Lec-7- Physiology

- **Iron-deficiency anemia**

Iron deficiency occurs in two main forms: absolute or functional. Absolute arises when total body iron stores are low or exhausted; functional iron deficiency is a disorder in which total body iron stores are normal or increased, but the iron supply to the bone marrow is inadequate. Functional iron deficiency present in many acute and chronic inflammatory states,

*Hepcidin: the master regulator of iron homoeostasis-has a key role in pathogenesis.

Causes

(1) Blood loss is the most common cause of iron deficiency.
In adult men and postmenopausal women: Iron deficiency anemia is most likely due to chronic gastrointestinal blood loss which is usually secondary to ulcers or drugs (aspirin) or infections (parasitic infections), or inflammatory bowel disease and malignancy.

(2) Lack of dietary iron may cause anemia in children. This is why iron supplements are given to infants. Iron deficiency is a major cause of anemia in pregnancy.

(3) Malabsorption of iron is a rare cause of iron deficiency but is seen in patients who have had a partial gastrectomy or who have a malabsorption disorder.

-Myeloperoxidase is an iron-containing enzyme that is essential to neutrophil phagocytosis and bacterial killing, both functions may be

diminished with iron depletion, so cell-mediated immunity (T cell function) can be impaired, but antibody production (B cell function) is normal.

-Iron deficiency anemia is associated with a deficiency of Hb in the red cells (hypochromic anemia) and cells that are smaller than normal (microcytic anemia).

Iron transportation & metabolism

-**Transferrin**, the major iron transport protein, is synthesized by the liver and macrophages.

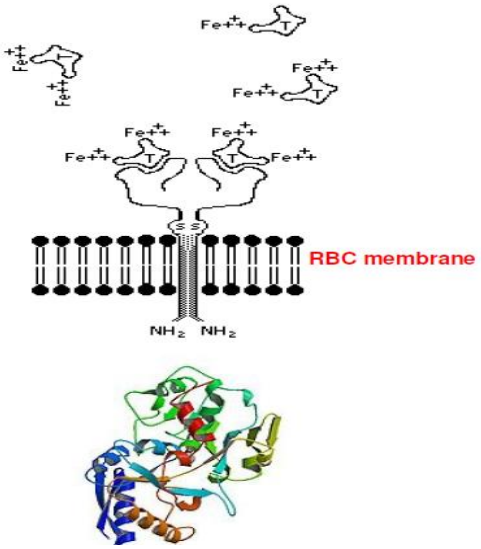
-Each molecule of transferrin can bind two atoms of iron.

- Usually about one-third (25 - 45%) of the total transferrin is bound to iron (referred to as % saturation).

- Transferrin carries iron via plasma to cells throughtout the body, and mainly to the erythroblast cells in the BM.

- Transferrin binds to transferrin receptors (CD71) on the erythroblast surface membrane.

- inside the cell, iron is released from transferrin as Fe++ (ferrous) and transported to mitochondria where it is complexed with protoporphyrin IX to form heme.



Iron absorption

Table 3.2 Iron absorption.

Factors favouring absorption	Factors reducing absorption
Haem iron	Inorganic iron
Ferrous form (Fe^{2+})	Ferric form (Fe^{3+})
Acids (HCl, vitamin C)	Alkalis—antacids, pancreatic secretions
Solubilizing agents (e.g. sugars, amino acids)	Precipitating agents—phytates, phosphates
Iron deficiency	Iron excess
Ineffective erythropoiesis	Decreased erythropoiesis
Pregnancy	Infection
Hereditary haemochromatosis	Tea
Increased expression of DMT-1 and ferroportin in duodenal enterocytes	Decreased expression of DMT-1 and ferroportin in duodenal enterocytes
	Increased hepcidin

Iron overload

There is no physiological mechanism for eliminating excess iron from the body.

• Iron absorption is carefully regulated to avoid accumulation.

• Iron overload can occur in disorders associated with excessive absorption or chronic blood transfusion.

• Excessive iron deposition in tissues can cause serious damage to organs, particularly the heart, liver and endocrine organs.

Lec-8-

Sickle cell anemia

- Sickle cell anemia (sickle cell disease) is a disorder of the blood caused by inherited abnormal hemoglobin (the oxygen-carrying protein within the red blood cells). Which affect people from Africa, India, Middle East and the Mediterranean regions.
- The sickled red blood cells are fragile and prone to rupture. This condition is referred to as sickle cell anemia. The irregular sickled

cells can also block blood vessels causing tissue and organ damage and pain.

- The main forms of sickle cell disease found in tropical countries are:
  - Homozygous sickle cell anemia (HbSS)
  - Sickle cell hemoglobin C (HbSC)
  - Sickle cell thalassaemia
  - Sickle cell trait (HbAS)

Hemoglobin composition in sickle cell disease

Hemoglobin	Normal	Sickle cell disease
HbA	95–98%	0%
HbS	0%	75–95%
HbF	< 2%	5–25%

Pathomechanism

- **HbS polymerizes when deoxygenated**, causing deformation of erythrocytes (“sickling”). This can be triggered by any event associated with reduced oxygen tension.
- Hypoxia (e.g., at high altitudes)
- In homozygotes, up to 100% of the hemoglobin molecules are affected, leading to sickle cell formation under minimally decreased oxygen tension.
- In heterozygotes, sickling only occurs due to severe reduction in oxygen tension.
- Infections
- Dehydration
- Acidosis

- Sudden changes in temperature
- Stress
- Pregnancy
- Sickle cells lack elasticity and adhere to vascular endothelium, which disrupts microcirculation and causes **vascular occlusion and subsequent tissue infarction**.
- Extravascular hemolysis and intravascular hemolysis are common and result in anemia.
- Hemolysis and the subsequent increased turnover of erythrocytes may increase the demand for folate, causing folate deficiency.
- The body increases the production of fetal hemoglobin (HbF) to compensate for low levels of HbA in sickle cell disease.

People who are known carriers of the disease often undergo genetic counseling before they have a child. A test to see if an unborn child has the disease takes either a blood sample from the fetus or a sample of amniotic fluid. Since taking a blood sample from a fetus has greater risks, the latter test is usually used. Children born with sickle-cell disease will undergo close observation by the pediatrician and will require management by a hematologist to assure they remain healthy. These patients will take a 1 mg dose of folic acid daily for life. From birth to five years of age, they will also have to take penicillin daily due to the immature immune system that makes them more prone to early childhood illnesses.

Normocytic anemia

- **Fanconi anemia**

HOMEOSTASIS

The concept of constancy of internal environment was further elaborated and championed as HOMEOSTASIS by American physiologist Walter Cannon (1871–1945).

• Life is a dynamic process

• Cells of the body work like machines consume fuels and produce waste

• Optimum environment required

- Right composition of ECF

- Appropriate pH

- Temperature etc

• Each organ-system makes some contribution towards providing optimum conditions for the functioning of all the cells of body

• With the cooperative/coordinated activity of all parts of body, the conditions under which cells function are maintained at a reasonably constant level

This constancy is known as

homeostasis : Homoio similar * Stasis position

• The basis of health is the organism's success in maintaining this balance, the concept elaborated by Cannon who named the dynamic state as homeostasis

• He showed that the body could adjust to meet serious external/internal danger

• The fact had been recognized by Hippocrates as long ago as 400 BC when he stated. "*The body possesses the means for its recovery from illness*"!

Control system

• A control system is basically designed to maintain a controlled variable at a **set point**

• The value of the controlled variable is continuously monitored by a **sensor**

• The current value of the controlled variable is conveyed by the sensor to controller in the form of a **feedback signal**

• The feedback signal is naturally affected by any **disturbance** which alters the value of the controlled variable

• The controller compares the feedback signal with the set point and the difference between the two is called the **error**

• The output of the controller conveyed to an **effecter**

Feedback Mechanism

1- Negative feedback m.
2- Positive feedback m.

Negative feedback

A control system such as this one is called a negative feedback system because the effecter response is negative to the initiating stimulus (disturbance).

Positive feedback

• If a disturbance increases the value of controlled variable, the controller will respond to disturbance by increasing the value of controlled variable still further

• Now the feedback signal gets still stronger resulting in a still stronger response

• Thus the control system actually increases the rate at which the disturbance would produce its effect and also increases magnitude of the effect.

• Less common in the body

• Whereas negative feedback systems are designed to resist change, positive feedback systems reinforce change

• Positive feedback systems move the controlled variable even further away from a steady state

Example: Using the furnace and temperature example, the room would get progressively hotter

• During labour, uterine contractions push the fetus towards cervix. Stretching of cervix stimulates uterine contraction by positive feedback

• Blood coagulation reactions are autocatalytic in nature, thrombin triggers the formation of more thrombin (Cascade)

*Positive feedback- Vicious cycle - harmful Force of contraction in heart decreases in circulatory shock

*Positive / Negative feedback Mild degree of positive feedback can be overcome by negative feedback and vicious cycle fails to develop

Temperature homeostasis

In humans, temperature is controlled by the hypothalamus. The thermoregulatory centre receives input from two sets of thermoreceptors

a. Receptors in the hypothalamus monitor the temperature of the blood as it passes through the brain (the core temperature)

b. receptors in the skin monitor the external temperature.

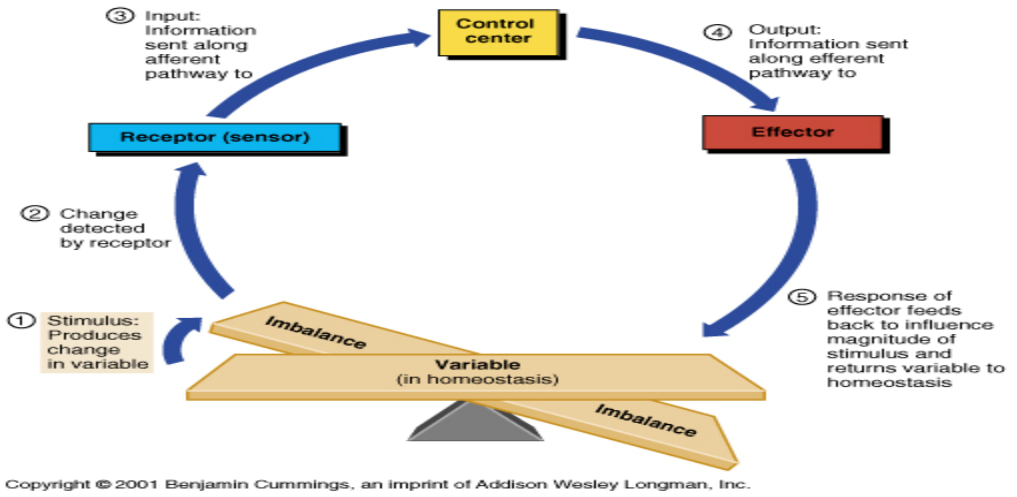
Thermoregulation

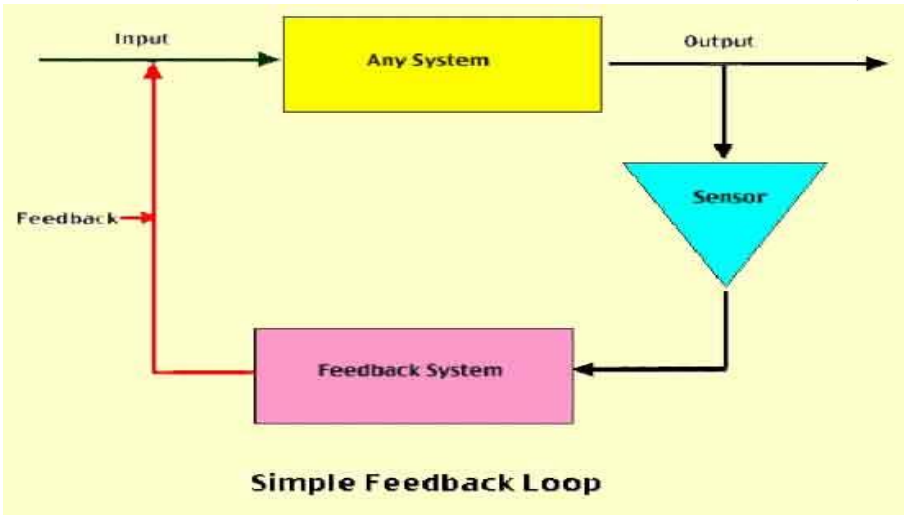
• The hypothalamic thermo-sensors detect changes in the controlled variable - body temperature

• In addition, the hypothalamic controller also monitors the environmental temperature by being in touch with the cutaneous thermoreceptors

• Thermoregulatory responses is initiated before the changes in environmental temperature have succeeded in changing body's core temperature

• That is why thermoregulation has such a high gain




Input
Any System
Output
Sensor
Feedback
Feedback System
Simple Feedback Loop

Protein synthesis from DNA

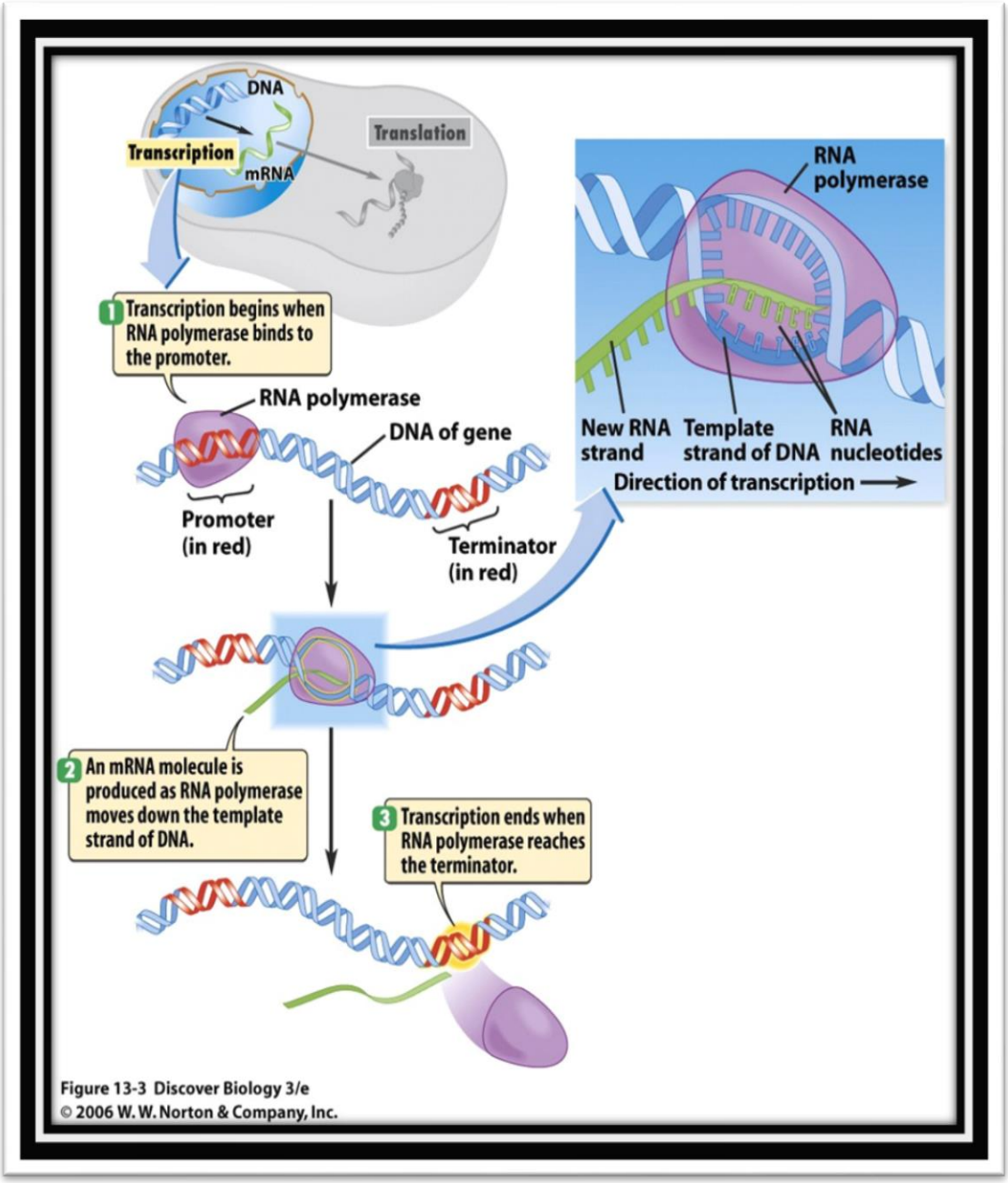
DNA – controls cell function via **transcription** and **translation** (in other words, by controlling protein synthesis in a cell).

Protein synthesis involves 2 steps:

Transcription (transcription of DNA sequences into mRNA): DNA is used to produce mRNA (Called Codon)

Transcription begins when RNA polymerase separates the DNA strands at the promoter (DNA sequence) and begins added RNA nucleotides in the 5' to 3' direction. It finishes it job when it reaches the terminator (DNA sequence).

The first stage of transcription is initiation. Transcription factors help RNA polymerase II bind to the promoter in eurkaryotes (not needed in prokaryotes). Elongation is the next step and this is where RNA nucleotides are added as the DNA is read. Termination is last step and this when a terminator portion of DNA is read. The mRNA is released. Eukaryotes add a 5' cap and poly-A tail to the mRNA before it is complete. The 5' cap allows the mRNA to attach to the ribosome. It is a guanine and two phosphate groups: GTP. The poly-A tail helps stabilize the mRNA as it leaves the nucleus. It is added to the 3' end and is made up of close to 200 adenine nucleotides.


DNA
Transcription
mRNA
Translation
1 Transcription begins when RNA polymerase binds to the promoter.
RNA polymerase
DNA of gene
Promoter (in red)
Terminator (in red)
2 An mRNA molecule is produced as RNA polymerase moves down the template strand of DNA.
3 Transcription ends when RNA polymerase reaches the terminator.
RNA polymerase
New RNA strand
Template strand of DNA
RNA nucleotides
Direction of transcription
Figure 13-3 Discover Biology 3/e
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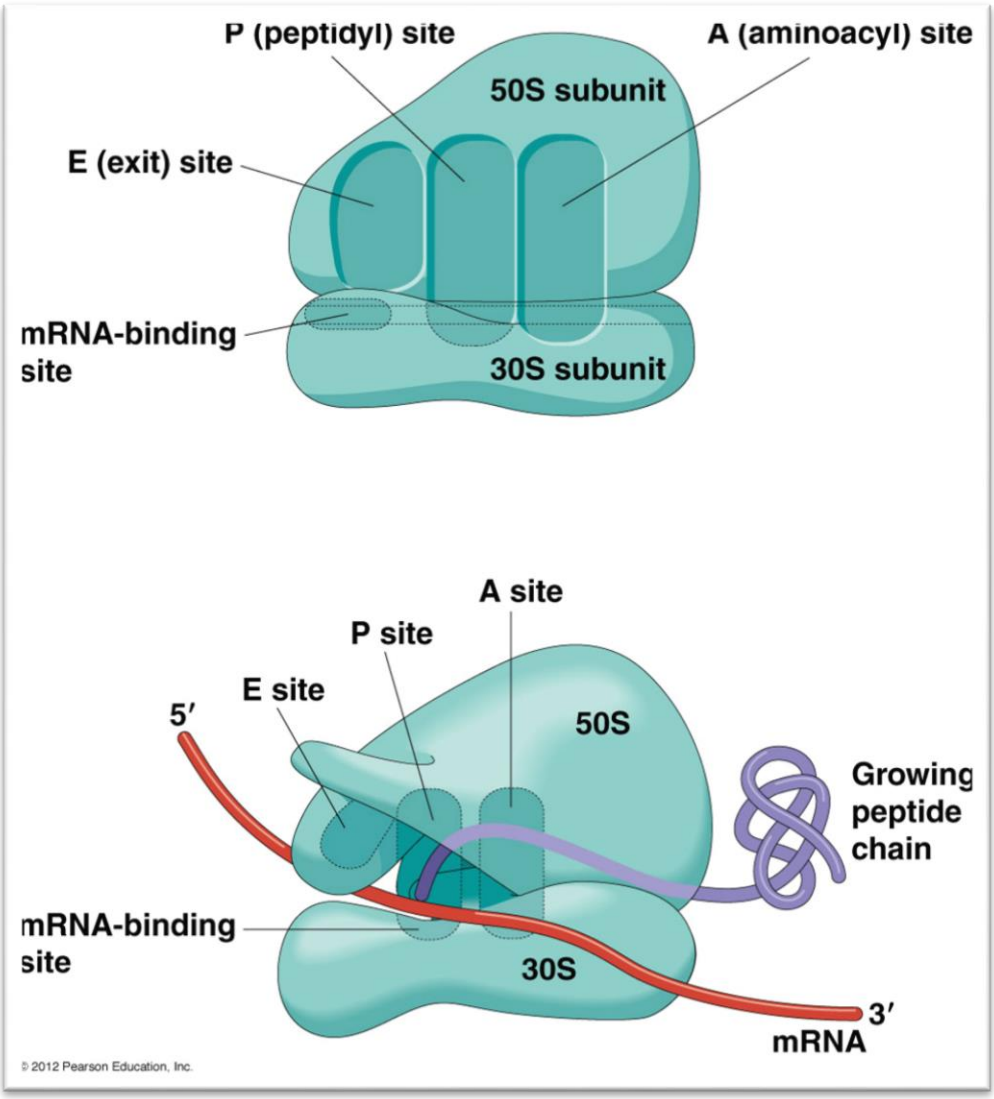
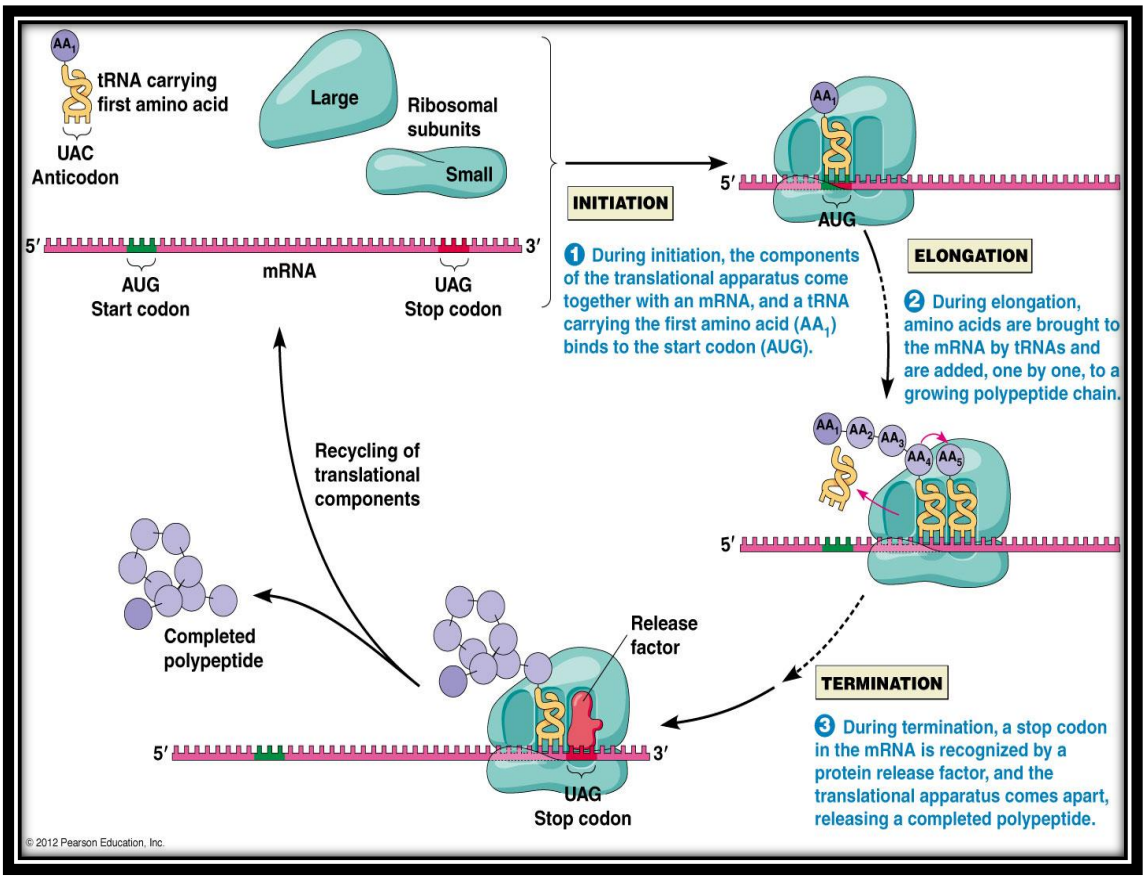
Translation (translation of mRNA into polypeptides): mRNA (messenger RNA) then moves from the nucleus into the cytoplasm and is used to produce a protein in the presence of tRNA (transfer RNA), Amino acids and aribosome.

Translation occurs at the ribosome where mRNA is read and tRNA carries in the corresponding amino acids to form a protein. There are three binding sites on the ribosome for the tRNA. The P site holds the tRNA carrying the protein chain, the A site holds the tRNA carrying the next amino acid and the E site is where the tRNA exits.




AA1
tRNA carrying first amino acid
UAC Anticodon
Large
Small
Ribosomal subunits
5′
3′
AUG
Start codon
mRNA
UAG
Stop codon
INITIATION
1 During initiation, the components of the translational apparatus come together with an mRNA, and a tRNA carrying the first amino acid (AA1) binds to the start codon (AUG).
ELONGATION
2 During elongation, amino acids are brought to the mRNA by tRNAs and are added, one by one, to a growing polypeptide chain.
AA2
AA3
AA4
AA5
Recycling of translational components
Completed polypeptide
Release factor
TERMINATION
3 During termination, a stop codon in the mRNA is recognized by a protein release factor, and the translational apparatus comes apart, releasing a completed polypeptide.
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Cell division :with 2 major events :

1-***Mitosis*** :division of the nucleus ;results in the formation of the daughter nucli.

2-***Cytokinesis*** :division of the cytoplasm ;begains when mitosis is near completed ;and results in the formation of two daughter cells.

Stages of mitosis:

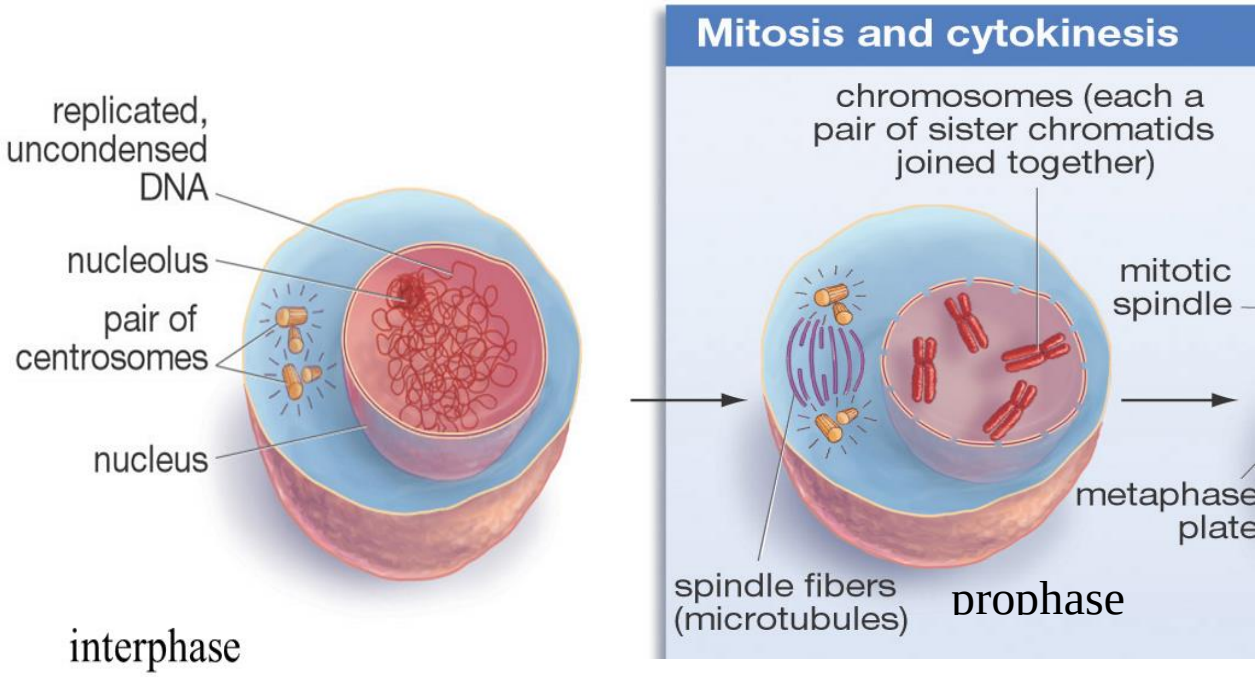
1-**interphase**: no cell division occurs. The cell carries out normal metabolic activity and growth.

2-**prophase**: first part of the cell division centrioles migrate to the poles chromosomes form, nuclear envelope disappears.

3-**metaphase**: chromosomes align midway between centrioles. Spindle from centrioles are attached to chromosoms.

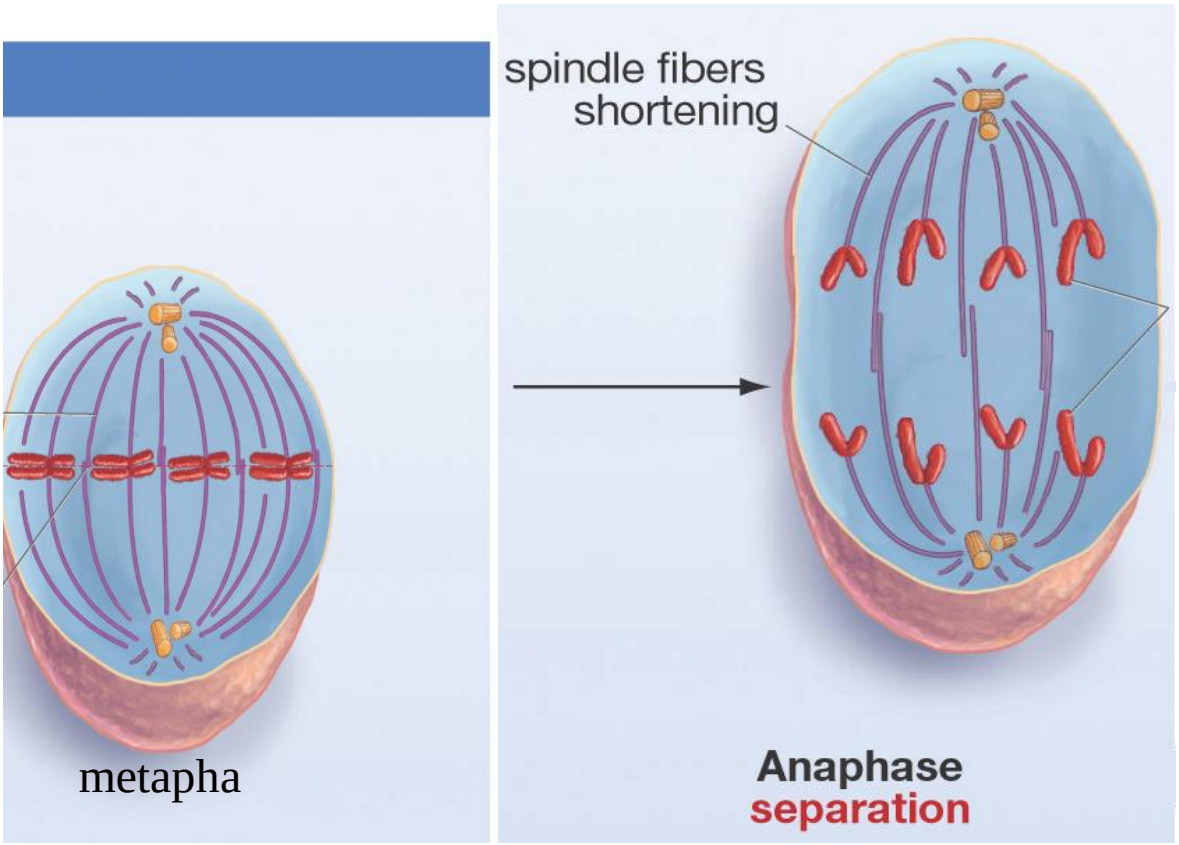
4-**anaphase:**chromosome separate and pulled toward centrioles(toward the poles). The cell begins to elongate (cytokinesis beginning).

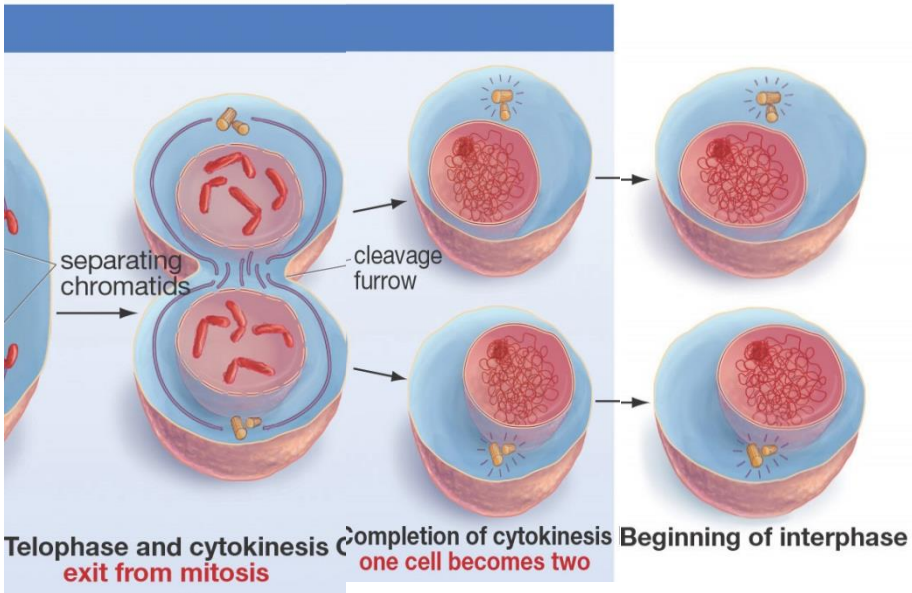
5-**Telophase**: chromatin form; nuclear envelope forms.

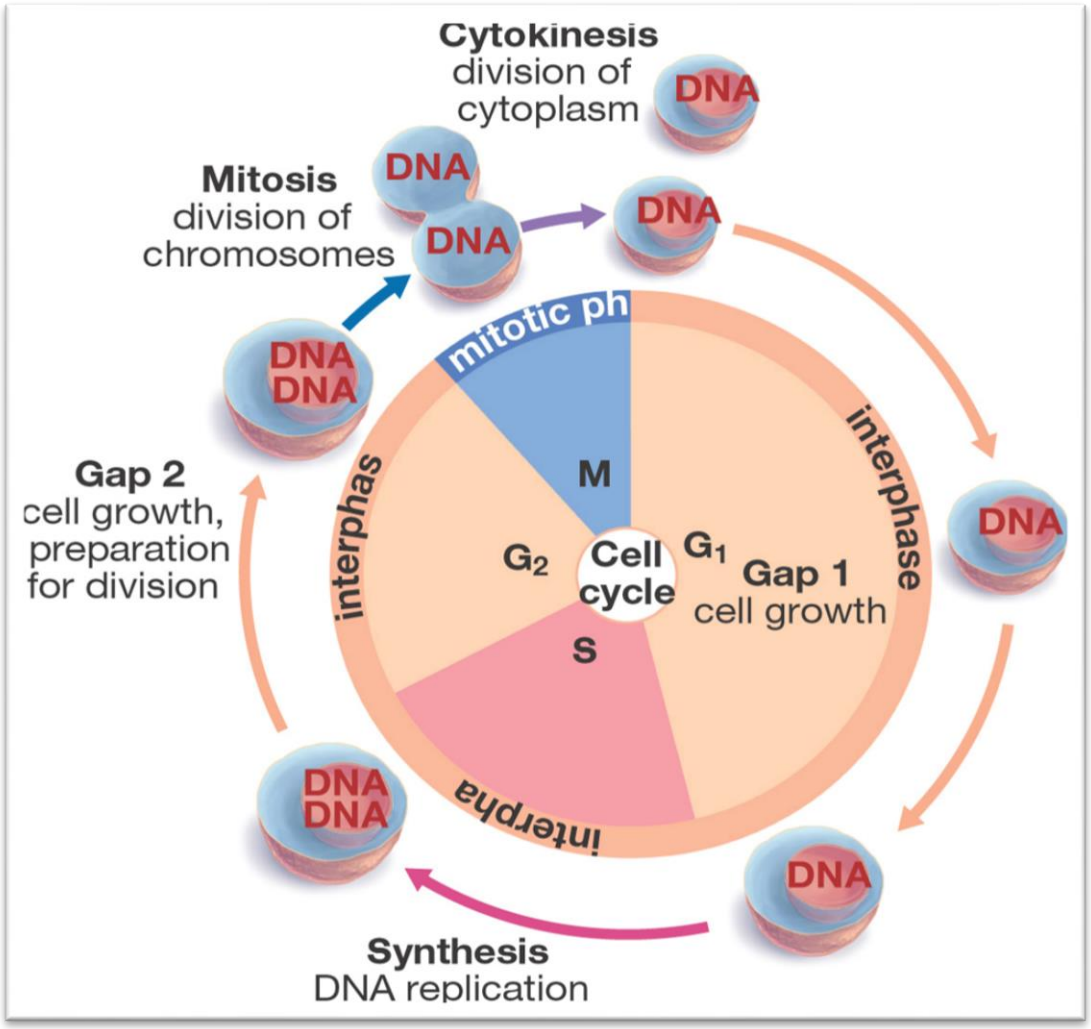


interphase

prophase


spindle fibers
shortening
metapha
Anaphase
separation


separating
chromatids
cleavage
furrow
Telophase and cytokinesis
exit from mitosis
Completion of cytokinesis
one cell becomes two
Beginning of interphase



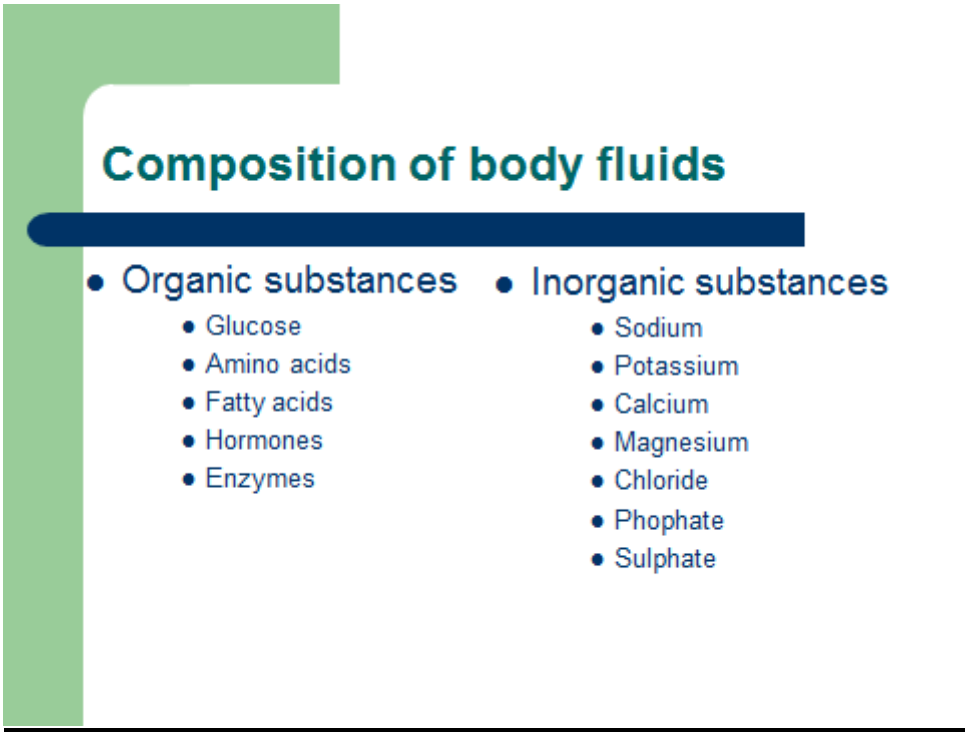
مدرس المادة: م.م ندى محمد

Body composition

In average young adult male

Body composition	% of body weight
Protein, & related substances	18%
Fat	15%
Mineral	7%
Water	60%

Body Fluids



Water content in body is divided into 2 compartments:

1. Extracellular fluid (ECF):

   - fluid outside the cells.

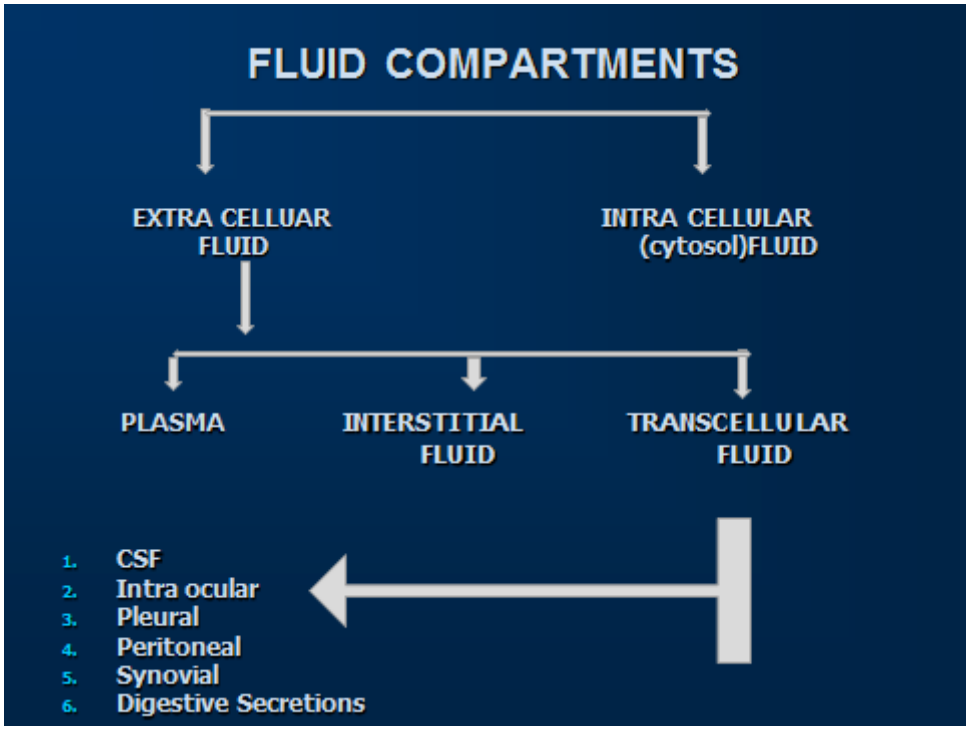
≈ 1/3 volume of fluids in body (≈ 33% of total body water).

- contains ions & nutrients needed for cellular life.

2. Intracellular fluid (ICF):

- fluid inside the cells.

≈ 2/3 volume of fluids in body (≈ 67% of total body water).



Control of body fluids

-Thirst

-Sweating

-Renal control (aldosterone)

-Neuronal (osmoreceptors, baroreceptors)

Types of transport

1. Diffusion (passive transport)

Movement of molecules & ions across a membrane from higher concentration to lower concentration (Down concentration gradient)

Doesn't require energy

1. Diffusion

(Passive transport)

a. Simple diffusion.

b. Facilitated diffusion. (Carrier-mediated)

c. Osmosis.

a. Simple diffusion

Non-Carrier mediated transport.

Diffusion from higher to lower concentration

Doesn't need energy

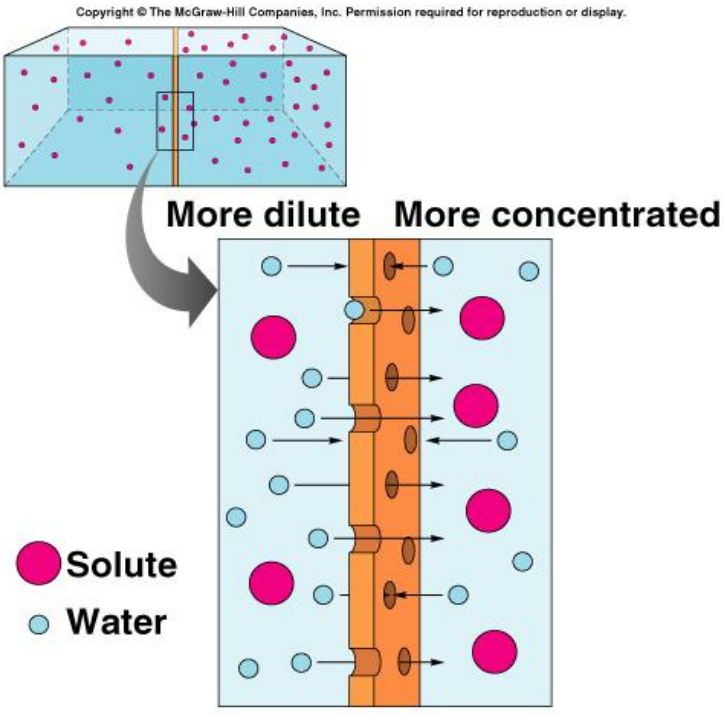
Net diffusion stops when the concentration is equal on both sides of the membrane.

b. Osmosis

Net diffusion of H_20 across a selectively permeable membrane

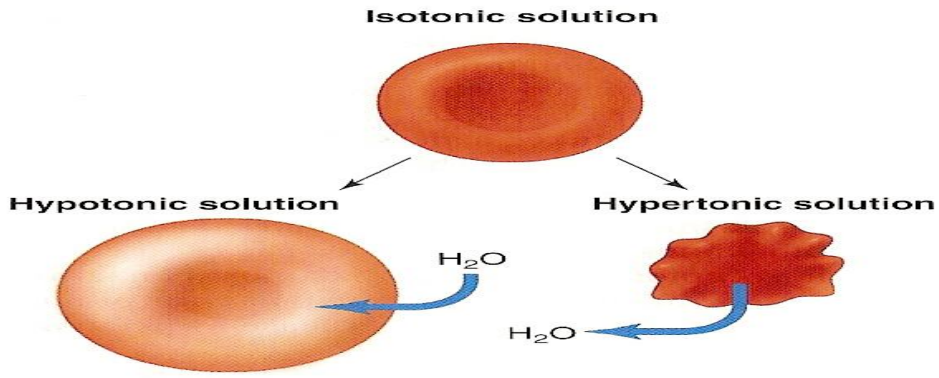
Movement of H_20 from a high [H_20] to lower [H_20] until equilibrium is reached

Examples for osmosis is blood red cell.



Red blood cells in isotonic, hypotonic & hypertonic solutions . As a result, water moves by osmosis into the red blood cells placed in hypotonic solutions, causing them to swell and

even to burst. Similarly, water moves out of red blood cells placed in a hypertonic solution, causing them to shrink.



c. Facilitated diffusion

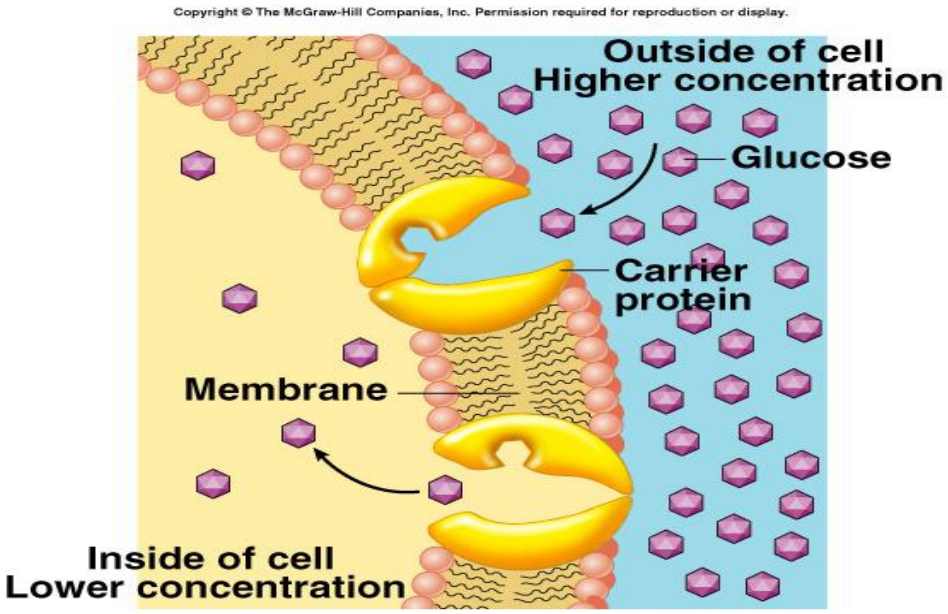
Protein-Carrier mediated transport, within the membrane.

Diffusion from higher to lower concentration

Does not need energy

Molecules that are too large & polar to diffuse are transported across plasma membrane by protein carriers.

e.g. Glucose, most of amino acids, & other organic molecules.



2. Active transport

Protein-Carrier mediated transport.

Involves net transport against concentration gradient (from lower to higher concentration)

Requires energy (ATP)

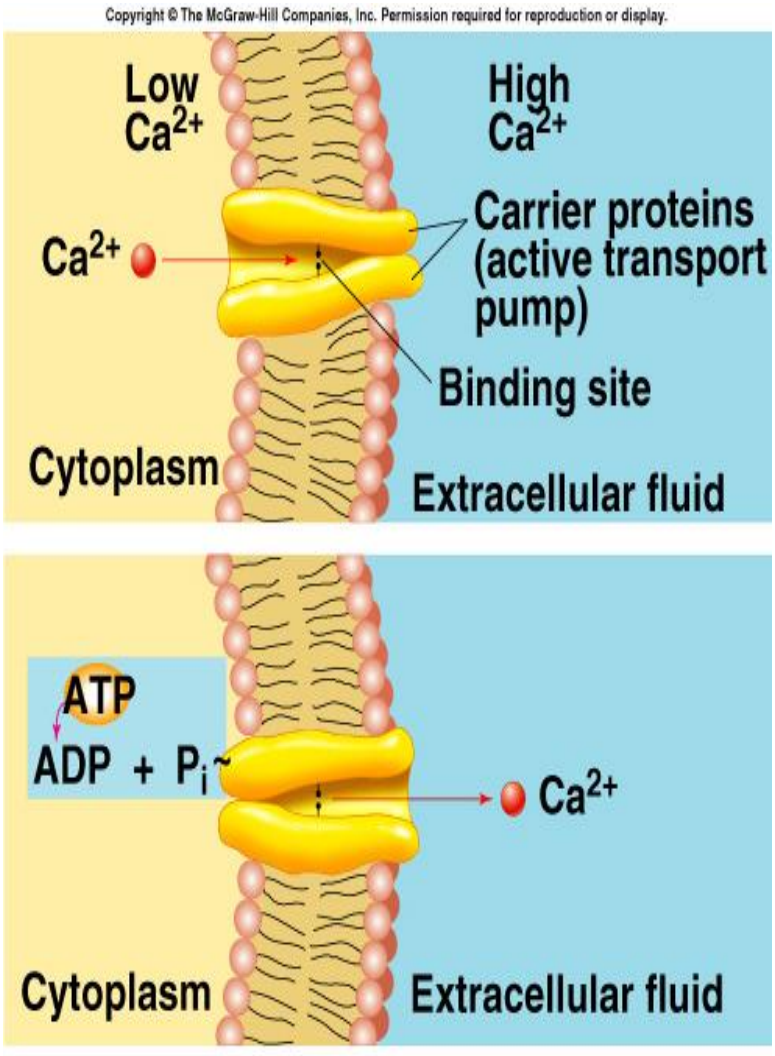
Types of active transport

I. Primary active transport

II. Secondary active transport

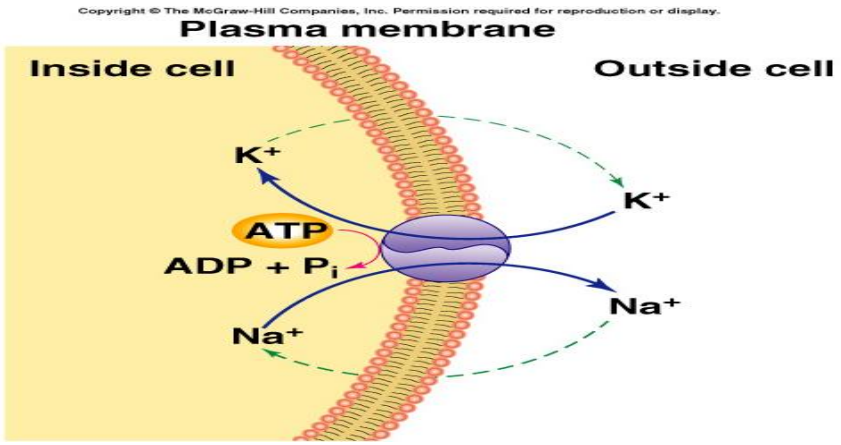
I. Primary Active Transport

Energy is supplied directly from hydrolysis of ATP for the function of the protein carriers. Molecule or ion binds to "recognition site" on one side of carrier protein. Binding stimulates phosphorylation (breakdown of ATP) of carrier protein. Carrier protein undergoes conformational change. This change releases transported molecules to opposite side of membrane. Some of these carriers transport only one molecule or ion for another.



Examples:

Sodium-Potassium pump (Na^+/K^+ pump).



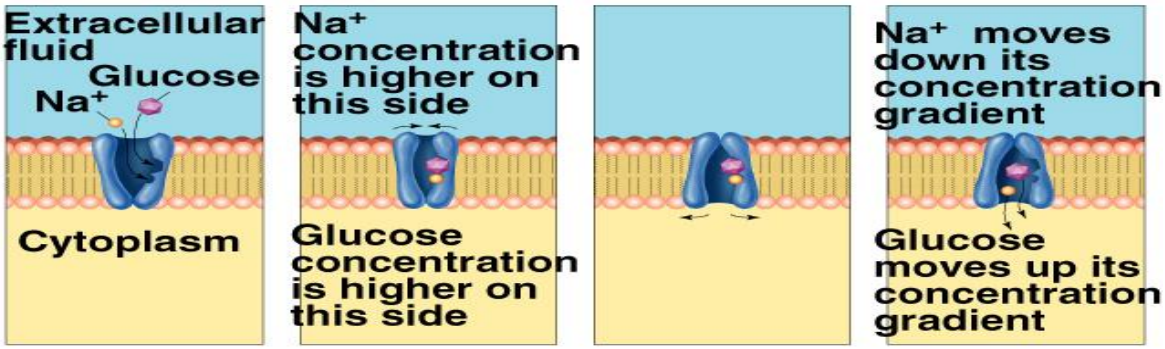
II. Secondary active transport: (Coupled Transport)

Transport of one or more solutes against an electrochemical gradient, coupled to the transport of another solute down an electrochemical gradient

Energy needed for "uphill" movement obtained from "downhill" transport of Na^+.

If the other molecule or ion is moved in the same direction as Na^+ (into the cell), the coupled transport is called either: '**cotransport**' or '**symport**'.

If the other molecule or ion is moved in the opposite direction as Na^+ (out of the cell), the process is called either: '**countertransport**' or '**antiport**'.

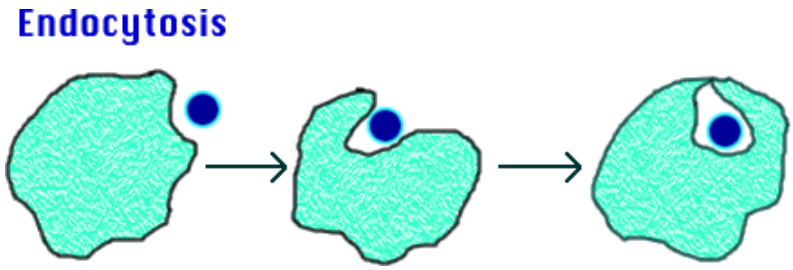


Endocytosis: taking bulky material into a cell

Uses energy

Cell membrane in-folds around food particle"cell eating"forms food vacuole & digests food

This is how white blood cells eat bacteria



Exocytosis: Forces material out of cell in bulk

Membrane surrounding the material fuses with cell membrane

Cell changes shape – requires energy

EX: Hormones or wastes released from cell

مدرس المادة: م.م ندى محمد

Human Physiology

Blood pressure

It is the force per unit area exerted on the vessel wall by the contained blood.

It is expressed in millimeters of mercury (mmHg).all vessels have an associated pressure ;however the term" blood pressure " typically refers to arterial pressure .

During ventricular systole(contraction),BP rises to **systolic blood pressure**.

Pressure then declines as the heart relaxes to the **diastolic blood pressure** .blood pressure (BP) is expressed as systolic pressure(the higher value)/diastolic pressure (the lower value).typical normal value for a 70 Kg man is **120/80mmHg**.

The recoil of the elastic arteries helps propel blood onward through the circulatory system as the heart relaxes. this is responsible for the diastolic pressure .arterial blood moves in a pulsatile flow ,so distinguishes a cut artery from a cut vein.

The major arteries of the body are located deep inside the tissues ,where they are protected from superficial trauma.in contrast ,the veins are closer to the surface of the body .although one cannot see the major arteries ,we can feel(palpate)them wherever we can find a pulse. major points of the body include the **carotid-arteries**, which are found in the neck on either side of the trachea ,the **femoral arteries** ,which found in the groin area ,the **brachial arteries** ,which are found on the inside of the arms just above the elbow ,and the **radial arteries**, which are found on the lateral side of the wrists.in these locations the arteries emerge closer to the body surface.

Arterial BP is estimated by using **sphygmomanometer** .the process is as follows :inflating the cuff with air cuts off blood flow as it exceeds the pressure in the vessel.gradually deflating the cuff allows blood flow to begin in turbulent flow that makes the korotkoff sound.first sound heard ;represent the systolic pressure and sound disappearance represent diastolic pressure.

Human Physiology

Maintaining blood pressure:

Systolic pressure (~110-120 mmHg)&diastolic pressure (~70-80mmHg)both maintained by mechanisms:

1-**short- term controls(neural):**handles acute changes in Bpi.e. rapid control by reflex arch through vasomotor center(located in the medulla oblongata)&its actions are modified by:

***baroreceptors**-detect stretch on the blood vessels,especially in the carotid arteries and the aortic arch

***chemoreceptors**-detects oxygen ,pH and carbon dioxide levels .located in the carotids and aortic arch.

2-**short-term controls (chemical):**also handles acute changes in BP(rapid control);by hormones:

-**epinephrine &norepinephrine**:cause vasoconstriction and increase BP

-**angiotensin II** :causes vasoconstriction and increases BP.

-**atrial natriuretic factor** :causes a decrease in blood volume and BP

-**antidiuretic hormone** :causes increase in blood volume and BP

-**endothelium-derived factors**:chemicals released in response to low blood flow and cause vasoconstriction and increase BP

-**nitric oxide:** secreted by the endothelium cells in response to high blood flow rate and causes vasodilatation and decrease BP

3-long-term controls(renal):

Increases in BP cause the kidneys to excrete more water (diuresis).this decrease in blood volume results in decrease BP

Human Physiology

When BP declines,the kidney activates the rennin-angiotensin mechanism which increases blood volume and vasoconstriction leading to increase BP.

Hypotension=low BP (≤110/70)

*usually not a problem in healthy individuals

***orthostatic hypotension:** sudden drop in pressure resulting from rapid postural changes ;often seen in the elderly

***chronic hypotension** :long-lasting decrease in BP ;can be due to:

Improper nutrition, additions disease ,hypothyroidism, or severe tissue wasting.

***acute hypotension**-sudden drop in BP (circulatory shock);due to

1-after hemorrhage or other severe fluid loss (e.g. severe diarrhea or vomiting ,or after severe burns

2- damage to the heart (myocardial infarction=MI)

3-extensive vasodilation(e.g. anaphylactic allergic reaction)

Hypertension=(high BP)sustained arterial pressure of 140/90 or greater.it is of 2 types according to duration of the hypertension:

Transient-during periods of fever,physical exertion,and emotional upset

Persistent-common in obese individuals,resulting in increased peripheral resistance

It strains the heart and damages the arteries; causing heart failure ,vascular disease ,renal failure, and stroke

According to cause of the hypertension ;it is of 2 types

Primary hypertension-(90%of cases) with no underlying cause ,therefore it can be controlled not cured.

Factors(not causes)that can contribute to primary hypertension:

Human Physiology

1-diets high in sodium, fat, or cholesterol

2-obessity-over ideal body weight

3-age-over 40 years

4-heredity-family history

5-stress-physical&mental

6- smoking-number of cigarettes/day

7-diabetes mellitus

8-hypercholesterolemia

Secondary hypertension-(10% of hypertensive individuals)with an identifiable disorder ,therefore it can be cured if we treat the underlying cause .e.g.:

Hyperthyroidism ,Cushing's disease, adrenal gland tumor ,or excessive renin secretion by the kidneys

(**Cholesterol level** one of the major risk factors for hypertension)

The **total cholesterol** value is quite important ,but it alone is not considered sufficient in evaluating the risk of hypertension& coronary heart disease.one must evaluate the **triglycerides** level (**TG**),the **high density lipids (HDL**)level "good cholesterol" and then calculate the **low density (LDL)"bad cholesterol**" and **very low density lipids(VLDL).**

All the lipid tests are done with the patient fasting(nothing by month for 10-16 hours).

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Lect3

The Cell and Its Functions

Cell: is the basic living unit of the body. Each organ is an aggregate of many different cells held together by intercellular supporting structures.

Functions: Each type of cell is specially adapted to perform one or a few particular functions. For instance, the red blood cells, transport oxygen from the lungs to the tissues. Although the red cells are the most abundant of any single type of cell in the body, there are about 75 trillion additional cells of other types that perform functions different from those of the red cell. The entire body, then, contains about 100 trillion cells.

Organization of the Cell: A typical cell, as seen by the light microscope, is shown in Figure 1. Its two major parts are the nucleus and the cytoplasm. The nucleus is separated from the cytoplasm by a nuclear membrane, and the cytoplasm is separated from the surrounding fluids by a cell membrane, also called the plasma membrane. The different substances that make up the cell are collectively called protoplasm. Protoplasm is composed mainly of five basic substances: water, electrolytes, proteins, lipids, and carbohydrates.

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Fig 1: Structure of the cell by the light microscope

Membranous Structures of the Cell

Most organelles of the cell are covered by membranes composed primarily of lipids and proteins. These membranes include the *cell membrane, nuclear membrane (envelope), membrane of the endoplasmic reticulum,* and *membranes of the mitochondria, lysosomes,* and *Golgi apparatus.*

Cell Membrane: The cell membrane (also called the plasma membrane),which envelops the cell, is a thin, pliable, elastic structure only 7.5 to 10 nanometers thick. It is composed almost entirely of proteins and lipids. The approximate composition is proteins, 55 per cent ;phospholipids, 25 per cent; cholesterol, 13 per cent; other lipids, 4 per cent; and carbohydrates, 3 per cent.

Cytoplasm and Its Organelles: The cytoplasm is filled with both minute and large dispersed particles and organelles. The clear fluid portion of the cytoplasm in which the particles are dispersed is called *cytosol;* this contains mainly dissolved proteins, electrolytes, and glucose. Dispersed in the cytoplasm are neutral fat globules, glycogen granules, ribosomes, secretory vesicles, and five especially important organelles:

1- **Endoplasmic Reticulum**

a network of tubular and flat vesicular structures in the cytoplasm. The tubules and vesicles interconnect with one another. Also, their walls are constructed of lipid bilayer membranes that contain large amounts of proteins, similar to the cell

membrane. The total surface area of this structure in some cells, the liver cells, for instance—can be as much as 30 to 40 times the cell membrane area.

2- **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 transported substances from endoplasmic reticulum are then processed in the Golgi apparatus to form lysosomes, secretory vesicles, and other cytoplasmic components.

3- **Lysosomes**

are vesicular organelles that form by breaking off from the Golgi apparatus and then dispersing throughout the cytoplasm. The lysosomes provide an *intracellular digestive system* that allows the cell to digest (1) damaged cellular structures (2) food particles that have been ingested by the cell, and (3) unwanted matter such as bacteria.

4- **Peroxisomes**

are similar physically to lysosomes, but they are different in two important ways. First, they are believed to be formed by self-replication (or perhaps by budding off from the smooth endoplasmic reticulum) rather than from the Golgi apparatus. Second, they contain oxidases rather than hydrolases.

5- **Secretory Vesicles**

One of the important functions of many cells is secretion of special chemical substances. Almost all such secretory substances are formed by the endoplasmic reticulum–Golgi apparatus system and are then released from the Golgi apparatus into the cytoplasm in the form of storage vesicles called *secretory vesicles* or *secretory granules.*

6- **Mitochondria**

are called the “powerhouses” of the cell. Without them, cells would be unable to extract enough energy from the nutrients, and essentially all cellular functions. Mitochondria are present in all areas of each cell’s cytoplasm, but the total number per cell varies from less than a hundred up to several thousand, depending on the amount of energy required by the cell. Mitochondria are self-replicative, which means that one mitochondrion can form a second one, a third one, and so on, whenever there is a need in the cell for increased amounts of ATP.

7- **Nucleus**

is the control center of the cell. Briefly, the nucleus contains large quantities of DNA, which are the *genes*. The genes determine the characteristics of the cell’s proteins, including the structural proteins, as well as the intracellular enzymes that control cytoplasmic and nuclear activities.

8- **Filament and Tubular Structures of the Cell**

The fibrillar proteins of the cell are usually organized into filaments or tubules. For example, large numbers of actin filaments frequently occur in the outer zone of the cytoplasm, called the *ectoplasm,* to form an elastic support for the cell membrane. Also, in muscle cells,actin and myosin filaments are organized into a special contractile machine that is the basis for muscle contraction.

Red blood cell disorders

RBC Physiology

The primary functions of red blood cells (RBCs) include carrying oxygen to all parts of the body, binding to hemoglobin, and removing carbon dioxide.

Red blood cells (RBCs) perform a number of human respiratory and cardiovascular system functions. Most of these functions are attributed to hemoglobin content. The main RBC functions are facilitating gas exchange and regulating blood pH.

There are multiple disorders of the red blood cells, including hemoglobinopathies, cytoskeletal abnormalities (spherocytosis and other membranopathies) and enzymopathies.

Hemoglobinopathies are a group of rare, inherited disorders involving abnormal structure of the hemoglobin molecule. These disorders include hemoglobin C disease, hemoglobin S-C disease, sickle cell anemia and various types of thalassemia.

Examples on RBCs disorders:

1- **Hemolytic anemia**
2- **Iron-deficiency anemia**
3- **Sickle cell anemia**
4- **Normocytic anemia**
5- **Fanconi anemia**

1- Hemolytic anemia

What is hemolytic anemia?

- Increased destruction of red blood cells in the peripheral blood without evidence of ineffective erythropoiesis is known as hemolytic anemia.
- Normally when the RBCs become senescent (after 120 days) they are removed from the peripheral blood by macrophages in the spleen and liver.
- Hemolysis is the e premature destruction of RBCs due to intrinsic inherited defects in the RBCs or because of acquired intravascular abnormalities.

Classification of hemolytic anemias

1-Hereditary: - Membrane: hereditary spherocytosis, hereditary elliptocytosis - Metabolism: G6PD deficiency

2- Acquired:

- Immune: Autoimmune and alloimmune - Infections: Malaria - Chemical and physical agents: Drugs burns.

Antibody Mediated Hemolysis

• In autoimmune hemolytic anemia (AIHA) RBCs are destroyed by antibodies made by a person against their own RBCs. • Divided into 'warm‘ and 'cold' types according to whether the antibody reacts more strongly with red cells at 37°C or 4°C, respectively. • The red cells in warm AIHA are coated usually with immunoglobulin G (IgG), and with IgM in cold AIHA.

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Alloimmune hemolytic anemias

In these anemias, antibody produced by one individual reacts with red cells of another - transfusion of ABO-incompatible blood - Rhesus disease of the newborn.

يتبع في المحاضرة اللاحقة

Lec-10-Human Physiology

Leucocytes (WBC)

Are nucleated cells & classified into : -

1. Granular leucocytes:- contain granules in their cytoplasm & posses lobed nuclie .

a. Neutrophils (10 – 12 micrometer in diameter). Their nuclei have 2-6 lobes connected by very thin strands . Their cytoplasm contain granules stained with acidic & basic stains .

b. Basophils :- Their nuclei are bi lobed or irregular in shape often in the form of a letter S. The cytoplasmic granules are round, variable in size, stain blue – black .

c. Eosinophils (Acidophils). contain nuclei usually bi lobed connected by isthmus . The cytoplasm contain large granules stained red – orange.

2. A granulocytes or a granular leukocytes.

a. lymphocytes (7-15 micrometer in diameter).Their nuclei are darkly stained , round. The cytoplasm stains sky blue , and forms a rim around the nucleus.

b. monocytes :- Their nuclei are kidney-Shaped & the cytoplasm has a foamy appearance .

Functions of leucocytes :-

The general function of leukocytes is to combat inflammation and infection by phagocytosis or antibody production .

- Neutrophils & monocytes are actively phagocytic (they can ingest bacteria & dead tissues . - Neutrophils are the most active leucocytes in responding to tissue destruction by bacteria. Neutrophils release lysosomes which destroys certain bacteria.

- Monocytes take longer to reach the site of infection than do neutrophils. They do so in larger numbers and destroy more microbes . Monocytes that have migrated to

infected tissues and differentiated into phagocytes are called wandering macrophages they clean up cellular debris & microbes following an infection .

Chemotaxis:-

Migration of phagocytes to inflamed tissues in response to a number of different chemicals.These chemicals called chemotaxic agents .

Diapedessis : - The ability of most leucocytes to migrate through the minute spaces between the cells that form the walls of capillaries & into connective and epithelial tissues .

Defensins :- are amino acids found in the neatrophils which has a broad range of antibiotic activity against bacteria , fungi , & viruses .

- Eosinophils:- release substances that combat the effects of histamine & other mediators of inflammation in allergic reactions .

Eosinophils are also effective against certain parasitic worms . Thus , a high eosinophil count indicates an allergic condition or a parasitic infection .

- Basophils :- also involved in allergic reactions . Basophils leave the capillaries, enter the tissues & liberate heparin , histamine, & serotonin . - Lymphocytes :- Are involved in the production of antibodies .

Antibodies : are special proteins that inactivate antigens .

Antigens : are substances that will stimulate the production of antibodies and are capable of reacting specifically with the antibody. antigens are proteins that make up the cell structures & enzymes bacteria and toxins released by bacteria .

Antigen – antibody complex:- When antigen enter the body , they react chemically with substances in the lymphocytes & stimulate some lymphocytes called B cells to become plasma cells .the plasma cells then produce antibodies (globulin – type proteins that attach to antigens in a vary precise way) . Antibodies cover their antigens so the antigens cannot come in contact with other chemicals in the body . In this way , bacterial poisons can be sealed up & become harmless . This process is called the antigen – antibody response. phagocytes in tissues destroy the antigen – antibody complexes . * Other type of lymphocytes are called T Cells .

* group are called cytotoxic or killer T cells . Which are activated by certain antigens and react by destroying them directly or indirectly by stimulating other lymphocytes & macrophages . T cells are effective against bacteria , viruses , fungi , transplanted cells & cancer cells .

* Neutrophilia = ↑ neturophils count : in case of 1- Infections (bacterial) 2- burns 3- stress 4- inflammation

* Neutropnea = ↓ neutrophils count : in case of 1- Radiation 2- certain drugs 3- vit. B12 deficiency .

* Eosinophilia = ↑ eosinophils count :- in case of 1- Allergic reactions 2- parasitic infections 3- autoimmune disease 4- adrenal insufficiency

* Eosinopnea = ↓ eosinphils count :- in case of

1- Certain drugs 2- stress 3- Cushing's syndrome.

* Basophilia = ↑ basophils count :- in case of 1-Allergic responses 2- leukemias 3- cancers 4- hypothyroidism

* Basopnea = ↓ basophils count :- case of 1-Pregnency 2- ovulation 3- stress 4- hyperthyroidism

* Lymphocytosis = ↑ lymphocyte count :- in case of 1-Viral infections 2- immune diseases 3- in some leukemias

* Lymphopnea = ↓ lymphocyte count :- in case of 1-Prolonged severs illness 2- high steroid levels 3- immune suppression .

* Monocytosis = ↑ monocyte count :- in case of

1-Certain viral infection 2- fungal infection 3- tuberculosis 4- some leukemias 5- chronic diseases

* Monocytopnea =↓ monocyts count :- rarely occur - Number of WBCs about 5000 – 10000 cell / mm3. - Life span from few hours to few days .

كلية الكوت الجامعة/قسم تقنيات المختبرات الطبية

المرحلة الثانية

محاضرة الفسلجة النظري

Anemia

Sickle cell anemia

-The RBCs contain an abnormal type of Hb called HbS, in which the α chains are normal but the β chains are abnormal, due to replacement of one glutamic acid residue by a valine residue.

-This abnormal Hb is insoluble at low O2 tensions, so when it is exposed to low concentration of O2, it precipitates into long crystals inside RBCs.

-These crystals elongate the cell and give it a sickle-like appearance rather than being a biconcave disc. The precipitated Hb also damages the cell membrane, so that the cells become highly fragile.

*Sickle cell anemia can lead to a host of complications, including:

- Stroke
- Acute chest syndrome
- Pulmonary hypertension
- Pulmonary hypertension
- Organ damage
- Blindness
- Leg ulcers
- Gallstones
- Pregnancy complications

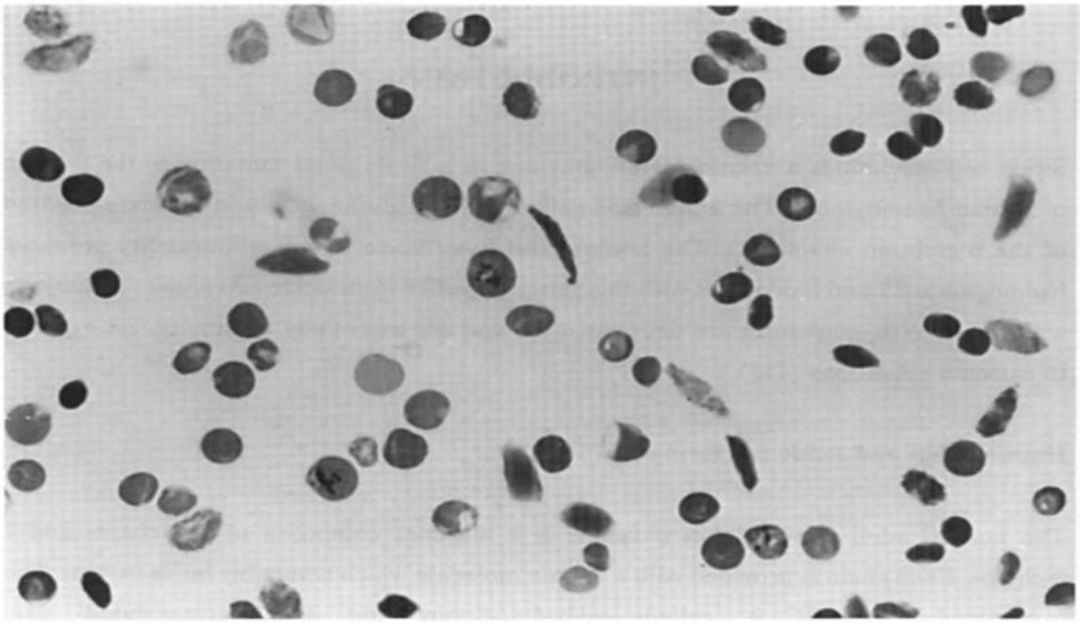


Figure of Sickle cell shape

Thalassemia

Is another hereditary type of anemia in which the RBCs are unable to synthesize adequate amounts of either the alpha or beta polypeptide chains required to form the Hb.

-There are two major types of thalassemia: Alpha thalassemia that is caused by a defect in the rate of synthesis of α chains and beta thalassemia that is caused by a defect in the rate of synthesis of β chains. Alpha thalassemias occur most often in people from Southeast Asia, the Middle East, China, and in those of African descent.

-Beta thalassemias occur most often in people of Mediterranean origin. To a lesser extent, Chinese, other Asians, and African Americans can be affected.

-There are many forms of thalassemia. Each type has many different subtypes. Both alpha and beta thalassemia include the following two forms:

- Thalassemia major
- Thalassemia minor

You must inherit the gene defect from both parents to develop thalassemia major.

Thalassemia minor occurs if you receive the faulty gene from only one parent. People with this form of the disorder are carriers of the disease. Most of the time, they do not have symptoms.

Beta thalassemia major is also called Cooley anemia.

Fanconi anaemia

Is an autosomal recessive condition first described in 1927 by the Swiss paediatrician Guido Fanconi. This disease reflects the cellular and phenotypic consequences of genetic instability: growth retardation, congenital malformations, bone marrow failure, high risk of neoplasia, and premature aging. At the cellular level, manifestations of genetic instability include chromosomal breakage, cell cycle disturbance, and increased somatic mutation rates. FA is caused by biallelic mutations in at least 11 different genes which appear to function in the maintenance of genomic stability.

*Clinical features:

1) Developmental Abnormalities

-Pre- and postnatal growth retardation

- Skeletal malformations

- Malformation of inner organs (kidney and heart) and auditory system

- Hypogonadism and reduced fertility

-Hyperpigmentation, hypopigmentation, café au le spots

2) Progressive bone marrow failure

3) Cancer predisposition (AML, squamous cell carcinomas).

بسم الله الرحمن الرحيم

second stage

Thermal Regulation

On the basis of body temperature animals are classified as warm blooded (**homeothermic**) animals which are capable of maintaining a relatively constant body temperature in spite of great variations of external temperature or cold blooded (**poikilothermic**) animals in which the body temperature varies with that of the environment. Poikilotherms include invertebrates and aquatic animals like fishes and amphibians.

Some animals have a high rate of thermal conductance and low rate of heat production. Such animals acquire heat from the environment and regulate their body temperature quite independent of the heat produced in the body; these animals are known as **ectothermic**. In contrast to this, a few animals produce sufficient heat due to their own oxidative metabolism and maintain body temperature at a constant level. Such animals are called **endothermic** which include homeotherms like birds and mammals. Another category of animals which do not maintain constant body temperature, but during activity they show endothermic regulation, these are called **heterothermic** animals, they are also called facultative endotherms since they are capable of regulating physiological temperature at certain time only.

The habitats of animals can be divided into **terrestrial**, **aquatic** and **aerial**. Animals living in terrestrial environment have an acute problem of temperature because of the radiant heat of the sun. Also air has a low specific heat and so it gains or loses heat rapidly. Animals living in aquatic habitats do not face acute thermal problems because water has a high specific heat and it gains or loses heat slowly, thus making little changes in temperature. Aerial animals like birds have a higher limit of thermal tolerance (35C º-42C º) due to higher rate of metabolism.

Body Temperature

The normal range of human body temperature is (36 C ºto 38C º), with an average oral temperature of (37C º). Within a 24-hour period, an individual's temperature fluctuates from 1C ºto 2C º, with the lowest temperatures occurring during sleep. At either end of the age spectrum, however, temperature regulation may not be as precise as it is in older children or younger adults. Infants have more surface area (skin) relative to volume and are likely to lose heat more rapidly.

In the elderly, the mechanisms that maintain body temperature may not function as efficiently as they once did, and changes in environmental temperature may not be compensated for as quickly or effectively. This is especially important to remember when caring for patients who are very young or very old.

Heat Production

Cell respiration, the process that releases energy from food to produce ATP, also produces heat as one of its energy products. Although cell respiration takes place constantly, many factors influence the rate of this process:

1. The hormone **thyroxin** (and T3), produced by the thyroid gland, increases the rate of cell respiration and heat production. The secretion of thyroxin is regulated by the body's rate of energy production, the metabolic rate itself. When the metabolic rate decreases, the thyroid gland is stimulated to secrete more thyroxin. As thyroxin increases the rate of cell respiration, a negative feedback mechanism inhibits further secretion until metabolic rate decreases again.
2. In stress situations, **epinephrine** and **norepinephrine** are secreted by the adrenal medulla, and the **sympathetic** nervous system becomes more active. Epinephrine increases the rate of cell respiration, especially in organs such as the heart, skeletal muscles, and liver. Sympathetic

stimulation also increases the activity of these organs. The increased production of ATP to meet the demands of the stress situation also means that more heat will be produced.

3. Organs that are normally active (producing ATP) are significant sources of heat when the body is at rest. The skeletal muscles, for example, are usually in a state of slight contraction called muscle tone. Because even slight contraction requires ATP, the muscles are also producing heat. This amounts to about 25% of the total body heat at rest and much more during exercise, when more ATP is produced.

The liver is another organ that is continually active, producing ATP to supply energy for its many functions. As a result, the liver produces as much as 20% of the total body heat at rest. The heat produced by these active organs is dispersed throughout the body by the blood. As the relatively cooler blood flows through organs such as the muscles and liver, the heat they produce is transferred to the blood, warming it.

4. The intake of food also increases heat production, because the metabolic activity of the digestive tract is increased. Heat is generated as the digestive organs produce ATP for peristalsis and for the synthesis of digestive enzymes.

5. Changes in body temperature also have an effect on metabolic rate and heat production. This becomes clinically important when a person has a **fever**, an abnormally high body temperature.

Heat Loss through the Skin

Because the skin covers the body, most body heat is lost from the skin to the environment. When the environment is cooler than body temperature (as it usually is), heat loss is unavoidable.

The amount of heat that is lost is determined by blood flow through the skin and by the activity of sweat glands. Blood flow through the skin influences the amount of heat lost by the processes of radiation,

conduction, and convection. **Radiation** means that heat from the body is transferred to cooler objects not touching the skin. **Conduction** is the loss of heat to cooler air or objects, such as clothing, that touch the skin.

Convection means that air currents move the warmer air away from the skin surface and facilitate the loss of heat; this is why a fan makes us feel cooler on hot days. The temperature of the skin and the subsequent loss of heat are determined by blood flow through the skin. The arterioles in the dermis may constrict or dilate to decrease or increase blood flow. In a cold environment, **vasoconstriction** decreases blood flow through the dermis and thereby decreases heat loss. In a warm environment, **vasodilation** in the dermis increases blood flow to the body surface and loss of heat to the environment.

The other mechanism by which heat is lost from the skin is sweating. The **sweat glands** secrete sweat (water) onto the skin surface and excess body heat evaporates the sweat. Sweating is most efficient when the humidity of the surrounding air is low. Humidity is the percentage of the maximum amount of water vapor the atmosphere can contain. A humidity reading of 90% means that the air is already 90% saturated with water vapor and can hold little more. In such a situation, sweat does not readily evaporate, but instead remains on the skin even as more sweat is secreted. If the humidity is 40%, however, the air can hold a great deal more water vapor, and sweat evaporates quickly from the skin surface, removing excess body heat. In air that is completely dry, a person may tolerate a temperature of 75C º for nearly 1 hour.

Although sweating is a very effective mechanism of heat loss, it does have a disadvantage in that it requires the loss of water in order to also lose heat. Water loss during sweating may rapidly lead to dehydration, and the water lost must be replaced by drinking fluids. Small amounts of heat are also lost in what is called “insensible water loss.” Because the

skin is not like a plastic bag, but is somewhat permeable to water, a small amount of water diffuses through the skin and is evaporated by body heat. Compared to sweating, however, insensible water loss is a minor source of heat loss.

Heat Loss through the Respiratory Tract

Heat is lost from the respiratory tract as the warmth of the respiratory mucosa evaporates some water from the living epithelial surface. The water vapor formed is exhaled, and a small amount of heat is lost. Animals such as dogs that do not have numerous sweat glands often pant in warm weather. Panting is the rapid movement of air into and out of the upper respiratory passages, where the warm surfaces evaporate large amounts of water. In this way the animal may lose large amounts of heat.

Heat Loss through the Urinary and Digestive Tracts

When excreted, urine and feces are at body temperature, and their elimination results in a very small amount of heat loss.

Regulation of Body Temperature

The **hypothalamus** is responsible for the regulation of body temperature and is considered the “thermostat" of the body. As the thermostat, the hypothalamus maintains the “setting” of body temperature by balancing heat production and heat loss to keep the body at the set temperature. To do this, the hypothalamus must receive information about the temperature within the body and about the environmental temperature. Specialized neurons of the hypothalamus detect changes in the temperature of the blood that flows through the brain. The temperature receptors in the skin provide information about the external temperature changes to which the body is exposed. The hypothalamus then integrates this sensory information and promotes the necessary responses to maintain body temperature within the normal range.

Mechanisms to Increase Heat Loss

In a warm environment or during exercise, the body temperature tends to rise, and greater heat loss is needed. This is accomplished by vasodilation in the dermis and an increase in sweating. Vasodilation brings more warm blood close to the body surface, and heat is lost to the environment. However, if the environmental temperature is close to or higher than body temperature, this mechanism becomes ineffective.

The second mechanism is increased sweating, in which excess body heat evaporates the sweat on the skin surface. As mentioned previously, sweating becomes inefficient when the atmospheric humidity is high. On hot days, heat production may also be decreased by a decrease in muscle tone. This is why we may feel very sluggish on hot days; our muscles are even slightly less contracted than usual and are slower to respond.

Mechanisms to Conserve Heat

In a cold environment, heat loss from the body is unavoidable but may be reduced to some extent. Vasoconstriction in the dermis shunts blood away from the body surface, so that more heat is kept in the core of the body. Sweating decreases, and will stop completely if the temperature of the hypothalamus falls below about 37C º. If these mechanisms are not sufficient to prevent the body temperature from dropping, more heat maybe produced by increasing muscle tone.

When this greater muscle tone becomes noticeable and rhythmic, it is called shivering and may increase heat production by as much as five times the normal. People also have behavioral responses to cold, and these too are important to prevent heat loss.

Low temperature effects

The protoplasm can exist in living state between 0C º and 45C º and freezes a few degrees below zero. Freezing causes:

1- Formation the ice crystals in the cell and disturbs the cell organization.
2- Metabolism is greatly lowered and as such the rate of oxygen consumption is also very low because the diffusion of O2 and CO2 through the ice is very low.
3- The enzymes become inactive.

Fever

A fever is an abnormally high body temperature and may accompany infectious diseases, extensive physical trauma, cancer, or damage to the CNS. The substances that may cause a fever are called **pyrogens**. Pyrogens include bacteria, foreign proteins, and chemicals released during inflammation. These inflammatory chemicals are called **endogenous pyrogens**. It is believed that pyrogens chemically affect the hypothalamus and "raise the setting" of the hypothalamic thermostat.

The hypothalamus will then stimulate responses by the body to raise body temperature to this higher setting. White blood cells increase their activity at moderately elevated temperatures, and the metabolism of some pathogens is inhibited. Thus, a fever may be beneficial in that it may shorten the duration of an infection by accelerating the destruction of the pathogen. A fever increases the metabolic rate, which increases heat production, which in turn raises body temperature even more. When the body temperature rises above 39.7C º, the hypothalamus begins to lose its ability to regulate temperature.

The proteins of cells, especially the enzymes, are also damaged by such high temperatures. Enzymes become denatured, that is, lose their shape and do not catalyze the reactions necessary within cells. As a result, cells begin to die. A medication such as aspirin is called an **antipyretic** because it lowers a fever, probably by affecting the hypothalamic thermostat.

Nervous System

The **nervous system** is one of the regulating systems. Electrochemical impulses of the nervous system make it possible to maintain homeostasis. The functions of the nervous system:

1. To detect changes and feel sensations
2. To initiate appropriate responses to changes
3. To organize information for immediate use and store it for future use

Nerve Tissue

Nerve cells are called **neurons (**figure 1) the **cell body** contains the nucleus. **Dendrites** are processes (extensions) that transmit impulses toward the cell body. The one **axon** of neuron transmits impulses away from the cell body. It is the cell membrane of the dendrites, cell body, and axon that carries the electrical nerve impulse. In PNS, axons and dendrites are "wrapped" in specialized cells called **Schwann cells**, enclosing them in several layers of Schwann cell membrane. These layers are the **myelin sheath**; myelin is phospholipid that electrically insulates neurons from one another. The spaces between adjacent Schwann cells are called nodes of **Ranvier**. These nodes are the parts of the neuron cell membrane that depolarize when an electrical impulse is transmitted. The nuclei and cytoplasm of the Schwann cells are wrapped around the outside of the myelin sheath and are called the **neurolemma**, In the CNS; the myelin sheaths are formed by **oligodendrocytes**, one of the **neuroglia**

Types of neurons

Neurons may be classified into three groups: **Sensory neurons** (or **afferent neurons**) carry impulses from receptors to the CNS. **Receptors** detect external or internal changes and send the information to the CNS in the form of impulses by way of the afferent neurons. **Motor**

neurons (or **efferent neurons**) carry impulses from the central nervous system to **effectors**. **Interneuron** is found entirely within the CNS.

Generation of Nerve Impulse:

Excitability

Excitability is that property of the nerve fiber by virtue of which it responds by generating a nerve signal (electrical impulses or the so-called action potentials) when it is stimulated by a suitable stimulus which may be mechanical, thermal, chemical or electrical.

Resting Membrane Potential

A steady potential difference of −70mV (inside negative) is observed in the nerve fiber (figure 2). This is the resting membrane potential (RMP) and indicates the resting state of cell**,** also called state of **polarization.**

Action Potential

The **action potential** may be defined as the brief sequence of changes which occur in the resting membrane potential when stimulated by a threshold stimulus. When the stimulus is subminimal or subthreshold, it does not produce action potential, but does produce some changes in the RMP. The adequate strength of stimulus necessary for producing the action potential in a nerve fiber is known as **threshold**.

Phases of action potential

The action potential basically occurs in two phases: depolarization and repolarization(figure 3). When the nerve is stimulated, the polarized state is altered, i.e. RMP is abolished and the interior of the nerve becomes positive as compared to the exterior. This is called **depolarization phase**. Within no time there occurs reversal to the nearly original potential and this second phase of action potential is

called **repolarization phase**. According to **Hodgkin-Huxley theory,** the sequences of events are:

1. **Polarization phase**. Resting membrane potential (−70 mV) is due to distribution of more cations outside the cell membrane and more anions inside the cell membrane, with Na+ ions more abundant outside the cell, and K+ ions and negative ions more abundant inside. Na^+ cannot enter the cell due to the impermeability of the membrane.
2. **Depolarization phase**. When threshold stimulus is applied to the cell membrane, at the point of stimulation the permeability of the membrane for Na^+ ions increases. There occurs a rapid influx of Na^+ ions into the cell. This rapid entry of Na^+ leads to depolarization.
3. **Repolarization phase**. Repolarization occurs due to decrease in further Na^+ influx and K^+ efflux. The net transfer of positive charge out of the cell serves to complete the repolarization. Then the sodium and potassium pumps return Na+ ions outside and K+ ions inside, and the neuron is ready to respond .

Main Characteristics of Nerve Excitability

1. **All or none response**. A single nerve fiber always obeys **'all or none law'**, that is:

- When a stimulus of subthreshold intensity is applied to the axon, then no action potential is produced **(none response);**
- A response in the form of spike of action potential is observed when the stimulus is of threshold intensity; and
- There occurs no increase in the magnitude of action potential when the strength of stimulus is more than the threshold level **{all response)**. This all or none relationship observed between the strength of stimulus and the response achieved is known as **'All or None Law'**.

2. **Refractory period**. Refractory period refers to the period following action potential (produced by a threshold stimulus) during which a nerve fiber either does not respond or responds subnormally to a stimulus of threshold intensity or greater than threshold intensity. It is of two types:

A - **Absolute refractory period (ARP)**. It is a short period following action potential during which second stimulus, no matter how strong it may be, cannot evoke any response (another action potential). In other words during absolute refractory period the nerve fiber completely loses its excitability.

B- **Relative refractory period (RRP)**. It is a short period during which the nerve fiber shows response if the strength of stimulus is more than normal.

Propagation of action potential in an unmyelinated axon

The steps of propagation of action potential along an unmyelinated axon are summarized:

1-In the resting phase (polarized state) the axonal membrane is outside positive and inside negative.

2-When an unmyelinated axon is stimulated at one site by a threshold stimulus, there occurs action potential at that site, i.e. that site is depolarized. In other words, at that site outside membrane become negative and inside positive (reversal of polarity) but the neighbouring areas until now remain in polarized state.

3-The circular current flow depolarizes the neighboring area of the membrane up to firing level and a new action potential is produced which in turn depolarizes the neighboring area ahead. Thus, due to successive depolarization of the neighboring area, the action potential is propagated along the entire length of the axon

Propagation of action potential in a myelinated axon

The myelinated nerve fibers have a wrapping of myelin sheath with gaps at regular intervals which are devoid of myelin sheath (nodes of Ranvier).The axonal membrane in the naked area (nodes of Ranvier) bears densely packed ion channels. The myelin sheath acts as an insulator and does not allow the current flow. Therefore, in myelinated nerve fibers the **local circuit of current flow** only occurs from one node of Ranvier to the adjacent node . That is, the impulse (action potential) jumps from one node of Ranvier to next. This is known as **saltatory conduction**. Since the impulse jumps from one node to other, the speed of conduction in myelinated fibers is much rapid (50 to 100 times faster) than the unmyelinated fiber.

Factors affecting conduction velocity

The velocity of conduction in nerve fibers varies from as little as 0.25 m/sec in very small unmyelinated fibers to as high as 100 m/sec in very large myelinated fibers. In general the factors affecting conduction velocity are:

1. Temperature: A decrease in temperature delays conduction i.e. slows down the conduction velocity.

2. Axon diameter: affects the conduction velocity through the resistance offered by the axoplasm to the flow of axoplasmic current. If the diameter of the axon is greater, the axoplasmic resistance is lesser and hence the velocity of conduction is higher.

3. **Myelination**: increases conduction velocity by increasing the axon diameter, and by the saltatory conduction.

Synapse

Neurons that transmit impulses to other neurons do not actually touch one another. The small gap or space between the axon of one neuron and

the dendrites or cell body of the next neuron is called the **synapse**. Within the synaptic knob (terminal end) of the presynaptic axon is a chemical **neurotransmitter** that is released into the synapse by the arrival of an electrical nerve impulse (figure 4).

The neurotransmitter diffuses across the synapse, combines with specific receptor sites on the cell membrane of the postsynaptic neuron, and there generates an electrical impulse that is, in turn, carried by this neuron's axon to the next synapse, and so forth. A chemical **inactivator** at the cell body or dendrite of the postsynaptic neuron quickly inactivates the neurotransmitter. This prevents unwanted, continuous impulses, unless a new impulse from the first neuron releases more neurotransmitter. Many synapses are termed **excitatory**, because the neurotransmitter causes the postsynaptic neuron to depolarize (become more negative outside as Na+ ions enter the cell) and transmit an electrical impulse to another neuron, muscle cell, or gland. Some synapses, however, are **inhibitory**, meaning that the neurotransmitter causes the postsynaptic neuron to hyperpolarize(become even more positive outside as K+ ions leave the cell or Cl^- ions enter the cell) and therefore **not** transmit an electrical impulse.

Such inhibitory synapses are important, for example, for slowing the heart rate, and for balancing the excitatory impulses transmitted to skeletal muscles. With respect to the skeletal muscles, this inhibition prevents excessive contraction and is important for coordination. An example of a neurotransmitter is **acetylcholine**, which is found at neuromuscular junctions, in the CNS, and in much of the peripheral nervous system. Acetylcholine usually makes a postsynaptic membrane more permeable to Na+ ions, which brings about depolarization of the postsynaptic neuron. **Cholinesterase** is the inactivator of acetylcholine.

Nervous System Divisions

The nervous system has two divisions. The **central nervous system** (**CNS**) consists of the brain and spinal cord. The **peripheral nervous system** (**PNS**) consists of cranial nerves and spinal nerves. The PNS includes the autonomic nervous system (ANS).

Spinal Cord Reflexes

A **reflex** is an involuntary response to a stimulus, that is, an automatic action stimulated by a specific change of some kind. **Spinal cord reflexes** are those that do not depend directly on the brain, although the brain may inhibit or enhance them.

Reflex Arc

A reflex arc is the pathway that nerve impulses travel when a reflex is elicited, and there are five essential parts:

1. **Receptors**—detect a change (the stimulus) and generate impulses.
2. **Sensory neurons**—transmit impulses from receptors to the CNS.
3. **Central nervous system**—contains one or more synapses (interneurons may be part of the pathway).
4. **Motor neurons**—transmit impulses from the CNS to the effector.
5. **Effector**—performs its characteristic action.

Patellar Reflex or Knee- Jerk

In this reflex, a tap on the patellar tendon just below the kneecap causes extension of the lower leg. This is a **stretch reflex**, which means that a muscle that is stretched will automatically contract. In the quadriceps femoris muscle are stretch receptors that detect the stretching produced by striking the patellar tendon. These receptors generate impulses that are carried along sensory neurons in the femoral nerve to the spinal cord. In the spinal cord, the sensory neurons synapse with motor neurons (this is a two-neuron reflex). The motor neurons in the femoral nerve carry impulses back to the quadriceps femoris, the effector,

which contracts and extends the lower leg. The patellar reflex is one of many used clinically to determine whether the nervous system is functioning properly. If the patellar reflex were absent in a patient, the problem could be in the thigh muscle, the femoral nerve, or the spinal cord. If the reflex is normal, however, that means that all parts of the reflex arc are intact. Since these are spinal cord reflexes, the brain is not directly involved.

The Autonomic Nervous System

The **autonomic nervous system** (**ANS**) is actually part of the peripheral nervous system in that it consists of motor portions of some cranial and spinal nerves. The ANS has two divisions: **sympathetic** and **parasympathetic**. Often, they function in opposition to each other.

Sympathetic Division

The sympathetic division brings about widespread responses in many organs. The sympathetic division is dominant in stressful situations, which include anger, fear, or anxiety, as well as exercise. For our prehistoric ancestors, stressful situations often involved the need for intense physical activity—the "fight or flight response. The heart rate increases, vasodilation in skeletal muscles supplies them with more oxygen, the bronchioles dilate to take in more air and the liver changes glycogen to glucose to supply energy. At the same time digestive secretions decrease and peristalsis slows; these are not important in a stress situation. Vasoconstriction in the skin and viscera shunts blood to more vital organs such as the heart, muscles, and brain.

Parasympathetic Division

The parasympathetic division dominates in relaxed (non-stress) situation to promote normal functioning of several organ systems.

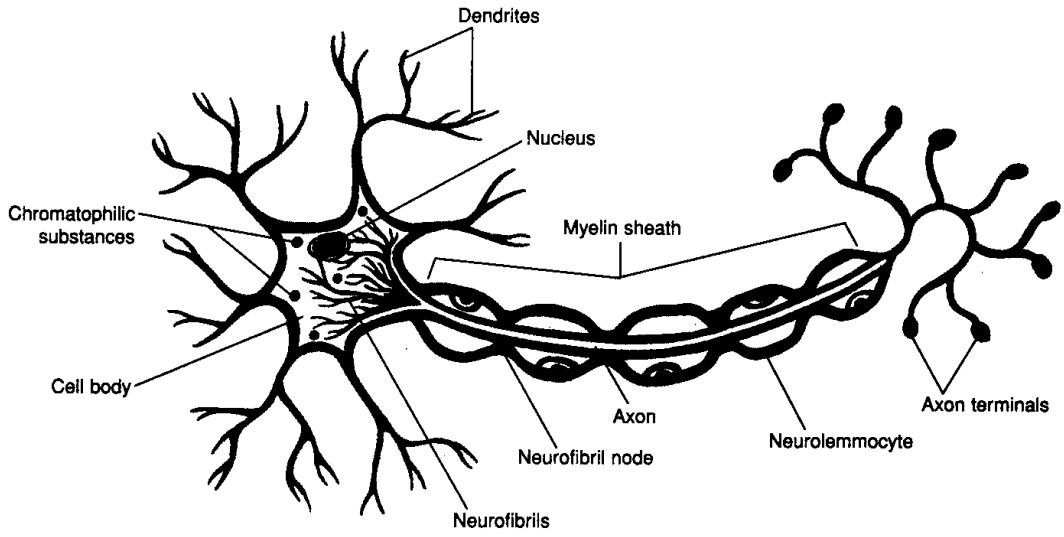


Figure (1): A nerve cell

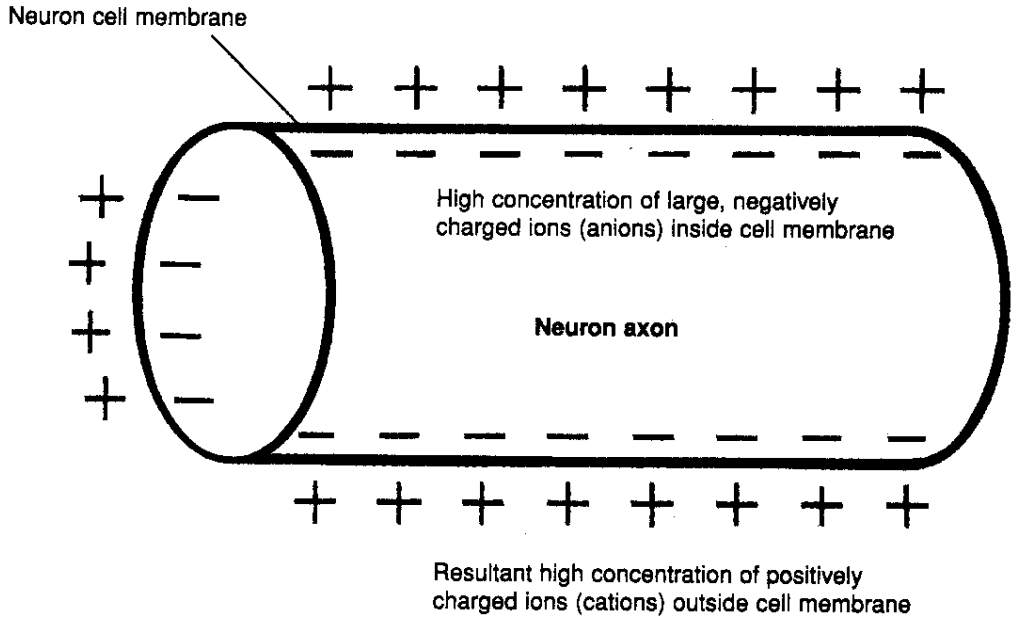


Figure (2): A segment of neuron showing the location of charges

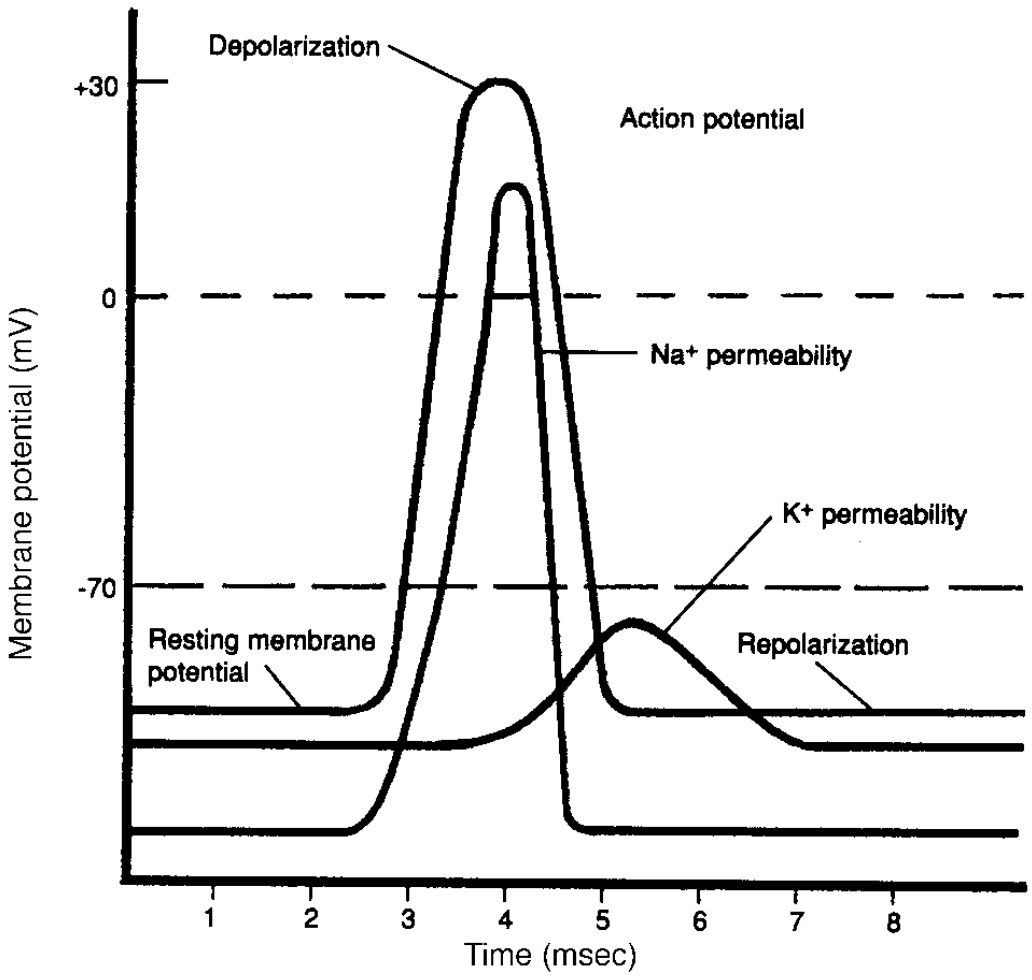


Figure (3): An action potential

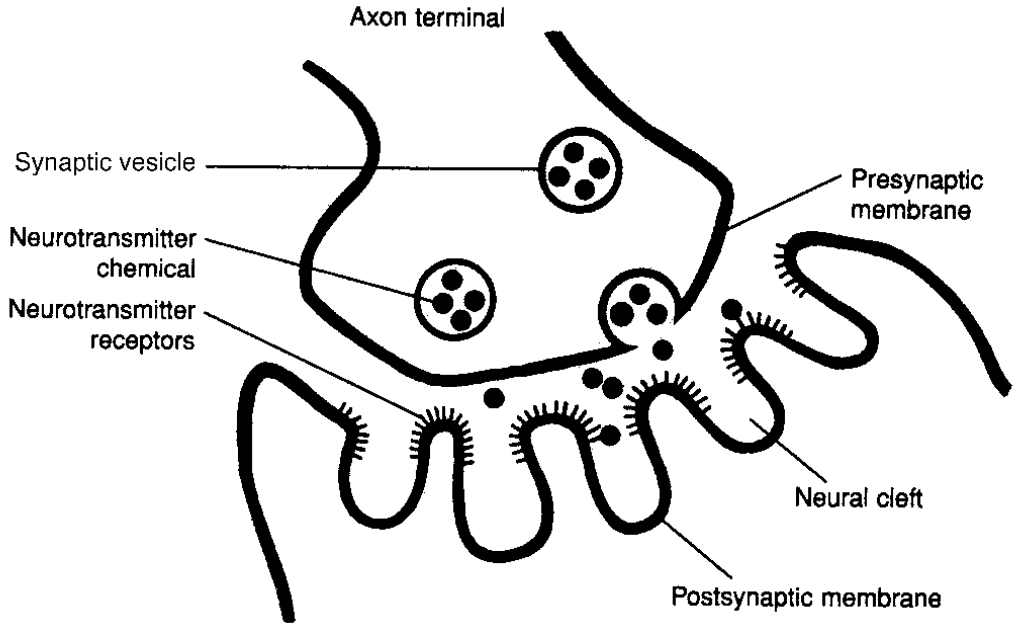


Figure (4): Synaptic transmission

Urinary System

Urinary System is a group of organs in the body concerned with filtering out excess fluid and other substances from the bloodstream. The substances are filtered out from the body in the form of **urine**. Urine is a transparent yellow fluid containing unwanted wastes mostly excess water, salts, and nitrogen compounds (In general 95% water and 5% solutes). Excretion is the process of eliminating, from an organism, waste products of metabolism and other materials that are of no use. The kidneys are the most important excretory organ; they also accomplish several other functions:

1- Regulation of plasma ionic composition such as sodium, potassium, calcium, magnesium, chloride, bicarbonate, and phosphates

2- Regulation of plasma volume by controlling how much water a person excretes. The plasma volume has a direct effect on the total blood volume, which has a direct effect on blood pressure. Salts such as NaCI can cause osmosis, the diffusion of water into the blood.

3- Regulation of plasma hydrogen ion concentration (pH) with the lungs (regulated the acid- base balance) because they control the amount of bicarbonate excreted or held onto. The kidneys help maintain the blood pH mainly by excreting hydrogen ions and reabsorbing bicarbonate ions as needed.

4- Removal of metabolic waste products and foreign substances from the plasma like nitrogenous waste(**urea**, **ammonia**, **creatinine** and **uric acid**) **urea** comes from combines that ammonia with carbon dioxide by the liver .The **creatinine** comes from the metabolic breakdown of creatine phospate (a high-energy phosphate in muscles). **Uric acid** comes from the break down of nucleotides. Uric acid is insoluble and too much uric

acid in the blood will build up and form crystals that can collect in the joints and cause gout.

5- Secretion of hormones like **Renin**, it is needed to stimulate the secretion of aldosterone by the adrenal cortex which promotes the kidneys to reabsorb the (Na+) ions. The kidneys also secrete **erythropoietin** when the blood doesn't have the capacity to carry oxygen; erythropoietin stimulates red blood cell production. Vitamin D from the skin is also activated with help from the kidneys. Calcium (Ca+) absorption from the digestive tract is promoted by vitamin D.

Kidneys and Their Structure:-

The **kidneys** are pair of bean shaped, reddish brown organs, weighs 140- 160 g, they are covered by the renal capsule, which is a tough capsule of fibrous connective tissue. Adhering to the surface of each kidney is two layers of fat to help cushion them. There is a concaved side of the kidney that has a depression where a renal artery enters, and a renal vein and a ureter exit the kidney. They are considered retroperitoneal, which means they lie behind the peritoneum.

Each kidney has an indentation called the **hilum** on its medial side, at the hilum, the renal artery enters the kidney, and the renal vein and ureter emerge, (figure 1)

There are three major regions of the kidney, **renal cortex**, **renal medulla** and the **renal pelvis**. The outer, granulated layer is the renal cortex; the cortex stretches down in between a radially striated inner layer. The inner radially striated layer is the renal medulla, this contains between 8 and 18 cone- shaped sections known as pyramids called the renal pyramids, separated by renal columns. The ureters are continuous with the renal pelvis and are the very center of the kidney.

The Nephron:-

The **nephron** is the structural and functional unit of the kidney; each kidney contains approximately 1 million nephrons. It is in the nephrons, with their associated blood vessels, that urine is formed. Each nephron has two major portions: a renal corpuscle and a renal tubule (figure 2), each of these major parts have further subdivisions.

Renal Corpuscle:

A **renal corpuscle** consists of a glomerulus surrounded by a Bowman's capsule. The **glomerulus** is a capillary network that arises from an **afferent arteriole** and empties Glomerular filtration into an **efferent arteriole**. The diameter of the efferent arteriole is smaller than that of the afferent arteriole (diameter of the afferent arteriole is 25% larger than normal), which helps maintain a fairly high blood pressure in the glomerulus. **Bowman's capsule** (or glomerular capsule) is the expanded end of a renal tubule; it encloses the glomerulus.

The inner layer of Bowman's capsule is made of **podocytes**; the name means "foot cells," and the "feet" of the podocytes are on the surface of the glomerular capillaries. The arrangement of podocytes creates pores, spaces between adjacent "feet," which make this layer very permeable. The space between the inner and outer layers of Bowman's capsule contains renal filtrate, the fluid that is formed from the blood in the glomerulus and will eventually become urine.

Renal Tubule:

The **renal tubule** continues from Bowman's capsule and consists of the following parts: **proximal convoluted tubule** (in the renal cortex and contains the microvilli), **loop of Henle** (or loop of the nephron, in the renal medulla), and **distal convoluted tubule** (in the renal cortex). The distal convoluted tubules from several nephrons empty into a **collecting tubule**. Several collecting tubules then unite to form a papillary duct that empties urine into a calyx of the renal pelvis. These anatomic

characteristics provide for efficient exchanges of materials. All parts of the renal tubule are surrounded by **peritubular capillaries**, which arise from the efferent arteriole. The peritubular capillaries will receive the materials reabsorbed by the renal tubules.

Blood Vessels of the Kidney:-

The pathway of blood flow through the kidney is an essential part of the process of urine formation (renal blood flow about 21% of cardiac output). Blood from the abdominal aorta enters the **renal artery**, which branches extensively within the kidney into smaller arteries. The smallest arteries give rise to afferent arterioles in the renal cortex. From the afferent arterioles, blood flows into the glomeruli (capillaries), to efferent arterioles, to peritubular capillaries, to veins within the kidney, to the **renal vein**, and finally to the inferior vena cava. The efferent arteriole drains the glomerulus.

Ureters:

The **ureters** are two tubes that drain urine from the kidneys to the bladder, each ureter is a muscular tube about (25 cm) long. Muscles in the walls of the ureters send the urine in small spurts into the bladder. After the urine enters the bladder from the ureters, small folds in the bladder mucosa act like valves preventing backward flow of the urine. The outlet of the bladder is controlled by a sphincter muscle.

Urinary Bladder:

The **urinary bladder** is a hollow, muscular and distensible or elastic organ that sits on the pelvic floor. When the bladder fills with urine (about half full), stretch receptors send nerve impulses to the spinal cord, which then sends a reflex nerve impulse back to the sphincter (muscular valve) at the neck of the bladder, causing it to relax and allow the flow of urine into the urethra. The Internal urethral sphincter is involuntary.

Urethra:

The **urethra** is a muscular tube that connects the bladder with the outside of the body. The function of the urethra is to remove urine from the body, it measures about (3.8 cm) in the human female. In the human male, the urethra is about (20 cm) long. Because the urethra is so much shorter in a woman it makes it much easier for a woman to get harmful bacteria in her bladder this is commonly called a bladder infection or a UTI.

The **urethral sphincter** is a collective name for the muscles used to control the flow of urine from the urinary bladder; these muscles surround the urethra, so that when they contract, the urethra is closed.

Formation of Urine:-

The formation of urine involves three major processes: The first is glomerular filtration, which takes place in the renal corpuscles. The second and third are tubular reabsorption and tubular secretion, which take place in the renal tubules (figure 3).

Glomerular Filtration:

Filtration is the process in which blood pressure forces plasma and dissolved material out of capillaries. In **glomerular filtration**, blood pressure forces plasma, dissolved substances, and small proteins out of the glomeruli and into Bowman's capsules, this fluid is no longer plasma but is called **renal filtrate**. The blood pressure in the glomeruli, compared with that in other capillaries, is relatively high, "up to four times", about 60 mmHg (because the diameter of the afferent arteriole going to the glomerulus is 25% larger than normal). The pressure in Bowman's capsule is very low, and its inner, podocyte layer is very permeable, so that approximately 20% to 25% of the blood that enters glomeruli becomes renal filtrate in Bowman's capsules.

The blood cells and larger proteins are too large to be forced out of the glomeruli, so they remain in the blood. Waste products are dissolved in

blood plasma, so they pass into the renal filtrate. Useful materials such as nutrients and minerals are also dissolved in plasma and are also present in renal filtrate. Filtration is not selective with respect to usefulness; it is selective only with respect to size. Therefore, renal filtrate is very much like blood plasma, except that there is far less protein and no blood cells are present.

The **glomerular filtration rate** (GFR) is the amount of renal filtrate formed by the kidneys in 1 minute, and averages 100 to 125 ml per minute (remove about 19% of blood plasma). GFR may be altered if the rate of blood flows through the kidney changes. If blood flow increases, the GFR increases, and more filtrate is formed. If blood flow decreases (as may happen following a severe hemorrhage), the GFR decreases, less filtrate is formed, and urinary output decreases.

Tubular Reabsorption:

Tubular reabsorption takes place from the renal tubules into the peritubular capillaries (the blood pressure in the peritubular capillaries is15 mmHg). In a 24-hour period, the kidneys form 150 to 180 liters of filtrate, and normal urinary output in that time is 1 to 2 liters. Therefore, it becomes apparent that most of the renal filtrate does not become urine. Approximately 99% of the filtrate is reabsorbed back into the blood in the peritubular capillaries. Only about 1% of the filtrate will enter the renal pelvis as urine.

Most reabsorption and secretion (about 65%) take place in the proximal convoluted tubules whose cells have **microvilli** that greatly increase their surface area. Water, Na^{+}, Cl^{-}, K^{+}, glucose, amino acid are reabsorbed in proximal convoluted tubules whale other does not reabsorb like inulin, creatinine .

About 20% of filtered Na^{+} and Cl^{-}, 15% of filtered water and cations such as K^{+}, Ca^{2+} and Mg^{2+} are reabsorbed in the loop of Henle.

The distal convoluted tubules and collecting tubules are also important sites for the reabsorption, approximately 7% of the filtered NaCl and about 8-17% of water is reabsorbed. Sodium chloride reabsorbed into the system increases the osmolarity of blood in comparison to the glomerular filtrate. This reabsorption process allows water (H_2O) to pass from the glomerular filtrate back into the circulatory system. Glucose and various amino acids also are reabsorbed (towards the end of the proximal convoluted tubules) into the circulatory system, these nutrients have carrier molecules that claim the glomerular molecule and release it back into the circulatory system. If all of the carrier molecules are used up, excess glucose or amino acids are set free into the urine.

Reabsorption of Water and Salt:

Direct control of water excretion in the kidneys is exercised by the anti-diuretic hormone (ADH), released by the posterior lobe of the pituitary gland. ADH causes the insertion of water channels into the membranes of cells lining the collecting ducts, allowing water reabsorption to occur. Without ADH, little water is reabsorbed in the collecting ducts and dilute urine is excreted. There are several factors that influence the secretion of ADH. The first of these happen when the blood plasma gets too concentrated, when this occurs, special receptors in the hypothalamus release ADH. When blood pressure falls, stretch receptors in the aorta and carotid arteries stimulate ADH secretion to increase volume of the blood.

Aldosterone is secreted by the adrenal cortex in response to a high blood potassium level, to a low blood sodium level, or to a decrease in blood pressure. Aldosterone promotes the excretion of potassium ions and the reabsorption of sodium ions, when aldosterone stimulates the reabsorption of Na^+ ions, water follows from the filtrate back to the blood. This helps maintain normal blood volume and blood pressure. The

release of Aldosterone is initiated by the secretion of renin the enzyme that converts angiotensinogen (a large plasma protein produced by the liver) into **Angiotensin I** and eventually into **Angiotensin II** which stimulates the adrenal cortex to produce aldosterone.

The antagonist to aldosterone is **atrial natriuretic peptide** (ANP), which is secreted by the atria of the heart when the atrial walls are stretched by high blood pressure or greater blood volume. ANP inhibits the secretion of renin by the juxtaglomerular apparatus and the secretion of the aldosterone by the adrenal cortex. This promotes the excretion of sodium. When sodium is excreted so is water. This causes blood pressure and volume to decrease.

Tubular Secretion:

Some substances are removed from blood through the peritubular capillary network into the distal convoluted tubule or collecting duct and K^+ and H^+ are secreted in these segments .This mechanism also changes the composition of urine. In **tubular secretion**, substances are actively secreted from the blood in the peritubular capillaries into the filtrate in the renal tubules. Waste products, such as ammonia and some creatinine, and the metabolic products of medications may be secreted into the filtrate to be eliminated in urine. Hydrogen ions (H^+) may be secreted by the tubule cells to help maintain the normal pH of blood.

Hypernatremia:

An increase in plasma sodium levels above normal is **hypernatremia**. Sodium is the primary solute in the extracellular fluid. Sodium levels have a major role in osmolarity regulation. For excitable cells the electrochemical gradient for sodium across the plasma membrane is critical for life. Water retention and an increased blood pressure usually are signs of hypernatremia. If the plasma sodium levels are below normal

it is called **hyponatremia**. Signs of this are low plasma volume and hypotension.

Diseases of the Kidney:-

1- Diabetic nephropathy; Is a progressive kidney disease caused by angiopathy of capillaries in the kidney glomeruli. It is characterized by nodular glomerulosclerosis. It is due to longstanding diabetes mellitus. In medicine **hematuria** (or "haematuria") is the presence of blood in the urine. It is a sign of a large number of diseases of the kidneys and the urinary tract, ranging from trivial to lethal.

2- Kidney stones: Also known as nephrolithiases, urolithiases or renal calculi, are solid accretions (crystals) of dissolved minerals in urine found inside the kidneys or ureters. They vary in size from as small as a grain of sand to as large as a golf ball. Kidney stones typically leave the body in the urine stream; if they grow relatively large before passing (on the order of millimeters), obstruction of a ureter and distention with urine can cause severe pain most commonly felt in the flank, lower abdomen and groin. Kidney stones are unrelated to gallstones.

3- Pyelonephritis: When an infection of the renal pelvis and calices, called pyelitis, spreads to involve the rest of the kidney as well, the result is pyelonephritis. It usually results from the spread of fecal bacterium Escherichia coli from the anal region superiorly through the urinary tract. In severe cases, the kidney swells and scars, abscesses form, and the renal pelvis fill with pus. Left untreated, the infected kidney may be severely damaged, but administration of antibiotics usually achieves a total cure.

4- Urinary tract infections (UTI's): The second most common type of bacterial infections is UTI's. In the hospital indwelling catheters and straight catheterizing predispose the opportunity for urinary tract infections. In females there are three stages in life that predispose urinary

tract infections that is menarche, manipulation between intercourse, and menopause.

5- Glomerulonephritis: Inflammation of the glomerular can be caused by immunologic abnormalities, drugs or toxins, vascular disorders, and systemic diseases. Glomerulonephritis can be acute, chronic or progressive.

Two major changes in the urine are distinctive of glomerulonephritis: hematuria and proteinuria with albumin as the major protein. There is also a decrease in urine as there is a decrease in GFR (glomerular filtration rate).

6- Renal Failure: Uremia is a syndrome of renal failure and includes elevated blood urea and creatinine levels. Acute renal failure can be reversed if diagnosed early. Acute renal failure can be caused by severe hypotension or severe glomerular disease.

Diabetes Insipidus:

This is caused by the deficiency of or decrease of ADH. The person with (DI) has the inability to concentrate their urine in water restriction, in turn they will void up 3 to 20 liters/day. There are two forms of (DI), neurogenic, and nephrogenic. In nephrogenic (DI) the kidneys do not respond to ADH. Usually the nephrogenic (DI) is characterized by the impairment of the urine concentrating capability of the kidney along with concentration of water. The cause may be a genetic trait, electrolyte disorder, or side effect of drugs. In the neurogenic (DI), it is usually caused by head injury near the hypophysisal tract.

The Urination Reflex:

Urination may also be called **micturition** or **voiding**. This reflex is a spinal cord reflex over which voluntary control may be exerted. The stimulus for the reflex is stretching of the detrusor muscle of the bladder. The bladder can hold as much as (500- 600) mL of urine, or even more,

but the reflex is activated long before the maximum is reached. When urine volume reaches 200 to 300 ml, the stretching is sufficient to generate sensory impulses that travel to the sacral spinal cord. Motor impulses return along parasympathetic nerves to the detrusor muscle, causing contraction. At the same time, the internal urethral sphincter relaxes. If the external urethral sphincter is voluntarily relaxed, urine flows into the urethra, and the bladder is emptied. Urination can be prevented by voluntary contraction of the external urethral sphincter. However, if the bladder continues to fill and be stretched, voluntary control is eventually no longer possible.

The Kidneys and Acid- Base Balance:-

The kidneys are the organs most responsible for maintaining the pH of blood (normal 7.35 - 7.45) and tissue fluid within normal ranges. They have the greatest ability to compensate for the pH changes that are a normal part of body metabolism or the result of disease, and to make the necessary corrections. Acid- base balance is controlled by renal regulation of $HCO3^{-}$ and H^{+} ions and by pulmonary excretion of $CO2$.

If body fluids are becoming too acidic, the kidneys will secrete more H^{+} ions into the renal filtrate and will return more $HCO3^{-}$ ions to the blood. This wills help raise the pH of the blood back to normal. If body fluids are becoming too alkaline, the kidneys will return H^{+} ions to the blood and excrete $HCO3^{-}$ ions in urine. This will help lower the pH of the blood back to normal.

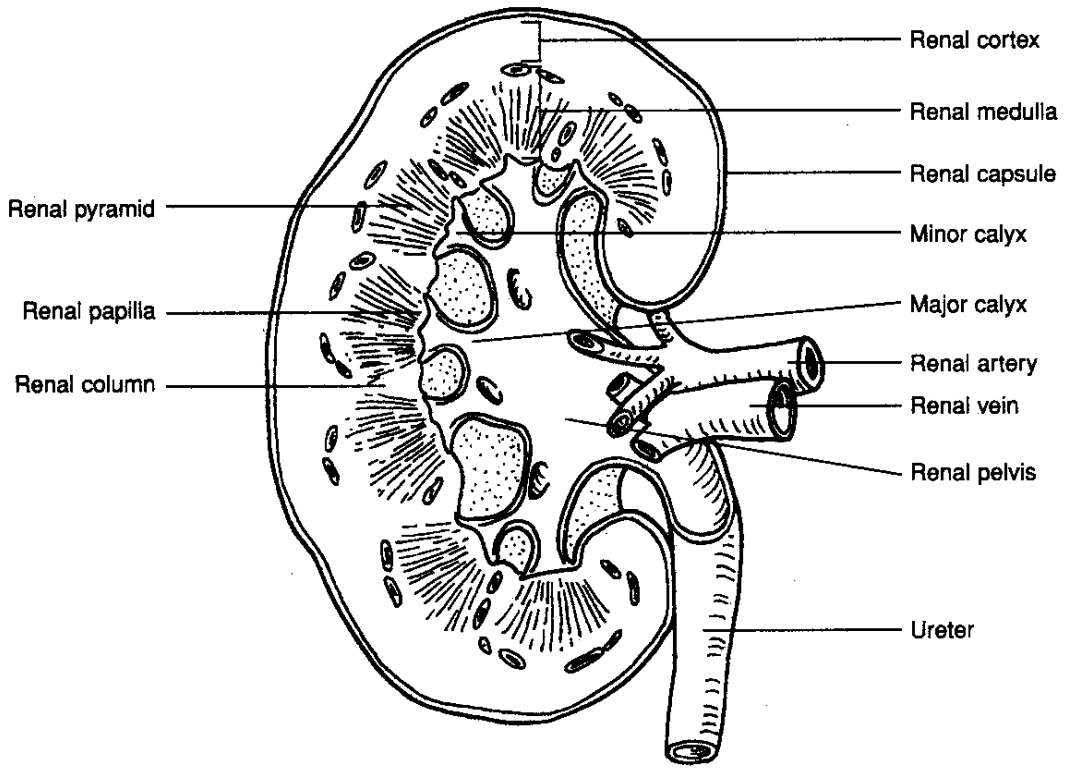
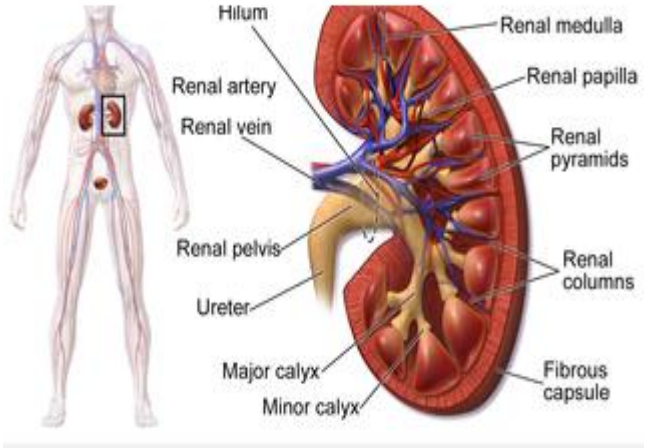


Figure (1): The kidney



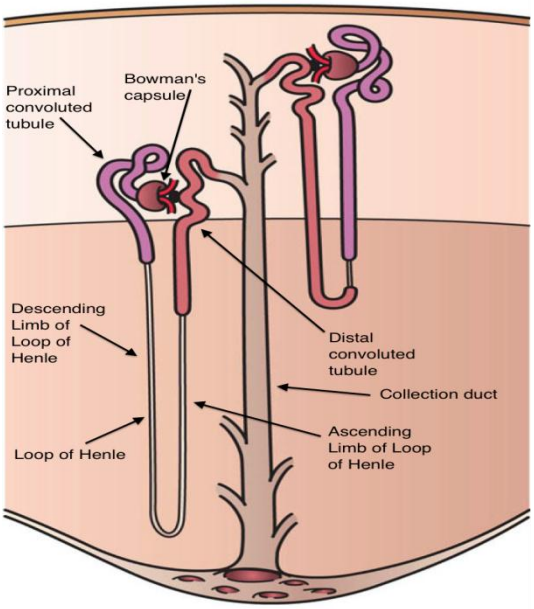


Figure (2): The nephron

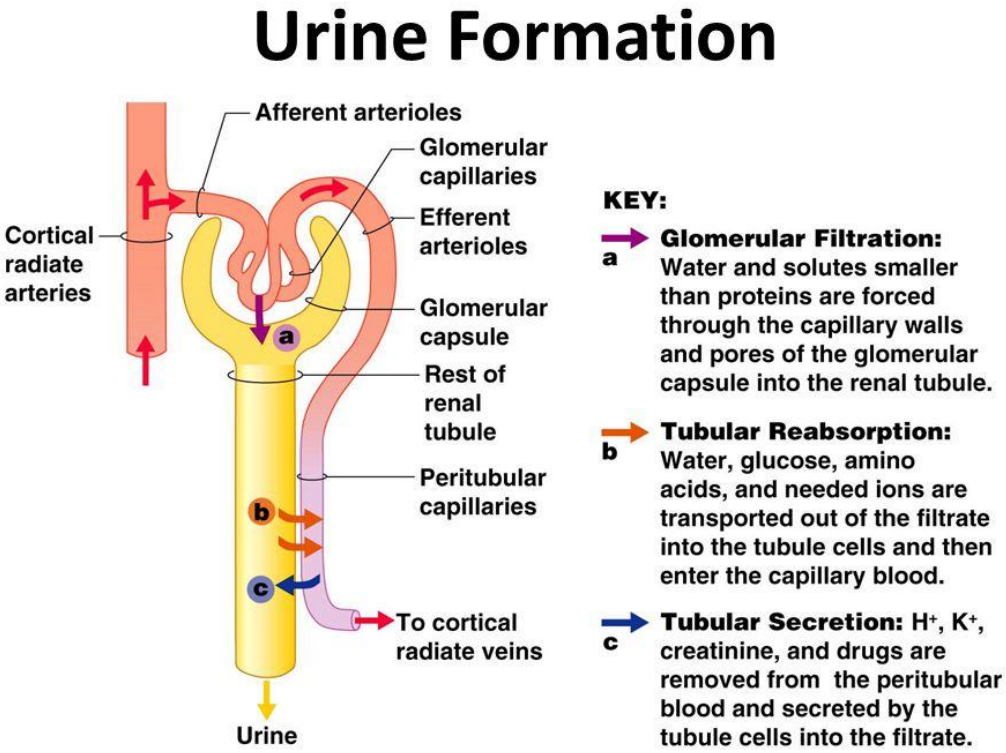
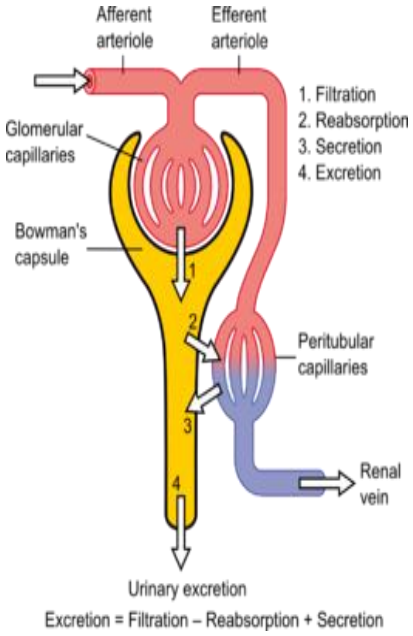
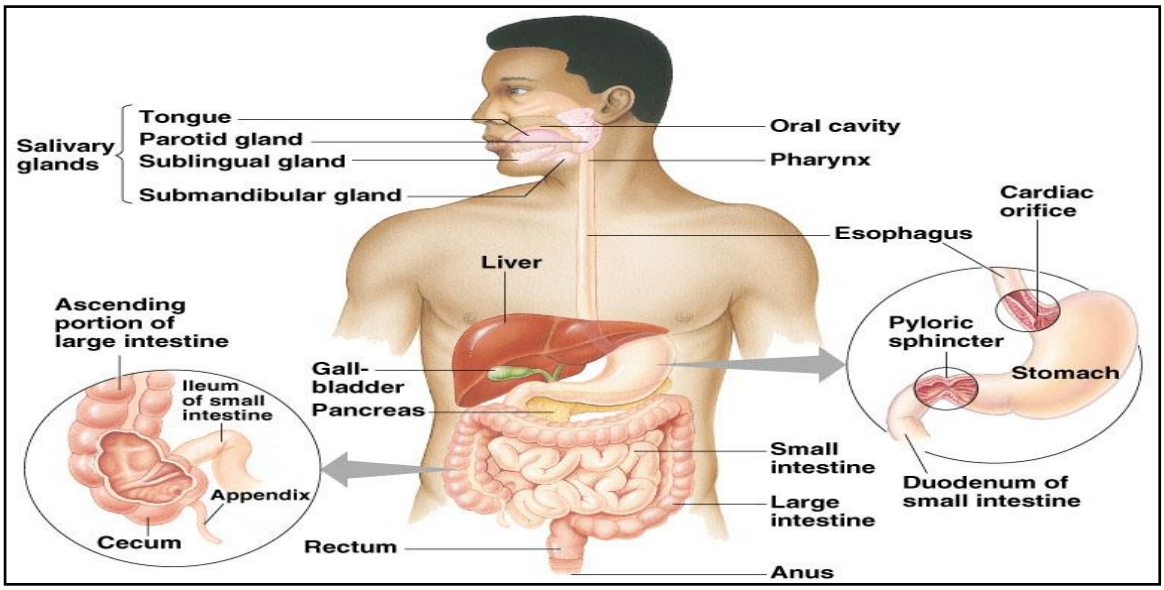


Figure (3): Formation of urine


Afferent arteriole
Efferent arteriole
1. Filtration
2. Reabsorption
3. Secretion
4. Excretion
Glomerular capillaries
Bowman's capsule
1
2
3
4
Peritubular capillaries
Renal vein
Urinary excretion
Excretion = Filtration – Reabsorption + Secretion

Digestive System

The **digestive system**, it is also referred to as the **gastrointestinal (GI) system**, includes the tubular **gastrointestinal (GI) tract** plus the **accessory digestive organs.** The GI tract which is approximately 9 m long; it includes the mouth, pharynx, esophagus, stomach, small intestine, and large intestine. The accessory digestive organs which are not part of the tract but secrete substances into it via connecting ducts; they include the salivary glands, liver, gallbladder, and pancreas.



The digestive system

Functions of the gastrointestinal system

The overall function of the GI system is to process ingested foods into molecular forms that are then transferred, along with salts and water to the body's internal environment, where they can be distributed to cells by the circulatory system.

The functions of the GI system can be described in terms of the following four processes:-

1. Digestion: This refers to the breakdown of food molecules into their smaller subunits, which can be absorbed. During digestion, two main processes occur at the same time:

a. Mechanical digestion: Larger pieces of food get broken down into smaller pieces while being prepared for chemical digestion. Mechanical digestion starts in the mouth and continues into the stomach.

b. Chemical digestion: Several different enzymes break down macromolecules into smaller molecules that can be absorbed. Chemical digestion starts in the mouth and continues into the intestines.

2. Secretion: This includes both exocrine and endocrine secretions.

a. Exocrine secretions: Water, hydrochloric acid, bicarbonate, and many digestive enzymes are secreted into the lumen of the GI tract.

b. Endocrine secretions: The stomach and small intestine secrete a number of hormones that help to regulate the digestive system.

3. Absorption: This refers to the passage of digested end products from the lumen of the GI tract across a layer of epithelial cells into the blood or lymph.

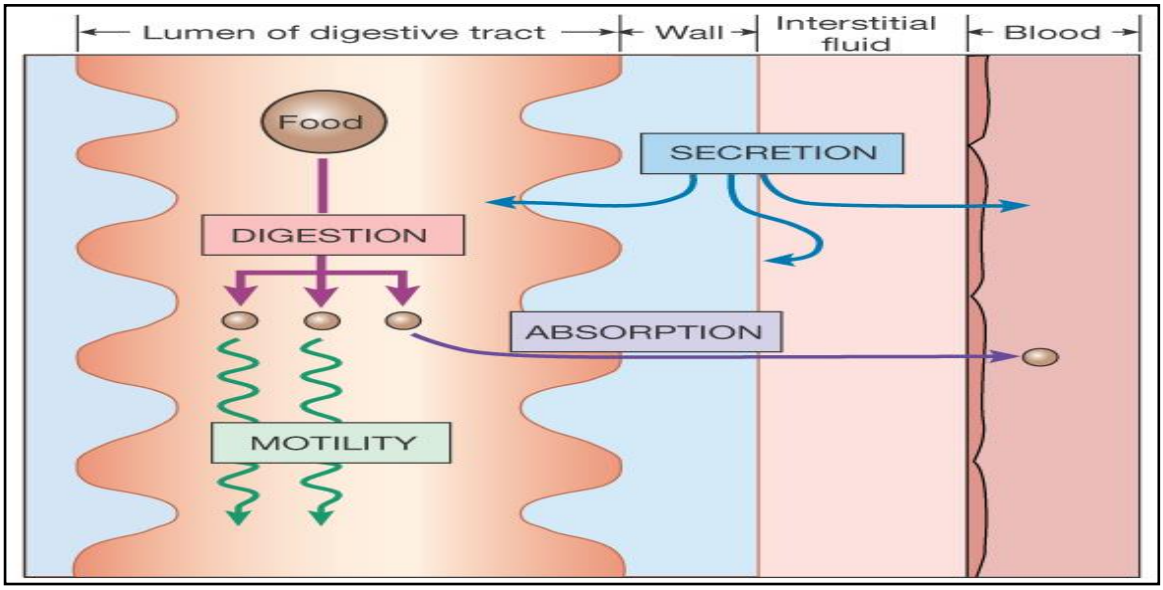
4. Motility: This refers to the movement of food through the digestive tract through the processes of:

a. Ingestion: Taking food into the mouth.

b. Mastication: Chewing the food and mixing it with saliva.

c. Deglutition: Swallowing the food.

d. Peristalsis: Rhythmic, wavelike contractions that move food through the GI tract.



Four processes carried out by the gastrointestinal tract

Layers of the gastrointestinal tract

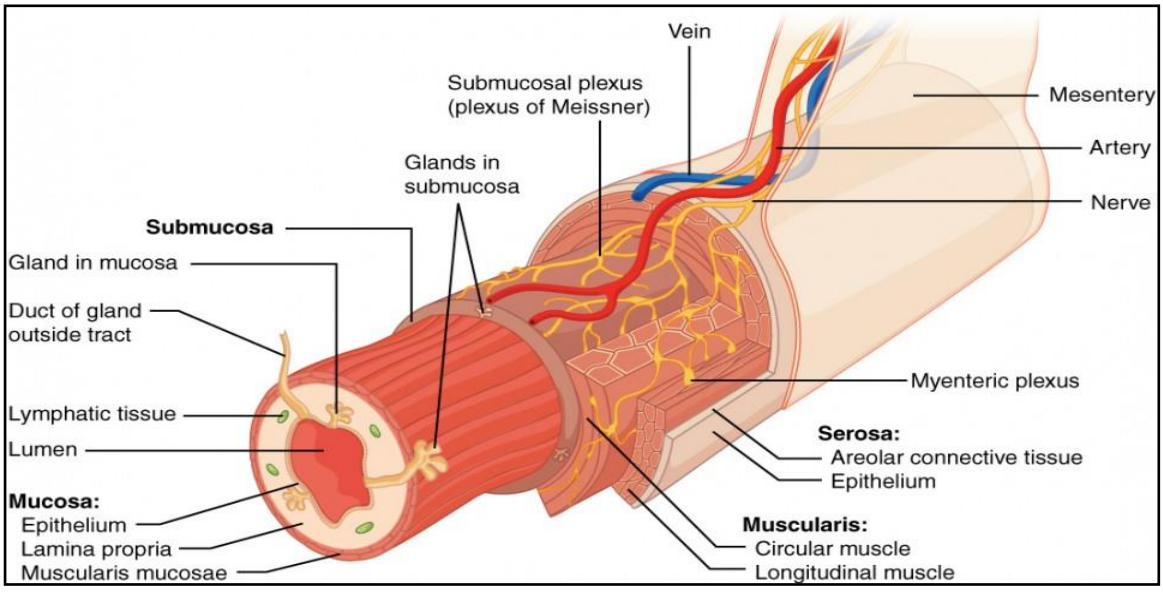
The GI tract is composed of four layers; each layer has different tissues and functions. From the inside out they are:

1. Mucosa: The mucosa is the inner most layer of the GI tract that is surrounding the lumen. It is composed of simple epithelium cells and a thin connective tissue. This layer comes in direct contact with the food and is responsible for absorption and secretion.

2. Submucosa: The submucosa consists of a dense irregular layer of connective tissue with large blood vessels, lymphatics and nerves branching into the mucosa and muscularis.

3. Muscularis: The muscularis is composed of two layers of muscle: an inner circular and outer longitudinal layer of smooth muscle. The circular muscle layer prevents the food from going backwards and the longitudinal layer shortens the tract (peristalsis). The muscularis is responsible for segmental contractions and peristaltic movement in the GI tract.

4. Serosa or adventitia: The serosa consists of several layers of connective tissue and simple squamous epithelium. This last layer is a protective layer, it secretes lubricating serous fluid.



Structure of the gastrointestinal wall

Phases of digestion

Oral cavity and esophagus

The GI tract begins with the **mouth,** and digestion starts there with chewing, which breaks up large pieces of food into smaller particles that can be swallowed. **Saliva** was secreted by three pairs of **salivary glands;** they are parotid glands, submandibular glands and sublingual glands. Saliva, which contains mucus, moistens and lubricates the food particles before swallowing. It also contains the enzyme **amylase,** which partially digests polysaccharides.

The next segments of the GI tract, the **pharynx** and **esophagus,** contribute nothing to digestion but provide the pathway by which ingested materials reach the stomach. The muscles in the walls of these segments control swallowing.

Stomach

The **stomach** is a saclike organ, located between the esophagus and the small intestine; it is the most distensible part of the GI tract. The stomach is divided into four sections:-

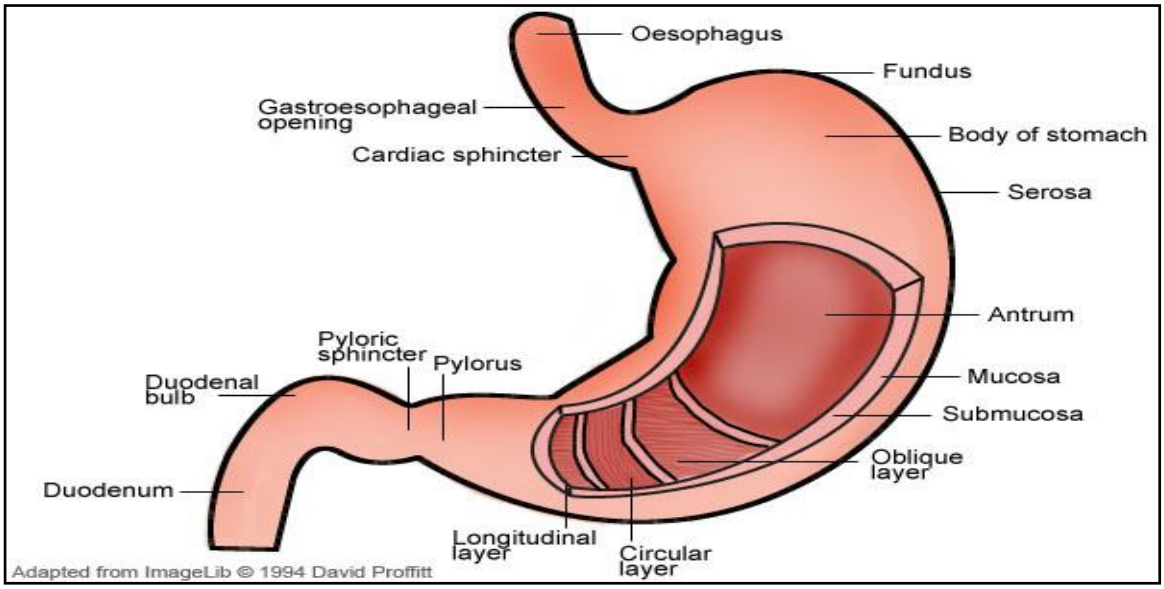
1- Cardiac region is where the contents of the esophagus empty into the stomach.

2- Fundus is formed by the upper curvature of the organ.

3- Body is the main central region.

4- Pylorus is the lower region that facilitates emptying the contents into the small intestine.

There are two sphincters keep the contents of the stomach: **cardiac or esophageal sphincter** dividing the tract above and **pyloric sphincter** dividing the stomach from the small intestine.



Regions of the stomach

The functions of the stomach are to store food, to initiate the digestion of proteins, to kill bacteria with the strong acidity of gastric juice, and to move the food into the small intestine as a pasty material called **chyme,** which contains molecular fragments of proteins and polysaccharides, droplets of fat, and salt, water, and various other small molecules ingested in the food.

The glands lining the stomach wall are called **gastric glands**; these glands contain several types of cells that secrete different products:-

1. Goblet cells secrete mucus.

2. Parietal cells secrete hydrochloric acid (HCl).

3. Chief cells secrete pepsinogen, an inactive form of the protein-digesting enzyme pepsin.

Small intestine

The small intestine is divided into three segments: An initial short segment, the **duodenum**, is followed by the **jejunum** and then by the longest segment, the **ileum**. Normally, most of the chyme entering from the stomach is digested and absorbed in the first quarter of the small intestine, in the duodenum and jejunum.

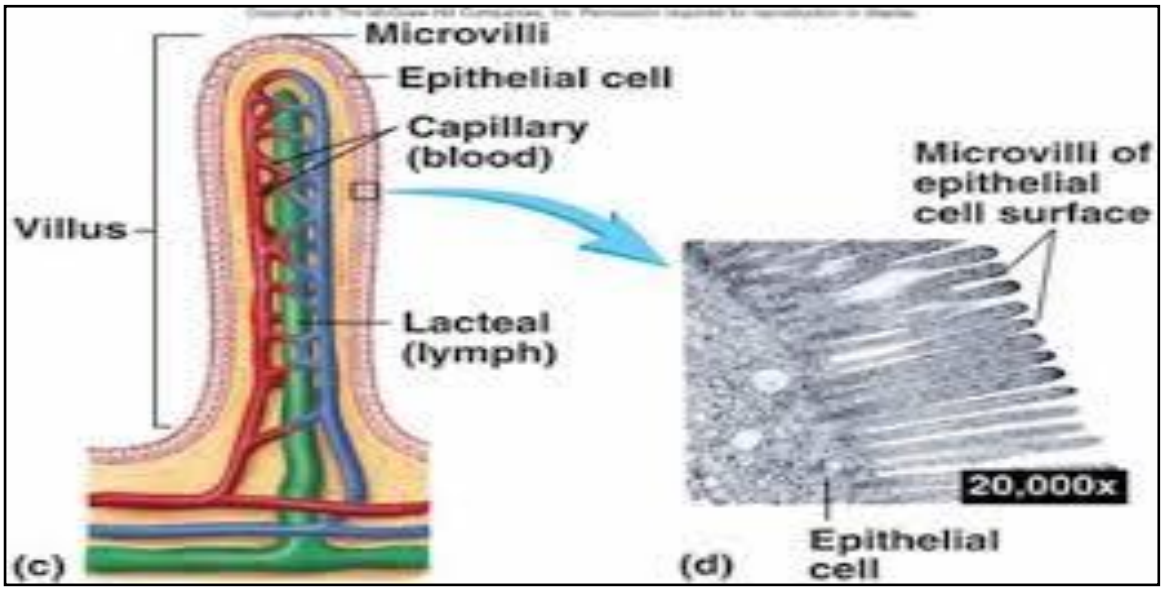
Digestion's final stages and most absorption occur in the small intestine. Here molecules of intact or partially digested carbohydrates, fats, and proteins are broken down by hydrolytic enzymes into monosaccharides, fatty acids, and amino acids. Some of these enzymes are on the luminal surface of the intestinal lining cells, while others are secreted by the pancreas and enter the intestinal lumen.

Digestive enzymes

Reaction	Enzymes	Produced by	Site of Occurrence
Starch + H_20 →maltose	a. Salivary amylase b. Pancreatic amylase	a. Salivary gland b. Pancreas	a. Mouth b. Small intestine
Maltose + H_20 → glucose	Maltase	Intestinal cells	Small intestine
Protein + H_20 → peptides	a. Pepsin b. Trypsin	a. Gastric glands b. Pancreas	a. Stomach b. Small intestine
Peptides+ H_20 → amino acids	Peptidase	Intestinal cells	Small intestine
Fats+ H_20 → glycerol + fatty acids	Lipase	Pancreas	Small intestine

The mucosa of the small intestine contains many folds that are covered with tiny fingerlike projections called **villi**. In turn, the villi are covered with microscopic projections called **microvilli**. These structures create a vast surface area through which nutrients can be absorbed. The products of digestion are absorbed across the epithelial cells and enter the blood and/or lymph.

Each villus has a network of capillaries and fine lymphatic vessels called **lacteals** close to its surface. The epithelial cells of the villi transport nutrients from the lumen of the intestine into these capillaries (amino acids and carbohydrates) and lacteals (lipids). The food that remains undigested and unabsorbed passes into the large intestine.



Structure of villi in small intestine

Large intestine

The large intestine is divided into the **cecum**, **colon**, **rectum**, and **anal canal**. The cecum is a blind pouch containing **appendix** (open only at one end) at the beginning of the large intestine.

The large intestine has little or no digestive function, but it does absorb water and electrolytes. Bacteria residing in the intestine, referred to as the **intestinal microflora,** ferment undigested nutrients, make gas, and produce vitamin K and folic acid which are absorbed in the large intestine. Waste materials pass through the ascending colon, transverse colon, descending colon, sigmoid colon, rectum, and anal canal. Then, the feces is excreted through the anus, the external opening of the anal canal.

Pancreas, Liver, and Gallbladder

Pancreas

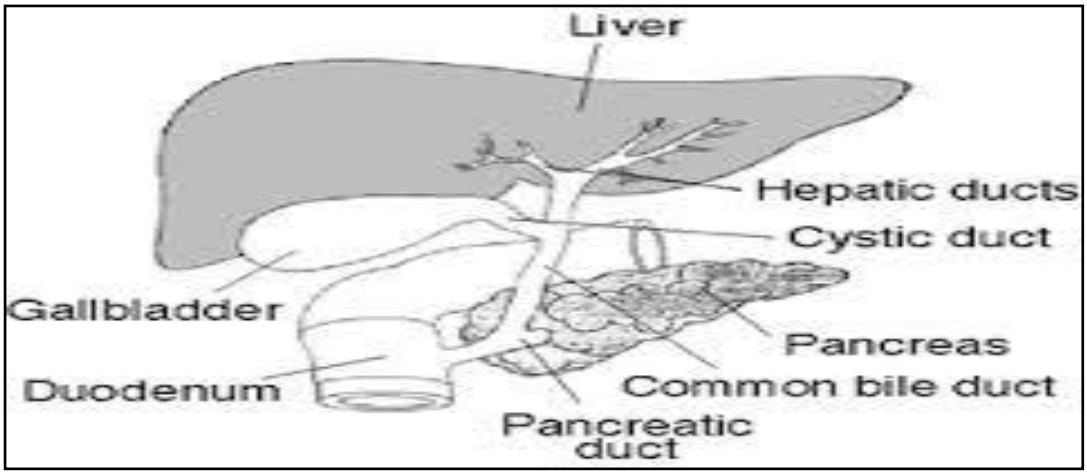
The pancreas is an elongated gland located behind the stomach. It has both endocrine and exocrine functions. The exocrine portion of the pancreas secretes digestive enzymes and a fluid rich in bicarbonate ions. The high acidity of the chyme coming from the stomach would inactivate the pancreatic enzymes in the small intestine if the acid were not neutralized by the bicarbonate ions.

Liver

The liver is located under the diaphragm on the right side of the upper abdomen; it makes a kind of bed for the gallbladder. The liver plays a major role in metabolism and has a number of functions. It also produces and excretes bile, which is necessary for adequate digestion and absorption of fats.

Gallbladder

The gallbladder is a pear shaped organ that stores about 50 ml of bile until the body needs it for digestion. Bile is stored between meals in the gallbladder. At mealtime, it is squeezed out of the gallbladder, through the bile ducts, and into the intestine to mix with the fat in food.



Pancreas, Liver, and Gallbladder

Neural and endocrine regulation of the digestive system

Neural and endocrine control mechanisms modify the activity of the digestive system.

Neural regulation

The GI tract has its own local nervous system, known as the **enteric nervous system,** in the form of two nerve networks, the **myenteric plexus,** lies between longitudinal and circular muscles layers and the **Meissner's or submucous plexus,** lies in the submucosa .In addition, nerve fibers from both the sympathetic and parasympathetic branches of the autonomic nervous system enter the intestinal tract and synapse with neurons in both plexuses. Parasympathetic nerves stimulate motility and secretions of the GI tract. The effects of the sympathetic nerves reduce peristalsis and secretory activity and stimulate the contraction of sphincter muscles along the GI tract

It should be noted that not all neural reflexes are indicated by signals within the tract. The sight or smell of food and the emotional state of an individual can have significant effects on the GI tract, effects that are mediated by the central nervous system via autonomic neurons.

Hormonal regulation

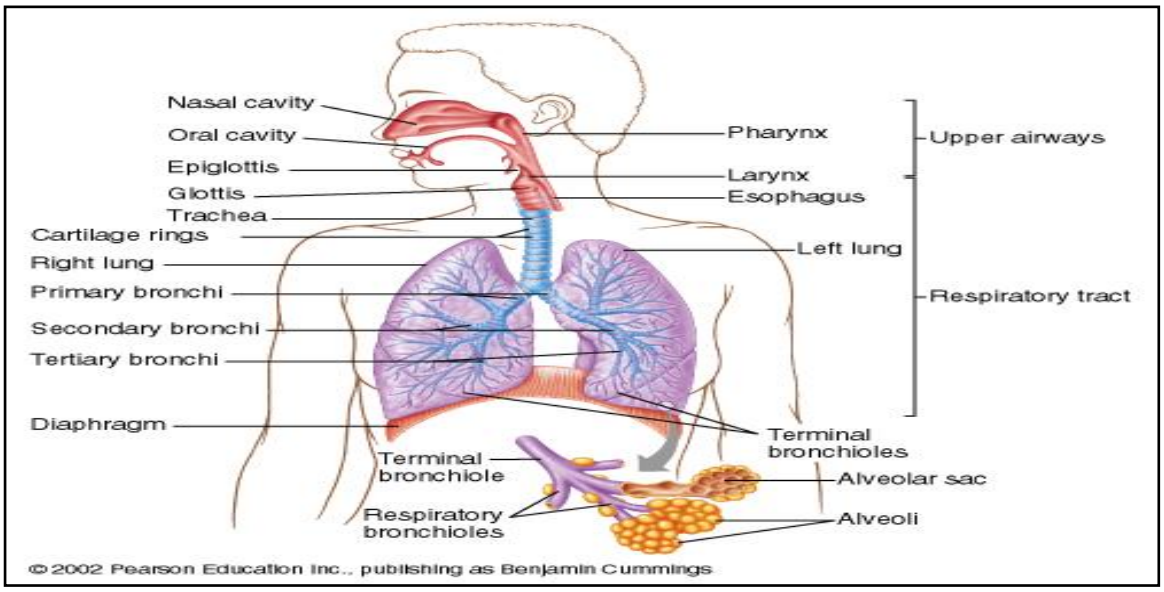
The major hormones that control the functions of the GI system are produced and released by endocrine cells in the mucosa of the stomach and small intestine. One surface of each endocrine cell is exposed to the lumen of the GI tract. At this surface, various chemical substances in the chyme stimulate the cell to release its hormones from the opposite side of the cell into the blood. The main hormones that control digestion and their effects are summarized in the following table:

Gastrointestinal Hormones

Hormone	Secreted by	Stimuli for hormone release	Effects
Gastrin	Stomach	Amino acids, peptides in stomach	Stimulates parietal cells to secrete HCl. Stimulates chief cells to secrete pepsinogen.
Secretin	Small intestine	Acid in small intestine	Stimulates secretion of bicarbonate by pancreas.
Cholecystokinin (CCK)	Small intestine	Amino acids, fatty acids in small intestine	Stimulates contraction of gallbladder. Stimulates secretion of pancreatic enzymes. Inhibits gastric motility and secretion.
Glucose-dependent insulinotropic peptide (GIP)	Small intestine	Glucose, fat in small intestine	Stimulates secretion of insulin from pancreatic islets. Inhibits gastric motility and secretion.

Respiratory System

The **respiratory system** or **respiratory tract** is the path of air from the nose to the lungs. The organs of the respiratory system ensure that oxygen enters the body and carbon dioxide leaves the body. As air moves along the respiratory tract, it is cleansed, warmed, and moistened. Anatomically, the respiratory tract is divided into two sections: **upper respiratory tract** and **lower respiratory tract**.



The respiratory system

Upper respiratory tract

Upper respiratory tract includes the organs located outside of the chest cavity (i.e. **nose**, **nasal cavity**, **pharynx**, and **larynx**). Its primary function is to receive the air from the external environment and filter, warm, and humidify it before it reaches the lungs where gas exchange will occur.

The **nose** opens at the nostrils through which air enters and is partially filtered by the nose hairs, then flows into the nasal cavity.

The **nasal cavity** is lined with epithelial tissue, containing blood vessels which help warm the air; and secrete mucous which further filters the air. The endothelial lining of the nasal cavity also contains tiny hair-like projections called cilia which serve to transport dust and other foreign particles, trapped in mucous, to the back of the nasal cavity and to the pharynx; there the mucus is either coughed out, or swallowed and digested by powerful stomach acids.

The **pharynx** is a tube-like structure that connects the nasal and oral cavities to the larynx and esophagus. The **tonsils** which are part of the lymphatic system form a ring at the connection of the oral

cavity and the pharynx, they protect against foreign invasion of antigens, therefore the respiratory tract aids the immune system through this protection. Then the air travels through the larynx.

The **larynx** known as the **voice box** because it contains **vocal cords**, in which it produces sound. Sound is produced from the vibration of the vocal cords when air passes through them. In order for the larynx to function and produce sound, we need air. That is why we can't talk when we're swallowing. At the top of the larynx is the **epiglottis** which acts as a flap that closes off the trachea during the act of swallowing to direct food into the esophagus instead of the trachea. Stimulation of the larynx by ingested matter produces a strong cough reflex to protect the lungs.

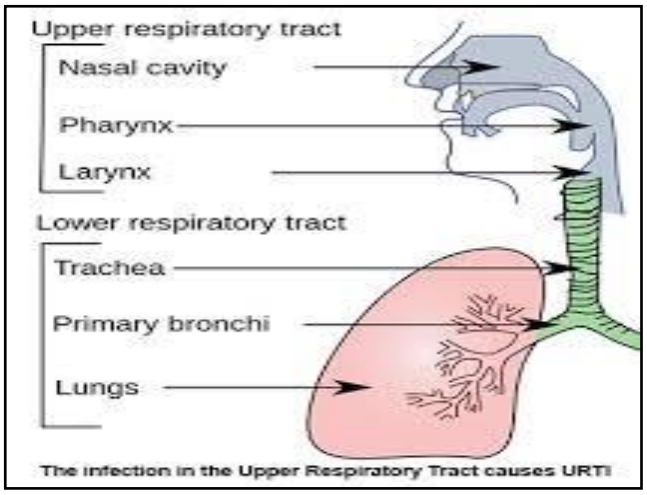
Lower respiratory tract

Lower respiratory tract includes the organs located entirely within the chest cavity (i.e. **trachea**, **bronchi**, **bronchioles**, and **alveoli**).

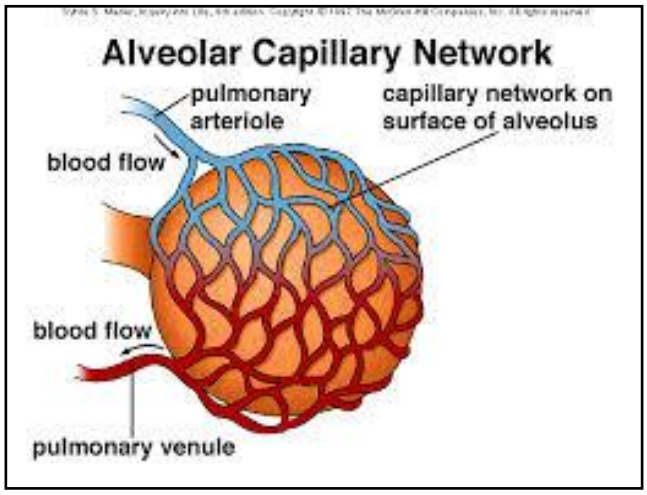
The **trachea** (windpipe) is a hollow tube connecting the larynx to the primary bronchi. It has ciliated cells and mucous secreting cells (goblet cells) lining it, and is held open by 18 to 20 C-shaped cartilage rings. One of its functions is protection from dust and other particles. The trachea lies ventral to the esophagus, the open part of the C-shaped rings faces the esophagus, and this allows the esophagus to expand when swallowing.

The trachea divides into right and left **primary bronchi** which lead into the right and left lungs. The bronchi branch into a great number of **secondary bronchi** that eventually lead to **bronchioles.** The bronchi resemble the trachea in structure, but as the bronchial tubes divide and subdivide their walls become thinner and the small rings of cartilage are no longer present. During an asthma attack, the smooth muscle of the bronchioles contracts causing bronchiolar constriction and characteristic wheezing. Each bronchiole supplies air to a lobule of the lung composed of tiny air sacs called ***alveoli***. The components of the bronchiole tree beyond the primary bronchi compose the **lungs**.

The **lungs** are paired, cone-shaped organs that occupy the thoracic cavity, except for the central area that contains the trachea, the heart, and esophagus. The right lung has three lobes, and the left lung has two lobes, allowing room for the heart, which points left. A lobe is further divided into lobules, and each lobule has a bronchiole serving many alveoli. The lungs have about 300 million **alveoli**, with a total cross sectional area of 50–70 m^2. Each alveolar sac is surrounded by blood capillaries; the wall of the sac and the wall of the capillary are largely simple squamous epithelium—thin flattened cells—and this facilitates gas exchange.



Upper and Lower Respiratory Tract



Alveolar Capillary Network

Respiration physiology

The primary function of the respiratory system is to supply the body with oxygen and remove carbon dioxide. In addition to this main process, the respiratory system serves for regulation of blood pH, defense against microbes, and control of body temperature.

The organs of the respiratory system can be divided functionally into the **conducting zone** and the **respiratory zone**. The conducting zone is the airway from the nose or mouth down to the bronchioles; it is responsible for transporting air and any foreign particles. The respiratory zone includes the respiratory bronchioles down to the alveoli, where gas exchange takes place through a diffusion process. There are four processes of respiration as following:-

1. Breathing or **Ventilation:** It is the exchange of air between the external environment and the alveoli. There are two phases of ventilation; **inspiration (inhalation)** and **expiration (exhalation)**. Air moves into the lungs from the nose or mouth during inspiration and then moves out of the lungs during expiration. During each phase the body changes the lung dimensions to produce a flow of air either in or out of the lungs depending on the pressure in the alveoli. All pressures in the respiratory system are relative to atmospheric pressure (760 mmHg at sea level). Air moves from an area of high pressure to low pressure. The body changes the pressure in the alveoli by changing the volume of the lungs; as volume increases pressure decreases and as volume decreases pressure increases.

2. External respiration: It is the exchange of gases (oxygen and carbon dioxide) between the air in the alveoli and the blood within the pulmonary capillaries.

3. Internal respiration: It is the exchange of gases (oxygen and carbon dioxide) between the blood and tissue fluids.

4. Cellular respiration: It is also called aerobic respiration. It is the process of moving energy from one chemical (glucose) into another (ATP), since all cells use ATP for all metabolic reactions. It is in the mitochondria of the cells where oxygen is actually consumed and carbon dioxide produced.

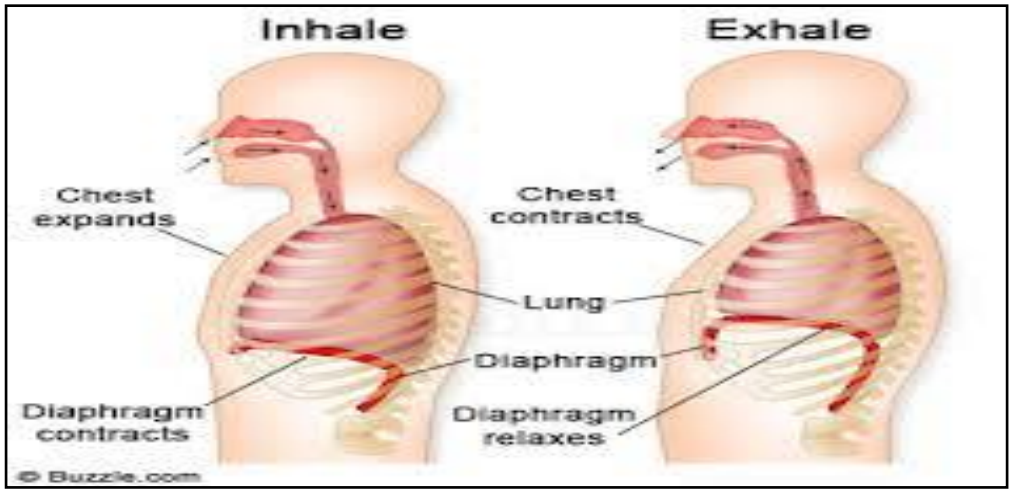
Inspiration and Expiration

Inspiration

Inspiration is the active phase of ventilation because it is the phase in which the diaphragm and the external intercostal muscles contract. In its relaxed state, the diaphragm is dome-shaped; during deep inspiration, it contracts and lowers. Also, the external intercostal muscles contract, and the rib cage moves upward and outward. Following contraction of the diaphragm and the external intercostal muscles, the volume of the thoracic cavity will be larger than it was before. As the thoracic volume increases, the lungs expand. Now the air pressure within the alveoli decreases, creating a partial vacuum. Because alveolar pressure is now less than atmospheric pressure, air naturally flows from outside the body into the respiratory passages and into the alveoli.

Expiration

Expiration is the passive phase of breathing, and no effort is required to bring it about. During expiration, the elastic properties of the thoracic wall and lungs cause them to recoil. In addition, the lungs recoil because the surface tension of the fluid lining the alveoli tends to draw them closed. The diaphragm and external intercostal muscles are usually relaxed when expiration occurs. Contraction of the internal intercostal muscles can force the rib cage to move down and inward. Also, during expiration, the abdominal organs press up against the diaphragm and the rib cage moves downward and inward. The increased pressure in the thoracic cavity helps expel air.



Inspiration and Expiration

Gas exchange

Respiration includes the exchange of gases in the lungs and the exchange of gases in the tissues. Gases exert pressure, and the amount of pressure each gas exerts is called its **partial pressure**. The exchange of O_2 and CO_2 occurs through **diffusion** which is the net movement of gas molecules from a region that has a higher partial pressure to another region that has a lower partial pressure.

External respiration

External respiration refers to the exchange of gases between air in the alveoli and blood in the pulmonary capillaries. In external respiration, gases diffuse in either direction across the walls of the alveoli; O_2 diffuses from the air into the blood and CO_2 diffuses out of the blood into the air. Most of the CO_2 is carried to the lungs in plasma as bicarbonate ions (HCO_3^-). When blood enters the pulmonary capillaries HCO_3^- and H^+ are converted to carbonic acid (H_2CO_3) and then back into CO_2 and H_2O.The enzyme **carbonic anhydrase,** present in red blood cells, speeds the breakdown of H_2CO_3.

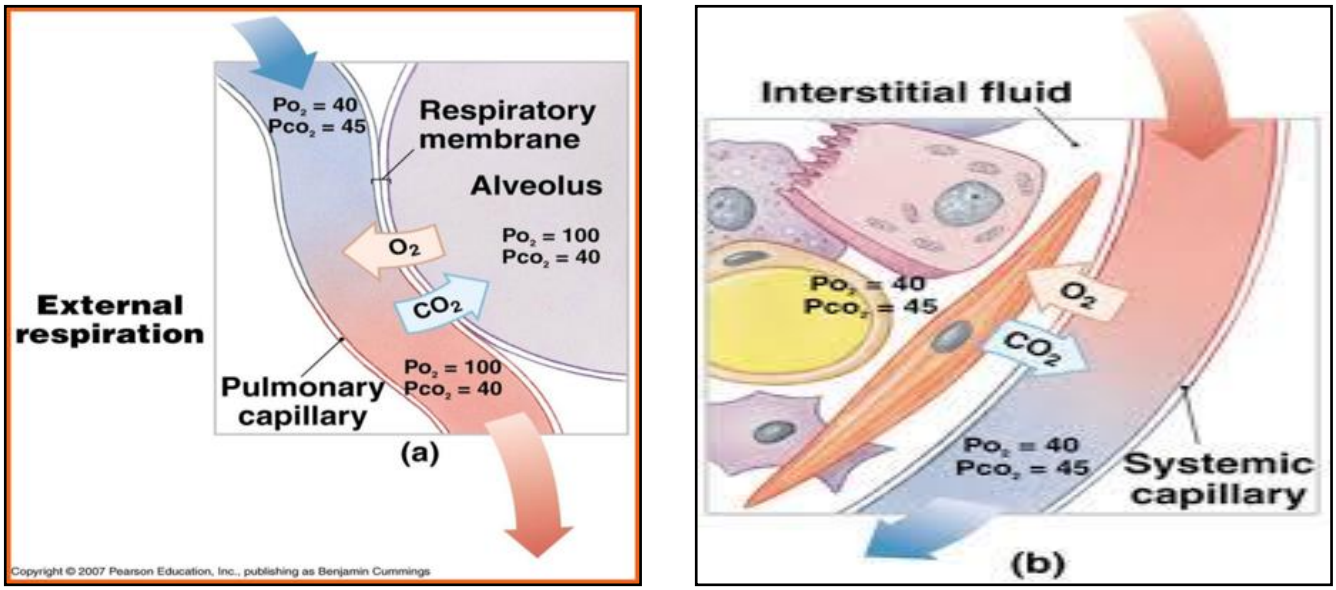
The pressure pattern for O_2 during external respiration is the reverse of that for CO_2. Blood in the pulmonary capillaries is low in O_2, and alveolar air contains a higher partial pressure of O_2. Therefore, O_2 diffuses into plasma and then into red blood cells in the lungs. Hemoglobin takes up this O_2 and becomes **oxyhemoglobin (HbO_2)**.

De-oxygenated blood coming from the pulmonary arteries has PO_2 of 40 mmHg and PCO_2 of 45 mmHg. Oxygenated blood leaving the lungs via the pulmonary veins has PO_2 of 100 mmHg and PCO_2 of 40 mmHg.

Internal respiration

Internal respiration refers to the exchange of gases between the blood in the systemic capillaries and the tissue fluid. Oxygen diffuses out of the blood into the tissues because the PO_2 of tissue fluid is lower than that of blood. Carbon dioxide diffuses into the blood from the tissues because the PCO_2 of tissue fluid is higher than that of blood. After CO_2 diffuses into the blood, it enters the red blood cells, where a small amount is taken up by hemoglobin, forming **carbaminohemoglobin ($HbCO_2$)**.

Most of the CO_2 combines with H_20 forming H_2CO_3, which dissociates to H^+ and HCO_3^-. HCO_3^- diffuses out of red blood cells and is carried in the plasma. The globin portion of hemoglobin combines with excess H^+ produced by the overall reaction, and Hb becomes **reduced hemoglobin (HHb).**



Gas exchange, (a) External respiration, (b) Internal respiration

Regulation of respiration

Normal adults have a breathing rate of 12-20 respirations per minute. The rhythm of ventilation is controlled by a **respiratory center** located in the **medulla oblongata** of the brain. During inspiration, the respiratory center stimulates the diaphragm to contract via the **phrenic nerve** and stimulates the external intercostal muscles to contract via the **intercostal nerves**. Expiration occurs due to a lack of stimulation from the respiratory center to the diaphragm and intercostal muscles.

Although the respiratory center automatically controls the rate and depth of breathing, its activity can also be influenced by nervous input and chemical input.

Nervous input: Following forced inspiration, stretch receptors in the alveolar walls initiate inhibitory nerve impulses that travel from the inflated lungs to the respiratory center. This stops the respiratory center from sending out nerve impulses.

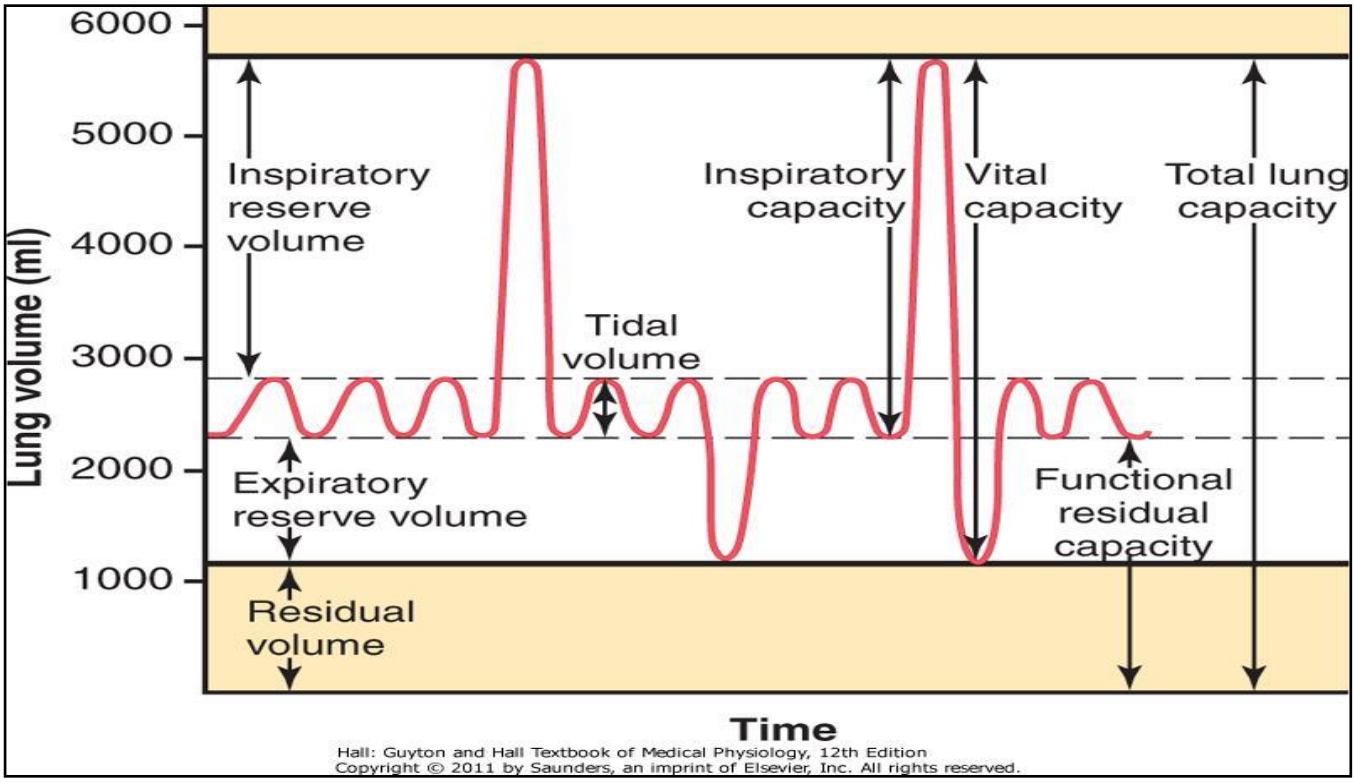
Chemical input: The respiratory center is directly sensitive to the levels of H^+. However, when CO_2 enters the blood, it reacts with H_2O and releases H^+. In this way, CO_2 participates in regulating the breathing rate. When H^+ rises in the blood; the respiratory center increases the rate and depth of breathing. The center is not affected directly by low O_2 levels. However, chemoreceptors in the **carotid bodies,** located in the carotid arteries, and in the **aortic bodies,** located in the aorta, are sensitive to the level of O_2 in the blood. When the concentration of O_2 decreases, these bodies communicate with the respiratory center, and the rate and depth of breathing increase.

Lung volumes and capacities

Several terms have been developed to describe the various physiological volumes and capacities of the lung. Normally the lung volumes are measured with a **spirometer**, while the lung capacity is inferred from the measurements.

Lung volumes and capacities

Volume or Capacity	Definition	Typical value
Tidal volume (TV)	The volume of air that is inspired and exhaled during normal breathing at rest.	500 ml
Inspiratory reserve volume (IRV)	The maximum volume that can be inhaled above the tidal volume.	3000 ml
Expiratory reserve volume (ERV)	The maximum volume of air that can be expired after the expiration of a tidal volume.	1100 ml
Residual volume (RV)	The volume of air in the lungs after maximal expiration.	1200 ml
Functional residual capacity (FRC)	The volume of air left in the lungs that can be exhaled after normal expiration.	2300 ml
Inspiratory capacity (IC)	The volume of maximum inhalation.	3500 ml
Vital capacity (VC)	The maximal volume of air that can be expelled following maximal inspiration.	4600 ml
Total lung capacity (TLC)	The volume of gas in the lungs following maximal inspiration.	5800 ml



Graph of lung volumes and capacities

The Circulatory System

The circulatory system consists of a muscular chambered **heart**, a network of closed branching **blood vessels** and **blood**, the fluid which is circulated. Together, the heart and blood vessels comprise the *cardiovascular system.* Humans have a **closed** circulatory system; this means that the blood is always contained in tubes and vessels.

The circulatory system has the following three main functions:

1. It transports gases, nutrients, waste materials, and chemical substances from one part of the body to the other.

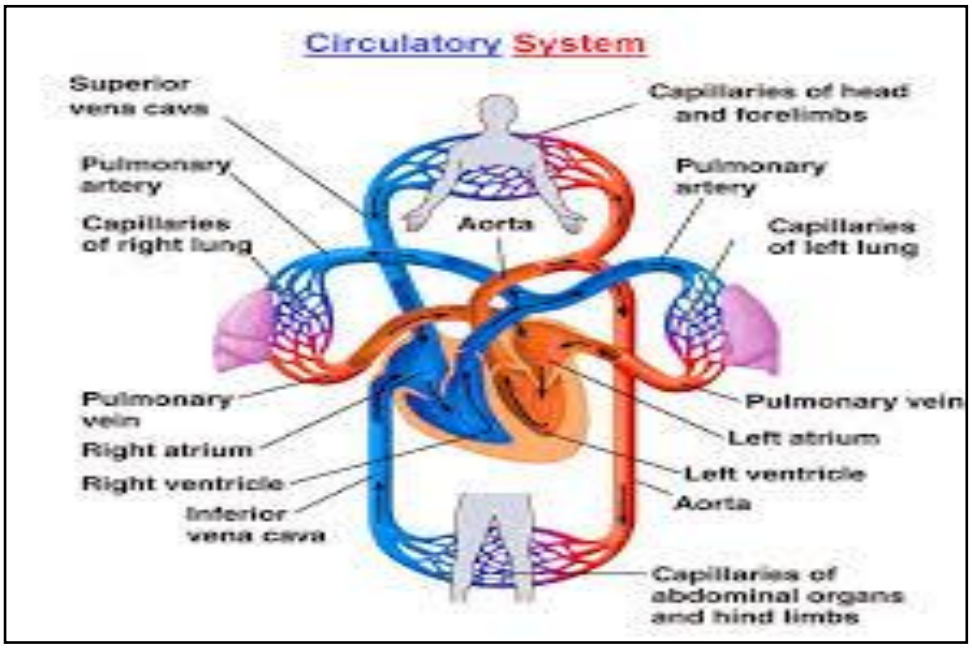
2. It regulates internal temperature by altering the blood flow through the skin.

3. It protects against blood loss from injury and against disease-causing microbes or toxic substances.

The heart

The heart is a muscular cone-shaped organ about the size of a closed fist; it is located in the centre of the thorax between the lungs, slightly tilted to the left**.** The heart wall is composed of three layers of tissue: the **epicardium**, the **myocardium**, and the **endocardium**. The heart has four chambers, two relatively small upper chambers called **atria** and two larger lower chambers called **ventricles**. The heart can be thought of as two pumps sitting side by side; vertically dividing the two sides of the heart is a wall, known as the **septum.** The septum prevents the mixing of oxygenated (left side) and deoxygenated (right side) blood.

The blood pumped by the right ventricle enters the pulmonary artery, whereas the left ventricle pumps blood into the aorta. The deoxygenated blood pumped into the pulmonary artery is passed on to the lungs from where the oxygenated blood is carried by the pulmonary veins into the left atrium. This pathway constitutes the **pulmonary circulation**. The oxygenated blood entering the aorta is carried by a network of arteries, arterioles and capillaries to the tissues from where the deoxygenated blood is collected by a system of venules, veins and vena cava and emptied into the right atrium. This is the **systemic circulation.** The heart itself is supplied by blood vessels that are in the heart muscle; the movement of blood through the heart tissues is called **cardiac circulation**.

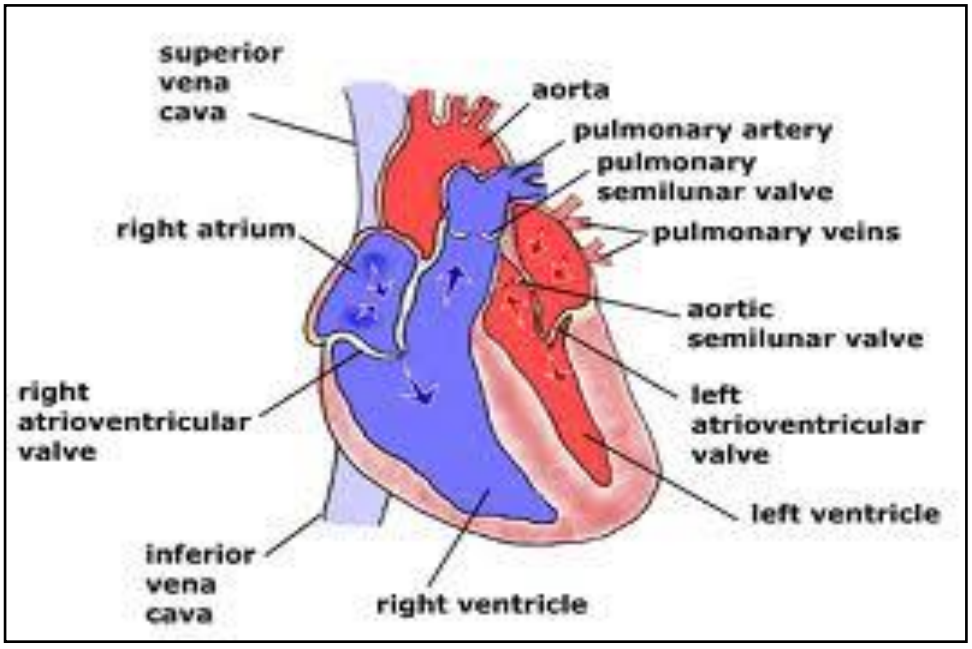


The circulatory system

Heart valves

The heart has four valves inside it. The atria and ventricles are separated from each other by two valves called **atrioventricular valves**. The atrioventricular valve on the right side is called the **tricuspid valve** because it is made up of three flaps. The atrioventricular valve on the left side is called the **bicuspid valve (or mitral valve)** because it has only two flaps.

The aorta and pulmonary trunk possess **aortic** and **pulmonary semilunar valves,** respectively. They so called because of their half-moon shape. The valves in the heart allow the flow of blood only in one direction, and prevent any backward flow.



The heart valves

Cardiac cycle

The **cardiac cycle** is the sequence of events in one heartbeat. It is the simultaneous contraction of both atria, followed a fraction of a second later by the simultaneous contraction of both ventricles. A heartbeat has two phases:

Phase 1: Systole is the term for contraction. This occurs when the ventricles contract, closing the atrioventricular valves and opening the semilunar valves to pump blood into the two major vessels leaving the heart.

Phase 2: Diastole is the term for relaxation. This occurs when the ventricles relax, allowing the back pressure of the blood to close the semilunar valves and opening the atrioventricular valves.

During each cardiac cycle two prominent sounds are produced which can be easily heard through a stethoscope. The **first heart sound (lub)** is associated with the closure of the tricuspid and bicuspid valves whereas the **second heart sound (dub)** is associated with the closure of the semilunar valves. These sounds are of clinical diagnostic significance. If any of the valves do not close properly, an extra sound called a **heart murmur** may be heard.

Cardiac output and Stroke volume

The amount of blood pumped by the heart is often referred to as **cardiac output** and is measured in ml/min. Cardiac output is an indicator of the level of oxygen delivered to the body. Two factors contribute to cardiac output: **heart rate** and **stroke volume**. Heart rate is the number of heart beats per minute. Stroke volume is the amount of blood forced out of the heart with each heartbeat.

Cardiac output = heart rate × stroke volume.

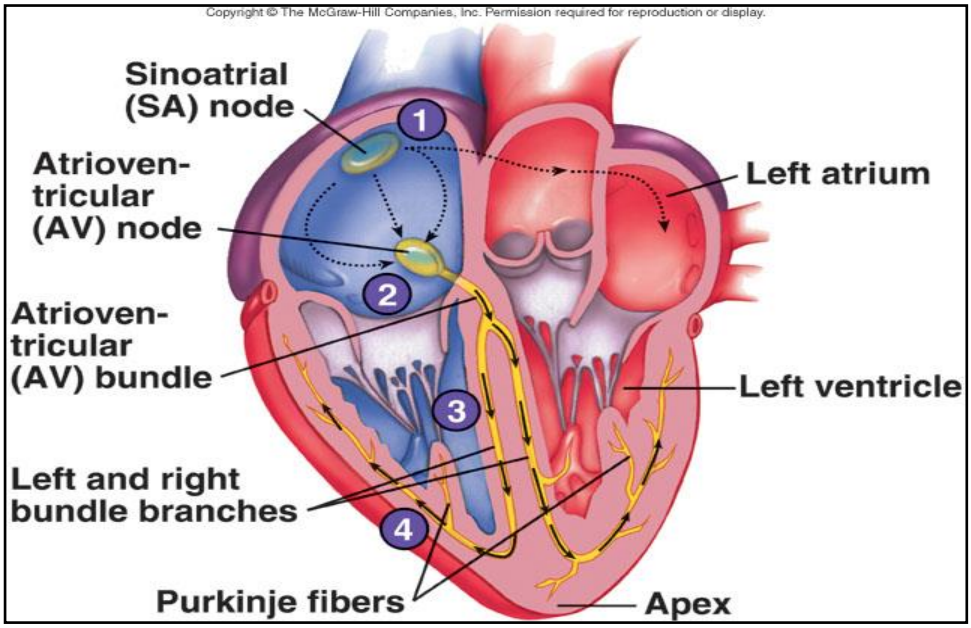
The average person has a **stroke volume** of about **70 ml** and a **resting heart rate** of about **70 beats per minute**. This means that the cardiac output for a typical adult at rest is 70 × 70= **4900 ml/minute**.

Contraction of the heart

Within the heart and in the wall of the right atrium, a specialized muscle tissue, called the **sinoatrial (SA) node**, stimulates the muscle cells to contract and relax rhythmically. The SA node is referred to as the **pacemaker**, because it sets the pace for cardiac activity. The SA node generates an electrical signal that spreads over the two atria and makes them contract simultaneously. As the atria contract, the signal reaches another node, called the **atrioventricular (AV) node** which transmits the electrical signal through a bundle of specialized fibers called the **bundle of His** which relay the signal through

two branches of bundles that divide into fast-conducting **Purkinje fibers**. The Purkinje fibers initiate the almost simultaneous contraction of all cells of the right and left ventricles.

A wave of contraction is initiated by the SA node, which forces blood from the atria into the ventricles. A subsequent wave of contraction begins at the apex of the heart causing the ventricles to forcibly expel blood into the pulmonary artery and the aorta.



The Conduction system of the heart

The electrocardiogram (ECG)

The electrical pulses that cause the heart to beat create small voltage changes that can be measured by electrodes placed on the skin of the chest. These voltage measurements produce an **electrocardiogram (ECG)** that physicians use to diagnose the health of the heart. ECG is a graphical representation of the electrical activity of the heart during a cardiac cycle.

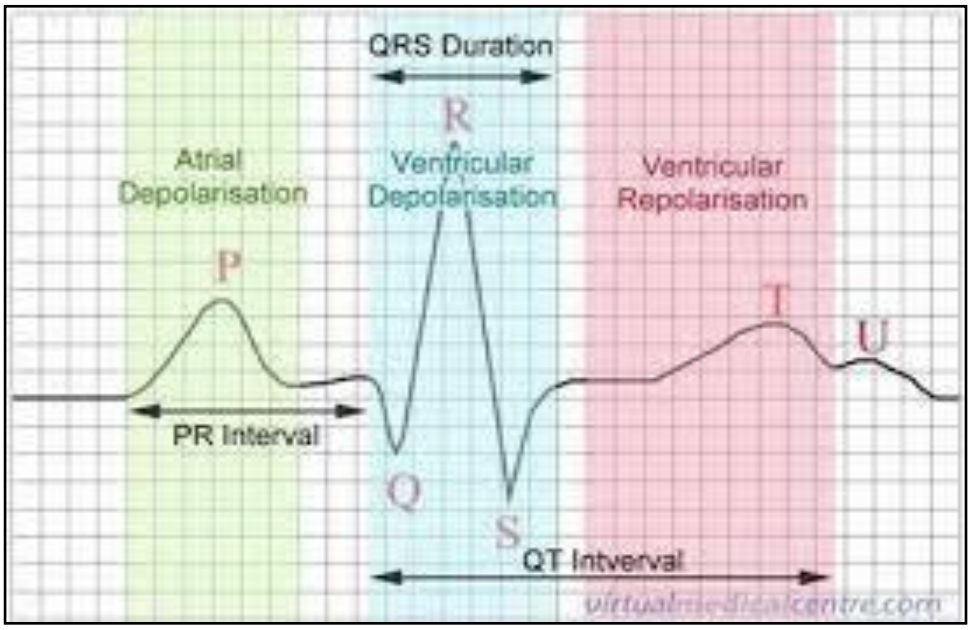
To obtain a standard ECG, a patient is connected to the machine (**electrocardiograph**) with three electrical leads (one to each wrist and to the left ankle) that monitor the heart activity.

Each peak in the ECG is identified with a letter from P to T that corresponds to a specific electrical activity of the heart.

The P wave: It represents the **depolarization of the atria**, which leads to the contraction of the atria.

The QRS complex: It represents the **depolarization of the ventricles**, which initiates the ventricular contraction. The contraction starts shortly after Q and marks the beginning of the systole.

The T wave: It represents the return of the ventricles from excited to normal state (**repolarization**). The end of the T-wave marks the end of systole.



Electrocardiogram

Regulation of cardiac activity

Normal activities of the heart are regulated intrinsically, i.e., auto regulated by specialized muscles (nodal tissue), hence the heart is called **myogenic**. A special neural centre in the medulla oblongata can moderate the cardiac function through autonomic nervous system (ANS). Neural signals through the sympathetic nerves (part of ANS) can increase the rate of heart beat, the strength of ventricular contraction and thereby the cardiac output. On the other hand, parasympathetic neural signals (another component of ANS) decrease the rate of heart beat, speed of conduction of action potential and thereby the cardiac output. Adrenal medullar hormones can also increase the cardiac output.

Blood vessels

There are three main types of blood vessels in the human body. **Arteries** carry blood away from the heart, and **veins** carry blood toward the heart. Smaller-diameter arteries are called **arterioles**, and smaller-diameter veins are called **venules**. A network of **capillaries** joins the arteries and arterioles with venules and veins. The one-cell-thick capillaries are the sites where gases, nutrients, and other materials are transferred from blood to tissue cells and from tissue cells to blood.

Artery versus Vein

- The wall of the artery is thicker.
- The lumen of the artery is much narrower.
- Arteries do not have valves along their length, veins do.
- Blood flows away from the heart in arteries; blood flows towards the heart in veins.

- Blood pressure in arteries is higher and so also the speed of blood flow.
- Pulsed flow in an artery, steady flow in a vein.

Capillaries

- Capillaries are the link between arteries and veins, where exchange with tissues occurs.
- The capillary wall is one cell thick and somewhat porous to allow materials to pass in and out.
- All tissue cells very close to a capillary so exchange is very efficient.
- Exchange at the capillaries is by diffusion, mass flow and active transport.
- Blood flow in capillaries is slow giving enough time for effective exchange.

Blood and Its components

An average adult human has about **5 liters** of blood moving continuously through the circulatory system. Blood consists of two distinct elements: a fluid portion and a solid portion. The fluid portion, called plasma makes up about 55% of the blood volume, consists of water plus dissolved gases, proteins, sugars, vitamins, minerals, and waste products. The solid portion consists of red blood cells, white blood cells, and platelets. The solid portion makes up the other 45% of the blood volume.

Plasma and its functions

Plasma is a clear, yellowish fluid composed of about 92% water and 7% dissolved blood proteins. The remaining 1% percent of plasma consists of other organic substances and inorganic ions such as Na^+, K^+ and Cl^-. The main proteins in blood are *albumin, globulins,* and *fibrinogen*. Other substances transported by the blood include nutrients (glucose, fatty acids, and vitamins), respiratory gases (O_2 and CO_2), and the waste products of metabolism.

Red blood cells and their functions

Red blood cells, also called *erythrocytes*, make up 44 % of the total volume of blood. Red blood cells are specialized for oxygen transport. The oxygen carrying capacity of the blood is dependent on the number of erythrocytes that are present and the amount of hemoglobin that each red blood cell contains. A mature mammalian erythrocyte is a disk-shaped cell with no nucleus. Hemoglobin releases oxygen in the presence of cells that need it. Hemoglobin also transports some of the carbon dioxide waste from cells. Red blood cells have an average life span of 120 days after which they are destroyed in the spleen.

White blood cells and their functions

White blood cells, also called leukocytes, are part of the body's response to infection. Leukocytes make up about 1 % of the total blood volume, but this may increase to more than double normal levels when the body is fighting an infection. All white blood cells have nuclei and appear to be colorless, they are generally short lived. There are two main categories of white blood cells: granulocytes (Neutrophils, eosinophils and basophils) and agranulocytes (lymphocytes and monocytes). Neutrophils are the most abundant cells of the total WBCs and basophils are the least among them. Neutrophils and monocytes are phagocytic cells which destroy foreign organisms entering the body. Basophils secrete histamine, serotonin, and heparin and are involved in inflammatory reactions. Eosinophils resist infections and are also associated with allergic reactions. Lymphocytes are of two major types – 'B' and 'T' forms. Both B and T lymphocytes are responsible for immune responses of the body.

Platelets and their functions

Platelets (thrombocytes) are the third major substance in the solid portion of the blood. Platelets are membrane-bound fragments of cells that form when larger cells in the bone marrow break apart. Platelets do not contain nuclei and they breakdown in the blood within 7 to 10 days after they have formed. Platelets play a key role in clotting blood, which prevents excessive blood loss after an injury.

Blood pressure

As blood passes through the vessels in the body, it exerts pressure against the vessel walls. This is called **blood pressure**. Changes in blood pressure correspond to the phases of the heartbeat; when the ventricles contract and force blood into the pulmonary arteries and the aorta, the pressure increases in these vessels.

The maximum pressure during the ventricular contraction is called **systolic pressure**. The phase during which this occurs is called *systole*. The ventricles then relax and the pressure in the pulmonary arteries and the aorta drops. The lowest pressure before the ventricles contract is called the **diastolic pressure**. The phase during which this occurs is called *diastole*.

A blood pressure reading shows how much pressure the blood exerts against the vessel walls and indicates the condition of the heart and arteries. Blood pressure is usually measured at an artery in the arm, using a device called a **sphygmomanometer.** The systolic pressure is presented over the diastolic pressure in the form of a fraction. The blood pressure of an average healthy young person is below 120 mmHg over 80 mmHg or 120/80 (systolic/diastolic).

Blood pressure is affected by genetics, activity, stress, body temperature, diet, and medications. Continuous high blood pressure, also called *hypertension*, causes the heart to work harder for extended periods of time. This can cause damage to arteries and increases the risk of heart attack, stroke, and kidney failure.

Blood groups

Various types of grouping of blood have been done. Two such groupings, the ABO and Rh, are widely used all over the world.

ABO grouping is based on the presence or absence of two surface antigens (chemicals that can induce immune response) on the RBCs namely A and B. Similarly, the plasma of different individuals contains two natural antibodies (proteins produced in response to antigens). During blood transfusion, any blood cannot be used; the blood of a donor has to be carefully matched with the blood of a recipient before any blood transfusion to avoid severe problems of clumping (destruction of RBC).

Rh grouping is based on the another antigen, the Rh antigen similar to one present in Rhesus monkeys (hence Rh), is also observed on the surface of RBCs of majority (nearly 80 per cent) of humans. Such individuals are called Rh positive (Rh+ve) and those in whom this antigen is absent are called Rh negative (Rh-ve).

An Rh-ve person, if exposed to Rh+ve blood, will form specific antibodies against the Rh antigens. Therefore, Rh group should also be matched before transfusions. A special case of Rh incompatibility (mismatching) has been observed between the Rh-ve blood of a pregnant mother with Rh+ve blood of the foetus. Rh antigens of the foetus do not get exposed to the Rh-ve blood of the mother in the first pregnancy as the two bloods are well separated by the placenta. However, during the delivery of the first child, there is a possibility of exposure of the maternal blood to small amounts of the Rh+ve blood from the foetus. In such cases, the mother starts preparing antibodies against Rh antigen in her blood. In case of her subsequent pregnancies, the Rh antibodies from the mother (Rh-ve) can leak into the blood of the foetus (Rh+ve) and destroy the foetal RBCs.

This could be fatal to the foetus or could cause severe anaemia and jaundice to the baby. This condition is called **erythroblastosis foetalis**. This can be avoided by administering anti-Rh antibodies to the mother immediately after the delivery of the first child.

The Lymphatic System

Water and plasma are forced from the capillaries into intracellular spaces; this interstitial fluid transports materials between the cells. Most of this fluid is collected in the capillaries of a secondary system which is called the **lymphatic system.** The lymphatic system consists of a fluid (lymph), lymphatic vessels that transport the lymph, and lymphatic organs. The lymphatic system has three basic functions:

1- Removal of excess fluids from body tissues and its return to the bloodstream.

2- Absorption of fatty acids and subsequent transport to the blood.

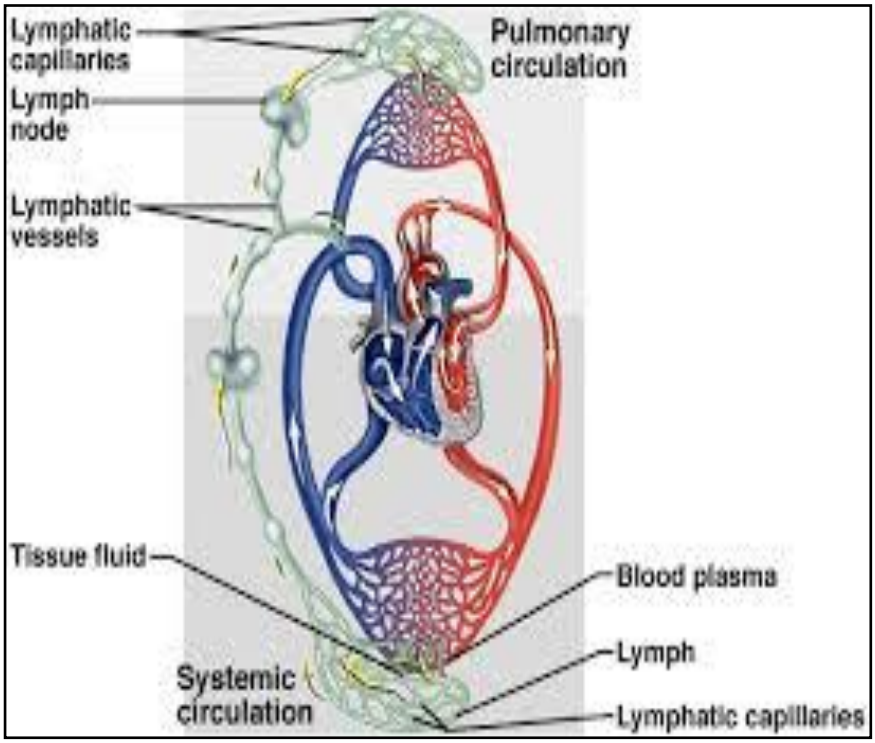
3- Formation of white blood cells, and initiation of immunity through the formation of antibodies.

Lymphatic vessels and ducts

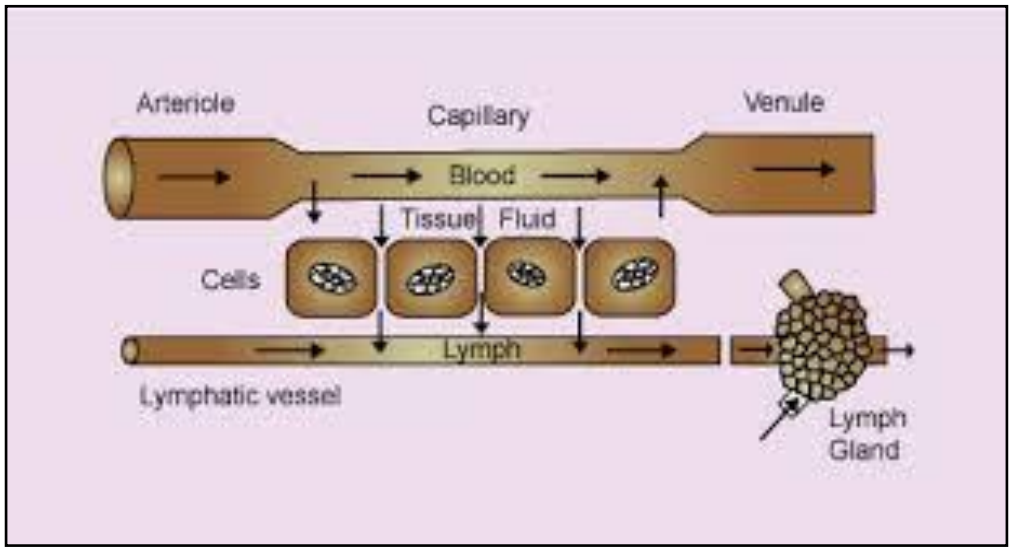
The lymphatic vessels are similar in structure to the cardiovascular veins, meaning they also have valves. They are dependent upon the contraction of skeletal muscle, respiratory movements and valves that do not allow backward flow. The vessels merge before entering one of two ducts:-

Thoracic duct: This duct serves the abdomen, lower extremities and the left side of the upper body.

Right lymphatic duct: This duct serves all of the right side of the upper body and thoracic area.



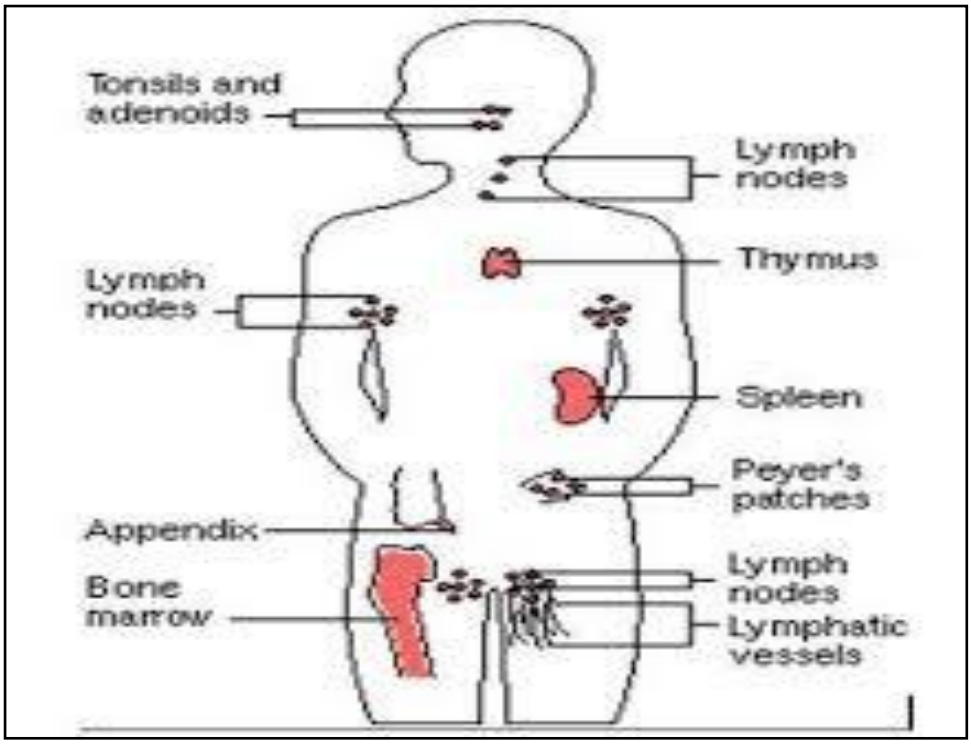
The lymphatic system



Components of the lymphatic system

Lymphatic organs

Lymphatic organs are subdivided into primary and secondary lymphatic organs. The **primary lymphatic organs** are the **red bone marrow** and the **thymus**. They are the site of production and maturation of lymphocytes, the type of white blood cell that carries out the most important work of the immune system. The **secondary lymphatic organs** include the **lymph nodes, spleen**, **tonsils**, **Peyer's patches**, and the **appendix**. They also play an important role in the immune system as they are places where lymphocytes find and bind with antigens.



The lymphatic organs

Red bone marrow

Red bone marrow, the soft, spongy, nutrient rich tissue in the cavities of certain long bones, is the organ that is the site of blood cell production. It is also the site of maturation of **B lymphocytes**.

Thymus gland

The thymus gland is a soft organ with two lobes that is located in the upper thoracic cavity posterior to the sternum. It is divided into an outer cortex and an inner medulla. It is an organ that is more active in children, and shrinks as we get older. **T lymphocytes** mature in the thymus. Also, the thymus gland produces a hormone, **thymosin** which thought to aid in the maturation of T lymphocytes.

Lymph nodes

The lymph nodes are small oval shaped structures located along the lymphatic vessels. They act as filters, with an internal connective tissue filled with lymphocytes that collect and destroy bacteria and viruses. They concentrated in the neck, armpit, groin, and abdominal cavity.

The spleen

The spleen is the largest of the lymphatic organs and lies in the left part of the abdominal cavity between the stomach and the diaphragm. It is divided into two partial compartments known as **white pulp** and **red pulp**. The white pulp contains lymphocytes and the red pulp contains venous sinuses. When blood enters the spleen and flows through the sinuses for filtration, lymphocytes react to pathogens; macrophages engulf debris and remove old, worn out red blood cells.

Tonsils

The tonsils are a group of small rounded organs in the pharynx. They are filled with lymphocytes, macrophages, and macrophage-like cells. Their lymphocytes respond to microbes that arrive by way of ingested food as well as inspired air.

Peyer's patches

Peyer's patches are lymphoid tissues found in the wall of the small intestine, although they're more concentrated in the ileum.

Appendix

Appendix extends from the inferior end of the large intestine's cecum. The submucosa of the appendix contains many masses of lymphoid tissue. The presence of lymphoid tissue suggests that the appendix may play a role in the immune system.