flowering until it is exposed to prolonged period of low temperature of the winter. The requirement of low temperature treatment for accelerating flowering is called **vernalization**.

The site of vernalization in the case of biennials and perennials, is believed to be the growing point (apical bud). Cold treated shoot apices when grafted on to untreated plants induce the latter to flower. This property is attributed to cold induced production of a stimulus called vernalin. But vernalin remains as a hypothetical substance and has never been isolated from plants. The plant hormone gibberellic acid can substitute the effect of low temperature treatment for germination, flowering and release of bud dormancy in many plants.

Vernalization effect is reversible and the reverse process is called devernalisation. If a vernalized seed or plant is kept under high temperature, the effect of low temperature treatment is completely removed. High temperature reversal can be counteracted if the duration of vernalization treatment is increased. Devernalized plants can, however, be vernalized under low temperature treatment.

14.9. PHOTOPERIODISM :

It is the phenomenon of physiological changes that occur in plants in response to relative length of day and night (i.e. photoperiod). The response of the plants to the photoperiod, expressed in the form of flowering is also called as photoperiodism. Garner and Allard (1920) noticed that Soybeans and Tobacco could be made to flower only if the plants were exposed to a series of short days. After a series of experiments they realized the importance of relative length of the day as a chief factor of importance for growth and development of plants.

Most plants can flower only if they are exposed to the light for less or more than a certain period , called **critical period** (Fig. 14.12). Depending on the photoperiod, the plants are classified into three categories:

(a) Short Day Plants (SDP) : These plants are exposed to photoperiod shorter than a critical period i.e. a relatively short day light period (usually 8-10 hours) and a continuous dark period of about 14-16 hours for subsequent flowering. These plants are also known as long-night plants e.g. Rice, coffee, soybean, tobacco and chrysanthemum.

In SDPs, the dark period is critical and should be continuous. If this dark period is interrupted even with a flash of light, the plants will not flower.

(b) Long Day Plants (LDP) : These plants require longer day light period (usually 14-16 hours) i.e. light period for more than the critical period for subsequent flowering. These plants are also called as short night plants. E.g. Wheat, radish, cabbage, sugar beet and spinach.

(c) Day Neutral Plants (DNP): These plants flower in all photoperiod and do not show any correlation between exposure to light duration and flowering response. E.g. Tomato, cotton, sunflower, cucumber, peas and certain varieties of tobacco.

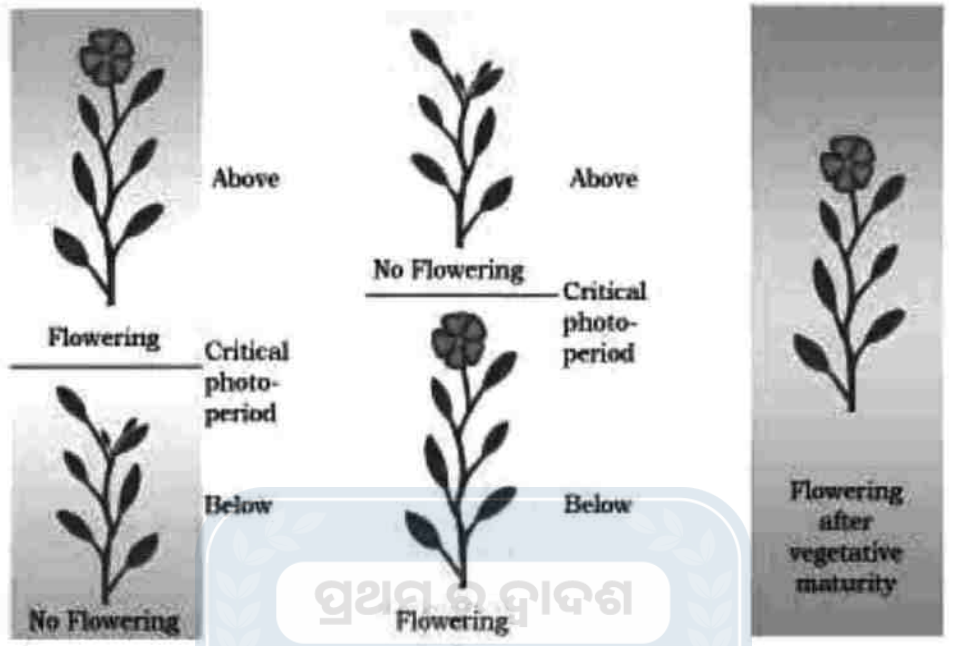


Fig 14.12: Photoperiodism in Long Day, Short Day and Day Neutral Plants.

The inhibition of flowering in short day plants by brief exposure of red light and stimulation of flowering in long day plants by the interruption of dark period involves the operation of a proteinaceous pigment called **phytochrome**.

Leaves are the sites of perception of light or dark period in plants. It is presumed that there is a hormonal substance called **florigen** which is responsible for flowering. When required photo-inductive period is given, the florigen synthesized and migrates from leaves to shoot apices to induce flowering in plants.

Photoperiodism is a process of physiological preconditioning. This has been of great importance to the commercial flower growers. They can be able to induce or retard the flowering by regulating the light and dark periods in controlled conditions to meet the market demand.

SAMPLE QUESTIONS

A. Multiple-choice questions :

1. Gibberellic acids do which of the following physiological effects:
   (a) yellowing of young leaves
   (b) elongation of genetically dwarf plants
   (c) shortening of genetically tall plants
   (d) yellowing of old leaves
2. What will happen when the dark period of short day plants is interrupted by a flash of light?
   (a) flowers immediately (b) will not flower
   (c) induce more flowering (d) converts to a long day plant
3. The plant hormone connected primarily with cell division is:
   (a) IAA (b) NAA
   (c) Kinetin (d) GA
4. Apical dominance is influenced by:
   (a) GA (b) Ethylene
   (c) Auxin (d) Coumarine
5. Abscisic acid causes:
   (a) stomatal closure (b) leaf expansion
   c) root formation (d) stem elongation
6. Richmond-Lang effect is due to :
   (a) auxin (b) abscisic Acid
   (c) cytokinin (d) ethylene
7. Auxin transport is
   (a) polar (b) non-polar
   (c) symplastic (d) apoplastic

B. Fill in the blanks :

1. Fruit ripening is induced by the hormone _____.
2. Mangrove plants generally show _____ type of germination.
3. Florigen is associated with _____.
4. The amino acid _____ is the precursor of ethylene.

C. Short answer type:

1. Growth curve
2. Apical dominance
3. Seed dormancy
4. Vernalization

D. Long answer type :

1. Describe the different types of seed germination.
2. Give an account of physiological effects of auxins in plants.
3. Discuss the physiological effects of gibberellins in plants.

❑ ❑ ❑

UNIT-V : HUMAN PHYSIOLOGY

CHAPTER 15

DIGESTION AND ABSORPTION

Organisms need food for their survival. It provides energy and inorganic and organic materials required for growth, repair of tissues and other purposes. The major bio-macromolecules present in our food are **carbohydrates**, **proteins** and **lipids**, Besides, **minerals** and **vitamins** are also present in food, which are needed by our body in small quantities. Water is very much essential for us as it constitutes about 55% of our body mass and is used in various metabolic processes. We get all these molecules from the food, we eat by a process called **ingestion**. The complex bio-macromolecules are then hydrolyzed into simple absorbable products by a process called **digestion**. The digested products pass into the blood or body fluid for distribution to all parts of the body. This process is called **absorption**. Cells and tissues, in all parts of the body, pick up the required amount of these nutrients from the blood or body fluid by a process called **assimilation**. Finally the residual undigested food is eliminated by **defaecation** or **egestion**. The sum total of all the above-mentioned five processes is known as **nutrition**. ***Thus, nutrition may be defined as a process by which an organism takes in or ingests food, hydrolyzes or digests it, absorbs and finally assimilates the digested food into the body and lastly eliminates the undigested residual food by egestion or defaecation.*** A part of the food is used as substrate for generation of energy by catabolism. Any excess of it is stored in the cells of storage organs, especially the liver, muscle and adipose tissue for use during exigency.

15.1. BIOMACROMOLECULES :

Carbohydrates : These have the general molecular formula $C_n(H_2O)_n$ and are classified into monosaccharides (e.g. glucose, fructose and galactose), oligosaccharides (e.g. maltose, lactose and sucrose) and polysaccharides (e.g. starch, glycogen and cellulose). These constitute the key source of energy for the body. The end products of carbohydrate digestion are monosaccharides, mostly glucose. The main sources of carbohydrates are rice, wheat, maize and patato.

Proteins : These are made up of many of the twenty different amino acids. The amino acids are joined linearly by peptide bonds to form long polypeptide chains. Animal sources of proteins are milk, egg, fish, meat etc. and plant sources include pulses, nuts, peas, beans etc. The proteins are hydrolyzed into amino acids at the end of digesation.

Lipids : These are water insoluble organic compounds, which mostly consist of oils and fats. They serve as the storage or reserve source of energy during exigency. The principal sources of dietery lipids are vegetable oils, vegetable or vanaspati ghee and animal fat or neutral fat. Most lipids are digested into falty acids and glycerol.

Nucleic Acids : DNA and RNA constitute and insignificant part of our food. During digestion they are converted first into nucleotides and then into nitrogenous bases, pentose sugar and phosphate.

15.2. TYPES OF DIGESTION :

Digestion is of two types based on the place of occurrence: **intra-cellular** and **extra-cellular.**

15.2.1. Intra-cellular digestion (Fig.15.1) :

It is the simplest type of digestion, which occurs entirely inside the cell. The food material is engulfed by the cell into a **food vacuole**. Then **lysosomes** containing digestive enzymes fuse with the food vacuole and consequently the food is digested. The digested products are absorbed into the surrounding cytoplasm by simple diffusion. The residual undigested food is eliminated to the outer side by **egestion** (*e.g.*; all protozoa, sponges and *Hydra*).

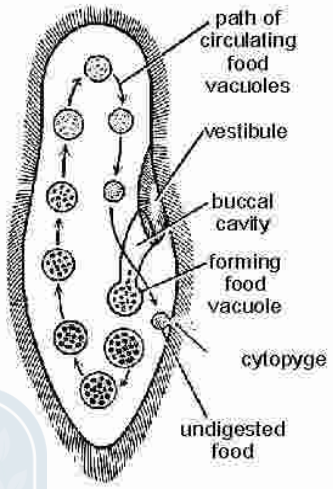


Fig. 15.1 : Intra-cellular digestion in Paramecium.

15.2.2. Extra-cellular digestion :

Here, the food is digested in the extra-cellular space i.e. the lumen of a digestive tract or gut. It is a more complex process, in which digestive enzymes are secreted by specialized digestive glands and released into the lumen of the gut to digest the complex micromolecular food. This type of digestion is a characteristic feature of animals included in the phyla form coelenterata to Chordata including human.

Coelenterates and some worms combine both types of digestion.

DIFFERENCES BETWEEN INTRACELLULAR AND EXTRACELLULAR DIGESTION

Intracelluear	Extracellular
1. Digestion occurs inside cells.	1. Digestion occurs outside the cell i.e. in the extracellular space or the lumen of the alimentary canal.
2. Food vacuoles are formed in the process.	2. No food vacuole is formed.
3. Digested food diffuses into the cytoplasm.	3. Digested products are absorbed into the body fluid such as lymph and blood.
4. Digestive enzymes are released into the food vacuoles by the lysosomes of the surrounding cytoplasm.	4. Digestive enzymes are secreted into the lumen of the gut by specialized digestive glands.

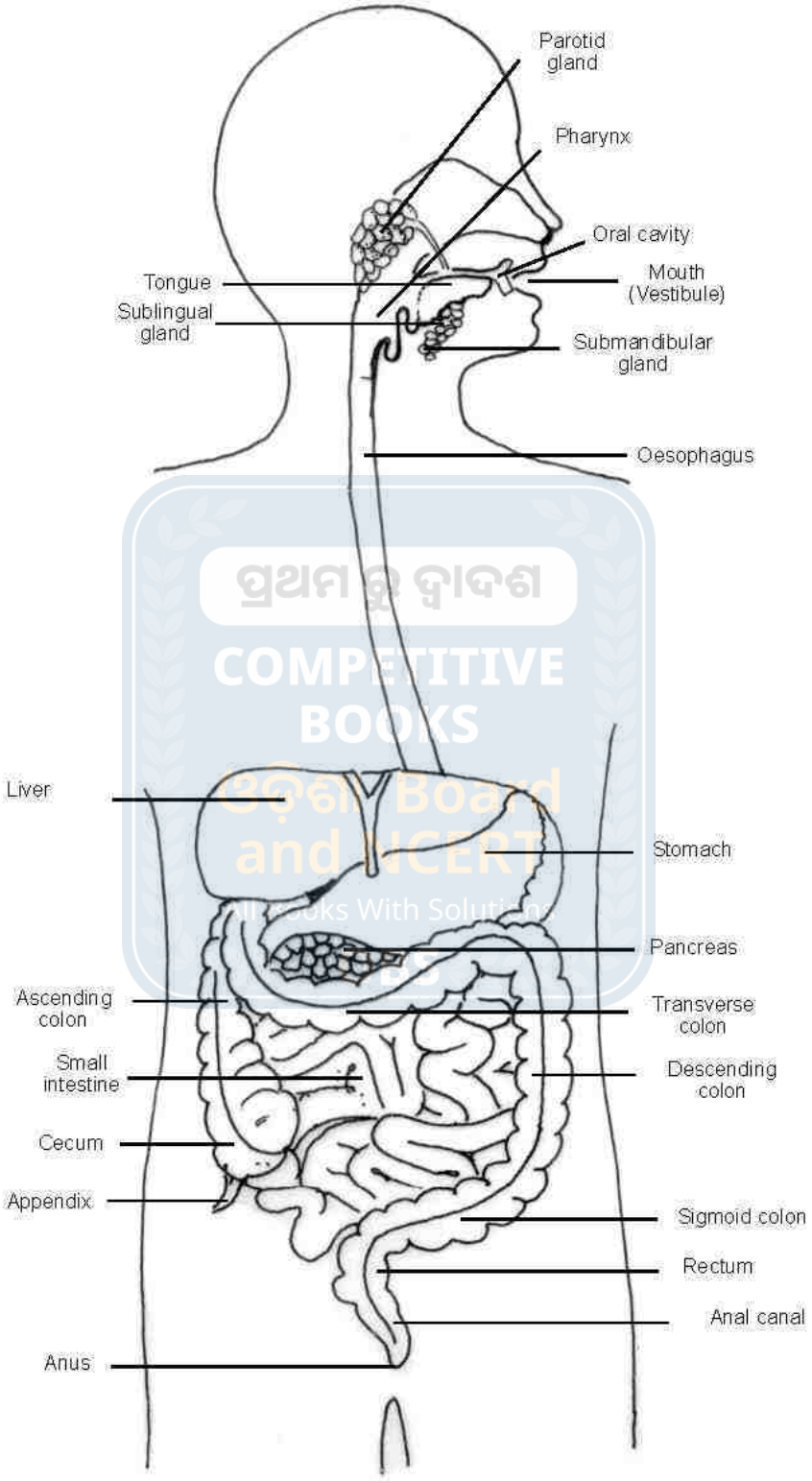


Fig. 15.2 : Alimentary canal of human with associated glands.

15.3. DIGESTIVE SYSTEM OF HUMAN :

The digestive system includes a long and differentiated **alimentary canal** and **associated glands** (Fig.15.2). The alimentary canal performs diverse functions such as **ingestion**, temporary storage **digestion** and **absorption** of food and elimination of undigested residue, known as the **faecal matter** or **stool**. The associated glands secrete digestive juice containing enzymes and other elements. The enzymes hydrolyze complex food materials into simple molecules that are easily absorbed into the body fluid (blood and lymph) for transport to all parts of the body and then assimilated by the cells.

15.3.1. Alimentary Canal :

The alimentary canal of human being is a long coiled tube having distinct regional parts. There is a variation in the diameter of the tube in different regions. It consists of: **(1) Mouth; (2) Buccal cavity or Oral cavity; (3) Pharynx; (4) Oesophagus; (5) Stomach; (6) Small intestine; (7) Large intestine; (8) Rectum; (9) Anal canal; and (10) Anus.**

Besides the alimentary canal, there are two associated glands : **(1) Liver**; and **(2) Pancreas**.

Mouth : The mouth is a transverse slit, bounded by two soft and movable lips. It is meant for the ingestion of food. It opens into a **vestibule**. The vestibule in turn, opens into a **buccal cavity** or **oral cavity**. The buccal cavity is closed and opened by a pair of jaws, a lower and upper. The jaws bear teeth.

15.3.2.1. Buccal cavity or Oral cavity : It is a large space bound dorsally by a **palate**, ventrally by the throat and infront by the jaws having teeth. The cavity is lined by **stratified squamous epithelium**. It has the following structures.

(a) Palate : Palate forms the roof of the buccal cavity and separates the buccal cavity from the nasal chamber. It is differentiated into anterior, **hard palate** and posterior, **soft palate**. The hard palate is provided with transverse ridges, called **palatine ridges** or **rugae**. The rugae help in securing a better grip on the food. The soft palate is smooth and fleshy. The posterior free part of the soft palate hangs down as a small, conical flap, the **uvula** or **velum palati**, which closes the internal nares during swallowing of food.

(b) Tongue : The tongue is a freely movable, muscular gustatory organ, situated on the floor of the oral cavity. Its base is fixed, but the tip is free and is protrusible. It is attached to the floor of the mouth cavity by a membrane called **frenulum**.

The upper surface bears **taste buds** situated on **taste papillae**. The papillae are connected by nerves.

(i) Taste papillae and Taste buds

The papillae are small projections found on the upper surface of the tongue. There are three types of papillae, namely, **filiform**; **fungiform**; and **circumvallate** (Fig.15.3).

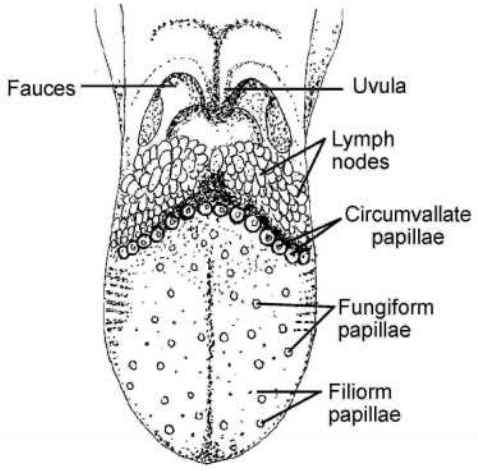


Fig.15.3 : Surface view of human tongue with papillae

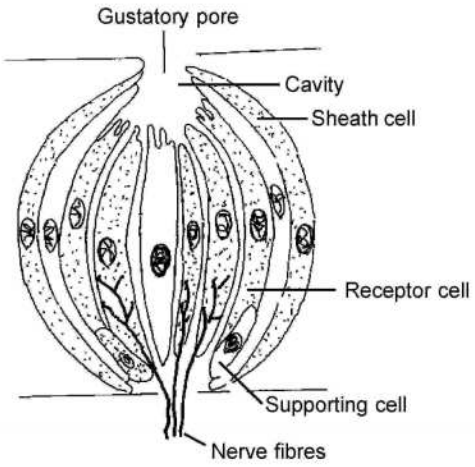


Fig.15.4 : Cellular srtructure of a taste bud

1. **Filiform papillae :** These are small, conical and most numerous, present on anterior two-third part of the tongue. These papillae do not bear taste buds.
2. **Fungiform papillae :** These are mushroom-shaped papillae and less numerous than filiform papillae, distributed on the tip and along the sides of the tongue. Each fungiform papilla bears up to five taste buds, situated at the tip.
3. **Circumvallate papillae :** These are large and circular papillae, few in number (8-12), lying along the margin of an inverted **V-shaped sulcus terminalis** near the base of the tongue. Each circumvallate papilla is encircled by a deep furrow, which bears the taste buds. Each papilla bears up to 100 taste buds, lying along the wall of the furrow.

The taste buds are the organs of taste. Besides the tongue, taste buds are also present on the soft palate, epiglottis, palatoglossal arches and posterior wall of the oropharynx. A taste bud is a pyriform structure made up of modified epithelial cells (Fig. 15.4). There is a small cavity that opens to the surface through a **gustatory pore**. Contrary to previously held idea that taste buds perceiving different tastes, such as sweet, sour, bitter and salty are specialized, it is undoubtedly established that all taste buds can perceive all tastes.

(ii) Functions of the tongue

1. It functions as a gustatory organ (an organ perceiving taste).
2. It helps in the act of chewing and mastication of the food.
3. It helps in the act of swallowing.
4. It plays a role in speech.

5. It acts as a brush to clean the teeth.

6. It keeps the mouth moist by secreting mucous and serous fluids.

(c) Teeth : Teeth are present on both jaws in the oral cavity. Human teeth are **thecodont** in nature i.e. the roots are lodged in bony sockets of the jaw bones. All the teeth of the upper jaw are lodged in sockets of maxilla bones and of the lower jaw in sockets of the dentary bones.

The number of teeth is fixed for a species and so is for human being. They develop in two sets : **milk** or **deciduous set** and **permanent set** (Fig. 15.5). The milk teeth appear during first 2 years after birth. These are smaller, weaker and temporary. They are replaced by the permanent teeth between 6 to 12 years of age. The teeth that appear in two sets are called **diphyodont**. The deciduous set consists of two incisors, one canine and two premolar teeth on each side of the upper and lower jaws. Permanent teeth of man are of four types, based on their functions : **incisors (8)**, **canines (4)**, **premolars (8)** and **molars (12) (Fig. 15.5)**. This is called **heterodont dentition**.

Incisors are present in the anterior part of the jaw. They have sharp cutting edges and hence, are called cutting teeth. The canines are pointed and are dagger-shaped. Premolars and molars are called **grinding** or **cheek teeth** having **cusps** or **grinding surfaces**. They are located farther back on the jaws. All the molars grow in the permanent set only. Thus, molars appear only once in the life time and therefore, they are **monophyodont**. The last molars are called **wisdom teeth**.

(i) Dental Formula

The numerical presentation showing the number and arrangement of teeth in one half of both the jaws is called **dental formula**. On adding all the teeth in one half of both the jaws, the number is multiplied by two. The resultant is the total number of teeth.

Dental Formula (permanent set)

$$= I\frac{2}{2}\ C\frac{1}{1}\ PM\frac{2}{2}\ M\frac{3}{3} \times 2 = 32 \text{ or } \frac{2123}{2123} \times 2 = 32$$

Dental Formula (Deciduous set)

$$= I\frac{2}{2},\ C\frac{1}{1},\ PM\frac{2}{2},\ M\frac{0}{0} \times 2 = 20 \text{ or } \frac{2102}{2102} \times 2 = 20$$

(N.B: I, Incisor; C, Canine; PM, Premolar; and M, Molar)

(ii) Structure of Tooth

A typical tooth consists of three regions: (i) **crown**, (ii) **neck**, and (iii) **root** (Fig.15.6). The crown is the exposed part of the tooth. Neck is usually covered by **fleshy gum or**

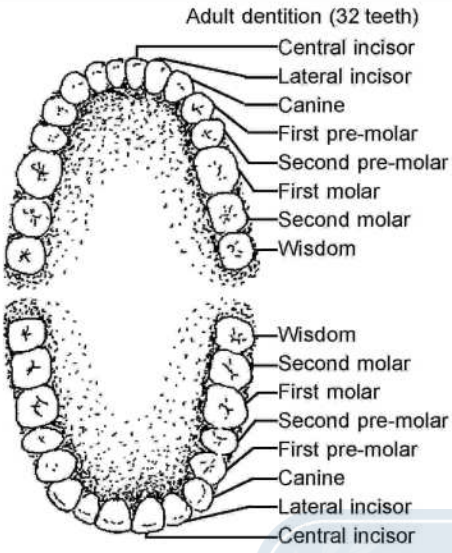


Fig.15.5 : Human dentition permanent set.

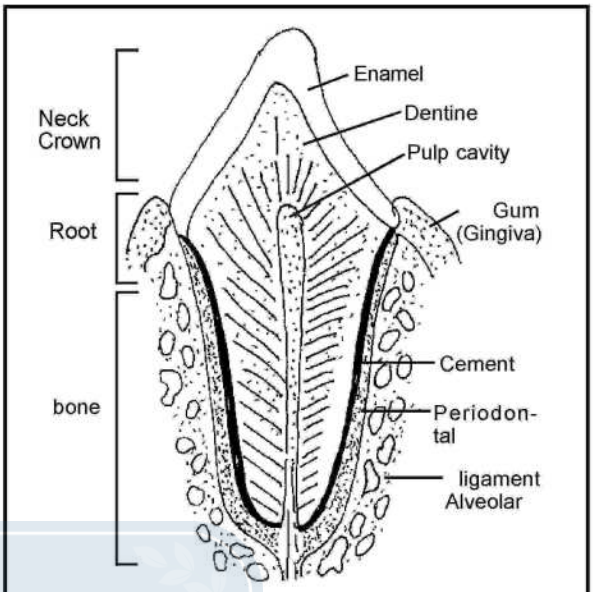


Fig.15.6 : Structure of a human tooth

gingiva. Root is embedded in a socket of the jaw bone. The root consists of one, two or three **fangs**. For example, an incisor and a canine, each have a single fang or root; upper molar has three roots; and lower molar two roots.

The main mass of a tooth consists of a hard and bone-like material, without blood vessels, called **dentine**. It is chiefly composed of phosphate and carbonate of calcium and magnesium and collagen fibers. In the region of the crown, the dentine is covered by a much harder shiny-white material called **enamel**. It is composed of large amount of calcium phosphate and organic substance. **Enamel is the hardest substance in the body**. The dentine is covered by a thin layer of cement in the root region. The cement adheres to the wall of the bony socket through a layer of fibrous connective tissue. The dentine is traversed by a **pulp cavity** containing a mass of cells, blood vessels and nerve endings that constitute a connective tissue, known as the **pulp**.

(d) Salivary glands

There are three pairs of salivary glands in human, namely, (a) **parotid** (b) **sublingual** and (c) **submaxillary** or **submandibular**. The ducts open into the oral or buccal cavity (Fig. 5.13). The glands secrete a watery, secretion called saliva into the oral cavity.

15.3.1.2. Pharynx : It is a continuation of the buccal or oral cavity behind. There is no physical demarcation between the two and therefore, the two often constitute a **bucco-pharyngeal cavity**. The nasal canals and the buccal cavity, both open into the pharynx. It is divided into three sections: (i) **nasopharynx** (ii) **oropharynx** and (iii) **laryngopharynx**.

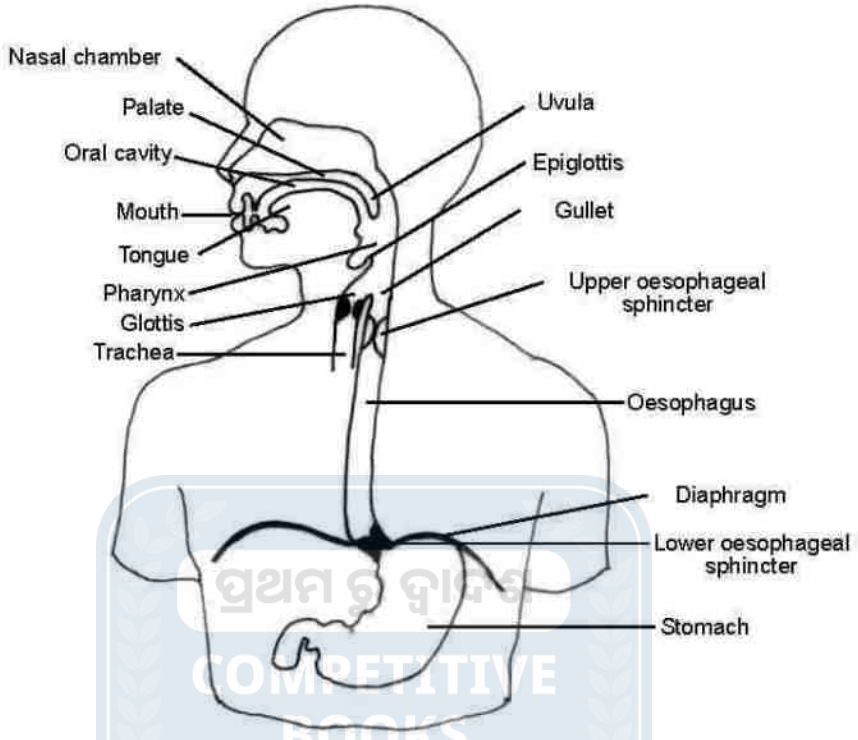


Fig.15.7 : Outline structure of the oral cavity, pharynx and oesophagus leading to the stomach

(a) Nasopharynx : The nasal canals open into a section of the pharynx, called the nasopharynx, through a pair of **internal nostrils** or **internal nares**. It serves for the passage of the inspired and expired air. There is a pair of small oval openings, called **openings of eustachian tubes,** on the roof. Each middle ear opens into the nasopharynx through an eustachian tube.

(b) Oropharynx : The buccal cavity opens into a section of the pharynx, called oropharynx. It serves as the passage for food.

(c) Laryngopharynx : Both the naso-and oropharynx open into a short laryngopharynx. The laryngopharynx, in turn, opens into the oesophagus or food pipe through **gullet** and into the larynx or the sound box through a **glottis**. The larynx is continued into the trachea or the wind pipe. The food pipe and the wind pipe cross each other at the end of the laryngopharynx. The glottis is guarded by a muscular flap called **epiglottis**. When we swallow the food, the glottis remains closed by the epiglottis. The presence of an epiglottis guarantees that the food and air enter into their respective pipes. A mass of lymphoid tissues, called **palatine tonsil**, lies on either side of oropharynx. Infection of tonsils by pathogenic microorganisms causes their inflammation. This pathological condition is known as **tonsillitis**.

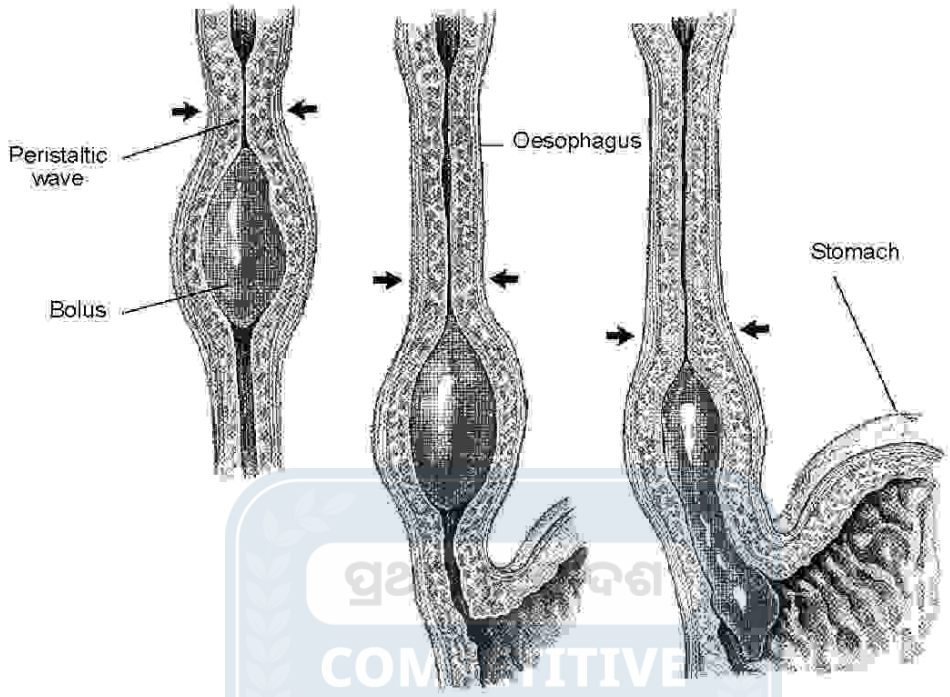


Fig. 15.8 : Peristalstic movement of the wall of the oesophagus.

15.3.1.3. Oesophagus : It is a 25 cm long, narrow muscular tube lined internally by stratified squamous epithelium containing mucous secreting gland cells. It runs downward from the gullet through the neck behind the trachea, passes through the diphragm and opens into the stomach in the abdomen. The mucosa (the innermost tissue layer) is raised into longitudinal folds, called **oesophageal rugae.** One each of two such folds is present at the beginning and the end, which regulate the entry and exit of food from the oesophagus. These folds are called **oesophageal sphincters** (Fig. 15.7). The oesophagus conducts the food to the stomach by successive contraction and relaxation of the muscle layers of the oesophageal wall. This phenomenon is known as **peristalsis** (Fig. 15.8). The contraction and relaxation in a reverse rhythm is known as **antiperistalsis**. It results in rhythmic **hiccups**.

15.3.1.4. Stomach : The stomach is a large J-shaped distensible sac-like muscular organ present on the upper left side of the abdomen, just below the diaphragm. It is about 30 cm long and 15 cm wide. It has a variable capacity ranging from **2.0 to 4.5** liters. It communicates in front with the oesophagus and behind with the first part of the small intestine, the duodenum. The stomach has four regions : (i) **cardiac region** (cardia); (ii) **fundus**; (iii) **body**; and (iv) **pyloric region** [Fig.15.9 (a)]. The pyloric region begins with a somewhat widened part, called **pyloric antrum**. It leads into a short and narrow **pyloric canal** that ends in a **pyloric sphincter**. Each of these parts contains a specific type of gland.

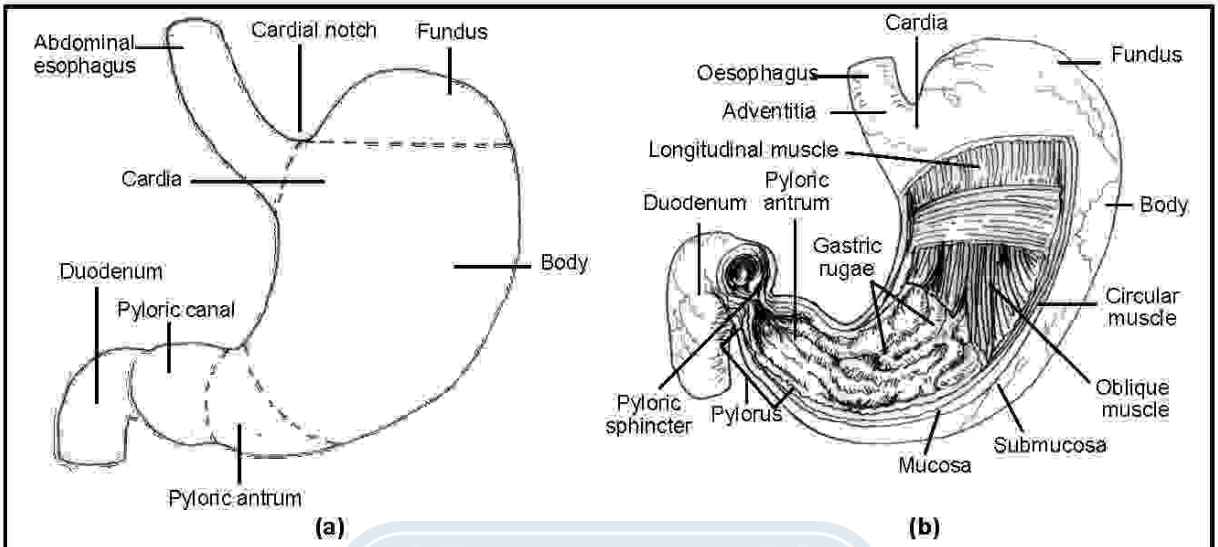


Fig. 15.9 : The structure of the stomach. (a) gross structure and divisions of the stomach and (b) stomach, partially cut open to exhibit the internal structure.

(a) Cardiac part (Cardia) : The oesophagus drains the food into the cardiac stomach through a cardiac aperture. It is guarded by a sphincter, the **lower oesophageal sphincter** or **cardiac sphincter** (Fig. 15.7), which prevents backward movement of the food into oesophagus.

(b) Fundus : It is the thickest part, lying to the left of cardiac aperture. It has a dome like upper part that projects above the cardiac aperture.

(c) Body : It is the main and middle part of the stomach.

(d) Pyloric part (Pylorus) : It is the narrow lower part of the stomach, which opens into the duodenum by a pyloric aperture, guarded by a **pyloric sphincter**. The pyloric sphincter regulates the passage of food into the duodenum.

(e) Functions of the stomach

1. It stores food temporarily, received from the oesophagus.
2. It helps in mechanical mixing of food, known as **churning**.
3. It helps in the digestion of food by enzyme.
4. It regulates the flow of food into the small intestine.
5. Some **enteroendocrine cells** in the mucosa of the stomach (antrum part) secrete a hormone, called **gastrin**. It regulates the secretion of gastric juice from the gastric glands. Some other cells secrete another hormone, called **motilin**, which promotes the smooth muscle contraction in the wall of the stomach and intestine. This hormone is also produced from the mucosa of the small intestine and colon.

15.3.1.5. Small Intestine: It is the longest part of the alimentary canal, measuring about seven meters. It extends from the end of the pybric stomach to the **ileo-caecal valve** guarding the caecum. It is divided into three parts : **duodenum**, **jejunum**, and **ileum**.

(a) Duodenum : It is the proximal part and is about 25 cm long. It forms a C-shaped curve. The common bile duct and the pancreatic duct open into the duodenum, marked by an **ampulla of Vater**. The opening is guarded by a **sphincter of Oddi**.

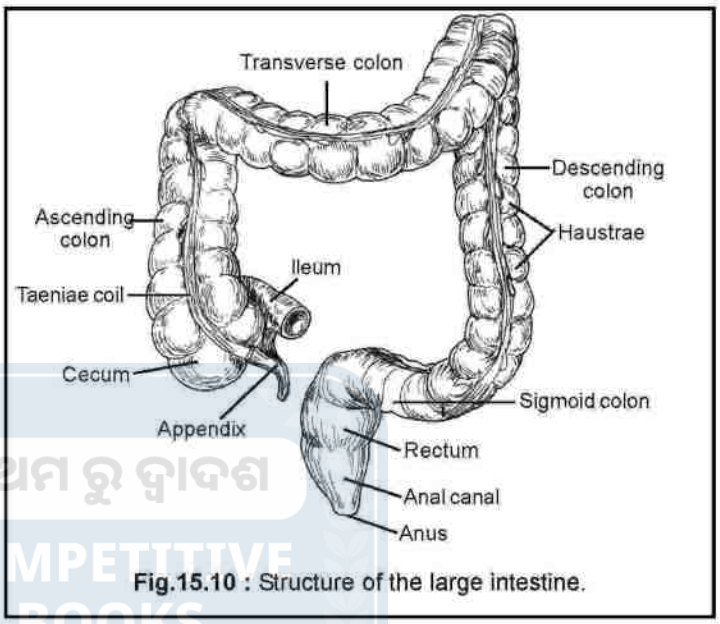


Fig.15.10 : Structure of the large intestine.

(b) Jejunum : It is the middle part of the small intestine. It follows the duodenum and is about 2.5 meters long.

(c) Ileum : It is the distal part of small intestine. It is the longest part and is about 3.5 meters long. It opens into the **caecum** of the large intestine. The opening of the ileum into the caecum is guarded by an **ileo-caecal valve,** which prevents the passage of food into the caeum. The jejunum and ileum are profusely coiled structures. Small intestine is the region where most of the digestion and absorption of food takes place.

(d) Peyer's Patches : Small nodules of lymphoid tissue are present along the lining through out the entire length of the small intestine. In the ileum, the nodules are clustered together in groups called **Peyer patches or Gut Associated Lymphoid Tissues (GALT)**. These are the places for maturation of bone marrow lymphocytes as B-lymphocytes. Though less conspicuous, lymph nodes are found throughout the length of the small intestine.

(e) Functions of small Intestine

1. It completes the digestion of food.
2. It helps absorb nutrients into blood and lymph.
3. It secretes gastro-intestinal hormones, such as, secretin; and cholecystokinin-pancreozymin, which regulate the release of bile and pancreatic juice, respectively into the duodenum.
4. The Peyer's patches serve as the maturation sites for B-lymphocytes, which mature as antibody secreting plasma cells.

15.3.1.6. Large Intestine : The large intestine is shorter than the small intestine. It measures about 1.5 meters long. It is much wider than the small intestine and is divided into three parts: **caecum**, **colon** and **rectum** (Fig.5.10). The colon has three longitudinal muscle strips or chords, called **taeniae coli**. The contractions of the taeniae coli form small pouches called **haustrae** or **haustras**.

(a) Caecum : It is a small, blind sac measuring about 6 cm in length and 7.5 cm in width. The caecum is extended as a small and finger shaped tubular structure called **vermiform appendix** (Fig.5.10). The appendix is a vestigial organ in human being. Occasionally, the appendix develops inflammation due to microbial infection. This pathological condition is known as **appendicitis**. In such cases, the infected appendix is removed surgically. Both the caecum and vermiform appendix are quite large and more developed in herbivores. Cellulose digesting bacteria harbour the appendix and help digest the cellulose, which the herbivores eat in bulk.

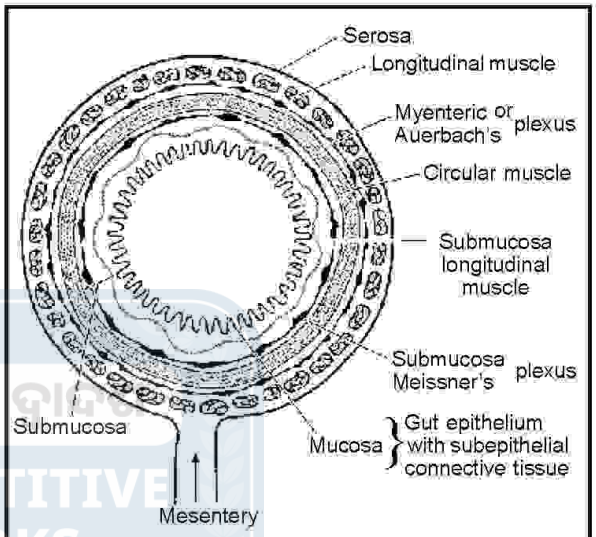


Fig. 5.11 : General histology of the wall of the alimentary canal (Complete outline)

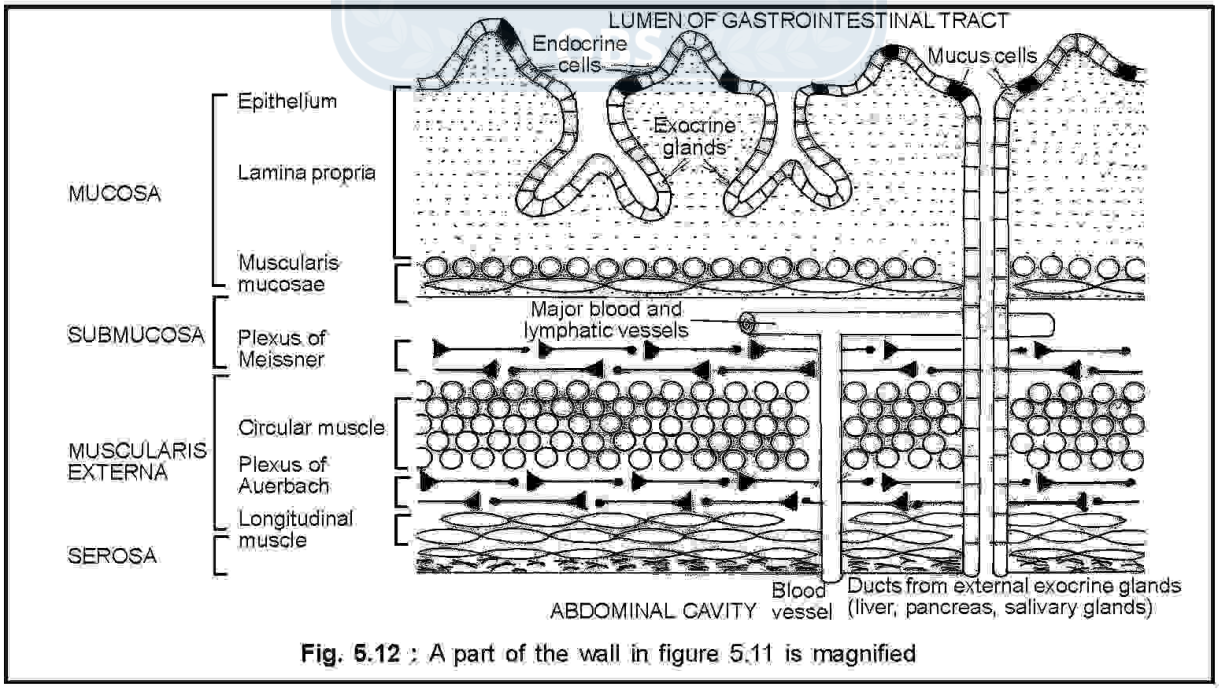


Fig. 5.12 : A part of the wall in figure 5.11 is magnified

(b) Colon : It is the longest part of the large intestine. It is about 130 cm long and acculated possessing pouches. It is differentiated into four regions : **ascending colon** extending up to the liver on the right side; **transverse colon** that bends to the left and crosses the abdominal cavity below the pancreas; **descending colon** running downward on the left side; and **sigmoid** or **pelvic colon** that runs to the right and joins the rectum (Fig. 15.10).

(c) Rectum : It is about 16 to 20 cm long. It is concerned with temporary storage of the faecal matter. The rectum has longitudinal folds which dilates it during storage. Its lower part is prolonged as an **anal canal**, which finally opens to the exterior through an **anal orifice** or **anus**, guarded by an **anal sphincter**.

(d) Functions of Large Intestine

1. It receives and temporarily stores undigested residual food from the small intestine.
2. It absorbs water and salts.
3. It provides a site for the action of bacteria that release the food substance and produce vitamins and gases.

15.3.1.7. Anus : The anus is guarded by **internal** and **external anal sphincters**. The enlargement of rectal veins in the wall of the anus causes a severe painful condition, called **haemorrhoid** or **piles**.

15.3.2. General Histology of the Alimentary Canal

Histologically, the alimentary canal consists of four primary layers: (a) **outer most serosa** or **visceral peritoneum**; (b) **muscular layer**; (c) **submucosa**; and (d) **innermost lining of mucosa** [Figs. 15.12 (a) & (b)].

(a) Serosa : It is the outer most visceral peritoneal layer made up of simple squamous epithelium. It is called serosa because it is lubricated by a serous or watery fluid.

(b) Muscular layer : It is present below the serosa and is composed of outer **longitudinal** and inner **circular** muscle layers. Both the muscle layers consist of smooth and unstriated muscle cells. An oblique layer may be present in some parts. These muscle layers help in **peristalsis**.

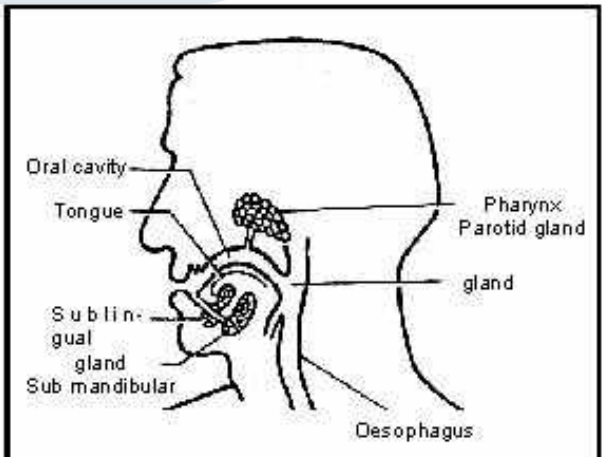


Fig. 15.13 : Human salivary glands emptying into the oral cavity.

(c) Submucosa : It lies between the muscular layer and mucosa. It consists of **loose connective tissue**, richly supplied with blood vessels and lymph vessels. In this layer, a nerve network, called **plexus of Meissner,** is present.

(d) Mucosa : This layer forms the inner most layer and it is named as mucosa because it secretes mucous to lubricate the inner lining of the gut. It is composed of three layers from outer to inner.

(i) A **muscularis mucosa** of a thin muscular layer, consisting of outer longitudinal muscle layer and inner circular muscle layer.

(ii) A middle thin layer of loose connective tissue called **lamina propria** or **tunica propria**. The tunica propria contains fine blood and lymph vessels.

(iii) The inner most layer is the mucous membrane, made up of columnar epithelial cells supported by a thin basement membrane. It forms **gastric glands** in the stomach and **villi** and **intestinal glands** in the small intestine.

15.3.3. Digestive Glands :

These glands secrete digestive juices for the digestion of food. The glands involved in the digestion process and their secretions are enlisted below :

1. **Salivary glands** (Oral cavity) : Saliva
2. **Gastric glands** (Stomach) : Gastric juice
3. **Intestinal glands** (Small intestine) : Intestinal juice or Succus entericus.
4. **Brunner's glands** (Duodenum) : Mucous
5. **Pancreas** : Pancreatic juice
6. **Liver** : Bile

All, except bile from liver and mucous from Brunner's glands, contain one or more digestive enzymes. Bile does not contain any enzyme; but still plays an important role in digestion. Mucous hydrates and lubricates the food.

15.3.3.1. Salivary Glands (Fig.15.13) : There are three pairs of salivary glands in human.

(a) Parotid Glands : These are the largest of the salivary glands, located anterior and inferior to the external ear or pinna. The parotid ducts or **Stenson's ducts** open into the vestibule, opposite to the upper second molar teeth. Inflammation of parotid gland due to viral infection causes the disease called **mumps**.

(b) Sublingual Glands : These are smallest of the salivary glands, located below the tongue. They open at the floor of the buccal cavity by a number of small sublingual ducts or **Bartholin's ducts** or **ducts of Rivinus**.

(c) Submandibular (Submaxillary) Glands : These are located inferior to the mandible on the floor of the oral cavity. They open below the tongue, by **submaxillary** or **Wharton's ducts**.

The salivary glands secrete a viscous, watery fluid called saliva into the oral cavity. It contains a starch-hydrolyzing enzyme called **ptyalin** or **salivary α-amylase**. Its pH is marginally in the acidic side i.e. 6.8. About 1.5 litres of saliva is secreted daily. The salivary α-amylase hydrolyzes starch into **maltose**, **maltotriose** and **limit dextrin (α-dextrin)**. A **lingual lipase** is also secreteel by **Ebner's glands**, present on the dorsal side of the tongue. This lipase, although secreted from the buccal cavity, becomes active only in the stomach. Saliva also contains a **bacteriolytic enzyme**, **lysozyme** and **immunoglobulin A (I_gA).** These two play an important role in the first line of defence of the body.

(d) Compostion of saliva

Water is about 99.5%

Total solids constitute 0.5%

(i) Cellular constituents

Few desquamated epithelial cells, bacteria etc.

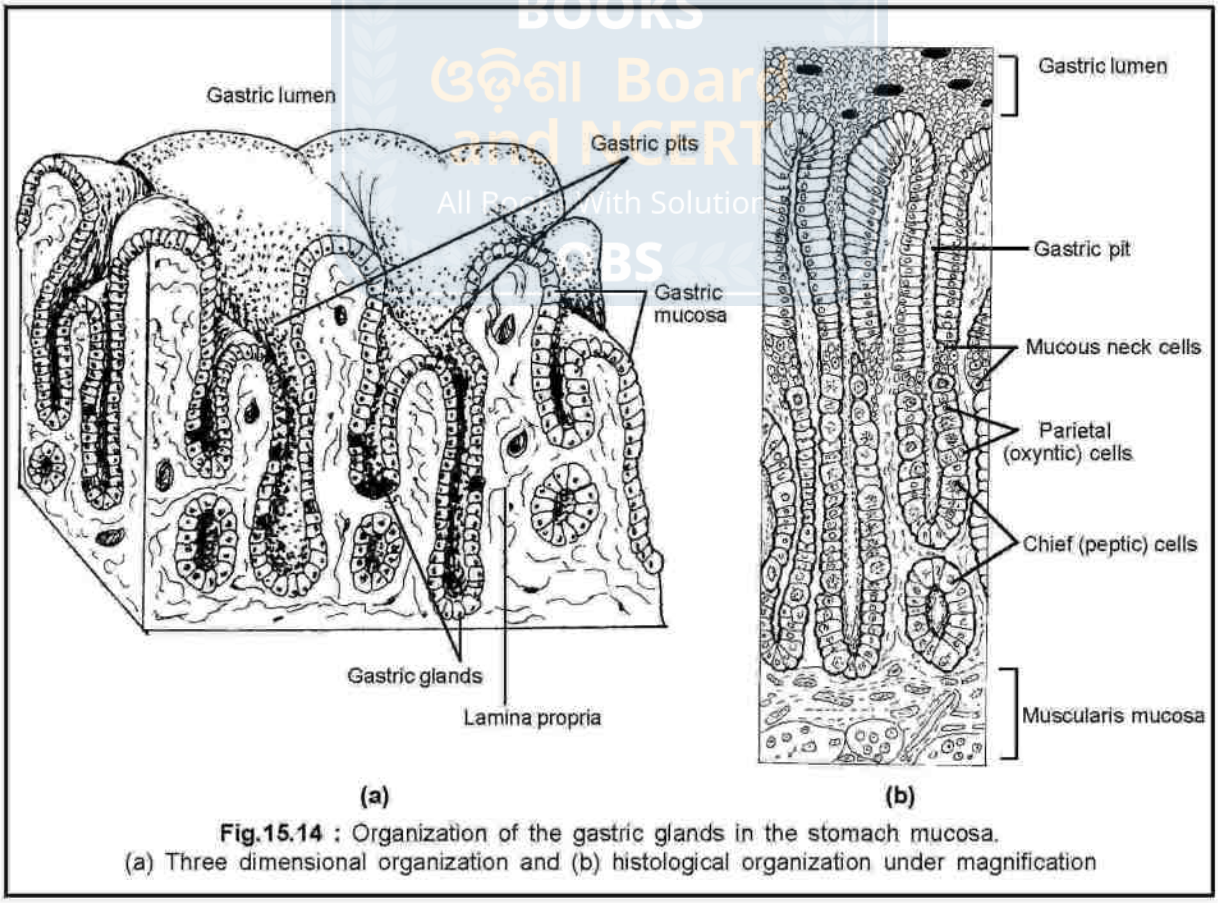


Fig.15.14 : Organization of the gastric glands in the stomach mucosa.
(a) Three dimensional organization and (b) histological organization under magnification

(ii) **Inorganic constituents : 0.2%**

Imporatant salt are Sodium chloride, Potassium chloride, Calcium carbonate, Calcium phosphate and Sodium bicarbonate.

(iii) **Organic constituents : 0.3%**

Enzymes : Salivary α-amylase (Ptyalin), lingual lipase, phosphatase, and bacteriolytic enzyme (lysozyme).

Other organic matter : Immunglobulin A(I_gA), mucin, urea, amino acids, cholesterol, etc.

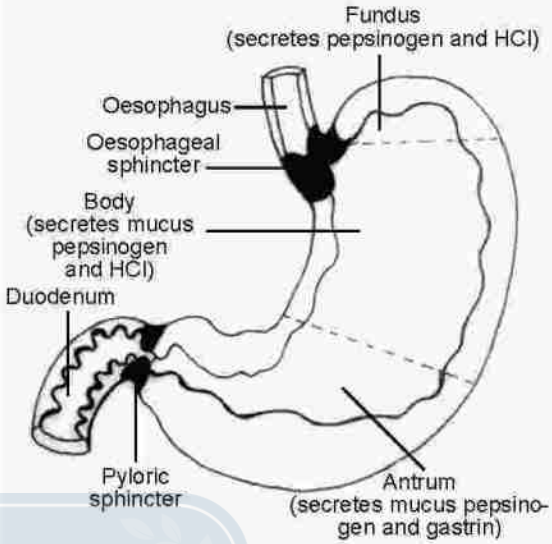


Fig.15.15 : An outline diagram of the stomach with different divisions.

(e) Functions

1. Mechanical function : Saliva keeps the mouth moist and helps in speech, masticates the food, prevents injury to the mucous membrane.

2. Digestive function : The enzyme ptyalin or salivary α-amylase splits starch into maltose, maltotriose and limit dextrin.

3. Bacteriolytic function : Lysozyme of saliva has bactericidal property i.e. it kills bacteria by dissolving their polysaccharide cell wall.

4. Contains an antibody, immunoglobulin A (I_gA) : It serves as the first line of defence of the body.

5. Maintenance of water balance : When body water is lost due to sweating, perspiration, diarrhoea, etc., saliva secretion is reduced and thirst sensation is aroused. Consequently, there is a stimulation for drinking more water to restore the water balance of the body.

6. Excretory Function : Saliva excretes urea; heavy metals like mercury, lead and arsenic; alkaloids like morphine; antibiotics such as penicillin and streptomycin; ethyl alcohol; thiocyanate; iodide; and some micro-organisms from the body.

15.3.3.2. Gastric Glands : The mucous membrane lining the stomach is well developed and is folded to form about 35 million simple or branched tubular glands called **gastric glands** [Fig.15.14 (a)]. These are of three types : **cardiac glands**, **pyloric glands** and **fundic glands**.

(a) Cardiac Glands : The cardiac glands are found in the cardiac region of the stomach, which secrete mucous, pepsinogen and HCl in traces.

(b) Pyloric Glands : They are found in the pyloric region, which secrete mucus as well as gastrin. It also secretes pepsinogen and HCl in traces.

(c) Fundic Glands [Fig. 15.14 (b)] **:** The gastric glands of the fundus are called fundic glands. Each fundic gland has three types of cells :

(i) **Chief or peptic (zymogen) cells** secrete two pro-enzymes; **pepsinogen**, and **prorennin,** and an enzyme **gastric lipase**. They are usually present in the basal part of gastric glands.

(ii) **Oxyntic (parietal) cells** secrete **hydrochloric acid.** These cells are large and are most numerous on the side walls of the gastric glands.

(iii) **Mucous neck cells** or **Goblet cells** are numerous at the neck of the glands. They secrete a watery lubricating substance, the mucus.

The secretions of these cells collectively form the gastric juice. The gastric juice is strongly acidic with a pH of 0.9 to 1.5. Approximately, 500-1000 ml of gastric juice is secreted per meal (2-3 liters / day)

Enterochromaffin cells or enteroendocrine cells present in the mucosa layer of the pyloric antrum secrete a hormone, called **gastrin**. These cells are stimulated by the arrival of food (bolus) from the oesophagus. Consequently, gastrin is secreted, which stimulates the gastric glands to secrete gastric juice.

15.3.3.3. Intestinal Glands : There are two types of intestinal glands: **crypts of Lieberkuhn** or **intestinal glands** and **Brunner's glands** or **duodenal glands**.

A crypt of Lieberkuhn is a multicellular simple tubular gland (Fig.15.16), present throughout the small intestine between the villi. It is a sunken or invaginated part of the mucosa into the lamina propria. It contains three main types of cells: **goblet cells**; **Paneth (zymogen) cells** and **enteroendocrine**

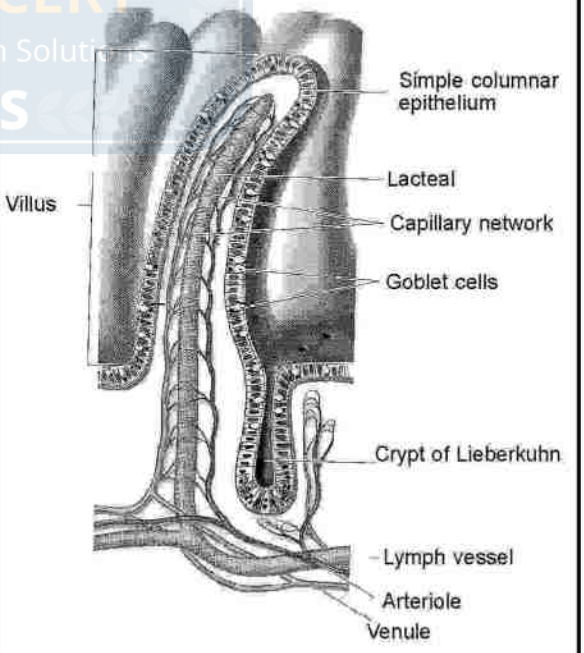


Fig. 15.16 : Intestinal villus with an associated crypt of Lieberkuhn in the ileum.

(**enterochromaffin**) **cells**. Goblet cells secrete mucous, while Paneth cells are believed to secrete lysozyme, an enzyme having anti-bacterial property. The enteroendocrine cells secrete several hormones, which regulate the secretion of gastric juice, pancreatic juice and bile. These hormones include **secretin**, **cholecystokinin-pancreozymin** and **gastric inhibitory peptide** (GIP). The cells of the crypts also secrete a number of enzymes, which complete the process of digestion. Similar crypts are also present in the large intestine, which secrete only mucus, but no enzyme.

The **Brunner's glands** are multicellular glands, present in the submucosa of the duodenum only. They are absent in the jejunum and ileum . They secrete mucous to protect the intestinal lining from the corrosive action of hydrochloric acid. Brunner's glands open into the crypts of Lieberkuhn of the duodenum.

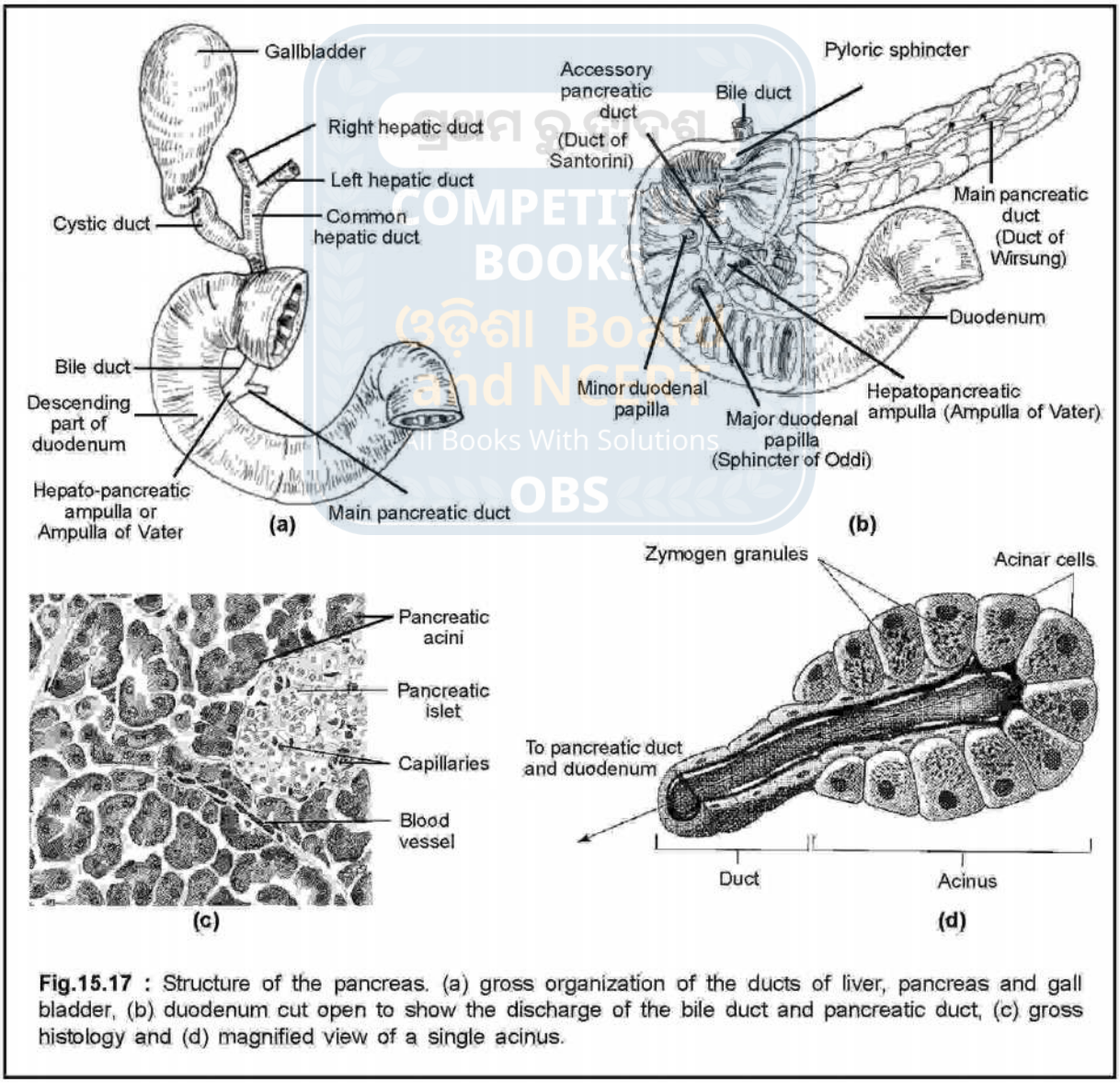


Fig.15.17 : Structure of the pancreas. (a) gross organization of the ducts of liver, pancreas and gall bladder, (b) duodenum cut open to show the discharge of the bile duct and pancreatic duct, (c) gross histology and (d) magnified view of a single acinus.

The secretion of intestinal glands is known as **intestinal juice** or **succus entericus**. About 2 to 3 litres of intestinal juice is secreted per day. The juice contains mucin and several enzymes such as **maltase**, **isomaltase**, **sucrase (invertase)**, **lactase**, α- or **limit dextrinase** (**α-1, 6 glycosidase**), **exopeptidases** (**aminopeptidase** and **carboxypeptidase**), **endopeptidases**, **dipeptidases**, **nucloside phosphorylase, nucleotidase** and **intestinal lipase**. These enzymes act on the partially digested food of the stomach. Intestinal juice also contains an activator enzyme called **enteropeptidase** or **enterokinase,** which activates inactive trypsinogen into active trypsin.

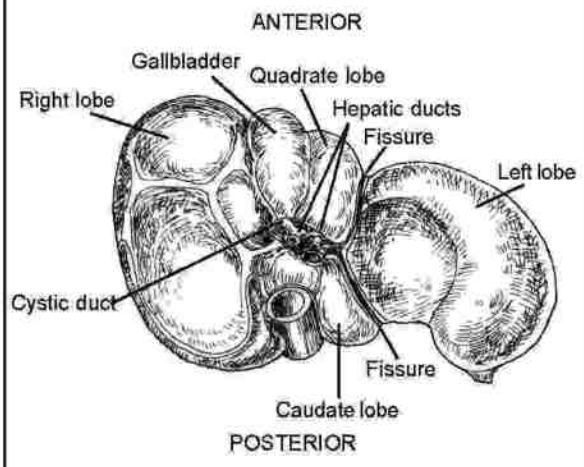


Fig.15.18 : Gross morphology of the liver of human.

In addition to the digestive glands, the entire mucosa layer of the alimentary canal has mucous glands that produce mucus. The mucous lubricates the digestive tract so that food passes through easily. The mucous coat protects the underlying cells of the mucosa layer from the digestive enzymes.

15.3.3.4. Pancreas : It is a pinkish gland located in the loop of the duodenum and extends up to the spleen behind the stomach. It is about 2.5 cm wide and 12-15 cm long. It is comprised of three parts: head, body and tail. Pancreas is the second largest gland and it functions both as an **exocrine** and an **endocrine gland**. Thus, it is a **mixocrine gland**. Its exocrine part is formed by large number of **lobules** or **acini** [Figs. 15.17 (c) & (d)]. Each acinus consists of a number of glandular cells, which secrete **pancreatic juice**. Pancreatic juice is carried by the pancreatic duct or **duct of Wirsung** [Figs. 15.17 (a) & (b)] into the duodenum through the **ampulla of Vater**. Sometimes, an accessory pancreatic duct, **duct of Santorini** [Fig. 15.17 (b)] is also present, which directly pours the pancreatic juice. The juice is alkaline (pH = 7.8) due to the presence of sodium bicarbonate. The endocrine part of the pancreas consists of spherical balls of cells called **Islets of Langerhans** scattered in the pancreatic tissue.

Pancreatic juice contains sodium bicarbonate and three pro-enzymes (inactive enzymes): **trypsinogen**, **chymotrypsinogen** and **procarboxypeptidase**. An intestinal activator enzyme, **enterokinase**, activates trypsinogen into trypsin. Activated trypsin then activates chymotrypsinogen and procarboxypeptidase into their respective active forms. Besides, the pancreatic juice also contains **elastase**, **nucleases** (**ribonuclease**, **deoxyribonuclease**), **pancreatic α-amylase**, **pancreatic lipase or steapsin**, **cholesteryl ester hydrolase** and

phospholipase. The pancreatic juice helps in the digestion of starch, proteins, lipids and nucleic acids.

Functions of Pancreatic Juice

1. It is alkaline in nature and hence, neutralizes the acidic chyme in the duodenum and makes the food alkaline (pH 8.4)
2. Pancreatic α-amylase acts on starch and converts it into maltose, maltotriose and limit dextrin.
3. Trypsinogen is activated into trypsin by **enterokinase**, present in the intestinal juice. Trypsin acts on proteins and converts them into peptones (polypeptides of variable length).
4. Chymotrypsin coagulates milk.
5. Elastase acts on elastic fibers of connective tissue.
6. Carboxypeptidase removes amino acids from the C (carboxyl)-terminus of polypeptides.
7. Panecratic lipase or steapsin completes fat digestion.
8. Pancreatic nucleases hydrolyze nucleic acids into their constituent nucleotides.

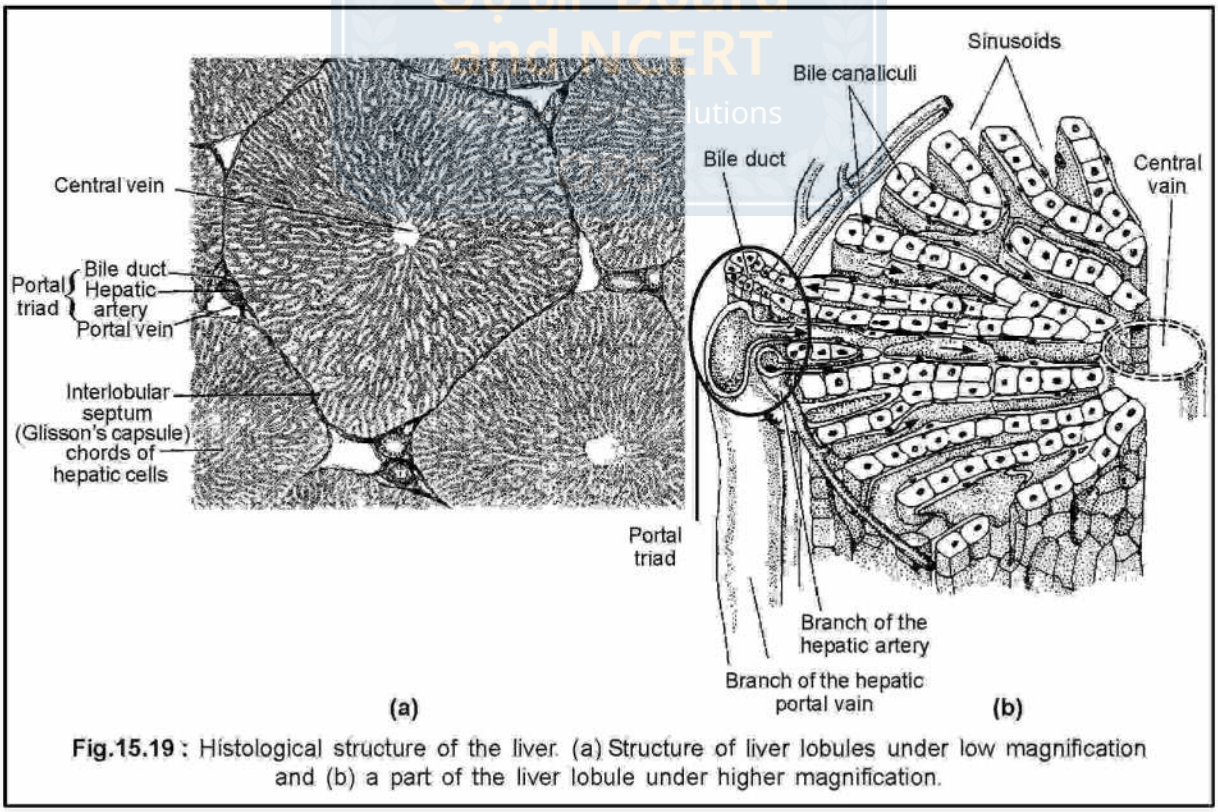


Fig.15.19 : Histological structure of the liver. (a) Structure of liver lobules under low magnification and (b) a part of the liver lobule under higher magnification.

15.3.3.5. Liver : The liver is the largest gland of the body. It is found in the upper right side of the abdominal cavity and is fitted against the lower face of the diaphragm. It is reddish brown in colour. It is larger in males than in females and weighs about 1.6 kg. The liver is divided into two lobes: a large **right lobe** and a small **left lobe.**

The right lobe consists of **right lobe proper, quadrate lobe** and **caudate lobe** (Fig.15.18). A thin-walled, pear-shaped sac, known as **gall bladder** is present on the lower surface of the right lobe. It stores bile, secreted by the liver. The right and left hepatic ducts from the corresponding liver lobes join to form a **common hepatic duct**. The latter joins with the cystic duct of the gall bladder to form a **common bile duct**. The common bile duct passes downward to join the pancreatic duct forming a **hepato-pancreatic ampulla** or **ampulla of Vater**. The ampulla opens into the duodenum. The opening is guarded by **sphincter of Oddi**. Another sphincter muscle or **muscle of Boyden** surrounds the opening of the common bile duct before it joins with the pancreatic duct. This muscle constricts the bile duct, when there is no food in the duodenum.

Histologically, each liver lobe is made up of a number of polygonal columns of hepatic cells, called **hepatic lobules** [Fig.15.19 (a)]. These are the structural and functional units of liver. Each lobule is separated from its adjacent ones by thin inter-lobular septa of connective tissue. Thus, a lobule has a complete connective tissue sheath called **Glisson's capsule** [Fig.15.19 (a)]. In addition to hepatic cells, the liver has Kupffer cells, which destroy bacteria and other germs by phagocytosis.

(a) Bile

Bile is a greenish-yellow, alkaline fluid secreted by the liver and stored in a pear-shaped thin walled bladder, called **gall bladder**, present on the lower surface of the right lobe of the liver. The hepatic bile has a the pH of 8.6 whereas pH of gall bladder bile is 7.6.

(b) Composition of bile

1.	**Water : 97%; Total Solids**	:	**3%**
(i)	**Inorganic constitutents**	:	**0.7%**
	Chlorides and phosphates of Sodium, Potassium and bicarbonates of Sodium and Calcium.		
(ii)	**Organic constituents**	:	**2.3%**
	Bile salts	:	**0.7%**
	(Sodium glycocholate and Sodium taurocholate)		
	Bile pigments	:	**0.2%**
	(Bilirubin and Biliverdin)		
	Other organic constituents	:	**1.4%**
	(Mucin, cholesterol, lecithin, fat, fatty acids and alkaline phosphatase).		

The bile pigment bilirubin is yellow in colour, while biliverdin is green. Accumulation of bilirubin in body fluids causes a disease, called jaundice, in which skin becomes yellow.

(c) Functions of bile

1. Bile is alkaline, hence, neutralizes the acidic chyme of the stomach and makes an optimum environment for the action of enzymes in the small intestine.
2. It prevents the food from bacterial contamination, as it kills germs.
3. Bile reduces the surface tension causing the fat to change into an **emulsion**. Bile salts break the larger fat droplets into smaller ones. This process is called **emulsification**. This increases lipase action on fat.
4. Bile facilitates the absorption of fat, fat soluble vitamins (A, D, E, K), iron, calcium etc.
5. Bile excretes heavy metals like copper; zinc; mercury; toxins; bacteria; bile pigments; cholesterol and lecithin.
6. It stimulates peristaltic movement.

(d) Functions of liver

1. The liver secretes bile.
2. It converts excess glucose into glycogen by **glycogenesis,** with the action of insulin hormone.
3. It converts glycogen into glucose by **glycogenolysis**, as and when necessary, regulated by glucagon hormone.
4. It detoxifies toxic substances.
5. Destroys bacteria by phagocytosis with the help of Kupffer cells.
6. It synthesizes **fibrinogen** and **prothrombin** which help in blood clotting or coagulation.
7. It forms the anticoagulant, called **heparin**.
8. The haemoglobin degrades into bile pigment in the liver.
9. **Deamination** of amino acids takes place in the liver cells.
10. The liver manufactures RBCs in embryos.
11. It synthesizes and stores vitamin B_{12}.
12. It stores iron and copper.
13. The liver is the site of formation of glucose and then glycogen form non-carbohydrate sources like proteins and lipids. This process is called **gluconeogenesis**.

14. Conversion of excess glucose and amino acids into fat takes place in the liver. This process is called **lipogenesis**.
15. Liver produces **angiotensinogen** which helps kidneys in maintaining body fluid homeostasis by osmoregulation.
16. Due to high metabolic activity of liver, heat is produced which is necessary for maintaing an optimum body temperature.

15.4. PHYSIOLOGY OF DIGESTION :

Digestion is a combination of mechanical or physical and chemical processes, in which complex macromolecular food is converted into simpler, smaller and easily diffusible products in the alimentary canal, which is absorbed into the body fluid (blood and lymph) for assimilation by the tissues.

The food is digested in a stepwise manner as it passes through different parts of the alimentary canal in a forward direction. Apart from digestion, the alimentary canal conducts, stores and absorbs the digested food. Thus, there is a physiological division of labour and on the basis of this, the alimentary canal is divided into four zones.

(a) Ingressive zone : It ingests and masticates the food. It includes mouth, buccal cavity, tongue and teeth.

(b) Progressive zone : It conducts, stores and partly, digests food, and includes pharynx, oesophagus and stomach.

(c) Digressive zone : It completes the digestion and absorbtion of the food. It includes small intestine.

(d) Egressive zone : It temporarily stores and finally eliminates the faecal matter to the exterior. It includes colon, rectum, anal canal and anus.

15.4.1. Digestion in the Buccal Cavity :

The digestion of food begins in the buccal cavity, where it is ground into finer particles; and moistened and masticated with saliva to form a soft and pulpy mass, called **bolus**. Food remains in the buccal cavity for about 14 to 18 seconds and then it is swallowed. The presence of food in the buccal cavity acts as a stimulus for the secretion of saliva from the salivary glands and swallowing.

(a) Mastication

Mastication or the act of chewing refers to a combined mechanical action of the salivary glands, teeth, tongue and cheek muscle. This leads to the secretion and mixing of the saliva with the food, which converts it into bolus. The saliva contains mucous and a carbohydrate digesting enzyme, **α-amylase** or **ptyalin and lingual lipase**. Lingual lipase is a lipolytic enzyme. However, it does not work in the buccal cavity and starts working with gastric lipase only in the stomach. Salivary α-amlylase acts on starch and hydrolyzes the **α (1-4) glycosidic bonds**. Consequently, starch converts into **maltose**; and **maltotriose** both

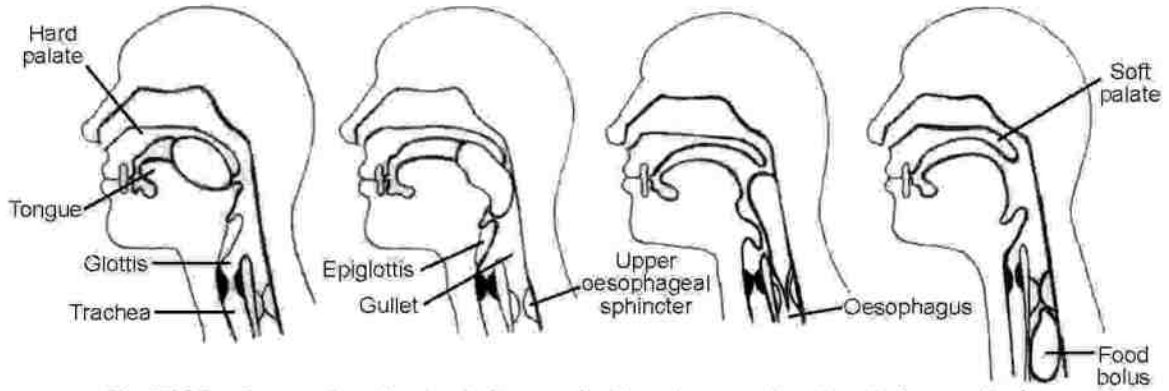


Fig.15.24 : Successive structural changes in the pharyngeal region during swallowing.

with α-1, 4 glycosicic bonds and a branched macromolecule called **limit dextrin** or **α-dextrin**, containing, on an average, eight molecules of glucose.Salivary amylase acts best in the presence of the activator, chloride ions at pH 6.7.

$$\textbf{Starch} \xrightarrow[\text{(pH-6.7)}]{\text{Salivary } \alpha\text{ - amylase}} \textbf{Maltose + Maltotriose + Limit Dextrin } (\alpha \text{ - Dextrin})$$

(b) Deglutition (Swallowing)

Deglutition or the **act of swallowing** is a process by which the bolus is transferred from the mouth to the stomach through the oesophagus (Fig.15.20). This process is a complicated muscular reflex, involving a series of coordinated muscular movements of the mouth; tongue; pharynx; and oesophagus.

The bolus passes down the oesophagus by a series of **peristaltic contraction** of the muscles in the oesophageal wall. This is assisted by the secretion of mucous from the mucosa of the oesophagus. The food does not undergo any chemical modification in the oesophagus.

15.4.2. Digestion in the Stomach :

The bolus remains inside the stomach for several hours and following its digestion, it passes into the intestine in slow spurts. The stomach plays three important roles: (1) it acts as a temporary reservoir of the partially digested food received from the oesophagus; (2) it acts as a mechanical mixer; and (3) it is the site of active **protein digestion**. **A little amount of fat is also digested in the stomach**. There is practically no carbohydrate digestion in the stomach, but the HCl can carry out the hydrolysis of sucrose into glucose and fructose to some extent.

(a) Mechanical Events : Due to the periodic muscular contractions and relaxations in the wall of the stomach, the bolus is thoroughly **churned** (Fig.15.21). The cardiac and pyloric sphincters remain closed during churning of the food. Then it is mixed with the gastric juice and the digestion of proteins commences.

(b) Biochemical Events : As soon as the food bolus reaches the stomach, the enteroendocrine cells of the antral mucosa secrete a hormone called **gastrin**. It stimulates the gastric glands to produce **gastric juice**. The gastric juice consists of **mucus**; **hydrochloric acid (HCl)**; pro-enzymes, **pepsinogen** and **pro-rennin**; and **gastric lipase**.

(c) Role of HCl in digestion

(i) It provides an optimum pH for pepsin activity.

(ii) It activates inactive pepsinogen and prorennin into active pepsin and rennin, respectively.

(iii) It inhibits the action of ptyalin.

(iv) It acts as an antibacterial agent.

(v) It causes denaturation and swelling of proteins, so that enzymes can act well on them.

(vi) It regulates the opening and closing of the pyloric sphincter.

(vii) It softens the food for enzyme action.

(d) Action of Pepsin : Inactive pepsinogen is first activated into active pepsin under the influence of HCl (Fig.15.22). Then the activated pepsin itself activates pepsinogen into pepsin. Such activation is known as **autocatalytic activation**. Pepsin is an **endopeptidase**, which digests proteins into **polypeptides of variable lengths** or **peptones** in an acidic medium. No free amino acid is released by pepsin digestion. The maximum activity of pepsin is exerted at two pH ranges, 1.6 to 2.4 and 3.4 to 3.9.

Pepsinogen $\xrightarrow{HCl}$ **Pepsin**

Protein $\xrightarrow[pH = 1.6 - 3.9]{Pepsin}$ **Acid Metaprotein** $\rightarrow$ **Primary Proteoses** $\rightarrow$ **Secondary Proteoses** $\rightarrow$ **Peptone (Short chain polypeptides)**

(e) Action of Rennin : **Prorennin** is a proenzyme that is inactive. It is activated by HCl into an active **rennin** or **chymosin**. Rennin hydrolyses the milk protein, **casein** into **para-casein** and **whey protein** (peptone-like substance). Para-casein is transformed into

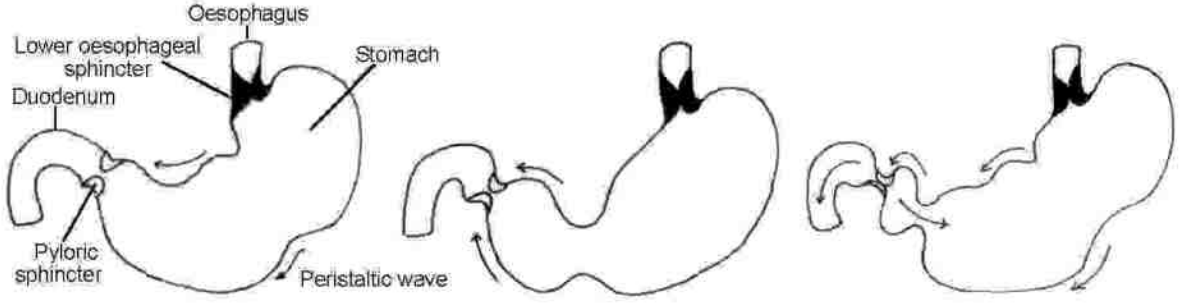


Fig.15.21 : Peristaltic movement of the stomach during churnimng of the food.

insoluble **calcium para-caseinate** in the presence of calcium ions. This is known as **clotting** or **curdling of milk**. The curd is acted upon by pepsin and forms peptone. The curd stays in the stomach for a relatively longer period for proper digestion by pepsin. Rennin is absent in adult human gastric juice. The clotting and digestion of milk in adult human stomach mainly takes place by means of HCl and pepsin, respectively.

Prorennin $\xrightarrow{HCl}$ **Rennin**
Casein $\xrightarrow{Rennin}$ **Paracasein**
Paracasein + Calcium $\rightarrow$ **Calcium paracaseinate (curd)**
Calciumparacaseinate $\xrightarrow{Pepsin}$ **Peptone**

(f) Action of Gastric Lipase : Gastric lipase is a weak lipolytic (lipid digesting) enzyme. It hydrolyzes fat into glycerol and fatty acids. Fat digestion in the stomach is not significant. Its complete digestion is carried out in the duodenum by pancreatic lipase.

The thick acidic mixture of gastric juice and partially digested food form a thick acidic paste, called **chyme** in the stomach. Gastric digestion takes about 3 to 5 hours. However, it depends upon the nature of food ingested. The chyme passes into the duodenum at intervals by the peristaltic contractions of the stomach. The pyloric sphincter of the stomach opens to release the chyme in spurts.

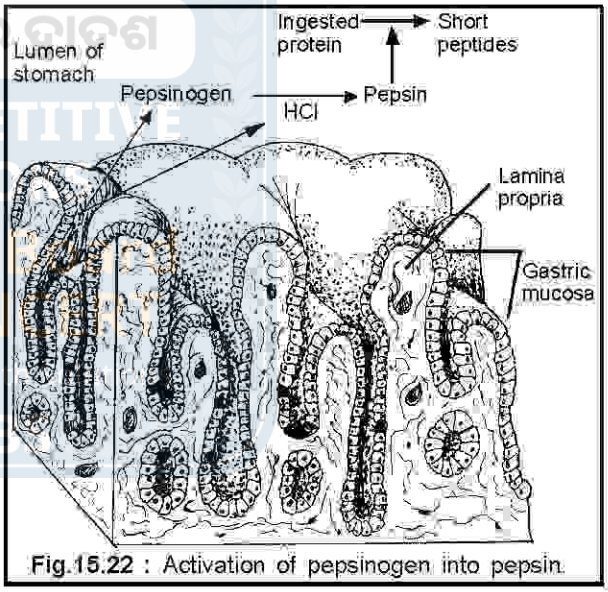


Fig.15.22 : Activation of pepsinogen into pepsin

15.4.3. Digestion in Small Intestine :

In the small intestine, the chyme undergoes further mechanical and chemical processing. The mechanical processing involves the segmented contraction of the wall of the intestine, which mixes the chyme with digestive juice and liquefies it still further (Fig.15.23). This act accelerates the subsequent chemical treatment by the enzymes. Digestion in the small intestine has been described in two parts : (a) digestion in the duodenum; and (b) digestion in the jejunum and ileum (enteric digestion).

(a) Digestion in the Duodenum

In the duodenum, the chyme is mixed with three alkaline juices; bile from the liver, pancreatic juice from the pancreas, and intestinal juice from intestinal glands (crypts of Lieberkuhn); and mucous from the Brunner's glands.

The enteroendocrine cells present in the mucosal layer of the duodenum are stimulated to secrete several gastro-intestinal hormones, when the acidified chyme of the stomach enters into it. Two such hormones bearing significant roles in the release of digestive juices are: **Cholecystokinin-Pancreozymin** (CCK-PZ) and **Secretin**.

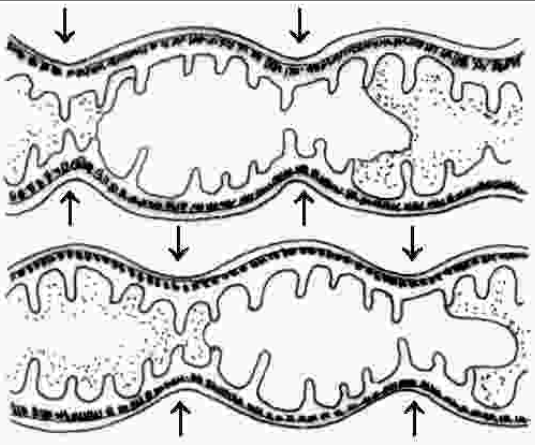


Fig.15.23 : Segmented contraction of the wall of the small intestine.

(i) Cholecystokinin-Pancreozymin (CCK-PZ) : It is a single hormone possessing two activities. Cholecystokinin (CCK) activity stimulates the gall bladder to contract and release bile into the duodenum, while pancreozymin activity stimulates the acinar cells of the pancreas to secrete increasing amounts of pancreatic juice, rich in enzymes.

(ii) Secretin : It stimulates the duct cells of the pancreatic acini to secrete sodium bicarbonate into the pancreatic juice and thus makes the pancreatic juice alkaline.

In addition, **enterogastrone** is presumed to be a separate hormone regulating gastro-intestinal functions. However, it is not a separate entity, but rather a collection of two hormones, secretin and cholecystokinin-pancreozymin, which inhibit gastric function.

(b) Action of Pancreatic Juice

(i) Digestion of Proteins

All proteases (proteolytic enzymes) of the pancreatic and intestinal juices fall under two broad categories : **endopeptidases** and **exopeptidases**. An endopeptidase hydrolyzes internal peptide bonds, while an exopeptidase hydrolyzes peptide bonds from C- or N- ends in a sequence. Accordingly, exopeptidases are **carboxypeptidases** and **aminopeptidases**, respectively.

Trypsin : Inactive proenzyme trypsinogen is activated to trypsin by an enteropeptidase, known as enterokinase, present in the intestinal juice. Trypsin is an **endopeptidase** that converts proteins and polypeptides into peptones (peptides of variable lengths).

Trypsinogen $\xrightarrow{\text{Enterokinase}}$ **Trypsin**

Proteins and Polypeptides $\xrightarrow[(pH = 7.8)]{\text{Trypsin}}$ **Peptones (peptides of variable lengths)**

Chymotrypsin : Once trypsin becomes active, it activates proenzyme **chymotrypsinogen** to **chymotrypsin**. It is also an **endopepdidase** that converts proteins and polypeptides into peptones.

Chymotrypsinogen $\xrightarrow{\text{Trypsin}}$ **Chymotrypsin**

Proteins and Polypeptides $\xrightarrow[(pH = 7.8)]{\text{Chymotrypsin}}$ **Peptones (peptides of variable length)**

Elastase : Proelastase is activated into elastase by trypsin. It is an **endopeptidase**, which acts on elastin and converts it into peptides of variable lengths.

Carboxypetidase : Proenzyme procarboxypeptidase is activated to carboxypeptidase by trypsin. It is an **exopeptidase**, which converts peptides into dipeptides and amino acids by removing amino acids from the C-terminus of peptides.

Procarboxypeptidase $\xrightarrow{\text{Trypsin}}$ **Carboxypeptidase**

Peptides $\xrightarrow[(pH = 7.8)]{\text{Carboxypeptidase}}$ **Dipeptides + amino acids**

Pancreatic nucleases : Pancreatic juice also contains nucleases (**ribonuclease** and **deoxyribonuclease**), which hydrolyze RNA and DNA, into their respective **constituent nucleotides**.

(ii) Digestion of carbohydrates

Pancreatic juice contains a carbohydrate digesting enzyme, called **pancreatic α-amylase**. This enzyme hydrolyzes starch, in a similar manner to salivary α-amylase. Starch is converted to a mixture of disaccharides and trisaccharides and limit dextrin in an alkaline medium.

Starch $\xrightarrow[(pH = 7.8)]{\text{Pancreatic } \alpha\text{- amylase}}$ **Maltose + Maltotriose + Limit Dextrin**

(iii) Digestion of Fat

Pancreatic juice contains pancreatic lipase (steapsin), which is the principal fat digesting enzyme. It digests about two third of the fat in stages.

Triglycerides (Fats) $\xrightarrow{\text{Bile salts}}$ **Emulsified Triglycerides**

Emulsified Triglycerides $\xrightarrow[(pH - 7.8)]{\text{Lipase}}$ **Fatty acids + Glycerol**

(b) Digestion in the Ileum

The ileum has simple tubular glands invaginated into the lamina propria of the mucosa. These glands are known as **crypts of Lieberkuhn**, which secrete **intestinal juice** or **succus entericus.** It contains: carbohydrate digesting enzymes; two proteases; an activator, enterokinase; intestinal lipase; and three nucleolytic enzymes, such as nucleotidase, nucleosidase and phosphatase.

(i) Digestion of carbohydrates

The intestinal juice contains a numbers of oligosaccharidases which hydrolyze oligosaccharides into their constituent monosaccharides.

Maltose $\xrightarrow{\text{Maltase}}$ **Glucose + Glucose**

Isomaltose $\xrightarrow{\text{Isomaltase}}$ **Glucose + Glucose**

Sucrose $\xrightarrow{\text{Sucrase (Invertase)}}$ **Glucose + Fructose**

Lactose $\xrightarrow{\text{Lactase}}$ **Glucose + Galactose**

Limit dextrin $\xrightarrow{\text{Limit dextrinase}}$ **Glucose**

Trehalose $\xrightarrow{\text{Trehalase}}$ **Glucose**

A major part of the hydrolysis occurs in the lumen of the small intestine. However, a small part of it occurs in the outer part of the brush border of the microvilli membrane.

Deficiency of one or more brush border enzymes may cause diarrhoea and flatulence following the ingestion of sugar. Absence of lactase from the intestinal juice leads to a serious disorder, called **lactose intolerance**. In such a case, the lactose can not be digested, which accumulates in the intestine and causes vomiting.

(ii) Digestion of proteins

Non digestive protease

(i) Enteropeptidase (Enterokinase) : It is an activating enzyme. It activates the proenzyme, trypsinogen into trypsin.

Digestive proteases

(i) Aminopeptidase (Erepsin) : It hydrolyzes the terminal peptide bonds at the N-terminus of the peptide to release amino acids one by one.

Peptides $\xrightarrow{\text{Aminopeptidase}}$ **Amino acids**

(i) Dipeptidase : It hydrolyzes the dipeptides into constituent amino acids.

Dipeptides $\xrightarrow{\text{Dipeptidase}}$ **Amino acids**

(iii) Digestion of fat

The intestinal lipase hydrolyzes some triglycerides, diglycerides and monoglycerides to fatty acids and glycerol.

(iv) Digestion of nucleic acids

The nucleic acids are digested in the ileum by the action of three nucleolytic enzymes.

Nucleases : These hydrolyze nucleic acids into nucleotides. These are of two types: deoxyribonuclease and ribonuclease. Deoxyribonuclease acts on DNA, while ribonuclease on RNA.

Phosphatase : It hydrolyzes a nucleotide into a nucleoside and phosporic acid.

Nucleosidase : It hydrolyzes nucleosides into free nitrogenous bases and pentose sugar.

The fully digested and alkaline food present in the small intestine is called **chyle**. The chyle is then passed into the large intestine by peristalsis.

15.4.4. Digestion in the large intestine :

There is practically no digestion in the large intestine or colon. The food entering into the colon is almost completely digested and absorbed in the small intestine with the exception of cellulose present in the vegetable matter. **Bacterial fermentation** in the large intestine breaks down cellulose tissue into vegetable cells which are then digested by enteric enzymes and partly absorbed. The microbial flora or bacteria of the colon convert (i) carbohydrate residue into organic acid and methane; (ii) lipids into fatty acids and glycerol and (iii) proteins into amino acids by decarboxylation. Some vitamins like vitamin K and vitamin B-complex are also produced in the large intestine.

15.5. ABSORPTION OF FOOD :

Absorption is the passage of end products of digestion, such as monosaccharides; amino acids; fatty acids and glycerol as well as minerals; vitamins; and water from the digestive tract into the blood and lymph through the intestinal epithelium.

No absorption takes place in the buccal cavity. In the stomach, the absorption is limited. Some mineral salts, alcohol, glucose, water and some easily diffusible drugs are absorbed directly at a very low rate. A comparatively smaller amount of these substances is absorbed in the duodenum. Practically all absorption takes place through the ileum, where the absorptive surface area is highly increased owing to the presence of around 5,000,000 villi. The villi are small (0.5 mm long) finger-like projections of the mucosal epithelium (Fig.15.24). Each villus contains capillary plexus and lymph vessels called **lacteals**. The surface area of the epithelial cells of the villus is increased due to the presence of many ultramicroscopic evaginations or cylindrical projections of the plasma membrane, called **microvilli.** The microvilli form a **brush border**.

15.5.1. Absorption of monosacharides :

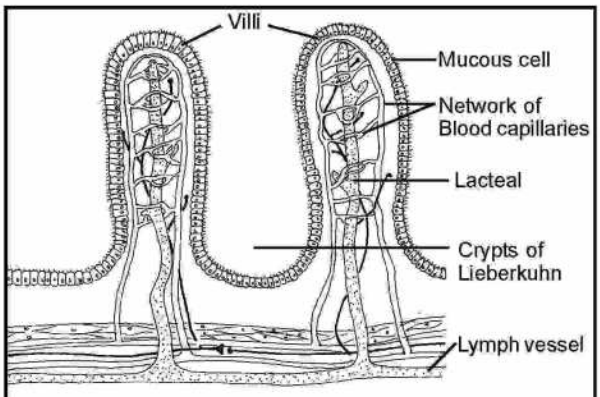


Fig.15.24 : Fine structure of two microvilli in the mucosa of ileum.

The end products of carbohydrate digestion, monosaccharides, such as glucose, fructose, galactose, etc. are rapidly absorbed into the blood stream across the wall of the small intestine. This absorption or transport is dependent on the concentration of Na^+ in the intestinal lumen. A high Na^+ concentration in the lumen facilitates the transport of glucose into the epithelial cells. Both glucose and Na^+ are transported into the cells by a **membrane transporter** (a transporter is a membrane integral protein), called **cotransporter** or more specifically, **sodium dependent glucose transporter** (**SGLT**). Following the transport into the epithelial cells, Na^+ is released back into the intestinal lumen, while glucose is released into the cytosol. Thus, glucose absorption is a **secondary active transport**. The energy for glucose transport is provided by the active transport of Na^+ out of the cell. The monosaccharides absorbed into the cytosol and then into the interstitium, enter into the hepatic portal circulation.

15.5.2. Absorption of amino acids :

Amino acids are directly absorbed into the intestinal epithelial cells and then released into the interstitium by simple diffusion. Larger peptides are never absorbed. However, di- and tripeptides are absorbed into the epithelial cells by **cotransport**. This transport is dependent on H^+, rather than Na^+. Like the monosaccharides, the amino acids enter into the hepatic portal circulation.

15.5.3. Absorption of fatty acids and glycerol :

Fatty acids combine with the bile salts forming small molecular aggregates, called **micelles**. These are absorbed into the cells, through the mediation of carriers. Short chain fatty acids (10-12 carbon atoms) pass directly into **lymph vessels** (**lacteals**), while those with more carbon atoms are re-esterified in the mucosal cells. Absorbed cholesterol is also esterified into cholestryl esters. All these esterified products are coated with proteins forming **chylomicrons**. These are then absorbed directly into the lymph vessels. The chylomicrons are absorbed into the hepatic portal circulation through the lacteal.

15.5.4. Absorption of water and electrolytes :

A healthy adult human drinks about 2000 ml of water and 7000 ml of secretions are poured into the alimentary canal in 24 hrs; 98% of this sum total fluid is reabsorbed with a loss of only 200 ml in the stool. As discussed above Na^+ absorption is linked to the presence

of glucose in the intestine. It is absorbed by a secondary active transport mechanism. This forms the basis for the oral rehydration of NaCl with glucose in diarrhoea patients. $2Cl^-$ are cotransported with one each of Na^+ and K^+. Na^+ and K^+ are driven into the cells by active transport mediated by $Na^+ - K^+$ ATPase of the membrane.

15.5.5. Absorption of vitamins :

Absorption of water soluble vitamins is rapid, while that of the fat soluble ones is depressed, if the pancreatic juice and bile secretions are inadequate. Most of the vitamins are absorbed in the jejunum, while B_{12} is absorbed in the ileum.

15.5.6. Absorption of minerals :

These are absorbed mostly in the small intestine. 30-80% of calcium is absorbed in the upper small intestine by active transport. Active transport of calcium is induced by a metabolite of vitamin D that is produced in the kidneys. Iron is another important mineral absorbed in the small intestine. The amount of iron absorbed, replenishes the amount lost due to various reasons. For the active absorption of sodium in intestine a sodium pump mechanism works in the cell membrane.

15.6. ASSIMILATION :

The required amount of absorbed food materials is transported from the blood to the cells and tissues of different parts of the body. This is known as assimilation. A part of the food materials undergoes biological oxidation to meet the energy requirement during work. Another part is used for building the extra organic matter during growth and repair of the body. Any excess of the food is stored as reserve food to be used during exigency.

15.6.1. Fate of Amino Acid :

Amino acids are not stored in the body. They are either metabolized through **transamination** and **oxidative deamination** or used in protein synthesis. Proteins are used for growth and repair of tissues or act as enzymes and hormones or act as antibodies, the defense molecules of the body. Some amino acids are converted to glucose by **gluconeogenesis** during exigency.

15.6.2. Fate of Monosaccharides :

Monosaccharides constitute a ready source of energy for the cells and tissues. Any excess is stored in the liver and muscle cells as **glycogen**. The synthesis of glycogen from these substrates in the presence of insulin, is known as **glycogenesis** Major part of the absorbed glucose acts as respiratory fuel and is utilised in the production of energy for various body activities. Some are converted into amino acids and fat.

15.6.3. Fate of lipids :

Lipids are used in the formation of biological membranes and insulation sheaths of **medullated** or **myelinated nerve fibers**. Excess fat is stored in the **adipose tissue**. Stored fat also serve as respiratory fuel for the cell.

15.6.4. Calorific value of food :

The amount of energy released from the food substrates in cellular oxidation is termed as their calorific value, which is expressed in calories (cal) or kilocalories (kcal). The value for one gram of carbohydrate is 4.1 kcal, for one gram of protein is 4.1 kcal and for one gram of lipid is 9.3 kcal. It is essential to know the calorific value of the food stuffs we consume to work out the ration, as the energy expenditures of persons of different ages, sexes and occupations vary. For a man of 80 Kg. body weight, maximum calorie intake is : 80 × 24 = 1920 cal, and the prescribed reduction is : 1920 – 500 = 1420 cal. However, daily intake should never go below 1000 cal. We get about 50% of our energy from carbodydrates, 15% from proteins and 35% from fats.

15.7. EGESTION :

The elimination of undigested residual food is called **egestion** or **defaecation**. The waste material discharged from the alimentary canal is called faeces or faecal matter. Following the absorption of essential food materials; water; minerals; and vitamins, the residue turns into a yellow coloured semisolid, called stool. The yellow colour of the stool is due to the excretion of bile pigments, especially billirubin into it. Methanogenic bacteria act upon the residue to generate methane that gives the stool a characteristic foul smell. It is finally eliminated through the anal aperture or anus. Summary of the physiology of digestion in human is depicted in Fig.15.25 and Table-15.1.

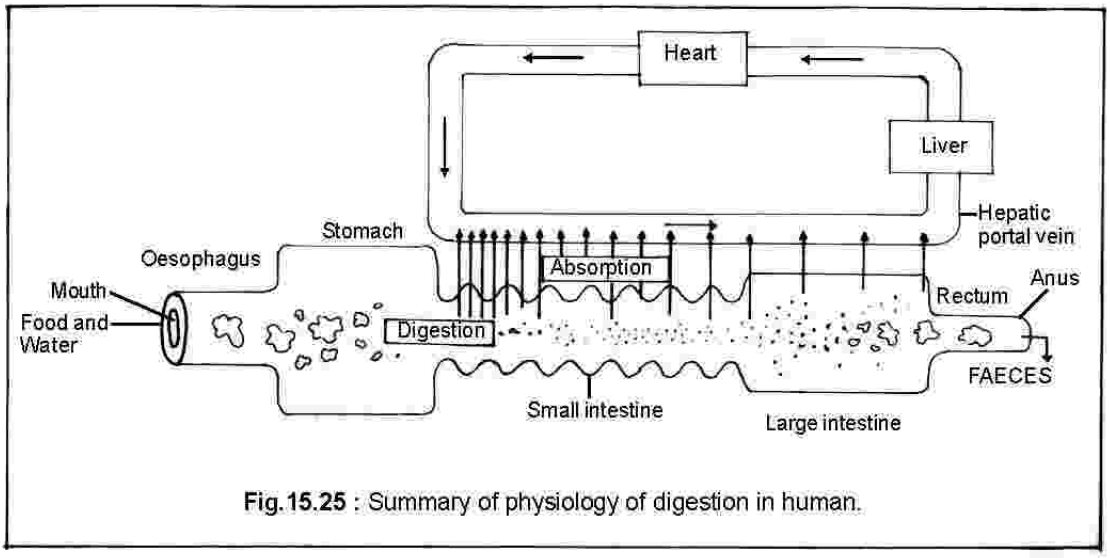


Fig.15.25 : Summary of physiology of digestion in human.

TABLE-15.1 : SUMMARY OF DIGESTIVE ENZYMES AND THEIR ACTIONS

Enzymes	Source	Substrate	Products
α-Amylase	Saliva and Pancreatic juice	Starch, glycogen	Disacharides, Trisaccharides and α-Dextrin
Pepsinogen	Gastric juice	Pepsinogen (inactive)	Pepsin (activated by HCl)
Pepsin	Gastric juice	Proteins	Peptones (Short chain polypeptides)
Rennin	Gastric juice	Milk protein (Casein)	Paracasein and Calcium para caseinate
Trypsinogen	Pancreatic juice	Trypsinogen (inactive)	Trypsin (activated by enterokinase)
Trypsin	Pancreatic juice	Proteins	Peptones (short chain polypeptides
Chymotrypsinogen	Pancreatic juice	Chymotrypsinogen (inactive)	Chymotrypsin (activated by trypsin)
Chymotrypsin	Pancreatic juice	Proteins	Polypeptides of variable lengths
Procarboxy-peptidase	Pancreatic juice	Procarboxypeptidase (inactive)	Carboxypeptidase (activated by trypsin)
Carboxypeptidase	Pancreatic juice	Polypeptides	Dipeptides and amino acids
Lipase	Pancreatic juice	Triglycerides (Neutral fat)	Fattyacids and glycerol
Nuclease	Pancreatic juice	Nucleic acids	Nucleotides
Enterokinase	Intestinal juice	Trypsinosen (Inactive)	Trypsin (active)
Aminopeptidase	Intestinal juice	Polypeptides	Amino acids
Dipeptidase	Intestinal juice	Dipeptides	Aminoacids
Maltase, Sucrase and Lactase	Intestinal juice	Maltose, sucrose and lactose, respectively	Monosacchrides
Limit dextrinase	Intestinal juice	Limit dextrin	Glucose

TABLE-15.2 : SUMMARY OF FUNCTIONS OF GASTRO-INTESTINAL HORMONES

Sl. No.	Hormone	Secreted from	Stimulated by	Inhibited by	Functions
1.	Gastrin	Gastric mucosa of the pyloric antrum	Presence of amino acids and peptides in the stomach	HCl in the stomach	Stimulates HCl and pepsinogen secretion from the oxyntic (parietal) and chief (peptic) cells, respectively.
2.	Cholecystokinin-Pancreozymin (CCK-PZ)	Mucosa of the duodenum	Presence of acidic chyme containing, amino acids and fatty acids in the duodenum	Empty duodenum	1.CCK stimulates the contraction of the gall bladder to release bile into the duodenum. 2. PZ stimulates the pancreas to release pancreatic juice containing enzymes.
3.	Secretin	Mucosa of the duodenum	Acidic chyme in the duodenum	Empty duodenum	Stimulates the pancreatic acinar duct cells to secrete bicarbonates into the pancreatic juice

15.8. NUTRITIONAL AND DIGESTIVE DISORDERS :

Every organism requires an adequate quantity of food (nutrients) in proper proportion for meeting the energy requirement and growth and development requirements.

15.8.1. Malnutrition :

Malnutrition is the intake of less than normal quantity of food, required by body. It is primarily due to inadequate intake of food both in quantity and quality. The nutritional deficiency, particularly of proteins of less calorific value for a long period of time causes many deficiency diseases. It is also known as **Protein energy malnutrion (PEM)**. It mostly affects infants and children of the developing countries. Two commonly occuring diseases due to PEM are (i) Kwashiorkor and (ii) Marasmus.

15.8.2. Kwashiorkor :

This disease is caused in children in the age group of 6 months to 3 years. It is caused by severe protein deficiency.

(a) Symptoms

1. Stunted growth and bulging of the belly and eyes.
2. Loss of appetite and anaemia.
3. Decreased immunity.
4. Darkening of skin and hair.
5. Recurrence of diarrhoea.
6. Atrophy of muscle and oedema in the hands, feet and face.

(b) Control

The disease is controlled by providing high quality protein in the diet.

15.8.3. Marasmus disease :

It is a type of disease, in which there is deficieny of proteins and calories. It is more common in infants under one year of age.

(a) Causes

It is caused by prolonged deficiency of proteins and or carbohydrates.

(b) Symptoms

1. Dry and wrinkled skin.
2. Stunted growth of the body with extreme thinning of the limbs.
3. Ribs protrude as the fat layer of the skin disappears.
4. Retarted Physical and mental growth.
5. Recurrence of diarrhoea.

(c) Control

It is controlled when the affected infant is given adequate proteins, fats and carbohydrates in the diet.

15.8.4. Indigestion (Dyspepsia) :

This is a condition in which food is not properly digested. The person gets a feeling of fullness during meal, thus not being able to finish eating. A burning sensation occurs in the stomach and osesophagus due to excessive gas formation. The causes of indigestion include insufficient enzyme secretion, food poisoning, over eating, eating of spicy or fatty food, anxiety cancer, ulcer, etc.

15.8.5. Constipation :

In this disorder, the faeces in the rectum are not removed properly as bowel movements become difficult, irregular or happen less than normal. This results in hardening of the stool. The abdomen swells acompanied by abdominal pain. Constipation occurs due to frequent changes in the food habit, least consumption of fiber-rich food and drinking less water than required.

15.8.6. Vomiting

It is the forcible emptying of the stomach contents through the mouth. This takes place due to violent contraction of the stomach. The causes of vomiting are varied and include food allergies; infections of the stomach and food poisoning. A feeling of nausea occurs before vomiting. The vomiting centre present in the medulla of the brain regulates vomiting through neural communication.

15.8.7. Jaundice (Icterus)

Jaundice or Icterus is a yellowish pigmentation of the skin, conjunctiva (white of the eyeball) and other mucous membrance caused by high blood bilirubin level. These symptoms are expressed in lever diseases, liver cancer and obstruction of the bile duct by gall bladder stone formation. Excess bilirubin is excreted in the urine imparting it an intense yellow colour. In hepatitis (inflammation of the lever) the symptoms of jaundice are often expressed. Jaundice occurs by drinking contaminated water. Medical treatment ranges from supportive care and rest to trnsfusion of fluid in case of dehydration and oral administration of liver rejuvenating drugs, antibiotics and antiviral drugs as per the advice of a registered medical practitioner.

15.8.8. Diarrhoea (Loose motion or Looseness of bowel)

In this disorder the faecal matter is discharged from the bowels frequently in a liquid form. The most common cause of diorrhoea is an infection of the intestine by a virus or bacterium or parasite. This may lead to dehydration due to an excess loss of fluid, decreased urination, loos of skin colour, increased heart rate and reduced responsiveness. Oral Rehydration Solution (ORS) and intravenous transfusion of rehydration solution treatments are essential to restore the fluid and salt loss from the body fluid. Diarrhoea can be prevented by improved sanitation, clean drinking water and hand washing with soap and administration of specific antibiotic drugs.

SAMPLE QUESTIONS

GROUP - A
(Objective-type Questions)

1. Choose the correct answer

(i) Glucose is stored as glycogen in :
(a) Pancreas (b) Liver
(c) Stomach (d) Kidney

(ii) Ascorbic acid is also known as :
(a) Vitamin B (b) Vitamin C
(c) Vitamin E (d) Vitamin D

(iii) Which gland functions as both exocrine and endocrine glands?
(a) Salivary gland (b) Gastric gland
(c) Pancreas (d) Liver

(iv) Pepsinogen is activated by :
(a) Trypsin (b) Chymotrypsin
(c) Hydrochloric acid (d) Pepsin

(v) Trypsin converts :
(a) Fats into fatty acids (c) Proteins into peptones
(b) Polysaccharides into maltose (d) Peptones into amino acids

(vi) The end products of fat digestion are fatty acids and
(a) Glycerol (b) Cholesterol
(c) Phospholipid (d) Glycolipid

(vii) The posterior free part of the soft palate is known as :
(a) Glottis (b) Gullet
(c) Epiglottis (d) Uvula

(viii) The number of teeth in the deciduous set of human being is :
(a) 32 (b) 20
(c) 18 (d) 24

(ix) The opening of the middle ear into the pharynx is known as
(a) Eustachian opening (c) External nostril
(b) Internal nostril (d) Glottis

(x) The gastro-intestinal hormone that stimulates the contraction of the gall bladder is known as :

(a) Gastrin (b) Cholecystokinin

(c) Secretin (d) Molitin

(xi) The wall of the stomach of human is histologically unique in possessing :

(a) Submucosa (b) Circular muscle

(c) Longitudinal muscle (d) Oblique muscle

(xii) Gastrin is secreted from the mucosa of :

(a) Antrum (b) Fundus

(c) Body (d) Pylorus

(xiii) Brunner's glands are present in the mucosa of :

(a) Ileum (b) Jejunum

(c) Duodenum (d) Colon

(xiv) Secretin stimulates the release of :

(a) Bicarbonate ions into the pancreatic juice

(b) Water into the pancreatic juice

(c) Enzymes into the pancreatic juice

(d) Ca^{2+} into the pancreatic juice

(xv) Kwashiorkor, a nutritional disorder, caused due to the deficiency of :

(a) Carbohydrates (b) Lipids

(c) Vitamins (d) Proteins

(xvi) In a polypeptide, the amino acids are joined together by :

(a) Glycosidic bonds (c) Phosphodiester bonds

(b) Peptide bonds (d) Hydrogen bonds

2. Answer each of the following in one or more words, wherever necessary.

(i) Name the mass of vascular connective tissue in a tooth.

(ii) Name the water soluble vitamins.

(iii) Enlist the fat soluble vitamins.

(iv) Name three divisions of the small intestine.

(v) Name the vestigial organ in the alimentary canal of human.

(vi) Which gland is the largest gland of the body ?

(vii) Name the term used for the presence of different types of teeth.

(viii) Name two bile pigments.

(ix) How many liver lobes are there in human ?

(x) Name the ampulla formed by the joining of the common bile duct and pancreatic duct before opening into the duodenum.

(xi) Name the phagocytic cell in the liver.

(xii) What is the non-digestive enzyme released in the small intestine?

(xiii) Name the enzyme that digests fat.

(xiv) Name the structure that is formed by the grouping of hepatic artery, hepatic portal vein and bile duct in the liver.

(xv) Give an alternate name for Ptyalin.

(xvi) Name the end product of protein digestion.

(xvii) Name the intestinal glands, which secrete succus entericus.

3. Fill in the blanks with appropriate words.

(i) The fibrous connective tissue that cements the root of the tooth to the socket is known as _____.

(ii) The last molar teeth in human are known as _____ teeth.

(iii) _____ is the hardest substance in the human body.

(iv) The longitudinal folds of the oesophageal mucosa are known as _____.

(v) The passage of the bolus through the lumen of oesophagus in spurts is known as _____.

(vi) The opening of the common bile duct and pancreatic duct into the duodenum is guarded by a sphincter, called _____.

(vii) The gastro-intestinal hormone that stimulates the secretion of enzymes into the pancreatic juice is known as _____.

(viii) The connective tissue sheath, surrounding a liver lobule is known as _____.

(ix) Bile facilitates the digestion of fat by dividing large fat droplets into a number of smaller droplets. This function of bile is known as _____.

(x) Intestinal juice is alternately known as _____.

(xi) There are _____ pairs of salivary glands in human.

(xii) _____ is the substrate for ptyalin.

(xiii) The yellow colour of the stool is due to the presence of a pigment _____.

(xiv) Limit dextrinase or α-Dextrinase is alternately known as _____.

(xv) Synthesis of glucose from non-carbohydrate sources is known as _____.

(xvi) Rennin acts on the milk protein _____ and changes it into _____ in the presence of Ca^{2+}.

(xvii) Bile is secreted by _____ and stored in _____.

(xviii) The coagulation factors, prothrombin and fibrinogen are synthesized in _____.

4. Match the words of Group A with those of B to make meaningful pairs.

Group A	Group B
1. Chief cell	(a) Small intestine
2. Meissner's plexus	(b) Insulin
3. Trypsinogen	(c) Bilirubin
4. Indigesation	(d) Food poisoning
5. Islets of Langerhans	(e) Pepsinogen
6. Marasmus	(f) HCl
7. Jaundice	(g) Lacteal
8. Chyle	(h) Pancreatic juice
9. Fatty acid	(i) Sub-mucosa
10. Oxyntic cell	(j) Nutritional deficiency

GROUP - B
(Short Answer-type Questions)

I. Answer the following (Answer each within 50 words)

(i) What do you mean by intracellular digestion ?

(ii) Explain the gustatory function of the tongue.

(iii) Write the dental formula of the permanent set of man.

(iv) Write the sub-divisions of the pharynx and the openings discharging into the pharynx and the openings leading from the pharynx.

(v) Mention about the divisions of the stomach of man.

(vi) What do you mean by peristalsis and antiperistalsis ?

(vii) What are Peyer's patches and what is their function ?

(viii) What are the four histological layers in the alimentary canal of man from outer to inner ?

(ix) How is the secretion of the gastric juice regulated ?

(x) Pancreas is a mixocrine gland – Explain it.

(xi) If enterokinase does not have a hydrolytic function in digestion, what specific role does it play?

(xii) What are the physiological roles of insulin and glucagon ? Where are these hormones secreted from the pancreas ?

(xiii) Distinguish between glycogenesis and glycogenolysis.

(xiv) What do you understand by curdling of milk ?

(xv) What are exo- and endopeptidases ?

(xvi) What do you understand by amino- and carboxypeptidases ?

(xvii) Comment on the absorption of glucose through the intestine following digestion.

(xviii) What are Kwashiorkor and Marasmus related to ?

2. Write short notes on

(a) Dental formula of man
(b) Salivary glands of man
(c) Larynx
(d) Pharynx
(e) Pristalsis
(f) Gastric glands
(g) Peyer's patches
(h) Islet of Langerhans
(i) Gastro-intestinal hormones
(j) Protein deficiency disorders
(k) Absorption of digested food
(l) Indigestion
(m) Constipation
(n) Vomiting
(o) Jaundice
(p) Diarrhoea

3. Distinguish between

(a) Intracellular and Extracellular digestions
(b) Teeth of Deciduous set and Permanent set
(c) Cardiac stomach and Pyloric stomach
(d) Duodenum and Ileum
(e) Exocrine pancreas and Endocrine pancreas
(f) Circumvallate papillae and Filliform papillae
(g) Brunner's gland and Crypt of Lieberkuhn
(h) Secretin and Pancreozymin
(i) Exopeptidase and Endopeptidase
(j) Aminopeptidase and Carboxypeptidase
(k) α-1, 4 glycosidase and α-1, 6 glycosidase

GROUP - C
(Long Answer-type Questions)

1. Describe the physiology of protein digestion in human alimentary canal.
2. Describe the physiology of digestion of different food stuffs in human digestive system.
3. Draw a neat labelled diagram of human alimentary canal (Description is not required).

❑ ❑ ❑

BREATHING AND RESPIRATION

CHAPTER 16

RESPIRATION :

Respiration is a catabolic process of biological oxidation that occurs either in the absence of oxygen (anaerobic respiration) or presence of oxygen (aerobic respiration). Anaerobic respiration occurs in microorganisms such as bacteria and yeast and some animal cells and tissues like erythrocytes and exercising muscle in mammals. In all other organisms aerobic respiration occurs through the process of oxygen uptake and release of carbon dioxide. In respiration potential energy (bond energy) trapped in the covalent bonds of bio-molecules is transformed into another form of energy i.e. chemical energy in the form of adenosine tri-phosphate (ATP).

Aerobic respiration includes external respiration and internal respiration. External respiration refers to the mechanisms by which O_2 is obtained from the environment in exchange with CO_2, which is expelled from the body. This occurs at the respiratory surface area, which may be integument, gill, trachea or lungs. In internal respiration, the respiratory surface is cell or tissue. Therefore, it is also called cellular or tissue respiration. In cells O_2 is utilized for production of energy and CO_2 is released as a by product.

16.1. MODES OF RESPIRATION :

Respiration is of the following types depending on the organs involved in the process.

(a) Cutaneous respiration
(b) Tracheal respiration
(c) Branchial respiration
(d) Pulmonary respiration

16.1.1. Cutaneous respiration :

Many small organisms obtain O_2 by diffusion through their body surfaces. They do not have any specialized respiratory organ nor do they have blood circulation. In animals that have defined circulatory system and readily permeable vascular skins, gaseous exchange occurs through the integument. Thus we find that animals like earthworms, leeches, and newly hatched fish fries are among the many animals that obtain the O_2 they need through their skin. Even larger animals such as many amphibians and fishes may rely on cutaneous respiration during emergencies or use it as a supplement to the gills or lungs. The integumentary contribution to

respiration may be as low as 20 percent in dry skinned toads to 76 percent in the urodele, *Triturus* and 90 percent in giant salamander *Cryptobranchus*. In frogs, cutaneous respiration accounts for about 25% of the body's O_2 requirement in normal life. During hibernation and aestivation the frog goes underground and mostly respires through skin.

The moist or mucous coated skin absorbs gaseous O_2 in exchange of CO_2. The O_2 diffuses through the skin and enters into the capillary plexus under the skin.

6.1.2. Tracheal respiration :

This type of respiration is seen in terrestrial arthropods like insects, centipedes and millipedes, in which the system comprises of a large number of chitinous tubes called **tracheae** (singular; trachea) and their branches, the **tracheoles**. These carry atmospheric air or oxygen to the tissues directly, without the need for transportation by the blood. The air enters into the system through several paired openings called **stigmata** or **spiracles** present on the lateral sides of the body. Direct exchange of the respiratory gases by the tissues occurs much faster and enables insects to maintain a higher metabolic rate particularly during flight.

In a typical example, such as in cockroach [Fig.16.1 (a)], there are ten pairs of these spiracles, of which, two pairs are present in the thorax, first pair in the mesothorax and the second pair in the metathorax and the rest eight pairs, one each in the first eight abdominal segments. The first pair of abdominal spiracles are present dorso-laterally, in the dorsal

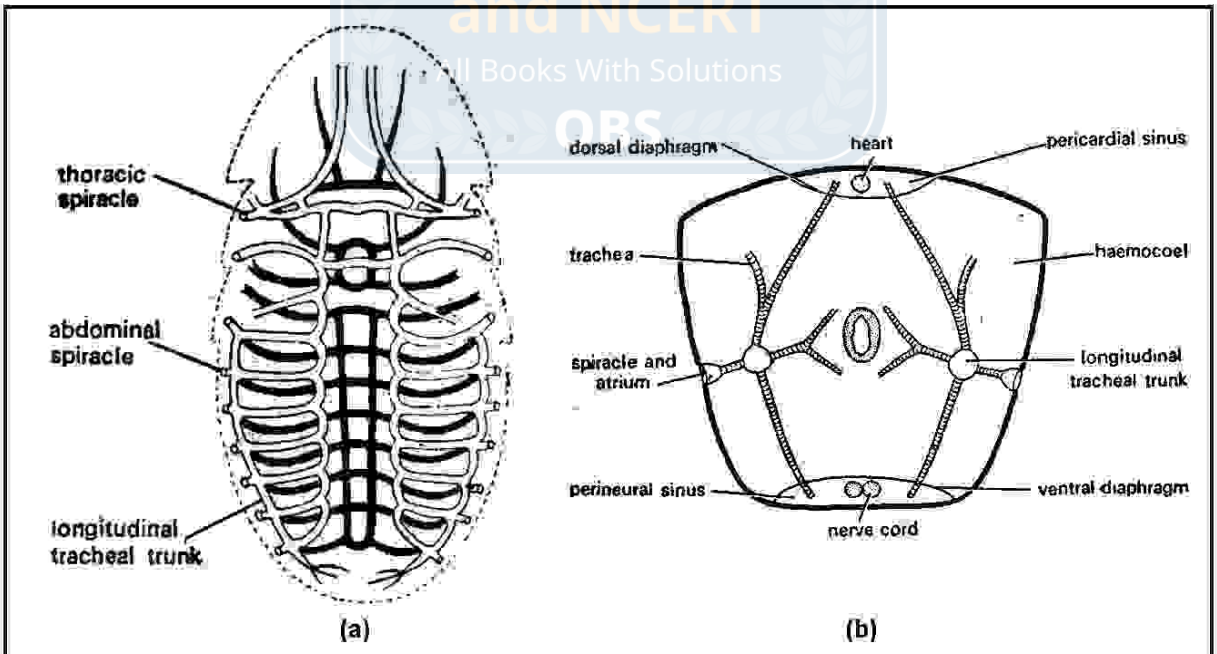


Fig. 16.1 : (a) Arrangement of spiracles (stigmata) and tracheae in cockroach. Dorsal and ventral tracheae are presented in white and black, respectively. (b) . Transverse section through the abdomen showing the branching of the longitudinal trachial trunk

chitinous plate or tergum. The rest are all located on the pleura, the lateral chitinous plates joining the terga and the sterna.

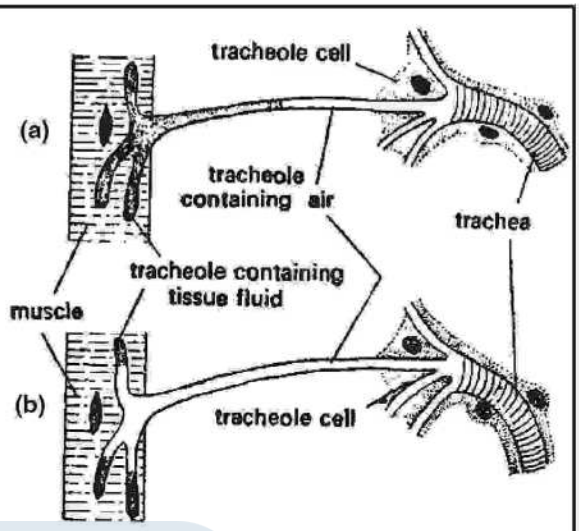


Fig. 16.2 : Tracheal activity in cockroach (a) during rest and (b) during activity.

Each spiracle leads into a short chamber or atrium, from which arises a main tracheal trunk. These tracheal trunks on each side divide and redivide to form fine tracheoles that enter into the tissues [Fig.16.1(b)]. The tracheae or the main trunks are ectodermal tubes supported by rings of chitin which keep the tracheae open even under conditions of reduced air pressure. These rings of chitin perform a function, similar to the cartilaginous rings of the trachea of human. The tracheoles on the other hand are fine tubes that lack chitinous support and are filled with tissue fluid, to which they reach out (Fig.16.2). The quantum of division of these tracheoles inside a tissue, depends on its metabolic requirement. At rest, atmospheric oxygen can diffuse into the tissue and carbon dioxide can diffuse out from the tissue through the tissue fluid that fills the tracheoles.

In the active state, such as during flight, requirement of oxygen increases in the body. Several abdominal muscles that span the dorso-ventral sides of the body, called the tergo-stenal muscles, alternately contract and relax. Their contraction flattens the body and helps to drive out air from the system (**expiration**) and relaxation helps the body to assume its normal shape or volume, when air rushes into the tracheae (**inspiration**).

In the active state, due to high metabolic rate, lactic acid is produced in the muscle tissue, which makes it hyper-osmolar. As a result, the tissue fluid in the tracheoles is withdrawn into the tissue by osmosis. This enables the air to enter further deep into the tissue. The amount of carbon dioxide in the tissues and the tracheal system is sensed by receptors in the body, which control a valve to open and close the spiracles by special muscles.

The thoracic and abdominal spiracles may open and close alternately and the air may take a one-way route, in through the thoracic spiracle and out through the abdominal spiracles.

16.1.3. Branchial Respiration :

Respiration by gills is known as **branchial respiration**. Gills are highly vascularised gaseous exchange membranes. It occurs in sea stars; crustaceans; some molluscs; many

amphibians, especially tadpole larvae and all fishes. Gill surface area must be large enough to provide adequate exchange of gases. For effective gaseous exchange a close contact between the gill and water is required. To understand how it happens let us have a close look at the surface of a gill in a bony fish. Gills are of two types : external and internal. External gills are external vascular membranous extensions having profuse gaseous exchange surface (e.g., tadpole larvae and Axolotl larva of salamander)

Internal gills are enclosed in a **branchical cavity** covered by an **operculum**. Gills of fishes consist of several gill arches on either side. From each gill arch extend two rows of gill filaments. Tips of the filaments of adjacent arches meet forming a sieve like structure through which the water flows.

In bony fishes the filaments are attached to an extremely reduced inter-branchial septum so that their distal ends hang freely in the gill chamber. This type of gill is called **filliform** or

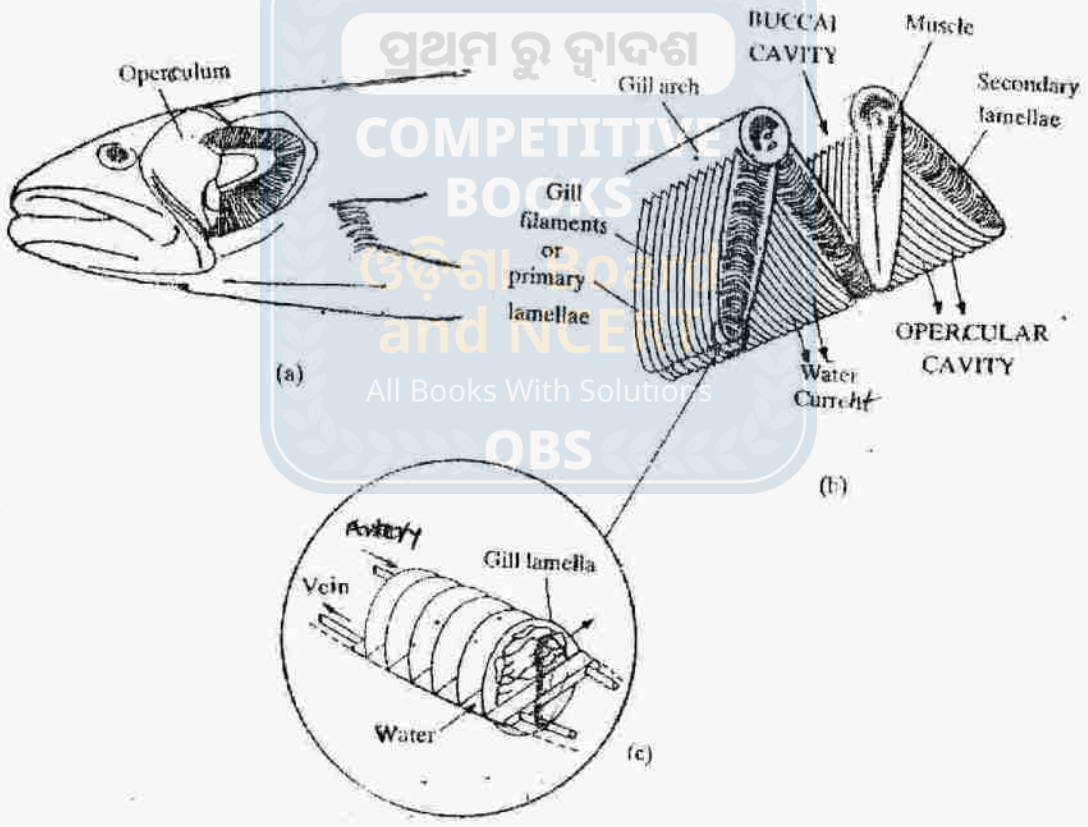


Fig. 16.3 : (a) Position of gill arches beneath the operculum on the left side of fish. The operculum has been lifted to show the arch.

(b) Part of two adjoining gill arches with their filaments. Note that the tips meet forming a sieve like arrangement for flow of water. The water moves through the mouth over the branched gills. Solid arrows show the flow of water.

(c) Part of a single filament showing the flat lamellae; the flow of water is opposite to the direction in which the blood moves.

pectenate. In contrast, the gills of cartilaginous fishes are called **Lamellibranch** in which the gill lamellae are attached throughout their length to an elongated septum.

16.1.4. Pulmonary respiration :

The respiration that takes place through lungs is called **pulmonary respiration**. Lungs are of two types: the **diffusion lungs**, which are very simple, characterized by an exchange with the surrounding environment by diffusion only. This type of lungs are found in small animals such as snails, small scorpions and some spiders. The other type i.e., **ventilation lungs** are typical to vertebrates. The air passes through a tube in to elastic lung where, gaseous exchange takes place.

16.2. RESPIRATORY SYSTEM IN HUMAN :

Human being, a terrestrial animal, respires by lungs, a pair of hollow air-filled bags situated in the thoracic cavity, one on either side of the heart. All vertebrates from amphibians to mammals possess a pair of lungs as respiratory organs for respiration on land. Even the aquatic vertebrates or mammals like whales, which have secondarily taken to water, respire by lungs. Respiration by lungs is **pulmonary respiration**. (L, *pulmone* : lungs)

16.2.1. Respitory Organs (Fig. 16.4) :

The respiratory system comprises of a pair of lungs and the air ways leading to and from the lungs, forming the respiratory tract. The respiratory tract begins with the nose containing a pair of openings or **external nostrils**, through which the air enters and ends with the finest of fine branches of the respiratory tract the **alveolar sacs** or **alveoli** (singular; alveolus) after passing through **larynx**, **trachea**, **bronchi** and **bronchioles**. The air way (passage) divides and redivides 23 times between the trachea and alveoli. Of these, 16 generations constitute the **conducting zone**, while the remaining 7 generations constitute the **transition** and the **respiratory zones (Fig. 16.7)**. The conducting zone spans between the trachea and terminal bronchiole. The respiratory zone spans between the respiratory bronchiole and alveoli. The conducting zone simply conducts the air into the respiratory zone. No diffusion takes place in this zone. The respiratory zone airways including the alveoli are concerned with the diffusion of respiratory gases into and out of the blood.

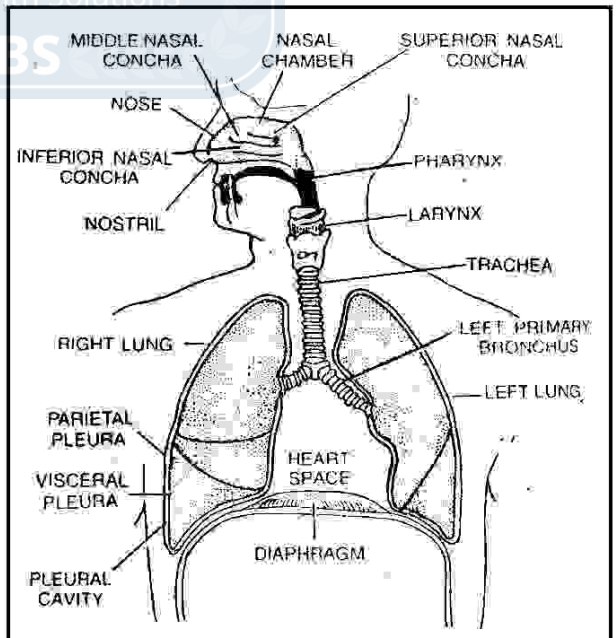


Fig.16.4 : Organization of human respiratory system

16.2.1.1. The Nose : It is a prominent feature of the human face with a small external portion followed by long internal passages. The external portion projects in front as a tringular structure, supported by a frame of bone and cartilage and contains two oval **external nostrils** or **external nares**, directed downwards.

As in the other mammals, in human, the nasal cavity is separated from the oral cavity by a horizontal **palate**. The palate is divided into an **anterior hard palate** and a **posterior soft palate**. The nasal cavity is divided by a perpendicular bony partition, the **nasal septum** into left and right nasal chambers. The nasal septum is formed by parts of nasal, ehtmoid and vomer bones. A small proximal part on each side is lined by hairy skin and constitutes the **vestibule**. A small upper area of the passage on each side forms the olfactory region containing the olfactary bulbs lined by the **schenederian membrane**, responsible for the sense of smell. The rest of the passage forms the respiratory region lined by pseudostratified epithelium containing many mucous secreting goblet cells. In this region, the air is moistened and warmed gently to equalise the temperature of the inspired air with that of the body.

The lateral wall of each nasal cavity contains scroll-like structure with three folds constituting, a **concha** projecting into the nasal cavity. It is covered by mucous membrane and is supplied with blood vessels. A concha has three divisions, designated as inferior, middle and superior from the vestibule upwards. The conchae are supported internally by bones.

The respiratory region of each nasal chamber opens into the **pharynx** by an **internal nare**. Passage of air into the pharyngeal region, however, can occur through the mouth also. This is useful when the nasal passage remains blocked for some reasons. Thus, breathing can be nasal as well as oral.

16.2.1.2. Pharynx : It is a region common to both digestive and respiratory systems. The pharynx is differentiated into an anterior and upper **naso-pharynx**, an anterior and lower **oro-pharynx** and a posterior **laryngo-pharynx**. The internal nostrils and the eustachial tubes from the middle ear cavity open into the nasopharynx. The oral or buccal cavity opens into the oropharynx. The soft palate proejcts into this region in the form of the **uvula** or **velum palatti**, which can be raised up to close the internal nostrils, at the time of swallowing to prevent the entry of food into the nasal chamber. Occasionally however, when the food is swallowed in a hurry, particles may enter through the internal nostrils into the nasal chambers causing a burning sensation.

The pharynx is a passage common to both air and food, where two passages cross each other. The **glottis**, the opening of the nasopharynx into the wind pipe is located on the floor, while the **gullet**, the opening of the oropharynx into the oesophagus is located above. However, to avoid the problem of food particles entering into the trachea, at the time of swallowing, the glottis remains covered by the epiglottis. Epiglottis is an elastic cartilaginous flap that is attached to the wall of the trachea near its origin.

16.2.1.3. Larynx : It is the first enlarged part of the trachea that is called the **voice box** as it contains the **vocal cords**. The vibration of the vocal cords produce the co-ordinated sound, which is interpreted as speech by the brain. Larynx is a triangular box-like structure that is supported by several paired and unpaired cartilages (Fig.16.5). it opens into the pharynx anteriorly by the glottis and posteriorly into the trachea. The cartilages in the larynx include a pair of **thyroid cartilages** present ventrally; a ring like **cricoid cartilage**, present antero dorsally; pair of **arytenoid cartilages**; a pair of elongated or rod shaped **cuneiform cartilages**, attached to the cricoid above; and a pair of **corniculate cartilages** at the top of the arytenoid. The corniculate cartilages are also known as **cartilages of Santorini**. The thyroid cartilages join ventrally forming a protuberance or projection, known as the socalled **Adam's apple**.

16.2.1.4. Vocal cords : There are two pairs of mucous membranous folds that extend into the lumen of the larynx from the sides. These are yellow elastic tissue covered by non-keratinized stratified squamous epithelium. The openings between the vocal cords is actually the glottis or true glottis. The lower pair of cords are known as **true vocal cords**. These vibrate, when the expired air is forced through them. Above the true vocal cords lie a pair of **false vocal cords**, that extend from the thyroid to the arytenoid cartilage. These have no role in sound

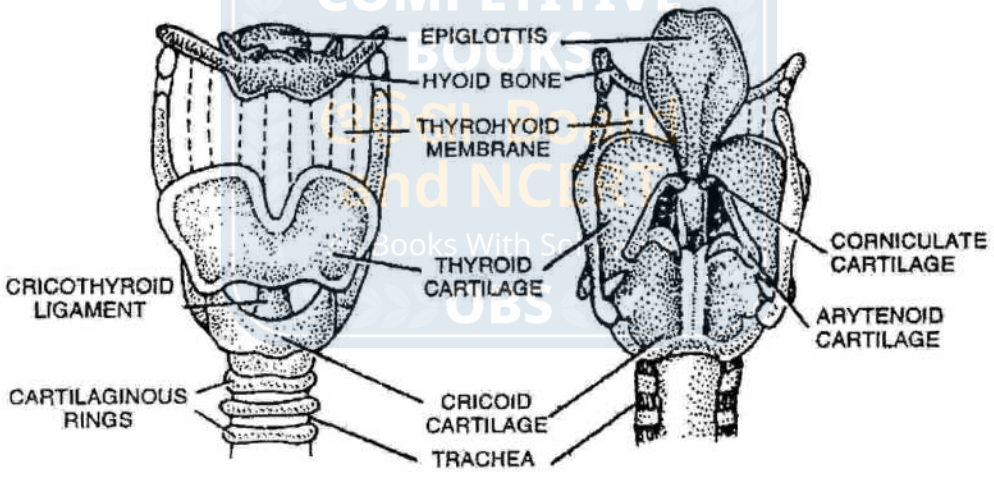


Fig.16.5 : The structure of the human larynx with its cartilaginous support.
(a) ventral view and (b) dorsal view

production. The vocal cords are usually thicker and longer in men than women. Thus, men produce a lower pitch sound than women.

16.2.1.5. Trachea (Fig.16.6) : The larynx passes into the wind pipe or trachea, 10-12 cm long, 2.5 cm wide, that extends through the neck into the thoracic cavity. The trachea is supported by a number of **incomplete C-shaped rings of hyaline cartilages**. The rings are somewhat elastic, held together by muscles in the wall. The tracheal wall around the passage is lined by mucus membrane containing cilia and goblet cells. The cartilaginous rings keep the trachea distended and prevent it from collapsing, when the air pressure in the lung falls. As the

trachea divides into bronchi and the bronchi enter into the lungs, the hyaline cartilage rings are replaced by hyaline cartilage plates. The cartilage plates decrease in size, as the bronchi divide into bronchioles. The plates completely disappear, when the diameter of bronchioles decreases to 1 mm.

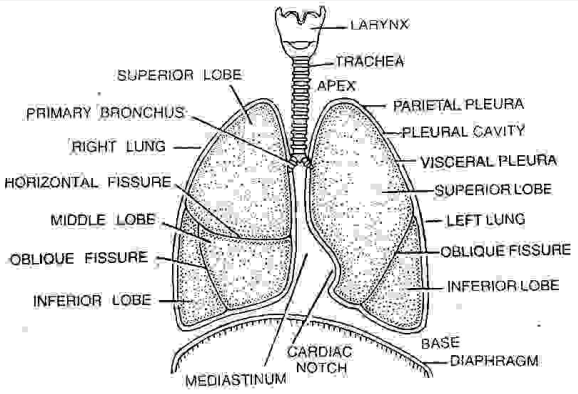


Fig.16.6 : Gross organization of the respiratory tract and lungs in human

16.2.1.6. Lungs, bronchi and bronchioles (Fig.16.6) : At the point of the entry into the thorax, the trachea divides into the first pair of branches, the **primary bronchi**. Each primary bronchus enters into a lung lodged in a **pleural cavity** of its own. There is a pair of lungs in the thoracic cavity, one on either side of the heart. Left lung is smaller, has a **cardiac notch** and has **two lobes**. Right lung is larger and has **three lobes**. Lungs are highly elastic and spongy in texture. In the new born, it is **rosy pink** in colour and **slaty grey** in the adult due to a deposition of carbonacious particles. Each lung is covered by two **pleural membranes**, an outer **perietal pleura** and an inner **visceral pleura.** Between the two pleural membrane, there is an obliterated **pleural cavity** containing a very little **pleural fluid**. The pleural membranes closely cover the lungs and they expand and contract in conformity with the lungs during inspiration and expiration. The two pleural coverings of the lungs are protective. They protect the lungs from friction during inflation and deflation. The inner membrane is in conact with the lungs, while the outer membrane lines the wall of the thorax and diaphragm. The pleural cavity is air tight and its pressure stays at 3-4 mm Hg, lower than that of the lung. This negative pressure is maintained during inspiration and helps the alveoli to inflate the lungs to fill any extra available space provided by the expanding thorax.

Inside the lung, the priamry bronchus divides into secondary and tertiary bronchi that further divide into bronchioles. **Bronchioles** are not supported by cartilaginous rings as seen in the trachea. Each bronchiole further divides, into **terminal bronchioles** and then into **respiratory bronchioles**. Each respiratory bronchiole subdivides into alveolar ducts. Each alveolar duct terminates in a small thin-walled, sac-like **alveolus.** Within the lungs, thus, there may be twenty generations of branchings, each resulting in a narrower, shorter and more numerous tubes. Each lung is estimated to contain 8×10^6 alveolar sacs or **alveoli**. Fig.16.7 depicts the increase in the number of airways following the division and sub-division of the trachea. The consequence is a great increase in the surface area for diffusion of gases.

The air ways beyond the larynx can be divided into two zones : **the conducting zone from the trachea to the terminal bronchioles and the respiratory zone from the respiratory bronchiole to the alveolar ducts**. Each alveolar duct opens into an **alveolus** or **air sac**.

The blood vessels supplying the lungs generally accompany the air ways. The conducting zone only conducts the air. No gaseous exchange takes place here, while gaseous exchange takes place in the respiratory zone. The pulmonary aorta undergoes numerous branchings. The smallest of these branches divides and redivides into a network of capillaries, which supplies the alveoli. The epithelial surfaces of the air ways to the end of the respiratory bronchioles is lined by psuedostratified ciliated epithelium containing goblet cell secreting mucous. Particulate matter such as dust and bacteria present in the inspired air stick to the mucous, which is moved by the cilia towards the pharynx and then it is either swallowed or thrown out. This helps the lungs to remain clear of dust and bacteria that enter through the inspired air. Ciliary activity can be inhibited by noxious agents such as those contained in the cigarette smoke, for several hours which may result in blockage and infection of the lung. Dust cells, present in the alveoli, also take up the dust and thus keep the airways clean.

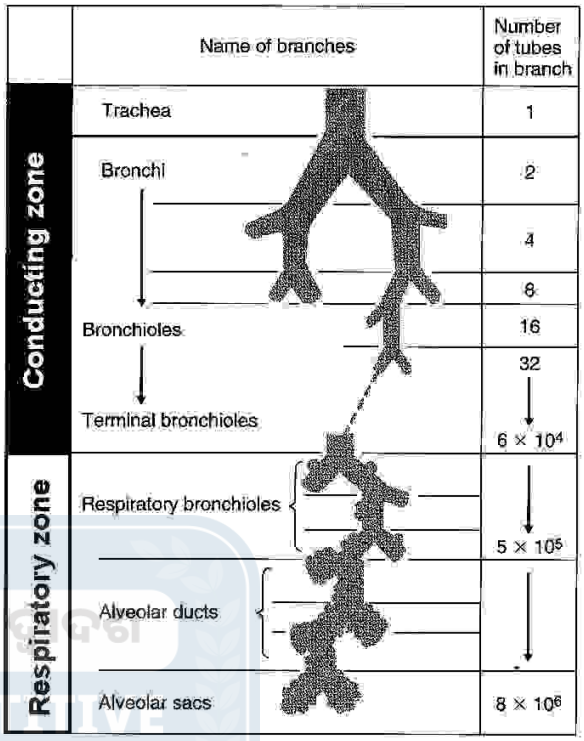


Fig.16.7 : Division and sub-division of the trachea in the lung forming a bronchial tree

16.2.1.7. Alveoli – Sites of gaseous exchange (Fig.16.8) : The alveoli are tiny hollow spaces, whose open ends are continuous with the lumens of the air ways through **alveolar ducts**. Typically, the air in the alveoli, is separated by a single layer of cells. The alveoli are lined by simple squamous epithelium containing **Type I pneumocytes.** In addition to these, the alveolar epitehlium, contains a small number of relatively larger and specialized cells, known as **type II pneumocytes** that produce a detergent like substance called **surfactant**. It lowers the surface tension of the fluid layer, lining the alveoli and thereby reduces the amount of effort needed to breathe in and inflate the lungs. The surfactant also speeds up the transport of oxygen and carbon dioxide between the air and the liquid, lining the alveoli and also helps to kill bacteria that reach the alveoli. It is constantly secreted and reabsorbed in the healthy lung. Without it, the surface tension of the fluid in the alveoli is about ten times higher than normal and the alveoli tend to collapse after each expiration. It also requires a much greater effort to expand them again when breathing in than when surfactant is present. The surfactant is generally a mixture of **dipalmitoylphosphatidylcholine, other lipids** and **proteins**. Surfactant begins to be produced in late fetal life. Therefore, the lungs of premature babies lack sufficient surfactant.

Consequently, the alveoli collapse following expiration. This condition is known as **respiratory distress syndrome**.

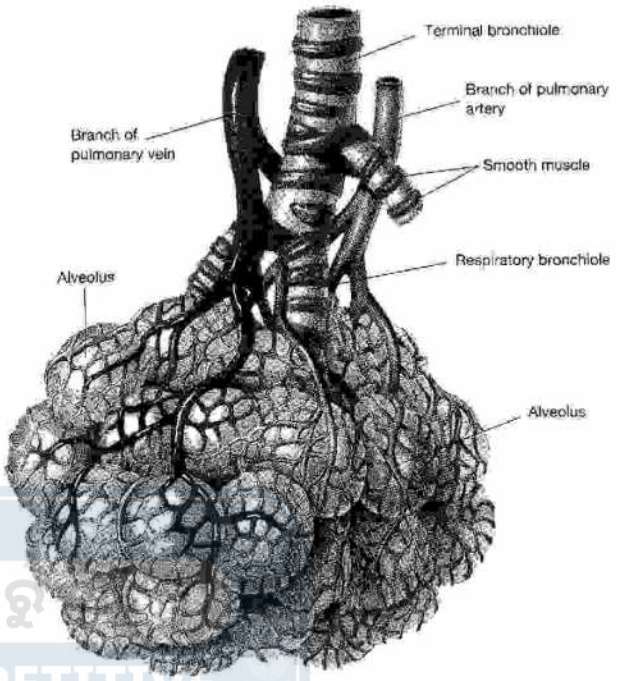


Fig. 16.8 : Alveoli with blood capillaries formed by pulmonary artery and vein.

The alveolar surface in contact with the air is kept moist by mucous. In some alveolar walls, there are pores that permit the flow of air between alveoli which is useful when the air way is blocked by diseases. The alveolar wall contains capillaries, the endothelial linings, which are separated from the alveolar epithelium by a basement membrane and a very narrow interstitial space containing interstitial fluid and a loose network of connective tissue. In places, the interstitial space may be absent altogether and the epithelium of the alveoli and the endothelium of the capillaries in the wall may fuse. Thus, the blood within an alveolar capillary is separated from the air by only about 0.2 μ (micron) compared to the 7.0 μ diameter of an erythrocyte. The total surface area of the alveoli is 80 times greater than the external body surface. The alveolar lumen contains **macrophages** or **phagocytic cells**, known as **dust cells**. These cells engulf dust particles that enter into the alveoli with the inspired air.

16.2.1.8. Rib cage and diaphragm : The lungs are contained in the thorax, the body division between the neck and the abdomen. The thorax is a closed compartment bound at the neck by muscle and connective tissue and completely separated off from the abdomen by a large dome-shaped sheet of skeletal muscle, the **diaphragm**. The wall of the thorax is formed at the back by the vertebral column and the ribs on the sides, which are movably attached to the vertebrae behind and the stenum or breast bone in front. There are 12 pairs of ribs which encircle the thoracic cavity from sides. Ribs are of 3 types:- (Fig. 16.9)

I. **True ribes** - 1st - 7th pairs. They are attached both to the thoracic vertebrae and sternum.

II. **False ribs** - 8th - 10th pairs. They are attached to costal cartilage of 7th rib.

III. **Floating ribs** - 11th and 12th pairs. They are attached to the vertebrae but do not reach the sternum. The muscles that connect the adjacent ribs are called **intercostal muscles**. Two sets of intercostal muscles connect the ribs : **external** and **internal (Fig. 16.10). The**

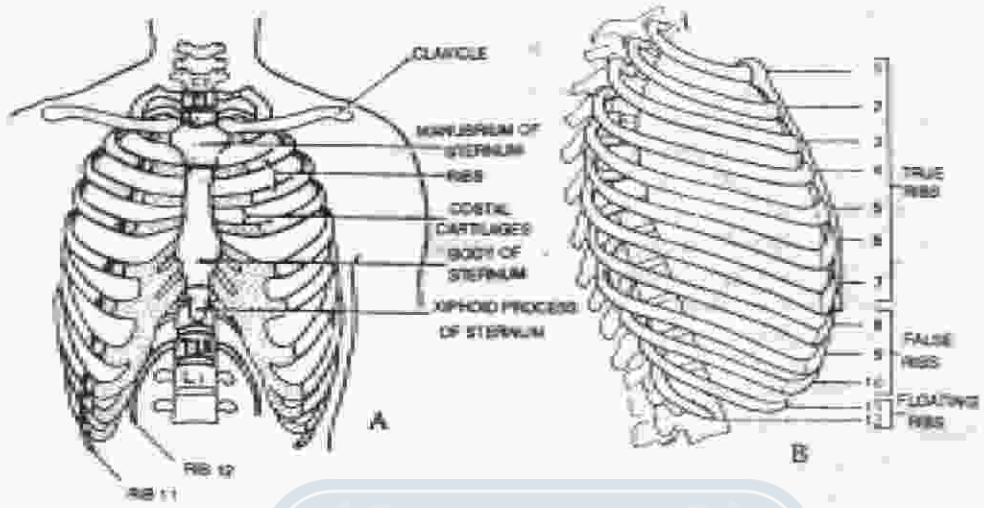


Fig. 16.9 : Thoracic cage. A. Anterior view, B. Lateral view

external intercostal muscles are the inspiratory muscles, which run obliquely downward and forward or inward from rib to rib. The **internal intercostal muscles are the expiratory muscles**, which run obliquely downward and backward or outward. These muscles are used during quiet respiration, while some accessory muscles, like **scalenes** and **sterno-cleidomastoid** are used during forced respiration (Fig.16.10).

16.3. MECHANISM OF BREATHING OR VENTILATION :

Each respiratory cycle comprises of two opposite physiological processes involving the lungs : **inspiration**, by which air is taken into the lungs and **expiration**, by which the used air is expelled out. Inspiration and expiration together constitute **breathing**, which is also known as **ventilation or external respiration**. Two types of breathings have been recognized : normal or quiet and forced (Table 16.1). The one described in the text below is normal or quiet breathing.

16.3.1. Inspiration :

Inspiration is an active process which is brought about by the contraction of the **external intercostal muscle** and the relaxation of the **internal intercostal muscle.** This pulls the rib cage forward and outward. Concurrently, the muscles of the **diaphragm** contract, which flatten it out. By this, the volume of the thoracic cavity is increased. The air pressure in the thorax and hence, in the lungs is reduced to less than the atmospheric pressure. Air, therefore, rushes into the lungs through the respiratory tract, inflating the alveoli untill the air pressure in the lungs is equal to that of the atmosphere. So our breathing is called **negative pressure breating**.

16.3.2. Expiration :

Expiration is a passive process under resting conditions. The events are a reversal of those of the inspiration. The **external intercostal muscles** relax and the **internal intercostal**

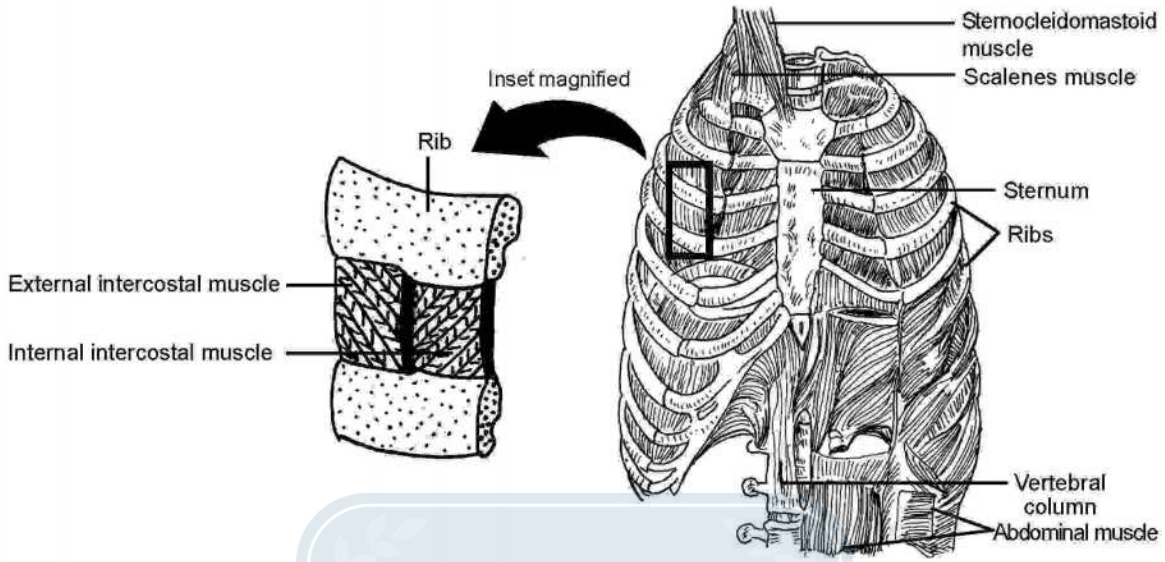


Fig. 6.10 : (a) The thoracic wall (rib cage) formed by the strnum, ribs and vertebral column and (b) a part of the lateral thoracic wall in the inset in (a) is magnified to show the external and internal intercostal muscles.

muscles contract. The rib cage move backward and inward. The muscles of the diaphragm relax as a result it becomes dome shape, pushing it up into the thoracic cavity. All these events reduce the volume of the thoracic cavity and raise the intrapulmonary pressure more than that of the atmosphere. Consequently, the air is forced out of the lungs.

Table 16.1: Comparative account of inspiration and expiration during quiet and forced breathing.

	Normal or Quiet	Forced
Inspiration	The diaphragm contracts. External intercostal muscles contract. The ribs move forward and outward. The thoracic volume increases. The intrapulmonary pressure decreases to about –3 mm Hg.	The action of the external intercostal muscles aided by the scalenes and sterrocleidomastoid muscles decreases the intrapulmonary pressure to –20 mm Hg.
Expiration	The diaphragm relaxes. Internal intercostal muscle contracts. The ribs move backward and inward. The thoracic volume decreases. The intrapulmonary pressure increases to about +3 mm Hg.	The contraction of the abdominal muscles and internal intercostal muscles decreases the intrapulmonary pressure to about +30 mm Hg.

Under condition of heavy exercise, forced breathing takes place. When this happens additional muscles are brought into action during inspiration and expiration. **Scalenes** and **sternocleidomastoid muscles** along with external intercostal muscle and diaphragm bring about inspiration. The **abdominal muscles** along with internal intercostal muscles and diaphragm bring about expiration. This type of ventilation also occur during sneezing and coughing. A comparative account of inspiration and expiration during quiet and forced breathing is presented in Table-16.1.

16.3.3. Control of ventilation or Breathing :

Under normal condition, breathing is controlled involuntarily and we are not conscious about it. Involuntary control is brought about by a breathing centre located in the **pons** and **medulla oblongata** of the brain. The ventral part of this centre is the **inspiratory centre** and the dorsal and lateral parts inhibit inspiration and stimulate expiration and hence form the **expiratory centre**. Nerve fibres reach out from these inspiratory and expiratory centres to the respective intercostal muscles and also by the phrenic nerve to the muscles of the diaphragm. Nerve impulses via these nerve fibres control the rhythmic movements of these muscles and hence, breathing. The bronchial tree, comprising of the bronchi and the bronchioles is also connected to the medulla of the brain by the vagus nerve.

Inspiration is also controlled by the **stretch receptors** (**propioreceptors**) located in the bronchial tree and the lung wall, which limit maximum inspiration. These receptors send impulses to the inspiratory centre to inhibit it when maximum inflation has reached. Impulses also reach the expiratory centre to stimulate it. External intercostal muscles relax as a result. This is known as **Herring-Breurer Reflex**. When inspiration is stopped, these receptors are no longer stimulated.

Besides, there are **chemoreceptors** in the medulla and in the **carotid** and **aortic bodies** in the large aorta that sense the blood for its carbon dioxide tension rather than the oxygen tension. When the carbon dioxide content rises, as during exercise, nerve impulses are sent out by them to the inspiratory centre and via this centre to the respiratory muscles to increase the rate of ventillation. Carbon dioxide, if allowed to accumulate, is harmful as it forms carbonic acid by combining wih the water of the plasma. Carbonic acid dissociates to form HCO_3^- and H^+. Increased H^+ concentration or decreased pH of the blood can denature the proteins particularly the enzymes. An increase of 0.25% in the concentration of carbon dioxide in the blood, duobles the ventilation rate. Reduction in oxygen concentration of 15 % only has the same effect. Since oxygen is available in higher concentration its effect is small in comparison to carbon dioxide Chemoreceptors sensitive to O_2 tension are also located in the medulla and the aortic bodies.

Within limits, the rate of breathing is also under voluntary control as is seen by the ability to hold the breathe. Voluntary control of breathing is also used during forced breathing, speech, singing, sneezing and coughing. Under these circumstances, the cerebral hemisphres send impulses from their centres to the medulla and then from the medulla to the breathing centre to carry out an approximate response.

Control of inspiration by Herring-Breurer reflex of the stretch receptors and the control throughh chemoreceptors are examples of negative feedbacks. Normal breathing rate per minute is 16-20.

16.4. LUNG VOLUMES AND CAPACITIES :

Human takes recourse to either quiet or forced breathing depending upon the situation. The lungs are very flexible and can hold variable volumes of air under different situations. However, there is an upper limit to the stretching of the lungs. Therefore, each lung has a volume range of holding air during quiet and forced breathing. The **lung volumes** and **lung capacities** (two or more lung volumes taken together) are described in Table-16.2 and Fig. 16.11. All four volumes added together make up the total lung capacity i.e., the maxium volume to which the lungs can be expanded. An instrument that measures the lung volumes and capacities is known as a **spirometer**.

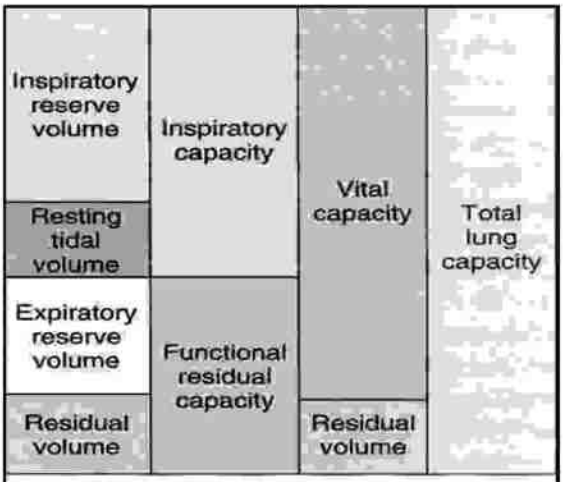


Fig. 16.11 : Lung volumes and capacities recorded on a spirometer

Table - 16.2 : Different lung volumes and capacities

Lung Volumes :	
Tidal volume (TV)	The volume of air inspired or expired in a quiet respiratory cycle. It is about 500 ml.
Inspiratory reserve volume (IRV)	It is the extra volume of air that can be inspired during forced breathing after normal inspiration. It is about 2000 to 3000 ml.
Expiratory reserve volume (ERV)	It is the extra volume of air that can be expired during forced breathing after normal inspiration.
Residual volume (RV)	The volume of air remaining in the lungs after a maximal expiration. It is about 1000 ml to 1500 ml.
Anatomical dead space	The volume of air remaining in the respiratory tubes of the conducting zone following inspiration (150 ml.)
Lung Capacities :	
Vital capacity (VC)	The maximum volume of air that can be expired after a maximum inspiration. VC = TV + IRV + ERV. It is about 3.5 - 4.5 litres
Inspiratory capacity (IC)	The maximum volume of air that can be expired following a normal tidal expiration. IC = TV + IRV. It is about 2.5 - 3.0 litres
Functional residual capacity (FRC)	The volume of air remaining in the lungs after a normal tidal expiration. FRC = ERV + RV
Total lung capacity (TLC)	The total volume of air in both lungs following a maximal inspiration (Vital capacity + Residual volume) TLC = VC + RV. It is about 5.0 - 6.0 litres

16.5. TRANSPORT OF RESPIRATORY GASES (Fig.16.12) :

Air is a mixture of several gases, of which, oxygen and carbondioxide are involved in respiration. Air has mass and therefore exerts a pressure. The pressure exerted by individual gases in a gaseous mixture is called its **partial pressure**, denoted by P. The sum total of the partial pressures of gases in the air is 760 mm Hg at sea level. The partial pressure of oxygen or Po_2 is 20.98% of 760 mm Hg. = 160 mm Hg at sea level. Similarly, the Pco_2 is 0.04% of 760 mm Hg = 0.3 mm Hg at sea level. The air that we breath becomes contaminated with water vapour, while it passes through the respiratory tract. The percentage of oxygen decreases to 19.67. Hence, Po_2 in the inspired air is calculated as 149.3 mm Hg. This air is known as humified air. The partial pressures of the different constituent gases in the inspired air is given below.

Gas	% in inspired humified air	Partial pressure (mm Hg)
O_2	19.67	149.3
CO_2	0.04	0.3
Water vapour	6.2	47.0

The humified air enters the lung alveoli and gets mixed up with the air that is already present (residual volume). The percentges and the partial pressures of the gases as a result change in the alveoli as noted below.

Gas	% in alveolar air	Partial pressure (mm Hg)
Oxygen	13.8	105
Carbon dioxide	5.3	40
Water vapour	6.2	47

The blood arriving at the lung alveoli through the pulmonary arterial capillaries in the alveolar wall has a lower Po_2 and a higher Pco_2. A comparison between the two is summarised below.

Respiratory gas	Partial pressure in alveolar air (mm Hg)	Partial pressure in the pulmonary arterial blood (mm Hg)
Oxygen	105	40
Carbon dioxide	40	46

Table-16.3

Comparative Po_2 and Pco_2 in the alveolar air and pulmonary blood vessels and the direction of diffusion of O_2 and CO_2. The direction of flow of blood is indicated by arravs.

	Po_2 (mm Hg)	Pco_2 (mm Hg)
Alveolus	105	40
$O_2 \downarrow$		
Pulmonary vein	100	40
$O_2 \downarrow$		
Systemic artery	100	40
$O_2 \downarrow$		
Cells	40	46
$CO_2 \downarrow$		
Systemic veins	40	46
$CO_2 \downarrow$		
Pulmonary artery	40	46

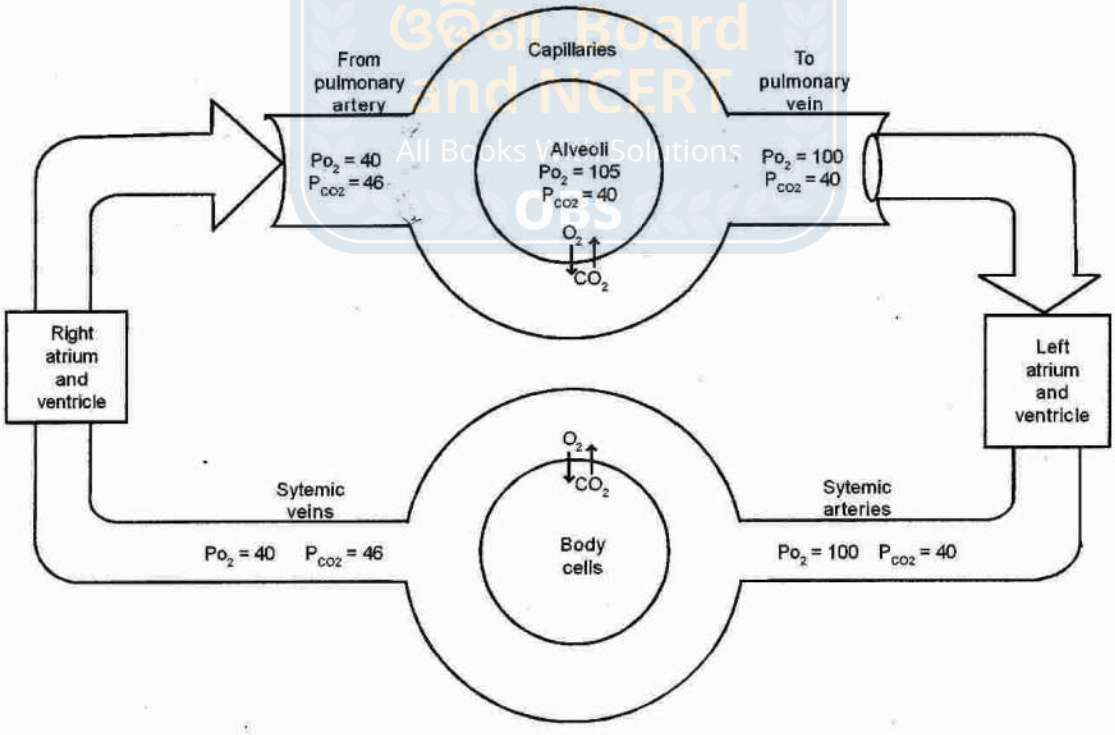


Fig.16.12 : Exchange of O_2 and CO_2 by diffusion between the tissues and alveoli

Gases always flow from a region of higher partial pressure to a region of lower partial pressure. In the alveolar air, the Po_2 is 100-105 mmHg, while the Po_2 in the pulmonary arterial blood is only 40 mm Hg. This blood reaches the alveoli after releasing oxygen at the tissue level. Oxygen, therefore, diffuses from the alveolar air into the pulmonary arterial blood. The thin wall separating the blood in the capillaries and the air in the alveoli is no barrier to this movement. Similarly, the Pco_2 is greater i.e. 46 mm Hg in the pulmonary arterial blood than the Pco_2 of the alveolar air i.e. 40 mm Hg. CO_2, therefore, diffuses out from the arterial blood into the alveolar air. The diffusion of oxygen and carbon dioxide in opposite direction continues till equilibrium is established on either side. Thus, Po_2 of the pulmonary blood rises from 40 to 100 mm Hg and that of carbon dioxide falls from 46 to 40 mmHg. This process is known as **oxygenation**. Following oxygenation, the pulmonary arterial blood changes to venous blood that is drained to the heart and then to tissues for delivery of oxygen.

Oxygen is transported from lungs to different parts of the body and carbon dioxide is transported from different parts of the body to lungs. Blood serves as a medium for this transport.

16.5.1. Transport of oxygen : Oxygen is transported by the blood in two forms.

I. As dissolved oxygen

Oxygen is soluble in water. Water is the major component of blood plasma. A fraction of the total oxygen is transported in dissolved state in the plasma. About 3% of oxygen is transported in this form.

II. As oxyhaemoglobin

R.B.C. contains a red-coloured respiratory pigment in its cytoplam called haemoglobin (Hb). Hamemoglobin is a conjugate protein having a protein part called **globin** and a non protein part called **heme.** Structurally, it is made up of four sub-units. Each sub-unit contains a heme conjugated to a globin polypeptide. A heme is an iron-containing porphyrin in ferrous (Fe^{2+}) valency state. The iron atom is bonded to globin polypeptide. There are two each of **α** and β globin polypeptides. Molecular oxygen (O_2) binds to the iron atom without changing its valency state. Each heme binds a molecule of oxygen. Thus, on saturation, haemoglobin is bound to four molecules of oxygen.

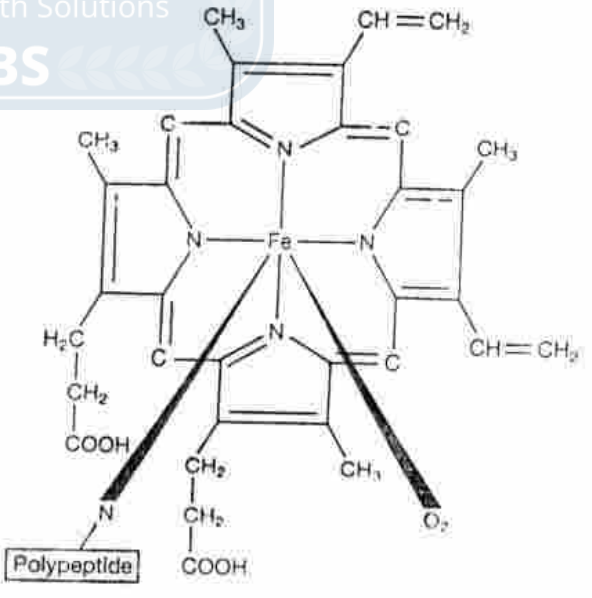


Fig.16.13 : Structure of a unit of haemoglobin molecule

However, this binding does not occure all at once. The binding of one molecule facilitates the binding of the second and so on. This type of binding is known as cooperative or allosteric binding. Haemoglobin on binding to oxygen forms **oxyhaemoglobin**. This type of binding is depicted below.

$Hb_4 + O_2 = Hb_4O_2$

$Hb_4O_2 + O_2 = Hb_4(O)_2)_2$

$Hb_4(O_2)_2 + O_2 = Hb_4(O_2)_3$

$Hb4(O_2)_3 + O_2 = Hb_4(O_2)_4$

Myoglobin is another such conjugate protein, present in the muscle. Structurally, it is more or less similar to haemoglobin. However, it contains one heme and one globin chain. It, thus, carries one molecule of oxygen. It can store oxygen in the muscle tissue and this is particularly important for diving mammals like seals, whales and porpoises who spend a lot of time under water.

16.5.2. Haemoglobin and oxygen association / dissociation curve :

16.5.2.1. Effect of Po_2 on haemoglobin saturation (Fig. 16.14) : The quantitative relationship between percentage saturation of haemoglobin and Po_2 is presented by an oxygen association/ dissociation curve (Fig.6.15). The curve is an S-shaped curve with a steep rise between 10 and 60 mm Hg Po_2 and a flat part between 70 and 100 mm Hg Po_2. Thus, the extent to which haemoglobin combines with oxygen increases very rapidly from 10 to 60 mm Hg so that at a Po_2 of 60 mm Hg, 90% of the total haemoglobin is combined with oxygen. From this point on, a further increase in Po_2 produces only a small increase in oxygen binding.

The importance of this plateau or flat region of the curve at higher Po_2 lies in many situations, including high attitudes and cardiac and pulmonary diseases, in which Po_2 of the alveolar or arterial blood is less. Even if the Po_2 falls below the normal value of 100 mm Hg to 60 mm Hg, the total quantity of oxygen carried by haemoglobin will decrease by only 10%, since at this Po_2, haemoglobin saturation is still close to 90%. The upper flat portion, therefore, provides an excellent safety factor in the supply of oxygen to the tissues.

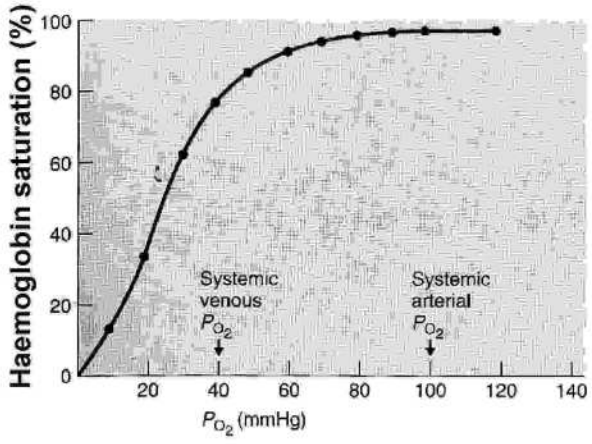


Fig.16.14 : Effect of Po_2 on percent saturation of haemoglobin

Since haemoglobin is neary fully saturated at 100 mm Hg only further increase in Po_2 or breathing 100% pure oxygen adds very little oxygen to the blood.

This is for normal people at sea level. Persons suffering from lung diseases or initially living at higher altitudes would benefit from such a situation, which would result in higher oxygen carriage.

The plasma and erythrocytes in the pulmonary arterial blood entering the lungs have a Po_2 of 40 mm Hg. At this Po_2 haemoglobin is 75% saturated. Oxygen diffuses from the alveolar air because of its higher Po_2 than the pulmonary arterial blood. Diffusion continues till the Po_2 of the pulmonary blood rises from 40 mm Hg to 100 mm Hg. Similarly, carbon dioxide diffuses out into the alveolar air from the pulmonary blood because of its higher partial pressure of 46 mm Hg, than the 40 mm Hg Pco_2 of the alveolar air. Diffusion continues till Pco_2 of the pulmonary blood falls to 40 mm Hg.

16.5.2.2. Effect of Pco_2, $[H^+]$, temperature and diphosphoglycerate concentration on oxygen-haemoglobin dissociation : Several factors influence the dissociation of oxyhaemoglobin and the release of oxygen. Among these are **hydrogen ion concentration (pH), temperature** and **2, 3-diphosphoglycerate (2, 3-DPG)** (Table 16.4). At higher temperature and lower pH, the oxyhaemoglobin dissociation curve shifts to the right i.e. higher Po_2 is required for haemoglobin to bind to oxygen. Alternately speaking, at higher temperature and lower pH, the affinity of haemoglobin for oxygen decreases [Fig. 16.15 (a) and (b)]. At higher body temperature, such as during heavy exercise and fever, the oxyhaemoglobin dissociates at the tissue level and thus the delivery of O_2 to the tissues increases in conformity with the demand. The effect of pH on this dissociation curve is described as **Bohr effect**.

The concentration of 2, 3-DPG has also a bearing on the oxyhaemoglobin dissociation curve. Erythrocytes lack mitochondria and hence, they obtain their energy from glycolysis or anaerobic breakdown of glucose. 2, 3-DPG, a product formed from 3-phosphoglycerate

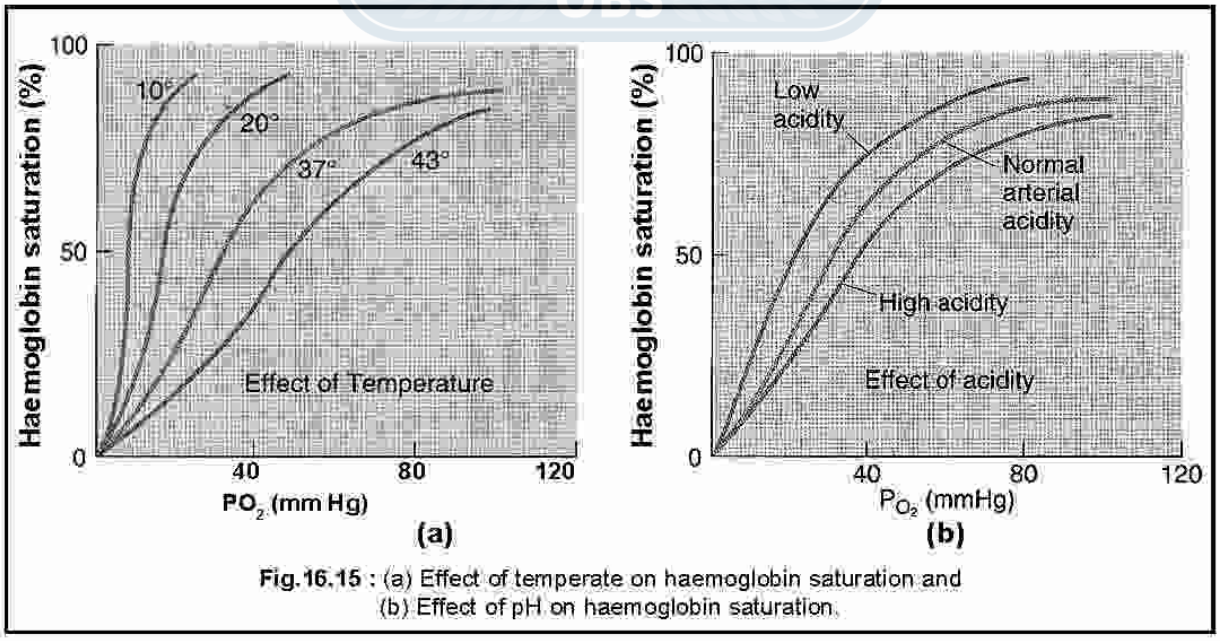


Fig.16.15 : (a) Effect of temperate on haemoglobin saturation and (b) Effect of pH on haemoglobin saturation.

during glycolysis, is plentiful in erythrocytes. It is a highly charged ion (anion) that binds to the β-globin polypeptide chain of deoxyhaemoglobin and thus affects the oxyhaemoglobin dissociation curve. An increased 2, 3-DPG in the red cells shifts the curve to the right side (Fig. 16.16). It favours the dissociation of oxyhaemoglobin into deoxyhaemoglobin and oxygen. Thus, 2, 3-DPG favours oxygen unloading from oxyhaemoglobin at the tissue level. At higher altitude, erythrocytes form more 2, 3-DPG. This facilitates the unloading of O_2 at the tissue level. A higher concentration of 2, 3-DPG also helps O_2 delivery to the tissues in anemia patients.

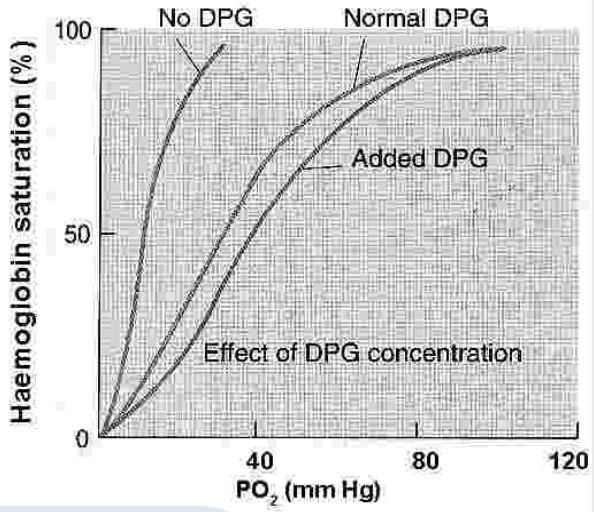


Fig.16.16 : Effect of 2, 3-DPG concentration an haemoglobin saturation

Table-16.4
Factors affecting the affinity of haemoglobin for oxygen :

Factor	Affinity for Oxygen	Feature of low curve	Inference
↓ pH	Decreased	Shifts to the right	Called Bohr effect. At lower pH (more H^+), oxyhaemoglobin dissociates into deoxyhaemoglobin and O_2.
↑ Temperature	Decreased	Shifts to the right	Increases oxygen unloading during exercise and fever.
↑ 2, 3-DGP	Decreased	Shifts to the right	Increases oxygen unloading in adaptation to anemia and high attitude living.

16.5.3. Transport of Carbon dioxide :

During oxidation of substrates at the cellular level, carbon dioxide is produced which diffuses out into the blood capillaries and transported to lungs for removal. Transport of carbon dioxide occurs in three major forms.

I. As dissolved carbon dioxide :

Carbon dioxide is sparingly soluble in water forming carbonic acid (H_2CO_3). So it is transported in dissolved condition by the blood plasma. About 7% of CO_2 is transported in this form.

$$CO_2 + H_2O \rightleftharpoons H_2CO_3$$

II. As carbaminohaemoglobin :

The globin part of haemoglobin helps in the transport of carbon dioxide. The terminal, amino group of globin polypeptide combines with carbon dioxide to form carbominohaemoglobin.

$$CO_2 + HbNH_2 \rightleftharpoons HbNHCOOH$$

Carbaminohaemoglobin is formed at the level of the tissue and dissociates at the level of lungs. Carbaminohaemoglblin is formed when haemoglobin is in deoxygenated from as oxyhaemoglobin can not hold as much of CO_2 as deoxyhaemoglobin. About 23% of carbon dioxide is transported by this process.

III. As bicarbonates

About 70% of carbon dioxide is transported by this method. After diffusing from the tissue into the blood capillaries, it enter into RBC. In the cytoplam of RBC, carbon dioxide combines with water to form **carbonic acid** (H_2CO_3) in the presence of an enzyme **carbonic anhydrase**. Carbonic acid spontaneously dissociates and liberates bicarbonate ions (HCO_3^-) and protons (H^+). HCO_3^- pass out from the RBC to the plasma. To restore ionic balance and electrochemical neutrality, chloride ions diffuse from the plasma into RBC. This is called **chloride shift or Hamburger shift**.

$$CO_2 + H_2O \xrightleftharpoons{\text{Carbonic anhydrase}} \underset{\text{(Carbonic acid)}}{H_2CO_3}$$

(Carbonic acid)

$$H_2CO_3 \rightleftharpoons H^+ + \underset{\text{(Bicarbonate)}}{HCO_3^-}$$

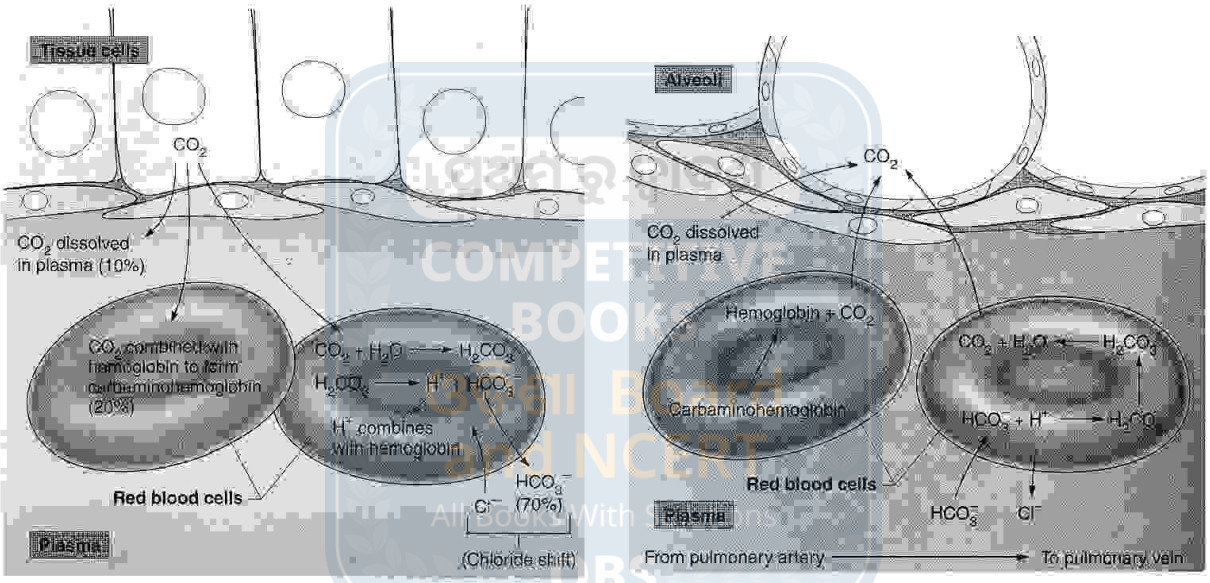
Inside the RBC, chloride ions combine with potassium ions to form KCl. Whereas, HCO_3^- in the plasma combines with Na^+ to form sodium bicarbonate ($NaHCO_3$). $NaHCO_3$ is carried by the blood to the lung alveoli, where is dissociates to release CO_2. Oxyhaemohglobin after reteasing oxygen combines with H^+ to form reduced haemoglobin, HHb.

At the level of the lungs, these reactions occur in a reverse way. Reduced haemoglobin becomes oxygenated forming oxyhaemoglobin and release H+. Cl^- ions of Kcl diffuse out of RBC and react with $NaHCO_3$ in the plasma forming Nacl and liberating HCO_3^- ions. HCO_3 combineions with H^+ ions inisde RBC and form carbonic acid. The lalter dissociates in the presence of carbonic anhydrase to produce H_2O & CO_2. Carbon dioxide diffuses out through the lungs. About 4 ml of CO_2 is released through the lungs by 100 ml of venous blood.

16.5.4. Gaseous exchanges at tissue and alveolar levels :

Two processes, such as Chloride Shift (Hamburger Shift) and Haldane Effect have been described to explain about gaseous exchanges at the tissue and alveolar levels, respectively.

16.5.4.1. Gaseous exchange at the tissue level : Chloride Shift (Hamburger Shift) [Fig. 16.7 (c)] explains about the gaseous exchange at the tissue level. This phenomenon has already been described in the Section 16.5.3 on Trasnport of CO_2. However, in this section, we make an attempt to explain about the unloading of O_2 from oxyhaemoglobin at the tissue level. Recall that following the buildup of H_2CO_3 in RBC cytoplasm of the systemic arterial capillaries, undergoes a spontaneous dissociation into H^+ and HCO_3^-. Thus, there is an increase in the H^+ concentration in the RBCs. Since, haemoglobin has a greater affinity for H^+ than O_2, oxyhaemoglobin dissociated into deoxyhaemoglobin and O_2. O_2 diffuses into the tissues based on the difference in the partial pressures of O_2 between the two sides. Excess of H^+ is buffered in combination with deoxyhaemoglobin.



[Fig.16.17 : (a) Chloride shift or Hamburger's phenomenon opuating in erythrocytes at the tissue level and (b) Haldane effect and release of CO_2 into the alveoli at the alveolar capillary level.]

16.5.4.2. Gaseous exchange at the alveolar level : Following the unloading of O_2 at the tissue level, CO_2 generated in the tissues, diffuses into the blood based on the difference in partial pressures of CO_2 on both sides. CO_2 is carried as bicarbonates to the lung via the heart. The blood containing deoxyhaemoglobin in the RBCs and bicarbonates in the plasma returns to the lungs via the heart and then pulmonary artery. This time again, due a partial pressure difference, O_2 gets into the pulmonary arterial blood and CO_2 gets out of it into the alveolus. This process is explained by Haldane Effect [Fig. 16.17 (b)]. The sequence of events is exactly reverse of what happens in the Chloride Shift. Due to a higher Po_2 in the pulmonary arterial blood. This makes way for association of O_2 with deoxyhaemoglobin, consequently forming oxyhaemoglobin. This is followed by an exchange of Cl^- with HCO_3^- in the RBC. The released H^+ from the deoxyhaemoglobin reacts with HCO_3^- in the RBC to from H_2CO_3. When there is a

build-up of H_2CO_3, it spontaneously dissociates into H_2O and CO_2. CO_2 diffuses into the alveoli and then expelled out by expiration. The blood, known as oxygenated blood is carried to the tissues by the palmonary vein via the heart and then systemic artery.

16.5.5. Acid-base regulation :

The blood within the arteries has an average pH of 7.40. This pH is maintained all throughout by buffering mechanisms. When the pH falls below 7.35, the pathological condition is known as **acidosis** and when it is raised above 7.45, it is known as **alkalosis.** A greater part of CO_2, generated in the tissues through aeorobic respiration is transported to the lungs as bicarbonates. Primarily CO_2 reacts with H_2O forming H_2CO_3 in the erythrocytes, catalyzed by the enzyme, **carbonic anhydrase**. H_2CO_3 is formed in the plasma, but to a lesser extent. When H_2CO_3 concentration builds up, it spontaneously dissociates into H^+ and HCO_3^-. Non-volatile metabolic acids like, lactic acid, fatty acids and ketone bodies also generate H^+. A major part of the H^+ is buffered by haemoglobin in erythrocytes and different buffering mechanisms in the plasma. HCO_3^-, generated in erythrocytes is exchanged with Cl^- of the plasma at the tissue level. (refer to chloride shift). HCO_3^- functions as an excellent buffer and absorbs excess of H^+, generated by nonvolatile acids. Any excess of the H^+ is excreted by the kidneys in the urine.

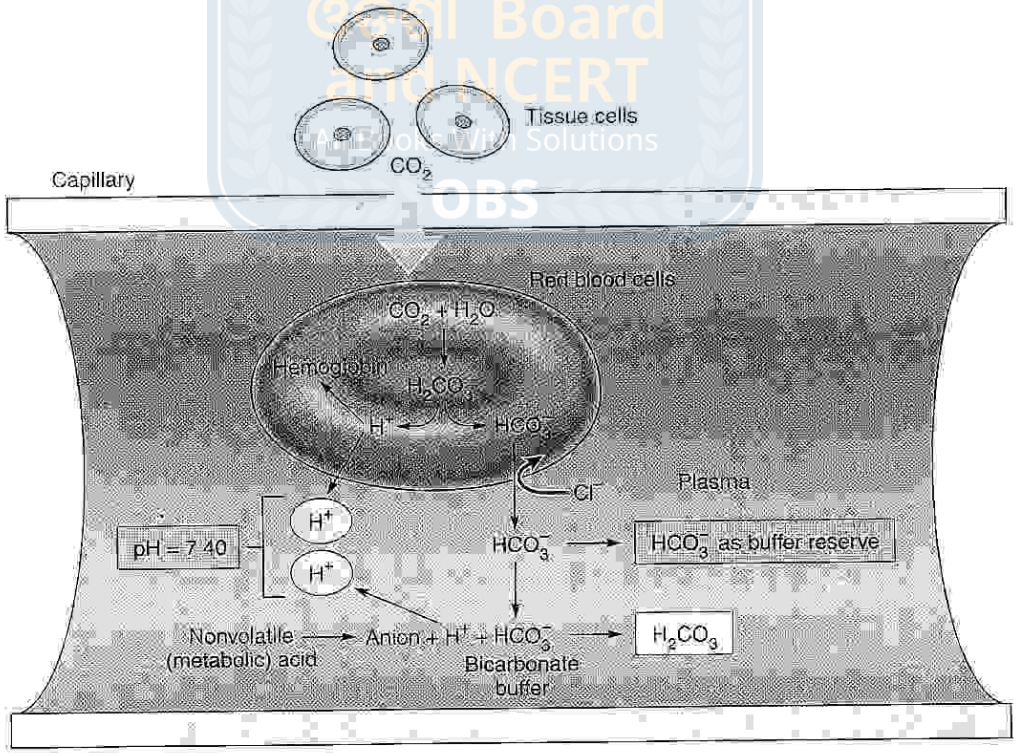


Fig.16.18 : Acid-base regulation in the blood by HCO_3^-.

Acidosis and alkalosis, mentioned earlier are categorized as respiratory and metabolic components. **Respiratory acidosis** is caused by **hypoventilation**, which results in the rise of plasma CO_2 concentration. **Metabolic acidosis** results from excess production of nonvolatile acids. **Respiratory alkalosis**, by contrast, results due to **hyperventilation**. Athletes, especially short distance runners, use hyperventilation to transiently build an alkaline pH of the blood, which consequently absorbs excess of H^+ from lactate, generated in the skeletal muscle due to inadequate oxygen supply during running. Metabolic alkalosis may be caused due to excess HCO_3^- or inadequate nonvolatile acids, caused due to vomiting. Vomiting may cause alkalosis through the loss of gastric juice, which is normally absorbed from the intestine into the blood.

16.6. COMMON RESPIRATORY DISORDERS : PREVENTION AND CURE :

The disorders relating to the functioning of lungs are classed as **restrictive** and **obstructive**. In restrictive disorders, the inspiratory vital capacity is reduced to a sub-normal value. The rate of expiratory vital capacity is, however, is normal. In obstructive disorders, by contrast, the vital capacity is usually normal, because the lung tissue is not damaged. The expiration is more difficult due to the obstruction of the airways. The degree of obstruction is measured by **forced expiratory volume** (**FEV**). An FEV less than 80% suggests the presence of an obstructive pulmonary disease. Chronic bronchitis, asthma and emphysema are grouped together as **chronic obstructive pulmonary disease** (**COPD**). COPD is the fifth leading cause of death in the world. Some common disorders relating to the respiratory system, especially the lungs and the airways are discussed in the underlying section.

Smoking :

Smoking has both short-term and long-term effects on the respiratory system and its functioning. Nicotine, present in the tobacco, causes constriction of finer bronchioles, increasing resistance to the passage of air Nicotine also paralyzes the cilia, present along the respiratory tract, which help to remove dirt and mucous, which would otherwise accumulate in the airways. Smoking also irritates the goblet cells and stimulates them to produce excess mucous. The mucous may constrict the airways causing difficulty in breathing. Long-term smoking may lead to several diseases, some of which are discussed in the succeeding sections.

16.6.1. Asthma :

It is a form of difficult and heavy breathing, caused by the spasm of the smooth or involuntary muscle, present in the wall of the airways, especially bronchioles. Contraction of such muscle results in the narrowing down of the bronchioles (**broncho-constriction**). The person experiences difficulty in breathing out than breathing in. Secretion of excess mucous aggravates the situation. This mucous may trap bacteria, which may cause serious infections of the bronchus and bronchioles, known as bronchitis. Difficulty in breathing due to broncho-constriction is compounded by the secretion of **immunoglobulin E** (**Ig E**) during exercise.

Ig E binds to the mast cell surface and stimulates it to release histamine, which causes inflammation and allergy.

The causes of asthma may be an over-reaction to one of several possible exogenous stimuli and allergy-causing agents (allergens), such as pollen grains, house-hold dust, specific types of food, feathers and particles of cotton. Emotional disturbances may also provoke an asthma attack. Cold, cigarette smoke, polluted air from vehicular exhaust also may cause asthma. Thus, the cause of asthma is not similar in all patients. The lung of the affected people has an increased number of mast cells and eosinophils. These cells are stimulated to produce **histamine** and **leukotrienes**, which produce **hypersensitivity** or **allergy** along the airways and alveoli.

Asthma is treated with **glucocorticoid drugs**, which inhibit inflammation and allergy. Anti-leukotriene drugs are also used to suppress the inflammatory response. **Epinephrine** is frequently used as an inhaled bronchodilator drug to relieve the symptoms of asthma. However, this drug binds to **adrenergic receptors**. Based on this finding, a drug, named as **terbutaline** is formulated, which specifically bind to the adrenergic receptors, present on the cells of the bronchioles and effect broncho-dilation.

Asthma can be prevented by avoiding exposure to sensitive allergens.

Bronchitis :

It is the inflammation of the lining of the airways and may be **chronic** or **acute**. Chronic bronchitis has a gradual onset and is of a long duration. Acute bronchitis, by contrast, flares up suddenly and dies down in a short period of time. It may be a side effect of an infection, like common cold.

Chronic bronchitis is a much more serious problem that may be caused and aggravated by smoking or inhaling polluted air. Excess mucous secretion in bronchi and bronchioles causes obstruction.

16.6.2. Emphysema :

Emphysema is a chronic lung disease, characterized by a damage to the air sacs (alveoli) in the lungs. The lung tissue supporting the alveoli loses its elasticity and the capillaries feeding the alveoli are destroyed. The air sacs are unable to deflate completely resulting in the trapping of the expired air inside. The lung cannot be renewed with fresh air thus impairing the exchange of O_2 and CO_2. This leads to the expression of symptoms such as, shortness of breath on exertion; hyperventilation and expanded chest; chronic cough and limited ability to exercise. These conditions together constitute emphysema. Emphysema and chronic bronchitis frequently co-exist together to comprise **chronic obstructive pulmonary disease**. The damage to the lung tissue may occur due to : (a) exposure to toxic chemicals; (b) long term exposure to tobacco smoke and (c) **alpha-1-antitrypsin** deficiency. The first two causes are extrinsic, while the third is intrinsic. Cigarette smoke is the most common cause of emphysema (80-90%). It stimulates the alveolar macrophages to secrete trypsin,

which digests and destroys the lining of the lung. In the rest, the disease results due to the deficiency of a protease inhibitor, alpha-1-antitrypsin. Alpha-1-antitrypsin is a protease, secreted by white blood cells, especially, neutrophils. This enzyme inhibits trypsin, secreted by alveolar macrophages. The enzyme is encoded by a gene, located on **chromosome 14.** Smoking must be avoided to prevent this disease.

Cystic fibrosis (CF) :

CF is an inherited disorder affecting many different parts of the body, including the lungs. It is characterized by chronic cough with thick mucus in the lungs. These symptoms lead to several secondary symptoms such as blockage of the airways of the lungs and infection leading to inflammation and pneumonia. The disease is caused by a mutation in the ***cystic fibrosis transmembrane conductance regulator*** (***CFTR***) ***gene***, located on **chromosome 7**. The normal gene encodes a trans-membrane CFTR protein. It is a chloride channel that regulates the movement of sodium chloride across the plasma membrane and thus regulates the concentration of salts in the extra-cellular secretions. The mutant gene encodes a defective chloride channel, which fails to regulate the flux of chloride ions in particular. The result is that the extra-cellular secretions become thicker and more viscous. This thicker and sticky mucus clogs the the airways of the lungs leading to infection and inflammation, impaired function and finally failure. **Francis Collins** and his coworkers have successfully mapped and cloned the gene. The mutant gene has been replaced by a cloned gene in gene therapy trials.

Pulmonary fibrosis :

Under certain conditions, not fully understood, the damage to the lunf tissue leads to pulmonary fibrosis instead of emphysema. The normal structure of the lungs is disrupted by the accumulation of fibrous connective tissue proteins. It can also result due to an inhalation of particles, less than 6 μm in size that accumulates in the respiratory zone of the lung. **Anthracosis** or **black lung** is a type of pulmonary fibrosis, produced by the inhalation of carbon particles from the coal dust.

Lung cancer :

It is one of the most common forms of cancer in men and is the third most common cause of death in developed countries after coronary heart disease and heart strokes. Cancer is caused by uncotrolled mitotic cell divisions forming tumors. Sometimes these cells breakaway from the original site and invade other tissues of the body to develop secondary tumors. Lung cancer usually starts in the epithelium of the bronchioles and then spreads throughout the lungs. It is caused exclusively by smoking (99.7%). Tobacco smoke contains a chemical like benzpyrene, which acts as a carrogen and causes cancer. So smoking must be avoided to prevent this disease.

Infectious Diseases of the respiratory system :

(i) **Tuberculosis (TB) :** caused by the bacterium *Mycobacterium tuberculosis*, a rod-shaped bacterium.

(ii) **Diptheria :** caused by the bacterium *Corynebacterium diptheria*, usually affecting children.

(iii) **Whooping cough (Petrusis) :** Caused by the bacterium *Bordetella petrusis*, affecting children.

(iv) **Pneumonia :** Caused by the diplococcus bacterium *Diplococcus pneumoniae*. In some cases, this is also caused by fungi, protozoa and viruses. The alveoli are inflammed. Lymph, mucous accumulate in the alveoli and bronchioles, adversely affecting the efficiency of the lungs.

16.6.3. Occupational Respiratory Disorders :

Workers in environments in several industries are often exposed to potential harmful chemicals, gases, dust particles and aerosols. **Silicosis** and **asbestosis** result from a chronic exposure to fine particles of silica, asbestos and cement which when inhaled tend to settle down on the walls of the airways and the alveoli, thereby causing irritation and blockage. This affects the respiratory efficiency and causes breathlessness.

16.6.4. Carbon monoxide poisoning :

The affinity of deoxyhaemoglobin (containing Fe^{2+}) for carbon monoxide is about 250 times greater than that of oxygen. Thus, haemoglobin quickly takes up any available carbon monoxide in preference to oxygen to form a stable compound called **carbon monoxyhaemoglobin** or **carboxyhaemoglobin**. If it happens, haemoglobin is not available to take up oxygen and tissues and vital organs like the heart and brain starve without oxygen. This results in **carbon monoxide poisoning** and the body collapses unless exposure to carbon monoxide is quickly stopped and pure oxygen and a small amount of CO_2 is inhaled, Carbon dioxide stimulates the respiratory centre in the medulla and breathing is made faster to flush out the carbon monoxide from the lungs. Carbon monoxide is present in the exhaust of the automobiles and tobacco smoke.

Some drugs and oxidizing agents oxidize the normal ferrous valency state of iron (Fe^{2+}) of haemoglobin to ferric state (Fe^{3+}). This haemoglobin is known as **methaemoglobin**. Some oxidation of haemoglobin to methaemoglobin occurs normally. However, an erythrocyte enzyme converts it back into normal haemoglobin. Congenital absence of this enzyme causes the hereditary disease, **methaemoglobinemia**.

SAMPLE QUESTIONS

GROUP - A
(Objective-type Questions)

1. Choose the correct answer :

(i) When does the frog respire by the skin ?
- (a) While in water
- (b) While on land
- (c) During hibernation
- (d) During all the times

(ii) The exchange of gases in the lung alveoli occurs by
- (a) Active transport
- (b) Passive transport
- (c) Diffusion
- (d) None of the above

(iii) The amount oxygen taken in and carbon dioxide released during quiet breathing is
- (a) 500 ml.
- (b) 1000 ml.
- (c) 3000 ml.
- (d) 5000 ml.

(iv) If the CO_2 concentration in the blood increases, the breathing will
- (a) Increase
- (b) Decrease
- (c) Stop
- (d) Remain unaffected

(v) If a tissue is having inadequate supply of oxygen, the condition is called
- (a) Hypoxia
- (b) Anoxia
- (c) Asphyxia
- (d) Anaemia

(vi) The respiratory centre that regulates breathing is located in which part of the brain ?
- (a) Cerebral hemispher
- (b) Diencephalon
- (c) Hypothalamus
- (d) Medulla oblongata

(vii) The quantity of 500 ml. of air during quiet breathing in man refers to the
- (a) Residual volume
- (b) Tidal volume
- (c) Vital capacity
- (d) Dead space air

(viii) Which structure in pharynx prevents the entry of food into the respiratory tract ?
- (a) Larynx
- (b) Gullet
- (c) Glottis
- (d) Epiglottis

(ix) Which of the following presents the collapse of the trachea ?
- (a) Diaphragm
- (b) Cartilaginous rings
- (c) Muscles in the wall
- (d) None of the above

(x) The enzyme involved in CO_2 transport by blood is
- (a) Carboxylase
- (b) Carboxykinase
- (c) Carbonic anhydrase
- (d) None

(xi) What is the rate of breathing in a normal healthy man at rest ?
- (a) 15-20 times/min
- (b) 10-15 times/min
- (c) 20-30 times/min
- (d) 40-50 times/min

2. Answer each of the following in one or two words :

(i) What type of respiration is seen in the frog during hibernation ?
(ii) What type of respiration is seen in endoparasites like the liver fluke and the filarial worm ?
(iii) What is the mode of respiration of the frog, while it is in water ?
(iv) What type of respiration is seen in insects ?
(v) In which part of the body is a schneiderian membrane located ?
(vi) What is the major form of oxygen is transport by the blood ?
(vii) What is the major form of CO_2 transport by the blood ?
(viii) Name the organ in man, which produces speech ?
(ix) What is the prosthetic group present in the haemoglobin molecule ?
(x) What is the respiratory pigment present in arthropods like the prawn ?
(xi) Which muscles in the thoracic wall bring about inspiration ?
(xii) What is the muscular partition that divides the thorasic and abdomnal cavities ?
(xiii) In which part of the mammalian brain the respiratory centre is located ?
(xiv) How many pair of spiracles are present in cockroach ?
(xv) What type of gill is found in cartilaginous fish ?
(xvi) What type of gill is found in the bony fish ?
(xvii) What is the oxygen carrying capacity of the human haemoglobin ?

GROUP - B
(Short Answer-type Questions)

1. Differentiate between :

(i) Anabolism and Catabolism
(ii) Anaerobic respiration and Aerobic respiration
(iii) Cutaneous respiration and Pulmonary respiration
(iv) Inspiration and Expiration
(v) External intercostal muscle and Internal intercostal muscle
(vi) Quiet breathing and Forced breathing
(vii) Tracheal respiration and Branchial respiration
(viii) Tidal volume and Vital capacity
(ix) Myoglobin and Haemoglobin.
(x) Deoxyhaemoglobin and Oxyhaemoglobin
(xi) Carbaminohaemoglobin and Carboxyhaemoglobin.
(xii) Substrate level phosphorylation and Oxidative phosphorylation
(xiii) Asthma and Emphysema.

2. Write brief notes on the following (within 50 words each) :

(i) Cutareous respiration
(ii) Disadvantages of tracheal respiration
(iii) Haldane effect
(iv) Bohr effect
(v) Chloride shift / Hamburger phenomenon
(vi) Residual volume
(vii) Vital capacity
(viii) Role of diaphragm in respiration
(ix) Advantages and disadvantages of cutaneous respiration
(x) Counter current flow in gill respiration
(xi) Structure and functions of larynx
(xii) Bronchial tree
(xiii) Control of ventillation
(xiv) Hering– Breur reflex
(xv) Structure of haemoglobin
(xvi) Myoglobin
(xvii) Role of haemoglobin as a buffer
(xviii) Carbon monoxide poisoning

GROUP - C
(Long Answer-type Questions)

1. Describe the mechanism of breathing and its regulation in human.
2. Describe the transport of respiratory gases in the blood of human.
3. Give an account of gaseous exchanges both are the tissues and alveolar levels.
4. Draw a neat labeled diagram of the respiratory organs of human. (Description is not required)

❑❑❑

BODY FLUIDS AND CIRCULATION

CHAPTER 17

The major constituent in the body of all living organisms is water. It is present in the form of different types of body fluids, which fall under two main categories: (1) **intracellular fluid**, containing 55% of the total body water and (2) **extracellular fluid**, containing 45% of the total body water. Intracellular fluid is present in the form of protoplasm in the cells, while extracellular fluid is present in the extracellular spaces. All body fluids contain water as the major constituent and dissolved solutes. The solutes are both organic and inorganic. There is a continuous exchange of water and all kinds of solutes between the internal and external environments. This creates disequilibrium in the homeostasis. Therefore, a continuous circulation of body fluids is essential for maintaining homeostasis in the body. Majority of multicellular animals possess defined circulatory systems, each with a pumping organ, the heart and walled vessels for circulation of the body fluid throughout the body. However, a few possess circulatory systems without walled blood vessels. This type of circulatory system has been designated as **open type**. The other type with walled vessels is designated as **closed type**. The circulatory system performs the following functions:

1. **Transportation :**
   - (i) **Transport of nutrients :** The digested food is carried from the alimentary canal to the cells and tissues for metabolism and / or storage.
   - (ii) **Transport of respiratory gases :** Respiratory gases, such as oxygen is transported to the tissues for cellular oxidation and carbon dioxide is transported from the site of cellular oxidation for elimination from the body.
   - (iii) **Transport of excretory wastes:** Nitrogenous excretory waste materials generated through catabolism of proteins and nucleic acids are transported from the site of their formation for elimination from the body.

2. **Regulation :**
   - (i) **Hormonal regulation :** Hormones secreted from endocrine glands are carried by the circulating fluid, such as the blood to the target tissues for action.
   - (ii) **Temperature regulation :** The circulating body fluid functions as a medium for even distribution of temperature throughout the body.

3. Protection :

(i) **Clotting :** The body fluid, especially blood of vertebrates possesses an intrinsic ability to prevent its loss by forming a plug by a clotting mechanism.

(ii) **Immunity :** Blood of vertebrates is the bearer of cells (leucocytes) and molecules (antibodies), which protect the body from invasive organisms and substances.

Different types of body fluids :

1. **Intracellular fluid : Protoplasm**
2. **Extracellular fluid :**
   - (i) **Plasma**
   - (ii) **Interstitial fluid** and **lymph**
   - (iii) **Fluid in bones**
   - (iv) **Fluid in cartilage**
   - (v) **Trans cellular fluid**
     - (a) Cerebrospinal fluid
     - (b) Intra-ocular fluid,
     - (c) Digestive juice,
     - (d) Serous fluid (intra pleural fluid, pericardial fluid and peritoneal fluid)
     - (e) Synovial fluid in joints
     - (f) Fluid in urinary tract.

Circulatory system of a vertebrate, especially of human has two components: **(1) cardio-vascular system**, consisting of heart; blood vessels; and a circulating fluid, the blood and (2) **lymphatic system**, consisting of lymphoid tissues, lymph vessels and lymph.

17.1. COMPOSITION OF BLOOD (Fig. 17.1) :

Blood is a special type of connective tissue, consisting of a cellular part, constituted by the **formed elements** or the **corpuscles**, suspended in a fluid part, the **plasma**. The plasma is the intercellular substance or matrix, which does not contain any fiber common to all other types of connective tissues. When a sample of blood is centrifuged, the formed elements settle at the bottom as sediment, leaving plasma at the top. More than 99% of the cells are erythrocytes, while leucocytes and platelets together account for very negligible percentages. The erythrocytes constitute approximately 45% and 42% of the total blood volume in men and women, respectively. This is known as the **hematocrit**. The plasma

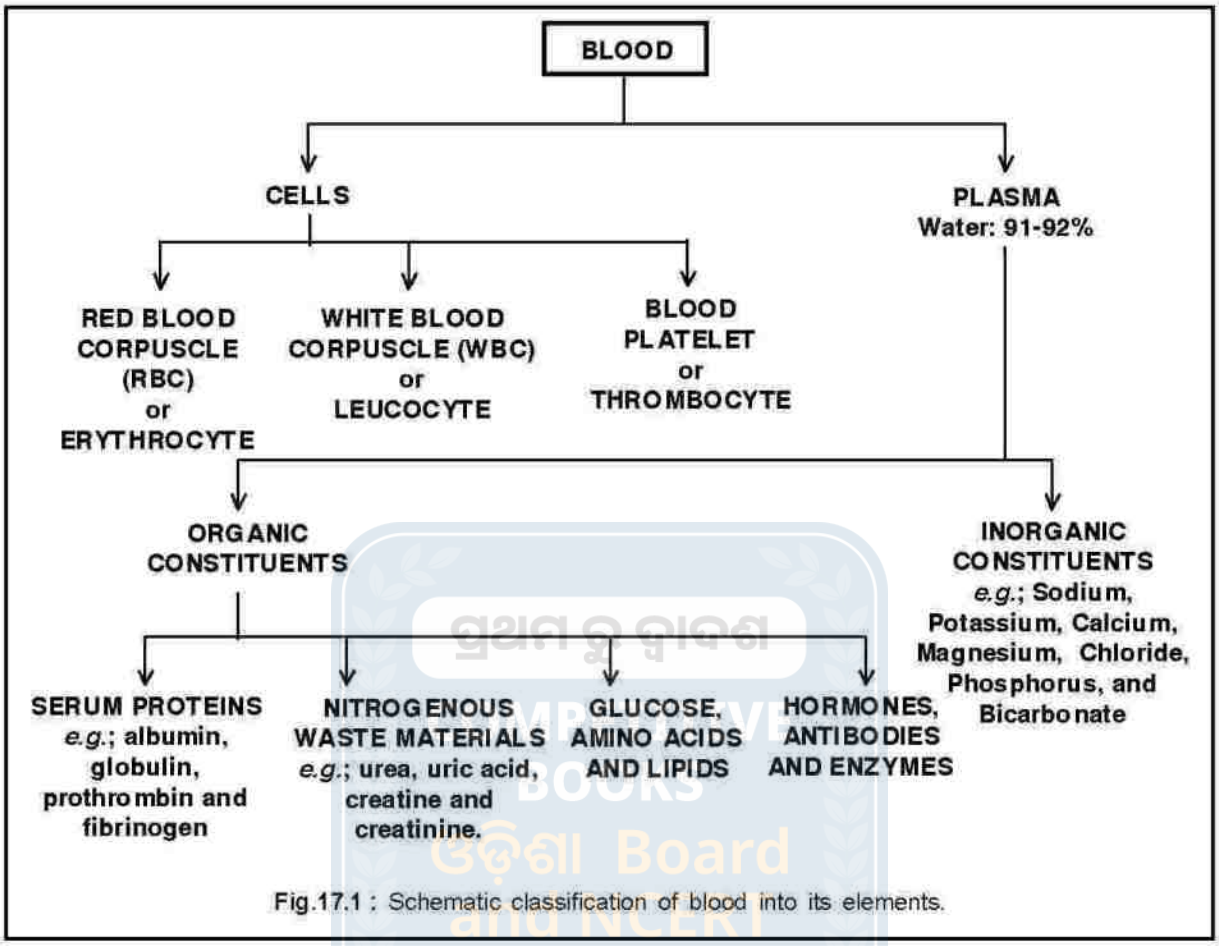


Fig.17.1 : Schematic classification of blood into its elements.

accounts for the remaining 55%. The total blood volume of an average person is approximately 5.5 L. If the hematocrit is taken as 45%, then : Total erythrocyte volume = 0.45 × 5.5 L = 2.5 L

Therefore, The plasma volume = 5.5 L – 2.5 L = 3.0 L

17.1.1. Plasma :

The plasma is a straw yellow coloured watery fluid containing many dissolved solutes. The water makes up 91-92% of the plasma. The rest are solutes, which are classed as: (1) **organic (colloids)** and (2) **inorganic (crystalloids)**. The organic constituents include 7-9% **plasma proteins**, such as **albumins**, **globulins**, **prothrombin** and **fibrinogen**. Albumins are produced by the liver and these help maintain the blood volume and pressure. Globulins are of three types : a, b and g. The a and b globulins are produced by the liver and help in transporting lipids and fat soluble vitamins. g globulins are produced by B-lymphocytes, which function as antibodies. Other proteins of the plasma are prothrombin and fibrinogen, which help in blood clotting or coagulation. Other organic constituents of the plasma are nutrients, such as glucose, amino acids and lipids; nitrogenous excretory wastes, such as urea, uric acid, creatine and creatinine; and hormones and enzymes. The straw yellow colour

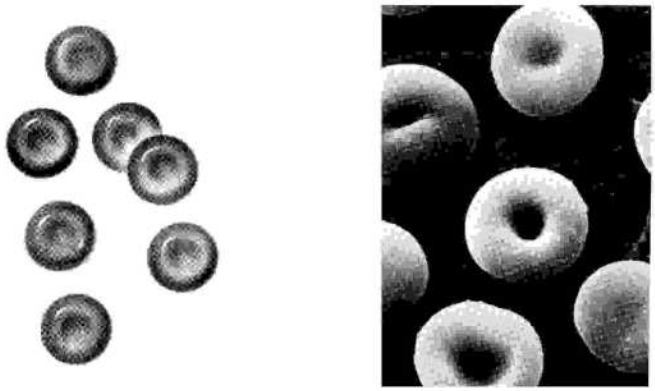


Fig.17.2 : Structure of human erythrocytes (RBCs). (a) Biconcave disc-shaped erythrocytes; (b) Scanning electron micrograph of human erythrocytes

of the plasma is due to the presence of substances, such as **bilirubin** and **carotene**. The inorganic constituents are ions of sodium, potassium, calcium, magnesium, phosphate and bicarbonate. The plasma that has been in equilibrium with RBCs, is slightly alkaline with a pH in the range of 7.35-7.45. A constant plasma volume is essential for normal functioning of the body. If the body loses water, the plasma becomes concentrated. This is detected by the osmoreceptors in the hypothalamus, resulting in the release of antidiuretic hormone (ADH) from the posterior pituitary. This hormone increases thirst and consequently intake of water and promotes water retention by the kidneys. This is a regulatory mechanism to maintain homeostasis of the plasma volume. Following the coagulation of the blood, a clear watery fluid, known as **serum**, oozes out from the wound. The serum is that part of plasma without fibrinogen and clotting factors II, V and VIII, which have been removed during the clotting reaction. The schematic classification of the blood into its constituents is presented in Fig.17.2.

17.1.2. Formed elements (Cells or Corpuscles) :

The blood has three types of formed elements or cells: erythrocytes or red blood corpuscles (RBCs); leucocytes or white blood corpuscles (WBCs); and thrombocytes or platelets.

(a) Erythrocytes (RBCs) : Erythrocytes of human are biconcave disc-like cells without nuclei and mitochondria (Fig.17.2). They lose their nuclei before entering the circulation. Due to the absence of mitochondria, they obtain energy by anaerobic respiration. An erythrocyte measures about 7 µm in diameter and 2.0 µm in thickness (1 µm = 10^{-6} m = 10^{-3} mm). The average number of erythrocytes is 5.5 millions/µL (1 µL = 1 mm^3) in a healthy adult man and 4.5 millions/µL in a woman. It survives in the circulation for an average of 120 days.

When suspended in a suitable medium, the erythrocytes pile up one above the other forming **rouleaux**. The erythrocytes maintain their normal shapes as long as they are

suspended in an isotonic medium. When the medium becomes hypotonic, the cells absorb water by **endo-osmosis** and swell up and ultimately burst releasing the haemoglobin into the medium [Fig. 17.3 (a)]. This phenomenon is known as **haemolysis**. Haemolysis results in the formation of ruptured erythrocyte plasma membranes, known as **red cell ghosts**. Alternately, if the erythrocytes are placed in a hypertonic solution, there is a loss of water from the cells due to **exo-osmosis** and consequently, the cells shrink developing irregularities at their surfaces. This phenomenon is known as **crenation** and the shrunken erythrocytes are known as **echinocytes** [Fig. 17.3(b)].

Fig.17.3 : Abnormal shapes of erythrocytes. (a) Swollen erythrocytes in hypotonic medium and (b) Echinocytes in hypertonic medium.

RBCs are so named due to the presence of a red coloured respiratory pigment, known as **haemoglobin**. Each erythrocyte contains 29 pg (pico gram; 1 pg = 10^{-12}g) of haemoglobin and thus, all the erythrocytes will contain 900 g of haemoglobin. The haemoglobin content of the blood must be maintained at a normal for normal respiratory function. Following senescence and death of RBCs, the heme iron is recycled in the liver and travels in the blood to the bone marrow, conjugated to a protein carrier, **transferrin**. Haemoglobin is a **conjugate protein** *i.e.*, a protein part, known as **globin** is conjugated to a non-protein part or prosthetic group, known as **heme**. The globin consists of two each of a and b polypeptides. The heme consists of four sub-units. Each sub-unit contains a porphyrin or tetra-pyrrole ring. There is an iron atom in ferrous valency state (Fe^{2+}) at the centre of the porphyrin. It is the element, iron that imparts a red colour to the haemoglobin. The Fe^{2+} is attached by four co-ordinate bonds to the four pyrrole rings and by two more co-ordinate bonds to the globin (α or β) chain (Fig.17.4). One of the co-ordinate bonds, by which it is attached to the globin chain, is displaced by molecular oxygen and consequently, oxyhaemoglobin is formed. Due to its oxygen carrying function, haemoglobin is known as a **respiratory pigment**. The haemoglobin, containing two each of a and b globin chains is termed as **adult haemoglobin** (**haemoglobin A**). The b globin chain in 25% of adult haemoglobin is substituted by d globin

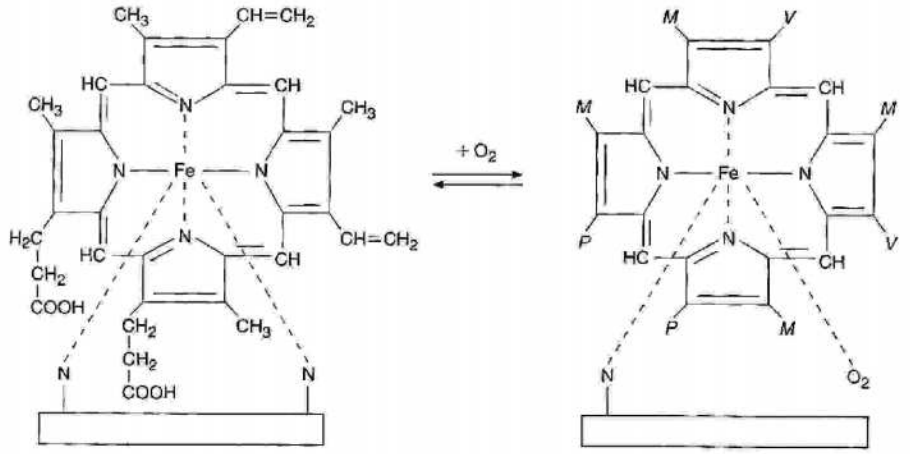


Fig.17.4 : Structure of human haemoglobin. (a) Deoxyhaemoglobin; (b) Oxyhaemoglobin.

Erythrocyte abnormality :

A normal number of erythrocytes is required for normal functioning. However, under situations, the number increases or decreases. An increase in number gives rise to a condition, known as, ***polycythemia****, while a decrease leads to a fall in the haemoglobin content of the blood, a condition, known as* ***anemia****. Anemia is of several types :*

Aplastic anemia **:** *Destruction of bone marrow stem cells by chemicals, such as benzene, arsenic and radiation.*

Microcytic anemia **:** *The erythrocytes remain smaller and hence, contain less haemoglobin than normal.*

Haemolytic anemia **:** *Excessive destruction of erythrocytes.*

Pernicious anemia **:** *Sub-normal absorption of vitamin B_{12} (cyanocobalamine) from the intestine due to a lack of intestinal protein, intrinsic factor, which assist in its absorption. Vitamin B_{12} helps in erythrocyte formation.*

Hereditary spherocytosis **:** *Absence of an erythrocyte cytoskeletal protein, ankyrin, leads to a spherical shape of erythrocytes, instead of the default biconcave shape. Such spherical erythrocytes squeeze and rupture spontaneously, leading to a loss of haemoglobin, a condition known as* ***hereditary hemolytic anemia****. It is an autosomal recessive disorder.*

Sickle cell anemia **:** *The haemoglobin is abnormal due to an amino acid substitution in the b-globin chain. The erythrocytes remain sickle shaped and the haemoglobin has a reduced oxygen carrying capacity. It is an autosomal recessive disorder.*

chain. In fetus, however, the b globin chains are substituted by g chains. This haemoglobin has been referred to as **fetal haemoglobin (haemoglobin F)**.

Each sub-unit of haemoglobin molecule binds to a molecule of oxygen. Thus, a complete deoxyhaemoglobin molecule binds to four molecules of oxygen at saturation. However, all the four molecules do not bind at once. In the first step, one molecule binds and this facilitates the binding of the second and so on. This type of binding is known as **co-operative** or **allosteric binding**.

(b) Leucocytes (WBCs) : Leucocytes (WBCs) are nucleated blood cells of variable shapes and sizes. These are so named because of the absence of pigments. The number

*There are two types of inherited disorders of haemoglobin production in human: **haemoglobinopathies** and **thalasemias**.*

*In **haemoglobinopathies**, abnormal polypeptides are produced. Mutant genes encode abnormal polypeptides, which make the haemoglobin abnormal. Many abnormal haemoglobins have been described in human. These are identified by alphabets, such as C, E, I, J, S, etc.*

*In **thlasemias**, the polypeptides are normal. However, there is a decresed synthesis of α- or β-globin. Accordingly, the disorder is either named as **α-thalasemia** or **β-thalasemia**.*

of leucocytes in a healthy human adult is in the range of 4,000-10,000/μL of blood. Under special pathological conditions, the number varies considerably. The increase in the number above normal is known as **leucocytosis**, while a decrease below normal is **leucopenia**. In an acute condition, known as **leukemia**, there is an uncontrolled release of a large number of immature leucocytes into the circulation.

Leucocytes are primarily classified as **granulocytes** or **polymorphonuclear leucocytes (PMNs)** and **agranulocytes** based on the presence or absence of characteristic granules in the cytoplasm. Based on the staining properties of the cytoplasmic granules, the granulocytes are of three types : **neutrophils**, **eosinophils** or **acidophils** and **basophils**. Agrnulocytes do not contain any granule in their cytoplasm. They are of two types: **lymphocytes** and **monocytes**. Each type of leucocyte has a specific percentage of occurrence in the blood (Table 17.1). Any serious deviation of the percentages points towards a pathological condition.

(i) Neutrophil [Fig.17.5 (a)] : The name is derived from the neutral staining properties of the cytoplasmic granules. It is characterized by the presence of a **multi-lobed nucleus**. In human female, the nucleus is seen to possess an additional smaller lobe at one end. This lobe is known as **drum stick**. The drum stick stains relatively darker and is considered as having the inactivated X chromosome (Barr Body). Neutrophils have a very short life span.

They circulate in the blood for approximately 10 hr and then enter into the connective tissue, where they live for another 2-3 days. These are attracted by chemotactic factors, secreted by bacteria at the site of infection. They leave the circulation by piercing through two adjacent endothelial cells of the capillary and enter into the connective tissue harbouring bacteria. This phenomenon is known as **diapedesis** or **extravasation**. They, then, turn into **phagocytes** and engulf and digest the bacterial cells.

(ii) Eosinophil (Acidophil) [Fig.17.5 (b)] : The name of this granulocyte is derived from the acidic staining property of the cytoplasmic granules. The granules preferably stain with eosin, an acidic dye. **The nucleus is bilobed** They have a short life span. They circulate

Table - 17.1

Number range and relative percentages of different corpuscles

Cell	Cells / µL	Approximate Normal Range/µL	%
Erythrocytes (Male)	5.5×10^6	—	—
Erythrocytes (Female)	4.5×10^6	—	—
Leucocytes	8,000	4,000-10,000	—
Granulocytes			
Neutrophils	5,400	3,000-6,000	50-70
Eosinophils	275	150-300	1-4
Basophils	35	0-100	0.4
Agranulocytes			
Lymphocytes	2750	1,500-4,000	20-40
Monocytes	540	300-600	2-8
Platelets	300,000	200,000-500,000	—

in the blood for around 10 hr and then migrate to the connective tissue by the same phenomenon of diapedesis and stay there for up to 10 days. Eosinophils are phagocytic cells having an affinity for antigen-antibody complexes, formed at the site of inflammation. They also migrate to the site of parasitic infection and specifically kill, engulf and digest helminth larvae. They are, especially abundant in the mucosa of the gastro-intestinal, respiratory and urinary tracts, where they defend against parasites.

(iii) Basophil [Fig.17.5 (c)] : This granulocyte has cytoplasmic granules having basic staining property. **The nucleus is bilobed.** They have a short life span and a negligible percentage in the blood. Their function is similar to that of a **mast cell**.Basophils store **histamine** and **heparin**. Release of histamine causes inflammation (allergic reaction) and vascular changes, which lead to fluid leakage from blood vessels. This causes severe **hypersensitivity** responses and **anaphylaxis**.

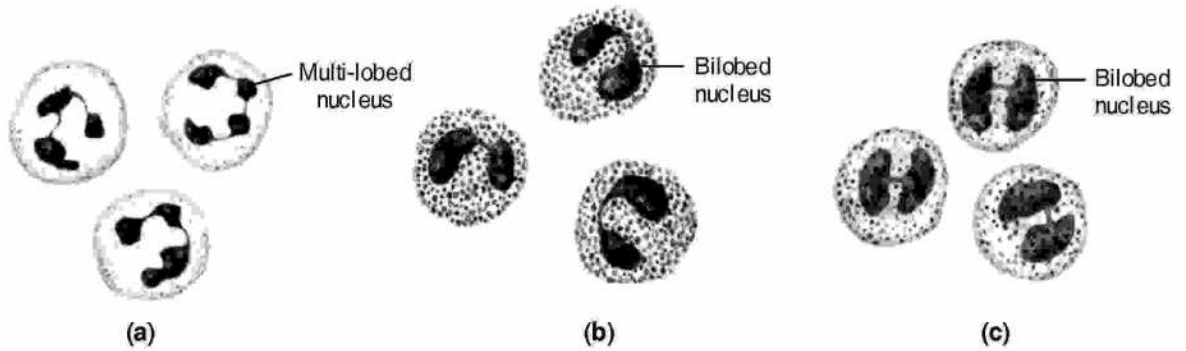


Fig. 17.5 : Structure of granulocytes. (a) Neutrophils; (b) Eosinophils (Acidophils); and (c) Basophils

(iv) Lymphocyte [Fig.17.6 (a)] : Lymphocytes have variable life spans, ranging from several days to months. A lymphocyte is characterized by the presence of an **indented nucleus**. They play a key role in the immune response of the body. Lymphocytes mature and become immunologically competent cells in the thymus and Bursa of Fabricius or its analogous structures. Thymus maturing lymphocytes are known as T-lymphocytes, while lymphocytes maturing in the Bursa of Fabricius are known as B-lymphocytes. T-lymphocytes act as killer or cytotoxic cells, killing pathogenic microorganisms and other alien cells entering into the body. They also help B-lymphocytes mature into antibody secreting plasma cells.

(v) Monocytes [Fig.17.6 (b)] : There is no cytoplasmic granule. **The nucleus is horse shoe shaped**. They live in the blood circulation for 2-3 days. Then they move into the connective tissue, where they live for a few months. In the connective tissue, monocytes become **phagocytes**. At the site of infection, monocytes differentiate as **tissue macrophages**, which then destroy bacteria, foreign particles and cellular debris.

(c) Thrombocytes (Platelets) : Thrombocytes or platelets are small anucleate oval or disc shaped granulated bodies, measuring 2-4 µm in diameter. These are pinched off from a giant cell in the bone marrow, known as **megakaryocyte**. Thrombocytes are second most numerous among the formed elements of the blood. The number ranges from 200,000-

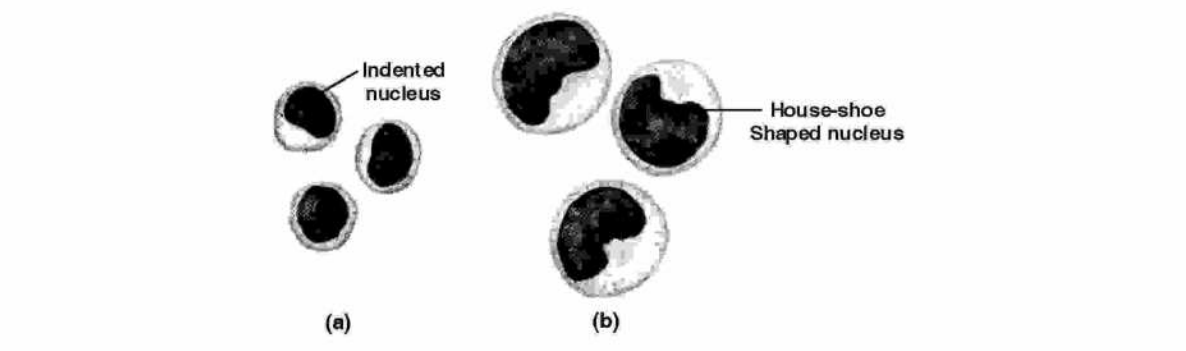


Fig.17.6 : Structure of agranulocytes. (a) Lymphocytes; and (b) Monocytes

500,000/µL of circulating blood. The life span is about 10 days. Each platelet has a ring of microtubules around the periphery. The cytoplasm is granular containing actin, myosin, glycogen, lysosomes and two types of granules. Some granules contain blood clotting factors and a growth factor, known as **platelet derived growth factor** (PDGF). PDGF promotes wound healing and mitotic divisions in the smooth muscle of the blood vessels. Platelets play a very important role in blood clotting. They contain an essential enzyme, **thromboplastin** that is essential in initiating the blood clotting cascade, ending in the formation of **fibrin mesh**. More than the normal number of platelets (thrombocytes) causes a pathological condition, known as **thrombocytosis**. Deficiency of platelets is known as **thrombocytopenia**, which leads to prolonged bleeding, following a minor injury.

Hematopoiesis :

Blood cells are continuously formed by a process known as **hematopoiesis** (also called **hemopoiesis**). The stem (undifferentiated) cells, which differentiate as blood cells originate in the yolk sac and then migrate to the liver. Thus, liver functions as the hematopoietic organ of the fetus.. These stem cells then migrate to the bone marrow. The liver ceases to function as the hematopoietic organ soon after birth. Thereafter, the bone marrow manufactures different kinds of blood cells till death.

Erythropoiesis refers to the formation of erythrocytes, while leucopoiesis to leucocytes. Similarly, thrombopoiesis refers to the formation of thrombocytes.

All blood cells descend from a single population of bone marrow stem cells, known as **pluripotent stem cells**. Thus stem cells are uncommitted cells, which divide and redivide to form new stem cells or become committed to a specific developmental pathway, leading to the formation of a particular type of blood cell. The first commitment is **dichotomous** *i.e.*, some stem cells are committed to becoming **lymphoid stem cells** and others **myeloid stem cells**. The lymphoid stem cells differentiate as lymphocytes, while the myeloid stem cells as the rest of the blood cells. At some point, the myeloid stem cells become committed to differentiate along one pathway, giving rise to a particular myeloid cell type.

The commitment is believed to be effected by several growth factors, collective called **hematopoietic growth factors**. These factors fall under four classes : **erythropoietin**, **colony stimulating factors**, **interleukins** and **thrombopoietin**. As the stem cells proliferate and differentiate, they express specific membrane receptors for growth factors. A specific growth factor binds to its receptor and thus stimulates the cell to differentiate along a specific line. The earliest cells, which can be distinguished under a microscope are the **erythroblasts** (become erythrocytes); **myeloblasts** (become granular leucocytes); **lymphoblasts** (become lymphocytes);and **monoblasts** (become monocytes).

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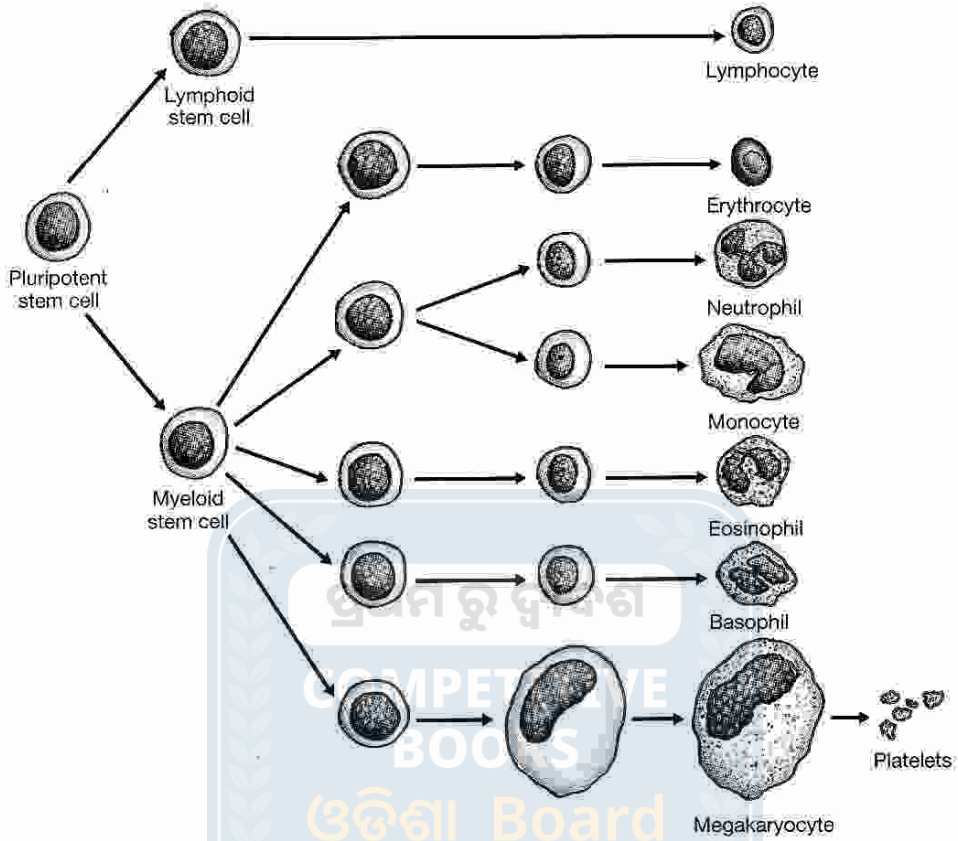

Haematopoiesis (haemopoiesis) of the formed elements (blood cells) in human.

Erythropoiesis is an extremely active process. It is estimated that about 2.5 million erythrocytes are produced every second in order to replenish the worn out and destroyed erythrocytes by the spleen and liver. The life span of an erythrocyte is 120 days. Erythropoiesis is regulated by the hormone **erythropoietin, secreted by the kidney**. The erythropoietin gene has been cloned and expressed by recombinant DNA technology and erythropoietin has been commercially synthesized. It is now commercially available for the treatment of anemia.

The formation of leucocytes is stimulated by biochemical agents, called **cytokines**. These cytokines fall under two classes: colony stimulating factors, such as **granulocyte colony stimulating factor (G-CSF)** and **granulocyte-macrophage colony stimulating factors (GM-CSF)**; and **interleukins (IL)**.

A specific cytokine, called **thrombopoietin** has also been identified. It stimulates a megakaryocyte to form a large number of platelets. This cytokine has commercially been prepared by recombinant DNA technology. It has been used to treat thrombocytopenia (low platelet count).

Bone marrow transplantation :

In some people, the bone marrow stem cells fail to form the normal number of blood cells, which leads to serious consequences like anemia, leukemia and immunodeficiencies. In these situations, bone marrow transplantation is the effective treatment. It involves the aspiration of marrow from the iliac crest and separation of the hematopoietic stem cells. Stem cells are also isolated from the peripheral blood of the donor, injected with G-CSF and GM-CSF. Another source of the stem cells is the umbilical cord of a neonatal baby. These cells are stored and used as and when necessary.

The stem cells are implanted into the bone marrow and necessary stimuli are given for their appropriate differentiation.

17.2. LYMPHATIC SYSTEM :

The lymphatic system is a network of **lymph capillaries**, **lymph vessels** and **lymph nodes**, through which a fluid, derived from the interstitial (tissue) fluid circulates. The amount of fluid, filtered from the blood into the surrounding tissues through the endothelial wall of the capillaries is known as the interstial or tissue fluid. This fluid needs to be reabsorbed back into the blood in order to maintain the osmolality of the blood so that the blood volume and blood pressure are maintained at an optimum level. Indeed, a part of it is reabsorbed. However, the remaining part i.e. 4 L is absorbed and returned to the cardiovascular system through the lymphatic system.

Like blood capillaries, the lymphatic capillaries are endothelium lined very narrow vessels, present in the interstitium of all organs and tissues (Fig.17.8). But, unlike blood capillaries, these are closed-ended i.e. these are not drained by vessels. The lymphatic capillaries join to form lymphatic vessels, which join to form two large lymphatic vessels, one of which is known as the the **right lymphatic duct** or **thoracic duct**. These ducts finally drain the lymph into the **right** and **left sub-clavian veins**, respectively (Fig.17.7). Structurally, the lymph vessels resemble the veins i.e. each has the same three-layered organization provided with valves at regular intervals to regulate unidirectional flow of the lymph. Before draining into the veins, the lymph is filtered in lymph nodes. The lymph node is a lymphoid tissue that contains lymphocytes, which locate and destroy pathogens, if any, present in the drained lymph.

There is no pumping organ for the circulation of lymph. The contractile tunica media, made by smooth muscle, contracts and propels the lymph forward. The backward flow is prevented by the prence of valves in the lymph vessels periodically.

Sometimes, the lymph vessels are occluded by parasites, consequently blocking the normal flow of the lymph. This results in the accumulation of excess interstitital fluid in the tissues and organs, causing massive swellings, known as **oedema** or **edema**. The commonest example is massive nodular tissues formed by the occluded lymphatic vessels by microfillariae of filarial worm. This condition is termed as **elephantiasis**.

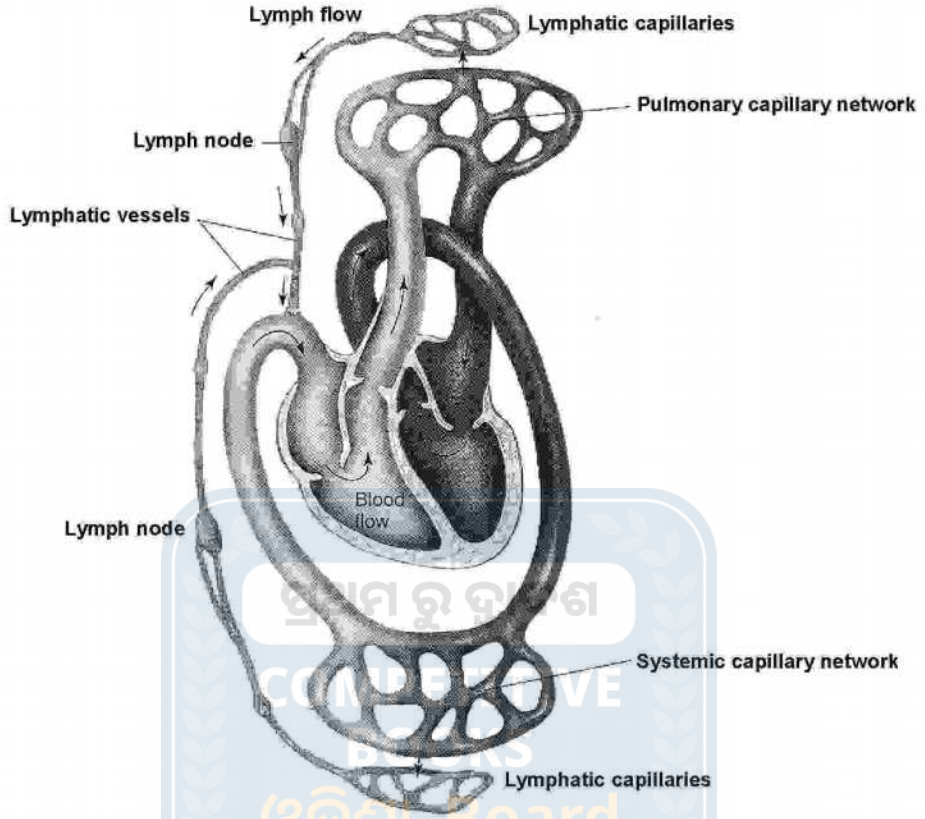

Fig.17.7 : Structure of the lymphatic system in close association with the cardio-vascular system.

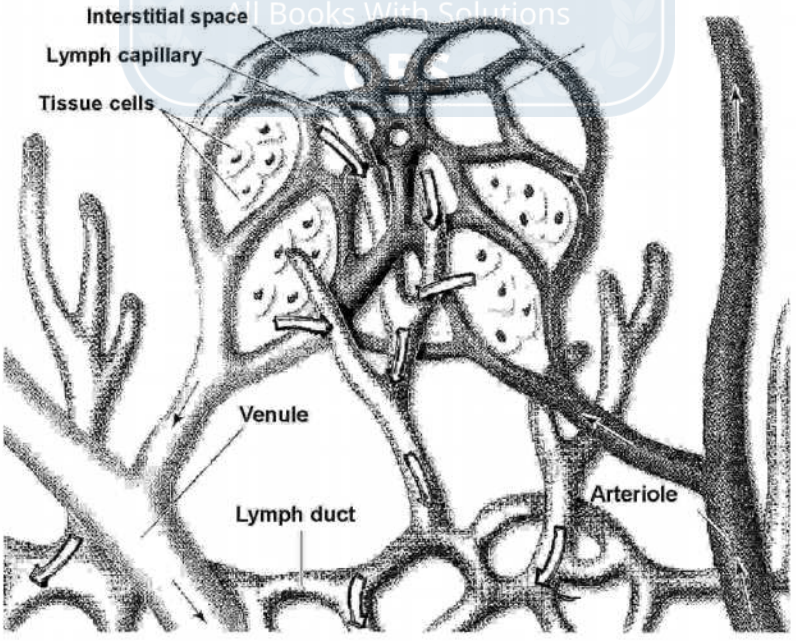

Fig.17.8 : Relationship between blood and lymph capillaries in the tissue interstitium.

(g) Atrial Natriuretic Peptide: A rise in the blood volume leads to an augmented urine formation. Increased urine formation is coupled to an **increased excretion of Na^+ in the urine (natriuresis)**. A natriuretic peptide is produced by the atria of the heart, which promotes the excretion of Na^+ and water in the urine in response to a rise in the blood volume. It, thus, lowers the blood volume and pressure. It antagonizes ADH, angiotensin II and aldosterone.

17.3. BLOOD GROUPS :

All cells of an individual bear, on their surfaces, characteristic molecules, which help them to identify as belonging to self. Any cell that bears a molecule of a different configuration is identified as **foreign** or **alien**. If, by chance, this foreign cell enters into the body of the individual, the immune system checks its surface, marks it as foreign and then destroys it. These surface molecules are known as **antigens** and are used as passport by all the cells of an individual. The cells bearing antigens of differing configuration are considered as foreign or from another individual. This is an important **biological basis of individuality**. Erythrocytes or red blood cells also bear surface molecules, which are known as **blood group antigens** or **agglutinogens**. The serum bears molecules, which are compatible with the blood group antigens. These are known as **antibodies** or **agglutinins**. Compatibility refers to the absence of an immune response. There are two main systems of human blood grouping: ABO system and Rh system.

Table - 17.2
Red cell surface antigens and compatible serum antibodies and genotypes in the ABO system

Blood Group	Red Cell Surface Antigen	Serum Antibody	Allelic Combination (Genotype)
A	A	Ani-B	I^AI^A and I^Ai
B	B	Anti-A	I^BI^B and I^Bi
AB	Both A and B	None	I^AI^B
O	None	Both Anti-A and Anti-B	ii

17.3.1. ABO System :

Karl Landsteiner (1901) found that reactions between red cell antigens of one sample of blood and serum antibodies of another sample caused the red cells to clump together, causing adverse reactions in recipients. He was able to identify three blood groups : A, B and C (C later was termed as O), based on the surface antigens of red cells. Two of his coworkers, **Alfred von Decastello** and **Adriano Sturli (1902)** added the fourth group, AB to the list. These findings led to blood group classification in the ABO system as A, B, AB and O.

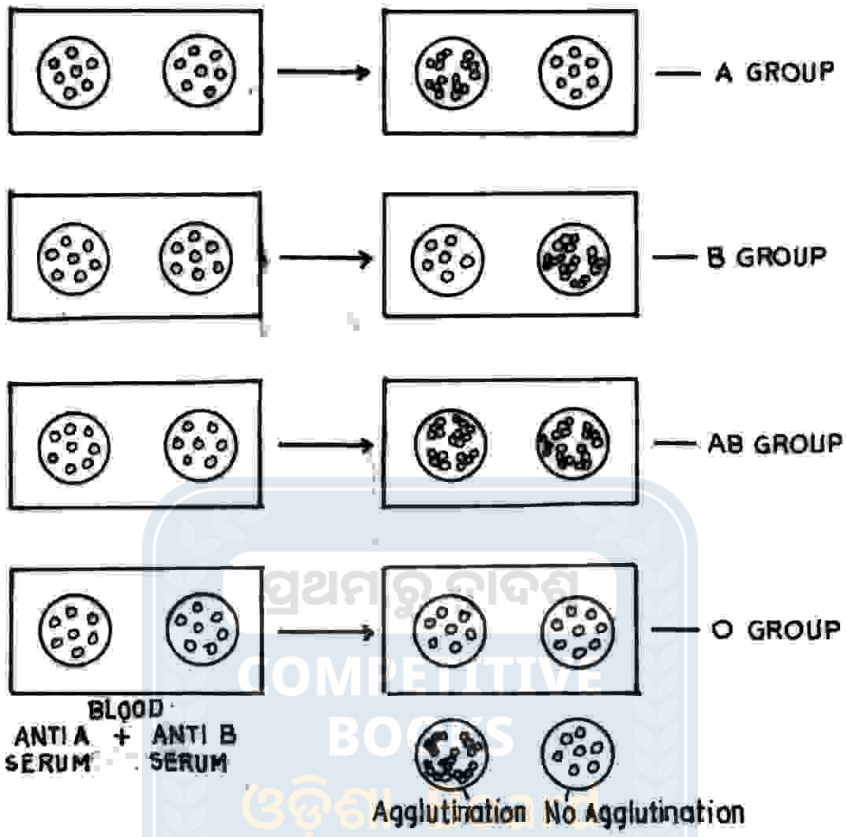

Fig.17.9 (a-d) : Blood transfusion reactions in the ABO system.

There are only two types of blood group antigens, such as A and B and two types of antibodies in the serum, such as anti-A and anti-B in the human population. A blood group may have A or B or both A and B or neither A nor B antigens on the surface of red cells. Similarly, the serum may have anti-B or anti-A or neither anti-A nor anti-B or both anti-A and anti-B antibodies. Table 17.2 summarizes the presence of red cell surface antigens and compatible Serum antibodies of the four types of blood groups in the ABO system.

(a) Transfusion Reaction :

Prior to blood transfusion, a cross-match is made by mixing the serum of the recipient and the blood cells of the donor. If the types do not match, for example the donor is type A and the recipient is type B, the recipient's serum antibody (anti A), will react with the red cell surface antigen (A) of the donor, in an antigen-antibody reaction forming a **clump** or **agglutinate**. From the agglutination reaction (Fig. 17.9), it is evident that a person possessing the blood group O is a **universal donor**, while a person with blood group AB is a **universal recipient**.

(b) Genetics of ABO system :

The blood group antigens are inherited in a dominant manner. Antigen A is expressed by the **dominant allele I^A**, while antigen B by the **dominant allele, I^B**. Both the alleles are dominant to the allele for O, i (lower case letter since the allele is recessive). Each person inherits two alleles, one from each parent. Thus, A and B have two allelic combinations, I^AI^A and I^Ai for antigen A and I^BI^B and I^Bi for antigen B. AB and O antigens have one combinations each, such as I^AI^B and ii, respectively (Table 17.2).

17.3.2. Rh Factor (Fig. 17.10) :

Alexander S. Wiener (**1937**) discovered another group of antigens, which are found on red cells of most people. This was named as the Rh factor. The notation, Rh is derived from rhesus monkey, in which these antigens were first discovered. There are a number of antigens in this group, such as C, D and E. However, the **antigen, D** is termed as Rh antigen and is important for its clinical significance. **If D antigens are present on the red cell surface of a person, the person is considered as Rh positive** and **if absent, the person is Rh negative.**

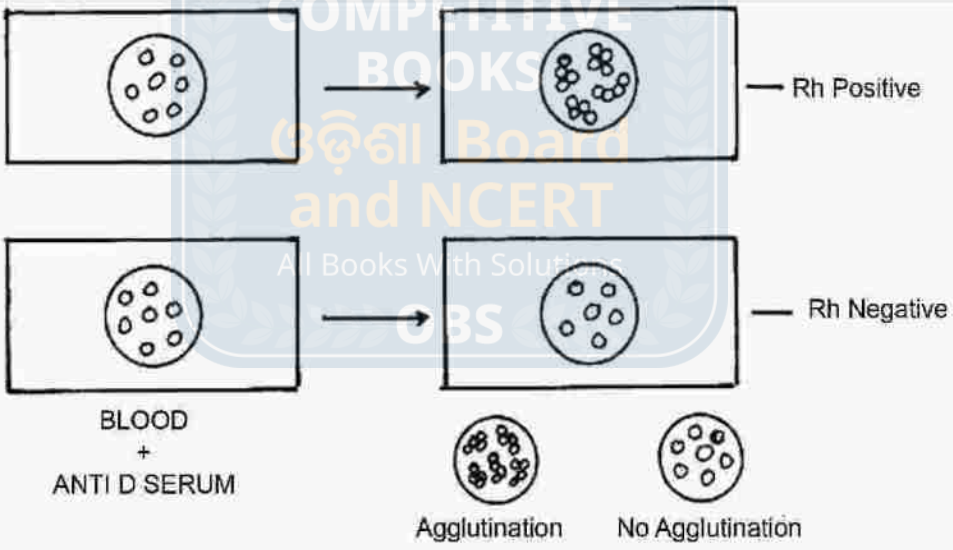

Fig.17.10 : Blood transfusion reactions in the Rh system.

The Rh factor is of particular significance, when Rh negative woman conceives and gives birth to Rh positive baby. The blood of the mother and the baby are normally kept apart by the placental barrier and hence, do not mix during the pregnancy period. Thus the Rh negative mother is not exposed to the Rh antigens. However, an exposure may occur at the time of birth. Consequently, the Rh negative mother's immune system may be sensitized and anti-Rh antibody may be synthesized. If the mother conceives Rh positive baby subsequently thereafter, the anti-Rh antibody may cross the placental barrier and enter into the fetal circulation. These antibodies react with the Rh antigen, present on the red cell surface of the

fetus and result in the clumping of the fetal red cells by antigen-antibody reaction. This causes haemolysis of the red cells of the fetus. The fetus is born, either dead or live and anemic with a condition, called **erythroblastosis fetalis** or **hemolytic disease of the new born**.

Erythroblastosis fetalis is prevented by injecting the Rh negative mother with an antibody preparation against the Rh antigen (**RhoGAM** is the trade name for this preparation). This preparation is injected within 72 hr after the birth of each Rh positive baby. This is a type of **passive immunization**, in which the antibodies inactivate the Rh antigen and thus prevent the mother from becoming **actively immunized** to them.

17.4. BLOOD CLOTTING (COAGULATION) :

The circulatory system has an intrinsic mechanism of preventing excess loss of blood from an injured part of the body. This is done by forming a **clot** or **thrombus**. The clot is made up of a mesh of an insoluble protein, fibrin. It holds back the blood cells. A clear fluid, called **serum**, oozes out from the wound. This process of forming clots in the walls of damaged blood vessels and preventing blood loss is known as **hemostasis**. When a blood vessel is injured, a number of physiological mechanisms are activated that promote hemostasis. The collagen protein from the sub-endothelial tissue of the damaged blood vessel is exposed. This initiates three events : **vasoconstriction**; **formation of a platelet plug**; and **formation of a fibrin mesh**.

17.4.1. Mechanism of clotting :

1. As long as the endothelium of a blood vessel is intact, the platelets circulating in it, repel each other and keep away from the endothelial cells by repulsion.
2. The endothelial cells secrete **prostacyclin** [prostaglandin (PGI_2)] and **nitric oxide** (NO). These act as vasodilators and inhibit platelet aggregation.

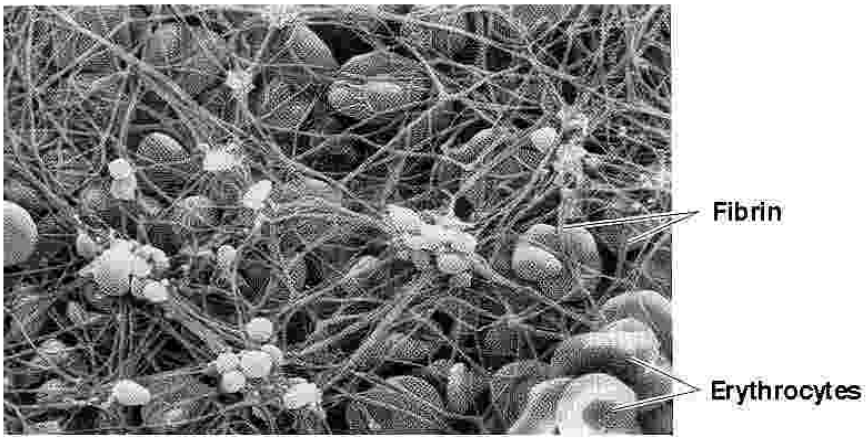

Fig.17.11 : Scanning electronmicrograph of a fibrin mesh.

3. The plasma membrane of endothelial cells has a **membrane bound enzyme, CD 39** that hydrolyzes ADP into AMP and Pi. ADP, as such, promotes platelet aggregation. The breakdown of ADP into AMP and Pi, thus, prevents platelet aggregation.

4. These are only a few protective mechanisms, which ensure that platelets do not form aggregates nor do they stick to the endothelium as long as the endothelium is intact.

5. When a blood vessel is injured, the endothelium is broken and consequently, the platelet plasma membrane bound proteins bind to collagen. This binding is facilitated by **von Willebrand's factor** (VWF), which binds to the platelet membrane on the one hand and to the collagen fibers on the other.

6. When platelets stick to collagen, they degranulate releasing **ADP**, **serotonin** and **thromboxane** A_2 (TxA_2). This phenomenon is known as **platelet release reaction (Fig. 17.12)**. ADP and TxA_2 recruit new platelets to the site, thus forming a second

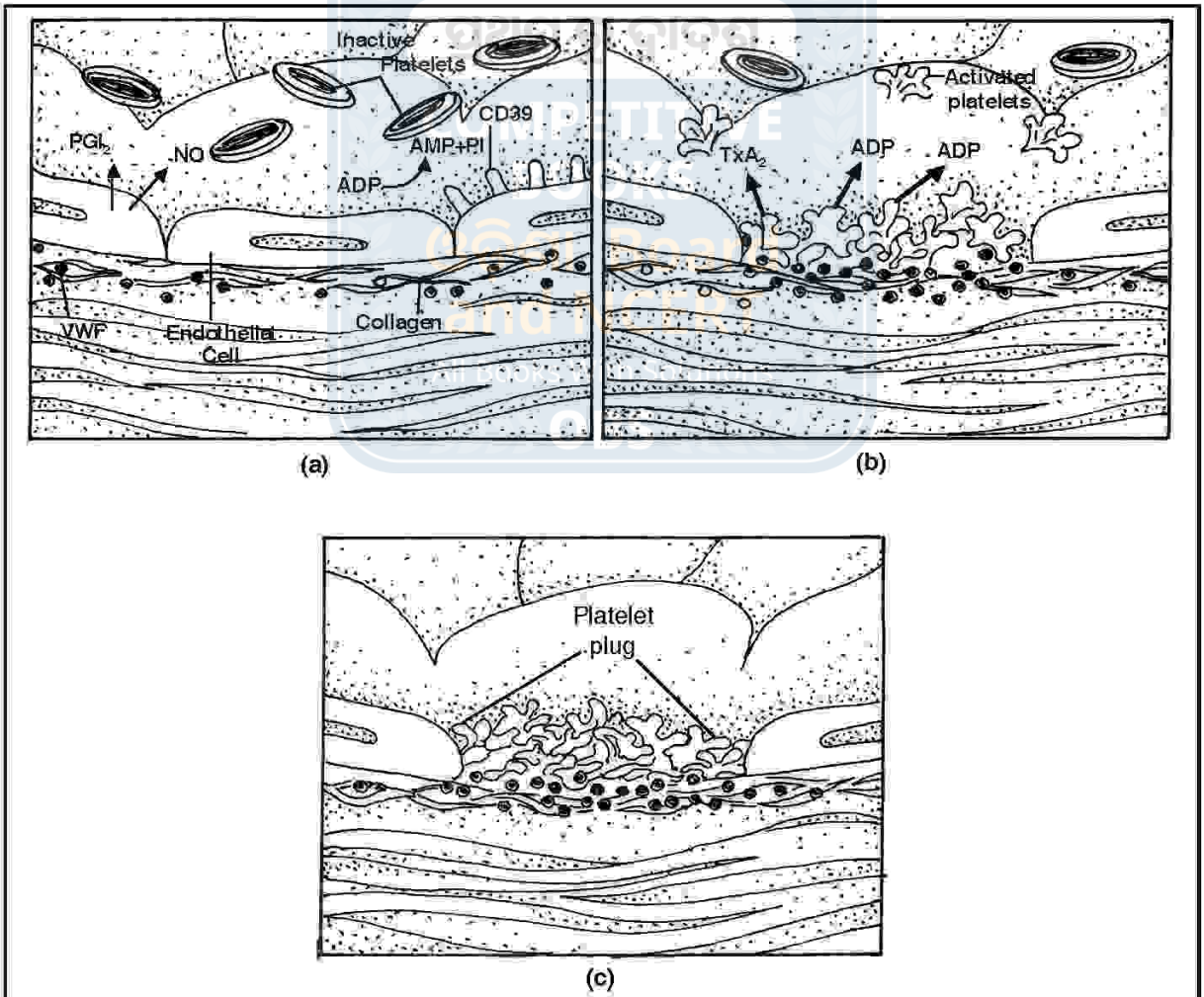

Fig.17.12 (a, b and c) : Mechanism of platelet plug formation.

layer. This second layer undergoes another platelet release reaction to form the third layer and so on. This produces a platelet plug (Fig.17.12) at the site of the injury.

7. The activated platelets then activate several plasma clotting factors in a cascade ending in soluble fibrinogen changing into insoluble fibrin mesh (Fig.17.11), which holds back the oozing out blood cells.

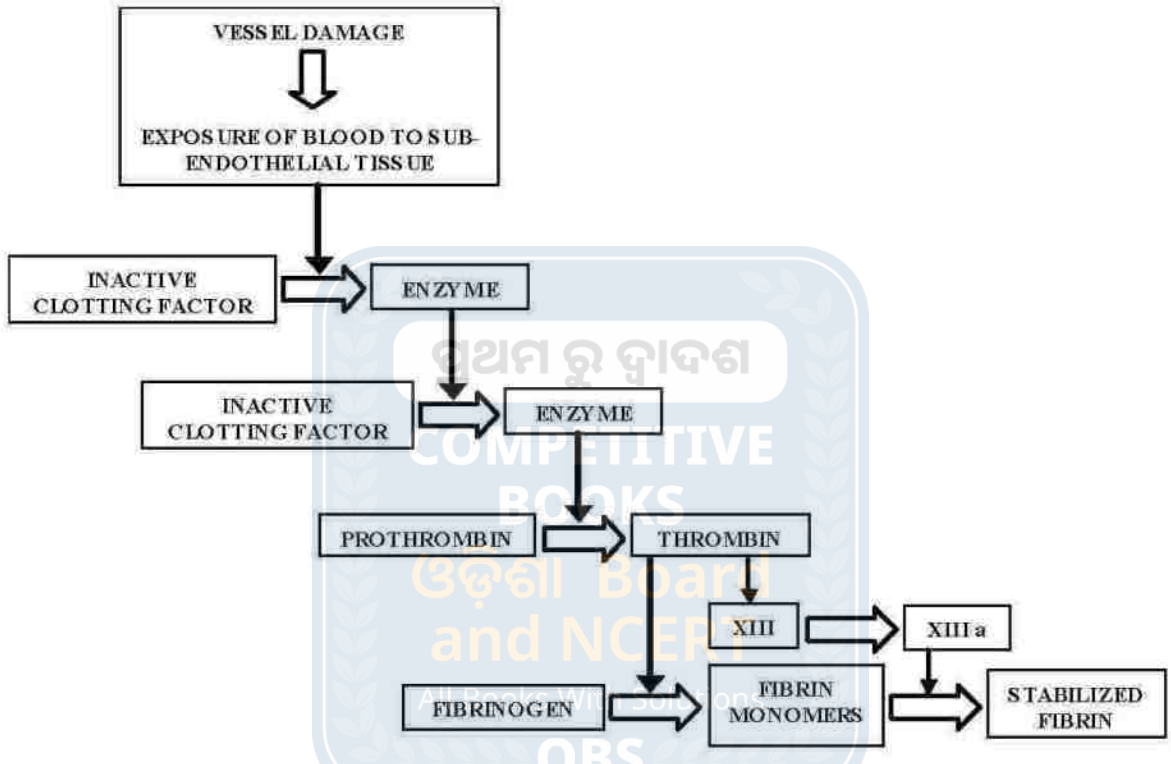

Fig.17.13 : A simplified cascade in the blood clotting reaction.

17.4.2. Plasma Clotting Factors and formation of Fibrin :

The conversion of fibrinogen into fibrin mesh occurs via either of the two pathways: **(1) intrinsic pathway** and **(2) extrinsic pathway**.

(1) Intrinsic pathway (Fig.17.14) : Blood left in a test tube will clot without the addition of any external chemical. This pathway also forms a clot in the damaged blood vessels. The pathway is initiated by the exposure of the plasma to a negatively charged surface like that of collagen at the site of a wound. The negatively charged surface is also provided by the glass surface of a test tube. This process activates a plasma protein, called factor XII (Hageman's factor). It is a protease (protein digesting enzyme). The activated factor XII activates the inactive factor XI, which activates yet another and so on. These sequential activation reactions constitute a cascade. A simplified blood coagulation cascade is presented in Fig.17.13.

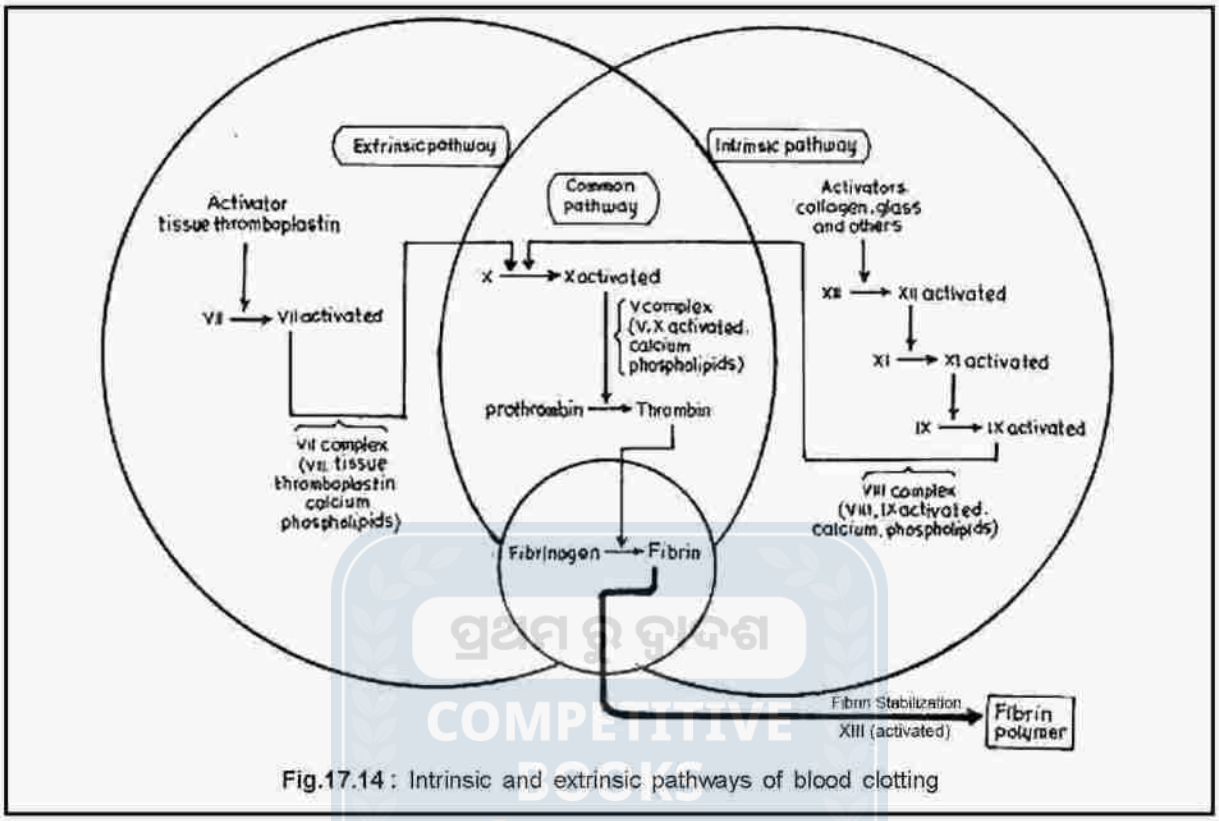

Fig.17.14 : Intrinsic and extrinsic pathways of blood clotting

In the next step, calcium ions and phospholipids convert an inactive glycoprotein enzyme, prothrombin into its active form, thrombin. In the final step, thrombin converts soluble fibrinogen into fibrin monomers. The fibrin monomers are joined forming insoluble fibrin polymers. The fibrin polymers are stabilized by the activated factor XIII. The fibrin polymer forms a mesh, supporting the platelet plug and thus prevents loss of blood.

(2) Extrinsic pathway [Fig.17.14] : In the extrinsic pathway, additional factors are required for the clot formation. For example, fibrin can be formed by a shortcut route by the release of **tissue thromboplastin** from the damaged tissue cells. The two pathways converge at the activation reaction of the inactive factor X.

17.4.3. Anticlotting mechanism :

Clotting reactions continue as long as there is a loss of blood. The moment the clot is formed and blood outflow is checked, the clotting reactions are suspended. There are several mechanisms, which prevent clotting inside blood vessels and break down any clot that is formed.

1. There is an interaction between the platelet aggregating effect of thromboxane A_2 and antiaggregating effect of prostacycline.
2. **Antithrombin III** is a circulating plasma protein, which inactivates thrombin and several other clotting factors. In order to do so, antithrombin III itself is activated by **heparin**, a substance that is present at the surface of endothelial cells.

Table - 17.3

The Plasma Clotting Factors

Clotting Factors	Name	Function
I	Fibrinogen	Converted to fibrin by thrombin
II	Prothrombin	Converted to thrombin
III	Tissue thromboplastin	Cofactor (Activator of factor VII)
IV	Calcium ions (Ca^{2+})	Cofactor (Conjugate activator of factor X and prothrombin)
V	Proaccelerin	Cofactor (Conjugate activator of prothrombin)
VII	Proconvertin	Enzyme (Conjugate activator of factor X)
VIII	Antihemophilic factor	Cofactor (Conjugate activator of factor X)
IX	Plasma thromboplastin Component (Christmas factor)	Enzyme (Conjugate activator of factor X)
X	Stuart-Prower factor	Enzyme (Conjugate activator of prothrombin)
XI	Plasma thromboplastin antecedent	Enzyme (Activates factor IX)
XII	Hageman factor	Enzyme (Activates factor XI)
XIII	Fibrin stabilizing factor	Enzyme (Stabilizes fibrin monomers into fibrin polymer)
HMW-K	High mol. Weight kininogen (Fitzgerald factor)	Activates XII to XIIa and XI to XIa
Pre-K_a	Prekallikrenin (Fletcher factor)	Inactive Kalikrenin, activated by factor XII
K_a	Kallikrenin	Activates plasminogen into plasmin.
PL	Platelet phospholipid	Activates many factors in conjunction with Ca^{2+} and other activated factors.

3. The plasma protein, **tissue factor pathway inhibitor** (**TFPI**) is a plasma protein that binds to activated factor VII complex and inhibits the formation of active factor X.

4. All endothelial cells, except those in the cerebral microcirculation produce **thrombomodulin**. It binds to thrombin. Thrombin alone activates factors V and VIII, while in combination with thrombomodulin, activates protein C. Activated protein C inactivates factors V and VIII.

5. **Plasmin** or **fibrinolysin** is the activated form of plasminogen. It is an enzyme, which lyses fibrin. However, plasminogen is present as such and when the clot formation is complete, it is activated by a protein activator, called **tissue plasminogen activator** (**tPA**). Human tPA is now produced by recombinant DNA technology and is available for clinical use.

Blood Clotting Disorders :

Many hereditary disorders occur due to the defective blood clotting factors. Three are noteworthy in this context. One is ***haemophilia A****, which is caused by the deficiency of a sub-unit of factor VIII. It is an* ***X-linked recessive disorder*** *that is prevalent in the royal families of Europe. A deficiency in another sub-unit of factor VIII results in* ***von Willebrand's disease****. In this disease, rapidly circulating platelets are unable to stick to collagen and consequently a platelet plug can not be formed. von Willebrand's disease is an* ***autosomal dominant disorder****. The deficiency of another factor, factor IX causes the inherited disorder,* ***haemophilia B*** *or* ***Christmas disease****. It is an* ***X-linked recessive disorder****. Blood coagulation factors, VIII and IX have been synthesized by recombinant DNA technology on a commercial basis and marketed for clinical use.*

6. Blood coagulation factor XII converts an inactive plasma component, **prekallikrenin** into an active **kallikrenin. Kallikrenin is an activator of plasminogen and activates it into active plasmin.** Plasmin is a protease, which acts on fibrin and dissolves it. A bacterial enzyme, **streptokinase** also activates plasminogen into plasmin. Streptokinase and tPA are injected into the general circulation to dissolve a clot or thrombus.

Types of heart :

There are two types of heart: **neurogenic** and **myogenic**. In a neurogenic heart, the muscle cells are incapable of initiating the heart beat. A group of nerve cells (ganglion) initiates the heart beat (*e.g.*; arthropods and molluscs). Conversely, in a myogenic heart, the nerve stimulation is not required for initiating the heart beat. A few localized cardiac muscle cells are specialized to initiate the heart beat. The collection of specialized cardiac muscle cells constitutes a **node**. For example, **sino-atrial (SA) node** in the right atrium of human heart initiates the heart beat (*e.g.*; vertebrates). It is known as the **pace maker**.

17.5. STRUCTURE OF HUMAN HEART (Figs. 17.15, 17.16 and 17.17) :

The heart is a conical muscular pumping organ, present in the middle mediatinum of the thoracic cavity. It is enclosed by a pericardium. The pericardium is a fibrous sac surrounding the heart and the roots of great vessels. It consists of an **outer fibrous** and an **inner serous layers.** The fibrous pericardium is a tough connective tissue outer layer that defines the boundary of the middle mediastinum. The serous pericardium, also known as the **epicardium,** consists of **outer parietal layer** and **inner visceral layer**. Both the layers are continuous at the roots of great vessels. There is a **pericardial fluid** in the space between the parietal and visceral layers. This fluid protects the heart from friction, caused during its contraction and relaxation.

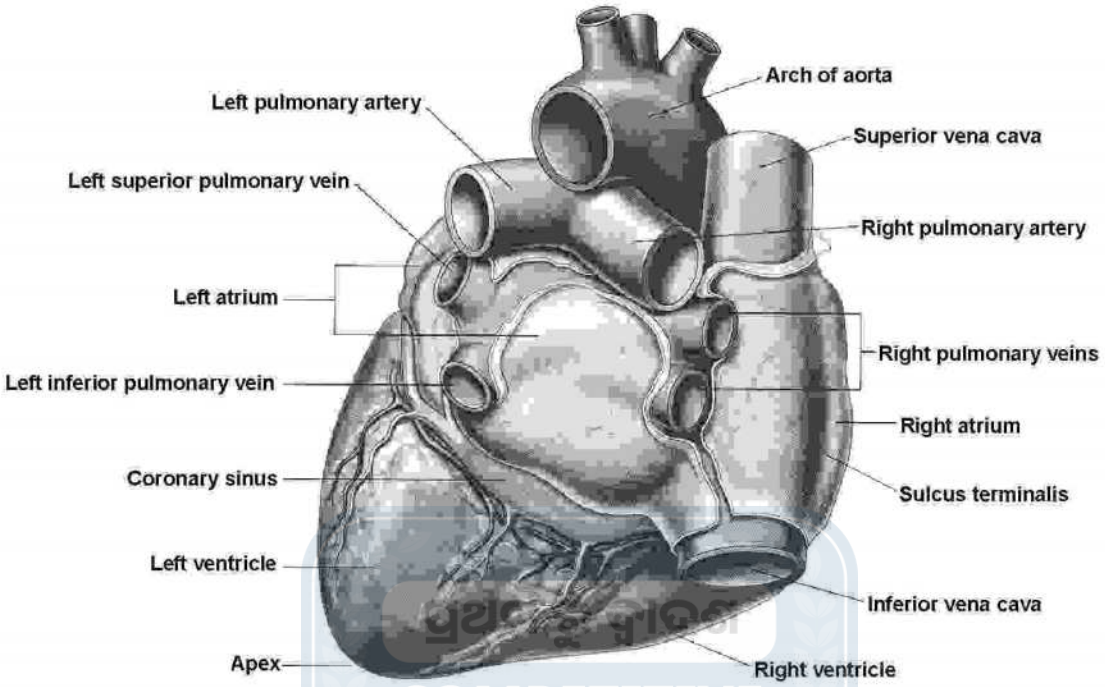

Fig.17.15 : External structure of human heart (anterior view)

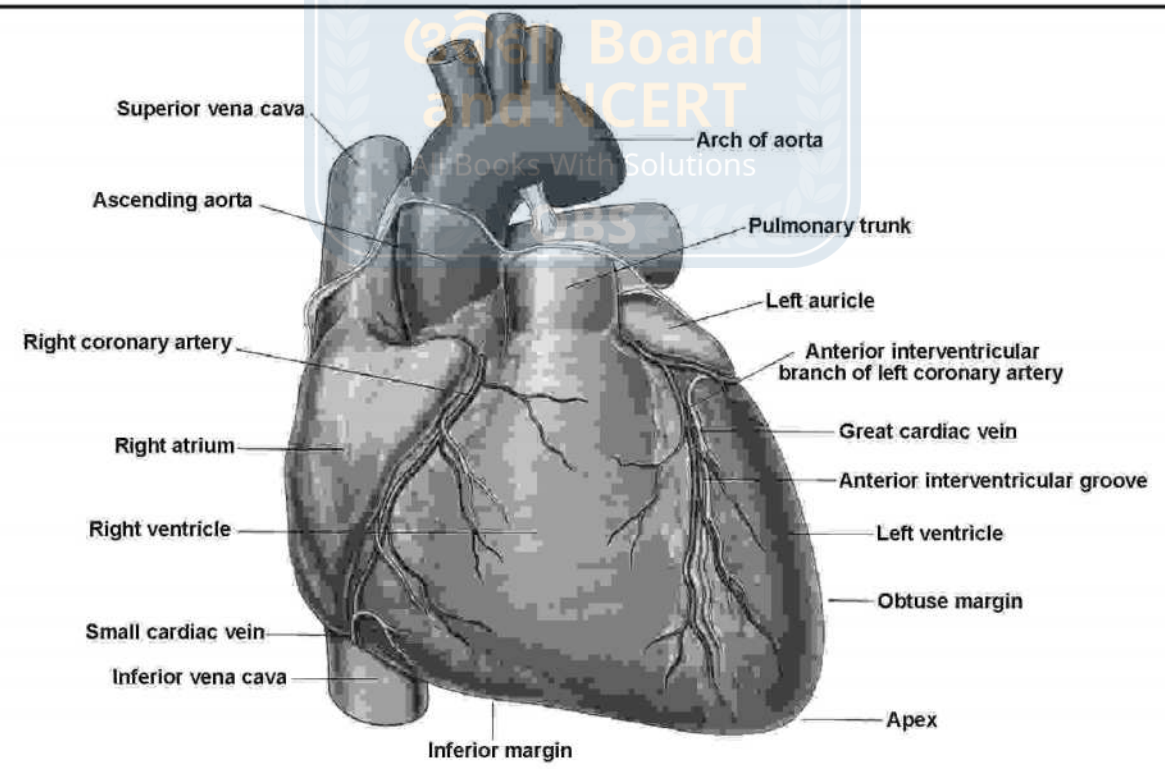

Fig.17.16 : External structure of human heart (posterior view)

The shape of the heart is conical or pyramidal. The shape is comparable to that of a pyramid that has fallen over and is resting on one side. The apex projects forward, downward and to the left. The heart is four chambered consisting of **two atria** and **two ventricles**. Internally, the chambers are separated from each other by partitions. These partitions conform to the external grooves, called **sulci** (singular; sulcus). The atria are separated from the ventricles by a **coronary sulcus**. This groove harbours the coronary sinus, cardiac vein, right coronary artery and a branch of left coronary artery. The ventricles are separated from each other by anterior and posterior inter-ventricular sulci.

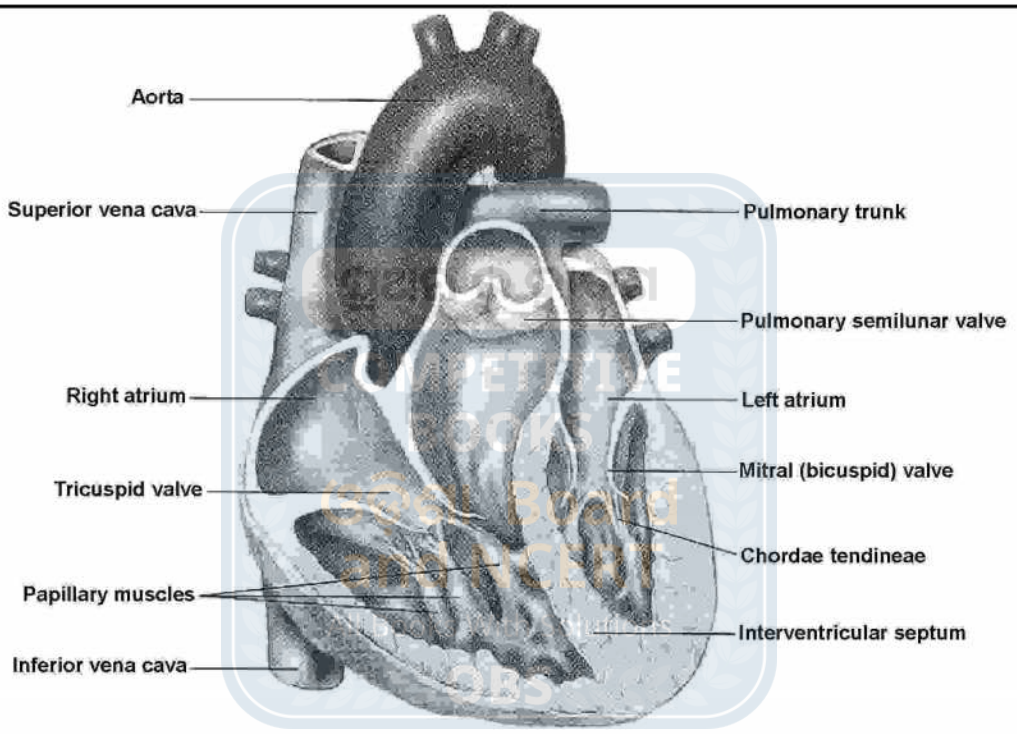

Fig.17.17 : Vertical (longitudinal) section of human heart showing internal structures.

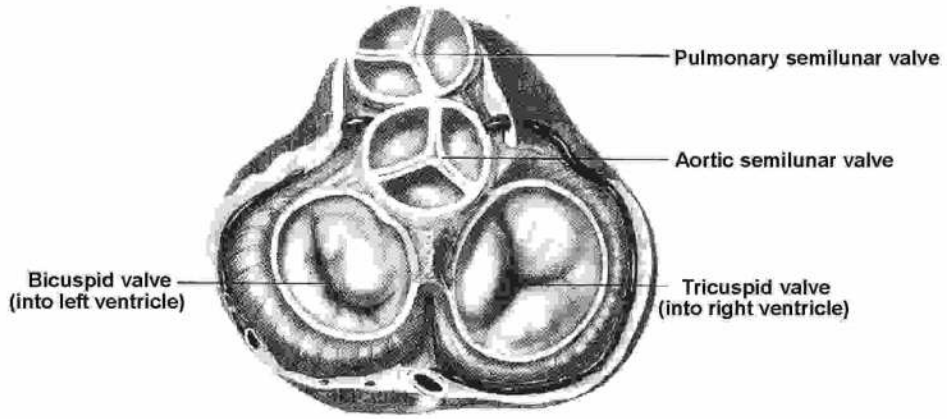

Fig.17.18 : Structure of bicuspid (mitral); tricuspid; and semilunar valves.

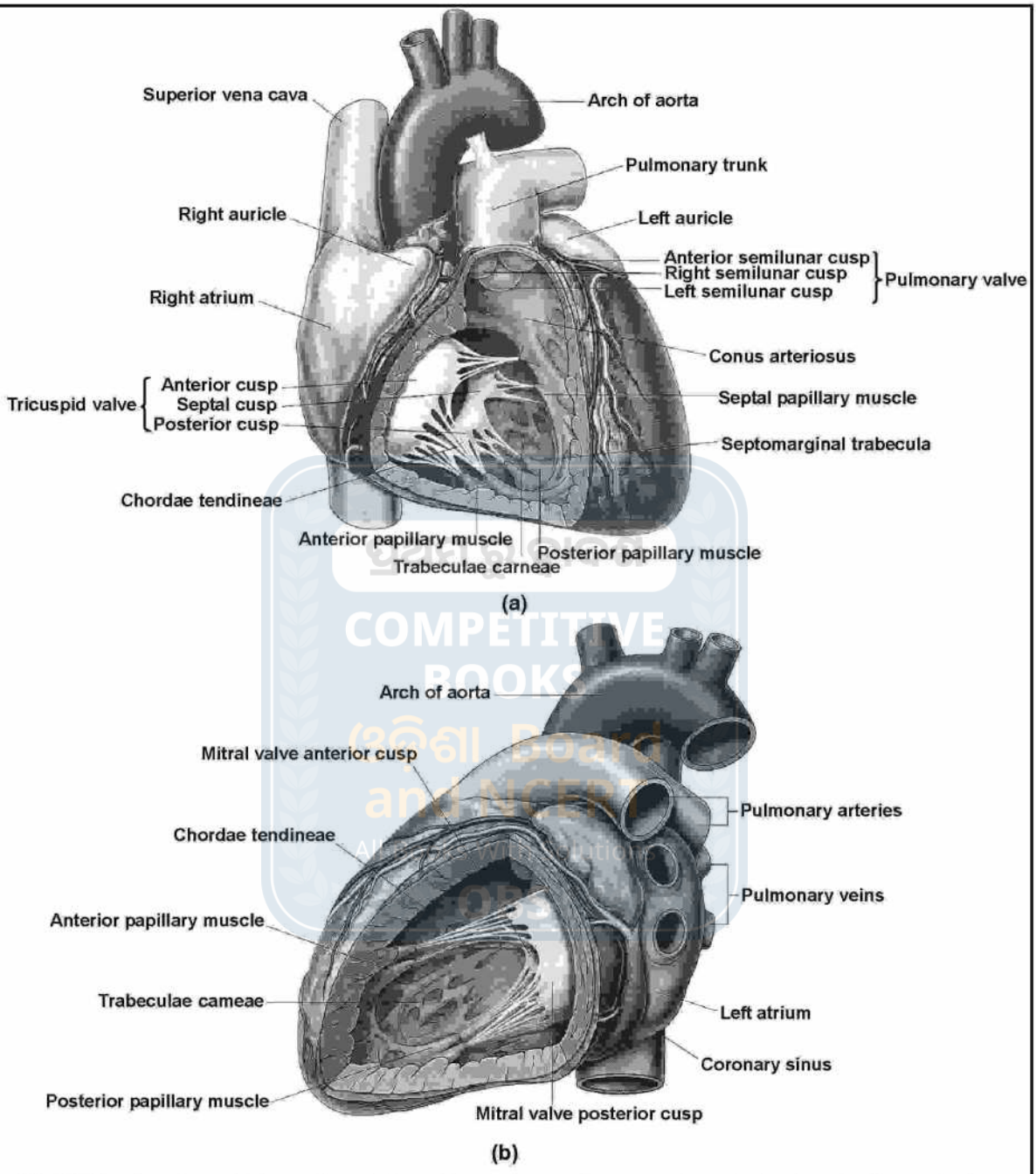

Fig.17.19 : Structure of tricuspid and bicuspid valves, papillary muscle and chordae tendineae in the ventricles of human heart. (a) In the right ventricle; and (b) In the left ventricle.

Foramen ovale and Ductus arteriosus :

The lungs of the fetus are collapsed and non-functional. Therefore, the circulating blood bypasses the pulmonary circulation by developing two features in the heart. One, known as ***foramen ovale****, is a communication between the two atria and the other, known as* ***ductus arteriosus****, a vascular connection between the pulmonary trunk and aorta. Both the communications close at birth except in few, where these structures exist as congenital deformities.*

The wall of the heart consists of three layers : **outer epicardium**, **middle myocardium** and **inner endocardium**. The epicardium is synonymous with the visceral layer of the serous pericardium. It consists of simple squamous epithelium, called **mesothelium** and an underlying layer of sub-epicardial layer of connective tissue. This layer contains blood vessels, nerve fibers and adipose tissue. The myocardium consists of cardiac muscle. The endocardium consists of an inner simple squamous epithelium, called **endothelium** and an outer thin layer of sub-endothelial connective tissue. This layer contains small blood vessels and Purkinje fibers.

The heart is considered as having two pumps, the right and left. The right pump is constituted by the right atrium and the right ventricle, while the left by the left atrium and left ventricle.

17.5.1. Atria :

Two atria are separated from each other by a complete partition, the **inter-atrial septum**. The septum is seen to have a depression just above the inferior venacava orifice, known as **fossa ovalis**. In human fetus, the two atria communicate with each other through a foramen, called **foramen ovale**. The oxygenated blood entering into the right atrium directly passes to the left atrium through this foramen, bypassing the lungs, since the lungs are collapsed in the fetus. However, foramen ovale closes soon after birth, leaving a footprint, called fossa ovalis. The right atrium receives deoxygenated blood from the **superior** and **inferior venacavae** and the **coronary sinus**. The left atrium receives blood from two **pulmonary veins**.

17.5.2. Ventricles :

There are two ventricles, right and left, separated by a relatively thicker **inter-ventricular septum**. The right atrium opens into the right ventricle through a right atrio-ventricular orifice, guarded by a valve, known as **tricuspid valve**. The valve is named so because it is made by three cusps or leaflets. A pulmonary trunk originates from the right ventricle, which later divides into two pulmonary arteries.

The opening of the pulmonary trunk is guarded by three **semilunar valves** or **cusps**. The wall of the right ventricle has a few irregular muscular structures, called **papillary muscles**. The free surface of each papillary muscle is attached to tendon-like fibrous cords, known as **chordae tendineae** [Fig.17.19 (a)]. These are joined to the free edges of the cusps of tricuspid valves. The left atrium communicates with the left ventricle through a left atrio-ventricular orifice, guarded by a **bicuspid** or **mitral valve**. The aortic trunk originates from the left ventricle. The opening of the trunk is guarded by three semilunar valves. The papillary muscles are fine and delicate in comparison to those of the right ventricle. Chordae tendineae are seen as attachments between papillary muscles and free edges of the bicuspid valve [Fig.17.19 (b)]. For tricuspid, bicuspid (mitral) and semilunar valves, see Fig.17.18.