

UNIT 1

NUTRITION AND DIGESTION

Structure

1.1	Introduction	1.6	Mechanism of Absorption in Vertebrate Animals
	Objectives		Absorption of Monosaccharides
1.2	Nutrition		Absorption of Amino Acids, Dipeptides, and Tripeptides
	Proteins		Absorption of Lipids
	Carbohydrates	1.7	Physiology of Digestion in Mammals
	Lipids		Digestion in Oral Cavity
	Vitamins		Digestion in Stomach
	Minerals and Trace Elements		Digestion and Absorption in Small Intestine
	Water		Absorption in the Large Intestine
1.3	Feeding Mechanisms in Animals	1.8	Energy Metabolism in Animals
1.4	Digestion in Animals	1.9	Summary
	Intracellular Digestion	1.10	Terminal Questions
	Extracellular Digestion in Alimentary Canal	1.11	Answers
1.5	Digestive Enzymes in Animals		
	Action of Proteolytic Enzymes		
	Action of Carbohydrase Enzymes		
	Action of Lipase Enzymes		
	Maintenance of Gut Lining		
	Coordination of Digestion in Animals		

1.1 INTRODUCTION

All organisms require a fairly steady supply of nutrient materials from the environment to obtain energy in order to stay alive. You will recall from the

compulsory course on environment, “Environmental Studies (BEVAE-181)” that animals are heterotrophs because they depend on already synthesized organic compounds from plants and other animals to obtain their food. Unlike autotrophs (plants and chemosynthetic bacteria) animals have only limited synthesizing abilities.

In the earlier courses, you have already read that in organisms cellular metabolism provides energy for various processes, like movement, locomotion, excretion, osmoregulation, synthesis of new materials for growth and maintenance and reproduction. To provide energy for these processes **raw material** or **nutrients** are required which are supplied by food. In addition, animals require certain amino acids, vitamins and minerals which their body is unable to synthesize. The study of nutrition involves both the need for food to provide energy and the need for specific food components for various other activities of the body.

The process by which animals acquire and ingest their food is referred to as **feeding**. Diverse types of feeding mechanisms have been evolved by different groups of animals. Virtually all food ingested by animals whether of plant or of animal origin has to be broken down into simple compounds by the process of **digestion**. Digestion and absorption of food constitute the essential link between nutrition and metabolism. In this unit we shall first discuss briefly the nature and components of food and the specialized feeding mechanisms. There exists a relationship between the nature of ingested food and type of feeding mechanisms used in acquiring of food. Then we will consider the digestion and absorption of nutrients that takes place within the body of the animals. Towards the end of the unit we shall discuss energy metabolism in animals.

Objectives

After studying this unit you should be able to:

- ❖ differentiate between essential and non-essential nutrients and explain why animals exhibit differences in their essential food requirements;
- ❖ list the various feeding strategies evolved by the animals in relation to the available food;
- ❖ distinguish between the process of digestion of proteins, carbohydrates and fats;
- ❖ explain the role of gastrointestinal hormones in digestion;
- ❖ summarise the process of absorption of food from the alimentary canal;
- ❖ describe the digestion process in humans as an example of mammalian digestion;
- ❖ explain energy metabolism in animals in relation to oxygen consumption.

1.2 NUTRITION

As mentioned earlier, all animals are heterotrophs and require food from the environment. What is this food made up of? If the food ingested by a number

of different animals is broken down we find that it consists of proteins, carbohydrates, fats, water, minerals and vitamins. All animals require these broad categories of nutrients although in different amounts.

Some of these nutrients are used mainly as fuel (carbohydrates and fats) by the animals, while others such as proteins, minerals and vitamins are required principally as structural and functional components of the animal. However, proteins, in addition to carbohydrates and fats can serve as fuel for the body's energy needs in times of emergency. The energy generated by the ingested nutrients is used to carry on both the internal and the external activities of the body. Some examples of internal activities required in the body are: functioning of the brain, beating of the heart, breathing, digestion of food, excretory processes etc. But we must remember that no animal can survive on fuel alone, therefore, a balanced diet is needed to meet all the requirements of the animal body which include energy, growth, maintenance, reproduction and physiological regulation. Nutrients also have a protective role in the body as proper nutrients helps to fight infections and increase the life span. Now let us see the importance of these different classes of food in relation to animal nutrition.

1.2.1 Proteins

Proteins are called body **building foods** as they are used as raw material by the animals for building the muscles, skin, blood and bones of their body. Proteins account for about 20 percent of the total body weight and repair the tissues of the body and so are required every day by the animals for survival. All proteins contain carbon, hydrogen, oxygen, and nitrogen. Smaller quantities of sulphur and phosphorus may also be present. Proteins are composed of amino acids and are continually synthesized in the cells of animals. Amino acids are simple organic compounds (monomers) that combine to form proteins (polymers) and are derived: i) largely from the diet and ii) partly from the breakdown of proteins available in the body. Proteins also help the animal body to fight infections. They can also serve as an energy source, under circumstances when carbohydrates and fats are unable to provide the energy needs of the body.

Generally all proteins are made from about 20 different amino acids in various combinations (you will learn more about the structure of proteins in Unit 9 of this course). However, it is not necessary for the animal to obtain all the 20 amino acids from outside sources. Some amino acids can be formed in the body using other amino acids and are termed as **non-essential amino acids**. The amino acids that are not formed in the body and have to be supplied through diet are known as **essential amino acids**.

The requirement of essential amino acids differs from organism to organism so how can we determine which amino acid is essential and which is non-essential? The nutritional requirements are determined by deletion experiments i.e., by removing a single nutrient from the diet and then observing the growth and health of the animal. By this method it has been found that 10 amino acids are essential for the growth and well-being of rats. Refer to Table 1.1 to see the essential and non-essential amino acid requirements of rats and humans of which some are the same while others differ.

The terms essential and non-essential amino acids are not very significant because the non-essential amino acids are just as important for the body. Maybe so important that the body cannot depend on them to be supplied externally and so has mechanisms to synthesize them.

Table 1.1: Amino acids classified according to dietary needs of rats and humans.

Essential Amino Acids			Non-essential Amino Acids		
S.No	Rats	Humans	S.No	Rats	Humans
1.	Lysine	Lysine	1.	Glycine	Glycine
2.	Tryptophan	Tryptophan	2.	Alanine	Alanine
3.	Phenylalanine	Phenylalanine	3.	Serine	Serine
4.	Leucine	Leucine	4.	Tyrosine	Tyrosine
5.	Isoleucine	Isoleucine	5.	Aspartate	Aspartate
6.	Threonine	Threonine	6.	Glutamate	Glutamate
7.	Methionine	Methionine	7.	Proline	Proline
8.	Valine	Valine	8.	Hydroxyproline	Hydroxyproline
9.	Arginine	Cystine	9.	Citrulline	Citrulline
10.	Histidine		10.	Cysteine	Histidine
					Arginine

To what extent an animal requires a particular amino acid in its diet depends on the **synthetic ability** of the body cells. Organisms with marked synthetic ability, for example bacteria, require only a few essential amino acids. Organisms like mammals, that require many essential amino acids have a marked **synthetic disability**.

1.2.2 Carbohydrates

A carbohydrate is an organic molecule that contains carbon, hydrogen, and oxygen in a ratio near to 1:2:1 (for more details on the structure of carbohydrates refer to Unit 9 Volume 2 of this course). Familiar carbohydrates include glucose; sugars and starches (Table.1.2). Fifty five to seventy per cent of the required energy in animals is derived from carbohydrates.

Most animals, however, use a variety of hexose sugars like glucose, fructose, mannose, and galactose as interchangeable sources of energy. In this way no particular carbohydrate is really considered essential in a way similar to amino acids. But even if no carbohydrate is considered essential, growth of certain animals will be better when feeding on a particular type of sugar than on another as revealed by experiments in animals (see Box 1.1).

Table.1.2: Carbohydrates Present in the Animal Body

S.No.	Types of carbohydrates	Examples	Main Function
1.	Monosaccharides (simple sugars)	Glucose, fructose	Energy source
2.	Disaccharides	Sucrose, lactose, maltose	Energy source
3.	Polysaccharides	Glycogen	Storage of glucose

Box 1.1

The results of an experiment in young locusts showed that when their dietary sugar was maltose then growth was **maximum** or **optimum** while growth was **minimum** when carbohydrate was not given at all. Other sugars supported **sub-optimal** growth. What could be the reason for this difference? One of the main reasons is the difference in the rate of movement of sugars across the gut wall into the blood. In the above experiment with locusts, maltose was the **preferred nutrient**. Thus in the experiments with locusts though maltose was the preferred nutrient for them it was however, not considered an obligatory nutrient for them.

1.2.3 Lipids

Like carbohydrates, lipids (lipos: fat) contain carbon, hydrogen, and oxygen, but the carbon-to-hydrogen ratio is near to 1:2. Lipids compared to carbohydrates, contain much less oxygen though both have the same ratio of carbon atoms (Refer to Unit 9, Volume 2 for their structure). All animal tissues contain lipids as essential components of the cell membrane. Many kinds of lipids exist in the body of which the most important classes are: fatty acids, eicosanoids, glycerides, steroids, and phospholipids and glycolipids. Lipids are also stored as fat in certain tissues and are essential for diverse functions synthesis of steroid hormones such as insulation and padding, and as carriers of fat soluble vitamins.

Many animals can live on little or no dietary fat as it can also be formed from proteins as well as carbohydrates. However, the synthetic ability of many animals is limited with respect to certain unsaturated fatty acids and cholesterol. For instance, vertebrates can synthesise cholesterol readily. In humans, excess cholesterol is considered harmful in diet because it is a major factor in the development of atherosclerosis or hardening of arteries. On the other hand, insects cannot synthesise cholesterol from their precursors. Therefore, it must be supplied in their diet. Studies on rats show that three fatty acids – **linoleic, linolenic** and **arachidonic acid** acids are not synthesized by their body and so these are considered **essential fatty acids for rats**. Several insects, birds and some mammals also reveal such a dietary requirement of fatty acids. Studies show that in general animals have a better synthetic ability for lipids than for amino acids.

1.2.4 Vitamins

Animals cannot sustain a healthy life if they feed on a diet having only carbohydrates, fats and proteins. They also require vitamins and minerals in small quantities in the range of milligrams or micrograms. A number of vitamins function as coenzymes in metabolic reactions. Prolonged deficiency of vitamins in the animal body results in various diseases. **Essential vitamins** and **minerals** are those which cannot be synthesized in the organism, either at all or not in sufficient quantities, and therefore must be obtained through the diet. Let us first discuss the requirement of vitamins by animals.

Vitamins are broadly classified into lipid/fat soluble (Table 1.3) and water soluble (Table 1.4).

Table 1.3: Lipid Soluble Vitamins and their Characteristics

Name and Formula	Functions	Results of Deficiency or Absence in Humans except as noted
Vitamin A or Retinol ($C_{20}H_{30}O$)	Component of visual pigments; maintenance of epithelial tissues; Supports immune system.	In humans Skin disorders, impaired immunity, night blindness, xerophthalmia (dry cornea, no tear secretion). In birds croup (hoarseness) disease.
Vitamin D ($C_{28}H_{44}O$)	Aids in absorption. Regulates calcium and phosphorus metabolism	In children in human adults, bone cause softening (osteomalacia) especially in Asian women; Rickets (bone deformities).
Vitamin E or Tocopheral ($C_{29}H_{50}O_2$)	Prevents damage to cell membranes & breakdown of vitamin A and fatty acids. Acts as an antioxidant.	In humans; Nervous system degeneration in male fowls and rats causes sterility.
Vitamin K or Phylloquinone) ($C_{31}H_{46}O_2$)	Essential for prothrombin synthesis in liver and for blood clotting.	Blood fails to clot or blood clotting is delayed.

Table 1.4: Water Soluble Vitamins and their Characteristics

Name and Formula	Functions	Results of Deficiency or Absence in Humans except as noted
B₁:Thiamine ($C_{12}H_{17}ON_4S$). Anti neuritic (prevents or relieves neuritis)	In humans as coenzyme involved in many pathways; function in removing CO_2 from organic compounds.	In human causes Beriberi (tingling, poor coordination, reduced heart function) and muscle weakness. In birds causes polyneuritis (nerve inflammation)
B₂:Riboflavin ($C_{17}H_{20}O_6N_4$)	In humans is component of coenzymes FAD and FMN. Essential for growth. Involved in food metabolism & electron transport system	In humans epithelial and mucosal damage; cheilosis (inflammation and skin lesions, such as cracks at corners of the mouth. In dogs causes digestive disturbances. "yellow liver" disease occurs. In chicks causes curled toe paralysis occurs.
B₃: Nicotinic acid, or niacin ($C_6H_5O_2N$), antipellagic	Component of coenzymes NAD^+ and $NADP^+$	In humans causes mental disturbances, gastrointestinal disorders & Pellagra disease (skin becomes red, sore, and swollen, & occasionally small blisters occurs). In monkeys results in mental disturbances
B₅ : Pantothenic acid	Component of coenzyme A	Vitamin B5 deficiency is rare, but if it occurs it causes insomnia, fatigue, depression, irritability,

(C₉H₁₇O₃N)		vomiting, stomach pains, burning feet, and upper respiratory infections.
B₆: Pyridoxine (C₈H₁₂O₂N)	Coenzyme in amino acid metabolism.	In human retarded growth, anaemia, irritability, convulsions, muscular twitching and epithelial changes in humans and pigs in dogs Anaemia. Paralysis and death Dermatitis in pig, rats and chicks in rats.
B₇: Biotin (Vitamin H) (C₁₀H₁₆O₃N)	Coenzyme in synthesis of fat, glycogen, and amino acids.	In humans Ffatigue, scaly skin, inflammation, neuromuscular disorders and nausea in rats and chicks. Causes dermatitis with thickening of skin in poultry causes metabolic disease perosis (slipped tendon) resulting in leg deformity and weakness
B₉ :Folic acid(folate) (C₁₉H₁₉O₆N₇)	Essential for growth and formation of blood cells; coenzyme in amino acid & nucleic acid metabolism.	In humans causes anaemia, sprue (defective intestinal absorption), haemorrhage from kidneys, nutritional cytopenia (reduction in cellular elements of blood). In chicks and rats causes slow growth and anaemia
B₁₂ : Cyanocobalamin (C₆₃H₉₀ N₁₄PCo)	Growth; formation of blood cells; coenzyme in nucleic acid metabolism;	In humans causes impaired RBC production, pernicious anemia, numbness, loss of balance in humans. In young animals slow growth in ruminants wasting disease.
C or ascorbic acid (C₆H₈O₆)	Used in collagen synthesis. Maintains integrity of capillary walls; involved in formation of "Intercellular cement." is an Antioxidant	In humans and guinea pigs deficiency of vitamin C causes scurvy (degeneration of skin and teeth) and delayed wound healing In humans and guinea pigs vitamin C has to be supplied by diet.

The synthetic ability for vitamins also varies among different animal species. For instance, most mammals can synthesise ascorbic acid but humans and guinea pigs cannot. We also depend on intestinal bacteria to synthesise vitamin K and B₁₂. Fat soluble vitamins like A, D, E and K can be stored in the fat deposits of the body but vitamins that are water soluble like B or C need to be supplied continually as they are lost through urine.

1.2.5 Minerals and Trace Elements

As we explained earlier, a balanced diet includes both minerals and vitamins. However, minerals which are inorganic substances in the form of elements or ions cannot be synthesized and are needed through not diet in small amounts for a variety of different functions in the body of animals. Animals obtain

The physiological role of vitamin K was discovered in birds that were fed a cholesterol free diet for the purpose of studying cholesterol synthesis. The birds developed severe bleeding which was traced to a vitamin deficiency. Only after this it was discovered that vitamin K is necessary not only for birds but for

minerals through diet and so the required minerals are deemed essential. Some minerals which are needed in slightly larger amounts than others are simply called principal elements or **macronutrients** or macroelements and include **sodium, potassium, chloride, calcium, phosphorous, magnesium, and sulphur**. These are necessary for the animal body and can only be obtained from diet, and so are categorized as **essential macronutrients**. In the adult human body the daily requirement of essential **macronutrients** or macroelements is above 200 mg/day. The deficiency of such elements usually proves fatal unless properly rectified. For example, calcium is an important element which is essential in the physiology of muscle contraction about which you will learn in Unit 5. It is also an essential structural component of bones. Similarly sodium and potassium have an absolutely essential role in maintaining the membrane potential of cells as you will study in Unit 6.

Those minerals or elements which are required in the animal body in smaller quantities are called trace minerals or trace micronutrients and include **copper, iron, zinc, chromium, cobalt, iodine, molybdenum, and selenium**. Of these, iodine is a nonmetal, while others are metals. The micronutrients which are necessary for the animal body similar to macro nutrients are also only obtained from diet and so these are also categorized as **essential micronutrients**. Although the essential trace elements are present in minute amounts they are just as necessary as the essential macro nutrients and amino acids. For instance, cobalt is needed in the specific form of B₁₂ and its deficiency leads to severe anaemia. In ruminants vitamin B₁₂ is formed in the rumen by bacteria, provided a sufficient amount of cobalt is present in the diet. Deficiency of essential trace minerals in the animal body may lead to disorders that may prove fatal.

Our body contains reserves of several important minerals, which can help reduce the effects of variations in the dietary supply. Chronic dietary decrease of mineral ions in the body can lead to a variety of clinical problems. Alternatively, a dietary excess of mineral ions can be equally dangerous, because storage capabilities of the body are limited.

The first conclusive evidence that cobalt is an essential trace element came from Australia where a serious disease of cattle and sheep developed. Addition of small amounts of cobalt prevented this disease. Nowadays each sheep is made to swallow a ceramic coated cobalt ball that remains in the rumen and slowly releases the cobalt over several years.

1.2.6 Water

Water is the most important constituent of all living tissue. It forms up to 95% of the fresh weight of some animals. We all know that water in the body is lost by evaporation from the respiratory surfaces or through sweat and excretion. Water must therefore, be replenished mainly by drinking water, through food and in small quantities by metabolic processes of the body like synthesis and oxidation of fats, proteins and carbohydrates.

SAQ 1

a) Match the words in Column I with description given Column II.

Column I	Column II.
i) Synthetic ability	a. Amino acids that are required for growth but have to be supplied through diet.
ii) Synthetic disability	b. Most bacteria can produce all the required amino acids from only one nutrient present in their growth medium.
iii) Essential nutrient	c. Humans can synthesise cholesterol from non-sterol precursors but insects cannot

b) Why don't domestic cats and dogs need fruit in their diet while humans do?

1.3 FEEDING MECHANISMS IN ANIMALS

In the previous sections we considered the nutritional requirements of animals. Food intake is used for obtaining energy or for building the body in animals. The has to be ingested by animals means of feeding mechanisms and the larger food molecules after ingestion have to be broken down into simpler constituents before they can be used by the body.

All animals have evolved successful methods for extracting their required nutrition from the environment. Thus we find a diversity of feeding mechanisms or strategies according to the nature of food that an animal can obtain.

You have already studied in detail the different feeding strategies adopted by various invertebrate groups in the Animal Diversity Course (BZYCT -131) and by different vertebrates in Unit 3 (Digestive System) of Volume 1 of BZYCT - 133. Therefore, in this unit we are only going to recapitulate by means of Table 1.5 the major feeding methods adopted by various animal groups, based on the type of food available to them. You can note that taxonomically different animal groups living in the same habitat obtain food in a similar manner. For example, many marine animals (annelids, molluscs, crustaceans, whales herring fish, petrel birds, flamingo birds, baleen whales etc) may be **filter feeders** though the organs concerned with the process of filtration may not be anatomically similar.

Table 1.5: Feeding methods classified according to type of food.

S.No.	Type of Food	Method of feeding	Animals using the method
I.	Small Particles	Digestive vacuoles	Amoeba, Radiolarians
		Use of cilia	Ciliates including Paramecium, Sponges, Bivalves, Tadpoles
		Mucous traps	Gastropods, Tunicates
		Tentacles	Sea cucumbers
		Filter feeding	Annelids, Molluscs, small Crustacean, Herring, Flamingoes, Petrels birds, Baleen Whales
II.	Large food masses	Ingestion of inactive masses	Detritus feeders, Earthworm
		Scraping, chewing, boring	Sea urchins, Snails, Insects, Vertebrates
		Capture and swallowing of prey	Coelenterates, Fishes, Snakes, Birds, Bats,
		Chewing and swallowing	Mammals
III.	Fluid or soft tissue	Sucking plant sap, nectar	Aphids, Bees, Humming-birds,
		Ingestion of blood	Leaches, Ticks, Lice, Insects, Vampire bats
		Sucking milk or similar secretions	Young Mammals and Birds
		External digestion	Spiders
		Nutrient molecules uptake through the integument from the host medium in which they live.	Parasites, Tapeworm
IV.	Dissolved organic solution	Uptake from dilute solution	Aquatic invertebrates
V.	Symbiotic supply of nutrients	Intracellular symbiotic algae	Sponges, Corals, Hydras, Flatworms, Clams

1.4 DIGESTION IN ANIMALS

The process by which the food is broken down into simpler molecules with the aid of enzymes is known as digestion. Fig 1.1 summarises the process of digestion and absorption of ingested food which is applicable to all animals. As you can see in the figure, ingested food which is in the form of complex macromolecules like proteins, carbohydrates and lipids and nucleic acids is digested or broken by means of enzymes into simpler food molecules into amino

acids, simple sugars and glycerols, fatty acids and nucleotides respectively, so that they can be easily absorbed by the body. Important minerals, vitamins, and water present in the ingested foods are also extracted and absorbed from the ingested food from the ingested food by the body during the process of digestion.

DIGESTION

The process by which food is converted into substances that can be absorbed and assimilated by the body

Mechanical and chemical breakdown of food into nutrients.

Four main macromolecules in food:

Nucleic acids, proteins, carbohydrates and fats.



Broken down into smaller molecules of:

Nucleotides, amino acids, simple sugars and fatty acids



being absorbed

Vitamins, minerals, water are also extracted from food during digestion.

Fig.1.1: Digestion is the breakdown of complex, ingested food into simpler food molecules with the help of digestive enzymes for absorption by the body. The digested simpler food molecules help in growth, tissue building and generating energy for various functions of the body.

When **digestion** takes place **within the cell** it is termed as **intracellular digestion** and when it takes place **outside the cell** it is termed as **extracellular digestion**. Extracellular digestion often takes place in a specialized digestive tract. Let us first consider intracellular digestion and see how it differs from extracellular digestion.

1.4.1 Intracellular Digestion

Most organisms that digest food by intracellular digestion belong to Kingdom Protista. This is because unicellular protist organisms do not have a separate alimentary canal system and so digestion in them occurs within their single celled body. Some protists like the amoeba can ingest food particles from any part of their body surface. However, other protists like the paramecium have a fixed point of entry for ingesting food particles and use their beating cilia to create a current for propelling the water that contains food particles into their cytostome (cell mouth). Fig. 1.2 shows the process of intracellular digestion in *Amoeba*. The single celled amoeba engulfs food particles with the help of pseudopodia through the process of phagocytosis/endocytosis. The engulfed food gets enclosed within the food vacuole inside the cell body. The food vacuoles fuse with one of the several lysosomes present in the cell. Lysosomes contain hydrolytic enzymes for digesting the engulfed food contained in the food vacuole. After food digestion by the lysosome the small

digested molecules are retained by the cell while the indigestible remains are released outside the cell into the surrounding environment.

Intracellular digestion occurs in some invertebrates such as sponges, some coelenterates, ctenophores and turbellarians. Although the process is called intracellular digestion, the food material is actually separated from the rest of the cellular material by a membrane that the food can cross only after digestion. In other invertebrate organisms such as cnidarians and platyhelminthes, a gut or enteron is present and both extra and intracellular digestion takes place. In them, extracellular digestion takes place by enzymes secreted into the enteron cavity, and intracellular digestion takes place within the cells that line the enteron cavity. In invertebrates such as annelids and molluscs, digestion is intracellular, though some extracellular digestion does occur. Digestion is entirely extracellular in invertebrates such as nematodes, insects, and echinoderms and in vertebrates.

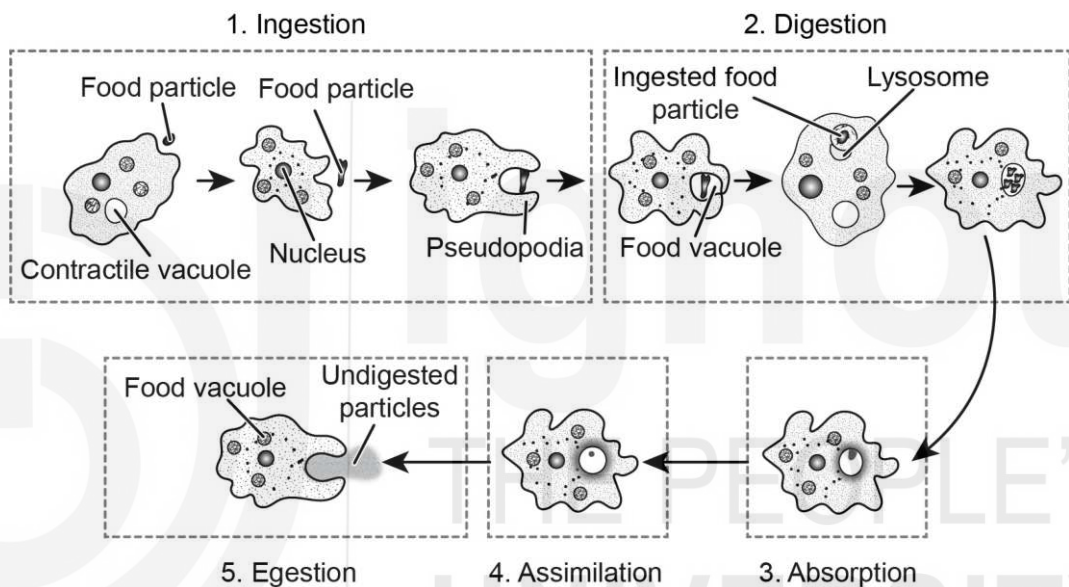


Fig. 1.2: Intracellular digestion in *Amoeba*.

1.4.2 Extracellular Digestion in Alimentary Canal

Extracellular digestion takes place in a tubular cavity that extends throughout the length of the organism. All animals after Phylum Platyhelminthes (flatworms) have a tubular alimentary tract that opens at both ends. The development of extracellular digestion freed many animals from feeding continuously on small particles. Animals could now quickly ingest a few large chunks of food. The overall tubular organization of the digestive tract also allows the food to travel in one direction passing through regions of digestive specialization (Fig. 1.3). In general the digestive system or tract of metazoan animals after Phylum Platyhelminthes is divisible into 4 major functional regions which are as follows :

1. reception region
2. conduction and storage
3. digestion and absorption
4. conduction and formation of faeces

1. Reception Region : Oral or buccal cavity

The region for reception of food is associated with structures i) mastication or chewing of food like teeth; ii) for maneuvering food within the mouth namely the tongue and the iii) salivary glands which secrete saliva containing mucous for lubricating the oral cavity enabling easy movement of the ingested food; iv) Some enzymes are secreted in the oral cavity for preliminary digestion of carbohydrates which may be present in the ingested food is the oral or buccal cavity.

2. Conduction and Storage : Oesophagus

The oesophagus of vertebrate animals and some invertebrate animal conducts the food bolus (mass of chewed food) from the oral or buccal cavity to the stomach by peristaltic movement. In some animals, like birds as you will recall, the oesophagus region has a crop for storage and for mildly fermenting or digesting food. The mildly digested food is later regurgitated by parent birds for their chicks. This storage region when present in a class/phylum of animal allows the animals to store food and use it when it is not easily available.

3. Digestion and Absorption : Stomach and small intestine

In the third digestive region the enzymes reduce the food to a form that can be absorbed by the body of the organism. As the food is digested, the absorbable food is passed into the blood stream for distribution to various parts of the body. Absorption occurs predominantly in the small intestine.

Conduction and Formation of Faeces

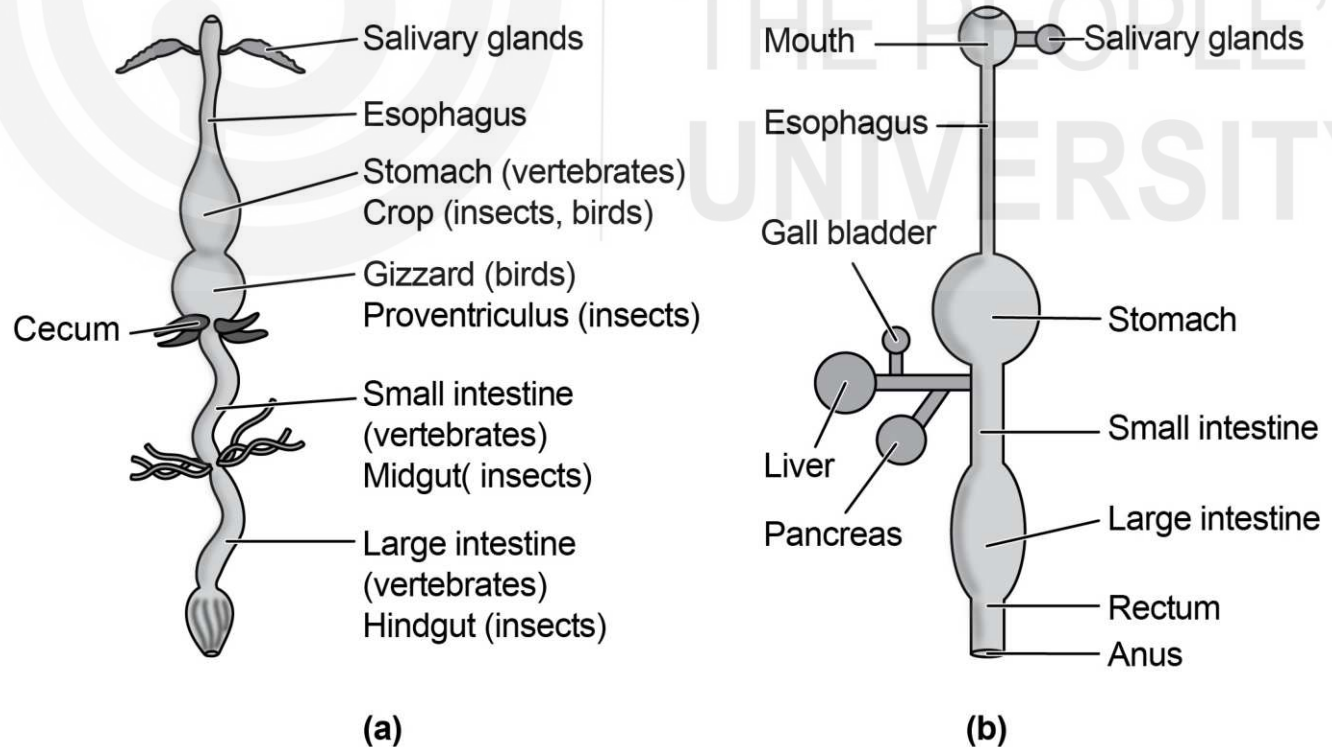


Fig. 1.3: Alimentary card of animals in which digestion is extra cellular a) Generalized digestive tract of invertebrates and vertebrates showing the one way passage of food which allows sequential stages in digestion; b) in humans as an example of vertebrates Dashed lines represent crop in some animals.

The remaining unabsorbed material is carried to the final section of the alimentary canal where further removal or resorption of excess water and consolidation of undigested material to form the faeces takes place. The faeces are stored briefly in the final section of the alimentary canal before being expelled outside the body. In vertebrates this function is carried out in the large intestine.

In higher vertebrates, each area of the alimentary canal or gut is specialized for a certain activity. In the digestive enzymes are produced by glands as by cells present well as in the wall of the alimentary canal. Let us now examine the process of digestion and absorption in greater detail.

SAQ 2

- a) What are the main advantages of having a digestive tract with a mouth and anus?
- b) Choose the correct answer.

Digestion is brought about by

- i) acids
 - ii) enzymes
 - iii) alkaline solutions
 - iv) vitamins and minerals
- c) Fill in the blanks with appropriate words.

In the process of digestion proteins are converted into, carbohydrates to fats to and and nucleic acids into

1.5 DIGESTIVE ENZYMES IN ANIMALS

Digestive enzymes as you know chemically breakdown complex, large ingested food molecules by **hydrolysis** into simpler, smaller, soluble units. The enzymes in order to digest food rupture the chemical bonds of the food to be digested by addition of one or more than one of their water molecules, so that the food is broken down into simpler molecules to the ingested food. You will be studying about the properties and mechanisms of action of enzymes in greater detail in Units 14 and 15 of this course. However, the properties and nature of digestive enzymes show specific differences from enzymes in general in the following ways:

1. Digestive enzymes are not as narrowly specific as other enzymes and instead show **group specificity**. For example, enzymes that digest carbohydrates can digest polysaccharides of both animal and plant origin.
2. Even though enzymes performing similar functions in different animals are given the same names, they are not however, identical chemically. For example, trypsin (an enzyme, that hydrolyses proteins) in humans is not identical to that found in fish. Temperature and pH for optimum

activity also differs. For example, trypsin from vertebrate pancreas acts best in the pH range of 7-9 while in silkworm the ideal pH range is 6.2-9.

3. Digestive enzymes secreted by pancreas particularly those that digest proteins are secreted in an inactive form.

The four major classes of digestive enzymes **in animals** are as follows:

- i) **Proteases** that hydrolyse peptide bonds in proteins,
- ii) **Carbohydrases** that hydrolyse glycosidic bonds in carbohydrate,
- iii) **Lipases** that hydrolyse ester bonds in fats
- iv) **Nuclease** that hydrolyse DNA and RNA into nucleotides

Now let us study the role of these four classes of digestive enzymes in digestion of food.

1.5.1 Action of Proteolytic Enzymes

Protein digestion begins in the stomach and is completed in the small intestine. It is brought about by proteolytic enzymes known as proteases that are synthesized as larger, inactive forms (zymogens) which after secretion, are cleaved to produce active proteases. Enzymes that digest proteins are categorized, based on the site of their action in the protein molecules into two groups : i) **endopeptidases** and ii) **exopeptidases** :

- i) **Endopeptidases** confine their attack to the interior part of the protein molecule so that the large peptide chains are broken into smaller fragments. These smaller fragments provide many more sites for exopeptidases to act upon as endopeptidases cannot breakdown proteins into their monomers.
- ii) **Exopeptidases** digest the smaller protein fragments produced by the action of the endopeptidases. They attack only peptide bonds present at the end of a peptide chain and cause the release of amino acids, dipeptides and tripeptides. There are several types of endopeptidases and exopeptidases of which the main ones are listed in Table 1.6.

As you can see, in the table, the exopeptidases and endopeptidases, attack specific peptide bonds depending on the chemical group near them. The inactive forms of the proteolytic enzymes need activators and autocatalysts for converting them into active forms. For example pepsinogen, secreted by chief cells of the vertebrate stomach is only activated when hydrochloric acid (HCl) which is secreted by the parietal cells of the stomach makes the medium of the stomach acidic (pH 2). The acidic environment of the stomach activates the inactive pepsinogen into the active **pepsin** by altering the conformation of pepsinogen so that it can cleave itself to yield active pepsin.

Table 1.6: Proteases of Animals. Some enzymes are secreted as zymogens that need other enzymes to be converted into their active forms while some proteases are secreted in their active forms but require the presence of ions to be active.

Extracellular Enzyme		
Inactive form (Origin)	Activator → autocatalyst	Active form
Preferred Peptide Link Attacked		
I. ENDOPEPTIDASES		
Pepsinogen (Stomach)	$\xrightarrow[\text{pepsin}]{\text{HCl}}$	Pepsin
		Link to amino group of aromatic amino acid (tyrosine, tryptophan, and phenylalanine)
Trypsinogen (Pancreas)	$\xrightarrow[\text{Trypsin}]{\text{Enterokinase}}$	Trypsin
		Link to carboxyl end of arginine or lysine
Chymotrypsinogen (Pancreas)	$\xrightarrow{\text{Trypsin}}$	Chymotrypsin
		Link to carboxyl group of aromatic amino acid (phenylalanine, tyrosine, tryptophan) and also bonds adjacent to methionine and leucine when they are present.
Proelastase (Pancreas)	$\xrightarrow{\text{Trypsin}}$	Elastase
		Link to carboxyl group of (alanine, glycine, and serine)
II. EXOPEPTIDASES		
Aminopeptidases (Mn^{2+} , Mg^{2+} , Zn^{2+}) (Lining of intestine)		
		Link to terminal amino acid with free amino group
Procarboxypeptidases	$\xrightarrow[\text{(Zn}^{2+})]{\text{Trypsin}}$	Carboxypeptidases
		Link to terminal amino acid with free carboxyl group
Dipeptidases (Mn^{2+} , Mg^{2+} , Zn^{2+}) (Lining of intestine)		
		Bonds between pairs of amino acids

Pepsin acts as endopeptidases and cleaves dietary proteins, composed of large polypeptide chains into a number of short fragments. Pepsin can hydrolyze virtually any peptide bond except for those present in keratin, mucoproteins, and protamines (protamine sulfate is a small positively charged protein derived from salmon sperm which is widely used to neutralize the anticoagulant activity of heparin following cardiac procedures). Pepsin thus, has a broad spectrum of specificity though it prefers to cleave specifically the peptide bond on the amino terminal end between a dicarboxylic and amine group of an aromatic amino acid (phenylalanine, tryptophan and tyrosine) (Table. 1.6 and Fig.1.4 a). In this way short fragments of polypeptide chains

are formed. Invertebrates seem to lack pepsin and their main endopeptidases is more like trypsin. In Table 1.6 you can further note that chymotrypsin also attacks a peptide bond involving an aromatic amino acid but on the carboxyl terminal end of the molecule while pepsin attacks on the amino terminal end.

The polypeptide fragments are further digested by the endopeptidases like **trypsin** (active form of inactive trypsinogen) and several other inactive digestive proenzymes (zymogens) that are secreted by the pancreas into the duodenum of the small intestine and which, when activated, collectively digest the peptides into single amino acids under alkaline conditions needed for digestion in the small intestine.

Trypsinogen secreted by the pancreas into the duodenum of the small intestine is activated into trypsin by another enzyme **enteropeptidase** (also called enterokinase), secreted by the brush border cells of the small intestine. As trypsin is formed, it autocatalytically activates more trypsinogen to be converted into trypsin. Trypsin acts in an alkaline medium between pH 7-9. It breaks a peptide bond next to a basic amino acid like arginine or lysine.

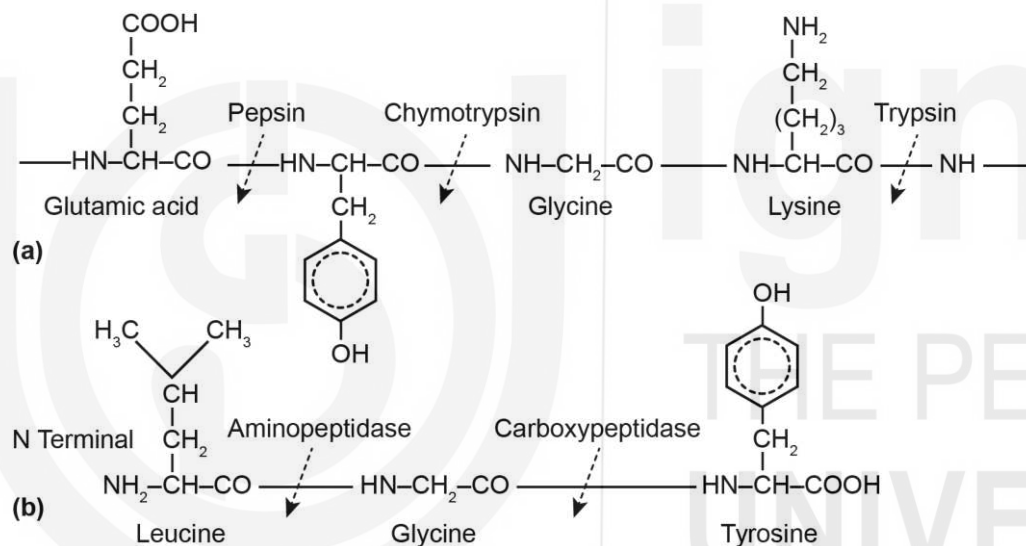


Fig.1.4: Protein digesting enzymes: a) attacking specific peptide bonds in a protein fragment; and b) breakdown of a tripeptide. However, both exopeptidases cannot attack the same tripeptide.

Trypsin cleaves the following proteolytic enzymes: 1) inactive chymotrypsinogen to yield active chymotrypsin; 2) inactive proelastase, to yield active elastase, and 3) inactive procarboxypeptidases, to yield active carboxypeptidases, an exopeptidase. Thus, trypsin plays a central role as the master activator because it cleaves dietary proteins and activates other proteases that cleave dietary protein. Chymotrypsin enzyme hydrolyses proteins that enter the duodenum, into smaller peptides and amino acids. Enzyme elastase breaks down elastin (an elastic fibre protein that, together with collagen, determines the mechanical properties of connective tissue). Enzyme carboxypeptidase splits one amino acid at a time.

Each of these protein digesting enzyme (protease) activated by trypsin exhibits cleavage specificity as you can see in Table 1.6 i) side of chymotrypsin cleaves at the carboxyl side of phenylalanine, tyrosine, tryptophan and leucine; ii) elastase cleaves at the carboxyl side of alanine,

glycine and serine. Carboxypeptidase in the presence of zinc ion and trypsin cleaves single amino acids from the carboxyl terminus. Apart from carboxypeptidase the other exopeptidases are secreted in an active form but all need metal ions as cofactors to increase their activity.

The polypeptide fragments produced due to endopeptidase proteolytic enzymes are further digested by the exopeptidases.

In the action of the endopeptidase is shown in Fig. 1.4 (b) illustrates the action of i) **aminopeptidase** which removes terminal amino acids having free amino groups and ii) **carboxypeptidase** which removes terminal amino acids possessing a free carboxyl group. In this way **aminopeptidase and carboxypeptidase** enzymes progressively remove peptides from each end until a dipeptide fragment consisting of only two amino acids remains. Bonds between these pairs of amino acids are split further by **dipeptidases** which results in release of free amino acids, the simplest components of protein that can be absorbed through the cells lining the wall of the small intestine.

1.5.2 Action of Carbohydrase Enzymes

Enzymes that digest carbohydrates are called **carbohydrases**. Simple sugars like glucose and fructose can be absorbed and metabolized directly by the lining of the small intestine, however, disaccharides such as sucrose or lactose and polysaccharides such as starch and glycogen have to be broken down to monosaccharides before they can be absorbed and used in metabolic pathways. **Carbohydrases** can be grouped into the following two categories:

- i) **Polysaccharases** that split polysaccharides into disaccharides or trisaccharides (oligosaccharides: short chains of three or more monosaccharides).
- ii) **Glycosidases** that break up the disaccharides or trisaccharides to monosaccharides.

The digestion of carbohydrates, similar to proteins occurs in a stepwise manner. The polysaccharase enzyme first splits the polysaccharides into disaccharides or oligosaccharides. After this, the disaccharides or oligosaccharides (the products resulting, due to the action of the polysaccharase enzyme) are further split by the action of glycosidase the second enzyme, into monosaccharides. The enzymes responsible for digestion of carbohydrates and the end products of carbohydrate digestion are given in Table 1.7

Carbohydrate digestion in vertebrates and invertebrates is very similar. All the enzymes shown in Table 1.7 are not required by all animals. However, amylase and maltase are of universal occurrence. The presence of enzymes in the digestive tract of an animal group is related to the food habits. For e.g., Carbohydrate digestion in the human alimentary tract occurs in the following two steps : (i) step one, involves digestion of carbohydrates by enzyme amylase of the salivary glands followed by digestion by alpha(α)-amylase enzyme of pancreas which is secreted into the duodenum in larger amounts in comparison to salivary amylase. The activity of amylase secreted by the salivary glands and pancreas of humans works best at pH of 6.7- 7.5. (ii) Step

two involves digestion of carbohydrates by the enzymes of the brush border cells present in the epithelial lining of the duodenum.

Table 1.7: Digestion of carbohydrates.

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

Enzyme production in some animals is also influenced by genetic characteristics and enzyme induction. For example, production of maltase and sucrase by the intestinal villi depends on the amount of ingested sugar. If a high maltose or sucrose diet is taken, it induces the villi to produce more maltase and sucrase within 2-5 days. Lactase production declines in humans as gut develops after infancy. It ceases in some individuals so that lactose sugar can no longer be digested by them.

Now let us consider the digestion of cellulose, the most important structural material of plants and a major component of the diet of herbivores. Very few animals possess the enzyme cellulase. Then how do animals that feed on plants breakdown this carbohydrate? Cellulase enzymes are synthesized by several microorganisms such as bacteria and protists that live symbiotically in the gut of many herbivores and insects. In herbivores such as ruminants (i.e. cow, sheep, etc.) cellulose digestion is carried on with the help of these **symbiotic microorganisms** which live in the stomach. The breakdown products of cellulose are then utilized by the host. In some invertebrates like the arthropod, silver fish (*Ctenolepisma lineate*) true cellulase enzymes have been reported but the insect cannot survive exclusively on a cellulose diet. Some other invertebrates also have some cellulases that partly digest cellulose. So far however, no conclusive evidence of a complete breakdown of cellulose into glucose without the help of symbionts has been reported.

Between 2-18 per cent of Caucasians lose the capacity to produce lactase and between 95-100 per cent of oriental and native African races lose the ability to produce lactase as they grow older. As a result they can no longer digest milk which as a consequence ferments in their gut and produces diarrhoea and related problems. Interestingly yoghurt and cheese do not create any problems as these contain less than 2 per cent lactose due to action of bacteria.

1.5.3 Action of Lipase Enzymes

Digestion of fats or lipids is similar in both invertebrates and vertebrates.

Lipases are the enzymes that hydrolyse fats in an alkaline medium. A single lipase can catalyse many steps in the breakdown of fat. In vertebrates, lingual

lipase secreted by the tongue, gastric lipase (these two lipases are acid stable) in the stomach and pancreatic lipase (works in alkaline medium) secreted into the duodenum are responsible for digesting lipids. Lipids are hydrophobic, and poorly soluble in the aqueous environment of the digestive tract, so they have to be broken down into fat droplets by the action of lingual lipase and gastric lipase before pancreatic lipase can act on them in an alkaline medium. As a result the fats form droplets and separate from the watery components. Gastric lipase begins to breakdown large aggregates of dietary triglyceride into diglycerides and fatty acids, however very little digestion of fat occurs in the stomach. The key players in the digestion of fats to yield monoglycerides and fatty acids are **bile and pancreatic lipase**.

Bile acids are steroid acids found predominantly in the bile of mammals and other vertebrates. Diverse bile acids are synthesized in the liver. Bile acids are conjugated with residues of amino acids taurine or glycine to give anions called **bile salts**. **Primary bile acids** are those synthesized by the liver while **secondary bile acids** result from bacterial actions in the colon.

Bile juice which is often simply referred to as bile is produced in the liver, flows through the biliary tract and gets stored in the gallbladder from where it is secreted into the duodenum of the small intestine. It is a complex fluid containing water, electrolytes and a large number of organic molecules including bile acids, cholesterol, phospholipids and bilirubin. The bile juice is largely responsible for making the environment in the duodenum alkaline which enables the pancreatic digestive enzymes to function. Bile acids that form bile salts play the first critical role in lipid assimilation by promoting emulsification. As derivatives of cholesterol, bile acids have both hydrophilic and hydrophobic domains (i.e. they are amphipathic). On exposure to a large aggregate of triglycerides, the hydrophobic portions of the bile acids get intercalated (inserted) into the lipid, while the hydrophilic domains remain at the surface. Such a coating by the bile acids aids in the breakdown of large aggregates or droplets into smaller and smaller droplets.

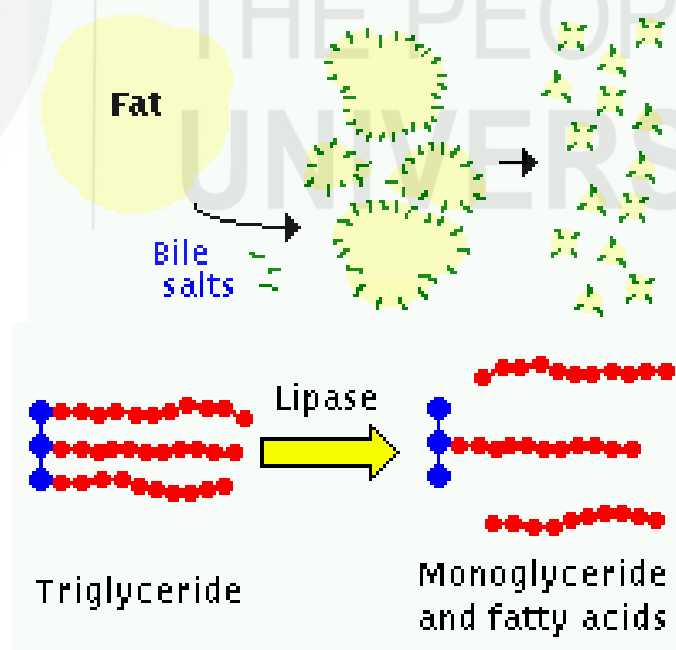


Fig. 1.5: Digestion of fats. a) bile emulsifies the fat globules into smaller droplets. b) pancreatic lipase cleaves the triglycerides and diglycerides in the emulsified fat droplets into free fatty acids and 2-monoglyceride. (Get this made using different colours or shapes the concept is useful)

As monoglycerides and fatty acids are liberated through the action of lipase, they retain their association with bile acids and form structures called **micelles**. Micelles reduce surface tension at the fat-water interface and micelles are essentially small aggregates (4-8 nm in diameter) of a mixture of lipids and bile acids, suspended within the aqueous medium of digested food in the intestine (ingesta). As the ingesta is mixed, the micelles bump into the brush border of the epithelium of the small intestine, with the result that the lipids, including monoglycerides and fatty acids, are taken up into the epithelial cells.

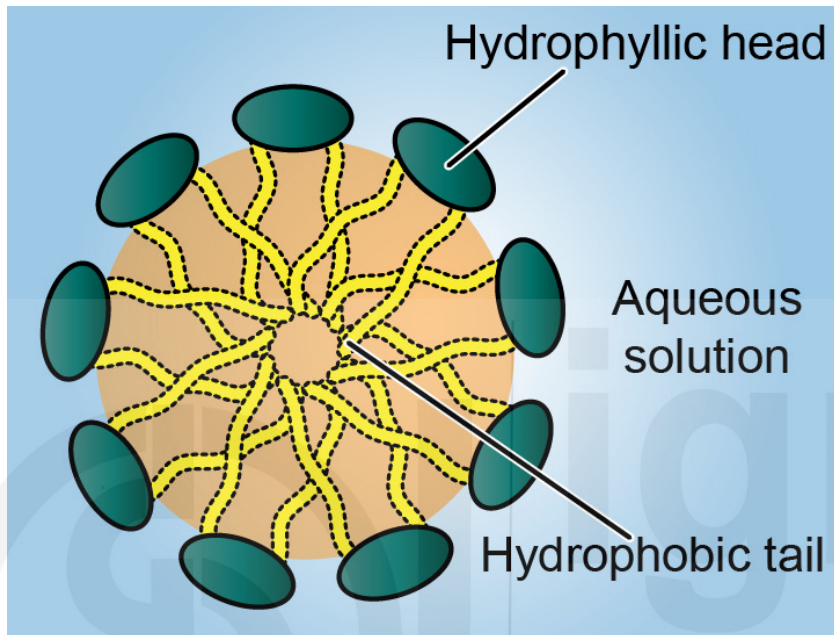


Fig. 1.6: Micelle formation with bile salts, monoglycerides, which is same for fatty acids, phospholipids and cholesterol. Hydrophilic heads of the bile salts make the micelles soluble in watery components in the small intestine.

SAQ 3

- a) Choose the correct answer from the following:
- Enzyme lipase digests lipids while trypsin digests proteins. Both these digestive processes:
 - occur inside cells.
 - add a water molecule to break bonds
 - require zinc to activate the enzymes
 - consume ATP.
 - What role do bile acids and salts play in digestion of complex fats?
 - They catalyze the cleavage of bonds that release fatty acids
 - They emulsify the large fat droplets
 - They digest the complex fats.
 - They activate the lipases

- iii) Carbohydrates are digested by:
 - a. Chymotrypsin in the duodenum
 - b. Lingual lipase in the oral cavity
 - c. Salivary and pancreatic amylase
 - d. HCl and pepsin in stomach
- b) Which of the following organ is **not correctly paired** with its function?
 - i) Stomach - protein digestion
 - ii) Gall bladder - bile juice synthesis
 - iii) Small intestine - nutrient absorption
 - iv) Pancreas - enzyme production
- c) Which of the following is **not a major activity** of the stomach?
 - i) Storage
 - ii) HCl production
 - iii) Nutrient absorption
 - iv) Churning of large food particles

Sometimes, some areas of stomach lining get damaged and gastric ulcers develop. Earlier it was thought that ulcers were caused by psychological stress which resulted in excess acid secretion. However, Australian researchers Barry Marshall and Robin Warren discovered that ulcers are due to infection by the acid-tolerant bacterium *Helicobacter pylori*. They also proved that an antibiotic could cure most gastric ulcers. They were awarded the Nobel Prize in 2005 for these findings.

1.5.4 Maintenance of Gut Lining

After studying the digestive enzymes you must be wondering as to why the gut linings are not digested themselves. This is because animals have several mechanisms that protect their gut lining from autodigestion that is self digestion. Mucous cells of the vertebrates secrete a slightly alkaline mucous that lubricates the food and protects the lining cells from corrosive secretions. In addition, the lateral surfaces of exposed epithelial cells are joined by tight junctions that prevent the digestive secretions from penetrating between them. Careful studies have also revealed that the entire lining of the gut is renewed every third day in rats and every 5-6 days in humans. Similar mechanisms are present in invertebrates also. In insects, the fore-gut and hind gut are lined by cuticle. This lining is known as **intima**. The epithelial cells are exposed only in the midgut, where most of the digestive occurs. The midgut is lined by a delicate lining the **peritrophic membrane** in some insects. This corresponds to the mucous of vertebrates.

1.5.5 Coordination of Digestion in Animals

You have learnt that digestion is a process in which large food molecules are broken down step by step into their constituents. In primitive metazoans that are continuous feeders, the enzyme producing cells secrete continuously. In higher animals more precise controls are needed to regulate the release of food from the stomach in intestine and also for the release of digestive

enzymes at the proper time. The interplay of nervous and hormonal control is beautifully illustrated when we study the coordination of digestive activity.

In the mammalian mouth, control of salivary gland secretion is entirely nervous; gastric secretions are under hormonal and neural control; and intestinal secretions are slower and are primarily under hormonal control.

Gastrointestinal secretion is largely under the control of gastrointestinal hormones secreted by the endocrine glands present in the gastric and intestinal mucosa.

Gastrointestinal Hormones

The three main mammalian gastrointestinal hormones are **secretin**, **gastrin** and **cholecystokinin** (CCK). There are several other hormones, all peptides. The physiology of only three major hormones is listed in Table 1.8. Fig. 1.7 summarizes the action of these three GI hormones.

Gastrin is secreted by the stomach and is responsible for control of HCl volume; the presence of HCl in turn inhibits further gastrin secretion.

Secretin regulates water homeostasis throughout the body and influences the environment of the duodenum by regulating secretions in the stomach, pancreas, and liver. It is a peptide hormone which is secreted in the duodenum in response to acidic chyme and stimulates the pancreas and gall bladder to release a large amount of water and bicarbonates causing the environment of the duodenum to become alkaline and thus neutralize the acid chyme. Secretin is also of some historical interest, as it was the first hormone to be discovered in 1902 by Sir William Maddock Bayliss and Ernest Starling.

Table 1.8: Mammalian gastrointestinal hormones; – denotes inhibition; + stimulation; +++ hormone more important than other two

	Gastrin	Secretin	Cholecystoldnin
Secreted by	Stomach	Duodenum	Duodenum
Stimulus for release	Peptides Parasympathetic	Acid (HCl)	Amino acids fatty acids
Effect on :	Nerves		
Gastric Motility	+	-	-
Gastric HCL Secretion	+++	-	-
Pancreatic secretion			
bicarbonates	+	+++	+
enzymes	+	+	+++

Cholecystokinin (CCK) hormone is produced by the cells lining the duodenum. Arrival of fat and partially digested proteins from the stomach into the duodenum initiates the release of CCK by the intestinal mucosa of the duodenum. CCK induces the secretion and flow of bile and pancreatic juice which are alkaline in nature into the duodenum. Bile juice aids in fat digestion in the duodenum by emulsifying fats while pancreatic juice digest the fats.

The two hormones Secretin and CCK inhibit stomach motility.

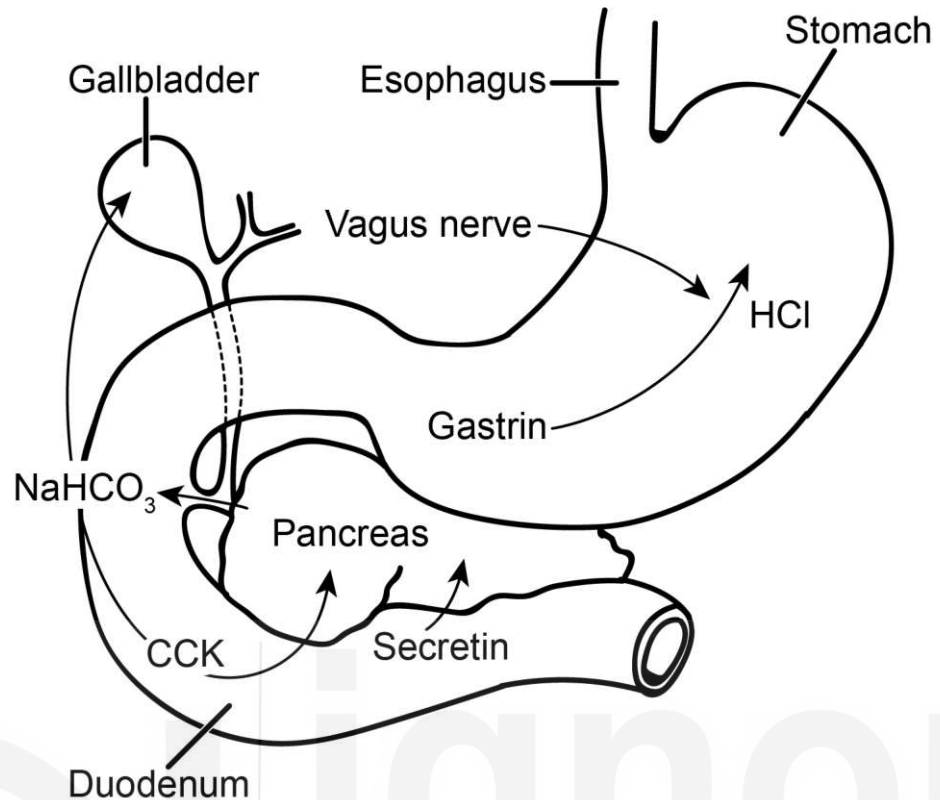


Fig. 1.7: Action of several gastrointestinal hormones. Gastrin is secreted in response to intragastric proteins, stomach distention and stimulation by the vagus nerve. Gastrin from the lower stomach stimulates HCl and pepsin secretion from the secretory cells. Cholecystokinin (CCK) stimulates pancreas to secrete digestive enzymes and alkaline secretions in order to neutralize and digest chyme. It also induces contraction of gall bladder to secrete bile salts. CCK is secreted in response to the arrival of amino acids and fatty acids in duodenum from stomach.

SAQ 4

Fill in the blanks:

Three hormones stimulate the release of digestive materials, ... stimulates the release of gastric juices, ... stimulates the release of bicarbonate ion stimulates release of bile and pancreatic enzymes.

1.6 MECHANISM OF ABSORPTION IN VERTEBRATE ANIMALS

In section 1.5 you have read that once the food has been digested it is absorbed in the small intestine. In animal physiology, **absorption** in higher multicellular organisms is defined as, “the transfer of products of extracellular digestion from the lumen of the gastrointestinal tract to the blood or lymph”. In extracellular digestion absorption occurs in sequence: digestion first,

absorption second. These organizing concepts, however, are inadequate for the animal kingdom as a whole. When digestion is only intracellular, the same cells are involved both in digestion and absorption. In those multicellular animals where some of the digestion is extracellular and most is intracellular, **absorption** in them is defined to be the transfer of food particles from the gut lumen into the cells that digest the particles intracellularly and only later are the digestive products passed into the blood. In higher multicellular animals However, in which digestion is totally extracellular there are usually separate tissues and areas of the gut for enzyme production, digestion and absorption. Thus a general definition of common to all **absorption - also called assimilation animal groups would be the entry of digested food molecules into tissues of the animal.**

In this section we will mainly be concerned with absorption of amino acids, sugars and fats released during extracellular digestion in vertebrates. All of the chemical and mechanical phases of digestion in the alimentary tract in the vertebrates are directed toward changing food into forms that can pass through the absorptive epithelial cells that line the mucosa of the small intestine. As you already know from earlier courses, the wall of the vertebrate intestine is folded and ridged to increase the absorptive surface (Fig. 1.8 a). These ridges or folds are covered by minute absorptive villi (Fig. 1.8 b) which further bear microvilli. The villi are highly specialized absorptive organs with a core containing a network of capillaries derived from blood vessels in the gut wall. Each villus also contains a central lymph capillary known as a lacteal which begins blindly at the tip of the villus and drains into the main lymph channels of the gut wall.

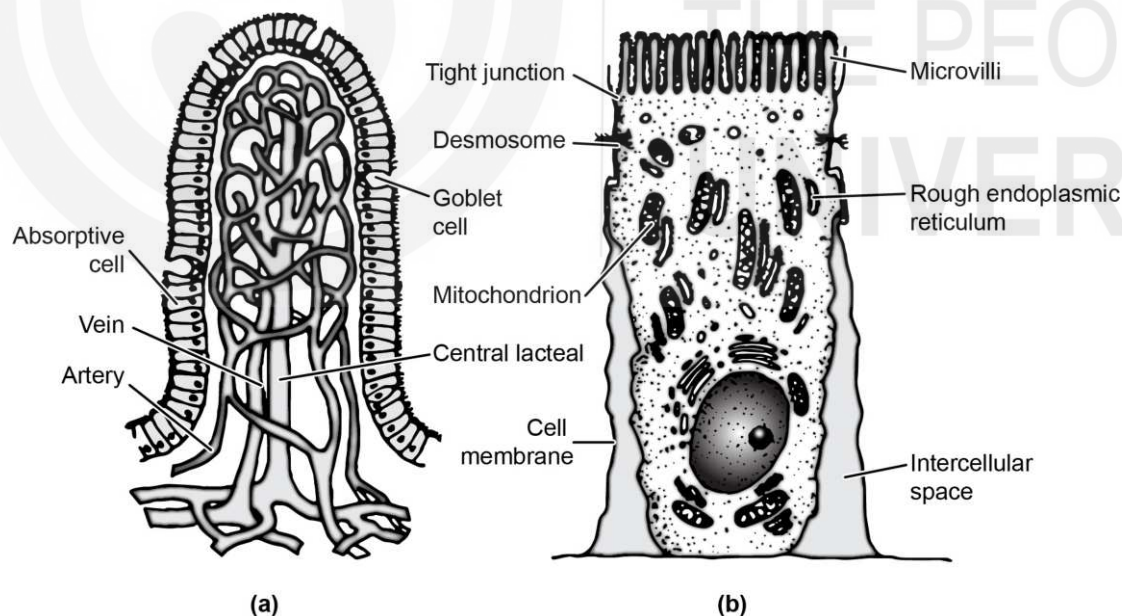


Fig. 1.8: Epithelial lining of the mammalian small intestine : a) Villus covered with digestive epithelium which consists of absorptive cell and occasional goblet cells. b) An absorptive cell under higher magnification showing its apical surface bearing a brush border of microvilli.

The end products of digestion, amino acids, monosaccharides and some of the lipids pass from the epithelial cells of the small intestine into the underlying blood capillaries. The rest of the lipids due to their large size cannot enter the

capillaries and so enter the underlying comparatively larger lacteal (lymphatic vessel). In the present section we will study the movement of the end products of digestion into the blood circulation which is accomplished via any of the following processes- 1) active transport, 2) passive diffusion, 3) facilitated diffusion, 4) co-transport (or secondary active transport), and 5) endocytosis which are briefly defined below:

The transport of sugars and of amino acids takes place through protein transport molecules that depend on the action of sodium pumps and can be blocked by metabolic inhibitors such as cyanide.

1. **Active transport** refers to the movement of a substance or solutes across a cell or biological membrane from an area of lower concentration to an area of higher concentration (against the concentration gradient). In this type of transport, proteins within the cell membrane act as “pumps,” using cellular energy (ATP) to move the substance. Electrolytes like Na ions (Na^+) are absorbed by active transport into the blood.
2. **Passive diffusion** refers to the movement of substances or solutes from an area of higher concentration to an area of lower concentration across a biological or cell membrane. The solute diffuses down its electrochemical gradient and at the end of the process the concentration inside the cell is equal to that of the outside.
3. **Facilitated diffusion** refers to the movement of solutes or substances across the biological or cell membrane along the concentration gradient. In facilitated diffusion, solutes from an area of higher concentration are transported to an area of lower concentration by means of a carrier protein molecule present in the cell membrane. The concentration gradient inside the cell never exceeds that of the outside.
4. **Co-transport (or secondary active transport)** uses the movement of one molecule through the membrane from a higher to lower concentration in order to power the movement of another molecule from lower to higher concentration.
5. **Endocytosis** is a transportation process in which the cell membrane engulfs material. It requires energy, generally in the form of ATP.

All animal groups make use of some of the five processes in the transport of digested nutrients. The absorption of most nutrients is through the mucosa of the intestinal villi via the epithelial cells lining the mucosa. This absorption is usually by means of usually requires active transport, and so is fueled by ATP. Sugars and amino acids are absorbed directly by the blood capillaries while most but not all of the digested lipids pass into the lacteals and then into the blood circulation. Now let us examine the actual processes involved in absorption of the digested food.

1.6.1 Absorption of Monosaccharides

All carbohydrates are absorbed as monosaccharides. All dietary carbohydrates that are normally digested are absorbed, leaving only indigestible cellulose and fibers in the faeces. Monosaccharides pass from the lumen of the small intestine through the apical cells of the epithelial membrane via facilitated diffusion or active transport.

Fructose, a monosaccharide found in fruits, is carried down its concentration gradient by facilitated diffusion. Glucose and galactose are transported into absorptive cells of the villi via secondary active transport process, by being coupled to the active transport of Na^+ (Fig 1.9). The best-known transporter molecule of glucose and galactose in the apical (epithelial) cells is a co-transporter protein molecule termed as sodium–glucose transporter 1 (SGLT1). The cotransporter protein molecule is so called because it couples the transport of a glucose or galactose molecule with that of a sodium ion. The energy needed in the transport of glucose or galactose is provided by the movement of sodium ion along its gradient. The co-transporter protein molecule enables the cells lining the lumen of the intestine to absorb even very small traces of glucose or galactose from the digested food despite, the fact that the epithelial cells may already have high concentrations of glucose or galactose inside them.

Once the glucose is inside the epithelial cell, the sodium ion is pumped out by ATP energized active transport and the glucose molecule is transferred to the blood stream through another transporter molecule, called **Glucose transporter 2** (Glu T2), along its concentration gradient (Fig. 1.9). Glu T2 transports glucose via facilitated diffusion into the blood capillaries of the villi. Glu T2 transports glucose into the blood capillaries in proportion to the sugar concentration present in the blood. If more glucose is present in the blood, then the transport of glucose slows down and if glucose content of blood is low then transport of glucose is accelerated. Galactose competes with glucose to ride the same transporter molecule which is also termed as a symporter (defined as an integral membrane protein involved in the movement of different molecules or ions in the same direction across a biological or phospholipid membrane) since Na^+ and both glucose or galactose move in the same direction, with the help of the same transporter molecule.

Glu T2 is one of the 5 glucose transport molecules known to carry glucose across cell membranes. These transporters are broadly similar in structure and function and are numbered in the order of their discovery. These transporters change their configuration, so that one shape of the transporter molecule binds glucose on its extracellular side and the other shape binds glucose in the intracellular side. This binding and transportation in a flip-flop manner is very rapid.

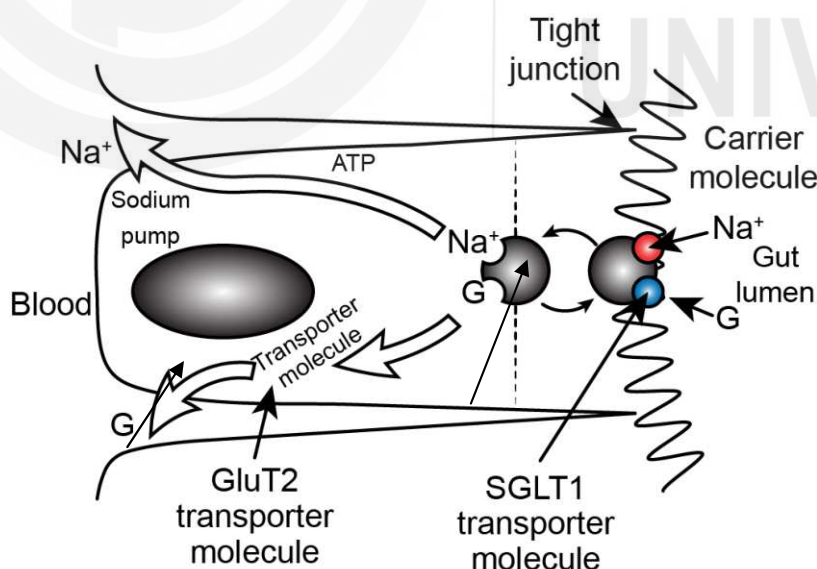


Fig. 1.9: Mechanism for absorption of glucose: Na^+ and glucose/galactose are transported together from the gut lumen into the intestinal epithelial cells of the by the carrier protein molecule SGLT1 also called as SGLT1 cotransporter molecule located on the epithelial cell membrane. Inside the cell, sodium (Na^+) is moved out by the ATP pump while the glucose is taken up by another transporter protein molecule termed as Glu T2 and transported into the blood capillaries via facilitated diffusion.

1.6.2 Absorption of Amino Acids, Dipeptides, and Tripeptides

Most proteins are absorbed as amino acids via active transport processes that occur mainly in the duodenum and jejunum of the small intestine during digestion. Normally, 95–98% of the proteins present in the small intestine are digested and absorbed. Absorption of most amino acids into the absorptive cells of the villi of the small intestine occurs via Na^+ dependent secondary active transport processes that are similar to the glucose transporter of monosaccharides. The plasma membrane of the absorptive cell of the small intestine bears at least four sodium-dependent amino acid transporters - of which two are for transport of neutral amino acids, one for basic and one for acidic amino acid. These transporter molecules are termed as **sodium-dependent amino acid transporters** since they bind to amino acids only after binding to a sodium ion. The fully loaded transporter molecule with the sodium ion and amino acid undergoes a conformational change that releases the sodium ion and the amino acid into the cytoplasm of the epithelial cells of the duodenum or jejunum of the small intestine. This is followed by the absorption of the amino acid by the blood capillaries surrounding the villi and reorientation of the transporter molecules back into their original form.

Another separate transport system exists for the absorption of dipeptides and tripeptides into the absorptive epithelial cells of the small intestine. A symporter molecule brings in dipeptides and tripeptides together with a hydrogen ion (H^+) inside the absorptive cells of the small intestine where they are hydrolyzed into single amino acids by intracellular peptidases.

There is virtually no absorption of peptides that are longer than four amino acids, except in neonates of humans and rodents who for a very few days after birth have the ability to absorb intact proteins after which this ability is rapidly lost (see Box 1.2).

Box 1.2

The ability to absorb intact proteins even for a few days after birth is of immense importance because it allows the newborn animal to acquire passive immunity by absorbing immunoglobulins in the colostral milk. In contrast to humans and rodents, there is no significant transfer of antibodies across the placenta in many animals (cattle, sheep, horses and pigs etc.) in which the young are born without circulating antibodies. However if the newborn babies of these animals are fed colostrum during the first day or soon after birth, they then absorb large quantities of immunoglobulins and acquire a temporary immune system that provides protection until they generate their own immune responses.

In the adult mammals, all the amino acids, which move into the absorptive epithelial cells of the small intestine after protein digestion, exit the absorptive cells via diffusion and enter the blood capillaries. The absorbed amino acids, similar to monosaccharides are ultimately transported via the blood stream into the liver by the hepatic portal system. If not removed by hepatocytes, they enter the general blood circulation.

1.6.3 Absorption of Lipids

The products of digestion of fats and oils (triacylglycerols) by the digestive activities of enzyme lipases are free fatty acids, glycerol, and 2-monoacylglycerols (glycerol with a single fatty acid). About 95 percent of lipids are absorbed in the small intestine. Small short-chain fatty acids are more water-soluble and can dissolve in the watery intestinal chyme, pass through the absorptive cells via simple diffusion, and follow the same route taken by monosaccharides and amino acids into a blood capillary of a villus (Fig. 1.10). However, large short-chain fatty acids (with more than 10-12 carbon atoms), long-chain fatty acids, and monoglycerides present in chyme that enter the duodenum from the stomach are large in size and are not water-soluble, due to which they have difficulty being suspended in the watery environment of the intestinal chyme. Bile salts formed from bile acids of the bile juice and lecithin present in the chyme resolve this by enclosing these insoluble fat molecules into a **micelle**, which is a tiny sphere with polar (hydrophilic) ends facing the watery environment and hydrophobic tails turned to the interior. The core of the **micelle** also includes cholesterol and fat-soluble vitamins. Once formed, the micelles move from the lumen of the small intestine into the brush border of the absorptive cells. At this point the insoluble fatty acids, cholesterol and fat-soluble vitamins diffuse out of the micelles into the absorptive epithelial cells of the small intestine, leaving the micelles behind in the chyme. The micelles continually repeat this ferrying function as they move from the brush border back through the chyme to the lumen of the small intestine to pick up more of insoluble fatty acids, monoglycerides cholesterol and fat soluble vitamins.

The free fatty acids and **monoacylglycerides** that enter the absorptive epithelial cells of the small intestine recombine together to reform into triglycerides within the absorptive cells. The recombined triglycerides mix with phospholipids and cholesterol present in the absorptive cells, and get enclosed in a protein coat, forming a new water-soluble complex lipoprotein called **chylomicron** (Fig.1.10). The large sized chylomicrons are processed by the Golgi apparatus within the epithelial absorptive cells after which they exit these epithelial cells of the small intestine. The chylomicrons are unable to directly enter the blood capillaries due to their large size and so instead enter into the lacteal, which is the lymph vessel located at the core of each villus. The lacteals contain patches of endothelial cells that are held together through specialized "button junctions" which are much more permeable to chylomicrons than the normal cellular junctions. The lymph containing the chylomicrons passes through the button junctions into the lacteals and from there into larger vessels of the lymphatic system and eventually reaches the circulatory system. Once in the circulatory system, the enzyme **lipoprotein lipase** breaks down the triglycerides of the chylomicrons into free fatty acids and glycerol which can then pass through capillary walls either to be used for energy by cells or for getting stored in adipose tissue as fat. Liver cells combine the remaining chylomicrons remnants with proteins, forming lipoproteins that transport cholesterol in the blood. Two or three hours after a meal, few chylomicrons remain in the blood. After participating in the emulsification and absorption of lipids, most of the bile salts are reabsorbed by

active transport in the ileum of the small intestine and are returned by the blood to the liver through the hepatic portal system for recycling.

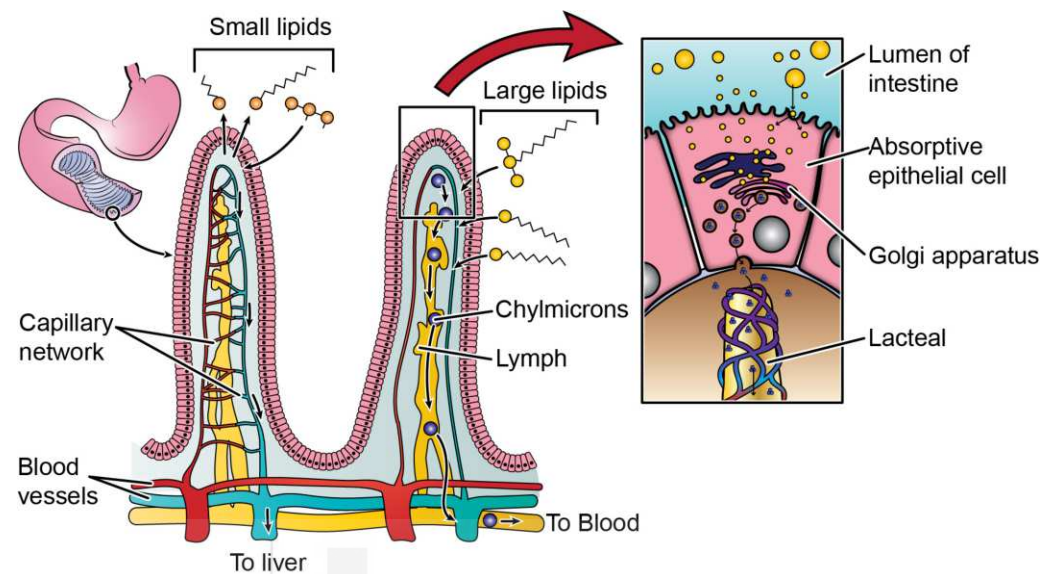


Fig. 1.10: Fatty acids and monoglycerides from the micelles within the small intestine are absorbed by the epithelial cells and resynthesised into triglycerides. These are then coated by protein to form chylomicrons which enter the lacteals of the small intestine.

SAQ 5

- a) Which nutrient of among following is absorbed mainly in the large intestine?
 - i) glucose
 - ii) amino acid
 - iii) sodium
 - iv) water
- b) Why are villi present in the small intestine and not in the stomach?

1.7 Physiology of Digestion in Mammals

In the earlier sections you read that the process of digestion is similar in vertebrates, including mammals. Now that you know the general mechanisms of digestion and absorption let us see how those can be applied in the physiology of digestion in humans that we take as an example of a mammal.

1.7.1 Digestion in Oral Cavity

A pair of lips protects the **oral cavity** (mouth) and helps retain the food as it is being chewed. The oral cavity contains the tongue and teeth (Figure 1.11). The process of food digestion begins in the oral cavity as soon as a bite of food

enters into it. The mechanical action of the teeth and tongue and the chemical action of saliva begin to break down the **ingested** food. **Three major pairs of salivary glands** constantly **secrete watery** fluid called saliva.

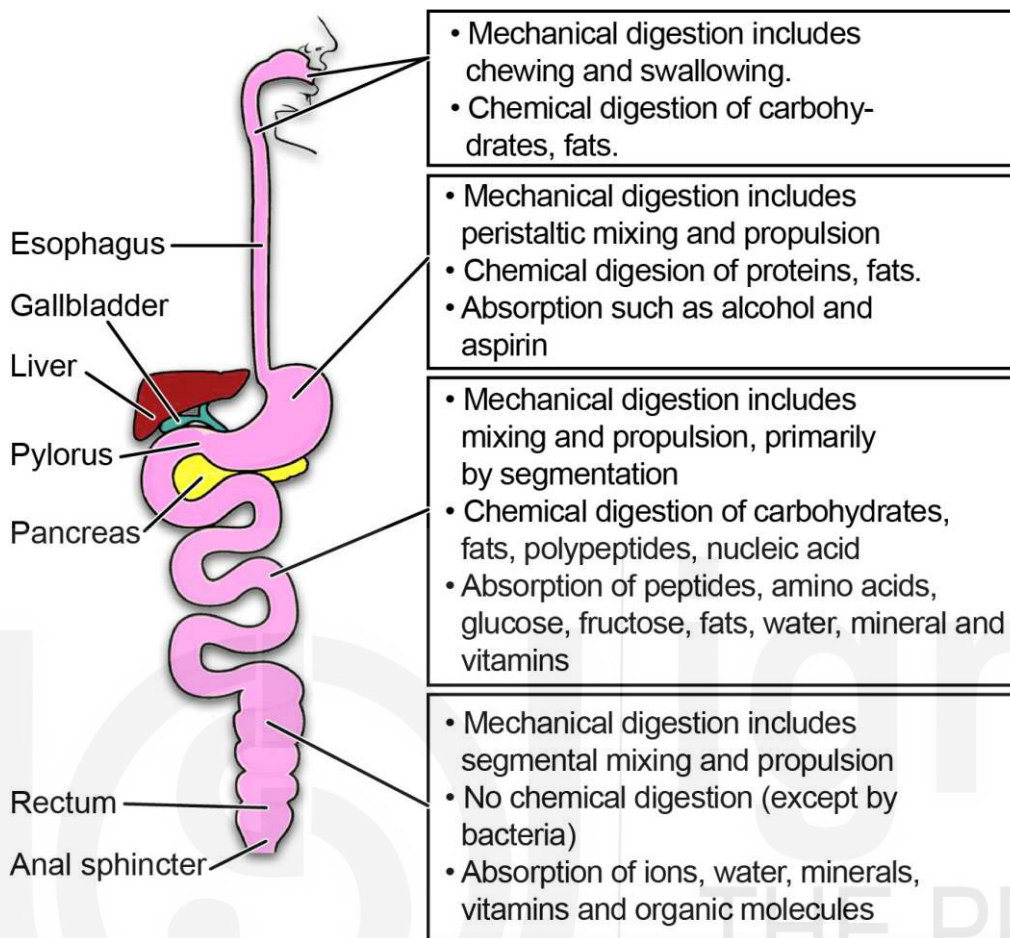


Fig.1.11: Human Digestive system and its associated glands. Digestion begins in the mouth and continues in the stomach and small intestine as the food travels through the alimentary canal. Most absorption also occurs in the small intestine while some absorption especially water takes place in the large intestine.

Among the three pairs of salivary glands: i) **parotid glands** produce a thin watery serum like secretion that contains a large amount of salivary amylase enzyme which breaks down starches (complex carbohydrates); ii) **sublingual glands** produce mucous that acts as a buffer and lubricant; and iii) **submandibular glands** secrete a mixture of buffers, salivary amylase and glycoproteins called mucins which in contact with water produce mucous, and. **Lingual glands are present in the tongue** and secrete both mucous and a watery **lingual lipase** which acts on as much as 30% of dietary triglycerides converting them into simpler fatty acids and diglycerides.

The salivary mucous serves to moisten and lubricate the food for easier swallowing, protects the gums against abrasion, and facilitates taste and smell. The saliva contains bicarbonate ions (HCO_3^-), which buffer chemicals in the mouth, and help prevent tooth decay. The saliva also contains lysozymes which kill microorganisms that enter the mouth with food.

The function of the salivary amylase is to begin starch (a polysaccharide) digestion by cleaving the bonds that link glucose monomers to produce

disaccharide such as maltose, trisaccharide such as maltotriose, and short-chain glucose polymers called α -dextrins.

The tongue movements manipulate the mixture of saliva and food, into a ball shaped structure called a food bolus. The food bolus, once formed is pushed with the help of the tongue to the back of the oral cavity (Fig. 1.12) and triggers swallowing or deglutition of the bolus into pharynx/throat. Swallowing can be voluntary, but most of the time it is involuntary. At the start of swallowing, food is prevented from entering into the respiratory system by the larynx which moves upwards, closing the epiglottis and so prevents the food from entering into the respiratory tract (Fig. 1.12). Once swallowing of food is begun the nervous system completes it due to a nerve reflex. Prior to the entry of the food bolus into the oesophagus, the oesophageal sphincter relaxes, allowing the bolus to enter from the pharynx. Unlike the pharynx the hollow, muscular tube like, oesophagus actively moves the food bolus into the stomach by peristalsis which is automatic and is caused by alternate contraction and relaxation of the circular and longitudinal muscles which line the alimentary canal from esophagus to anus. Mucous secreted by the esophageal glands lubricates the bolus and reduces friction. The passage of solid or semisolid food from the mouth to the stomach takes 4 to 8 seconds; very soft foods and liquids pass through in about 1 second. **Neither the pharynx nor the esophagus contributes to digestion.**

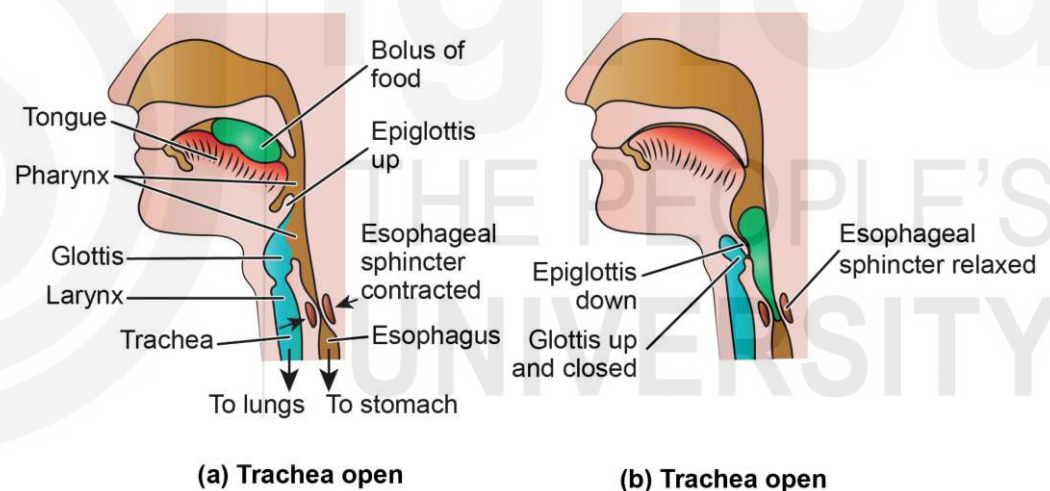


Fig. 1.12: Intersection of the human airway and digestive tract: In humans, the pharynx is the common passage for the oesophagus of the digestive system and the trachea, of the respiratory system and at most times a) a contracted sphincter seals off the oesophagus while the trachea remains open; b) When a food bolus arrives at the pharynx, the swallowing reflex is triggered due to which the upper part of the airway, the larynx moves upwards which tips a flap of tissue called the epiglottis downwards, thus preventing the food from entering the trachea. At the same time, the esophageal sphincter relaxes, allowing the bolus to pass into the oesophagus. Once the bolus passes into the oesophagus the trachea then reopens, and peristaltic contractions of the esophagus move the bolus to the stomach.

1.7.2 Digestion in Stomach

The stomach, located just below the diaphragm is a muscular, distensible sac with accordion-like folds to accommodate about 2 liters of food and fluid and is

guarded by valves called **sphincters** on both its ends (the gastro-oesophageal sphincter at the oesophageal end of the stomach and the pyloric sphincter located at the lower end of the stomach). The stomach mechanically and chemically digests the food bolus by its muscular contractions and by the action of hydrochloric acid and gastric enzymes. The wall of the stomach as you have learnt earlier in the second semester is composed of the same four layers that make up most of the gastrointestinal (GI) tract: inner most mucosa, submucosa, muscularis, and serosa (Fig1.13). The epithelial layer of the stomach mucosa is a **secretory sheet** consisting of simple columnar epithelium that contains many types of cells.

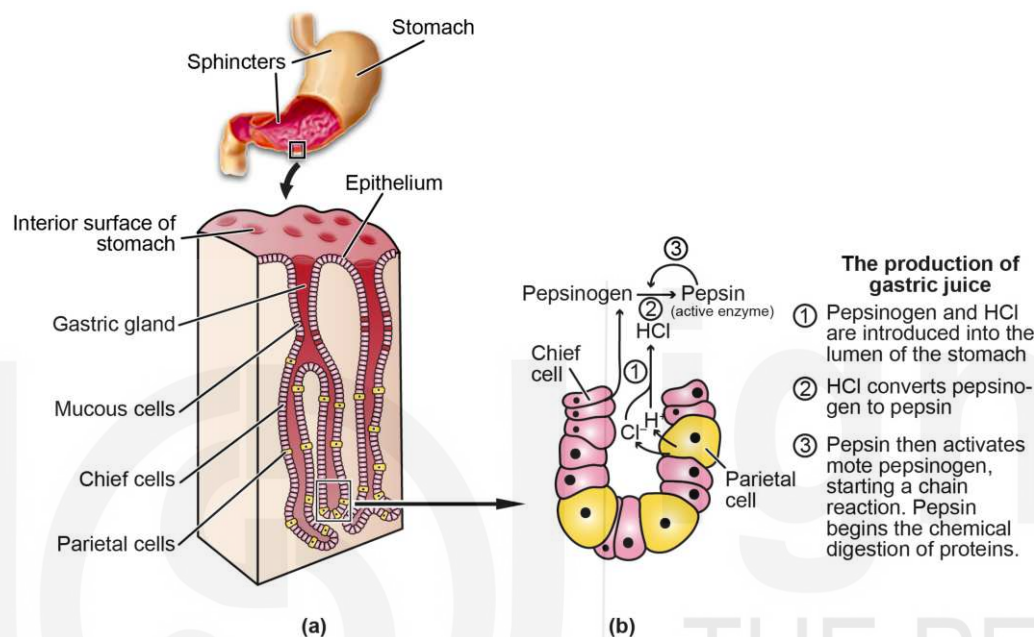


Fig.1.13: a) The human stomach with its absorptive cells and secretions; b) Production of HCl by the parietal cells.

Glands in the pyloric part of the stomach secrete alkaline mucous rather than enzymes or acids. Mucous covers the entire surface of the stomach protecting its inner epithelial lining against the action of acid and enzymes secreted by the stomach cells. The fundus region of the stomach contains thousands of gastric glands that secrete gastric juices. Gastric glands are dominated by two types of secretory cells namely, **parietal cells** and **chief cells**. **Parietal cells secrete** hydrogen ions that form the hydrochloric acid in the lumen of the stomach. **Parietal cells also secrete** an intrinsic factor, a glycoprotein that helps in the absorption of vitamin B₁₂ across the lining of the small intestine. The **chief cells secrete pepsinogen**, the precursor of the protease enzyme pepsin. Both the cells are in the pits of the gastric glands. The secretions of the mucous, parietal, and chief cells constitute the **gastric juice**, which totals 2000–3000 milliliter (ml)/day and which is a nearly colorless, strongly acidic, liquid consisting of mucous, hydrochloric acid (HCl), and the proteolytic digestive enzymes pepsin and rennin (found primarily in the gastric juice of infants which acts on milk proteins converting casein into paracasein).

In addition, several types of enteroendocrine cells are scattered among the mucous secreting cells lining the stomach. These enteroendocrine cells produce at least seven hormones, of which the most notable Gastrin, is produced by **G cells**, which are most abundant in the gastric pits of the pyloric

region. Gastrin stimulates the secretion of both parietal and chief cells, as well as contractions of the gastric wall that mix and stir the gastric contents. The pyloric region also contains enteroendocrine **D cells** which secrete somatostatin, a hormone that inhibits the release of gastrin. D cells continuously release their secretions into the interstitial fluid adjacent to the G cells. Neural and hormonal stimuli can override this inhibition of gastrin production when the stomach is preparing for digestion or is already engaged in digestion. Several other hormones play a role in hunger and satiety (feeling of not being hungry). Another hormone from the stomach and small intestine, the **obestatin**, is thought to decrease appetite and inhibit thirst.

The food bolus may remain in the stomach for about an hour without becoming mixed with gastric juice. During this time, digestion by salivary amylase from the salivary glands continues. Soon, however distention of the stomach due to the arrival of food as well as the act of eating causes the gastric pits to secrete HCl and pepsinogen. The HCl inactivates the salivary amylase and activates the lingual lipase that acts in an acidic medium.

Parietal cells use an ATP driven pump to expel hydrogen ions produced by them into the stomach lumen. At the same time, chloride ions present in the parietal cells diffuse into the stomach lumen through specific membrane channels of the parietal cells. It is therefore only within the stomach lumen that hydrogen and chloride ions combine to form HCl (see Fig. 1.13 b). The concentration of HCl is high, causing the pH of gastric juice to be about 2, which is acidic enough to dissolve iron nails (and to kill most bacteria)

The gastro-oesophageal sphincter at the proximal of the stomach occasionally, allows a back movement, or flux, of the chyme from the stomach back into the lower end of the esophagus which causes painful irritation of the esophagus. This is referred to as acid reflux but is more commonly known as "heartburn."

Hydrochloric acid (HCl) in the stomach lumen disrupts the extracellular matrix that binds cells together in meat and plant material. It further increases the exposure of the peptide bonds of the food present in the stomach for the digestive enzymes to act upon. Protein digestion in humans starts only from the stomach. HCl converts pepsinogen to active enzyme pepsin (a **protease**, or protein-digesting enzyme), by clipping off a small portion of it and exposing its active site. As you must have noted, both HCl and the active pepsin form in the lumen (cavity) of the stomach and not within the cells of the gastric epithelium ensuring that parietal and chief cells are not digested from within by their secretions. Furthermore, the lining of the stomach is replaced every 5-6 days to prevent damage to the stomach. The hydrochloric acid converts a small amount of inactive pepsinogen into active pepsin by clipping off a small portion of it and exposing its active site. The pepsin, then itself autoactivates pepsinogen into pepsin. Pepsin, similar to HCl, can clip pepsinogen to expose the enzyme's active site (see section 1.4 again). Digestion of protein is also aided by the mechanical action of smooth mucosal muscles of the stomach which contract and vigorously churn and mix the stomach contents about every 20 seconds. About three to four hours after a meal, the stomach contents are sufficiently mixed to form an acidic semi-liquid chyme which contains the hydrolysed proteins that have been converted into smaller and simpler polypeptides by the action of enzyme pepsin.

The pyloric sphincter regulates the passage of chyme into the small intestine, allowing only one squirt of chyme to enter at a time." When the stomach is empty, peristaltic waves cease. However, after about 10 hours of fasting, new

waves may occur in the upper region of the stomach. These waves can cause “hunger pangs” as sensory nerve fibers carry impulses to the brain.

1.7.3 Digestion and Absorption in Small Intestine

The stomach leads into the small intestine which is the longest section of the digestive tube and begins at the pyloric sphincter of the stomach. The small intestine coils through the central and inferior part of the abdominal cavity, and eventually opens into the large intestine. In humans the small intestine consists of three segments that form a passage from the beginning of the small intestine upto the beginning of the large intestine. The three segments of the small intestine are as follows:

- **Duodenum:** is the first segment of the small intestine. It is a short section that receives secretions from the pancreas and liver via the **pancreatic and common bile ducts**.
- **Jejunum:** is the mid segment part of the small intestine after the duodenum and roughly forms 40% of the small intestine in humans,
- **Ileum:** is the **posterior most part of the small intestine after the jejunum** and forms about 60% of the small intestine in humans. Ileum empties into the large intestine.

The wall of the small intestine similar to the stomach is composed of: mucosa, submucosa, muscularis, and serosa and similarly the mucosa is lined by a layer of epithelium consisting of simple columnar epithelium that contains many types of cells. As you will recall from the previous course BZYCT-133, the total surface area of the small intestine is greatly increased by large circular folds present in them and by the finger shaped projections called **villi** that project from the epithelial lining of the circular folds (Fig.1.8 a also see Fig.1.14 again). This total surface area of the small intestine is further increased by the fact that the villi also have microvilli which are projections of the apical (free) membrane of the villi (Fig.1.8 b& c).

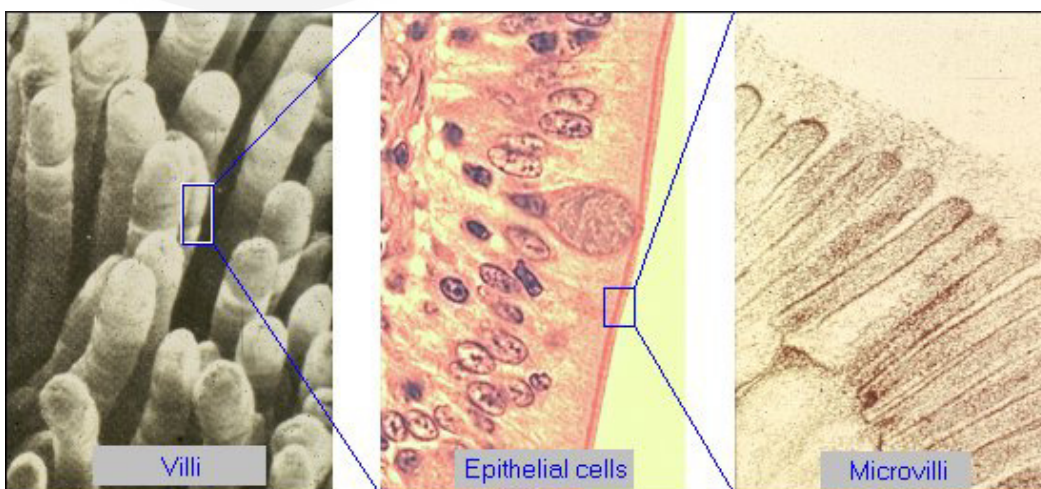


Fig.1.14: Micrographs of Intestinal folds or villi enlarged to show their composition in the human intestine. Source
(<http://www.vivo.colostate.edu/hbooks/pathphys/digestion/smallgut/anatomy.html>)

Absorptive cells (Fig. 1.15) present in the intestinal epithelium take up and deliver into blood virtually all nutrients from the ingested food. These cells also release enzymes that digest the food in chyme and absorb nutrients through the microvilli. Also present in the epithelium are **goblet cells**, which secrete mucous (Fig. 1.15). The mucosa of the small intestine contains many deep crevices lined with glandular epithelium. Cells lining the crevices between the villi form **crypts of Lieberkühn** (Fig. 1.15) which are lined largely with younger epithelial cells which are involved primarily in secretion of electrolytes.

Besides absorptive cells and goblet cells, the intestinal epithelial lining of the small intestine also contains paneth cells and three types of enteroendocrine cells (Fig. 1.15). **Paneth cells** may have a role in regulating the microbial population in the small intestine as they are capable of phagocytosis and secrete the bactericidal enzyme lysozyme. The three types of enteroendocrine cells found in the intestinal epithelium of the small intestine are **S cells**, **CCK cells**, and **K cells**, which secrete the hormones **secretin**, **cholecystokinin (CCK)** and **glucose-dependent insulinotropic peptide (GIP)** respectively. Importantly, towards the base of the crypts of Lieberkühn are **stem cells** (Fig. 1.15), which continually divide and provide the source of all the epithelial cells in the crypts and on the villi. Stem cells in the crypts divide to form daughter cells. One daughter cell from each stem cell division is retained as a stem cell. The other becomes committed to differentiate along one of four pathways to become absorptive cells, or goblet cells, or paneth cells, or enteroendocrine cells.

The chyme containing, partially digested carbohydrates, proteins, and lipids, enters the duodenum which is the first section of the small intestine, primarily involved in further digestion of the food. The **submucosa** of the duodenum contains duodenal glands, called **Brunner's glands** (Fig. 1.15), which secrete an alkaline mucous that helps neutralize gastric acid in the chyme coming from the stomach. As a result complete digestion of carbohydrates, proteins, and partial digestion of lipids, is accomplished in the duodenum by the collective action of: (1) intestinal gland cells, located in the duodenum wall, which secrete daily about 1–2 liters of **intestinal juice which is** a clear slightly alkaline (pH 7.6), yellow fluid, containing water and mucous. The alkaline pH of intestinal juice is due to its high concentration of bicarbonate ions (HCO_3^-). (2) alkaline bile juice containing bile salts, produced by liver, stored in the gall bladder and released from it into the duodenum and (3) the alkaline digestive juices from the pancreas. Thus an alkaline liquid medium is provided that aids the digestion and absorption of nutrients from chyme in the small intestine.

The presence of nutrients partially digested proteins and entry of the acidic chyme into the duodenum, trigger **the CCK cells** in the small intestine to secrete hormone cholecystokinin. Pancreatic enzymes enter the duodenum in response to secretion of cholecystokinin. Most of the digestive enzymes that act on the chyme in the small intestine are secreted by the pancreas and enter the small intestine via the pancreatic duct. You already know from section 1.5 that the pancreatic enzymes include the following: (1) proteolytic enzymes which include- (i) proteases which break apart large protein complexes, and

(ii) peptidases, which break small peptide chains into individual amino acids. (2) alpha-amylase, a carbohydrate digesting enzyme that breaks down certain starches (pancreatic alpha (α)-amylase is almost identical to salivary amylase). (3) pancreatic lipase, which breaks down certain complex lipids/fats, releasing products (such as fatty acids) that can be easily absorbed. (4) Nucleases, which break down RNA or DNA. Nucleotides that result from the action of the nucleases are further digested by brush-border enzymes called **nucleosidases** and **phosphatases** into pentoses, phosphates, and nitrogenous bases. These products are absorbed via active transport by the small intestine.

Only a **few starches** are **digested in** chyme leaving the **stomach**. Most of the carbohydrate digestion also occurs in the duodenum of the small intestine. The pancreatic enzyme amylase digests those starches that have not already been broken down in the stomach. Although pancreatic amylase acts on both glycogen and starches, it has no effect on another polysaccharide called cellulose, an indigestible plant fiber that is commonly referred to as “roughage” as it moves through the digestive system.

Recall from Section 1.5 that the brush-border cells secrete four carbohydrate-digesting enzymes called α -dextrinase, maltase, sucrase, and lactase which digest ingested molecules of carbohydrates into disaccharides and into monosaccharides. **α -dextrinase** acts on α -dextrins, clipping off one glucose unit at a time. **Maltase** splits maltose and maltotriose into two or three molecules of glucose, **Sucrase** breaks sucrose into a molecule of glucose and a molecule of fructose and **lactase** digests lactose into a molecule of glucose and a molecule of galactose. Digestion of carbohydrates ends with the production of monosaccharides, which the small intestine is able to absorb.

Fats in the form of triglycerides and phospholipids and are also digested primarily in the duodenum of the small intestine. We have already learnt how triglycerides are emulsified by bile secretion before pancreatic lipases cleaves them into fatty acids and 2- monoglyceride and before it diffuses into the absorptive cells of the small intestine.

The contents of the duodenum next move by peristalsis into the jejunum which is involved in both digestion and absorption of nutrients and so also secretes fluids. From jejunum, the contents of the duodenum move by peristalsis into the ileum, which is the posterior most part of the small intestine and is primarily involved in absorption of nutrients digested in duodenum. Thus the digestion of carbohydrates and proteins is completed in the small intestine. Most of the lipids are also digested in the small intestine.

Once digestion is largely complete in the duodenum the absorption of the end products of digestion namely amino acids, simple sugars, fatty acids, glycerol, and nucleotides) takes place across the lining of the jejunum and ileum of the small intestine. In addition to absorbing nutrients, the jejunum and ileum also absorbs most of the water, vitamins and dissolved mineral ions. Depending on the nutrients, absorption of the digested nutrients across the epithelial cells of the small intestine can be passive or active. Much of this absorption involves

Bile secretion also contributes to the destruction of red blood cells that are no longer fully functional. Pigments released as a result of red blood cell destruction are incorporated into bile pigments, and eliminated from the body along with faeces. In some liver and blood disorders, bile pigments accumulate in the skin, resulting in a yellowing called jaundice.

The fat-soluble vitamins A, D, and E are absorbed in the upper small intestine. The factors that cause the malabsorption of fat can also affect the absorption of these vitamins. Vitamin B12 is absorbed in the ileum and must be bound to an intrinsic factor, a protein secreted in the stomach, in order to be absorbed. If intrinsic factor is missing, then Vitamin B12 is not absorbed and pernicious anemia results.

active transport and sodium dependent ATPase pump about which you have already learnt in section 1.6 in greater detail.

1.7.4 Absorption in Large Intestine

The digested food from the small intestine reaches the large intestine. The large intestine includes as you know the colon, caecum and rectum (see Fig. 1.11 again). The caecum is important in mammals that eat large amounts of plant material as fermenting of ingested material, occurs in it. Compared with many other mammals, humans have a small caecum.

The wall of the large intestine contains the typical (Fig. 1.16) four layers found in the rest of the GI tract: mucosa, submucosa, muscularis, and serosa. The mucosa is similarly covered by simple columnar epithelium, which contains mostly goblet and absorptive cells. The goblet cells secrete mucous that lubricates the passage of the colonic contents while the absorptive cells are primarily involved in water re-absorption (Fig. 1.16). The major function of the large intestine is reabsorption of water and minerals, and formation and storage of faeces. It takes 12-24 hours for food material to travel the length of the colon which similar to small intestine also osmotically recovers some of the remaining water that is returned to the lymphatic system and bloodstream. Typically most of the water consumed by a person in a day is reabsorbed by the small and large intestines per day and only about 0.1 litre of the water is not reabsorbed. By the time chyme has remained in the large intestine for 3-10 hours, it becomes increasingly solid or semisolid because of water absorption. Insufficient, water reabsorption by the small and large intestine causes diarrhea while excessive reabsorption of water by the small and large intestine causes the faecal matter to become too thick, resulting in constipation.

Minerals diffuse or are actively transported from the food residue across the epithelial surface of the large intestine into the bloodstream as peristaltic waves move food residue along in the large intestine.

The final stage of digestion occurs in the colon through the activity of bacteria that inhabit the lumen. Bacterial products that are absorbed in the colon include several vitamins needed for normal metabolism. Chyme is prepared for elimination, by the action of bacteria, which ferment any remaining carbohydrates and release hydrogen, carbon dioxide, and methane gases. These gases contribute to **flatulence** in the colon. Bacteria also convert any remaining proteins to amino acids and breakdown the amino acids into simpler substances, some of which get eliminated in the faeces and contributes to the odour of the faeces while the rest are absorbed and transported to the liver. In the liver these compounds are converted to less toxic compounds and excreted in the urine. Bacteria also decompose bilirubin of the bile juice into simpler pigments, including stercobilin, which gives faeces their brown color. The faeces is a mixture of water, inorganic salts, bacteria, products of bacterial decomposition, undigested plant fiber, sloughed-off intestinal cells, and other waste products and is stored in the **rectum**, before being discharged outside by the anus. **This process of the faeces being discharged outside through the anus is called egestion (take care not to confuse egestion with excretion).**

SAQ 6

- a) The mammalian trachea and esophagus both connect to the:
- pharynx
 - stomach
 - large intestine.
 - Rectum
- b) Where does the chemical digestion of starch begin?
- mouth
 - esophagus
 - stomach
 - small intestine
- c) Which among these enzymes is involved in the chemical digestion of protein?
- pancreatic amylase
 - trypsin
 - sucrase
 - pancreatic nuclease
- d) Digestion **does not take place** in the:
- duodenum
 - oesophagus
 - mouth
 - stomach
- e) Which group of nutrients **do not require to be digested**?
- Protein, and vitamins, water
 - Fats, minerals and proteins
 - Minerals, vitamins and water
 - Water, carbohydrates and minerals
- f) What would happen if the stomach is unable to secrete hydrochloric acid?
- g) Why is bile juice important in digestion?
-

1.8 ENERGY METABOLISM IN ANIMALS

In the preceding sections we have studied how the products of digestion are absorbed and transported to the tissues via the blood. You have also learnt

that generally carbohydrates and fats are the fuel that provide energy. The oxidation of these compounds yields virtually all the chemical energy required by the body of the animal. This use of chemical energy is the animal's **energy metabolism**. We can also define energy metabolism as the process of generation of ATP from the nutrients by a series of interconnected pathways that function in the presence or absence of oxygen (you will learn more about the chemical pathways in Volume 2 of this course. Aerobic metabolism converts one molecule of glucose into 30-32 ATP molecules.

The rate at which energy is used by the body during both external and internal activities is known as the metabolic rate. Most of the body's energy expenditure or usage eventually appears in the form of heat, and so metabolic rate is normally expressed in terms of the rate of heat production in kilocalories per hour. The basic unit of heat energy is the calorie, which if you can recall "is the amount of heat required to raise the temperature of 1 g of water (H₂O) by 1°C". This unit is however, considered too small to be convenient when discussing the enormous amount of heat involved in the human body and so as a result the energy in the human or mammalian body is calculated in kilocalorie or Calorie, which is equivalent to 1000 calories. Thus, when nutritionists speak of "calories" in quantifying the energy content of various foods, they are actually referring to kilocalories or Calories.

One of the ways used to find out the **rate of metabolism** or the actual amount of energy liberated in oxidative metabolism is to measure the total heat produced by the organism per unit of time that is

Metabolic rate = energy expenditure/unit of time or

Metabolic rate = Rate of energy intake – rate of energy loss /unit time

Energy is the chemical energy content of the ingested food over a given time and energy loss is the chemical energy that remains in the faeces and urine produced by the animal. Through experiments it has been found out that the carbohydrates and lipids are fully oxidized to carbon dioxide and water during metabolism but proteins are not fully oxidized as the end product of protein metabolism which is urea possesses some energy. The energy contained in energy-yielding nutrients such as carbohydrates and lipids differ because the energy-yielding nutrients are composed of different types of chemical bonds. Carbohydrate or protein in a food yields approximately 4 kilocalories per gram of energy, whereas the triglycerides that compose fat in a food yield 9 kilocalories per gram of energy.

Although carbohydrates, proteins, and fats require different amounts of O₂ for their oxidation and yield different amounts of kilocalories when oxidized, an average estimate referred to as energy equivalent of O₂, can be made on the basis of the quantity of heat produced per liter of O₂ consumed. The most convenient and commonly used measure to determine metabolic rate of an animal is to find the oxygen consumption per unit of time since the heat produced for each liter of oxygen used is the same for all nutrients (proteins, lipid and carbohydrates) irrespective of the type of food oxidized. Therefore, it was found that on an average the value of energy (in the form of heat) liberated per liter of O₂ consumed, is 4.8 kcal. It was also determined that oxygen consumption per unit weight per unit time decreases with higher body weight of animals. In other words a mouse or shrew has a much higher metabolic rate than an elephant; consequently smaller animals need to feed constantly while larger animals can survive without food for a longer time.

Energy storage

As we said above, food intake and energy expenditure for animals is approximately equal. If energy expenditure exceeds food intake, then the excess energy is taken up by utilization of body fat. However, if food intake is excess, then the surplus is stored as fat irrespective of the kind of food eaten.

Excess carbohydrates are changed to fats. This is because fats contain relatively less oxygen and the excess oxygen of carbohydrates is used in the metabolism. This reduces the oxygen uptake and as a result the respiratory carbon dioxide to oxygen ratio is increased. For this reason fat is an ideal storage material for energy. It is much lighter and yields twice as much energy as the carbohydrates. Migratory birds that may have to fly more than 1000 km non-stop, carry fat as 40% to 50% of their body weight.

Nonetheless, some carbohydrates are important in energy storage. Glycogen, a starch-like carbohydrate polymer is stored as granules in the skeletal muscles and liver of vertebrates. During heavy muscular exercise when blood does not deliver sufficient oxygen to meet demands, glycogen provides the energy. It is broken down directly into glucose-6-phosphate, providing fuel for carbohydrate metabolism more directly than fat does.

On the other hand, many animals that do not move about, also store glycogen as excess energy source. For example, clams, oysters and many intestinal parasites like *Ascaris* use glycogen as the energy storage material. These animals have to face anaerobic conditions and in such situations glycogen breaks down to acetic acid to yield energy.

SAQ 7

A person who is on a diet and does not consume any fat but only rice and sweets still keeps still gaining weight. Why?

1.9 SUMMARY

In this unit you have studied that:

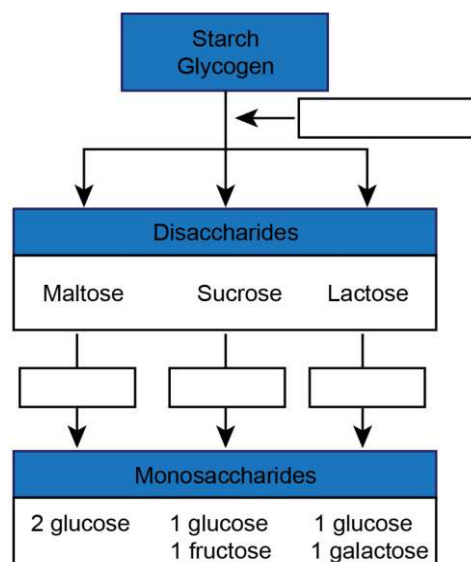
- All heterotrophic organisms require a balanced diet of nutrients to survive, grow and meet their energy demands. Nutrients that must be supplied to the animals in diet are called essential nutrients and the requirement for these essential nutrients indicates the animal's synthetic ability. Animals also have a quantitative requirement for nutrients and if they don't get the required amount, deficiency syndromes and suboptimal growth results.
- Food is obtained by animals in different ways and the feeding strategies have evolved according to the nature of food required.
- Digestion is the breakdown of complex food molecules into simpler constituents and two broad categories of chemical digestion are seen - intracellular and extracellular. Intracellular digestion is characteristic of primitive animals and extracellular digestion of the higher forms. Extracellular digestion of proteins, carbohydrates and lipids is a step by step process in which large food molecules are broken down by the

action of specific enzymes. Lipases are not as specific as carbohydrases and proteases.

- Secretion of digestive juices is under neural and hormonal control. All gastrointestinal hormones are peptides. Both direct activation by the arrival of food chyme in the gut and neural activation stimulate the endocrine cells of the alimentary canal to secrete hormones.
- The products of digestion are taken up by the absorptive cells of the intestine and transferred to the blood capillaries and lymphatic system. Transport of some sugars occurs by facilitated diffusion which does not require metabolic energy. Most sugars and amino acids are transported with Na^+ and a carrier molecule requiring energy. The products of fat digestion are absorbed by diffusion across cell membranes.
- The absorbed nutrients provide fuel for body metabolism. The chemical energy used in metabolism can be measured as heat energy. A given class of food will liberate the same amount of heat and require same amount of oxygen when oxidized to its end products of carbon dioxide and water. The heat production and oxygen consumption helps provide the metabolic rate of an animal.

1.10 Terminal Questions

1. What are essential nutrients? Why is it that certain nutrients are essential for some animals and non-essential for others?
2. Make a table that shows the characteristics of intracellular and extracellular digestion. List out some advantages of extracellular digestion from that information.
3. What prevents the walls of the stomach of animals from being digested by the HCl secreted by it?
4. What are the end-products of food that can be absorbed by the body? Explain how absorption of fats differs from absorption of proteins and sugars.
5. Fill in the names of the enzymes associated with carbohydrate digestion in humans in the chart given below:



1.11 Answers

Self-Assessment Questions

1.
 - a)
 - i) matches b
 - ii) matches c
 - iii) matches a
 - b) Because these animals can synthesise vitamin C while humans and some fruit eating mammals have lost the ability to synthesise vitamin C.
2.
 - a) It permits different parts of gut to specialize for performing different digestive functions.
 - b) ii) enzymes
 - c) amino acids, monosacchrides, fatty acids and glycerol, nucleotides.
3.
 - a)
 - i) b. add a water molecule to break bonds
 - ii) b. They emulsify the large fat droplets
 - iii) c. Pancreas - enzyme production
 - b) ii) Gall bladder— bile juice synthesis
 - c) iii) Nutrient absorption
4. gastrin, secretin, cholecystokinin.
5.
 - a) iv) water
 - b) The small intestine is mainly responsible for the absorption of the end products of digestion. The villi and their microvilli in the small intestine increase the absorptive surface area of the small intestine so that a considerably larger amount of the end products of digestion can be absorbed. The stomach, on the other hand, secretes HCl and digestive enzymes which aid in food digestion and so the stomach have not requires villi structures.
6.
 - a) i) pharynx
 - b) i) mouth
 - c) ii) trypsin
 - d) ii) oesophagus
 - e) iii) Minerals, vitamins and water
 - f) Hydrochloric acid disrupts the extracellular matrix that binds cells together in meat and plant material ingested by the mammal and activates pepsinogen into pepsin in an acidic environment in the stomach which digests proteins. Lingual lipase also acts on lipids in an acidic medium. Digestion will not take place in stomach if HCl is

not secreted by it as in the absence of HCl the extracellular matrix that binds the cells together in meat and plant material will not be disturbed and partial lipid and protein digestion by lingual and gastric lipase and pepsin respectively will not take place as both lipase and pepsin act in an acidic medium. Furthermore, activation of pepsinogen into pepsin will not take place so protein will not be digested in the stomach. HCl also kills the harmful bacteria in the stomach and so in the absence of its production the growth of these harmful bacteria may occur in the stomach which may adversely affect the health of the individual.

- g) Bile is secreted by the liver. It plays an important role in digestion. First being alkaline in nature the bile juice helps in neutralizing the acidic chyme and making the environment of the duodenum of the small intestine alkaline. The most important role the bile juice plays is that it causes the emulsification of fats. Bile juice also helps in the absorption of fats. The bile salts reduce the surface tension of the large fat droplets and make them into smaller droplets. Lipase which acts on these smaller fat droplets is activated by bile salts.

7. Excess carbohydrates that are not used for metabolism are converted to fats and stored in the body. This increases the body weight.

Terminal Questions

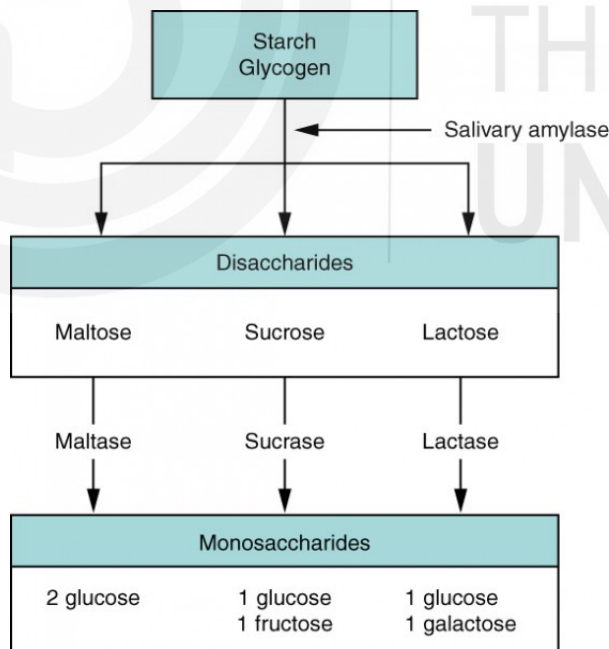
1. Essential nutrients are materials the animals need to sustain life but cannot synthesise in their cells. The nutrients that are essential differ for each type of animal because the ability to synthesise is genetic and species specific. For example, most vertebrates can synthesise vitamin C but human and guinea pigs have lost this synthetic ability. Therefore, vitamin C is essential for us but non-essential for some others.

2.	Intracellular	Extracellular
	Ingestion of small particles	Ingestion of large food masses
	Digestive enzymes enclosed in a small area. One kind of enzyme acts at one time in digestive vacuole	Usually well-developed digestive tract that allows secreted enzymes to act on food in different parts at the same time, digestion occurs in different phases at the same time.
	Suited to continuous feeding	Suited to discontinuous feeding
		Two opening, a mouth and anus in complex animals so that food passes in one direction

For more complex, freely moving organisms extracellular digestion is more advantageous because they don't have to feed continuously and a division of labour in the digestive tract occurs so that only a few cells are devoted to the digestive processes. Digestion can occur in different phases at the same time.

3. A lining of mucous is secreted by the goblet cells which coats the entire digestive tract and prevents the action of HCl and enzymes. Furthermore, most of the digestive enzyme especially the proteases are present in inactive form and HCl does not form in the cells lining the stomach, instead it forms in the lumen of the stomach and so the cells lining the stomach are not corroded by the action of HCl. In addition the stomach lining is replaced within a few days so in case the lining gets damaged it would soon be replaced.
4. Carbohydrates are hydrolysed to monosaccharides. Proteins are hydrolysed to amino-acids and fats are hydrolysed to the free fatty acids and glycerol.
- Amino acids and glucose enter the intestinal epithelial cells by a carrier or cotransporter protein molecules that depend on the action of a sodium ion pump. Free fatty acids or monoglycerides form micelles with bile salts before entering the intestinal epithelium through diffusion.
 - Amino acids and glucose are passed on to the blood stream through another transporter molecule while fatty acids and monoglycerides form chylomicrons within the epithelial cells of the mucosa of the small intestine chylomicrons then move from the epithelial cells of the mucosa of the small intestine and enter the lacteals from where they enter the blood stream.

5)



RESPIRATION |

Structure

2.1	Introduction	2.6	Transport of Gases in Blood
	Objectives		Hemoglobin
2.2	Respiratory Gases		Oxygen Transport in Blood
	Partial Pressure		Carbon Dioxide Transport in Blood
	Solubility	2.7	Summary
	Diffusion of Gases	2.8	Terminal Questions
2.3	Modes of Respiration	2.9	Answers
2.4	Human Respiratory System		
	Upper Airways		
	Lower Airways		
2.5	Lungs		
	Structure		
	Pulmonary Ventilation		
	Lung Volumes and Capacities		
	Gas Exchange in Alveoli		
	Regulation of Respiration		

2.1 INTRODUCTION

You have learnt in Unit 1 that virtually all animals depend on oxidation of food materials for their energy requirements. They utilize oxygen and produce carbon dioxide during the course of their metabolism. The process of oxygen uptake and release of carbon dioxide is called respiration. Respiration, includes two processes: 1) **external respiration**, which involves the absorption of O_2 and removal of CO_2 from the body as a whole; and 2) **internal respiration**, that involves utilization of O_2 and production of CO_2 by cells and the gaseous exchanges between the cells and their fluid medium. You have already learnt about the aspects of external respiration from the course BZYCT-133 (Comparative Anatomy and Developmental Biology of Vertebrates) which you had studied earlier in semester two. Animals as you are aware take up oxygen from the medium they live in. Aquatic animals take up oxygen from water and terrestrial animals take in air from the atmosphere

from air. In this unit, the processes involved in the uptake of O_2 and removal of CO_2 by the lungs will be discussed along with the transport of O_2 and CO_2 to and from the tissues.

In the beginning of this unit, we will explain some of the physical properties of gases as, it is important for you to understand the underlying principles of gases and their behavior. This will help you in understanding respiratory physiology. The exchange of oxygen and carbon dioxide within an organism can occur only when they cross a barrier of living tissue. In the simplest animals gas exchange, takes place through the skin or through the plasma membrane (unicellular). In most multicellular animals respiration is more complex as all the cells of the multicellular organism are not in direct contact with the respiratory medium (air or water). Therefore, respiratory strategy of animals depends on the medium in which the animal lives (aquatic or terrestrial). You have already learnt about respiration of aquatic vertebrates Unit 4 of the second semester course “Comparative Anatomy and Developmental Biology of Vertebrates”. This unit focuses on the acquisition of oxygen by animals from the environment and its distribution to the cells where it is needed for cellular respiration. You will also learn in this unit how the same distribution system elements carbon dioxide or metabolic wastes. In the present unit we will study the mechanisms involves in the process of respiration in mammals by using the example of a human lung which is a good example of an air breathing organ. Later in this unit you will also learn about the respiratory pigment (haemoglobin) that aid in the transport of oxygen.

In this unit, you will note that the circulatory system has been referred to quite often within it is somewhat difficult to discuss one system with the exclusion of the other. As we go further through the course you will realise that in higher animals all systems function in an integrated manner and no system is able to function alone. In the next unit we will discuss circulatory system in detail where we will again discuss some of the mechanisms from this unit.

Objectives

After studying this unit you should be able to:

- ❖ define and calculate the partial pressure of each of the important gases in the atmosphere at sea level,
- ❖ explain the need for gas exchange between the environment and respiratory surfaces in animals,
- ❖ explain the process of ventilation of human lung and list the passages through which air passes from the exterior to the alveoli in the lungs
- ❖ name and define lung volumes and capacities and give approximate values for each in a normal human adult,
- ❖ explain the process of gas transport between the blood and tissues in mammals; and
- ❖ discuss the role of haemoglobin in the transfer of oxygen and compare it to the transport of carbon dioxide in blood.

2.2 RESPIRATORY GASES

You must have studied in Class XI that physiologically the most important gases are oxygen, carbon dioxide and nitrogen. Molecular oxygen comprises 21% of the atmospheric air; carbon dioxide makes up only 0.3% while nitrogen forms 78.0%. All the gases present in the air exert a combined pressure which is referred to as **one atmosphere** (760 mm Hg = millimeters of mercury) or 101.3 k Pa (kilogram Pascal). You must remember that all the gases of concern in respiratory physiology are simple molecules that are free to move among one another, by the process called “diffusion.”

Most of the oxygen is in the air but some of it is also dissolved in the water bodies. An animal's immediate source of oxygen or respiratory medium depending on its habitat therefore, is either air or water. Comparison of the gaseous composition and physical characteristics of air and water highlight the adaptations made by terrestrial and aquatic animals to overcome the problems of respiration. For example, the oxygen content of air is about 20 times that of water saturated with air. The diffusion rate for oxygen in air is much more than the diffusion rate in water. Moreover, carbon dioxide diffuses more rapidly from air into water. Thus, extraction of oxygen and elimination of carbon dioxide from different media (water and air) require special strategies depending on the physical properties of gases.

To understand the physiology of respiration, you must have a basic knowledge of some of the physical properties of gases. The exchange of oxygen and carbon dioxide either in the respiratory organ or at the tissue level is dependent on the partial pressure, concentration and diffusion of gases. Let us consider them one by one.

2.2.1 Partial Pressure

Have you ever got the pressure of air in the tire/ tube of your car/bike/scooty/cycle checked? When you do this, you are measuring the pressure exerted by the gas molecules colliding with the walls of the tire/ tube. You all know that air is a mixture of different gases. Therefore, the total pressure P in that tire/tube will be a sum of the **partial pressures** exerted by all the gases in the mixture. This is **Dalton's law of partial pressures**.

Dalton's law of partial pressures states that the total pressure of a mixture of gases is equal to the sum of the partial pressures of the component gases:

$$P_{\text{Total}} = P_{\text{gas 1}} + P_{\text{gas 2}} + P_{\text{gas 3}} \dots$$

So, we can calculate partial pressure of a gas x as:

$$P_x = (x/100)P \quad \dots(1)$$

where P_x is the partial pressure of the gas

x is the percentage of the specific gas in the total volume

P is the total pressure of the mixture (101.3 k Pa or 760 mm Hg, for dry air).

Thus partial pressure for oxygen at sea level would be

$$P_{O_2} = \frac{21}{100} \times 760 = 159.6 = 160 \text{ mmHg}$$

and for carbon dioxide the value would be

$$P_{O_2} = \frac{0.03}{100} \times 760 = 0.228 = 0.3 \text{ mm Hg}$$

When you calculate the partial pressure of a gas in air, you must remember that atmospheric air is not always dry. It usually contains water vapour which contributes to the total pressure of atmospheric gases. The amount of water vapour varies with temperature. For instance at 37°C the partial pressure of water vapour – P_{wv} is about 47.26 mm Hg. Under these conditions we subtract the water vapour from total atmospheric pressure as gases contribute only 712.74 mm Hg of the total pressure. Therefore, the equation (1) given above must be modified to accommodate water vapour.

$$p_x = \frac{x}{100} (P - P_{wv}) \quad \dots(2)$$

Therefore, when we calculate the partial pressures at sea level of the other gases in the air reaching the lungs we will get P_{O_2} (partial pressure of oxygen) = 160 mm Hg; P_{CO_2} (partial pressure of carbon dioxide) = 0.3 mm Hg; and P_{N_2} (partial pressure of nitrogen + including the other inert gases) = 564 mm Hg.

2.2.2 Solubility

We know that gases are soluble in liquids and this solubility of gases is dependent on partial pressure, temperature and presence of other solutes in the liquid. When the solubility of oxygen, carbon dioxide and nitrogen in water were compared at different temperatures, it was seen that carbon dioxide has the highest solubility followed by oxygen and nitrogen which was the least soluble. The solubility of all three gases decreased as temperature was raised from 0 to 30 degrees Celsius showing that for any given partial pressure of a gas, solubility of the gas is inversely proportional to temperature. It is important to note that the solubility of gases decreases in the presence of other solutes or salinity.

The amount of a gas in a liquid is directly proportional to the partial pressure of that gas in contact with the liquid. This is known as “**Henry’s Law of gas solubility**” and explains why deep sea divers may suffer from decompression symptoms if they rise out of water very rapidly. Gas solubility is given by the following equation

$$P = H_v \times M$$

where P is the pressure, H_v is Henry’s proportionality constant which is a value different for different gases and M is the molar concentration of the gas.

It should be noted that a gas that is highly soluble in a liquid has a lower partial pressure than a gas which is less soluble.

2.2.3 Diffusion of Gases

Diffusion is the movement of a substance from an area of high concentration to an area of low concentration. Diffusion happens in liquids and gases

because their particles move randomly from place to place. Diffusion is an important process for living organisms as most substances move in and out of cells.

In the case of gases moving between different body compartments, diffusion occurs from areas of higher partial pressure to areas of lower partial pressure. You already know from sections 2.2.1 and 2.2.2 that partial pressure of a gas in a solution is determined by its concentration and also by the solubility of the gas in the solution. The diffusion of gases on the basis of their partial pressure gradient, ends only when the partial pressure in both areas becomes equal. This phenomenon is true in aqueous solutions, within mixtures of gases and across gas-water interphase.

In later sections we shall see how the movement of oxygen and carbon dioxide depends on the partial pressure gradient that exists at the inter phase between **vascular fluids** and **air in lungs**. Within the body at the capillary level the intracellular fluids and vascular fluids develop opposed partial pressure gradients and hence gases move in opposite directions.

Having studied the physical basis of gas diffusion we can now proceed to see how animals exchange gases across their respiratory surfaces. First, we shall discuss various arrangements for respiratory gas exchange in animals.

SAQ 1

- a) Pick out the correct statements from the following:
 - i) Partial pressure of a gas in solution is defined as the partial pressure of that gas in atmosphere in equilibrium with the solution.
 - ii) As the partial pressure of a gas in a water sample is reduced, the gas tends to move out of the solution.
 - iii) As temperature decreases the solubility of gases decreases too.
 - iv) The diffusion of a gas along a partial pressure gradient is always along the concentration gradient.
- b) Suppose air at 30°C and 735.18 mm Hg is saturated with water vapour at 18.00 mm Hg. What would the partial pressure of oxygen be in this saturated air?

2.3 MODES OF RESPIRATION

Many small organisms obtain oxygen by diffusion through their body surfaces. They do not have any specialized respiratory organs nor do they have blood circulation. Larger and more complex organisms, however, need specialized surfaces for gas exchange and a circulatory system that transports oxygen more readily than that possible by simple diffusion across the body surface.

Calculations based on metabolic demands and rate of diffusion in protoplasm show that simple diffusion is sufficient only to meet the demands of organisms

not larger than 1 mm in diameter. These calculations appear reasonable when we see that animals like protists (protozoans) and flatworms that meet their respiratory requirements through diffusion are either quite small or have very low metabolic rates (Fig. 2.1). Giant land planarians which are 50 cm long are exceptions as they are flat with very large surfaces in relation to mass, therefore, diffusion is sufficient to meet their oxygen demand. Coelentrates like corals and sponges often reach very large sizes but have very modest metabolic demands. They maintain a circulation of water by cilia over the surfaces of cells which line their canal systems. Thus, sufficient gas exchange takes place without the aid of a circulatory system or respiratory pigments.

In animals that have inefficient circulatory systems and readily permeable vascular skins, gas exchange occurs through the integument. Thus we find that animals like earthworms, leeches and many larval fishes are among the many animals that obtain the oxygen they need across their general body surface. Even larger animals such as many amphibians and fish may rely on **cutaneous respiration** during emergencies or use it as a supplement to the gills or lungs.

The ability to respire through the integument is developed the most in eels, and amphibians that have moist and highly vascularised skins. The integumentary contribution to respiration may be as high as 90 per cent in the giant salamander (*Cryptobranchus alleganiensis*) and as low as 20 per cent in dry-skinned toads. Giant salamander is 25 to 60 cm in length and may weigh over 1 kg. It lacks gills and the unspecialized lungs play little or no part in respiration. This aquatic amphibian is the largest animal relying exclusively on cutaneous breathing.

Animals that are large and have higher metabolic rates have specialised respiratory organs. These organs have a thin respiratory surface to help in gas exchange (Fig. 2.1).

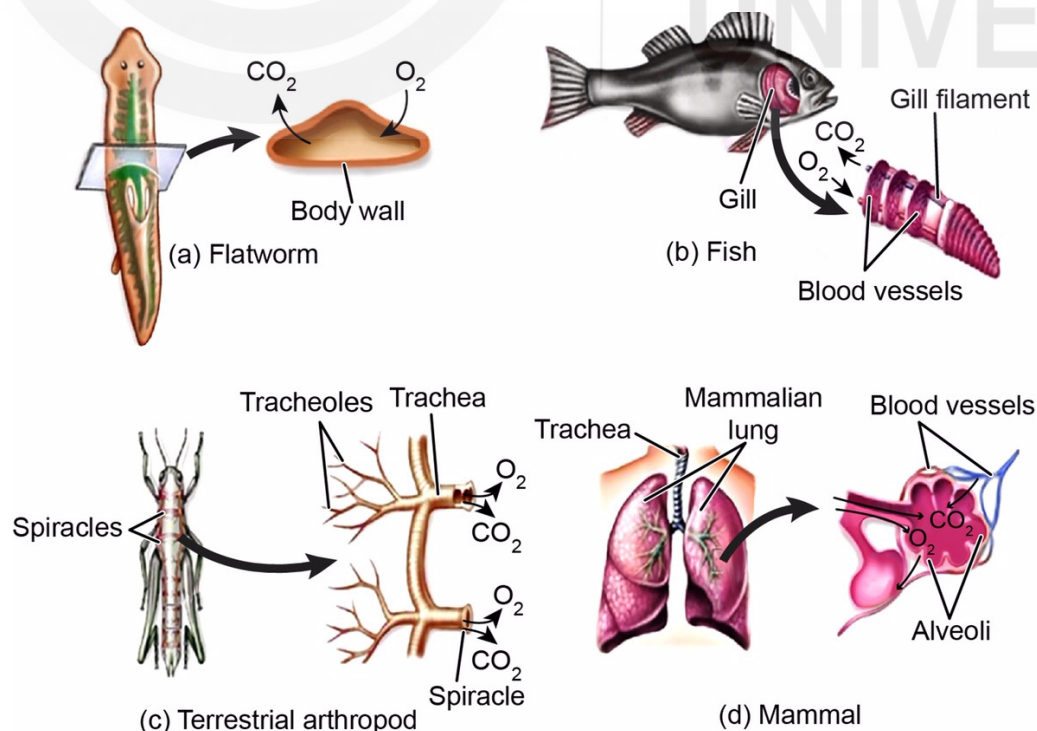


Fig. 2.1: Respiratory System of a) flatworm; b) insect; c) fish; and d) humans.

Insects have a special respiratory system (Fig.2.1b). Small openings on the insect's body surface are connected to small tubes or trachea that branch and spread throughout the body. The gases diffuse through these branches directly into the cells.

Generally gills are for aquatic breathing (Fig. 2.1 c) and lungs (Fig. 2.1 d) for breathing air. You have already studied how gills are used for respiration in Comparative Anatomy and Developmental Biology of Vertebrates (Unit 4). Gills are highly vascularised extensions of gas exchange membranes. Gill surface area must be large enough to provide adequate exchange of gases. Therefore, highly active fish have largest relative gill area.

Gas exchange takes in fishes place in the gill lamellae as water flows between them in one direction and blood within them in the other direction. This is known as **countercurrent flow** (refer again to Unit 4 of BZYCT-133 theory course). This type of flow has an important consequence. It permits the blood leaving the fish gills to have the highest possible oxygen levels.

In Section 2.2, you studied that air has more oxygen than water. The atmosphere provides a constant supply of oxygen almost everywhere. The greatest disadvantage however, is that air tends to dry out membranes involved in gas exchange. To overcome this, terrestrial animals have to live in extremely moist environments or find some ways to keep their respiratory surfaces moist. In order to accomplish this the water loss is membranes into lungs in amphibians, reptiles, birds and mammals, and trachea in insects that are contained with the body they bathed by body fluid and so are kept moist Table 2.1 compares oxygen availability in respiration using air and water.

Table 2.1: Major advantages of breathing air.

Properties	Air	Water
Solubility of oxygen at 15°C	Air contains 209 ml of oxygen per litre	7 ml of oxygen per litre
Energy needed to move medium (air or water) over the respiratory surface	Less energy needed to move air over the respiratory surface	More energy needed to move water over the respiratory surface as water is much more viscous than air,
Diffusion of Oxygen	Oxygen diffuses some 10,000 times more rapidly in air than in water and so can diffuse in lungs over several millimeters	Oxygen diffusion is slow from water to the respiratory surface in fish gill that thus take place only in a tiny fraction of a millimeter.

Lungs are of two types i) **diffusion lungs** which are characterised by air exchange with surrounding environment by means of diffusion only and are present in small animals such as pulmonate snails, small scorpions, some spiders and some isopods; ii) **ventilation lungs** which are typical of vertebrates. The air passes through a tube into inflatable lungs where gas exchange takes place and oxygen poor air and carbon dioxide rich air is then forced out usually through the same tube. This is known as **tidal flow of air**.

In this unit, you will study the process of respiration mainly in mammalian lungs as they are the best representative of a respiratory surface adapted for terrestrial respiration. For this purpose, human lung has been taken as the model of study.

SAQ 2

Why does diffusion alone suffice to supply oxygen in both protists (protozoans) and flatworms?

2.4 HUMANS RESPIRATORY SYSTEM

The respiratory system begins at the nose and ends in the most distal **alveolus** (plu: alveoli) contained within the lung (Fig 2.2). **Alveolus** refers to any of the many tiny air sacs of the lungs which allow for rapid gaseous exchange. The Respiratory system is divided into: upper airway and lower airway. The **upper airway** consists of all structures from the nose to the vocal cords, including sinuses and the larynx, whereas the **lower airway** consists of the trachea and airways (namely, paired bronchi and bronchioles and alveoli in the lungs).

The respiratory system is made up of the following:

1. The **nasal cavity**,
2. the **posterior pharynx**,
3. the **glottis** and **vocal cords**,
4. the **trachea**, and
5. Main stem bronchus
6. Lung with the **tracheobronchial tree structure**, consisting of the single tracheary paired lobar bronchi (plu: bronchus), branched segmental bronchi, branched **bronchioles**, and (sing : alveolus).

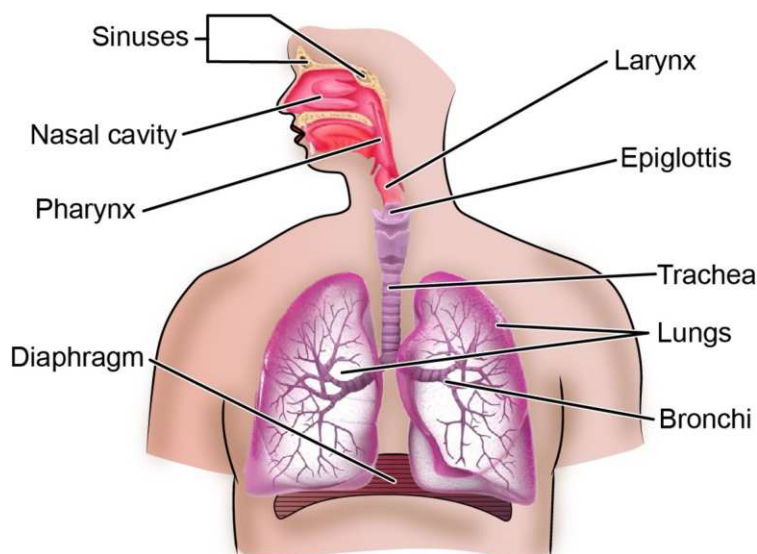


Fig. 2.2: The human respiratory system.

2.4.1 Upper Airways

The **upper airway** as you know consists of all structures from the nose to the vocal cords, including sinuses and the larynx. The major function of the upper airways from nose to vocal cords, is to "condition" or prepare the inspired (taken in) air such a way so that by the time it reaches the trachea, it is at body temperature and fully humidified. The nose which opens outside the body, by paired nares, not only provides the sense of smell but also functions to filter, entrap, and clear particles larger than 10 μm in size from the inspired air. In humans, the volume of air entering the **nares** each day is in the order of 10,000 to 15,000 L (Litres).

The interior of the nose is lined by respiratory epithelium interspersed with surface secretory cells and cilia which facilitate the flow of mucous from the upper airways and clear the main nasal passages approximately every 15 minutes.

The major structures of the larynx or voice box include the **epiglottis**, **paired arytenoid cartilages** and **vocal cords**. The **arytenoids are located** at the back of the larynx, and the vocal folds (vocal cords) are attached to them. These allow and aid in the vocal cords' movement (Fig. 2.3). With some infections, these structures can become **edematous** (swollen) and contribute significantly to airflow resistance. The epiglottis and arytenoids or "hood" cover the vocal cords during swallowing. So it can be said that under normal circumstances, the epiglottis and arytenoids function to prevent aspiration of food and liquid into the lower respiratory tract.

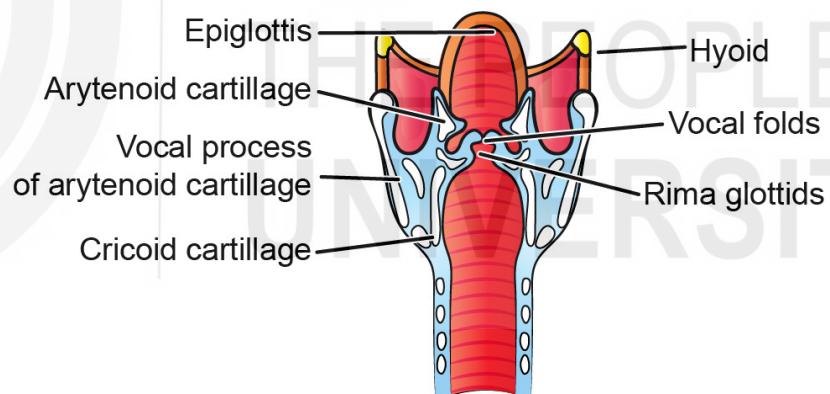


Fig. 2.3: Structure of larynx.

After **mastication** (chewing) the act of swallowing food usually occurs within 2 seconds, and it is closely synchronized with muscle reflexes that coordinate opening and closing of the airway. Hence, air is allowed to enter the lower airways and food and liquids are kept out. Patients with some neuromuscular diseases have altered muscle reflexes and can lose this coordinated swallowing mechanism. Thus, they may become susceptible to aspiration of food and liquid, which poses a risk of developing pneumonia.

2.4.2 Lower Airways

The lower airways include the single trachea, paired bronchi, branched bronchioles and alveoli in the lungs. The trachea or wind pipe (Figs. 2.2 and 2.4) is a tubular passageway for air and is about five inches long. The anterior

part of the trachea is composed of 16-20 "C" shaped cartilaginous rings. The posterior portion of the trachea is composed of fibrous tissue and extends from the lower end of the larynx till it bifurcates into two bronchi (singular: bronchus) which pass into the lungs.

- i) Right primary bronchus which goes into the right lung, and
- ii) Left primary bronchus which goes into the left lung.

Each primary **bronchi** divides into smaller secondary bronchi called the **lobar bronchi**, one for each lobe of the lung (the right lung has three lobes and the left lung has two). The lobar bronchi continue to branch forming smaller bronchi called **tertiary bronchi** that divide further to form the **bronchioles**. The airways continue to divide in a dichotomous or asymmetric branching pattern until they form **terminal bronchioles** that are distinguished by being the smallest airways without alveoli. The terminal bronchioles branch out into several **respiratory bronchioles**. Each branching of the respiratory bronchiole results in decreased diameter, however, the total surface area increases in size and number until the respiratory bronchiole terminates in an opening leading to a group of blind sacs called **alveoli** where the actual exchange of respiratory gases takes place. This extensive branching from the trachea resembles an inverted tree and is commonly referred to as the **bronchial tree** (Fig. 2.4 a and Fig. 2.2).

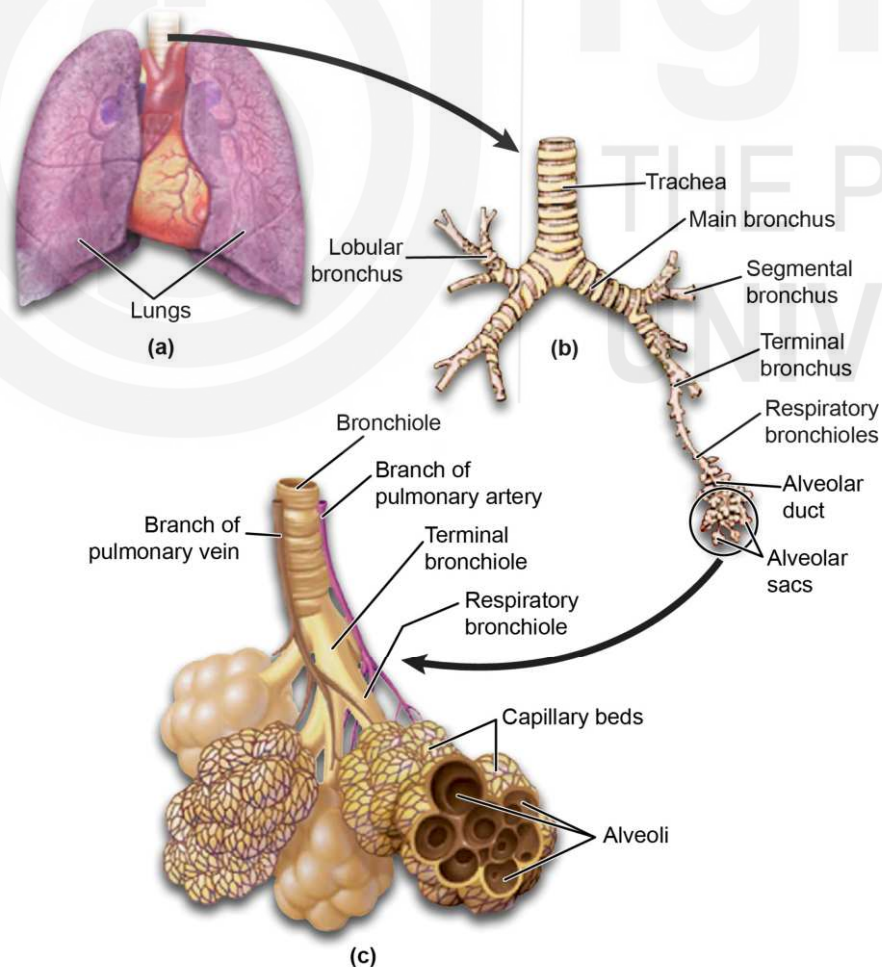


Fig. 2.4 : a) Human lung; b) The bronchial tree of the respiratory tract; c) The terminal bronchiole enlarged to show the respiratory bronchioles ending in clusters of alveoli.

A pair of human lungs contain about 300 million alveoli and the total surface area is about 70 meter square. This area is nearly equal to a tennis court! The alveoli have thin walls and capillaries from the pulmonary artery extensively occupy the vascular side of the alveoli (Fig. 2.4 b).

Let us now examine the structure and working of the human lungs in the next section.

2.5 LUNGS

The lungs are pyramid-shaped, paired organs protected by the chest wall (rib cage, sternum, thoracic vertebrae, intercostals muscles and connective tissue) (Fig .2.5). The lungs on their posterior side are bordered by the diaphragm which is the flat, dome-shaped muscle located at the base of the lungs and thoracic cavity.

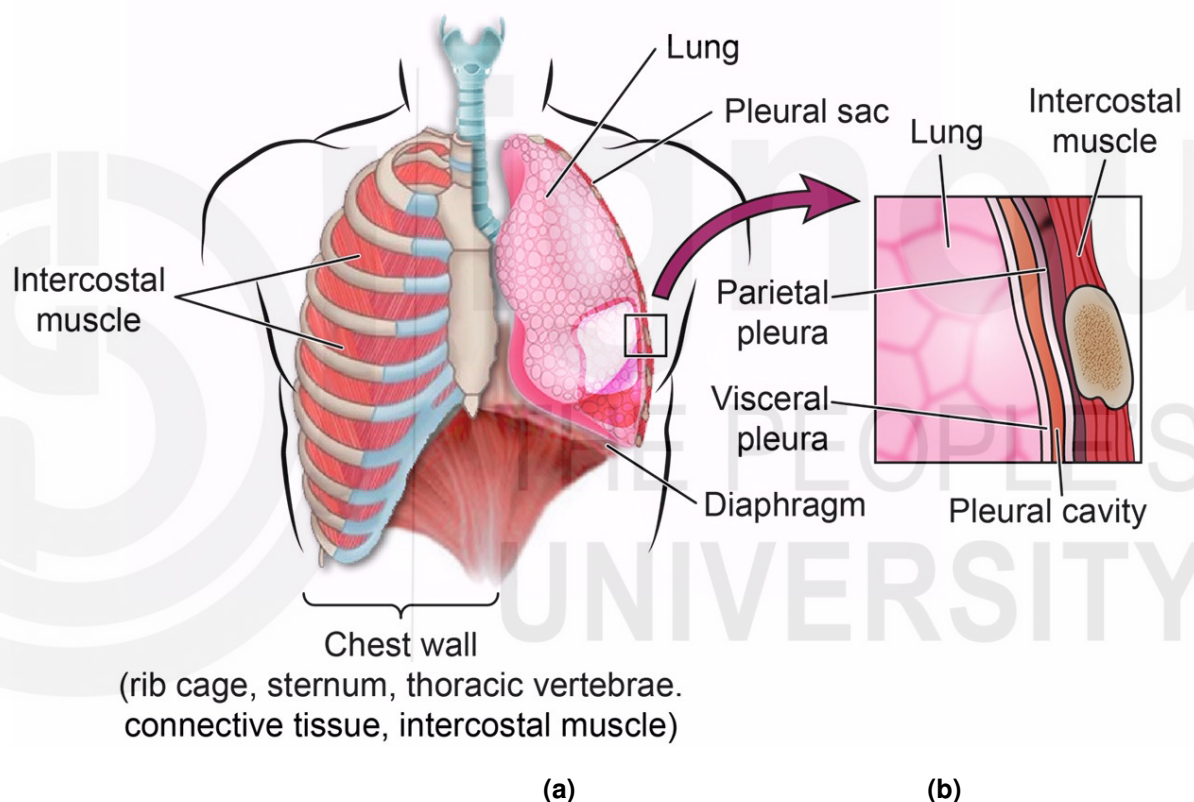


Fig. 2.5 : a) The lungs with their protective chest wall. The wall is made up of the rib cage, sternum, thoracic vertebrae, connective tissue and intercostals muscles; b) section of chest cavity wall showing visceral and parietal pleura and pleural cavity.

2.5.1 Structure

In the Fig 2.6 you can see that each lung is composed of smaller units called lobes. These lobes are separated from each other by fissures. The right lung consists of three lobes: the superior, middle, and inferior lobes. The left lung consists of two lobes: the superior and inferior lobes. A cardiac notch which is the form of an indentation on the surface of the left lung is present, and it allows the space for the heart.

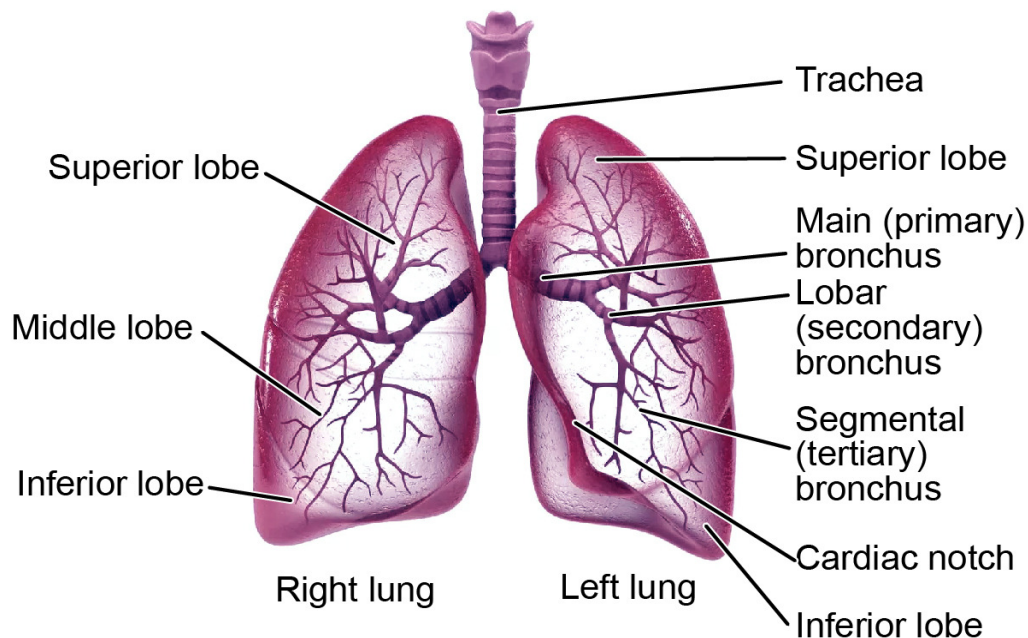


Fig. 2.6: The right lung consists of 3 lobes while the left lung is made up of 2 lobes there is an indentation called the cardiac notch on the left lung for the placement of heart against the left lobe.

The lungs are covered by a thin membrane called the visceral pleura and are encased by another membrane called the parietal pleura (look again at Fig 2.5 b). The interface of these two pleuras allows for smooth gliding of the lungs as they expand in the chest. Air can only enter between the visceral and parietal pleurae in case of either trauma, surgery, or rupture of a group of alveoli causing a condition known as pneumothorax.

The Respiratory Muscles

Several muscles are involved in respiration (Fig. 2.7). The main two layers of muscles connected with the ribs and are as follows: 1) External intercostals muscles which pass downwards and forwards and 2) Internal intercostals which pass downwards and backwards and are present between the ribs. The primary inspiratory muscles are the diaphragm and external intercostals. There are several accessory inspiratory muscles among them the important ones include the sternocleidomastoid, the scalenus group, the pectoralis major and minor. Technically any muscle attached to the upper limb and the thoracic cage can act as an accessory muscle of inspiration through reverse muscle action (muscle work from distal to proximal). Inspiration is an active process and the primary inspiratory muscles are the external intercostals and the diaphragm located at the base of the lungs (Figs 2.2 & 2.5).

Relaxed normal expiration is a passive process, and happens because of the elastic recoil of the lungs and surface tension. However there are a few muscles that help in forceful expiration and include the internal intercostals, intercostalis intimi, subcostals and the abdominal muscles.

The processes of both inspiration and expiration require changes in the pressure within the chest cavity. The respiratory muscles achieve this by changing the size of the thoracic cavity.

Muscles of inspiration**Accessory**

Sternocleidomastoid
(elevates sternum)

Scalenes group
(elevate upper ribs)

External intercostals
interchondral part of
internal intercostals
(also elevates ribs)

Diaphragm
(dome descends, thus
increasing vertical
dimension of thoracic
cavity; also elevates
lower ribs)

Muscles of expiration**Quite breathing**

Expiration results from
passive, elastic recoil
of the lungs, rib cage
and diaphragm

Active breathing

Internal intercostals,
excepts interchondral
part (pull ribs down)

Abdominals
(pull ribs down,
compress abdominal
contents thus pushing
diaphragm up)

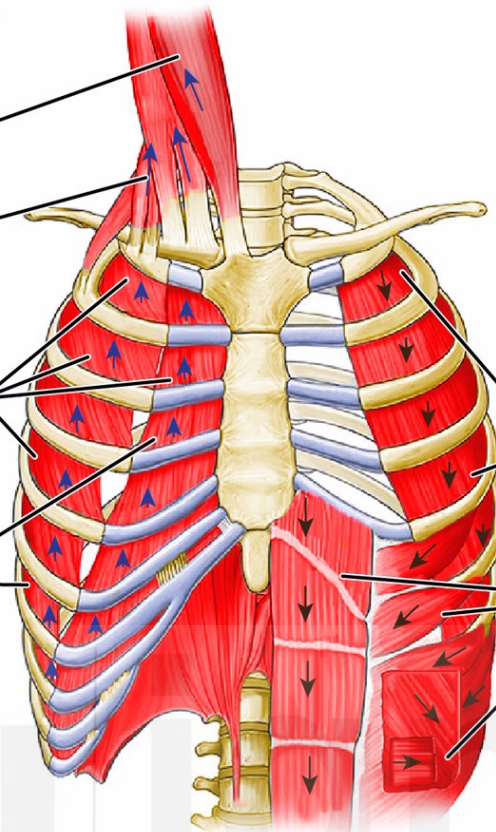


Fig. 2.7: Muscles involved in respiration

SAQ 3

Fill in the blanks with appropriate words.

- i) The main two layers of respiratory muscles connected with the ribs are and
- ii) The right lung consists of lobes and the left lung consists of lobes.
- iii) The lungs present in the lower airways consist of single, branched paired, ... and in the lungs.

2.5.2 Pulmonary Ventilation

Pulmonary (Pulmon: lung) ventilation or breathing is the mechanical flow of air into (inspiration) and out of (expiration) the lungs. During breathing, the contraction and relaxation of muscles act to change the volume of the thoracic cavity by which the volume of the lungs and the pressure inside change correspondingly. Mammalian lungs work through **negative pressure ventilation**. The pressure inside the lungs is always 5 mm to 8 mm Hg less than atmospheric pressure. This negative pressure, is enough to keep them expanded and prevents them from collapsing. Ventilation of lungs takes place in two steps:

Inhalation : Inhalation or inspiration as you can see from Fig. 2.8(a) is initiated by the diaphragm and is supported by the external intercostals muscles. Under normal conditions (Fig. 2.8 a), the diaphragm, is the primary driver of inhalation. When the diaphragm contracts, the intercostal muscles contract, and elevate the sternum and ribs. As a result the ribcage expands and the contents of the abdomen are moved downwards. This results in a larger thoracic volume and negative (suction) pressure (with respect to atmospheric pressure) inside the thorax. As the pressure in the chest falls, atmospheric air moves into the mouth and from it into the air conducting tubes. Here, the air is filtered, warmed, and humidified as it flows to the lungs. Normal resting respirations are 10 to 18 breaths per minute, with a time period of 2 seconds

Exhalation : Exhalation or expiration is generally a passive process (Fig. 2.8 b). The diaphragm returns to its resting position and the intercostals muscles relax, depressing the sternum and ribs. The lungs have a natural elasticity and so as they recoil back from the stretch of inhalation and their return to their normal position, air flows back to outside from them into the atmosphere till the pressures in the chest and the atmosphere reach an equilibrium. However, active or forced exhalation can be voluntarily achieved by the abdominal and the internal intercostals muscles. During active the process of active or forced exhalation, as when blowing out a candle, expiratory muscles including the abdominal muscles and internal intercostals muscles generate abdominal and thoracic pressure, which forces air out of the lungs.

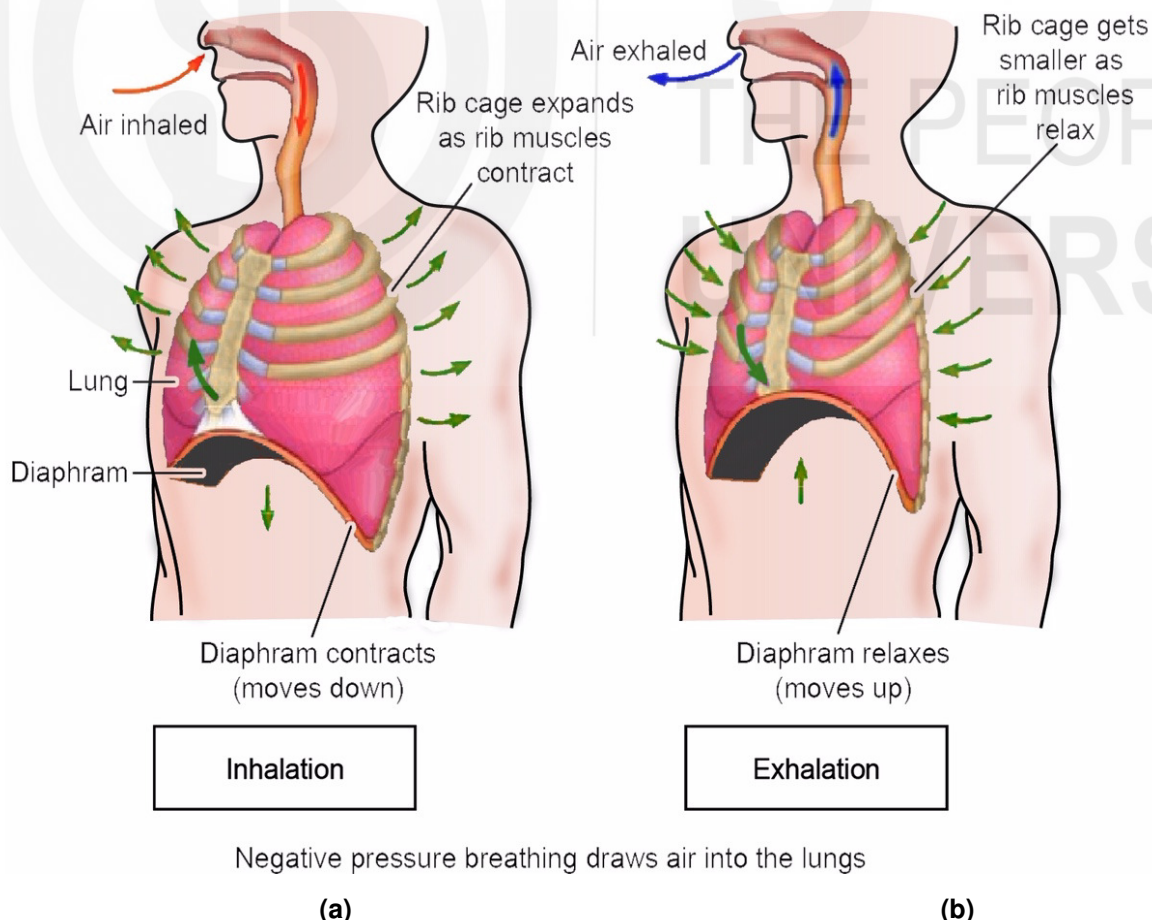


Fig 2.8: Pulmonary ventilation during respiration: a) inhalation in which the diaphragm contracts and move down; and b) exhalation in which the diaphragm relaxes and moves up.

2.5.3 Lung Volumes and Capacities

An average lung at rest maximum capacity can hold 6 liters of air, but lungs do not operate at maximum capacity. The total space within the lungs is measured in terms of lung volumes and lung capacities. Lung volume measures the amount of air required for one function of the lung that is, volume of inspired air, while lung capacity is the sum of two or more volumes. During the normal course of respiration when you breathe out or during exhalation, the exhaled air coming out from, some of the used air deficient in oxygen remains in the connecting tubes *i.e.*, trachea, bronchi and their branches is of the lungs and when you breathe in or inspire space occupied by the used air that remain in this used air is pushed back into the lungs first, before the fresh air enters. The volume of used present in air in the air passages thus reduce the volume of fresh air that can enter the lungs. Therefore, the space is called **anatomical dead space** and the volume occupied by this used air is learned. The **dead space** volume and is 150 ml. Let us look at some definitions related to lung volumes and capacities with the help of Table 2.2. You can see from the table that the volume of air inhaled in one breath at rest is 500 ml, therefore only 350 ml ($500-150=350$) of fresh air reaches the alveoli. In exercise the dead space volume is insignificant as an adult male may inhale 3000 ml of air in a single breath, in which case 150 ml is hardly significant.

Table 2.2 : Respiratory volumes and capacities in men. The pulmonary volume and capacities are usually 20-25% less in women.

Terms	Definition	Normal Volumes
Tidal volume (TV)	The volume of air inhaled and expired in one breath at rest.	500 ml
Inspiratory reserve volume (IRV)	The additional volume of air that can be taken in by forced inspiration, over and above the tidal volume.	3000 mL.
Expiratory reserve volume (ERV)	The volume of air in excess of tidal volume that can be exhaled forcibly.	1100 mL.
Residual volume (RV)	The volume of air which remains in the lungs after maximum expiration.	1200mL.
Vital capacity (VC)	The sum of inspiratory reserve volume, tidal volume and expiratory reserve volume. ($IRV+TV+ERV$)	4600 mL
Inspiratory capacity (IC)	Volume of air that can be inhaled in addition to a normal exhalation. ($TV+IRV$)	3500 mL
Total Lung capacity.	Total volume of air in the lungs after a maximal inspiration (The sum of $TV+IRV+RV+ERV$)	5800 mL

No matter how hard one may try the lungs are never empty of air. There is still about 1200 ml of air left in it. This is the **residual volume** after maximum

expiration. If the lungs were emptied out completely the lung surfaces would stick together and the energy required to re-inflate them would be huge. During inhalation 350 ml of fresh air reaches and mixes with the 1200 ml of the residual air. This ensures that there is a constant composition of 15% O₂ and 5% CO₂ in the lungs. This remains the same even during exercise and the extra requirement of O₂ is met by the extra ventilation of the lungs.

The lung/respiratory volumes and capacities are studied for diagnosis of respiratory disease. These respiratory volumes are obtained by using an instrument called the spirometer. However, the residual volume cannot be measured and can only be calculated.

SAQ 4

Match the following :

- | | |
|--------------------------------|--|
| i) Tidal volume | a. The sum of inspiratory reserve volume, tidal volume and expiratory reserve volume. |
| ii) Inspiratory reserve volume | b. The sum of tidal volume, inspiratory reserve volume, expiratory reserve volume and residual volume. |
| iii) Vital capacity | c. The additional volume of air that can be taken in by forced inspiration, over and above the tidal volume. |
| iv) Total Lung capacity. | d. The volume of air taken in, in one breath |

2.5.4 Gas Exchange in Alveoli

The major function of the lungs is to enable gas exchange between the inspired oxygen rich and the deoxygenated blood that comes from the body tissues to the heart and from there by the pulmonary artery to the lungs. Erythrocytes also known as red blood cells the respiratory tract is richly supplied with blood vessels both arteries and veins. In this pigment lungs or RBC of blood, pick up oxygen from the oxygen rich inspired air and transport it to tissues throughout the body on its return journey. Thus the circulatory system of the body plays an important role in gas exchange. The pulmonary artery branches multiple times as it follows the bronchi, and each branch becomes progressively smaller in diameter. One arteriole and an accompanying venule supply and drain respectively one alveolar lobule. As they reach near the alveoli, the pulmonary arterioles become the pulmonary capillary network. The pulmonary capillary network consists of tiny vessels with very thin walls that lack smooth muscle fibers. The capillaries branch and follow the respiratory bronchioles and structure of the alveoli. It is at this point that the capillary wall meets the alveolar wall, creating the respiratory membrane. Once the blood is oxygenated, it drains from the alveoli by way of multiple bronchial veins.

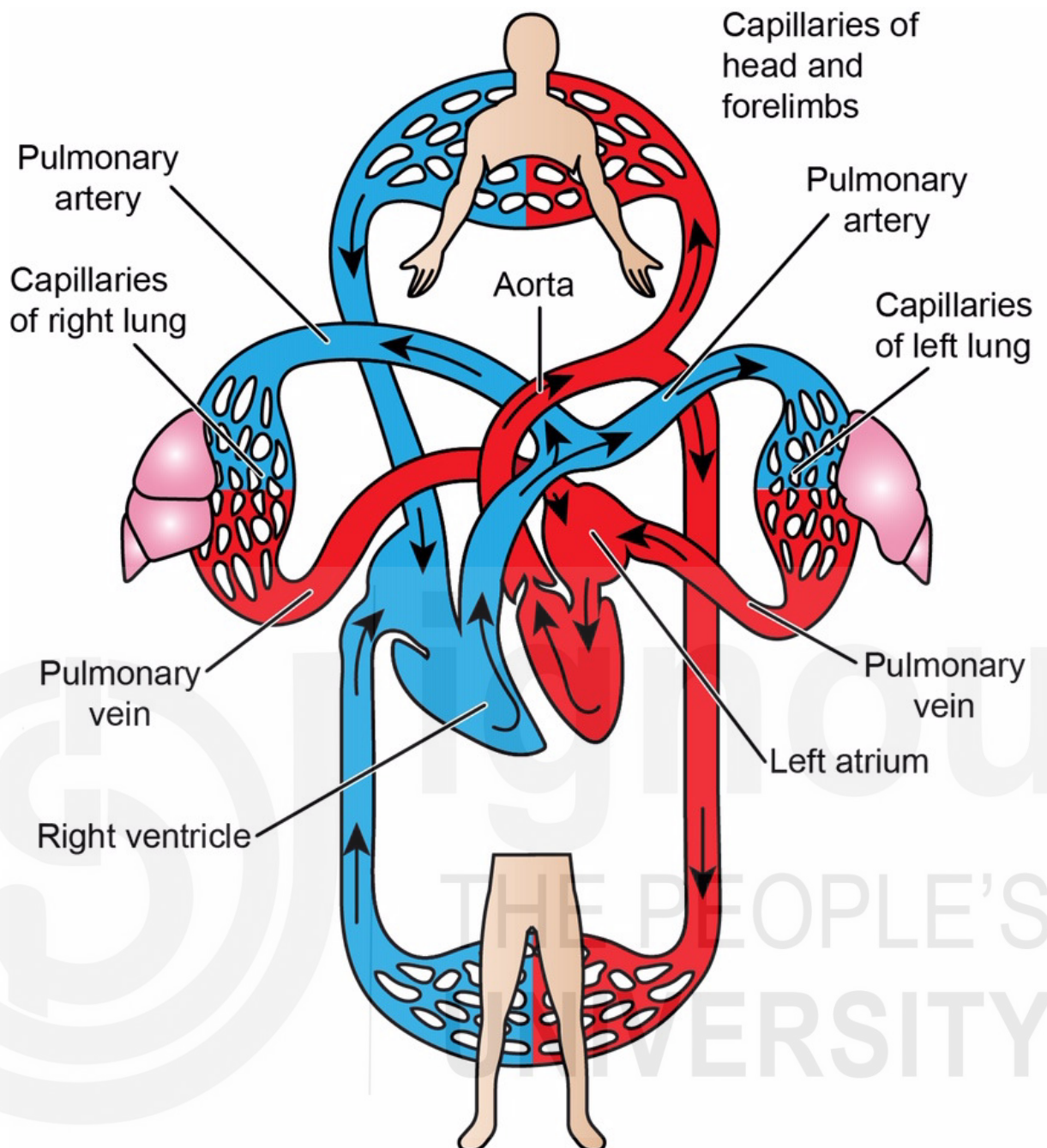


Fig. 2.9: Blood supply to lungs.

Trachea, bronchi and their branches are only connecting tubes and no exchange of gases take place in them. **Gas exchange takes place only in the respiratory bronchioles, alveolar ducts and alveolar sacs.** The oxygenated blood that enters the lungs from the heart is routed through body tissue where mitochondrial respiration, depletes the oxygen content. Thus lowers the partial pressure of oxygen (PO_2 = about 40 mm Hg). At the same time metabolic activity increases partial pressure of carbon dioxide in the cells of body tissue which increase partial pressure of carbon dioxide of blood entering the alveoli is 45 mm Hg. Thus, compared to partial pressures in the atmosphere, ($PO_2=158$ and $P_{CO_2}=0.3$) the blood entering lungs from the body tissue has low PO_2 and high P_{CO_2} . This difference in partial pressure of oxygen in alveoli which contains the oxygen rich atmospheric air causes the oxygen and carbon dioxides gases to diffuse along their partial pressure gradient. The whole process of exchange is depicted in Fig. 2.9.

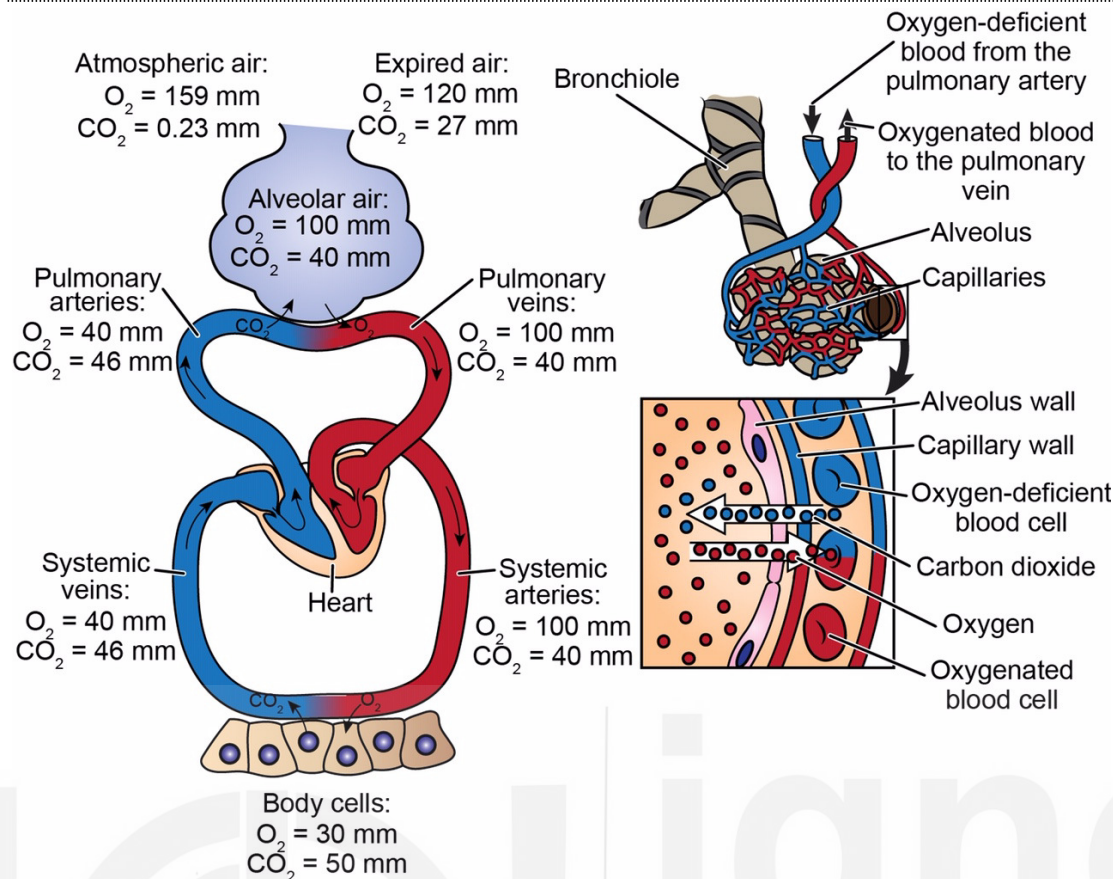


Fig. 2.10: Exchange of respiratory gases in alveoli in lungs and tissue cells.

2.5.5 Regulation of Respiration

In mammals, during respiration ventilation is operated by separate groups of neurons that work alternatively. Ventilation is regulated primarily by the amount of carbon dioxide present in the lung air. Even a slight increase in CO_2 level in the inspired air increases the rate of ventilation. Oxygen on the other hand has a much smaller effect on ventilation. If the O_2 concentration is decreased from 21% to 18.5% there is virtually no effect on ventilation.

The rhythmic contractions of the diaphragm and of the intercostal muscles are controlled by respiratory centres which consists of clusters of neurons located in the area of the medulla oblongata and pons of the brain. Chemoreceptors that are located in the respiratory centers are sensitive to increased carbon dioxide levels and increased acidity of the blood and cerebrospinal fluid and respond by increasing the ventilation so that more CO_2 is able to leave the lungs and its levels return to normal. **It is peculiar that even though metabolism requires oxygen yet the respiratory centre is not very sensitive to decreased oxygen levels.**

There are four respiratory groups that regulate respiration in the body : two in the medulla and two in the pons. The two groups in the pons are known as the pontine respiratory group.

1. Dorsal respiratory group – in the medulla
2. Ventral respiratory group – in the medulla

3. Pneumotaxic center – various nuclei of the pons
4. Apneustic center – nucleus of the pons

Whenever the need for oxygen in the body increases, ventilation of the respiratory organs also increases. For this purpose nerve impulses are transmitted from these centres in the brain to the respiratory muscles in particular the diaphragm and intercostals muscles which become activated and cause air to move in and out of the lungs.

Chemoreceptors that are sensitive to changes in arterial carbon dioxide, oxygen, and pH (resulting from changes in the levels of carbon dioxide) transmit the information of these changes to the respiratory centres so that they can respond appropriately by sending impulses to increase or decrease ventilation (Fig.2.10). These chemoreceptors are located centrally and peripherally.

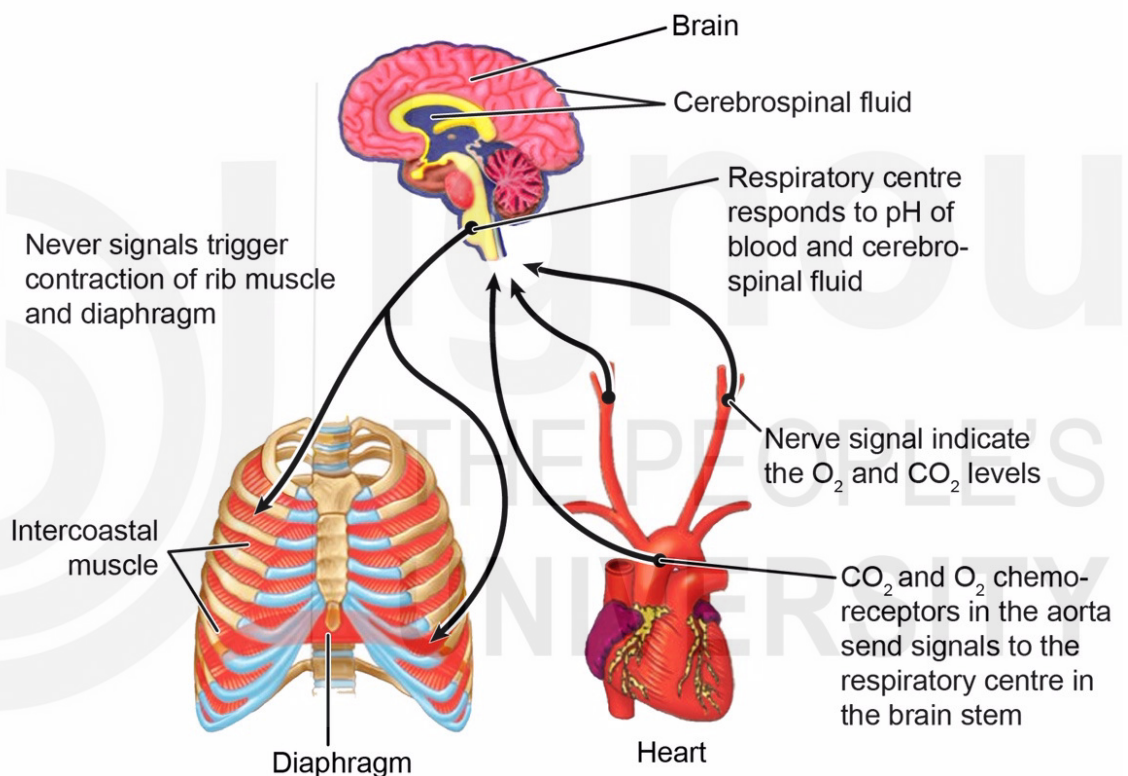


Fig. 2.11: Respiratory centre in brain.

Central chemoreceptors are located on the medulla oblongata, near the medullary respiratory groups of the respiratory center. They are mainly sensitive to changes in the pH in the blood, (resulting from changes in the levels of carbon dioxide).

The peripheral chemoreceptors are present in the carotid bodies and aortic arch near the heart and are sensitive to changes in arterial carbon dioxide, oxygen, and pH. Chemoreceptors located in the carotid bodies and aortic arches respond to decreased Po_2 levels by increasing the depth and frequency of breathing. The carotid bodies in general are more important in mediating this response and provide the principal mechanism by which mammals sense decreased levels of oxygen. Information from the peripheral

chemoreceptors is conveyed along nerves to the respiratory groups of the respiratory center.

2.6 TRANSPORT OF GASES IN BLOOD

We know that two types of gas exchanges are constantly occurring in the animal body-one at the interphase of the respiratory membrane and external environment (which you have studied in the previous section) and the other in the rest of the animal tissues. The underlying principle is the same at both places - passive diffusion occurs along a pressure gradient.

In many invertebrates oxygen and carbon dioxide are carried dissolved in blood or haemolymph. Since the amount of oxygen carried in a simple solution is small, therefore, in highly organised animals (many invertebrates and all vertebrates) oxygen is transported by being bound reversibly to proteins that are oxygen carriers. These proteins contain a metal, commonly iron or copper and are coloured. These proteins are thus, metalloproteins and are known as **respiratory pigments**. There are four major classes of respiratory pigments in animals. They are all metalloproteins that bind reversibly to oxygen at specific sites on the metal ion in their molecular structure. These are haemocyanins (copper containing), haemerythrins, chlorocruorins and haemoglobins (all three have iron). Out of all these haemoglobins are the most widespread respiratory pigment in most vertebrates.

2.6.1 Haemoglobin

Among the respiratory pigments we shall consider haemoglobin in some detail as this is the most familiar, and widespread and is present in human. It is also the most efficient respiratory pigment. In vertebrates haemoglobins are packed into the red blood cells and combine with far greater amounts of oxygen than other respiratory pigments that are found dissolved in the plasma. If the amount of haemoglobin that is packed in the cells was to be free in plasma, the viscosity of blood would be viscous (thick) like syrup and blood would not be able to flow in the blood as it does.

Let us now consider the structure of haemoglobin in more detail so as to know why haemoglobin has better oxygen carrying capacity. In Fig 2.11 a and b you can see that hemoglobin(Hb) molecule is made up of four polypeptide subunits 2 alpha(α) and 2 (β) beta subunits and so is a tetramer. Each subunit has a haeme group (an iron-containing compound of the porphyrin class) embedded in it. Each haemoglobin molecule forms a tetrahedral structure. Haeme, which accounts for only 4 percent of the weight of the molecule, is composed of a ring like organic compound known as a porphyrin to which an iron atom is attached (Fig. 2.11b). It is the iron atom that binds oxygen as the blood travels between the lungs and the tissues. Thus as there are four iron atoms in each molecule of haemoglobin, each haemoglobin can accordingly bind to four atoms of oxygen forming **oxyhaemoglobin** in a reversible reaction. The unoxygenated haemoglobin compound is called **deoxyhaemoglobin**. Another molecule in the body that has the ability to bind oxygen is **myoglobin**. It is a single unit or monomeric form of haemoglobin and consists of a single polypeptide chain the globin in which the haeme group is embedded.

Myoglobin is found in striated muscles of vertebrates and combines with one molecule of oxygen.

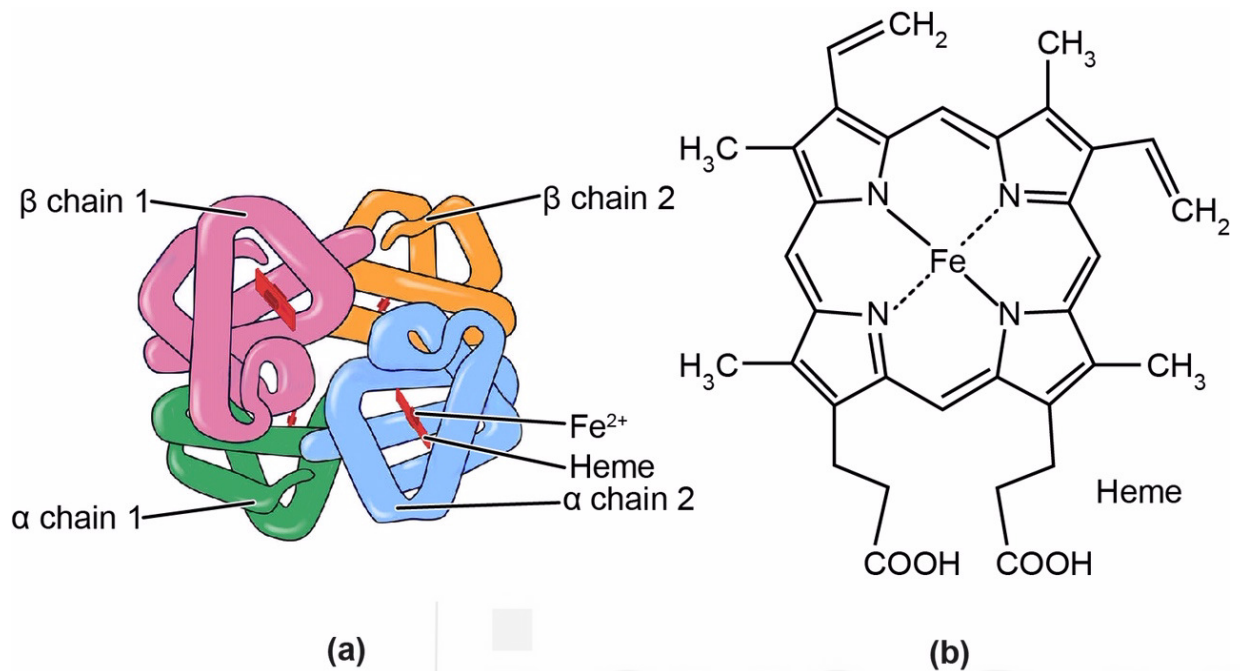


Fig. 2.12: a) Chemical structure of haeme group; b) Schematic representative of a single subunit of haemoglobin.

2.6.2 Oxygen Transport in Blood

Haemoglobin has even a stronger affinity for carbon monoxide than oxygen. The bond is 210 times stronger. Carbon monoxide tends to displace oxygen in haemoglobin and remains attached as the blood passes through the tissues. The transport of oxygen is impaired leading to dangerous consequences and even death.

When no oxygen is bound to the haemoglobin molecule it is said to be in a tense state (**T-state**). Haemoglobin molecule has the ability to change its shape when it binds to the first molecule of oxygen. As a result of the first binding the affinity for oxygen increases and the molecule is said to be in a relaxed state (**R-state**). This change in the state of the haemoglobin molecule allows subsequent binding of oxygen molecules to the rest of the 3 haemes easier and rapid. This type of binding is known as **cooperative binding between active sites**.

The transport of oxygen in the blood takes place in two ways: 1) the first and major one is through formation of oxyhaemoglobin (HbO_2) and 2) the second is through oxygen dissolved in plasma. In the amount of oxygen bound as oxyhaemoglobin is 20 ml/ 100 ml of blood and oxygen transported through plasma is only 0.2mL /100mL of blood.

The transport of oxygen in blood depends on : i) the Po_2 (partial pressure of oxygen) of the environment and ii) the bond strength or affinity between haemoglobin and oxygen. In the lungs where Po_2 in the inhaled air is high almost all deoxyhaemoglobin molecules bind to oxygen (Fig. 2.13). Low Po_2 in the systemic capillaries promotes unloading of oxygen. Haemoglobin has bond strength (affinity) which permits 97% of haemoglobin to combine with oxygen when leaving the lung. However, it has a stronger affinity for H^+ ions than oxygen. Therefore, in the presence of H^+ ions the oxyhaemoglobin molecule has the ability to unload or disassociate from its oxygen in the systemic capillaries. We will explain this as we study about oxygen disassociation curves.

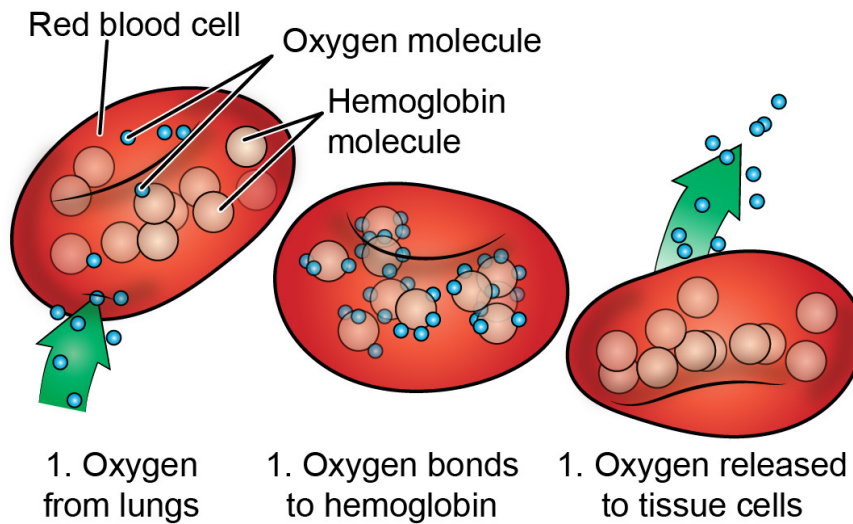


Fig. 2.13: Oxygen from the lungs binds to hemoglobin molecules and is carried through blood vessels to the rest of the body.

Oxygen Dissociation Curves

Recall we had said earlier in the section that in humans the oxygen carrying capacity is 20 ml oxygen per 100 ml blood. The relationship of oxygen carrying capacity to surrounding oxygen concentration can be shown graphically by the **oxygen dissociation curves (ODC)** (Fig. 2.14) which give us information about the most important function of red blood cells and the haemoglobin contained within them which is, the affinity of haemoglobin for oxygen and its delivery to the tissues. These curves are obtained by subjecting blood samples to different partial pressures of oxygen. The percentage of oxyhaemoglobin saturation at different partial pressures of oxygen is plotted.

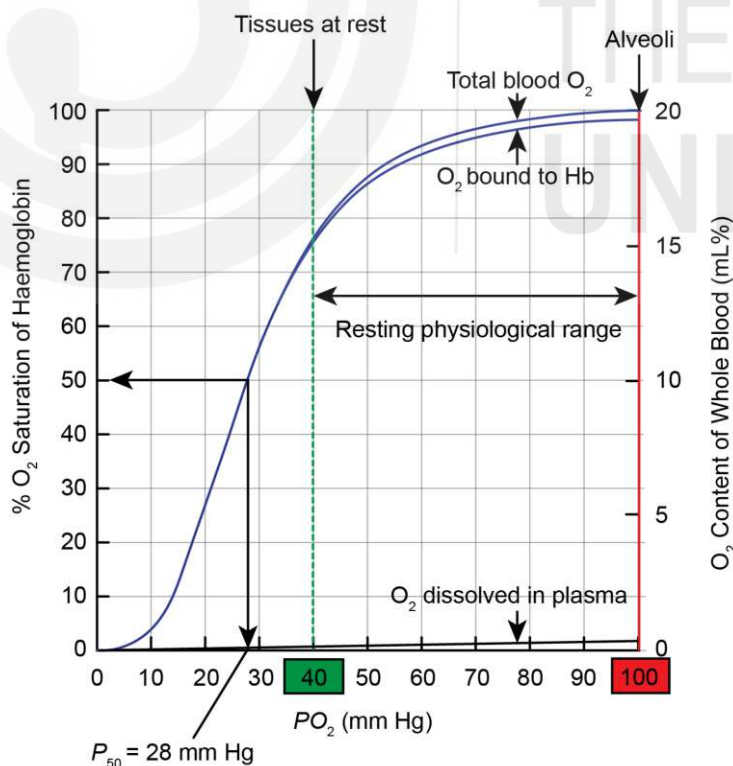


Fig. 2.14: Oxygen dissociation curve shows how haemoglobin's oxygen binding capacity depends on partial pressure of oxygen. Note that there is a 22% decrease in the percent of oxygen as blood passes from arteries to veins in the tissue. This results in unloading of approximately 5 ml of oxygen per 100 ml of blood.

The oxygen dissociation curve is S-Shaped or a sigmoid curve with the percentage of oxygen saturation of Hb shown on the Y (vertical) axis and the partial pressure of oxygen depicted on the X (horizontal) axis. You must remember that the amount of oxygen bound to hemoglobin i.e. the percentage O_2 saturation of hemoglobin at any time is related to partial pressure of O_2 that surrounds it. In the oxygen dissociation curve in Figure 2.14 we can see that as P_{O_2} increases the oxygen saturation of haemoglobin also increases. We can see that total saturation of Hb occurs in the lungs where partial pressure of oxygen is above 95 mm Hg. We can also see that at 60 mm Hg partial pressure of oxygen the curve begins to flatten out even if P_{O_2} levels are increased sharply. The steep portion of the curve indicates that when P_{O_2} drops (in systemic capillaries of tissues) the oxygen is dissociated from Hb and is released to the tissue. The curve shows that changes in P_{O_2} values from arterial to venous blood result in $97-75 = 22\%$ unloading when resting.

The P_{O_2} of oxygen when Hb is 50% saturated is about 28mmHg for healthy person and this point in graph is called P_{50} . In disease, the affinity of O_2 changes and the graph shifts to right or left.

Oxygen dissociation curve for a sample of blood is affected by several factors. The most important of them are:

1. Temperature
2. pH
3. CO_2
4. 2,3 – Diphosphoglycerate (DPG) –Organic phosphate

The importance of 2,3-DPG within the red blood cells is now recognized in blood banking. Old stored red cells lose their ability to produce 2,3-DPG which means that such cells will not unload their oxygen easily. Modern techniques for storage of blood, therefore, include the addition of energy substrates for respiration and phosphate sources needed for production of 2,3-DPG.

1. **Temperature** : Haemoglobin, at higher temperature gives up oxygen more readily and thus the dissociation curve shifts to the right (Fig 2.15). This is of physiological importance because increased temperature means higher metabolic rate or higher oxygen requirement by the organism.
2. **pH** : Another important factor that influences the oxygen dissociation curve is pH. An increase in carbon dioxide or other acids in the blood lowers the pH of the plasma and shifts the dissociation curve to the right (Fig. 2.15). At high carbon dioxide concentration more oxygen is unloaded at any given oxygen pressure. This effect is known as **Bohr effect**, after the Danish scientist who first described it. Therefore, as carbon dioxide enters the blood from respiring tissues it encourages the release of more oxygen. This is an important characteristic because it allows more oxygen to be released to the tissues which need it the most. More oxygen is loaded in the lungs and more is unloaded at the tissues as a result of **Bohr Effect**, than would be the case if only diffusion along the concentration gradient was responsible.
3. **Carbon dioxide** : Carbon dioxide lowers the oxygen affinity of haemoglobin even if the pH-is kept constant. This effect is due to the binding of carbon dioxide to the terminal amino groups of haemoglobin

molecule forming carbaminohaemoglobin. This site is not the same site on the molecule where oxygen is bound.

4. **2, 3-diphosphoglycerate (DPG)** : The presence of organic phosphate namely 2,3-diphosphoglycerate (DPG), in the red blood cells helps to explain many peculiarities of the oxygen dissociation curve. Previously the red blood corpuscle was considered to be a bag full of haemoglobin with no metabolism of its own because of the absence of a nucleus. Now we know that it has an active carbohydrate metabolism and the RBC has a high content of ATP and 2, 3-diphosphoglycerate (DPG). 2, 3-diphosphoglycerate is a product of glycolysis and binds to the beta chain of the globin and reduces oxygen affinity. Experimentally it has been shown that pure haemoglobin has greater oxygen affinity than whole blood (the dissociation curve for pure haemoglobin is far to the left of the curve as compared to that for the whole blood) Fig. 2.15. If 2, 3-DPG is added to pure haemoglobin solution the oxygen affinity decreases and approaches that of whole blood.

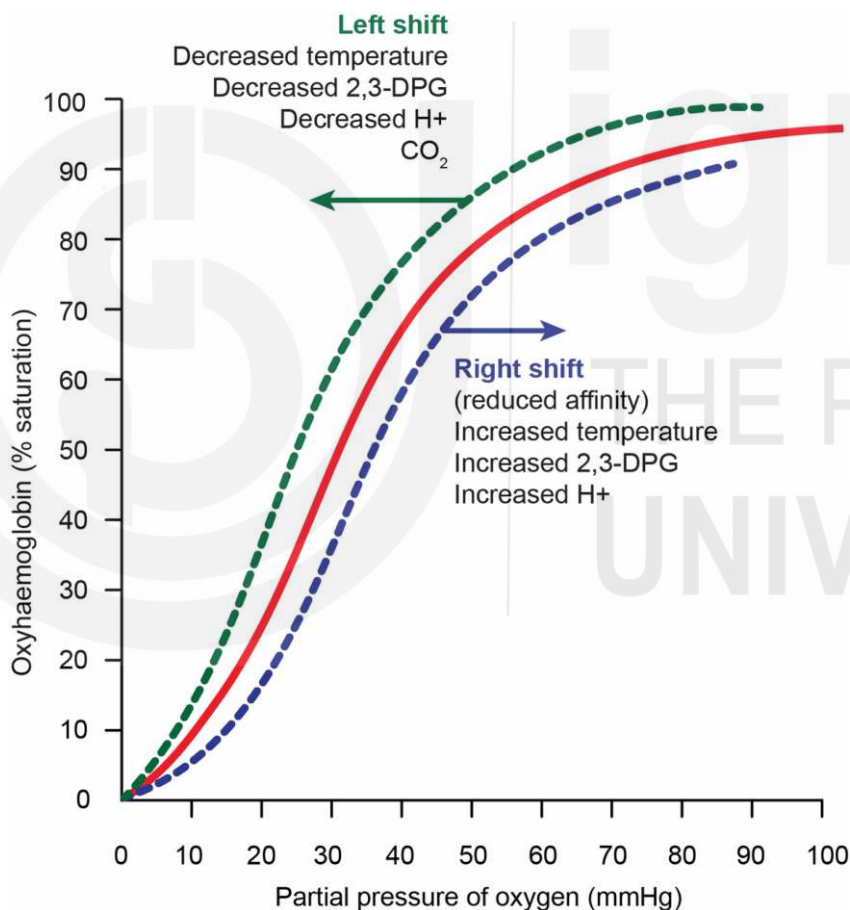


Fig. 2.15: The oxygen dissociation curve shifts to the right or left depending on temperature, carbon dioxide, pH, or 2,3-DPG levels . Due to Bohr effect oxyhaemoglobin surrenders its oxygen more readily in the presence of increasing acidity which is the case in metabolically active cells where more CO_2 is released.

We have learnt about the S shaped curve for haemoglobin. Let us now see how the oxygen dissociation curve of haemoglobin is different from the curve showing oxygen affinity in myoglobin. In myoglobin the haem reacts to oxygen independently. It does not show cooperativity binding as in the case of

haemoglobin. Fig. 2.16 shows the dissociation curve for myoglobin which in contrast to the curve for haemoglobin is rectangular. Myoglobin is described as middleman in the transfer of oxygen from blood to mitochondria within muscle cells. Myoglobin has a much stronger affinity for oxygen and stores oxygen in the muscles. It binds to oxygen at a much lower partial pressure than haemoglobin and dissociates from its bound oxygen only when the partial pressure of oxygen is very low as found in the mitochondria.

Fig. 2.16 also indicates that the myoglobin remains oxygenated until quite low levels of P_{O_2} in the surrounding fluids is reached. You can see from the figure that at 20 mm Hg the haemoglobin in the blood is about 30% saturated but the myoglobin in the muscles is above 80% saturated.

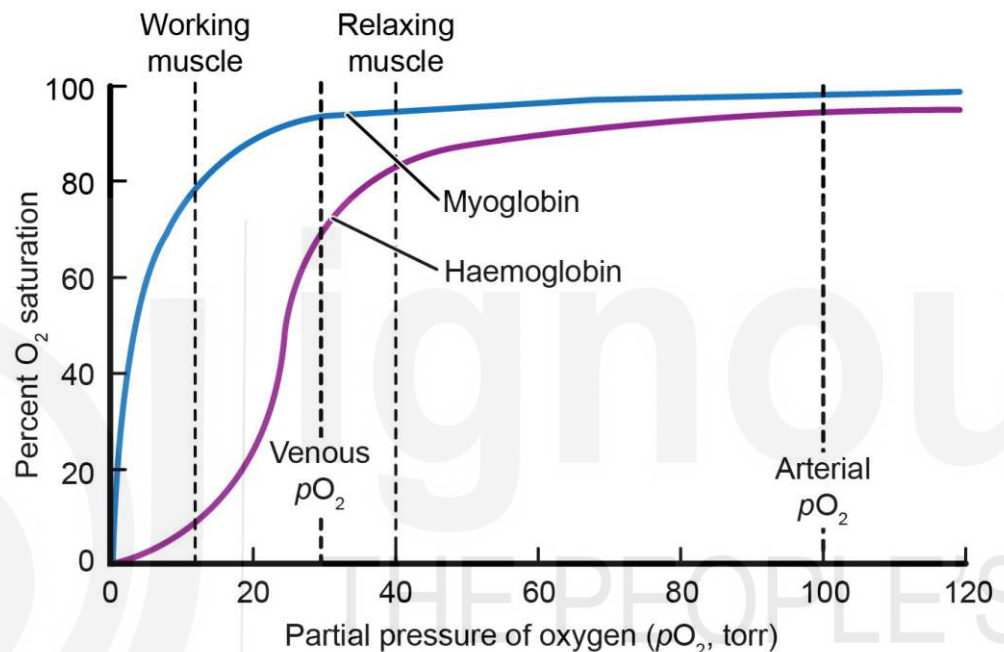


Fig. 2.16: A comparison of the dissociation curves for haemoglobin and for myoglobin. At the P_{O_2} of venous blood, the myoglobin retains almost all of its oxygen, indicating a higher affinity than haemoglobin for oxygen. The myoglobin does, however, release its oxygen at the very low PO_2 values found inside the mitochondria.

SAQ 5

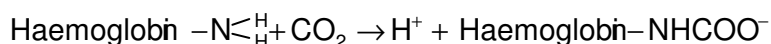
Pick out the true statements from those given below :

- The haemoglobin of adults contains four identical subunits and a haem group.
- When haem and globin fractions are separated the haem group binds, reversibly with oxygen.
- Bohr's effect facilitates transfer of oxygen to the tissues because of increased CO_2 levels in blood.
- Haemoglobin molecule has the ability to change its shape when it binds to the first molecule of oxygen due to which its affinity for oxygen increases.

2.6.3 Carbon Dioxide Transport in Blood

The same transport system that brings oxygen to the tissues must take back carbon dioxide to the environment across the respiratory surface present in the alveoli. However, unlike oxygen that is transported exclusively by haemoglobin, carbon dioxide is transported in three ways:

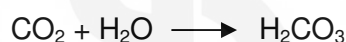
1. as **dissolved carbon dioxide** in plasma (about 8%),
2. **in red cell as carbaminohaemoglobin**. About 25% of the total blood carbon dioxide is carried attached to the amino groups in haemoglobin.



Carbaminohaemoglobin is carried to the lungs where haemoglobin releases the carbon dioxide in exchange for oxygen,

3. as **carbonic acid** (H_2CO_3) and **bicarbonate/ bicarbonate** ion (HCO_3^-) which accounts for most of the carbon dioxide (67%) carried by blood.

Carbon dioxide is generated in the tissues and diffuses freely into the venous plasma and then into the RBCs. In the RBCs, CO_2 combines with H_2O to form carbonic acid (H_2CO_3).

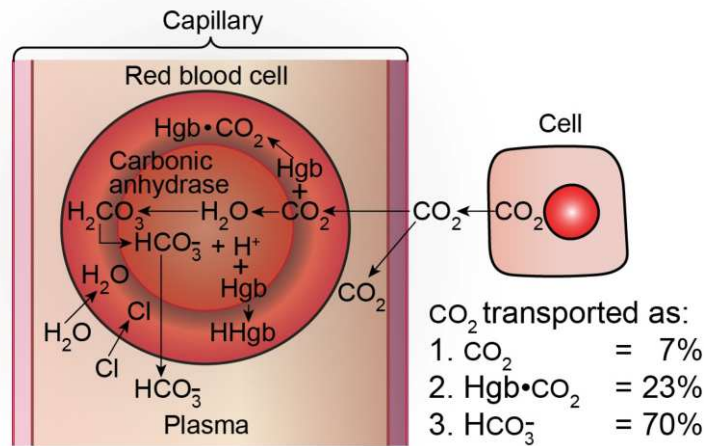


This reaction occurs spontaneously in plasma at a very slow rate but much more rapidly within the blood cell due to the catalytic reaction of an enzyme, **carbonic anhydrase**.

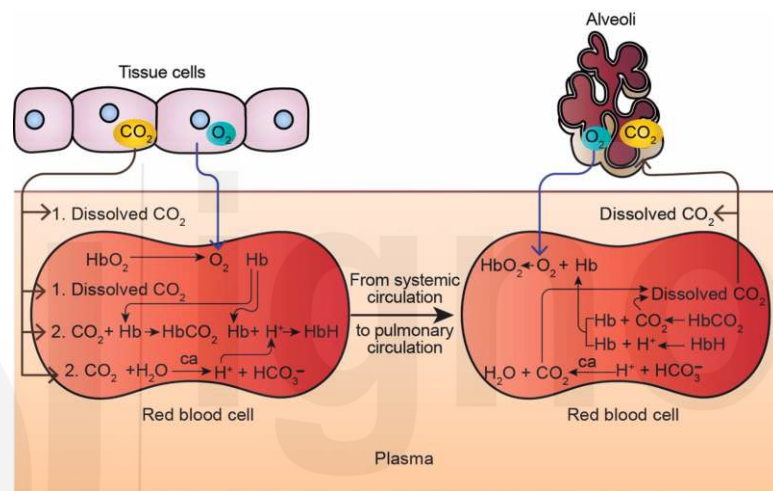
The formation of carbonic acid is favoured by high PCO_2 in the capillaries of tissues. Carbonic acid dissociates rapidly in the red blood cells into hydrogen ion (H^+) and bicarbonate ion (HCO_3^-).



The H^+ (hydrogen ions) released are buffered by combining with haemoglobin and HCO_3^- moves out of the cells. The inside of the cell thus gains a net positive charge. This attracts the chloride ion (Cl^-) which moves inside the red blood cells. This exchange of anions as the blood moves through capillaries in tissue is known as **chloride shift** (Fig. 2.17 a). The red blood cells are very permeable to both Cl^- and HCO_3^- ; because the membrane has a high concentration of a special anion carrier protein called band III protein that binds Cl^- and transfers them in opposite direction through the RBC membrane.



(a)

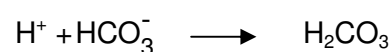


(b)

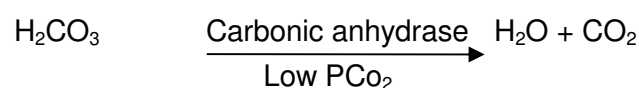
Fig. 2.17: Carbon dioxide transport in blood. a) carbon dioxide is transported in three forms: (i) as dissolved CO₂ gas in plasma, attached to haemoglobin as carbaminohaemoglobin, and as carbonic acid and bicarbonate in plasma due to chloride shift; b) carbon dioxide is released from the blood as it travels through pulmonary capillaries. A reverse chloride shift occurs and carbonic acid is transformed into CO₂ and H₂O releasing CO₂ in the alveolus.

The formation of carbonic acid enhances oxygen unloading (Bohr Effect) and oxygen unloading in turn improves the ability of blood to form carbonic acid and transport carbon dioxide.

When blood reaches the pulmonary capillaries deoxyhaemoglobin is converted to oxyhaemoglobin which has a lower affinity for H⁺. The H⁺ is released in the red blood cells. This attracts HCO₃⁻ from plasma which combines with H⁺ to form H₂CO₃



Under low PCO₂ of pulmonary vessels carbonic anhydrase catalyses the formation of carbonic acid to carbon dioxide and water



Therefore, a **reverse chloride** shift occurs in the pulmonary capillaries to convert carbonic acid, and biocarbonate to CO_2 gas which is eliminated in the expired breath (Fig. 2.17b).

After having discussed the properties of blood and its role in the transport of respiratory gases we can now proceed to discuss the movement of blood in animals in the next unit on circulation.

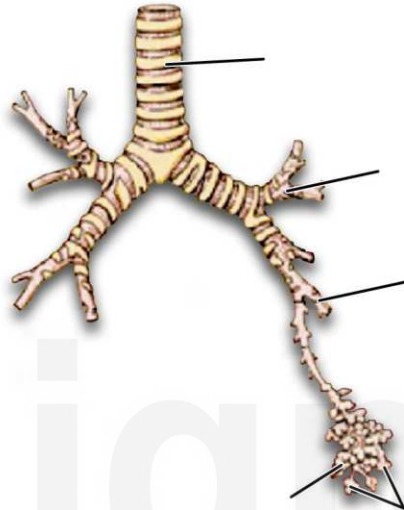
2.7 SUMMARY

In this Unit you have studied that :

- The physiological basis of gas exchange in animals depends on some simple physical principles like solubility of gases, their diffusion rates which in turn depends on the nature of gas, its partial pressure, temperature and presence of other solutes.
- The four basic categories of animal gas exchange mechanisms are diffusion through body surface, gills, lungs and trachea. The design of respiratory surface and the mechanism of breathing are related to the nature of the medium in which the animals live.
- Most aquatic animals exchange gases through gills that are evaginations of respiratory surfaces. The air breathing vertebrate lung is a highly branched inpocketing of respiratory surface containing numerous air sacs or alveoli, intimately associated with capillaries and ventilated by a tidal flow of air.
- Gas exchange in lungs takes place in the alveoli where partial pressure of oxygen is higher than that in blood hence oxygen diffuses from alveoli to blood. In body tissues the partial pressure of oxygen is low hence oxygen diffuses from blood into tissues. Respiration is regulated more by levels of PCO_2 than by PO_2 as the respiratory centre in the brain is sensitive to blood PCO_2 .
- Respiratory gases are transported mainly by respiratory pigments in blood. The most well-known pigment is haemoglobin which combines with oxygen to form oxyhaemoglobin. Oxygen dissociation curve depicts per cent oxyhaemoglobin saturation at different values of PO_2 . Carbon dioxide, pH, temperature and presence of organic compounds in blood influence this curve. A fall in pH decreases the oxygen affinity of haemoglobin for oxygen. This is Bohr effect. Decreased affinity causes unloading of oxygen to the tissue. Oxygen affinity also decreases in the presence of 2, 3-DPG and in conditions of increased blood temperature.
- Carbon dioxide from the tissues is transported to the lungs mainly by formation of carbonic acid in red blood cells; as carboxyhaemoglobin and due to dissolved CO_2 in plasma. Carbonic acid ionizes into H^+ and HCO_3^- . Hydrogen ion is buffered by combining with haemoglobin it and anion balance is maintained by chloride shift. Reverse chloride shift occurs in the pulmonary capillaries and carbon dioxide is formed from carbonic acid dissociation into water and carbon dioxide and hence carbon dioxide in gas form is exhaled outside.

2.8 TERMINAL QUESTIONS

1. Write a formula representing the reaction between haemoglobin and oxygen. What factors influence the rate and direction of the reaction?
2. How carbon dioxide transported when it is released by the tissues into the blood in mammals? What is the role of carbonic anhydrase?
3. Label the Following :



2.9 ANSWERS

Self-Assessment Questions

1. a) ii) and iv) are the correct statements.
b) knowing that oxygen percentage in air is 21

$$PO_2 = \frac{21 \times (735.18 - 18)}{100} = 150 \text{ mm Hg}$$
2. Calculations by scientists, based on metabolic demands and rate of diffusion in protoplasm show that simple diffusion is sufficient to meet the demands of organisms not larger than 1 mm in diameter and since protists (protozoans) and flatworms are less than 1 mm in diameter their respiratory requirements are met through diffusion.
3. i) external intercostal muscles, internal intercostal muscles.
ii) 3, 2
iii) trachea, paired bronchi, bronchioles, alveoli.
4. i) d. The volume of air taken in, in one breath.
ii) c. The additional volume of air that can be taken in by forced inspiration, over and above the tidal volume.
iii) a. The sum of inspiratory reserve volume, tidal volume and expiratory reserve volume.

- iv b. The sum of inspiratory reserve volume, tidal volume and expiratory reserve volume.

5. i) False; ii) False; iii) True; iv) True

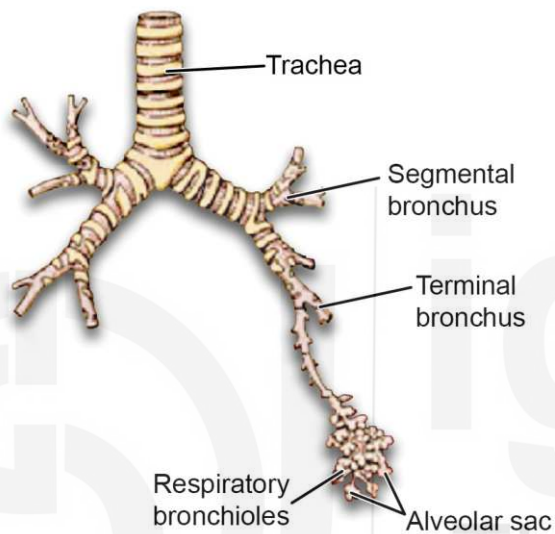
Terminal Questions

1. $\text{Hb} + \text{O}_2$ respiratory membrane HbO_2 (oxyhaemoglobin).

Hint : Temperature, CO_2 , pH and organic phosphates.

2. Refer to Subsection 2.6.3.

3.



CIRCULATION |

Structure

3.1	Introduction	3.6	Blood Vessels
	Objectives		Arteries
3.2	Composition of body fluids		Veins
	Blood		Capillaries
	Lymph		Blood Pressure
3.3	Haemostatic Mechanisms	3.7	Summary
	Primary Haemostasis	3.8	Terminal Questions
	Secondary Haemostasis	3.9	Answers
	Fibrinolysis		
3.4	Plan of Circulatory System in Animals		
3.5	Heart		
	Structure of heart		
	Blood flow in heart		
	Initiation of Heartbeat and Cardiac Cycle		
	Cardiac Output		

3.1 INTRODUCTION

You have learnt in Unit 2 that for cellular respiration to take place there must be a steady supply of nutrients and oxygen and continual removal of the waste products including carbon dioxide. In single celled organisms the supply of nutrients and removal of waste products is easier as their cell surface is in direct contact with their environment which facilitates easy diffusion. In small organisms (diameter < 1mm) gas exchange can take place by simple diffusion across the cell membrane. Such small organism do not need any internal system of transport, However, most multicellular organisms (except sponges, cnidarians and flatworms) require a system for transport of nutrients, waste products and respiratory gases. Such a transport system is called the **cardiovascular system** or the circulatory system. The body fluids which transport the nutrients, waste products and respiratory gases are the blood and lymph.

In this unit, we will study about the composition of blood and its functions in a vertebrate body. The general plan of cardiovascular system (heart as a pump and network of arteries, veins and capillaries as the connected vessels) and the principles associated with circulation of blood will also be discussed. The cardiovascular system of humans which is best known is taken as a representative model and so discussed in detail in this unit.

Objectives

After studying this unit you should be able to:

- ❖ describe the composition and functions of body fluids-blood and lymph;
- ❖ discuss the haemostatic mechanisms;
- ❖ describe structure of human heart, cardiac cycle and calculate cardiac output;
- ❖ explain the flow of blood and blood pressure in arteries and veins; and;
- ❖ describe the process of microcirculation and exchange of fluid across capillary beds.

3.2 COMPOSITION OF BODY FLUIDS

With the evolution of multicellular animals, the development of body fluids *i.e.* tissue fluids, blood and lymph took place so that cells of the body had a constant or stable environment. The body fluid can be divided into: i) the fluid within cells that is the **intracellular fluid (ICF)**; and ii) the fluid outside the cell called the **extracellular fluid (ECF)** (Fig. 3.1a). With the exception of the simplest multicellular animals the cells of all organisms, both aquatic and terrestrial, exist in an “internal sea” of **extracellular fluid** from which the cells take up O₂ and nutrients; and discharge metabolic waste products into it.

In animals with a closed vascular system, the extracellular fluid is subdivided into two components: **the interstitial fluid** and the **circulating blood plasma**. The plasma and the cellular elements of the blood, principally red blood cells, fill the vascular system, and together they constitute the **total blood volume**. The interstitial fluid also termed as tissue fluid is outside the vascular system, and bathes the cells so that the gases and nutrients can pass between cells and blood vessels. The interstitial fluid is formed constantly by filtration from the blood plasma through the capillary walls.

All body fluids - ECF (blood plasma, interstitial fluid) and ICF have one common feature *i.e.*, **they are formed mostly of water**. You would be surprised to know that though we appear solid, we are made mostly of water and so our body consists of 70% water by weight; of which 40% of the body weight is due to intracellular fluid and about 20% of the body weight is due to extracellular fluid. Apart from water, body fluids contain many inorganic and organic substances. These are mainly inorganic proteins and electrolytes. An electrolyte as you may recall is an element or compound that breaks up into ions when dissolved in fluid and is essential to maintaining healthy body functions. The most common electrolytes are sodium, chloride, calcium, and

bicarbonate Fig. 3.1b shows the difference in composition in intracellular and extracellular fluids. These differences are always maintained despite continuous flow of materials in and out of cells.

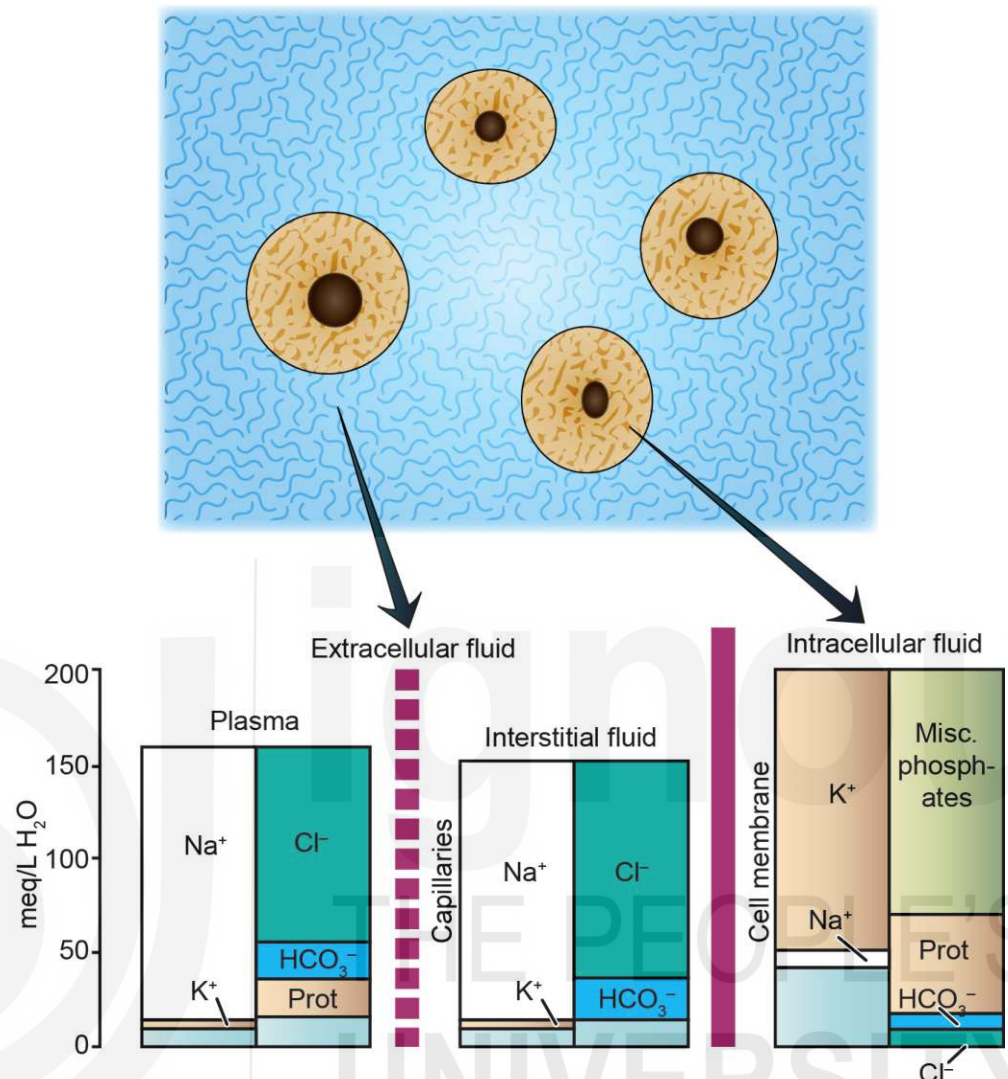


Fig. 3.1: a) Extracellular and intracellular fluid; b) Fluid compartments of the body and electrolyte composition of body fluids. All exchanges with the environment occur across cell membrane. Equal amounts of cations and anions are present in each fluid compartment. Na⁺ and Cl⁻ are virtually absent from intracellular fluids where amount of proteins is much more.

3.2.1 Blood

Among lower invertebrates like cnidarians and flatworms that lack a circulatory system true 'blood' is not found. Only a clear watery fluid with a few phagocytes, some proteins and a mixture of salts similar to seawater is found. The higher invertebrates possess **haemolymph** which is more complex than the fluid found in lower invertebrates. In vertebrates, however, blood is present which is a complex liquid tissue composed of plasma, and formed elements or corpuscles (Fig 3.2). The formed elements are the red blood cells (RBC also called erythrocytes), white blood cells (WBC also called leucocytes/teukocytes) and platelets. The structure of blood makes it an important system of rapid mass transport of nutrients gases and metabolites over distances where diffusion is inadequate.

Blood in vertebrates circulates through blood vessels which are as follows: arteries, veins, arterioles, venules and capillaries. Blood is bright red or scarlet in colour when it flows in the arteries and dark red or purple in colour when it flows in the veins. It is slightly alkaline with a pH of 7.4. The plasma of the blood is a watery fluid and transports dissolved glucose, wastes, carbon dioxide and hormones. The plasma also regulates the water balance for the blood cells.

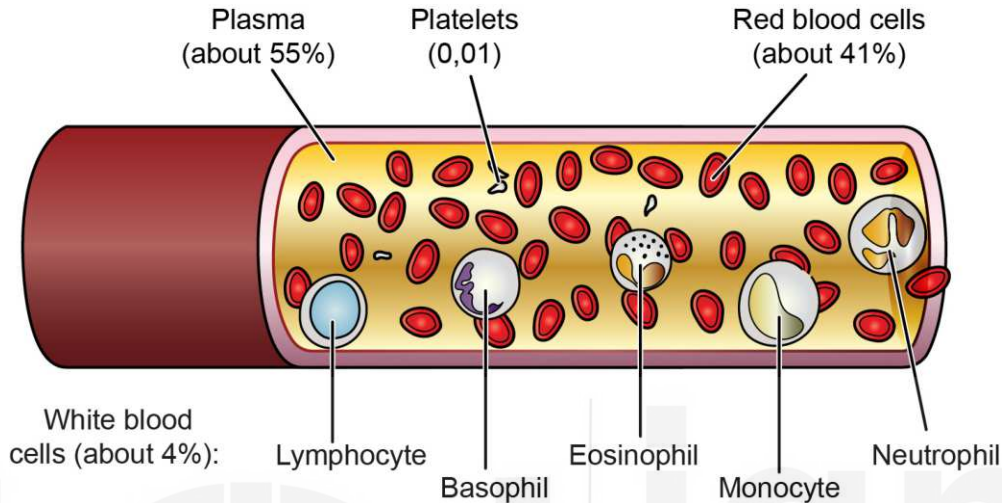


Fig. 3.2: Blood and its components in humans.

Blood Plasma

The fluid portion of the blood as mentioned earlier is the **plasma**. Plasma can be isolated by separating it from the cellular components contained in it by means of spinning a tube of whole blood in a centrifuge. This results in the separation of blood into two portions – a packed mass of cells which constitute around 45 per cent of the volume of the blood and an almost clear, straw coloured fluid called the plasma, which makes up the remaining 55 per cent (Fig 3.3).

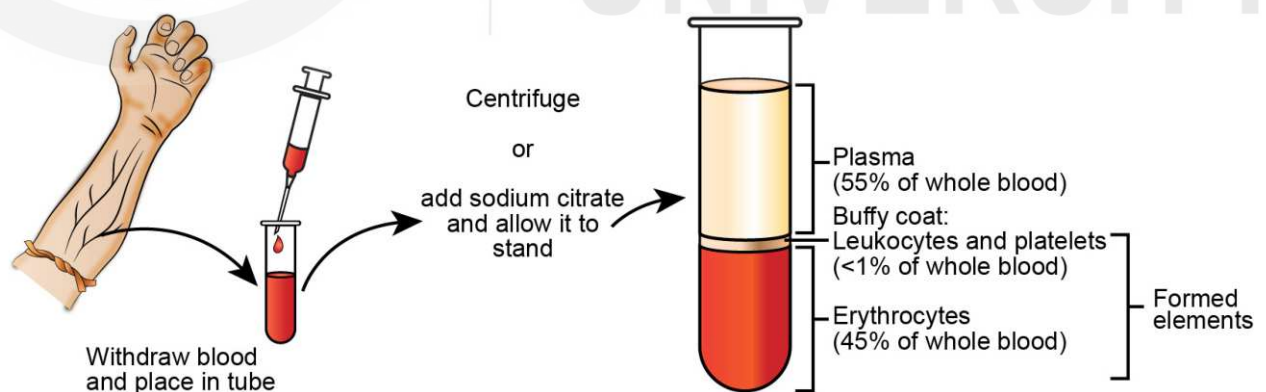


Fig.3.3: Separation of plasma from blood by centrifugation of blood.

Plasma contains a large number of ions, inorganic molecules, and organic molecules which help in the transport of other substances. The composition of human blood plasma is given in Table 3.1. If whole blood is allowed to clot, the fluid that separates is called **serum**. Serum has essentially the same composition as plasma, except for also having fibrinogen and clotting factors II, V, and VIII.

The concentrations of water, mineral ions, plasma proteins, and glucose in plasma are maintained. However, the plasma concentration of urea, CO₂, O₂, various foods, hormones, vitamins and others may vary.

Plasma Proteins

The Reticuloendothelial System (RES) consists of cells descending from the monocytes which are able to perform phagocytosis of foreign materials and particles. 90% of the RES are located in the liver.

The plasma proteins consist of albumin, globulin, and fibrinogen fractions. The total protein concentration of the plasma is around 7% only. The plasma proteins are of three types - serum albumin (4%), serum globulin (2.7%) and fibrinogen (0.3%). Serum albumin and fibrinogen are produced in the liver. The serum globulin is derived from the reticular endothelial system of the body.

Table 3.1 : The main components of blood plasma and their functions.

Components	Percent	Functions
1) Water	90.0	Maintains blood volume and pressure, forms lymph, provides water supply of cells, provides vehicle for transport of other constituents.
2) Mineral ions	Less than 1.0	Maintains osmotic balance, pH balance, buffer capacity, has varied effects on tissue cells.
3) Plasma proteins	7.0	All maintain osmotic and pH balance.
Albumin	(4.0)	Maintains osmotic pressure, regulates blood volume and acts as a carrier protein.
Globulins	(2.7)	Related to immunological reactions and acts as a carrier for certain molecules.
Fibrinogen	(0.3)	Participates in blood clotting.
Prothrombin	(0.3)	Participates in blood clotting
4) Glucose, other organic metabolites	2.0	In transit(moves) to and from cells
5) Urea, CO ₂ , O ₂ , various foods, hormones, vitamins and others	—	In transit to and from cells

The proteins of plasma have several important functions which have been listed in Table 1.3. However we will now briefly describe some of the functions which are as follows:

- 1) The major function of albumin is to provide colloidal osmotic pressure (pressure created by the concentration of colloidal proteins) which ranges between 25-30 mm Hg in the plasma and which prevents plasma loss from the capillaries, thus regulating blood volume, plasma water content and interstitial water content.
- 2) They act as carrier molecules for some hormones, vitamins and iron.
- 3) They act as buffers as you have read in Unit 2.

- 4) The globulins have three fractions and perform a number of enzymatic functions in the plasma. Equally important, they are principally responsible for both natural and acquired immunity of the body against invading organisms. The gamma fraction of the serum globulin (gamma globulin) is associated with production of immune bodies called antibodies. The concentration of these proteins increases during immunisation.
- 5) Fibrinogen plays an essential role in coagulation of the blood. Fibrinogen polymerizes into long fibrin threads during blood coagulation, thereby forming blood clots that help repair leaks in the circulatory system.
- 6) Plasma proteins along with the cellular component of blood give viscosity to the blood and thus aid to some degree in the maintenance of the blood pressure.
- 7) Plasma proteins also act as a source of protein for the tissues, whenever the need arises.

Most of the organic constituents of the plasma other than protein represent waste products of metabolism (e.g. urea, uric acid etc.), together with nutritive materials (e.g. amino acids, glucose and fats) absorbed from the intestinal tract. Among the inorganic constituents of plasma, which consist of sodium chloride potassium, calcium, magnesium, sodium bicarbonate phosphoresce and minute amounts of iodine and iron, the sodium chloride is in the highest concentration.

Cellular Component of blood

The cellular components of blood include red corpuscles also termed as **erythrocytes**, white corpuscles also called **leukocytes** and platelets also called **thrombocytes** (Table 3.2). Erythrocytes and thrombocytes are anucleated cells which perform most of their functions within the blood. Leukocytes (Leucocytes) are nucleated cells and are of five types which are as follows: neutrophils, eosinophils, basophils, monocytes and lymphocytes. Leukocyte cells can migrate out of post capillary venules into the connective tissue or the lymphatic tissue. They perform their functions both within and outside the blood stream.

Red blood cells (RBC)

The red blood cells or red blood corpuscles are also referred to as **erythrocytes** or as RBCs. The red blood cells are specialized cells that contain haemoglobin and circulate through the body and deliver oxygen to tissues and carbon dioxide to the lungs. In humans the normal RBC count in adult males is 5.4 million/ μL of blood and in adult females it is 4.8 million/ μL . The human RBCs are circular, biconcave, disc shaped, non-nucleated cells which contain as you know the oxygen carrying and carbon dioxide carrying pigment the haemoglobin (Table 3.2). Lack of a nucleus makes additional space for hemoglobin in the RBC thus increasing its oxygen carrying capacity. Moreover, the small size and biconcave shape of the RBCs increases the surface area-to-volume ratio, improving gas exchange, while, lack of mitochondria in them prevents red blood cells from using any of the oxygen

they're carrying, maximizing the amount of oxygen, which is to be delivered to tissues of the body. These characteristics allow red blood cells to effectively perform their task of oxygen transport.

RBCs are manufactured in the bone marrow and survive in the circulation for an average of 120 days. Old or damaged red blood cells are broken down in the liver and spleen, and new ones are produced in the bone marrow. Production of RBC is controlled by the hormone erythropoietin, which is released by the kidneys in response to low oxygen levels. This negative feedback loop ensures that the number of RBCs in the body remains relatively constant over time.

In Unit 2, you have already learnt how RBCs with the help of haemoglobin takes up oxygen, and circulate and releases the oxygen to the surrounding tissues. You have also already learnt how it also plays an important role in the transport of carbon dioxide, a waste product, from the tissues, back to the lungs for removal to the outside of the body.

White Blood Corpuscles (WBCs)

The white blood corpuscles or white blood cells are also called **leukocytes** or WBCs. These cells, unlike RBCs are nucleated (have nucleus) and do not have the oxygen carrying pigment haemoglobin. They are mainly involved in immune responses, recognizing and neutralizing invaders such as bacteria and viruses that enter the body and cancerous cells that develop in the body. The total WBC count in blood of humans is 4000 - 11,000/mm³.

The WBCs are subdivided, based on the presence of type of granules in their cytoplasm into the following categories :

- a) **Agranulocytes** (includes Lymphocytes and Monocytes).
- b) **Granulocytes** (includes Neutrophils, Eosinophils and Basophils)

a) **Agranulocytes (Nongranular)**

Agranulocytes as the name indicates are characterized by the absence of granules in their cytoplasm. There are two types of agranulocyte cells (see Table 3.2):

- i) **Lymphocytes** : which are of **two types** namely, **B lymphocytes** cells and **T cells lymphocytes**. The bone marrow constantly produces cells that will become lymphocytes. About 25 percent of the new lymphocytes remain in the bone marrow and become B lymphocyte which are commonly referred as B cells. The other 75 percent lymphocytes travel to the thymus and become T lymphocyte cells commonly referred to as T cells. B cells and T cells work together to fight infection though their mechanism of action in fighting infection differs.
- ii) **Monocytes** : are the largest type of leukocytes. In human blood there are at least three subclasses of monocytes which are classified based on their phenotypic receptors.

b) Granulocytes

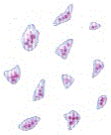
Granulocytes (Table 3.2) are white blood cells that are characterized by the presence of granules in their cytoplasm. They are also called polymorphonuclear leukocytes (PMN or PML) because of the varying shapes of the nucleus, which is usually lobed into segments.

Granulocytes are further divided into (Refer to Table 3.2) :

- i) Neutrophils,
- ii) Eosinophils, and
- iii) Basophils.

Granulocytes are characterized by the colour their granules present in the cytoplasm show when stained with hematoxylin and eosin stain which can be observed under a microscope. This is because staining characteristics of granulocytes are based on hematoxylin and eosin (H&E) staining. Most of granulocytes contain neutrophilic granules (neutrophils), a few contain granules that stain with acidic dyes (eosinophils), and some have basophilic granules (basophils). Whereas **basophilic white blood cells stain dark blue** and **eosinophilic white blood cells stain bright red**, **neutrophils stain a neutral pink**.

Table 3.2 : Formed units of blood. (get this remade slightly different from this) geetas comment.

CELL TYPE	ILLUSTRATION	DESCRIPTION*	CELLS/ μL (mm^3) OF BLOOD	DURATION OF DEVELOPMENT (D) AND LIFE SPAN (LS)	FUNCTION
Erythrocytes (red blood cells)		Biconcave, anucleate disc; salmon-colored; diameter 7–8 μm	4–6 million	D: about 15 days LS: 100–120 days	Transport oxygen and carbon dioxide
Leucocytes (white blood cells)		Spherical, nucleated cells	4800–10,800		
Granular					
Neutrophil		Nucleus multilobed; inconspicuous cytoplasmic granules; diameter 10–12 μm	3000–7000 (65–75% of leucocytes)	D: about 14 days LS: 6 hours to a few days	Phagocytize bacteria
Eosinophil		Nucleus bilobed; red cytoplasmic granules; diameter 10–14 μm	100–400 (2–5% of leucocytes)	D: about 14 days LS: about 5 days	Kill parasitic worms; complex role in allergy and asthma
Basophil		Nucleus bilobed; large purplish-black cytoplasmic granules; diameter 10–14 μm	20–50 ($\frac{1}{2}$ to 1% of leucocytes)	D: 1–7 days LS: a few hours to a few days	Release histamine and other mediators of inflammation; contain heparin, an anticoagulant
Nongranular					
Lymphocyte		Nucleus spherical or indented; pale blue cytoplasm; diameter 5–17 μm	1500–3000 (20–25% of leucocytes)	D: days to weeks LS: hours to years	Mount immune response by direct cell attack or via antibodies
Monocyte		Nucleus U or kidney shaped; gray-blue cytoplasm; diameter 14–24 μm	100–700 (3–8% of leucocytes)	D: 2–3 days LS: months	Phagocytosis; develop into macrophages in the tissues
Platelets		Discoid cytoplasmic fragments containing granules; stain deep purple; diameter 2–4 μm	150,000–400,000	D: 4–5 days LS: 5–10 days	Seal small tears in blood vessels; instrumental in blood clotting

*Appearance when stained with Wright's stain.

The White blood cells, especially the neutrophils and monocytes in the body act as the first line of defence, or provide immunity against invasion by microbes. These cells engulf (take inside) the invading organism through the process of phagocytosis and destroy them. Acting together, these cells provide the body with powerful defenses against viral, bacterial, and parasitic infections and cancer as well. You will study about immunity in detail in your Zoology Elective course 'Immunology'.

Platelets (thrombocytes)

Platelets are a component of blood. They are small, round or oval, non-nucleated (nucleus absent) bodies of varying size (See table 3.2) and are fragments of cytoplasm. Platelets are derived from large bone marrow cells called the megakaryocytes. The megakaryocyte cells, form platelets by pinching off bits of their cytoplasm and extruding them into the circulation. Between 60% and 75% of the platelets that have been extruded from the bone marrow are in the circulating blood, and the remainder are mostly in the spleen. Removal of spleen (splenectomy) causes an increase in the platelet count (thrombocytosis) in the blood.

The function of platelets (along with the coagulation factors) is to aggregate at sites of vascular injury and react with the blood from the injured blood vessel injury by clumping it, thereby initiating a blood clot formation.

The platelets are required for the process of repair of capillary leaks, clot retraction, initiation of blood clot, etc. We will discuss in detail the role of platelets in sections which deals with the process of clothing.

Stem cells and blood cell production

Red blood cells, white blood cells, and platelets are produced in the bone marrow and have a common precursor: a **hematopoietic** stem cell. Stem cells have a characteristic ability to divide asymmetrically i.e., one daughter cell continues to be a stem cell identical to the mother stem cell, while at the same time the other daughter cell acquires a new identity forming a different type of stem cell: either a myeloid stem cell or a lymphoid stem cell (Fig. 3.4).

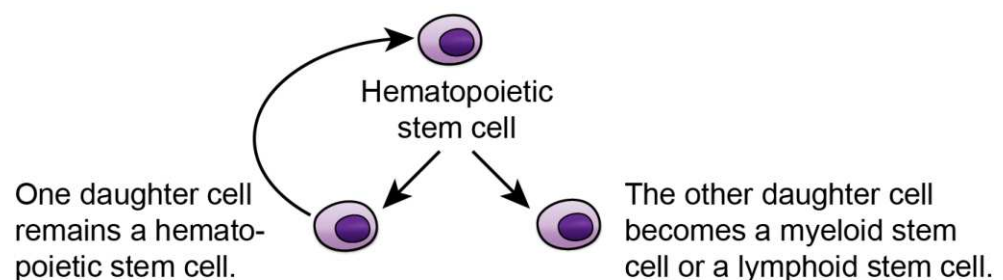


Fig. 3.4: Asymmetrical division of haemopoietic stem cell.

The myeloid stem cells and lymphoid stem cells also divide asymmetrically, with their non-stem cell daughters generating the mature cell types of the blood. **Myeloid stem cells** give rise to red blood cells, platelets, and some types of white blood cells. **Lymphoid stem cells** on the other hand give rise to the types of white blood cells that are classified as lymphocytes (Fig. 3.5).

Hematopoietic, myeloid, and lymphoid stem cells divide throughout a person's lifetime, generating new blood cells to replace old and worn-out ones.

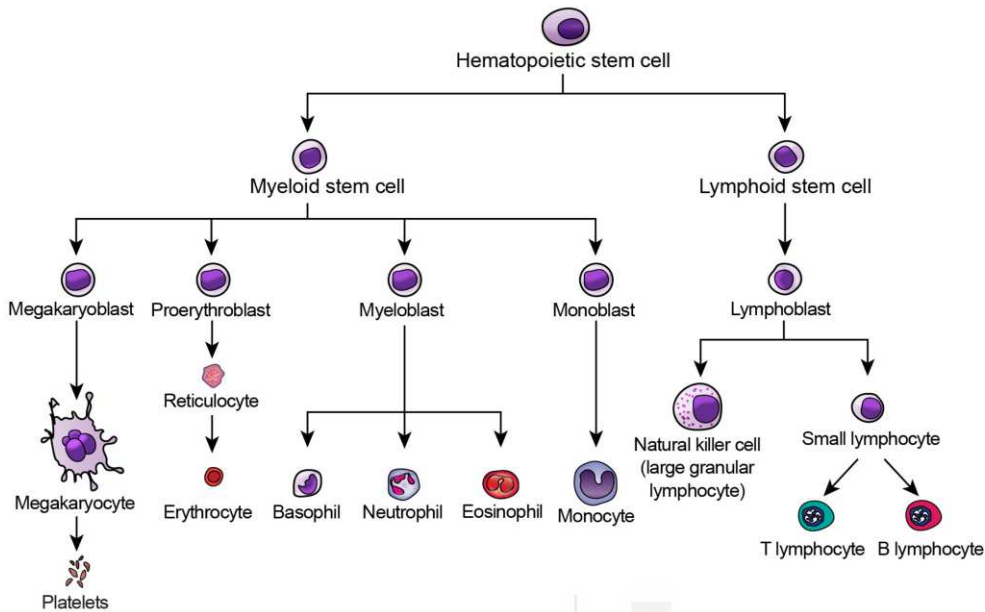


Fig. 3.5: Formation of blood cells from stem cells in bone marrow.

3.2.2 Lymph

Lymph is a modified fluid tissue containing 94% water and 6% solids. It differs from blood in the fact that only lymphocytes or the white blood cells are present in it and red blood cells are absent. The protein concentration of lymph is generally lower than that of plasma, but lymph protein content varies with the region from which the lymph drains (e.g., lymph drained from liver has a protein content of 6.2 mg/dL and from skin has a protein content of 2 mg/dL). Lymph contains clotting factors similar to blood, and so it also clots. Lymph flows in the lymphatic system. This system includes the lymphoid tissues, such as bone marrow and the thymus, as well as lymph glands, sinuses and lymph vessels. Lymph vessels are also referred to as lymphatics or lymphatic vessels and are thin-walled. They carry lymph and are similar to blood vessels that carry blood. The lymph enters the venous system by the main lymphatic vessels - the thoracic and right lymphatic ducts. Water-insoluble fats are absorbed from the intestine into the lymphatics. Lymphocytes enter the circulation principally through the lymphatics, and there are substantial numbers of lymphocytes in the thoracic duct lymph.

SAQ 1

- State the differences between blood and plasma.
- How do intercellular fluids differ from intracellular fluids?
- Match the following:

i) RBC	a. acidophilic granules
ii) Eosinophils	b. agranulocytes
iii) Basophils	c. haemoglobin
iv) Lymphocytes	d. basophilic granules

3.3 HAEMOSTATIC MECHANISMS

When we get hurt or cut our finger, blood starts flowing but within a few minutes the bleeding stops. Haemostasis (from the Greek word *haem* meaning blood and *stasis* meaning halting or stopping) is the body's normal physiological response for the prevention and stopping of bleeding also called haemorrhage at the site of injury while maintaining normal blood flow in the circulation. This mechanism is enough to stop bleeding in case of minor blood vessel injury, but when larger blood vessels rupture surgical intervention is needed.

Let us now study the normal physiological response involved in stopping bleeding at the site of injury while maintaining normal blood flow in the circulation. As soon as bleeding starts, due to damage to the blood vessels the first physiological response is the contraction of blood vessels at the site of the injury so that the blood flow decreases. This is followed by repair of the injured blood vessel by formation of a blood plug or clot. This mechanism is finely tuned so that it happens rapidly and is localized to the site of injury. Abnormalities in haemostasis can result in bleeding (haemorrhage) or blood clots (thrombosis).

The clotting mechanism or coagulation has been well studied in mammals especially humans, as it is of great medical importance and is broadly summarized in Fig 3.6. Let us try to understand the process.

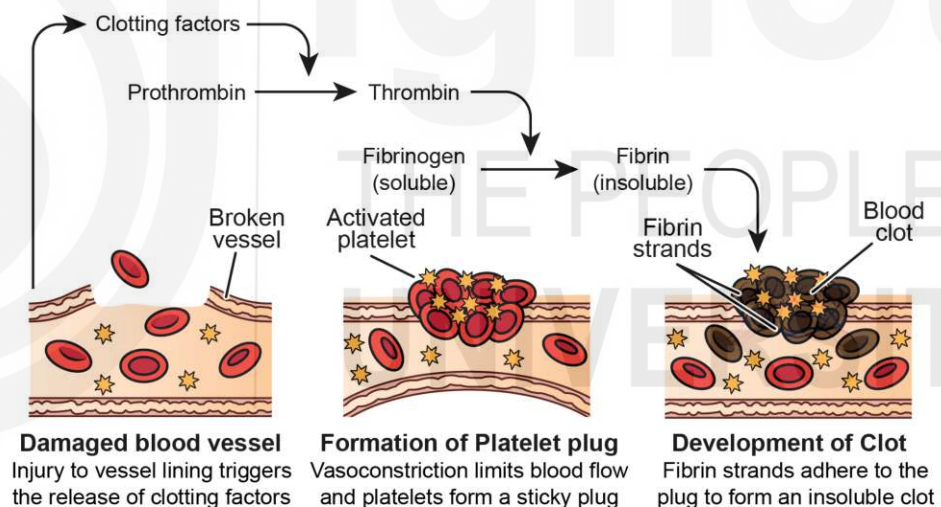


Fig. 3.6: The mechanism of haemostasis.

Haemostasis can be divided into two steps:

- Primary Haemostasis** involving local vasoconstriction and platelet plug formation;
- Secondary Haemostasis** or coagulation involving the formation of a more stable blood clot.

Later another important pathway known as fibrinolysis is activated to restore normal blood flow in the injured area.

3.3.1 Primary Haemostasis

When the lining of a blood vessel (vascular endothelium) is damaged (for instance, if you cut your finger deeply enough for it to bleed), the pain

receptors on the blood vessels and the injured cells of the blood vessel get activated and release several chemicals called endothelins that cause vasoconstriction of the cut vessel. This phenomenon lasts upto 30 minutes and sometimes up to an hour. As is shown in Fig 3.6 damage to the blood vessel releases clotting factors and platelet activating factor (PAF). The activated platelets release signals, which attracts other platelets to the site of injury and make them sticky. Platelet plug formation takes place with help of a glycoprotein called von Willebrand factor (VWF), which is found in plasma.

3.3.2 Secondary Haemostasis

Once the platelet plug formation occurs further bleeding is stopped by formation of a blood clot. This process is characterized by a chain or cascade of reactions (like a multistep waterfall). In the coagulation cascade chemicals called clotting factors activate other clotting factors finally leading to the formation of a mesh of fibrin which is an insoluble protein. There are 12 clotting factors including Ca^{+2} (see Table 3.3) numbered in the order they were discovered. Clotting factors are mostly plasma proteins and are synthesized in the liver and vitamin K is required for the production of many of them.

Table. 3.3: Blood Coagulation factors and their role in clotting pathways

Factor	Synonym	Pathway
I	Fibrinogen	Common pathway. It is converted to fibrin when bleeding occurs.
II	Prothrombin	Common pathway; It is converted to thrombin when bleeding occurs.
III	Tissue thromboplastin or tissue factor	Activates extrinsic pathway
IV	Calcium ions	Essential for all stages of coagulation ; always present
V	Proaccelerin (labile factor)	Common pathway
VI	Now considered identical to factor V so not used	
VII	Proconvertin (stabilising factor)	Both extrinsic and extrinsic pathways
VIII	Antihæmophilic factor A	Intrinsic pathway; deficiency results in hæmophilia A
IX	Antihæmophilic factor B (Christmas factor)	Intrinsic pathway; deficiency results in hæmophilia B
X	Stuart- Prower factor	Common pathway
XI	Plasma thromboplastin antecedent	Intrinsic pathway; deficiency results in hæmophilia C
XII	Hageman factor	Intrinsic pathway; activation initiates inflammation; activates plasmin
XIII	Fibrin stabilizing factor	Cross-links fibrin; forms strong stable clot

Coagulation as we have mentioned earlier is a complex series of reactions. It takes place through two pathways that lead to a common pathway as shown in Fig. 3.7:

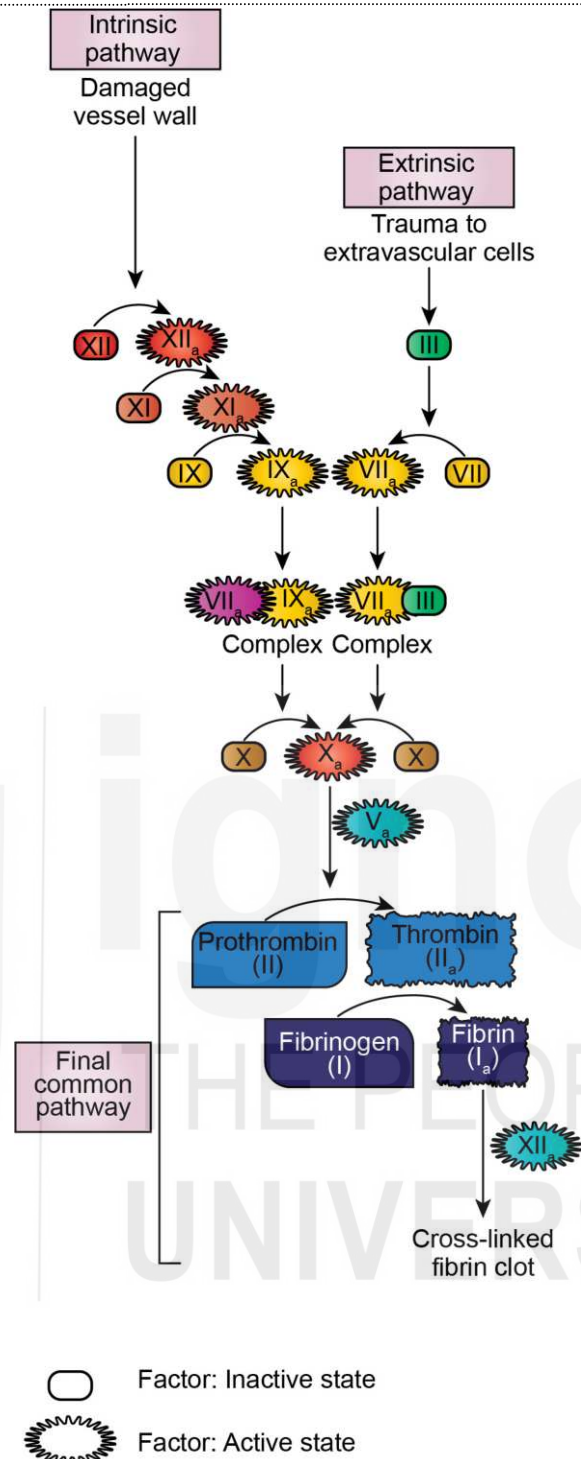


Fig. 3.7: Secondary haemostatic mechanisms. The cascade of clotting reactions begin with the secretion of factor III (tissue factor) secreted from injured vascular endothelium. The extrinsic and intrinsic pathways get activated and converge to form the common pathway during which the fibrin mesh cross-linking occurs resulting in a stable clot. Ca^{+2} is required throughout the whole process.

- i) **Extrinsic pathway** which begins when the tissue around the injury are damaged and come in contact with plasma, therefore, it is known as the tissue pathway. It is faster and more direct and takes place within seconds. It is activated when factor III namely, tissue thromboplastin is released from the damaged extravascular tissue. In the sequence Ca^{+2} and factor VII proconvertin are added to form an enzyme complex which goes to activate factor X (Stuart- Prower factor) which in turn activates the common pathway (see Fig.3.7).

- ii) **Intrinsic pathway** also known as contact activation pathway begins in the blood stream and is triggered by internal damage to the endothelial lining of the blood vessels. It is more complex and longer. Factor XII (Hageman factor) is activated by the damaged endothelial cells and XIIa in turn activates XI (plasma thromboplastin antecedent) which activates factor IX (antihaemophilic factor) which forms a complex with factor VIII and enters the common pathway by activating factor X.

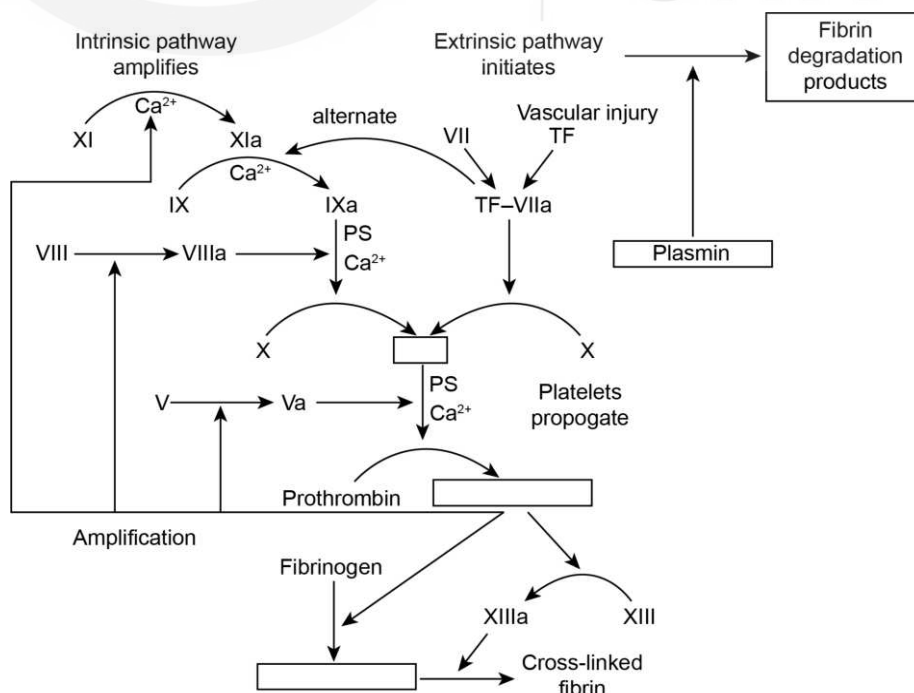
In either pathway the Factor Xa which is the activated form of the coagulation factor X, then binds to prothrombin (a precursor thrombin) to generate thrombin. When the amount of thrombin generation is optimal (right amount), then fibrin is formed from activation of inactive fibrinogen thrombin which causes activation of factor XIII (fibrin stabilizing factor). The fibrin forms threads that reinforce the platelet plug, making a clot that prevents further loss of blood. Thus, fibrin together with platelets forms a haemostatic plug over the wound site. Factor XIII covalently links the side chains of soluble fibrin monomers to form a stable polymer and provide strength and stability to fibrin incorporated in the platelet plug.

3.3.3 Fibrinolysis

The normal blood flow must be restored as the vessel heals and the process that mediates it is known as **fibrinolysis**. It is an enzymatic process in which inactive plasma protein plasminogen is converted to plasmin that helps in breakdown of fibrin in the blood clot and regulates the size of the clot. Plasmin cuts the fibrin mesh at various places into small fragments which are cleared by proteases (enzyme that helps in protein lysis). A vasodilator bradykinin is released that allows the muscles of the vessel to relax reversing the effect of vasoconstriction.

SAQ 2

- State the two steps of Haemostasis.
- Fill in the blanks in the given figure.



3.4 PLAN OF CIRCULATORY SYSTEM IN ANIMALS

We already explained in the introduction of this unit that almost all multicellular animals need a system of transportation or a circulatory system for movement of nutrients, respiratory gases and waste products in the body. You have learnt in the section 3.2 that the medium of this transportation is blood and other body fluids.

Circulation of blood in animals may take place either by :

- i) rhythmic contraction of a pump namely, the heart, or
- ii) through the **peristaltic movements of muscles** that surround the blood vessels and sometimes by the squeezing of the vessels through body movements.

Another common feature of the circulatory systems of all animal is the presence of **one way valves** that control the direction of the flow of the fluid.

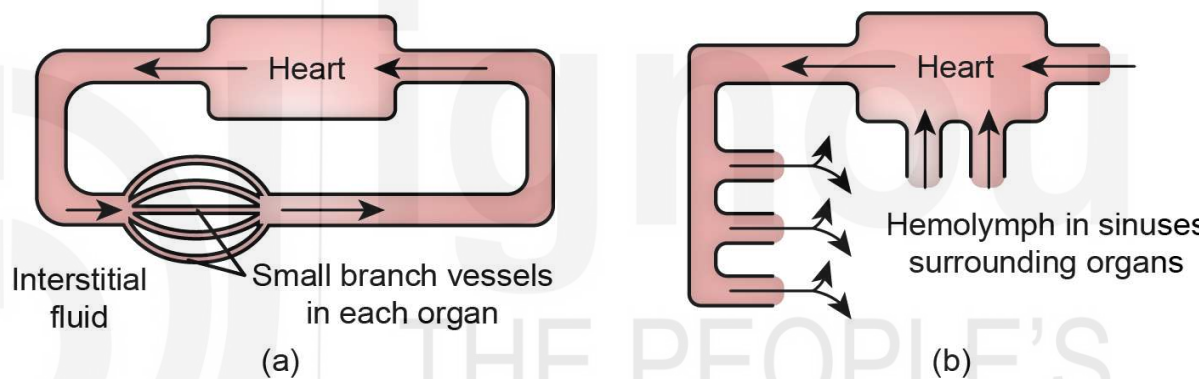


Fig.3.8: Diagrammatic representation of a) Open circulatory system seen in invertebrates like arthropods, mollusks. The haemolymph returns to the heart by ostia; b) closed circulatory system seen in all vertebrates and some invertebrates like annelids, echinoderms and cephalopods.

In many invertebrates the circulation of blood or fluid is aided by the heart which pumps the blood or fluid into a main vessel. This main vessel then empties its contents into open fluid spaces called sinuses and lacunae. Thus the tissues and organs lie directly in the blood filled sinuses **and** are bathed in the blood directly. In such cases the blood is known as haemolymph because it mixes with the interstitial fluid. The **haemolymph** is thus, **confined to vessels for only a part of its circuit through the body**. The remainder of its journey takes place within the body cavity called the **hemocoel**. In this type of circulation the capillaries or small vessels do not connect the main vessels (Fig.3.8b). Network of fine capillaries or minute sinuses are found at some points in a blood sinus which drain into the open ends of the returning main vessel that return the blood to the heart. This type of circulatory system is known as **open circulatory system**. In **open circulatory system** blood pressure is very low. Organisms with an open circulatory system typically have a relatively high volume of haemolymph and very low blood pressure. Thus, this is only a suitable system for animals with low metabolisms that do not require quick energy or immune defenses, or for blood to reach to far extremities.

In animals that have a heart, the circulating fluid or blood is carried from the heart within channels or vessels and eventually returns to the heart for recirculation. Vertebrates and several invertebrates like annelids, cephalopods, echinoderms, possess such a system. In them blood and lymph are pumped by the heart and carried through a system of elastic tubes the **arteries** and **veins**. These arteries and veins are connected through a system of fine vessels called capillaries. The blood leaves the heart through arteries and returns back to the heart through veins without ever leaving these vessels or tubes. Since blood and lymph remain in this closed system of vessels, the circulation is known as **closed circulatory system** (Fig.3.8 a).

In closed circulation the heart is the main pump that propels the blood in the arterial system and maintains high blood pressure in the arteries. The arterial system in turn acts as a pressure reservoir forcing blood through the capillary network. The walls of the capillaries are thin and exchange of material and gases takes place here between the tissues and blood. Each tissue has many capillaries in it and so all the cells of the tissues are very close to the blood supply. Blood leaving the capillaries enters venules that converge to form veins that return the blood to the heart. The venous system maintains low pressure as the veins have much thinner walls than do arteries, Veins can widen (dilate) as the amount of fluid in them increases and therefore contains most of the volume reserves.

In the next section we will study the structure and function of the human heart as the example of a highly developed pump in vertebrate circulation.

SAQ 3

Chose the in correct answer.

- a) A closed circulatory system is required by all animals that have
- i) an immune defense system
 - ii) Interstitial fluids
 - iii) Extracellular digestion
 - iv) Many layers of cells
- b) In the open circulatory system blood is not segregated from:
- i) Interstitial fluid
 - ii) Cytoplasm
 - iii) Digestive cavity
 - iv) Excretory system

3.5 HEART

You all must have felt or heard your heart beating. Did you know that on an average an individual's heart beats at about **80 beats per minute** that is **4,800 beats per hour, 115,200 beats per day**, and more than **42 million**

beats per year, which calculates to roughly **3 billion beats if you live to the age of 72**. This signifies the vital role of the heart in our survival. To comprehend the significance of the heart, you must remember that our body is made up of over 10 trillion cells and each cell has essential needs: oxygen, nutrients, fluid environment and removal of waste. To transport, the above to each and every cell of the body a very efficient transport system is needed. You already know that O_2 is transported through blood which flows in a system of arteries, veins and capillaries. To maintain the flow of blood in the arteries, veins and capillaries a pump is needed. The heart acts as a muscular pump which maintains rhythmic blood flow. You have already studied in Unit 5, in your previous course (BZYT-133-Comparative Anatomy and Developmental Biology of Vertebrates) the structure of the heart of various vertebrates. In the present unit we will be describing the structure and function of mammalian heart in greater detail.

3.5.1 Structure of Heart

Figure 3.9 (a) and (b) shows the position of a human heart in the chest or thorax. The heart lies in the upper left part of the chest under the sternum (breast bone) and is protected by the ribcage. It lies in between the lungs forming a cardiac notch in the left lung.

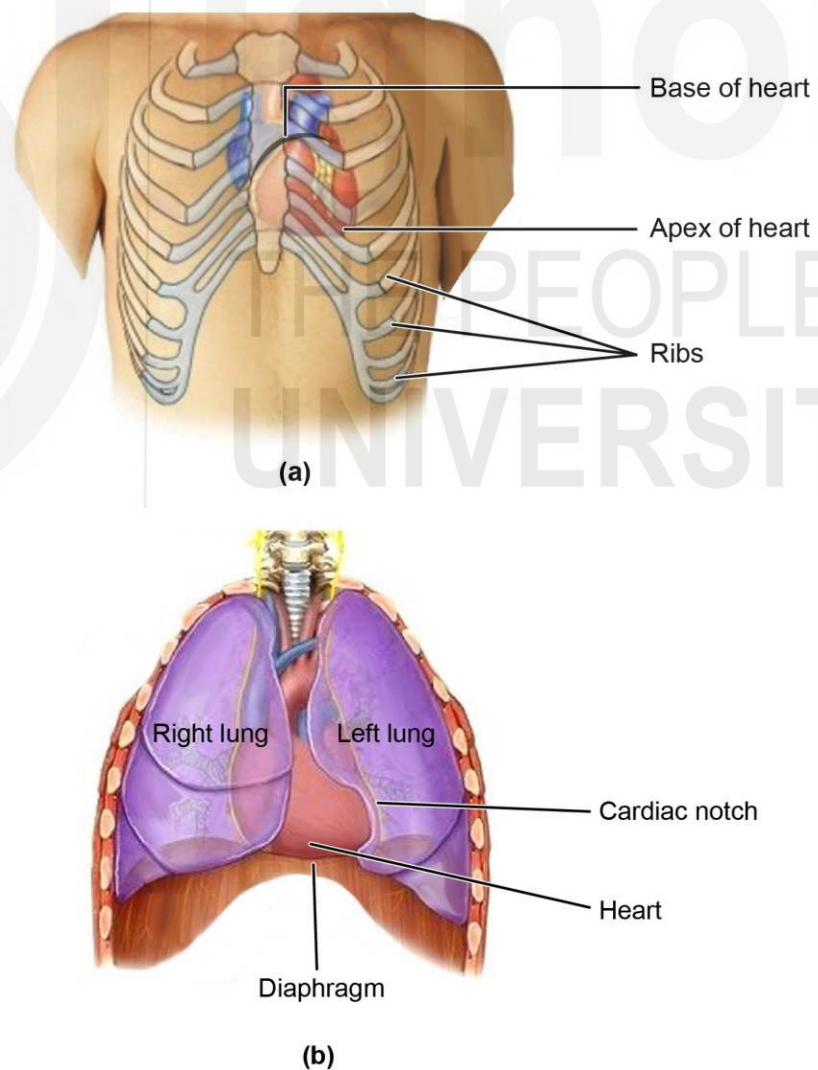


Fig. 3.9: Position of a human (mammal) heart in the thorax: a) heart is protected by the rib cage; b) heart lies in between the lungs forming a cardiac notch in the left lung.

The mammalian heart is a muscular organ and is located within the pericardial space or cavity which is within the mediastinum (central compartment of the thoracic cavity). The heart is covered by a tough fibrous sheath the pericardium which separates the heart from the rest of the organs of the thoracic region. The pericardium has two layers— an inner **visceral layer** that covers the heart from outside and external to it a **parietal layer** that forms a sac around the outside of pericardial cavity (see Fig. 3.10). The pericardial cavity contains fluid which lubricates the heart and permits it to contract with minimal friction.

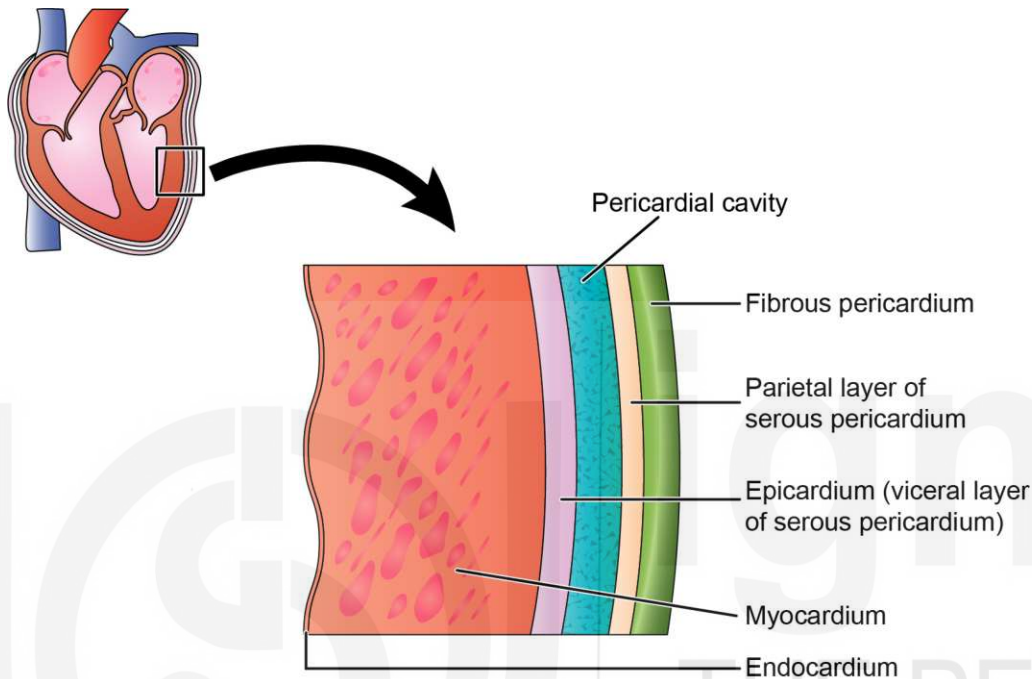


Fig. 3.10: Layers of heart - epicardium, myocardium and endocardium surrounded by the pericardial cavity that contains the pericardial fluid and enclosed in the outmost layer of pericardium.

The wall of the heart is made up of three layers (Fig 3.10) and its thickness varies in different parts of the heart. Just internal to the pericardium is the: i) **epicardium**, also called the **visceral layer of pericardium**. It forms the outermost protective layer of the heart; ii) inner to the **epicardium**, is the middle layer of the heart called the **myocardium which** consists of cardiac muscles. The myocardium is the muscular part of the heart and makes up for most of the thickness and mass of heart wall. It is responsible for the pumping of blood; iii) inner to the myocardium is the innermost layer of the heart which is called the **endocardium**. The endocardium is a thin layer which is made up of an endothelial layer.

Internal structure of the heart

The mammalian heart has four chambers, which consist of two upper chambers and two lower chambers. The upper chambers are called atria (singular atrium) or auricles and the lower chambers are called ventricles. Each half of the heart as shown in Figure 3.11 is made up of an upper, thin walled atrium and a posterior, thick walled ventricle. The thin walled atrium serves as a filling reservoir and the thick walled ventricle pushes the blood into the circulation. The right atrium and the right ventricle are connected by a

tricuspid valve and the left atrium and the left ventricle are connected by a **bicuspid valve also called the mitral valve**. These two sets of valves collectively called the **atrioventricular valves**. Another set of valves called the semilunar valves are also present in the heart. They are present at the region where the pulmonary artery leaves the right ventricle (pulmonary semilunar valve) and the aorta leaves the left ventricle (aortic semilunar valve). Both the atrioventricular valves and the semilunar valves prevent the backflow of blood.

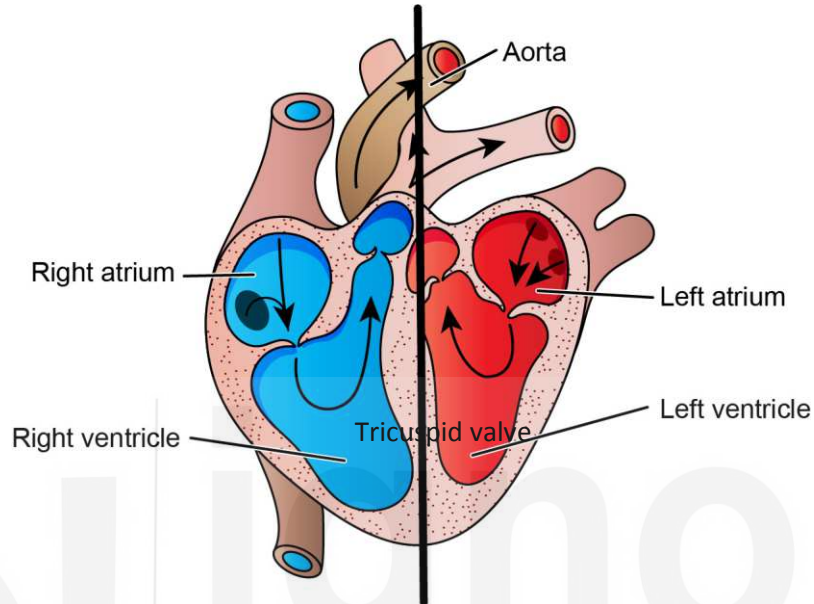


Fig. 3.11: Internal structure of heart Blue shows the flow of deoxygenated blood and red shows the flow of oxygenated blood.

3.5.2 Blood Flow in Heart

You are already familiar from Unit 2 that oxygenated blood from the heart flows in arteries and it releases the oxygen bound to haemoglobin in the tissues and collects the carbon dioxide released from the tissues becomes deoxygenated as it returns to the heart. This is known as **systemic circulation**.

Deoxygenated blood enters the heart from the systemic circulation via the large veins that bring blood back from the top and bottom of the body namely via superior vena cava and inferior vena cava respectively. The deoxygenated blood (**Blue in colour** in Fig. 3.12) is received in the right atrium which is a transit chamber from where the blood goes through the **tricuspid valve** to the right ventricle. The valves make sure that blood only goes one way *i.e.* from right atrium to right ventricle and prevents backflow. The right ventricle (**pump-1**) has muscular walls that constrict and gently push the deoxygenated blood through the tricuspid pulmonary semilunar valve into the pulmonary artery.

The pulmonary artery is the only artery that carries deoxygenated blood.

The tricuspid pulmonary semilunar valve ensures that blood only goes one way. The pulmonary artery carries the deoxygenated blood to the lungs where oxygen from an area of high oxygen concentration (alveoli) diffuses to an area of low concentration (blood) so that the blood becomes oxygenated. This oxygenated blood (**red in colour** in Fig. 3.12) then returns through pulmonary veins to the left atrium of the heart. This part of circulation is known as

pulmonary circulation. Pulmonary vein is the only vein that carries **oxygenated blood**.

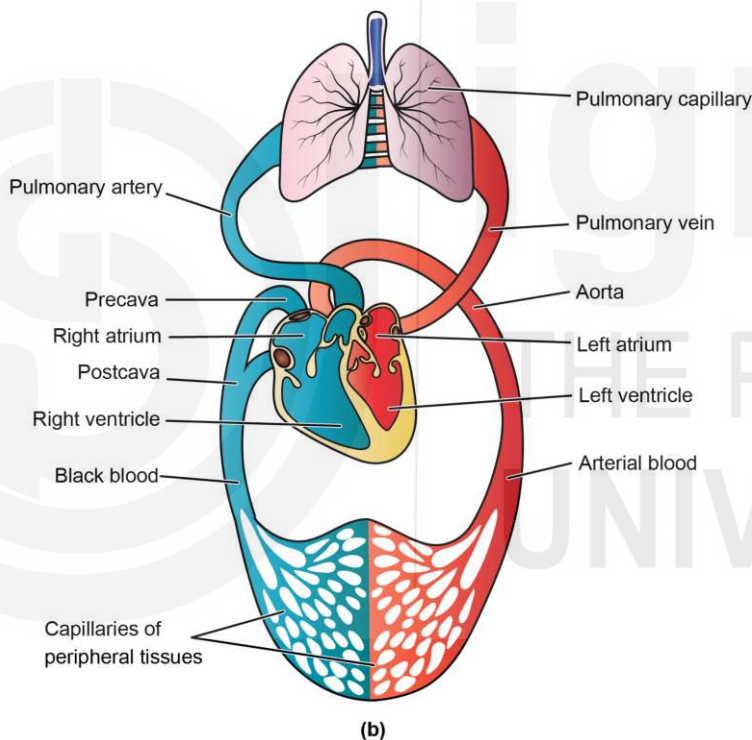
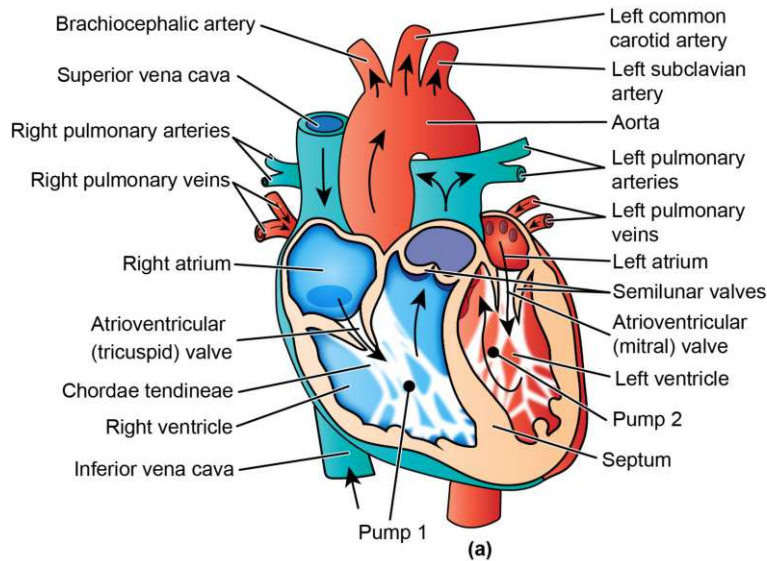


Fig.3.12: a) Cross-section of the human heart, with the right ventricle labeled “pump 1” and the left ventricle labeled “pump 2”. (Adapted from Wikipedia image from Zoofari). B) Fig 6.15 Systemic and Pulmonary circulation.

Just like the right atrium, the left atrium can be thought of as a transit chamber from where the blood passes through the bicuspid valve (mitral valve) to the left ventricle. The left ventricle is stronger, thicker, and more muscular than the right ventricle. As a result, the left ventricle (**pump-2**) forcefully pushes the blood through the aortic semilunar valves into the aorta for the systemic circulation. The muscle wall of the left ventricle is thicker than that of the right ventricle because the left ventricle has to apply greater force for pumping the blood through the systemic circulation. The aorta forks and the blood is divided between major arteries which supply the upper and lower body. The major

artery divides into smaller arteries which further divide into arterioles and then into capillaries of the body in order to supply oxygen to trillions of cells and to take up their carbon dioxide. The relatively deoxygenated blood then travels to the venules, which are the smallest types of veins. The venules coalesce into veins, which are larger vessels. The veins then join to form the inferior and superior venae cavae which finally enter back into the right atrium carrying deoxygenated blood where the process began (Fig. 3.12 b).

The contraction of the heart is known as **systole** and its relaxation is known as **diastole**. The **rhythmic contraction and relaxation of the heart** makes up **one heart beat or one cardiac cycle**. Let us now see how this heart beat is generated.

3.5.3 Initiation of Heartbeat and Cardiac Cycle

Do you know that the heart continuously pumps or beats because of a small electrical current that is generated by the cardiac conduction system of the heart without any external stimulus? The normal human heart beats continuously due to its own inherent and rhythmical electrical activity.

The electrical activity begins in a region of the heart known as **pacemaker**. The cells **of the pacemaker** are capable of spontaneous activity and maybe either composed of neurons or muscle cells. If the heartbeat is initiated in a pacemaker consisting of neurons, then the pacemaker is called neurogenic pacemaker as found in animals with open circulation and if the heartbeat is initiated in a pacemaker composed of muscle cell then the pacemaker is known as myogenic pacemaker as seen in animals with closed circulatory system. Based on the type of pacemaker, hearts are classified as **neurogenic or myogenic**.

In vertebrates the heart is myogenic which means that the source of stimulation for the beating of the heart is a network of specialized self-excitabile cardiac muscle cells called the **autorhythmic cells**. Proof of **autorhythmicity of cardiac muscle cells** can be observed when we see that the heart in a developing chick embryo begins to beat even before any nerve has reached it and also when heart muscle cells grown in a culture contract rhythmically without any external stimulus. These autorhythmic cells have two important functions: (i) They act as you are aware as a pacemaker and set the rhythm for the entire heart, and (ii) they form the conduction system, which is the route for propagating action potentials or electric stimulus throughout the heart muscle for it to contract or relax.

The conduction system ensures that the four heart chambers namely the two atria and two ventricles become stimulated to function as effective pumps. The main components of the cardiac conduction system as shown in Fig 3.13a are the sinoatrial node (**SA node**), **atrioventricular node (AV node)**, **bundle of His**, **bundle branches**, and **Purkinje fibers**.

Sinoatrial node (SA node) is the pacemaker of the heart which initiates electric impulse (Fig. 3.13b). The spontaneous electric impulse or wave of excitation produced by the SA node spreads across both atria **via gap junctions**, causing both atria to contract (atrial systole). Contraction of atria causes the

Cardiac muscle cells are rectangular shaped cells connected by regions called intercalated discs. Intercalated discs contain gap junctions and desmosomes. The gap junctions, are protein-lined tunnels, which allow direct transmission of the depolarizing current from cell to cell, across the chambers of the heart, so that the cells contract in unison. The desmosomes hold the cardiac muscle cells together during contraction. Depolarizations of myocardial cells occur, when they are stimulated by electrical system of the heart which results in their contraction. Cardiac cells at rest are considered polarized. Repolarization is the process in which the cardiac cells return to the resting state before they can be electrically simulated again.

flow of blood from the atria into the ventricle. After the electrical impulses spread across the atria, they converge at the atrioventricular node (AV node) – located within the atrioventricular septum. The atrioventricular septum is the membranous part of the interventricular septum, and is present, near the opening of the coronary sinus which is located along the heart's posterior (rear) surface between the left ventricle and left atrium. AV node after a brief delay sends the electrical impulse forward which ensures that the atria have enough time to fully eject blood into the ventricles before ventricular systole. The **delay** between atrial and ventricular excitation corresponds to the PR interval of the electrocardiogram and it is 120-200 ms in **humans**. The impulse **from** the AV node is conducted through the **bundle of His** (atrioventricular bundle) to the **Purkinje fibres** of the ventricles. From the AV node the impulse descends down the membranous part of the interventricular septum, before dividing into two main bundles: **Right bundle branch** which conducts the impulse to the Purkinje fibres of the right ventricle and **Left bundle branch** which conducts the impulse to the Purkinje fibres of the left ventricle.

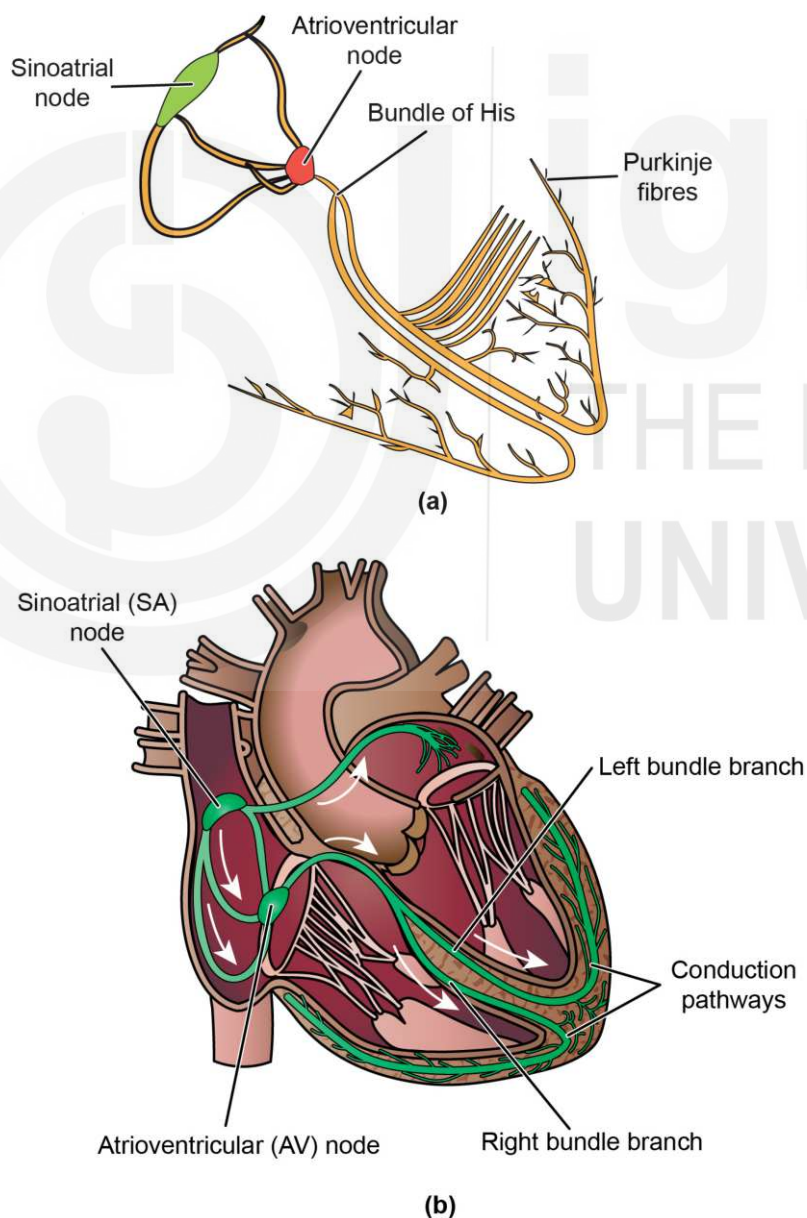


Fig. 3.13: a) The individual components of the human heart (mammal) conduction pathway; b) The pathway of the conducting system of the human heart.

Purkinje fibres are a network of specialised cells which are connected together by desmosomes and **gap junctions**, but not by intercalated discs. The Purkinje cells have extensive gap junctions that help in rapid transmission of cardiac action potentials from the atrioventricular bundle to the myocardium of the ventricles. This rapid conduction allows **coordinated ventricular contraction** (ventricular systole) and blood is moved from the right and left ventricles to the pulmonary artery and aorta respectively. This arrangement allows the contraction to begin at the tip of the ventricles and to spread upwards in order to squeeze out blood in the most efficient way. Thus cardiac conduction is the driving force behind the cardiac cycle. This cycle is the sequence of events of : systole and diastole that occur when the heart beats. Cardiac muscles contracts when electric impulse reaches them. Contraction of heart muscle means that the heart pushes in; making the heart chambers smaller which results in pushing the blood out of the heart and into the blood vessels. Once the heart contracts and pushes out the blood, its muscles then relax, due to which the chambers of the heart get bigger and the blood comes back to the heart and fills the chambers. Therefore, the sequence of events are: atrial systole → ventricular systole → cardiac diastole (Fig. 3.14). When this sequence of events happens one time, it is called a cardiac cycle

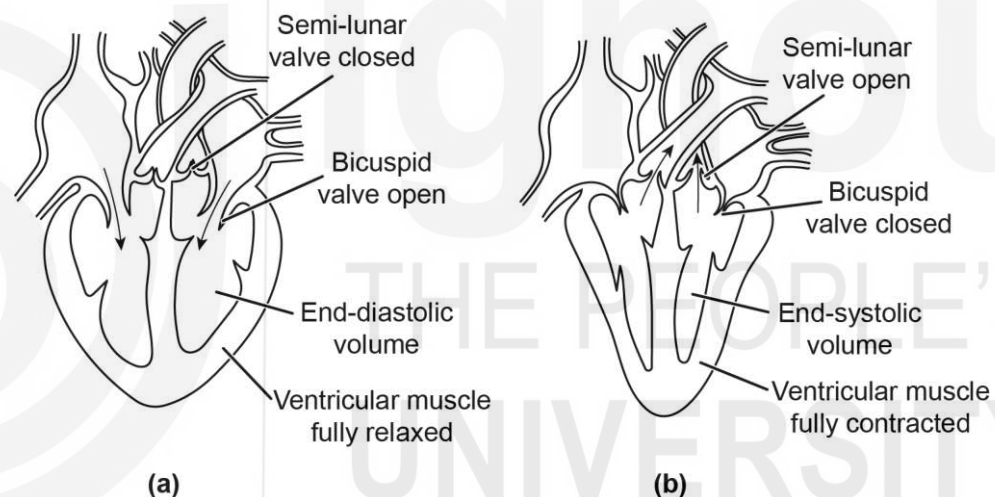


Fig. 3.14: Cardiac Cycle: a) During diastole the heart relaxes and blood is sucked into the heart. The semilunar valves are closed; b) while during systole heart contracts and blood is prevented from going back to atria by the atrioventricular valves. Blood is pumped out through the open semilunar valves.

3. 5.4 Cardiac Output

Now that you know how blood is pumped out by the heart, let us see how much blood is pumped out with each heartbeat and whether it is related to the oxygen requirements of the animal. Heartbeat frequency or pulse rate or heart rate is usually given as the number of heartbeats per minute. The pulse rate for an adult human being is 72 per minute at rest. The volume of blood ejected from the heart per minute is called **cardiac output**. The volume of blood ejected from the left ventricle in one contraction or with each beat is called **stroke volume** (SV). So we can calculate cardiac output as the product of the heart rate, which is the number of beats per minute, and the stroke volume, which is amount of blood pumped by the left ventricle per beat.

$$CO = HR \times SV$$

The cardiac output is usually expressed in liters/minute. For someone weighing about 70 kg, stroke volume at rest is about 70 ml/beat and the heart rate is 72 beats/min. Then the cardiac output (70x72) would be a little more than 5 liters/minute.

Heart rate is affected by autonomous innervations, hormones, age and fitness level of an individual. A nerve branch of parasympathetic origin slows the heart rate by releasing acetylcholine while another nerve of sympathetic origin releases epinephrine and norepinephrine at the pacemaker region to increase the heart rate. Apart from these the pacemaker is influenced by temperature and electrolytes.

SAQ 4

- a) Tick mark the correct answer.
- i) Stroke volume is the
 - a) volume of blood pumped from the heart
 - b) volume of blood pumped into the heart
 - c) volume of blood pumped by one ventricle during a single heartbeat
 - d) number of heart beats per minute
 - ii) Cardiac output equals
 - a) stroke volume multiplied by heart rate
 - b) stroke volume divided by heart rate
 - c) stroke volume added to the heart rate
- b) Fill in the blanks with appropriate words from the text.
- i) Sinoatrial node is the..... of the heart. The electrical impulse starts at this small piece of muscle and spreads to the..... from where it spreads to the.....
 - ii) In the heart the impulse from the AV node is conducted through the..... to the..... of the ventricles.

3.6 BLOOD VESSELS

There are two main types of blood vessels – arteries and veins with characteristic differences among them. Arteries have relatively thick walls that consist of heavy, strong layers of elastic fibres and smooth muscles. As the arteries branch, their diameter becomes smaller and the relative amount of muscle tissue increases in proportion to the elastic tissue. The smallest units of the arteries are the capillaries which are single cell thick. and play a major

role in all exchange between tissue and blood that take place through the walls of the capillaries. The veins also contain smooth muscles and fibres.

The walls of the arteries and veins are largely composed of living cells and need to be supplied with nutrition and they also produce waste. For this the vessels have their own blood supply in the form of a capillary network known as vasa vasorum or 'vessels within vessels'. There are also minute nerves within the walls of these vessels that control and coordinate the constriction and relaxation of these vessels.

3.6.1 Arteries

The arteries except for the pulmonary artery carry the oxygenated blood from the heart to various cells and tissues. Figure 3.15 shows the structure of arteries and the different layers of the vessel wall.

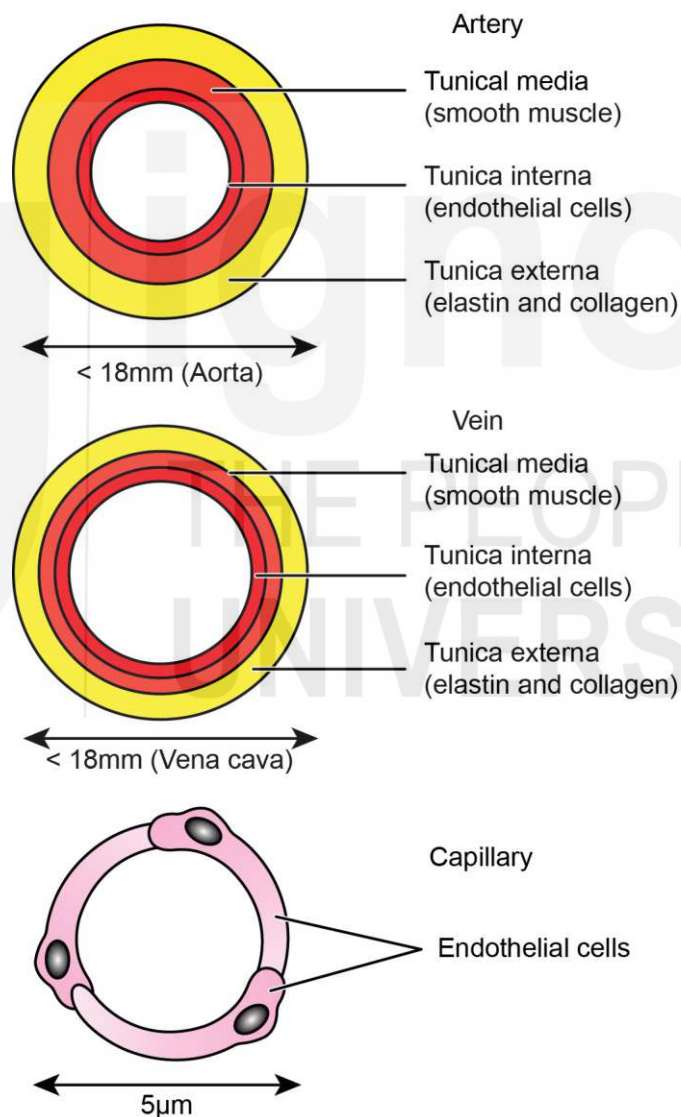


Fig. 3.15: Characteristic features of artery, vein and capillary.

The arteries have four main functions:

1. to act as a conduit for oxygenated blood(except for pulmonary artery which carries deoxygenated blood) between heart and capillaries,

2. to act as a pressure reservoir for forcing blood into small diameter arterioles,
3. to produce a more or less even flow of blood through the capillaries,
4. to control distribution of blood to different capillary networks via selective constriction of the terminal branches.

There is a precise control on arterial blood pressure. The nature of the arterial wall and the volume of blood pumped into the arteries determines the pressure. If any of these are changed, the pressure will also change. Normally, arterial blood pressure varies very little as cardiac output and capillary flows are evenly matched.

The elastic properties of arterial walls vary. Close to the heart the arteries are elastic and dampen (reduce) the oscillations in pressure and blood flow, generated by the contractions of the heart.

3.6.2 Veins

The veins bring back the deoxygenated blood (except for pulmonary vein which carries oxygenated blood) to the heart from the capillaries via the venules. They form a large volume low pressure system. The vessels have a larger internal diameter (Fig.3.15). In mammals 50% of the total blood volume is present in the veins and pressure is approximately 10-5 mm Hg. If there is any blood loss, the venous volume is decreased and not the arterial volume. So that arterial blood pressure and capillary blood flow is maintained. A flow of blood in veins is affected by several factors. Pressure exerted by the diaphragm on the gut and activity of the limbs both help to squeeze the veins of those regions. This squeezing and action of pocket valves (that prevent back flow) help the flow of blood towards the heart. Breathing in mammals also helps in drawing the blood from the veins in the head and abdominal cavity.

Smooth muscles in veins also help in regulating blood supply in the venous system. When a person changes his position from sitting to standing the change in the relative position of heart and brain with respect to gravity activates the nerve fibres that are present in the veins of the limb. This causes a contraction of the smooth muscles and results in the pooled blood to be, redistributed.

3.6.3 Capillaries

We had said earlier that most tissues have such an extensive network of capillaries that any single cell is hardly 2-3 cells away from any capillary. The small terminal arteries subdivide to form arterioles which divide to form metarterioles and then capillaries. The capillaries join the venules which contain the venous blood of the capillaries. Several venules join together to form the veins. The smooth muscles of the arterioles become discontinuous in the metarterioles and end in a muscle ring the precapillary sphincter that controls the blood supply to each capillary bed. Through the precapillary sphincters, fresh blood supply to the capillary bed can be bypassed altogether and blood can be diverted to areas of greater demand. All capillaries of an

animal have the potential to hold 14% of the total blood volume. However, only 30% to 50% of all capillaries are open at a time and thus only 5-7% of the total volume is contained in them.

Capillaries are made up of a single layer of endothelial cells surrounded by a basal membrane. The walls are thin and fragile but because of their small diameter can resist stretching in response to capillary blood pressure. Water and dissolved substances of small molecular weight (gases, salts, sugars, amino acids etc.) can diffuse easily in and out of the capillaries. In addition, fluid is forced out through the capillary walls. Substances of molecular weight more than 70,000 dalton (mostly proteins) do not pass in or out of the capillary walls. These proteins of molecular weight more than 70,000 dalton present in the capillaries exert an osmotic pressure called the **colloidal osmotic pressure**, which tends to draw water back into the capillary from the surrounding tissue fluid (**reabsorption**). Another force, known as hydrostatic pressure of blood **tends** to push the water across the endothelial cell layer and so out of the capillaries (**filtration**). When the hydrostatic pressure within the capillary exceeds colloidal osmotic pressure, fluid is passed out through the capillary wall into the tissues; when the hydrostatic pressure in the capillary falls below the colloidal osmotic pressure the fluid is drawn in from the tissues. At the arterial end of the capillary the hydrostatic pressure is higher than the colloidal osmotic pressure while at the venous end it is often lower. Therefore, fluid is filtered out at the arterial end and taken at the venous end (see Fig.3.16).

The amount of fluid which is forced out and the amount of fluid re-entering varies greatly. Usually outflow exceeds inflow and excess fluid remains in the interstitial spaces. This as you already know forms the lymph.

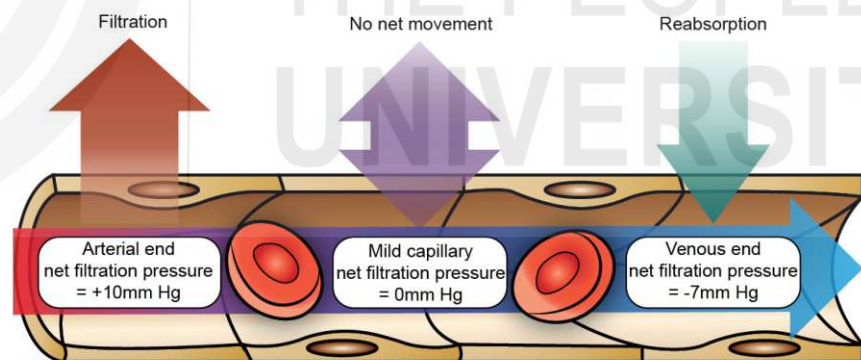


Fig. 3.16: Fluid exchange across the capillary wall, showing differences in blood pressure and colloidal osmotic pressure. Net filtration occurs near the arterial end of the capillary since capillary hydrostatic pressure (35mmHg) is greater than the blood colloidal osmotic pressure (25mmHg). There is no net movement of fluid near the midpoint of the capillary. At the venous end, fluid is reabsorbed as capillary hydrostatic pressure is less (18mm Hg) than colloidal blood pressure (25mm Hg).

3.6.4 Blood Pressure

We are all familiar with the term high blood pressure. What exactly does this term mean? By this term we really mean only arterial blood pressure. When

systemic blood pressure is measured it is recorded as a ratio of systolic and diastolic pressure. In a normal human adult individual blood pressure is 120/80mm Hg. The higher value of 120mmHg is the arterial pressure resulting from the ejection of blood during ventricular contraction and is termed systolic pressure. The lower value of 80mmHg is the arterial blood pressure during the relaxation of the heart and is termed as diastolic blood pressure. The difference between the two is referred to as pulse pressure which is normally 25 % of the systolic pressure. Persistently lower values of pulse pressure could indicate lower stroke volume and possibly congestive heart failure. Higher values can temporarily be attained during exercise but may indicate a diseased condition.

SAQ 5

Select the four true statements:

- a) Arteries generally have larger diameter than veins.
- b) Capillaries are made up of a single layer of endothelial cells surrounded by a basal membrane
- c) The arteries near the heart are more elastic and dampen the oscillation in blood flow.
- d) Whole blood is more viscous than plasma because of the presence of blood cells.
- e) Viscosity of blood changes with decreasing radius of blood vessels.
- f) The maximum pressure during a heartbeat is known as diastolic pressure.

3.7 SUMMARY

In this unit you have studied that :

- Plasma, interstitial and intracellular fluids make up the body fluids in animals. These fluids are mostly water but differ from each other in their solute composition.
- Blood is the fluid transport system which transports nutrients, wastes, heat, regulatory materials and the oxygen carrying pigments in the body.
- Blood is made up of red blood cells, white blood cells, platelets and plasma. Each RBCs contains a hemoglobin which carry oxygen , WBCs provide immunity and platelets are responsible for the haemostatic mechanism.
- Haemostatic mechanism includes primary haemostasis, secondary haemostasis and fibrinolysis. Haemostatic mechanisms like contraction of blood vessels and coagulation help to prevent blood loss during injury. Coagulation is a complex process involving an enzyme cascade which results finally in the formation of a blood clot.

- The vertebrate heart is a myogenic muscular pump that ejects blood into the arterial system. Excitation of the heart starts in a patch of muscle tissue the pacemaker and the contraction spreads to the rest of muscle tissue of the heart. The heartbeat consists of rhythmic contraction (systole) and relaxation (diastole) of the whole muscle mass.
- Cardiac output is dependent on the heart rate and stroke volume.
- The arterial system is the pressure reservoir and conduit for blood between heart and capillaries. The elastic arteries dampen the oscillations in pressure and flow caused by the contractions of the heart. Blood to the capillaries is controlled by muscular sphincters at the arteriole end. The velocity is maximum in arteries and minimum in capillaries.
- The venous system acts as a conduit for blood between capillaries and the heart and as a blood reservoir. In mammals 50% of the total blood is contained in veins.
- Exchange of materials between blood and tissue takes place through capillary walls. Changes in the composition of extracellular fluid and blood in capillaries causes the fluids to leave the capillaries at the arterial end and to be reabsorbed at the venous end.

3.8 TERMINAL QUESTIONS

1. List the components of blood. What is the difference between blood, serum and plasma?
2. Explain with help of a flow chart the cascade of events occurring in secondary haemostasis.
3. Describe in brief the cardiac conduction pathway and cardiac cycle.
4. Differentiate between artery and vein.
5. Explain with help of a diagram **fluid exchange across the capillary wall**,

3.9 ANSWERS

Self-Assessment Questions

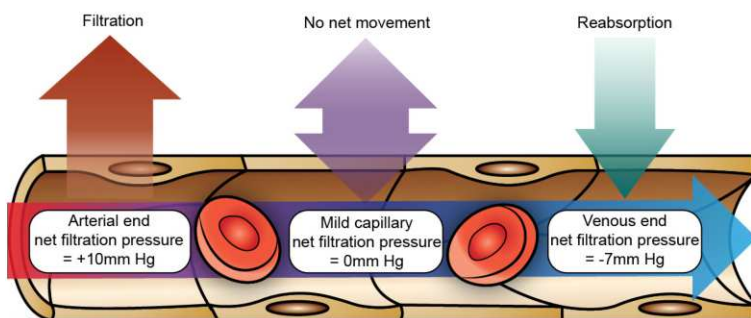
1. a) Blood is complex liquid tissue composed of plasma, and formed elements or corpuscles red and white blood cells and platelets. Plasma is the liquid portion of blood in which the formed elements or corpuscles are absent are suspended in plasma as they move throughout our bodies.
b) The body fluid can be divided into: i) the fluid within cells that is the **intracellular fluid (ICF)**; and ii) the fluid outside the cell called the **extracellular fluid (ECF)**.
c) i) c. haemoglobin

- ii) a. acidophilic granules
 - iii) d. basophilic granules
 - iv) b. agranulocytes
2. a) The two steps of Haemostasis are
- i) **Primary Haemostasis** involving local vasoconstriction and platelet plug formation;
 - ii) **Secondary Haemostasis** or coagulation involving the formation of a more stable blood clot.
3. a) ii) low metabolism
- b) i) Interstitial fluid, ii) Cytoplasm, iv) Excretory system
4. a) i) a. volume of blood pumped from the heart
- ii) a stroke volume multiplied by heart rate
- b) i) PACEMAKER, AV node, ventricles,
- ii) Bundle of His, Purkinje fibres.
5. a); b); c); d).

Terminal Questions

Blood is complex liquid tissue composed of plasma, and formed elements or corpuscles. The cellular components of blood include red corpuscles also termed as **erythrocytes**, white corpuscles also called **leukocytes** and platelets also called **thrombocytes**. Serum has essentially the same composition as plasma, except for also having fibrinogen and clotting factors II, V, and VIII.

1. Refer to Subsection 3.2.1.
2. Refer to Subsection 3.3.2.
3. Refer to Subsection 3.3.5.
4. Refer to Subsections 3.6.1 and 3.6.2.
- 5.



Fluid exchange across the capillary wall, occurs near the arterial end of the capillary since capillary hydrostatic pressure (35mmHg) is greater than the blood colloidal osmotic pressure (25mmHg). There is no net movement of fluid near the midpoint of the capillary. At the venous end, fluid is reabsorbed as capillary hydrostatic pressure is less (18mm Hg) than colloidal blood pressure (25mm Hg) Fig. 3.16.



UNIT 4

OSMOREGULATION AND EXCRETION

Structure

4.1	Introduction	Green Glands
	Objectives	Malpighian Tubules
4.2	Principles of Osmoregulation	4.5 Vertebrate Kidney
	Transport of Electrolytes Across Cell Membranes	4.6 Process of Urine Formation
	Ion Channels in Osmoregulation	Formation of Primary Urine
	Osmoconformers and Osmoregulators	Modification of Urine
4.3	Nitrogen Excretion	Countercurrent Multiplication
4.4	Osmoregulatory Organs and Excretory Function	Urine Volume and Concentration in Dct
	Functional Principles	4.7 Regulation of Kidney Function
	Contractile Vacuoles	4.8 Summary
	Nephridia of Worms	4.9 Terminal Questions
	Molluscan Kidney	4.10 Answers

4.1 INTRODUCTION

In the previous unit you have studied that water accounts for 99 percent of the fluid environment outside cells and is an essential component of the cytoplasm. Distribution of gases; transportation of nutrients and waste products inside the body, all depend on water as a diffusion medium. If the water content of the body changes, all cellular activities are disrupted and life is jeopardized as all chemical reactions inside the body of an organism occur in an aqueous environment. Thus maintaining water balance or **homeostasis** inside the body is of paramount importance. This water balance in the body is

Homeostasis: refers to the body's ability to maintain a stable internal environment. Animal organs and organ systems constantly adjust to internal and external changes in order to maintain this steady state.

In humans electrolyte imbalances lead to muscle spasms, confusion irregular heart beats, fatigue, paralysis and even death.

maintained if the intake of water is equal to water loss; it is also linked to the balance of solutes throughout the body. To survive, an animal must maintain normal volume and composition of the extracellular fluids as well the intracellular fluids, which means that the ionic (electrolyte) concentrations and pH of the fluids have to be maintained along with their volume. The process of maintaining osmotic pressure by maintaining the concentration of ions and water in the body fluids is known as **osmoregulation**.

How this water and electrolyte balance is maintained is the subject of the first part of this unit. We will first look into the processes through which water moves in and out of the cells, then we will investigate how animals regulate the volume of water and ionic concentration in the body in accordance with their external environment. You will learn even though the environments are different, the molecular mechanisms for facing these challenges are the same in many cases. You will also understand how organs such as **kidneys, gills, salt glands** all work to achieve the ionic and water balance in the body of different animals.

Osmoregulation and **excretion** are intimately related as the ultimate aim of these two processes is to maintain homeostasis. Excretion is the removal of toxic waste products of metabolism from the body. The end products of metabolism are either eliminated or conserved by an animal depending on its physiology. We know that carbon, hydrogen, oxygen and nitrogen are the end products of catabolism. Of these carbon atoms are eliminated in the form of carbon dioxide, hydrogen in water and oxygen in carbon dioxide and in water. When amino acids are catabolised, the amino group NH_2 is released and is either transferred to another group for reuse or removal. Any amino groups that are not reused need to be dissolved in water and excreted as soon as possible to avoid toxic rise of waste products in the plasma or must be converted into a less toxic form before being excreted.

The process of excretion and osmoregulation are performed by the same set of organs. In the latter half of this unit we will discuss the structure and function of excretory organs in different animal groups. We will also then learn about the role of hormones in excretion, osmotic and ionic regulation.

Objectives

After studying this unit you should be able to:

- ❖ explain the meaning of osmoregulation and excretion;
- ❖ discuss how osmoregulators and osmoconformers adapt to their environments;
- ❖ discuss anatomical diversity and functional principles of renal organs in animals;
- ❖ describe the process of urine formation in the mammalian kidney;
- ❖ discuss the role of hormones in regulating water and electrolyte balance in the body fluids.

4.2 PRINCIPLES OF OSMOREGULATION

You are familiar with the processes of diffusion and osmosis. After reading Unit 2 Respiration of this course, you already know that diffusion involves the movement of substances from a region of higher concentration to a region of lower concentration. In living organisms solutes move between cells and extracellular spaces along their concentration gradient across a selectively permeable membrane. When the solutes are randomly distributed throughout the solutions on both sides of the membrane then they are said to be in equilibrium and molecules can move back and forth at equal rates. The concentration of solutes in the solution is known as the solution's **osmolarity**. However, when solutes cannot cross the selectively permeable membrane then water moves from the region where solutes are less to the region where the solutes are more concentrated. We can say that water moves across a semi permeable membrane from regions of lower osmolarity to regions of higher osmolarity. This movement of water is called **osmosis** and pressure that would have to be applied to water to prevent it from passing across a semi permeable membrane is the **osmotic pressure**.

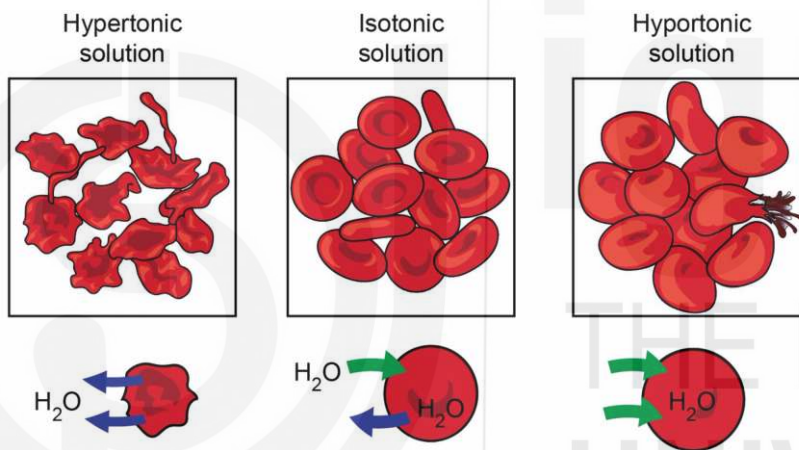


Fig. 4.1: Cells placed in a hypertonic environment tend to shrink due to loss of water. In a hypotonic environment, cells tend to swell due to intake of water. The blood maintains an isotonic environment so that cells neither shrink nor swell. (credit: Mariana Ruiz Villareal).

Recall we had defined osmoregulation as the process of maintenance of salt and water balance (osmotic balance) across membranes within the body's fluids, which are composed of water, plus electrolytes and non-electrolytes. An **electrolyte** is a solute that dissociates into ions when dissolved in water. In most animals the most abundant solutes or electrolytes are sodium, potassium, chlorine and calcium ions. A **non-electrolyte**, in contrast, doesn't dissociate into ions during water dissolution. Both electrolytes and non-electrolytes contribute to the osmotic balance. The body's fluids which you all know includes blood plasma, the cytosol within cells, and interstitial fluid - the fluid that exists in the spaces between cells and tissues of the body. The membranes of the body (such as the pleural, serous, and cell membranes) are semi-permeable membranes. Semi-permeable membranes are permeable (or permissive) to certain types of solutes and water. Solutions on two sides of a semi-permeable membrane tend to equalize in solute concentration by movement of solutes and/or water across the membrane. As seen in Figure 4.1, a cell placed in water tends to swell due to gain of water from the

hypotonic or “low salt” environment. A cell placed in a solution with higher salt concentration, on the other hand, tends to make the membrane shrivel up due to loss of water into the hypertonic or “high salt” environment. Isotonic cells have an equal concentration of solutes inside and outside the cell; this equalizes the osmotic pressure on either side of the cell membrane which is a semi-permeable membrane.

4.2.1 Transport of Electrolytes Across Cell Membranes

Electrolytes, such as sodium chloride, ionize in water, meaning that they dissociate into their component ions. In water, sodium chloride (NaCl), dissociates into the sodium ion (Na^+) and the chloride ion (Cl^-). The most important ions, whose concentrations are very closely regulated in body fluids, are the cations sodium (Na^+), potassium (K^+), calcium (Ca^{+2}), magnesium (Mg^{+2}), and the anions chloride (Cl^-), carbonate (CO_3^{-2}), bicarbonate (HCO_3^-), and phosphate (PO_3^-). Electrolytes are lost from the body during urination and perspiration. For this reason, in very hot weather and during strenuous exercise people are encouraged to replace electrolytes and fluids.

Water can pass through membranes by passive diffusion. If electrolyte ions could passively diffuse across membranes, it would be impossible to maintain specific concentrations of ions in the body therefore **ion channels on cell membranes have a vital role to play in osmoregulation.**

4.2.2 Ion Channels in Osmoregulation

Ion channels are protein molecules that span across the cell membrane allowing the passage of **ions** from one side of the membrane to the other (see Box 4.1). Some of the ions channels which play an important role in osmoregulation and their mechanism of action are as given below :

- **Na^+/K^+ ATPase pump** in cell (plasma) membranes: Powered by ATP, the pump moves sodium and potassium ions in opposite directions, each against its concentration gradient. In a single cycle of the pump, three sodium ions are taken out from the cell when the ATP molecule provides it energy. Then there is a conformational change in the ion protein and two potassium ions are imported into the cell and the phosphate is dissociated from the pump (Fig. 4.2). Na^+/K^+ ATPase pump produces and helps to maintain osmotic equilibrium and a membrane potential (difference in charge) across cell membranes.
- A **$\text{Na}^+/\text{Cl}^-/\text{K}^+$ cotransporter** is a protein which uses the electric gradient produced by Na^+/K^+ ATPase pump to bring the three ions: sodium, potassium and chloride into the cell across the membrane. The cotransporter brings in 1 Na^+ , 2 Cl^- and 1 K^+ together into the cell. There is an abundance of these cotransporters in the kidney where it extracts Na, K and Cl ions from the urine so that they can be reabsorbed into the blood.
- The Na^+ ion is again taken out of the cell by Na^+/K^+ ATPase pumps into the extracellular fluid but concentration of Cl^- and K^+ builds up in the cell.

Selective ion channels allow passive diffusion of ions. K^+ diffuses out of the cell into the extracellular fluid through **potassium channels** and Cl^- is secreted down the concentration gradient via **chloride channels**.

- Sodium ions also diffuse down the concentration gradient through **sodium channels**.
- Aquaporins (AQP) are integral membrane proteins that serve as channels in the transfer of water, and in some cases, small solutes across the membrane.

Box 4.1

Passive transport : Diffusion along an electrochemical gradient without the use of energy. Ions move across the membrane through protein channels, in passive transport there may be specific channels for particular ions and there could be carriers too that bind to specific proteins and undergo shape changes to deposit the bound protein inside the cell, this is known as facilitated diffusion.

Active transport : ATP powered movement of ions. Through special membrane bound proteins, ions are brought inside the cell against the electrochemical gradient. Once an electrochemical gradient has been established inside the cell a cotransporter or an antiporter uses the same energy to bring in a different ion against the concentration gradient.

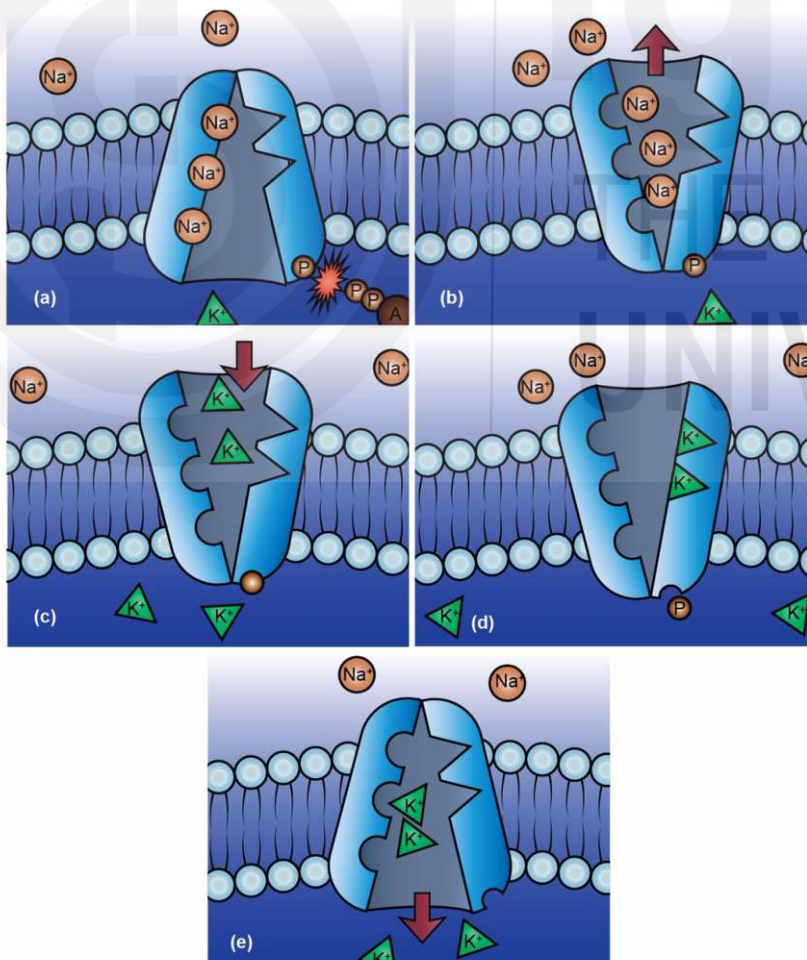


Fig.4.2: Na^+/K^+ ATPase pump functions to maintain osmotic balance and electric gradient across membranes by taking 3 Na^+ out of the cell and at the same time bringing back 2 K^+ into the cell. The energy required for this comes from the phosphorylation of this protein by ATP.

4.2.3 Osmoconformers and Osmoregulators

Biological systems constantly interact and exchange water and nutrients with the environment by way of consumption of food and water and through excretion in the form of sweat, urine, and feces. As there is a constant flow of water and electrolytes, diffusion and osmosis affect animals differently in freshwater, salt water and terrestrial environments, and thus pose different challenges in maintaining water and electrolyte balances.

Aquatic habitats may have varying osmolarities ranging from a few milliosmoles (mOsm) per liter in fresh water lakes to about 1000 mOsm/L in seawater. Landlocked saltwater lakes may have even higher concentrations of salts. Animals living in such environments face constant osmotic challenges as their whole body and even the respiratory surfaces are constantly immersed in water. The animals that can tolerate a wide range of salinities are known as **euryhaline** and those that can tolerate only a narrow range of salinity are termed as **stenohaline**. Let us examine the osmoregulatory challenges in marine and freshwater animals.

Marine invertebrates such as sponges, flatworms, cnidarians etc., face no difficulty in maintaining homeostasis with respect to water and ionic concentration, as their internal fluids resemble the concentrations found in seawater. Thus relative to seawater they are **isotonic**. Animals that do not actively regulate the osmolarity of their tissue though they do regulate their solute composition are known as **osmoconformers**.

Marine fish and other marine vertebrates on the other hand, are **osmoregulators** as they regulate the osmolarity of their internal fluids. Their tissues are **hypotonic** in relation to the sea water (the solutes inside their body are less than the solutes present in seawater). This becomes important in their gills that are constantly exposed to seawater. There is considerable difference between the ion concentration of the cells and the surrounding water, as a consequence the water tends to leave the gill epithelium cells. If this water is not replaced then the cells will shrivel and die. Marine teleosts make up this water loss by drinking large quantities of seawater. Most of the ingested water is absorbed across the intestinal epithelium and along with it the NaCl and KCl is also transported into the blood stream. The excess salts absorbed in the blood stream are removed by active transport of Na^+ , Cl^- and some K^+ by the gill epithelium by specialized **chloride cells** into the seawater and the divalent ions like Ca^{2+} , Mg^{2+} and SO_4^{2-} are secreted through the urine which has a much higher concentration of electrolytes than seawater. Thus the urine of marine teleosts is isotonic to blood but rich in those salts that are not secreted by the gills. (See Fig.4.3 a).

Elasmobranchs have blood plasma **iso-osmotic** to seawater. These fishes however have plasma and interstitial fluid levels of sodium, potassium and chloride ions similar to other vertebrates but to make up the solute levels similar to seawater they have large quantities of soluble compounds like urea and trimethylamine oxide (TMAO) thus preventing the loss of water from the body by osmosis. Sharks still need to excrete the excess NaCl that enters the body through the gills and they do so by special excretory organs, the **rectal**

glands, located at the end of the alimentary canal. This salt excretion is done by active transport of ions against the concentration gradient and requires energy. The Na^+/K^+ ATPase pump is involved in concentration of the sodium and chloride ions inside the epithelial cells so that they are excreted in to the lumen of the gut.

Animals that live in fresh water are also osmoregulators as they have to maintain their body fluids **hypertonic** to their external environment (solutes inside their body fluids are more than the solutes in water). Therefore, these animals have evolved various physiological and behavioural adaptations to cope up with this osmotic stress. An example is freshwater fish. The gills actively take up salt from the environment by the use of mitochondria-rich cells. Water will diffuse into the fish, so it excretes a very hypotonic (dilute) urine to expel all the excess water (Fig.4.3b)

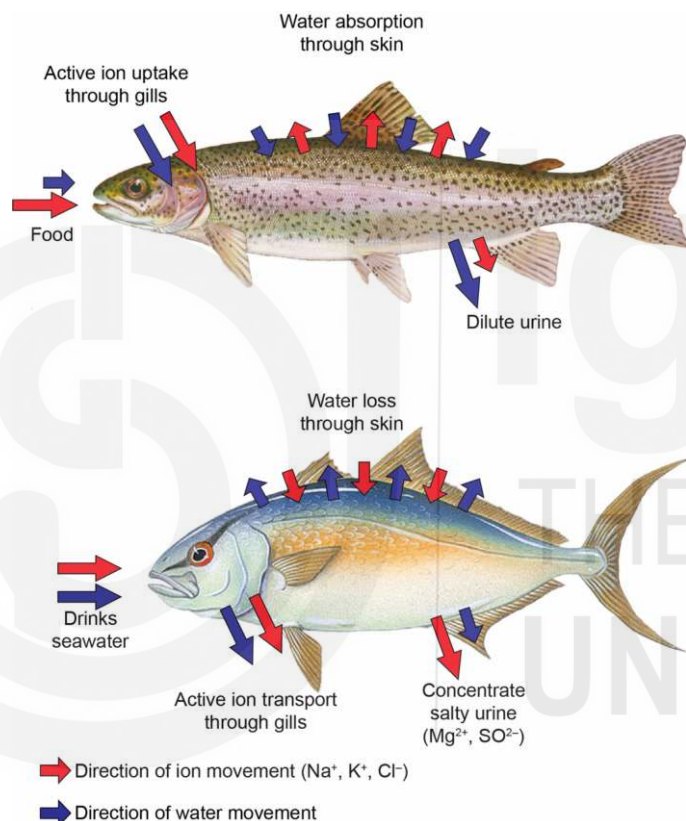


Fig.4.3: Saltwater and freshwater face different osmotic challenges. a) In marine fish water is lost by osmosis and electrolytes are gained by diffusion; b) In freshwater fish water is gained by osmosis and electrolytes are lost by diffusion. Red arrows show direction of ion movement and blue arrows show water movement.

Unlike marine teleosts, marine reptiles for example, iguanas, estuarine sea turtles, crocodiles, sea snakes and marine birds do not produce urine which is hyperosmotic to their body fluids. Instead they have specialized organs for salt secretion. These are the **salt glands** located in the cranium. In birds these are found above the orbit of the eye and in lizards, near the nose or eyes (Fig.4.4). Brackish water crocodiles have salt glands on the tongue. Although neither reptilian nor avian kidney is capable of producing a very hypertonic urine, the salt glands of marine reptiles and birds secrete enough salt to enable them to drink seawater get rid of the excess salt and still produce urine which is isoosmotic to seawater.

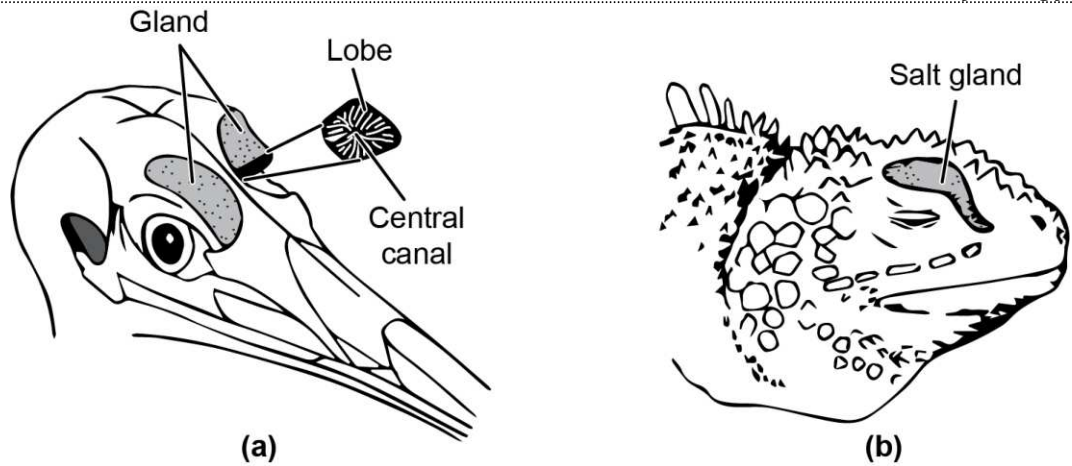


Fig. 4.4: Salt glands in a) bird; b) iguana a reptile.

Terrestrial animals also face water loss challenges. They lose water through evaporation. Land animals exchange gases through moist respiratory surfaces and as a byproduct lose some water too. The situation is further complicated in some species that lose water by sweating or panting to lower their body temperature; and most land animals lose water in the form of urine. These animals need to replace their water loss by drinking water or through food.

SAQ 1

- Osmolarity of an organism depends on the concentration of in their body fluid.
 - The marine environment is to the invertebrates occupying that habitat.
 - The body fluids of marine fish are to their environment while the body fluids of elasmobranchs are to the surrounding sea water
 - Look at Fig 4.2 and describe the process used by the Na^+/K^+ ATPase in your own words. Why is this protein essential?
-

4.3 NITROGEN EXCRETION

Excretion is the removal of toxic waste products of metabolism from the body. The end products of metabolism are either eliminated or conserved by an animal depending on its physiology. We know that carbon, hydrogen, oxygen and nitrogen are the end products of catabolism. Of these carbon atoms are eliminated in the form of carbon dioxide, hydrogen in water and oxygen in carbon dioxide and in water. When amino acids are catabolised, the amino group NH_2 is released and is either transferred to another group for reuse or removed. Any amino groups that are not reused need to be dissolved in water and excreted as soon as possible to avoid toxic rise of waste products in the plasma or must be converted into a less toxic form before being eventually excreted.

You are aware that nitrogen is a characteristic constituent of amino acids and proteins. Animals receive amino acids in diet and use them to synthesise a variety of functional nitrogenous compounds such as nucleic acids, proteins both enzymic and non-enzymic, some hormones, and neurotransmitters. The amount of amino acids obtained in diet is usually in excess of the need for the synthesis of the functional nitrogenous compounds. The excess of amino acids is either catabolised for the release of energy or is used for the synthesis of glycogen and fat. When amino acids, proteins or nucleic acids are catabolised, nitrogen-containing excretory end-product ammonia (NH_3) is formed. Ammonia is a strong base and it gains a proton to form the ammonium ion (NH_4^+). Ammonia is toxic to cells and high concentration raises the pH of intracellular and extracellular fluids enough to poison enzymes in the cells. Different animal species have evolved various strategies to prevent this from happening depending on their habitat. Those that are aquatic can get rid of the ammonia because it diffuses easily in water according to a concentration gradient. However, in terrestrial species ammonia is converted to less toxic compounds like urea that can be excreted in urine, and uric acid a white paste like substance that you must have seen in bird faeces. You will learn about the formation of these catabolic products of nitrogenous compounds in the body in Unit 13 - Protein Metabolism, in Block 4 of this course.

Animals are often grouped according to their main excretory products.

- i) Those that excrete mainly ammonia (NH_3) as the end-product of protein metabolism are called **ammonotelic**.
- ii) Those that excrete mostly urea are **ureotelic**.
- iii) Those that form mainly uric acid are **uricotelic**.
- iv) Those that secrete guanine are **guanotelic**.

Excretion of nitrogen as ammonia, urea or uric acid is closely related to the normal habitat of the animal and to the availability of water. Table 4.1 shows the type of nitrogenous waste produced by an animal correlates with the type of osmotic stress it has to face in its natural habitat. The nitrogen excretion is not restricted to a single product. Animals are designated as ammonotelic, ureotelic, uricotelic or guanotelic only to indicate the predominant form in which nitrogen is excreted. The term uricotelism, for example, does not preclude the excretion of ammonia and urea in minor quantities. The mode of nitrogen excretion may vary within a given group of animals depending on the habitat of the species. For example, South African frog, *Xenopus laevis*, which is aquatic in adult life is ammonotelic whereas, many of the truly amphibious frogs and toads (e.g. Bufo species) excrete urea as adults. Similarly, the aquatic chelonians (tortoise and turtles) excrete more or less equal proportions of urea and ammonia, the semiaquatic forms are ureotelic and the desert living are uricotelic.

Table 4.1: Characteristics of nitrogenous wastes produced by animals.

Characteristic	Ammonia	Urea	Uric acid
Solubility in water	High	Medium	Very low
Amount of water required for excretion	High	Medium	Very low
Amount of energy (ATP) required for its excretion	Low	High	High
Toxicity	High	Low	Medium
Animal group where it is the primary waste	Fish, aquatic invertebrates	Mammals, sharks	Birds, reptiles most terrestrial insects, spiders
Method of synthesis	Breakdown of amino acids and nucleic acids	In liver starting with amino groups from amino acids	Synthesis starts with amino acids and nucleic acids
Method of excretion	In urine and diffuses through gills	In urine (mammals); diffuses across gills (sharks)	In feces (in birds uric acid is derived from urine but excreted with the feces)

4.4 OSMOREGULATORY ORGANS AND EXCRETORY FUNCTION

The process of excretion and osmoregulation are performed by the same set of organs in most animals and they maintain homeostasis in the body. In this section we will discuss the structure and function of excretory organs in different animal groups to learn how the three basic nitrogenous excretory products - ammonia, urea and uric acids have affected the mechanism of their excretion in different habitats.

Recall that marine invertebrates are isoosmotic to their environment and do not need organs of water and ionic balance, therefore, no special organs of excretion are present in marine protozoans and sponges. Similarly the cnidarians and echinoderms that are restricted to the sea are devoid of excretory organs. Discharge of nitrogenous wastes is carried out through the general body surface. In all other animal groups, there are discrete organs that function in osmotic, ionic regulation and nitrogen excretion. These are the contractile vacuoles of protozoans and poriferans; the nephridia of flatworms, annelids and roundworms; the green glands of crustaceans; Malpighian tubules of insects and the metanephric kidneys of vertebrates.

4.4.1 Functional Principles

Though the excretory organs are different in different animal groups the basic function principles are the same. In this section we will discuss some basic functional principles which are common to all excretory organs.

You all know that epithelia are a sheet of cells that cover most of the body surfaces, form the functional unit of secretory glands and line the inner surface of blood vessels. The **apical** surface of the epithelial cells faces the *external environment* which may be the sea or freshwater or the internal lumen of the gut or tubule and the **basal** surface faces the *internal environment* that is, the internal part of the body that contains the intercellular spaces with the extracellular fluid (Fig.4.5). It is important that homeostasis be maintained in this internal environment. And this homeostasis depends on the osmoregulatory capabilities of the epithelial cells.

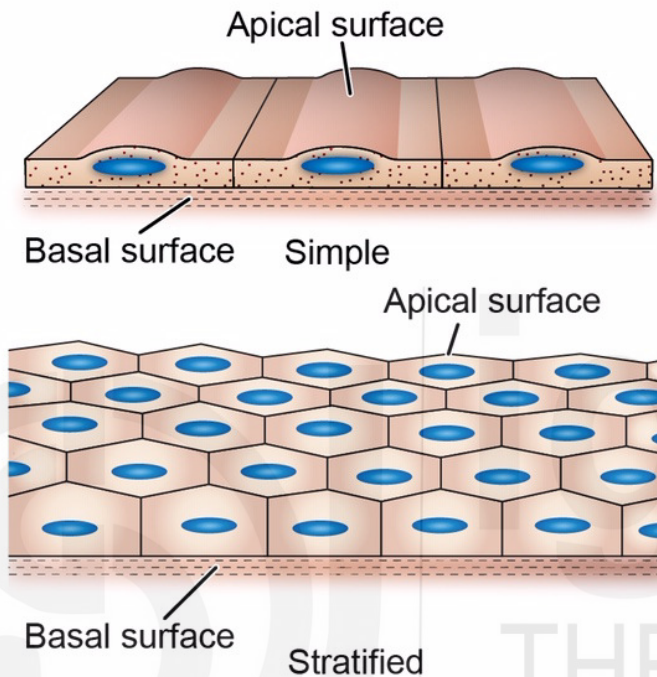


Fig. 4.5: Epithelial cells showing apical and basal surfaces.

The same basic cellular mechanisms are involved in the transport of substances across these two surfaces and these mechanisms are used in all osmoregulatory and excretory organs. For example, similar salt excreting cells are found in the nasal chambers of birds, in reptiles in the kidneys of mammals and in rectal glands of elasmobranches and in the gills of teleosts. Even their activities are regulated by similar hormones. However, the cells are not the same in each case. They are modified according to the requirements of the osmoregulatory or excretory organ in question.

In all animals renal function involves the initial appearance of a dilute fluid in the tubular lumen. This is the **primary urine** and it is isoosmotic to blood or body fluid from which it is derived. The composition and volume of the primary urine are later altered by **reabsorption** of substances useful to the body for example glucose etc., *into the blood* and the **secretion** of substances not wanted by the body for example, urea into the tubular lumen *from the blood*. Both reabsorption and secretion involve active transport. These modifications in the composition and volume result in the formation of the final urine that will be excreted from the body of the animal.

The mechanisms underlying the formation of urine are different in different animals. In many cases it is by the physical process of **ultrafiltration** in

which the blood is forced at hydrostatic pressure to pass through one or more membranes into the lumen of the renal tubule. The resulting **ultrafiltrate is the primary urine**. It is similar in its osmolarity to blood and in the composition of small solutes but does not contain formed blood cells or proteins with molecular weight larger than 67,000kDa. In principle this is similar to the filtration that you perform in your chemistry lab. There you use a funnel and a filter paper. Only those solutes pass through the filter paper along with water by gravitational force that is not larger than the pore size of the filter paper. Only in a few cases (insects) the primary urine though isoosmotic to haemolymph is strikingly different in composition and is formed by active secretion of substances from the haemolymph into the tubular lumen. Whether the primary urine is formed by ultrafiltration or secretion, its volume and composition are subsequently modified by reabsorption and secretion of molecules. In the following subsections we will study the structure and function of various excretory organs.

SAQ2

Fill in the blanks:

- a) The surface of the epithelial cells faces the *environment* which may be the sea or freshwater or the internal lumen of the gut or tubule and the surface faces the *environment* that is, the internal part of the body that contains the intercellular spaces with the extracellular fluid.
- b) is the removal of toxic waste products of metabolism from the body.
- c) Animals that excrete mainly ammonia (NH_3) as the end-product of protein metabolism are called and those that excrete mostly urea are

4.4.2 Contractile Vacuoles

The contractile vacuole complex (CVC) in protists is an osmoregulatory organelle composed of cisternae and interconnecting ducts. Large cisternae act as bladders that periodically fuse with the plasma membrane, forming pores to expel water.

Contractile vacuoles are present in freshwater protozoans and sponges, but are absent from their marine counterparts. Since freshwater animals are hyperosmotic to their surrounding water they gain water by diffusion and need to pump out water continuously. Microscopic examination has revealed that in protozoans contractile vacuoles exhibit a cyclic function (Fig. 4.6). A vacuole gets filled with fluid and increases in volume (diastole) till it reaches a critical volume and then it moves to the cell boundary and suddenly expels its contents to the exterior of the cell and decreases in size (systole). Contractile vacuoles are the primary organs of osmoregulation and any role they may have in excretion of ammonia is considered secondary.

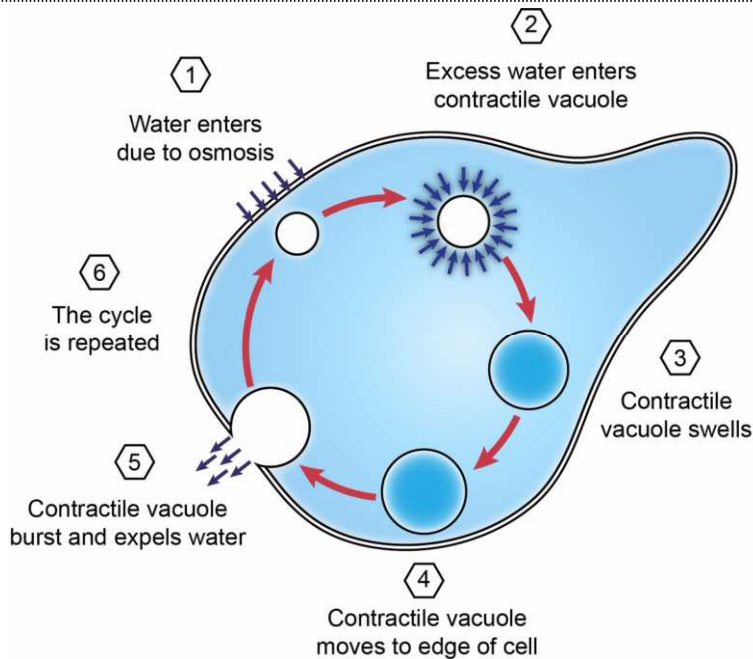


Fig. 4.6: Cyclic function of osmoregulation in amoeba.

4.4.3 Nephridia of Worms

Nephridia are the excretory tubules in many invertebrates. While all nephridia open to the exterior by an excretory pore known as **nephridiopore**, some have their internal end closed and others open into the body cavity by a ciliated funnel known as **nephridiostome**. The former type of nephridia are known as **protonephridia** and the latter type as **metanephridia**.

Protonephridia are more primitive and found in acoelomates and pseudocoelomates. An animal may have one or two more extensively branched protonephridia each terminating in a bulb like **flame cells**. Inside each flame cell is a tuft of cilia that moves to drive the fluid through the tubules (Fig 4.7a). Metanephridia are found in coelomates and are closely associated with their circulatory system. An isoosmotic fluid is filtered into the nephridium through the nephrostome, later salt is reabsorbed and a dilute urine is discharged.

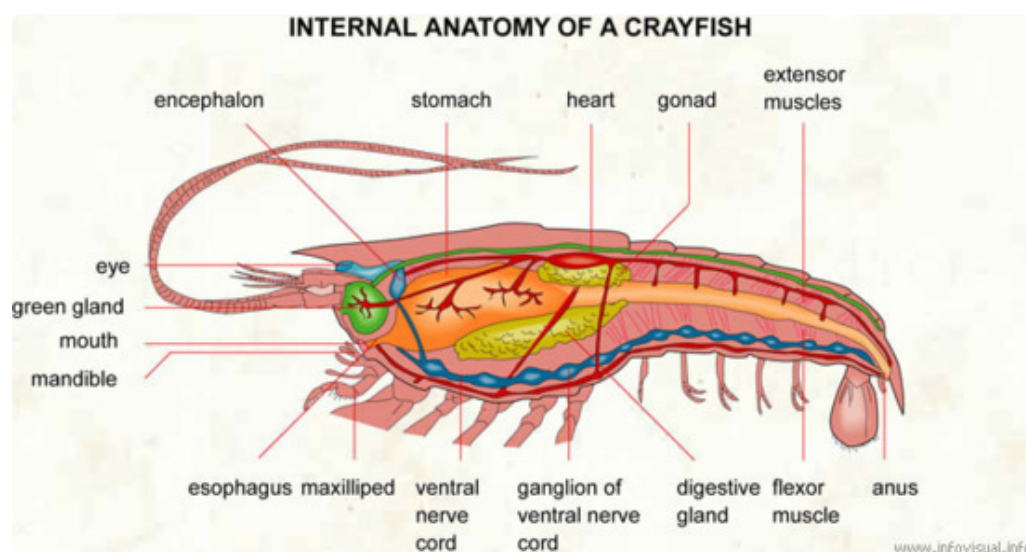
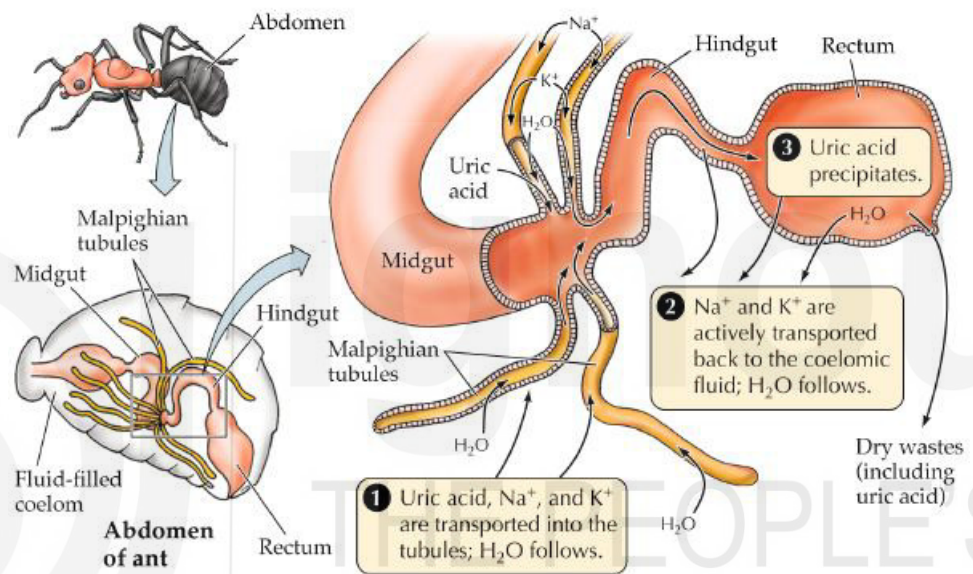


Fig. 4.7: Excretory system of a) planarian with flame cell in protonephridium; b) metanephridium of an earthworm.

4.4.4 Molluscan Kidney

In molluscs the coelom is reduced to the pericardial cavity and the cavities enclosing the kidneys and gonads. The pericardial coelom opens into the renal cavity via the reno-pericardial duct (Fig.4.8). Thus the molluscan kidney is a modified metanephridial coelomoduct with one end opening in the pericardial coelom and the other end opening to the mantle cavity. The initial urine is formed by ultra filtration of the blood through the wall of the heart and the pre-urine enters the renal cavity through the reno-pericardial duct. Reabsorption of valuable materials like glucose and other ions and secretion of unwanted salts and molecules takes place in the kidney sac and ureter resulting in the final urine. Most freshwater snails are able to maintain their body fluids hyperosmotic to the exterior environment in a varying range of osmolarities..



© 1998 Sinauer Associates, Inc.

Fig.4.8: Kidney and its relationship to the pericardium in freshwater snail.

4.4.5 Green Glands

Crustaceans have a pair of renal organs, each of which contain a closed end sac with a labyrinth and a coiled nephridial canal ending in a bladder that opens to the exterior through an excretory pore located at the base of the antennae in which case they are known as the **antennary glands** or opening at the base of the maxillae, where they are known as **maxillary glands**. The end sac in many cases is green hence these are also known as the green glands (Fig. 4.9 a). Urine formation in crustaceans too involves filtration, reabsorption and secretion. In the **antennal gland** of the freshwater **crayfish** (*Astacus*), fluid is filtered from the blood into an **end sac** and passes through a tubular labyrinth. Cl^- is reabsorbed from the isoosmotic ultrafiltrate during its passage in the nephridial canal so that the final urine is hypoosmotic (Fig. 4.9b). Like other freshwater invertebrates the urine is hypoosmotic and very dilute and in brackish water crustaceans the urine is closer to blood osmolarity. This may be due to the absence of the salt reabsorbing segment in the nephridial tubule. The hydrostatic pressure of the blood drives the force of filtration.

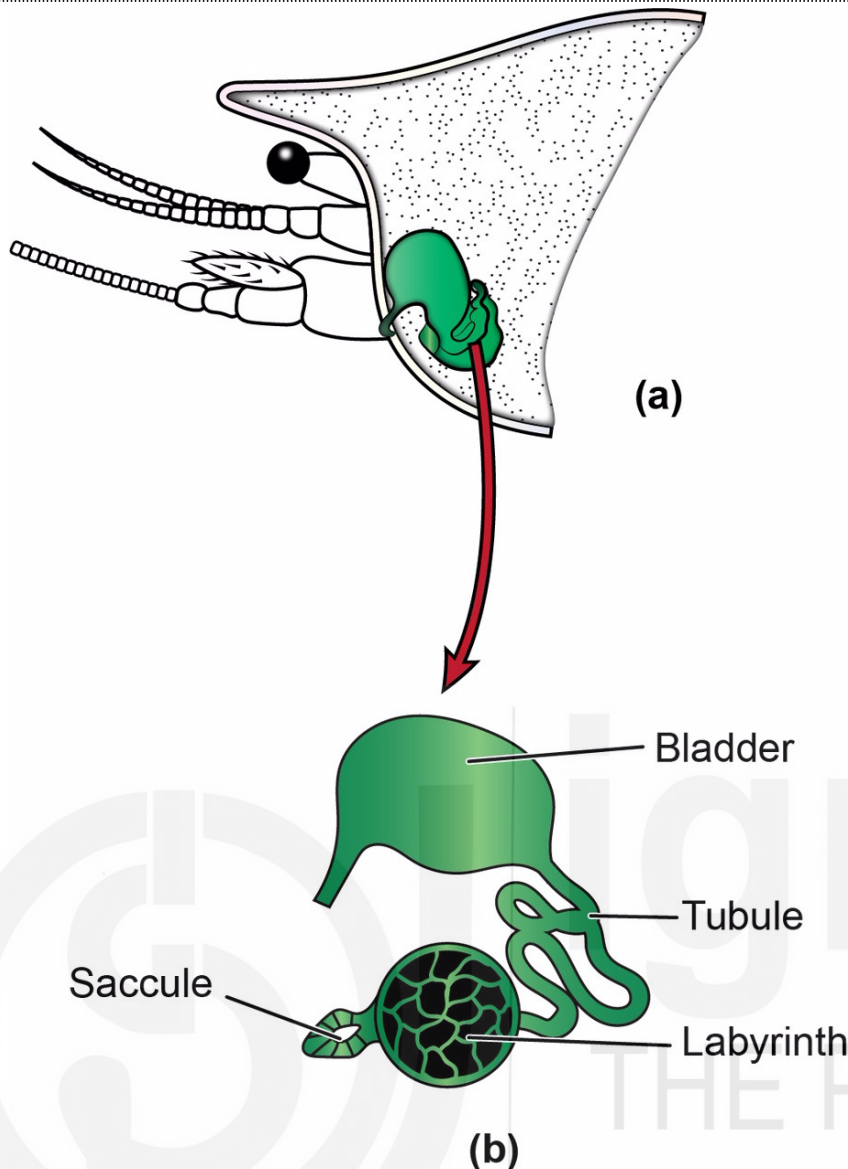


Fig. 4.9: a) location of green gland b) Structure of the renal organ and urine formation in crayfish

4.4.6 Malpighian Tubules

The osmoregulatory and excretory organs of insects are the **Malpighian tubules** that may be two to several hundred in number, and the hind gut (ileum, rectum and colon). Each tubule is similar to a protonephridium in that, one end is blind and the other end opens in the gut between the midgut and hindgut. The tubule as a whole is bathed in the haemolymph (Fig. 4.10a). The mechanism of primary urine formation, however is different. The tracheal system of insects eliminates the necessity of a pressurized arterial circulatory system, therefore, the formation of primary urine takes place by secretion rather than ultrafiltration. Most of the molecules present in the haemolymph are also present in the Malpighian tubules. Before excretion the essential ions molecules etc., are reabsorbed in the hind gut. Reabsorption is highly selective and takes place because of chloride pumps and Na^+/K^+ ATPase and valuable ions are retained while waste products and faeces are eliminated from the body. The whole process of reabsorption is tightly regulated allowing precise control over water and ionic balance. Figure 4.10b summarizes the process of urine formation in gut of locust.

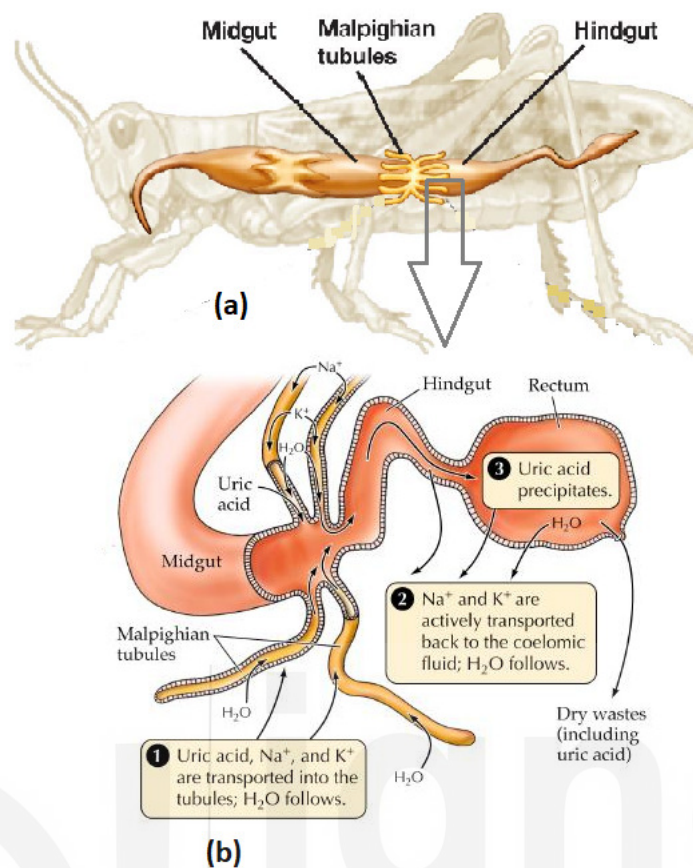


Fig. 4.10: a) Location of malpighian tubule b) Formation of urine in the Malpighian tubules and gut of locust

SAQ 3

- a) Match the following in column A with terms in column B.

Column A	Column B
i) Malpighian tubule	a Crustacean
ii) contractile vacuole	b Amoeba
iii) nephridia	c mammals
iv) green gland	d worm
	e insects

- b) describe with help of diagram the cyclic function of osmoregulation in amoeba.

4.5 VERTEBRATE KIDNEY

Typically all vertebrates have a pair of kidneys, which function on the filtration, reabsorption and secretion principle. Only in a few teleost fish the kidney is aglomerular and functions on absorption-reabsorption-secretion principle as in

the Malpighian tubules of insects. We will describe the mammalian kidney here as we understand its functions the best though it is not a representative of all vertebrates as it performs several functions that in lower vertebrates are shared by other organs such as skin and bladder in amphibians, gills in fish and salt glands in reptiles and birds.

You have studied the structure of the mammalian kidney in Unit 6 of your previous course BZYCT-133 (Comparative Anatomy and Development Biology of Vertebrates). You all know that there are two kidneys in the body that are bean shaped organs. A large blood vessel the **renal artery** brings in blood containing nitrogenous wastes to each kidney and the **renal vein** takes away the filtered blood. The urine that is formed is collected in the **ureters** leading to a storage organ the **bladder** from where it is transported to the body surface by a tube called the **urethra** and excreted. Figure 4.11 shows the human urinary system and longitudinal section of a kidney with its internal parts.

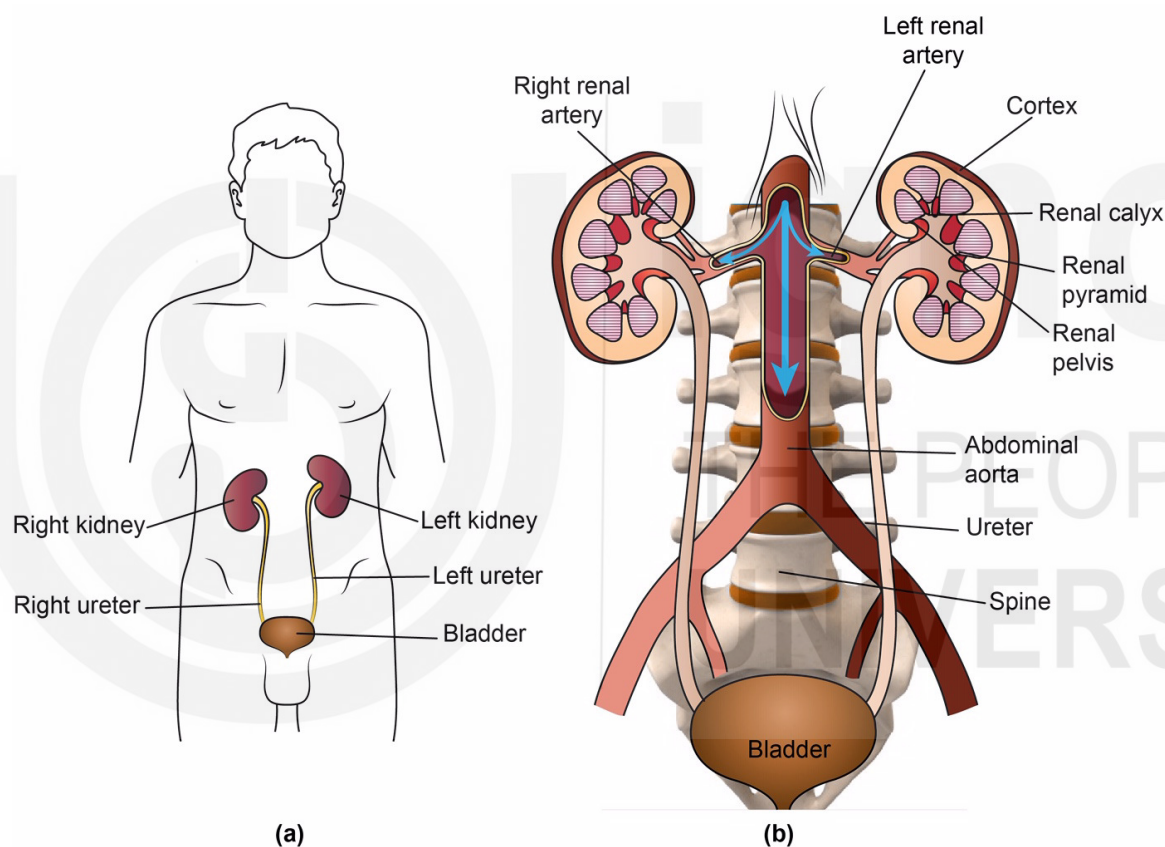


Fig.4.11: Anatomy of the human urinary system. a) A pair of kidneys are located near the spinal column. (b) L S of Kidney Cortex - the outer part of the kidney; Medulla - the inner portion of the kidney; Pyramids - the triangular-shaped divisions of the medulla of the kidney; Papilla - narrow, innermost tip of the pyramid; Pelvis - the kidney or renal pelvis is an extension of the upper end of the ureter (the tube that drains urine into the bladder); Calyx - each calyx is a division of the renal pelvis; opening into each calyx is the papilla of a pyramid

The functional unit of the vertebrate kidney is the **nephron** or the **uriniferous tubule**. A small fish may have its kidney made up of just a few nephrons; a large mammal may have several million nephrons organized into the bean shape structure that we associate with the kidney. Most of the nephrons in a human kidney (approximately one million) are located in the outer layer or

cortex however some nephrons extend in to the inner region known as **medulla**. As you can see in Figure 4.12 each nephron begins as a closed tube in the shape of a double walled cup called the **Bowman's capsule** (imagine a balloon that has been pushed in from one end forming a cup) and extends into a narrow tube that empties into a collecting duct along with other nephrons. Several such collecting ducts combine to form papillary ducts that finally empty into the ureter. The Bowman's capsule in each nephron encloses a knot of fine capillaries forming the **glomerulus**. Together the Bowman's capsule and glomerulus form the **renal capsule**. The Bowman's capsule of each nephron continues to form the long convoluted tubule that can be distinguished into - **proximal** and **distal convoluted tubules** respectively. In mammals and birds there is a 'U' shaped region of the nephron that is present between the proximal and distal tubules, the **loop of Henle**.

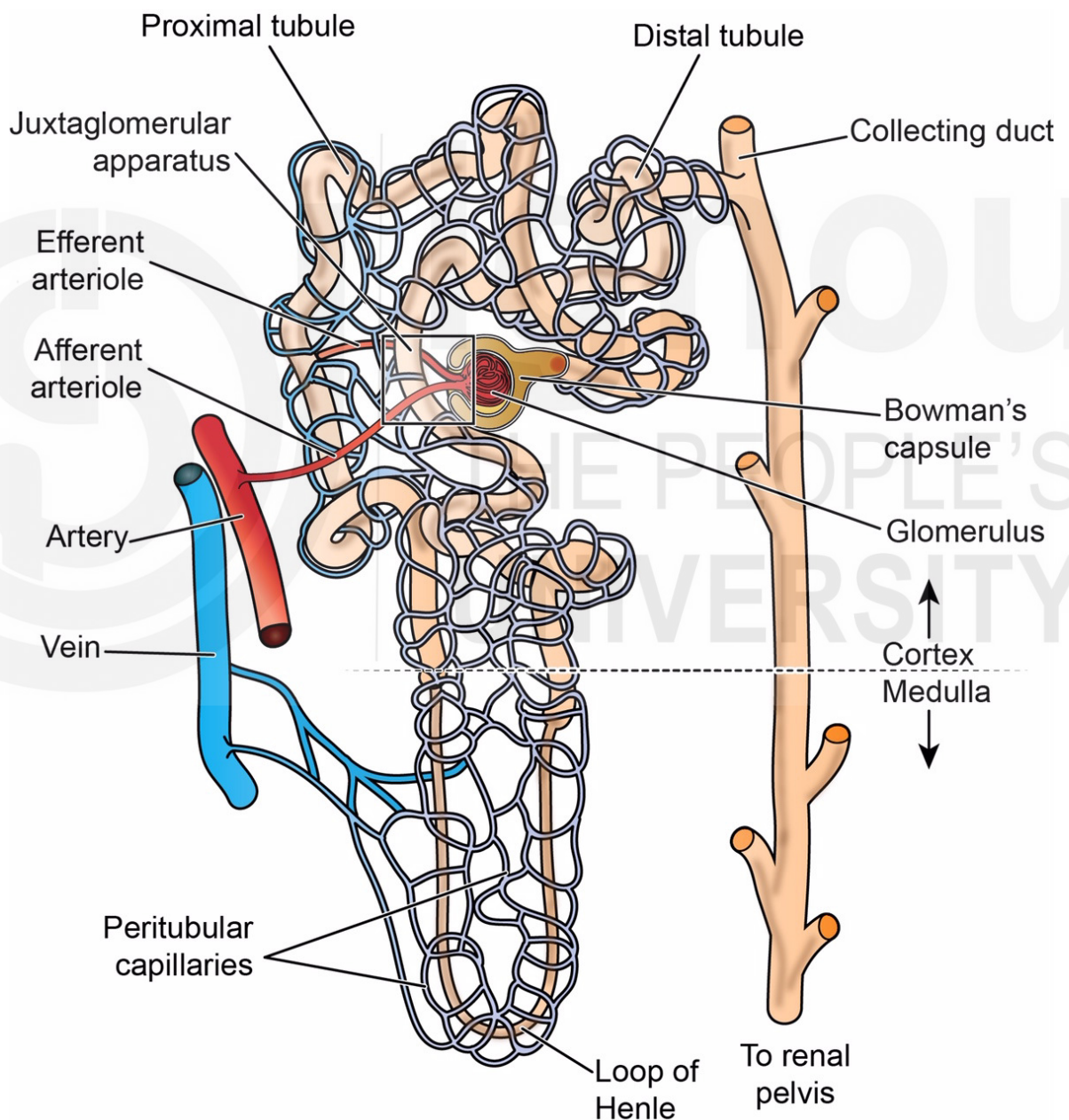


Fig. 4.12: Structure of nephron in the kidney.

Vertebrates that lack a loop of Henle are incapable of producing urine hypertonic to blood. In mammals the nephrons are so arranged in the kidney

that their collecting tubules are arranged parallel to each other giving the characteristic striated appearance to the interior of the kidney. The glomeruli are located in the cortex of the kidney and the loops of Henle are located in the medullary region. Two types of nephrons are found in the mammalian and avian kidneys:

- Juxtamedullary nephrons- that have their glomeruli in the interior of the cortex and loops reaching in the papillae of the medulla
- Cortical nephrons- that have their glomeruli buried in the cortex with short loops in the medulla.

The arrangement of the blood vessels in the kidney is suited to the mechanism of urine formation. The blood enters via the **afferent arteriole** in the glomerular capillaries and leaves via the **efferent arteriole** rather than via a vein as is the case with other capillary networks. After leaving the renal capsule the efferent arteriole forms another interconnecting capillary network around the loop of Henle known as vasa recta before leaving the kidney via a vein. The flow of blood is about 10% less in the efferent arteriole than in the afferent arteriole because the glomerulus filters about 10% of the fluid into the Bowman's capsule. Let us now see how urine formation takes place in vertebrates using the example of mammals.

SAQ 4

Correct the following statements.

- Cortical nephrons- that have their glomeruli in the interior of the cortex and loops reaching in the papillae of the medulla
- Juxtamedullary nephrons- that have their glomeruli buried in the cortex with short loops in the medulla.
- The blood enters via the efferent arteriole in the glomerular capillaries.
- The blood leaves via the afferent arteriole rather than via a vein as is the case with other capillary networks.

4.6 PROCESS OF URINE FORMATION

As mentioned earlier three main processes take place in the formation of final urine that is excreted as summarized in Figure 4.13:

- Filtration of blood plasma to form an ultrafiltrate in the Bowman's capsule
- Tubular reabsorption of about 99% of the water and other salts from the ultrafiltrate leaving behind waste products such as urea
- Tubular secretion of substances via active transport

In addition, some substances are formed in the tubular cells and in the lumen that assist in the formation of nitrogenous waste.

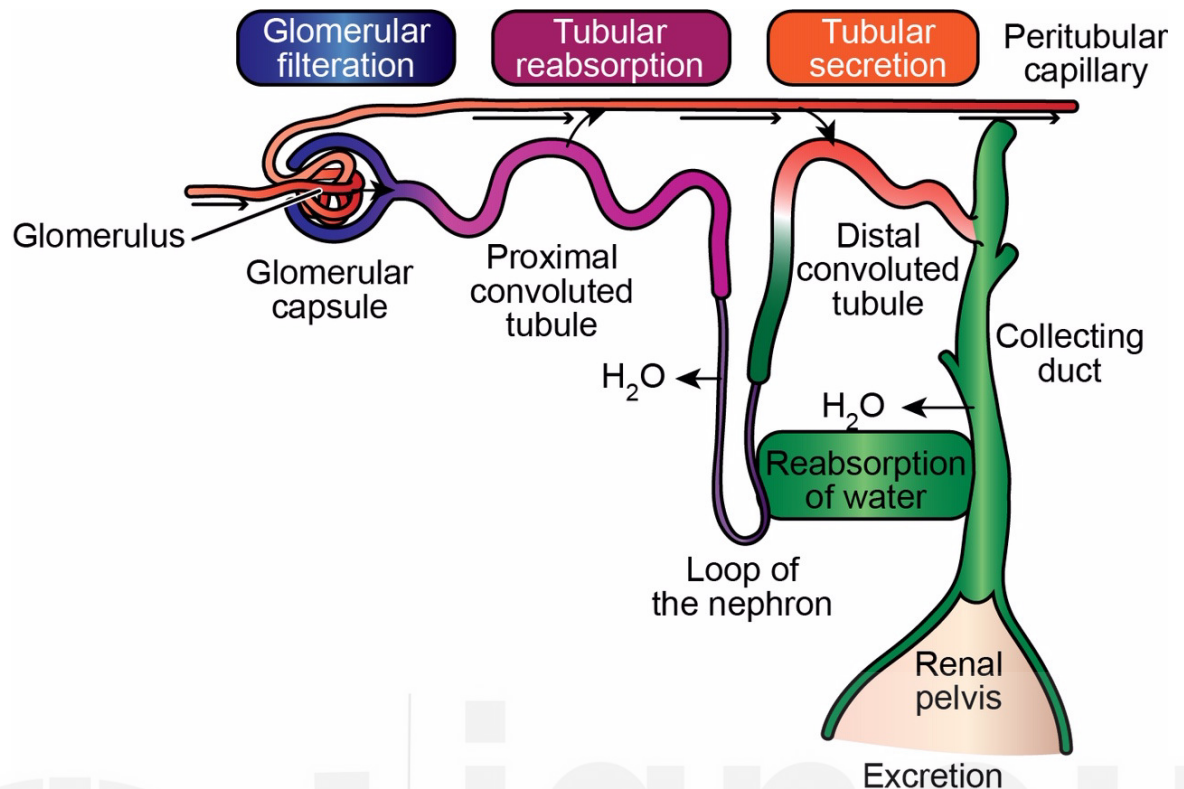


Fig. 4.13: Process of urine formation in a mammalian nephron.

4.6.1 Formation of Primary Urine

You know that in each nephron in the kidneys there is a microscopic filter, called a glomerulus that constantly filters the blood (Fig 4.14 a). Blood which is to be filtered enters the glomerulus, which consists of fenestrated capillaries, which have openings or pores and are 100 times more permeable than continuous capillaries found in other parts of the body. The physical characteristics of the glomerular capillary wall determine what is filtered and how much is filtered into the glomerular capsule. Working from the inside out, the capillary walls are made up of three layers to make the filtration membrane:

- i) *Endothelium* this has relatively large pores (70-100 nanometers in diameter), through which, solutes, and fluid can pass but not plasma proteins and blood cells. The proteins associated with these pores are negatively charged, so they tend to repel negatively charged substances and allow positively charged substances to pass more readily.
- ii) *Glomerular Basement membrane*-this membrane is also made up of complex mesh of intracellular proteins and is fused to the endothelial layer. Its job is to prevent plasma proteins from being filtered out of the bloodstream;
- iii) *Epithelium*-this layer consists of specialized cells called podocytes extending finger like arms (pedicels) to cover the glomerular capillaries. They wrap around the capillaries, but leave gaps/ slits between the pedicels, known as filtration slits. A thin diaphragm between the slits acts as a final filtration barrier before the fluid containing small solutes and water enters the glomerular space (Fig 4.14b &c).

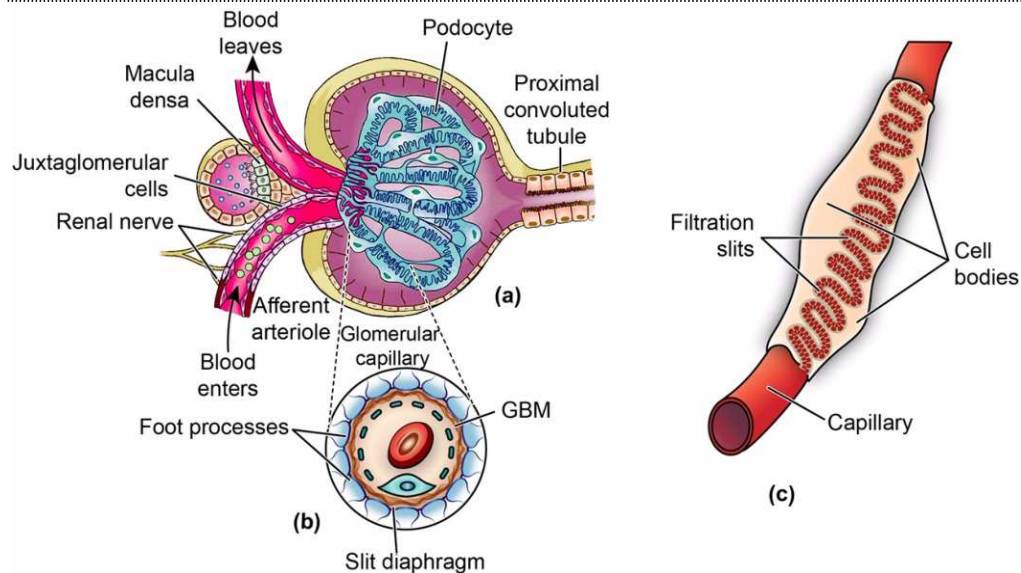


Fig.4.14: Structure of the renal capsule in humans a) Bowman's capsule containing the glomerulus; b) enlargement showing the position of pedicels; around the (c) fenestrated capillaries (adapted from *The Glomerulus: The Sphere of Influence: Martin R. Pollak, et al CJASN May 2014, CJN.09400913; DOI: <https://doi.org/10.2215/CJN.09400913>*).

Urine formation starts with a size dependent filtration step. The fluid filtered from the blood into the glomerulus consists of water and small solutes that are pushed out from the pores in the capillaries and through the filtration slits into the fluid filled space inside the Bowman's capsule. The force required for filtration is supplied by the blood pressure.

Most capillary beds in the glomerulus, are sandwiched between two arterioles - afferent arterioles which deliver blood to the glomerulus, and efferent arterioles which carry it away. Constriction of efferent arterioles as blood exits the glomerulus provides resistance to blood flow in the capillary, preventing a pressure drop. The two arterioles change in size to increase or decrease blood pressure in the glomerulus. In addition, efferent arterioles are smaller in diameter than afferent arterioles. As a result, pressurized blood enters the glomerulus through a relatively wide tube, but is forced to exit through a narrower tube. Together, these unique features plus the fact that the heart supplies the kidneys with over a liter of blood per minute (around 20% of its output) maintain a high glomerular capillary pressure and the filtration function of the kidney, regardless of fluctuations in blood flow.

It is interesting to note that during the formation of this filtrate upto 25% of the water and solutes are removed from the blood; the renal corpuscles of the human kidney are capable of producing 180L of pre-urine a day (how many crates of cola bottles would that be?) **but** we produce only about 1-2 L of urine a day which means that about 98% of the fluid volume is reabsorbed and returned to the bloodstream.

SAQ 5

- Name the three layers of the capillary walls which make the filtration membrane.
- Name the three main processes which take place in the formation of final urine that is excreted

4.6.2 Modification of Urine

As pre-urine which is isosmotic to plasma, leaves the glomerulus it enters the **proximal convoluted tubule (PCT)** where it begins to be modified and is reduced by about 80%. The fluids inside the tubule contain water, small solutes such as glucose, urea, amino acids, vitamins and electrolytes. It is important to remember that some of these molecules are waste while the others are valuable nutrients.

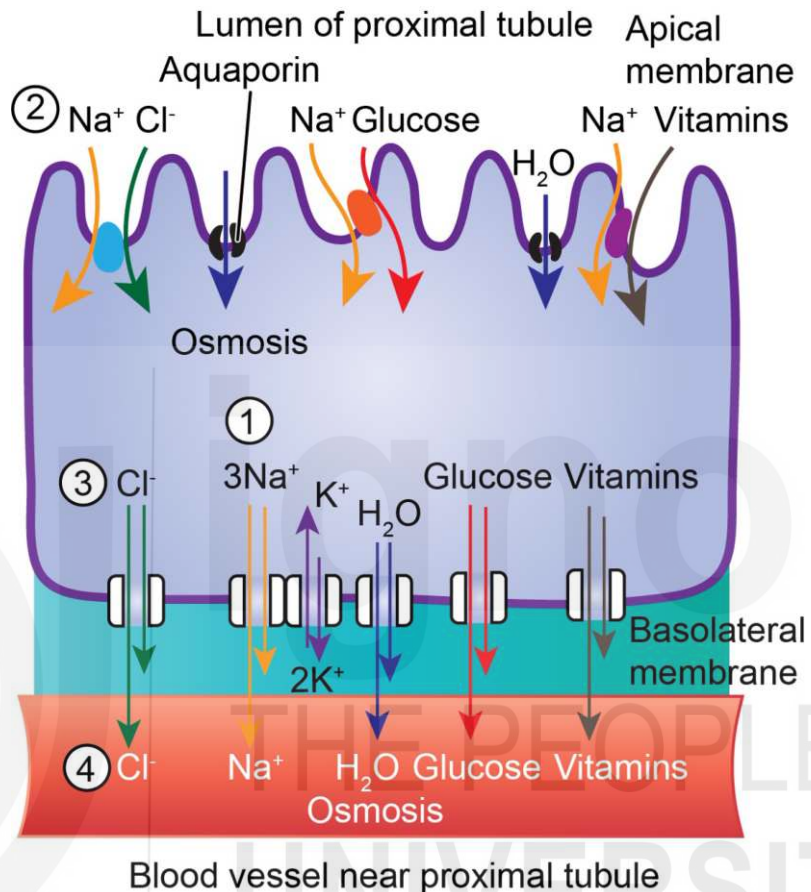


Fig.4.15: Water and electrolyte are reabsorbed in the proximal convoluted tubule. Brush border on the apical membrane of the epithelial cells increases the surface area, facilitating the entry of solutes through cotransporter molecules and water through aquaporins. The basolateral membrane has sodium potassium ATPase to transport the sodium ions and other electrolytes and glucose back to the blood through channels, water follows by osmosis.

The epithelial cells of the PCT bear series of projections termed microvilli - facing the lumen. These microvilli increase the surface area of these cells providing more space for membrane proteins that act as pumps, cotransporters and channels. The epithelial cells in the proximal tubule have a greater number of mitochondria as movement of substances across the epithelium takes place through active transport mechanisms. The proximal tubule is the region of the nephron where reabsorption of water and varying amounts of salts and other solutes from the pre-urine takes place. Figure 4.15 summarizes the molecular mechanism believed to be responsible for this selective reabsorption. You can see in the figure that the basolateral membrane of the cells in the proximal tubule contains the Na^+/K^+ -ATPase and the apical membrane has various channels and cotransporters. The Na^+/K^+ -

ATPase pumps **out** sodium ions from the cells and this creates a gradient for the Na ions to enter in the cell from the lumen. In the apical membrane adjacent to the lumen Na⁺ - dependent cotransporters use this gradient to remove valuable ions and nutrients selectively from the pre-urine. Thus along with the Na⁺, another solute like glucose, amino acids, Cl⁻ and vitamins are transported **in to** the cell against their gradient.

As these solutes are removed, the tubular fluid becomes hypoosmotic and the interstitial fluid surrounding the tubular wall becomes hyperosmotic. This causes passive diffusion of water out of the tubule to restore isoosmotic condition between the tubular fluid and the surrounding cortical interstitium. Water from the lumen enters the cells through special channels known as **aquaporins** that can bring in 3 billion water molecules per second. Aquaporins located in the basolateral membrane of the epithelial cells transport back the water into the blood from the interior of the epithelial cells. This reabsorption of water is secondary to solute transport and occurs inevitably irrespective of the water requirements of the body. Hence, it is called the **obligatory reabsorption of water**. It has been determined that two thirds of the NaCl and water that is filtered through the glomerulus is reabsorbed in the proximal tubule. However the osmolarity of the fluid in the tubule does not change as the water reabsorption is proportional to the solute reabsorption.

The pre-urine that enters the proximal tubule is dilute but the fluid that leaves the proximal tubule is isotonic but reduced in volume and as it enters the next part of the tubule it contains a high concentration of waste molecules and low concentration of nutrients.

4.6.3 Countercurrent Multiplication

In mammals and birds the fluid from the PCT enters a hairpin shaped loop. In most nephrons the loop is short and does not enter the medulla deep or leave the cortex but in about 20% nephrons the loop is long and enters deep into the medulla. You know from Figure 4.13 that the loop of Henle consists of three regions thin descending limb, thin ascending limb and thick ascending limb. The thin and thick ascending limbs differ in the thickness of their walls. **Ion transport is different in each of these segments as the descending limb is permeable to water and the ascending limb is permeable to solutes.** It took almost a century, before an explanation was offered for its function. In 1951 B Hargitay and Werner Kuhn proposed that the Loop of Henle acts as a **countercurrent multiplier system** of urine-concentrating mechanism in mammalian kidneys. This means that the loop of Henle sets up an osmotic gradient exchanging water and solutes between cell of different regions of the loop as it goes down from the cortex to the medulla. As a results water is reabsorbed from the tubular fluid and concentrated urine is produced. This is the mechanism that prevents you from producing litres and litres of dilute urine every day, and is the reason why you don't need to be continually drinking in order to stay hydrated. The three segments of the loops of Henle have different characteristics that enable countercurrent multiplication (Fig 4.16).

Jacob Henle described this part of the nephron first in 1860s hence it has been named loop of Henle.

- The *thin descending* limb is passively permeable to water but almost impermeable to solutes. As the loop of Henle enters in the medulla region the surrounding fluid is rich in salt concentration because of

reabsorption of solutes from the ascending limb of the loop of Henle. This increases the concentration of solutes within the interstitial space (space between cells), and causes the water to move down the concentration gradients until the concentrations within the descending limb and the interstitial space have equilibrated. In other words we can say, the tubular fluid becomes steadily more concentrated or hypertonic (compared to surrounding fluid) as it travels down the thin descending limb of the tubule. Once it begins to flow up the ascending limb it stops losing water.

- The *thin ascending* limb membrane is highly permeable to small solutes (Na^+ and Cl^-), moderately permeable to urea, but impermeable to water, which means no more water is lost from this part of the loop. But Na^+ and Cl^- move out of the tubular fluid passively, and the tubular fluid becomes hypotonic as it moves up the ascending limb of the tubule.
- The *thick ascending* limb actively transports sodium, potassium and chloride out into the interstitial fluid by a combination of Na^+/K^+ ATPase, Cl^- channels and $\text{Na}^+/\text{2Cl}^-/\text{K}^+$ cotransporters leaving behind urea as the primary solute in the urine. This segment is also impermeable to water, which again means that water cannot escape from this part of the loop. This segment is sometimes called the “diluting segment”.

Because two sides of the loop of Henle perform opposing functions, as illustrated in Figure 4.16, it acts as a **countercurrent multiplier**. The vasa recta around the loop of Henle acts as the **countercurrent exchanger** as the water and salt that move out of the loop quickly diffuse in the network of blood vessels that surround the loop (vasa recta).

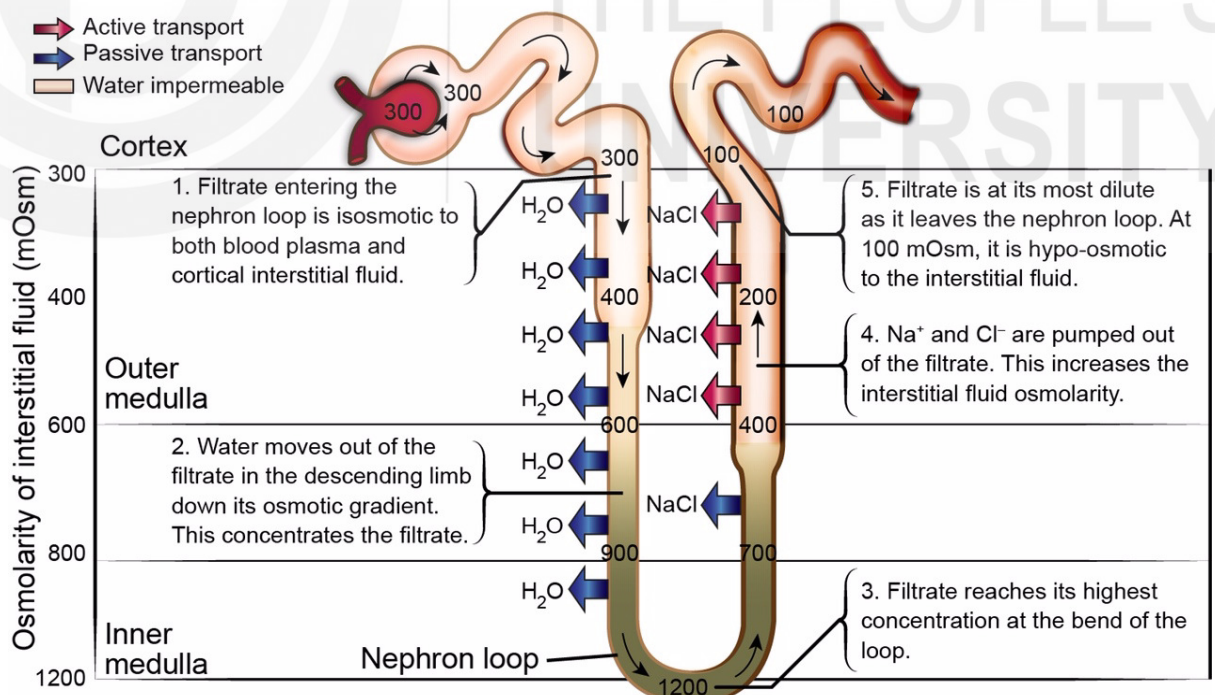


Fig. 4.16: Urine concentration in the nephron. The Loop of Henle with its three distinct regions. The descending limb is highly permeable to water; the thin ascending limb is permeable to sodium and chloride ions while its impermeable to water; the ascending thick limb removes NaCl by active transport against the concentration gradient.

Because the blood flow through these capillaries is very slow, any solutes that are reabsorbed into the bloodstream have time to diffuse back into the interstitial fluid, which maintains the solute concentration gradient in the medulla. This passive process is known as countercurrent exchange.

4.6.4 Urine Volume and Concentration in DCT

By the time the filtrate reaches DCT most of the solutes have been reabsorbed. The filtrate entering the distal convoluted tubule (DCT) has a high concentration of urea and other wastes though it is hypo-osmotic to the interstitial fluid as NaCl has been transported out of the tubular lumen. This region is important for transportation of K^+ , H^+ and NH_3 into the tubule and Na^+ , Cl^- and HCO_3^- out of the tubule into the interstitial fluid. As the salts are pumped out of the lumen, water also moves out passively. If the body requires additional water it is reabsorbed here. The activity of the cells of DCT depends on the conditions or osmotic stress faced by the body and is under hormonal control. Under conditions of diuresis that is if no water has to be conserved in the body then the fluid passes unchanged from the DCT in to the collecting duct. When water needs to be conserved then the hypothalamus secretes antidiuretic hormone (ADH) which change the permeability of the DCT walls to water. When ADH titers are high in the body more aquaporins are recruited in the epithelial cells of the tubule, water diffuses out and the fluid becomes iso-osmotic to blood when it enters the collecting duct.

In amphibians and reptiles there is no loop of Henle so the fluid from the proximal tube passes into the distal tubule directly and the final urine may be hypoosmotic or at best isoosmotic to blood. Urine in these animals is made hypo osmotic by resorption of salts and under dry conditions the volume is also reduced by resorption of water in the distal tubule under the influence of ADH. In lower vertebrates ADH is referred to as vasotocin.

Collecting duct : The fluid that reaches the collecting duct may be hypoosmotic or isoosmotic depending on the water status of the animal. Final adjustments in urine composition are made in the collecting ducts whose walls become permeable only under the influence of ADH. In the absence of ADH the hypo-osmotic urine that enters the collecting ducts is excreted unchanged that is, relatively large volume of urine is excreted. Under situations demanding water conservation, ADH is secreted and the walls of the collecting ducts become permeable to water. The fluid passing through the collecting ducts becomes progressively concentrated and a urine hyperosmotic to blood and isoosmotic to interstitial fluid is excreted.

Tubular secretion : Apart from K^+ , H^+ , NH_3 , some organic acids and organic bases that are not bound to plasma proteins are secreted from the plasma into the tubular lumen for excretion. Organic anions are secreted along the sodium gradient that is established by the Na^+/K^+ pump. These secretory mechanism are non specific and so many other new substances including drug molecules and toxins can be secreted coupled to the transporting molecules. Most of the tubular secretion happens in the DCT, but some occurs in the early part of the collecting duct. Kidneys also maintain an acid-base balance by secreting excess H^+ ions.

SAQ 6

- a) Tick the structures impermeable to water
- i) Thin ascending limb of Henle
 - ii) Thick ascending limb of Henle
 - iii) Thin descending limb of Henle
 - iv) PCT
 - v) DCT
- b) What is counter current multiplier?

4.7 REGULATION OF KIDNEY FUNCTION

After studying about the structure of kidney and formation of urine in it, we shall now learn how the function of kidney is regulated and water and electrolyte balance is maintained. You have studied earlier in this unit that urine production is dependent upon the filtration process. Reduction in blood supply to the kidney results in a drop in the net filtration pressure and so, urine production is greatly reduced. Under these conditions, a series of events are initiated in the kidney itself to develop a hypertensive state so that there is better flow of blood to the kidney and resumption of urine production. The autoregulation of renal blood flow involves a neuroendocrine mechanism related to the **juxtaglomerular apparatus** in the kidney that is responsible for the rennin- angiotensin - aldosterone regulatory system

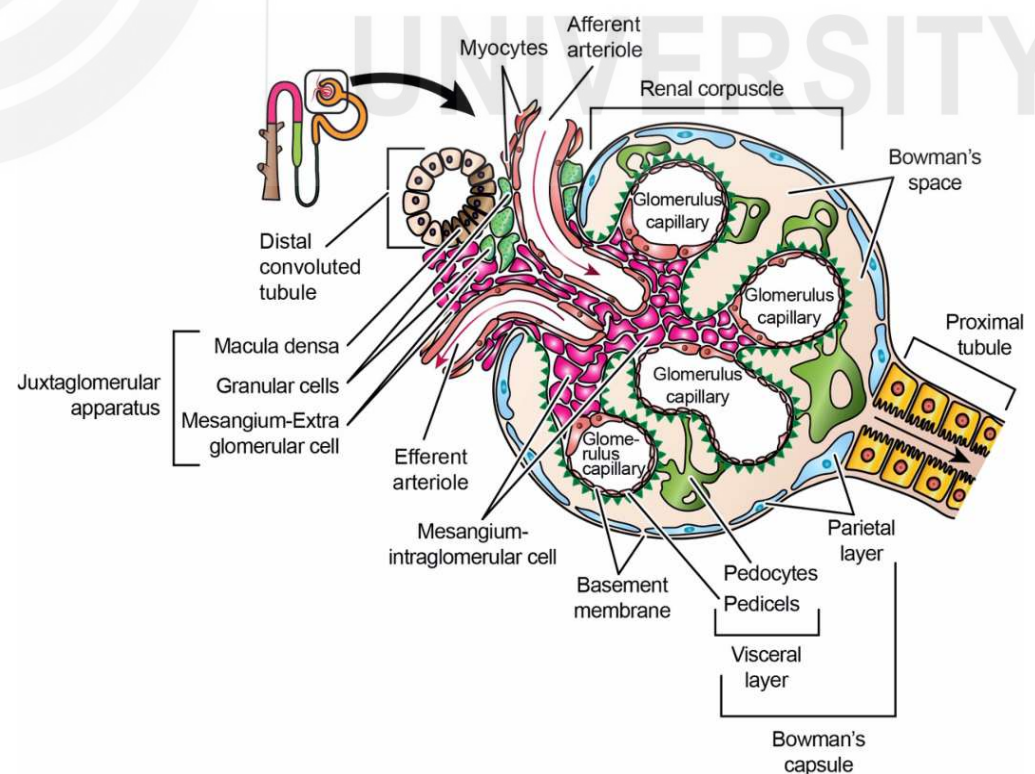


Fig. 4.17: Structure of Juxtaglomerular apparatus.

You can note in Fig. 4.17 that the juxtaglomerular apparatus (JGA) is located between the afferent arteriole and the returning distal convoluted tubule of the same nephron. It is responsible for regulating both renal and entire body fluid volume status.

Note in Fig. 4.17 that the juxtaglomerular apparatus has three components :

1. the **juxtaglomerular cells** of the afferent arteriole. Juxtaglomerular cells synthesize and store renin. Renin acts as an enzyme and hormone that is part of a physiological system that regulates blood pressure. Renin is secreted when there is decrease in arterial blood pressure or a decrease in sodium load delivered to the distal tubule or sympathetic nervous system activity. Renin participates in the body's renin-angiotensin-aldosterone system (RAAS) - also known as the renin-angiotensin-aldosterone axis,
2. the **macula densa**, a region of the distal convoluted tubule which is characterized by densely-packed tubular epithelial cells in comparison to other regions of the nephron (and thereby leading to its characteristic appearance under light microscopy). Macula densa detects sodium concentration of the fluid in the tubule. In response to elevated sodium, the macula densa cells trigger contraction of the afferent arteriole, reducing flow of blood to the glomerulus thus reducing the glomerular filtration rate,
3. **mesangial cells**, have smooth muscle activity, the mesangial cell contracts or relaxes in response to a number of vasoactive agents. This ability allows the cells to modify glomerular filtration locally.

Renin-angiotensin-aldosterone system (RAAS)

Figure 4.17 will help you to understand RAAS. When the afferent arterial blood pressure is low, the stretch sensitive receptors of the arterioles initiate nerve impulses which induce the secretion of a proteolytic enzyme called renin by the juxtaglomerular cells into the blood. This enzyme causes the release of a decapeptide called **angiotensin-I** from a large globular plasma protein known as angiotensinogen which is secreted by the liver. Another proteolytic enzyme the **angiotensin converting enzyme (ACE)**, removes two amino acids from angiotensin-I to form an octapeptide called **angiotensin-II**. ACE is found mainly in lung capillaries and within the renal endothelium. Angiotensin II is about 200 times more powerful than norepinephrine in its vasopressor activity. It increases the blood pressure by two mechanisms. Firstly, it acts on the smooth muscle of the arterioles and causes strong vasoconstriction. Secondly, it stimulates the secretion of **aldosterone** by the adrenal cortex. Aldosterone acts on the aldosterone receptors on the distal tubules and collecting tubules and enhances the reabsorption of Na⁺ from the kidney tubules and hence causes a rise in the plasma Na⁺ level. This results in an increase in the extracellular fluid volume and consequently an elevation in blood pressure. Angiotensin-II is degraded by an enzyme called **angiotensinase**, present in plasma.

Anti-diuretic hormone

ADH is also known as vasopressin and helps in retention of water. It is synthesized in the neurosecretory cells of the hypothalamus and stored in the posterior pituitary. ADH acts in the kidney to regulate the volume and

osmolarity of the urine. Specifically, it acts in the distal convoluted tubule (DCT) and collecting ducts (CT) cells.

Let's consider an example where there is an increase in osmolarity of the plasma. The increase in ADH release will mean that the permeability of the DCT and CT cells to water increases, (water leaves the tubules) and urine output decreases. This happens because ADH increases the aquaporin channels in the apical membrane of the DCT and CT cells. This allows water to move down its concentration gradient, out of the nephron and back into the blood stream. This increases the water reabsorbed from the urine, and decreases plasma osmolarity and increases total blood volume. Water reabsorption in this manner is a passive process.

Alternatively, when there is a decrease in osmolarity of the plasma then ADH release is inhibited. This results in a decrease in the number of aquaporin channels on the apical membrane of the DCT and CT cells. Therefore, there is a reduction in the amount of water reabsorbed from the nephron back in the blood stream.

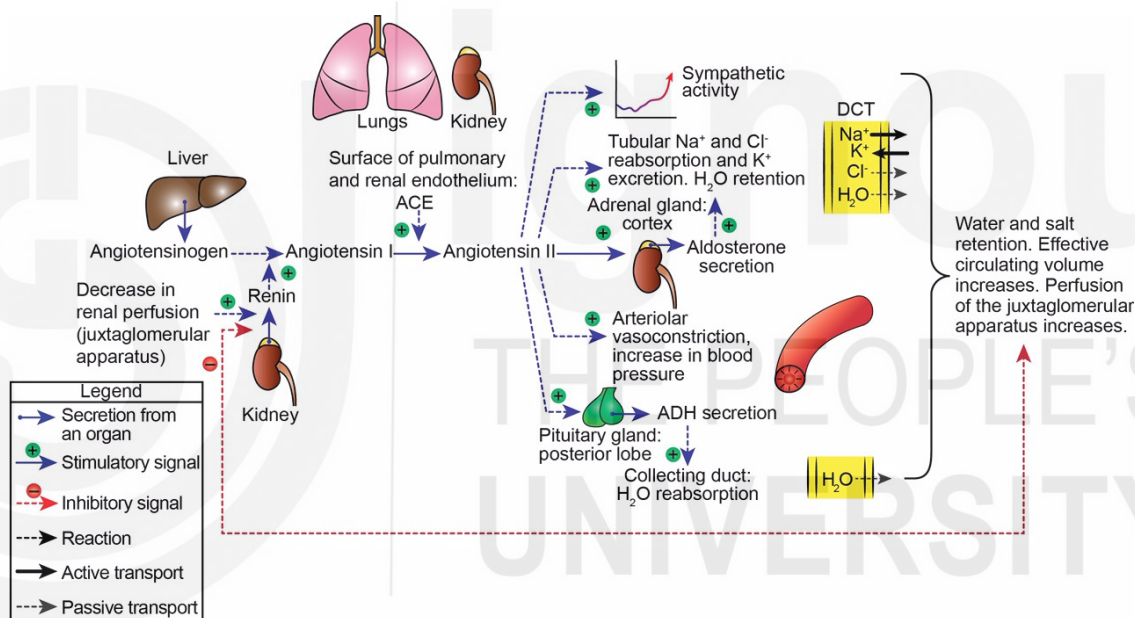


Fig. 4.18: The rennin – angiotensin - aldosterone system that regulates the ionic and water balance in the system. (Wikipedia)

SAQ 7

Fill in the blank spaces in the table

Hormone/Enzyme	Action
Renin	
	helps in retention of water
Angiotensin converting enzyme (ACE)	
Aldosterone	

4.8 SUMMARY

Let us sum up what we have learnt in this unit:

- Osmoregulation is a process for the maintenance of osmotic concentration of the body fluids. Animals have adapted various physiological and behavioural mechanisms to cope up with the rigors of the osmotic environments.
- Osmoregulatory and excretory organs are contractile, vacuoles of protozoa, nephridia of worms, molluscan kidney, green glands of crustaceans, Malpighian tubules of insects and vertebrate kidney.
- catabolism of proteins gives rise to nitrogen which is highly toxic to the animal. Therefore, animals get rid of the toxic nitrogen in the form of ammonia or convert it into less toxic forms such as urea and uric acid before it is being excreted,
- animals which predominantly excrete ammonia are called ammonotelic, those that excrete urea are known as urotelic and uric acid excreting animals are known as uricotelic,
- a variety of tubular renal organs are present in animals for the elimination of unwanted materials and for osmotic and ionic regulation. Despite their morphological diversity, their functional principles are remarkably similar,
- the nephron is the functional unit of the kidney, which actively filters blood and generates urine. The nephron filters and exchanges water and solutes with two sets of blood vessels and the tissue fluid in the kidneys,
- The glomerulus is a capillary bed that filters blood principally based on particle size. The filtrate is captured by Bowman's capsule and directed to the PCT. A filtration membrane is formed by the fused basement membranes of the podocytes and the capillary endothelial cells that they wrap around,
- the filtrate enters the PCT where absorption and secretion of solutes several substances and water occur in the descending and ascending limbs of the loop of Henle. Absorption and secretion continue in the DCT but to a lesser extent than in the PCT. Each collecting duct collects forming urine from several nephrons and responds to the posterior pituitary hormone ADH by inserting aquaporin water channels into the cell membrane to fine tune water recovery,
- osmoregulation and excretion from kidneys is regulated by hormones. Contractile mesangial cells further perform a role in regulating the rate at which the blood is filtered in the glomerulus. Specialized cells in the JGA produce signals to regulate blood flow and filtration rates of the glomerulus by triggering the rennin - angiotensin- aldosterone system, which plays a central role in homeostasis and blood pressure regulation.

4.9 TERMINAL QUESTIONS

1. Draw a well labelled diagram of the nephron of mammal.
2. Write short notes on :
 - a) green gland
 - b) ion channels
3. Differentiate between osmoregulators and conformers?
4. Draw a simple flow chart to show how kidney function is hormonally regulated.
5. Explain the role of the loop of Henle in urine formation.

4.10 ANSWERS

Self-Assessment Questions

1.
 - a) ions
 - b) isotonic.
 - c) hypotonic, isoosmotic
 - d) Na^+/K^+ ATPase pump functions to maintain osmotic balance and electric gradient across membranes by taking 3 Na^+ out of the cell and at the same time bringing back 2 K^+ into the cell. The energy required for this comes from the phosphorylation of this protein by ATP. Na^+/K^+ ATPase pump is essential as it helps to maintain resting potential, maintains the osmolarity, affects transport and regulate cellular volume.
2.
 - a) apical, external, basal, internal
 - b) excretion
 - c) ammonotelic, ureotelic
3.
 - a)
 - i) Malpighian tubule - insects, mammals
 - ii) contractile vacuole - Amoeba
 - iii) nephridia - worm
 - iv) green gland - Crustacean
 - b) Draw figure 4.6 and explain with help of Subsection 4.4.2
4.
 - a) Cortical nephrons- that have their glomeruli buried in the cortex with short loops in the medull.
 - b) Juxtamedullary nephrons- that have their glomeruli in the interior of the cortex and loops reaching in the papillae of the medulla.
 - c) The blood enters via the afferent arteriole in the glomerular capillaries.

- d) The blood leaves via the efferent arteriole rather than via a vein as is the case with other capillary networks.
5. a) The three layers of the capillary walls which make the filtration membrane.
- i) Epithelium
 - ii) Glomerular Basement membrane
 - iii) Endothelium
- b) Name the three main processes which take place in the formation of final urine that is excreted
- i) Filtration
 - ii) Tubular reabsorption
 - iii) Tubular secretion
6. a) Thick ascending limb of Henle, Thin descending limb of Henle
- b) Refer to Section 4.6.3.

Hormone/Enzyme	Action
Renin	regulates blood pressure
Anti diuretic enzyme	helps in retention of water
Angiotensin converting enzyme (ACE)	removes two amino acids from angiotensin-I to form an octapeptide called angiotensin-II
Aldosterone	increase in the extracellular fluid volume and consequently an elevation in blood pressure

Terminal Questions

1. Refer to Fig. 4.12.
2. Refer to (a) subsection 4.4.5 (b) subsection 4.2.2.
3. Refer to Subsection 4.2.3.
4. Refer to Fig 4.17.
5. Refer to Subsection 4.6.3.