Physiology of urinary system

Organ system that produced , stores and carries urine. Include **two kidneys, two ureters, the urinary bladder , two sphincter muscles and the urethra.** Human produced about 1.5 liters of urine over 24 hours, although this amount may vary according to the circumstance .

Structure of Urinary System

The kidneys (paired organ weight about 300g) are on either side of vertebral column below diaphragm **(About size of fist)**. each kidney consist of cortex and medulla, and consist of **8-10 conical pyramids with base in the cortex and apices project toward the pelvis. Each pyramid has outer cortex and inner medulla**. Medulla in turn subdivided into **outer and inner zones.**

The outer zone splits into outer and inner stripes. Each pyramid pours its urine into **a minor calyx**, and then **every 2-3 calyces unit to form a major calyx**. Major calyces unites to form the renal pelvis that leads urine through the ureter. Renal pelvis emerges through the hilum of kidney from which renal artery , enters and renal vein leaves. Two ureters pour into single urinary bladder from which urethra emerges.

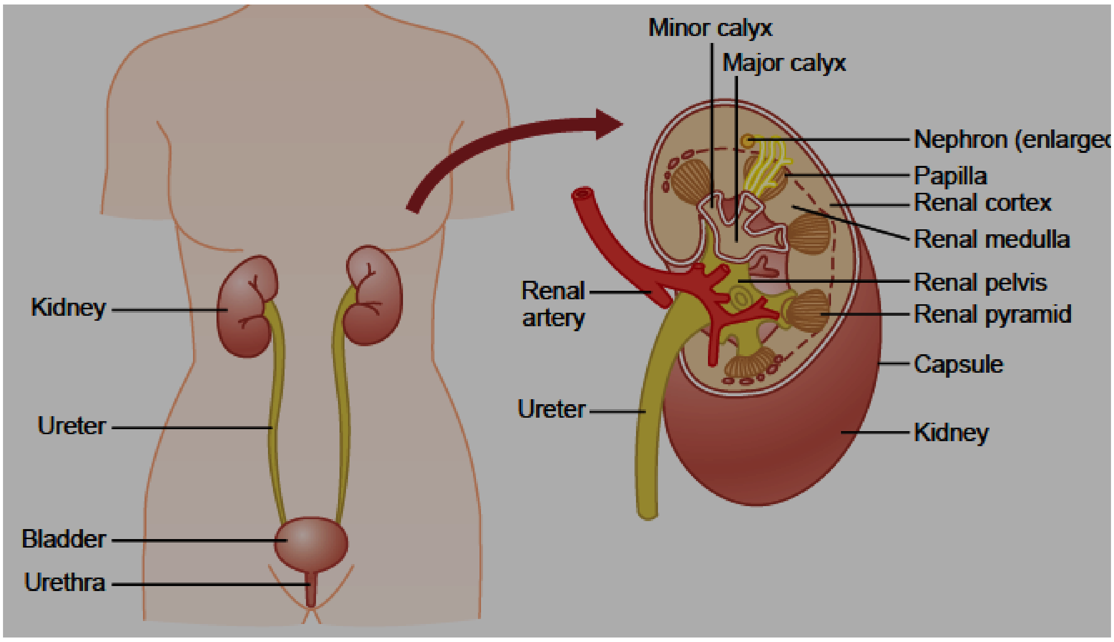


Figure (1). General organization of the kidneys and the urinary system.

Renal blood supply

Blood enters kidney through renal artery and renal artery divides into **interlobar arteries** that divide into **arcuate arteries** that give rise to **interlobular arteries** .Interlobular arteries give rise to **afferent arterioles** which supply glomeruli. Glomeruli are mass of capillaries inside glomerular capsule that gives rise to filtrate that enters nephron tubule.

Efferent arteriole drains glomerulus and delivers that blood to peritubular capillaries (a.k.a. the vasa recta) which is the only example in the body, where a capillary bed is drained by an arteriole, as opposed to a venule.

Blood from peritubular capillaries enters interlobular veins.

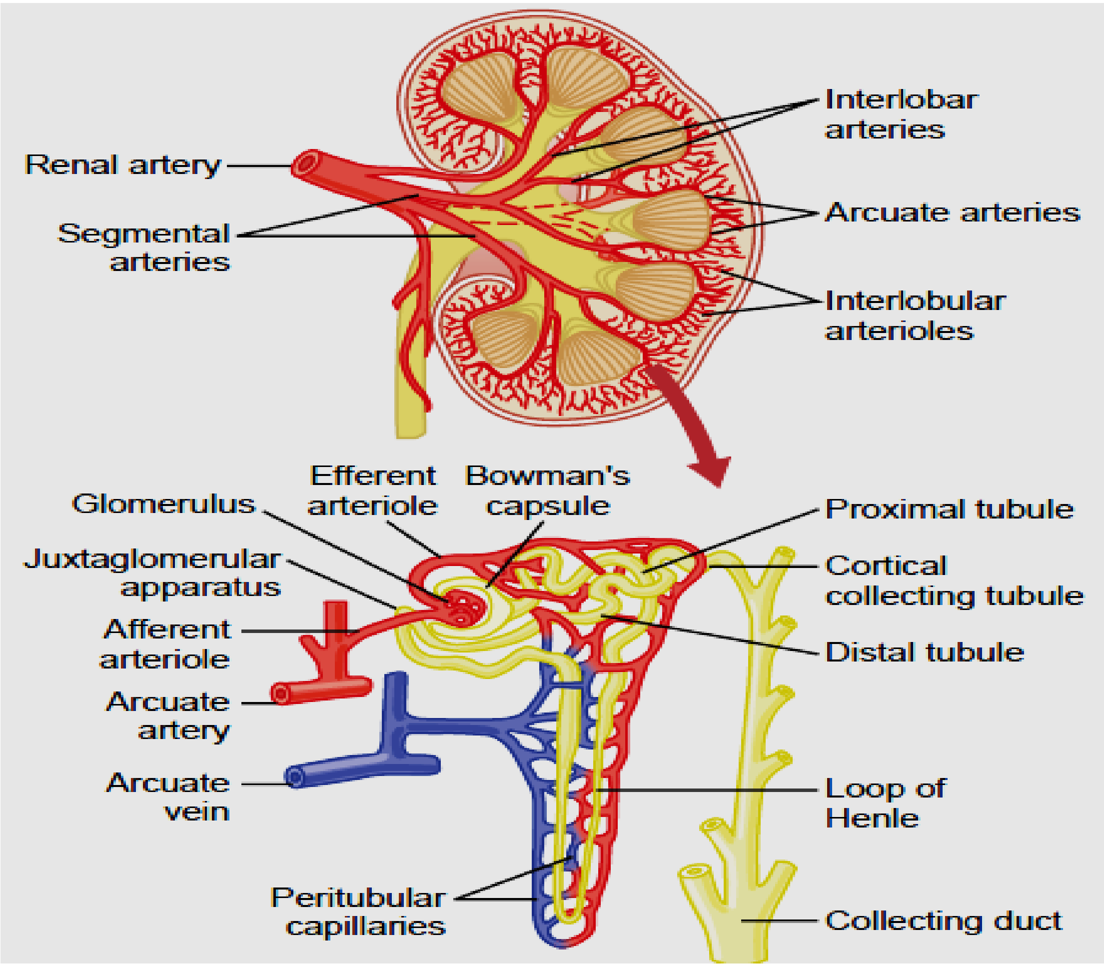


Figure (2). Section of the human kidney showing the major vessels that supply the blood flow to the kidney and schematic of the microcirculation of each nephron.

Characteristics of the renal blood flow

1. Large blood flow :200 ml /min (20 % of cardiac output) and 94 % to the cortex.
2. 1 ry and 2 ry capillary networks:
- primary network : glomerular capillary network , between afferent and efferent arterioles , high hydrostatic pressure(60 mm/hg), favor glomerular filtration .
- secondary network : peritubular capillary network , made by branch of efferent arterioles , low pressure(13 mm/hg), favor tubular reabsorption.
3. Autoregulation of renal blood flow.
4. Tubuloglomerular feedback.
5. Nervous and hormonal regulation.

N.B.

- There are 2 sets of capillaries and 2 sets of arterioles.

- the only circulation where there are capillaries, which are drained by arterioles.

Glomerular capillary bed	Peritubular capillary bed
1. Received blood from afferent arterioles.	Received blood from efferent arterioles.
2. High pressure bed 45-55 mm/hg.	low pressure bed 10-13 mm/hg.
3. Represent arterial end of capillary.	Represent venous end of capillary.
4. Allow fluid filtration.	Allow fluid reabsorption.

Autoregulation of RBF determines GFR:

1. RBF is about 20 % of the cardiac output : very large flow relative to the Wight of the kidneys (~ 350 g).
2. RBF also modifies solute and water reabsorption and delivers nutrients to nephron cells.

3. RBF kept constant in blood pressure of 80-180 mm/Hg by varying renal vascular resistance. (the resistance of the interlobular artery , afferent arteriole and efferent arteriole.
4. RBF autorgulation is vital to prevent large changes in gfr that would greatly affect urinary output and to allow normal renal excretion of water and solute.
5. RBF autorgulation occurs in denervated and isolated kidney (intrinsic property).

Nephron: Is define as the structural and functional unit of kidney responsible for forming urine (more than 1 million nephrons/ kidney).the kidney cannot regenerate new nephrons. The number of nephrons starts decreasing after about 45 to 50 years of age at the rate of 0.8% to 1% every year.

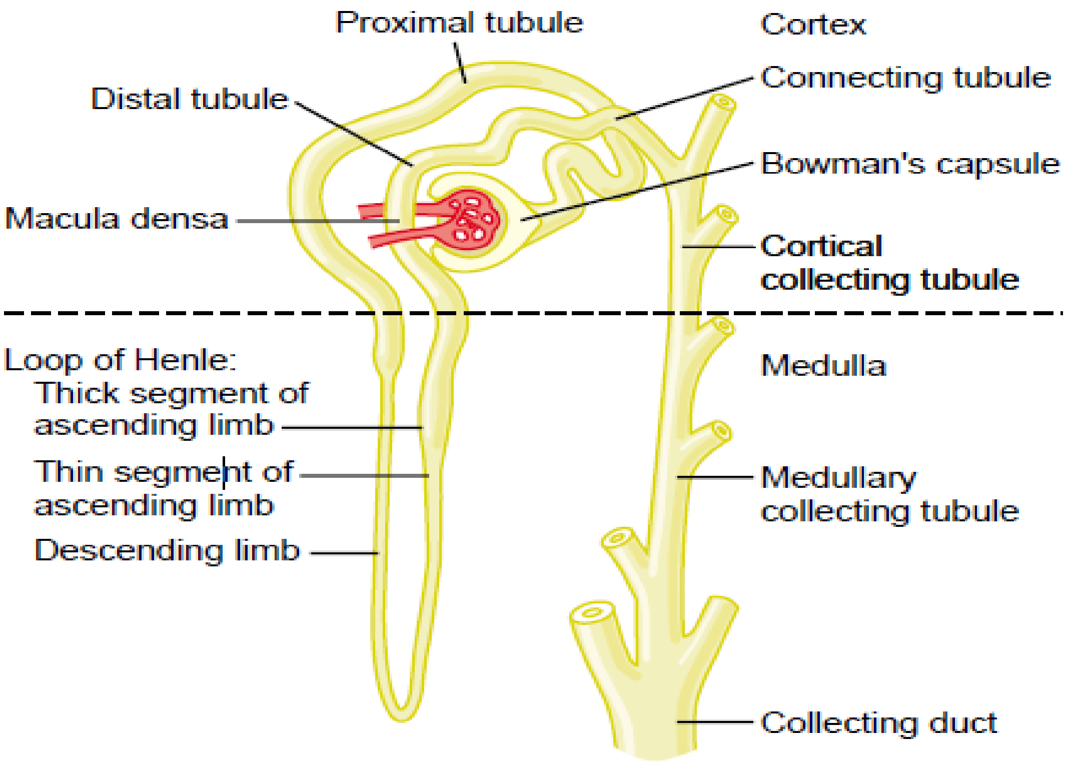


Figure (3). Basic tubular segments of the nephron. The relative lengths of the different tubular segments are not drawn to scale.

General Nephron Function

1. Glomerular filtration

2. Tubular reabsorption

3. Tubular secretion

Nephrons are composed of major parts:

1. **A glomerulus**
2. **A long tube (renal tube)**

Glomerulus , which is a globular tuft of capillaries supplied by afferent arteriole and drained by efferent arteriole and enclosed inside tightly sealed bowman's capsule. Blood that is filtered inside the glomerulus is transferred from bowman's capsule to the renal tubules.

Nephron Tubules: Tubular part of nephron begins with glomerular capsule which transitions into **proximal convoluted tubule (PCT)** or **called pars convolute** , which then straightens to be called **proximal** straight tubule (PST) or **called pars recta.**

At the junction between outer and inner stripes of outer medullary zone, starts the **thin descending limb of Henles Loop (tDHL)**, **tDHL** turns back to become thin **ascending limbs of Henles Loop (tAHL),** which thickens at the junction between the inner and **outer medullary zones to be referred to as ascending limbs** of **Henles Loop (tAHL) which enter the cortex again as distal tubule(DT)** .

The **distal tubule** passes between the afferent and efferent arteriole of the same nephron making with the afferent arteriole a special contact called juxtaglomerular apparatus (JGA), and then continues as **distal convolute tubule(DCT).**

Distal convolute tubule unite as collecting tubules , which pour in large collecting tubes, and then cortical and medullary collecting ducts to end in main duct of renal pyramid supplying minor calyx.

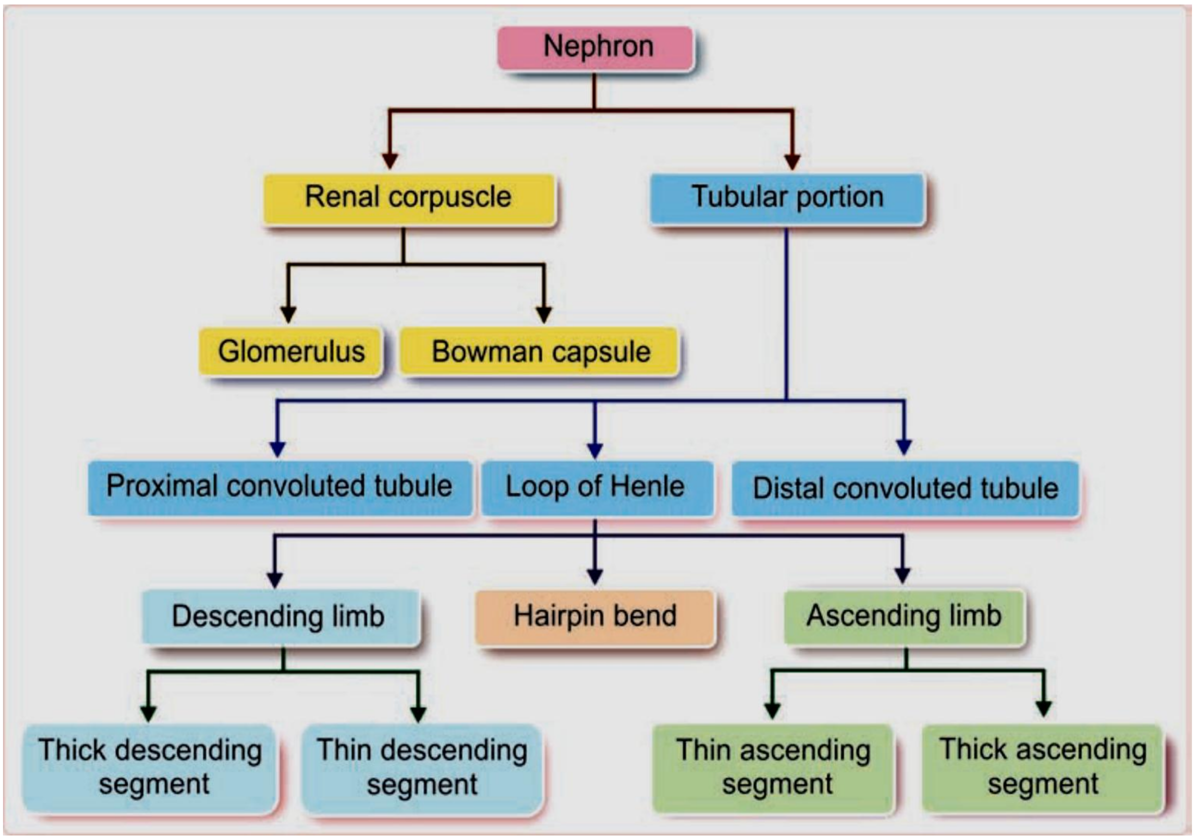


Figure (4). Parts of nephron

Type of Nephrons

There are two types of Nephrons:-

1- Cortical nephrons: originate in outer 2/3 of cortex, more numerous (70 – 80% lying in the outer layer of cortex. the tubular system is relatively short, no tAHL and efferent narrower than afferent arterioles. Has per tubular capillaries , but no vasa recta.na reabsorption occurs mainly here, and JG apparatus is well developed hence, share in the process of an autoregulation.

2- Juxtamedullary nephrons: originate in inner 1/3 cortex , less numerous (20 -30 % , lying in the inner third off cortex, long tubules with long tAHL dip deeply down into the medulla toward the pyramids and efferent wider than afferent arteriole (because efferent arteriole here supplies a much extensive peritubular capillary network) so vasa recta is active . It is important in producing concentrated urine.

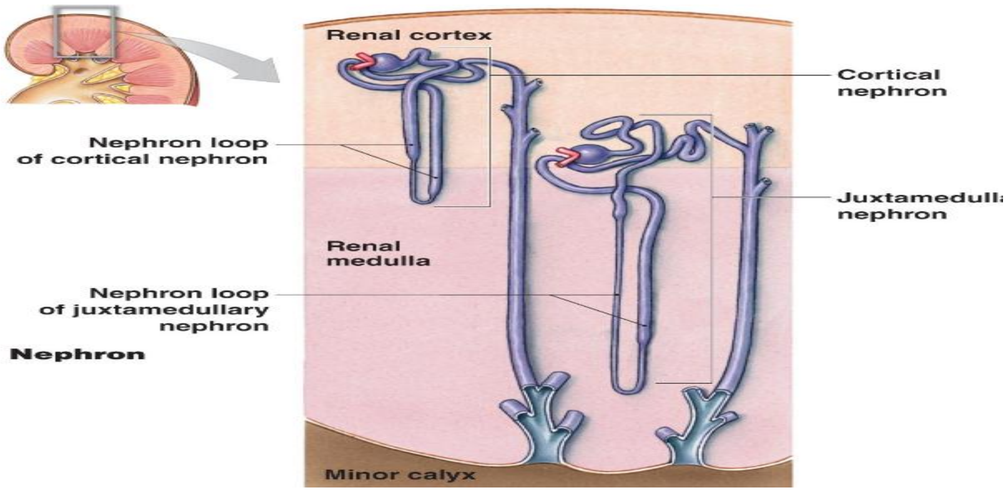


Figure (5). Types of nephron

<u>Intrinsic Controls: Regulation of Glomerular Filtration</u>

1. renal autoregulation - rate of FILTRATE production must be coordinated with reabsorption rate.

2. myogenic mechanism - circular muscle around the glomerular arterioles reacts to pressure changes.

a. increased blood pressure -> vasoconstriction.

b. decreased blood pressure -> vasodilation.

3. tubuloglomerular feedback mechanism - macula densa cells (of juxtaglomerular apparatus) sense the solute concentration of the FILTRATE.

a. low concentration > vasodilation.

b. high concentration -> vasoconstriction.

4. renin-angiotensin mechanism.

renin (released by juxtoglomerular cells) -> angiotensinogen -> angiotensin I -> angiotensin II -> global vasoconstrictor (rise in blood pressure) release of aldosterone (resorption of more Na+).

Factors causing release of Renin:

a. reduced stretch of juxtaglomerular cells.

b. stimulation by macula densa cells (as above).

c. stimulation of juxtaglomerular cells by sympathetics.

Extrinsic Controls: Sympathetic Innervation

1 sympathetics - cause increased release of renin.

2 epinephrine - causes increased vasoconstriction.

Tubular Reabsorption: Reabsorbing the Glomerular Filtrate

A. Overview of Reabsorption

1. filtrate :all fluid and its solutes pushed into the capsule.

2. urine : filtrate minus reabsorbed substances + secreted substances.

3. route of reabsorption (transepithelial process).

luminal surface of tubule cells >>

basolateral membrane of tubule cells >>

interstitial fluid between tubule cells and capillaries >>

endothelium of the peritubular capillary.

4. most sugars and amino acids are reabsorbed.

5. water and ion reabsorption depends on hormonal control.

B. Active Tubular Reabsorption

1. glucose, amino acids, lactate, vitamins, ions.

a. move across luminal surface by diffusion.

b. actively transported across basolateral membrane.

i. cotransported with Na^+.

c. diffuse into capillary by diffusion.

2. transport maximum (Tm) when "carrier proteins" for specific solute becomes saturated and cannot carry the substance across the membrane.

a. diabetes mellitus - lower Tm (glucose lost).

C. Passive Tubular Reabsorption

1. Na+ driven into interstitial space actively (above).

2. HCO_3^- and Cl^- follow Na+ into the space.

3. obligatory water reabsorption - water follows ions into the interstitial space between tubule & capillary.

4. solvent drags - solutes will begin to move into tubule from filtrate, following water (especially some urea and lipid-soluble molecules).

D. Non reabsorbed Substances

1. urea, creatinine, uric acid - most is not reabsorbed because of the following reasons

a. no carrier molecules for active transport.

b. not lipid-soluble.

c. too large (as with most proteins).

E. Absorption in Different Regions of Renal Tubule

1. proximal tubule - closest to the glomerular capsule.

a. almost all glucose & amino acids.

b. 75-80% of water and Na+.

c. most active transport of ions.

2. Loop of Henle - connects proximal & distal tubules.

Regulates Total water retained or lost:

a. descending limb - water can return to blood vessels.

b. ascending limb – water impermeable but releases ions to the interstitial space increasing osmotic pressure so that water can be reabsorbed from other parts of the renal tubule.

3. distal tubule & collecting duct - final passageway.

a. antidiuretic hormone (ADH) - causes increased permeability to Na+ and water, allow resorption.

b. aldosterone - stimulated by renin-angiotensin, enhances Na+ resorption (water follows). Triggered by :

i. lower blood pressure.

ii. low Na+ concentration (hyponatremia).

c. atrial natriuretic factor (ANF) - reduces Na+ permeability, less water (in response to high B.P.)

Tubular Secretion

A. Movement from Capillaries to Tubular Cells

1. K+, creatinine, ammonia, organic acids, drugs

2. Primary functions of tubular secretion:

a. moving drugs into the urine.

b. moving more urea & uric acid into urine.

c. removing excess K+ from blood.

d. regulating pH (H+ ion removal).

Q \ why is the henles loop useful?

The longer of the loop, the more concentration the filtrate in the medulla become.

*** importance** : the collecting tubule runs through the hyperosotic medulla more ability to reabsorb H_2O.

Renal pelvis

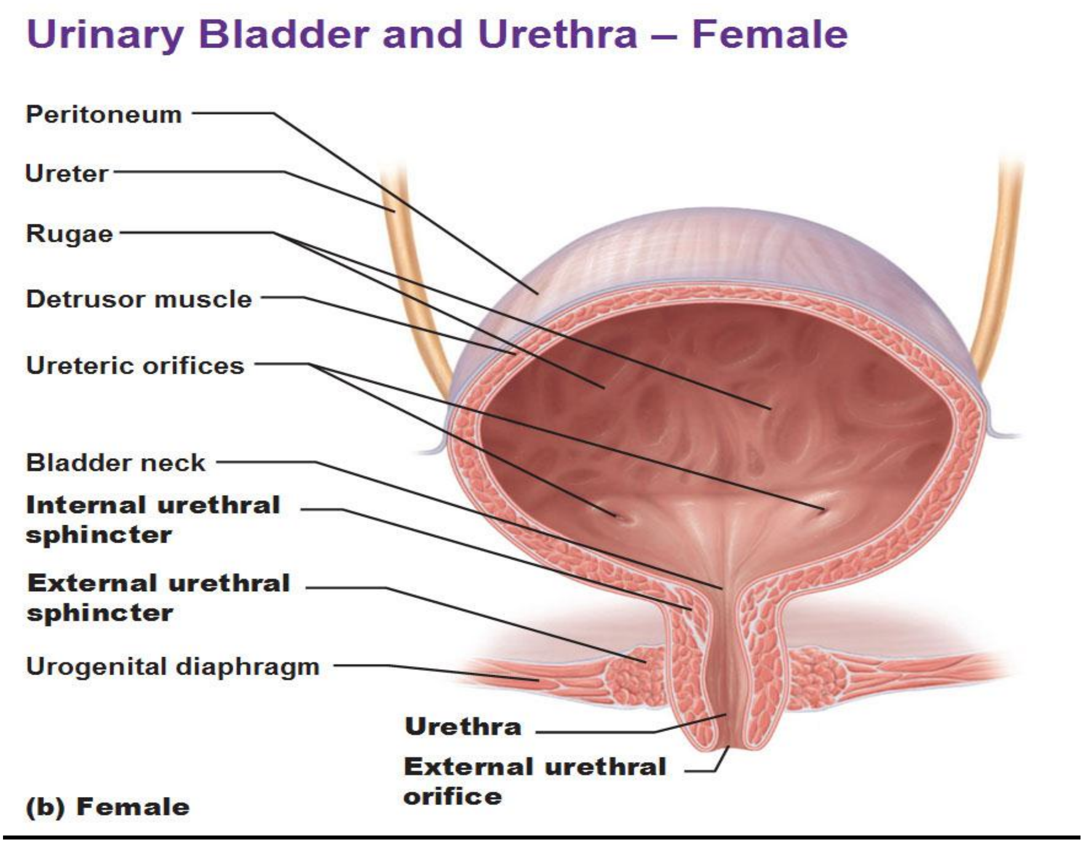
The major function of the renal pelvis is to act a funnel for urine flowing to the ureter. It is the point of convergence of two or three major calices. A branch of the renal pelvis called calyx surrounds each renal papilla.

Ureters

The ureters are about 200 to 250 mm long, urine is collected in the renal pelvis(or pyelum) , which connects to the ureters , which carry urine to the bladder. The urine peristaltically forced downward through smooth muscular tissue in the ureteric walls.

Urinary bladder

A balloon shape hollow muscular organ.it can stores up to 500 ml of urine comfortably (2-5 hours). Its sphincters (circular muscles) regulate the flow of urine from the bladder. Internal urethral sphincters in the beginning of urethra (smooth muscle- involuntary) while , external (skeletal - muscle- voluntary). In males , both sphincters are more powerful, able to retain urine for twice as long as females.



Functions of kidney

1. Regulation of ECF volume, osmolality and composition.
2. Regulation of blood pressure.
3. Regulation of acid- base balance.
4. Regulation of bone metabolism by regulation of excretion of calcium and phosphate ions and formation of active the form of vitamin D3 (1, 25 dicalcipherol).
5. Production of hormones : erythropoietin , renin and prostaglandins.
6. Excretion of various metabolic waste products, drugs, toxic substances :

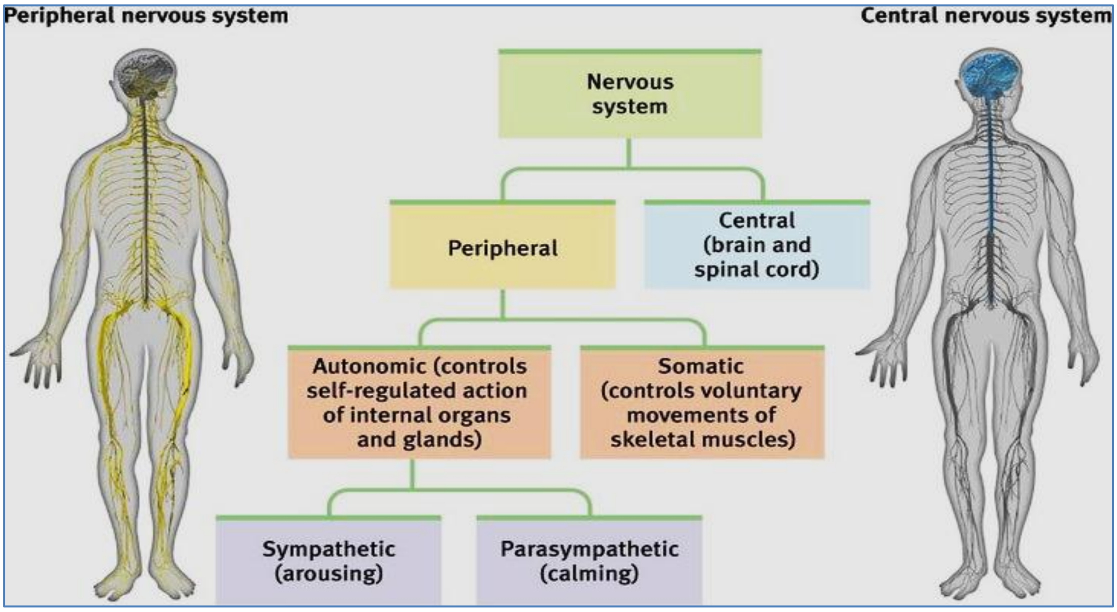
a. Urea from protein breakdown
b. Uric acid from nucleic acid breakdown.
c. Creatinine from muscles creatine breakdown.
d. End products of hemoglobin breakdown.

Physiology of Nerves

Nerves : are the excitable tissues , they are excitable because they have electrical phenomenon (they are polarized).

The nervous system has two major divisions:-

- The central nervous system (CNS) consisting of the brain and spinal cord.
- The peripheral nervous system (PNS) consisting of somatic and the autonomic nervous system.



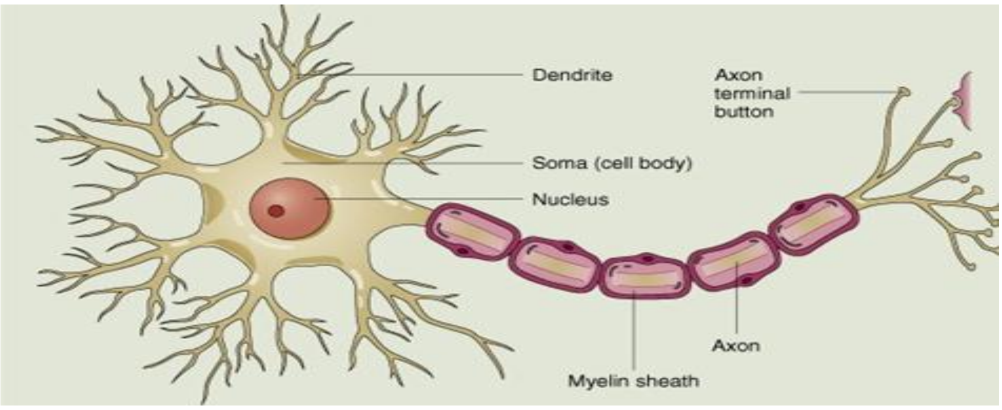
The neuron are excitable cells specialized for reception , integration and transmission of nerve impulses.

The neuron **in general are composed of three major parts:-**

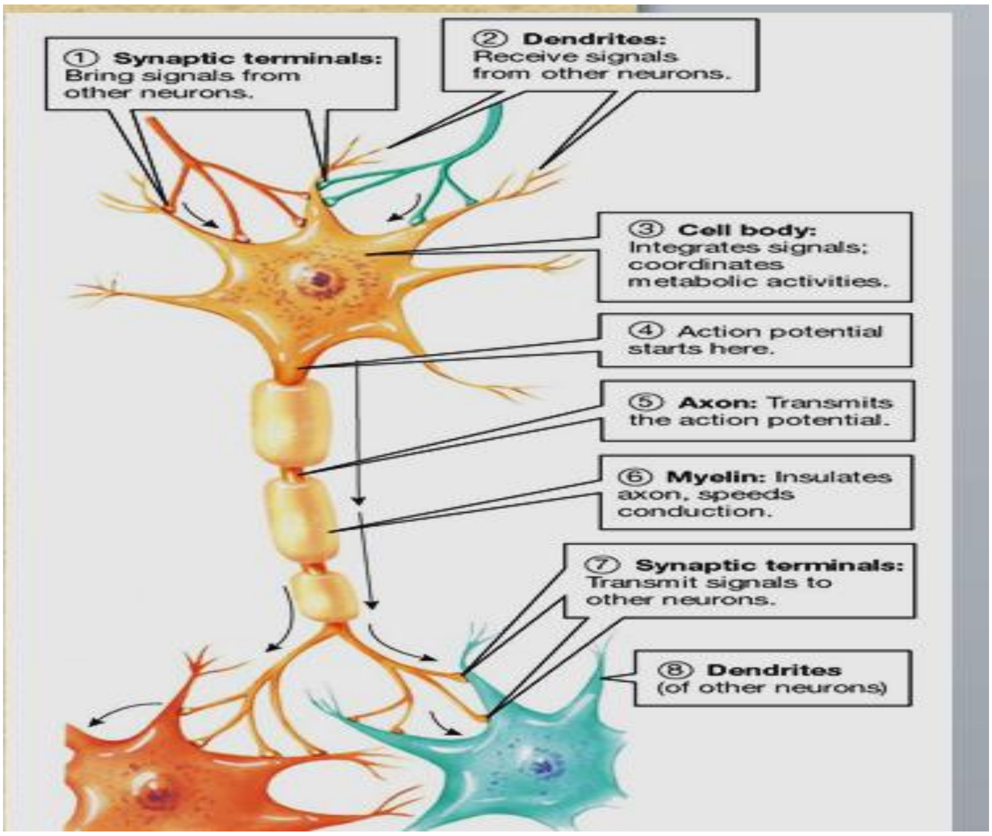
1. **The soma,** the main body of the neuron, contain specialized cytoplasm, single nucleus, and other granules (Nissl granules) **.**
2. **Dendrites** (2-7) which are great number of branching projection from the soma that conduct toward the cell body.

The soma and dendrites form a large area which is specialized for reception and the processes of other neurons terminate at this area to form what is caller synapses by which the neurons communicate with each other.

3. **Single axon** , which extends from the soma membrane to the periphery , it conducts away from the cell body . it starts from a thick area called the axon hillock, after that the part of the axon is called the initial segment (thinner), then the axon remains the same diameter until its termination (axon knob), where the chemical substance (neurotransmitter) is released in response to nerve impulse.
4. **Nerve endings or Terminal Buttones :** The side of synthesis storage and molecules of neurotransmitters (NTS).



(Nerve cell)



Each axon in the peripheral nervous system after a short distance from its origin is covered by a series of Schwan cells which are the supporting cells of the peripheral nervous system, they form the myelin sheath of the nerve.

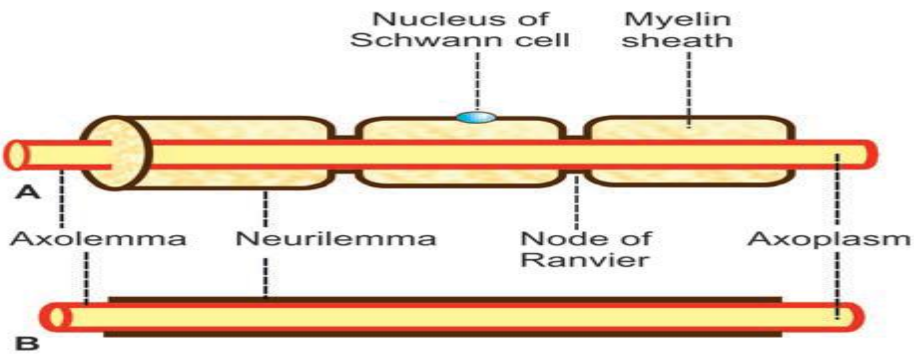
The myelin : - is a lipoprotein complex formed of many layers , and it is not continuous , it is interrupted by a small exposed area of 1 micron in length which is called **(node of Ranvier)** that forms the myline sheath between 2 adjacent nodes.

The process of myelin sheath forming (myelination) involves the following:-

1. The Schwan cell membrane first envelop the axon .
2. Then the cell rotates around the axon many times laying down multiple layers of Schwan cell membrane containing the lipid substance sphingomeylin which is an electrical insulator decreasing the ion flow through the membrane , this sheath has a main role in conduction because , it increased the velocity of conduction 5- 50 times , so diseases like multiple sclerosis causes demyelination and sever nerve defect which block conduction.

At the junction of 2 successive Schwan cell along the axon there is an area that is not insulated where ions can flow called the (node of Ranvier).

Not all the nerve fibers are mylinated , some are not mylinated but surround by Schwan cell without the deposition of myline (axon more than 1 micrometer in diameter is mylinated, but less than 0.5 micrometer in diameter are not mylinated.

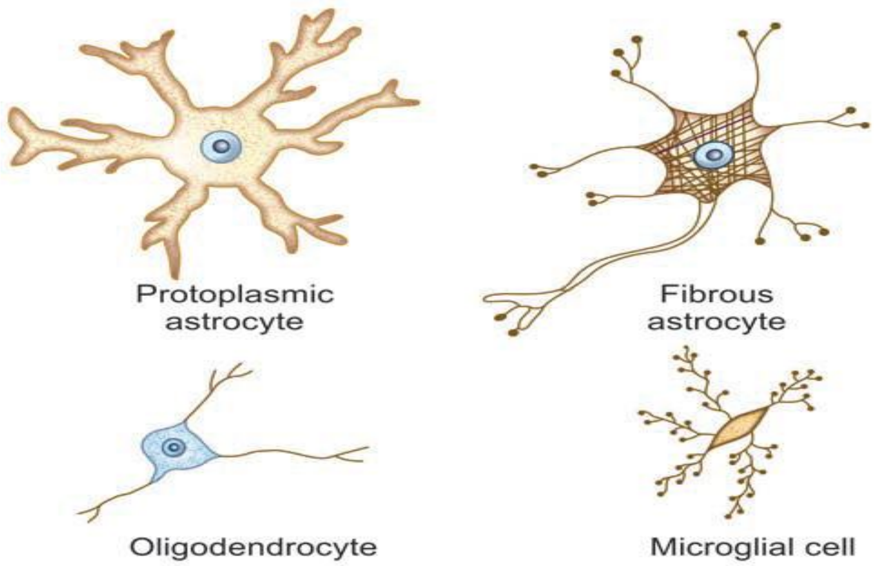


A. Myelinated nerve fiber; **B.** Non-myelinated nerve fiber.

In the CNS the myelination is done by other cells which are called the oligodendrocytes , which send multiple processes to the number of adjacent nerve fibers forming the myline sheath of many axon (by one cell).

In addition to the neurons , the nervous system contain glial cells (neuroglia), there are 10-50 times as many glial cells as neurons.

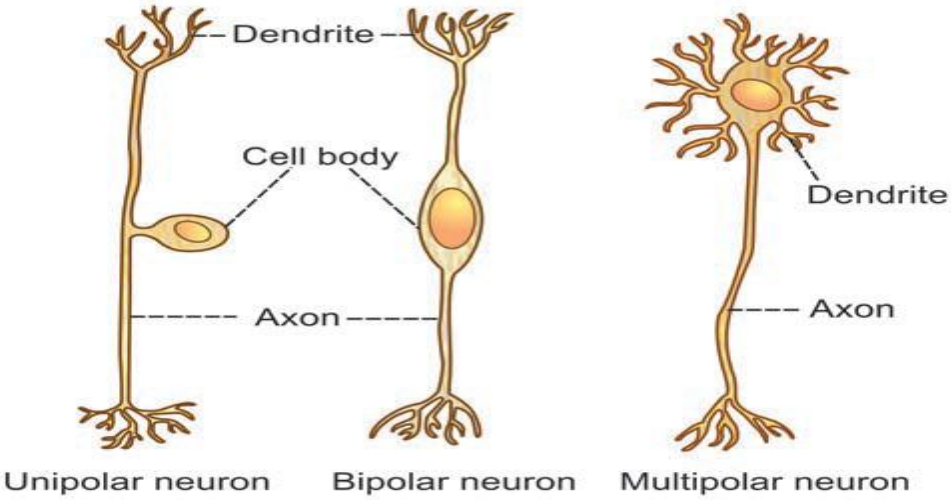
In the CNS there is **microglia, oligodendrocytes** and **astrocyte**. Microglia, provide support and phagocyte bacteria. Oligodendrocytes produced the myline sheath. The astrocyte support the CNS and transport substances between the neurons and the blood vessels and contribute in making blood brain barrier (BBB).



Neuroglial cells in CNS

Types of neurons

- Bipolar neurons:- the cell body has only two processes , one is the axon and the other is the dendrite . examples (in nose , eye and ears).
- Unipolar neurons :- has a single process extending from the cell body then after a short distance it will divide into 2 branches.
- Multipolar neurons:- has many processes arising from the cell body, only one is the axon , the rest are the dendrites.



Types of neuron

Functionally they are divided in to :-

1. Sensory
2. Motor
3. Interneuron

Functional organization of the neuron:-

1. **The receptor zone or dendritic zone :-** it represents the site for the reception of nerve signals, and much local potential are going to be formed in this area.
2. **The initial segment zone :-** it is site and origin of the conducting impulses , it is the site where the nerve impulses are generated.
3. **The axonal zone :-** or called the transmitting zone where the nerve impulses are propagated and transmitted.
4. **The nerve ending zone :-** the site where the nerve impulses causes the release of the neurotransmitter to affect other neuron or muscle fiber.

The neurons are secretory . there is synthesis of proteins which are transmitted by the axoplasmic transport from the cell body to the axon terminal and it is of **3 types:-**

1. Fast
2. Slower axoplasmic flow
3. Slowest axoplasmic flow

There is another type of transport in the neuron , which is called retrograde transport : this type is for the transport of substances , which are taken by the nerve ending , and nerve growth factor and some viruses from the endings to the soma.

Neural communication

The neurons communicate with each other by 2 types of communication:-

1. The electronic potential (generator potential) : local , no propagated potentials called , synaptic , generator , or electronic potential.
2. The action potential (nerve impulse):

Both types are physiochemical disturbances due to change in conduction across the cell membrane . the first type is a local non propagated potentials used for communication between neurons which are very close to each other (e.g. the brain and the eye , where large number of information are sent or received by adjacent cells.

The second type is a propagated disturbances used to send information for long distance without any loss of energy.

The Synapse

Synapse is the junction between two neurons. It is not an anatomical continuation. But, it is only a physiological continuity between two nerve cells.

Classification of synapse

Synapse is classified by two methods:

A. Anatomical classification

B. Functional classification.

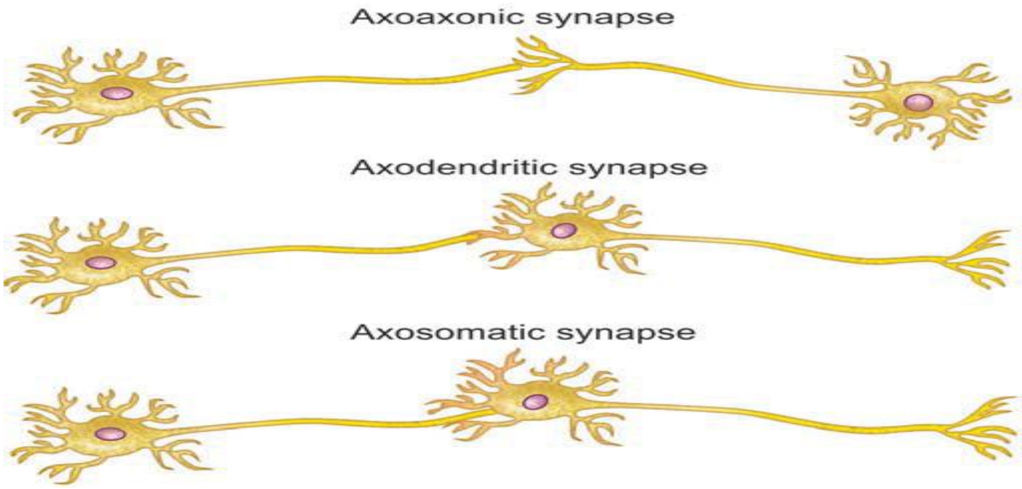
Anatomical classification

Usually synapse is formed by axon of one neuron ending on the cell body, dendrite or axon of the next neuron. Depending upon **ending of axon,** synapse is classified into three types:

1. **Axoaxonic synapse** in which axon of one neuron terminates on axon of another neuron.

2. **Axodendritic synapse** in which the axon of one neuron terminates on dendrite of another neuron

3. **Axosomatic synapse** in which axon of one neuron ends on soma (cell body) of another neuron.



Anatomical synapses

Functional classification

Functional classification of synapse is on the basis of **mode of impulse transmission.** According to this, synapse is classified into two categories:

1. Electrical synapse

2. Chemical synapse.

However, generally the word synapse refers to a chemical synapse.

1. Electrical Synapse

Electrical synapse is the synapse in which the physiological continuity between the presynaptic and the postsynaptic neurons is provided by **gap junction** between the two neurons . There is **direct exchange** of ions between the two neurons through the gap junction. Because of this reason, the action potential reaching the terminal portion of presynaptic neuron directly enters the postsynaptic neuron.

Important feature of electrical synapse is that the synaptic delay is very less because of the direct flow of current. Moreover, the impulse is transmitted in either direction through the electrical synapse.

This type of impulse transmission occurs in some tissues like the cardiac muscle fibers, smooth muscle fibers of intestine and the epithelial cells of lens in the eye.

2. Chemical Synapse

Chemical synapse is the junction between a nerve fiber and a muscle fiber or between two nerve fibers, through which the signals are transmitted by the release of chemical transmitter. In the chemical synapse, there is no continuity between the two neurons because of the presence of a space called **synaptic cleft** between the two neurons. Action potential reaching the presynaptic terminal causes release of neurotransmitter substance from the vesicles of this terminal. Neurotransmitter reaches the postsynaptic neuron through synaptic cleft and causes the production of potential change. Structure and functions of the chemical synapse are given here.

Neurotransmitter:- is a chemical substance that acts as a mediator for the transmission of nerve impulse from one neuron to another neuron through a synapse.

Some Neurotransmitters

Neurotransmitter	Location	Some Functions
Acetylcholine	Neuron-to-muscle synapse	Activates muscles
Dopamine	Mid-brain	Control of movement
Epinephrine	Sympathetic system	Stress response
Serotonin	Midbrain, pons, medulla	Mood, sleep
Endorphins	Brain, spine	Mood, pain reduction
Nitric Oxide	Brain	Memory storage

*Action potential transport:

Electrical potentials exist across the membranes of virtually all cells of the body. In addition, some cells, such as nerve and muscle cells, are capable of generating rapidly changing electrochemical impulses at their membranes, and these impulses are used to transmit signals along the nerve or muscle membranes. In still other types of cells, such as glandular cells, macrophages, and ciliated cells, local changes in membrane potentials also activate many of the cells' functions.

*Ion distribution across cell membranes:

In intracellular fluid there are high concentration of K^+ and large organic anions and little con. Of Na^+,Cl^- and Ca^{2+} . in extracellular fluid .

Origin of the Normal Resting Membrane Potential

The important factors in the establishment of the normal resting membrane potential of –90 millivolts. They are as follows**:**

1- **Contribution of the potassium diffusion potential:** diffusion of potassium through the potassium leaky channels play an important role in establishment of the resting membrane potential**.** If potassium ions were the only factor causing the resting potential, the resting potential inside the fiber would be equal to –95 millivolts**.**
2- **Contribution of sodium diffusion through the nerve membrane.**
3- **Contribution of the Na+-K+ Pump.** this creates an additional degree of negativity (about –4 millivolts additional) on the inside beyond that which can be accounted for by diffusion alone.

Selective Permeability of the Cell Membrane

Membrane potentials are set up because the membrane is selectively permeable to different ions. The permeability of the membrane to ions occurs by way of channel proteins; membrane-spanning transport proteins that allow ions to permeate.

These **ion channels** are characterized by:

1.**Selectivity:** the channel lets through only one (or a few) ion species. Channels selective for Na^+,K^+,Ca^{2+},Cl^-, and with non-selective cation permeability are known.

2.**Gating**: the channel can be open or closed by a conformational change in the protein molecule.

3.**A high rate of ion flow** that is always down the electrochemical gradient for the ion. So, depending on which types of channel are open, the resting membrane can be selectively permeable to certain ion species.

Setting up the Resting Potential

Ionic concentrations in atypical mammalian cell (mM)

Intracellular	**Extracellular**
Na+ 10 mM	Na+ 145 mM
K+ 160 mM	K+ 4.5 mM
Cl - 3 mM	Cl - 114 mM
A- 167 mM	A- 40 mM

*Nerve Action Potential

Nerve signals are transmitted by action potentials, which are rapid changes in the membrane potential that spread rapidly along the nerve fiber membrane.

The successive stages of the action potential are as follows:

1- Resting Stage. This is the resting membrane potential before the action potential begins. The membrane is said to be "polarized" during this stage because of the –90 milli volts negative membrane potential that is presence .

2- Depolarization Stage. At this time, the membrane suddenly becomes very permeable to sodium ions, allowing tremendous numbers of positively charged sodium ions to diffuse to the interior of the axon. The normal "polarized" state of –90 millivolts is immediately neutralized by the inflowing positively charged sodium ions, with the potential rising rapidly in the positive direction. This is called depolarization.

3- Repolarization Stage. Within a few 10,000 ths of a second after the membrane becomes highly permeable to sodium ions, the sodium channels begin to close and the potassium channels open more than normal. Then, rapid diffusion of potassium ions to the exterior re-establishes the normal negative resting membrane potential. This is called repolarization of the membrane.

As a summery: (Action potential)

1- Stimulus open chemical gated Na^+ channels until the membrane potential reach to threshold potential

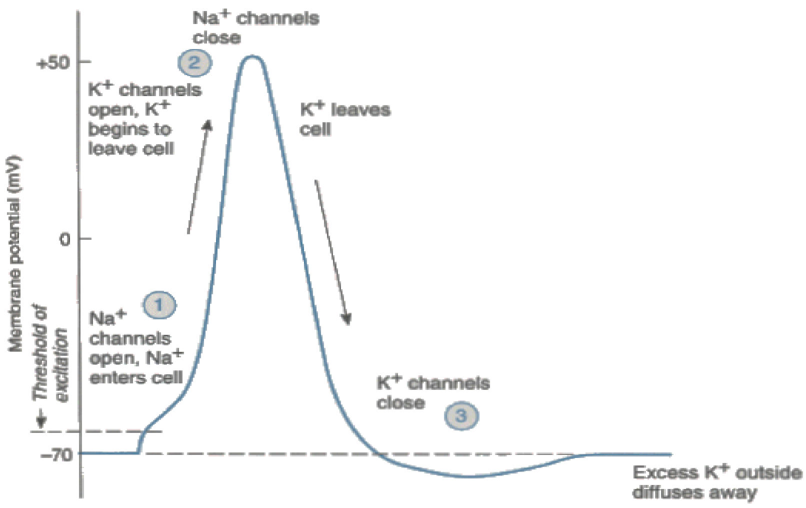
2- when threshold reached the voltage gated Na^+ channels open, Na^+ diffuses in, leading to decrease polarity briefly reaching down to about +35 mV

3-Then Na^+ channels inactivated then it will close.

3- After reaching the peak of depolarization and inactivation of the Na^+ channels, then K^+ channels open, K^+ diffuses out, Potential returns to zero

4- All channels closed, Na-K pump moves Na^+ back out & K^+back in.

5- A brief period of Hyperpolarization occurs due to slow closure of K^+ channels.
6- Resting potential restored



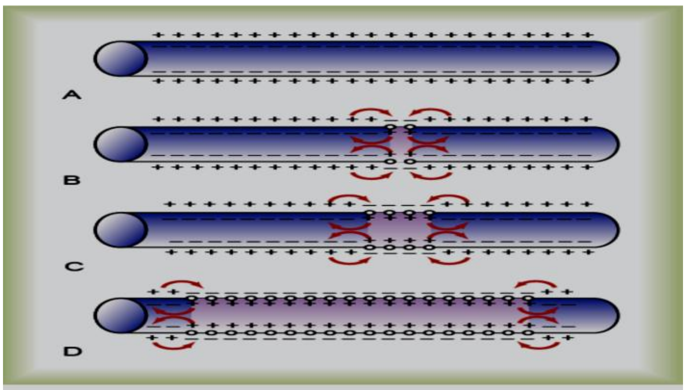


Figure 5–11

Propagation of action potentials in both directions along a conductive fiber.

Actions of sympathetic and parasympathetic divisions of autonomic nervous system

Effector organ		Sympathetic division	Parasympathetic division
1. Eye	Ciliary muscle	Relaxation	Contraction
	Pupil	Dilatation	Constriction
2. Lacrimal glands		Decrease in secretion	Increase in secretion
3. Salivary glands		Decrease in secretion and vasoconstriction	Increase in secretion and vasodilatation
4. Gastrointestinal tract	Motility	Inhibition	Acceleration
	Secretion	Decrease	Increase
	Sphincters	Constriction	Relaxation
	Smooth muscles	Relaxation	Contraction
5. Gallbladder		Relaxation	Contraction
6. Urinary bladder	Detrusor muscle	Relaxation	Contraction
	Internal sphincter	Constriction	Relaxation
7. Sweat glands		Increase in secretion	–
8. Heart – rate and force		Increase	Decrease
9. Blood vessels		Constriction of all blood vessels, except those in heart and skeletal muscle	Dilatation
10. Bronchioles		Dilatation	Constriction

Physiology: is the study of the functions of the human body. In other words, the mechanisms by which the various organs and tissues carry out their specific activities are considered.

The cells can be considered as the basic function unit of the living organisms . however it is possible to go down to the cellular organelles, macromolecules , molecules, atoms and even to the basic components of the atoms. From the cells it is also possible to go up to tissues , organs and systems in functions are accompanied with the necessary modifications in structure.

Water means life , the biological in living organisms is water. Solutes of the biological systems dissolved in water different concentrations , consequently, fluid compartments have their own specifications.

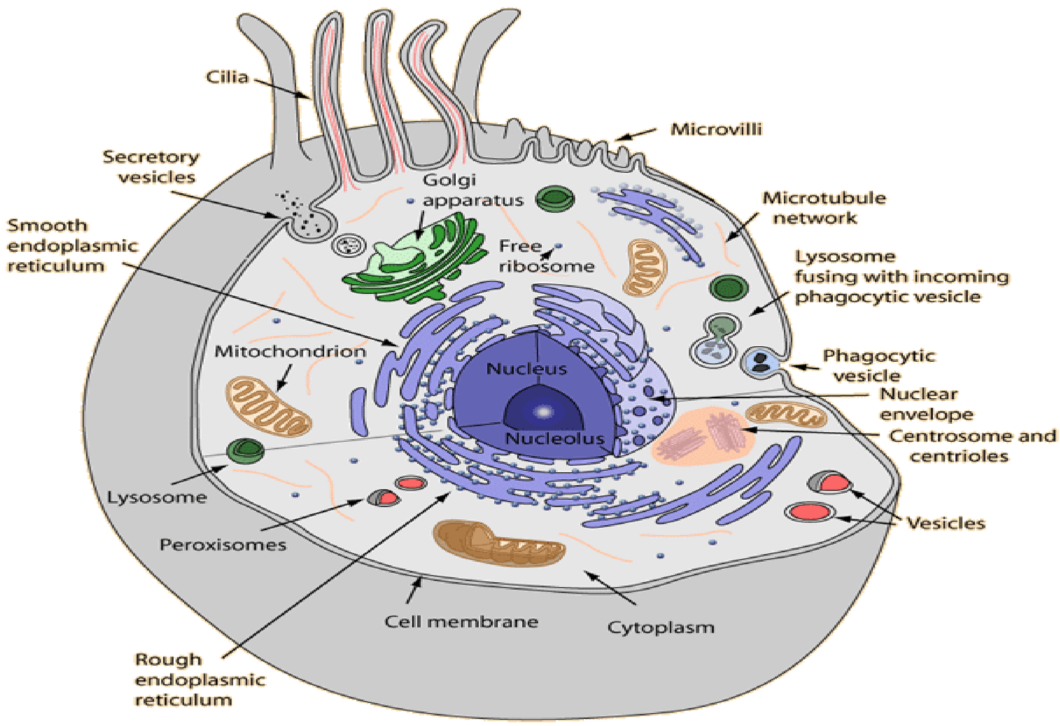
Homeostasis: refers to a system's ability to maintain a range of values. Think of how your body maintains certain levels of substances in your blood. For example, your blood contains a sugar called glucose.
Remember that for normal cellular function water and essential nutrients are required:

1.maneral elements 2. essential amino acids 3. essential fatty acids

4. water-soluble vitamins 5. fat- soluble vitamins

Cell structures and functions

Cells: are a major part of our bodies, Is a structure and function units in all organisms.
The human body has something on the order of 10 trillion cells all working in harmony to keep us alive. Cells are fundamental building blocks for many of the tissues and organs of our bodies.



Cell structures

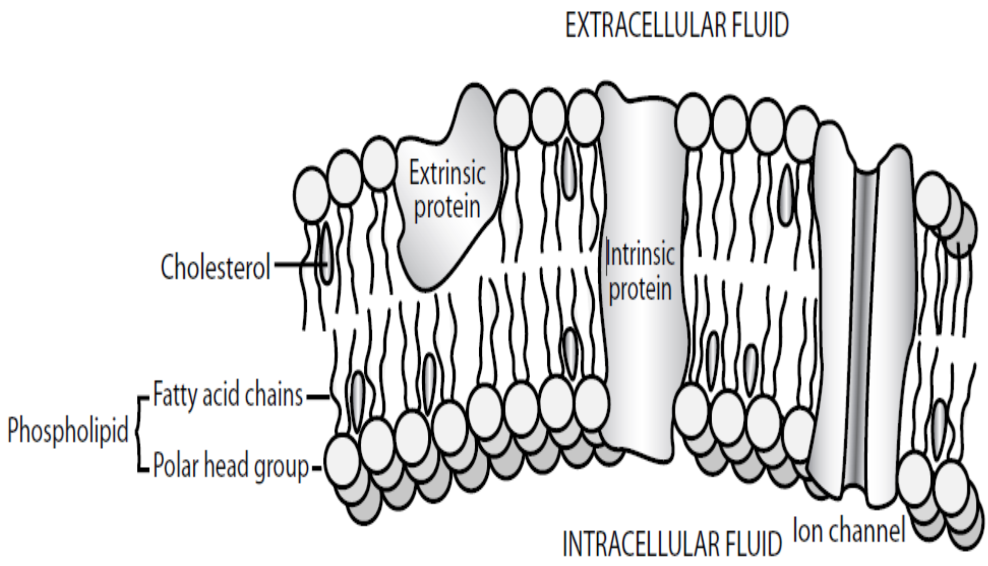
Cell Membrane

The cell membrane is composed of molecules called phospholipids.

The phosphate head of the phospholipid **likes** water so it is called **hydrophilic** while the lipid tail is called **hydrophopic** or “water hating.” Because of the water loving and hating characteristics of the heads and tails, phospholipids arrange themselves in what is known as a **bilayer**.

The cell membrane also lets certain substances in or out. We say that it is **selectively permeable**. For example, lipid soluble substances can pass right through the cell membrane. Examples oxygen, carbon dioxide and steroids.

Water soluble substances cannot pass through the cell membrane and require carrier proteins in order to get in or out of the cell.



The cell membrane also contains a number of proteins. Some of these proteins are **imbedded** on the surface of the cell and some go all the way through the cell membrane.

Some proteins act as **channels** to allow substances to pass through the membrane. Others act as **receptors** that receive information carried by proteins. Still others act as **connection points** for other cells to attach. These are known as **intercellular junctions.**

Cytoplasm

The cytoplasm or cytosol is the fluid inside the cell. It contains a network of channels and support structures called the **cytoskeleton.**

Endoplasmic Reticulum

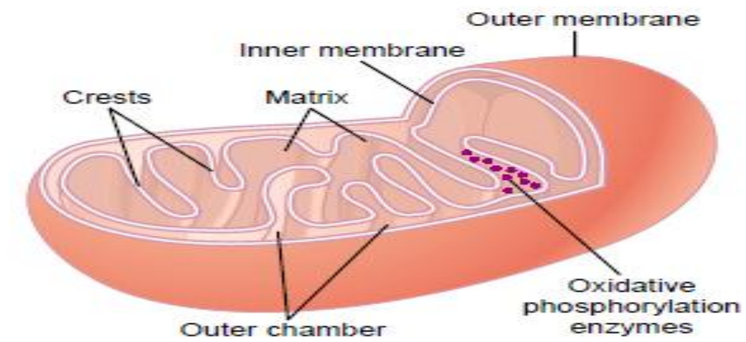
Another important organelle is the endoplasmic reticulum. The endoplasmic reticulum comes in two varieties; rough and smooth. Rough endoplasmic reticulum is studded with ribosomes. The ribosomes function in making proteins (protein synthesis). Smooth endoplasmic reticulum does not contain ribosomes. It functions in making lipids (lipid synthesis). Ribosomes contain RNA, protein and the enzymes needed for protein synthesis.

After the endoplasmic reticulum synthesizes the proteins they need to be packed up and shipped out to other parts of the cell or to other cells. That’s where the Golgi apparatus takes over. The Golgi apparatus packs up the proteins.

Besides the vesicles from the Golgi apparatus, there are other vesicles containing enzymes for breaking up debris in the cell. These are called **lysosomes.**

Mitochondrion

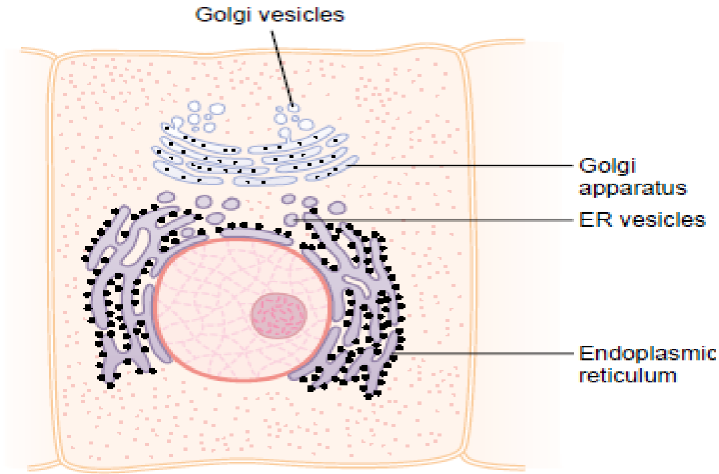
The function of it is produces energy that is needed throughout the body. It is known as the "powerhouse" of the cell. The mitochondrion takes in fuel such as glucose and extracts the energy from it to make ATP. The inner portion of the mitochondrion is folded into shelves called cristae. These are studded with enzymes needed for the many chemical reactions used to make ATP.



Golgi Apparatus

The Golgi apparatus, is closely related to the endoplasmic reticulum. It has membranes similar to those of the a granular endoplasmic reticulum. It usually is composed of four or more
stacked layers of thin, flat, enclosed vesicles lying near one side of the nucleus.

The Golgi apparatus functions concentrates, modifies and sorts proteins arriving from the granular endoplasmic reticulum prior to their distribution by way of the Golgi vesicles , to other organelles or their secretion from cells.



Centrosome

The centrosome is important in producing a structure called the mitotic spindle that helps to separate the chromosomes during mitosis. The centrosome consists of 2 hollow cylinders called centrioles. The centrioles are constructed from tubular proteins.

Cilia and Flagella

The cell contains other protein structures called cilia and flagella, and important in cellular movements .

A flagellum is a long protein structure from Cilia. Cells may have many cilia but will only have one flagellum.

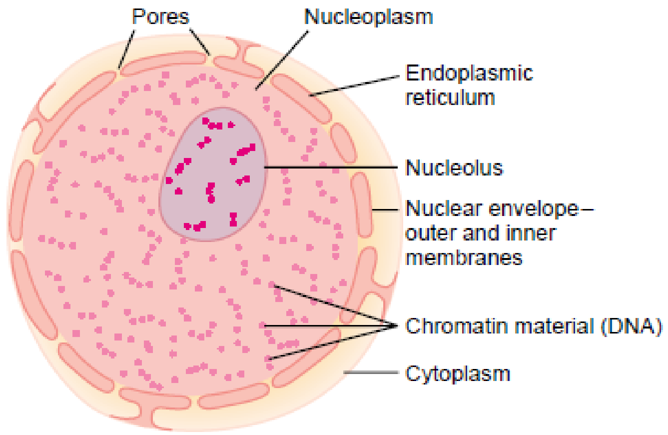
Microfilaments and Microtubules

Microfilaments are solid protein structures that form the cytoskeleton to support the cell.

Microtubules are hollow and can transport substances around the cell.

Nucleus

The nucleus contains the DNA of the cell. It is surrounded by a membrane much like the cell membrane. Inside the nucleus is the nucleolus which contains RNA and proteins. This is where ribosomes are synthesized.



Substance Transport in Cells

Diffusion

Diffusion is the movement of substances from an area of higher concentration toward an area of lower concentration until reaching equilibrium. The force that drives diffusion comes from differences in concentration called concentration gradients.

Facilitated Diffusion

Many solutes do not simply diffuse across plasma membrane. they are transported by means of proteins carriers within the membranes. Examples of substances that move via facilitated diffusion include sodium, potassium, and chloride.

1. Active transport: minerals, and some of sugars and most amino acids move against a concentration gradient with expenditure of energy.
2. Passive transport: the moving force is the concentration gradient. So the molecules move with gradient without expenditure of energy.

Osmosis

Water moves from an area of higher concentration to lower concentration.

So you could think of osmosis in 2 ways:

1. Water moves across a semipermeable membrane from a higher area of concentration of water to a lower concentration of water.

2. Water moves across a semipermeable membrane from an area of lower concentration of solute to an area of higher concentration of solute.

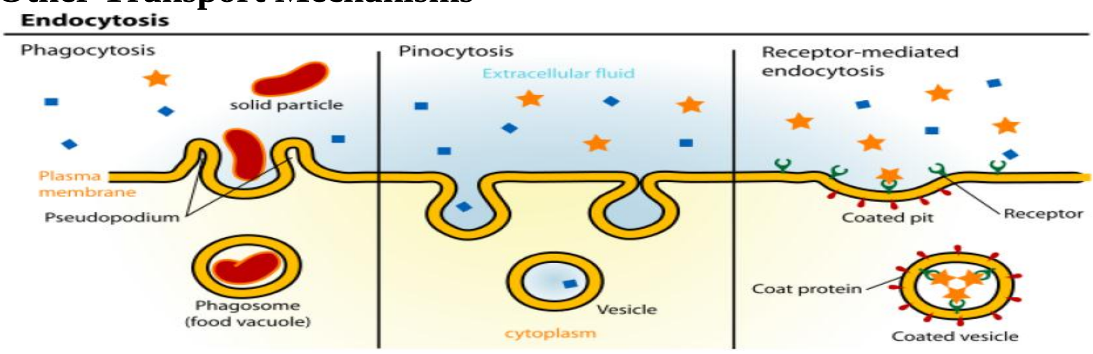
Active Transport

In active transport substances are moved against their concentration gradients by carrier proteins. However, there is an energy cost to be paid for this action. So the carrier proteins use ATP as an energy source.

An example of an active transport protein is the sodium potassium pump . Normally there is more sodium outside of the cell than in so sodium would move from outside to in.

Also, there is usually more potassium inside the cell than out, so potassium would follow its concentration gradient and move out of the cell.

Other Transport Mechanisms



The Respiratory System Physiology

Introduction:

- **Ventilation (mechanics of respiration)**
- **Gas exchange and transport**
- **Control of respiration**

The function of respiratory system

*The major function of the respiratory system can be divided in two categories : **Respiratory and Non-respiratory.**

The first function is to carry out gas exchange. The respiratory system must obtain oxygen from the environment and must eliminate carbon dioxide (co_2) produced by cellular mechanism. These processes must be coordinated so that the demand for oxygen is met and so that the carbon dioxide (co_2) that is produced is eliminated.

The respiratory system is also involved in non- respiratory functions. It participates in maintaining acid-base balance, since increased in co2 in the body leads to increased H^+ , the lungs also metabolized naturally occurring compounds such as angiotensin I, prostaglandins and epinephrine. The lungs are also responsible for protecting the body from inhaled particles.

Functional anatomy of the respiratory system

Functionally , the respiratory air passages are divided into two zones:

- **Conductive zone**
- **Respiratory zone**

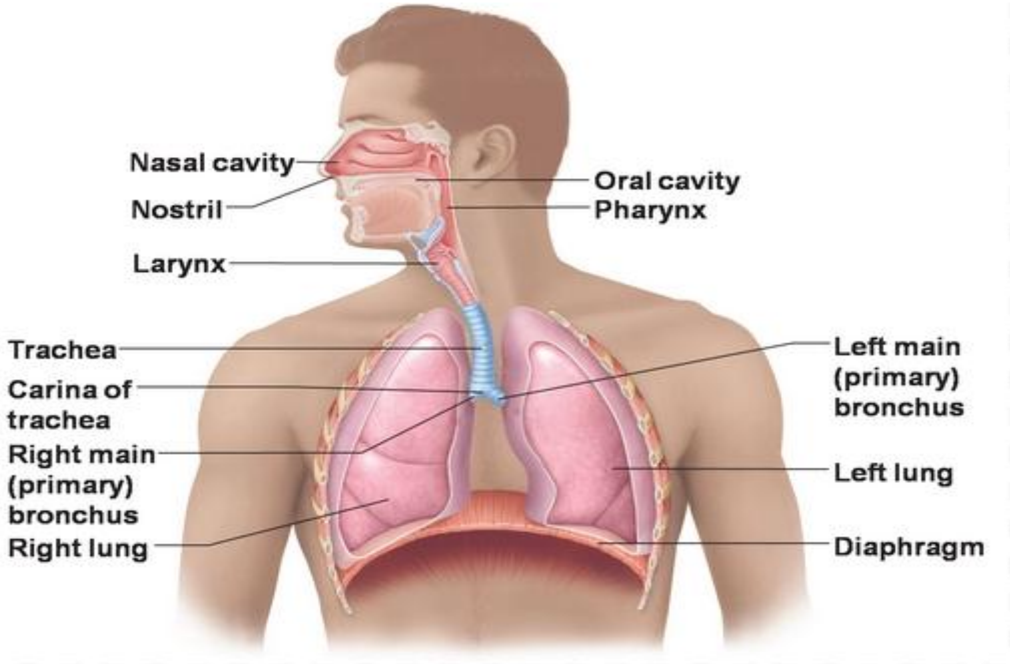


Figure : general structure of respiratory system

*Conducting zone:

The Conducting zone includes all of the anatomical strictures through which air passes before reaching respiratory zone.

It consists of the following parts:

- Mouth and nose then pharynx →larynx → trachea → primary bronchi → all successive branches of bronchioles including terminal bronchioles. The air way tree consists of a series of highly branched hollow tubes that decrease in diameter and become more numerous at each branching**.**
- Trachea , the main air way in turn branches into two bronchi, one of which enters each lung. Within each lung, these bronchi branches many times progressively smaller bronchi, which in turn branch into terminal bronchioles analogous to twigs of a tree. The terminal bronchioles redivide to form respiratory bronchioles, which end as alveoli, analogous to leaves on a tree.

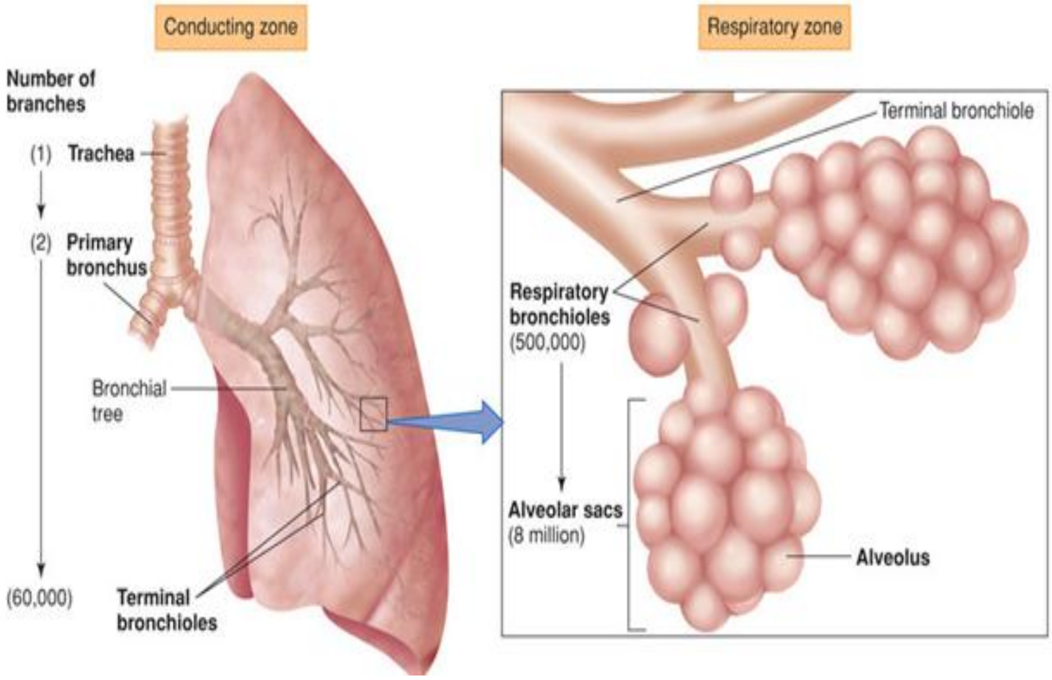


Figure : structure of the airway

Function of the Conducting zone

1. Warming and humidification of the inspired air.

Regardless of the temperature and the humidity of the atmosphere, when the inspired air reaches the respiratory zone it is at a body temperature of 37 c (body temperature) and it is saturated with water vapor. This ensures that a constant internal body temperature will be maintained.

2. Filtration and cleaning.

Mucous secreted by the cells of the Conducting zone serves to trap small particles in the inspired air and thereby performs a filtration function. this mucus is moved along at a rate of 1-2 cm/min by cilia projecting from the tops of the epithelial cells that line the Conducting zone. There are about 300 cilia per cell that bend in a coordinated fashion to move mucus toward the pharynx, where it can either be swallowed or expectorated . as a result of this filtration function, particles larger than about 6 µm do not enter the respiratory zone of the lungs. The cleaning action of cilia and macrophages in the lungs is diminished by cigarette smoke.

3. **Distribute air to the gas exchange surface of the lung.**

* Respiratory zone

The respiratory zone includes the :

- respiratory bronchioles (because they contain separate out pouching of alveoli).
- Alveolar ducts
- Alveolar sacs
- The alveoli

Alveoli : are tiny air sacs, having a diameter of 0.25 – 0.50 mm. there are about 300- 500 million Alveoli in each lung. The numerous numbers of these structures provides a large surface area (60 – 80 m2) for diffusion of gases.

The pleural cavities and pleural membrane

Each lung covered by one pleura. Pleura is a serious membrane lining the pleural cavity. It is divided into partial pleura that forms the outer layer and visceral pleura that adheres to the surface of the lungs, pleural fluids fill and lubricates the space between the pleura.

Pulmonary blood flow

Pulmonary blood flow is the cardiac output of the right heart . it is delivered to the lungs via the Pulmonary artery. Pulmonary capillaries form dense network around the alveoli. Pulmonary blood flow is not distributed equally in the lungs because of gravitational effects. when a person is standing , blood flow is lowest at apex (top) and higher at base (bottom) of the lungs. when a person is in supine (lying down) position gravitational effects disappear. As in other organs , regulation of blood flow is accomplished by altering arteriolar resistance. Bronchial circulation is the blood supply to the conducting air way and is a small fraction of total Pulmonary blood flow.

Ventilation:

Ventilation: is the exchange of air between the external environment and the alveoli. Air moves by bulk flow from area of high pressure to low pressure. All pressures in the respiratory system are relative to atmospheric pressure (760 mm Hg at sea level). Air will move in or out of the lungs depending on the pressure in the alveoli. The body changes the pressure in the alveoli by the changing the volume of the lungs.

The pathway of air:

When one breathes air in at sea level , the inhalation is composed of different gases. These gases and their quantities are oxygen which makes up 21%, nitrogen which is 78%, carbon dioxide with 0.04% and others with significantly smaller portions.

In the process of breathing , air enters into the nasal cavity through the nostrils and is filtered by coarse hairs and mucous that are found there. The hair filter macro particles, which are particles of large size. Dust, pollen, smoke and fine particles are trapped in the mucous that lines the nasal cavities. Air then travels through the nasopharynx, oropharynx and laryngopharynx, which are the three portions that make up the pharynx. The pharynx is a funnel – shaped tube that connects nasal and oral cavities to the larynx.

The tonsils which are part of the lymphatic system, form a ring at the connection of the oral cavity and the pharynx. Here, they protect against foreign invasion of antigens. Therefore the respiratory tract aides the immune system through, this protection. Then the air travels through the larynx. **The larynx** closes at the epiglottis to prevent the passage of food or drink as a protection to trachea and lungs. The larynx is also voice box ; it contains vocal cords, in which it produces sound. Sound is produced from the vibration of the vocal cord when air passes through them. Through the trachea, the air is now able to pass into the bronchi.

There are two phases of Ventilation :

- **Inspiration**
- **Expiration**

During each phase the body changes the lungs dimensions to produce a flow of air either in or out of the lungs.

* Inspiration

Is an active process requiring the contracting of skeletal muscles. The primary muscles of inspiration include the external intercostal muscles (located between the ribs) and the diaphragm(a sheet of muscles located between the thoracic and abdominal cavities). the external intercostal plus the diaphragm contract to bring about inspiration.

contraction of external intercostal muscles causes elevation of ribs and sternum causing increased front to back dimension of thoracic cavity and this lowers air pressure in lungs so air moves into lungs.

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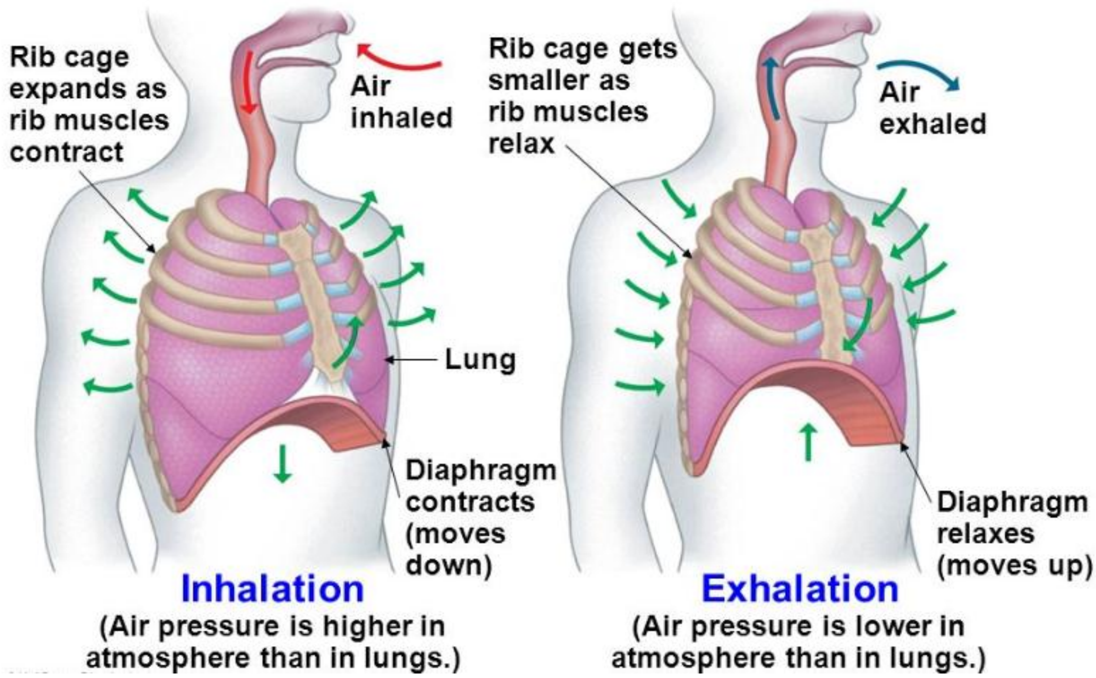
Intra- alveolar pressure during inspiration and expiration

As the external intercostal and diaphragm contract, the lungs expand. The expiration of the lungs causes the pressure in the lungs(and alveoli) to become slightly negative relative to atmospheric pressure. As a result , air moves from an area of higher pressure (the air) to an area of lower pressure (lungs and alveoli). During expiration, the respiration muscles relax and lung volume decreases. This causes pressure in the lungs (and alveoli) to become slight positive relative to atmospheric pressure. As a result, air leaves the lungs.



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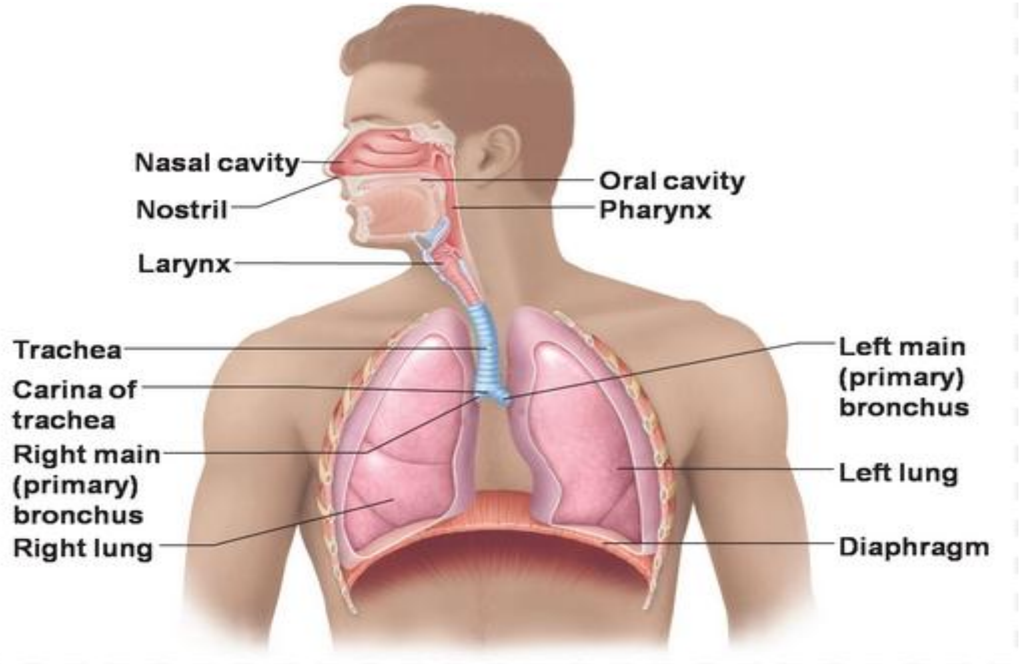

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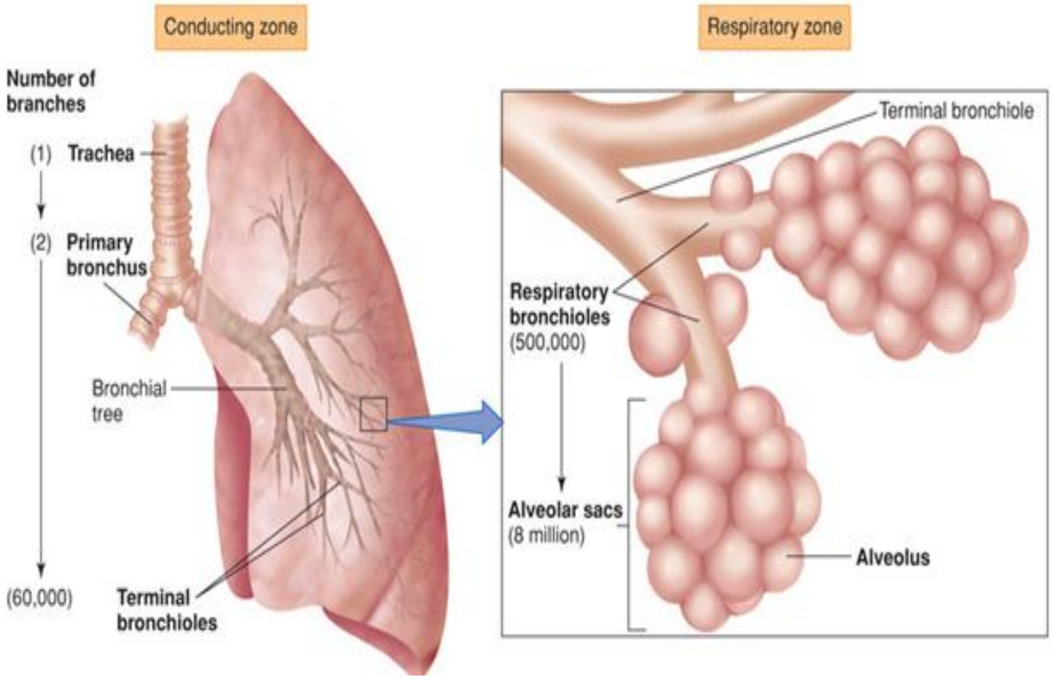

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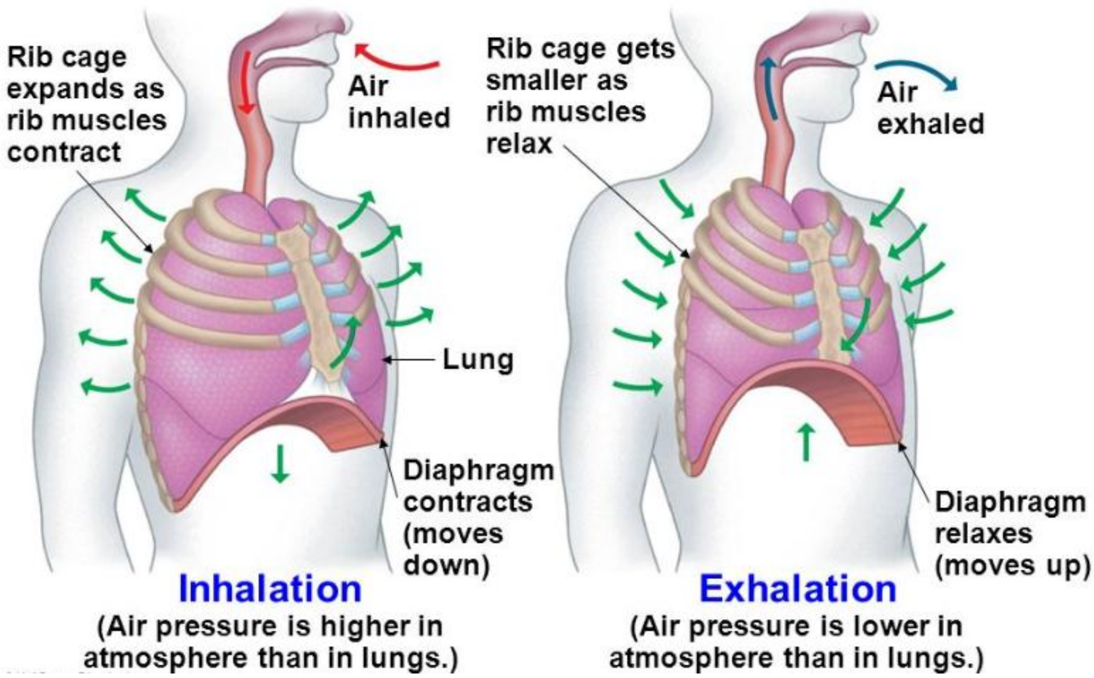


The Blood

Blood : - is a connective tissue in fluid form. It is considered as the **'fluid of life'** because it carries oxygen from lungs to all parts of the body and carbon dioxide from all parts of the body to the lungs. It is known as **'fluid of growth'** because it carries nutritive substances from the digestive system and hormones from endocrine gland to all the tissues. The blood is also called the **'fluid of health'** because it protects the body against the diseases and gets rid of the waste products and unwanted substances by transporting them to the excretory organs like kidneys.

Properties of Blood

1. *Color:* Blood is red in color. Arterial blood is scarlet red because it contains more oxygen and venous blood is purple red because of more carbon dioxide.

2. *Volume:* Average volume of blood in a normal adult is 5 L. In a newborn baby, the volume is 450 ml. It increases during growth and reaches 5 L at the time of puberty. In females, it is slightly less and is about 4.5 L.

3. *Reaction and pH:* Blood is slightly alkaline and its pH in normal conditions is 7.4.

4. *Specific gravity:*

Specific gravity of total blood : 1.052 to 1.061
Specific gravity blood cells : 1.092 to 1.101
Specific gravity of plasma : 1.022 to 1.026

5. *Viscosity:* Blood is five times more viscous than water. It is mainly due to red blood cells and plasma proteins.

Composition of Blood

Blood contains the blood cells which are called formed elements and the liquid portion known as plasma.

Blood cells

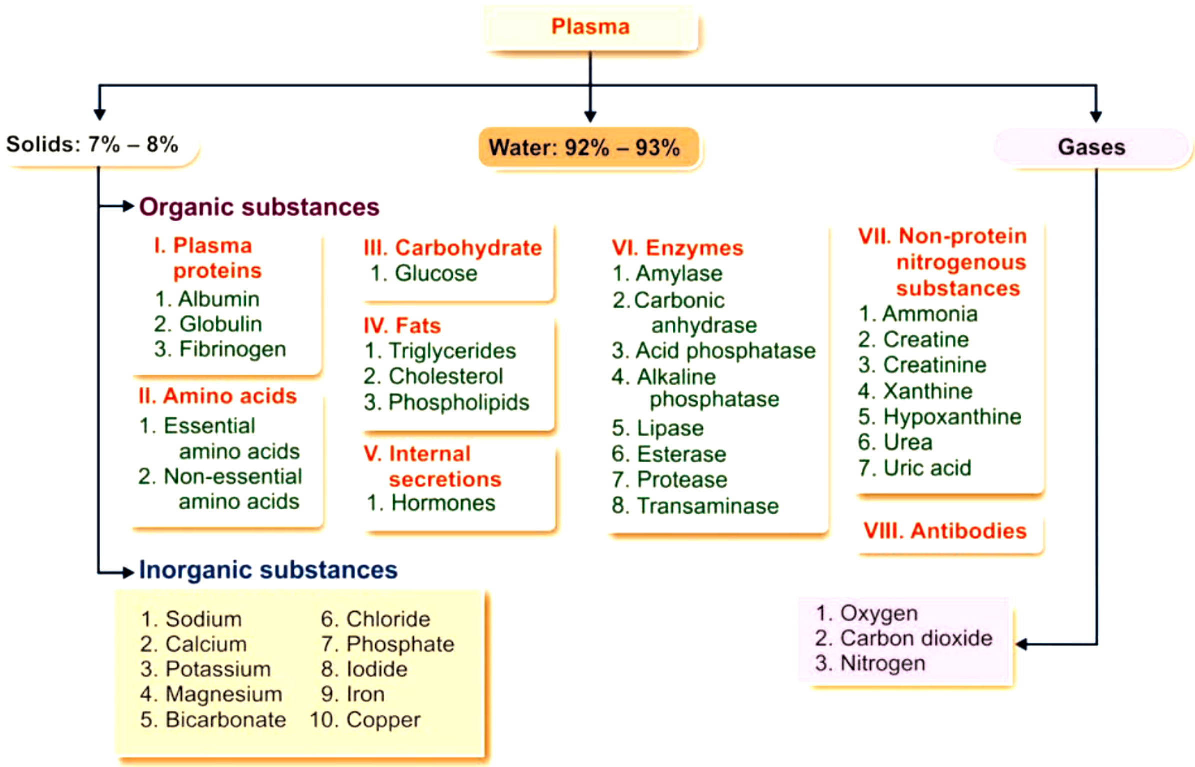
Three types of cells are present in the blood:
1. Red blood cells or erythrocytes
2. White blood cells or leukocytes
3. Platelets or thrombocytes.

Plasma

Plasma is a straw-colored clear liquid part of blood. It contains 91% to 92% of water and 8% to 9% of solids. The solids are the organic and the inorganic substances.

Plasma proteins are:
1. Serum albumin
2. Serum globulin
3. Fibrinogen.

Fibrinogen is absent in serum because, it is converted into fibrin during blood clotting. Because of this, the albumin and globulin are usually called serum albumin and serum globulin.



Some important substances in blood.

Normal Values

Normal values of the plasma proteins are:
Total proteins : 7.3 g/dL (6.4 to 8.3 g/dL)
Serum albumin : 4.7 g/dL
Serum globulin : 2.3 g/dL
Fibrinogen : 0.3 g/dL

„ **Albumin/Globulin Ratio**

Ratio between plasma level of albumin and globulin is called albumin/globulin (A/G) ratio.
It is an important indicator of some diseases involving liver or kidney.
Normal A/G ratio is 2 : 1.

Separation of plasma proteins

Plasma proteins are separated by the following methods.

„ **1. Precipitation Method**
„ **2. Salting-out Method**
3. Electrophoretic Method
4. Cohn's fractional (Precipitation Method)

„ **5. Ultracentrifugation Method**
„ **6. Gel filtration chromatography**
7. Immunoelectrophoretic Method

Origin of plasma proteins

„ **1. In Embryo**

In embryonic stage, the plasma proteins are synthesized by the **mesenchyme cells.** The albumin is synthesized first and other proteins are synthesized later.

„ 2. **In Adults**

In adults, the plasma proteins are synthesized mainly from **reticuloendothelial cells** of liver. The plasma proteins are synthesized also from spleen, bone marrow, disintegrating blood cells and general tissue cells. Gamma globulin is synthesized from B lymphocytes.

Functions of Plasma Proteins

Plasma proteins are very essential for the body. Following are the functions of plasma proteins:

„ **1. Role in Coagulation of Blood**

Fibrinogen is essential for the coagulation of blood .

„ **2. Role in Defense Mechanism of Body**

Gamma globulins play an important role in the defense mechanism of the body by acting as antibodies (immune substances). These proteins are also called immunoglobulins. Antibodies react with antigens of various microorganisms, which cause diseases like diphtheria, typhoid, streptococcal infections, influenza, hepatitis, rubella, etc.

„ **3. Role in Transport Mechanism**

Plasma proteins are essential for the transport of various substances in the blood like (hormones, enzymes, etc). The alpha and beta globulins play an important role in the transport of metals in the blood.

4. Role in Maintenance of Osmotic Pressure in Blood

At the capillary level, most of the substances are exchanged between the blood and the tissues. However, auto because of their large size, the plasma proteins cannot pass through the capillary membrane easily and remain in the blood. In the blood, these proteins exert the colloidal osmotic (oncotic) pressure. Osmotic pressure exerted by the plasma proteins is about 25 mm Hg. Since the concentration of albumin is more than the other plasma proteins, it exerts maximum pressure. Globulin is the next and fibrinogen exerts least pressure.

5. Role in Regulation of Acid-Base Balance

Plasma proteins, particularly the albumin, play an important role in regulating the acid base balance in the blood.

6. Role in Viscosity of Blood

Plasma proteins provide viscosity to the blood, which is important to maintain the blood pressure.

7. Role in Erythrocyte Sedimentation Rate

8. Role in Suspension stability of Red Blood Cells

9. Role in Production of Trephone Substances

10. Role as Reserve Proteins

Serum

Serum is the clear straw-colored fluid that oozes from blood clot. When the blood is shed or collected in a container, it clots. In this process, the fibrinogen is converted into fibrin and the blood cells are trapped in this fibrin forming the blood clot. After about 45 minutes, serum oozes out of the blood clot. For clinical investigations, serum is separated from blood cells and clotting elements by centrifuging. Volume of the serum is almost the same as that of plasma (55%). It is different from plasma only by the absence of fibrinogen, i.e. serum contains all the other constituents of plasma except fibrinogen.

Serum = Plasma – Fibrinogen

Functions of Blood

„ **1. Nutritive Function**

Nutritive substances like glucose, amino acids, lipids and vitamins derived from digested food are absorbed from gastrointestinal tract and carried by blood to different parts of the body for growth and production of energy.

„ **2. Respiratory Function**

Transport of respiratory gases is done by the blood.

„ **3. Excretory Function**

Waste products formed in the tissues during various metabolic activities are removed by blood and carried to the excretory organs like kidney, skin, liver, etc. for excretion.

„ **4. Transport of Hormones and Enzymes**

Hormones which are secreted by ductless (endocrine) glands are released directly into the blood. The blood transports these hormones to their target organs/tissues. Blood also transports enzymes.

„ **5. Regulation of Water Balance**

This helps in the regulation of water content of the body.

„ **6. Regulation of Acid-base Balance**

Plasma proteins and hemoglobin act as buffers and help in the regulation of acid-base balance.

„ **7. Regulation OF Body Temperature**

Because of the high specific heat of blood, it is responsible for maintaining the thermoregulatory mechanism in the body.

8. Storage Function

Water and some important substances like proteins, glucose, sodium and potassium are constantly required by the tissues. Blood serves as a readymade source for these substances. And, these substances are taken from blood during the conditions like starvation, fluid loss, electrolyte loss, etc.

„ 9. Defensive Function

Blood plays an important role in the defense of the body. The white blood cells are responsible for this function. Neutrophils and monocytes engulf the bacteria by phagocytosis. Lymphocytes are involved in development of immunity. Eosinophils are responsible for detoxification, disintegration and removal of foreign proteins.

Body Fluids

Body is formed by solids and fluids. Fluid part is more than two third of the whole body. Water forms most of the fluid part of the body. In human the total body water varies from **45% to 75%** of body weight. In a normal young adult male, body contains **60% to 65%** of water and 35% to 40% of solids. In a normal young adult female, the water is 50% to 55% and solids are 45% to 50%. In females, water is less because of more amount of subcutaneous adipose tissue. In thin persons, water content is more than that in obese persons. In old age, water content is decreased due to increase in adipose tissue. Total quantity of body water in an average human that weigh about 70 kg is about 40 L.

Importance Of Body Fluids

1. In Homeostasis

Body cells persist in the fluid medium called **internal environment.** Internal environment contains substances **such as** glucose, amino acids, lipids, vitamins, ions, oxygen, etc. which are essential for growth and functioning of the cell. Water not only forms the major constituent of internal environment but also plays an important role in homeostasis.

2. In Transport Mechanism

Body water forms the transport medium by which nutrients and other essential substances enter the cells; and unwanted substances come out of the cells. Water forms an important medium by which various enzymes, hormones, vitamins, electrolytes and other substances are carried from one part to another part of the body.

3. In Metabolic Reactions

Water inside the cells forms the medium for various metabolic reactions, which are necessary for growth and functional activities of the cells.

4. In Texture Of Tissues

Water inside the cells is necessary for characteristic form and texture of various tissues.

5. In Temperature Regulation

Water plays a vital role in the maintenance of normal body temperature.

Distribution Of Body Fluids

Total water in the body is about 40 L. It is distributed into two major compartments

1. ***Intracellular fluid (ICF)****:* Its volume is 22 L and it forms 55% of the total body water
2. ***Extracellular fluid (ECF):*** Its volume is 18 L and it forms 45% of the total body water. ECF is divided into 5 subunits:

i. Interstitial fluid and lymph (20%)
ii. Plasma (7.5%)
iii. Fluid in bones (7.5%)
iv. Fluid in dense connective tissues like cartilage (7.5%)
v. Transcellular fluid (2.5%) that includes:
a. Cerebrospinal fluid
b. Intraocular fluid
c. Digestive juices
d. Serous fluid – intrapleural fluid and pericardial fluid
e. Synovial fluid in joints
f. Fluid in urinary tract.

Composition Of Body Fluids

Body fluids contain water and solids. Solids are organic and inorganic substances.

1. **Organic Substances**

Organic substances are glucose, amino acids and other proteins, fatty acids and other lipids, hormones and enzymes.

2. **Inorganic Substances**

Inorganic substances present in body fluids are sodium, potassium, calcium, magnesium, chloride, bicarbonate, phosphate and sulfate. ECF contains large quantity of sodium, chloride, bicarbonate, glucose, fatty acids and oxygen. ICF contains large quantities of potassium, magnesium, phosphates, sulfates and proteins. **The pH of ECF is 7.4. The pH of ICF is 7.0.**

Concentration Of Body Fluids

Concentration of body fluids is expressed in three ways:

„ 1. **Osmolality**

Measure of a fluid’s capability to create osmotic pressure is called osmolality or osmotic concentration of a solution. In simple words, it is the concentration of osmotically active substance in the solution.

„ **Osmolality**

Osmolarity is another term to express the osmotic concentration. It is the number of particles (osmoles) per liter of solution (osmoles/L).

Tonicity

movement of water between the fluid compartments is not influenced by small molecules **like urea and alcohol**, which cross the cell membrane very rapidly. These small molecules are called ineffective molecules . On the contrary, the larger molecules like sodium and glucose, which cross the cell membrane slowly, can influence the movement of water, such molecules are called effective molecules. Effective molecules are responsible for this. Depending On **tonicity**, the solutions are classified into three types:

i. ***Isotonic Fluid***

Fluid which has the same effective molecules concentration (tonicity) of body fluids is called isotonic fluid. Examples are 0.9% sodium chloride solution (normal saline) and 5% glucose solution. Red blood cells or other cells placed in isotonic fluid (normal saline) neither gain nor lose water by osmosis This is because of the **osmotic equilibrium** between inside and outside the cell across the cell membrane.

ii. ***Hypertonic Fluid***

Fluid which has greater effective molecules concentration than the body fluids is called hypertonic fluid. Example is 2% sodium chloride solution. When red blood cells or other cells are placed in hypertonic fluid, water moves out of the cells (exosmosis) resulting in shrinkage of the cells.

iii. ***Hypotonic Fluid***

Fluid which has less effective molecules concentration than the body fluids is called hypotonic fluid. Example is 0.3% sodium chloride solution. When red blood cells or other cells are placed in hypotonic fluid, water moves into the cells (endosmosis) and causes swelling of the cells

Applied Physiology

„ **Dehydration**

Dehydration is defined as excessive loss of water from the body. Body requires certain amount of fluid intake daily for normal functions. Minimum daily requirement of water intake is about 1 L. This varies with the age and activity of the individual. Dehydration occurs when fluid loss is more than what is taked.

Classification

Basically, dehydration is of three types:

1. ***Mild dehydration****:* It occurs when fluid loss is about 5% of total body fluids. Dehydration is not very serious and can be treated easily by rehydration.

2. ***Moderate dehydration**:* It occurs when fluid loss is about 10%. Dehydration becomes little serious and immediate treatment should be given by rehydration.
3. ***Severe dehydration**:* It occurs when fluid loss is about 15%. Dehydration becomes severe and requires hospitalization and emergency treatment. When fluid loss is more than 15%, dehydration becomes very severe and life threatening.

Causes

1. Severe diarrhea and vomiting due to gastrointestinal disorders
2. Excess urinary output due to renal disorders
3. Excess loss of water through urine due to endocrine disorders such as diabetes mellitus, diabetes insipidus and adrenal insufficiency
4. Insufficient intake of water
5. Prolonged physical activity without consuming adequate amount of water in hot environment.

Water Intoxication Or Overhydration

Water intoxication is the condition characterized by great increase in the water content of the body. It is also called overhydration, hyperhydration, water excess or water poisoning.

Causes

Water intoxication occurs when more fluid is taken than that can be excreted. Water intoxication due to drinking excess water is rare when the body's systems are functioning normally. But there are some conditions that can produce water intoxication.

1. Heart failure in which heart cannot pump blood properly
2. Renal disorders in which kidney fails to excrete enough water in urine
3. Hypersecretion of antidiuretic hormone as in the case of syndrome of inappropriate hypersecretion of antidiuretic hormone (SIADH)
4. Intravenous administration of unduly large amount of medications and fluids than the person's body can excrete
5. Infants have greater risk of developing water intoxication in the first month of life, when the filtration mechanism of the kidney is underdeveloped and cannot excrete the fluid rapidly
6. Water intoxication is also common in children having swimming practice, since they are more prone to drink too much of water while swimming
7. An adult (whose heart and kidneys are functioning normally) can develop water intoxication, if the person consumes about 8 L of water every day regularly.

The Digestive system physiology

Digestion : is defined as the process by which food is broken down into simple chemical substances that can be absorbed and used as nutrients by the body. A normal young healthy adult consumes about 1 kg of solid diet and about 1 to 2 liter of liquid diet every day.

The functions of digestive system include:

1. Ingestion or consumption of food substances.
2. Breaking them into small particles.
3. Transport of small particles to different areas of the digestive tract.
4. Secretion of necessary enzymes and other substances for digestion.
5. Digestion of the food particles.
6. Absorption of the digestive products (nutrients).
7. Removal of unwanted substances from the body.

Functional anatomy of digestive system

Digestive system is made up of **gastrointestinal tract** (GI tract) or alimentary canal and accessory organs, which help in the process of digestion and absorption . GI tract is a tubular structure extending from the mouth up to anus, with a length of about 30 feet. It opens to the external environment on both ends. GI tract is formed by two types of organs:

1. Primary digestive organs.
2. Accessory digestive organs.

1. *Primary Digestive Organs*

Primary digestive organs are the organs where actual digestion takes place. Primary digestive organs are:

1. Mouth
2. Pharynx
3. Esophagus
4. Stomach
5. Small intestine
6. Large intestine.

2. *Accessory Digestive Organs*

Accessory digestive organs are those which help primary digestive organs in the process of digestion.

Accessory digestive organs are:

1. Teeth
2. Tongue
3. Salivary glands
4.. Exocrine part of pancreas
5. Liver
6. Gallbladder.

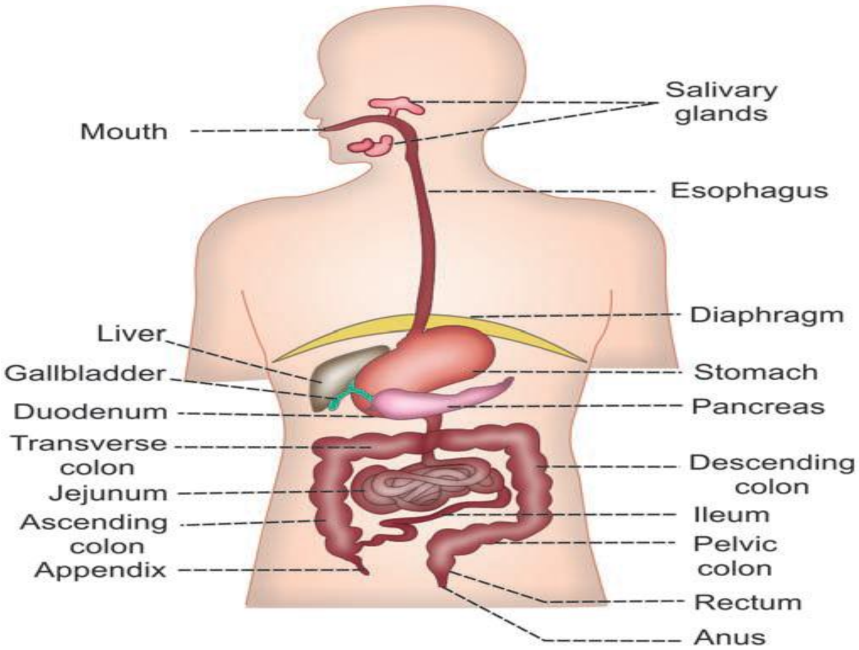


Figure (1): Gastrointestinal tract

Control of Conditions in the GI Tract

GIT possess two kinds of receptor ;mechanoreceptors and chemoreceptors which respond to **1.stretching of the lumen by foodstuffs and solute concentration 2. pH within the lumen 3. presence of digestible and digested molecules these receptors initiated activate or inhibit the following processes:**

1. secretions into the lumen
2. muscular "mixing" activity
3. secretion of hormones
4. local "nerve plexuses" .

There are 2 types of digestive reflex processes: **short reflex** which controlled by "nerve plexus" within the GI tract (enteric plexus) **and**

long reflex which involving the CNS and extrinsic autonomic nerves.

Enteric plexus organized into ganglia interconnected by 2 plexuses:

1- Outer myenteric (Auerbach's) plexus found along entire length of GI tract.

2-Inner submucosal (meissner's plexus) located only in small and large intestine enteric plexuses contains 100 million neurons and similar diversity of neurotransmitters as CNS and has **interneurons**, **sensory**, **autonomic**, and **ganglia** .Peristalsis is controlled by enteric plexuses.

Layers of GI Tract

There are 4 tunics composed the GIT (from inside to outside) :-

1-Mucosa: Is the absorptive and secretory layer lining lumen of GI tract. In places is highly folded with villi to increase absorptive area .Contains lymph nodules, mucus secreting goblet cells, and thin layer of muscle.

2- Submucosa: Is a thick, highly vascular layer of connective tissue where absorbed molecules enter blood and lymphatic vessels . Contains glands and nerve plexuses (submucosal plexus) that carry ANS activity to muscularis mucosae of small and large in it.

3-muscularis: Is responsible for segmental contractions and peristaltic movement through GI tract. Has an inner circular and outer longitudinal layer of smooth muscle.

Activity of these layers moves food through tract while pulverizing and mixing it. Myenteric plexus between these layers is major nerve supply to GI tract .Includes fibers and ganglia from both Sympathetic and Parasympathetic systems.

4 - serosa : Is outermost layer; serves to bind and protect .Consists of

areolar connective tissue covered with layer of simple squamous epithelium.

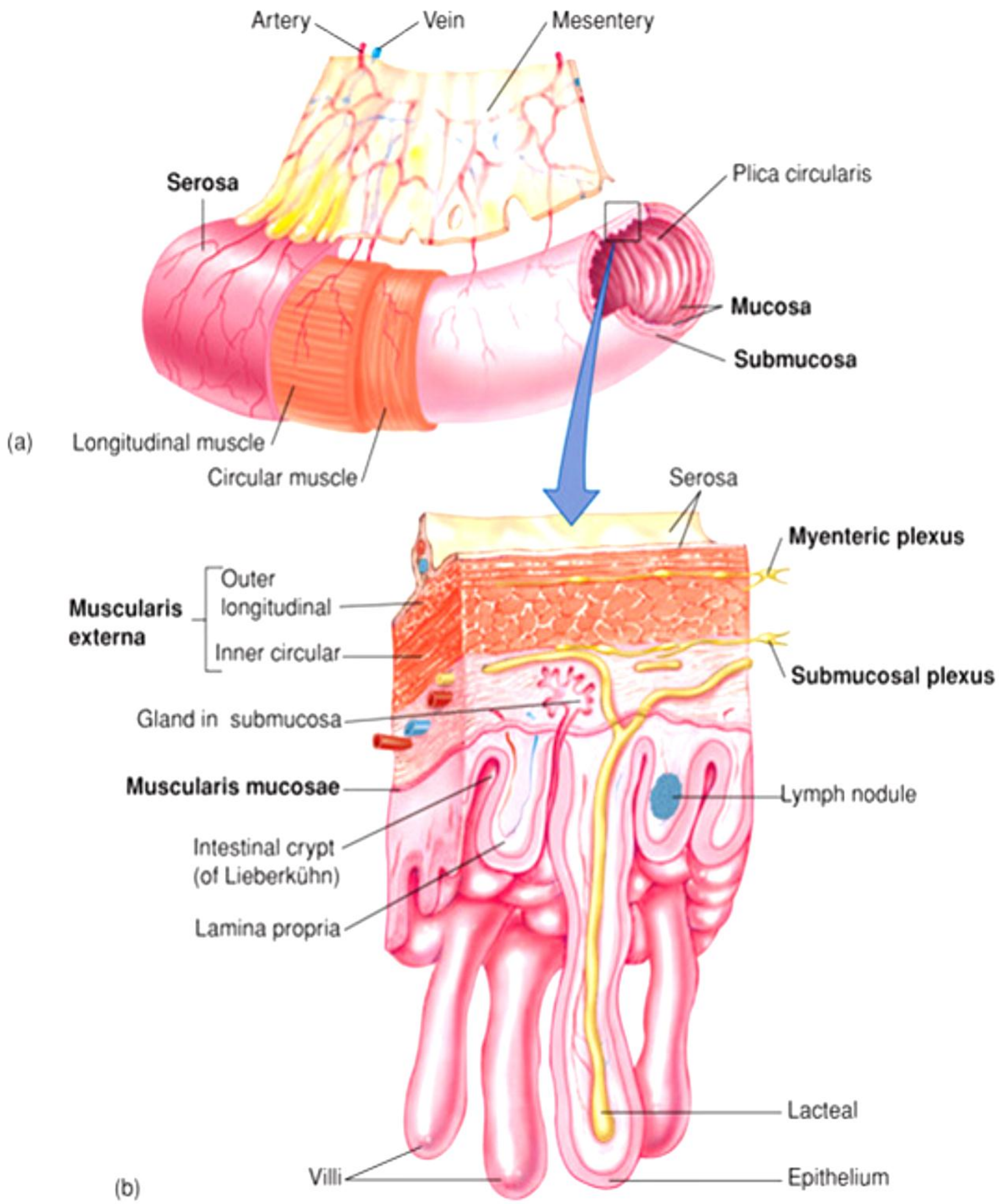


Figure (2): Layers of GI Tract

Digestive Processes Occurring in the Mouth, Pharynx, Esophagus:

This digestion involving mechanical Processes and salivation the mechanical processes are :

1. Prehension and mastication (chewing) - cheeks, tongue, and teeth involved in both voluntary and involuntary grinding, ripping, and tearing of foodstuffs. Chewing is mixes food with saliva which contains salivary amylase, which is an enzyme that catalyzes partial digestion of starch .

2. Deglutition (swallowing) : moving "bolus" on its way it is begins as voluntary activity. Oral phase is voluntary and forms a food bolus. Pharyngeal and esophageal phases are involuntary and cannot be stopped To swallow, larynx is raised so that epiglottis covers entrance to respiratory tract. A swallowing center in medulla orchestrates complex pattern of contractions required for swallowing. **Esophagus connects pharynx to stomach .Upper third of esophagus contains skeletal muscle ,middle third contains mixture of skeletal and smooth and terminal portion contains only smooth muscle esophagus passes through diaphragm via esophageal hiatus.**

Peristalsis propels food through GI tract it is wave-like muscular contractions .After food passes into stomach, the gastroesophageal sphincter constricts, preventing reflux.

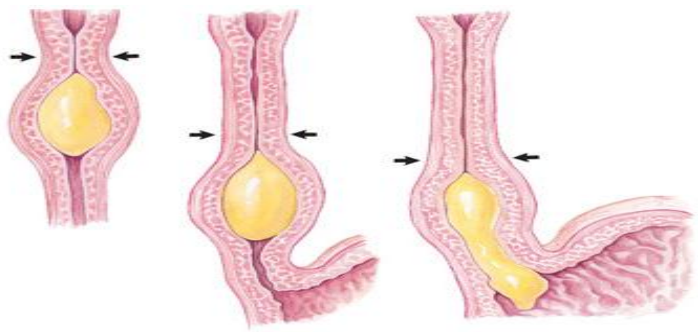


Figure (3): Peristalsis movement

Composition of Saliva & Control of Salivation

1. major components of saliva:

a. water (97-99.5%).

b. electrolytes: Na^+, K^+, Cl^-, PO_4^- .

c. mucin - protein that forms thick, slimy mucus .

d. IgA antibodies - immune defense.

e. lysozyme - antibacterial enzyme.

f. salivary amylase - starts breakdown of carbo's.

2. control of salivation: ingestion of foodstuffs → activate chemoreceptors and pressoreceptors →. Salivatory nuclei (pons & medulla) →Parasympathetic nerve activation → Facial (VII) anGlassopharyngeal (IX) nerves →secretion by salivary glands.

Sympathetic nerve activation →decreased salivation

<u>Stomach:</u> there are two types of stomach in mammalian **1-simple stomach** that present in human an non ruminants animals this type consist of one compartment **2- complex stomach** its consist of four compartment (rumen, reticulum ,omasum and abomasums) this type present in ruminant animals . In general stomach is most distensible part of GI tract, empties into the duodenum its functions are:

1- storage of food.

2- initial digestion of proteins.

3-killing bacteria with high acidity.

4- moving soupy food mixture (chyme) into intestine.

Simple stomach is enclosed by gastroesophageal sphincter on top and pyloric sphincter on bottom. Its divided into 3 regions: Fundus ,Body and Antrum . Inner surface of stomach is highly folded into rugae. Contractions of stomach churn chyme, mixing it with gastric secretions. Eventually these will propel food into small intestine.

Gastric mucosa has gastric pits in its folds. Cells that line folds deeper in the mucosa, are exocrine gastric gland which contain cells that secrete different products that form gastric juice .**1-Goblet cells** secrete mucus **2- Parietal cells** secrete HCl and intrinsic factor (necessary for B12 absorption in intestine) **3- Chief cells** secrete pepsinogen (precursor for pepsin) **4-Enterochromaffin-like cells** secrete histamine and serotonin **5- G cells** secrete gastrin **6- D cells** secrete somatostatin . See the figure (4).

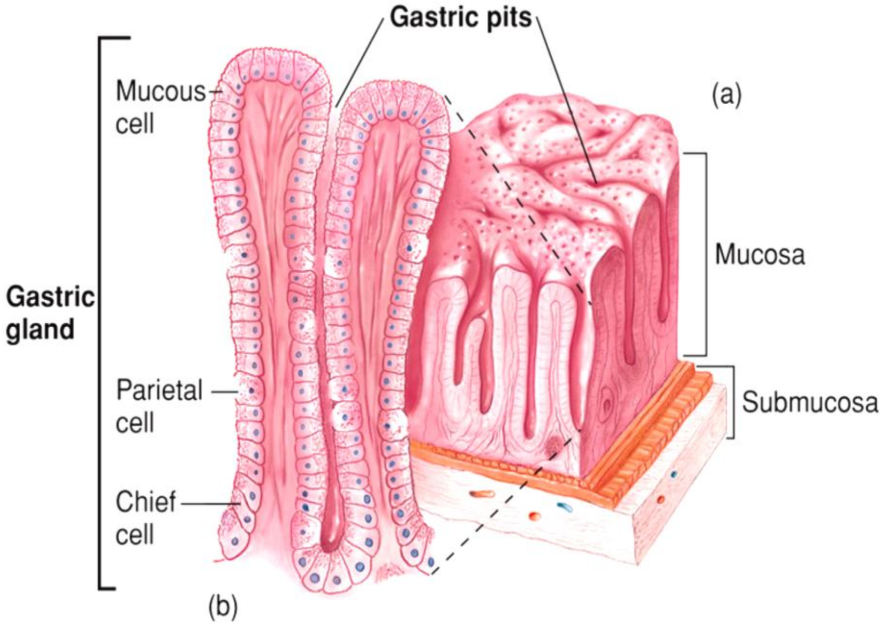


Figure (4): Gastric gland

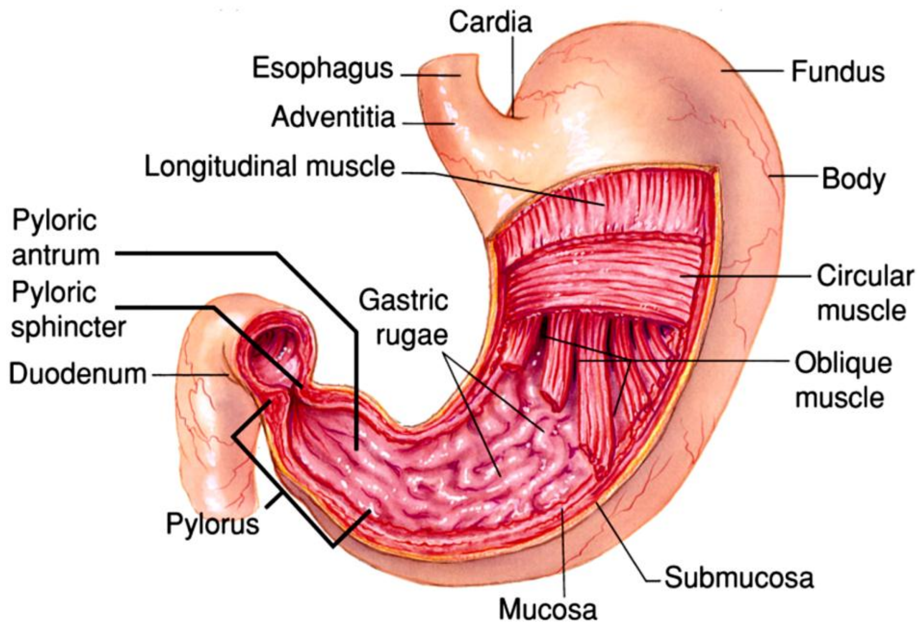


Figure (5): Simple stomach

HCl in Stomach Is produced by parietal cells which pump H+ into lumen via an H+/ K+ pump (pH ~1).

1- Cl- is secreted by facilitated diffusion.

2- H+ comes from dissociation of H2CO3

3- Cl- comes from blood side of cell in exchange for HCO3 ,see figure (6).

HCl is secreted in response to the hormone gastrin; and ACh from vagus, these are indirect effects since both stimulate release of histamine which causes parietal cells to secrete HCl.

HCl in Stomach Makes gastric juice very acidic which denatures proteins to make them more digestible and converts pepsinogen into pepsin.

Both HCL and pepsin can damage lining and produce a peptic ulcer . 1st line of defense is the adherent layer of mucus which is a stable gel of mucus coating the gastric epithelium and contains bicarbonate for neutralizing HCL also gastric epithelial cells contain tight junctions to prevent HCL and pepsin from penetrating the surface.

Gastric epithelial cells are replaced every 3 days.

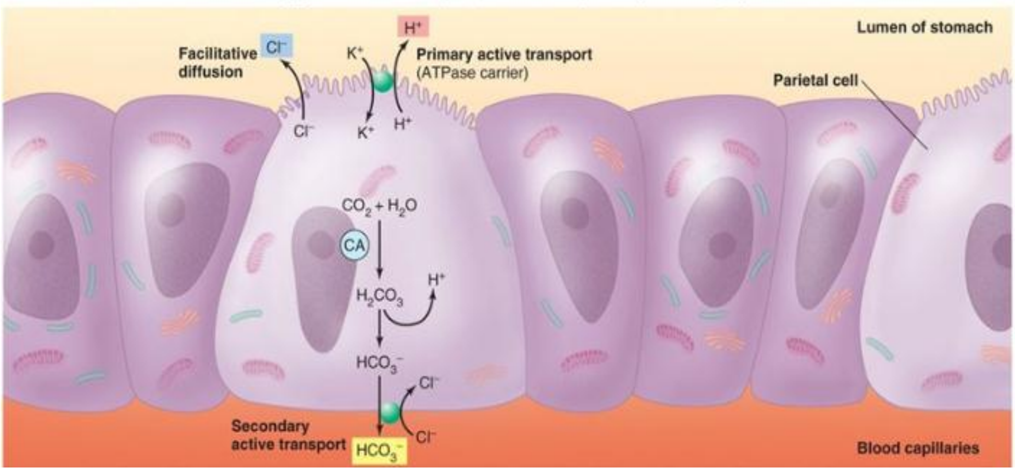


Figure (6)

Regulation of Gastric Secretion, Motility, and Emptying

(A) . Regulation of Gastric Secretion ("Gastric Juice")

1. Cephalic (reflex) phase

sight, aroma, taste, thought → hypothalamus gustatory centers → vagal nuclei of medulla → vagus nerve (parasympathetic) → increased gastric secretion.

2. Gastric phase accrues when food reaches the stomach by 2 mechanisms:

A-neural mechanism	**B-hormonal mechanism**
distention & low acidity --->	digested proteins --->
vagal afferents to medulla --->	increase in pH --->
vagal efferents to stomach --->	gastrin released --->
parasympathetic ACh release --->	enzymes & HCl released
increased gastric secretion	

3. intestinal phase :

excitatory phase	**inhibitory phase**
chyme enters the duodenum ->	inhibition of vagal nuclei
release of intestinal gastrin ->	inhibition of local reflexes
continued gastric secretion	activation of sympathetics
	release of inhibitory hormones:(secretin, cholecystokinin CCK, gastric inhibitory peptide GIP)

(B) . Gastric Motility and Emptying

1. Receptive relaxation - trilayer of muscles in wall of the stomach relax to allow filling to occur.
2. Plasticity - smooth muscle tension specially regulated to prevent regurgitation of food.
3. Basic electrical rhythm - pacemaker cells of longitudinal muscle allow rhythmic contractions.
4. Emptying to duodenum - regulated by amount and type of chyme entering into the duodenum; faster with high carbo, slower with higher fats.
5. Vomiting (emesis) - irritants activate neurons which stimulate the "emetic center" of medulla.

Small Intestine (SI)

Is longest part of GI tract; approximately 3m long in human. Duodenum is 1st 25cm after pyloric sphincter ,jejunum is next 2/5 of length and ileum is last 3/5 of length; empties into large intestine. Absorption of digested food occurs in SI and facilitated by long, length and tremendous surface area .Surface area increased by foldings and projections; the large folds are plicae circulares and microscopic fingerlike projections are villi In addition to apical hair-like projections which are called microvilli. figure (7).

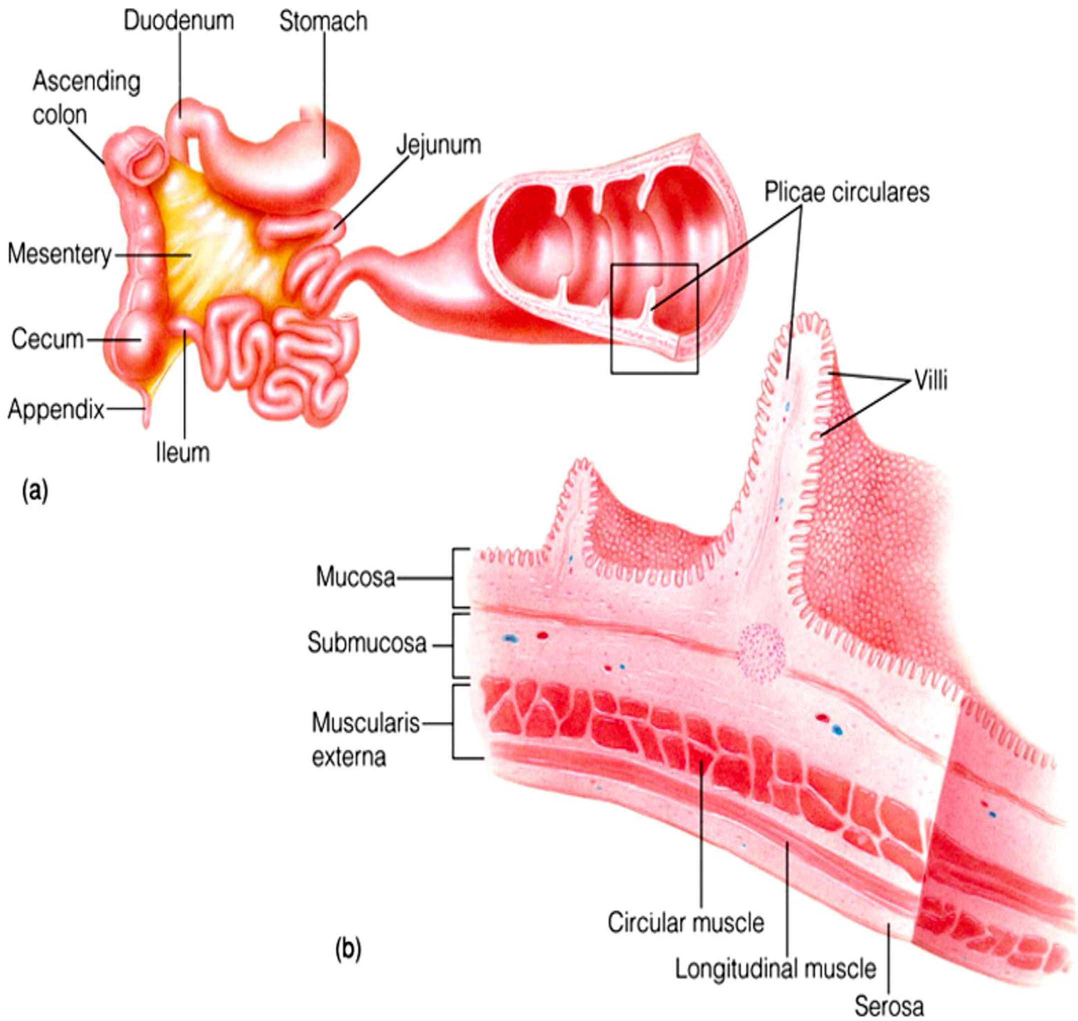


Figure (7).

Each villus is covered with columnar epithelial cells interspersed with goblet cells .Epithelial cells at tips of villi are exfoliated and replaced by mitosis in crypts of Lieberkuhn. Inside each villus are lymphocytes, capillaries, and central lacteal. see figure (8).

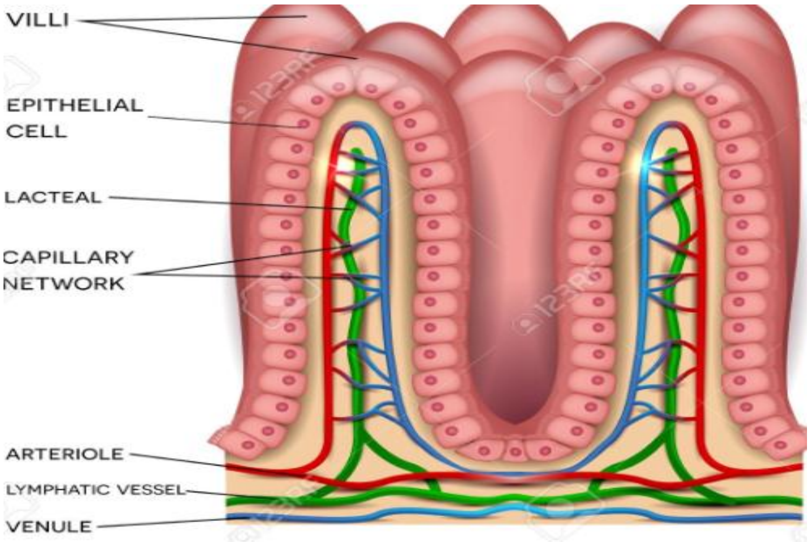


Figure (8)

Intestinal Enzymes: Attached to microvilli are brush border enzymes that are not secreted into lumen but enzyme active sites are exposed to chime**.**

Types	**Enzyme**	**Comments**
Disaccharides	**Sucrase** **Maltase** **Lactase**	**Digest sucrose to glucose and fructose.** **Digest maltose to glucose** **Digest lactose to glucose And galactose**
Peptidase	**Amino peptidase** **Enterokinase**	**Products free amino acids, di and tripeptidase** **Activates trypsin**
Phosphatase	**Ca +2, Mg +2, At pase** **Alkaline phosphatase**	**Needed for absorption of dietary calcium , enzyme activity regulated by v D.** **Remove phosphate groups from organic , enzyme activity regulated by v D.**

Intestinal Contractions and Motility : 2 major types of contractions occur in SI:

1- Peristalsis is weak and slow and occurs mostly because pressure at pyloric end is greater than at distal end.

2-Segmentation is major contractile activity of SI Its contraction of circular smooth muscle to mix chyme (shown in figure 8).

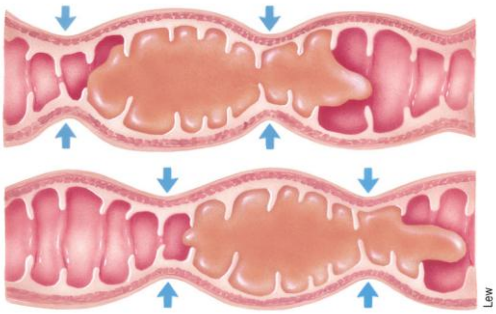
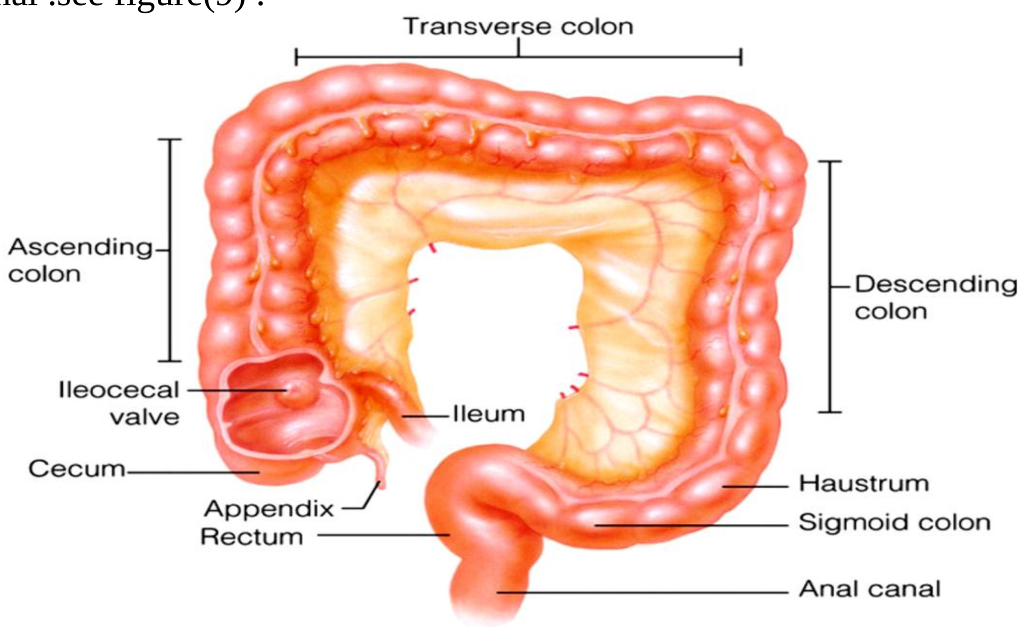


Figure (8) Segmentation in SI

<u>Large Intestine (LI)</u> : Has no digestive function but absorbs H2O, electrolytes, B and K vitamins, and folic acid .Internal surface has no villi or crypts and is not very elaborate and contains large population of microflora 1013 to 1014 commensal bacteria of 400 species which produce folic acid and vitamin K and ferment indigestible food to produce fatty acids and reduce ability of pathogenic bacteria to infect LI ,antibiotics can negatively affect commensals. LI extends from ileocecal valve at end of SI to anus .Outer surface of LI bulges to form pouches (haustra) ,Chyme from SI enters cecum, then passes to ascending colon, transverse colon, descending colon, sigmoid colon, rectum, and anal canal .see figure(9) .



<u>Structure of Liver</u> : Liver is the largest internal organ, hepatocytes form hepatic plates that are 1–2 cells thick Plates are separated by sinusoids which are fenestrated and permeable even to proteins and contain phagocytic Kupffer cells. A damaged liver can regenerate itself from mitosis of surviving hepatocytes In some cases, such as alcohol abuse or viral hepatitis, regeneration does not occur and can lead to liver fibrosis and ultimately cirrhosis

Hepatic Portal System:

Food absorbed in SI is delivered first to live .Capillaries in digestive tract drain into the hepatic portal vein which carries blood to liver and hepatic vein drains liver .Liver also receives blood from the hepatic artery(figure 10).

Liver Lobules are functional units formed by hepatic plates ,in middle of each is a central vein and at edge of each lobule are branches of hepatic portal vein and artery which open into sinusoids . Bile is secreted by hepatocytes in bile canaliculi and empty into bile ducts which flow into hepatic ducts that carry bile away from liver .

Enterohepatic Circulation :

Is recirculation of compounds between liver and intestine .Many compounds are released in bile, reabsorbed in SI, and returned to liver to be recycled .Liver excretes drug metabolites into bile to pass out in feces.

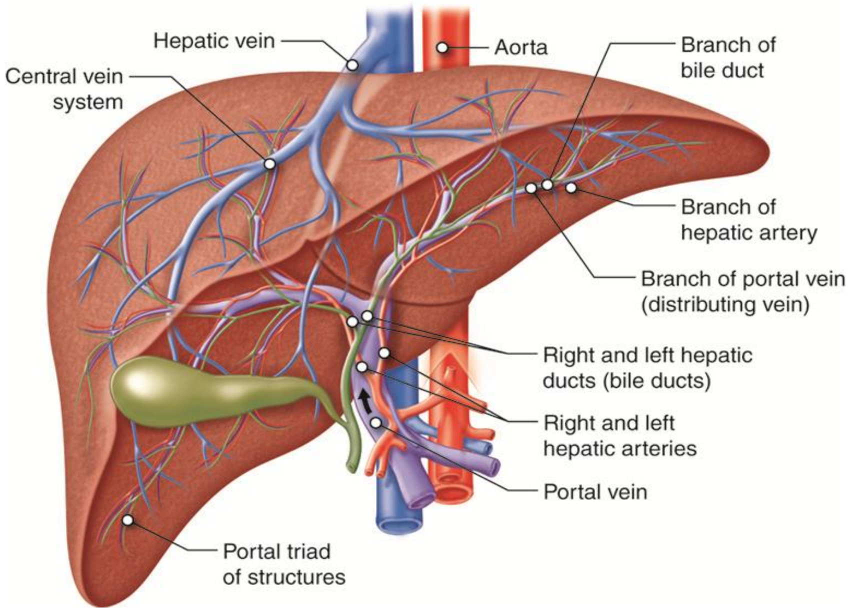


Figure (10) structure of liver

Content of Bile and Bile Release into Small Intestine

A. Content of Bile (made in Liver, released by Gall Bladder): bile consist of bile salts, bile pigments, cholesterol neutral fats, phospholipids and electrolytes .Bile salts are derivatives of cholesterol (cholic acid, chenodeoxycholic acid) its emulsify fats (separate fats into tiny droplets for digestion & absorption) ,bile salts reabsorbed in distal small intestine

to liver via hepatic portal blood and then resecreted as bile from gall bladder this process named enterohepatic circulation.
Bile pigment (bilirubin) is waste product of heme from broken-down erythrocytes ,urobilinogen is breakdown product of bilirubin, causes darker coloration of feces.

B. Regulation of Bile Release to Small Intestine

1. hepatocytes - cells of the liver that produce 0.5-1.0 liters of bile each day.
2. parasympathetic - stimulates gall bladder release.
3. cholecystokinin (CCK) - hormone released by cells of the mucosa of the duodenum.

acidic, fatty chyme enters duodenum →
duodenal mucosa secretes CCK →

a. gall bladder contracts to release bile.
b. pancreas secretes pancreatic juices.
c. hepatopancreatic sphincter opens.

4. gallstones - crystallized formation of cholesterol and salts, causing obstruction of bile release.

<u>Composition of Pancreatic Juice and Regulation of Secretion</u>

A. Composition of Pancreatic Juice.

1. 1.2 - 1.5 liters per day.
2. water and electrolytes (mainly bicarbonate ions).
3. enzymes - precursors and active digestive forms.

a. trypsinogen ------> trypsin
enterokinase

b. procarboxypeptidase --------> carboxypeptidase
trypsin

chymotrypsinogen --------> chymotrypsin
trypsin

c. amylase (carbohydrates), lipases (fats), nucleases (nucleic acids)

B. Regulation of Pancreatic Secretion.

1. parasympathetic causes release during cephalic and gastric phases of gastric secretion.
2. secretin - hormone that causes release of "bicarbonate-rich" pancreatic juices in response to the presence of HCl.
3. cholecystokinin - hormone that causes release of "enzyme-rich" pancreatic juice in response to the presence of proteins and fats.

Digestive Processes of the Small Intestine

A. Optimal Conditions for Digestion & Absorption.

1. pancreatic juice & bile - enzymes, emulsifying fats, and pH are essential for proper intestinal processes
2. small intestine is PRIMARY site for absorption of nutrients into the cardiovascular system.

B. Movement in the Small Intestine.

1. segmentation - longitudinal flow of chyme through the tube (duodenum -> ileum).
2. migrating mobility complex - activity that moves the chyme from the ileum to the cecum through the ileocecal valve.

Digestive Processes of the Large Intestine

A. Bacterial Flora.

1. digest remaining carbohydrates.
2. responsible for producing gas (flatus).
3. synthesize & complex B vitamins and vitamin K.

B. Digestion and Absorption.

1. reclaim most of the water.
2. reclaim some of the electrolytes (Na^+ and Cl^-).

C. Motility of the Large Intestine.

1.haustral contractions - slow acting segmental motion; moves chyme from one segment to next.
2. mass movements - peristaltic waves that move food to the rectum during/after eating:
diverticula - herniation of the mucosa through the wall of the colon (sigmoid colon).

D. Defecation

1. defecation reflex when feces (stool) enters rectum, spinal

cord reflex is triggered.
a. internal sphincter (involuntary).
b. external sphincter (voluntary).

2. Valsalva's maneuver - contraction of diaphragm and abdominal muscles to increase pressure for defecation.
3. diarrhea - too much water in the stool.

4. constipation - insufficient water or fiber.

Chemical Digestion

A. Enzymatic Hydrolysis ("water" "breaking").

1. hydrolysis - a water molecule is added between two "monomers" of a complex organic molecule in order break it down into its component parts.

B. Carbohydrate Digestion.

1. monosaccharides - "monomers" such as glucose, fructose, and galactose.
2. disaccharides - sucrose (table sugar), lactose (milk sugar), and maltose (grain sugar).
3. polysaccharides - starch (grains), glycogen (muscle).
4. carbohydrate hydrolyzing enzymes.
   a. salivary amylase - produces "oligosaccharides"
   b. pancreatic amylase - in small intestine.
   c. intestinal enzymes - dextranase & glucoamylase (> 3 sugars), maltase, sucrase, and lactase.
5. lactose intolerance - decreased ability to digest lactose in the diet (use "lactase" supplements).

C. Protein Digestion.

1. amino acids - the "monomer" components of protein.
2. stomach - pepsinogen --------> pepsin (low pH).
3. small intestine.

a. enzymes that cleave throughout the protein.

trypsinogen ----------> trypsin
chymotrypsinogen -----> chymotrypsin

b. carboxypeptidase (carboxyl end of protein).

c. aminopeptidase, dipeptidase (amino end).

D. Lipid (Fat) Digestion.

1. lipid structure - glycerol + 3 triglycerides.
2. lipases - enzymes that break down lipids.
3. bile salts - "emulsify" fats in 1 micron "micelles".

E. Nucleic Acid Digestion.

pancreatic nucleases - break down DNA and RNA

<u>Absorption of Nutrients</u>

A. General Features

1. transepithelial transport - nutrients must pass across the epithelial lining of the small intestine.

2. active transport - most nutrients must be transported across membrane using ATP of the cells.

B. Carbohydrate Absorption

1. facilitated diffusion - glucose and galactose (coupled with active transport of Na^+)

   a. "carrier molecule" has binding sites for both sugar and Na^+; relies on Na^+ gradient

C. Protein (Amino Acid) Absorption

1. facilitated diffusion - amino acids and small peptides (coupled with Na+ active transport)

   a. "carrier molecule" has binding sites for both amino acid and Na+; relies on Na+ gradient

2. food allergies - absorption of proteins in infant gut causes early immune reaction.

D. Lipid Absorption

1. micelles - tiny balls of fats that result from bile salt emulsification and "lecithin".

   a. contain cholesterol and fat-soluble vitamins.
   b. diffuse through lipid bilayer of membrane.
   c. chylomicrons - micelles combined with associated proteins within the cell; enter the lacteals of the lymphatic system.

E. Nucleic Acid Absorption

1. pentoses, nitrogen bases, phosphates - absorbed by similar processes as sugars and amino acids.

F. Vitamin Absorption

1. fat soluble - Vitamins A, D, E, K are absorbed by epithelial cells along with lipid micelles.
   a. OLESTRA - will carry fat-soluble vitamins out in feces with it.

2. water soluble - Vitamins B & C absorbed by diffusion.

3. Vitamin B_{12} - large and electrically charged, must bind with "intrinsic factor" before being taken into the cell by endocytosis.

G. Electrolyte Absorption

1. Fe and Ca - primarily absorbed in small intestine.

   a. ferritin - sequesters Fe in intestinal cells.
   b. transferrin - transfers Fe into circulation when need is present (menstruation).
   c. Vitamin D - facilitates Ca absorption.

2. Na - exchanged for sugars and amino acids.

3. Cl - absorbed into cells and exchanged for HCO_3^-.

4. K - absorbed into cells due to osmotic gradients.

H. Water Absorption

1. small intestine - 95% of water absorbed by small intestine following transport of solutes.
2. large intestine - absorbs remaining water before moving the chyme on to the rectum.

Malabsorption of Nutrients

1. impairment of bile or pancreatic juice release.
2. infections of the intestinal mucosa.
3. gluten enteropathy - "gluten" protein in grains damages the mucosa of the intestines.

Physiology of White blood cells (WBCs)

White blood cells (WBCs) or leukocytes :- are the colorless and nucleated formed elements of blood and its Mobile units of the body's resistance to infection (defense mechanism) formed in the bone marrow and some in the lymph nodes. leuko is derived from Greek word leukos = white).

Compared between WBCs and RBCs

WBCs differ from RBCs in many aspects. The differences between WBCs and RBCs are given in Table 1.
1. Larger in size.
2. Irregular in shape.
3. Nucleated.
4. Many types.
5. Granules are present in some type of WBCs.
6. Lifespan is shorter.

General structure and functions

1- protection from microbes , parasites , toxins , cancer
2- 1% of blood volume , 4-11,000 per cubic mm blood
3- Diapedesis – can slip between capillary wall
4- Amoeboid motion – movement through the body
5- Chemotaxis – moving in direction of a chemical substance
6- Leukocytosis – increased WBC count in response to bacteria / viral infection
7- Granulocytes – contain membrane – bound granules (neutrophil, eosinophil , basophil)
8- a granulocytes – no membrane bound granules (monocyte & lymphocyte)

- **Granulocytes** – granules in cytoplasm can be stained with wrights´ , bilobar nuclei , 10 – 14 micron diameter, all are phagocytes cells (engulf material)

1- Neutrophils : destroy and ingest bacteria & fungi (polymorphonuclear leuks ,polys)

a- most numerous WBC in human and some animal

b- the granules basophilic (blue) & acidophilic (red)

c- defenses – antibiotic – like proteins (granules) d- polymorphonuclear – many lobed nuclei, The number of lobes in the nucleus depends upon the age of cell.

e- causes analysis of infecting bacteria / fungi

f- high poly count = likely infection

g- In poultry there is no neutrophils but heterophils.
h- The neutrophils are ameboid in nature.

Feature	WBCs	RBCs
Color	Colorless	Red
Number	Less: 4,000 to 11,000/cu mm	More: 4.5 to 5.5 million/cu mm
Size	Larger Maximum diameter = 18 μ	Smaller Maximum diameter = 7.4 μ
Shape	Irregular	Disk-shaped and biconcave
Nucleus	Present	Absent
Granules	Present in some types	Absent
Types	Many types	Only one type
Lifespan	Shorter ½ to 15 days	Longer 120 days

”

TABLE 1: Differences between WBCs and RBCs

2- Eosinophils – Eosinophils have coarse (larger) granules in the cytoplasm lead attack against parasitic worms.

a- only 1- 4% of all leukocytes.

b- two – lobed , purplish nucleus.

c- acidophilic (red) granules with digest enzymes.

d- phagocytose antigen & antigen / antibody complex.

e- inactivate chemicals released during allergies.

f- Diameter of the cell varies between 10 and 14 µ.

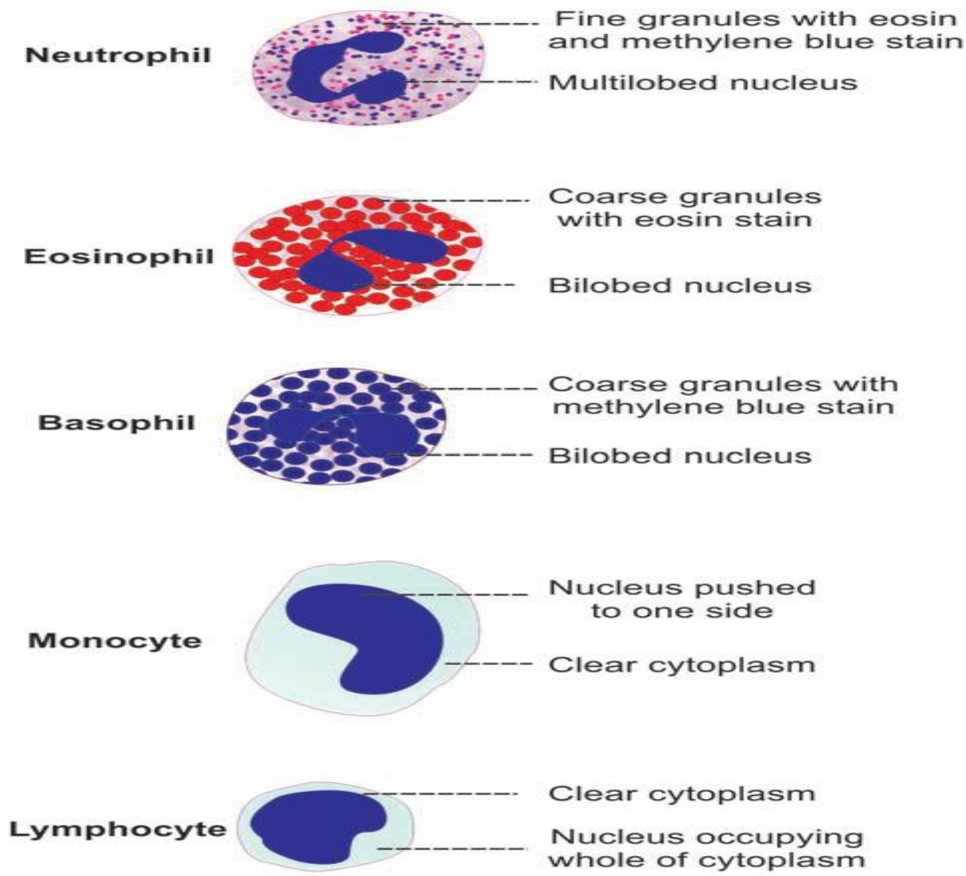


FIGURE 1: Different white blood cells

3- basophils – release histamine which causes inflammation , vasodilution , attraction of WBCs.

a- rarest of all leukocytes (0.5%).

b- deep purple U or S shaped nucleus.

c- basophilic (blue) granules with histamine.

d- related to mast cells of connective tissue.

e- both release histamine with IgE signal.

f- anti histamine – blocks the action of histamine in response to infection or allergic antigen.

g- Diameter of the cell is 8 to 10 µ.

- **A granulocytes** – WBCs without granules in cytoplasm.

1- Lymphocytes – two types of lymphocytes

A- T lymphocytes – (thymus) respond against virus infected cells and tumor cells
B- B lymphocytes – (bone) differentiate in to different plasma cells which each produce antibodies against different antigens
C- Lymphocytes primarily in lymphoid tissues
D- Very large (purple) nucleus
E- Small lymphocytes in blood (5-8 microns)
F- Larger lymphocytes in lymph organs (10 – 17mic)

2- Monocytes – differentiate to become macrophages , serious appetites for infectious microbes

A- largest of all leukocytes (18 microns)

B- dark purple , kidney shaped nucleus

TABLE 16.2: Diameter and lifespan of WBCs

WBC	Diameter (μ)	Lifespan (days)
Neutrophils	10 to 12	2 to 5
Eosinophils	10 to 14	7 to 12
Basophils	8 to 10	12 to 15
Monocytes	14 to 18	2 to 5
Lymphocytes	7 to 12	½ to 1

”

*** leukopoiesis and colony stimulating factors (CSFs)**

1- leucopoiesis : is the production , differentiation and development of WBC.

2- colony stimulating factors (CSFs): is hematopoietic hormones that promote leucopoiesis produced by macrophages and T lymphocytes

3- leucopoiesis – all cells derived from hemocytoblast(figure 2)

1- myeloid stem cell

Myeloblast monoblast
Promyelocyte promonocyte
Metamyelocyte monocyte
Band cell (macrophages)
(3 month lifespan)

Eosiophil }
Neutrophil} (0.5 to 9 day lifespan)
basophil}

2- lymphocyte stem cell

lymph oblast
prolymphocyte
lymphocyte
(B- cell → plasma cell , memory cells,T-cells)
(days – decades lifespan)

*** Disorders of leukocytes**

1- **leucopenia :** it is abnormally low WBC count occur in HIV , glucocorticoids & chemotherapy.
2- **leukemia :** it is a cancerous condition of line of WBCs characterized by anemia , fever , weight loss . bone pain then death from internal hemorrhage or infection . chemotherapy & radiation therapy used to treat there are many types:

a- myelocytic leukemia (myelocytes)
b- lymphocytic leukemia (lymphocytes)
c- acute leukemia – cancer spreads rapidly
d- chronic leukemia – cancer progresses slowly

physiology of platelets

Platelets or thrombocytes are the formed elements of blood. These formed elements of blood are considered to be the fragments of cytoplasm.

General characteristics

1- colorless, non-nucleated, very small , 2-4 microns in diameter
2- approximately 250 – 500,000 per cubic millimeter
3- essential for clotting of damaged vasculature
4- thrombopoietin – regulates platelet production
5- Volume : 7.5 cu μ (7 to 8 cu μ).

6- platelets are of several shapes, spherical, or rod-shaped and become oval or disk-shaped when inactivated.
7- Normal platelet count is 2,50,000/cu mm of blood. It ranges between 2,00,000 and 4,00,000/cu mm of blood.
8- Average lifespan of platelets is 10 days.

Structure and composition

1. Cell membrane or surface membrane
2. Microtubules
3. Cytoplasm.

* Cell membrane of platelet contains lipids in the form of phospholipids, cholesterol and glycolipids, carbohydrates as glycocalyx and glycoproteins and proteins. Of these substances, glycoproteins and phospholipids are functionally important.

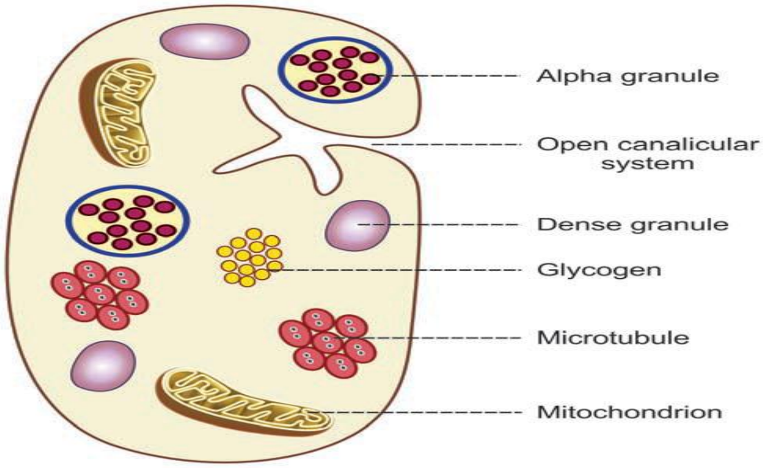
- **Glycoproteins** prevent the adherence of platelets to normal endothelium, but accelerate the adherence of platelets to collagen and damaged endothelium in ruptured blood vessels. Glycoproteins also form the receptors for adenosine diphosphate (ADP) and thrombin.
- **Phospholipids** accelerate the clotting reactions. The phospholipids form the precursors of thromboxane A2 and other prostaglandin-related substances.

Platelet Granules:-

Granules present in cytoplasm of platelets are of two types:
1. Alpha granules
2. Dense granules.

Alpha granules	Dense granules
Clotting factors: fibrinogen, V and XIII	Nucleotides
Platelet-derived growth factor	Serotonin
Vascular endothelial growth factor	Phospholipid
Basic fibroblast growth factor	Calcium
Endostatin	Lysosomes
Thrombospondin	

Substances present in platelet granules



Platelet under electron microscope

*** Formation of platelets:**

1. Hemocytoblast 2. Myeloid stem cell 3. Megakaryoblast

4. Promegakaryocyte 5. Megakaryocyte (large multilobed nucleus).

6. Platelets (a nucleated parts of megakaryocyte cytoplasm).

Properties of platelets

1. Adhesiveness 2. Aggregation 3. Agglutination.

Hemostasis (stoppage of blood flow after damage)

Hemostasis : Is cessation of bleeding or as arrest or stoppage of bleeding.

*** General stages of hemostasis**

1- Promoted by reactions initiated by vessel injury:

2- Vasoconstriction restricts blood flow to area.

3- Platelet plug forms.

4- Plug and surroundings are infiltrated by web of fibrin , forming clot

***Blood Clot: -** The clot is composed of a mesh work of fibrin fibers running in all directions and entrapping blood cells, platelets, and plasma. The fibrin fibers also adhere to damaged surfaces of blood vessels; therefore, the blood clot becomes adherent to any vascular opening and thereby prevents further blood loss.

*Role of Platelets

 Platelets don't stick to intact endothelium because of presence of **prostacyclin** (PGI2--a prostaglandin) and **NO**

1- Keep clots from forming and are vasodilators.

2- Damage to endothelium allows platelets to bind to exposed collagen

3- **Von Willebrand factor:** increases bond by binding to both collagen and platelets.

4- Platelets stick to collagen and release **ADP**, **serotonin**, and thromboxane **A2 = platelet release Reaction.**

5- Serotonin and thromboxane A2 stimulate vasoconstriction, reducing blood flow to wound.

6- ADP and thromboxane A2 cause other platelets to become sticky and attach and undergo platelet release reaction. This continues until **platelet plug** is formed.

*Role of Fibrin

 Platelet plug becomes infiltrated by meshwork of fibrin.

 Clot now contains platelets, fibrin and trapped RBCs.

 Platelet plug undergoes **plug contraction** to form more compact plug.

Conversion of Fibrinogen to Fibrin

Can occur via 2 pathways: -

1- **Intrinsic pathway** clots damaged vessels and blood left in test tube

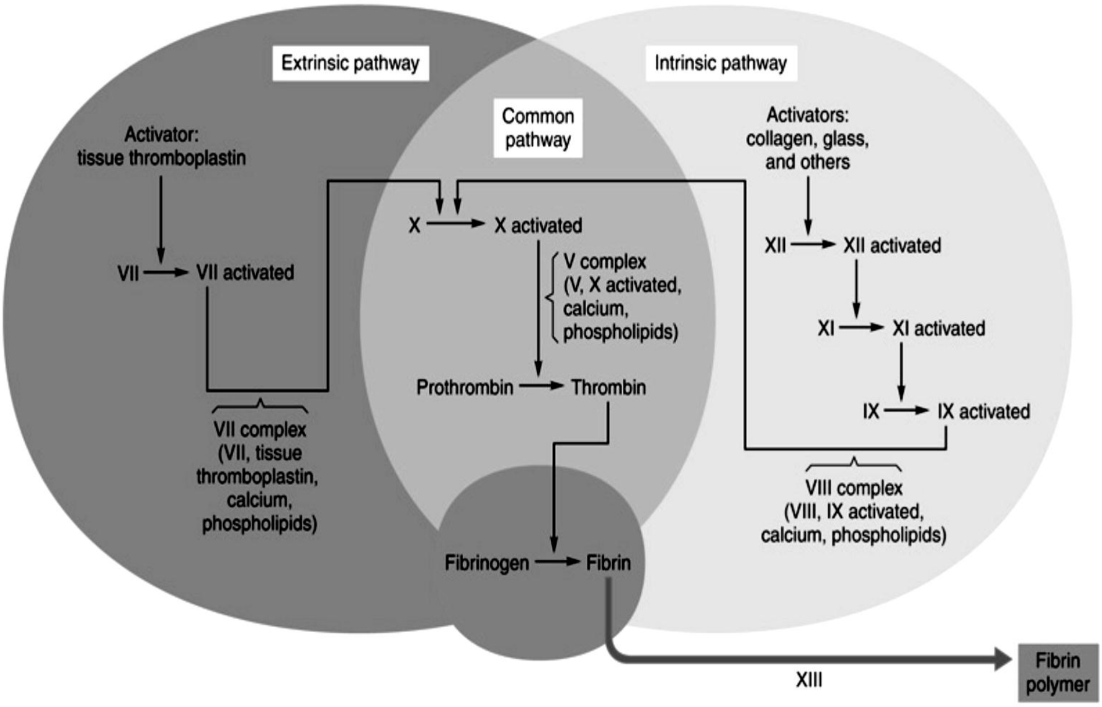
A- Initiated by exposure of blood to negatively charged surface of glass or blood vessel collagen.

B- This activates factor XII (a protease) which initiates a series of clotting factors.

 Ca^{2+} and phospholipids convert prothrombin to thrombin.

 Thrombin converts fibrinogen to fibrin ,polymerizes to form a mesh.

 Damage outside blood vessels releases tissue thromboplastin that triggers a clotting shortcut (= extrinsic pathway).



Factor	Name	Function	Pathway
I	**Fibrinogen**	**Converted to fibrin**	**Common**
II	**Prothrombin**	**Converted to thrombin(enzyme)**	**Common**
III	**Tissue thromboplastin**	**Cofactor**	**Extrinsic**
IV	**Calcium ions (Ca^{2+})**	**Cofactor**	**Intrinsic – Extrinsic and common**
V	**Proaccelerin**	**Cofactor**	**Common**
VII	**Proconvertin**	**Enzyme**	**Extrinsic**
VIII	**Antihemophilic factor**	**Cofactor**	**Intrinsic**
IX	**Plasma thromboplastin compenant, christma factor**	**Enzyme**	**Intrinsic**
X	**Stuart – prower factor**	**Enzyme**	**Common**
XI	**Plasma thromboplastin antecedent**	**Enzyme**	**Intrinsic**
XII	**Hageman factor**	**Enzyme**	**Intrinsic**
XIII	**Fibrin stabilizing factor**	**Enzyme**	**Common**

*** The plasma clotting factors**

* Dissolution of Clots

- When damage is repaired, activated factor XII causes activation of **kallikrein**
- Kallikrein converts **plasminogen** to plasmin
- Plasmin digests fibrin, dissolving clot

*Anticoagulants

- Clotting can be prevented by Ca^{+2} chelators (e.g. **sodium citrate** or **EDTA**)
- or **heparin** which activates **antithrombin III** (blocksn thrombin)
- **Coumarin** blocks clotting by inhibiting activation of **Vit K** , Vit K works indirectly by reducing Ca^{+2} availability.

Blood Types

*Reactions of Blood

When blood transfusions from one person to another were first attempted, immediate or delayed agglutination and hemolysis of the red blood cells often occurred, resulting in typical transfusion reactions that frequently led to death. Soon it was discovered that the bloods of different people have different antigenic and immune properties, so that antibodies in the plasma of one blood will react with antigens on the surfaces of the red cells of another blood type. If proper precautions are taken, one can determine ahead of time whether the antibodies and antigens present in the donor and recipient bloods will cause a transfusion reaction.

* O-A-B Blood Types

Two antigens—type A and type B—occur on the surfaces of the red blood cells.

In a large proportion of human beings. It is these antigens (also called agglutinogens because they often cause blood cell agglutination) that cause most blood transfusion reactions. Because of the way these agglutinogens are inherited, people may have neither of them on their cells, they may have one, or they may have both immediately.

* Major antigen group is ABO system

Type A blood has only A antigens

Type B has only B antigens

Type AB has both A and B antigens

Type O has neither A or B antigens

Blood Group	Antigens on RBCs	Antibodies in Serum	Genotypes
A	A	Anti-B	AA or AO
B	B	Anti-A	BB or BO
AB	A and B	Neither	AB
O	Neither	Anti-A and Anti-B	OO

People with Type A blood make antibodies to Type B RBCs, but not to Type A. Type B blood has antibodies to Type A RBCs but not to Type B . Type AB blood doesn't have antibodies to A or B therefore called "universal recipient".(can recipient all types of blood) Type O has antibodies to both Type A and B therefore called "universal donor"(can´t recipient all types of blood except O type but donor to all types) . If incompatible blood types are mixed, antibodies will cause mixture to agglutinate

*Rh Factor

Is another type of antigen found on RBCs called (D) antigen, if this antigen found in blood , the type of blood is Rh^+. If does not found the type of blood is Rh^- .

* Rh Blood Types

Along with the O-A-B blood type system, the Rh blood type system is also important when transfusing blood. The major difference between the O-A-B system and the Rh system is the following :

In the O-A-B system, the plasma agglutinins responsible for causing transfusion reactions develop immediately, whereas in the Rh system, spontaneous agglutinins almost never occur. Instead, the person must first be massively exposed to an Rh antigen, such as by transfusion of blood containing the Rh antigen, before enough agglutinins to cause a significant transfusion reaction will develop. Can cause problems when Rh^- mother has Rh^+ babies At birth, mother may be exposed to Rh+ blood of fetus In later pregnancies mom produces Rh antibodies In Erythroblastosis fetalis, Rh antibodies from mom cross placenta and combine with Rh+ antigens oan fetal blood cells causing hemolysis of fetal RBCs.

Physiology of Red blood cells (RBCs)

Red blood cells (RBCs) :- are also known as erythrocytes (erythros = red). Normally, the RBCs are **non-nucleated**, **disk shaped** and **flat biconcave** . Central portion is thinner and periphery is thicker. The biconcave contour of RBCs has some mechanical and functional advantages.

Diameter : 7.2 μ (6.9 to 7.4 μ).

Average volume : 90-95 mm^3.

Specific gravity of RBC : 1.092 to 1.101.

Flexible

Normal value :- RBC count ranges between 4 and 5.5 million/cu mm of blood. In adult males, it is 5 million/cu mm and in adult females, it is 4.5 million/cu mm.

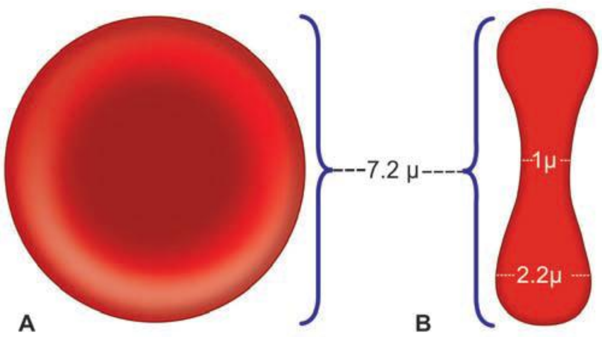


figure 1: Dimensions of RBC.

A. Surface view, B. Sectioned view.

Functions of red blood cells

Major function of RBCs is the transport of respiratory gases. Following are the functions of RBCs:

1. Transport of Oxygen from the Lungs to the Tissues
2. Transport of Carbon Dioxide from the Tissues to the Lungs
3. Buffering Action in Blood
4. In Blood Group Determination
5. Regulation of blood flow
6. Regulation of blood pressure , how? Nitric oxide (NO)released by endothelial cells bind with Hb . then Hb under condition releases NO causes vasodilation and increased blood flow and decreased BP.

Lifespan of red blood cells

- Erythrocytes lack a nucleus and mitochondria

  *They get energy from anaerobic respiration .

  *More surface area / volume allows the RBCs to accommodate change through the capillaries.

- Importance of the unique shape : provides an increased surface area through which gas can diffuse.
- Lifespan about: 120 days.

Hematopoiesis

All cells arise from same blood stem cells (pluripotent hematopoietic stem cells) . Hematopoiesis involves the proliferation , maturation and destruction of blood cells. Hematopoiesis in bone marrow is called **medullary hematopoiesis**. While in other area is called **extramedullary hematopoiesis.**

Erythropoiesis

The production of new RBCs to replace the old and died ones. It is stimulated by erythropoietin hormone.in the adults , all the RBCs are produced in marrow with a rate of 2.5 million RBCs/ sec. old RBCs removed from blood by phagocytic cells in liver, spleen and bone marrow. iron of the destroyed RBCs recycled back into hemoglobin production.

- Early few weeks of embryo nucleated RBCs are formed in yolk sac.
- Middle trimester mainly in liver, spleen and lymph nodes.
- Last month RBCs are formed in bone marrow and all bones.
- bone marrow of flat bone continue to produce RBCs into adult life.
- Slaft of long bones stop to produced RBCs at puberty while epiphysis continued.

Hormonal control of RBCs production (major events) :

1. The kidney and liver tissues experience hypoxia.
2. These tissues release the hormone EPO.
3. EPO travel to bone marrow and stimulate production in RBCs.
4. Increasing in RBCs in the circulation rise O_2 carrying ability of the blood.
5. O_2 concentration in the kidney and liver↑ and the release of EPO ↓.

Erythropoietin

Erythropoietin is a glycoprotein with 165 amino acids.

Source of secretion

Major quantity of erythropoietin is secreted by **tubular epithelial cells of kidney (90%)**. A small quantity is also secreted from **liver and brain (10%). M wt. 34.000 D, T1/2 = 6-9hrs.**

Stimulant for secretion

Hypoxia is the stimulant for the secretion of erythropoietin.

Actions of Erythropoietin

Erythropoietin causes formation and release of new RBCs into circulation. After secretion, it takes 4 to 5 days to show the action.

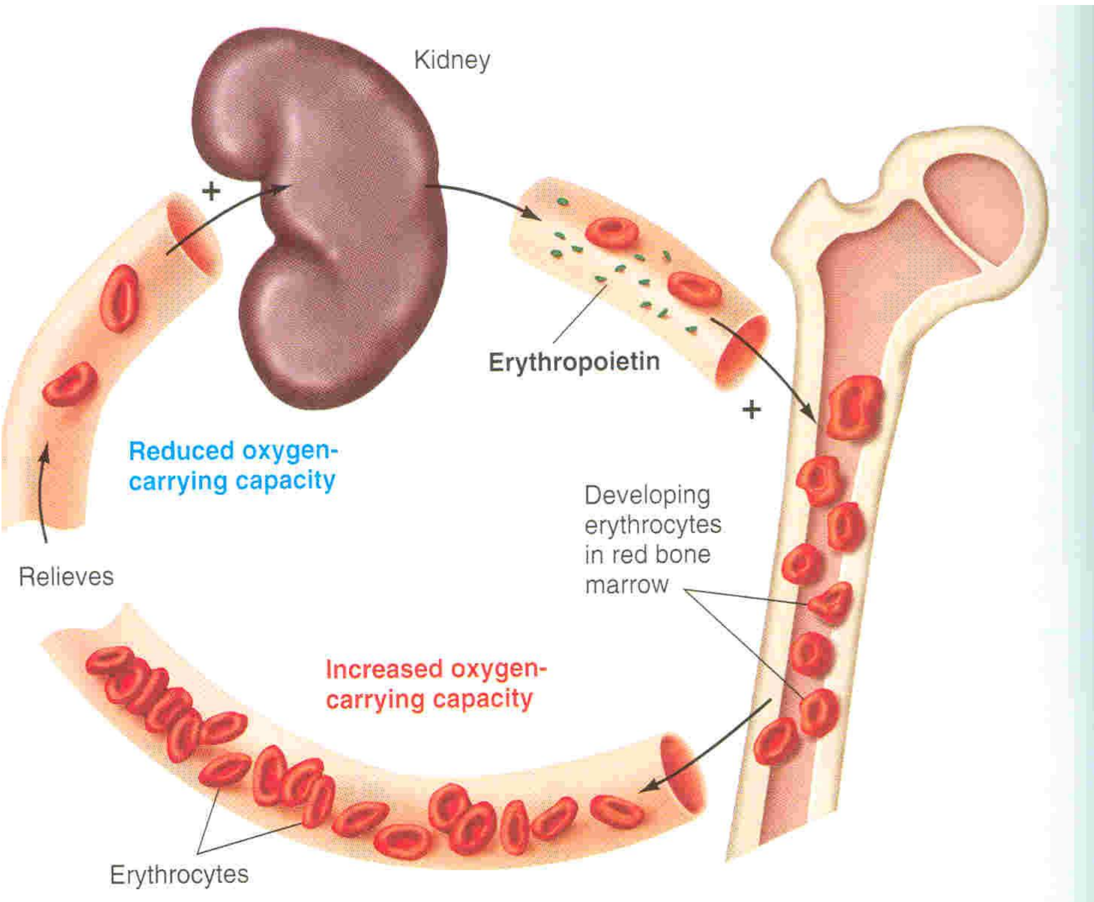
Erythropoietin promotes the following processes:

a. Production of proerythroblasts from CFU-E of the bone marrow**.**

b. Development of proerythroblasts into matured RBCs through the several stages – **early normoblast**, **intermediate normoblast**, **late normoblast** and **reticulocyte**.

c. Release of matured erythrocytes into blood. Even some reticulocytes (immature erythrocytes) are released along with matured RBCs.

Blood level of erythropoietin increases in anemia.



Effect of Erythropoietin

- Stimulates the proliferation and differentiation of the committed RBCs precursor.
- Accelerates hemoglobin synthesis.
- Shortens the period of RBCs development in the BM.

Stimulus : (Renal hypoxia and non-Renal hypoxia)

- Increased in EPO concentration after min- hrs. and max level after 24 hrs.
- After 3-5 days : ↑ RBCs numbers 10x.
- Other non-Renal hypoxia sensors act through : E, NE , PG and EPO production (+).
- Absence results in apoptosis (programmed cell death) of erythroid committed cells.

Hypoxia caused by : -

- Low RBCs count (anemia)
- Hemorrhage
- High altitude
- Prolonged heart failure
- Lung disease

Factors necessary for erythropoiesis

Development and maturation of erythrocytes require variety of factors, which are classified into three categories:

1. General factors
2. Maturation factors
3. Factors necessary for hemoglobin formation.

General factors

General factors necessary for erythropoiesis are:

i. Hormones : (Erythropoietin, Thyroxine, androgens, and growth hormone). But estrogen inhibits it.

ii. Proteins, amino acids , lipids and carbohydrates.

iii. Iron for hemoglobin synthesis.

iv. Vitamins : Vitamin B_{12} and folic acid for DNA synthesis.

v . cytokines.

Stages of erythropoiesis

Various stages between CFU-E cells and matured RBCs are : -

1. Proerythroblast
2. Early normoblast
3. Intermediate normoblast.
4. Late normoblast
5. Reticulocyte

6. Matured erythrocyte.

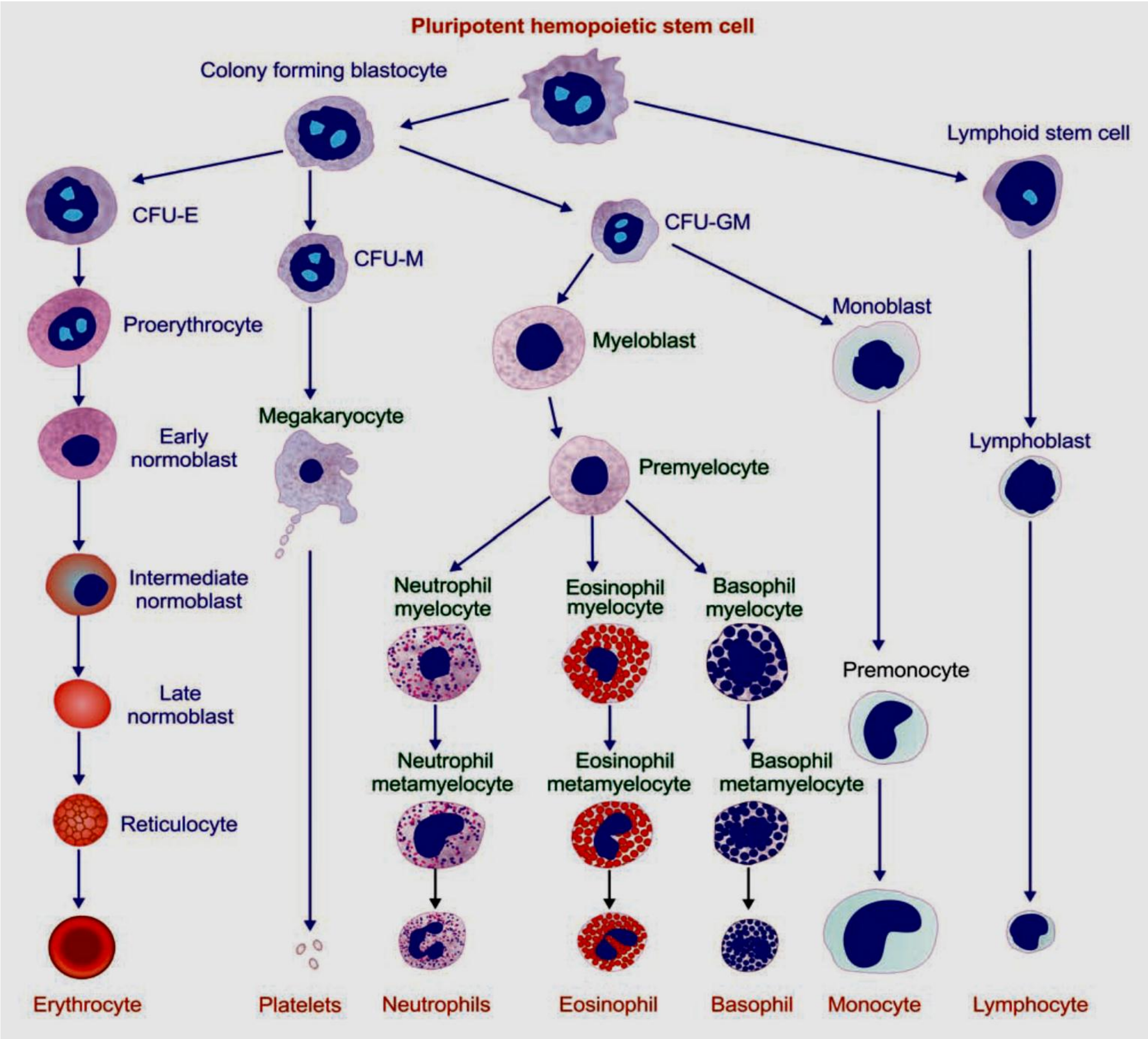


figure 2: Stages of erythropoiesis. CFU-E = Colony forming unit-erythrocyte, CFU-M = Colony forming unit-megakaryocyte, CFU-GM = Colony forming unit-granulocyte/monocyte.

Vitamin B12 and folic acid

Vitamin B12, intrinsic factor and folic acid are necessary for the maturation of RBCs. Vitamin B12 is called **extrinsic factor** since it is obtained mostly from diet. Its absorption from intestine requires the presence of **intrinsic factor of Castle.** Vitamin B12 is stored mostly in liver and in small quantity in muscle. When necessary, it is transported to the bone marrow to promote maturation of RBCs. It is also produced in the large intestine by the intestinal flora.

*Action

Vitamin B12 is essential for synthesis of DNA in RBCs. Its deficiency leads to failure in maturation of the cell and reduction in the cell division. Also, the cells are larger with fragile and weak cell membrane resulting in macrocytic anemia.
Deficiency of vitamin B12 causes **pernicious anemia.** So, vitamin B12 is called antipernicious factor.

*Folic Acid

Folic acid is also essential for maturation. It is required for the synthesis of DNA. In the absence of folic acid, the synthesis of DNA decreases causing failure of maturation. This leads to anemia in which the cells are larger and appear in megaloblastic (proerythroblastic) stage. And, anemia due to folic acid deficiency is called **megaloblastic anemia.**

Importance of the erythropoiesis

- Maintain RBCs numbers remarkably constant.
- Replace the requirement in anemia if there is :-

(1)- decreased rate of erythropoiesis or increased rate of RBCs destruction.

(2)- decreased numbers of RBCs and Wight of Hb .

Regulation of erythropoiesis

- Neural : hypothalamus
- Hormonal: specific erythropoietin (kidneys).
- Non-specific: (+) androgens, thyroxin, GH, corticoids and (-) estrogen .

Hematocrit (Packed red Cell Volume or PCV)

Definition :- is fraction of the blood composed of RBC or part of blood volume occupied by packed RBC volume (pcv). **Values ~ 35% - 45% .**
Hematocrit is greatly related to the blood viscosity.
If we centrifuged blood in a calibrated (hematocrit tube) the heavier red cells settle to the bottom of the tube. The straw-colored plasma remains at the top.

Hemoglobin (Hb)

Hemoglobin (Hb) :- is the iron containing coloring matter of red blood cell (RBC). It is a chromoprotein forming 95% of dry weight of RBC and 30% to 34% of wet weight. Function of hemoglobin is to carry the respiratory gases, oxygen and carbon dioxide. It also acts as a buffer.

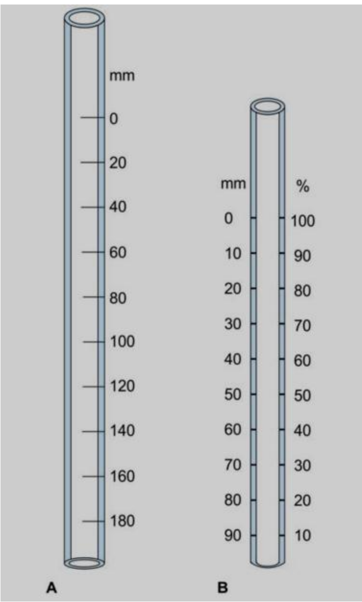
Molecular weight of hemoglobin is 68,000.

Types of normal hemoglobin

Hemoglobin is of two types:
1. Adult hemoglobin – HbA
2. Fetal hemoglobin – HbF

Replacement of fetal hemoglobin by adult hemoglobin starts immediately after birth. It is completed at about 10th to 12th week after birth. Both the types of hemoglobin differ from each other structurally and functionally.

Erythrocyte sedimentation rate (ESR) is the rate at which the erythrocytes settle down. Normally, the red blood cells (RBCs) remain suspended uniformly in circulation. This is called suspension stability of RBCs. If blood is mixed with an anticoagulant and allowed to stand on a vertical tube, the red cells settle



A. Westergren tube:
B. Wintrobe tube

down due to gravity with a supernatant layer of clear plasma. Determination of ESR is especially helpful in assessing the progress of patients treated for certain chronic inflammatory disorders such as:
1. Pulmonary tuberculosis
2. Rheumatoid arthritis
3. Polymyalgia rheumatic (inflammatory disease characterized by pain in shoulder and hip)
4. Temporal arteritis (inflammation of arteries of head).

Normal values of ESR

By Westergren Method

In males : 3 to 7 mm in 1 hour
In females : 5 to 9 mm in 1 hour
Infants : 0 to 2 mm in 1 hour

By Wintrobe Method

In males : 0 to 9 mm in 1 hour
In females : 0 to 15 mm in 1 hour
Infants : 0 to 5 mm in 1 hour

The factors influencing the ESR

Increased ESR

- Elevated fibrinogen (pregnancy)
- Decreased albumin concentration
- Anemia
- Macrocytic red cells

Decreased ESR

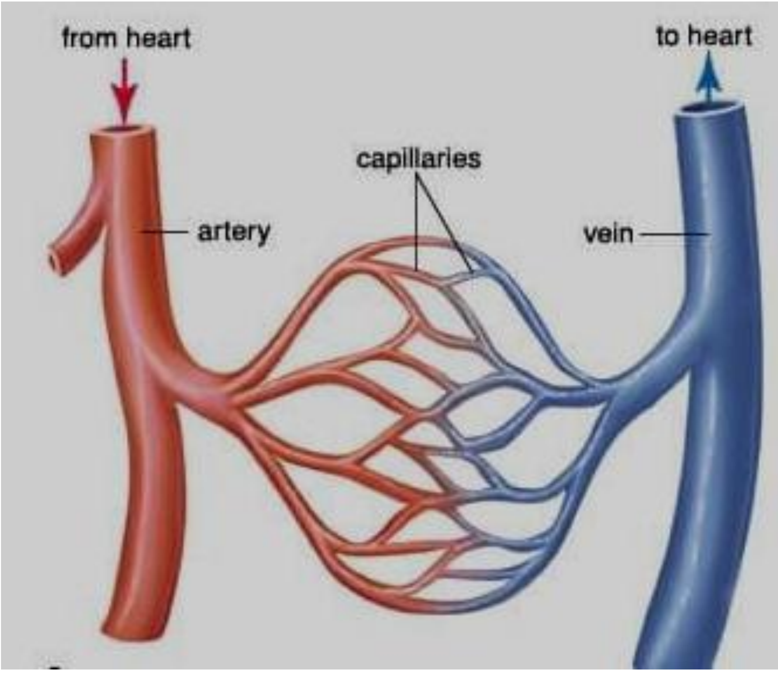
- Polycythemia
- RBCs disease with abnormal shape
- Hypofibrinogenemia

Major events in RBC destruction

1. **Formation of bilirubin in reticuloendothelial system (RES).**
2. **Uptake, conjugation and secretion of bilirubin by the liver.**
3. **Catabolism of bilirubin in the gut.**

Vascular system

Blood vessels: are the organ of the vascular system , they form a closed circuit of tubes that carries oxygenated blood from left ventricle to the circulation through the aorta and form the aorta to the arterioles and then finally the capillaries.

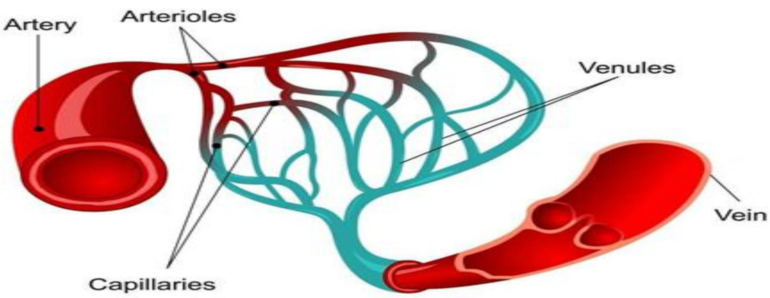


Types of blood vessels

1. **Arterial system** :(artery and arterioles) , the arterioles have a narrow lumen than arteries. The artery walls thick because the blood enters under pressure therefore the wall can be expand.
2. **Capillaries** : the Capillaries beds are network of small blood vessels present through the body. They are carried **25%** of the mount of blood . the wall them are thin layer to allowed the molecules such as oxygen , water and lipid can be pass through them by diffusion to enter the tissue . the blood flow slowly through the capillary.
3. **Veins and venules**: then returning the deoxygenated blood from the capillaries to the heart is occur through asset of collecting tubules called venules and the veins and then vena cave the right atrium.

*Most the blood volume found in the venous system about **70%.**

*Veins have low blood pressure compared to arteries and need to skeletal muscles to bring blood back to the heart.

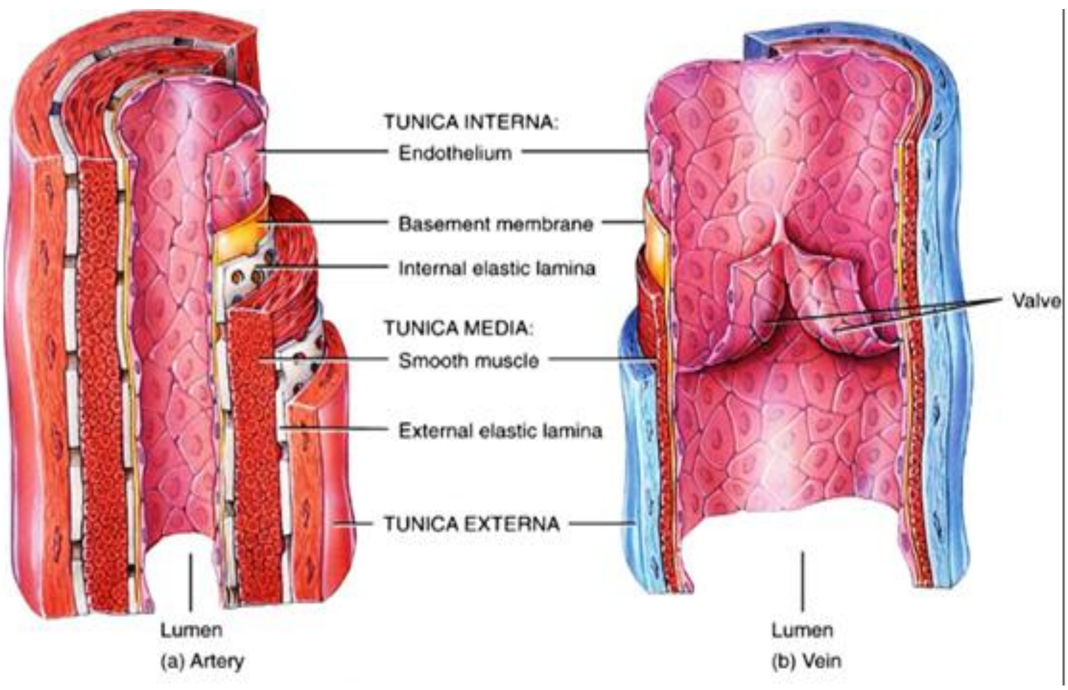


What are the venous valve?

- Most veins have one valve called **venous valve** to prevent backflow caused by the gravity.
- If the person standing still for long time or is bedridden , the blood accumulation in veins and can be caused varicose vein.

Structure of blood vessels wall:

- **The wall of arteries** : are thick wall that consist of three layers **:(1)** the inside layer is called the endothelium (tunica interna) **(2)** the middle is mostly smooth muscle (tunica media) **(3)**the outside layer is connective tissue (tunica externa).
- **The wall of capillaries** : are composed of single layer cells.
- **The wall of venus**: have the same layers the artery , differing only because a lake of smooth muscles in the inner layer and less connective tissue on outer layer.



Systemic circuit

A. Pulmonary circulation (Pulmonary circuit):

- The blood is pumped to the lungs from the right ventricle of the heart via Pulmonary artery.
- At lungs , oxygen in the alveoli diffuses to the capillary that surrounding the alveoli and Carbone dioxide inside the blood diffuses to the alveoli.
- As the result, blood is oxygenated which is then carried to the hearts left to the right atrium via Pulmonary veins.

B. Arterial circulation (Systemic circuit):

- They supplied oxygenated blood to the organ system.
- Oxygenated blood from lungs returned to the left atrium, then the ventricles contracts and pumps blood into the aorta.
- Systemic arteries split from the aorta and direct blood into the capillaries that surrounding the cells.
- Cells consume oxygen and nutrient and add the Carbone dioxide, wastes, enzymes and hormones.
- The vein deoxygenated blood from the capillary and return the blood to the right atrium.

C. **Hepatic circulation**:

The blood vessels carried the deoxygenated blood from the lower half of the body (stomach, intestine, pancreas and colon) to the right atrium of the heart via vena cave.

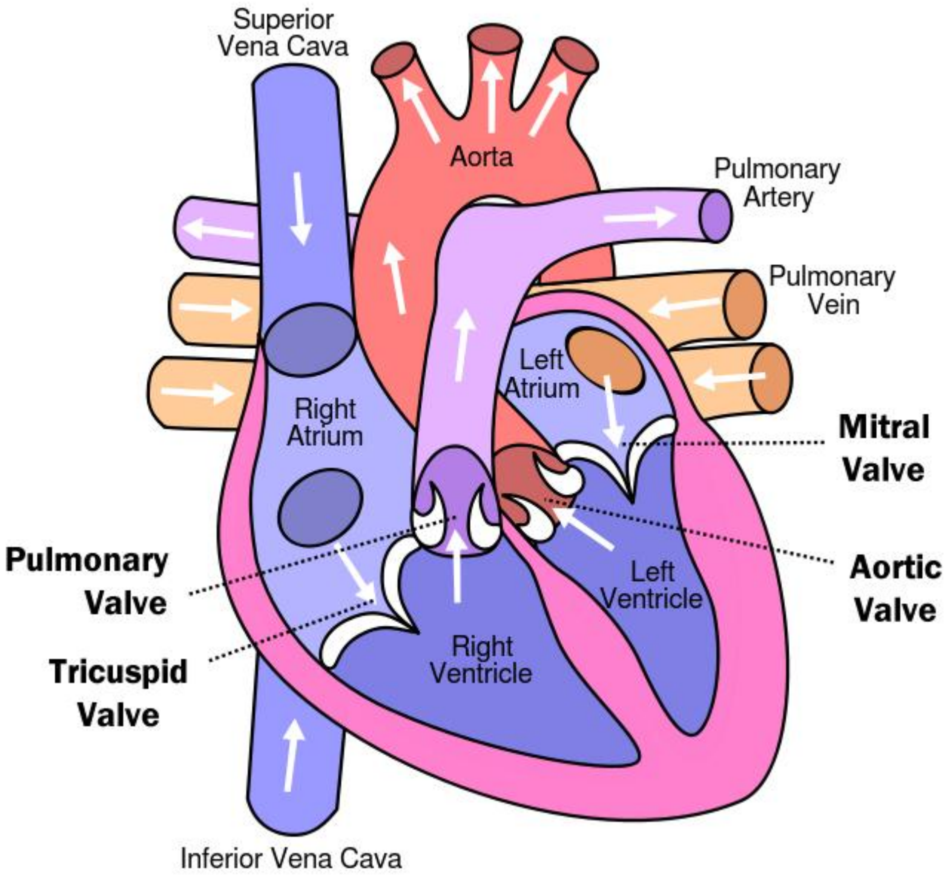
The Heart

Heart: is a hollow, muscular organ about the size of a fisit.it is responsible for pumping blood throughout the circulatory system. It is situated in the thoracic cavity between two lungs .

The heart for the average human will contract about 3 million times , never resting , never stopping to take break except for a fraction of a second between beats.

*It is made up of four chambers, two atria and two ventricles. The musculature of ventricles is thicker than that of atria. Force of contraction of heart depends upon the muscles.

Heart's chamber's:



1. **Atria**

There are two Atria on either side of the heart . on the Right side, it is holds blood oxygen. Right atrium is a thin walled and low pressure chamber. The left atrium holds that blood oxygenated and is ready to be sent to the body.

2. **ventricle**

the ventricle is a heart chumber which collects blood from an atrium and pumps it out of the heart. Ventricle have thicker walls than atria, because the ventricle needs to pump blood to the whole body. This leads to the common misconception that the heart lies on the left side of the body.

3. **Valves:**

The right atrium leading to the right ventricle, the left atrium leading to the left ventricle. There are two atrioventricular valve(AV) are a one way valve that ensures blood flow from atria to the ventricle. The right (AV) valve is called the tricuspid valve because it has three flaps. The left (AV) valve has two flaps is called bicuspid. It is also mitral valve.

Layers of wall of the heart

Heart is made up of three layers of tissues:

1. **Outer pericardium (epicardium)**
2. **Middle myocardium**
3. **Inner endocardium.**

„ **Pericardium**

It is thick, membranous sac that surrounding the heart. It is made up of two layers: fibrous pericardium and serious pericardium. The serious pericardium is divided into two layers(Outer parietal pericardium and Inner visceral pericardium) .

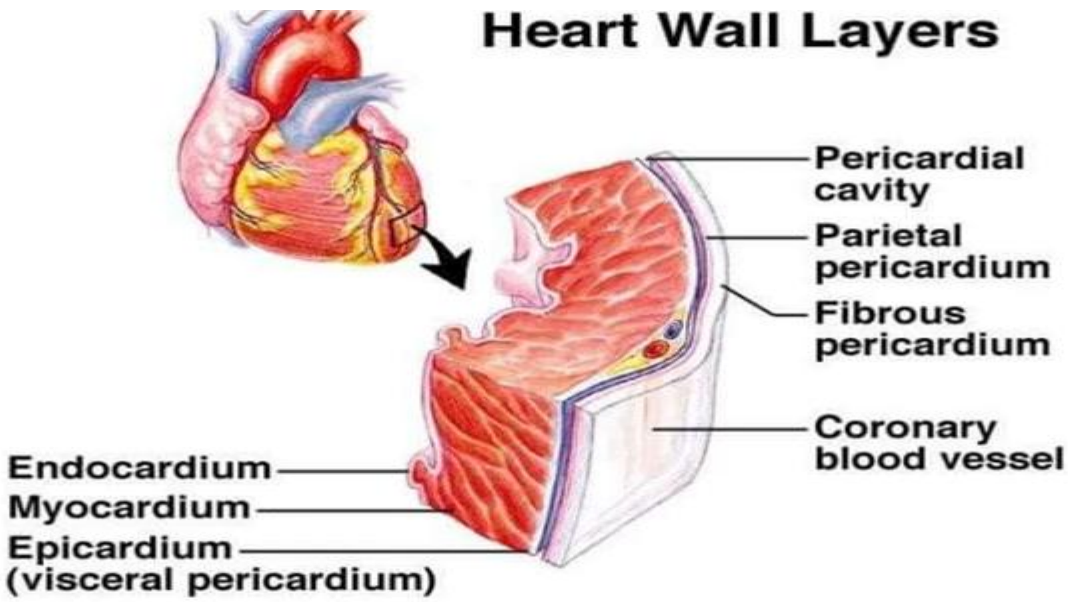
The space between the two layers is called pericardial cavity or pericardial space and it contains a thin film of fluid.

Myocardium

Myocardium it is active functionally which is cardiac muscle that is responsible for the pressure generated by each heart chamber during contraction. Thickness of Myocardium is different according parts of the heart, so the atrial Myocardium is thin while the ventricles Myocardium is thick , specially that the left ventricle which generated the highest pressure.

Endocardium

Endocardium is the visceral layer of heart wall which continues as endothelium of the blood vessels that consist connective tissue.



<u>Heart action</u>

The heart chamber's function in coordinated fashion. Their actions are regulated so that atria contract, called atrial systole, while ventricles relax, called ventricles diastole, then ventricles contract called ventricular systole while atria relax (atrial diastole) then the atria and ventricles both relax for a brief interval. This series of events constitutes a complete heartbeat, or cardiac cycle.

Cardiac cycle:

During a Cardiac cycle, the pressure within the heart chamber rise and falls. the pressure difference between atria and ventricles causes the AV- valve is open and the ventricles to fill.

- **Atrial systole :** when the atria contract , the AV- valve is open the blood is pushed into the ventricles, and ventricles pressure increased a bit more.
- **ventricular systole**: then, as the ventricles contract, ventricles pressure rises sharply, and as soon as the ventricles pressure exceeds atrial pressure, the AV- valve close.

-The atria are now relaxed and pressure in the atria is quite low, even lower than venous pressure. As the result, blood flow into the atria from the large attached vein. **<u>The ventricular are contracting , the atria are filling , already preparing for the next cardiac cycle.</u>**

Ventricular pressure continues to increase until it exceeds the pressure in the pulmonary trunk (right side) and aorta (left side). Then the semilunar valves is open , and blood is rejected from each Ventricular into these arteries.

General diastolic : Ventricular pressure begin to drop gradually even the ventricles begin to relax.

When Ventricular pressure is lower than the blood pressure in the aorta and the pulmonary trunk , the semilunar valves close. The

Ventricular continue to relax , this is lead to the A.V valves is opened , and the Ventricular begin to fill once more.