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

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

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

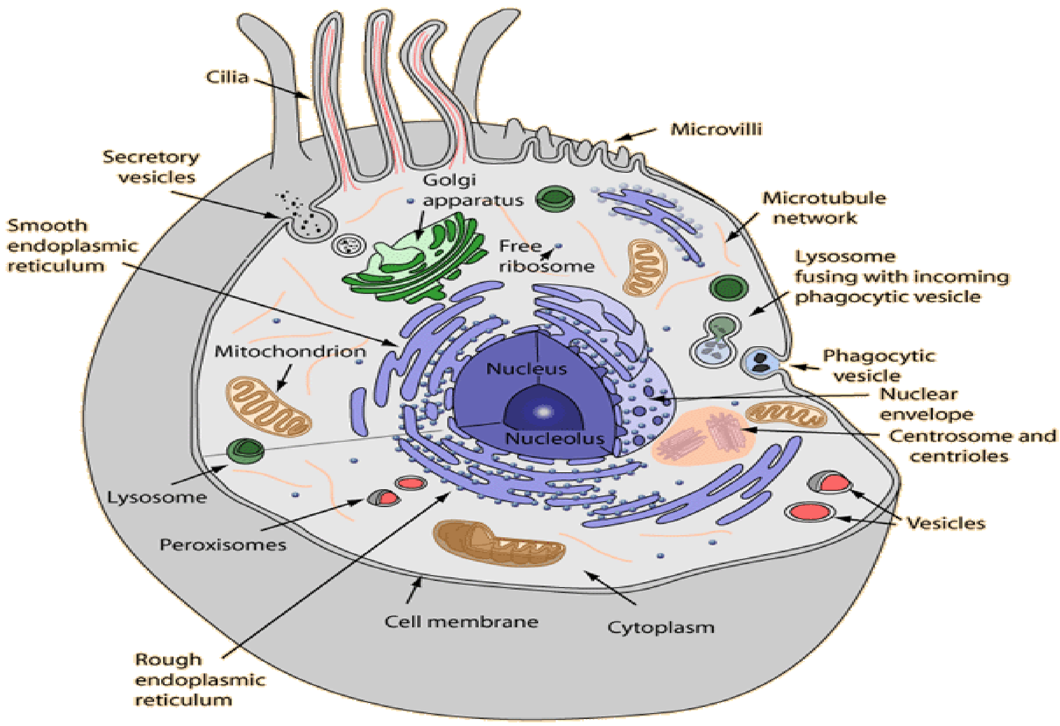
Homeostasis: refers to a system's ability to maintain a range of values. Think of how your body maintains certain levels of substances in your blood. For example, your blood contains a sugar called glucose.
Remember that for normal cellular function water and essential nutrients are required:

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

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

Cell structures and functions

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

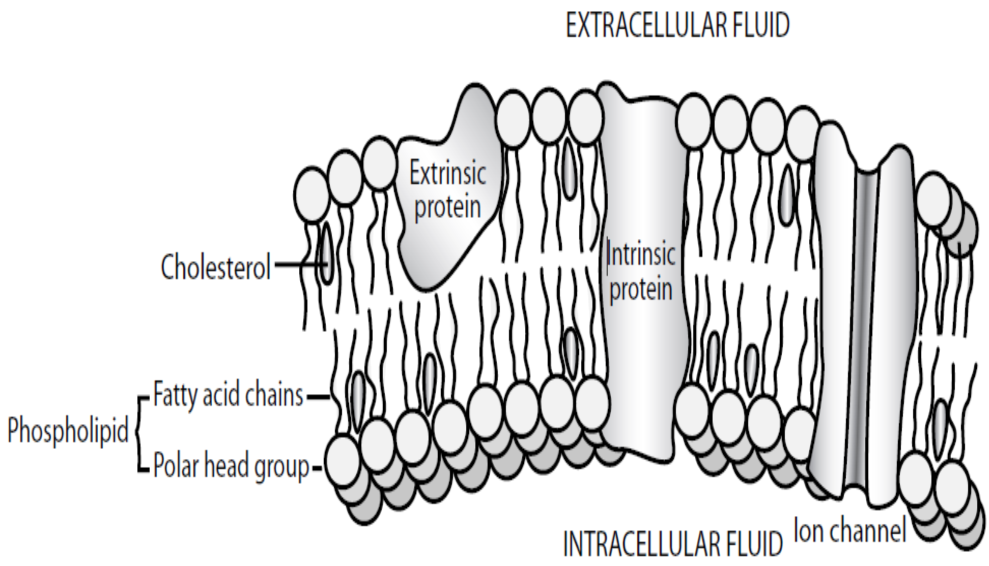


Cell structures

Cell Membrane

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

The cell membrane also lets certain substances in or out. We say that it is **selectively permeable**. For example, lipid soluble substances can pass right through the cell membrane. Examples oxygen, carbon dioxide and steroids.
Water soluble substances cannot pass through the cell membrane and require carrier proteins in order to get in or out of the cell.



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

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

Cytoplasm

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

Endoplasmic Reticulum

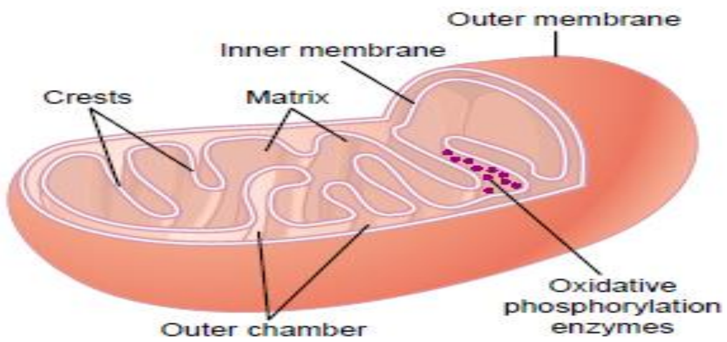
Another important organelle is the endoplasmic reticulum. The endoplasmic reticulum comes in two varieties; rough and smooth. Rough endoplasmic reticulum is studded with ribosomes. The ribosomes function in making proteins (protein synthesis). Smooth endoplasmic reticulum does not contain ribosomes.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

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

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

Mitochondrion

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

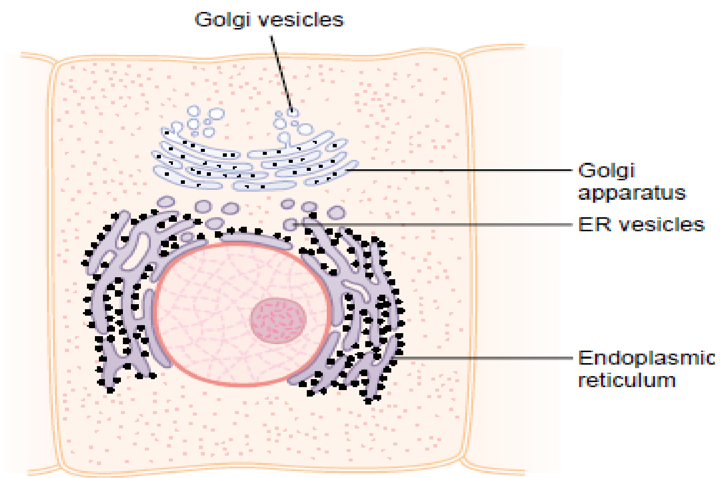


Golgi Apparatus

The Golgi apparatus, is closely related to the endoplasmic reticulum. It has membranes similar to those of the a granular endoplasmic reticulum. It usually is composed of four or more

stacked layers of thin, flat, enclosed vesicles lying near one side of the nucleus.

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



Centrosome

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

Cilia and Flagella

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

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

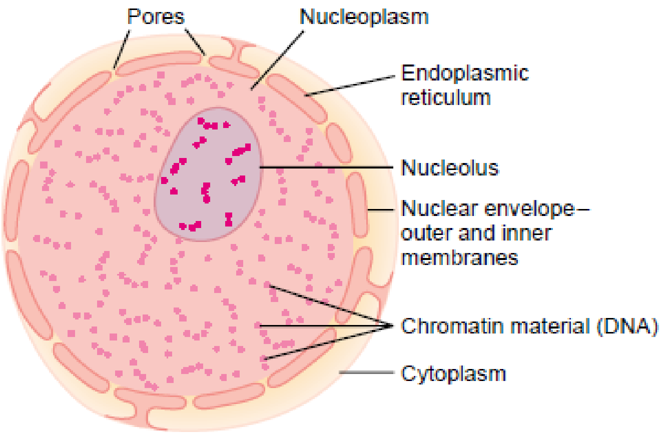
Microfilaments and Microtubules

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

Microtubules are hollow and can transport substances around the cell.

Nucleus

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



Substance Transport in Cells

Diffusion

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

Facilitated Diffusion

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

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

Osmosis

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

So you could think of osmosis in 2 ways:

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

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

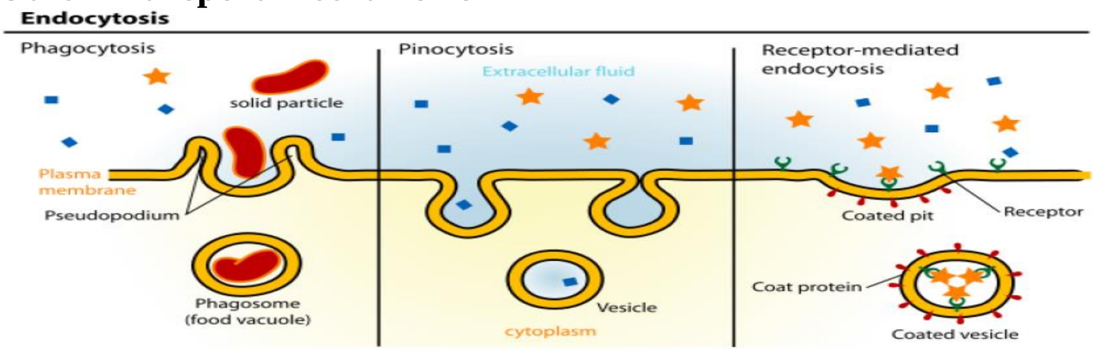
Active Transport

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

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

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

Other Transport Mechanisms



Body Fluids

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

Importance Of Body Fluids

1. In Homeostasis

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

2. In Transport Mechanism

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

3. In Metabolic Reactions

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

4. In Texture Of Tissues

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

5. In Temperature Regulation

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

Distribution Of Body Fluids

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

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

i. Interstitial fluid and lymph (20%)
ii. Plasma (7.5%)
iii. Fluid in bones (7.5%)
iv. Fluid in dense connective tissues like cartilage (7.5%)
v. Transcellular fluid (2.5%) that includes:

a. Cerebrospinal fluid
b. Intraocular fluid
c. Digestive juices
d. Serous fluid – intrapleural fluid and pericardial fluid
e. Synovial fluid in joints
f. Fluid in urinary tract.

Composition Of Body Fluids

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

1. **Organic Substances**

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

2. **Inorganic Substances**

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

Concentration Of Body Fluids

Concentration of body fluids is expressed in three ways:

„ 1. **Osmolality**

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

„ **Osmolality**

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

Tonicity

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

i. ***Isotonic Fluid***

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

ii. ***Hypertonic Fluid***

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

iii. ***Hypotonic Fluid***

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

Applied Physiology

„ **Dehydration**

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

Classification

Basically, dehydration is of three types:

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

2. ***Moderate dehydration****:* It occurs when fluid loss is about 10%. Dehydration becomes little serious and immediate treatment should be given by rehydration.

3. ***Severe dehydration****:* It occurs when fluid loss is about 15%. Dehydration becomes severe and requires hospitalization and emergency treatment. When fluid loss is more than 15%, dehydration becomes very severe and life threatening.

Causes

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

Water Intoxication Or Overhydration

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

Causes

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

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

The Blood

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

Properties of Blood

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

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

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

4. *Specific gravity:*

Specific gravity of total blood : 1.052 to 1.061

Specific gravity blood cells : 1.092 to 1.101

Specific gravity of plasma : 1.022 to 1.026

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

Composition of Blood

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

Blood cells

Three types of cells are present in the blood:

1. Red blood cells or erythrocytes
2. White blood cells or leukocytes
3. Platelets or thrombocytes.

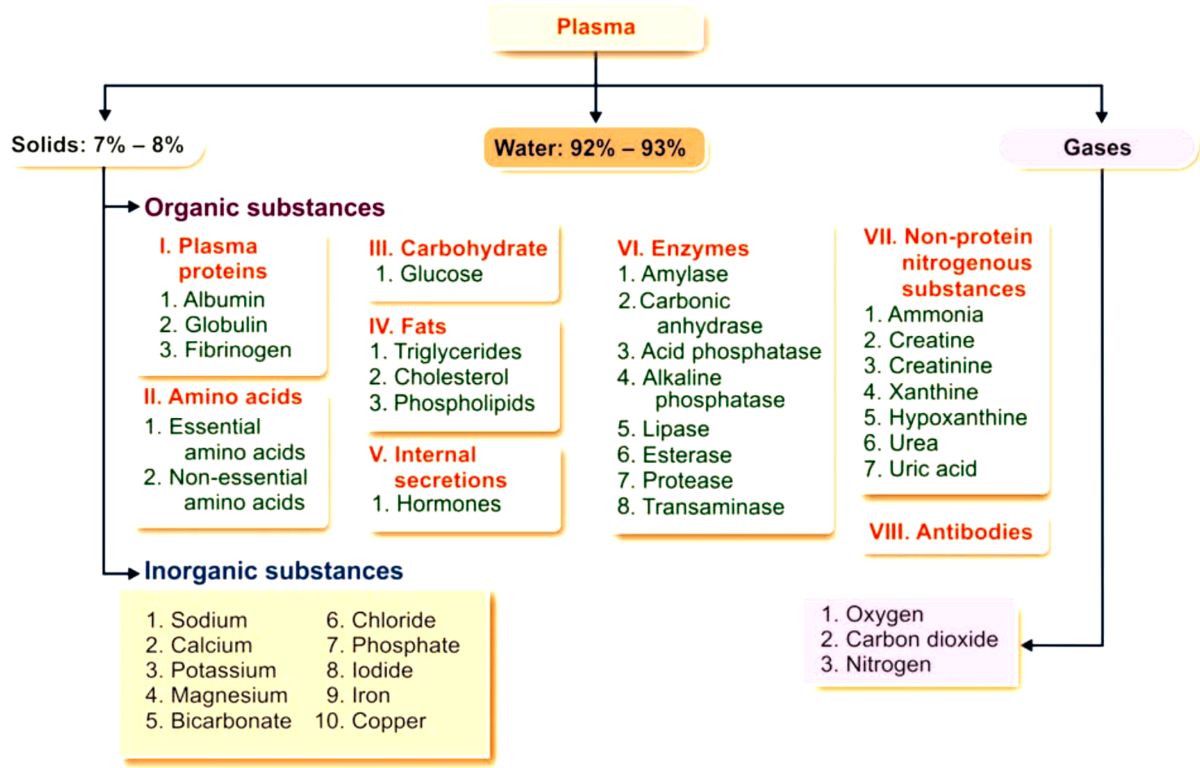
Plasma

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

Plasma proteins are:

1. Serum albumin
2. Serum globulin
3. Fibrinogen.

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



Some important substances in blood.

Normal Values

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

„ **Albumin/Globulin Ratio**

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

Separation of plasma proteins

Plasma proteins are separated by the following methods.

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

„ **5. Ultracentrifugation Method**

„ **6. Gel filtration chromatography**

7. Immunoelectrophoretic Method

Origin of plasma proteins

„ **1. In Embryo**

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

„ 2. **In Adults**

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

Functions of Plasma Proteins

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

„ **1. Role in Coagulation of Blood**

Fibrinogen is essential for the coagulation of blood .

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

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

„ **3. Role in Transport Mechanism**

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

4. Role in Maintenance of Osmotic Pressure in Blood

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

5. Role in Regulation of Acid-Base Balance

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

6. Role in Viscosity of Blood

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

7. Role in Erythrocyte Sedimentation Rate

8. Role in Suspension stability of Red Blood Cells

9. Role in Production of Trephone Substances

10. Role as Reserve Proteins

Serum

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

Serum = Plasma – Fibrinogen

Functions of Blood

„ **1. Nutritive Function**

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

„ **2. Respiratory Function**

Transport of respiratory gases is done by the blood.

„ **3. Excretory Function**

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

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

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

„ **5. Regulation of Water Balance**

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

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

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

„ **7. Regulation OF Body Temperature**

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

8. Storage Function

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

„ **9. Defensive Function**

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

Physiology of Red blood cells (RBCs)

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

Diameter : 7.2 μ (6.9 to 7.4 μ).

Average volume : 90-95 mm^3.

Specific gravity of RBC : 1.092 to 1.101.

Flexible

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

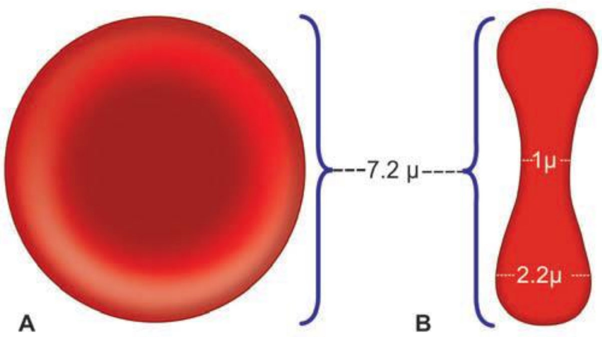


figure 1: Dimensions of RBC.
A. Surface view, B. Sectioned view.

Functions of red blood cells

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

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

Lifespan of red blood cells

- Erythrocytes lack a nucleus and mitochondria
  *They get energy from anaerobic respiration .
  *More surface area / volume allows the RBCs to accommodate change through the capillaries.

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

Hematopoiesis

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

Erythropoiesis

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

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

Hormonal control of RBCs production (major events) :

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

Erythropoietin

Erythropoietin is a glycoprotein with 165 amino acids.

Source of secretion

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

Stimulant for secretion

Hypoxia is the stimulant for the secretion of erythropoietin.

Actions of Erythropoietin

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

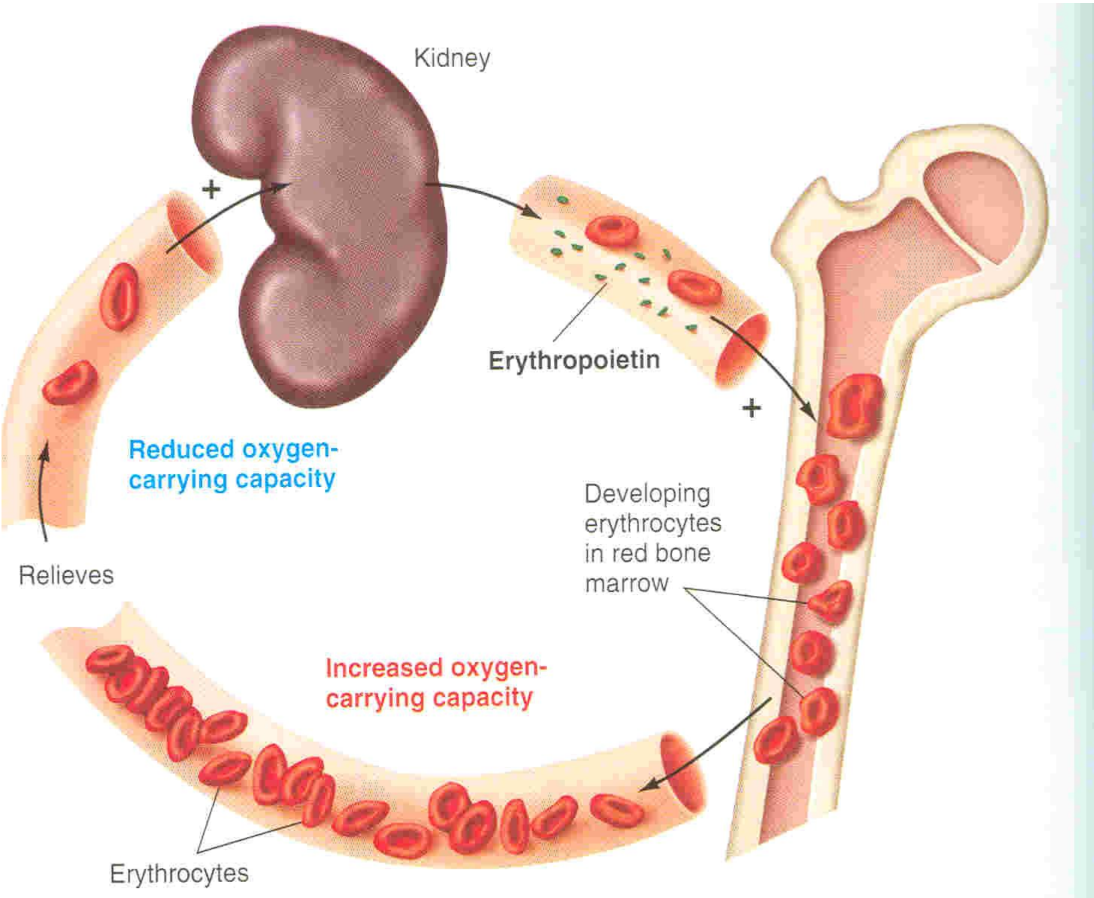
Erythropoietin promotes the following processes:

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

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

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

Blood level of erythropoietin increases in anemia.



Effect of Erythropoietin

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

Stimulus : (Renal hypoxia and non-Renal hypoxia)

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

Hypoxia caused by : -

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

Factors necessary for erythropoiesis

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

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

General factors

General factors necessary for erythropoiesis are:

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

ii. Proteins, amino acids , lipids and carbohydrates.

iii. Iron for hemoglobin synthesis.

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

v . cytokines.

Stages of erythropoiesis

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

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

6. Matured erythrocyte.

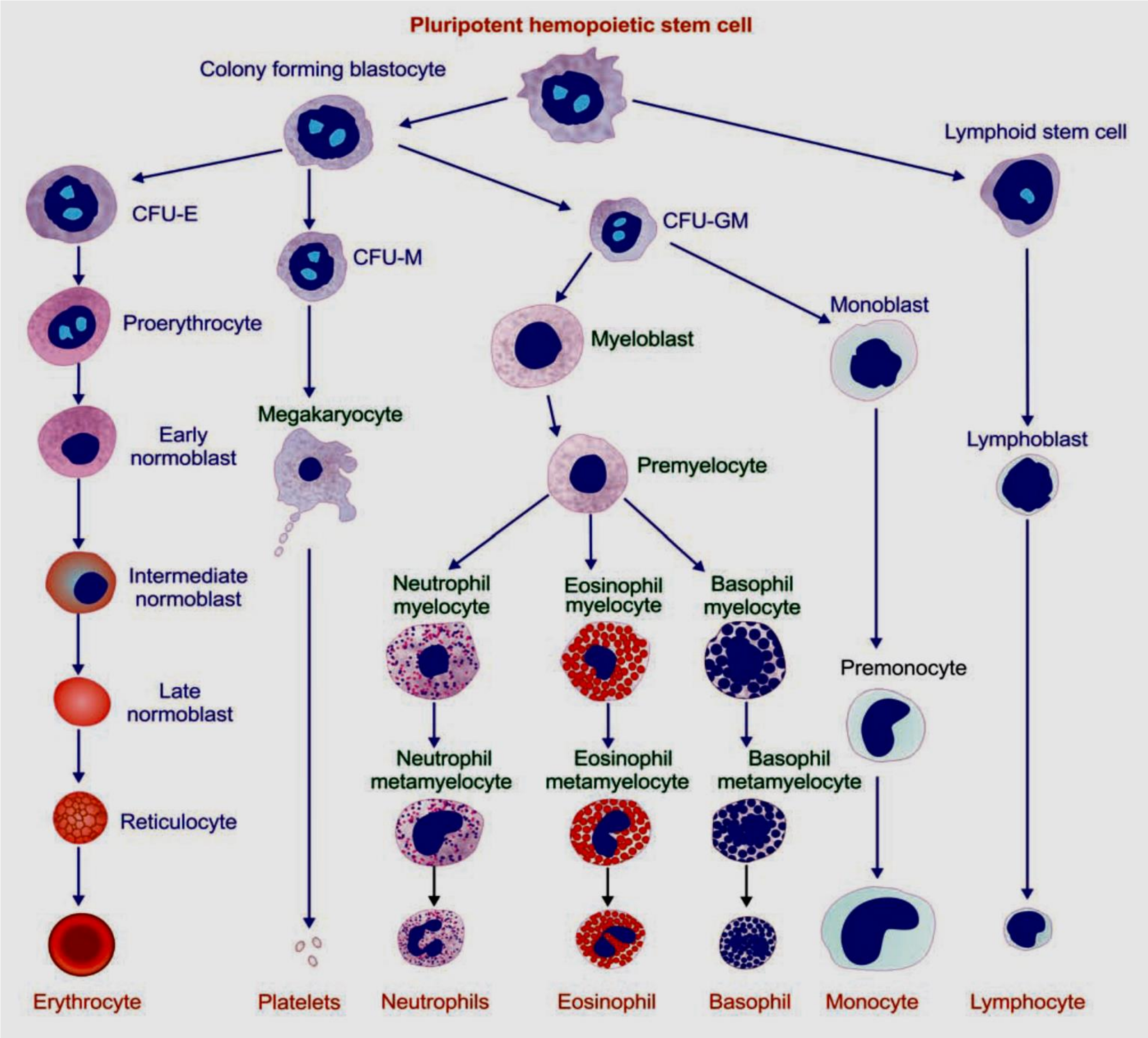


figure 2: Stages of erythropoiesis. CFU-E = Colony forming unit-erythrocyte, CFU-M = Colony forming unit-megakaryocyte, CFU-GM = Colony forming unit-granulocyte/monocyte.

Vitamin B12 and folic acid

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

*Action

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

*Folic Acid

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

Importance of the erythropoiesis

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

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

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

Regulation of erythropoiesis

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

Hematocrit (Packed red Cell Volume or PCV)

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

Hemoglobin (Hb)

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

Molecular weight of hemoglobin is 68,000.

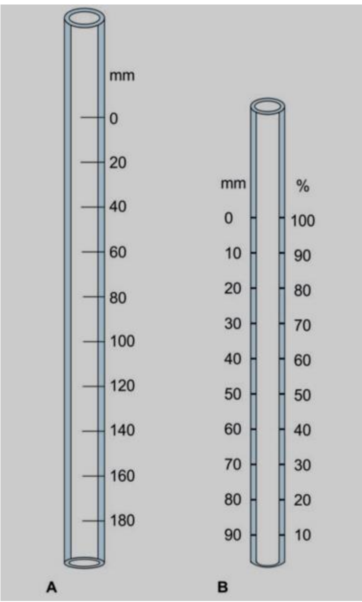
Types of normal hemoglobin

Hemoglobin is of two types:

1. Adult hemoglobin – HbA
2. Fetal hemoglobin – HbF

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

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



A. Westergren tube:
B. Wintrobe tube

down due to gravity with a supernatant layer of clear plasma. Determination of ESR is especially helpful in assessing the progress of patients treated for certain chronic inflammatory disorders such as:

1. Pulmonary tuberculosis
2. Rheumatoid arthritis
3. Polymyalgia rheumatic (inflammatory disease characterized by pain in shoulder and hip)
4. Temporal arteritis (inflammation of arteries of head).

Normal values of ESR

By Westergren Method

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

By Wintrobe Method

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

The factors influencing the ESR

Increased ESR

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

Decreased ESR

- Polycythemia
- RBCs disease with abnormal shape
- Hypofibrinogenemia

Major events in RBC destruction

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