First Lec… Introduction

Physiology is the branch of science dealing with the study of the functions of living beings. It is a dynamic study of life describing the vital functions of the living organisms at organ, cellular, and molecular levels. The term physiology is a combination of Greek word "*Physis*" meaning nature and "*logos*" meaning science or study.

Physiologists have attempted to understand the intricate control system and regulatory mechanisms that influence the body to function survive and maintain stability in the ever-changing external environment. Ability of the body to maintain constancy of the internal environment is termed **"Homeostasis"**. Alteration in the normal physiology lead to causation of disease and pathology.

Cell physiology

Each organ is made up of various tissues and each tissue is made up of millions and millions of small units, termed "Cells". Cell is the basic unit of living beings. Our body is made up of 75 trillion cells.

Components of cell

Each cell contains:

1- Water 2- Electrolytes 3- Proteins

4- Lipids 5- Carbohydrates

1- Water

70-75% of the cell is made up of water. It contains dissolves chemicals and suspended particles. Water helps in transport of substances from one part of the cell to another.

2- Electrolytes

Major electrolytes include Potassium, Sodium, Magnesium, Phosphate, Sulfate Bicarbonate, Chloride and Calcium. They are dissolved in water and necessary for cellular control mechanisms.

3- Proteins

They constitute 10-20% of the cell mass. Proteins are of two types:

a. Structural proteins: Present in the form of filaments, ex: cilia, collagen and elastic fiber.

b. Globular proteins: Shaped like a globe or a ball, ex: enzymes.

4- Lipids

Lipids constitute 2% of cell mass. They are made up of phospholipids and cholesterol, they are insoluble in water.

5- Carbohydrates

Carbohydrates form around 1% of cell mass. They play a major role in providing nutrition to the cell. They are present as a glucose or glycogen, which are used for providing energy to the body.

Structure of cell

Cell is the structural and functional unit of all living beings; cell is made up of two major parts: **nucleus** and **cytoplasm**, which is the fluid part of the cell containing the organelles; it is covered by an envelope termed **cell membrane**.

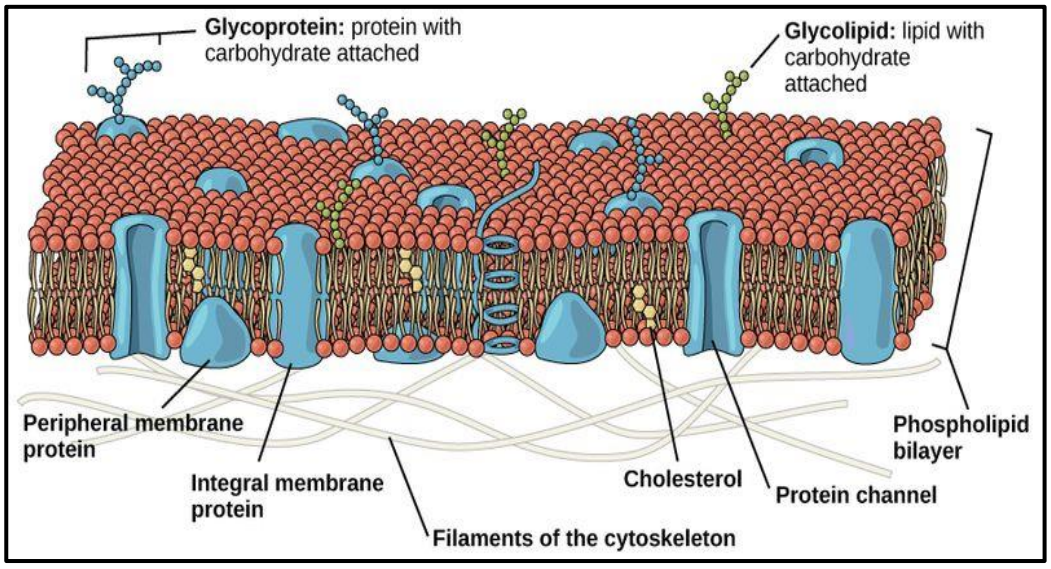
Cell membrane

All plasma membrane are made up of lipids and proteins plus small amount of carbohydrate. Phospholipids are most abundant with a lesser amount of cholesterol. Phospholipids bilayer have a polar charged head having a negatively charged phosphate group and two non- polar (electrically neutral) fatty acid tails. The polar end is hydrophilic (water loving) because it can interact with water molecule which is also polar, the non-polar end is hydrophobic (water fearing) and will not mix with water.

The water surface (outer layer) of the layer is exposed to extracellular fluid (ECF), whereas the inner layer is in contact with the intracellular fluid

(ICF). Cholesterol provides stability; cholesterol lies in between the phosphate molecules, preventing the fatty acid chain from packing together and crystallizing that could decrease fluidity of the membrane. Cholesterol also provide a framework for the arrangement of proteins and carbohydrate on the cell membrane.

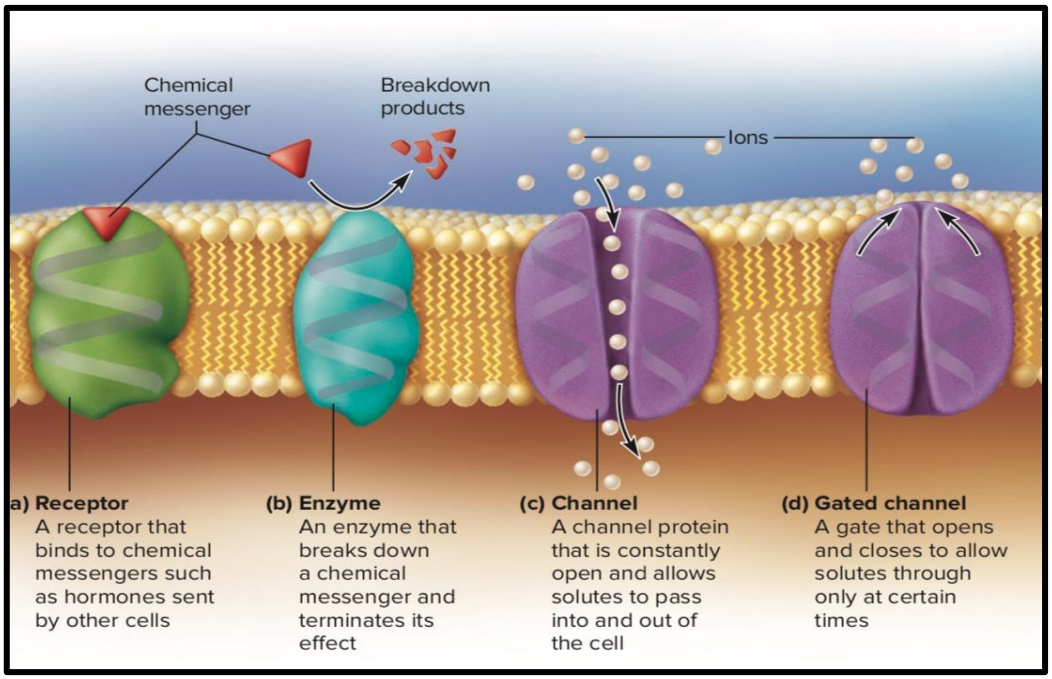
Protein are globular masses floating in the lipid bilayer. They are mostly glycoprotein. They are two types: Integral proteins and Peripheral proteins



Function of proteins

1- Act as structural proteins, which provide framework for the cell.
2- Act as a pump, which helps in active transport.
3- Act as carriers in facilitated diffusion.
4- Form ion channels.
5- Act as receptors.
6- Act as enzymes.

Only the outer surface of the plasma membrane contains a small amount of carbohydrate as glycoproteins or glycolipids, which act as receptors for binding hormones and participate in immune reactions.



Function of cell membrane

1- Separation between the extracellular fluid and the internal components of the cell.
2- Communication with other cells.
3- Recognition of external substances.
4- Structural support.
5- Transport of materials, it controls passage of various molecules- including sugars, amino acids, ions, and water into and out of the cell.

Second Lec. Transport across cell membrane

One of the important functions of the cell membrane is facilitating the transport of materials from the outside to the inside of the cells. Transport of materials is accomplished via number of possible mechanisms. These include:

1-Passive transport: Cell does not use energy.

2-Active transport: Cell does use energy.

Types of Passive Transport:

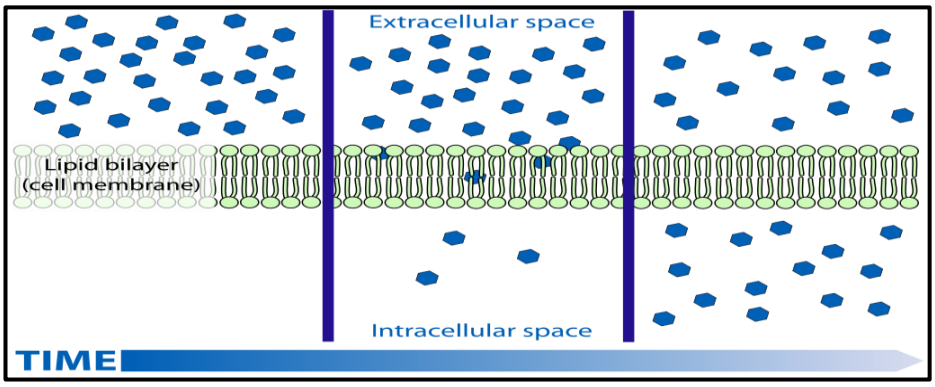
- Simple diffusion
- Facilitated Diffusion
- Filtration
- Osmosis

Simple diffusion

The process of the net movement of solutes from a region of high concentration to region of low concentration is known as "Diffusion". The differences of concentration between the two regions are termed as "Concentration gradient", diffusion occurs down the concentration gradient.

A biological example of diffusion is the gas exchange that occurs during respiration within the human body. Upon inhalation, oxygen is brought into the lungs and quickly diffuses across the membrane of alveoli and enters the circulatory system by diffusing across the membrane of the pulmonary capillaries. Simultaneously, carbon dioxide moves in the opposite direction, diffusing across the membrane of the capillaries and entering into the alveoli, where it can be exhaled.

The process of moving oxygen into the cells, and carbon dioxide out, occurs because of the concentration gradient of these substances, each moving away from their respective areas of higher concentration toward areas of lower concentration. Because the gasses are small and uncharged, they are able to pass directly through the cell membrane without any special membrane proteins. No energy is required.



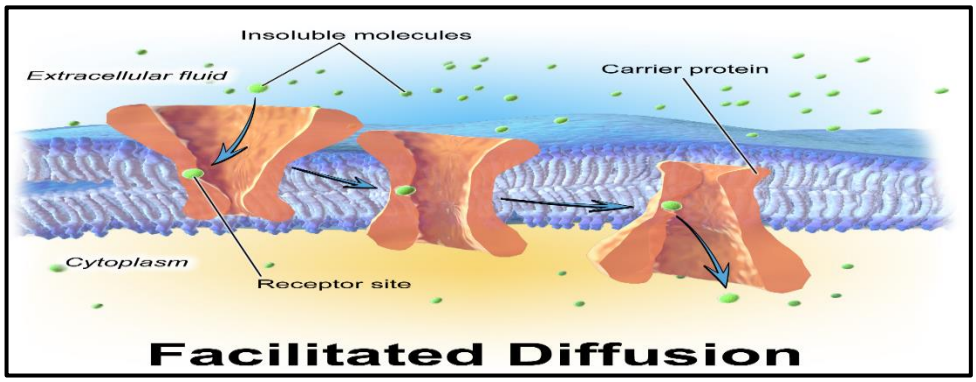
Facilitated Diffusion

The process of the movement of molecules across the cell membrane via special transport proteins that are embedded within the cellular membrane is known as "Facilitated Diffusion" or called "Carrier- mediated diffusion". Many large molecules such as glucose and ions such as Cl^-, Na^+ cannot pass through plasma membrane.

An example of facilitated diffusion is when glucose is absorbed into cells through Glucose transporter 2 ($GLUT_2$) in the human body. There are many other types of glucose transport proteins, some that do require energy, and are therefore not examples of passive transport. Since glucose is too large molecule to fit into the pores of cells and insoluble in lipids, it requires a specific channel to facilitate its entry across plasma membranes and into cells. When diffusing into a cell through $GLUT_2$, the driving force that moves glucose into the cell is still the concentration gradient.

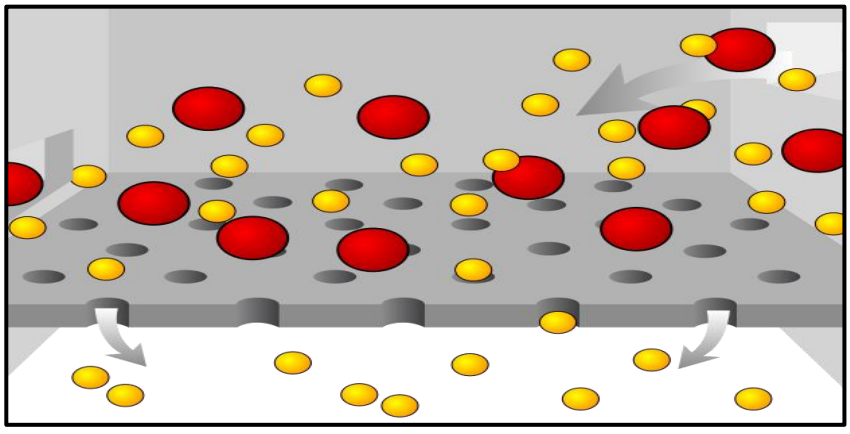
The main difference between simple diffusion and facilitated diffusion is that facilitated diffusion requires a transport protein to 'facilitate' or

assist the substance through the membrane. After a meal, the cell is signaled to move $GLUT_2$ into membranes of the cells lining the intestines called enterocytes. With $GLUT_2$ in place after a meal and the relative high concentration of glucose outside of these cells as compared to within them, the concentration gradient drives glucose across the cell membrane through $GLUT_2$.



Filtration

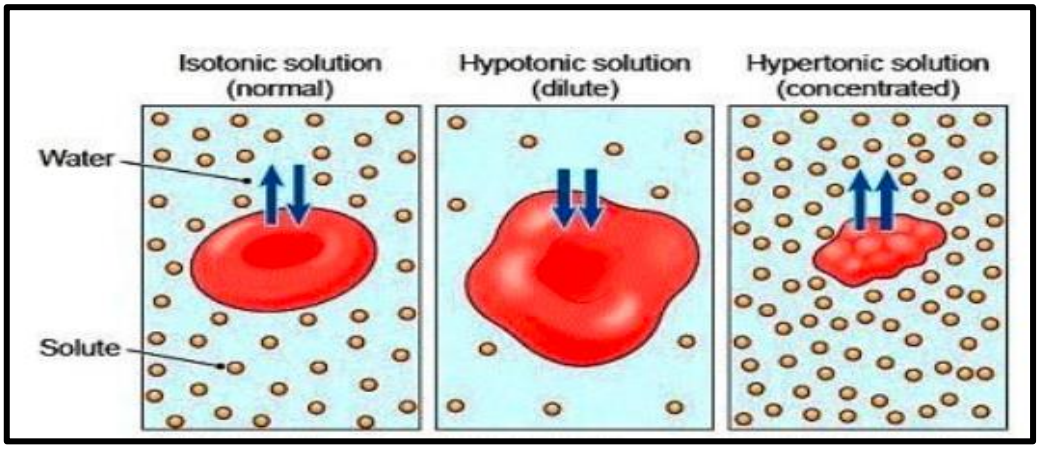
Filtration is the process of the movement of water and solute molecule across the cell membrane due to hydrostatic pressure generated by cardiovascular system. Depending on the size of the membrane pores, only solutes of a certain size may pass through it. The membrane pores of the Bowman's capsule in the kidneys are very small, and only albumins (smallest proteins) can filter though it. On the other hand, the membrane pores of liver cells are extremely large to allow a variety of solutes to pass through it and be metabolized.



Osmosis

Osmosis is the type of diffusion of water molecules across a selectively permeable membrane, from a solution of high water potential to a region of low water potential (from a region of lower solute concentration to a region of higher solute concentration).

Depending on the condition of the extracellular environment, different things can happen to the cell. If the cell is exposed to an "**Isotonic**" environment (same solutes concentration inside and outside the cell), the movement of water into and out of the cell occur at the same rate. If the cell exposed to a "**Hypertonic**" environment (outside of the cell has higher solute concentration than the inside), the cell will shrivel because of loss of water. If the cell is exposed to a "**Hypotonic**" environment (inside of the cell has higher concentration than outside), the cell take up more water and becomes bloated and will eventually burst.



Third Lec. Active Transport

Active transport is the movement of substance against its concentration gradient (from low to high concentration), utilizing energy.

Types of active transport:

- Primary active transport
- Secondary active transport
- Endocytosis and Exocytosis

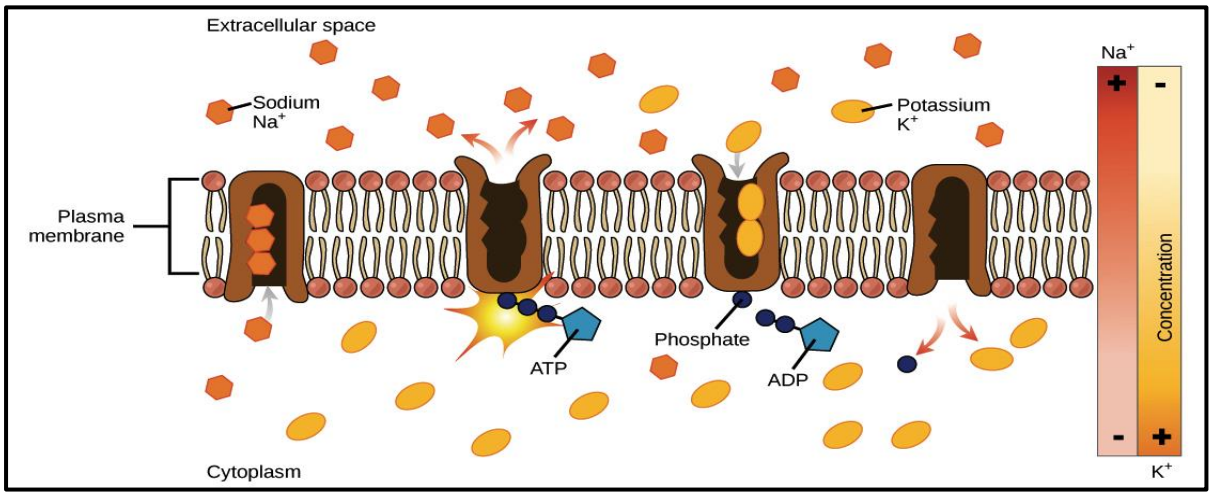
Primary active transport

Primary active transport is the process in which solutes are moved across cell membranes against electrochemical gradients using energy supplied directly by ATP or some other high- energy phosphate compound, so it is called "**direct active transport**". The action of the $Na^{+}-K^{+}$ pump is an important example of primary active transport. The sodium-potassium pump transports sodium out of and potassium into the cell in a repeating cycle. In each cycle, three sodium ions exit the cell, while two potassium ions enter. This process takes place in the following steps:

1- To begin, the pump is open to the inside of the cell. In this form, the pump really likes to bind (has a high affinity for) sodium ions, and will take up three of them.
2- When the sodium ions bind, they trigger the pump to hydrolyze (break down) ATP. One phosphate group from ATP is attached to the pump, which is then said to be phosphorylated. ADP is released.
3- Phosphorylation makes the pump change shape, re-orienting itself so it opens towards the extracellular space. In this conformation, the pump no longer likes to bind to sodium ions (has a low affinity for them), so the three sodium ions are released outside the cell.
4- In its outward-facing form, the pump switches allegiances and now really likes to bind to (has a high affinity for) potassium ions. It will bind two of them, and this triggers removal of the phosphate group attached to the pump in step 2.

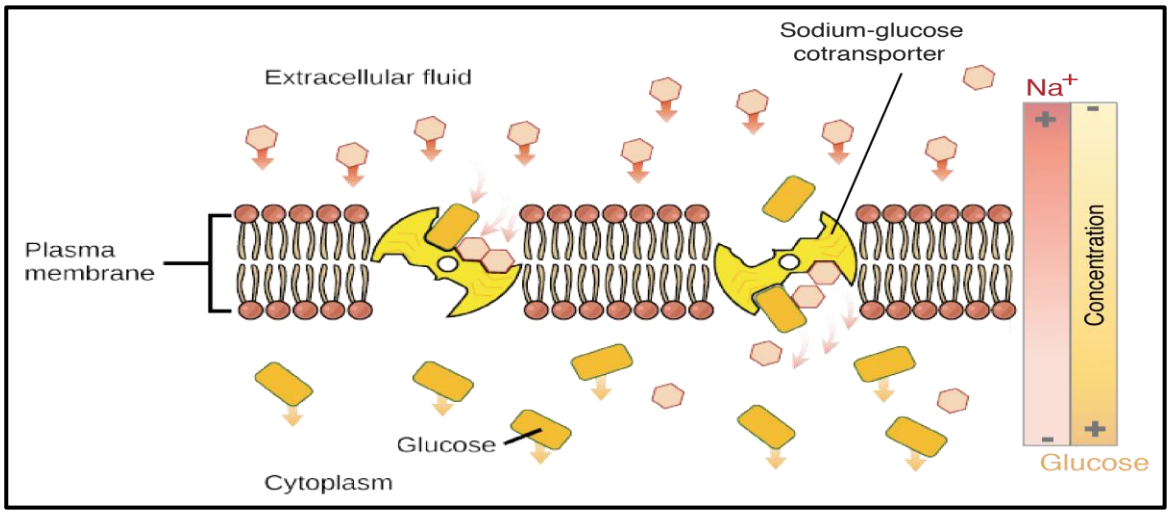
5- With the phosphate group gone, the pump will change back to its original form, opening towards the interior of the cell.

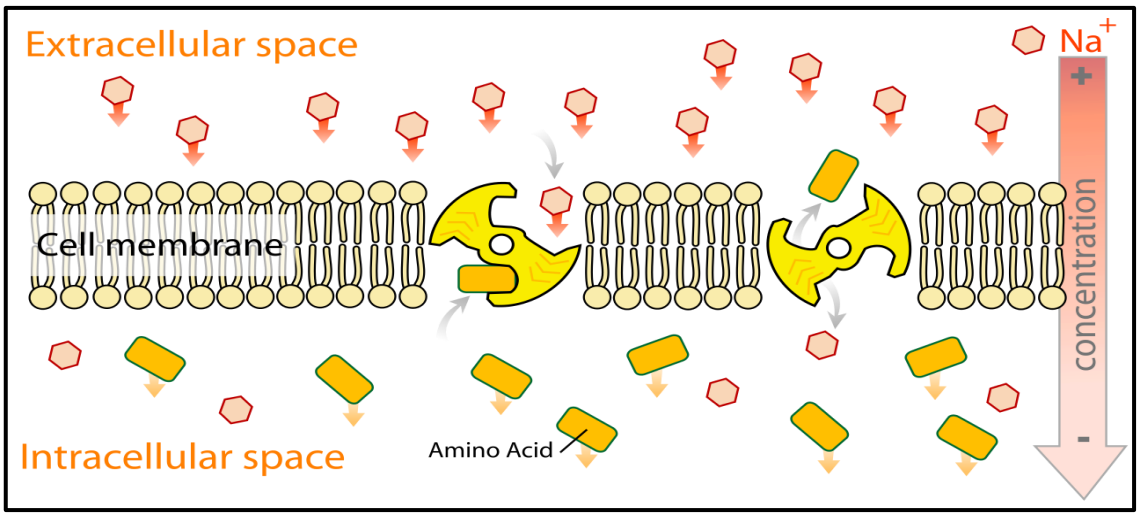
6- In its inward-facing shape, the pump loses its interest in (has a low affinity for) potassium ions, so the two potassium ions will be released into the cytoplasm. The pump is now back to where it was in step 1, and the cycle can begin again.



Secondary active transport

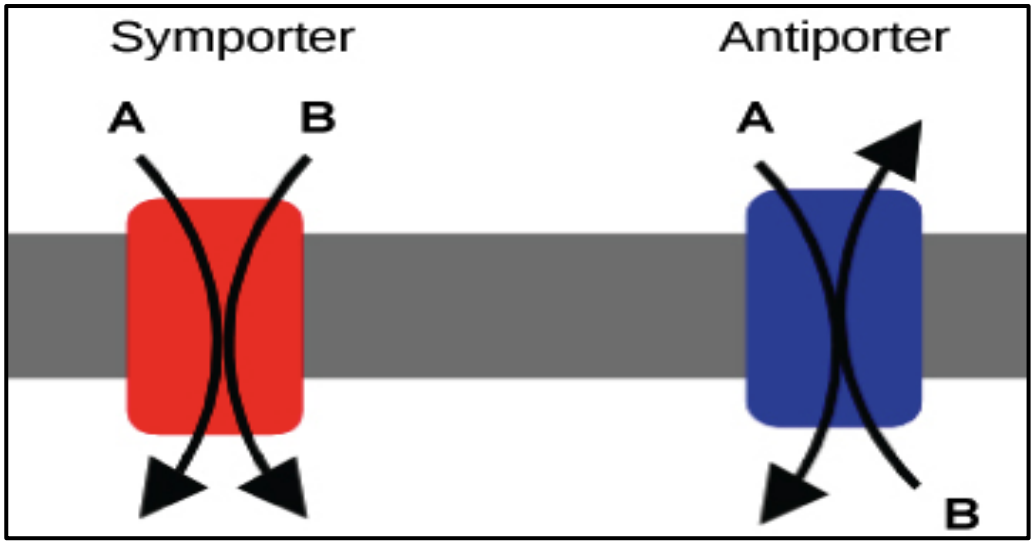
Secondary active transport or co- transport, also uses energy to transport molecules across membrane; however, in contrast to primary active transport, there is no direct use of ATP (energy in other forms than ATP); instead, energy derived from the transport of one substance helps the movement of the other substances. The action of the Na^+–glucose (Amino-acids) pump is an important example of secondary active transport.





In secondary active transport, the movement of the sodium ions down their gradient is coupled to the uphill transport of other substances by a shared carrier protein (a **cotransporter**). For instance, in the figure below, a carrier protein lets sodium ions move down their gradient, but simultaneously brings a glucose molecule up its gradient and into the cell. The carrier protein uses the energy of the sodium gradient to drive the transport of glucose molecules.

In secondary active transport, the two molecules being transported may move either in the same direction (i.e., both into the cell), or in opposite directions (i.e., one into and one out of the cell). When they move in the same direction, the protein that transports them is called a **symporter**, while if they move in opposite directions; the protein is called an **antiporter**.



Fourth Lec. Endocytosis and Exocytosis

Some molecules or particles are just too large to pass through the plasma membrane or to move through a transport protein. So cells use two other **active transport** processes to move these macromolecules into or out of the cell. Vesicles or other bodies in the cytoplasm move macromolecules across the plasma membrane. There are two types of vesicle transport, **endocytosis** and **exocytosis** also called **vesicle transport.**

Endocytosis is the process by which cells internalize substances from their external environment. It is how cells get the nutrients they need to grow and develop. Substances internalized by endocytosis include fluids, electrolytes, proteins, and other macromolecules. Endocytosis is also one of the means by which white blood cells of the immune system capture and destroy potential pathogens including bacteria and protists. The process of endocytosis can be summarized in three basic steps.

The Basic Steps of Endocytosis

1. The plasma membrane folds inward (invaginates) forming a cavity that fills with extracellular fluid, dissolved molecules, food particles, foreign matter, pathogens, or other substances.
2. The plasma membrane folds back on itself until the ends of the in-folded membrane meet. This traps the fluid inside the vesicle. In some cells, long channels also form extending from the membrane deep into the cytoplasm.
3. The vesicle is pinched off from the membrane as the ends of the in-folded membrane fuse together. The internalized vesicle is then processed by the cell.

There are three primary types of endocytosis

Phagocytosis is also called "cell eating" and involves the intake of solid material or food particles.

Pinocytosis, also called "cell drinking", involves the intake of molecules dissolved in fluid.

Receptor-mediated endocytosis involves the intake of molecules based upon their interaction with receptors on a cell's surface.

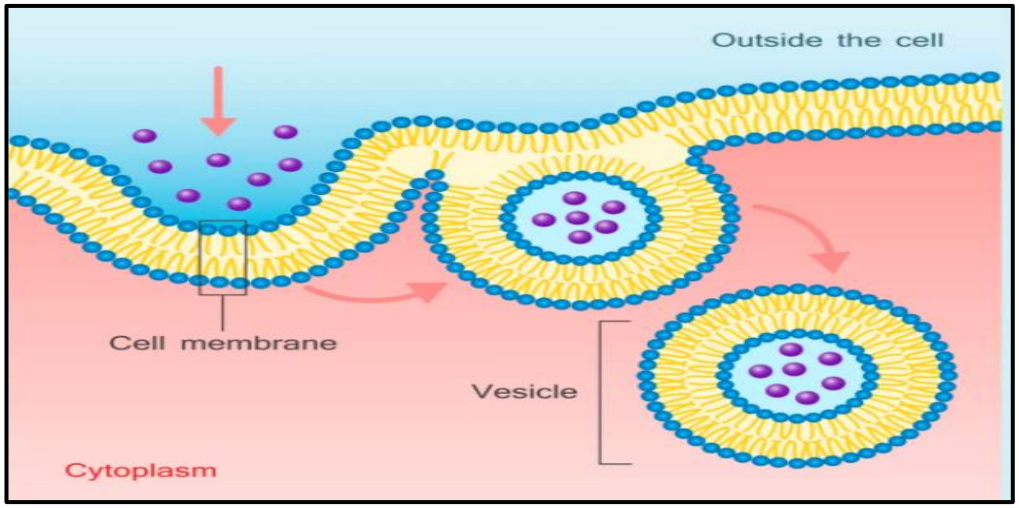
Phagocytosis is a form of endocytosis that involves the engulfing of large particles or cells. Phagocytosis allows immune cells, like macrophages, to rid the body of bacteria, cancer cells, virus-infected cells, or other harmful substances. It is also the process by which organisms such as amoebas obtain food from their environment. In phagocytosis, the phagocytic cell or **phagocyte** must be able to attach to the target cell, internalize it, degrade it, and expel the refuse. This process, as it occurs in immune cells, is described below.

Basic Steps of Phagocytosis

- **Detection:** The phagocyte detects the antigen (substance provoking an immune response), such as a bacterium, and moves toward the target cell.
- **Attachment:** The phagocyte makes contact with and attaches to the bacterium. This binding initiates the formation of **pseudopodia** (extensions of the cell) that surround the bacterium.
- **Ingestion:** The surrounded bacterium is enclosed within a vesicle formed when pseudopodia membranes fuse. This vesicle with bacterium enclosed, called a **phagosome**, is internalized by the phagocyte.
- **Fusion:** The phagosome fuses with an organelle called a lysosome and becomes known as a **phagolysosome**. Lysosomes contain enzymes that

digest organic material. The release of digestive enzymes within the phagolysosome degrades the bacterium.

- **Elimination:** The degraded material is expelled from the cell by exocytosis.



Pinocytosis: While phagocytosis involves cell eating, **pinocytosis** involves cell drinking. Fluids and dissolved nutrients are taken into a cell by pinocytosis. The same basic steps of endocytosis are utilized in pinocytosis to internalize vesicles and to transport particles and extracellular fluid inside the cell. Once inside the cell, the vesicle may fuse with a lysosome. The digestive enzymes from the lysosome degrade the vesicle and release its contents into the cytoplasm for use by the cell. In some instances, the vesicle does not fuse with a lysosome but travels across the cell and fuses with the cell membrane on the other side of the cell. This is one means by which a cell can recycle cell membrane proteins and lipids.

Receptor-mediated endocytosis: is the process used by cells for the selective internalization of specific molecules. These molecules bind to specific receptors on the cell membrane before they are internalized by endocytosis. Membrane receptors are found in regions of the plasma membrane coated with the protein clatherine known as **clatherine-coated pits**. Once the specific molecule binds to the receptor, the pit regions are internalized and clatherine-coated vesicles

are formed. After fusing with early **endosomes**, the clatherine coating is removed from the vesicles and the contents are emptied into the cell.

Basic Steps of Receptor-mediated Endocytosis

1- (Binding): receptors in clathrine-coated pits bind with specific materials.

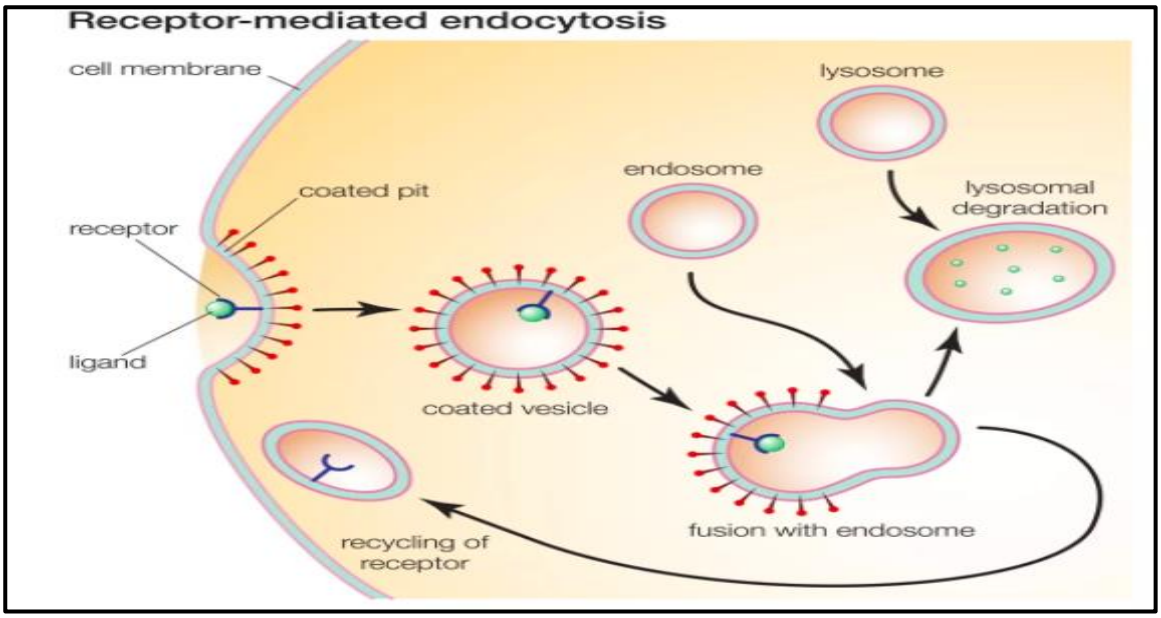
2- (Invagination): invagination of the plasma membrane occurs forming a clathrine- coated vesicle.

3- (Un-coating): the vesicle loses its clathrine coat and becomes an uncoated vesicle.

4- (Fusion): the vesicle fuses with an endosome.

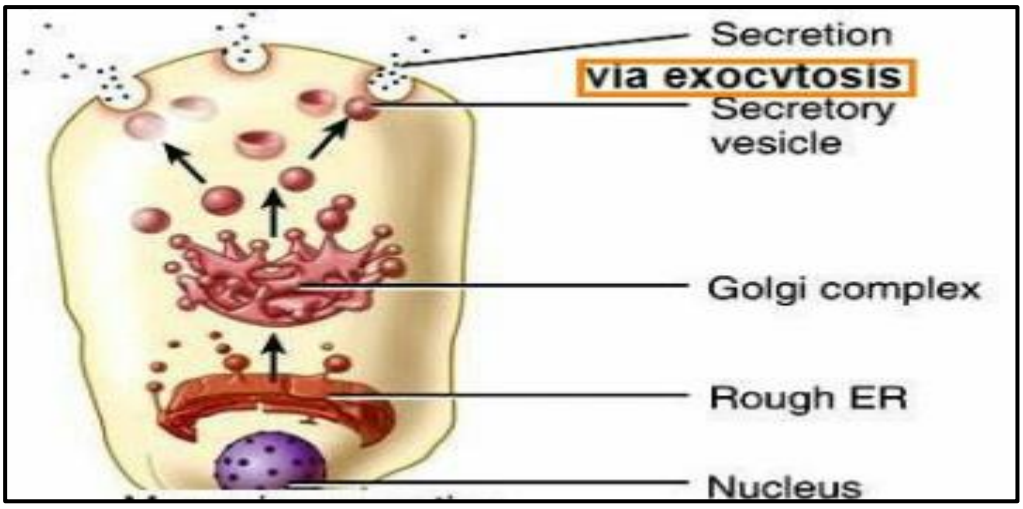
5- (Recycling): the vesicle divides and recycles the receptors to the plasma membrane via transport vesicles.

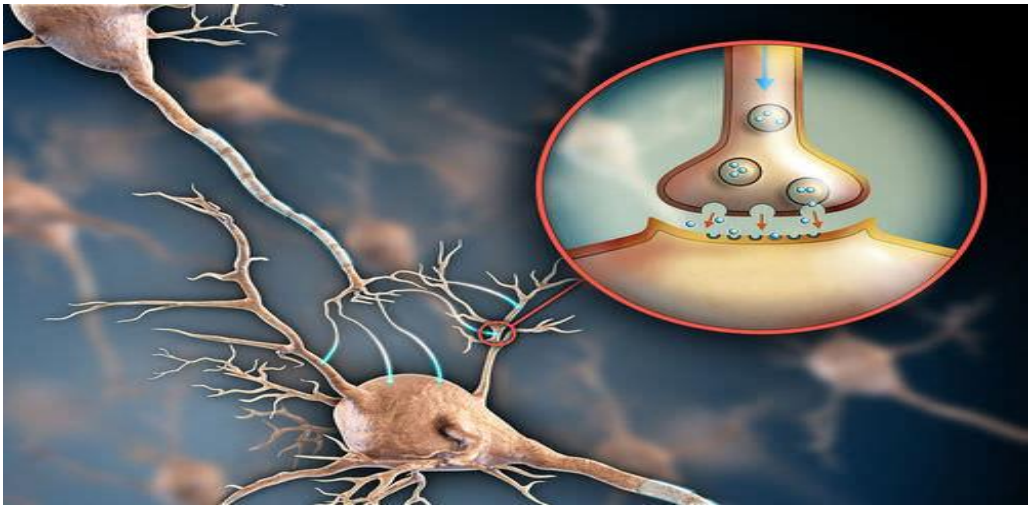
6- (Digestion): another transport vesicle transports the ligands toward a lysosome; enzymes in the lysosome digest the ligands. The specific substances that attach to these receptor proteins actually have a specific name, called "ligands".



Exocytosis

It is also called cell vomiting. The process by which the cells direct the contents of secretory vesicles out of the cell membrane is known as exocytosis. Theses vesicles contain soluble proteins to be secreted to the extracellular environment, as well as membrane. It is the final step in the secretory pathway that typically begins in the endoplasmic reticulum, passes through the Golgi apparatus, the membrane of the vesicle fuses to the plasma membrane upon secretion of the materials (ends at the outside of the cell). Some of the examples include secretion of proteins like enzymes, peptide hormones and antibodies from cells and release of neurotransmitter from neurons.





Fifth Lec. Blood physiology

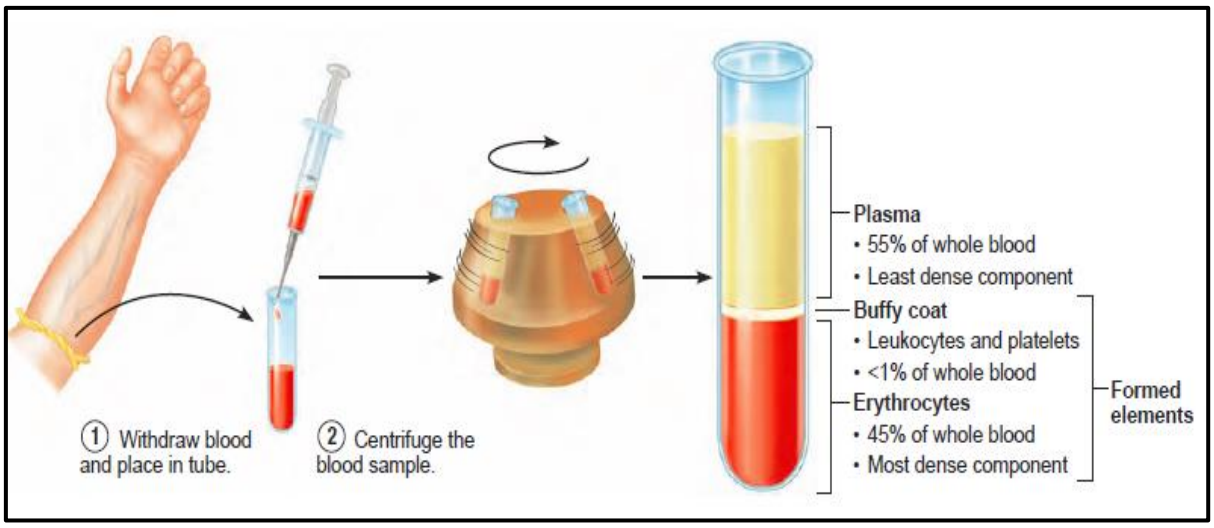
Blood is a specialized type of connective tissue in which living blood cells, called the ***formed elements***, are suspended in a nonliving fluid matrix called ***plasma***. The collagen and elastic fibers typical of other connective tissues are absent from blood, but dissolved fibrous proteins become visible as fibrin strands during blood clotting. Blood is a tissue present in the circulatory system. It is a red in color due to presence of hemoglobin.

Blood is made up of:

1- **Fluid component**: Plasma

2- **Formed elements**: Erythrocytes (RBCs), Leukocytes (WBCs), and Thrombocytes (Platelets).

Plasma constitutes 55% of blood and formed elements constitute 45%.



Physical Characteristics and Volume

Blood is a sticky, opaque fluid with a characteristic metallic taste. Depending on the amount of oxygen it is carrying, the color of blood varies from scarlet (oxygen rich) to dark red (oxygen poor).

Blood is more dense than water and about five times more viscous, largely because of its formed elements. Blood is slightly alkaline with a pH between 7.35 and 7.45, and its temperature (38 C) is always slightly higher than body

temperature. Blood accounts for approximately 8% of body weight. Its average volume in healthy adult males is 5-6 L, somewhat greater than in healthy adult females 4-5 L.

Functions

Blood performs a number of functions, all concerned in one way or another with distributing substances, regulating blood levels of particular substances, or protecting the body.

Distribution

Distribution functions of blood include

1- Delivering oxygen from the lungs and nutrients from the digestive tract to all body cells.
2- Transporting metabolic waste products from cells to elimination sites (to the lungs for elimination of carbon dioxide, and to the kidneys for disposal of nitrogenous wastes in urine).
3- Transporting hormones from the endocrine organs to their target organs.

Regulation

Regulatory functions of blood include

1- Maintaining appropriate body temperature by absorbing and distributing heat throughout the body and to the skin surface to encourage heat loss.
2- Maintaining normal pH in body tissues. Many blood proteins act as buffers to prevent excessive or abrupt changes in blood pH that could affect normal cell activities.
3- Maintaining adequate fluid volume in the circulatory system. Salts (sodium chloride and others) and blood proteins act to prevent excessive fluid loss from the bloodstream into the tissue spaces. As a result, the fluid volume in the blood vessels remains ample to support efficient blood circulation to all parts of the body.

Protection

Protective functions of blood include

1- Preventing blood loss. When a blood vessel is damaged, platelets and plasma proteins initiate clot formation, halting blood loss.

2- Preventing infection. Blood contain antibodies, complement proteins, and white blood cells, all of which help defend the body against foreign invaders such as bacteria and viruses.

Plasma

Blood **plasma** is a straw-colored, sticky fluid. Although it is mostly water (about 90%), plasma contains over 100 different dissolved solutes, including nutrients, gases, hormones, wastes and products of cell activity, ions, and proteins.

Plasma proteins are the most abundant solutes in plasma. Except for antibodies and protein-based hormones, the liver makes most plasma proteins.

Plasma proteins serve a variety of functions, but they are ***not*** taken up by cells to be used as fuels or metabolic nutrients as are most other plasma solutes, such as glucose, fatty acids, and amino acids.

1-Albumin: Accounts for some 60% of plasma protein, produced by liver. It acts as a carrier to transport certain molecules through the circulation like bilirubin, hormones, and drugs. It is the major blood protein contributing to the plasma osmotic pressure (the pressure that helps to keep water in the bloodstream).

2- Fibrinogen: A coagulation protein, accounts for some 4% of plasma proteins; produced by liver; forms fibrin threads of blood clot.

3- Globin: 36% of plasma proteins, including:

A- **alpha and beta**, which produced by liver; most are transport proteins that bind to lipids, metal ions, and fat-soluble vitamins.

B- **Gamma**: Antibodies released by plasma cells during immune response.

4-Prothrombin: Is the inactive precursor of thrombin. The normal concentration in plasma is 15 mg/ dL, it is formed in the liver with the help of vitamin K.

Sixth Lec. Formed Elements of blood

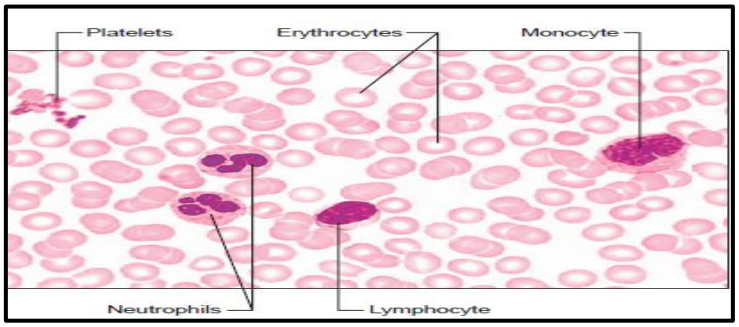
There are, ***erythrocytes, leukocytes***, and ***platelets***, have some unusual features:

(1) Two of the three are not even true cells: Erythrocytes have no nuclei or organelles, and platelets are cell fragments. Only leukocytes are complete cells.

(2) Most of the formed elements survive in the bloodstream for only a few days.

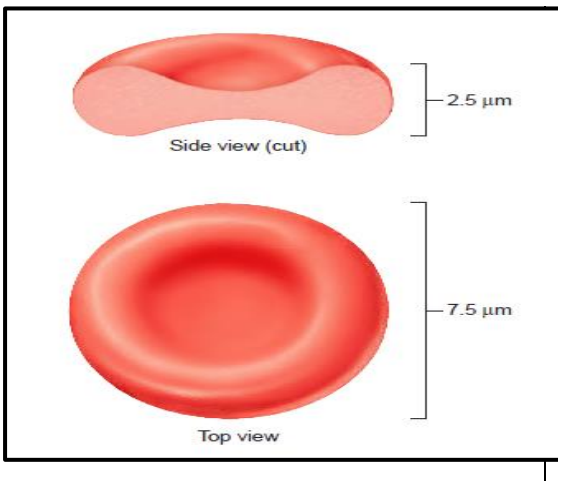
(3) Most blood cells do not divide. Instead, they are continuously renewed by division of cells in red bone marrow, where they originate.

If you examine a stained smear of human blood under the light microscope, you will see disc-shaped red blood cells, stained spherical white blood cells, and some scattered platelets that look like debris. Erythrocytes vastly outnumber the other types of formed elements.



Red blood cell (erythrocyte): Structural Characteristics

Erythrocytes or **red blood cells (RBCs)** are small cells, about 7.5 µm in diameter. Shaped like biconcave discs—flattened discs with depressed centers—they appear lighter in color at their thin centers than at their edges. Consequently, erythrocytes look like miniature doughnuts when viewed with a microscope.



Red blood cells lose nuclei upon maturation and have essentially no organelles. RBC's live about 120 days and do not self-repair. RBC's contain

hemoglobin, which transports oxygen. The hemoglobin gets its red color from their respiratory pigments. In fact, RBCs are little more than "bags" of hemoglobin (Hb), the RBC protein that functions in gas transport.

Other proteins are present, such as antioxidant enzymes that rid the body of harmful oxygen radicals, but most function mainly to maintain the plasma membrane or promote changes in RBC shape. For example, the biconcave shape of an erythrocyte is maintained by a network of proteins, especially one called **spectrin**, attached to the cytoplasmic face of its plasma membrane. The spectrin net is deformable, giving erythrocytes flexibility to change shape as necessary.

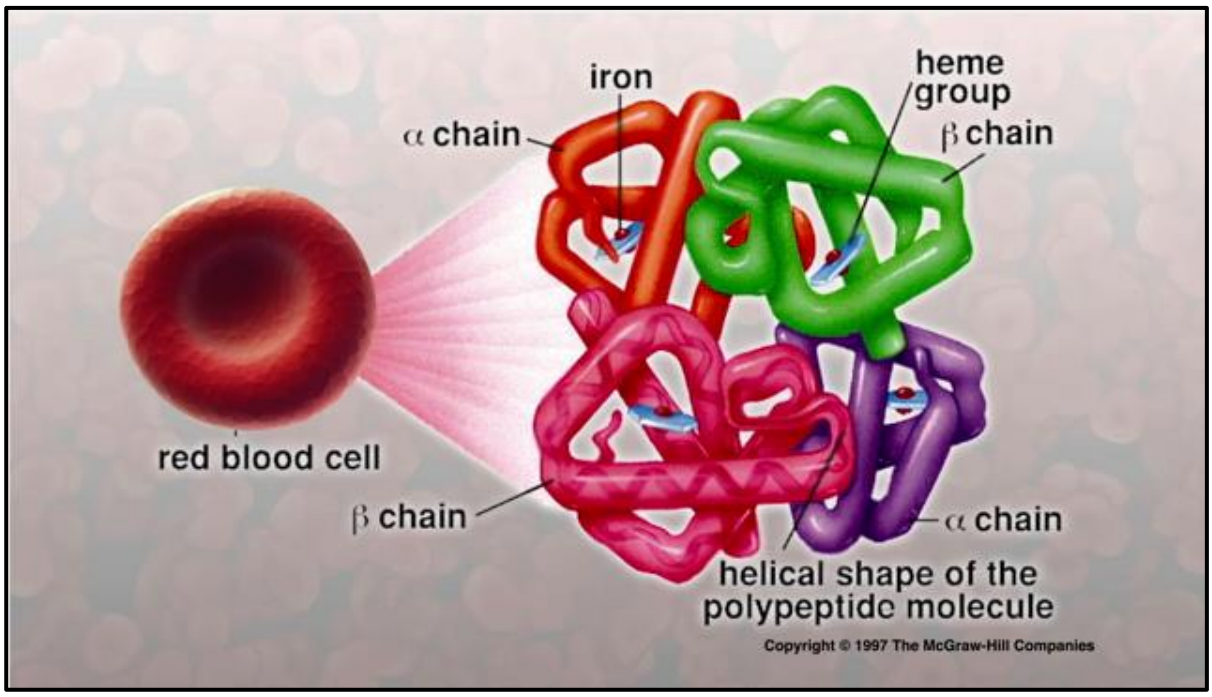
Women typically have a lower red blood cell count than men [4.3–5.2 million cells per microliter (1 μl = 1 mm3) of blood versus 5.1–5.8 million cells/μl respectively].

Function

Erythrocytes are completely dedicated to their job of transporting respiratory gases (oxygen and carbon dioxide). **Hemoglobin**, the protein that makes red blood cells red, binds easily and reversibly with oxygen, and most oxygen carried in blood is bound to hemoglobin. Normal values for hemoglobin are 14–20 grams per 100 milliliters of blood (g/100 ml) in infants, 13–18 g/100 ml in adult males, and 12–16 g/100 ml in adult females.

Hemoglobin is made up of the protein **globin** bound to the red **heme** pigment. Globin consists of four polypeptide chains—two alpha and two beta each binding a ring like heme group. Each heme group bears an atom of iron set like a jewel in its center. A hemoglobin molecule can transport four molecules of oxygen because each iron atom can combine reversibly with one molecule of oxygen.

A single red blood cell contains about 250 million hemoglobin molecules, so each of these tiny cells can scoop up about 1 billion molecules of oxygen.



Production of Erythrocytes

Blood cell formation is referred to as **hematopoiesis**, or **hemopoiesis**. This process occurs in the **red bone marrow (myeloid tissue)**, which is composed largely of a soft network of reticular connective tissue bordering on wide blood capillaries called *blood sinusoids*, although when the body is under severe conditions the yellow bone marrow, which is also in the fatty places of the marrow in the body will also make RBC's. The formation of RBC's is called **erythropoiesis**.

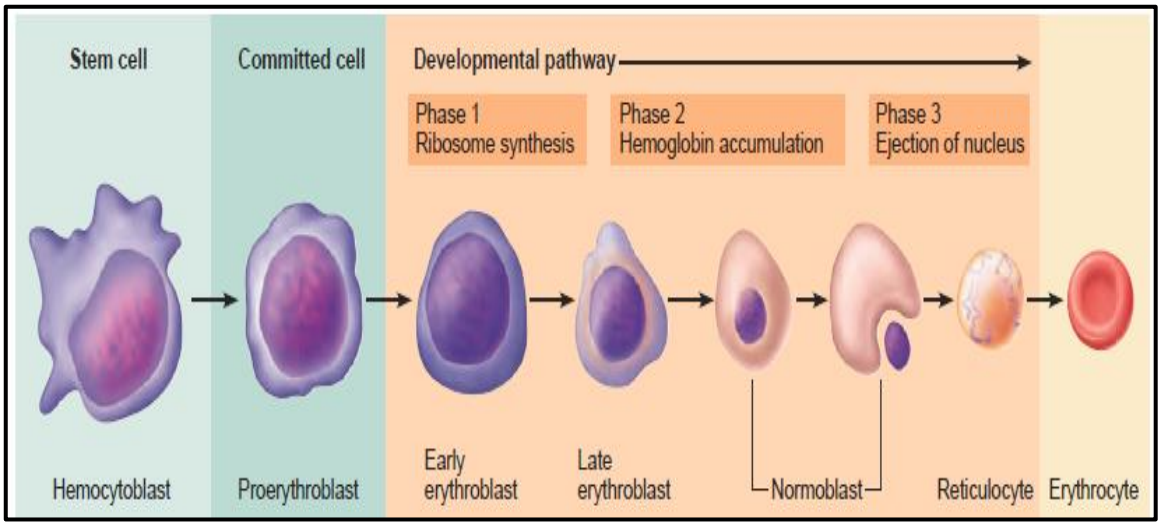
Each type of blood cell is produced in different numbers in response to changing body needs and different regulatory factors. As blood cells mature, they migrate through the thin walls of the sinusoids to enter the bloodstream. On average, the marrow turns out an ounce of new blood containing some 100 billion new cells each and every day. All arise from the same type of *stem cell*, the **hemocytoblast**.

These undifferentiated precursor cells reside in the red bone marrow. The maturation pathways of the various formed elements differ, however, and once a cell is committed to a specific blood cell pathway, it cannot change. This

commitment is signaled by the appearance of membrane surface receptors that respond to specific hormones or growth factors, which in turn "push" the cell toward further specialization.

Erythrocyte production, or **erythropoiesis** begins when a hemocytoblast descendant called a **myeloid stem cell** is transformed into a **proerythroblast**. Proerythroblasts, in turn, give rise to the **early erythroblasts** that produce huge numbers of ribosomes. During these first two phases, the cells divide many times. Hemoglobin is synthesized and iron accumulates as the early erythroblast is transformed into a **late erythroblast** and then a **normoblast**. The "color" of the cell cytoplasm changes as the blue-staining ribosomes become masked by the pink color of hemoglobin. When a normoblast has accumulated almost all of its hemoglobin, it ejects most of its organelles.

Additionally, its nuclear functions end and its nucleus degenerates and is pinched off, allowing the cell to collapse inward and eventually assume the biconcave shape. The result is the **reticulocyte** (essentially a young erythrocyte), so named because it still contains a scant *reticulum* (network) of clumped ribosomes.



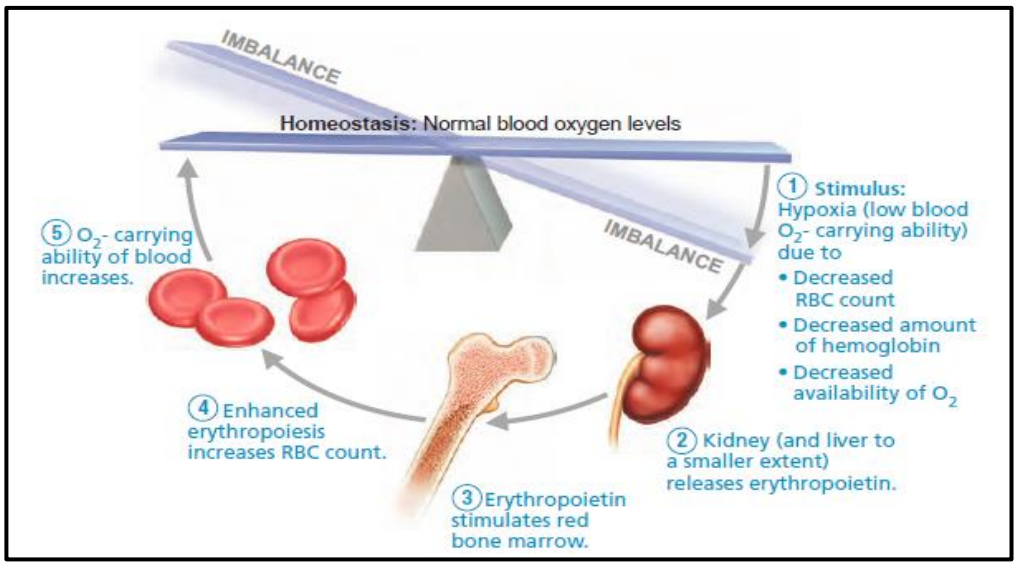
The entire process from hemocytoblast to reticulocyte takes about 15 days. The reticulocytes, filled almost to bursting with hemoglobin, enter the bloodstream to begin their task of oxygen transport. Usually they become fully mature erythrocytes within two days of release as their ribosomes are degraded by intracellular enzymes.

Reticulocytes account for 1–2% of all erythrocytes in the blood of healthy people. **Reticulocyte counts** provide a rough index of the *rate* of RBC formation. If this counts below or above this percentage range indicate abnormal rates of erythrocyte formation.

Regulation and Requirements for Erythropoiesis

The number of circulating erythrocytes in a given individual is remarkably constant and reflects a balance between red blood cell production and destruction. This balance is important because having too few erythrocytes leads to tissue hypoxia (oxygen deprivation), whereas having too many makes the blood undesirably viscous. To ensure that the number of erythrocytes in blood remains within the homeostatic range, new cells are produced at the incredibly rapid rate of more than 2 million per second in healthy people. This process is controlled hormonally and depends on adequate supplies of iron, amino acids, and certain B vitamins.

Hormonal Controls The direct stimulus for erythrocyte formation is provided by **erythropoietin (EPO)**, a glycoprotein hormone. Normally, a small amount of EPO circulates in the blood at all times and sustains red blood cell production at a basal rate. The kidneys play the major role in EPO production, although the liver produces some. When certain kidney cells become *hypoxic* (i.e., have inadequate oxygen), it accelerates the synthesis and release of erythropoietin.



Dietary Requirements The raw materials required for erythropoiesis include the usual nutrients and structural materials— amino acids, lipids, and carbohydrates. Iron is essential for hemoglobin synthesis. Iron is available from the diet, and its absorption into the bloodstream is precisely controlled by intestinal cells in response to changing body stores of iron.

Approximately 65% of the body's iron supply is in hemoglobin. Most of the remainder is stored in the liver, spleen, and bone marrow. Free iron ions (Fe^{2+},Fe^{3+}) are toxic, so iron is stored inside cells as proteiniron complexes such as **ferritin** and **hemosiderin**.

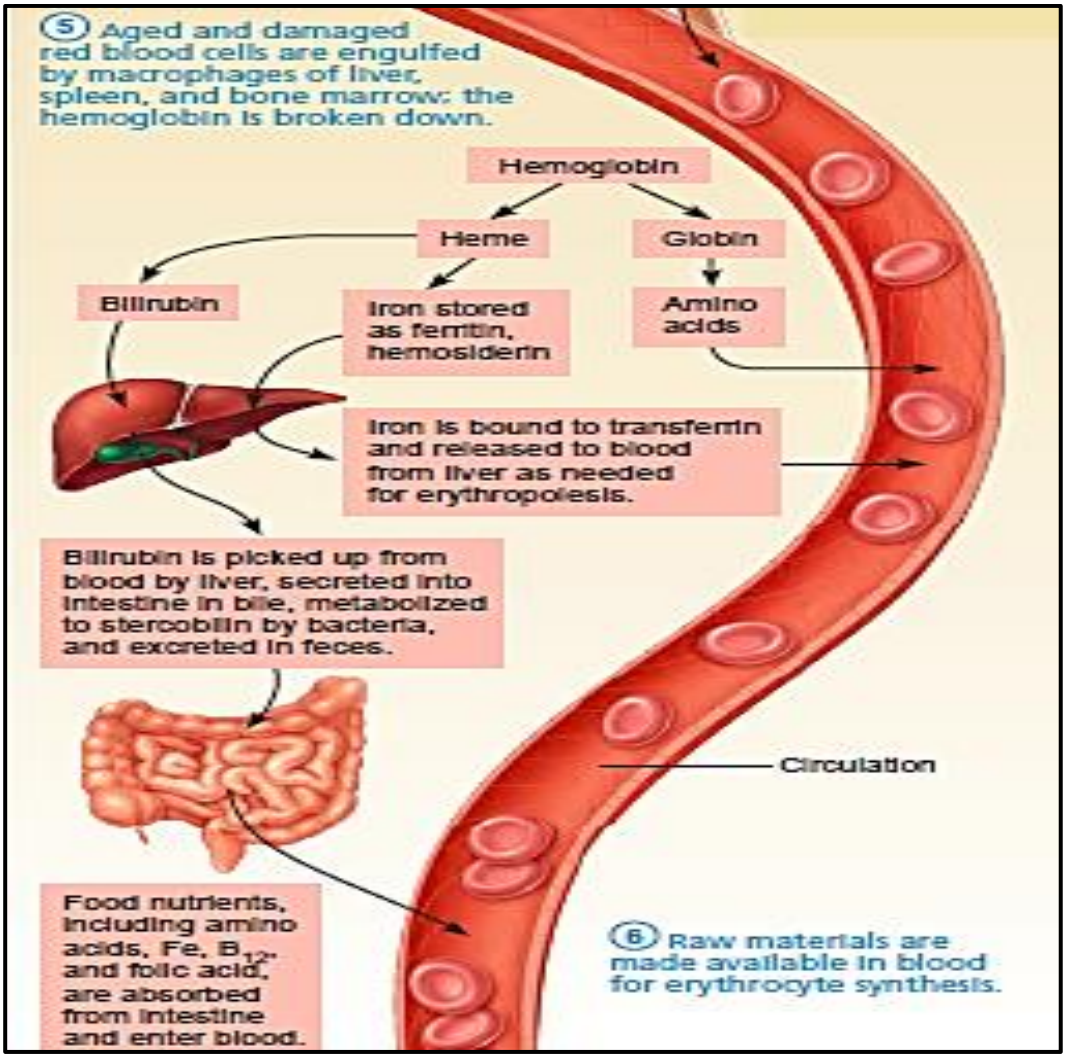
Two B-complex vitamins—vitamin B12 and folic acid—are necessary for normal DNA synthesis. Thus, even slight deficits jeopardize rapidly dividing cell populations, such as developing erythrocytes.

Fate and Destruction of Erythrocytes

Red blood cells have a useful life span of 100 to 120 days. Their a-nucleate condition carries with it some important limitations. Red blood cells are unable to synthesize new proteins, to grow, or to divide. Erythrocytes become "old" as they lose their flexibility and become increasingly rigid and fragile, and their contained hemoglobin begins to degenerate.

Dying erythrocytes are engulfed and destroyed by macrophages of spleen, liver and bone marrow, the spleen is sometimes called the "red blood cell graveyard". The heme of their hemoglobin is split off from globin. Its core of iron is salvaged, bound to protein (as ferritin or hemosiderin), and stored for reuse in bone marrow. The balance of the heme group is degraded to **bilirubin**, a yellow pigment that is released to the blood and binds to albumin for transport.

Bilirubin is picked up by liver cells, which in turn secrete it (in bile) into the intestine. Most of this degraded pigment leaves the body in feces, as a brown pigment called *stercobilin*. The protein (globin) part of hemoglobin is metabolized or broken down to amino acids, which are released to the circulation, which in turn are recycled by the body.



Seventh Lec. Erythrocyte Disorders

Most erythrocyte disorders can be classified as **anemia** or **polycythemia**.

Anemia is a condition in which the blood has abnormally low oxygen-carrying capacity. Its hallmark is blood oxygen levels that are inadequate to support normal metabolism. Anemic individuals are fatigued, often pale, short of breath. Common causes of anemia include the following:

1. **An insufficient number of red blood cells:** Conditions that reduce the red blood cell count include blood loss, excessive RBC destruction, and bone marrow failure.

Hemorrhagic anemia result from blood loss. In acute hemorrhagic anemia, blood loss is rapid (as might follow a severe stab wound). Slight but persistent blood loss (due to an undiagnosed bleeding ulcer, for example) causes chronic hemorrhagic anemia.

In ***hemolytic anemia*** erythrocytes rupture, or lyse, prematurely, for example: transfusion of mismatched blood, certain bacterial and parasitic infections are possible causes.

Aplastic anemia may result from destruction or inhibition of the red marrow by certain drugs and chemicals, ionizing radiation, or viruses. In most cases, the cause is unknown. Because marrow destruction impairs formation of *all* formed elements, anemia is just one of its signs. Defects in blood clotting and immunity are also present.

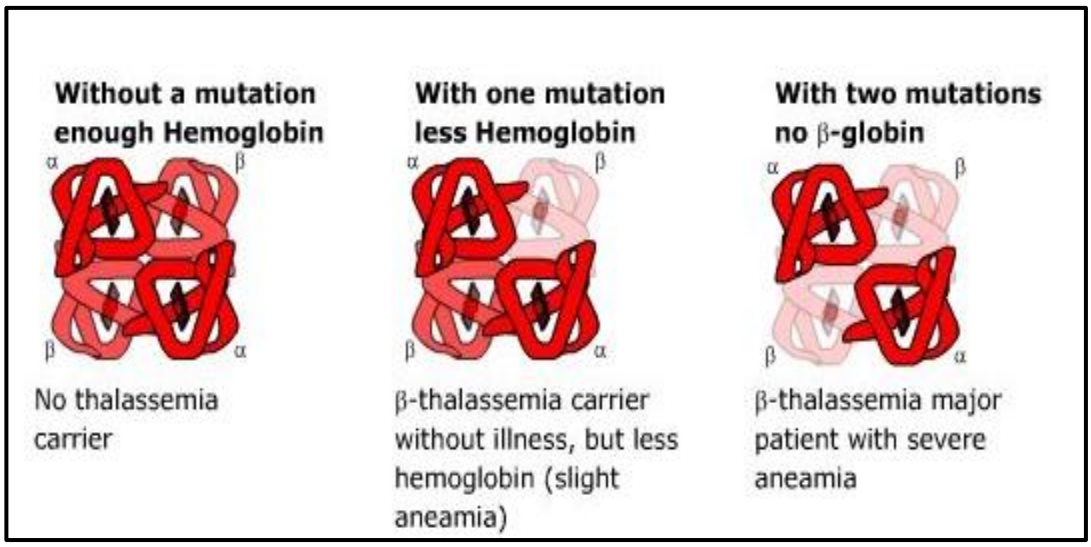
2. **Low hemoglobin content:** When hemoglobin molecules are normal, but erythrocytes contain fewer than the usual number, a nutritional anemia is always suspected.

Iron-deficiency anemia is generally a secondary result of hemorrhagic anemias, but it also results from inadequate intake of iron-containing foods and impaired iron absorption. The erythrocytes produced, called **microcytes**, are small and pale. The obvious treatment is iron supplements, but if chronic hemorrhage is the cause, red cell transfusions may also be needed.

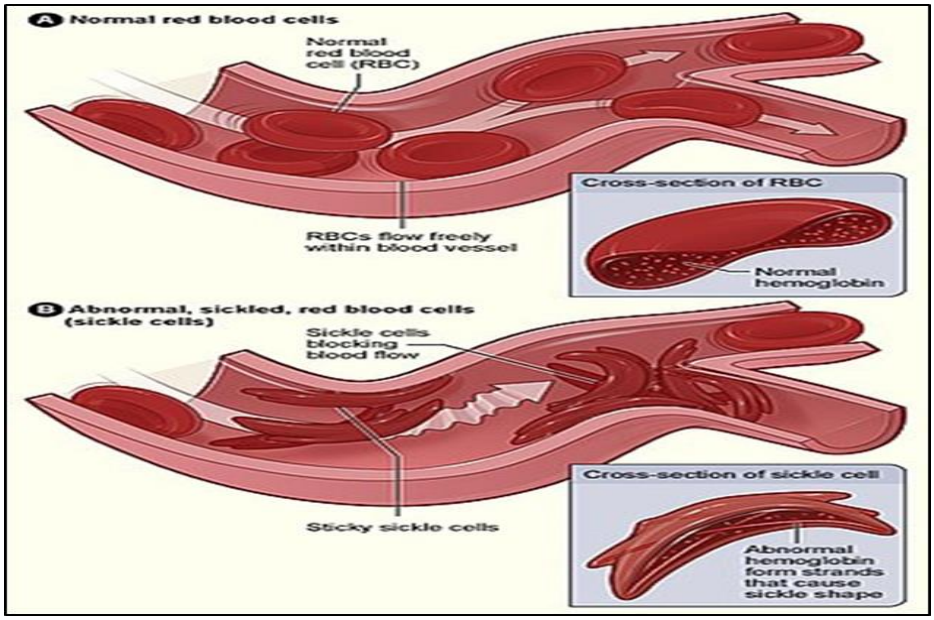
Pernicious anemia is due to a deficiency of vitamin B_{12}. Because meats, poultry, and fish provide ample amounts of the vitamin, diet is rarely the problem except for strict vegetarians. A substance called **intrinsic factor**, produced by the stomach mucosa, must be present for vitamin B12 to be absorbed by intestinal cells. In most cases of pernicious anemia, intrinsic factor is deficient. Consequently, the developing erythrocytes are large, pale cells called **macrocytes**. Pernicious anemia is an autoimmune disease in which the stomach mucosa atrophies. Treatment involves regular intramuscular injections of vitamin B_{12}.

3. Abnormal hemoglobin. Production of abnormal hemoglobin usually has a genetic basis. Two such examples, thalassemia and sickle- cell anemia, can be serious, incurable, and sometimes fatal diseases. In both diseases the globin part of hemoglobin is abnormal and the erythrocytes produced are rupture prematurely.

***Thalassemia*:** are typically seen in people of Mediterranean ancestry, such as Greeks and Italians. One of the globin chains is absent or faulty, and the erythrocytes are thin, delicate, and deficient in hemoglobin. There are many subtypes of thalassemia, classified according to which hemoglobin chain is affected and where, ranging in severity from mild to so severe that monthly blood transfusion is required.



sickle-cell anemia, the havoc caused by the abnormal hemoglobin, *hemoglobin S* (*HbS*), results from a change in just one of the 146 amino acids in a beta chain of the globin molecule. This alteration causes the beta chains to link together under low-oxygen conditions, forming stiff rods so that hemoglobin S becomes spiky and sharp. This, in turn, causes the red blood cells to become crescent shaped when they unload oxygen molecules or when the oxygen content of the blood is lower than normal. The stiff, deformed erythrocytes rupture easily and tend to dam up in small blood vessels. These events interfere with oxygen delivery.



Blood transfusion is still the standard treatment for an acute sickle-cell crisis, but preliminary results using inhaled nitric oxide to dilate blood vessels. Sickle-cell anemia occurs chiefly in black people who live in the malaria belt of Africa and among their descendants. It strikes nearly one of every 400 black newborns in the United States. Globally, 300–500 million people are infected with malaria and more than a million die each year. While individuals with gene of this anemia have a better chance of surviving in regions where malaria is present. Sickling appears to reduce the parasites' ability to survive and enhances macrophages' ability to destroy infected RBCs and the parasites they contain.

Polycythemia is an abnormal excess of erythrocytes that increases blood viscosity, causing it to sludge, or flow sluggishly.

Polycythemia vera, a bone marrow cancer, is characterized by dizziness and an exceptionally high RBC count (8–11 million cells/µl). The hematocrit may be as high as 80% and blood volume may double, causing the vascular system to become engorged with blood and severely impairing circulation.

Secondary polycythemias result when less oxygen is available or EPO production increase. The secondary polycythemia that appears in individuals living at high altitudes is a normal physiological response to the reduced atmospheric pressure and lower oxygen content of the air in such areas. RBC counts of 6–8 million/µl are common in such people. Severe polycythemia is treated by blood dilution, in other words, removing some blood and replacing it with saline.

Leukocytes

(*leuko* = white), or **white blood cells (WBCs)**, are the only formed elements that are complete cells, with nuclei and the usual organelles. Accounting for less than 1% of total blood volume. On average, there are 4800–10,800 WBCs/mm^3 of blood.

Leukocytes are crucial to our defense against disease. They form a mobile army that helps protect the body from damage by bacteria, viruses, parasites, toxins, and tumor cells. As such, they have some special functional characteristics. Red blood cells are confined to the bloodstream, and they carry out their functions in the blood, but white blood cells are able to slip out of the capillary blood vessels- a process called **diapedesis**. Once out of the bloodstream, leukocytes move through the tissue spaces by **amoeboid motion**, by following the chemical trail of molecules released by damaged cells or other leukocytes, a phenomenon called **positive chemotaxis**, they can pinpoint areas of tissue damage and infection and gather there in large numbers to destroy foreign substances or dead cells. Leukocytes are grouped into two major categories on the basis of structural and chemical characteristics. *Granulocytes* contain obvious membrane-bound cytoplasmic granules, and *a granulocytes* lack obvious granules

Granulocytes

Granulocytes, which include neutrophils, basophils, and eosinophils, are spherical in shape, have lobed nuclei. They are larger than erythrocytes. ***Neutrophils:*** are the most numerous of the white blood cells, accounting for 50-70% of the WBC population. The neutrophil cytoplasm stains pale lilac and contains very fine granules. Some of these granules contain hydrolytic enzymes, and are regarded as lysosomes. Others, especially the smaller granules, contain potent antimicrobial proteins, called **defensins**.

Eosinophils: account for 2-4% of all leukocytes. Large, coarse granules contain digestive enzymes. The most important role of eosinophils is to lead the

counterattack against parasitic worms that are too large to be phagocytized. Eosinophils have complex roles in many other diseases including allergy and asthma.

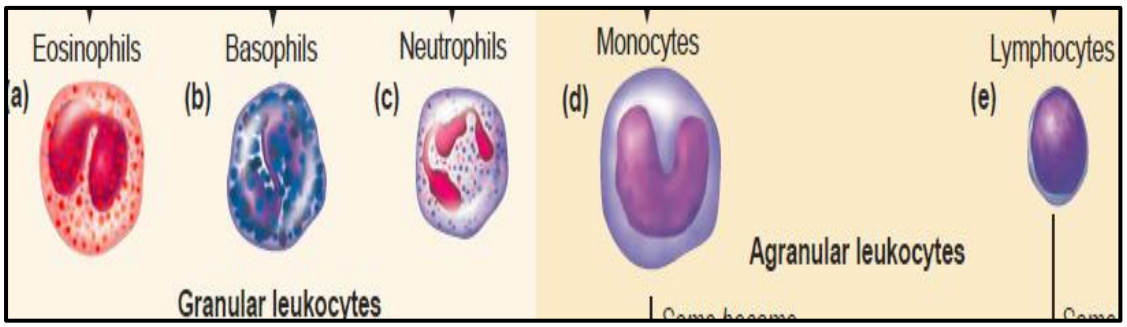
***Basophils*:** are the rarest white blood cells, averaging only 0-1% of the leukocyte population. The deep purple nucleus is generally U or S shaped. Their cytoplasm contains large, coarse, histamine-containing granules that have an affinity for the basic dyes. *Histamine* is an inflammatory chemical that acts as a vasodilator (makes blood vessels dilate) and attracts other white blood cells to the inflamed site; drugs called antihistamines counter this effect.

Agranulocytes

The **agranulocytes** include lymphocytes and monocytes, WBCs that lack *visible* cytoplasmic granules. Their nuclei are typically spherical or kidney shaped.

***Lymphocytes*:** accounting for 25%. Lymphocytes are closely associated with lymphoid tissues (lymph nodes, spleen), where they play a crucial role in immunity. **T lymphocytes (T cells)** function in the immune response by acting directly against virus-infected cells and tumor cells, it is processed in the thymus gland. **B-lymphocytes (B cells)** give rise to *plasma cells*, which produce **antibodies** that are released to the blood. They are processed in fetal liver and bone marrow in human.

***Monocytes*:** account for 3–8% of WBCs. When circulating monocytes leave the bloodstream and enter the tissues, they differentiate into highly mobile **macrophages**. Macrophages are actively phagocytic, and they are crucial in the body's defense against viruses, certain intracellular bacterial parasites, and *chronic* infections such as tuberculosis, macrophages are also important in activating lymphocytes to mount the immune response.



Platelets

Platelets are cytoplasmic fragments of extraordinarily large cells called **megakaryocytes**. In blood smears, each platelet exhibits a blue-staining outer region and an inner area containing granules that stain purple. The granules contain an impressive array of chemicals that act in the clotting process, including serotonin, Ca^{2+}, a variety of enzymes, ADP, and platelet-derived growth factor (PDGF). Platelets are essential for the clotting process that occurs in plasma when blood vessels are ruptured or their lining is injured. Platelets age quickly because they are a-nucleate, and they degenerate in about 10 days if they are not involved in clotting.

Hemostasis

Normally, blood flows smoothly past the intact blood vessel lining (endothelium). But if a blood vessel wall breaks, a whole series of reactions is set in motion to accomplish **hemostasis (**stoppage of bleeding). Without this plug-the-hole defensive reaction, we would quickly bleed out our entire blood volume from even the smallest cuts.

The hemostasis response is fast, localized, and carefully controlled, three steps occur in rapid sequence:

1- Vascular spasm.

2-Platelet plug formation.

3-Coagulation or blood clotting.

Vascular Spasm

In the first step, the damaged blood vessels respond to injury by constricting (vasoconstriction). Factors that trigger this **vascular spasm** include direct injury to vascular smooth muscle, chemicals released by endothelial cells and platelets, and reflexes initiated by local pain receptors.

The spasm mechanism becomes more and more efficient as the amount of tissue damage increases, and is most effective in the smaller blood vessels. The spasm response is valuable because a strongly constricted artery can significantly reduce blood loss for 20-30 minutes, allowing time for platelet plug formation and blood clotting to occur.

Platelet Plug Formation

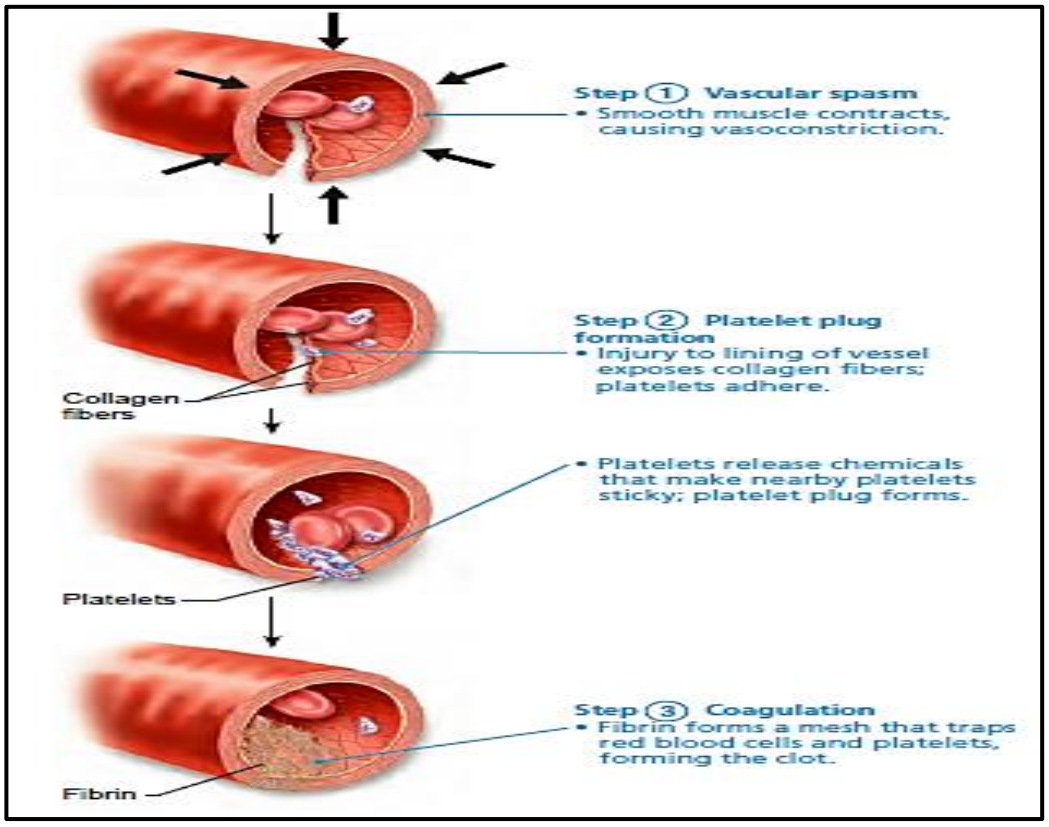
In the second step, platelets play a key role in hemostasis by aggregating (sticking together), forming a plug that temporarily seals the break in the vessel wall.

As a rule, platelets do not stick to each other or to the smooth endothelial linings of blood vessels. Intact endothelial cells release nitric oxide and a prostaglandin called **prostacyclin**. Both chemicals prevent platelet aggregation in undamaged tissue and restrict aggregation to the site of injury.

However, when the endothelium is damaged and underlying collagen fibers are exposed, platelets adhere tenaciously to the collagen fibers. A large plasma protein called *von Willebrand factor* stabilizes bound platelets by forming a bridge between collagen and platelets. Platelets swell, form spiked processes, become stickier, and release chemical messengers including the following:

- **Adenosine diphosphate (ADP):** a potent aggregating agent that causes more platelets to stick to the area and release their contents
- **Serotonin** and **thromboxane A2** (a short-lived prostaglandin derivative): messengers that enhance vascular spasm and platelet aggregation.

As more platelets aggregate, they release more chemicals, aggregating more platelets. Within one minute, a platelet plug is built up, further reducing blood loss. Platelets alone are sufficient for sealing the thousands of minute rips and holes that occur unnoticed as part of the daily wear and tear in your smallest blood vessels. Because platelet plugs are loosely knit, larger breaks need additional reinforcement.



Coagulation or blood clotting

The third step, **coagulation** or **blood clotting**, reinforces the platelet plug with fibrin threads that act as a glue for the aggregated platelets. Blood is transformed from a liquid to a gel in a multistep process that involves a series of substances called **clotting factors.**

Most clotting factors are plasma proteins synthesized by the liver. They are numbered I to XIII. All (except tissue factor) normally circulate in blood in inactive form until mobilized. Although vitamin K is not directly involved in coagulation, this fat-soluble vitamin is required for the synthesis of four of the clotting factors.

Coagulation occurs in three phases, each with a specific end point:

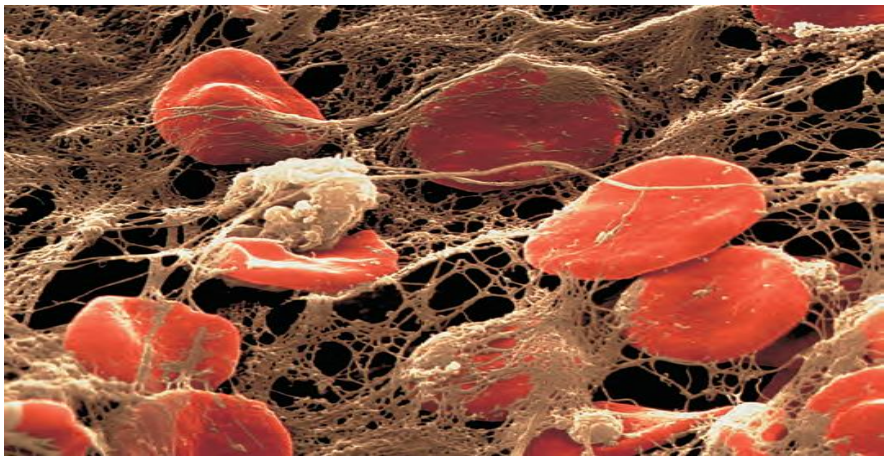
■ *Phase 1: Two pathways (Intrinsic and Extrinsic pathways) to prothrombin activator.* A complex substance called *prothrombin activator* is formed.

■ *Phase 2:* Prothrombin activator converts a plasma protein called *prothrombin* into *thrombin*, (an enzyme) in the presence of Ca^{+2}.

■ *Phase 3: Pathway to the fibrin mesh.* Thrombin catalyzes the joining of *fibrinogen* molecules present in plasma to a *fibrin mesh*, which traps blood cells and effectively seals the hole until the blood vessel can be permanently repaired.

Thrombin catalyzes the transformation of the *soluble* clotting factor **fibrinogen** into **fibrin**. The fibrin molecules then polymerize (join together) to form long, hairlike, *insoluble* fibrin strands. The fibrin strands glue the platelets together and make a web that forms the structural basis of the clot. Fibrin makes plasma become gel-like and traps formed elements that try to pass through it.

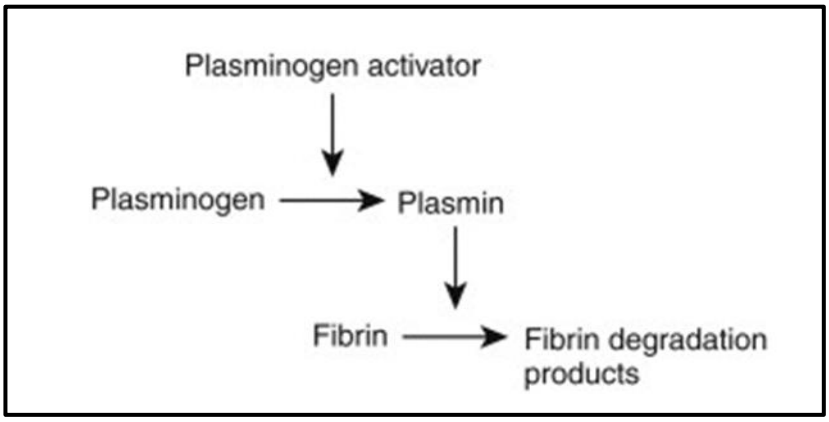
In the presence of calcium ions, thrombin also activates **factor XIII (fibrin stabilizing factor)**, a cross-linking enzyme that binds the fibrin strands tightly together, forming a fibrin mesh.



Fibrinolysis

A clot is not a permanent solution to blood vessel injury, and a process called **fibrinolysis** removes unneeded clots when healing has occurred. Without fibrinolysis, blood vessels would gradually become completely blocked.

There is a fibrin-digesting enzyme called **plasmin**, which is produced when the plasma protein **plasminogen** is activated. Large amounts of plasminogen are incorporated into a forming clot, where it remains inactive until appropriate signals reach it. The presence of a clot in and around the blood vessel causes the endothelial cells to secrete **tissue plasminogen activator (tPA)**. Activated factor XII and thrombin released during clotting also serve as plasminogen activators. As a result, most plasmin activity is confined to the clot, and any plasmin that strays into the plasma is quickly destroyed by circulating enzymes. Fibrinolysis begins within two days and continues slowly over several days until the clot is finally dissolved.



Animal Physiology

Digestive system

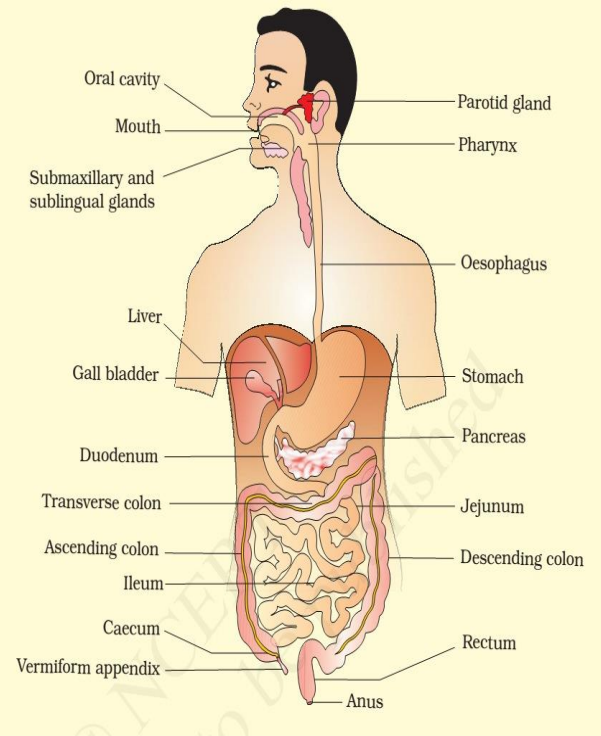


Figure 16.1 The human digestive system

Dr. muntaha mhmood

Chapter One - Digestion and Gastrointestinal physiology

Contents : Gastrointestinal functions : Digestion in the Mouth and Pharynx, major components of saliva & control, Stomach and Gastric glands, Small intestine , Liver functions, biliary system , Pancreas , Colon .

Mechanisms of digestion , Mechanical and Chemical Digestion.

Digestion and absorption of: Fat , Carbohydrate , DNA and RNA , protein, vitamin and minerals ,

Stages in the Digestive Process ,

Regulation of Gastrointestinal functions, appetite, Control of Digestion, Gastrointestinal hormones.

Objectives

1. Describe the structure and general function of each digestive organ and the liver.
2. Describe the structure of the wall of the alimentary canal.
3. Explain how the contents of the alimentary canal are mixed and moved.
4. Describe the mechanisms of Digestion, Absorption , Control.

Chapter One - Digestion and Gastrointestinal physiology

Functions of Gastrointestinal System

The main two functions of the digestive system are digestion and absorption including followings:

1-Is responsible for the breakdown and convert food into energy .

2-absorption of various foods and liquids needed to sustain life.

3-Movement of nutrient molecules from the external environment to the internal environment

Steps of food processing

Animals process food in four stages which are : ingestion , digestion , absorption , elimination . these processes occur by two mechanisms:

1-Mechanical Digestion: larger pieces of food broken down into smaller pieces to be prepared for chemical digestion. Mechanical digestion starts in the mouth and continues into the stomach by action of muscles

2-Chemical Digestion: starts in the mouth and continues into the intestines. Several different enzymes break down macromolecules into smaller molecules that can be absorbed by chemical reactions.

Stages in the Digestive Process

Digestion of the large molecules into smaller components involves following process:

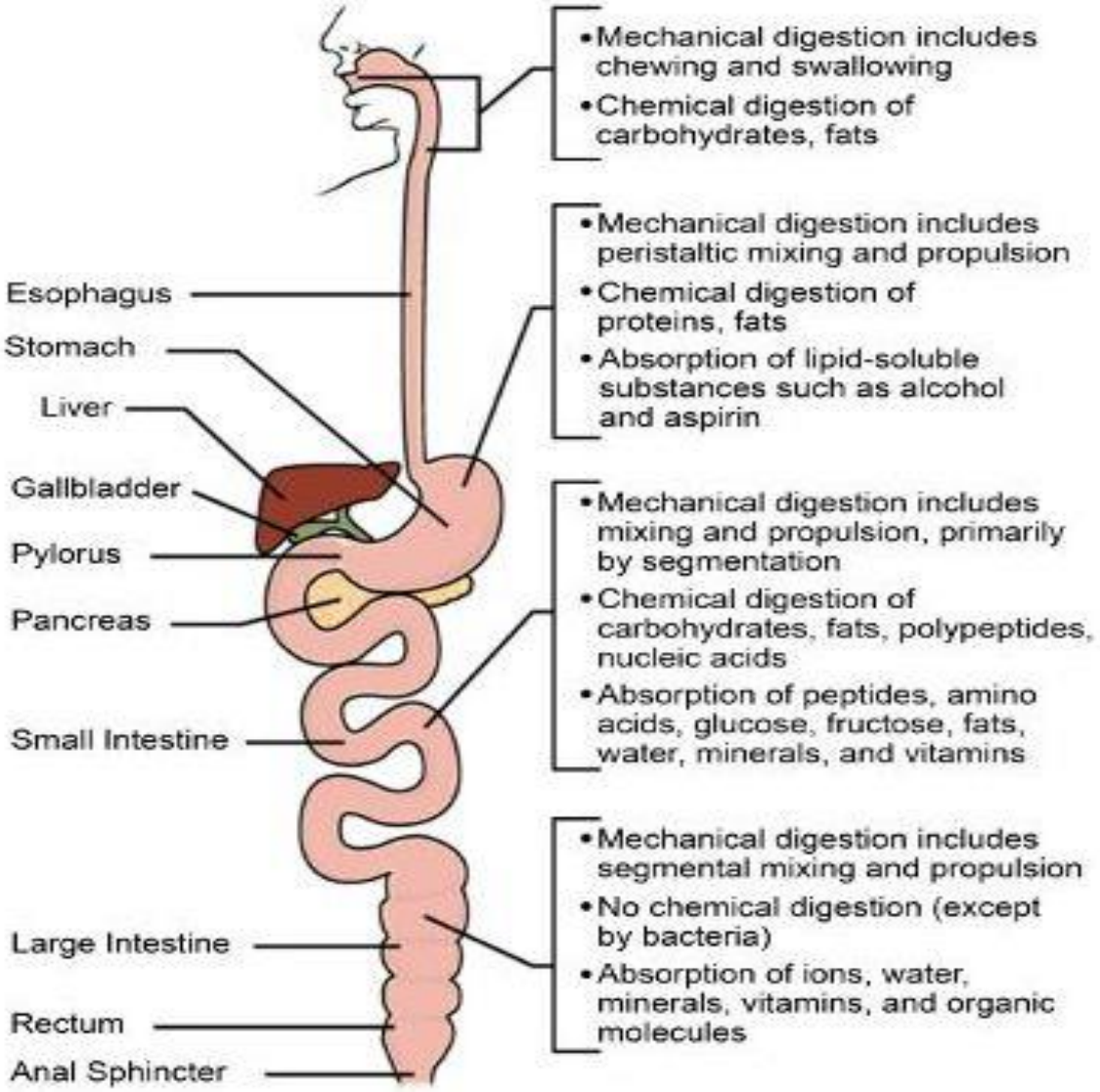
Movement: propels food through the digestive system

Secretion: release of digestive juices in response to a specific stimulus.

Digestion: breakdown of food into molecular components small enough to cross the plasma membrane.

Absorption: passage of the molecules into the body's interior and their passage throughout the body.

Elimination: removal of undigested food and wastes


Esophagus
Stomach
Liver
Gallbladder
Pylorus
Pancreas
Small Intestine
Large Intestine
Rectum
Anal Sphincter
•Mechanical digestion includes chewing and swallowing
•Chemical digestion of carbohydrates, fats
•Mechanical digestion includes peristaltic mixing and propulsion
•Chemical digestion of proteins, fats
•Absorption of lipid-soluble substances such as alcohol and aspirin
•Mechanical digestion includes mixing and propulsion, primarily by segmentation
•Chemical digestion of carbohydrates, fats, polypeptides, nucleic acids
•Absorption of peptides, amino acids, glucose, fructose, fats, water, minerals, and vitamins
•Mechanical digestion includes segmental mixing and propulsion
•No chemical digestion (except by bacteria)
•Absorption of ions, water, minerals, vitamins, and organic molecules

Digestion in different parts of the digestive tract

Mouth and Pharynx

Mechanical breakdown begins in the mouth by chewing with teeth and actions of the tongue. Chemical breakdown of starch start by production of salivary amylase from the salivary glands, salivary amylase, begins the breakdown of starch .

Salivary glands are: Parotid gland, submandibular gland, sublingual gland , these are exocrine glands that produces saliva which begins the process of digestion with amylase, Salivary glands also produce an estimated three liters of saliva per day.

Control of salivation:

ingestion of foodstuffs activate chemoreceptors and pressoreceptors salivatory nuclei (pons & medulla) parasympathetic nerve activation Facial (VII) and Glassopharyngeal (IX) nerves secretion by salivary glands.

sympathetic nerve activation decreased salivation.

Stomach

The stomach a thick walled organ. It is on the left side of the abdominal cavity; food reaches the end of the esophagus, it enters the stomach through a muscular valve called the lower esophageal sphincter. The stomach secretes acid and enzymes that digest food. The stomach muscles contract periodically, churning food to enhance digestion. The pyloric sphincter is a muscular valve that opens to allow food to pass from the stomach to the small intestine.

Gastric glands :

Three type of secretary cells found in each gland:

A-Parietal cells , B-chief cells , C-mucus cells .

Parietal cells (oxyntic cells): Secrete gastric Hcl.

Chief cells (Digestive cells): It synthesize and secrete in active pepsinogen which activated by gastric Hcl into active pepsin that digest proteins by cleaving peptide bonds and breaks long polypeptide chains into shorter ones .

Food in the stomach is in semi-liquid form, which upon completion is known as chyme. The gastric juice is highly acidic with a pH of 1-3. It may cause or compound damage to the stomach wall or its layer of mucus, causing a peptic ulcer.

Function of gastric Hcl

1-It has a role in digestion .

2-Making the medium of the stomach acidic (pH-2) .

3-Stimulate pancreatic and bile secretion where it enter intestine

4- Kills much of bacteria that may be ingested along with food

5-Stops activity of salivary amylase, but promotes pepsin activity

Phases of gastric secretion

The secretion of gastric juices occurs in three phases: cephalic, gastric, and intestinal.

1-Cephalic phase - This phase occurs before food enters the stomach and involves preparation of the body for eating and digestion.
2-Gastric phase - This phase takes 3 to 4 hours. It is stimulated by distension of the stomach, presence of food in stomach and decrease in pH.
3-Intestinal phase -The intestinal phase blocks the effect of the cephalic and gastric phases.
Control of secretion and motility
The movement and the flow of chemicals into the stomach are controlled by both the nervous system and by the various digestive system hormones.
Gastrin hormone
That is causes an increase in the secretion of HCL pepsinogen and intrinsic factor from parietal cells in the stomach.
It also causes increased motility in the stomach.Gastrine is relaesed pH normally less than 4 by G-cells into the stomach. It is inhibited by (high acid) as well as the hormone somatostatin.

Cholecystokinin (CCK)

Cholecystokinin (CCK) has most effect on the gall bladder, but it also decreases gastric emptying, has most effects on the pancreas.

Gastric inhibitory peptide (GIP)

Gastric inhibitory peptide (GIP) and enteroglucagon decrease both gastric motility and secretion of pepsin.

Small Intestine

The small intestine is the site where most of the chemical and mechanical digestion is carried out. Tiny projections called villi line the small intestine which absorbs digested food into the capillaries. Most of the food absorption takes place in the jejunum and the ileum.

The functions of a small intestine is, the digestion of proteins into peptides and amino acids principally occurs in the stomach but some also occurs in the small intestine. Peptides are

degraded into amino acids; lipids (fats) are degraded into fatty acids and glycerol; and carbohydrates are degraded into simple sugars. Two ducts enter the duodenum which are:

1-Common duct which is composed from liver duct and bile duct –it draining the gall bladder and liver secretions into duodenum .

2-Pancreatic duct which draining the exocrine product from pancreas into duodenum .

Parts of intestine

The Duodenum

It is the first and shortest part of the small intestine. The duodenum is also where the bile and pancreatic juices enter the intestine.

The Jejunum

The inner surface of the jejunum, its mucous membrane, is covered in projections called villi, which increase the surface area of tissue available to absorb nutrients from the gut contents.

The Ileum

Its function is to absorb vitamin B12 and bile salts. The wall itself is made up of folds, each of which has many tiny fingerlike projections known as villi, on its surface. The villi contain large numbers of capillaries which take the amino acids and glucose produced by digestion to the hepatic portal vein and the liver.

Liver

It plays a major role in metabolism and has a number of functions, It also produces bile, which is important in digestion. The bile produced in the liver is collected in bile canaliculi, which merge from bile ducts. These eventually drain into the right and left hepatic ducts, which in turn merge to form the common hepatic duct. The cystic duct from the gallbladder joins with the common hepatic duct to form the common bile duct.

Bile can either drain directly into the duodenum via the common bile duct or be temporarily stored in the gallbladder via the cystic duct. The common bile duct and the pancreatic duct enter the duodenum together. The branching's of the bile ducts resemble those of a tree, and indeed term "biliary tree" .
The various functions of the liver are carried out by the liver cells or hepatocytes.

1. detoxify blood - remove and metabolize poisonous substances.
2. destroy old RBC - hemoglobin converted to bile -- bile stored in gall bladder and used in digestion of fats.
3. stores glucose as glycogen - converts glycogen to glucose to keep blood sugar concentration in blood constant
4. production of urea from amino groups and ammonia.
5-synthesis of blood proteins.
6-The liver produces and excretes bile requires for dissolving fats.

7-The liver produces coagulation factors I (fibrinogen), II (prothrombin), V, VII, IX, X and XI, as well as protein C, Protein S and antithrombin.

Bile Release into Small Intestine

The liver is stimulated by the hormones “secretin” and “cholecystokinin” (CCK) to produce bile. The bile enters the right and left hepatic ducts and travels to the common hepatic duct. The bile is stored in the gallbladder. The gallbladder is stimulated to release the bile by the vagal nerve and CCK. The bile enters the duodenum via the bile duct.

Function of bile juice

Emulsification of ingested fat by breaking large fat droplets into smaller &changing fast from insoluble material into water soluble that could digested by lipase . Also bile juice helps in absorption of fat soluble vitamins (E,D,A,K).

Role of the Bile

1. Neutralize the stomach acid;
2. Inhibit the act of stomach proteases;
3. Increase the activity of pancreatic lipase;
4. Emulsificates the lipids by help of bile acids actions;
5. Bile acids help stabilizing of emulsion;
6. Increase absorption of fatty acids, carrotin,vitamins K, D, E;
7. Increase tone and motor function of intestines .
8. Decrease the activity of intestine micro flora;
9. Take place of enzymes fixation on the intestines su

Pancreas

Is an gland has two type of secretions :

1-Exocrine functions:

Exocrine secretion whose drain in to duodenum and called pancreatic juice

its pH (8) and contains :

1-sodium bicarbonate – neutralize the acidity of gastric Hcl in duodenum.

2-Ions of Cl-
, So4-
, Hpo4, K+
, Ca+ , Mg+
.
3-Many digestive enzymes that are :
A- Pancreatic amylase hydrolyze starch .
B- pancreatic lipase hydrolyze fats .
C- trypsin hydrolyze proteins .
D- chemotrypsin hydrolyze proteins .
E- Elastase hydrolyze proteins .
F- Carboxypeptidase hydrolyze polypeptides .
G- nuclease hydrolyze nucleic acids .
2-Endocrine functions:
Endocrine secretions from islets of langerhans , which are following hormones insuline , glucagune , somatostatin .
o Somatostatin: inhibits the function of insulin.
Produced if the body is getting too much glucose.

o Glucagon: stimulates the stored glycogen in the liver to convert to glucose. Produced if the body does not have enough glucose.
o Insulin: made in the beta cells of the Islets of Langerhans of the pancreas. Insulin is a hormone that regulates blood glucose.

Regulation of Pancreatic Secretion

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

Digestion of foods

Fat digestion

All fats ingested digested into three type of molecules which are :Glycerol,Triglycerides, Fatty acids, These products are absorbed into intestinal lymphatic circulation not into the blood circulation .And then thy pass to the fat deposts of the body either in the abdomen or under the skin .

Lipid Absorption

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

contain cholesterol and fat-soluble vitamins , diffuse through lipid bilayer of membrane .

2.hylomicrons - micelles combined with associated proteins within the cell; enter the lacteals of the lymphatic system.

Carbohydrate digestion

Starches are broken down into sugars (glucose and fructose) by amylase and hydrochloric acid in the stomach.

DNA and RNA digestion

DNA and RNA are broken down into mononucleotides by the nucleases deoxyribonuclease and ribonuclease (DNase and RNase) from the pancreas.

Nucleic Acid Absorption

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

Digestion of protein

Ingested proteins broken down into amino acids by enzymatic activity : Food protein by action of pepsin converted to long chain peptides , then by action of trypsin changed to short chain peptides then by action of erepsin converted to amino acids.

Protein (Amino Acid) Absorption

by facilitated diffusion - amino acids and small peptides (coupled with Na+ active transport), "carrier molecule" has binding sites for both amino acid and Na+; relies on Na+ gradient

Vitamin Absorption

1-fat soluble - Vitamins A, D, E, K are absorbed by epithelial cells along with lipid micelles by aids of bile juice.

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

3.Vitamin B12 - large and electrically charged, must bind with "intrinsic factor" before being taken into the cell by endocytosis.

Electrolyte Absorption

1. Fe and Ca - primarily absorbed in small intestine
2. Na - exchanged for sugars and amino acids
3. Cl - absorbed into cells and exchanged for HCO_3^-
4. K - absorbed into cells due to osmotic gradients

Water Absorption

1.small intestine - 95% of water absorbed by small intestine following transport of solutes

2.large intestine - absorbs remaining water before moving the chyme on to the rectum

Control of Digestion

1- by Nervous System: Two Phases controlled by N. system:

1-Cephalic Phase - Triggered by the site, smell, and taste of food. This stimulates the stomach to prepare for the entry of food.

2-Gastric Phase - Stomach distension by food stimulates the release of gastric juices.

2- by Hormons

1-Gastrin - Produced by the stomach; stimulates the release of gastric juices.

2-Secretin - Produced by the small intestine; stimulates the pancreas and gall bladder to release pancreatic juices and bile.

3-Cholecystokinin (CCK) - Produced by the small intestine; stimulates the pancreas and gall bladder to release pancreatic juices and bile.

Large Intestine

The large intestine (colon) extends from the end of the ileum to the anus. It is about 5 feet long, being one-fifth of the whole extent of the intestinal canal.

The large intestine is divided into the cecum, colon, rectum, and anal canal.

Digestive Enzymes

Location	Enzyme	Targets
Salivary glands	Amylase Lipase	Starch Triglycerides
stomach	Pepsin lipase	Protien Triglycerides
pancreas	Amylase Lipase and colipase Phospholipase Trypsin chymotrypsin	Starch Triglycerides Phospholipides Peptides Peptides
intestine	Enterokinase Disaccharidases Peptidase	Activates trypsin Complex sugers peptides

Muscular system

Muscle is one of the four primary types of tissues.

General characteristics of muscles

- The structural and functional unit of muscles are formed of special elongated cells known as **muscle fiber**.
- The cell membrane of these muscles fibers is known as **sarcolemma**.
- The cytoplasim of these muscles fibers is known as **sarcoplasm.**
- Smooth endoplasmic reticulum is called **sarcoplasmic reticulum.**
- The muscle fibers may have transverse striations as the skeletal and cardiac muscle fibers, or they may show no striation as smooth muscle fiber (myocytes).

Function of muscles

1- Producing body movements
2- Stabilizing body position.
3- Regulating organ volumes.
4- Movement of substances within the body (blood, lymph, air, sperms).
5- Producing heat {involuntary contractions of skeletal muscle (shivering)}.

Histologically, there are three types of muscles tissue:

(1) Skeletal muscle (2) Cardiac muscle (3) Smooth muscle.

Skeletal muscle

Sites

- The skeletal muscles attached to the skeleton.
- They are present also in the diaphragm, tongue, muscles of face, eye, pharynx, and upper third of esophagus.

Structure of skeletal muscle

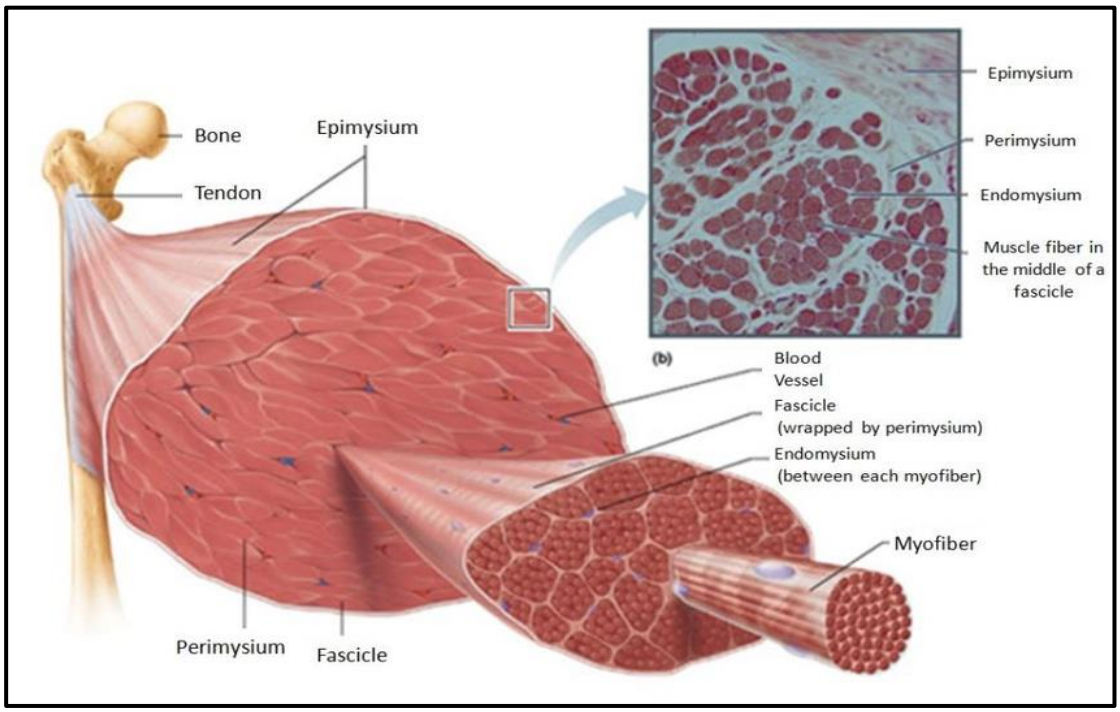
1- The entire muscle surrounded by a connective tissue called the **epimysium**.

2- Fascicles are bundles of individual muscle cells (myofibers or myocytes).

3- These bundles surrounded by a connective tissue sheath called the **perimysium.**

4- Each fascicles made up of several muscle cells known as myocytes or myofibers or delicate muscle fibers

5- Each muscle cell surrounded by a connective tissue sheath known as the **endomysium.**



Muscle fiber (muscle cell) of skeletal muscle

1- Sarcolemma

2- Sarcoplasm (mitochondria, Sarcoplasmic reticulum, Myofibrils).

Myofibrils

Contain contractile protein units called Sarcomeres, these contain:

1- Thin filaments (Actin).

2- Thick filaments (Myosin).

Regions of sarcomere:

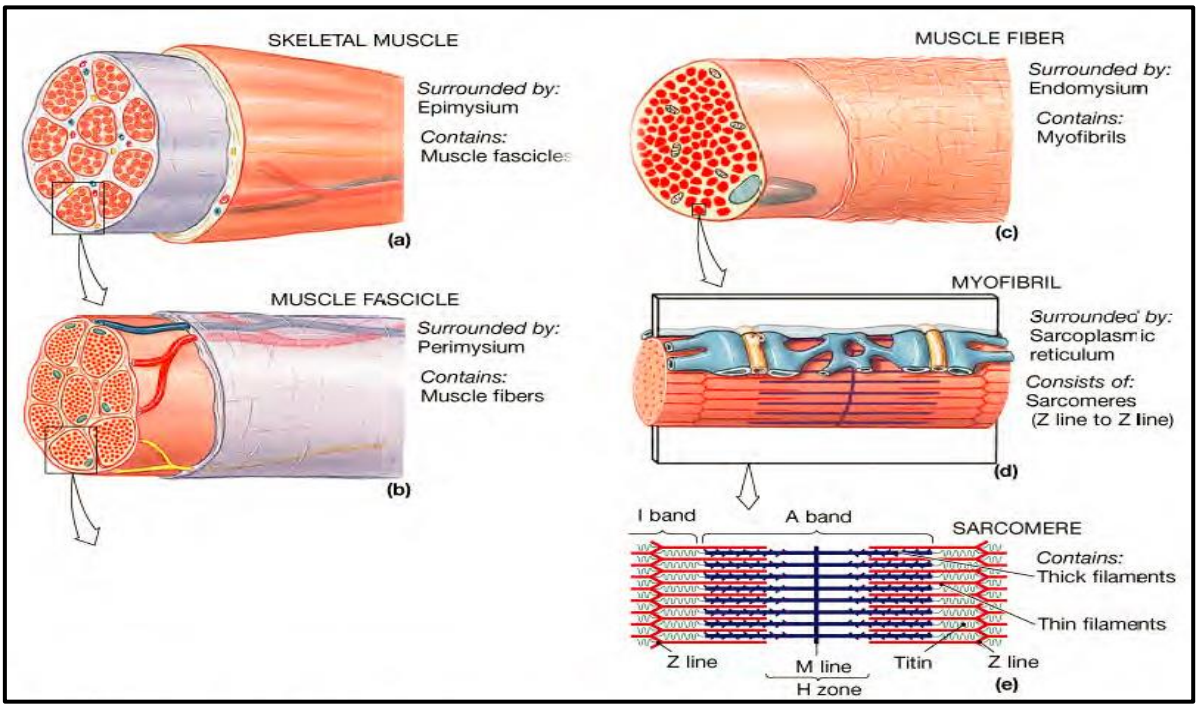
1- A- band = whole width of thick filaments, looks dark microscopically.

2- M- line = center of each thick filament, middle of A- band.

3- H- zone = light region either side of M- line, contains thick filaments only.

4- I- band = area that contains thin filaments.

5- Z- line = center of I band, Z- line mark ends of each sarcomere.



Skeletal Muscle Contractions (The Sliding Filament Theory (Huxley 1954)

Our muscles contract when the myosin heads binds to actin (**cross bridge formation**) causing it to slide overtop of itself, the length of the thin and the thick filaments have not changed, Then we must know the structure of this filaments

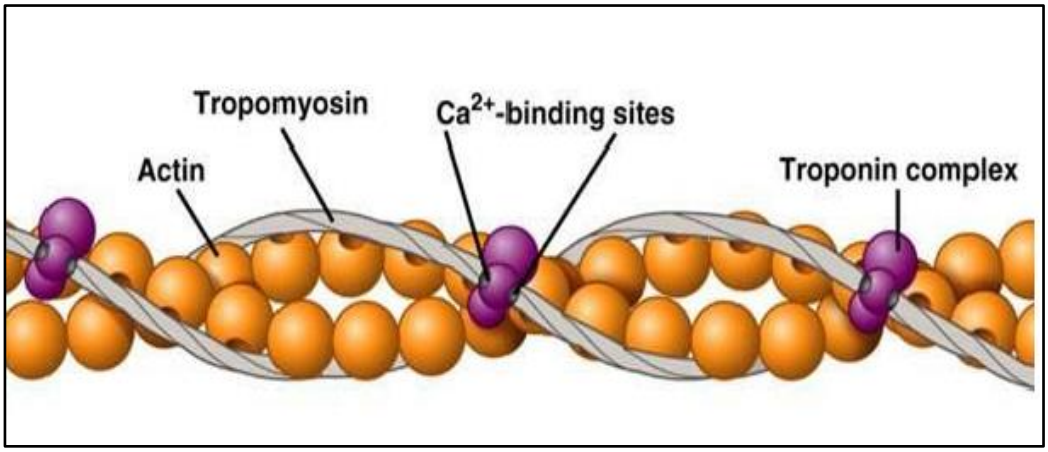
Actin filaments

Consist of Three types of Proteins**:**

a- Actin: It is globular protein, has an active site that can bind to myosin.

b- Tropomyosin: Strand like protein wrapped around actin that blocks the myosin binding sites on the actin.

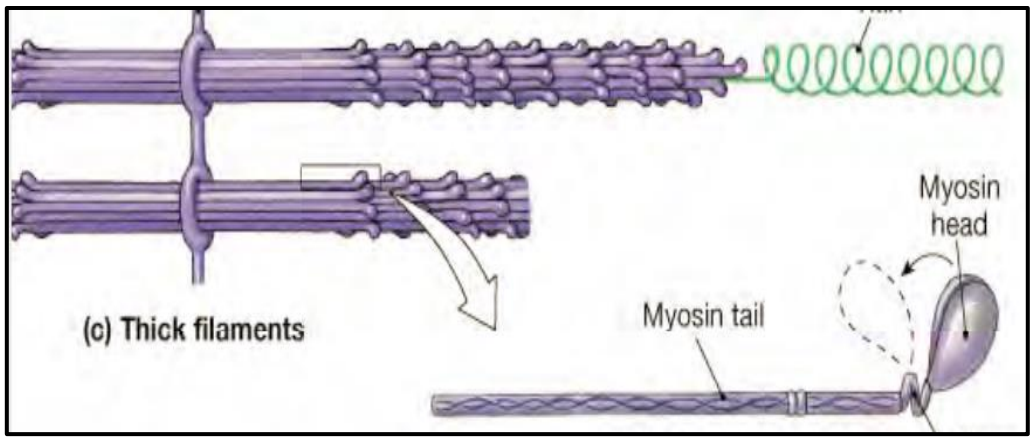
c- Troponin: Globular shaped molecules, which sit on top of tropomyosin and have calcium ion (Ca^{2+}) binding sites.



Myosin Filaments

Composed of bundled myosin molecules, each myosin molecule has two parts:

1. **Tail**: tails bundled together to make length of thick filament.
2. **Head**: will bind actin at active site on actin protein



Two problems:

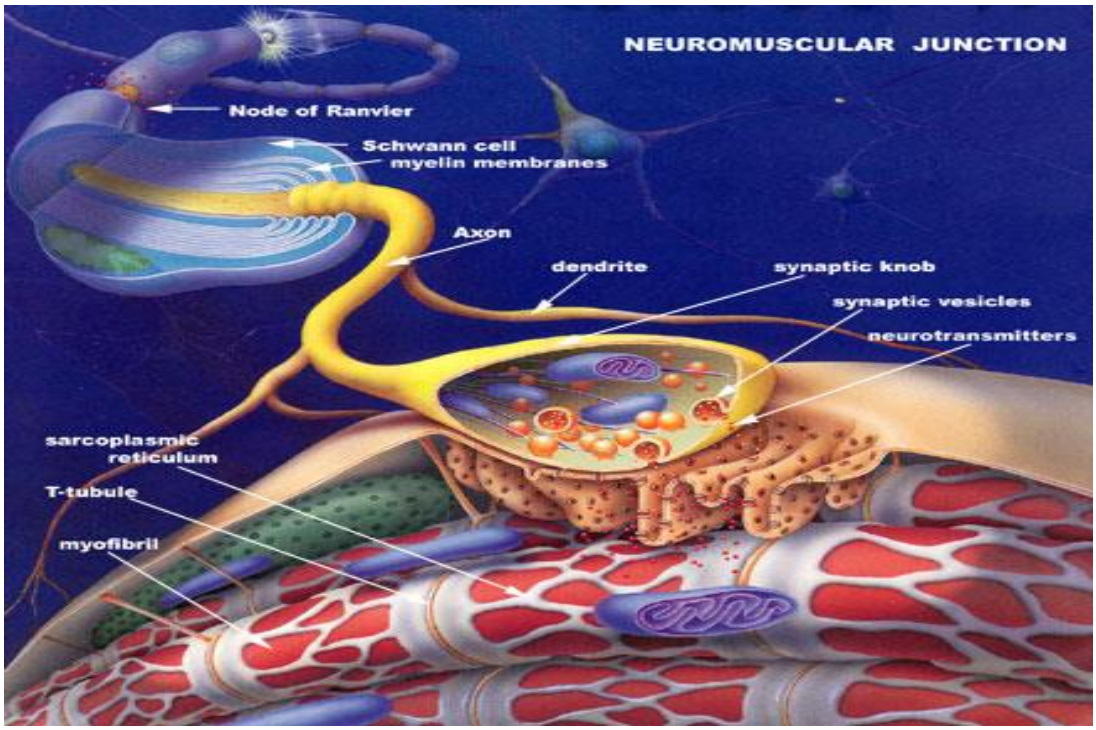
1- The **binding sites on actin are blocked** by tropomyosin.

2- Myosin needs **energy** to bind and move the actin.

The Sliding Filament Theory

- An action potential reaches the axon of the motor neuron.
- The action potential activates voltage gated calcium ion channels on the axon, and calcium rushes in.

- The calcium causes acetylcholine vesicles in the axon to fuse with the membrane, releasing the acetylcholine into the cleft between the axon and the motor end plate of the muscle fiber.
- The skeletal muscle fiber is excited by large nerve fibers.
- The acetylcholine diffuses and cause the sarcoplasmic reticulum to release calcium ions (Ca^{2+}).



- The calcium binds to the troponin present on the thin filaments of the myofibrils. The troponin then allosterically modulates the tropomyosin. Normally the tropomyosin physically obstructs binding sites for cross-bridge; once calcium binds to the troponin, the troponin forces the tropomyosin to move out of the way, unblocking the binding sites, each Ca^{2+} bind to troponin will exposed 7 sites on actin to combined with myosin.
- Contraction stage, myosin heads attach to actin and form cross bridges, ATP is broken down during this stage by ATPase enzyme from Myosin. Myosin binds at this point to the exposed binding sites and through the sliding filament mechanism the muscles contract, by sliding actin towered the central region of sarcomere without movement of A band.

- The calcium is actively (ATP is also broken down) pumped back into the sarcoplasmic reticulum after the action potential ends. When no longer present on the thin filament, the tropomyosin changes back to its previous state, so as to block the binding sites again by releasing from myosin, ATP is also broken down during this stage.
  - Decrease the concentration of Ca^{2+} out of sarcoplasmic reticulum finishing the combination between actin and myosin then case muscle relaxation.