Unit 1

Homeostasis and the organization of body fluid compartments :

Intracellular, extracellular and interstitial fluid. Homeostasis, control system and their components. Plasma as an extracellular fluid, RBC, molecular mechanism of blood coagulation, role of vitamin K in coagulation, anticoagulant and fibrinolytic systems. Anemias, polycythemia, haemophilia and thrombosis.

Respiration : Organization of the pulmonary system. Mechanism of respiration, pulmonary ventilation and related volumes, pulmonary circulation. Principles of gas exchange and transport. Regulation of respiration. Pulmonary oedema and regulation of pleural fluid. Hypoxia, hypercapnea, pulmonary distress, emphesema, ARDS.

TEXTBOOKS

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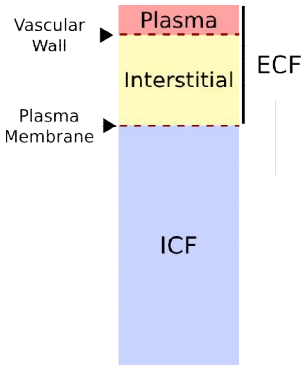
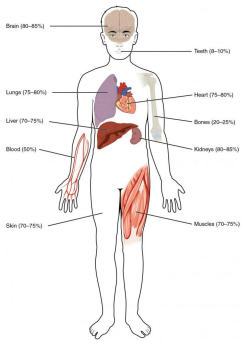
1. Homeostasis and the organization of body fluid compartments

1.1. Intracellular, extracellular and interstitial fluids

Distribution of body fluids

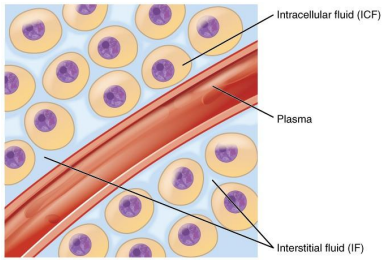
- Roughly 60% of the total body weight is water.
- Two-thirds of total body water is held within cells as Intracellular Fluid (ICF).
- The remainder is within the extracellular space as the Extracellular Fluid (ECF).
- The ECF is itself divided between fluid within the vasculature itself, known as plasma, and that outside the vasculature, known as the interstitial fluid.
- Each of these compartments is separated by the barriers shown above with unique physio-chemical properties.
- The plasma membrane is permeable to water but not small solutes or proteins.
- The vascular wall is permeable to water and small solutes but not proteins.





Fluid Compartments

This diagram shows a small blood vessel surrounded by several body cells. The fluid between the body cells is the interstitial fluid (IF), which is a type of extracellular fluid (ECF). The fluid in the blood vessel is also an example of extracellular fluid. The fluid in the cytoplasm of each body cell is intracellular fluid, or ICF.



Body fluids can be discussed in terms of their specific fluid compartment, a location that is largely separate from another compartment by some form of a physical barrier. The intracellular fluid (ICF) compartment is the system that includes all fluid enclosed in cells by their plasma membranes. Extracellular fluid (ECF) surrounds all cells in the body. Extracellular fluid has two primary constituents: the fluid component of the blood (called plasma) and the interstitial fluid (IF) that surrounds all cells not in the blood.

Intracellular Fluid Compartment

- ✓ The Intracellular Fluid (ICF) refers to the fluid present inside cells and is considered the sum total of the fluid volume in all of the body's cells.
- ✓ The ICF is separated from the Extracellular Fluid by the plasma membrane of each, individual cell.
- ✓ Although the plasma membrane is permeable to water, it is highly impermeable to both ionic and small solutes as well as proteins.
- ✓ The ICF contains roughly two-thirds of the total body water or about 40% of total body weight.

Extracellular Fluid Compartment

- ✓ The Extracellular Fluid (ECF) refers the total volume of fluid outside of cells.
- ✓ The ECF is separated from the ICF by the plasma membrane of each cell which is impermeable to nearly all classes of solutes.
- ✓ The ECF contains roughly one-third of the total body water or about 20% of total body weight.
- ✓ The ECF is sub-divided into two other fluid compartments known as the Interstitial Fluid and the Plasma. These compartments are separated by the vasculature.
- ✓ ECF is found in blood, lymph, body cavities lined with serous (moisture-exuding) membrane, cavities and channels of the brain and spinal cord, and in muscle and other body tissues
- ✓ The ECF is primarily a NaCl and $NaHCO_3$ solution. The Ionic Composition of ECF
- ✓ Na^+ 150 (mM), K^+ 5 (mM), Cl^- 110 (mM)
- ✓ The ECF is distributed into three subcompartments:

(i) Interstitial Fluid (ISF)

- It surrounds the cells, but does not circulate. It comprises about 3/4 of the ECF. (Approximately 80% of extracellular fluid surrounds the cells of the body -16% of human body weight)

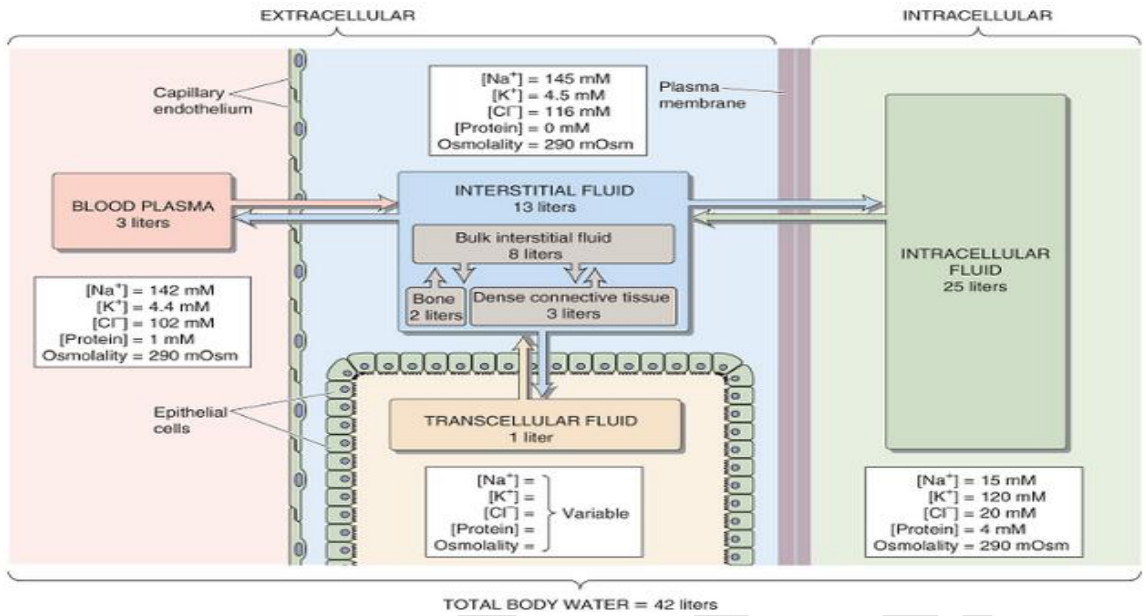
- About 75% (13 liters) of the ECF is outside the intravascular compartment, where it bathes the nonblood cells of the body.
- Within this interstitial fluid are two smaller compartments that communicate only slowly with the bulk of the interstitial fluid: dense connective tissue, such as cartilage and tendons, and bone matrix.
- The barriers that separate the intravascular and interstitial compartments are the walls of capillaries.
- Water and solutes can move between the interstitium and blood plasma by crossing capillary walls and between the interstitium and cytoplasm by crossing cell membranes.

(ii) Plasma

- Plasma circulates as the extracellular component of blood. It makes up about 1/4 of the ECF.(20% of the extracellular fluid is the plasma portion of the blood-4% of human body weight).
- Of the 17 liters of ECF, only 20% (3 liters) is contained within the cardiac chambers and blood vessels, that is, within the intravascular compartment.
- The total volume of this intravascular compartment is the blood volume, 5.5 liters. The extracellular 3 liters of the blood volume is the plasma volume.
- The balance, 2.5 liters, consists of the cellular elements of blood: erythrocytes, leukocytes, and platelets.
- The fraction of blood volume that is occupied by these cells is called the hematocrit. The hematocrit is determined by centrifuging blood that is treated with an anticoagulant and measuring the fraction of the total volume that is occupied by the packed cells.

(iii) Transcellular fluid

- Finally, 5% (1 liter) of ECF is trapped within spaces that are completely surrounded by epithelial cells.
- This transcellular fluid includes the synovial fluid within joints and the cerebrospinal fluid surrounding the brain and spinal cord.
- Transcellular fluid does not include fluids that are, outside the body, such as the contents of the gastrointestinal tract or urinary bladder.



1.2. Homeostasis control system and their components

The biological definition of homeostasis is "the tendency of an organism or cell to regulate its internal environment and maintain equilibrium, usually by a system of feedback controls, so as to stabilize health and functioning". Generally, the body is in homeostasis when its needs are met and its functioning properly.

Every organ in the body contributes to homeostasis. A complex set of chemical, thermal, and neural factors interact in complex ways, both helping and hindering the body while it works to maintain homeostasis.

Homeostatic control

To maintain homeostasis, communication within the body is essential. The image below is an example of how a homeostatic control system works. Here is a brief explanation:

1. **Stimulus**– produces a change to a variable (the factor being regulated).
2. **Receptor**– detects the change. The receptor monitors the environment and responds to change (stimuli).
3. **Input**– information travels along the (afferent) pathway to the control center. The control center determines the appropriate response and course of action.
4. **Output**– information sent from the control center travels down the (efferent) pathway to the effector.
5. **Response**– a response from the effector balances out the original stimulus to maintain homeostasis.

Afferent pathways– carry nerve impulses into the central nervous system. For instance, if you felt scorching heat on your hand, the message would travel through afferent pathways to your central nervous system.

Efferent pathways– carry nerve impulses away from the central nervous system to effectors (muscles, glands).

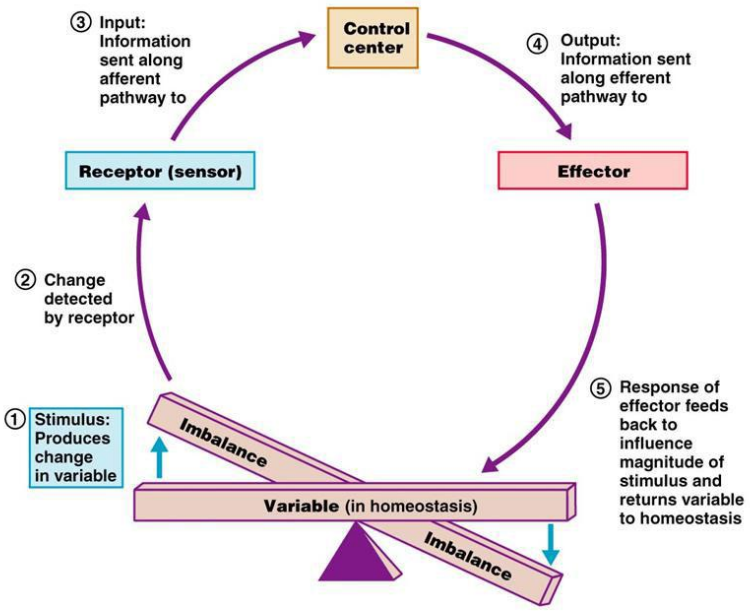
The feeling of heat would travel through an afferent pathway to the central nervous system. It would then interact with the effector and travel down the efferent pathway, eventually making the person remove their hand from the scorching heat.

Negative feedback mechanisms

Almost all homeostatic control mechanisms are negative feedback mechanisms. These mechanisms change the variable back to its original state or "ideal value".

A good example of a negative feedback mechanism is a home thermostat (heating system). The thermostat contains the receptor (thermometer) and control center. If the heating system is set at 70 degrees Fahrenheit, the heat (effector) is turned on if the temperature drops below 70 degrees Fahrenheit. After the heater heats the house to 70 degrees Fahrenheit, it shuts off effectively maintaining the ideal temperature.

The control of blood sugar (glucose) by insulin is another good example of a negative feedback mechanism. When blood sugar rises, receptors in the body sense a change . In turn, the control center (pancreas) secretes insulin into the blood effectively lowering blood sugar levels. Once blood sugar levels reach homeostasis, the pancreas stops releasing insulin.

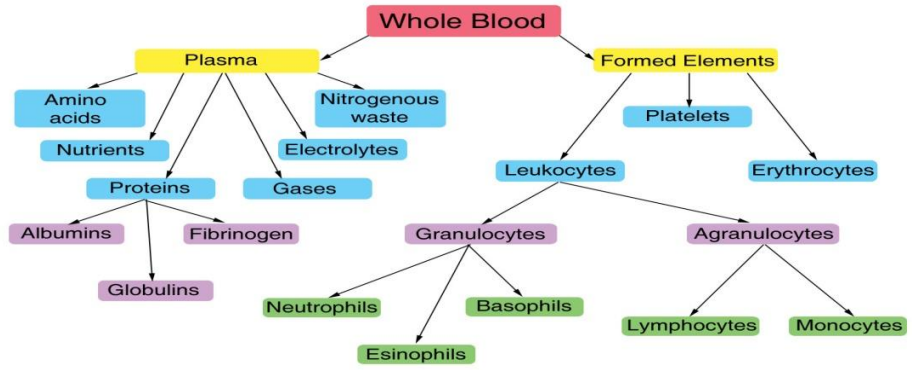


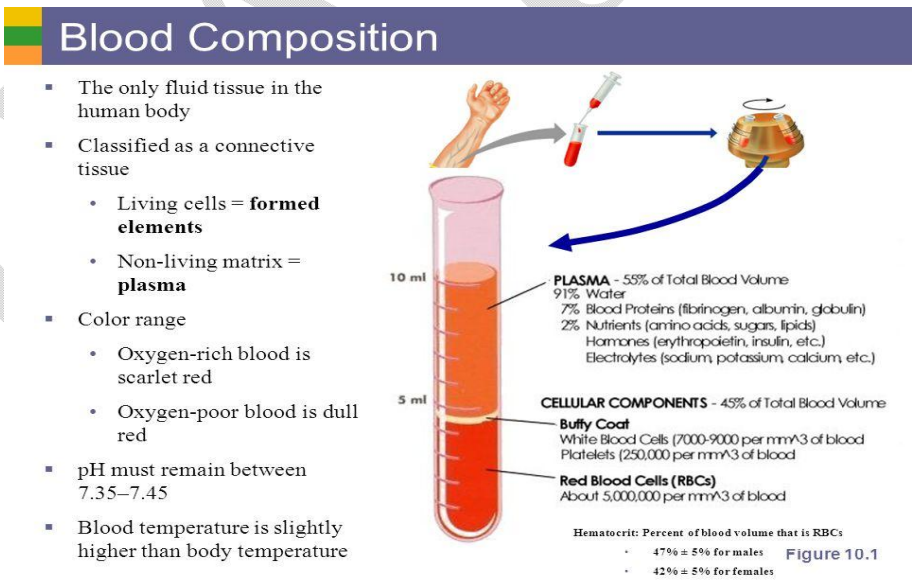
1.3. Red blood cells (RBC)

Composition of Blood

The **blood** is responsible for the following:

- Transportation of gases (oxygen O2) and carbon dioxide (CO2), chemical substances (hormones, nutrients, salts), and cells that defend the body.
- Regulation of the body's fluid and electrolyte balance, acid-base balance, and body temperature.
- Protection of the body from infection.
- Protection of the body from loss of blood by the action of clotting.



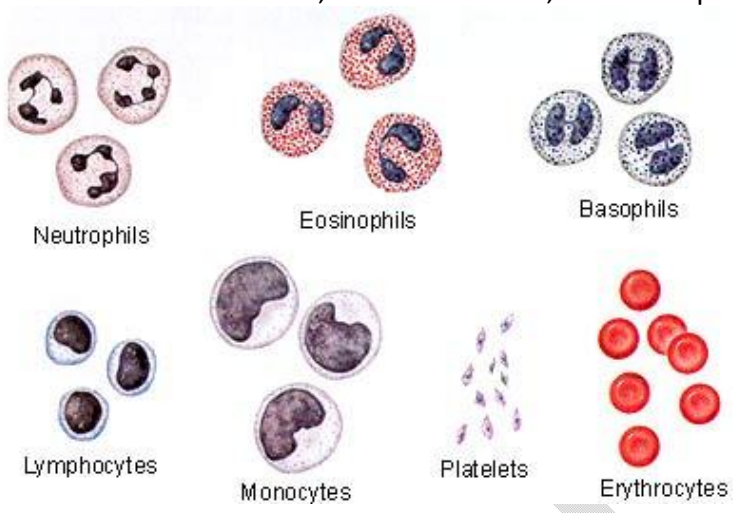


A. Blood consists of two portions—**Formed elements and Plasma**.

B. Formed elements

1. Make up 45% of the total volume of whole blood.

2. Contains red blood cells, white blood cells, and blood platelets.



C. Plasma

Plasma, the liquid portion of blood,:

1. Makes up 55% of the total volume of whole blood.
2. Contains a variety of inorganic and organic molecules suspended in water.

(I)PLASMA

A. Plasma is the liquid portion of blood. Contains a variety of inorganic and organic molecules suspended in water

B. Approximately 92% of plasma is water. The other 8% consists of various salts (help maintain pH) and organic molecules (nutrients, wastes, hormones, proteins).

1. Water, or H2O (90%)
2. Inorganic substances (calcium, potassium, sodium)
3. Organic substances (glucose, amino acids, fats, cholesterol, hormones)
4. Waste products (urea, uric acid, ammonia, creatinine)
5. Plasma proteins (serum albumin, serum globulin, and two clotting proteins: fibrinogen and prothrombin)

Serum is plasma minus the clotting proteins

C. The **Plasma Proteins**

1. The three major types are the albumins, globulins, and fibrinogen.
2. Most are made in the liver, except antibodies which are produced by B lymphocytes.

Have many functions that help maintain homeostasis:

1. Buffer the blood and keep the pH around 7.4.
2. Contribute to osmotic pressure which keeps water in the blood — Albumins.
3. Transport large organic molecules.
4. Antibodies help defend the body against disease—Gamma Globulins.
5. The plasma protein fibrinogen is important in the process of blood clotting.

(II) THE FORMED ELEMENTS:

Red blood cells, White blood cells, and Platelets

1. **RED BLOOD CELLS (ERYTHROCYTES)**

-Small, biconcave disks that lack a nucleus when mature.

- 4-6 million rbcs per mm3 of whole blood.

-Contains hemoglobin-respiratory pigment that carries oxygen and is red.

1. Each rbc contains about 280 million hemoglobin molecules.
2. Hemoglobin contains four globin proteins, each with an iron-containing heme group.
3. Iron atom of a heme group loosely binds with oxygen. Thus, blood carries oxygen.
4. Oxyhemoglobin which is formed in the lungs has a bright red color.
5. Deoxyhemoglobin has given up oxygen to tissue fluid and is a dark maroon color.
6. Carbon monoxide combines with hemoglobin more readily than oxygen, making hemoglobin unavailable for oxygen transport.

Production of Red Blood Cells

1. All blood cells are formed from special red bone marrow cells called stem cells.

2.THE WHITE BLOOD CELLS (LEUKOCYTES)

- WBCs are found not only in the blood, but also in tissue fluid and lymph.
- Larger than rbcs, have a nucleus, lack hemoglobin, and w/o staining, appear translucent.
- 5000-11,000 per mm3 of blood. Not as numerous as rbcs.
- Fight infections and in this way contribute to homeostasis.
- WBCs are derived from stem cells in the red bone marrow and undergo several maturation stages.
- When there is an infection, wbcs greatly increase in number.
- Life span of wbcs is a few days to months to years.
- 9. Types of WBCs

1. Classified into the granular and agranular leukocytes.

- Both contain granules in the cytoplasm surrounding the nucleus, but the granules are more visible after staining in granular leukocytes.
- Granules contain various enzymes and proteins which help wbcs defend the body.

(a) Granular leukocytes-3 types

- **Neutrophils**

  Most abundant of the wbcs; have a multi-lobed nucleus; do not take up stain well; first type of wbc to respond to infection.
- **Eosinophils**

  Have a bi-lobed nucleus; stain red; function is not clear, but they increase in number due to parasitic worm infections and allergic reactions.
- **Basophils**

  Have a U-shaped or lobed nucleus; stain dark-blue; release histamine associated with allergic reactions.

(b) Agranular Leukocytes-2 types

Monocytes

- Largest of the wbcs; have a kidney-shaped nucleus.
- Differentiate into macrophages once in tissues.
- Macrophages phagocytize pathogens, old cells, and cellular debris.
- Stimulate other wbcs to defend the body.

Lymphocytes

- **2 types: B cells and T cells.**
  - **B cells produce antibodies.**
  - **T cells directly destroy foreign cells.**

3. THE PLATELETS (THROMBOCYTES)

- Result from fragmentation of large cells called mega karyocytes in the red bone marrow.
- 200 billion platelets are produced per day.
- Blood contains 150,000-300,000 platelets per mm3
- Platelets are involved in the process of blood clotting or coagulation.
- When a blood vessel is damaged, platelets clump at the site of the puncture and seal the break, if it is not too extensive.
- A large break may also require a blood clot to stop the bleeding.
- There are at least 12 clotting factors that participate in the formation of a blood clot.

Hemophilia is an inherited clotting disorder due to a deficiency in a clotting factor. Most frequent cause of death is bleeding into the brain with accompanying neurological damage.

1.4. Molecular Mechanism of Blood Coagulation (BLOOD CLOTTING)

Blood Clotting is one of three mechanisms that reduce the loss of blood from broken blood vessels.

The three mechanisms are:

1. Vascular Spasm - The smooth muscle in blood vessel walls contracts immediately the blood vessel is broken. This response reduces blood loss for some time, while the other hemostatic mechanisms become active.

2. Platelet Plug Formation - When blood platelets encounter a damaged blood vessel they form a "platelet plug" to help to close the gap in the broken blood vessel.

The key stages of this process are:

- platelet adhesion,
- platelet release reaction, and
- platelet aggregation

3. Blood Clotting (Coagulation)

- Following damage to a blood vessel, vascular spasm occurs to reduce blood loss while other mechanisms also take effect:

- Blood platelets congregate at the site of damage and amass to form a platelet plug. This is the beginning of the process of the blood "breaking down" from is usual liquid form in such a way that its constituents play their own parts in processes to minimise blood loss.
- Blood normally remains in its liquid state while it is within the blood vessels but when it leaves them the blood may thicken and form a gel (coagulation).
- Blood clotting (technically "blood coagulation") is the process by which (liquid) blood is transformed into a solid state.
- This blood clotting is a complex process involving many clotting factors (incl. calcium ions, enzymes, platelets, damaged tissues) activating each other.

The stages of this process are:

1. Formation of Prothrombinase

Prothrombinase can be formed in two ways, depending of which of two "systems" or "pathways" apply. These are

Intrinsic System: This is initiated by liquid blood making contact with a foreign surface, i.e. something that is not part of the body; or

Extrinsic System: This is initiated by liquid blood making contact with damaged tissue.

2. Both the intrinsic and the extrinsic systems involve interactions between coagulation factors. These coagulation factors have individual names but are often referred to by a standardised set of Roman Numerals, e.g. Factor VIII (antihaemophilic factor), Factor IX (Christmas factor).

3. Prothrombin converted into the enzyme Thrombin

Prothrombinase (formed in stage 1.) converts prothrombin, which is a plasma protein that is formed in the liver, into the enzyme thrombin.

4. Fibrinogen (soluble) converted to Fibrin (insoluble)

In turn, thrombin converts fibrinogen (which is also a plasma protein synthesized in the liver) into fibrin. Fibrin is insoluble and forms the threads that bind the clot.

Figure: The clotting process

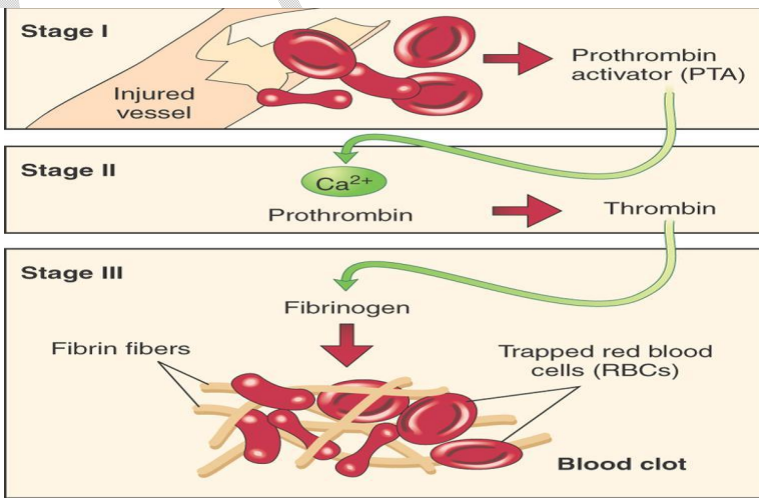
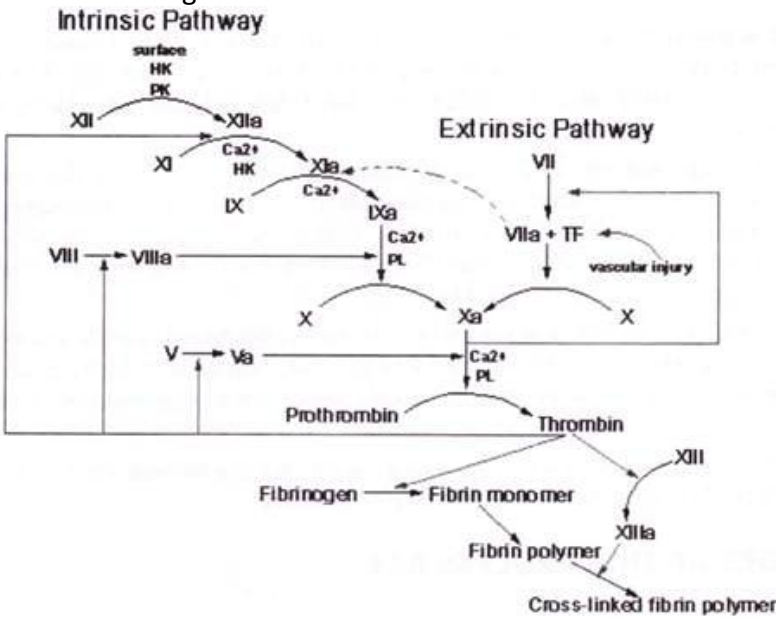


Figure-Cascade mechanism of blood clotting

Intrinsic: Damage to the blood vessel inside
Extrinsic: Damage to the tissue outside the blood vessel



Blood Clotting Problems:

If blood clots too quickly/easily then thrombosis may occur. This blood clotting in an unbroken blood vessel is dangerous and can lead to strokes or heart-attacks.

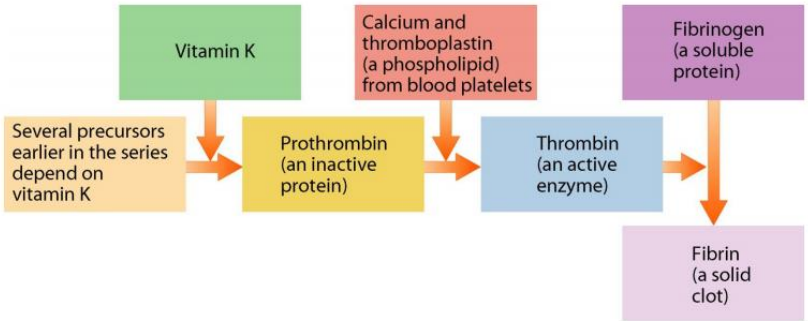
Conversely, if blood takes too long to clot hemorrhage may occur. In this case much blood may be lost from the blood vessels, which is also dangerous.

Clotting disorder

The hereditary disorder, **haemophilia** is a condition in which certain coagulation factors are missing from the blood, as a result of which the blood cannot form clots (without medical intervention).

1.5. Role of Vitamin K in coagulation

- Chief functions in the body
- Synthesis of blood-clotting proteins and bone proteins that regulate blood calcium



NATURAL ANTICOAGULANTS:

1. PGI-2.
2. Antithrombin.
3. Protein-C.
4. TFPI.
5. Heparin.
6. Fibrinolytic system.

CLASSIFICATION:

A) Anticoagulants.
B) Thrombolytic agents.
C) Antiplatelet agents.

ANTICOAGULANTS:

1. Parenteral

- Heparin Sulphate.
- Danaparoid.
- Lepirudin.

2. Oral

- Warfarin sodium.
- Dicumarol.
- Phenprocoumon.
- Acenocoumarol.
- Anisindione.

THROMBOLYTIC AGENTS:

- Streptokinase.
- t-PA.
- Urokinase.
- Alteplase.

ANTIPLATELET AGENTS:

- Aspirin
- Dipyridamole
- Ticlopidine
- Clopidogrel

HEPARIN SULPHATE:

- Glycosaminoglycan found in mast cells.
- UDP sugar precursors.
- Extracted from porcine intestinal mucosa or bovine lung.
- Available as USP units/mg.
- LMWH are 4500 daltons or 15 monosaccharide units.
- Isolated from standard heparin.

Mechanism of action:

- Acts via heparin co-factor or antithrombin III.
- Inhibits thrombin by PAI-1, protein-C inhibitor & protease nexin-1.
- Inhibits factor Xa by TFPI.
- Releases lipoprotein lipase enzyme.
- Interferes with platelet aggregation.

What are their bad effects? (Adverse effects)

- Bleeding.
- Allergy.
- Increase in serum potassium level (Hyperkalaemia).
- Decrease in platelet count (Thrombocytopenia).
- Softening of bones (Osteoporosis).
- Loss of hairs (Alopecia).

Fibrinolytic system

The fibrinolytic system dissolves fibrin blood clots, acting in reverse to the coagulation system.

Plasminogen, the inactive, zymogen form of plasmin, is incorporated into fibrin clots as they form. Cleavage of plasminogen by tissue plasminogen activator (PLAT, tPA) and urokinase converts plasminogen to the active serine protease plasmin form. Acting as a serine protease, the kringle domains of plasmin bind to arginine and lysine residues and cleave fibrin into fibrin degradation products (fibrinolysis).

Tissue plasminogen activator (PLAT, tPA) is a serine protease secreted by cells of the arteriolar endothelium. Urokinase, also termed urokinase-type plasminogen activator (uPA), is also a serine protease that contains a serine protease domain, a kringle domain, and a growth factor domain. The serpins, plasminogen activator inhibitor-1 (PAI-1) and plasminogen activator inhibitor-2 (PAI-2) irreversibly inhibit the protease (peptidase) activity of tPA and uPA.

In the extracellular matrix, urokinase binds to the urokinase receptor, tethering urokinase to the cell membrane. Through its interaction with the urokinase receptor, urokinase participates in cell adhesion, migration, and cellular mitotic pathways. It appears that tissue degradation following plasminogen activation facilitates tissue invasion and contributes to establishment of tumor metastasis, making urokinase an attractive potential target for anticancer inhibitors. Urokinase is employed as a thrombolytic agent in the treatment of deep venous thrombosis (DVT) and pulmonary embolism (PE). Both urokinase and recombinant tissue plasminogen activator (PLAT, tPA) are employed in treatment of myocardial infarction (MI), and recombinant PLAT is used in treatment of acute stroke (CVA, cerebrovascular accident).

Conversely, antifibrinolytics, such as aminocaproic acid (ε-aminocaproic acid) and the more potent tranexamic acid are employed as inhibitors of fibrinolysis. They act by blocking the lysine-binding site in the kringle domains on plasminogen, and are employed in treatment of menorrhagia, excessive post-operative bleeding, and bleeding dyscrasias.

Anemia

Anemia is a condition that develops when your blood lacks enough healthy red blood cells or hemoglobin. Hemoglobin is a main part of red blood cells and binds oxygen. If you have too few or abnormal red blood cells, or your hemoglobin is abnormal or low, the cells in your body will not get enough oxygen. Symptoms of anemia -- like fatigue -- occur because organs aren't getting what they need to function properly.

Anemia is the most common blood condition in the U.S. It affects about 3.5 million Americans. Women, young children, and people with chronic diseases are at increased risk of anemia. Important factors to remember are:

Certain forms of anemia are hereditary and infants may be affected from the time of birth.

Women in the childbearing years are particularly susceptible to iron-deficiency anemia because of the blood loss from menstruation and the increased blood supply demands during pregnancy.

Older adults also may have a greater risk of developing anemia because of poor diet and other medical conditions.

There are many types of anemia. All are very different in their causes and treatments. Iron-deficiency anemia, the most common type, is very treatable with diet changes and iron supplements. Some forms of anemia -- like the mild anemia that develops during pregnancy -- are even considered normal. However, some types of anemia may present lifelong health problems. Polycythemia is a condition that results in an increased level of circulating red blood

cells in the bloodstream. People with polycythemia have an increase in hematocrit, hemoglobin, or red blood cell count above the normal limits.

Polycythemia

Polycythemia is normally reported in terms of increased hematocrit (hematocrit is the ratio of the volume of red blood cells to the total volume of blood) or hemoglobin concentration (hemoglobin is a protein responsible for transporting oxygen in the blood).

- **Hematocrit (HCT)**: Polycythemia is considered when the hematocrit is greater than 48% in women and 52% in men.
- **Hemoglobin (HGB)**: Polycythemia is considered when a hemoglobin level of greater than 16.5g/dL in women or hemoglobin level greater than18.5 g/dL in men.

Polycythemia can be divided into two categories; primary and secondary.

- **Primary polycythemia:** In primary polycythemia the increase in red blood cells is due to inherent problems in the process of red blood cell production.
- **Secondary polycythemia:** Secondary polycythemia generally occurs as a response to other factors or underlying conditions that promote red blood cell production.

Red cell production (erythropoiesis) takes place in the bone marrow through a complex sequence of tightly regulated steps. The main regulator of the red cell production is the hormone erythropoietin (EPO). This hormone is largely secreted by the kidneys, although, about 10% may be produced and secreted by the liver.

Erythropoietin secretion is up-regulated in response to low oxygen levels (hypoxia) in the blood. More oxygen can be carried to tissues when erythropoietin stimulates red blood cell production in the bone marrow to compensate for the hypoxia.

Neonatal (newborn) polycythemia can be seen in 1% to 5% of newborns. The most common causes may be related to transfusion of blood, transfer of placental blood to the infant after delivery, or chronic inadequate oxygenation of the fetus (intrauterine hypoxia) due to placental insufficiency.

Hemophilia

Hemophilia is an inherited bleeding disorder in which a person lacks or has low levels of certain proteins called “clotting factors” and the blood doesn’t clot properly as a result. This leads to excessive bleeding. There are 13 types of clotting factors, and these work with platelets to help the blood clot. Platelets are small blood cells that form in your bone marrow. According

to the World Federation of Hemophilia (WFH), about one in 10,000 people are born with this disease.

People with hemophilia bleed easily, and the blood takes a longer time to clot. People with hemophilia can experience spontaneous or internal bleeding and often have painful, swollen joints due to bleeding into the joints. This rare but serious condition can have life-threatening complications.

The three forms of hemophilia are hemophilia A, B, and C.

Hemophilia A is the most common type of hemophilia, and it's caused by a deficiency in factor VIII. According to the National Heart, Lung, and Blood Institute (NHLBI), eight out of 10 people with hemophilia have hemophilia A.

Hemophilia B, which is also called Christmas disease, is caused by a deficiency of factor IX.

Hemophilia C is a mild form of the disease that's caused by a deficiency of factor XI. People with this rare type of hemophilia often don't experience spontaneous bleeding. Hemorrhaging typically occurs after trauma or surgery.

Hemophilia is an inherited genetic condition. This condition isn't curable, but it can be treated to minimize symptoms and prevent future health complications.

In extremely rare cases, hemophilia can develop after birth. This is called "acquired hemophilia." This is the case in people whose immune system forms antibodies that attack factors VIII or IX.

Thrombosis

Thrombosis is the process of a blood clot, also known as a thrombus, forming in a blood vessel. This clot can block or obstruct blood flow in the affected area, as well as cause serious complications if the clot moves to a crucial part of the circulatory system, such as the brain or the lungs.

It is normal for the body to produce clotting factors like platelets and fibrin when a blood vessel is injured, to prevent an excessive loss of blood from the body. If this effect is over productive it can obstruct the flow of blood and form an embolus that moves around the blood stream.

Thrombosis Types

Thrombosis can be broadly classified as either venous thrombosis or arterial thrombosis, according to where the thrombus presents in the body.

Venous thrombosis occurs in the veins and is categorized further according to where it occurs including:

- Deep vein thrombosis
- Portal vein thrombosis
- Renal vein thrombosis
- Jugular vein thrombosis
- Budd-Chiari Syndrome
- Paget-Schoetter disease
- Cerebral venous sinus thrombosis

Arterial thrombosis, also known as atherothrombosis due to its association with atheroma rupture, occurs in the arteries. The blood stasis caused by atrial fibrillation may also cause this type of thrombosis.

There are multiple causes for stroke, including ischemia, hemorrhage and embolus in the brain. Stroke due to a blood clot in the brain usually builds gradually around an atherosclerotic plaque.

Myocardial infarction may also be caused by a thrombus in the coronary artery and is associated with ischemia. The reduced oxygen supply to the heart cells, as a result of the blockage, results in cell death and myocardial infarction.

2. RESPIRATORY SYSTEM

The **respiratory system** (or **ventilatory system**) is a biological system consisting of specific organs and structures used for the process of respiration in an organism. The respiratory system is involved in the intake and exchange of oxygen and carbon dioxide between an organism and the environment.

In air-breathing vertebrates, respiration takes place in the respiratory organs called lungs. The passage of air into and out of the lungs to supply the body with oxygen (and expel carbon dioxide) is called breathing. In humans and other mammals, the anatomical features of the respiratory system include **trachea, bronchi, bronchioles, lungs, and diaphragm.**

The Human Respiratory System

Lungs: The lungs are large, lobed, paired organs in the chest (also known as the thoracic cavity). Thin sheets of epithelium (pleura) separate the inside of the chest cavity from the outer surface of the lungs. The bottom of the thoracic cavity is formed by the diaphragm.Ventilation is the mechanics of breathing in and out(moving air in and out of the lungs)

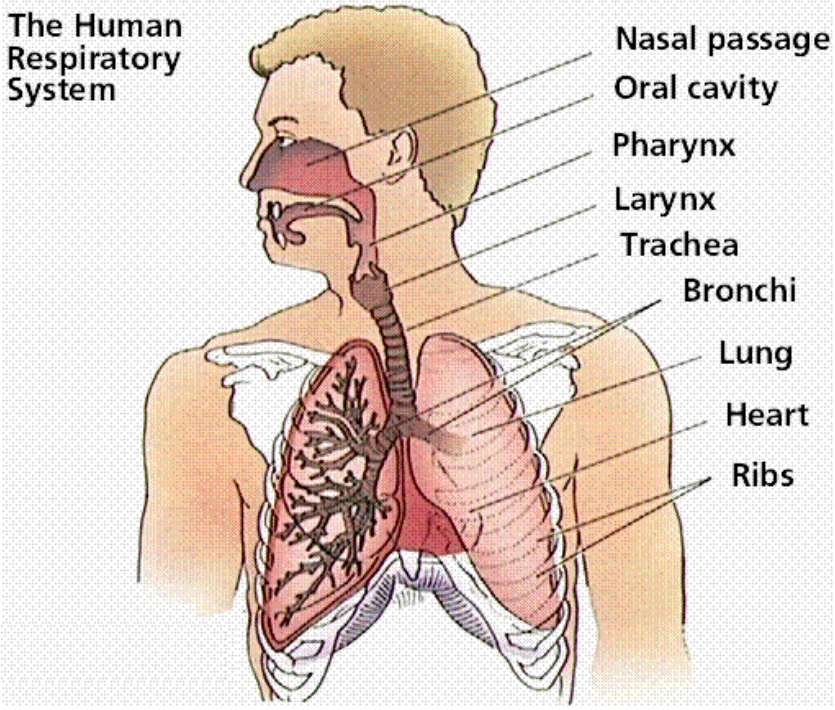
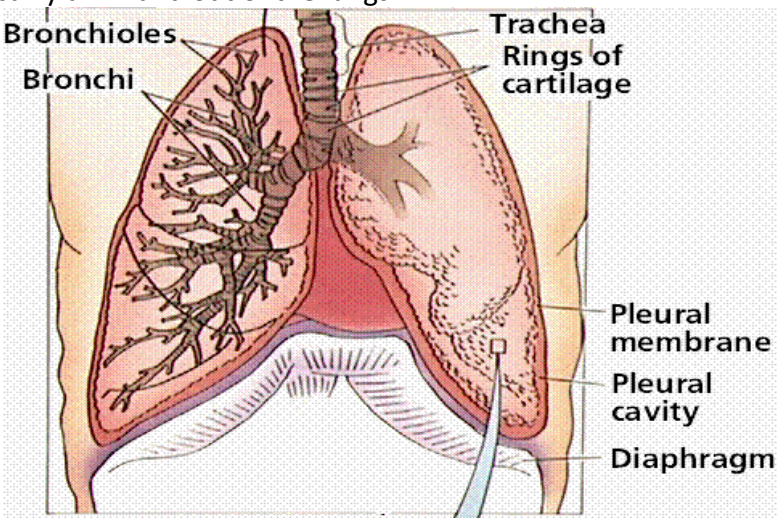


Figure: The human respiratory system.

Air enters the body through the **nose,** is warmed, filtered, and passed through the nasal cavity. Air passes the **pharynx** (which has the epiglottis that prevents food from entering the trachea).The upper part of the trachea contains the **larynx**. The vocal cords are two bands of tissue that extend across the opening of the larynx. After passing the larynx, the air moves into the **bronchi** that carry air in and out of the lungs.



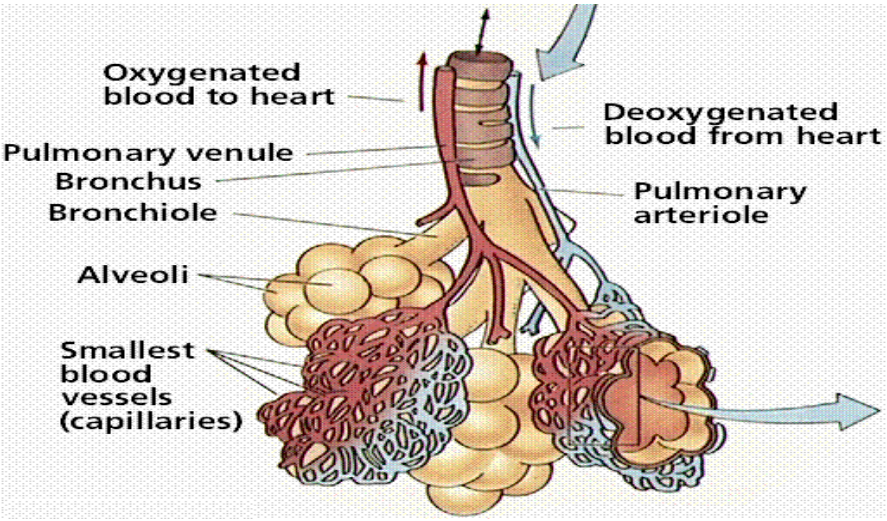


Figure: The lungs and alveoli and their relationship to the diaphragm and capillaries.

Bronchi are reinforced to prevent their collapse and are lined with ciliated epithelium and mucus-producing cells. Bronchi branch into smaller and smaller tubes known as **bronchioles.** Bronchioles terminate in grape-like sac clusters known as **alveoli.** Alveoli are surrounded by a network of thin-walled capillaries. Only about 0.2 µm separate the alveoli from the capillaries due to the extremely thin walls of both structures.

Four Respiration Processes

- Breathing (ventilation): air in to and out of lungs
- External respiration: gas exchange between air and blood
- Internal respiration: gas exchange between blood and tissues
- Cellular respiration: oxygen use to produce ATP, carbon dioxide as waste

This breathing in (inspiration) and breathing out (expiration) is controlled via nervous impulses from the respiratory centre in the medulla of the brain.

Both the intercostal muscles (in between the ribs) and the diaphragm receive impulses from the respiratory centre. Stretch receptors in the lungs send impulses to the respiratory centre in the brain giving information about the state of the lungs.

Process of inspiration (breathing in)

1. External intercostal muscles contract
2. Ribs and sternum move up and out
3. Width of thorax increases front to back and side to side
4. Diaphragm contracts
5. Diaphragm moves down, flattening
6. Depth of thorax increases top to bottom so the...
7. Volume of thorax increases.
8. Pressure between the pleural surfaces decreases.

9. Lungs expand to fill thoracic cavity.
10. Air pressure in alveoli is less than atmospheric pressure.
11. Air is forced in by the higher external atmospheric pressure.

As the lungs fill with air the stretch receptors send impulses to the expiratory part of the respiration centre to end breathing in.

Process of expiration (breathing out)

1. External intercostal muscles relax
2. Ribs and sternum move down and in
3. Width of thorax decreases front to back and side to side
4. Diaphragm relaxes
5. Diaphragm moves up
6. Depth of thorax decreases top to bottom. So the ...
7. Volume of thorax decreases.
8. Pressure between the pleural surfaces increases.
9. Lung tissue recoils from sides of thoracic cavity
10. Air pressure in alveoli is more than atmospheric pressure.
11. Air is forced out.

As the air leaves, the stretch receptors are no longer stimulated. The inhibition of breathing in (via the expiratory part of the centre) stops so breathing in can start again.

Chemoreceptors

There are also chemoreceptors in the medulla and certain blood vessels that are sensitive to changes in carbon dioxide levels in the blood.

If the level is too high (the pH would drop, enzyme action would be affected with serious results), impulses are sent from these cells to the inspiratory part of the centre so that breathing rate increases.

This means that carbon dioxide is got out of the body as quickly as possible and more oxygen comes in.

Cellular respiration involves the breakdown of organic molecules to produce ATP. A sufficient **supply of oxygen** is required for the aerobic respiratory machinery of Kreb's Cycle and the Electron Transport System to efficiently convert stored organic energy into energy trapped in ATP. **Carbon dioxide** is also generated by cellular metabolism and must be removed from the cell. There must be an exchange of gases: carbon dioxide leaving the cell, oxygen entering.

The Respiratory System and Gas Exchange

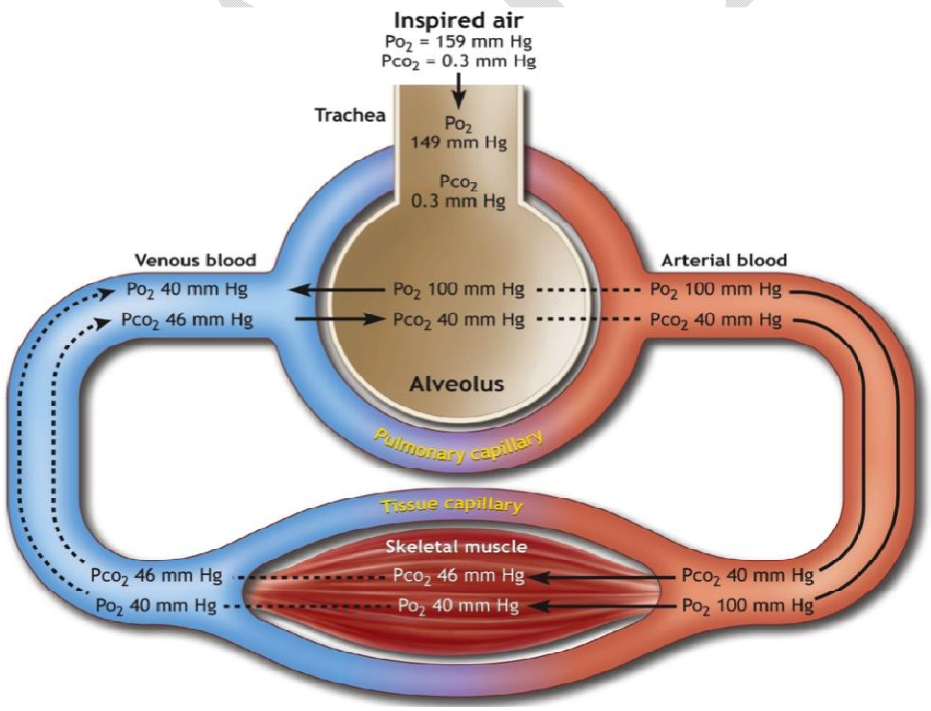
- Gases diffuse according to their partial pressures

Partial Pressures of O2 and CO2 in the body

- Alveoli
  - PO2 = 100 mm Hg
  - PCO2 = 40 mm Hg
- Alveolar capillaries
  - Entering the alveolar capillaries
    - PO2 = 40 mm Hg (relatively low because this blood has just returned from the systemic circulation & has lost much of its oxygen)
    - PCO2 = 45 mm Hg (relatively high because the blood returning from the systemic circulation has picked up carbon dioxide)
  - Body cells (resting conditions)
    - PO2 = 40 mm Hg
    - PCO2 = 45 mm Hg

Blood leaving the systemic capillaries returns to the heart (right atrium) via venules & veins (and no gas exchange occurs while blood is in venules & veins). This blood is then pumped to the lungs (and the alveolar capillaries) by the right ventricle.

Figure: Partial pressure in respiration

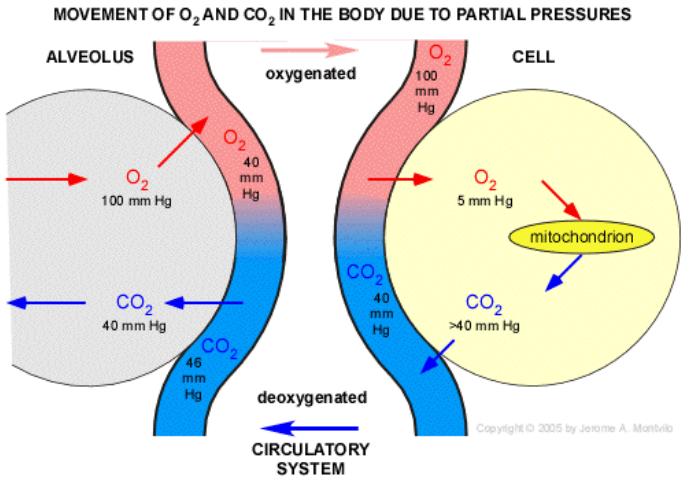


Gas exchange at lungs (Alveoli Gas Exchange)

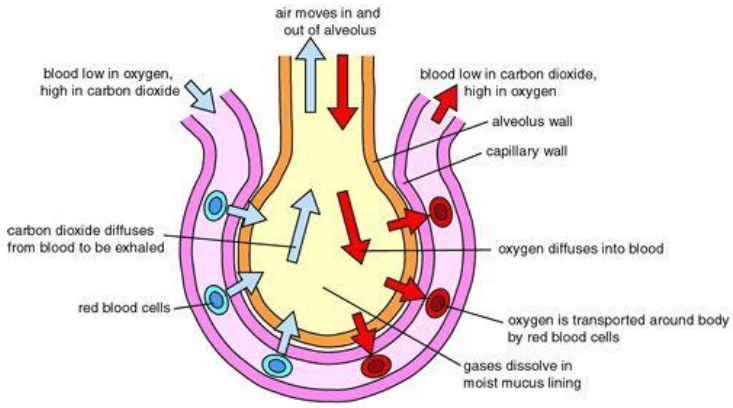
There are numerous **alveoli** - air sacs, supplied with gases via a system of tubes (**trachea**, splitting into two**bronchi** - one for each lung - and numerous **bronchioles**) connected to the outside by the mouth and nose.

These alveoli provide a massive surface area through which gases can diffuse. These gases diffuse a very short distance between the alveolus and the blood because the lining of the lung and the capillary are both only one cell thick.

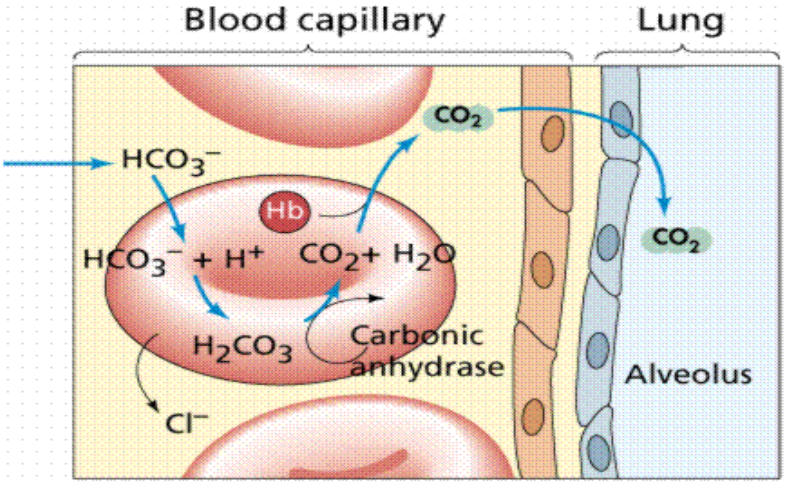
The blood supply is extensive, which means that oxygen is carried away to the cells as soon as it has diffused into the blood. Ventilation movements also maintain the concentration gradients because air is regularly moving in and out of the lungs.



Gas exchange across capillary and alveolus walls.



Diffusion is the movement of materials from a higher to a lower concentration. The differences between oxygen and carbon dioxide concentrations are measured by partial pressures. The greater the difference in partial pressure the greater the rate of diffusion.



- In the alveoli capillaries, bicarbonate combines with a hydrogen ion (proton) to form carbonic acid, which breaks down into carbon dioxide and water. The carbon dioxide then diffuses into the alveoli and out of the body with the next exhalation..

Transport of Oxygen By Blood

Oxygen is transported in two forms in the blood:

1. Physically dissolved in plasma (2 %)
   - Compared to carbon dioxide, oxygen is relatively insoluble in plasma
   - 100 ml blood contains 0.3 ml of oxygen at PO2= 100 mmHg

2. Chemically bound to the hemoglobin molecule (Hb) in the red blood cells (98 %)

Hb can combine rapidly and reversibly with oxygen. The reversibility of this reaction allows oxygen to be released to the tissues.

$$Hb + O_2 \leftrightarrow HbO_2$$

deoxyhemoglobin a.k.a reduced Hb — oxyhemoglobin

- Each gram of Hb can combine with 1.34 ml of oxygen. Normally, blood contains ≈ 15g Hb/100ml of blood [or 150g/L]. Hence theoxygen carrying capacity of Hbis 15 X 1.34 = 20 ml oxygen/100 ml blood.
- The amount of oxygen in the blood (sum of both forms, dissolved and bound to hemoglobin) is called the oxygen content of blood and is described in ml O2per 100 ml blood (or volume %).
- The O2 content of arterial blood (CaO2) is ≈20 vol% ; the O2content of venous blood (CvO2) ≈15 vol%.Therefore, each time blood circulates through the circulation, 5 vol% of oxygen is taken up by the tissues

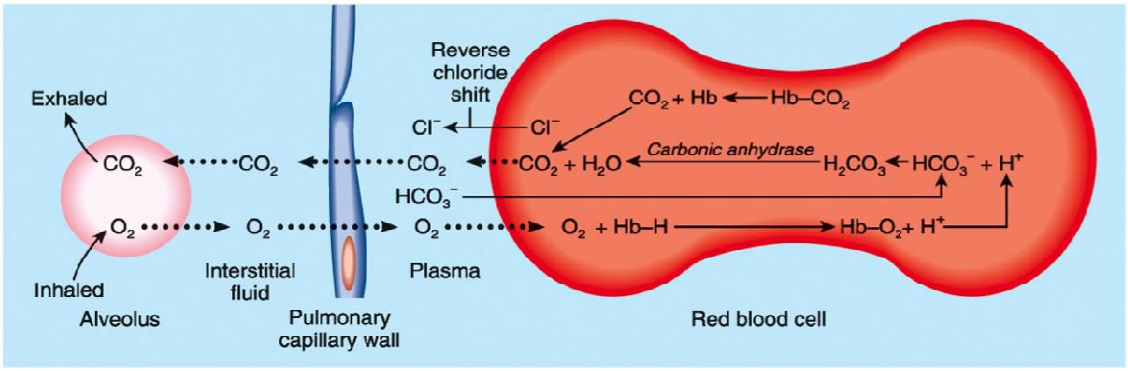
Gas exchange at tissues

Respiratory pigments increase the oxygen-carrying capacity of the blood. Humans have the red-colored pigment hemoglobin as their respiratory pigment. Hemoglobin increases the oxygen-carrying capacity of the blood between 65 and 70 times. Oxygen concentration in cells

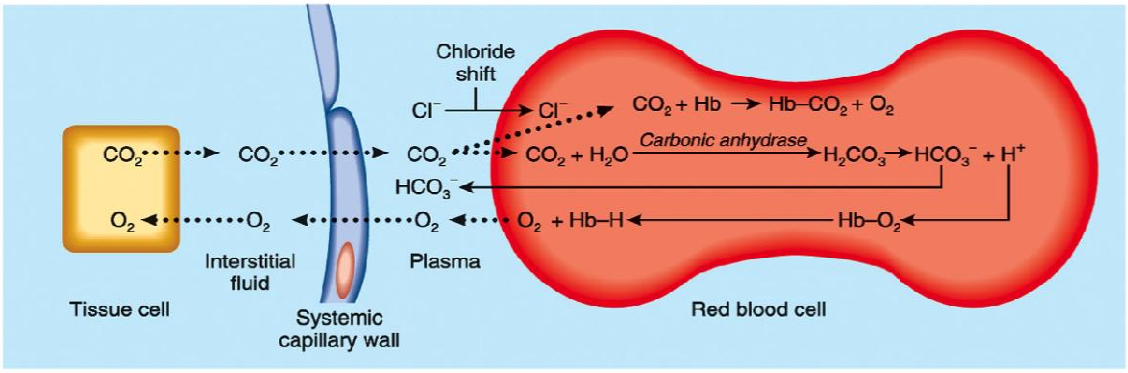
is low (when leaving the lungs blood is 97% saturated with oxygen), so oxygen diffuses from the blood to the cells when it reaches the capillaries.

Carbon dioxide concentration in metabolically active cells is much greater than in capillaries, so carbon dioxide diffuses from the cells into the capillaries. Water in the blood combines with carbon dioxide to form bicarbonate. This removes the carbon dioxide from the blood so diffusion of even more carbon dioxide from the cells into the capillaries continues yet still manages to "package" the carbon dioxide for eventual passage out of the body.

- This reaction also occurs outside the red blood cells, in the plasma, but is much slower due to the lack of carbonic anhydrase.
- The hydrogen ions, formed from the dissociated carbonic acid, combine with the haemoglobin in the red blood cell.
- Bicarbonate ions diffuse out of the red blood cell into the plasma whilst chloride ions (Cl^-) diffuse in to take their place. This is known as the chloride shift.



(a) Exchange of O_2 and CO_2 in pulmonary capillaries (external respiration)

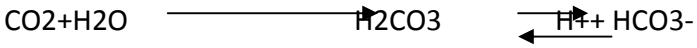


(b) Exchange of O_2 and CO_2 in systemic capillaries (internal respiration)

Carbon dioxide transport from tissues to lungs

There are 3 ways in which carbon dioxide is transported in the blood:

1. DISSOLVED CO_2
   - Carbon dioxide is much more soluble in blood than oxygen
   - About 5 % of carbon dioxide is transported unchanged, simply dissolved in the plasma
2. BOUND TO HAEMOGLOBIN AND PLASMA PROTEINS
   - Carbon dioxide combines reversibly with haemoglobin to form carbaminohaemoglobin. Carbon dioxide does not bind to iron, as oxygen does, but to amino groups on the polypeptide chains of haemoglobin.
   - Carbon dioxide also binds to amino groups on the polypeptide chains of plasma proteins
   - About 10 % of carbon dioxide is transported bound to haemoglobin and plasma proteins
3. BICARBONATE IONS (HCO_3^-)
   - The majority of carbon dioxide is transported in this way
   - Carbon dioxide enters red blood cells in the tissue capillaries where it combines with water to form carbonic acid (H_2CO_3). This reaction is catalysed by the enzyme carbonic anhydrase (C.A.), which is found in the red blood cells. Carbonic acid then dissociates to form bicarbonate ions (HCO_3^-) and hydrogen ions (H^+).



Factors that affect the transport of gases

- lower pH- **lowering** of **blood pH** (making blood more acidic)caused by presence of H+ ions from lactic acid or carbonic acid,**reduces affinity of Hb for O2**
- **increased** blood **temperature-reduces haemoglobin affinity for O2,**hence more O2 is delivered to warmed-up tissue
- increased levels of CO2 and lower O2 - the **higher CO2 concentration** in tissue,the **less the affinity of Hb for O2,** so the harder the tissue is working, the more O2 is released

Factors affecting alveolar PO2 and PCO2

- PO2 and PCO2 of inspired air
- alveolar ventilation rate of air exchange
- Rate of CO2 production and O2 use by tissue -gas pressure of venous blood

Factors affecting gas exchanges in alveoli

- Gas partial pressure --- mountain sickness
- Surface area for gas exchange--- emphysema
- Diffusion distance ---- pulmonary edema
- Rate and depth of breath --- high anatomical dead space, low RR

Oxygen transport in the blood

- O2 from the alveoli diffuse into the blood
- Then O2 enters the RBC and binds to hemoglobin
- 2% of O2 is dissolved in plasma while 98% is bound to Hb ◊ oxyHb
- The binding Hb to O2 is reversible

Control of Respiration

Muscular contraction and relaxation controls the rate of expansion and constriction of the lungs. These muscles are stimulated by nerves that carry messages from the part of the brain that controls breathing, the medulla. Two systems control breathing: an automatic response and a voluntary response. Both are involved in holding your breath.

Although the automatic breathing regulation system allows you to breathe while you sleep, it sometimes malfunctions. Apnea involves stoppage of breathing for as long as 10 seconds, in some individuals as often as 300 times per night. This failure to respond to elevated blood levels of carbon dioxide may result from viral infections of the brain, tumors, or it may develop spontaneously. A malfunction of the breathing centers in newborns may result in SIDS (sudden infant death syndrome).

As altitude increases, atmospheric pressure decreases. Above 10,000 feet decreased oxygen pressures causes loading of oxygen into hemoglobin to drop off, leading to lowered oxygen levels in the blood. The result can be mountain sickness (nausea and loss of appetite). Mountain sickness does not result from oxygen starvation but rather from the loss of carbon dioxide due to increased breathing in order to obtain more oxygen.

Diseases of the Respiratory System

Many diseases affect the condition of the airways

- Asthma narrows the airways by causing allergy-induced spasms of surrounding muscles or by clogging the airways with mucus.
- Bronchitis is an inflammatory response that reduces airflow and is caused by long-term exposure to irritants such as cigarette smoke, air pollutants, or allergens.

Cystic fibrosis is a genetic defect that causes excessive mucus production that clogs the airways.

Unit 2

Cardiovascular physiology: Pressure, flow and resistance. Anatomy of heart. Physiology of the cardiac muscle, automacity of the cardiac muscle contraction, excitation contraction coupling, relationship between cardiac cycle, heart sound, ventricular volumes and the ECG, control of cardiac function and output. The arterial system, venous system, the microcirculation and mechanics of capillary fluid exchange. Control of blood flow to the tissues. Portal circulations. Arterial pressure and its regulation. Hypertension, congestive heart disease, atherosclerosis and myocardial infarction.

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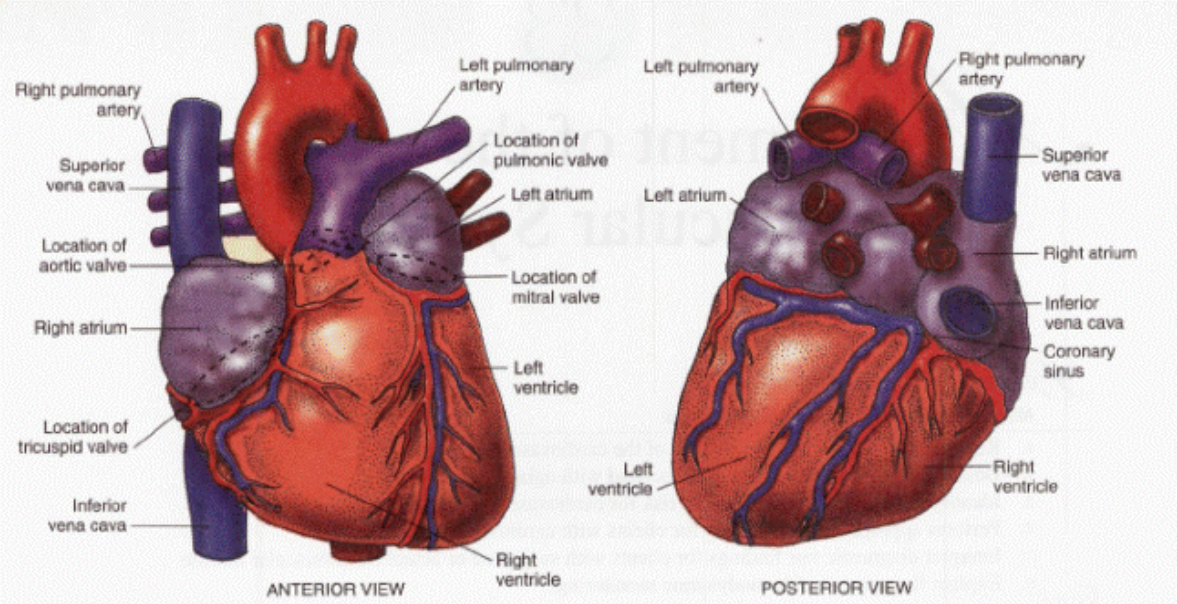
Cardiovascular Physiology

HEART

Structure. The human heart is a cone-shaped, hollow, muscular organ located in the mediastinum between the lungs. It is approximately the size of an adult fist. The heart rests on the diaphragm, tilting forward and to the left in the client's chest. This small organ must pump continuously. Each beat of the heart pumps approximately 60 mL of blood, or approximately 5 L/min. During strenuous physical activity, the heart can double the amount of blood pumped to meet the increased oxygen needs of the peripheral tissues.

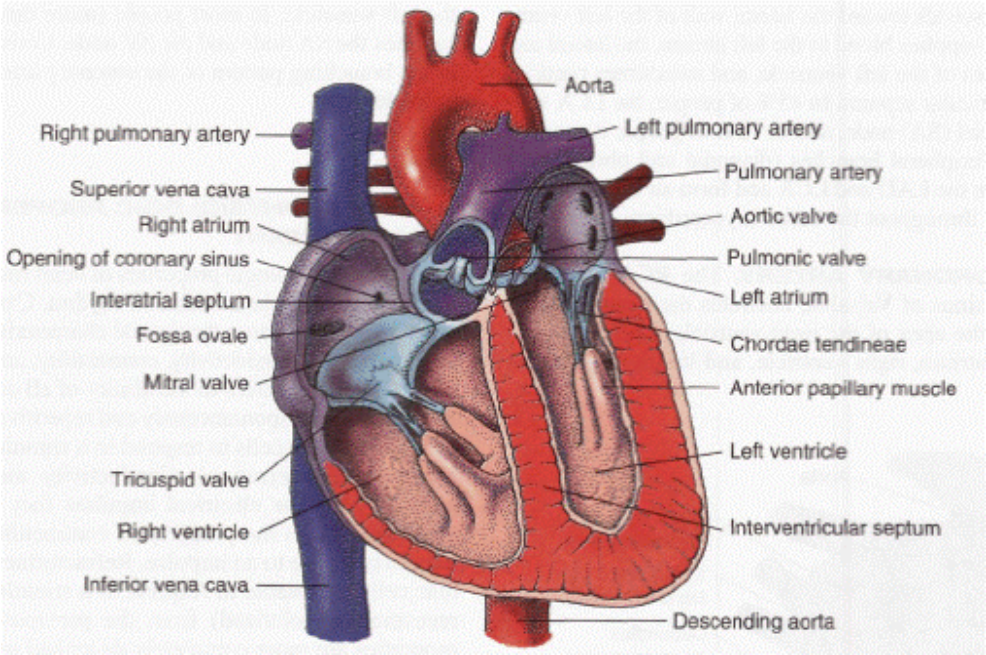


Surface anatomy of the heart.

The heart is encapsulated by a protective covering called the pericardium. Cardiac muscle tissue is composed of three layers: epicardium, myocardium, and endocardium. The epicardium, the outer surface, is a thin, transparent tissue. The myocardium, the middle layer, is composed of striated muscle fibers interlaced into bundles. This layer is responsible for the contractile force of the heart. The innermost layer, the endocardium, is composed of endothelial tissue. This tissue lines the inside of the chambers of the heart and covers the four heart valves.

CHAMBERS OF THE HEART

A muscular wall (septum), separates the heart into two halves: right and left. Each half has an upper chamber (atrium) and a lower chamber (ventricle).

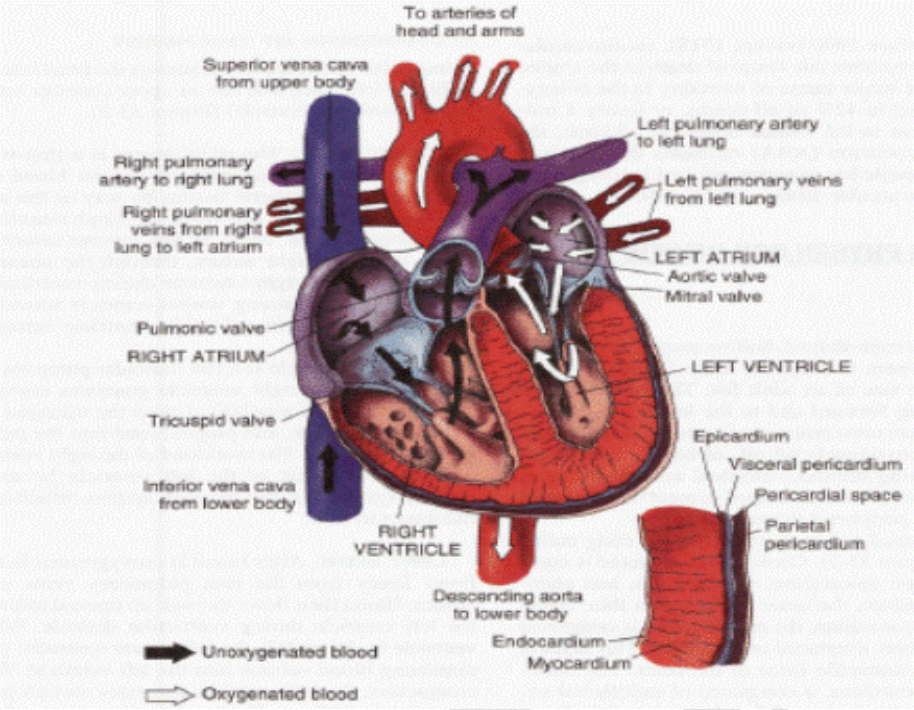


RIGHT SIDE. The right atrium is a thin-walled structure that receives deoxygenated venous blood (venous return) from all peripheral tissues by way of the superior and inferior venae cavae and from the heart muscle by way of the coronary sinus.

Most of this venous return flows passively from the right atrium, through the opened tricuspid valve, and to the right ventricle during ventricular diastole, or filling. The remaining venous return is actively propelled by the right atrium into the right ventricle during atrial systole, or contraction.

The right ventricle is a flat muscular pump located behind the sternum. The right ventricle generates enough pressure (approximately 25 mm Hg) to close the tricuspid valve, open the pulmonic valve, and propel blood into the pulmonary artery and the lungs. The workload of the right ventricle is light compared with that of the left ventricle because the pulmonary system is a low-pressure system, which imposes less resistance to flow.

LEFT SIDE. After blood is reoxygenated in the lungs, it flows freely from the four pulmonary veins into the left atrium. Blood then flows through an opened mitral valve into the left ventricle during ventricular diastole. When the left ventricle is almost full, the left atrium contracts, pumping the remaining blood volume into the left ventricle. With systolic contraction, the left ventricle generates enough pressure (approximately 120 mm Hg) to close the mitral valve and open the aortic valve. Blood is propelled into the aorta and into thesystemic arterial circulation.



The left ventricle is ellipsoid in shape and is the largest and most muscular chamber of the heart. Its wall is two to three times the thickness of the right ventricular wall. The left ventricle must generate a higher pressure than the right ventricle because it must contract against a high-pressure systemic circulation, which imposes a greater resistance to flow.

Blood is propelled from the aorta throughout the systemic circulation to the various tissues of the body; blood returns to the right atrium because of pressure differences. The pressure of blood in the aorta of a young adult averages approximately 100 to 120 mm Hg, whereas the pressure of blood in the right atrium averages about 0 to 5 mm Hg. These differences in pressure produce a pressure gradient, with blood flowing from an area of higher pressure to an area of lower pressure. The heart and vascular structures are responsible for maintaining these pressures.

HEART VALVES

The four cardiac valves are responsible for maintaining the forward flow of blood through the chambers of the heart. These valves open and close passively in response to pressure and volume changes within the cardiac chambers. The cardiac valves are classified into two types: atrioventricular (AV) valves and semilunar valves. Both AV valves are supported by chordae tendineae, which keep them from everting into the atria during systole.

ATRIOVENTRICULAR VALVES.

The AV valves separate the atria from the ventricles. The tricuspid valve is composed of three leaflets and separates the right atrium from the right ventricle. The mitral (bicuspid) valve is composed of two leaflets and separates the left atrium from the left ventricle.

During ventricular diastole, the valves act as funnels and facilitate the flow of blood from the atria to the ventricles. During systole, the valves close to prevent the backflow (re-gurgitation) of blood into the atria.

SEMILUNAR VALVES. There are two semilunar valves: the pulmonic valve and the aortic valve. The pulmonic valve separates the right ventricle from the pulmonary artery. The aortic valve separates the left ventricle from the aorta. Each semilunar valve consists of three cuplike cusps, or pockets, around the inside wall of the artery. These cusps prevent blood from flowing back into the ventricles during ventricular diastole. During ventricular systole, these valves are open to permit blood flow into the pulmonary artery and the aorta.

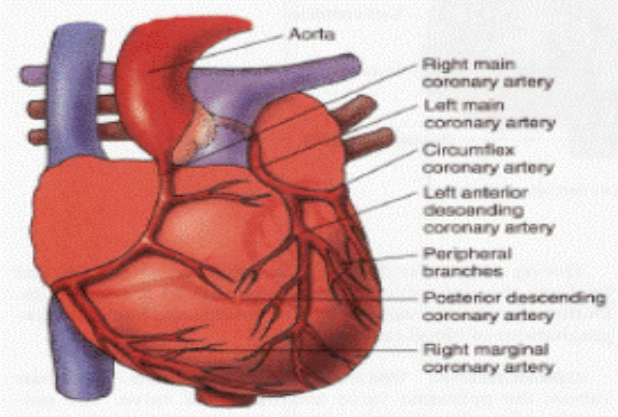
CORONARY ARTERIES

The heart muscle receives blood to meet its metabolic needs through the coronary arterial system . The coronary arteries originate from an area on the aorta just beyond the aortic valve. There are two main coronary arteries: the left coronary artery (LCA) and the right coronary artery (RCA). Coronary artery blood flow to the myocardium occurs primarily during diastole, when coronary vascular resistance is minimized. To maintain adequate blood flow through the coronary arteries, diastolic blood pressure must be at least 60 mm Hg.

LEFT CORONARY ARTERY.

The LCA divides into two branches: the left anterior descending (LAD) and the circumflex coronary artery (LCX). The LAD branch descends toward the anterior wall and the apex of the left ventricle. It supplies blood to portions of the left ventricle, ventricular septum, chordae tendineae, papillary muscle, and right ventricle.

The LCX descends toward the lateral wall of the left ventricle and apex. It supplies blood to the left atrium, the lateral and posterior surfaces of the left ventricle, and sometimes portions of the interventricular septum. In 45% of people, the LCX supplies the sinoatrial (SA) node, and in 10% of people it supplies the AV node. Peripheral branches (diagonal and obtuse marginal) arise from the LAD and LCX and form an abundant network of vessels throughout the entire myocardium.



RIGHT CORONARY ARTERY. The RCA originates from the right sinus of Valsalva, encircles the heart, and descends toward the apex of the right ventricle.

The RCA supplies the right atrium, right ventricle, and inferior portion of the left ventricle. In most people (more than 50%), the RCA supplies the SA node and the AV node. Considerable variation in the branching pattern of the coronary arteries exists among individuals.

■ **FUNCTION**

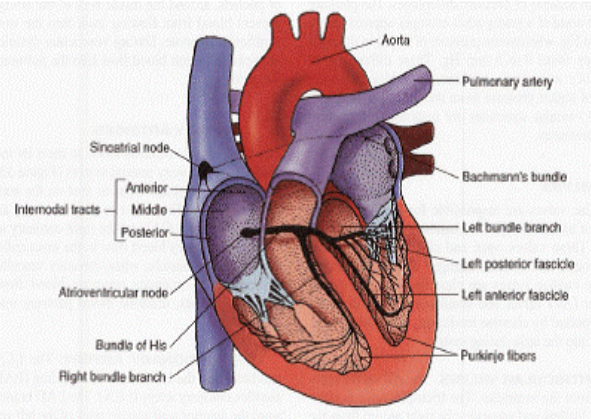
■ **ELECTROPHYSIOLOGIC PROPERTIES OF THE HEART**

The electrophysiologic properties of heart muscle are responsible for regulating heart rate and rhythm. Cardiac muscle cells are unique and possess the special characteristics of automaticity, excitability, conductivity, contractility, and refractoriness.

Automaticity refers to the ability of all cardiac cells to initiate an impulse spontaneously and repetitively. Excitability is the ability of the cells to respond to a stimulus by initiating an impulse (depolarization). Conductivity means that cardiac cells transmit the electrical impulses they receive.

Because the cells possess the property of contractility, they also contract in response to an impulse. Refractoriness means that cardiac cells are unable to respond to a stimulus until they have recovered (repolarized) from the previous stimulus. .

CONDUCTION SYSTEM OF THE HEART



The cardiac conduction system is composed of specialized tissue capable of rhythmic electrical impulse formation. It can conduct impulses much more rapidly than other cells located in the myocardium. The SA node, located at the junction of the right atrium and the superior vena cava, is considered the main regulator of heart rate. The SA node is composed of pacemaker cells, which spontaneously initiate impulses at a rate of 60 to 100 times per minute and myocardial working cells, which transmit the impulses to the surrounding atrial muscle. An impulse from the SA node initiates the process of depolarization and hence the activation of all myocardial cells. The impulse travels through both atria to the atrioventricular (AV) node located in the junctional area. After the impulse reaches the AV node, conduction of the impulse is delayed briefly. This delay allows the atria to contract completely before the ventricles are stimulated to contract. The intrinsic rate of the AV node is 40 to 60 beats/min.

The Bundle of His is a continuation of the AV node and is located in the interventricular septum. It divides into the right and left bundle branches. The bundle branches extend downward through the ventricular septum and fuse with the Purkinje fiber system. The Purkinje fibers are the terminal branches of the conduction system and are responsible for carrying the wave of depolarization to both ventricular walls. Purkinje fibers can act as an intrinsic pacemaker, but their discharge rate is only 20 to 40 beats/min. Thus these intrinsic pacemakers seldom initiate an electrical impulse.

SEQUENCE OF EVENTS DURING THE CARDIAC CYCLE

The phases of the cardiac cycle are generally described in relation to changes in pressure and volume in the left ventricle during filling (diastole) and ventricular contraction (systole). Diastole, normally about two thirds of the cardiac cycle, consists of relaxation and

filling of the atria and ventricles, whereas systole consists of the contraction and emptying of the atria and ventricles.

Cardiac muscle contraction results from the release of large numbers of calcium ions from the sarcoplasmic reticulum. These ions diffuse into the myofibril sarcomere (the basic contractile unit of the myocardial cell). Calcium ions promote the interaction of actin and myosin protein filaments, causing these filaments to link and overlap. Cross-bridges, or linkages, are formed as the protein filaments slide over or overlap each other. These cross-bridges act as force-generating sites. The sliding of these protein filaments of multiple myofibril sarcomeres shortens the sarcomeres, producing myocardial contraction. Cardiac muscle relaxes when calcium ions are pumped back into the sarcoplasmic reticulum, causing a decrease in the number of calcium ions around the myofibrils. This reduced number of ions causes the protein filaments to disengage or dissociate, the sarcomere to lengthen, and the muscle to relax.

MECHANICAL PROPERTIES OF THE HEART

The electrical and mechanical properties of cardiac muscle determine the function of the cardiovascular system. The heart is able to adapt to various pathophysiologic conditions (e.g., stress, infections, and hemorrhage) to maintain adequate blood flow to the various body tissues.

Blood flow from the heart into the systemic arterial circulation is measured clinically as cardiac output (CO), the amount of blood pumped from the left ventricle each minute. CO depends on the relationship between heart rate (HR) and stroke volume (SV); it is the product of these two variables:

Cardiac output = Heart rate x Stroke volume

CARDIAC OUTPUT AND CARDIAC INDEX. Cardiac output (CO) is the volume of blood (in liters) ejected by the heart each minute. In adults, the CO ranges from 4 to 7 L/min. Because cardiac output requirements vary according to body size, the cardiac index is calculated to adjust for differences in body size.

The cardiac index can be determined by dividing the CO by the body surface area. The normal range is 2.7 to 3.2 L/min/m^2 of body surface area.

HEART RATE. Heart rate refers to the number of times the ventricles contract each minute. The normal resting heart rate for an adult is between 60 and 100 beats/min.

Increases in heart rate increase myocardial oxygen demand. Heart rate is extrinsically controlled by the autonomic nervous system, which adjusts rapidly when necessary to regulate cardiac output. The parasympathetic system slows the heart rate, whereas sympathetic stimulation has an excitatory effect. An increase in circulating endogenous catecholamine (e.g., epinephrine and norepinephrine) usually causes an increase in heart rate, and vice versa.

Other factors, such as the central nervous system (CNS) and baroreceptor (pressoreceptor) reflexes, influence the effects of the autonomic nervous system on heart rate. Pain, fear, and anxiety can increase heart rate. The baroreceptor reflex acts as a negative-feedback system. If a client experiences hypotension, the baroreceptors in the aortic arch sense a lessened pressure in the blood vessels. A signal is relayed to the parasympathetic system to have less of an inhibitory effect on the sinoatrial (SA) node; this results in a reflex increase in heart rate.

STROKE VOLUME. Stroke volume is the amount of blood ejected by the left ventricle during each systole. Several variables influence stroke volume and, ultimately, CO. These variables include heart rate, preload, after load, and contractility.

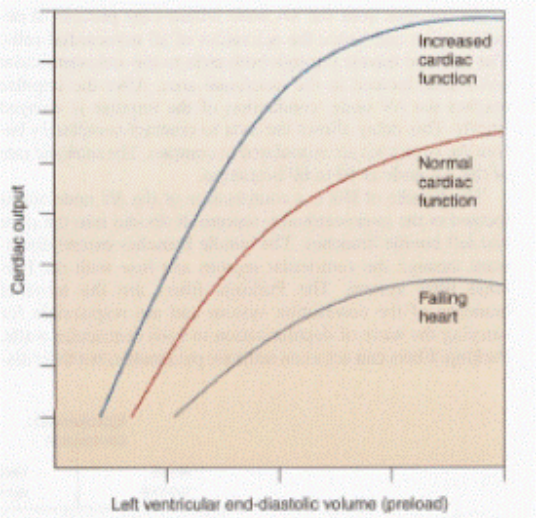
PRELOAD. Preload refers to the degree of myocardial fiber stretch at the end of diastole and just before contraction. The stretch imposed on the muscle fibers results from the volume contained within the ventricle at the end of diastole. Preload is determined by left ventricular end-diastolic (LVED) volume.

An increase in ventricular volume increases muscle fiber length and tension, thereby enhancing contraction and improving stroke volume. This statement is derived from Starling's law of the heart: the more the heart is filled during diastole (within limits), the more forcefully it contracts. However, excessive filling of the ventricles results in excessive LVED volume and pressure and a decreased cardiac output

AFTERLOAD. Another determinant of stroke volume is after load. After load is the pressure or resistance that the ventricles must overcome to eject blood through the semilunar valves and into the peripheral blood vessels. The amount of resistance is directly related to arterial blood pressure and the diameter of the blood vessels.

Impedance, the peripheral component of afterload, is the pressure that the heart must overcome to open the aortic valve. The amount of impedance depends on aortic compliance and total systemic vascular resistance, a combination of blood viscosity and arteriolar constriction. A decrease in stroke volume can result from an increase in afterload without the benefit of compensatory mechanisms.

CONTRACTILITY. Contractility also affects stroke volume and CO. Myocardial contractility is the force of cardiac contraction independent of preload. Contractility is increased by factors such as sympathetic stimulation and calcium release. Factors such as hypoxia and acidemia decrease contractility.



The heart is the pump responsible for maintaining adequate circulation of oxygenated blood around the vascular network of the body. It is a four-chamber pump, with the right side receiving deoxygenated blood from the body at low pressure and pumping it *to* the lungs (the pulmonary circulation) and the left side receiving oxygenated blood *from* the lungs and pumping it at high pressure around the body (the systemic circulation).

The myocardium (cardiac muscle) is a specialised form of muscle, consisting of individual cells joined by electrical connections. The contraction of each cell is produced by a rise in intracellular calcium concentration leading to spontaneous depolarisation, and as each cell is electrically connected to its neighbour, contraction of one cell leads to a wave of depolarisation and contraction across the myocardium.

This depolarisation and contraction of the heart is controlled by a specialised group of cells localised in the sino-atrial node in the right atrium- the *pacemaker cells*.

1. These cells generate a rhythmical depolarisation, which then spreads out over the atria to the atrio-ventricular node.

2. The atria then contract, pushing blood into the ventricles.

3. The electrical conduction passes via the Atrio-ventricular node to the bundle of His, which

divides into right and left branches and then spreads out from the base of the ventricles across the myocardium.

4. This leads to a 'bottom-up' contraction of the ventricles, forcing blood up and out into the pulmonary artery (right) and aorta (left).

5. The atria then re-fill as the myocardium relaxes.

The 'squeeze' is called systole and normally lasts for about 250ms. The relaxation period, when the atria and ventricles re-fill, is called diastole; the time given for diastole depends on the heart rate.

The ECG

The Electrocardiograph (ECG) is clinically very useful, as it shows the electrical activity within the heart, simply by placing electrodes at various points on the body surface. This enables clinicians to determine the state of the conducting system and of the myocardium itself, as damage to the myocardium alters the way the impulses travel through it.

When looking at an ECG, it is often helpful to remember that an upward deflection on the ECG represents depolarisation moving *towards* the viewing electrode, and a downward deflection represents depolarisation moving *away* from the viewing electrode. Below is a normal lead II ECG.

- The P wave represents atrial depolarisation- there is little muscle in the atrium so the deflection is small.
- The Q wave represents depolarisation at the bundle of His; again, this is small as there is little muscle there.
- The R wave represents the main spread of depolarisation, from the inside out, through the base of the ventricles. This involves large ammounts of muscle so the deflection is large.
- The S wave shows the subsequent depolarisation of the rest of the ventricles upwards from the base of the ventricles.
- The T wave represents repolarisation of the myocardium after systole is complete. This is a relatively slow process- hence the smooth curved deflection.

The Heart Sounds

The closure of the heart valves and the contraction of the heart muscle produce sounds that can be heard through the thoracic wall by the unaided ear, although they can be heard better when amplified by a stethoscope. The sounds of the heart may be represented as lubb-dubb-pause-lubb-dubb-pause. The lubb sound indicates the closing of the valves between the atria and ventricles and the contracting ventricles; the dubb sound indicates the closing of the semilunar valves. In addition, there may also be cardiac murmurs, especially when the valves are abnormal. Some heart murmurs, however, may also occur in healthy persons, mainly during rapid or pronounced cardiac action. The study of heart sounds and murmurs furnishes valuable information to physicians regarding the condition of the heart muscle and valves.

The Heartbeat

The heart muscle pumps the blood through the body by means of rhythmical contractions (systole) and relaxations or dilations (diastole). The heart's left and right halves work almost synchronously. When the ventricles contract (systole), the valves between the atria and the ventricles close as the result of increasing pressure, and the valves to the pulmonary artery and the aorta open. When the ventricles become flaccid during diastole, and the pressure decreases, the reverse process takes place.

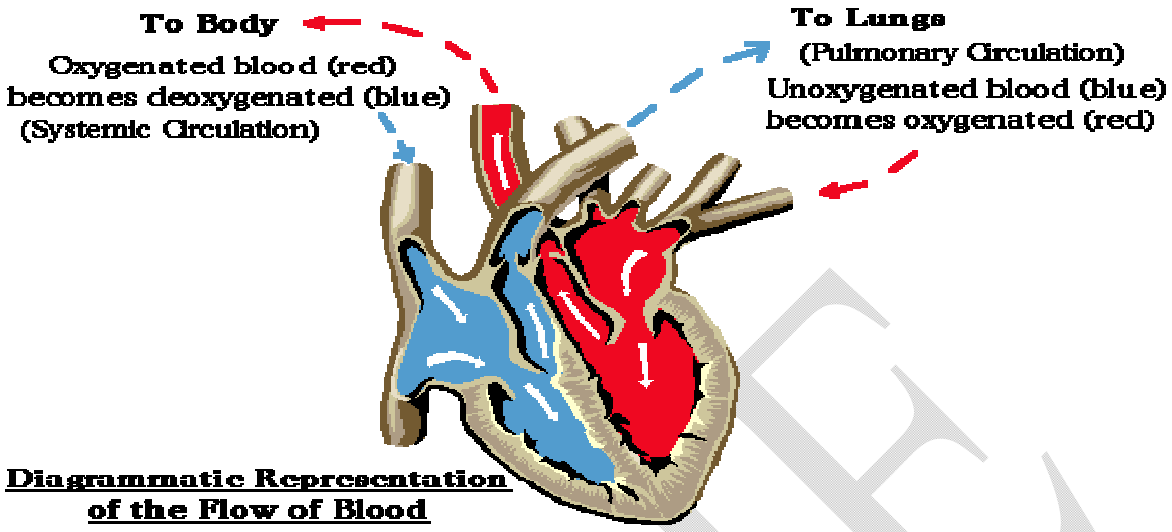
The Pulmonary Circulation

From the right atrium the blood passes to the right ventricle through the tricuspid valve, which consists of three flaps (or cusps) of tissue. The tricuspid valve remains open during diastole, or ventricular filling. When the ventricle contracts, the valve closes, sealing the opening and preventing backflow into the right atrium. Five cords attached to small muscles, called papillary muscles, on the ventricles' inner surface prevent the valves' flaps from being forced backward.

From the right ventricle blood is pumped through the pulmonary or semilunar valve, which has three half-moon-shaped flaps, into the pulmonary artery. This valve prevents backflow from the artery into the right ventricle. From the pulmonary artery blood is pumped to the lungs where it releases carbon dioxide and picks up oxygen.

The Systemic Circulation

From the lungs, the blood is returned to the heart through pulmonary veins, two from each lung. From the pulmonary veins the blood enters the left atrium and then passes through the mitral valve to the left ventricle.



Diagrammatic Representation of the Flow of Blood

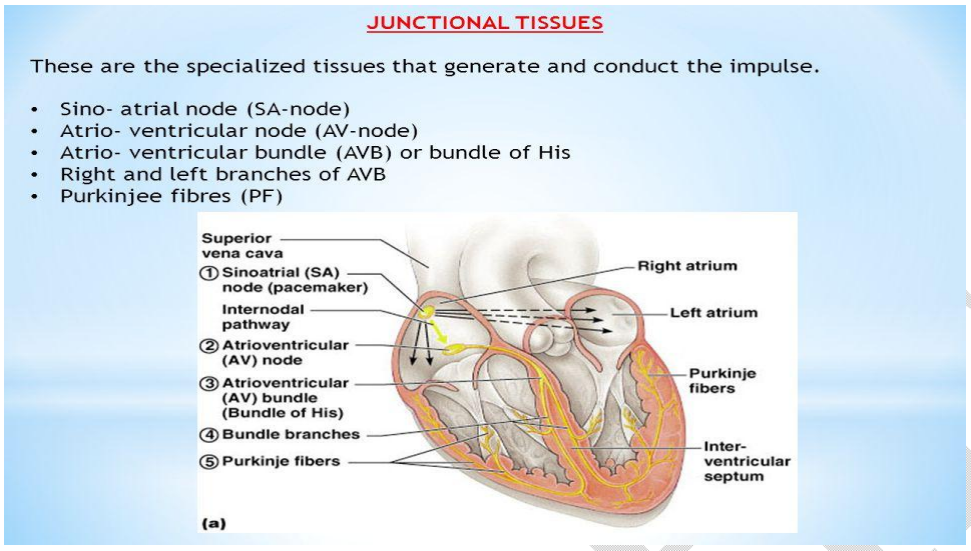
As the ventricles contract, the mitral valve prevents backflow of blood into the left atrium, and blood is driven through the aortic valve into the **aorta, the major artery that supplies blood to the entire body**. The aortic valve, like the pulmonary valve, has a semilunar shape.

The aorta has many branches, which carry the blood to various parts of the body. Each of these branches in turn has branches, and these branches divide, and so on until there are literally millions of small blood vessels. The smallest of these on the arterial side of the circulation are called arterioles. They contain a great deal of smooth muscle, and because of their ability to constrict or dilate, they play a major role in regulating blood flow through the tissues.

Special junctional tissue of the heart

The junctional tissues is a network of fibers that transmit the electrical signal between the atria and ventricles of the heart. They are the atrioventricular node and the bundle of His. They, along with the sinoatrial node, form the excitoconductory system of the heart. The rhythm of the healthy heart is given by the sinoatrial node (about 70 80 bpm, which is normal). If this node doesn't work, then the atrioventricular node (40 bpm) takes over, and gives a slower rhythm. Finally, if the av node doesn't work either, the His bundle takes over, with an even slower rhythm (25 bpm). All 3 of them cooperate to transmit the electrical signal, contracting the miocardium as an end result, but only one of them can be the regulatory center, regulating the rhythm (physiologically the sinoatrial node, but in some pathologies the other ones take over). So to resume, the junctional tissues have the role of conducting

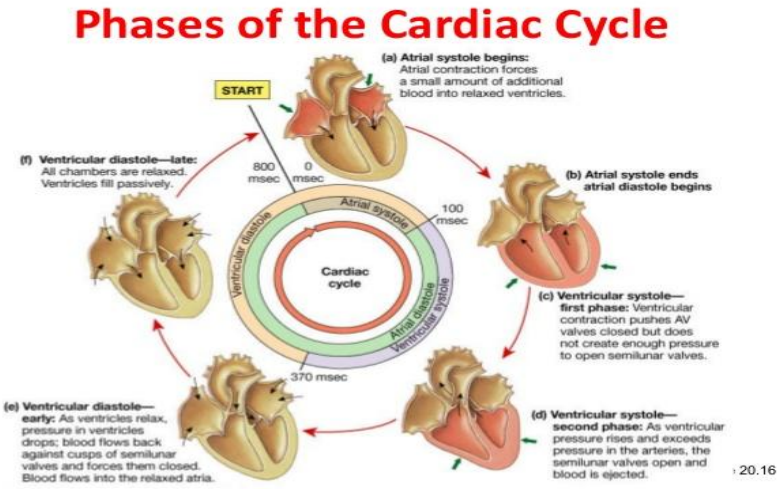
electricity through the heart, under the control of the sinoatrial node, but in some pathological cases they might have to substitute the lack of control by imposing a rhythm for themselves (much slower and less efficient)



CARDIAC CYCLE

Definition

Cardiac cycle is defined as the succession of (sequence of) **coordinated events** taking place in the heart during each beat. Each heartbeat consists of two major periods called systole and diastole. During systole,heart contracts and pumps the blood through arteries. During diastole, heart relaxes and blood is filled in the heart. All these changes are repeated during everyheartbeat, in a cyclic manner.



Events of cardiac cycle

Events of cardiac cycle are classified into two:

1. Atrial events

2. Ventricular events.

DIVISIONS AND DURATION OF CARDIAC CYCLE

When the heart beats at a normal rate of 72/minute, duration of each cardiac cycle is about 0.8 second.

ATRIAL EVENTS

Atrial events are divided into two divisions:

1. Atrial systole = 0.11 (0.1) sec

2. Atrial diastole = 0.69 (0.7) sec.

VENTRICULAR EVENTS

Ventricular events are divided into two divisions:

1. Ventricular systole = 0.27 (0.3) sec
2. Ventricular diastole = 0.53 (0.5) sec.

In clinical practice, the term 'systole' refers to ventricular systole and 'diastole' refers to ventricular diastole. Ventricular systole is divided into two subdivisions and ventricular diastole is divided into five subdivisions.

Ventricular Systole

Time (second)

1. Isometric contraction = 0.05
2. Ejection period = 0.22

Ventricular Diastole

1. Protodiastole = 0.04
2. Isometric relaxation = 0.08
3. Rapid filling = 0.11
4. Slow filling = 0.19
5. Last rapid filling = 0.11

Among the atrial events, atrial systole occurs during the last phase of ventricular diastole. Atrial diastole is not considered as a separate phase, since it coincides with the whole of ventricular systole and earlier part of ventricular diastole.

DESCRIPTION OF ATRIAL EVENTS

ATRIAL SYSTOLE

Atrial systole is also known as **last rapid filling phase** or **presystole.** It is usually considered as the last phase of ventricular diastole. Its duration is 0.11 second. During this period, only a small amount, i.e. 10% of blood is forced from atria into ventricles. Atrial systole is not essential for the maintenance of circulation. Many persons with atrial fibrillation survive for years, without suffering from circulatory insufficiency. However, such persons feel difficult to cope up with physical stress like exercise.

Pressure and Volume Changes

During atrial systole, the intra-atrial pressure increases.Intraventricular pressure and ventricular volume also
increase but slightly.

Fourth Heart Sound

Contraction of atrial musculature causes the production of fourth heart sound.

ATRIAL DIASTOLE

After atrial systole, the atrial diastole starts. Simultaneously,
ventricular systole also starts. Atrial diastole lasts for about 0.7 sec (accurate duration is 0.69 sec).This long atrial diastole is necessary because, this is the period during which atrial filling takes place. Right atrium receives deoxygenated blood from all over the
body through superior and inferior venae cavae. Left atrium receives oxygenated blood from lungs through pulmonary veins.

Atrial Events Vs Ventricular Events

Out of 0.7 sec of atrial diastole, first 0.3 sec (0.27 sec accurately) coincides with ventricular systole. Then,ventricular diastole starts and it lasts for about 0.5 sec (0.53 sec accurately). Later part of atrial diastole coincides with ventricular diastole for about 0.4 sec. So,the heart relaxes as a whole for 0.4 sec.

ISOMETRIC CONTRACTION PERIOD

Isometric contraction period in cardiac cycle is the first phase of ventricular systole. It lasts for 0.05 second.Isometric contraction is the type of muscular contraction characterized by increase in tension, without any change in the length of muscle fibers. Isometric contraction of ventricular muscle is also called **isovolumetric contraction.**Immediately after atrial systole, the atrioventricular valves are closed due to increase in ventricular
pressure. Semilunar valves are already closed. Now,ventricles contract as closed cavities, in such a way that there is no change in the volume of ventricular chambers or in the length of muscle fibers. Only the tension increases in ventricular musculature.
Because of increased tension in ventricular musculature during isometric contraction, the pressure increases sharply inside the ventricles.

First Heart Sound

Closure of atrioventricular valves at the beginning of this
phase produces first heart sound.

Significance of Isometric Contraction

During isometric contraction period, the ventricular pressure increases greatly. When this pressure increases above the pressure in the aorta and pulmonary artery, the semilunar valves open. Thus,
the pressure rise in ventricle, caused by isometric contraction is responsible for the **opening of semi-lunar valves,** leading to ejection of blood from the ventricles into aorta and pulmonary artery.

EJECTION PERIOD

Due to the opening of semilunar valves and isotonic contraction of ventricles, blood is ejected out of both the ventricles. Hence, this period is called ejection period.Duration of this period is 0.22 second. Ejection period is of two stages:

1. ***First Stage or Rapid Ejection Period***

First stage starts immediately after the opening of semilunar valves. During this stage, a large amount of blood is rapidly ejected from both the ventricles. It lasts for 0.13 second.

2. ***Second Stage or Slow Ejection Period***

During this stage, the blood is ejected slowly with much less force. Duration of this period is 0.09 second.

End-systolic Volume

Ventricles are not emptied at the end of ejection period and some amount of blood remains in each ventricle.Amount of blood remaining in ventricles at the end of ejection period (i.e. at the end of systole) is called endsystolic volume. It is 60 to 80 mL per ventricle.

Measurement of end-diastolic volume

Endsystolic volume is measured by radionuclide angiocardiography(multigated acquisition – MUGA scan)

and **echocardiography.** It is also measured by cardiac **catheterization,** computed tomography **(CT) scan** and

magnetic resonance imaging **(MRI)**

Ejection Fraction

Ejection fraction refers to the fraction (or portion) of enddiastolic

volume (see below) that is ejected out by each ventricle per beat. From 130 to 150 mL of enddiastolic

volume, 70 mL is ejected out by each ventricle (stroke

volume). Normal ejection fraction is 60% to 65%.

BLOOD PRESSURE

Definition: The pressure exerted by the blood on the walls of the blood vessels.

Blood pressure (BP) is the pressure of circulating blood on the walls of blood vessels. When used without further specification, "blood pressure" usually refers to the pressure in large arteries of the systemic circulation. Blood pressure is usually expressed in terms of the systolic pressure (maximum during one heart beat) over diastolic pressure (minimum in between two heart beats) and is measured in millimeters of mercury (mmHg), above the surrounding atmospheric pressure (considered to be zero for convenience).

May be regarded as

1.Arterial B.P.
2.Venous B.P.
3.Capillary B.P.

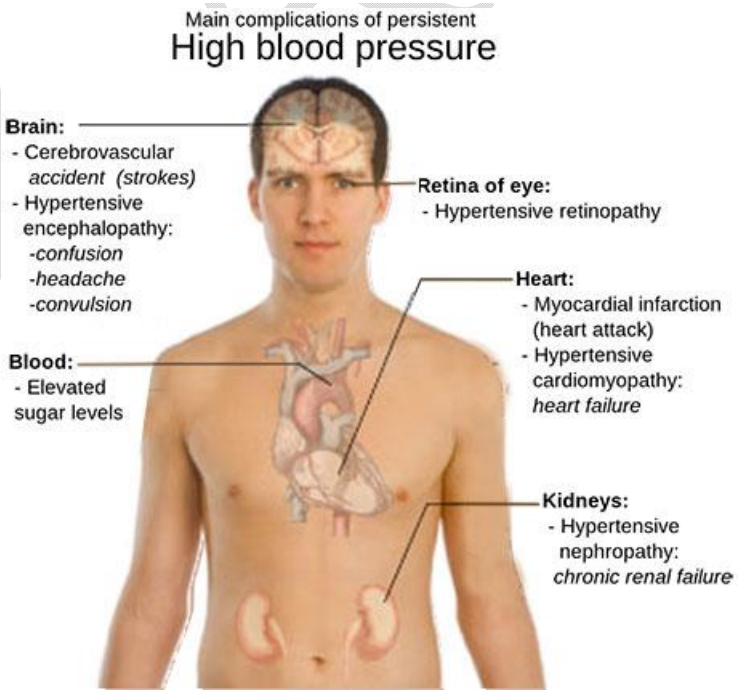
The phases of the blood pressure are

- **Systolic B.P**: max pressure during the systole of the heart
- **Diastolic B.P**: min pressure during the diastole of the heart

- **Pulse pressure**: diff. between systolic and diastolic pressure Normal range of B.P. (mmHg) Standard B.P. (mmHg) SP110-145125 DP70-9080 PP40-5540

Physiological Variations in BP

- Age:
  - SBP and DBP gradually rise with age (after about 30 years), the SBP more so and more sustained than the DBP
- Sex:
  - the rise in BP with age is greater in males
- Circadian variation (diurnal variation):
  - lowest during sleep (nocturnal dip) and highest in the mornings after waking up
- Increased transiently during physical stress (e.g. muscular exercise), mental stress(anger, apprehension, resentment, mental concentration), emotional excitement
- The effect of Gravity: When erect, BP in any vessel varies in relation to the vertical distance from the heart level



SIGNIFICANCE OF BLOOD PRESSURE:

Systolic pressure: It indicates the force with which the heart works. It is highly variable Increases with excitement, exercise, meals and decreases with shock, sleep, rest etc.

Diastolic pressure: It indicates the extent of peripheral resistance (peripheral resistance that heart has to withstand) It is generally constant Variations in diastolic pressure are of great clinical importance

Pulse pressure: It indicates the strength of stroke volume of cardiac output. Does not have any clinical significance

Methods of Blood Pressure measurement:

It is commonly measured by sphygmomanometer Two methods for the measurement of B.P:

- Palpatory method
- Ausclatory method

Palpatory method:

The cuff is tied at the lower part of upper arm. The arterial pulse at the wrist is felt BP is raised upto 200mmHg till pulse stops The bulb is unscrewed and pressure is lowered till reappearance of the pulse The reading in the sphygmomanometer is recorded when the pulse reappears It gives the systolic pressure.

Ausulatory method: The cuff is tied and the pressure is raised up to 200 mmHg. The stethoscope is placed in cubital fossa at the bifurcation of the brachial artery The first sound heard at lowering of the pressure indicates the systolic pressure Now the pressure is further lowered, the disappearance of the sound indicates the diastolic pressure.

Factors maintaining B.P:

Heart: The force and frequency of the heart affects the pumping of the heart which indeed maintains the B.P.

Cardiac output: Depends on the venous return and pumping capacity of the heart.

Peripheral resistance: It is governed by the elasticity and lumen of the blood vessels as well as the velocity and viscosity of the blood. The peripheral resistance maintains the diastolic blood pressure.

Blood volume: Total circulating blood also affects the B.P. the increase in the volume raise where as decrease in volume lower the pressure

Vasomotor center**:** Situated in medulla oblongata It receives the information about the pressure through baroreceptors and chemoreceptors

REGULATION

The endogenous regulation of arterial pressure is not completely understood, but the following mechanisms of regulating arterial pressure have been well-characterized:

- Baroreceptor reflex: Baroreceptors in the high pressure receptor zones detect changes in arterial pressure. These baroreceptors send signals ultimately to the medulla of the brain stem, specifically to the rostral ventrolateral medulla (RVLM). The medulla, by way of the autonomic nervous system, adjusts the mean arterial pressure by altering both the force and speed of the heart's contractions, as well as the systemic vascular resistance. The most important arterial baroreceptors are located in the left and right carotid sinuses and in the aortic arch.[48]
- Renin-angiotensin system (RAS): This system is generally known for its long-term adjustment of arterial pressure. This system allows the kidney to compensate for loss in blood volume or drops in arterial pressure by activating an endogenous vasoconstrictor known as angiotensin II.
- Aldosterone release: This steroid hormone is released from the adrenal cortex in response to angiotensin II or high serum potassium levels. Aldosterone stimulates sodium retention and potassium excretion by the kidneys. Since sodium is the main ion that determines the amount of fluid in the blood vessels by osmosis, aldosterone will increase fluid retention, and indirectly, arterial pressure.
- Baroreceptors in low pressure receptor zones (mainly in the venae cavae and the pulmonary veins, and in the atria) result in feedback by regulating the secretion of antidiuretic hormone (ADH/Vasopressin), renin and aldosterone. The resultant increase in blood volume results in an increased cardiac output by the Frank–Starling law of the heart, in turn increasing arterial blood pressure.

These different mechanisms are not necessarily independent of each other, as indicated by the link between the RAS and aldosterone release. When blood pressure falls many physiological cascades commence in order to return the blood pressure to a more appropriate level.

1. The blood pressure fall is detected by a decrease in blood flow and thus a decrease in Glomerular filtration rate (GFR).
2. Decrease in GFR is sensed as a decrease in Na^+ levels by the macula densa.
3. The macula densa cause an increase in Na^+ reabsorption, which causes water to follow in via osmosis and leads to an ultimate increase in plasma volume. Further, the macula densa releases adenosine which causes constriction of the afferent arterioles.
4. At the same time, the juxtaglomerular cells sense the decrease in blood pressure and release renin.
5. Renin converts angiotensinogen (inactive form) to angiotensin I (active form).
6. Angiotensin I flows in the bloodstream until it reaches the capillaries of the lungs where angiotensin converting enzyme (ACE) acts on it to convert it into angiotensin II.
7. Angiotensin II is a vasoconstrictor which will increase bloodflow to the heart and subsequently the preload, ultimately increasing the cardiac output.
8. Angiotensin II also causes an increase in the release of aldosterone from the adrenal glands.
9. Aldosterone further increases the Na^+ and H_2O reabsorption in the distal convoluted tubule of the nephron.

Hypertension

Blood pressure is the force exerted by the blood against the walls of blood vessels, and the magnitude of this force depends on the cardiac output and the resistance of the blood vessels.4

The blood flowing inside vessels exerts a force against the walls - this is blood pressure.

More information on the biology and physics of normal blood pressure is available, along with details of how blood pressure is measured, what normal measurements look like, and how they change with age and exercise.

Hypertension is defined as having a blood pressure higher than 140 over 90 mmHg, with a consensus across medical guidelines.1,5

This means the systolic reading (the pressure as the heart pumps blood around the body) is over 140 mmHg (millimeters of mercury) and/or the diastolic reading (as the heart relaxes and refills with blood) is over 90 mmHg.

This threshold has been set to define hypertension for clinical convenience as patients experience benefits once they bring their blood pressure below this level.6

However, medical experts consider high blood pressure as having a continuous relationship to cardiovascular health.1,6 They believe that, to a point, the lower the blood pressure the better (down to levels of 115-110 mmHg systolic, and 75-70 mmHg diastolic).1

This view has led the American Heart Association (AHA), for example, to define the following ranges of blood pressure (in mmHg):

- Normal blood pressure is below 120 systolic and below 80 diastolic
- Prehypertension is 120-139 systolic or 80-89 diastolic
- Stage 1 high blood pressure (hypertension) is 140-159 systolic or 90-99 diastolic
- Stage 2 high blood pressure (hypertension) is 160 or higher systolic or 100 or higher diastolic
- Hypertensive crisis (a medical emergency) is when blood pressure is above 180 systolic or above 110 diastolic.

What is congestive heart failure?

Congestive heart failure (CHF) is a chronic progressive condition that affects the pumping power of your heart muscles. While often referred to simply as "heart failure," CHF specifically refers to the stage in which fluid builds up around the heart and causes it to pump inefficiently.

You have four heart chambers. The upper half of your heart has two atria, and the lower half of your heart has two ventricles. The ventricles pump blood to your body's organs and tissues, and the atria receive blood from your body as it circulates back from the rest of your body.

CHF develops when your ventricles can't pump blood in sufficient volume to the body. Eventually, blood and other fluids can back up inside your:

Lungs
Abdomen
Liver
Lower body
CHF can be life-threatening. If you suspect you or someone near you has CHF, seek immediate medical treatment.

TYPES

What are the most common types of CHF?

Left-sided CHF is the most common type of CHF. It occurs when your left ventricle doesn't properly pump blood out to your body. As the condition progresses, fluid can build up in your lungs, which makes breathing difficult.

There are two kinds of left-sided heart failure:

Systolic heart failure occurs when the left ventricle fails to contract normally. This reduces the level of force available to push blood into circulation. Without this force, the heart can't pump properly.

Diastolic failure, or diastolic dysfunction, happens when the muscle in the left ventricle becomes stiff. Because it can no longer relax, the heart can't quite fill with blood between beats.

Right-sided CHF occurs when the right ventricle has difficulty pumping blood to your lungs. Blood backs up in your blood vessels, which causes fluid retention in your lower extremities, abdomen, and other vital organs.

It's possible to have left-sided and right-sided CHF at the same time. Usually, the disease starts in the left side and then travels to the right when left untreated.

Congestive heart failure stages

Stage	Main symptoms	Outlook
Class I	You don't experience any symptoms during typical physical activity.	CHF at this stage can be managed through lifestyle changes, heart medications, and monitoring.
Class II	You're likely comfortable at rest, but normal physical activity may cause fatigue, palpitations, and shortness of breath.	CHF at this stage can be managed through lifestyle changes, heart medications, and careful monitoring.
Class III	You're likely comfortable at rest, but there's a noticeable limitation of physical activity. Even mild exercise may cause fatigue, palpitations, or shortness of breath.	Treatment can be complicated. Talk with your doctor about what heart failure at this stage may mean for you.
Class IV	You're likely unable to carry on any amount of physical activity without symptoms, which are present even at rest.	There's no cure for CHF at this stage, but there are still quality-of-life and palliative care options. You'll want to discuss the potential benefits and risks of each with your doctor.

CAUSES AND RISKS

What are the causes of CHF?

CHF may result from other health conditions that directly affect your cardiovascular system. This is why it's important to get annual checkups to lower your risk for heart health problems, including high blood pressure (hypertension), coronary artery disease, and valve conditions.

Hypertension

When your blood pressure is higher than normal, it may lead to CHF. Hypertension occurs when your blood vessels become restricted by cholesterol and fat. This makes it harder for your blood to pass through them.

Coronary artery disease

Cholesterol and other types of fatty substances can block the coronary arteries, which are the small arteries that supply blood to the heart. This causes the arteries to become narrow. Narrower coronary arteries restrict your blood flow and can lead to damage in your arteries.

Valve conditions

Your heart valves regulate blood flow through your heart by opening and closing to let blood in and out of the chambers. Valves that don't open and close correctly may force your ventricles to work harder to pump blood. This can be a result of a heart infection or defect.

Other conditions

While heart-related diseases can lead to CHF, there are other seemingly unrelated conditions that may increase your risk, too. These include diabetes, thyroid disease, and obesity. Severe infections and allergic reactions may also contribute to CHF.

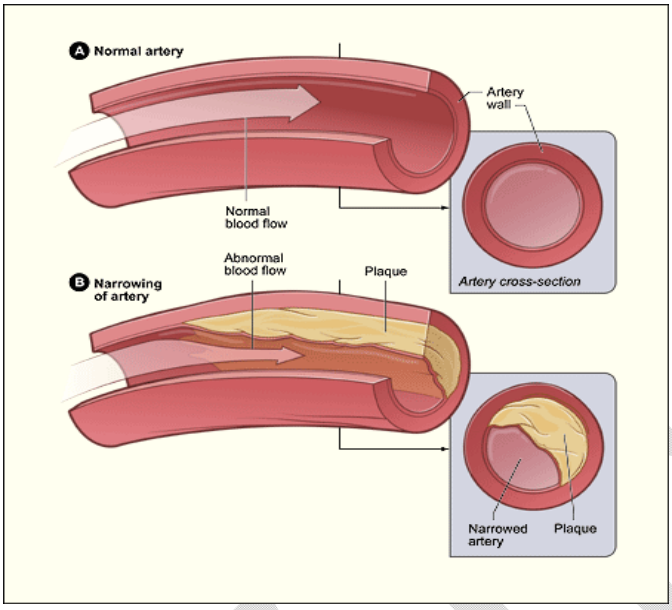
Atherosclerosis

Atherosclerosis is a disease in which plaque builds up inside your arteries. Arteries are blood vessels that carry oxygen-rich blood to your heart and other parts of your body.

Plaque is made up of fat, cholesterol, calcium, and other substances found in the blood. Over time, plaque hardens and narrows your arteries. This limits the flow of oxygen-rich blood to your organs and other parts of your body.

Atherosclerosis can lead to serious problems, including heart attack, stroke, or even death.

Figure A shows a normal artery with normal blood flow. The inset image shows a cross-section of a normal artery. Figure B shows an artery with plaque buildup. The inset image shows a cross-section of an artery with plaque buildup.



Myocardial Infarction (MI)

The pathogenesis can include:

- Occlusive intracoronary thrombus - a thrombus overlying on plaque causes 75% of myocardial infarctions, with superficial plaque erosion present in the remaining 25%.
- Vasospasm - with or without coronary atherosclerosis and possible association with platelet aggregation.
- Emboli - from left sided mural thrombosis, vegetative endocarditis, or paradoxic emboli from the right side of heart through a patent foramen ovale.

In 2000, the European Society of Cardiology and the American College of Cardiology Consensus group redefined myocardial infarction, with the definition being based on myocyte necrosis as determined by troponins in the clinical setting of ischaemia. (White and Chew, 2008)

The molecular events during MI relate to the initial ischemic event, reperfusion, and subsequent inflammatory response. Up to 6 hours following the initial ischemic event, most cell loss occur via apoptosis. After that, necrosis predominates. Ischemic endothelial cells express adhesion molecules that attract neutrophils that subsequently migrate into damaged myocardium.

The gross morphologic appearance of a myocardial infarction can vary. Patterns include:

- Transmural infarct - involving the entire thickness of the left ventricular wall from endocardium to epicardium, usually the anterior free wall and posterior free wall and septum with extension into the RV wall in 15-30%. Isolated infarcts of RV and right atrium are extremely rare.
- Subendocardial infarct - multifocal areas of necrosis confined to the inner 1/3-1/2 of the left ventricular wall. These do not show the same evolution of changes seen in a transmural MI.

Gross morphologic changes evolve over time as follows:

Time from Onset	Gross Morphologic Finding
18 - 24 Hours	Pallor of myocardium
24 - 72 Hours	Pallor with some hyperemia
3 - 7 Days	Hyperemic border with central yellowing
10 - 21 Days	Maximally yellow and soft with vascular margins
7 weeks	White fibrosis

Microscopic morphologic changes evolve over time as follows:

Time from Onset	Microscopic Morphologic Finding
1 - 3 Hours	Wavy myocardial fibers but no inflammatory cells
2 - 3 Hours	Staining defect in myocardial fiber cytoplasm with tetrazolium or basic fuchsin dye

4 - 12 Hours	Coagulation necrosis with loss of cross striations, contraction bands, edema, hemorrhage, and early neutrophilic infiltrate
18 - 24 Hours	Continuing coagulation necrosis, pyknosis of nuclei, and marginal contraction bands
24 - 72 Hours	Total loss of nuclei and cross striations along with heavy neutrophilic infiltrate
3 - 7 Days	Macrophage and mononuclear infiltration begins, fibrovascular response begins
10 - 21 Days	Fibrovascular response with prominent granulation tissue containing capillaries and fibroblasts
7 Weeks	Fibrosis with dense collagenous connective tissue and no inflammation

The above gross and microscopic changes over time can vary. In general, a larger infarct will evolve through these changes more slowly than a small infarct. Clinical complications of myocardial infarction will depend upon the size and location of the infarction, as well as pre-existing myocardial damage. Complications can include:

- Arrhythmias and conduction defects, with possible "sudden death"
- Extension of infarction, or re-infarction
- Congestive heart failure (pulmonary edema)
- Cardiogenic shock
- Pericarditis
- Mural thrombosis, with possible embolization
- Myocardial wall rupture, with possible tamponade
- Papillary muscle rupture, with possible valvular insufficiency
- Ventricular aneurysm formation

Sudden death occurs within an hour of onset of symptoms. Such an occurrence often complicates ischemic heart disease. Such patients tend to have severe coronary atherosclerosis (>75% lumenal narrowing). Often, a complication such as coronary thrombosis or plaque hemorrhage or rupture has occurred. The mechanism of death is usually an arrhythmia.

Unit 3

Renal physiology: Anatomy of the kidney and the nephron. Regulation of renal blood flow. Cell biology of the Bowmans' capsule. Physiology of glomerular filtration and GFR. Tubular processing of the glomerular filtrate. Micturition reflex and voluntary control of micturition. Regulation of ECF electrolyte and water content, blood volume and long term blood pressure. Blood buffer systems, renal and pulmonary control of blood pH, renal clearance. Assessment of kidney function. Acidosis and alkalosis. Glomerular nephritis, renal failure, dialysis and diuretics.

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Renal Physiology

KIDNEY

The **kidneys** are organs that serve several essential regulatory roles in vertebrate animals. They are essential in the urinary system and also serve homeostatic functions such as the regulation of electrolytes, maintenance of acid–base balance, and regulation of blood pressure (via maintaining salt and water balance). They serve the body as a natural filter of the blood, and remove wastes, which are diverted to the urinary bladder. In producing urine, the kidneys excrete wastes such as urea and ammonium, and they are also responsible for the reabsorption of water, glucose, and amino acids. The kidneys also produce hormones including calcitriol, erythropoietin, and the enzyme renin. Located at the rear of the abdominal cavity in the retroperitoneum, the kidneys receive blood from the paired renal arteries, and drain into the pairedrenal veins. Each kidney excretes urine into a ureter, itself a paired structure that empties into the urinary bladder.

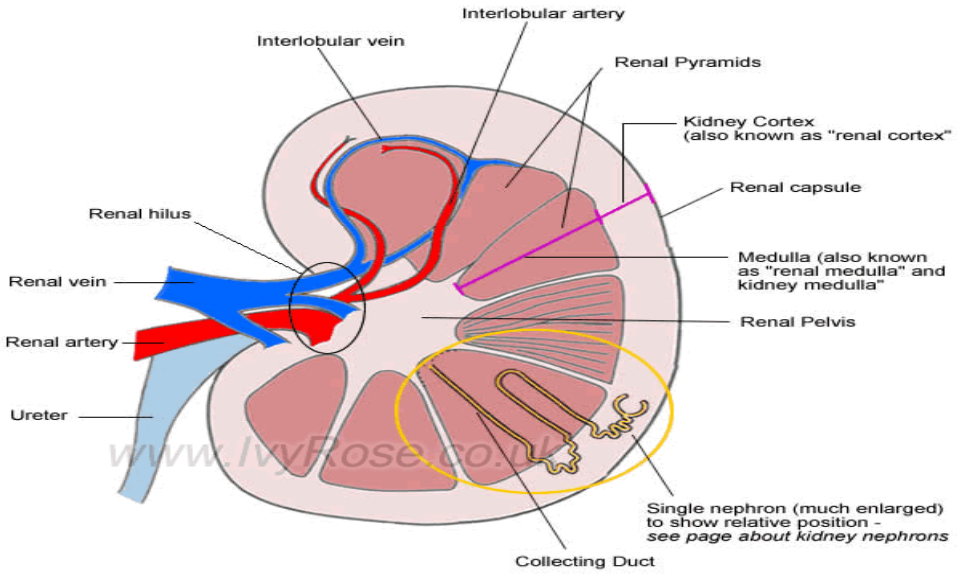
Structure

The kidneys are bean-shaped with the convex side of each organ located laterally and the concave side medial. The indentation on the concave side of the kidney, known as the renal hilus, provides a space for the renal artery, renal vein, and ureter to enter the kidney.

A thin layer of fibrous connective tissue forms the renal capsule surrounding each kidney. The renal capsule provides a stiff outer shell to maintain the shape of the soft inner tissues.

Deep to the renal capsule is the soft, dense, vascular **renal cortex**. Seven cone-shaped renal pyramids form the renal medulla deep to the renal cortex. The **renal pyramids** are aligned with their bases facing outward toward the renal cortex and their apexes point inward toward the center of the kidney.

Each apex connects to a minor calyx, a small hollow tube that collects urine. The minor calyces merge to form 3 larger major calyces, which further merge to form the hollow renal pelvis at the center of the kidney. The renal pelvis exits the kidney at the renal hilus, where urine drains into the ureter.



- *The cortex is characterized by renal corpuscles and their associated tubules.*
- *The medulla is characterized by straight tubules, collecting ducts, and a special capillary network, the vasa recta.*
- *The number of lobes in a kidney equals the number of medullary pyramids. Each human kidney contains 8 to 18 lobes. The lobes of the kidney are further subdivided into lobules. A lobule consists of a collecting duct and all the nephrons that it drains*

Blood Supply

1. The renal arteries branch directly from the abdominal **aorta** and enter the kidneys through the renal hilus.
2. Inside our kidneys, the **renal arteries** diverge into the smaller afferent arterioles of the kidneys.
3. Each afferent arteriole carries blood into the renal cortex, where it separates into a bundle of capillaries known as a glomerulus.
4. From the glomerulus, the blood recollects into smaller efferent arterioles that descend into the renal medulla.
5. The efferent arterioles separate into the peritubular capillaries that surround the renal tubules.
6. Next, the peritubular capillaries merge to form veins that merge again to form the large **renal vein**.
7. Finally, the renal vein exits the kidney and joins with the **inferior vena cava**, which carries blood back to the heart.

STRUCTURE OF NEPHRON

The Nephron

The nephron is the structural and functional unit of the kidney.

The **nephron** is the fundamental structural and functional unit of the kidney. Each human kidney contains approximately 2 million nephrons. Nephrons are responsible for the production of urine and correspond to the secretory part of other glands. The collecting ducts are responsible for the final concentration of the urine and are analogous to the ducts of exocrine glands that modify the concentration of the secretory product.

General Organization of the Nephron

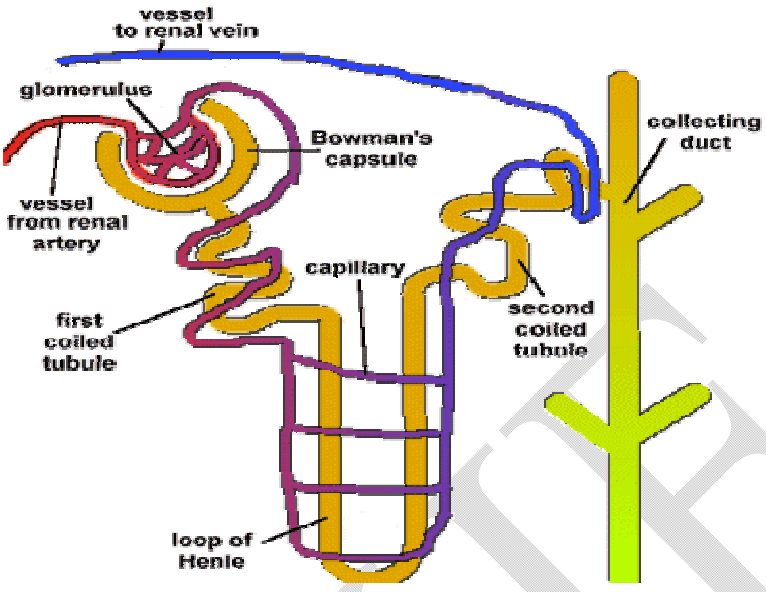
The nephron consists of the renal corpuscle and a tubule system.

As stated previously, the **renal corpuscle** represents the beginning of the nephron. It consists of the **glomerulus**, a tuft of capillaries composed of 10 to 20 capillary loops, surrounded by a double-layered epithelial cup, the renal or **Bowman's capsule**. Bowman's capsule is the initial portion of the nephron, where blood flowing through the glomerular capillaries undergoes filtration to produce the **glomerular ultrafiltrate**. The glomerular capillaries are supplied by an **afferent arteriole** and are drained by an **efferent arteriole** that then branches, forming a new capillary network to supply the kidney tubules. The site where the afferent and efferent arterioles penetrate and exit from the parietal layer of Bowman's capsule is called the **vascular pole**. Opposite this site is the **urinary pole** of the renal corpuscle, where the proximal convoluted tubule begins. Continuing from Bowman's capsule, the remaining parts of the nephron (the tubular parts) are as follows:

- **Proximal thick segment**, consisting of the proximal convoluted tubule (pars convoluta) and the proximal straight tubule (pars recta)
- **Thin segment**, which constitutes the thin part of the loop of Henle
- **Distal thick segment**, consisting of the distal straight tubule (pars recta) and the distal convoluted tubule (pars convoluta)

The **distal convoluted** tubule connects to the **collecting tubule**, often through a connecting tubule, thus forming the uriniferous tubule (i.e., the nephron plus collecting tubule).

Fig-Structure of nephron



The kidney tubule or nephron is the working unit of the kidney. There are one million of these in each kidney. Branches of the renal artery form tiny capillaries. Along the length of each capillary is a knot called a glomerulus.

The capillary entering the glomerulus is wider than the capillary leaving it. This makes the pressure inside the glomerulus high. This forces some of the blood plasma out of the vessels. Large objects like proteins and blood cells are too big to leak out. The smaller particles like water, salts, urea, glucose & amino acids leak out of the capillary and are termed the glomerular filtrate. This filtrate is collected in a cup like structure called the Bowman's capsule. This is the first part of the kidney tubule and leads into the first coiled tubule.

The cells lining the first coiled tubule actively reabsorb the nutrients and other chemicals the body needs, leaving behind the unwanted urea, salts and some water. The cells are adapted for this. They have lots of mitochondria for active transport and they have microvilli (tiny finger-like folds of the cell membrane) which increase the surface area for absorption. By the time the filtrate reaches the end of this coiled tubule, all the important chemicals (i.e. glucose, amino acids & vitamins etc) have been reabsorbed along with 99% of the water. What remains in the filtrate is the unwanted salts, urea and water, along with any other chemical the body does not need (like alcohol, drugs etc).

The rest of the kidney tubule (the loop of Henle, the second coiled tubule and the collecting duct) is designed to reabsorb some of the remaining water as necessary. The remaining fluid, called urine, passes down the collecting duct to the pelvis of the kidney and then onto the bladder (via the ureter) where it is temporarily stored.

The blood leaving the kidney differs from the blood entering the kidney in a number of ways.

Blood entering the kidney	Blood leaving the kidney
High in urea	No urea
High in oxygen	Low in oxygen (due to respiration)
No carbon dioxide	High in carbon dioxide (due to respiration)
Glucose levels high	Glucose present but lowering in concentration. (due to respiration)

Tubes of the Nephron

The tubular segments of the nephron are named according to the course that they take (convoluted or straight), location (proximal or distal), and wall thickness (thick or thin).

Beginning from Bowman's capsule, the sequential parts of the **nephrons** consist of the following tubules:

- **Proximal convoluted tubule** originates from the urinary pole of Bowman's capsule. It follows a very tortuous or convoluted course and then enters the medullary ray to continue as the proximal straight tubule.
- **Proximal straight tubule**, commonly referred to as the *thick descending limb of the loop of Henle,* descends into the medulla.
- **Thin descending limb** is the continuation of the proximal straight tubule within the medulla. It makes a hairpin turn and returns toward the cortex.
- **Thin ascending limb** is the continuation of the thin descending limb after its hairpin turn.
- **Distal straight tubule**, which is also referred to as the *thick ascending limb of the loop of Henle*, is the continuation of the thin ascending limb. The distal straight tubule ascends through the medulla and enters the cortex in the medullary ray to reach the vicinity of its renal corpuscle of origin. The distal straight tubule then leaves the medullary ray and makes contact with the vascular pole of its parent renal corpuscle. At this point, the epithelial cells of the tubule adjacent to the afferent arteriole of the glomerulus are modified to form the **macula densa**. The distal tubule then leaves the region of the corpuscle and becomes the distal convoluted tubule.
- **Distal convoluted tubule** is less tortuous than the proximal convoluted tubule; thus, in a section showing the cortical labyrinth, there are fewer distal tubule profiles than proximal tubule profiles. At its termination, the distal convoluted tubule empties into a collecting duct that lies in the medullary ray via either an **arched collecting tubule** or a shorter tubule simply called the connecting tubule.

- *The loop of Henle forms the entire U-shaped portion of a nephron.*

- The proximal straight tubule, the thin descending limb with its hairpin turn, the thin ascending limb, and the distal straight tubule are collectively called the **loop of Henle**. In some nephrons, the thin descending and ascending segments are extremely short; therefore, the hairpin turn may be made by the distal straight tubule.

- **Types of Nephrons**

- Several types of nephrons are identified, based on the location of their renal corpuscles in the cortex (see Fig. 20.3):

- **Subcapsular nephrons** or **cortical nephrons** have their renal corpuscles located in the outer part of the cortex. They have short loops of Henle, extending only into the outer medulla. They are typical of the nephrons described previously, wherein the hairpin turn occurs in the distal straight tubule.
- **Juxtamedullary nephrons** make up about one eighth of the total nephron count. Their renal corpuscles occur in proximity to the base of a medullary pyramid. They have long loops of Henle and long ascending thin segments that extend well into the inner region of the pyramid. These structural features are essential to the urine-concentrating mechanism, which is described in a further section.
- **Intermediate nephrons** or **midcortical nephrons** have their renal corpuscles in the midregion of the cortex. Their loops of Henle are of intermediate length.

MECHANISM OF URINE FORMATION

The urine is a pale yellow coloured fluid. The yellow colour is due to the presence of urochrome pigment formed from the haemoglobin of dead RBC's in the liver cells. It is acidic in nature and has a pH of 6.0. It has a faint anamalic odour due to the presence of urinod. It soon gets a strong smell of ammonia which forms as a result of degradation of urea.Daily urine output is 1.5 to 1.8 lts. The volume of urine output is directly proportional to the fluid intake.

Chemically it is formed of water 95 - 96%, urea 2%, other wastes like uric acid, hip puric acid, createnine, phosphates and oxalates 2-3%. It also contains non-nitrogenous organic compounds like vitamin C, oxalic acid and phenolic substances.

Formation of urine

- Basic function of nephrons is to clear out the blood plasma from unwanted substances. Urea, creatininie, uric acids, hippuric acids and drug remains etc cleaned by nephrons.The fluid comings out from the nephrons, containing these unwanted substances is called urine.

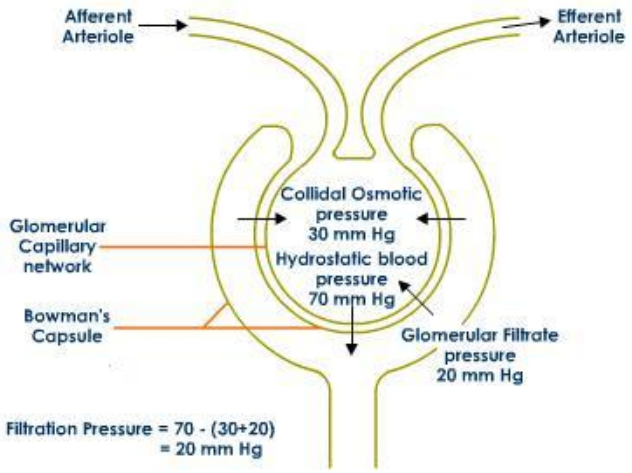
Principle Mechanism of urine formation includes three basic processes

- **Ultrafiltration** in Bowman's capsule.
- **Selective reabsorption** of wanted substances from tubular filtrate.
- **Tubular Secretion** of unwanted substances from tubular filtrate.

1. Ultra filtration

- Ultrafiltration means the filtration of blood present in golmerular capillary through glomerular capillary wall, a basement membrane and wall of Bowman's capsule.
- The filtrate is called glomerular filtrate or tubular filtrate or ultrafiltrate, which reaches the tubular lumen.
- The unfiltered volume of the blood remains the glomerular capillary which is moved to efferent arteriole.
- This membrane is almost completely impermeable to all plasma proteins.

Due to the efferent arterioles being narrower than the afferent arteriole, the blood pressure is twice that in the capillary network. Blood enters the glomerulus at a hydrostatic pressure of 60 mm Hg., to filter out some fine components of blood. The glomerular filteration pressure is about 10 mm Hg and is responsible for filtering a large amount of water, glucose, amino acids, vitamins, Na^+ and a number of harmful substances like urea, uric acid, creatinine, ammonium salts. Pigments, K^+. The proteins, fats and carbohydrates are not filtered out.



The glomerular filtrate is same as blood minus cells and proteins. It resembles the protein free plasma in composition and Osmotic pressure. About 650 ml of blood passes through the glomerular capillaries in all nephrons of both kidneys, but in one minute about 125

ml of filtrate is filtered out. So about 150 - 180 lts of nephric filtrate is formed per day but only 1.5 - 1.8 lts of urine is excreted out per day and this is called urine output.

Factor effecting GFR

- Change in renal blood flow – If BP rises than EFP would also rise. This will increase the GFR.
- Change in capillary ghdrostatic pressure .
- Change in capsular pressure.
- Change in the permeability of capillary wall or capsular wall.

Glomerular filtration rate is controlled by two intrinsic mechanisms, which provide autoregulation. They are:

1) Myogenic mechanism

2) Justaglomerular apparatus.

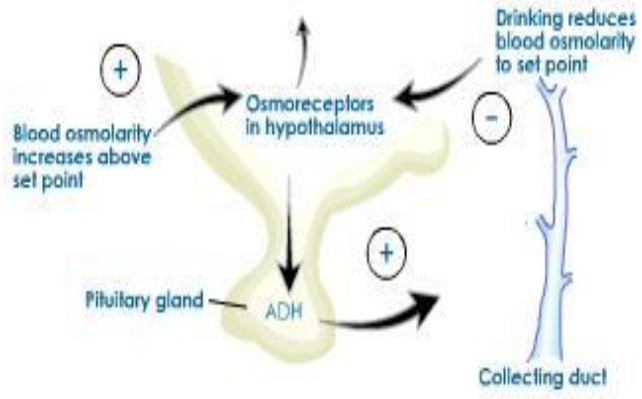
1) Myogenic mechanism

Myogenic mechanism helps to control variations of the blood flow to the glomerulus due to fluctuations in blood pressure. An increase in blood pressure makes the wall of the afferent arteriole contract thus reducing the diameter of the arteriole and increasing the resistance to flow.

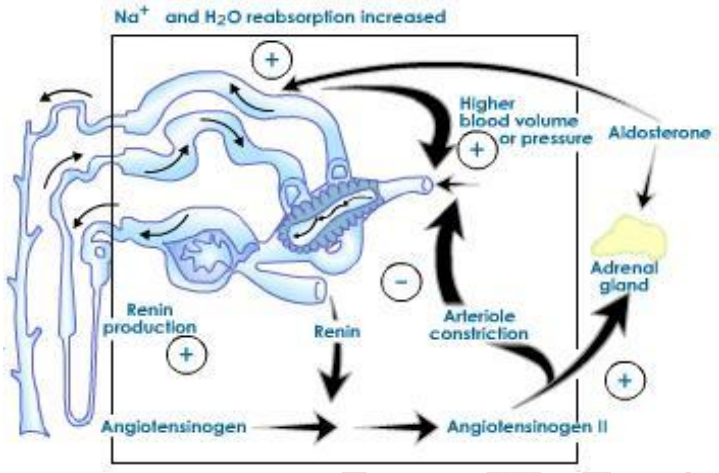
2) Juxtaglomerular apparatus

When there is a decrease in blood pressure or blood volume in the afferent arteriole of the glomerulus, the Justaglomerular Apparatus (TGA) that is situated between the afferent and efferent arterioles release an enzyme 'renin' into the blood stream. A plasma protein angiotensinogen is converted to apeptide angiotensin II by renin.

Fig: Regulation of renal function by feedback circuits:



(a) control by ADH;



(b) control by RAAS

Composition of glomerular filtrate

- The fluid that enters the PCT, is called glomerular filtrate. It contains no RBC and blood cells.
- It also does not have plasma proteins.
- But this filtrate contains other soluble substances, which are present normally in plasma.
- The substances present in filtrate are glucose, urea, amino acids, calcium ions, sodium ions, bicarbonate ions, potassium ions, protons and a large amount of water.

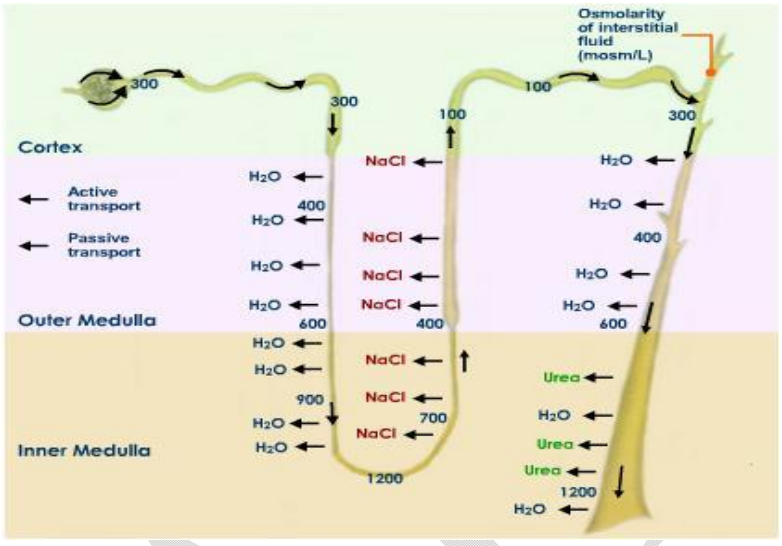
2. Selective reabsorption

This process by which only useful substances are reabsorbed from the nephric filtrate is called selective reabsorption.

- The glomerular filtrate contains some very useful substances like glucose, water and various ions.These substances are useful for the body, hence must not pass out with urine.
- Therefore these are to be reabsorbed from the tubular lumen. As the nephric filtrate moves in the nephron towards the collecting tubule, about 99% of water, whole of glucose and amino acids, most of the $Na^+$and Cl, are reabsorbed back into the blood.
- Water and some ions are reabsorbed from all parts of the nephrons .
- Almost all sugars, vitamins, amino acids and other organic nutrients are reabsorbed in PCT.

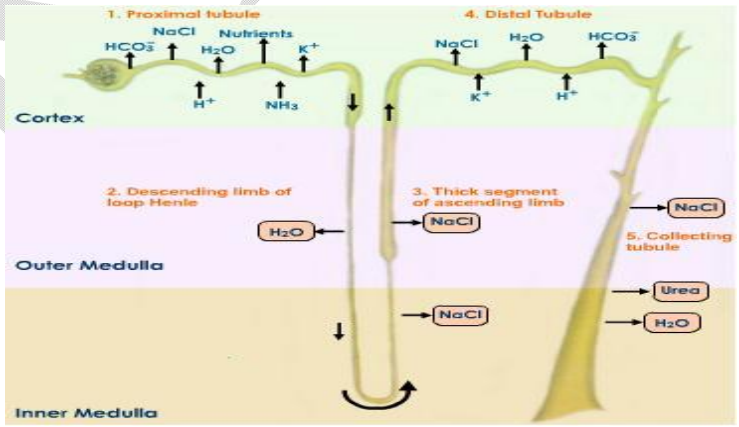
- About 99% of the filtered water is reabsorbed.
- Major amount of water is absorbed in PCT. Nephron carries out a 'counter current system' to absorb more and more water from tubular filtrate.

Fig: Water conservation and production of concentrated urine in renal tubule



The PCT actively absorbs almost whole of glucose, 75% of amino acids and Vitamin C, about 70% Na^+, about 75% of K^+ and a large amount of Ca^{++} from the glomerular filtrate. The ascending limb of Henle's loop actively reabsorbs about 25% of K^+ and some Cl^- ions. DCT and the collecting tubules actively reabsorb some Na^+ from nephric filtrate in exchange with K^+ of the interstitial fluid. The main function of reabsorption is to maintain homeostasis so that volume, electrolytic balance composition, pH and osmotic pressure of blood are kept constant.

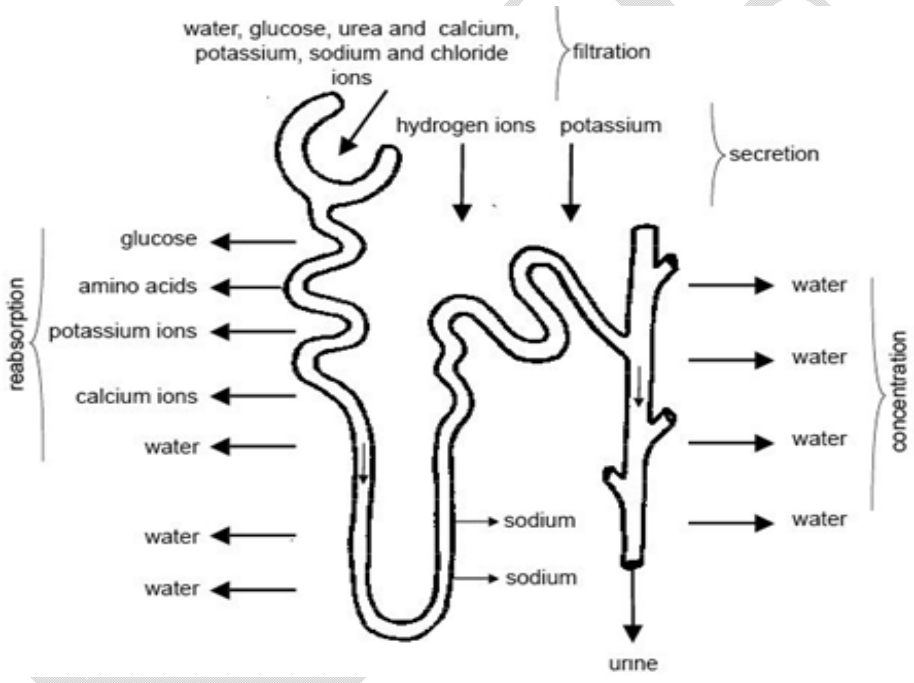
Fig: Filtration, reabsorption and secretion at different parts of the nephron



3- Tubular secretion:

- It is a process by which the glandular cells of nephron especially of DCT, extract the wastes like uric acid, creatinine, hippuric acid, K^+, H^+, ammonia from the blood in the capillaries by active transport and secrete them in the nephric filtrate.
- Most of the secretion occurs in DCT.
- In DCT, for each Na^+ ion reabsorbed, either one K^+ or one H^+ ion is secreted.
- Excess of water soluble vitamins, remains of drugs etc. are also secreted in DCT.

Fig: Tubular secretion



URINE AND ITS COMPOSITION

- As a result of all the three processes, the fluid that comes out from collecting duct is called urine.
- It is a non viscous aqueous solution, containing various impurities.

Volume

- The amount of urine passed out from the body varies from 800 ml to 2 litre. The average value is about 1.5 litre.

Specific gravity

- Its specific gravity varies between 1.001 to 1.040.
- In 'Diabetes mellitus', the specific gravity becomes very high.

Colour

- Urine has a pale lemon yellow colour.
- The colour is due to the presence of pigment called urochrome urobilin and uroerythrin.

Chemical composition of urine

- 95% water/5% solutes
- Nitrogenous waste products:
- Urea – from normal breakdown of AAs
- Uric acid – end product of nucleic acid metabolism
- Creatinine – a metabolite of creatine phosphate (regeneration of ATP—sk mm)
- Urea, Na, K, Ph, SO4, creatinine, uric acid
- Smaller amts of Ca, Mg, HCO3 ions
- A healthy adult produces:
    - 1200 ml per day (0.6% of filtrate)
    - with osmotic concentration of 800–1000 mOsm/L

Regulation of Urine Concentration and Volume

- Osmolality
    - The number of solute particles dissolved in 1L of water
    - Reflects the solution's ability to cause osmosis
- Body fluids are measured in milliosmols (mOsm)
- The kidneys keep the solute load of body fluids constant at about 300 mOsm
- This is accomplished by the countercurrent mechanism

Formation of Dilute Urine

- Filtrate is diluted in the ascending loop of Henle
- Dilute urine is created by allowing this filtrate to continue into the renal pelvis
- This will happen as long as antidiuretic hormone (ADH) is not being secreted
- Collecting ducts remain impermeable to water; no further water reabsorption occurs
- Sodium and selected ions can be removed by active and passive mechanisms
- Urine osmolality can be as low as 50 mOsm -one-sixth that of plasma

Formation of Concentrated Urine

- Antidiuretic hormone (ADH) inhibits diuresis
- This equalizes the osmolality of the filtrate and the interstitial fluid
- In the presence of ADH, 99% of the water in filtrate is reabsorbed
- ADH-dependent water reabsorption is called facultative water reabsorption
- ADH is the signal to produce concentrated urine
- The kidneys' ability to respond depends upon the high medullary osmotic gradient

Abnomalities in urine

- Metabolic errors of kidney may severely affect the composition of urine. Occurrence of ketone bodies,glucose, albumin, blood cells, excess pigments, pus cells, calculi are some of the major abnormal constituents of urine.

Some important abnormalities, have been listed below-

- **Proteinuria** – Excess protein level in urine.
- **Albuminuria** – Presence of albumin in urine.
- **Glycosuria –** Presence of glucose in urine, as in the case of Diabetes mellitus.
- **Ketnuria** – Presence of abnormally high ketone bodies.
- **Hematuria** – Presence of blood or blood cells in urine.
- **Haemoglobinura** – Presence of haemoglobin in urine.

MICTURATION

- Micturition is the act of voiding the urine.
- The release of urine is done by contraction of the smooth muscle of the urinary bladder wall and the relaxation of the skeletal muscle sphincter around the opening of the bladder.
- The gradual filling of the bladder stretches the walls of the bladder.
- The stretch receptors in the bladder wall in response generate impulses that are carried by afferent fibres to the spinal cord and also to, brain.
- Spinal cord stimulates the efferent fibres which cause the contraction of detrussor muscles, and simultaneously relaxation of internal sphincter.

Physiology of Micturation

Micturation is the discharge of urine from the bladder via the urethra. The bladder is a loose sack that can accommodate a range of volumes of urine - from 0 ml (immediately after the bladder has been emptied), to a maximum of around 300-400ml in normal adults, less in cases of children and adults of below average size. When the quantity of urine contained in the bladder exceeds that necessary to cause tension in the walls of the bladder this is communicated to the brain (i.e. the **Central Nervous System, CNS**) and is perceived consciously as a sensation recognised as due to a "full" bladder.

Urine is released from the bladder into the urethra, and then out of the body, as a result of the actions of muscles. These muscles are innervated by nerve cells called motor neuronsacting at neuromusclar junctions (NMJs).

Nervous System control of Micturation

Peripheral Nervous System (PNS) which includes all nervous system tissue outside of the brain and spinal cord, may be subdivided into the:

- **Somatic Nervous System (SNS)**, the
- **Autonomic Nervous System (ANS)**, and the
- **Enteric Nervous System (ENS)**, which relates to the nerves of the gut.

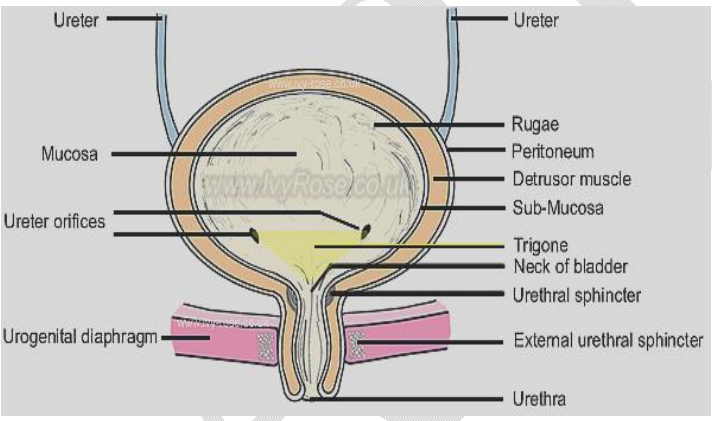
Of these, the ENS is an involuntary part of the nervous system that relates only to the gut and therefore plays no part in micturation. However, both the SNS and the ANS are involved in this process because the SNS controls skeletal (also known as striated or voluntary muscles) and the ANS controls smooth (involuntary) muscles. More specifically, the part of the ANS that controls motor neurons (and therefore ultimately muscles) consists of the **sympathetic division** and

the **parasympathetic division**. Many tissues are innervated by both of these divisions. In the cases of tissues innervated by both sympathetic and parasympathetic divisions of the ANS, the nerves of these two divisions generally have opposing effects.

Control of Muscles involved in Micturation

The **detrusor muscle** is the (smooth) muscle of the bladder wall and, together with the **urethral (internal) sphincter muscle** located at the neck of the bladder, is innervated by the ***sympathetic*** nerve fibres from the lumbar sections of spinal cord, and also by the ***parasympathetic*** nerve fibres from sacral segments 2 - 4 of the spinal cord. and these muscles are NOT under voluntary control.However, the external **urethral sphincter muscle** is under voluntary control, and as such is innervated by the SNS.

Fig: Urinary Bladder with associated muscles



Micturation Reflex

The micturation reflex is an autonomic spinal cord reflex that initiates urination.

Involuntary Action:

The bladder wall can accomodate increasing volumes of urine with little change in the tension of the bladder wall until the volume of urine reaches certain a threshold (which is typically in the range 300-400 ml for normal adults). If/when this "*threshold volume*" (of urine) for a particular individual is reached then he/she experiences the significant discomfort associated with the increased tension in the bladder wall - ***and the micturation reflex is triggered***. In this situation, micturation would occur involuntarily. That is, it would have been triggered by the Peripheral Nervous System (PNS).

Voluntary Action:

The micturation reflex can also be triggered consciously - that is, by the Cental Nervous System (CNS).

This is the more usual situation. Proof that the micturation (emptying) reflex can also be triggered by the brain/CNS is demonstrated by the fact that the bladder can be emptied at any volume.

In most normal cases micturation is voluntary (consciously triggered at the person's convenience). If not triggered voluntarily then the spinal cord reflexes that would give rise to immediate micturation may be *temporarily* inhibited by the brain until either it is appropriate to urinate, or the autonomic reflex can no-longer be inhibited.

If the autonomic reflex has been temporarily inhibited by the brain, or the micturation reflex was triggered consciously (e.g. before the volume of urine was sufficient to increase the tension in the bladder wall), then when the micturation reflex is finally triggered, it is assisted by the CNS relaxing the external urethral sphincter muscle to facilitate flow of urine from the body.

Regardless of how it is activated, once in progress, the flow of urine is aided by additional reflexes from the urethra that are stimulated by the flow of urine and which also reinforce contraction of the bladder muscle and relaxation of the sphincter muscle.

Completion of the emptying of the bladder is also facilitated by contration of the abdominal wall and pelvic floor muscles.

REGULATION OF HOMEOSTATIS BY KIDNEYS

Water Homeostasis

The kidneys are able to control the volume of **water in the body** by changing the reabsorption of water by the tubules of the nephron. Under normal conditions, the tubule cells of the nephron tubules reabsorb (via osmosis) nearly all of the water that is filtered into urine by the glomerulus.

Water reabsorption leads to very concentrated urine and the conservation of water in the body. The hormones **antidiuretic hormone (ADH) and aldosterone both increase the reabsorption of water until almost 100% of the water filtered by the nephron is returned to the blood.** ADH stimulates the formation of water channel proteins in the collecting ducts of the nephrons that permit water to pass from urine into the tubule cells and on to the blood. Aldosterone functions by increasing the reabsorption of Na+ and Cl- ions, causing more water to move into the blood via osmosis.

In situations where there is too much water present in the blood, our **heart** secretes the hormone **atrial natriuretic peptide (ANP)** in order to increase the excretion of Na+ and Cl- ions. Increased concentration of Na+ and Cl- in urine draws water into the urine via osmosis, increasing the volume of urine produced.

Acid/Base Homeostasis

The kidneys regulate the pH level of the blood by controlling the excretion of hydrogen ions (H+) and bicarbonate ions (HCO3-). Hydrogen ions accumulate when proteins are metabolized in the liver and when carbon dioxide in the blood reacts with water to form carbonic acid (H2CO3). Carbonic acid is a weak acid that partially dissociates in water to form hydrogen ions and bicarbonate ions. Both ions are filtered out of the blood in the glomerulus of the kidney, but the tubule cells lining the nephron selectively reabsorb bicarbonate ions while leaving hydrogen ions as a waste product in urine. The tubule cells may also actively secrete additional hydrogen ions into the urine when the blood becomes extremely acidic.

The reabsorbed bicarbonate ions enter the bloodstream where they can neutralize hydrogen ions by forming new molecules of carbonic acid. Carbonic acid passing through the capillaries of the **lungs** dissociates into carbon dioxide and water, allowing us to exhale the carbon dioxide.

Electrolyte Homeostasis

The kidneys maintain the homeostasis of important electrolytes by controlling their excretion into urine.

- *Sodium (Na+)*: Sodium is a vital electrolyte for muscle function, neuron function, blood pressure regulation, and blood volume regulation. Over 99% of the sodium ions passing through the kidneys are reabsorbed into the blood from tubular filtrate. Most of the reabsorption of sodium takes place in the proximal convoluted tubule and ascending loop of Henle.

- *Potassium (K+)*: Just like sodium, potassium is a vital electrolyte for muscle function, neuron function, and blood volume regulation. Unlike sodium, however, only about 60 to 80% of the potassium ions passing through the kidneys are reabsorbed. Most of the reabsorption of potassium occurs in the proximal convoluted tubule and ascending loop of Henle.

- *Chloride (Cl-)*: Chloride is the most important anion (negatively charged ion) in the body. Chloride is vital to the regulation of factors such as pH and cellular fluid balance and helps to establish the electrical potential of neurons and muscle cells. The proximal convoluted tubule and ascending loop of Henle reabsorb about 90% of the chloride ions filtered by the kidneys.

- *Calcium (Ca2+)*: Calcium is not only one of the most important minerals in the body that composes the bones and teeth, but is also a vital electrolyte. Functioning as an electrolyte, calcium is essential for the contraction of muscle tissue, the release of neurotransmitters by neurons, and the stimulation of cardiac muscle tissue in the heart. The proximal convoluted tubule and the ascending loop of Henle reabsorb most of the calcium in tubular filtrate into the blood. Parathyroid hormone increases the reabsorption of calcium in the kidneys when blood calcium levels become too low.

- *Magnesium (Mg2+)*: Magnesium ion is an essential electrolyte for the proper function of enzymes that work with phosphate compounds like ATP, DNA, and RNA. The proximal

convoluted tubule and loop of Henle reabsorb most of the magnesium that passes through the kidney.

Blood Pressure Homeostasis

The kidneys help to control blood pressure in the body by regulating the excretion of sodium ions and water and by producing the enzyme **renin.** Because blood is mostly made of water, an increased volume of water in the body results in an increase in the volume of blood in the blood vessels. Increased blood volume means that the heart has to pump harder than usual to push blood into vessels that are crowded with excess blood. Thus, increased blood volume leads to increased blood pressure. On the other hand, when the body is dehydrated, the volume of blood and blood pressure decrease.

The kidneys are able to control blood pressure by either reabsorbing water to maintain blood pressure or by allowing more water than usual to be excreted into urine and thus reduce blood volume and pressure. Sodium ions in the body help to manage the body's osmotic pressure by drawing water towards areas of high sodium concentration. To lower blood pressure, the kidneys can excrete extra sodium ions that draw water out of the body with them. Conversely, the kidneys may reabsorb additional sodium ions to help retain water in the body.

Finally, the kidneys produce the enzyme renin to prevent the body's blood pressure from becoming too low. The kidneys rely on a certain amount of blood pressure to force blood plasma through the capillaries in the glomerulus. If blood pressure becomes too low, cells of the kidneys release renin into the blood. Renin starts a complex process that results in the release of the hormone aldosterone by the adrenal glands. Aldosterone stimulates the cells of the kidney to increase their reabsorption of sodium and water to maintain blood volume and pressure.

Dialysis

The kidneys are a pair of organs, each about the size of a fist, located on either side of your spine. They're responsible for purifying your blood by removing waste and excess fluid from your body. When the kidneys don't work properly, dialysis is used to perform the function of the kidneys.

Dialysis is a treatment that filters and purifies the blood using a machine. This helps keep your body in balance when the kidneys can't do their job. Dialysis has been used since the 1940s to treat people with kidney problems.

PURPOSE

Why Is Dialysis Used?

Properly functioning kidneys prevent extra water, waste, and other impurities from accumulating in your body. They also help control blood pressure and regulate the levels of

chemicals in the blood, such as sodium, or salt, and potassium. They even activate a form of vitamin D that improves the absorption of calcium.

When your kidneys can't perform these functions due to disease or injury, dialysis can help keep the body running as normally as possible. Without dialysis, salts and other waste products will accumulate in the blood and poison the body. However, dialysis isn't a cure for kidney disease or other problems affecting the kidneys. Different treatments may be needed to address those concerns.

Diuretics

Diuretics, sometimes called water pills, help rid your body of salt (sodium) and water. Most work by making your kidneys release more sodium into your urine. The sodium then takes water with it from your blood. That decreases the amount of fluid flowing through your blood vessels, which reduces pressure on your vessel walls.

Examples of diuretics

There are three types of diuretics: thiazide, loop and potassium-sparing. Each type affects a different part of your kidneys and may have different uses, side effects and precautions.

Examples of thiazide diuretics include:

- Chlorothiazide (Diuril)
- Chlorthalidone
- Hydrochlorothiazide (Microzide)
- Indapamide
- Metolazone

Examples of loop diuretics include:

- Bumetanide (Bumex)
- Ethacrynic acid (Edecrin)
- Furosemide (Lasix)
- Torsemide (Demadex)

Examples of potassium-sparing diuretics include:

- Amiloride
- Eplerenone (Inspra)
- Spironolactone (Aldactone)
- Triamterene (Dyrenium)

Some pills combine more than one type of diuretic or combine a diuretic with another blood pressure medication.

Unit 4

Gastrointestinal and hepatic physiology: Histology of the gastrointestinal tract. Propulsion and motility of food and digested material. Enteric reflexes, secretory functions of the gastrointestinal tract, digestion and absorption of macro and micronutrients. Peptic ulcer, Sprue, celiac disease, IBD, regurgitation, diarrhoea and constipation. Anatomy of the hepatic lobule and blood flow into the liver. Formation and secretion of bile. enterohepatic cycle, reticuloendothelial system, metabolic importance of liver. Liver function tests. Jaundice, liver cirrhosis and fatty liver.

Musculosketetal system: Bone structure and formation. Physiology of muscle contraction in striated and non-striated muscle.

TEXTBOOKS

Chatterjee, C.C., (2012). Human Physiology, 11th edition, Mical Alli Agency, Calcutta.

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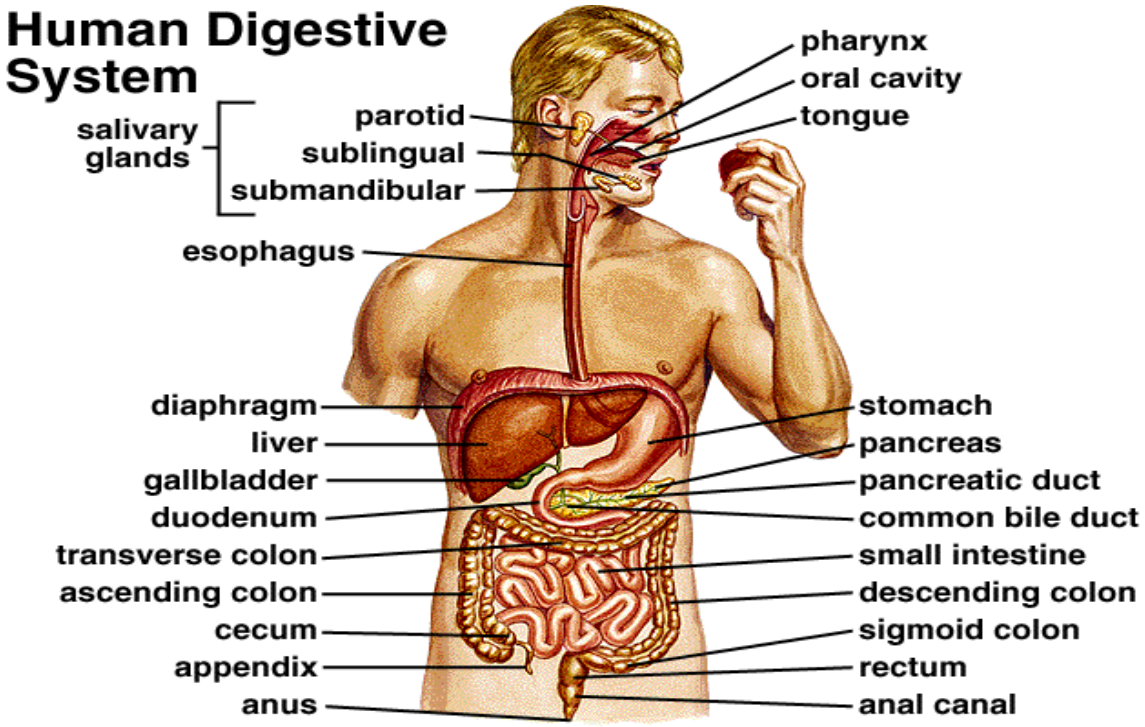
Gastrointestinal and hepatic physiology

DIGESTIVE SYSTEM

The digestive system is a group of organs working together to convert food into energy and basic nutrients to feed the entire body. Food passes through a long tube inside the body known as the alimentary canal or the gastrointestinal tract (GI tract). The alimentary canal is made up of the **oral cavity, pharynx, esophagus, stomach, small intestines, and large intestines.** In addition to the alimentary canal, there are several important accessory organs that help your body to digest food but do not have food pass through them. Accessory organs of the digestive system include the **teeth, tongue, salivary glands, liver, gallbladder, and pancreas.**



Oral cavity

This is the place where the ancient of food carried out this consists of tongues helps in chewing and swallowing the food. There are 3 pairs of salivary glands namely parotid, submaxilary and sublingual glands. One of each pair remains on one side of oral cavity. They secrete saliva rich in salivary amylase (ptyalln). The saliva also contains calcium iodide. The salivary amylase helps in the digestion of CHO pharynx or throat cavity. It is a musculo membranous tube whose constricted end, ends in the oesophagus. It is made up of mucous membrane having sensor receptors essential in the mechanism of swallowing. It acts as a channel to transport food from mouth to oesophagus.

Pharynx

It is a musculo membranous tube whose contricted end, ends in oesophagus. This helps in the process of swallowing of food.

Oesophagus

It is otherwise called as **food pipe** which connects pharynx and stomach. The main function of it is to receive food from pharynx and pass it to stomach by series of pesistatic construction.

Stomach

It is J in shape and divided into 3 parts. Namely the find us body and pylorus. In find us and the parietal cells secrete HCl.

The main functions of stomach are

- Access reservoir of food
- To secrete gastric juice
- Digestion of protein and lipid
- Absorption of water alcohol and glucose

Small intestine

It has 3 parts namely

- Duodenum- Upper part
- Jejunum- middle part
- Ileum – lower part

Functions: Duodenum and jejunum involved in digestion where as ileum involved in absorption of food. In duodenum part the secretion of gall bladder (bile salts) and pancreatic amylase, pancreatic lipases are released and they help in digestion of CHO and lipids.

In small intestine the presence of villi, the projections of SI increase the surface are and helps in the rapid absorption of food.

Large intestine:

It has following parts

- Ascending colon

- Descending colon
- Transverse colon
- Sigmoid colon

Rectum and anal canal

They are last part of GI tract, through which only the stored faeces evacuated. Rectum acts as reservoir of semisolid faeces. During defecation, the muscular sling relaxes and the rectum becomes straight to permit the easy passage of stool.

Accessory organs

Liver, Gallbladder

Anatomy

- Connected to gallbladder via bile duct and then to small intestine
- Contains sinusoidal capillaries which are permeable to most substances
- Unusual vasculature: G.I. capillaries Liver , vena cava. This allows filtration of ingested substances.
- Enterohepatic circulation: from liver via bile duct to small intestine and then from small intestine back through portal vein to liver

Major functions

- production and secretion of bile
- detoxication of blood
- secretion and storage of glucose
- production of albumin
- Liver clears substances via the bile duct in a similar manner to the way the kidney clears substances into the nephron.

Production and secretion of bile

- Components of bile
- bile pigment or bilirubin: removes hemoglobin breakdown products
- bile salts: adds in fat absorption

- Phospholipids, cholesterol, inorganic ions.
- Gallbladder stores bile. Bile entering gallbladder is controlled by the sphincter of Oddi.

Pancreas

Endocrine versus exocrine function:

- Endocrine: involves secretion into blood inside the body, endo: insulin and glucagons
- Exocrine: involves secretion into GI system outside the body, exo.

Pancreatic juice contains:

- water: H_2O
- bicarbonate: HCO_3^-
- amylase: digests starch
- trypsin: digests protein
- lipase: digests fatty acids

To achieve the goal of providing energy and nutrients to the body, six major functions take place in the digestive system:

- Ingestion
- Secretion
- Mixing and movement
- Digestion
- Absorption
- Excretion

DIGESTION AND ABSORPTION OF CARBOHYDRATES:

DIGESTION

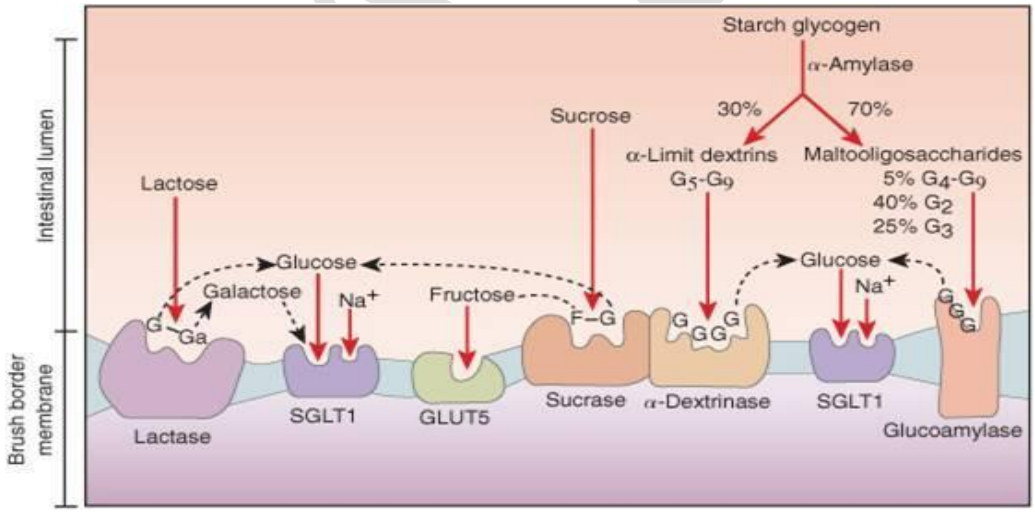
Carbohydrates are composed of chains of simple sugars. The term polysaccharide refers to the largest molecules, oligosaccharides contain from 3 to 10 sugars, disaccharides are double sugars, and monosaccharides are simple sugars.

In the mouth, amylase in saliva breaks polysaccharides into oligosaccharides. No carbohydrate digestion occurs in the stomach. In the small intestine, polysaccharides that survived digestion in the mouth are broken down to oligosaccharides by pancreatic amylase.

The remaining enzymes involved in carbohydrate digestion are membrane bound. Dextrinase breaks oligosaccharides into the disaccharidessucrose, maltose, and lactose. Next, disaccharidases--sucrase, maltase, lactase--break the corresponding disaccharides into monosaccharides that are absorbed into the blood stream.

Figure: Digestion and absorption of carbohydrates

Polysaccharides ($(C_6H_{10}O_5)_x$)	Polysaccharases	Disaccharides ($C_{12}H_{22}O_{11}$)	Glycosidases	Monosaccharide ($C_nH_{2n}O_n$)
Glycogen (animals)	Amylases	Maltose	Maltase	Glucose
Starch (Plants)	Amylases	Maltose	Maltase	Glucose
Cellulose (Plants & animals)	Cellulases	Cellobiose	Cellobioses	Glucose
		Trehalose (insects and some plants)	Trehalase	Glucose
		Lactose	Lactase	Galactose Glucose
		Sucrose	Invertase	Fructose Glucose



Arrows point from each disaccharide to their corresponding monosaccharides. Sucrose yields a molecule of glucose and a molecule of fructose. Dextrin yields many molecules of glucose. Lactose yields one glucose and one galactose.

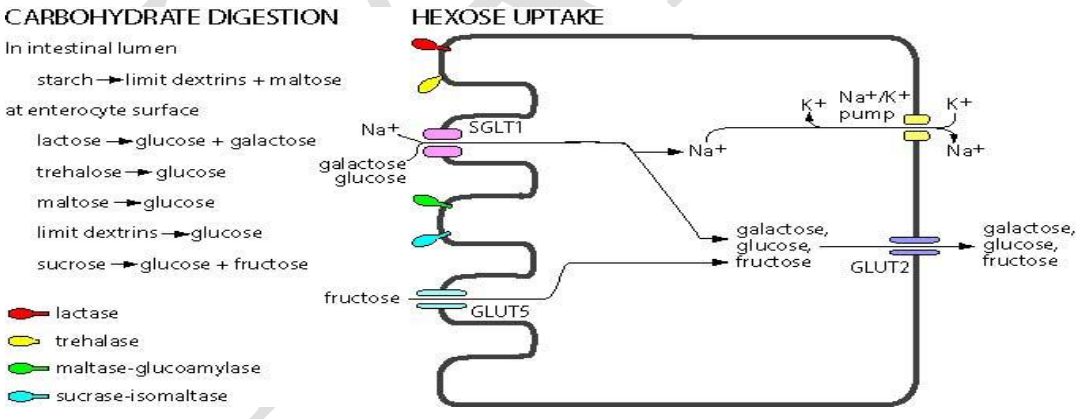
ABSORPTION

Once carbohydrates are broken down into their simplest forms, they are quickly absorbed along the upper and lower parts of the small intestine through the small, finger-like projections, called villi and then they are transferred to the blood stream and carried to muscles and the liver. It is not only with **simple diffusion** of substances, but also with **active transport** that requires energy.

During the phase of carbohydrate absorption, fructose is transported into the intestinal cell's cytosol, **glucose and galactose competes with other Na + transporter** required for operation**. Fructose** is absorbed into the blood by means of **facilitated diffusion**. From the cytosol, **monosaccharides p**ass into the capillaries by **simple or facilitated diffusion**.

Carbohydrates that are not digested in the small intestine, including resistant starch foods such as potatoes, beans, oats, wheat flour, as well as several non-polisacacáridos oligosaccharides and starch, are digested in a variable when they reach the large intestine. The bacterial floras metabolize these compounds in the absence of oxygen. This produces gases (hydrogen, carbon dioxide and methane) and short-chain fatty acids (acetate, propionate, butyrate). The gases are absorbed and excreted by breathing or through the anus.

Figure: Absorption carbohydrates

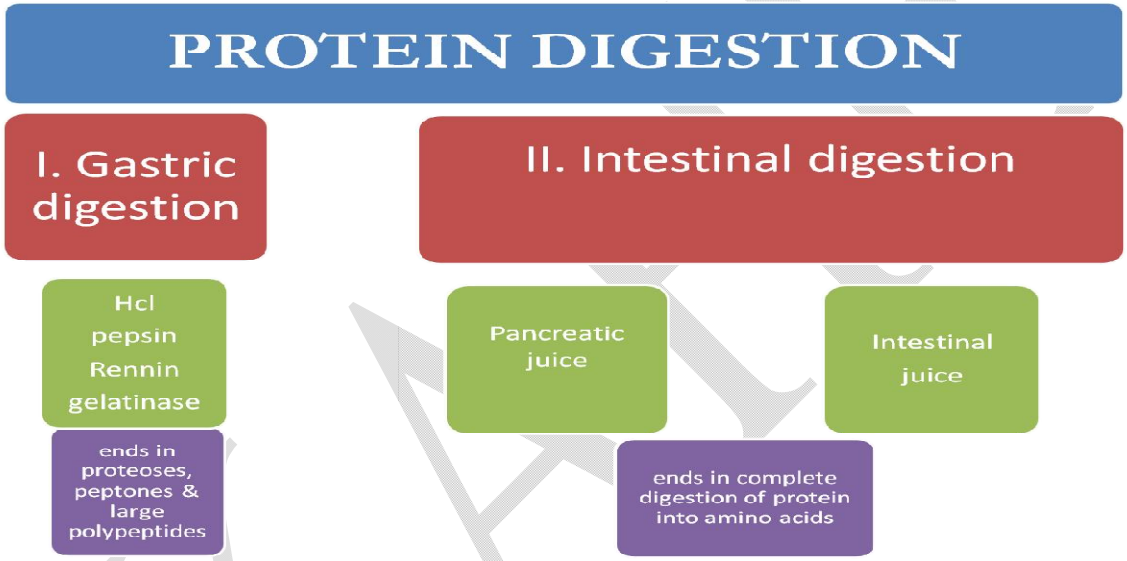


DIGESTION & ABSORPTION OF PROTEINS

- Protein digestion occurs in the **stomach** and in **small intestine.** Dietary proteins must be digested to small simple molecules that are amino acids which are easily absorbed from the intestine.

- Dietary proteins are cleaved by hydrolases with specificity for the peptide bond (peptidases).
- **Endopeptidases** (aka **Proteases**): attack **internal protein bonds** liberating large peptide fragments.
- **Exopeptidases**: cleave off **one amino acid** at a time from either from the amino terminal end(**amino**peptidases) carcoxy termninal end (**carboxy** peptidase)
- Endo- and Exopeptidases work in concert

Figure: Over view of protein digestion



(I) DIGESTION OF PROTEINS

Protein digestion and absorption takes place in two place of gastric intestine track. There are

- Stomach
- Small intestine.

Dietary proteins must be digested to small simple molecules that are amino acids to easily absorbed from the intestine.

I-Digestion in the stomach

When food is enter into the stomach it stimulate the secretion of hormone, gastrin. The gastrin stimulates the HCl secretion and pepsinogen. The gastric juice contains

- Gastric HC1 4
- Pepsin
- Rennin
- Gelatinase

1- Role of gastric HC1

- Gastric acid **kills microorganisms** and it causes denaturation of proteins. ie unfolding of protein and preparing them for hydrolysis by proteases.
- It activates pepsinogen to pepsin.
- Proteins are converted into polypeptide in the presence of pepsin and HCl, which are easily digested.
- It makes pH in the stomach suitable for the action of pepsin

2- Pepsin

- It is secreted in an inactive form called pepsinogen.
- Its optimum pH: 1.5-2.2
- It is activated by HC1 then by autoactivation.

HCl

Pepsinogen ————► Pepsin

- **Acting on central peptide bond in which amino group belongs to aromatic amino acids** e.g. phenyl alanine, tyrosine and tryptophan.

Since gastric juices contain the **acid stable** proteases of the **pepsin family**, it produce **large peptide fragments** and some free amino acids.

3-Rennin

- It is a milk-clotting enzyme.
- It is present in stomachs of infants and young animals.
- Its optimum pH 4
- **It acts on casein (main milk protein) converting it to soluble paracasein.**

Casein paracasein + calcium ions-------→ Calcium paracaseinate (milk clot)

- Calcium paracaseinate is then digested by pepsin.

4- Gelatinase

It is an enzyme that liquefies gelatin.

The end products of protein digestion in the stomach are smaller polypeptides.

II- DIGESTION IN THE SMALL INTESTINE

Dietary protein includes the proteins of cereals, egg, meat and chicken. Protein digestion at this stage is partial, digestion of proteins is then completed in the small intestine by proteolytic enzymes present in pancreatic and intestinal juices.

As foods enter into small intestine due its lower pH, stimulate the hormone secretin. This secretin stimulate the pancrease to secrete HCO_3^-. It neutralise the acidic food from stomach to pH 7. When this food which contain the amino acids and small proteins enter the duodenum, it release the hormone cholectystokinin-pancreozymin (**CCK-PZ**) and this release initiates the **secretion** of **protease zymogens** from the **pancreas** and release of **enteropeptidase** in the **gut**.

A. Pancreatic Juice contains

1-Trypsin

2- Chymotrypsin

3- Elastase

4- Carboxy peptidase

1-Trypsin

- ✓ It is secreted in an inactive form called trypsinogen.
- ✓ Its optimum pH: 8
- ✓ It is activated by enterokinase enzyme (produced by intestinal mucosa) then by auto activation
- ✓ It is an **endopeptidase** that hydrolyzes central peptide bond in which the amino group belongs to the basic amino acids. e.g. arginine, lysine and histidine.

2- Chymotrypsin

- ✓ It is secreted in an inactive form called chymotrypsinogen.
- ✓ It is activated by trypsin.
- ✓ Its optimum pH: 8
- ✓ It is an endopeptidase that hydrolyzes central peptide bond in which the carboxyl group belongs to aromatic amino acids. E.g – phenyl alanine, tyrosine

3- Elastase

- ✓ It is secreted in an inactive form called proelatase.
- ✓ It is activated by trypsin.
- ✓ It digests elastin and collagen.

- ✓ Its optimum pH: 8
- ✓ It is an endopeptidase acting on peptide bonds formed by glycine, alanine and serine.

4- Carboxy peptidase

- ✓ It is secreted in an inactive form called procarboxy peptidase.
- ✓ It is activated by trypsin.
- ✓ Its optimum pH: 7.4
- ✓ It is an exopeptidase that hydrolyzes the terminal (peripheral) peptide bond at the carboxyl terminus (end) of the polypeptide chain.

B. INTESTINAL JUICE (DIGESTION AT THE BRUSH BORDER -surface of intestinal epithelial cells)

Since pancreatic juice does not contain appreciable aminopeptidase activity, final digestion of di- and small peptides depends on brush border enzymes.

2. The surface of intestinal epithelial cells is rich in **endopeptidases** and **aminopeptidases**.

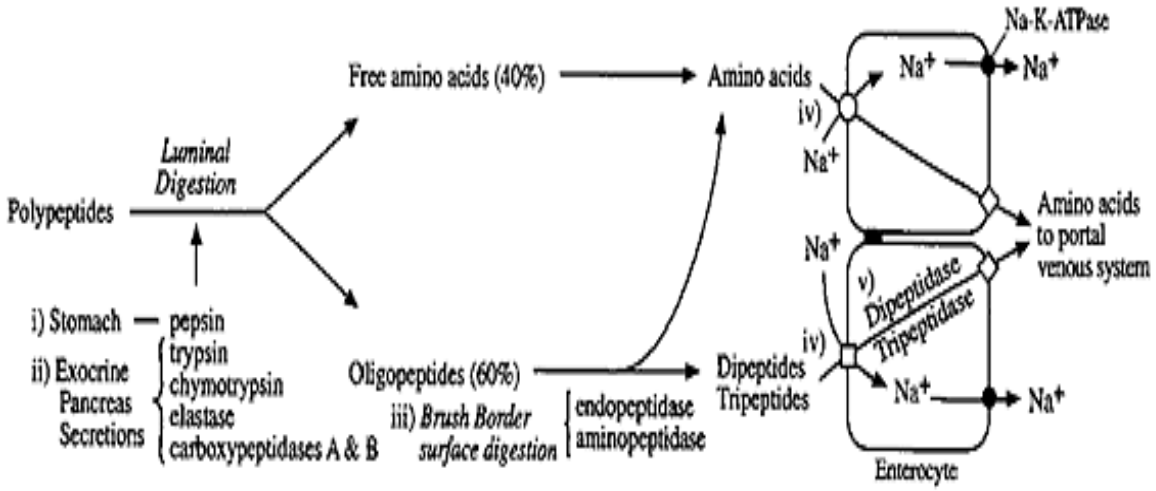
3. The end products of cell surface digestion are **free amino acids** and **di-** and **tripeptides**.

1-Aminopeptidase

2-Tripeptidase

3-Dipeptidase

Figure: **Protein Digestion and Absorption**



PROTEIN ABSORPTION

Absorption occurs in small intestine and absorption of amino acids is rapid in the duodenum and jejunum, but slow in the ileum. Free aminoacids absorbed from small intestine and enter into blood through portal vein.

Following digestion, amino acids and small peptides are co-absorbed w/ sodium via group specific amino acids or peptide transport systems.

The transport of amino acid is **carrier mediated**, they **discriminate** between natural **L amino acids** and D-amino acids, **require energy** (for the Na^+ gradient, Na-K ATPase) and **physiologic temperatures**.

There are two mechanisms for amino acids absorption.

1- Carrier proteins transport system

2- Glutathione transport system (γ- Glutamyl cycle)

CARRIER PROTEINS TRANSPORT SYSTEM

- It is the main system for amino acid absorption.
- It is an active process that needs energy.
- The energy needed is derived from ATP.
- Absorption of one amino acid molecule needs one ATP molecule.
- There are 7 carrier proteins, one for each group of amino acids.
- Each carrier protein has two sites one for amino acid and one for Na+
- It co-transports amino acid and Na+ from intestinal lumen to cytosol of intestinal mucosa cells.
- The absorbed amino acid passes to the portal circulation,

At least five brush border transport systems exist for:

1. neutral amino acids (uncharged aliphatic and aromatic)

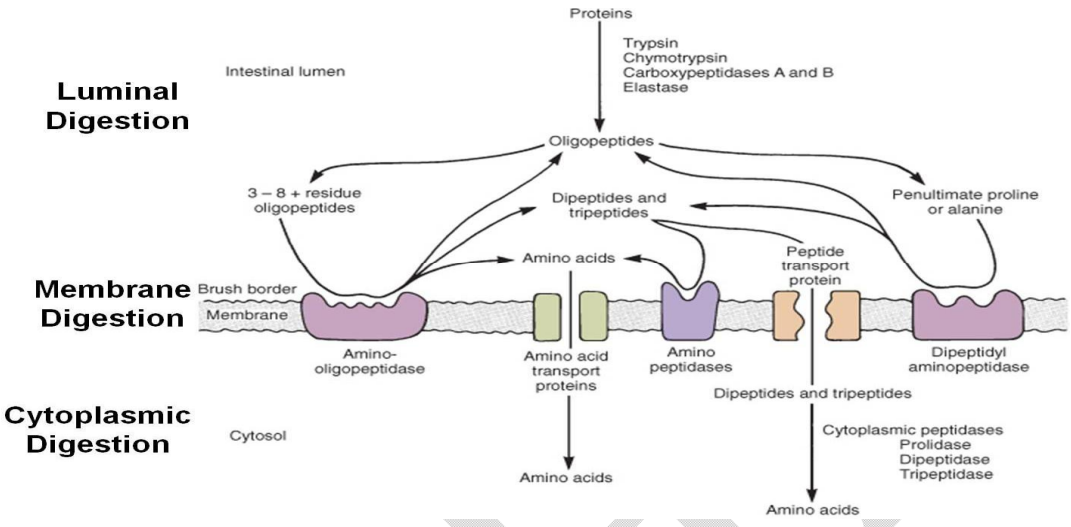
2. basic amino acids (Lys, Arg, Cys, Cys-Cys)

3. acidic amino acids (Asp, Glu)

4. imino acids (Pro, Hydroxyproline)

5. di- and tripeptides

Figure : Digestion and absorption of amino acids



DIGESTION AND ABSORPTION OF LIPID

The bulk of dietary lipid is triglyceride, phospholipids, sterols like cholesterol and many minor lipids, including fat-soluble vitamins.

In order for the triglyceride to be absorbed, two processes must occur:

- Large aggregates of dietary triglyceride, which are virtually insoluble in an aqueous environment, must be broken down physically and held in suspension - a process called emulsification.
- Triglyceride molecules must be enzymatically digested to yield monoglyceride and fatty acids, both of which can efficiently diffuse or be transported into the enterocyte.

The key players in these two transformations are **bile acids and pancreatic lipase,** both of which are mixed with chyme and act in the lumen of the small intestine. Bile acids are also necessary to solubilize other lipids, including cholesterol.

DIGESTION

Most of the fat in the human diet is in the form of triacylglycerol (TAG), which consists of three fatty acids linked to glycerol.

In the digestive tract, TAG is hydrolyzed by the enzyme lipase, to release free fatty acids and monoglycerides.

The key issue in the digestion and absorption of fats is one of solubility: lipids are hydrophobic, and thus are poorly soluble in the aqueous environment of the digestive tract. The digestive enzyme, lipase, is water soluble and can only work at the surface of fat globules. Digestion is greatly aided by emulsification, the breaking up of fat globules into much smaller emulsion droplets. Bile salts and phospholipids are amphipathic molecules that are present in the bile.

Minor digestion of lipid occurs in **mouth**. Where,

TAG —Lingual lipase→ Free fatty acid + Glycerol

In **Stomach,**

TAG —Gastric lipase→ Free fatty acid + Monoacyl glycerol

In **Small intestine**,

(I) Emulsification of lipids occurs by three complementary mechanisms

(i) Detergent action of bile salts

Lipids in the presence of bile salts converted into smaller particles. The bile salts also prevent the reaggregation of smaller lipid droplets into larger aggregates

TAG —Bile salts→ smaller partilcles

(ii) Surfactant action of degraded lipids

Initial digestion products like free fatty acids and MAG promote emulsification. Here the Initial digestion products and phospholipids are called surfactants.

(iii) Mechanical mixing of food

Motility in the small intestine breaks fat globules apart into small droplets that are coated with bile salts and phospholipids, which prevent the emulsion droplets from re-associating.

(II) Digestion by pancreatic enzymes

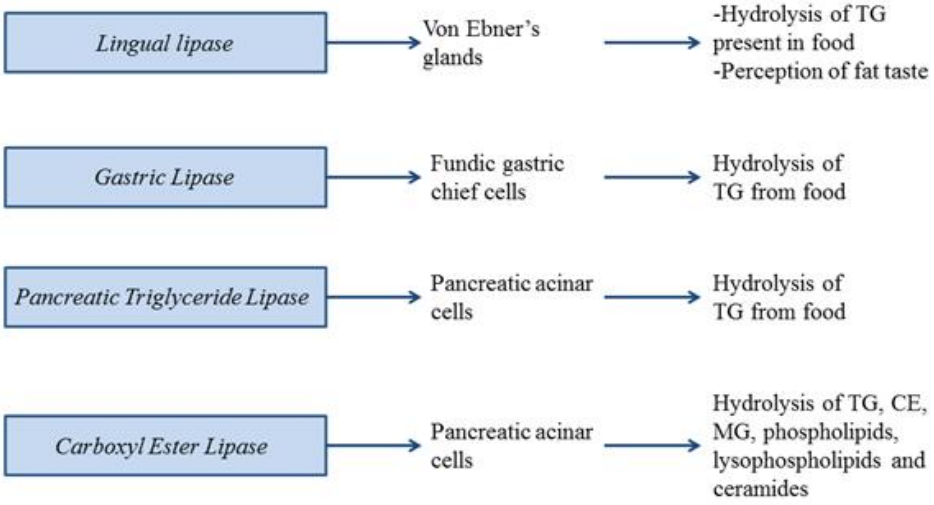
TAG —Pancreatic lipase→ Free fatty acid + Glycerol

Cholesterol ester —lipid esterase→ Cholesterol+ free fatty acid

Lipid ester

Phospholipid —phospholipase→ Glycerol+ free fatty acid+ nitrogenous base

Figure: Emulsification and digestion of lipids



The emulsion droplets are where digestion occurs. Emulsification greatly increases the surface area where water-soluble lipase can work to digest TAG. Another factor that helps is colipase, an amphipathic protein that binds and anchors lipase at the surface of the emulsion droplet.

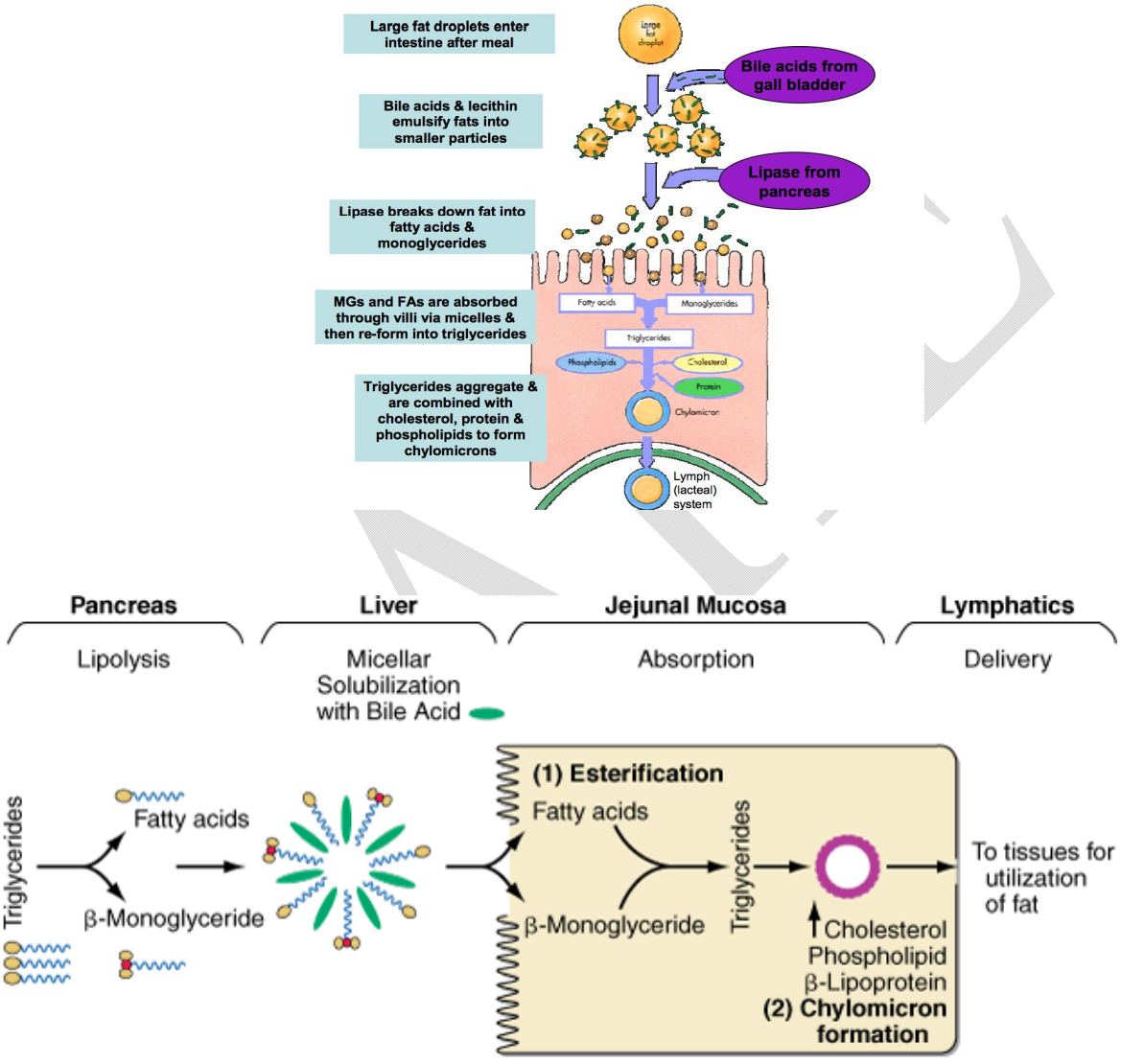
ABSORPTION

Micelles

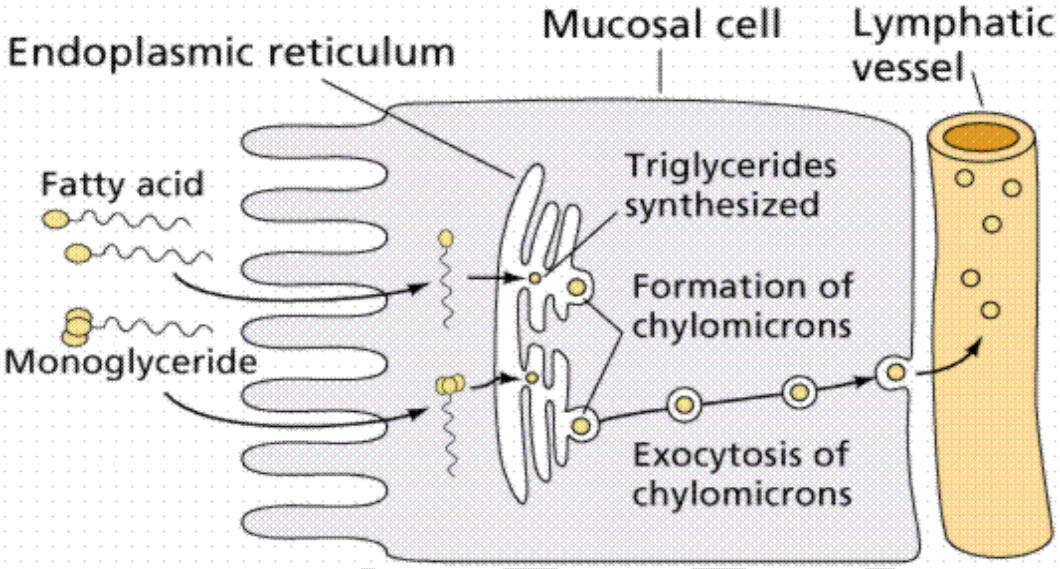
After digestion, monoglycerides and fatty acids associate with bile salts and phopholipids to form micelles. Micelles are about 200 times smaller than emulsion droplets (4-7nm versus 1µm for emulsion droplets). Micelles transport the poorly soluble monoglycerides

and fatty acids to the surface of the enterocyte where they can be absorbed. As well, micelles contain fat soluble vitamins and cholesterol. Because of their nonpolar nature, monoglycerides and fatty acids can just diffuse across the plasma membrane of the enterocyte. Some absorption may be facilitated by specific transport proteins.

Figure: Digestion and absorption of lipid

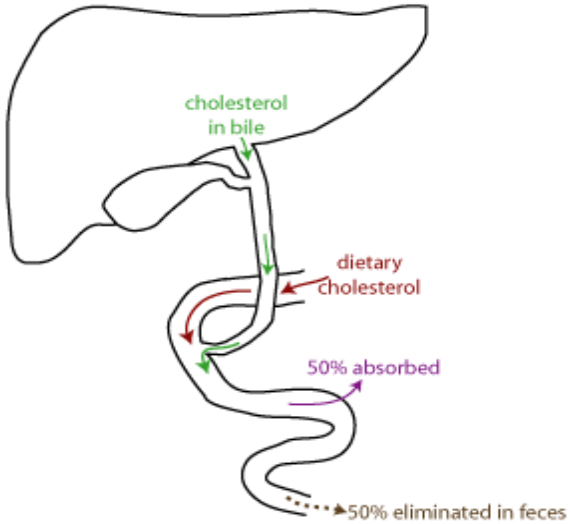


Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: http://www.accessmedicine.com



Cholesterol absorption

As shown in the figure, some of the cholesterol in the small intestine is dietary cholesterol, and some is put there by the liver, arriving via the bile. Of the total cholesterol that passes through the small intestine, only half is typically absorbed, and the rest is eliminated in the feces. **Figure: Digestion and absorption of cholesterol**



Peptic ulcers are sores that develop in the lining of the stomach, lower esophagus, or small intestine (the duodenum), usually as a result of inflammation caused by the bacteria H. pylori, as well as from erosion from stomach acids. Peptic ulcers are a fairly common health problem.

There are three types of peptic ulcers:

- gastric ulcers: ulcers that develop inside the stomach
- esophageal ulcers: ulcers that develop inside the esophagus
- duodenal ulcers: ulcers that develop in the upper section of the small intestines, called the duodenum

CAUSES

Causes of Peptic Ulcers

Different factors can cause the lining of the stomach, the esophagus, and the small intestine to break down. These include:

- Helicobacter pylori (H. pylori): a bacteria that can cause a stomach infection and inflammation
- frequent use of aspirin, ibuprofen, and other anti-inflammatory drugs (risk associated with this behavior increases in women and people over the age of 60)
- smoking
- drinking too much alcohol
- radiation therapy
- stomach cancer

SYMPTOMS

Symptoms of Peptic Ulcers

The most common symptom of a peptic ulcer is burning abdominal pain that extends from the navel to the chest, which can range from mild to severe. In some cases, the pain may wake you up at night. Small peptic ulcers may not produce any symptoms in the early phases.

Other common signs of a peptic ulcer include:

- changes in appetite
- nausea

- bloody or dark stools (melena)
- unexplained weight loss
- indigestion
- vomiting
- chest pain

Celiac Disease - Sprue

Celiac disease is a condition that creates inflammation and damages the lining of the small intestine. This prevents absorbing components of food that are important for staying healthy. The damage is due to a reaction to eating gluten, which is found in wheat, barley, rye, and possibly oats.

Causes

The exact cause of celiac disease is unknown. The lining of the intestines is covered by villi, which help absorb nutrients. When people with celiac disease eat foods or use products that contain gluten, their immune system reacts by damaging these villi.

This damage affects the ability to absorb nutrients properly. A person becomes malnourished, no matter how much food he or she eats.

The disease can develop at any point in life, from infancy to late adulthood.

Symptoms

The symptoms of celiac disease can be different from person to person. This is part of the reason why the diagnosis is not always made right away. For example, one person may have constipation, a second may have diarrhea, and a third may have no problem with stools.

Gastrointestinal symptoms include:

- Abdominal pain, bloating, gas, or indigestion
- Constipation
- Decreased appetite (may also be increased or unchanged)
- Diarrhea, either constant or off and on
- Lactose intolerance (common when the person is diagnosed, usually goes away after treatment)
- Nausea and vomiting

- Stools that are foul smelling, oily, or and stick to the toilet when flushed
- Unexplained weight loss (although people can be overweight or of normal weight)

Diarrhea is an increase in the frequency of bowel movements or a decrease in the form of stool (greater looseness of stool). Although changes in frequency of bowel movements and looseness of stools can vary independently of each other, changes often occur in both.

Diarrhea needs to be distinguished from four other conditions. Although these conditions may accompany diarrhea, they often have different causes and different treatments than diarrhea. These other conditions are:

1. Incontinence of stool, which is the inability to control (delay) bowel movements until an appropriate time, for example, until one can get to the toilet
2. Rectal urgency, which is a sudden urge to have a bowel movement that is so strong that if a toilet is not immediately available there will be incontinence
3. Incomplete evacuation, which is a sensation that another bowel movement is necessary soon after a bowel movement, yet there is difficulty passing further stool the second time
4. Bowel movements immediately after eating a meal

Constipation

Being constipated means your bowel movements are tough or happen less often than normal. Almost everyone goes through it sooner or later.

Although it's not usually serious, you'll feel much better when your body is back on track.

The normal length of time between bowel movements varies widely from person to person. Some people have them three times a day. Others have them only once or twice a week.

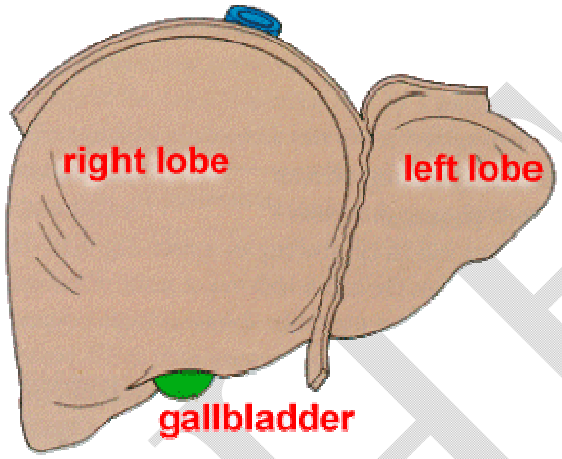
Going longer than 3 or more days without one, though, is usually too long. After 3 days, the stool or feces become harder and more difficult to pass.

Symptoms

- Few bowel movements
- Trouble having a bowel movement (straining to go)
- Hard or small stools
- A sense that everything didn't come out

- Swollen belly or belly pain
- Throwing up

Anatomy of the Liver- front view



The liver is the largest organ in the body, normally weighing about 1.5kg (although this can increase to over 10kg in chronic cirrhosis). The liver is the main organ of metabolism and energy production; its other main functions include:

- Bile production
- Storage of iron, vitamins and trace elements
- detoxification
- conversion of waste products for excretion by the kidneys

The liver is functionally divided into two lobes, right and left. The external division is marked on the front of the liver by the *falciform ligament*, which joins the *coronary ligament* at the superior margin of the liver.

- The **right lobe** is separated from the other lobes by the gallbladder fossa and the fossa for the *inferior vena cava* on the visceral surface of the liver.
- The **left lobe** includes the caudate and quadrate lobes. It is separated from these two lobes by the attachment of the *ligumentum teres*, and the fissures for the ligumentum teres and the *ligamentum venosum.*
- The **caudate lobe** lies between the fissure for the ligamentum venosum and the fossa for the inferior vena cava.

- The **quadrate lobe** is partly covered by the gallbladder in normal patients; anatomically, it lies between the fissure for the ligamentum teres and the gallbladder fossa.

Each lobe hs its own arterial and venous supply and its own billiary drainage. all the lobes perform the same functions- there are no areas of specialization.

The Portal Circulation

The liver is unusual in that it has a double blood supply; the right and left hepatic arteries carry oxygenated blood to the liver, and the portal vein carries venous blood from the GI tract to the liver.

The venous blood from the GI tract drains into the superior and inferior mesenteric veins; these two vessels are then joined by the splenic vein just posterior to the neck of the pancreas to form the portal vein. This then splits to form the right and left branches, each supplying about half of the liver. On entering the liver, the blood drains into the **hepatic sinusoids**, where it is screened by specialised macrophages (Kupffer cells) to remove any pathogens that manage to get past the GI defences. The plasma is filtered through the endothelial lining of the sinusoids and bathes the **hepatocytes**; these cells contain vast numbers of enzymes capable of braking down and metabolising most of what has been absorbed.

The portal venous blood contains *all* of the products of digestion absorbed from the GI tract, so all useful and non-useful products are processed in the liver before being either released back into the hepatic veins which join the inferior vena cava just inferior to the diaphragm, or stored in the liver for later use.

Secretion of Bile and the Role of Bile Acids In Digestion

Bile is a complex fluid containing water, electrolytes and a battery of organic molecules including bile acids, cholesterol, phospholipids and bilirubin that flows through the biliary tract into the small intestine. **There are two fundamentally important functions of bile in all species:**

- Bile contains bile acids, which are critical for digestion and absorption of fats and fat-soluble vitamins in the small intestine.
- Many waste products, including bilirubin, are eliminated from the body by secretion into bile and elimination in feces.

Adult humans produce 400 to 800 ml of bile daily, and other animals proportionately similar amounts. The secretion of bile can be considered to occur in two stages:

- Initially, hepatocytes secrete bile into canaliculi, from which it flows into bile ducts. This hepatic bile contains large quantities of bile acids, cholesterol and other organic molecules.

- As bile flows through the bile ducts it is modified by addition of a watery, bicarbonate-rich secretion from ductal epithelial cells.

In species with a gallbladder (man and most domestic animals except horses and rats), further modification of bile occurs in that organ. **The gall bladder stores and concentrates bile during the fasting state.** Typically, bile is concentrated five-fold in the gall bladder by absorption of water and small electrolytes - virtually all of the organic molecules are retained.

Secretion into bile is a major route for eliminating cholesterol. Free cholesterol is virtually insoluble in aqueous solutions, but in bile, it is made soluble by bile acids and lipids like lecithin. Gallstones, most of which are composed predominantly of cholesterol, result from processes that allow cholesterol to precipitate from solution in bile.

Role of Bile Acids in Fat Digestion and Absorption

Bile acids are derivatives of cholesterol synthesized in the hepatocyte. Cholesterol, ingested as part of the diet or derived from hepatic synthesis is converted into the bile acids cholic and chenodeoxycholic acids, which are then conjugated to an amino acid (glycine or taurine) to yield the conjugated form that is actively secreted into cannaliculi.

Bile acids are facial amphipathic, that is, they contain both hydrophobic (lipid soluble) and polar (hydrophilic) faces. The cholesterol-derived portion of a bile acid has one face that is hydrophobic (that with methyl groups) and one that is hydrophilic (that with the hydroxyl groups); the amino acid conjugate is polar and hydrophilic.

Their amphipathic nature enables bile acids to carry out two important functions:

- **Emulsification of lipid aggregates:** Bile acids have detergent action on particles of dietary fat which causes fat globules to break down or be emulsified into minute, microscopic droplets. Emulsification is not digestion per se, but is of importance because it greatly increases the surface area of fat, making it available for digestion by lipases, which cannot access the inside of lipid droplets.
- **Solubilization and transport of lipids in an aqueous environment:** Bile acids are lipid carriers and are able to solubilize many lipids by forming **micelles** - aggregates of lipids such as fatty acids, cholesterol and monoglycerides - that remain suspended in water. Bile acids are also critical for transport and absorption of the fat-soluble vitamins.

Role of Bile Acids in Cholesterol Homeostasis

Hepatic synthesis of bile acids accounts for the majority of cholesterol breakdown in the body. In humans, roughly 500 mg of cholesterol are converted to bile acids and eliminated in bile every day. This route for elimination of excess cholesterol is probably important in all animals, but particularly in situations of massive cholesterol ingestion.

Interestingly, it has recently been demonstrated that bile acids participate in cholesterol metabolism by functioning as hormones that alter the transcription of the rate-limiting enzyme in cholesterol biosynthesis.

Enterohepatic Recirculation

Large amounts of bile acids are secreted into the intestine every day, but only relatively small quantities are lost from the body. This is because approximately 95% of the bile acids delivered to the duodenum are absorbed back into blood within the ileum.

Venous blood from the ileum goes straight into the portal vein, and hence through the sinusoids of the liver. Hepatocytes extract bile acids very efficiently from sinusoidal blood, and little escapes the healthy liver into systemic circulation. Bile acids are then transported across the hepatocytes to be resecreted into canaliculi. The net effect of this enterohepatic recirculation is that each bile salt molecule is reused about 20 times, often two or three times during a single digestive phase.

It should be noted that liver disease can dramatically alter this pattern of recirculation - for instance, sick hepatocytes have decreased ability to extract bile acids from portal blood and damage to the canalicular system can result in escape of bile acids into the systemic circulation. Assay of systemic levels of bile acids is used clinically as a sensitive indicator of hepatic disease.

Pattern and Control of Bile Secretion

The flow of bile is lowest during fasting, and a majority of that is diverted into the gallbladder for concentration. When chyme from an ingested meal enters the small intestine, acid and partially digested fats and proteins stimulate secretion of cholecystokinin and secretin. As discussed previously, these enteric hormones have important effects on pancreatic exocrine secretion. They are both also important for secretion and flow of bile:

- **Cholecystokinin**: The name of this hormone describes its effect on the biliary system - cholecysto = gallbladder and kinin = movement. The most potent stimulus for release of cholecystokinin is the presence of fat in the duodenum. Once released, it stimulates contractions of the gallbladder and common bile duct, resulting in delivery of bile into the gut.
- **Secretin**: This hormone is secreted in response to acid in the duodenum. Its effect on the biliary system is very similar to what was seen in the pancreas - it simulates biliary duct cells to secrete bicarbonate and water, which expands the volume of bile and increases its flow out into the intestine.

The enterohepatic circulation of bile salts.

Bile salts are recycled out of the small intestine in four ways: (1) passive diffusion along the small intestine (plays a relatively minor role); (2) carrier-mediated active absorption in the

terminal ileum (the most important absorption route); (3) de-conjugation to primary bile acids before being absorbed either passively or actively; (4) conversion of primary bile acids to secondary bile acids with subsequent absorption of deoxycholic acid.

Although bile salt and bile acid absorption is extremely efficient, some salts and acids are nonetheless lost with every cycle of the enterohepatic circulation. About 500 mg of bile acids are lost daily. They are replenished by the synthesis of new bile acids from cholesterol. The loss of bile acid in feces is, therefore, an efficient way to excrete cholesterol.

Absorbed bile salts are transported in the portal blood bound to albumin or high-density lipoproteins (HDLs). The uptake of bile salts by hepatocytes is extremely efficient. In just one pass through the liver, more than 80% of the bile salts in the portal blood is removed. Once taken up by hepatocytes, bile salts are secreted into bile. The uptake of bile salts is a primary determinant of bile salt secretion by the liver.

Reticuloendothelial system

Definition:

Reticuloendothelial system is part of the immune system of human body and consists of phagocytic cells. It is closely related to lymphatic system because the two are independent structurally and functionally. This system is made up of highly phagocytic cells which are widely distributed in the body. These cells include:

The endothelial cells, fibroblasts, and most leukocytes arc not included in this system because of their poor power of phagocytosis.

Functions of Reticuloendothelial system:

1. The system forms first line of defense of the body against microorganisms, because of the amoeboid and phagocytic properties of its cells.

2. The macrophages of lymphoid tissue are now considered to be intimately concerned with mounting specific immune responses by the neighboring cells.

3. Many of the prominent sites of RES are also important sites of hemopoiesis.

METABOLIC FUNCTIONS OF THE LIVER

Hepatocytes are metabolic overachievers in the body. They play critical roles in synthesizing molecules that are utilized elsewhere to support homeostasis, in converting molecules of one type to another, and in regulating energy balances. *If you have taken a course in biochemistry, you probably spent most of that class studying metabolic pathways of the liver.* At the risk of damning by faint praise, the major metabolic functions of the liver can be summarized into several major categories:

Carbohydrate Metabolism

It is critical for all animals to maintain concentrations of glucose in blood within a narrow, normal range. Maintainance of normal blood glucose levels over both short (hours) and long (days to weeks) periods of time is one particularly important function of the liver.

Hepatocytes house many different metabolic pathways and employ dozens of enzymes that are alternatively turned on or off depending on whether blood levels of glucose are rising or falling out of the normal range. Two important examples of these abilities are:

- Excess glucose entering the blood after a meal is rapidly taken up by the liver and sequestered as the large polymer, glycogen (a process called **glycogenesis**). Later, when blood concentrations of glucose begin to decline, the liver activates other pathways which lead to depolymerization of glycogen (**glycogenolysis**) and export of glucose back into the blood for transport to all other tissues.
- When hepatic glycogen reserves become exhaused, as occurs when an animal has not eaten for several hours, do the hepatocytes give up? No! They recognize the problem and activate additional groups of enzymes that begin synthesizing glucose out of such things as amino acids and non-hexose carbohydrates (**gluconeogenesis**). The ability of the liver to synthesize this "new" glucose is of monumental importance to carnivores, which, at least in the wild, have diets virtually devoid of starch.

Fat Metabolism

Few aspects of lipid metabolism are unique to the liver, but many are carried out predominantly by the liver. Major examples of the role of the liver in fat metabolism include:

- The liver is extremely active in oxidizing triglycerides to produce energy. The liver breaks down many more fatty acids that the hepatocytes need, and exports large quantities of acetoacetate into blood where it can be picked up and readily metabolized by other tissues.
- A bulk of the lipoproteins are synthesized in the liver.
- The liver is the major site for converting excess carbohydrates and proteins into fatty acids and triglyceride, which are then exported and stored in adipose tissue.
- The liver synthesizes large quantities of cholesterol and phospholipids. Some of this is packaged with lipoproteins and made available to the rest of the body. The remainder is excreted in bile as cholesterol or after conversion to bile acids.

Protein Metabolism

The most critical aspects of protein metabolism that occur in the liver are:

- Deamination and transamination of amino acids, followed by conversion of the non-nitrogenous part of those molecules to glucose or lipids. Several of the enzymes used in these pathways (for example, alanine and aspartate aminotransferases) are commonly assayed in serum to assess liver damage.
- Removal of ammonia from the body by synthesis of urea. Ammonia is very toxic and if not rapidly and efficiently removed from the circulation, will result in central nervous system disease. A frequent cause of such hepatic encephalopathy in dogs and cats are malformations of the blood supply to the liver called portosystemic shunts.
- Synthesis of non-essential amino acids.
- Hepatocytes are responsible for synthesis of most of the plasma proteins. Albumin, the major plasma protein, is synthesized almost exclusively by the liver. Also, the liver synthesizes many of the clotting factors necessary for blood coagulation.

LIVER FUNCTIION TESTS

What Are Liver Function Tests?

Liver function tests help determine the health of your liver by measuring the levels of proteins, liver enzymes, or bilirubin in your blood.

A liver function test is often given in the following situations:

- to screen for liver infections, such as hepatitis C
- to monitor the side effects of certain medications known to affect the liver
- if you already have a liver disease, to monitor the disease and how well a particular treatment is working
- to measure the degree of scarring (cirrhosis) on the liver
- if you're experiencing the symptoms of a liver disorder
- if you're planning on becoming pregnant

Many tests can be performed on the liver, but most of them don't measure the overall function of the liver. Commonly used tests to check liver function are the alanine transaminase (ALT), aspartate aminotransferase (AST), albumin, and bilirubin tests. The ALT and AST tests measure enzymes that your liver releases in response to damage or disease. The albumin and bilirubin tests measure how well the liver creates albumin, a protein, and how well it disposes of bilirubin, a waste product of the blood.

Abnormal results on any of the liver function tests don't necessarily mean you have liver disease or damage. Talk to your doctor about the results of your liver function test.

TYPES OF LIVER FUNCTION TESTS

What Are the Most Common Liver Function Tests?

Liver function tests are used to measure specific enzymes and proteins in your blood. Depending on the test, either higher- or lower-than-normal levels of these enzymes or proteins can indicate a problem with your liver.

Some common liver function tests include:

Alanine Transaminase (ALT) Test

Alanine transaminase (ALT) is used by your body to metabolize protein. If the liver is damaged or not functioning properly, ALT is released into the blood. This causes ALT levels to increase. A high result on this test can be a sign of liver damage.

Aspartate Aminotransferase (AST) Test

Aspartate aminotransferase (AST) is an enzyme found in several parts of your body, including the heart, liver, and muscles. Since AST levels aren't specific for liver damage, it's usually measured together with ALT to check for liver problems. Your doctor may use an ALT-to-AST ratio to help with their diagnosis. When the liver is damaged, AST is released into the bloodstream. A high result on an AST test might indicate a problem with the liver or muscles.

Alkaline Phosphatase (ALP) Test

Alkaline phosphatase (ALP) is an enzyme found in your bones, bile ducts, and liver. An ALP test is typically ordered in combination with several other tests. High levels of ALP may indicate liver damage, blockage of the bile ducts, or a bone disease.

Children and adolescents may have elevated levels of ALP because their bones are growing. Pregnancy can also raise ALP levels.

Albumin Test

Albumin is the main protein made by your liver. It performs many important bodily functions. For example, albumin:

- stops fluid from leaking out of your blood vessels
- nourishes your tissues
- transports hormones, vitamins, and other substances throughout your body

An albumin test measures how well your liver is making this particular protein. A low result on this test indicates that your liver isn't functioning properly.

Bilirubin Test

Bilirubin is a waste product ordinarily processed by the liver. The breakdown of red blood cells creates this waste product. It passes through the liver before being excreted through your stool.

A damaged liver can't properly process bilirubin. This leads to an abnormally high level of bilirubin in the blood. A high result on the bilirubin test indicates that the liver isn't functioning properly.

JAUNDICE

A yellow tinge to the whites of the eyes is a common symptom of jaundice

Bilirubin (bil-ih-ROO-bin) is a yellow-colored substance that is responsible for the yellowing of the skin and sclerae in jaundice.

Bilirubin is a waste product that remains in the bloodstream after iron is removed from hemoglobin in red blood cells. When there is an excess of bilirubin, it can leak out into surrounding tissues, saturating them with this yellow substance. Bilirubin that is circulating freely in the blood is called unconjugated bilirubin.

One of the liver's functions is to filter out waste, such as bilirubin, from the blood.

Once bilirubin is in the liver, other chemicals are latched on to it, creating a substance called conjugated bilirubin, which is secreted in bile (a digestive juice released by the liver) and then excreted. A product of bilirubin is what gives feces its brown color.

Causes of jaundice

Jaundice most often occurs as a result of an underlying disorder that either causes overproduction of bilirubin or prevents the liver from disposing of it, both of which result in bilirubin being deposited in tissues.

Some underlying conditions that may cause jaundice are:

- **Acute inflammation of the liver** - may impair the ability of the liver to conjugate and secrete bilirubin, resulting in a buildup.
- **Inflammation of the bile duct** - may prevent the secretion of bile and removal of bilirubin, causing jaundice.
- **Obstruction of the bile duct** - prevents the liver from disposing of bilirubin.

- **Hemolytic anemia** - production of bilirubin increases when large quantities of red blood cells are broken down.
- **Gilbert's syndrome** - an inherited condition that impairs the ability of enzymes to process the excretion of bile.
- Cholestasis - a condition where the flow of bile from the liver is interrupted. The bile containing conjugated bilirubin remains in the liver instead of being excreted.

More rare conditions that may cause jaundice include:

- **Crigler-Najjar syndrome** - an inherited condition that impairs the specific enzyme responsible for processing bilirubin
- **Dubin-Johnson syndrome** - an inherited form of chronic jaundice that prevents conjugated bilirubin from being secreted out of the liver's cells
- **Pseudojaundice** - a harmless form of jaundice in which the yellowing of the skin results from an excess of beta-carotene, not from an excess of bilirubin; usually from eating lots of carrots, pumpkin, or melon

Symptoms of jaundice

Symptoms of jaundice include:

- Yellow tinge to the skin and the whites of the eyes, normally starting at the head and spreading down the body
- Pruritis (itchiness)
- Fatigue
- Abdominal pain - typically indicates a blockage of the bile duct
- Weight loss
- Vomiting
- Fever
- Paler than usual stools
- Dark urine

Types of jaundice

There are three main types of jaundice:

- **Hepatocellular jaundice** - occurs as a result of liver disease or injury
- **Hemolytic jaundice** - occurs as a result of hemolysis (an accelerated breakdown of red blood cells) leading to an increase in production of bilirubin
- **Obstructive jaundice** - occurs as a result of an obstruction in the bile duct (a system of tubes that carries bile from the liver to the gallbladder and small intestine), which prevents bilirubin from leaving the liver

CIRRHOSIS OF THE LIVER

Cirrhosis is an abnormal liver condition in which there is irreversible scarring of the liver. The main causes are sustained excessive alcohol consumption, viral hepatitis B and C, and fatty liver disease - however, there are many possible causes.

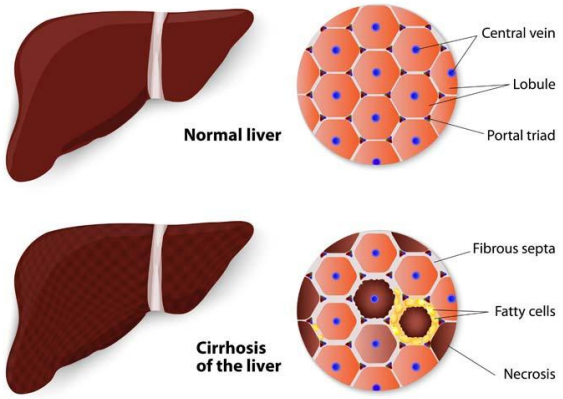
People with cirrhosis may develop jaundice (yellowing of the skin, eyes and tongue), itching and extreme tiredness.

For cirrhosis to develop long-term, continuous damage to the liver needs to occur. When healthy liver tissue is destroyed and replaced by scar tissue the condition becomes serious, as it can start blocking the flow of blood through the liver.

Cirrhosis is a progressive disease, developing slowly over many years, until eventually it can stop liver function (liver failure).

The liver carries out several essential functions, including the detoxification of harmful substances in the body. It also purifies the blood and manufactures vital nutrients.

If cirrhosis is mild the liver can make repairs and continue functioning properly. If the cirrhosis is advanced and more and more scar tissue forms in the liver, the damage is irreparable. The liver tissue is replaced by fibrous scar tissue as well as regenerative nodules (lumps that appear as a consequence of a process in which damaged tissue is regenerated).



Causes of cirrhosis

Common causes of cirrhosis are long-term alcohol abuse, hepatitis B and C infection, and fatty liver disease. Of those, hepatitis B and C together are said to be the leading cause of cirrhosis (WHO). We will take a look at each of these causes in detail below.

Overconsumption of alcohol

According to the NHS (National Health Service), UK, excessive alcohol consumption is when a man drinks more than 21 units and a woman drinks more than 14 units per week.

Alcohol is one of the leading causes of liver cirrhosis.

Toxins, including alcohol, are broken down by the liver. However, if the amount of alcohol is too high the liver will be overworked and liver cells can eventually become damaged.

Heavy, regular, long-term drinkers are much more likely to develop cirrhosis, compared to other healthy people. It is a myth that only alcoholics are at risk - regular and heavy social drinking is also linked to a higher probability of developing cirrhosis.

Typically, heavy drinking needs to be sustained for at least ten years for cirrhosis to develop. The period varies according to each individual.

Regular heavy female drinkers are more likely to develop symptoms compared to men who consume the same amount.

Heavy drinkers will eventually develop *fatty liver*. The liver breaks down alcohol into carbon dioxide and water, causing fatty liver. As soon as excessive drinking stops the symptoms of fatty liver go away. However, 20% to 30% of those who continue drinking heavily will develop alcoholic hepatitis, the next stage. Approximately 10% of heavy drinkers will subsequently develop cirrhosis - the third stage of alcoholic liver disease.

Health authorities in the UK urge males not to exceed three to four units of alcohol consumption per day, and women should not have more than two to three units daily - to reduce the risk of developing alcohol hepatitis and cirrhosis.

Hepatitis

Hepatitis C, a bloodborne infection, can damage the liver and eventually lead to cirrhosis. Hepatitis C is a common cause of cirrhosis in Western Europe, North America, and many other parts of the world. Cirrhosis can also be caused by hepatitis B and D.

Non-alcoholic steatohepatitis (NASH)

NASH is more likely to occur with people who are obese, diabetes patients, those with high blood lipid (fat) levels, as well as individuals with hypertension (high blood pressure). NASH, in its early stages, begins with the accumulation of too much fat in the liver. The fat causes inflammation and scarring, resulting in possible cirrhosis later on.

Autoimmune hepatitis

The person's own immune system attacks healthy organs in the body as though they were foreign substances. Sometimes the liver is attacked. Eventually the patient can develop cirrhosis.

Some genetic conditions

- Hemochromatosis - iron accumulates in the liver and other parts of the body.
- Wilson's disease - copper accumulates in the liver and other parts of the body.

Blockage of bile ducts

Some conditions and diseases, such as cancer of the bile ducts, or cancer of the pancreas can block the bile ducts, increasing the risk of cirrhosis.

Budd-Chiari syndrome

There is thrombosis (blood clots) in the hepatic vein, the blood vessel that carries blood from the liver, leading to liver enlargement and the development of collateral vessels.

Other diseases and conditions

Some of the other diseases and conditions that can contribute to cirrhosis are:

- Cystic fibrosis
- Primary sclerosing cholangitis - hardening and scarring of the bile ducts

- Galactosemia - inability to process sugars in milk
- Schistosomiasis - a parasite commonly found in some developing countries
- Biliary atresia - badly formed bile ducts in babies
- Glycogen storage disease - problems in the storage and energy release vital for cell function.

Symptoms of cirrhosis

A symptom is something the patient feels and reports, while a sign is something other people, including a doctor or a nurse may detect. For example, pain may be a symptom while a rash may be a sign.

Symptoms are not common during the early stages of cirrhosis. However, as scar tissue accumulates the liver's ability to function properly is undermined. **The following signs and symptoms may occur:**

- Blood capillaries become visible on the skin on the upper abdomen
- Fatigue
- Insomnia
- Itchy skin
- Loss of appetite
- Loss of bodyweight
- Nausea
- Pain or tenderness in the area where the liver is located
- Red or blotchy palms
- Weakness.

The following signs and symptoms may appear as liver cirrhosis progresses:

- Abdomen fills up with fluid, giving the patient a large tummy (ascites)
- Accelerated heartbeat
- Altered personality (as blood toxins build up and affect the brain)
- Bleeding gums
- Body and upper arms lose mass

- Body finds it harder to process alcohol
- Body finds it harder to process drugs
- Confusion
- Dizziness
- Fluid buildup on ankles, feet and legs (edema)
- Hair loss
- Higher susceptibility to bruising
- Jaundice (yellowing of the skin, whites of the eyes, and tongue)
- Walking problems (staggering).

Fatty Liver

Fatty liver, or steatosis, is a term that describes the buildup of fat in the liver. While it's normal to have some fat in your liver, more than 5 to 10 percent of your liver weight is fat in the case of fatty liver.

Fatty liver is a reversible condition that can be resolved with changed behaviors. It often has no symptoms and typically does not cause permanent damage.

The liver is the second largest organ in the body. The liver's function is to process everything we eat or drink and filter any harmful substances from the blood. This process is interrupted if too much fat is in the liver. The liver commonly repairs itself by rebuilding new liver cells when the old ones are damaged. When there's repeated damage to the liver, permanent scarring takes place. This is called cirrhosis.

Fatty liver is common. Around 10 to 20 percent of Americans have too much fat in their liver, but no inflammation or damage is present. Most cases of fatty liver are detected in people between ages 40 and 60. When fatty liver is caused by an underlying condition, it can become harmful to the liver if the cause is not recognized and treated.

What Are the Types of Fatty Liver?

There are four types of fatty liver.

Nonalcoholic Fatty Liver

Nonalcoholic fatty liver (NAFL) develops when the liver has difficulty breaking down fats, which causes a buildup in the liver tissue. The cause is not related to alcohol. NAFL is diagnosed when more than 10 percent of the liver is fat.

Alcoholic Fatty Liver

Alcoholic fatty liver is the earliest stage of alcohol-related liver disease. Heavy drinking damages the liver, and the liver cannot break down fats as a result. Abstaining from alcohol will likely cause the fatty liver to subside. Within six weeks of not drinking alcohol, the fat will disappear. However, if excessive alcohol use continues, cirrhosis may develop.

Nonalcoholic Steatohepatitis (NASH)

When the fat builds up enough, it will cause the liver to swell. If the original cause is not from alcohol, it's called nonalcoholic steatohepatitis (NASH). This disease can impair liver function.

Symptoms can be seen with this disease. These include:

- appetite loss
- nausea
- vomiting
- abdominal pain
- yellowing of the skin (jaundice)

If left untreated, NASH can progress to permanent scarring of the liver and eventual liver failure.

Acute Fatty Liver of Pregnancy

Acute fatty liver is a rare complication of pregnancy that can be life-threatening.

Symptoms begin in the third trimester. These include:

- persistent nausea and vomiting
- pain in the upper-right abdomen
- jaundice
- general malaise

Women who are pregnant will be screened for this condition. Most women improve after delivery and have no lasting effects.

Musculoskeletal System

The musculoskeletal system provides form, support, stability, and movement to the body. It is made up of the bones of the skeleton, muscles, cartilage, tendons, ligaments, joints, and other connective tissue that supports and binds tissues and organs together.

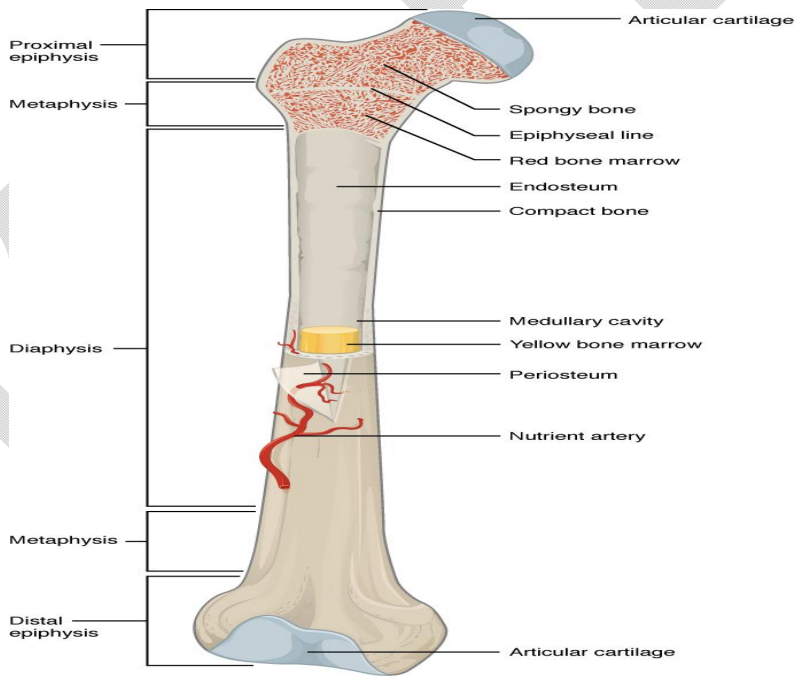
Bone Structure

Bone tissue (osseous tissue) differs greatly from other tissues in the body. Bone is hard and many of its functions depend on that characteristic hardness. Later discussions in this chapter will show that bone is also dynamic in that its shape adjusts to accommodate stresses. This section will examine the gross anatomy of bone first and then move on to its histology.

Gross Anatomy of Bone

The structure of a long bone allows for the best visualization of all of the parts of a bone ([link]). A long bone has two parts: the **diaphysis** and the **epiphysis**. The diaphysis is the tubular shaft that runs between the proximal and distal ends of the bone. The hollow region in the diaphysis is called the **medullary cavity**, which is filled with yellow marrow. The walls of the diaphysis are composed of dense and hard **compact bone**.

Anatomy of a Long Bone



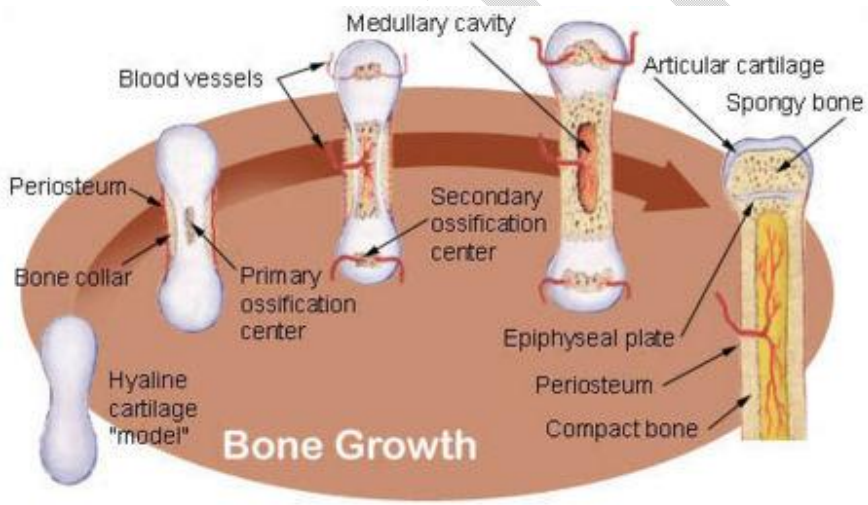
A typical long bone shows the gross anatomical characteristics of bone.

The wider section at each end of the bone is called the epiphysis (plural = epiphyses), which is filled with spongy bone. Red marrow fills the spaces in the spongy bone. Each epiphysis meets the diaphysis at the metaphysis, the narrow area that contains the **epiphyseal plate** (growth

plate), a layer of hyaline (transparent) cartilage in a growing bone. When the bone stops growing in early adulthood (approximately 18–21 years), the cartilage is replaced by osseous tissue and the epiphyseal plate becomes an epiphyseal line.

The medullary cavity has a delicate membranous lining called the **endosteum** (end- = "inside"; oste- = "bone"), where bone growth, repair, and remodeling occur. The outer surface of the bone is covered with a fibrous membrane called the **periosteum** (peri- = "around" or "surrounding"). The periosteum contains blood vessels, nerves, and lymphatic vessels that nourish compact bone. Tendons and ligaments also attach to bones at the periosteum. The periosteum covers the entire outer surface except where the epiphyses meet other bones to form joints. In this region, the epiphyses are covered with **articular cartilage**, a thin layer of cartilage that reduces friction and acts as a shock absorber.

BONE FORMATION



Thirteen weeks after conception, the fetus begins to develop bones. They begin with 300 bones, and end up with 206 bones. At first, the bones are not actually bones. They are cartilage that hardens to become bone with the assistance of calcium. This process of bone hardening is called ossification. During childhood, bones grow very differently. Long bones (such as the bones in your arms or legs) grow lengthwise. Flat bones (bones in your skull) grow expand outward. Bone also continuoulsy undergoes remodeling, replacing the old bone with new bone. Remodeling also allows bone to reapond to changes in mechanical forces, such as pregnancy or exterme weight gain or loss.

Bone remodeling cycle.

Two main types of cells are responsible for bone renewal: the osteoblasts involved in bone formation and the osteoclasts involved in bone resorption.

- Activation: Preosteoclasts are stimulated and differentiated under the influence of cytokine and growth factors to mature into active osteoclasts.
- Resorption: Osteoclasts digest mineral matrix, old bone.
- Reversal: End of resorption

Formation: Osteoblasts are responsible for bone matrix synthesis (collagen). Two other non-collagenous proteins are also formed: ostocalcin and osteonectin.

Bone Remodeling

The renewal of bone is responsible for bone strength throughout our life. Old bone is removed (resorption) and new bone is created (formation). During childhood and the beginning of adulthood, bone becomes larger, heavier and denser, bone formation is then more important than bone resorption.

The Bone Mass actually increases until the age of 20, 25 where it reaches its maximum value: the Peak Bone Mass in denisty and strength. The higher the Peak Bone Mass is, the lower the risk of osteoporosis is. Bone Mass remains stable for a few years (for women, till about 45 years old). After a certain age, bone mass starts to decrease.

Bone remodeling cycle

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Osteoblasts

Osteoblasts are responsible for bone matrix synthesis. They secrete a collagen rich ground substance essential for later mineralization of hydroxyapatite and other crystals. Osteoblasts cause calcium salts and phosphorus to precipitate from the blood, these minerals bond with the newly formed osteoid to mineralize the bone tissue. The osteoblasts also have estrogen receptors. Estrogens can actually increase the number of osteoblasts, increasing therefore collagen production.

Osteocytes

Osteoblasts Osteocytes maintain bones, they play a role in controlling the extracellular concentration of calcium and phosphate, and are directly stimulated by calcitonin and inhibited by PTH (Parathyroid hormone). Their exact role is actually still to be defined.

Osteoclasts

These cells derive from bone marrow mononuclear cells. Their characteristic feature is a ruffled edge where active resorption takes place. The osteoclasts secrete bone-reabsorbing enzymes, which digest bone matrix. The mode of differentiation, recruitment and inhibition is controlled by numerous hormonal and growth factors. The osteoclasts also have estrogen receptors (Estrogens can inhibit their recruitment).

Regulation of bone remodeling Bone formation and resorption are influenced by many factors like:

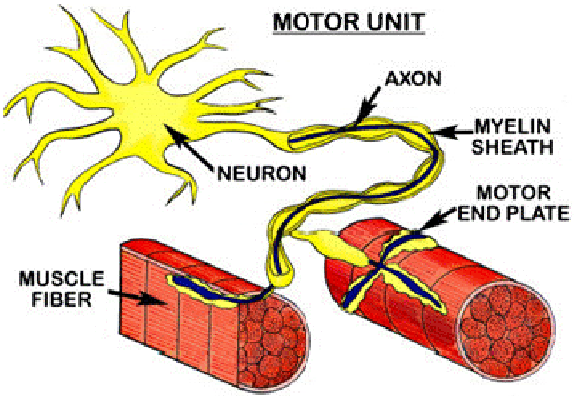
Parathyroïd Hormone (PTH): The PTH can increase the recruitment and the cavity of osteoblasts and osteoclasts. Therefore if the PTH secretion is too high, there is an acceleration of the bone turnover. If the increase occurs along a Vitamin D deficiency, the bone cycle is accelerated and entails bone loss.

Vitamin D: Vitamin D tends to increase the recruitment of osteoclasts, and also plays a part in the mineralization of bone matrix. A lack of Vitamin D results in osteomalacia (impaired mineralization) and too much Vitamin D entails bone loss.

THE PHYSIOLOGY OF SKELETAL MUSCLE CONTRACTION

The Sliding Filament Theory

For a contraction to occur there must first be a stimulation of the muscle in the form of an impulse (action potential) from a motor neuron (nerve that connects to muscle).



Note that one motor neuron does not stimulate the entire muscle but only a number of muscle fibres within a muscle.

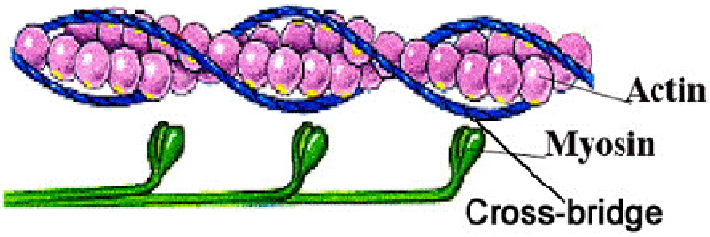
The individual motor neuron plus the muscle fibres it stimulates, is called a motor unit. The motor end plate (also known as the neuromuscular junction) is the junction of the motor neurons axon and the muscle fibres it stimulates.

When an impulse reaches the muscle fibres of a motor unit, it stimulates a reaction in each sarcomere between the actin and myosin filaments. This reaction results in the start of a contraction and the sliding filament theory.

The reaction, created from the arrival of an impulse stimulates the 'heads' on the myosin filament to reach forward, attach to the actin filament and pull actin towards the centre of the sarcomere. This process occurs simultaneously in all sarcomeres, the end process of which is the shortening of all sarcomeres.

Troponin is a complex of three proteins that are integral to muscle contraction. Troponin is attached to the protein tropomyosin within the actin filaments, as seen in the image below. When the muscle is relaxed tropomyosin blocks the attachment sites for the myosin cross bridges (heads), thus preventing contraction.

When the muscle is stimulated to contract by the nerve impulse, calcium channels open in the sarcoplasmic reticulum (which is effectively a storage house for calcium within the muscle) and release calcium into the sarcoplasm (fluid within the muscle cell). Some of this calcium attaches to troponin which causes a change in the muscle cell that moves tropomyosin out of the way so the cross bridges can attach and produce muscle contraction.



In summary the sliding filament theory of muscle contraction can be broken down into four distinct stages, these are;

1. Muscle activation: The motor nerve stimulates an action potential (impulse) to pass down a neuron to the neuromuscular junction. This stimulates the sarcoplasmic reticulum to release calcium into the muscle cell.

2. Muscle contraction: Calcium floods into the muscle cell binding with troponin allowing actin and myosin to bind. The actin and myosin cross bridges bind and contract using ATP as energy (ATP is an energy compound that all cells use to fuel their activity – this is discussed in greater detail in the energy system folder here at pt direct).

3. Recharging: ATP is re-synthesised (re-manufactured) allowing actin and myosin to maintain their strong binding state

4. Relaxation: Relaxation occurs when stimulation of the nerve stops. Calcium is then pumped back into the sarcoplasmic reticulum breaking the link between actin and myosin. Actin and myosin return to their unbound state causing the muscle to relax. Alternatively relaxation (failure) will also occur when ATP is no longer available.

In order for a skeletal muscle contraction to occur;

1. There must be a neural stimulus
2. There must be calcium in the muscle cells
3. ATP must be available for energy

So, a few things can stop a contraction;

1. Energy system fatigue: There is no more ATP left in the muscle cell so it can't keep contracting.

2. Nervous system fatigue: The nervous system is not able to create impulses sufficiently or quickly enough to maintain the stimulus and cause calcium to release.

3. Voluntary nervous system control: The nerve that tells the muscle to contract stops sending that signal because the brain tells it to, so no more calcium ions will enter the muscle cell and the contraction stops.

4. Sensory nervous system information: For example, a sensory neuron (nerves that detect stimuli like pain or how heavy something is) provides feedback to the brain indicating that a muscle is injured while you are trying to lift a heavy weight and consequently the impulse to that muscle telling it to contract is stopped.

In the gym or during exercise virtually all muscular fatigue occurring is energy system fatigue. That is, the rate of work within the muscle cannot be maintained because ATP (energy) can no longer be provided. Strength and hypertrophy (training to make muscles stronger or bigger) training are prime examples of the types of training that can cause muscle failure due to energy system fatigue.

Unit 5

Reproductive physiology: Sex determination and differentiation. Development of female and male genital tracts. Spermatogenesis, capacitation and transport of sperm, blood testis barrier. Ovarian function and its control. Uterine changes, fertilization and implantation. Placenta as a feto- maternal unit, gestation and parturition.

Neurochemistry and neurophysiology: Central Nervous system. Peripheral Nervous system. Blood brain barrier and CSF. Membrane potentials. Synaptic transmission. Neurotransmitters. Sensory receptors and neural pathways. Somatic sensation, EEG, sleep, coma, learning and memory.

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Reproductive Physiology

MALE REPRODUCTIVE SYSTEM

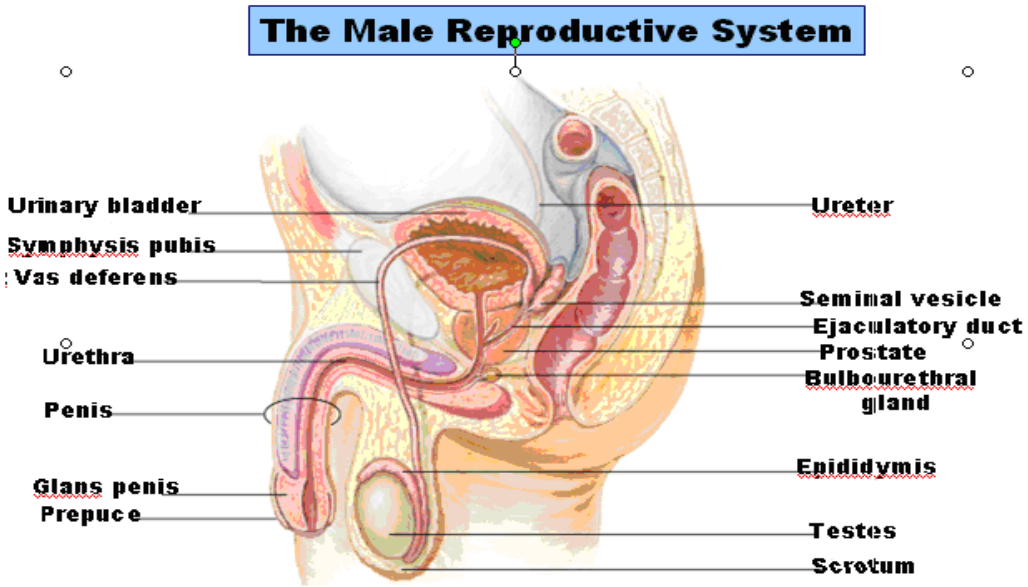
Male reproductive system structure and functions:

The purpose of the organs of the male reproductive system is to perform the following functions:

- To produce, maintain, and transport sperm (the male reproductive cells) and protective fluid (semen)
- To discharge sperm within the female reproductive tract during sex
- To produce and secrete male sex hormones responsible for maintaining the male reproductive system.

STRUCTURE:

Male reproductive system is located outside of the body. **These external structures include the penis, scrotum, and testicles.**



Penis: It has three parts: the root, which attaches to the wall of the abdomen; the body, or shaft; and the glans, which is the cone-shaped part at the end of the penis. The glans, also called the head of the penis, is covered with a loose layer of skin called foreskin. This skin is sometimes removed in a procedure called circumcision. The opening of the urethra, the tube

that transports semen and urine, is at the tip of the penis. The penis also contains a number of sensitive nerve endings. The body of the penis is cylindrical in shape and consists of three circular shaped chambers. These chambers are made up of special, sponge-like tissue. Semen, which contains sperm (reproductive cells), is expelled (ejaculated) through the end of the penis.

Scrotum: This is the loose pouch-like sac of skin that hangs behind and below the penis. It contains the testicles (also called testes), as well as many nerves and blood vessels. The scrotum acts as a "climate control system" for the testes. For normal sperm development, the testes must be at a temperature slightly cooler than body temperature. Special muscles in the wall of the scrotum allow it to contract and relax, moving the testicles closer to the body for warmth or farther away from the body to cool the temperature.

Testicles (testes): These are oval organs about the size of large olives that lie in the scrotum, secured at either end by a structure called the spermatic cord. Most men have two testes. The testes are responsible for making testosterone, the primary male sex hormone, and for generating sperm. Within the testes are coiled masses of tubes called seminiferous tubules. These tubes are responsible for producing sperm cells.

The internal organs of the male reproductive system, also called accessory organs, include the following:

1. Epididymis: The epididymis is a long, coiled tube that rests on the backside of each testicle. It transports and stores sperm cells that are produced in the testes. It also is the job of the epididymis to bring the sperm to maturity, since the sperm that emerge from the testes are immature and incapable of fertilization. During sexual arousal, contractions force the sperm into the vas deferens.

2. Vas deferens: The vas deferens is a long, muscular tube that travels from the epididymis into the pelvic cavity, to just behind the bladder. The vas deferens transports mature sperm to the urethra, the tube that carries urine or sperm to outside of the body, in preparation for ejaculation.

3. Ejaculatory ducts: These are formed by the fusion of the vas deferens and the seminal vesicles (see below). The ejaculatory ducts empty into the urethra.

4. Urethra: The urethra is the tube that carries urine from the bladder to outside of the body. In males, it has the additional function of ejaculating semen when the man reaches orgasm. When the penis is erect during sex, the flow of urine is blocked from the urethra, allowing only semen to be ejaculated at orgasm.

5. Seminal vesicles: The seminal vesicles are sac-like pouches that attach to the vas deferens near the base of the bladder. The seminal vesicles produce a sugar-rich fluid (fructose) that provides sperm with a source of energy to help them move. The fluid of the seminal vesicles makes up most of the volume of a man's ejaculatory fluid, or ejaculate.

6. Prostate gland: The prostate gland is a walnut-sized structure that is located below the urinary bladder in front of the rectum. The prostate gland contributes additional fluid to the ejaculate. Prostate fluids also help to nourish the sperm. The urethra, which carries the ejaculate to be expelled during orgasm, runs through the center of the prostate gland.

7. Bulbourethral glands: Also called Cowper's glands, these are pea-sized structures located on the sides of the urethra just below the prostate gland. These glands produce a clear, slippery fluid that empties directly into the urethra. This fluid serves to lubricate the urethra and to neutralize any acidity that may be present due to residual drops of urine in the urethra.

FUNCTIONS:

The entire male reproductive system is dependent on hormones, which are chemicals that regulate the activity of many different types of cells or organs. The primary hormones involved in the male reproductive system are follicle-stimulating hormone, luteinizing hormone, and testosterone.

Follicle-stimulating hormone is necessary for sperm production (spermatogenesis), and luteinizing hormone stimulates the production of testosterone, which is also needed to make sperm. Testosterone is responsible for the development of male characteristics, including muscle mass and strength, fat distribution, bone mass, facial hair growth, voice change, and sex drive.

STRUCTURE AND FUNCTION OF THE TESTES

The testes consist of a series of tubules containing testosterone and sperm-producing cells, which are covered by a multi-layered tunica. The primary function of the testes is sperm production and the main components of the testes which play a role in sperm production are the seminiferous tubules, Sertoli and Leydig cells. There are also a series of ducts and tissues within the testis which play an accessory role in producing and/or transporting sperm from the testes.

1. Tunica

The multi-layered tunica covers the testes, It facilitate blood supply to the testes and creates a partition between sperm producing regions of the testes. There are three layers to the tunica, the tunica vasculosa, tunica albuginea and tunica vaginalis.

Tunica vasculosa

The tunica vasculosa is the inner layer of the tunica and consists of blood vessels and connective tissue. It is covered by the tunica albuginea and **facilitates blood supply to the testes.**

Tunica albuginea

Tunica albuginea (Latin for white coat) is a dense layer of tissue which encases the testes and connects to the layers of fibres which surround the epididymis, the first in a series of ducts which transport sperm out of the testes and into the penis.The tunica albuginea also extends into the testis, creating partitions between seminiferous tubules where sperm is produced. It has a bluish-white appearance and covers most of the inner layer of the tunica, the tunica vasculosa. Overlying this structure is the outer layer of the tunica, the tunica vaginalis.

Tunica vaginalis

There are two layers of the tunica vaginalis: the visceral and the parietal. The visceral layer overlies the tunica albuginea (middle layer of the tunica) while the parietal layer lines the scrotal cavity. A thin fluid layer separates the two sections of the tunica vaginalis and reduces friction between the testes and the scrotum. An increased quantity of fluid between these layers can form a hydrocele (an accumulation of fluid).

2. Seminiferous tubules

Seminiferous tubules lie within the testes and are separated by partitions, which are extensions of the tunica albuginea, the middle layers of the testes' covering. They house germ cells (23 chromosome cells which in men replicate to produce sperm) and are the site of spermatogenesis (sperm production).

Partitions divide the testes into lobules which contain the seminiferous tubules. Each lobule contains 1–4 seminiferous tubules and each testis may contain up to 900 of these tubules. The tubules average 50 cm in length and are tightly coiled within the testis. A typical testis contains up to 800 m of tightly coiled seminiferous tubules.

3. Mediastinum

The mediastinum is a region of tissue which connects to the rete testis. The mediastinum supports the blood vessels and lymphatic system (the system which removes excess fluid from body tissues) of the testis and the ducts within the testis which transport sperm.

4. Straight tubules

Straight tubules connect seminiferous tubules to the rete testis facilitating sperm transport. They cross from within partitions which separate seminiferous tubules inside the testes.

5. Rete testis

The seminiferous tubules open into a series of channels called the rete testis. The rete testis facilitate the transport of sperm from the testes to the sperm transport ducts of the penis.

6. Efferent ducts

Efferent ducts are located between the rete testes and the epididymis. They connect the testes to the male ducts and facilitate the transport of sperm from the testes.

7. Leydig cells (interstitial cells)

In the adult male, the soft connective tissues surrounding the seminiferous tubules contain interstitial cells of Leydig. These cells are almost non-existent prior to the commencement of testicular testosterone production at the onset of puberty.

The primary function of the Leydig cells is production and secretion of androgens particularly testosterone which is the key male hormone. The primary function of testosterone produced in the Leydig cells is to **stimulate spermatogenesis** (sperm production) and support the development of immature spermatozoa (sperm). Some 95% of testosterone produced by the male body post-puberty is produced in the Leydig cells. Men who do not produce enough testosterone in their testicles develop a condition called hypogonadism (testosterone deficiency).

Testosterone also has a number of **secondary functions** related to giving the male body a typically male appearance, including:

- Regulation of central nervous system functions which influence libido and sexual behaviour;
- Stimulation of the metabolism, particularly those functions involved in protein synthesis and muscle growth;
- Maintaining glands and organs in the male reproductive system; and
- Developing and maintaining male secondary sexual characteristics which, compared to female characteristics include:
    - Fully developed male genitals;
    - Male pattern body hair distribution, that is facial hair, baldness (because testosterone decreases hair follicle growth on the top of the head) and body hair;
    - Deepening of the voice;
    - Muscle development;
    - Increased bone density and calcium retention;
    - Increased basal metabolic levels;

- Increased number of red blood cells;
- Increased body water due to increased renal reabsorption of water and electrolytes.

Sertoli cells (sustentacular cells)

Sertoli cells are also found in the seminiferous tubules; however they do not play a direct role in sperm or testosterone production. Unlike Leydig cells which proliferate at the onset of puberty, Sertoli cells are abundant pre-puberty and in the elderly. Sertoli cells have numerous important functions which facilitate spermatogenesis and sperm transport.

Their primary function in an adult is to provide support for germ cells as they grow and develop into mature spermatozoa. Stimulated by follicle stimulating hormone (FHS) which is produced in the pituitary gland and in the presence of testosterone (produced by the testes following puberty), Sertoli cells secrete proteins which bind to testosterone and other hormones in the androgen group. These androgen-binding proteins are thought to stimulate spermatogenesis by increasing the concentration of androgens in the seminiferous tubules. The Sertoli cells also secrete a nutritious protein-rich fluid into the seminiferous tubules, which sustains the germ cells and assists in their transport.

Sertoli cells further play an endocrinological (hormone-secretion) role in spermatogenesis, by producing inhibin, a peptide hormone which down-regulates pituitary FSH secretion (signals the pituitary to produce less FSH). Increases in inhibin production correlate to increases in the rate of spermatogenesis. Sertoli cells are thought to also influence the secretion of gonadotrophin releasing hormone (GnRH) from the hypothalamus (a hormone secreting gland in the brain which influences numerous reproductive functions).

Sertoli cells are linked by tight junctions and form the blood-testes barrier.

Blood-testes barrier

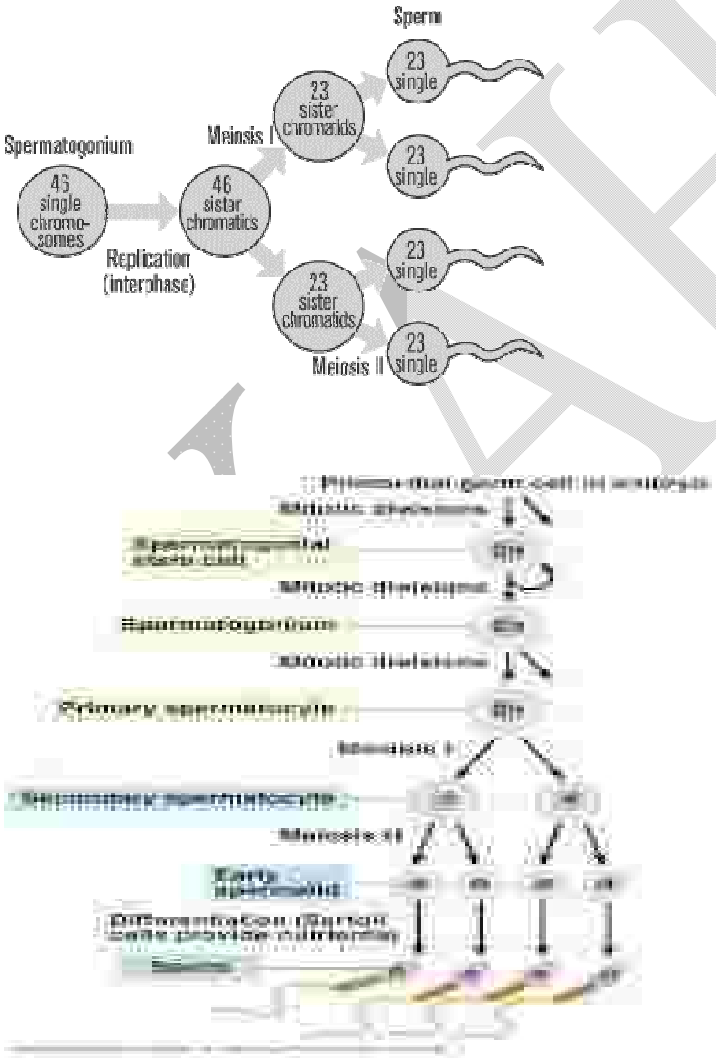
The blood-testes barrier functions in a similar way to the blood-brain barrier, separating the testes from the normal circulatory processes of the body (the processes through which blood and other body fluids circulate to cells in the body). The barrier prevents blood and other body fluids entering the testes; it allows only secretions from Sertoli cells (androgen-binding proteins, protein-rich fluid) to enter the lumen of the seminiferous tubules. In doing so the blood-testes barrier enables the testes to maintain a fluid balance conducive to sperm development.

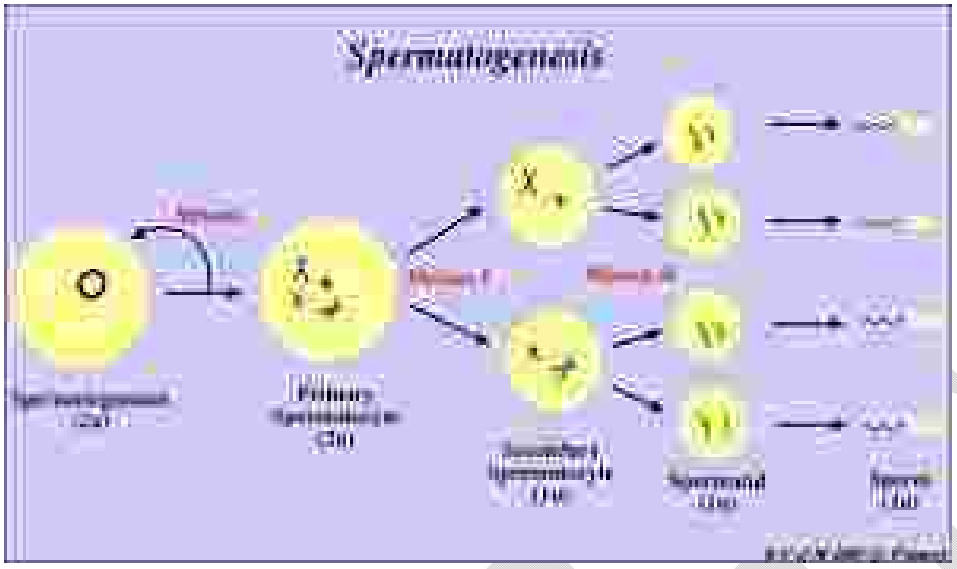
The blood-testes barrier also protects developing sperm from the body's immune system, which attacks immature sperm if the blood-testis barrier is compromised. The auto-immune response occurs because developing sperm contain sperm-specific antigens in their cell membranes, which the immune system recognises as foreign (because these antigens do not occur in other body cells) and attacks.

SPERMATOGENESIS:

Spermatogenesis

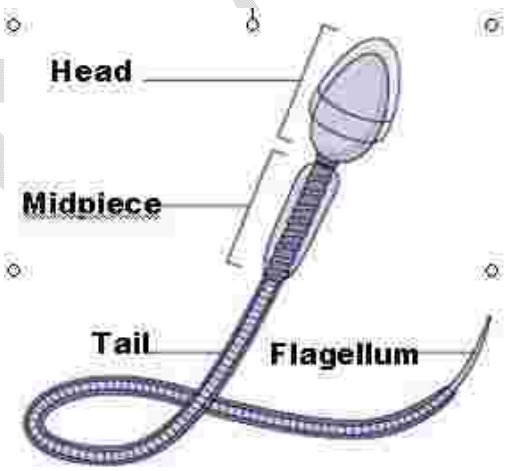
The male testes have tiny tubules containing diploid cells called spermatogonium that mature to become sperm. The basic function of spermatogenesis is to turn each one of the diploid spermatogonium into four haploid sperm cells. This quadrupling is accomplished through the meiotic cell division detailed in the last section. During interphase before meiosis I, the spermatogonium's 46 single chromosomes are replicated to form 46 pairs of sister chromatids, which then exchange genetic material through synapsis before the first meiotic division. In meiosis II, the two daughter cells go through a second division to yield four cells containing a unique set of 23 single chromosomes that ultimately mature into four sperm cells. Starting at puberty, a male will produce literally millions of sperm every single day for the rest of his life.





Spermatozoon

- It is a microscopic cell
- Consists of a head and tail- flagellum
- Genetic material are located in the head
- Motility occurs by means of the flagellum



CAUSES OF INFERTILITY IN MALE

A variety of disorders ranging from hormonal disturbances to physical problems, to psychological problems can cause male infertility.

- In many instances, male infertility is caused by **testicular damage** resulting in an inability of the testicle to produce sperm. This aspect of male infertility is analogous to menopause for women and cannot usually be treated.
- Besides testicular damage, the main causes of male infertility are **low sperm production and poor sperm quality.**

Sperm-related problems include

- low sperm count
- sperm that don't move quickly enough — they die before they reach the egg
- sperm that are not formed correctly
- seminal fluid that is too thick — sperm can't move around in it very easily
- no sperm

Sperm-related problems may result from too much or too little of some of the hormones that guide sperm making.

- Another cause of male infertility is a problem with ejaculation. In some cases, tubes inside the male reproductive organs are blocked. In some cases, there is no known reason for someone's infertility. This is called unexplained infertility.

The Causes of Male Infertility

Male infertility has many causes- hormonal imbalances, to physical problems, to psychological and/or behavioral problems.

(i) The following list highlights some **lifestyle choices** that negatively impact male fertility

- Smoking--significantly decreases both sperm count and sperm cell motility
- Prolonged use of marijuana and other recreational drugs.
- Chronic alcohol abuse.
- Anabolic steroid use--causes testicular shrinkage and infertility.

- Intense exercise--produces high levels of adrenal steroid hormones which cause a testosterone deficiency resulting in infertility.
- Inadequate vitamin C and Zinc in the diet.
- Tight underwear--increases scrotal temperature which results in decreased sperm production.
- Exposure to environmental hazards and toxins such as pesticides, lead, paint, radiation, radioactive substances, mercury, benzene, boron, and heavy metals Malnutrition and anemia.
- Excessive stress

Modifying these behaviors can improve a man's fertility and should be considered while treating infertility

(ii) Hormonal Problems

A small percentage of male infertility is caused by hormonal problems. The hypothalamus-pituitary endocrine system regulates the chain of hormonal events that enables testes to produce and effectively disseminate sperm. Several things can go wrong with the hypothalamus-pituitary endocrine system:

- The brain can fail to release gonadotrophic-releasing hormone (GnRH) properly. GnRH stimulates the hormonal pathway that causes testosterone synthesis and sperm production. A disruption in GnRH release leads to a lack of testosterone and a cessation in sperm production.
- The pituitary can fail to produce enough lutenizing hormone (LH) and follicle stimulating hormone (FSH) to stimulate the testes and testosterone/sperm production. LH and FSH are intermediates in the hormonal pathway responsible for testosterone and sperm production.
- The testes' Leydig cells may not produce testosterone in response to LH stimulation.
- A male may produce other hormones and chemical compounds which interfere with the
  sex-hormone balance.

The following is a list of hormonal disorders which can disrupt male infertility:

Hyperprolactinemia:

Elevated prolactin--a hormone associated with nursing mothers, is found in 10 to 40 percent of infertile males. Mild elevation of prolactin levels produces no symptoms, but greater elevations

of the hormone reduces sperm production, reduces libido and may cause impotence. This condition responds well to the drug Parlodel (bromocriptine).

Hypothyroidism:

Low thyroid hormone levels--can cause poor semen quality, poor testicular function and may disturb libido. May be caused by a diet high in iodine. Reducing iodine intake or beginning thyroid hormone replacement therapy can elevate sperm count. This condition is found in only 1 percent of infertile men.

Congenital Adrenal Hyperplasia:

Occurs when the pituitary is suppressed by increased levels of adrenal androgens. Symptoms include low sperm count, an increased number of immature sperm cells, and low sperm cell motility. Is treated with cortisone replacement therapy. This condition is found in only 1 percent of infertile men.

Hypogonadotropic Hypopituitarism:

Low pituitary gland output of LH and FSH. This condition arrests sperm development and causes the progressive loss of germ cells from the testes and causes the seminiferous tubules and Leydig (testosterone producing) cells to deteriorate. May be treated with the drug Serophene. However, if all germ cells are destroyed before treatment commences, the male may be permanently infertile.

Panhypopituitafism:
Complete pituitary gland failure--lowers growth hormone, thyroid-stimulating hormone, and LH and FSH levels. Symptoms include: lethargy, impotence, decreased libido, loss of secondary sex characteristics, and normal or undersized testicles. Supplementing the missing pituitary hormones may restore vigor and a hormone called hCG may stimulate testosterone and sperm production.

(iii) Physical Problems

A variety of physical problems can cause male infertility. These problems either interfere with the sperm production process or disrupt the pathway down which sperm travel from the testes to the tip of the penis. These problems are usually characterized by a low sperm count and/or abnormal sperm morphology. The following is a list of the most common physical problems that cause male infertility:

Variocoele:

A varicocele is an enlargement of the internal spermatic veins that drain blood from the testicle to the abdomen (back to the heart) and are present in 15% of the general male population and 40% of infertile men.

Damaged Sperm Ducts:

Seven percent of infertile men cannot transport sperm from their testicles to out of their penis. This pathway may be blocked by a number of conditions:

- A genetic or developmental mistake may block or cause the absence of one or both tubes (which transport the sperm from the testes to the penis).
- Scarring from tuberculosis or some STDs may block the epididymis or tubes.
- An elective or accidental vasectomy may interrupt tube continuity.

Torsion:

Is a common problem affecting fertility that is caused by a supportive tissue abnormality which allows the testes to twist inside the scrotum which is characterized by extreme swelling. Torsion pinches the blood vessels that feed the testes shut which causes testicular damage. If emergency surgery is not performed to untwist the testes, torsion can seriously impair fertility and cause permanent infertility if both testes twist.

Infection and Disease:

Mumps, tuberculosis, brucellosis, gonorrhea, typhoid, influenza, smallpox, and syphilis can cause testicular atrophy. A low sperm count and low sperm motility are indicators of this condition. Also, elevated FSH levels and other hormonal problems are indicative of testicular damage. Some STDs like gonorrhea and chlamydia can cause infertility by blocking the epididimis or tubes. These conditions are usually treated by hormonal replacement therapy and surgery in the case of tubular blockage.

Klinefelter's Syndrome:

Is a genetic condition in which each cell in the human body has an additional X chromosome--men with Klinefelter's Syndrome have one Y and two X chromosomes. Physical symptoms include peanut-sized testicles and enlarged breasts. A chromosome analysis is used to confirm this analysis. If this condition is treated in its early stages (with the drug hCG), sperm production may commence and/or improve. However, Klinefelter's Syndrome eventually causes all active testicular structures to atrophy. Once testicular failure has occurred, improving fertility is impossible.

Retrograde Ejaculation:

Is a condition in which semen is ejaculated into the bladder rather than out through the urethra because the bladder sphincter does not close during ejaculation. If this disorder is present, ejaculate volume is small and urine may be cloudy after ejaculation. This condition affects 1.5 percent of infertile men and may be controlled by medications like decongestants which

contract the bladder sphincter or surgical reconstruction of the bladder neck can restore normal ejaculation.

(iv) Psychological/Physical/Behavioral Problems:

Several sexual problems exist that can affect male fertility. These problems are most often both psychological and physical in nature: it is difficult to separate the physiological and physical components.They are

- **Erectile Disfunction (ED)**
- **Premature Ejaculation**
- **Ejaculatory Incompetence**

FEMALE REPRODUCTIVE SYSTEM

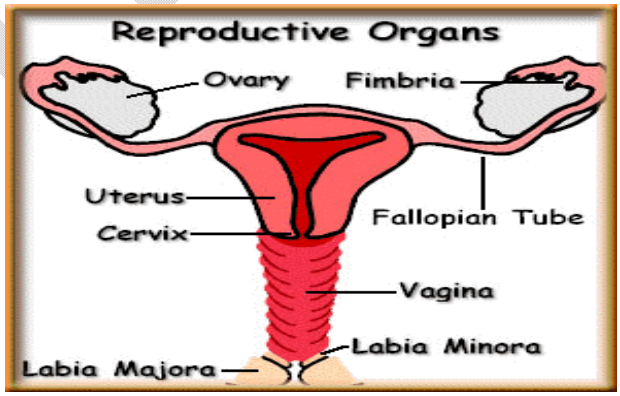
The female reproductive system includes

Major Organs

- Ovaries [gonads]
- Uterine tubes [fallopian tubes]
- Uterus
- Vagina
- Accessory glands
- External genitalia
- Breasts

These organs are involved in the production and transportation of gametes and the production of sex hormones. The female reproductive system also facilitates the fertilization of ova by sperm and supports the development of offspring during pregnancy

Fig : Female reproductive system



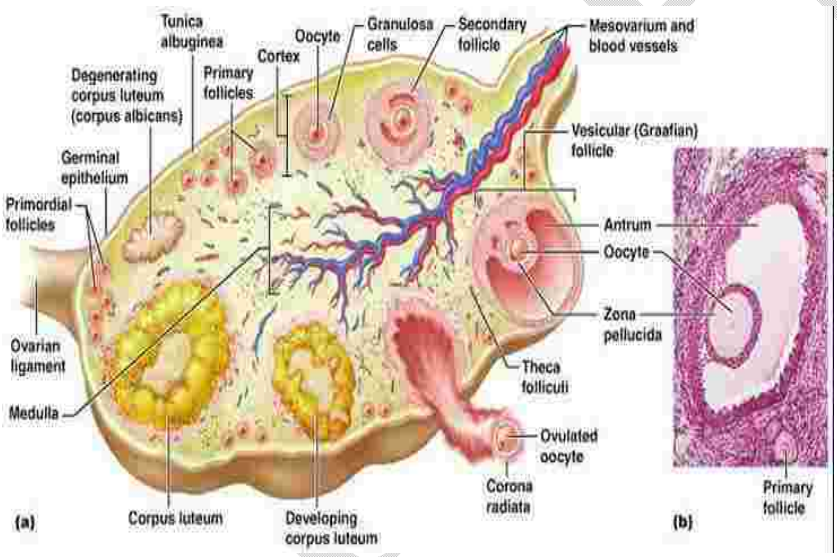
(i)Ovaries

The ovaries are the female pelvic reproductive organs that house the ova and are also responsible for the production of sex hormones. They are paired organs located on either side of the uterus within the broad ligament below the uterine (fallopian) tubes. The ovaries are responsible for housing and releasing ova, or eggs, necessary for reproduction. At birth, a female has approximately 1-2 million eggs, but only 300 of these eggs will ever become mature and be released for the purpose of fertilization.

The ovaries are small, oval-shaped, and grayish in color, with an uneven surface. The actual size of an ovary depends on a woman's age and hormonal status; the ovaries, covered by a modified peritoneum, are approximately 3-5 cm in length during childbearing years and become much smaller and then atrophic once menopause occurs. A cross-section of the ovary reveals many cystic structures that vary in size. These structures represent ovarian follicles at different stages of development and degeneration.

Structure of Ovaries

The ovaries have two layer soft tissue.



The medulla.

This lies in the centre and consists of fibrous tissue, blood vessels and nerves.It is highly vascularised and contains hilus cells, which are similar to the Leydig cells of the testes.

The cortex. This surrounds the medulla. It has a frame work of connective tissue ,or **stroma,** covered by germinal epithelium. It contains ovarian follicles in various stages of maturity, each of which contains an ovum. Before puberty the ovaries are inactive but the stroma already contains immature (primordial) follicles, which the female has from birth. During the

childbearing years, about every 28 days, one ovarian follicle (Graffian follicle) matures, ruptures and releases its ovum into the peritoneal cavity. This is called ovulation and it occurs during most menstrual cycles.

Stroma

- The body of the ovary (ovarian stroma) consists of:
  - spindle-shaped cells
  - fine collagen fibres
  - ground substance
- Stromal cells resemble fibroblasts, but some contain lipid droplets.
- Bundles of smooth muscle cells are scattered throughout the stroma.

Ovarian follicles

The ovarian follicles are found within the stroma of the ovarian cortex. A follicle consists of an oocyte surrounded by follicular cells called granulosa cells. Follicles go through stages of development each month, with the goal of their maturation to release the oocyte for the purpose of fertilization and reproduction. If the follicle fails to release the egg, it goes through degeneration.

Ovarian ligament

Several paired ligaments support the ovaries. The ovarian ligament connects the uterus and ovary. The posterior portion of the broad ligament forms the mesovarium, which supports the ovary and houses its arterial and venous supply. The suspensory ligament of the ovary (infundibular pelvic ligament) attaches the ovary to the pelvic sidewall. This larger structure also contains the ovarian artery and vein, as well as nerve supply to the ovary.

(ii) Fallopian Tubes

The fallopian tubes are a pair of muscular tubes that extend from the left and right superior corners of the uterus to the edge of the ovaries. The fallopian tubes end in a funnel-shaped structure called the infundibulum, which is covered with small finger-like projections called fimbriae. The fimbriae swipe over the outside of the ovaries to pick up released ova and carry them into the infundibulum for transport to the uterus. The inside of each fallopian tube is covered in cilia that work with the smooth muscle of the tube to carry the ovum to the uterus.

(iii)Uterus

The uterus is a hollow, muscular, pear-shaped organ located posterior and superior to the urinary bladder. Connected to the two fallopian tubes on its superior end and to the vagina (via

the cervix) on its inferior end, the uterus is also known as the womb, as it surrounds and supports the developing fetus during pregnancy. The inner lining of the uterus, known as the endometrium, provides support to the embryo during early development. The visceral muscles of the uterus contract during childbirth to push the fetus through the birth canal.

(iv) Vagina

The vagina is an elastic, muscular tube that connects the cervix of the uterus to the exterior of the body. It is located inferior to the uterus and posterior to the urinary bladder. The vagina functions as the receptacle for the penis during sexual intercourse and carries sperm to the uterus and fallopian tubes. It also serves as the birth canal by stretching to allow delivery of the fetus during childbirth. During menstruation, the menstrual flow exits the body via the vagina.

(v)Breasts and Mammary Glands

The breasts are specialized organs of the female body that contain mammary glands, milk ducts, and adipose tissue. The mammary glands are a special type of sudoriferous glands that have been modified to produce milk to feed infants.

Blood supply, lymph drainage and nerve supply to ovary

Arterial supply: This is by the **ovarian arteries,** which branch from the abdominal aorta just below the renal arteries.

Venous drainage: This is into a plexus of veins behind the uterus from which the ovarian veins arise. The right ovarian vein opens into the inferior vena cava and the left into the left renal vein.

Lymph drainage: This is to the lateral aortic and preaortic lymph nodes. The lymph vessels follow the same route as the arteries.

Nerve supply: The ovaries are supplied by parasympathetic nerves from the sacral outflow and sympathetic nerves from the lumbar outflow. Their precise functions are not yet fully understood.

The ovarian cycle

- The ovarian cycle is a series of events in the ovaries that occur during and after the maturation of the oocyte (egg or ovum).
- During their reproductive years, nonpregnant females usually experience a cyclical sequence of changes in their ovaries and uterus
- A typical female cycle lasts 28 days; however, this can range from 21-35 days and involves both oogenesis, the process of formation and development of oocyte, and preparation of the uterus to receive a fertilized ovum.

- Hormones secreted by the hypothalamus, anterior pituitary gland -the follicle stimulating hormone (FSH) and the luteinizing hormone (LH), -and ovaries control the principal events.
- The uterine (menstrual) cycle is a concurrent series of changes in the endometrium of the uterus to prepare it for the arrival of a fertilized ovum that will develop in the uterus until birth. If fertilization does not occur, the lining of the endometrium is shed during menstruation

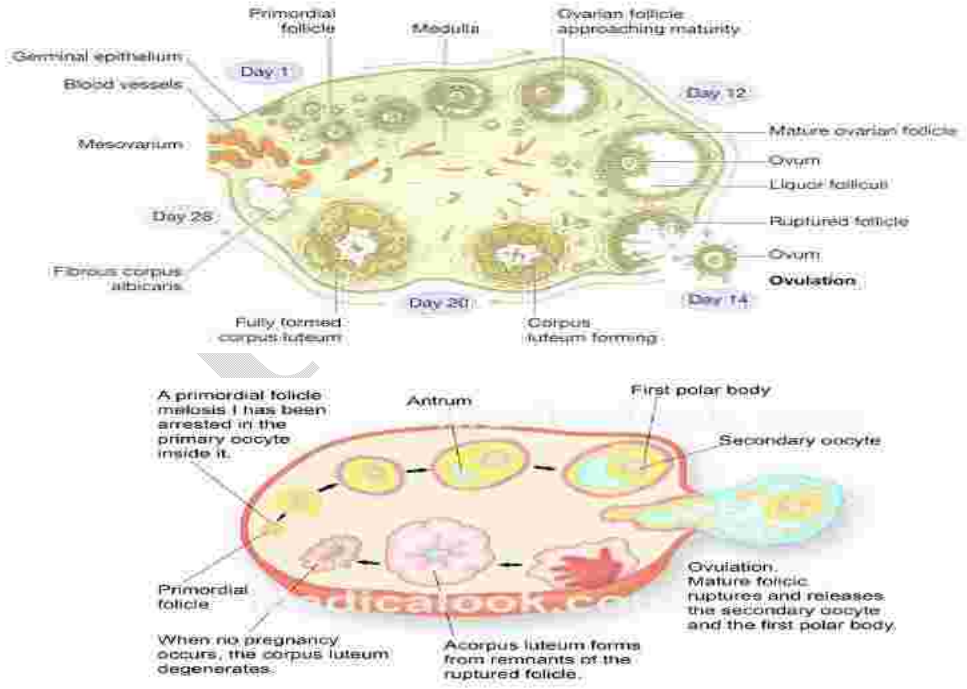
The ovarian cycle has 2 distinct phases:

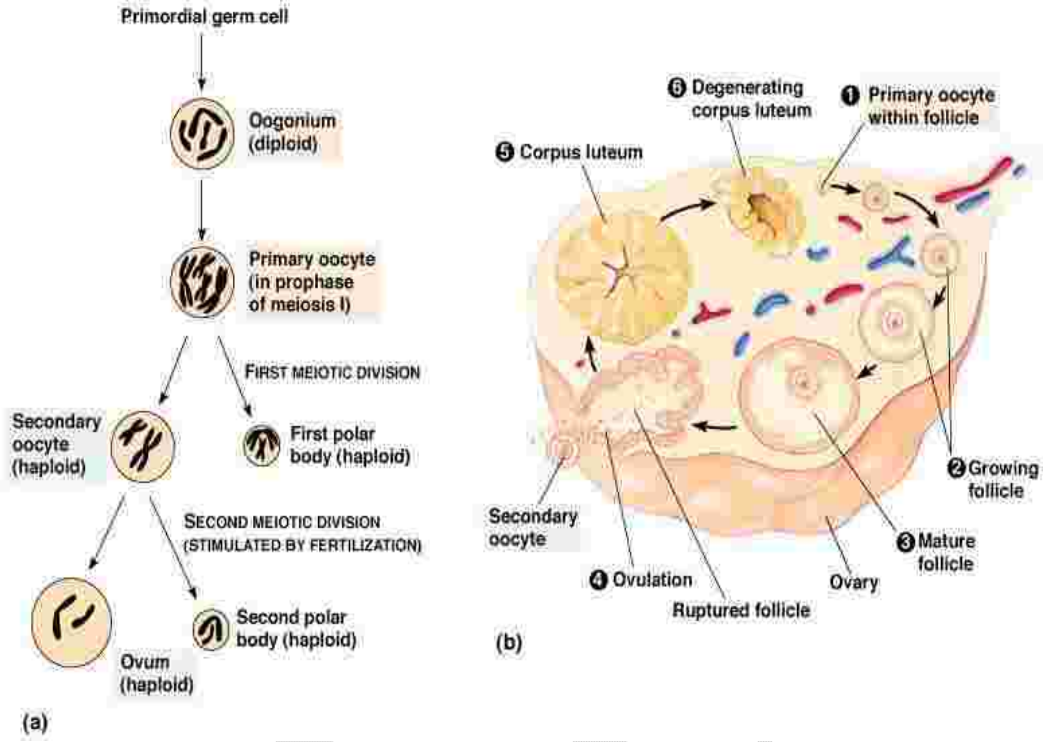
(i) Follicular phase (days 1-14)

(ii) **Luteal phase** (days 14-28).

The follicular phase is characterized by follicle development and growth, where one follicle matures and releases an egg at the time of ovulation, around day 14 of the female cycle. The remaining immature follicles go through stages of degeneration up until day 28, when the cycle repeats itself. The egg that is released is picked up by the fimbriae of the uterine tube, and the egg is transported toward the uterus. If fertilization does not occur, the egg degenerates, and menstruation occurs.

. Fig: Ovarian cycle





Menstruation

Menstruation is the elimination of the thickened lining of the uterus (endometrium) from the body through the vagina. Menstrual fluid contains blood, cells from the lining of the uterus (endometrial cells) and mucus. The average length of a period is between three days and one week.

The menstrual cycle

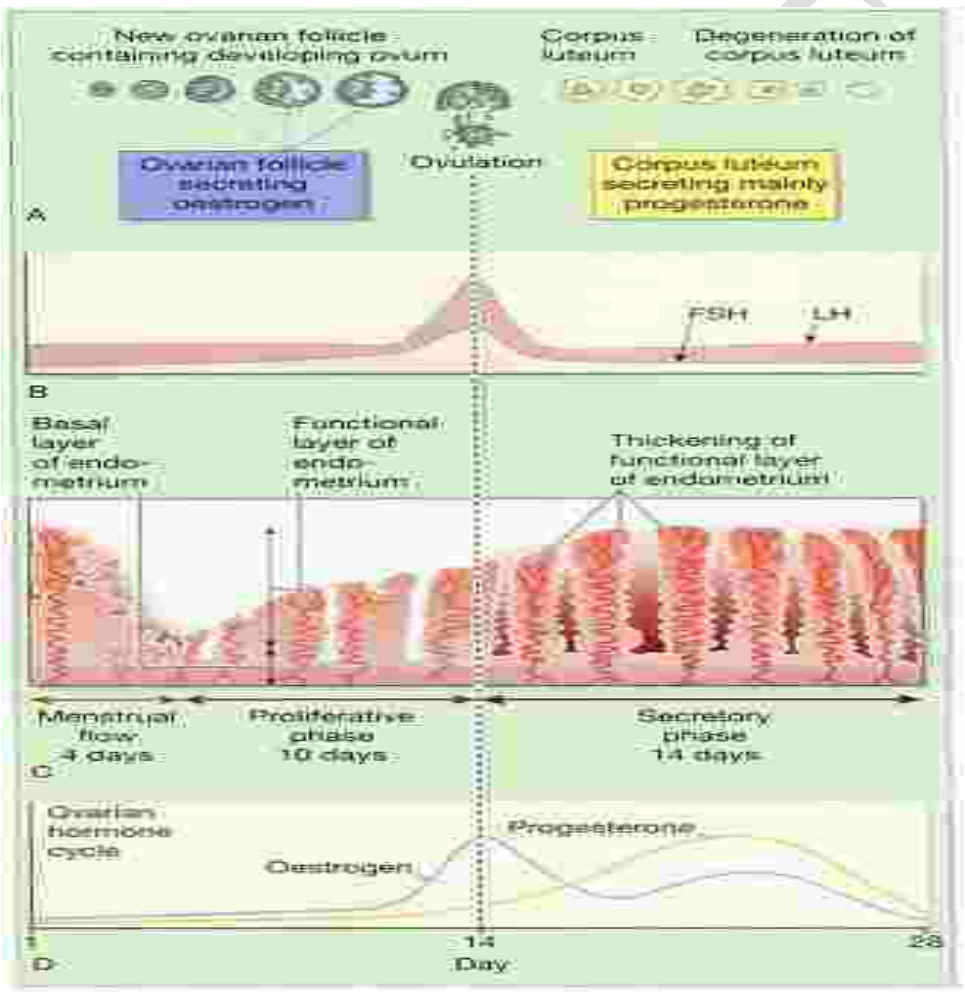
This is a series of events, occurring regularly in females every 26 to 30 days throughout the child bearing period of about 36years. The cycle consists of a series of changes that take place concurrently in the ovaries and Uterine walls, stimulated by changes in the blood concentrations of hormones. Hormones secreted in the cycle are regulated by negative feedback mechanisms. The hypothalamus secretes Luteinizing Hormone Releasing Hormone (LHRH) which stimulates the anterior pituitary to secrete. Follicle Stimulating Hormone (FSH) ,which promotes the maturation of ovarian follicles and the secretion of oestrogen, leading to ovulation.

The average length of menstrual cycle is 28 days. It vary between women and from one cycle to next cycle. It is the hormonal driven cycle; day 1 is the first day of period while day 14 is the approximate day of ovulation and if an egg is not fertilized, hormone levels eventually drop

and at about day 25; the egg begins to dissolve and the cycle begins again with the period at about day 30.

- The average age for a girl to get her first period in the US is 12, but the range of age is about 8 to 15 years old.
- Women usually have periods until about ages 45 to 55.

Fig: Menstrual cycle



The four main phases of the menstrual cycle are:

(i) Menstruation
(ii) The follicular phase
(iii) Ovulation
(iv) The luteal phase

Follicular phase

The follicular phase starts on the first day of menstruation and ends with ovulation. Prompted by the hypothalamus, the pituitary gland releases follicle stimulating hormone (FSH). This hormone stimulates the ovary to produce around five to 20 follicles (tiny nodules or cysts), which bead on the surface.

Each follicle houses an immature egg. Usually, only one follicle will mature into an egg, while the others die. This can occur around day 10 of a 28-day cycle. The growth of the follicles stimulates the lining of the uterus to thicken in preparation for possible pregnancy.

Ovulation

Ovulation is the release of a mature egg from the surface of the ovary. This generally occurs mid-cycle, around two weeks or so before menstruation starts. During the follicular phase, the developing follicle causes a rise in the level of oestrogen. The hypothalamus in the brain recognises these rising levels and releases a chemical called gonadotrophin-releasing hormone (GnRH). This hormone prompts the pituitary gland to produce raised levels of luteinising hormone (LH) and FSH.

Within two days, ovulation is triggered by the high levels of LH. The egg is funnelled into the fallopian tube and towards the uterus by waves of small, hair-like projections. The life span of the typical egg is only around 24 hours. Unless it meets a sperm during this time, it will die.

Luteal phase

During ovulation, the egg bursts from its follicle, but the ruptured follicle stays on the surface of the ovary. For the next two weeks or so, the follicle transforms into a structure known as the corpus luteum. This structure starts releasing progesterone, along with small amounts of oestrogen. This combination of hormones maintains the thickened lining of the uterus, waiting for a fertilised egg to stick (implant).

If a fertilised egg implants in the lining of the uterus, it produces the hormones that are necessary to maintain the corpus luteum. This includes human chorionic gonadotrophin (HCG), the hormone that is detected in a urine test for pregnancy. The corpus luteum keeps producing the raised levels of progesterone that are needed to maintain the thickened lining of the uterus.

If pregnancy does not occur, the corpus luteum withers and dies, usually around day 22 in a 28-day cycle. The drop in progesterone levels causes the lining of the uterus to fall away. This is known as menstruation. The cycle then repeats.

Hormones and the menstrual cycle

The menstrual cycle is complex and is controlled by many different glands and the hormones that these glands produce. A brain structure called the hypothalamus causes the nearby pituitary gland to produce certain chemicals, which prompt the ovaries to produce the sex hormones oestrogen and progesterone.

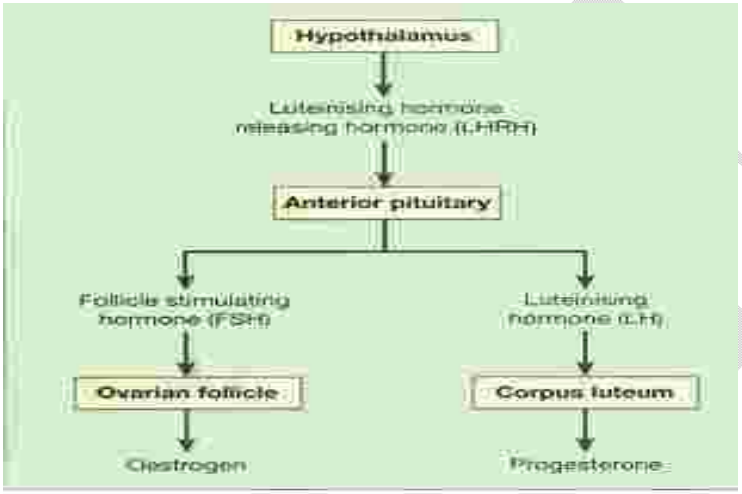


Figure 19.8 Female reproductive hormones and target tissues.

- Maturation of the follicle is stimulated by follicle stimulating hormone (FSH) from the anterior pituitary, and oestrogen secreted by the follicle lining cells.
- Ovulation is triggered by a surge of luteinising hormone (LH) from the anterior pituitary, which occurs a few hours before ovulation.
- After ovulation, the follicle lining cells develop into the corpus luteum (yellow body), under the influence of LH from the anterior pituitary. The corpus luteum produces the hormone progesterone and some oestrogen.
- If the ovum is fertilised it embeds itself in the wall of the uterus where it grows and develops and produces the hormone human chorionic gonadotrophin (hCG),which stimulates the corpus luteum to continue secreting progesterone and oestrogen for the first 3 months of the pregnancy after which time this function is continued by the placenta.
- If the ovum is not fertilised the corpus luteum degenerates and a new cycle begins with menstruation. At the site of the degenerate corpus luteuman inactive mass of fibrous tissue forms, called the corpus albicans. Sometimes more than one follicle matures at a time, releasing two or more ovum in the

same cycle. When this happens and the ova are fertilised the result is a multiple pregnancy.

Common menstrual problems:

Premenstrual syndrome: side effects before periods-water retention, headache, fatigue, irritability: Treatment- exercise, dietary modification.

Dysmenorrhoea-pianful period-treatment- pain relieving medication

Menorrhagia- heavy menstrual flow-cause anemia- treatment- hormonal intra uterine device

Anenorrhoea-absence of menstrual periods-abnormal and causes are low or high body weight, excessive exercise.

FEMALE INFERTILITY

Women are born with a finite number of eggs. Thus, as the reproductive years progress, the number and quality of the eggs diminish. The chances of having a baby decrease by 3% to 5% per year after the age of 30. This reduction in fertility is noted to a much greater extent after age 40.

Causes Female Infertility

Female infertility can be also be caused by a number of factors, including the following:

- **Damage to fallopian tubes.** Damage to the fallopian tubes (which carry the eggs from the ovaries to the uterus) can prevent contact between the egg and sperm. Pelvic infections, endometriosis, and pelvic surgeries may lead to scar formation and fallopian tube damage.
- **Hormonal causes.** Some women have problems with ovulation. Synchronized hormonal changes leading to the release of an egg from the ovary and the thickening of the endometrium (lining of the uterus) in preparation for the fertilized egg do not occur. These problems may be detected using basal body temperature charts, ovulation predictor kits, and blood tests to detect hormone levels.
- **Cervical causes.** A small group of women may have a cervical condition in which the sperm cannot pass through the cervical canal. Whether due to abnormal mucus production or a prior cervical surgical procedure, this problem may be treated with intrauterine inseminations.
- **Uterine causes.** Abnormal anatomy of the uterus; the presence of polyps and fibroids.
- **Unexplained infertility**. The cause of infertility in approximately 20% of couples will not be determined using the currently available methods of investigation.

Detection of Infertility

If male infertility is suspected, a semen analysis is performed. This test will evaluate the number and health of his sperm. A blood test can also be performed to check his level of testosterone and other male hormones.

If female infertility is suspected several tests are performed:

- A blood test to check hormone levels
- An endometrial biopsy to check the lining of the uterus
    - Two diagnostic tests that may be helpful in detecting scar tissue and tubal obstruction are hysterosalpingography and laparoscopy.
    - Hysterosalpingography (HSG). This procedure involves either ultrasound or X-rays taken of the reproductive organs. Either dye or saline and air are injected into the cervix and travel up through the fallopian tubes. This enables the ultrasound or X-ray to reveal if the fallopian tubes are open or blocked.
    - Laparoscopy. In this procedure, a laparoscope (a slender tube fitted with a fiberoptic camera) is inserted into the abdomen through a small incision near the belly button. The laparoscope enables the doctor to view the outside of the uterus, ovaries, and fallopian tubes to detect abnormal growths, as in endometriosis.

PREGNANCY AND PARTURITION

I. Development of the Fetus

A. The fetus is the result of differentiation of the inner cell mass of the embryo into ectoderm, mesoderm and endoderm.

Endoderm -- becomes the lining of the gut, glands and bladder

Mesoderm -- becomes connective tissue, vascular system, bones, muscle and the adrenal cortex.

Ectoderm -- becomes the nervous system and the covering of the body.

Organogenesis

The organs of the fetus grow at differential rates resulting in a constant changing of shape.

1. The liver and heart are highly functional in the early embryo and greatly enlarged. The lungs, however, develop functionally just before delivery. In the fetus, the placenta functions as a lung and oxygen-rich blood travels from the umbilical vein through the ductus venous, the caudal vena cava, and through an opening between right and left

atrum (foramen ovale) directly into the left atrium. A ductus arteriosus shunts right ventricular blood away from the lungs and directly into the aorta.

2. The brain and nervous system develop early and the brain (especially its hypothalamus and pituitary) plays a major role in controlling the functional development of other systems of the body. Interference with hypothalamic function at the stage when a particular process is under development can cause permanent defects (birth defects).

B. Growth is orderly and fetal age can be easily determined from crown rump length or length of the long bones or from the time specific structures develop.

C. Factors affecting prenatal development.

1. Heredity.
2. Maternal size and age influence account for 50-75% of the variation in birth weight. For example, the Shire horse x Shetland pony cross produces a foal nearly the size of a pony when the dam is a pony.
3. Restricted feed intake in the last 1/3 of gestation results in reduced birth weight, most weight increase occurs in the last trimester.
4. Large litter cause reduced birth weight and there are preferred locations in the uterus in litter bearing species.
5. Ambient temperature. Ewes subjected to high temperature produce lighter lambs and have less mammary development.

II. Establishment of Pregnancy:

A. After fertilization embryos spend a short period of time trapped on the ampulla side of the ampullary-isthmic junction of the oviduct. They then pass rapidly through the isthmus to the uterus. In horses the ampullary-isthmic junction allows egg passage only after a fertile mating. It has been suggested that a humoral agent is produced by the embryo which promotes opening or transfer across the ampullary-isthmic junction. Embryos fail to develop beyond the early blastocyst if confined to the oviduct.

Hormonal events associated with the first 14 days of the estrous cycle and pregnancy are essentially identical; however, by day 16 the female must decide if she is pregnant and intends to maintain corpora lutea or to cause their regression and thereby start a new estrous cycle.

Since uterine PGF2a causes corpus luteum (CL) regression and terminates progesterone production in farm animals its secretion, transport or effectiveness at the ovary must be prevented for maintenance of corpora lutea. The way this is accomplished differs for each species.

B. Swine -- Pregnancy is established when the embryo starting at day 12 produces estrogen which acts on the uterus preventing the release of the luteolytic factor (PGF2a) into the uterine vein. The corpora lutea are saved from regression. LH from the sow's pituitary gland is required to maintain the CL throughout pregnancy. The placenta of the sow converts all its produced progesterone to estrogen. Therefore, functional ovaries are the only source of progesterone and needed to prevent uterine contraction throughout pregnancy.

C. Sheep -- The ovine blastocyst prevents CL regression by production of a protein from its trophoblast cells called "ovine interferon tau (oIFN-t). The oIFN-t acts on the endometrium of the uterus to prevent the syntheses of PGF2a. Thus by preventing synthesis of the CL luteolytic agent, PGF2a, the CL is protected and maintained.

D. Cattle -- The bovine blastocyst prevents CL regression by a mechanism similar to that described for sheep except the protein produced by the blastocyst is called bovine interferon tau (bIFN-t) . One half of this protein appears to be similar to oIFN-t of the sheep.

F. Human -- In humans and other primates maintenance of the corpus luteum, progesterone production and pregnancy are dependent on a placental hormone called Human Chorionic Gonadotropin. This hormone, abbreviated hCG, has LH like activity. It is the LH activity that protects the corpus luteum from regression and stimulates its production of progesterone, The hCG is produced initially by the trophectoderm of the blastocyst embryo (8-10 days after conception). As soon as the placenta forms, cells of its chorion layer derived from trophectoderm cells produce and continue to produce hCG. The presence of hCG in maternal blood provides the basis for rapid and accurate immunological assay and pregnancy diagnosis.

III. Maintenance of Gestation:

The maintenance of pregnancy in mammals is dependent on prevention of uterine contraction except in the elephant and perhaps the mare at the end of pregnancy. A "progesterone block" of myometrial activity prevents uterine contraction. The source of progesterone and control of its production differ between species and stages of pregnancy. Species or stages in which the ovary is required generally require a functional pituitary gland except for rodents where the corpora lutea are maintained by a placental gonadotropin.

A. Species with Progesterone from the CL

1. Swine -- progesterone from the CL and CL maintenance are essential for prevention of uterine contraction and maintenance of pregnancy in this species throughout the 114 day gestation. Production of progesterone by the CL is dependent on continued secretion of LH from the anterior pituitary gland. During the first 1/4 of gestation each uterine horn must contain at least 2 piglets, total of 4, to produce sufficient signal to tell the sow she is pregnant and to prevent regression of the CL by PGF2a.

2. Cattle -- One blastocyst is usually sufficient to signal maintenance of pregnancy although early conception rates are higher when 2 blastocysts are transferred into the uterus. Later they compete and 1 usually dies. The CL and ovarian progesterone are essential for pregnancy maintenance through 215 days of the 280 day bovine gestation. After day 215 the maternal adrenals produce enough progesterone to maintain pregnancy to term. Maintenance of the CL is likely dependent on pituitary LH.

3. Horses -- The original corpus luteum is maintained through day 140. However, mare will remain pregnant when the ovaries are removed after day 70. About day 35, cells of fetal trophoblast origin from the chorioallantoic girdle invade the endometrial cups of the uterus and by day 40 produce equine chorionic gonadotropin (eCG). The gonadotropic hormone stimulates follicular growth on the ovaries, occasional ovulation and considerable luteinization occurs by day 50 to form numerous accessory corpora lutea. The eCG levels remain high and accessory corpora lutea greatly elevate plasma progesterone through day 140. The accessory and original CL regress and pregnancy is maintained by low levels of progestin or some as yet unexplained mechanism.

   Equine blastocysts do not undergo elongation immediately after hatching from the zona as in other species. Rather they remain spherical until day 50 due to a large prominent fluid filled yolk sac. Blastocyst elongation and true implantation occur after day 50. Abortion often occurs at this time of transition from yolk sac attachment to true placentation. Progesterone from the original and eCG induced accessory corpora lutea is essential around this time to prevent abortion.

B. Species with Pregnancy Maintained by the Placenta

1. Sheep -- The CL and anterior pituitary LH needed to cause CL secretion of progesterone are essential for the first 55 days of ovine pregnancy. Thereafter the placenta produces sufficient progesterone for maintenance of pregnancy until the end of the 146 day gestation when the placenta converts its produced progesterone to estrogen.

2. Human -- After 2 months of pregnancy the human placenta produces sufficient progesterone to maintain the pregnancy and corpus luteum and its maintenance by hCG are no longer required. There is also evidence that the hormone relaxin is produced during human pregnancy. It also causes some suppression of uterine contraction.

IV. Length of Gestation

A. Length of gestation is calculated as the interval from the last fertile mating to parturition. It is quite precise in swine (114 ± 2 days), especially within breeds, variable in cattle (280 ± 5 days) and sheep (148 ± 5 days) and highly variable in horses (338 ± 15 days) and humans (252-274 days).

B. The length of gestation is influenced by:

1. Heredity -- genotypes of the offspring. In horses, mares have a gestation of 5 days longer when bred to a stallion than when bred to a Jack. Interestingly, the eCG levels in the mare are 10 times higher and found for over a month longer in mares carrying a foal from a stallion than from a Jack. Pony mares have a gestation of approximately 330 days while large saddle mares average 338 days.

2. Fetal sex -- Male calves and foals are carried 1 to 2 days longer than female.

3. Twinning -- Twin calves are carried 3 to 6 days less than singles yet litter size in swine has very effect on gestation length until the litter is reduced to one pig, then there is a tendency for prolonged gestation.

4. Life of the fetus -- late fetal death or abnormalities of the pituitary or adrenal glands will extend gestation in swine, sheep and cattle.

V. Parturition

Parturition is not a decisive single-step terminal event. Preparation for parturition involves coordinated changes in both mother and fetus. The mother must develop the ability to produce and eject milk in order to feed the newborn. In some species, she must develop nest building or protective senses as well. Her uterus must be removed from progesterone influence and stimulated to undergo contraction. These and other events must be, and are, synchronized. Meanwhile, the fetus must develop the ability to respire air, to circulate blood to and from the lungs, to metabolize milk products, to regulate its own body temperature, immune protection from its new environment, and other essential functions. These events are coordinated by the fetus and they in turn are synchronized with the maternal changes.

A. Mechanisms initiating parturition -- for delivery to occur, the uterus must undergo massive contraction and the birth canal (cervix, and pelvis in some species) must be opened. For this to happen, a progesterone block of uterine contraction must be removed. In species such as swine where progesterone is from the corpus luteum, regression of the corpus luteum must occur. In species such as sheep where progesterone is from the placenta, this production must cease.

1. Sheep: Parturition is prevented by removal of the fetal pituitary or adrenal glands and prematurely induced along with lung maturation and other necessary life systems by Adrenal Corticotrophic Hormone (ACTH) or the hormone of the fetal adrenal cortex, cortisol. Thus, the message initiating parturition starts with the fetal brain, its control of ACTH release from the pituitary, and increased cortisol production by the fetal adrenal. The cortisol stimulates placental enzymes which cause placental progesterone to be made into estrogen. The placental estrogen acts on a uterus which is no longer under progesterone influence causing the myometrium to contract. This stimulates the uterus to release prostaglandin F2a which in turn, and in the absence of progesterone, stimulates release of oxytocin and prolactin from the pituitary gland. Prostaglandin F2a and oxytocin cause a cascading effect on the uterus; that is, the more

it is stimulated to contract, the more prostaglandin is released and the more prostaglandin released, the more the uterus contracts until delivery occurs. Relaxin release to soften the cervix appears to be stimulated by the elevated estrogen in maternal blood.

2. Swine: Parturition is prevented by removal of the pituitary glands of the fetuses, fetal decapitation or late fetal death of an entire litter. After day 100, parturition can be prematurely induced by ACTH, glucocorticoids (cortisol is a glucocorticoid) or prostaglandin F2a. Parturition does not occur if prostaglandin synthesis is inhibited. The initiation of parturition is controlled by the fetus as in sheep but different mechanism exists for terminating production of progesterone because it is produced by the corpora lutea in this species. As in sheep, the message initiating parturition starts with the fetal brain and after day 100, the following events: ACTH release, elevation of adrenal cortisol, stimulation of some as yet unknown intermediate which causes the uterus to produce and release prostaglandin F2a. The prostaglandin F2a stimulates release of prolactin and oxytocin cause a cascading of uterine contraction until delivery is complete. Delivery requires about 15 minutes per pig and stillbirths occur if delivery is prolonged. Prostaglandin F2a causes the corpora lutea to release relaxin. Relaxin is capable of softening and relaxing the cervix as well as pelvic ligaments to expand the birth canal. This is essential for rapid and live birth.

3. Cattle. The mechanisms controlling parturition are similar to those in swine.

4. Horses. Hormonal events change very rapidly preceding parturition in the mare perhaps because the contractile property of the myometrium is not under heavy progesterone suppression. There is a rapid and high elevation of prostaglandin F2a and oxytocin at the time of labor and delivery is rapidly completed without much prior warning. It is likely that the fetus controls the initiation of parturition in this species but the mare can suppress this stimulation for days if disturbed and nearly all mares choose to foal at night when they are not disturbed. As in sheep, swine and cattle, both glucocorticoids and prostaglandin F2a can be used to induce preterm delivery.

5. Primates: In the human, the control of corpus luteum function is not dependent on the uterus and in fact the ovary and maternal pituitary gland are not necessary for completion or termination of pregnancy. Although exogenous corticosteroids do not induce labor in the human, the fact that fetal pituitary or adrenal failure prolongs gestation suggests the involvement of these two glands in human parturition as in other species. Present evidence from the rhesus monkey and the human suggests that endogenous prostaglandins play some part in limiting progesterone production. As in other species there is a dramatic increase in placental estrogen production before parturition. This estrogen is known to stimulate the synthesis of prostaglandin F2a by placenta and uterus and to thereby cause uterine contraction. Estrogen also promotes development of receptors for oxytocin and communication junctions between cells of

the uterus. There is firm evidence that prostaglandins increase during labor, and that inhibition of prostaglandin activity delays labor in primates. Prostaglandins clearly have a role in labor and along with oxytocin, they cause the uterine contractions of delivery. Extensive clinical experience in the prostaglandins for induction of labor has revealed no ill effects on the fetus.

B. Stages of labor:

1. Preparation stage. Uterine contractions provide the major driving force for this stage of delivery (uterine 90%, abdominal contraction 10%). The preparatory stage is characterized by rhythmic peristaltic and segmental contraction of the uterus which force fetal fluids and membranes against a relaxed cervix causing it to dilate. Uterine contractions are stimulated by extrinsic autonomic neural reflex mechanisms and most importantly, by the local characteristic of automatic contractibility of this smooth muscle.

2. Expulsion of the fetus. This stage is characterized by violent contractions of the diaphragm and abdominal muscles as well as the myometrium. In ruminants, the fetus is expelled while attached to the umbilical cord and placenta. However, in swine and horses, the placental connections are often broken before delivery. Therefore live birth in these species is dependent on rapid delivery.

3. Expulsion of the placenta. Peristaltic contraction of the uterus causes inversion of the chorioallantoic placenta and its expulsion. In the pig, placental membranes are sometimes shed between delivered piglets and the remainder at the end of delivery. In ruminants, loosening of the chorionic villi from crypts of the caruncles does not always occur. These are held in place by a swelling or engorgement with blood. Failure of separation results in a retained placenta. These are most frequent in cows that deliver before full term.

Neurochemistry and neurophysiology

THE CENTRAL NERVOUS SYSTEM

1. The central nervous system CNS is responsible for integrating sensory information and responding accordingly. It consists of two main components:
    1. The **spinal cord** serves as a conduit for signals between the brain and the rest of the body. It also controls simple musculoskeletal reflexes without input from the brain.
    2. The **brain** is responsible for integrating most sensory information and coordinating body function, both consciously and unconsciously. Complex functions such as thinking and feeling as well as regulation of homeostasis are attributable to different parts of the brain.

2. The brain and spinal cord share some key anatomic features:
    1. The entire CNS is encased in bone. The brain is within the **cranium**, while the spinal cord runs within a canal through the **vertebrae**.
    2. Within its bony case, the entire CNS is bathed in a **cerebrospinal fluid (CSF)**, a colorless fluid produced by special structures in the brain. CSF provides a special chemical environment for nervous tissue, as well as an additional buffer against physical damage.
    3. The special chemical environment of nervous tissue is maintained by the relatively impermeable membranes of capillaries in the CNS. This feature is known as the **blood-brain barrier**.
    4. There are two general types of tissue in the CNS:
        - **Gray matter** consists of nerve cell bodies, dendrites, and axons. Neurons in gray matter organize either in layers, as in the cerebral cortex, or as clusters called **nuclei**.
        - **White matter** consists mostly of axons, causing it to look white due to the myelin sheathing of the axons.

The Meninges

Both the spinal cord and brain are covered in three continuous sheets of connective tissue, the meninges. From outside in, these are the

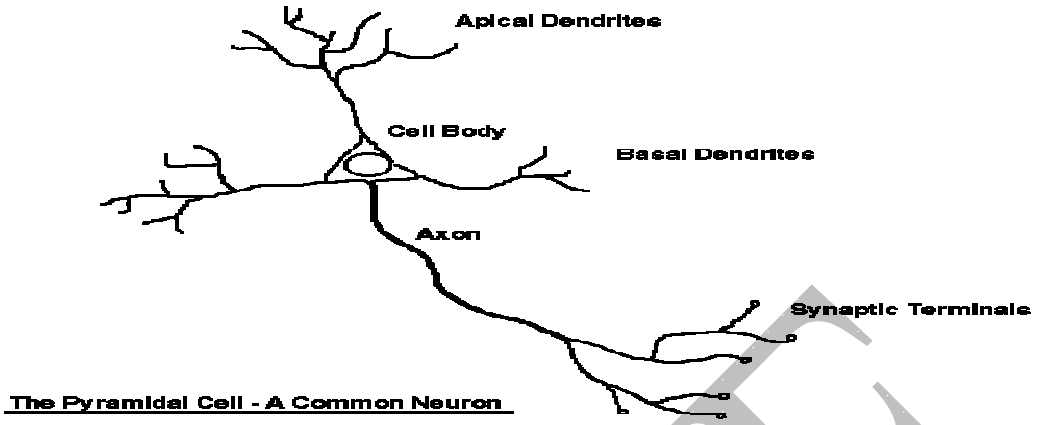
- **dura mater** — pressed against the bony surface of the interior of the vertebrae and the cranium
- the **arachnoid**
- the **pia mater**

The region between the arachnoid and pia mater is filled with **cerebrospinal fluid** (**CSF**).

(i) BRAIN

- The brain is one of the largest and most complex organs in the human body. It is made up of more than 100 billion neurons that communicate in trillions of connections called synapses.
- While variable in size and shape, all neurons have three parts.
    - **Dendrites** receive information from another cell and transmit the message to the cell body.
    - The **cell body** contains the nucleus, mitochondria and other organelles typical of eukaryotic cells.
    - The **axon** conducts messages away from the cell body.

Figure-Structure of neuron



The Pyramidal Cell - A Common Neuron

The brain is made of three main parts:

- **forebrain** (prosencephalon)
- **midbrain** (mesencephalon)
- **hindbrain** (rhombencephalon)

THE FOREBRAIN

The human forebrain (prosencephalon) consists of the cerebrum, thalamus, and hypothalamus.

- Cerebrums consist of a pair of large **cerebral hemispheres**, called the **telencephalon**. Because of crossing over of the spinal tracts, the left hemisphere of the forebrain deals with the right side of the body and vice versa.
- a group of structures located deep within the cerebrum, that make up the **diencephalon**.-, which is composed of two major parts:

The **thalamus** processes and integrates all sensory information going to the higher regions of the brain.

The **hypothalamus** is critical for homeostasis, the maintenance of the body's internal environment.

THE MIDBRAIN

The midbrain along with the medulla and pons are often referred to as the "brainstem. It is primarily responsible for eye movement

THE HINDBRAIN

The main structures of the hindbrain (rhombencephalon) are the

- **medulla oblongata** - make breathing possible and regulate heartbeat
- **pons** - he pons seems to serve as a relay station carrying signals from various parts of the cerebral cortex to the cerebellum.participates in the reflexes that regulate breathing
- **cerebellum-** to coordinate body movements

(i) The Cerebrum: The cerebrum or cortex is the largest part of the human brain, he cerebrum fills up most of our skull. It is involved in remembering, problem solving, thinking, and feeling. It also controls movement.The cerebral cortex is divided into four sections, called "lobes": **the frontal lobe, parietal lobe, occipital lobe, and temporal lobe.**

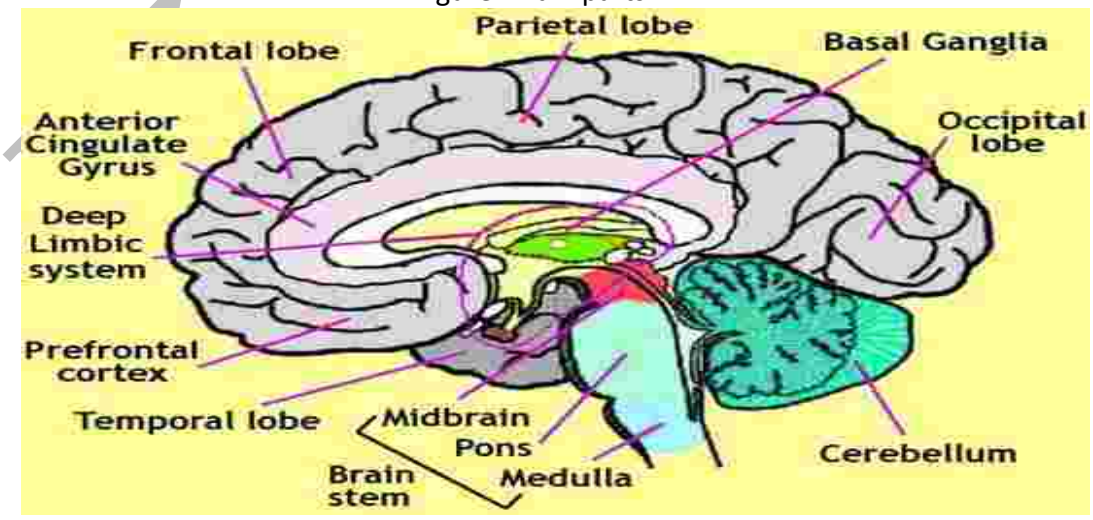
- **Frontal Lobe-** associated with reasoning, planning, parts of speech, movement, emotions, and problem solving
- **Parietal Lobe-** associated with movement, orientation, recognition, perception of stimuli
- **Occipital Lobe**- associated with visual processing
- **Temporal Lobe**- associated with perception and recognition of auditory stimuli, memory, and speech
- deep furrow divides the cerebrum into two halves, known as the **left and right hemispheres.** The two hemispheres look mostly symmetrical yet it has been shown that each side functions slightly different than the other. Sometimes the right hemisphere is associated with creativity and the left hemispheres is associated with logic abilities. The corpus callosum is a bundle of axons which connects these two hemispheres.

(ii)The Cerebellum: The cerebellum sits at the back of our head, under the cerebrum. The cerebellum, or "little brain", is similar to the cerebrum in that it has two hemispheres and has a highly folded surface or cortex. This structure is associated with regulation and coordination of movement, posture, and balance.

(iii)Limbic System: The limbic system, often referred to as the "emotional brain", is found buried within the cerebrum. This system contains the thalamus, hypothalamus, amygdale and hippocampus.

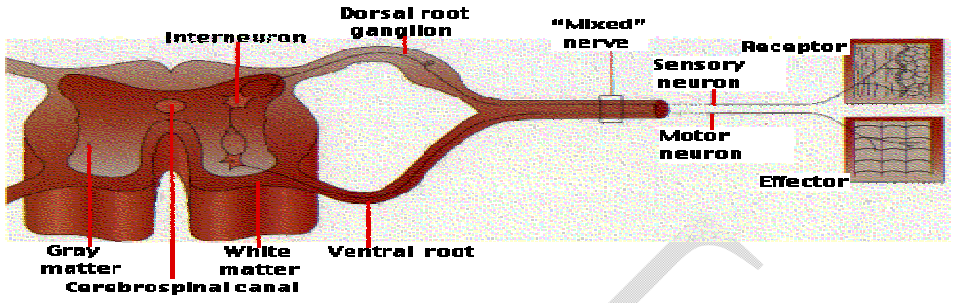
(iv)Brain Stem: Underneath the limbic system is the brain stem.It sits beneath our cerebrum in front of our cerebellum. The brain stem is made of the midbrain, pons, and medulla. It connects the brain to the spinal cord and controls automatic functions such as breathing, sleep , digestion, heart rate and blood pressure.

Figure: Brain parts



- The human brain receives nerve impulses from **spinal cord** and 12 pairs of **cranial nerves**

(2) THE SPINAL CORD



31 pairs of **spinal nerves** arise along the spinal cord. These are **"mixed" nerves** because each contain both sensory and motor axons. However, within the spinal column,

- all the **sensory axons** pass into the **dorsal root ganglion** where their cell bodies are located and then on into the spinal cord itself.
- all the **motor axons** pass into the **ventral roots** before uniting with the sensory axons to form the mixed nerves.

The spinal cord carries out two main functions:

- It connects a large part of the peripheral nervous system to the brain. Information (nerve impulses) reaching the spinal cord through sensory neurons are transmitted up into the brain. Signals arising in the motor areas of the brain travel back down the cord and leave in the motor neurons.
- The spinal cord also acts as a minor coordinating center responsible for some simple reflexes like the withdrawal reflex.

The interneurons carrying impulses to and from specific receptors and effectors are grouped together in **spinal tracts**. Impulses reaching the spinal cord from the left side of the body eventually pass over to tracts running up to the right side of the brain and vice versa

(II) PERIPHERAL NERVOUS SYSTEM

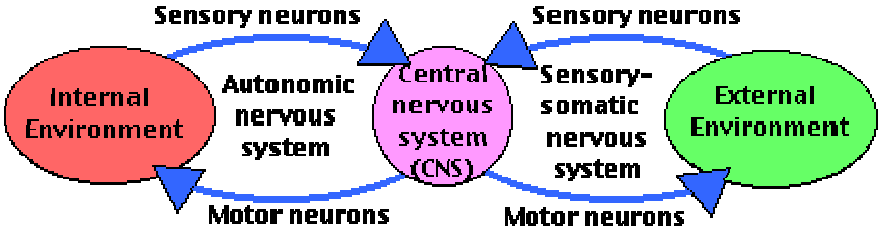
The **PNS** consists of

- **sensory neurons** running from stimulus **receptors** that inform the CNS of the stimuli
- **motor neurons** running from the CNS to the **muscles and glands** - called **effectors** - that take action.

The **peripheral nervous system** is subdivided into the

- **sensory-somatic nervous system**
  The cranial nerves
- **autonomic nervous system**
  Sympathetic nervous system
  Para sympathetic nervous system

(I) THE SENSORY-SOMATIC NERVOUS SYSTEM



The sensory-somatic system consists of

- 12 pairs of **cranial nerves** and
- 31 pairs of **spinal nerves**.

(i)The Cranial Nerves

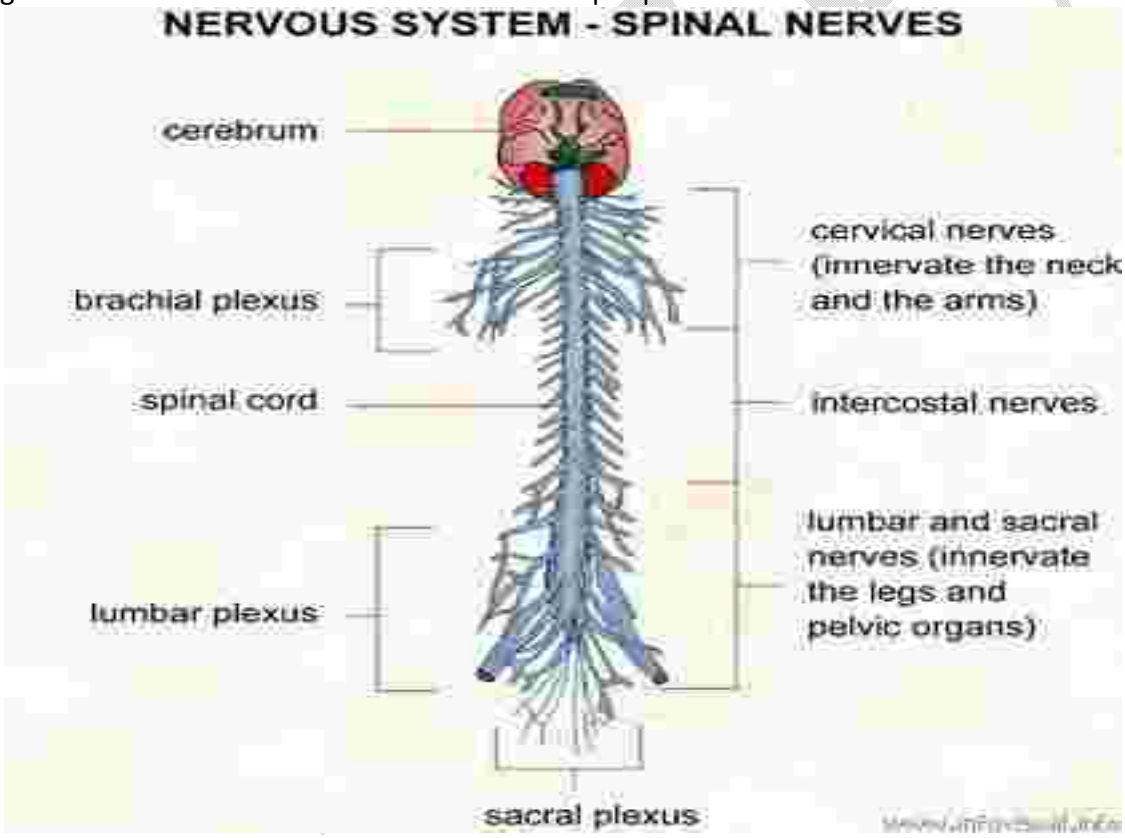
- Some of the cranial nerves are "mixed", containing both sensory and motor axons
- Some, e.g., the optic and olfactory nerves (numbers I and II) contain sensory axons only
- Some, e.g. number III that controls eyeball muscles, contain motor axons only.

Nerves	Type	Function
I Olfactory	sensory	olfaction (smell)
II Optic	sensory	vision (Contain 38% of all the axons connecting to the brain.)
III Oculomotor	motor*	eyelid and eyeball muscles
IV Trochlear	motor*	eyeball muscles
V Trigeminal	mixed	Sensory: facial and mouth sensation Motor: chewing
VI Abducens	motor*	eyeball movement
VII Facial	mixed	Sensory: taste Motor: facial muscles and salivary glands
VIII Auditory	sensory	hearing and balance
IX Glossopharyngeal	mixed	Sensory: taste Motor: swallowing
X	mixed	main nerve of the parasympathetic nervous system (PNS)

Vagus		
XI Accessory	motor	swallowing; moving head and shoulder
XII Hypoglossal	motor*	tongue muscles

(ii) The Spinal Nerves

All of the spinal nerves are "mixed"; that is, they contain both sensory and motor neurons Spinal nerves join together in plexuses. A plexus is an interconnection of fibers which form new combinations. There are four voluntary plexuses (there are some autonomic plexuses) they are the cervical plexus, the brachial plexus, the lumbar plexus, and the sacral plexus. Each plexus gives rise to new combinations of fibers as the peripheral nerves.



All our conscious awareness of the external environment and all our motor activity to cope with it operate through the sensory-somatic division of the PNS.

(II) THE AUTONOMIC NERVOUS SYSTEM

The autonomic nervous system consists of sensory neurons and motor neurons that run between the central nervous system (especially the **hypothalamus** and **medulla oblongata**) and various internal organs such as the:

- heart
- lungs
- viscera
- glands (both exocrine and endocrine)

It is responsible for monitoring conditions in the internal environment and bringing about appropriate changes in them. The contraction of both smooth muscle and cardiac muscle is controlled by motor neurons of the autonomic system.

The actions of the autonomic nervous system are largely **involuntary** (in contrast to those of the sensory-somatic system). It also differs from the sensory-somatic system is using two groups of motor neurons to stimulate the effectors instead of one.

- The first, the **preganglionic neurons**, arise in the CNS and run to a ganglion in the body. Here they synapse with
- **postganglionic neurons**, which run to the effector organ (cardiac muscle, smooth muscle, or a gland).

The autonomic nervous system has two subdivisions, the

1. **Sympathetic nervous system**
2. **Parasympathetic nervous system**.

(I)The Sympathetic Nervous System

The **preganglionic** motor neurons of the sympathetic system arise in the spinal cord. They pass into sympathetic ganglia which are organized into two chains that run parallel to and on either side of the spinal cord.

The preganglionic neuron may do one of three things in the sympathetic ganglion:

- synapse with **postganglionic** neurons (shown in white) which then reenter the spinal nerve and ultimately pass out to the sweat glands and the walls of blood vessels near the surface of the body.
- pass up or down the sympathetic chain and finally synapse with postganglionic neurons in a higher or lower ganglion
- leave the ganglion by way of a cord leading to special ganglia (e.g. the solar plexus) in the viscera. Here it may synapse with postganglionic sympathetic neurons running to the smooth muscular walls of the viscera. However, some of these preganglionic neurons pass right on through this second ganglion and into the **adrenal medulla**. Here they synapse with the highly-modified postganglionic cells that make up the secretory portion of the adrenal medulla.

The neurotransmitter of the preganglionic sympathetic neurons is **acetylcholine** (**ACh**). It stimulates action potentials in the postganglionic neurons.

The neurotransmitter released by the postganglionic neurons is **noradrenaline** (also called **norepinephrine**).

- The action of noradrenaline on a particular gland or muscle is excitatory is some cases, inhibitory in others.

In short, stimulation of the sympathetic branch of the autonomic nervous system prepares the body for emergencies: for "**fight or flight**" (and, perhaps, enhances the memory of the event that triggered the response).

(ii) The Parasympathetic Nervous System

The main nerves of the parasympathetic system are the tenth cranial nerves, the **vagus nerves**. They originate in the **medulla oblongata**. Other preganglionic parasympathetic neurons also extend from the brain as well as from the lower tip of the spinal cord.

.**Acetylcholine** (**ACh**) is the neurotransmitter at all the pre- and many of the postganglionic neurons of the parasympathetic system. However, some of the postganglionic neurons release nitric oxide (NO) as their neurotransmitter.

Parasympathetic stimulation causes

- slowing down of the heartbeat (as Loewi demonstrated)
- lowering of blood pressure
- constriction of the pupils
- increased blood flow to the skin and viscera
- peristalsis of the GI tract

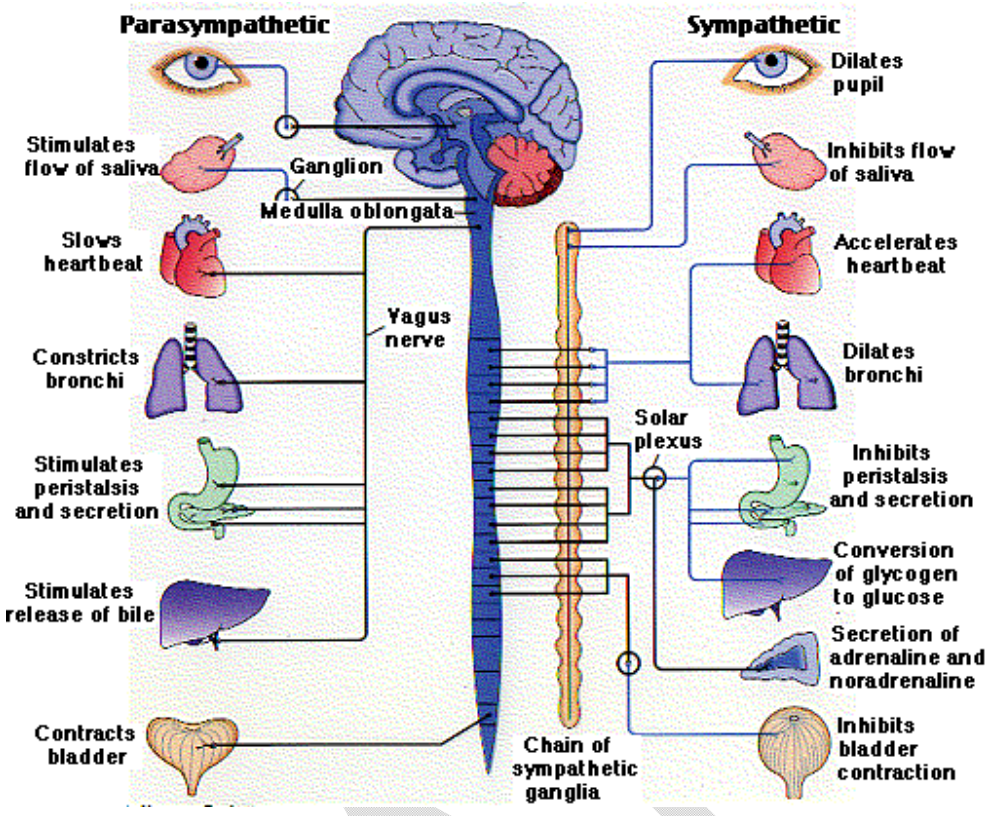
In short, the parasympathetic system returns the body functions to normal after they have been altered by sympathetic stimulation. In times of danger, the sympathetic system prepares the body for violent activity. The parasympathetic system reverses these changes when the danger is over.

Although the autonomic nervous system is considered to be involuntary, this is not entirely true. A certain amount of conscious control can be exerted over it as has long been demonstrated by practitioners of Yoga and Zen Buddhism. During their periods of meditation, these people are clearly able to alter a number of autonomic functions including heart rate and the rate of oxygen consumption. These changes are not simply a reflection of decreased physical activity because they exceed the amount of change occurring during sleep or hypnosis.

A detailed comparison between the sympathetic nervous system and parasympathetic nervous system:

Both the sympathetic nervous system (SNS) and parasympathetic nervous system (PSNS, or occasionally PNS) are part of the autonomic nervous system . They play an important role in maintaining homeostasis in the body, especially during stressful conditions such as sickness and starvation. The parasympathetic and sympathetic nervous system are opposite systems that operate independently in some functions but act in collaboration to control some physiological functions.

Figure: Autonomous nervous system



The main purpose of the SNS is to activate the response of the body during stressful situations, including the fight-or-flight mechanism of the body.It dilates the pupil, so one can see better especially in the dark, it increases heart rate, so that one may have better circulation of oxygen to the muscles, decreases digestion, so that the energy be better utilized for fighting,

The parasympathetic nervous system is responsible for stimulation of "rest-and-digest" or "feed and breed" activities that occur when the body is at rest. These activities include sexual arousal, salivation, tearing up, urination, digestion, and defecation.

	Sympathetic	Parasympathetic
Part of	Autonomic Nervous System	Autonomic Nervous System
Nerve origination	The lumbar and thoracic regions	The midbrain, hindbrain and sacral region
Nerves	Short postsynaptic nerves located near or on the organs	Long postsynaptic nerves that synapse at a distance from the organs
Neurotransmitter	Norepinephrine	Acetylcholine

Innervates	Eyes, lungs, kidneys, gastrointestinal tract, heart, etc.	Eyes, lungs, kidneys, gastrointestinal tract, heart, etc.
Purpose	Mediate involuntary responses, such as "fight or flight"	Mediate vegetative functions, controls feeding, breeding, and resting functions.
Function	Allows the body to adjust in stressful situations, such as arousing excitement, fear, anger, and embarrassment, increases the heart rate, thus, causing an increase in the blood pressure, dilates the respiratory bronchioles to increase uptake of oxygen, decreases gallbladder secretions and dilates blood vessels to increase blood supply to the skeletal muscles.	Constriction of pupils, decreases the heart rate, thus, causing a drop in the blood pressure, stimulation of digestive glands, stimulation of secretion of saliva, stimulates the processes of urination and defecation, and constricts the bronchi and thus, decreasing the diameter of airway,

SYNAPTIC TRANSMISSION

Introduction

Neurons receive information from sensory organs, send information to motor organs, or share information with other neurons. The process of communicating information is very similar, whether it is to another neuron or to a muscle or gland cell. However, by far the largest number of neuronal connections is with other neurons. The transmission of information is accomplished in two ways:

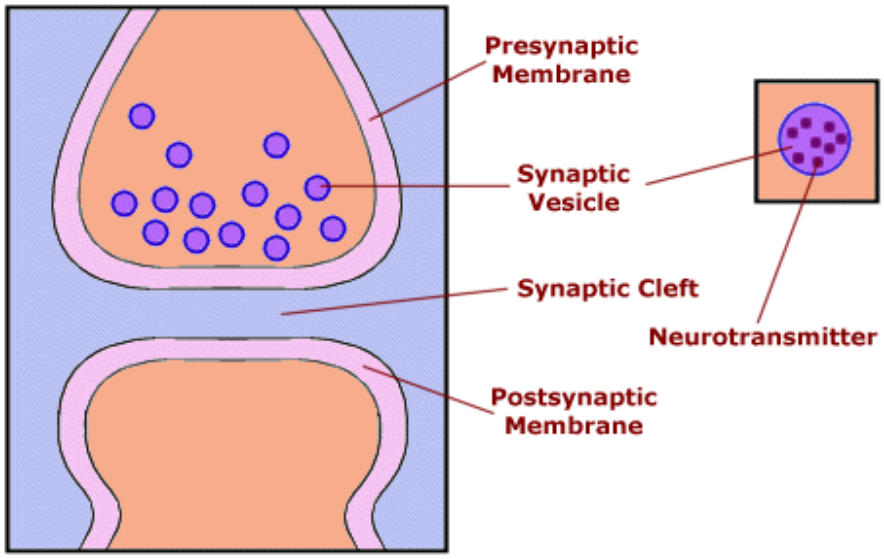
- **Electrically:** the neuron is directly adjacent to other neurons. Small holes in each cell's membrane, called *gap junctions*, are juxtaposed so that as the action potential reaches the end of the axon (at the terminal boutons), the depolarization continues across the membrane to the postsynaptic neuron directly.
- **Chemically:** there is a space (the synaptic cleft) between the axon terminus and the adjacent neuron. As the action potential reaches the end of the axon, a chemical is released that travels across the synaptic cleft to the next neuron to alter its electric potential.

With very few exceptions, mammalian organisms use chemical means to transmit information.

Synapse Structure

- The part of the synapse that belongs to the initiating neuron is called the *presynaptic membrane*.
- The part of the synapse that belongs to the receiving neuron is called the *postsynaptic membrane*.

- The space between the two is called the *synaptic cleft*. It is approximately 20 nm wide (20×10^{-9} m).
- Presynaptic terminals contain numerous *synaptic vesicles*
- Synaptic vesicles contain *Neurotransmitters*, chemical substances which ultimately cause postsynaptic changes in the receiving neuron, is contained within the synaptic vesicles. Common neurotransmitters include:
  - Acetylcholine
  - Dopamine
  - Norepinepherine (a.k.a., noradrenaline)
  - Serotonin



Synaptic Transmission

Electrical transmission occurs by virtue of the fact that the cells are in direct contact with each other: depolarization of the presynaptic cell membrane causes a depolarization of the postsynaptic cell membrane, and the action potential is propagated further. Here transmission of information is always excitatory: the conduction of information always causes a depolarization of the adjacent cell's membrane.

Chemical transmission, albeit more complex allows for far more control, including the ability to excite or inhibit the postsynaptic cell. Here the conduction of information can cause either depolarization or hyperpolarization, depending on the nature of the chemical substance.

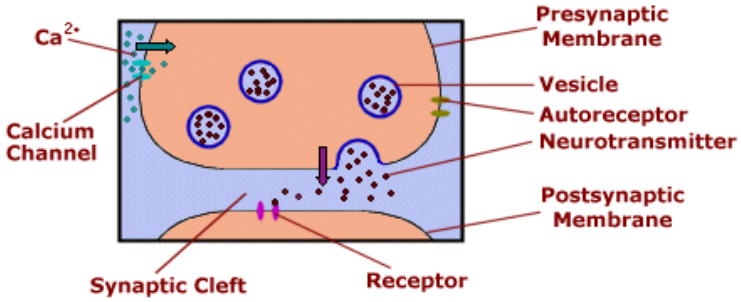
The sequence of events that lead to postsynaptic changes is as follows:

1. The action potential signal arrives at the axon terminal (the bouton).
2. The local depolarization causes Ca^{2+} channels to open. (Is this channel voltage, chemically, or mechanically gated?
3. Ca^{2+} enters the presynaptic cell because its concentration is greater outside the cell than inside.
4. The Ca^{2+}, by binding with calmodulin, causes vesicles filled with neurotransmitter to migrate towards the presynaptic membrane.

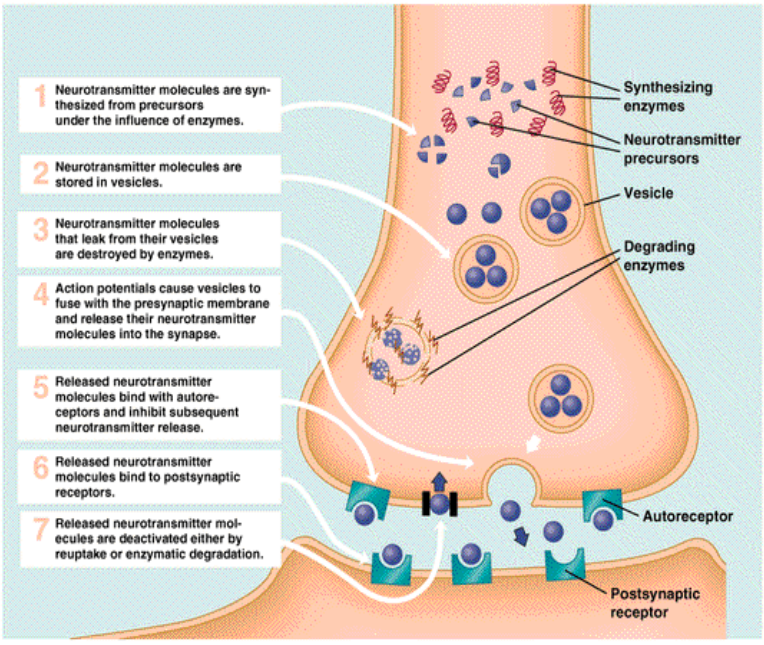
5. The vesicle merges with the presynaptic membrane.
6. The presynaptic membrane and vesicle now forms a continuous membrane, so that the neurotransmitter is released into the synaptic cleft. This process is called *exocytosis*.
7. The neurotransmitter diffuses through the synaptic cleft and binds with receptor channel membranes that are located in both presynaptic and postsynaptic membranes. The time period from neurotransmitter release to receptor channel binding is less than a millionth of a second.

The process is depicted in the diagram below:

Figure: Synaptic transmission



► **Seven Processes in Neurotransmitter Action**



Direct and Indirect Binding to Postsynaptic Receptor
There are two kinds of receptor channels: direct and indirect

1. Direct: the receptor channel allows ions to pass through the membrane. The neurotransmitter acts like a key which opens the ion channel. This is the fastest kind of channel (about 0.5 ms). This is called an ionotropic receptor.
2. Indirect: the binding of neurotransmitter to the receptor channel causes the release of a molecule, called a secondary messenger, that indirectly activates nearby ion channels. This is called a metabotropic receptor.
    - This process is much slower than direct receptor ion channels: from 30 ms up to 1 second.
    - However, this is the most common type of postsynaptic receptor channel

Postsynaptic Stimulation

Once the postsynaptic ion channel is opened, whether directly or indirectly, the effect can be either excitatory (depolarizing) or inhibitory (hyperpolarizing).

- Excitatory Postsynaptic Potentials (EPSP)
    - Excitatory ion channels are permeable to Na^+ and K^+
    - Because of the electrical and concentration gradient, more Na^+ moves into the cell than K^+
    - The inside of the cell becomes more positive, hence causing a local depolarization
    - If enough depolarization occurs (for example, because the neurotransmitter released caused nearby ion channels to open), an action potential is generated
- Inhibitory Postsynaptic Potentials (IPSP)
    - Inhibitory ion channels are permeable to Cl^- and K^+
    - Because of the concentration gradient (not electrical), Cl^- moves into the cell and K^+ moves out of the cell
    - The inside of the cell thus becomes more negative, hence causing a local hyperpolarization
    - The hyperpolarization will make it more difficult for the cell membrane potential to reach threshold, thereby making it less likely that an action potential will be generated

Neurotransmitter Deactivation

If neurotransmitters were continually in the synaptic cleft, the postsynaptic channels would be continually stimulated and the membrane potential would not be able to become stable. There are three ways in which neurotransmitter is deactivated:

1. *Degradation*: Enzymes located in the synaptic cleft break down the neurotransmitter into a substance which has no effect on the receptor channel
2. *Reuptake*: The neurotransmitter can reenter the presynaptic cell through channels in the membrane.
3. *Autoreceptors*: Receptors for a particular neurotransmitter are located on the presynaptic membrane that act like a thermostat. When there is too much neurotransmitter released in the synapse, it decreases the release of further neurotransmitter when the action potential arrives at the presynaptic membrane. It

may accomplish this by decreasing the number of Ca^{2+}channels that open when the next action potential arrives at the presynaptic terminal.

NEUROTRANSMITTERS

A molecule is considered a neurotransmitter if it meets the following criteria:

- Synthesis of the neurotransmitter occurs in the neuron itself
- It can be found in the presynaptic membrane (because it was carried there from the soma, or because it was synthesized there directly)
- Its release into the synaptic cleft causes a change in the postsynaptic membrane
- Its effect on a neuron is the same whether released exogenously (i.e., from outside the organism as a drug) or endogenously (from the presynaptic terminal)
- Once released, the molecule is specifically removed from the synaptic cleft either by reuse or degradation

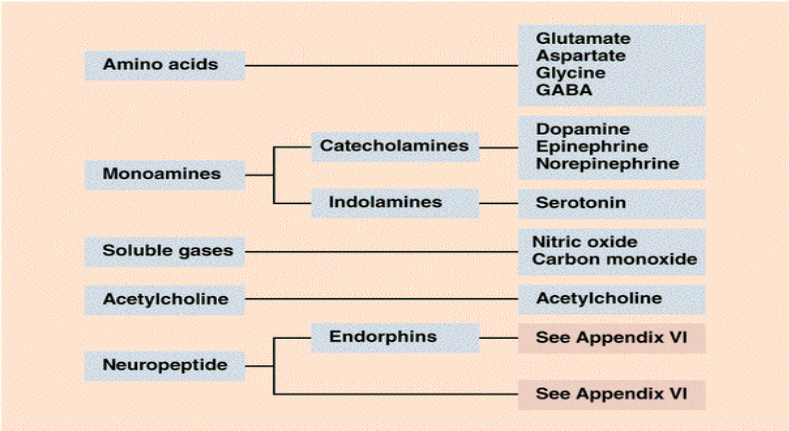
Classes of neurotransmitter

There are two classes of neurotransmitters:

  - Small molecules, such as acetylcholine (ACh) or dopamine are packaged in small vesicles
  - they are released in a pulse into synaptic clefts each time an action potential reaches a button
  - Are released by exocytosis at active zones associated with Ca^{2+} channels
- Large molecules made up of chains of amino acids
  - Are packaged in large vesicles (which can contain small molecules as well)
  - large-molecule neurotransmitters are released gradually in response to general increases in neuron firing
  - Are released by exocytosis generally anywhere from the presynaptic membrane

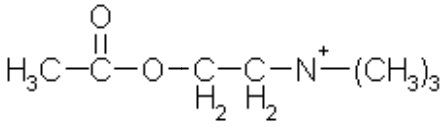
- Most neurons contain both types of vesicles, but in different concentrations.

► Classes of Neurotransmitters



Small Molecules

Acetylcholine (ACh)

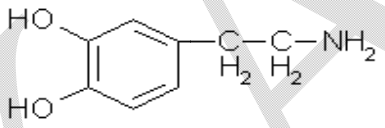


- The only small molecule that is not an amino acid or derived from one
- Uses *choline* as a precursor
- Choline cannot be synthesized by the body and must be obtained from external food sources
- Used by motor neurons as an excitatory neurotransmitter in the spinal cord
- Used at neuromuscular junctions as an excitatory neurotransmitter to influence muscle activation
- Used by the Autonomic Nervous System, such as smooth muscles of the heart, as an inhibitory neurotransmitter in preganglionic neurons and postganglionic parasympathetic neurons
- Used everywhere in the brain. For example, memory systems of the CNS (may be related to Alzheimer's Disease).
- Most receptors for acetylcholine are ionotropic

Monoamines

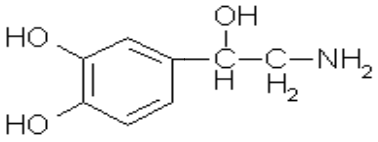
a. Synthesized from tyrosine

1. Dopamine



- Is synthesized in three steps from the amino acid tyrosine
- Is the direct precursor to norepinepherine.
- Enzyme converts tyrosine to L-DOPA
- Generally involved in regulatory motor activity
- In the basal ganglia, involved in mood, sensory perception, and attention
- Schizophrenics have too much dopamine, patients with Parkinson's Disease have too little

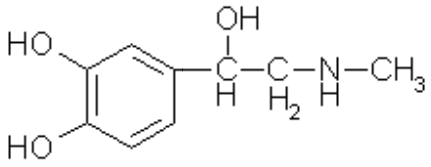
2. Norepinepherine



- Synthesized directly from dopamine, and forms the direct precursor to epinepherine. It is synthesized in four steps from tyrosine
- Synthesized within vesicles (the only neurotransmitter synthesized this way)

- Also known as *noradrenaline*
- Used in the CNS by neurons that project in the cortex, cerebellum, and spinal cord; as such has many uses including sleep/wakefulness regulation
- Activates sympathetic and parasympathetic neurons in the Autonomic Nervous System

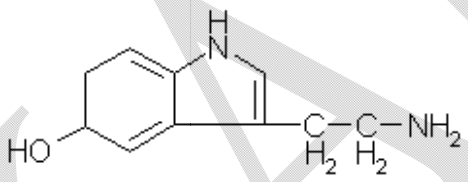
3. Epinepherine



- Synthesized in five steps from tyrosine, and directly from norepinepherine in the biosynthetic pathway
- Also known as *adrenaline* (from Latin: *ad* means "above" and *renal* means "kidney," while in Greek, *epi* means "above" and *nephron* means "kidney")
- Produced by the adrenal medulla, a gland above the kidney
- Few neurons in the brain use this neurotransmitter
- Activates sympathetic neurons in the Autonomic Nervous System

b. Synthesized from tryptophan

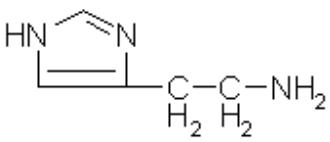
1. Serotonin (5-HT)



- Synthesized in two steps from the amino acid tryptophan
- Actual name: 5-hydroxytryptamine (5-HT)
- Regulates attention and other complex cognitive functions, such as sleep (dreaming), eating, mood, pain regulation
- Neurons which use serotonin are distributed throughout the brain and spinal cord
- Directly implicated in depression (also norepinepherine)
- Used by metabotropic receptors

c. Synthesized from histidine

Histamine

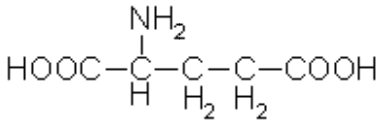


- Synthesized from the amino acid histidine
- Used in control of smooth muscle, exocrine glands, and vasculature

- High concentration in the hypothalamus, which regulates the secretion of horomones
- Used during inflammatory reactions

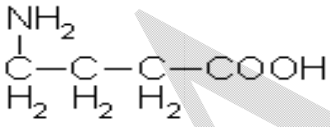
Amino Acids

Glutamate (Glu)



- Most prevalent neurotransmitter in the Central Nervous System. Used by more that 50% of neurons
- Derived from a -ketoglutarate
- Glutamate is the most important excitatory (EPSP) neurotransmitter, exciting about 90% of the postsynaptic terminals to which it contacts
- As an excitatory neutrotransmitter, it binds to with ionotropic receptors, causing depolarization by opening Na^+ ion channels
- At metabotropic receptors, it is modulatory

g-Aminobutyric Acid (GABA)



- Synthesized directly from glutamate
- GABA is the most important inhibitory (IPSP) neurotransmitter
- Present in high concentrations in the CNS, preventing the brain from becoming overexcited
- As an inhibitory neutrotransmitter, it binds to both ionotropic and metabotropic receptors, causing hyperpolarization by opening Cl^- ion channels
- Used by inhibitory interneurons in the spinal cord

Soluble Gas Neurotransmitters

- this class of recently identified neurotransmitters includes nitric oxide and carbon monoxide
- the gasses are produced in the neural cytoplasm, diffuse immediately through the cell membrane into the extracellular fluid and into nearby cells to stimulate production of second messengers
- they are difficult to study as they act rapidly and are immediately broken down, existing for only a few seconds

Large Molecules

Neuropeptides

- Derived from secretory proteins formed in the cell body
- They are first processed in the endoplasmic reticulum (ER) and are moved to the Golgi apparatus before being secreted as large vesicles and transported down the axon in preparation for exocytosis
- More than 50 peptides have been isolated in nerve cells. For example,
    - ***Substance P* and *enkephalins*:** Active during inflammation and pain transmission in the PNS
    - ***Endorphins*:** Endogenous opiates which cause euphoria, suppress pain, or regulate responses to stress
- Are either excitatory or inhibitory, and can also act as neuromodulators, affecting the amount of neurotransmitter released
- Some form part of the neuroendocrine system by functioning both as hormones and neurotransmitters

As neurotransmitters, each one of these molecules undergo a similar life cycle:

1. ***Synthesis*:** Neurotransmitters are synthesized by the enzymatic transformation of precursors. The biosythetic pathway can be immediate (as in GABA from glutamate) or in multiple steps (as in epinepherine from norepinepherine from dopamine, etc.). The synthesis occurs either at the terminal boutons of the axon, or in the soma. In the latter case, it is transported to the axon terminals probably by way of microtubular tracks.
2. ***Storage*:** They are packaged inside synaptic vesicles. These vesicles vary in size, depending on the size of the neurotransmitter.
3. ***Release*:** The neurotransmitters are released from the presynaptic terminal by exocytosis and diffuse across the synaptic cleft to the postsynaptic membrane
4. ***Binding*:** The neurotransmitters bind to receptor proteins imbedded in the postsynaptic cell's membrane. There are two kinds of receptors: ionotropic (direct) and metabotropic(indirect).
5. ***Inactivation***: The neurotransmitter is degraded either by being broken down enzymatically, or reused by active reuptake in which case the cycle begins again

Neurotransmitter - Receptors

It was initially assumed that there is only one kind of receptor for each neurotransmitter; it is now clear that each neurotransmitter binds to *more than one class of receptor*; for example, **muscarinic** (found in internal organs) and **nicotinic** (found at neuromuscular junctions) bind to acetylcholine receptors, with each subtype binding, then producing fundamentally different responses.

Receptor subtypes are located in different brain areas; this allows the same neurotransmitter to signal differently at various locations; postsynaptic neurons are differentially influenced based on the receptor subtype

Ion-channel linked receptors chemically open or close an ion channel inducing an immediate postsynaptic potential, these receptors are not prevalent but are fast acting

G-protein linked receptors consist of a protein chain that winds in and out of the cell membrane seven times and each is located next to a guanine sensitive protein; the binding breaks away the G-protein and leads to one of two actions; the binding may trigger the synthesis of a second messenger that diffuses through the cytoplasm to bind to ion channels (for an EPSP or IPSP), and influence the metabolic activities of the cell, or bind to DNA in the nucleus to influence gene expression

The Somatic Senses

The somatic (general) senses collect information about cutaneous sensations (tactile sensations on the surface of the skin) and proprioceptive sensations. The following stimuli are detected:

- Tactile stimuli are detected by mechanoreceptors and produce sensations of touch and pressure:
- Merkel discs are receptors with free nerve endings that detect surface pressure (light touch). They are located deep in the epidermis.
- Root hair plexuses are receptors with free nerve endings that surround hair follicles and detect hair movement.
- Corpuscles of touch (Meissner's corpuscles) are receptors with encapsulated nerve endings located in the dermal paillae (near the surface) of the skin that detect surface pressure (light touch).
- Pacinian corpuscles are encapsulated nerve receptors that detect deep pressure and are located in the subcutaneous layer (below the skin).
- Thermal stimuli are detected by free nerve ending thermoreceptors sensitive to heat or cold.
- Pain stimuli are detected by free nerve ending nociceptors.
- Proprioceptive stimuli are detected by the following receptors:
- Muscle spindles are mechanoreceptors located in skeletal muscles. They consist of specialized skeletal muscle fibers enclosed in a spindle-shaped capsule made of connective tissue.
- Golgi tendon organs are mechanoreceptors located at the junctions of tendons and muscles.
- Joint kinesthetic receptors are mechanoreceptors located in synovial joints.

EEG

An **electroencephalogram (EEG)** is a test used to evaluate the electrical activity in the brain. Brain cells communicate with each other through electrical impulses. An EEG can be used to help detect potential problems associated with this activity.

The test tracks and records brain wave patterns. Small, flat metal discs called electrodes are attached to the scalp with wires. The electrodes analyze the electrical impulses in the brain and send signals to a computer, where the results are recorded.

The electrical impulses in an EEG recording look like wavy lines with peaks and valleys. These lines allow doctors to quickly assess whether there are abnormal patterns. Any irregularities may be a sign of seizures or other brain disorders.

USES

Why Is an EEG Performed?

An EEG is used to detect problems in the electrical activity of the brain that may be associated with certain brain disorders. The measurements given by an EEG are used to confirm or rule out various conditions, including:

- seizure disorders (such as epilepsy)
- a head injury
- encephalitis (an inflammation of the brain)
- a brain tumor
- encephalopathy (a disease that causes brain dysfunction)
- memory problems
- sleep disorders
- stroke
- dementia

When someone is in a coma, an EEG may be performed to determine the level of **Sleep** is a naturally recurring state of mind and body characterized by altered consciousness, relatively inhibited sensory activity, inhibition of nearly all voluntary muscles, and reduced interactions with surroundings. It is distinguished from wakefulness by a decreased ability to react to stimuli, but is more easily reversed than the state of being comatose. Sleep occurs in repeating periods, in which the body alternates between two highly distinct modes known as non-

REM and REM sleep. Although REM stands for "rapid eye movement", sleep affects other brain-body functions, including virtual paralysis of the body.

SLEEP

During sleep, most systems are in an anabolic state, helping to restore the immune, nervous, skeletal, and muscular systems. The internal circadian clock promotes sleep daily at night. However, sleep patterns vary among individuals. In the last century, artificial light has substantially altered sleep timing in industrialized countries.

The diverse purposes and mechanisms of sleep are the subject of substantial ongoing research. Sleep seems to assist with improvements in the body and mind. Research in the 21st century is investigating whether sleep is a period of maintenance for removing metabolic waste compounds from the brain.

A well-known feature of sleep is the dream, an experience typically recounted in narrative form, which resembles waking life while in progress, but which usually can later be distinguished as fantasy. Sleep is sometimes confused with unconsciousness, but is quite different in terms of the thought process.

In a comatose state, the patient cannot be awakened and does not respond to pain, light or sound in a normal way - the comatose individual cannot react to the surrounding environment. A person in a coma does not make voluntary actions and does not have sleep-wake cycles.

A coma is a medical emergency that requires rapid action to preserve life and brain function. Generally, doctors will order a series of blood tests and imaging scans to try to ascertain what the cause of the coma is. Determining the cause usually decides what type of treatment to apply.

Coma may occur for various reasons, such as intoxication, CNS (central nervous system) diseases, a serious injury and hypoxia (oxygen deprivation). Coma can be induced deliberately with pharmaceutical agents - perhaps in order to protect the patient from intense pain during a healing process, or to preserve higher brain function following another form of brain trauma.

Comas generally do not last for more than a few weeks. A patient whose state does not change after an extended period is often reclassified as being in a persistent vegetative state. Unfortunately, those in a persistent vegetative state for over twelve months rarely wake up.

The English medical word "coma" comes from the Ancient Greek word *Koma*, meaning "deep sleep."

MEMORY AND LEARNING

Memory and learning are so closely connected that people often confuse them with each other. But the specialists who study them consider them two distinct phenomena.

These specialists define learning as a process that will modify a subsequent behaviour. Memory, on the other hand, is the ability to remember past experiences.

You learn a new language by studying it, but you then speak it by using your memory to retrieve the words that you have learned.

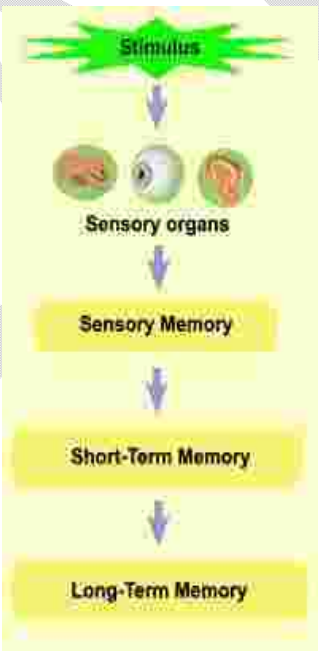
Memory is essential to all learning, because it lets you store and retrieve the information that you learn. Memory is basically nothing more than the record left by a learning process.

Thus, memory depends on learning. But learning also depends on memory, because the knowledge stored in your memory provides the framework to which you link new knowledge, by association. And the more extensive your framework of existing knowledge, the more easily you can link new knowledge to it.

SENSORY, SHORT-TERM AND LONG-TERM MEMORY

Human memory is not a unitary process. Research suggests, that, at the psychological level, various types of memory are at work in human beings. It also seems increasingly likely that these various systems bring different parts of the brain into play.

Types of memory can be classified in a number of ways, depending on the criterion used. With duration as the criterion, at least three different types of memory can be distinguished: sensory memory, short-term memory, and long-term memory.



Sensory memory takes the information provided by the senses and retains it accurately but very briefly. Sensory memory lasts such a short time (from a few hundred milliseconds to one

or two seconds) that it is often considered part of the process of perception. Nevertheless, it represents an essential step for storing information in short-term memory.

Short-term memory temporarily records the succession of events in our lives. It may register a face that we see in the street, or a telephone number that we overhear someone giving out, but this information will quickly disappear forever unless we make a conscious effort to retain it. Short-term memory has a storage capacity of only about seven items and lasts only a few dozen seconds. Just as sensory memory is a necessary step for short-term memory, short-term memory is a necessary step toward the next stage of retention, long-term memory.

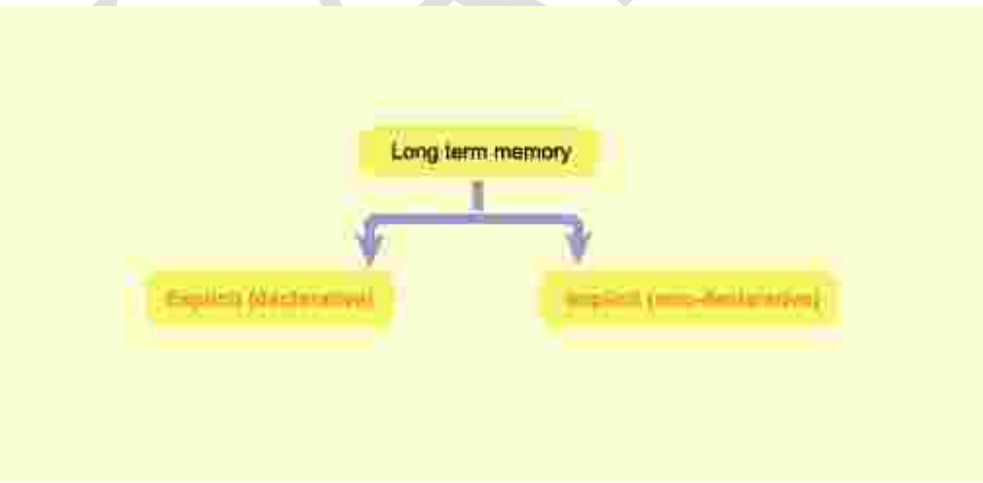
Long-term memory not only stores all the significant events that mark our lives, it lets us retain the meanings of words and the physical skills that we have learned. Its capacity seems unlimited, and it can last days, months, years, or even an entire lifetime! But it is far from infallible. It sometimes distorts the facts, and it tends to become less reliable as we age.

Though each of these types of memory has its own particular mode of operation, they all cooperate closely in the process of memorization.

DIFFERENT TYPES OF LONG-TERM MEMORY

Long-term memory as a whole is defined by the criterion of long duration. But other criteria can be applied to break down the complex phenomenon of memory into separate components.

One such criterion is whether or not the long-term memory in question can be verbalized. On the basis of this criterion, two main forms of long-term memory can be distinguished.



The first is **declarative memory**: your memory of all those things that you are aware of remembering and that you can describe in words, such as your birthday, or the meaning of the word "cradle", or what you ate last night. This form of memory is also called explicit memory, because you can name and describe each of these remembered things explicitly.

The other form of long-term memory is **non-declarative memory**. It is also known as **implicit memory**, because you express it by means other than words. For example, when you ride a bike, juggle some balls or simply tie your shoelaces, you are expressing memories of motor skills that do not require the use of language. Such "motor memories" are just one type of implicit memory. There are others as well.

KARPAGAM ACADEMY OF HIGHER EDUCATION
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Coimbatore – 641 021.

LECTURE PLAN
DEPARTMENT OF BIOCHEMISTRY

STAFF NAME: Dr. L. HARIPRASATH
SUBJECT NAME: HUMAN PHYSIOLOGY SUB.CODE:17BCU203
SEMESTER: II CLASS: I B.Sc Biochemistry

S. No.	Duration of period	Topics covered	Books referred	Page No.	Web page referred
Unit I					
1	1	Intracellular, extracellular and interstitial fluid	T1	187-191	W1, W2
2	1	Homeostasis, control system and their components	T1	187-191	
3	1	Plasma as an extracellular fluid, RBC, molecular mechanism of blood coagulation	T1	131-140	
4	1	Role of vitamin K in coagulation, anticoagulant and fibrinolytic systems	T2	51-63	
5	1	Anemias, polycythemia, Haemophilia and thrombosis			W1
6	1	Respiration : Organization of the pulmonary system			W1
7	1	Mechanism of respiration, pulmonary ventilation and related volumes, pulmonary circulation	T1 T2 R1	365-425 213-226 474-513	
8	1	Principles of gas exchange and transport			
9	1	Regulation of respiration			
10	1	Pulmonary oedema and regulation of pleural fluid			W2
11	1	Hypoxia, hypercapnea, pulmonary distress, emphesema, ARDS			
12	1	Revision			
13	1	Class test			
Total: 13 Hours					
Unit II					
1	1	Pressure, flow and resistance	T1	226-234	
2	1	Anatomy of heart			
3	1	Physiology of the cardiac muscle	T2	109-110	W3
4	1	Automacity of the cardiac muscle contraction, excitation contraction	T1	242-248	

		coupling			
5	1	Relationship between cardiac cycle, heart sound, ventricular volumes and the ECG	T1 T2	249-283 112-131	
6	1	Control of cardiac function and output	T1	291-297	
7	1	The arterial system, venous system, the microcirculation and mechanics of capillary fluid exchange	T2	139-179	
8	1	Control of blood flow to the tissues, Portal circulations, Arterial pressure and its regulation	T2	180-189	
9	1	Hypertension, congestive heart disease, Atherosclerosis and myocardial infarction	T1	328-329	
10	1	Revision			
11	1	Class test	T1	197-209	
Total: 11 Hours					
Unit III					
1	1	Anatomy of the kidney and the nephron, Regulation of renal blood flow	T2	411-420 424-439	
2	1	Cell biology of the Bowmans' capsule, Physiology of glomerular filtration and GFR			
3	1	Tubular processing of the glomerular filtrate			
4	1	Micturition reflex and voluntary control of micturition	T2	453-454	
5	1	Regulation of ECF electrolyte and water content, blood volume and long term blood pressure			
6	1	Blood buffer systems, Renal and pulmonary control of blood pH, renal clearance	T2	440-444 446-452 453-458	
7	1	Assessment of kidney function. Acidosis and alkalosis			
8	1	Glomerular nephritis, renal failure, dialysis and diuretics			
9	1	Revision			
10	1	Class test			
Total: 10 Hours					
Unit IV					
1	1	Histology of the gastrointestinal tract.	T2	299-363	
2	1	Propulsion and motility of food and digested material			
3	1	Enteric reflexes, secretory functions of the gastrointestinal tract			
4	1	Digestion and absorption of macro and micronutrients			
5	1	Peptic ulcer, Sprue, celiac disease	T2	369-385	

6	1	IBD, regurgitation, diarrhoea and constipation			
7	1	Anatomy of the hepatic lobule and blood flow into the liver	T2	338-339	
8	1	Formation and secretion of bile.	T1 T2	657 333	
9	1	Enterohepatic cycle	T1	448, 474	
10	1	Reticuloendothelial system	T1	51, 203	
11	1	Metabolic importance of liver	T2	342-345	
12	1	Liver function tests. Jaundice, liver cirrhosis and fatty liver	T2 T1 T1	344-345 451, 664 553, 663	
13	1	Bone structure and formation. Physiology of muscle contraction in striated and non-striated muscle	T2	621-647	
14	1	Class test			
Total: 14 Hours					
Unit V					
1	1	Sex determination and differentiation	T2	572-598	
2	1	Development of female and male genital tracts	R1	961-963	
3	1	Spermatogenesis, capacitation and transport of sperm, blood testis barrier			
4	1	Ovarian function and its control, Uterine changes, fertilization and implantation	T2	581-591	
5	1	Placenta as a feto- maternal unit, Gestation, Parturition			
6	1	Central Nervous system, Peripheral Nervous system	T2	696-698 824-832	
7	1	Blood brain barrier and CSF, Membrane potentials. Synaptic transmission.			
8	1	Neurotransmitters. Sensory receptors and neural pathways.			
9	1	Somatic sensation, EEG, sleep, coma, Learning and memory	T2	642-670	
10	1	Revision			
Total: 10 Hours					
1	1	Previous year ESE question paper Discussion			
2	1	Previous year ESE question paper Discussion			
Grand Total: 58 + 2 = 60 Hours					

Textbook

T1: Chatterjee, C.C., (2012). Human Physiology, 11th edition, Mical Alli Agency, Calcutta.

T2: Saradha, S., (2004). Textbook of Human Physiology, S. Chand and Company, New Delhi.

References

R1: Guyton, C., and Hall, J.E., (2010). Textbook of Medical Physiology, 12th Editon. Prism Indian edition, W.B. Saunders Company, New Delhi.

R2: Murray, R.K., Bender, D.A., Botham, K.M., and Kennelly, P.J., (2012).Harper's illustrated Biochemistry, 29th edition.. McGraw-Hill Medical. London.

Web references

Unit 1: https://courses.lumenlearning.com/ap2/chapter/body-fluids-and-fluid-compartments-no-content/
http://www.pathwaymedicine.org/body-fluid-compartments
W1:
http://intranet.tdmu.edu.ua/data/kafedra/internal/meds/classes_stud/en/nurse/en/BSN-(4y)/4%20year/fall%20semester/Health%20Alterations%202%20Practicum/02.%20Red%20blood%20cell%20disorders%20Anemias,%20Polycythemia%20Vera.htm
W2: www5.zzu.edu.cn/sie/upload/attachments/uncategoried/20150625154638859.pdf
W3: http://www.innerbody.com/image/card01.html

I BSc Biochemistry

17BCU203 Human Physiology

S. No.	Question	Opt A	Opt B	Opt C	Opt D	Answer
1	“Adam’s apple” is used to refer to	the trachea	the epiglottis	the thyroid cartilage	the larynx	the thyroid cartilage
2	A rapid and shallow ventillation is called	Apnea	Hyperpnea	Hyperventillation	Tachypnea	Tachypnea
3	Amount of air in the lungs that remains after deep breathing is called _____.	Dead space	Residual volume	Vital capacity	Ventilation rate	Residual volume
4	As you breathe, this contracts and flattens to give your lungs room to fill up with	Larnynx	Lung balloon	Diaphragm	Bronchiole	Diaphragm
5	At high altitude, RBCs of human blood will	Increase in number	Decrease in number	Decrease in size	Increase in size	Increase in number
6	At rest, the average breathing rate of an adult is	60 to 65 breaths per n	100 + breaths per min	3 to 5 breaths per min	12 to 15 breaths per minute	12 to 15 breaths per minute
7	Bronchi branch into the tubes of smaller diameters (less than 1 mm) known as _	Microtrachea	Bronchioles	Alveoli	Eustachian tubes	Bronchioles
8	Coagulation factor IX is:	Stuart-Prower factor	Hageman factor	Anti-hemophilic acid	Christmas factor	Christmas factor
9	Coagulation factor VIII is:	Stuart-Prower factor	Hageman factor	Anti-hemophilic acid	Christmas factor	Anti-hemophilic acid
10	Coagulation factor X is:	Stuart-Prower factor	Hageman factor	Anti-hemophilic acid	Christmas factor	Stuart-Prower factor
11	Coagulation factor XII is:	fibrinogen	Stuart-Prower factor	FSF	Hageman factor	Hageman factor
12	Complete the following statement using the choices below. Air moves out of the	less than the pressure	greater than the press	equal to the pressure i	greater than the intra-alveo	greater than the pressure in the atmosphere.
13	Complete the following statement using the choices below. Air moves out of the	less than the pressure	greater than the press	equal to the pressure i	greater than the intra-alveo	greater than the pressure in the atmosphere
14	During inspiration, how does alveolar pressure compare to atmospheric pressure	Alveolar pressure is gr	Alveolar pressure is le	Alveolar pressure is th	Alveolar pressure is one of t	Alveolar pressure is less than atmospheric.
15	During swallowing of food, _____ is the opening covered by epiglottis.	Glottis	Trachea	Epiglottis	Larynx	Trachea
16	Human lungs are situated in	Abdominal cavity	Thoracic cavity	Inside diaphragm	Without any cavity	Thoracic cavity
17	In a hot summer after noon, if your body's Homeostatic machinery keep your int	Positive feedback	Negative feedback	Osmoregulation	Feed back	Negative feedback
18	In case of low blood glucose concentration, negative feedback is	To avoid sweets	to workout	to rest	convert glycogen to glucose	convert glycogen to glucose
19	In expiration, diaphragm becomes	Flattened	Relaxed	Straightened	Arched	Relaxed
20	In which disease lung tissue degenerate?	Bronchitis	Pneumonia	Emphysema	Asthma	Emphysema
21	In which of these compartments is Na+ concentration the lowest?	interstitial fluid	plasma	intracellular fluid	extracellular fluid	intracellular fluid
22	Intrapulmonary pressure is the _____.	pressure within the pl	pressure within the al	negative pressure in th	difference between atmosp	pressure within the alveoli of the lungs
23	Lack of pulmonary surfactant produces	Asthma	Respiratory distress sy	Cystic fibrosis	Emphysema	Emphysema
24	Opening to the trachea is covered by a small flap of tissues termed as the _____	Glottis	Trachea	Epiglottis	Larynx	Epiglottis
25	Patients with which of the following diseases may have a normal PTT?	von Willebrand’s disea	Hemophilia A	Hemophilia B	Factor V Leiden	von Willebrand’s disease
26	Protection of internal environment from harms by external environment is term	Thermoregulation	Homeostasis	Osomoregulation	nerve impulse	Homeostasis
27	Proteins C and S are dependent on which vitamin for synthesis?	Vitamin A	Vitamin B	Vitamin E	Vitamin K	Vitamin K
28	Respiration rate is the lowest during	Running	Playing	Eating	Sleeping	Sleeping
29	The _____ produces red blood cells, which transport _____ and some ____	Liver; oxygen; mineral	Liver; oxygen; carbon	Bone marrow; oxygen;	Bone marrow; oxygen; carb	Bone marrow; oxygen; carbon dioxide
30	The amount of air a person takes in during normal, restful breathing is called the	Deadspace	Tidal volume	Vital capacity	Ventilation rate	Tidal volume
31	The average percentage of oxygen in inhaled air is 21%. Which one of the followi	0%	21%	16%	25%	16%
32	The life span of RBC is	100 days	110 days	120 days	130 days	120 days
33	The lowermost portion of the pharynx is the _____.	oropharynx	nasopharynx	laryngopharynx	pharyngeal tonsils	laryngopharynx
34	The major sign of hypoventilation is	Cyanosis	Dyspnea	Hypercapnia	Hypoxia	Hypercapnia
35	The metal ion present in haemoglobin is	Iron	Magnesium	Copper	Zinc	Iron
36	The most powerful respiratory stimulus for breathing in a healthy person is ____	loss of oxygen in tissu	increase of carbon dio	pH (acidosis)	pH (alkalosis)	increase of carbon dioxide
37	The nose, pharynx, and associated structures are all part of the _____	respiratory division	upper respiratory syst	lower respiratory syste	bronchial tree	upper respiratory system
38	The relationship between the pressure and volume of gases is given by _____	Boyle's law	Henry's law	Charles' law	Dalton's law	Boyle's law
39	The term “Red Puffers” describes a person with which type of disease?	Emphysema	Bronchitis	Tuberculosis	ARDS	Emphysema
40	The type of hypoxia present in high altitute is	Anemic hypoxia	Hypoxic hypoxia	Stagnant hypoxia	Histotoxic hypoxia	Hypoxic hypoxia
41	The volume of air that can be exhaled during forced breathing in addition to tida	residual volume	expiratory reserve volu	vital capacity	total lung capacity	expiratory reserve volume
42	The walls of the alveoli are composed of two types of cells, type I and type II. Th	secrete surfactant	trap dust and other de	replace mucus in the a	protect the lungs from bacti	secrete surfactant
43	The walls of the alveoli are composed of two types of cells, type I and type II. Th	secrete surfactant	trap dust and other de	replace mucus in the a	protect the lungs from bacti	secrete surfactant
44	This disease is due to allergens	Bronchitis	Pneumonia	Emphysema	Asthma	Asthma
45	Tidal volume in adult is	125 ml	500 ml	1500 ml	2200 ml	500 ml
46	What is another name for the windpipe?	Lungs	Larynx	Trachea	Oesophagus	Trachea
47	What is pulmonary edema?	Excessive leakage of fl	Excessive leakage of fl	Excessive leakage of fl	Edema of the larynx	Excessive leakage of fluid into the interstitial compartment in the lungs
48	What is pulmonary embolism?	A blood clot obstructir	A blood clot obstructir	A blood clot in the dee	Right sided heart failure	A blood clot obstructing a pulmonary artery
49	What is the instrument that measures the amount of air inhaled and exhaled wit	Sphygmomanometer	Hygrometer	Stethoscope	Spirometer	Spirometer
50	When a person takes a very deep breath of air just prior to diving into water, thi	tidal volume	vital capacity	residual volume	inspiratory reserve volume	inspiratory reserve volume
51	When the “wind” is knocked out of a football player because of a hard blow to t	tidal volume	vital capacity	residual volume	inspiratory reserve volume	residual volume
52	Which lung disorder is related to profession?	Silicosis	Emphysema	Pneumonia	Asthma	Silicosis
53	Which of the following cations is required for the conversion of Prothrombin into	Ca2+	Fe2+	Mg2+	Mn2+	Ca2+
54	Which of the following initiates the coagulation cascade IN VIVO?	Factor XII	Thrombin	Tissue factor	Factor X	Tissue factor
55	Which of the following is known as Royal disease?	Sickle cell anaemia	Haemophilia	Alzheimer’s disease	Color blindness	Haemophilia
56	Which of the following is not a form of lung cancer?	adenocarcinoma	Kaposi's sarcoma	small cell carcinoma	squamous cell carcinoma	Kaposi's sarcoma
57	Which of the following is not an event necessary to supply the body with O2 and	pulmonary ventilation	blood pH adjustment	internal respiration	external respiration	blood pH adjustment
58	Which of the following is the correct order for air passing through the lungs?	trachea, bronchus, brc	bronchus, alveoli, trac	bronchus, trachea, brc	trachea, alveoli, bronchi, br	trachea, bronchus, bronchiole, alveoli
59	Which statement concerning body fluid composition is correct?	Intracellular fluid cont	Interstitial fluid contai	Extracellular fluid cont	Extracellular fluid contains a	Extracellular fluid contains a higher concentration of sodium than intracellular fluid.
60	Why can't Heparin be administered orally?	It is large	It is negatively charge	It contains too much n	It is large and negatively cha	It is large and negatively charged

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S. No.	Question	Opt A	Opt B	Opt C	Opt D	Answer
1	A blockage within the heart arteries caused by the death of heart muscle cells is	an embolism	an infarct	an abscess	a trachanter	an infarct
2	All arteries of the body flow:	to the liver	to the brain	away from the lungs	away from the heart	away from the lungs
3	All the following apply to the bicuspid valve except:	it is also called the mit	it is a semilunar valve	it is found on the left s	it prevents blood from back	it is a semilunar valve
4	All the following have the ability to regulate blood flow in the body except:	antidiuretic hormone	epinephrine and norep	chemoreceptors	enzymes from the salivary g	enzymes from the salivary glands
5	A-V valve on the right side is:	Mitral valve	Tricuspid valve	Aortic valve	Pulmonary valve	Mitral valve
6	Back flow of blood is prevented by valve classified as	Bronchial valve	Lymphatic valve	Atria vale	Thebesian valve	Thebesian valve
7	Blood flowing through a vein tends to:	pulse	flow smoothly	carry oxygen to the bo	flow at a faster rate than in	flow smoothly
8	Blood returning to the heart from the body organs enters the:	left atrium through th	right atrium through t	left ventricle by the pu	right ventricle by the pulmo	right atrium through the vena cava
9	BP component, which does not show fluctuations:	Systolic pressure	Diastolic pressure	Pulse pressure	Mean pressure	Diastolic pressure
10	Bradycardia in athletes is because:	Increased sympathetic	Increased vagal tone	Decreased cardiac out	Low venous return	Increased vagal tone
11	Cardiac index is the ratio of	Cardiac output to the	Cardiac output to the	Cardiac output to worl	Stroke volume to body surfa	Cardiac output to the body surface area
12	Cardiac output is not decreased in	Acute venous dilation	Beriberi	Cardiac tamponade	Myocardial infarction	Beriberi
13	Each small square in ECG paper represents a voltage of:	1 mV	0.1 mV	0.2 mV	0.5 mV	0.1 mV
14	Each small square in EEG paper represents:	0.02 sec	0.04 sec	0.5 sec	1 sec	0.04 sec
15	Fourth heart beat sound is heard in:	Early ventricular diast	Late ventricular diasto	Early ventricular systo	Late ventricular systole	Late ventricular diastole
16	If the heart's natural pacemaker fails to fire, then:	no blood would enter	no blood would enter	the node on the floor c	the node on the floor of the	the node on the floor of the right atrium would act as a secondary pacemaker
17	If you decrease a blood vessel's radius in half, by what fraction does the blood fl	1/2	1/4	1/8	1/16	1/16
18	Immediately following strenuous and vigorous exercise, which of the following is	blood will be rapidly d	the skin will be cold ar	capillaries of the activ	blood flow to the kidneys q	capillaries of the active muscles will be engorged with blood
19	Intercalated disks are found:	between the right side	between the flaps of t	where the aorta joins l	between the cardiac muscle	between the cardiac muscle cells
20	Mean blood pressure means	Systolic pressure + dia	Systolic pressure + dia	Systolic pressure + 1/3	Diastolic pressure + 1/3 pul	Diastolic pressure + 1/3 pulse pressure
21	Most of the cardiac muscle of the heart is found in the:	endocardium	epicardium	myocardium	pericardium	myocardium
22	Nervous control of the heart can be exerted by:	nerves from the thora	the second and third c	by fibers of the sensor	by fibers of the autonomic r	by fibers of the autonomic nervous system
23	Normal end diastolic volume is:	75 mL	100 mL	110-120 mL	130-150 mL	110-120 mL
24	Normal end systolic volume is:	40-50 mL	50-60 mL	60-70 mL	75-80 mL	40-50 mL
25	Prime contributor of atherosclerosis is	accumulation of monc	accumulation of meso	accumulation of album	accumulation of cholesterol	accumulation of mesophyll
26	Study of properties of blood flow is classified as	physiology	hemodynamic	hemorheology	cardiology	hemorheology
27	The arteries supplying blood to the tissue of the heart are the:	renal arteries	myocardial arteries	coronary arteries	vena cavae	coronary arteries
28	The blood pressure is measured by an instrument known as a:	electrocardiogram	electroencephalograpl	sphygmomanometer	CAT scan machine	sphygmomanometer
29	The bundle of His:	is found in the aorta	is a group of Purkinje f	prevents the mitral va	is a group of arteries that su	is a group of Purkinje fibers
30	The circulatory pathway that carries blood from the digestive tract towards the l	coronary circuit	cerebral circuit	hepatic portal circuit	pulmonary circuit	hepatic portal circuit
31	The condition called arrhythmia is characterized by:	rapid heart contractio	irregular heart rhythm	mitral valve prolapse	semilunar valve dysfunction	irregular heart rhythms
32	The exchange of gases and nutrients between blood and tissues is a major functi	arterioles	arteries	capillaries	veins	capillaries
33	The heart's electrical conduction network found within the ventricular myocardi	sinoatrial node	bundle of His/atrioven	left and right bundle b	Purkinje fibers	Purkinje fibers
34	The heart's natural pacemaker is termed the:	sinoatrial node	bundle of His/atrioven	left and right bundle b	Purkinje fibers	sinoatrial node
35	The hepatic portal vein transports blood:	from the heart to the l	from the liver to the sy	from the gastrointsest	from the liver to the gastroi	from the gastrointsestinal tract to the liver
36	The interventricular septum and the intra-atrial septum separate the:	chambers of the heart	chambers of the lungs	aorta and pulmonary a	bicuspid and tricuspid valve	chambers of the heart
37	The lining of the inner walls of the heart's chambers is termed the:	visceral pericardium	epicardium	myocardium	endocardium	endocardium
38	The only vein in the body that transports oxygen-rich blood is the:	coronary vein	hepatic portal vein	pulmonary vein	aortic vein	pulmonary vein
39	The outermost layer of the heart's serous pericardium is termed the:	visceral pericardium	parietal pericardium	epicardium	myocardium	parietal pericardium
40	The peak pressure of atrial systole is:	7-8 mm Hg	8-15 mm Hg	15-20 mm Hg	20-25 mm Hg	7-8 mm Hg
41	The pericardium is the double sac membrane that:	encloses the heart	line the aorta	makes up the heart va	is found only in the capillari	encloses the heart
42	The PR interval of ECG corresponds to	ventricular repolarizat	ventricular repolarizat	atrial repolarization ar	repolarization of AV node ar	atrial repolarization and conduction through AV node
43	The pulse rate of a normal individual averages about:	10 beats per minute	40 beats per minute	50 beats per minute	70 beats per minute	70 beats per minute
44	The semilunar valves prevent blood from flowing backwards:	into the atria	into the ventricles	into the brain	into the liver	into the ventricles
45	The systemic circuit of the cardiovascular system extends:	from the heart to the l	from heart to the coro	from the heart to the l	from the gastrointestinal tra	from the heart to the body's organs and tissues
46	The 'T' wave in ECG is above the isoelectric line because of	depolarisation of vent	depolarisation of bunc	change in the direction	repolarisation of purkinje fi	change in the direction of repolarisation from the wave of depolarization of the ventricles
47	The term vasoconstriction refers to:	increasing the size of t	decreasing the size of	delivering oxygen and	delivering waste products to	decreasing the size of the lumen of the blood vessel
48	The terms systole and diastole refer to:	sounds from the heart	the major artery and v	heart contractions and	rates of heart pulse	heart contractions and relaxations
49	Venous return depends upon	Velocity of blood	Increased mean syster	Cardiac output	Stiffness of vessel	Increased mean systemic filling pressure
50	Ventricular depolarization in ECG is seen as:	P-wave	QRS complex	T-wave	ST segment	QRS complex
51	Which is the most desirable blood pressure (taken as average of 2 consecutive m	180/110mmHg	140/80mmHg	120/80mm	80/60mmHg	120/80mm
52	Which of the following agents helps to increase the Ca storage capacity of the SF	dihydropyridines	ryanodine	calsequestrin	acetylcholine	calsequestrin
53	Which of the following applies to the sinoatrial node?	it is a mass of nerve ce	it produces important	it generates autorhyth	it contains both bicuspid an	it generates autorhythmic impulses to contract the heart
54	Which of the following blood vessels has the greatest compliance?	Arteries	Veins	Arterioles	Capillaries	Veins
55	Which of the following is a correct formula for the mean arterial blood pressure?	MAP = CO X SV	MAP = CO X HR	MAP = SV X HR X TPR	MAP = HR X TPR	MAP = SV X HR X TPR
56	Which of the following is usually the dominant pacemaker and fires the fastest?	SA node	AV node	His bundle	Purkinje fibers	SA node
57	Which of the following represents the flow of blood from the heart to the body c	venules to capillaries t	arteries to capillaries t	capillaries to arteriole	veins to arteries to capillari	arteries to capillaries to veins
58	Which of the following statements best describes arteries?	all arteries carry oxyge	all arteries contain val	all arteries carry blood	only large arteries are lined	all arteries carry blood away from the heart
59	Which of these vessels does not have sympathetic control	cerebral	splanchnic	cardiac	cutaneous	cerebral
60	Which tunic of an artery contains endothelium?	tunica interna/intima	tunica media	tunica externa	tunica adventitia	tunica interna/intima

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17BCU203 Human Physiology

S. No.	Question	Opt A	Opt B	Opt C	Opt D	Answer
1	An increase in the concentration of plasma potassium causes increase in:	release of renin	secretion of aldosteror	secretion of ADH	production of angiotensin II	secretion of aldosterone
2	Amino acids are almost completely reabsorbed from the glomerular filtrate via act	proximal tubule	loop of Henle	distal tubule	collecting duct	proximal tubule
3	Glomerular filtration rate would be increased by :	constriction of the affe	a decrease in afferent	compression of the ren	a decrease in the concentrat	a decrease in the concentration of plasma protein
4	The greatest amount of hydrogen ion secreted by the proximal tubule is associate	excretion of potassium	excretion of hydrogen	reabsorption of calciur	reabsorption of bicarbonate	reabsorption of bicarbonate ion
5	In controlling the synthesis and secretion of aldosterone , which of the following f	angiotensin II	concentration of plasm	concentration of plasm	adrenocorticotropic hormon	adrenocorticotropic hormone (ACTH)
6	Renal correction of acute hyperkalemia will result in :	alkalosis	acidosis	increased secretion of	increased secretion of Na+	acidosis
7	Most of the glucose that is filtered through the glomerulus undergoes reabsorptic	proximal tubule	descending limp of the	ascending limb of the l	distal tubule	proximal tubule
8	Ammonia is an affective important urinary buffer for which of the following reaso	its production in the ki	the walls of the renal t	the walls of the renal t	its acid base reaction has a k	the walls of the renal tubules are impermeable to NH4
9	The amount of potassium excreted by the kidney will decreases if :	distal tubular flow incr	circulating aldosterone	dietary intake of potas	Na+ reabsorption by the dist	Na+ reabsorption by the distal nephron decreases
10	In the presence of ADH, The distal nephron is least permeable to :	water	ammonia	urea	sodium	urea
11	Which of the following substances will be more concentrated at the end of the pr	glucose	creatinine	sodium	bicarbonate	creatinine
12	When a person is dehydrated, hypotonic fluid will be found in the:	glomerular filtrate	proximal tubule	loop of Henle	distal convoluted tubule	loop of Henle
13	Which one of the following statements about aldosterone is correct?	it produces its effect b	it produces its effect by	it causes an increased i	it has its main effect on the g	it produces its effect by increasing membrane permeability to potassium
14	The effect of antidiuretic hormone (ADH)	increase the permeabi	increase the excretion	increase the excretion	increase the diameter of the	increase the permeability of the distal nephron to water.
15	In the distal tubules, sodium reabsorption is increased directly by increased :	sympathetic nerve stir	atrial natriuretic hormo	antidiuretic hormone s	aldosterone secretion	aldosterone secretion
16	The ability of the kidney to excrete a concentrated urine will increase if :	the permeability of the	the rate of blood flow	the rate of flow throug	the activity of the Na-K pum	the rate of blood flow through the medulla decreases .
17	The glomerular filtration rate will increase if :	circulating blood volur	the afferent arteriolar	the efferent arteriolar	the plasma protein concentr	the plasma protein concentration decreases .
18	The volume of plasma needed each minute to supply a substance at the rate at wl	diffusion constant of t	clearance of the substa	extraction ratio of the	tubular mass of the substanc	clearance of the substance
19	An increase in the osmolarity of the extracellular compartment will:	stimulate the volume r	inhibit the volume and	inhibit the volume and	stimulate the volume and os	stimulate the volume and osmoreceptors , and stimulate ADH secretion.
20	Select the correct answer about proximal tubules :	K+ is secreted in excha	aldosterone	glucose , amino acids &	only 10% of the filtered wate	aldosterone
21	The primary renal site for the secretion of organic ions e.g urate, creatinine is :	proximal tubule	loop of Henle	distal tubule	collecting duct .	proximal tubule
22	Reabsorption of Na+ :	takes place in associati	occurs only in PT	is under control of parr	is a passive process .	takes place in association with CL- & HCO3 –
23	Diamox causes :	water diuresis	hypokalaemia	alkalosis	acidosis	hypokalaemia
24	K+ excretion is markedly influenced by :	aldosterone	amount of Na+ deliver	rate of tubular secretic	insulin	aldosterone
25	More hydrogen is secreted in :	alkalosis	administration of diam	hypokalaemia	hyperventilation.	hypokalaemia
26	Major determinants of plasma osmolarity include all the following except:	sodium	hemoglobin	chloride	albumin	hemoglobin
27	The hypothalamus will effect the release of ADH in response to all the following st	dehydration	severe hemorrhage	pain , anxiety , or surgi	nicotine	nicotine
28	H+ secretion in the distal nephron is enhanced by all the following except :	an increase in the leve	an increase in the tubu	hyperkalemia	metabolic acidosis	hyperkalemia
29	Urinary volume is increased by all the following except :	diabetes insipidus	diabetes mellitus	sympathetic stimulatio	increased renal arterial press	sympathetic stimulation
30	Significant buffers for hydrogen ions generated in the body from anaerobic metat	extracellular bicarbonz	plasma proteins	plasma lactate	inorganic phosphate	plasma lactate
31	Extracellular bicarbonate ions serve as effective buffer for all the following except	phosphate acid	lactic acid	carbonic acid	ß- hydroxybutyric acid	carbonic acid
32	All the following statements are true of the H+ secreted into the lumen of the dist	can combine with NH4	can combine with HCO	can combine with HPO	can remains as free H	can combine with NH4+
33	The glomerular filtration barrier is composed of all the following except :	fenestrated capillary e	macula densa .	basement membrane .	podocytes .	macula densa .
34	The amount of H+ excreted as titratable acid bound to phosphate would be increa	an increase in the amo	an increase in the pH o	an increase in the diet	an increase in the level of pl	an increase in the pH of the urine .
35	Carbonic anhydrase plays an important role in all the following except :	the renal handing of H	the renal handling of H	the renal handling of H	the renal handling of HCO3 –	the renal handling of HCO3 – within the lumen of the tubules of the distal nephron
36	About the proximal convoluted tubules , all are true except :	reabsorb most of Na+	reabsorb most of Cl- io	reabsorb most of K+ io	contains JGCs which secrete	contains JGCs which secrete renin
37	About urea , all are true except :	concentration rises in	nephron	is actively secreted by	concentration in the blood r	nephron
38	Which of the following would cause an increase in both glomerular filtration rate (	Hyperproteinemia	A ureteral stone	Dilation of the afferent	Dilation of the efferent arter	Dilation of the afferent arteriole
39	Subjects A and B are 70 kg men. Subject A drinks 2 L of distilled water, and subje	greater change in intra	higher positive free-wa	greater change in plas	higher urine osmolarity	higher urine osmolarity
40	Use the values below to answer the following question. Glomerular capillary hydr	57 mmHg	47 mmHg	37 mmHg	10 mmHg	10 mmHg
41	Glucose reabsorption occurs in the	proximal tubule	loop of Henle	distal tubule	cortical collecting duct	proximal tubule
42	Which agent is released or secreted after a hemorrhage and causes an increase in	Aldosterone	Angiotensin I	Angiotensin II	Antidiureis hormone（ADH）	Aldosterone
43	Which of the following causes hyperkalemia?	Exercise	Alkalosis	Insulin injection	Decreased serum osmolarity	Exercise
44	In the presence of vasopressin, the greatest fraction of filtered water is absorbec	proximal tubule	loop of Henle	distal tubule	cortical collecting duct	proximal tubule
45	On which of the following does aldosterone exert its greatest effect?	Proximal tubule	Thin portion of the loo	Thick portion of the loo	Cortical collecting duct	Cortical collecting duct
46	What is the clearance of a substance when is concentration in the plasma is 10 mg	2 ml/min	10 ml/min	20 ml/min	200 ml/min	20 ml/min
47	As urine flow increases during osmotic diuresis	the osmolality of urine	the osmolality of urine	the osmolality of urine	the osmolality of urine appr	the osmolality of urine approaches that of plasma because an increasingly large fraction of the excreted urine is isotonic proximal tubular fluid
48	If the clearance of a substance which is freely filtered is less than that of insulin	there is net reabsorpti	there is net secretion c	the substance is neithe	the substance becomes bou	there is net reabsorption of the substance in the tubules
49	A negative free-water clearance (-CH2O) will occur in a person who	drinks 2 L of distilled w	begins excreting large v	is receiving lithium trea	has an oat cell carcinoma of	has an oat cell carcinoma of the lung, and excretes urine with an osmolarity of 1000 mOsm/L
50	At plasma concentrations of glucose higher than occur at transport maximum（Tr	clearance of glucose is	excretion rate of gluco	reabsorption rate of gl	excretion rate of glucose inc	excretion rate of glucose increases with increasing plasma glucose concentrations
51	One gram of mannitol was injected into a woman. After equilibration, a plasma s	extracellular fluid（EC	intracellular fluid (ICF)	ECF volume is 10 L	ICF volume is 10 L	ECF volume is 10 L
52	Which of the following would produce an increase in the reabsorption of isosmoti	Increased filtration fra	Extracellular fluid (ECF	Decreased peritubular	Increased peritubular capilla	Increased filtration fraction
53	Which of the following is an action of parathyroid hormone（PTH）on the renal t	Stimulation of adenlat	Inhibition of distal tubl	Inqibition of distal tubl	Stimulation of proximal tubu	Stimulation of adenlate cyclase
54	At plasma para-aminohippuric acid（PAH）concentrations below the transport m	reabsorption is not sat	clearance equals inulin	secretion rate equals P	concentration in the renal ve	concentration in the renal vein is close to zero
55	Compared with a person who ingests 2 L of distilled water, a person with water c	lower plasma osmolari	lower circulating level	higher tubular fluid/pl	higher rate of H2O reabsorp	higher rate of H2O reabsorption in the collecting ducts
56	Which of the following would best distinguish an otherwise healthy person with s	Free-water clearance	Urine osmolarity	Plasma osmolarity	Circulating levels of antidiure	Plasma osmolarity
57	Which of the following causes a decrease in renal Ca2+ clearance?	Hypoparathyroidism	Treatment with chloro	Treatment with furose	Extracellular fluid（ECF）vo	Treatment with chlorothiazide
58	Which of the following substances has the highest renal clearance?	Para-aminohippuric ac	Inulin	Glucose	Na+	Para-aminohippuric acid（PAH）
59	A woman runs a marathon in 90 weather and replaces all volume lost in sweat b	decreased total body v	decreased hematocrit	decreased intracellular	decreased plasma osmolarit	decreased plasma osmolarity
60	The glomerular filtration rate in ml/min is:	120	180	240	400	120

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S. No.	Question	Opt A	Opt B	Opt C	Opt D	Answer
1	Slow waves in small intestinal smooth muscle cells are	action potentials	phasic contractions	tonic contractions	oscillating resting membran	oscillating resting membrane potentials
2	Which of the following substances is released from neurons in the GI tract and p	Secretin	Gastrin	Cholecystokinin (CCK)	Vasoactive intestinal peptid	Vasoactive intestinal peptide（VIP）
3	Which of the following is characteristic of saliva?	Hypotonicity relative t	A lower HCO3- concen	The presence of prote	Secretion rate that is increa	Hypotonicity relative to plasma
4	Which of the following is the site of secretion of gastrin?	Gastric antrum	Gastric fundus	Duodenum	Ileum	Gastric antrum
5	Secretion of which of the following substances is inhibited by low pH?	Secretin	Gastrin	Cholecystokinin（CCK	Vasoactive intestinal peptid	Gastrin
6	When parietal cells are stimulated, they secrete	HCl and intrinsic facto	HCl and pepsinogen	HCl and HCO3-	HCO3- and intrinsic factor	HCl and intrinsic factor
7	Which of the following abolishes "receptive relaxation"of the stomach?	Parasympathetic stimu	Sympathetic stimulatic	Vaotomy	Administration of gastrin	Vaotomy
8	Which of the following is the site of secretion of intrinsic factor?	Gastric antrum	Gastric fundus	Duodenum	Ileum	Gastric fundus
9	Which of the following is true about the secretion from the exocrine pancreas?	It has a higher Cl- conc	It is stimulated by the	Pancreatic HCO3- secr	Pancreatic enzyme secretio	Pancreatic enzyme secretion is increased by cholecystokinin（CCK）.
10	Which of the following are incorrectly paired?	Pancreatic amylase : s	Elastase : tissues rich	Enteropeptidase : pol	Rennin : coagulated milk	Enteropeptidase : polypeptides
11	Which of the following has the highest pH?	Gastric juice	Bile in the gallbladder	Pancreatic juice	Saliva	Pancreatic juice
12	Cholecystokinin (CCK) has some gastrin like properties because both CCK and ga	are released from G ce	are released from I cel	are members of the se	have five identical C-termin	have five identical C-terminal amino acids
13	Which of the following is the site of Na+-bile acid cotransport?	Gastric antrum	Gastric fundus	Duodenum	Ileum	Ileum
14	Peristalsis of the small intestine	mines the food bolus	is coordinated by the c	involves contraction o	involves contraction of smo	involves contraction of smooth muscle behind the food bolus and relaxation of smooth muscle in front of the bolus
15	Which of the following changes occurs during defecation?	Internal anal sphincter	External anal sphincter	Rectal smooth muscle	Intra-abdominal pressure is	Internal anal sphincter is relaxed
16	In infants, defecation of ten follows a meal. The cause of colonic contractions in	the gastroileal reflex	increased circulating le	the gastrocolic reflex	increased circulating levels	the gastrocolic reflex
17	Water is absorbed in the jejunum, ileum, and colon and excreted in the feces. Ar	colon, jejunum, ileu	feces, colon, ileum,	jejunum, ileum, colo	colon, ileum, jejunum, fi	jejunum, ileum, colon, feces
18	Which of the following substances must be further digested before it can be abs	Fructose	Sucrose	Alanine	Dipeptides	Sucrose
19	The pathway from the intestinal lumen to the circulating blood for a short-chain	intestinal mucosal cell	intestinal mucosal cell	space between mucos	space between mucosal cell	intestinal mucosal cell→hepatic portal vein blood→systemic venous blood
20	Which type of hepatitis can be transmitted through feco-oral?	hepatitis A	hepatitis B	hepatitis G	hepatitis D	hepatitis A
21	What is type III primary biliary cirrhosis?	Positive LKM	No auto antibodies de	All antibodies negative	Positive ANA and ASMA, rais	All antibodies negative, positive antibodies against soluble liver antigen (SLA)
22	_____ measurement is sensitive in detecting mild cirrhosis.	AST	GGT	ALP	ALT	GGT
23	The best liver function test is:	AST/ALT	Alkaline phosphatase	Bilirubin	INR	INR
24	Feaces gets	Hard and wet in const	Soft and dry in constip	Hard and dry in consti	Soft and wet in constipation	Hard and dry in constipation
25	Main cause of indigestion of food is due to	Lack of chewing	Lack of water in the bc	Lack of Saliva	Infection	Lack of chewing
26	Diarrhea takes out too much water and minerals which causes	Dehydration	Hunger	Dryness	Lack of energy	Dehydration
27	Diarrhea takes place due to	Mosquitoes	Infected Food	Infected Syringes	Cold	Infected Food
28	Liver synthesizes all, except	C3 complement comp	Haptoglobin	Fibrinogen	Immunoglobulin	Immunoglobulin
29	The hepatocyte	is usually diploid and	closest to the portal t	has great variation in	is supplied principally by he	is usually diploid and uninucleate
30	The primary diseases of the liver include all of the following except	hepatitis C	alcoholic liver disease	ascending cholangitis	hepatocellular carcinoma	ascending cholangitis
31	The most common cause for chronic liver disease in the West is	Hepatitis C	alcoholic liver disease	non-alcoholic fatty liv	drug induced hepatitis	hepatitis C
32	Concerning patterns of hepatic injury	centrilobular necrosis	alcoholic fatty liver aff	fibrotic change is gen	necrosis is usually liquefact	alcoholic fatty liver affects virtually every hepatocyte
33	Regarding hepatic failure	60-70% of hepatic cap	Mortality of hepatic fa	Paracetamol overdos	Hepatitis C is a cause of ma	Paracetamol overdose is the most common cause of massive hepatic necrosis
34	Regarding the clinical findings in hepatic failure	patients suffering fro	patients are often pro	asterixis is the non rh	jaundice occurs in 60% of p	asterixis is the non rhythmic movement of the extremities
35	Regarding hepatic failure (old paper)	60% of hepatic capaci	Encephalopathy is the	The liver is the predo	Encephalopathy is universa	The liver is the predominant site of albumin synthesis
36	Regarding hepatorenal syndrome (old paper)	it is irreversible	the ability to concentr	the urine is high is soc	the urine is hyperosmolar d	the urine is hyperosmolar devoid of proteins and sediment and low in sodium
37	Cirrhosis of the liver (old paper)	results in changes to t	shows a basically norr	rapid development of	can usually be reversed if tl	results in changes to the vascular channels
38	Clinical features of cirrhosis include all except	osteoporosis	atrophy of the spleen	anorexia	development of hepatocelli	atrophy of the spleen
39	In cirrhosis (old paper)	fibrosis is confined to	nodularity is uncomm	vascular architecture	The Ito cell is a major sourc	The Ito cell is a major source of excess collagen
40	Which of the following is most correct regarding portal hypertension (old paper)	prehepatic + splenic v	intrahepatic + Budd Cl	post hepatic + cirrhos	schistosomiasis + prehepati	intrahepatic + Budd Chiari syndrome
41	Oesophageal varices (old paper)	occur in one third of c	account for more thar	are most often as a re	have a 40% mortality during	have a 40% mortality during the first episode of rupture
42	Ascites	is clinically detectable	caused by cirrhosis re	can cause a hydrotho	with the presence of red ce	with the presence of red cells points to possible disseminated intra-abdominal cancer
43	Bilirubin	is formed exclusively	is produced in quantit	is formed in the liver	is soluble in aqueous soluti	is produced in quantities of 0.2-0.3g per day
44	Conjugated hyperbilirubinaemia results from (old paper)	Gilbert's syndrome	Physiologic jaundice	Excess production of l	Cholestasis	Cholestasis
45	Regarding jaundice (old paper)	Unconjugated bilirubi	Excess conjugated bili	Unconjugated bilirubi	Unconjugated bilirubin is tig	Unconjugated bilirubin is tightly bound to albumin
46	Which of the following conditions is associated with an unconjugated hyperbiliru	Haemolysis	Rotor syndrome	Dubin Johnson syndrc	Pancreatic cancer	Haemolysis
47	Hepatitis A	has a chronic carrier s	has an associated mo	infection is not affect	has an incubation period of	has an incubation period of 2-6 weeks
48	Regarding hepatitis B	HBe antigen amounts	IgG anti Hepatitis A vi	Anti He antibody amo	it has an incubation period	HBe antigen amounts to active replication by the virus
49	In hepatitis B	anti-HBs appears soo	infection is not associ	HBsAg appears soon a	acute infection causes sub-	acute infection causes sub-clinical disease in 65% of cases
50	Hepatitis C	has a high association	transmission increase	causing fulminant hep	infections become chronic i	infections become chronic in greater than 50% of infected patients
51	Hepatitis D	is a double stranded r	induces anti-HD surfa	is unable to replicate	does not cause fulminant h	is unable to replicate independently
52	Hepatitis E infection (old question)	is transmitted primari	accounts for a greater	is common in Russia	is associated with chronic d	accounts for a greater than 20% mortality in pregnant mothers
53	Regarding acute viral hepatitis infection	Acute viral hepatitis is	Chronic disease result	Icterus is common in :	Most patients with acute di	Icterus is common in adults with hepatitis A infection, but is rare in children
54	Concerning biliary lithiasis p928	stones are produced i	50% of stones are sym	50% are cholesterol st	Caucasian women are twice	Caucasian women are twice as likely to be affected than men
55	Concerning the pathogenesis of cholesterol stones, all the following defects are r	Infection of the biliary	Bile must be supersat	Gallbladder hypomoti	Cholesterol nucleation acce	Infection of the biliary tract by E coli

I BSc Biochemistry

17BCU203 Human Physiology

S. No.	Question	Opt A	Opt B	Opt C	Opt D	Answer
1	_____ Hormone stimulates leydig cells to secrete testosterone	Scrotum	Epididymis	prostrate gland	cowpers gland	scrotum
2	Acetylcholinesterase is	nodes of Ranvier	dendrites	synapses	Schwann cells	Schwann cells
3	Action potentials	serotonin	dopamine	neuropeptides	norepinephrine	neuropeptides
4	After passing stimulus from receptors to sensory neurons , it passes then to	urea	concentrated urine	uric acid	ammonia	concentrated urine
5	All of the following neurotransmitters are biogenic amines except	axons	dendrites	neuron cell bodies	myelin sheaths	dendrites
6	Autonomic nervous system controls	motor neurons	sensory neurons	associative neurons	relay neurons	motor neurons
7	Autonomic nervous system is further divided into	voluntary movements	reflex actions	semi-voluntary moven	involuntary movements	involuntary movements
8	Between two neurons a microscopic gap exists which is the contact point of neu	sleep membrane pote	resting membrane pot	passive membrane pot	dormant membrane potenti	resting membrane potential
9	Corpus luteum secretes	Placenta	Pregnancy	Fertilization	Ejaculation	Pregnancy
10	During saltatory conduction, a nerve impulse jumps from one _____	neuromuscular junctio	nodes of Ranvier	inhibitory synapses	excitatory synapses	inhibitory synapses
11	Each testis is encased by a white fibrous membrane known as	Spermatogenesis	spermatic cord	spermiation	spermetazoa	spermiation
12	Fertilisation of human ovum is due to	Aldosterone	Testosterone	Coticosterone	Vasopressin	Testosterone
13	For each impulse autonomic nervous system utilizes only	axons	dendrites	cell body	myelin	myelin
14	GABA (gamma aminobutyric acid) is normally found at	dendrites	axon	myelin sheaths	hormones	dendrites
15	Graded potentials may become action potential by	are summable	are amplifiable	result from facilitated	are all-or-nothing events	are all-or-nothing events
16	Human spermatozoa	Penetration of the ovu	Only one sperm is allo	May occur one week a	Usually occurs at the ampul	Penetration of the ovum by the sperm brought about by a lysosomal enzyme present
17	In hydra nervous system is a network of neurons present between the	effectors	motor neurons	associative neurons	Back to receptors	associative neurons
18	In myelinated neurons the impulse jumps from node to node. This is called	node of ranvier	neuron bridges	synapse	gaps	synapse
19	In normal menstrual cycle	Require temperature l	They are motile even v	In the absence of fertil	Take about 45 min to pass f	Require temperature lower than that of the interior of body for their genesis
20	In sensory neurons, stimuli are received by the	summation	multiplication	hypopolarization	decreasing frequency	summation
21	Interstial cells of Leydig secrete	Prostrate gland	Epidymis	Seminiferous tubules	Ampulla	Seminiferous tubules
22	Leutinizing hormone releasing hormone is secreted in	Thyroxin	Calcitonin	Estrogen	Progesterone	Progesterone
23	Most of the sperms are stored in	Castration	Enuuchism	Frohlich's syndrome	Fibro adenoma	Castration
24	Name the hormone that regulates the water reabsorption in the distal tubule	Spermatogenesis	Cytogenesis	Oogenesis	Embryogenesis	Spermatogenesis
25	Nephrons have extensive blood supply by	cortical nephrons	medullar nephrons	juxtamedullary nephrc	cortical and medullar nephr	juxtamedullary nephrons
26	Nerve impulses are normally carried toward a neuron cell body by the neuron's	neurotransmitter	synapse	node of Ranvier	threshold	synapse
27	Neurons at rest (non-conducting neuron) has electric potential called	ectoderm and mesode	ectoderm and endode	endoderm and mesod	mesoderm and pericarp	ectoderm and endoderm
28	Neurotransmitters are released from vesicles at the	a neurotransmitter	an enzyme that breaks	a stimulant that trigge	a hormone	an enzyme that breaks down a neurotransmitter
29	Oxytocin is secreted in	LH	Growth hormone	ACTH	PRL	LH
30	Postsynaptic membranes are most likely to be found on	myelin sheath	synapse	node of Ranvier	dendrite	node of Ranvier
31	Prolactin is secreted by	Vasderferens	Spermatids	Spermatogonia	Sertoli cells	Vasderferens
32	Semen also contains a hormone like substance known as	graffian follicle	zona pellucida	ovulation	ophorous	zona pellucida
33	Somatic nervous system is made up of	four neurons and two	two neurons and one g	one neuron and one ga	one neuron and two ganglio	two neurons and one ganglion
34	Spermatogenesis occurs in	Pituitary gland	Ovaries	Hypothalamus	Adrenal gland	Hypothalamus
35	Sympathetic nervous system is associated with	three parts	two parts	four parts	five parts	two parts
36	The cell membrane of the oocyte is called as	Ovulation	cumulus oophorous	corpus leuteum	theca interna	Ovulation
37	The development of the young within the female reproductive system from the f	4 phases	3 phases	5 phases	6 phases	4 phases
38	The formation of sperm is known as	Sperm	Ovum	Both	None	Ovum
39	The hormone which is responsible for ovulation,formation of the corpus luteum	Diuretic hormone	Antidiuretic hormone	Lutenizing hormone	Follicle stimulating hormon	Antidiuretic hormone
40	The hormone which stimulus secretion of "Uterine milk" is	Adrenal gland	Posterior pituitary	Anterior pituitary	Parathyroid gland	Posterior pituitary
41	The inner end of nephrons is a cup shaped swelling structure known as	hormonal secretions	fear and rage	skeletal muscles	fight and flight	fight and flight
42	The junction between a neuron and its target cell is called a	cell body	dendrite	cell nucleus	presynaptic membrane	presynaptic membrane
43	The juxtamedullary nephrons are specialized for the production of	renal veins	renal arteries	hepatic arteries	peritoneal veins	renal arteries
44	The male organ for copulation is	Testosterone	Androgens	cumulus oophorus	antaglutins	Androgens
45	The menstrual fluid is normally non clotting because of the presence of	Proliferation	Ovulation	Secretory phase	Menstrual phase	Ovulation
46	The meta estrone phase is otherwise termed as	LH	Aldosterone	Vasopressin	FSH	FSH
47	The midbrain of vertebrates is also called the	cerebrum	forebrain	midbrain	hindbrain	hindbrain
48	The myelin sheath is formed by _____, which wrap around the axons	maintain proper ionic	generate the nerve im	transmit the nerve imp	provide a source of Na+ and	maintain proper ionic concentration gradients across the neuron membrane
49	The nephrons which are arranged along the border of medulla looping deep in in	glomerulus	Bowman's capsule	medulla	cortex	Bowman's capsule
50	The neurotransmitter at neuromuscular junctions is	an unmyelinated, sma	an unmyelinated, largi	a myelinated, small di	a myelinated, large diamete	an unmyelinated, small diameter nerve
51	The outer surface of the ovary is covered by	Thrombolysin	Proteolysin	Anticoagulin	Fibrinolysin	Fibrinolysin
52	The phenomenon of the release of ovum from the graffian follicle is described as	LH	FSH	Relaxin	Progesterone	Progesterone
53	The primary function of the Graffian follicle is to form	Hypothalamus	Posterior pituitary	Anterior pituitary	Adrenal cortex	Anterior pituitary
54	The progestational phase of the endometrial cycle occur after	Pre-ovulatory phase	Ovulatory phase	Post ovulatory phase	None of the above	Ovulatory phase
55	The release of sperms from the sertoli cells is known as	Penis	Spermetagenisis	Spermetocytes	Spermetazoa	Penis
56	The role of the Na+/K+ pump in the nervous system is to	GABA	serotonin	acetylcholinesterase	acetylcholine	acetylcholine
57	The testes are small ovoid organs lodged in a pouch like structure called as	Tunica albicans	tunica albuginea	tunica degeneratum	septum	tunica albuginea
58	The testicular hormones are known as	Primordial follicles	Ligaments	Mesovaria	prostaglandins	prostagladins
59	When a boy loses his testes prior to puberty it leads to a condition called	Primodial follicle	Hilar connective tissue	Germinal epithelium	Fallopian tubes	Germinal epithelium
60	Which of the following should have the slowest conduction velocity?	medulla	mesencephalon	diencephalon	hypothalamus	mesencephalon

KARPAGAM ACADEMY OF HIGHER EDUCATION

(Deemed to be University Established Under Section 3 of UGC Act 1956)
Coimbatore - 641021.

(For the candidates admitted from 2015 onwards)

DEPARTMENT OF BIOCHEMISTRY

SUBJECT	**:**	**HUMAN PHYSIOLOGY**		
SEMESTER	**:**	**II**		
SUBJECT CODE	**:**	**17BCU203**	**CLASS**	**: I B.Sc. Biochemistry**

Programme Objective: Understanding of the working of different systems of our body and their functions. The purpose of this course is to promote knowledge in the integration of theories, methods, and research in human physiology.

Programme learning outcome:

The students after completion of this course would have

- Gained knowledge on different systems of our body and their role.
- Obtained knowledge on the working of various organs of our body.
- Understood the basics of human anatomy and physiology.

Unit 1

Homeostasis and the organization of body fluid compartments :

Intracellular, extracellular and interstitial fluid. Homeostasis, control system and their

components. Plasma as an extracellular fluid, RBC, molecular mechanism of blood coagulation, role of vitamin K in coagulation, anticoagulant and fibrinolytic systems. Anemias, polycythemia, haemophilia and thrombosis.

Respiration : Organization of the pulmonary system. Mechanism of respiration, pulmonary ventilation and related volumes, pulmonary circulation. Principles of gas exchange and transport. Regulation of respiration. Pulmonary oedema and regulation of pleural fluid. Hypoxia, hypercapnea, pulmonary distress, emphesema, ARDS.

Unit 2

Cardiovascular physiology: Pressure, flow and resistance. Anatomy of heart. Physiology of the cardiac muscle, automacity of the cardiac muscle contraction, excitation contraction coupling, relationship between cardiac cycle, heart sound, ventricular volumes and the ECG, control of cardiac function and output. The arterial system, venous system, the microcirculation and mechanics of capillary fluid exchange. Control of blood flow to the tissues. Portal circulations. Arterial pressure and its regulation. Hypertension, congestive heart disease, atherosclerosis and myocardial infarction.

Unit 3

Renal physiology: Anatomy of the kidney and the nephron. Regulation of renal blood flow. Cell biology of the Bowmans' capsule. Physiology of glomerular filtration and GFR. Tubular processing of the glomerular filtrate. Micturition reflex and voluntary control of micturition. Regulation of ECF electrolyte and water content, blood volume and long term blood pressure. Blood buffer systems, renal and pulmonary control of blood pH, renal clearance. Assessment of kidney function. Acidosis and alkalosis. Glomerular nephritis, renal failure, dialysis and diuretics.

Unit 4

Gastrointestinal and hepatic physiology: Histology of the gastrointestinal tract. Propulsion and motility of food and digested material. Enteric reflexes, secretory functions of the gastrointestinal tract, digestion and absorption of macro and micronutrients. Peptic ulcer, Sprue, celiac disease, IBD, regurgitation, diarrhoea and constipation. Anatomy of the hepatic lobule and blood flow into the liver. Formation and secretion of bile. enterohepatic cycle, reticuloendothelial system, metabolic importance of liver. Liver function tests. Jaundice, liver cirrhosis and fatty liver.

Musculosketetal system :Bone structure and formation. Physiology of muscle contraction in striated and non-striated muscle.

Unit 5

Reproductive physiology : Sex determination and differentiation. Development of female and male genital tracts. Spermatogenesis, capacitation and transport of sperm, blood testis barrier. Ovarian function and its control. Uterine changes, fertilization and implantation. Placenta as a feto- maternal unit, gestation and parturition.

Neurochemistry and neurophysiology: Central Nervous system. Peripheral Nervous system. Blood brain barrier and CSF. Membrane potentials. Synaptic transmission. Neurotransmitters. Sensory receptors and neural pathways. Somatic sensation, EEG, sleep, coma, learning and memory**.**

TEXTBOOKS

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Murray, R.K., Bender, D.A., Botham, K.M., and Kennelly, P.J., (2012).Harper's illustrated Biochemistry, 29th edition.. McGraw-Hill Medical. London.