محاضرات فسلجة

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Lecture 1 The Cell

Introduction

Anatomy It is the study of the structure and shape of the body; body parts and their relationships to one another . Physiology: It is the study of how the body and its parts work or function .

The cells

Cell is the smallest basic unit of structure and function in the body . They are variable in shape , size and functions . They are grouped together form tissues, each of which has a specialized function , e.g. blood , bone, muscle Different tissues are grouped together to form organs , e.g. heart, stomach, brain, kidney each of which performs Organs are grouped together to form systems particular function that maintains homeostasis and contributes to the health of the individual A cell consist of a membrane surrounded it called (plasma membrane) inside which a number of organelles suspended in watery fluid called (cytoplasm) Organelles functions, and are often enclosed in their own membrane in the cytoplasm are a smali organs have individual and highly specialized they include

Nucleus

Mitochondria

Ribosomes

Endoplasmic reticulum

Golgi apparatus

Lysosomes

Cytoskeleton

The Plasma Membrane

Plasma membrane consist of two layers of (phospholipids) with protein and sugar (carbohydrates) molecules embedded in them There are two type of sugar (glycoprotein and glycolipid) , type of proteins (peripheral and integral) peripheral proteins partially embedded in one face of the membrane, whereas integral proteins span the membrane from side to the other. In addition to phospholipids, the cholesterol is also present in the plasma membrane so there was two are The phospholipid molecules have a head which is electrically charged and hydrophilic (meaning water loving) , and a tail which has no hydrophobic (meaning water charge and is hating) The phospholipid bilayer is arranged like a sandwich with the hydrophilic head aligned forming a central water repelling layer on the outer surface of the membrane and the hydrophobic tails Those proteins that extend all the way through the membrane may provide channels that allow the passage of, e.g. (water , electrolytes and non pidii Whereas the hydrophobic middle of the membrane soluble substances) restricts the passage of water and water-soluble molecules and ions . This arrangement of the phospholipid and protein known as the Fluid-mosaic model of membrane structure Those different influence the transfer of substances across the membrane

Functions of plasma membrane:

1. It separates the contents of the cell from its outside environment and it regulates what enters and exits the cell

2. Plasma membrane plays interior of the cell by allowing only selected substances into the cell and keeping other substances out.

3. It also serves as a base of attachment for the cytoskeleton in some organisms and the cell wall in others. Thus the cell membrane supports the cell and helps in maintaining the shape of the cell.

4. The cell membrane is primarily composed of proteins and lipids. While lipids help to give membranes their flexibility and proteins monitor and maintain the cell's chemical climate and assist in the transfer of molecules across the membrane. bilayer pidi selected molecules to diffuse across the membrane

5. The lipid bilayer is semi-permeable, which allows only selected molecules to diffuse across the membrane.

The Organelles

1. Nucleus

Every cell in the body has a nucleus except the mature erythrocytes . Some other cells have several nuclei e.g. skeletal muscle and liver cells The nucleus is the largest organelles , surrounded by two membrane (an inner membrane and an outer membrane) that together envelop that which some substances can pass between it and the cytoplasm . The are called the nuclear , a membrane similar to the plasma membrane but with tiny pores nucleus is variable in shape (e.g. spherical , oval, kidney-shape, lobbed). The nucleus contains the body's genetic material, which direct all the metabolic activities of the cell. This consist of (46 chromosomes) which are made from DNA , except during cell division the chromosomes resemble a fine network of threads called (chromatin) . Within the nucleus is a roughly spherical structure called (nucleolus), which is involved in manufacture (or synthesis) and assembly of the components or ribosomes NO

2.Mitochondria

membranous, finger-shaped Mitochondria (single mitochondrion) structure in the cytoplasm , sometimes described as the "power house" of the are Each mitochondrion is surrounded by an inner and outer membrane separated by inner and outer membranes of mitochondria , it has an a

narrow intermembranous space : is the region between the important role in the primary function of mitochondria which is oxidative phosphorylation The outer membrane is smooth and is a relatively simple phospholipid bilayer containing protein structures called porins permeable to molecules of about 10 kilodaltons or less (the size of the smallest proteins) . Ions, nutrient molecules, ATP, ADP, etc. can pass through the outer membrane with easy Which render it The inner membrane is characterized by many folds called cristae (singular : crista) which project like shelves into the matrix of mitochondrion The cristae greatly increase the total surface area of the inner membrane The inner membrane is freely permeable only to oxygen , carbon dioxide and water. Mitochondria serve as sites for the production of most of the energy. The most active cells have the greatest number of mitochondria e.g. liver muscles and spermatozoa

3. Endoplasmic reticulum (ER) :

Endoplasmic reticulum ER is a tubules in the complex series of There are two types : smooth and rough , smootn cytoplasm of the cell endoplasmic reticulum SER synthesised lipids and steroid hormones and is also associated with the detoxification of some drugs, some of the lipids replace and repair the plasma membrane and membranes of are used to organelles

Rough endoplasmic reticulum RER is studded with ribosomes on it surface , these are the site of synthesis of proteins, some of which are exporte from cell e.g. enzymes and hormones that leave the cell by exocytosis to be used by cells in another place.

4. Golgi apparatus:

It consists of stacks of closely folde flattened membranous sacs , it is present in all cells but is larger in those that synthesise and export proteins The Golgi apparatus is usually found close to the cell nucleus, it has two faces' - the cis (receiving or forming or entry) face and the trans (or maturing or exit) face The proteins move from the ER to the Golgi apparatus where they are 'packaged' into membrane-bound vesicles called (secretory granules) , the vesicles are stored

and when needed they move to the plasma membrane and fuse with it, the contents then leave the cell by exocytosis

5. Ribosomes

These are tiny granules composed of RNA and protein . They synthesise protein from amino acid using RNA as the template When the ribosomes present in free unit or in small clusters in the cytoplasm they make proteins for use within the cell, these include the enzymes required for metabolism Ribosomes are also found on the outer surface of the nuclear envelope and rough endoplasmic reticulum , where they manufacture proteins for export from the cell.

6. Lysosomes

A tiny spherical vesicles , Primary lysosomes are produced by the Golgi apparatus. They form secondary lysosomes by fusing with other membrane- hound vesicles in the cytoplasm, these vesicles may contain extracellular material that has entered the cell by phagocytosis and require digesting or organelles that require degrading because they have reached the end of their active life They ccntain about 40 different types of hydrolytic enzymes including proteases, nucleases and lipases (they are all acid hydrolyses, which need an acid pH to work optimally) This process is also used for degrading internal organelles in a process called 'autophagy' in which cell organelles are marked for destruction. Also when lysosomes fuse with the organelles to form secondary lysosomes

7 .Cytoskeleton:

This consist of an extensive network of tiny protein fibers , they include

Microfilaments : These are the smallest protein fibers , they provide structural support, maintain the characteristic shape of the cell and permit contraction e.g. in muscle cells .

Microtubules : These are larger contractile protein fibers that are involved in movement of (organelles in the cell , chromosomes during cell division , cell extensions).

Centrosome: This directs organization of microtubules in the cell , it consist of a pair of (centrioles) a small cluster of microtubules and plays an important role during cell division

Cell extensions : These project from the plasma membrane in some types of cell and their main components are microtubules which allow movement, they include: (microvilli, cilia, flagella).

Transport of Substances across Cell membrane

Passive transport: This occurs when substances can cross the semipermeable plasma and organelles membranes and move down the concentration gradient (downhill) without using energy , there are three types

1- Diffusion : Is refers to the movement of a chemical substances from 1. an area of high concentration to an area of low concentration and occur mainly in gases , liquids and solution. The process of diffusion is speeded up if the

temperature of solution rises.

the concentration of the diffusing substance is increased

The permeability of the membrane to the diffusing substances

The surface area of the membrane through which the substances are diffusing Osmosis

2- **Osmosis** is the movement of water through a plasma membrane from a region of low solute concentration to a region of high concentration of solute to which the membrane is impermeable When a substance is dissolved in water, the concentration of water molecules in the solution is less than that in pure water because the addition of solute to the water results in a solution that occupies a greater volume than does the water alone The force with which osmotic process occurs is called the osmotic pressure it is also defined as the minimum pressure needed to nullify osmosis . e.g. Imaging two solutions of sugar separated by a semipermeable membrane whose pores are too small to let the sugar molecules through, on one side the sugar solution is twice as concentrated as on the other side . After a period of time the concentration of sugar molecules will have equalised on both sides of the membrane, not because sugar molecules have diffused across the membrane but because osmotic pressure across the membrane pulls water

from the dilute solution into the concentrated solution (water has moved down its concentration gradient). Osmosis proceeds until equilibrium is reached at which point the solutions on each side of the membrane are of the same concentration and are said to be isotonic .

3- **Facilitated diffusion :** This passive process is used by some substances that are able to diffuse through the semipermeable membrane unaided (e.g. Glucose , amino acids). Specialized protein carrier molecules in the membrane have specific sites that attract and bind substances to be transferred like a (lock and key mechanism The carrier then changes its shape and deposits the substances on the other side of the membrane , the carrier sites are specific can be used by only one substances

Active transport: This is the transport of substances from lower to a higher concentration , chemical energy in the form of (ATP) . Its a include two types:

1- **The Sodium-Potassium Pump** : Also known as Na+-K+ ATPase (Sodium-potassium adenosine triphosphatase) , its located in the plasma membrane of all animal cells This active transport mechanism maintains the 'unequal concentrations of sodium (Na+) and potassium (K+) ions on either side of the plasma membrane, it may use up to (30%) of cellular ATP requirements Potassium levels are much higher inside the cell than outside , it is the principal intracellular cation. Wheres sodium levels are much higher outside the cell than inside and it is the principal extracellular cation . These ions tend to diffuse down their concentration gradients (K+) outwards and (Na+ into the cell in order to maintain their concentration gradients excess (3 Na+) is constantly pumped out across the cell membrane in exchange for (2 K+ 8)

2- Bulk Transport

membrane occurs by pinocytosis or engulfed by extensions of the cytoplasm which enclose them, forming a membrane-bound vacuole . When the vacuole is small pinocytosis occurs, Transport of particles too large to cross cell phagocytosis these particles are : and in phagocytosis larger particles (e.g. cell fragments , foreign materials , microbes) are taken into the cell this process called endocytosis Lysosomes then adhere to the vacuole membrane

releasing enzymes which digest the contents. An exocytosis is a process by which cellular products are secrete into the extracellular environment . Secretory granules formed by the Golgi apparatus usually leave the cell in this way , so as do an indigestible residues of phagocytosis . Exocytosis and endocytosis together provide (bulk transport) out of and into the cell respectively

The Tissues:

The tissues of the body consist of large numbers of cells and they are classified according to the size , shape and functions of these cells. There are four main types of tissues that each have subdivision:

1. Epithelial tissue o epithelium

2. Connective tissue

3. Muscle tissue

4. Nervous tissue

1- Epithelial tissue this group of tissues is found covering the body and lning cavities, hollow organs and tubes. The cells are very closely packed and the intercellular substance called "matrix" is minimal . Te cells usually lie on a "basement membrane" which is an inert connective tissue made by the epithelial cells themselves. It is also found in glands , the structure of epithelium is closely related to its functions which include:

Protection of underlying structures from (e.g. dehydration , chemical and mechanical damage).
Secretion
Excretion
Absorption
Sensory reception

Reproduction

Epithelial tissue divided into two groups

: Simple a single layer of cells

Stratified: several layers of cells

The simple Epithelial tissues : Simple epithelium consists of a single layer of identical cells , it is usually found on a thin membrane called the "basement membrane" . The types are named according to the shape of the cells which differs according to their functions ; there four types included

1**. Simple squamous epithelium :** This is composed of a single layer of flattened cells lining on the basement membrane . The cells have one nucleus central in position , this tissue lining the blood vessels (endothelium), alveoli and the heart (endocardium)

2**. Simple cuboidal epithelium :** This consists of a single layer of shaped cells lning on the basement membrane , The cells have one nucleus central in position . This tissue is lining the kidney tubule , ducts of glad and the ovary surface .

3. **Simple columnar epithelium :** Consists of a single layer of cells taller than cuboidal tissue they are wide , and have one nucleus oval in shape located near to the base of the cells . This tissue is found in the stomach , oviduct cube- and intestine

4. Pseudo-stratified columnar epithelium : This tissue found in the trachea

The stratified epithelial tissues : stratified epithelial tissue consists oi several layers of cells (two or more) of various shapes . Continual cell division in the lower (basal) layers pushes cells above nearer and nearer to the surface , where they are shed . Basement membranes are the main function of stratified epithelium is to protect underlying structures from mechanical wear and tear. There are many types of this tissue included usually absent

1. **Stratified squamous epithelium :** This tissue composed of a number of layers of cells . in the deepest layers the cells are mainly columnar and as they grow towards the surface they become flattened and are then shed. There are two types of this tissue:

   Keratinized stratified squamous epithelium : found in the skin and nails

   Non-keratinized squamous epithelium found in the pharynx oesophagus and nasal cavity

   2. **Stratified cuboidal epithelium** : usually two layers of cube-shaped cells, this tissue found in sweat glands salivary glands and pancreas

   3. **Transitional epithelium** : This is composed of several layers of pear- shaped cells . It found lining the urinary bladder , ureter and urethra

2. Connective Tissues : connective tissue is the most abundant tissue in the body, the connective tissue cells are more widely separated from each other than in epithelial issues ; and intercellular substance (matrix) is present in considerably larger amounts.there are usually fibers present in the matrix which form a supporting network for the cells to attach to . Most types of connective tissue have a good blood supply , major functions of connective tissue are

Binding and structural support

Protection

Transport

Insulation

Cells in the connective tissue

1- Fibroblasts these are large cells with irregular processes , they are produce collagen and elastic fibers and a matrix of extracellular material

2- Fat cells also known "adipocytes" these cells occur singly or in group in many types of connective tissue and are especially abundant in adipose tissue . They vary in size and shape according to the amount of fat granules that they contain

3- Macrophages : These are irregular-shaped cells with granules in the cytoplasm Some are fixed (attached to connective tissue fibers) and others are motile. They are an important part of the body's defense mechanisms These develop from B-lymphocytes , they synthesis and secret

4- Plasma cells specific defensive antibodies into the blood and tissues .

5- Mast cells: These cells are similar to basophil leukocytes , they are found in loose connective tissue and under the fibrous capsule of some organs (e.g. liver and spleen). They produce granules containing heparin and histamine and other substances, which are released when the cells are damaged by disease or injury

Types of Fibers in the connective tissue:

1. Collagenous or White fibers.
2. Elastic or Yellow fibers.
3. Reticular fibers

Loose connective tissues:

1- Areolar connective tissue: it composed of collagen fibers , elastic fibers and proximately most of connective tissue cells , which embedded in a gelatin matrix muscles and in alimentary tract between the This tissue is found under the skin

2- Adipose connective tissue : it composed of large number of fat cells (adipocytes) , and between these cells some of connective cells like fibroblast and mast cell . This tissue is found under the skin surrounded the kidney and surrounded the ureter

3- Mucous connective tissue : it is found in umbilical cord of fetus (embryo)

4- . Lymphoid connective tissue : it is found in all organs of lymphatic tissue lymph node, thymus gland and spleen

Dens connective tissues:

1. Fibrous connective tissue : composed of collagenous (or white) fibers , this tissue formed the tendons (which connect muscles and bones).

2. Elastic connective tissue : composed of elastic (or yellow) fibers and consists a few number of white fibers and fibroblast cells . This tissue is found in large artery , trachea and true vocal cords

Lecture2BLOOD PHYSIOLOGY

Blood :is a type of liquid connective tissue, the major function of blood is transport

Blood composition: blood consists of

1- (55- 60 %1- volume about liquid plasma

2- Formed elements (cells) (volume about 40-45 %)

Blood Formed elements include

- Erythrocytes (red blood cells);

-Leukocytes (white blood cells)

-Thrombocytes (platelets)

Functions of Blood

1- Respiration: supplies oxygen to cells and tissues

2-Trophic : supplies essential nutrients to cells, such as amino acids, fatty acids, and glucose, either dissolved in the blood or bound to plasma proteins

3- Messenger functions transports hormones released by a cell in one part of the body that sends out messages that affect cells elsewhere in the body

4-Excretive removes carbon dioxide, urea and lactic acid (waste products)

5- Regulative: regulates body acidity (pH) levels regulates body temperature and maintenance of water content in the body

6-Protective (immunological functions) : Its white blood cells have antibodies ch defend the body from infection and foreign bodies

Physical Characteristics of Blood

-Thicker (more viscous) than water and flows more slowly than water

-Temperature of 100.4 degrees F

- pH 7.4 (7.35-7.45)

- 8% of total body weight

- Blood volume about (5 -6 liters) in average male ; and (4- 5 liters) in average female

- Hormonal negative feedback systems maintain constant blood volume and osmotic pressure

Blood plasma Composition:

- 90-92% of water

- 8-10% of dry substance mainly consisting from proteins (6-8%)

Dry substance includes: inorganic (minerals) and organic components

-The main (inorganic) mineral (0.9-1.5 %) components :

-Cations: Sodium (Na), Potassium (K'), Calcium (Ca), Magnesium (Mg2)

-Anions : Chlorides (Cl''), Phosphates (PO4''), Bicarbonates (HCO3).

-The organic components of plasma include : proteins , lipids and carbohydrates

plasma proteins:

- albumin (65-85 g/l)

-globulins (28 g/l)

- clotting proteins (fibrinogen) - (3 g/l)

- Plasma normally contains varying amounts of hormones enzymes , pigments and vitamins . -The composition of plasma varies with the body's activity and different physiological states

-plasma proteins provide a role in balancing osmotic pressure and water flow between the blood and extracellular fluid/tissues

- loss of plasma proteins from blood decreases osmotic pressure in blood and results in water flow out of blood into tissues (swelling)

. Blood formed elements 45% of blood is the cellular elements or formed elements includes:

1- 99% of this (44.55% of total blood) is erythrocytes or RBCS

2- 1% found in the Buffy coat is leukocytes or WBCS

Erythrocytes (Red Blood Cells)

- RBCS are the most abundant type of blood cells. Approximately 2.4 million new erythrocytes are produced per second

- Structure : In humans, mature RBCS are oval biconcave disks and they are flexible

-A typical human erythrocyte has a disk diameter of approximately (6.2-8.2 um), they lack a cell nuc) and most organelles, in order to accommodate maximum space for haemoglobin

-Since RBCS have a elastic membrane, they are able to change their shape when they pass through the capillaries.

- RBCS develop in the bone marrow and its life span about (100-120 days) in the body before their components are recycled by macrophages

-Human red blood cells take on average (20 seconds) to complete one cycle of circulation

- - 1/3 of erythrocytes consisting hemoglobin (Hb) , the protein that carries oxygen in blood. -RBCS Count Normal range : In male (4.0-5.0 x 10/L), and In female (3.5-4.5 x 10 12/L) of blood

Red Blood Cells Classification

1-According to size

- Normocytic: normal sized RBCS

- Microcytes: small sized RBCS

-Macrocytes: large sized RBCS

2-According to color :

- Normochromia : normal colored RBCS

-Hyperchromia darker, due to increased hemoglobin

-Hypochromia paler, due to decreased hemoglobin

They are determined by measuring the:

-Mean corpuscular haemoglobin (MCH)

-Mean corpuscular hemoglobin concentration (MCHC)

functions of RBCS

1- The major function of red blood cells is a transport of haemoglobin, which in turn carries oxygen from lungs to the tissues (transport of O 2)

2-RBCS contain carbonic anhydrase which catalyzes the reaction between carbon dioxide and water, that has a significance in transporting (CO 2) from tissues to lungs

3-Maintenance of acid-base balance (haemoglobin is an excellent acid-base buffer).

4-Blood group determination.

The HAEMOGLOBIN:

-Iron-containing protein (Globin)

- Binds strongly, but reversibly to oxygen

- Each hemoglobin molecule has four oxygen binding sites

- Each erythrocyte has 250 million hemoglobin molecules

- Globin protein consisting of 4 polypeptide chains (a2B2)

-One heme pigment attached to each polypeptide chain

-Each heme contains an iron ion (Fe *2) that can combine reversibly with one oxygen molecule.

-Each hemoglobin molecule can carry 4 oxygen molecules from lungs to tissue cells

-Haemoglobin transports 23% of total CO2 waste from tissue cells to lungs for excreted

-Hemoglobin transports nitric oxide (NO) & super nitric oxide (SNO) helping to regulate Blood Pressure Iron ions pick up nitric oxide (NO) & super nitric oxide (SNO) and transport its to and while SNO from the lungs - NO causing vasoconstriction is released in the lungs causing vasodilatation is picked up in the lungs

-The blood test, hemoglobin Alc (Hb Alc), can be used to monitor blood glucose levels in diabetics

Leukocytes (White Blood Cells)

- WBCS are nucleated cells and do not contain hemoglobin

- Size about (9-12 uk) they make up approximately 1% of the total blood volume ina healthy adult.

-They live for about (3 -4 days) in the average human body.

-Less numerous than RBCS (5000 10,000 cells) per drop of blood (4 -9 x 10 /L)

-The major function of leucocytes is : Protective function ; it provides immunity and thus defends the body.

-WBCS leave the blood stream by emigration, some WBCs particularly neutrophils and macrophages, are active in phagocytosis.

- The chemical attraction of WBCS to a disease or injury site is termed chemotaxis

Have two principal types are:

-Granulocytes: contain cytoplasmic granules

- A granulocytes: lack cytoplasmic granules

Granulocytes : have three types of cells:

1. Neutrophils

2. Eeosinophils

3. Basophils

1. Neutrophils:

- Multi-lobed (3-5 lobes) nucleus with granules stain light purple in acid-base combination stains .

-First line of defense (first white blood cells that arrive at place of infection).

Defend against bacteria (by releasing lysozymes which destroy/digest bacteria -

-They constitute (54% - 62%) of the total leukocytes

-Older neutrophils are called segs (segments) or polymorph-nuclear leukocytes due to nuclear appearance

-Younger neutrophils are called bands

2.Eosinophils

-Contain coarse deep red staining granules in acid stains

-Nucleus has two lobes

--Active during moderate allergic reactions (contains histaminases, so it reduces allergic reaction)

-Defend against parasitic worm infectio

- Constitute (1% -3%) of total leukocytes

Phagocytes antibody-antigen complexes

3- Basophils:

-Granules stain deep blue in basic stain

- Nuclei have two lobes .

-Migrate to damaged tissue Leave capillaries & enter connective tissue as mast cells .

- Release histamine to promote inflammation, and heparin to inhibit blood clotting.

-Constitute less than (1%) of total leukocytes

A granulocytes: have two types of cells :

1. Monocytes .

2. Lymphocytes

Monocytes:

-Are the largest of white blood cells

- Have kidney-shape nucleus

Function as macrophages , its important in fighting chronic infection-

-Take longer to get to site of infection, but arrive in larger numbers

-Destroy microbes and clean up dead tissue following an infection

-Constitute (3% to 9%) of total leukocytes

Lymphocytes

-Nucleus fills most of the cell

-Play an important role in the immune response

-Have two types B cells , T cells and natural killer cells

-B cells - destroy bacteria and their toxins - turn into plasma cells that produces antibodies

- T cells- attack viruses , fungi , transplanted organs , cancer cells & some bacteria.

- Natural killer cells - attack many different microbes and some tumor cells destroy foreign invaders by direct attack

Thrombocytes (Blood platelets)

-Derived from ruptured multinucleate cells "Megakaryocytes" in the red bone marrow Platelets are smaller and lack a nucleus-

- Function in the blood clotting process

-Help repair broken blood vessels.

-Release serotonin Normal platelet count :(150.000 300.000/mm) of blood

-They live for about (5 -9 days) in the average human body

The ABO Blood Group System

Although all blood is made of the same basic elements, not all blood is identical, there are four major blood groups determined by the presence or absence of two (antigens - A and antigens - B) on the surface of red blood cells and the Antibodies which present in the blood plasma . It allows doctors to determine what type of blood to give if a transfusion is necessary, the wrong blood can cause agglutination in a patient leading to death

Antigens-molecules on the outer surface of the cell

Antibodies -molecules floating in plasma that help fight infections

The four types are :

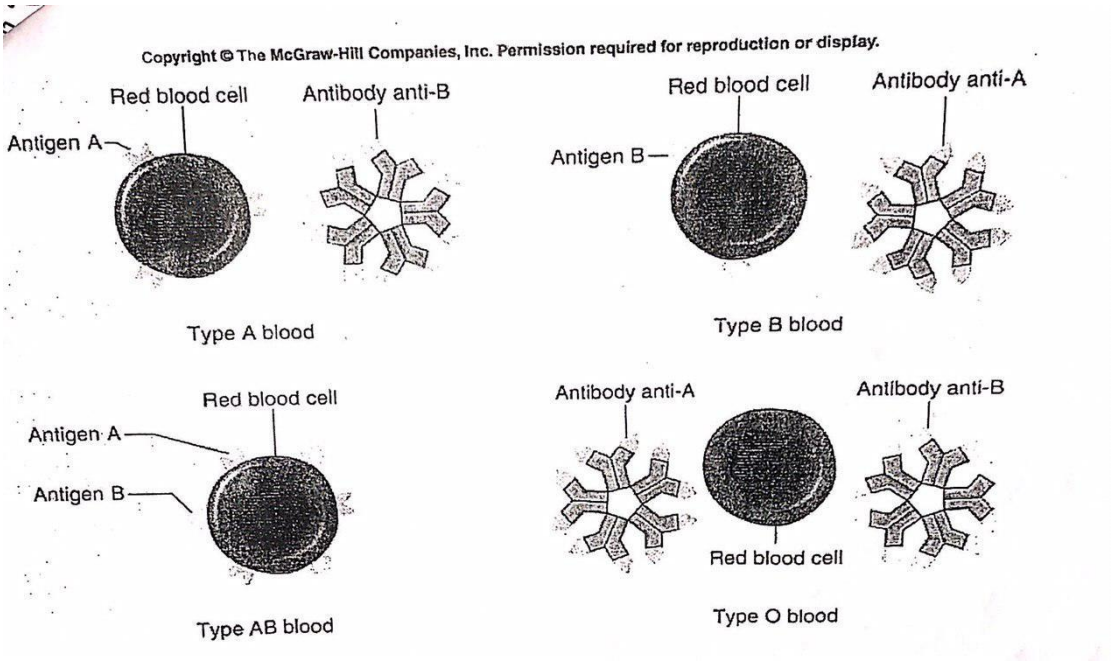
(1) Group A : is most common (47%) has only the A-antigen on red blood cells and B-antibody in the plasma . This group can only receive blood from groups A or O , and given to group A and group AB

(2) Group B : is about (41%) has only the B-antigen on red blood cells and A-antibody in the plasma . This group can receive blood from gro B and O, and given to group B and group AB.

(3) Group AB : is about (9%) has both (A-antigen& B-antigen) on red blood cells , but neither (A nor B antibody) in the plasma . This group can generally receive blood from any group , and given to group AB only

(4)Group O : is about (3%) has ither (A nor B antigens) on red blood cells , but both (A and B antibody) are in the plasma .This group can given to people of virtually any blood type , and receive blood from group O only.

The Blood RhD (Rhesus) factor



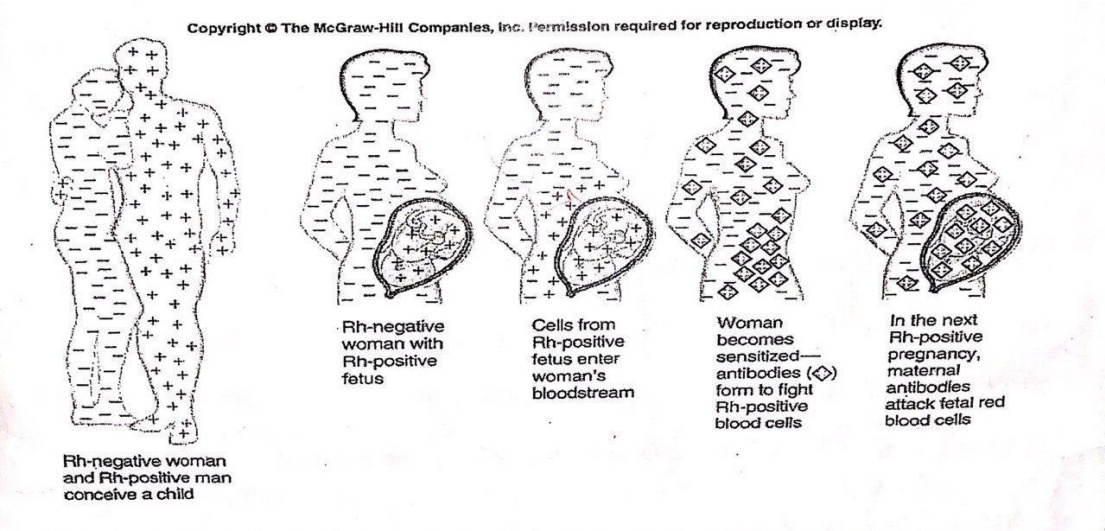
The RhD factor on blood refers to the positive or negative part of the blood type . If the blood type (RhD positive) it means that a protein (D-antigen) is found on the surface of the red blood cells , and if do not have the D-antigen the blood type will be RhD negative

RhD and the pregnancy:

Rhesus status only matters if a mother is an (RhD-negative) who is carrying an (RhD-positive) baby he child will have inherited this from (RhD-positive) father If some of the baby's blood enters the mother's bloodstream , the immune system of her may react to the D-antigen in the baby's blood . It will be treated as a foreign invader and the mother body will produce antibodies against it , this is known as a "sensitizing event"

Sensitizing is not usually harmful if it is the first pregnancy. But it can cause problems i the woman become pregnant again with another RhD-positive baby . The antibodies that mother body made in her first pregnancy can cross the placenta and attack the blood cells of the baby When the baby's blood cells are attacked, it can cause anaemia and if the anaemia becomes severe, it can lead to life-

threatening problems for the baby such as heart failure and fluid retention Having an injection of anti-D can prevent the mother system from making antibodies. It's important to prevent antibodies from being made, because once they're produced they stay in the mother blood forever.



Lecture 3Anemia

Anemia :

- Is a reduction in the hemoglobin concentration in the peripheral blood below that expected for a healthy person of the same ***age*** and ***gender***.
- Decline of hemoglobin is usually accompanied by a fall in R.B.C. count and P.C.V. (Hct.).
- The normal values can vary between laboratories but typical values to be considered as anemia would be as following :
  * Adult male : Hemoglobin concentration < ***135 g/L*** (13.5 g/dl).
  * Adult female : Hemoglobin concentration < ***115 g/L*** (11.5 g/dl).
  * 2 y. – puberty : Hemoglobin concentration < ***110 g/L*** (11 g/dl).
  * Newborn infants : Hemoglobin concentration < ***140 g/L*** (14 g/dl).

Table 2.1 : Classification of anemia.

Hypochromic Microcytic	Normochromic Normocytic	Normochromic Macrocytic
M.C.V. < 80 fl	**M.C.V. = 80-95 fl (Normal)**	**M.C.V. > 95 fl**
M.C.H. < 27 pg	**M.C.H. = 27-34 pg (Normal)**	**Normal M.C.H.**
M.C.H.C. < 300 g/L	**M.C.H.C. = 300-350 g/L (Normal)**	**Normal M.C.H.C.**
Iron deficiency anemia.	Many hemolytic anemias.	Megaloblastic anemia.
Thalassemia.	Anemia of chronic diseases (some cases).	Non-megaloblastic : alcoholism , liver disease , myelodysplastia , aplastic anemia , hypothyroidism , drugs , smoking.
Anemia of chronic diseases (some cases).	After acute blood loss (hemorrhage).	
Lead poisoning.	Renal disease.	
Sideroblastic anemia (some cases).	Mixed deficiencies.	
	Bone marrow failure. e.g.: post-chemotherapy, Infiltration.	

Iron deficiency anemia (I.D.A.) :

Iron deficiency is the ***most common cause of anemia*** in every country of the world, affecting about 500 million people worldwide, which is the most common form of ***nutritional deficiency***, it is the most important cause of a ***hypochromic microcytic anemia*** (as shown in table 2.1 above). The appearance of blood film that show hypochromic (reduced MCH) and microcytic (reduced MCH) red blood cells, is caused by a ***defect in hemoglobin synthesis***.

Iron physiology and metabolism :

- Iron is present in food in two forms : Haem iron form (90%) and Non-Haem iron form (10%).
  - Haem form is present in ***red meat*** and particularly in ***liver***. It is a better source of iron and is ***absorbed rapidly***.
  - Non-Haem form is present in vegetables, cereals, eggs or dairy foods. It is needed to be converted into ferrous state (Fe^{+2}).
- ***Ferrous (Fe^{+2}) iron*** is better absorbed than ferric (Fe^{+3}) iron.
- Following the oral intake of iron in the ferric state (Fe^{+3}), stomach secretions reduce the iron to the ferrous state (Fe^{+2}).
- Iron is absorbed in small intestine (***duodenum and upper jejunum***).
- Factors that ***favoring*** iron absorption are : Haem iron, Ferrous (Fe^{+2}) iron, Acids, Vitamin C and Sugars.
- Factors that ***decreasing*** iron absorption are : Non-Haem iron, Ferric form (Fe^{+3}), Alkalis-antacids and tea.
- The iron is carried (transferred) in blood bound to ***transferrin***, which is a glycoprotein formed in the liver.
- The ***transferrin*** can contain up to two atoms of iron ***(Fe^{+3})***, it delivers iron to tissues that have transferrin receptors.
- When iron is absorbed , it is transferred to the bone marrow for the synthesis of hemoglobin and to a lesser extent for the synthesis of myoglobin (in the muscles) and cytochromes, succinic dehydrogenase and catalase (iron-containig enzymes).
- Most of the body iron is present in the ***hemoglobin*** (65-70 % of total iron).
- At the end of their life, RBCs are broken down in the macrophages of the reticuloendothelial system (RES) and the Fe is released from hemoglobin (from haem by haem oxygenase and is largely reused for haem synthesis), enters the plasma and provides most of the iron on transferrin.
- When RBC_s are destroyed, and the body has sufficient iron to meet its needs (functional iron), the remainder iron is stored in the RES (Bone marrow, Liver and Spleen) as ***Hemosiderin*** (insoluble form) and ***Ferritin*** (soluble form), about 30 % of iron (500-1000 mg) is present in the stores.
- Every day about 30 mg iron is used to make new hemoglobin and most of this is obtained from the breakdown of old RBCs.
- The adult has average 3.5-5 grams of iron.
- Normal iron loss is very small, it is about less than 1 mg per day. Iron is lost from the body through exfoliation of intestinal epithelium, skin cells, bile and through urinary excretion.
- The daily intake of iron is 10 mg and only 10 % is absorbed, so daily requirements for an adult male is 1 mg/day and that is doubled in females because of menses.
- During pregnancy, iron requirement is 3 mg/day. In children, the requirement for iron is 1.5 mg / day because of growth requirement.

Causes of iron deficiency anemia :

1- Excessive blood loss (Hemorrhage or bleeding) :
   - Is the **most common cause** of iron deficiency in adults.
   - Half a liter of whole blood contains approximately 250 mg of iron.
   - It can occur after chronic hemorrhage such as : peptic ulcers, carcinoma of stomach, colon or rectum, heavy menstruation in females, hematuria, bleeding hemorrhoids and worm infestation by the hook worm *Ancylostoma duodenale*.

2- Nutritional deficiency (Insufficient dietary intake) :
   In which not enough iron is consumed to meet the normal and daily amount (e.g. poor diet and imbalanced vegetarian diet), therefore it occurs among low social class people.

3- Malabsorption (Faulty or incomplete iron absorption) :
   As in achlorhydria in certain disorders, chronic diarrhea associated with gluten-induced enteropathy (Celiac disease), sprue, Crohn's disease, gastrectomy (gastric resection) and resection of small bowel.

4- Increased physiological iron requirements (demands) :
   - During prematurity, infancy, adolescence, pregnancy, lactation and in menstruating women.
   - It is highest in ***pregnancy*** , ***adolescent*** and ***menstruating females***.
   - For that reason these groups are most likely to develop iron deficiency if there is additional iron loss or prolonged reduced intake.

Clinical manifestations (features) of Iron deficiency anemia :

- The reticuloendothelial stores (hemosiderin and ferritin) become completely depleted (Latent iron deficiency) before iron deficiency anemia becomes apparent.
- As the condition develops, the patient develop general symptoms and signs of anemia such as :
  Shortness of breath (S.O.B.) particularly on exercise, Weakness, Impairment of work performance, Lethargy, Lassitude, Dizziness, Tinnitus, Palpitation, Headache, Pallor, Painless glossitis and Angular stomatitis.
- Also the patient has specific symptoms and signs of I.D.A. :
  Flat-Brittle nails then become spoon-shaped nails (***Koilonychia***) (as shown in figure 2.1 below), Dysphagia as a result of pharyngeal webs (Paterson Kelly or Plummer-Vinson syndrome) and Unusual dietary craving (***Pica***) when the patient ingests strange non-nutritive items like soil, chalk, ice and papers.

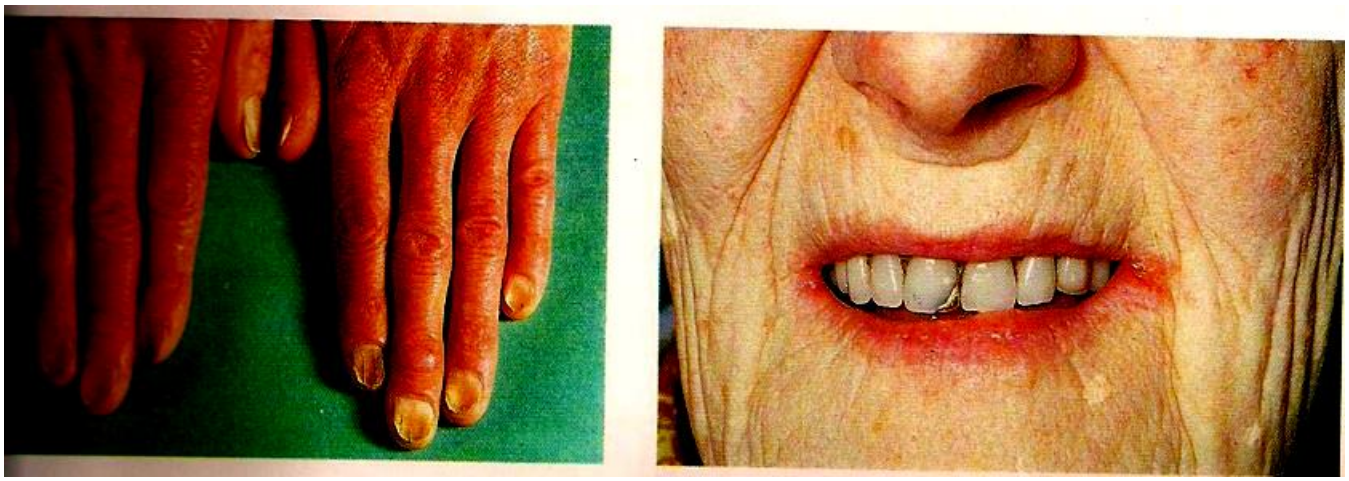


Fig. 2.1 : Clinical features of iron deficiency anemia , (Left) Koilonychia , (Right) Angular stomatitis.

Laboratory tests (findings) of iron deficiency anemia :

1- Hemoglobin concentration and P.C.V. are low, the red blood cells count is frequently reduced.

2- Red cell indices :

M.C.V., M.C.H. and M.C.H.C. are reduced while ***R.D.W. is increased***.

3- Blood film (as shown in figure 2.2 below) :

Red blood cells become obviously ***microcytic and hypochromic***, pencil-shaped poikilocytosis and target cells may be present.

- When iron deficiency is associated with severe folate or vitamin B12 deficiency → Dimorphic blood film which occurs with a dual population of red cells of which :
  -- One population of cells is macrocytic.
  -- Other population of cells is hypochromic microcytic ; the indices may be normal.

4- ***Reticulocyte count is low*** for the degree of anemia (as this is a nutritional anemia), but it is increased when the patient takes iron as the treatment.

5- Leukocytes and platelets count :

- Leukocytes are usually normal in count. In IDA due to parasitic infestation, eosinophilia may be present.
- The platelet count is often moderately raised in IDA, particularly when hemorrhage is continuing.

6- Serum total iron binding capacity ***(T.I.B.C.) rises*** and serum ***iron falls***, so that the transferrin saturation percentage is usually less than 10% (serum Iron / T.I.B.C. X 100).

7- Serum soluble ***transferrin receptor is increased***.

8- Serum ***ferritin is low***.

9- Bone marrow study :

The bone marrow shows ***depleted iron stores*** by staining the bone marrow with iron stain (Perls' (Prussain blue) reaction).

10- Hemoglobin ***electrophoresis*** test :

It is ***normal*** in I.D.A.
This test will differentiate between I.D.A. and thalassemia trait (minor).

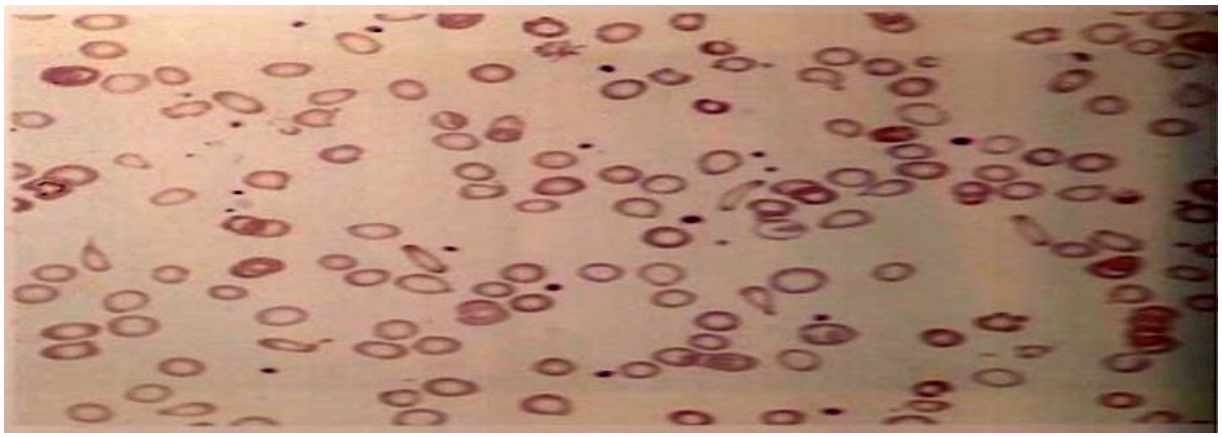


Fig. 2.2 : Photograph of the blood film from the patient with iron deficiency anemia, showing hypochromic microcytic with pencil-shaped poikilocytes and few target cells.

Iron Overload :

- There is no physiological mechanism for eliminating excess iron from the body and so iron absorption is normally and carefully regulated to avoid accumulation.
- Iron overload can occur in disorders associated with excessive absorption or chronic blood transfusion.
- Excessive Fe deposition in tissues can cause serious damage to organs, mainly the : Heart, Liver and Endocrine organs.

Anemia of chronic disorder (or disease) (A.C.D.) :

- It is one of the most common anemias occurs in patients with a variety of chronic inflammatory diseases (such as Rheumatoid arthritis (***R.A.***) and Systemic Lupus Erythematosus (***S.L.E.***)) and malignant diseases (such as ***Carcinoma***).
- The characteristic features are :

● ***Mild*** and non-progressive anemia (Hemoglobin concentration is rarely less than 90 g/L),
the severity being related to the severity of the disease.

● Normochromic normocytic or ***mildy*** hypochromic (MCV is 75-82 fl).
● Serum iron is ***low***.
● T.I.B.C. is ***normal or reduced***.
● Transferrin saturation percentage is ***reduced***.
● Serum ferritin is ***normal or raised***.
● Serum transferrin receptor assay is ***normal or reduced***.
● Bone marrow storage (RES) iron is ***normal*** but erythroblast iron is ***reduced***.
● Hemoglobin electrophoresis test is ***normal***.
● C-reactive protein : Usually ***raised***.
● E.S.R. : Usually ***raised***.

Lecture 4 Jaundice :

Jaundice :

Is the yellowish discoloration or pigmentation of the skin, sclera (white of the eyes), other mucous membranes and body fluids, is caused by hyperbilirubinemia (which is the increased levels of bilirubin in the blood).

Jaundice itself is not a disease, but rather a sign of one of many possible underlying pathological processes.

Normal range of total serum bilirubin (TSB) :

* In adults :

0.3-1.0 mg/ dl (5.1-17.0 mmol/ L).

* In Newborns (Infants) :

- Full-Term Baby :

1 day old (less than 24 hours) = Less than 6.0 mg/dl or 103 mmol/L.
2 day old (less than 48 hours) = Less than 10.0 mg/dl or 170 mmol/L.
3-5 days = Less than 12.0 mg/dl or 205 mmol/L.

- Premature Baby :

1 day old (less than 24 hours) = Less than 8.0 mg/dl or 137 mmol/L.
2 day old (less than 48 hours) = Less than 12.0 mg/dl or 205 mmol/L.
3-5 days = Less than 15.0 mg/dl or 256 mmol/L.

Bilirubin Cycle (Bilirubin Catabolism) :

1- Red blood cell (***RBC***) destruction usually occurs after a mean life span of 120 days when the cells are removed from the extravascular system by the macrophages of the reticuloendothelial system (RE) especially in the marrow and also the liver and spleen.

2- The ***hemoglobin*** of the RBC is released into the blood stream.

3- The hemoglobin is then phagocytosed by macrophages and split into it's ***heme*** and ***globin*** portions.

4- The globin portion (which is a protein) is degraded into ***amino acids*** and plays no role in jaundice.

5- The breakdown of heme liberates ***iron*** and ***protoporphyrin***.

6- The iron is for re-circulation via plasma transferrin to bone marrow erythroblasts.

7- The protoporphyrin is broken down to ***bilirubin*** by two reactions :

a- The 1st reaction is catalyzed by heme oxygenase enzyme and results in ***biliverdin*** (green color pigment).

b- The 2nd reaction is the reduction of biliverdin to ***bilirubin*** (yellow color pigment) by biliverdin reductase enzyme.

NOTE **:** This bilirubin is ***Unconjugated*** , ***Free*** or ***Indirect bilirubin*** , which is insoluble in water.

8- The unconjugated bilirubin then travels to the liver through blood stream bound to plasma albumin.

9- Once it arrives to the liver, it is conjugated with glucoronic acid to form bilirubin diglucuronide (catalysed by uridine diphosphate glucoronosyl transferase) or just ***Conjugated (Direct) bilirubin*** to become water soluble.

10- The conjugated bilirubin is excreted from the liver into the biliary duct as part of bile, and thus
secreted out into small intestine (duodenum) to aid in the digestion of fats.

11- Intestinal bacteria convert the bilirubin into ***Urobilinogen***.

12- Urobilinogen can take two pathways :

a- It can either be further converted to ***Stercobilinogen*** , which is then oxidized to ***Stercobilin*** and passed out in the faeces.

b- Or it can be reabsorbed by the intestinal cells, transported in the blood to the kidneys, and passed out in the urine as the oxidized product ***Urobilin***.

NOTE **:** Stercobilin is the product responsible for the coloration of faeces.
Urobilin is the product responsible for the coloration of urine.

13- In the newborn, much of the conjugated bilirubin in the intestine is hydrolyzed back to unconjugated bilirubin reaction catalyzed by the enzyme Beta glucoronidase that is present in the intestinal mucosa. The unconjugated bilirubin is reabsorbed into the blood stream by way of the ***enterohepatic circulation*** adding an additional bilirubin load to the already overstressed liver. This enterohepatic circulation of bilirubin is an important contributor to neonatal jaundice, by contrast, in the adult conjugated bilirubin is reduced rapidly by the action of colonic bacteria to urobilinogens and very little enterohepatic circulation occurs (as shown in figure 1.1).

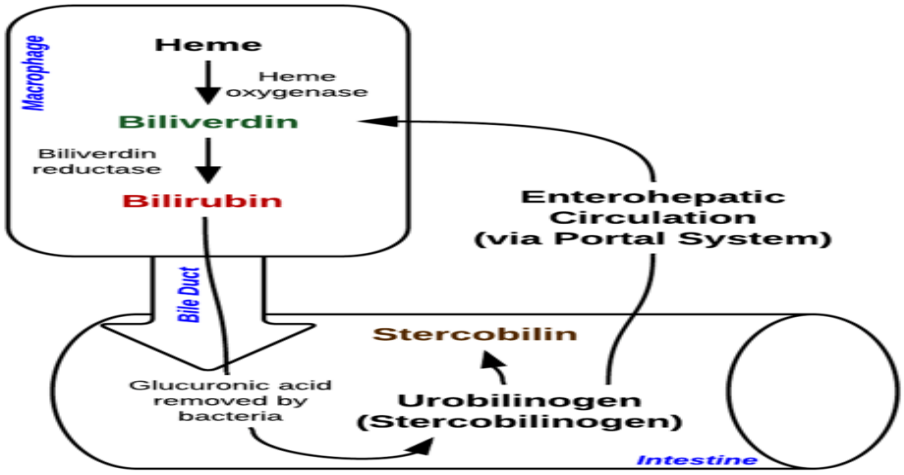


Fig. 1.1 : Diagram of bilirubin cycle.

Types of neonatal jaundice :

1- Physiological jaundice.

2- Pathological jaundice.

- **Physiological jaundice :**
  - Neonatal jaundice is usually harmless and often seen in most newborns around the ***second day*** after birth, lasting until day 8 in normal births or around day 14 in premature births.
  - Serum bilirubin normally drops to a low level without any intervention required.
  - Most infants develop visible jaundice due to :
    a- Elevation of unconjugated bilirubin concentration which accumulates due to increased red cell destruction (shorter life span of RBC in the baby).
    b- Inability of underdeveloped (immature) liver to metabolize this high quantity of unconjugated bilirubin concentration because of low activity of glucuronyl transferase.
  - In extreme cases, a brain damaging condition known as **kernicterus** can occur, leading to significant lifelong disability due to the passage of bilirubin through the infant's blood-brain barrier (there is increase permeability of the blood brain barrier in neonates).

- **Pathological jaundice :**
  Any of the following features characterizes pathological jaundice :
  - Clinical jaundice appearing in the ***first 24 hours***.
  - Increases in the level of total bilirubin by more than 0.5 mg/dl per hour or 5 mg/dl per 24 hours.
  - Total bilirubin more than 19.5 mg/dl.
  - Direct bilirubin more than 2 mg/dl.

Causes of pathological neonatal jaundice :

A- Increased production of bilirubin load on the liver due to :

1- Hemolytic disease such as :
- Immune mediated :
  - Rh alloimmunization (Hemolytic disease of newborn (HDN)).
  - ABO and other blood groups incompatibility.
- Non immune :
  ~ Hereditary RBC membrane defect such as :
  - Hereditary spherocytosis.
  - Hereditary elliptocytosis.

  ~ RBC enzymopathies such as :
  - G6PD deficiency.
  - Pyruvate kinase deficiency.

  ~ Hemoglobinopathies such as :
  - α (Alpha) thalassemia.
  - β (Beta) thalassemia.

2- Other causes of increased production :
- Sepsis.
- DIC (Disseminated intravascular coagulopathy).
- Extravasations of blood as in hematoma or pulmonary, abdominal and cerebral hemorrhage.

3- Increased enterohepatic circulation of bilirubin :
   - Breast milk jaundice.
   - Pyloric obstruction.
   - Small or large bowel obstruction or ileus.

B- Decreased clearance of bilirubin due to :

1- Prematurity.
2- G6PD deficiency.
3- Inborn errors of metabolism such as : Gilbert Syndrome or Grigler-Najjar Syndrome.
4- Metabolic (hypothyroidism or hypopituitary).

C- Other causes :

- Hepatitis B.
- Galactosemia.
- Biliary atresia.

Breast feeding jaundice :

- Is the jaundice associated with breastfeeding in the first 2^{nd} to 4^{th} postnatal days it may persist for three months in some infants.
- Caused by insufficient breast milk intake resulting in inadequate quantities of bowel movements to remove bilirubin from the body (An increase in the enterohepatic circulation of bilirubin).
- This can be improved by frequent breastfeeding sessions of sufficient duration to stimulate adequate milk production.

Breast milk jaundice :

- In 1-2 % of breastfed babies, jaundice may be caused by substances produced in their mother's breast milk that can cause the bilirubin level to rise.
- This substance is unusual metabolite of progesterone that inhibit glucuronyl transferase.

Symptoms and signs of neonatal jaundice :

- The symptoms and signs of neonatal jaundice largely depend on the underlying causes.
- In the physiological type of jaundice the baby usually feeds well and the physical examination reveals a normal liver. The urine color is dark while the stool appears normal.
- Extremely high levels of bilirubin lead to kernicterus a condition where the brain is severely damaged.

Laboratory tests for neonatal jaundice :

1- TSB.
2- Complete blood count (PCV, reticulocyte count and blood film to see RBC morphology).
3- ABO and Rh type in mother and infant.
4- DAT (Direct antiglobulin test).
5- Screening tests for G6PD deficiency.
6- LFT (Liver function test).
7- Test for viral/parasitic infection.
8- Reducing substances in urine (e.g. in Galactosemia).

9- Thyroid function test (T3, T4 and TSH).

Complications of jaundice :

1- Cholangitis. **2-** Biliary cirrhosis. **3-**Pancreatitis. **4-** Coagulopathy. **5-** Renal failure. **6-** Liver failure.

Types of jaundice :

Jaundice is classified into three categories depending on which part of the physiological mechanism is affected :

Table 1.1 : Catogories of jaundice.

Category	Definition
Pre-hepatic	The pathology occurs prior to the liver.
Hepatic	The pathology is located within liver.
Post-hepatic	The pathology is located after the conjugation of bilirubin in the liver.

Pre-hepatic Jaundice :

- It is caused by anything which causes an increased rate of hemolysis (break down of red blood cells).
- This will leads to an increase in the amount of unconjugated bilirubin present in the blood and deposition of it into various tissues which can lead to a jaundiced appearance.
- In jaundice secondary to hemolysis, the increased production of bilirubin leads to the increased production of urine urobilinogen.
- In urine, there is no conjugated bilirubin but high urobilinogen.
- Kernicterus is associated with increased unconjugated bilirubin.

Hepatic (Hepatocellular) Jaundice :

- It can be caused by something that cause reduction in the liver ability to metabolize and excrete bilirubin leading to a buildup of unconjugated bilirubin in the blood.
- Or it can be caused by something that cause impairment of excretion of conjugated bilirubin into the bile leading to an increase in plasma conjugated bilirubin.
- The blood contains abnormally raised amount of conjugated bilirubin and bile salts which are excreted in the urine.
- Kernictirus is not associated with increased conjugated bilirubin.

Post-hepatic Jaundice :

- Also called obstructive jaundice, it is caused by any interruption to the drainage of bile in the biliary system.
- The most common causes are gallstones in the common bile duct and pancreatic cancer in the head of pancreas.
- In case of complete obstruction of the bile duct, no urobilinogen is found in the urine, since bilirubin has no access to the intestine and it is in the intestine that bilirubin gets converted to urobilinogen to be later released into blood.
- In this case, presence of bilirubin (conjugated) in the urine without urine urobilinogen suggests obstructive jaundice, either intra-hepatic or post-hepatic.

- The presence of pale stools and dark urine suggests an post-hepatic cause as normal faeces get their color from bile pigments.

Table 1.2 : Differentiation between types of jaundice.

	Pre-hepatic jaundice	Hepatic jaundice	Post-hepatic jaundice
Causes	• Infection such as malaria. • Sickle cell anemia. • Spherocytosis. • Thalassemia. • G6PD deficiency. • Hemolytic uremic disease. • Gilbert's syndrome. • Grigler-Najjar syndrome.	• Acute or chronic hepatitis. • Hepatotoxicity. • Cirrhosis. • Drug-induced hepatitis. • Alcoholic liver disease. • Primary biliary cirrhosis.	• Gallstones in the common bile duct. • Pancreatic cancer in the head of pancreas. • Strictures of the common bile duct such as : - Ductal carcinoma. - Pancreatitis. - A group of parasites known as liver flukes.
TSB	Normal/Increased Indirect>Direct	Increased All high (Direct and Indirect)	Increased Direct >Indirect
Indirect Bilirubin	Increased	Normal/Increased	Normal
Direct Bilirubin	Normal	Increased	Increased
Urine color	Normal	Dark	Dark
Urine Urobilinogen	Increased	Normal	No
Stool color	Normal	Normal	Pale
Conformational tests	High K^+ (Potassium). Low Hemoglobin level.	High GPT (ALT). High GOT (AST). Low plasma albumin level. High plasma globulins level.	High ALP (Alkaline phosphatase).

Management (Treatment) :

- Reduce level of serum bilirubin and prevent bilirubin toxicity and prevent Kernicterus.
- Phototherapy (bili light) is often the tool used for early treatment which often consist of exposing the baby to intensive ultraviolet light to change non-water soluble bilirubin into water soluble which can be excreted from the kidneys.
- Regular and proper feedings are especially important.
- Exchange transfusions should be used for any newborn with a total serum bilirubin of greater than 25 mg/dl.
- Drugs : use of Phenobarbital promotes liver enzymes and protein synthesis.

Lecture 5 ***Cardiovascular system***

****A closed system of the heart and blood vessels.***

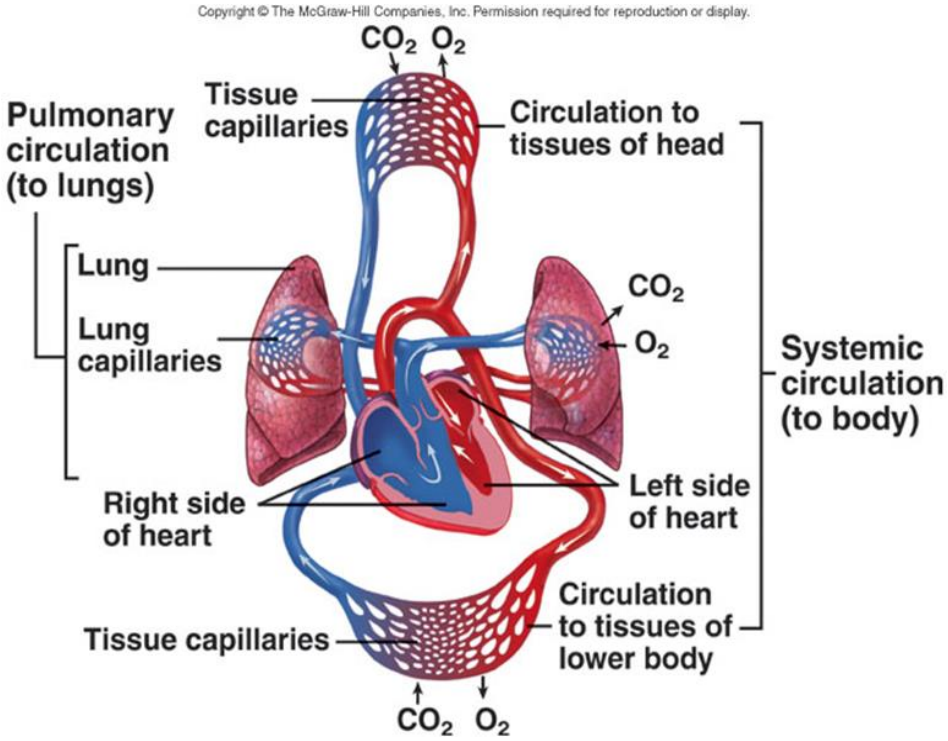
- The heart pumps blood.

- Blood vessels allow blood to circulate to all parts of the body.

*****The function of the cardiovascular system :***

is to deliver oxygen and nutrients

and to remove carbon dioxide and other waste products



***Pulmonary circuit**

The blood pathway between the right side of the heart, to the lungs, and back to the left side of the heart.

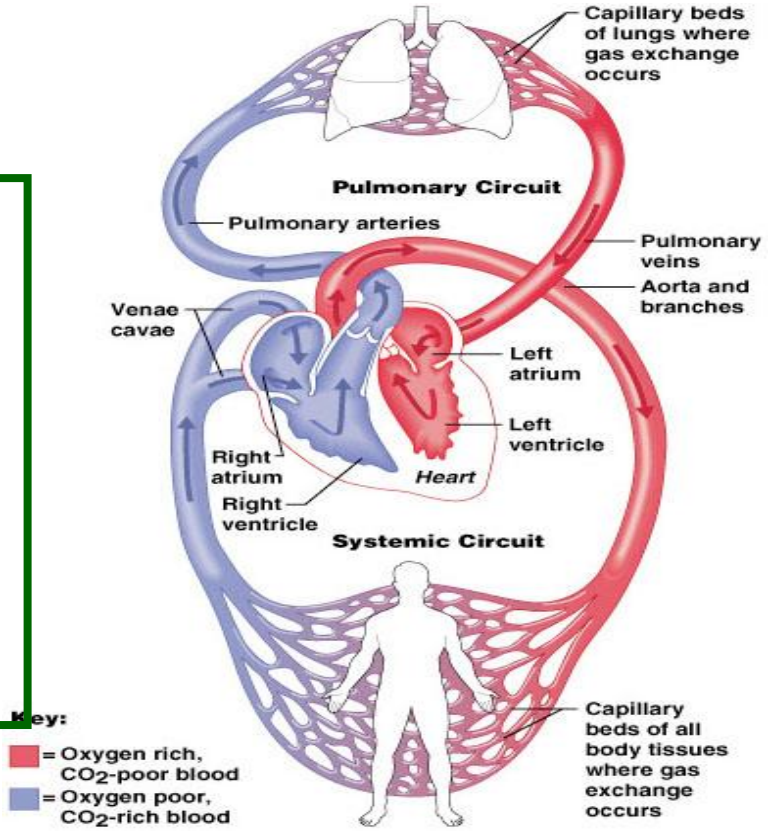
***Systemic circuit**

The pathway between the left and right sides of the heart.

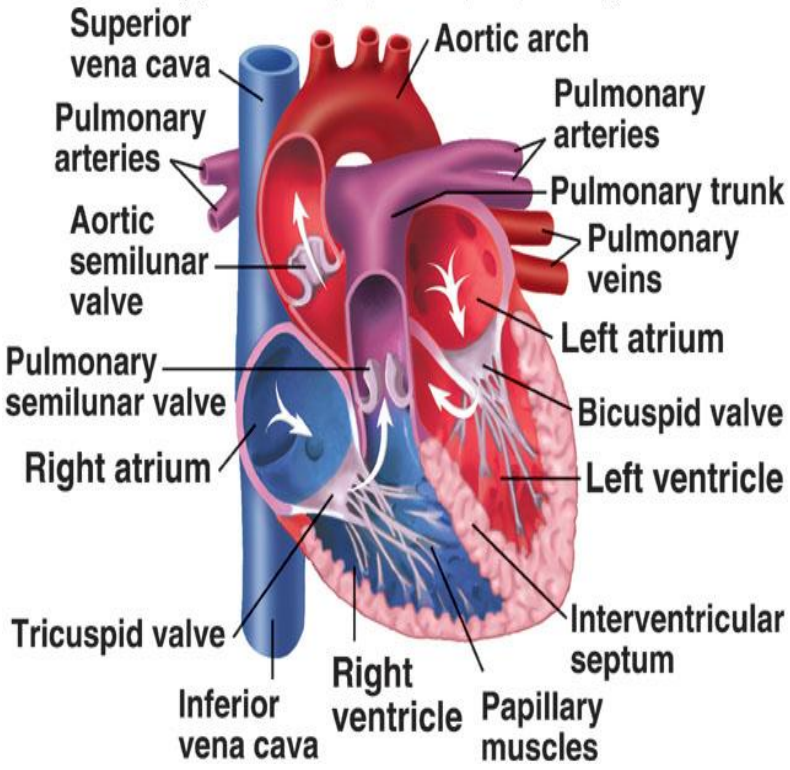
***The human circulatory system consists of:**

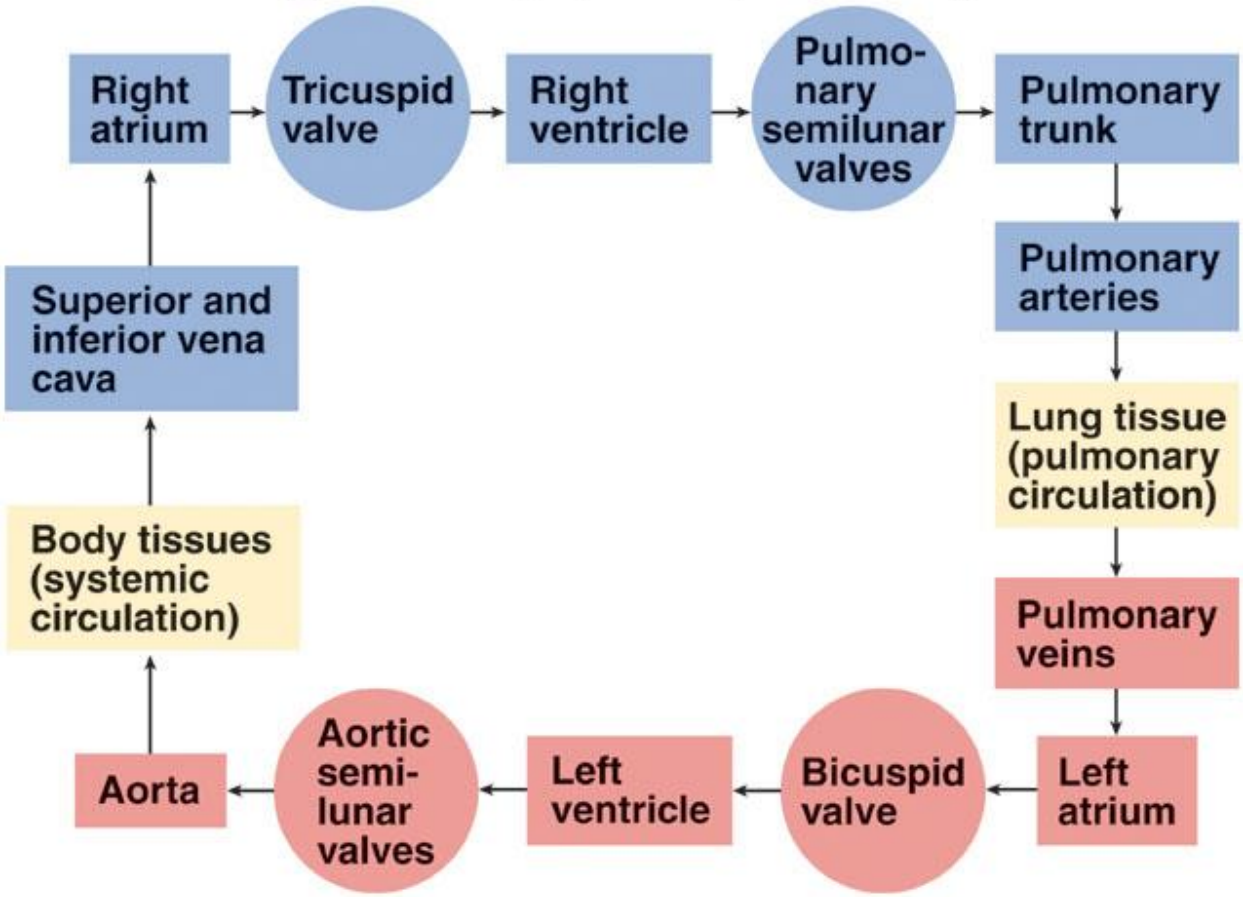
- *The heart.*
- *A series of blood vessels.*
- *Blood that flows through them.*

the **right** side of the system deals with **deoxygenate d** blood.



the **left** side of the system deals with **oxygenated** blood.

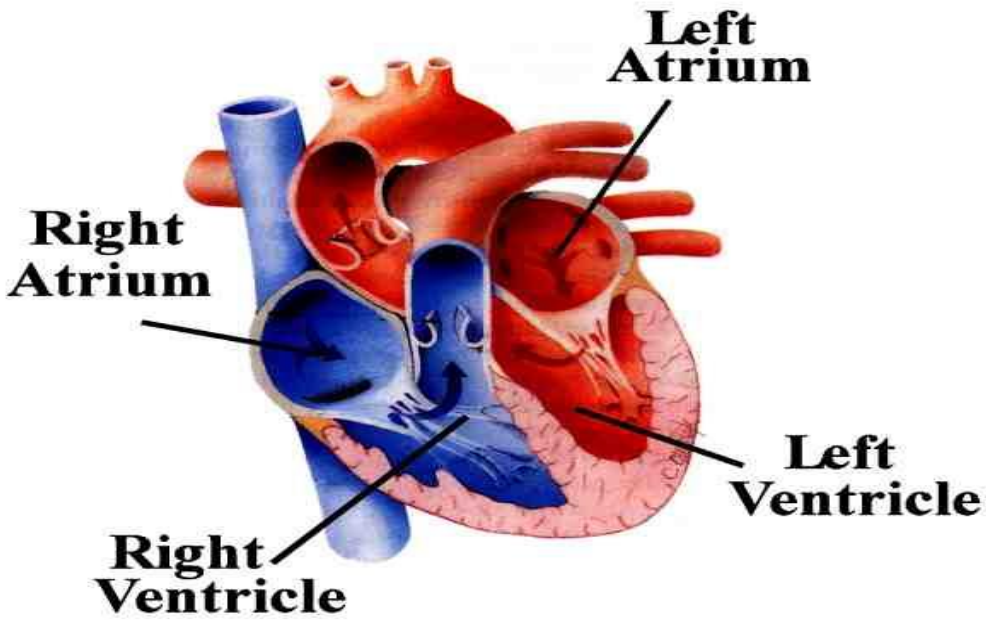




Cardiovascular system (Heart)

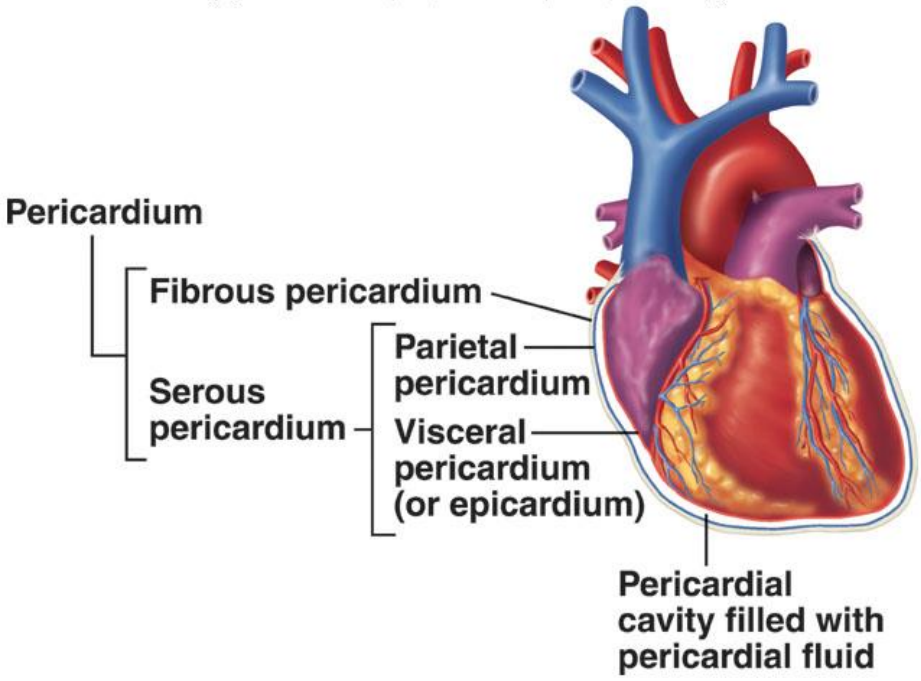
Located near the center of your chest
A hollow organ about the size of our fist composed of cardiac muscle

Right and left side act as separate pumps
Has four chambers
a - Atria
- Receiving chambers.
-Right atrium
-Left atrium
b - Ventricles
- Discharging chambers.
-Left ventricle
-Right ventricle



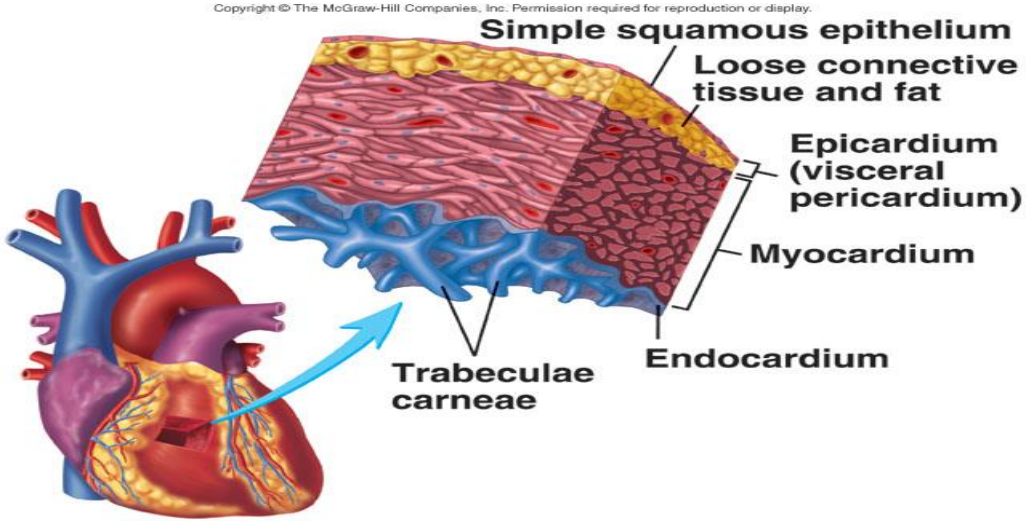
5. *The heart Covered by Pericardium a double serous membran:*

- *Visceral pericardium*
- *Parietal pericardium*
- *Serous fluid fills the space between the layers of pericardium*



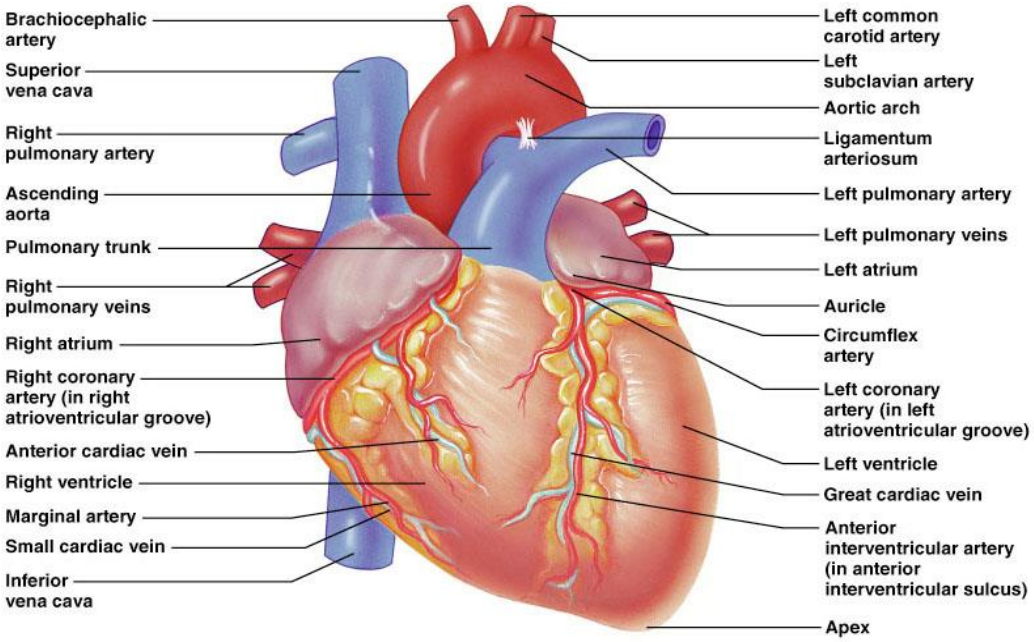
6. The wall of the heart composed of:

- ***Three layers of tissue:***
  - *Epicardium: This serous membrane of smooth outer surface of heart.*
  - *Myocardium: Middle layer composed of cardiac muscle cell and responsibility for heart contracting.*
  - *Endocardium: Smooth inner surface of heart chambers..*



7. *Vessels returning blood to the heart include:*
   - a. *Right and left pulmonary veins.*
   - b. *Superior and inferior venae cavae.*

8. *Vessels conveying blood away from the heart include:*
   - a. *Aorta.*
   - b. *Right and left pulmonary arteries.*



. Heart valves ensure unidirectional blood flow through the heart.

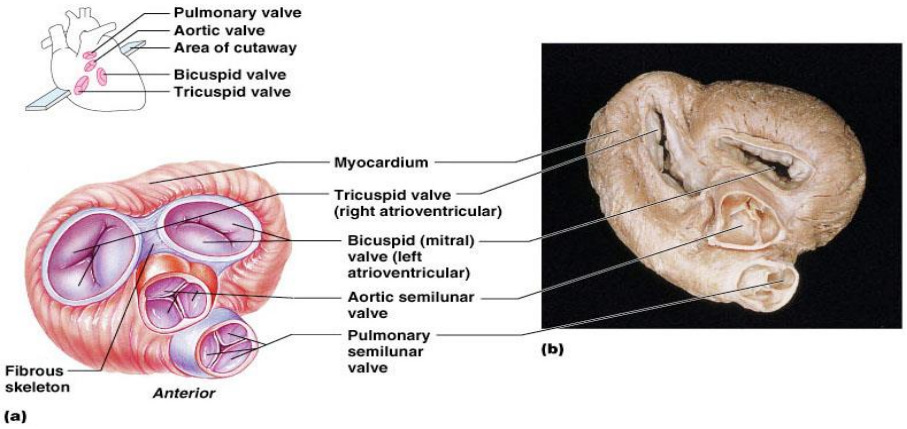
1. Atrioventricular (AV) valves lie between the atria and the ventricles

- AV valves prevent backflow into the atria when ventricles contract
- (tricuspid v.in the right& bicuspid v. in the left).

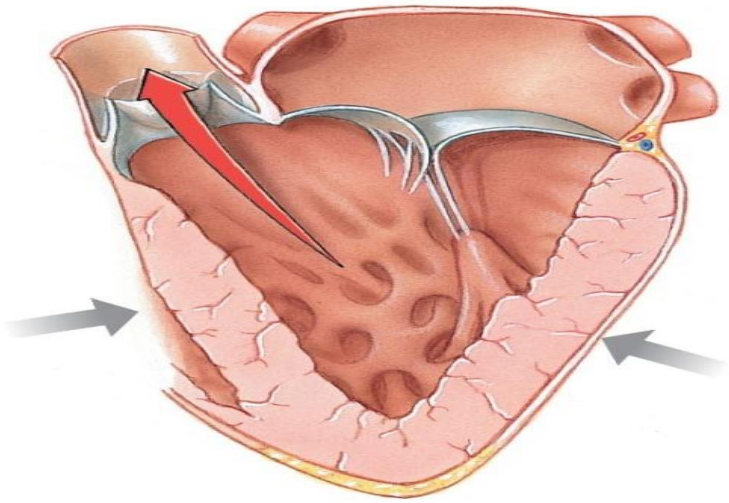
2. Semilunar valves prevent backflow of blood into the ventricles

- Aortic semilunar valve lies between the left ventricle and the aorta

-Pulmonary semilunar valve lies between the right ventricle and pulmonary trunk



3. *Valves open as blood is pumped through.*
    - *Close to prevent backflow.*



The Heart: Cardiac Cycle

Cardiac cycle : is the sequence of events as blood enters the atria, leaves the ventricles and then starts over.

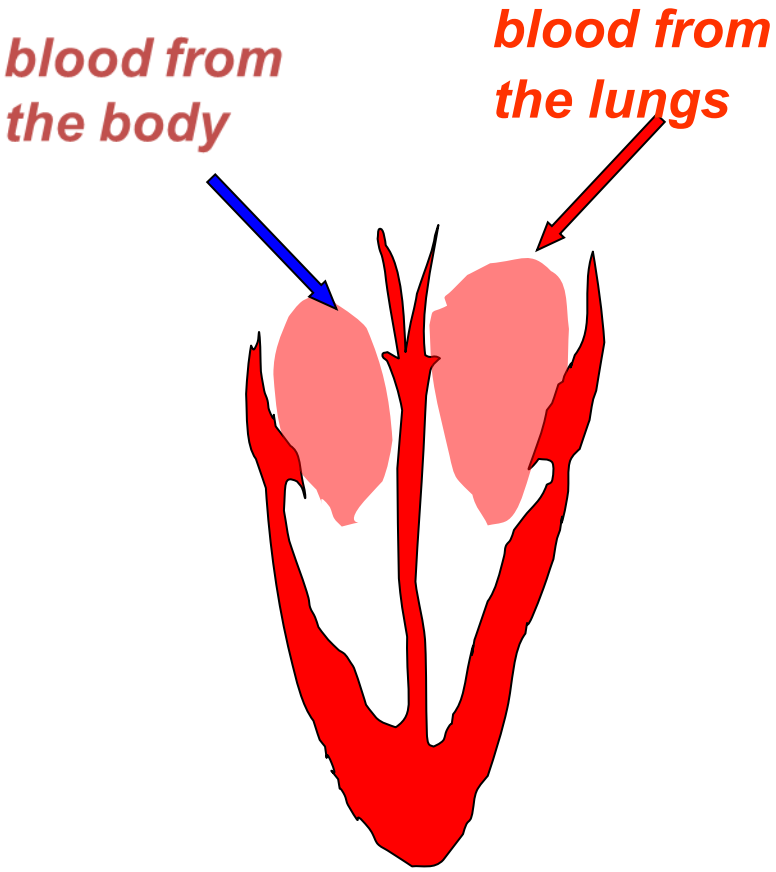
- is events of one complete heart beat

- is alternating periods of systole and diastole-

Systole = period of contraction
Diastole = period of relaxation

- When the atria contract, blood flows into the ventricles
- When the ventricle contract, blood flows out of the heart

Cardiac cycle

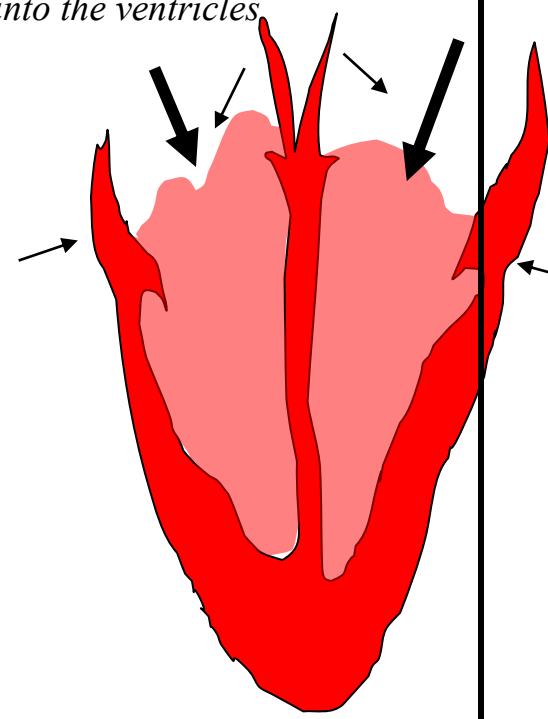


STEP ONE

The heart beat begins when the heart muscles relax and blood flows into the atria.

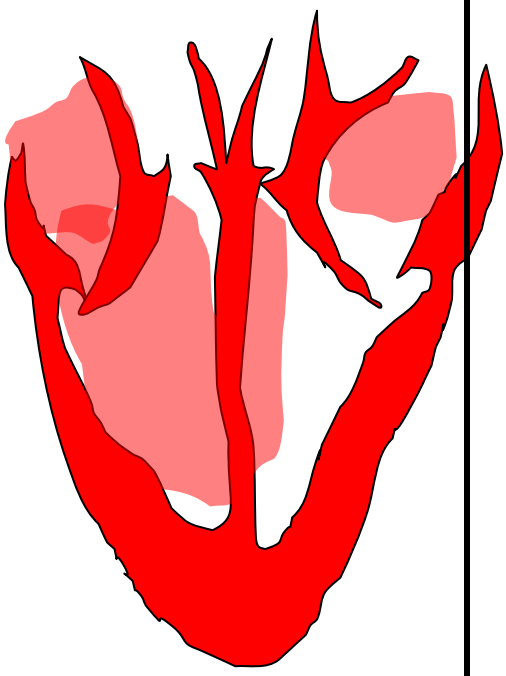
STEP TWO

The atria then contract andthe valves open to allow blood into the ventricles



Cardiac cycle

STEP THREE



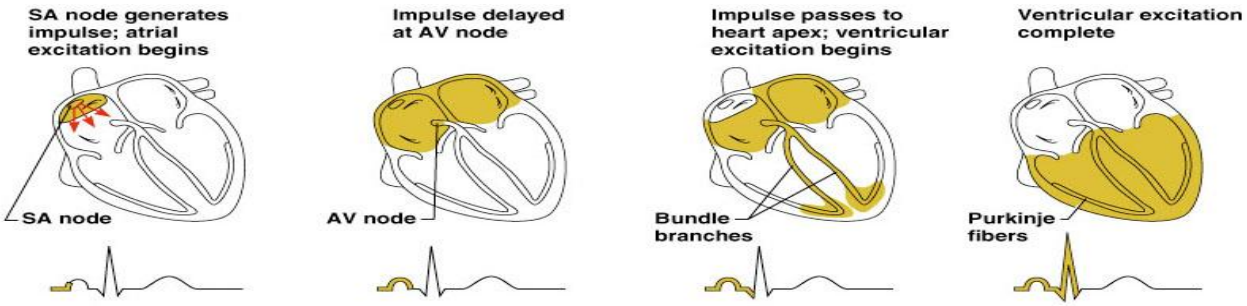
The valves close to stop blood flowing backwards.

The ventricles contract forcing the blood to leave the heart.

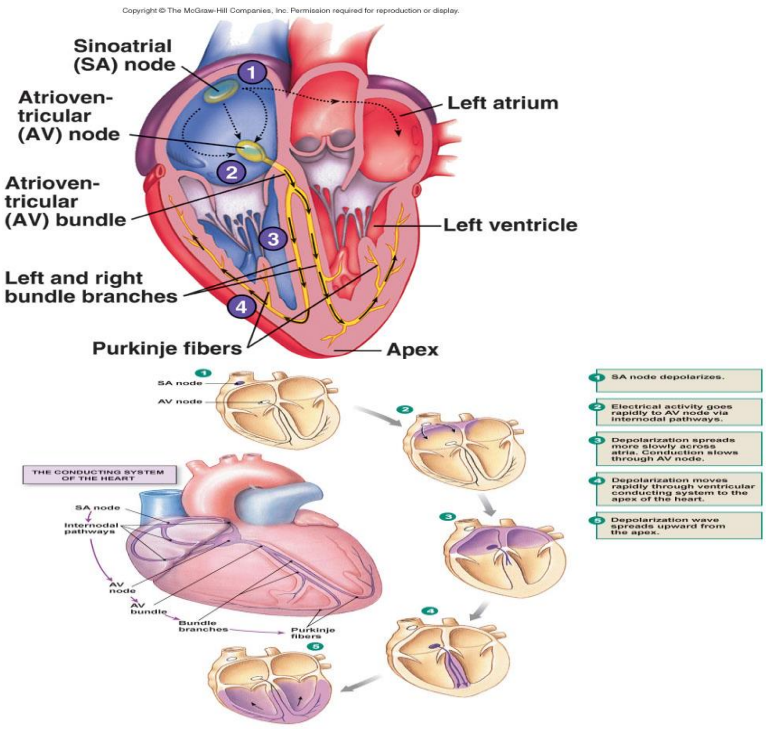
At the same time, the atria are relaxing and once again filling with blood.

The Heart: Conduction System

- *Each contraction begins in a small group of cardiac muscle cells in the right atrium that stimulate the rest of the muscle cells = sinoatrial node (SA node)*
  - *Since the sinoatrial node sets the pace for the heart it is also called "the pacemaker"*
    - *Impulse passes from atria to ventricles via the atrioventricular bundle (bundle of His)*
      - *AV bundle splits into two pathways in the interventricular septum (bundle branches)*
      - *Bundle branches carry the impulse toward the apex of the heart*
      - *Purkinje fibers carry the impulse to the heart apex and ventric ular walls*



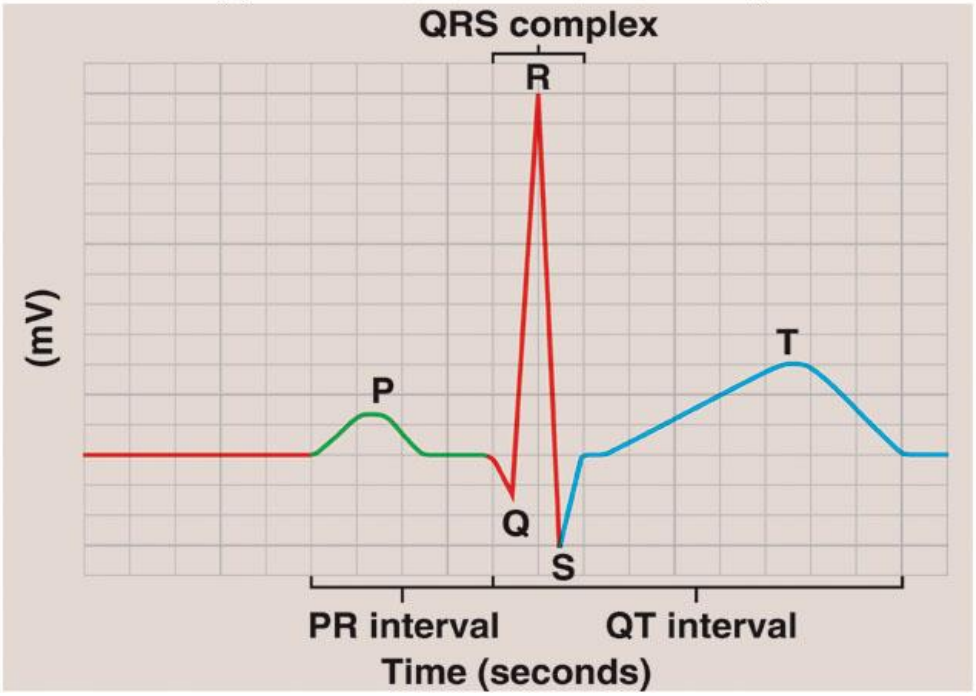
The Heart: Conduction System



The Heart: Conduction System

- *Action potentials through myocardium during cardiac cycle produces electric currents than can be measured* by *electrocardiogram (ECG)*
  - *Pattern*
    - *P wave*
      - *Atria depolarization*
    - *QRS complex*
      - *Ventricle depolarization*

  - *Atrial repolarization record is masked by the larger QRS complex.*
    - *T wave:*
      - *Ventricle repolarization*



Cardiovascular system (Heart)

11.Heart sounds (lub-dup) are associated with closing of heart valves.

- First sound occurs as AV valves close and signifies beginning of systole (contraction)

- Second sound occurs when SL valves close at the beginning of ventricular diastole (relaxation).

Tachycardia: Heart rate in excess of 100bpm .

Bradycardia: Heart rate less than 60 bpm .

Heart Murmur : abnormal heart beat , caused by valve problems.

Cardiac Output is the amount of blood pumped by each ventricle in one minute

Regulation of the Heart rate

12. *Changing heart rate is the most common way to change cardiac output.*

- *Increased heart rate*
  - *Sympathetic nervous system*
    - *Crisis*
    - *Low blood pressure*
  - *Hormones*
    - *Epinephrine*
    - *Thyroxine*
  - *Exercise*
  - *Decreased blood volume*
- *Decreased heart rate*
  - *Parasympathetic nervous system*
  - *High blood pressure or blood volume*
  - *Decreased venous return*

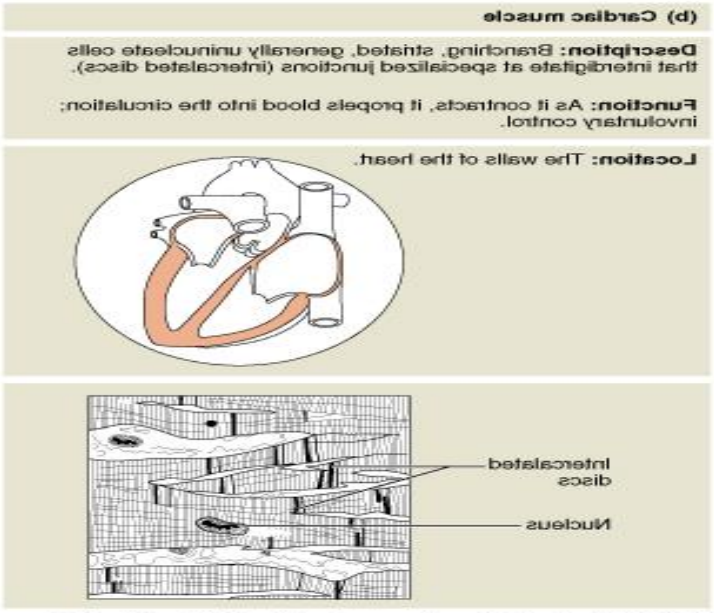
Lecture 6Muscle Physiology

Muscle Tissue

- Skeletal Muscle
- Cardiac Muscle
- Smooth Muscle

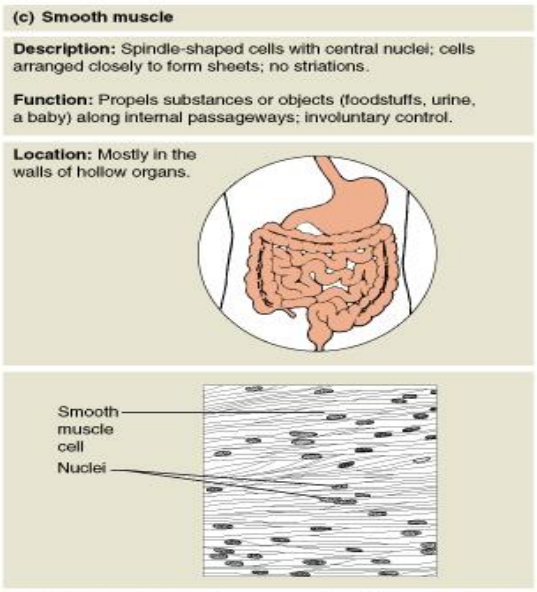
Cardiac Muscle

- Branching cells
- One/two nuclei per cell
- Striated
- Involuntary
- Medium speed contractions



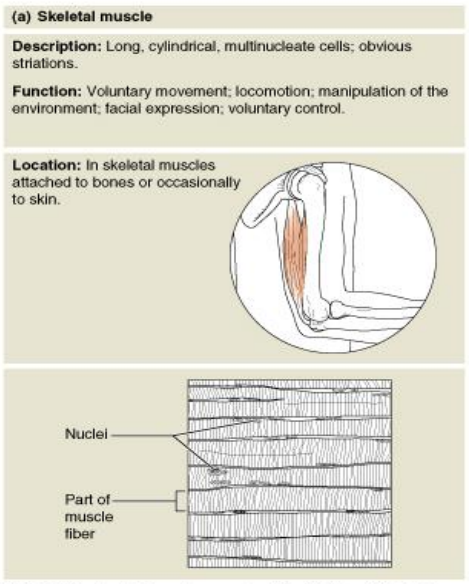
Smooth Muscle

- Fusiform cells
- One nucleus per cell
- Nonstriated
- Involuntary
- Slow, wave-like contractions



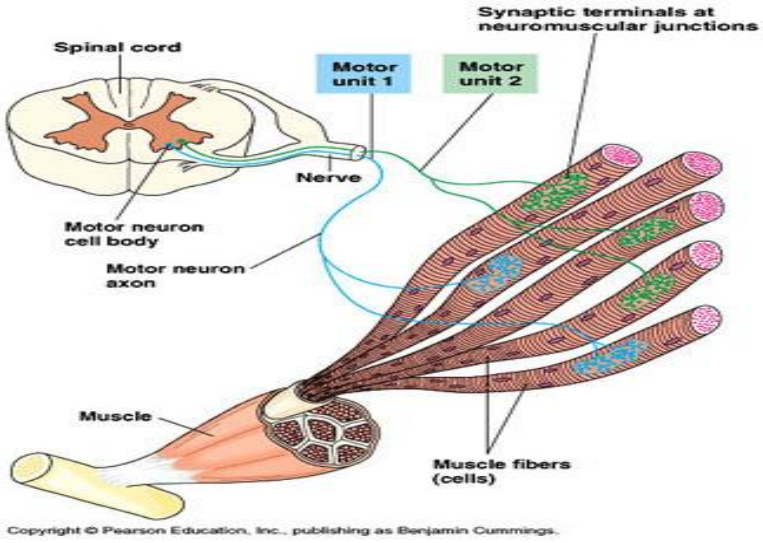
Skeletal Muscle

- Long cylindrical cells
- Many nuclei per cel
- Striated
- Voluntary
- Rapid contraction

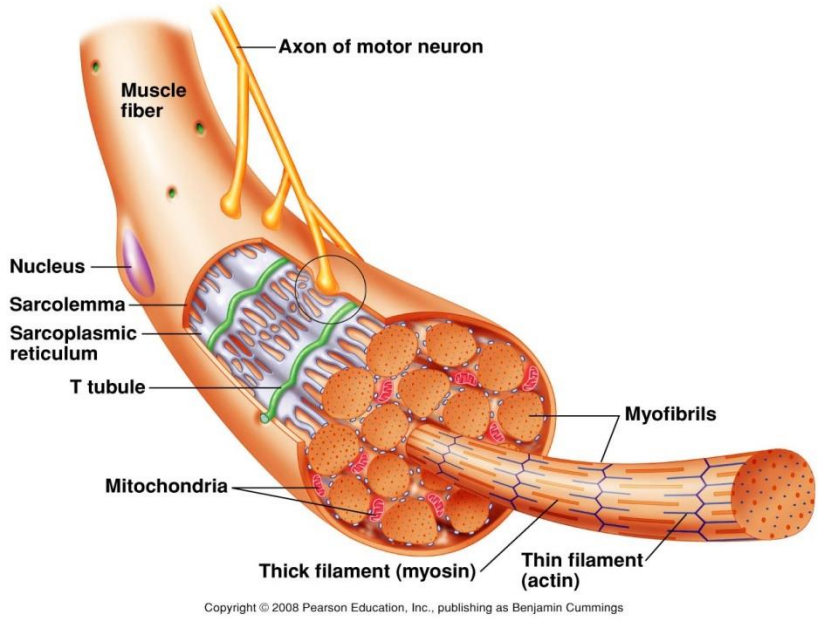


Motor units

- Motor unit: Composed of one motor neuron and all the muscle fibers that it innervates
- There are many motor units in a muscle
- The number of fibers innervated by a single motor neuron varies (from a few to thousand)
- The fewer the number of fibers per neuron → the finer the movement (more brain power)

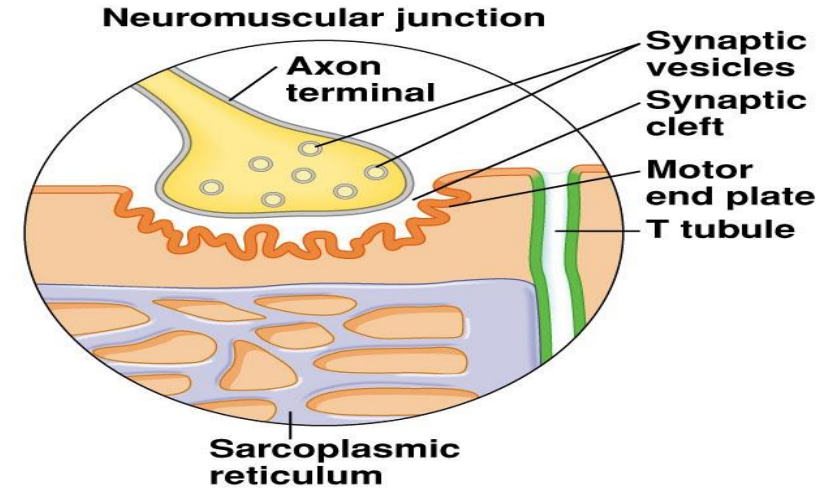


Components of a muscle fiber



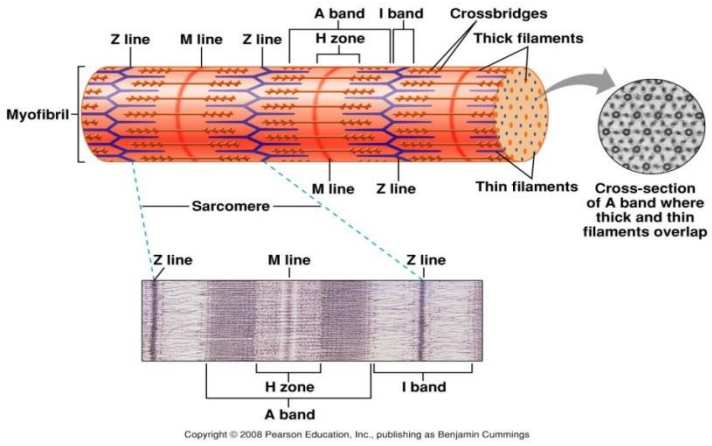
Muscle fiber components

- Sarcolemma: muscle cell membrane
- Sarcoplasma: muscle cell cytoplasm
- Motor end plate: contact surface with axon terminal
- T tubule: cell membrane extension into the sarcoplasm (to reach the myofibrils)
- Cisternae: areas of the ER dedicated to Ca++ storage (located on each side of the T-tubules)
- Myofibrils: organized into sarcomeres

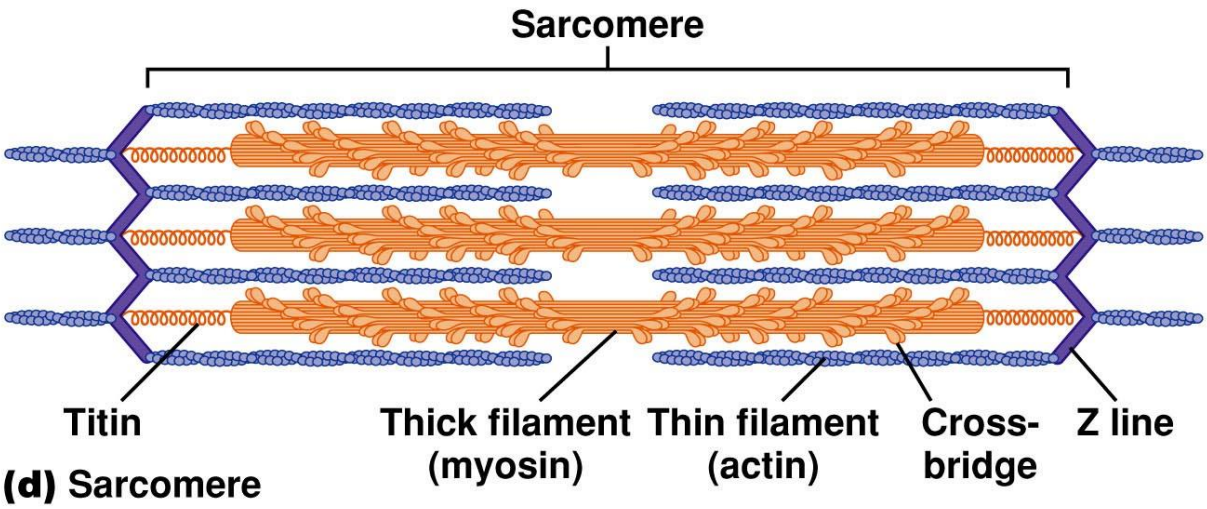


The sarcomere

- The myofibrils are organized into a repetitive pattern, the sarcomere
- Myosin: thick filament
- Actin: thin filament
- Bands formed by pattern: A and I and H bands
- Z line: area of attachment of the actin fibers
- M line: Myosin fiber centers

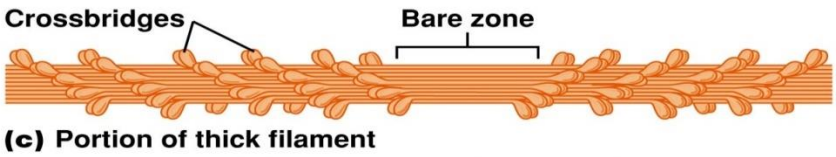


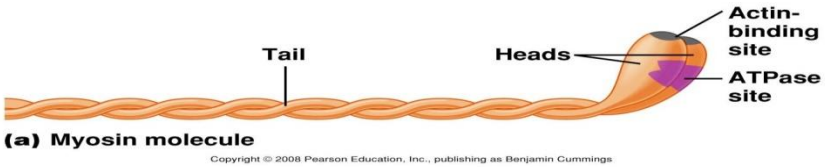
The sarcomere



Myosin structure

- Many myosin molecules per filament,
- Long tail topped by a thickening: the head → forms crossbridges with the thin filament
- Presence of the enzyme, ATPase in the head → release energy for contraction





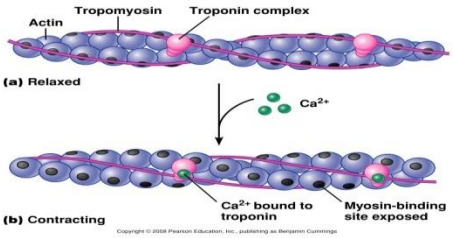
Actin structure

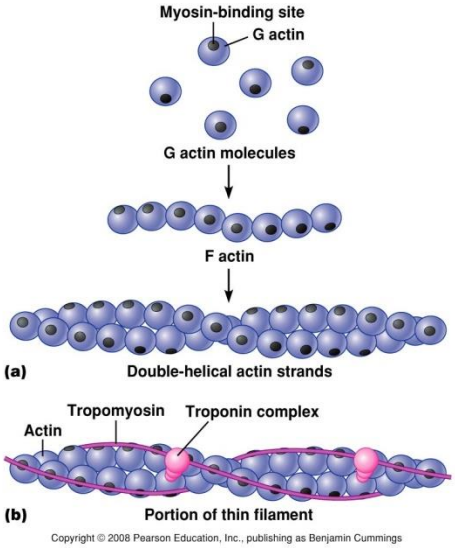
- Formed by 3 different proteins:

- globular (G) actins: bind to myosin heads
- tropomyosin: long, fibrous molecule, extending over actin, and preventing interaction between actin and myosin
- troponin: binds reversibly to calcium and able to move tropomyosin away from the actin active site

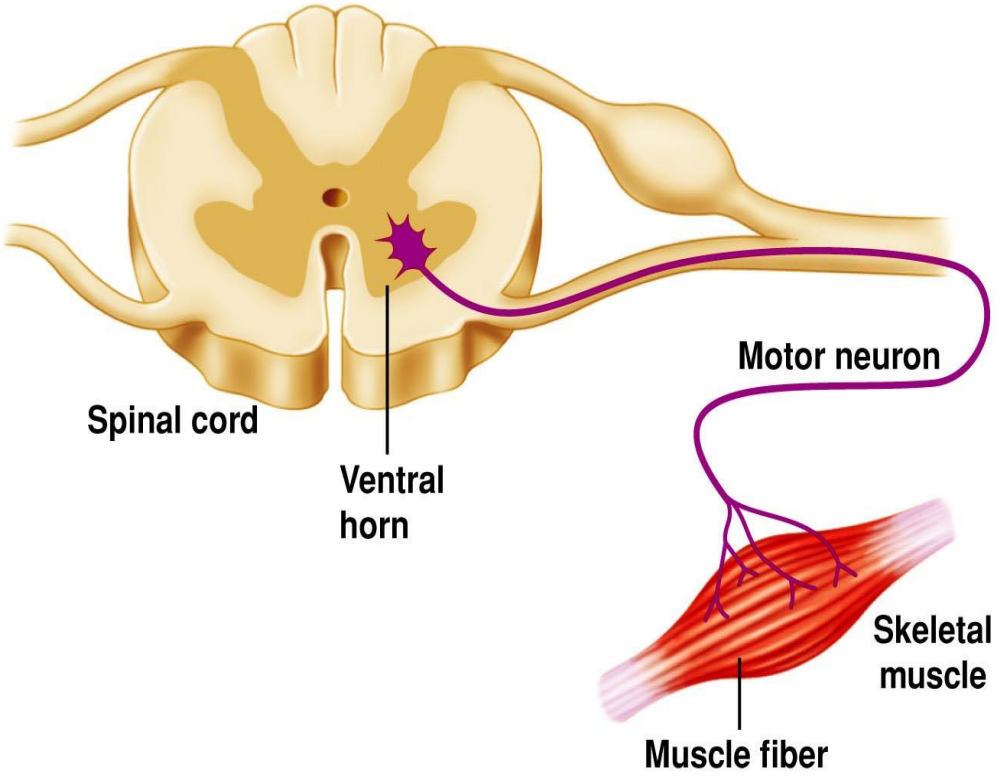
- Formed by 3 different proteins:

- globular (G) actins: bind to myosin heads
- tropomyosin: long, fibrous molecule, extending over actin, and preventing interaction between actin and myosin
- troponin: binds reversibly to calcium and able to move tropomyosin away from the actin active site



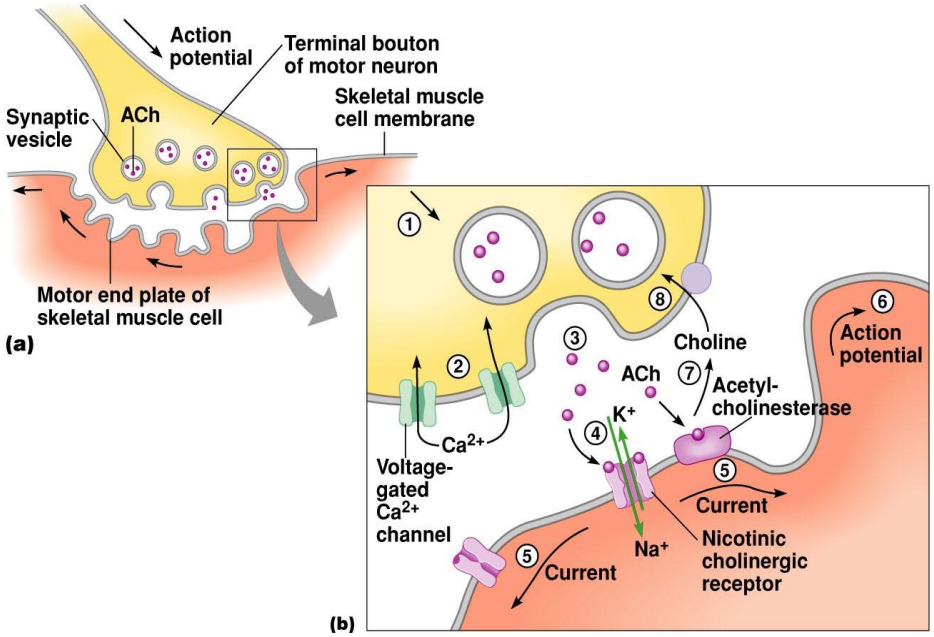


2- Muscle contraction: Cell events



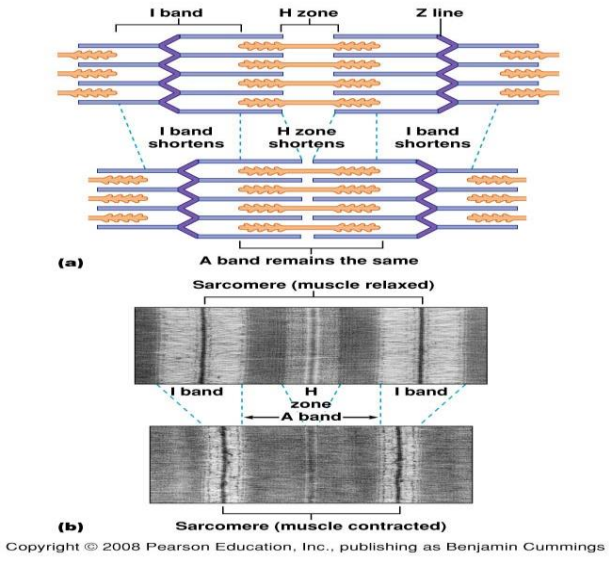
Synaptic events

- The AP reaches the axonal bulb
- Voltage-gated calcium channels open
- The influx of calcium in the bulb activates enzymes →the vesicles containing the neurotransmitter molecule dock and release the neurotransmitter in the synapse
- The neurotransmitter for skeletal muscles is always acetylcholine
- The receptors on the muscle fiber are cholinergic receptors
- These receptors are nicotinic (fast) acting receptors



Muscle relaxation

- Ach is removed from the receptors by acetylcholinesterase
- Ligand-gated Na+channels close
- Ca++ ions leave troponin and are brought back into the cisternae (this process needs energy)
- Tropomyosin moves back over the actin active site
- The myosin heads release their binding to actin
- The filaments passively move back into resting position



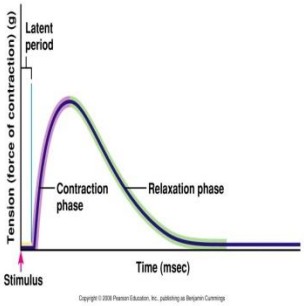
3- Muscle contraction: Mechanical events

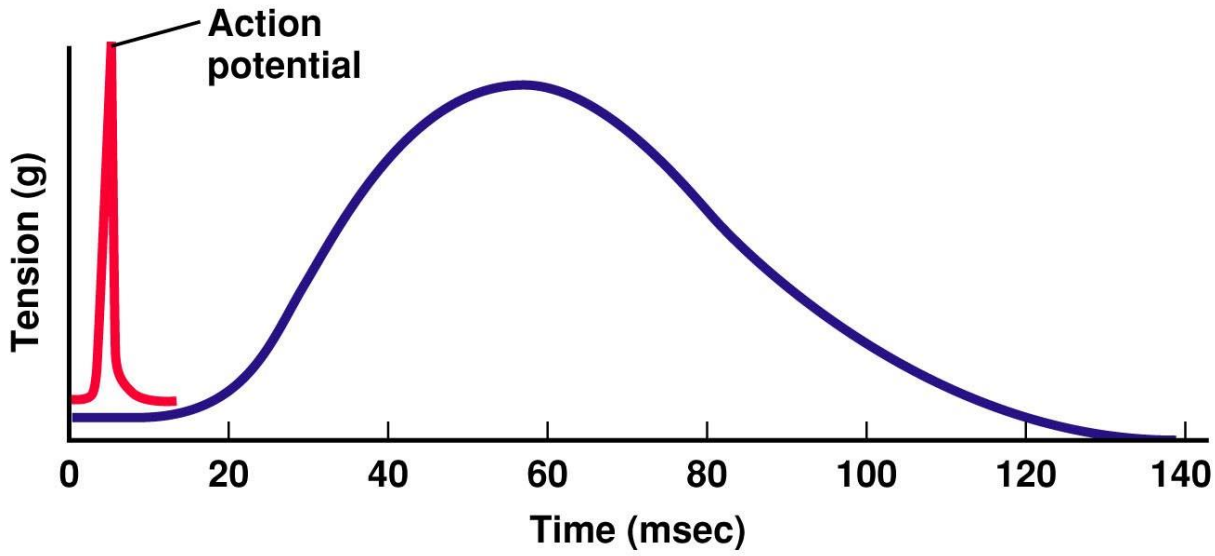
- 1 stimulation → 1 twitch
- Muscle twitch: 3 phases:

- latent phase

- contraction phase

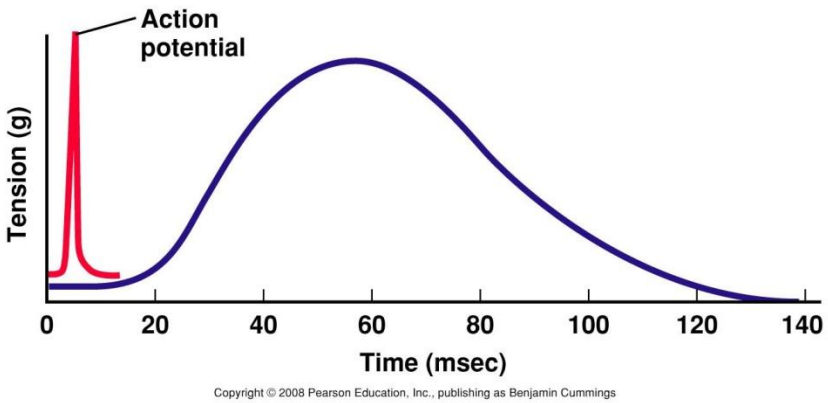
- relaxation phase





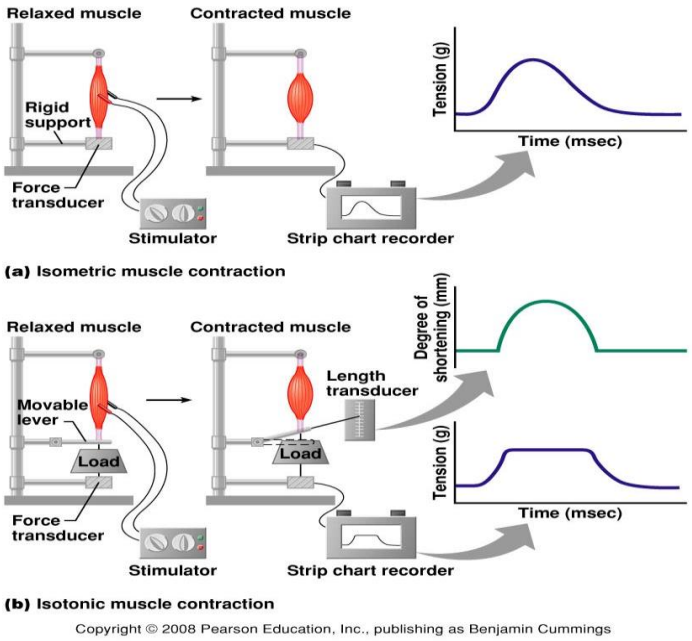
Events during the twitch

- Latent phase: Stimulus to beginning contraction: to myosin binding to actin active site
- Contraction phase: beginning to end of muscle tension → myosin heads slide along the actin filaments
- Relaxation phase: peak tension to no tension → Ca++ ions moved back into the cisternae, tropomyosin moves back over actin, myosin head release actin and the filaments move back into resting position



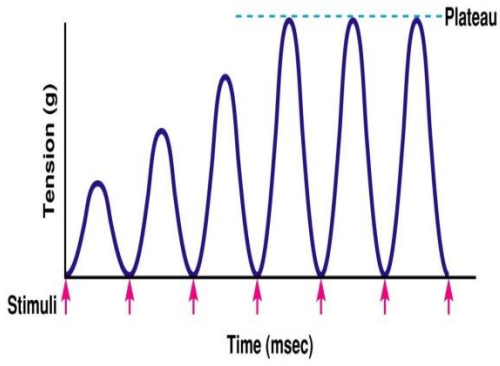
Isometric/isotonic contractions

- Isometric: muscle contraction without movement → no muscle shortening
- Isotonic: muscle contraction with movement → muscle shortens



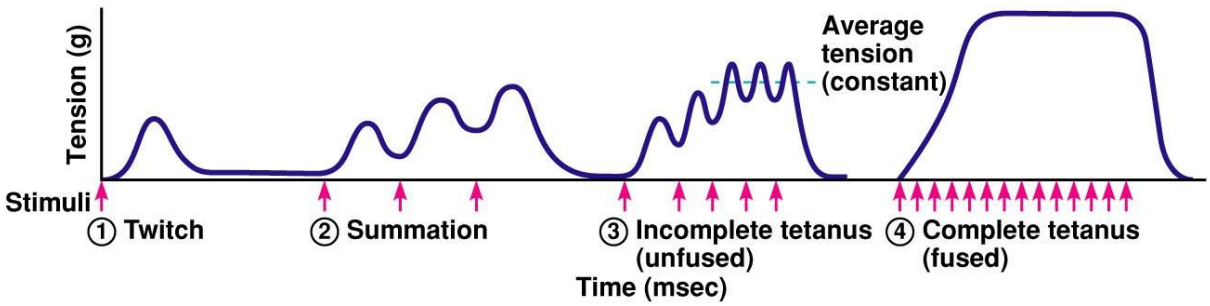
Effect of consecutive stimuli: Treppe

- Treppe: gradual increase in contraction intensity during sequential stimulation
- Might be due to calcium ions accumulating in the cytoplasm with each stimulation



Summation and tetanus

- Summation: Rapid sequence of stimuli→ muscle twitches fuse into each other, each subsequent one being stronger that its precedent (due to Ca++?)
- Tetanus: very rapid sequence of stimuli: no relaxation



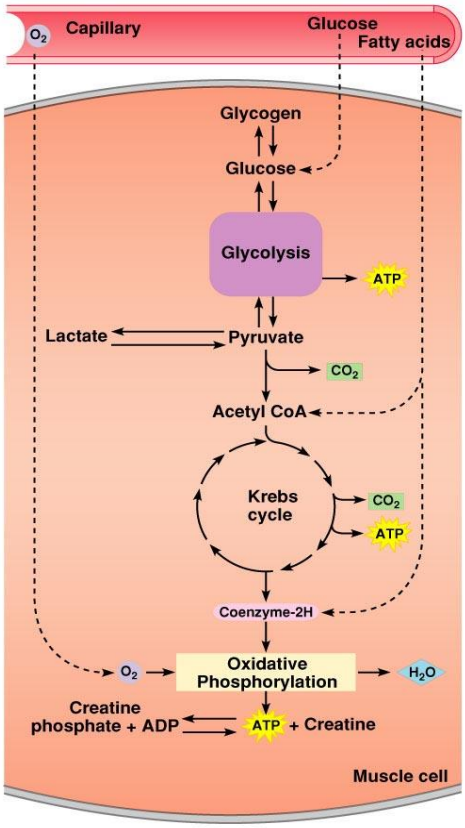
IV- Muscle metabolism

- Muscle fibers use ATP (only first few seconds) for contraction
- ATP must then be generated by the muscle cell:

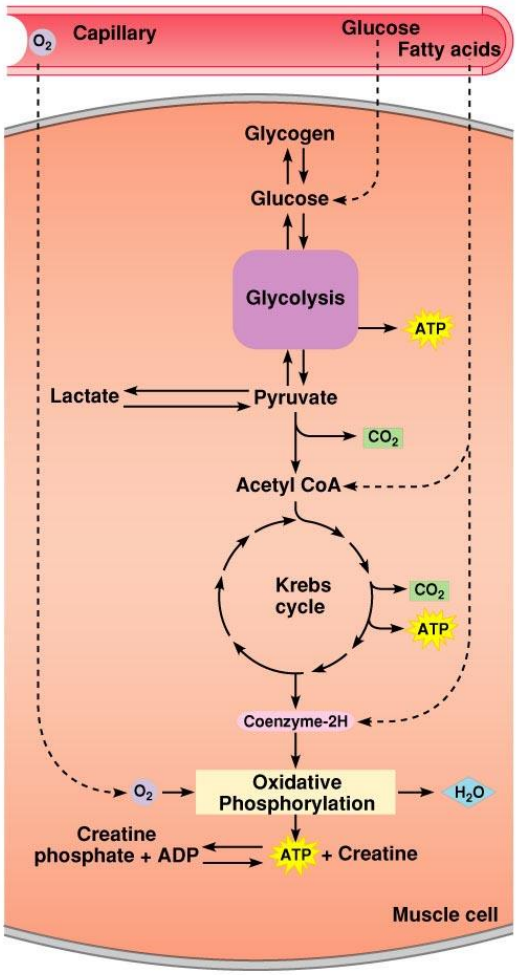
- from creatine phosphate, first
- from glucose and glycogen
- from fatty-acids

ATP formation from the above compound is possible if oxygen is present (oxidative phosphorylation: 36 ATP per glucose)

Oxygen is delivered to the muscle by myoglobin, a molecule with high affinity to oxygen and related to hemoglobin



If the effort is strong and sustained, the muscle might not have enough oxygen delivered to it by myoglobin → anaerobic glycolysis with only 2 ATP formed per glucose and synthesis of lactic acid



Muscle fatigue

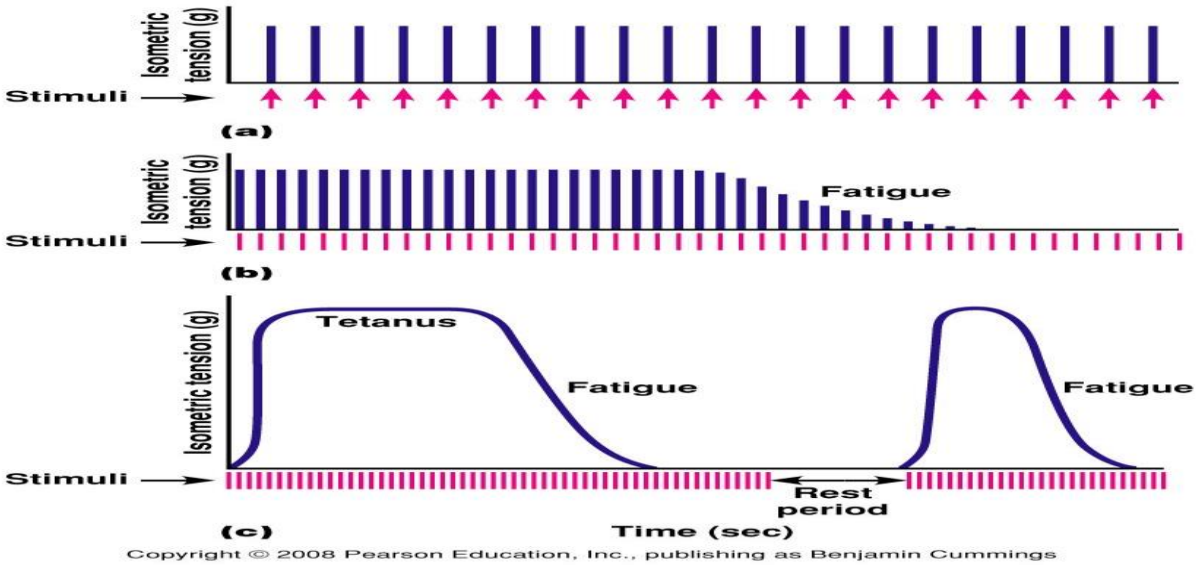
- Muscle fatigue: a decline in the ability of the muscle to sustain the strength of contraction
- Causes:

- rapid build-up of lactic acid

- decrease in oxygen supply

- decrease in energy supply (glucose, glycogen, fatty-acids)
  - Decreased neurotransmitter at the synapse

- psychological causes



Basis for classification

- Velocity of contraction: slow vs fast
- Energy source: oxidative vs glycolytic

Oxydative

Oxydative	Glycolytic

Primary energy through oxidative phosphorylation

Many mitochondria

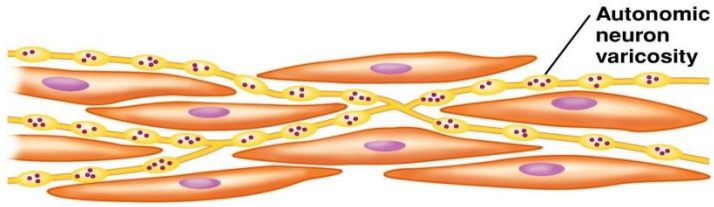
Myoglobin (red)

Resistant to fatigue

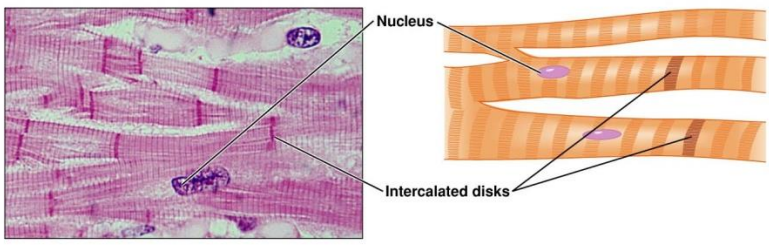
Primary energy through anaerobic glycolysis

- Fewer mitochondria
- Many glycolytic enzymes
- High glycogen stores
- Use little oxygen—anaerobic
- Quick to fatigue

VI- Smooth and Cardiac Muscles



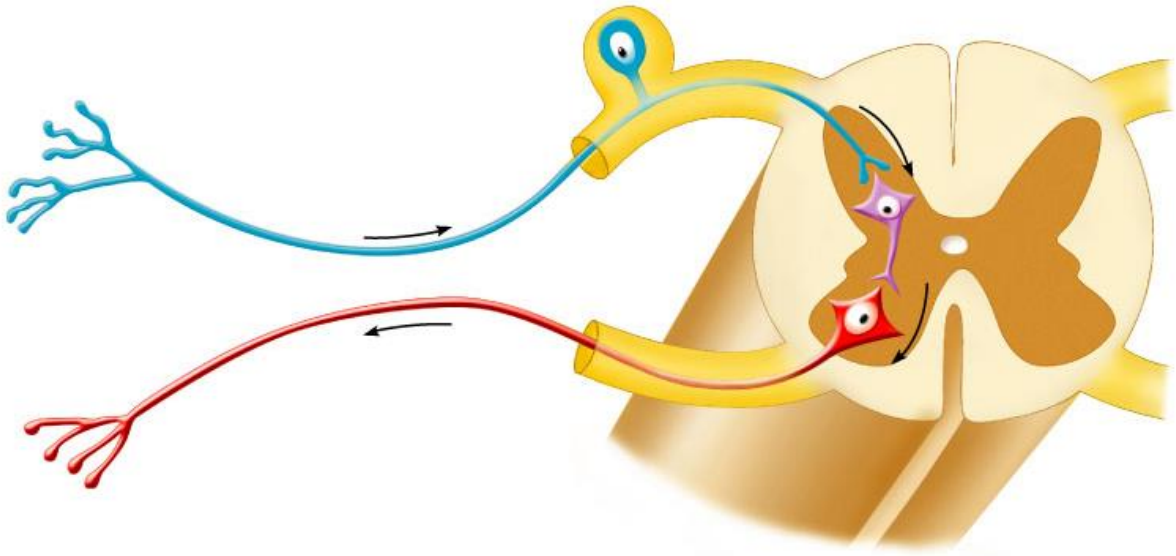
(a) Multi-unit smooth muscle



(c) Cardiac muscle

	Skeletal	Cardiac	Smooth
Appearance			
Control	voluntary	unvoluntary	Unvoluntary
Hormone	0	Epi	Epi/others
Ca++ prot	Troponin	Troponin	Calmodulin
Gap junctions	No	Yes	Yes
Pacemaker	No	Yes	No

Lecture 7 Fundamentals of the Nervous System



Basic division of the Nervous System (although there is only ***one*** NS)

- **Central nervous system ("CNS") – occupies cranium and vertebral column**
    - Brain
    - Spinal cord
- **Peripheral nervous system ("PNS")**
    - Cranial nerves
    - Spinal nerves
    - Ganglia (clusters of cell bodies)

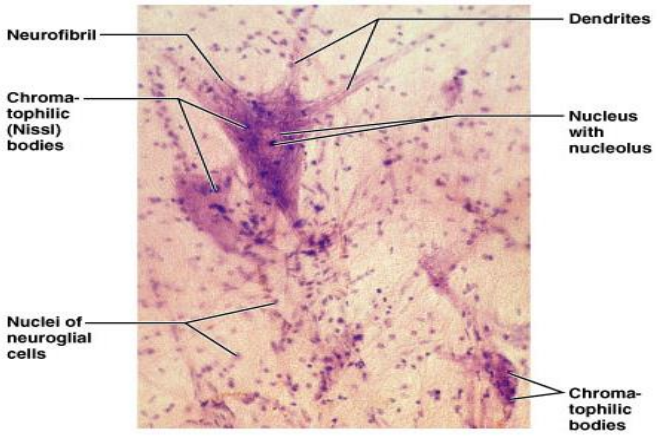
Nervous tissue: 2 types of cells

1. ***Neurons***
    - Excitable nerve cells
    - Transmit electrical signals
2. Supporting cells: ***neuroglia*** or just ***glia***
    - Means "nerve glue"

Neurons

- All have a cell body: with nucleus and cytoplasm
- Cell bodies are in clusters
    - CNS: clusters called ***nuclei***
    - PNS: clusters are called ***ganglia***

      (are *outside* the CNS)



Neurons

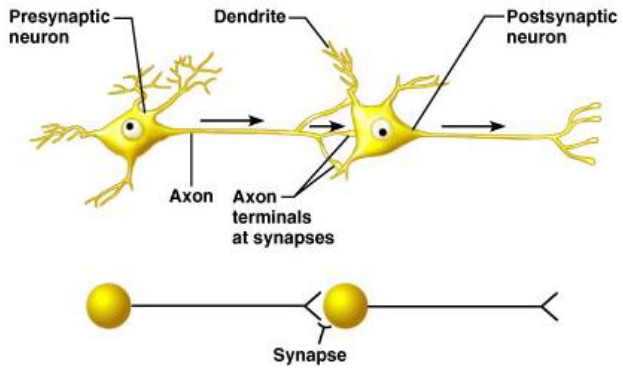
- Can live for a lifetime (i.e. over 100 years)
- Do not divide
    - (exception: recent neural stem cells identified)
    - Cannot replace themselves
    - High metabolic rate
    - Require continuous oxygen and glucose
    - Die within a few minutes without oxygen

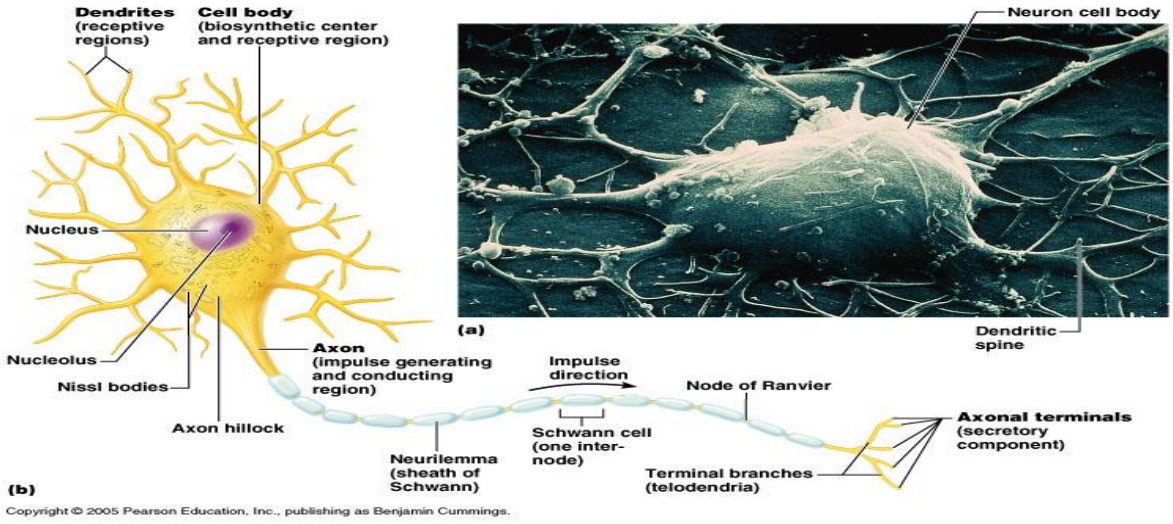
Neuron "processes"

(armlike; extend from the cell body)

- Nerve fibers = ***axons***
    - Nerve impulse generators & transmitters
    - One per neuron, although can branch into "collaterals"
    - At terminal end branch *a lot* (e.g. 10,000/terminus)

- Receptive regions called ***dendrites***
  - Have receptors for neurotransmitters (chemicals released by other neurons)
  - Neurons may have many



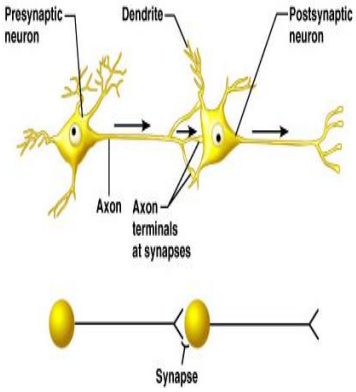


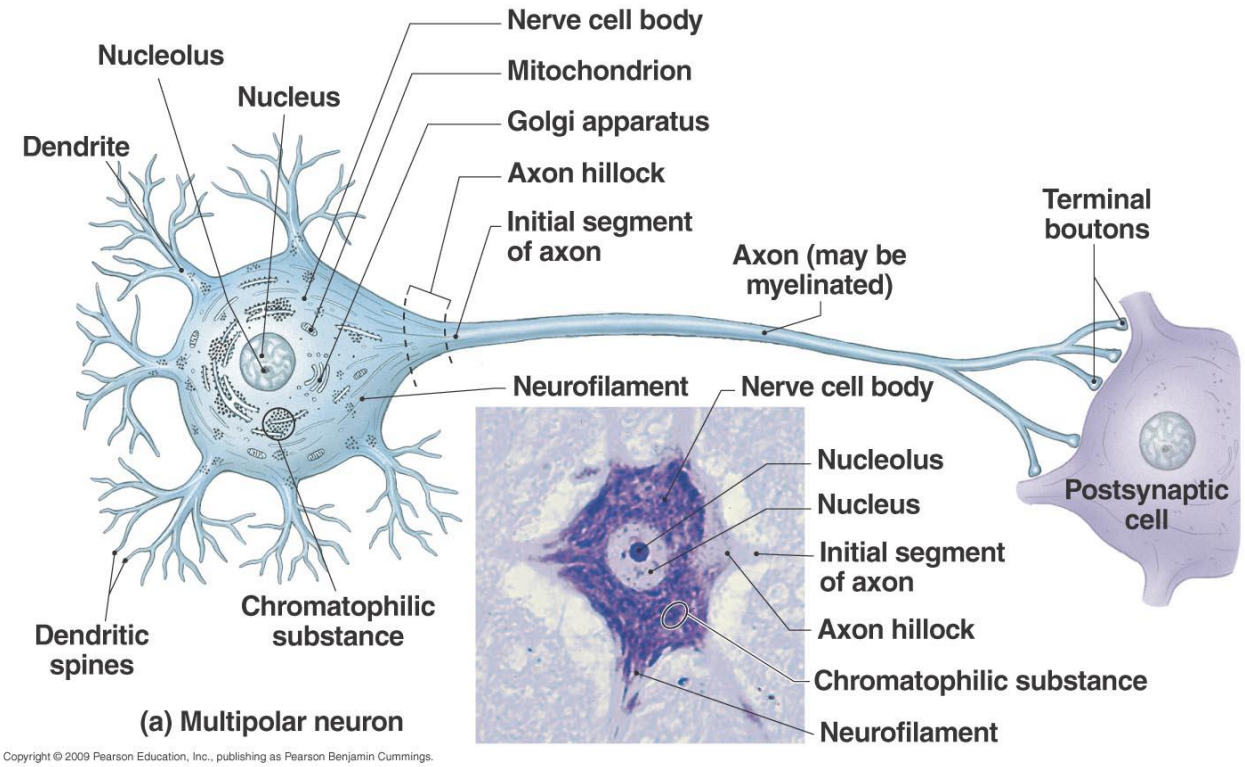
Neuron processes

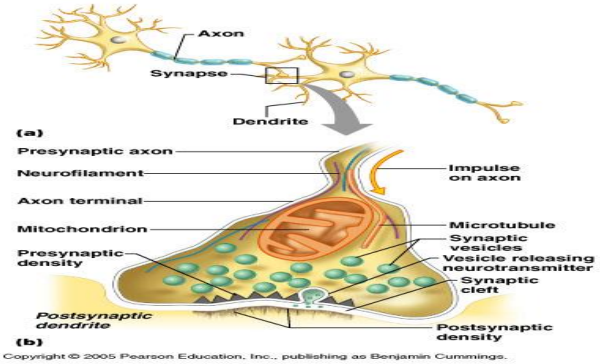
- Run through CNS in ***tracts*** of white matter
- Run through the PNS forming peripheral ***nerves***

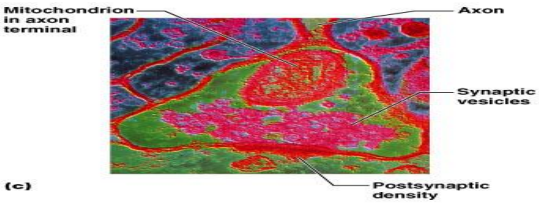
Synapses

- Junctions between neurons
- Information is passed (usually chemically)
- Unidirectional
- Presynaptic (*toward* synapse) vs postsynaptic (*away from* synapse): most neurons function as both
- Synaptic cleft (tiny gap)



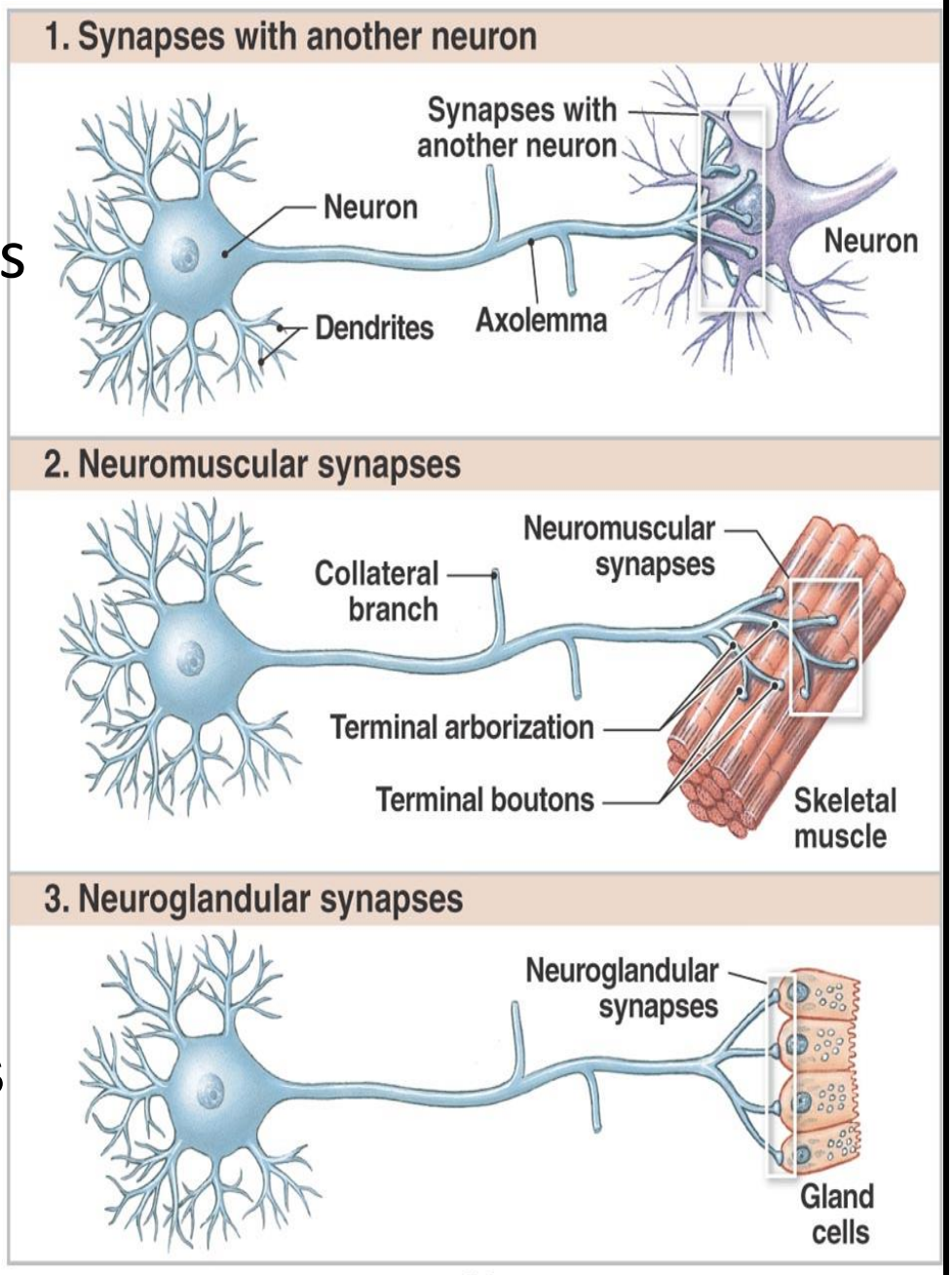






Neurons can synapse with:

1. Neurons
2. Muscle
3. Glands



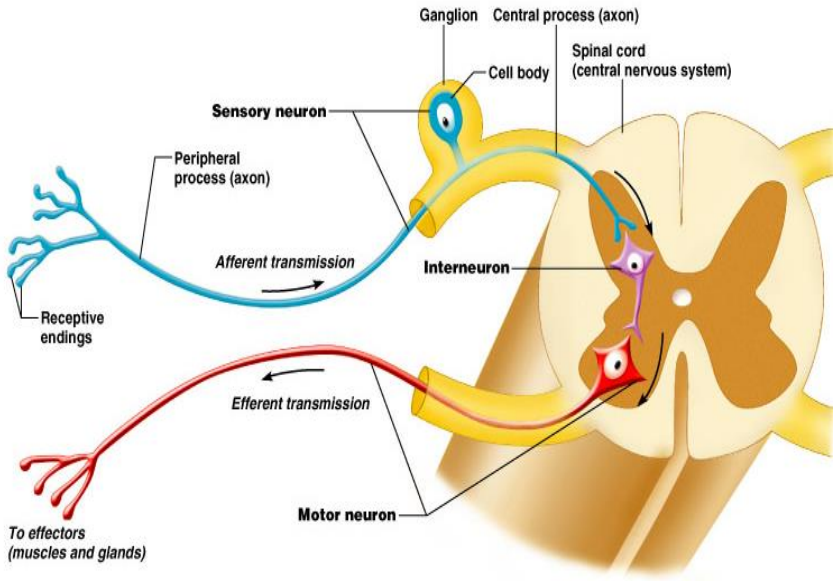
simplified

- Info passed between neurons by chemicals
  - Can be excitatory or inhibitory
  - Along the axons, the information passes electrically

Neurons by function/direction *(relative to the CNS)*

- Sensory or afferent (toward CNS from sensory receptor in PNS)
  - Dendrites with specialized sensory receptors

    (in skin, muscles, viscera, etc)
  - Cell bodies **always** in ganglion* outside CNS
- Motor or efferent
  - From CNS to muscles, glands or viscera
  - Cell bodies almost always in CNS*
- Interneurons*: 99.98% of neurons (within CNS; can be long, e.g. travel down the spinal cord)



Nervous tissue: 2 types of cells

1. (Neurons and their processes: we just did)
2. Supporting cells = neuroglia ("nerve glue") or just glial cells
    - CNS
        - Astrocytes
        - Oligodendrocytes
        - Microglia
        - Ependymal cells
    - PNS
        - Schwann cells
        - Satellite cells

Supporting cells

- Neuroglia usually refers to CNS ones
- Just "glia" to both
- Divide throughout life
- Smaller and darker than neurons
- Outnumber neurons 10 to 1

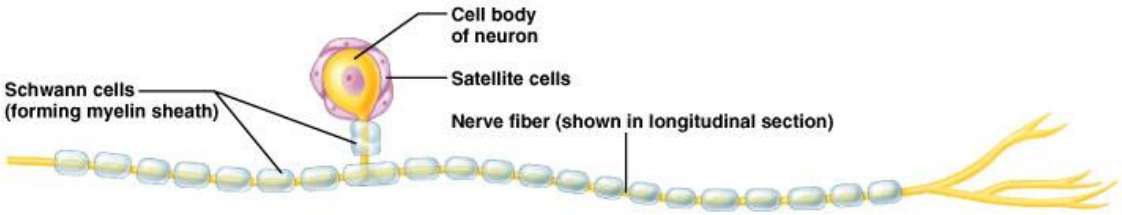
Neuroglia (CNS glial cells)

- Astrocytes
    - Star shaped; the most numerous
    - Involved in metabolism & synapse formation
- Microglia
    - Phagocytes
- Ependymal cells
    - Line the cavities of CNS and spinal cord; cilia

- Oligodendrocytes
    - Produce myelin sheaths in CNS (see later slide)

PNS supporting cells

- Satellite cells
- Surround neuron cell body
- Schwann cells
- Form myelin (see next slide) in PNS

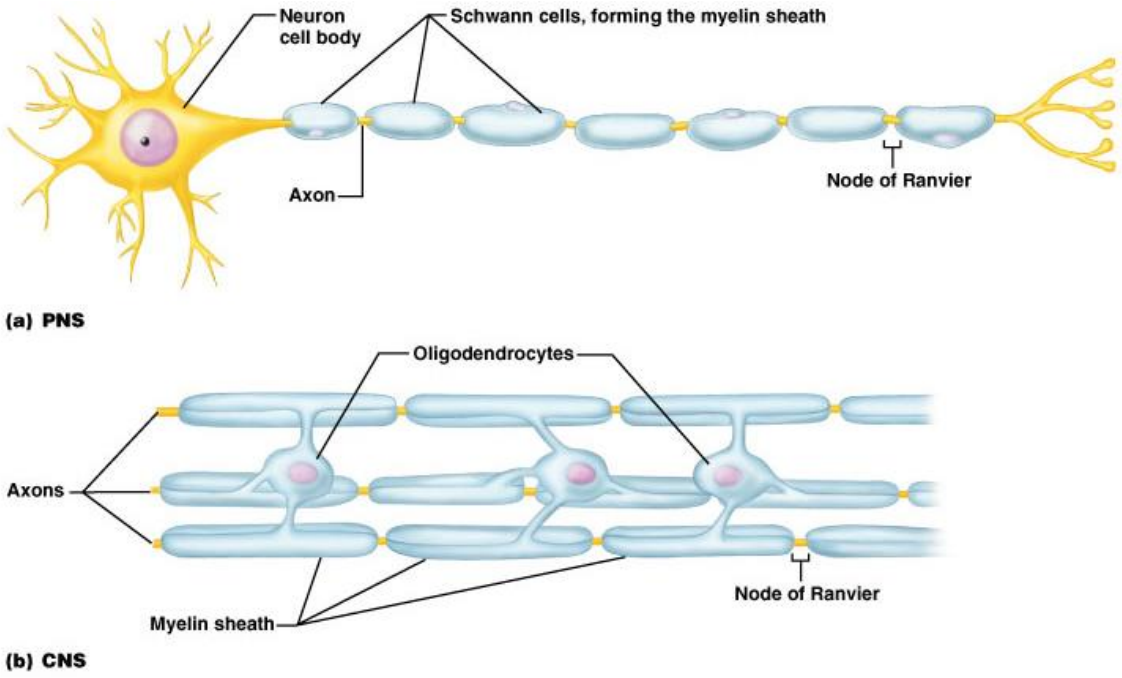


Sensory neuron with Schwann cells and satellite cells

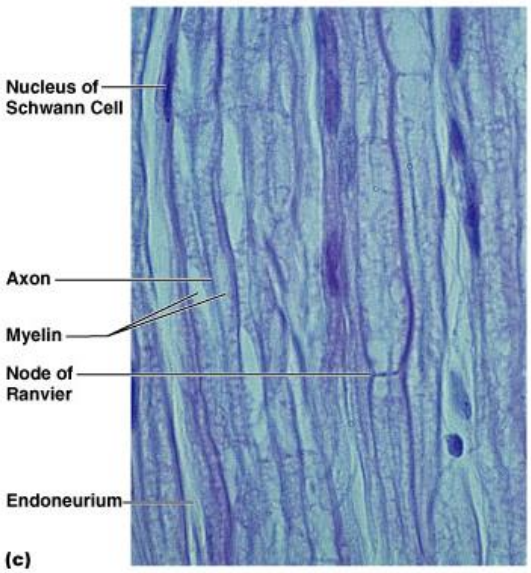
Myelin

- Lipoprotein
- Increases speed of conduction, large axons
    - Are “insulation”
    - Prevent leakage of electric current
- Layers with spaces (nodes of Ranvier) between cells
- Impulse “jumps” from node to node
- “Unmyelinated” axons – smaller, slower

- **Myelin in the Peripheral and Central Nervous Systems**



- **Schwann cells**
  - Myelin sheath
  - Neurolemma (nucleus and most of cytoplasm squeezed to outside)



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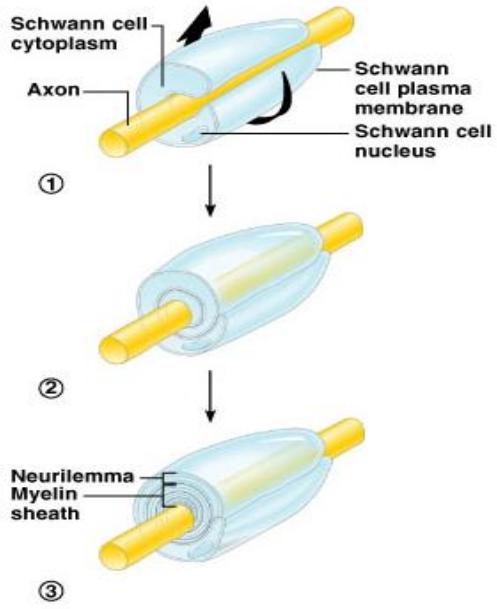
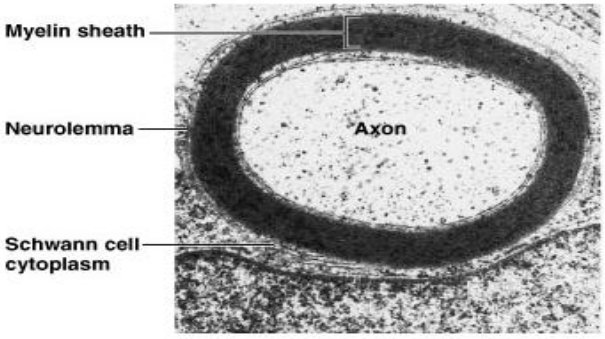




(a) Schwann cells on myelinated axon

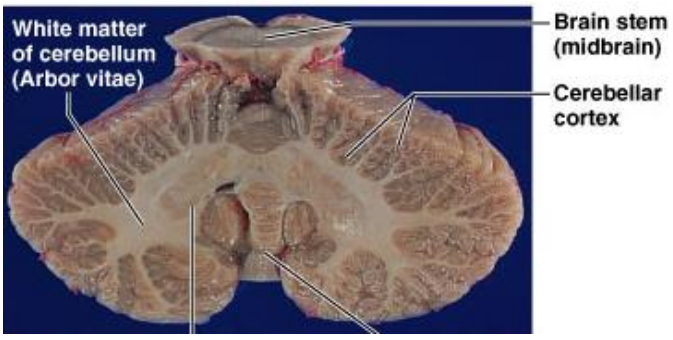
Gray and White Matter of the CNS

(GROSS ANATOMY OF THE CNS)

- Gray matter: gray-colored
- Where neuron cell bodies are clustered
- White matter: white-colored
- Where millions of axons are running between different part of CNS, in bundles of "tracts"
  - Remember, *tracts* are in CNS, vs *nerves* in PNS
- White is from the myelin sheaths

Usual pattern of gray/white in CNS

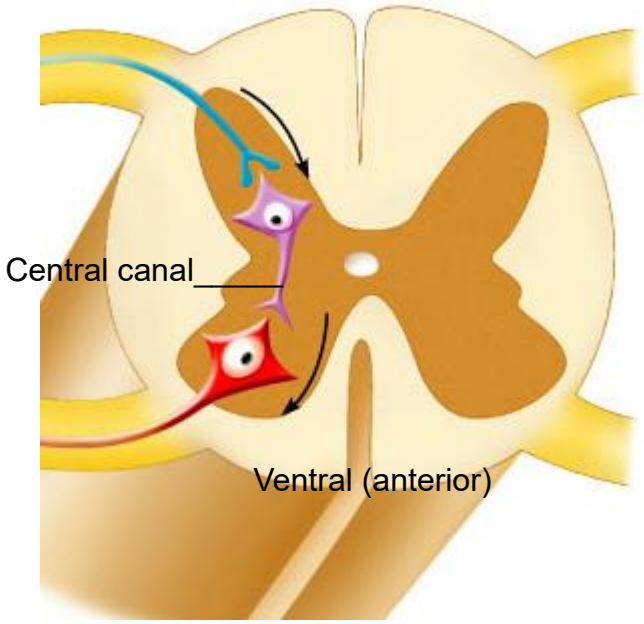
- White exterior to gray
- Gray surrounds hollow central cavity
- Two regions with additional gray called "cortex"
  - Cerebrum: "cerebral cortex"
  - Cerebellum: "cerebellar cortex"



Gray/White in spinal cord

- Hollow central cavity ("central canal")
- Gray matter surrounds cavity

- White matter surrounds gray matter (white: ascending and descending tracts of axons)
- "H" shaped on cross section
- Dorsal half of "H": cell bodies of interneurons
- Ventral half of "H": cell bodies of motor neurons
- No cortex



From earlier: neuron processes

- Run through CNS in ***tracts*** of white matter
- Run through the PNS forming peripheral ***nerves***

Nerves are bundles of nerve fibers (long axons) in connective tissue

- To or from CNS to periphery
- Classified according to direction, like neurons
- ***Mixed***: carry both sensory (afferent) and motor (efferent) fibers
    - All spinal nerves are mixed
- ***Sensory*** or afferent nerves: ***to*** CNS
- ***Motor*** or efferent nerves: ventral roots of spinal cord

Interneurons

(99% of all neurons)

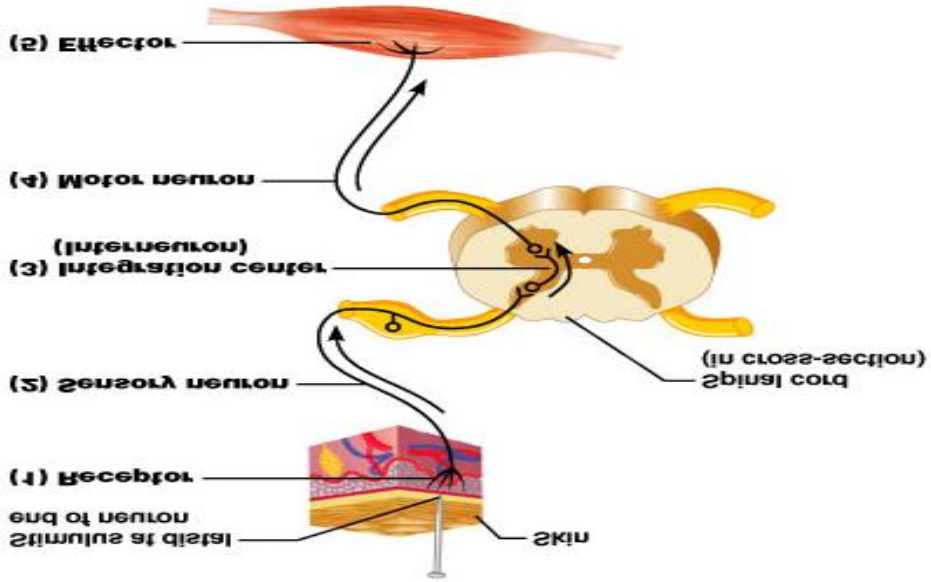
- In gray matter:
    - They process received sensory information
    - They direct this info to specific regions of the CNS
    - They initiate the appropriate motor response
- Via axons in white matter
    - They transmit info (sensory and motor) from one region of the CNS to another

Reflex arcs: our "reflexes"

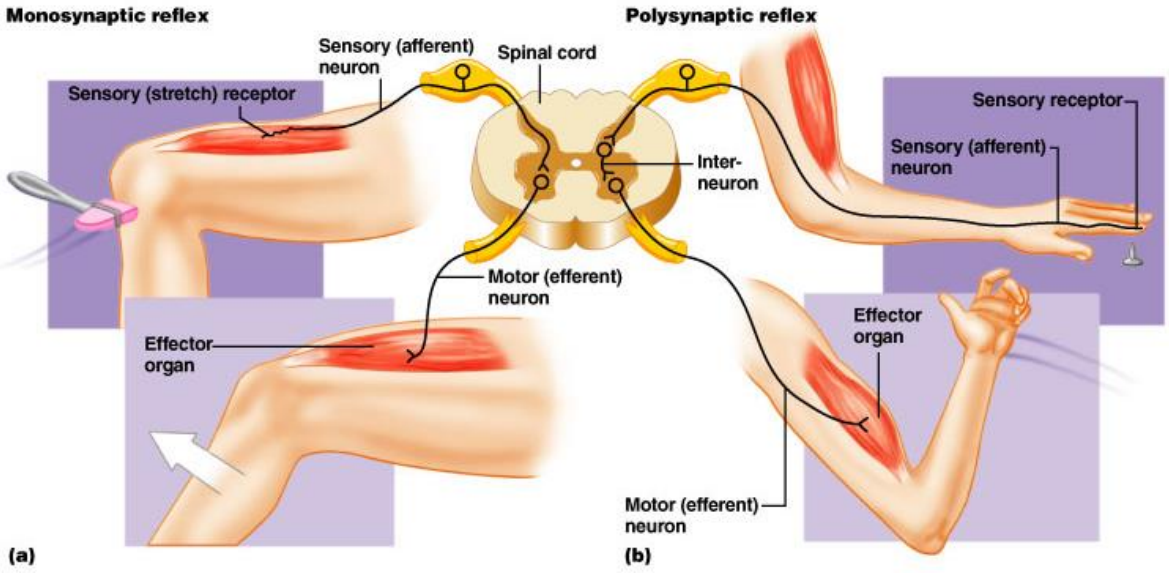
- Fast, automatic, involuntary
- Somatic or visceral
- Motor responses
- Monosynaptic or polysynaptic

- 5 components:

see right

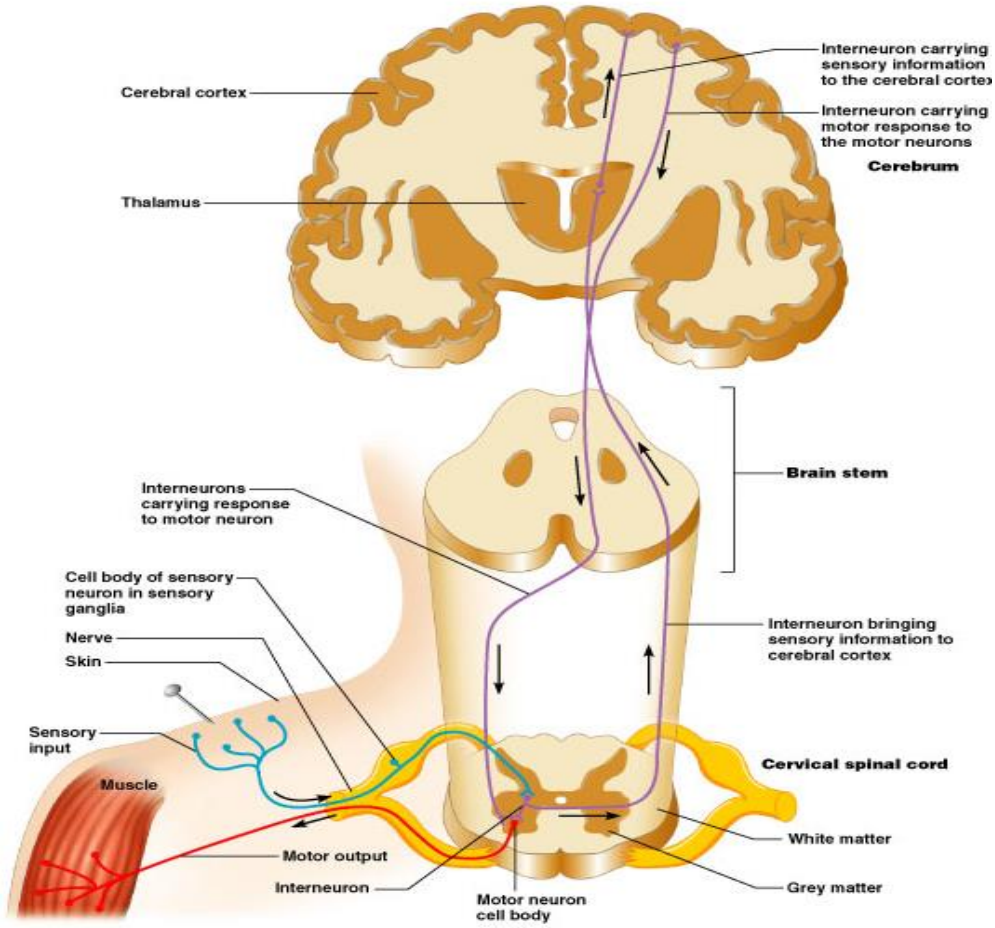


Reflex arcs: monosynaptic or polysynaptic



Basic neuronal organization

- Coronal section of cerebrum
- Cross sections of spinal cord and brains stem
- Note gray matter (brown) and white matter (tan)
- Reflex arc and information processing are shown



Terminology for quiz

- ***Neuron*** = nerve cell
- ***Neuroglia*** = supporting cell
- ***Nerve fiber*** = long axon
- ***Nerve*** = collection of nerve fibers (axons) in ***PNS***
- ***Tract*** = collections of nerve fibers (axons) in ***CNS***
- ***Nucleus*** = cluster of cell bodies in CNS

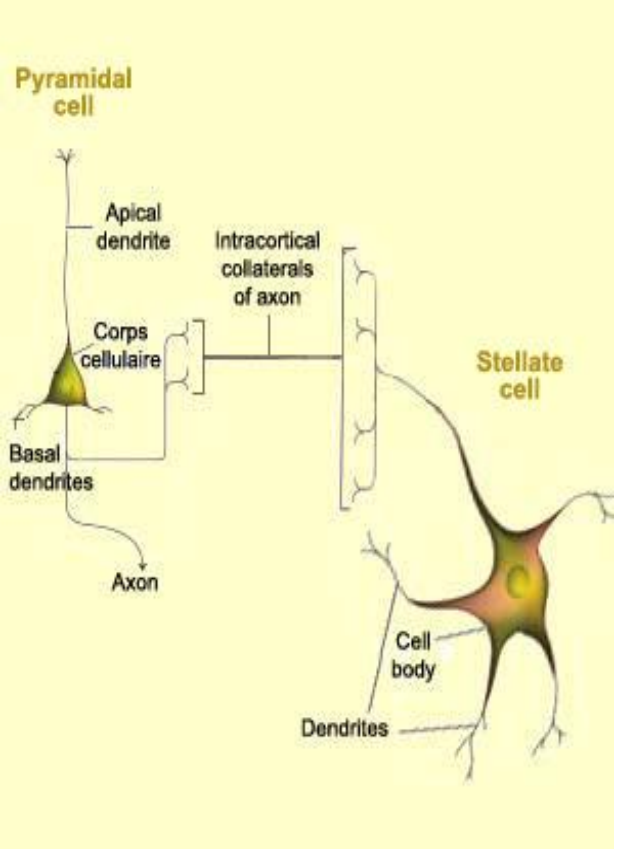
- ***Ganglia*** = cluster of cell bodies in PNS

New:

- ***Unilateral:*** on ***one*** side
- ***Ipsilateral:*** on the ***same*** side
- ***Contralateral:*** on the ***opposite*** side

Remember also:

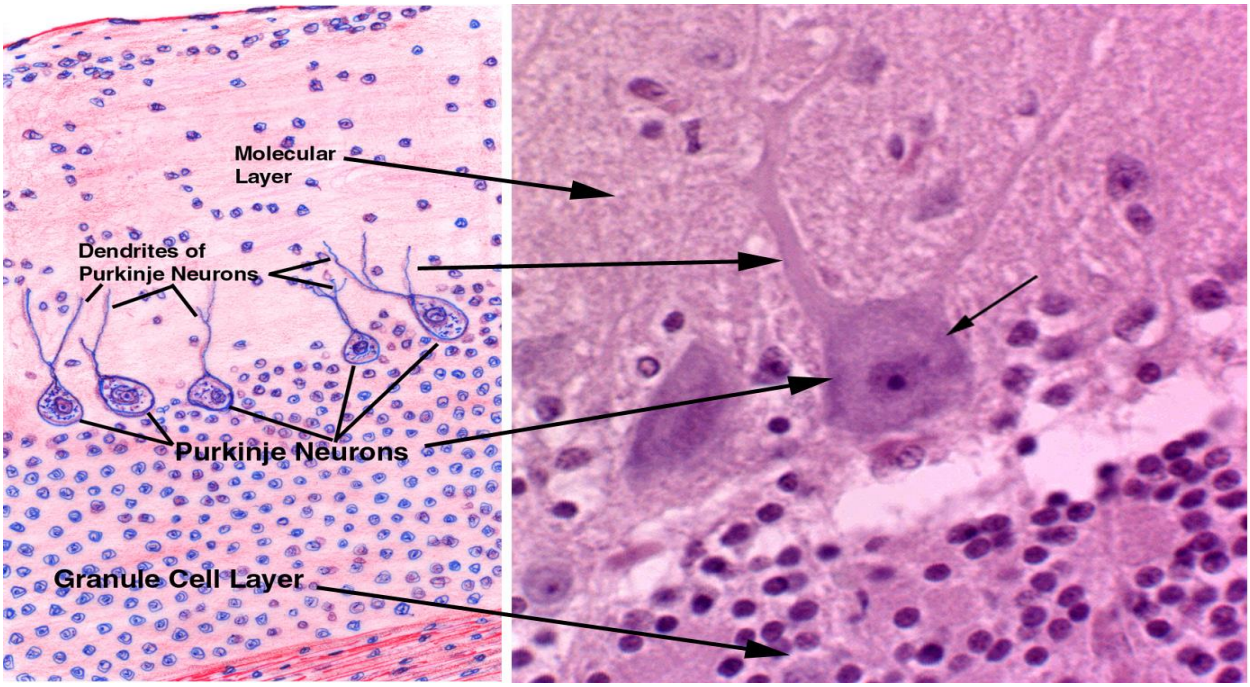
- ***CNS vs PNS***
- ***Input: sensory: afferent: to brain***
- ***Output: motor : efferent: from brain***

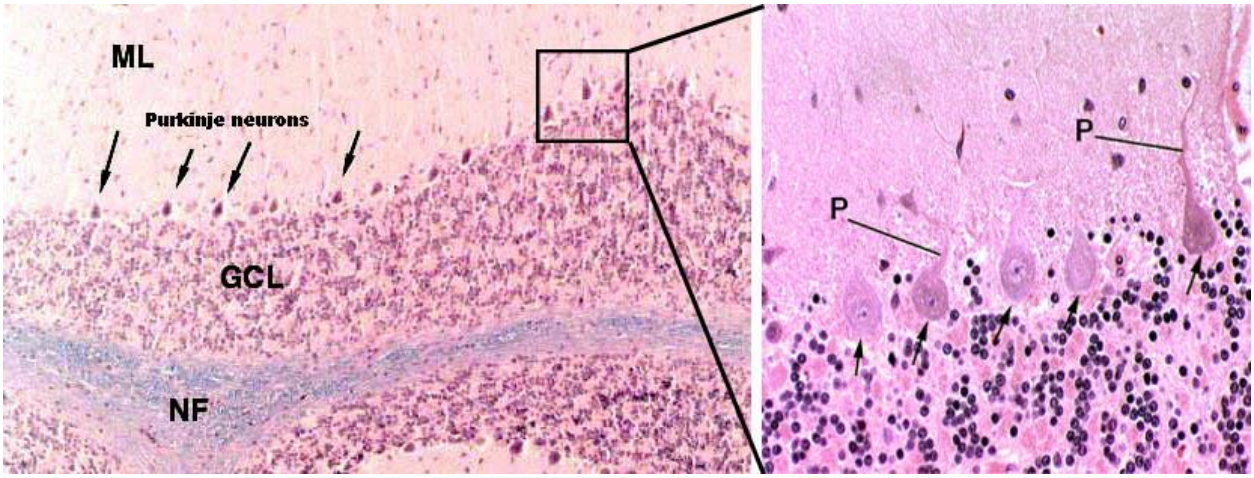


Pyramidal cells of cerebral cortex

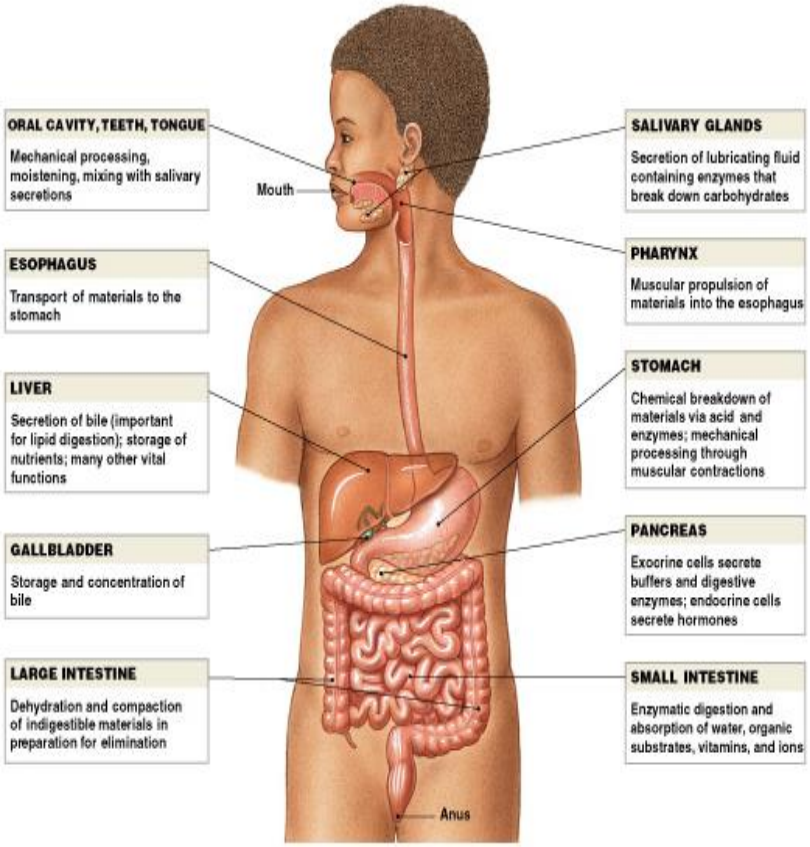
- This is where the “pyramidal” tract gets its name (the main motor tract from the cerebral cortex); also pyramids of medulla, pyramidal decussation

Cerebellar purkinje cells




ML
Purkinje neurons
GCL
NF
P
P

Lecture 8 Components of the Digestive System



Digestive Tract

- Extends from oral cavity to anus
- Passes through:
  - pharynx
  - esophagus
  - stomach
  - small intestine
  - large intestine
  - anus

Functions of the Digestive System

1. Ingestion:
   - occurs when materials enter digestive tract via the mouth
2. Mechanical processing:
   - crushing and shearing
   - makes materials easier to propel along digestive tract
3. Digestion:
   - is the chemical breakdown of food
   - into small organic fragments
   - for absorption by digestive epithelium

Functions of the Digestive System

4. Secretion:
   - is the release of water, acids, enzymes, buffers, and salts
   - by epithelium of digestive tract
   - by glandular organs
5. Absorption:
   - movement of organic substrates, electrolytes, vitamins, and water
   - across digestive epithelium
   - into interstitial fluid of digestive tract
6. Excretion:
   - removal of waste products from body fluids

Lining of the Digestive Tract

- Protects surrounding tissues against:
  - corrosive effects of digestive acids and enzymes
  - mechanical stresses, such as abrasion
  - bacteria

Peritoneal Cavity

- Is located within the abdominopelvic cavity
- Lined with serous membrane consisting of: superficial mesothelium covering a layer of areolar tissue
- Peritoneal Fluid-is produced by serous membrane lining
- Provides essential lubrication

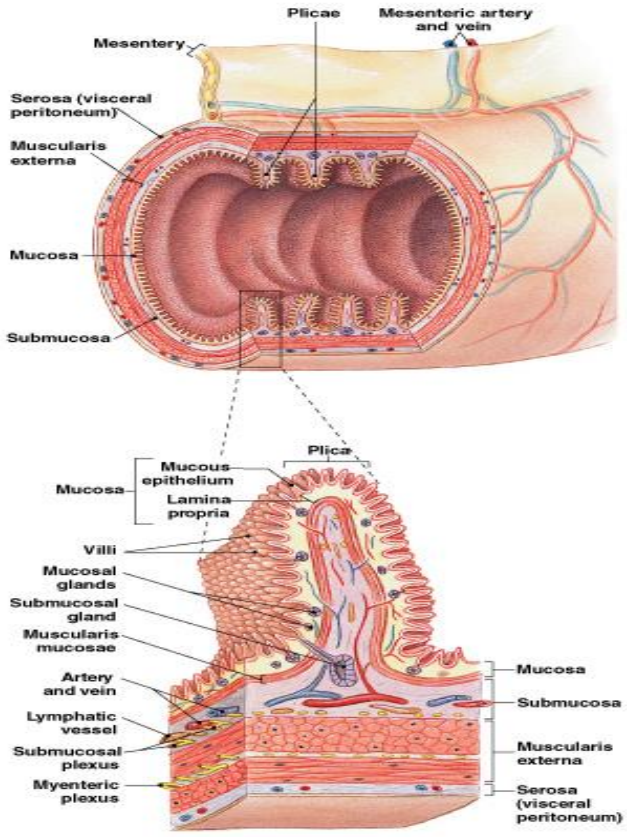
Histological Organization of the Digestive Tract

- Major layers of the digestive tract:
  - Mucosa- Is the inner lining of digestive tract

    Is a mucous membrane consisting of:

    epithelium, moistened by glandular secretions
  - submucosa
  - muscularis externa
  - serosa

Structure of the Digestive Tract



The Digestive Epithelium

- Mucosal epithelium is simple or stratified:
  - depending on location, function, and stresses
- Oral cavity, pharynx, and esophagus:
  - mechanical stresses
  - lined by stratified squamous epithelium
- Stomach, small intestine, and most of large intestine:
  - absorption
  - simple columnar epithelium with goblet cells

Lining of Digestive Tract

- Folding increases surface area for absorption:
  1. longitudinal folds, disappear as digestive tract fills
  2. permanent transverse folds (plicae)

Muscularis Mucosae

- Smooth muscle cells arranged in 2 concentric layers:inner layer encircles lumen (circular muscle)
  outer layer contains muscle cells parallel to tract (longitudinal layer)

Submucosa

- Is a layer of dense irregular connective tissue
- Surrounds muscularis mucosae
- Has large blood vessels and lymphatic vessels
- May contain exocrine glands:
  - secrete buffers and enzymes into digestive tract

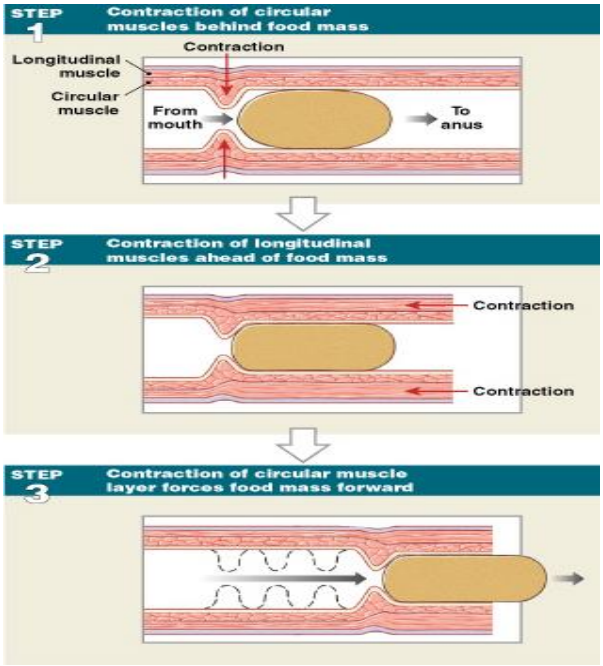
Muscularis Externa Structure

- Is dominated by smooth muscle cells
- Are arranged in:
  - inner circular layer
  - outer longitudinal layer
  - Function:
- Involved in:
  - mechanical processing
  - movement of materials along digestive tract
- Movements coordinated by enteric nervous system (ENS):
  - sensory neurons
  - interneurons
  - motor neurons

Peristalsis

Consists of waves of muscular contractions

Moves a bolus along the length of the digestive tract-Bolus is a small, oval mass of digestive contents



Peristaltic Motion

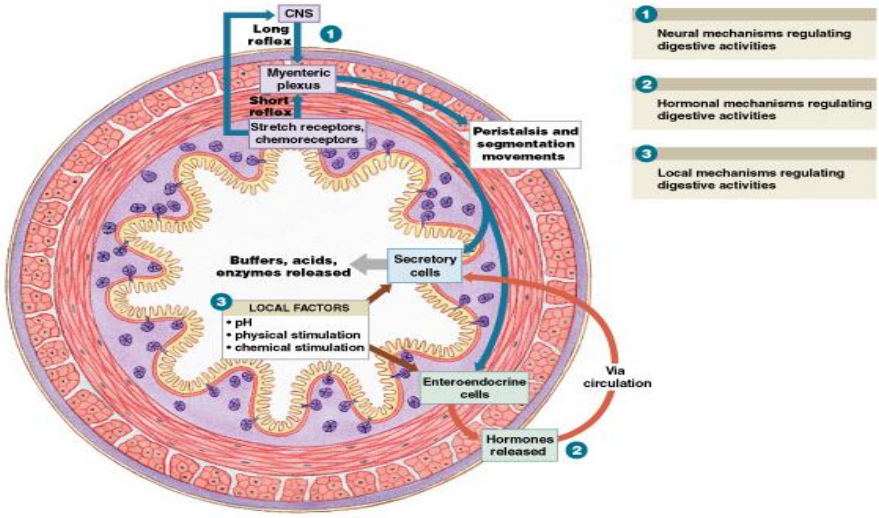
1. Circular muscles contract behind bolus:
   - while circular muscles ahead of bolus relax
2. Longitudinal muscles ahead of bolus contract:
3. Wave of contraction in circular muscles:
   - forces bolus forward

Segmentation

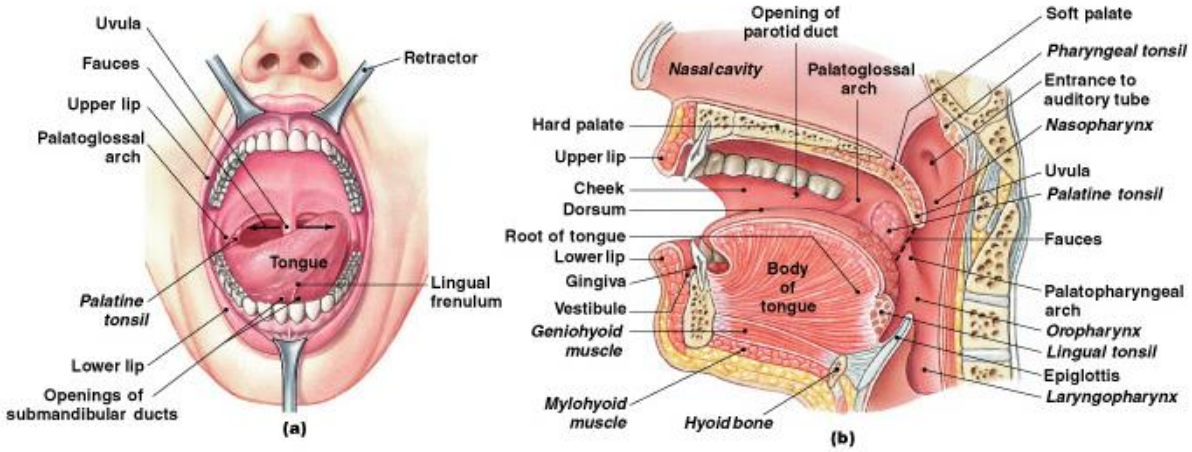
- Cycles of contraction:
  - Churn and fragment bolus
  - mix contents with intestinal secretions

The Regulation of Digestive Activities

Neural mechanisms Hormonal mechanisms Local mechanisms



The Oral Cavity



4 Functions of the Oral Cavity

- Sensory analysis:
  - of material before swallowing
- Mechanical processing:
  - through actions of teeth, tongue, and palatal surfaces
- Lubrication:
  - mixing with mucus and salivary gland secretions
- Limited digestion:
  - of carbohydrates and lipids

Oral Mucosa

- Lining of oral cavity
- Has stratified squamous epithelium

The Mucosa Inferior to the Tongue

- Is thin and vascular enough to rapidly absorb lipid-soluble drugs
- Cheeks- Are supported by pads of fat and the buccinator muscles
- Lips- labia - the mucosa of each cheek is continuous with that of the lips

The Tongue

- Manipulates materials inside mouth
- May bring foods into oral cavity

4 Functions of the Tongue

1. Manipulation:
2. Mechanical processing:
   - compression, abrasion, and distortion
   - assists in chewing
   - prepares material for swallowing

4 Functions of the Tongue

3. Sensory analysis:
   - , temperature, and taste receptors
4. Secretion:
   - mucins
   - enzyme lingual lipase

- Lingual Papillae has fine projections on superior surface (dorsum) of tongue which are covered in thick epithelium

Muscles of the Tongue

- Extrinsic tongue muscles-Perform all gross movements of the tongue
- Are large muscles
- Intrinsic tongue muscles- Change shape of the tongue
- Assist extrinsic muscles during precise movements, as in speech

Sublingual Glands

- Small glands extend into underlying lamina propria
- Secretions flush tongue's epithelium
- Contain water, mucins, and enzyme lingual lipase - Enzyme, works over broad pH range (3.0–6.0)
- Starts lipid digestion immediately

Lecture 9The Urinary System

- Filter 200 liters of blood daily, allowing toxins, metabolic wastes, and excess ions to leave the body in urine
- Regulate volume and chemical makeup of the blood
- Maintain the proper balance between water and salts, and acids and bases

Other Renal Functions

- Gluconeogenesis during prolonged fasting
- Production of rennin to help regulate blood pressure and erythropoietin to stimulate RBC production
- Activation of vitamin D

Other Urinary System Organs

- Urinary bladder – provides a temporary storage reservoir for urine
- Paired ureters – transport urine from the kidneys to the bladder
- Urethra – transports urine from the bladder out of the body

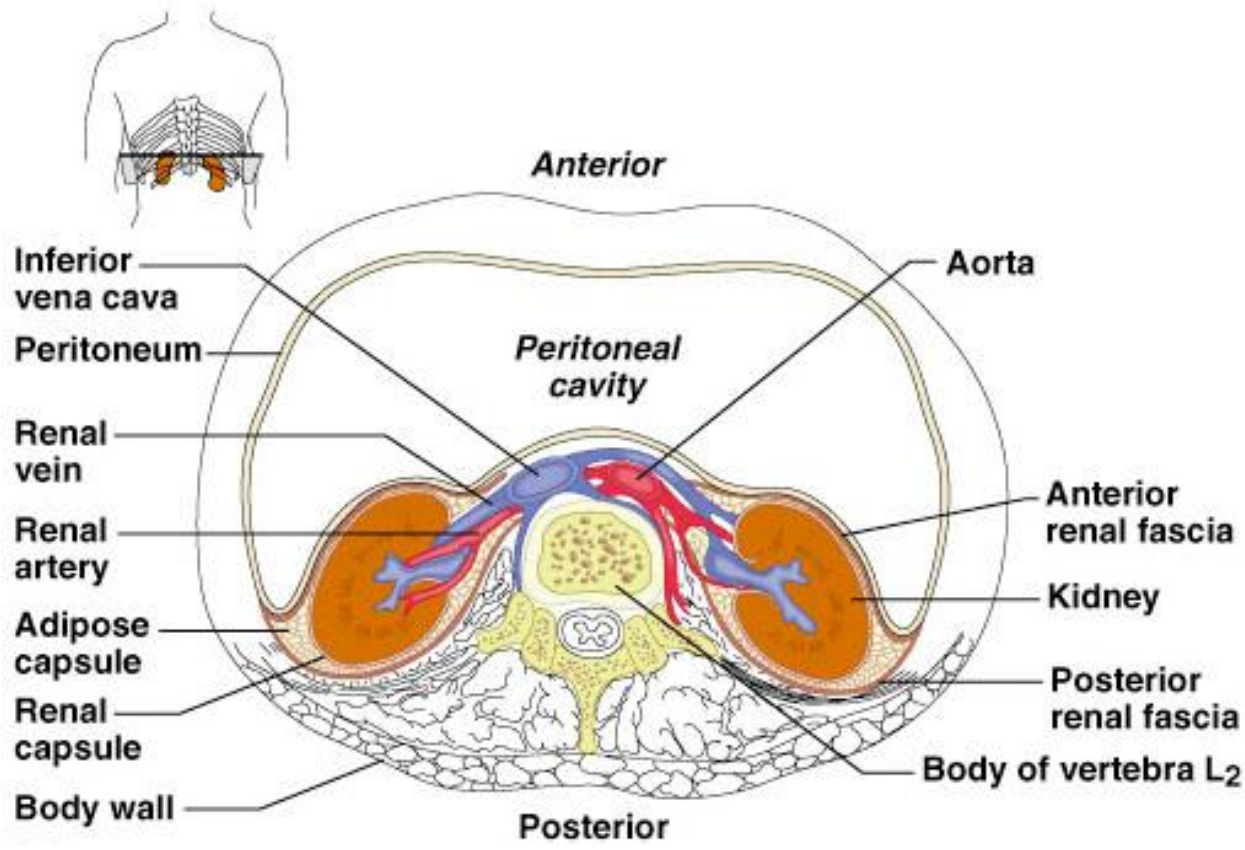
Kidney Location and External Anatomy

- The bean-shaped kidneys lie in a retroperitoneal position in the superior lumbar region and extend from the twelfth thoracic to the third lumbar vertebrae
- The right kidney is lower than the left because it is crowded by the liver
- Ureters, renal blood vessels, lymphatics, and nerves enter and exit at the hilus

Layers of Tissue Supporting the Kidney

- Renal capsule – fibrous capsule that prevents kidney infection
- Adipose capsule – fatty mass that cushions the kidney and helps attach it to the body wall
- Renal fascia – outer layer of dense fibrous connective tissue that anchors the kidney

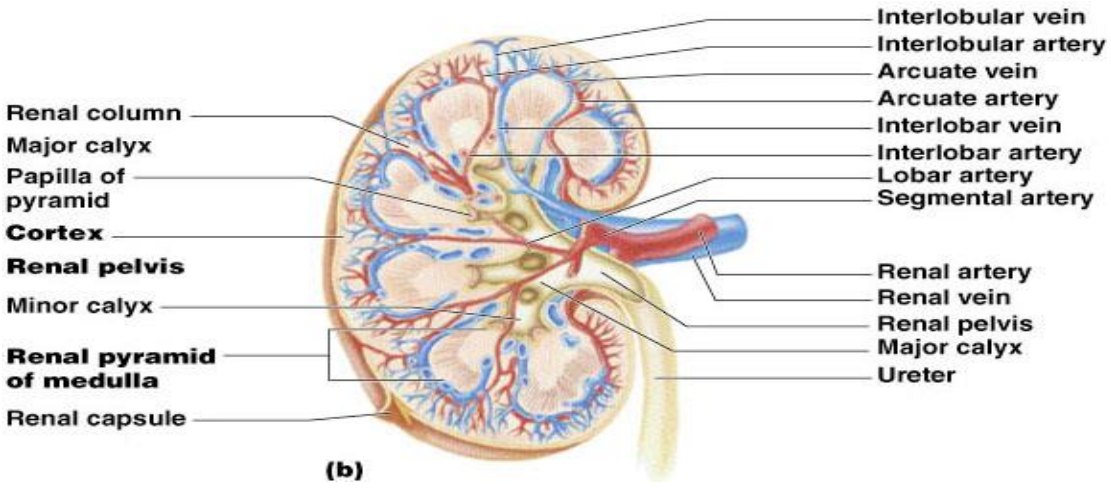
Kidney Location and External Anatomy



Internal Anatomy

- A frontal section shows three distinct regions
    - Cortex – the light colored, granular superficial region
    - Medulla – exhibits cone-shaped medullary (renal) pyramids
        - Pyramids are made up of parallel bundles of urine-collecting tubules
        - Renal columns are inward extensions of cortical tissue that separate the pyramids
        - The medullary pyramid and its surrounding capsule constitute a lobe
        - Renal pelvis – flat, funnel-shaped tube lateral to the hilus within the renal sinus
- Major calyces – large branches of the renal pelvis
    - Collect urine draining from papillae
    - Empty urine into the pelvis
- Urine flows through the pelvis and ureters to the bladder

Internal Anatomy



Blood and Nerve Supply

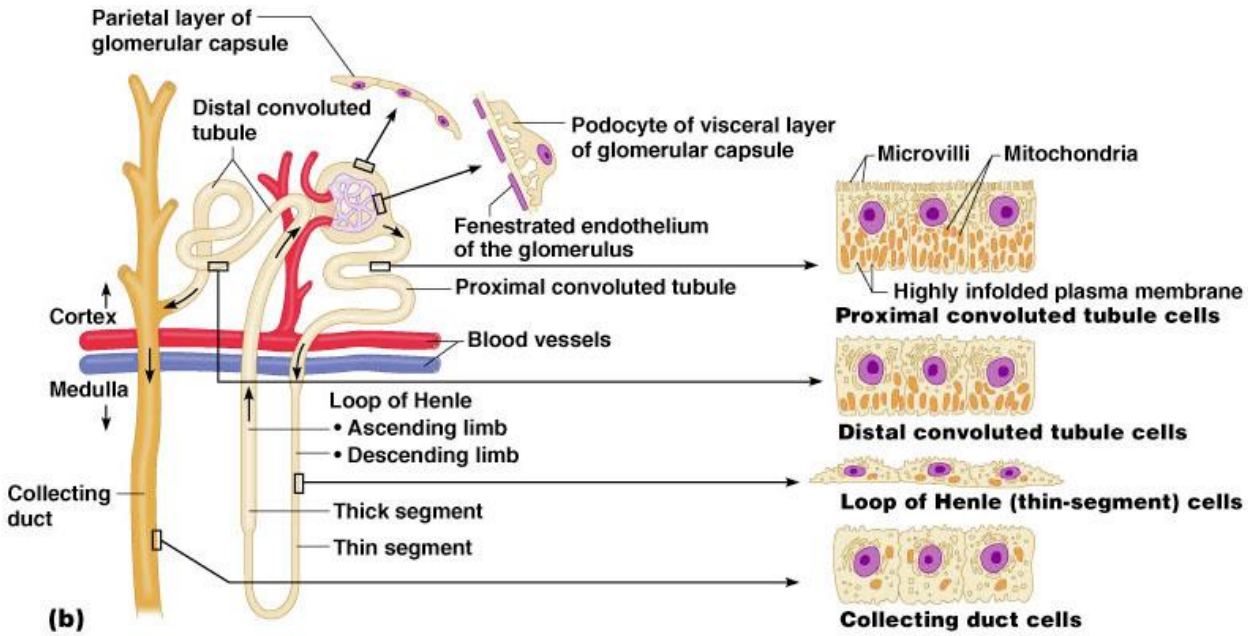
- Approximately one-fourth (1200 ml) of systemic cardiac output flows through the kidneys each minute
- Arterial flow into and venous flow out of the kidneys follow similar paths
- The nerve supply is via the renal plexus

The Nephron

- Nephrons are the structural and functional units that form urine, consisting of:
    - Glomerulus – a tuft of capillaries associated with a renal tubule
    - Glomerular (Bowman's) capsule – blind, cup-shaped end of a renal tubule that completely surrounds the glomerulus

- Renal corpuscle – the glomerulus and its Bowman's capsule
- Glomerular endothelium – fenestrated epithelium that allows solute-rich, virtually protein-free filtrate to pass from the blood into the glomerular capsule

The Nephron



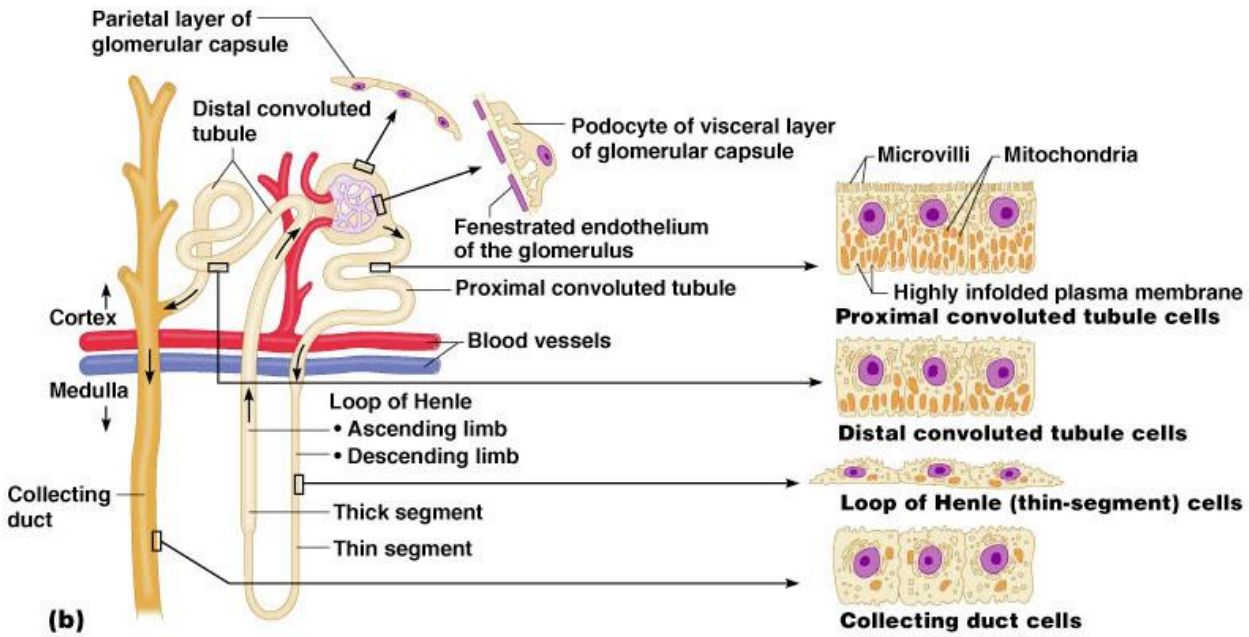
Anatomy of the Glomerular Capsule

- The external parietal layer is a structural layer
- The visceral layer consists of modified, branching epithelial podocytes
- Extensions of the octopus-like podocytes terminate in foot processes
- Filtration slits – openings between the foot processes that allow filtrate to pass into the capsular space

Renal Tubule

- Proximal convoluted tubule (PCT) – composed of cuboidal cells with numerous microvilli and mitochondria
- Reabsorbs water and solutes from filtrate and secretes substances into it
- Loop of Henle – a hairpin-shaped loop of the renal tubule
  - Proximal part is similar to the proximal convoluted tubule
  - Proximal part is followed by the thin segment (simple squamous cells) and the thick segment (cuboidal to columnar cells)
- Distal convoluted tubule (DCT) – cuboidal cells without microvilli that function more in secretion than reabsorption

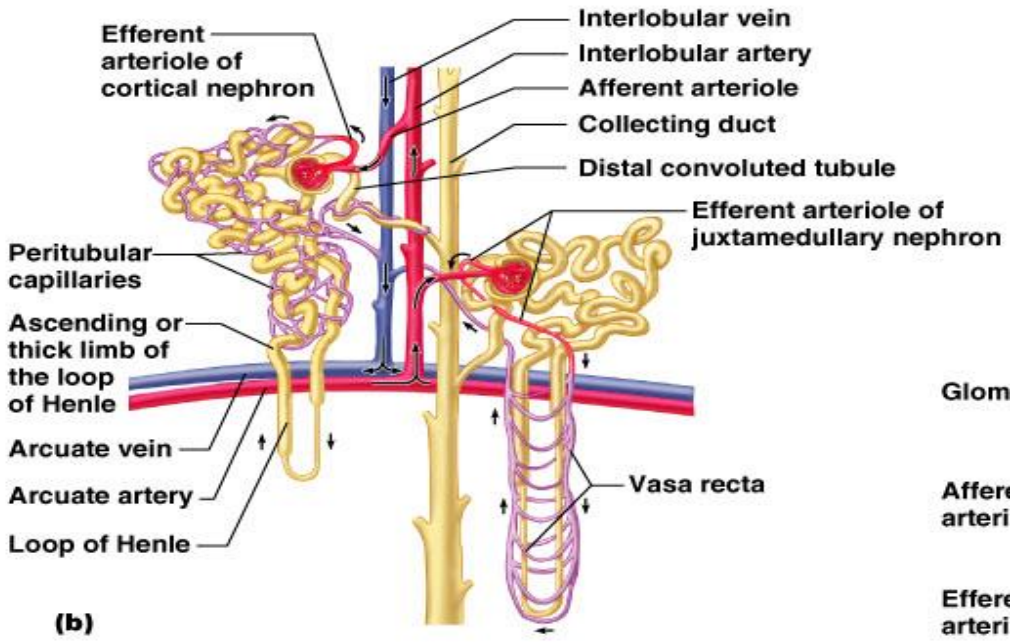
Renal Tubule



Nephrons

- Cortical nephrons – 85% of nephrons; located in the cortex
- Juxtamedullary nephrons:
  - Are located at the cortex-medulla junction
  - Have loops of Henle that deeply invade the medulla
  - Have extensive thin segments
  - Are involved in the production of concentrated urine

Nephrons

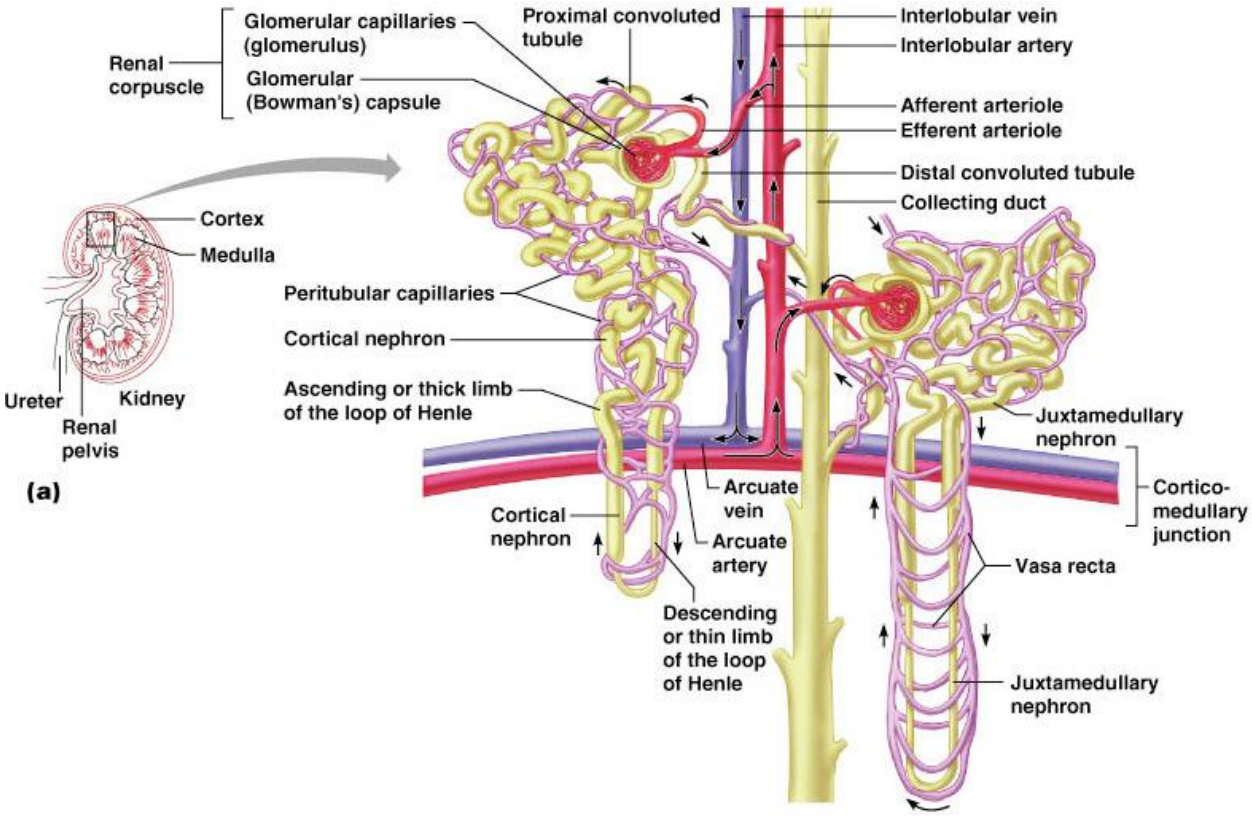


- **Blood pressure in the glomerulus is high because:**
  - Arterioles are high-resistance vessels

- Afferent arterioles have larger diameters than efferent arterioles

Fluids and solutes are forced out of the blood throughout the entire length of the glomeru

Capillary Beds



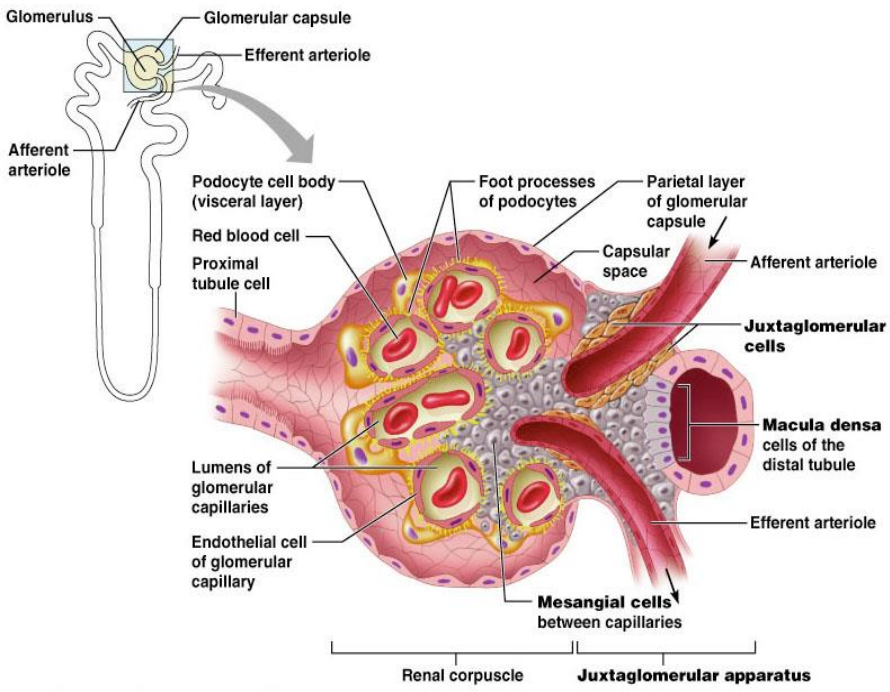
Vascular Resistance in Microcirculation

- Afferent and efferent arterioles offer high resistance to blood flow
- Blood pressure declines from 95mm Hg in renal arteries to 8 mm Hg in renal veins
- Resistance in afferent arterioles:
  - Protects glomeruli from fluctuations in systemic blood pressure
- Resistance in efferent arterioles:
  - Reinforces high glomerular pressure
  - Reduces hydrostatic pressure in peritubular capillaries

Juxtaglomerular Apparatus (JGA)

- Where the distal tubule lies against the afferent (sometimes efferent) arteriole
- Arteriole walls have juxtaglomerular (JG) cells
  - Enlarged, smooth muscle cells
  - Have secretory granules containing renin
  - Act as mechanoreceptors

Juxtaglomerular Apparatus (JGA)

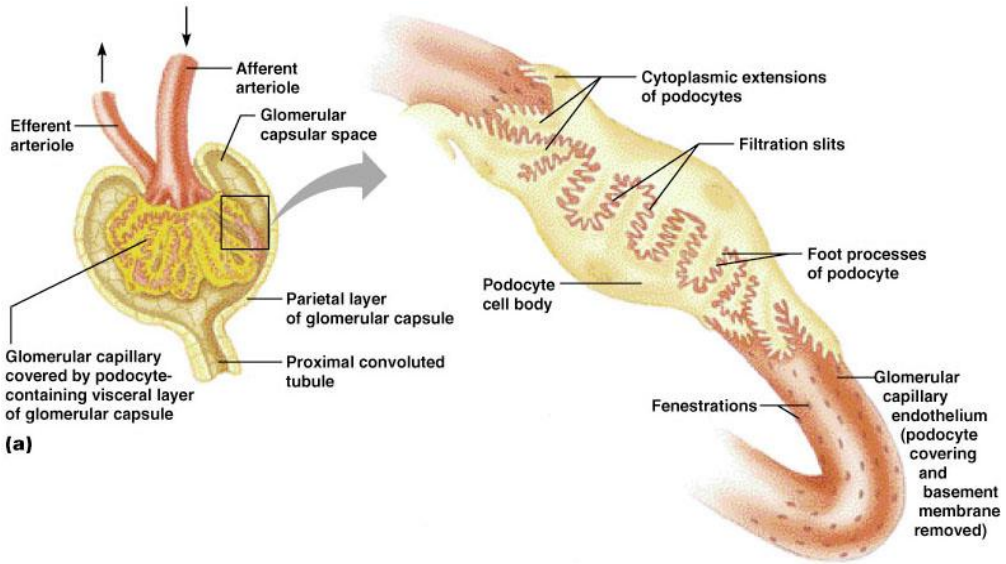


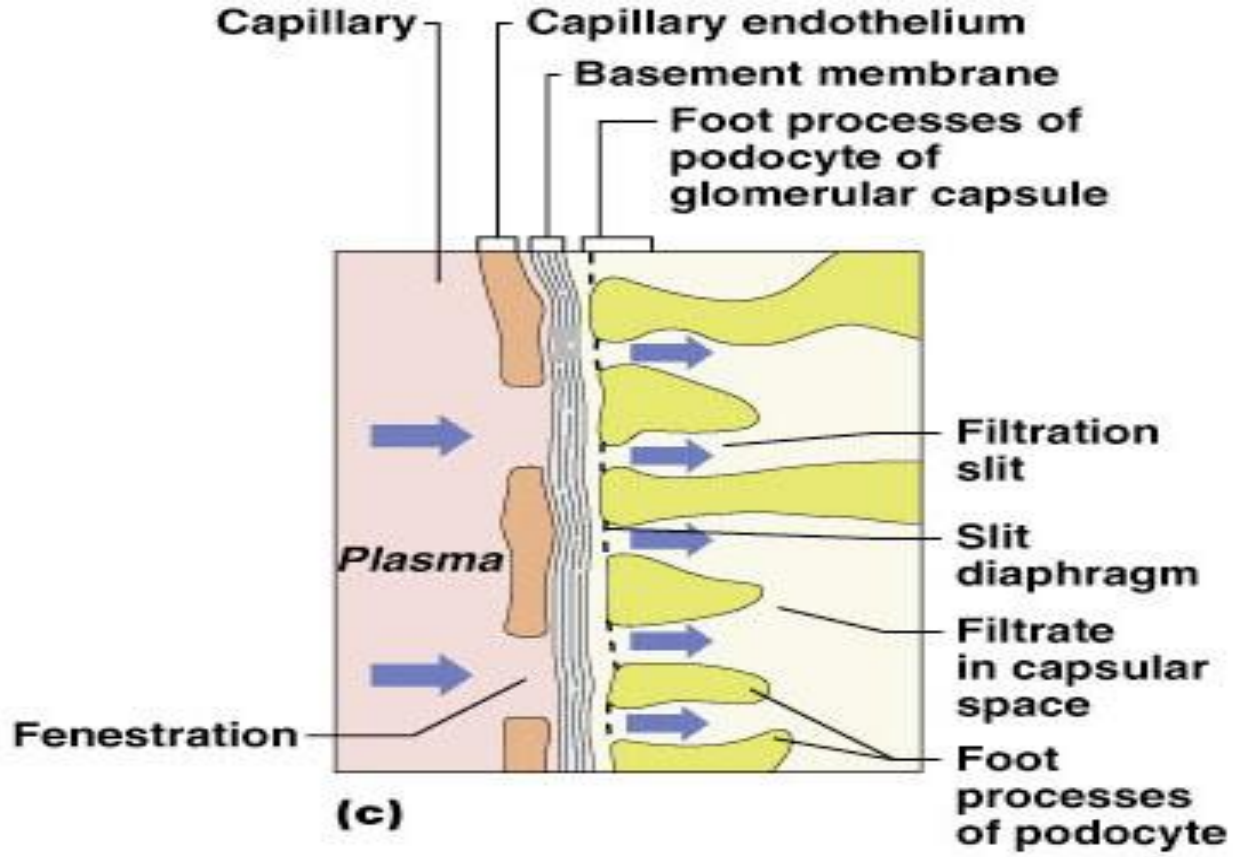
- Macula densa
  - Tall, closely packed distal tubule cells
  - Lie adjacent to JG cells
  - Function as chemoreceptors or osmoreceptors

Filtration Membrane

- Filter that lies between the blood and the interior of the glomerular capsule
- It is composed of three layers
    - Fenestrated endothelium of the glomerular capillaries
    - Visceral membrane of the glomerular capsule (podocytes)
    - Basement membrane composed of fused basal laminae of the other layers

Filtration Membrane





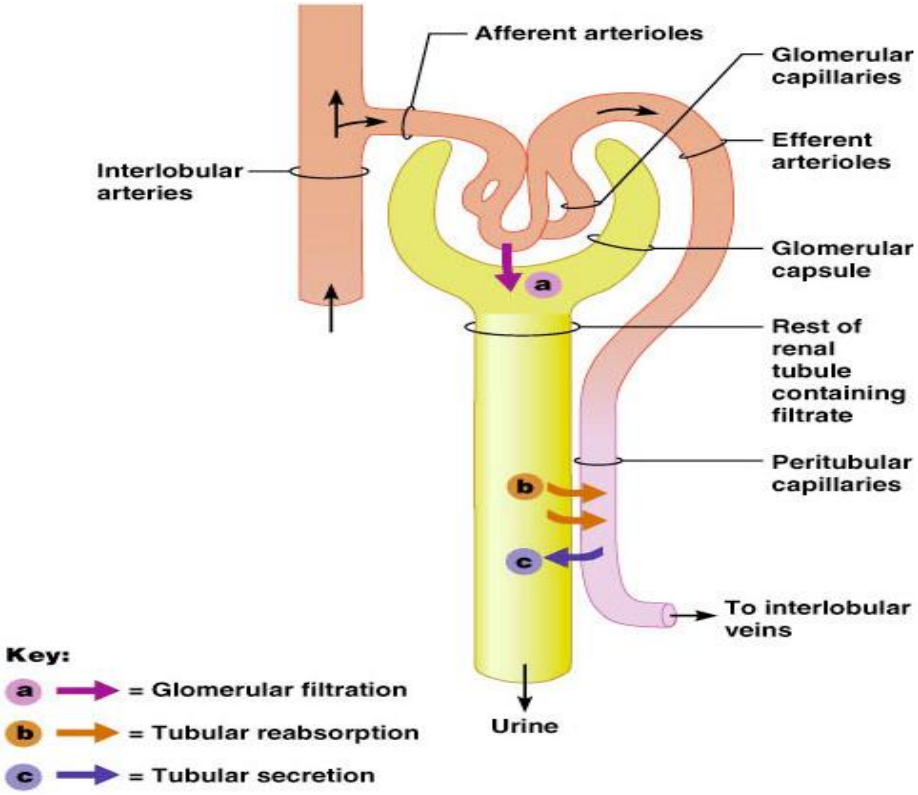
Mechanisms of Urine Formation

- The kidneys filter the body's entire plasma volume 60 times each day

- The filtrate:
    - Contains all plasma components except protein
    - Loses water, nutrients, and essential ions to become urine
- The urine contains metabolic wastes and unneeded substances

Mechanisms of Urine Formation

- Urine formation and adjustment of blood composition involves three major processes
    - Glomerular filtration
    - Tubular reabsorption



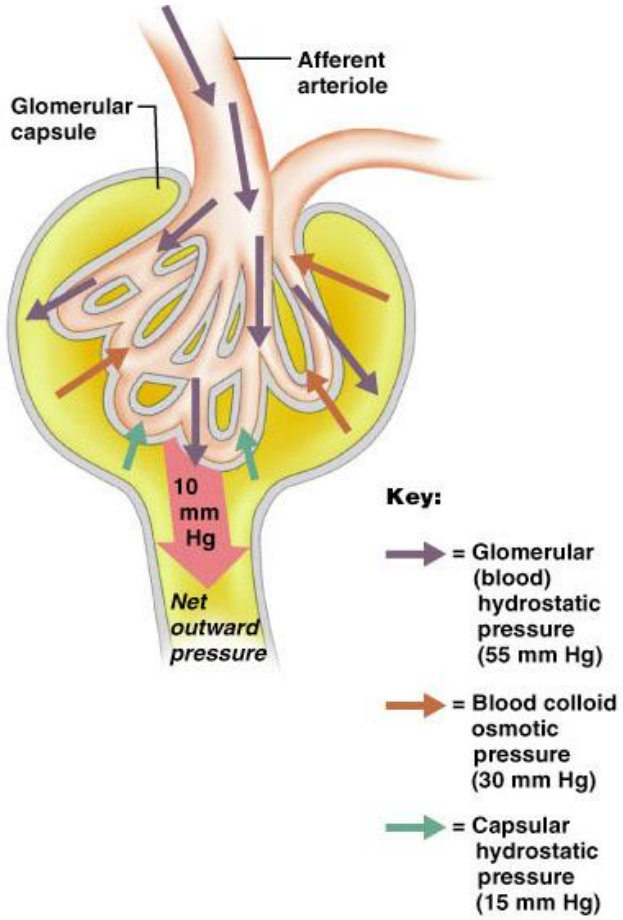
Glomerular Filtration

- Principles of fluid dynamics that account for tissue fluid in all capillary beds apply to the glomerulus as well
  - The glomerulus is more efficient than other capillary beds because:
    - Its filtration membrane is significantly more permeable
    - Glomerular blood pressure is higher
    - It has a higher net filtration pressure
  - Plasma proteins are not filtered and are used to maintain oncotic pressure of the blood

Glomerular Filtration Rate (GFR)

- The total amount of filtrate formed per minute by the kidneys
- Factors governing filtration rate at the capillary bed are:
    - Total surface area available for filtration
    - Filtration membrane permeability
    - Net filtration pressure

Glomerular Filtration Rate (GFR)



Regulation of Glomerular Filtration

- If the GFR is too high:
    - Needed substances cannot be reabsorbed quickly enough and are lost in the urine
- If the GFR is too low:
    - Three mechanisms control the GFR
        - Renal autoregulation (intrinsic system)
        - Neural controls
        - Hormonal mechanism (the renin-angiotensin system)

Intrinsic Controls

- Under normal conditions, renal autoregulation maintains a nearly constant glomerular filtration rate
- Autoregulation entails two types of control
    - Myogenic – responds to changes in pressure in the renal blood vessels
    - Flow-dependent tubuloglomerular feedback – senses changes in the juxtaglomerular apparatus

Extrinsic Controls

- Under stress:
  - Norepinephrine is released by the sympathetic nervous system
  - Epinephrine is released by the adrenal medulla
  - Afferent arterioles constrict and filtration is inhibited
- The sympathetic nervous system also stimulates the renin-angiotensin mechanism

Renin-Angiotensin Mechanism

- Is triggered when the JG cells release renin
- Renin acts on angiotensinogen to release angiotensin I
- Angiotensin I is converted to angiotensin II
- Angiotensin II:
  - Causes mean arterial pressure to rise
  - Stimulates the adrenal cortex to release aldosterone
- As a result, both systemic and glomerular hydrostatic pressure rise

Renin Release

- Renin release is triggered by:
  - Reduced stretch of the granular JG cells
  - Stimulation of the JG cells by activated macula densa cells
  - Direct stimulation of the JG cells via β_1-adrenergic receptors by renal nerves
  - Angiotensin II

Lecture 10 Endocrine System

- **Local pathways**
  - Paracrine and autocrine responses
  - In or in the vicinity of the cells or tissues
- **Long-Distance pathways**
  - Response loops
    - Stimulus
    - Sensor/receptor
    - Afferent pathway
    - Integrating center
    - Efferent pathway
    - Effector
    - Responses

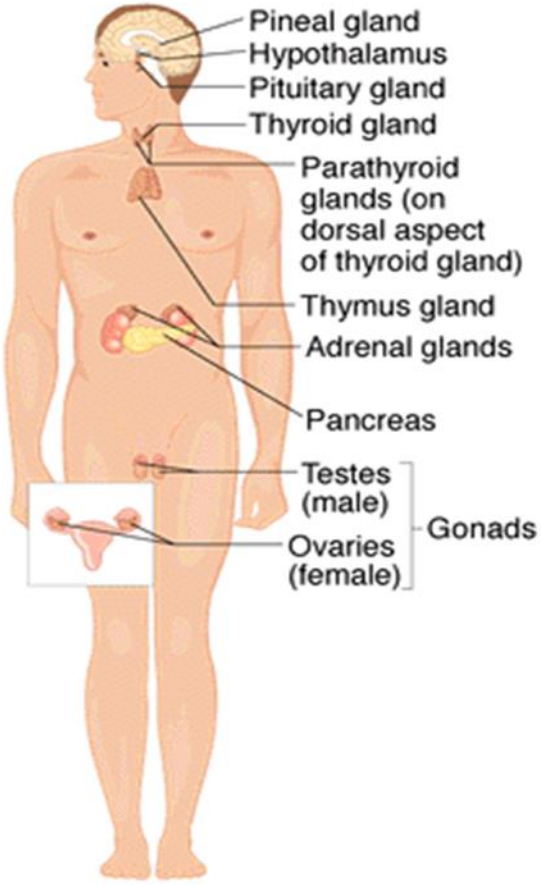
- **ControNegative feedback loops**
  - Stabilizing a function and maintain it withing a normal range
  - Response is in opposition to stimuli
  - Homeostatic control
- **Positive feedback loops**
  - Response reinforces the stimulus
  - Response destabilizes the variable
  - Requires an event outside the loop to stop them

- **Feedforward control**
  - Anticipates change
  - Starts the response loop before the change has occurred

- **Control systems vary in their speed & specificity**
  - Specificity
    - Nervous control very specific
    - Hormonal control more general
  - Nature of signal
    - Nervous system uses both electrical and chemical
    - Endocrine system uses only chemicals
  - Speed
    - Nervous system much faster, up to 120 m/sec
    - Endocrine system much slower
  - Duration of action
    - Nervous system shorter, very brief
    - Endocrine system lasts longer

  - **It brings about changes via chemical messengers, hormones, released into the blood stream and carried to target organs.**
  - **Endocrinology** - the study of hormones and the endocrine organs.
  - **Endocrine system** - all of the glands that secrete hormones
    - Endocrine and exocrine glands

- **Exocrine glands** - have ducts through which their nonhormonal products travel to the membrane surface and to the exterior (epithelial surface)
- **Endocrine glands** - release their substances into the surrounding fluid (*ductless glands).* They include the pituitary, thyroid, parathyroid, adrenal, pineal, and the thymus glands. Also included are the pancreas and gonads. The hypothalamus is called a *neuroendocrine organ*.



Endocrine System

Endocrine System, Hormones

- **Hormones** - chemical messengers carried by the blood from endocrine glands to the cell upon which they act.
  - Are chemical messengers
  - Secreted into the blood by endocrine cells or neurons
  - Affect distal targets
- Affect target cells by controlling
  - Rate of enzymatic reactions
  - Transport of molecules across cell membrane

- Gene expression and protein synthesis
- Stimulation of mitosis

- **Classification**
  - Peptide hormones - 3 or more amino acids
  - Steroid hormones - derived from cholesterol
  - Amine hormones - single amino acids

- **Classification, Peptide hormone - eg: Insulin**
  - Synthesis - RER, preprohormone
  - Packaged in vescicles
  - In Golgi apparatus, pre to pro hormone then to hormone and fragments
  - Released into ECF when cell is signaled to do so
  - Transported in blood, half-life - minutes
  - Mechanism of action - bind to cell surface receptors. Many use cAMP and some use tyrosine kinase

Action - open or close membrane channels or modulate metabolic enzymatic activity or transport proteins

- **Classification, Steroid hormones, eg: estradiol**
  - Synthesis - SER, lipophilic, sythesized as needed
  - Found bound (inactive) to protein carriers in blood
  - Half-life - hours
  - Mechanism - diffuses across cell membrane to cytoplasmic and nuclear receptors. Interact with DNA
  - Slow response by cells - hours

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Slow response by cells - hours

- **Classification, Amine hormones**
    - Nitrogen-containing
    - Most derived from tryptophan or tyrosine
    - They behave like peptide hormones (catecholamines) or like steroid hormones (thyroid hormones)
    - Thyroid hormones: produced by thyroid gland found in the lower part of the neck. It secretes 3 hormones:
        - Thyroxine - T_4
        - Triiodothyromine - T_3
        - Calcitonin
    - The first two are collectively known as thyroid hormones (TH) and contain iodine
    - Virtually every tissue in the body is affected by TH

- **Amine hormone, Adrenal medullary hormones**
  - The adrenal gland consists of a medullary and cortical section. The cortex secretes steroid hormones.
  - The adrenal medulla secretes two hormones
    - Epinephrine (E) and
    - Norepinephrine (NE)
  - These are also called catecholamines
- **It takes much longer for sex hormones and other steriods to produce their effects than it takes nonsteroid hormones. Why**?
  - A. Steroids are bigger, slower molecules
  - B. Steroids usually must be carried longer distances in the blood
  - C. Steroids cause target cells to make new proteins, which takes time
  - D. Steroids must relay their message via a second messenger
  - E. It takes longer for endocrine cells to make and secrete steroids
- **List the hormones produced by the adrenal gland.**
- **Steroid hormones**
  - Produced by the adrenal cortex, the gonads, and the placenta
  - Precursor is cholesterol

Synthesis of steroid hormones

- Hormonal Specificity
  - All major hormones circulate to virtually all tissues (target cells), but for these cells to respond to a hormone, they must have a specific protein receptor on their plasma membrane or in their interior.
- Hormone-target interaction depends on:

- Blood levels of the hormone
- The relative number of receptors for that hormone
- The *affinity* of the bond between the hormone and the receptor

- Up-regulation and down-regulation
- Onset, Duration, and Half-life
  - Onset varies greatly, from almost immediately to hours or days
  - Duration can range from several minutes to several hours
  - Half-life is the length of time the hormone concentration takes to drop by half
    - From a fraction of a minute to several hours

Concentration determined by its rate of release and the speed of deactivation and removal

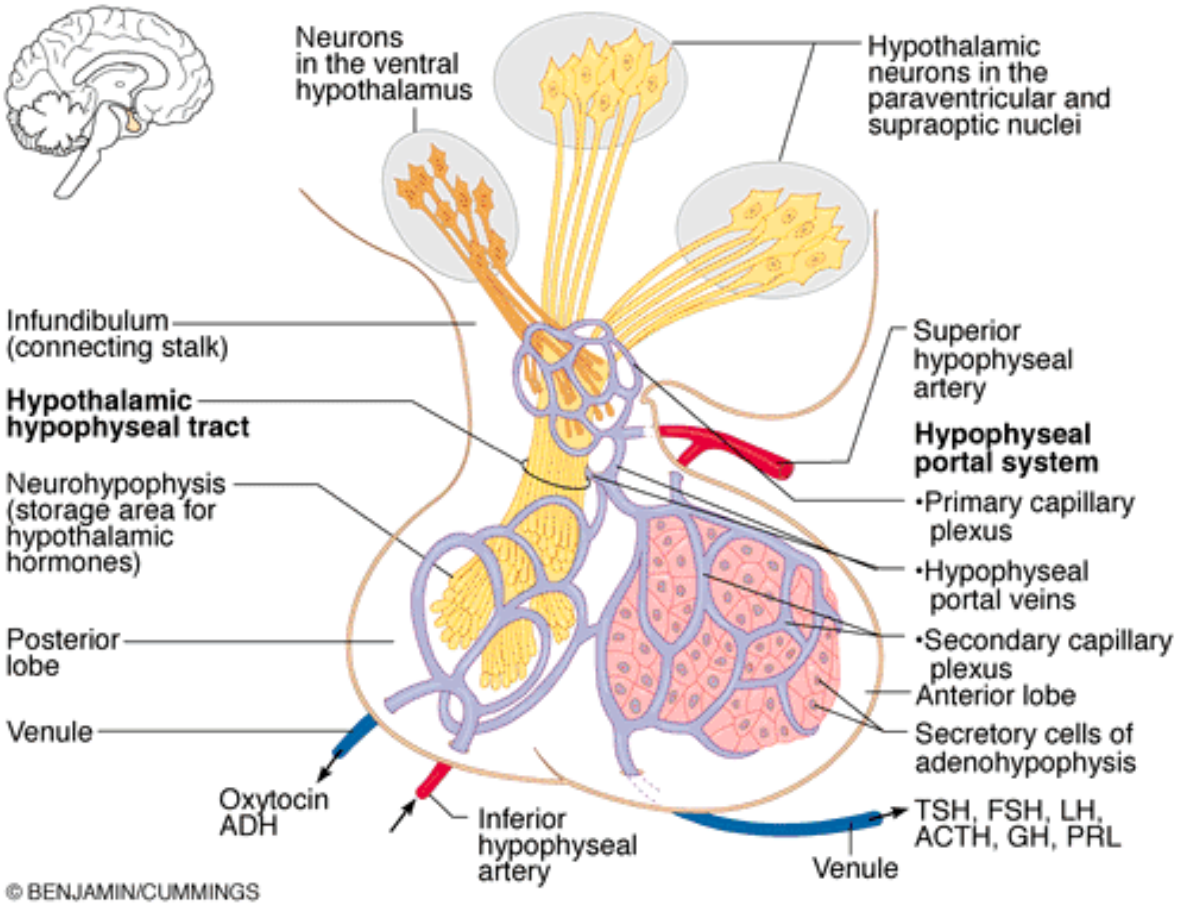
Endocrine System, Control of Hormone Release

- Endocrine glands are stimulated by humoral, neural and hormonal means.
  - Humoral stimuli - changing levels of blood ions and nutrients. Example:-↓calcium →↑parathyroid hormone
  - Neural stimuli - nerve fiber stimulates hormonal release. Example:-↑nervous input to adrenal medulla → release of catecholamines
  - Hormonal stimuli (tropic hormones) - endocrine glands release their hormones in response to hormones produced by other endocrine organs. Example:-hypothalamic hormones → anterior pituitary to release hormones → other endocrine glands to produce even more hormones

- **Hypothalamic-pituitary system**
- Pituitary gland - lies just below hypothalamus, in pocket of bone at base of brain. Consists of two adjacent lobes - the anterior pituitary and the posterior piruitary
  - Posterior pituitary hormones
    - Oxytocin and vasopressin are released
    - Made in hypothalamus, move down the neural axons and accumulate in the axon terminals in the posterior pituitary
    - Vasopressin - blood pressure and kidney function
    - Oxytocin - breasts and uterine contractions

Endocrine System, Neurohormones

- Hypothalamus and Anterior Pituitary
  - The hypothalamus also secretes hormones that control the secretion of ALL the anterior pituitary hormones. The basic pattern is as follows:
    - Secretion of a hypothalamic hormone, which controls secretion of
    - An anterior pitiutary hormone, which controls the secretion of
    - A hormone from some other endocrine organ/gland
  - Anterior Pituitary Hormones
    - At least eight secreted, six with well-established functions


Neurons in the ventral hypothalamus
Hypothalamic neurons in the paraventricular and supraoptic nuclei
Infundibulum (connecting stalk)
Hypothalamic hypophyseal tract
Neurohypophysis (storage area for hypothalamic hormones)
Posterior lobe
Venule
Oxytocin ADH
Inferior hypophyseal artery
Superior hypophyseal artery
Hypophyseal portal system
•Primary capillary plexus
•Hypophyseal portal veins
•Secondary capillary plexus
Anterior lobe
Secretory cells of adenohypophysis
TSH, FSH, LH, ACTH, GH, PRL
Venule
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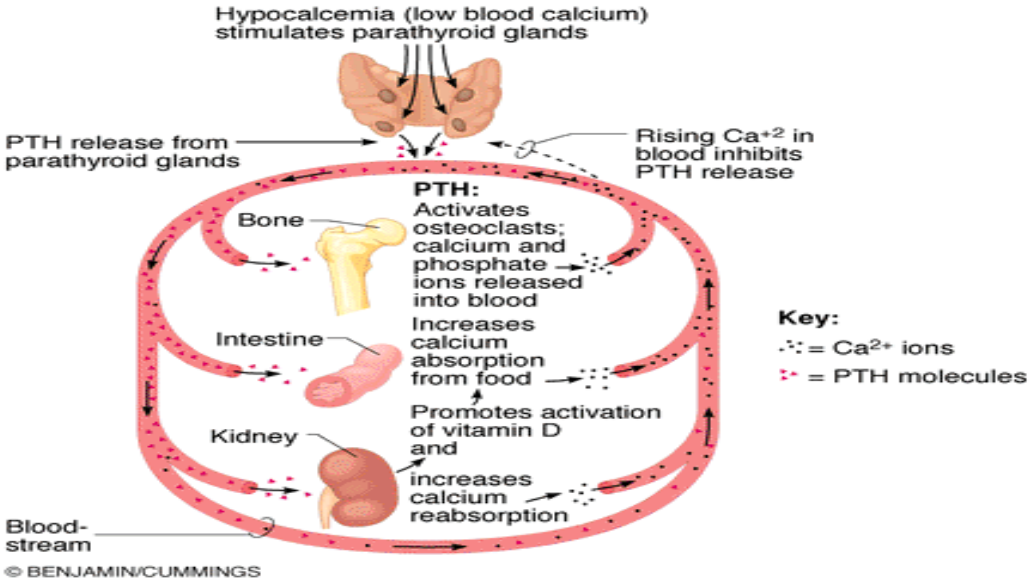
- **Hypothalamic Releasing Hormones**
  - Corticotropin Releasing Hormone (CRH)
  - Thyrotropin Releasing Hormone (TRH)
  - Growth Hormone Releasing Hormone (GHRH)
  - Somatostatin (SS) also called Growth hormone releasing Inhibitin Hormone (GIH)
  - Gonadotropin Releasing Hormone (GnRH)
  - Prolactin Releasing Hormone (PRH)
  - Prolactin releasing Inhibiting Hormone (PIH)

- **Anterior Pituitary Hormones**
  - Gonadotropic Hormones
    - Follicle-Stimulating Hormone (FSH)
    - Luteinizing Hormone (LH)
  - Growth Hormone (GH)
  - Thyroid-stimulating Hormone (TSH)
  - Prolactin
  - AdrenoCorticoTropic Hormone (ACTH)
  - β-Lipotropic Hormone

    β-Endorphi


Hypocalcemia (low blood calcium) stimulates parathyroid glands
PTH release from parathyroid glands
Rising Ca+2 in blood inhibits PTH release
PTH:
Activates osteoclasts; calcium and phosphate ions released into blood
Bone
Intestine
Increases calcium absorption from food
Promotes activation of vitamin D and increases calcium reabsorption
Kidney
Blood-stream
Key:
= Ca2+ ions
= PTH molecules
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