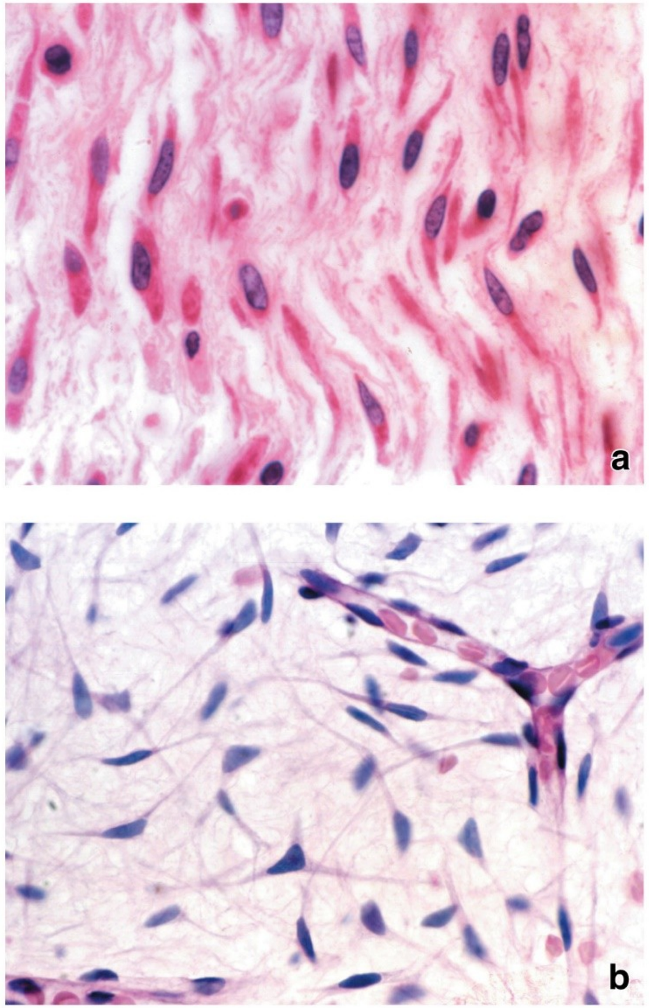
- tendons, ligaments, and aponeuroses.
- fibers are the prominent feature
- little ECM

a) Electron micrograph of a tendinocytes (fibroblasts) and their thin processes (*arrows*) lying between the collagen bundles.
b) higher magnification. The collagen fibers (*C*). Orderly and regular alignment of the bundles of collagen fibers.

❯❯ MEDICAL APPLICATION

Overuse of tendon-muscle units can result in **tendonitis,** characterized by inflammation of the tendons and their attachments to muscle. Common locations are the elbow, the Achilles tendon of the heel, and the shoulder rotator cuff. The swelling and pain produced by the localized inflammation restricts the affected area’s normal range of motion and can be relieved by injections of anti-inflammatory agents such as cortisone. Fibroblasts eventually repair damaged collagen bundles of the area.

Embryonic Connective Tissue



a) Although morphologically the mesenchymal cells appear as a homogeneous population, they give rise to cells that will differentiate into various cell types.
b) Wharton's jelly consists of a specialized, almost gelatin like ground substance that occupies large intercellular spaces located between the spindle-shaped mesenchymal cells

MEDICAL APPLICATION

Some cells in mesenchyme are multipotent stem cells potentially useful in regenerative medicine after grafting to replace damaged tissue in certain patients.

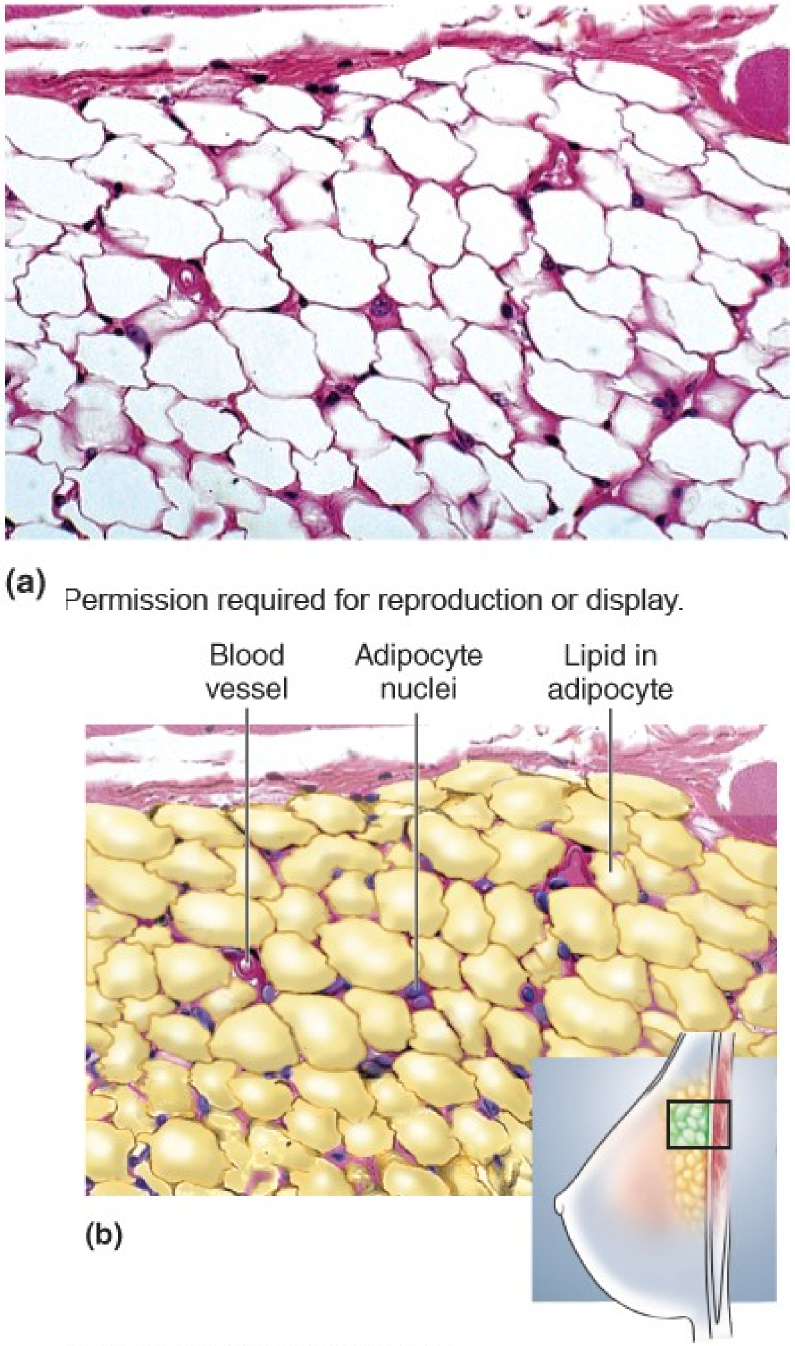
Stem cells to allow growing new teeth: https://www.youtube.com/watch?v=_Gyv-BVniAw

Chapter 6 Adipose Objectives

1. Adipose tissue is a specialized connective tissue that plays an important role in energy homeostasis (stores energy in lipid droplets in the form of triglycerides) and hormone production (adipokines).
2. White adipose tissue with supporting collagen and reticular fibers forms the subcutaneous fascia, is concentrated in the mammary fat pads, and surrounds several internal organs.
3. White adipocytes differentiate from mesenchymal stem cells
4. Brown adipose tissue is abundant in newborns (5% of total body mass) but is markedly reduced in adults.
5. Adipocytes are able to undergo white-to-brown and brown-to-white transformation (transdiferentiation) in response to the thermogenic needs of the body.

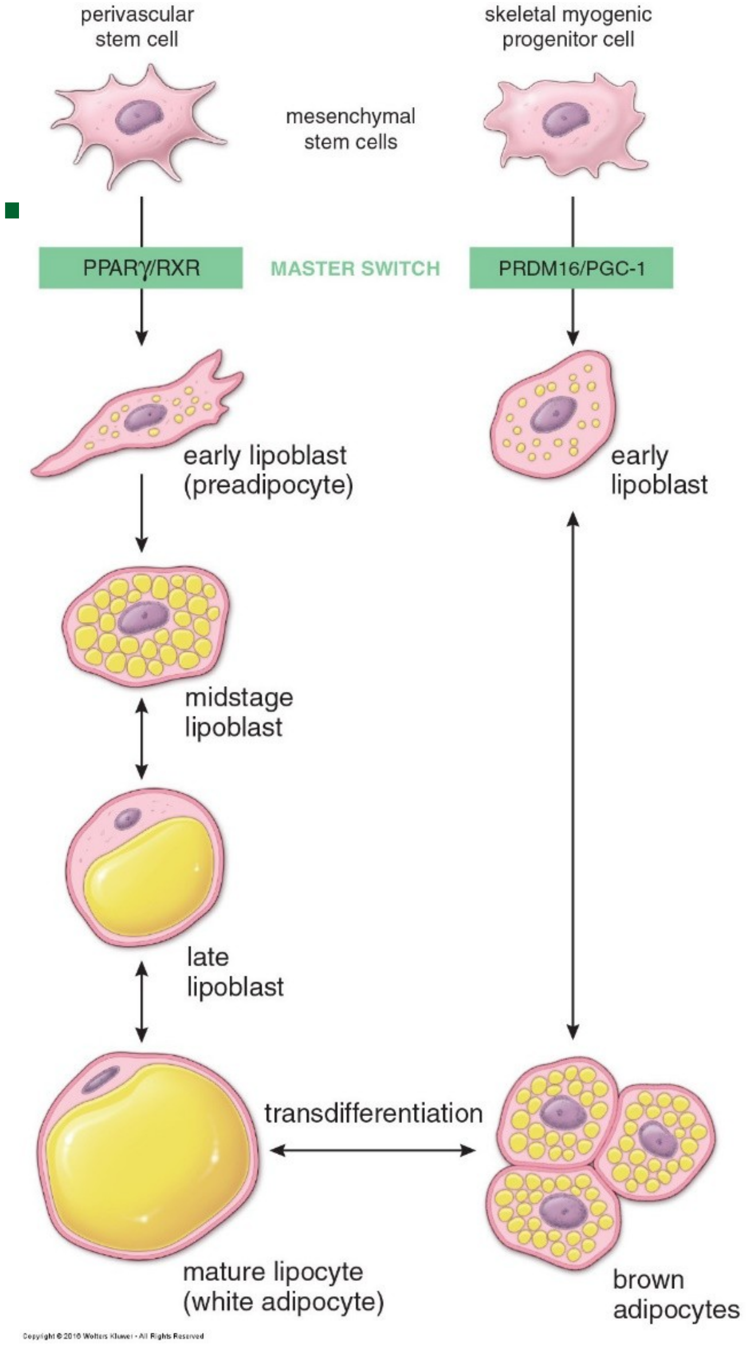
Adipose Tissue

- Description
  - Closely packed adipocytes, nucleus pushed to one side by fat droplet Function
  - Provides reserve food fuel
  - Insulates against heat loss
  - Supports and protects organs
  - Most adult fat is called white fat
  - Brown fat: in fetuses, infants, children. a heat-generating tissue
  - Empty-looking cells with thin margins; nucleus pressed against cell membrane
  - Space between adipocytes is occupied by areolar tissue, reticular tissue, and blood capillaries
- Location: Under skin, around kidneys, Behind eyeballs, within abdomen and in breasts



Inc./Dennis Strete, photographer

White adipose tissue begins to form midway through fetal development.

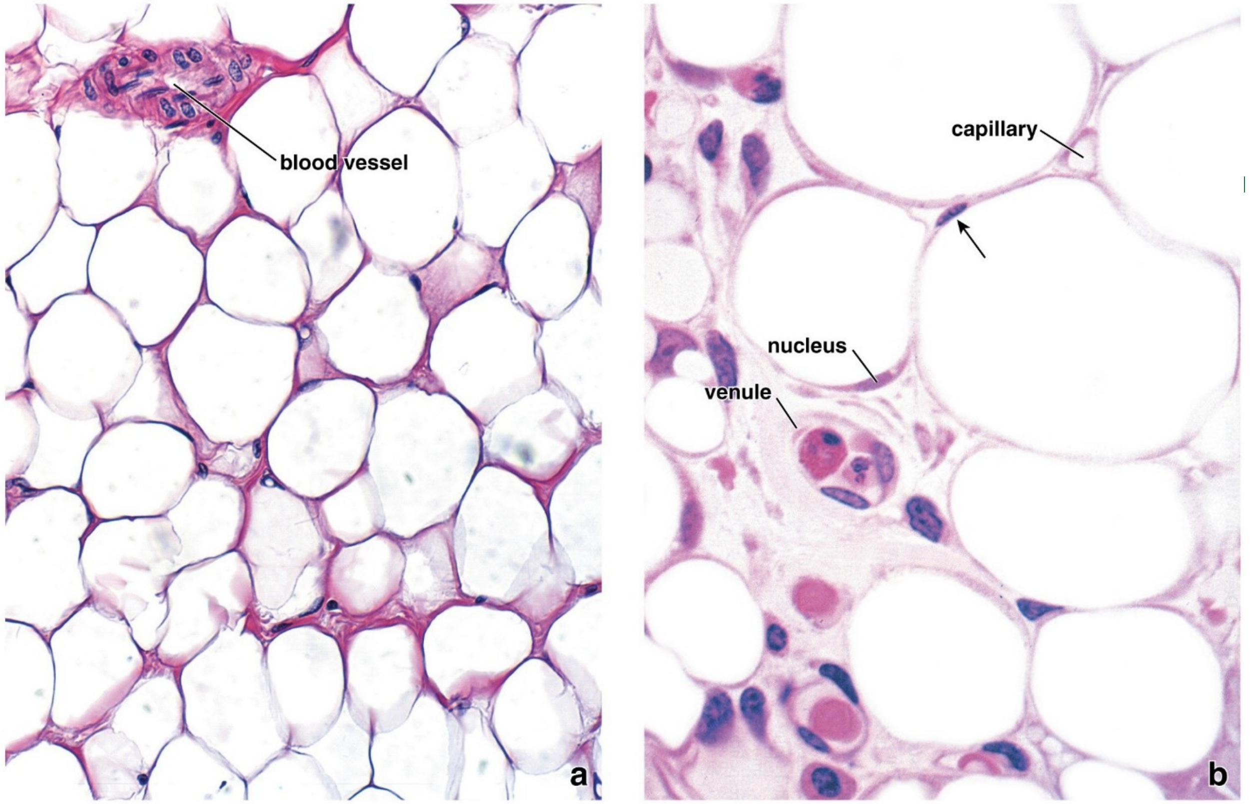


- White adipocytes differentiate from mesenchymal stem cells under the control of **PPARγ/RXR** transcription factors ("master switch" for white adipocyte differentiation).
- Brown adipocytes differentiate from mesenchymal stem cells under the control of **PRDM16/PGC-1** transcription factors ("master switch" for brown adipocyte differentiation).
- **Transdifferentiation**: white to brown conversion is induced by cold or physical activity
- **Research application:** Mice with abundant natural or induced brown adipose tissue are resistant to obesity, Genetically modified mice without functional brown adipocytes are prone to obesity and type 2 diabetes.

White Adipose Tissue

White adipose tissue represents at least 10% of body weight in a normal healthy adult.

- Forms subcutaneous fascia, is concentrated in the mammary fat pads, and surrounds several internal organs.



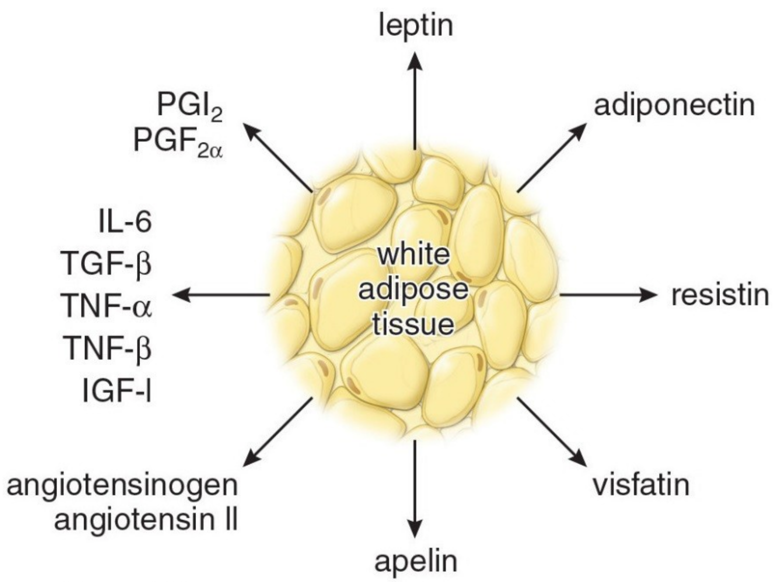
White adipocytes are very large cells (100 µm or more in diameter) with a single, large lipid droplet (unilocular), a thin rim of cytoplasm, and a flattened, peripherally displaced nucleus.
A single large lipid droplet within the white adipocyte represents cytoplasmic inclusion and is not membrane bound.

White adipose tissue secretes a variety of adipokines, which include hormones (e.g., leptin), growth factors, and cytokines.

White adipose tissue produces a variety of hormones, growth factors, and cytokines.

Leptin: **circulating satiety factor** that controls food intake when the body's store of energy is sufficient.

❯❯ **MEDICAL APPLICATION**: In most obese humans adipocytes produce adequate or excess quantities of leptin, but target cells are not responsive due to mechanisms downstream of leptin receptors.

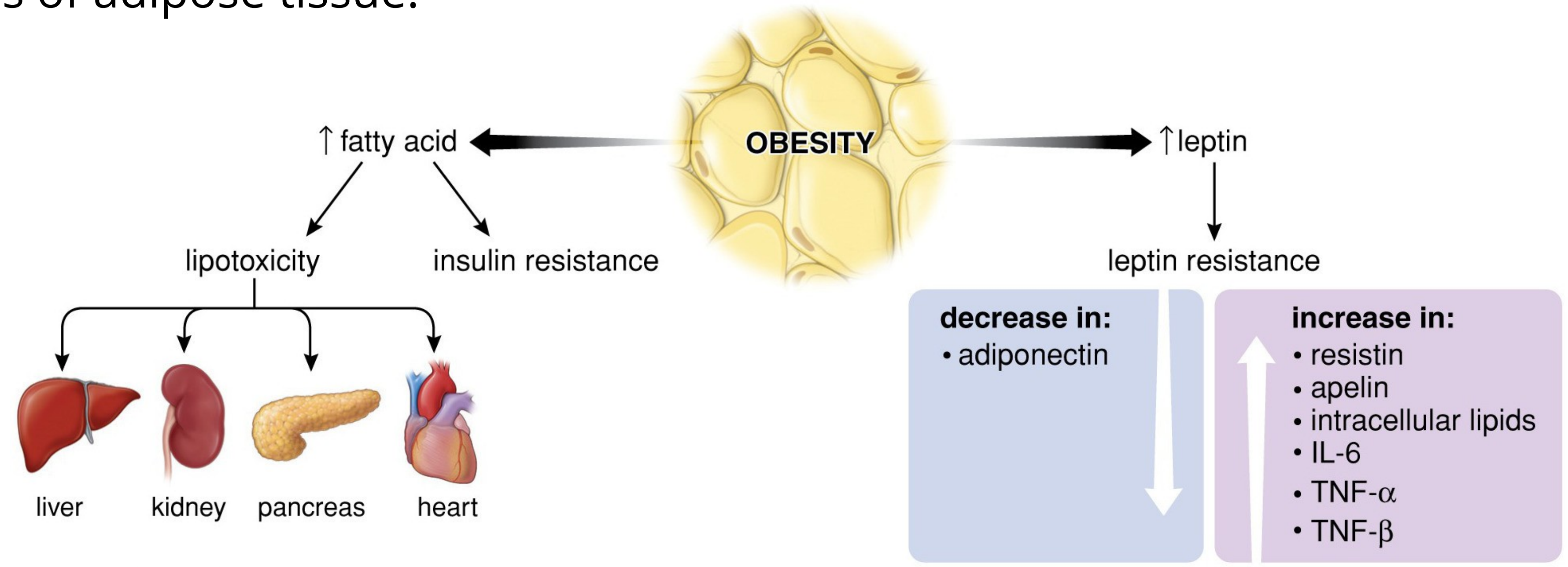


❯❯ **MEDICAL APPLICATION**

In addition to leptin, white adipose tissue secretes numerous other cytokines. It is not clear whether these are produced by adipocytes or other cells of the tissue such as macrophages or fibroblasts. With its increased amounts of white adipose tissue, obesity is characterized by a state of chronic mild inflammation and inflammation-related disorders associated with obesity, such as diabetes and heart disease.

Clinical Correlation: Obesity

Adult-onset obesity is very often associated with age related metabolic changes and may involve reduced activity of the hormone-sensitive lipases of adipocytes, causing less effective fat mobilization out of the cells. The increased number of adipocytes produced during childhood obesity predisposes an individual to obesity in later life. Despite claims of various fad diets, there is no evidence that any particular type of caloric restriction is more effective than others; rather, any intake of calories that is lower than the energy expenditure will result in loss of adipose tissue.



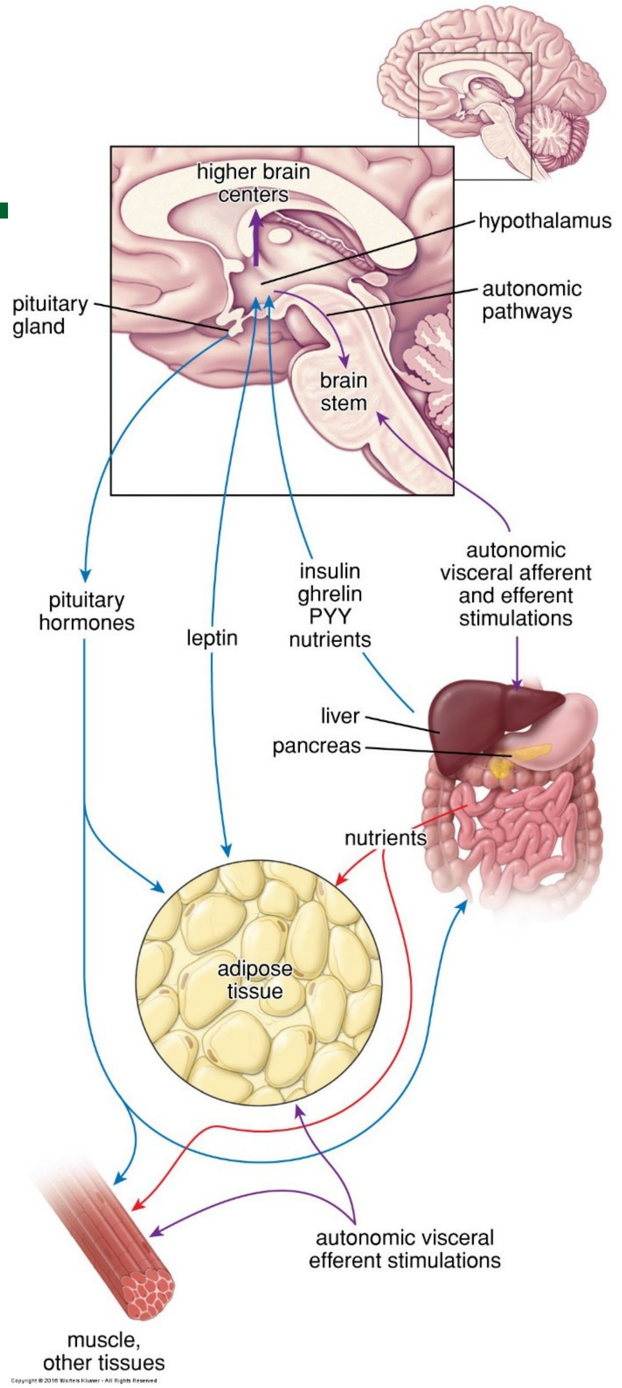
Regulation of Adipose Tissue: brain-gut-adipose axis

Short-term weight regulation: controls appetite via GI tract hormones **ghrelin** (appetite stimulant) and **peptide YY** (PYY, appetite suppressant)

Long term weight regulation:

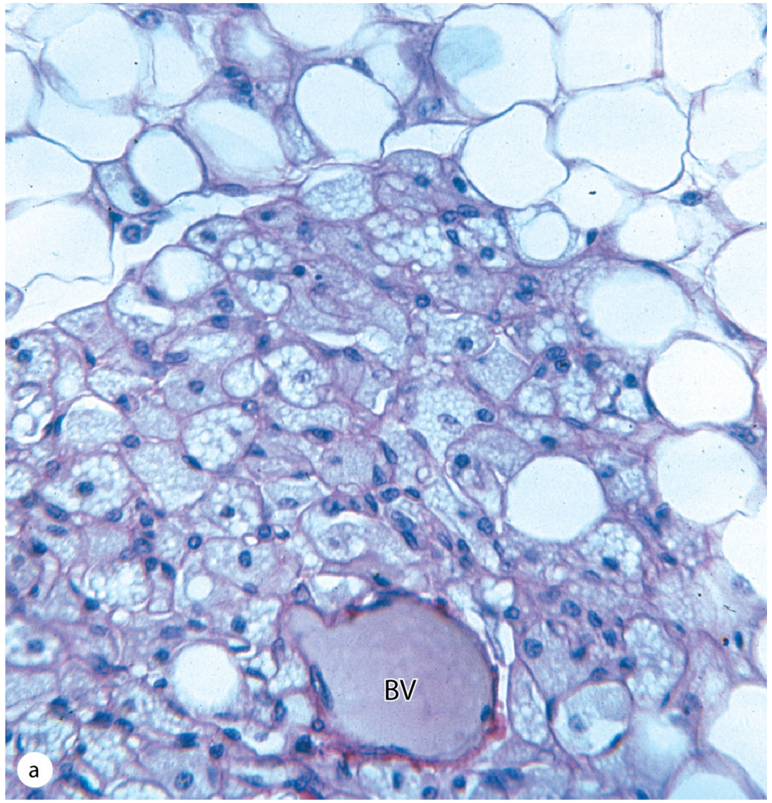
Leptin: controls food intake. Mice lacking leptin are obese, however obese humans overexpress leptin. The effect of leptin in satiety may be downstream of the receptor.

Insulin: regulates blood glucose levels by encouraging conversion of glucose to triglyceride. It also acts on the hypothalamus.



http://www.hhmi.org/biointeractive/leptin-feedback-control-system

Brown adipose tissue, abundant in newborns, is markedly reduced in adults.

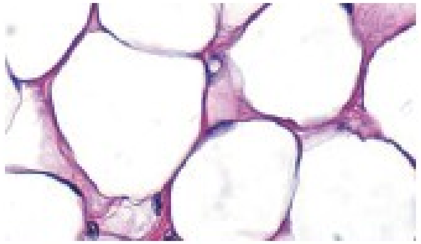
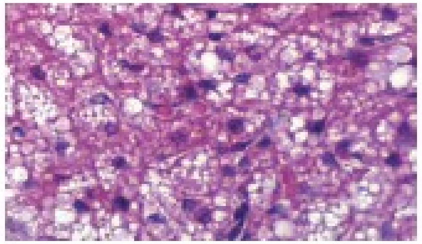


In newborns, brown adipose tissue makes up about 5% of the total body mass which helps to offset the extensive heat loss that results from the newborn's high surface-to-mass ratio and to avoid lethal hypothermia (a major risk of death for premature babies).

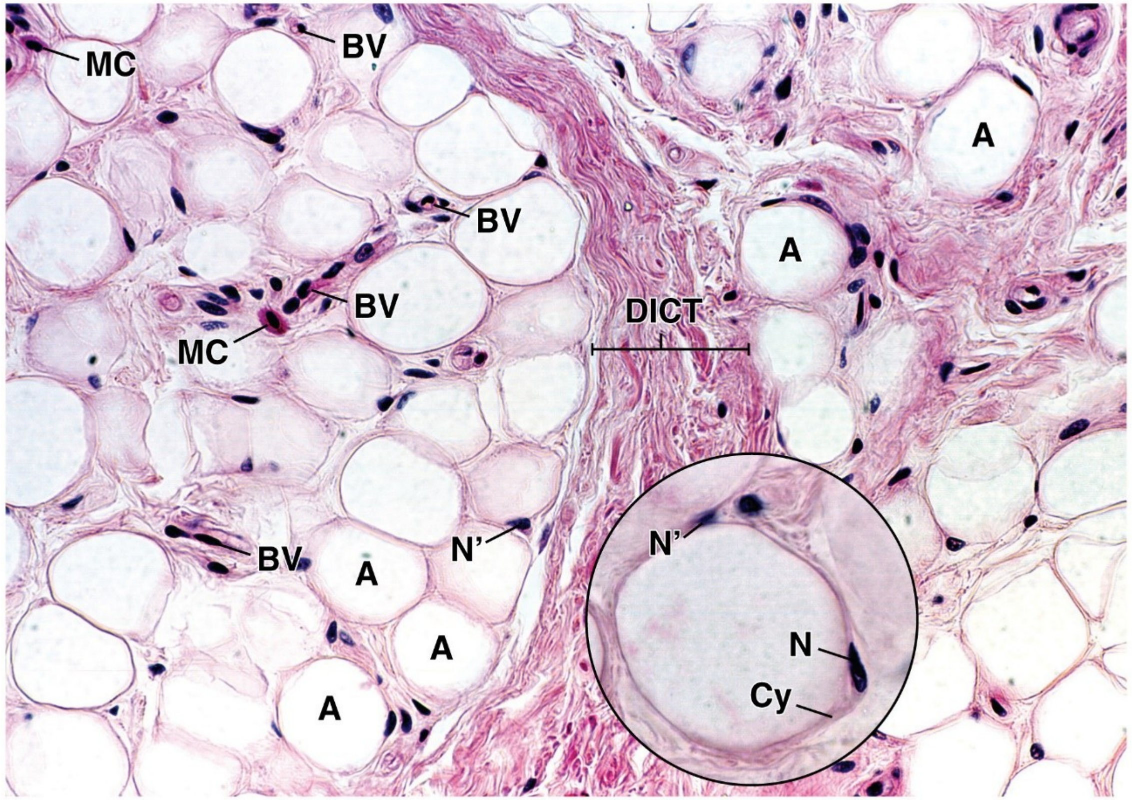
Brown (multilocular, multiple fat droplets) adipose tissue cells are smaller than those of white adipose tissue.

Brown adipose tissue can expand in response to increased blood levels of norepinephrine

Nonshivering themogenesis: Metabolism of lipid in brown adipose for heat, common in hibernating animals. UCP-1 (uncoupling protein 1 in mitochondria) uncouples oxidation of fatty acids from ATP production in favor of heat production.

TABLE 9.2 Summary of Adipose Tissue Features		
Features	**White Adipose Tissue**	**Brown Adipose Tissue**
		
Location	Subcutaneous layer, mammary gland, greater omentum, mesenteries, retroperitoneal space, visceral pericardium, orbits (eye sockets), bone marrow cavity	Large amounts in newborn Remnants in adults at the retroperitoneal space, deep cervical and supraclavicular regions of the neck, interscapular, paravertebral regions of the back, mediastinum
Function	Metabolic energy storage, insulation, cushioning, hormone production, source of metabolic water	Heat production (thermogenesis)
Adipocyte morphology	Unilocular, spherical, flatten nucleus, rim of cytoplasm Large diameter (15–150 μm)	Multilocular, spherical, round eccentric nucleus Smaller diameter (10–25 μm)
Transcription factors "master switch" in differentiation	PPAR-γ/RXR	PRDM16/PGC-1
UCP-1 genes expression	No	Yes (unique to brown fat)
Mitochondria	Few, poorly developed	Many, well developed
Innervation	Few sympathetic nerve fibers	High density of sympathetic nerve fibers
Vascularization	Few blood vessels	Highly vascularized tissue
Response to environmental stress (cold exposure)	Decreased lipogenesis Increased lipoprotein lipase activity	Increased lipogenesis Decreased lipoprotein lipase activity
Growth and differentiation	Throughout entire life from stromal-vascular cells	Only during fetal period Decreases in adult life (exception: individuals with pheochromocytoma and hibernoma)

White adipose tissue, human, H&E



Dense irregular connective tissue (DICT) separates the lobules from surrounding structures.

adipocytes (A) with very thin rim of cytoplasm surrounding a single, large fat-containing vacuole fat is lost during tissue preparation

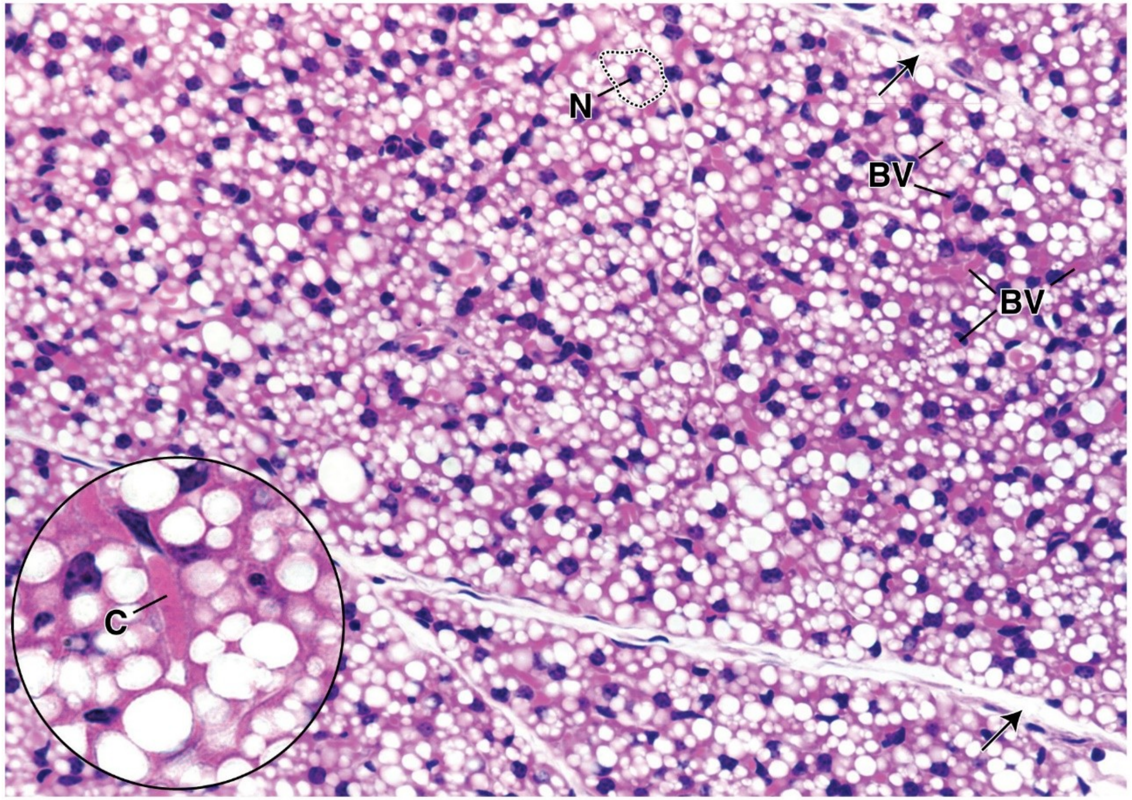
blood vessels (BV), mostly capillaries and venules.

inset shows an adipocyte whose nucleus (N) is relatively easy to identify. It appears to reside within the rim of cytoplasm (Cy), giving the adipocyte the classic " signet ring" appearance.

Because of the relatively large size of the adipocyte, it is very infrequent that the nucleus of the cell is included in the plane of section of a given cell.

Other cells that may be seen within the delicate connective tissue stroma are mast cells (MC) and Nuclei of Fibroblasts (N')

Brown adipose tissue, human, H&E



Small fat cells that are very closely packed with minimal intercellular space.

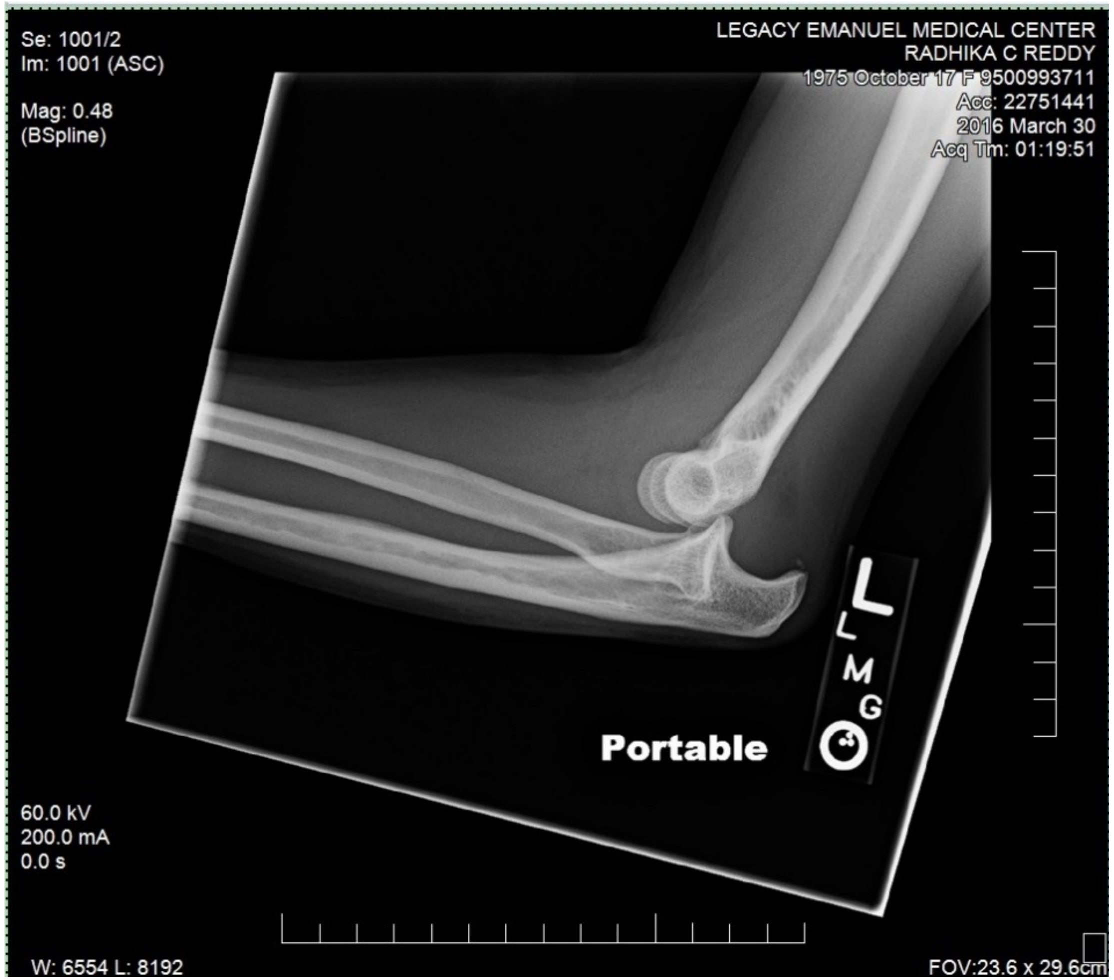
Each cell contains many small, fat-containing vacuoles surrounded by cytoplasm. Included in this cell is its nucleus (N).

Brown adipose tissue is highly vascularized

A capillary (C) can be identified in the inset

Chapter 7 Cartilage Objectives

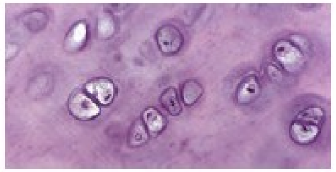
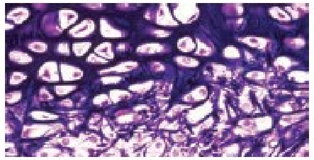
1. General properties of cartilage: Chondrocytes, lacunae, ECM, avascularity
2. Hyaline cartilage
3. Fibrocartilage
4. Elastic cartilage
5. Formation, growth and repair



Cartilage is a form of connective tissue composed of cells called chondrocytes and a highly specialized extracellular matrix.

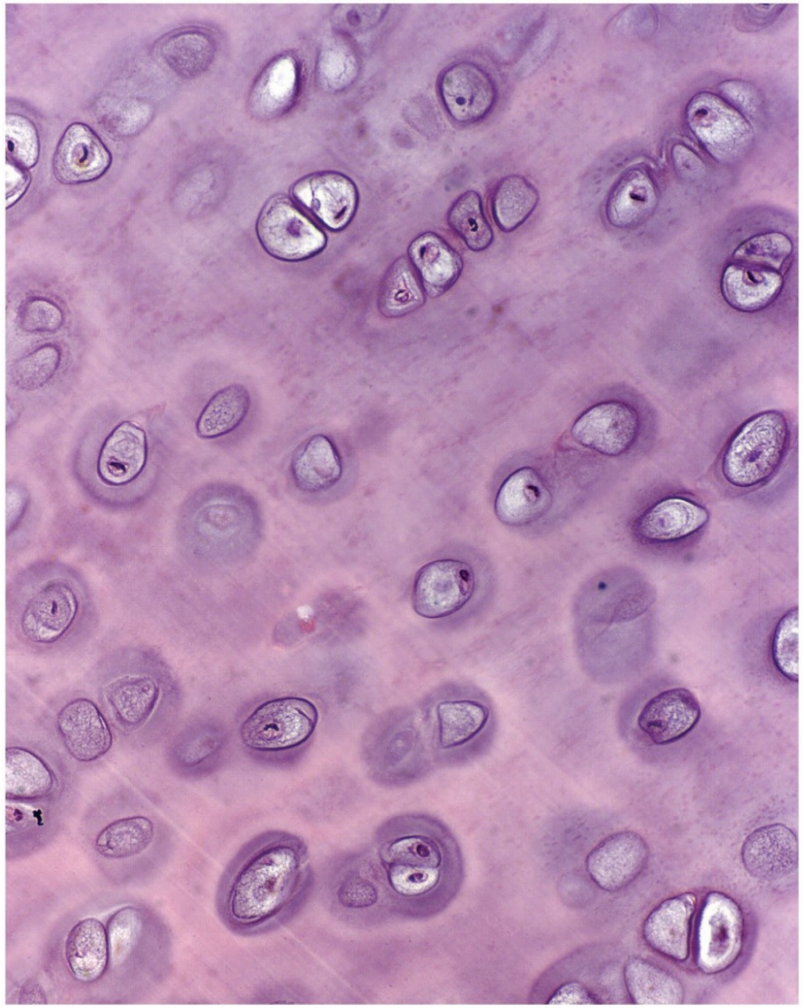
- Supportive connective tissue with flexible, rubbery matrix that gives shape to ear, tip of nose, and larynx
- **Chondroblasts** produce matrix and surround themselves until they become trapped in little cavities (lacunae)
- **Chondrocytes**: cartilage cells in lacunae
- **Perichondrium**: sheath of dense irregular connective tissue that surrounds elastic and most hyaline cartilage (not articular cartilage)
  - Contains a reserve population of chondroblasts that contribute to cartilage growth throughout life
- **No blood vessels**: Diffusion brings nutrients and removes wastes, heals slowly
- Matrix rich in chondroitin sulfate and contains collagen fibers

TABLE 7.1 Summary of Cartilage Features

Features	Hyaline Cartilage	Elastic Cartilage	Fibrocartilage
			
Location	Fetal skeletal tissue, epiphyseal plates, articular surface of synovial joints, costal cartilages of rib cage, cartilages of nasal cavity, larynx (thyroid, cricoid, and arytenoids), rings of trachea and plates in bronchi	Pinna of external ear, external acoustic meatus, auditory (Eustachian) tube, cartilages of larynx (epiglottis, corniculate, and cuneiform cartilages)	Intervertebral discs, symphysis pubis, articular discs (sternoclavicular and temporomandibular joints), menisci (knee joint), triangular fibrocartilage complex (wrist joint), insertion of tendons
Function	Resists compression Provides cushioning, smooth, and low-friction surface for joints Provides structural support in respiratory system (larynx, trachea, and bronchi) Forms foundation for development of fetal skeleton and further endochondral bone formation and bone growth	Provides flexible support	Resists deformation under stress
Presence of perichondrium	Yes (except articular cartilage and epiphyseal plates)	Yes	No
Undergoes calcification	Yes (i.e., during endochondral bone formation, during aging process)	No	Yes (i.e., calcification of fibrocartilaginous callus during bone repair)
Main cell types present	Chondroblasts and chondrocytes	Chondroblasts and chondrocytes	Chondrocytes and fibroblasts
Characteristic features of extracellular matrix	Type II collagen fibrils and aggrecan (the most important proteoglycan)	Type II collagen fibrils, elastic fibers, and aggrecan	Types I and II collagen fibers and versican (a proteoglycan secreted by fibroblasts)
Growth	Interstitially and appositionally, very limited in adults		
Repair	Very limited capability, commonly forms scar, resulting in fibrocartilage formation		

Hyaline cartilage is distinguished by a homogeneous, amorphous matrix.

- extensive extracellular matrix
- sparse population of chondrocytes
- Throughout the **cartilage matrix** are spaces called **lacunae**.
- **Chondrocytes** within these lacunae provides a low-friction surface, participates in lubricating synovial joints, and distributes applied forces to the underlying bone.



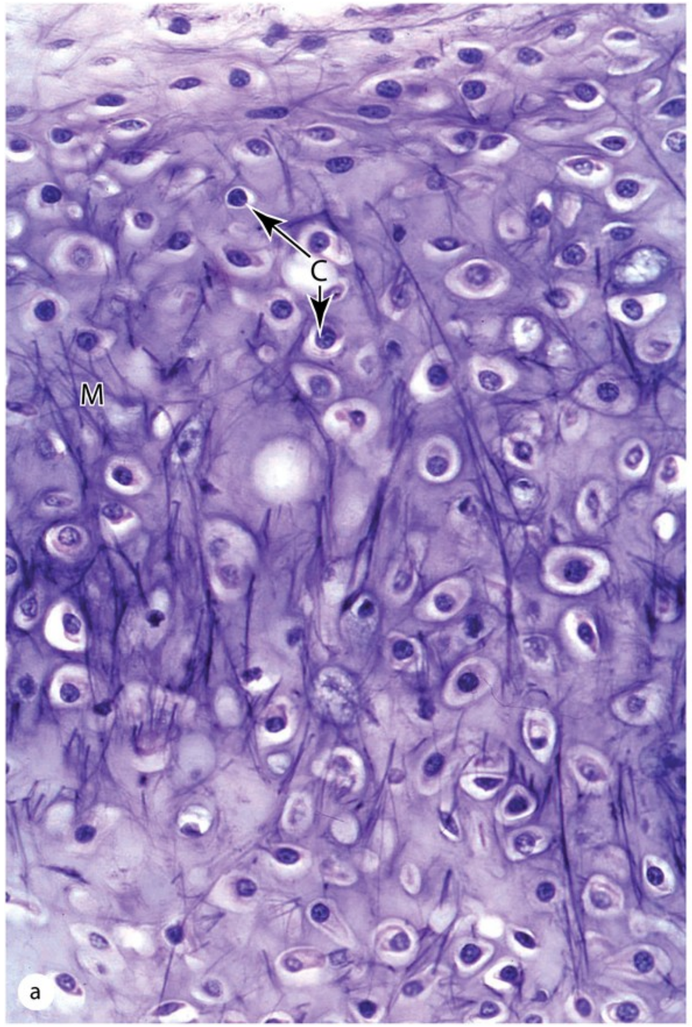
MEDICAL APPLICATION

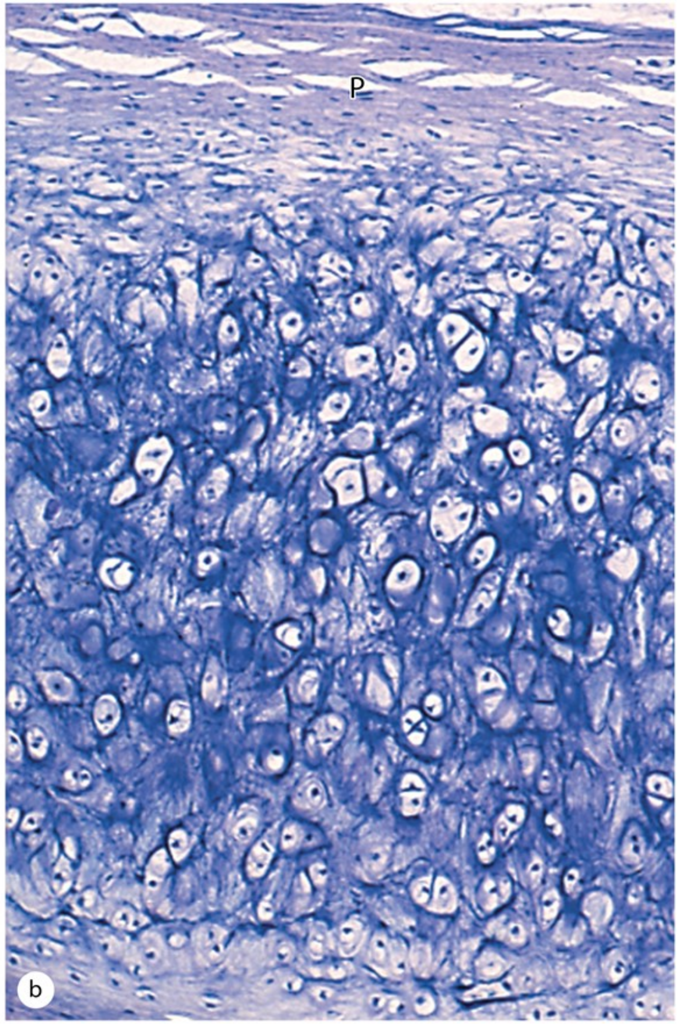
Many genetic conditions in humans or mice that cause defective cartilage, joint deformities, or short limbs are due to recessive mutations in genes for collagen type

MEDICAL APPLICATION

Osteoarthritis, a chronic condition that commonly occurs during aging, occurs most in joints that are weightbearing (knees, hips) or heavily used (wrist, fingers) are most prone to cartilage degeneration

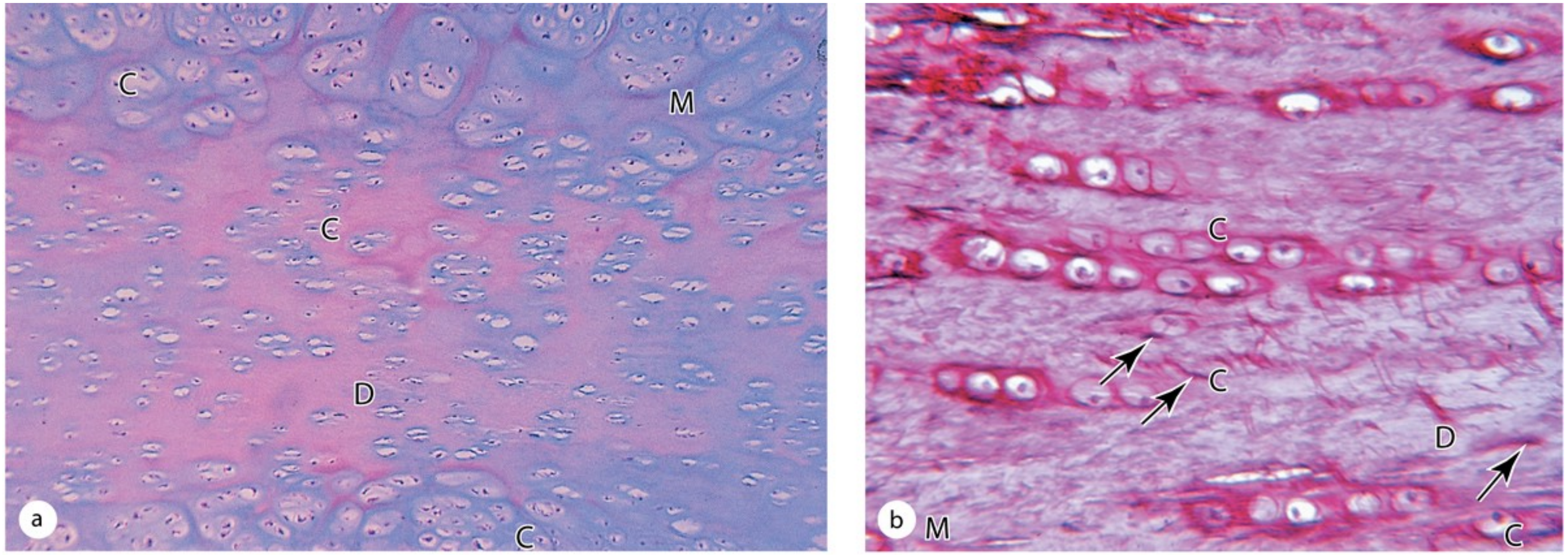
The chondrocytes (C) and overall organization of elastic cartilage are similar to those of hyaline cartilage.





Stains for elastin, however, reveal many dark-staining elastic fibers in the matrix (**M**), in addition to the major components found in hyaline matrix. Elastic fibers provide greater flexibility to this form of cartilage. The section in part **b** includes perichondrium (**P**) that is also similar to that of hyaline cartilage. **(a)** X160. Hematoxylin and orcein. **(b)** X100. Weigert resorcin-fuchsin.

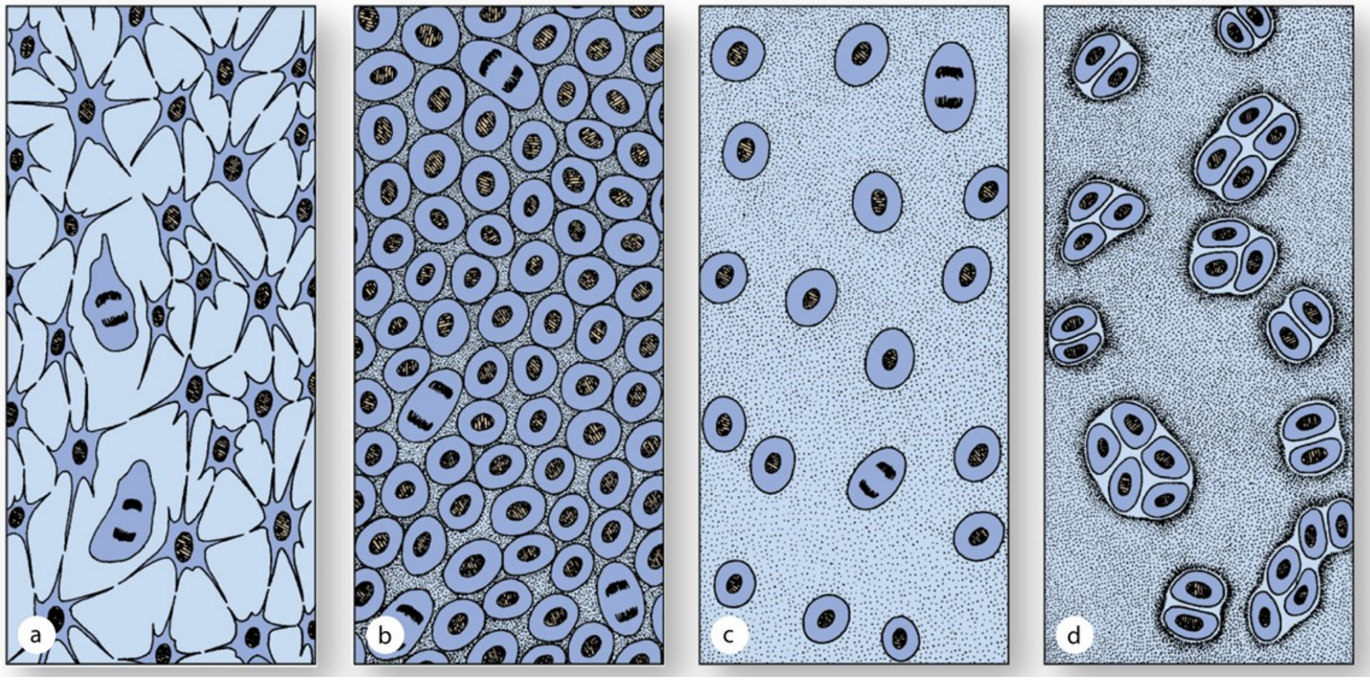
Fibrocartilage varies in different organs, but is essentially a mixture of hyaline cartilage and dense connective tissue.



Shotgun Histology Fibro-Cartilage: https://www.youtube.com/watch?v=imDyTwvgNaQ

(a) A section of pubic symphysis shows lacunae with isolated and grouped chondrocytes (**C**) surrounded by matrix (**M**) and separated in some areas by dense regions (**D**) containing more concentrated acidophilic type I collagen. No separate perichondrium is present on fibrocartilage. X100. H&E.
(b) At higher magnification in a small region of intervertebral disc, the axially arranged aggregates of chondrocytes (**C**) are seen to be surrounded by small amounts of matrix and separated by larger regions with dense collagen (**D**) and a small number of fibroblasts with elongated nuclei (arrows). X250. Picrosirius-hematoxylin.

Major stages by which embryonic cartilage is formed



(a) Mesenchyme is the precursor for all types of cartilage.
(b) Mitosis and early differentiation produces a tissue with **chondroblasts**.
(c) Chondroblasts are then separated from one another again by their production of ECM.
(d) Multiplication of chondroblasts within the matrix gives rise to **isogenous cell aggregates** surrounded by a condensation of territorial matrix.

Bone, Nervous, Muscle

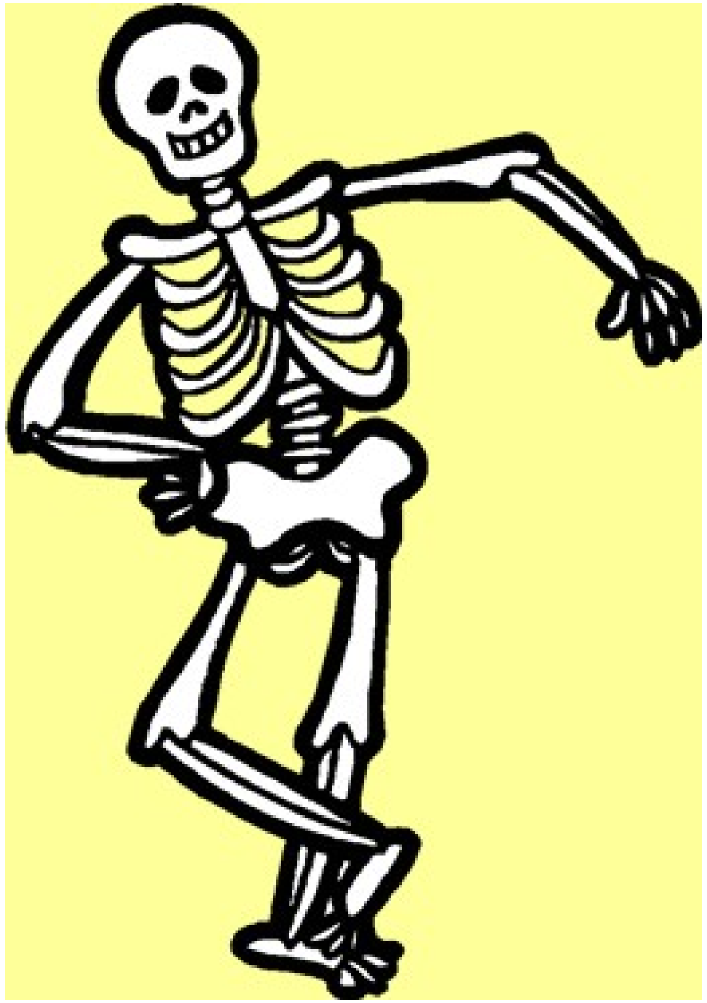
BI 455 CHAPTER 8-10

Chapter 8 Bone Objectives

1. Cells and ECM: Osteoblasts, osteocytes, bone matrix
2. Mineralized extracellular matrix
3. General structure of bone tissue: lamellar bone, osteons, perforating canals, lacunae
4. Bone formation: membranous ossification, endochondral ossification
5. Bone growth, remodeling, and repair: interstitial and appositional growth
6. Calcium homeostasis

Functions of the Skeleton

- Support: holds up the body, supports muscles, mandible and maxilla support teeth
- Protection: brain, spinal cord, heart, lungs
- Movement: limb movements, breathing, action of muscle on bone
- Electrolyte balance: calcium and phosphate ions
- Acid–base balance: buffers blood against excessive pH changes
- Blood formation: red bone marrow is the chief producer of blood cells



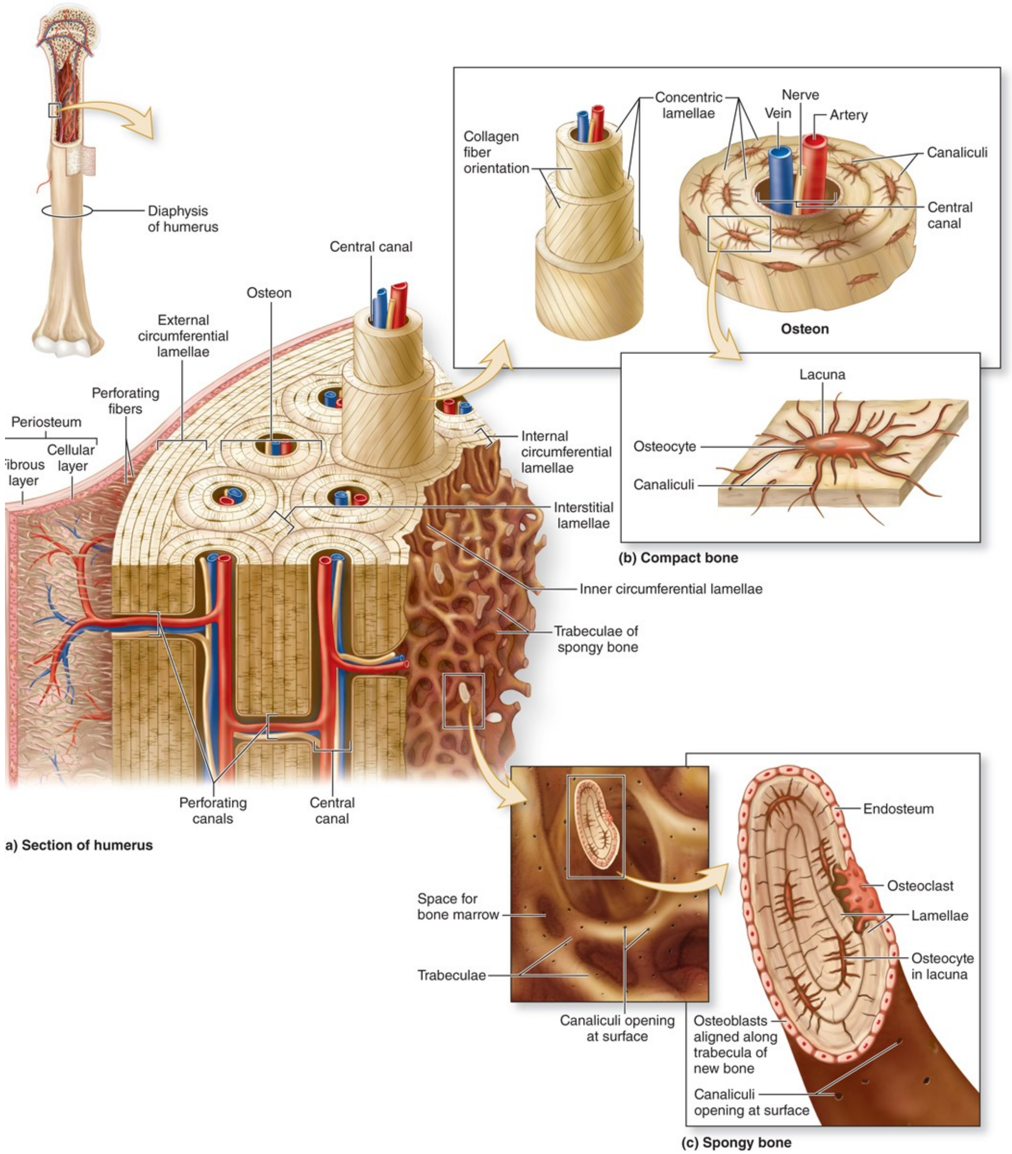
brasheranatomy.wikispaces.com

Bone cells

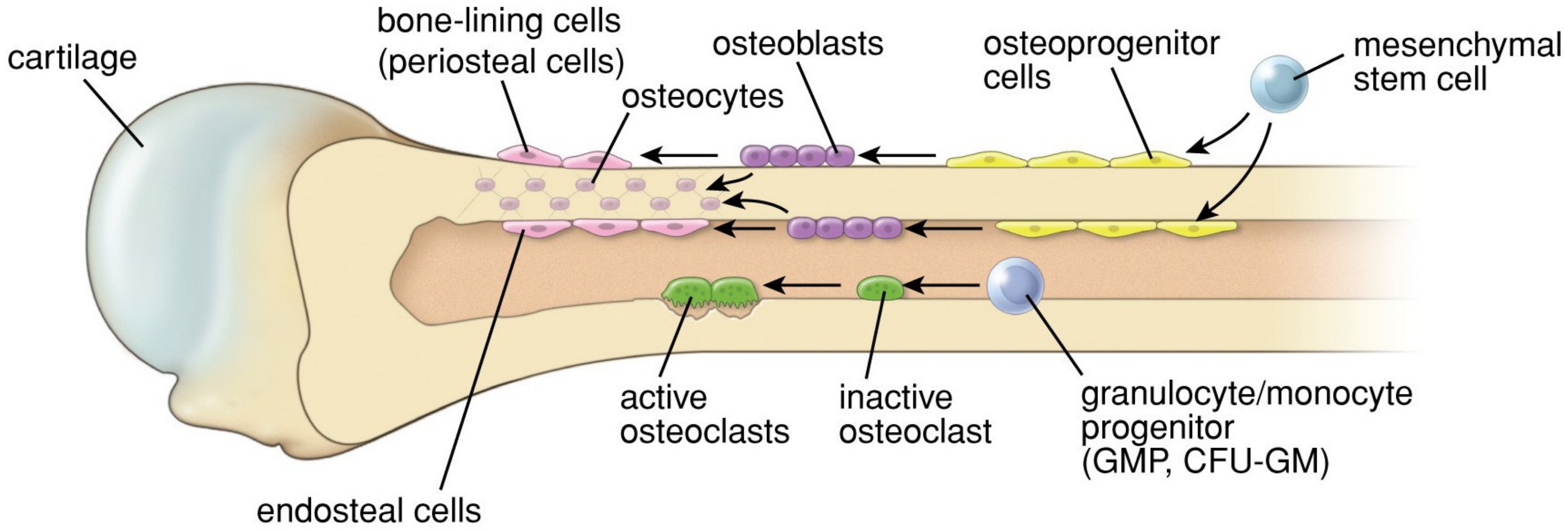
Bone Density Decreases in Space - What to Do? | Video: https://www.youtube.com/watch?v=nHbj7kqYoVk

Osteoprogenitor cells: derived from mesenchymal stem cells; give rise to osteoblasts.
Osteoblasts: secrete the extracellular matrix of bone; becomes **osteocyte** once the cell is surrounded with its secreted matrix
Osteoclasts: bone-resorbing cells on bone surfaces, for remodeling and repair

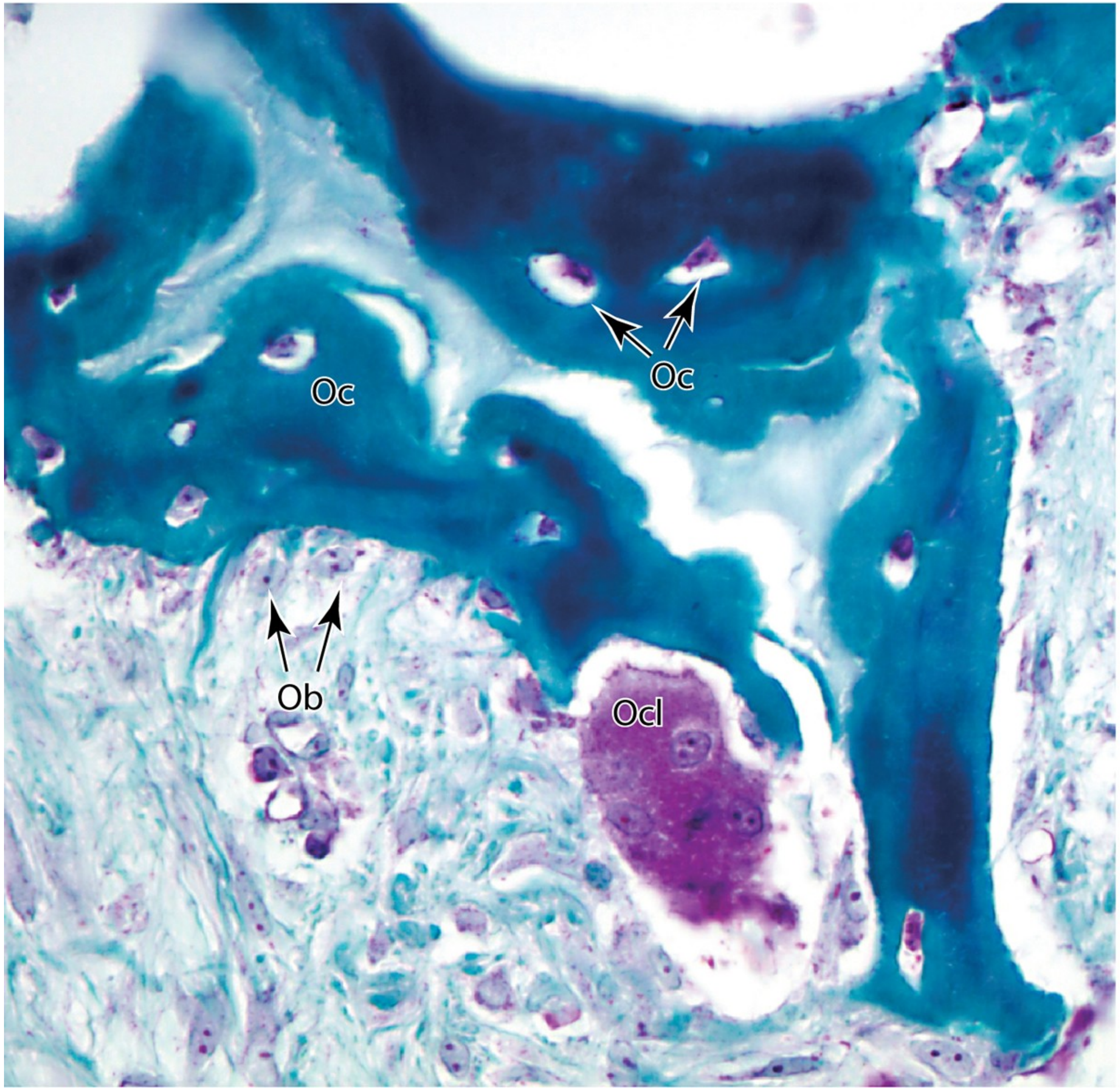
MEDICAL APPLICATION: dendritic processes of osteocytes detect load and maintain the matrix accordingly. Lack of exercise or the weightlessness experienced by astronauts leads to decreased bone density.



Bone Cells



MEDICAL APPLICATION: Osteoporosis, frequent in immobilized patients and postmenopausal women, is an imbalance where bone resorption exceeds bone formation. This leads to calcium loss and reduced bone mineral density (BMD).



Osteoblasts, osteocytes, and an osteoclast (400X Mallory trichrome)

- Bone-forming osteoblasts (**Ob**) differentiate from osteoprogenitor cells in the periosteum and endosteum.
- These cells differentiate further as osteocytes (**Oc**)
- The much less numerous large, multinuclear osteoclasts (**Ocl** reside on bony surfaces

Bones and Osseous Tissue

- **Bone (osseous tissue):** connective tissue with the matrix hardened by calcium phosphate and other minerals
- **Mineralization or calcification: the hardening process of bone**
  - Continually remodels itself and interacts physiologically with all of the other organ systems of the body
  - Permeated with nerves and blood vessels, which attests to its sensitivity and metabolic activity

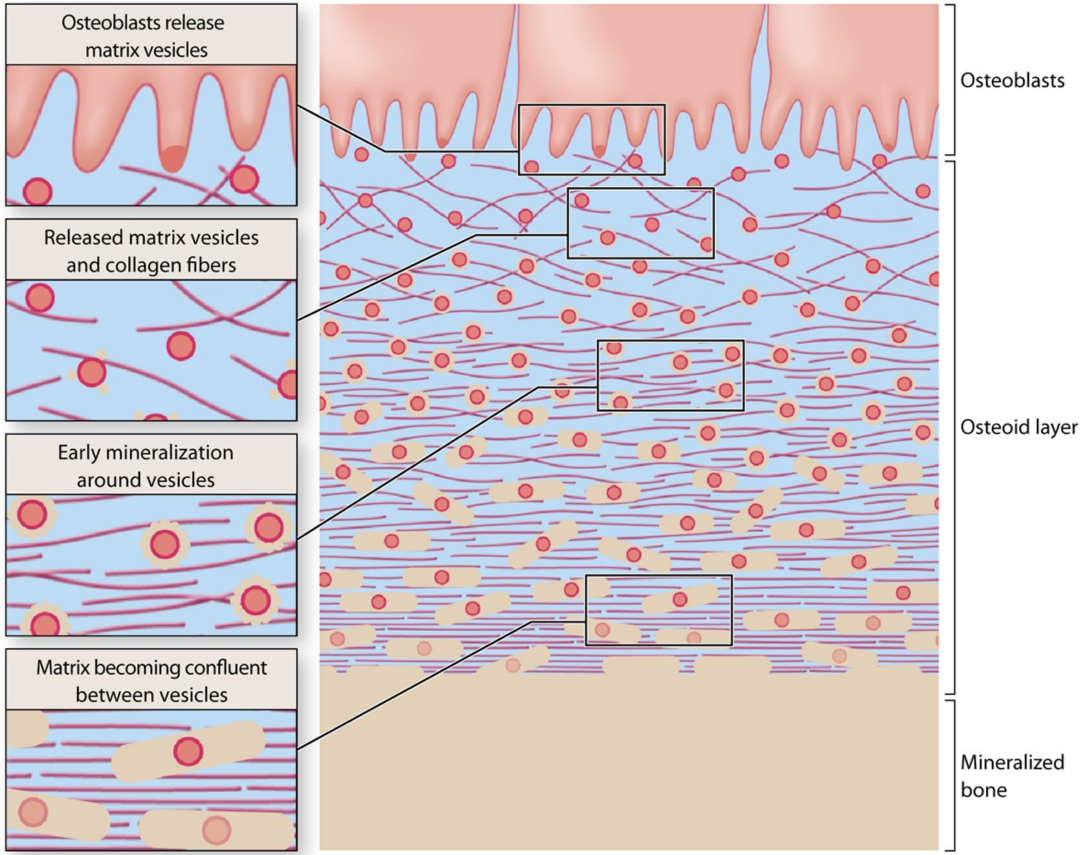
TEM: osteocyte surrounded by matrix, which calcifies around the processes, giving rise to canaliculi (**C**) in the bony matrix.

Bone matrix contains mainly type I collagen along with other matrix (noncollagenous) proteins.

Osteoblasts secrete type I collagen, several glycoproteins, and proteoglycans.

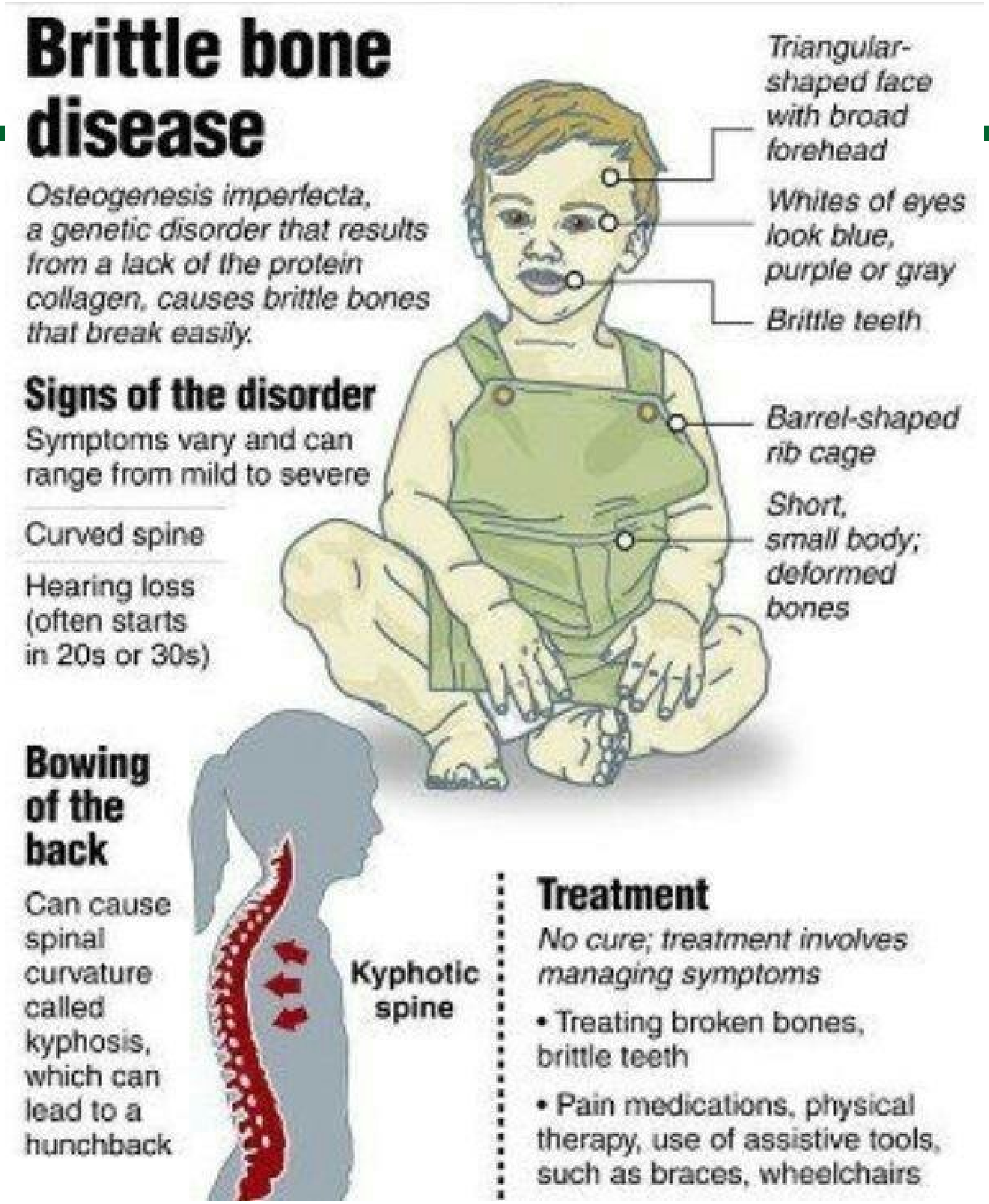
- Glycoproteins bind Ca^{2+} raising it'slocal concentration of these ions.

- Osteoblasts also release very small membrane-enclosed **matrix vesicles:** filled with enzymes that hydrolyze PO_4^- ions from various macromolecules,
- Calcified nanocrystals of calcium hydroxyapatite $[Ca_{10}(PO_4)_6(OH)_2]$ surround the collagen fibers and form bony matrix



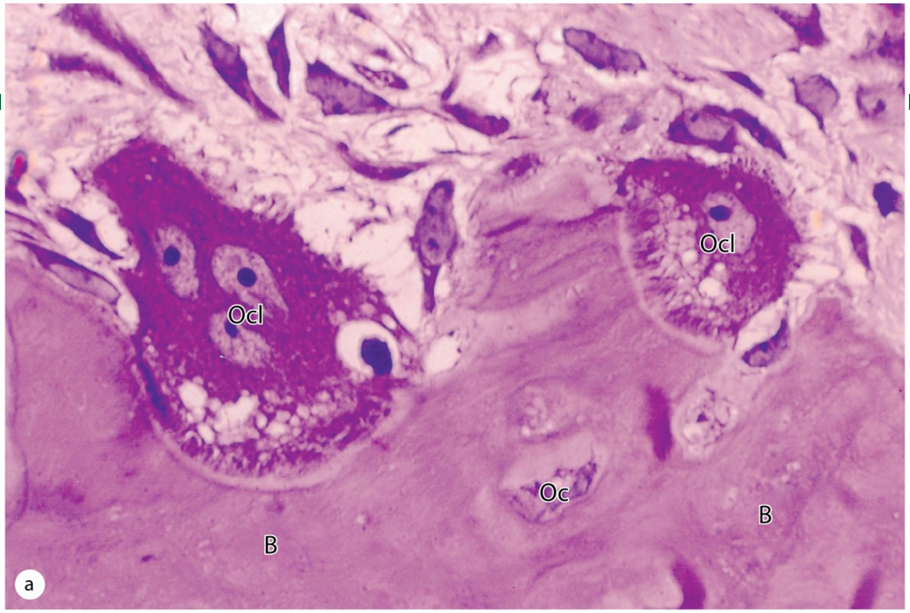
Osteogenesis imperfecta

Osteogenesis imperfecta, or “brittle bone disease,” refers to a group of related congenital disorders in which the osteoblasts produce deficient amounts of type I collagen or defective type I collagen due to genetic mutations. Such defects lead to a spectrum of disorders, all characterized by significant fragility of the bones. The fragility reflects the deficit in normal collagen, which normally reinforces and adds a degree of resiliency to the mineralized bone matrix.



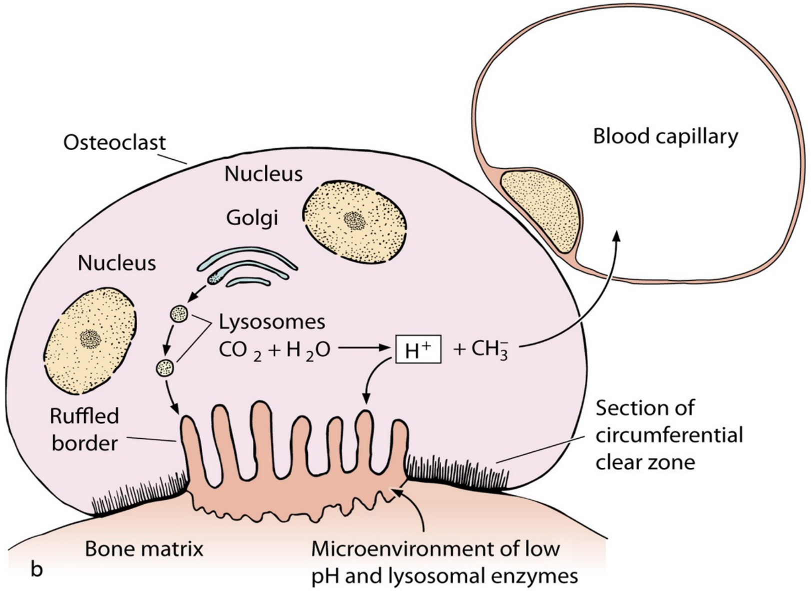
Osteoclasts

The osteoclast is a large cell with several nuclei derived by the fusion in bone of several blood-derived monocytes. Osteoclasts (**Ocl**) digest bone matrix (**B**) in resorption cavities on the matrix surface.



<u>**Medical Application**</u>

Osteopetrosis: dense, heavy bones (“marble bones”). Osteoclasts lack ruffled borders and bone resorption is defective. Most patients with osteopetrosis have mutations in genes for the cells’ proton-ATPase pumps or chloride channels.



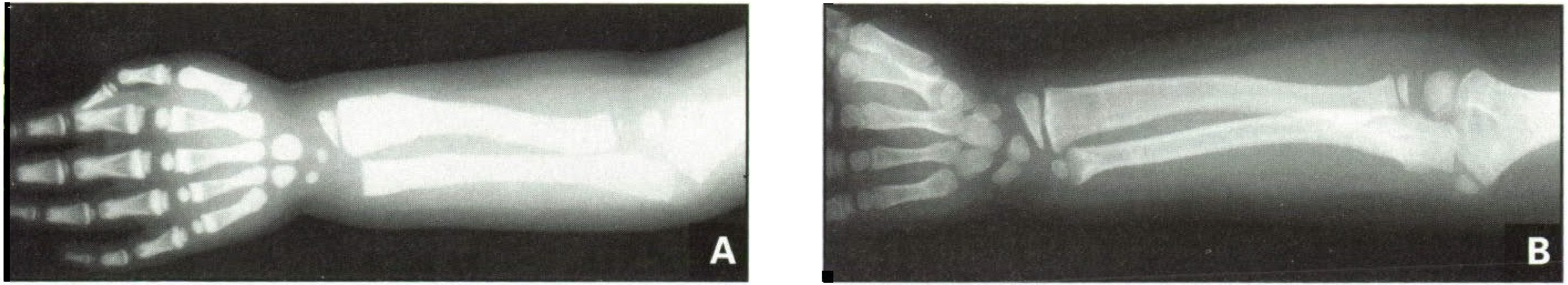
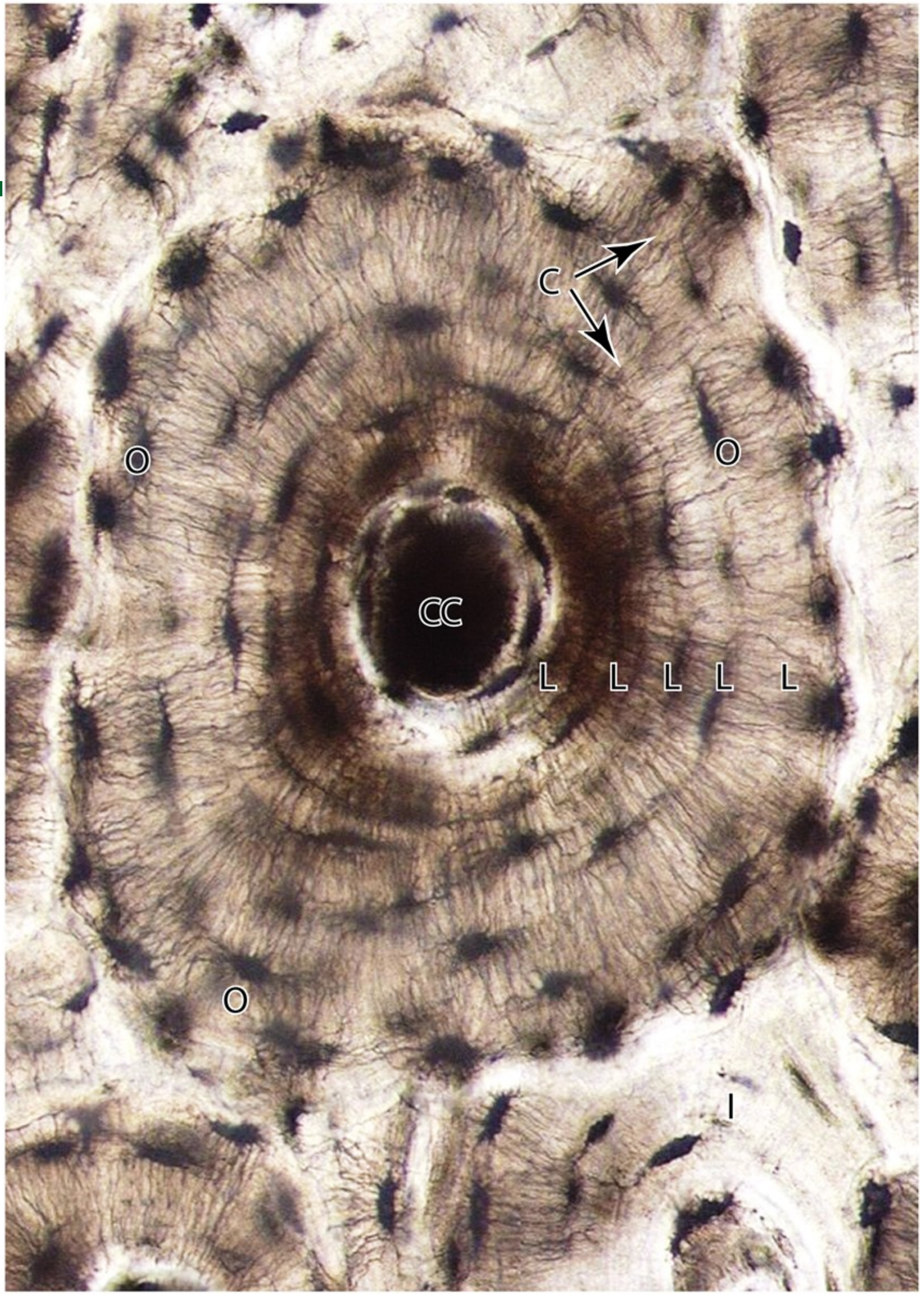


FIGURE 1: X-ray of arm prior to (A) and 6 months after (B) bone marrow transplantation. The high bone density, absent medullary cavity, and abnormal epiphyseal plates of osteopetrosis have largely resolved following bone marrow transplantation.

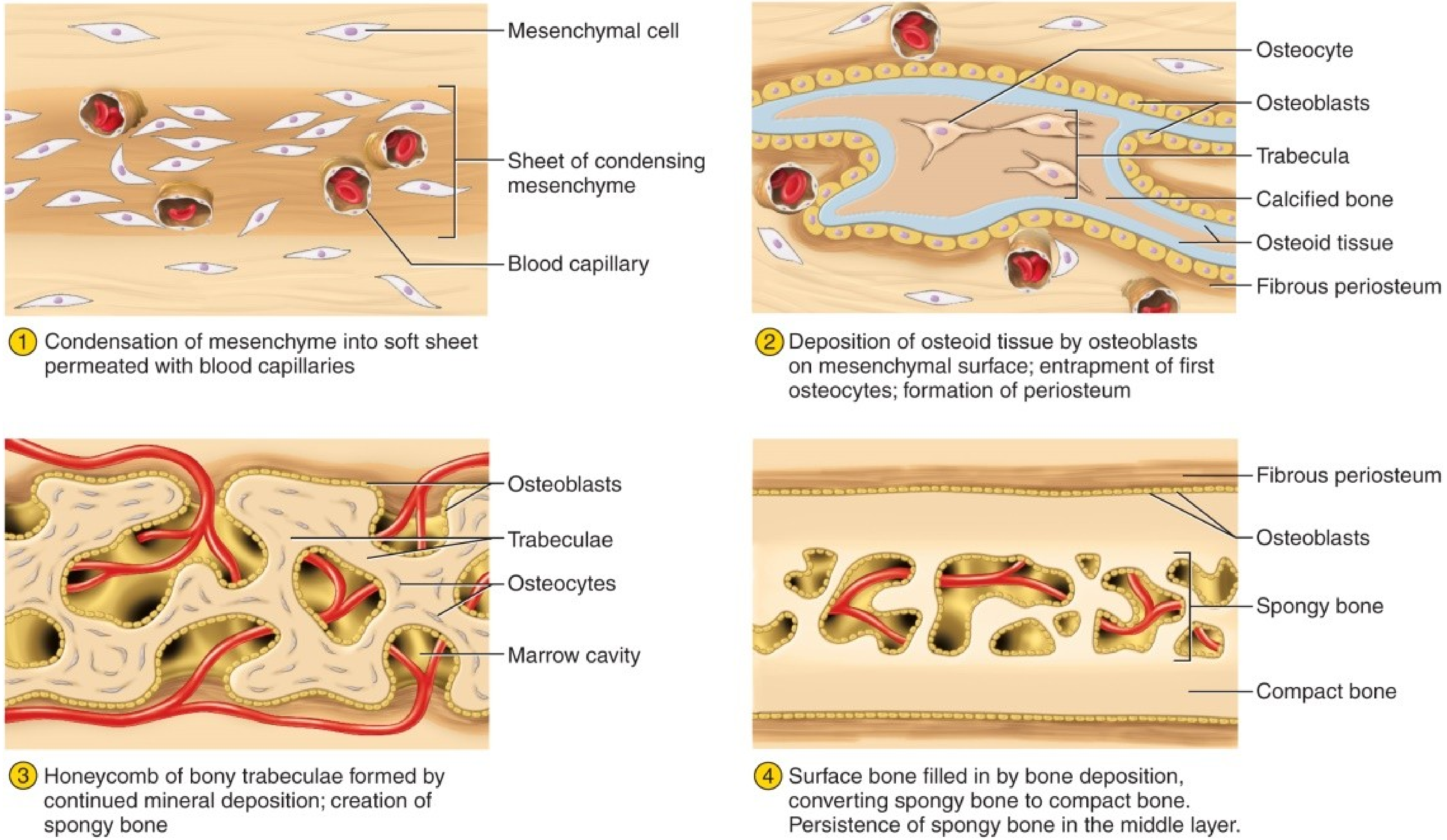
An Osteon

Osteons (Haversian systems) constitute most of the compact bone. Shown here is an osteon with four to five concentric lamellae (**L**) surrounding the central canal (**CC**). Osteocytes (**O**) in lacunae are in communication with each other and with the central canal and periphery of the osteon via through hundreds of dendritic processes located within fine canaliculi (**C**). Also shown are the partial, interstitial lamellae (**I**) of an osteon partially eroded when the intact osteon was formed. Ground bone

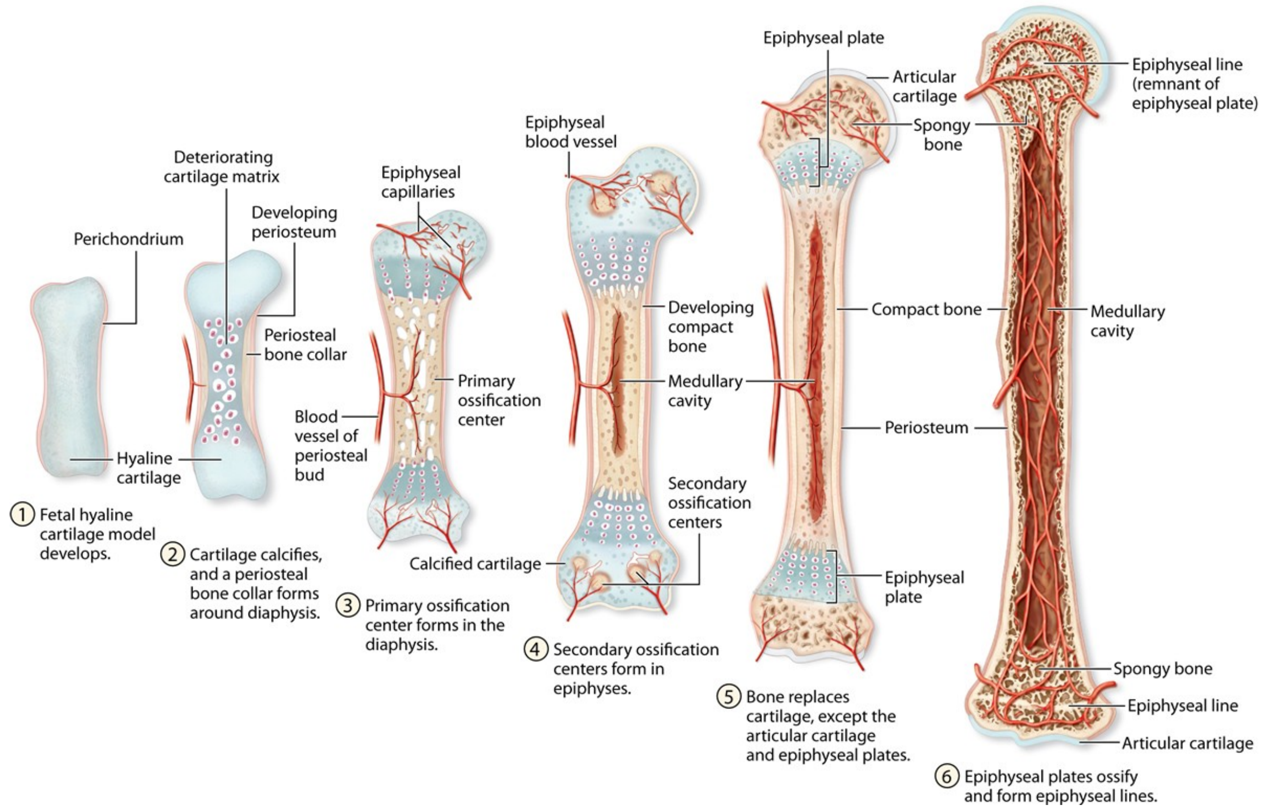
http://highered.mheducation.com/sites/0072507470/student_view0/chapter6/animation__bone_growth_in_width.html



Intramembranous ossification produces flat bones of skull and clavicle from mesenchymal tissue



Osteogenesis of long bones by endochondral ossification from hyaline cartilage



Development of Bone: https://www.youtube.com/watch?v=xXgZap0AvL0&nohtml5=False

(**1**) Bone collar develops beneath the perichondrium

(**2**) Invasion of the degenerating cartilage by capillaries and osteoprogenitor cells to produce a **primary ossification center**

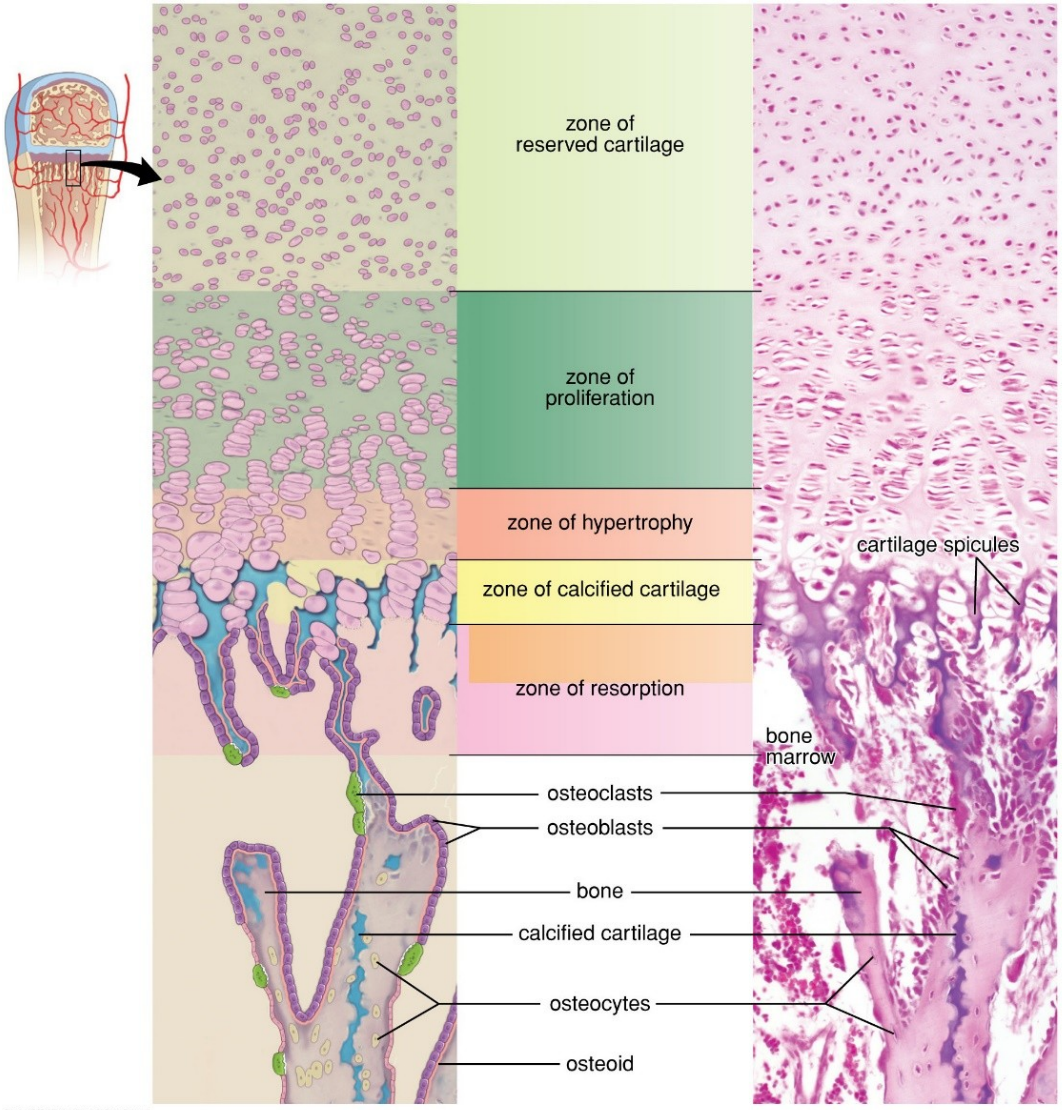
(**3**) Osteoid is deposited, calcified into woven bone, and is remodeled as compact bone.

(**4**) **Secondary ossification centers** develop by a similar process in the epiphyses. Ossification centers gradually come to be separated only by the **epiphyseal plate**.

(**5**) Continued bone elongation. The two ossification centers do not merge until the epiphyseal plate disappears

(**6**) When full stature is achieved, osteoblasts of the periosteum provide for growth in the bone's diameter.

Zones in the Epiphyseal Cartilage



Zone of reserve cartilage exhibits no cellular proliferation or active matrix production.

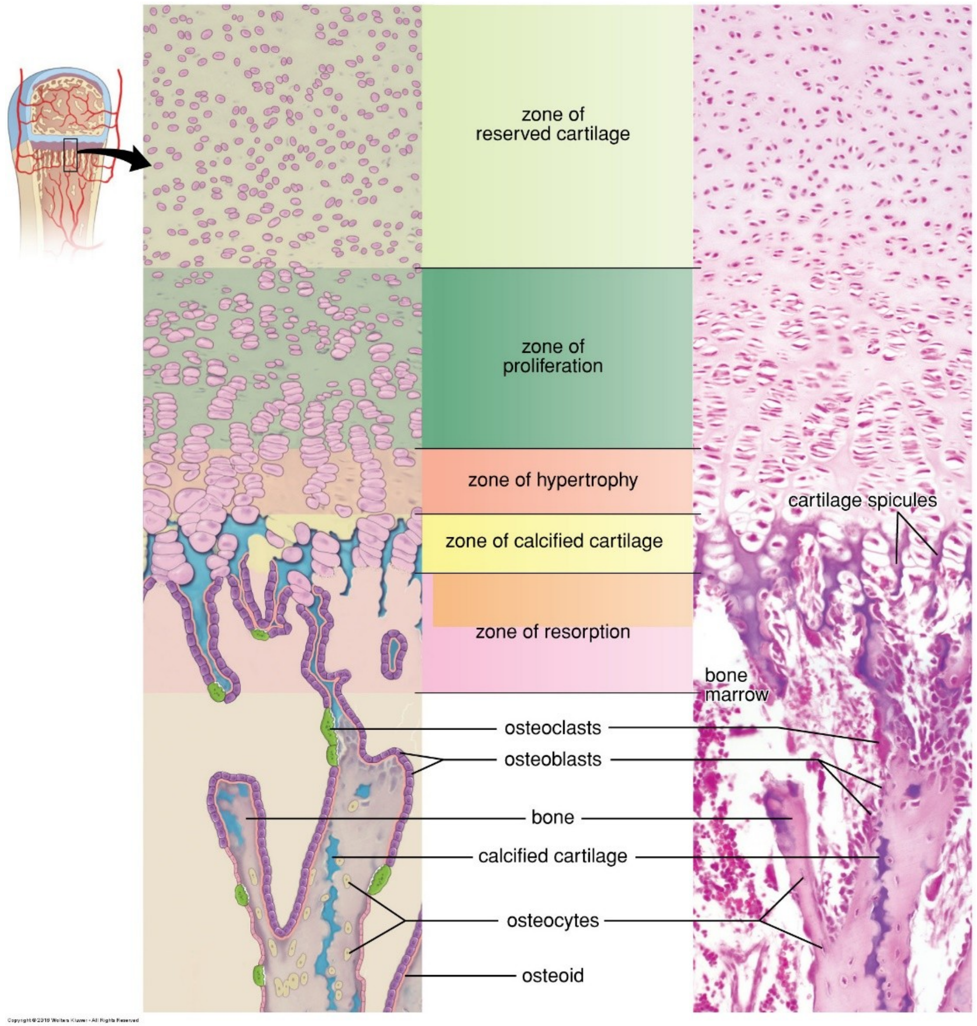
Zone of proliferation is adjacent to the zone of reservecartilage in the direction of the diaphysis. In thiszone, the cartilage cells undergo division and organize into distinct columns.

Zone of hypertrophy contains greatly enlarged (hypertrophic) cartilage cells.

Zone of calcified cartilage, the hypertrophied cells
begin to degenerate and the cartilage matrix becomes calcified. The calcified cartilage then serves as an initial scaffold for deposition of new bone.

Zone of resorption is the zone nearest the diaphysis. The calcified cartilage here is in direct contact with the connective tissue of the marrow cavity.

Zones in the Epiphyseal Cartilage

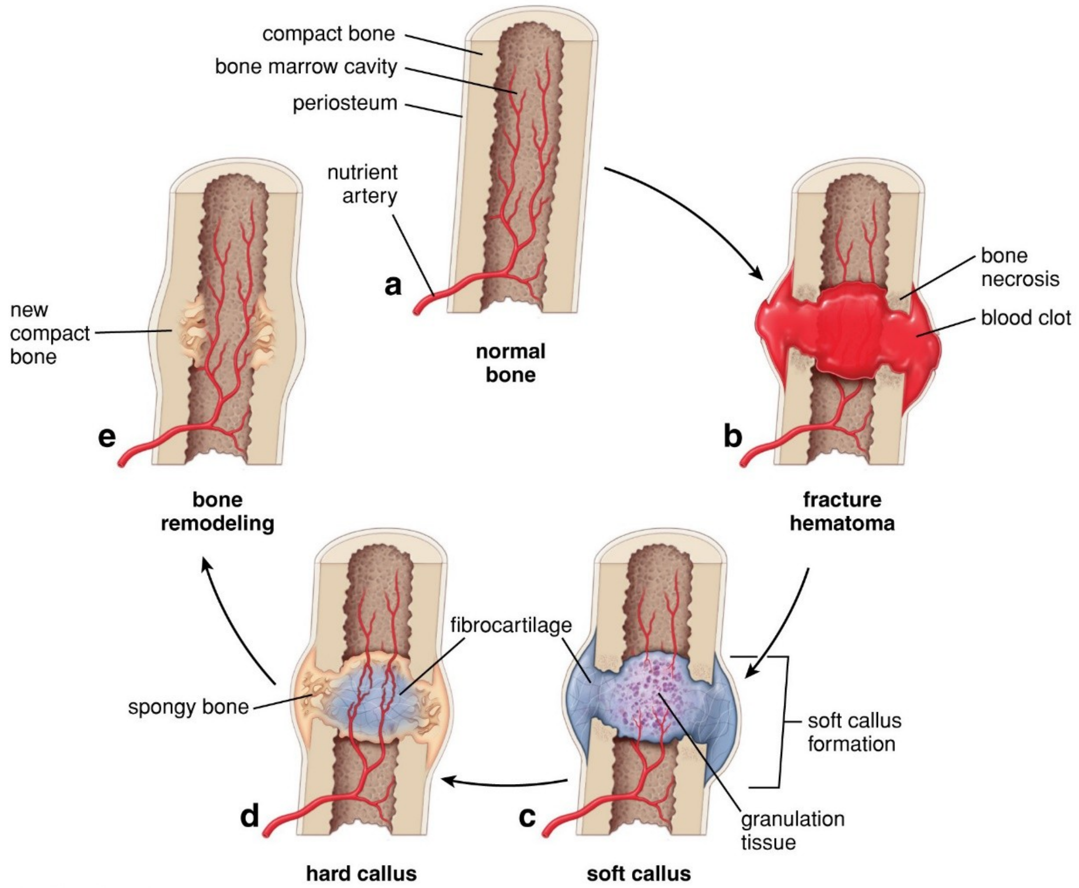


MEDICAL APPLICATION

Calcium deficiency in children can lead to rickets, a disease in which the bone matrix does not calcify normally and the epiphyseal plate can become distorted by the normal strains of body weight and muscular activity. Ossification processes are consequently impeded

http://highered.mheducation.com/sites/0072507470/student_view0/chapter6/animation__osteoporosis.html

Bone fractures and the stages of the bone healing process



MEDICAL APPLICATION

Bone fractures are repaired fibrocartilage formation and osteogenic activity of the major bone cells.

Bone fractures disrupt blood vessels, causing bone cells near the break to die.

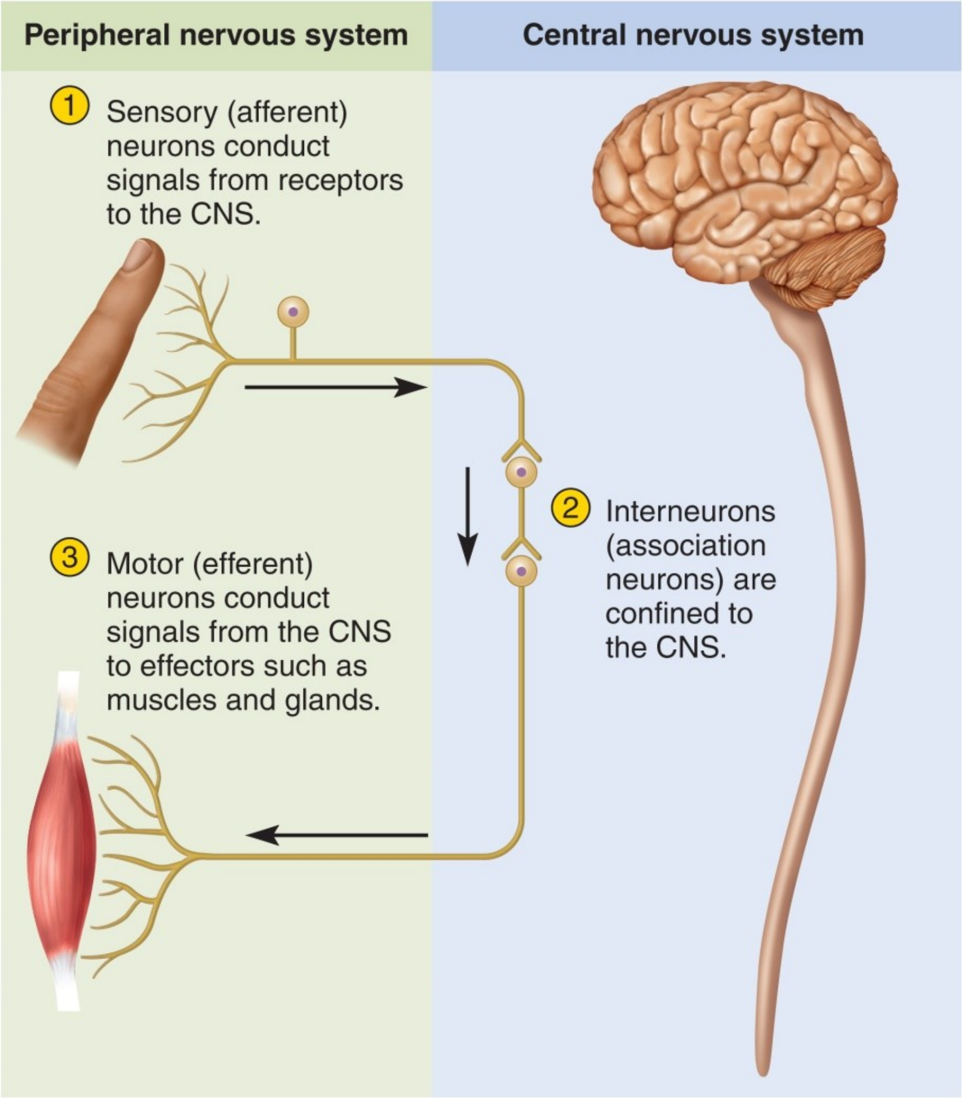
The damaged blood vessels produce a localized hemorrhage or hematoma. Clotted blood is removed along with tissue debris by macrophages and the matrix of damaged, cell-free bone is

Chapter 9 Nerve Tissue & The Nervous System Objectives

1. Overview of Nervous System
2. Neurons
3. Nerves
4. Glia
5. Meninges

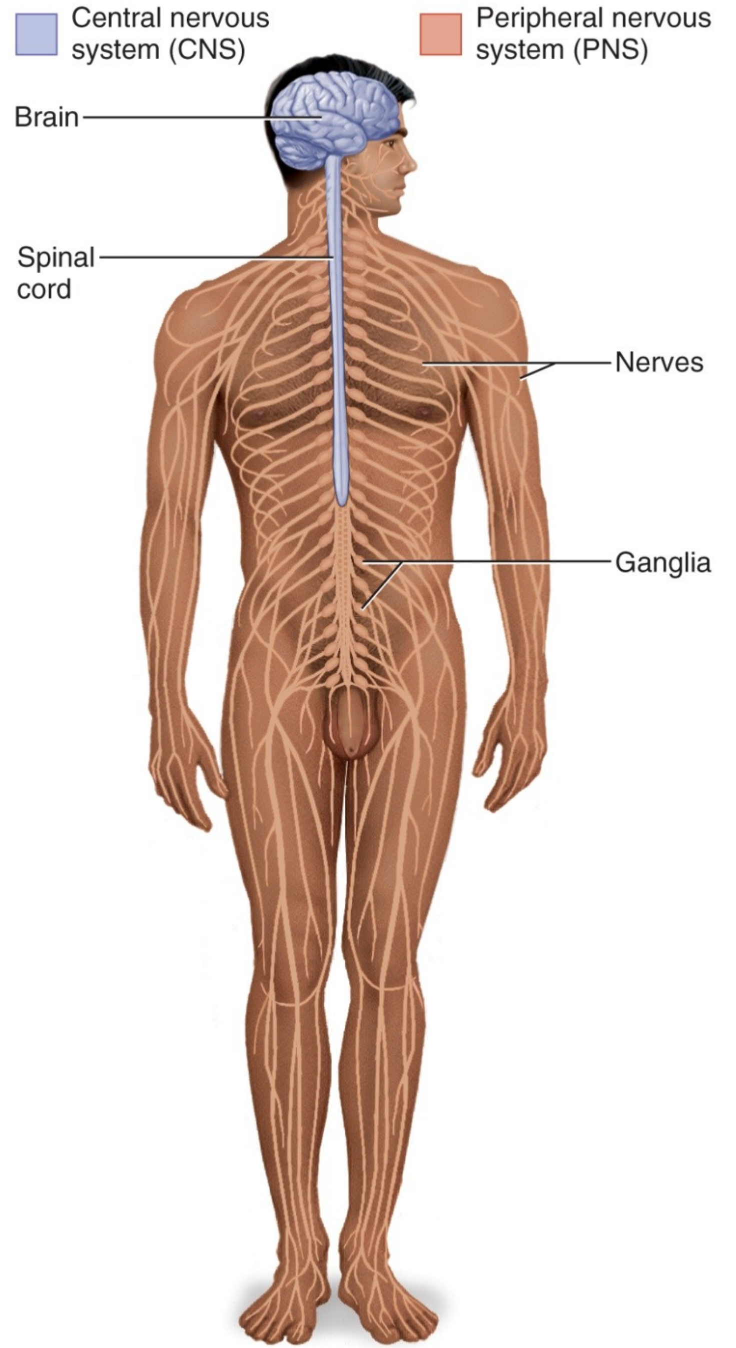
Cells and Tissues of the Nervous System: Functions and Divisions

- **Sensory function:** Respond to stimuli
- **Integrative function:** Receive and process information
- **Motor function:** Issue outgoing signals



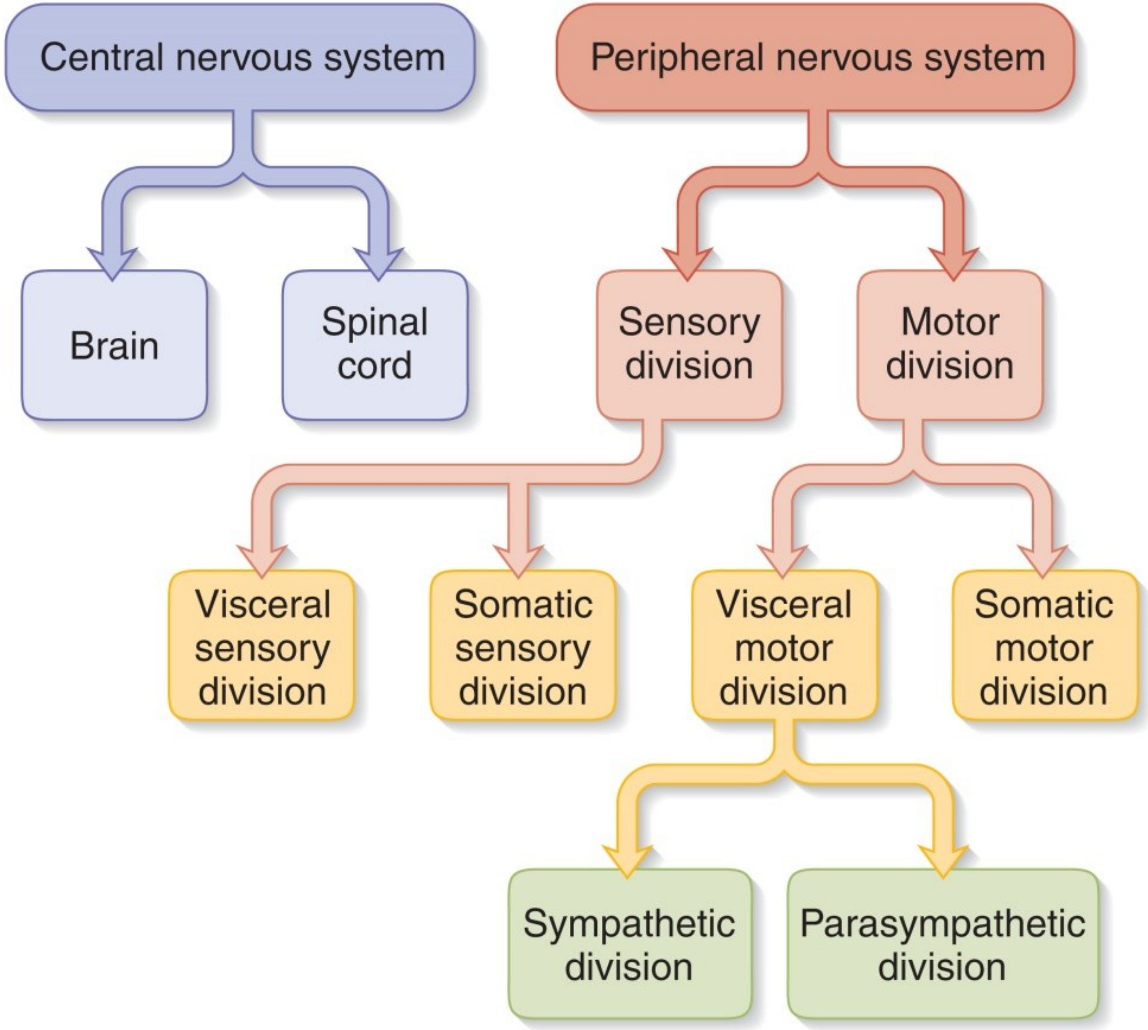
Two main anatomical subdivisions

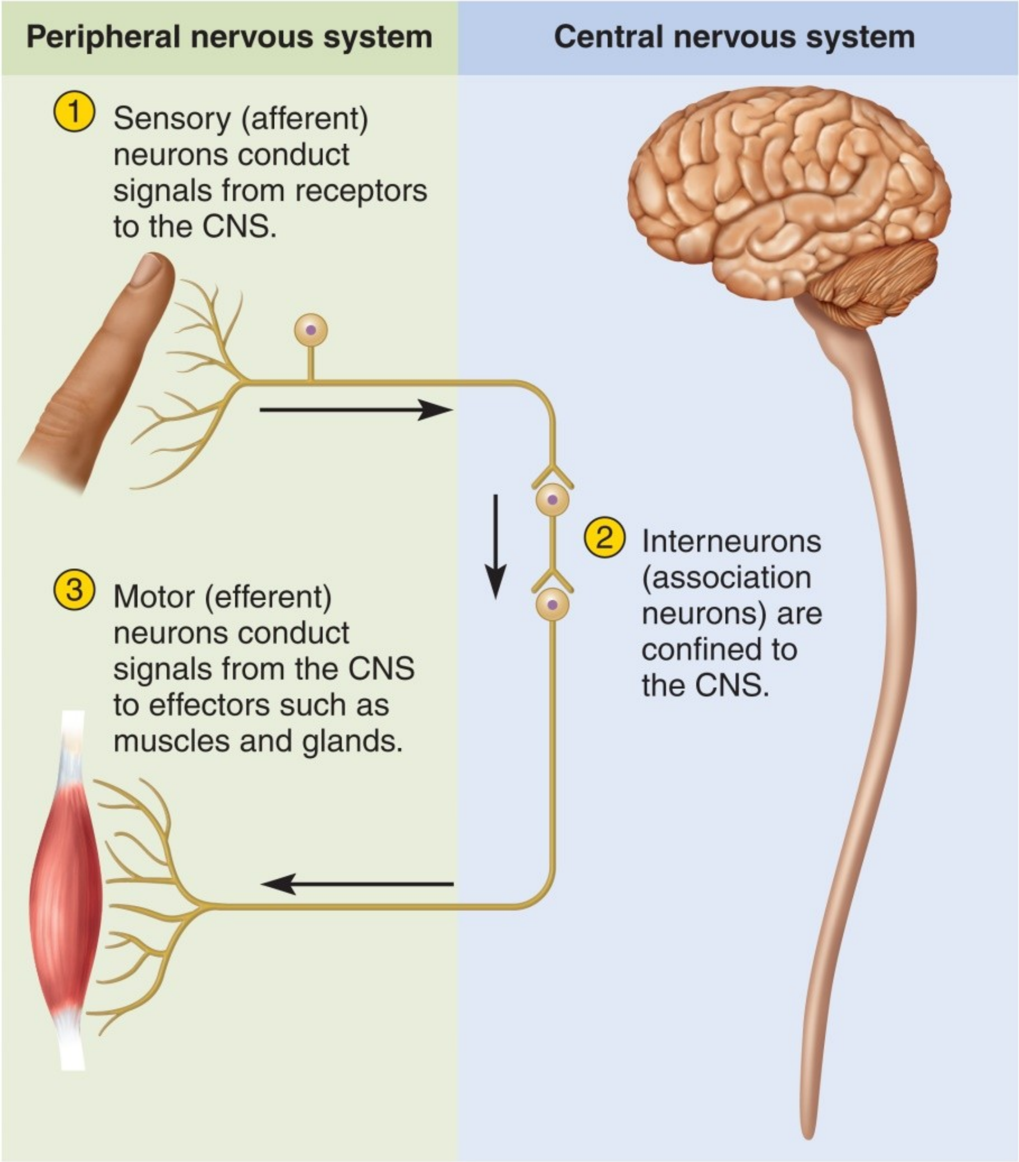
- **Central nervous system (CNS)**
  - Brain and spinal cord
  - Protected by cranium and vertebral column
  - Carries out integrative functions
- **Peripheral nervous system (PNS)**
  - Nerves leading to and from CNS
  - Provides pathway of signal input and output
  - Connects CNS to body's sense organs, muscles, and glands
  - Carries out sensory and motor functions



Overview of the Nervous System

- Peripheral nervous system has two major functional subdivisions
  - Sensory (afferent) division: carries sensory signals from various receptors to the CNS
    - Informs the CNS of stimuli within or around the body
  - Somatic sensory division: carries signals from receptors in the skin, muscles, bones, and joints
  - Visceral (Autonomic) sensory division: carries signals from the viscera of the thoracic and abdominal cavities
    - Heart, lungs, stomach, and urinary bladder





❯❯ MEDICAL APPLICATION

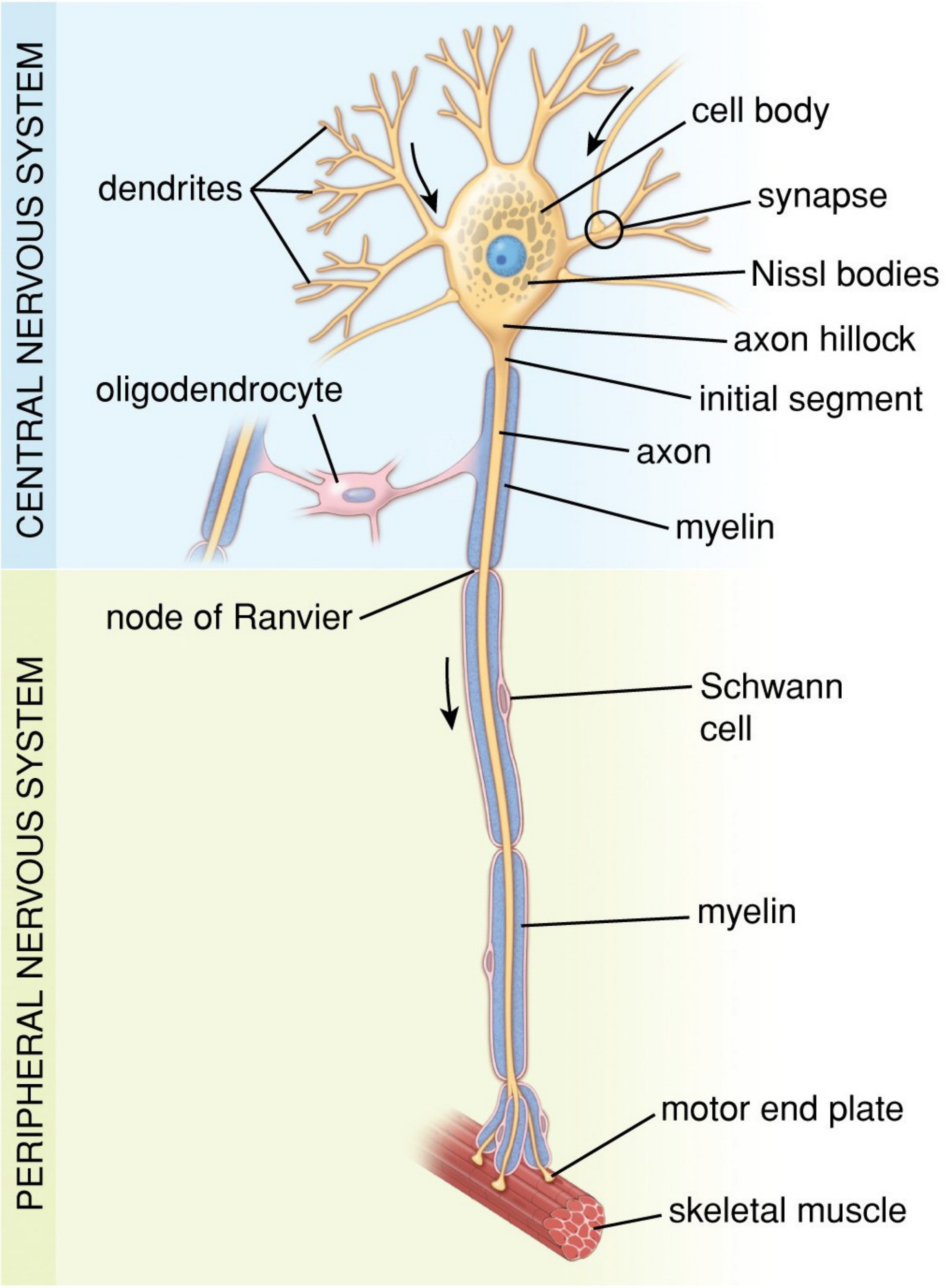
Parkinson disease is a characterized by muscle tremors, reduced activity of the facial muscles, loss of balance, and postural stiffness.

It is caused by gradual loss by apoptosis of dopamine-producing neurons whose cell bodies lie within the nuclei of the CNS substantia nigra. Parkinson disease is treated with l-dopa (L-3,4-dihydroxyphenylalanine), a precursor of dopamine which augments the declining production of this neurotransmitter.

http://abcnews.go.com/Health/video/dr-oliver-sacks-real-life-awakenings-29088197

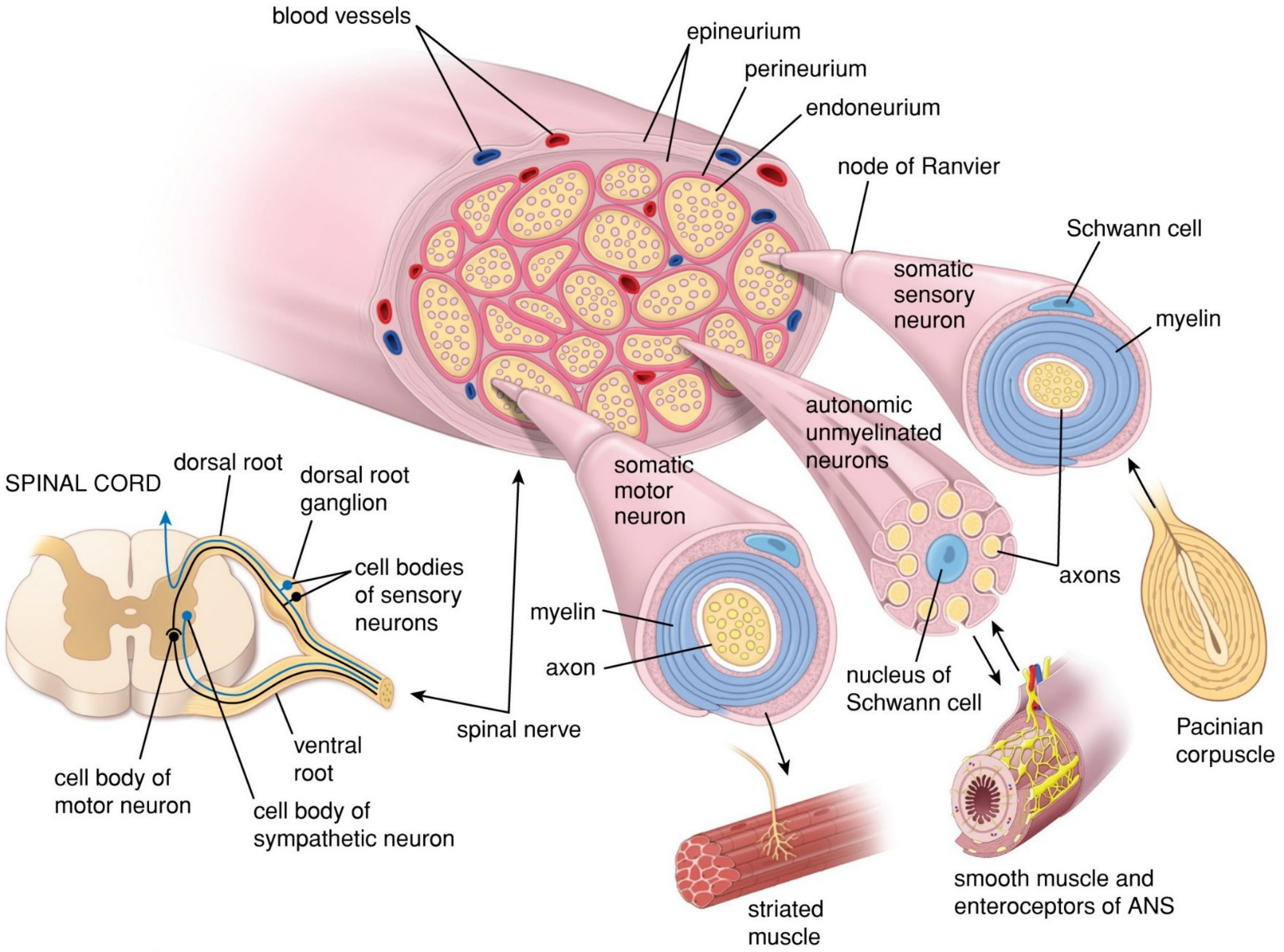
Neuron structure

- **Neurosoma (soma** or **cell body):** control center of neuron
- **Neurofibrils:** Cytoskeleton of protein bundles
- **Dendrites:** thick arms arising from soma, receives signals from other neurons
- **Axon (nerve fiber):** output pathway for signals to other cells not more than one, sometimes none
- **Synaptic knob:** bulb at terminus of axon
- **Axon hillock**: conical mound on soma side gives rise to axon
- **Axonal transport:** process of carrying substances to and from soma



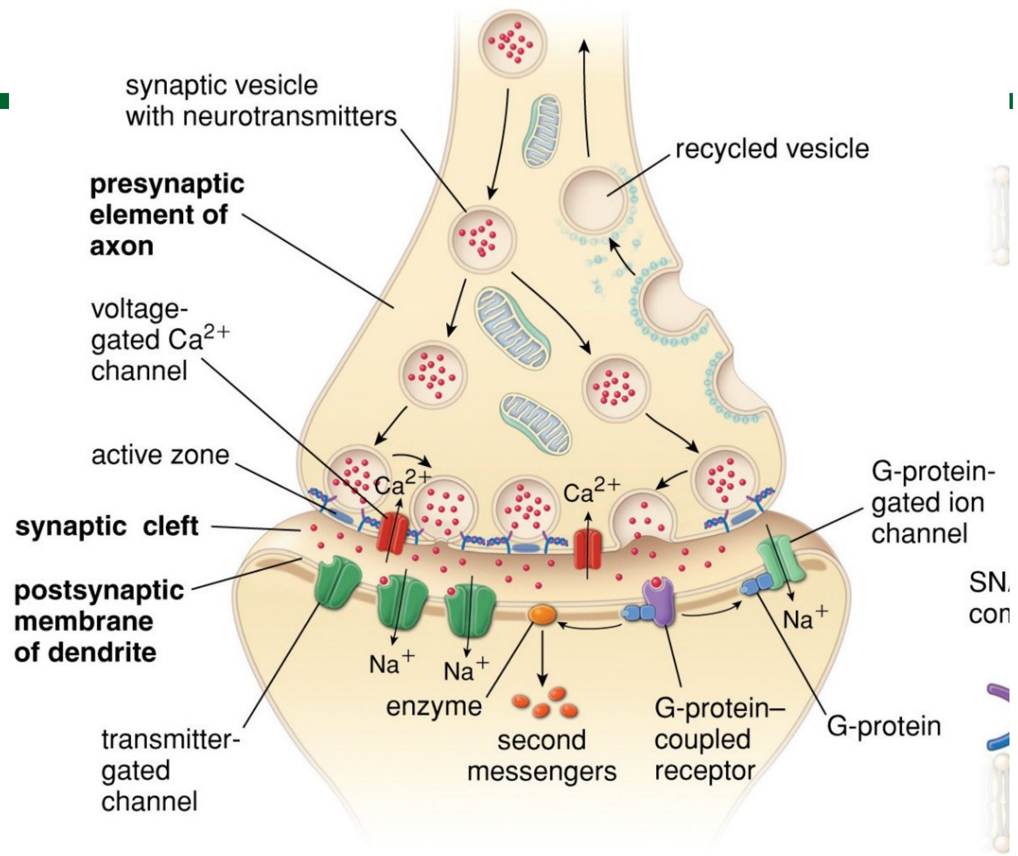
Nerve: Bundle of nerve fibers and connective tissue wrappings with internal blood vessels

- **Endoneurium:** thin loose connective tissue covering nerve fiber
- **Perineurium:** epithelium-like cells, wrapped bundles of nerve cells, **fascicles**
- **Epineurium:** fibrous sleeve wrapping several fascicles
- **Ganglion:** Swelling, usually near end of nerve that contains cell bodies of peripheral neurons



Review of the Synapse

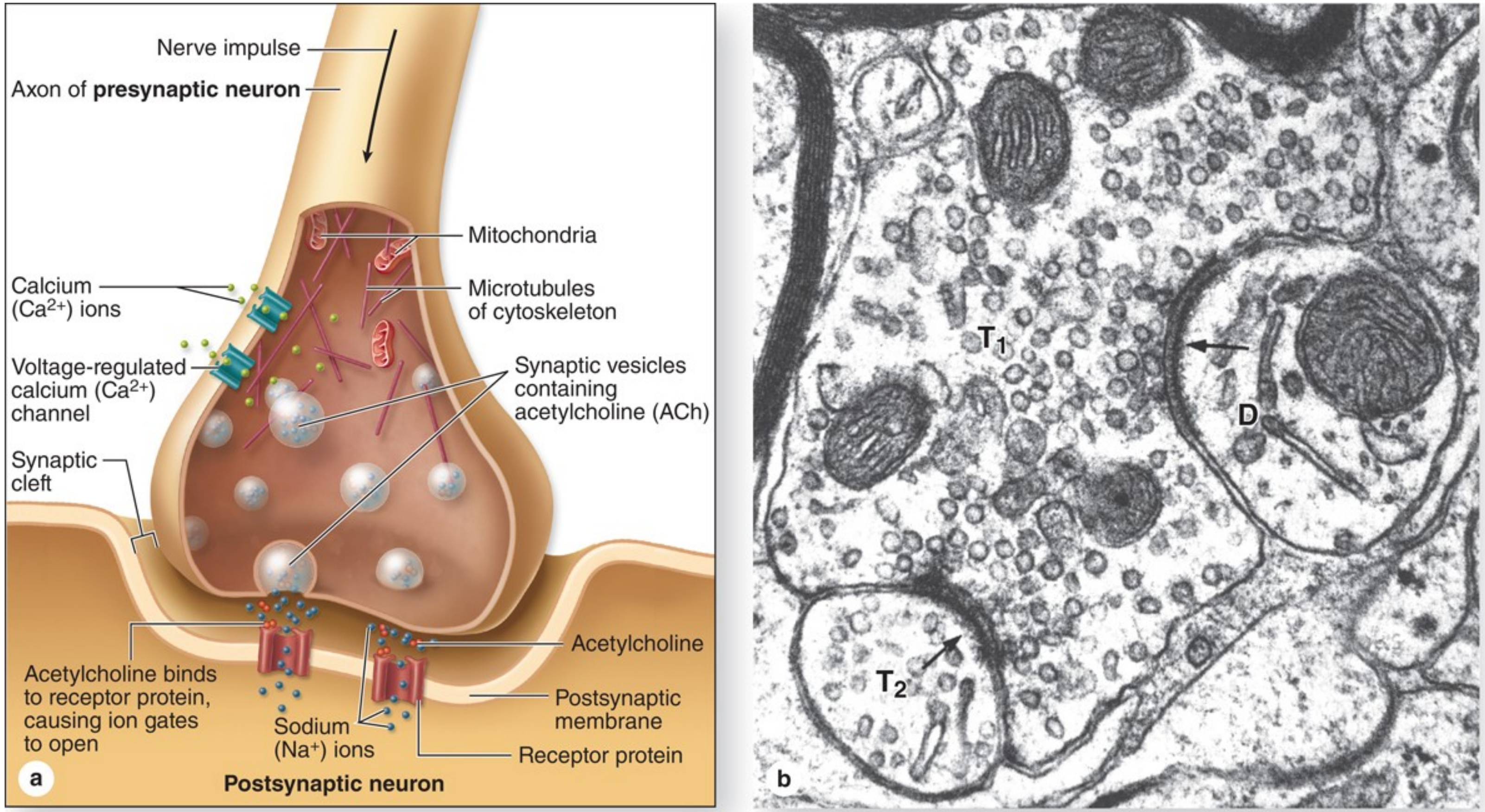
Presynaptic neuron: sends signal
Postsynaptic neuron: stimulated neuron
Synaptic cleft: gap between two neurons
Synaptic knob: Dilated tip of presynaptic neuron
Synaptic vesicles: spherical vesicles with
Neurotransmitters: chemical signals, undergo exocytosis with arrival of nerve signal



❯❯ MEDICAL APPLICATION

Most local anesthetics are low-molecular-weight molecules that bind to the voltage-gated sodium channels of the axolemma, interfering with sodium ion influx and, consequently, inhibiting the action potential responsible for the nerve impulse.

http://highered.mheducation.com/sites/0072495855/student_view0/chapter14/animation__transmission_across_a_synapse.html



❯❯ MEDICAL APPLICATION

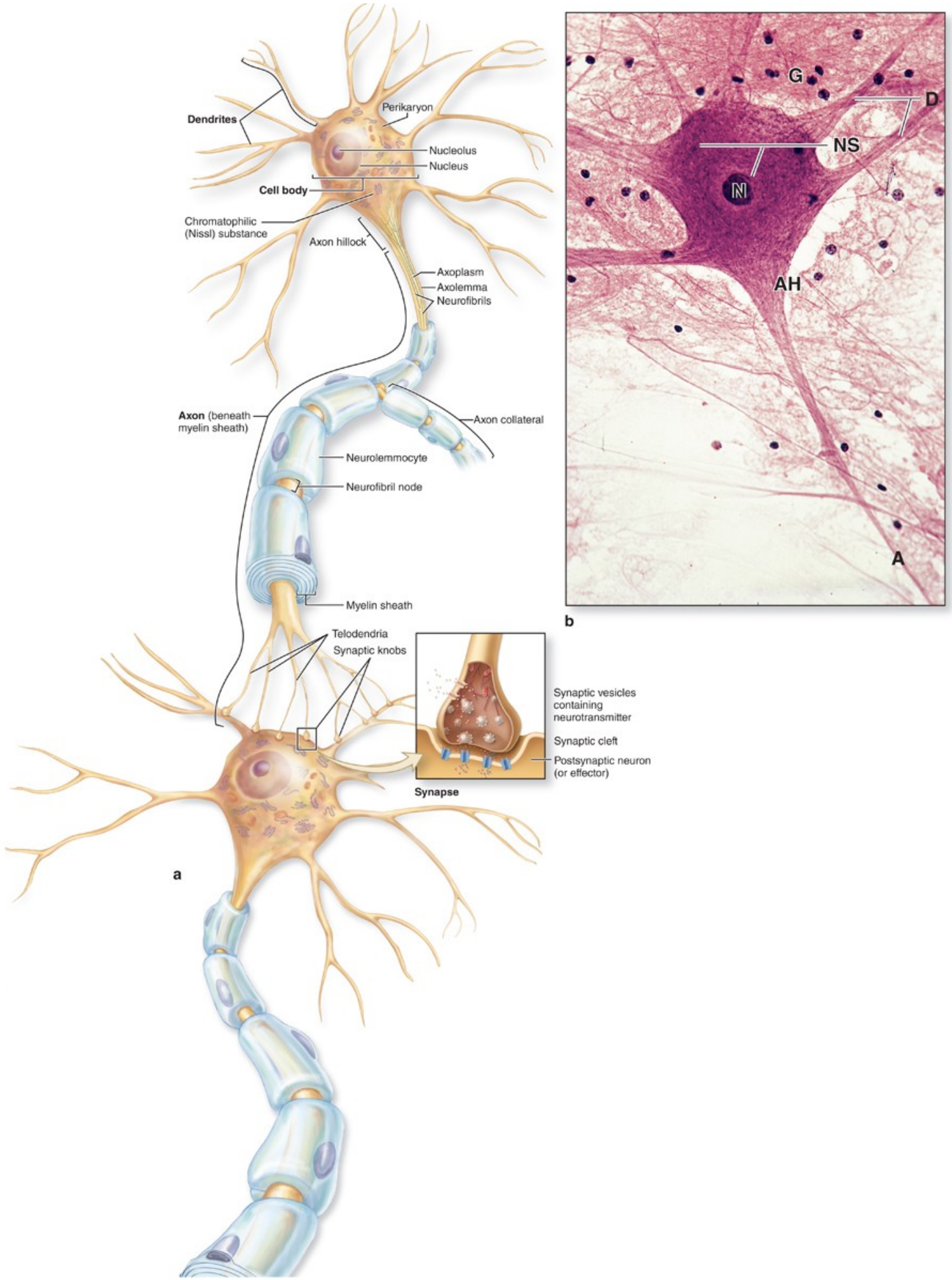
Alzheimer's disease, a common type of dementia in the elderly, affects both neuronal perikarya and synapses within the cerebrum. Functional defects are due to neurofibrillary tangles, which are accumulations of tau protein associated with microtubules of the neuronal perikaryon and axon hillock regions, and neuritic plaques, which are dense aggregates of β-amyloid protein that form around the outside of these neuronal regions.

❯❯ MEDICAL APPLICATION

Levels of neurotransmitters in the synaptic cleft and available for binding postsynaptic receptors are normally regulated by several local mechanisms. Selective serotonin reuptake inhibitors (SSRIs), a widely used class of drugs for treatment of depression and anxiety disorders, were designed to augment levels of this neurotransmitter at the postsynaptic membrane of serotonergic CNS synapses by specifically inhibiting its reuptake at the presynaptic membrane.

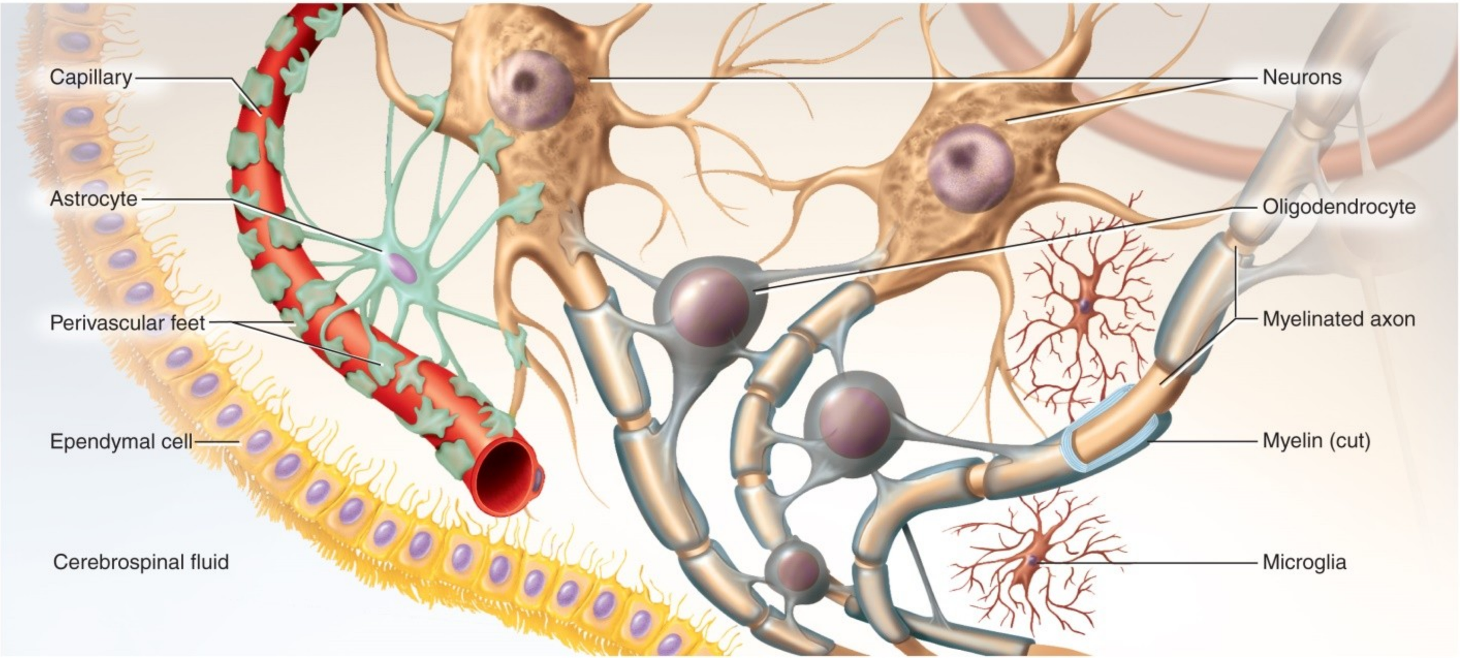
Supportive Cells (Neuroglia)

- Neuroglia outnumber the neurons by as much as 50 to 1
- Neuroglia or glial cells
  - Support and protect the neurons
  - Bind neurons together and form framework for nervous tissue
  - In fetus, guide migrating neurons to their destination
  - If mature neuron is not in synaptic contact with another neuron it is covered by glial cells
    - Prevents neurons from touching each other
    - Gives precision to conduction pathways



Types of Neuroglial Cells: CNS

- **Oligodendrocytes** form myelin sheaths in CNS: each wraps around many nerve fibers
- **Ependymal** cells line cavities and produce CSF
- **Microglia** (macrophages) formed from monocytes in areas of infection, trauma or stroke
- **Astrocytes:** contribute to BBB and regulate composition of brain tissue fluid



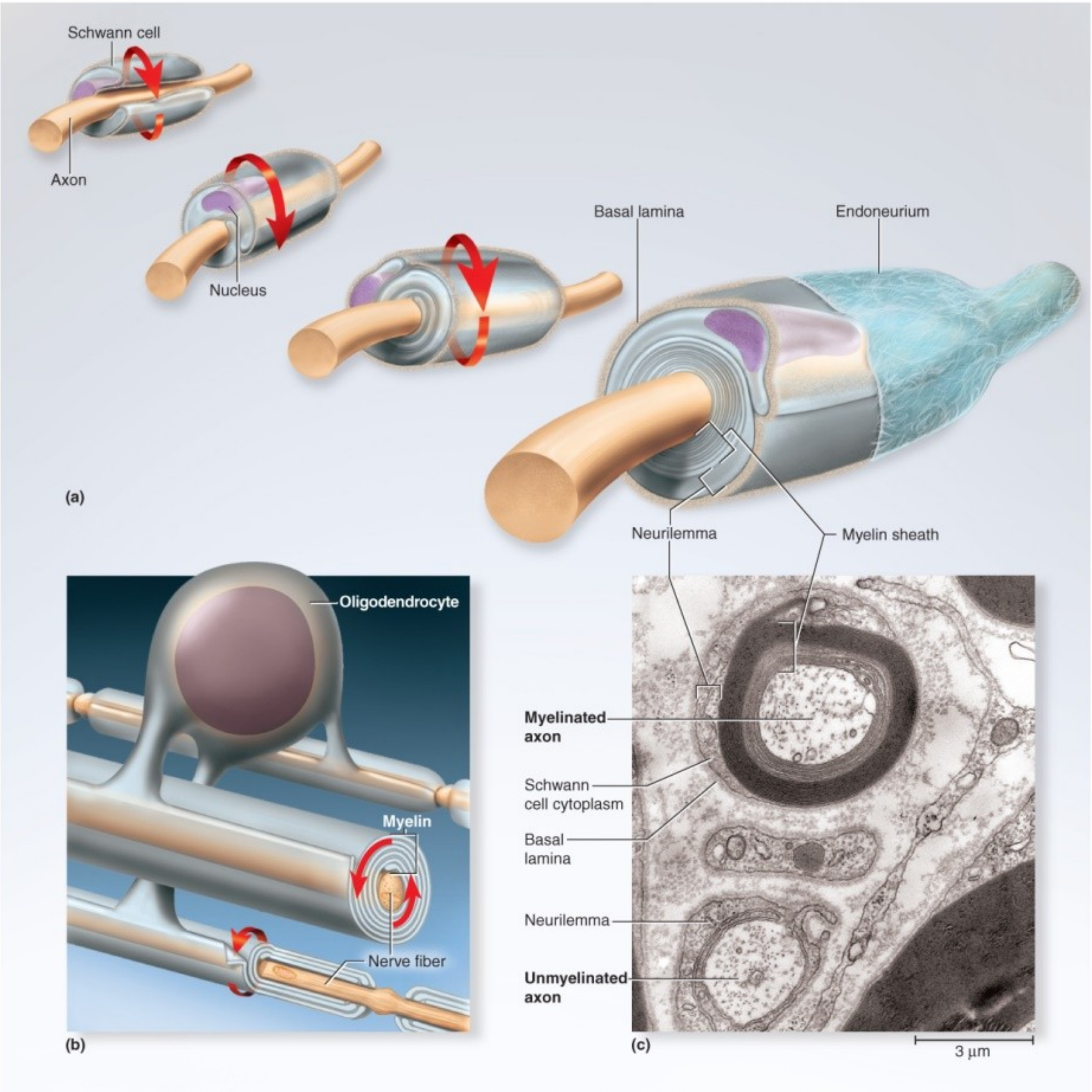
Types of Neuroglial Cells PNS

Schwann cells myelinate fibers of PNS
Satellite cells thought to have same function as astrocytes

❯❯ MEDICAL APPLICATION

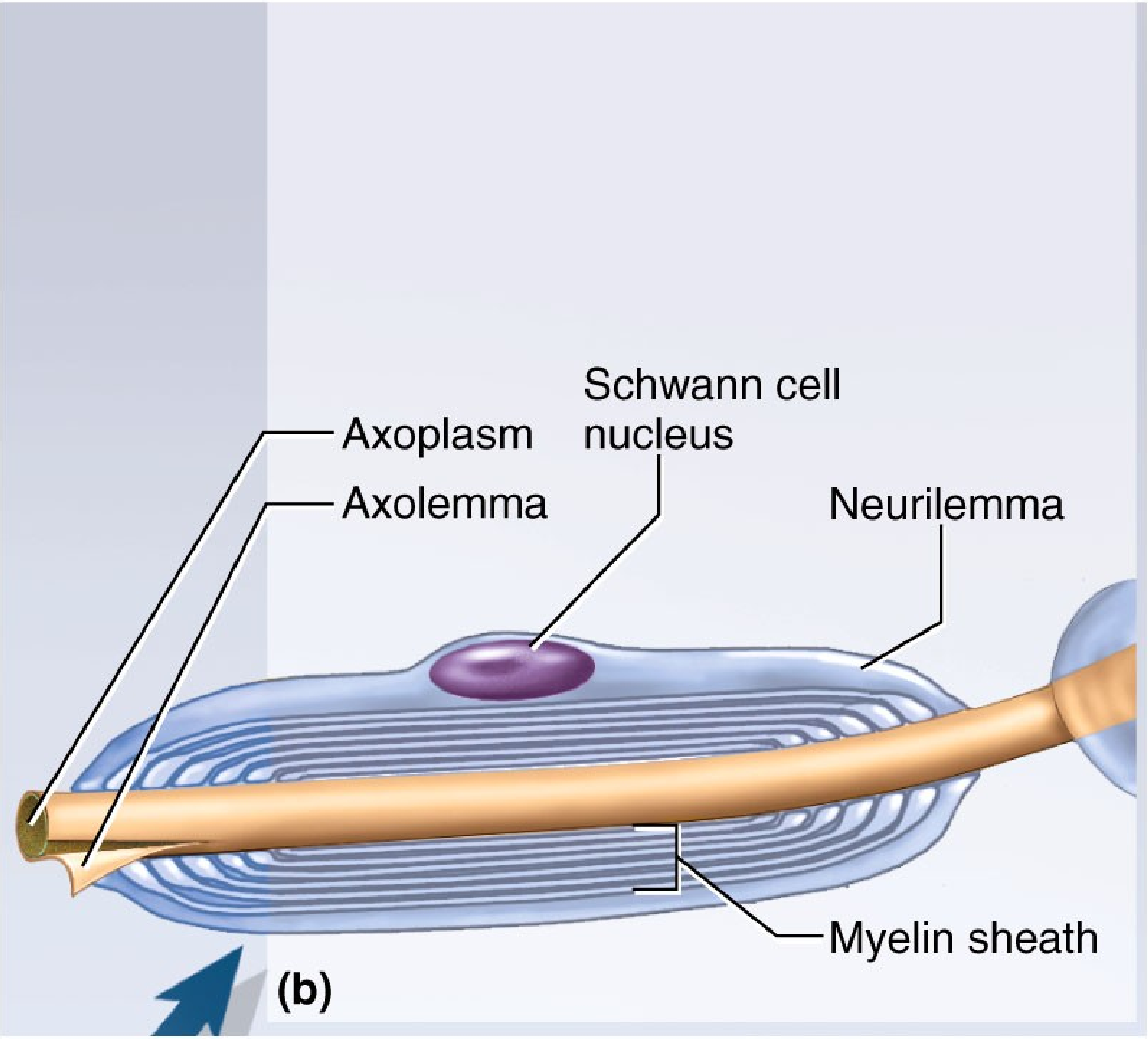
In multiple sclerosis (MS) myelin sheaths are damaged by an autoimmune mechanism. T lymphocytes and microglia degrade myelin.

Introduction to Multiple Sclerosis - Medical Animation Short: https://www.youtube.com/watch?v=VIoDr8ugbqI



The Myelin Sheath

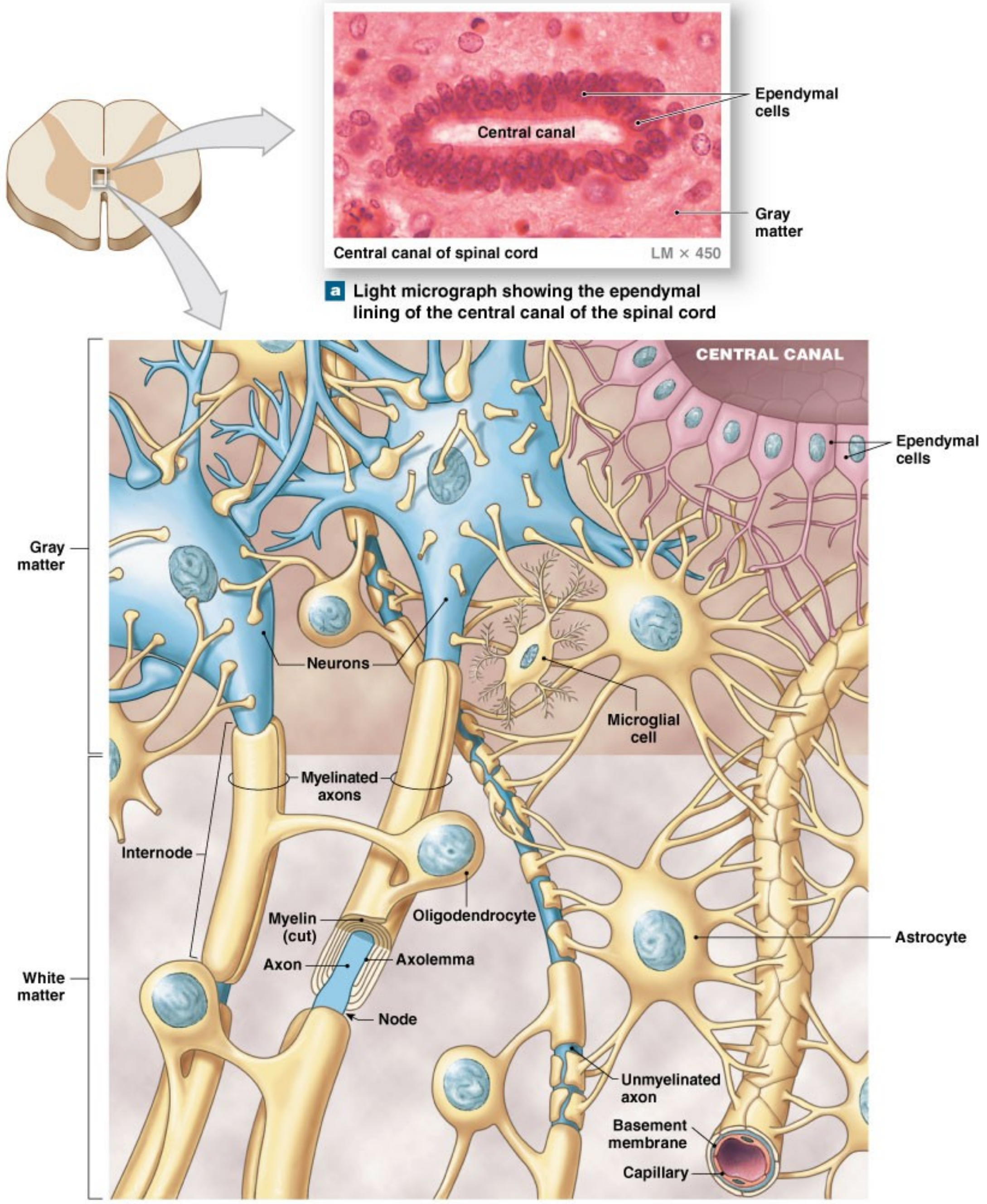
- **Myelin sheath characteristics**
  - Layers wrapped around fiber, insulating it
    - like electrical tape around wire
  - Requires many cells to myelinate one nerve
  - **Nodes of Ranvier**
    - gaps between myelinated segments
  - Myelin covered segments termed **internodes**



Myelination

White matter: Regions of CNS with many myelinated nerves
- Bundles of nerve fibers called tracts, each with similar origin, destination, and function
- Myelination giving white color

Gray matter: Unmyelinated areas of CNS where neurosomas, dendrites, and synapses are located
- Little myelin, so duller color
- Information-processing part of CNS



a Light micrograph showing the ependymal lining of the central canal of the spinal cord

b A diagrammatic view of neural tissue in the CNS, showing relationships between neuroglia and neurons

Meninges: Protective Membranes

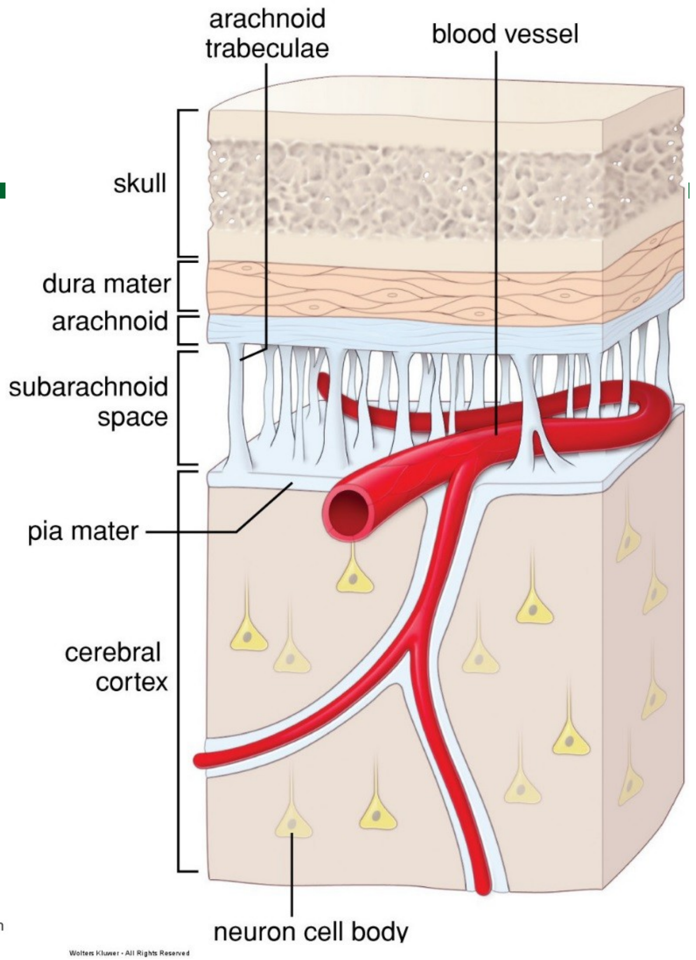
Meninges: Fibrous membranes between nervous tissue and bone

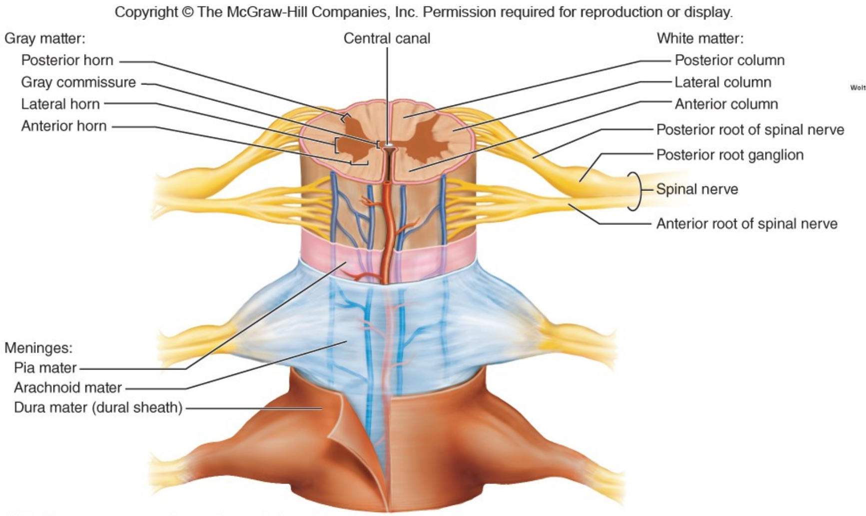
Dura mater: Tough collagenous outermost membrane

- Separated from bone by epidural space, anesthetics often used here

Arachnoid mater: Delicate middle layer, Loose webby appearance

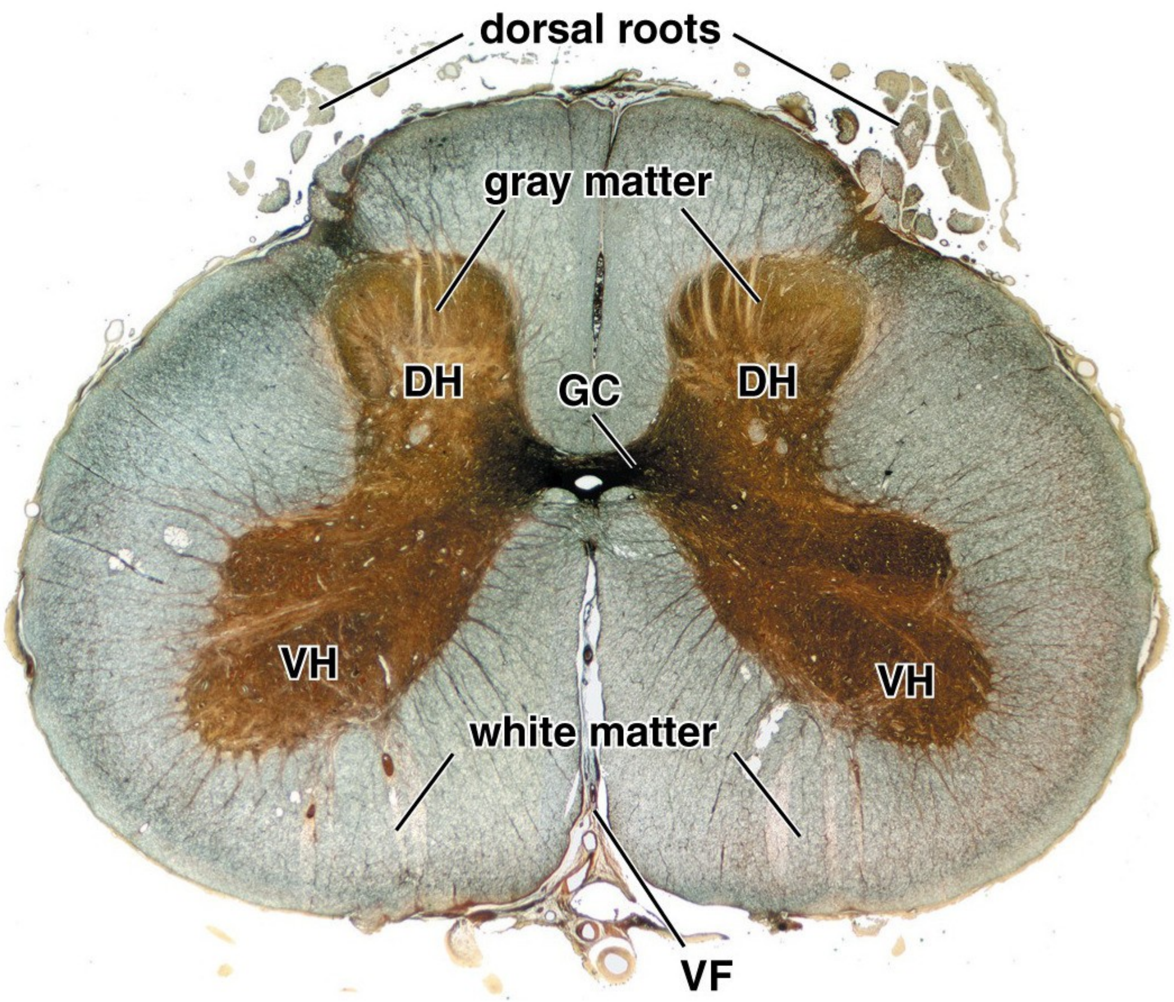
Pia mater: Innermost thin layer of connective tissue, follows contours of brain and spinal cord





(b) Spinal cord and meninges (thoracic)

Cross-section of the human spinal cord



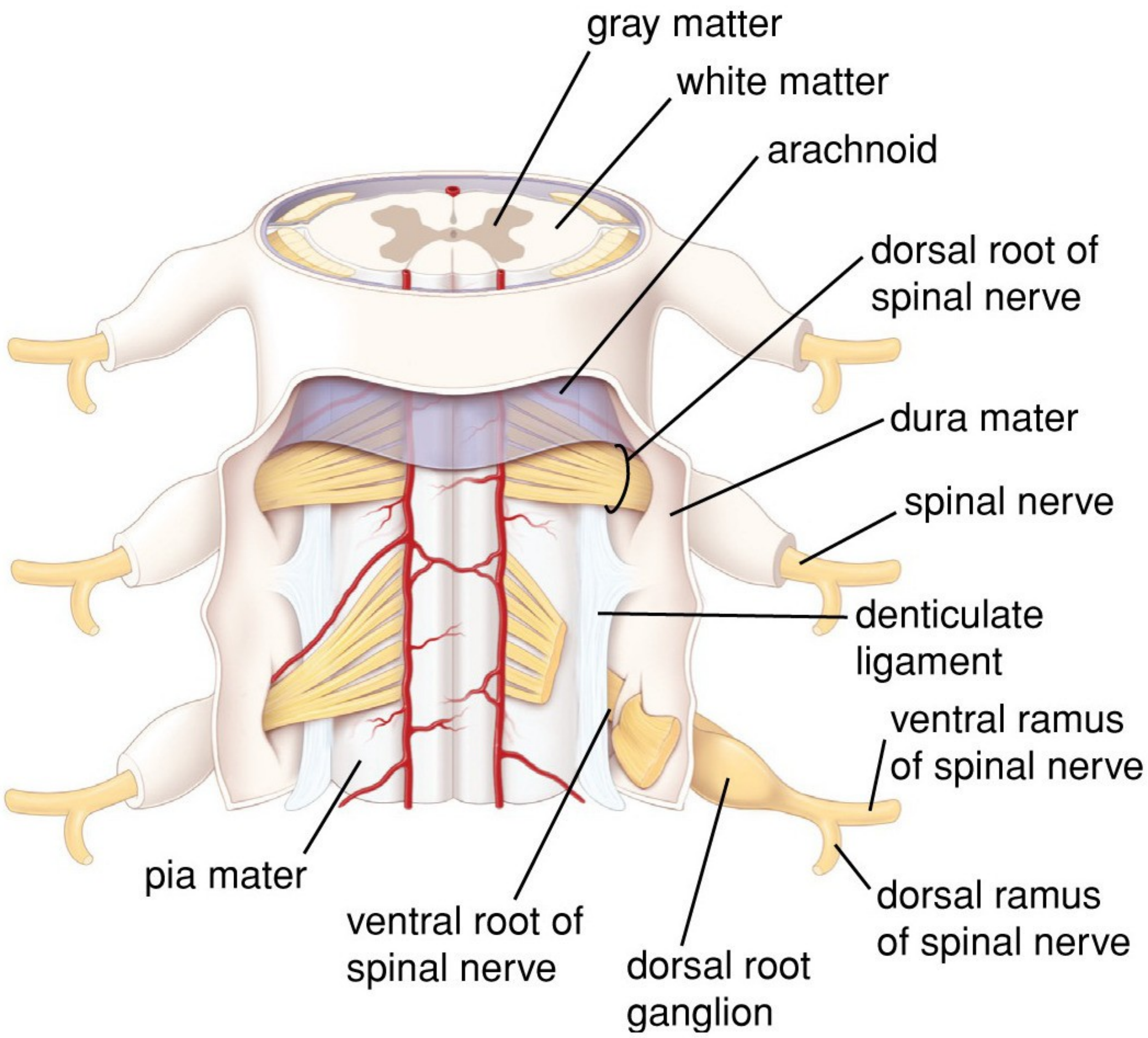
The spinal cord is organized into an outer part, the white matter, and an inner part, the gray matter that contains nerve cell bodies and associated nerve fibers.

The gray matter of the spinal cord appears roughly in the form of a butterfly. The anterior and posterior prongs are referred to as ventral horns (VH) and dorsal horns (DH), respectively. They are connected by the gray commissure (GC).

The white matter contains nerve fibers that form ascending and descending tracts. The outer surface of the spinal cord is surrounded by the pia mater.

Cord cross section

Posterior (dorsal) horns: sensory reception
Anterior (ventral) horns: motor neurons give motor commands through axons/spinal nerve
Lateral horn: neurons of sympathetic nervous system
Gray commissure: connects right and left halves of cord. May have **central canal** filled with spinal fluid or closed

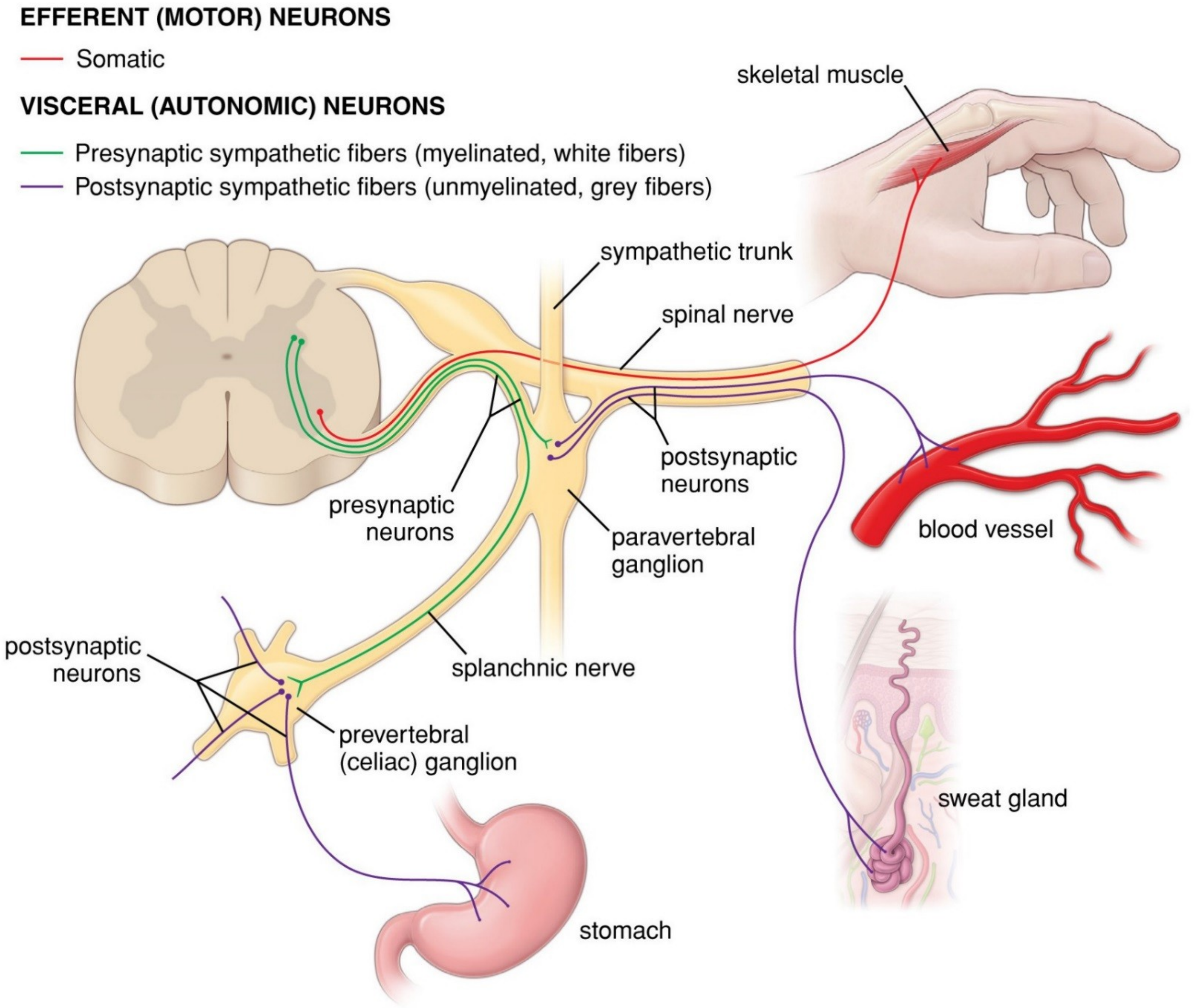


❯❯ **MEDICAL APPLICATION** regeneration of peripheral nerves is functionally efficient only when the fibers and the columns of Schwann cells are directed properly. In a mixed nerve, if regenerating sensory fibers grow into columns formerly occupied by motor fibers connected to motor end plates, the function of the muscle will not be reestablished.

Flow of information through the spinal cord

Somatic efferent (motor) system: one neuron conducts the impulses from the CNS to the effector (skeletal muscle).

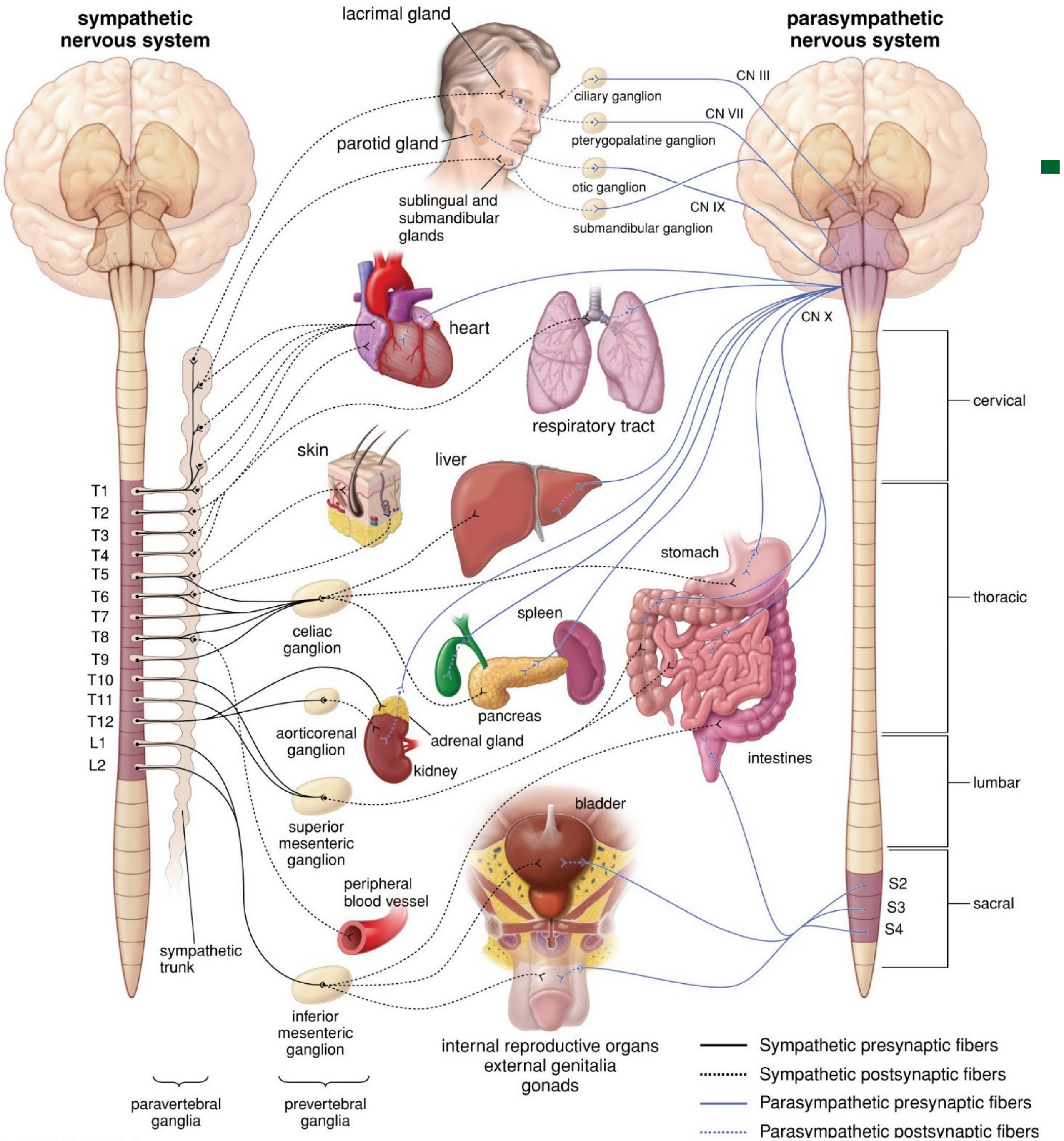
Visceral (autonomic) efferent system: chain of two neurons conducts the impulses, a presynaptic neuron located within the CNS and a postsynaptic neuron located in the paravertebral or prevertebral ganglia.



Autonomic Nervous System

The sympathetic outflow is shown on the left, the parasympathetic on the right.

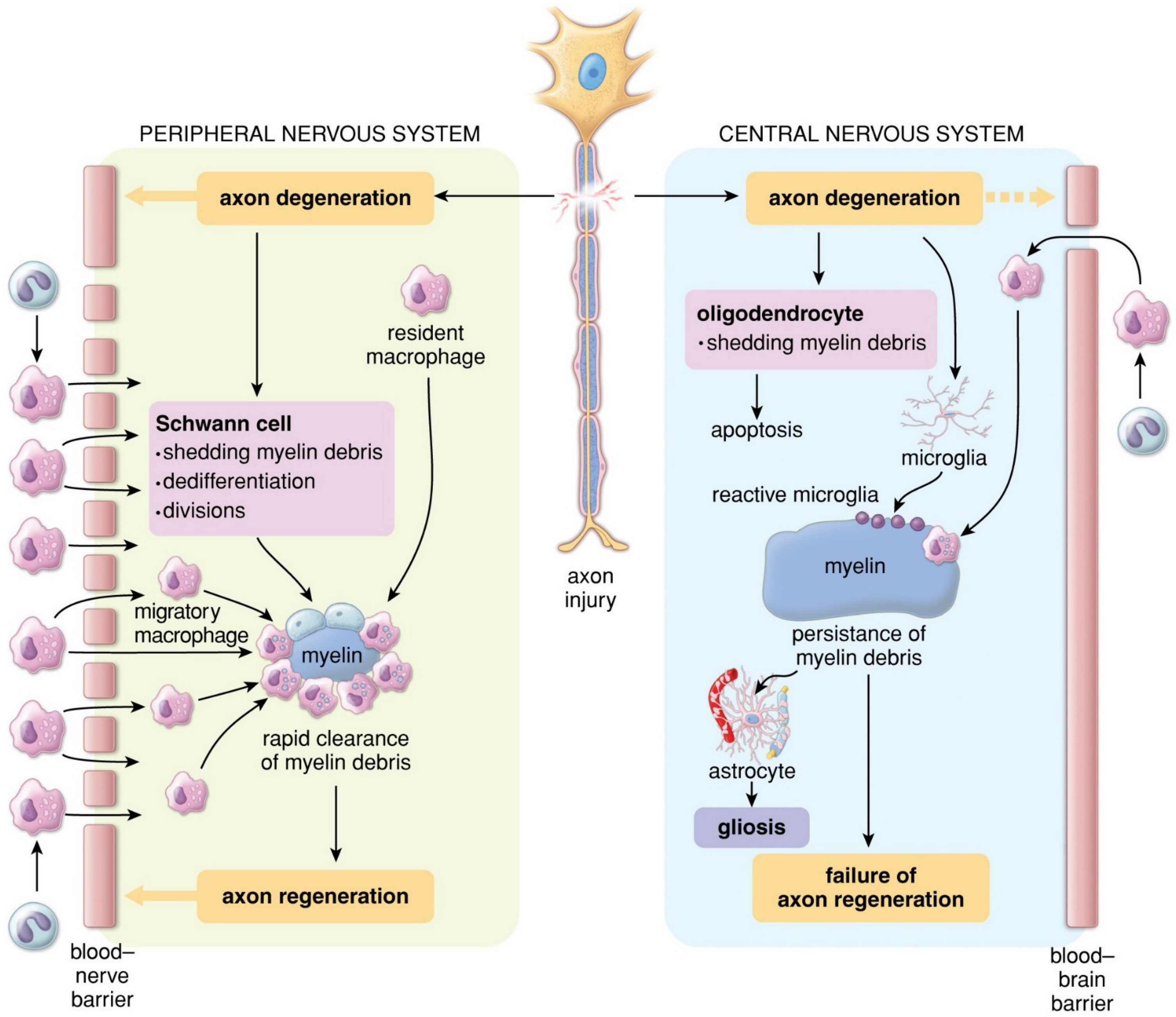
The sympathetic (thoracolumbar) outflow leaves the CNS from the thoracic and upper lumbar segments (T1 to L2) of the spinal cord.



Response to neuronal injury within peripheral and central nervous systems

Injuries induces axonal degeneration and neural regeneration.

Involves neurons, Schwann cells, oligodendrocytes, macrophages and microglia.



Chapter 10 Muscle Objectives

1. Skeletal muscle: Organization and physiology
2. Cardiac Muscle
3. Smoot Muscle

Functions of the Muscular system

Muscle is composed of elongated cells that contract

- Converts chemical energy of ATP into mechanical energy

Movement: Externally visible movements

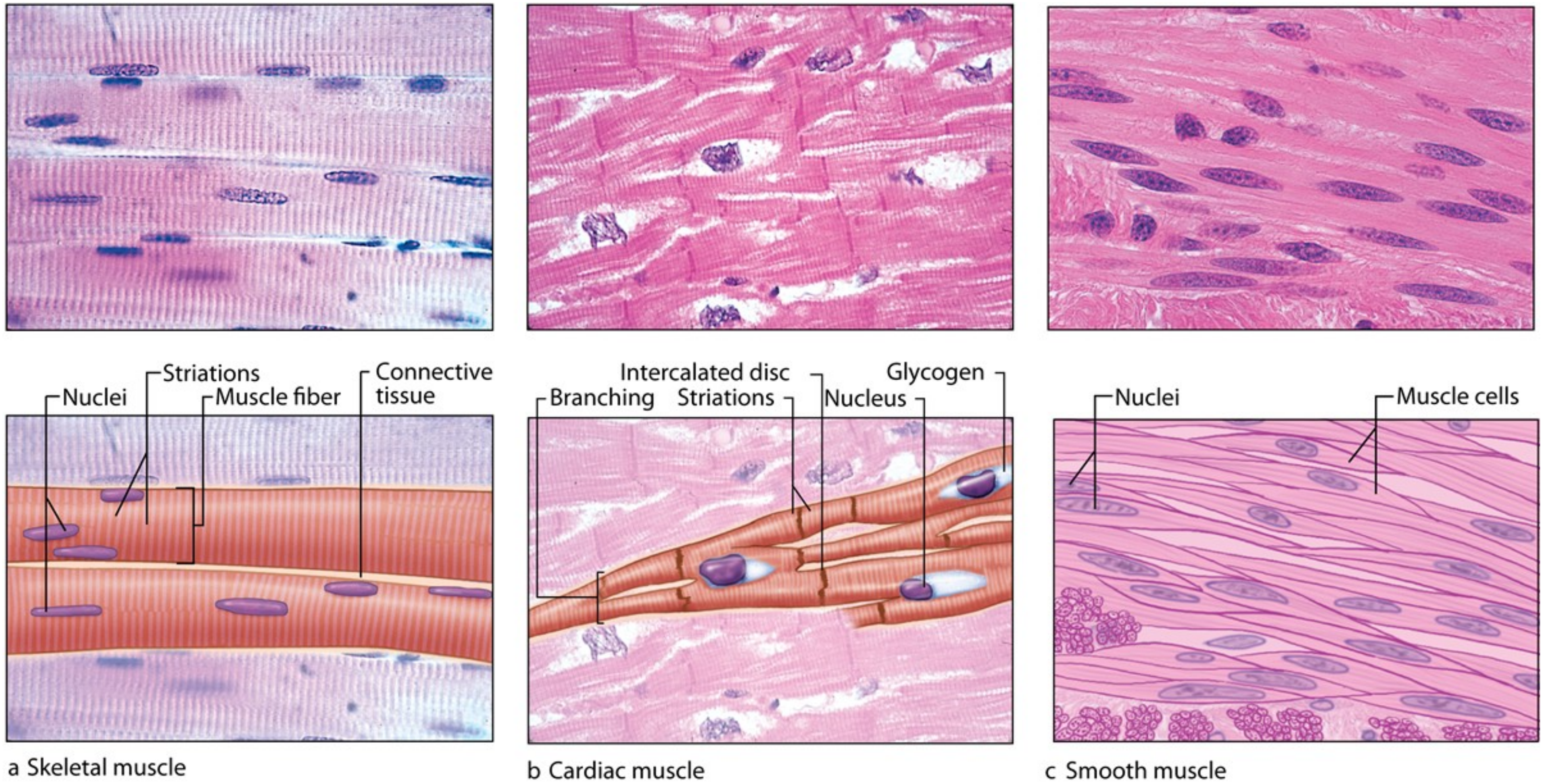
- Also internal movements e.g., propulsion of digestive tract and expulsion of urine
- Important roles in communication: speech, writing, etc.

Stability: Prevent unwanted movement e.g., posture and holding bones in place

Control of body openings and passages E.g., **sphincter muscles** around eyelids, regulating waste elimination

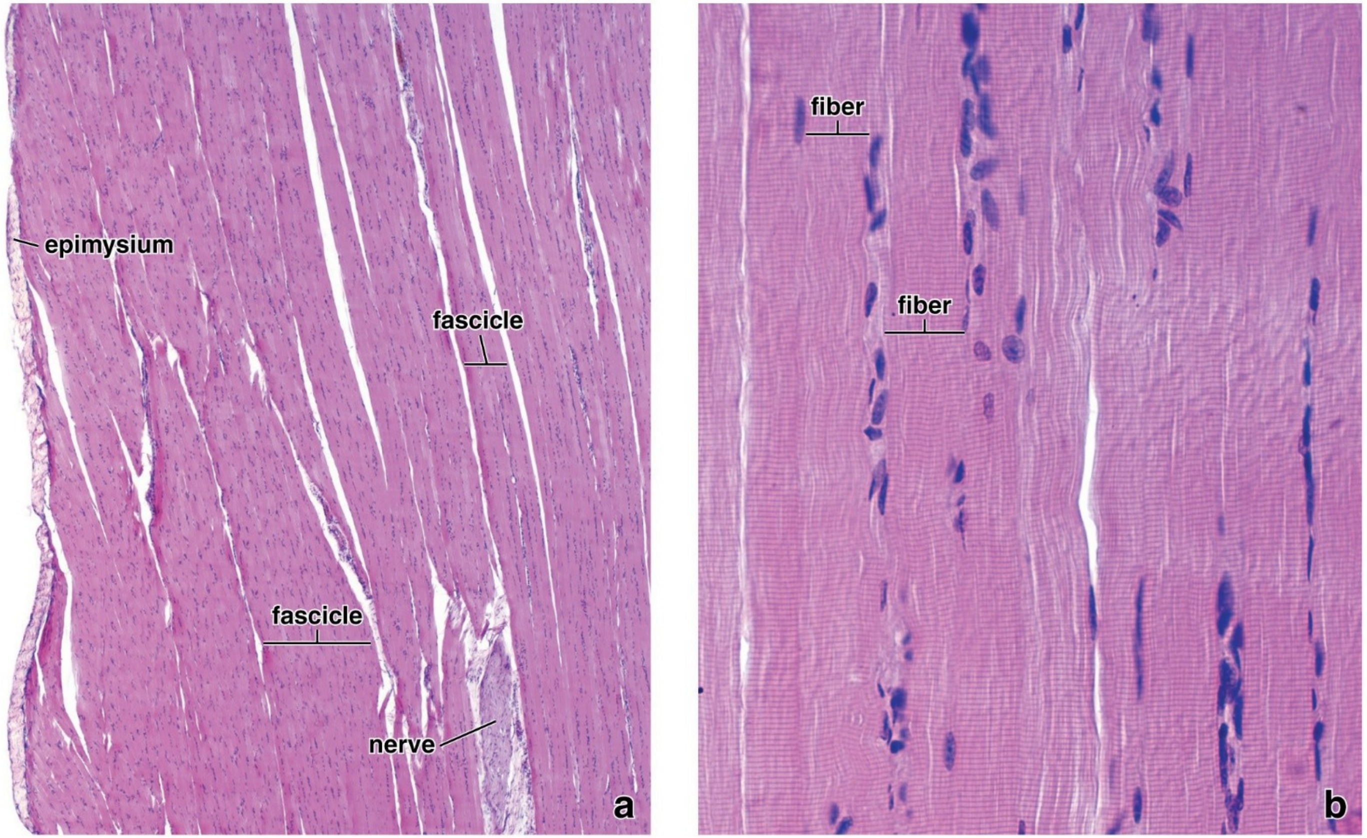
Heat generation: Muscles generating 20 to 30% of body heat at rest

Glycemic control: Aids regulation of blood glucose



(a) **Skeletal muscle:** large, elongated, multinucleated fibers that show strong, quick, voluntary contractions.
(b) **Cardiac muscle:** irregular branched cells bound together longitudinally by intercalated discs and shows strong, involuntary contractions.
(c) **Smooth muscle:** grouped, fusiform cells with weak, involuntary contractions.

Skeletal Muscle Fibers



Voluntary: subject to conscious control

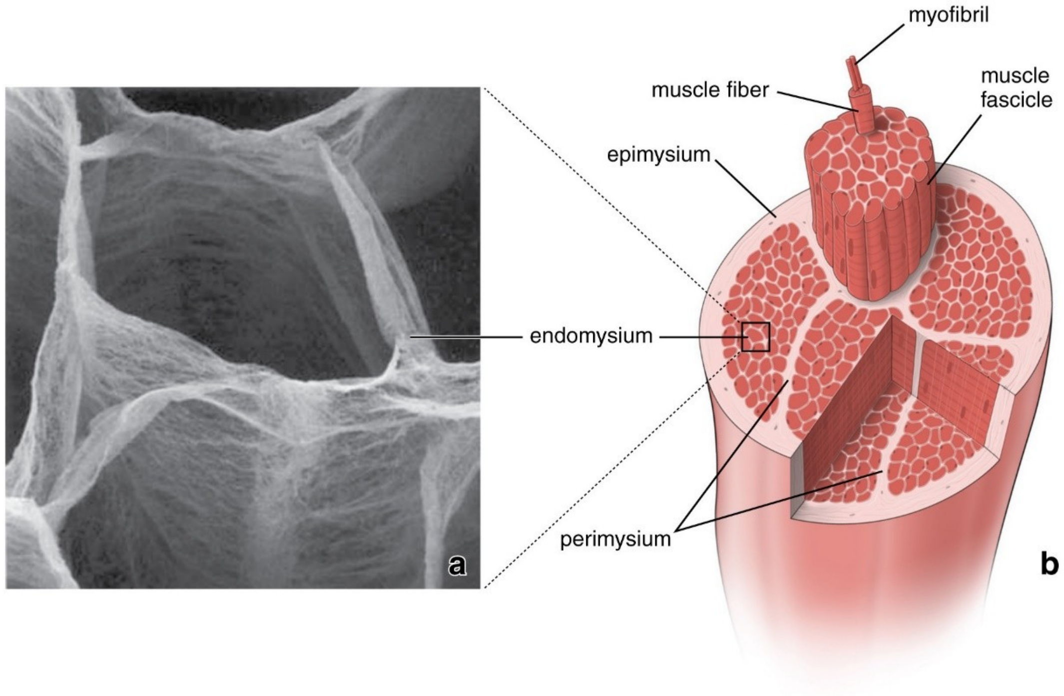
Striated: alternating light and dark bands, or **striations** reflect overlapping arrangement of internal proteins

Skeletal muscle cells: multinucleate termed **muscle fibers** due to long slender shape

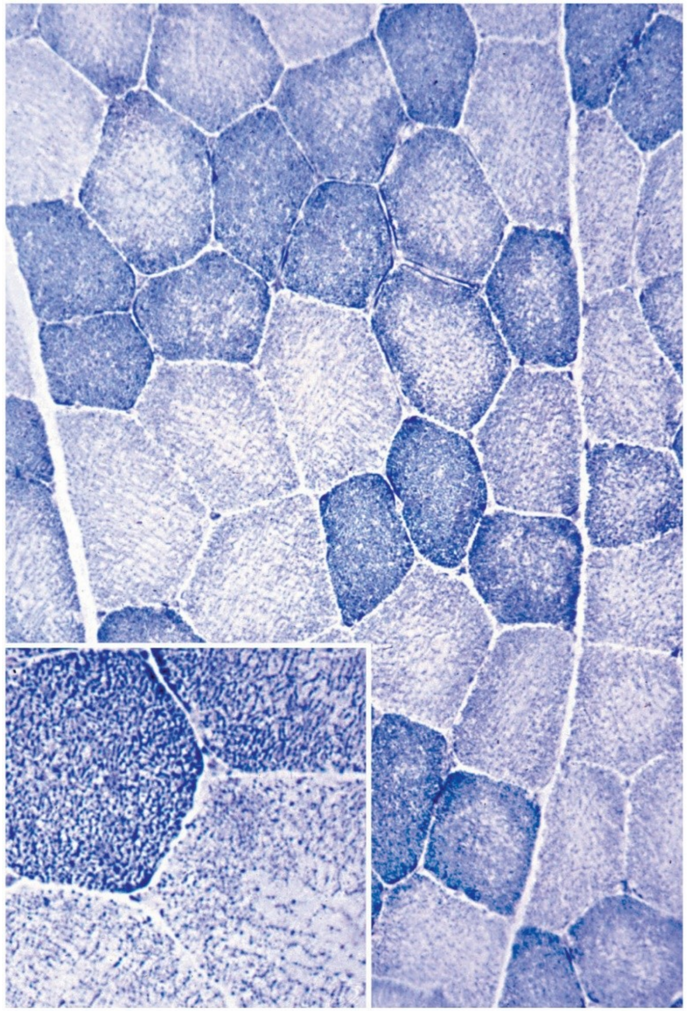
Connective tissue layers in skeletal muscle

Endomysium: thin layer enclosing each muscle fiber, allows room for blood capillaries and nerve fibers. Reticular fibers.
Perimysium: layer of thicker connective tissue surrounds bundles of muscle fibers, **fascicles**
Epimysium: layer surrounding muscle as a whole, dense ct

Fasciae: fibrous sheets separating muscles from each other, may separate functionally related muscles into **compartments.** Contains nerves and vessels supplying muscle group



Skeletal Muscle Fiber Types: High levels of mitochondrial oxidative enzymes → strong succinic dehydrogenase and NADH histochemical staining reactions

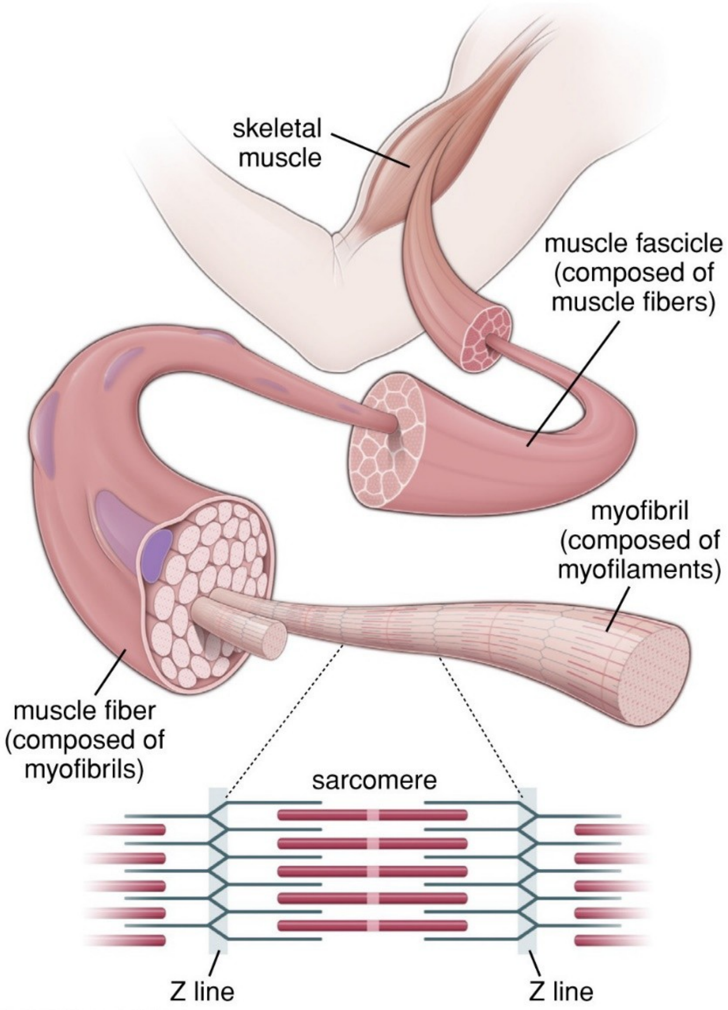


Type I fibers (slow oxidative): slow-twitch, fatigue-resistant motor units small, many mitochondria. Postural muscles.
Type IIa fibers (fast oxidative glycolytic): fast-twitch, fatigue- resistant motor units that generate high peak muscle tension. 400-800m runners.
Type IIb fibers (fast glycolytic fibers): low level of oxidative enzymes, high anaerobic enzyme activity. Eyes and fingers.

❯❯ MEDICAL APPLICATION

The variation in diameter of muscle fibers depends on factors such as the specific muscle, age, gender, nutritional status, and physical training of the individual. Exercise enlarges the skeletal musculature by stimulating formation of new myofibrils and growth in the diameter of individual muscle fibers. This process, characterized by increased cell volume, is called **hypertrophy** (gr. *hyper* , above + *trophe* , nourishment). Tissue growth by an increase in the number of cells is termed **hyperplasia** (hyper + gr. *plasis*, molding), which takes place very readily in smooth muscle, whose cells have not lost the capacity to divide by mitosis.

Organization of a skeletal muscle



Striations:

A bands: regions in which thick and thin filaments overlap. Middle part composed of myosin only

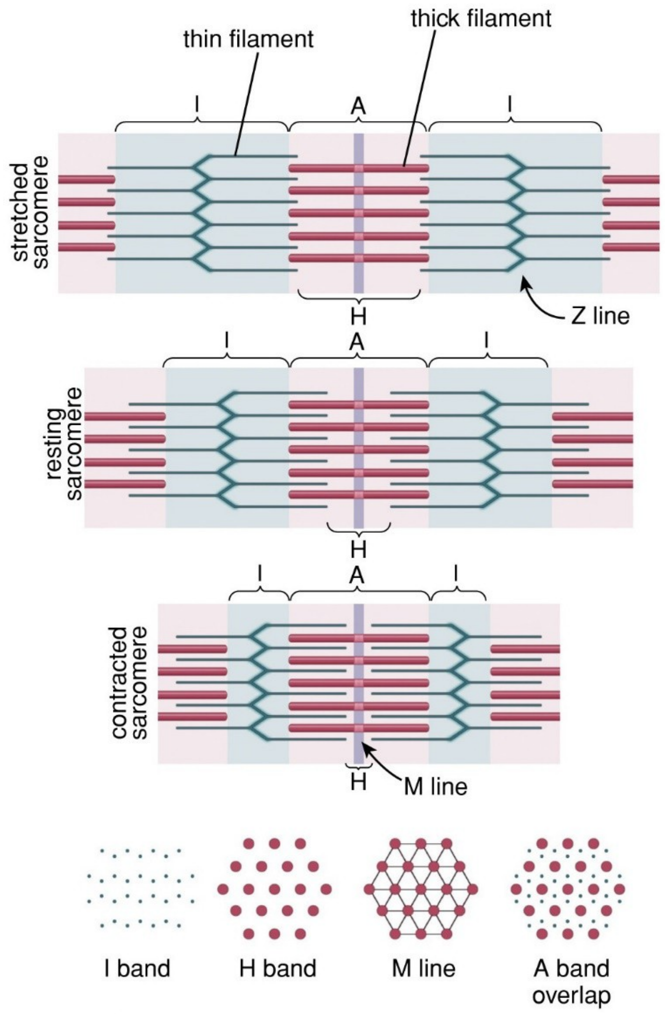
I bands: consists only of thin filaments bisected by thin dark line, **Z disc (**protein providing anchorage for thin filaments)

Sarcomere: Segment from one Z disc to the next, functional unit of muscle fiber

Muscle shortening due to sarcomeres shortening pull Z discs closer

http://highered.mheducation.com/sites/0072495855/student_view0/chapter10/animation__sarcomere_contraction.html

The functional unit of the myofibril is the sarcomere, the segment of the myofibril between two adjacent Z lines

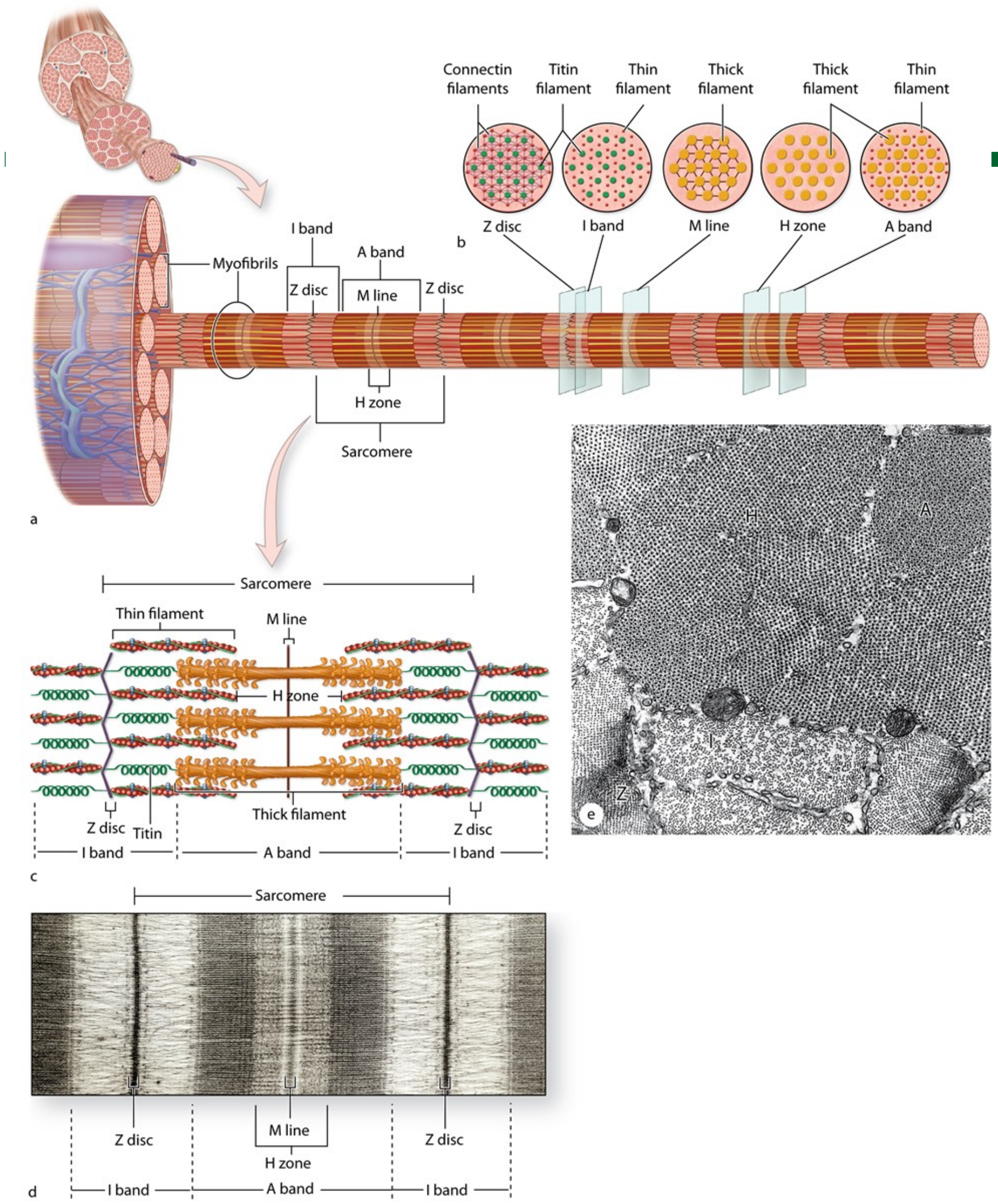


In the resting state (middle), interdigitation of thin (actin) and thick (myosin) filaments is not complete; the H and I bands are relatively wide.

In the contracted state (bottom), the interdigitation of the thin and thick filaments is increased according to the degree of contraction.

In the stretched state (top), the thin and thick filaments do not interact; the H and I bands are very wide. The length of the A band always remains the same and corresponds to the length of the thick filaments; the lengths of the H and I bands change

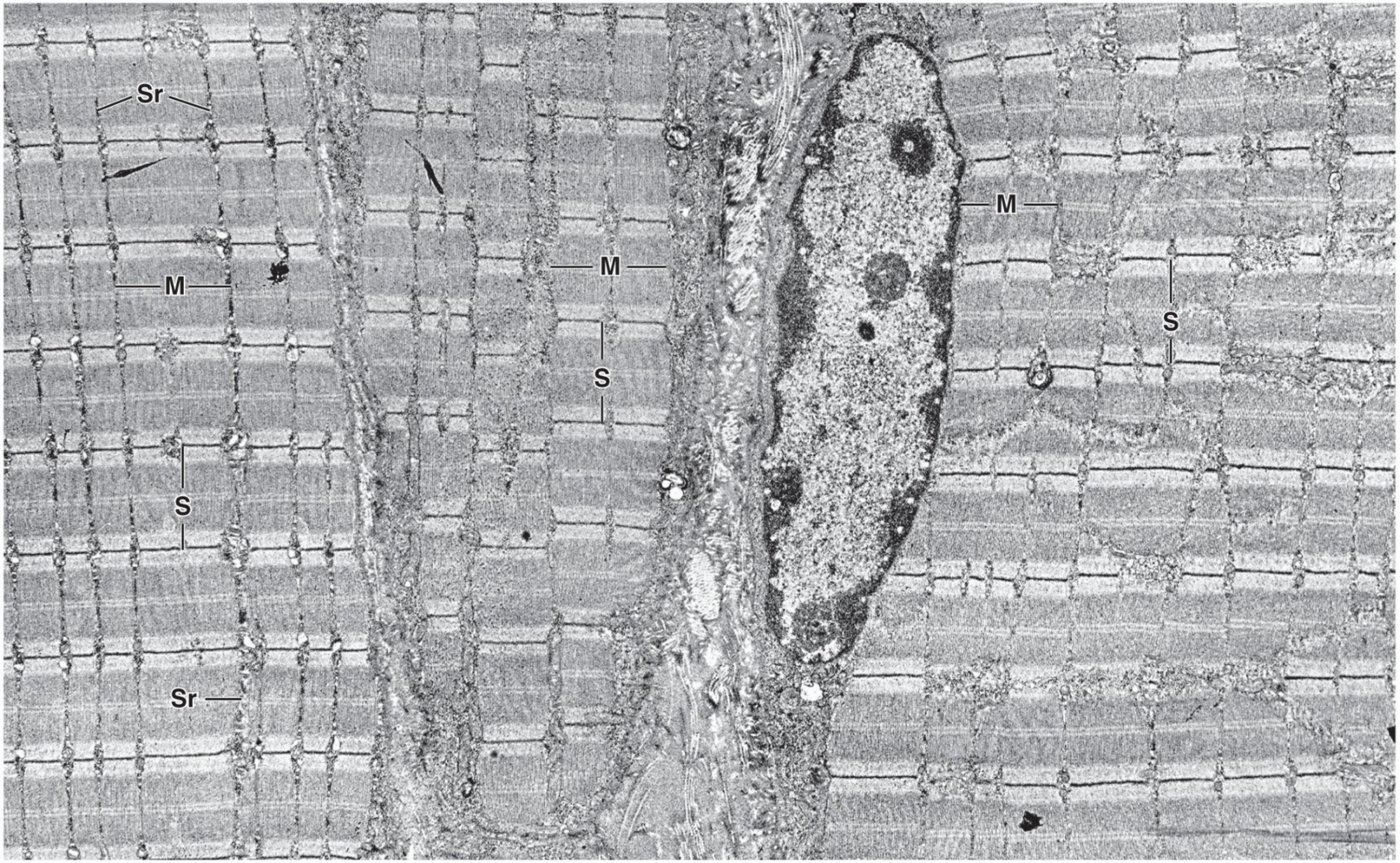
Structure of a myofibril: A series of sarcomeres.



The myosin-containing thick filaments are restricted to the central portion of the sarcomere (i.e., the A band).

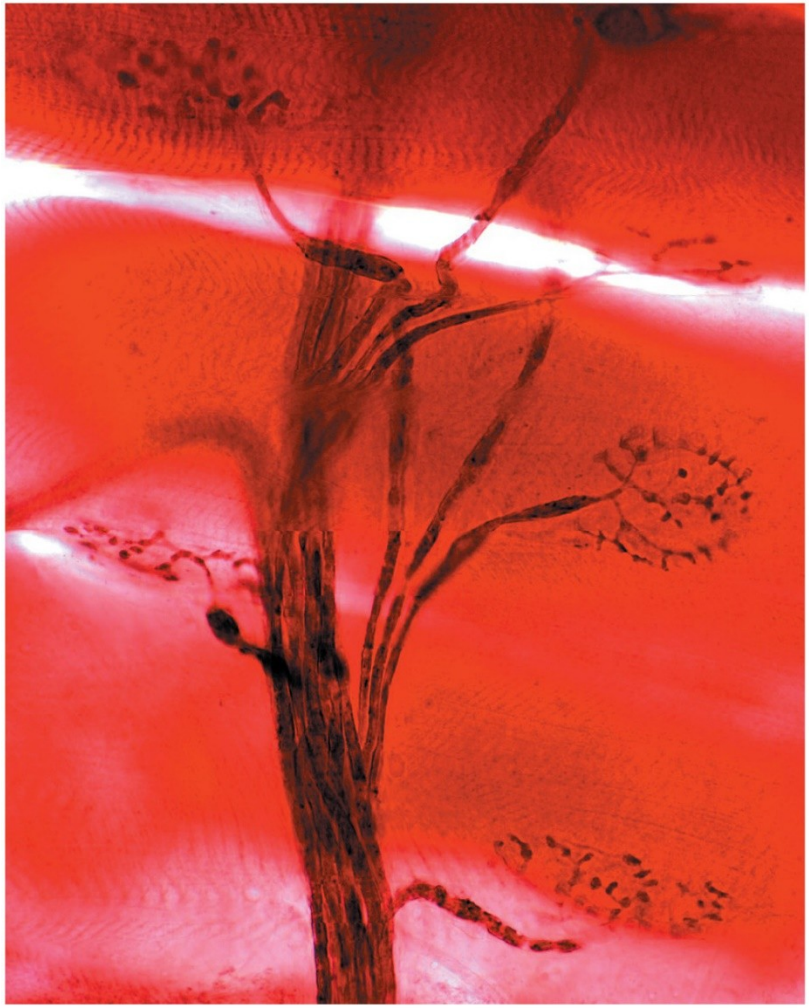
Actin-containing thin filaments attach to the Z line and extend into the A band to the edge of the H band.

When a muscle contracts, each sarcomere shortens, but the myofilaments remain the same length.

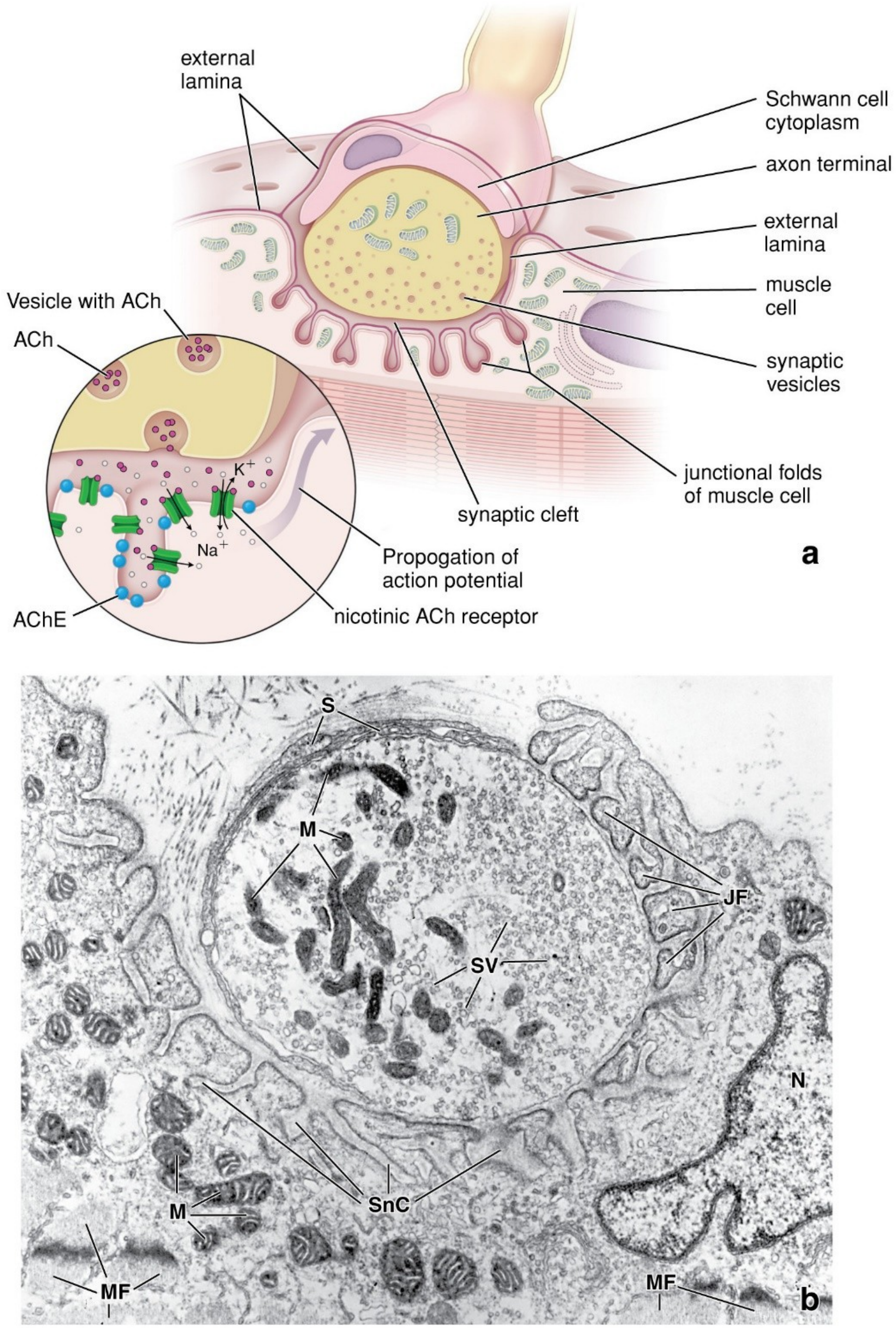


Two fibers—one in the middle and another on the left—exhibit regular profiles of myofibrils separated by a thin layer of surrounding sarcoplasm (Sr). Each repeating part of the myofibril between adjacent Z lines is a sarcomere (S). The cross-banded pattern visible on this micrograph reflects the arrangement, in register, of the individual myofibrils (M); a similar pattern found in the myofibril reflects the arrangement of myofilaments.

The neuromuscular junction is the contact made by the terminal branches of the axon with the muscle fiber



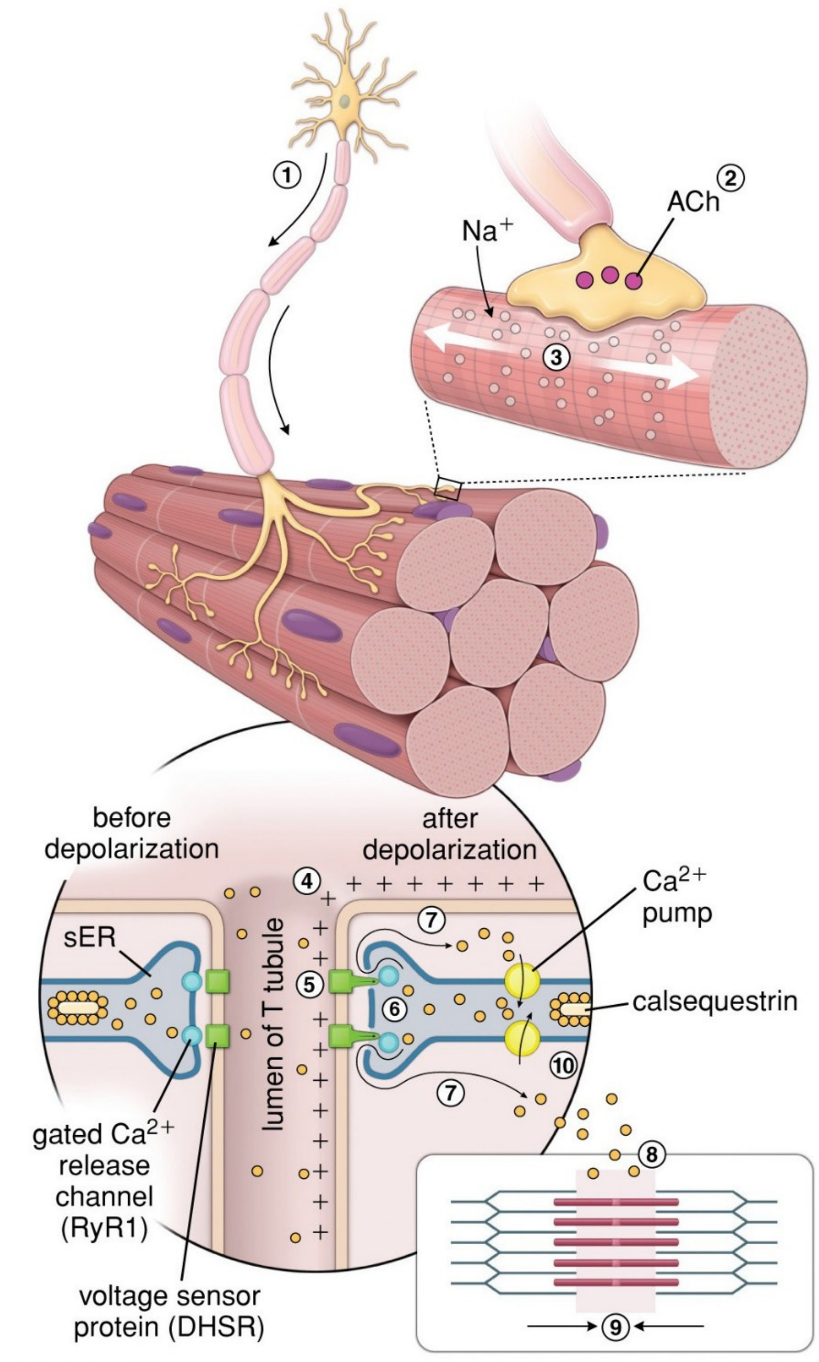
A motor nerve and its final branches that lead to the neuromuscular junctions (motor end plates). The skeletal muscle fibers are oriented horizontally in the field and are crossed perpendicularly by the motor nerve fibers. Note that these fibers distally lose their myelin sheath and divide extensively into small swellings, forming a cluster of neuromuscular junctions.



Release of acetylcholine into the synaptic cleft initiates depolarization of the plasma membrane, which leads to muscle cell contraction.

If the nerve supply to a muscle is disrupted, the muscle cell undergoes regressive changes known as tissue atrophy

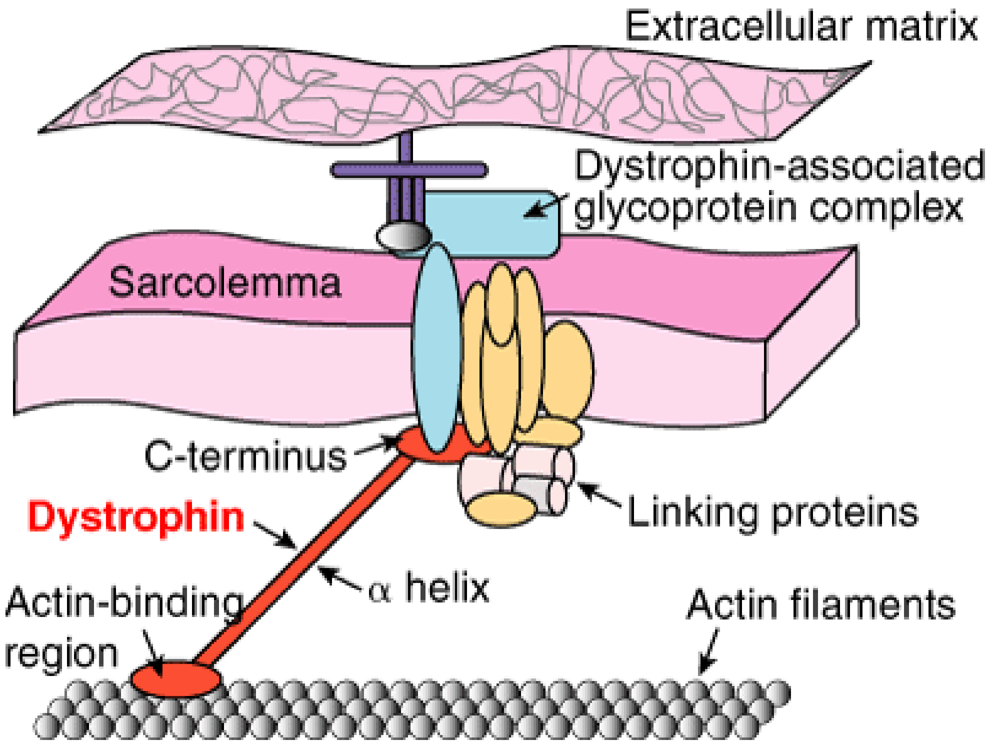
MEDICAL APPLICATION Myasthenia gravis is an autoimmune disorder that involves circulating antibodies against proteins of acetylcholine receptors. The disease follows a progressive course. The extraocular muscles of the eyes are commonly the first affected.



The events leading to contraction of skeletal muscle

1. Nerve impulse.
2. release of acetylcholine into the synaptic cleft, ACh-gated Na channels cause local depolarization of sarcolemma.
3. Voltage-gated Na channels open
4. General depolarization spreads of the muscle cell
5. Voltage sensors in the plasma membrane of T tubules change their conformation.
6. At the muscle cell triads, sarcoplasmic reticulum gated Ca release activated
7. Ca is rapidly released
8. Ca binds troponin complex.
9. Acto-myosin cross-bridge cycle is initiated.
10. Ca is returned to the terminal cisternae of the sarcoplasmic reticulum.

Duchenne muscular dystrophy

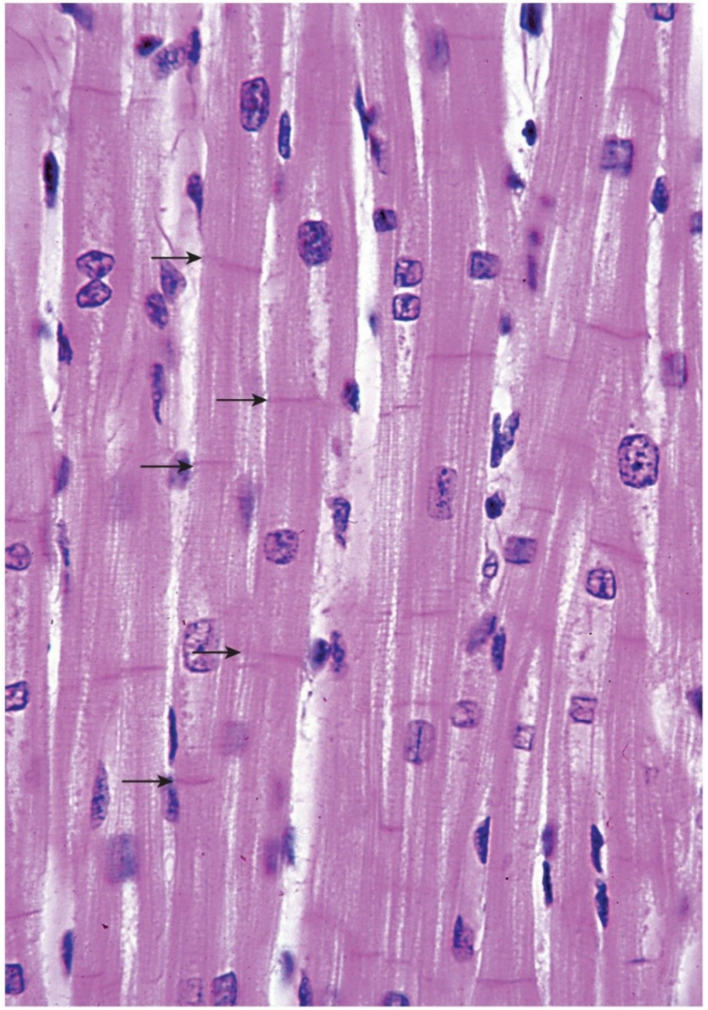


MEDICAL APPLICATION

Dystrophin is a large actin-binding protein located just inside the sarcolemma of skeletal muscle fibers which is involved in the functional organization of myofibrils.

Research on Duchenne muscular dystrophy revealed that mutations of the dystrophin gene can lead to defective linkages between the cytoskeleton and the extracellular matrix (ECM). Muscle contractions can disrupt these weak linkages, causing the atrophy of muscle fibers typical of this disease.

Cardiac muscle has the same types and arrangement of contractile filaments as skeletal muscle



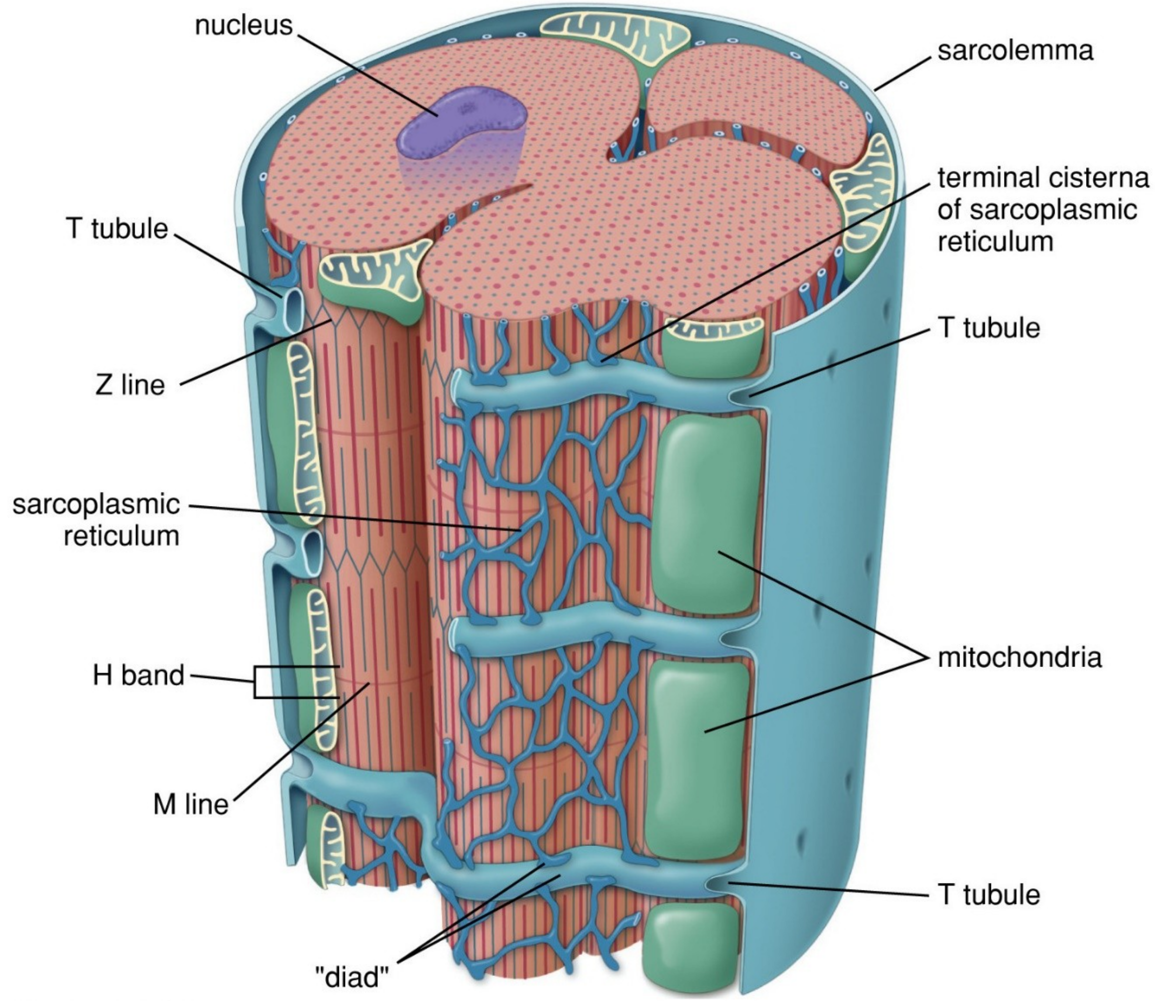
Unlike skeletal and visceral striated muscle fibers that represent multinucleated single cells, cardiac muscle fibers consist of numerous cylindrical cells arranged end to end.

In addition, cardiac muscle fibers exhibit densely staining cross-bands, called **intercalated discs.**

Gap junctions (communicating junctions) constitute the major structural element of the lateral component of the intercalated disc. Gap junctions provide ionic continuity between cells, permitting cardiac muscle fibers to behave as a syncytium while retaining cellular integrity and individuality

The central location of the nucleus in cardiac muscle cells is one feature that helps distinguish them from multinucleated skeletal muscle fibers.

Organization of cardiac muscle fiber

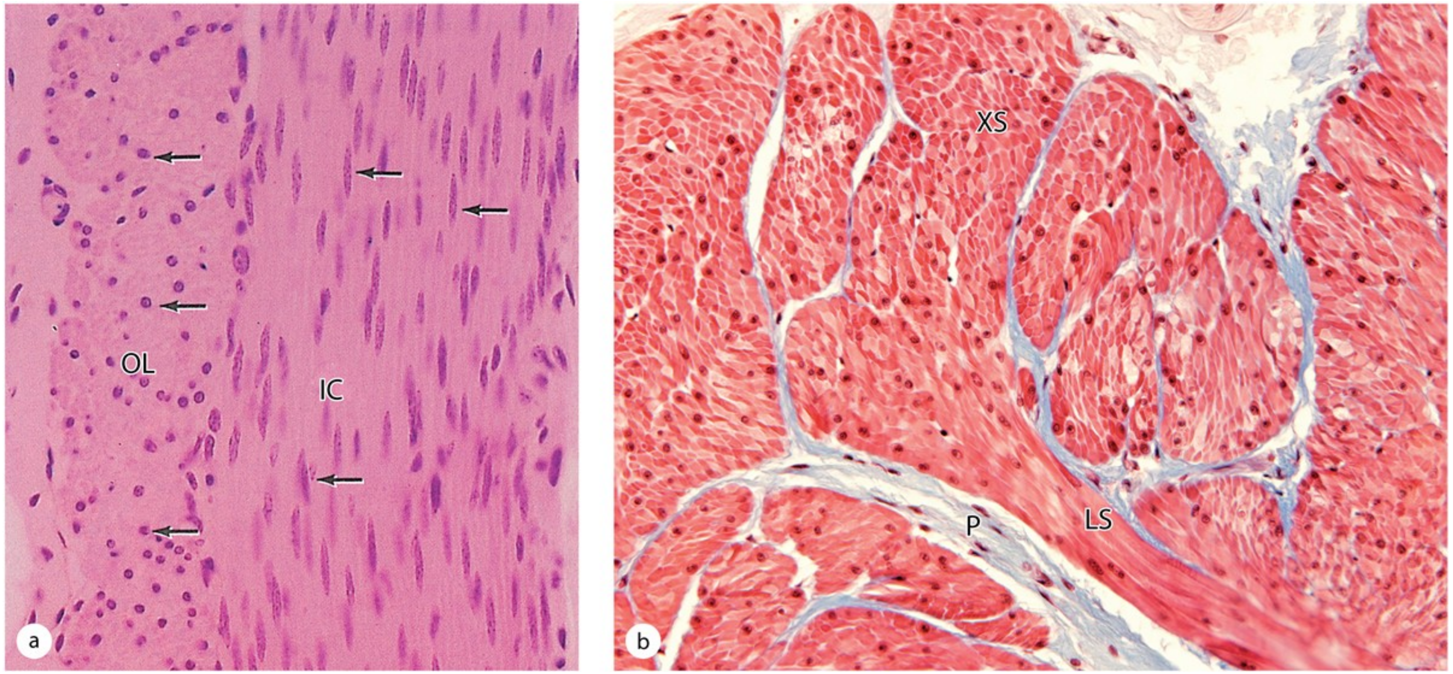


The T tubules of cardiac muscle are much larger than the T tubules of skeletal muscle
They also differ in that they are located at the level of the Z line.

MEDICAL APPLICATION
Ischemia: tissue damage due to lack of oxygen when coronary arteries are occluded by heart disease.

Adult mammalian cardiac muscle has little potential to regenerate after injury. However, certain fish and amphibians, as well as newborn mice, do form new muscle when the heart is partially removed, despite the lack of satellite cells. Research on the possibility of mammalian heart muscle regeneration builds on work with the animal models, focusing primarily on the potential of mesenchymal stem cells to form new, site-specific muscle.

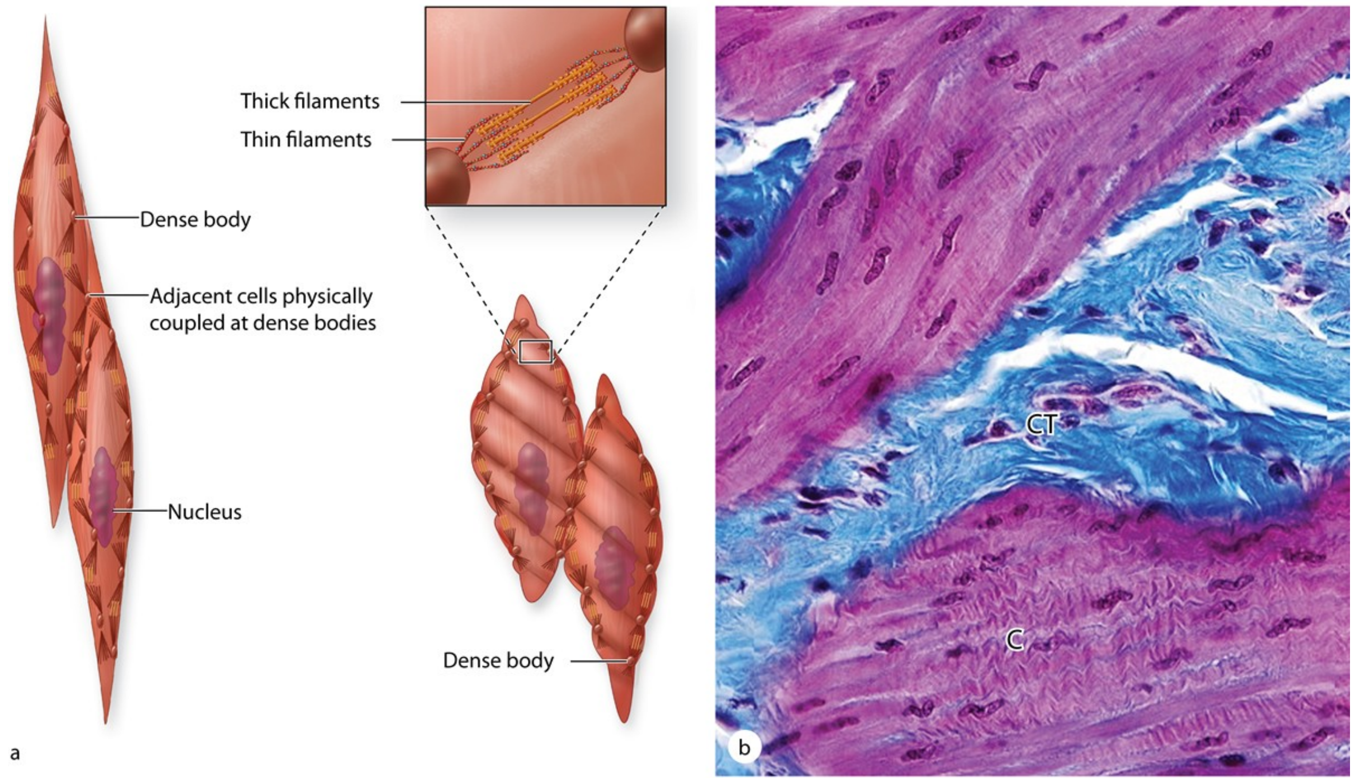
Cells of smooth muscle are long, tapering structures with elongated nuclei centrally located at the cell's widest part.



(a) wall of the small intestine cells of the inner circular (**IC**) layer are cut lengthwise and cells of the outer longitudinal layer (**L**) are cut transversely.

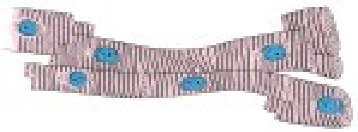
(b) Section of smooth muscle in bladder shows fibers in cross section (**XS**) and longitudinal section (**LS**) with the same fascicle.

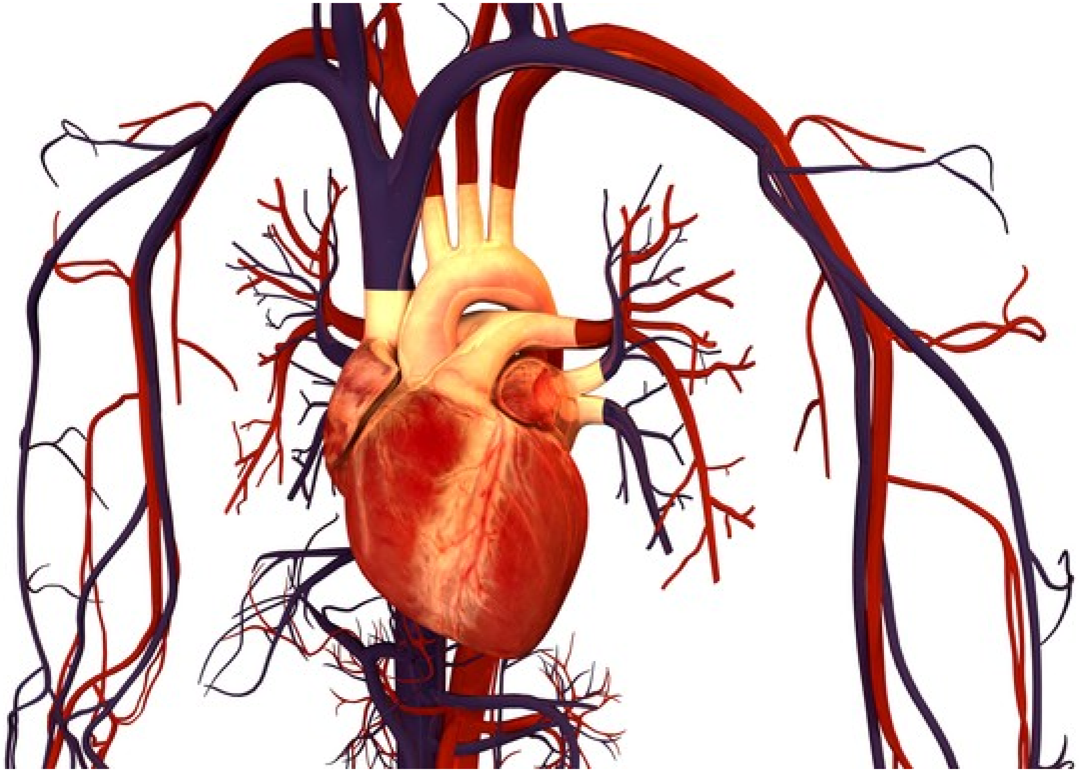
Filaments of smooth muscle are arranged differently and appear less organized.



(a) thin filaments attach to **dense bodies** located at the cell membrane and deep in the cytoplasm. This arrangement of both the cytoskeleton and contractile apparatus allows the multicellular tissue to contract as a unit, providing better efficiency and force.

(b) Contracted (**C**) region of smooth muscle, with contraction decreasing the cell length and deforming the nuclei. The long nuclei of individual fibers assume a cork-screw shape when the fibers contract, reflecting the reduced cell length at contraction. Connective tissue (**CT**) of the perimysium outside the muscle fascicle is stained blue.

	Skeletal	Cardiac	Smooth
			
Structural features			
Muscle cell	Large, elongate cell, 10–100 μm in diameter, up to 100 cm in length (sartorius m.)	Short, narrow cell, 10–15 μm in diameter, 80–100 μm in length	Short, elongate, fusiform cell, 0.2–2 μm in diameter, 20–200 μm in length
Location	Muscles of skeleton visceral striated (e.g., tongue, esophagus, diaphragm)	Heart, superior and inferior vena cava, pulmonary veins	Vessels, organs, and viscera
Connective tissue components	Epimysium, perimysium, endomysium	Endomysium (subendocardial and subpericardial connective tissue)	Endomysium, sheaths, and bundles
Fiber	Single skeletal muscle cell	Linear branched arrangement of several cardiac muscle cells	Single smooth muscle cell
Striation	Present	Present	None
Nucleus	Many peripheral	Single central, surrounded by juxtanuclear region	Single central
T tubules	Present at A-I junction (triad: with two terminal cisternae), two T tubules/sarcomere	Present at Z lines (diad: with small terminal cisternae), one T tubule/sarcomere	None, well-developed sER, many invaginations and vesicles similar to caveolae
Cell-to-cell junctions	None	Intercalated discs containing 1. Fasciae adherentes 2. Macula adherens (desmosome) 3. Gap junctions	Gap junctions (nexus)
Special features	Well-developed sER and T tubules	Intercalated discs	Dense bodies, caveolae, and cytoplasmic vesicles
Functions			
Type of innervation	Voluntary	Involuntary	Involuntary
Efferent innervation	Somatic	Autonomic	Autonomic
Type of contraction	"All or none" (type I and type II fibers)	"All or none" rhythmic (pacemakers, conductive system of the heart)	Slow, partial, rhythmic, spontaneous contractions (pacemakers of stomach)
Regulation of contraction	By binding of Ca^{2+} to TnC, causes tropomyosin movement and exposes myosin-binding sites on actin filaments	By binding of Ca^{2+} to TnC, causes tropomyosin movement and exposes myosin-binding sites on actin filaments	By phosphorylation of myosin light chain by myosin light chain kinase in the presence of Ca^{2+}-calmodulin complex
Growth and regeneration			
Mitosis	None	None (in normal condition)	Present
Response to demand	Hypertrophy	Hypertrophy	Hypertrophy and hyperplasia
Regeneration	Limited (satellite cells and myogenic cells from bone marrow)	None (in normal condition)	Present



The Circulatory System, Blood, Hemopoiesis

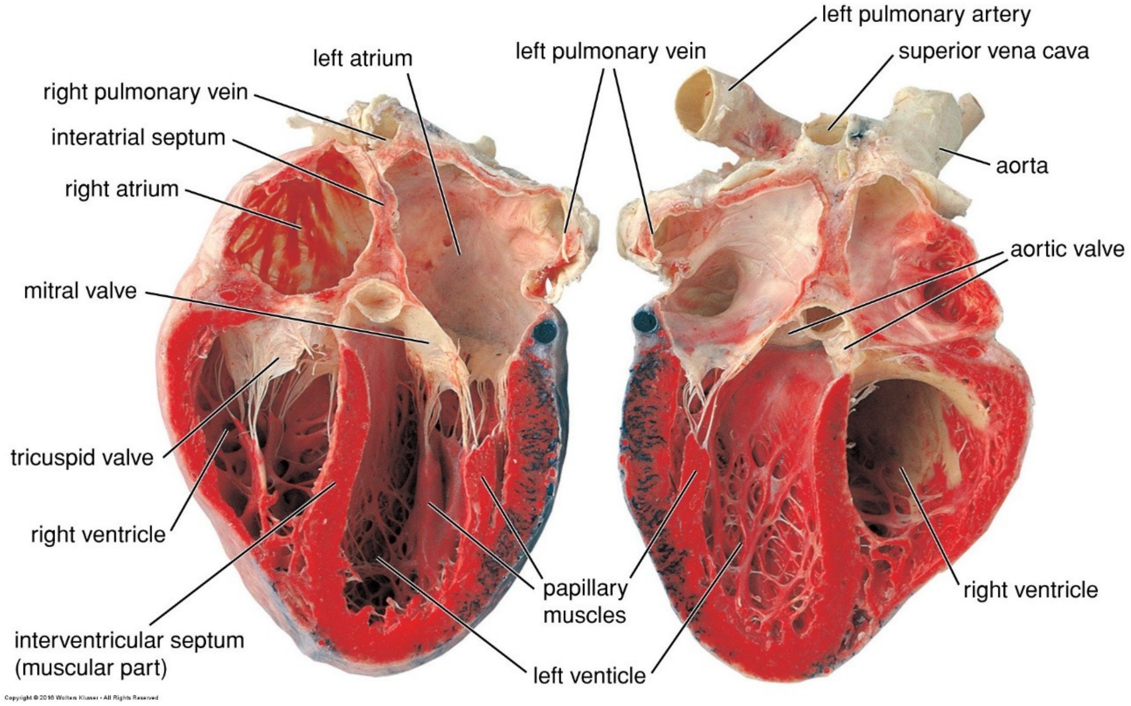
BI 455 CHAPTER 11-13

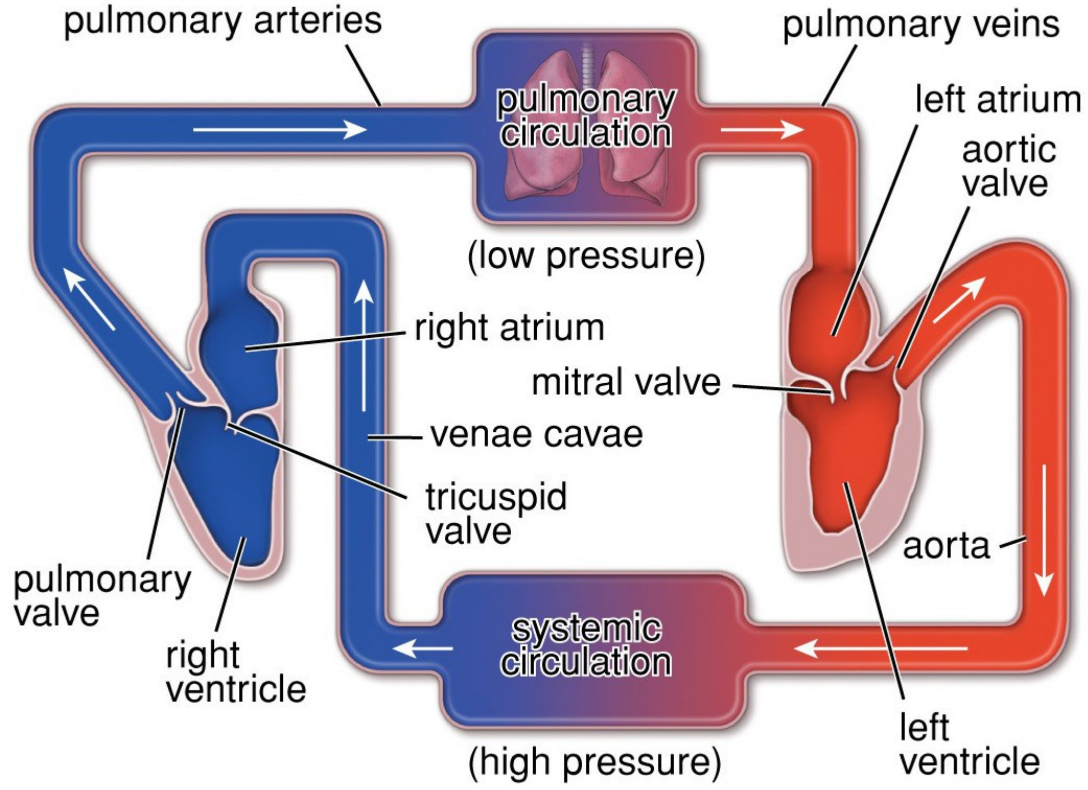
Chapter 11 Circulatory System
Key Points

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

http://ed.ted.com/lessons/how-the-heart-actually-pumps-blood-edmond-hui

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



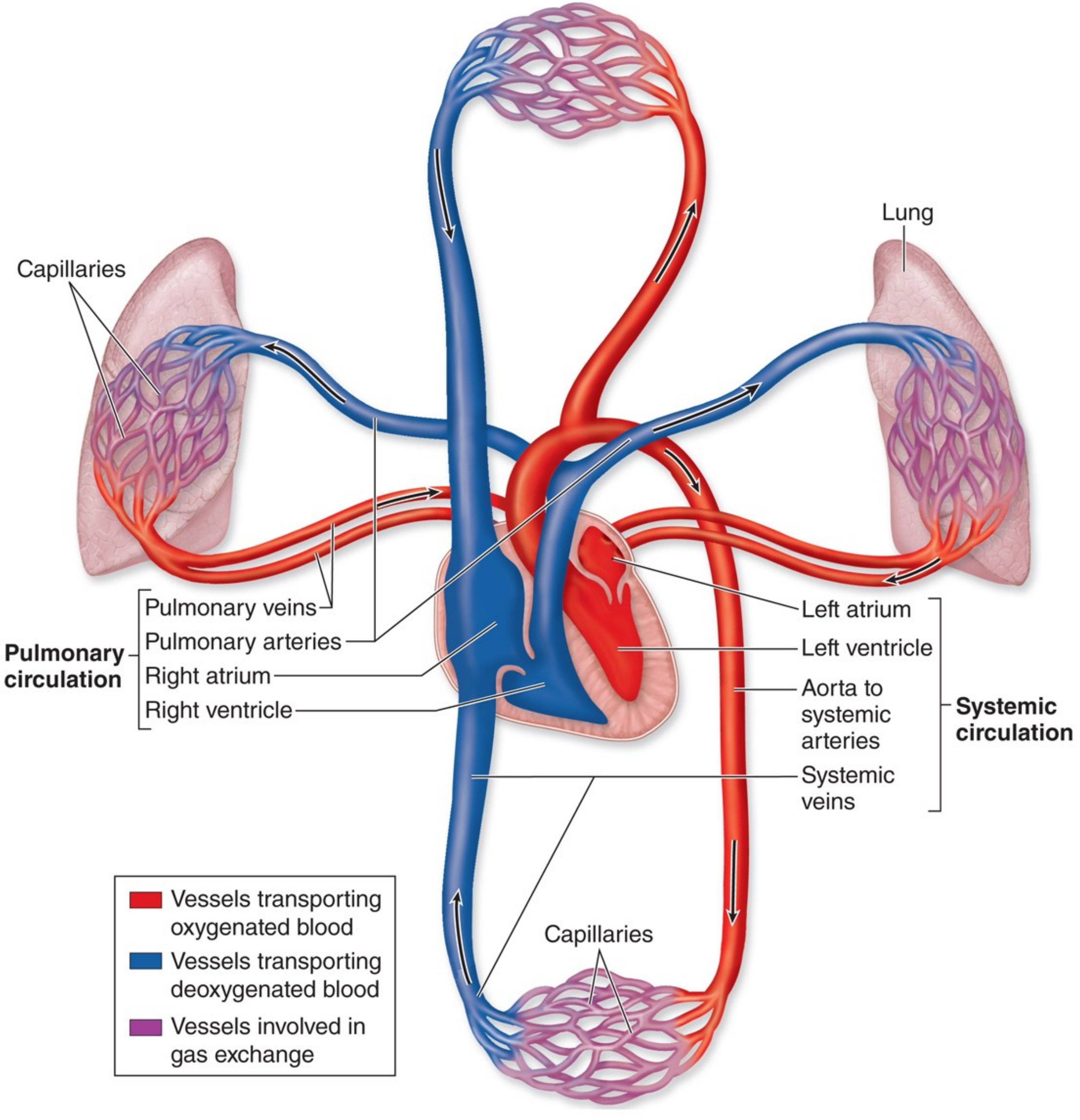


http://ed.ted.com/lessons/how-blood-pressure-works-wilfred-manzano

Circulation

Systemic circuit: tissues → superior and inferior venae 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

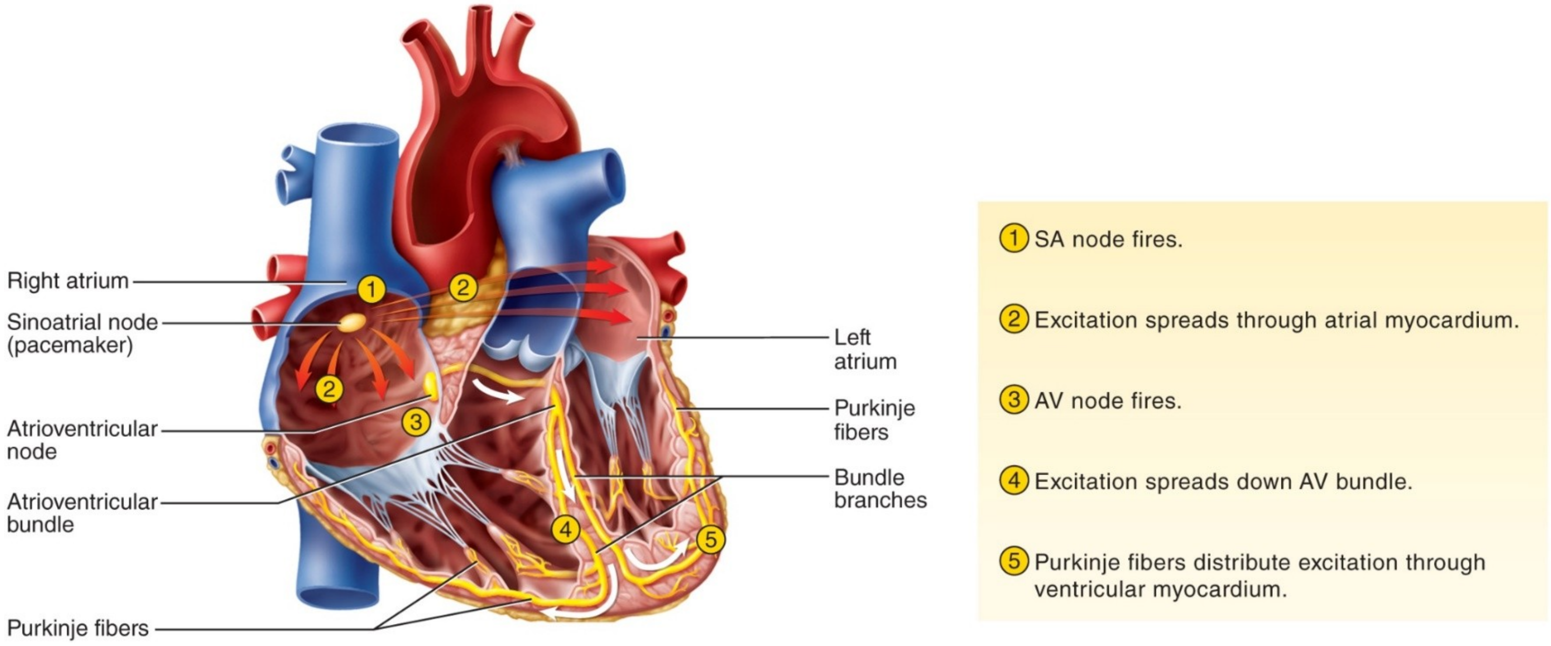


Cardiovascular System

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)

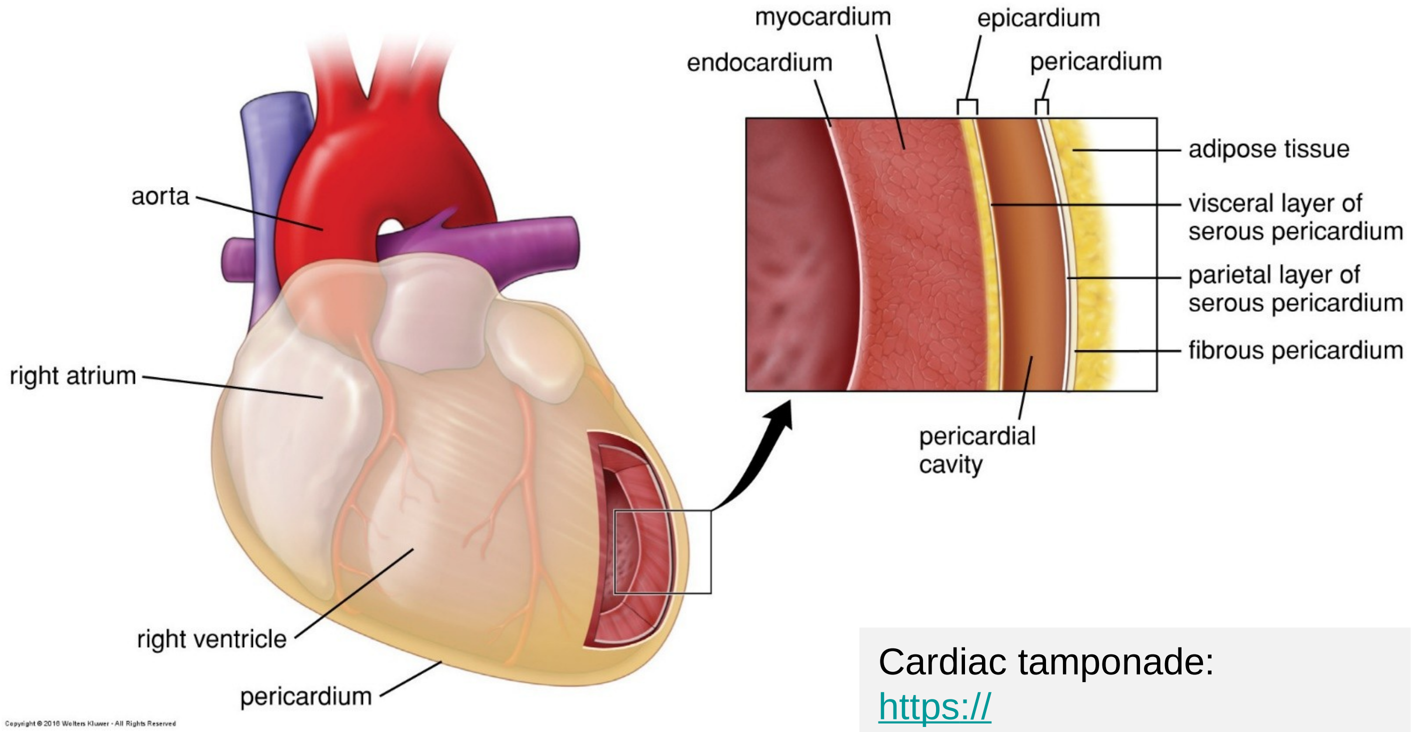
Sinoatrial node(SA) fires automatically → Internodal conduction → Atrioventricular (AV) node → Atrioventricular (AV) bundle (bundle of His) → Purkinje fibers



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

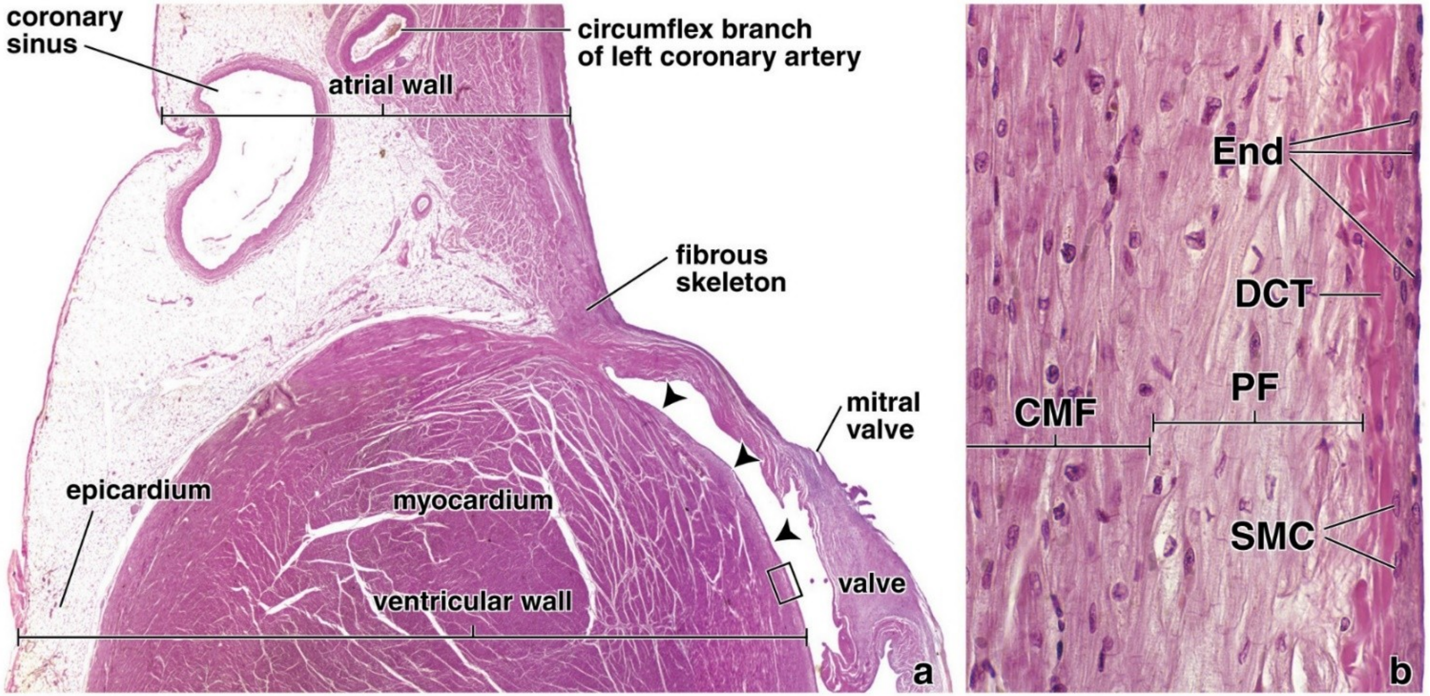
Outside the heart wall: Pericardial cavity, parietal serous pericardium, Fibrous pericardium, adipose tissue
Cardiac tamponade: Fluid accumulation on pericardial cavity compresses heart. Caused by chest injury or pericarditis (inflammation of pericardium)



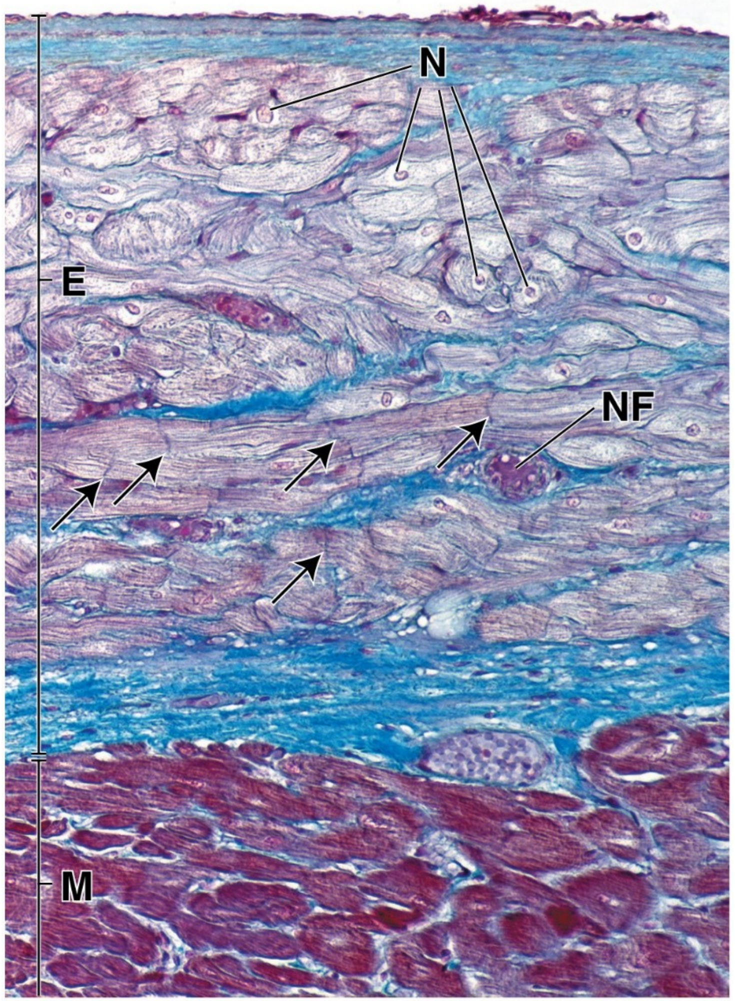
Cardiac tamponade: https://www.youtube.com/watch?v=QwqfuDeqC5Y

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

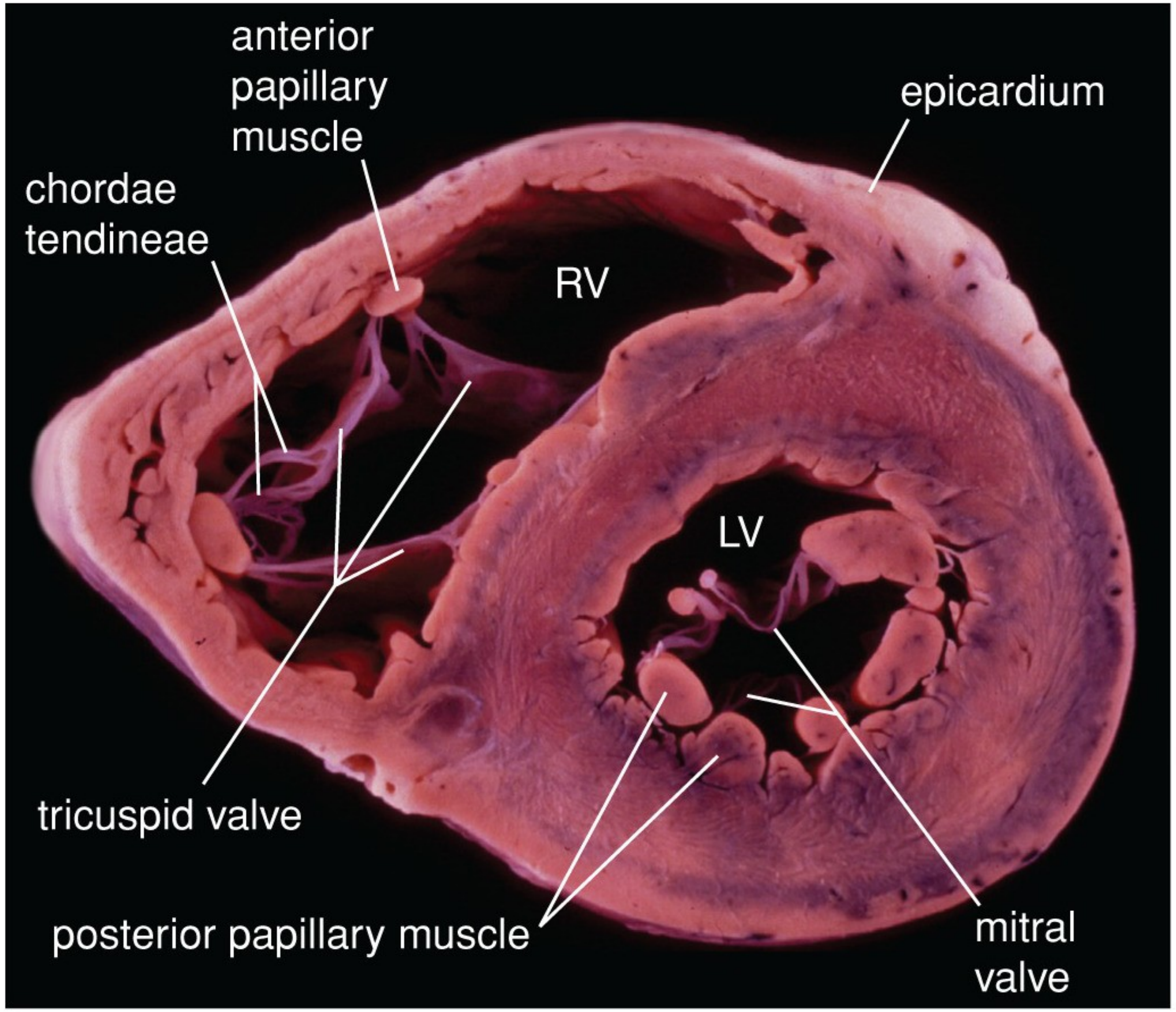


- **Endocardium (E):** The free luminal surface of the ventricle (top) is covered by endothelium and an underlying layer of subendothelial connective tissue (stained blue).

- **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



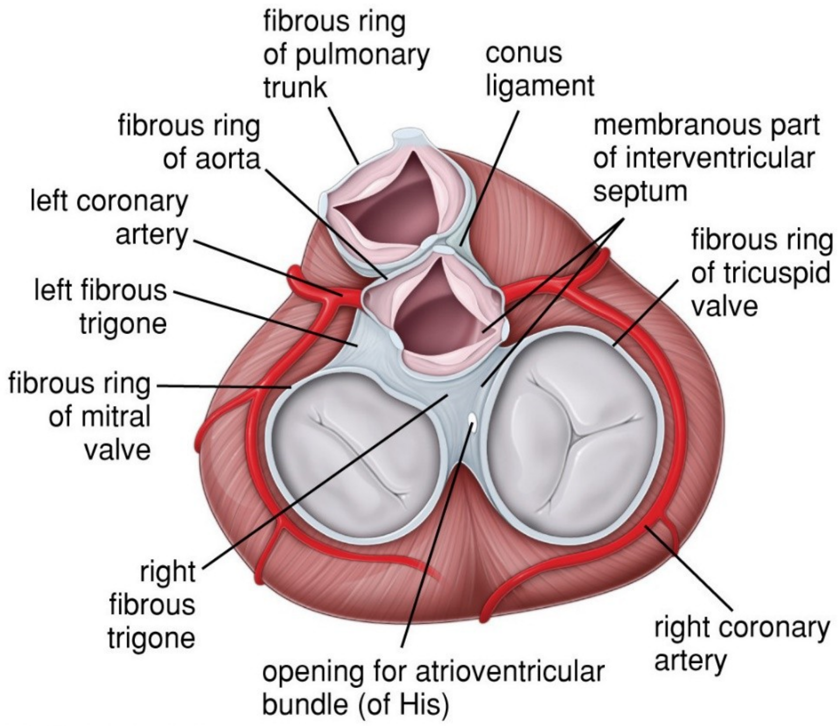
- Atria myocardium is thinner than ventricles
- Atria deliver blood to ventricles, while ventricles deliver to pulmonary and systemic circulations.
- Left ventricle delivers to systemic circulation, which requires more force.

Live Beating Heart and Heart Surgery:
https://www.youtube.com/watch?v=uR4t__B-Zwg

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.

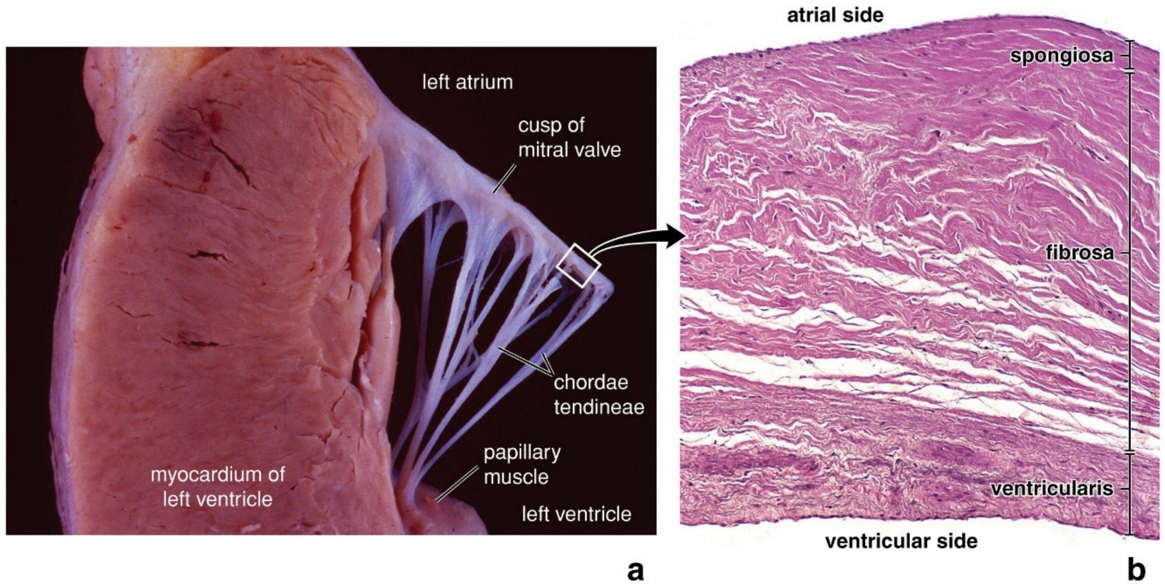


http://www.webmd.com/heart-disease/video/aortic-valve-replacement

Heart Valve: Connective tissue with overlying endocardium

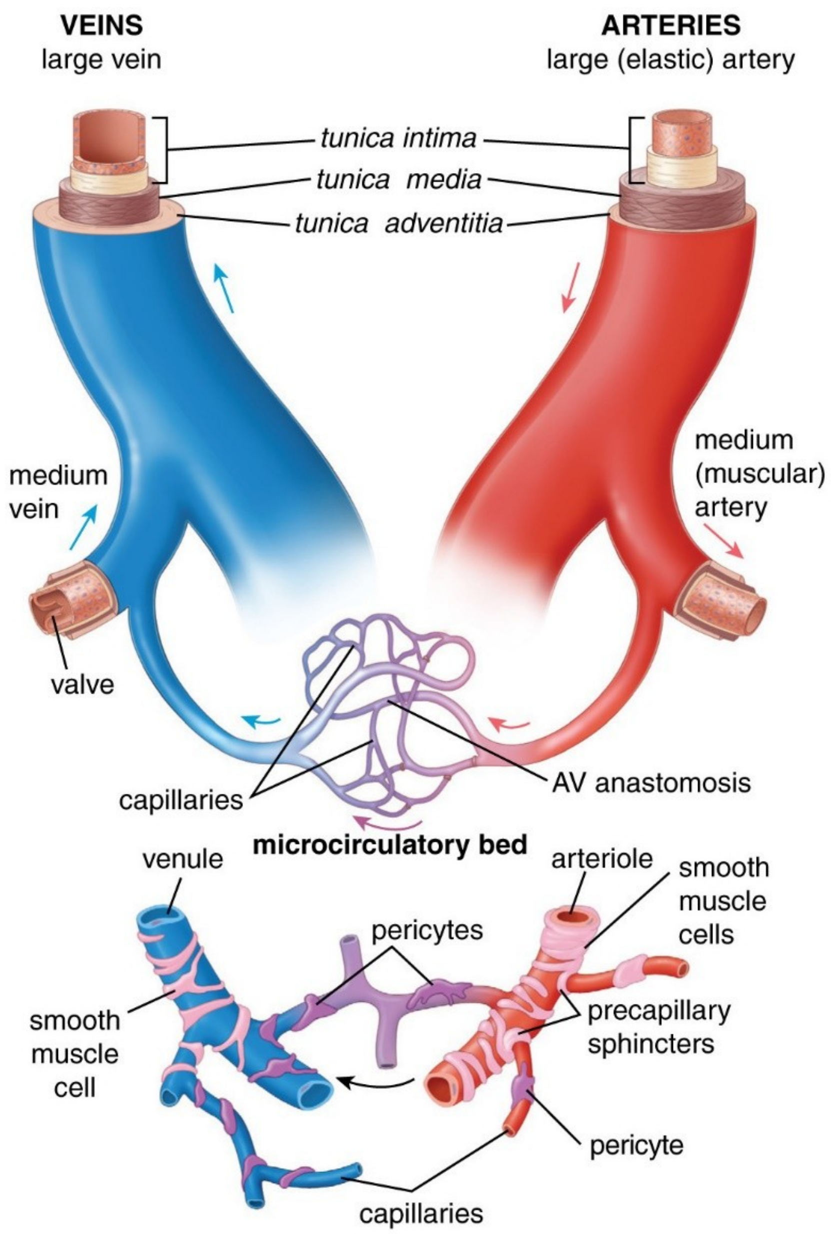
Valve cusps are normally avascular, but cusps are thin enough to allow nutrient diffusion from chamber blood.

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



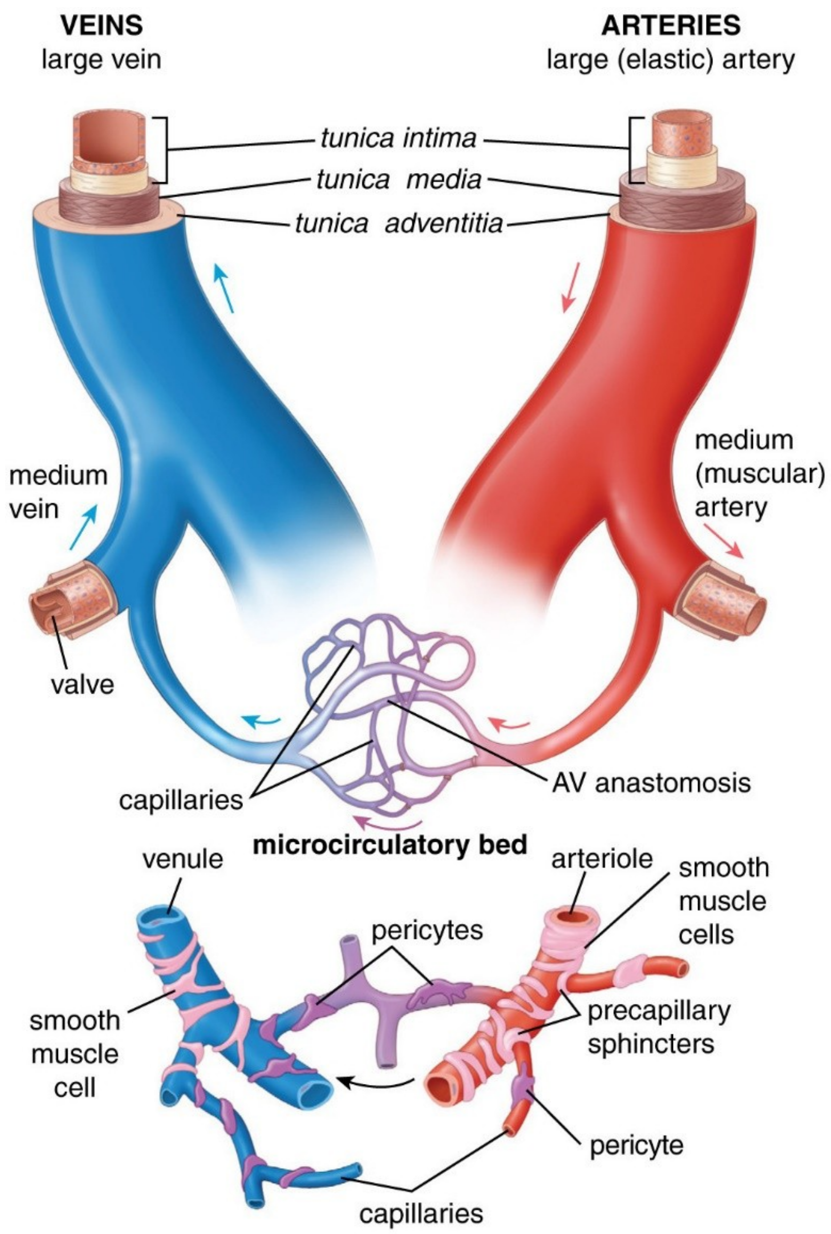
Arteries

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 µm	Endothelium Connective tissue Smooth muscle	Smooth muscle (1–2 cell layers)	Thin, ill-defined sheath of connective tissue
Capillary	4–10 µm	Endothelium	None	None

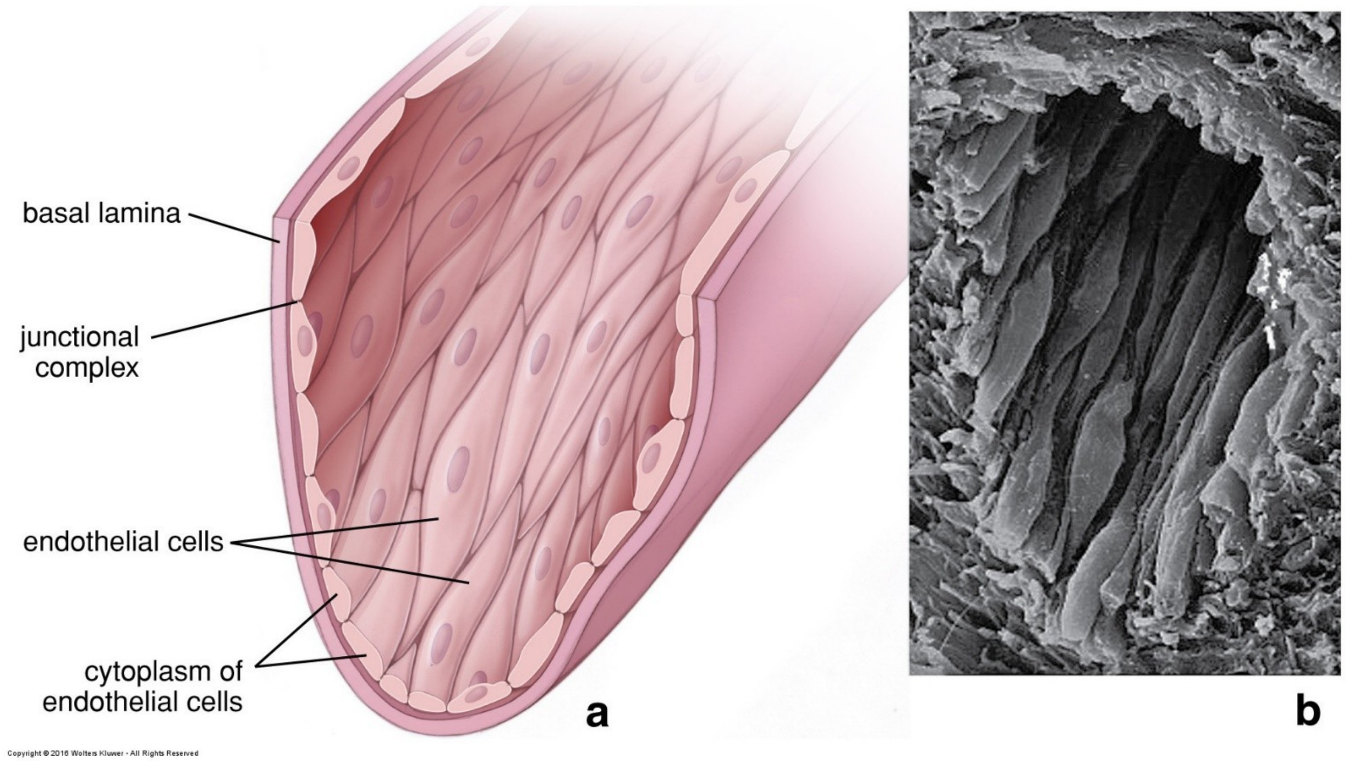


Veins

Vessel	Diameter	Tunica intima (inner layer)	Tunica media (middle layer)	Tunica adventitia (outer layer)
Postcapillary venule	10–50 µm	Endothelium Pericytes	None	None
Muscular venule	50–100 µm	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



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.

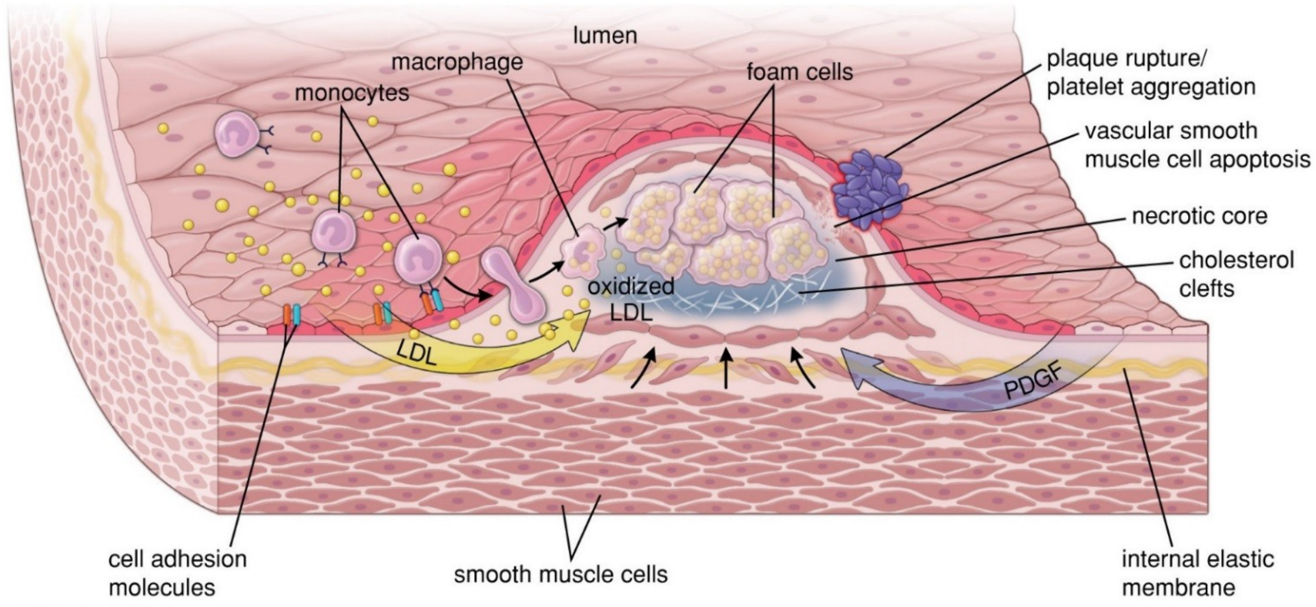
b. Scanning electron micrograph of a small vein, showing the cells of the endothelial lining. Note the spindle shape with the long axis of the cells running parallel to the vessel.

Vascular endothelium: continuous layer of fattened, 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.

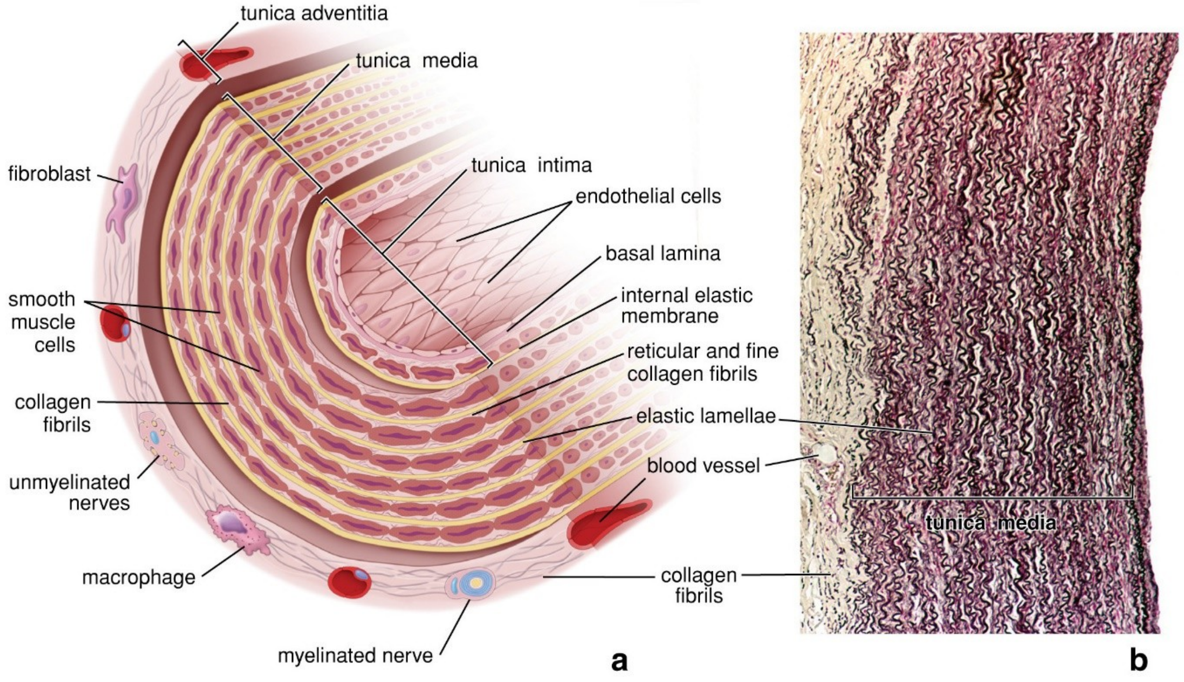
❯❯ **MEDICAL APPLICATION**: Tissue injury → platelet aggregation → clotting.

Emboli (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.



http://ed.ted.com/lessons/what-happens-during-a-heart-attack-krishna-sudhir

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



ELASTIC ARTERY

http://www.webmd.com/heart-disease/video/atherosclerosis

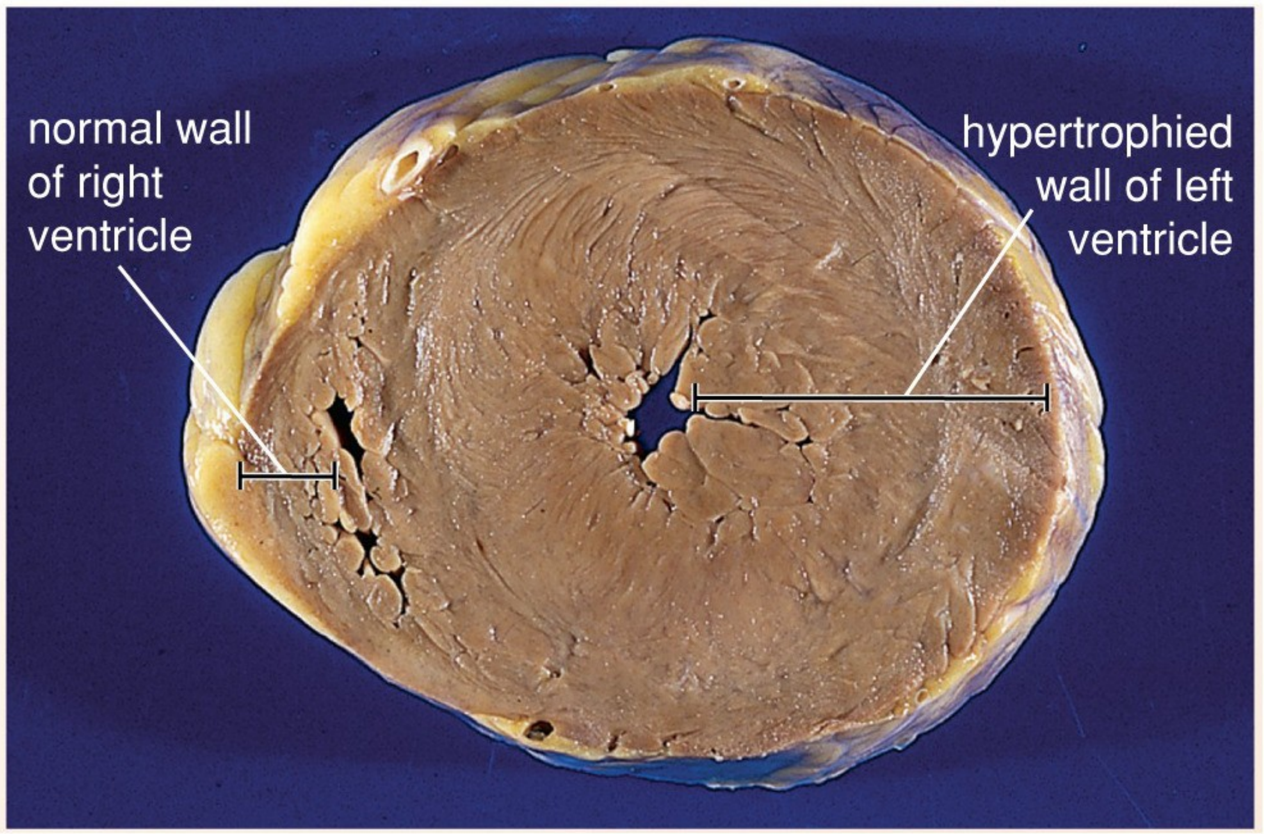
❯❯ MEDICAL APPLICATION

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.

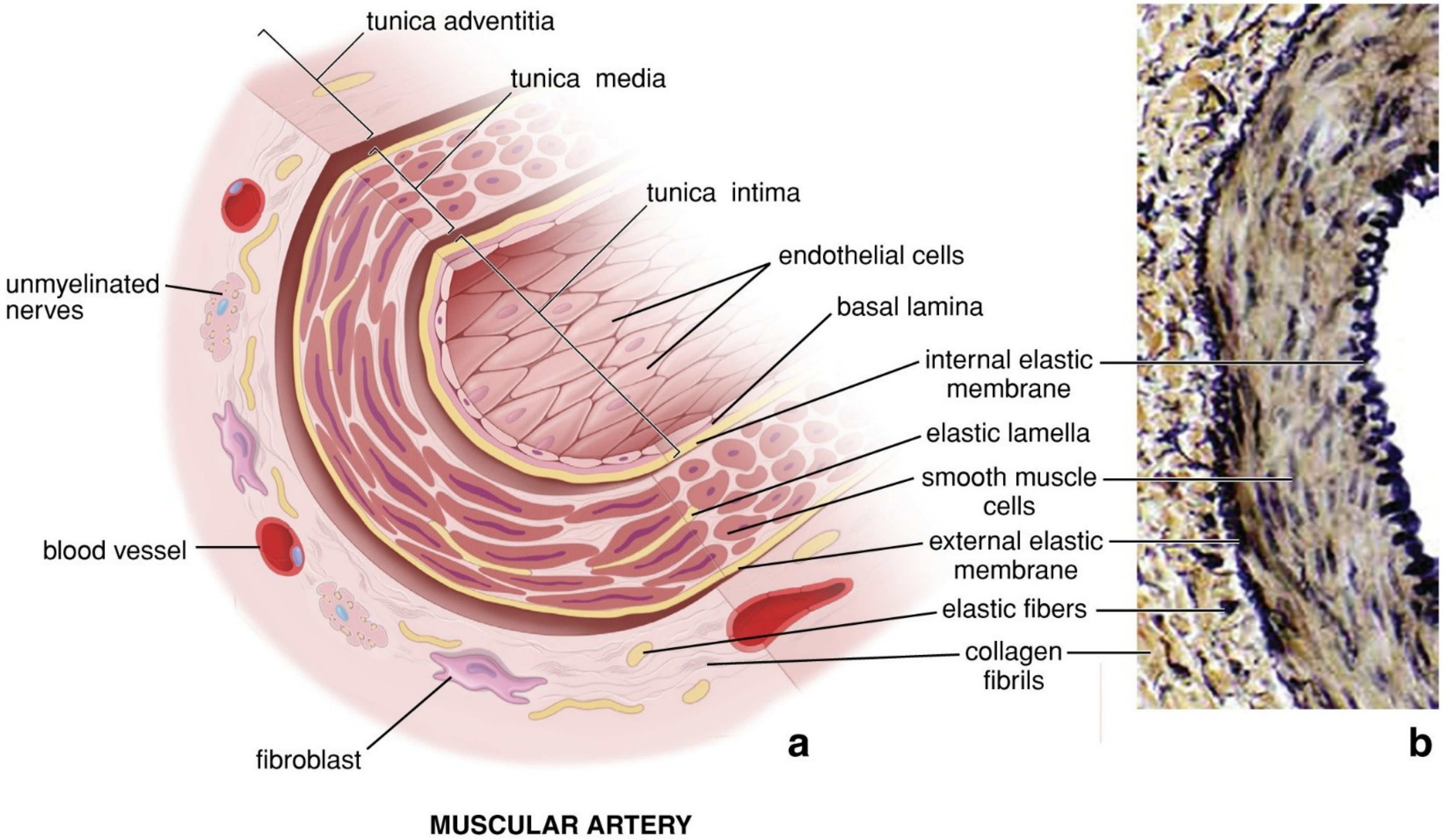
Hypertension



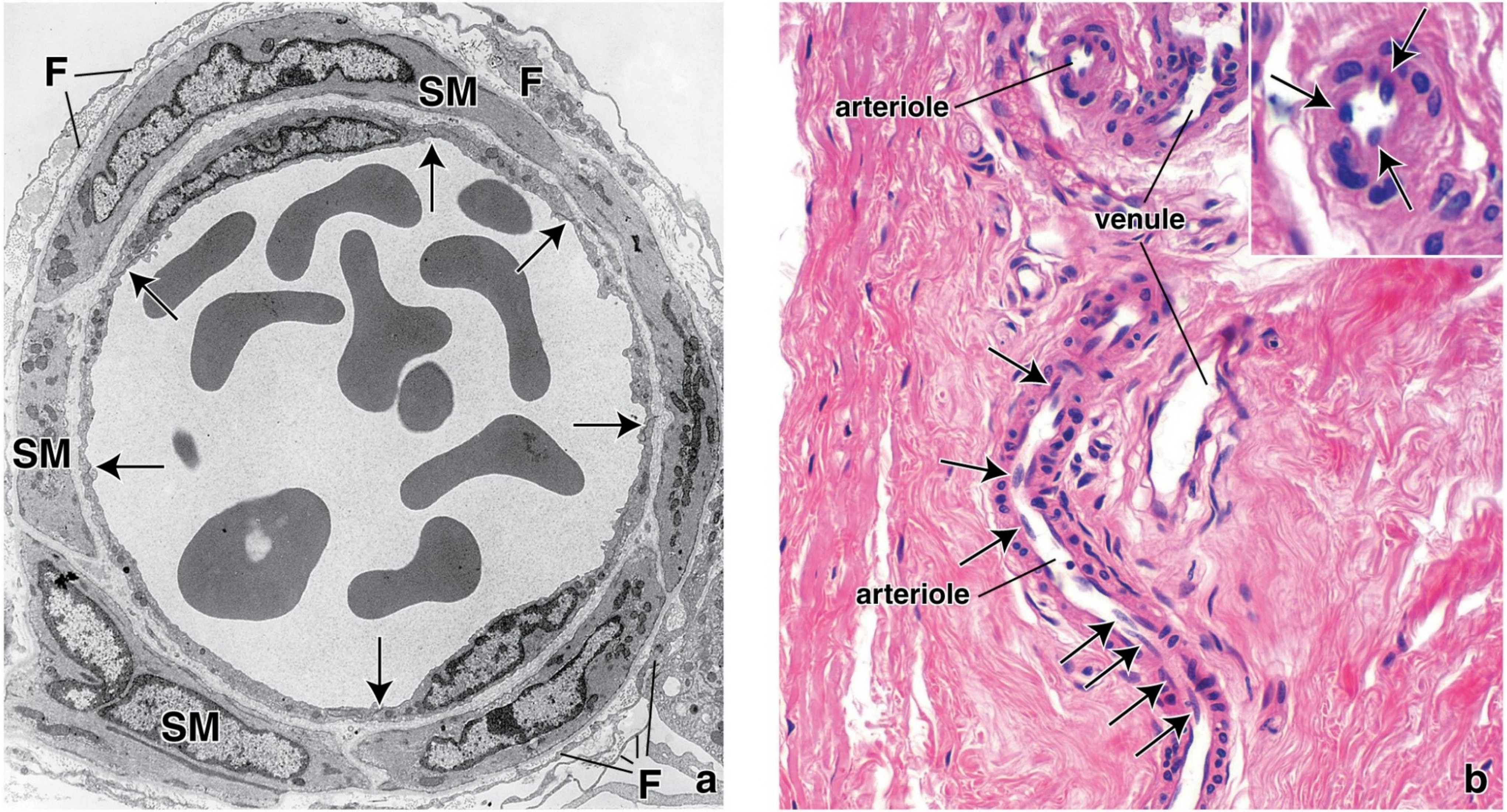
Atherosclerosis reduces diameter of small muscular arteries and arterioles is reduced, which leads to increased vascular resistance.

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**

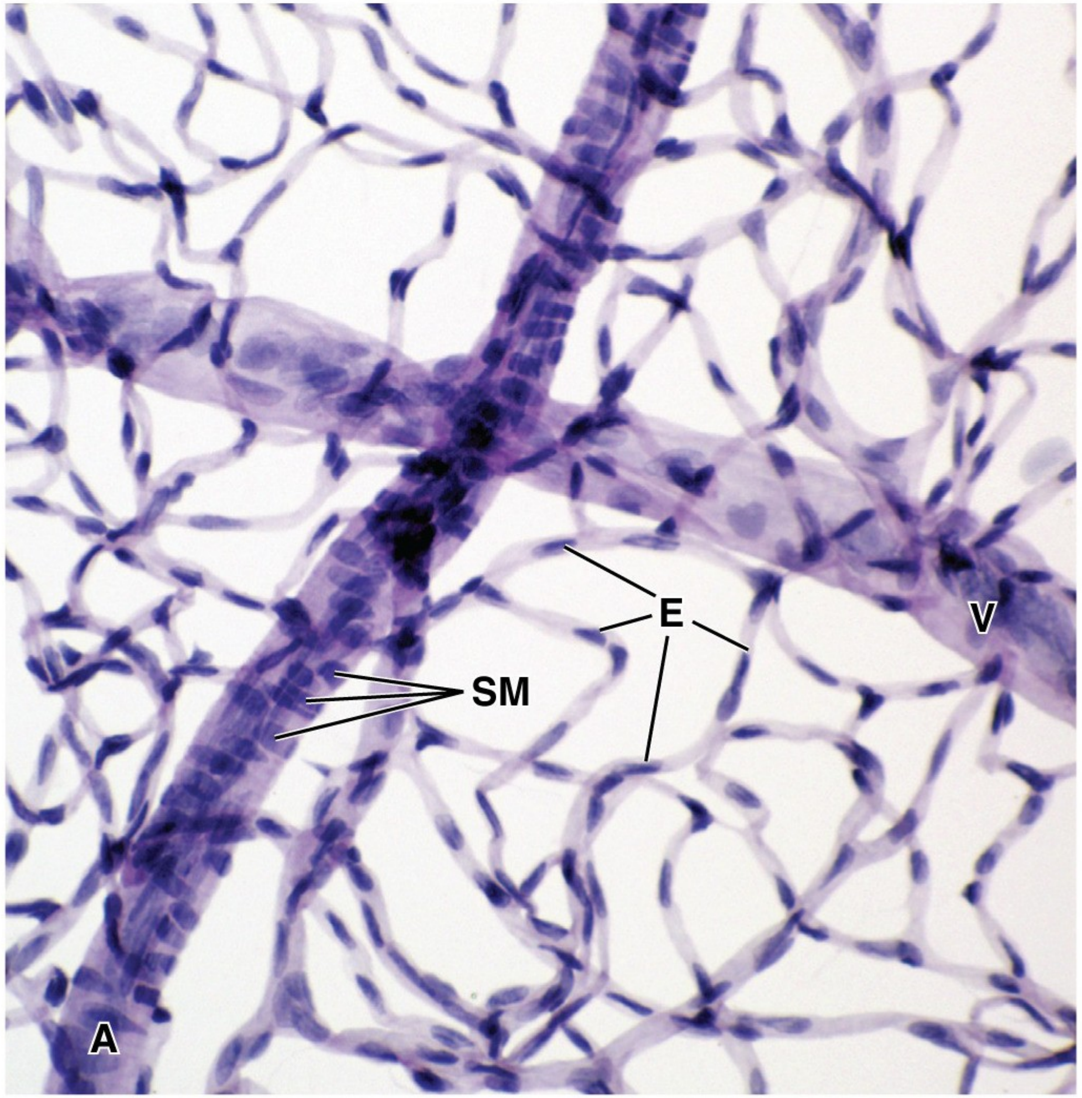
Medium (muscular) arteries: more smooth muscle and less elastin in tunica media



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



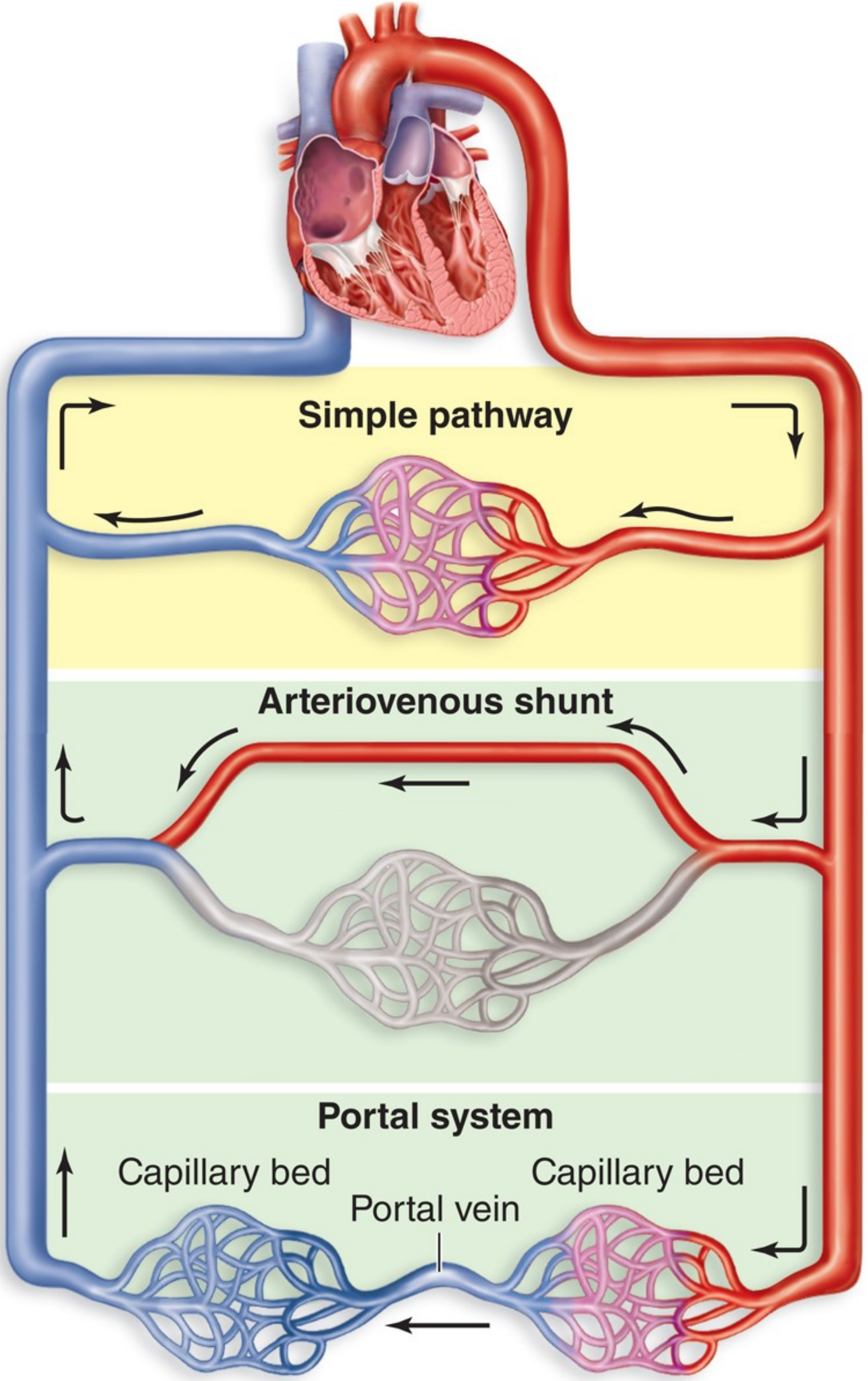
Capillaries allow fluids containing gases, metabolites, and waste products to move through their thin walls.

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.

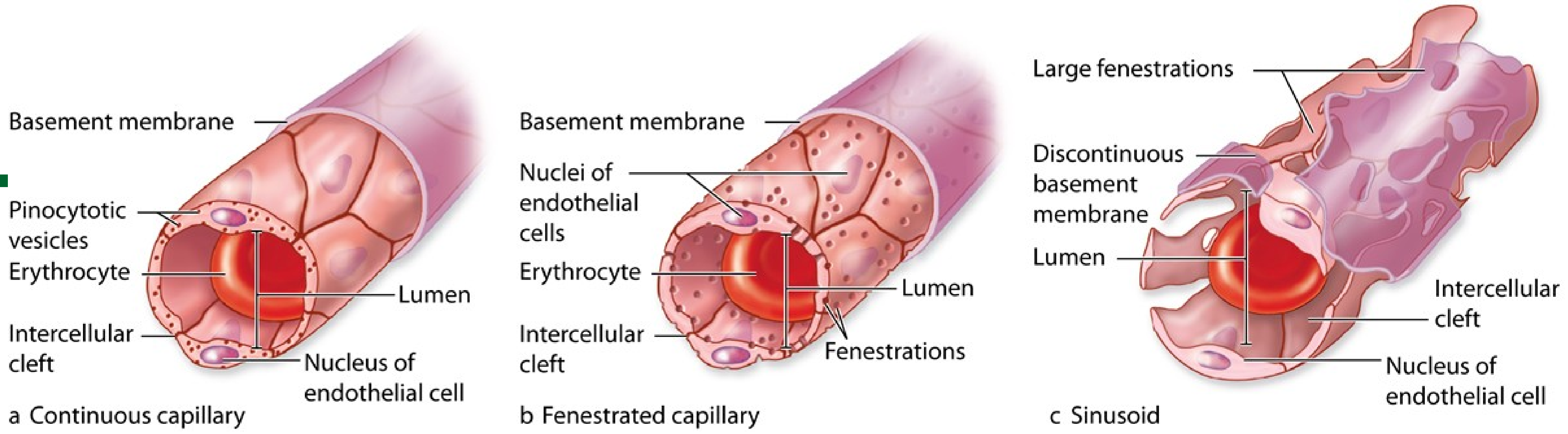
Microvascular pathways

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

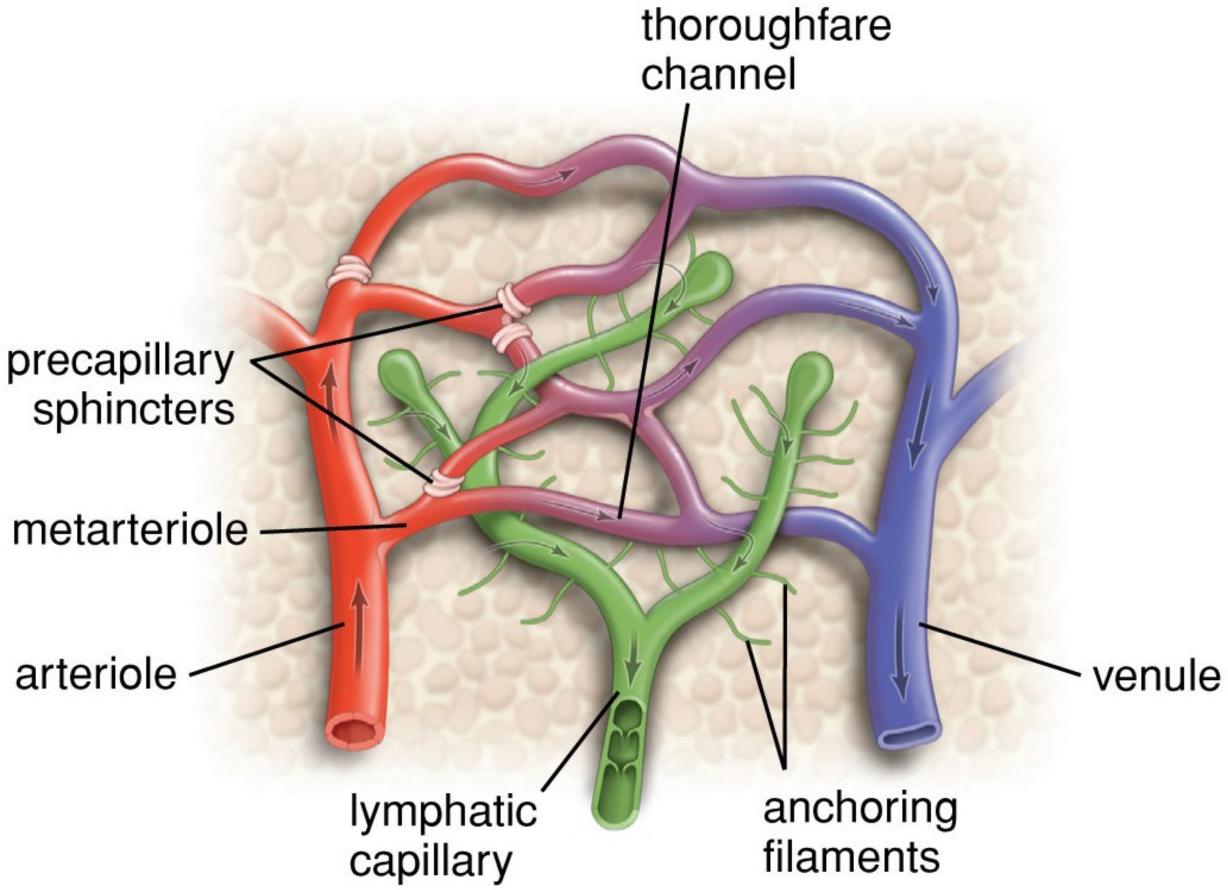


(a) Continuous capillaries, the most common type, have tight, occluding junctions sealing the intercellular clefts between all the endothelial cells to produce minimal fluid leakage. All molecules exchanged across the endothelium must cross the cells by diffusion or transcytosis.

(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



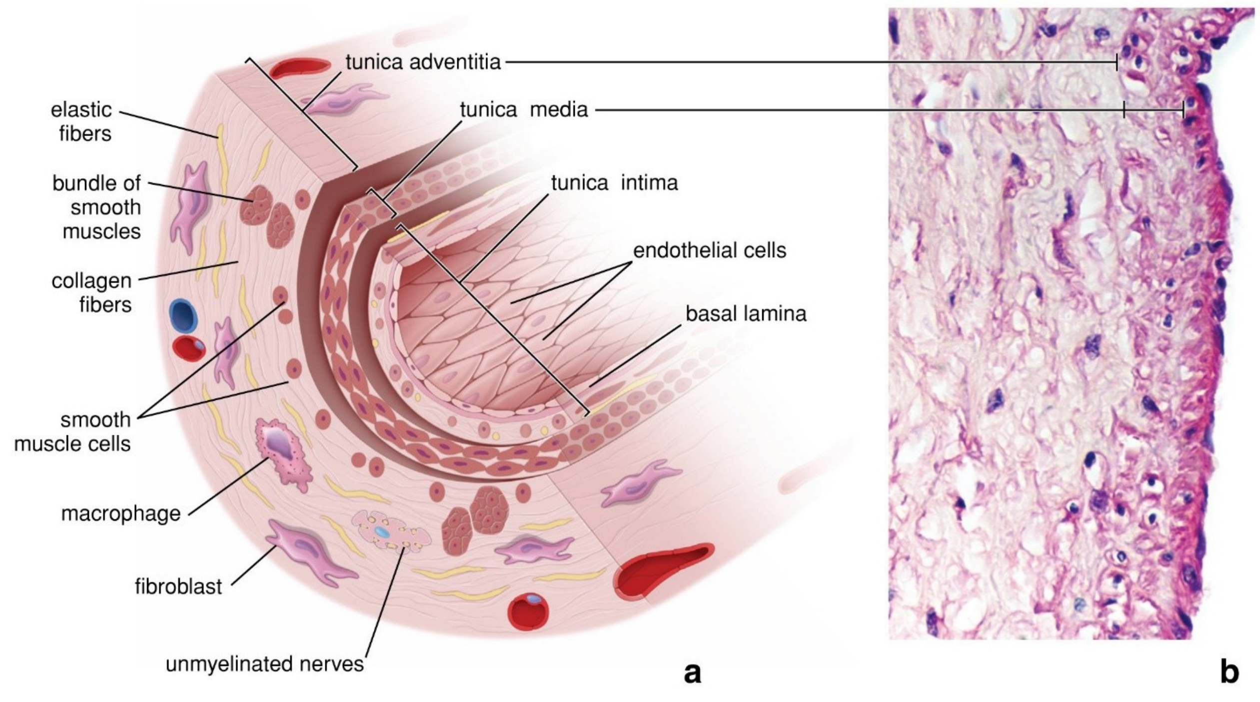
❯❯ MEDICAL APPLICATION

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



MEDIUM-SIZED VEIN

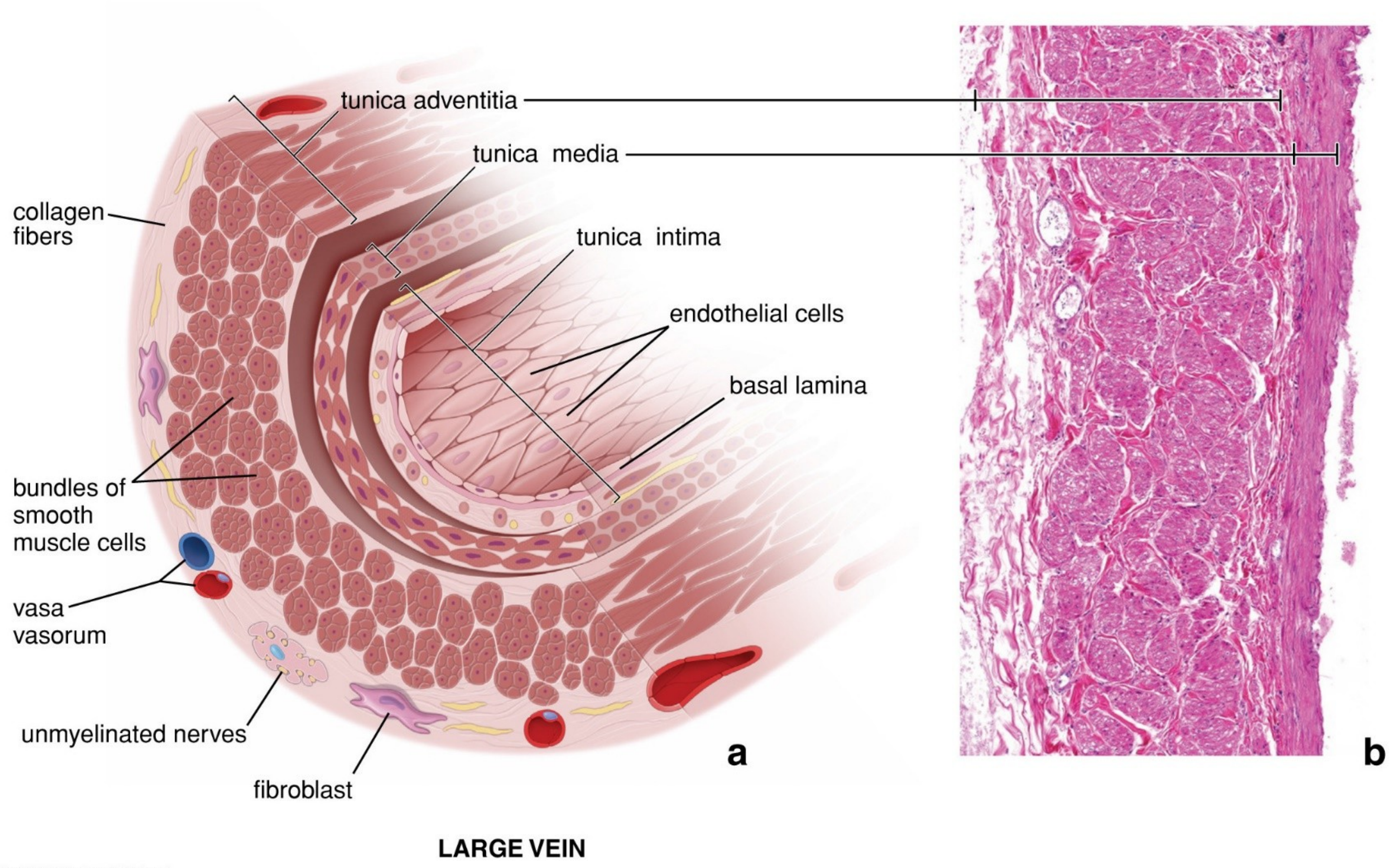
Tunica media: less smooth muscle than similar sized arteries, as flow back to heat is largely passive

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



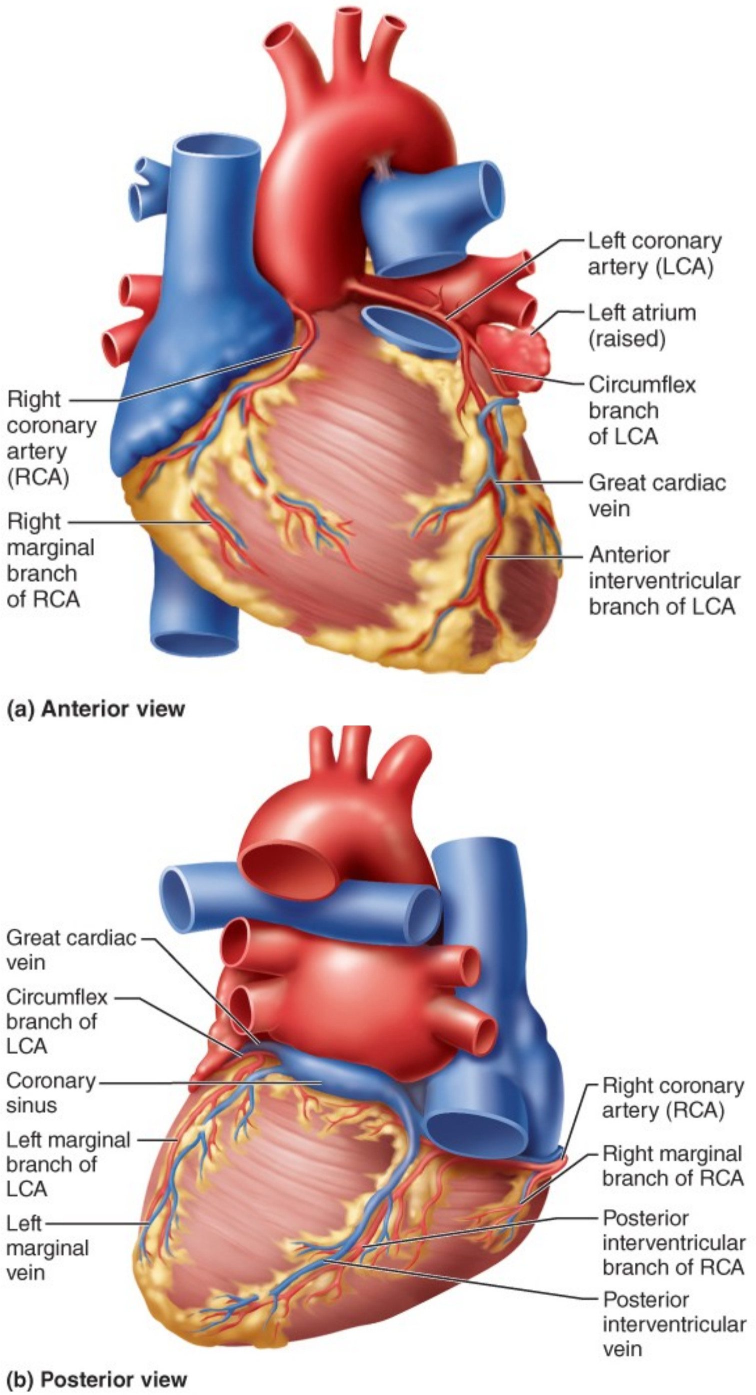
Thick layer of smooth muscle cells in vessels nearest to heart may participate in initiating atrial fibrillation.

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

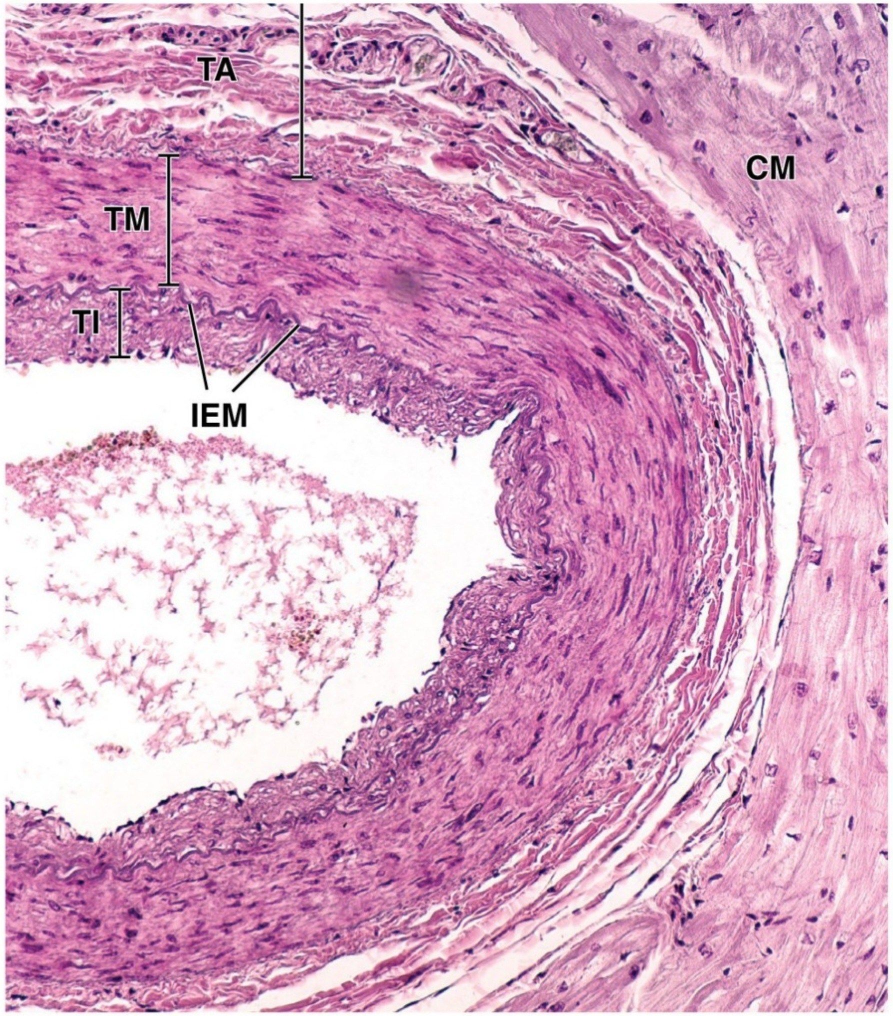
Left coronary artery (LCA)
- **Anterior interventricular branch** (left anterior descending)
- **Circumflex branch**

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**



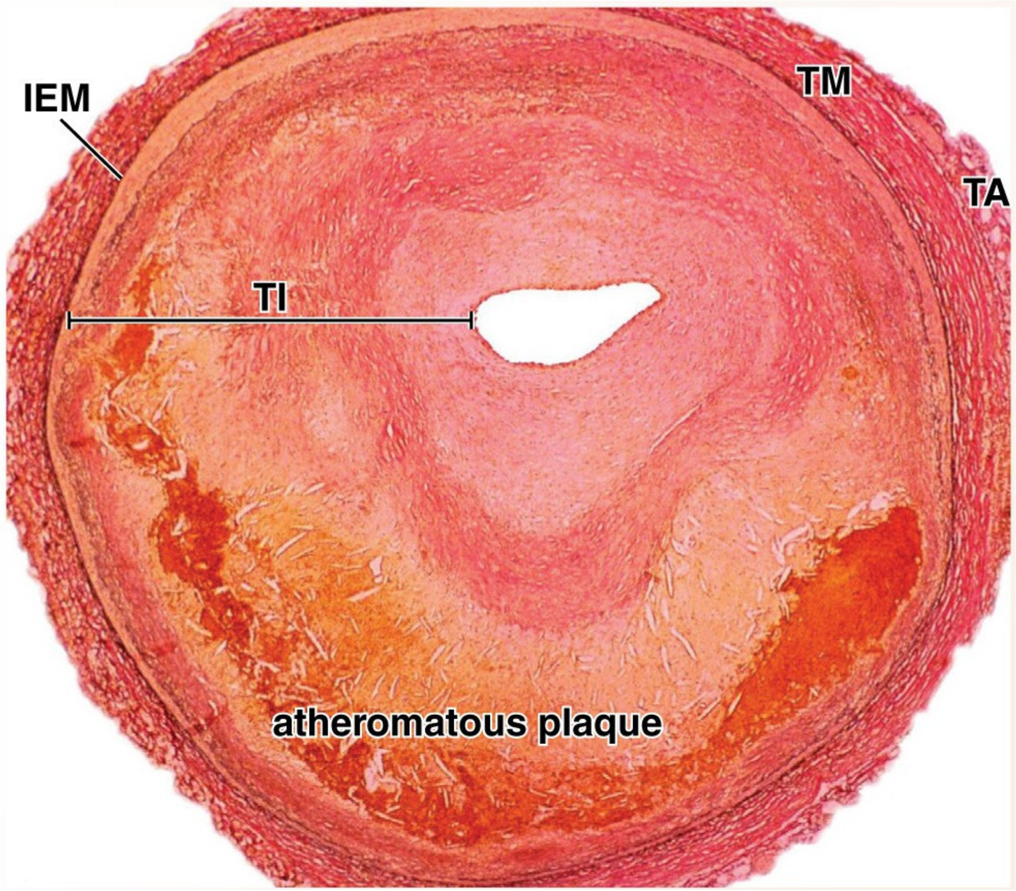
The Coronary artey: medium muscular arteries



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

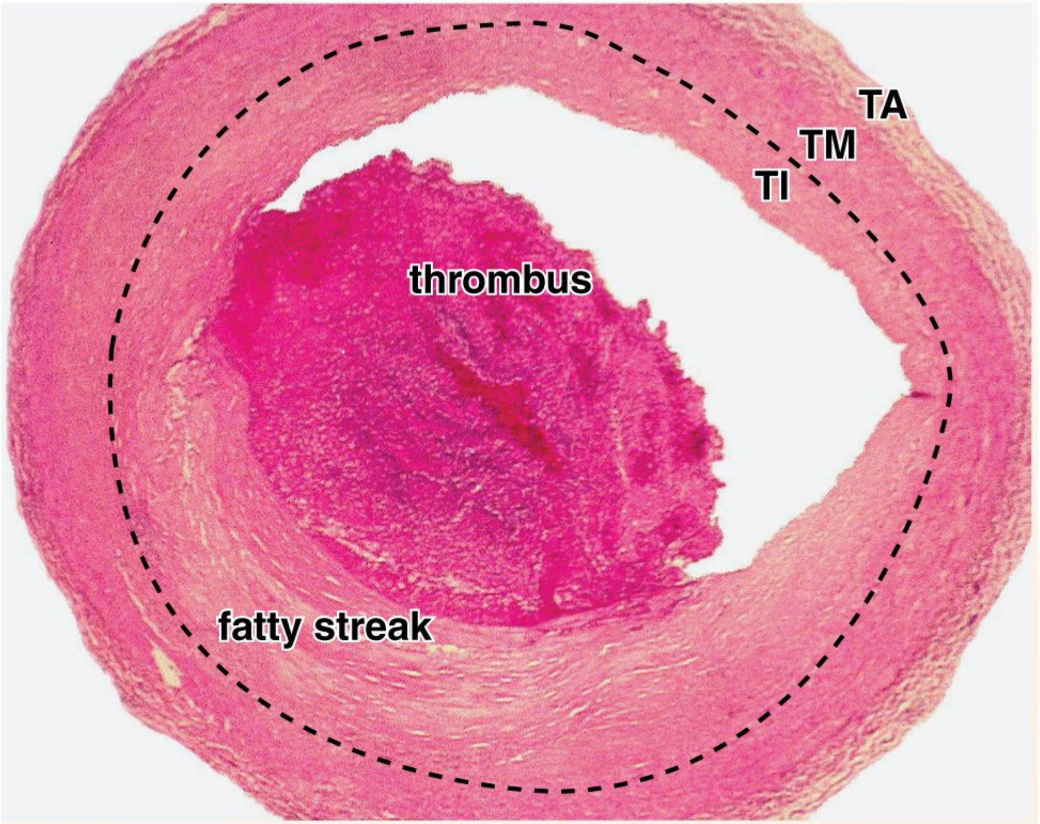
Atherosclerotic changes in coronary arteries that restrict blood flow and oxygen supply to cardiac muscle leads to **ischemic heart disease**

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

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, bicon-cave discs (7.8 μm 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).

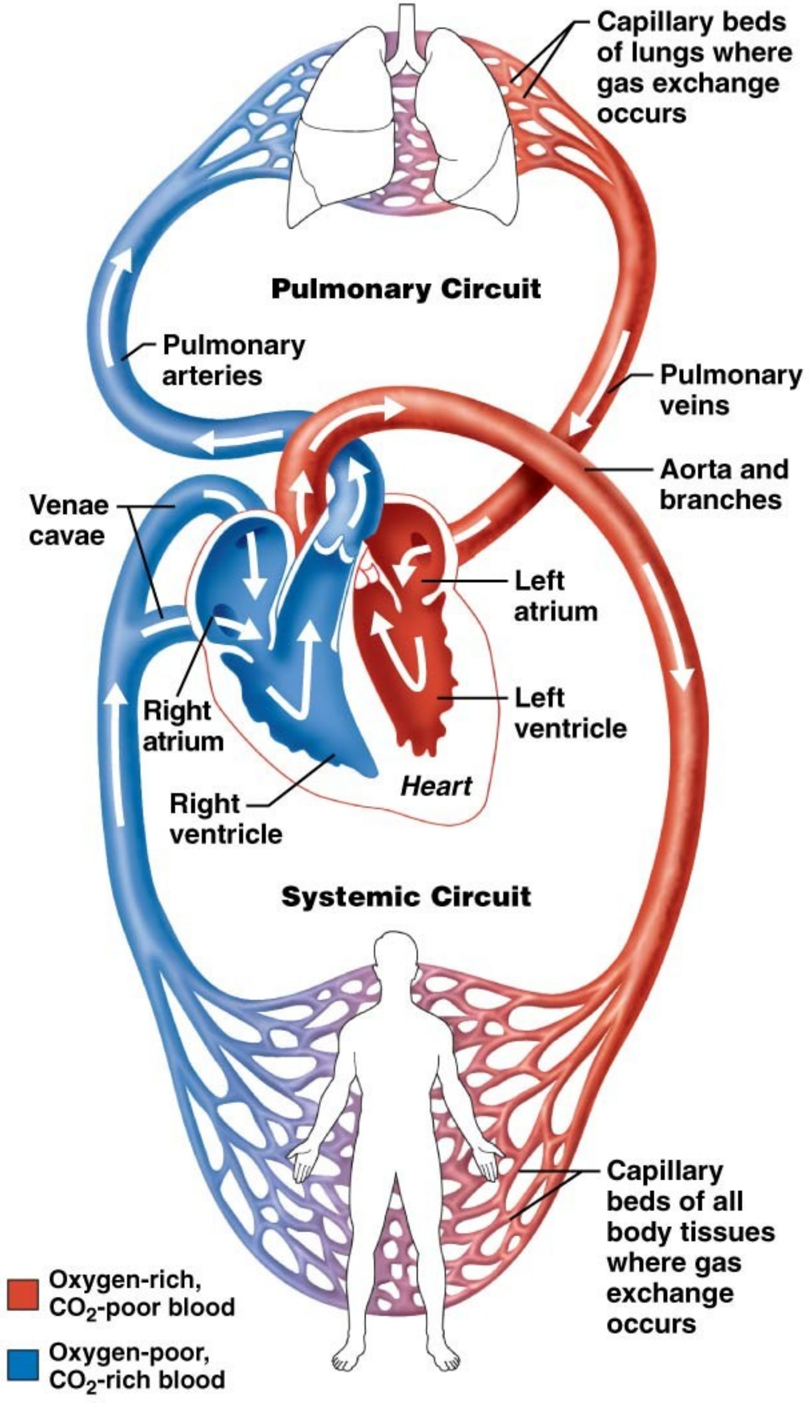
Circulatory system consists of the heart, blo vessels, and blood

Functions of circulatory system

- **Transport:** O_2, CO_2, 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

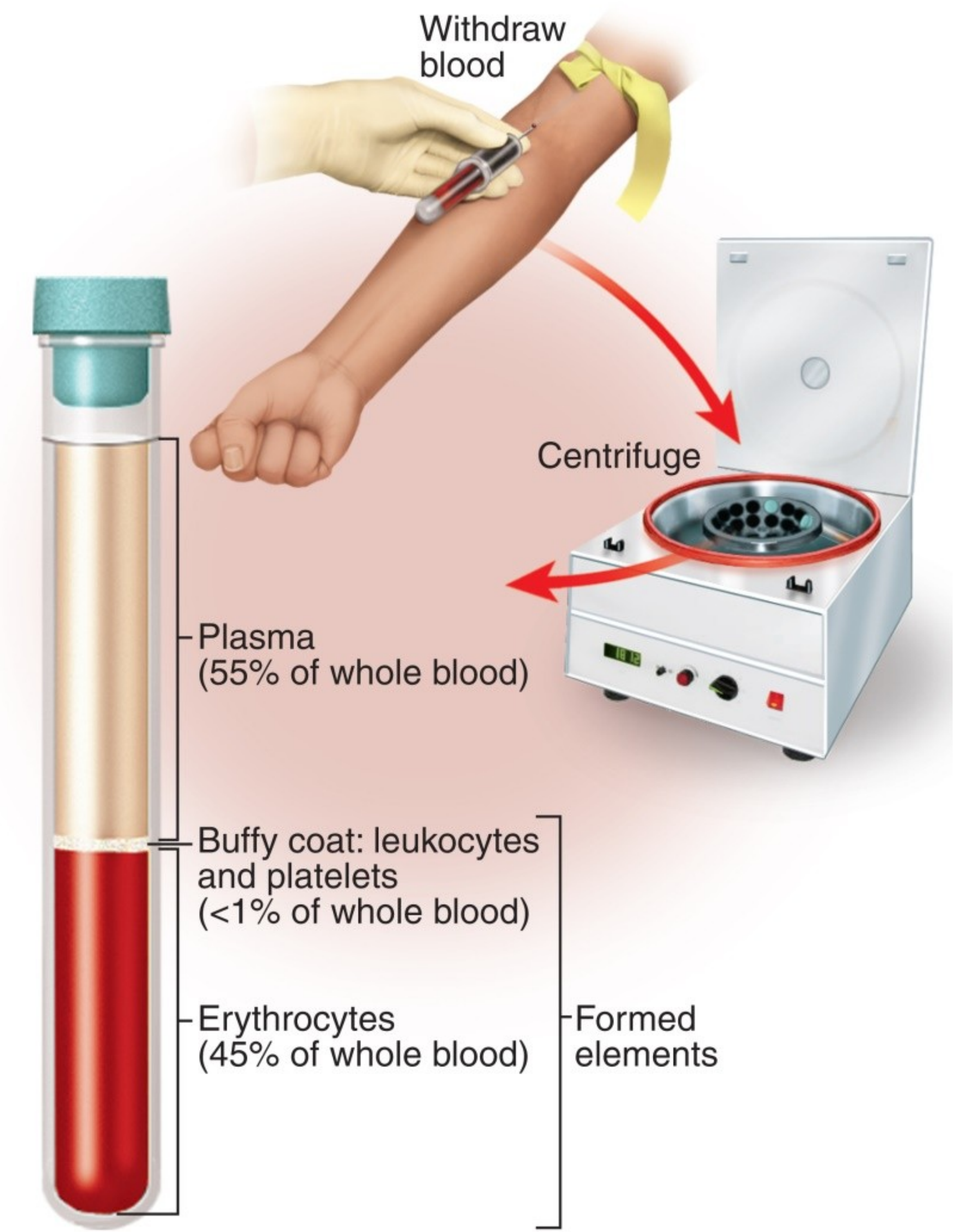


Components and General Properties of Blood

Adults have 4 to 6 L of blood
Blood is a liquid connective tissue consisting of cells and extracellular matrix

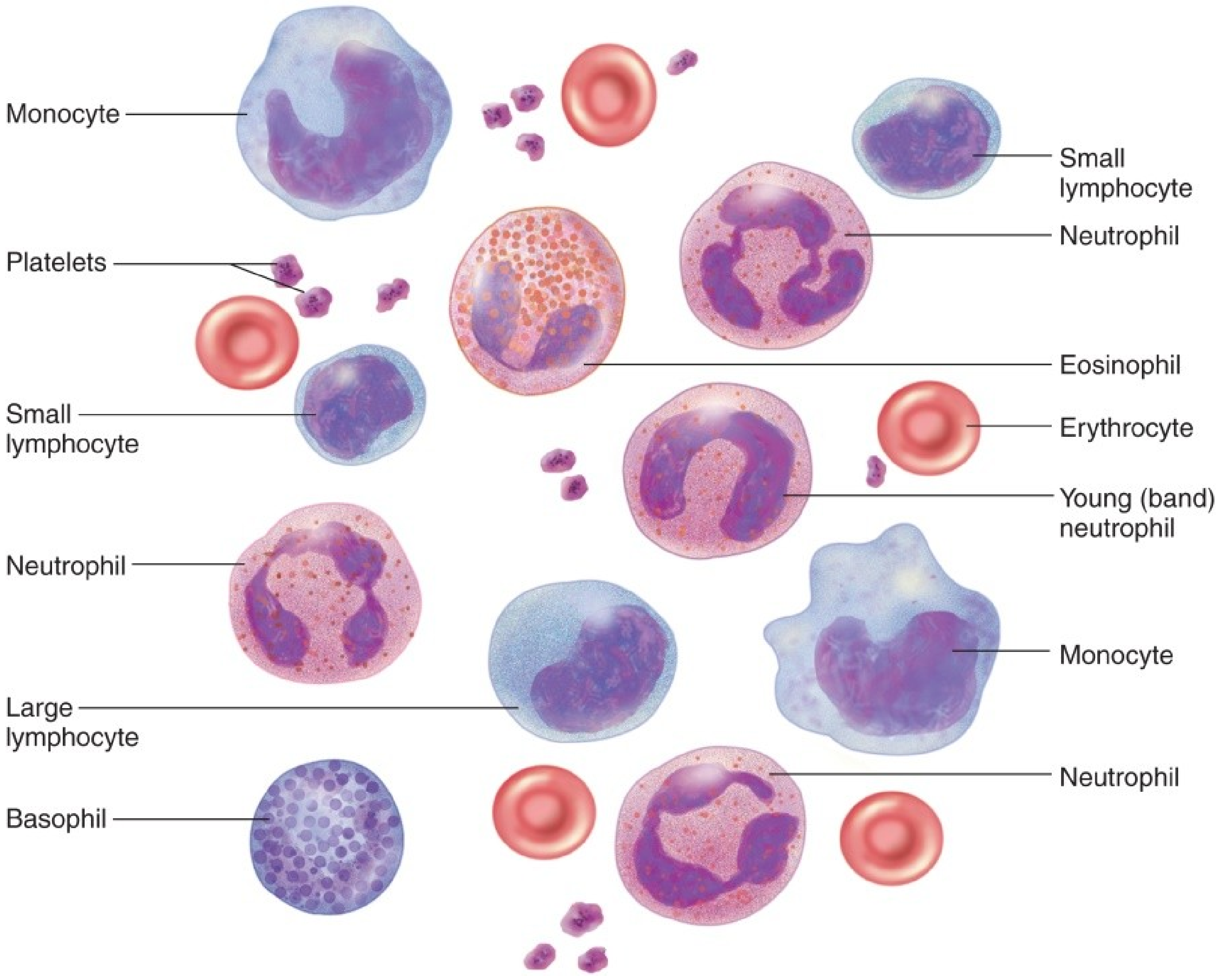
- **Plasma**: matrix of blood. Clear, light yellow fluid
- **Formed elements**: blood cells and cell fragments
    - Red blood cells, white blood cells, and platelets

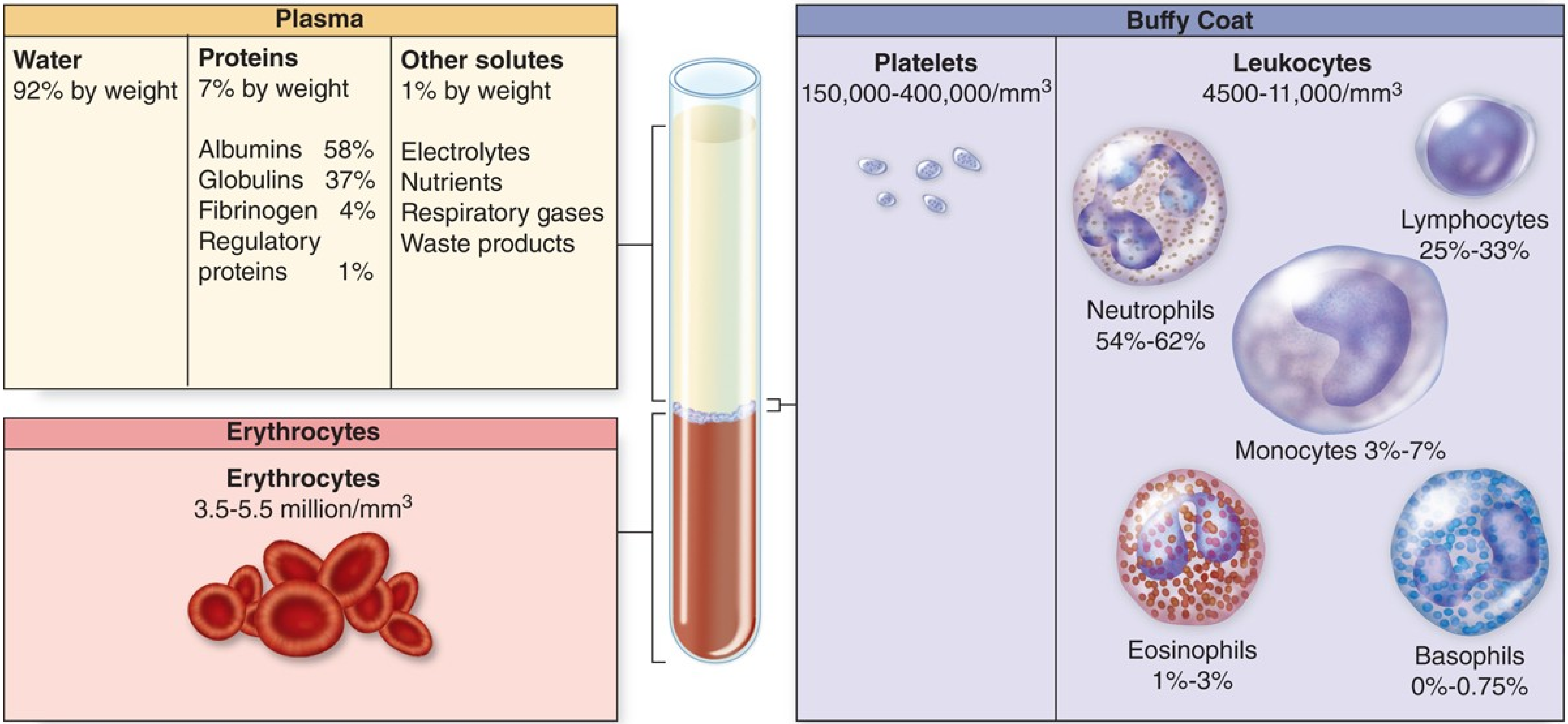
Hematocrit (packed cell volume): percentage of whole blood volume composed of RBCs



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




Plasma
Water
92% by weight
Proteins
7% by weight
Albumins 58%
Globulins 37%
Fibrinogen 4%
Regulatory proteins 1%
Other solutes
1% by weight
Electrolytes
Nutrients
Respiratory gases
Waste products
Erythrocytes
Erythrocytes
3.5-5.5 million/mm3
Buffy Coat
Platelets
150,000-400,000/mm3
Leukocytes
4500-11,000/mm3
Neutrophils
54%-62%
Lymphocytes
25%-33%
Monocytes 3%-7%
Eosinophils
1%-3%
Basophils
0%-0.75%

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

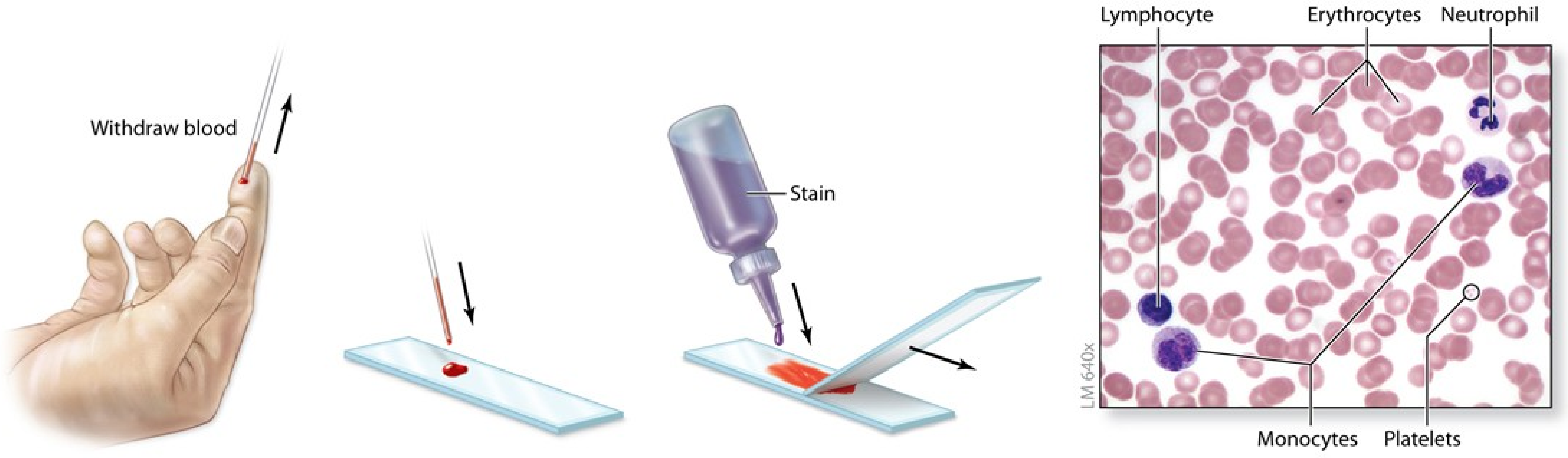
2) Globulins (antibodies): Provide immune system functions
- Alpha, beta, and gamma globulins

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 (Na^+, K^+, Ca^{2+}, Mg^{2+}, Cl^-, HCO^{3-}, PO_4^{3-}, 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.

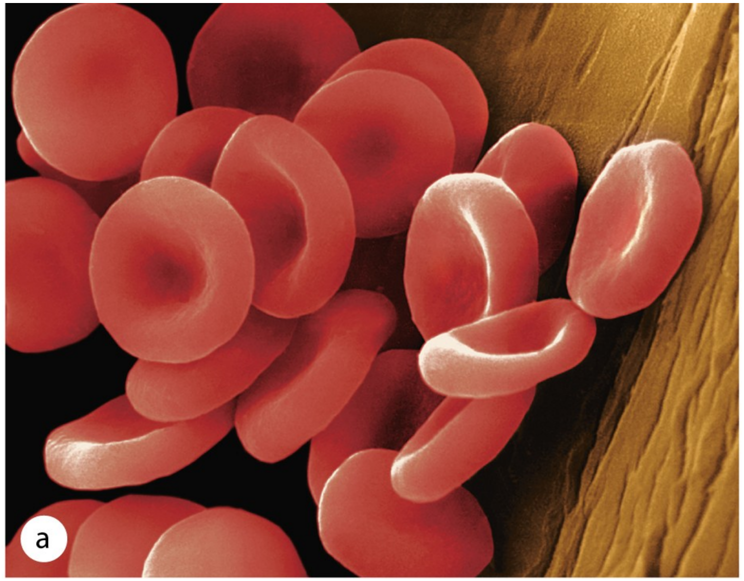
3b. After the blood dries, apply a stain briefly and rinse. Place a coverslip on top.

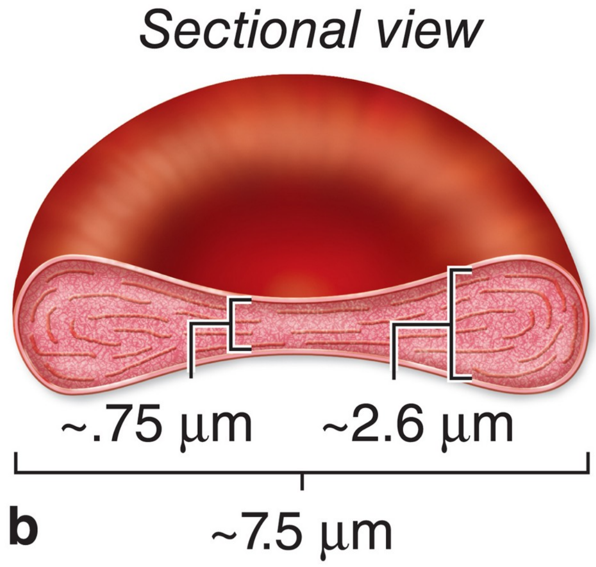
4. When viewed under the microscope, blood smear reveals the components of the formed elements.

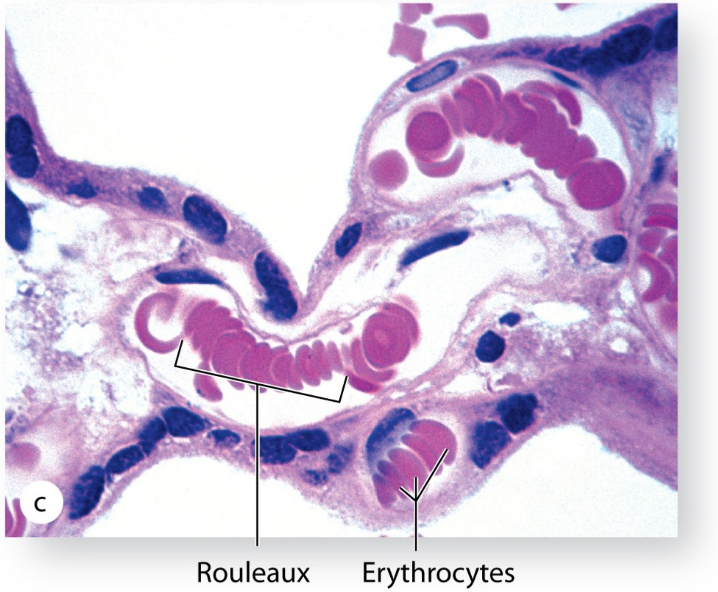
Erythrocytes

- Two principal functions
  - Carry oxygen from lungs to cell tissues
  - Pick up CO_2 from tissues and bring to lungs

- Insufficient RBCs may kill in minutes due to lack of oxygen to tissues

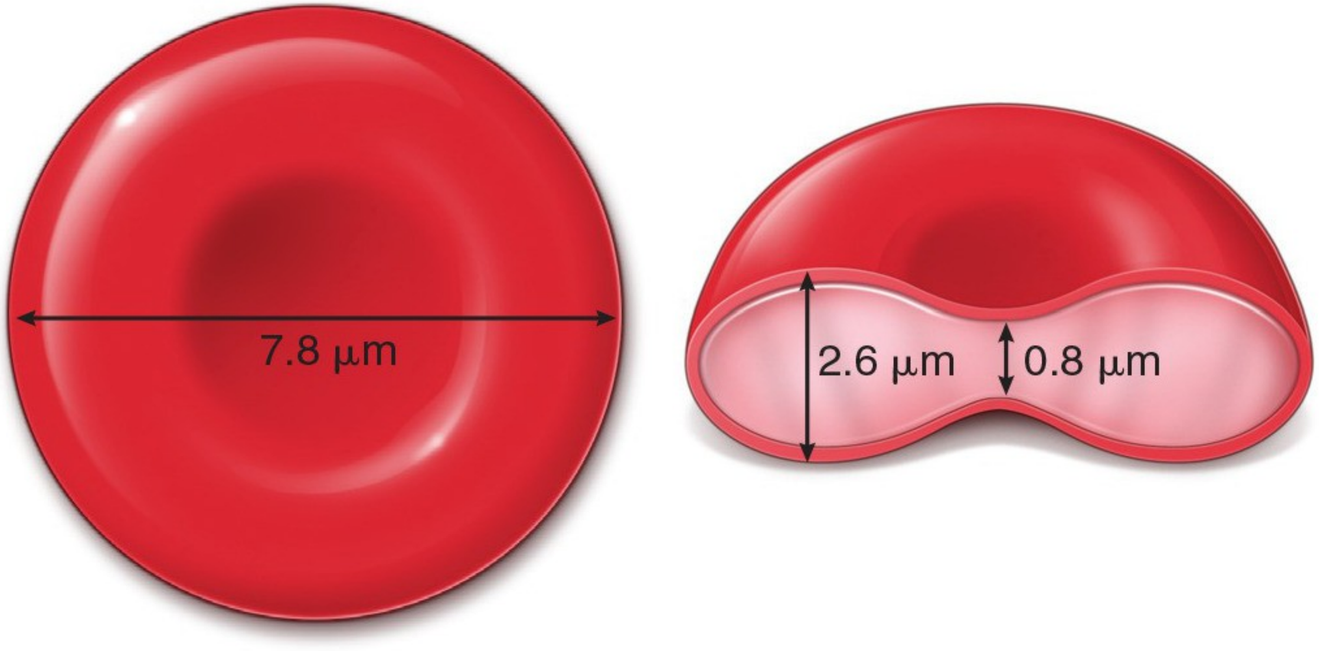




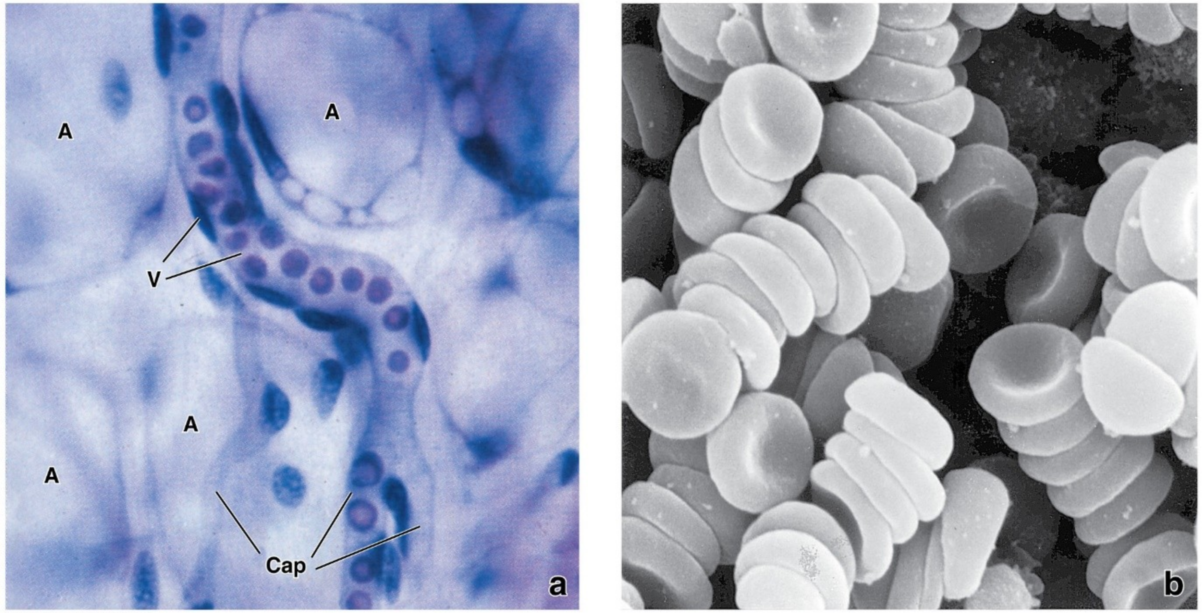


Form and Function

- Disc-shaped cell with thick rim
  - 7.8 µm diameter and 2.0 µm 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

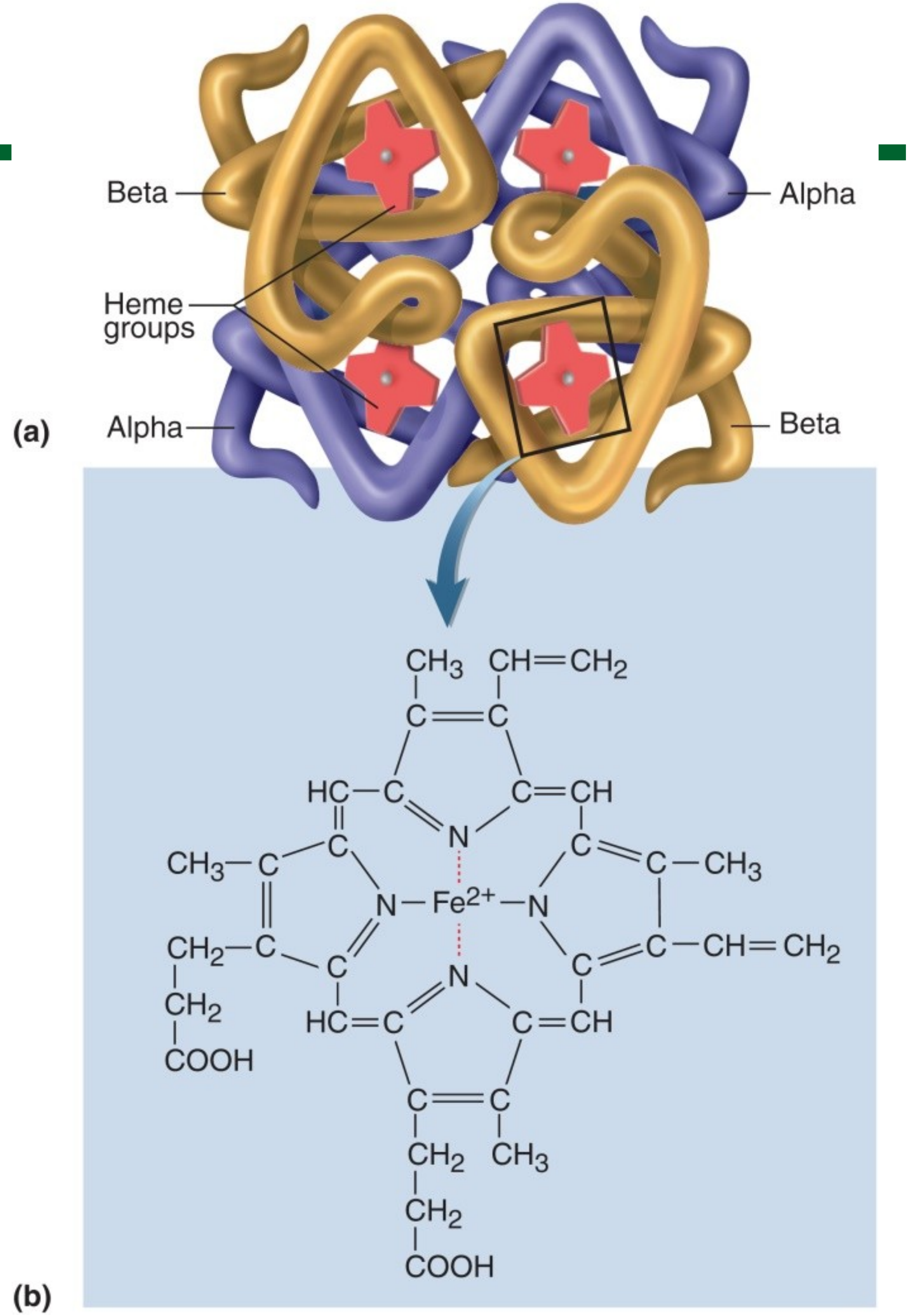
❯❯ MEDICAL APPLICATION

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_2. 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.

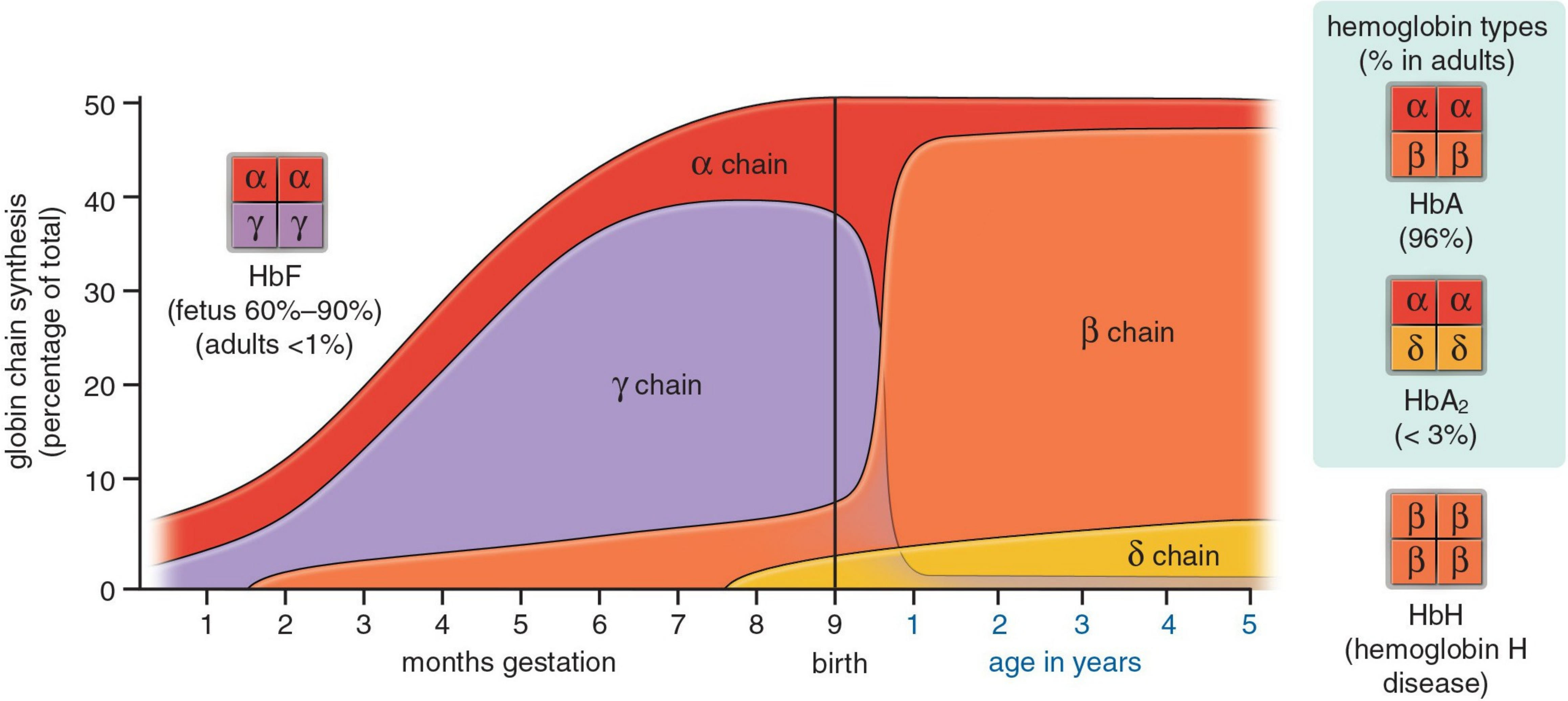
An increased concentration of erythrocytes in blood (**erythrocytosis**, or **polycythemia**) may be a physiologic Adaptation found, for example, in individuals who live at high altitudes, where O_2 is low. Elevated hematocrit increases blood viscosity, putting strain on the heart, and, if severe, can impair circulation through the capillaries.

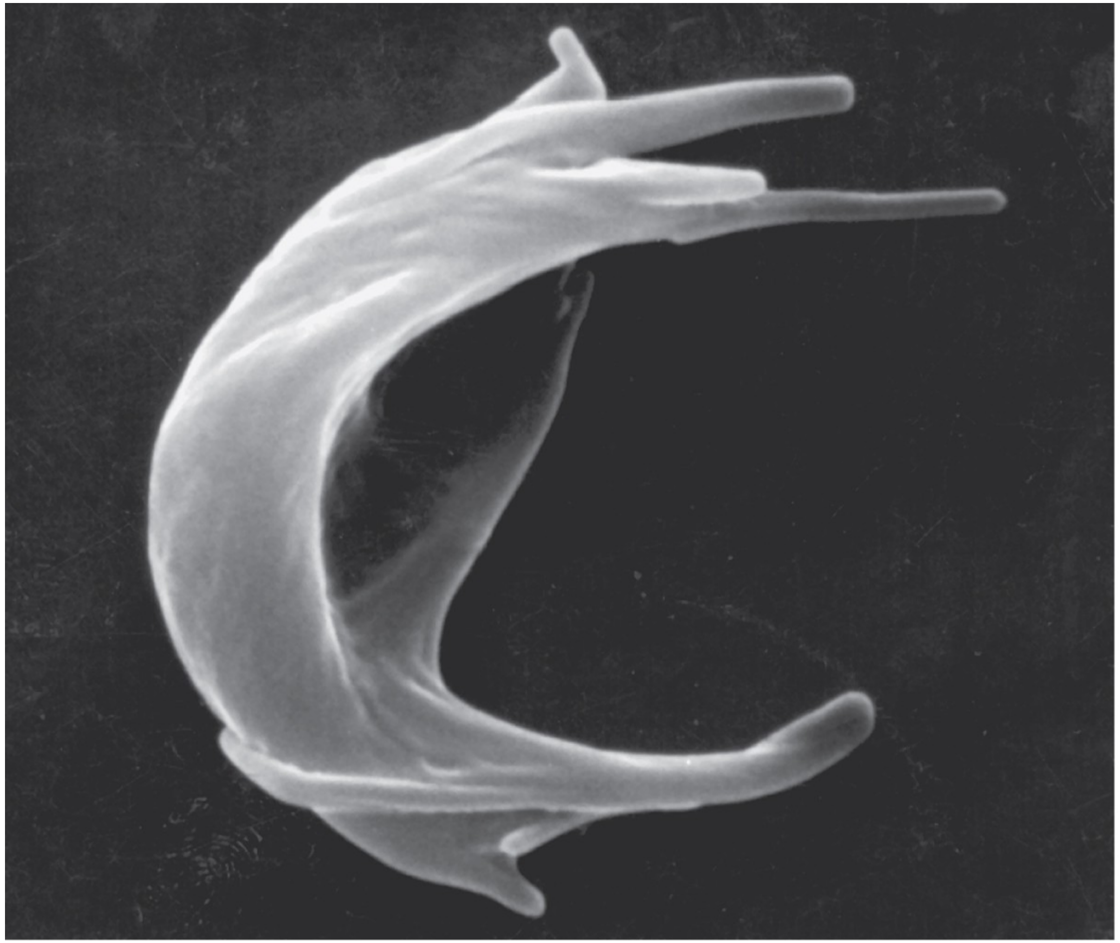
Hemoglobin

- Each Hb molecule consists of:
  - Four protein chains—globins
  - Four heme groups
- Heme groups
  - Nonprotein moiety that binds O_2 to ferrous ion (Fe^{2+}) at its center
- RBC count and hemoglobin concentration indicate amount of O_2 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

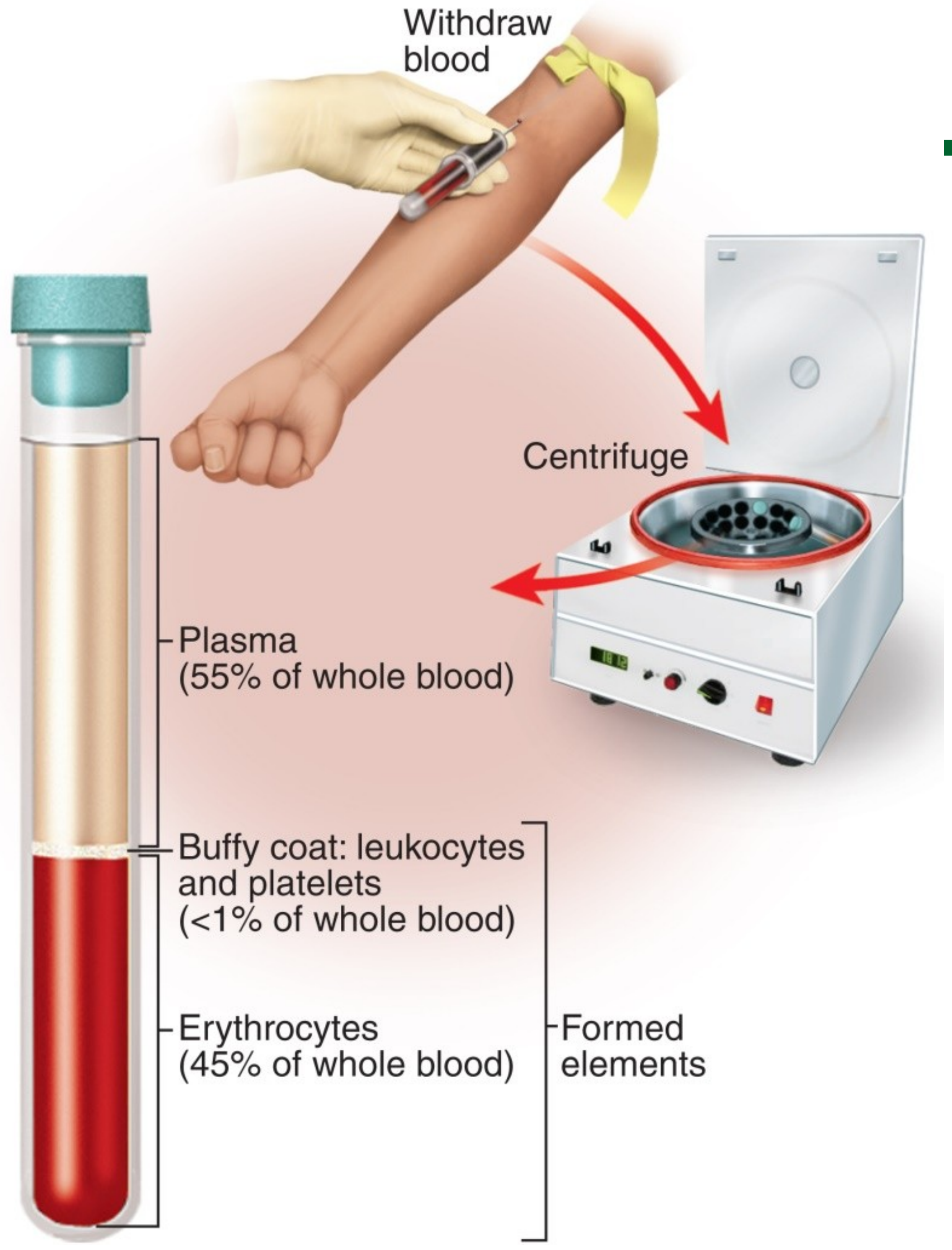
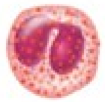
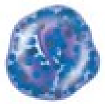
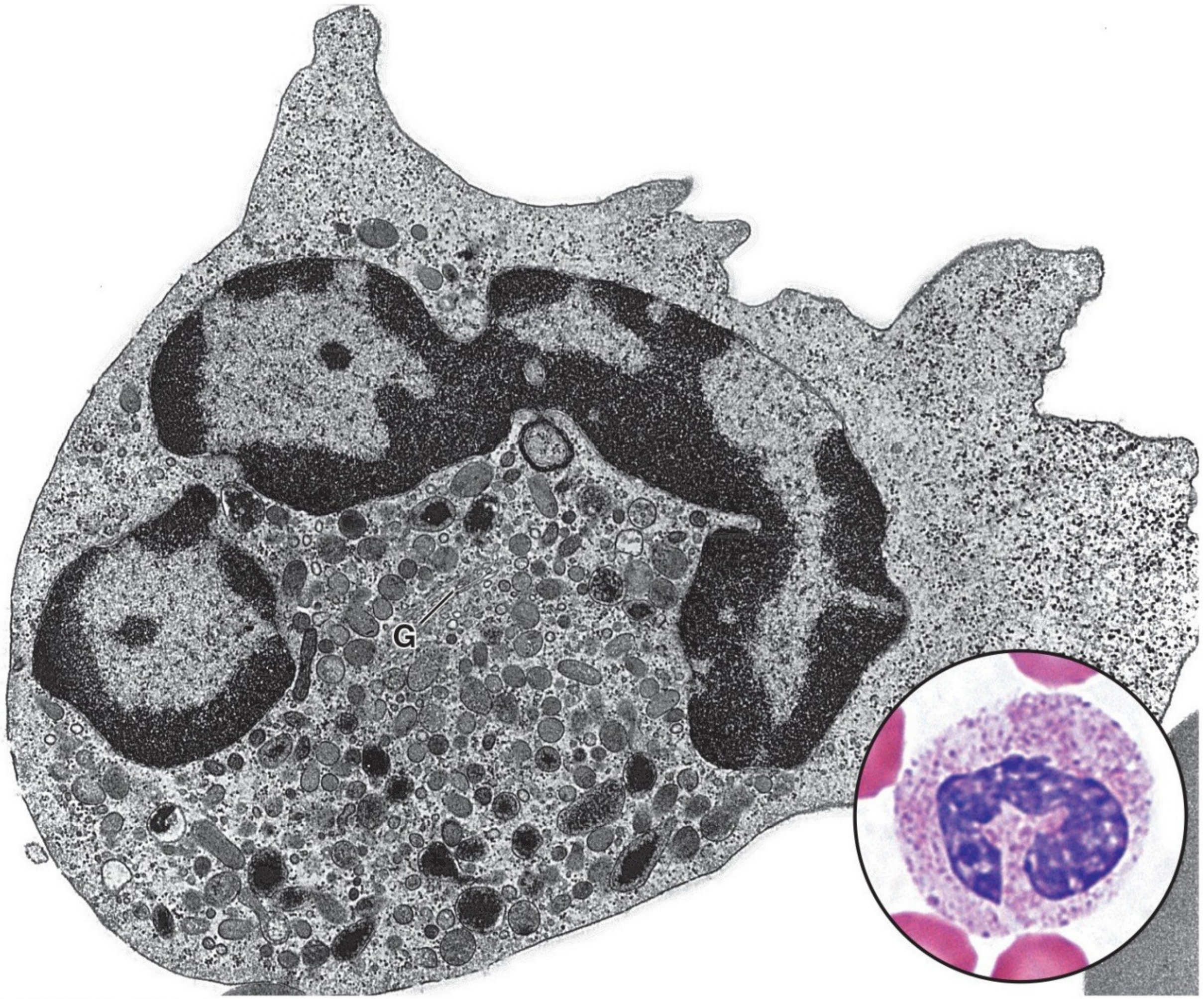


Table 29.1 Summary of Formed Elements of the Blood

Cell type	Illustration	Description*	Cells/mm3 (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.

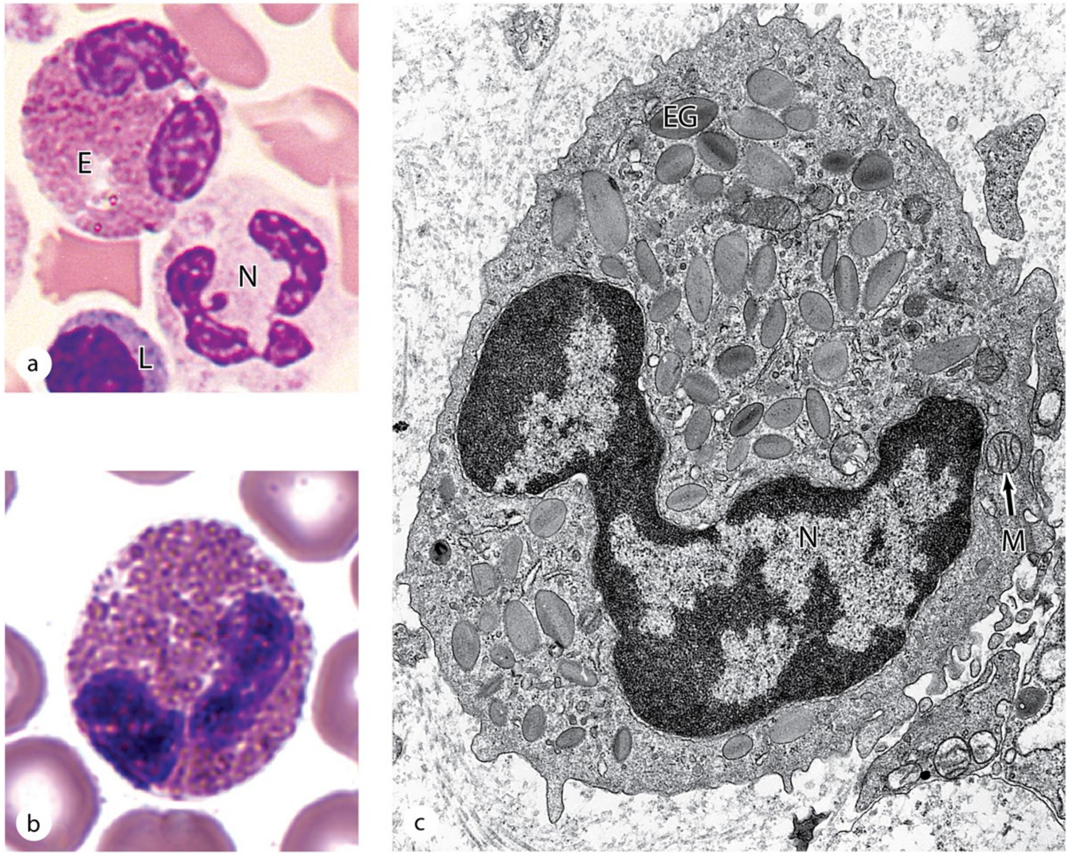


The nucleus shows the typical multilobed configuration with the heterochromatin at the periphery and the euchromatin more centrally located.

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

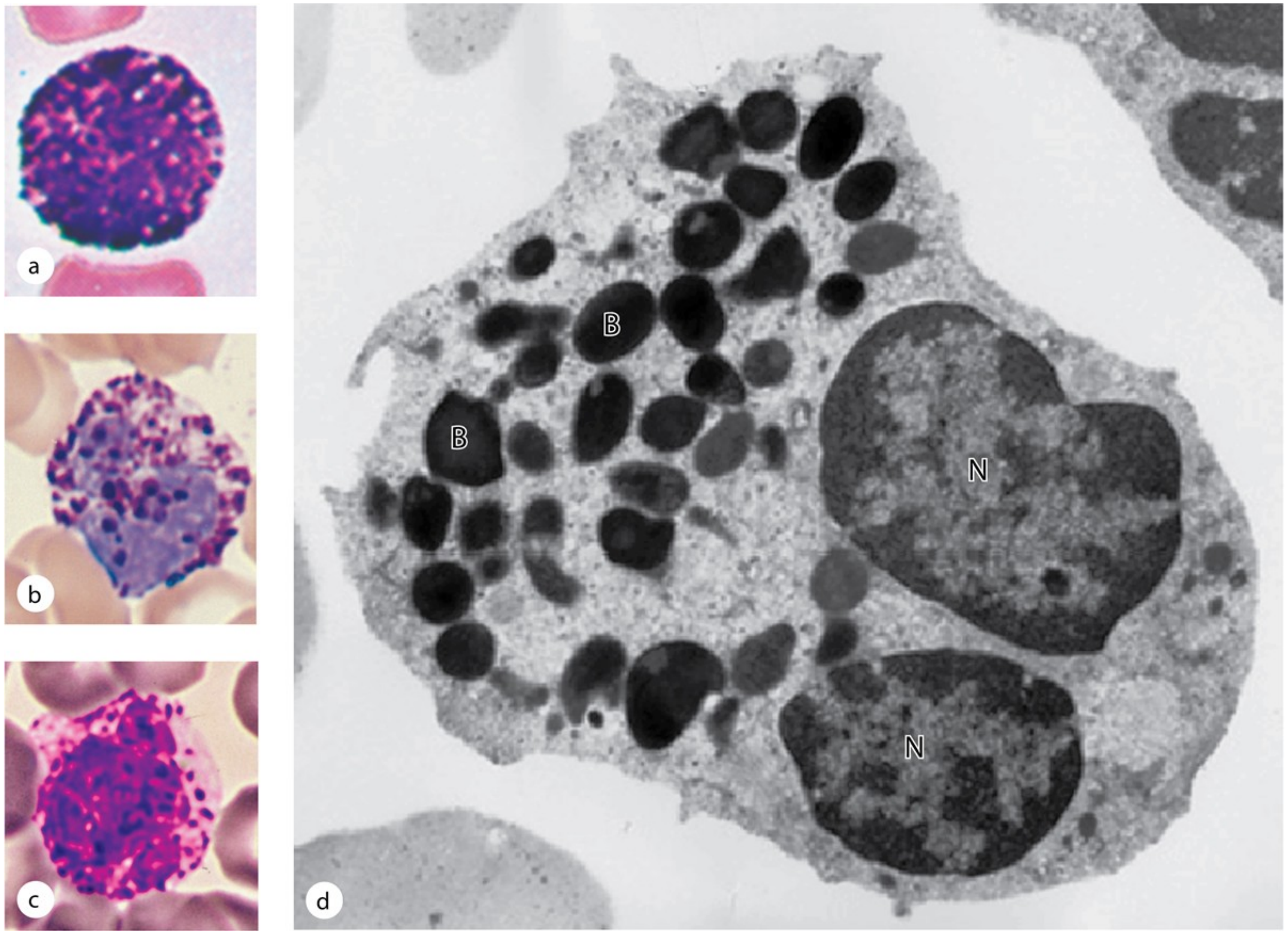


Eosinophils are associated with allergic reactions, parasitic infections, and chronic inflammation.

❯❯ 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

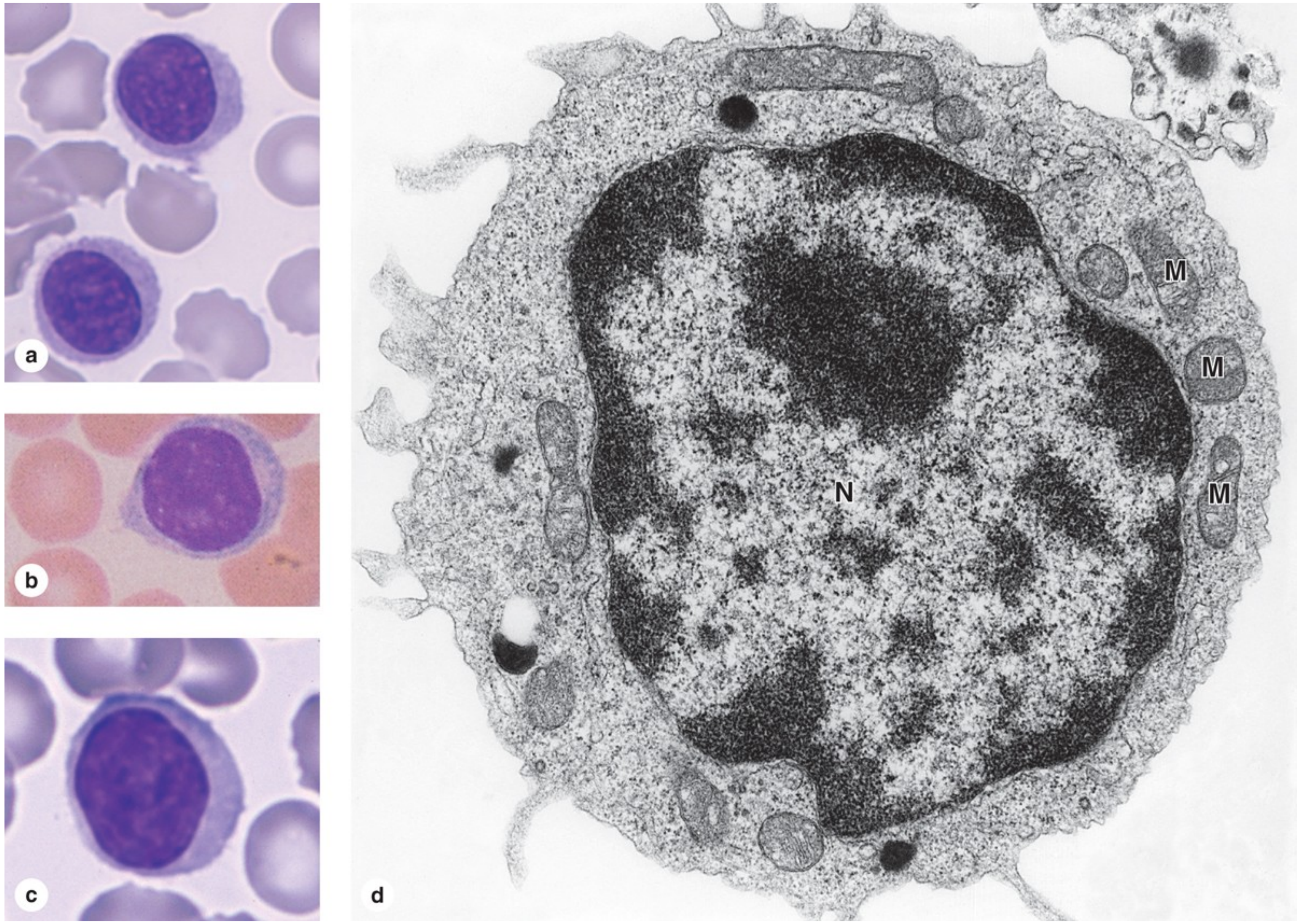


Basophils have large, strongly basophilic specific granules that usually obstruct the appearance of the nucleus which usually has two large irregular lobes

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



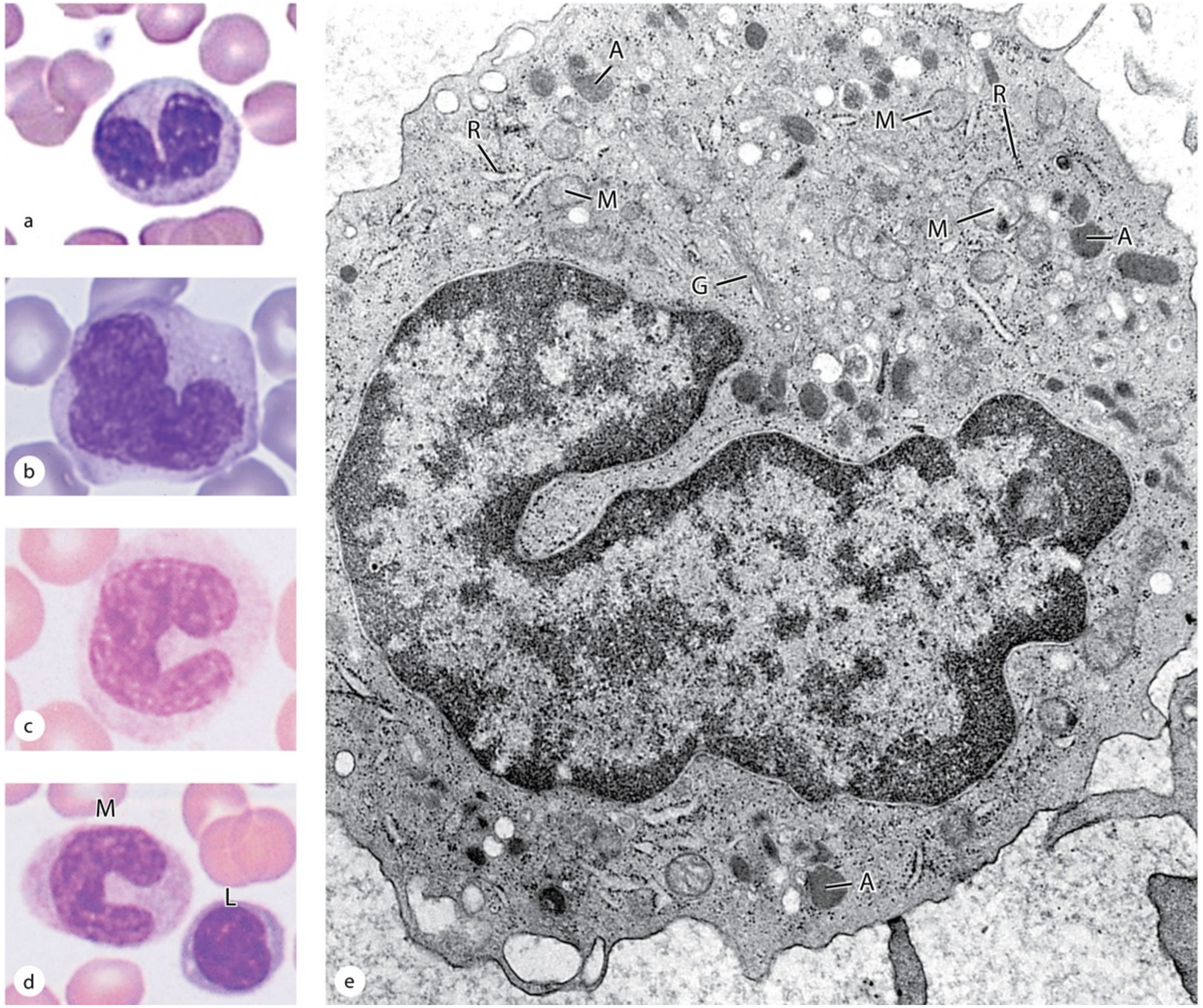
[http://
ed.ted.com/lessons/what-is-leukemia-danilo-alle
gra-and-dania-puggioni](http://ed.ted.com/lessons/what-is-leukemia-danilo-allegra-and-dania-puggioni)

Lymphocytes circulating in blood generally range in size from 6 to 15 µm 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 µm that circulate as precursors to macrophages

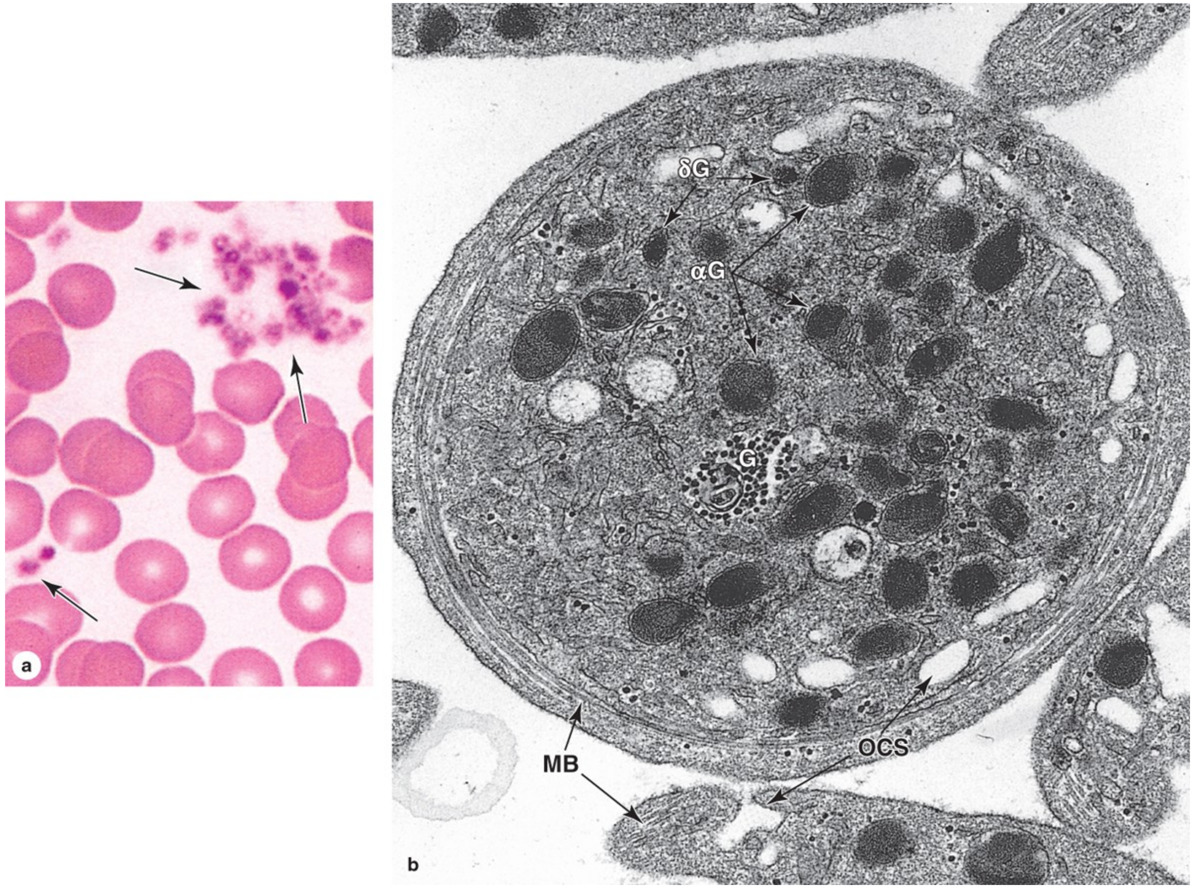


Monocytes have distinctive nuclei which are indented, kidney-shaped, or C-shaped

❯❯ 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 µm in diameter derived from megakaryocytes of bone marrow



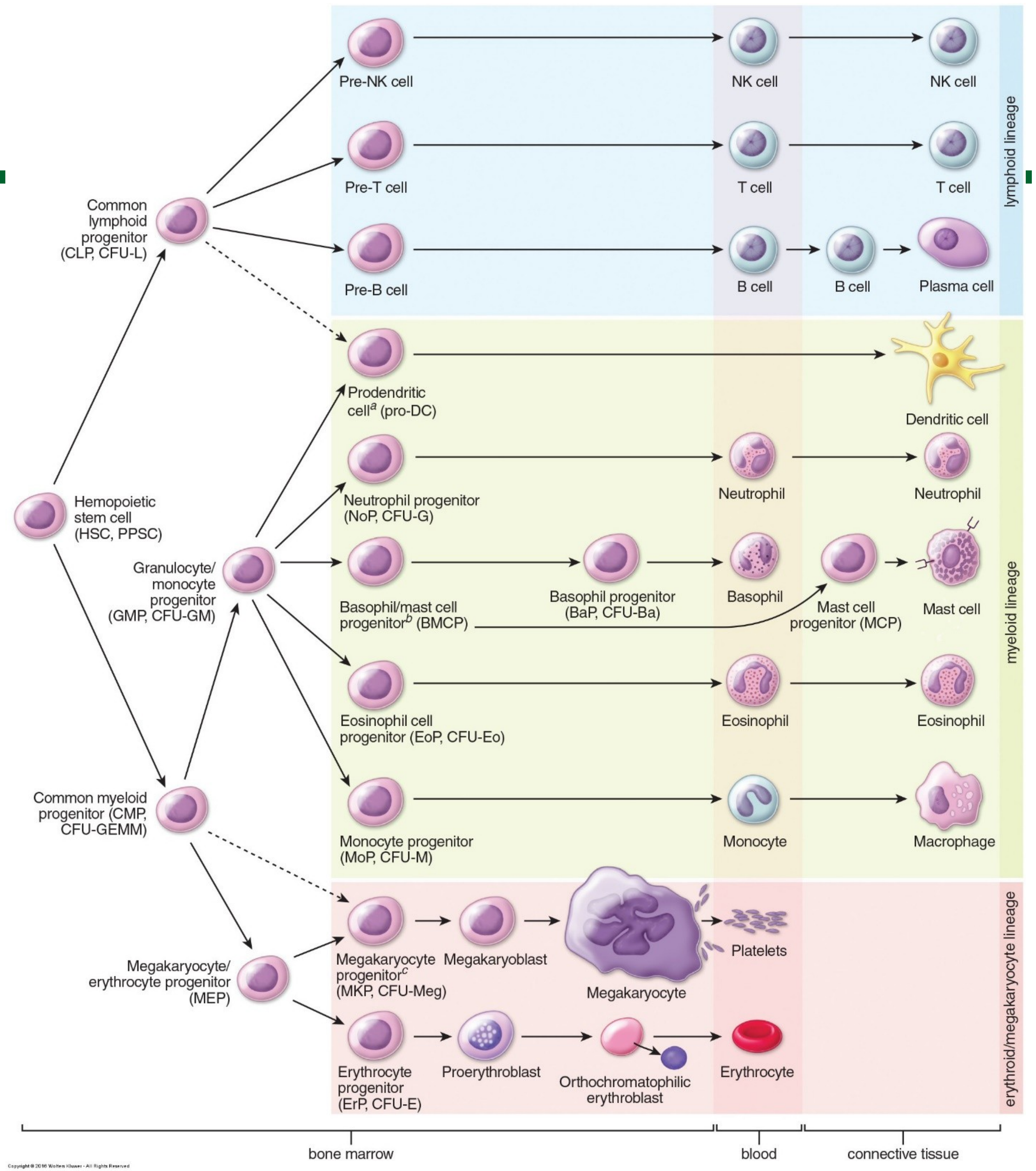
Platelets: release the content of their granules upon contact with collagen (or other materials outside of the endothelium) to begin the process of clot formation and reduce blood loss from the vasculature.

❯❯ 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).



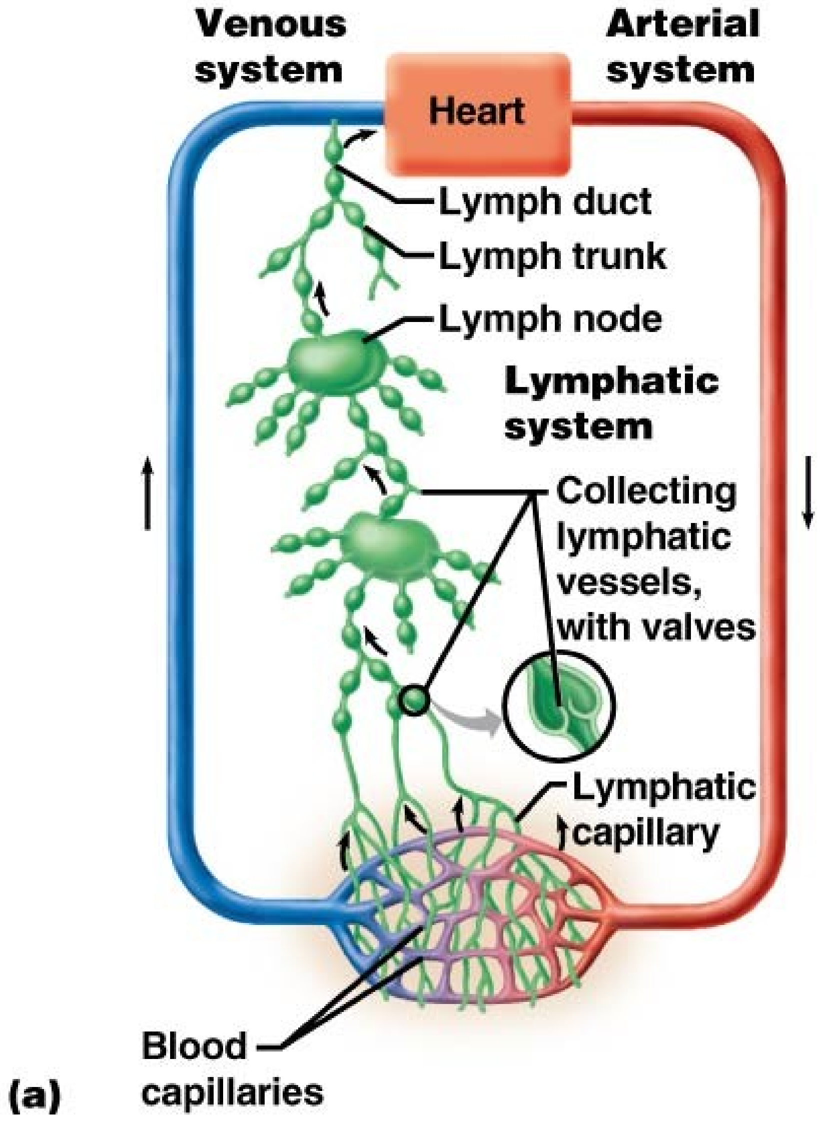
Lymphatic, Digestive, and Associated Organs of the Digestive System

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



The immune system explained (watch at home after class): http://ed.ted.com/on/uJ4BVyIr

Mechanisms of Immune Defense

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

- **1st defense**: External barriers, skin, and mucous membranes
- **2nd defense**: Leukocytes and macrophages, antimicrobial proteins (interferons, complement system), immune surveillance, inflammation, and fever

Adaptive (Specific) Immunity

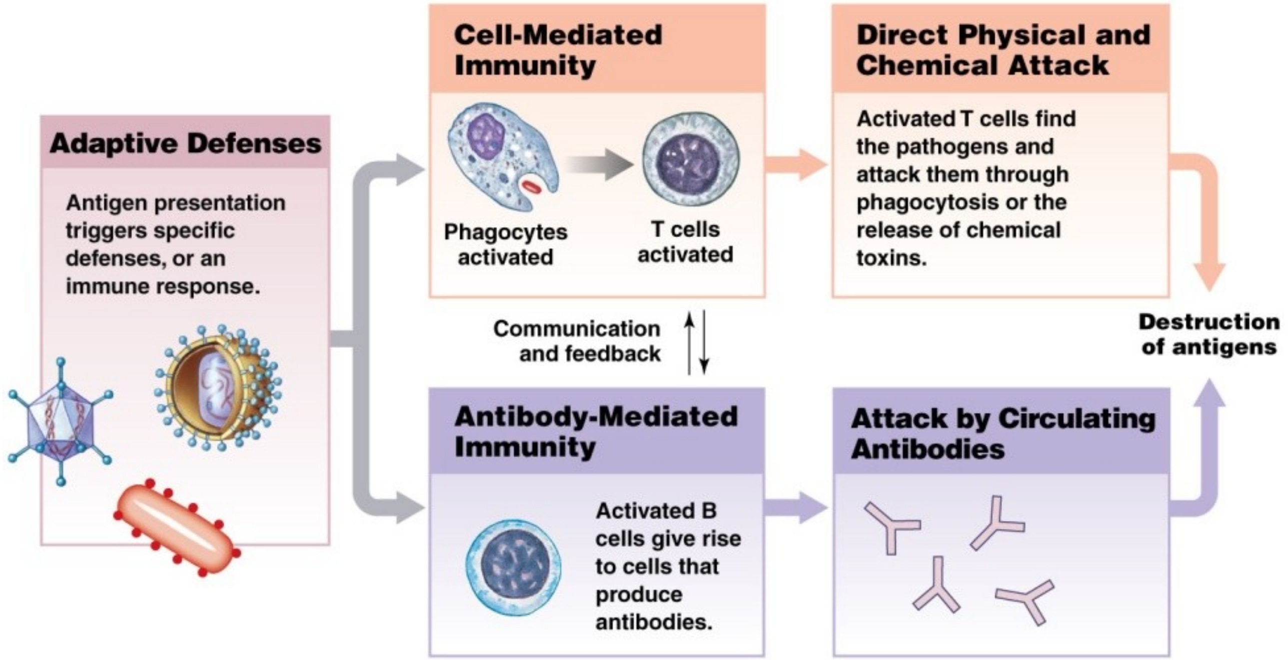
- **3rd defense:** Relies on prior exposure of memory of pathogen, enabling faster defense in the future
  - Humoral: antibody marks invaders for other immune cells
  - Cellular: infected cells are destroyed by “killer” cells

Overview of Immune System: http://www.youtube.com/watch?v=IWMJIMzsEMg
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

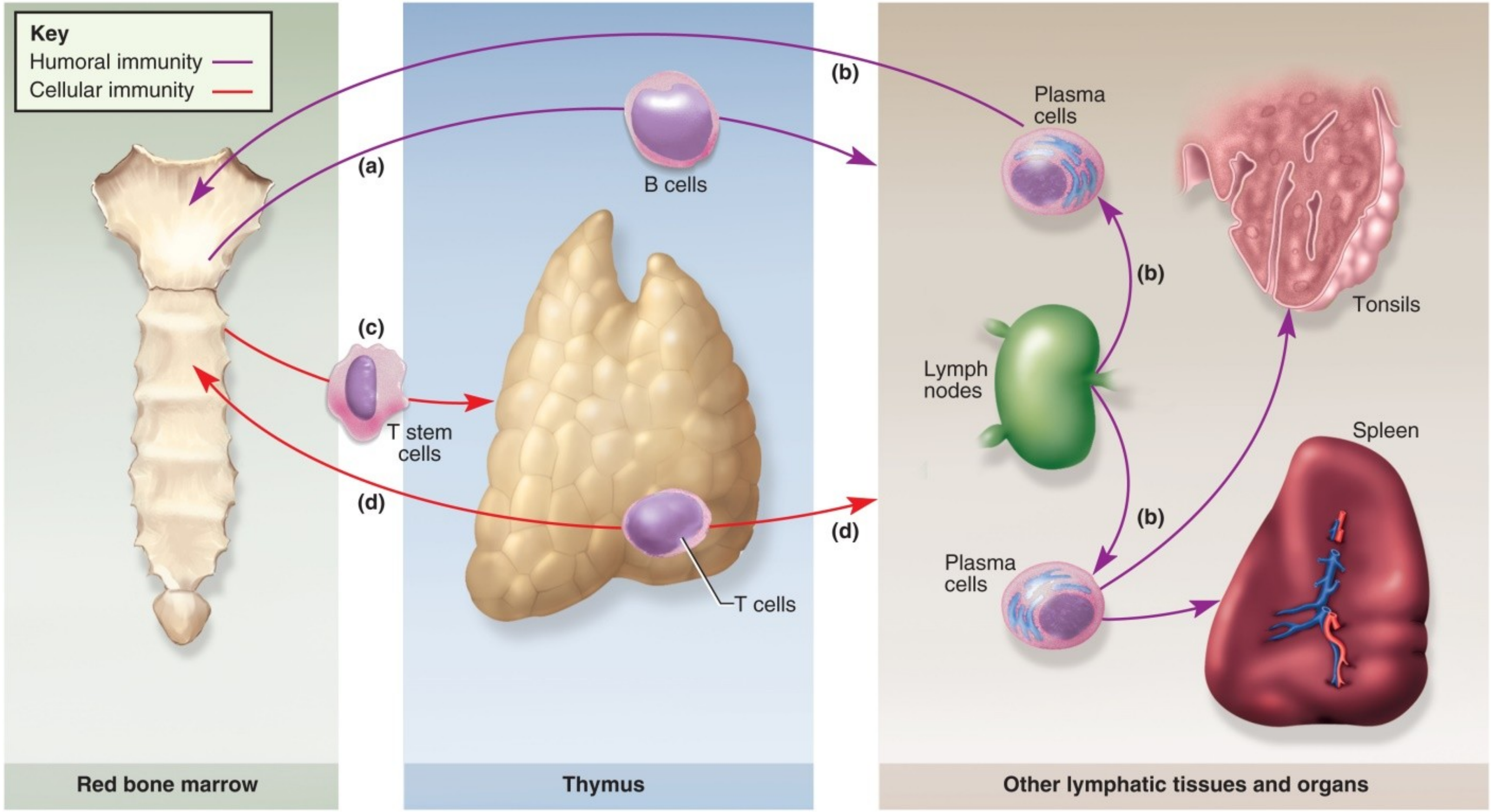
Cellular (<u>cell-mediated</u>) immunity: T cells respond to intracellular pathogens which are inaccessible to antibodies, and kill cells that harbor them

Humoral (<u>antibody-mediated</u>) 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

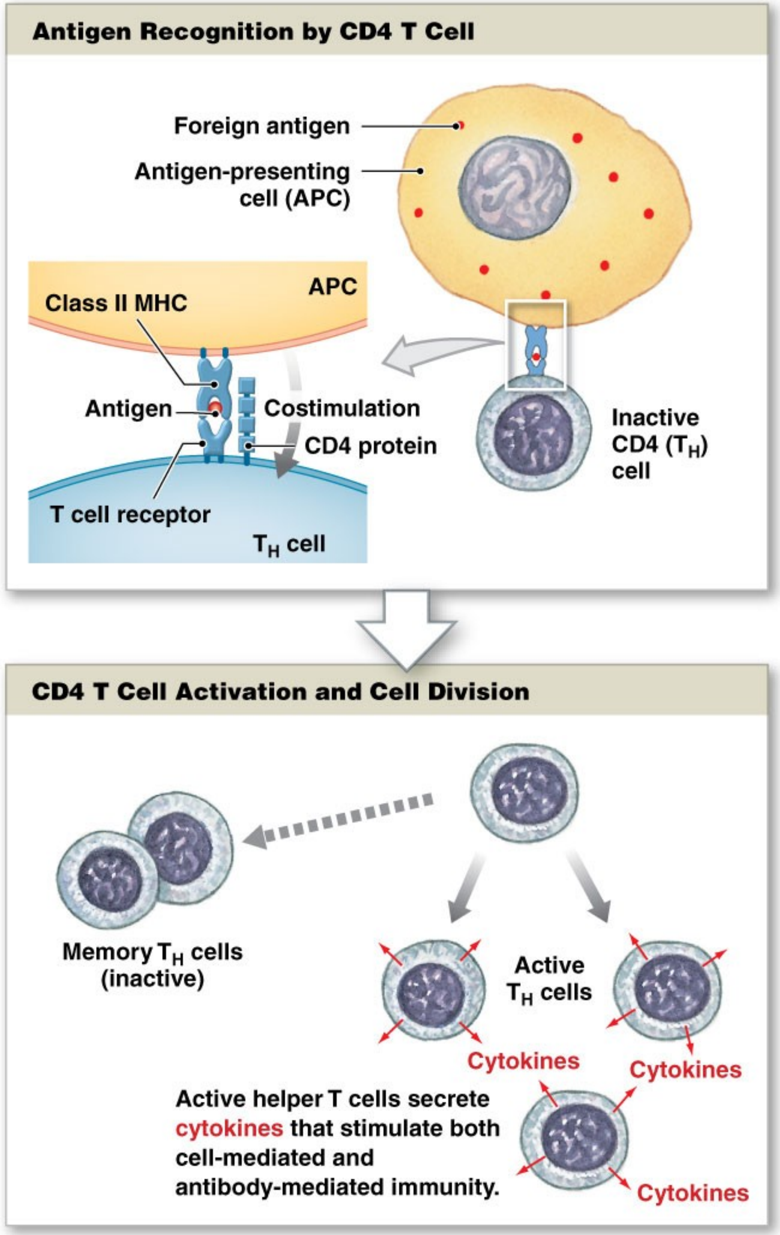
Some T_C and T_H cells become **memory cells**

- 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

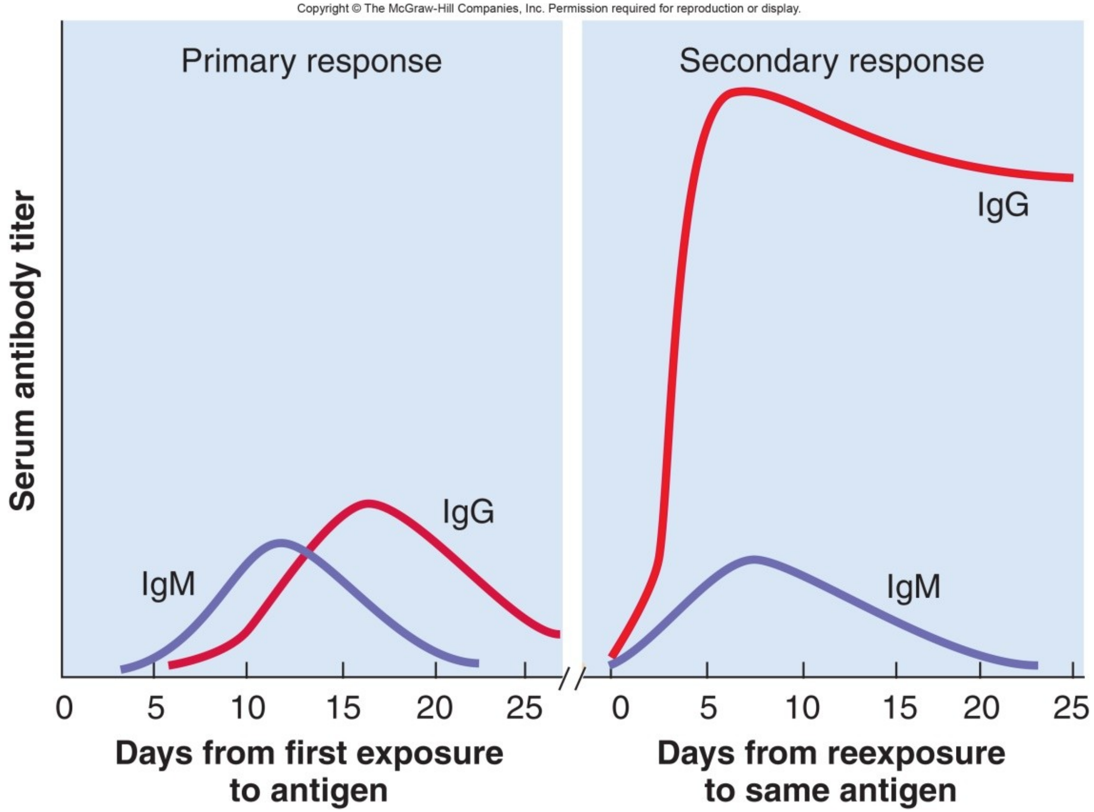
The retrovirus that produces acquired immunodeficiency syndrome (AIDS) infects and rapidly kills helper T cells, crippling the immune system rendering them susceptible to other infections.

http://ed.ted.com/lessons/why-it-s-so-hard-to-cure-hiv-aids-janet-iwasa



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

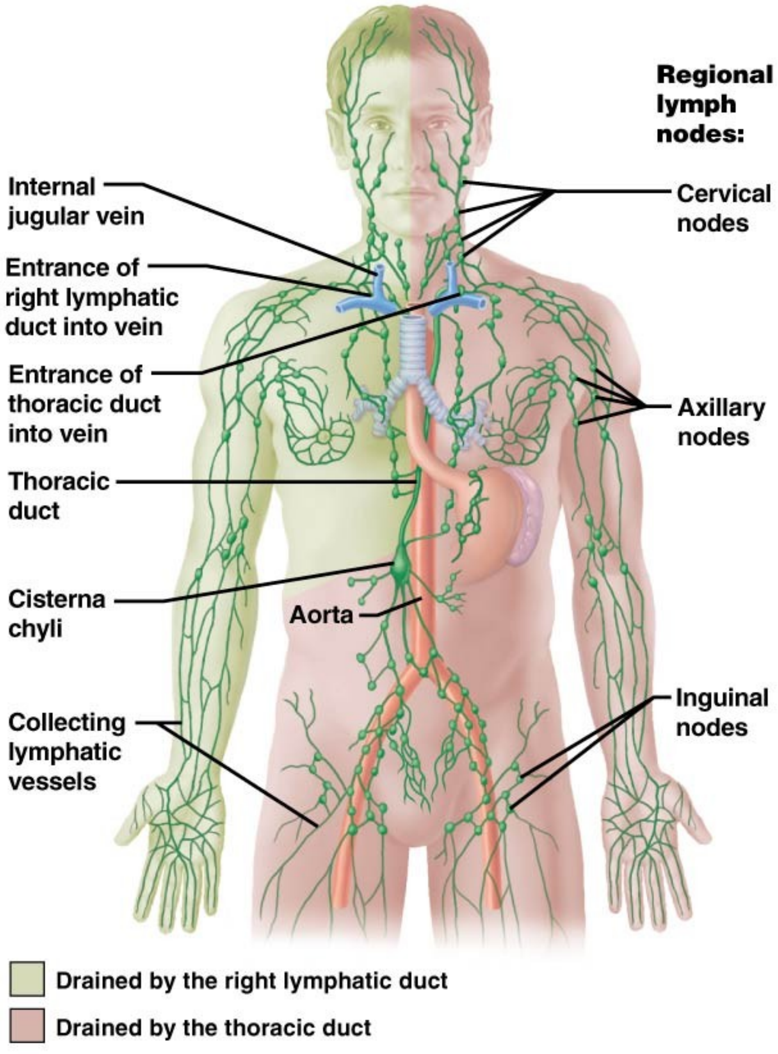


The immune response animation: http://highered.mheducation.com/sites/0072495855/student_view0/chapter24/animation__the_immune_response.html

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



(b)

Lymphatic Tissues

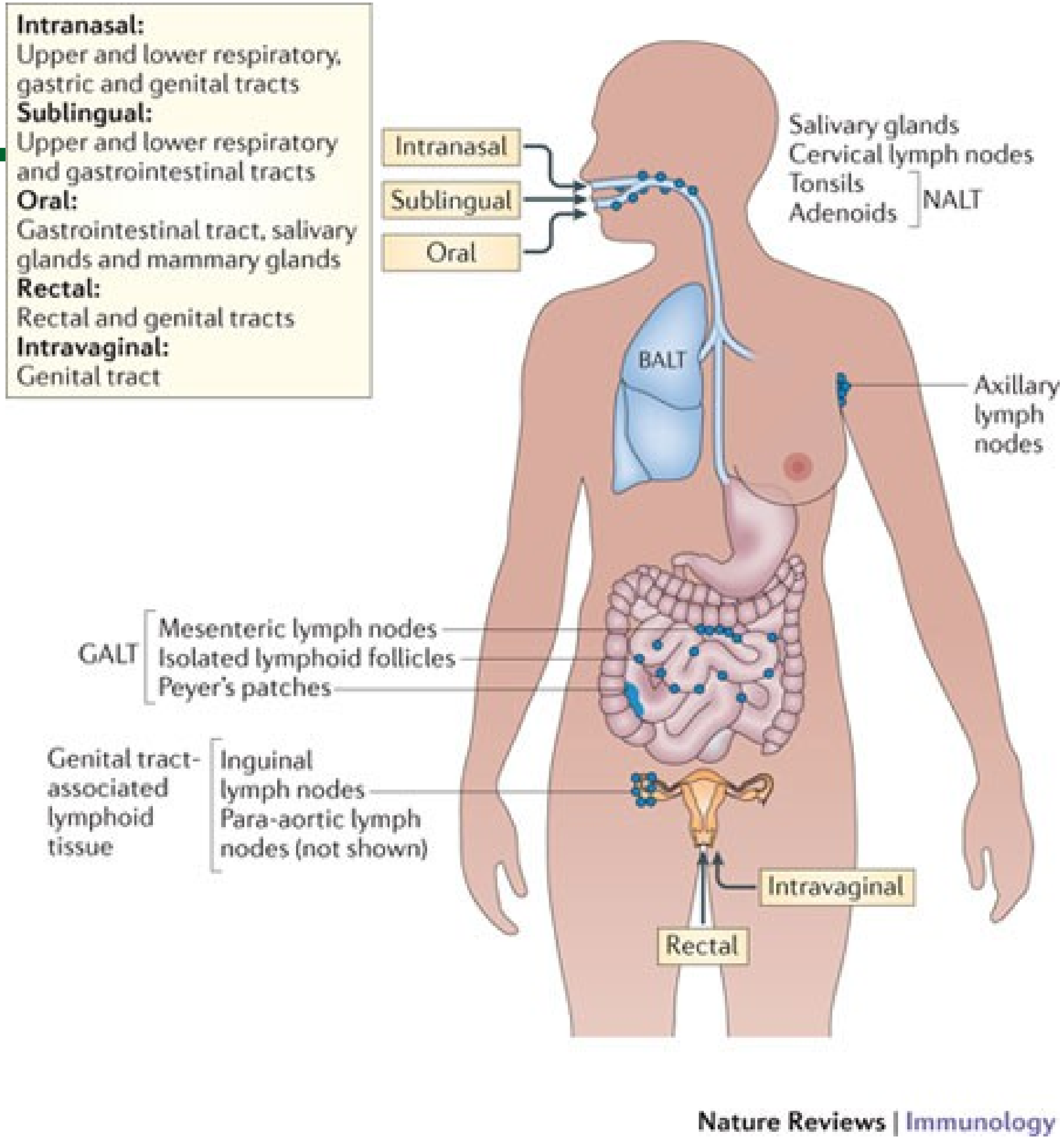
Diffuse lymphatic tissue: simplest form

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



Lymphatic Organs

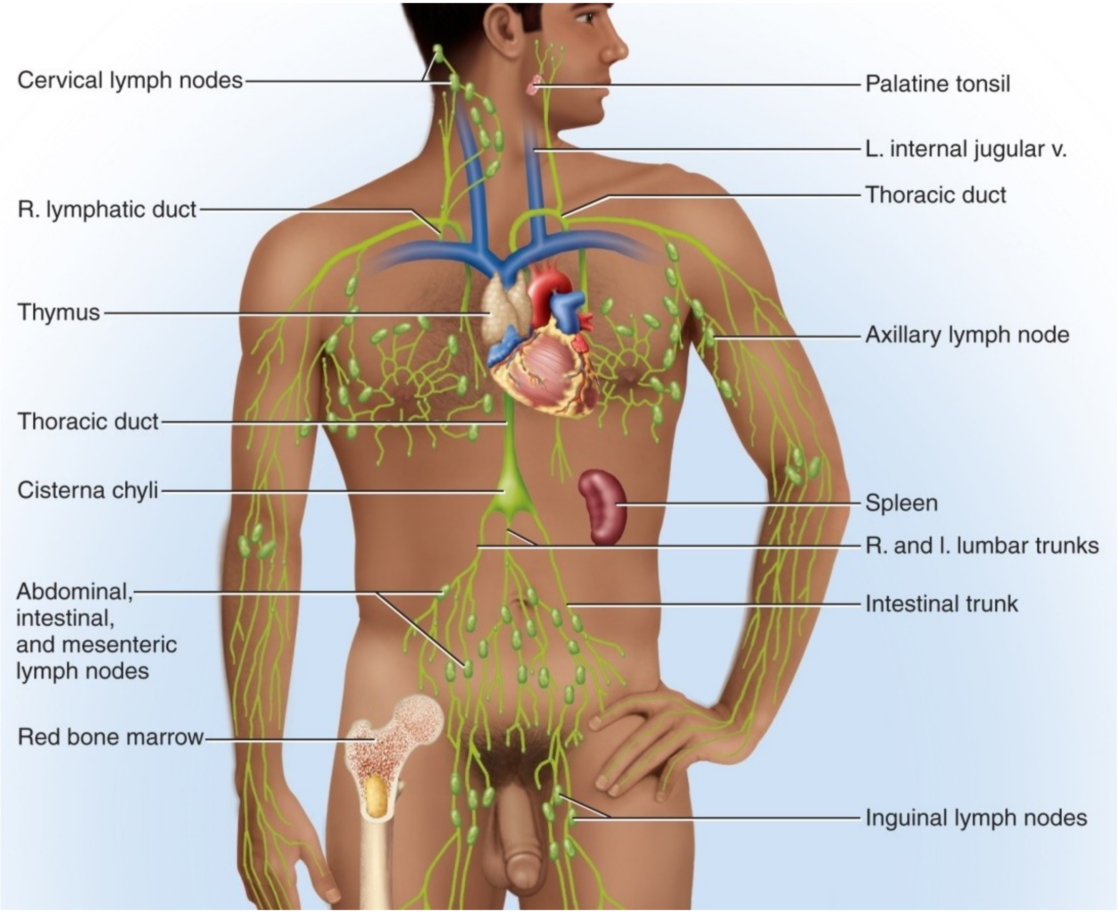
Lymphatic organs are surrounded by connective tissue capsule, separating them from neighboring tissues

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

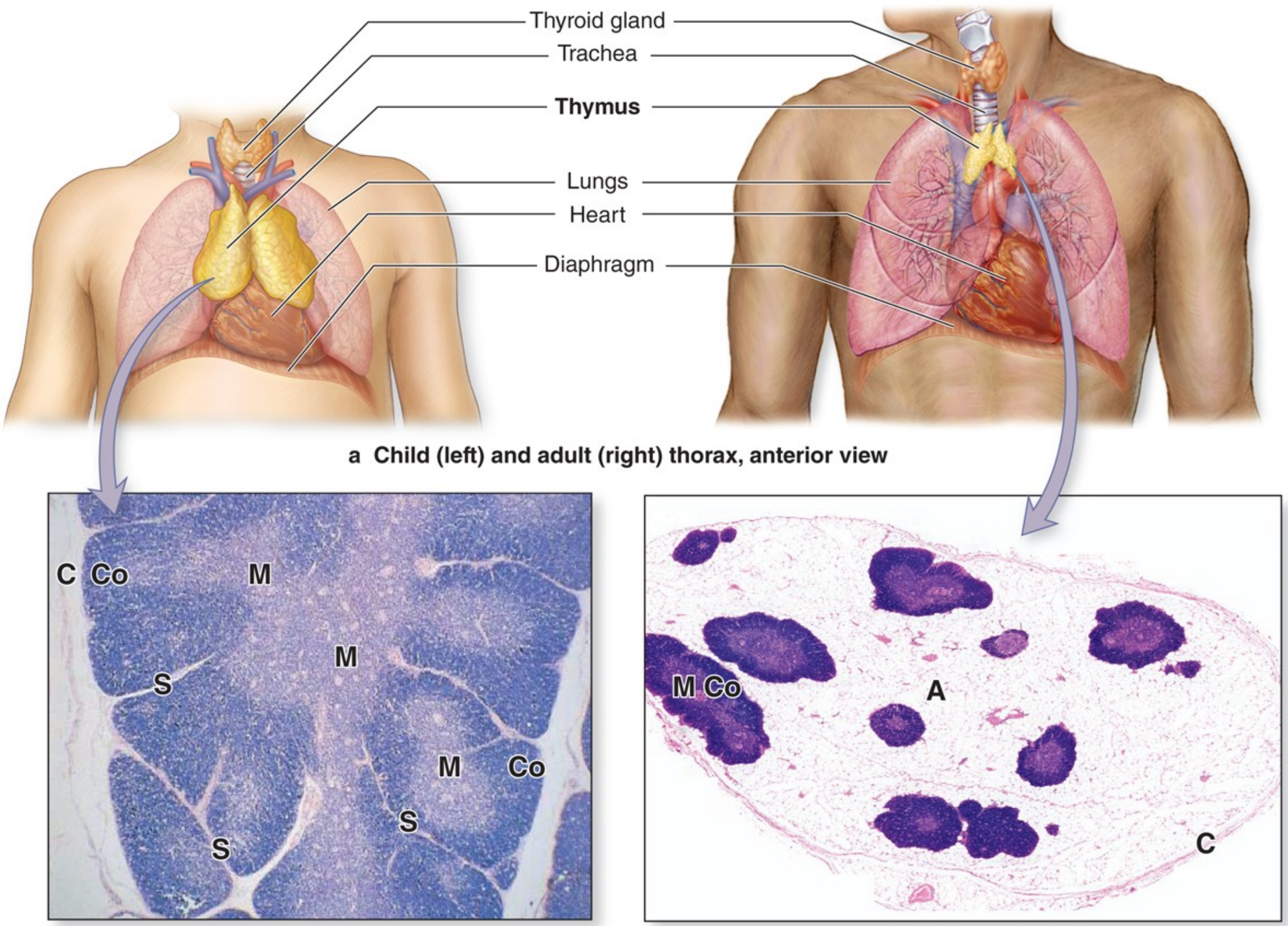
1. Red bone marrow
2. Thymus

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.



a Child (left) and adult (right) thorax, anterior view

b Micrograph of child's thymus

c Micrograph of adult's thymus

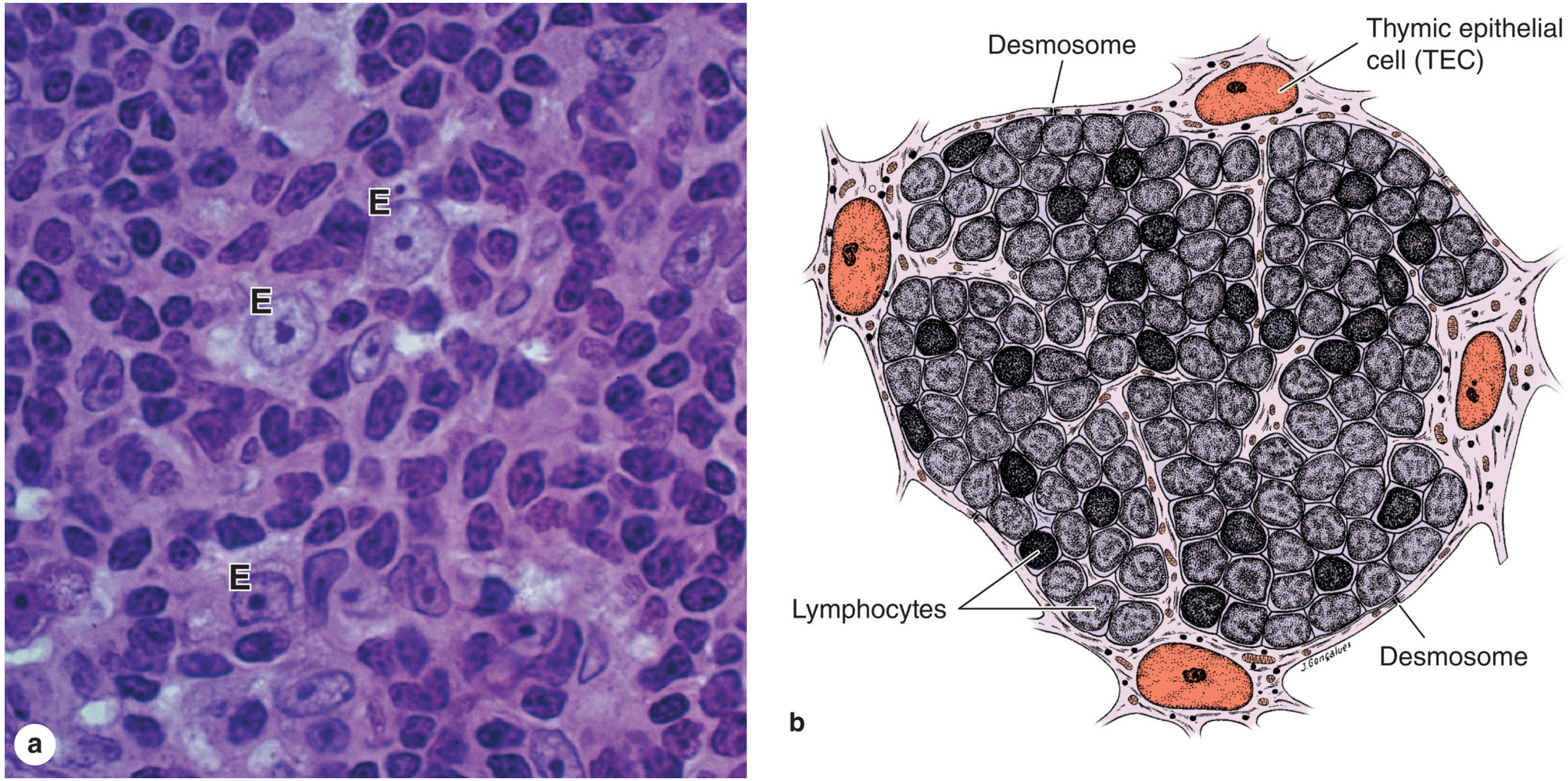
(b) A child's thymus, showing connective tissue of the capsule (**C**) and septa (**S**) -between thymic lobules, each having an outer cortex (**Co**) and -incompletely separated medulla (**M**) of lymphoid tissue.

(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

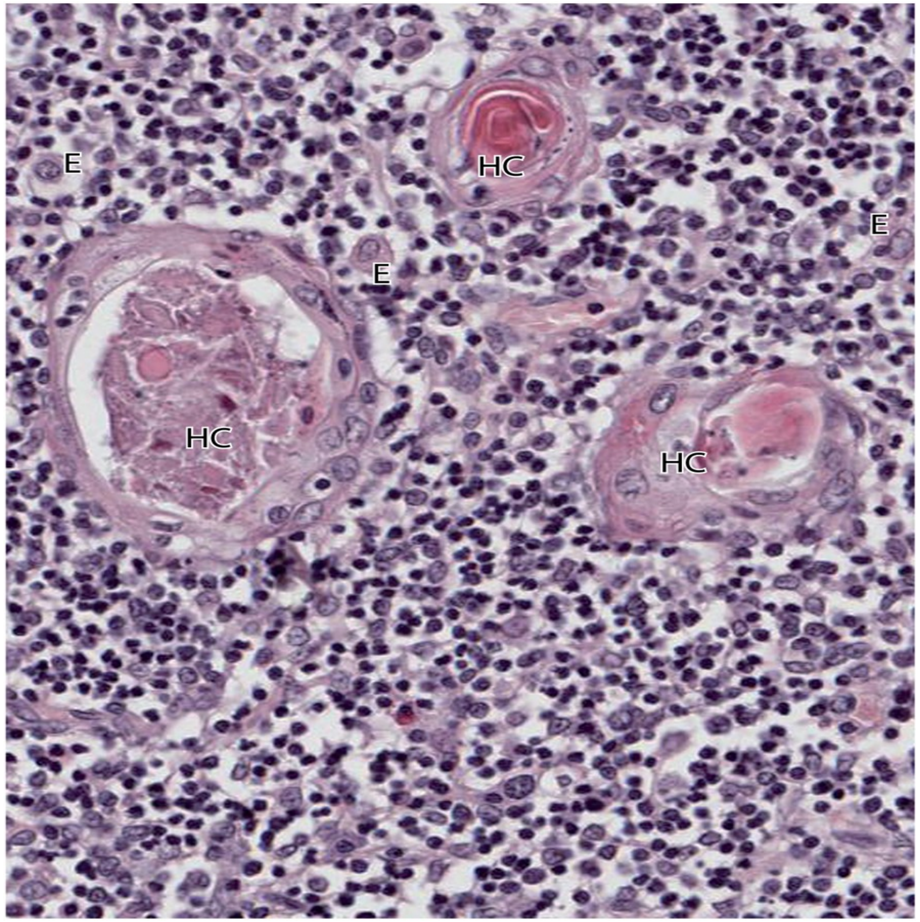
Thymic Cortex: early T cell development

(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) Corpuscles are a distinguishing feature of the thymic medulla

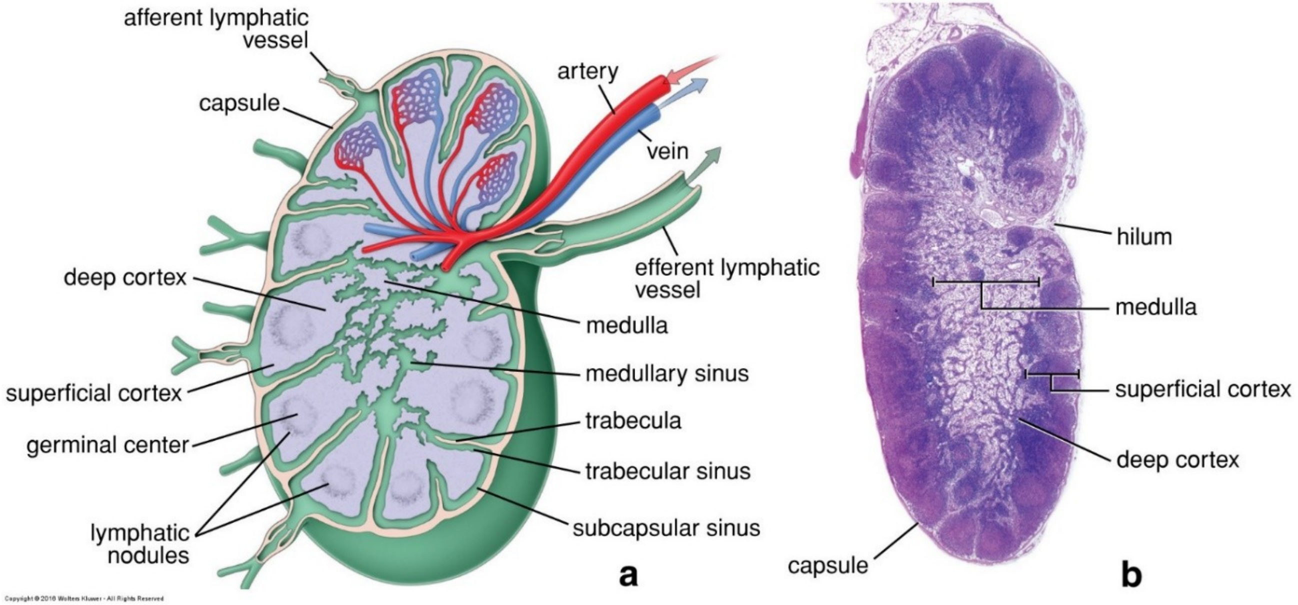


The most characteristic feature of the medulla in humans is the presence of thymic (Hassall) corpuscles (**H**).

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.

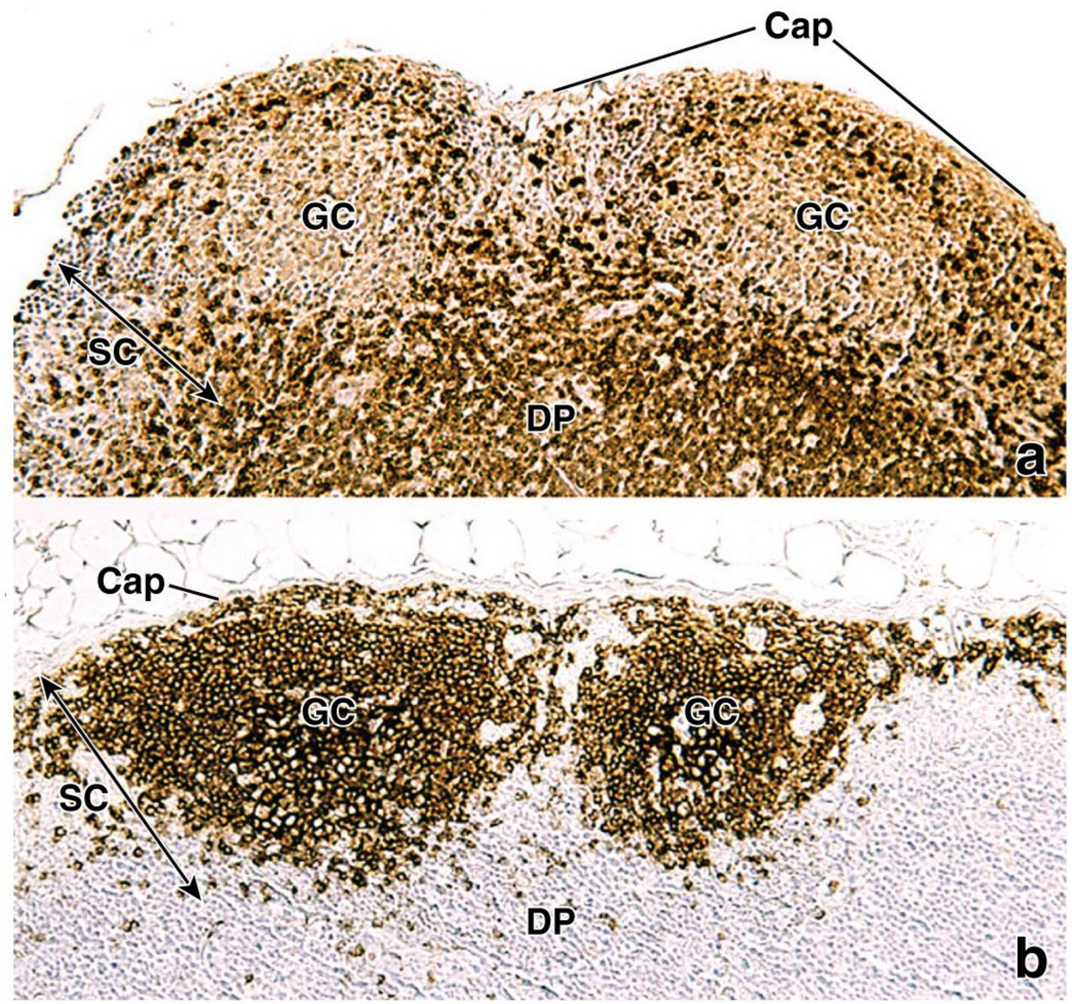


❯❯ MEDICAL APPLICATION

Metastatic cancer cells can are 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

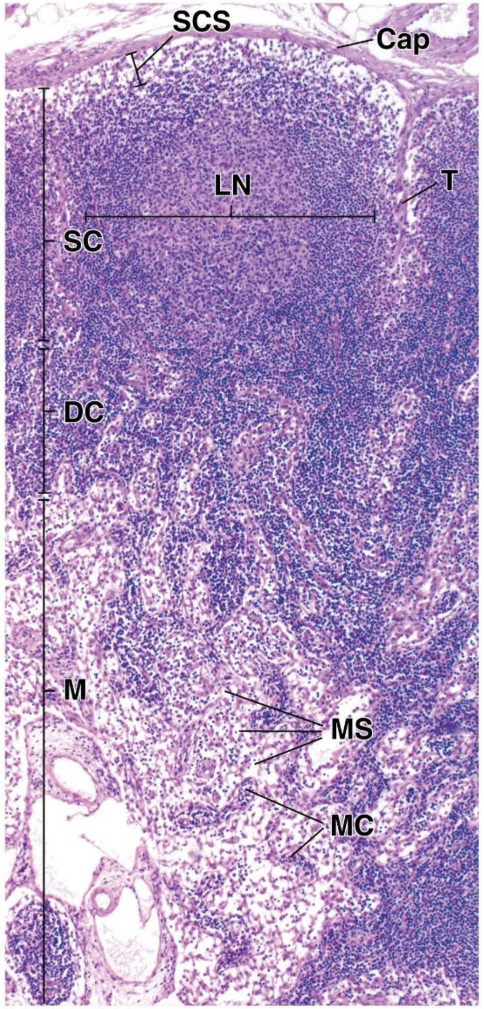
B and T Lymphocytes in the Superficial Cortex of a Marmoset Monkey Lymph Node



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).

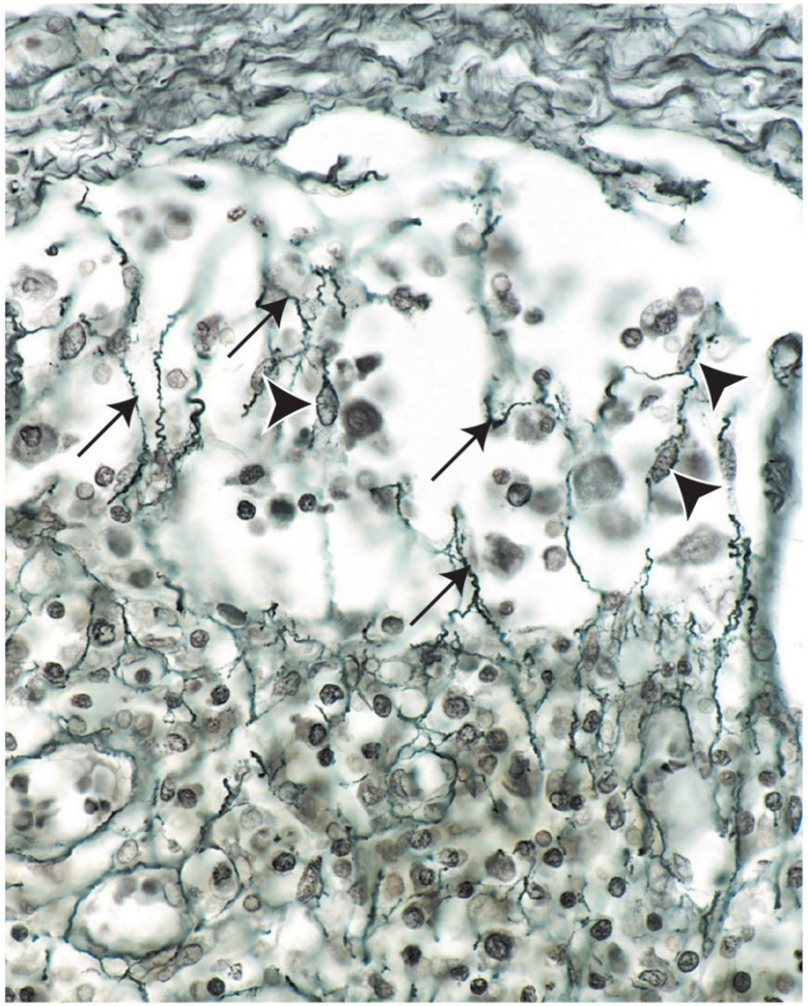
b: anti CD20 (**B lymphocytes marker**) stain: B cells accumulate in germinal centers (GC) of the superficial cortex (SC)

H & E of a lymph node



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.

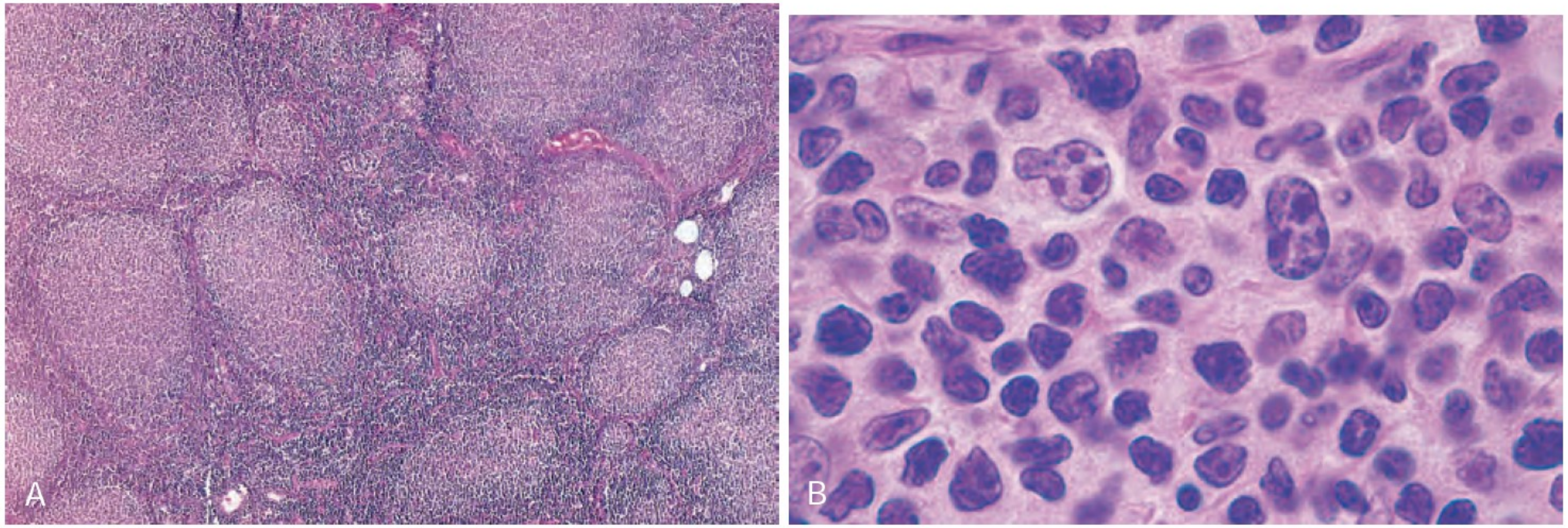
Silver Stain of a Lymph Node



Connective tissue capsule (at the top) Subcapsular sinus, and the superfcial 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

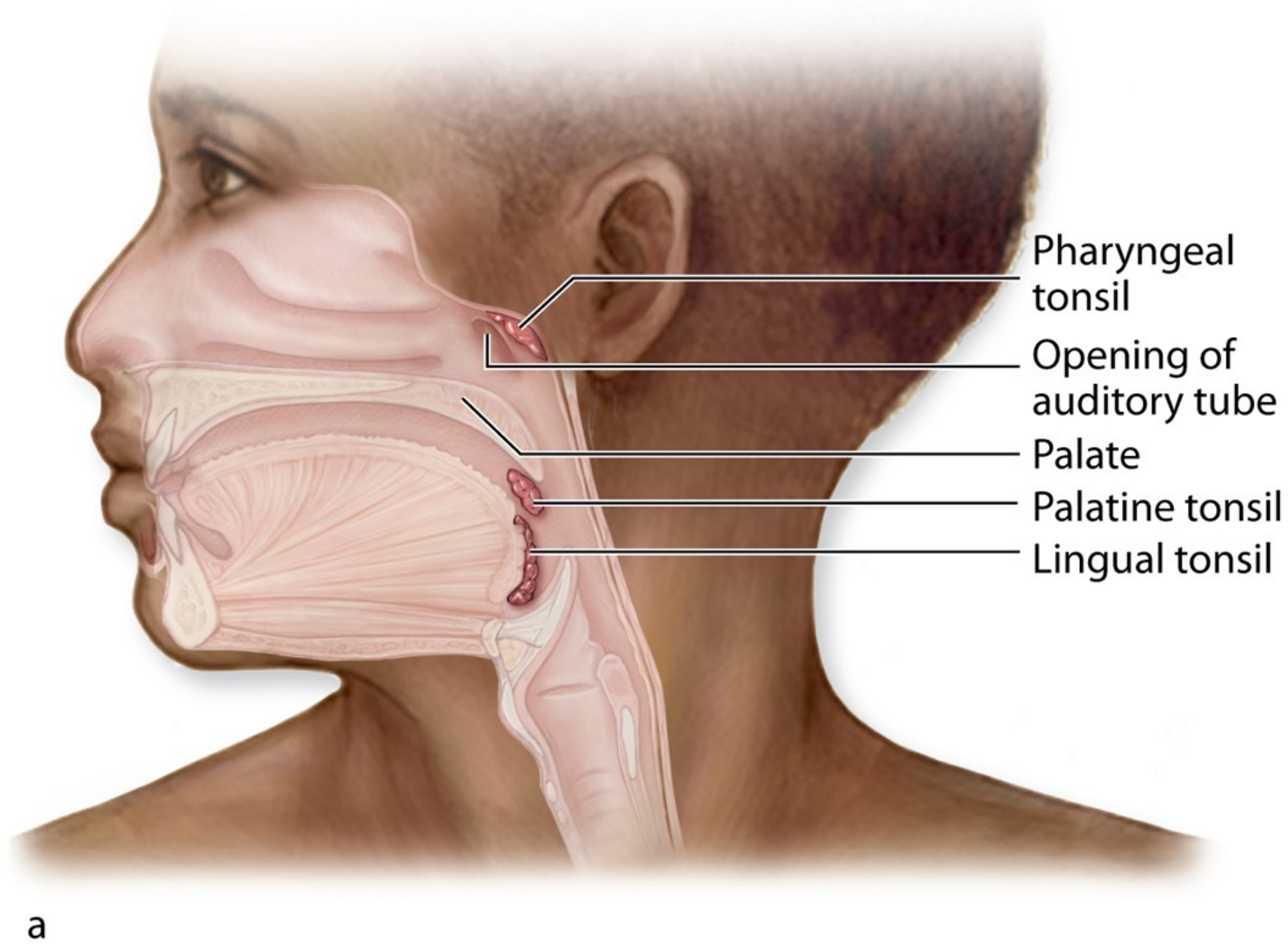


❯❯ MEDICAL APPLICATION

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.

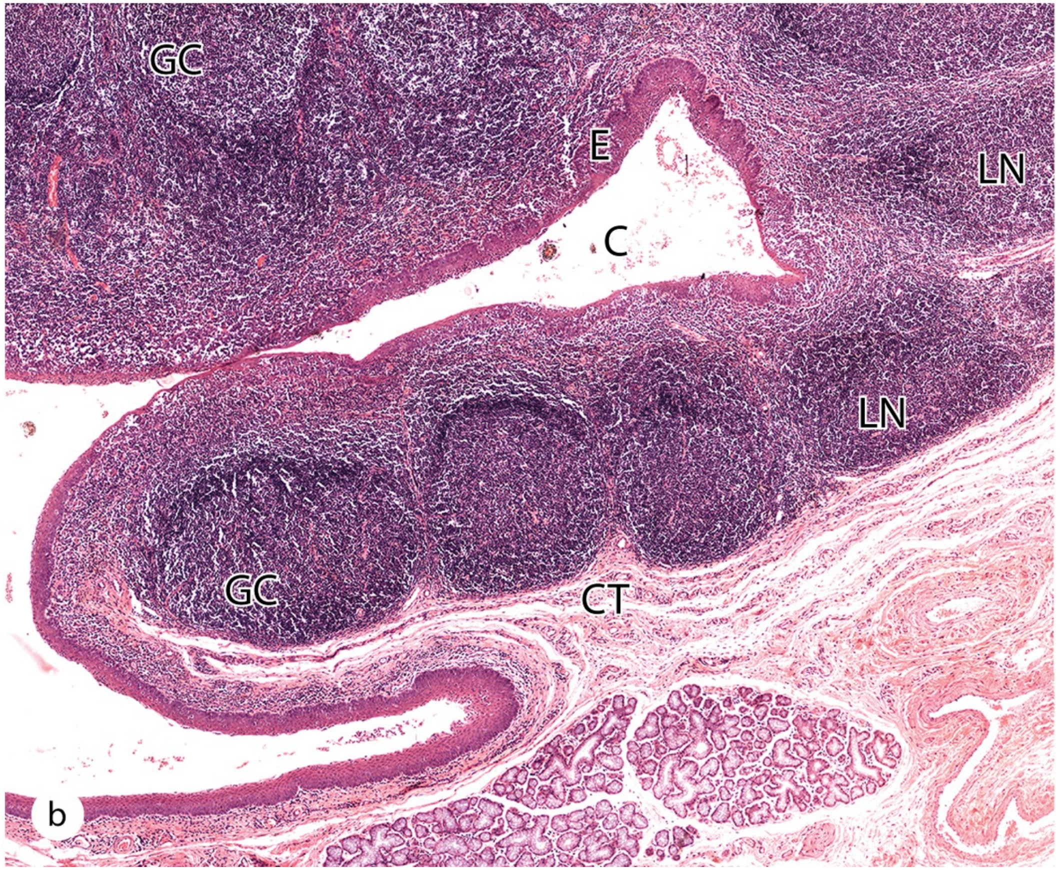


Palatine tonsils: posterior
Lingual tonsils: posterior third of the tongue. Both are covered with stratified squamous epithelium.
Pharyngeal tonsil: single medial mass situated in the posterior wall of the nasopharynx. It is usually covered by ciliated pseudostratified columnar epithelium,

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

https://sites.psu.edu/siowfa15/2015/09/14/why-do-we-have-tonsils/

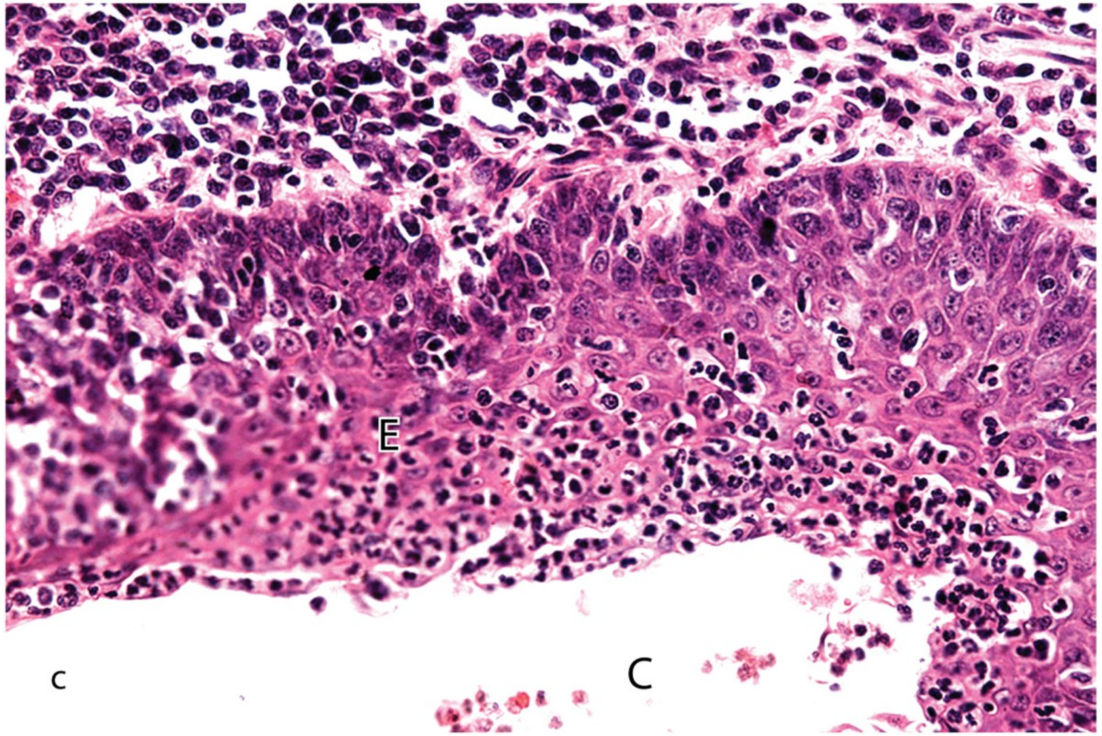
Lymphoid Nodules of the Tonsils



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.

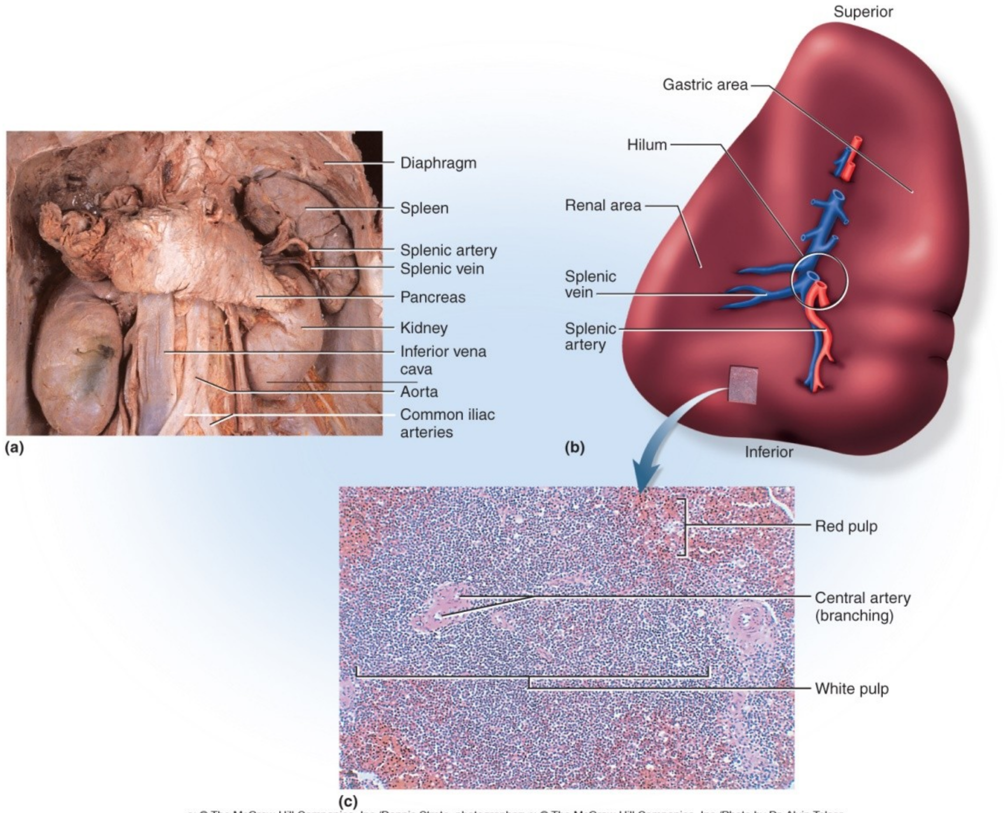
❯❯ **MEDICAL APPLICATION** Chronic inflammation of the pharyngeal lymphoid tissue and tonsils of children often produces hyperplasia and enlargement of the tonsils to form “adenoids,” which can obstruct the eustachian tube and lead to middle ear infections.

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

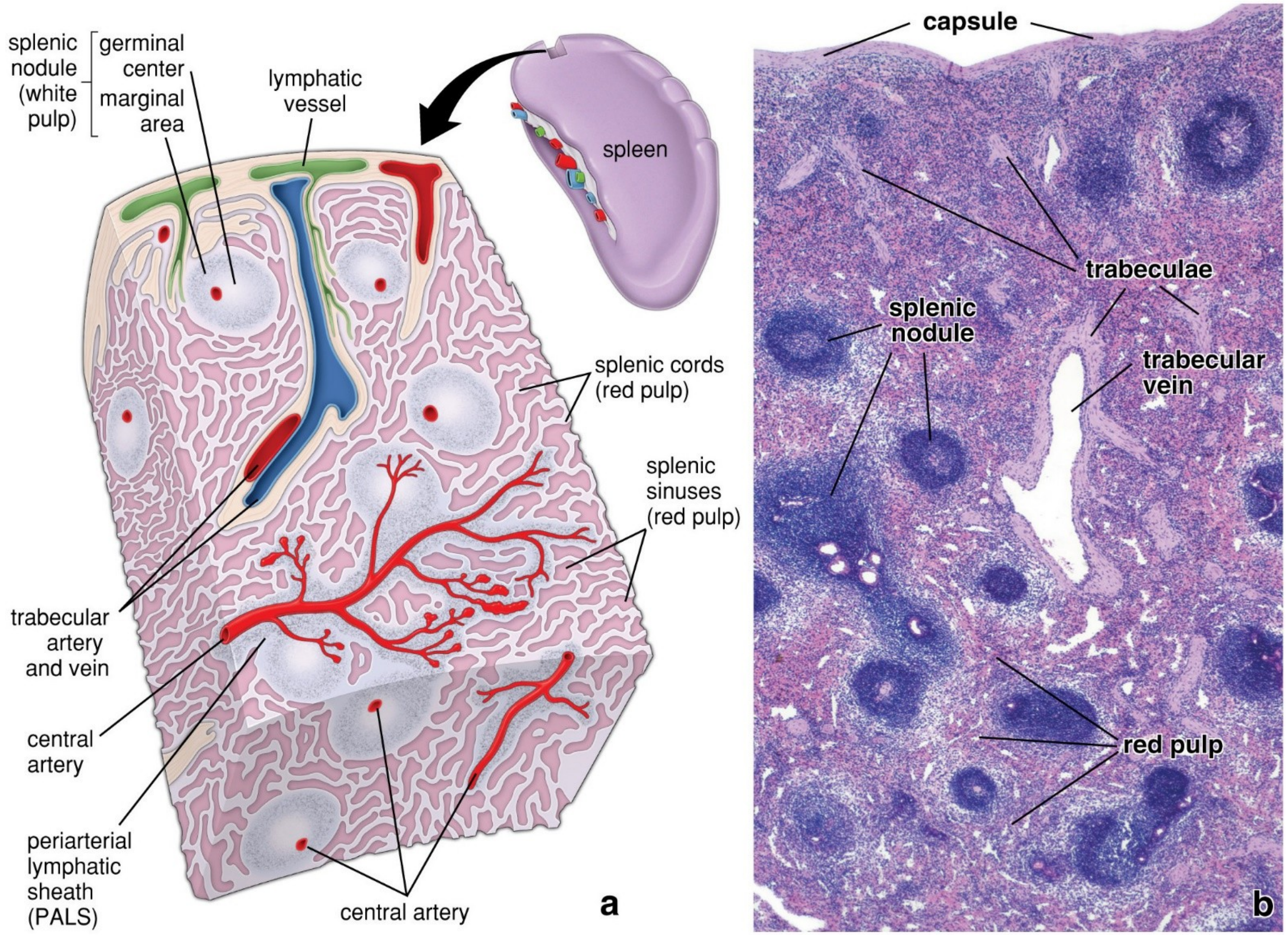
Ruptured spleen requires splenectomy

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



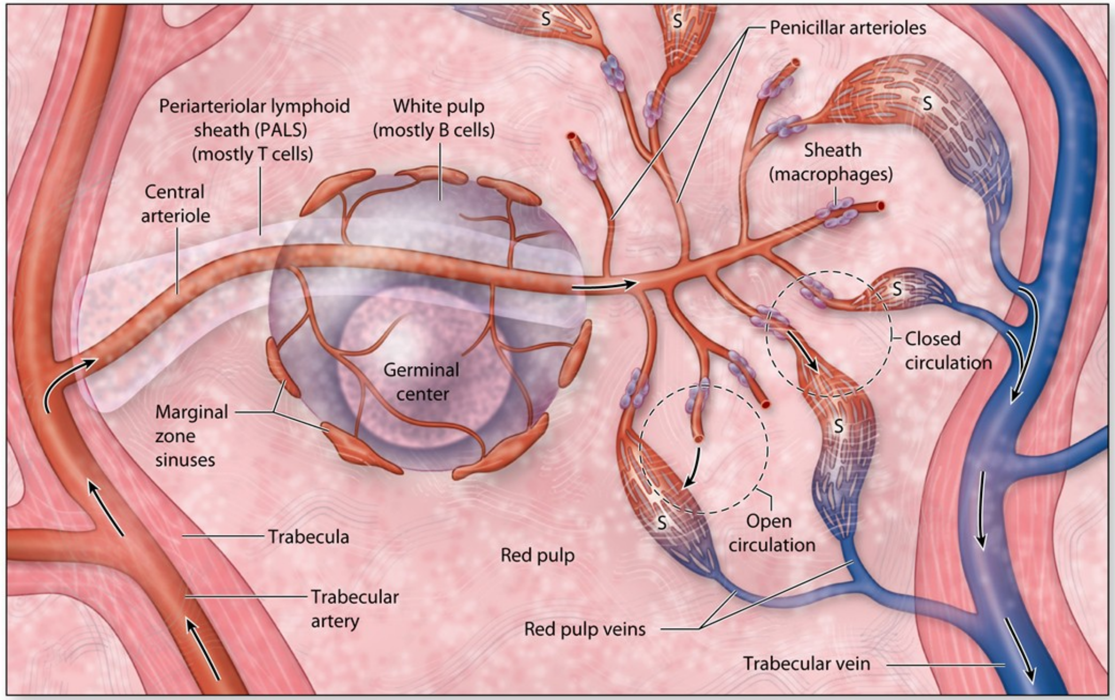
Splenic Structure



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

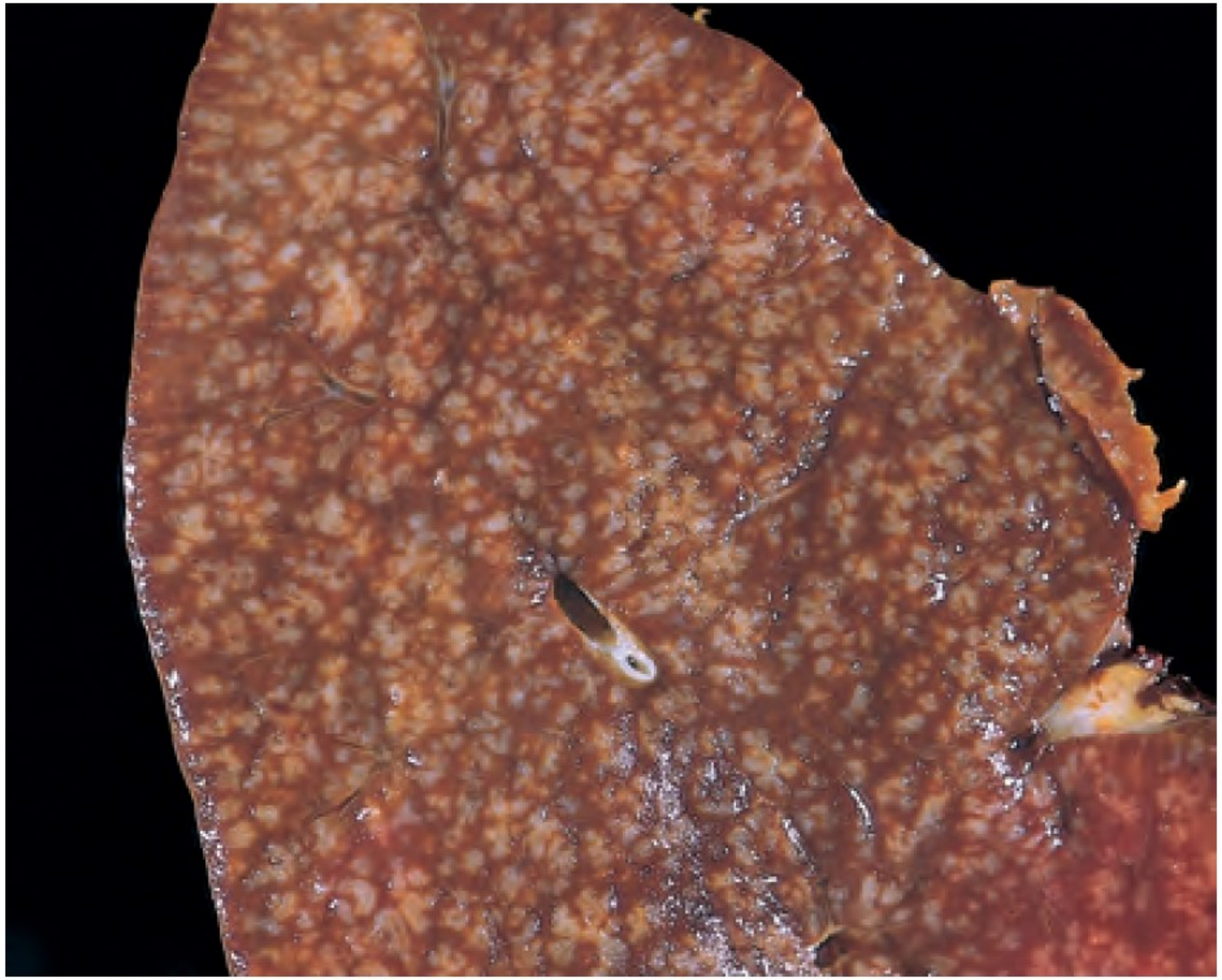


central arterioles are enclosed by lymphoid cell rich **periarteriolar lymphoid sheath (PALS),** in white pulp.

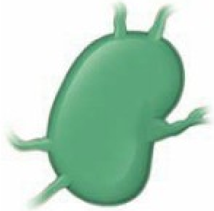
B cells in these sheaths can form nodules as the largest masses of white pulp

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
				
Major function	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
Connective tissue capsule	No	Yes	Yes	Yes; contains myofibroblasts
Cortex	No	Yes	Yes	No
Medulla	No	Yes	Yes	No
Lymph nodules	Yes	Yes; in the superficial cortex only	No	Yes; in white pulp only
Afferent lymphatic vessels	No	Yes; passing through the capsule	No	No
Efferent lymphatic vessels	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
High endothelial venules (HEVs)	Yes; in well-established lymph nodules (i.e., tonsils, appendix, Peyer's patches)	Yes; associated with deep cortex	No	No
Characteristic features	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

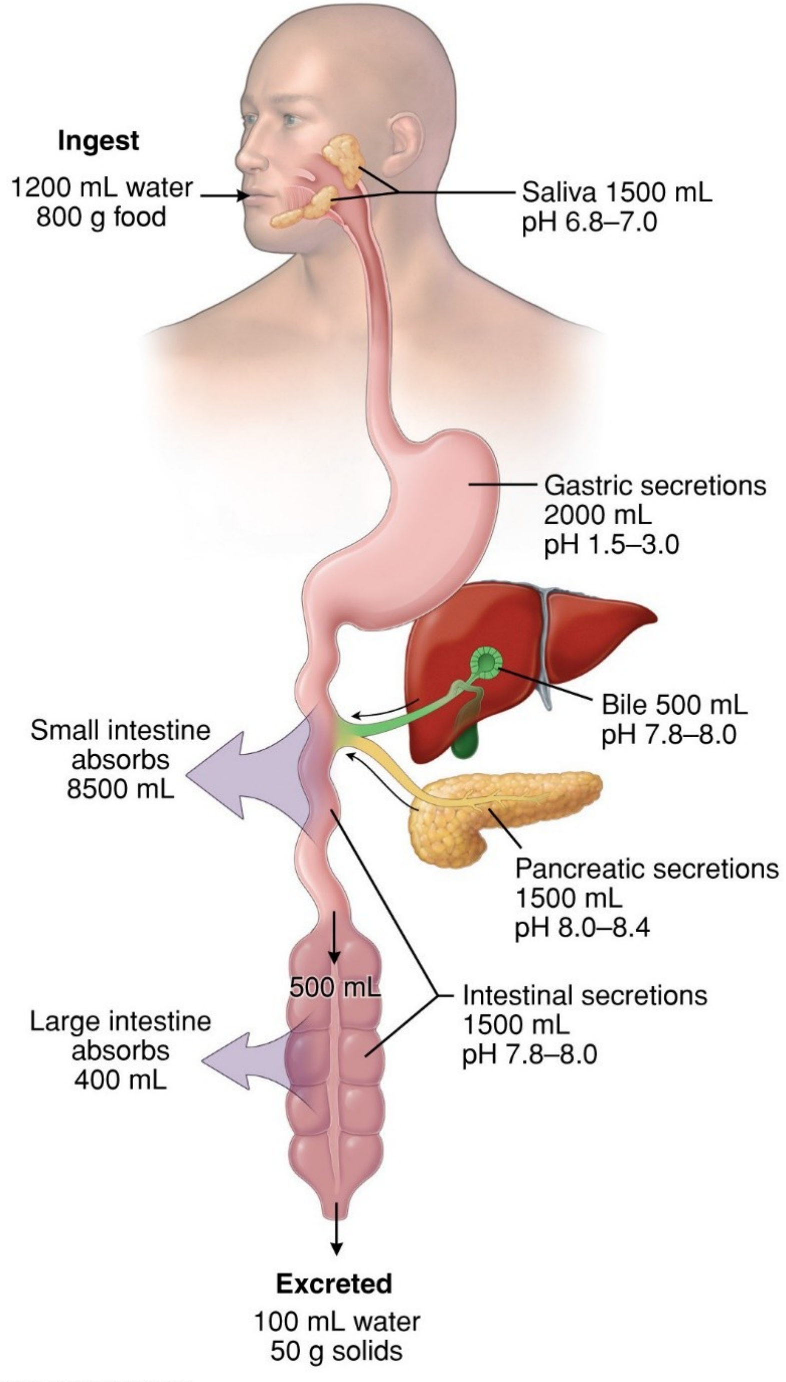
BI 455 CHAPTER 15

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

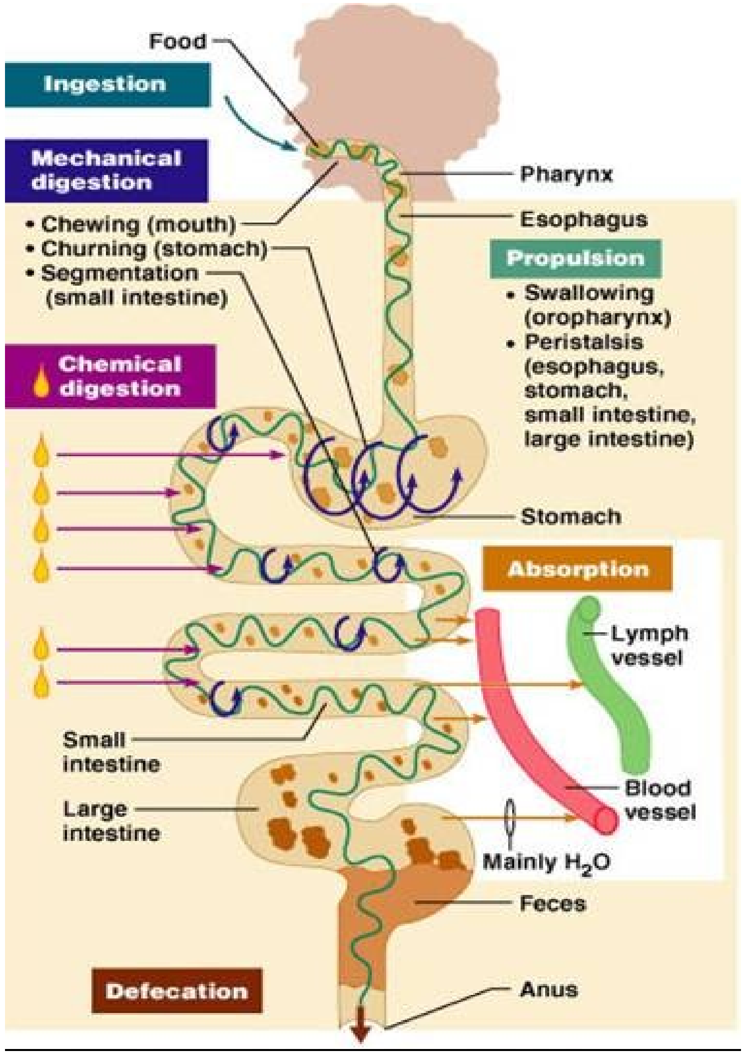
2. **Gastrointestinal (GI) tract**: stomach and intestines

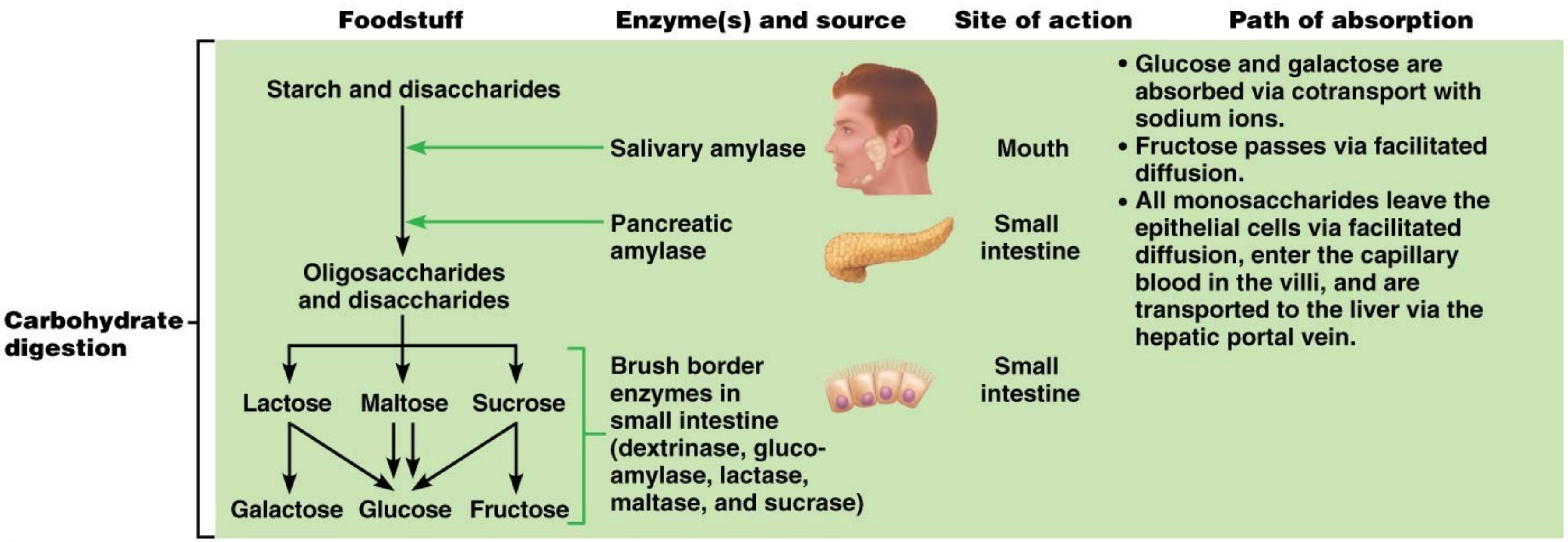
Accessory organs: Teeth, tongue, salivary glands, liver, gallbladder, and pancreas

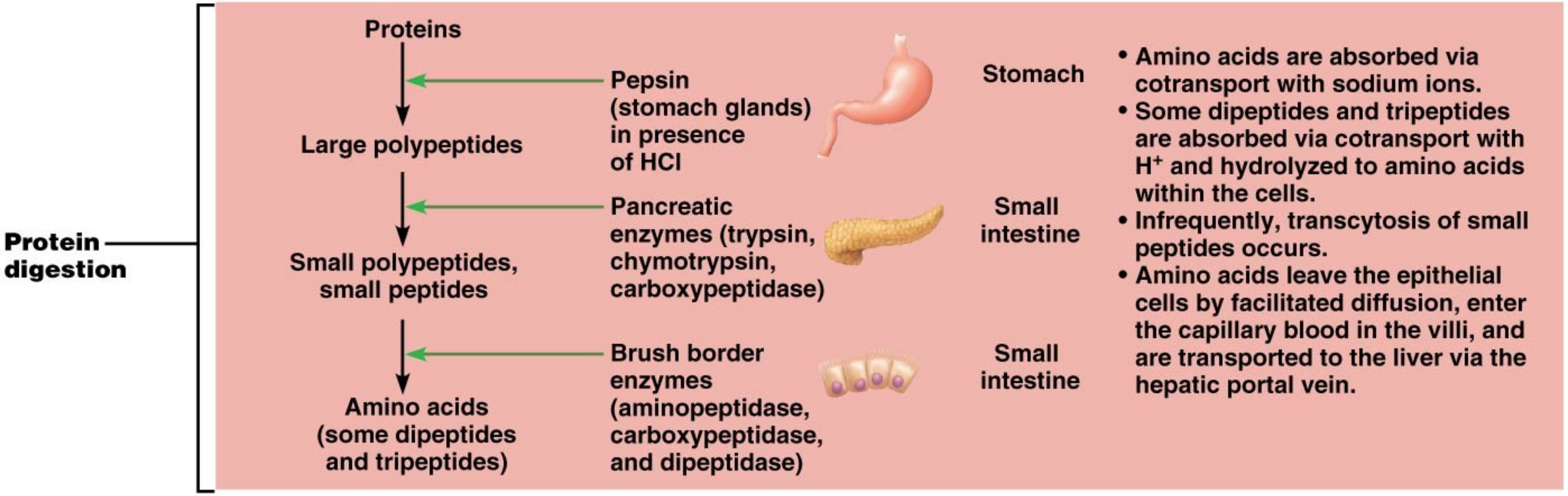


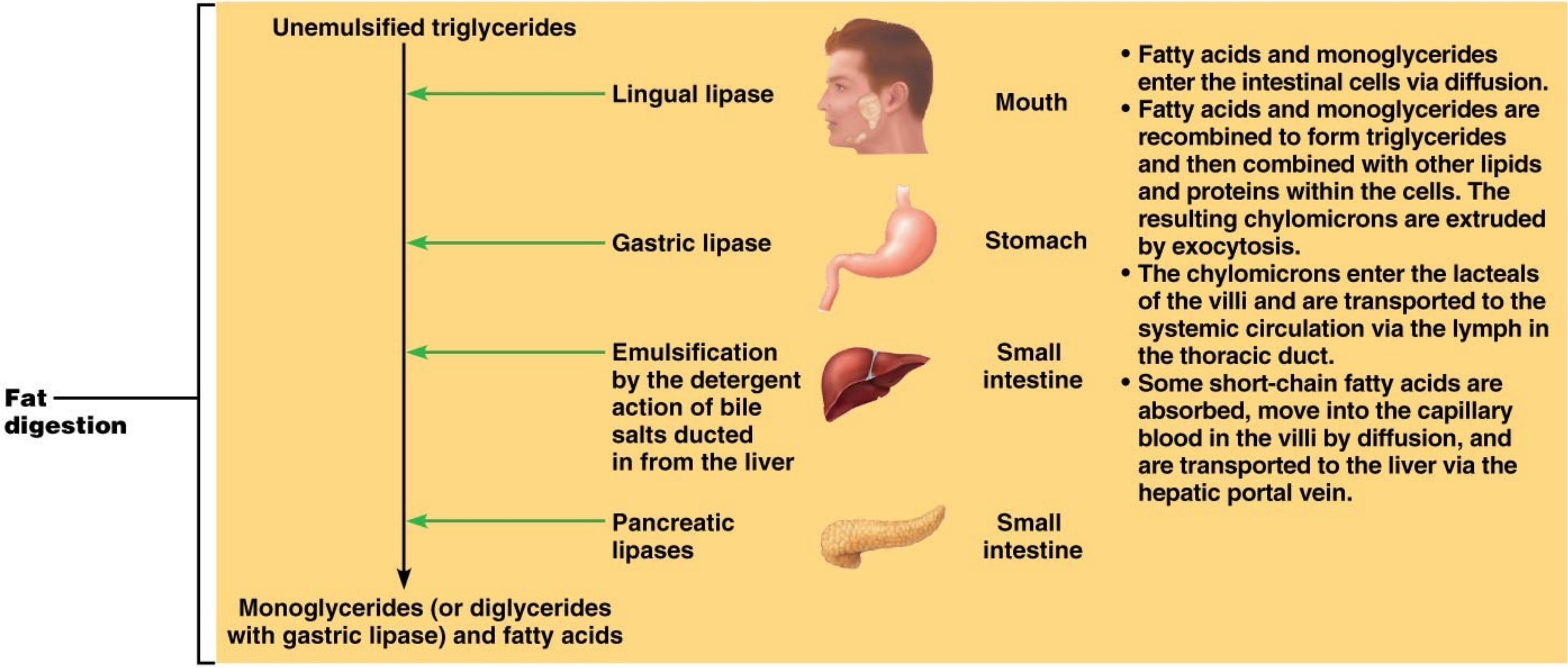
Five stages of digestion

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

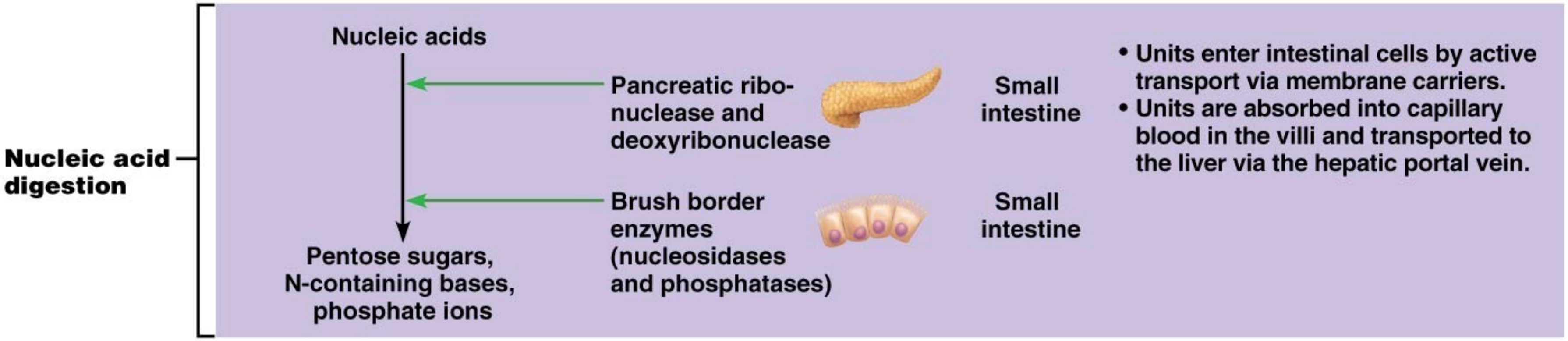



Foodstuff
Enzyme(s) and source
Site of action
Path of absorption
Carbohydrate digestion
Starch and disaccharides
Salivary amylase
Mouth
Pancreatic amylase
Small intestine
Oligosaccharides and disaccharides
Lactose
Maltose
Sucrose
Brush border enzymes in small intestine (dextrinase, gluco-amylase, lactase, maltase, and sucrase)
Small intestine
Galactose
Glucose
Fructose
• Glucose and galactose are absorbed via cotransport with sodium ions.
• Fructose passes via facilitated diffusion.
• All monosaccharides leave the epithelial cells via facilitated diffusion, enter the capillary blood in the villi, and are transported to the liver via the hepatic portal vein.


Protein digestion
Proteins
Pepsin (stomach glands) in presence of HCl
Stomach
Large polypeptides
Pancreatic enzymes (trypsin, chymotrypsin, carboxypeptidase)
Small intestine
Small polypeptides, small peptides
Brush border enzymes (aminopeptidase, carboxypeptidase, and dipeptidase)
Small intestine
Amino acids (some dipeptides and tripeptides)
• Amino acids are absorbed via cotransport with sodium ions.
• Some dipeptides and tripeptides are absorbed via cotransport with H+ and hydrolyzed to amino acids within the cells.
• Infrequently, transcytosis of small peptides occurs.
• Amino acids leave the epithelial cells by facilitated diffusion, enter the capillary blood in the villi, and are transported to the liver via the hepatic portal vein.

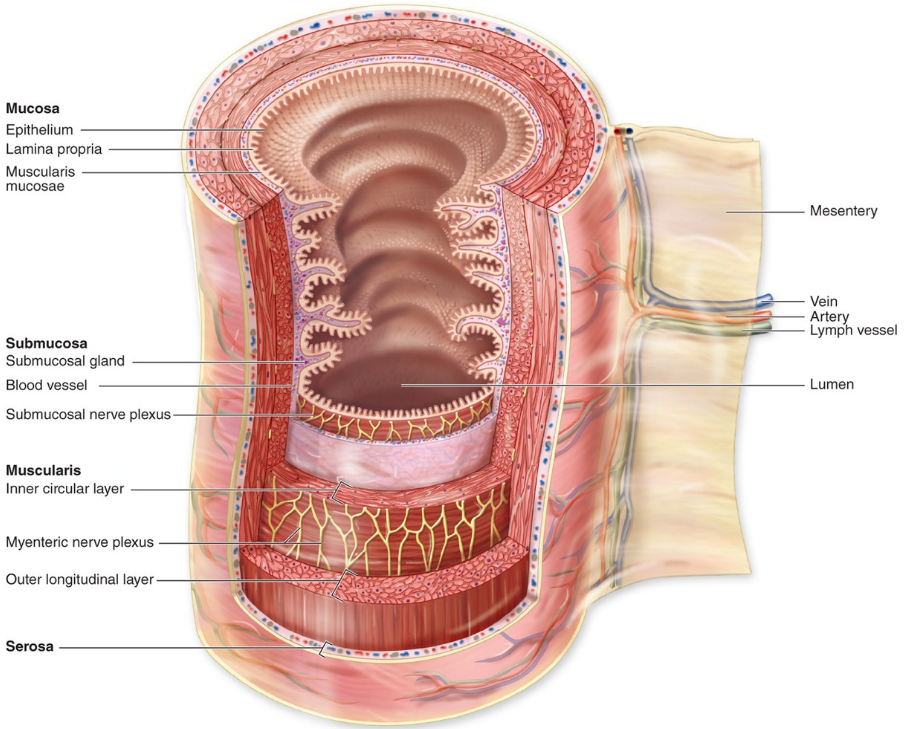


Fat digestion
Unemulsified triglycerides
Lingual lipase
Mouth
Gastric lipase
Stomach
Emulsification by the detergent action of bile salts ducted in from the liver
Small intestine
Pancreatic lipases
Small intestine
Monoglycerides (or diglycerides with gastric lipase) and fatty acids
• Fatty acids and 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.



Nucleic acid digestion
Nucleic acids
Pancreatic ribo-nuclease and deoxyribonuclease
Small intestine
Brush border enzymes (nucleosidases and phosphatases)
Small intestine
Pentose sugars, N-containing bases, phosphate ions
• Units enter intestinal cells by active transport via membrane carriers.
• Units are absorbed into capillary blood in the villi and 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

Musclularis externa

Inner circular layer: valves (sphincters)

Outer longitudinal layer: propels food and residue through the tract

Serosa (sometimes adventitia)

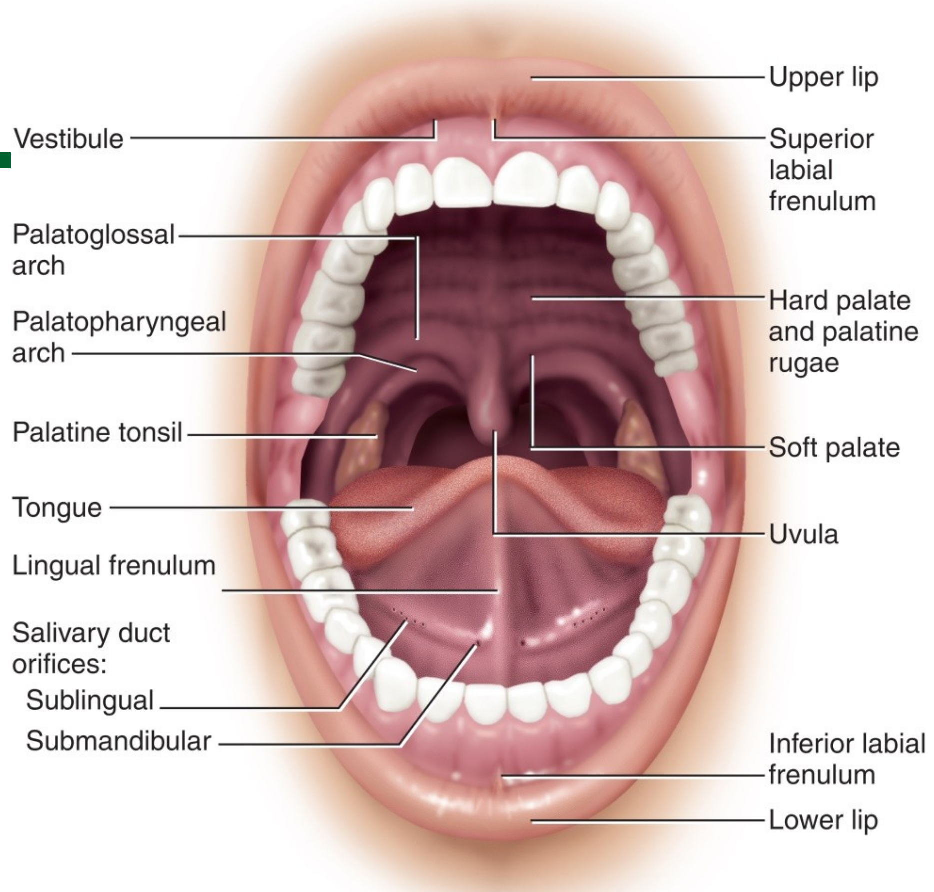
❯❯ **MEDICAL APPLICATION** Infection disturbs plexuses in the digestive tract’s enteric nervous system which then digestive tract motility and produces dilations in some areas. The rich autonomic innervation of the enteric nervous system also provides an anatomic explanation of the well-known actions 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

<u>Stratified squamous epithelium lining</u>

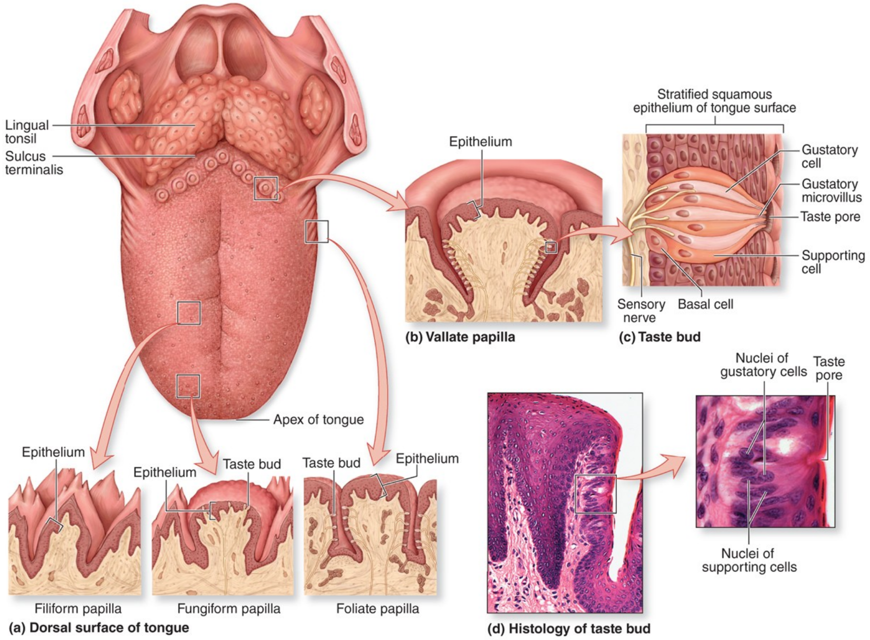
- **Keratinized** in areas subject to food abrasion: gums and hard palate
- **Nonkeratinized** in other areas: floor of mouth, soft palate, and insides of cheeks and lips



❯❯ **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.

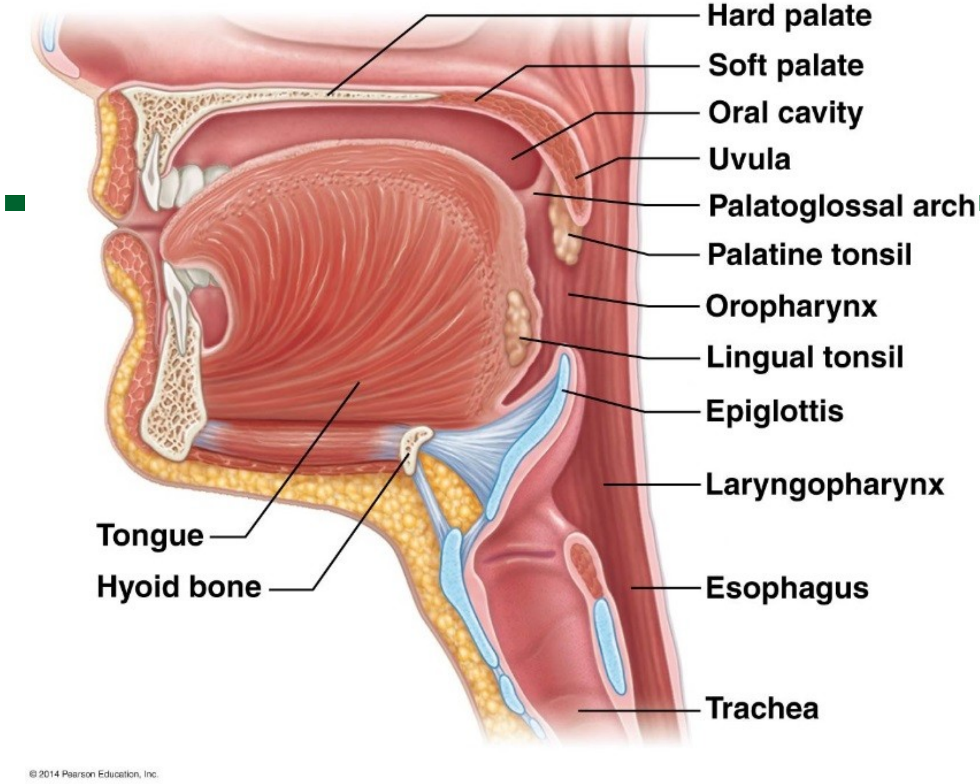


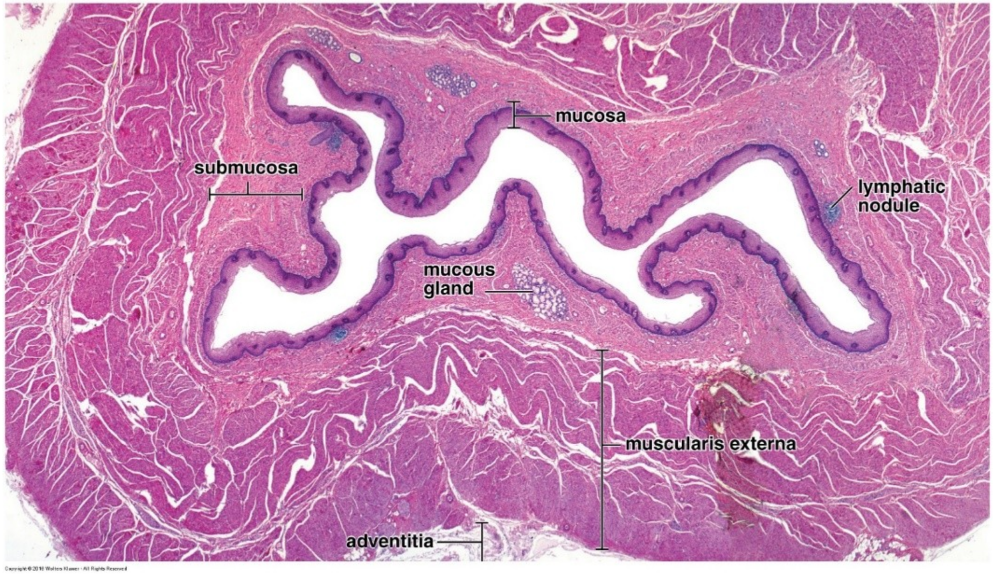
Filiform papillae provide friction to help move food during chewing.
Foliate papillae: sides of the tongue, best developed in young children
Fungiform papillae: dorsal surface,
Vallate papillae: V-shaped line near the terminal sulcus.

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.

The Esophagus





Mucosa:

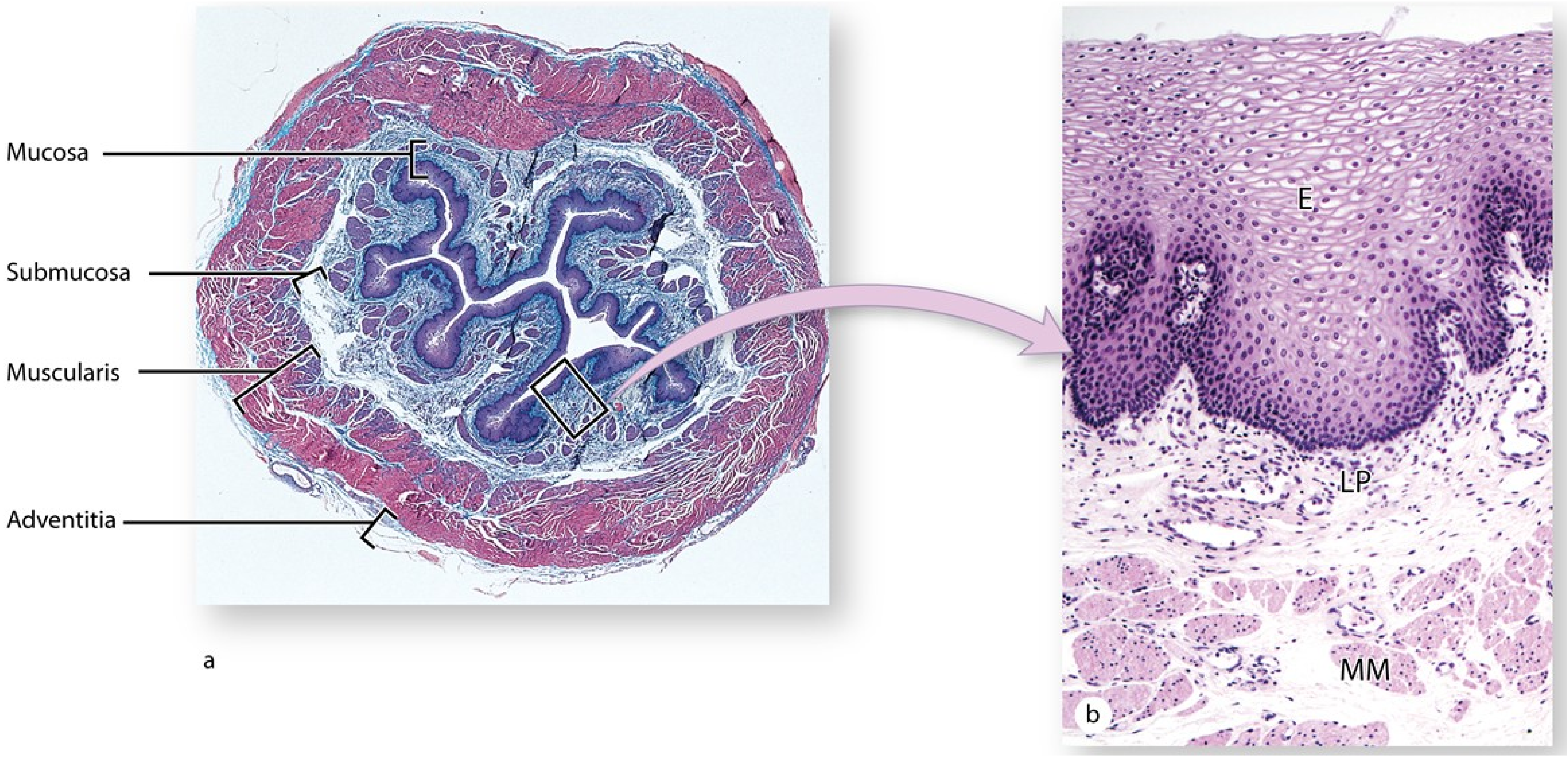
- thick stratified squamous epithelium,
- thin lamina propria containing occasional lymphatic nodules
- muscularis mucosae.

Submucosa:
Mucous glands with ducts emptying into esophagus

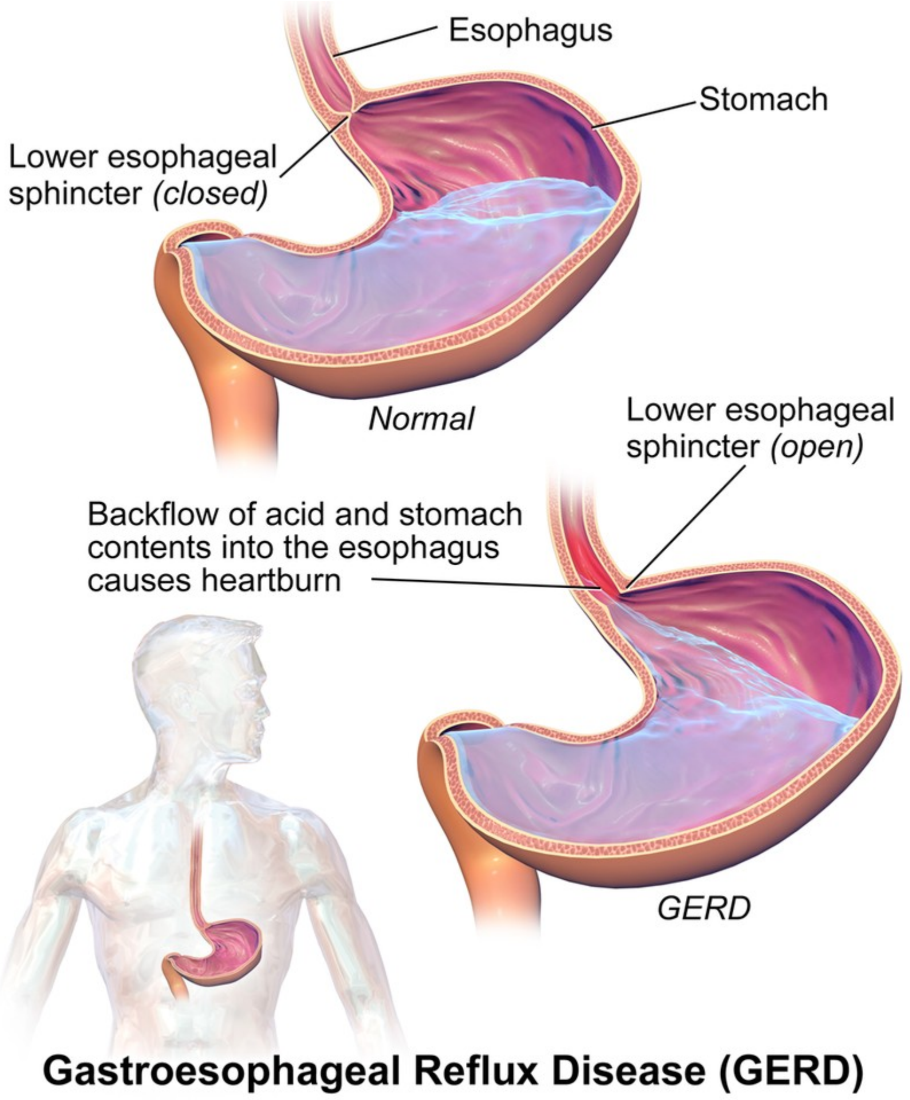
Muscularis externa: Thick inner layer circular smooth muscle outer layer longitudinal smooth muscle

Adventitia

The esophagus



The esophagus transports swallowed material from the larynx to the stomach



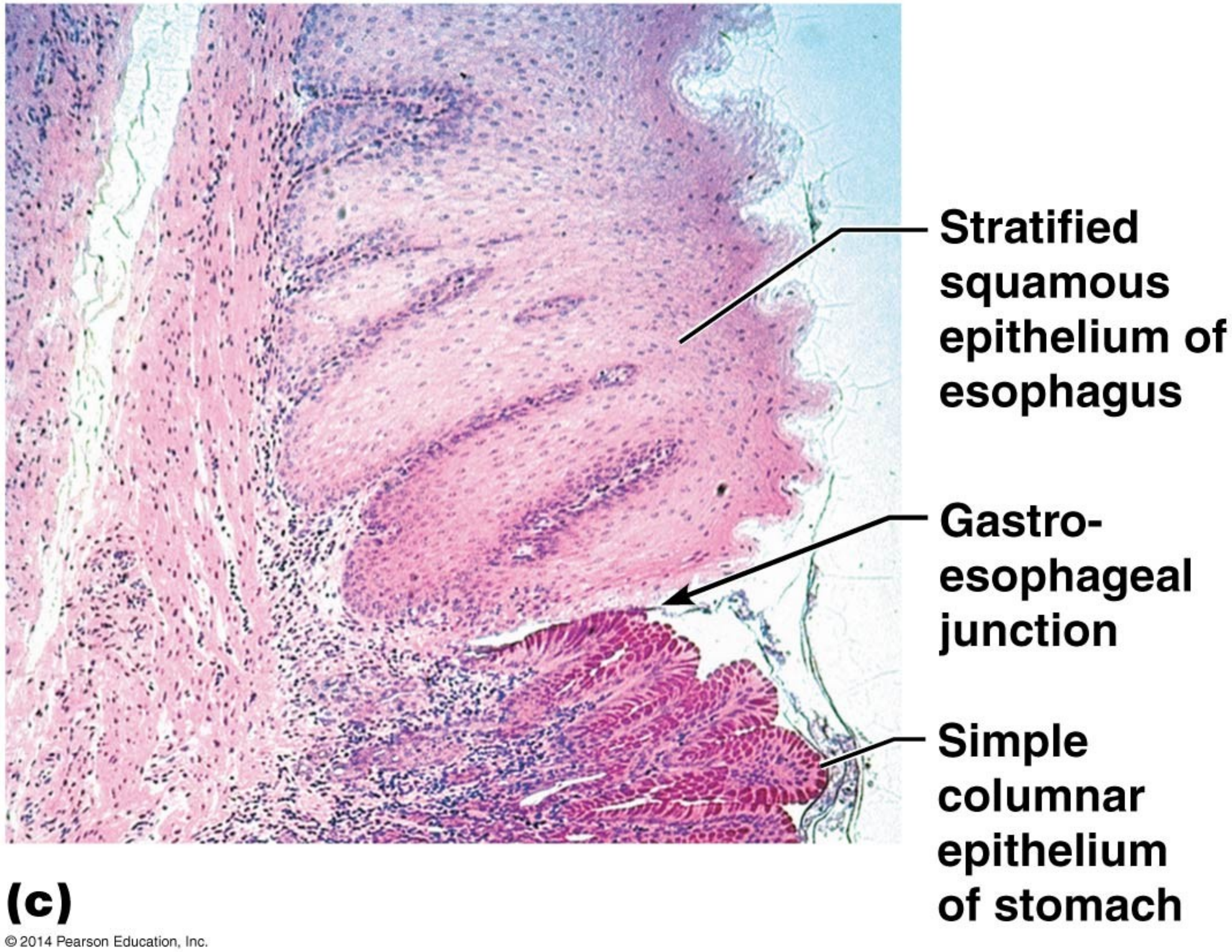
❯❯ MEDICAL APPLICATION

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

Esophagastric Junction



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

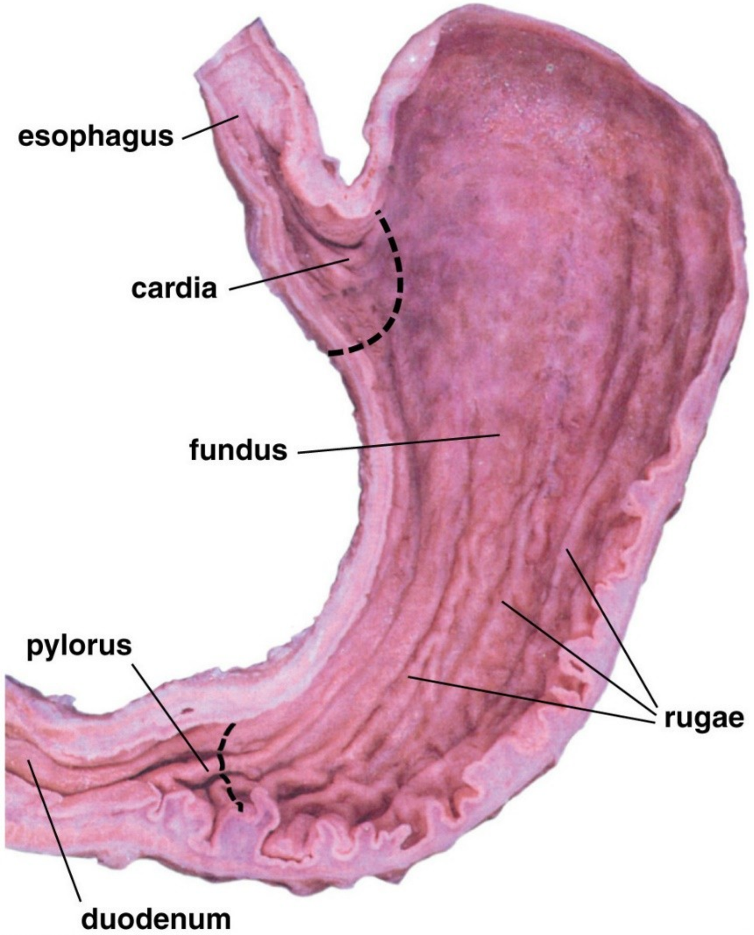
Stomach: **simple columnar epithelium** (secretory & some absorptive functions), acid resistance

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.

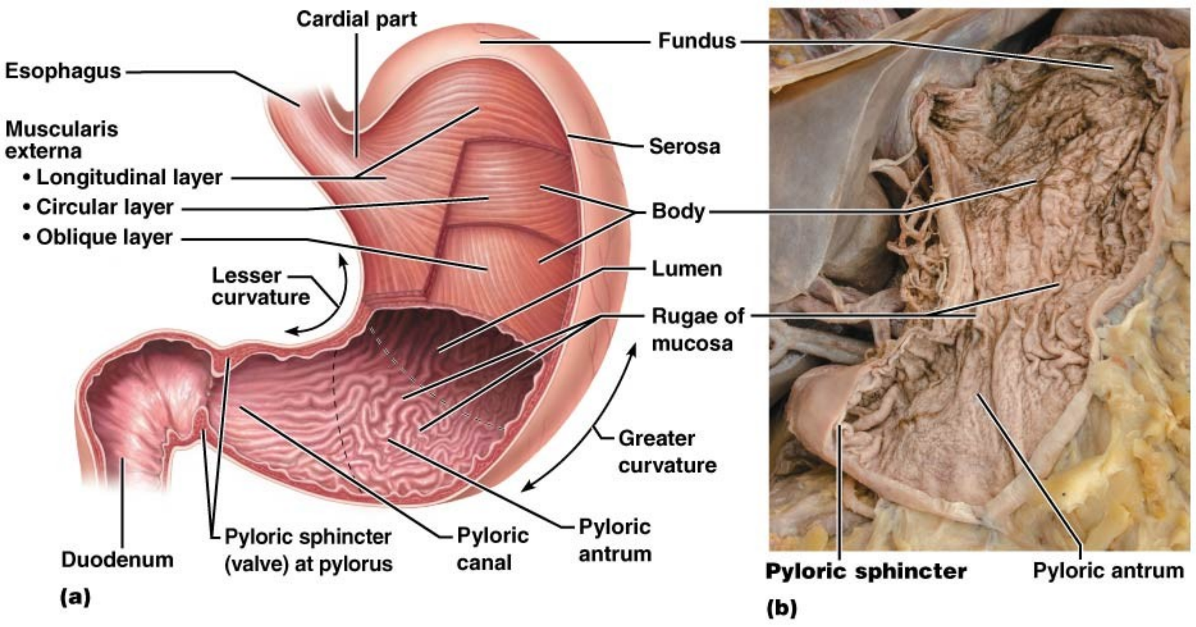
The stomach is divided histologically into three regions based on the type of gland that each contains.

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 <u>anatomical</u> (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

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

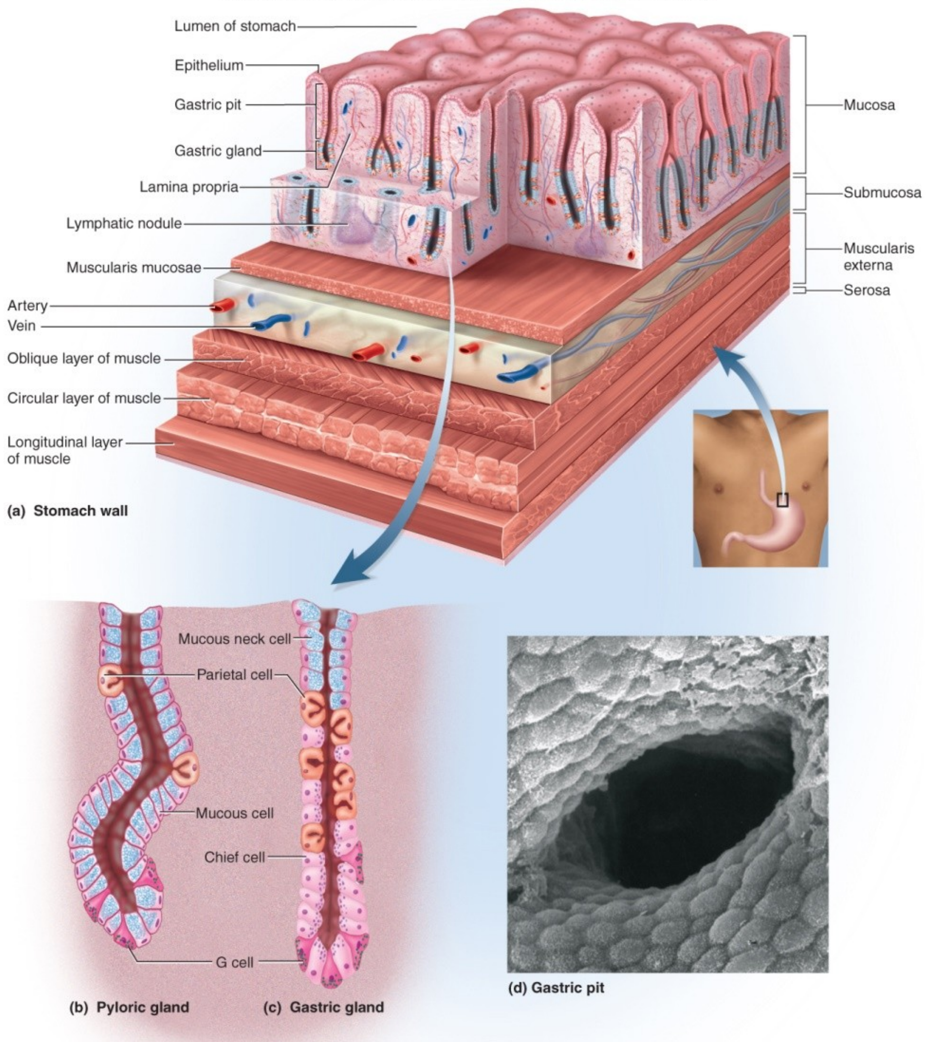
3 layers of **muscular externa** serves vigorous churning of food.

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



(a) Stomach wall

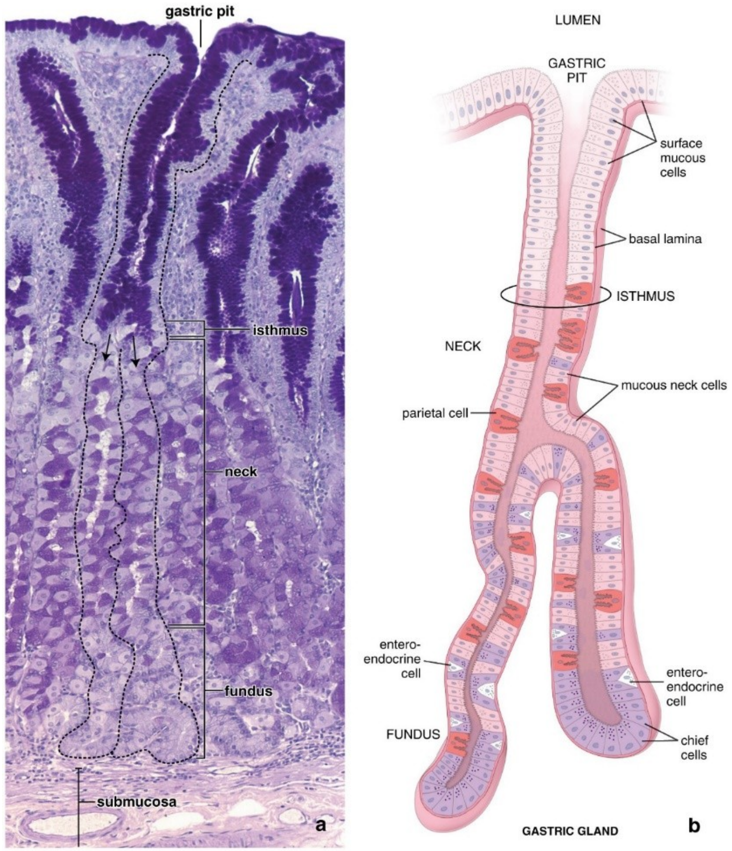
(b) Pyloric gland (c) Gastric gland

(d) Gastric pit

TABLE 25.1 Major Secretions of the Gastric Glands

Secretory Cells	Secretion	Function
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 (Fe^{2+}); destroys ingested pathogens
	Intrinsic factor	Enables small intestine to absorb vitamin 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**

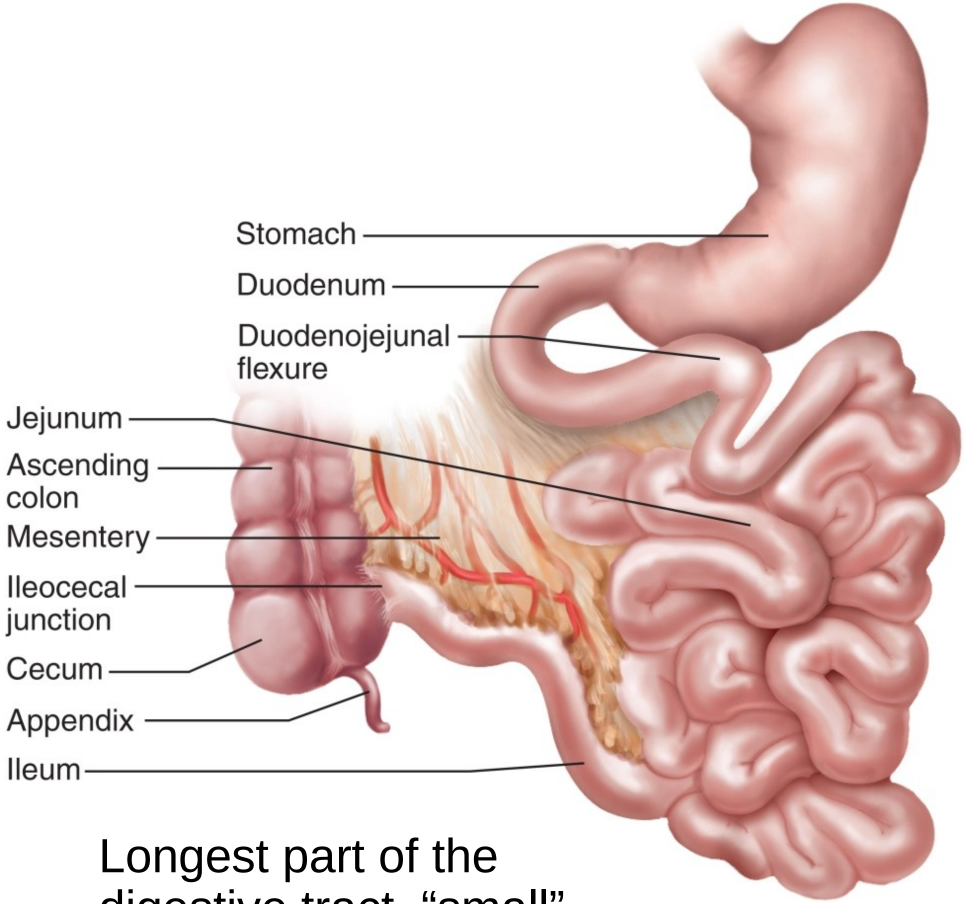
- Receives stomach contents, pancreatic juice, and bile
- Neutralizes stomach acid is neutralized here
- Breaks down fats
- Pancreatic enzymes perform chemical digestion

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



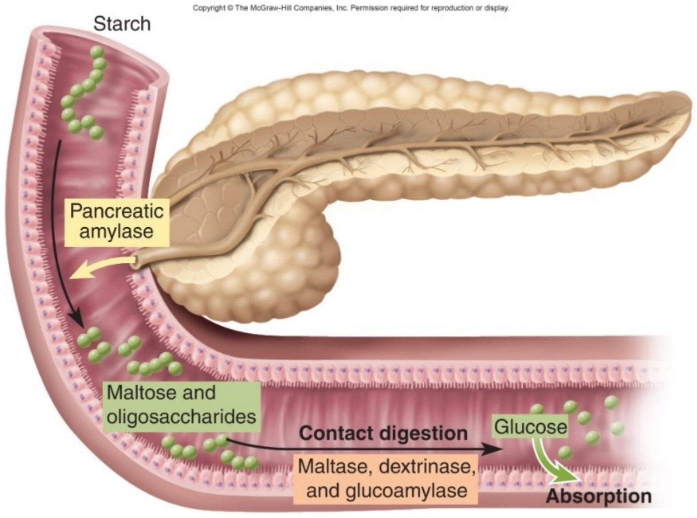
Longest part of the digestive tract, “small” refers to diameter

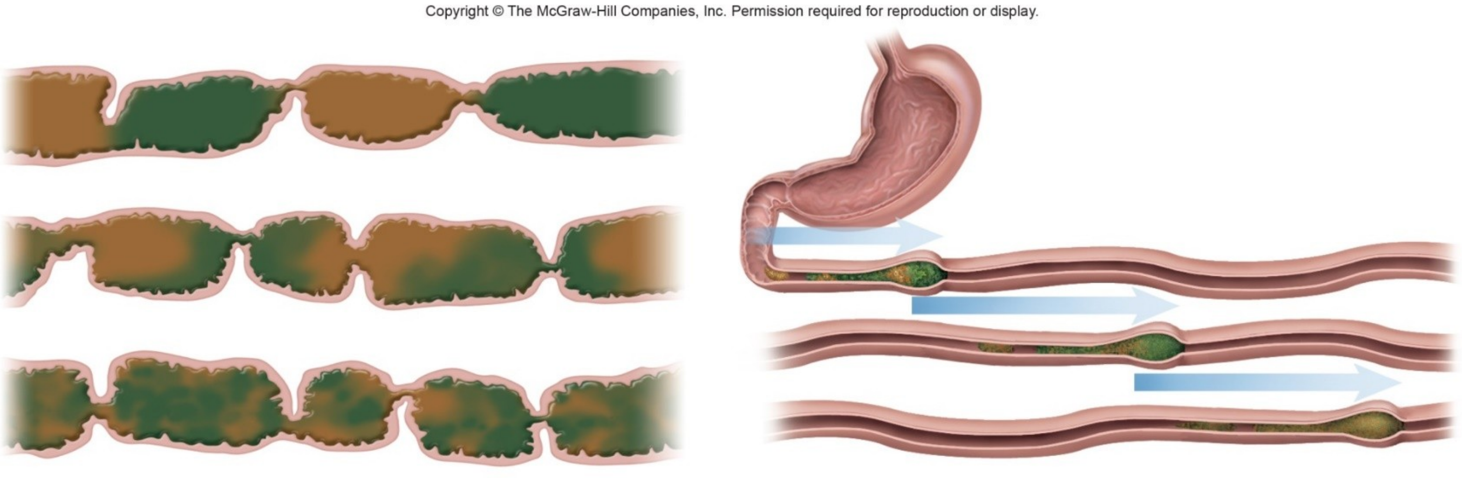
Digestion Small Intestine

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





(a) Segmentation

(b) Peristalsis

Microscopic Anatomy of Small Intestine

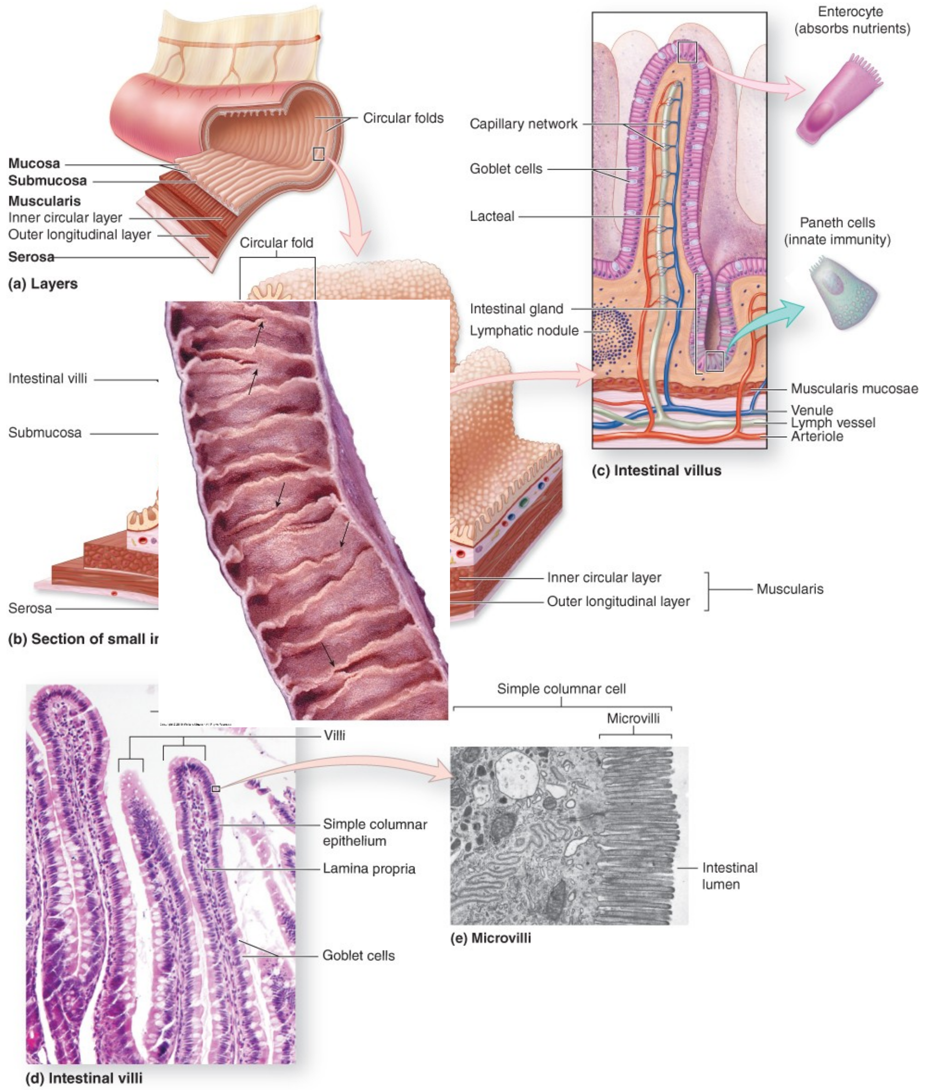
Surface area for effective digestion and absorption increased by:

- **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)

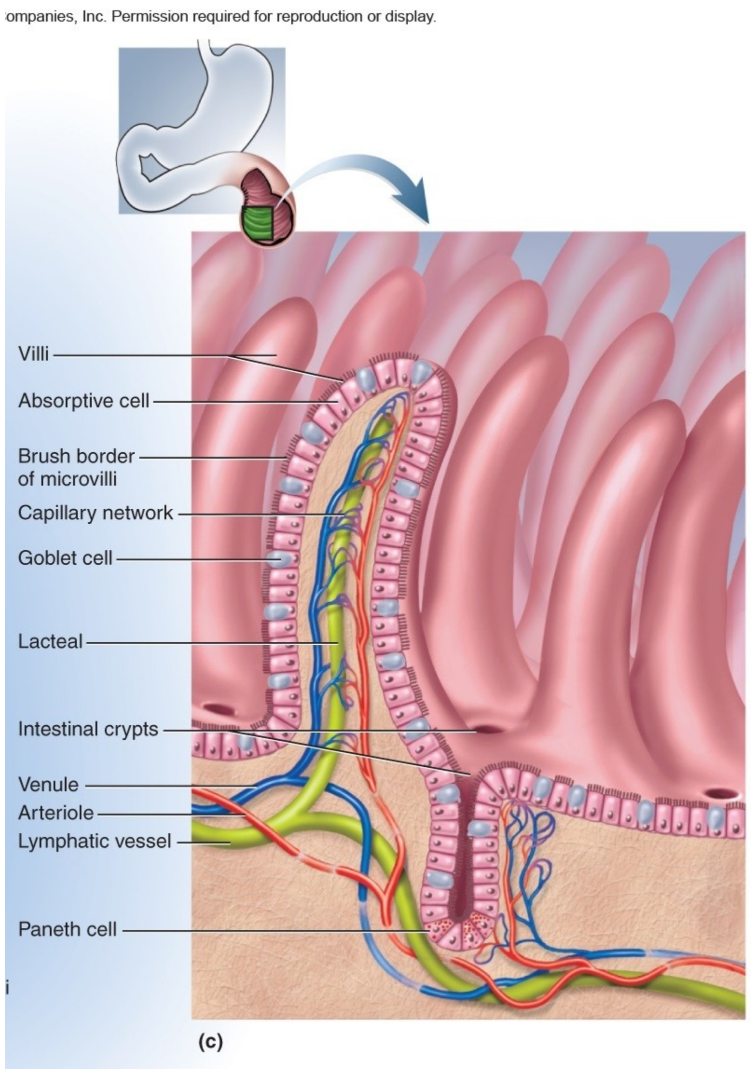
Duodenal glands: Neutralize stomach acid and shield the mucosa from its erosive effects



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

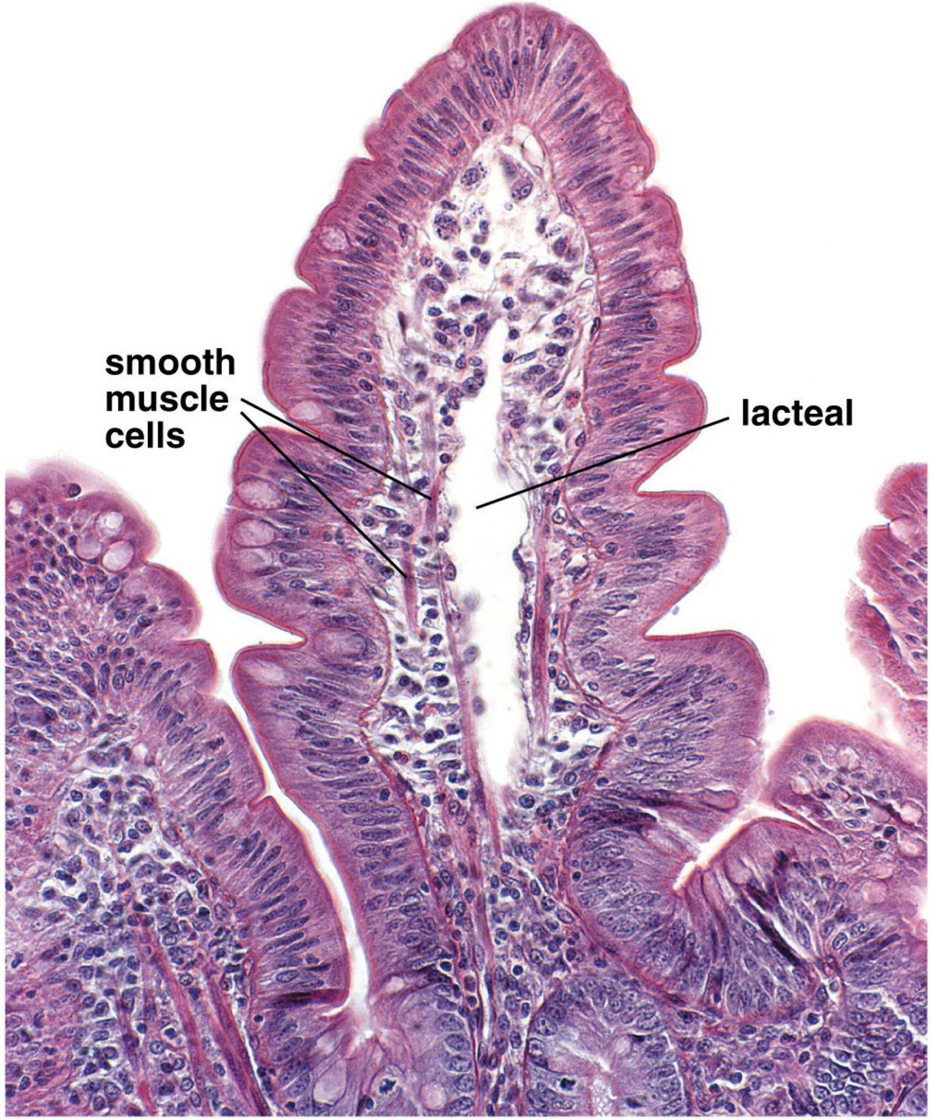
MEDICAL APPLICATION:
Celiac disease (celiac sprue) is a disorder of the small intestine mucosa that causes malabsorption and can lead to damage or destruction of the villi. The cause of celiac disease is an immune reaction against gluten or other proteins in wheat and certain other types of grain. The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

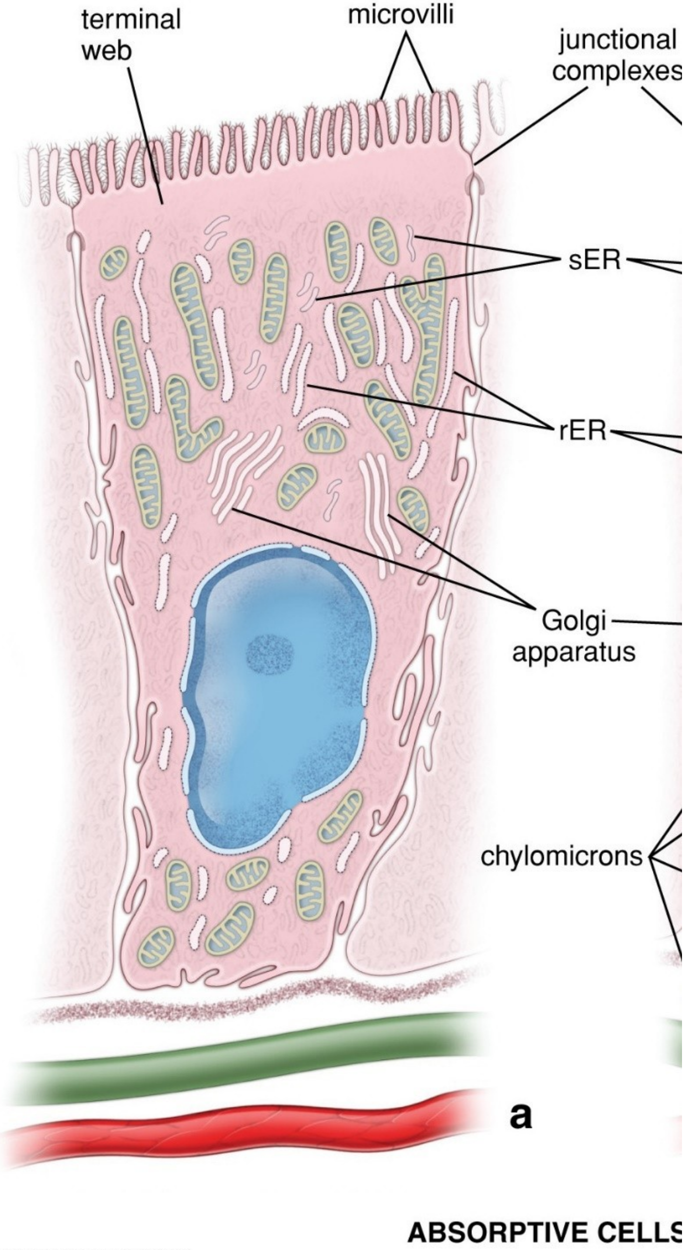


Enterocytes Absorb and Transport Substances to Circulation

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.



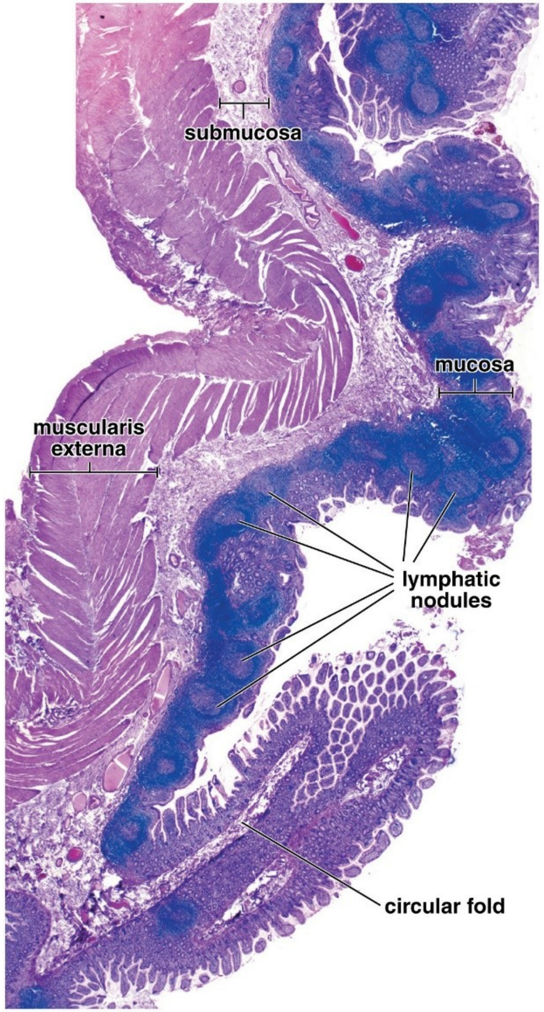


Duodenal Brunner's Glands De-acidify Stomach Chyme

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

Brunner's Glands are branched, tubular glands with secretions of 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.

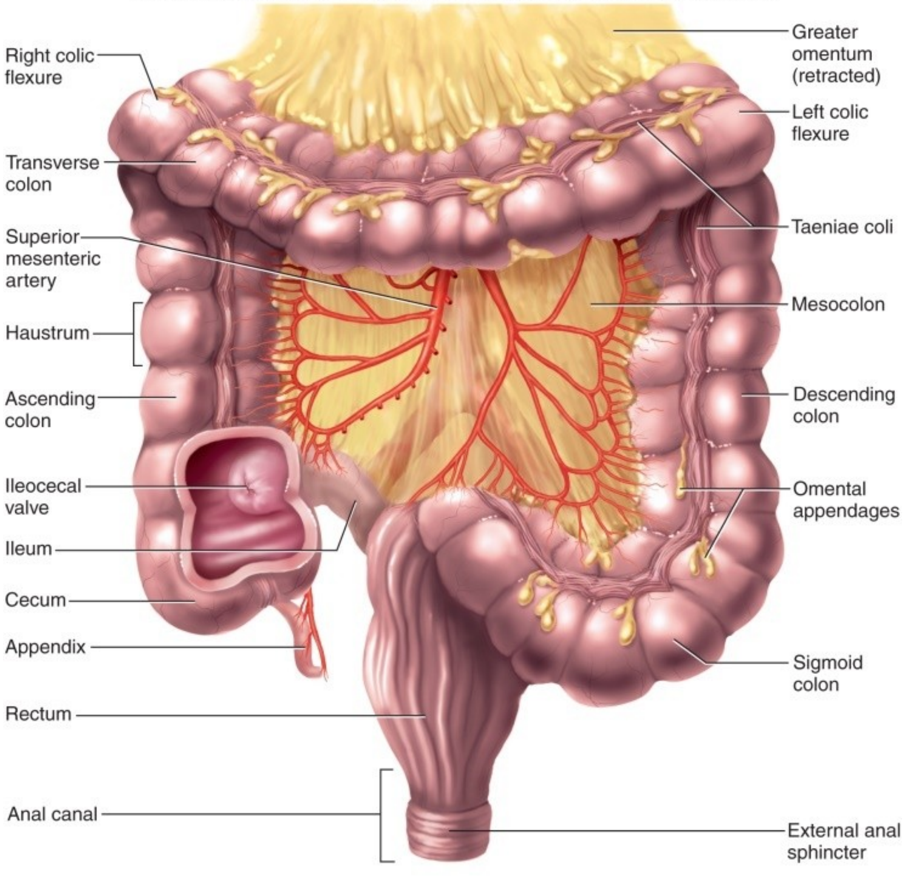
GALT serves as an immunologic barrier throughout the length of the gastrointestinal tract.

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

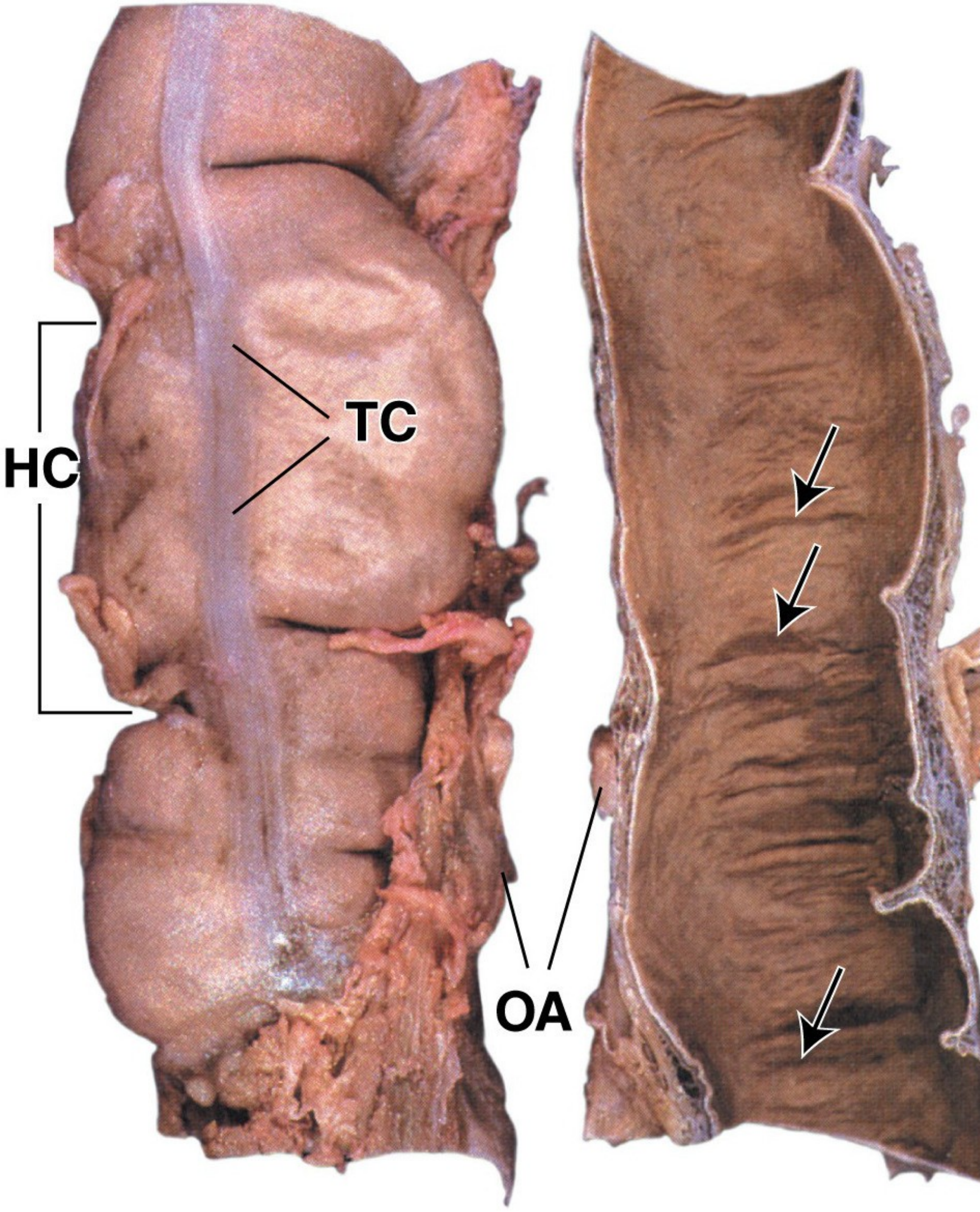
Herniation: outpocketing of the mucosa and submucosa of the colon can occur between the teniae coli resulting from structural defects in the colon wall or from high intraluminal pressure or constipation.

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

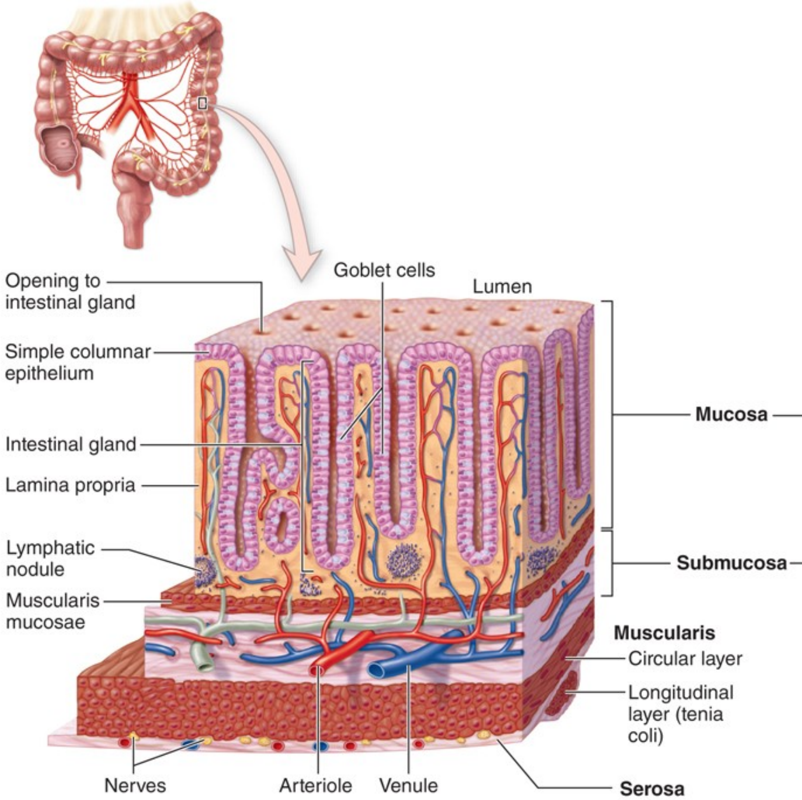
Flatus (intestinal gas): Average person produces 500 mL per day (flatus) from 7 to 10 L of gas present but reabsorbed

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

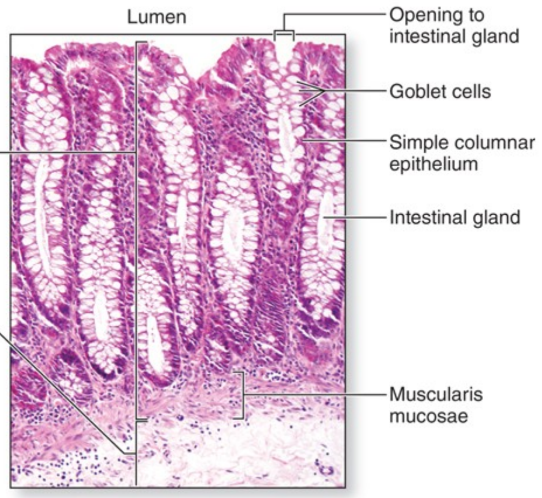
FMT: https://www.youtube.com/watch?v=MUhJoTF6ZMc



Wall of the Large Intestine



(a) Large intestine tunics



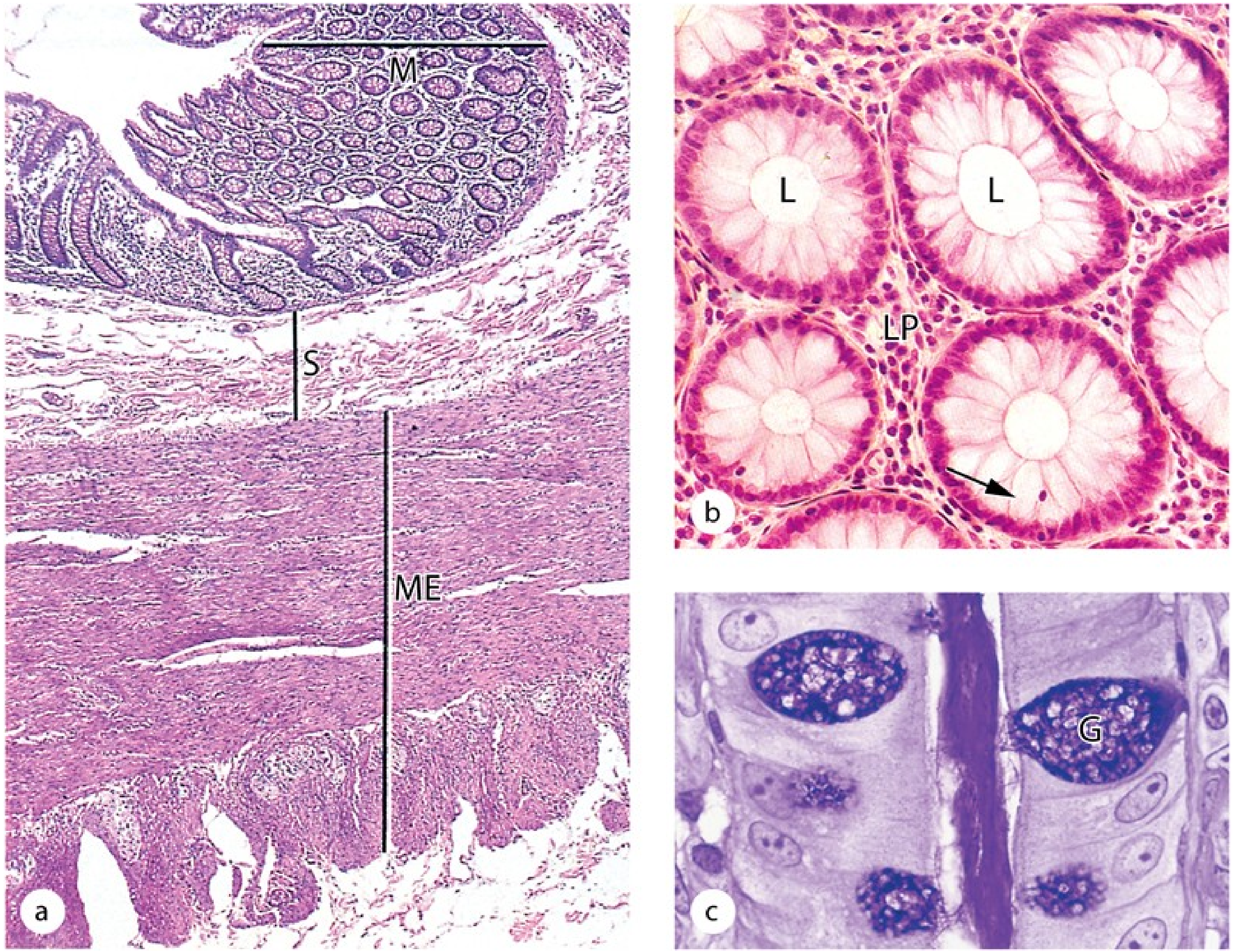
(b) Large intestine mucosa and submucosa

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**).

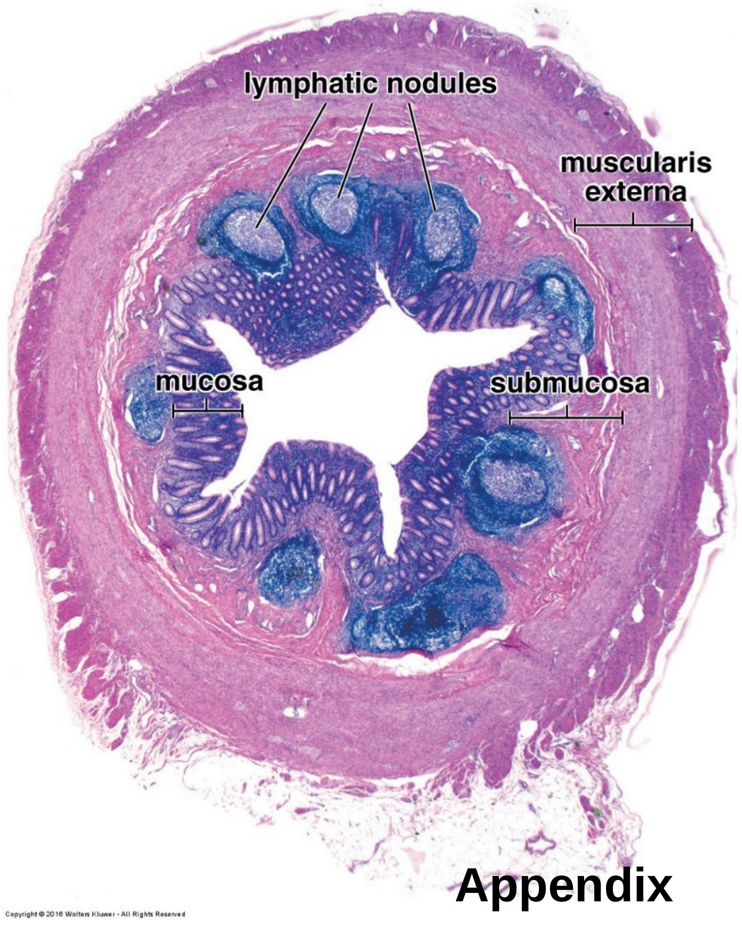
(c) Longitudinal section of one intestinal gland stained for glycoproteins shows **mucus** in the lumen and two major cell types in the epithelium: goblet cells (**G**) and the neighboring columnar cells specialized for water absorption.

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.

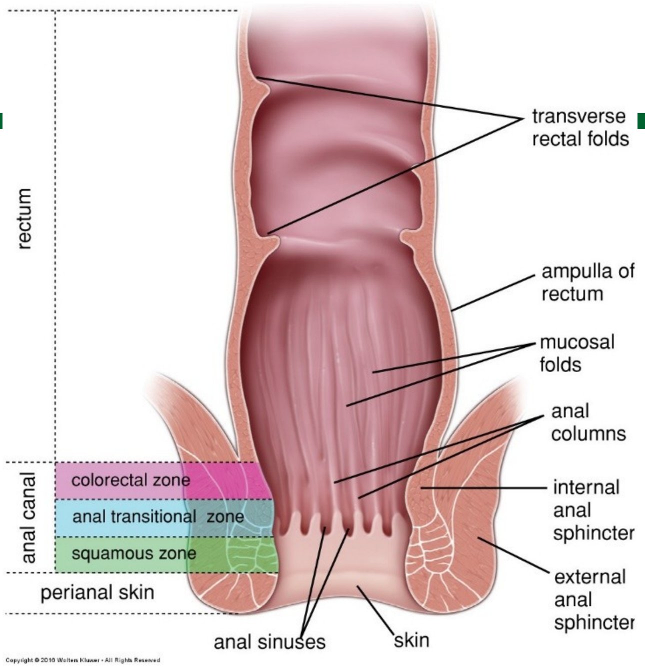


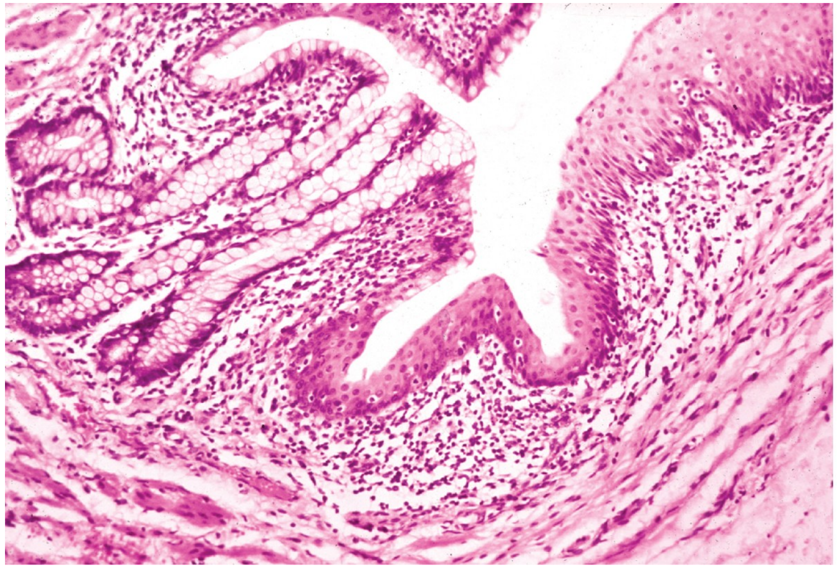
Appendix

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





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

http://highered.mheducation.com/sites/0072943696/student_view0/chapter16/animation__reflexes_in_the_colon.html

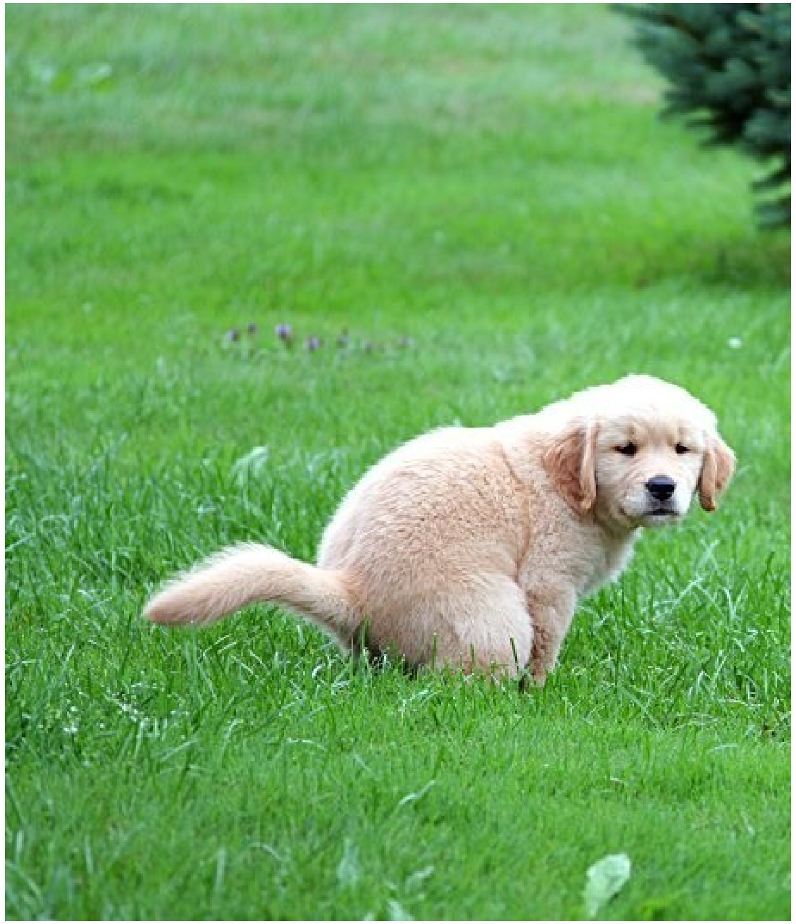
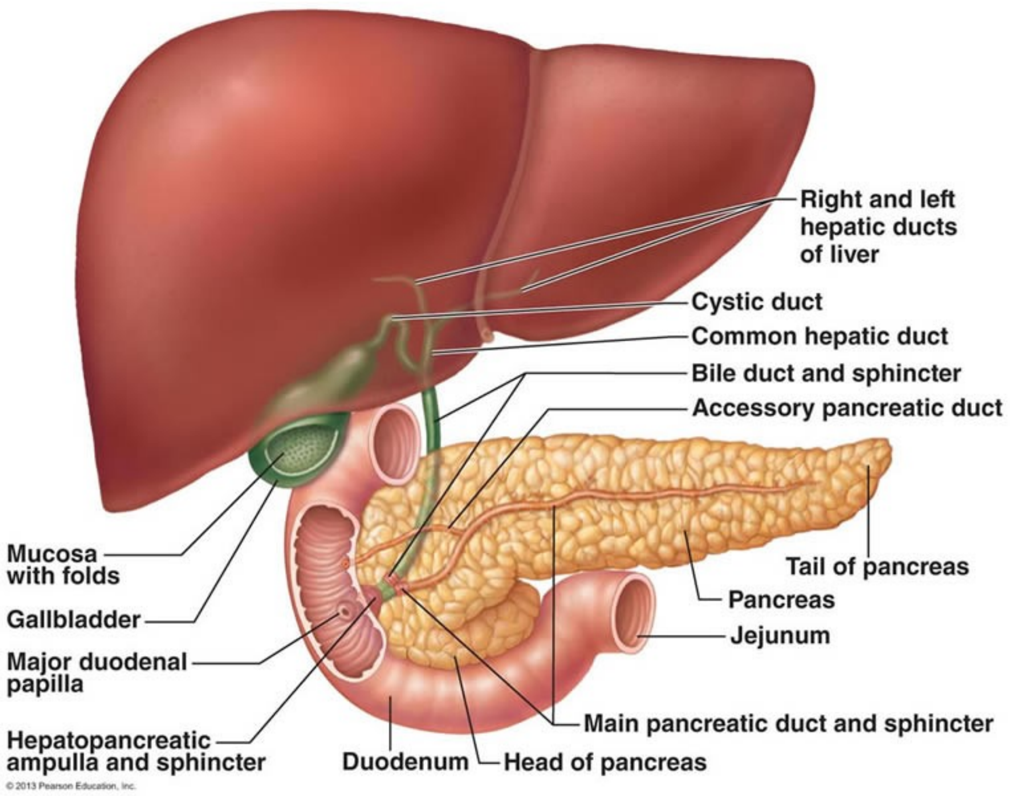


TABLE 15–2 **Summary of distinguishing digestive tract features, by region and layers.**

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

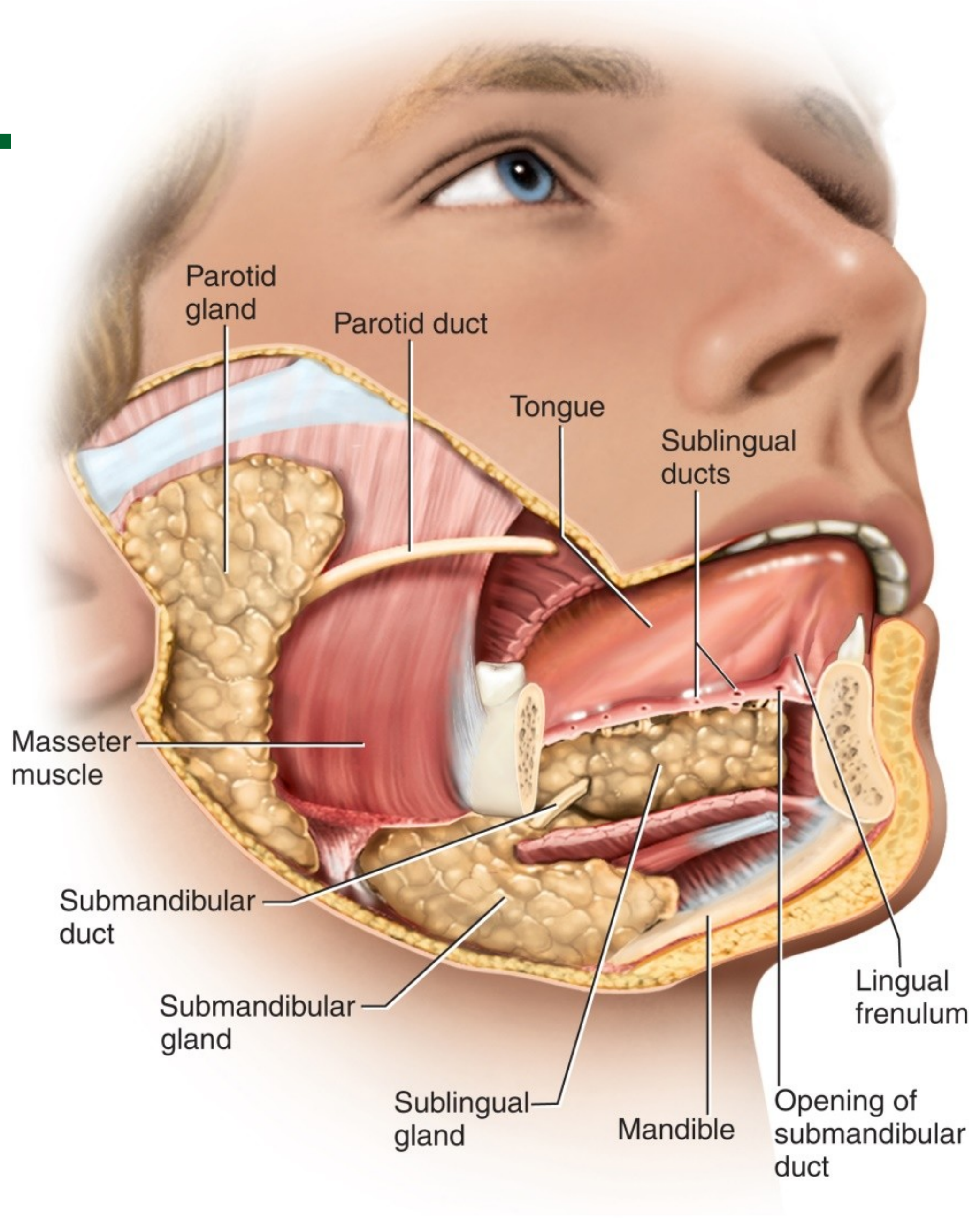
Saliva: starch and fat digestion, inhibits bacterial growth
Salivary amylase: starch digestion in the mouth
Lingual lipase: digests fat in stomach acid,
Mucus: lubricates food for swallowing
Lysozyme: kills bacteria
Immunoglobulin A (IgA): inhibits bacterial growth
Electrolytes: Na^+, K^+, Cl^-, phosphate, 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

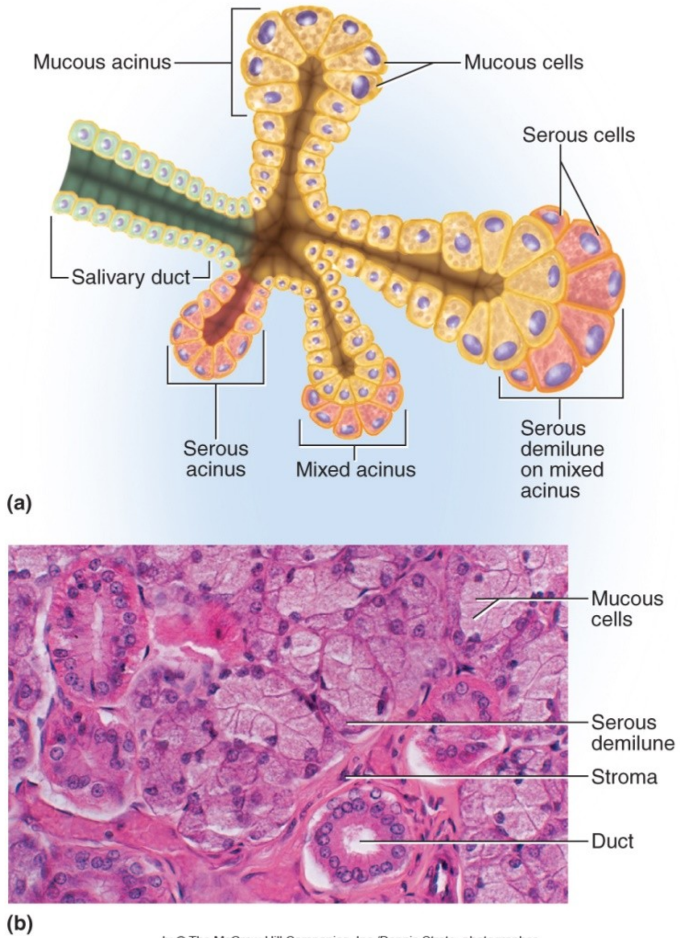
- **Parotid**: Mumps is viral infection of parotid gland
- **Submandibular gland**: empties near the lower central incisors
- **Sublingual glands**: multiple ducts that empty posterior to submandibular duct



Histology of Salivary Glands

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

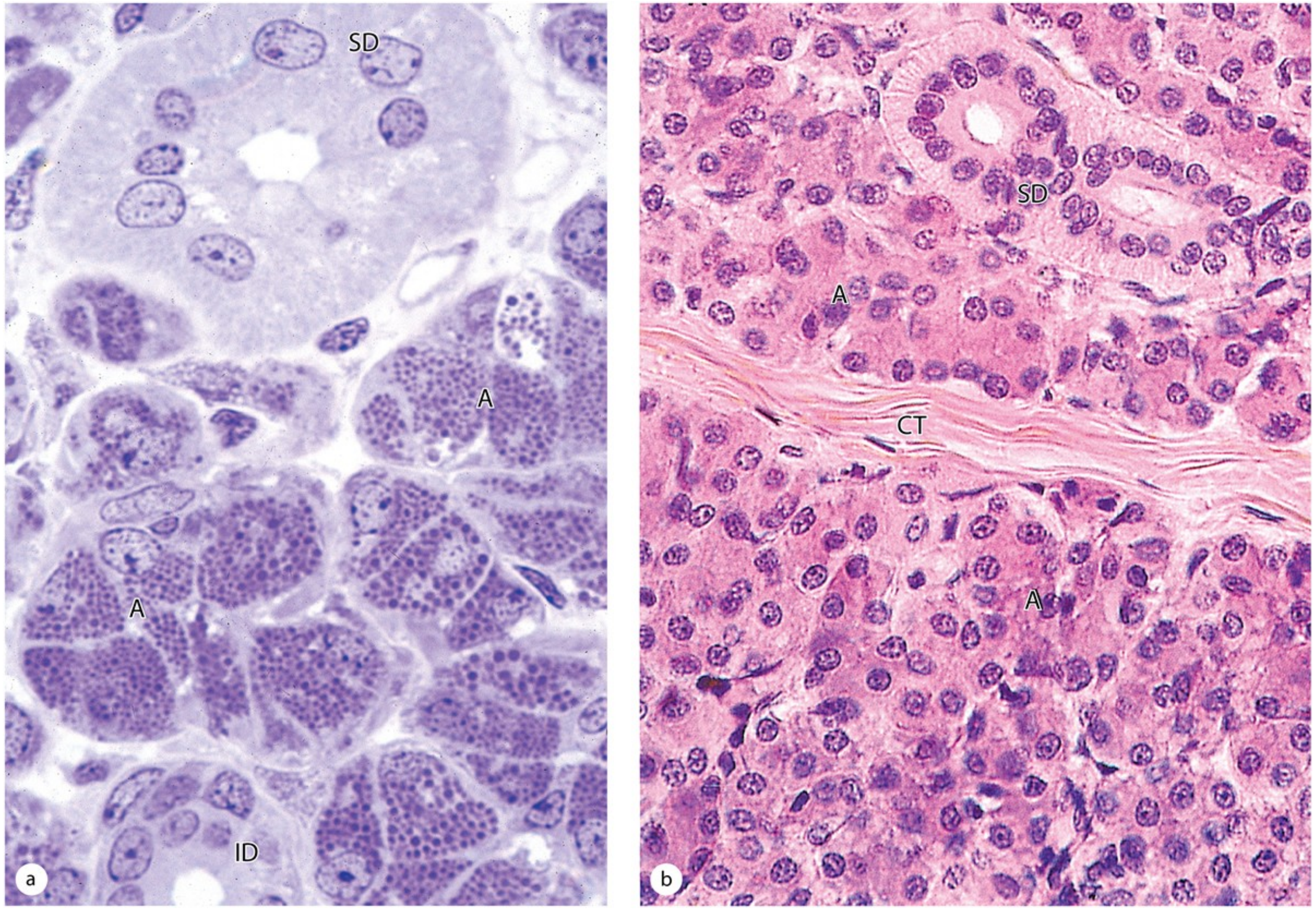


❯❯ MEDICAL APPLICATION

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

Pavlov's Dogs: https://www.youtube.com/watch?v=hChO1Gim8b0

Parotid gland



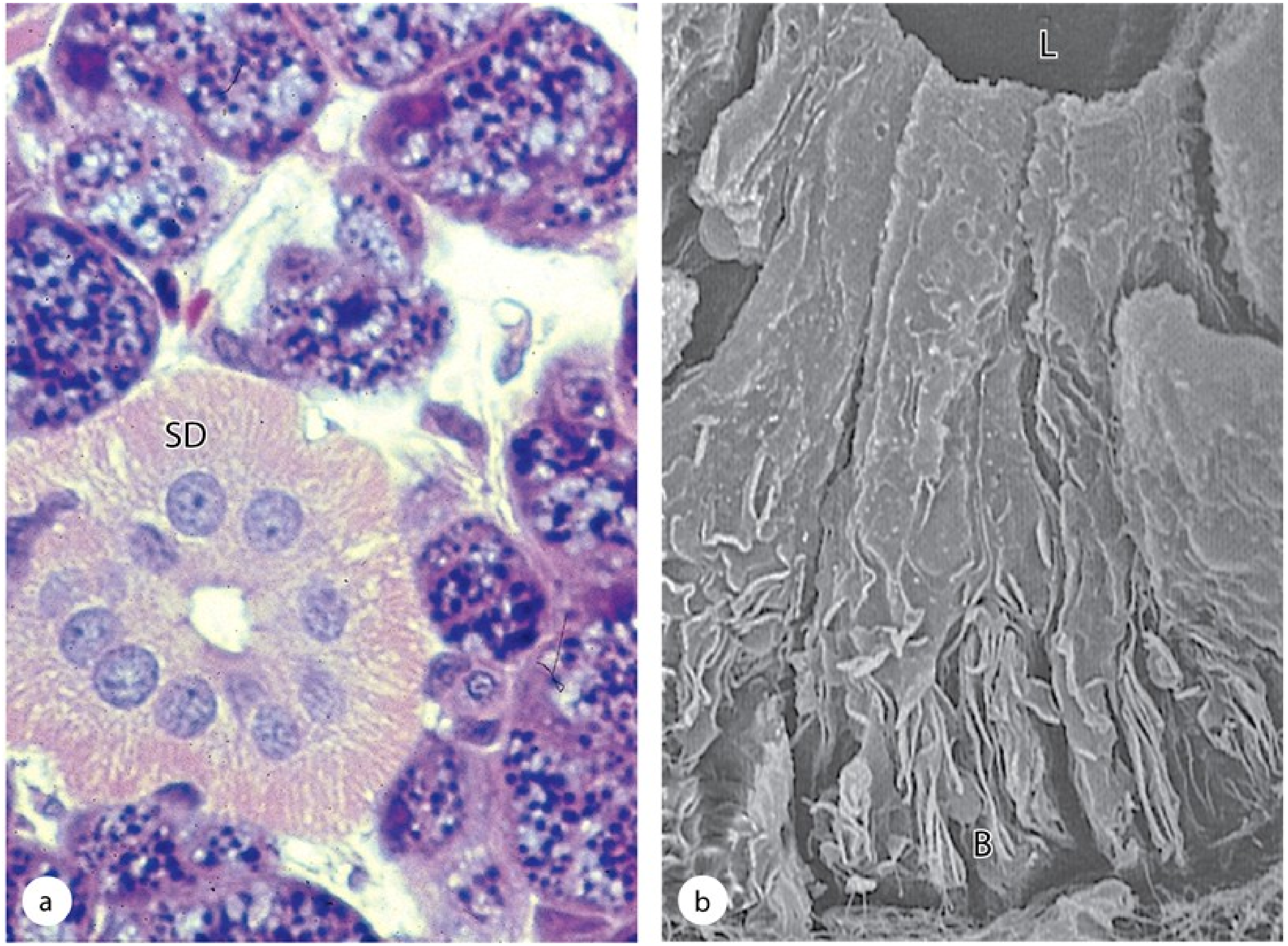
The large parotid gland consists entirely of serous acini with cells producing amylase and other proteins for storage in secretory granules.

(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.

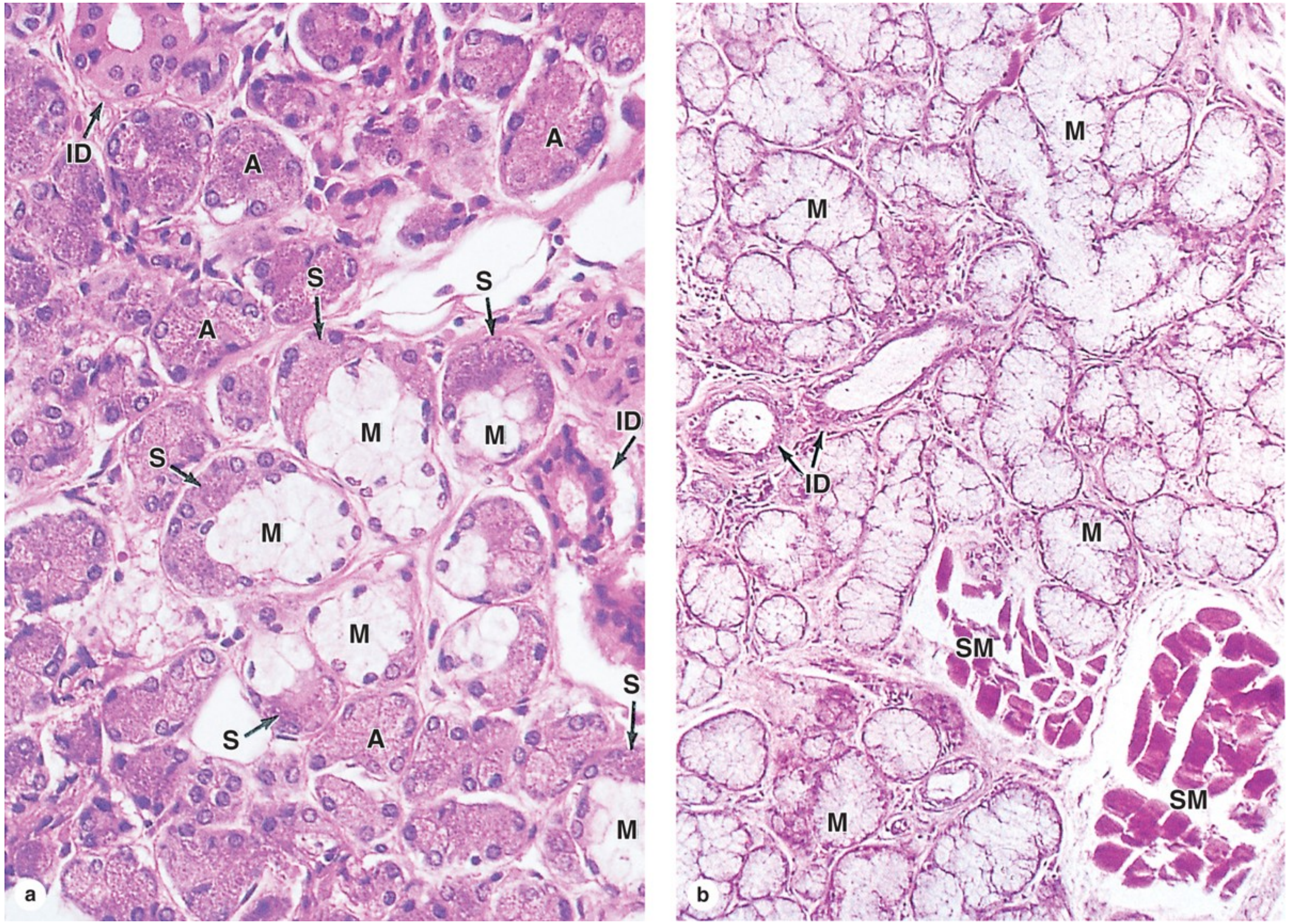
Striated ducts



(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.

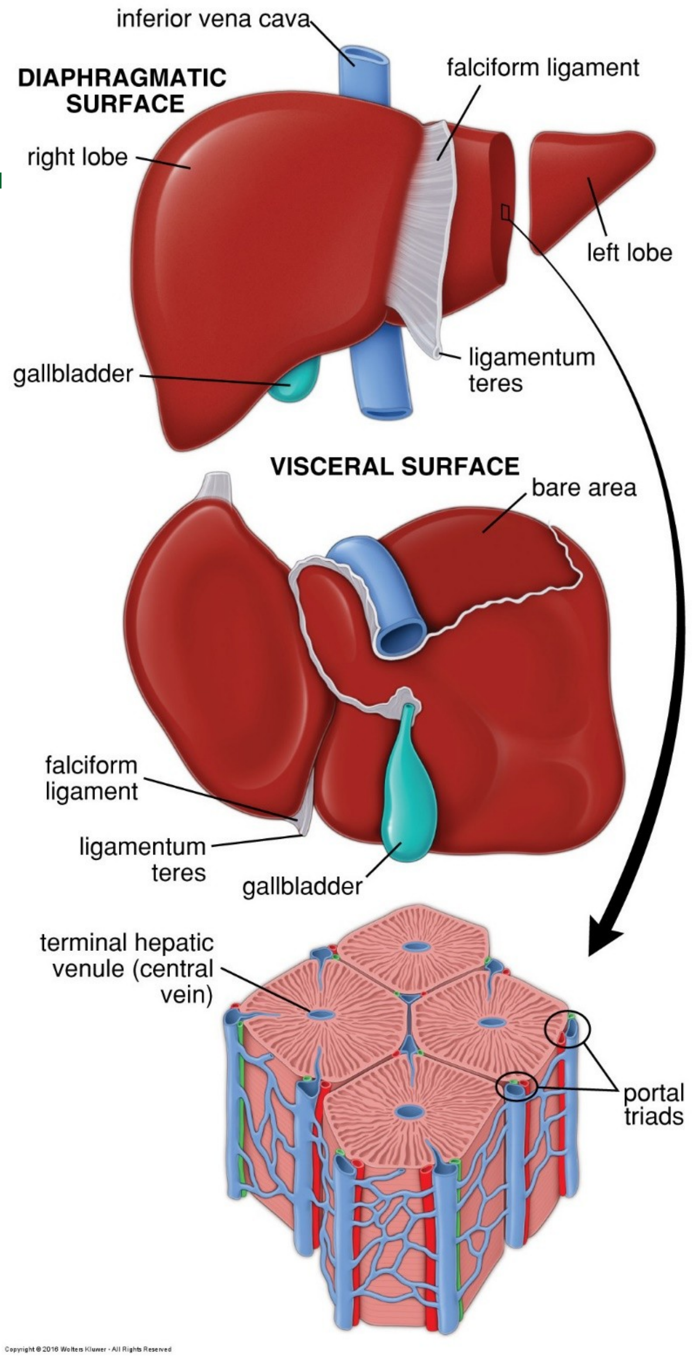
(b) The **sublingual gland** is a mixed but largely mucous gland with a tubuloacinar arrangement of poorly stained mucous cells (**M**). Small intralobular ducts (**ID**) are seen in connective tissue, as well as small fascicles of lingual striated muscle

The Liver Secretes Digestive Bile

Functions

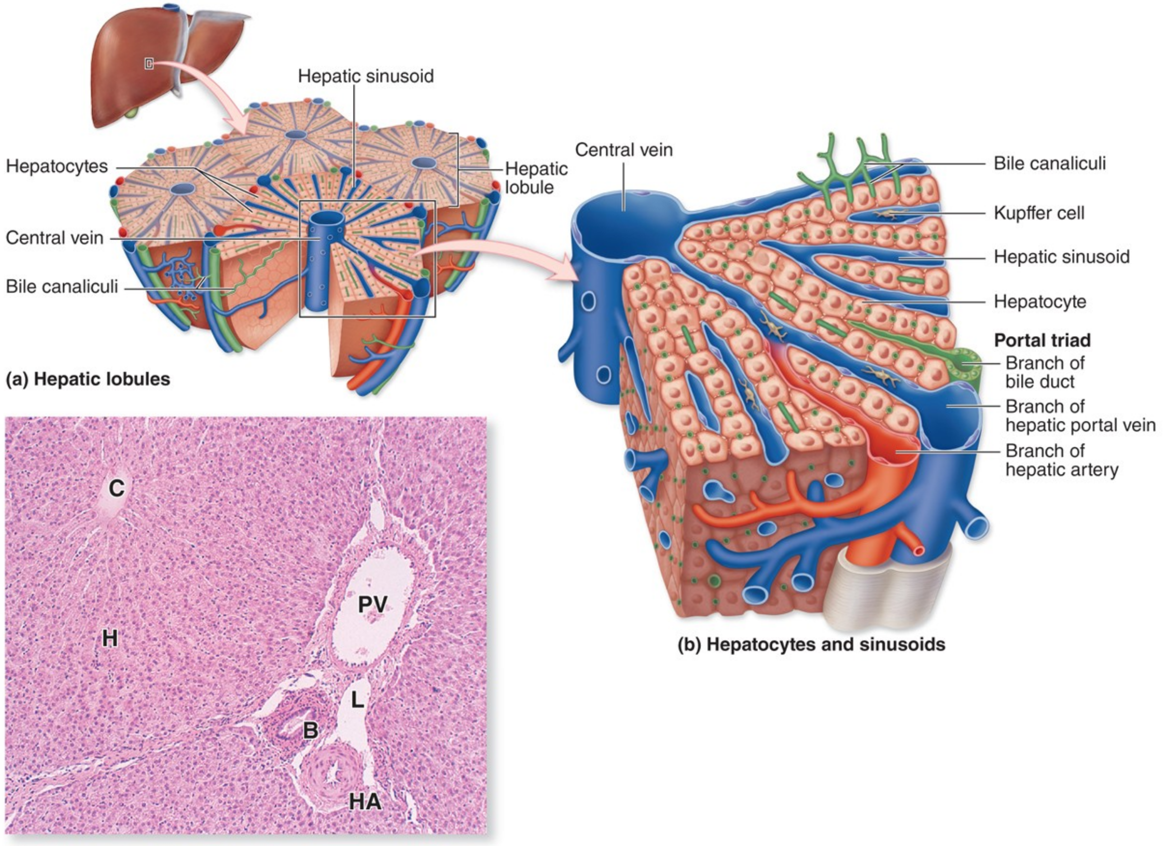
- Produces circulating plasma proteins (albumins, β-globulins, fibrinogen)
- Stores vitamins and iron
- Degrades drugs and toxins
- Secretes bile

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.



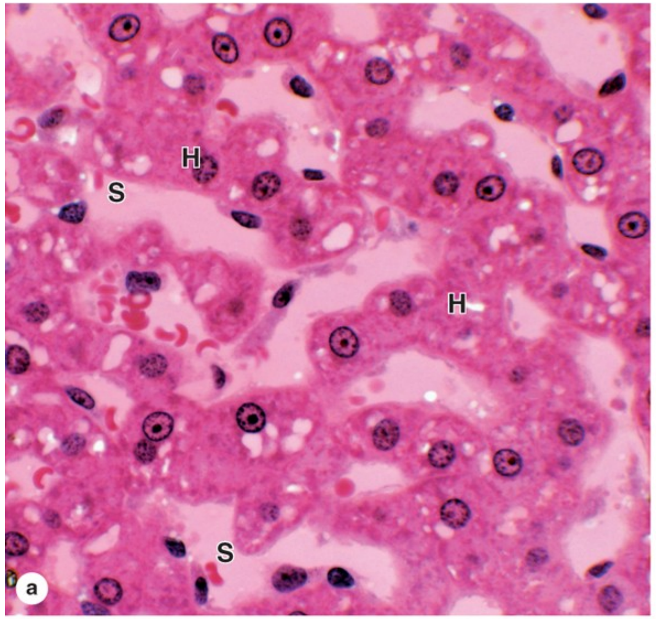
Microscopic Anatomy

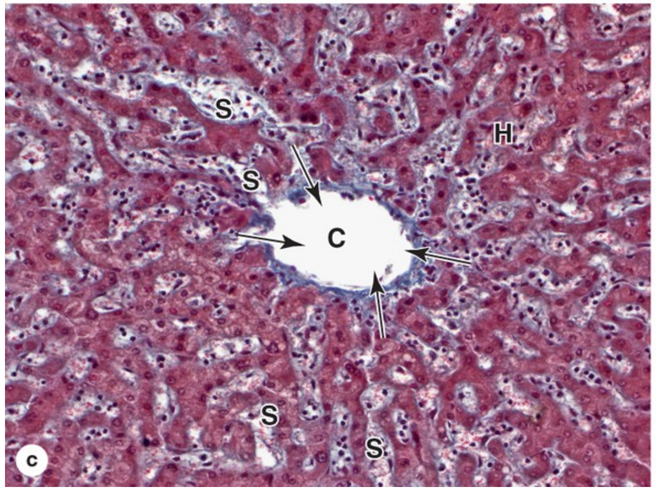
Hepatic lobules: basic functional units
Central vein: passing down the core
Hepatocytes: cuboidal cells, absorb nutrients from blood
Hepatic sinusoids: blood from stomach
Hepatic macrophages (Kupffer cells): phagocyets
Bile: aids in digestion of lipids
Bile canaliculi: narrow channels into which the 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.

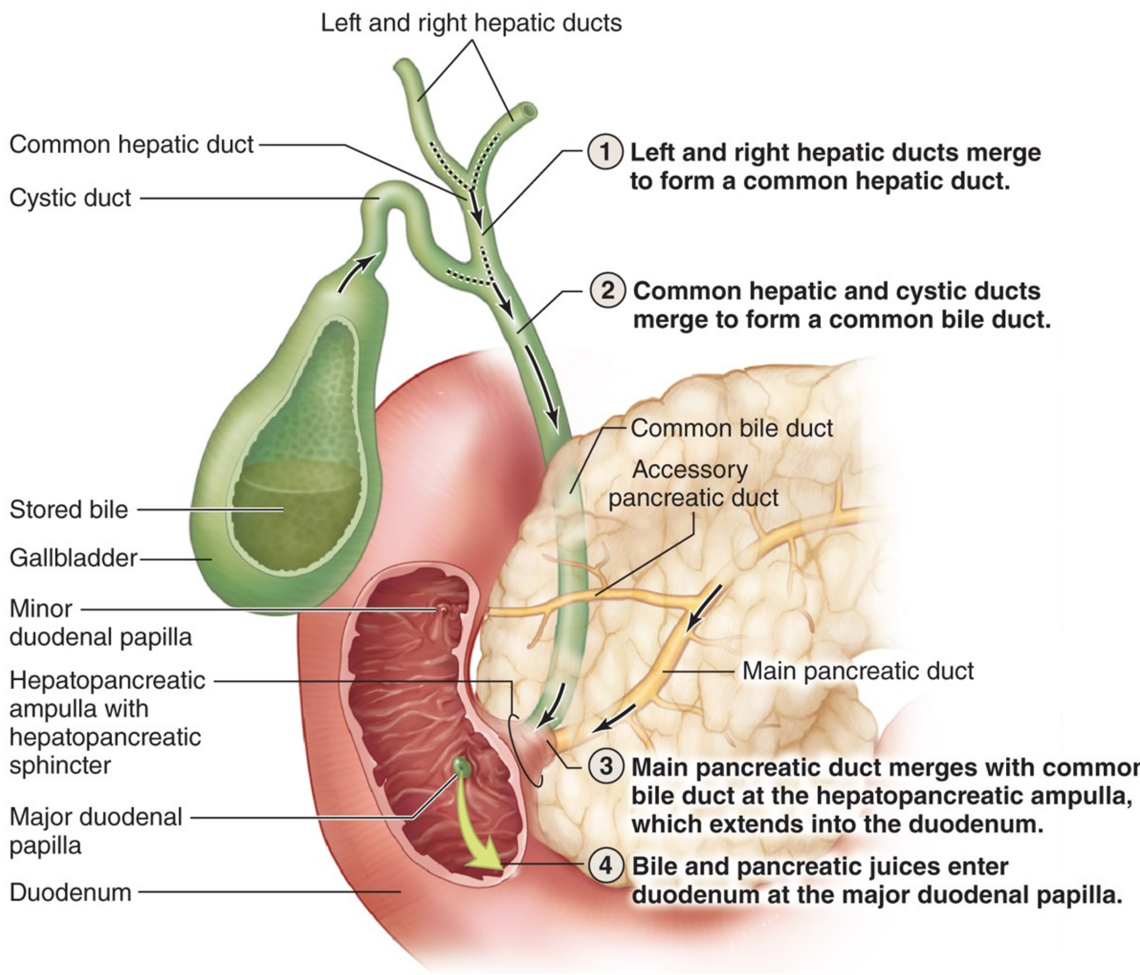
Fatty liver disease is a reversible condition in which large lipid droplets containing triglycerides accumulate abnormally in hepatocytes via the process called steatosis. This disorder has multiple causes, but it occurs most commonly in individuals with alcoholism or obesity. Accumulation of fat in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

Bile: produced by liver
Bile duct: formed from union of hepatic ducts.

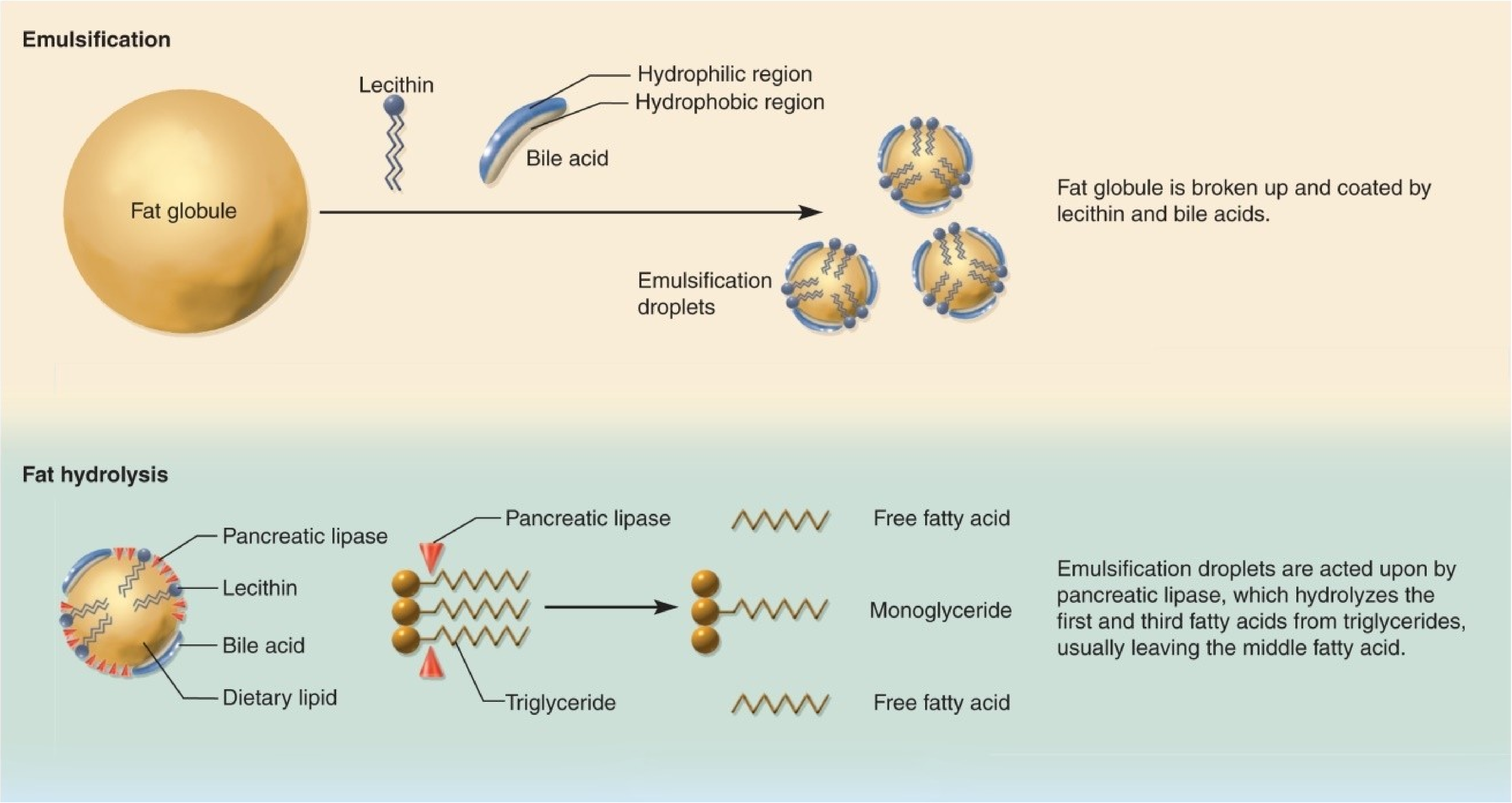
Bile and pancreatic juices are mixed before release into the duodenal lumen

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.

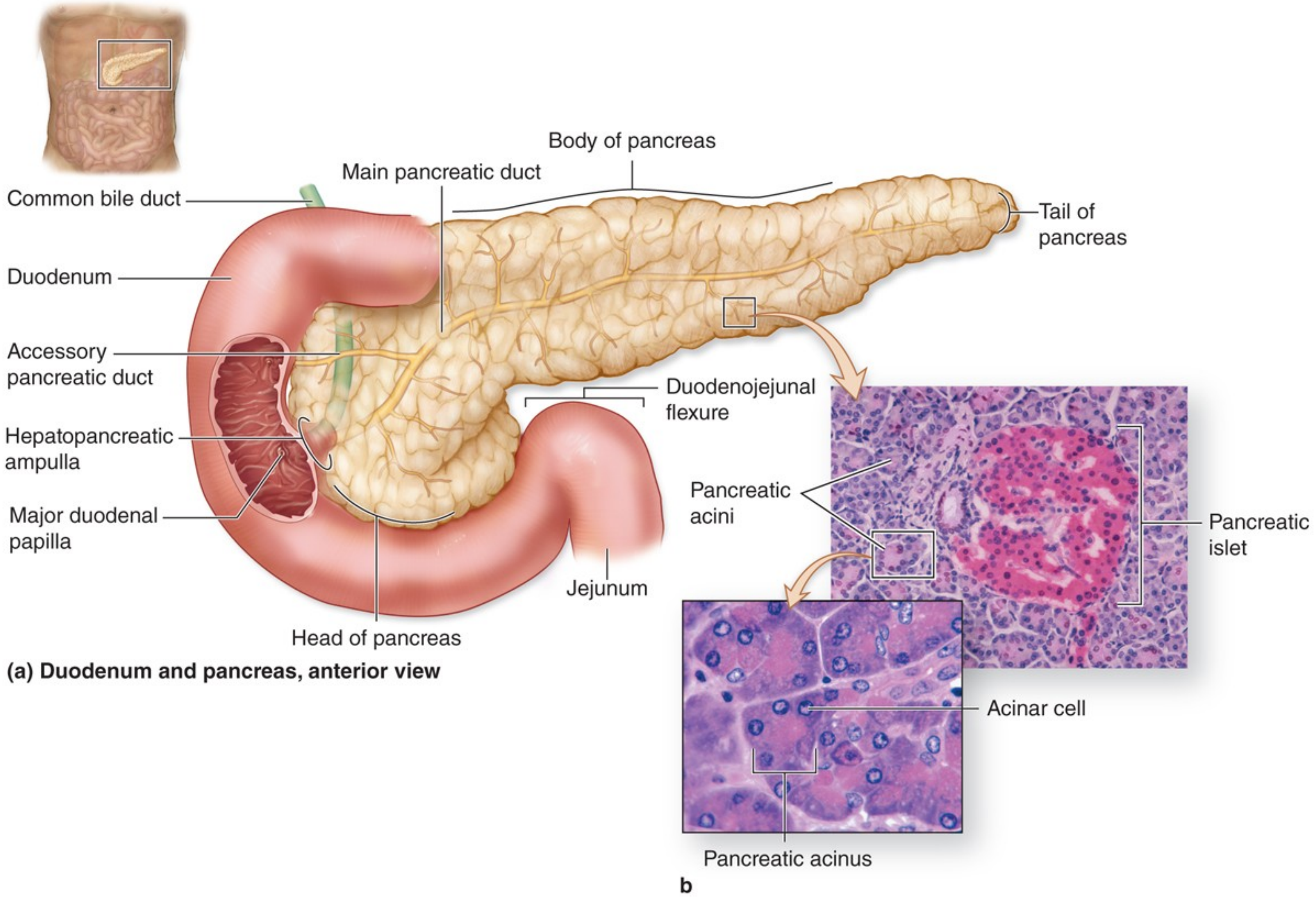
The Gallbladder Stores and Concentrates Bile



Bile Acid Emulsifies Fat So Pancreatic Enzymes Can Access Their Substrate



Pancreas and duodenum



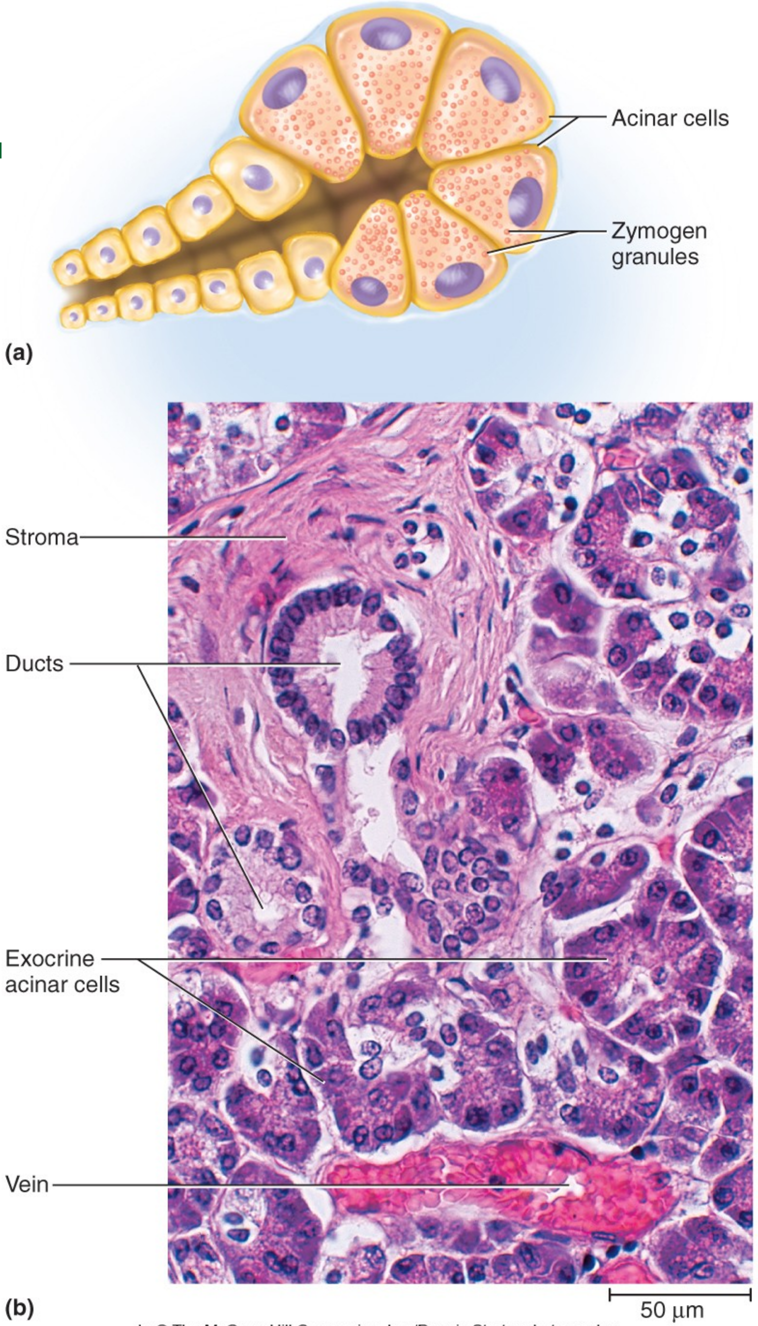
(a) Duodenum and pancreas, anterior view

(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

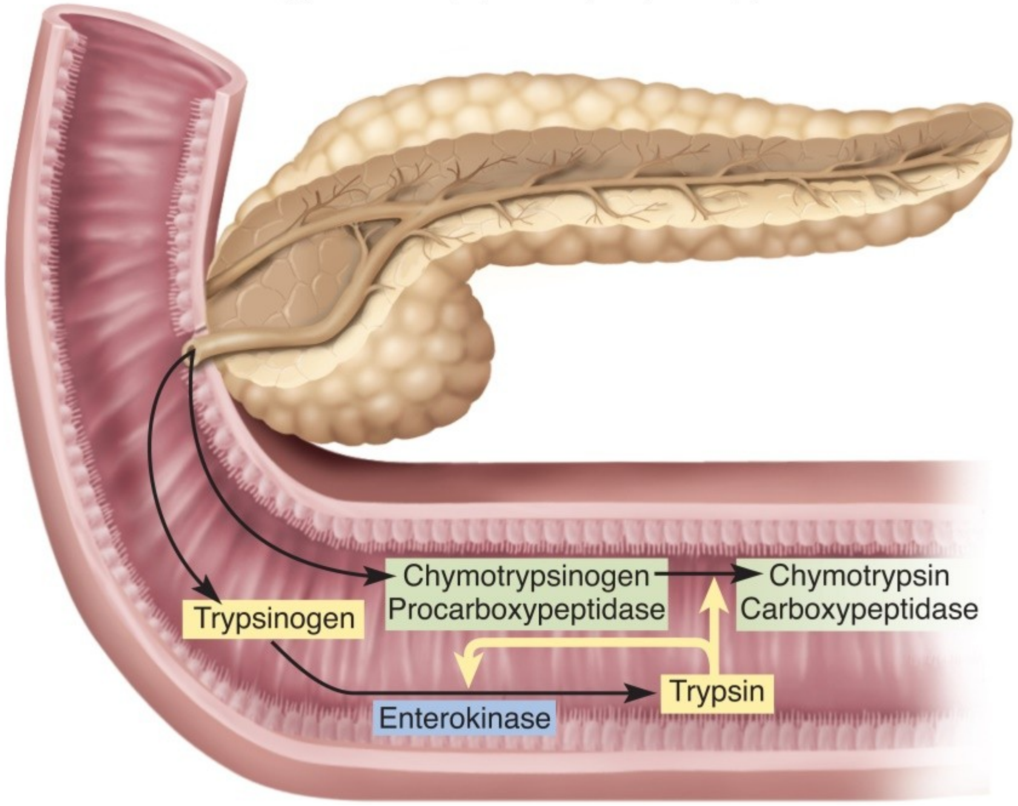
The Pancreas is a Gland

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



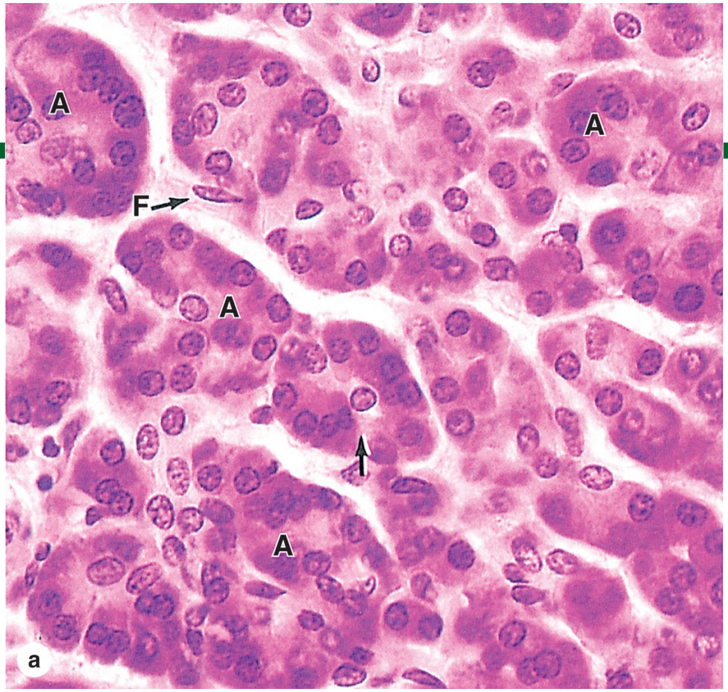
Trypsin: peptide cleavage
Trypsinogen: Converted to trypsin by enterokinase
Chymotrypsinogen: converted to chymotrypsin by trypsin
Procarboxypeptidase: converted to carboxypeptidase by trypsin
Pancreatic amylase: digests starch
Pancreatic lipase: digests fat
Ribonuclease and deoxyribonuclease: digest RNA and DNA Control of Release of pancreatic juice and bile

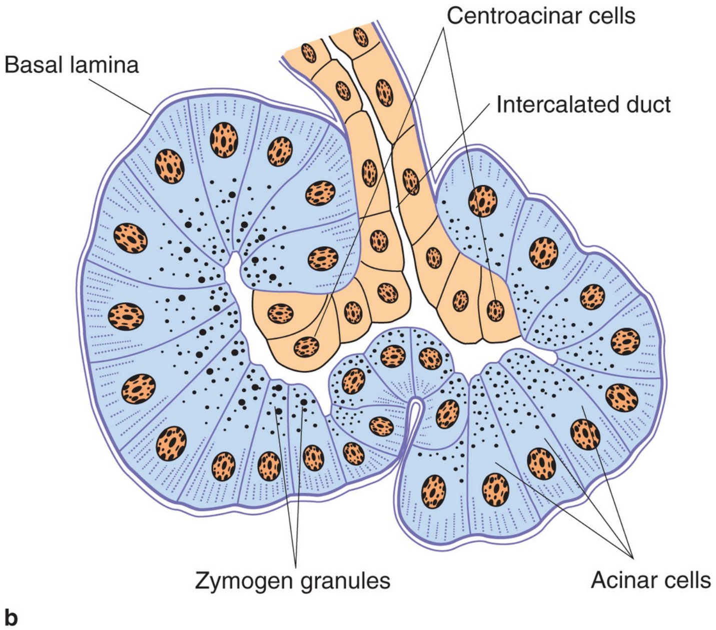
Pancreatic Enzymes



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.

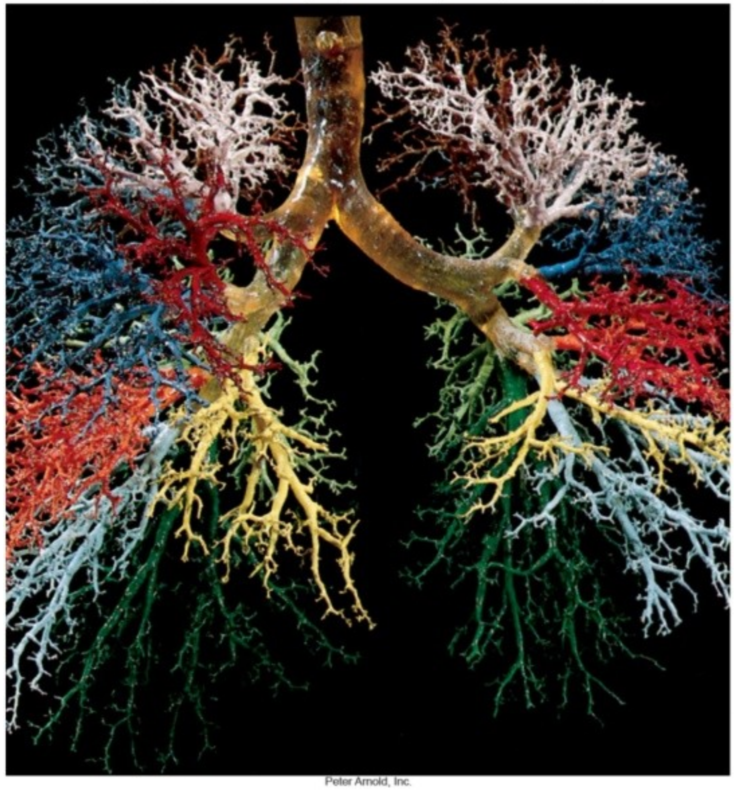
Pancreatic acini





(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 HCO_3^--rich fluid that hydrates, flushes, and alkalinizes the enzymatic secretion of the acini.



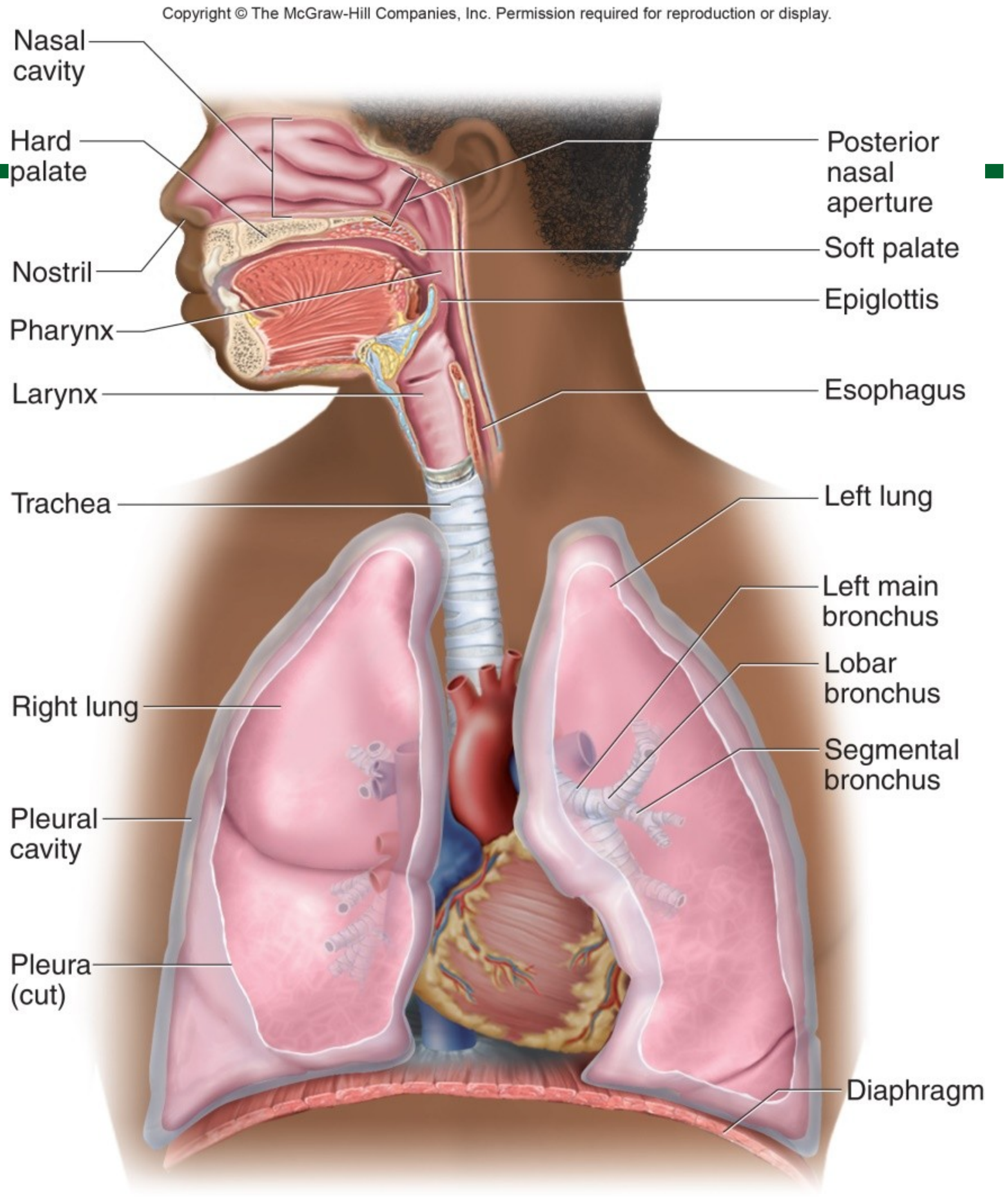
Peter Arnold, Inc.

Respiratory

BI 455 CHAPTER 17

What is respiration?

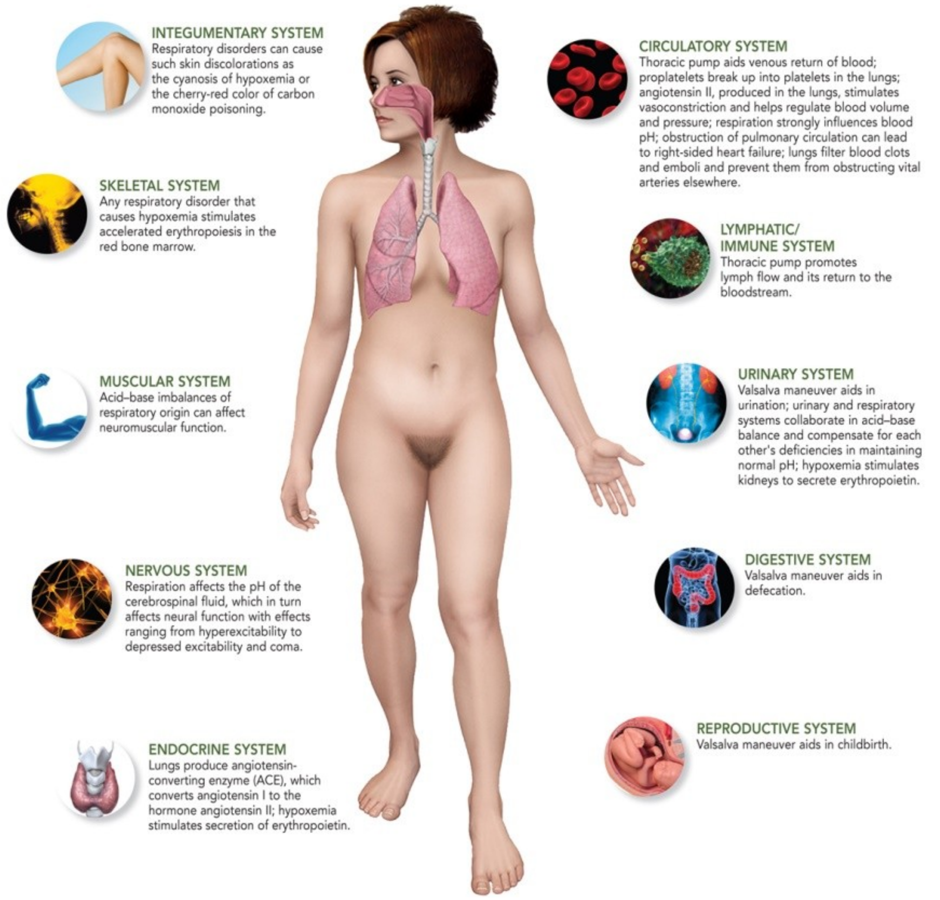
1. Ventilation of the lungs (breathing)
2. The exchange of gases between the air and blood, and between blood and the tissue fluid
3. The use of oxygen in cellular metabolism (ATP production)



http://www.bozemanscience.com/respiratory-system

Functions of the Respiratory System

1. O_2 and CO_2 exchange between blood and air
2. Speech
3. Provides the sense of smell
4. Affects pH of body fluids by eliminating CO_2
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)



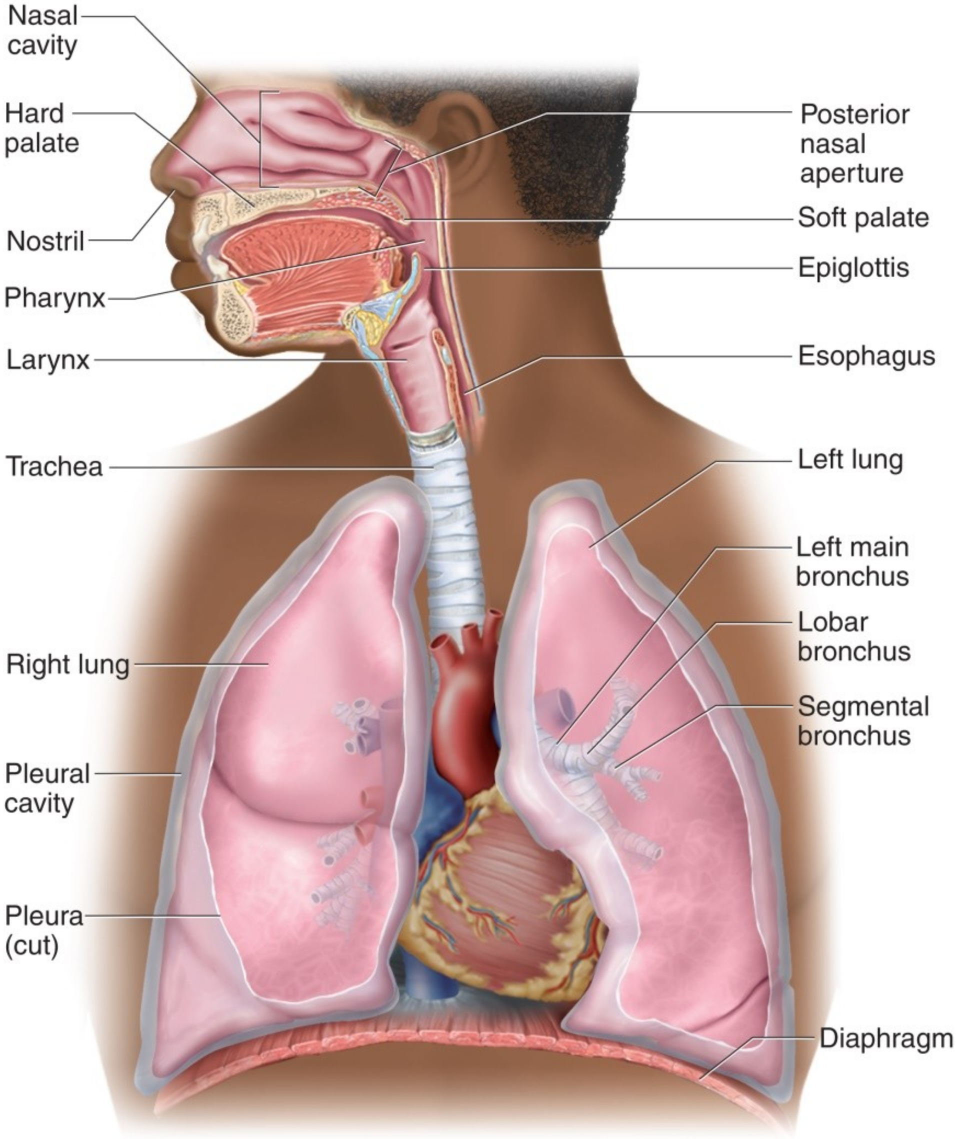
Conducting Division of the Respiratory System

Nose, pharynx, larynx, trachea, bronchi, lungs

- Those passages that serve only for airflow
- No gas exchange
- Nostrils through major bronchioles

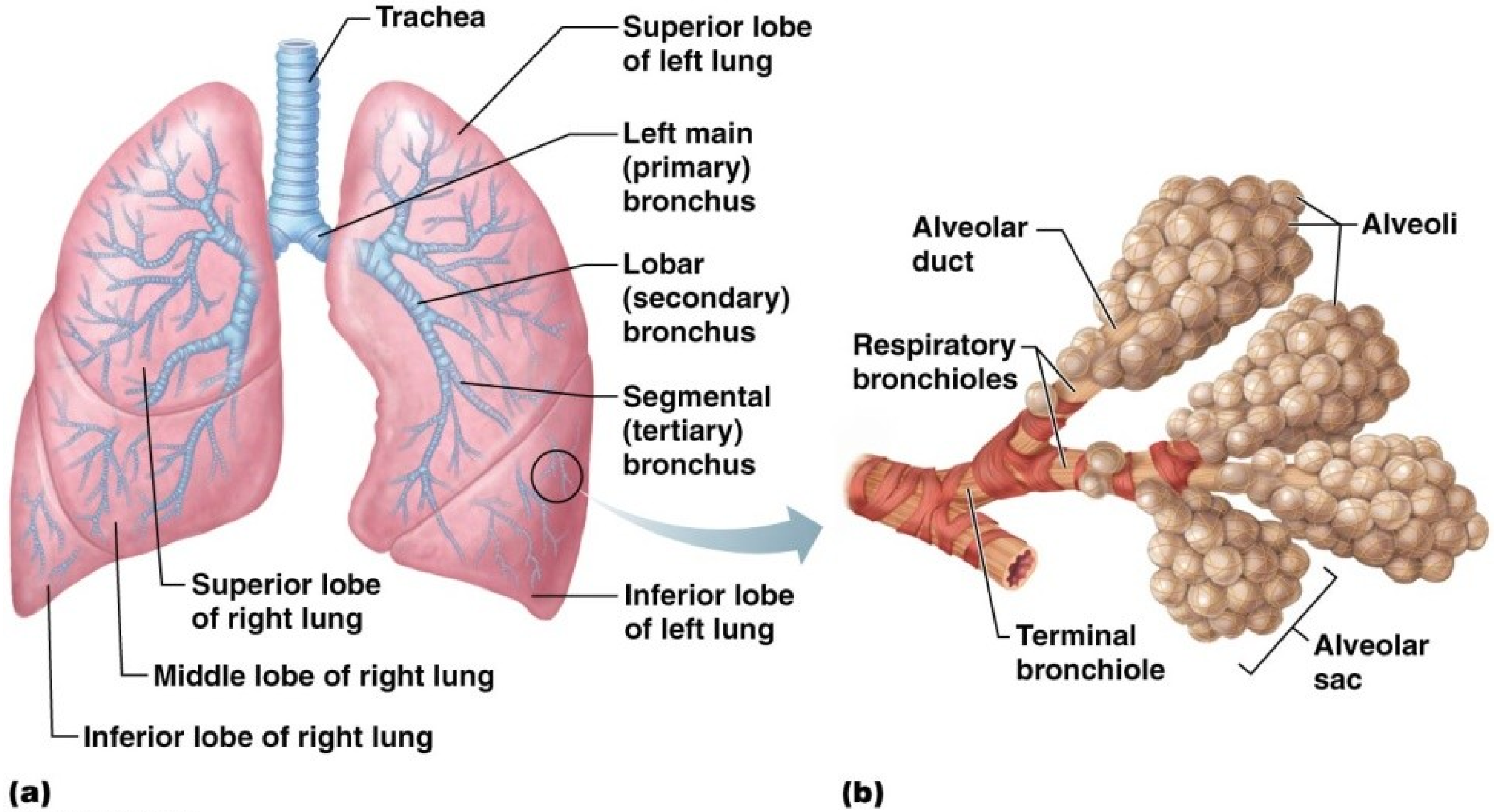
- **Upper respiratory tract**: Nose through larynx
- **Lower respiratory tract**: Trachea through lungs

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

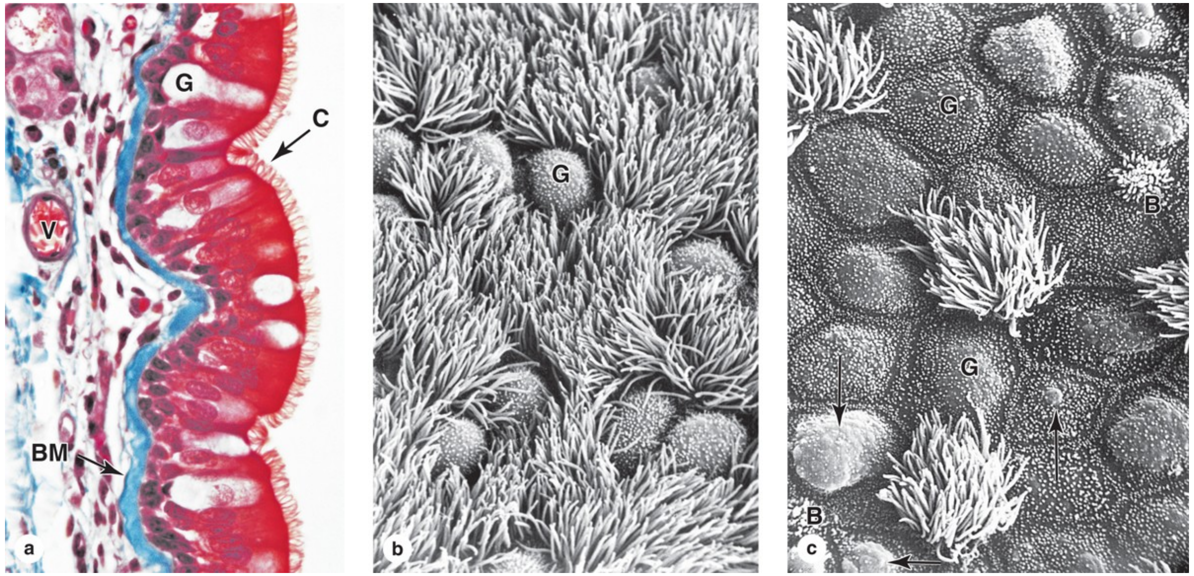


Respiratory Division of the Respiratory System: respiratory bronchioles, alveolar ducts, alveolar sacs, alvaoli

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



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



<u>Respiratory mucosa cell types</u>

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

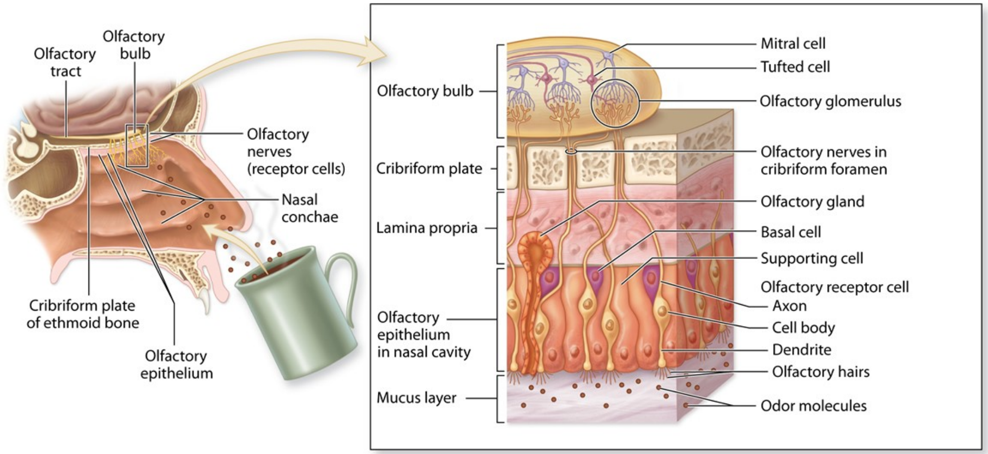
Brush cells (B): a general name for those cells in the respiratory tract that bear short, blunt microvilli

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)

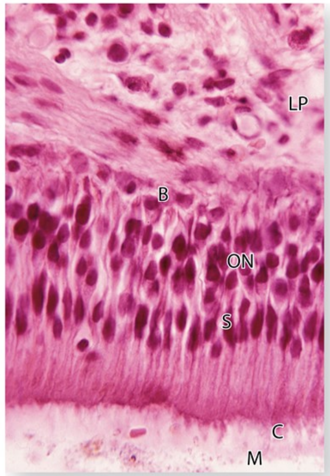
Olfactory Region Sends Axons to the Brain

MEDICAL APPLICATION: The loss or reduction of the ability to smell, anosmia or hyposmia, respectively, can be cause 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.



a

Aging and the loss of smell, taste: https://www.youtube.com/watch?v=A_aevsFwlJA



b

Pseudostratified epithelium

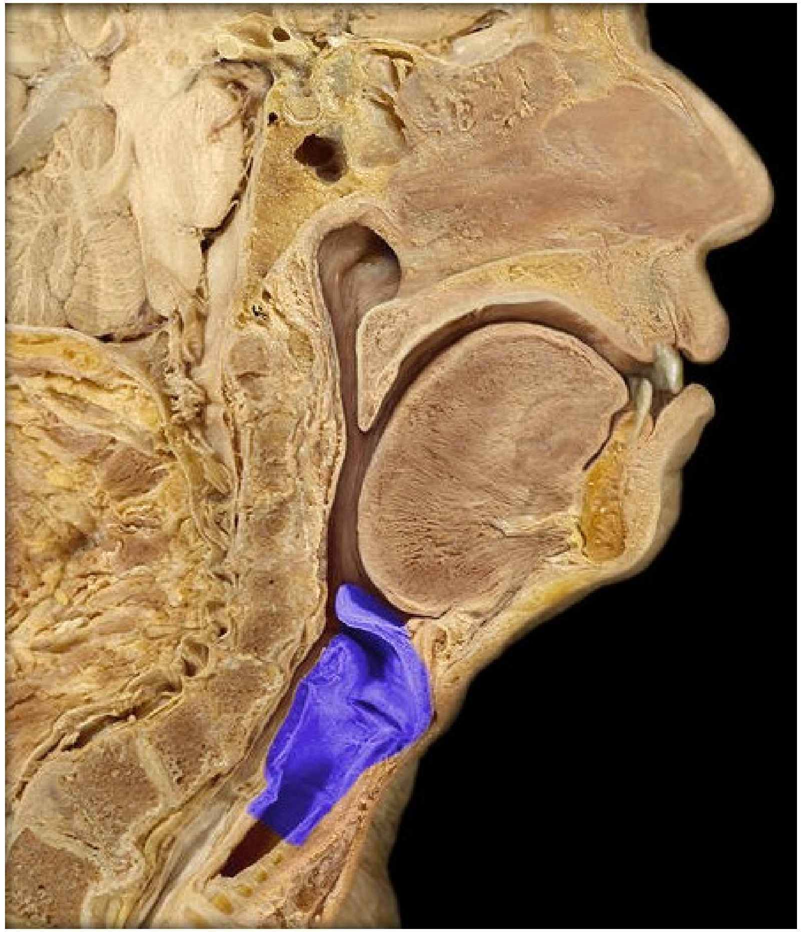
(Only a thin basement membrane separates the olfactory basal cells (**B**) from the underlying lamina propria (**LP**). Nuclei of the bipolar olfactory neurons (**ON**) lie in the middle of the pseudostratified olfactory epithelium, with a zone of supporting cell (**S**) nuclei above it. At the apical 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

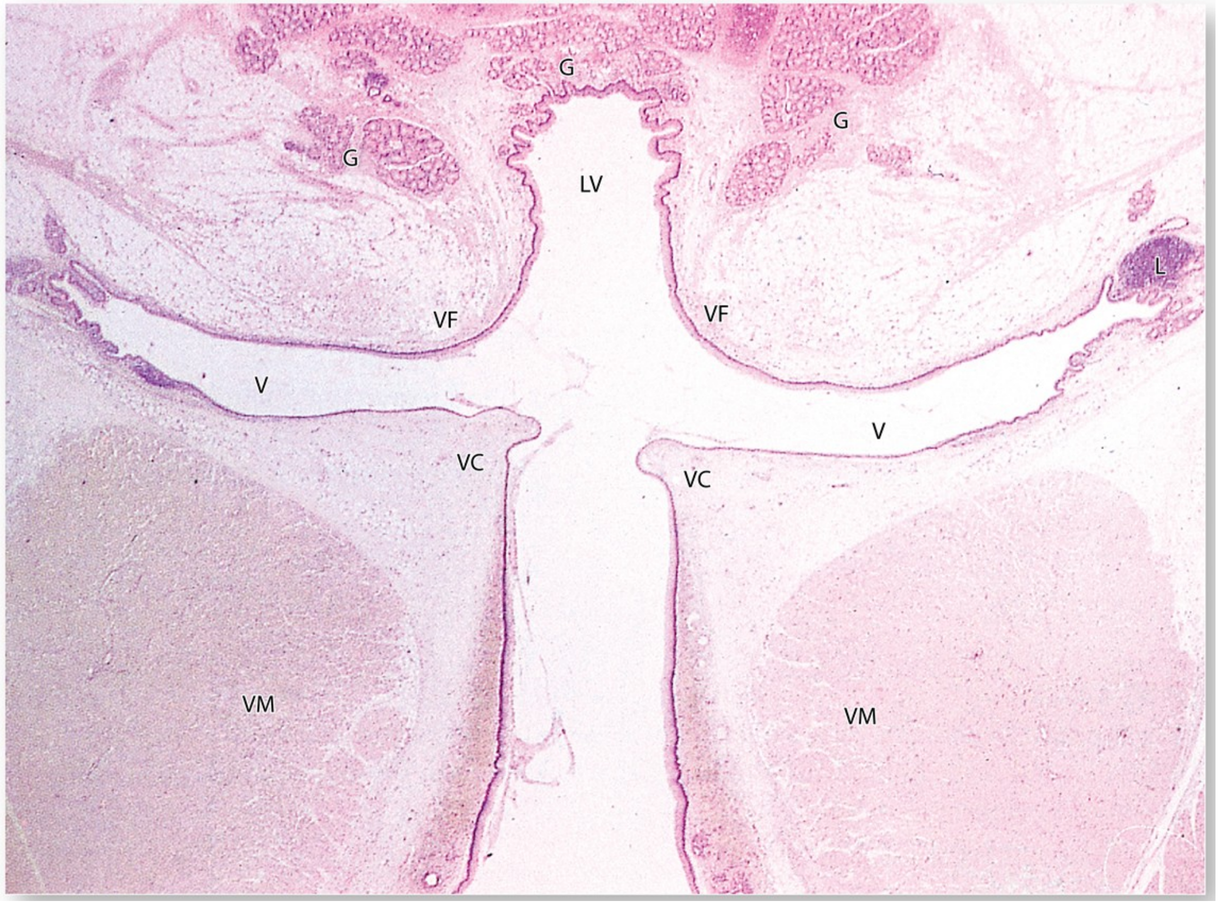


Laryngitis https://www.youtube.com/watch?v=puqe3_HkDZA

❯❯ **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

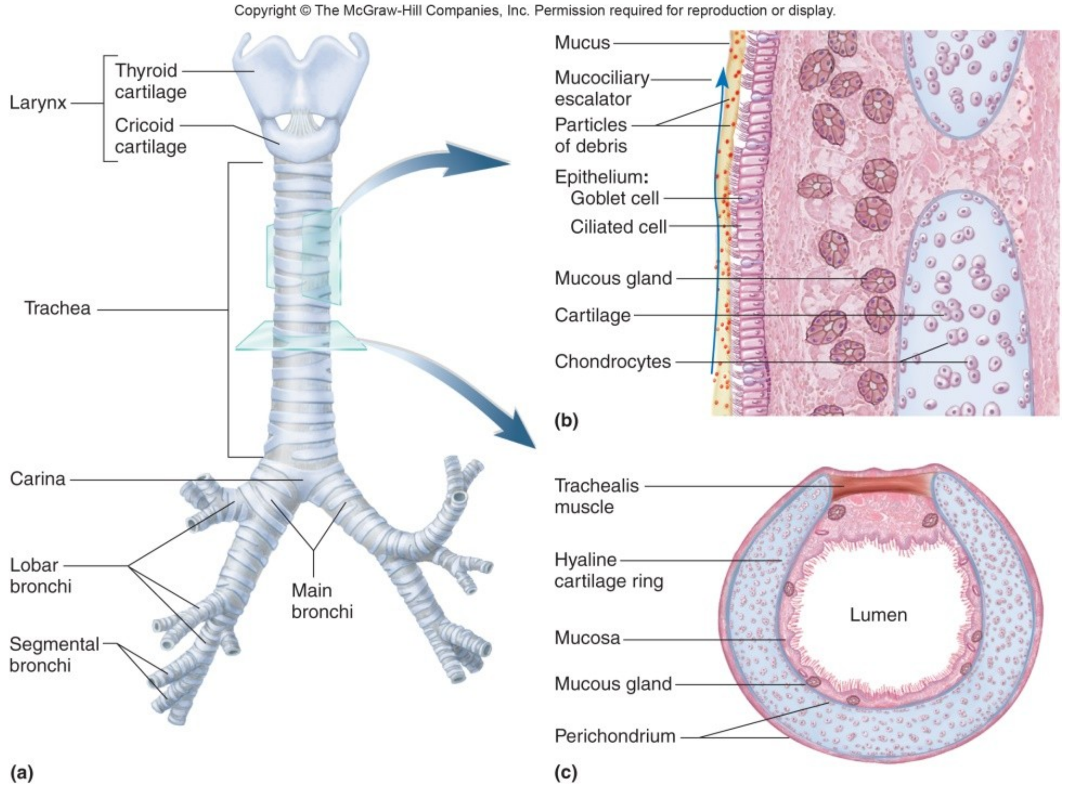
Larynx: short air passage between the pharynx and trachea



- 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

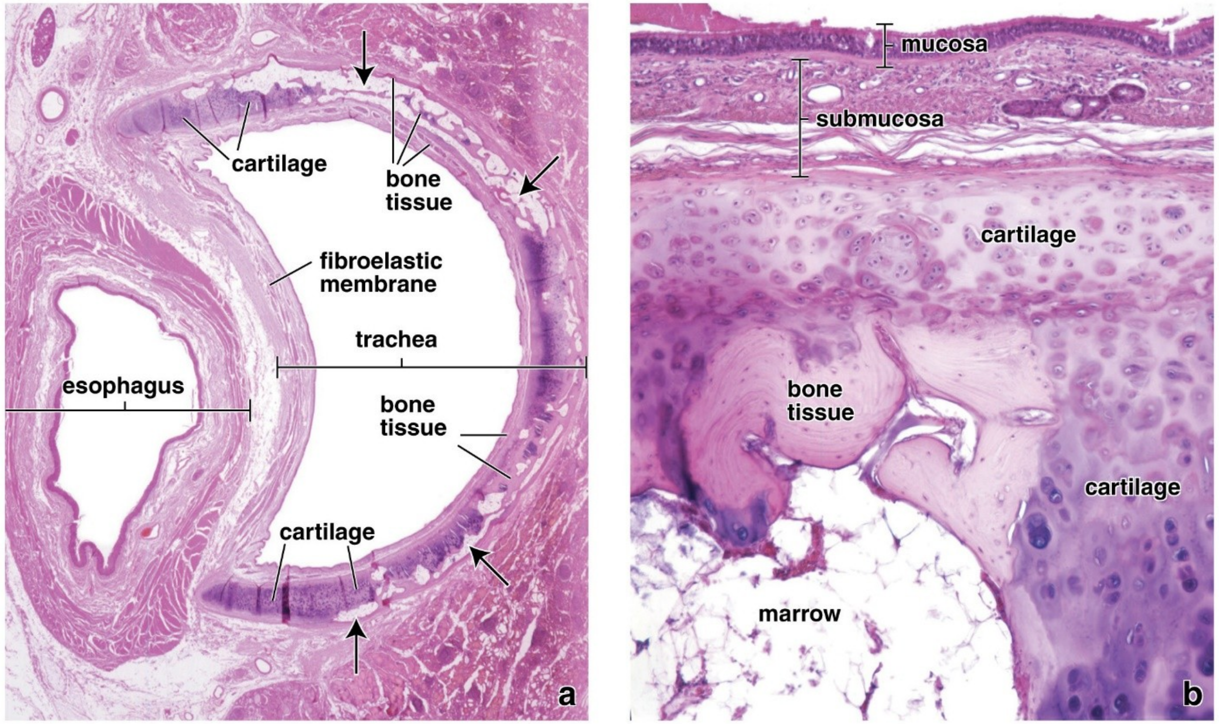
Inner lining : mucous secreting pseudostratified columnar epithelium
Mucociliary escalator: Mucus traps inhaled particles, upward beating cilia drives mucus toward pharynx where it is swallowed
Middle tracheal layer: connective tissue; contains lymphatic nodules, mucous and serous glands, and the tracheal 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

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

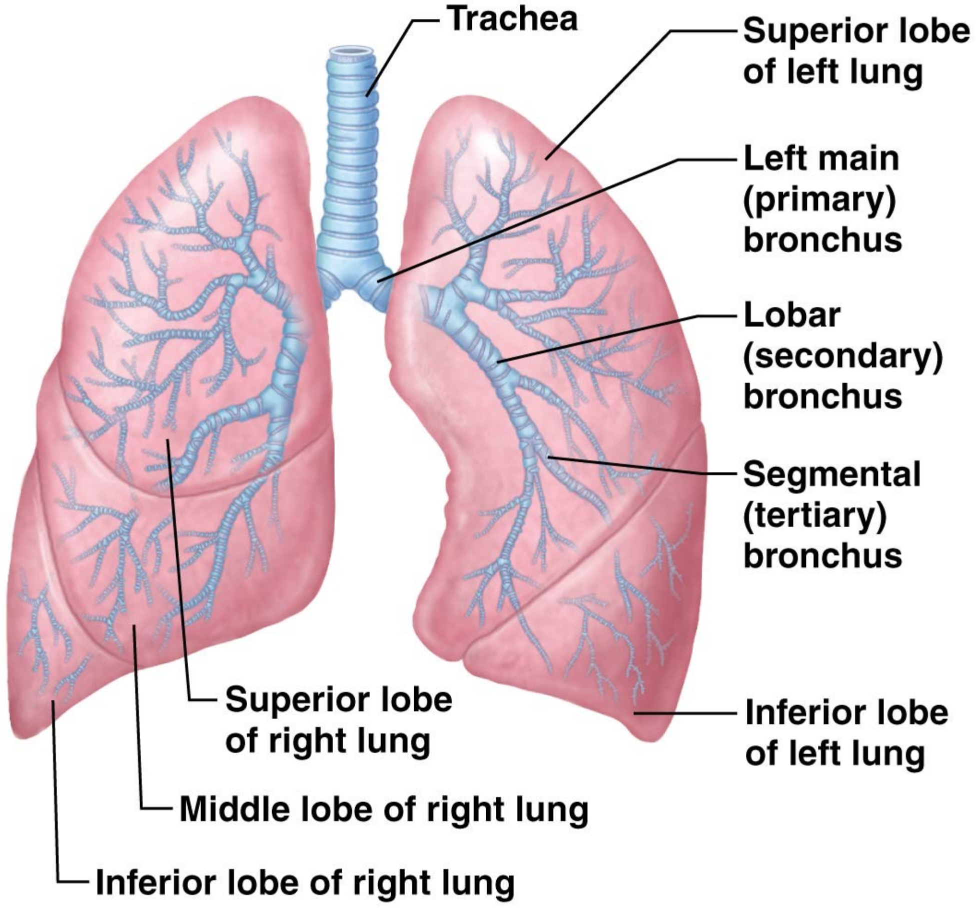
Lungs are crowded by adjacent organs and are asymmetrical

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

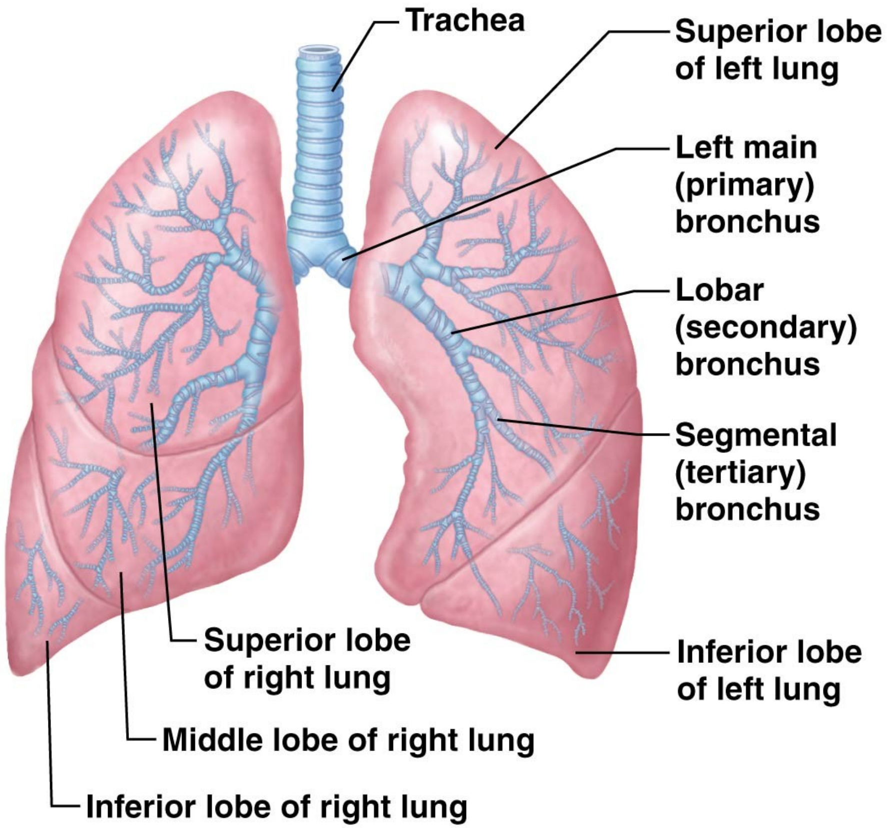


(a)

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



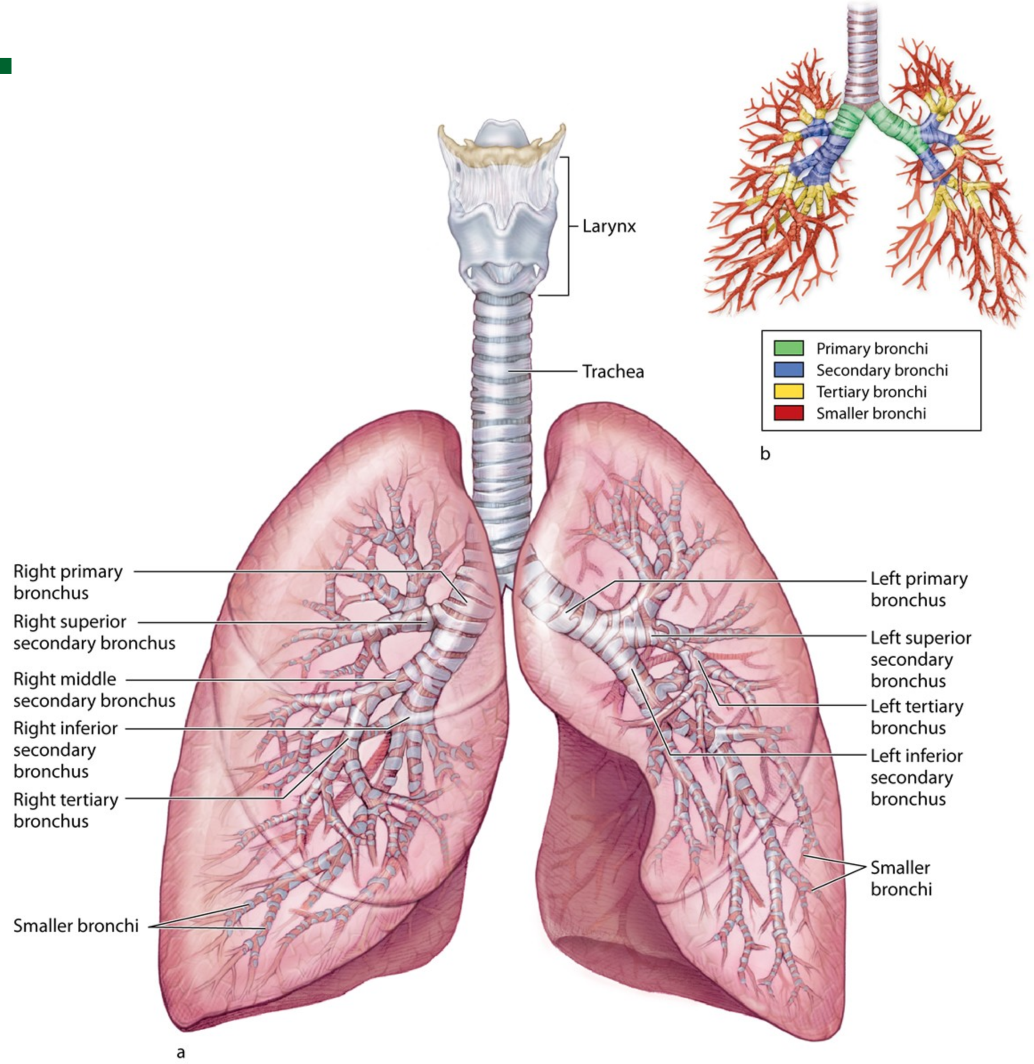
(a)

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

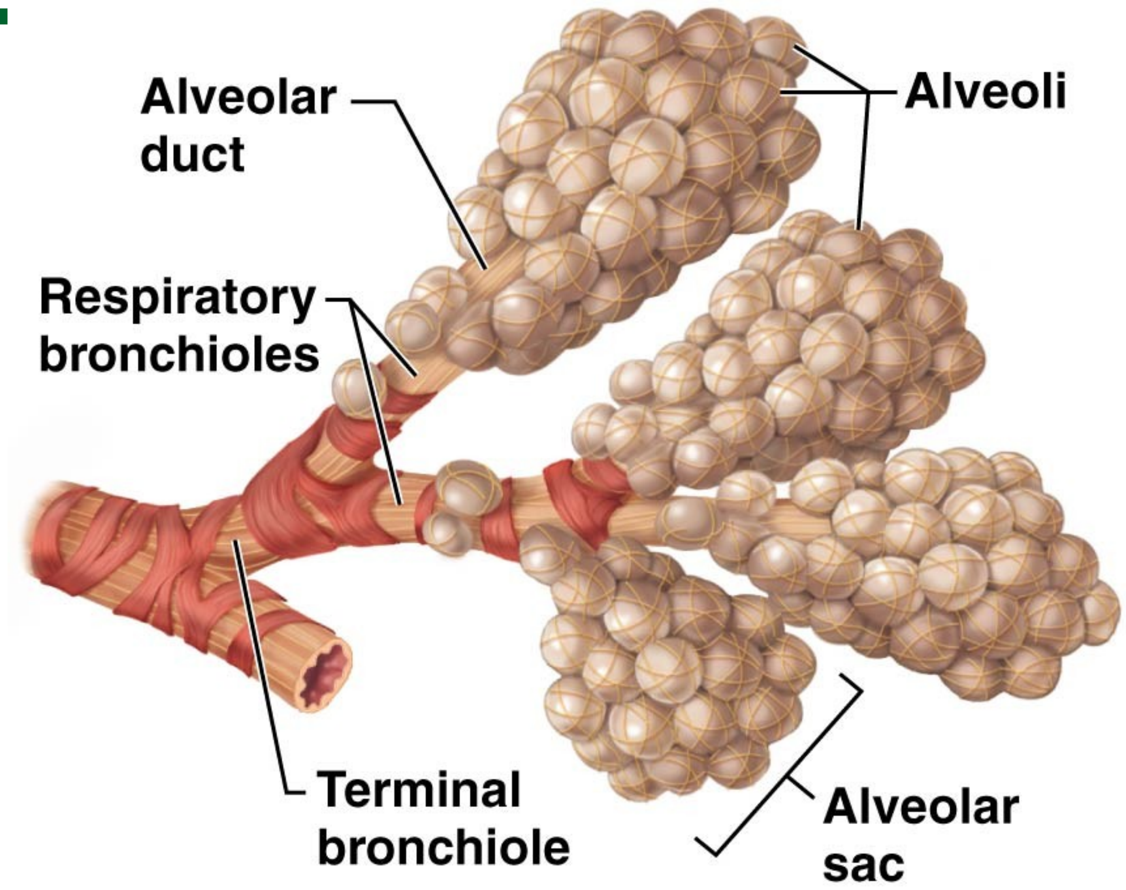
Primary → secondary → tertiary → bronchiole → terminal brochiole → respiratory bronchiole → alveolar duct → alveolar sac → alveoli



Respiratory bronchioles

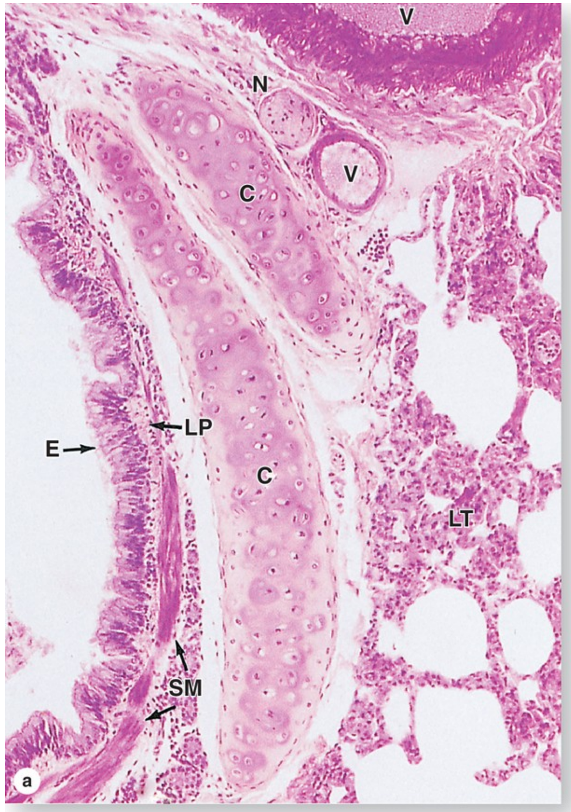
- Have **alveoli** budding from their walls
- Considered the beginning of the **respiratory division** since alveoli participate in gas exchange
- Divide into 2 to 10 **alveolar ducts**
- End in **alveolar sacs**: grapelike clusters of alveoli arrayed around a central space called the **atrium**

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



(b)

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.

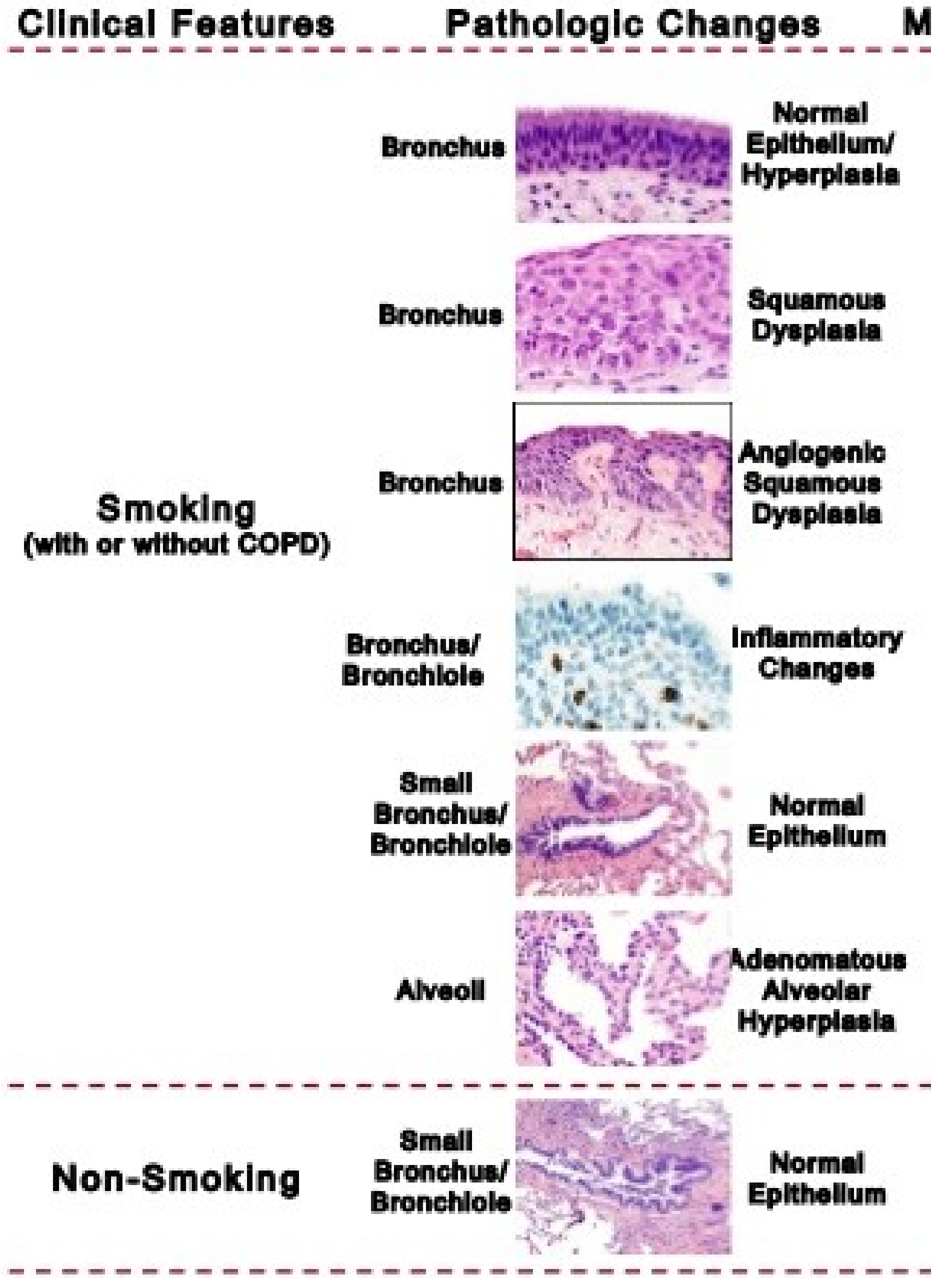
The lamina propria has both smooth muscle (**SM**) and small serous glands (**G**) near cartilage (**C**).

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.



Dysplasia: The Progression of Cancer: https://www.youtube.com/watch?v=Gh_1PfLKqg4

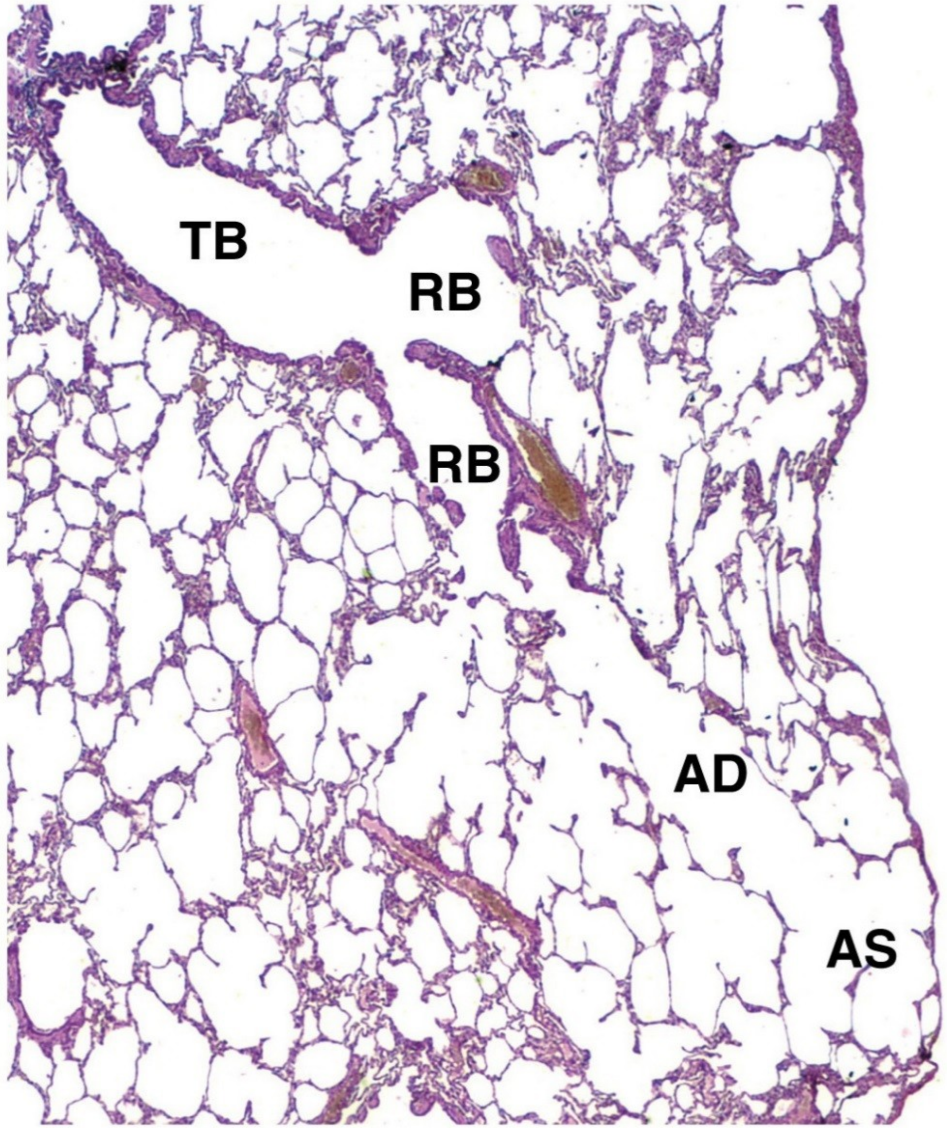
Terminal bronchiole tissue lacks cartilage, has ciliated cuboidal epithelium and well developed layer of smooth muscle

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)**

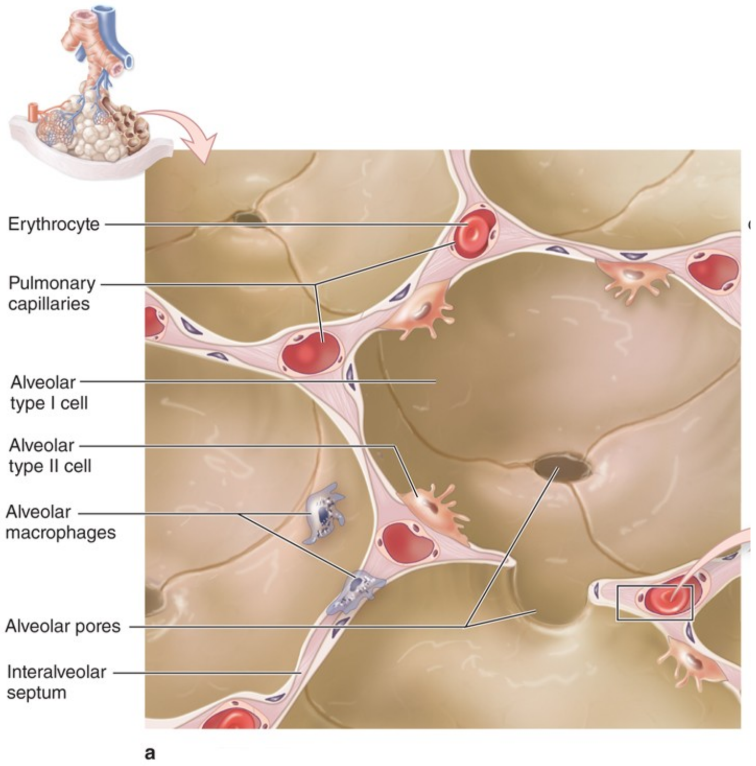
Alveolar Ducts (AV) & Alevolar Sacs (AS)

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



Cells of the alveolus

- **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



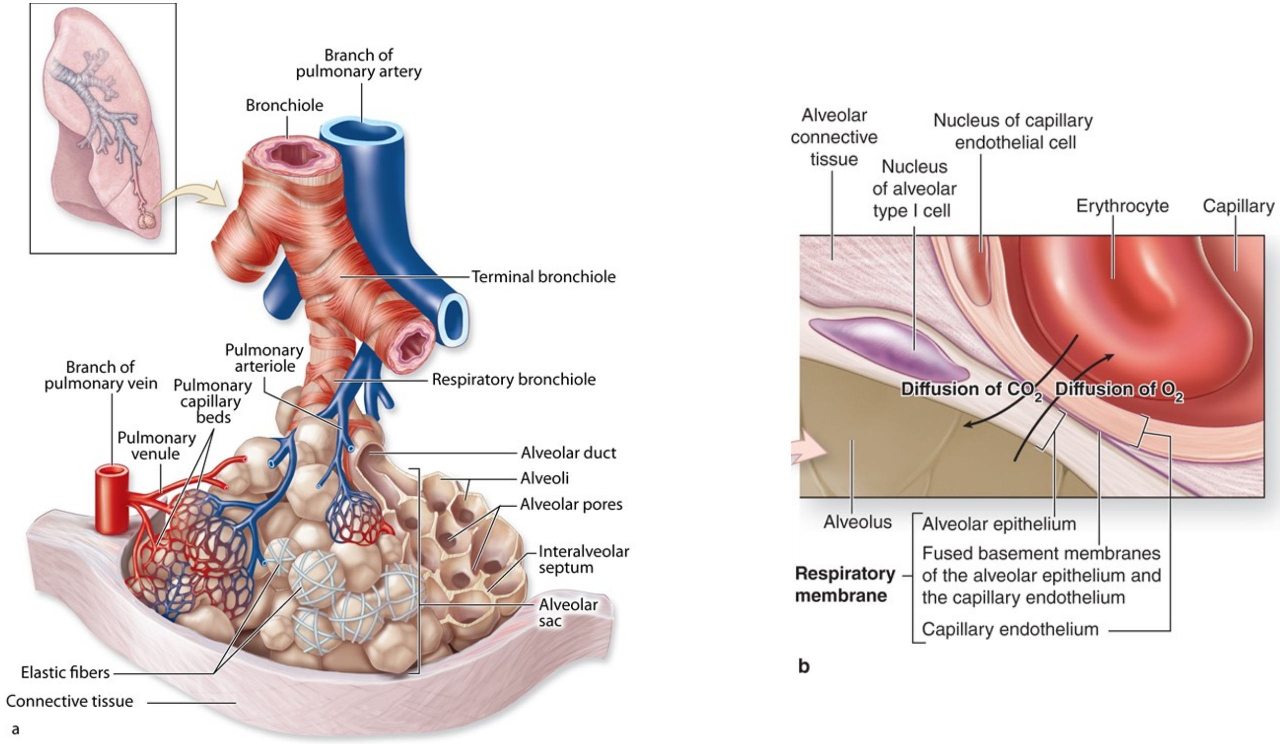
MEDICAL APPLICATION: Infant respiratory distress syndrome, the leading cause of death in premature babies, is due to incomplete differentiation of type II alveolar cells and a resulting deficit of surfactant and difficulty in expanding the alveoli in breathing.

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

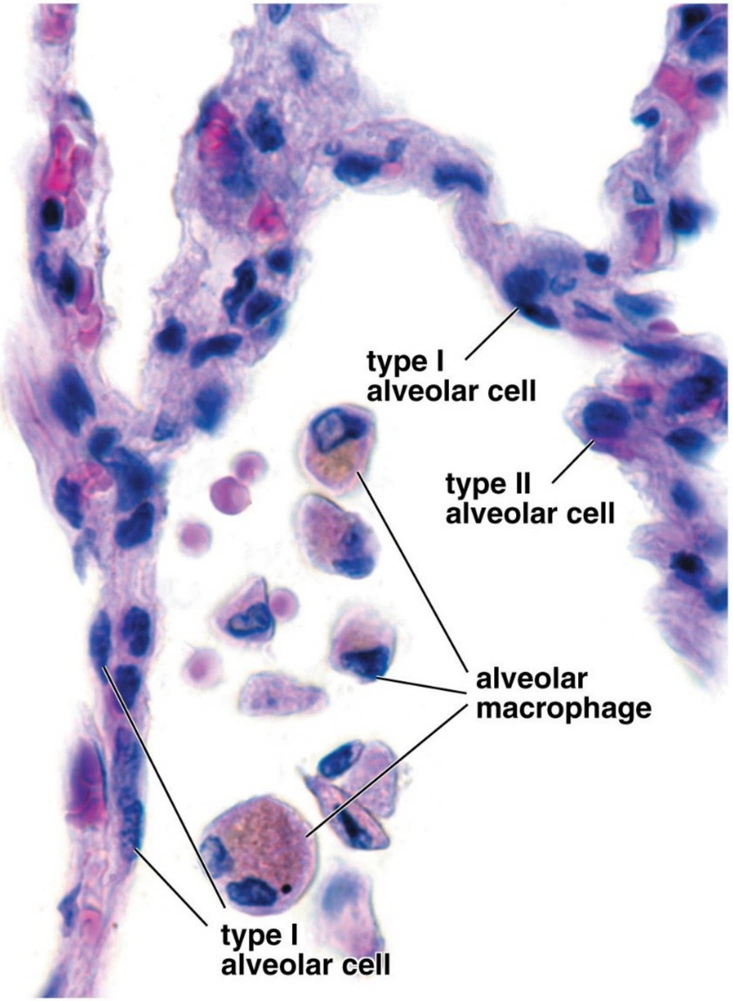
Each alveolus is surrounded by a basket of blood capillaries supplied by the pulmonary artery

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



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

BI 455 CHAPTER 18

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

<u>Functions</u>

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 Ca2+ absorption

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

Thermoregulation

Nonverbal communication

Intro to the integument:
http://www.youtube.com/watch?v=BVIIgHyNRdI&feature=related
(watch till 5:20)

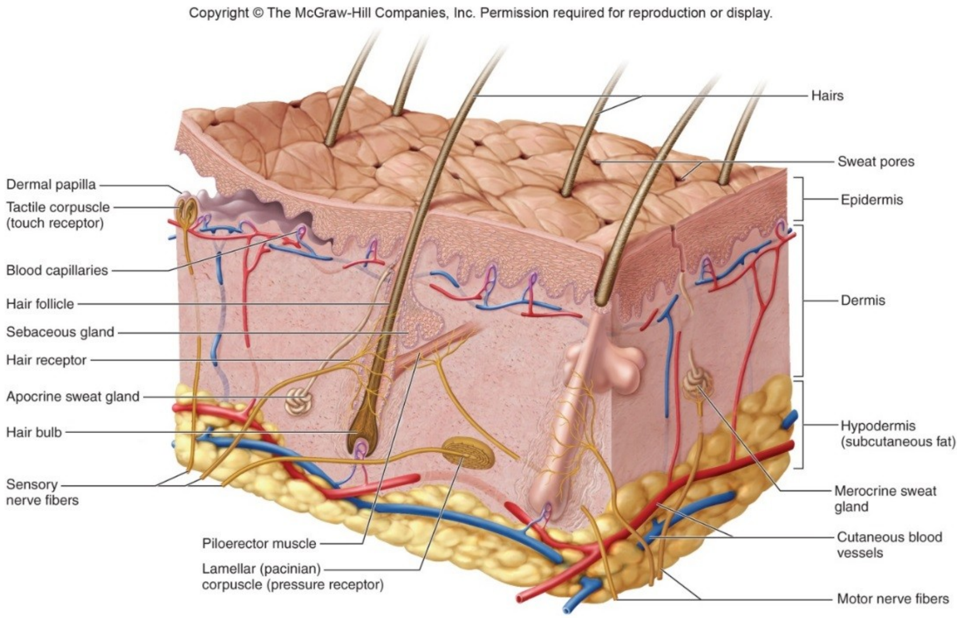
The Skin and Subcutaneous Tissue

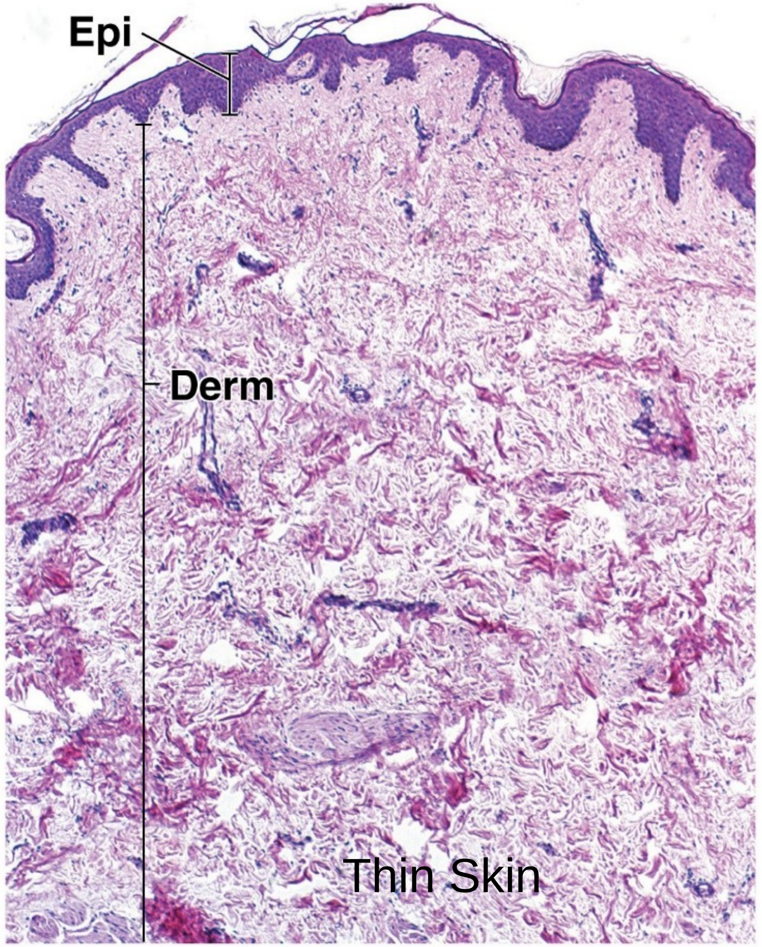
Skin: 2 layered membrane covering external surface of body

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

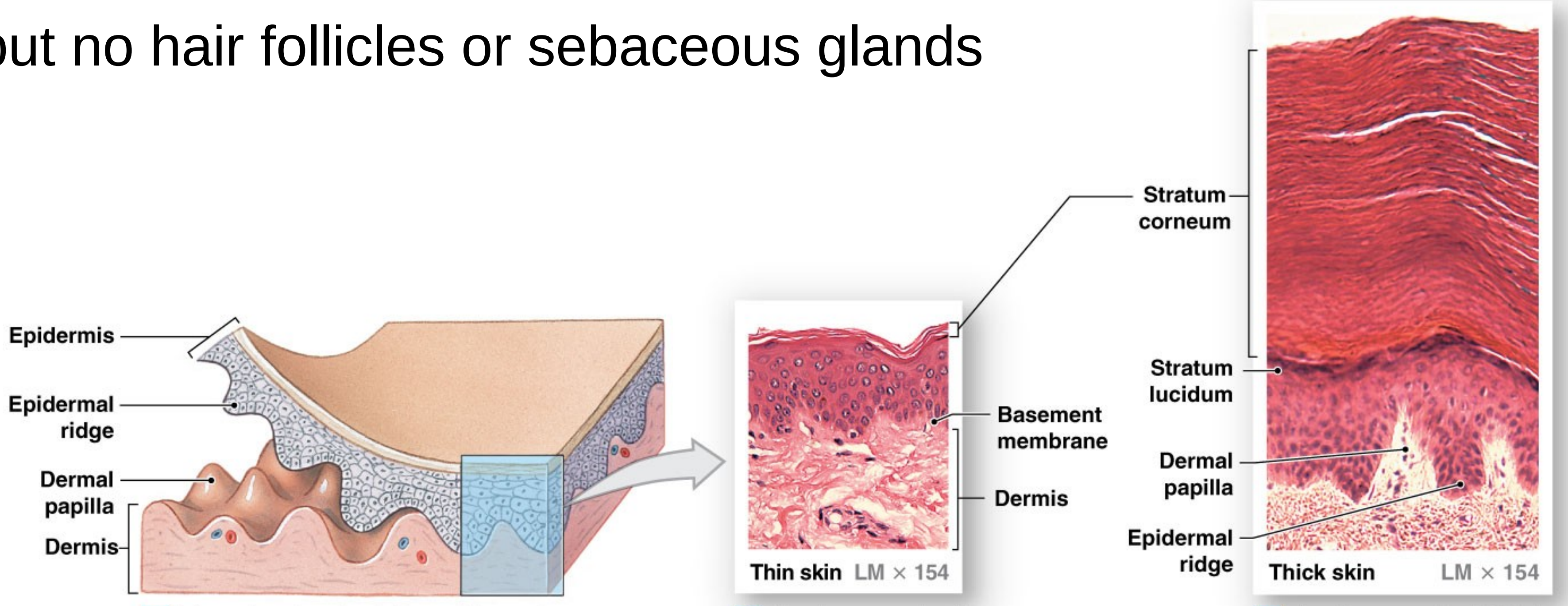
15% of body weight, ranges from 0.5mm to 6 mm, due mostly to variations in dermis

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.

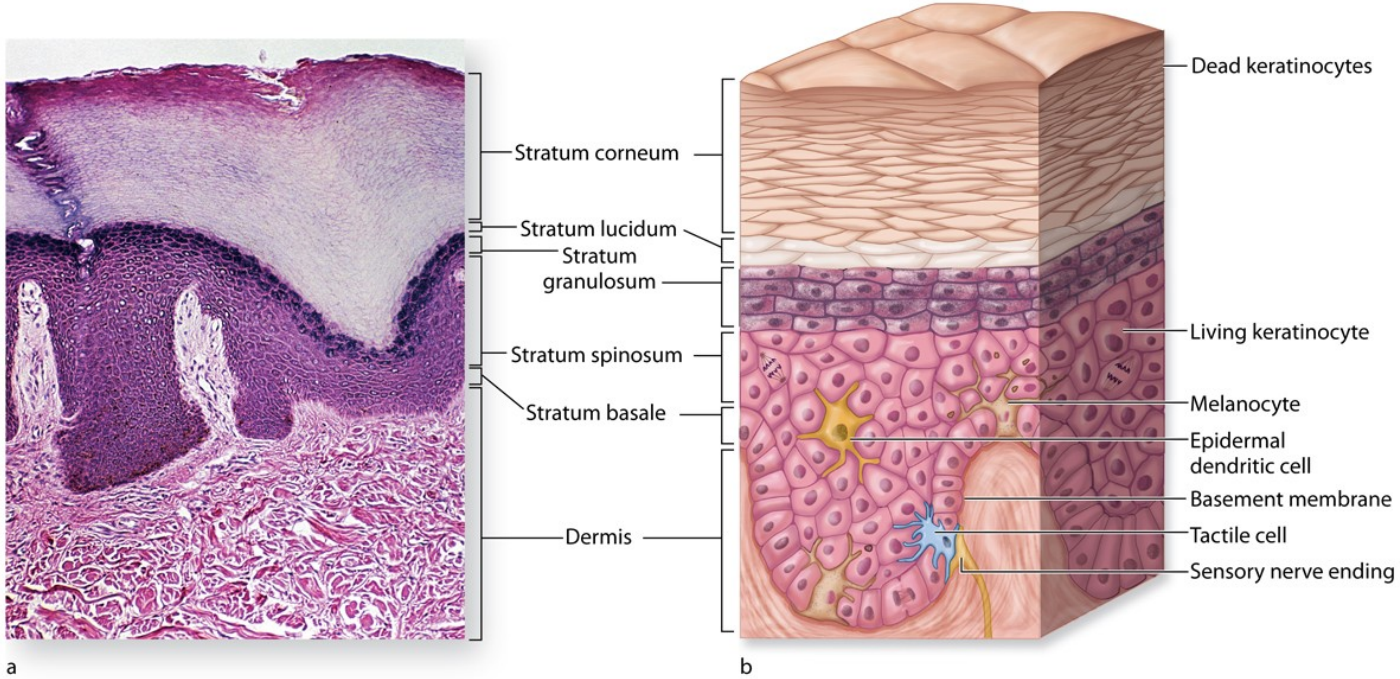
b A micrograph of thin skin, which covers most of the exposed body surface.

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

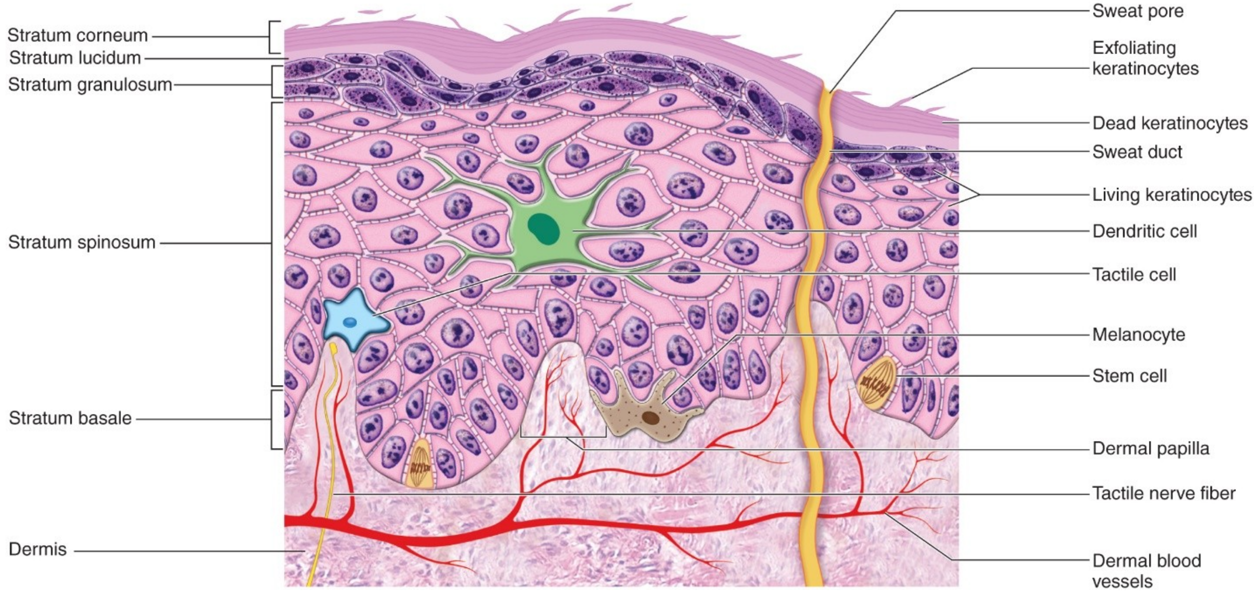
Keratinized stratified squamous epithelium is mostly **keratinocytes** packed with keratin

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

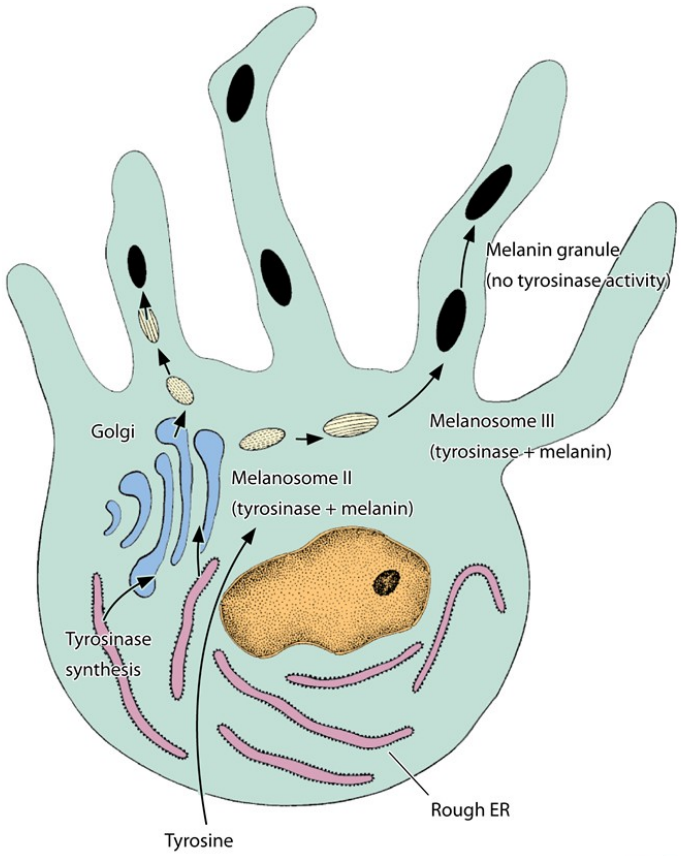


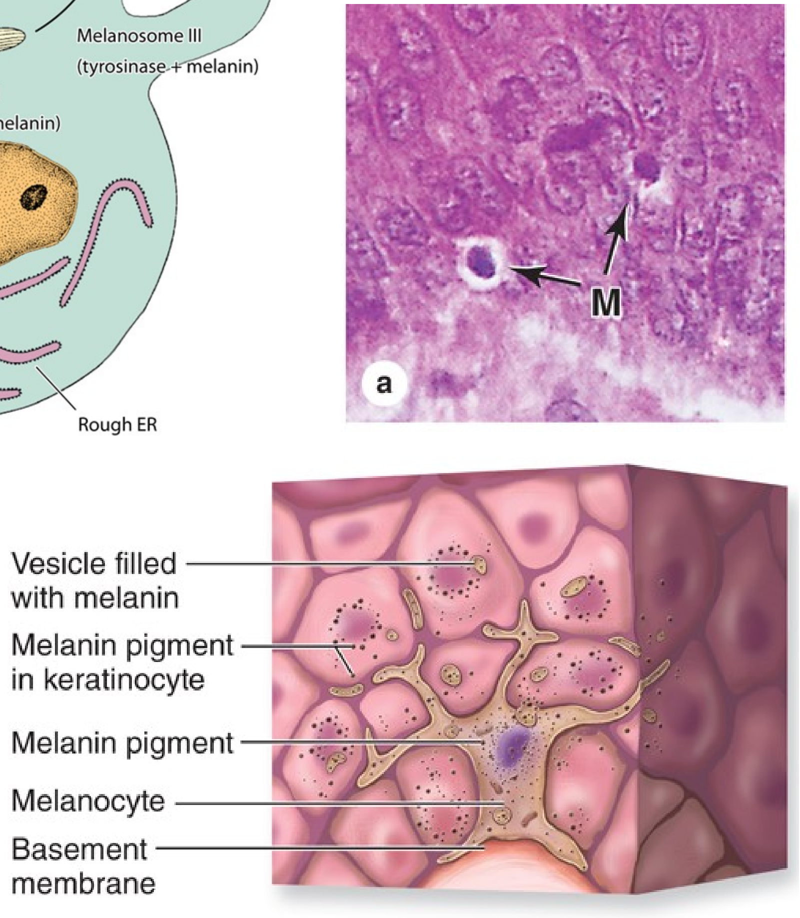
❯❯ MEDICAL APPLICATION

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





b

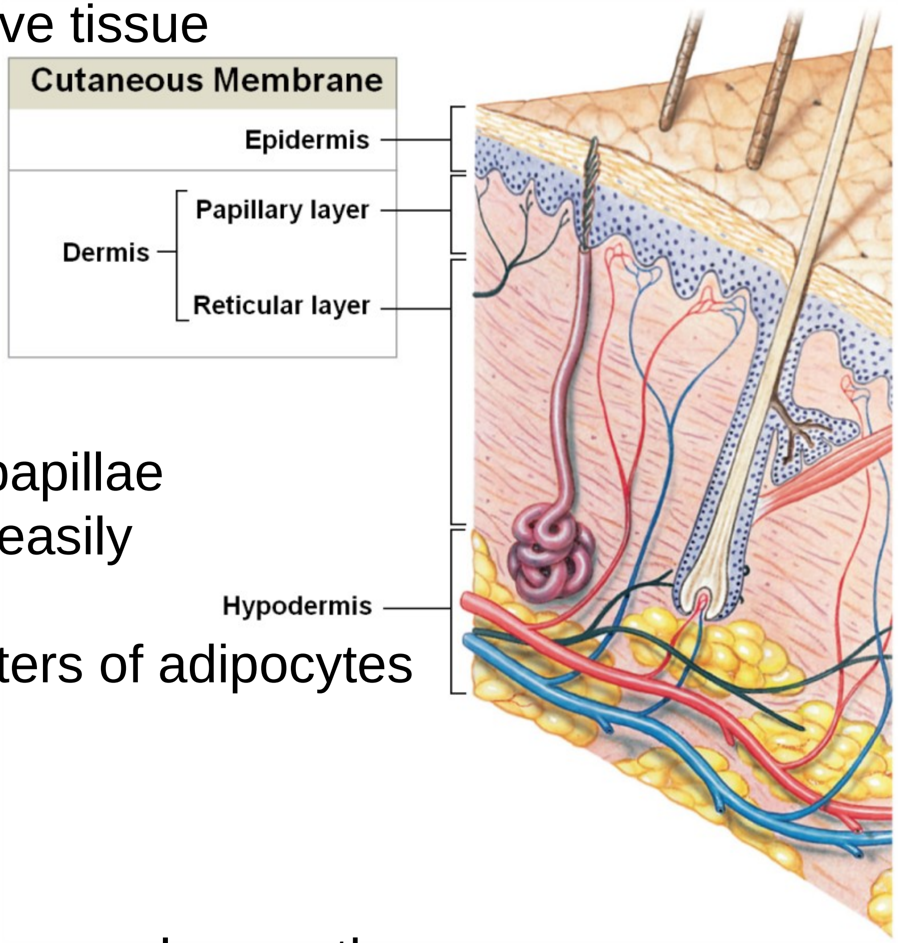
Melanocytes synthesize **melanin granules** and transfer them into neighboring **keratinocytes** of the basal and spinous layers. Typically melanocytes are pale-staining cells on the basement membrane, with lower total melanin content than the keratinocytes

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



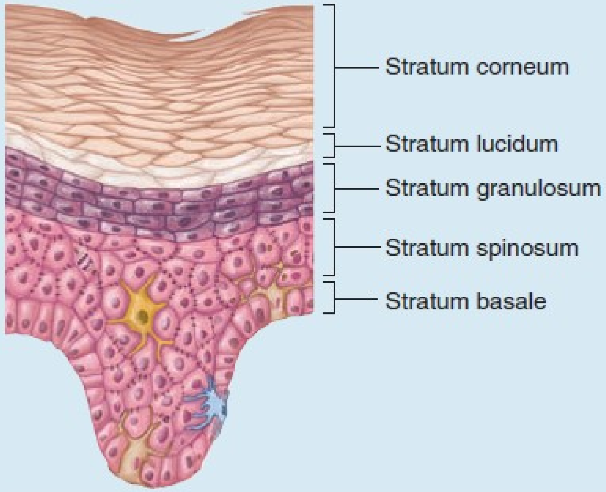
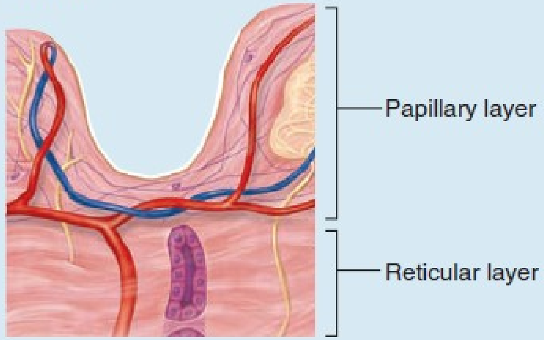
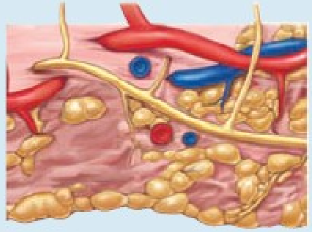
Zones of Dermis

- **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

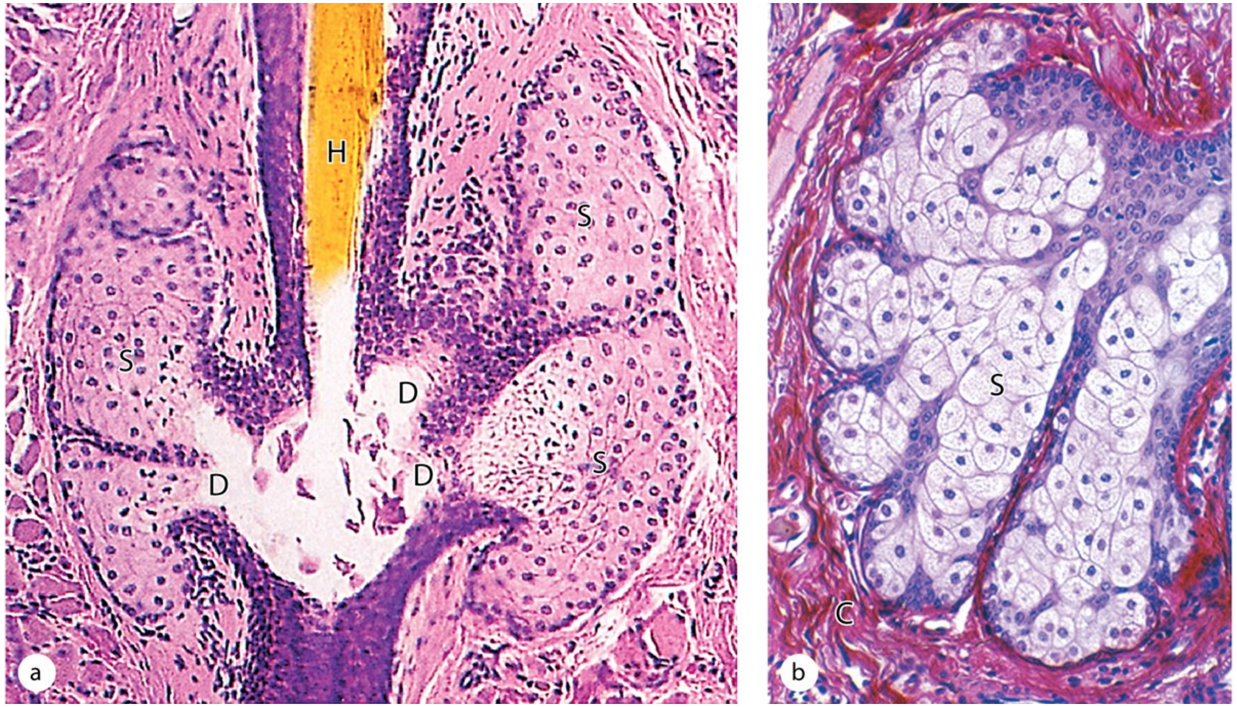
TABLE 18–1 Skin layers and the subcutaneous layer.

Layer	Specific Layer	Description
Epidermis 	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	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



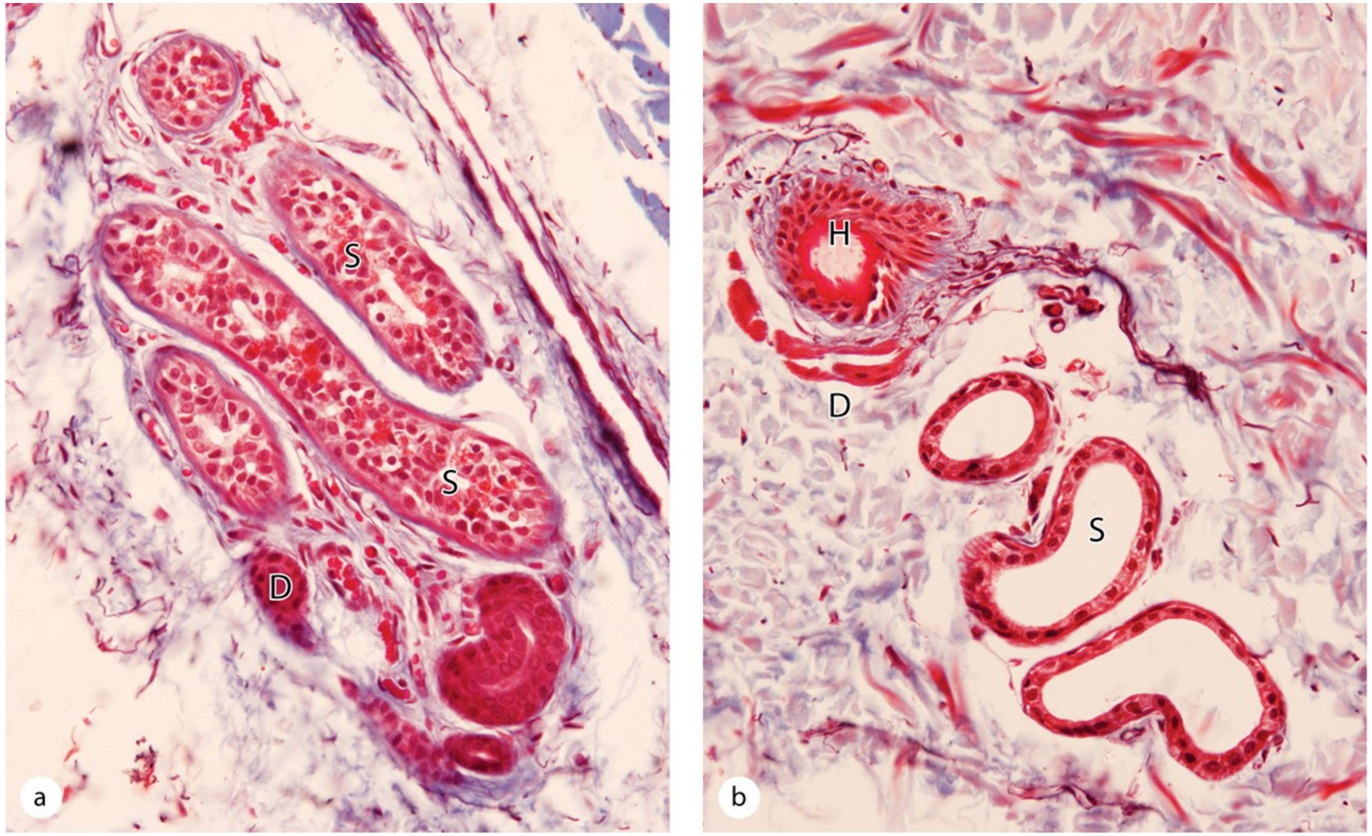
Holocrine secretion

(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.



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

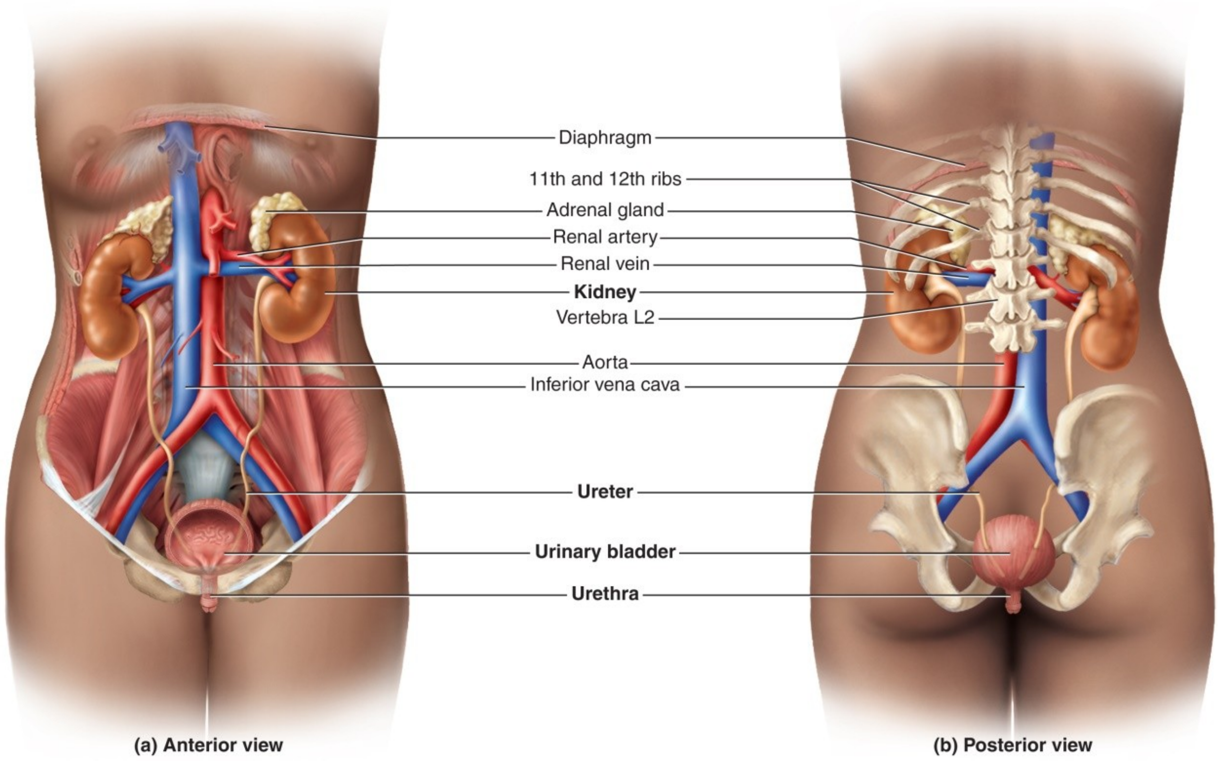
The sweat of infants with cystic fibrosis (CF) is often salty and is commonly taken as indicative of this genetic disease. CF patients have defects in a transmembrane conductance regulator (CFTR) of epithelial cells that lead to disruptive accumulations of thick mucus in the respiratory and digestive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

Urinary

BI 455 CHAPTER 19

Urinary system rids the body of waste products

- The urinary system is closely associated with the reproductive system
- Shared embryonic development and adult anatomical relationship
- Collectively called the urogenital (UG) system
- **Urinary system** consists of six organs: two kidneys, two ureters, urinary bladder, and urethra



Chapter 19 Key Points

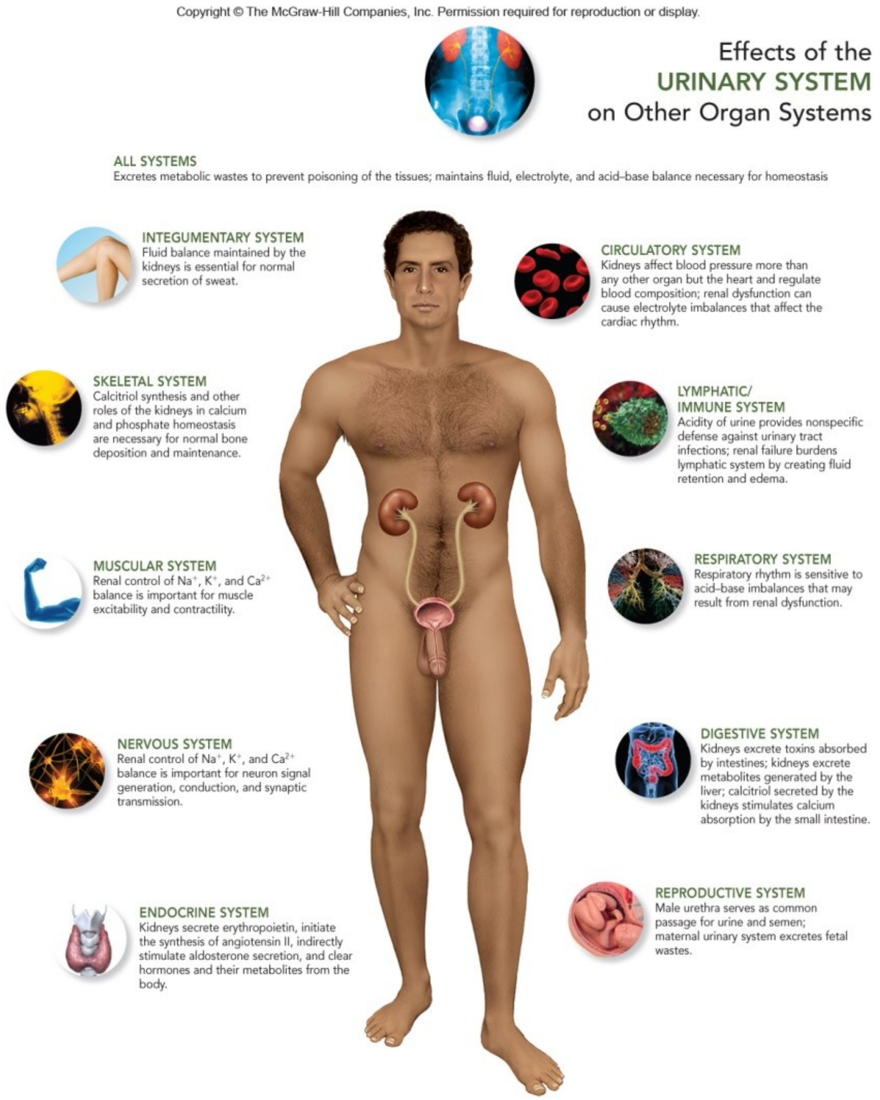
1. Urinary system function
2. Urinary anatomy
3. Urine formation
    1. Glomerular filtration
    2. Tubular reabsorption
    3. Water conservation
4. Urine function and renal tests
5. Urine storage and elimination

Bozeman Science: http://www.bozemanscience.com/osmoregulation

Crash Course: https://www.khanacademy.org/partner-content/crash-course1/crash-course-biology/v/crash-course-biology-128

Excretion: separation of wastes from body fluids and the elimination of them

Respiratory system: CO_2, small amounts of other gases, and water
Integumentary system: Water, inorganic salts, lactic acid, urea in sweat
Digestive system: Water, salts, CO_2, lipids, bile pigments, cholesterol, other metabolic waste, and food residue
Urinary system: Many metabolic wastes, toxins, drugs, hormones, salts, H^+, and water



Nitrogenous Wastes

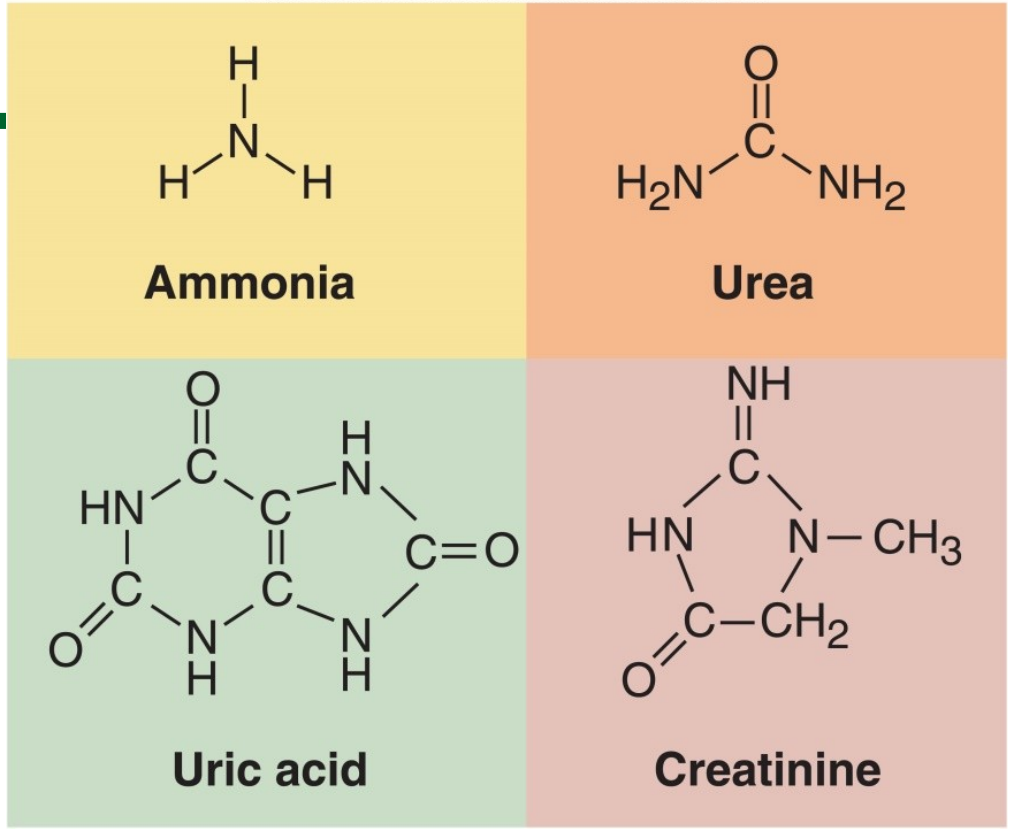
Urea: Proteins→ amino acids → NH_2 removed → forms ammonia, liver converts to urea

Uric acid: Product of nucleic acid catabolism

Creatinine: Product of creatine phosphate catabolism

Blood urea nitrogen (BUN): level of nitrogenous waste in the blood

- Normal BUN: 10 to 20 mg/dL
- **Azotemia**: elevated BUN, indicates renal insufficiency
- **Uremia**: syndrome of diarrhea, vomiting, dyspnea, and cardiac arrhythmia stemming from the toxicity of nitrogenous waste
- Treatment: hemodialysis or organ transplant

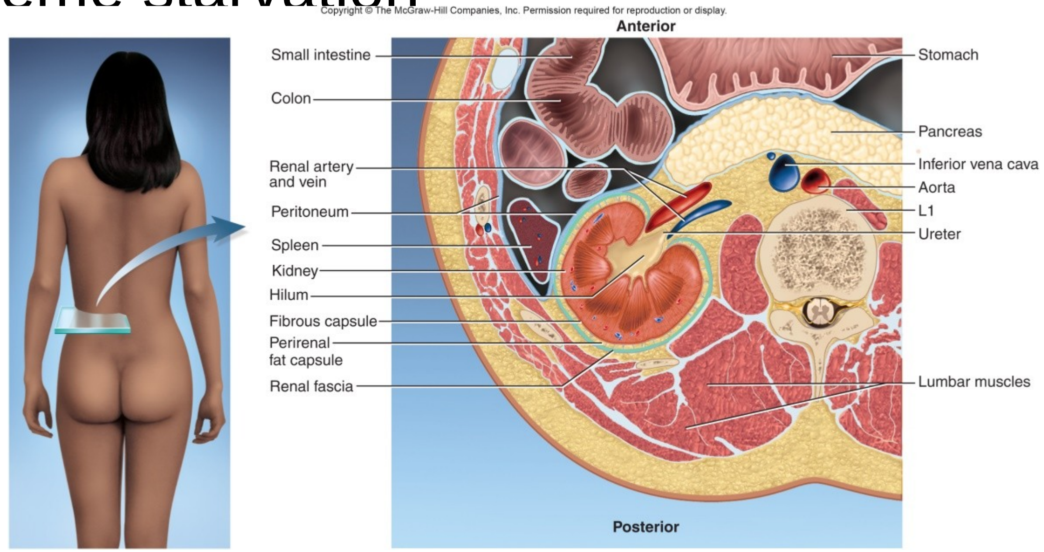


Waste: useless or present in excess of the body's needs

Metabolic waste: produced by the body

Functions of the Kidneys

1. Filters blood plasma
2. Regulates **blood volume** and **body fluid osmolarity** via elimination of water and solutes
3. Secretes **renin**, controlling blood pressure and electrolyte balance
4. Secretes **erythropoietin**, stimulating RBC production
5. Contributes to **PCO_2** and **acid–base balance** of body fluids
6. Final step in synthesizing hormone, **calcitriol** (Vitamin D)
7. Gluconeogenesis in extreme starvation



Gross Anatomy of the kidney

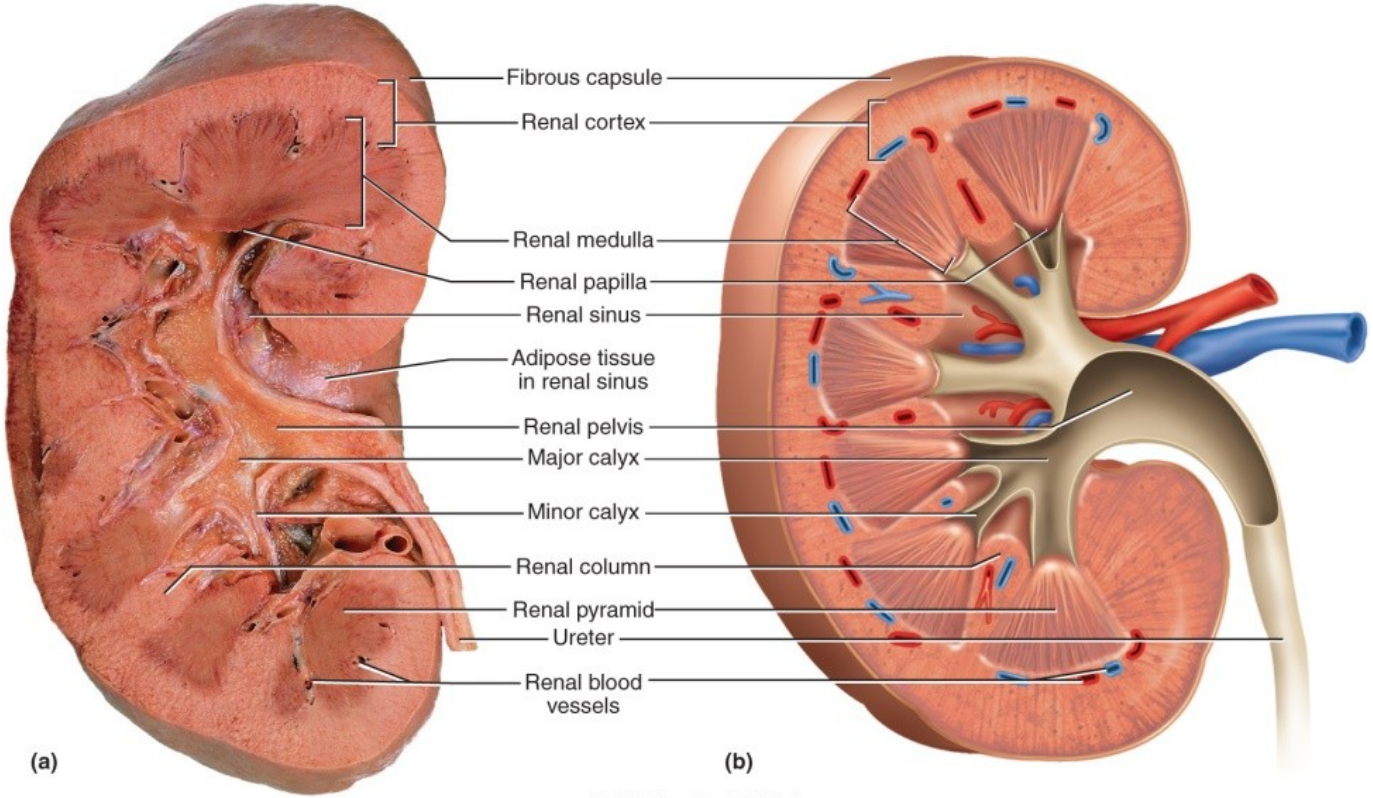
Renal sinus: blood lymphatic vessels, nerves, and urine-collecting structures

Renal parenchyma: glandular tissue that forms urine, Encircles the renal sinus

Two zones of renal parenchyma

- **Outer renal cortex**
- **Inner renal medulla**: **Renal columns** & Renal pyramids:

Lobe of the kidney: one pyramid and its overlying cortex



a: Ralph Hutchings/Visuals Unlimited

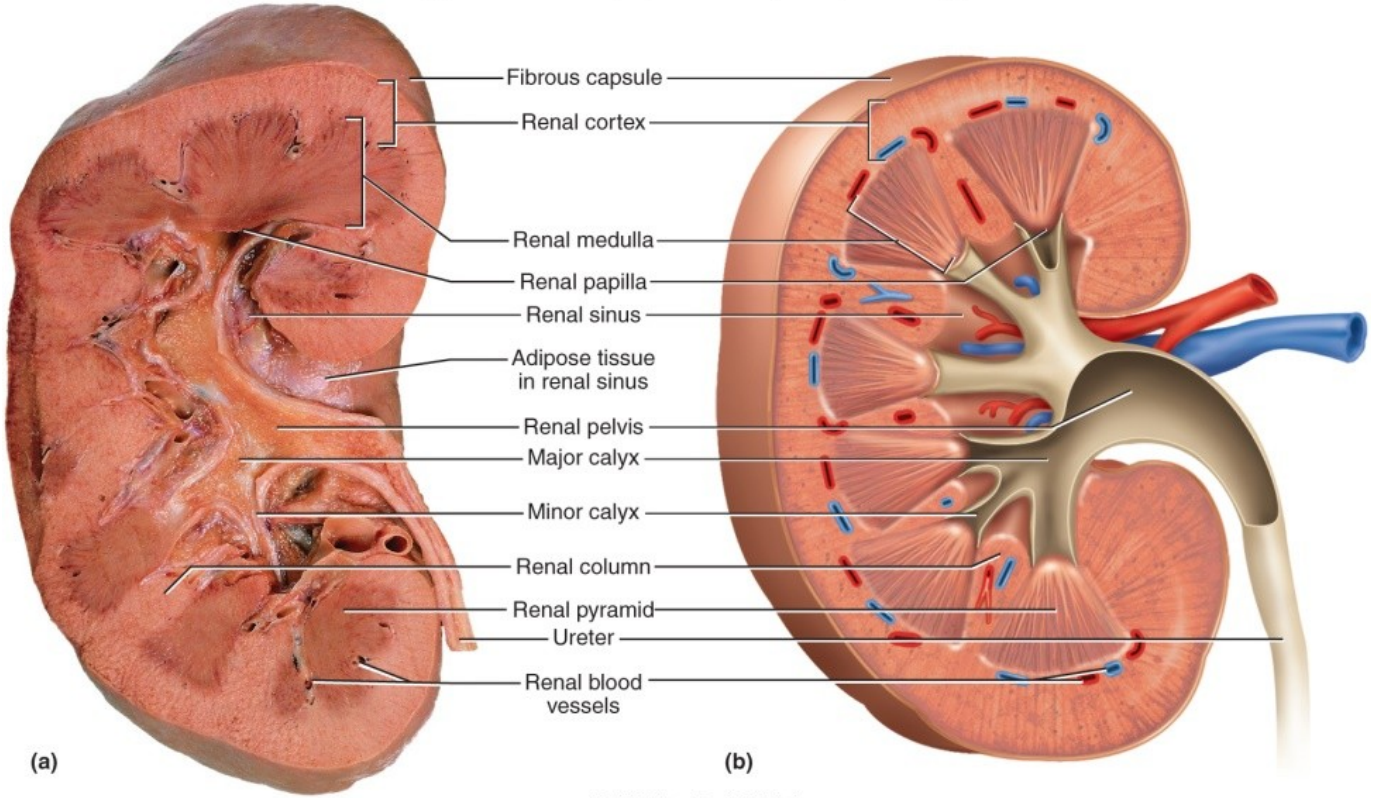
Gross Anatomy of the kidney

Minor calyx: cup nestled in papilla of each pyramid; collects it urine

Major calyces: convergence of two or three minor calyces

Renal pelvis: convergence of two or three major calyces

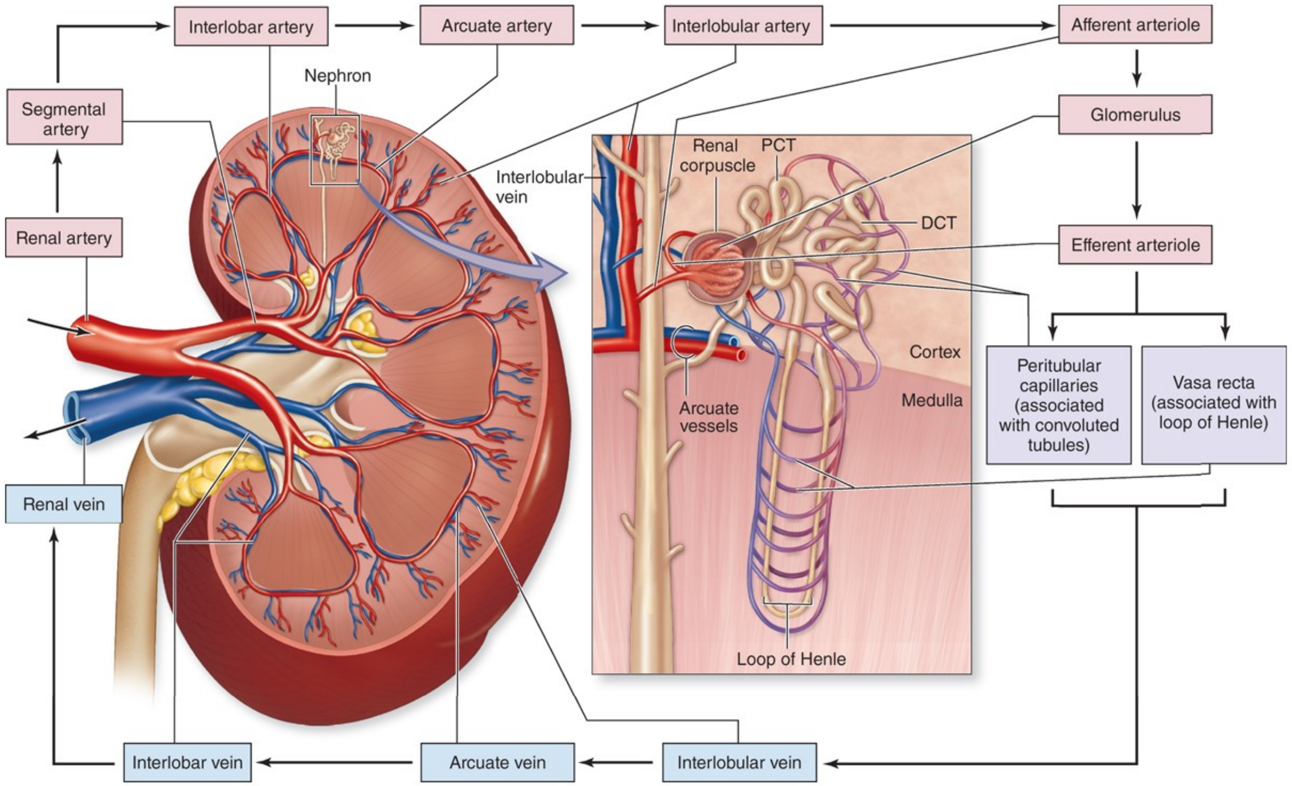
Ureter: tubular continuation of the pelvis that drains the urine down to the urinary bladder



a: Ralph Hutchings/Visuals Unlimited

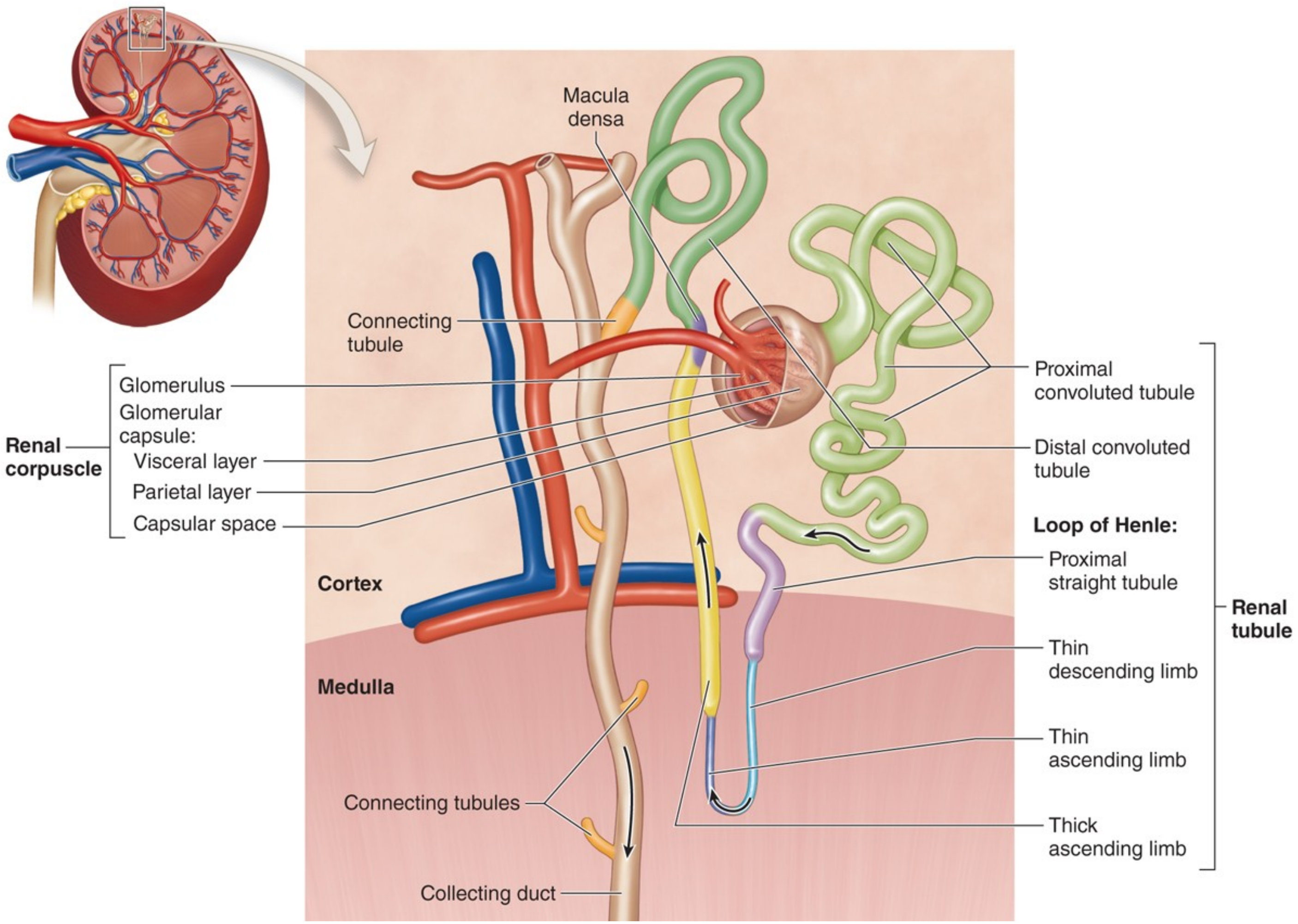
Renal Circulation: 0.4% of body weight, 21% of cardiac output

Renal artery→ Interlobar arteries → Arcuate arteries: over pyramids → Interlobular (cortical radiate) arteries → afferent arterioles → 1 nephron → efferent arterioles → peritubular capillaries or vasa recta → Interlobular veins (cortical radiate)→arcuate veins → interlobar veins → Renal vein→ inferior vena cava



Medical Application: Distance runners and swimmers often experience temporary proteinuria or hematuria (protein or blood in urine). Prolonged, strenuous exercise greatly reduces perfusion of kidney Glomerulus deteriorates under prolonged hypoxia

Each kidney contains approximately 1 million functional units called nephrons, which carry waste from blood to calyx



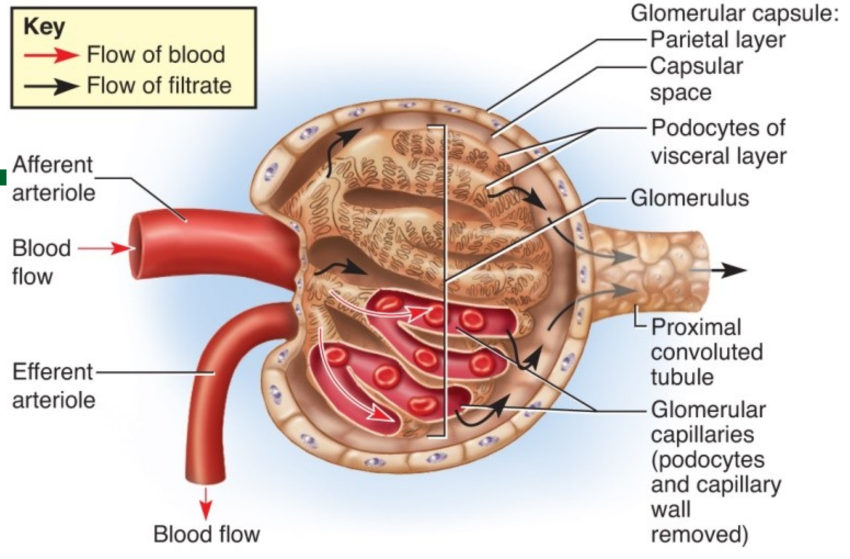
renal corpuscle →proximal convoluted tubule → loop of Henle (proximal straight tubule → thin descending limb → thin ascending limb → thick ascending limb → macula densa → distal convoluted tubule → connecting tubule → collecting duct → calyx

The Nephron

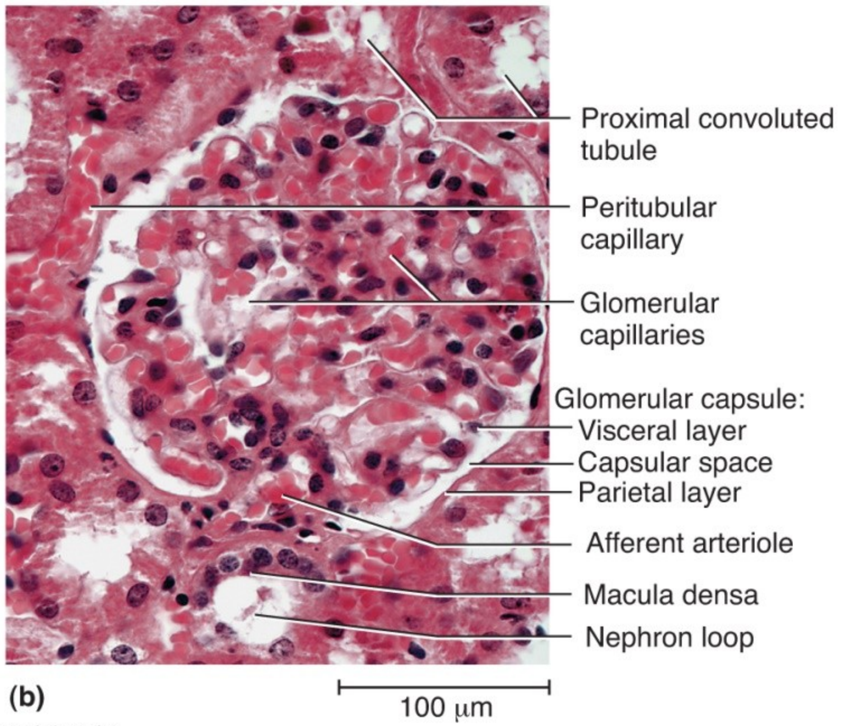
Glomerular filtrate: fluid exits glomulerular capillary → capsular space → convoluted tubule.
Note the afferent arteriole is larger than the efferent arteriole.

- **Vascular pole**: the side of the corpuscle where the afferent arterial enters the corpuscle and the efferent arteriole leaves
- **Urinary (Tubular) pole**: the opposite side of the corpuscle where the renal tubule begins

MEDICAL APPLICATION: In diseases such as diabetes mellitus and glomerulonephritis, the glomerular filter is altered and becomes much more permeable to proteins, with the subsequent release of protein into the urine (**proteinuria**). Proteinuria is an indicator of many potential kidney disorders.



(a)



(b)

Renal corpuscle is small mass of capillaries called the glomerulus housed within a bulbous glomerular capsule: filters the blood plasma

Parietal (outer) layer of capsule: simple squamous epithelium

Visceral (inner) layer of capsule

> **podocytes** surround capillaries and create barrier against escape of large molecules
>
> **pedicels:** foot processes of podocytes

Capsular space separates the two layers of Bowman capsule

Blood enters and leaves the glomerulus through the afferent and efferent arterioles, respectively.

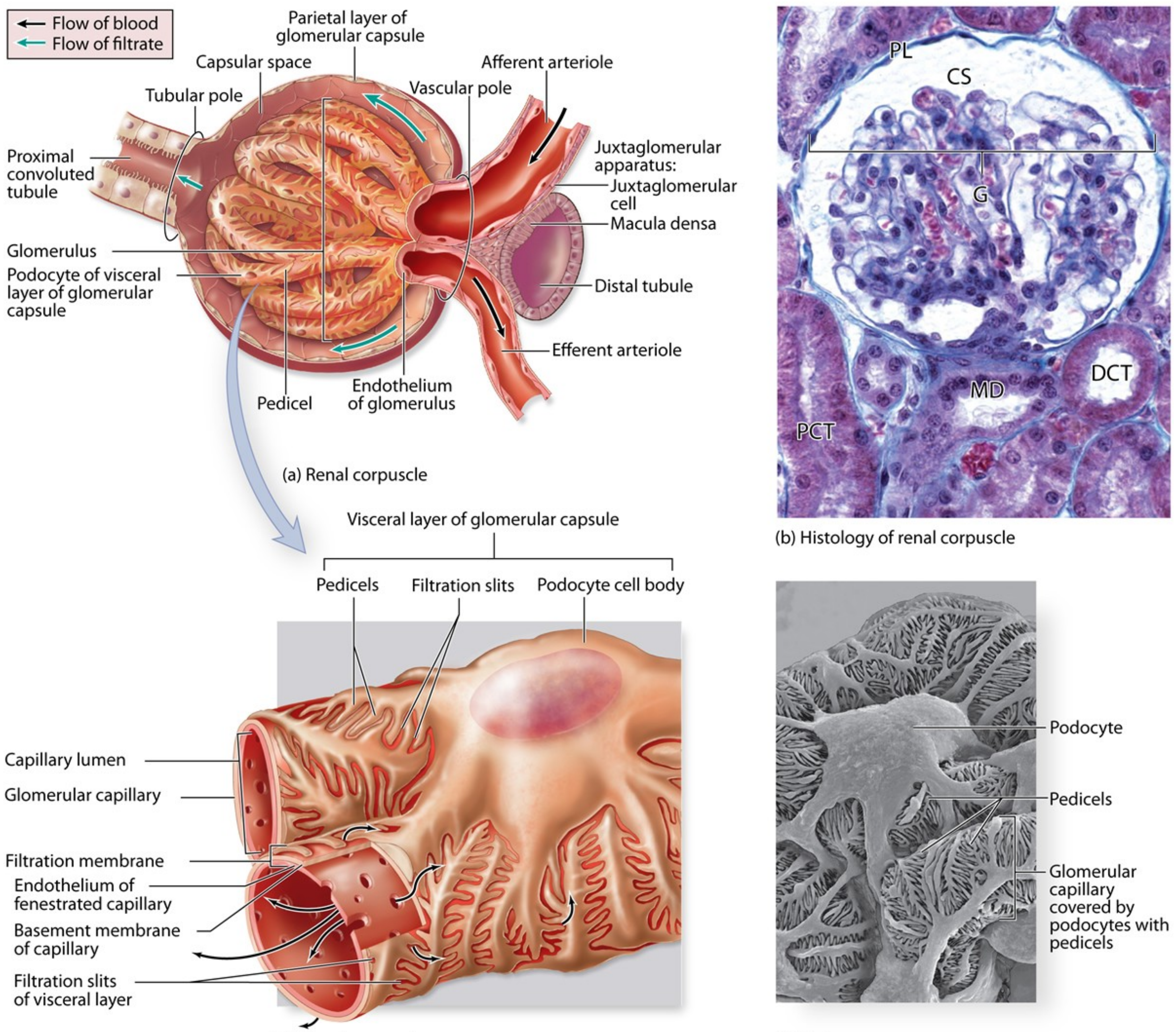
G glomerulus

CS capsular space

PL: simple squamous parietal layer of Bowman capsule. **MD** macula densa

PCT proximal convoluted tubules

DCT distal convoluted tubules



(a) Renal corpuscle

(b) Histology of renal corpuscle

(c) Filtration membrane

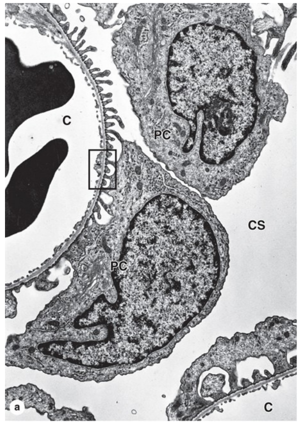
(d) Podocytes

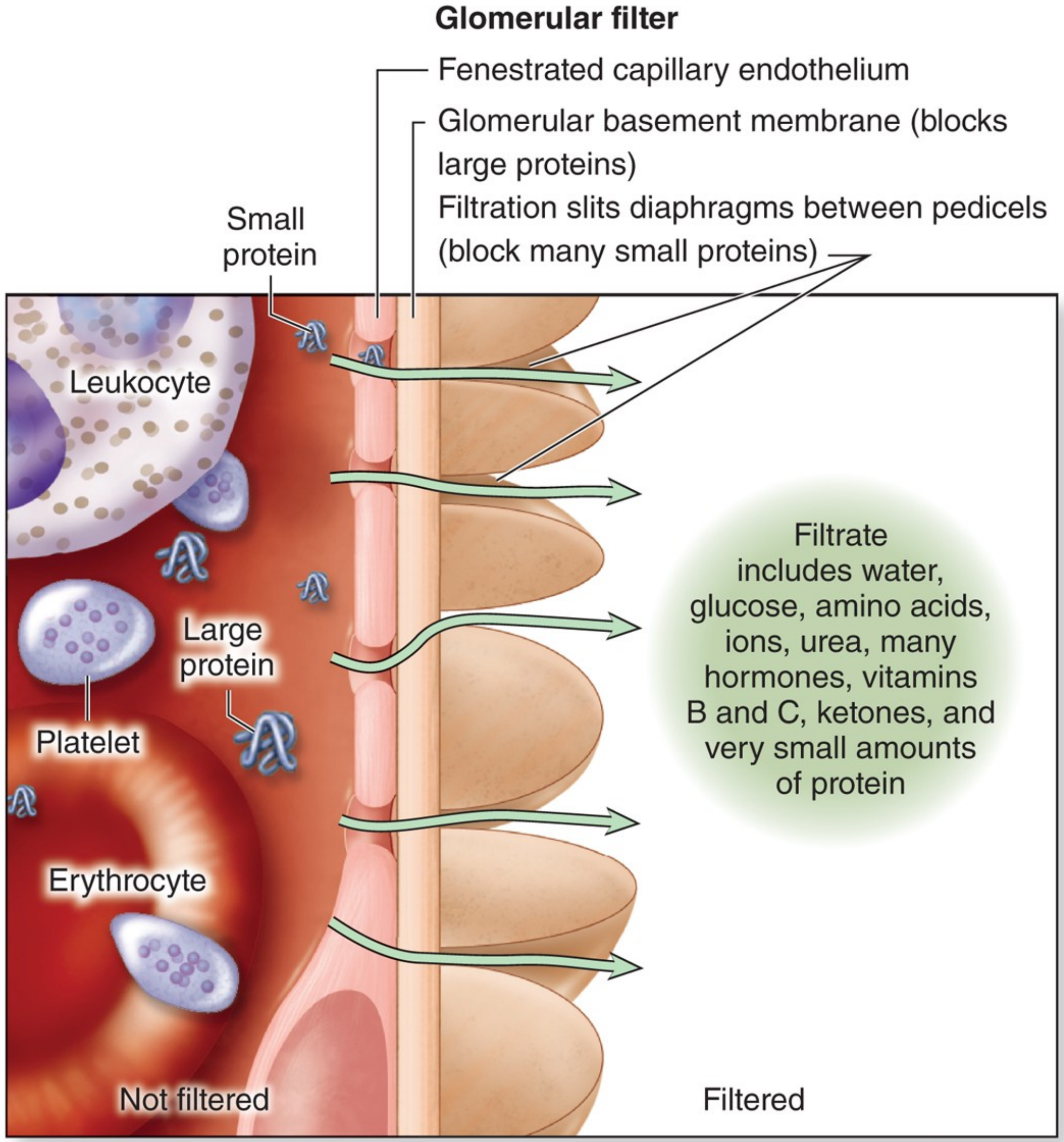
Glomerular Filter

Filtrate is produced in the corpuscle when blood plasma is forced under pressure through the **capillary fenestrations**, across the filtration **membrane** or surrounding the capillary, and through the **filtration slit** diaphragms located between the podocyte pedicels

The glomerular filtration barrier = fenestrated **capillary endothelium**, the **glomerular basement membrane (GBM)**, and **filtration slit**

MEDICAL APPLICATION Diabetic glomerulosclerosis, the thickening and loss of function in the GBM produced as part of the systemic microvascular sclerosis in diabetes mellitus, is the leading cause of (irreversible) end-stage kidney disease in the United States. Treatment requires either a kidney transplant or regular artificial hemodialysis.





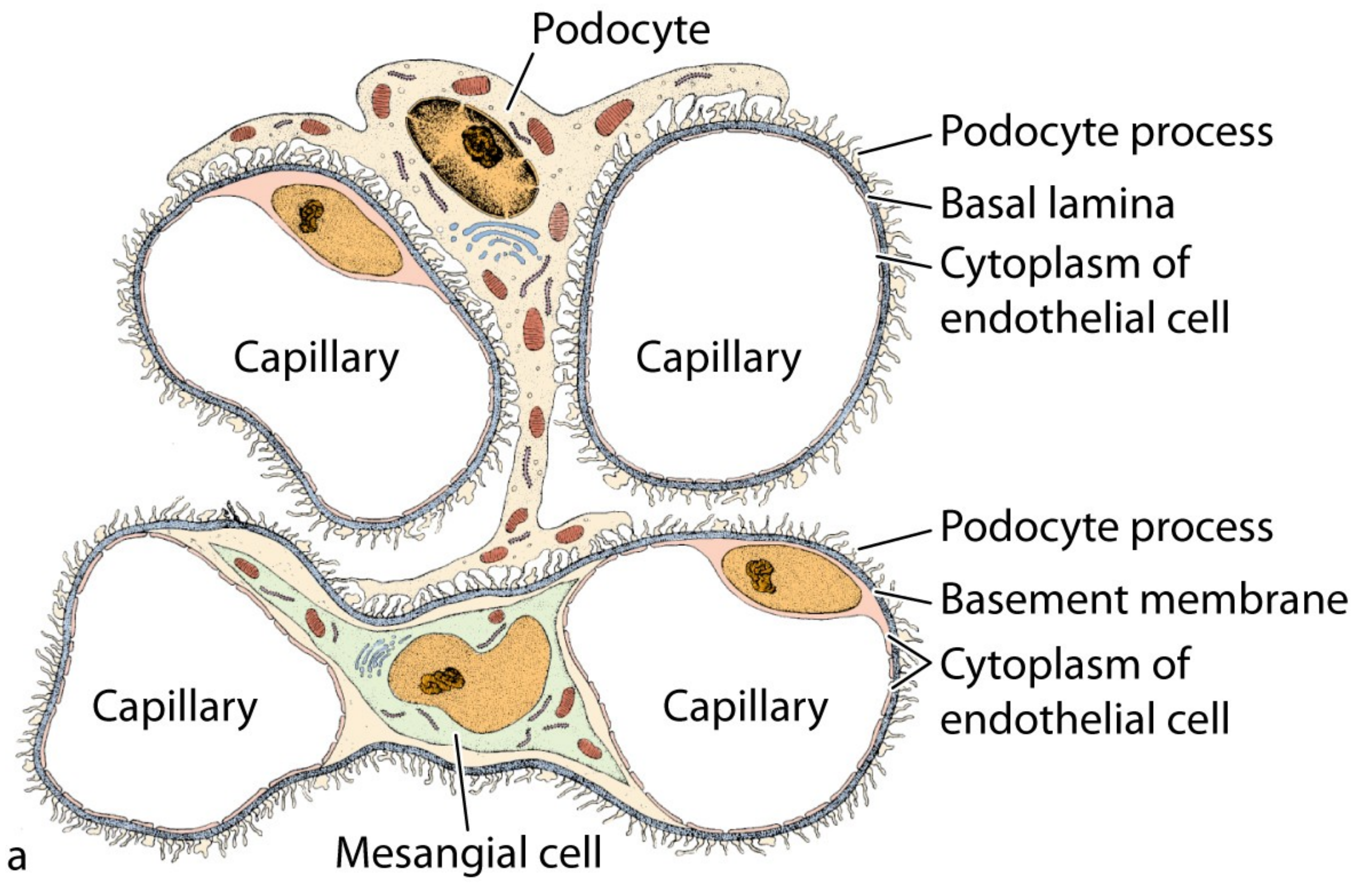
(c) Substances filtered by filtration membrane

Mesangial cells extend contractile processes (arrows) along capillaries that help regulate blood flow in the glomerulus

Mesangial cells in renal corpuscles are located between capillaries and cover those capillary surface not covered by podocyte processes.

Some mesangial processes appear to pass between endothelial cells into the capillary lumen where they may help remove or endocytose adherent protein aggregates.

Podocytes and their pedicels open to the urinary space and associate with the capillary surfaces not covered by mesangial cells



The Renal (Uriniferous) Tubule: glomerular capsule → tip of medullary pyramid

4 regions of renal tubule:

1. Proximal convoluted tubule (PCT): most coiled , Simple cuboidal epithelium with prominent microvilli for majority of absorption

2. Nephron loop (loop of Henle): long U-shaped portion of renal tubule

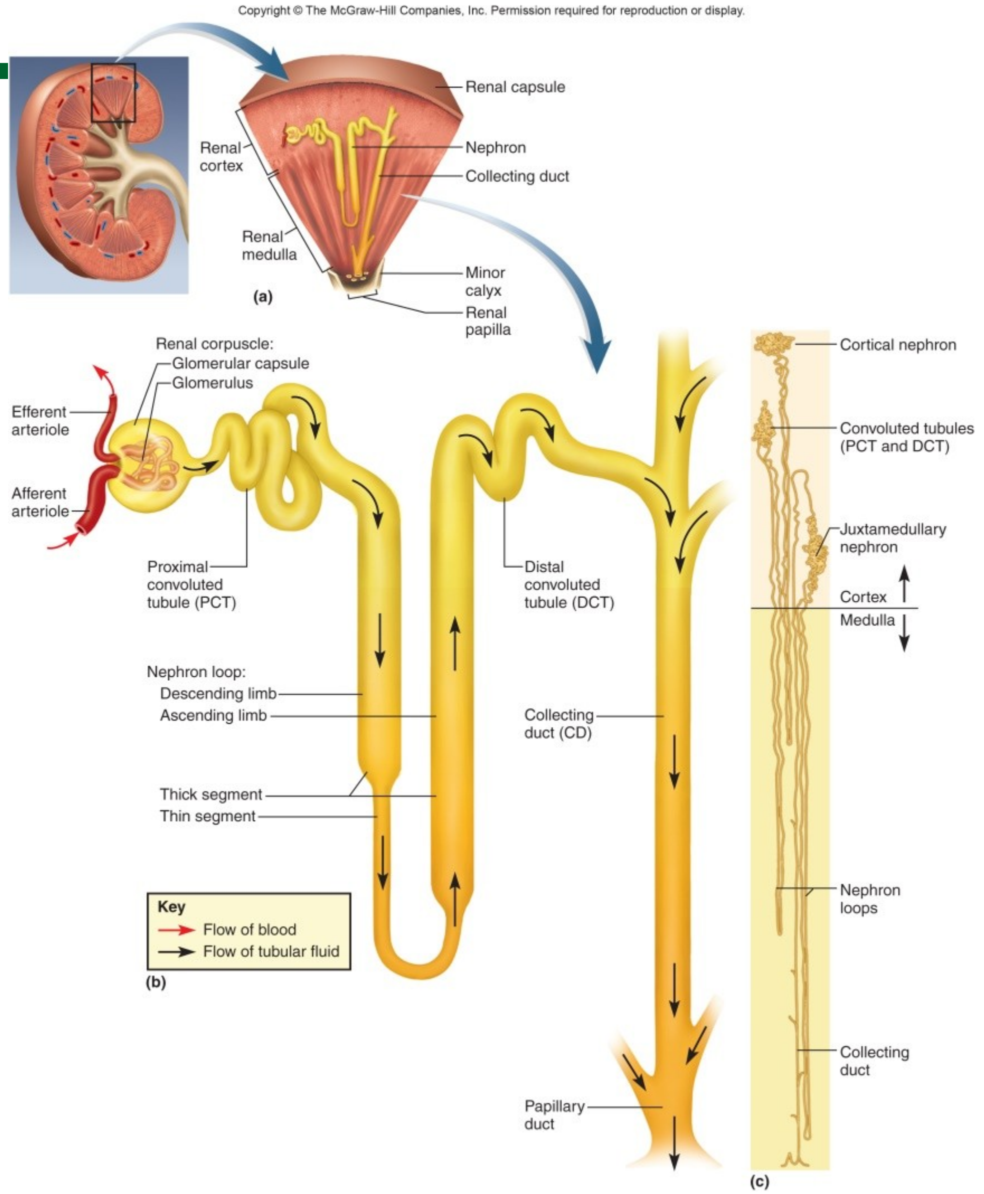
Thick segments: simple cuboidal epithelium, active transport of salts, many mitochondria

Thin segment: simple squamous epithelium, very permeable to water

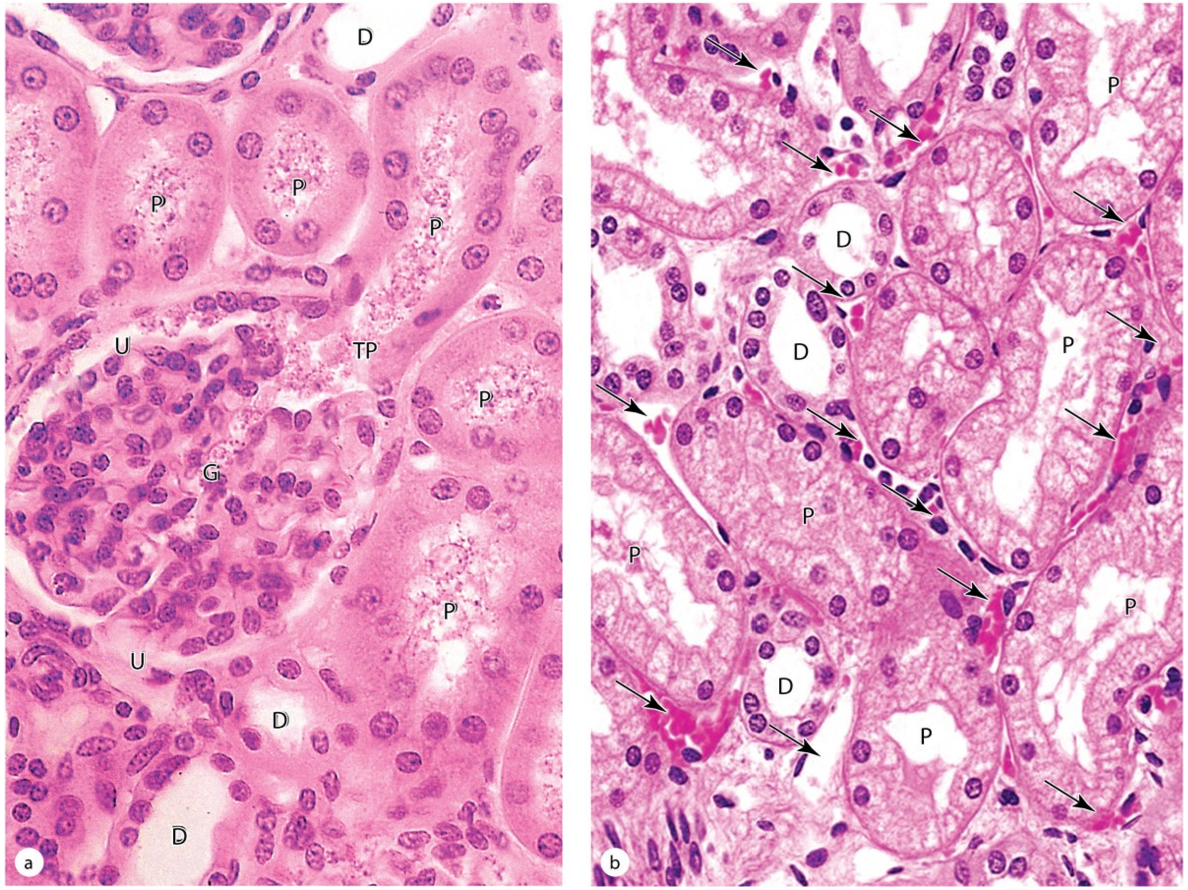
3. **Distal convoluted tubule (DCT, end of nephron)**: Cuboidal epithelium without microvilli

4. **Collecting duct**: receives from several DCTs, simple cuboidal ep.

collecting duct → papillary duct → minor calyx → major calyx → renal pelvis → ureter → urinary bladder → urethra



Renal cortex: proximal and distal convoluted tubules

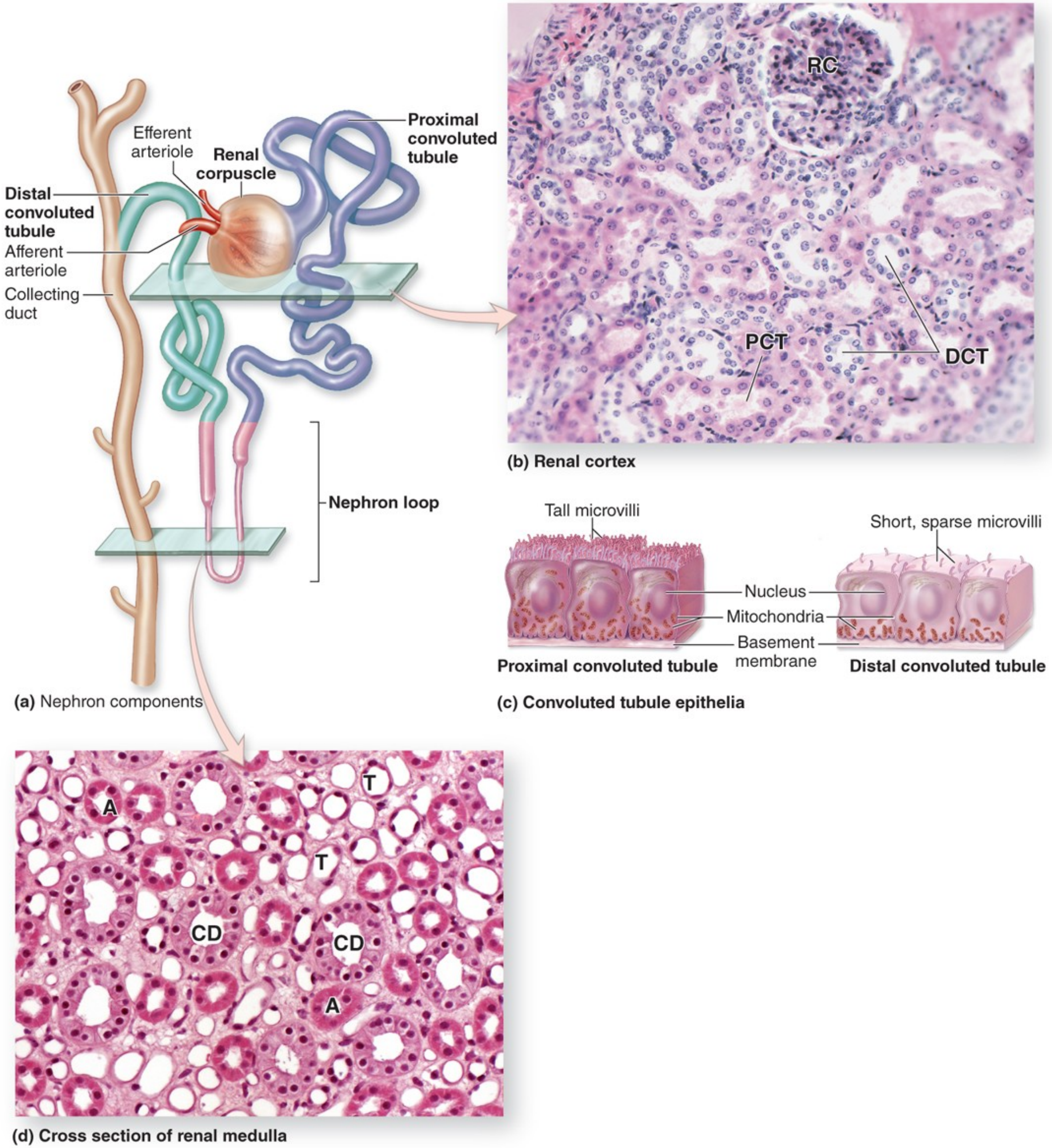


Note the **continuity at a renal corpuscle's tubular pole** (**TP**) between the simple cuboidal epithelium of a **proximal convoluted tubule** (**P**) and the simple squamous epithelium of the **capsule's parietal layer**.

The urinary space (**U**) between the parietal layer and the glomerulus (**G**) drains into the lumen of the proximal tubule. The lumens of the proximal tubules appear filled, because of the long microvilli of the brush border and aggregates of small plasma proteins bound to this structure. By contrast, the lumens of distal convoluted tubules (**D**) appear empty, lacking a brush border and protein.

Abundant **peritubular capillaries** and **draining venules** (arrows) that surround the proximal (**P**) and distal (**D**) convoluted tubules are clearly seen.

Convoluted tubules, nephron loops, and collecting ducts



RC: renal corpuscle
PCT: eosinophilic proximal convoluted tubules smaller
DCT: Less well-stained distal convoluted tubules.

Cuboidal cells of proximal and distal tubules have structural differences.

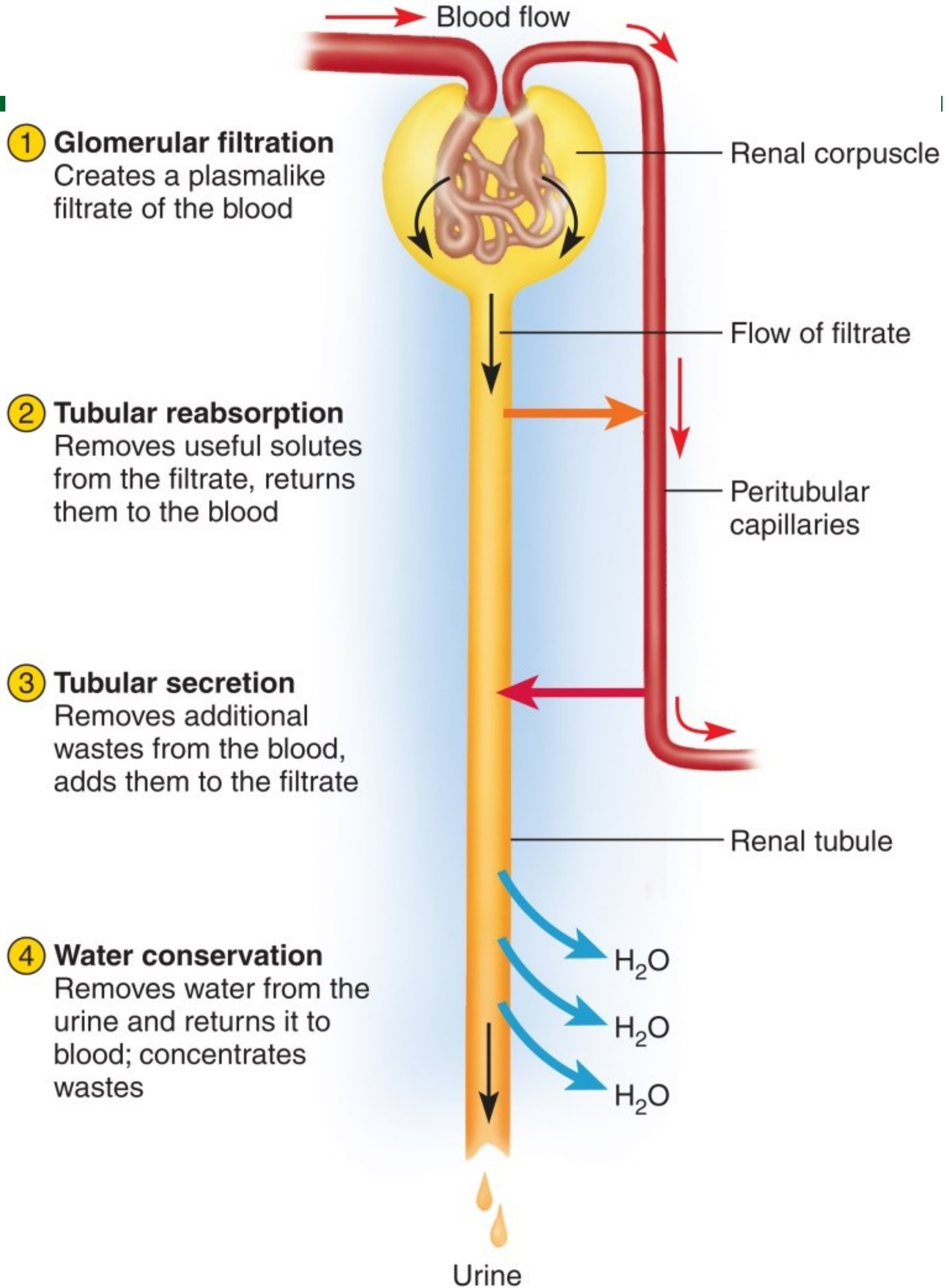
T: loops of Henle in cross section through a medullary pyramid. Simple squamous epithelium of the thin descending and ascending limbs of and its thick ascending limbs (**A**), as well as the pale columnar cells of collecting ducts (**CD**).

Urine Formation I: Glomerular Filtration

Kidneys convert blood plasma to urine in three stages

1. Glomerular filtration
   <u>Glomerular filtrate</u>: fluid in the capsular space, like blood plasma but almost no protein.
2. Tubular reabsorption and secretion
3. Water conservation

<u>Urine</u>: fluid that enters the collecting duct, little alteration beyond this point except for changes in water content



Juxtaglomerular apparatus

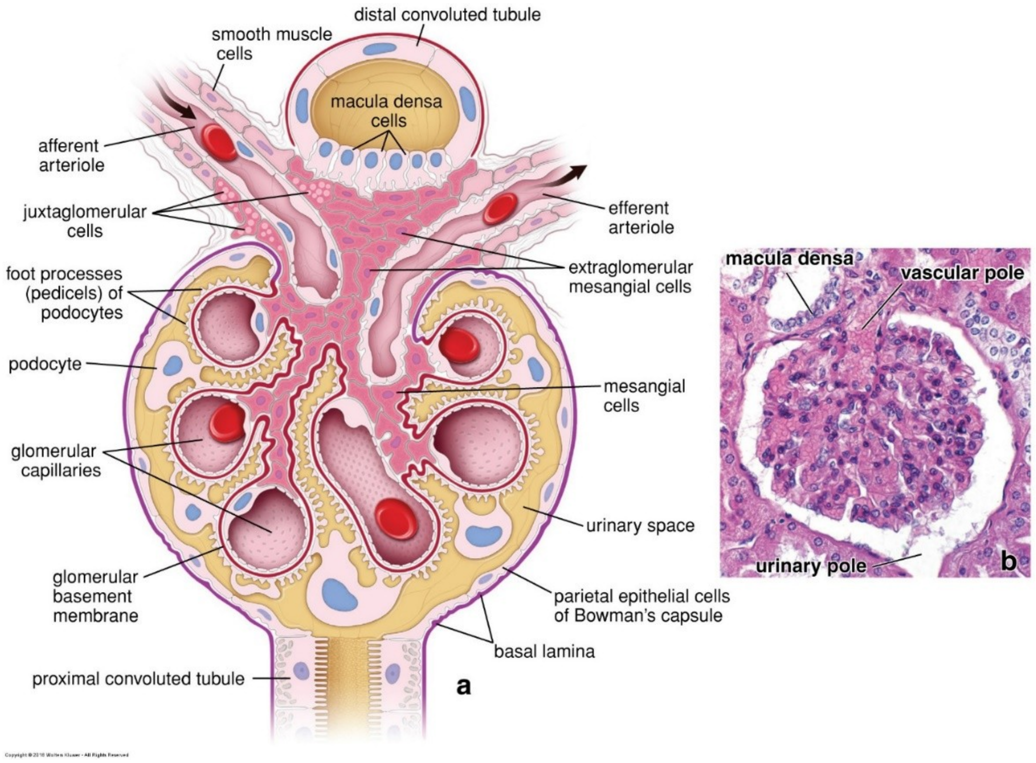
Macula densa: epithelial cells at end of the nephron facing the arterioles

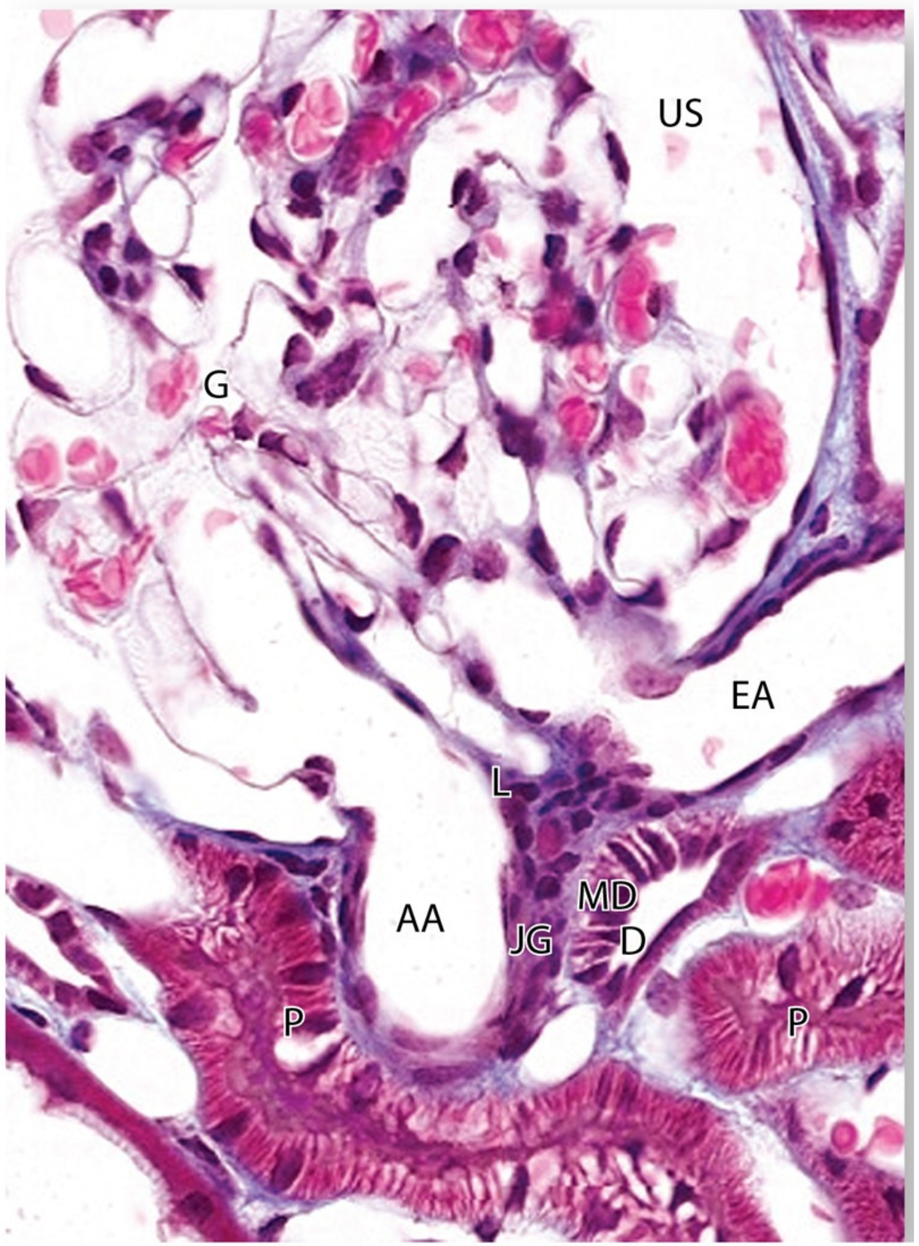
- Senses flow or fluid composition, secretes a paracrine signal that stimulates JG cells

Juxtaglomerular (JG) cells: smooth muscle cells of afferent arteriole across from macula dens, control arteriole diameter.

- Secrete in renin in response to drop in blood pressure
- Renin activates the renin-angiotensin system

angiotensinogen → angiotensin I → angiotensin II → constricts blood vessels, increases the secretion of ADH and aldosterone (to decrease urine volume), and stimulates the hypothalamus to activate the thirst reflex → increase in blood pressure





JGA forms at the point of contact between a nephron’s distal tubule (D) and the vascular pole of its glomerulus (G).

Cells of the distal tubule become columnar as a thickened region called the macula densa (**MD**).

Smooth muscle cells of the afferent arteriole’s (**AA**) tunica media are converted from a contractile to a secretory morphology as juxtaglomerular granule cells (**JG**).

Also present are lacis cells (**L**), which are extraglomerular mesangial cells adjacent to the macula densa, the afferent arteriole, and the efferent arteriole (**EA**).

TABLE 19–1 Histologic features and major functions of regions within renal tubules.

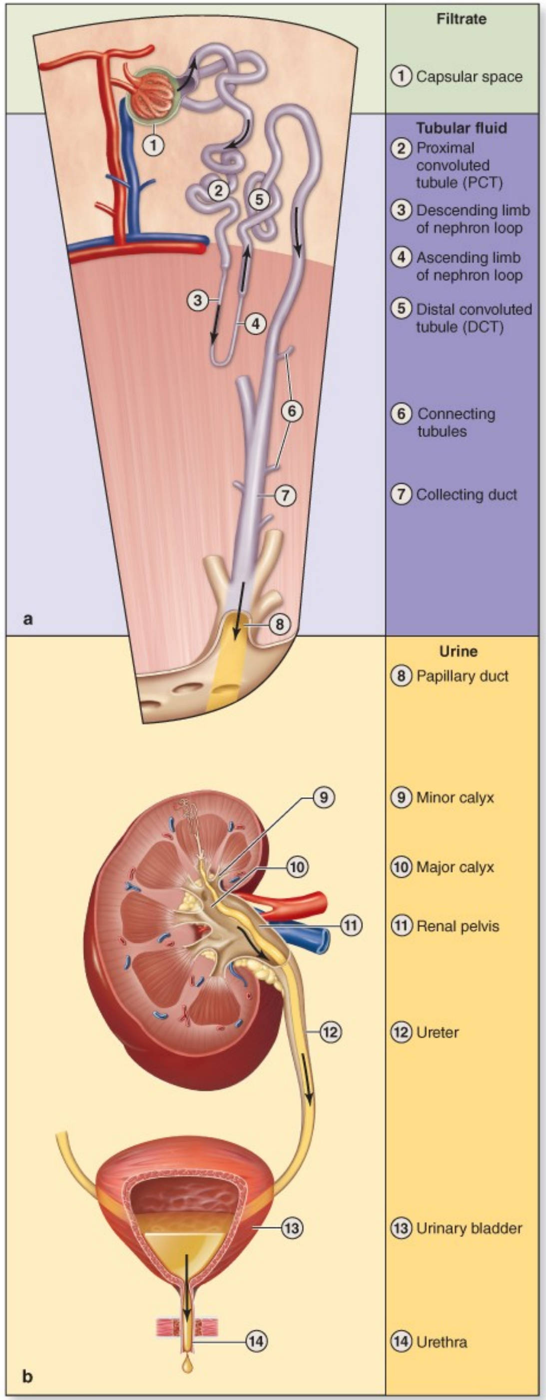
Region of Tubule	Histological Features	Locations	Major Functions
PCT	Simple cuboidal epithelium; cells well-stained, with numerous mitochondria, prominent basal folds and lateral interdigitations; long microvilli, lumens often occluded	Cortex	Reabsorption of all organic nutrients, all proteins, most water and electrolytes; secretion of organic anions and cations, H^+, and NH_4^+
Loop of Henle			
Thin limbs	Simple squamous epithelium; few mitochondria	Medulla	Passive reabsorption of Na^+ and Cl^-
TAL	Simple cuboidal epithelium; no microvilli	Medulla and medullary rays	Active reabsorption of various electrolytes
DCT	Simple cuboidal epithelium; cells smaller than in PCT, short microvilli and basolateral folds, more empty lumens	Cortex	Reabsorption of electrolytes
Collecting system			
Principal cells	Most abundant, cuboidal to columnar; pale-staining, distinct cell membranes	Medullary rays and medulla	Regulated reabsorption of water & electrolytes; regulated secretion of K^+
Intercalated cells	Few and scattered; slightly darker staining	Medullary rays	Reabsorption of K^+ (low-K^+ diet); help maintain acid-base balance

DCT, distal convoluted tubule; PCT, proximal convoluted tubule; TAL, thick ascending limb.

Fluid transport in the urinary system

Upon delivery at a minor calyx, filtrate is no longer modified by reabsorption or secretion and is called **urine**. It flows passively into the renal pelvis but moves by peristalsis along the ureters for temporary storage in the urinary bladder, which is emptied through the urethra.

MEDICAL APPLICATION: A common problem involving the ureters is their obstruction by renal calculi (**kidney stones**) formed in the renal pelvis or calyces, usually from calcium salts (oxalate or phosphate) or uric acid. While urate stones are usually smooth and small, calcium stones can become large and irritate the mucosa. Problems caused by such stones can be corrected by either surgical removal of the stone or its disintegration using focused ultrasonic shock waves in a procedure called **lithotripsy** (https://www.youtube.com/watch?v=fR_CjlVXhzw)

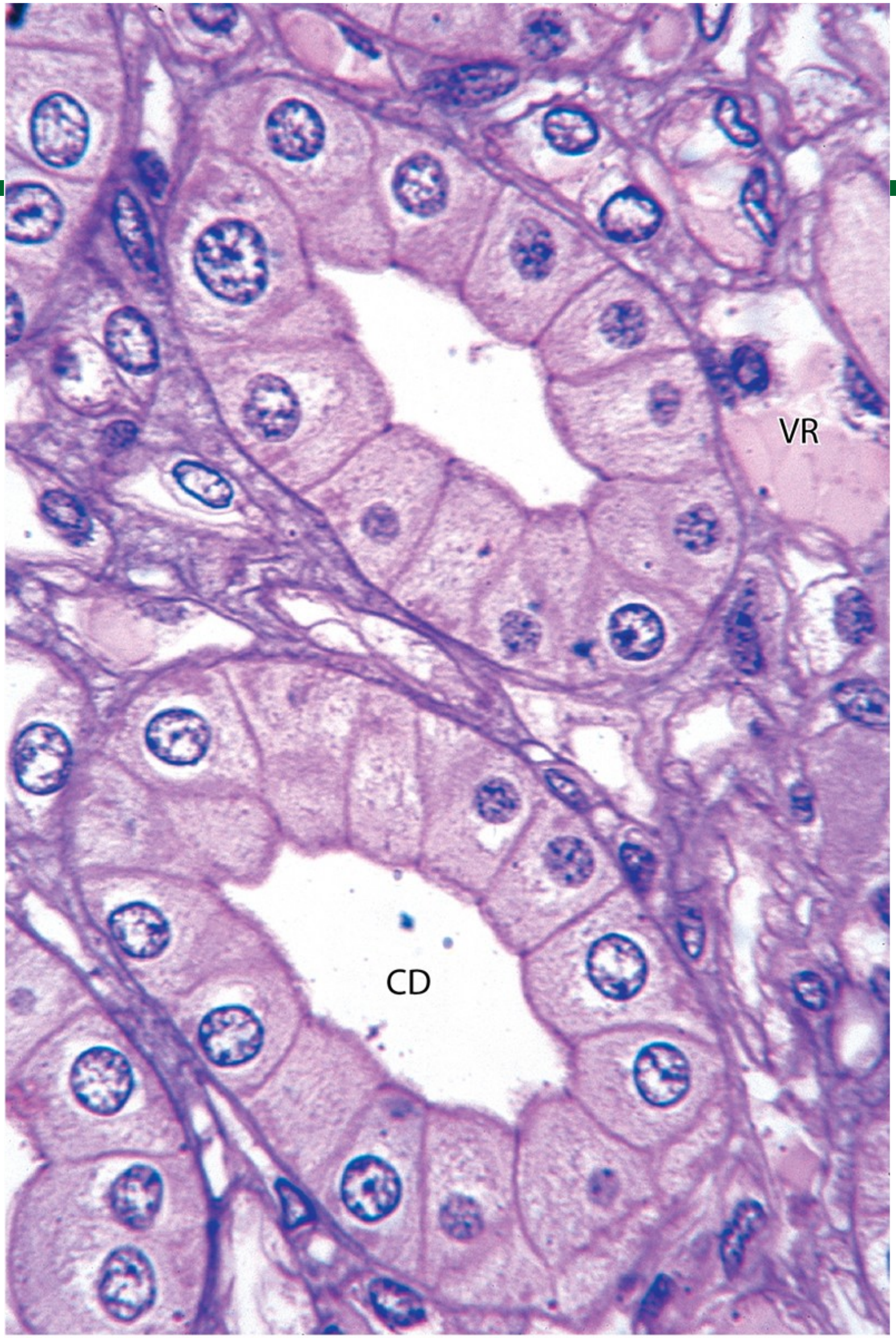


Collecting Ducts

Pale-staining columnar **principal cells**, in which ADH-regulated aquaporins of the cell membrane allow more water reabsorption, are clearly seen in these transversely sectioned collecting ducts (**CD**), surrounded by interstitium with vasa recta (**VR**)

MEDICAL APPLICATION:

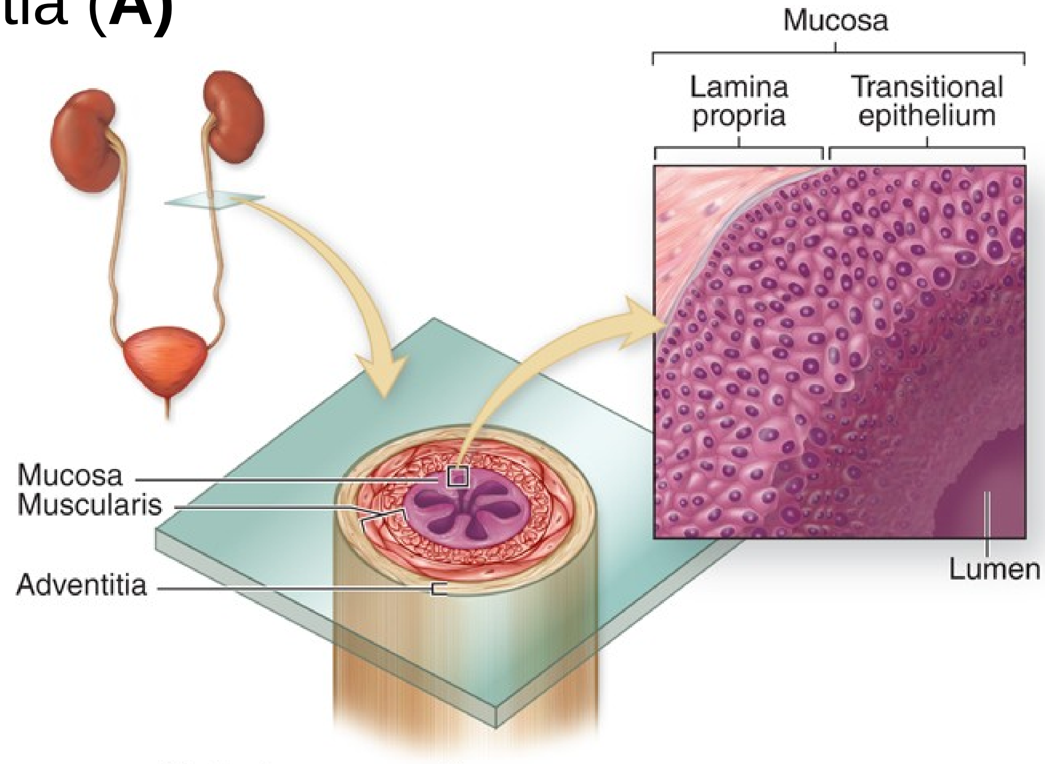
Bacterial infections of the urinary tract can lead to inflammation of the renal pelvis and calyces, or pyelonephritis In acute pyelonephritis bacteria often move from one or more minor calyx into the associated renal papilla, causing accumulation of neutrophils in the collecting ducts.



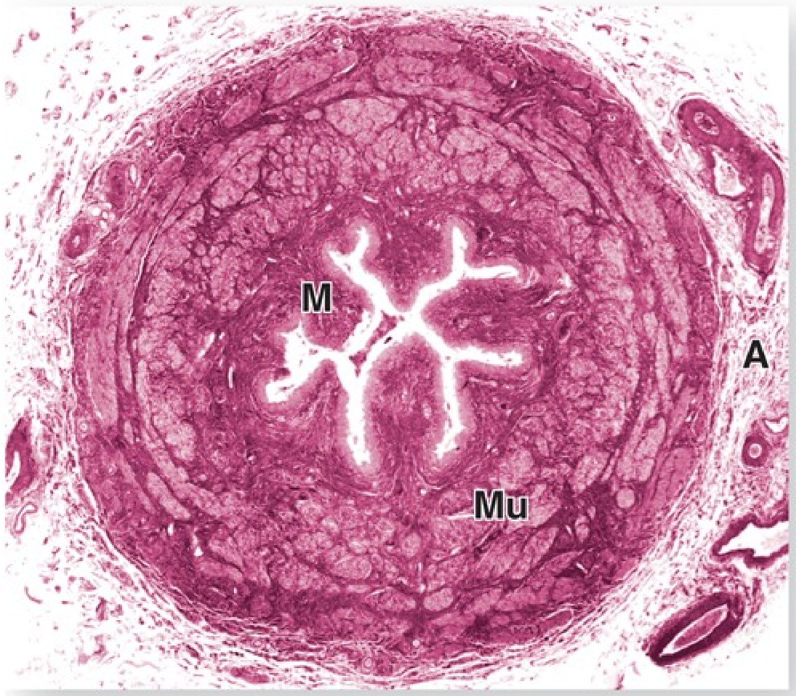
Ureter in cross section shows a characteristic pattern of longitudinally folded mucosa, surrounded by a thick muscularis that moves urine by regular waves of peristalsis.

The lamina propria is lined by a unique stratified epithelium called **transitional epithelium** or **urothelium** that is resistant to the potentially deleterious effects of contact with hypertonic urine.

Histologically the muscularis (**Mu**) is much thicker than the mucosa (**M**) and adventitia (**A)**



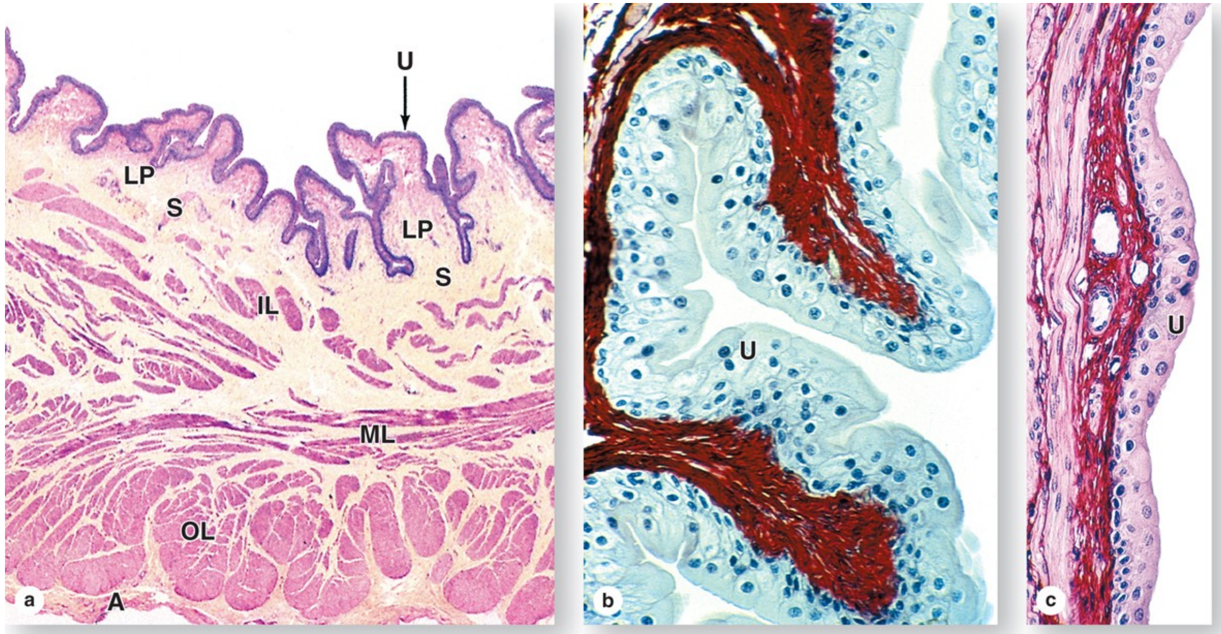
(a) Ureter cross section



(b)

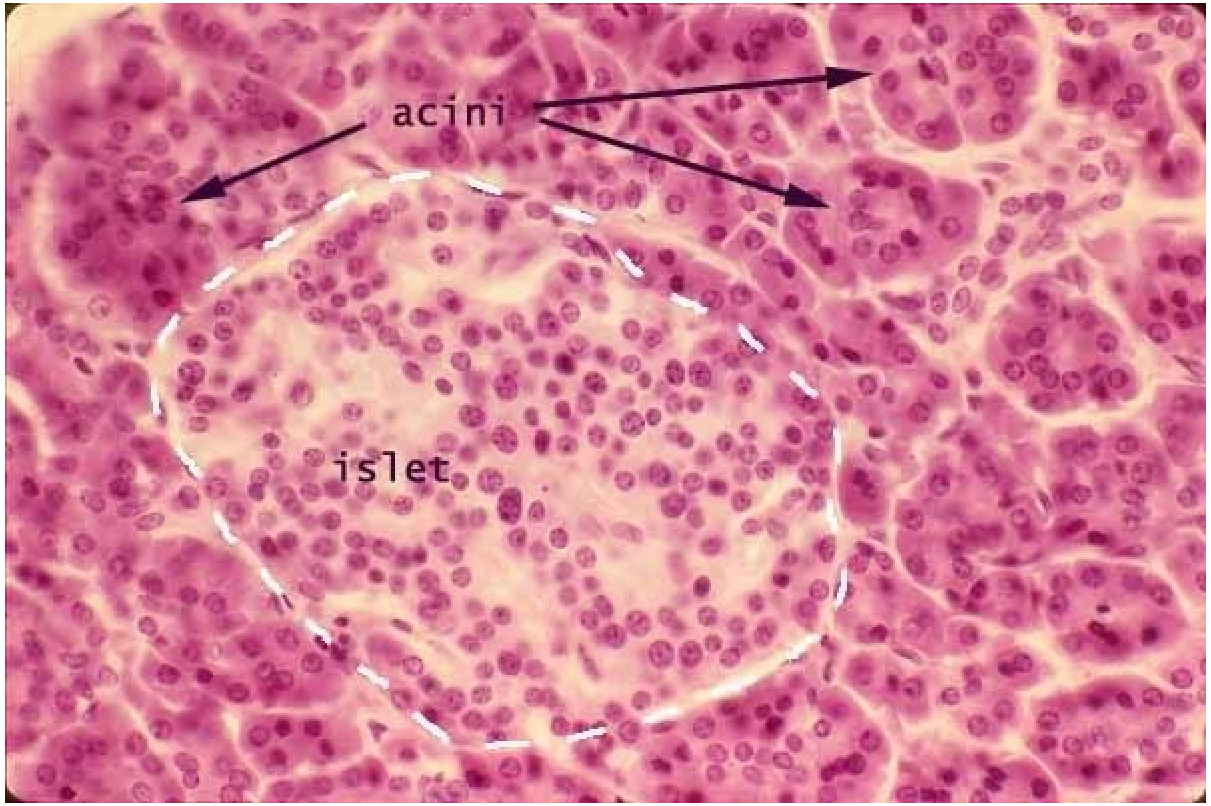
Bladder

(a) In the neck of the bladder, near the urethra, the wall shows four layers: the mucosa with urothelium (**U**) and lamina propria (**LP**); the thin submucosa (**S**); inner, middle, and outer layers of smooth muscle (**IL**, **ML**, and **OL**); and the adventitia (**A**). **(b)** When the bladder is empty, the mucosa is highly folded and the urothelium (**U**) has bulbous umbrella cells. **(c)** When the bladder is full, the mucosa is pulled smooth, the urothelium (**U**) is thinner, and the umbrella cells are flatter.



MEDICAL APPLICATION Cystitis, or inflammation of the bladder mucosa, is the most frequent problem involving this organ. Such inflammation is common during urinary tract infections, but it can also be caused by immunodeficiency, urinary catheterization, radiation, or chemotherapy.

Bladder cancer is usually some form of transitional cell carcinoma arising from unstable urothelium.



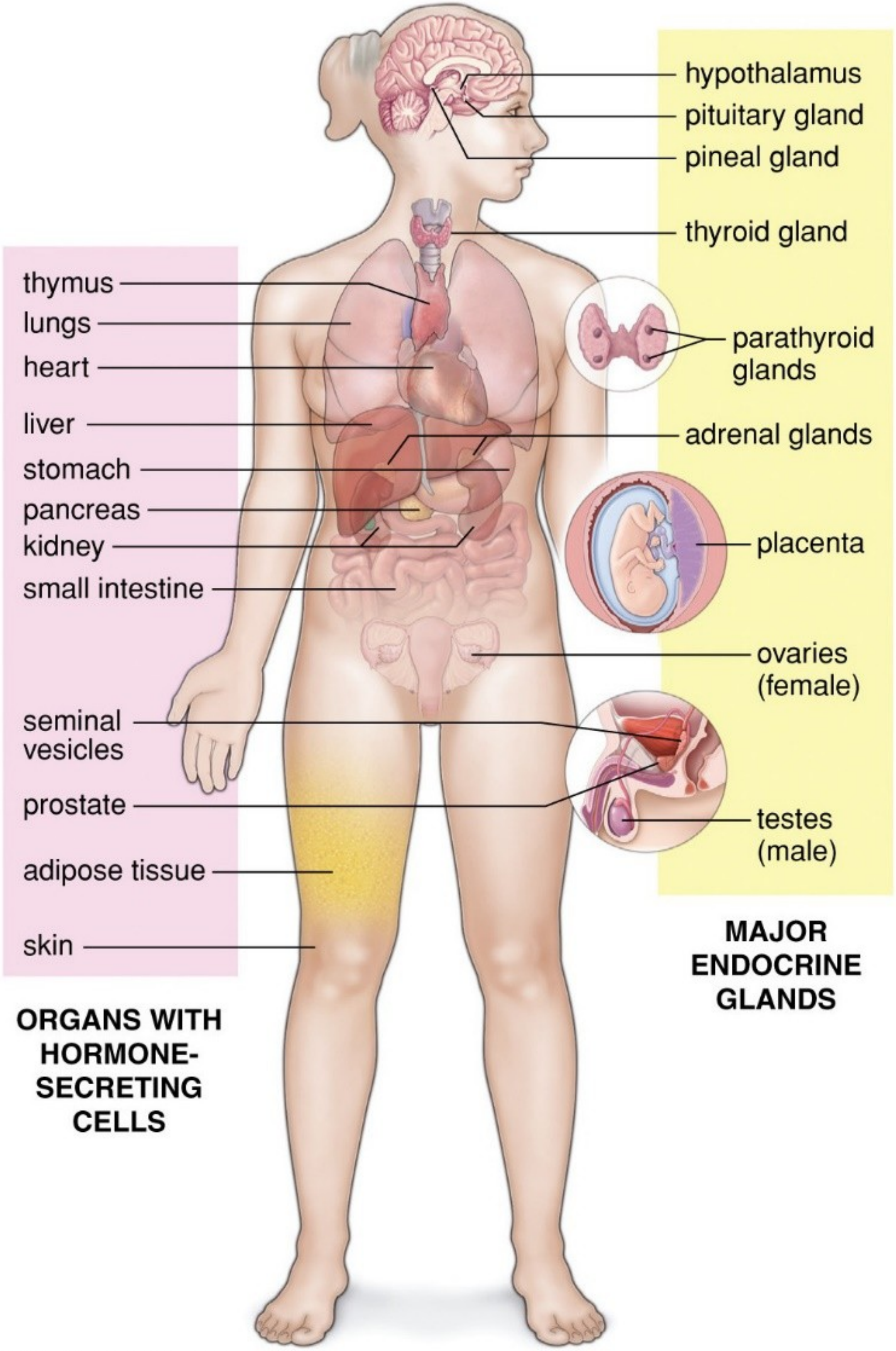
Endocrine

BI 455 CHAPTER 20

Crash Course Endocrine
https://www.khanacademy.org/partner-content/crash-course1/partner-topic-crash-course-bio-ecology/crash-course-biology/v/crash-course-biology-132

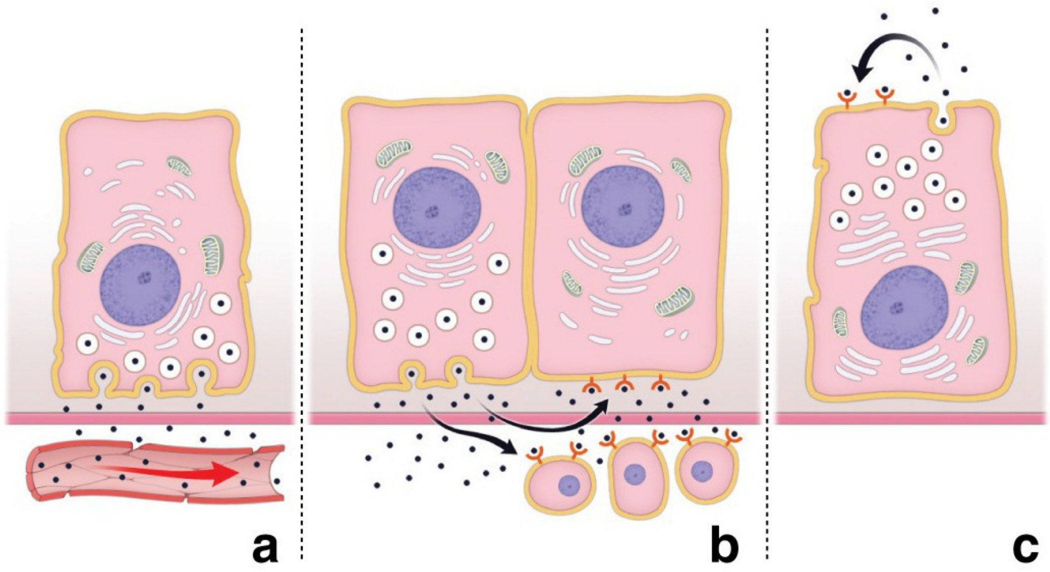
Overview of the Endocrine System

- **Endocrine system:** glands, tissues, and cells that secrete hormones
- **Endocrinology**: the study of this system and the diagnosis and treatment of its disorders
- **Endocrine glands**: organs that are traditional sources of hormones
- **Hormones**: chemical messengers that are transported by the bloodstream and stimulate physiological responses in cells of another tissue or organ, often a considerable distance away



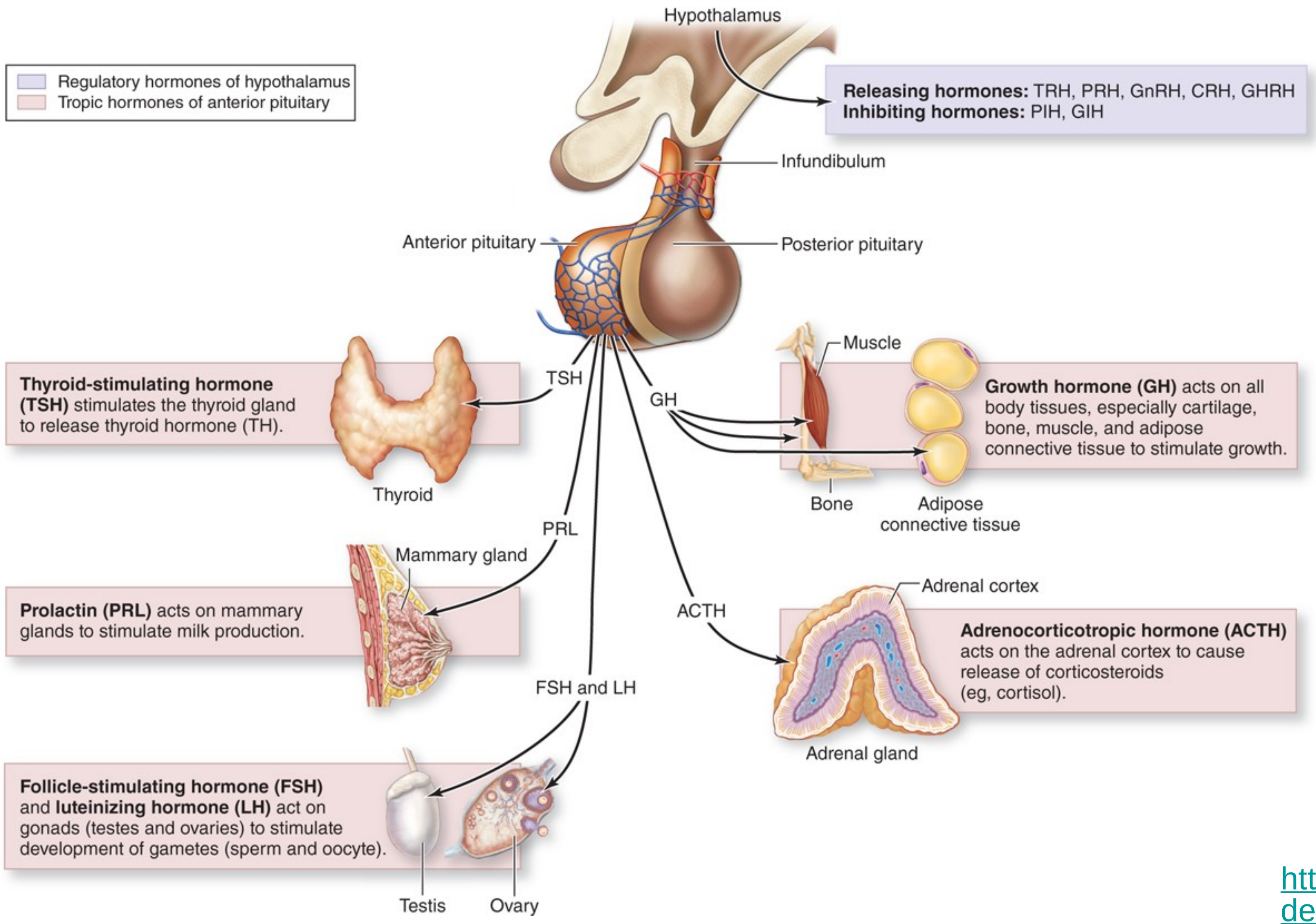
Comparison of Endocrine and Exocrine Glands

- **Exocrine glands**: Have ducts carry secretion to an epithelial surface or the mucosa of the digestive tract: “external secretions”
- **Endocrine glands**: No ducts, Contain dense, fenestrated capillary networks which allow easy uptake of hormones into bloodstream
  - “Internal secretions”, Intracellular effects such as altering target cell metabolism



Endocrine: hormone is discharged from a cell into the bloodstream and is transported to the effector cells.
Paracrine: hormone is secreted from one cell and acts on adjacent cells that express specific receptors.
Autocrine: hormone responds to the receptors located on the cell that produces it

Hormones of the Hypothalamus and Pituitary Gland are the <u>Master Regulators</u> of the Endocrine System



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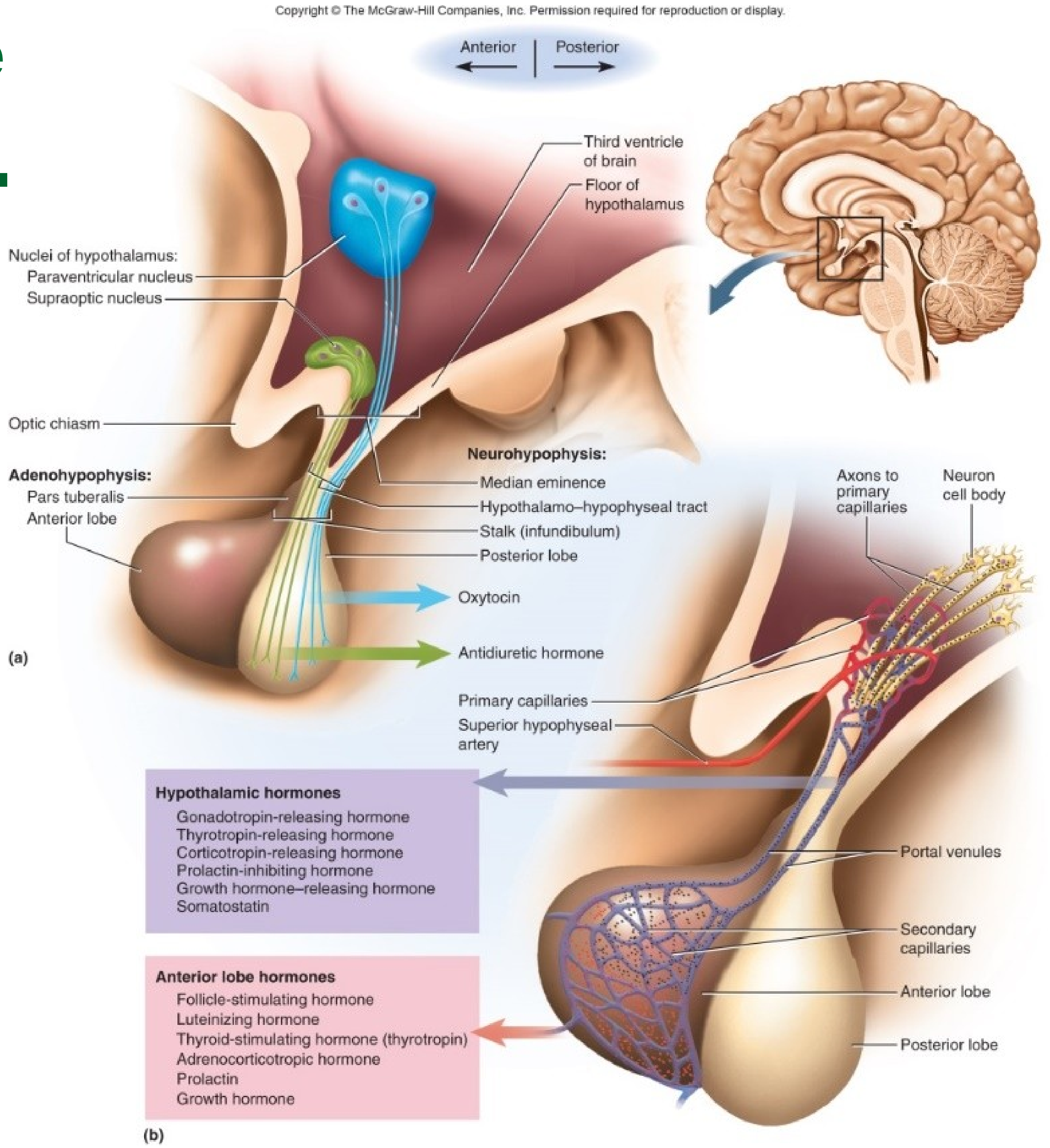
Hypothalamus is attached to poste pituitary by infundibulum stalk

Hypothalamo-hypophyseal tract: Hypothalamic nuclei (NOT posterior pituitary) synthesize oxytocin and antidiuretic hormone

- transport down fibers for storage in posterior pituitary

Hypophyseal portal system: hypothalamus → anterior pituitary gland

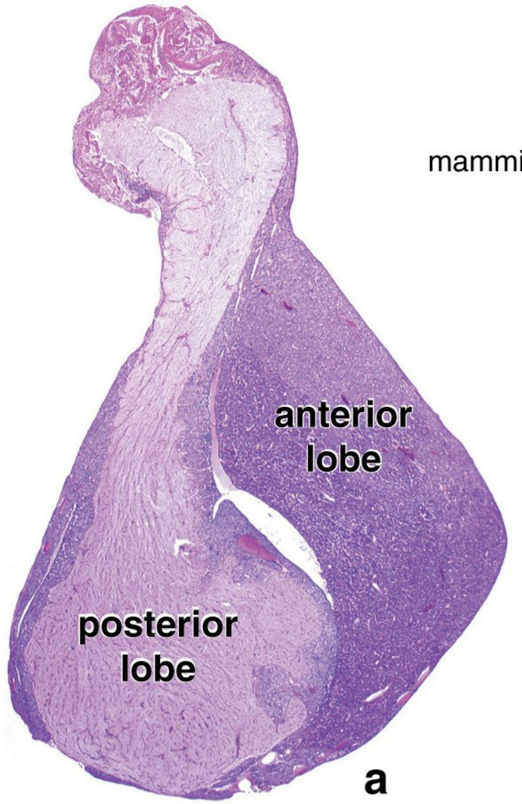
- **Portal system**: blood flows from one capillary bed to another
- **Hypothalamic Hormones** stimulate anterior pituitary via portal system

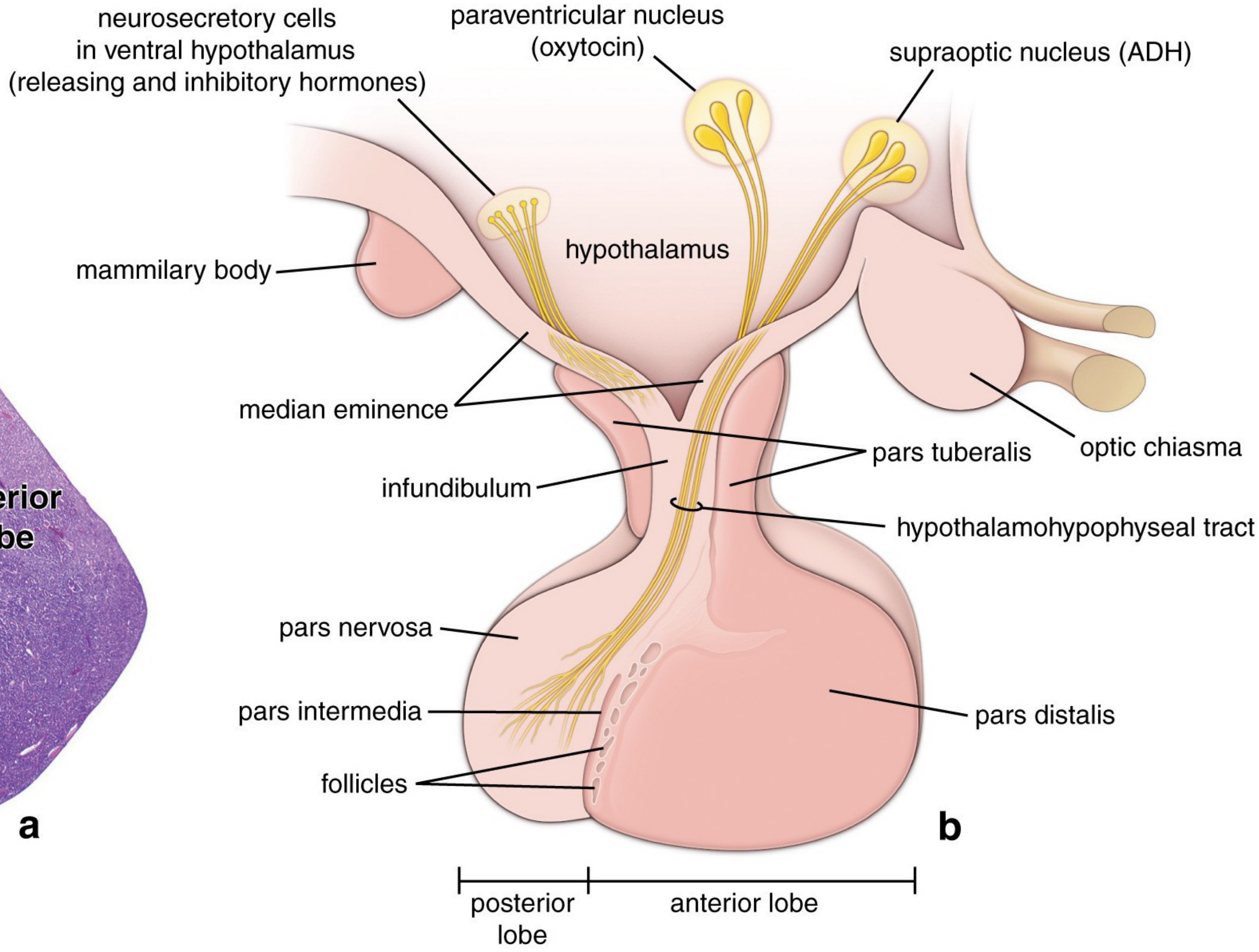


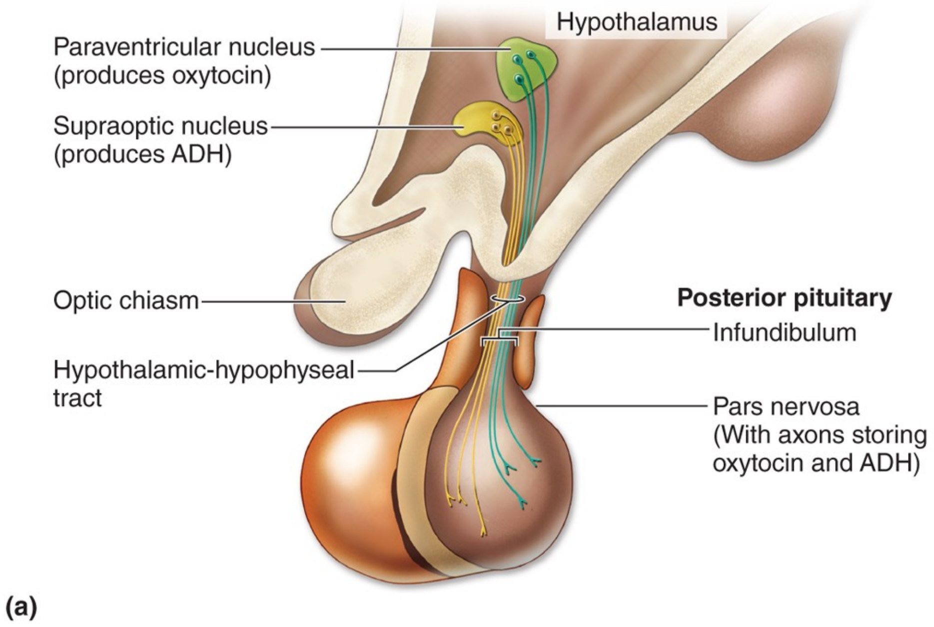
Pituitary gland (hypophysis) is sheltered in sella turcica, of sphenoid bone

Anterior pituitary (adenohypophysis): develops from pouch in roof of embryonic pharynx. Tissue looks glandular.

Posterior pituitary (neurohypophysis): Down growth from hypothalamus, retains connection to brain. Tissue looks nervous.





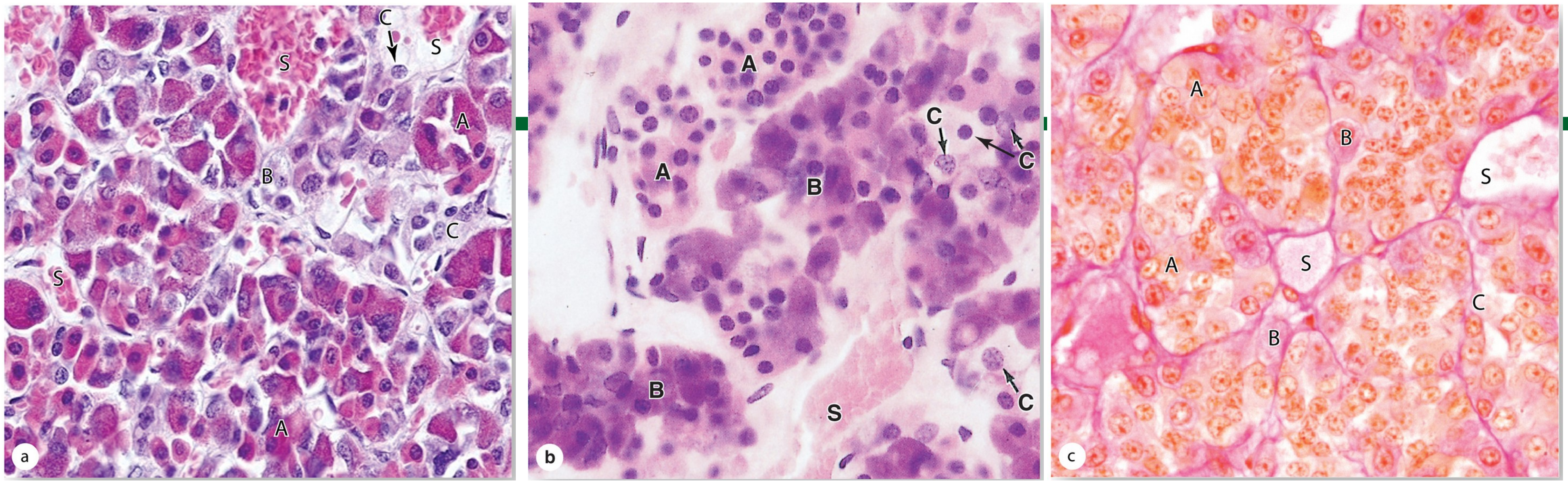


Adenohypophysis

Pars distalis: 75% of the adenohypophysis. Chromophils: basophils and acidophils, based on affinities for basic and acidic. Store hormones in granules. Chromophobes: lightly staining cells

Pars intermedia: thin zone of basophilic cells between the pars distalis and the pars nervosa of the neurohypophysis

Pars tuberalis: smaller funnel-shaped region surrounding the infundibulum of the neurohypophysis Most of the cells of the pars tuberalis are **gonadotrophs**.



Pars Distalis

acidophil cells (**A**)
basophils (**B**)
chromophobes (**C**)
capillaries and sinusoids (**S**)

TABLE 21.2 **Staining Characteristics of Cells Found in the Anterior Lobe of the Pituitary Gland**

Cell Type	Percentage of Total Cells	General Staining	Specific Staining	Product
Somatotrope (GH cell)	50	Acidophil	Orange G (PAS −)	Growth hormone (GH)
Lactotrope (PRL cell)	15–20	Acidophil	Orange G (PAS −) Herlant's erythrosine Brooke's carmosine	Prolactin (PRL)
Corticotrope (ACTH cell)	15–20	Basophil	Lead hematoxylin (PAS +)	Proopiomelanocortin (POMC), which is cleaved in human into adrenocorticotropic hormone (ACTH) and β-lipotrophic hormone (β-LPH)
Gonadotrope (FSH and LH cells)	10	Basophil	Aldehyde-fuchsin Aldehyde-thionine (PAS +)	Follicle-stimulating hormone (FSH) and luteinizing hormone (LH)
Thyrotrope (TSH cell)	~5	Basophil	Aldehyde-fuchsin Aldehyde-thionine (PAS +)	Thyroid-stimulating hormone (TSH)

MEDICAL APPLICATION: Benign pituitary adenomas often produce excessive numbers of functional acidophils or basophils. Adenomas involving somatotropic cells can cause gigantism if occurring in children before closure of the long bones' epiphyseal plates or acromegaly in adults, with musculoskeletal, neurologic, and other medical consequences.

https://vimeo.com/62985496 (0-4:30)

Neurohyphophysis: Pars nervosa and the infundibular stalk

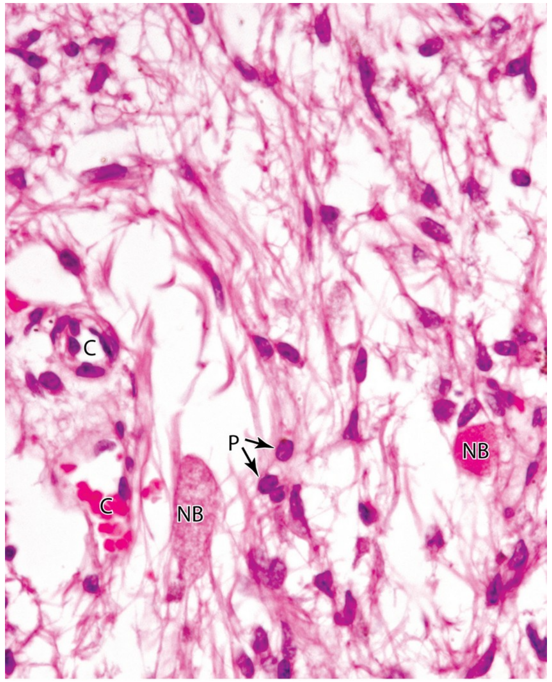


TABLE 20–3	Hormones of the posterior pituitary.
Hormone	**Function**
Vasopressin/antidiuretic hormone (ADH)	Increases water permeability of renal collecting ducts
Oxytocin	Stimulates contraction of mammary gland myoepithelial cells and uterine smooth muscle

The neurohypophysis does NOT synthesize its two hormones

Neurosecretory (**Herring**) **bodies** (**NB**): swellings at the end unmyelinated axons of hypothalamic neurons of which release oxytocin or vasopressin **(ADH)**. Released hormones are picked up by capillaries (**C**) for distribution

Pituicytes (**P**): Glial cells that resemble astrocytes

MEDICAL APPLICATION: Posterior pituitary function can be adversely affected by heritable mutations in the gene for vasopressin (ADH)-neurophysin, by compression from a tumor in adjacent tissues, and by head trauma. By lowering levels of vasopressin, such conditions can produce diabetes insipidus, a disorder characterized by inability to concentrate urine, which leads to frequent urination (polyuria) and increased thirst (polydipsia).

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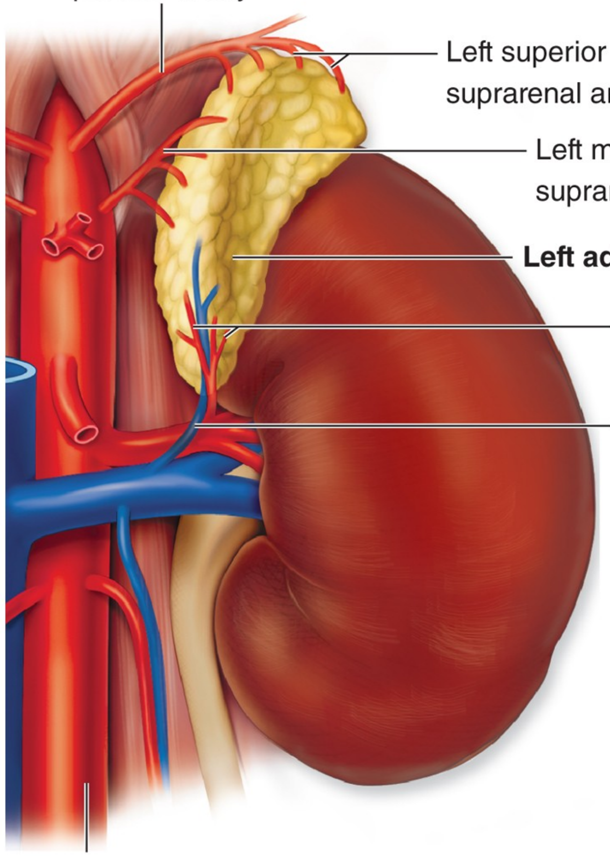
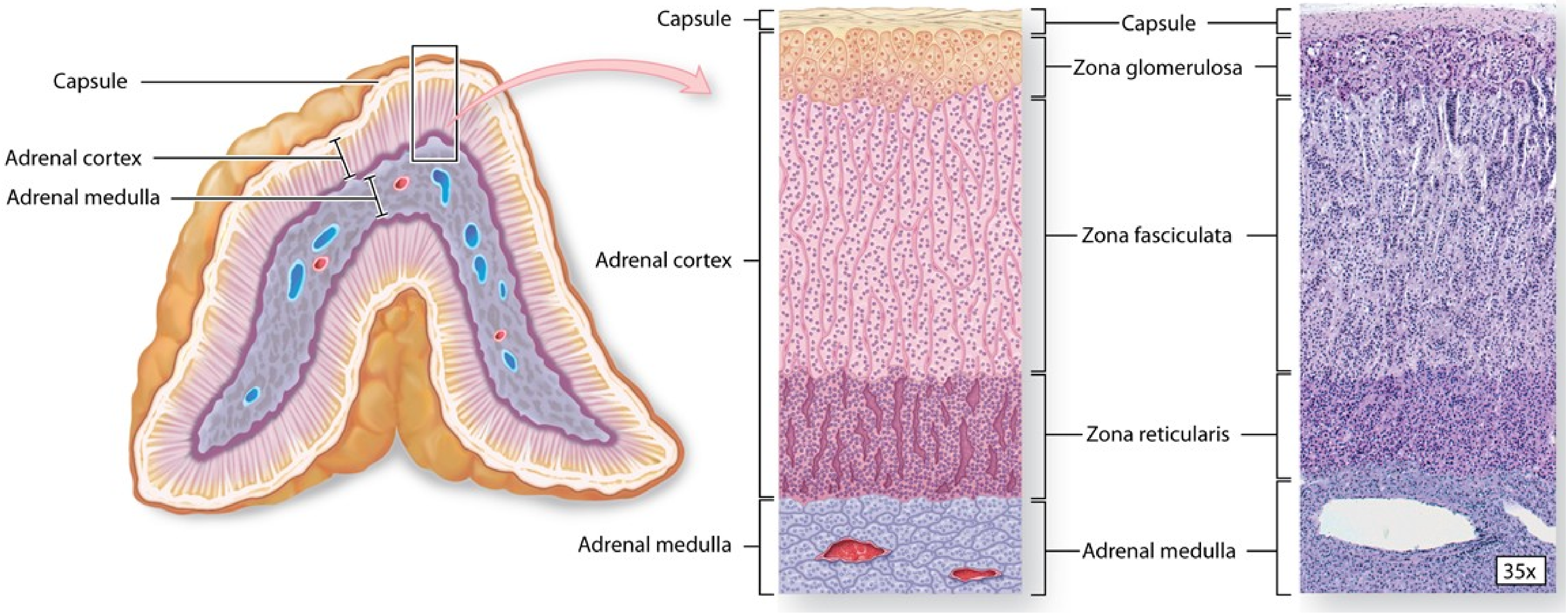
Location and blood supply of the adrenal glands



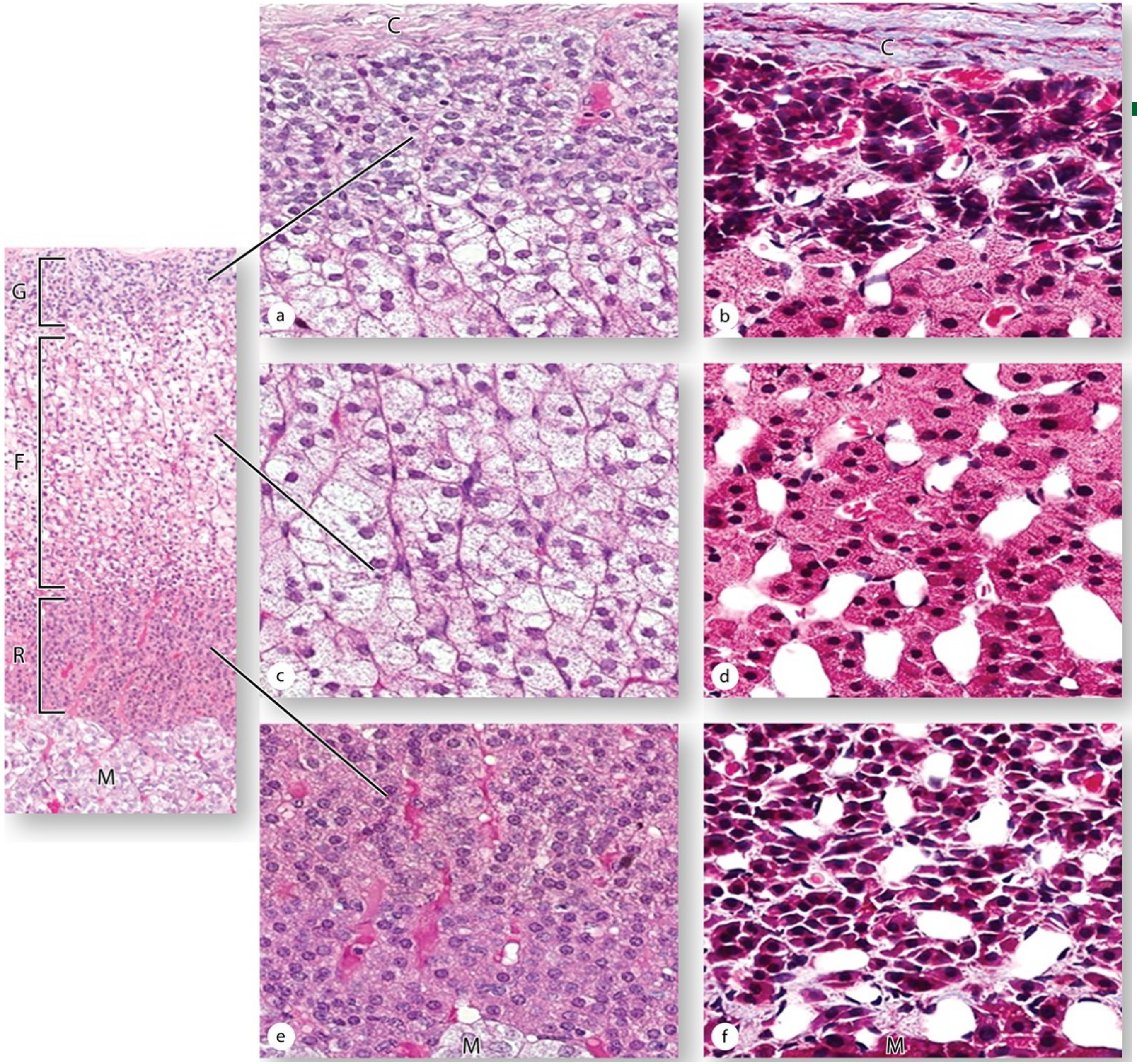
The paired adrenal glands are located at the superior pole of each kidney and each consists of an outer cortex that produces a variety of steroid hormones and an inner medulla that produces epinephrine and norepinephrine.

This anterior view of the left adrenal gland and kidney shows the blood vessels supplying these glands.

Inside the capsule of each adrenal gland is an adrenal cortex



MEDICAL APPLICATION: Addison disease or adrenal cortical insufficiency is a disorder, usually autoimmune in origin, which causes degeneration in any layer of adrenal cortex, with concomitant loss of glucocorticoids, mineralocorticoids, or androgen production.



Adrenal cortex

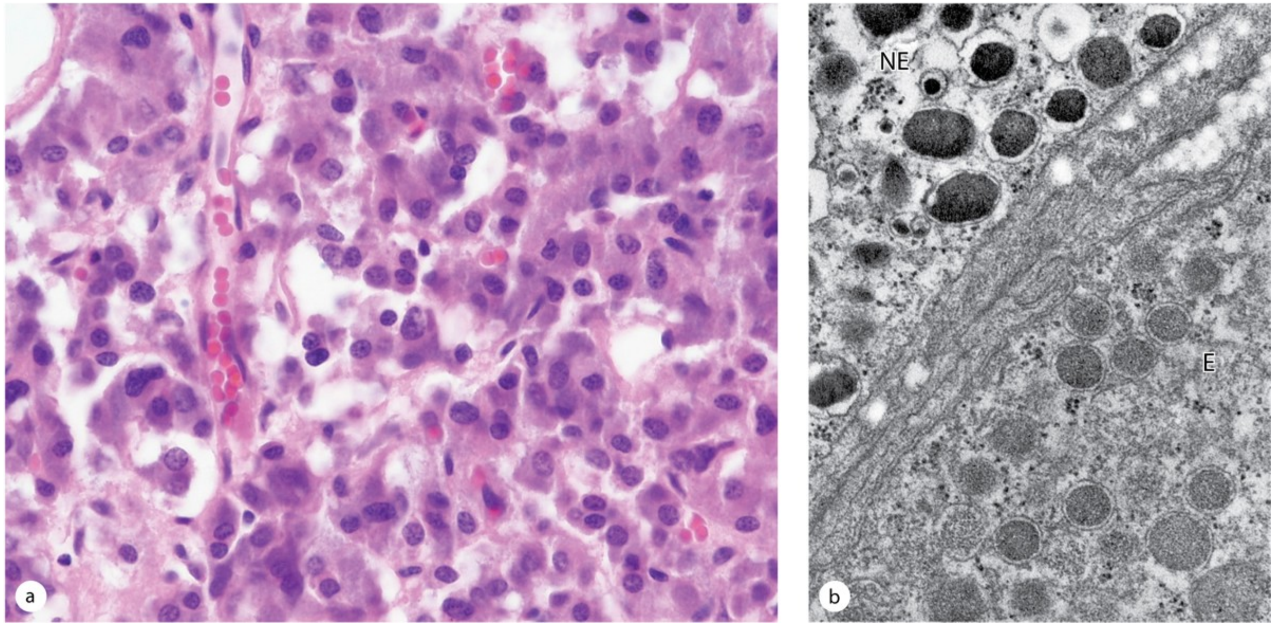
capsule (**C**), zonae glomerulosa (**G**), fasciculata (**F**), and reticularis (**R**), surrounding the medulla (**M**). Shown here are sections from two adrenal glands, stained with H&E (left) and Mallory trichrome, in which the sparse collagen appears blue (right).

(a, b) zona glomerulosa: rounded clusters of columnar cells principally secreting the mineral corticoid **aldosterone**.
(c, d) zona fasciculate: long cords of large, spongy-looking cells mainly secreting glucocorticoids such as **cortisol**.
(e, f) zona reticularis: better stained, arranged in a close network and secrete mainly **sex steroids**.

Cells of all the layers are closely associated with sinusoidal capillaries.

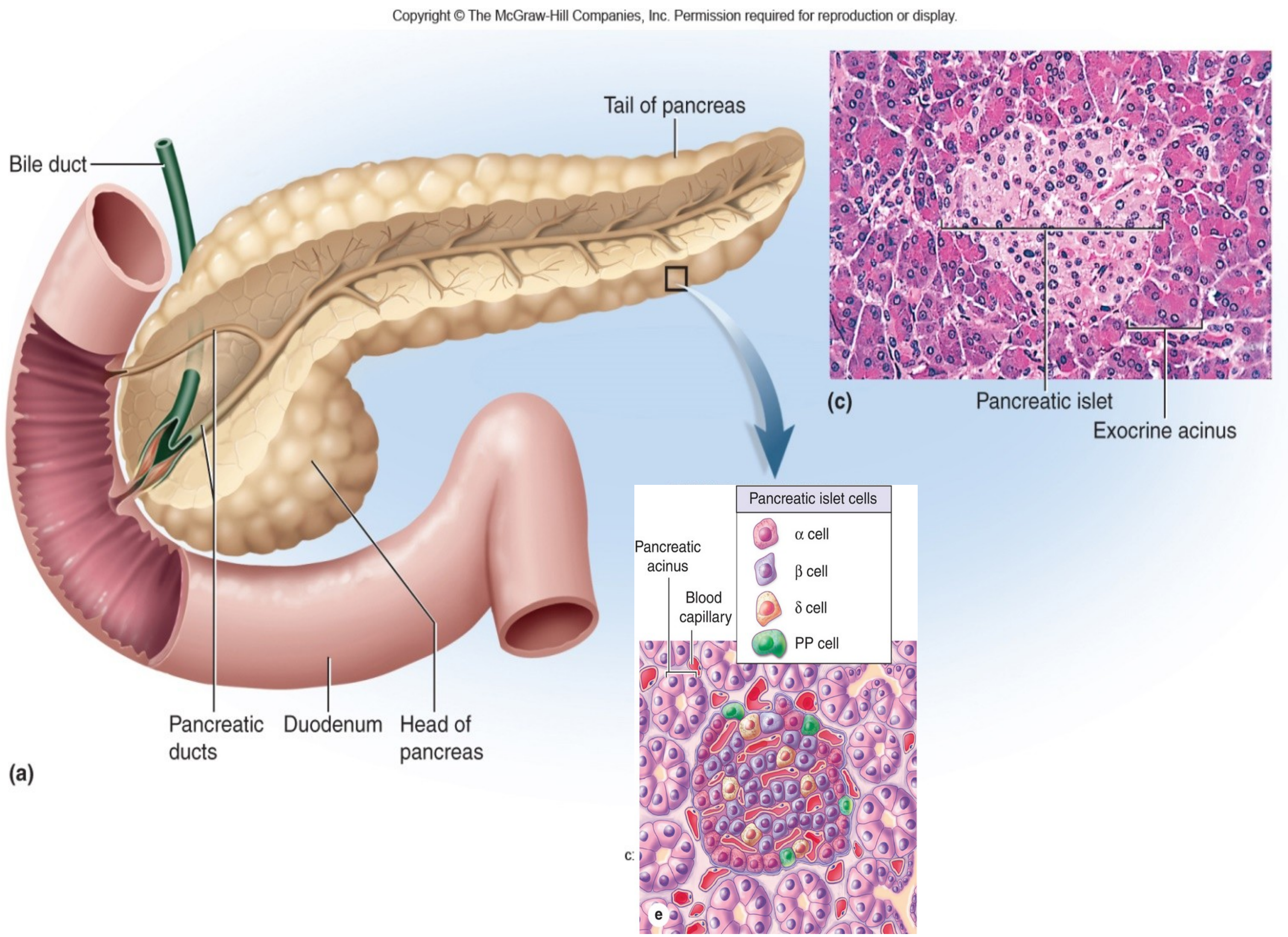
The hormone-secreting cells of the adrenal medulla are chromaffin cells, which resemble sympathetic neurons.

Chromaffin Cells: large pale-staining cells, arranged in cords interspersed with wide capillaries.
Granules of norepinephrine-secreting cells (**NE**) are more electron-dense than those of cells secreting epinephrine (**E**). Most of the hormone produced is epinephrine, which is only made in the adrenal medulla



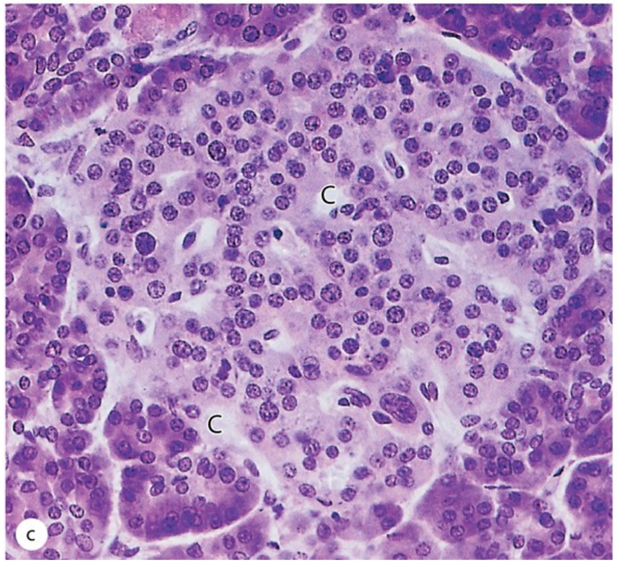
❯❯ **MEDICAL APPLICATION** In the adrenal medulla, **benign pheochromocytomas** periodically secrete high levels of atecholamines that cause swings in blood pressure between hypertension and hypotension.

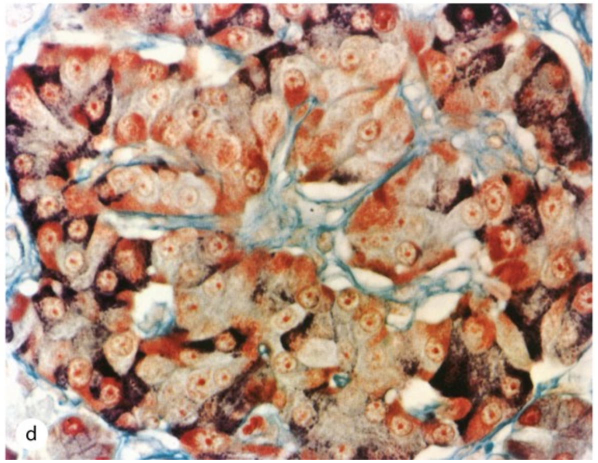
The Pancreatic Islets: endocrine cell clusters



α: glucagon breaks down **glycogen** and **fat** to increases blood glucose
β: insulin causes cell uptake of glucose, decrease of blood glucose
δ: Somatostatin inhibits release of GH and TSH in anterior pituitary and HCl secretion by gastric parietal cells
PP: Pancreatic polypeptide Polypeptide (rare) stimulates activity of gastric chief cells; inhibits bile secretion, pancreatic enzyme and bicarbonate secretion, and intestinal motility

Pancreatic islets are clumped masses of pale-staining endocrine cells embedded in the exocrine acinar tissue of the pancreas.





C: Fenestrated capillaries. This local vascular system allows specific islet hormones to help control secretion of other islet cells and the neighboring acini.

(d) An islet prepared with a modified aldehyde fuchsin stain shows that granules in the **peripheral α cells** are a deep brownish purple and the **central β cells** granules are brownish orange

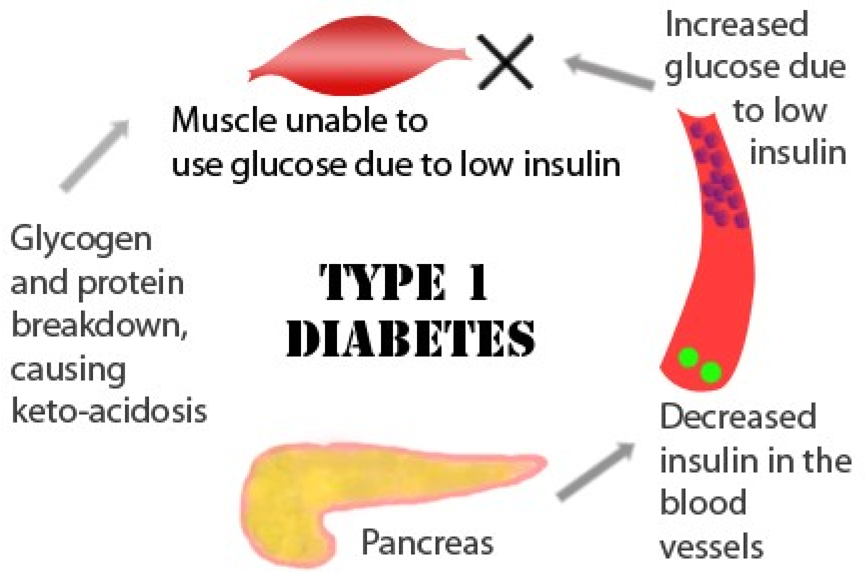
Immunohistochemistry with antibodies against the various islet polypeptide hormones allows definitive identification of each islet cell type.

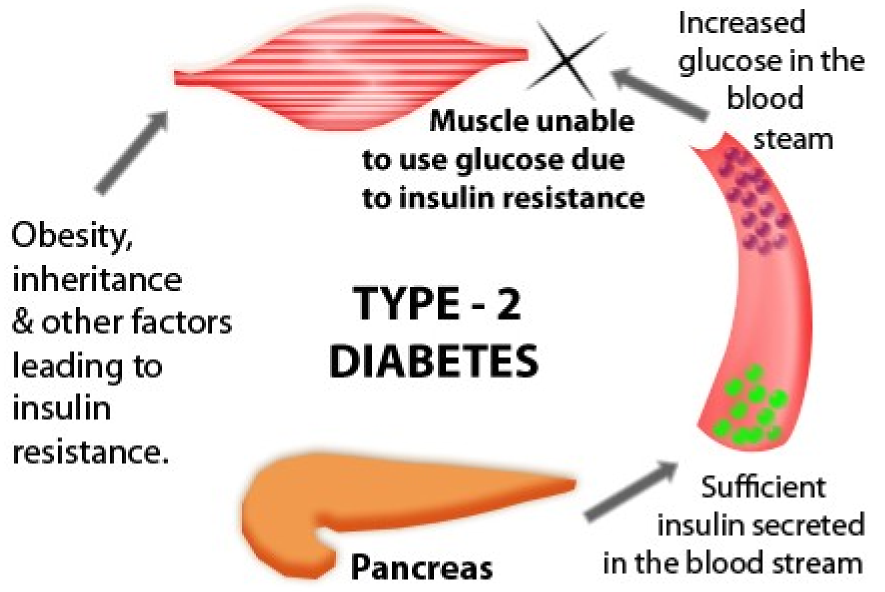
MEDICAL APPLICATION: Diabetes mellitus is characterized by loss of the insulin effect and a subsequent failure of cells to take up glucose, leading to elevated blood sugar or hyperglycemia.

Type 1 diabetes or insulin-dependent diabetes mellitus (IDDM) is caused by loss of the β cells from autoimmune destruction and is treated by regular injections of insulin.

Type 2 diabetes or non–insulin-dependent diabetes mellitus (NIDDM), β cells are present but fail to produce adequate levels of insulin in response to hyperglycemia and the peripheral target cells "resist" or no longer respond to the hormone. Type 2 diabetes commonly occurs with obesity, and poorly understood, multifactorial genetic components are also important in this disease's onset.

http://highered.mheducation.com/sites/0072507470/student_view0/chapter18/animation__blood_sugar_regulation_in_diabetics.html





The Thyroid Gland

Largest endocrine gland: Composed of two lobes and an isthmus below the larynx

- Dark reddish brown color due to rich blood supply

Thyroid follicles: sacs that compose most of thyroid

- Contain protein-rich colloid
- Follicular cells: simple cuboidal epithelium that lines follicles

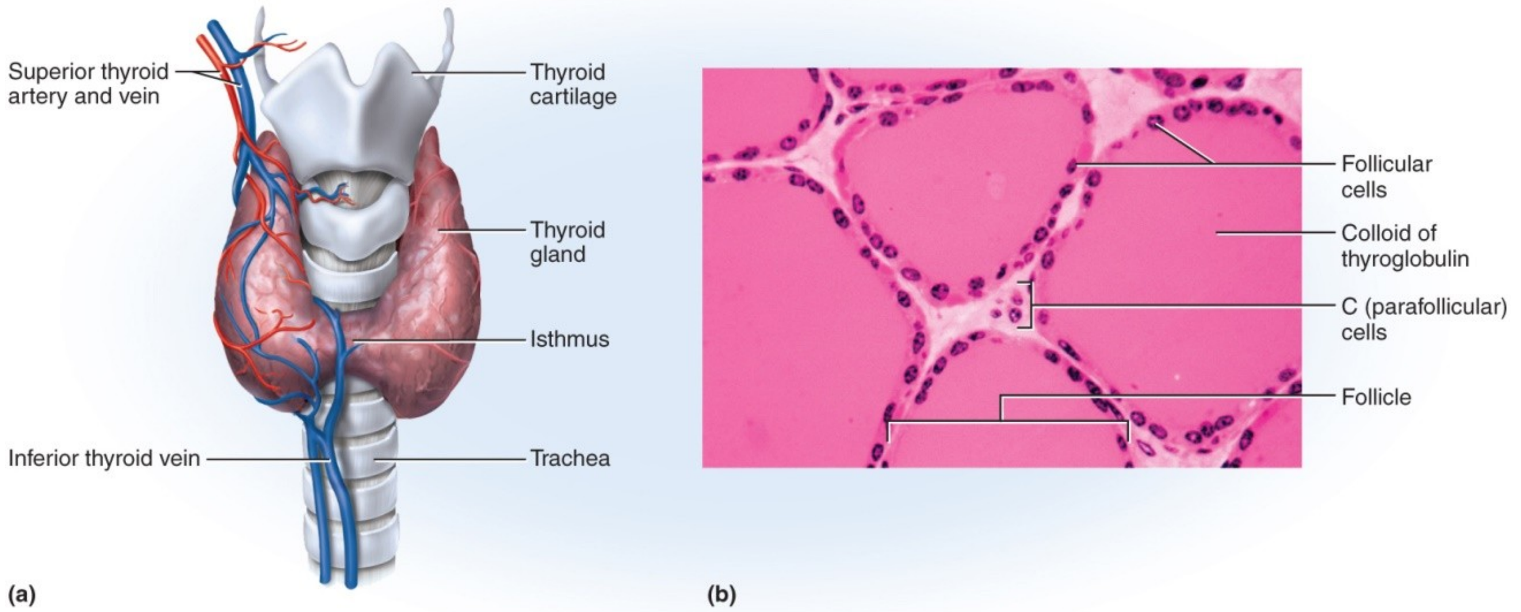
The Thyroid Gland

Thyrocytes (Follicular cells) secretes thyroxine (T_4 because of four iodine atoms) and triiodothyronine (T_3)—T_4 which is converted to T_3

- Increases metabolic rate, O_2 consumption, heat production (calorigenic effect), appetite, growth hormone secretion, alertness, quicker reflexes

Parafollicular (C or clear) cells secrete calcitonin with rising blood calcium

- Stimulates osteoblast activity and bone formation

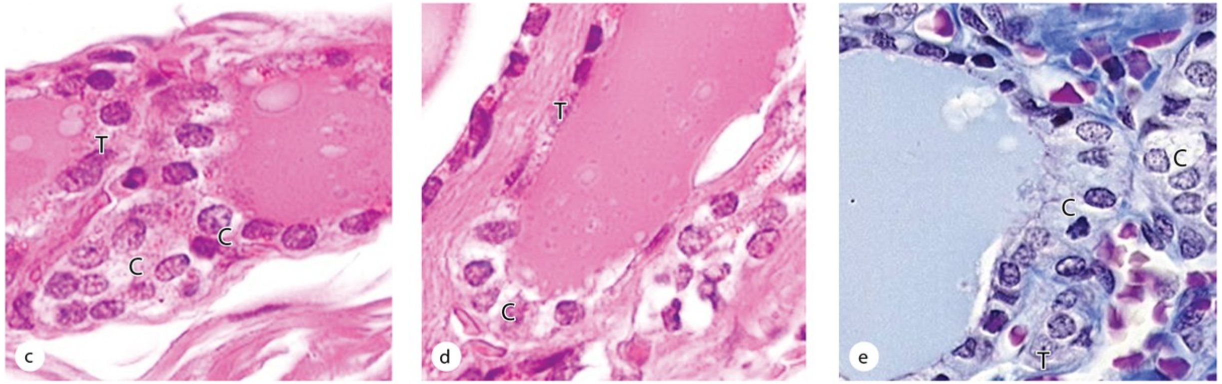


MEDICAL APPLICATION: Chronic dietary iodine deficiencies inhibit thyroid hormone production, causing thyrotropic cells of the anterior pituitary gland to produce excess TSH. This leads to excessive growth of thyroid follicles and enlargement of the thyroid gland, a condition known as goiter

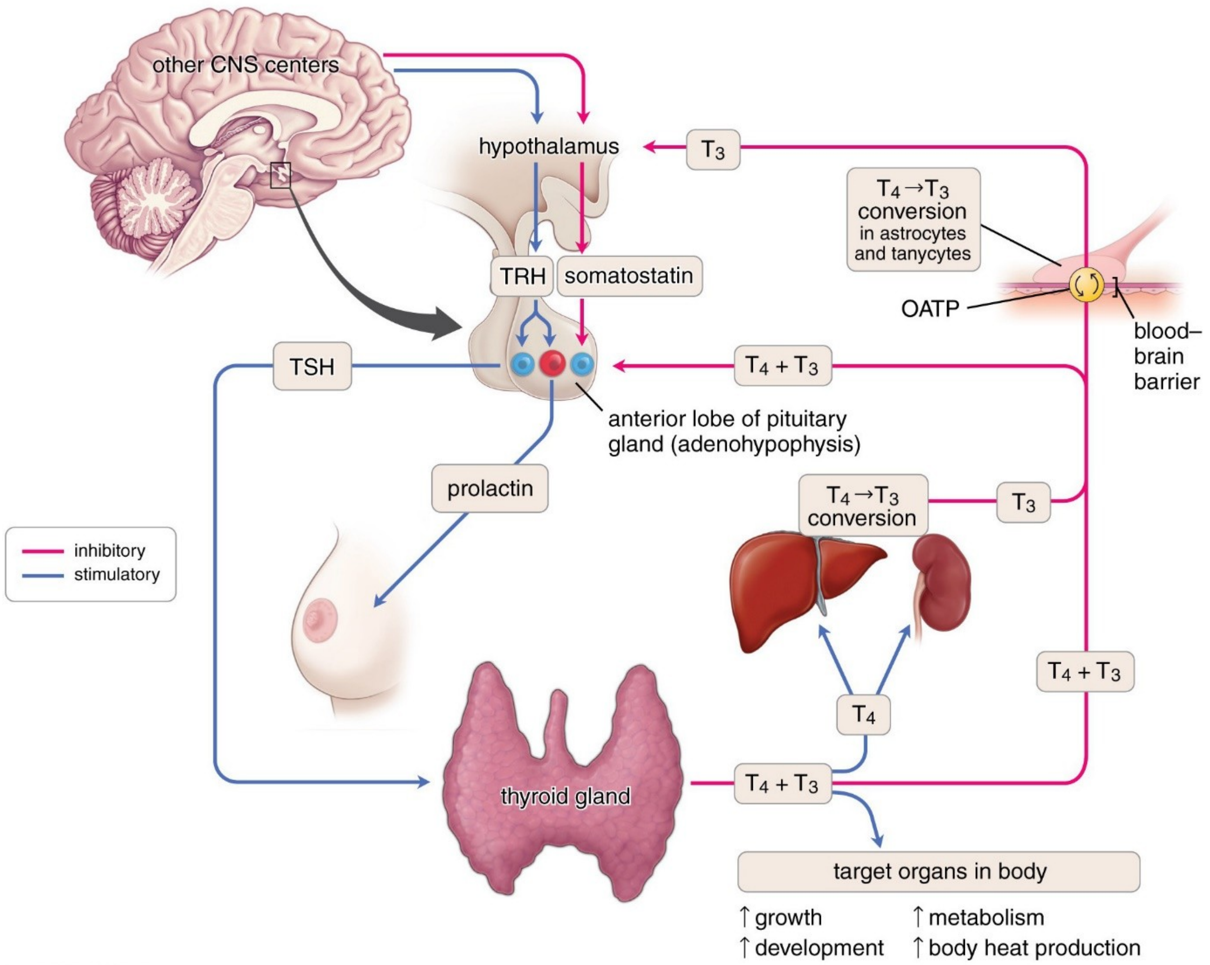
MEDICAL APPLICATIONS

Graves disease is an autoimmune disorder in which antibodies produce chronic stimulation of the follicular cells and release of thyroid hormones (hyperthyroidism), which causes a hypermetabolic state marked by weight loss, nervousness, sweating, heat intolerance, and other features.

Hypothyroidism, with reduced thyroid hormone levels, can be caused by local inflammation (thyroiditis) or inadequate secretion of TSH by the anterior pituitary gland and is often manifested by tiredness, weight gain, intolerance of cold, and decreased ability to concentrate.



Production, transport, and regulation of thyroid hormones is regulated through a negative feedback system



Follicular cells: produce 20X more T4 than T3. T4 → T3 (more active) in peripheral organs (e.g., liver, kidney)

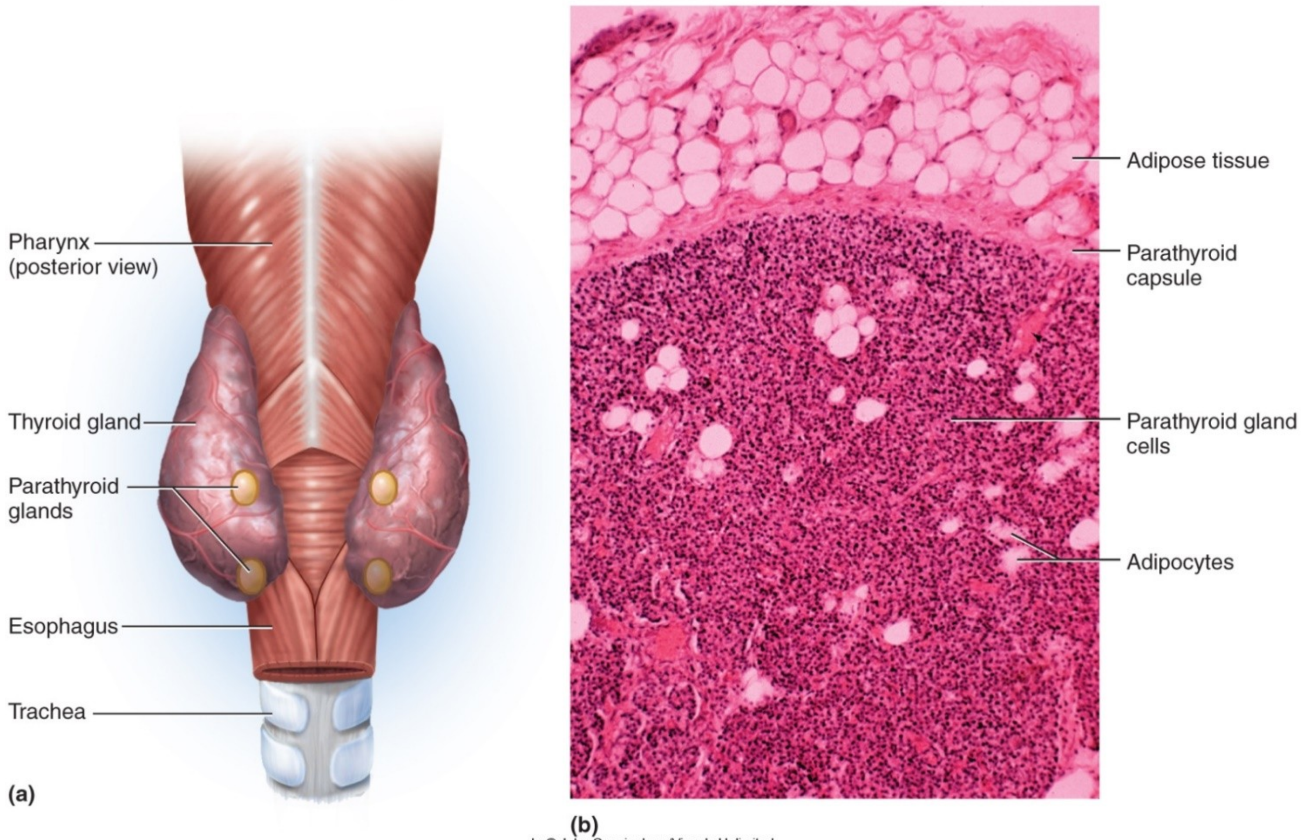
99% of T4 and T3: bound to thyroglobulin for solubility

Remaining free (unbound) T4 and T3: Crosses BBB for negative feedback on the system and inhibit further release In the hypothalamus, T3 inhibits TRH and stimulates somatostatin.

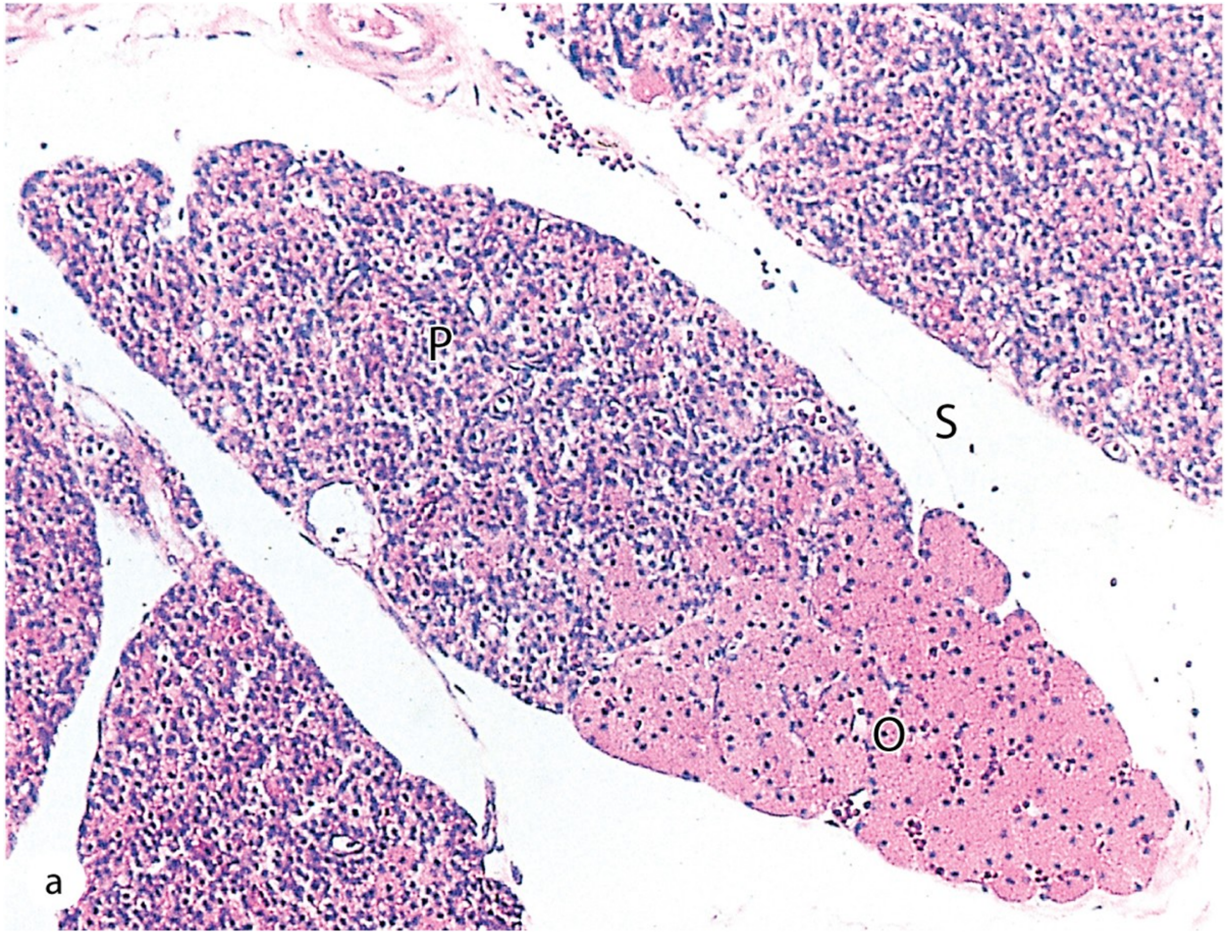
http://highered.mheducation.com/sites/9834092339/student_view0/chapter46/mechanism_of_thyroxine_action.html

The Parathyroid Glands

- Four glands partially embedded in posterior surface of thyroid gland
  - Can be found from as high as hyoid bone to as low as aortic arch
- **Secrete parathyroid hormone (PTH):**
  - Increases blood Ca^{2+} levels: decreased urinary excretion, promotes synthesis of calcitriol → increased digestive absorption of Ca^{2+}
  - Increased bone resorption via increase osteoclast activity



Parathyroid histology



A small lobe of parathyroid gland, surrounded by connective tissue septa (**S**), shows mainly densely packed cords of small principal cells (**P**). Older parathyroid glands show increasing numbers of much larger and acidophilic nonfunctional oxyphil cells (**O**) that may occur singly or in clumps of varying sizes

MEDICAL APPLICATION In **hypoparathyroidism**, diminished secretion of PTH can cause bones to become more mineralized and denser and striated muscle to exhibit abnormal contractions due to inadequate calcium ion concentrations.

Excessive PTH produced in **hyperparathyroidism** stimulates osteoclast number and activity, leading to increased levels of blood calcium that can be deposited pathologically in cartilage, arteries, or the kidneys.

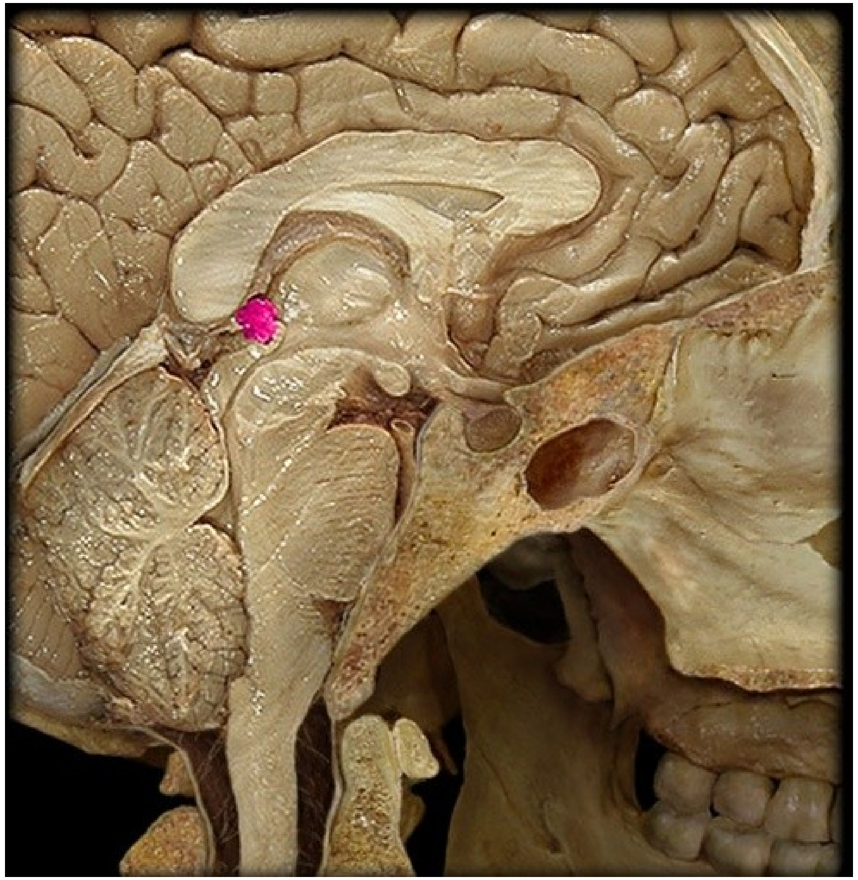
The Pineal Gland

After age 7, it undergoes **involution** (shrinkage), 75% by end of puberty

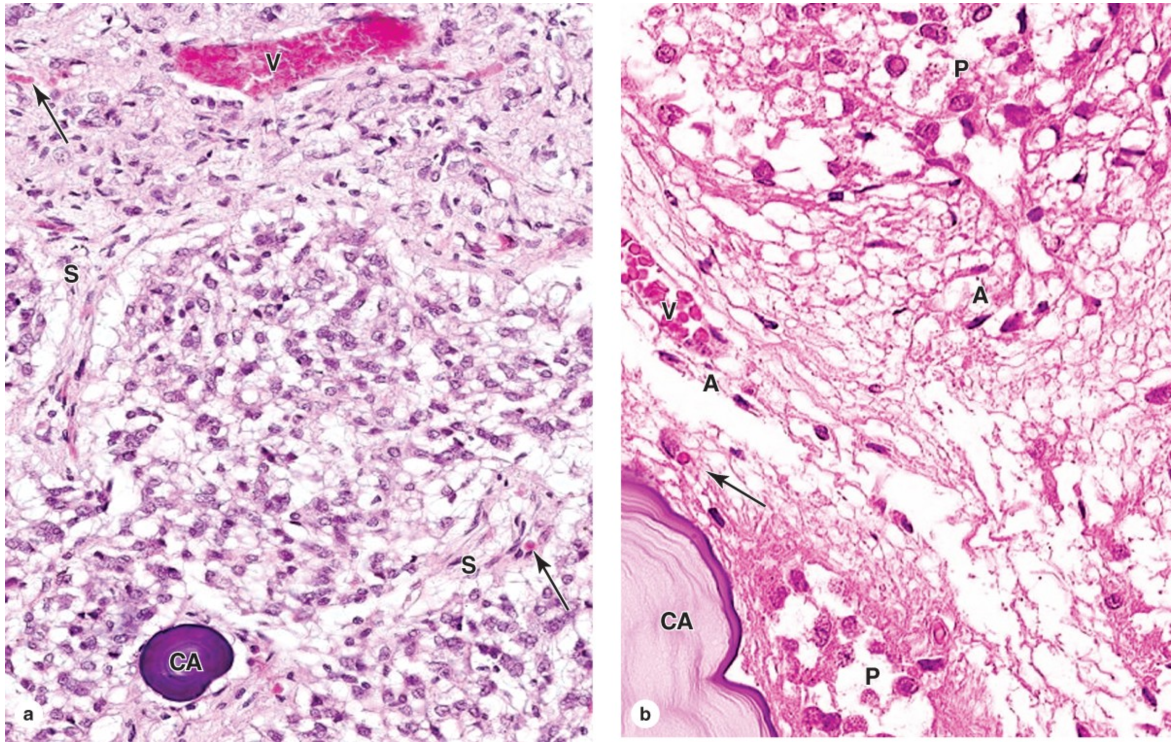
- Tiny mass of shrunken tissue in adults
- May regulate timing of puberty in humans

May synchronize physiological function with 24-hour **circadian rhythms** of daylight and darkness

- Synthesizes **melatonin** from serotonin during the night
- Fluctuates seasonally with changes in day length →
- **Seasonal affective disorder (SAD)** occurs in winter or northern climates
- Symptoms: depression, sleepiness, irritability, and carbohydrate craving
- Two to 3 hours of exposure to bright light each day reduces the melatonin levels and the symptoms (phototherapy)



Pineal Histology



Pinealocytes (**P**) surrounded by septa (**S**) containing venules (**V**) and capillaries (arrows
Corpus arenaceum (**CA**): extracellular mineral deposit called a of unknown physiologic significance but an excellent marker for the pineal

astrocytes (**A**): darker, more elongated nuclei
small blood vessels (**V**)
Capillaries (arrow) are not nearly as numerous as in other endocrine glands.

Along the septa run unmyelinated tracts of sympathetic fibers, associated indirectly with photoreceptive neurons in the retinas and running to the pinealocytes to stimulate melatonin release in periods of darkness.

MEDICAL APPLICATION

Densely calcified corpora arenacea can be used as landmarks for the midline location of the pineal gland in a various radiological examinations of the brain. Tumors originating from pinealocytes are very rare, but they can be either benign or highly malignant.

TABLE 20–5 Cells, important hormones, and functions of other major endocrine organs.

Gland	Endocrine Cells	Major Hormones	Major Functions
Adrenal glands: Cortex	Cells of zona glomerulosa	Mineralocorticoids	Stimulate renal reabsorption of water and Na^+ and secretion of K^+ to maintain salt and water balance
	Cells of zona fasciculata	Glucocorticoids	Influence carbohydrate metabolism; suppress immune cell activities
	Cells of zona reticularis	Weak androgens	Precursors for testosterone or estrogen
Adrenal glands: Medulla	Chromaffin cells	Epinephrine	Increases heart rate and constricts vessels
		Norepinephrine	Dilates vessels and increases glucose release
Pancreatic islets	α Cells	Glucagon	Raises blood glucose levels
	β Cells	Insulin	Lowers blood glucose levels
	δ Cells	Somatostatin	Inhibits secretion of insulin, glucagon, and somatotropin
	PP cells	Pancreatic polypeptide	Inhibits secretion of pancreatic enzymes and HCO_3^-
Thyroid glands	Follicular cells	Thyroid hormones (T_3 and T_4)	Increase metabolic rate
	Parafollicular or C cells	Calcitonin	Lowers blood Ca^{2+} levels by inhibiting osteoclast activity
Parathyroid glands	Chief cells	Parathyroid hormone (PTH)	Raises blood Ca^{2+} levels by stimulating osteoclast activity
Pineal gland	Pinealocytes	Melatonin	Regulates circadian rhythms

Male Reproductive

CHAPTER 21

Sex Determination: More Complicated Than You Thought: http://ed.ted.com/on/C1lWtSAb

Overview of the Reproductive System

Male reproductive system: produce sperm, introduces gametes into female

Female reproductive system: produces eggs, receives sperm, provides for the union of the gametes, harbors the fetus, and nourishes the offspring

Primary sex organs (**gonads**): Produce gametes (**testes** or **ovaries**)

Secondary sex organs: necessary for reproduction, but don't produce gametes

- Male: system of ducts, glands; penis delivers sperm cells
- Female: uterine tubes, uterus, and vagina receive sperm and harbor developing fetus

TABLE 27.1 The External and Internal Genitalia

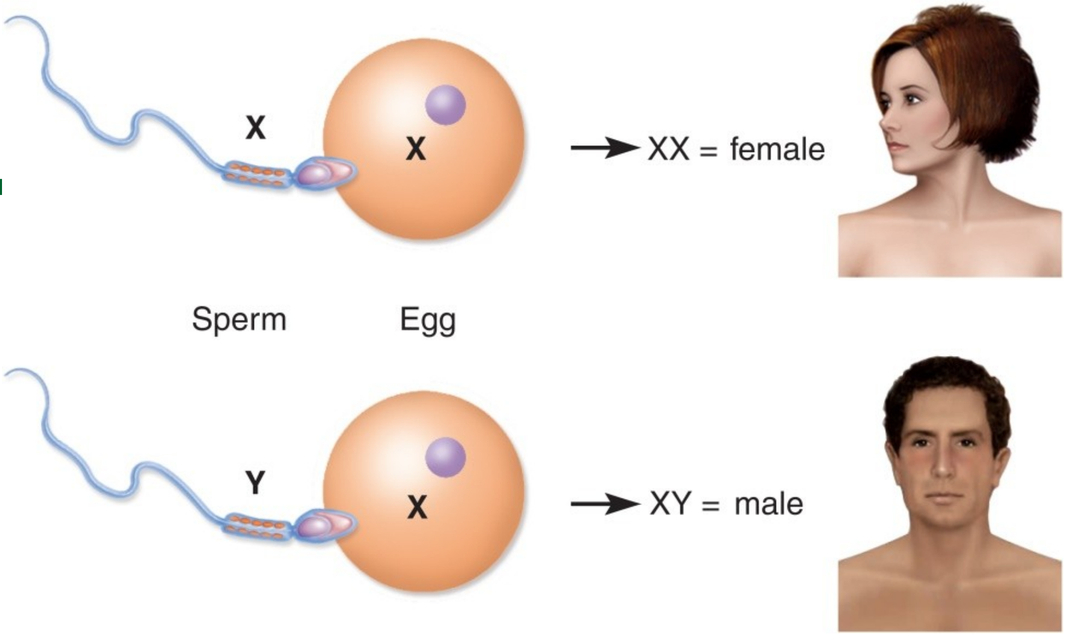
External Genitalia	Internal Genitalia
Male	
Penis	Testes (s., *testis*)
Scrotum	Epididymides (s., *epididymis*) Ductus deferentes (s., *ductus deferens*) Seminal vesicles Prostate Bulbourethral glands
Female	
Mons pubis	Ovaries
Labia majora (s., *labium majus*)	Uterine tubes
Labia minora (s., *labium minus*)	Uterus
Clitoris	Vagina
Vaginal orifice	
Vestibular bulbs	
Vestibular glands	
Paraurethral glands	

Sexual reproduction

Male parent: Y chromosome, gamete (sperm, spermatozoon) has motility

Female parent: lacks Y chromosome, gamete (egg, ovum) contains nutrients for developing embryo

Mammals: female parent provides sheltered internal environment and prenatal nutrition of the embryo



Androgen-Insensitivity Syndrome: XY chromosomes, testes produce normal male levels of testosterone but target cells lack receptors. External genitalia develop female anatomy as if no testosterone were present, presence of testes in the abdomen, no uterus or menstruation

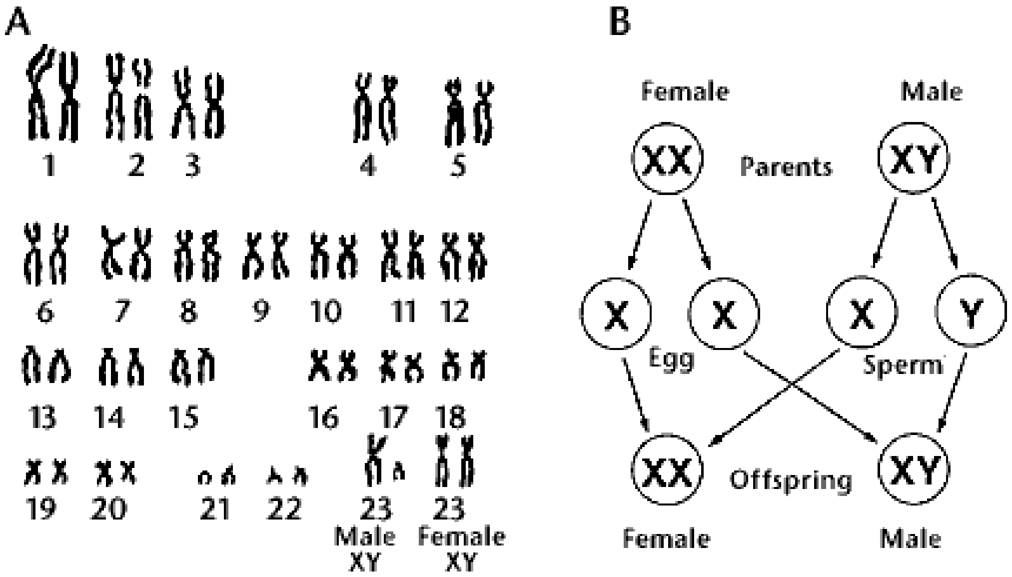
http://www.dailymail.co.uk/video/news/video-1155630/Doctors-explain-androgen-insensitivity-syndrome.html

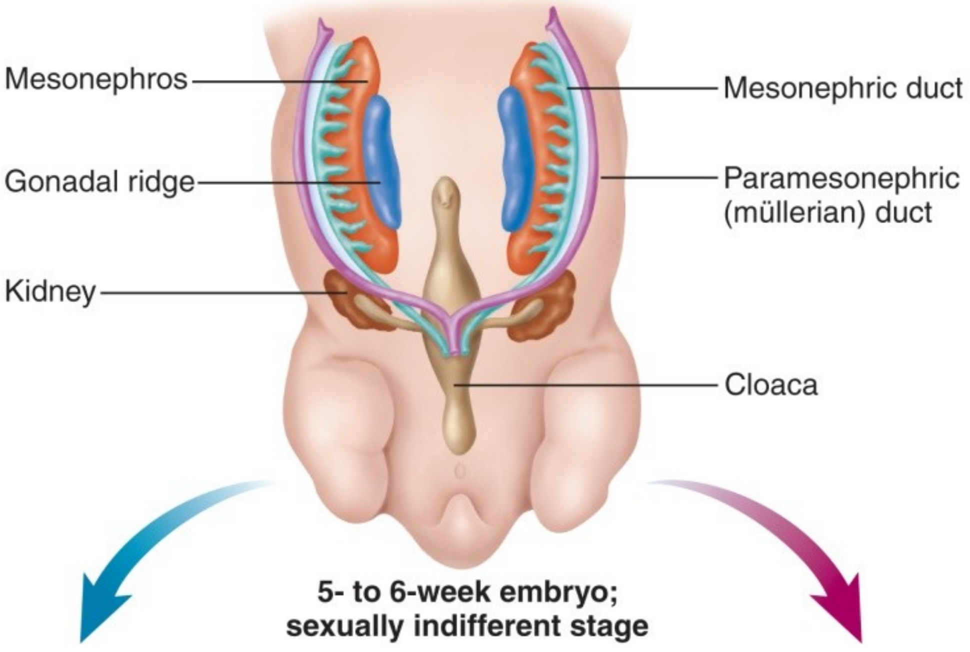
Chromosomes and Sex Determination

Human cells: 22 pairs of autosomes, 1 pair of sex chromosomes (XY males: XX females)

<u>Initially, a fetus is sexually undifferentiated</u>
SRY gene (sex-determining region of Y chromosome): codes for a protein, testes-determining factor (TDF), that initiates development of testes

Gonads begin to develop at 5 or 6 weeks as gonadal ridges

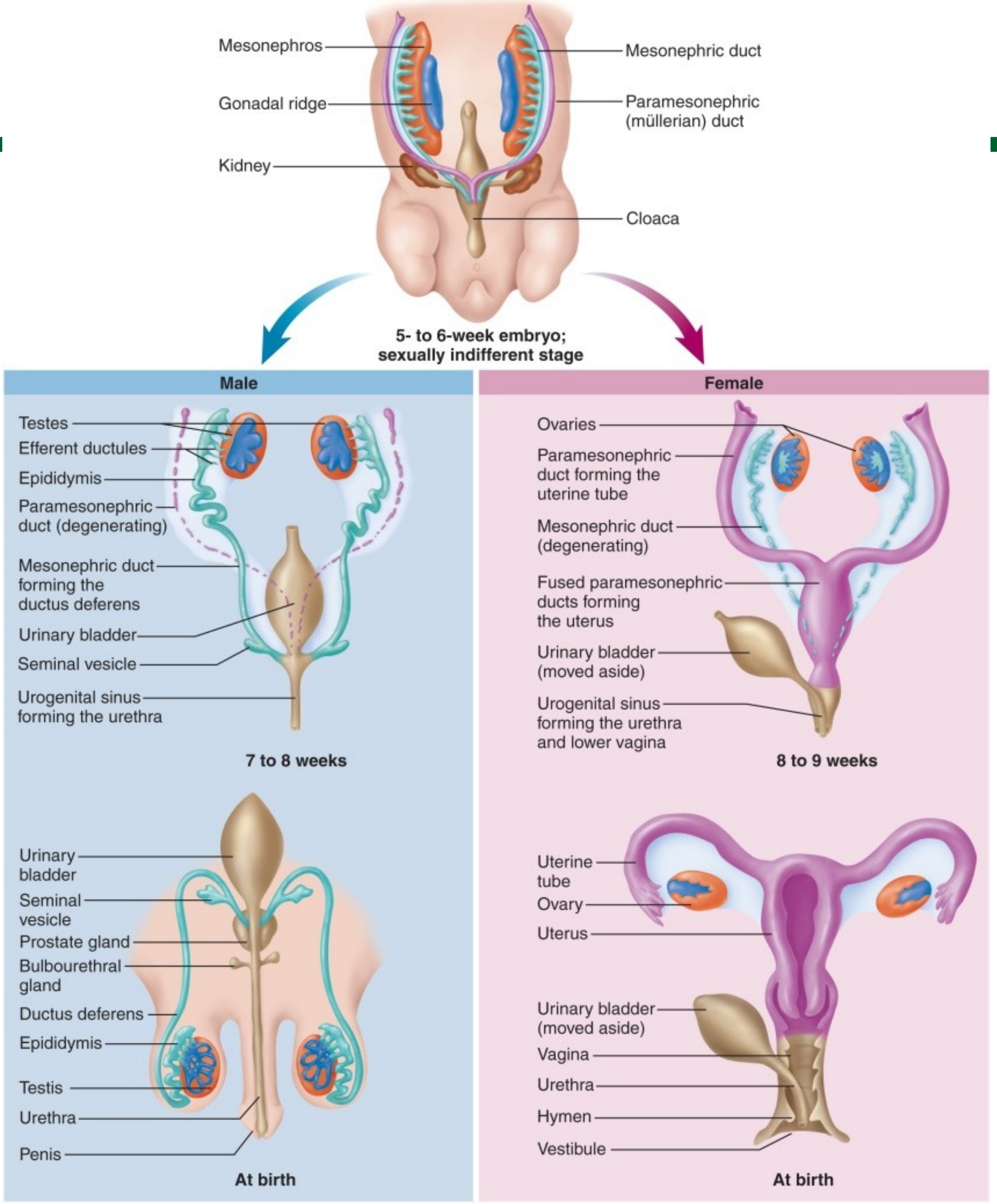




Sexual Differentiation

Male: gonads secrete testosterone at 8 to 9 weeks, **stimulate mesonephric (wolffian) ducts** → male reproductive system;
Testes secrete **müllerian-inhibiting factor** causing **paramesonephric ducts degeneration**
Female: Paramesonephric (müllerian) ducts → female reproductive tract; mesonephric ducts degenerate

If estrogen was the hormone that directed the female development, all fetuses would be feminized (estrogen levels are always high in pregnancy)



Similarity of external genitalia

Male:

Genital tubercle → head (glans) of penis

Urogenital folds encloses urethra → penis

Labioscrotal folds → scrotum

Female:

Genital tubercle → glans of clitoris

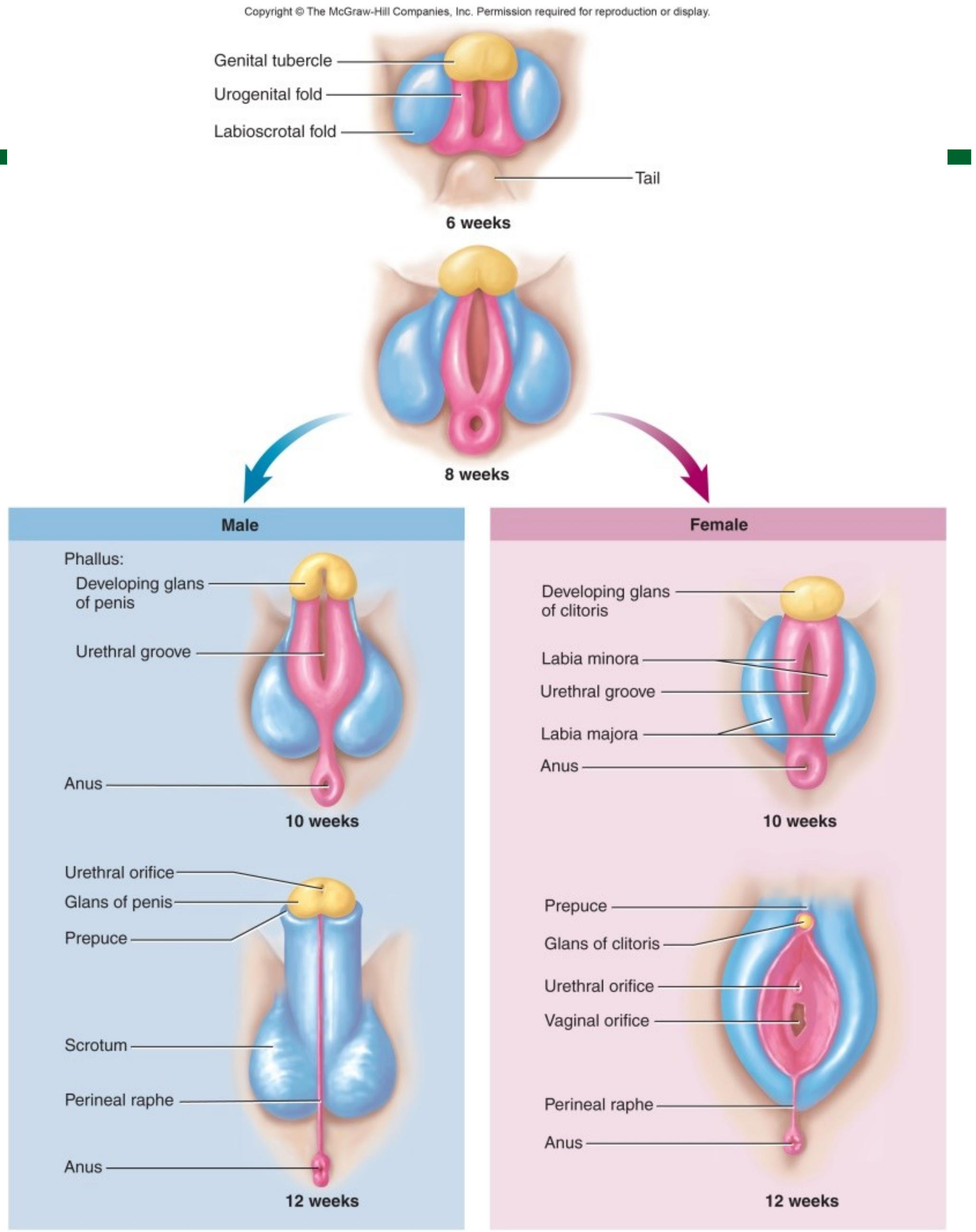
Urogenital folds → labia minora

Labioscrotal folds → labia majora

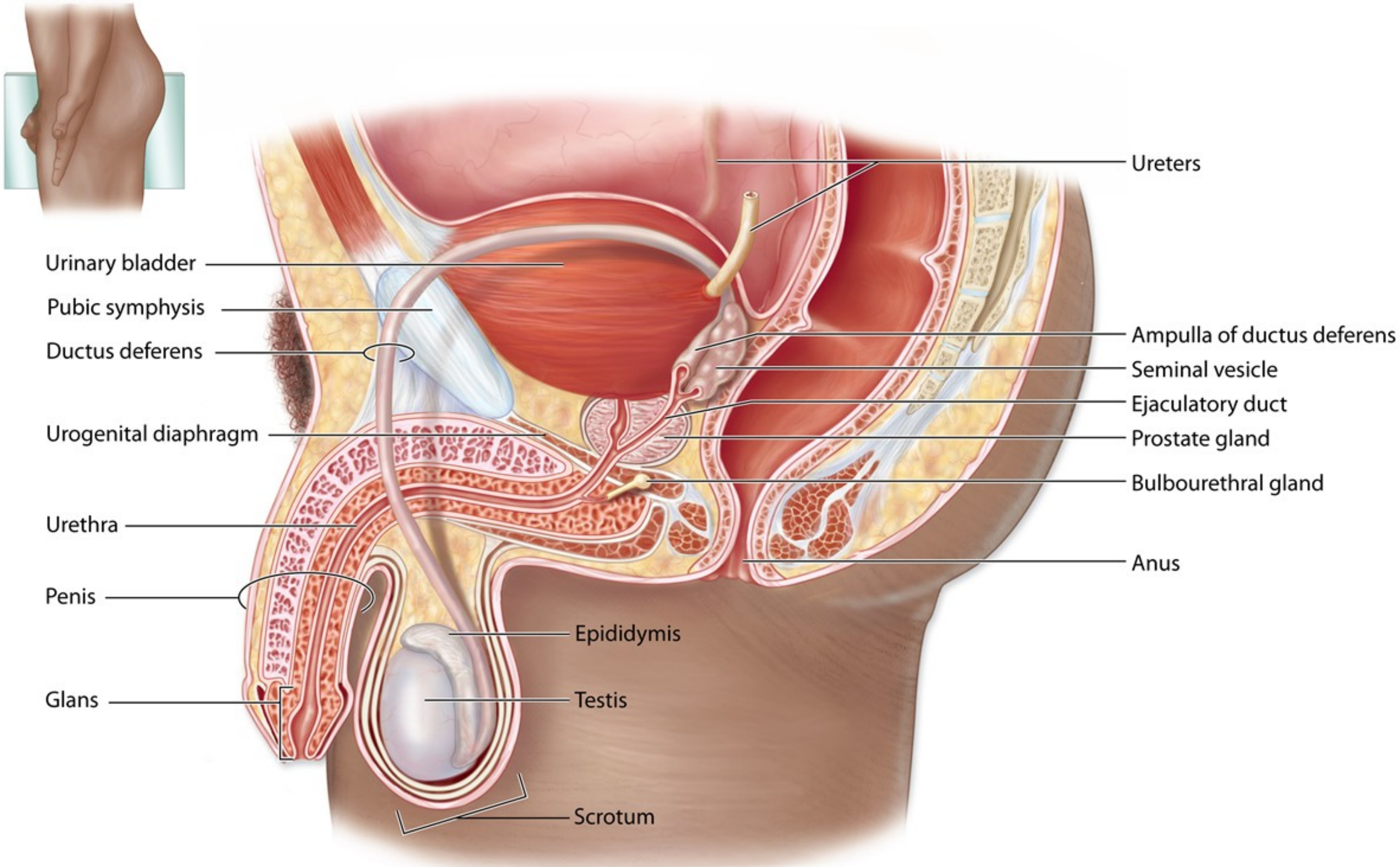
Genitalia formed by week 12

Male and female organs from same embryonic structure are homologous

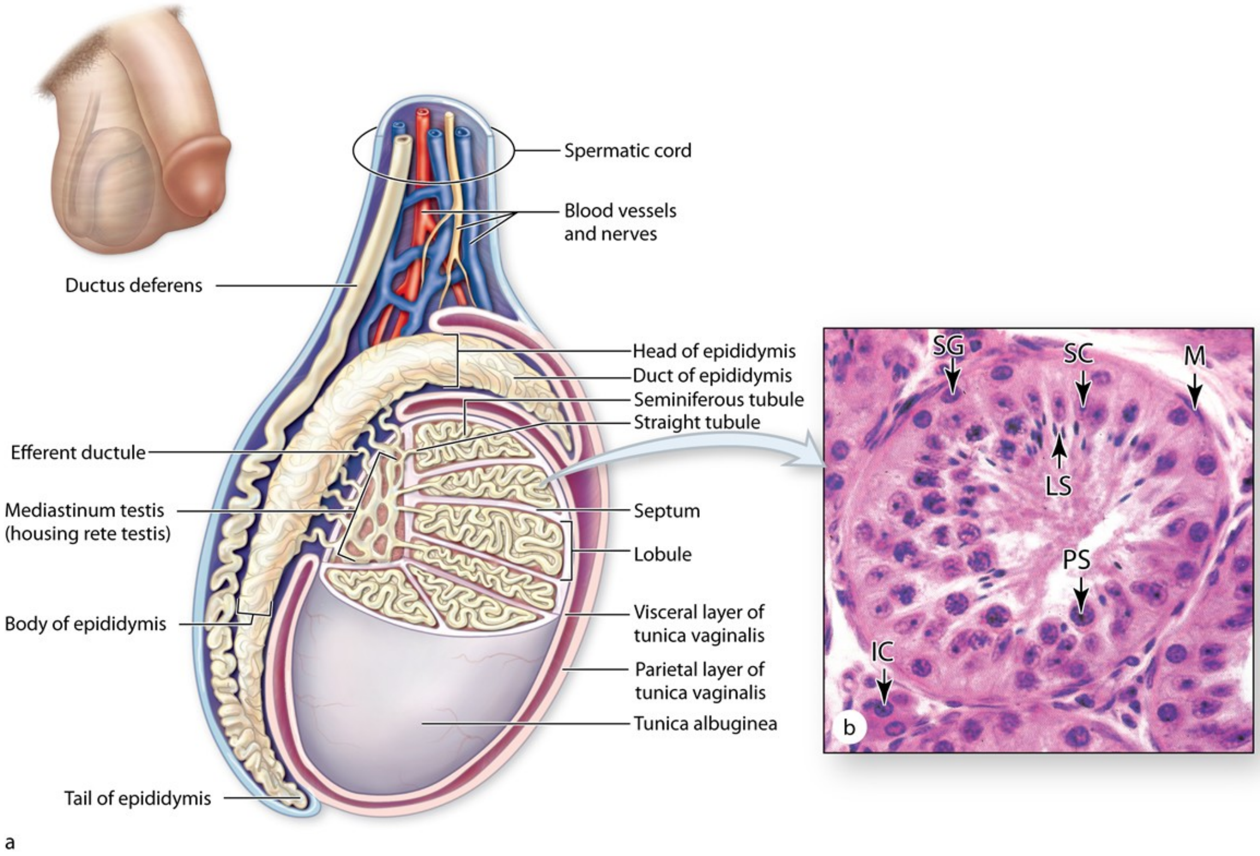
Penis~clitoris, scrotum~labia majora



The male reproductive system



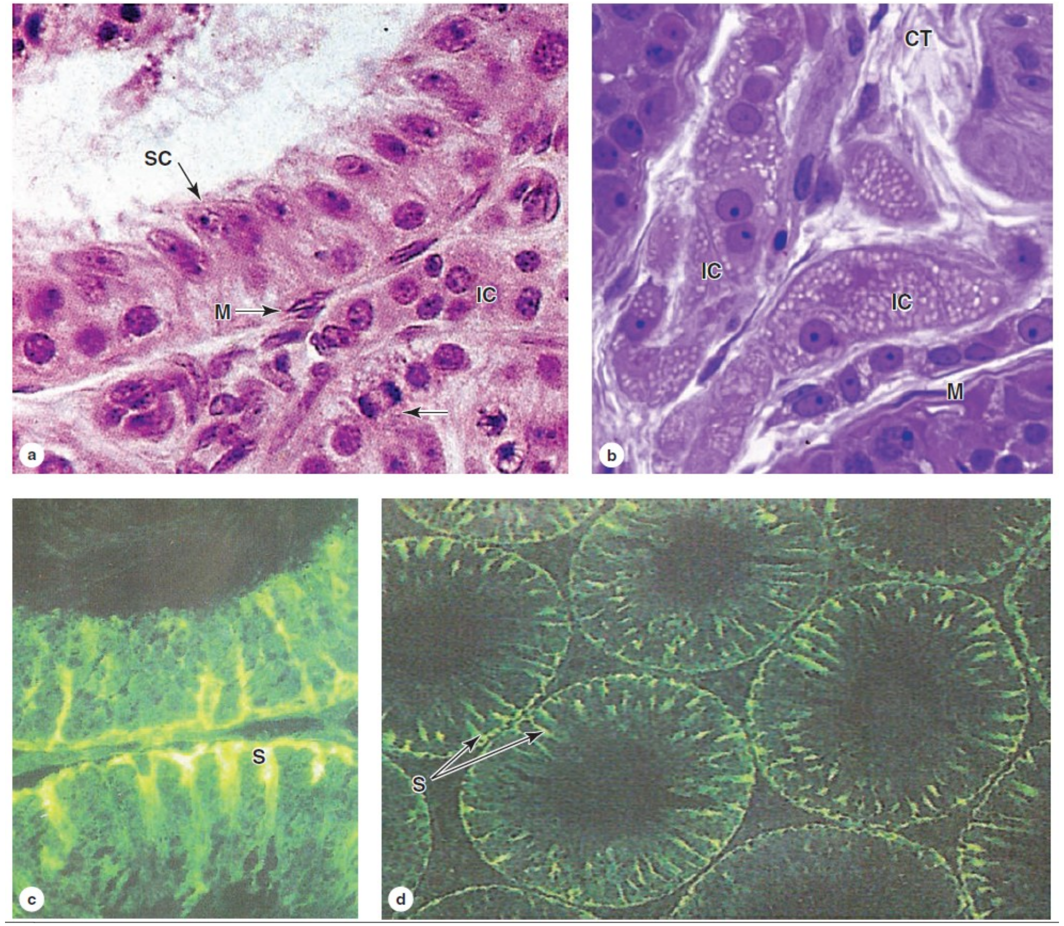
The Testes: (testicles: endocrine /exocrine glands that produce sex hormones and sperm



Spermatogonia (SG) **Sertoli Cells (SC)**
primary spermatocytes (PS) **late spermatids (LS)**
interstitial cells (IC)

Tunica Vaginalis: anterior cover
Tunica Albuginea: white fibrous capsule
Connective tissue septa: divides testes 250 to 300 lobules
Seminiferous tubules: 1 to 3 per lobule, lined with a thick germinal epithelium for sperm generation
Interstitial (Leydig) cells: between tubules produce testosterone
Sustentacular (Sertoli) Cells: between germ cells, protect the germ cells, and promote their development
Germ cells depend on them for nutrients, waste removal, growth factors, and other needs

Seminiferous tubule and interstitial cells



(a-b) Seminiferous tubules are surrounded by connective tissue (**CT**) containing many large interstitial cells (**IC**) that secrete androgens. Sertoli cells (**SC**),
Dividing spermatogenic stem cells with round nuclei (**arrow**).

(c-d) Immunohistochemistry (antibody against sulfated glycoprotein-1 of Sertoli cells (**S**) in the seminiferous tubules.

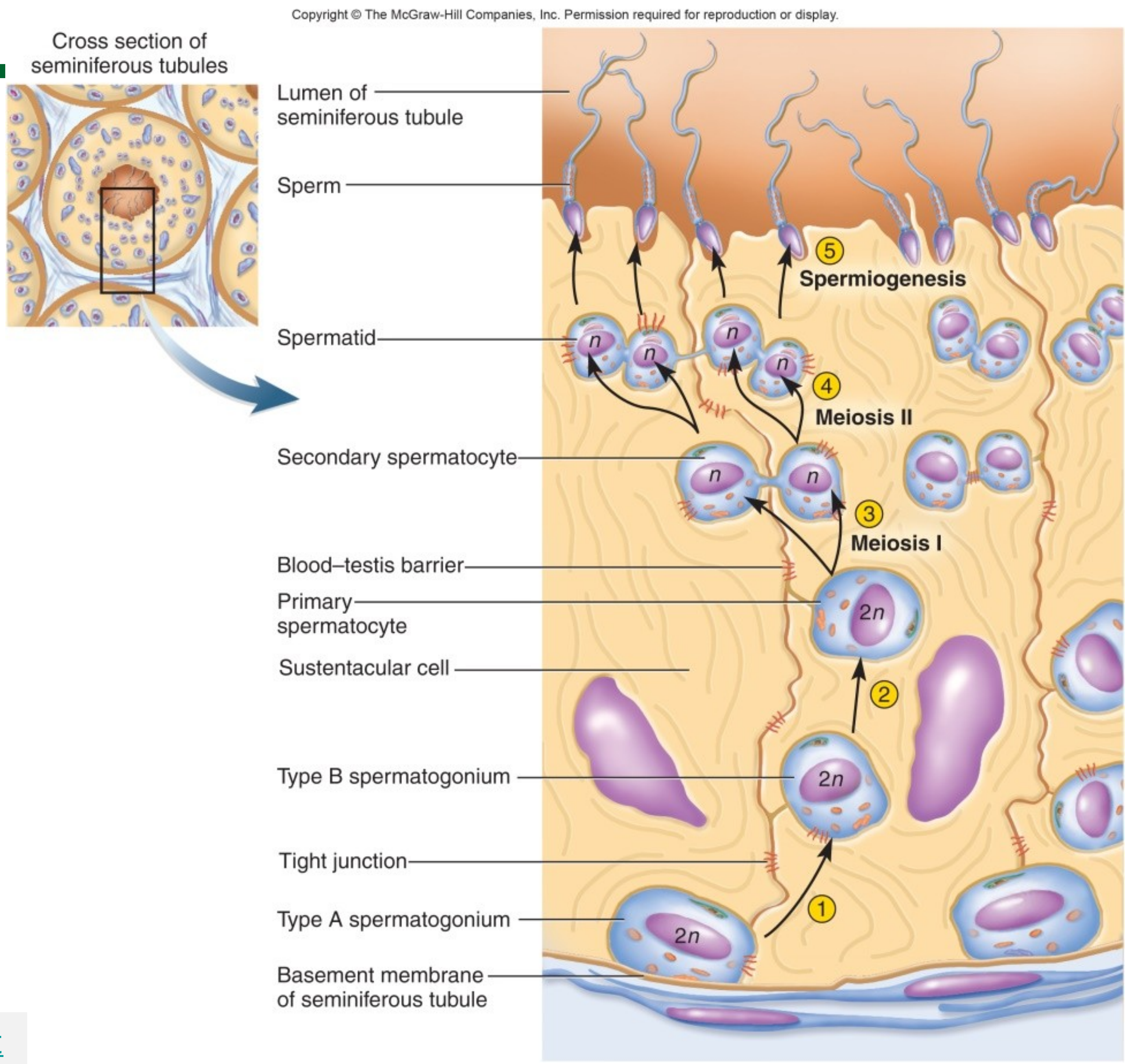
MEDICAL APPLICATION Both interstitial cell tumors and Sertoli cell tumors are rare. Most (95%) testicular cancer involves germ cell tumors, which only appear after puberty and are much more likely to develop in men with untreated cryptorchidism.

Spermatogenesis

Spermatogonia: divide by mitosis in seminiferous tubules

- One daughter cell of each division remains in tubule wall as stem cell: **Type A spermatogonium**
- Other daughter cell migrates slightly away from wall and is on its way to producing sperm: **Type B spermatogonium**

Primary spermactye (protected by the blood–testis barrier) → secondary spermacyte → spermatid → sperm



http://highered.mheducation.com/sites/0072495855/student_view0/chapter28/animation__spermatogenesis__quiz_1_.html

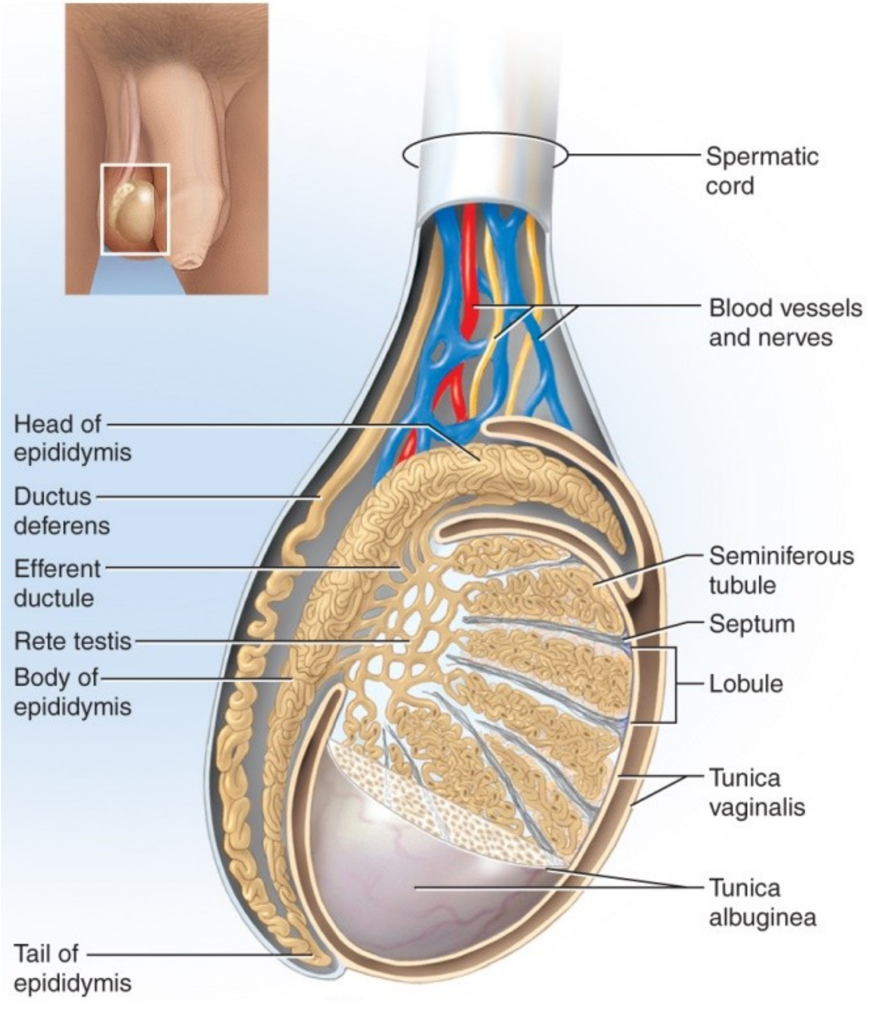
Rete Testes

Rete testis: collects sperm from seminiferous tubules, move with flow of fluid secreted by the sustentacular cells. Sperm do not swim while in the male reproductive tract.

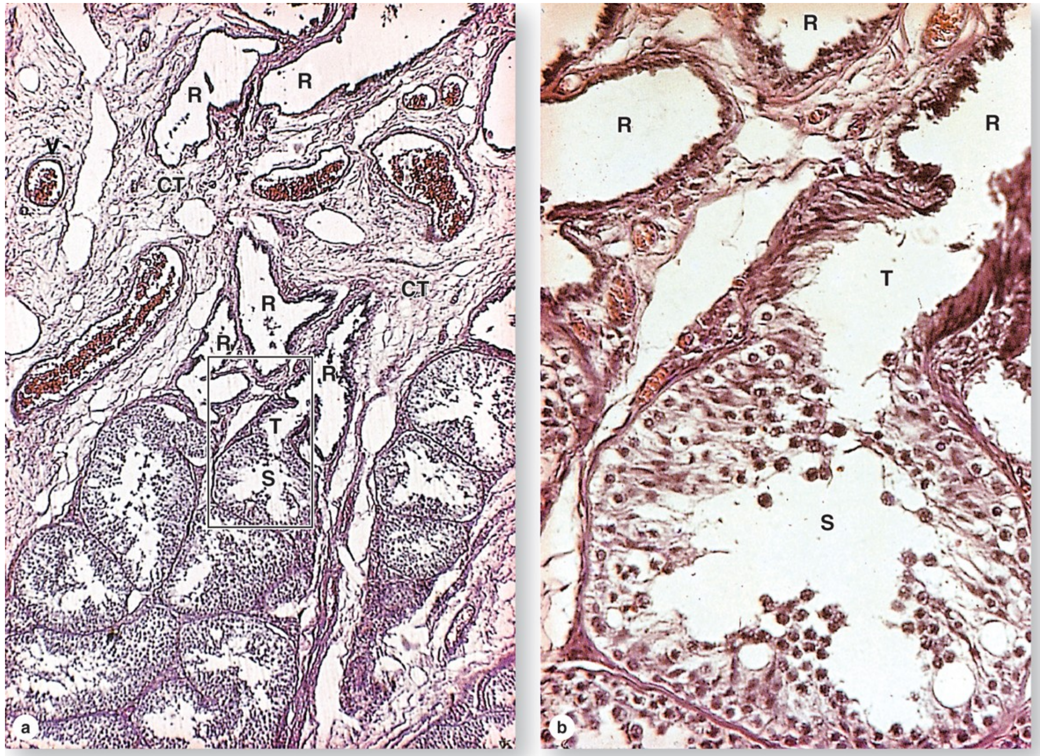
Testicular artery: Low BP, poor O2 supply to the testes.

Blood flow: Testicular artery → pampiniform → testicular veins → inferior vena cava (R) or left renal vein (L)

Blood–testis barrier (BTB): tight junctions between sustentacular cells, keeps Abs out, as germ cells are immunologically different from body cells and would be attacked by the immune system



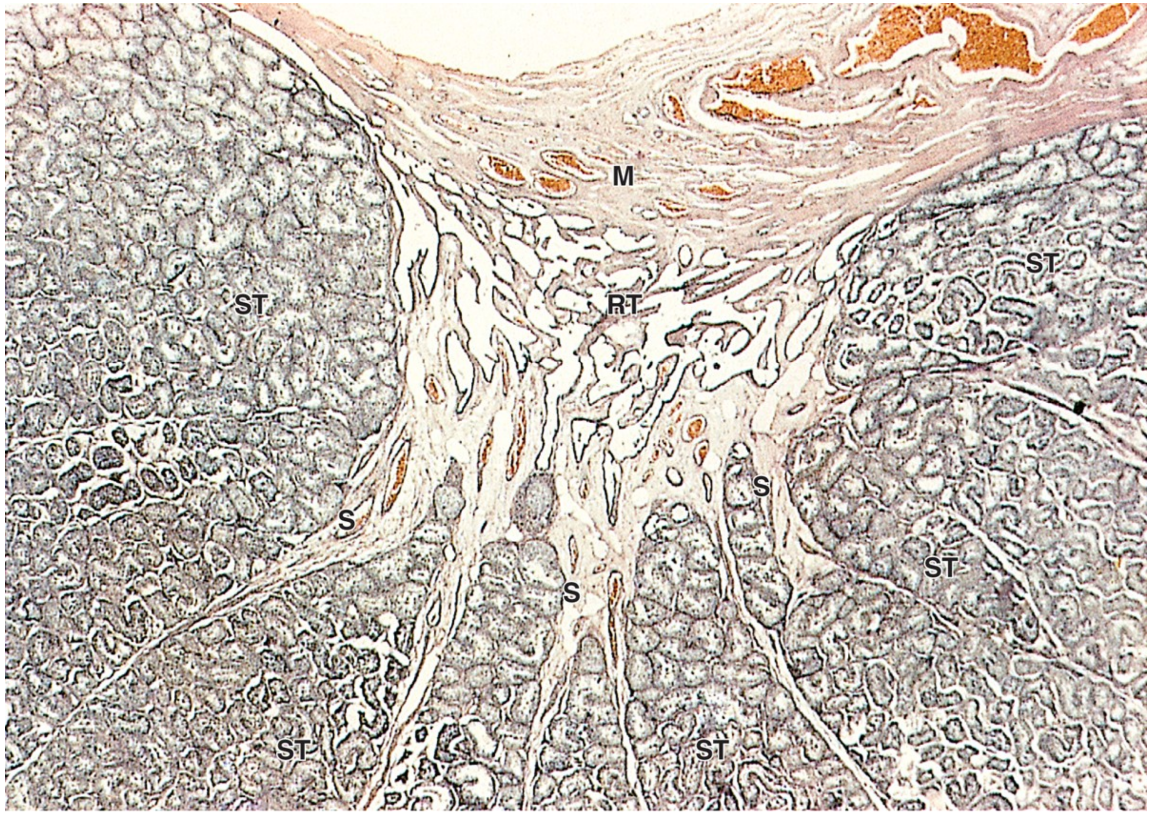
Seminiferous tubules, straight tubules and rete testis



(a) The seminiferous tubules (**S**) drain into short, much narrower straight tubules (**T**), which connect to the rete testis (**R**), a network of channels embedded along with blood vessels (**V**) in the connective tissue (**CT**) of the mediastinum testis.

(b) At higher magnification the enclosed portion of part **a** shows the transition from wide seminiferous tubule (**S**) to the straight tubule (**T**). Initially the straight tubule wall has only tall Sertoli cells devoid of germ cells. The wall becomes a **simple cuboidal epithelium** near its connection to the rete testis (**R**), which is also lined with simple cuboidal epithelium

Lobules converging at rete testis



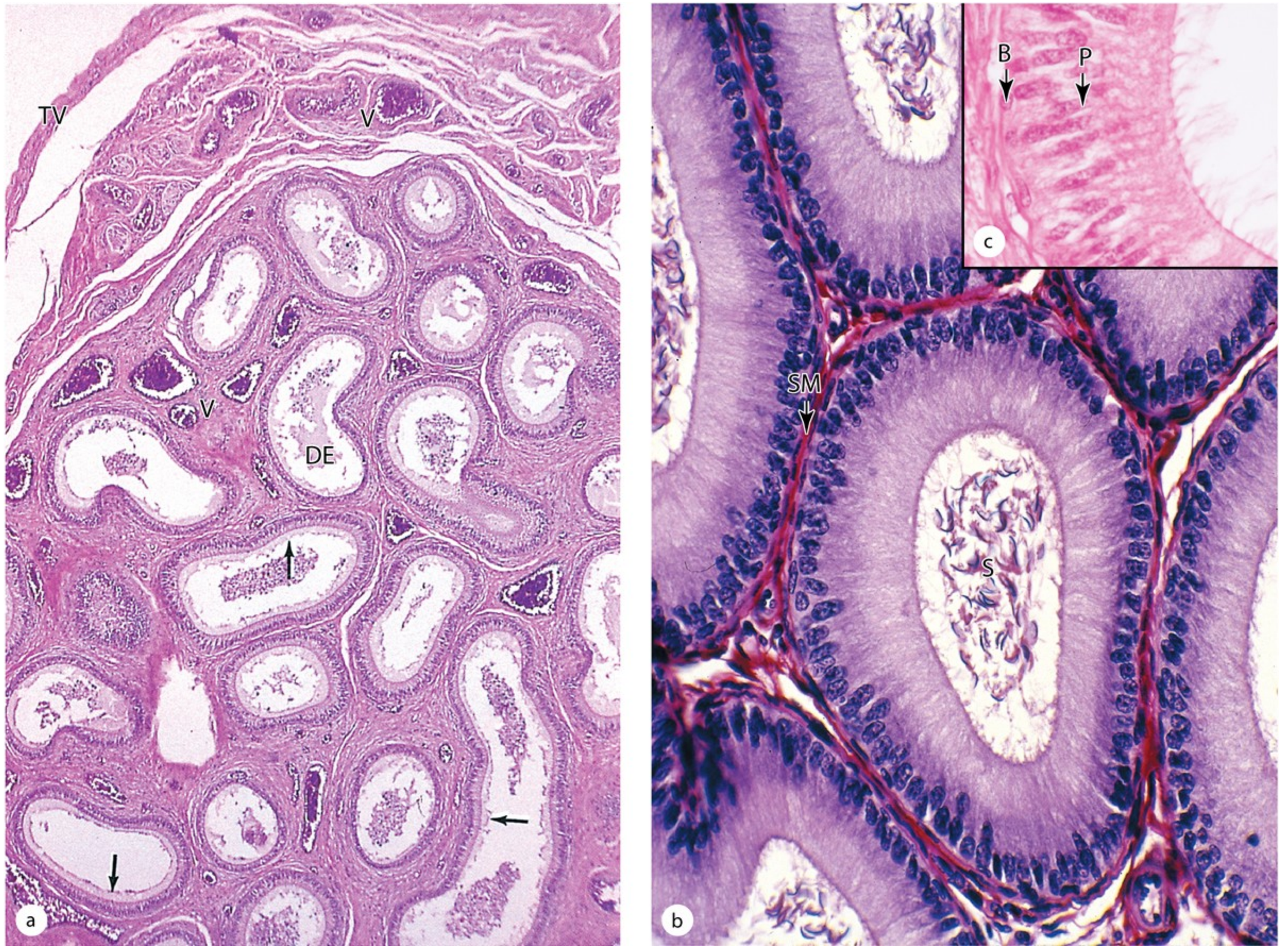
Mediastinum testis (**M**) form thin septa (**S**) to subdivide testis.
Seminiferous tubules (**ST**) form rete testis (**RT): **move sperm into the epididymis.

MEDICAL APPLICATION Acute or chronic inflammation of the testis ducts (**orchitis)** can be caused by urinary tract infection or *Chlamydia* or *Neisseria gonorrhoeae*.

Persistent inflammation (**epididymitis)** causes massive invasion by leukocytes into the infected duct, stimulating fibrosis that obstructs the epididymis and is a common cause of male infertility.

Killer Sex Disease Now DRUG RESISTANT! https://www.youtube.com/watch?v=0b2ngu5Vr4Y

Epididymis: sperm undergo maturation and short-term storage



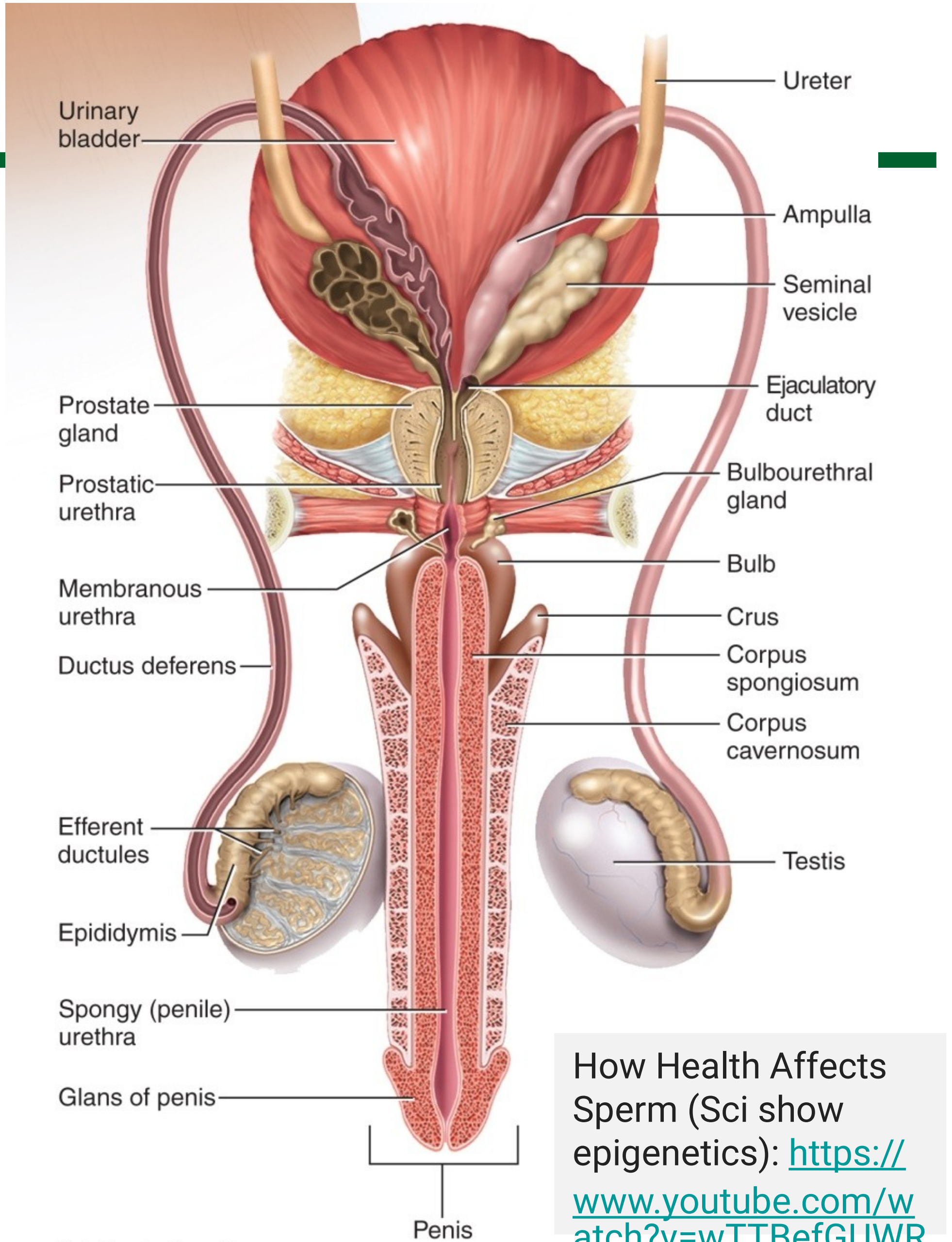
Epididymis (**DE**) is enclosed by connective tissue with many blood vessels (**V**) and covered by a capsule and the tunica vaginalis (**TV**). Lined by a <u>pseudostratified columnar epithelium</u> with long stereocilia (**arrows**).

The <u>columnar epithelium</u> of the epididymal duct is surrounded by a thin circular layer of smooth muscle (**SM**) cells and its lumen contains sperm (**S**).

The spermatic ducts: testis to urethra

Efferent ductules: ~12 small ciliated ducts collecting sperm from rete testes and transporting it to epididymis
Duct of the epididymis: Site of sperm maturation and storage (fertile for 40 to 60 days)
Ductus (vas) deferens: from scrotum to bladder
Seminal vesicle: form semen secretion
Semen passes through prostate via **Ejaculatory duct** to empty into urethra

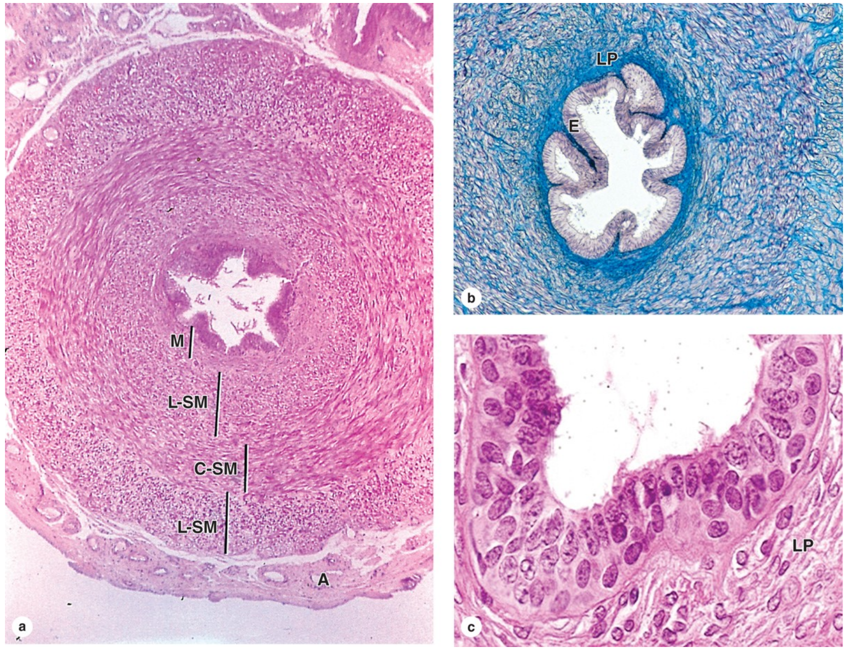
MEDICAL APPLICATION Male infertility is frequently idiopathic (unknown causes). Poor semen quality results from reduces sperm cell density, abnormal sperm morphology, and flagellar defects that impair sperm motility.



(b) Posterior view

How Health Affects Sperm (Sci show epigenetics): https://www.youtube.com/watch?v=wTTBefGUWRA

Ductus deferens



Mucosa (**M**), a thick muscularis with inner and outer layers of longitudinal smooth muscle (**L-SM**) and an intervening layer of circular smooth muscle (**C-SM**), and an external adventitia (**A**). The muscularis is specialized for powerful peristaltic movement of sperm at ejaculation.

(b) The lamina propria (**LP**) is rich in elastic fibers and the thick epithelial lining (**E**) shows longitudinal folds. Mallory trichrome.

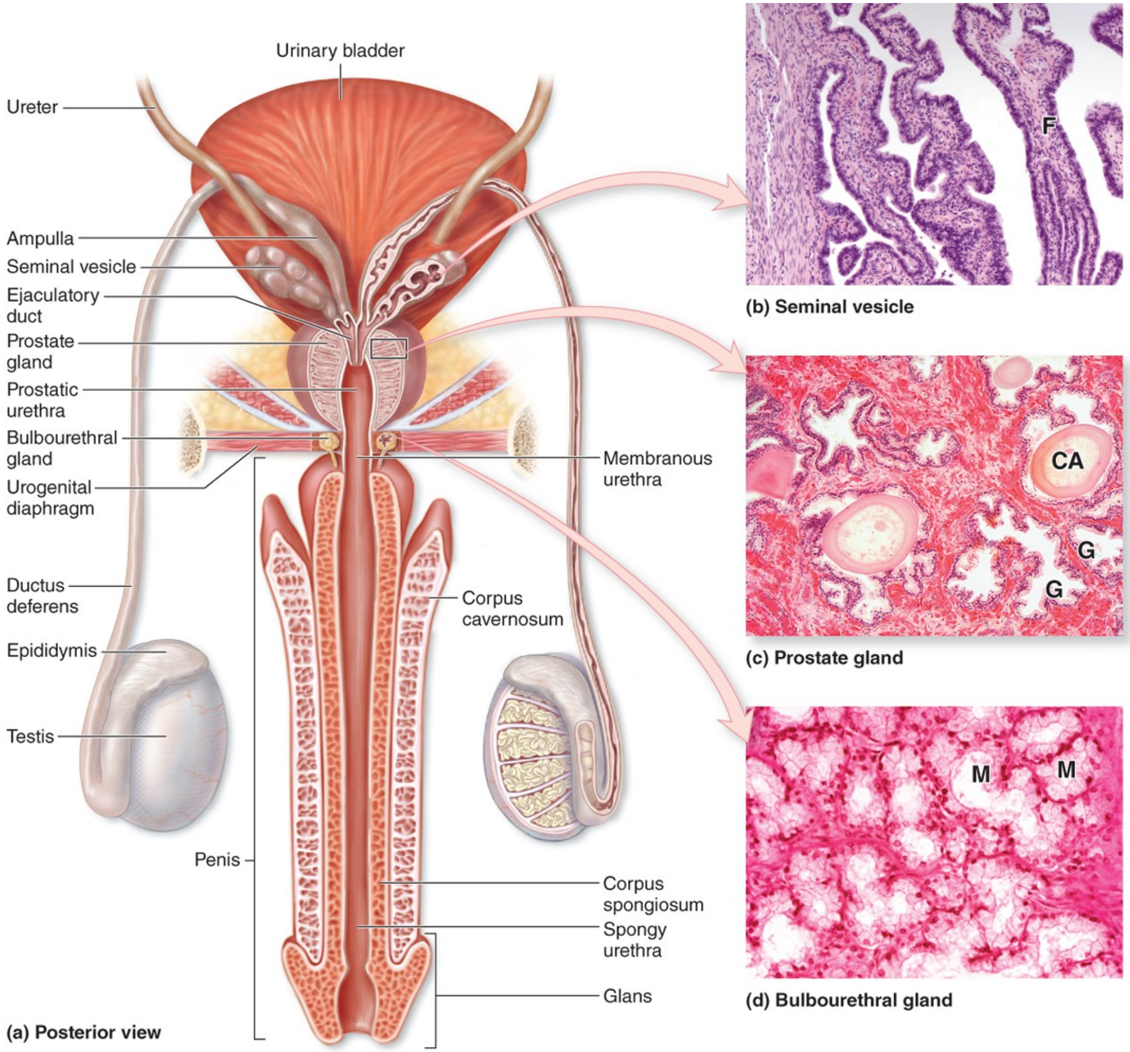
(c) Higher magnification of the mucosa shows that the epithelium is pseudostratified with basal cells and many columnar cells, some with stereocilia.

MEDICAL APPLICATION: In **vasectomy,** a small incision is made through the scrotal skin near the two ducts and the two ends (or only the end leading to the abdomen) are cauterized and tied. After vasectomy sperm are still produced, but they degenerate and are removed by macrophages in the epididymis (and in the scrotal sac if the short portion of the vas is left open-ended.)

The Accessory Glands

Seminal vesicles: Forms 60% of semen. Fructose (energy), prostaglandins (stimulates female activity), fibrinogen (semen coagulation)
Prostate gland: Thin milky secretion forms 30% of semen. Prostoglandins, enzymes
Bulbourethral (Cowper) glands: lubricates the head of the penis in preparation for intercourse, neutralizes acidity of residual urine in the urethra

MEDICAL APPLICATION Prostate cancer (adenocarcinoma), the most common cancer in nonsmoking men, occurrs mainly in glands of the peripheral zone.



(a) Posterior view

(b) Seminal vesicle

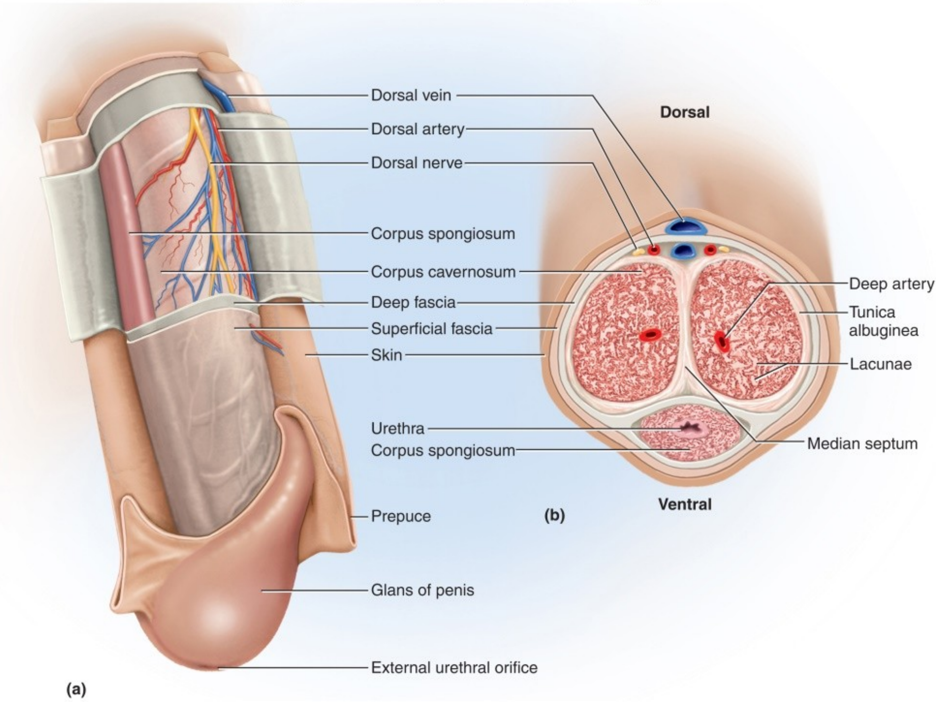
(c) Prostate gland

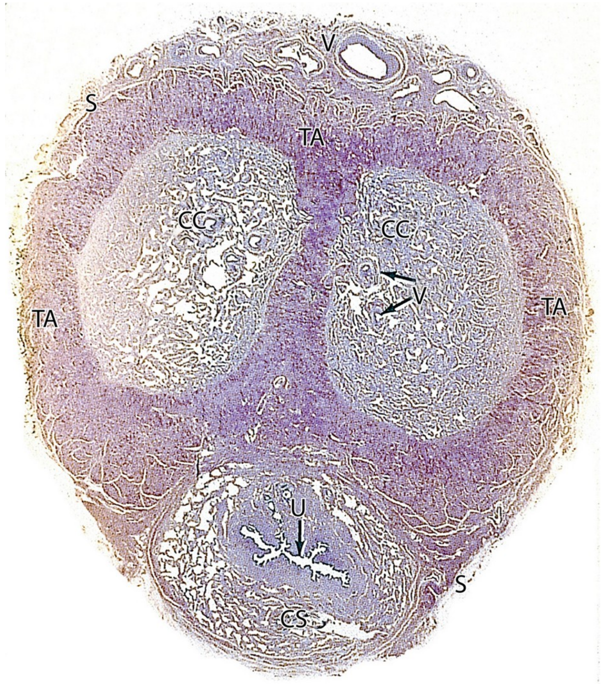
(d) Bulbourethral gland

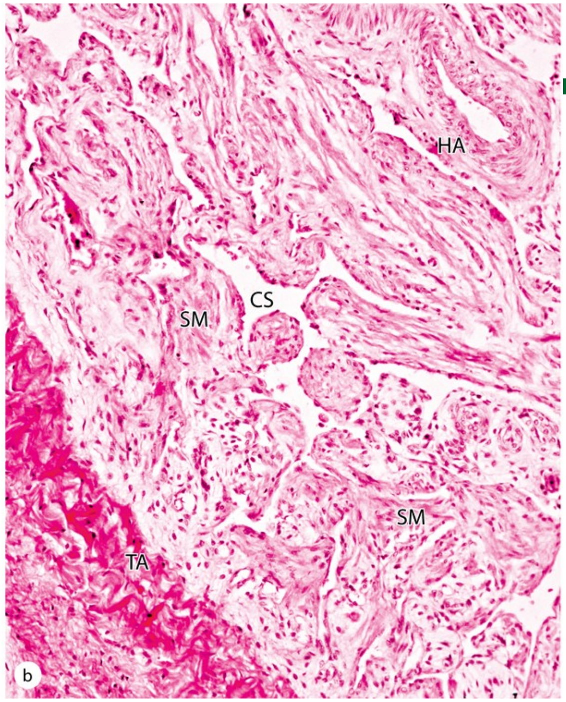
The penis

Foreskin: Extends over glans as **prepuce**, removed by circumcision
Three cylindrical bodies of erectile tissue: fill with blood during sexual arousal → enlargement → erection
Corpus spongiosum: encloses spongy (penile) urethra
Corpora cavernosa: Diverge like arms (crus) of a Y, attaches penis to pubic arch,
Lacunae: blood sinuses
Trabeculae: partitions between lacunae

corpus spongiosum (**CS**) urethra (**U**) corpora cavernosa (**CC**) tunica albuginea (**TA**) blood vessels (**V**) skin (**S**), which distally forms the large foreskin fold and becomes thin over the glans







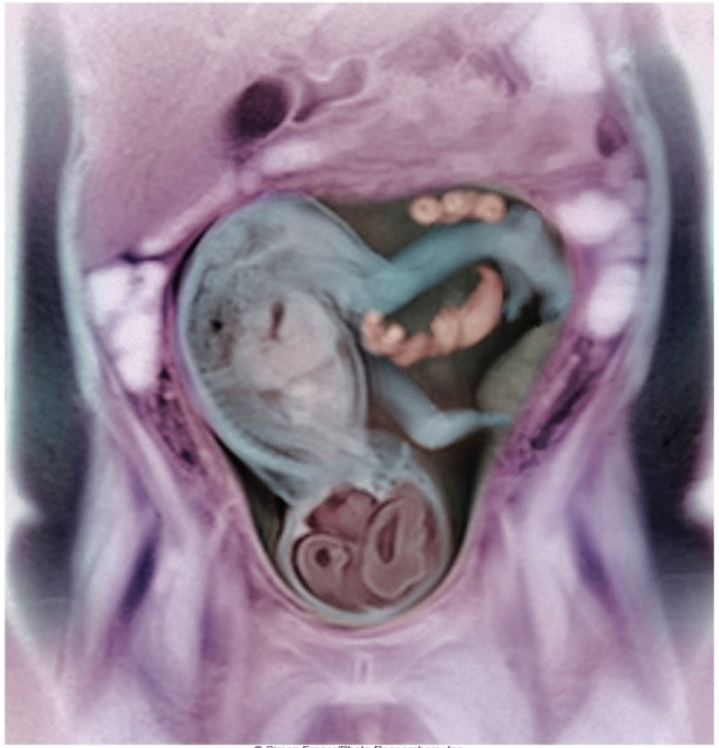
Penile urethra and erectile tissue

(a) The corpus spongiosum (**CS**) surrounds the longitudinally folded wall of the penile urethra (**PU**). Small urethral glands (**UG**) with short ducts to the urethra release mucus during erection, supplementing the similar secretion from the bulbourethral glands. The two dorsal corpora cavernosa (**CC**) are ensheathed by dense, fibrous tunica albuginea (**TA**) and in one here a small helicine artery (**HA**)
(b) A higher magnification of erectile tissue is shown with a small portion of tunica albuginea (**TA**) and fibrous, elastic connective tissue containing smooth muscle (**SM**) and many small, cavernous spaces (**CS**) lined by vascular endothelium. Very little blood normally passes through this vasculature due to constriction of the helicine arteries (**HA**) serving them.

MEDICAL APPLICATION: Acetylcholine from parasympathetic nerves causes the vascular endothelial cells of the helicine arteries and cavernous tissue to release nitric oxide (NO). NO causes surrounding smooth muscle cells to relax and promotes blood flow for the erection.

Erectile dysfunction , or impotence , can result from diabetes, anxiety, vascular disease, or nerve damage during prostatectomy. Drugs may alleviate the problem by inhibiting smooth muscle cells of helicine arteries and erectile tissue.

Duct	Location	Epithelium	Support Tissues	Function(s)
Seminiferous tubules	Testicular lobules	Spermatogenic, with Sertoli cells and germ cells	Myoid cells and loose connective tissue	Produce sperm
Straight tubules (tubuli recti)	Periphery of the mediastinum testis	Sertoli cells in proximal portions, simple cuboidal in distal portions	Connective tissue	Convey sperm into the rete testis
Rete testis	In mediastinum testis	Simple cuboidal	Dense irregular connective tissue	Channels with sperm from all seminiferous tubules
Efferent ductules	From rete testis to head of epididymis	Alternating patches of simple cuboidal nonciliated and simple columnar ciliated	Thin circular layer of smooth muscle and vascular loose connective tissue	Absorb most fluid from seminiferous tubules; convey sperm into the epididymis
Epididymal duct	Head, body, and tail of the epididymis	Pseudostratified columnar, with small basal cells and tall principal cells bearing long stereocilia	Circular smooth muscle initially, with inner and outer longitudinal layers in the tail	Site for sperm maturation and short-term storage; expels sperm at ejaculation
Ductus (vas) deferens	Extends from epididymis to ejaculatory ducts in prostate gland	Pseudostratified columnar, with fewer stereocilia	Fibroelastic lamina propria and three very thick layers of smooth muscle	Carries sperm by rapid peristalsis from the epididymis to the ejaculatory ducts
Ejaculatory ducts	In prostate, formed by union of ductus deferens and ducts of the seminal vesicles	Pseudostratified and simple columnar	Fibroelastic tissue and smooth muscle of the prostate stroma	Mix sperm and seminal fluid; deliver semen to urethra, where prostatic secretion is added



Female Reproductive System

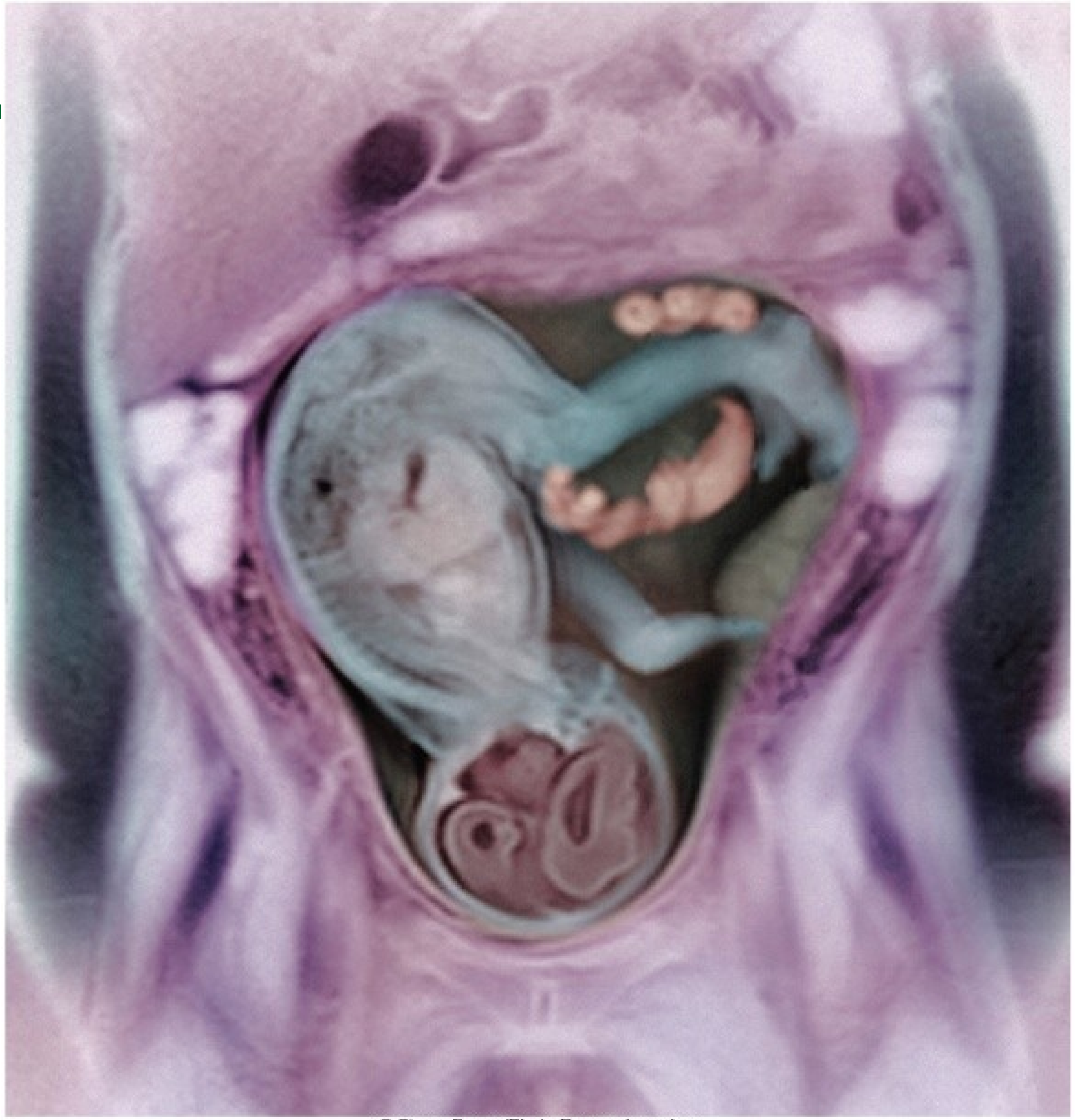
BI 455 CHAPTER 23

Introduction

The female reproductive system is more complex than the male system because it serves more purposes

- Produces and delivers gametes
- Provides nutrition and safe harbor for fetal development
- Gives birth
- Nourishes infant

Female system is more cyclic, and the hormones are secreted in a more complex sequence than the relatively steady secretion in the male



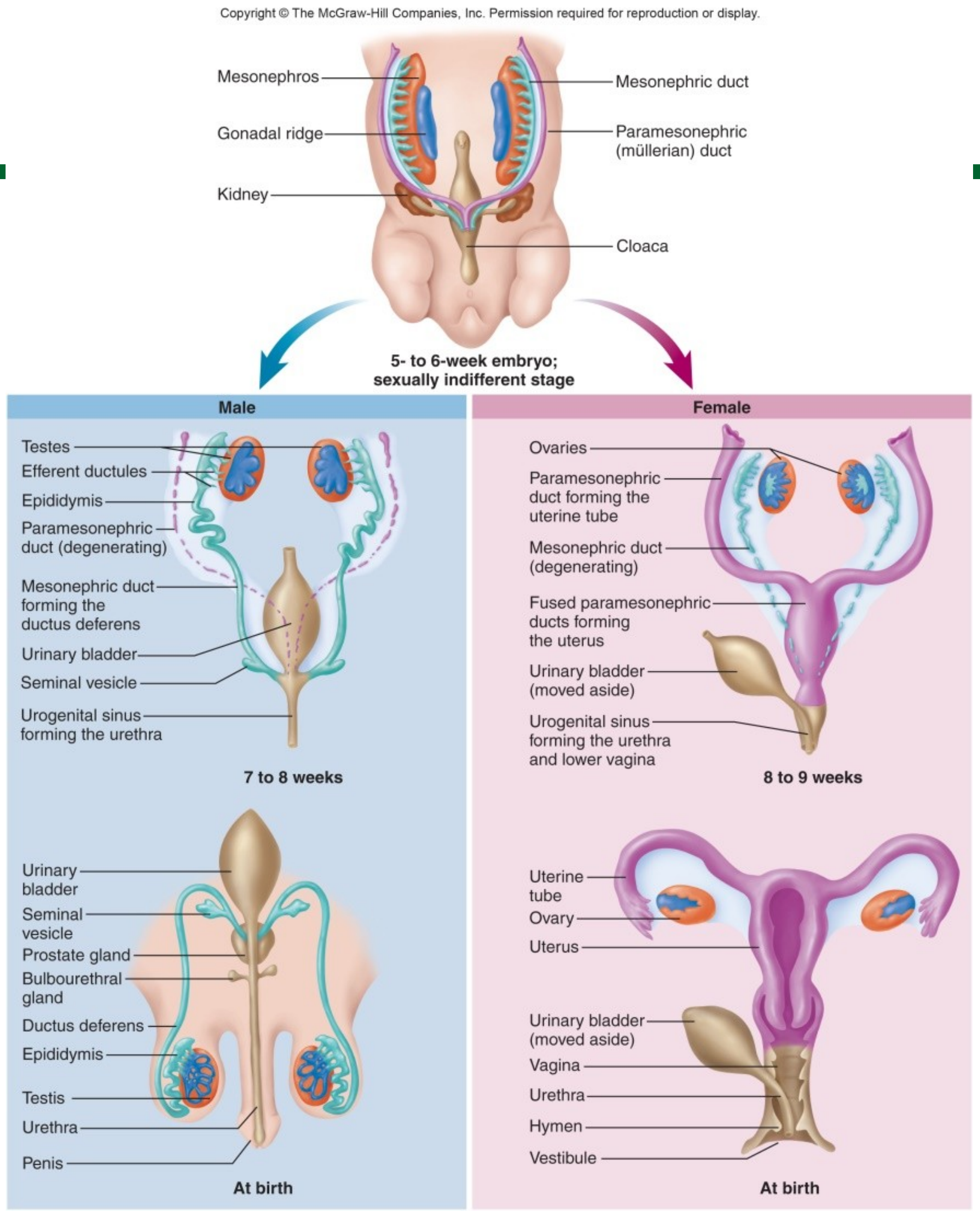
Sexual Differentiation: indistinguishable for 8 to 10 weeks

Female reproductive tract develops from the paramesonephric ducts in absence of testosterone and müllerian-inhibiting factor (MIF)

Without testosterone:

- Mesonephric ducts to degenerate
- Genital tubercle becomes the glans clitoris
- Urogenital folds become the labia minora
- Labioscrotal folds develop into the labia majora

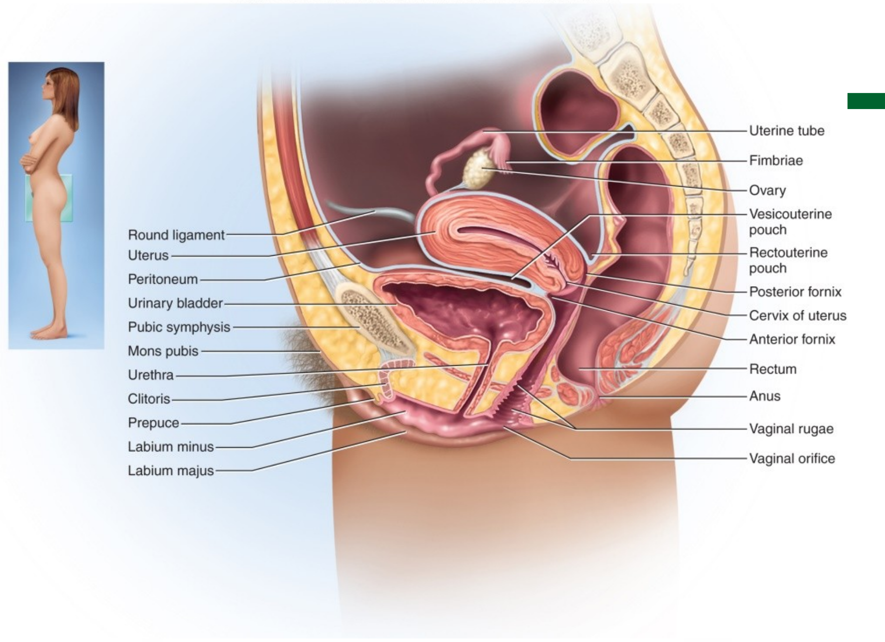
Without MIF: Paramesonephric ducts develop into the uterine tubes, uterus, and vagina

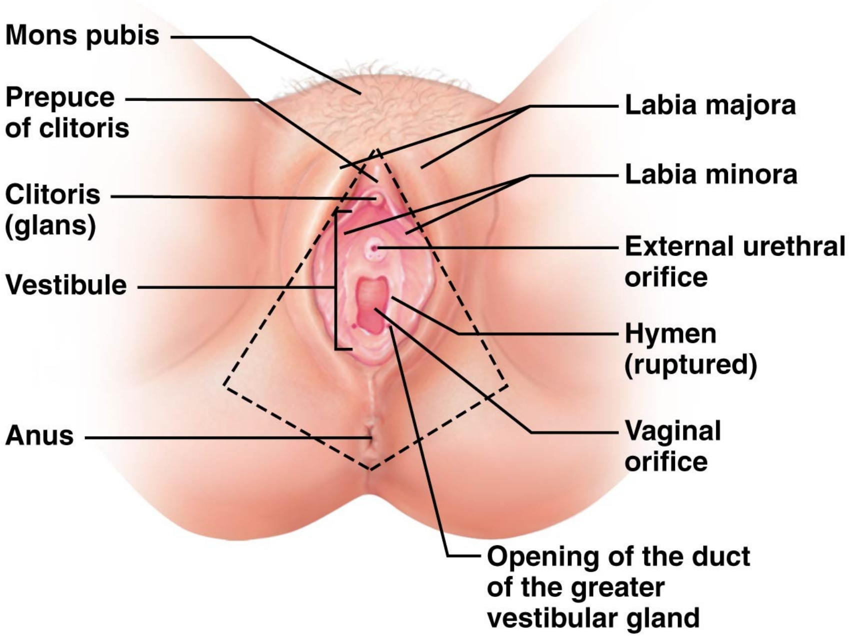


The Genitalia

- Internal genitalia: Ovaries, uterine tubes, uterus, and vagina
- External genitalia: Clitoris, labia minora, and labia majora

- **Primary sex organs**: Ovaries
- **Secondary sex organs**: Other internal and external genitalia

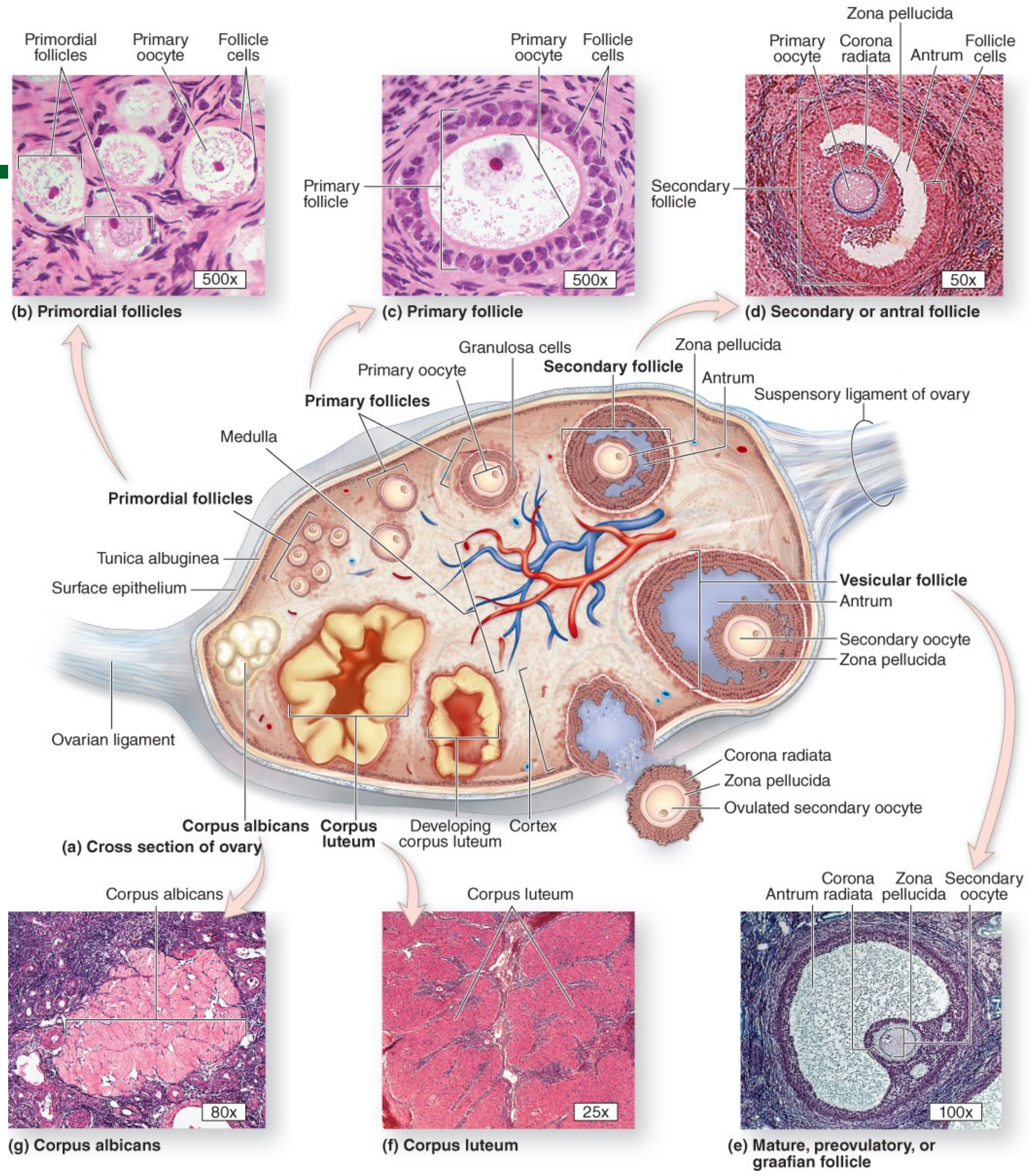




The ovary produces both oocytes and sex hormones.

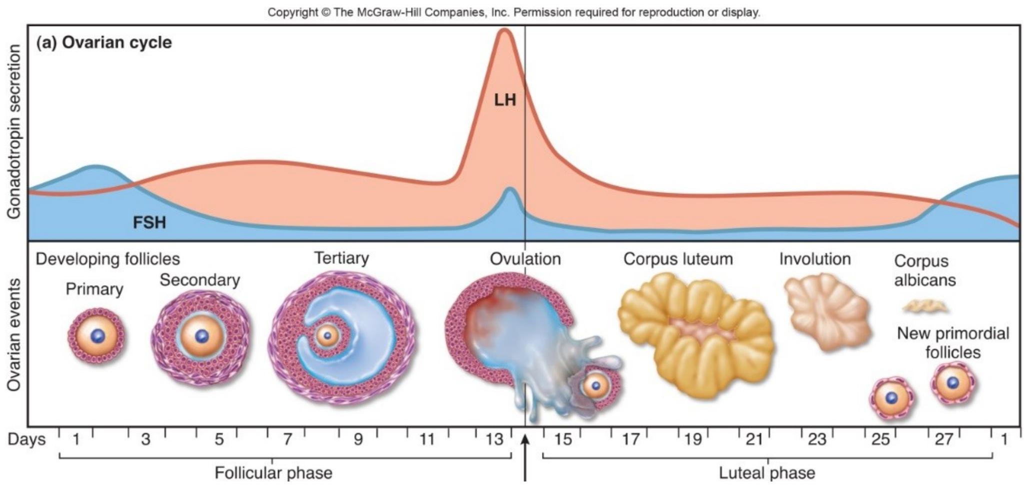
Tunica albuginea: capsule, like on testes
Outer cortex: germ cells develop
Inner medulla: major arteries and veins.
Ovulation: bursting of the follicle and releasing the egg

primordial follicles **(b)**→primary follicle **(c)**→ secondary follicle **(d)** → large vesicular follicle **(e)**. After ovulation, remains form corpus luteum **(f)** → degenerates into the corpus albicans **(g)**

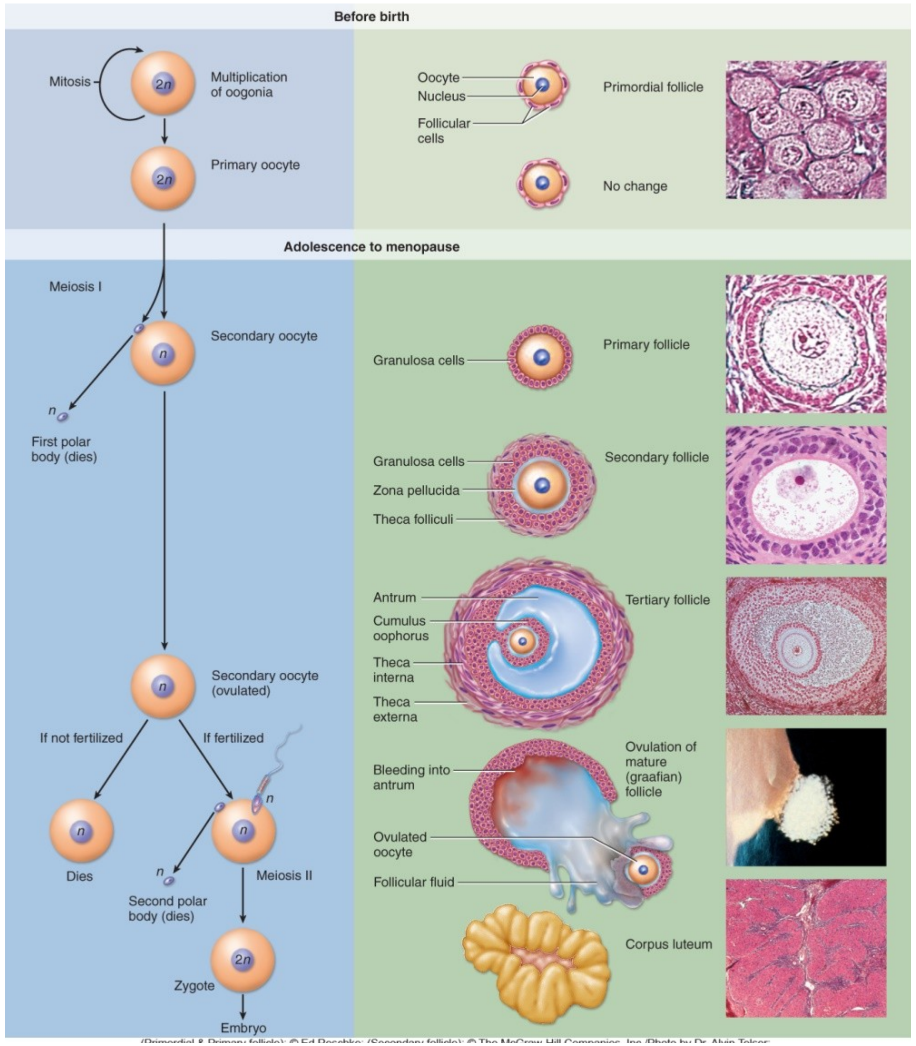


Embryonic development of ovary

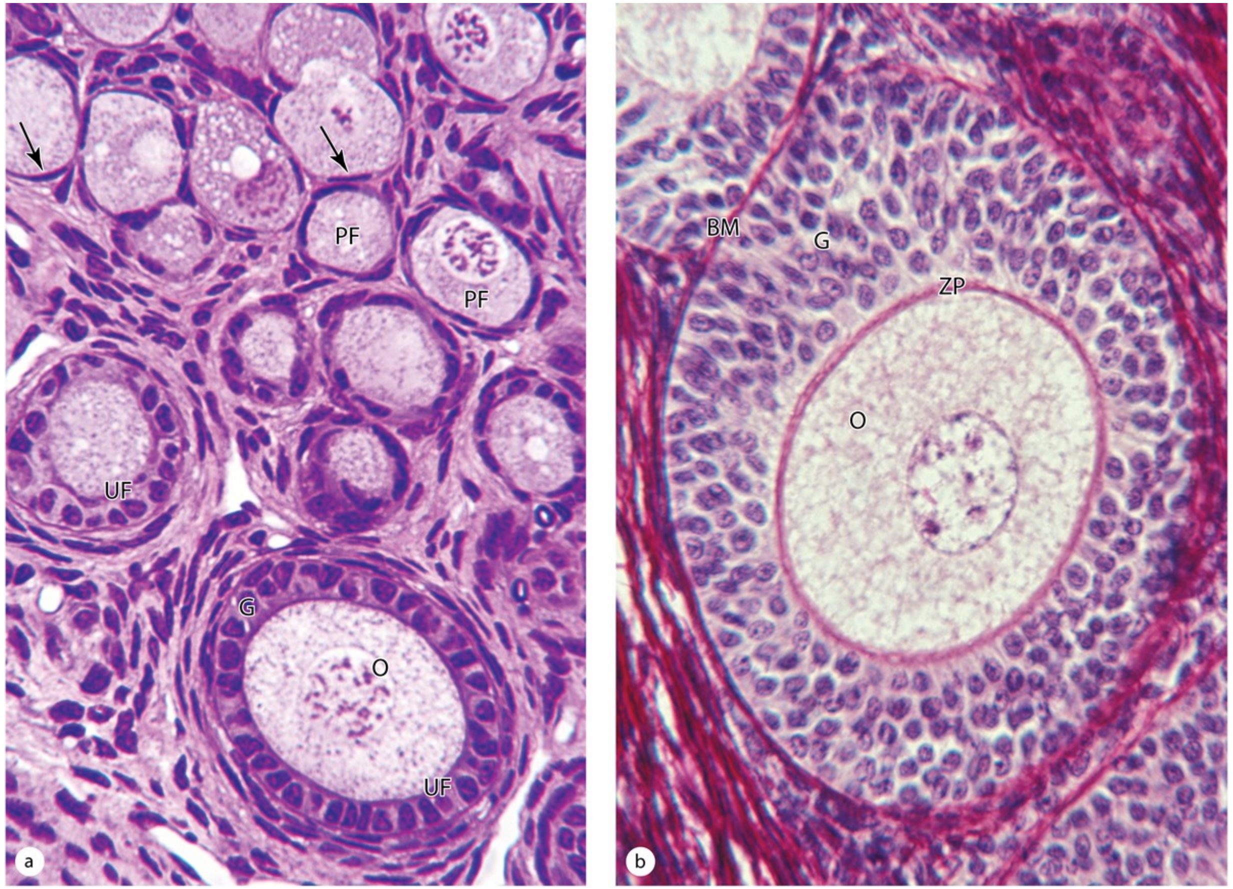
Females are born with lifetime supply of **primary oocytes,** surrounded by simple squamous **primordial follicles**: arresting in early meiosis I
Egg, or ovum: any stage from the primary oocyte to the time of fertilization
FSH: stimulates monthly cohorts of oocytes to complete meiosis I
First polar body: Disintegrates after meiosis I
Secondary oocyte: proceeds to metaphase II. Simple cuboidal **primary follicles,** stratified cuboidal granulosa cells in **secondary follicles,** hormone secreting **Tertiary follicles**
Fertilization triggers completion of Meiosis II



http://highered.mheducation.com/sites/0072495855/student_view0/chapter28/animation__maturation_of_the_follicle_and_oocyte.html



(a) Primordial and (b) Primary follicles



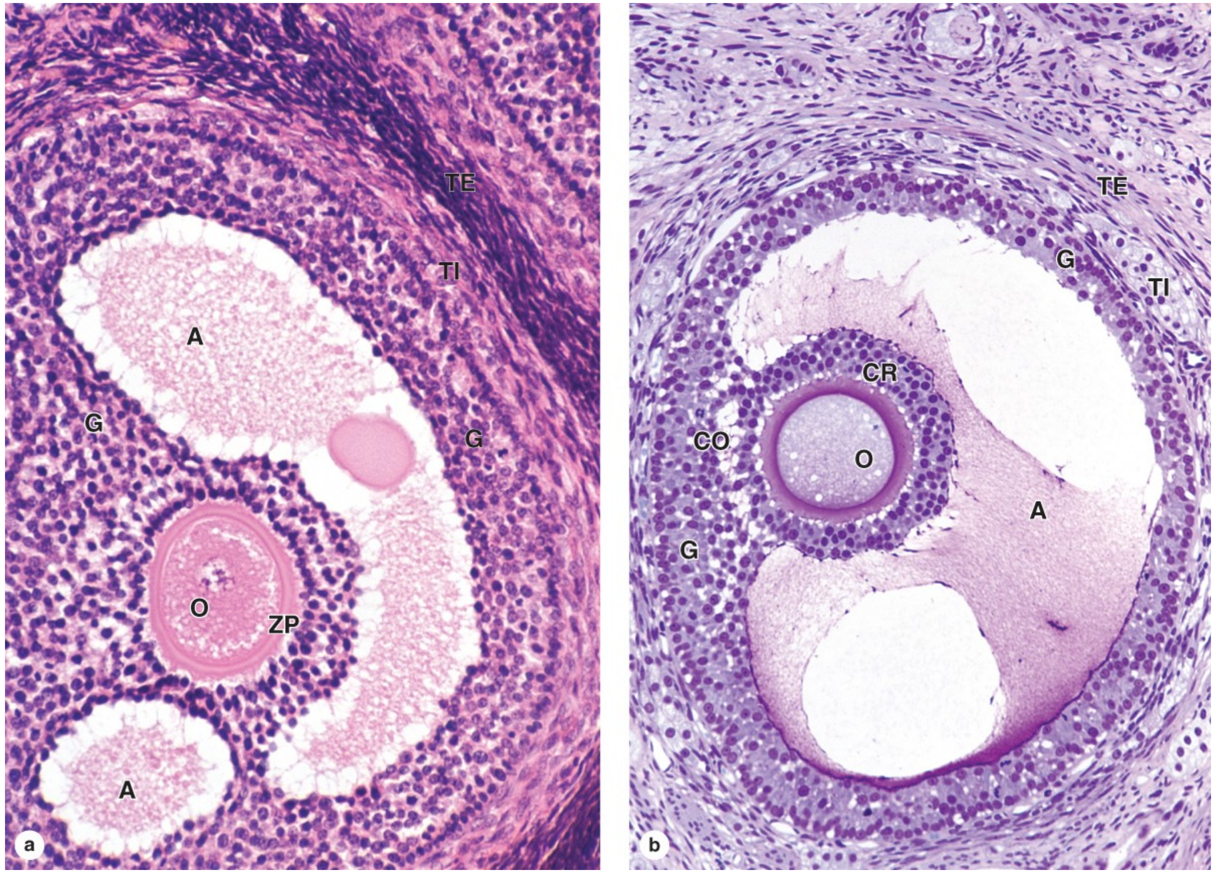
(a) primordial follicles (**PF**) and their flattened follicle cells (**arrows**)
granulosa cells (**G**) form a single cuboidal layer around the large primary oocyte (**O**)

(b) larger multilayered primary follicle. Granulosa cells (**G**) have now proliferated to form several layers. zona pellucida (**ZP**): glycoprotein layer produced by the oocyte that is required for sperm binding and fertilization. The primary oocyte is now a very large cell. basement membrane (**BM**)

MEDICAL APPLICATION Polycystic ovary syndrome (PCOS) is characterized by enlarged ovaries with numerous cysts and an anovulatory state (with no follicles completing maturation successfully).
Increased androgen production by the ovaries or adrenals is likely involved.
PCOS is a common cause of **infertility** in women.

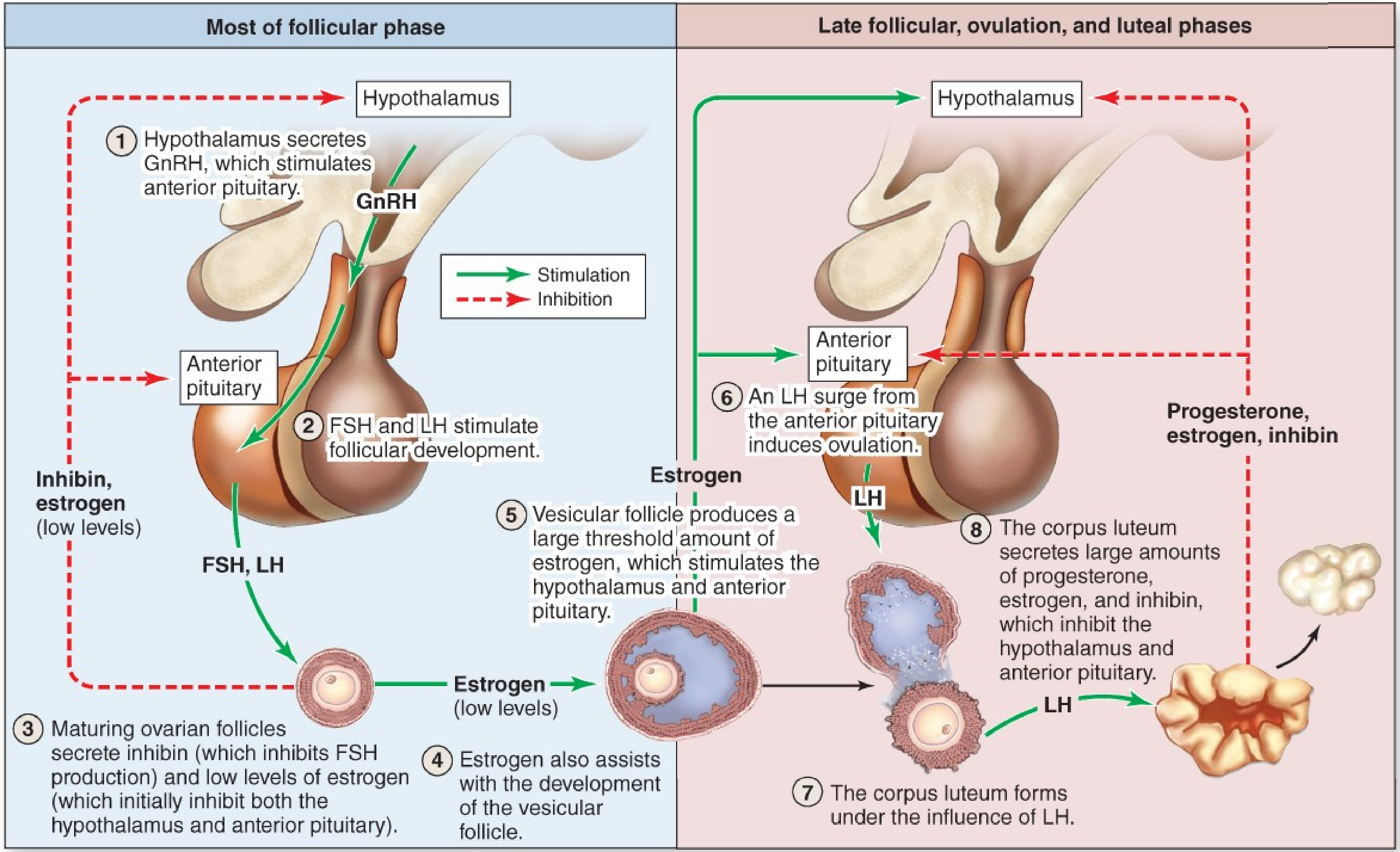
(a) An antral follicle shows the large, fluid-filled antral cavities or vesicles (**A**)
The oocyte (**O**) is surrounded by the zona pellucida (**ZP**) and granulosa cells (**G**), Steroid-secreting theca interna (**TI**) and a covering theca externa (**TE**).

(b) A slightly more developed preovulatory follicle shows a very large single antrum (**A**). The oocyte (**O**) is surrounded by granulosa cells that now make up the corona radiata (**CR**). The corona radiata and oocyte are attached to the side of the follicle within a larger mass of granulosa cells called the **cumulus oophorus** (**CO**)



MEDICAL APPLICATION Late primary or antral follicles can produce **follicular cysts**, which are thin-walled, fluid-filled structures with both granulosa and thecal endocrine cells. Follicular cysts are common and usually benign, but can produce high estrogen levels and lead to menstrual irregularities. If cyst formation disrupts blood vessels blood enters the fluid, often rapidly, and produces a **hemorrhagic cyst**.

The ovarian cycle is initiated by hypothalamic GnRH, causing the AP to secrete FSH and LH

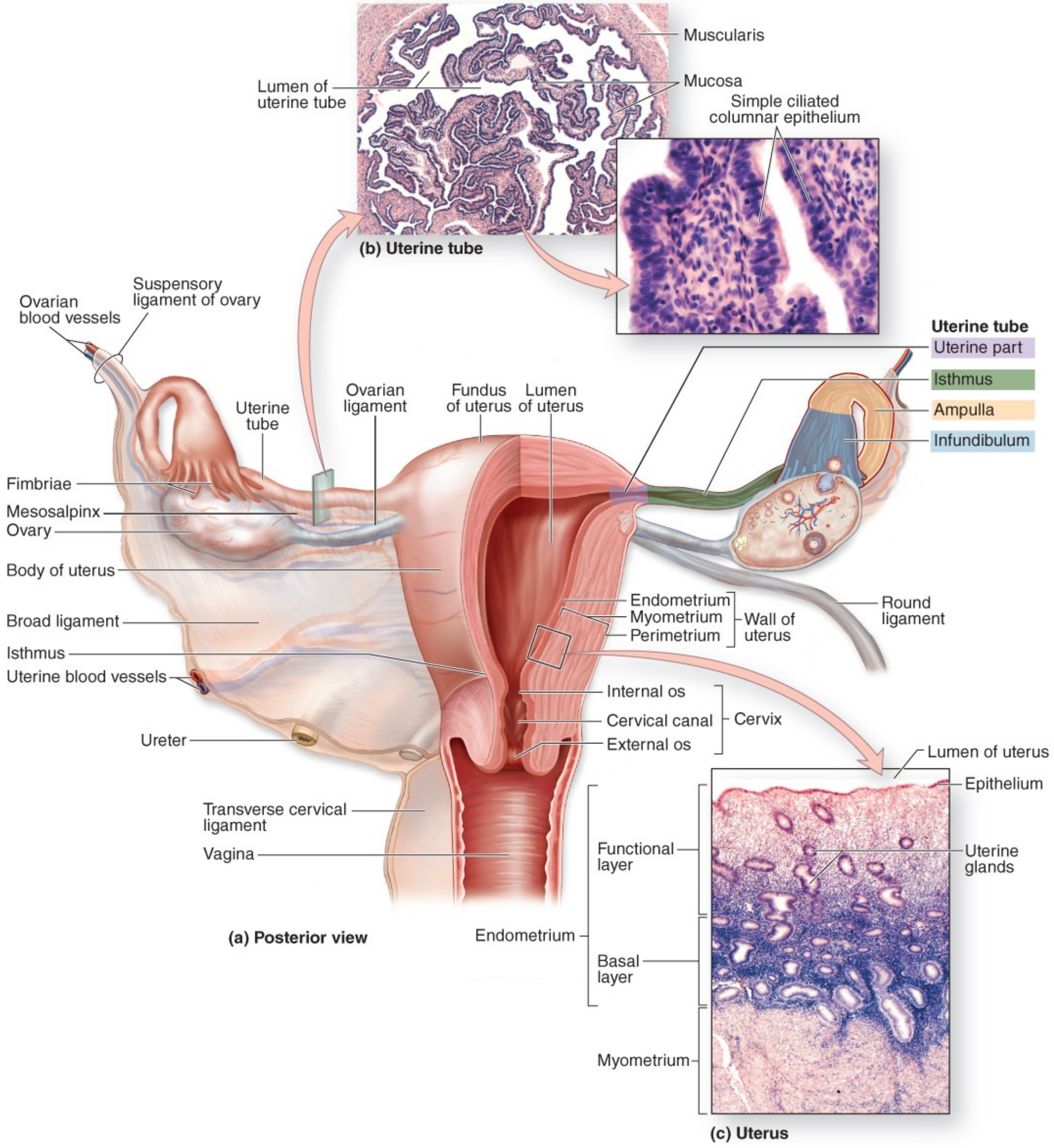


Uterine tubes and uterus

The uterine tubes catch the ovulated secondary oocyte, nourish both the oocyte and sperm, provide the microenvironment for fertilization, and transport the embryo undergoing cleavage to the uterus.

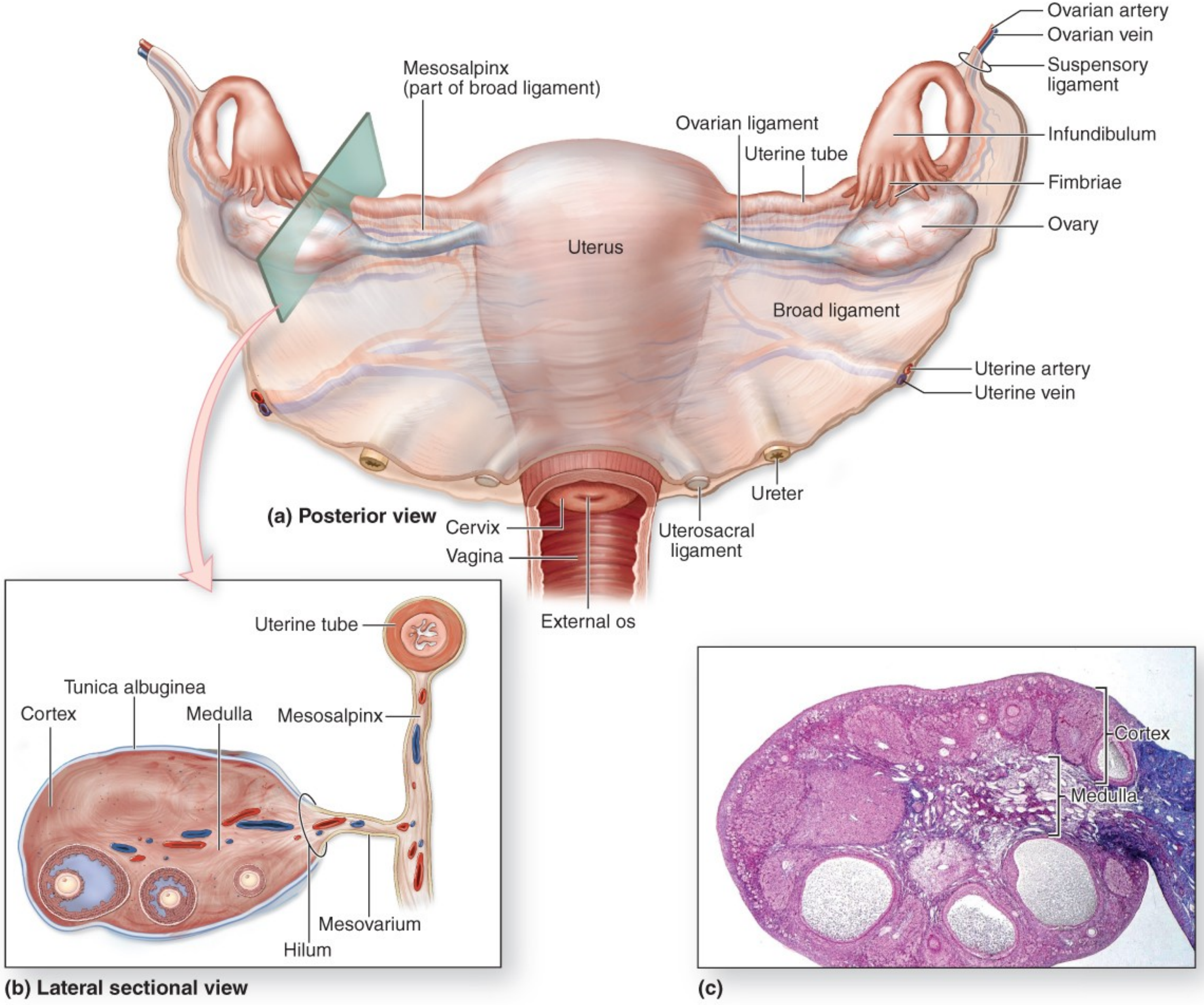
MEDICAL APPLICATION: Mucosal damage or adhesions can lead to **infertility** or an **ectopic (tubal) pregnancy** if there is blockage of oocyte or embryo transport to the uterus.
The tube cannot contain the growing embryo and will rupture, causing potentially fatal hemorrhage.

Tubal ligation is a common surgical type of contraception.

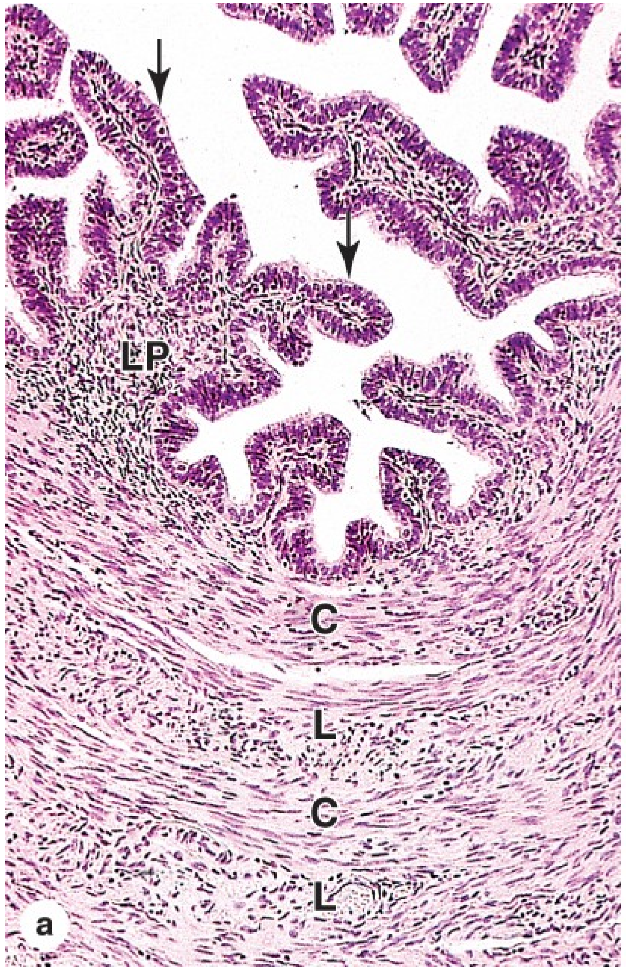


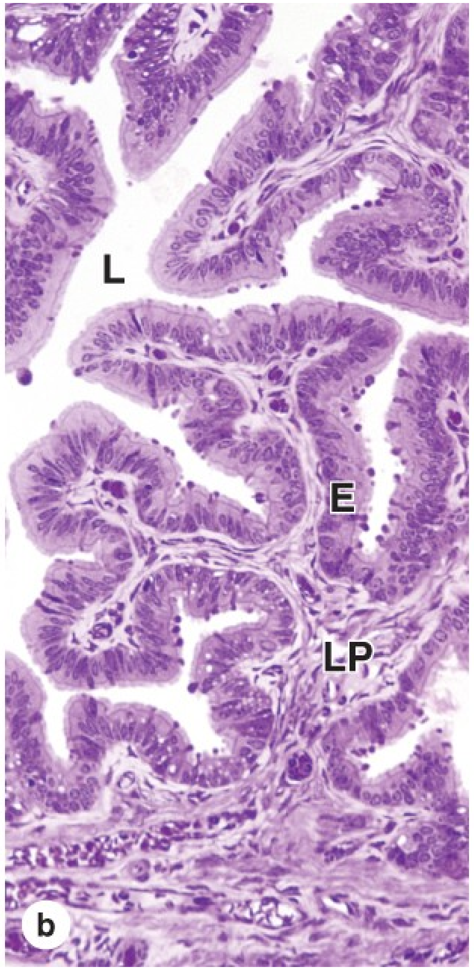
The Uterine Tubes (Oviduct/Fallopian Tube): Muscular tube lined with ciliated cells

Highly folded into longitudinal ridges
Infundibulum: flared, trumpet-shaped distal (ovarian) end
Fimbriae: feathery projections on infundibulum
Mesosalpinx: the superior portion of the broad ligament that enfolds uterine
Ovarian ligament: ovaries→uterus
Suspensory ligament: ovaries→pelvic wall. Contains ovarian artery, vein, and nerves
Mesovarium: ovaries→ broad ligament



Mucosa of the uterine tube wall

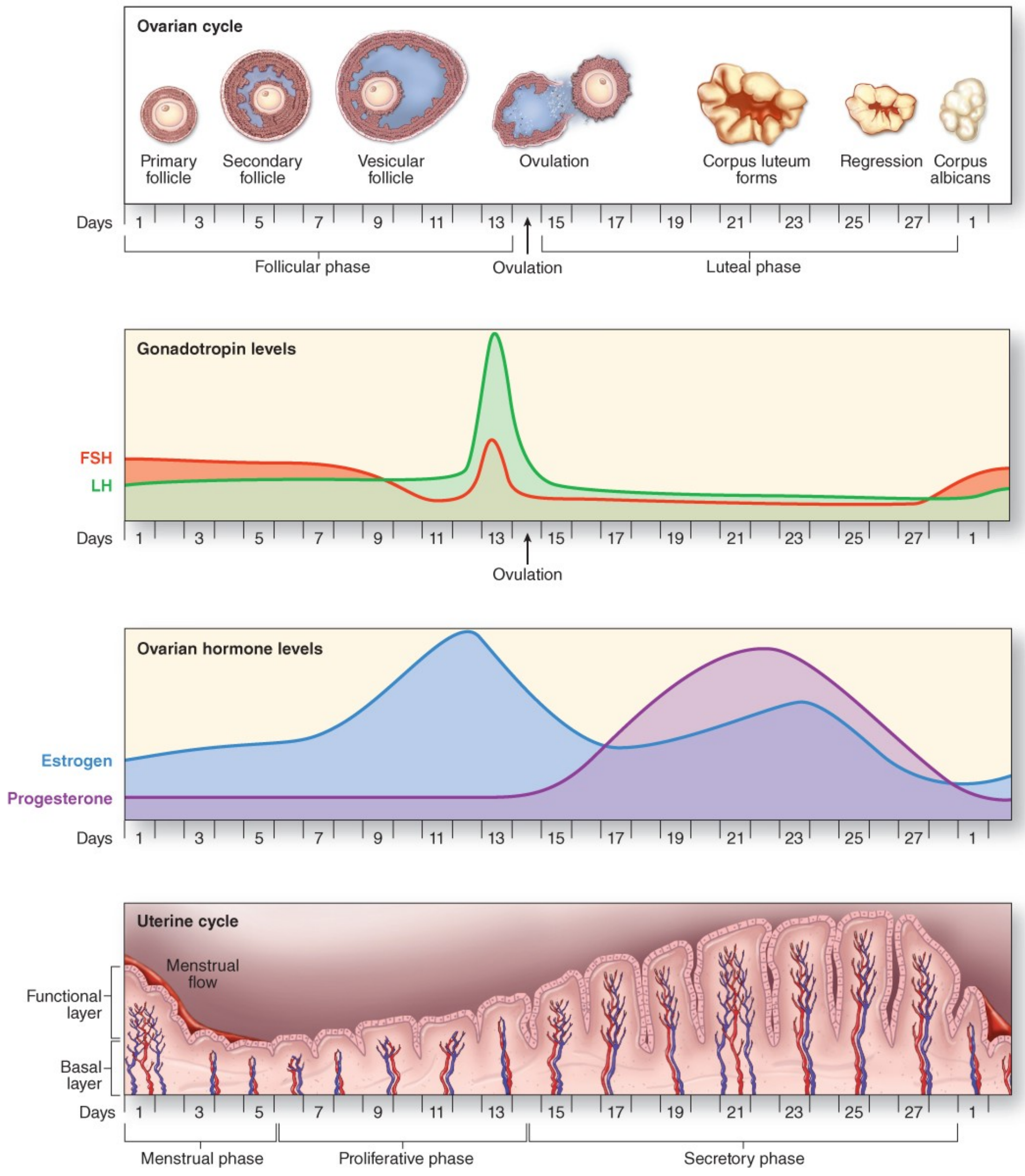




(a) A cross section of the uterine tube at the ampulla shows the interwoven circular (**C**) and longitudinal (**L**) layers of smooth muscle in the muscularis and in the complex of folded mucosa, the lamina propria (**LP**) underlying a simple columnar epithelium (arrows).

(b) The oviduct mucosa, with folds projecting into the lumen (**L**), has simple columnar epithelium (**E**) on the lamina propria (**LP**).

MEDICAL APPLICATION: Endometriosis results when endometrial tissue grows on the ovaries, oviducts, or elsewhere. Under the influence of estrogen and progesterone, the ectopic tissue grows and degenerates monthly but cannot be removed effectively from the body. In addition to pain endometriosis can produce inflammation, ovarian cysts, adhesions, and scar tissue that can cause infertility



Correlation of ovarian and menstrual cycles with levels of their controlling hormones.

The cyclic development of **ovarian follicles** and the **corpus luteum**, controlled by the pituitary **gonadotropins** FSH and LH, lead to cyclic shifts in the levels of the major ovarian hormones: steroidal **estrogens and progesterone**.

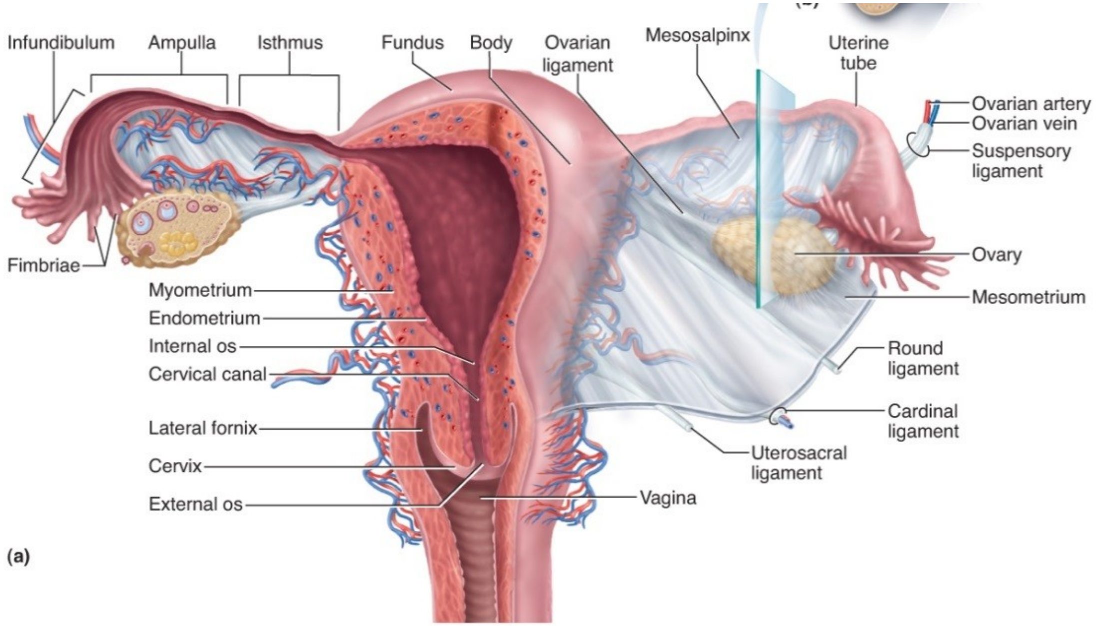
Estrogen stimulates the proliferative phase of the uterine cycle and its level peaks near the day of ovulation,
After ovulation the corpus luteum forms and produces both progesterone and estrogens, which together promote growth and development of the endometrial **functional layer.**

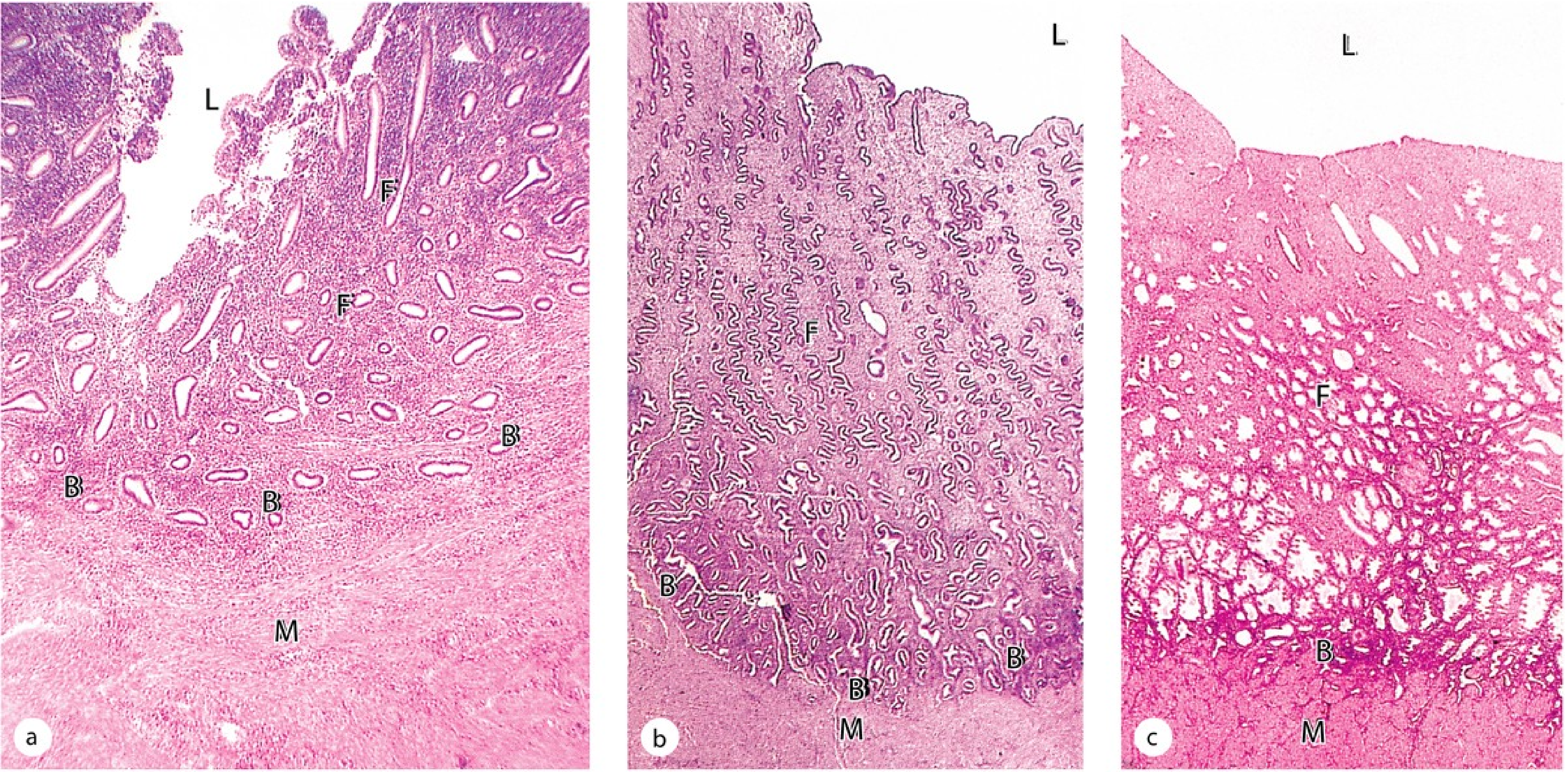
Without fertilization, regression of the corpus luteum leads to declining levels of the steroid hormones endometrial issue sloughs off as the menstrual flow,

http://ed.ted.com/lessons/how-menstruation-works-emma-bryce

The Uterus: thick muscular chamber that opens into roof of the vagina and usually tilts forward over the urinary bladder

Fundus: broad superior curvature
Body (corpus): middle portion
Cervix: cylindrical inferior end
Lumen is roughly triangular
Upper two corners are openings to **uterine tube**
Cervical canal connects lumen to vagina
Internal os: superior opening of canal into body of uterus
External os: inferior opening of canal into vagina
Cervical glands: secrete mucus that prevents spread of microorganisms from vagina to uterus





Proliferative, secretory, and premenstrual phases in the uterus.

Endometrium:
Functional layer (**F**) closest to the lumen (**L**)
Basal layer (**B**)

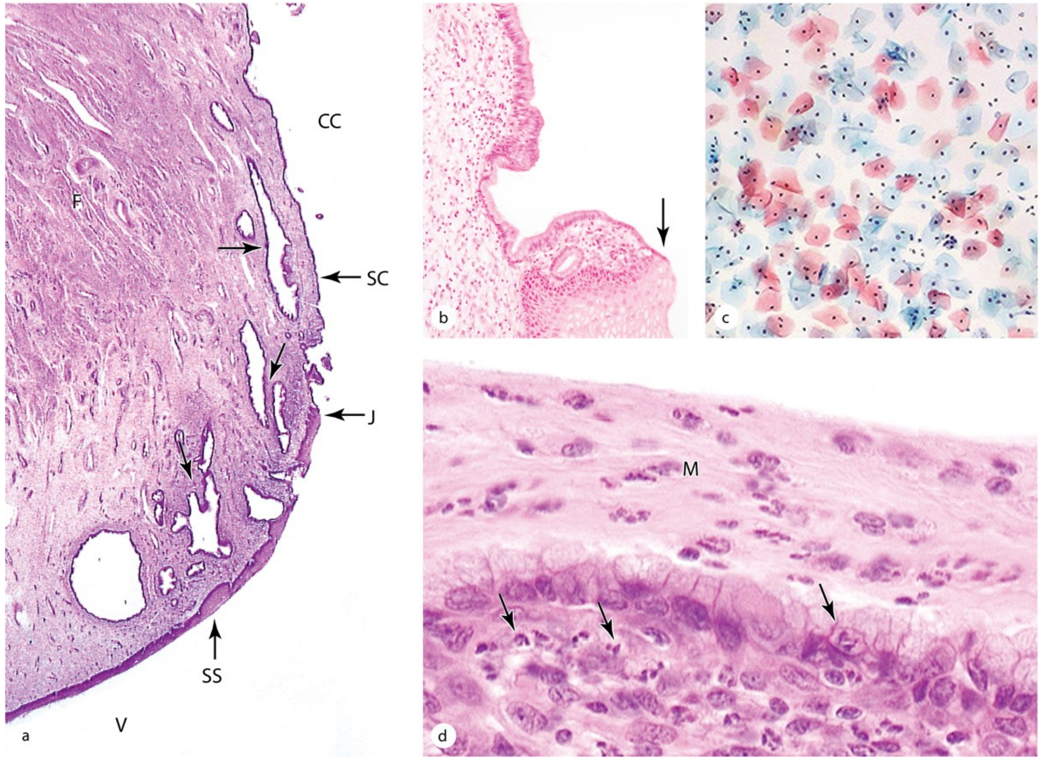
Myometrium (**M**).

(a) proliferative phase: the functional layer is still relatively thin, the stroma is more cellular, and the glands (**G**) are relatively straight, narrow, and empty.
(b) secretory phase: functional layer is four times thicker than the basal layer. The tubular glands have wider lumens containing secretory product and coil tightly up through the stroma
(c) premenstrual phase: constriction of arteries produces hypoxia. Glands (**G**) dissolve, breakdown of the stromal matrix.

TABLE 22–1 Summary of events of the menstrual cycle.

	Stage of Cycle				
	Proliferative	**Secretory or Luteal**			**Menstrual**
Main actions of pituitary hormones	Follicle-stimulating hormone stimulates rapid growth of ovarian follicles	Peak of luteinizing hormone at the beginning of secretory stage, secreted after estrogen stimulation, induces ovulation and development of the corpus luteum			
Main events in the ovary	Growth of ovarian follicles; dominant follicle reaches preovulatory stage	Ovulation	Development of the corpus luteum	Degeneration of the corpus luteum	
Dominant ovarian hormone	Estrogens, produced by the growing follicles, act on vagina, tubes, and uterus	Progesterone, produced by the corpus luteum, acts mainly on the uterus		Progesterone production ceases	
Main events in the endometrium	Growth of the mucosa after menstruation	Further growth of the mucosa, coiling of glands, secretion			Shedding of part of the mucosa about 14 days after ovulation

Cervix



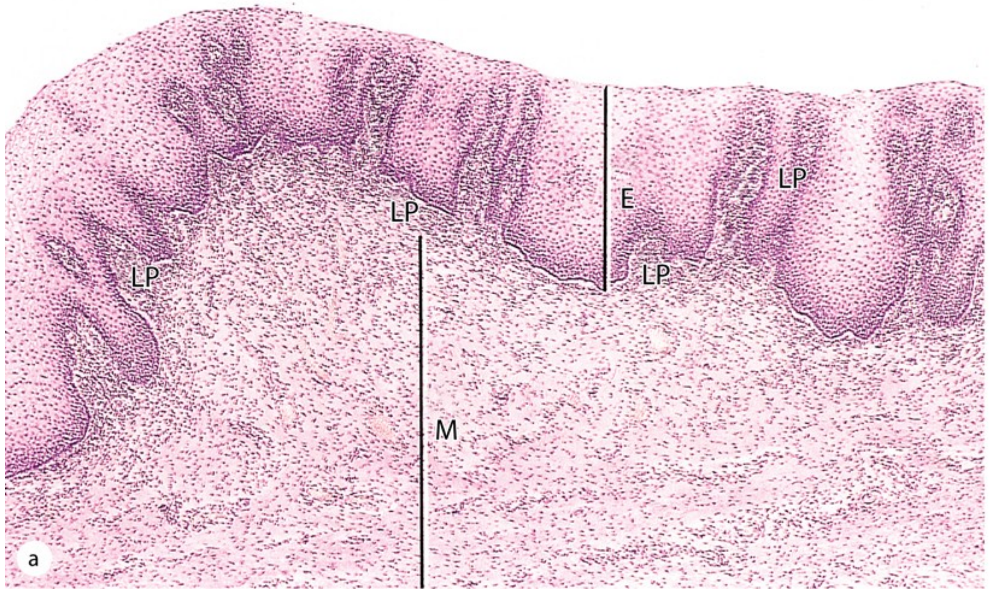
The mucosa of the cervical canal (**CC**) is continuous with the endometrium and like that tissue is lined by simple columnar epithelium (**SC**) and cervical mucous glands (**arrows**).

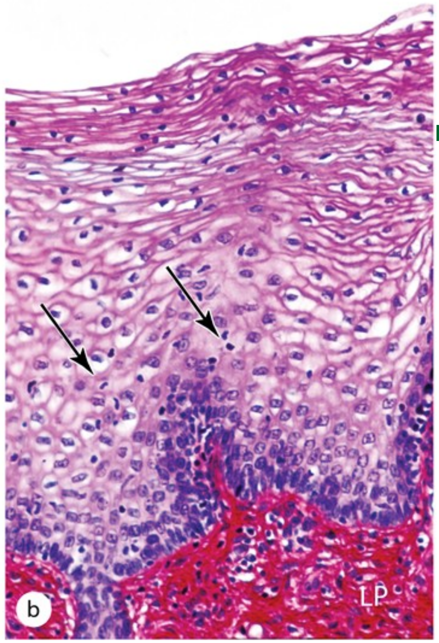
At the external os, columnar epithelium → stratified squamous epithelium (**SS**) covering the exocervix and vagina.

(c) Exfoliative cytology of epithelial cells from the exocervical mucosa in a routine cervical smear. The squamous cells, stain differently according to their content of keratins. Cells with atypical nuclei or other abnormalities can be detected by this method that is used routinely to check for cervical carcinoma.

(d) The endocervical mucosa is exposed to a relatively high population of microorganisms and normally has a large number of neutrophils and other leukocytes (**arrows**)

MEDICAL APPLICATION: The incidence of cervical cancer worldwide has been greatly reduced by widespread, routine screening by exfoliative cytology to examine for dysplasia of the cervical epithelium. The test called the Pap smear after its developer George Papanicolaou, who introduced this diagnostic technique in the 1920s, uses cells that have been lightly scraped from cervix. Abnormal cells suggestive of precancerous changes in the epithelium are then detected microscopically. The epithelial dysplasia that precedes squamous cell neoplasia, the most common type of cervical cancer, occurs in metaplastic cells of the transformation zone at a mean age of 54 years. The human papillomas virus (HPV) is strongly implicated in the pathogenesis





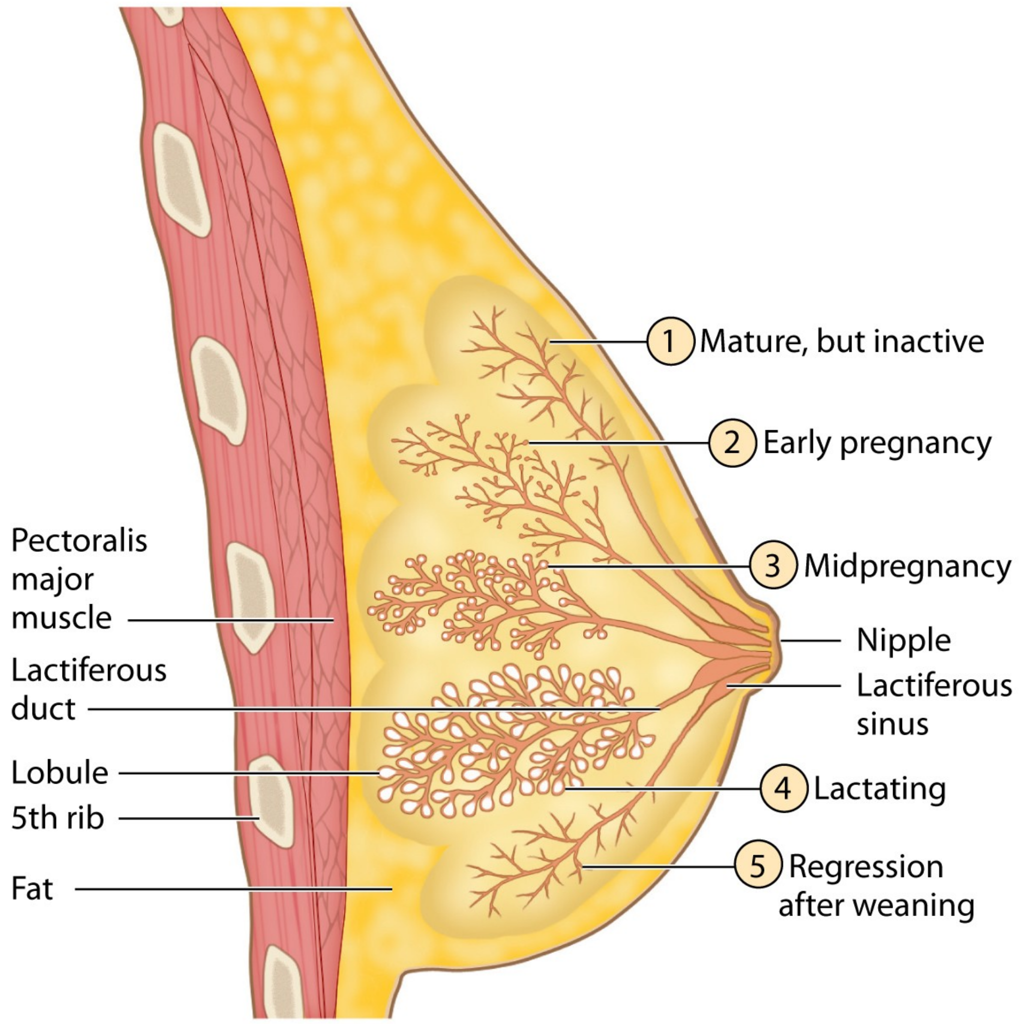
Vagina

The vagina has mucosal, muscular, and adventitial layers.
Lamina propria (**L**) is highly cellular and extends narrow papillae into the thick, nonkeratinized stratified squamous epithelium (**E**). The muscular layer (**M**) has bundles of smooth muscle arranged in a circular manner near the mucosa and longitudinally near the

❯❯ MEDICAL APPLICATION

Atrophic vaginitis involves thinning or atrophy of the vaginal epithelium caused by diminished estrogen levels and occurs most often in postmenopausal woman. This change allows the more frequent inflammation and infections characteristic of this condition. Primary squamous cell carcinoma of the vagina occurs rarely, with most vaginal malignancies having spread secondarily from the cervix or vulva.

Mammary gland

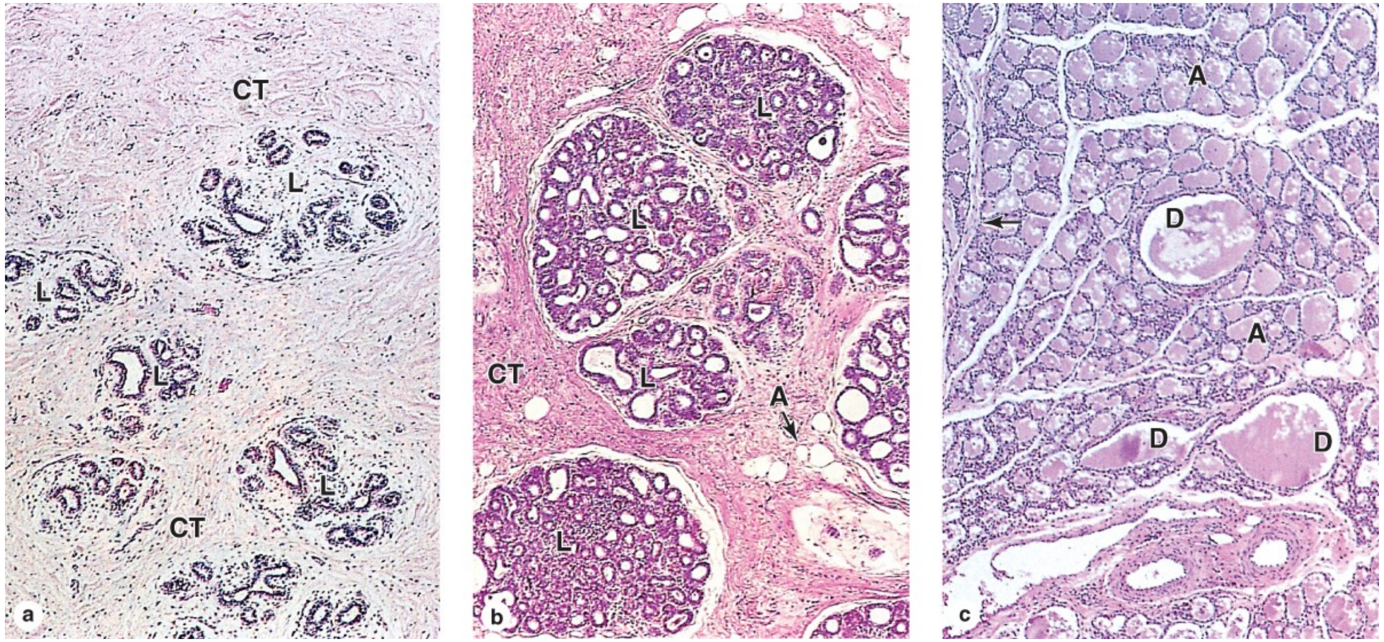


(**1**) Before pregnancy, the gland is inactive, with small ducts and only a few small secretory alveoli.
(**2**) Alveoli develop and begin to grow early in a pregnancy.
(**3**) By midpregnancy, the alveoli and ducts have become large and have dilated lumens.
(**4**) At parturition and during the time of lactation, the alveoli are greatly dilated and maximally active in production of milk components.
(**5**) After weaning, the alveoli and ducts regress with apoptotic cell death.

MEDICAL APPLICATION When a woman is breast-feeding, the nursing action of the child stimulates tactile receptors in the nipple, resulting in liberation of the posterior pituitary hormone **oxytocin.** This hormone causes contraction of the smooth muscle of the lactiferous sinuses and ducts, as well as the myoepithelial cells of alveoli, resulting in the milk-ejection reflex.

Negative emotional stimuli, such as frustration, anxiety, or anger, can inhibit the liberation of oxytocin and thus prevent the reflex.

Alveolar development in the breast during pregnancy



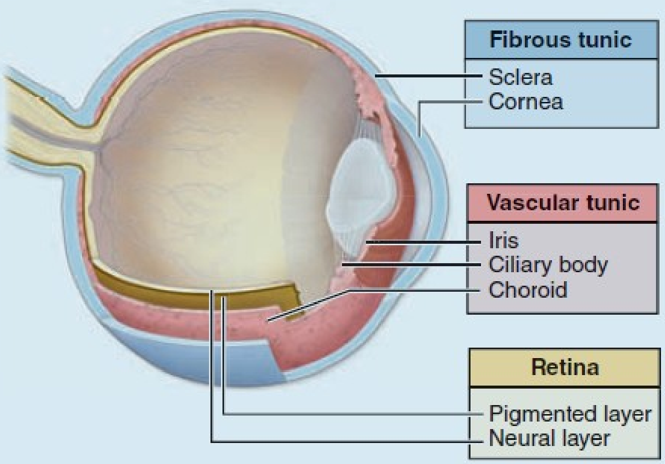
(a) Nonpregnant glands inactive, with small ducts and few lobules (**L**) having secretory alveoli which are not well-developed.
(b) During pregnancy: duct system grows, secretory units much larger and more extensively branched.
(c) During lactation, the lobules are greatly enlarged and the lumens of both the numerous glandular alveoli (**A**) and the excretory ducts (**D**) are filled with milk.

MEDICAL APPLICATION Breast cancer is almost always derived from epithelial cells in the terminal lobules of the glands. **Invasive ductal carcinoma**: intralobular ducts invade the surrounding stroma, forming a fixed, palpable mass. If the treatment is mastectomy, axillary lymph nodes are usually also removed surgically and examined histologically for the presence of metastatic mammary carcinoma cells. Early detection (eg, through self-examination, mammography, ultrasound, and other techniques) and consequent early treatment have significantly reduced the mortality rate.
Bacterial infection of a mammary gland, or **acute mastitis**, may occur in the lactating or involuting breast, usually
after obstruction by milk left within small components of the duct system.

Eye & Ear

BI 455 CHAPTER 23

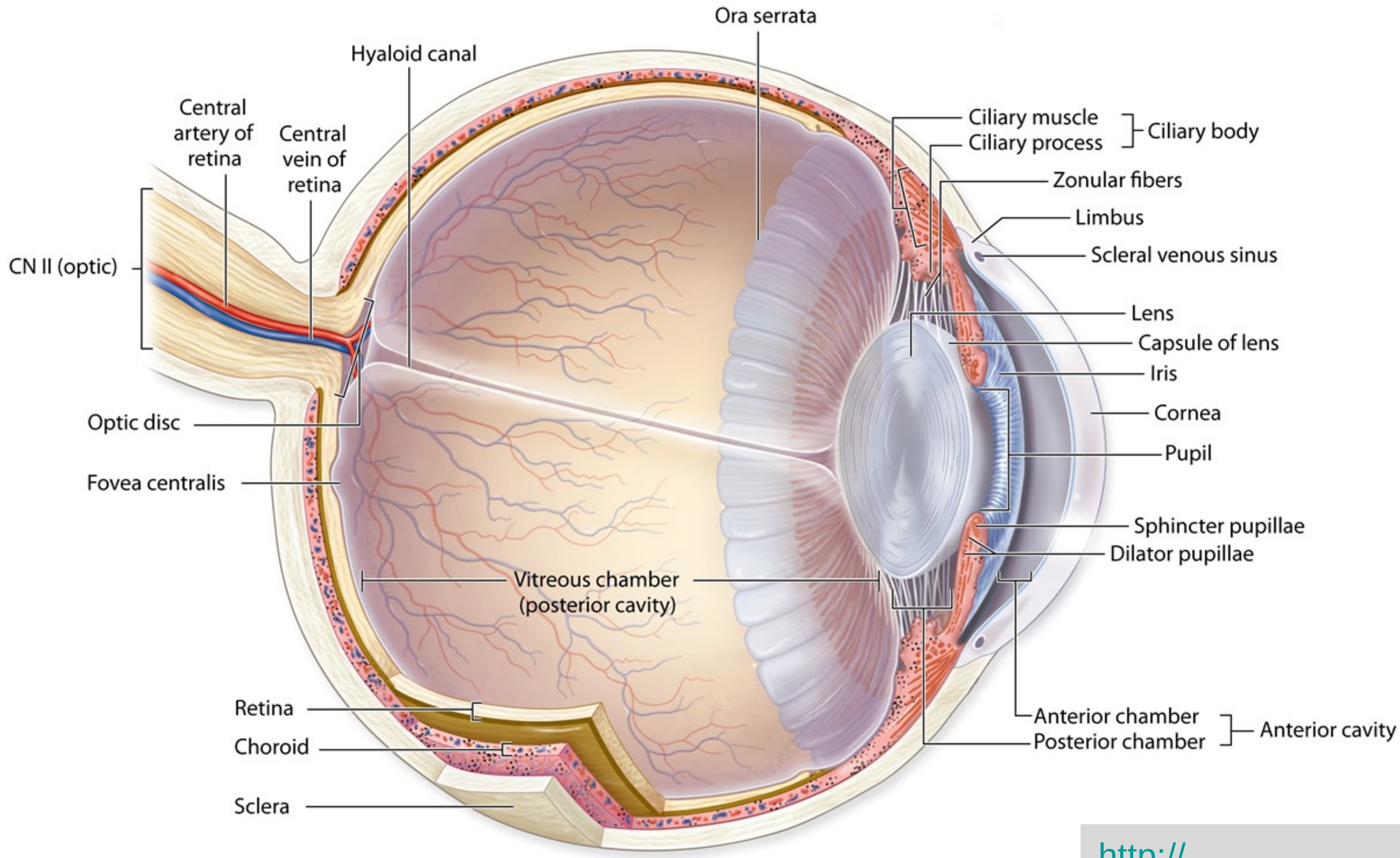
http://ed.ted.com/lessons/the-evolution-of-the-human-eye-joshua-harvey



Structures	Components	Function
Fibrous Tunic (External Layer)		
Sclera	Dense irregular connective tissue	Supports eye shape Protects delicate internal structures Extrinsic eye muscle attachment site
Cornea	Two layers of epithelium with organized connective tissue in between	Protects anterior surface of the eye Refracts (bends) incoming light
Vascular Tunic (Middle Layer)		
Choroid	Areolar connective tissue; highly vascularized	Supplies nourishment to retina Pigment absorbs extraneous light
Ciliary body	Ciliary smooth muscle and ciliary processes; covered with a secretory epithelium	Holds suspensory ligaments that attach to the lens and change lens shape for far and near vision Epithelium secretes aqueous humor
Iris	Two layers of smooth muscle (sphincter pupillae and dilator pupillae) and connective tissue, with a central pupil	Controls pupil diameter and thus the amount of light entering the eye
Retina (Internal Layer)		
Pigmented layer	Pigmented epithelial cells	Absorbs extraneous light Provides vitamin A for photoreceptor cells
Neural layer	Photoreceptors, bipolar neurons, ganglion cells, and supporting Müller cells	Detects incoming light rays; light rays are converted to nerve signals and transmitted to the brain

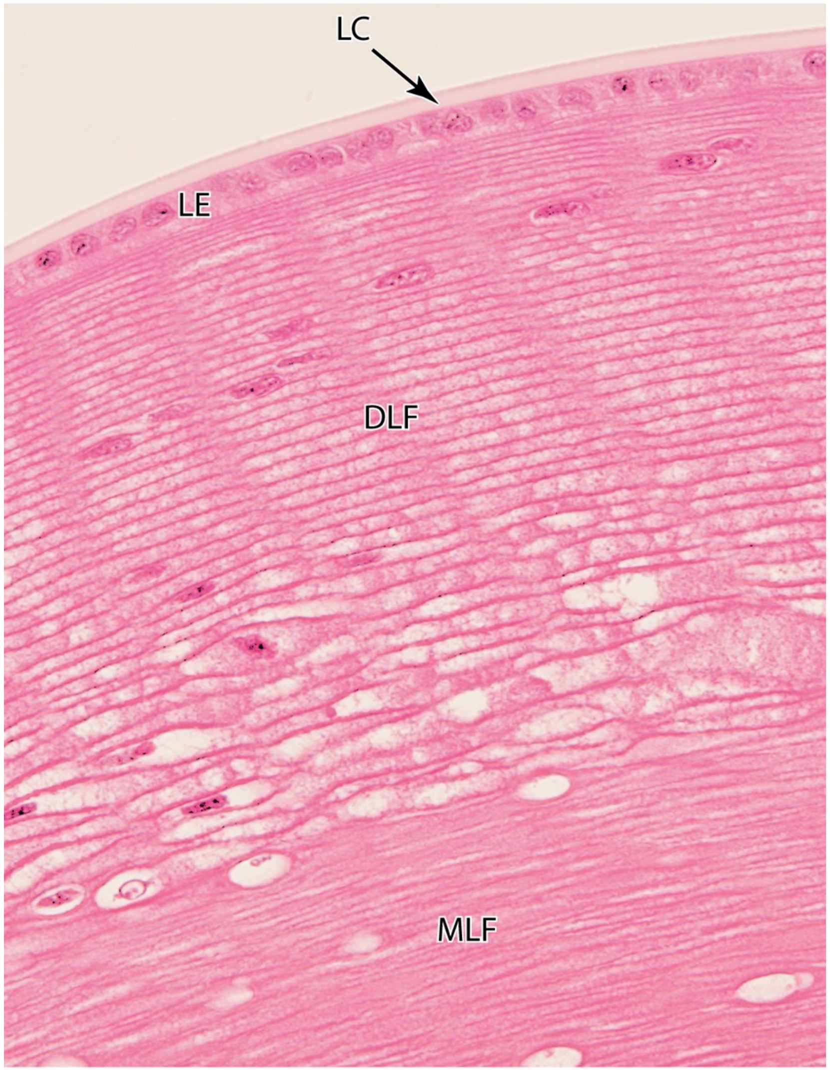
Internal anatomy of the eye

Three major layers or tunics of the wall
Refractive elements: cornea, lens, and vitreous



http://ed.ted.com/lessons/eye-vs-camera-michael-mauser

The lens: transparent, elastic tissue that focuses light on the retina.



Lens capsule (**LC**): thick, external lamina

Columnar lens epithelium (**LE**): Epithelial cells proliferate and give rise to lens fibers.

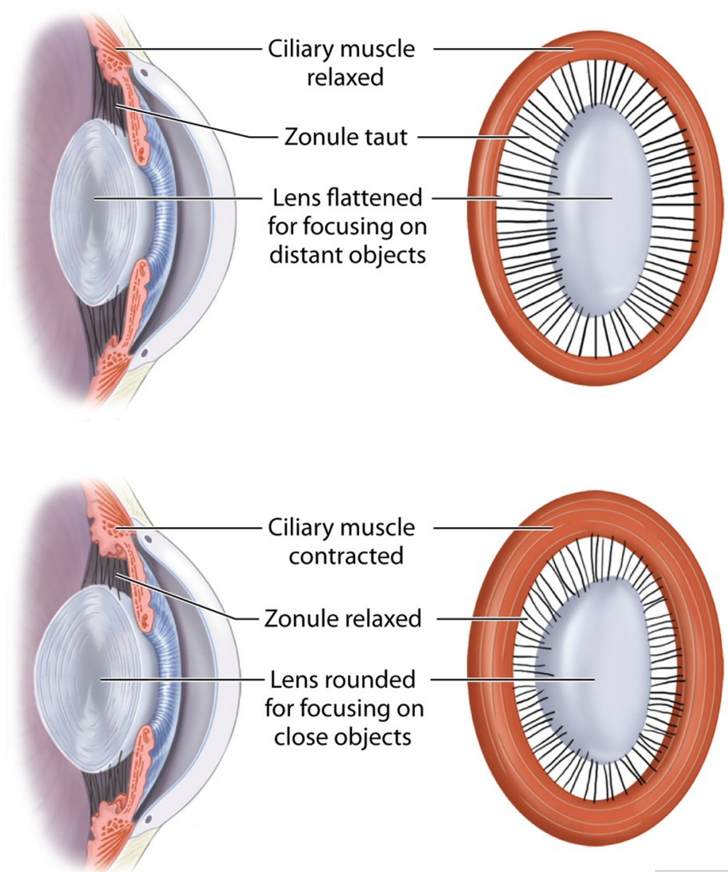
Differentiating lens fibers (**DLF**): have nuclei, making crystallin proteins

Mature lens fibers (**MLF**): No nuclei, densely packed, transparent

Accommodation: changes in shape of lens keep images focused on the retina

(a) <u>Distant vision:</u> Ciliary muscle relaxes, lens flattens

(b) <u>Near vison:</u> Ciliary muscle contracts, lens rounds



(a)

(b)

MEDICAL APPLICATION

Presbyopia (far sightedness): Denaturation of crystallins commonly begins to occur in lens fibers, making them less transparent.

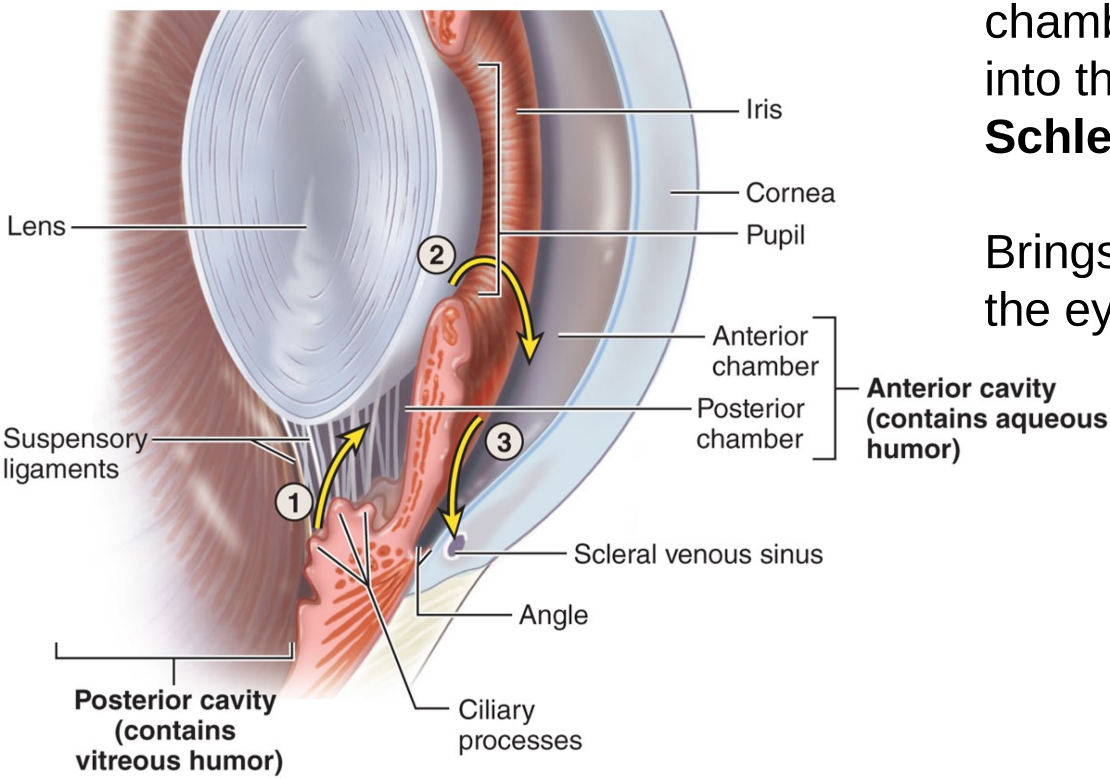
Cataract: areas of lens become opaque. the condition is termed a Causes: excessive UV exposure, trauma, diabetes mellitus, and hypertension.

Lens accommodation: https://

Production and removal of aqueous humor

Aqueous humor secreted from **ciliary processes** into posterior chamber of the anterior cavity, flows into the anterior chamber through the **pupil**, and drains into the **scleral venous sinus (canal of Schlemm)**.

Brings nutrients to the **anterior cavity** of the eye.

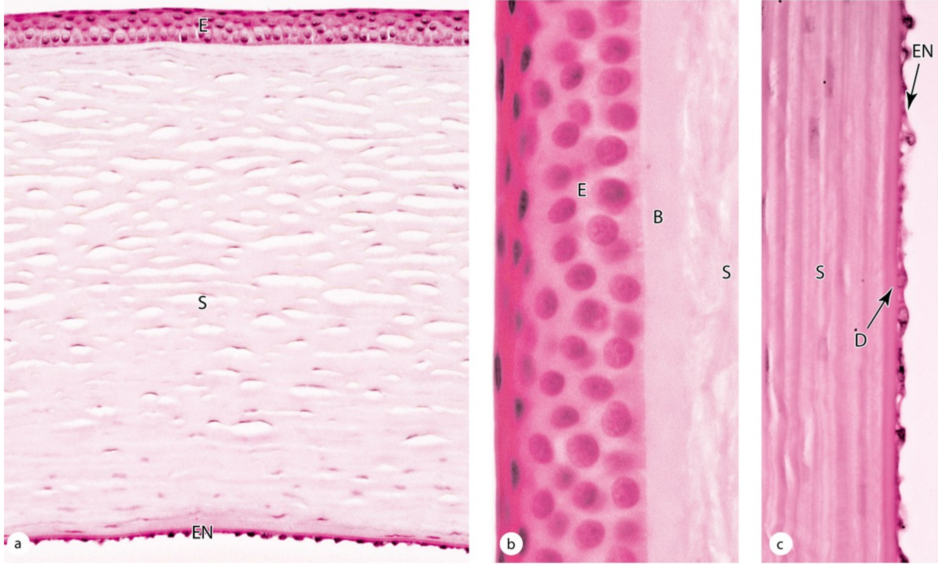


1. Aqueous humor is secreted by the ciliary processes into the posterior chamber.
2. Aqueous humor moves from the posterior chamber, through the pupil, to the anterior chamber.
3. Excess aqueous humor is resorbed via the scleral venous sinus.

Eye Anatomy- Vitreous and Aqueous Humor: https://www.youtube.com/watch?v=7E40NZsQO4E

MEDICAL APPLICATION:.
Glaucoma: If aqueous humor drainage is impeded, intraocular pressure pushes vitreous body against the retina

Cornea



External stratified squamous epithelium (**E**): nonkeratinized, sensory-free nerve endings that trigger the blinking reflex.
Stroma (**S**): Collagen fibers with flattened **keratocytes**. Avascular, nutrients diffuse aqueous humor behind the cornea

Medical Application: The shape of the cornea can be changed via laser - assisted in situ keratomileusis **(LASiK)** surgery. The corneal epithelium is displaced as a flap and the stroma reshaped by an excimer laser which vaporizes collagen and keratocytes in a highly controlled manner with no damage to adjacent cells or ECM. LASiK surgery is used to correct myopia (near-sightedness), hyperopia (far-sightedness), or astigmatism (irregular curvature of the cornea).

Corneal grafts (transplants) between unrelated individuals can usually be accomplished successfully without immune rejection due in part to this tissue's lack of both a vascular supply and lymphatic drainage.

https://www.youtube.com/watch?v=TL4m7cPYyUY

Corneoscleral junction (limbus) and ciliary body

Corneoscleral junction (**CSJ**): corneal stroma merges with the opaque, vascular sclera (**S**).

Conjunctiva (**C**) cover the anterior sclera and lining the eyelids.

Scleral venous sinus (**SVS**), or canal of Schlemm: receives aqueous humor from an adjacent trabecular meshwork at the surface of the anterior chamber (**AC**).

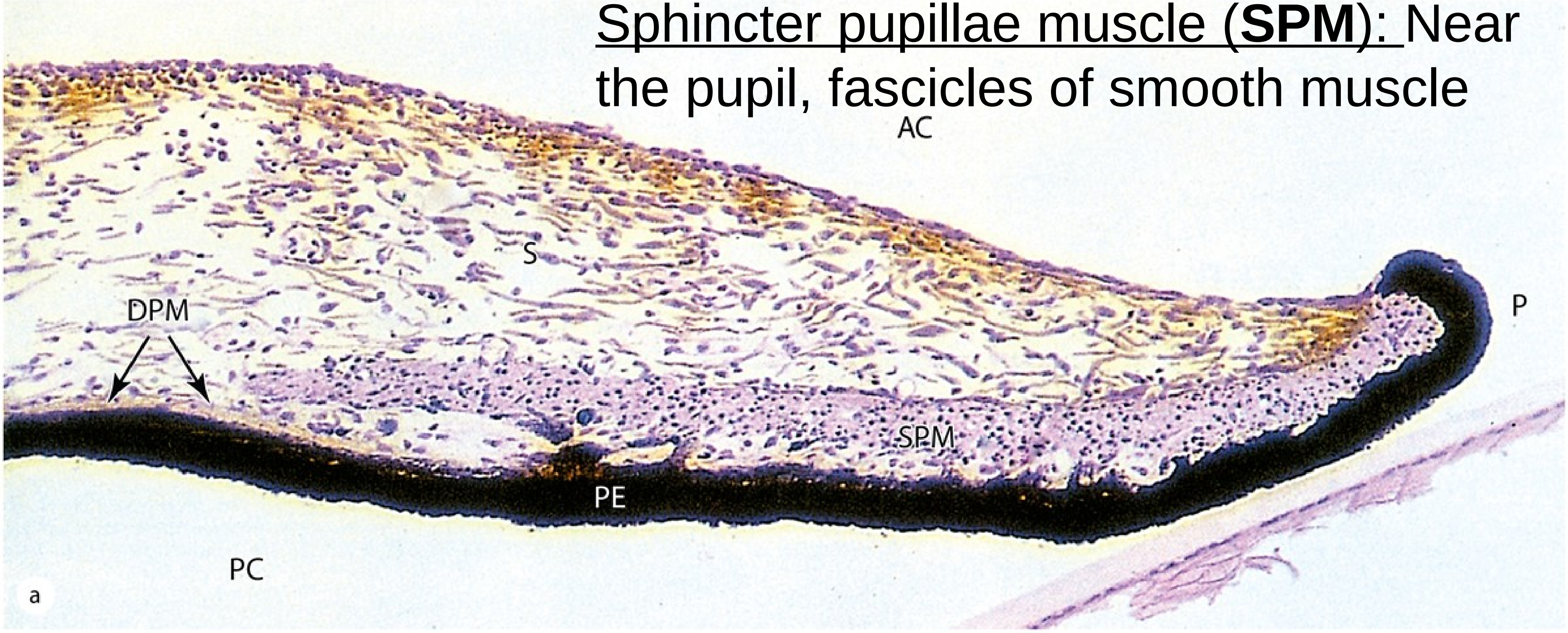
Iris (**I**): anterior extension of ciliary body and Ciliary body:

- Ciliary muscle (**CM**): smooth muscle
- Ciliary processes (**CP**): epithelium, produces aqueous humor that flows through pupil into the anterior chamber
- Ciliary zonule (**CZ**): fibrillin-rich fibers that attach to the capsule of the lens (**L**)

Posterior chamber (**PC**)
Vitreous chamber (**VC**)

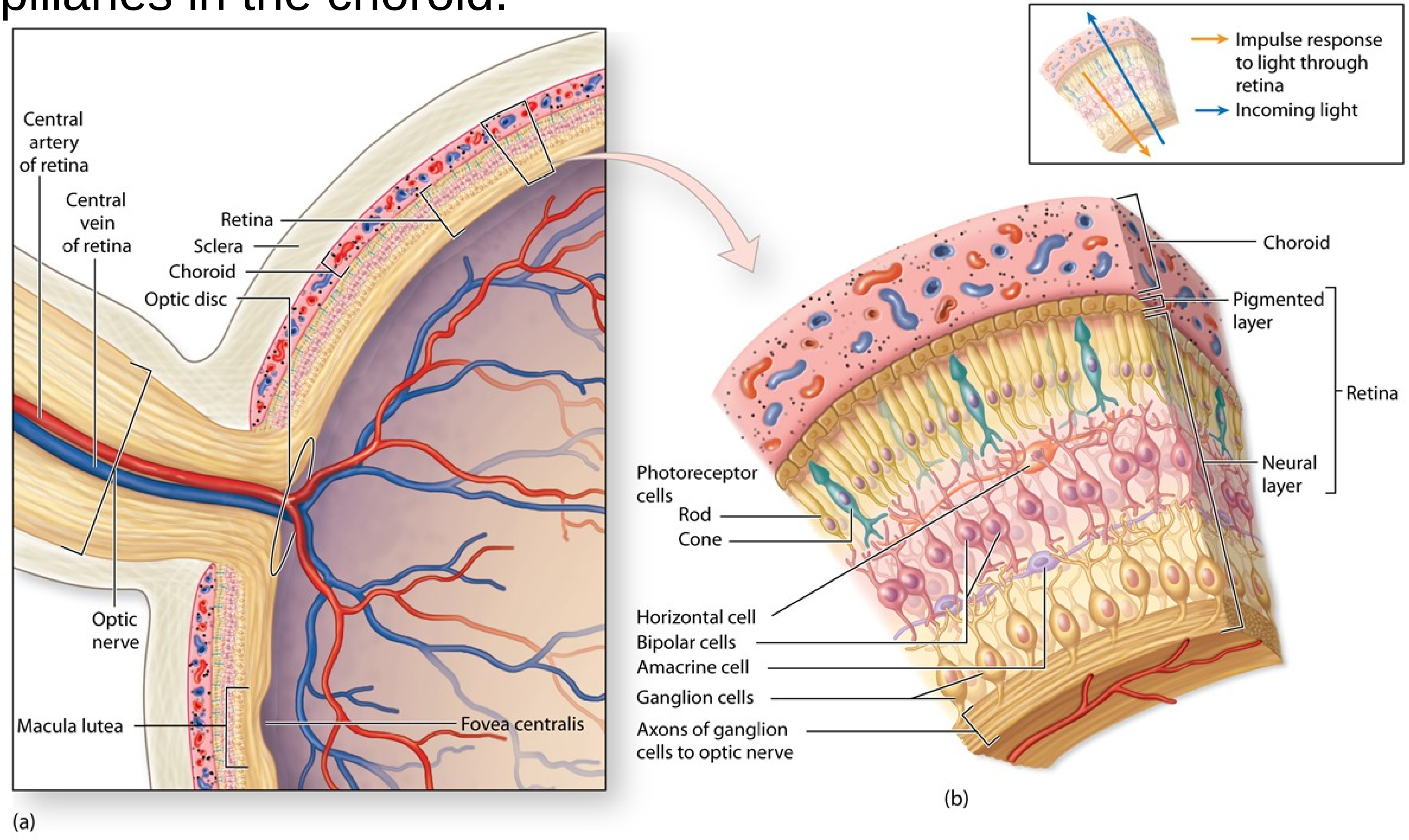
The iris regulates the amount of light to which the retina is exposed

Pupil (**P**): Space between iris
Anterior chamber (**AC**): On anterior surface of iris,
External pigmented epithelium (**PE**): Rich in melanin granules to protect the eye's interior from an excess of light. Dilator pupillae muscle (**DPM**): Extends along most of the iris.
Sphincter pupillae muscle (**SPM**): Near the pupil, fascicles of smooth muscle



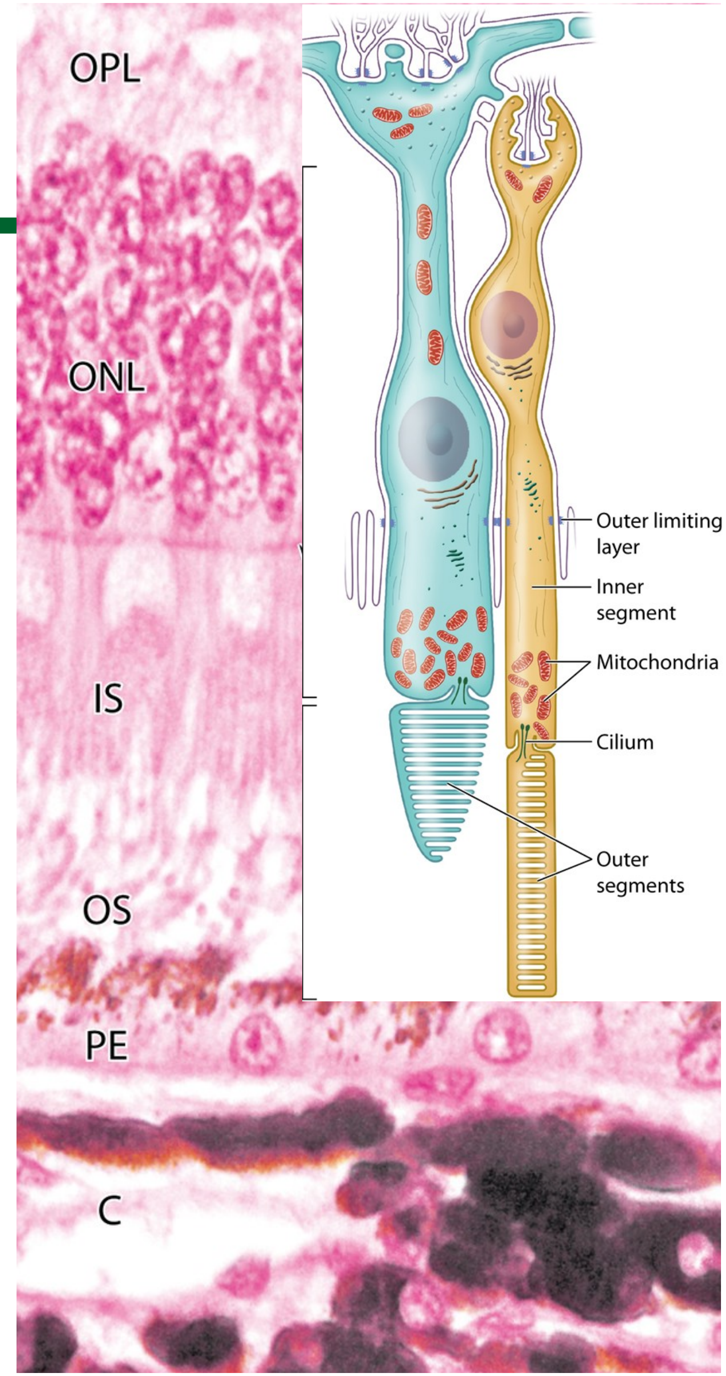
The retina is the thick layer of the eye inside the choroid.

Nutrients and O_2 for the outer retinal layers diffuse from capillaries in the choroid.

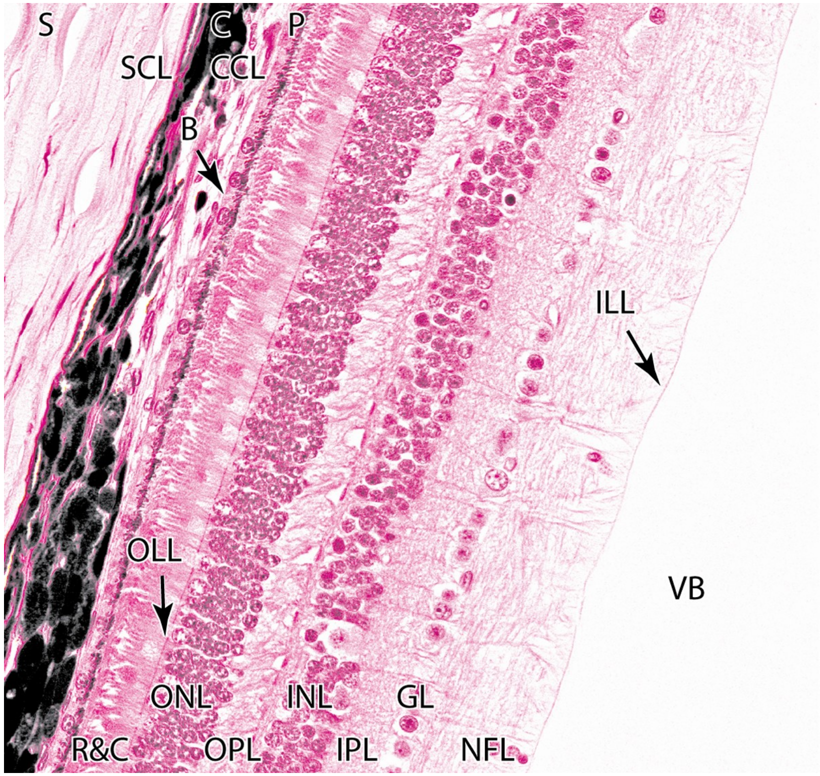


Retina: pigmented epithelium and photosensitive neural layer

<u>Outer plexiform layer (**OPL**):</u>
Axons of rods and cones
<u>Outer nuclear layer (ONL):</u>
Nuclei of rods and cones
<u>Inner segments (**IS**):</u>
mitochondria-rich
<u>Outer segments (**OS**):</u>
Photosensitive stacks of folded membranes with visual pigments
<u>Pigmented epithelium (PE):</u>
simple cuboidal cells inside choroid (C).



Lateral wall of the eye: sclera, choroid, and retina

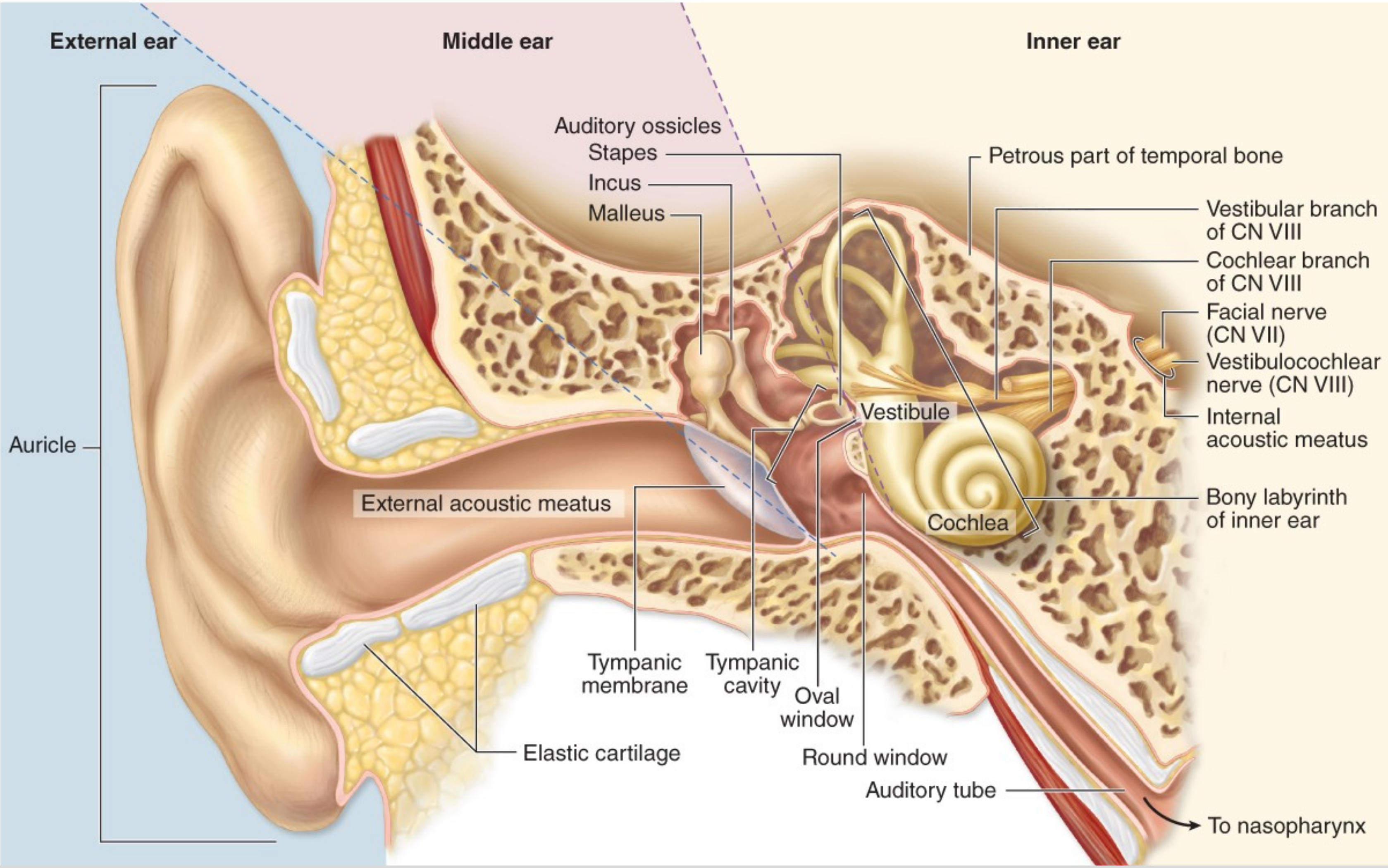


MEDICAL APPLICATION:

Retinal detachment: The pigmented epithelium and the photoreceptor layer of the retina, can be separated by head trauma. Loss of metabolic support causes this area of retina to dies. Prompt repositioning of the retina and reattaching it with laser surgery is an effective treatment.

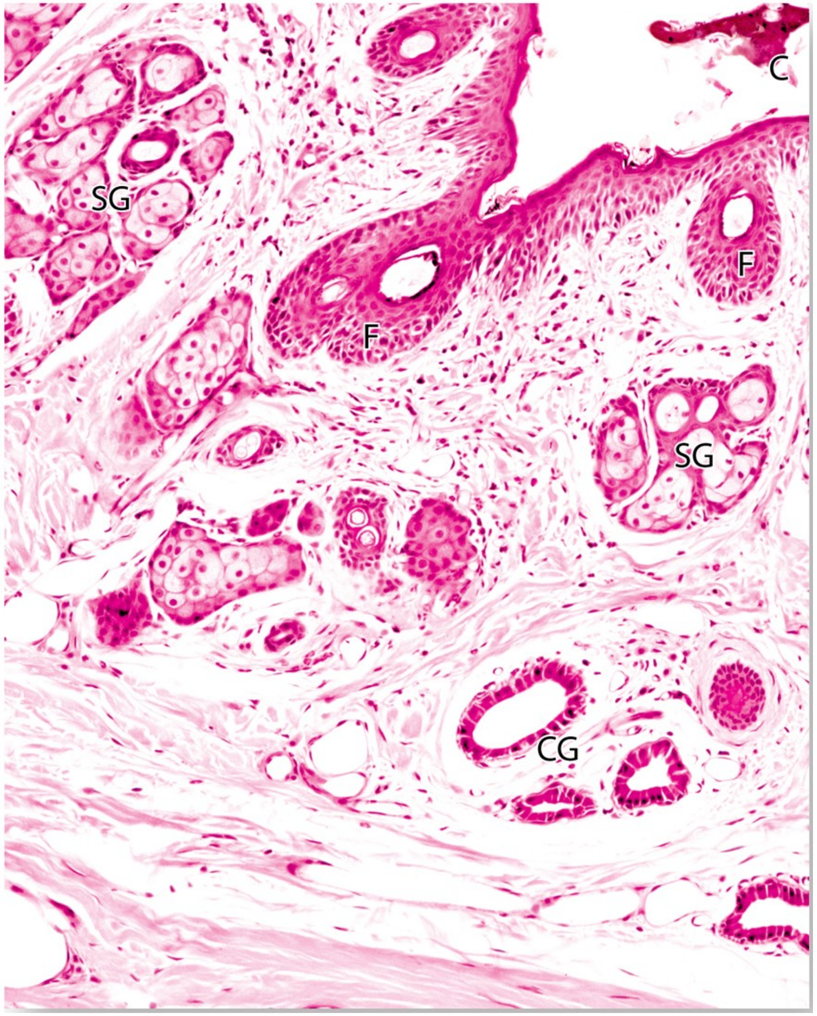
http://ed.ted.com/lessons/could-a-blind-eye-regenerate-david-davila

Major divisions of the ear: external, middle, and internal



Ear Anatomy | Inside the ear | 3D Human Ear animation video | Biology | Elearnin: https://www.youtube.com/watch?v=p3Oy4lodZU4

The external acoustic meatus leads from the opening in the auricle to the tympanic membrane (or eardrum).



Outer third of the acoustic meatus is lined with skin.

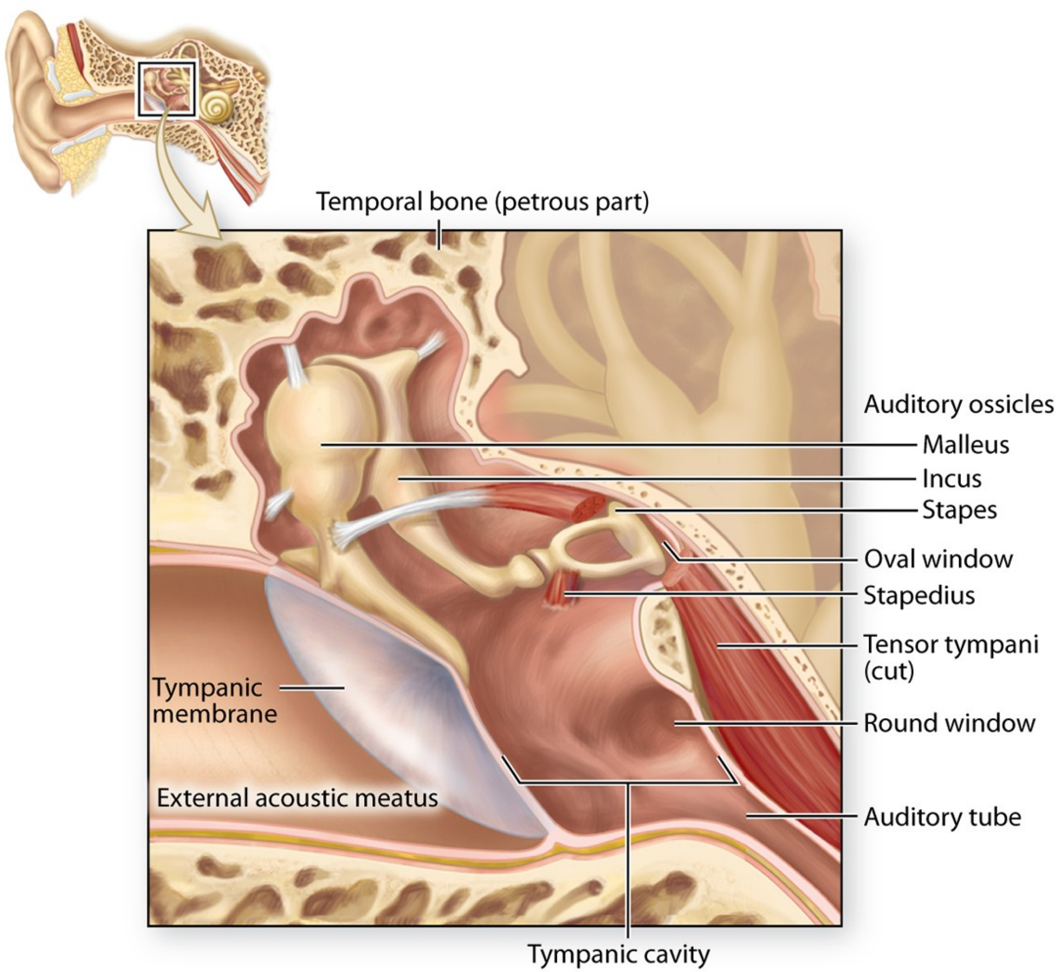
Small hair follicles (**F**)

Sebaceous glands (**SG**)
Ceruminous glands (**CG**): and modified apocrine sweat glands

Secretions from these two glands form a yellowish, waxy product called **cerumen (C)**

Middle Ear

Three **auditory ossicles** are enclosed by the **temporal bone** and the **tympanic membrane**



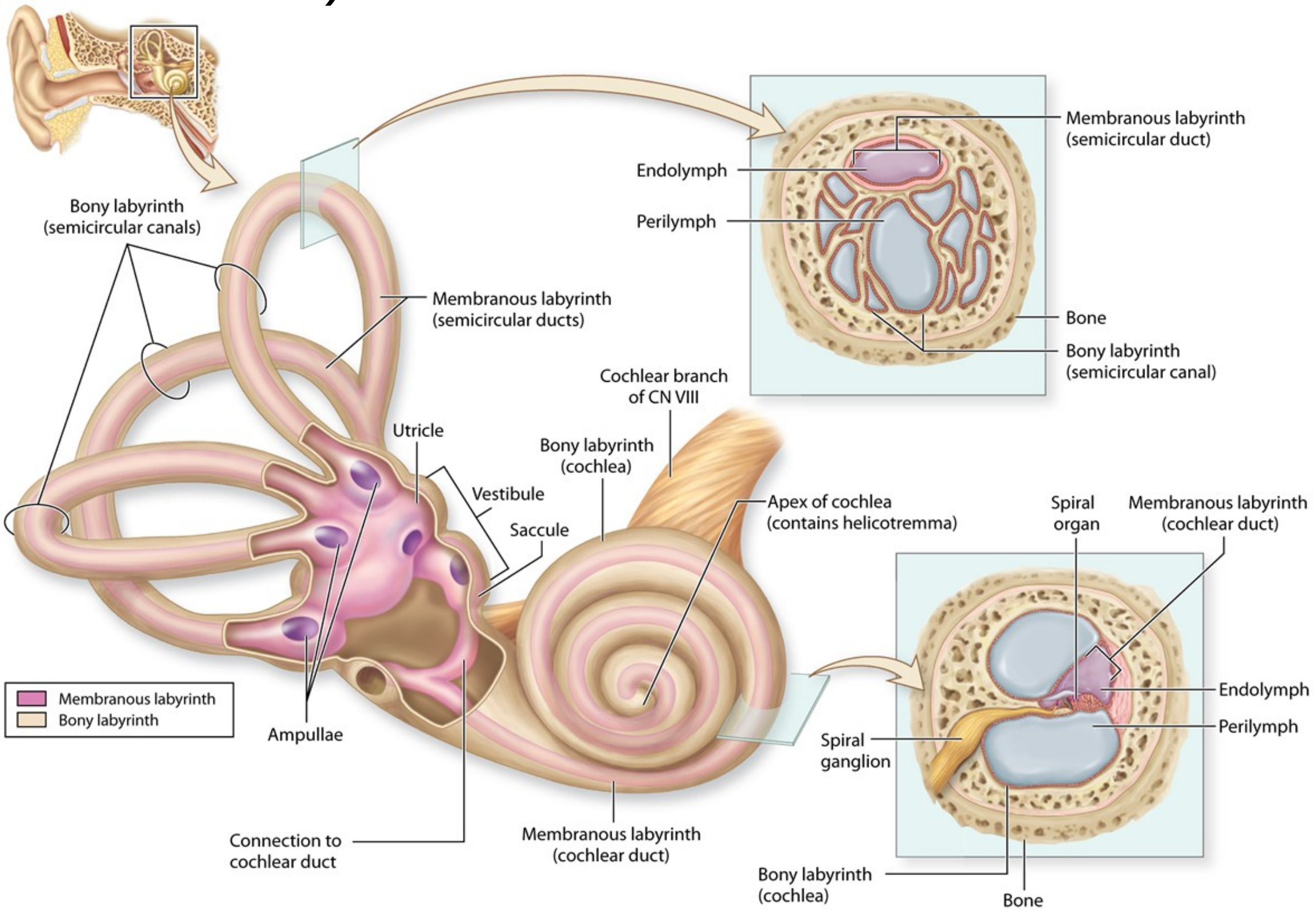
MEDICAL APPLICATION

Inflammation **(otitis media)** of middle ear vua viral or bacterial infections from the upper respiratory tract via the auditory tubes.

Otitis media is common in children, as short auditory tubes facilitate infection of the tympanic cavity.

The internal ear consists of a cavity in the temporal bone, the bony labyrinth, which houses a fluid-filled membranous labyrinth.

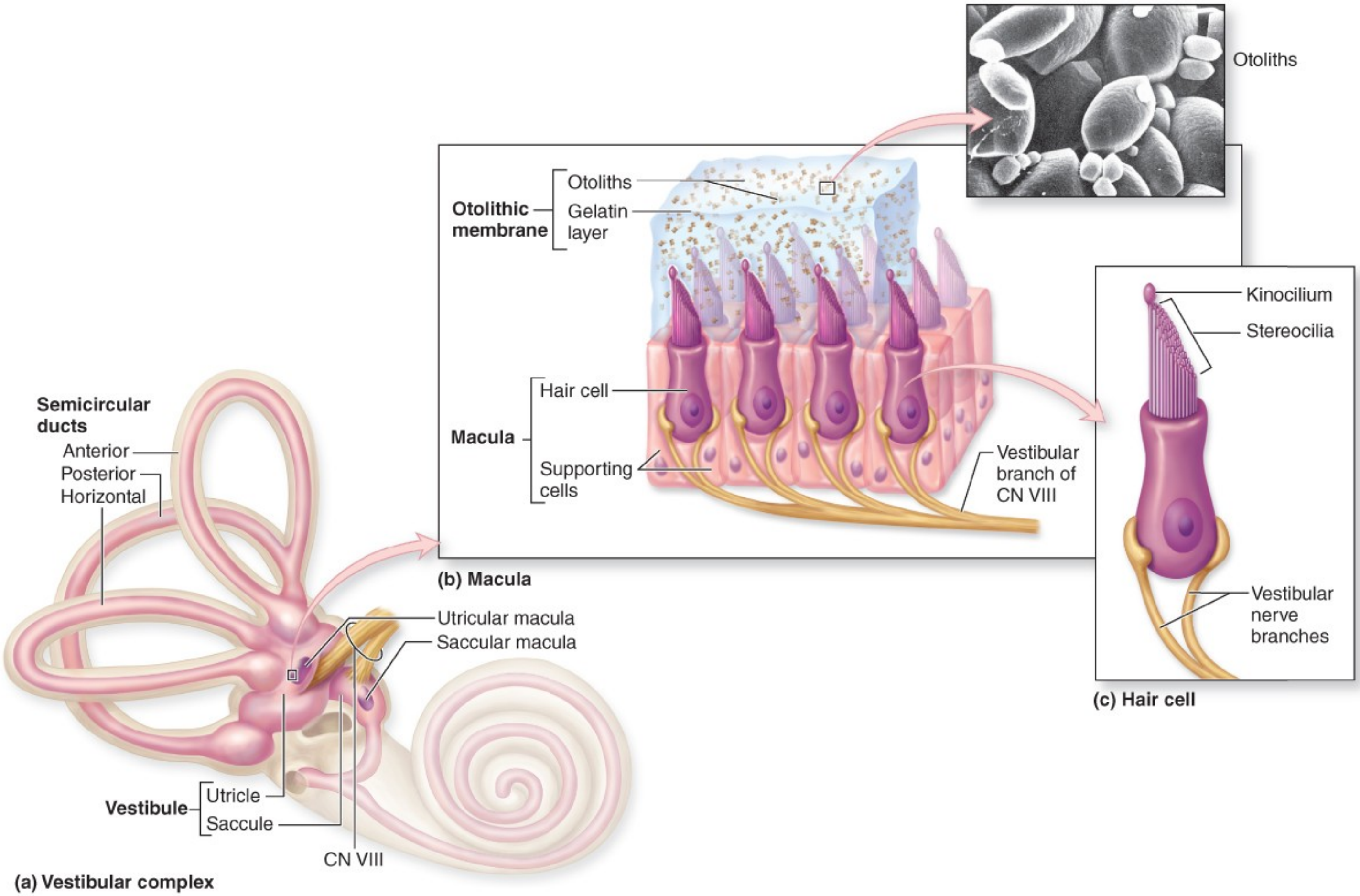
The membranous labyrinth includes the vestibular organs for the sense of equilibrium and balance (the **saccule, utricle**, and **semicircular ducts**) and the **cochlea** for the sense of hearing.



Vestibular maculae are specialized for detecting gravity and endolymph movements.

Hair cells: covered by a gelatinous otolithic layer, basal ends of the cells have synaptic connections with the nerve fibers.

Kinocilia and **stereocilia**: moved by gravity or movement of the head.

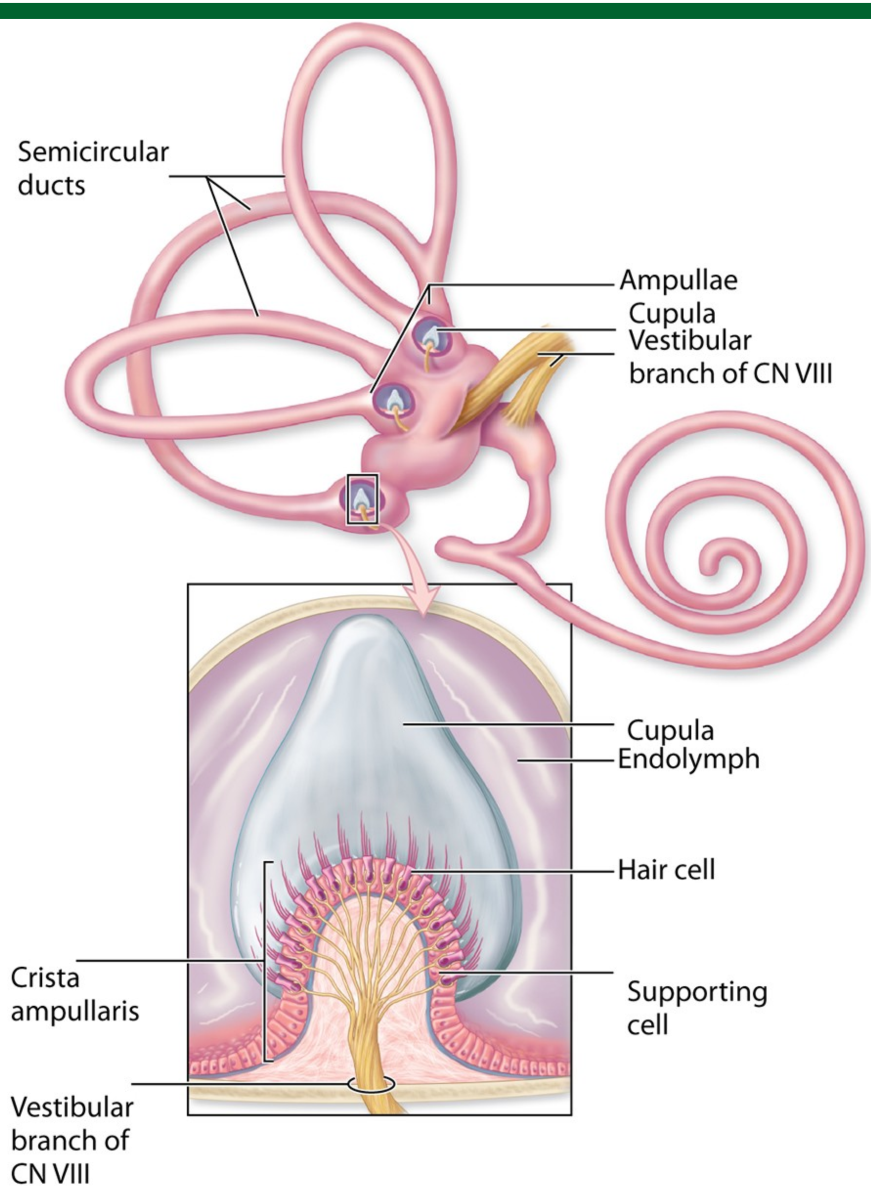


(b) Macula

(c) Hair cell

(a) Vestibular complex

Ampullae and cristae of the semicircular ducts



Ampulla: end of semicircular ducts
Crista ampullaris: Contain hair cells with hair bundles projecting into layer of proteoglycan called the cupula.

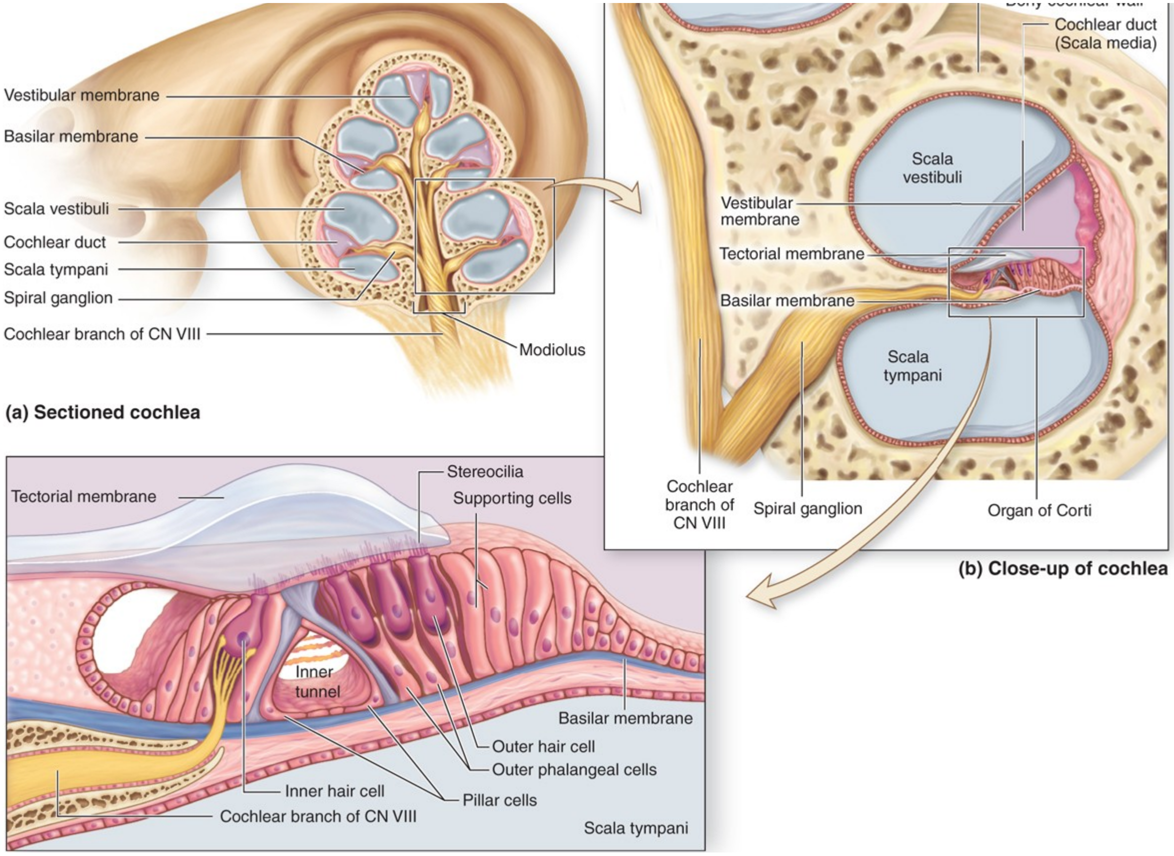
Cupula is moved by endolymph movement within the semicircular duct.

MEDICAL APPLICATION: Vertigo caused by internal ear inflammation or neurologic conditions.

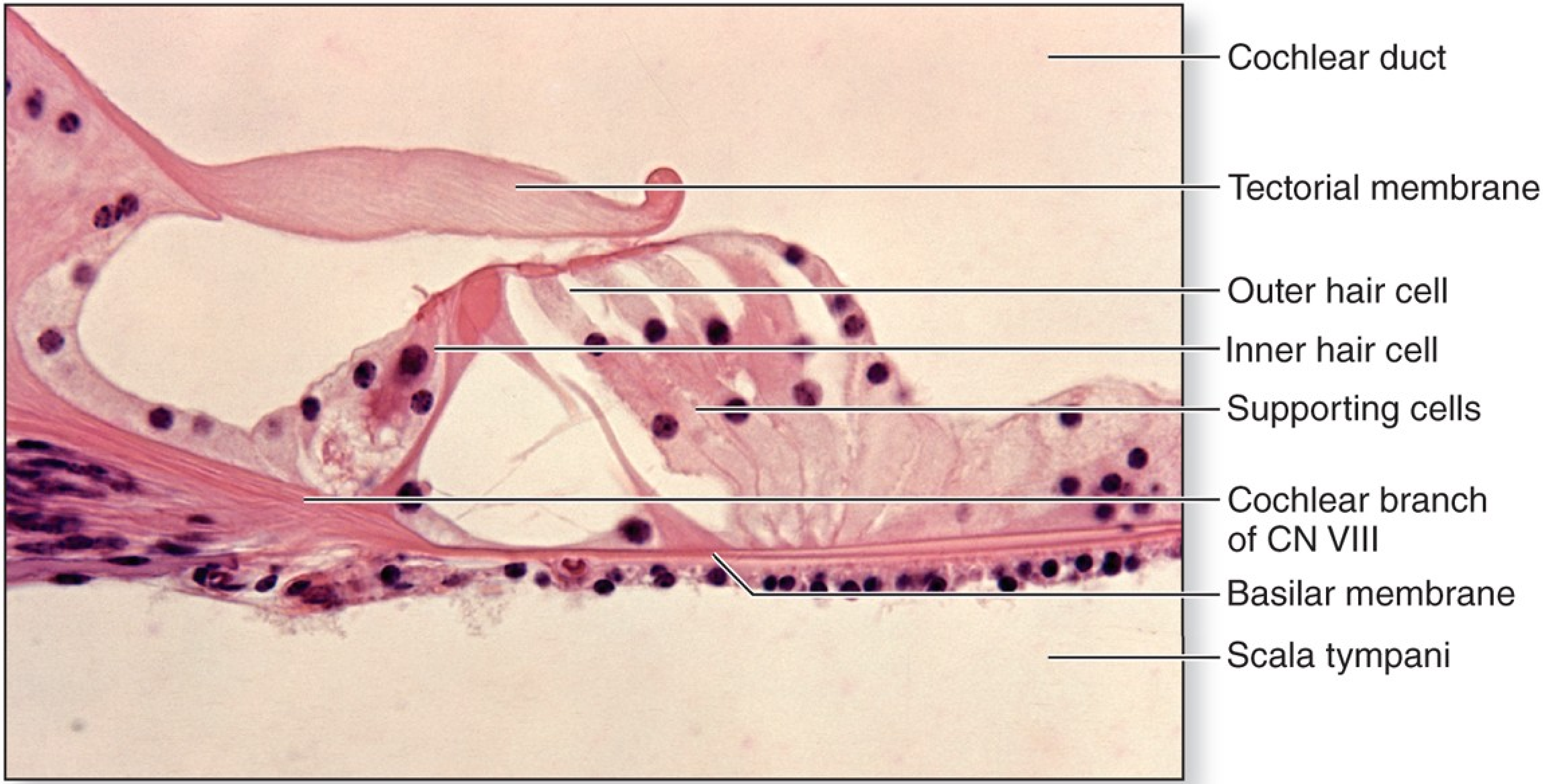
Brief periods of vertigo produced by sudden changes in position of head, such as standing up quickly or sitting up after lying in bed, may result when otoliths detach from the otolithic membrane.

Cochlea and spiral organ (of Corti)

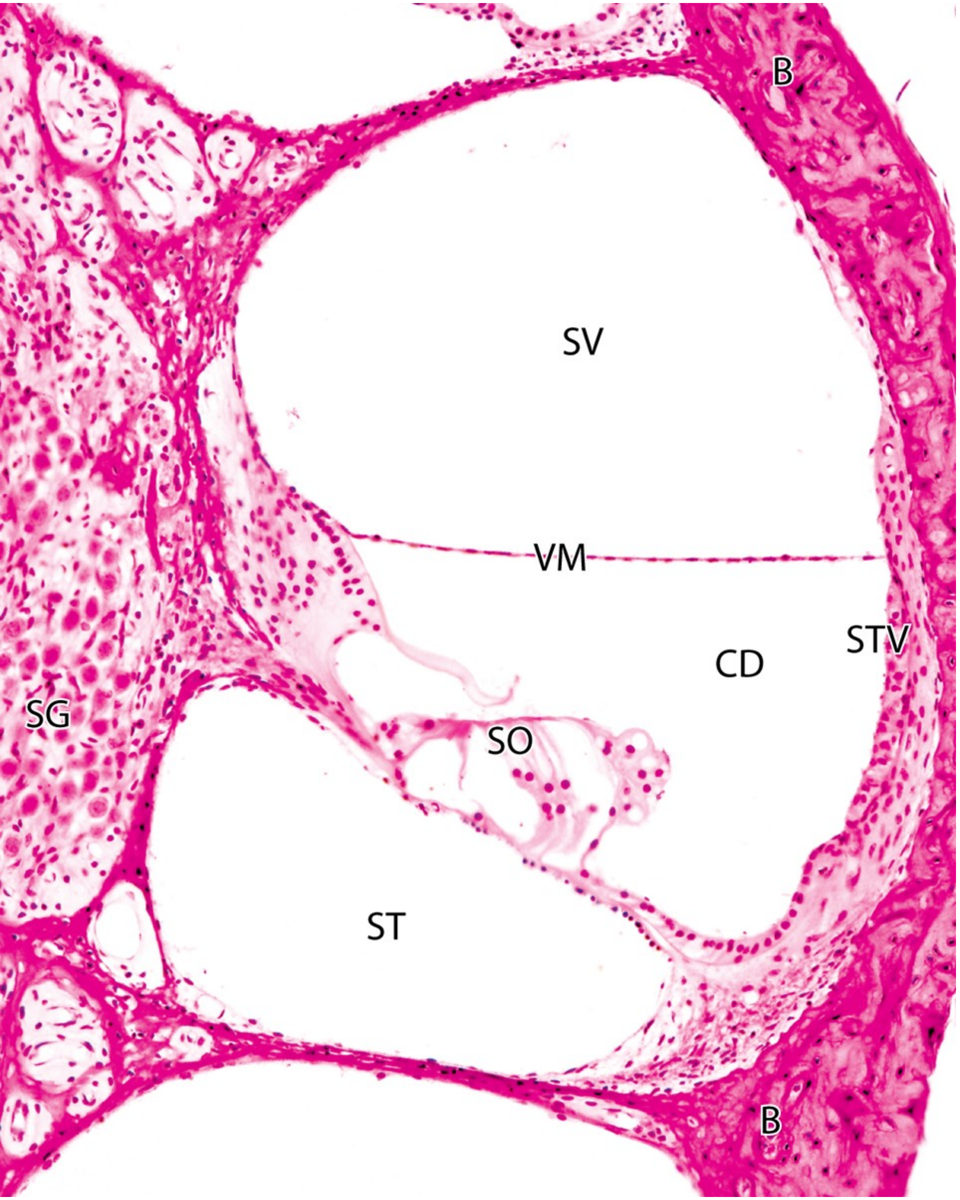
Cochlea: snail-like spiral bony and membranous labyrinths.
Cochlear duct (scala media): Endolymph filled
Organ of Corti: on the basilar membrane,
Perilymph-filled spaces: scala vestibuli and scala tympani.



http://highered.mheducation.com/sites/0072495855/student_view0/chapter19/animation__effect_of_sound_waves_on_cochlear_structures__quiz_1_.html



(d) Organ of Corti



Cochlear duct and spiral ganglion:

Cochlear duct (**CD**): filled with endolymph produced in the epithelial cells of stria vascularis (**STV**),

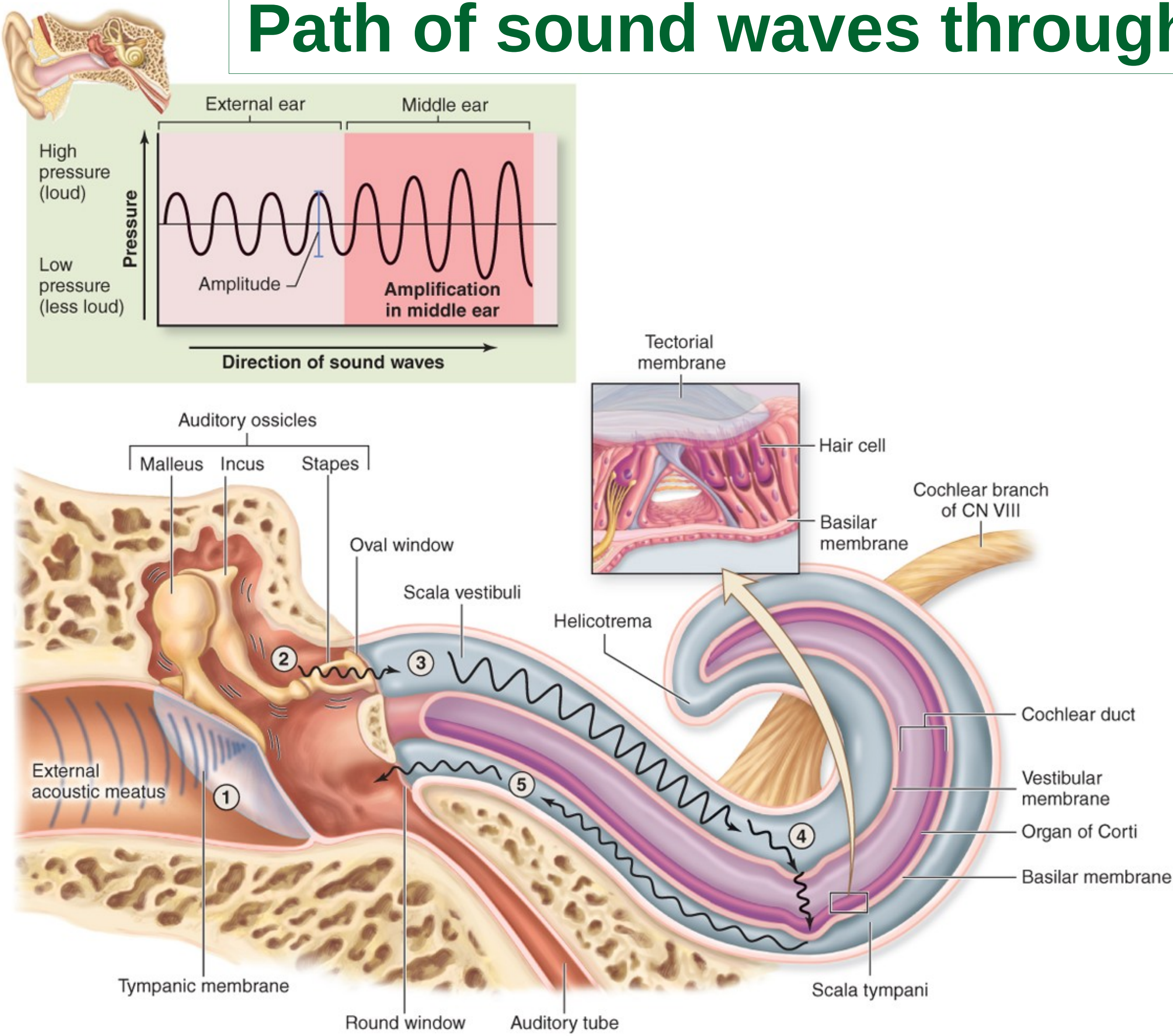
Bone (B)

Scala vestibuli (**SV**) and scala tympani (**ST**): filled with perilymph

Vestibular membrane (**VM**): separates perilymph in the scala vestibuli from endolymph in the cochlear duct.

Spiral ganglion (**SG**): Contains cell bodies of bipolar neurons which send axons to the cochlear nuclei of the brain.

Path of sound waves through the ear

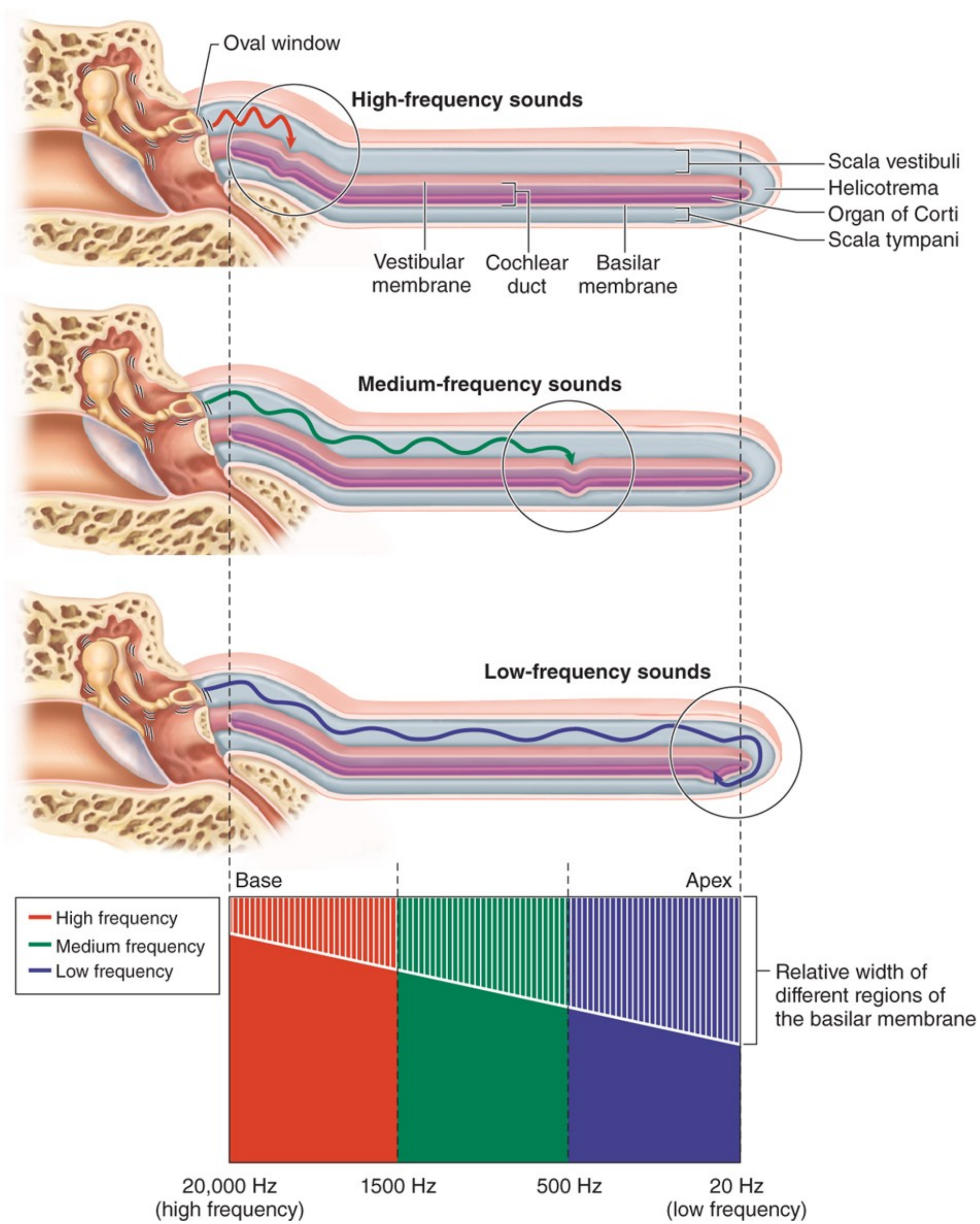


1. Sound waves enter ear and cause the tympanic membrane to vibrate.
2. Tympanic membrane vibration moves auditory ossicles; sound waves are amplified.
3. The stapes at the oval window generates pressure waves in the perilymph within the scala vestibuli.
4. Pressure waves cause the vestibular membrane to move, resulting in pressure wave formation in the endolymph within the cochlear duct and displacement of a specific region of the basilar membrane. Hair cells in the organ of Corti are distorted, initiating a nerve signal in the cochlear branch of CN VIII.
5. Remaining pressure waves are transferred to the scala tympani and exit the inner ear via the round window.

MEDICAL APPLICATION

Conductive hearing loss: conduction of vibrations by the chain of ossicles from the tympanic membrane to the oval window reduced

Sensorineural deafness: defects in any structure or cell from the cochlea to the auditory centers of the brain



Interpretation of sound waves in the cochlea

High-frequency sound waves (red arrow) generate pressure waves that displace the basilar membrane near the base of the cochlea, close to the oval window.
Medium-frequency sound waves (green arrow) and low-frequency sound waves (blue arrow) displace the membrane closer to the apex

MEDICAL APPLICATION
Cochlear implant: A microphone transmits signals to a receiver that stimulates nerve branches appropriate for those frequencies.

https://www.youtube.com/watch?v=zeg4qTnYOpw