Physiology

-Physiology is the study of the normal functioning of a living organism and its component parts, including all its chemical and physical processes.

-The goal of physiology is to explain the physical and chemical factors that are responsible for the origin, development, and progression of life. Each type of life, from the simple virus to the largest tree or the complicated human being, has its own functional characteristics.

In human physiology, we attempt to explain the specific characteristics and mechanisms of the human body that make it a living being.

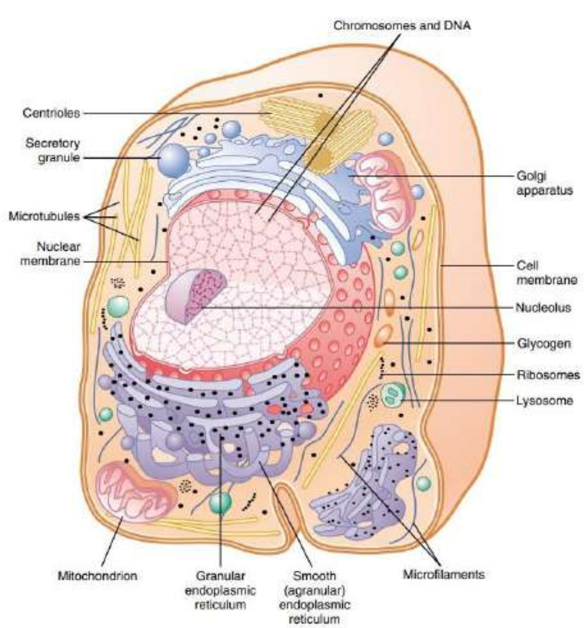
Cells as the Living Units of the Body

The basic living unit of the body is the cell. Each organ is an aggregate of many different cells held together by intercellular supporting structures. Each type of cell is specially adapted to perform one or a few particular functions. The entire body contains about 100 trillion cells of different types that perform different functions.

Component of the Cell

A typical cell, as seen by the light microscope, has two major parts: the nucleus and the cytoplasm.

The nucleus is separated from the cytoplasm by a nuclear membrane, and the cytoplasm is separated from the surrounding fluids by a cell membrane, also called the plasma membrane.



The different substances that make up the cell are collectively called protoplasm that is composed mainly of five basic substances:

1. Water: The principal fluid medium of the cell, which is present in most cells in a concentration of (70 to 85%). Many cellular chemicals are dissolved in the water; chemical reactions take place among these dissolved chemicals.

2. Ions: The most important ions in the cell are potassium, magnesium, phosphate, sulfate, bicarbonate, and smaller quantities of sodium, chloride, and calcium.

3. Proteins: After water, the most abundant substances in most cells are proteins, which normally constitute (10 to 20%) of the cell mass.

4. Lipids: Are several types of substances that are grouped together because of their common property of being soluble in fat solvents. Especially important lipids are phospholipids and cholesterol, which are used to form the cell membrane.

5. Carbohydrates: They play a major role in nutrition of the cell.

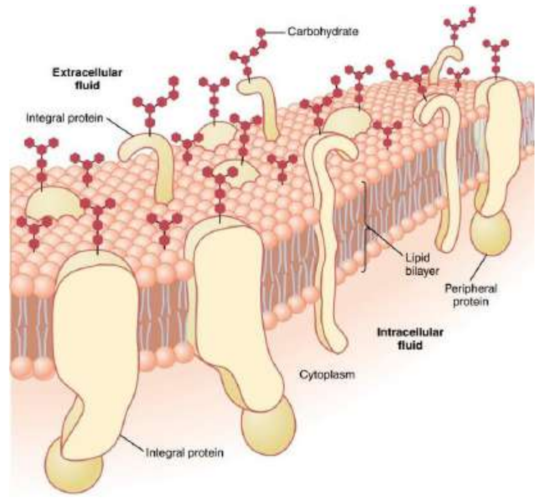
Cell membrane

-The cell membrane (also called the plasma membrane), is a thin elastic structure which envelops the cell. It is composed almost entirely of proteins and lipids.

-Its basic structure is a lipid bilayer, interspersed in this lipid membrane are large globular protein molecules.

-The lipid layer in the middle of the membrane is impermeable to the usual water-soluble substances, such as ions, glucose, and urea. Conversely, fat-soluble substances, such as oxygen, carbon dioxide, and alcohol, can penetrate this portion of the membrane with ease.

-There are two types of cell membrane proteins:



1- integral proteins that protrude all the way through the membrane

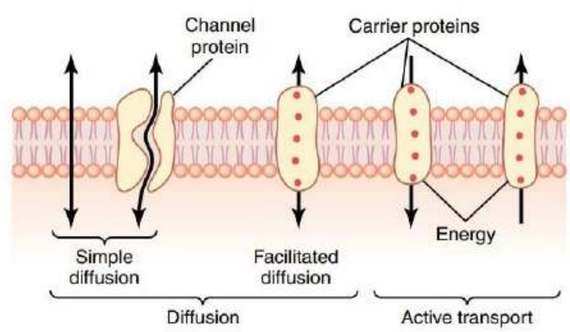
2- peripheral proteins that are attached only to one surface of the membrane and do not penetrate all the way through.

-Many of the integral proteins provide structural channels (or pores) through which water molecules and water-soluble substances, especially ions, can diffuse between the extracellular and intracellular fluids.

Cell Membrane Transport Mechanism

-Transport through the cell membrane, either directly through the lipid bilayer or through the proteins, occurs by one of two basic processes: diffusion or active transport.

1- Diffusion: is the movement of molecules from area of high concentration to the area of low concentration through the cell membrane. Diffusion is divided into two subtypes called simple diffusion and facilitated diffusion.



- Simple diffusion means that kinetic movement of molecules or ions occurs through a membrane opening without any interaction with carrier proteins in the membrane.

- **Facilitated diffusion** requires interaction of a carrier protein that aids passage of the molecules or ions through the membrane by binding chemically with them.

2- Active Transport: is the movement of molecules or ions against a concentration gradient through the cell membrane using energy.

Osmosis and Body fluids

-The most abundant substance that diffuses through the cell membrane is water. Enough water ordinarily diffuses in each direction through the cell membrane.

- Normally the amount that diffuses in the two directions is balanced so precisely that zero net movement of water occurs. Therefore, the volume of the cell remains constant.

- However, under certain conditions, a concentration difference for water can develop across a membrane, just as concentration differences for other substances can occur.

- When this happens, net movement of water does occur across the cell membrane, causing the cell either to swell or shrink, depending on the direction of the water movement.

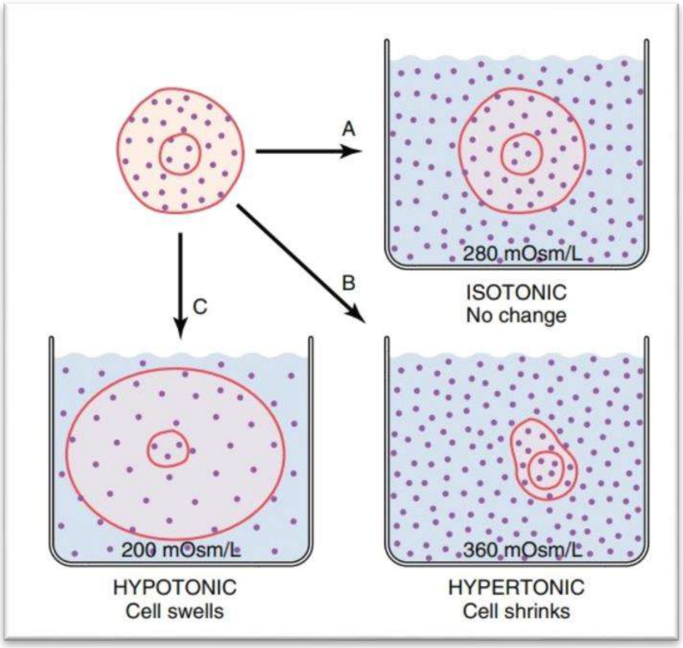
- **Osmosis:** is the process of net movement of water caused by a concentration difference of water through semipermeable membrane.

Isotonic, Hypotonic, and Hypertonic Fluids

- If a cell is placed in a solution having an equal osmolarity with the cell, the cells will not shrink or swell because the water concentration in the intracellular and extracellular fluids is equal and the solutes cannot enter or leave the cell. Such a solution is said to be **isotonic**.

- If a cell is placed into a **hypotonic** solution that has a lower concentration of solutes, water will diffuse into the cell, causing it to swell.

- If a cell is placed in a **hypertonic** solution having a higher concentration of solutes, water will flow out of the cell into the extracellular fluid causing the cell to shrink.



Fluid Intake and Output

- The relative constancy of the body fluids is remarkable because there is continuous exchange of fluid and solutes with the external environment as well as within the different compartments of the body.

- Water is added to the body by two major sources:

(1) It is ingested in the form of liquids or water in the food.

(2) It is synthesized in the body as a result of oxidation of carbohydrates.

Daily Loss of Body Water

1- Insensible Water Loss: there is a continuous loss of water by evaporation from the respiratory tract and diffusion through the skin, which together account for about 700ml/day of water loss under normal conditions.

2- Fluid Loss in Sweat: The amount of water lost by sweating is highly variable, depending on physical activity and environmental temperature. The volume of sweat normally is about 100ml/day, but in very hot weather or during heavy exercise water loss in sweat increased.

3- Water Loss in Feces: Only a small amount of water (100ml/day) normally is lost in the feces. This can increase to several liters a day in people with severe diarrhea.

4- Water Loss by the Kidneys: The remaining water loss from the body occurs in the urine excreted by the kidneys.

Body Fluid Compartments

- The total body fluid is distributed mainly between two compartments:

the extracellular fluid and the intracellular fluid, The extracellular fluid is divided into the interstitial fluid and the blood plasma.

- In the average 70-kilogram adult man, the total body water is about 60 percent of the body weight, or about 42 liters. This percentage can change, depending on age, gender, and degree of obesity. As a person grows older, the percentage of total body weight that is fluid gradually decreases.

- Women normally have more body fat than men, their total body water averages about 50 percent of the body weight. In premature and newborn babies, the total body water ranges from 70 to 75 percent of body weight.

Intracellular Fluid Compartment

- About 28 of the 42 liters of fluid in the body are inside the 100 trillion cells and are collectively called the intracellular fluid. Thus, the intracellular fluid constitutes about 40 percent of the total body weight in an “average” person.

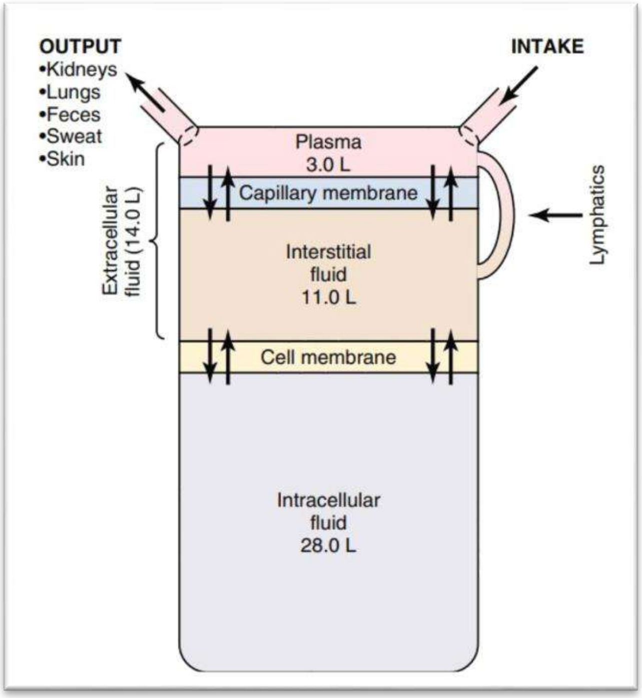
Extracellular Fluid Compartment

- All the fluids outside the cells are collectively called the extracellular fluid. Together these fluids account for about 20 percent of the body weight, or about 14 liters in a normal 70-kilogram man.

- The two largest compartments of the extracellular fluid are the interstitial fluid, which makes up more than three fourths (11 liters) of the extracellular fluid, and the plasma, which makes up almost one fourth of the extracellular fluid, or about 3 liters.

- The plasma is the noncellular part of the blood; it exchanges substances continuously with the interstitial fluid through the pores of the capillary membranes. These pores are highly permeable to almost all solutes in the extracellular fluid except the proteins.

- Therefore, the extracellular fluids are constantly mixing, so the plasma and interstitial fluids have about the same composition except for proteins, which have a higher concentration in the plasma.



Blood volume

- Blood contains both extracellular fluid (the fluid in plasma) and intracellular fluid (the fluid in the red blood cells).

-The average blood volume of adults is about 7 percent of body weight, or about 5 liters. About 60 percent of the blood is plasma and 40 percent is red blood cells, but these percentages can vary considerably in different people, depending on gender, weight, and other factors.

Ionic Composition of Plasma and Interstitial Fluid

- Because the plasma and interstitial fluid are separated only by highly permeable capillary membranes, their ionic composition is similar.

- The most important difference between these two compartments is the higher concentration of protein in the plasma; because the capillaries have a low permeability to the plasma proteins, only small amounts of proteins are leaked into the interstitial spaces in most tissues.

- Because of the Donnan effect, the concentration of positively charged ions (cations) is slightly greater (≈2 percent) in the plasma than in the interstitial fluid. The plasma proteins have a net negative charge and, therefore, tend to bind cations, such as sodium and potassium ions, thus holding extra amounts of these cations in the plasma along with the plasma proteins.

- Conversely, negatively charged ions (anions) tend to have a slightly higher concentration in the interstitial fluid compared with the plasma, because the negative charges of the plasma proteins repel the negatively charged anions.

Intracellular Fluid Constituents

- The intracellular fluid is separated from the extracellular fluid by a cell membrane that is highly permeable to water but not to most of the electrolytes in the body.

- In contrast to the extracellular fluid, the intracellular fluid contains only small quantities of sodium and chloride ions and almost no calcium ions.

- Instead, it contains large amounts of potassium and phosphate ions plus moderate quantities of magnesium and sulfate ions, all of which have low concentrations in the extracellular fluid. Also, cells contain large amounts of protein, almost four times as much as in the plasma.

Regulation of Fluid Exchange and Osmotic Equilibrium Between Intracellular and Extracellular Fluid

- The relative amounts of extracellular fluid distributed between the plasma and interstitial spaces are determined mainly by the balance of hydrostatic and colloid osmotic forces across the capillary membranes.

- The distribution of fluid between intracellular and extracellular compartments, in contrast, is determined mainly by the osmotic effect of the smaller solutes especially sodium, chloride, and other electrolytes acting across the cell membrane.

- The reason for this is that the cell membranes are highly permeable to water but relatively impermeable to even small ions such as sodium and chloride.

Blood

- Blood is the fluid that circulates in the cardiovascular system**,** it's a connective tissue composed of cellular elements suspended in an extensive fluid matrix called plasma.

- Plasma makes up one-fourth of the extracellular fluid, the internal environment that bathes cells and acts as a buffer between cells and the external environment.

- Blood is the circulating portion of the extracellular compartment, responsible for carrying material from one part of the body to another.

Plasma

- Plasma is the fluid matrix of the blood, within which cellular elements are suspended.

- Water is the main component of plasma, accounting for about 92% of its weight. Proteins account for another 7%. The remaining 1% is dissolved organic molecules (amino acids, glucose, lipids, and nitrogenous wastes), ions, trace elements and vitamins, and dissolved oxygen and carbon dioxide.

- Plasma is identical in composition to interstitial fluid except for the presence of plasma proteins.

- Albumins are the most prevalent type of protein in the plasma, making up about 60% of the total. Albumins and nine other proteins— including globulins, the clotting protein fibrinogen, and the iron-transporting protein transferrin—make up more than 90% of all plasma proteins.

- The presence of proteins in the plasma makes the osmotic pressure of the blood higher than that of the interstitial fluid. This osmotic gradient tends to pull water from the interstitial fluid into the capillaries and offset filtration out of the capillaries created by blood pressure.

- Plasma proteins participate in many functions, including blood clotting and defense against foreign invaders. In addition, they act as carriers for steroid hormones, cholesterol, drugs, and certain ions such as iron.

Cellular Elements

- Three main cellular elements are found in blood: red blood cells (RBCs), also called erythrocytes {erythros, red}; white blood cells (WBCs), also called leukocytes {leukos, white}; and platelets or thrombocytes {thrombo-, lump, clot}.
- White blood cells are the only fully functional cells in the circulation. Red blood cells have lost their nuclei by the time they enter the bloodstream, and platelets, which also lack a nucleus, are cell fragments that have split off a relatively large parent cell known as a megakaryocyte.

- Red blood cells play a key role in transporting oxygen from lungs to tissues, and carbon dioxide from tissues to lungs.

Red blood cells

- Erythrocytes, or red blood cells, are the most abundant cell type in the blood. A microliter of blood contains about 5 million red blood cells, compared with only 4000–11,000 leukocytes and 150,000– 450,000 platelets.

- Normal red blood cells, are biconcave discs having a mean diameter of about 7.8 micrometers. The shapes of red blood cells can change remarkably as the cells squeeze through capillaries. Actually, the red blood cell is a “bag” that can be deformed into almost any shape.

- The red blood cells have other functions besides transport of hemoglobin. For instance, they contain a large quantity of carbonic anhydrase, an enzyme that catalyzes the reversible reaction between carbon dioxide (CO_2) and water to form carbonic acid (H_2CO_3).

White blood cells

- White blood cells play a key role in the body's immune responses, defending the body against foreign invaders, such as parasites, bacteria, and viruses. Most white blood cells circulate through the body in the blood, but their work is usually carried out in the tissues rather than in the circulatory system.

- Blood contains five types of mature white blood cells: (1) lymphocytes, (2) monocytes, (3) neutrophils, (4) eosinophils, and (5) basophils.

- Monocytes that leave the circulation and enter the tissues develop into macrophages. Tissue basophils are called mast cells.

- The types of white blood cells may be grouped according to common morphological or functional characteristics.

- Neutrophils, monocytes, and macrophages are collectively known as phagocytes because they can engulf and ingest foreign particles such as bacteria (phagocytosis).

- Lymphocytes are sometimes called immunocytes because they are responsible for specific immune responses directed against invaders.

- Basophils, eosinophils, and neutrophils are called granulocytes because they contain cytoplasmic inclusions that give them a granular appearance.

Platelets

- Platelets are cell fragments produced in the bone marrow from huge cells called megakaryocytes.

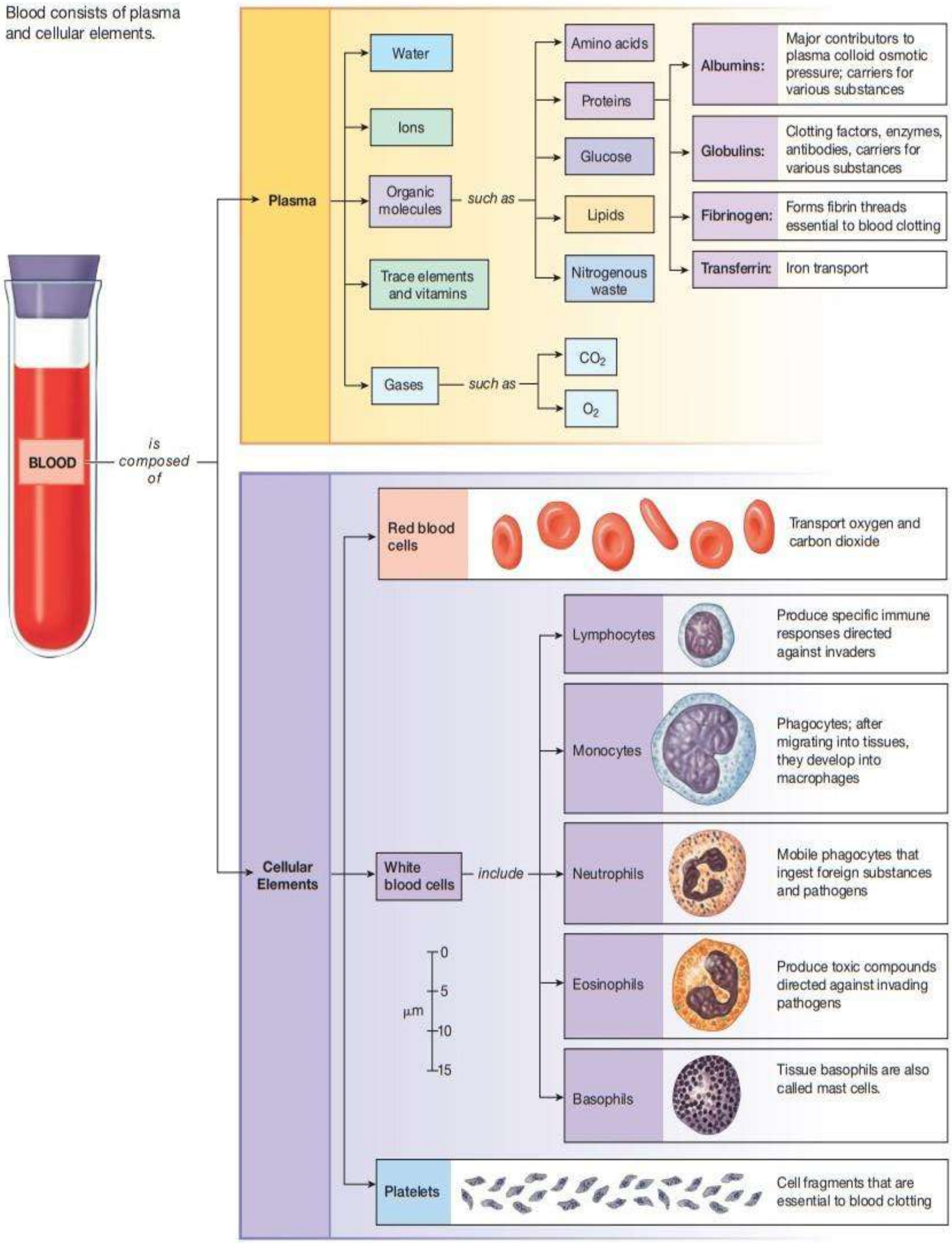
- Platelets are smaller than red blood cells, are colorless, and have no nucleus. Their cytoplasm contains mitochondria, smooth endoplasmic reticulum, and numerous membrane-bound vesicles called granules that are filled with a variety of cytokines and growth factors.

- Platelets are always present in the blood and their typical life span is about 10 days. They are best known for their role in helping stop blood loss, but in recent years, scientists have shown that platelets also act as immune cells and mediators of the inflammatory response.

Serum

- Within a few minutes after a clot is formed, it begins to contract and usually expresses most of the fluid from the clot within 20 to 60 minutes. The fluid expressed is called serum because all its fibrinogen and most of the other clotting factors have been removed; in this way, serum differs from plasma.

Serum cannot clot because it lacks these factors.


Blood consists of plasma and cellular elements.
BLOOD
is composed of
Plasma
Water
Ions
Organic molecules
such as
Trace elements and vitamins
Gases
such as
Amino acids
Proteins
Glucose
Lipids
Nitrogenous waste
CO_2
O_2
Albumins:
Major contributors to plasma colloid osmotic pressure; carriers for various substances
Globulins:
Clotting factors, enzymes, antibodies, carriers for various substances
Fibrinogen:
Forms fibrin threads essential to blood clotting
Transferrin:
Iron transport
Cellular Elements
Red blood cells
Transport oxygen and carbon dioxide
White blood cells
include
Lymphocytes
Produce specific immune responses directed against invaders
Monocytes
Phagocytes; after migrating into tissues, they develop into macrophages
Neutrophils
Mobile phagocytes that ingest foreign substances and pathogens
Eosinophils
Produce toxic compounds directed against invading pathogens
Basophils
Tissue basophils are also called mast cells.
μm
0
5
10
15
Platelets
Cell fragments that are essential to blood clotting

Blood cell production

- All different blood cells descendants of a single precursor cell type known as the *pluripotent hematopoietic stem cell.* This cell type is found primarily in **bone marrow**, a soft tissue that fills the hollow center of bones.

- Pluripotent stem cells have the remarkable ability to develop into many different cell types.

- Hematopoiesis: the synthesis of blood cells, begins early in embryonic development and continues throughout a person's life.

- Hematopoiesis continues in the marrow of all the bones of the skeleton until age five. As the child continues to age, the active regions of marrow decrease. In adults, the only areas producing blood cells are the pelvis, spine, ribs, cranium, and proximal ends of long bones.

- Active bone marrow is red because it contains hemoglobin, the oxygen-binding protein of red blood cells. Inactive marrow is yellow because of an abundance of adipocytes (fat cells).

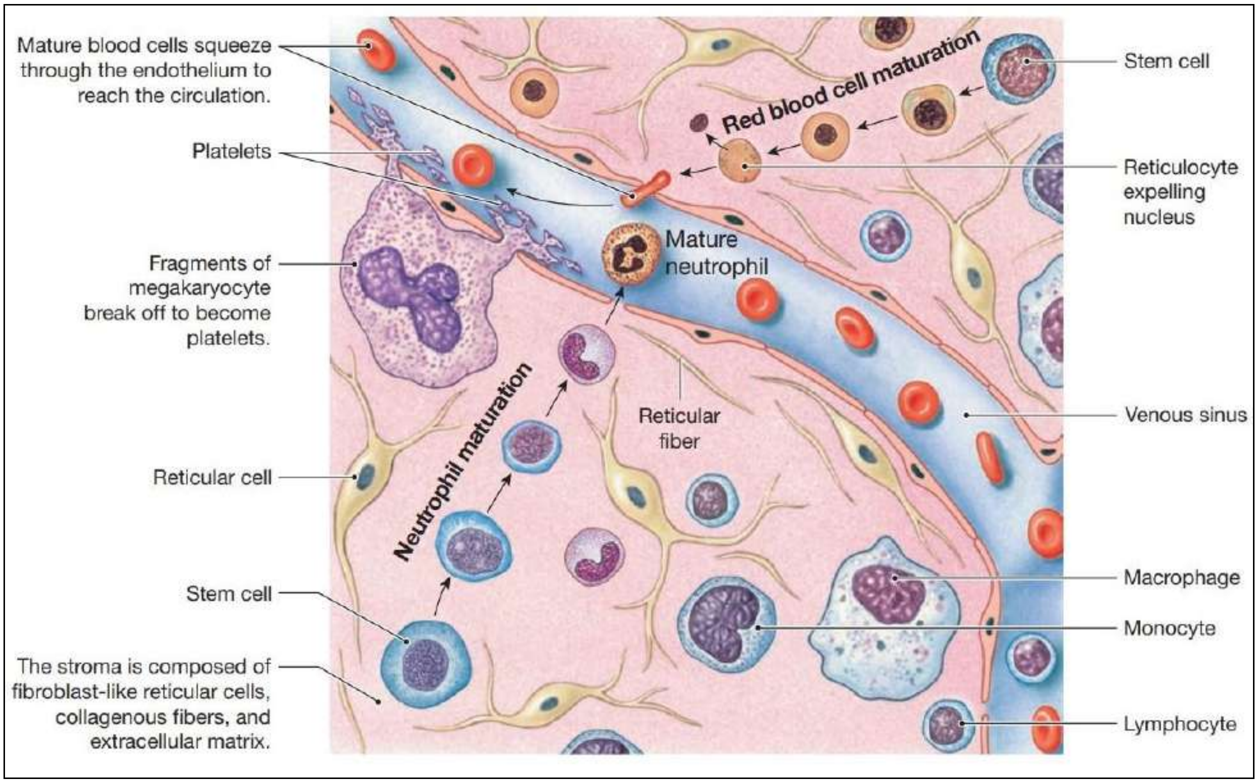
- In the regions of marrow that are actively producing blood cells, about 25% of the developing cells are red blood cells, while 75% are destined to become white blood cells.

- The life span of white blood cells is considerably shorter than that of red blood cells, and so WBCs must be replaced more frequently.

Erythropoietin Regulates RBC Production

-Red blood cell production (erythropoiesis) is controlled by the glycoprotein erythropoietin (EPO), assisted by several cytokines. Erythropoietin is made primarily in the kidneys of adults.

- The stimulus for EPO synthesis and release is hypoxia, low oxygen levels in the tissues. Hypoxia stimulates EPO synthesis. This pathway helps the body maintain homeostasis. By stimulating the synthesis of red blood cells, EPO puts more hemoglobin into the circulation to carry oxygen.



Mature RBCs Lack a Nucleus

- In the bone marrow, committed progenitor cells differentiate through several stages into large, nucleated erythroblasts.

- As erythroblasts mature, the nucleus condenses and the cell shrinks in diameter. In the last stage before maturation, the nucleus is pinched off and phagocytized by bone marrow macrophages.

- At the same time, other membranous organelles (such as mitochondria) break down and disappear. The final immature cell form, called a reticulocyte, leaves the marrow and enters the circulation, where it matures into an erythrocyte in about 24 hours.

Hemoglobin Synthesis

- **Hemoglobin**, the main component of red blood cells, is best known for its role in oxygen transport. Hemoglobin (Hb) is a large, complex protein with four globular protein chains, each of which is wrapped around an iron-containing heme group.

- There are several isoforms of globin proteins in hemoglobin. The most common isoforms are designated *alpha (α), beta (β), gamma (γ), and delta (δ),* depending on the structure of the chain. Most adult hemoglobin (designated HbA) has two alpha chains and two beta chains.

- About 70% of the iron in the body is found in the heme groups of hemoglobin. Consequently, hemoglobin synthesis requires an adequate supply of iron in the diet.

- Iron is absorbed in the small intestine by active transport. A carrier protein called **transferrin** binds iron and transports it in the blood. The bone marrow takes up iron and uses it to make the heme group of hemoglobin for developing red blood cells.

- Excess ingested iron is stored, mostly in the liver. Iron stores are found inside a spherical protein called molecule **ferritin**. The core of the sphere is an iron-containing mineral that can be converted to soluble iron and released when needed for hemoglobin synthesis.

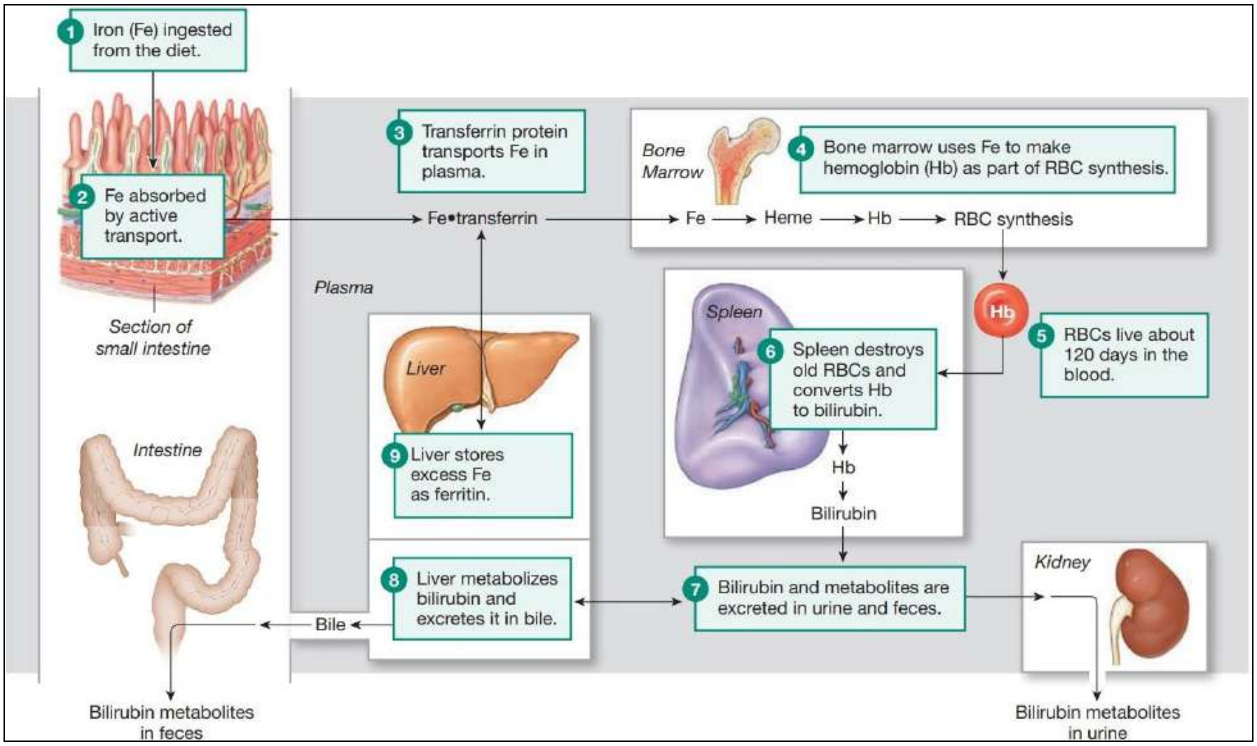
RBCs Live about Four Months

- Red blood cells in the circulation live for about 120. Old red blood cells may rupture as they try to squeeze through narrow capillaries, or they may be engulfed by scavenging macrophages as they pass through the spleen.

- Many components of the destroyed cells are recycled. Amino acids from the globin chains of hemoglobin are incorporated into new proteins, and some iron from the heme groups is reused to make new heme groups.

- The spleen and liver convert remnants of the heme groups to a colored pigment called **bilirubin**. Bilirubin is carried by plasma albumin to the liver, where it is metabolized and incorporated into a secretion called bile.

- In some circumstances, bilirubin levels in the blood become elevated (hyperbilirubinemia). This condition, known as **jaundice**, causes the skin and whites of the eyes to take on a yellow cast.



Hemostasis and Coagulation

- **Hemostasis** is the process of keeping blood within a damaged blood vessel. Hemostasis has three major steps: 1 vasoconstriction, 2 blockage by a platelet plug, and 3 coagulation.

- The first step is immediate constriction of damaged vessels to decrease blood flow and pressure within the vessel.

- The second step is the mechanical blockage of the hole by a platelet plug, when platelets stick to exposed collagen in the damaged area.

- The third step is the formation of a fibrin protein mesh that stabilizes the platelet plug to form a clot. Fibrin is the end product of a series of reactions known as the coagulation cascade.

The Heart

The heart is a muscular organ, about the size of a fist. It lies in the center of the thoracic cavity. Within the thoracic cavity, the heart lies on the ventral side, between the two lungs, with its apex resting on the diaphragm.

The heart is encased in a tough membranous sac, the pericardium. A thin layer of clear pericardial fluid inside the pericardium lubricates the external surface of the heart as it beats within the sac.

The heart itself is composed mostly of cardiac muscle, or myocardium covered by thin outer and inner layers of epithelium and connective tissue.

Seen from the outside, the bulk of the heart is the thick muscular walls of the ventricles, the two lower chambers. The thinner walled atria lie above the ventricles.

The major blood vessels all emerge from the base of the heart. The aorta and pulmonary trunk (artery) direct blood from the heart to the tissues and lungs, respectively. The venae cavae and pulmonary veins return blood to the heart.

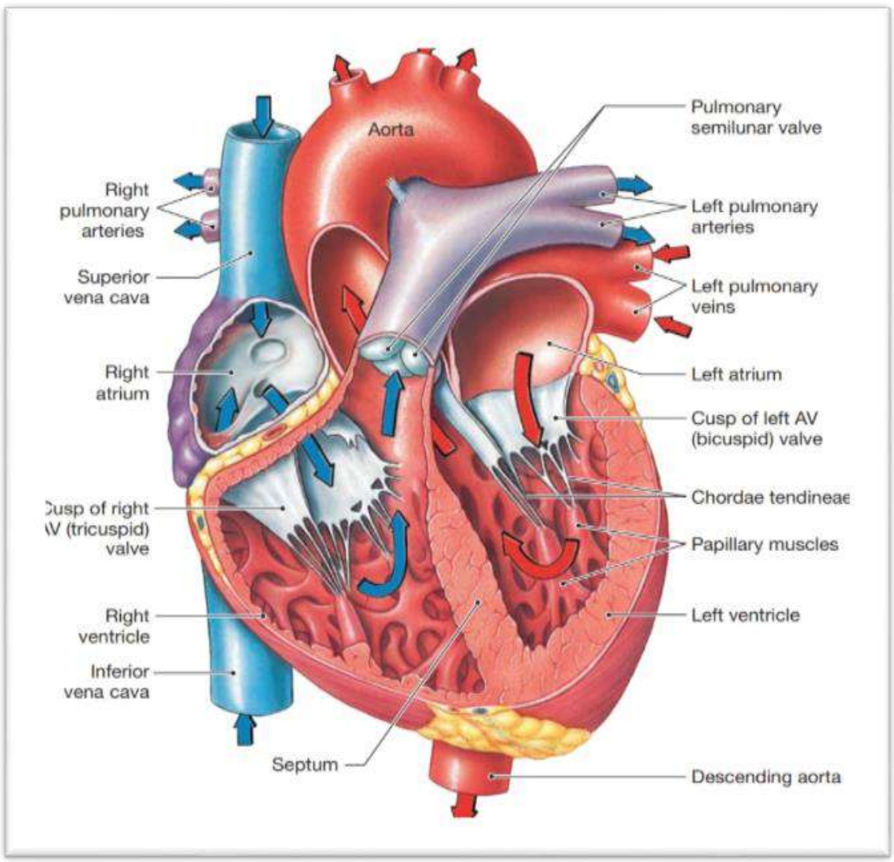
The left and right sides of the heart are separated by a septum, so that blood on one side does not mix with blood on the other side.

The two sides contract in a coordinated fashion. First, the atria contract together, then the ventricles contract together. Blood flows from veins into the atria and from there through one-way valves into the ventricles, the pumping chambers. Blood leaves the heart via the pulmonary trunk from the right ventricle and via the aorta from the left ventricle. A second set of valves guards the exits of the ventricles so that blood cannot flow back into the heart once it has been ejected.

The Heart Valves

Two sets of heart valves ensure the one-way flow: one set (the atrioventricular valves) between the atria and ventricles, and the second set (the semilunar valves) between the ventricles and the arteries. The two sets of valves are very different in structure, they serve the same function: preventing the backward flow of blood.

The two AV valves are not identical. The valve that separates the right atrium and right ventricle has three flaps and is called the tricuspid valve. The valve between the left atrium and left ventricle has only two flaps and is called the bicuspid valve.



The semilunar valves separate the ventricles from the major arteries. The aortic valve is between the left ventricle and the aorta, and the pulmonary valve lies between the right ventricle and the pulmonary trunk.

The Coronary Circulation

The heart has its own special blood supply known as the coronary circulation. The major coronary arteries run across the surface of the heart, branching into smaller and smaller arteries until finally the arterioles disappear into the heart muscle itself. In general, the major coronary veins run in parallel with the coronary arteries.

The two primary coronary arteries originate at the start of the aorta, just superior to the semilunar valve leaflets of the aortic valve.

The Heart as a Pump

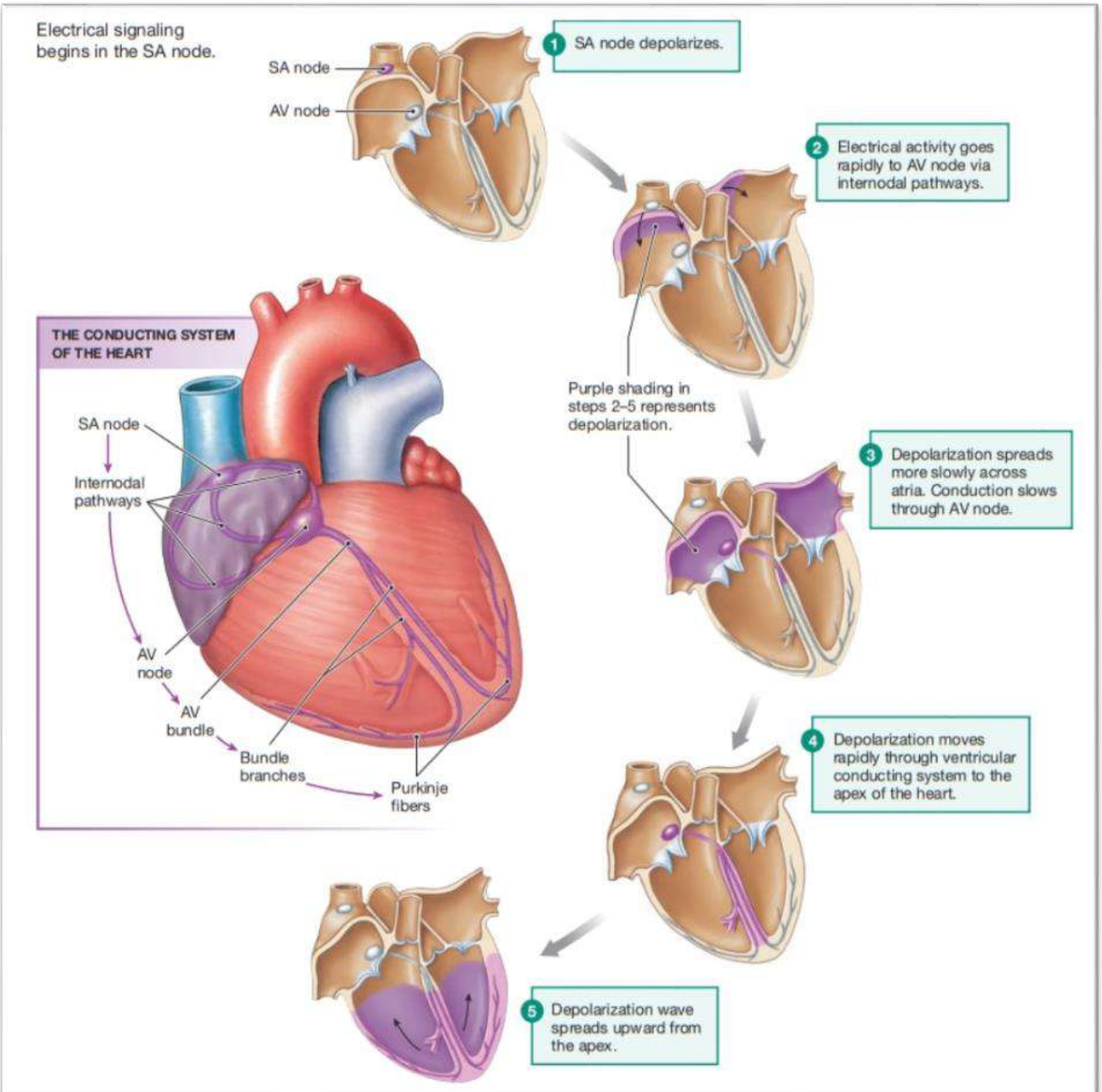
The signal for myocardial contraction comes not from the nervous system but from specialized myocardial cells known as autorhythmic cells. The autorhythmic cells are also called pacemakers because they set the rate of the heartbeat.

Electrical communication in the heart begins with an action potential in an autorhythmic cell. The depolarization spreads rapidly to adjacent cells. The depolarization wave is followed by a wave of contraction that passes across the atria, then moves into the ventricles.

The depolarization begins in the sinoatrial node (SA node), autorhythmic cells in the upper wall of right atrium that serve as the main pacemaker of the heart. The depolarization wave then spreads rapidly through autorhythmic fibers. A branched internodal pathway connects the SA node to the atrioventricular node (AV node), a group of autorhythmic cells near the floor of the right atrium.

From the AV node, the depolarization moves into the ventricles. Purkinje fibers, specialized conducting cells of the ventricles, transmit electrical signals very rapidly down the atrioventricular bundle (AV bundle), also called the bundle of His ("hiss"), in the ventricular septum. A short way down the septum, the AV bundle fibers divide into left and right bundle branches. The bundle branch fibers continue downward to the apex of the heart, where they divide into smaller Purkinje fibers that spread outward among the contractile cells.

A second function of the AV node is to slow down the transmission of action potentials slightly. This delay allows the atria to complete their contraction before ventricular contraction begins.



The Electrocardiogram ECG

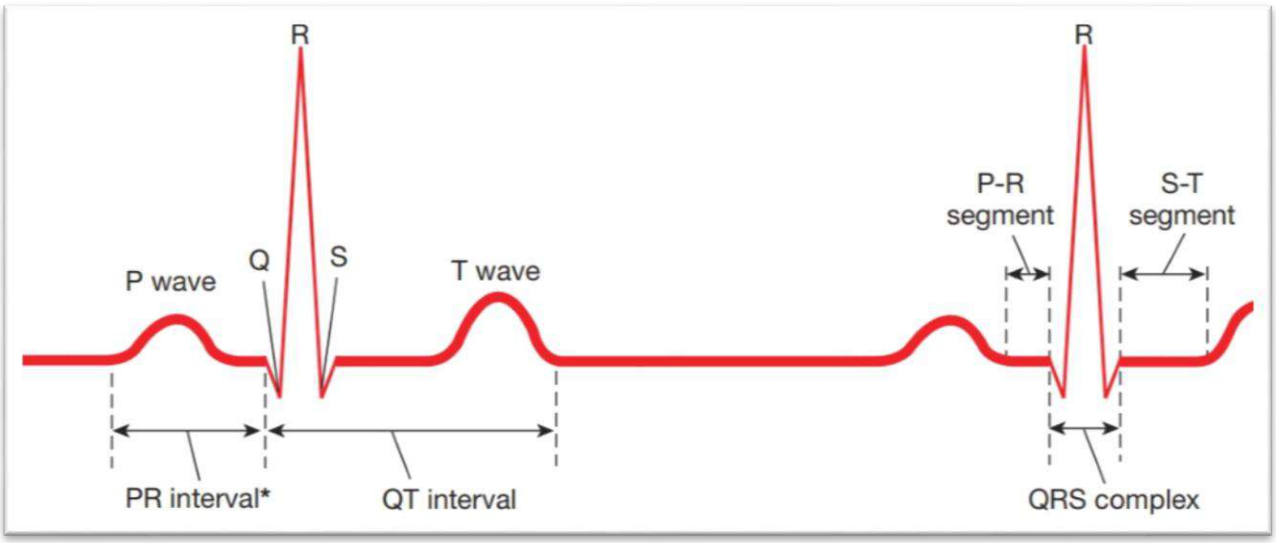
At the end of the nineteenth century, physiologists discovered that they could place electrodes on the skin's surface and record the electrical activity of the heart. It is possible to use surface electrodes to record internal electrical activity because salt solutions, such as our NaCl-based extracellular fluid, are good conductors of electricity.

Action potentials conducted through the heart during the cardiac cycle produce electric currents that can be measured at the surface of the body. Electrodes placed on the surface of the body and attached to a recording device can detect the small electric changes resulting from the action potentials in all of the cardiac muscle cells. The record of these electrical events within the heart is an electrocardiogram (ECG).

The normal ECG consists of tracing waves and the intervals between them have time duration:

- The P wave results from depolarization of the atrium and precedes the onset of atrial contraction. its duration $<$80 ms.
- The QRS complex results from depolarization of the ventricles and precedes ventricular contraction. its duration 80-100 ms.
- The T wave represents repolarization of the ventricles and precedes ventricular relaxation. its duration 160 ms. Atrial contraction occurs during the P-Q interval and the ventricles contract and relax during the Q-T interval.

The ECG is an extremely important diagnostic tool. Any deviation from the normal tracing or intervals is potentially pathological and therefore of clinical significance. Analysis of an ECG can be used to identify abnormal heart rates or rhythms, abnormal conduction pathways, hypertrophy or atrophy of portions of the heart and the approximate location of damaged cardiac muscle.



- Heart rate is normally timed either from the beginning of one P wave to the beginning of the next P wave or from the peak of one R wave to the peak of the next R wave.

- A normal resting heart rate is 60–100 beats per minute. A faster-than-normal rate is known as tachycardia, and a slower-than-normal rate is called bradycardia.

- An irregular rhythm, or arrhythmia, can result from a benign extra beat or from more serious conditions such as atrial fibrillation, in which the SA node has lost control of the pacemaking.

The Heart Contracts and Relaxes during the cardiac cycle

Each cardiac cycle has two phases: diastole, the time during which cardiac muscle relaxes, and systole, the time during which the muscle contracts. Because the atria and ventricles do not contract and relax at the same time.

1) **Late diastole**: both sets of chambers are relaxed and ventricles fill passively.
2) **Atrial systole**: atrial contraction forces a small amount of additional blood into ventricles.
3) **Isovolumic ventricular contraction:** first phase of ventricular contraction pushes AV valves closed but does not create enough pressure to open semilunar valves.
4) **Ventricular ejection**: as ventricular pressure rises and exceeds pressure in the arteries, the semilunar valves open and blood is ejected.
5) **Isovolumic ventricular relaxation:** as ventricles relax, pressure in ventricles falls. Blood flows back into cusps of semilunar valves and snaps them closed.

Blood pressure

Ventricular contraction is the force that creates blood flow through the cardiovascular system. As blood under pressure is ejected from the left ventricle, the aorta and arteries expand to accommodate it.

When the ventricle relaxes and the aortic valve closes, the elastic arterial walls recoil, propelling the blood forward into smaller arteries and arterioles. By sustaining the driving pressure for blood flow during ventricular relaxation, the arteries keep blood flowing continuously through the blood vessels.

Blood pressure is highest in the arteries and decreases continuously as blood flows through the circulatory system. The decrease in pressure occurs because energy is lost as a result of the resistance to flow offered by the vessels.

In the systemic circulation, the highest pressure occurs in the aorta and results from pressure created by the left ventricle. Aortic pressure reaches an average high of 120 mm Hg during ventricular systole (systolic pressure), then falls steadily to a low of 80 mm Hg during ventricular diastole (diastolic pressure). By the time blood reaches the veins, pressure has decreased because of friction, and a pressure wave no longer exists.

Changes in Blood Volume Affect Blood Pressure

The volume of the blood in the circulation is usually relatively constant, changes in blood volume can affect arterial blood pressure.

Small increases in blood volume occur throughout the day due to ingestion of food and liquids. Adjustments for increased blood volume are primarily the responsibility of the kidneys. If blood volume increases, the kidneys restore normal volume by excreting excess water in the urine.

Compensation for decreased blood volume is more difficult. If blood volume decreases, the kidneys cannot restore the lost fluid. The kidneys can only conserve blood volume and thereby prevent further decreases in blood pressure.

Factors that influence mean arterial pressure:

1) blood volume
2) effectiveness of the heart as a pump
3) resistance of the system to blood flow
4) relative distribution of blood between arterial and venous blood vessels

The Lymphatic System

The lymphatic system includes lymph, lymphocytes, lymphatic vessels, lymph nodes, tonsils, the spleen and the thymus gland. The lymphatic system is part of the body's defense system against microorganisms and other harmful substances. In addition, it helps to maintain fluid balance in tissues, through returning accessory amount of plasma from interstitial fluid to the blood vessels, and to absorb fats from the digestive tract.

The Lymph

Lymph is the fluid that circulates throughout the lymphatic system. It is similar to blood plasma except that it doesn't contain red blood cells. The lymph is formed when the interstitial fluid (the fluid which lies in the intervening spaces of all body tissues) is collected through lymph capillaries, then transported through larger lymphatic vessels to lymph nodes, ultimately it mixes back with the blood. Lymph returns proteins and excess interstitial fluid to the blood stream. Lymph may pick up bacteria and bring them to lymph nodes to destroyed. Lymph also transports fats from the digestive system to the blood.

The Lymphocytes

A lymphocyte is one of the subtypes of white blood cell, more lymphocytes include T cells and B cells. They are the main type of cell found in lymph, therefore it named "lymphocyte". The lymphocytes originate from red bone marrow and are carried by the blood to lymphatic organs. When the body is exposed to microorganisms or foreign substances the lymphocytes divide and increase in number. The increased number of lymphocytes is part of the immune system response that causes the destruction of microorganisms and foreign substances. Bone marrow is responsible for both the production and maturation of

B cells, and creation of T cells. From the bone marrow, B cells immediately travel to lymphoid organs. T cells, travel from the bone marrow to the thymus, where they develop and matured.

Lymphatic Vessels

Fluid moves from blood into tissue spaces and some of the fluid remove from tissues by lymphatic system, where enters lymphatic capillaries to become lymph. The removal of fluid begins in lymphatic capillaries, which are tiny closed-ended vessels, mainly responsible for the absorption of interstitial fluid from the tissues. The lymphatic capillaries empty lymph into lymphatic vessels which converge into larger ducts that return the lymph to the blood.

Three factors assist in the transport of lymph through the lymphatic vessels:

1. contraction of surrounding skeletal muscles during activity.
2. contraction of smooth muscles in the lymphatic vessel wall.
3. pressure changes in the thorax during respiration.

The lymphatic vessels converge and eventually empty into the blood at two location in the body. Lymph vessels from the upper right limb and the right half of the head, neck and chest form the right lymphatic duct, which empties into the right subclavian vein. Lymphatic vessels from the rest of the body enter the thoracic duct, which empties into the left subclavian vein.

Lymphatic Organs

Lymphatic organs include the tonsils, lymph nodes, the spleen and the thymus gland. Lymphatic tissue, which consist of many lymphocytes and other cells, is found within lymphatic organs.

Tonsils

There are three groups of tonsils. The palatine tonsils usually are referred to as the "tonsils" and they are located on each side of the posterior opening of the oral cavity. The pharyngeal tonsils are located near the internal opening of the nasal cavity. The lingual tonsils are on the posterior face of the tongue. The tonsils form a protective ring of lymphatic tissue around the opening between the nasal and oral cavities and the pharynx. They provide protection against pathogens and other potentially harmful material entering from the nose and mouth.

Lymph Nodes

Lymph nodes are rounded structures, varying in size. Lymph nodes are distributed along the various lymphatic vessels. Although lymph nodes are found throughout the body, there are three superficial aggregation of lymph nodes on each side of the body: inguinal nodes in the groin, axillary nodes in axilla and cervical nodes in the neck. Lymph nodes are divided into compartments contain lymphatic tissue and lymph sinuses. The lymphatic tissue consist of lymphocytes and other cells that can form dense aggregation of tissue called lymph nodules. Lymph sinuses are spaces between lymphatic tissue which contain macrophages on a network of fibers. Lymph enters the lymph nodes through afferent vessels, passes through the lymphatic tissue and sinuses and exits through efferent vessels. As lymph moves through the lymph nodes two functions are performed:

1. Activation of the immune system. Microorganisms or other foreign substances in the lymph can stimulate lymphocytes in the lymphatic tissue to start dividing.

2. The removal microorganisms and foreign substances from the lymph by macrophages.

Spleen

The spleen is located in the left, superior corner of the abdominal cavity. The spleen filters blood instead of lymph and contains two specialized types of lymphoid tissue. White pulp surrounds the arteries within the spleen and red pulp is associated with the veins. 1 Lymphocytes in the white pulp can be stimulated in the same manner as in lymph nodes. Before blood leaves the spleen through veins, it passes through the red pulp. Macrophages in the red pulp remove foreign substances and worn out red blood cells through phagocytosis. The main functions of the spleen are: to produce immune response against blood-borne antigens, to remove particulate matter and aged blood cells, mainly erythrocytes, to produce blood cells during fetal life. The spleen also functions as a blood reservoir, holding a small volume of blood, in emergency situation such as hemorrhage, provide a small amount of blood to the circulation.

Thymus

The thymus is a bilobed gland. It's located in the superior mediastinum, (the partition dividing thoracic cavity into left and right parts). The thymus continues to grow until puberty. After puberty, the thymus decreases in size and in adults the thymus may be so small that it is difficult to find during dissection. The thymus functions as a site for the maturation of (T cells) lymphocytes. After thymic lymphocytes have matured, they enter the blood and travel to other lymphatic tissues, where they help to protect against microorganisms and other foreign substances.

The Respiratory system

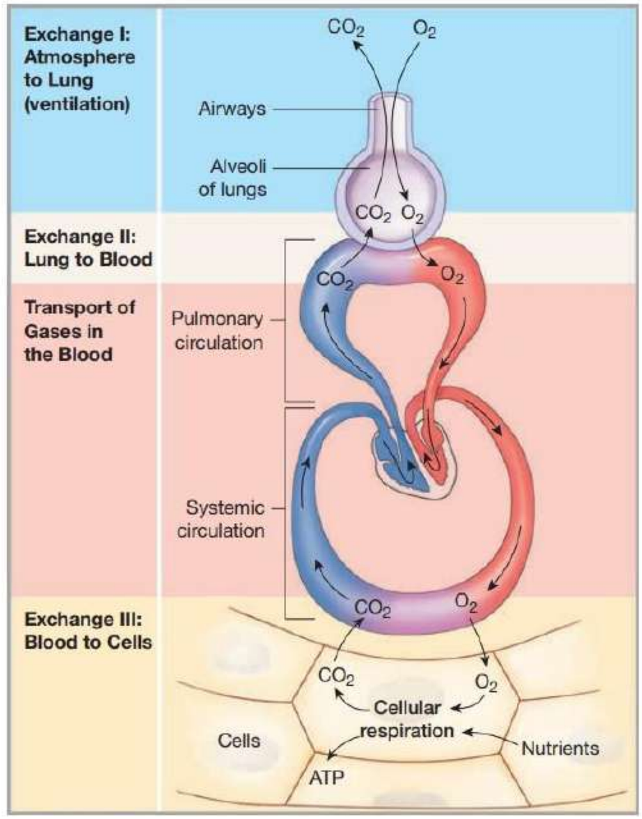
Respiration is the movement of gases between the environment and the body's cells. External respiration can be subdivided into four integrated processes:

1. The exchange of air between the atmosphere and the lungs.

2. The exchange of O2 and CO2 between the lungs and the blood.

3. The transport of O2 and CO2 by the blood.

4. The exchange of gases between blood and the cells.



The respiratory system consists of structures involved in ventilation and gas exchange:

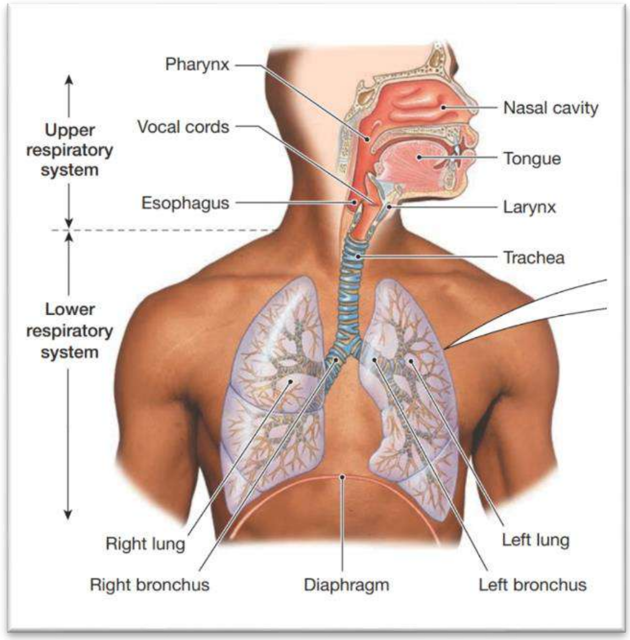
1. The conducting system of passages, or airways.

2. The alveoli, a series of interconnected sacs and their associated pulmonary capillaries. These structures form the exchange surface, where oxygen moves from inhaled air to the blood, and carbon dioxide moves from the blood to air that is about to be exhaled.

3. The bones and muscles of the thorax and abdomen that assist in ventilation.

The respiratory system can be divided into two parts. **The upper respiratory tract** consists of the mouth, nasal cavity, pharynx, and larynx. **The lower respiratory tract** consists of the trachea, two primary bronchi, their branches, and the lungs.

The lungs



The lungs consist of light, spongy tissue. These irregular cone-shaped organs fill the thoracic cavity, with their bases resting on the diaphragm. The bronchi connect the lungs to the main airway, the trachea. Each lung is surrounded by a double-walled pleural sac whose membranes line the inside of the thorax and cover the outer surface of the lungs. Each pleural membrane, contains several layers of elastic connective tissue. The opposing layers of pleural membrane contain a thin film of pleural fluid in between.

Pleural fluid has two purposes. First, it creates a moist surface so that the opposing membranes can slide across one another as the lungs move within the thorax. Second, it holds the lungs tight against the thoracic wall.

Airways

Air enters the upper respiratory tract through the mouth and nose and passes into the pharynx, a common passageway for food, liquids, and air. From the pharynx, air flows through the larynx into the trachea, or windpipe. The larynx contains the vocal cords, connective tissue bands that vibrate and tighten to create sound when air moves past them.

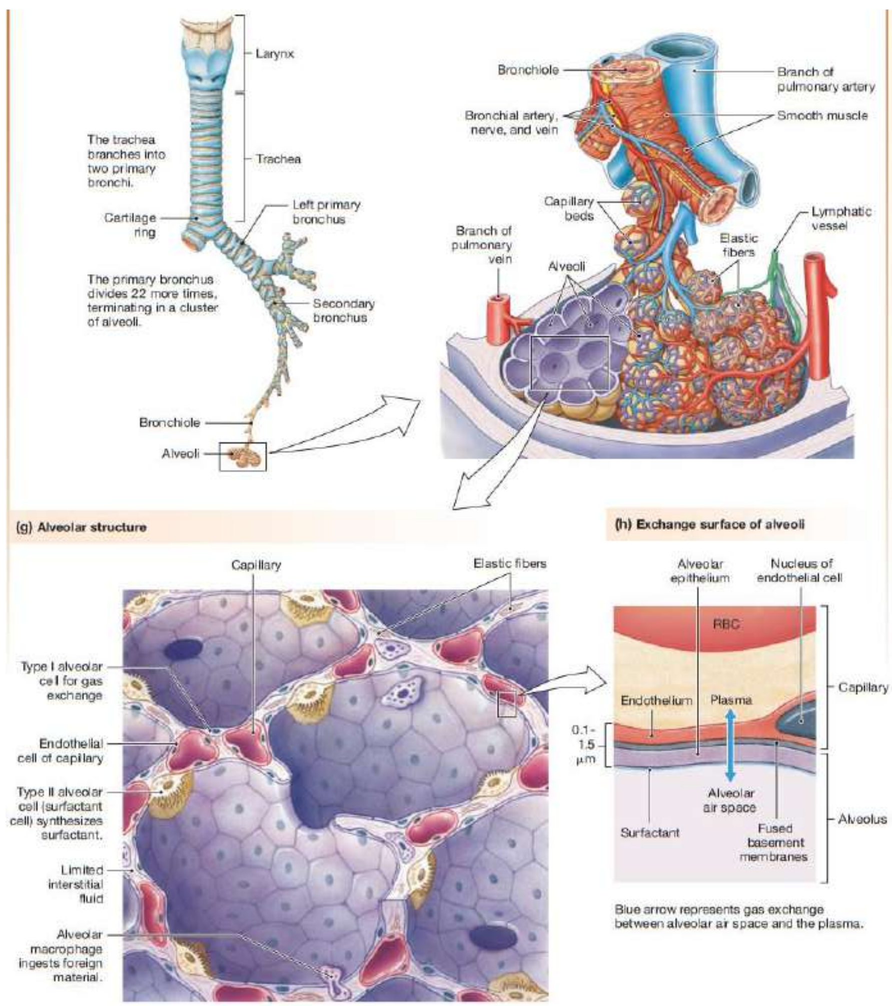
The trachea is a semiflexible tube held open by 15 to 20 C-shaped cartilage rings. It extends down into the thorax, where it branches into a pair of primary bronchi, one bronchus to each lung. Within the lungs, the bronchi branch repeatedly into progressively smaller bronchi.

Within the lungs, the smallest bronchi branch to become bronchioles, small passageways. The bronchioles continue branching until the respiratory bronchioles form a transition between the airways and the exchange epithelium of the lung.

Inhaled air is warmed by the body's heat and moistened by water evaporating from the mucosal lining of the airways. Air is filtered both in the trachea and in the bronchi.

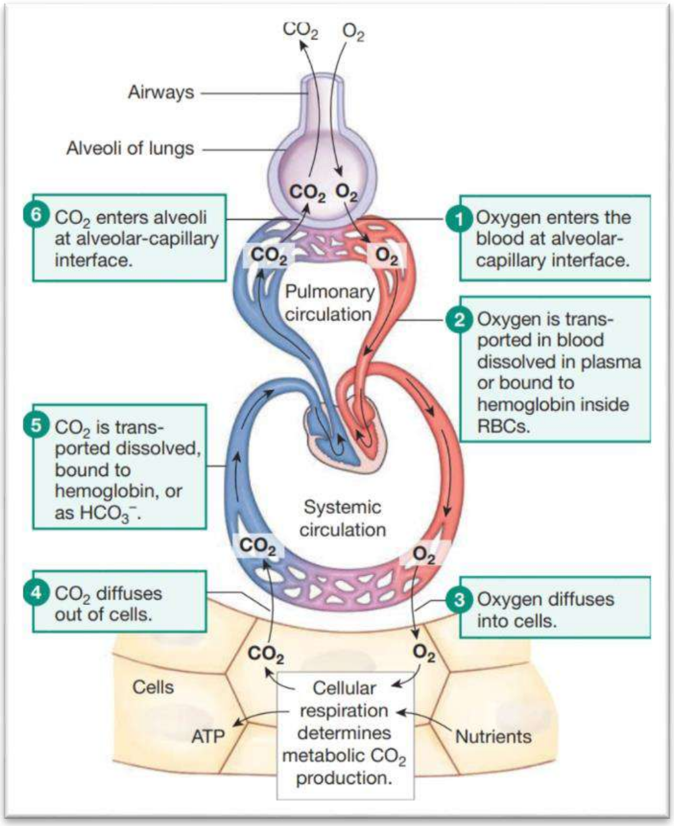
Alveoli

The air-filled alveoli, clustered at the ends of terminal bronchioles, make up the bulk of lung tissue. Their primary function is the exchange of gases between themselves and the blood. Each tiny alveolus is composed of a single layer of epithelium. The thin walls of alveoli do not contain muscle. As a result, lung tissue itself cannot contract. Blood vessels fill 80–90% of the space between alveoli, making the blood in close contact with the air-filled alveoli.



Gas Exchange

Breathing is the flow of air into and out of the lungs. Once air reaches the alveoli, gases such as oxygen and CO2 diffuse from the alveolar air space into the blood. Recall that diffusion is movement of a molecule from a region of higher concentration to one of lower concentration.

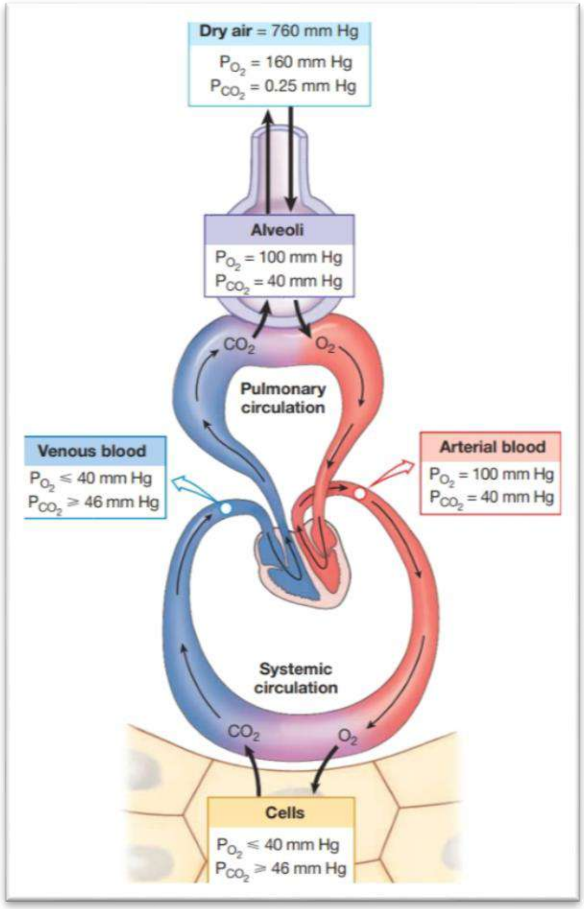


Normal alveolar PO2 at sea level is about 100 mm Hg. The PO2 of "deoxygenated" venous blood arriving at the lungs is about 40 mm Hg. Oxygen therefore diffuses down its partial pressure (concentration) gradient from the alveoli into the capillaries. Diffusion goes to equilibrium, and the PO2 of arterial blood leaving the lungs is the same as in the alveoli: 100 mm Hg.

When arterial blood reaches tissue capillaries, the gradient is reversed. Cells are continuously using oxygen for oxidative phosphorylation. In the cells of a person at rest, intracellular PO2 averages 40 mm Hg. Arterial blood arriving at the cells has a PO2 of 100 mm Hg. Because PO2 is lower in the cells, oxygen diffuses down its partial pressure gradient from plasma into cells. Once again, diffusion goes to equilibrium. As a result, venous blood has the same PO2 as the cells it just passed.

Conversely, PCO2 is higher in tissues than in systemic capillary blood because of CO2 production during metabolism. Cellular PCO2 in a person at rest is about 46 mm Hg, compared to an arterial plasma PCO2 of 40 mm Hg. The gradient causes CO2 to diffuse out of cells into the capillaries. Diffusion goes to equilibrium, and systemic venous blood averages a PCO2 of 46 mm Hg.

At the pulmonary capillaries, the process reverses. Venous blood bringing waste CO2 from the cells has a PCO2 of 46 mm Hg. Alveolar PCO2 is 40 mm Hg. Because PCO2 is higher in the plasma, CO2 moves from the capillaries into the alveoli. By the time blood leaves the alveoli, it has a PCO2 of 40 mm Hg, identical to the PCO2 of the alveoli.



Gas Transport in the Blood

Gases that enter the capillaries first dissolve in the plasma. But dissolved gases play only a small part in providing the cells with oxygen. The red blood cells have a critical role in ensuring that gas transport between lung and cells is adequate.

Oxygen transport in the blood in two ways: the oxygen that is dissolved in the plasma (the PO2) and oxygen bound to hemoglobin (Hb). Oxygen is only slightly soluble in aqueous solutions, and less than 2% of all oxygen in the blood is dissolved. That means hemoglobin transports more than 98% of our oxygen. Hemoglobin, the oxygen-binding protein, binds reversibly to oxygen. With four heme groups per hemoglobin molecule, one hemoglobin molecule binds four oxygen molecules. Hemoglobin bound to oxygen is known as ***oxyhemoglobin***, abbreviated HbO2.

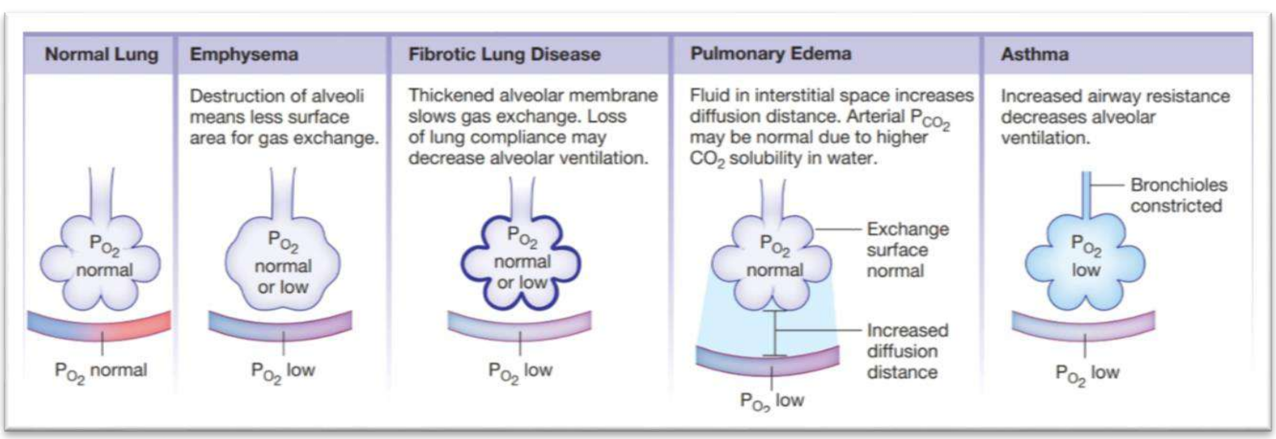
Carbon dioxide is more soluble in body fluids than oxygen is, but the cells produce far more CO_2 than can dissolve in the plasma. Only about 7% of the CO_2 carried by venous blood is dissolved in the plasma. The other 93% diffuses into red blood cells, where 23% binds to hemoglobin (HbCO2) while the remaining 70% is converted to bicarbonate ion (HCO_3^-).

The conversion of CO_2 to HCO_3^- serves two purposes: (1) it provides an additional way to transport CO_2 from cells to lungs, and (2) HCO_3^- is available to act as a buffer for metabolic acids, thereby helping stabilize the body's pH.

Hypoxia

Is a state of too little oxygen. It results from impaired diffusion of gases between alveoli and blood or inadequate oxygen transport in the blood.

The factors of surface area, diffusion distance, and membrane permeability do come into play with various diseases. Pathological changes that adversely affect gas exchange include (1) a decrease in the amount of alveolar surface area available for gas exchange, (2) an increase in the thickness of the alveolar-capillary exchange barrier, and (3) an increase in the diffusion distance between the alveolar air space and the blood.



Digestive System

The digestive system begins with the oral cavity (mouth and pharynx), which serves as a receptacle for food. Swallowed food enters the gastrointestinal tract (GI tract) consisting of esophagus, stomach, small intestine, and large intestine. The portion of the GI tract running from the stomach to the anus is also called the gut.

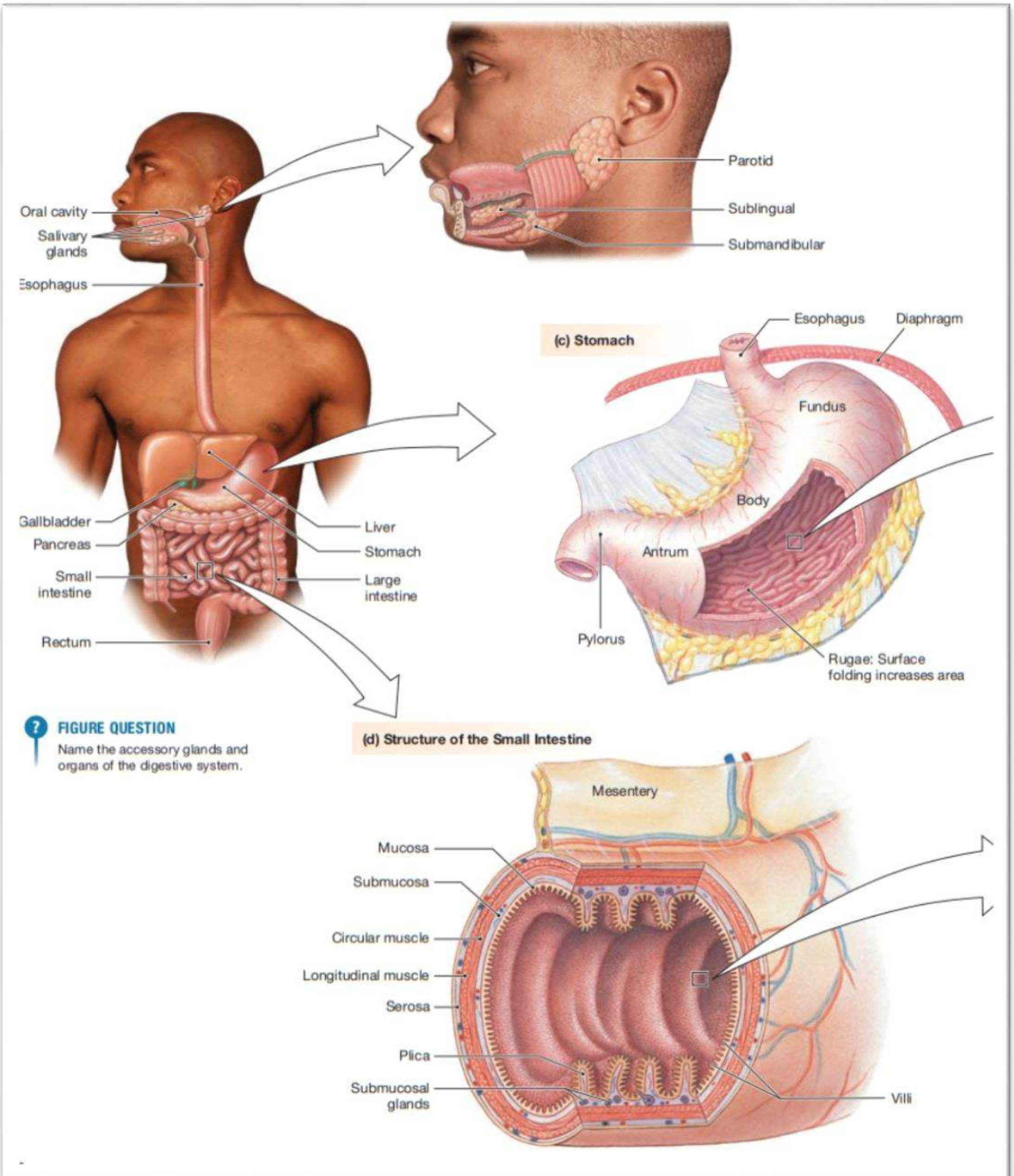
Digestion, the chemical and mechanical breakdown of food, takes place primarily in the lumen of the gut. Along the way, secretions are added to ingested food by secretory epithelial cells and by accessory glandular organs that include salivary glands, the liver, the gallbladder, and the pancreas. The liquid mixture of food and secretions is known as chyme.

The digestive system parts

In the oral cavity, the first stages of digestion begin with chewing and the secretion of saliva by three pairs of salivary glands: sublingual glands, submandibular glands, and parotid glands. Swallowed food passes into the esophagus, a narrow tube that travels through the thorax to the abdomen. Just below the diaphragm, the esophagus ends at the stomach, a baglike organ that can hold as much as 2 liters of food and fluid when fully expanded.

The stomach has three sections: the upper fundus, the central body, and the lower antrum. The stomach continues digestion that began in the mouth by mixing food with acid and enzymes to create chyme. The pylorus {gatekeeper} or opening between the stomach and the small intestine is guarded by the pyloric valve.

Most digestion takes place in the small intestine, which has three sections: the duodenum (the first 25 cm), jejunum, and ileum (the latter two together are about 260 cm long). Digestion is carried out by intestinal enzymes, aided by exocrine secretions from two accessory glandular organs: the pancreas and the liver.



The GI Tract Wall

The basic structure of the gastrointestinal wall is similar in the stomach and intestines. The gut wall is crumpled into folds to increase its surface area. The intestinal mucosa also projects into the lumen in small fingerlike extensions known as villi.

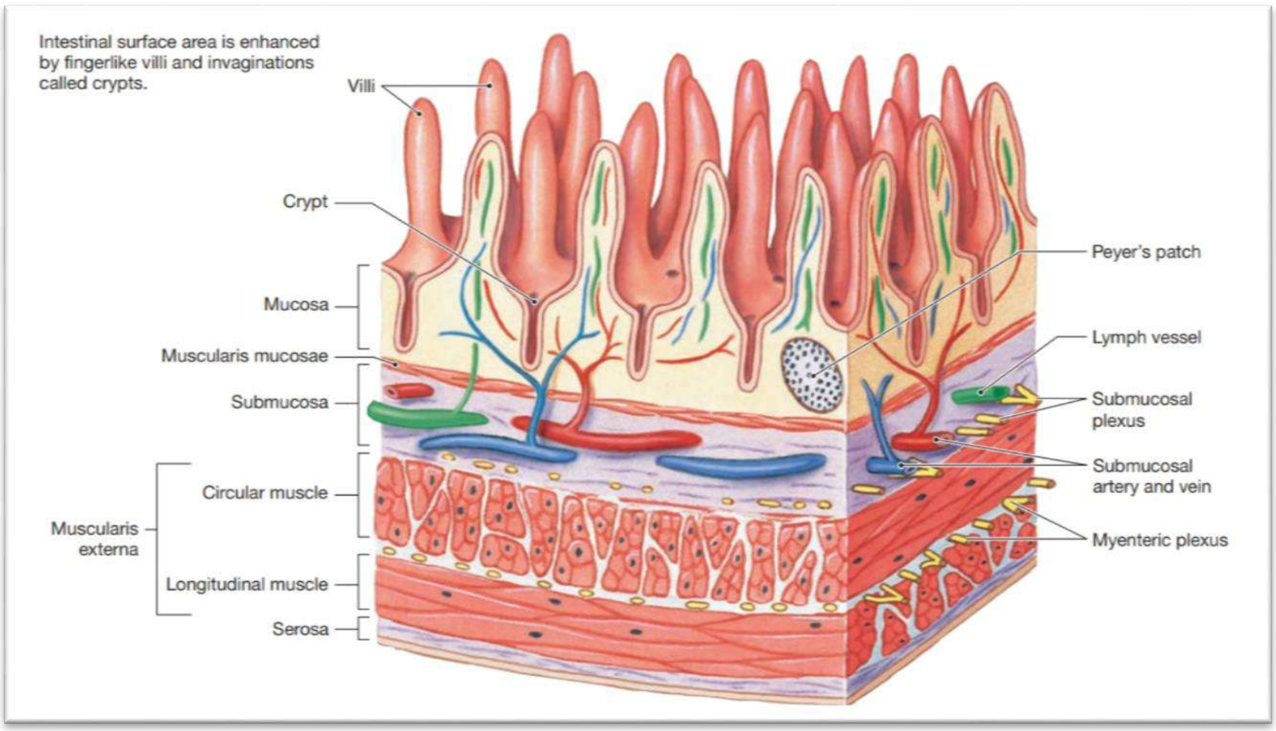
The gut wall consists of four layers:

(1) an inner mucosa facing the lumen,

(2) a layer known as the submucosa.

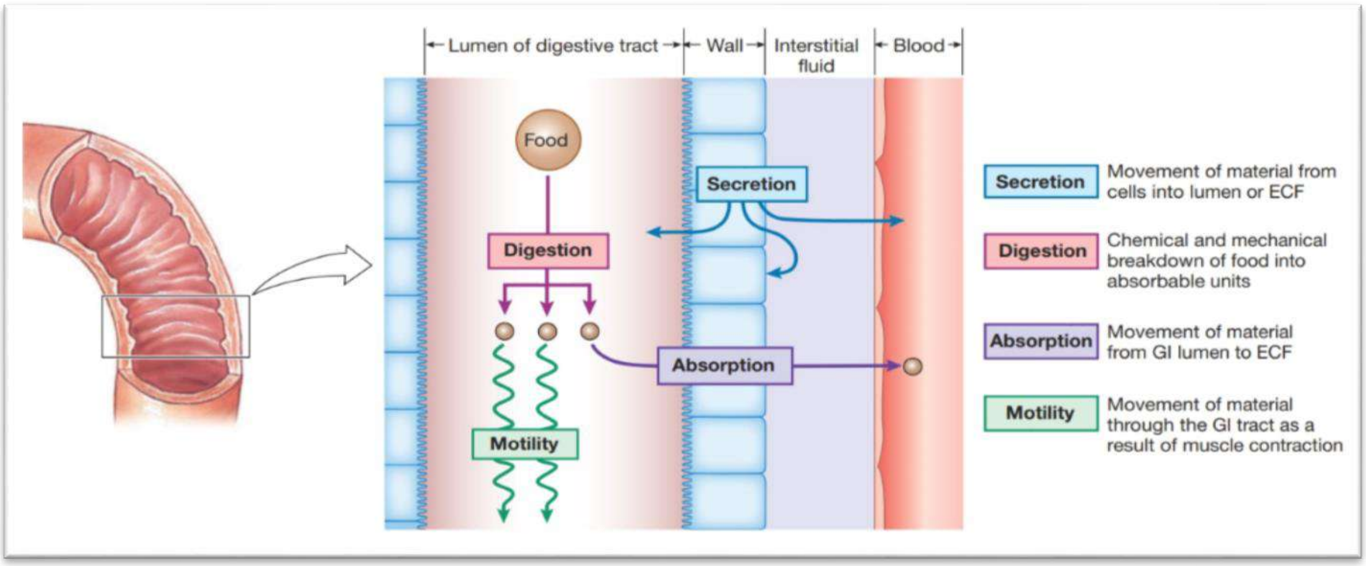
(3) layers of smooth muscle known collectively as the muscularis externa.

(4) a covering of connective tissue called the serosa.



Digestive Function and Processes

The primary function of the digestive system is to move nutrients, water, and electrolytes from the external environment into the body's internal environment. To accomplish this, the system uses four basic processes: digestion, absorption, secretion, and motility.



Digstion

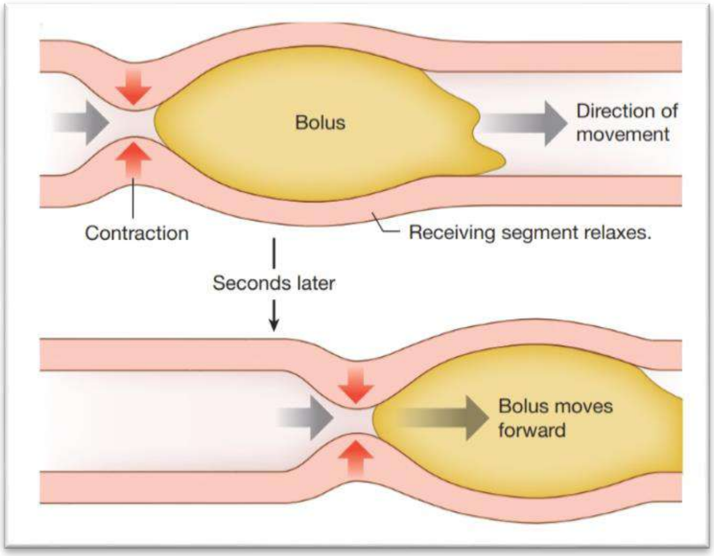
When food first enters the mouth, it is met by a flood of the secretion we call saliva. Saliva has four important functions:

1. Soften and moisten food. 2. Digestion of starch.

3. Taste. 4. Defense.

Mechanical digestion of food begins in the oral cavity with chewing. The lips, tongue, and teeth all contribute to the mastication of food, creating a softened, moistened mass (bolus) that can be easily swallowed.

As the bolus moves down toward the esophagus, the epiglottis folds down, completing closure of the upper airway and preventing food and liquid from entering the airways. At the same time, respiration is briefly inhibited. When the bolus reaches the esophagus, the upper esophageal sphincter relaxes.



If the lower esophageal sphincter does not stay contracted, gastric acid and pepsin can irritate the lining of the esophagus, leading to the pain and irritation of gastroesophageal reflux, more commonly called heartburn.

About 3.5 liters of food, drink, and saliva enter the fundus of the stomach each day. The stomach has three general functions: **1. Storage. 2. Digestion. 3. Defense.**

When food arrives from the esophagus, the stomach relaxes and expands to hold the increased volume. The storage function of the stomach is perhaps the least obvious aspect of digestion. However, whenever we ingest more than we need from a nutritional standpoint, the stomach must regulate the rate at which food enters the small intestine.

The stomach produces two enzymes: pepsin and a gastric lipase. Pepsin carries out the initial digestion of proteins. It is particularly effective on collagen and therefore plays an important role in digesting meat. Lipases are enzymes that break down triglycerides.

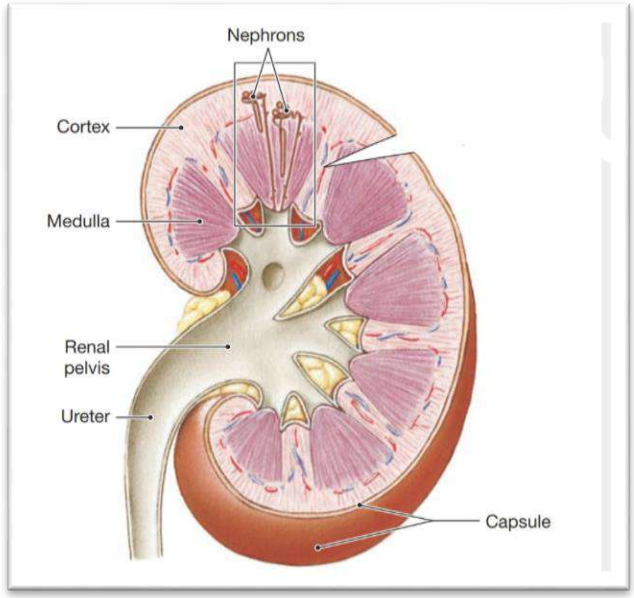
About 5.5 liters of food, fluid, and secretions enter the small intestine each day, and about 3.5 liters of hepatic, pancreatic, and intestinal secretions are added there, making a total input of 9 liters into the lumen. All but about 1.5 liters of this volume is absorbed in the small intestine, mostly in the duodenum and jejunum. The anatomy of the small intestine facilitates secretion, digestion, and absorption by maximizing surface area.

Most nutrients absorbed across the intestinal epithelium move into capillaries in the villi for distribution through the circulatory system. The exception is digested fats, most of which pass into lacteals of the lymphatic system. Venous blood from the digestive tract does not go directly back to the heart. Instead, it passes into the hepatic portal system. This specialized region of the circulation has two sets of capillary beds: one that picks up absorbed nutrients at the intestine, and another that delivers the nutrients directly to the liver.

Each day, the liver, pancreas, and intestine produce more than 3 liters of secretions whose contents are necessary for completing the digestion of ingested nutrients. The added secretions include digestive enzymes, bile, bicarbonate, mucus, and an isotonic NaCl solution.

By the end of the ileum, only about 1.5 liters of unabsorbed chyme remain. The colon absorbs most of this volume so that normally only about 0.1 liter of water is lost daily in feces. Chyme enters the large intestine through the ileocecal valve.

The urinary system

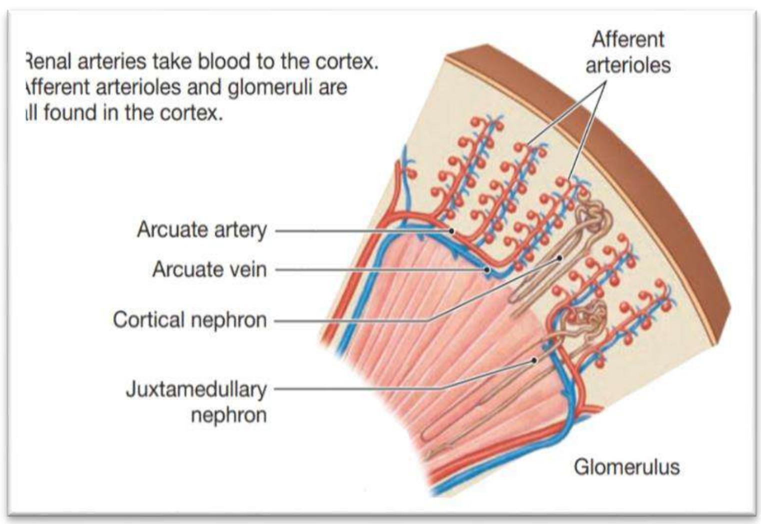


The urinary system is composed of two kidneys, two ureters, a bladder, and a urethra.

Each kidney has about 1 million microscopic nephrons. In cross section, a kidney is arranged into an outer cortex and inner medulla. Renal blood flow goes from afferent arteriole to glomerulus to efferent arteriole to peritubular capillaries. The vasa recta capillaries dip into the medulla.

The Functional Unit of the Kidney

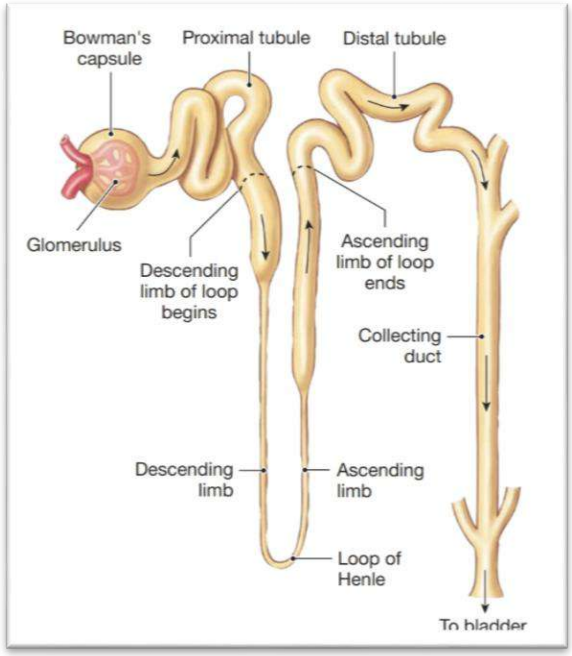
A cross section through a kidney shows that the interior is arranged in two layers: an outer cortex and inner medulla. The layers are formed by the organized arrangement of microscopic tubules called nephrons. About 80% of the nephrons in a kidney are almost completely contained within the cortex (cortical nephrons), but the other 20% dip down into the medulla.



The nephron is the functional unit of the kidney. Each of the 1 million nephrons in a kidney is divided into sections, and each section is closely associated with specialized blood vessels

The nephron begins with a hollow, ball-like structure called Bowman's capsule that surrounds the glomerulus. The endothelium of the glomerulus is fused to the epithelium of Bowman's capsule so that fluid filtering out of the capillaries passes directly into the lumen of the tubule. The combination of glomerulus and Bowman's capsule is called the renal corpuscle.

From Bowman's capsule, filtered fluid flows into the proximal tubule, then into the loop of Henle, a U-shaped segment that dips down toward the medulla and then back up. The loop of Henle is divided into two limbs, a thin descending limb and an ascending limb with thin and thick segments. The fluid then passes into the distal tubule. The distal tubules of up to eight nephrons drain into a single larger tube called the collecting duct. (The distal tubule and its collecting duct together form the distal nephron.) Collecting ducts pass from the cortex through the medulla and drain into the renal pelvis. From the renal pelvis, the filtered and modified fluid, now called urine, flows into the ureter on its way to excretion.



Kidneys Filter, Reabsorb, and Secrete

Three basic processes take place in the nephron: filtration, reabsorption, and secretion.

Filtration is the movement of fluid from blood into the lumen of the nephron. Filtration takes place only in the renal corpuscle, where the walls of glomerular capillaries and Bowman's capsule are modified to allow bulk flow of fluid. Bowman's capsule epithelium has specialized cells called podocytes that wrap around the glomerular capillaries and create filtration slits. Filtered solutes must pass first through glomerular capillary endothelium, then through a basement membrane, and finally through podocyte filtration slits before reaching the lumen of Bowman's capsule.

Filtration allows most components of plasma to enter the tubule but excludes blood cells and almost all plasma proteins.

Reabsorption is the process of moving substances in the filtrate from the lumen of the tubule back into the blood flowing through peritubular capillaries. Most reabsorption takes place in the proximal tubule.

Most reabsorption involves transepithelial transport, but some sol utes and water are reabsorbed by the paracellular pathway. Most renal transport is mediated by membrane proteins and exhibits saturation, specificity, and competition. Peritubular capillaries reabsorb fluid along their entire length.

Secretion selectively removes molecules from the blood and adds them to the filtrate in the tubule lumen. Although secretion and glomerular filtration both move substances from blood into the tubule.

Secretion enhances excretion by removing solutes from the peritubular capillaries. K+, H+, and a variety of organic compounds are secreted.