MBCDSE 1.3: HUMAN PHYSIOLOGY, BLOCK-I: PHYSIOLOGY.

UNIT 1: BASIC BODY PLAN IN HUMANS AND LOCATION OF ORGANS

STRUCTURE OF THE UNIT

1.0 OBJECTIVES: After studying this unit, you should be able to:

- Identify various body plans and symmetry.
- Describe different levels of organization in human body.
- List out the principal organ systems of the human body.
- Explain the life processes or characteristics of life.
- Describe the requirements for maintenance of life or survival needs.

1.1 INTRODUCTION: It is believed that around 600 million years ago the development of organisms started based on the fossil evidences available at the Ediacara Hills of Australia. The Ediacaran organisms comprise a group of Late Precambrian fossils named for the place where they were first found and described, the Ediacara Hills of Australia. Some of these fossils show similarities to present invertebrates like cnidarians, echinoderms, worms, or arthropods. The basic human body plan starts from earliest stages of embryonic development. The embryo is a small ball like structure in early stage with dividing cells. The embryo later starts to form the tissue and organs following further cell divisions. At the end of the third week the human embryo has Bilateral symmetry, with left and right sides mirror images of each other. The body plan originates with left and right sides of embryo with clarity in developing the vertebrate body supporting the upright body.

1.2 BODY PLAN: A body plan can be thought of as a cross-section through an animal, showing only the most fundamental arrangement of the tissue layers. It does not show any detail, such as the position of the internal organs.

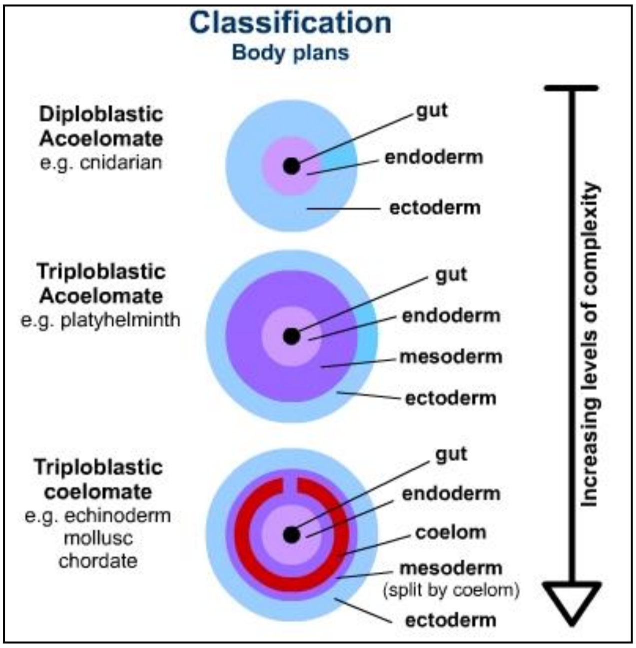
Coelom: a fluid-filled space in the mesoderm of more advanced organisms which divides the gut muscles from those of the body wall. This provides a protective place for specialized organs, which are held in position, supported and lubricated. The main advantages are:

1. Separating the gut muscles from the body wall means that digestion can become more efficient (e.g. peristalsis can occur)
2. Aids locomotion as muscles and bones can develop. In earthworms, coelomic fluid itself provides a hydrostatic "skeleton".
3. Allows for the development of internal organs

Organisms that have a coelom are known as **coelomate** organisms, all others are **acoelomate**. When we talk about complexity in phyla, we refer to the number of tissue layers and whether it has a coelom or not.

1.3 CLASSIFICATION OF BODY PLANS:

Diploblastic acoelomate: An animal possessing 2 major tissue layers. These include the outer layer (the ectoderm) and the inner layer (the endoderm).



Triploblastic acoelomate: An animal possessing 3 major tissue layers. It has a middle layer (the mesoderm), between the endoderm and the ectoderm.

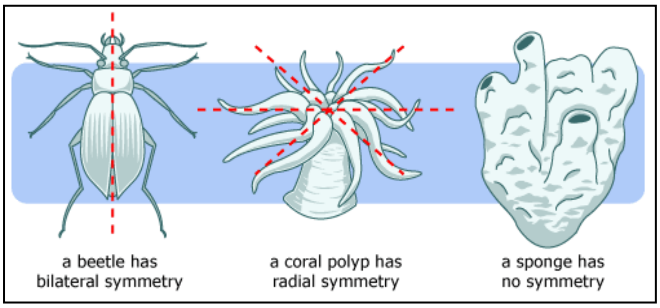
Triploblastic coelomate: An animal possessing 3 major tissue layers. It has a middle layer, the mesoderm, which contains the coelom between the endoderm and the ectoderm.

All phyla fit into one of the three body plans shown in the diagram above.

The more tissue layers and the presence of a coelom the more complex the animal system will be. Humans, for example, have a coelom and are triploblastic, making them one of the most complex organisms in terms of their body plan. The presence of coelom,

- enables independent movement of the gut wall and the body wall.
- provides space for the enlargement and development of internal organs.
- may act as a circulatory medium for transport of materials or a storage area of excess or waste materials.

1.4 SYMMETRY IN ANIMALS:



1. **Asymmetry** is the absence of, or a violation of, symmetry. e.g. sponge.
2. **Radial symmetry:** Slow moving or sessile (non-moving) organisms

have a point of symmetry. Sensory, feeding and defense structures are spread out around the whole organism, e.g. jellyfish and adult starfish.

3. Bilateral symmetry: Active animals have an axis of symmetry. They often exhibit cephalisation (all sense organs on a distinct head). e.g. insects, human.

1.5 DIFFERENT LEVELS OF ORGANIZATION: The evolution of animal body plan originated over 600 million years ago. A body plan is the blue print for the way to locate the organs. Every organism has a body plan. The symmetry and number of segments, organs etc., are related to body plan in the early stage of formation of body. The DNA controls the development of structural features, location and position of cells and organs. The humans had a "pipe" alimentary canal in early stage of body plan. The humans developed basic symmetry in body plan which gave advantage of movement, survival and reproduction.

The human body starts at a Chemical level, that consist of atoms and molecules which forms cellular level -> tissue level -> organ level -> organ system level -> organism -> Body. Let us understand each level of development of human body in detail.

1. **Chemical level:** The chemicals that make up the human body may be divided into two major categories: Inorganic and organic.

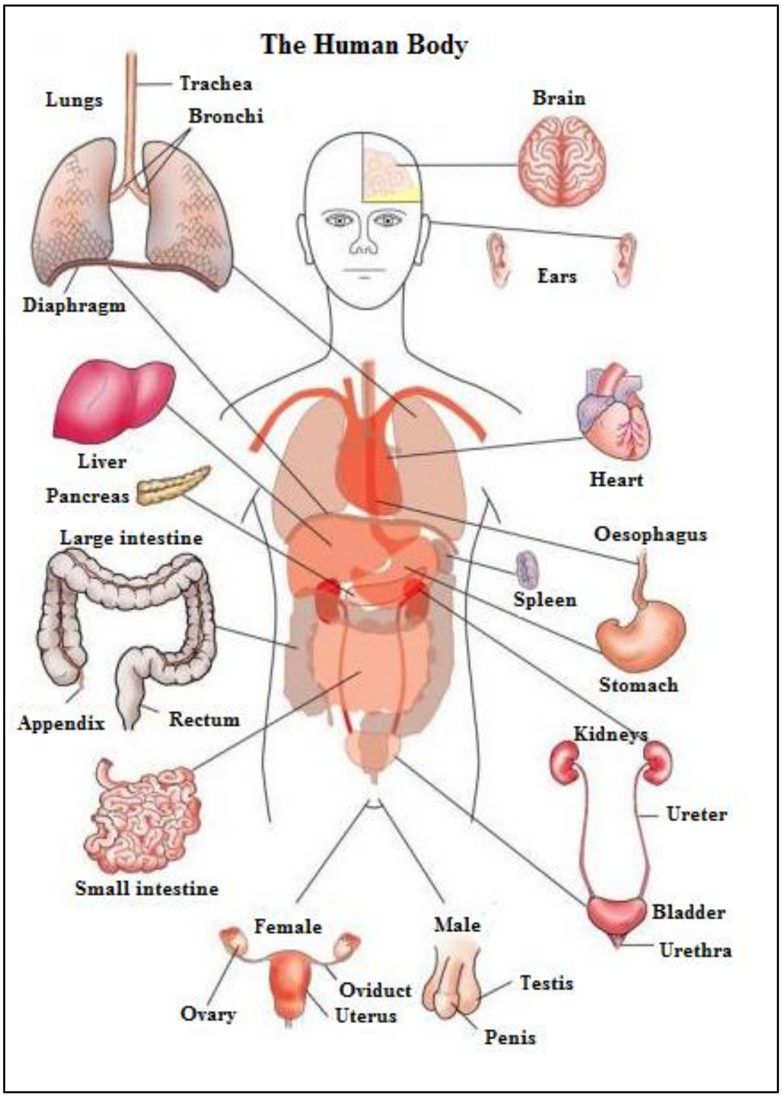
Inorganic chemicals: These are usually simple molecules made up of one or more elements other than Carbon. Examples: Water, Oxygen, Carbon Dioxide (an exception), and minerals such as iron, calcium, and sodium.

Organic chemicals: These are often very Complex and always contain the elements carbon and hydrogen. Examples: Carbohydrates, Fats, Proteins, and Nucleic Acids.

2. **Cellular level:** The smallest living units of structure and function are cells. Anything less than a complete structure of a cell does not ensure independent living. Hence, cell is the fundamental structural and functional unit of all living organisms such as a human being. There are many different types of cells; each is made of chemicals and carries out specific chemical reactions.

3. Tissue level: A tissue is a group of cells with similar structure and function. There are four groups of tissues.

Epithelial tissue: Cover or line body surfaces; some are capable of producing secretions with specific functions. The outer layer of the skin and sweat glands are examples of epithelial tissue.



Connective tissue: Connects and supports parts of the body; some transport or store materials. Blood, Bone, and Adipose Tissue (Fat) are examples.

Muscle tissue: Specialized for contraction, which brings about movement. Our skeleton muscles and the heart are examples.

Nerve tissue: Specialized to generate and transmit electrochemical impulses that regulate body functions. The brain and optic nerves are examples.

4. Organ level: An organ is a group of two or more different types of tissues precisely arranged so as to accomplish specific functions and usually have recognizable shape. Heart, Brain, Liver, Lungs are examples.

5. Organ system level: An organ system is a group of organs that all contribute to a particular function. Examples are the Circulatory, Respiratory, and Digestive Systems. Each organ system carries out its own specific function, but for the organism to survive the organ systems must work together this is called integration of organ systems.

6. Organism level: Organism level is the most complicated and complete level of the body plan. All the organ systems of the body functioning with one another constitute the total organism or a living individual, a human being.

Check your progress exercise-1

Answer in few words.

a) What is Coelom?

b) What are Diploblastic acoelomate?

c) Name different types of body symmetry in animals.

d) What are connective tissues?

Fill in the blanks with appropriate answers.

e) Organisms that have a coelom are known as __________.

f) Humans have ________symmetry.

g) _______ are specialized to generate and transmit electrochemical impulses.

1.6 PRINCIPAL ORGAN SYSTEMS OF THE HUMAN BODY: There are about 11 organ systems that function together in human body. The organ systems are comprised of various organs. Let us know in brief the organ systems present in human body. In the following units we will study these organ systems and their function in detail.

1. Integumentary system: Integumentary system consists of the skin and structures derived from it, such as hair, nails, sweat and oil glands. Mainly integumentary system serves as a barrier to pathogens and chemicals to protect human body, and helps regulate body temperature, eliminates waste, and helps synthesize vitamin D. In addition, the integumentary system receives environmental stimuli due to exposure to temperature, pressure, and pain.

Integumentary system is the most visible system and more attention paid to this organ system. Inspection of the skin, hair, and nails is significant part of a physical examination. Skin is the most vulnerable organ due to exposure to radiation, trauma, infection, and injurious chemicals.

2. Skeletal system: All the bones of the body (206), their associated cartilage, and the joints of the body constitute skeletal system. Bones support and protect the body, assist in body movement. Skeletal system houses cells that produce blood cells, and also store minerals. Skeletal system supports the muscle attachment in turn movement of body.

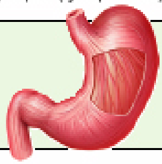
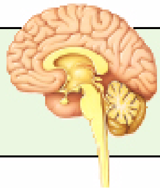
3. Muscular system: Specifically refers to skeletal muscle tissue and tendons. Participates in bringing about movement, maintaining posture, and produces heat.

4. Circulatory and cardiovascular system: The heart, blood and blood vessels constitute this system. Transports oxygen and nutrients to tissues and removes waste.

5. Lymphatic system: The lymph, lymphatic vessels, and structures or organs (spleen and lymph nodes) containing lymph tissue constitute this system. Cleans and returns tissue fluid to the blood and destroys pathogens that enter the body. Most of the times the lymphatic system functions very closely with the immune system or circulatory system hence studied and classified together with these systems.

6. Nervous system: The brain, spinal cord, nerves, and sense organs, such as the eyes and ears. Interprets sensory information, regulates body functions such as movement by means of electrochemical impulses.

7. Endocrine system: All hormone producing glands and cells such as the Pituitary Gland, Thyroid Gland, and Pancreas constitute this system. Regulate body functions by means of secretion of hormones into the circulation.

System	Major structures	Functions
Circulatory	Heart, blood vessels, blood (cardiovascular) lymph nodes and vessels, lymph (lymphatic)	Transports nutrients, wastes, hormones, and gases
Digestive	Mouth, throat, esophagus, stomach, liver, pancreas, small and large intestines 	Extracts and absorbs nutrients from food; removes wastes; maintains water and chemical balances
Endocrine	Hypothalamus, pituitary, pancreas and many other endocrine glands	Regulates body temperature, metabolism, development, and reproduction; maintains homeostasis; regulates other organ systems
Excretory	Kidneys, urinary bladder, ureters, urethra, skin, lungs	Removes wastes from blood; regulates concentration of body fluids
Immune	White blood cells, lymph nodes and vessels, skin	Defends against pathogens and disease
Integumentary	Skin, nails, hair	Protects against injury, infection, and fluid loss; helps regulate body temperature
Muscular	Skeletal, smooth, and cardiac muscle tissues	Moves limbs and trunk; moves substances through body; provides structure and support
Nervous	Brain, spinal cord, nerves, sense organs 	Regulates behavior; maintains homeostasis; regulates other organ systems; controls sensory and motor functions
Reproductive	Testes, penis (in males); ovaries, uterus, breasts (in females)	Produces gametes and offspring
Respiratory	Lungs, nose, mouth, trachea	Moves air into and out of lungs; controls gas exchange between blood and lungs
Skeletal	Bones and joints 	Protects and supports the body and organs; interacts with skeletal muscles, produces red blood cells, white blood cells, and platelets

8. Respiratory system: The Lungs and a series of associated passageways such as the Pharynx (Throat), Larynx (Voice Box), Trachea (Windpipe), and Bronchial Tubes leading into and out of them constitute this system. Primary function of this system is to participate in the exchange of oxygen and carbon dioxide between the air and blood.

9. Digestive system: A long tube called the Gastrointestinal (GI) Tract and associated organs such as the Salivary Glands, Liver, Gallbladder, and Pancreas together form this system. The role of this system is to break down and absorb food for use by cells and eliminates solid and other waste.

10. Urinary and excretory system: The Kidneys, Urinary Bladder, and Urethra that together produce, store, and eliminate Urine form this system. Primary function is to remove waste products from the blood and regulate volume and pH of blood.

11. Immune system: The immune system consists of several organs, as well as white blood cells present in the blood and Lymphatic system of an individual. The main organs of this system are lymph nodes, spleen, lymph vessels, blood vessels, bone marrow, and white blood cells (Lymphocytes). Provide protection against infection and disease.

12. Reproductive system: Organs that produce, store, and transport reproductive cells (sperm and eggs) form the part of this system. Produces eggs (in female) and sperm (in male) and provides a site for the developing embryo-foetus.

1.7 LIFE PROCESSES OR CHARACTERISTICS OF LIFE: All living organisms carry on certain processes that set them apart from nonliving things. The following are several of the more important life processes carried out by humans. The following terminologies are important for further understanding of human body.

Metabolism: Is the sum of all the chemical reactions that occur in the body. One phase of metabolism is called catabolism which provides the energy needed to sustain life by breaking down substances such as food molecules. The other phase is called anabolism which uses the energy from catabolism to make various substances that form body structures and enable them to function.

Assimilation: The changing of absorbed substances into forms that is chemically different from those that entered body fluids.

Responsiveness: The ability to detect and respond to changes outside or inside the body. Seeking water to quench thirst is a response to water loss from body tissue.

Movement: Includes motion of the whole body, individual organs, single cells, or even structures inside cells.

Growth: Refers to an increase in body size. It may be due to an increase in the size of existing cells, the number of cells, or the amount of substance surrounding cells. It occurs whenever an organism produces new body materials faster than old ones are worn out or replaced.

Differentiation: This is the process whereby unspecialized cells become specialized cells. Specialized cells differ in structure and function from the cells from which they originated.

Reproduction: Refers to either the formation of new cells for growth, repair, or replacement or to the making of a new individual.

Others process which we will come across in the coming units include:

Respiration: Obtaining oxygen.

Digestion: Chemically and mechanically breaking down food substances.

Absorption: The passage of substances through certain membranes.

Circulation: The movement of substances within the body in body fluids.

Excretion: Removal of wastes that the body produces.

1.8 MAINTENANCE OF LIFE OR SURVIVAL NEEDS: The structures and functions of almost all body parts help maintain the life of an Organism. The only exceptions are the organism's reproductive structures, which ensure that its species will continue into the future. In addition life requires certain environmental factors, including the following:

Water: This is the most abundant chemical in the body and it is required for many metabolic processes and provides the environment in which most of them take place. Water also transports substances within the organism and is important in regulating body temperature.

Food: The substances that provide the body with necessary Chemicals (Nutrients) in addition to Water. Food is used for energy, supply the raw materials for building new living matter and still others help regulate vital chemical reactions.

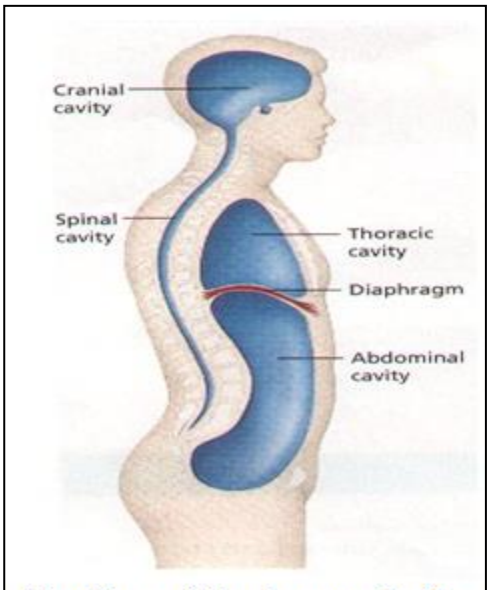
Oxygen: It is required to release energy from food substances. This energy, in turn, drives metabolic processes. Approximately 20% of the air we breathe is oxygen.

Heat (Body temperature): A form of energy, it is a product of Metabolic Reactions. Normal Body Temperature is around 37^{o}C or 98^{o}F. Both low and high body temperatures are dangerous to the organism.

Pressure: Atmospheric pressure is necessary for breathing.

1.9 HOMEOSTASIS OF HUMAN BODY: All of the above systems function together to help the Human Body to Maintain homeostasis. A person who is in good health is in a state of Homeostasis. Homeostasis reflects the ability of the body to maintain relative stability and to function normally despite constant changes. These changes may be external or internal, and the body must respond appropriately. As we continue to study the human body, keep in mind that the proper functioning of each organ and organ system has a role to perform in maintaining homeostasis. Further, the human body uses homeostasis mechanisms to maintain its stable internal environment. Homeostasis mechanisms work much like a Thermostat (negative feedback) that is sensitive to temperature and maintains a relative constant room temperature whether the room gets to hot or cold.

1.10 BODY CAVITIES: Many organs and organ systems in the human body are housed in compartments called body cavities.



Cavities of the human body

These cavities protect delicate internal organs from injuries and from the daily wear of walking, jumping, or running.

The body cavities also permit organs such as the lungs, the urinary bladder, and the stomach to expand and contract while remaining securely supported.

The human body has four main body cavities:

1. Cranial cavity - encases the brain.

2. Spinal cavity - extending from the cranial cavity to the base of the spine, surrounds the Spinal Cord.

The two main cavities in the trunk of the human body are separated by a wall of muscle called the diaphragm.

3. Thoracic cavity - The upper compartment contains the heart, the esophagus, and the organs of the respiratory system - the lungs, trachea, and bronchi.

4. Abdominal cavity - The lower compartment contains organs of the digestive, reproductive, and excretory systems.

Check your progress exercise-2

Answer in few words.

a) What is the role of integumentary system?

b) What is assimilation of food?

c) What is homeostasis?

d) Which are the four main body cavities?

Fill in the blanks with appropriate answers.

e) _____ system participates in bringing about movement, maintaining posture, and produces heat

f) _______ is the process where unspecialized cells become specialized

g) ________ is the wall of muscle that separates two main cavities in the trunk of the human body.

1.11 SUMMARY: Humans belong to Triploblastic coelomate class which means, an animal possessing 3 major tissue layers, such as endo, meso and ectoderm layers. Further, in humans there is a coelom between the endoderm and the ectoderm in addition to gut.

Animals show different patterns of body symmetry. Some groups, such as the phylum Porifera, show no particular pattern of symmetry (asymmetry). That is, no line of bisection exists that could divide the organism into similar-looking halves. Other groups, including the Cnidaria and Echinodermata show **radial symmetry**, where more than one hypothetical bisections can be visualized. A third pattern, seen in most phyla of animals, is **bilateral symmetry**, where only one hypothetical bisection can be visualized.

One of the primary ways zoologist's group animals has to do with the presence or absence of a coelom, and how the coelom is formed. A **coelom** is a fluid-filled cavity between the alimentary canal and the body wall. The peritoneal cavity in our abdomen is one part of our coelom, and there are similar spaces around our heart and lungs. However, the type of coelom (or even its existence) differs among groups of

animals – both in its structure (such as what types of tissues surround it) and its mode of development. There are three structural types of body plans related to the coelom. These are,

1. **Acoelomate**, in which no coelomic cavity exists.
2. **Pseudocoelomate**, in which a coelom exists, but it is lined by mesoderm only on the body wall, not around the gut.
3. **Coelomate**, in which the coelom is lined both on the inside of the body wall and around the gut by mesoderm.

1.12 GLOSSARY:

Organ: Organs are then formed by the functional grouping together of multiple tissues.

Symmetry: Symmetry in biology is the balanced distribution of duplicate body parts or shapes within the body of an organism.

Homeostasis: The tendency towards a relatively stable equilibrium between interdependent elements, especially as maintained by physiological processes.

Body cavity: A body cavity is any fluid-filled space in a multicellular organism other than those of vessels (such as blood vessels and lymph vessels).

1.13 QUESTIONS FOR SELF STUDY:

1) What is body plan, what body plan does humans belong to?
2) Explain various types of symmetry
3) Describe different levels of organization in human body
4) List out the principal organ systems of the human body
5) Explain characteristics of life
6) Describe the requirements for maintenance of life or survival needs
7) With the help of a diagram describe the body cavities and their function

1.14 Answers to check your progress

Exercise-1

a) It is a fluid filled space in the mesoderm of advanced organisms.

b) Animal possessing two major tissue layers. They are ectoderm and the endoderm.

c) Bilateral symmetry, Radial Symmetry and Asymmetry.

d) Tissues which connects and supports parts of the body.

e) Coelomate organisms.

f) Bilateral.

g) Nerve tissues.

Exercise-2

a) It serves as a barrier to pathogens and chemicals to protect body, helps to regulate body temperature, and eliminates waste.

b) It is the changing of absorbed substances into forms that are chemically different from those that entered body fluids.

c) Homeostasis reflects the ability of the body to maintain relative stability and to function normally despite constant changes

d) Cranial cavity, Spinal cavity, Thoracic cavity, Abdominal cavity

e) Muscular

f) Differentiation

1.15 FURTHER REFERENCES:

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BC 1.3: PHYSIOLOGY AND NUTRITION

BLOCK-I: PHYSIOLOGY

UNIT 2: BLOOD: COMPOSITION, CELLS. ERYTHROCYTES – STRUCTURE & FUNCTION. STABILITY OF RBCS: HYPO & HYPERTONIC SOLUTIONS.

WBC: TYPES & FUNCTIONS, DIFFERENTIAL COUNT. PLATELETS & THEIR FUNCTIONS. BUFFER SYSTEMS.

BLOOD VOLUME, BLOOD PRESSURE AND ITS REGULATION.

HEMOSTASIS: BLOOD CLOTTING, DIGESTION OF CLOT; ANTICOAGULANTS. CSF-COMPOSITION & FUNCTION, LYMPH & ITS COMPOSITION.

STRUCTURE OF THE UNIT

2.0 OBJECTIVES: After studying this unit, you should be able to:

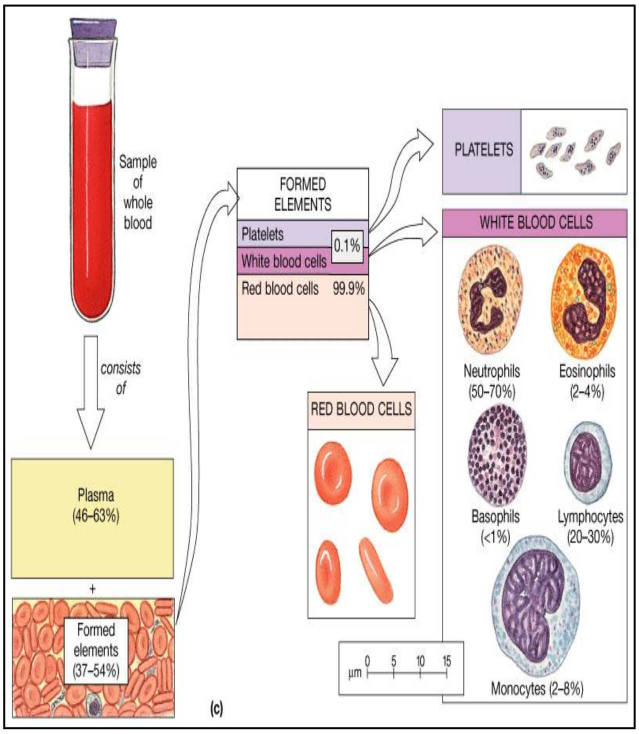
- Describe the composition of blood (Cells and plasma).
- Identify erythrocytes, and list their properties and functions.
- Describe different types of White blood cells and their functions.
- List the role of platelets in the human blood.
- Describe the importance of hemostasis.
- Understand the composition and functions of Cerebrospinal fluid.
- Describe lymph and its composition.

2.1 INTRODUCTION: Blood is called the 'River of the life'. About 400 years ago, the blood circulation around the human body was discovered and 200 years back the first human blood transfusion was performed. We have a complex circulatory system to carry the blood. The average adult has about five litre of blood inside their body, coursing through their vessels, delivering essential elements, and removing harmful wastes. Without blood, the human body would stop working. It is estimated that 8 million blood cells die in human body every second with the same number being born each second.

The blood looks like a red liquid, but it is made up of billions of cells in a pale yellow-coloured fluid called plasma. The bone marrow is a blood factory from where most of the blood cells arise. There are 3 main types of blood cells: red blood cells, white blood cells and platelets. The red blood cells give blood its red colour. Blood is the only tissue that flows throughout your body. This red liquid carries oxygen and nutrients to all parts of the body and waste products back to your lungs, kidneys and liver for disposal. It is also an essential part of your immune system, crucial to fluid and temperature balance, a hydraulic fluid for certain functions and a highway for hormonal messages. This wonderful tissue may be the easiest to transplant (transfuse). In the present unit we will study about blood, its composition and how blood functions as a buffer. In addition, we will discuss key concepts such as blood pressure, blood clotting and about anticoagulants which prevent blood from clotting. Finally, we will study about the other two important liquids present in the body (apart from blood) the cerebrospinal fluid and lymph.

2.2 BLOOD COMPOSITION: Blood is a constantly circulating fluid providing the body with nutrition, oxygen, and waste removal. Blood is mostly liquid, with numerous cells and proteins suspended in it, making blood "thicker" than pure water. The average person has about 5 litres (more than a gallon) of blood.

Liquid called plasma makes up about half of the content of blood. Plasma contains proteins that help blood to clot, transport substances through the blood, and perform other functions. Blood plasma also contains glucose and other dissolved nutrients.

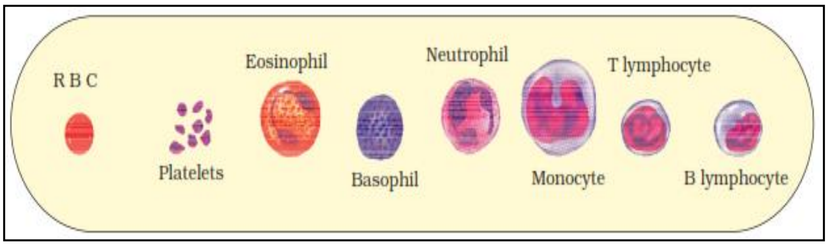


About half of blood volume is composed of blood cells which are also called formed elements of blood:

- Red blood cells, which carry oxygen to the tissues
- White blood cells, which fight infections
- Platelets, smaller cells that help blood to clot

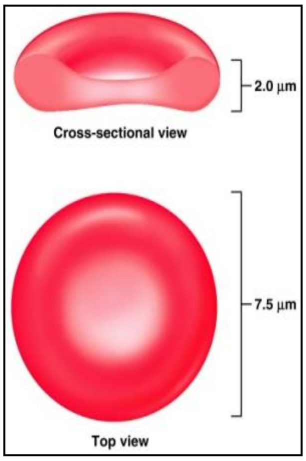
Blood is conducted through blood vessels (arteries and veins). Blood is prevented from clotting in the blood vessels by their smoothness, and the finely tuned balance of clotting factors.

Blood plasma: It is a mixture of proteins, enzymes, nutrients, wastes, hormones and gases. The proteins are categorized in three groups majorly- 1) albumin, 2) globulin, and 3) fibrinogen. The plasma contains nitrogen wastes, abundant sodium ions, gases mostly oxygen and carbon dioxide.



The formed elements: Formed elements are RBC's, WBC's and platelets. The RBC's are also called Erythrocytes, WRC's are also called Leucocytes. These formed elements are enclosed in a membrane and have a definite structure and shape. All formed elements are cells except for platelets from fragments of bone marrow cells. The WBC is mainly of two types. 1) granulocyte and 2) agranulocyte. They have different shape and they can change their shape also. They secret coagulants. They also digest and destroy bacteria.

2.3 ERYTHROCYTES STRUCTURE AND FUNCTIONS: Red blood cells (RBC) also called as Erythrocytes is a simple cell. The RBC does not contain any cell organelles. It has no mitochondria (ATP generating machinery), Ribosome, endoplasmic reticulum, centriole etc. RBC is a biconcave cell. After maturity it loses its nucleus and the mature RBC is a very simple living cell containing Haemoglobin (Hb). Nearly 95% RBC is made up of Hb. The diameter of an average RBC is 7.5 µm and the thickness is 1-2 µm. A healthy RBC can enter a very narrow capillary by sequencing itself and afterwards it regains its original shape. The life span of a RBC is 120 days.



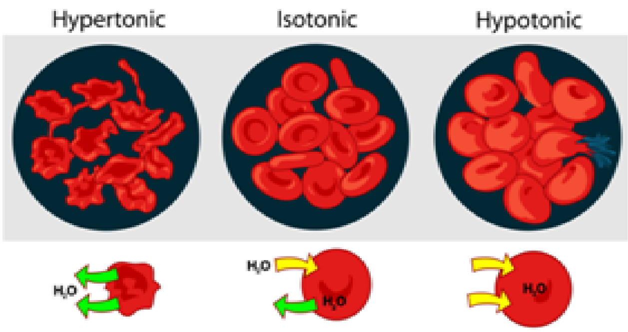
The biconcave shape of RBC gives an increased surface area, allowing the cell to contain more Hb. The small size and large surface area both increase the rate of diffusion of O_2 and CO_2. The reddish colour of RBC's is derived from Hb. The protein globin (containing 4 polypeptide chains) combines with haem, which contains an iron atom. One O_2 molecule binds to each iron atom. Therefore, each haemoglobin molecule can bind $4O_2$ molecules. Cell shape is maintained by a protein cytoskeleton. RBC's are very flexible and can squeeze through minute gaps, such as capillary walls.

Functions of RBC: RBC's carries O_2 from the lungs and transports it to cells through the body. In a reversible process Hb binds O_2 in the lungs to form oxyhaemoglobin, which is taken to the cells where it gives up it's O_2. Haemoglobin also carries CO_2 from the cells, which is returned to the lungs. 95% of CO_2 generated is carried by RBC's (containing the enzyme carbon anhydrase to speed up the process). About 5% of CO_2 is dissolved in blood plasma. If all CO_2 were carried this way the blood pH would drop to an instantly fatal 4.5. It is essential that blood pH is maintained, and Hb acts as a powerful buffer in maintaining a pH of about 7.4.

Stability of RBC: The stability of RBC is very essential in blood stream. The RBC stabilization depends on its movement in capillaries. During passage through the circulation the RBC which has 7 to 8 microns in diameter must elongate otherwise deformed. If the RBC enters 3 micron diameter capillaries or it may enter endothelial sites having 1 micron diameter. Then more deformity occurs and stability lost. The stabilization is very essential in all this conditions. During 120 days life span it must undergo deformation however the stability of RBC is maintained until it dies.

Hypertonic solution or Hypertonicicty: When the osmotic pressure of the solution outside the blood cells is higher than the osmotic pressure inside the red blood cells, the solution is hypertonic. The water inside the blood cells exits the cells in an attempt to equalize the osmotic pressure, causing the cells to shrink.

Isotonic solution or Isotonicity: When the osmotic pressure outside the red blood cells is the same as the pressure inside the cells, the solution is isotonic with respect to the cytoplasm. This is the usual condition of red blood cells in plasma. The cells are normal.



The effect of osmotic pressure on red blood cells. From left to right, the effect is depicted of a hypertonic, isotonic, and hypotonic solution on red blood cells.

Hypotonic solution or Hypotonicity: When the solution outside of the red blood cells has a lower osmotic pressure than the cytoplasm of the red blood cells, the solution is hypotonic with respect to the cells. The cells take in water in an attempt to equalize the osmotic pressure, causing them to swell and potentially burst.

The red cell "skeleton": The lipid bilayer is stabilised by a protein framework on the inside of the cell. This is the most important factor in RBC stabilization, which is regulated by the membrane property that is elasticity, different modules of RBC like bending module etc. The "**skeleton**" is made of **spectrin**, an asymmetric two-chained molecule which is attached to the inside of the cell wall by other proteins including **actin** and **ankyrin**. The ankyrin binds to an integral protein and the actin to a peripheral protein. Spectrin gives the cell membrane its flexibility and strength. The red cell distorts as it passes through tiny capillaries, but once through the capillary, it immediately returns to its biconcave shape. If spectrin is denatured, e.g. by heat, the red cell assumes a spherical shape and loses its flexibility (spherocytosis).

2.4 WBC TYPES AND FUNCTIONS: The WBC also called as Leucocytes. The white blood cells are mainly two types.

(1) Granulocytes and (2) Agranulocytes or Mono nuclear cells without granules. WBCs are totally 5 types. The granulocytes are of three types 1) Neutrophils (60 to 70%) (2) Eosinophils (1 to 4%) (3) Basophils (0.1 to 1 %). The Agranulocytes are of two types (1) Lymphocytes (2) Small lymphocytes.

Neutrophils: Neutrophils contain very fine cytoplasmic granules. They are also called as polymorphonuclear (PMN) cells, because they have a variety of nuclear shapes. The most important function of neutrophils is phagocytosis. Neutrophils kill the bacteria by phagocytosis.

Type of WBC	% by volume of WBC	Description	Function
Neutrophils	60 – 70 %	Nucleus has many interconnected lobes; blue granules	Phagocytize and destory bacteria; most numerous WBC
Eosinophils	2 – 4 %	Nucleus has bilobed nuclei; red or yellow granules containing digestive enzymes	Play a role in ending allergic reactions
Basophils	< 1 %	Bilobed nuclei hidden by large purple granules full of chemical mediators of inflammation	Function in inflammation medication; similar in function to mast cells
Lymphocytes (B Cells &T Cells)	20 – 25 %	Dense, purple staining, round nucleus; little cytoplasm	the most important cells of the immune system; effective in fighting infectious organisms; act against a specific foreign molecule (antigen)
Monocytes	4 – 8 %	Largest leukocyte; kidney shaped nucleus	Transform into macrophages; phagocytic cells

Eosinophils: Eosinophils made up of large granules and a prominent nucleus. They secrete histamine which increases tissue blood flow via dialating blood vessels and secret heparin which is a anticoagulant.

Basophils: Basophils have pale colored nucleus with hidden granules. They secrete histamine which increases tissue blood flow via dilating blood vessels and secrete heparin which is a anticoagulant.

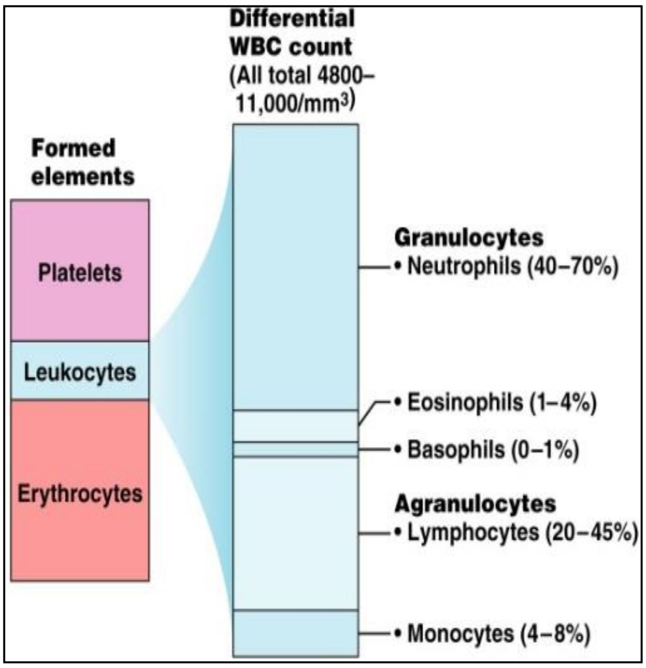
Agranulocytes or mononuclear cells:

Lymphocytes: They are divided into large and small lymphocyte. They help in destroying cancer cells, cells infected by viruses, stimulate cells of the immune system to secrete antibodies.

Monocytes: They are large in shape, their cytoplasm is abundant they are Macrophages. They phagocyte and digest pathogen and repair the tissues. They produce Antigens like lymphocytes.

Platelets and their functions: Platelets are also called thrombocytes. Unlike red and white blood cells, platelets are not actually cells but rather small fragments of bone marrow cells. Platelets help the blood clotting process (or coagulation) by gathering at the site of an injury, sticking to the lining of the injured blood vessel, and forming a platform on which blood coagulation can occur. This results in the formation of a fibrin clot, which covers the wound and prevents blood from leaking out. Fibrin also forms the initial scaffolding upon which new tissue forms, thus promoting healing. Platelets also secrete vasoconstrictor and arrest haemorrhage, that is hemostasis. They aggregate to stop bleeding and secrete coagulants to promote clotting. Platelets also participate in destruction of bacteria.

.**Differential count:** Differential count is the percentage of each type of blood cell. It reveals normal as well as abnormal percentage of white cells in our blood. The differential white cells count is usually calculated by examination of the stained blood film and counting different white cells and expressed in percentage. A healthy adult result would be Neutrophil- 60%, Lymphocytes- 30%, Monocytes- 6%, Eosinophil- 3%, Basophils- 1%. In almost any illness may alter the total or differential white cell count. In differential count each cell count is significant for the blood defense activity. The Neutrophil count



signifies phagocytosis. Lymphocyte count signifies the activity related to defense mechanism. Eosinophil count is increased during allergy.

2.5 BLOOD PROTEINS/PLASMA PROTEINS: Plasma proteins also termed serum proteins, are proteins present in blood plasma. They serve many different functions, including transport of lipids, hormones, vitamins and metals in the circulatory system and the regulation of acellular activity and functioning and in the immune system. Other blood proteins act as enzymes, complement components, protease inhibitors or kinin precursors. Contrary to popular belief, hemoglobin is not a blood protein, as it is carried within the RBC, rather than in the blood serum. Serum albumin accounts for 55% of blood proteins, and is a major contributor to maintaining the osmotic pressure of plasma to assist in the transport of lipids and steroid hormones. Globulins make up 38% of blood proteins and transport ions, hormones and lipids assisting in immune function. Fibrinogen comprises 7% of blood proteins; conversion of fibrinogen to insoluble fibrin is essential for blood clotting. The remainder of plasma proteins (1%) is made up of regulatory proteins such as enzymes, proenzymes and hormones. All blood proteins are synthesized in liver except for the gamma globulins. Separating serum proteins by electrophoresis is a valuable diagnostic tool as well as a way to monitor plasma proteins in normal and clinical conditions.

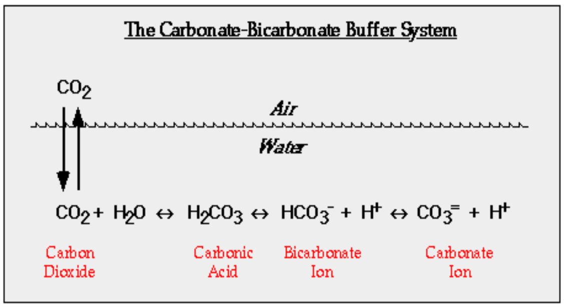
Blood proteins	**Normal level**	**%**	**Functions**
Albumins	3.5-5.0 gm/dl	55 %	Maintain colloid osmotic pressure, Create oncotic pressure and transport insoluble molecules
Globulins	2.0-2.5gm/dl	38%	Participate in immune system
Fibrinogen	0.2-0.45gm/dl	7%	Blood coagulation
Regulatory proteins		<1 %	Regulation of gene expression
Clotting factors		<1 %	Conversion of fibrinogen into Fibrin

Biological buffering of blood/ Buffering systems of human body: There are three important buffer systems which are major contributors to regulating the pH of blood.

1. Bicarbonate buffer system
2. Phosphate buffer system
3. Protein buffer system

Blood pH must be kept close to 7.4. Hydrogen ion generated in the blood is extremely reactive and effects many molecules which regulate physiological processes. Blood pH is set at a slightly alkaline level of 7.4 (pH 7.0 is neutral). A change of pH of 0.2 units in either direction is considered serious. Blood pHs below 6.9 or above 7.9 are usually fatal if they last for more than a short time. All three buffer systems work similarly, when these buffer systems are exposed to very acidic solution (free hydrogen ions) the base component of the buffer neutralize the excess hydrogen ions. And these buffer systems are exposed to strong base (lack free hydrogen ions), they donate their hydrogen ions to the solution neutralizing its basic nature. In other words, these buffer systems turn strong acids into weak acids and turn strong bases into weak bases.

1. Bicarbonate buffer system: The bicarbonate system is the most important and is controlled by the rate of respiration. Carbon dioxide in water reacts to form carbonic acid, CO_2 (g) <-> CO_2 (aq) + H_2O -> H_2CO_3 (Carbonic acid). The pKa of carbonic acid is 6.35. the pH of blood is 7.4 so the acid is greater than 1 pH away from the pKa and it is primarily dissociated to H_2CO_3 -> H^+ + HCO_3 (Bicarbonate) under physiological conditions the equilibrium for the first reaction is far to the left, and the combined pKa for the two reactions is 6.4. At first glance this does not look like a good buffer for blood. The buffering capacity is poor. To maintain a pH of 7.4 there would have to be a ratio of 11 to 1 of bicarbonate to carbon dioxide.



pH = 6.4 + Log $[HCO_3^-]/[CO_2]$

Because this is an open system, the CO_2 dissolved and the bicarbonate can rapidly change. Changes resulting in loss of carbonic acid are replaced by CO_2 dissolving - This is an open system. Normal concentration of carbon dioxide is 1.2 mM and bicarbonate is 15 mM.

2. Phosphate buffer system: Phosphate buffer system is a relatively unimportant buffer system when it comes to buffering the pH changes in the blood due to its low concentration of hydrogen phosphate and dihydrogen phosphate ions. However, when it comes to intracellular compartment and urine, the concentration of these two ions would be rather high and therefore its buffering capacity would also be at a higher level. The importance of phosphate buffer system can be illustrated with regard to the buffering action of urine. Thus, the phosphates promote holding of H+ in the urine and thereby eliminating the same via urine. At the same time, because of the phosphate effect, the kidneys are able to absorb the bicarbonates back into the body without dragging the H+ back in to the system. This allows the body to maintain a acid base balance, even in instances where the body produce higher concentration of H+ due to various reasons.

The nucleic acid and phosphoprotein break down yields phosphoric acid. Phosphoric acid is H_3PO_4, which changes pretty quickly into dihydrogen phosphate, or $H_2PO_4^-$. This dihydrogen phosphate is an excellent buffer, since it can react with a hydrogen ion and reform phosphoric acid, or it can give off another hydrogen ion and become monohydrogen phosphate, or HPO_4^{2-}. In extremely basic conditions, monohydrogen phosphate can even give up its remaining hydrogen ion.

The Phosphate Buffer System

$$H_3PO_4 \leftrightarrow H_2PO_4^{-1} + H^+ \leftrightarrow HPO_4^{-2} + H^+ \leftrightarrow PO_4^{-3} + H^+$$

If the $H_2PO_4^-$ is in an acidic solution, the above reactions go to the left, and if the $H_2PO_4^-$ is in a basic solution, the reactions above proceed to the right. Therefore, the phosphate buffer system can accept or donate hydrogen ions depending on the condition of the body.

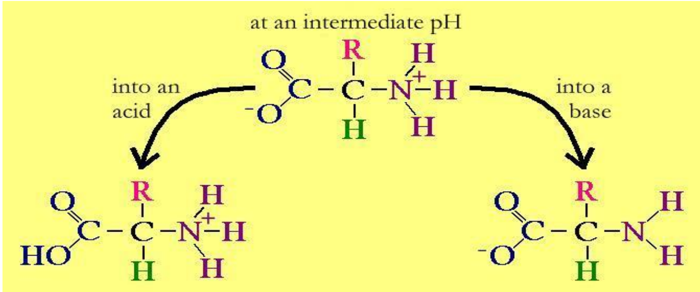
3. Protein buffer system

While bicarbonate buffer system accounts for most of the buffering in the extra-cellular compartment, protein buffer system contributes mainly to the intra-cellular buffering although it exerts extra-cellular buffering as well. As such, protein buffer system is also known as 'cellular buffering'. Among the intracellular protein buffers, hemoglobin is the main contributor while plasma proteins are the main sources of extracellular protein buffering. However, the buffering capacity of hemoglobin is around six times more than the buffering capacity of the plasma proteins. In addition, the deoxy form of hemoglobin is far more effective than its saturated oxyhemoglobin.

To understand in detail how proteins work as buffers, proteins are made up of amino acids. Amino acids have a central carbon with four groups:

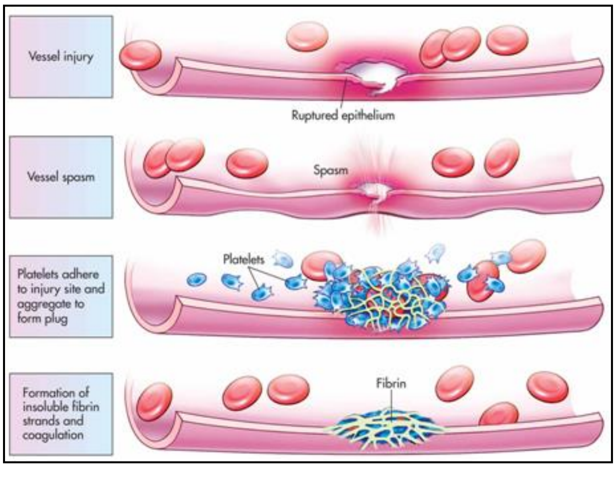
1. a carboxyl group (COOH)
2. an amino group (NH_2)

3. a hydrogen atom
4. an R group



The carboxyl and amino groups are what enable proteins to act as buffers. The carboxyl group at a near neutral pH, like the pH of blood, the carboxyl group is actually COO^- instead of COOH. At acidic pH, the carboxyl group will bind with extra hydrogen ions and return to the COOH configuration. Further the amino group, at a near neutral pH, like in blood, exists as NH_3^+ rather than just NH_2. It actually tends to carry an extra hydrogen ion on it at a normal pH. In a basic environment, its amino groups on its amino acids can actually release their hydrogen ions and return to NH_2. So amino acids can accept or donate hydrogen ions, making them excellent buffers. Any given protein typically has number of amino acids with their R group free to interact with the environment and they are found in very high concentration in intracellular solutions and in blood.

2.6 HAEMOSTASIS: The term Haemostasis means to stop the loss of blood. This Haemostasis mechanism occurs whenever a vessel is ruptured or damaged. There are three mechanisms that work together in the process of Hemostasis.



1) Vasoconstriction 2) Platelet aggregation or plug formation and 3) Clotting of blood. The vasoconstriction of a damaged blood vessel slows the flow of blood. This is initiated by vasoconstrictors such as thromboxane, at the site of injury and also epinephrine released by adrenal glands. The adrenaline stimulates general vasoconstriction. The formation of platelet plug is generated by platelets called thrombocytes. When a vessel is damaged the collagen fibers and platelets stick together. The clotting process (Hemostasis) is a vital process by which the body prevents blood loss is referred to as coagulation. Coagulation involves the formation of a blood clot (thrombus) that prevents further blood loss from damaged tissues, blood vessels or

organs. This is a complicated process with a cellular system comprised of cells called platelets that circulate in the blood and serve to form a platelet plug over damaged vessels and a second system based upon the actions of multiple proteins (called clotting factors) that act in concert to produce a fibrin clot.

These two systems work in concert to form a clot; disorders in either system can yield disorders that cause either too much or too little clotting. Platelets serve three primary functions: 1) sticking to the injured blood vessel (called platelet adherence), 2) attaching to other platelets to enlarge the forming plug (called platelet aggregation), and 3) providing support (molecules on the surface of platelets are required for many of the reactions) for the processes of the coagulation cascade. When a break in a blood vessel occurs, substances are exposed that normally are not in direct contact with the blood flow. These substances (primarily collagen and von Willebrand factor) allow the platelets to adhere to the broken surface. Once a platelet adheres to the surface, it releases chemicals that attract additional platelets to the damaged area, referred to as platelet aggregation. These two processes are the first responses to stop bleeding. The protein based system (the coagulation cascade) serves to stabilize the clot that has formed and further seal up the wound.

Clotting of blood: The blood contains 13 clotting factors. These factors are proteins in the blood not activated in healthy vessels. Whenever the vessels are damaged these factors are activated and they help in formation of clot. The clots are formed using fibrin, fibrinogen, thrombin, prothrombin in the presence of calcium. The fibrinogen activates fibrin. Prothrombin to thrombin. The platelets aggregate to form the clot.

2.7 BLOOD VOLUME, BLOOD PRESSURE AND ITS REGULATION: Blood volume is a measurement of the volume, or amount of space, that the blood takes up in a given person. This includes both red blood cells and plasma; it is not limited to one particular part of blood. Maintaining a normal volume of blood is very important as it carries oxygen and essential nutrients throughout the body. If a person loses too much blood because of a bleeding wound or because of inadequate blood cell synthesis, dangerously low blood pressure can result and may cause vital organs to receive inadequate amounts of oxygen and nutrients. The blood volume is regulated mainly by kidneys. The kidney regulates the amount of water and sodium lost through urine.

There are many different factors that affect blood volume from person to person. Females, on average, have less blood than males do, and the bodies of children tend to contain less than those of grown men or women. Most people have roughly 1.2 gallons (4.7 litres) of blood in their bodies. Blood makes up approximately 1/11 of human body weight. People who live at high altitudes tend to have a higher volume because there is less oxygen in the air; the extra blood is needed to carry additional oxygen throughout the body.

2.7.1 Blood pressure: Blood pressure is a measurement of the force of blood against the arterial walls when the heart pumps. Sometimes, it is also referred to as arterial blood pressure, and is one of the principal vital signs. During each heart beat, blood pressure varies between a maximum (systolic) and a minimum (diastolic) pressure. Differences in mean blood pressure are responsible for blood flow from one location to another in the circulation. The rate of mean blood flow depends on the resistance to flow presented by the blood vessels. Mean blood pressure decreases as the circulating blood moves away from the heart through arteries and capillaries due to viscous losses of energy. Mean blood pressure drops over the whole circulation, although most of the fall occurs along the small arteries and arterioles. Gravity affects blood pressure via hydrostatic forces, and the valves in veins, breathing and pumping from contraction of skeletal muscles also influence blood pressure in veins.

Arterial pressure is most commonly measured via a sphygmomanometer, which historically uses the height of a column of mercury to reflect the circulating pressure. The measurement of blood pressure is done at a person's upper arm and is the measure of the pressure in the bronchial artery, the major artery in the upper arm. Blood pressure is measured in millimeters of mercury (mmHg) and is expressed as two numbers. For example, the optimal blood pressure for an adult is 120 over 80, or 120/80. The top number, called the systolic pressure, measures the highest pressure exerted when the heart contracts. The bottom number, called the diastolic pressure, shows the minimum pressure against the arteries when the heart rests between beats. The blood pressure depends on volume of blood in our body. Depending on the body size, and change of vascular resistance the load on the heart varies in order to pump the blood for circulation. The blood pressure therefore depends on 1) Blood volume 2) vessel resistance (artery, vein) or elasticity of vessel or dilation and contractibility of vessel. and 3) Cardiac output.

Blood pressure varies in healthy people and animals, but its variation is under control by the nervous and endocrine systems. Blood pressure that is pathologically low is called hypotension, and that which is pathologically high is hypertension. Both have many causes and can range from mild to severe.

Classification of blood pressure for adults		
Category	Systolic (mmHg)	Diastolic (mmHg)
Hypertension	< 90	<60
Desired/ Normal	90-119	60-79
Pre-hypertension	120-139	80-89
Stage 1: Hypertension	140-159	90-99
Stage 2: Hypertension	160-179	100-109
Hypertension levels	≥ 180	≥ 110

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

1. *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. 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 total peripheral resistance. The most important arterial baroreceptors are located in the left and right carotid sinuses and in the aortic arch.

2. *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.

3. *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.

4. 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 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. Currently, the RAS is targeted pharmacologically by ACE inhibitors and angiotensin II receptor antagonists. The aldosterone system is directly targeted by spironolactone an aldosterone antagonist. The fluid retention may be targeted by diuretics; the antihypertensive effect of diuretics is due to its effect on blood volume. Generally, the baroreceptor reflex is not targeted in hypertension because if blocked, individuals may suffer from orthostatic hypotension and fainting.

2.7.3 Blood coagulation/ Blood clotting: When blood is shed, it loses its fluidity within few minutes and sets into a semisolid jelly called clot. This phenomenon of formation of clot is called as coagulation or clotting of blood. The clot gradually retracts and a fluid separates out, called serum. Blood coagulation is a property of plasma, RBC, WBC, do not directly take part in clotting process but get caught up in the meshes of the clot. Blood platelets play important role in coagulation.

2.7.4 Significance of blood coagulation: The phenomenon of coagulation is of enormous physiological importance as it prevents further haemorrhage. When bleeding occurs, the shed blood coagulates and the bleeding vessel is plugged off by the clot. The retraction of clot, compresses the ruptured vessel further and bleeding stops.

Mechanism of blood coagulation: Coagulation of blood is a complicated process in which about 13 coagulation factors are involved. All these factors are blood proteins or their derivatives. Even if one of the factors is defective, the whole clotting process is impaired leading to haemorrhage. These factors are from F-I to F-XIII. Clotting mechanism begins by Trauma to tissues or trauma to blood. In each case it leads to formation of prothrombin activator which causes conversion of prothrombin in to thrombin. There are two pathways of formation of prothrombin activator:

i) Extrinsic Pathway: It begins with trauma to vascular wall or to the tissues outside the blood vessel.

ii) Intrinsic pathway: It begins with trauma to blood itself.

In both pathways, different blood clotting factors play important roles. Davie and Ratnoff (1965) have proposed a waterfall sequence hypothesis to explain the events taking place in coagulation process. Whereas Macfarlane has suggested a scheme of coagulation called enzyme cascade which is similar to waterfall sequence. Blood clotting factors exist in inactive form and are activated sequentially until finally prothrombin activator is formed.

Extrinsic pathway: Mechanism of Extrinsic pathway for formation of prothrombin activator includes number of steps.

1) It begins with trauma to blood vessel or tissues outside the blood vessel. It releases tissue factor and Tissue phospholipids and clotting process starts.

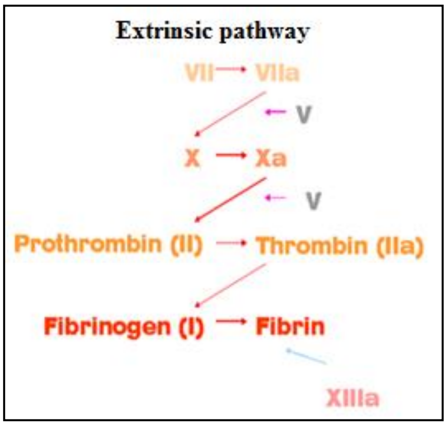
2) The tissue factor complexes with blood clotting factor VII and activates it.

3) Activated factor VII in presence of Ca^{2+} and tissue phospholipids acts on factor –X and activates it.

4) Activated factor X acts on Factor V and activates it.

5) Activated F-X complexes with tissue phospholipids, Factor-V, Ca^{2+} and forms a complex called prothrombin activator.

6) Prothrombin activator converts prothrombin in to thrombin under influence of Ca^{2+}



7) Thrombin acts on fibrinogen and converts it in to fibrin monomers

8) Fibrin monomers polymerize with other fibrin monomers and form long fibrin threads that form reticulum of the clot.

9) At first clot is weak but later on with the help of active fibrin stabilizing factor (F- X III) clot becomes strong.

10) WBCs and RBCs get trapped into reticulum of the clot

11) Clots adhere to the damaged surface of the blood vessel and thereby prevent the blood loss.

12) Clot retraction following clot formation, the volume of the clot decreases, this is called as clot retraction platelets are necessary for clot retraction, contain contractile protein Thrombosthenin, which contracts and reduces the volume of the clot. Following this a clear fluid is separated out called as serum.

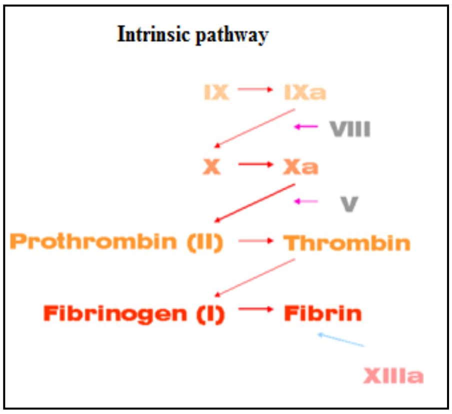
Intrinsic pathway: Intrinsic Mechanism begins with injury to blood itself and continues through following steps (F-III, F-XII-F-XI-F-IX-FVIII-F-X-F-V)

1) Trauma to blood alters two important clotting factors in the blood Factor XII and Platelet Phospholipids i.e. F- III

2) When F-XII comes in contact with collagen outside the blood vessel, it gets activated and acts as an enzyme for activation of F-XI

3) Damaged platelets adhere to the wet surface of blood vessel and release platelet phospholipids i.e. F- III.

4) Activated factor XII acts enzymatically on F-XI i.e. Plasma Thromboplastin Antecedent (PTA –Factor) and activates it.



5) Activated factor XI acts enzymatically on F- IX i.e. Christmas factor and activates it (Ca^{2+} are nessessory)

6) Factor IX activates F-VIII (Anti Haemophilic Factor)

7) Activated F-IX, F-VIII and platelet phospholipids,activate factor-X.

8) Activated Factor X acts enzymatically on Factor V (Proaccelarin) and activates it, (Ca^{2+} are nessessory).

9) Activated F-V, activated X, Platelet phospholipids and ca++ form a complex called prothrombin activator Prothrombin activator converts prothrombin in to thrombin under influence of Ca^{2+}

10) Thrombin acts on fibrinogen and converts it in to fibrin monomers

11) Fibrin monomers polymerize with other fibrin monomers and form long fibrin threads that form reticulum of the clot.

12) At first clot is weak but later on with the help of active fibrin

12) At first clot is weak but later on with the help of active fibrin stabilizing factor (F- X III) clot becomes strong.

13) WBCs and RBCs get trapped in to reticulum of the clot

14) Clots adhere to the damaged surface of the blood vessel and thereby prevent the blood loss.

Failure of clotting mechanisms: Blood fails to clot due to following defects:-

1) Lack of Fibrinogen i.e. Factor–I: Blood fails to clot due to absence of protein Fibrinogen. In a rare congenital disease fibrinogen is lacking in the blood causing fibrinogenopenia. Such condition also occurs in abnormal pregnancy.

2) Diminution of Prothrombin or Factor-II: Prothrombin is produced in liver so in liver diseases like cirrhosis of liver, cancer of liver etc. There is diminution of synthesis of prothrombin in the liver. Vitamin K helps in formation of prothrombin in liver. And it is absorbed from small intestine in presence of bile salts. In liver diseases like obstructive jaundice, liver cirrhosis etc. secretion of bile salts is affected and in absence of bile salts Vitamin K is not absorbed. Due to this synthesis of prothrombin and proaccelarin i.e. Factor V is decreased and clotting is affected.

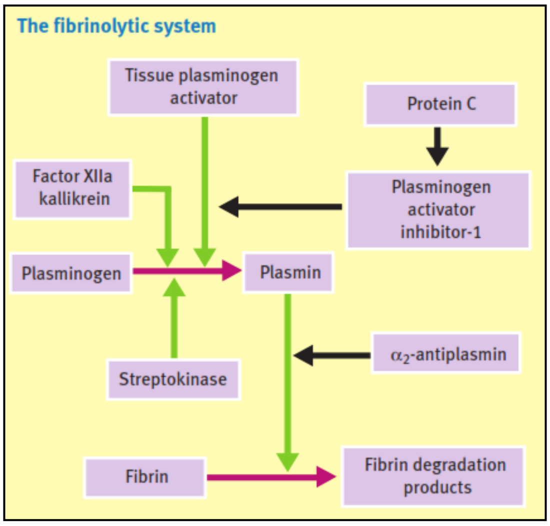
3) Due to lack of antihaemophilic Factor i.e. Factor VIII (Haemophilia A) in blood, person suffers from disease haemophilia in which blood fails to clot. Haemophilia is a hereditary disease which occurs in males but is transmitted through females. In this disease clotting time is abnormally prolonged. Patient shows tendency to bleed. Haemophilic person dies very early in life due to repeated hemorrhage.

4) Due to diminuation of Factor V, VII, IX (Haemophilia B) XI (Haemophilia C) in blood person shows pseudohaemophilia and develops a tendency to bleed.

5) Thrombocytopenia means presence of very low quantities of platelets in the circulatory system. Blood fails to coagulate. Bleeding occurs from small capillaries therefore there is haemorrhage all over the body. Person displays thrombocytic purpura. Platelets are important in repairing minute capillaries. They aggregate and plug small bleeding vessels. Normal count of platelets 200000 to 400000 Cm^3 when count falls below 50000 Cm^3 blood coagulation is affected.

6) Vitamin K deficiency: Vitamin K is necessary for some intermediate stages in formation of clotting factor. It is continuously synthesized in the gastrointestinal tract by bacteria and absorbed in blood along with fat. Vitamin K defficiency occurs due to poor absorption of fat by gastrointestinal tract. In liver diseases bile production is decreased hence fat digestion is affected which in turn affects absorption of vitamin K.

2.7.5 Digestion of clot or Fibrinolysis: Fibrinolyis (the dissolution of fibrin) also occurs, through the action of plasmin, which degrades fibrin and fibrinogen into fibrin-degradation products. Plasmin is present in plasma as an inactive precursor, plasminogen. Its conversion to plasmin is brought about primarily by tissue-type



plasminogen activator (t-PA), a protein released from endothelium, in addition to limited conversion by factor XIIa and kallikrein. Bradykinin is a powerful stimulator of t-PA release, whereas the activity of t-PA is inhibited in plasma due to the presence of plasminogen activator inhibitor-1 (PAI-1). However, this inhibitor is itself inhibited by activated protein C. Thus activated protein C stimulates fibrinolysis. The action of plasmin is limited to the site of the clot since any plasmin free in plasma is inactivated by the enzyme α_2-antiplasmin found in blood.

2.8 ANTICOAGULANTS: Substances which prevent coagulation of blood are called as anticoagulants. Richard Lewshan discovered anticoagulants in 1914, discovered that, Blood remains in fluid state when mixed with citrate solution. This lead to opening of blood banks during 1st world war. There are four types of substances which prevent coagulation of blood. These are:

1. Natural anticoagulants
2. Anticoagulants used in blood banks (A.C.D. and C.P.D.)
3. Anticoagulants used in laboratory
4. Therapeutic anticoagulants.

1. Natural Anticoagulants: These are present within the body hence the name natural anticoagulants. They keep the blood in fluid state in the vessels. Physical characteristic of endothelium of blood vessel and Smoothness of the vascular Endothelium prevents contact activation of the intrinsic clotting mechanism. As soon as endothelium of blood vessel is damaged, the clotting mechanism is initiated.

Monomolecular layer of negatively charged proteins absorbed on the inner surface of the endothelium repels the clotting factors and blood platelets and prevent clotting. As soon as the endothelium of the blood vessel is damaged, its smoothness and negative charge are lost and intrinsic pathway is activated.

Antithrombin III: This is normally present in the blood. Antithrombin III inhibits the activation of IX, X, XI, XII factors. Antithrombin III action is facilitated by heparin. Its deficiency leads to venous thrombosis.

Heparin: To maintain blood in a fluid state in blood vessels, blood contains an anticoagulant called as heparin. It is a powerful anticoagulant but has short duration of activity. It is secreted by the basophil or mast cells. These cells contain granules which are supposed to be the precursor of heparin Heparin helps to maintain the normal fluidity of the blood. It inhibits transformation of prothrombin in to thrombin.

Protein 'C': Thrombin in combination with thrombomodulin (protein present in plasma) activates protein C which inhibit activated factor VIII and V.

α-2 macroglobulin: is a large globulin molecule. This also has anticoagulant property. It acts as binding agent for coagulation factors until they are destroyed.

Fibrin threads: 85 to 90% thrombin formed from prothrombin is absorbed on fibrin threads and thus they prevent spreading thrombin into remaining blood and prevent excessive spread of blood clot.

Antithrombin heparin co-factor: also acts as anticoagulant. Thrombin which does not get absorbed on fibrin threads combines with co-factor and get inactivated.

Fibrinolytic System: exists in body which brings about clot lysis. Small clots are immediately lysed by this system. Plasminogen co precipitates with fibrin as plasmin. When activated the plasmin in clots digest the fibrin into soluble fragments dissolving the clots.

2. Anticoagulants used in Blood banks:

a) Acid citrate Dextrose (ACD): It forms a complex with Ca^{2+} and decreases its level.

b) Citrate Phosphate Dextrose (CPD): Mechanism is similar to ACD. CPD is better than ACD as the O_2 transport function is better preserved by CPD.

c) CPD is added to collected blood to store the blood up to 14 days. It binds with plasma Ca ions.

3. Anticoagulants used in Laboratory:

In laboratory Citrate or oxalate of Na (3.8%) or potassium (3%), 0.3% Sodium Fluride, EDTA are used as Anticoagulants for various investigations like ESR, Blood urea etc. By adding various salt solutions like $1/4^{th}$ of the blood volume of magnesium sulfate or equal volume of half saturated Sodium sulfate solution, clotting is prevented.

4. Therapeutic anticoagulants:

These substances are used to prevent thrombus formation in vivo.

a) Heparin: given intravenously

b) Dicoumarol: It is a synthetic product. Patients with hyper coagulity are given this anticoagulant for preventing the formation of thrombus. It prevents synthesis of clotting factors mainly prothrombin as it is antagonistic to Vitamin K

c) Thrombin is sprayed on the bleeding surfaces along with fibrinogen to arrest the bleeding.

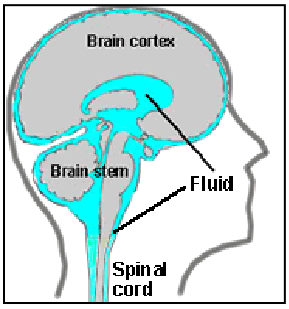
d) Foam of fibrin can be spread on the bleeding surface.

e) Sodium alginate when comes in contact with blood it is converted in to calcium alginate which clots and forms tenacious layer thus prevent bleeding.

f) Cellulose gauze made up of oxidized cellulose swells when socked with blood and prevents further bleeding.

Some other substances of biological origin which also serve as anticoagulants are, Protamine a simple protein found in fish. Peptones when injected into veins stop coagulation. Extract of cray fish and mussels (Sea clam) increase the secretion of heparin by mast cells hence prevents coagulation of blood. Hirudin is a naturally occurring peptide in the salivary glands of leeches that have a blood anticoagulant property. Venom of certain snakes inhibits activation of prothrombin and thrombin fibrinogen reaction. Azodyes, synthetic products like Chicago blue, trypan red, trypan blue can also act as anticoagulants.

2.9 CEREBROSPINAL FLUID (CSF): It is formed by the choroid plexus and secreted into the lateral ventricle from where it enters the third and fourth ventricles and is finally absorbed through the subarachnoid space. Its volume is about 5 ml in the new born and reaches 100 to 150 ml in the adult.



Under normal conditions, secretion of CSF is slow and may not exceed 100-150 ml a day. If a lumbar puncture is performed with the subject in the reclining (horizontal) position, the fluid exerts the same pressure as on cisternal puncture and is about 110-130mm water (Ringer saline) or 7-10mm mercury. Composition of the jugular vein causes a rise in the CSF pressure.

The main function of CSF is to provide a protective water jacket around the brain and spinal cord, and to enable alteration in the volume of these viscera without causing their compression in the rigid bony encasement. Other functions like nutrition and excretion are only incidental.

Composition of CSF: It can be considered to be an ultrafiltrate of the plasma. Protein is present only in trace amounts. Lipids and bilirubin are absent. Glucose, urea and other organic constituents have about the same concentration as in plasma; pH is also same as in plasma. The calcium concentration is that of the diffusible portion in plasma (2.3-2.8 m.eq/litre). The concentration of sodium and chloride are determined by the Donnan membrane equilibrium phenomenon and are somewhat higher than in plasma. The magnesium level is nearly double that in plasma; potassium an inorganic phosphate, a little more than one half. The concentration of the more important constituents of CSF are presented and compared with those of serum in the table below.

Concentration of Constituents in cerebrospinal fluid and in serum of normal persons

Constituent	Serum	CSF
Glucose, mg/ 100ml	55-80	55-80
Urea nitrogen, mg/100ml	6-23	6-23
Non-protein nitrogen, mg/100ml	20-30	20-30
Uric acid, mg/100ml	3-5	0.6-0.7
Protein, mg/100ml	6500-8500	20-30
Bilirubin, mg/100ml	0.2-1.0	0.0
Sodium, m. eq/litre	138-148	142-150
Potassium, m. eq/litre	4.5-5.5	2.3-3.2
Magnesium, m. eq/litre	1.6-2.1	2.5-3.0
Calcium, m. eq/litre	4.8-5.2	2.3-2.8
Chloride, m. eq/litre	100-110	120-130
Bicarbonate, m. eq/litre	24-29	24-29
pH	7.4	7.4

The final composition of the CSF is dependent on two factors-

1) Secretion of an ultrafiltrate by the choroid plexus and 2) Addition and removal of constituents by meninges and nervous tissue. The prolonged contact with the meninges and the nervous tissues results in profound alterations in the secretion. Glucose, amino acids, phosphate and potassium are all taken up and magnesium is added.

Absorption of CSF into the bloodstream takes place in the superior sagittal sinus through structures called arachnoid villi. When the CSF pressure is greater than the venous pressure, CSF will flow into the bloodstream. However, the arachnoid villi act as one-way valves: if the CSF pressure is less than the venous pressure, the arachnoid villi will not let blood pass into the ventricular system.

Functions of the CSF include:

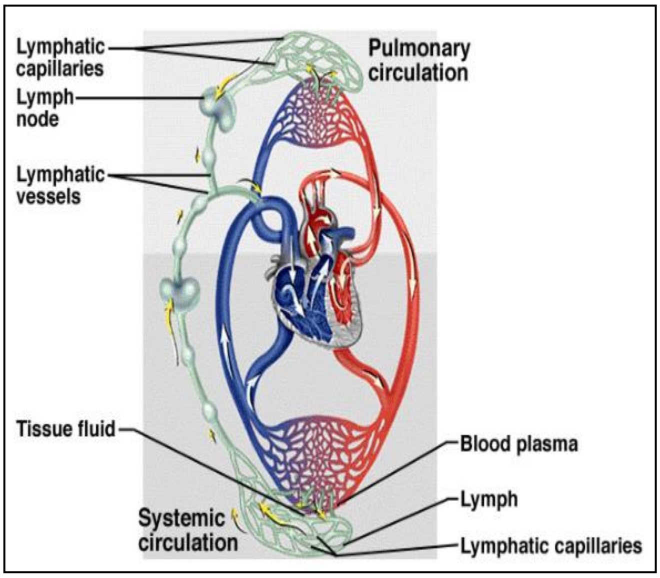
Protection: The CSF protects the brain from damage by "buffering" the brain. In other words, the CSF acts to cushion a blow to the head and lessen the impact.

Buoyancy: Because the brain is immersed in fluid, the net weight of the brain is reduced from about 1400gm to about 50gm. Therefore, pressure at the base of the brain is reduced.

Excretion of waste products: The one-way flow from the CSF to the blood takes potentially harmful metabolites, drugs and other substances away from the brain.

Endocrine medium for the brain: The CSF serves to transport hormones to other areas of the brain. Hormones released into the CSF can be carried to remote sites of the brain where they may act.

2.10 LYMPH: Arterial blood carries oxygen, nutrients, and hormones for the cells. To reach these cells it leaves the small arteries and flows into the tissues. This fluid is now known as *interstitial fluid* and it delivers its nourishing products to the cells. Then it leaves the cell and removes waste products. After this task is complete, 90% of this fluid returns to the circulatory system as venous blood. The remaining 10% of the fluid that stays behind in the tissues as a clear to yellowish fluid is known as lymph. The interstitial fluid is collected by



lymph capillaries which empty ultimately into the thoracic duct and right lymphatic duct which join the left and right subclavian veins and thus enter the systemic circulation. The daily lymph flow appears to be 1 to 2 litres in the human adult. Diffusible non-electrolytes like urea and glucose have the same concentration as in plasma. Diffusible non-electrolytes like K^+, Na^+, Cl^- and HCO_3^- tend to be somewhat higher than in plasma. This is on account of the lower protein content of lymph which creates Donnan effect. The protein content of lymph varies with the location from which lymph is collected. It is highest in lymphatics of liver (about 6.0 gm%) and lowest in subcutaneous lymphatics (0.25gm%). It averages about 3% in thoracic duct. The albumin/globulin ratio is much higher than in plasma. The lymph is protein-rich due to the undigested proteins that were removed from the cells.

Unlike blood, which flows throughout the body in a continue loop, lymph flows in only one direction within its own system. This flow is only upward toward the neck. Here, it flows into the venous blood stream through the subclavien veins which are located on either sides of the neck near the collarbones.

Main functions of lymphatic system:

- The lymphatic system aids the immune system in removing and destroying waste, debris, dead blood cells, pathogens, toxins, and cancer cells.
- The lymphatic system absorbs fats and fat-soluble vitamins from the digestive system and delivers these nutrients to the cells of the body where they are used by the cells.
- The lymphatic system also removes excess fluid, and waste products from the interstitial spaces between the cells.

2.10.1 Lymphatic circulation: The lymph is moved through the body in its own vessels making a one-way journey from the interstitial spaces to the subclavian veins at the base of the neck.

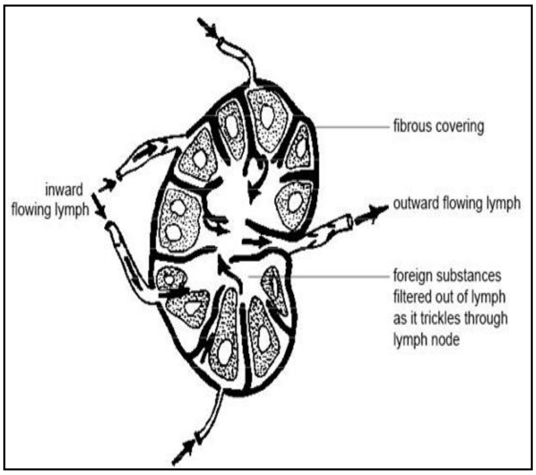
- Since the lymphatic system does not have a heart to pump it, its upward movement depends on the motions of the muscle and joint pumps.
- As it moves upward toward the neck the lymph passes through lymph nodes which filter it to remove debris and pathogens.
- The cleansed lymph continues to travel in only one direction, which is upward toward the neck.
- At the base of the neck, the cleansed lymph flows into the *subclavian veins* on either side of the neck.

2.10.2 Lymphatic capillaries: In order to leave the tissues, the lymph must enter the lymphatic system through specialized lymphatic capillaries. Approximately 70% of these are *superficial capillaries* located near, or just under, the skin. The remaining 30%, which are known as *deep lymphatic capillaries*, surround most of the body's organs. Lymphatic capillaries begin as blind-ended tubes that are only a single cell in thickness. These cells are arranged in a slightly overlapping pattern, much like the shingles on a roof. Each of these individual cells is fastened to nearby tissues by an *anchoring filament*.

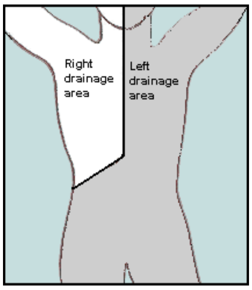
2.10.3 Lymphatic vessels: The lymphatic capillaries gradually join together to form a mesh-like network of tubes that are located deeper in the body.

- As they become larger, and deeper, these structures become lymphatic vessels.
- Deeper within the body the lymphatic vessels become progressively larger and are located near major blood veins.
- Like veins, the lymphatic vessels, which are known as lymphangions, have one-way valves to prevent any backward flow.
- Smooth muscles in the walls of the lymphatic vessels cause the angions to contract sequentially to aid the flow of lymph upward toward the thoracic region. Because of their shape, these vessels are previously referred to as a string of pearls.

2.10.4 Lymph node: There are between 600-700 lymph nodes present in the average human body. It is the role of these nodes to filter the lymph before it can be returned to the circulatory system. Although these nodes can increase or decrease in size throughout life, any nodes that has been damaged or destroyed does not regenerate.



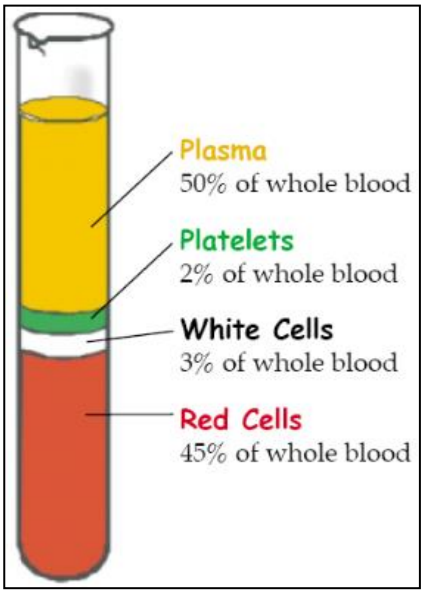
- *Afferent lymphatic vessels* carry unfiltered lymph into the node. Here waste products, and some of the fluid, are filtered out.
- In another section of the node, lymphocytes, which are specialized white blood cells, kill any pathogens that may be present. This causes the swelling commonly known as swollen glands.
- Lymph nodes also trap and destroy cancer cells to slow the spread of the cancer until they are overwhelmed by it.
- *Efferent lymphatic vessels* carry the filtered lymph out of the node so that it can continue its return to the circulatory system.



2.10.5 Drainage areas: Lymphatic system drainage is organized into two separate and very unequal drainage areas. The right drainage area clears the right arm and chest. The left drainage area clears all of the other areas of the body including both legs, the lower trunk upper left of the chest, and the left arm.

2.11 SUMMARY:

- Blood, which consists of cells and cell fragments suspended in an intercellular matrix, is one of the connective tissues in the body.
- Formed elements are the cellular components of the blood, and the liquid part is plasma. The plasma is the river in which the blood cells travel. It carries not only the blood cells but also nutrients (sugars, amino acids, fats, salts, minerals, etc.), waste products (CO_2, lactic acid, urea, etc.), antibodies, clotting proteins (called clotting factors), chemical messengers such as hormones, and proteins that help maintain the body's fluid balance.



- Blood is the primary transport medium that is responsible for continuously supplying nutrients and oxygen to the active cells in the body.
- The three activities of the blood are transportation, regulation, and protection.
- Erythrocytes are tiny biconcave disks, and their primary function is to transport oxygen and, to a lesser extent, carbon dioxide.
- In the tissue spaces leukocytes provide a defense against organisms that cause disease and either promote or inhibit inflammatory responses.
- Two main groups of leukocytes in the blood are granulocytes and agranulocytes; the cells that develop granules in the cytoplasm are called granulocytes, and those that do not have granules are called agranulocytes.
- Thrombocytes/ platelets become sticky and clump together to form platelet plugs that close breaks and tears in blood vessels. Platelets are fragments of a much larger cell, the megakaryocyte that stays in the bone marrow after it differentiates and matures from the stem cell. The platelets leave the bone marrow and circulate throughout the body. When stimulated by substances from damaged tissue, the platelets release substances necessary to help blood clot. This helps initiate the clotting sequence and protect the integrity of the vasculature.

- CSF is produced by choroid plexuses of the lateral, third and forth ventricles. It is a clear, colorless liquid, whose total volume is maintained at 80 ~ 150 mL. CSF, supports and cushions the CNS against trauma ("protective buffer"). Provides buoyancy; reduces momentum and acceleration. Removes waste products of metabolism and drugs/toxins ("blood/CSF barrier"). Integrates brain endocrine function i.e. hypothalamic releasing factors are secreted directly into the CSF and controls microenvironment of neurons and glial cells.
- Lymph is a clear to yellowish watery fluid that is found throughout the body. It circulates through body tissues picking up fats, bacteria, and other unwanted materials, and filtering them out through the lymphatic system. It is sometimes possible to see this fluid; cuts sometimes weep it rather than blood, for example. Its circulation through the body is an important part of immune system health.
- This fluid contains white blood cells, known as lymphocytes, along with a small concentration of red blood cells and proteins. It circulates freely through the body, bathing cells in needed nutrients and oxygen while it collects harmful materials for disposal. We can think of it as the milkman of the body, dropping off fresh supplies and picking up discarded containers for processing elsewhere.
- As lymph circulates, it is pulled into the lymphatic system, an extensive network of vessels and capillaries that is linked to lymph nodes, small nodules that act as filters to trap unwanted substances. The nodes also produce more white blood cells, refreshing the fluid before it is pumped back into the body. The fluid may not be as showy as blood, but it is related to an equally complex and ornate system of vessels.
- Lymph also explains why things like intramuscular shots at the doctor's office work. When a medical professional injects a substance into muscle tissue, it is picked up by the fluid and then slowly filtered into the bloodstream. When people wear tight clothing or their circulation is otherwise impeded, fluids can build up in the tissue, causing oedema, a condition that can be both painful and dangerous. Edema happens when lymph cannot circulate to pull these fluids out.

2.12 KEY WORDS: Blood Composition, Erythrocytes, White Blood Cells (WBC), Platelets, Blood Volume, Blood Pressure, Hemostasis, Blood Clotting, Anticoagulants, Cerebro Spinal Fluid, Lymph.

2.13 QUESTIONS FOR SELF STUDY:

1. Write in detail about the composition of blood
2. Write a note on the following :
    a) RBC b) WBC c) Platelets d) Plasma
3. Describe buffering actions of blood
4. What is blood pressure? How is blood pressure regulated?
5. Write in detail about a) Hemostasis b) Blood coagulation c) Intrinsic pathway d) Extrinsic pathway.
6. What are anticoagulants?
7. Explain the types of anticoagulants and their applications
8. What is CSF? Briefly explain its composition.
9. With the help of a diagram explain lymph and its functions.

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BC 1.3: PHYSIOLOGY AND NUTRITION

BLOCK-I: PHYSIOLOGY

UNIT 3: NERVOUS SYSTEM: TYPES OF NEURONS, BRAIN, SPINAL CORD AND TRANSMISSION OF IMPULSES.

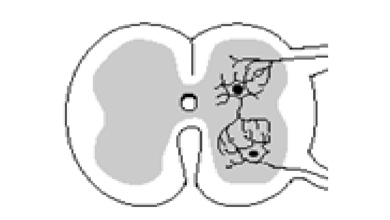
STRUCTURE OF THE UNIT

3.0 OBJECTIVES: After studying this unit thoroughly, you should be able to:

- Identify various parts of human nervous system.
- Describe different function of human brain and spinal cord.
- List out the parts of a neuron and its types.
- Understand how a nerve impulse is transmitted.

3.1 INTRODUCTION: We have studied about various organ systems of the human body in Unit 1 of this Block. We will study in detail about the nervous system in the present unit. The nervous system has three main functions: sensory input, integration of data and motor output. Sensory input is when the body gathers information or data, by way of neurons, glia and synapses. The nervous system is composed of excitable nerve cells (neurons) and synapses that form between the neurons and connect them to centres throughout the body or to other neurons. These neurons operate on excitation or inhibition. Although nerve cells can vary in size and location, their communication with one another determines their function. These nerves conduct impulses from sensory receptors to the brain and spinal cord. The data is then processed by way of integration of data, which occurs only in the brain. After the brain has processed the information, impulses are then conducted from the brain and spinal cord to muscles and glands, which are called motor output. Glia cells are found within tissues and are not excitable but help with myelination, ionic regulation and extracellular fluid.

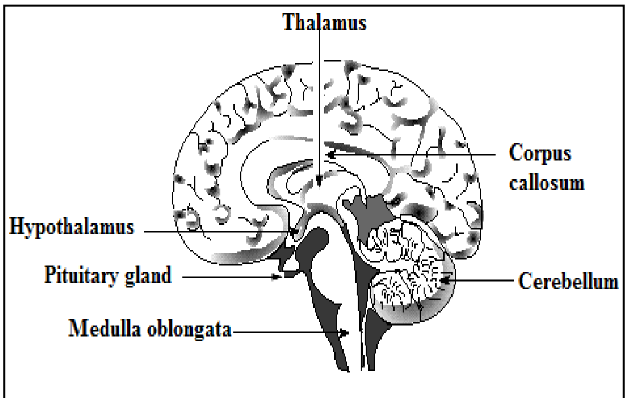
3.2 THE CENTRAL NERVOUS SYSTEM: The CNS consists of the brain and spinal cord, the CNS lies in the mid-line of the body and is the place where sensory information is received and motor control is initiated. Protected by bone (skull & vertebrae). They are also wrapped up in three protective membranes called meninges. Spaces between meninges are filled with cerebrospinal fluid for cushioning and protection. This fluid also found within central canal of the spinal cord and ventricle of brain.



Transverse section of spinal cord

SPINAL CORD: The nervous system's "superhighway" contains central canal filled with cerebrospinal fluid. The gray matter (inner layer) containing cell bodies of neurons and short fibers. Looks kind of like a butterfly with open wings. In grey matter, dorsal cell bodies function primarily in receiving sensory information, and ventral cell bodies send along primarily motor information. White matter (outer layer) containing long fibers of interneuron's that run together in bundles called tracts that connect the cord to the brain. Within white matter, ascending tracts take information to the brain; descending tracts in the ventral part carry information down from the brain.

THE BRAIN: The brain itself contains parts which function in the coordination of movement, sensing, and consciousness (and all that entails), as well as areas that are below the level of conscious control. The brain has a volume, on average, or 1,370 cubic centimetres (with a normal range of 950 to 2,200 cm^2). It weighs about 1.35 kg (or 3 pounds), and consists of hundreds of billions of neurons and glial cells. You had the maximum number of neurons when you were born. Thousands are lost daily, never to be replaced and apparently not missed, until the cumulative loss builds up in very old age. The brain is vastly complex, and is certainly not thoroughly understood. There are many ways of looking at the brain functionally and structurally. The simplest first way of looking at it is dividing it up into parts that run "automatically" (the unconscious brain) and the parts in which our consciousness resides (the conscious brain).



Parts of brain

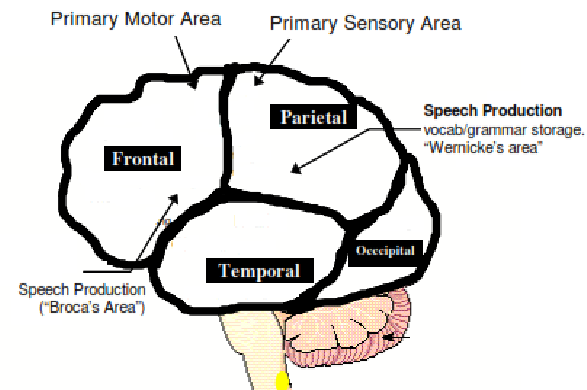
Medulla oblongata: Lies closest to spinal cord. Controls heart rate, breathing, blood pressure, reflex reactions like coughing, sneezing, vomiting, hiccoughing, and swallowing. **Thalamus:** Receives sensory information from all parts of the body and channels them to the cerebrum. It is the last portion of the brain for sensory input before the cerebrum. Serves as a central relay station for sensory impulses coming up spinal cord and other parts of brain to the cerebrum. Receives all sensory impulses (except for smell) and sends them to appropriate regions of the cortex for interpretation. The thalamus has connections to various parts of the brain, and is part of the RAS (the *reticular activating system*), which sorts out incoming stimuli, passing on to the cerebrum only those that require immediate attention. i.e. it lets you ignore input (like your teacher talking) so you can do other things. The RAS extends from the medulla oblongata to the thalamus.

Cerebellum: Controls balance and complex muscular movement. It is the *second largest portion of the brain.* Butterfly-shaped. Functions in *muscle coordination* and makes sure *skeletal muscles work together smoothly.* Responsible for maintaining normal muscle tone, posture and balance. It receives sensory information from the inner ear (which senses balance).

Hypothalamus: One of the most important sites for the regulation of homeostasis. It maintains internal environment, contains centres for hunger, sleep, thirst, body temperature, water balance, blood pressure etc. Controls pituitary gland (serves as a link between the nervous system and the endocrine systems). The hypothalamus plays a role in sexual response and mating behaviours, and the "fight-or-flight" response, and pleasure. Yes, there are *pleasure centers* in the hypothalamus (these have been stimulated experimentally with electrodes in studies using rats).

Corpus callosum: Horizontal connecting piece between the two hemispheres of the brain. Transmits information between the two cerebral hemispheres. It has been noted that severing the corpus callosum can control severe epilepsy (which is thought to be caused by a disturbance of the normal communication between the RAS and the cortex), but also means the two halves of brain don't communicate with each other normally and will function separately. Each half has its own memories and "style" of thinking. Sometimes you'll hear this discussed as "right brain" versus "left brain" thinking. The right hemisphere of the brain controls the left side of the body (except for smell), and vice versa. Thus, an image viewed with the right eye is actually "seen" with the left occipital lobe. The left hand is controlled by the right frontal lobe, and so on.

THE CEREBRUM: Largest, most prominent, most highly developed portion of the brain is also called the conscious brain since consciousness resides only in this part of the brain. The intellect, learning, memory, sensations are formed here. Outer layer is the cortex (gray in colour). It is the largest and most complex part of the human brain, and the part that has changed the most during vertebrate evolution. The highly folded human cortex has a surface area of about 0.5 m^2. Divided into right and left cerebral hemispheres, each consisting of four lobes: frontal, parietal, temporal, and occipital lobes. The fifth lobe called the insula, that lies below the surface. Its function is poorly understood. The cerebral cortex has been "mapped" in some detail. All the lobes have association areas that receive information from other lobes and integrate it into higher, more complex levels of consciousness. Association areas are concerned with intellect, artistic, and creative abilities, learning, and memory.



The Cerebrum

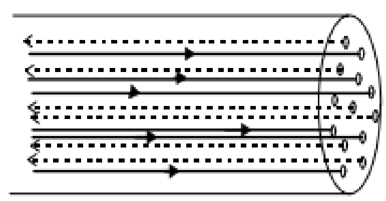
1. **FRONTAL:** Movement, higher intellectual processes (e.g. problem solving, concentration, planning, judging the consequences of behavior, moving your tongue and mouth to speak (left side only).

2. **PARIETAL:** Sensations, e.g. touch, temperature, pressure, pain. Understanding the speech, using words, communication skills etc.

3. **TEMPORAL:** Hearing, smelling, interpretation of experiences, memory of visual scenes, music, and complex sensory patterns.

4. **OCCIPITAL:** Vision, combining visual experiences with other sensory experiences.

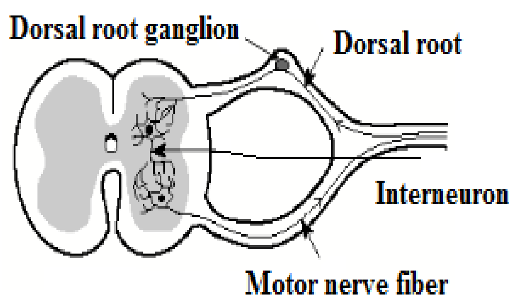
3.3 THE PERIPHERAL NERVOUS SYSTEM: Voluntary and involuntary control. The peripheral nervous system consists of nerves that contain only long dendrites and/or long axons. This is because neuron cell bodies are found only in the brain, spinal cord, and ganglia. Ganglia are collections of cell bodies within the PNS.


A mixed nerve

There are 3 types of nerves:

1. **Sensory nerves**: contain only long dendrites of sensory neurons.

2. **Motor nerves**: contain only the long axons of motor neurons.



3. **Mixed nerves**: contain both the long dendrites of sensory neurons and the long axons of motor neurons.

Humans have **12 pairs** of cranial nerves attached to the brain. Some are sensory, some are motor, and others are mixed. The cranial nerves are a part of the PNS. The cranial nerves serve the head, neck, and face regions except for the vagus nerve, which branches to serve internal organs. Humans have 31 pairs of Spinal Nerves. Spinal nerves are *mixed nerves* leaving the spinal cord by two short branches (called roots) which lie within the vertebral column. Of these, the dorsal root can be identified by the presence of an enlargement called the dorsal root ganglion, which contains the cell bodies of the sensory neurons whose dendrites conduct impulses toward the cord. The ventral root of each spinal nerve contains axons of motor neurons that conduct impulses away from the cord. The two roots join just before the spinal nerve leaves the vertebral column.

SOMATIC NERVOUS SYSTEM: Includes all the nerves that serve the musculoskeletal system and the exterior sense organs (including skin). Exterior sense organs are receptors (receive environmental stimuli and begin nerve impulses). Muscle fibers are effectors that react to the stimulus.

THE AUTONOMIC NERVOUS SYSTEM: Is part of the PNS - made of motor neurons that control the internal organs automatically (usually unconsciously). Autonomic nervous system is divided into sympathetic and parasympathetic nervous systems. These two systems connect to the same organs by have opposite effects. Each system functions unconsciously on internal organs and utilize two motor neurons and one ganglion for each nerve impulse.

SYMPATHETIC NERVOUS SYSTEM: Is especially important during emergency situations and is associated with "fight or flight" reaction. For example, in an emergency, it causes the following: energy directed away from digestion, pupils dilate, heart rate increases, perspiration increases, salivation decreases, breathing rate increases, the neurotransmitter released by the postganglionic axon of the Sympathetic nervous system is noradrenalin (which is closely related to adrenalin; a known heart stimulant). Noradrenalin is released by postganglionic axon; heart rate accelerates. Fibres for this system arise from middle part (thoracic-lumbar) of the spinal cord. Pre-ganglionic fibre is short, postganglionic fibre (which contacts the organ) is long.

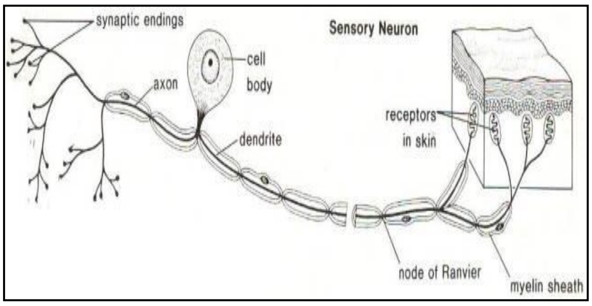
PARASYMPATHETIC NERVOUS SYSTEM: The parasympathetic system promotes all the internal responses associated with a relaxed state. For example: causes the pupils to contract, energy diverted for digestion of food, heart rate slows. Important neurotransmitter in this system is acetylcholine. Fibers for this system arise from upper and lower part of spinal cord (cranial and sacral nerves). Preganglionic fiber is long, postganglionic fiber is short because the ganglia lie near or within the organ.

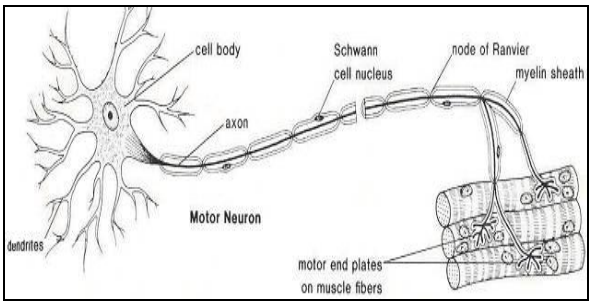
3.4 NEURONS: Nerve cells are called "Neurons". All neurons have three parts: i) dendrite (s) conduct nerve impulses towards the cell body. ii) cell body and iii) axon (conducts nerve impulses away from the cell body). Dendrites and axons are sometimes called fibers. Most long fibers are covered by a myelin sheath. The sheath has spaces in it exposing the axon called nodes of Ranvier. The sheath is secreted by Schwann cells, each of which has a nucleus.

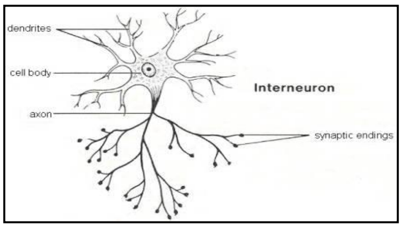
There are three types of neurons:

1. Sensory neuron: (=*afferent* neuron) takes a message from a sense organ to CNS. Has long dendrite and short axon**.**

2. Motor neuron: (=*efferent* neuron) takes message away from CNS to a muscle fiber or gland. Has short dendrites and long axon.



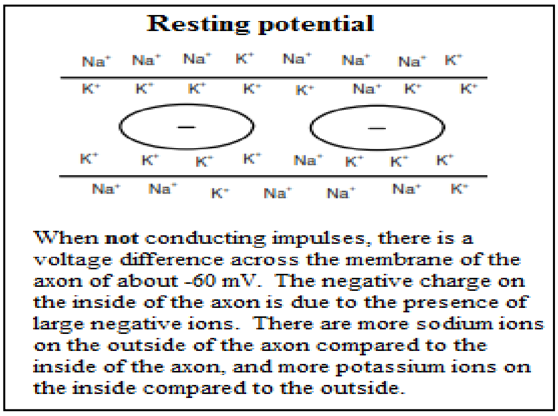




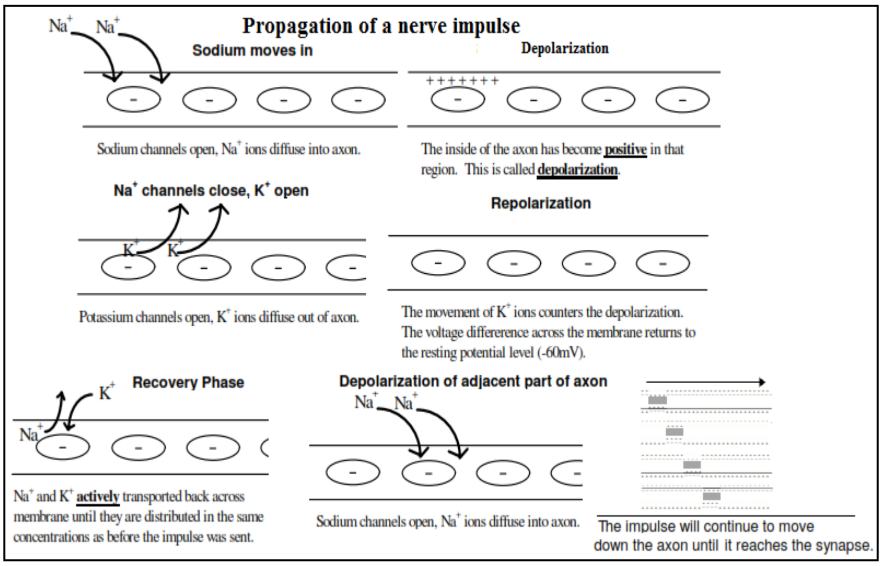
3. Interneuron: (= *association* neuron or *connector* neuron): Completely contained within CNS. Conveys messages between parts of the system. Dendrites and axons may be long or short.

3.5 GENERATION AND TRANSMISSION OF NERVE IMPULSES: Scientists used giant axons in squids to figure out how nerve impulses are generated. Nerve conduction is an electrochemical change that moves in one direction along the length of a nerve fiber. It is electrochemical because it involves changes in voltage as well as in the concentrations of certain ions. Since it is electric, we can use an oscilloscope (a type of voltmeter that shows a graph of voltage changes) to measure potential differences (voltages). There are three distinct phases in the generation of a nerve impulse along an axon: the resting phase and the action phase, followed by a recovery phase.

RESTING POTENTIAL: The potential difference across the membrane of the axon when it is not conducting an impulse is equals -60 mV. This negative polarity is caused by the presence of large organic negative ions in the axoplasm (the cytoplasm inside an axon). During the resting potential, Na^+ ions are more concentrated on the outside of the membrane than the inside. K^+ ions are more concentrated on the inside of the axon. This uneven distribution of K and Na ions is maintained by active transport across Na^+/K^+ pumps which operate whenever the neuron is not conducting an impulse.



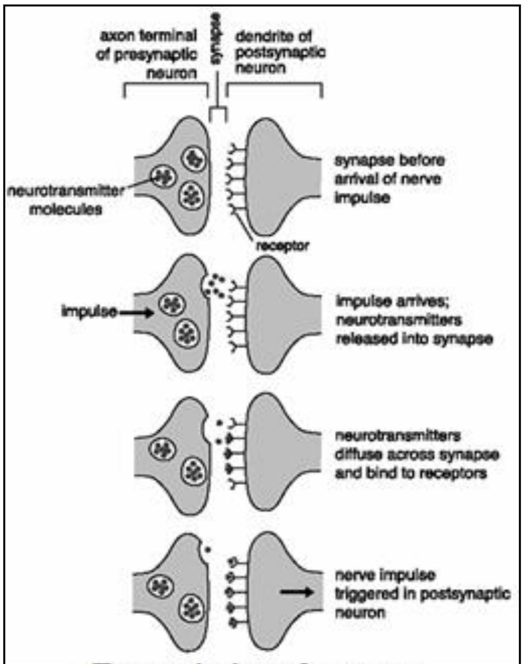
ACTION POTENTIAL: If nerve is stimulated by electric shock, pH change, mechanical stimulation, a nerve impulse is generated, and a change in potential can be seen on the oscilloscope. This nerve impulse is called the action potential. Readings on the oscilloscope, can be broken into an upswing and downswing. During the upswing (-60



mV to +40 mV), membrane becomes permeable to Na^+ ions. Na moves from outside to inside of axon (i.e. "depolarization" occurs and the inside of the axon becomes positive). In the downswing (+40 mV to 60 mV), membrane becomes permeable to K^+. K^+ moves from outside to inside of axon. This is called repolarization (since the inside of axon becomes negative again).

RECOVERY PHASE: Between transmissions, K^+ ions are returned to inside of axon, Na^+ to the outside. The speed of nerve impulses is quite rapid. This is due to the structure of the nerves. Specifically, the myelin sheath of most nerve fibers (this sheath is formed by tightly packed spirals of the cell membrane of Schwann cells) and the interruptions or gaps of the sheath called the nodes of Ranvier. This sheath gives nerves their characteristic white appearance. The speed of transmission is ~200 m/s in myelinated fibers, but only 0.5 m/s in non-myelinated fibers. The reason is that the nerve impulse "jumps" from node to node in myelinated fibers. In non-myelinated fiber, the nerve impulse must depolarize and repolarize each point along the nerve fiber.

3.6 TRANSMISSION OF IMPULSES ACROSS SYNAPSES: What happens to a nerve impulse once it reaches the end of an axon? How does one nerve communicate with another? The answer lies in the specialized regions at the ends of axons called synapses. Synapse is the region between end of an axon and the cell body or dendrite to which it is attached. The synaptic endings are swollen terminal knobs on the ends of axon terminal branches. The Presynaptic membrane and Postsynaptic membrane are the membrane of the axon synaptic ending and the membrane of the next neuron just beyond the axon's synaptic membrane respectively. The space between the presynaptic and the postsynaptic membranes synaptic cleft. Neurons contain neurotransmitter substances



Transmission of a nerve impulse across a synapse

(neurotransmitters); the chemicals that transmit the nerve impulses across a synaptic cleft.

The Synaptic vesicles contain the neurotransmitters located near the surface of synaptic endings. Acetylcholine, Noradrenalin, Serotonin, Adrenalin (epinephrine) are some important neurotransmitters. Transmission across a synapse is one-way because only the ends of axons have synaptic vesicles that are able to release neurotransmitters to affect the potential of the next neurons. Stimulation or inhibition of postsynaptic membranes can occur. A neuron is on the receiving end of many synapses, some may be giving inhibitory and some may give stimulatory impulses. Whether or not the neuron they are attached to fibres depends on the summary effect of all the excitatory neurotransmitters received. If amount of excitatory neurotransmitters received is sufficient to overcome the amount of inhibitory neurotransmitters received, the neuron fires. If not, only local excitation occurs. The total process allows neurons to fine-tune to the environment.

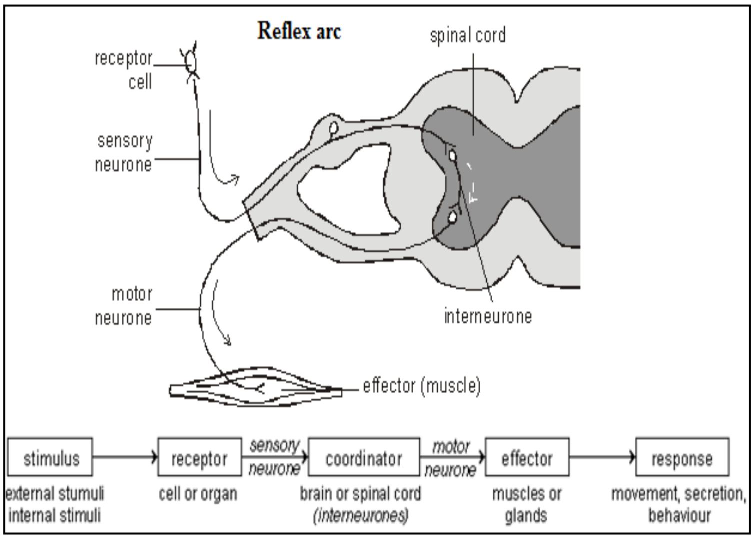
Sequence of events:

1. Nerve impulse travel along axon, reach a synaptic ending.
2. Arrival of nerve impulse at synaptic ending changes membrane → Ca^{2+} flows into ending.
3. Ca^{2+} ions cause contractile proteins to pull synaptic vesicles to inner surface of the presynaptic membrane.
4. Vesicle fuses with presynaptic membrane, releasing neurotransmitters into synapse.
5. Neurotransmitters diffuse across synaptic cleft to receptors on postsynaptic membrane. The receptors control selective ion channels; binding of a neurotransmitter to its specific receptors opens the ion channels.
6. The resulting ion flux (not shown on diagram) changes the voltage of the postsynaptic membrane. This either moves the membrane voltage closer to the 'threshold voltage' required for an action potential (an excitatory synapse), or hyperpolarizes the membrane (an inhibitory synapse). In this case, the neurotransmitters binding to receptors on the dendrite causes the nerve impulse to be transmitted down the dendrite of the second neuron. The nerve impulse has now been transmitted from the first neuron to the second neuron.
7. Neurotransmitters are quickly deactivated to prevent them from continually acting on postsynaptic membrane. This can occur by: a) neurotransmitter is degraded by

enzymes (e.g., acetylcholinesterase (= "cholinesterase") breaks down acetycholine). b) Synaptic ending reabsorbs the neurotransmitter. e.g. this is what happens to Serotonin.

3.7 THE REFLEX ARC:

• Reflexes are automatic, involuntary responses to changes occurring inside or outside the body. Can involve the brain (e.g. blinking) or not involve brain (e.g. withdraw hand from hot stove).

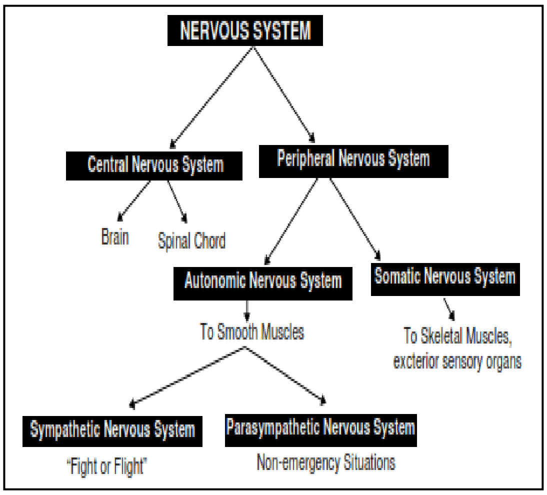


• The Reflex arc is the main functional unit of the nervous system. It allows us to react to internal and external stimuli.

Path of a simple Reflex Arc:

1. Receptor (e.g. in skin) - generates a nerve impulse.
2. Sensory Neuron: Takes message to CNS. Impulses move along dendrite, proceed to cell body (in dorsal root ganglia) and then go from cell body to axon in gray matter of cord.
3. Interneuron - passes message to motor neuron.
4. Motor neuron - takes message away from CNS to axon of spinal nerve.
5. Effector - receives nerve impulses and reacts: glands secrete and muscles contract.

3.8 SUMMARY:



- The **central nervous system (CNS)** includes the **brain** and **spinal cord**. The brain and spinal cord are protected by bony structures, membranes, and fluid. The brain is held in the cranial cavity of the skull and it consists of the **cerebrum**, **cerebellum**, and the **brain stem**. The nerves involved are cranial nerves and spinal nerves.
- The nervous system is our **processing**

system, and the system that keeps us in contact with the outside world. It tells us that we exist, and along with the muscles allows us to move and react to stimuli. Our **consciousness** resides in our nervous systems, as do our thoughts and emotions.

- In short, the roles of the nervous system are: responsible for coordination of movement, response to environmental stimuli, intelligence, **self-awareness**, **thought**, **and emotion**.
- **Nervous system is composed** of nerve cells called **neurons**, which are specialized to carry nerve impulses.
- Nervous system has **two major divisions**: (the division is arbitrary; the two systems work together and are connected to one another). The two systems are:

  1. **Central Nervous System**: (CNS) - includes spinal cord and brain and is the "center" of the body.

  2. **Peripheral Nervous System**: (PNS) - the rest of the nervous system: PNS is further divided into the **Somatic Nervous System** (connects to skeletal muscle) and **Autonomic Nervous System** (connects to smooth (involuntary) muscles).
- The Autonomic Nervous System is further divided into the **Sympathetic Nervous System** (usually causes effects associated with emergency situations) and the **Parasympathetic Nervous System** (promotes activities associated with a normal state).

Axons	**Dendrites**
Take information away from the cell body	Bring information to the cell body
Smooth Surface	Rough Surface (dendritic spines)
Generally only one axon per cell	Usually many dendrites per cell
No ribosomes	Have ribosomes
Can have myelin	No myelin insulation
Branch further from the cell body	Branch near the cell body

	Sensory neuron	Interneuron	Motor Neuron
Length of Fibers	Long dendrites and short axon	Short dendrites and short or long anxon	Short dendrites and long axons
Location	Cell body and dendrite are outside of the spinal cord; the cell body is located in a dorsal root ganglion	Entirely within the spinal cord or CNS	Dendrites and the cell body are located in the spinal cord; the axon is outside of the spinal cord
Function	Conduct impulse to the spinal cord	Interconnect the sensory neuron with appropriate motor neuron	Conduct impulse to an effector (muscle or gland)

3.9 KEY WORDS: Nervous system, Neurons, Brain, Spinal cord, Transmission of impulses, Axon, Dendrites, Synapse, Acetyl choline, Reflex arc.

3.10 QUESTIONS FOR SELF STUDY:

1. What are the major divisions of nervous system?
2. Depict the parts of a human brain
3. Write about the functions of cerebellum
4. Explain the roles of spinal cord
5. What are the types of neurons?
6. What is reflex arc?
7. Explain transmission of impulse through the synapse.

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BC 1.3: PHYSIOLOGY AND NUTRITION

BLOCK-I: PHYSIOLOGY.

UNIT 4: EXCRETORY SYSTEM: ULTRASTRUCTURE OF NEPHRON, GLOMERULAR FILTRATION, FORMATION OF URINE, ACID-BASE BALANCE AND ITS REGULATION.

STRUCTURE OF THE UNIT

4.0 OBJECTIVES:

- To understand the excretory systems of human body
- To study the structure of kidney and ultra structure of nephron.
- To understand the process of glomerular filtration and formation of urine.
- To learn about the process of acid-base balance and its regulation by kidney.

4.1 INTRODUCTION: The living cells of the body produce wastes during cell metabolism. If the wastes are not removed, they would build up in the cells, organs, and blood to such a degree that nutrients and oxygen wouldn't be able to enter the cells to be used for energy. There are different systems of the body that work together to keep the body functioning properly. One of the most important systems is the excretory system which eliminates wastes from the body. Within each kidney are one million microscopic nephrons where filtering takes place. A cluster of capillaries called a glomerulus is surrounded by a cup-shaped sac called the Bowman's capsule. Water, urea, glucose, and minerals in the blood move into the Bowman's capsule. Reabsorption of some of this material and most of the water takes place while the blood continues to weave around the renal tubule. Wastes that are left after reabsorption collect as urine and are sent to the bladder. As perspiration is released to the surface of the skin, it evaporates, or changes from a liquid into a gas. To make this change, heat from the body is used up, and as a result, there is a loss of heat from the body, resulting in a cooling effect. The top layer of the skin is called the epidermis. Below this layer is the dermis. Urine is made up water, urea, and inorganic salts. The bladder collects the urine before it is eliminated from the body through the urethra. Homeostatsis is a term that refers to the balance of chemicals and elements within the body. The lungs are a part of the respiratory and excretory systems. The lungs collect the metabolic waste carbon dioxide and eliminate it from the body. The circulatory system gathers the carbon dioxide from living body cells and returns it to the alveoli of the lungs. The carbon dioxide moves from the blood to the alveoli where it is then exhaled. Water vapor is also released during exhaling. The kidneys are about the size of a large bar of soap and are shaped like kidney beans. They are located on either side of the spinal cord at about waist height.

4.2 THE HUMAN EXCRETORY SYSTEM: Excretion is the process of removing the body waste in order to maintain homeostasis. The excretory system works to maintain proper water balance in the body and to also remove liquid waste (urine). Aside from the kidneys, other organs are also involved in excretion process. Structures involved in excretion include:

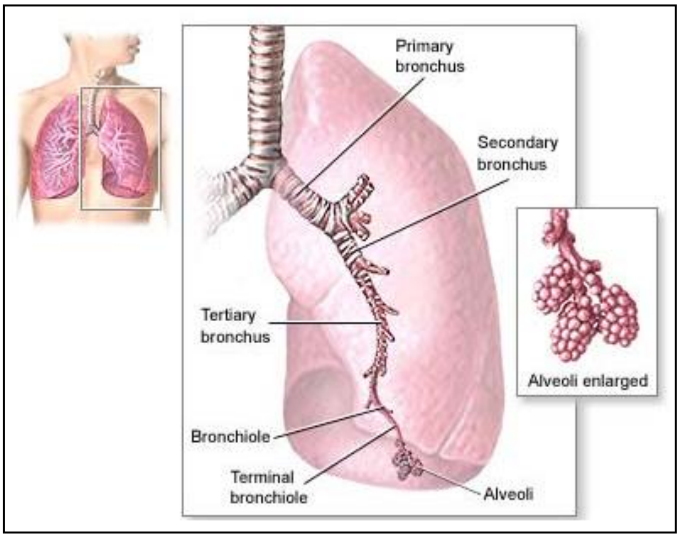
a. Skin: Sweat is removed by the skin as a waste product (trying to remove heat)

b. Lungs: Removes waste gases such as CO_2.

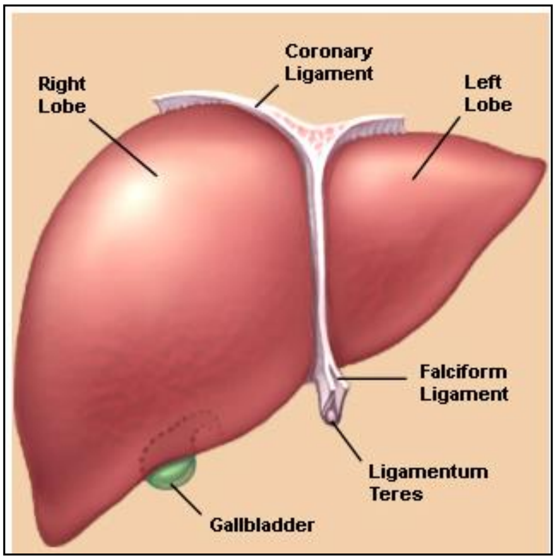
c. Liver: Removes Nitrogenous waste (Urea).

Let us understand in brief about these accessory organs and their role in excretion before we move on to the major organ involved in human excretory system the kidneys.

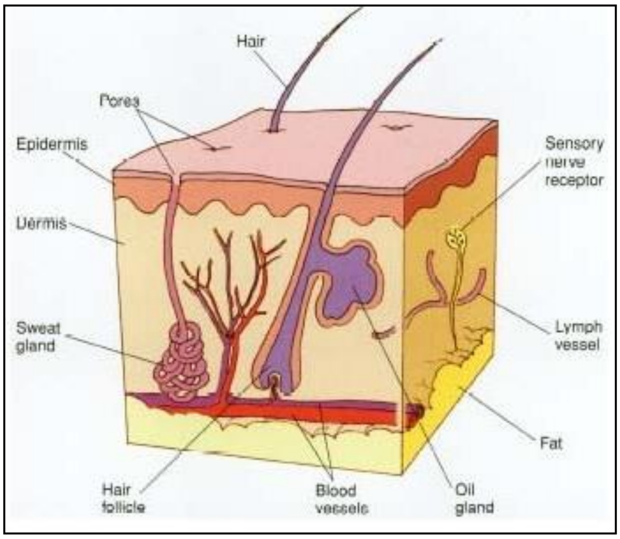
Lungs: The lungs are a part of the respiratory system and the excretory system. Air is breathed into the lungs and a gas exchange takes place inside the tiny air sacs of the lungs called alveoli. Oxygen from the air moves through the thin walls of the alveoli and through the walls of the capillaries or microscopic blood vessels that surround the alveoli. The oxygen is attracted to and held by the hemoglobin in the red blood cells. The oxygen rich blood will move back to the heart and receive a giant push to travel throughout the body. The oxygen will then be released to living cells. The cells need oxygen to carry on respiration, which is the releasing of energy from food and oxygen within the individual cells. The waste product carbon dioxide is produced during this process. It is released to the red blood cells and then carried back to the lungs for elimination from the body. The carbon dioxide travels from the red blood cells and moves into the alveoli. From there it is exhaled from the body when a person breathes out. Water vapor is also exhaled during this process.



Liver: The liver, which is located just to the right of the stomach, is another organ that plays a major role in excretion. Food that has been digested in the small intestine travels to the liver where some of it is stored and released back to the blood stream in a controlled fashion. Sugar in the blood is removed in the liver and stored as glycogen. When the sugar level in the blood goes down, the liver breaks down the glycogen and releases sugar back into the blood. If there is no room in the liver to store glycogen, the liver changes the sugar to fat and stores it in other parts of the body. Blood sugar level is important because sugar is the energy provider for all the cells of the body. If the liver's supply of glycogen runs out, it converts these fats to sugars. Amino acids release nitrogen when they are changed into sugars, glycogen, or fats. This nitrogen is changed by the liver into urea which is carried to the kidneys by the blood stream. The urea will be eliminated from the body from the kidneys. The liver also removes from our bodies poisonous substances, such as mercury in fish, poisonous fumes from paint, and chemicals sprayed on food. The liver is our bodies' main defense from poisons like those mentioned above. The liver also changes hemoglobin from dead red blood cells into bile, which is used in the small intestine to breakdown fats. Bacteria from the large intestine are removed from the blood by the liver.

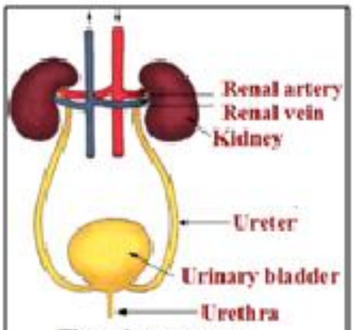


Skin: The last member of the excretory team is the skin. The skin is the largest organ of the body. It covers an area of 1.5 to 2 square meters in an average adult. That represents a space about the size of a small area rug. The thickness of the skin varies from a .5 millimeters on the eyelids to 6 millimeters on the soles of the feet. There are two general layers of the skin. The outer layer is called the epidermis and is made up of layers of flat cells. The surface cells of this layer are dead. They are constantly rubbing off and being replaced by cells below

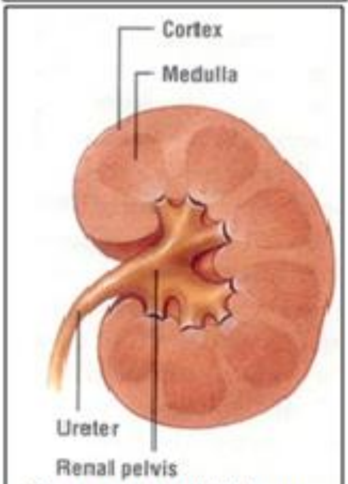


them. This outer layer of skin provides a waterproof shield against germs and bacteria. Under the epidermis is a layer called the dermis. The cells in this layer are all alive. This layer contains blood vessels, nerve endings, sweat and oil glands, hair follicles, and fat cells. The sweat glands have tubes that lead to the surface of the skin at points called sweat pores. Perspiration is released at these sweat pores. Water, urea, and inorganic salts are included in perspiration. Besides ridding the body of these wastes, perspiration also cools the body and helps maintain a proper body temperature. When you exercise, work hard, or if the temperature of your surroundings is high you sweat or perspire. The sweat evaporates when it reaches the surface of the skin. During evaporation, heat is required to change the liquid to a gas. This heat comes from the body. Therefore, the body is cooled as the sweat evaporates.

4.3 A. STRUCTURE OF THE KIDNEY: Parts of the excretory system that are associated with kidneys are Ureters, Urinary bladder and Urethra. Kidney is a lima bean shaped structure found on both sides of the spinal column in the lower back. Part of the urinary system, our kidneys are vital organs that serve to remove waste from the bloodstream through ultrafiltration and the formation of urine, and to aid the body in maintaining proper hydration through a process called osmoregulation. Situated to the back of the abdominal wall, the kidneys are snugged up underneath the diaphragm, behind the liver on one side and the stomach on the other, partially shielded in the back by the ‘floating’ ribs. The kidney has three distinct regions:



The urinary system



Structure of kidney

1. Renal Cortex : The outer region of kidney that helps in blood filtration.

2. Renal Medulla: This is the middle region of the kidney. Made up of collecting ducts. Collects filtrate (filtered materials from the blood) and carries it to the renal pelvis.

3. Renal Pelvis : This is the inner section of the kidney. It is a cavity in the center of a kidney connected to the ureters. Filtrate (now called urine) drains from the pelvis into ureters for removal.

B. Ureters: Hollow tubes connecting the renal pelvis to the Urinary bladder. Carry urine from the kidney to the urinary bladder.

C. Urinary bladder: Hollow muscular pouch located in the pelvic area of a human. Hold urine until it is released from the body. A typical bladder is able to hold up to about 500 mL of urine.

D. Urethra: Hollow tube leading from the urinary bladder to the outside of the human body. Carry urine from the bladder to the outside of the body.

4.4 ULTRA STRUCTURE OF NEPHRON:

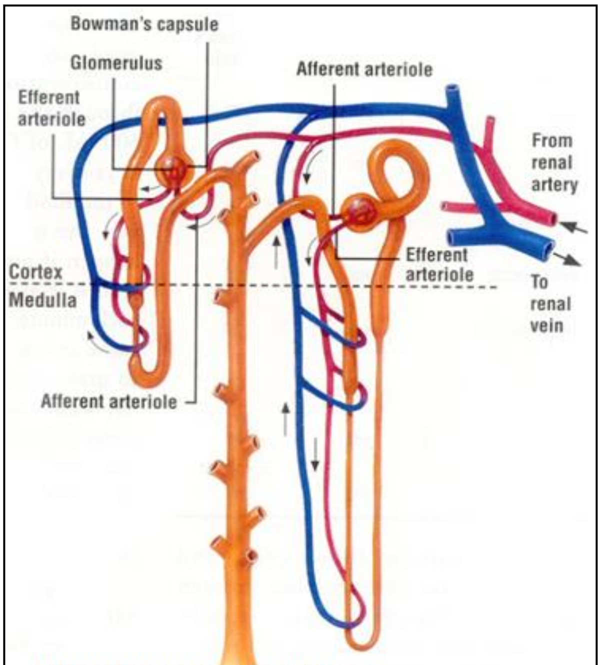
• The basic functional unit of a kidney.

• This is the structure responsible for filtering the blood and maintaining proper water balance.

• There are about 1.25 million nephrons per kidney.

• The kidney Nephron extends from the renal cortex (glomerulus/Bowman's capsule) into the renal medulla (Loop of Henle).

Structures called nephrons residing in the cortex and medulla produce urine from filtrate removed from the bloodstream, passing it to the bladder via a series of collecting tubules that continuously merge, ultimately reaching the renal pelvis and finally the ureter. The question is,"Exactly how is urine produced?" It can hardly pass into the bladder until it actually exists. In order to understand that process, we have to take a deeper look into the structure of the kidney– specifically looking to the nephron and the renal vessels, since this is where waste products leave the blood and enter kidney tissue. There are about one million nephrons in a kidney, each feeding into a nest of collecting ducts. A nephron is a rather intricate structure and it serves two basic purposes: to filter and remove waste products and maintain the body's water supply. At one end of the nephron, residing in the cortex, is an approximately 0.2mm



Ultrastructure of Nephron

diameter structure known as the Malpighian Corpuscle, and about 3.0cm away at the other end, a collecting duct. A complicated array of blood vessels intertwines this structure.

Parts of nephron include;

a. **Renal Artery**: Artery that carries blood to the kidney to be filtered.

b. **Renal Vein**: Vein that carries blood from the kidney after it has been filtered.

c. **Glomerulus:** A tight ball of blood capillaries located in the bowman's capsule of Nephron. Blood Pressure created here causes materials to be filtered from the blood.

d. **Bowman's Capsule:** A cup-shaped structure that receives filtrate from the glomerulus.

e. **Proximal Tubule**: Tube connected to the Bowman's capsule. Filtrate enters the proximal tube from the Bowman's capsule. ***Reabsorption of amino acids and glucose occurs here.***

f. **Loop of Henle**: Long U-shaped tube that extends into the renal medulla. Responsible for maintaining the salt balance by reabsorbing or releasing salt in the filtrate.

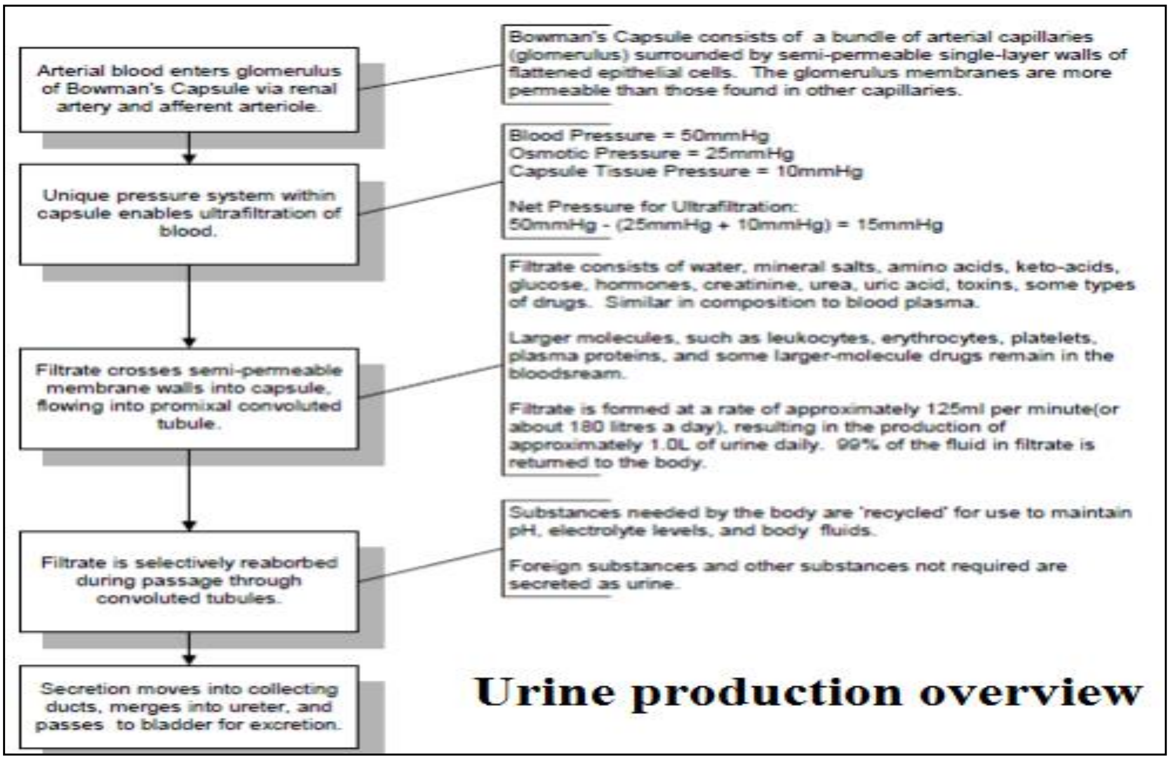
g. **Distal Tubule**: Tube extending from the loop of henle. It also reabsorbs materials from the filtrate. ***Tubular secretion occurs here.*** Materials such as creatinine and drugs are **added** to the filtrate.

H. **Collecting Tubule:** Tube that extends from the distal tubule to the renal pelvis. This portion of the Nephron is mainly responsible for reabsorption of water.

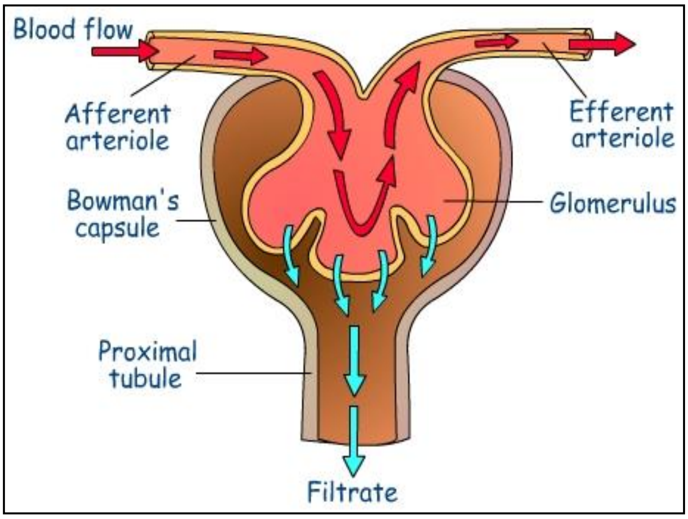
4.5 THE FORMATION OF URINE:

Filtration, reabsorption and secretion.

Every one of us depends on the process of urination for the removal of certain waste products in the body. The production of urine is vital to the health of the body. Most of us have probably never thought of urine as valuable, but we could not survive if we did not produce it and eliminate it. Urine is composed of water, certain electrolytes, and various waste products that are filtered out of the blood system. Remember, as the blood flows through the body, wastes resulting from the metabolism of foodstuffs in the body cells are deposited into the bloodstream, and this waste must be disposed of in some way. A major part of this "cleaning" of the blood takes place in the kidneys and, in particular, in the nephrons, where the blood is filtered to produce the urine. Both kidneys in the body carry out this essential blood cleansing function. Normally, about 20% of the total blood pumped by the heart each minute will enter the kidneys to undergo filtration. This is called the **filtration fraction**. The rest of the blood (about 80%) does not go through the filtering portion of the kidney, but flows through the rest of the body to service the various nutritional, respiratory, and other needs that are always present.



For the production of urine, the kidneys do not simply pick waste products out of the bloodstream and send them along for final disposal. The kidneys' 2 million or more nephrons (about a million in each kidney) form urine by three precisely regulated processes: filtration, reabsorption, and secretion.



Glomerular Filtration: Urine formation begins with the process of filtration, which goes on continually in the renal corpuscles. As blood courses through the glomeruli, much of its fluid, containing both useful chemicals and dissolved waste materials, soaks out of the blood through the membranes (by osmosis and

diffusion) where it is filtered and then flows into the Bowman's capsule. This process is called glomerular filtration. The water, waste products, salt, glucose, and other chemicals that have been filtered out of the blood are known collectively as glomerular filtrate. The glomerular filtrate consists primarily of water, excess salts (primarily Na^+ and K^+), glucose, and a waste product of the body called urea. Urea is formed in the body to eliminate the very toxic ammonia products that are formed in the liver from amino acids. Since humans cannot excrete ammonia, it is converted to the less dangerous urea and then filtered out of the blood. Urea is the most abundant of the waste products that must be excreted by the kidneys. The total rate of glomerular filtration (glomerular filtration rate or GFR) for the whole body (i.e., for all of the nephrons in both kidneys) is normally about 125 ml per minute. That is, about 125 ml of water and dissolved substances are filtered out of the blood per minute. The following calculations may help you visualize how enormous this volume is. The GFR per hour is:
125 ml/min X 60min/hr= 7500 ml/hr.
The GFR per day is: 7500 ml/hr X 24 hr/day = 180,000 ml/day or 180 liters/day.

Now, what we have just calculated is the **amount of water** that is removed from the blood each day - about 180 liters per day. (Actually it also includes other chemicals, but the vast majority of this glomerular filtrate is water.) Imagine the size of a 2-liter bottle of soda pop. About 90 of those bottles equal 180 liters. Obviously no one ever excretes anywhere near 180 liters of urine per day! Why? Because almost all of the estimated 180 liters, that leaves the blood by glomerular filtration, the first process in urine formation, returns to the blood by the second process - reabsorption.

Reabsorption: Reabsorption, by definition, is the movement of substances out of the renal tubules back into the blood capillaries located around the tubules (called the peritubular copillaries). Substances reabsorbed are water, glucose and other nutrients, and sodium (Na^+) and other ions. Re-absorption begins in the proximal convoluted tubules and continues in the loop of Henle, distal convoluted tubules, and collecting tubules. Let's discuss for a moment the three main substances that are reabsorbed back into the bloodstream.

Large amounts of water - more than 178 liters per day - are reabsorbed back into the bloodstream from the proximal tubules because the physical forces acting on the water in these tubules actually push most of the water back into the blood capillaries. In other words, about 99% of the 180 liters of water that leaves the blood each day by glomerular filtration returns to the blood from the proximal tubule through the process of **passive reabsorption**.

The nutrient glucose (blood sugar) is **entirely** reabsorbed back into the blood from the proximal tubules. In fact, it is **actively transported** out of the tubules and into the peritubular capillary blood. None of this valuable nutrient is wasted by being lost in the urine. However, even when the kidneys are operating at peak efficiency, the nephrons can reabsorb only so much sugar and water. Their limitations are dramatically illustrated in cases of diabetes mellitus, a disease which causes the amount of sugar in the blood to rise far above normal. As already mentioned, in ordinary cases all the glucose that seeps out through the glomeruli into the tubules is reabsorbed into the blood. But if too much is present, the tubules reach the limit of their ability to pass the sugar back into the bloodstream, and the tubules retain some of it. It is then carried along in the urine, often providing a doctor with her first clue that a patient has diabetes mellitus. The value of urine as a diagnostic aid has been known to the world of medicine since as far back as the time of Hippocrates. Since then, examination of the urine has become a regular procedure for physicians as well as scientists.

Sodium ions (Na^+) and other ions are only partially reabsorbed from the renal tubules back into the blood. For the most part, however, sodium ions are **actively transported** back into blood from the tubular fluid. The amount of sodium reabsorbed varies from time to time; it depends largely on how much salt we take in from the foods that we eat. (As stated earlier, sodium is a major component of table salt, known chemically as sodium chloride.) As a person increases the amount of salt taken into the body that person's kidneys decrease the amount of sodium reabsorption back into the blood. That is, more sodium is retained in the tubules. Therefore, the amount of salt excreted in the urine increases. The process works the other way as well. The less the salt intake, the greater the amount of sodium reabsorbed back into the blood, and the amount of salt excreted in the urine decreases.

Secretion: Now, let's describe the third important process in the formation of urine. Secretion is the process by which substances move into the distal and collecting tubules from blood in the capillaries around these tubules. In this respect, secretion is re-absorption in reverse. Whereas re-absorption moves substances out of the tubules and into the blood, secretion moves substances out of the blood and into the tubules where they mix with the water and other wastes and are converted into urine. These substances are secreted through either an active transport mechanism or as a result of diffusion across the membrane. Substances secreted are hydrogen ions (H+), potassium ions (K+), ammonia (NH3), and certain drugs. Kidney tubule secretion plays a crucial role in maintaining the body's acid-base balance, another example of an important body function that the kidney participates in.

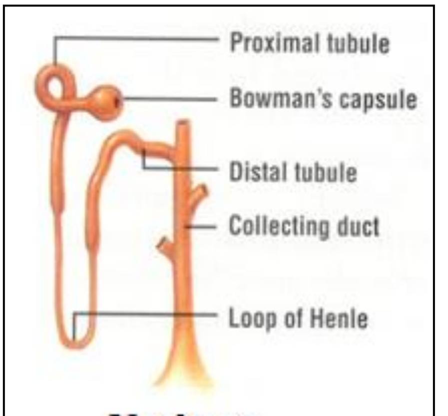
4.6 ACID-BASE BALANCE: Acid–base imbalance occurs when a significant insult causes the blood pH to shift out of the normal range (7.35 to 7.45). In the fetus, the normal range differs based on which umbilical vessel is sampled (umbilical vein pH is normally 7.25 to 7.45; umbilical artery pH is normally 7.18 to 7.38). An excess of acid in the blood is called academia and an excess of base is called alkalemia. The process that causes the imbalance is classified based on the etiology of the disturbance (respiratory or metabolic) and the direction of change in pH (acidosis or alkalosis). There are four basic processes: metabolic acidosis, respiratory acidosis, metabolic alkalosis, and respiratory alkalosis. One or a combination may occur at any given time.

Acid–base balance is the part of human homeostasis concerning the proper balance between acids and bases, also called body pH. The body is very sensitive to its pH level, so strong mechanisms exist to maintain it. Outside the acceptable range of pH, proteins are denatured and digested, enzymes lose their ability to function, and death may occur. The body's acid–base balance is normally tightly regulated, keeping the arterial blood pH between 7.38 and 7.42. Several buffering agents that reversibly bind hydrogen ions and impede any change in pH exist. Extracellular buffers include bicarbonate and ammonia, whereas proteins and phosphate act as intracellular buffers. The bicarbonate buffering system is especially key, as carbon dioxide (CO_2) can be shifted through carbonic acid (H_2CO_3) to hydrogen ions and bicarbonate (HCO_3^-) as shown below.

$$H_2O + CO_2 \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

Acid–base imbalances that overcome the buffer system can be compensated in the short term by changing the rate of ventilation. This alters the concentration of carbon dioxide in the blood, shifting the above reaction according to Le Chatelier's principle (If a chemical system at equilibrium experiences a change in concentration, temperature, volume, or partial pressure, then the equilibrium shifts to counteract the imposed change and a new equilibrium is established), which in turn alters the pH. For instance, if the blood pH drops too low (*acidemia*), the body will compensate by increasing breathing thereby expelling CO_2, and shifting the above reaction to the left such that fewer hydrogen ions are free; thus the pH will rise back to normal. For *alkalemia*, the opposite occurs.

The kidneys are slower to compensate, but renal physiology has several powerful mechanisms to control pH by the excretion of excess acid or base. In response to acidosis, tubular cells reabsorb more bicarbonate from the tubular fluid, collecting duct cells secrete more hydrogen and generate more bicarbonate, and ammonia genesis leads to increased formation of the NH_3 buffer. In responses to alkalosis, the kidney may excrete more bicarbonate by decreasing hydrogen ion secretion from the tubular epithelial cells, and lowering rates of glutamine metabolism and ammonium excretion.



Nephron

4.7 SUMMARY: We have taken a close look at the excretory system of the human being. This system works with other systems to maintain a healthy body. The liver, kidneys, lungs, and skin are the organs of the excretory system. The lungs are responsible for releasing carbon dioxide and water vapor from the body. The liver and kidneys filter materials from the blood. The skin has sweat glands that release water, salts, and urea. Perspiration also cools the body and helps to keep a balanced body temperature. Particularly, we have studied in detail the role of kidney in the process of excretion. The excretory system is crucial to survival. If the system doesn't perform properly the consequence can mean death. In summary, three processes occurring in successive portions of the nephron accomplish the function of urine formation: Glomerular Filtration of water and dissolved substances out of the blood in the glomeruli and into Bowman's capsule; reabsorption of water and dissolved substances out of the kidney tubules back into the blood (note that this process prevents substances needed by the body from being lost in the urine). Secretion of hydrogen ions (H^+), potassium ions (K^+), ammonia (NH_3), and certain drugs out of the blood and into the kidney tubules, where they are eventually eliminated in the urine.

4.8 KEY WORDS: Excretory System, Ultrastructure of Nephron, Glomerular Filtration, Formation of Urine, Acid-Base Balance, Metabolism, Kidneys, Homeostasis, Urine, Ureter, Bladder, Urethra Liver, Epidermis, Skin.

4.9 QUESTIONS FOR SELF STUDY:

1. Which are the four organs of the excretory system?
2. Why is the excretory system important to the human body?
3. How do kidneys clean the blood?
4. How is perspiration important to regulating body temperature?
6. What is urine?
7. What jobs does the bladder perform?
8. What does the term homeostasis mean?
9. Explain the role of lungs in the excretory system?
10. How big are the kidneys and where are they located?

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