Text Book for

INTERMEDIATE

Second Year

Zoology

Permission & Support by:

National Council of Educational Research and Training
New Delhi

Board of Intermediate Education, Andhra Pradesh

Telugu and Sanskrit Akademi, Andhra Pradesh

Intermediate

Second Year Text Book

Zoology

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Y.S. JAGAN MOHAN REDDY

CHIEF MINISTER
ANDHRA PRADESH

AMARAVATI

MESSAGE

I congratulate Akademi for starting its activities with printing of textbooks from the academic year 2021 – 22.

Education is a real asset which cannot be stolen by anyone and it is the foundation on which children build their future. As the world has become a global village, children will have to compete with the world as they grow up. For this there is every need for good books and good education.

Our government has brought in many changes in the education system and more are to come. The government has been taking care to provide education to the poor and needy through various measures, like developing infrastructure, upgrading the skills of teachers, providing incentives to the children and parents to pursue education. Nutritious mid-day meal and converting Anganwadis into pre-primary schools with English as medium of instruction are the steps taken to initiate children into education from a young age. Besides introducing CBSE syllabus and Telugu as a compulsory subject, the government has taken up numerous innovative programmes.

The revival of the Akademi also took place during the tenure of our government as it was neglected after the State was bifurcated. The Akademi, which was started on August 6, 1968 in the undivided state of Andhra Pradesh, was printing text books, works of popular writers and books for competitive exams and personality development.

Our government has decided to make available all kinds of books required for students and employees through Akademi, with headquarters at Tirupati.

I extend my best wishes to the Akademi and hope it will regain its past glory.

(YS JAGAN MOHAN REDDY)

Dr. Nandamuri Lakshmiparvathi
M.A., M.Phil., Ph.D.
Chairperson, (Cabinet Minister Rank)
Telugu and Sanskrit Akademi, A.P.

Message of Chairperson, Telugu and Sanskrit Akademi, A.P.

In accordance with the syllabus developed by the Board of Intermediate, State Council for Higher Education, SCERT etc., we design high quality Text books by recruiting efficient Professors, department heads and faculty members from various Universities and Colleges as writers and editors. We are taking steps to print the required number of these books in a timely manner and distribute through the Akademi's Regional Centers present across the Andhra Pradesh.

In addition to text books, we strive to keep monographs, dictionaries, dialect texts, question banks, contact texts, popular texts, essays, linguistics texts, school level dictionaries, glossaries, etc., updated and printed and made available to students from time to time.

For competitive examinations conducted by the Andhra Pradesh Public Service Commission and for Entrance examinations conducted by various Universities, the contents of the Akademi publications are taken as standard. So, I want all the students and Employees to make use of Akademi books of high standards for their golden future.

Congratulations and best wishes to all of you.

Nandamuri Lakshmiparvathi
Chairperson, Telugu and Sanskrit Akademi, A.P.

J. SYAMALA RAO, I.A.S.,
Principal Secretary to Government

Higher Education Department
Government of Andhra Pradesh

MESSAGE

I Congratulate Telugu and Sanskrit Akademi for taking up the initiative of printing and distributing textbooks in both Telugu and English media within a short span of establishing Telugu and Sanskrit Akademi.

Number of students of Andhra Pradesh are competing of National Level for admissions into Medicine and Engineering courses. In order to help these students Telugu and Sanskrit Akademi consultation with NCERT redesigned their Textbooks to suit the requirement of National Level Examinations in a lucid language.

As the content in Telugu and Sanskrit Akademi books is highly informative and authentic, printed in multi-color on high quality paper and will be made available to the students in a time bound manner. I hope all the students in Andhra Pradesh will utilize the Akademi textbooks for better understanding of the subjects to compete of state and national levels.

(J. SYAMALA RAO)

THE CONSTITUTION OF INDIA

PREAMBLE

WE, THE PEOPLE OF INDIA, having solemnly resolved to constitute India into a [SOVEREIGN SOCIALIST SECULAR DEMOCRATIC REPUBLIC] and to secure to all its citizens:

JUSTICE, social, economic and political;

LIBERTY of thought, expression, belief, faith and worship;

EQUALITY of status and of opportunity; and to promote among them all

FRATERNITY assuring the dignity of the individual and the [unity and integrity of the Nation];

IN OUR CONSTITUENT ASSEMBLY this twenty-sixth day of November, 1949 do HEREBY ADOPT, ENACT AND GIVE TO OURSELVES THIS CONSTITUTION.

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Foreword

The Government of India vowed to remove the educational disparities and adopt a common core curriculum across the country especially at the Intermediate level. Ever since the Government of Andhra Pradesh and the Board of Intermediate Education (BIE) swung into action with the task of evolving a revised syllabus in all the Science subjects on par with that of COBSE, approved by NCERT, its chief intention being enabling the students from Andhra Pradesh to prepare for the National Level Common Entrance tests like NEET, ISEET etc for admission into Institutions of professional courses in our Country.

For the first time BIE AP has decided to prepare the Science textbooks. Accordingly an Academic Review Committee was constituted with the Commissioner of Intermediate Education, AP as Chairman and the Secretary, BIE AP; the Director SCERT and the Director Telugu Akademi as members. The National and State Level Educational luminaries were involved in the textbook preparation, who did it with meticulous care. The textbooks are printed on the lines of NCERT maintaining National Level Standards.

The Education Department of Government of Andhra Pradesh has taken a decision to publish and to supply all the text books with free of cost for the students of all Government and Aided Junior Colleges of newly formed state of Andhra Pradesh.

We express our sincere gratitude to the Director, NCERT for according permission to adopt its syllabi and curriculum of Science textbooks. We have been permitted to make use of their textbooks which will be of great advantage to our student community. I also express my gratitude to the Chairman, BIE and the honorable Minister for HRD and Vice Chairman, BIE and Secretary (SE) for their dedicated sincere guidance and help.

I sincerely hope that the assorted methods of innovation that are adopted in the preparation of these textbooks will be of great help and guidance to the students.

I wholeheartedly appreciate the sincere endeavors of the Textbook Development Committee which has accomplished this noble task.

Constructive suggestions are solicited for the improvement of this textbook from the students, teachers and general public in the subjects concerned so that next edition will be revised duly incorporating these suggestions.

It is very much commendable that Intermediate text books are being printed for the first time by the Akademi from the 2021-22 academic year.

Sri. V. Ramakrishna I.R.S.
Director
Telugu and Sanskrit Akademi,
Andhra Pradesh

Preface

This Edition, as you are aware, is the 'Brain Child' of BIE, AP. Preparing a Text Book is no small job. It requires months of preparation, innumerable discussions ,editing, and uncompromising efforts to maintain quality. The '***central dogma***' of this exercise is to bring out the best in us. Barring some minor possible errors, which are generally common in the first Edition of any book written by ordinary mortals like us, we know we did a pretty good job of this book. And, we know – "***The proof of pudding lies in eating***". It is ultimately the students and well intentioned Teachers that decide the quality of our work. I request my young friends, the Lecturers in Zoology, AP, who are giving their life to the 'GREATER GLORY' of 'ZOOLOGY' to read in depth, and help us weed out errors, if any. The doors of wisdom must never shut, hence our efforts to give valid comments their due. We tried very sincerely to present updated information, while not forgetting the so called 'common' student. We tried to present Zoology in a readable way. We also tried ways to draw the attention of the students to points that matter, in view of the Public Examinations they face, and also tried in our own little way to cater to the needs of students who aspire to MAKE IT BIG. This book gave me immense pleasure, thanks to my esteemed Authors and the Editor. They always reposed immense confidence in my capabilities as the Chief Editor. And, should there be any errors, I would like to categorically state that I own the total responsibility. The fact that I am currently the senior most Lecturer in Zoology in AP, does not necessarily mean that I am 'error proof', but I must say, I tried my best to avoid errors. We consulted some recent Reference Editions liberally. However, we must admit that we had to follow the NCERT books in letter and spirit, keep to the perimeters and parameters of the syllabus prepared by the COBSE, with some freedom to update information. We presented some new illustrations, which are self explanatory. The First Page of each Chapter is a 'Preview' of the contents in that chapter and the CAPTIONS and TAGS given are aimed at 'raising curiosity' in the reader of that Chapter and are just 'cosmetic' in nature. The IGNITED MINDS, at the end of each Chapter, is aimed at giving a 'taste' of 'application' of the subject learnt.

It has been a pleasure working with the BIE, its esteemed Secretary, the ever inspring Commissioner and the wonderful Officials of the BIE.

Chief Editor

Preface to the Reviewed Edition

In view of advancements in Science, periodical review of Text Books at different levels of study has become necessary. Taking into consideration the syllabus for the students of Zoology of Senior Intermediate, Board of Intermediate Education, Andhra Pradesh, the present book is thoroughly reviewed. **The additional information presented in the previous edition is retained as boxed items in colour. Those topics are not meant for evaluation.** They may be useful for the advanced learners. Lapses in some units are fulfilled and now the present book is as per the prescribed syllabus.

In spite of the best efforts in preparation of this book, some errors may crept in. We welcome the constructive criticism from the academic fraternity. It will be reviewed and incorporated in the coming edition.

We gratefully acknowledge the help received from the Director, Telugu Akademi and the team of dedicated Officials.

Editor
(Reviewed Edition)

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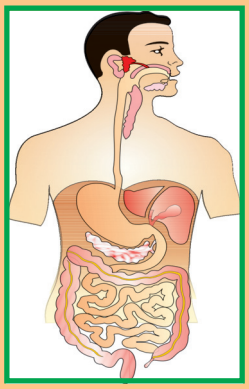


Unit-I

Human Anatomy and Physiology-I

Digestive System-
The 'Fuel Provider' and 'Life Sustainer'

Digestive system consists of the alimentary canal and associated glands such as salivary glands, liver, pancreas etc. Vertebrates (heterotrophs) are either herbivores or carnivores. Human beings are mostly 'omnivores' in food habits. The dental formula of man shows all the four types of teeth indicating his fundamentally omnivorous nature. Complex items of food have to be broken down (digested/hydro-lysed) into simple, absorbable substances. Human food has essential substances such as carbohydrates (chief energy providers), proteins (body builders and enzymes), fats (energy reserves) mostly stored in adipose tissue. Insufficient intake of food materials causes nutritional deficiency disorders. If protein intake is deficient, in spite of normal caloric intake, a person suffers from Kwashiorkor. Protein-calorie under nutrition (severe malnutrition and energy deficiency), leads to 'Marasmus'. Alimentary canal is generally long in the herbivores as much of what they eat (cellulose) is not digested and they require a larger absorptive surface area to absorb fully of what little they digested. Carnivores have comparatively shorter alimentary canal, as digestion is more efficient in them. The major site of digestion in the human gut is the small intestine. Water and some minerals are reabsorbed and faeces is formed in the large intestine. The movements of the gut are controlled by nerve plexuses present in the muscle layers. Enzymes are produced in their inactive forms such as pepsinogen, trypsinogen, chymotrypsinogen.Thus the cells which secrete these inactive enzymes escape from 'autodigestion'. Only activated enzymes can act on the cells of the wall of the gut. The 'Brush Border Enzymes' embedded in the plasma membrane hydrolyse disaccharides into monosaccharides. The 'intestinal flora' is important in producing some vitamins. Hyper acidity causes peptic ulcers in the wall of the stomach. However scientists found that peptic ulcers are caused by the bacterium ***Helicobacter pylori****. Thus, nowadays, antibiotic treatment is given for treating ulcers.*

UNIT I A

Digestion and Absorption

1.1 Digestive System

Food is one of the basic requirements of all living organisms as it provides energy and organic material for growth and repair of tissues. The water we drink plays an important role in metabolic processes and also prevents 'dehydration' of the body. Vitamins, minerals and water can be absorbed into the cells directly whereas bio-macromolecules of food such as carbohydrates, proteins and fats cannot be absorbed and utilised by our body in their original form. The breakdown of bio-macromolecules into simple substances is required for their absorption into cells. **The process of conversion of the complex food substances into their simple absorbable forms is called digestion,** and it is carried out by our digestive system. Digestion involves both mechanical and biochemical processes.

1.1 Digestive System

Human digestive system consists of the alimentary canal and the associated glands.

1.1.1 Alimentary canal/digestive tract

The alimentary canal of man begins with the anterior opening, the mouth, and ends with the posterior opening, the anus. Parts of the alimentary canal between the mouth and the anus include buccal cavity, pharynx, oesophagus, stomach, small intestine and the large intestine in the given order.

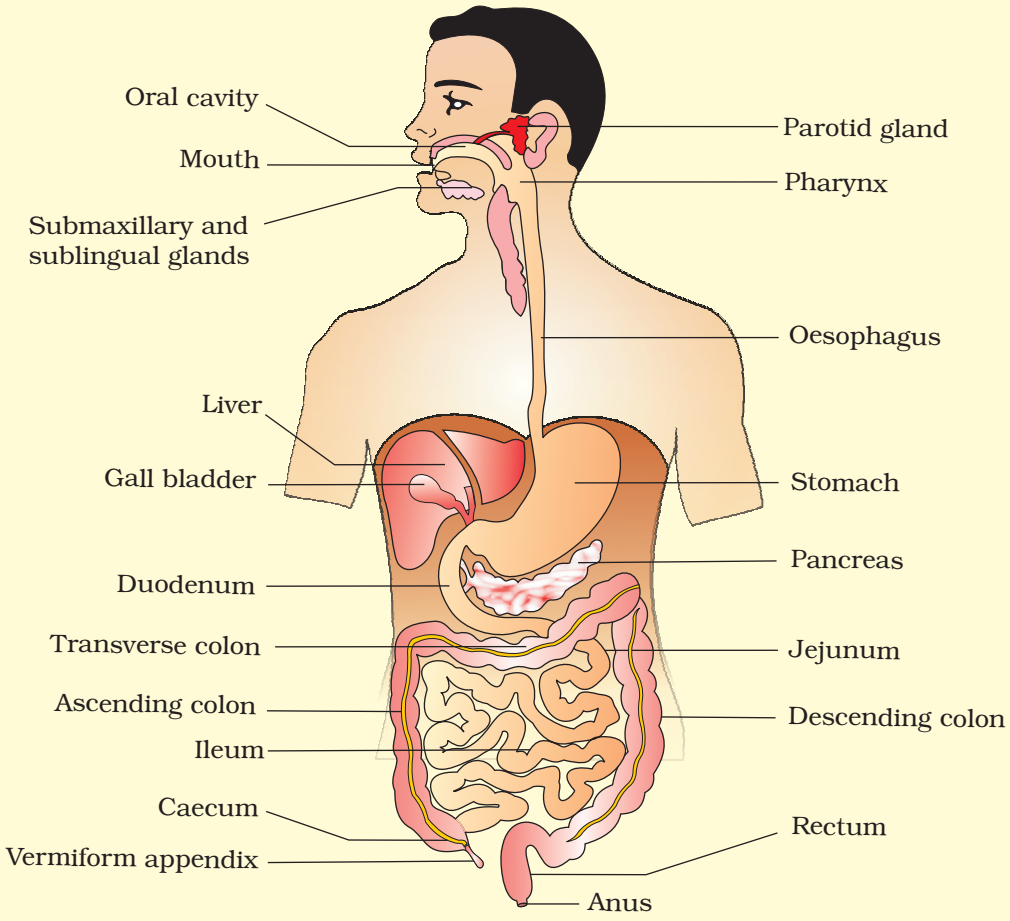


Figure 1.1 The human digestive system

I. Mouth and Buccal (oral) cavity

The mouth, bordered by the movable upper and lower lips (***labia***), leads into the buccal or oral cavity. The **palate** separates the ventral buccal cavity from the dorsal nasal chamber and facilitates *chewing* and *breathing* simultaneously. The anterior bony **hard palate** is lined by **palatine rugae**. The posterior **soft palate** that hangs down into the pharynx is called **uvula**. The jawbones bear four kinds of teeth and a tongue occurs at the base of the buccal cavity.

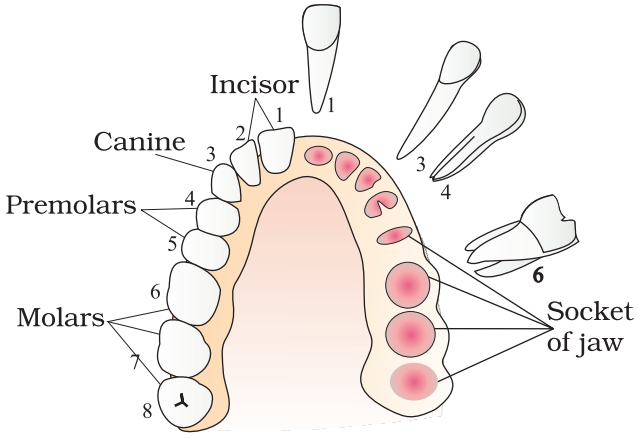


Figure 1.2 Arrangement of different types of teeth in the jaw on one side and the sockets on the other side

i. Teeth

These are **ecto-mesodermal** in origin. Teeth of human beings are embedded in the sockets of the jaw bones, hence called **thecodont**. Majority of mammals including human beings form two sets of teeth during their life time, a set of temporary/ **milk teeth** or **deciduous teeth** replaced by a set of **permanent teeth** or **adult teeth**. This type of dentition is called **diphyodont dentition**. An adult human has **32** permanent teeth, which are of four different types namely, incisors (I), canines (C), premolars (PM), and molars (M), and such a type of dentition is called **heterodont dentition**. The arrangement of different types of teeth in each half of both the jaws in the order I, C, PM, M is represented by the **dental formula** in adult humans is $I\frac{2}{2}C\frac{1}{1}PM\frac{2}{2}M\frac{3}{3}$ 32 . The dental formula of the 'milk dentition' of a baby is teeth. The third molar teeth appear very late (usually at about 21 years of age) and are called **wisdom teeth**. Incisors, the 'chisel shaped' teeth are useful in cutting, canines, the dagger like teeth help in tearing, premolars and molars, the **cheek teeth**, help in **grinding** the food.

The Structure of a Tooth

Tooth has three parts namely **crown** (the exposed part), **neck** (the middle part) and **root** (the inner most part embedded in the socket of jaw bone). The bulk of a tooth is formed by a hard material called **dentine**, which is secreted by **odontoblasts**, of mesodermal origin. Dentine of the crown is covered by

enamel (the hardest substance in the body), which is secreted by **ameloblasts** of **ectodermal** origin. A small cavity present inside the tooth is called **pulp cavity**, which is filled with **pulp** (odontoblasts, nerves,blood vessels etc) and lined by a layer of odontoblasts. Dentine of the root is covered by **cementum**. The root is fixed in the socket (**alveolus**) of the jaw bone by cementum and **periodontal membrane.** The basal parts of teeth (neck and root) are covered by the **gums** (**gingiva**).

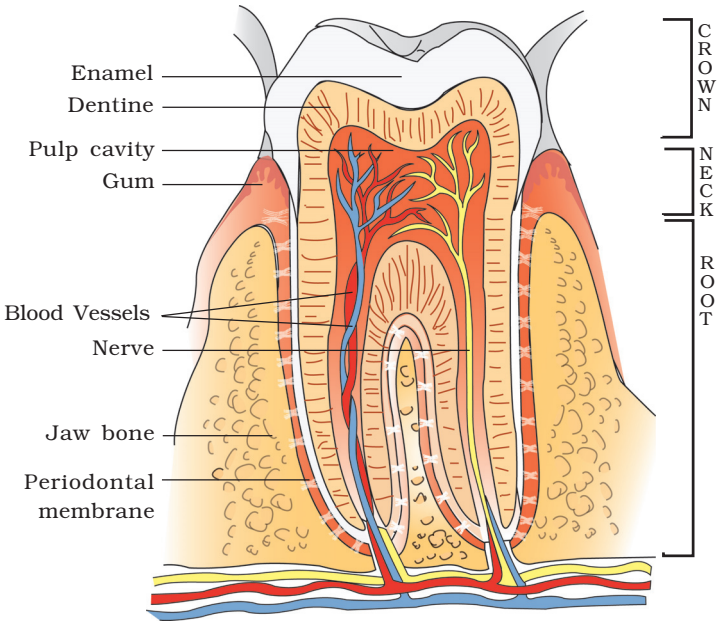


Figure 1.3 L.S. of tooth

ii. Tongue

It is a freely movable, muscular sense organ, attached to the floor of the oral cavity by a fold of tissue called **frenulum**. The upper surface of the tongue has small projections called **papillae**, some of which bear **taste buds**. In humans the tongue bears 4 types of papillae namely 1. **fungi form** (at the anterior margin and tip of tongue), 2. **filiform** (on the surface of the tongue) and 3. **circumvallate** (on the posterior surface/base of the tongue) and 4. **foliate** papillae (on the lateral sides of posterior 1/3rd of the tongue, rudimentary in adults). The tongue acts as '**universal tooth brush**', and helps in mixing saliva with food, taste detection, deglutition and speaking.

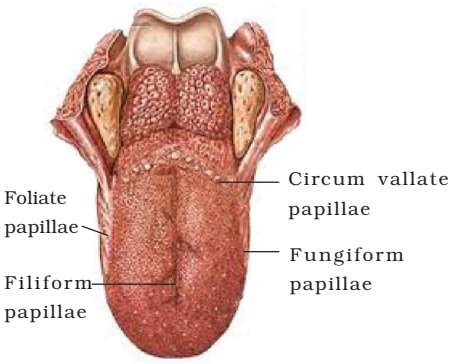


Figure 1.4 Tongue

II. Pharynx

The oral cavity leads into a short pharynx which serves as a common passage for food and air. It is divided into **nasopharynx** (lies above the soft palate), **oropharynx** (the middle part) and **laryngopharynx** (the lower part). The trachea opens into the larynx and from there into the laryngopharynx through the **glottis**. A cartilaginous flap called **epiglottis** prevents the entry of food into glottis during swallowing. Pharynx possesses voluntary muscles to assist in swallowing. Tonsils (**lymphoid tissues**) present in the pharynx , include i) **pharyngeal tonsils** or **adenoids**, ii) a pair of **palatine tonsils** and iii) a pair of **lingual tonsils**. **Eustachian tubes** from the middle ear cavities open into the nasopharynx.

III. Oesophagus

The oesophagus is a thin long tube which extends posteriorly, passing through the neck, thorax and diaphragm and it finally leads into the stomach. A muscular sphincter (gastro-oesophageal/cardiac sphincter) regulates the opening between the oesophagus and the stomach. There is an upper oesophageal sphincter at the beginning of the oesophagus.

IV. Stomach

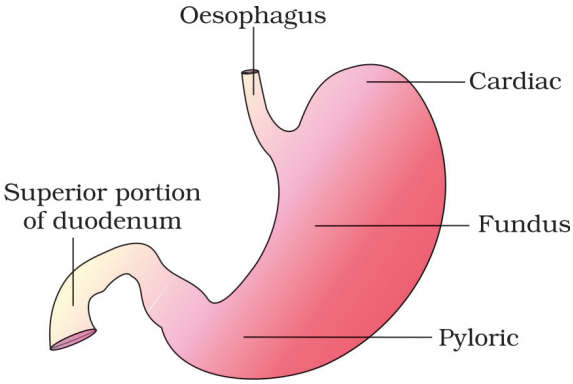


Figure 1.5 Anatomical regions of human stomach

The stomach is a wide, J-shaped, distensible muscular bag like structure, located in the upper left portion of the abdominal cavity just below the diaphragm. It has three major parts, an anterior **cardiac portion** into which the oesophagus opens, a middle large **fundic region** (main body) and a posterior **pyloric portion** which opens into the first part of the small intestine through the pyloric aperture which is guarded by the **pyloric sphincter**.

V. Small intestine

The small intestine is the **longest part** of the alimentary canal. It is distinguished serially into three regions namely proximal **duodenum**, middle long coiled **jejunum** and distal highly coiled **ileum**. Duodenum receives the **hepato-pancreatic duct**. Ileum opens into the large intestine,and the opening bears the **ilio-caecal valve** and a sphincter to prevent backward flow of faecal matter into the ileum.

VI. Large Intestine

It consists of caecum, colon and rectum. Caecum is a small blind sac which hosts some **symbiotic microorganisms**. A narrow finger-like tubular projection, the **vermiform appendix** (**abdominal tonsil**) which is a vestigial organ, arises from the caecum. The caecum opens into the colon which is divided into - an **ascending**, a **transverse**, a **descending** parts and a **sigmoid** colon that continues behind into the rectum. Colon shows the external bulged out pouches called **haustra** and three longitudinal smooth muscle folds called **taenia coli**. Rectum is a small dilated sac which leads into **anal canal** that opens out through the anus. It is guarded by an **internal anal sphincter** formed by '***smooth muscle***' and **external anal sphincter** formed by a ring of ***voluntary***, ***striped*** muscle. There is no significant digestive activity in the large intestine. It is concerned with the absorption of some water, minerals and certain drugs. It secretes mucus which helps in keeping the undigested particles together and lubricating their passage to the exterior.

Histology of alimentary canal

The wall of the alimentary canal from the oesophagus to the rectum possesses four layers namely serosa, muscularis externa, sub mucosa and mucosa.

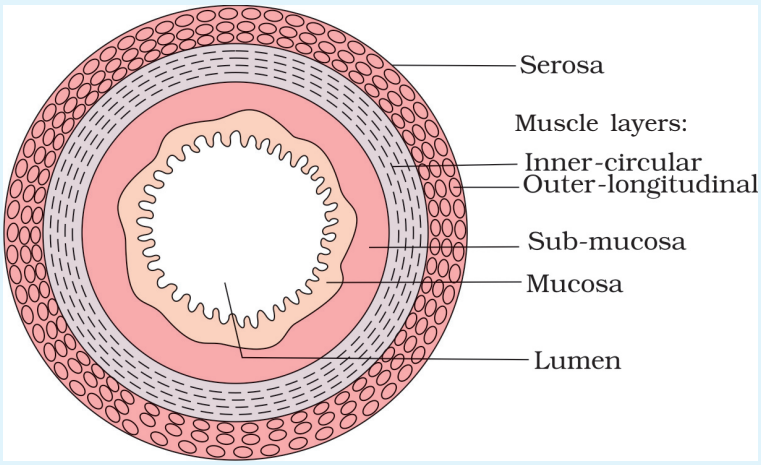


Figure 1.6 Diagrammatic representation of transverse section of gut

i) Serosa: it is the outermost layer and is made up of a thin mesothelium with some connective tissue. **ii) Muscularis externa:** It is formed by smooth muscles usually arranged into outer longitudinal and inner circular muscles. An oblique muscle layer may be present in some regions such as stomach, **iii) Sub mucosa:** It is formed of loose connective tissue containing nerves, blood vessels and lymph vessels. Sub mucosa of duodenum has Brunner's glands which secrete mucus, **iv) Mucosa:** It is the innermost layer lining the lumen of the alimentary canal. Mucosa of the stomach forms irregular folds called gastric rugae in between which there are many microscopic gastric glands. The mucosa of the small intestine forms small folds called **villi**. The columnar epithelial cells that line the villi produce numerous microscopic projections called **microvilli** giving a 'brush border' appearance. These modifications increase the surface area of absorption. Plasma membrane of microvilli bears enzymes such as disaccharidases,which are called 'brush border enzymes'. Each villus has a network of capillaries and a large lymph capillary called **lacteal**. Mucosal epithelium has goblet cells which secrete mucus, that helps in the protection of the wall from the action of the enzymes. It also helps in the lubrication of the passage of food. Mucosa of the small intestine forms crypts of Lieberkuhn between the bases of villi.

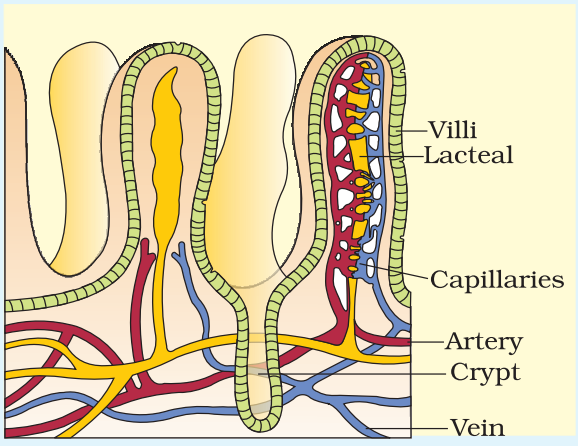


Figure 1.7 A section of small intestinal mucosa showing villi

1.1.2 Digestive glands

The digestive glands present in the wall of the alimentary canal are **gastric glands**, **Brunner's glands**, and **crypts of Lieberkuhn**. The salivary glands, liver and pancreas are the digestive glands associated with the gut (extra alimentary canal glands).

I. Salivary glands

There are *three pairs* of salivary glands in man, the **parotid glands** (present below the pinna/inner surface of the cheeks), the **sub maxillary/sub mandibular glands** (angles of lower jaw) and the **sublingual glands**(below the tongue). These are formed of ***serous cells*** and ***mucous cells*** which secrete **saliva**. Saliva contains water, salts, mucin, the enzyme **ptyalin** or **salivary amylase** (-amylase) and **lysozyme** (which kills bacteria). The **pH** of saliva is **6.8**.

> **Note:** Mumps, a painful inflammation of the parotid salivary glands is caused by a virus of the group 'Paramyxovirus'.

II. Gastric glands

These are located in the wall of the stomach beneath the surface epithelium. Gastric glands are of three types namely: i) **Cardiac glands** (secrete mucus for protection), ii) **Pyloric glands** (secrete mucus and the hormone '**gastrin**') and iii) **Fundic/Oxyntic glands** (They are composed of three different types of cells, the mucous **neck cells** which secrete mainly mucus; the **peptic/ chief cells** which secrete large quantities of the '***proenzymes***' **pepsinogen**, **prorennin** and the **oxyntic/parietal cells** which secrete **hydrochloric acid** and **Castle's Intrinsic Factor** (essential for the absorption of vitamin B_{12}). Secretions of all these glands form the 'gastric juice' with the pH ranging from **0.9 to 1.8**. Chief cells of gastric glands also secrete some amount of **gastric lipase**.

III. Intestinal glands

They are of two types, i) **Brunner's glands** (secrete mucus), ii) **Crypts of Lieberkuhn**. The secretion of Brunner's glands along with that of crypts of Lieberkuhn constitutes the **intestinal juice** or **succus entericus**, with the pH ranging from 7.5 to 8.0. Succus entericus contains **peptidases** such as **tripeptidases**, **dipeptidases**, **aminopeptidases** and **disaccharidases** such as **sucrase** (**invertase**), **maltase**, and **lactase**. It also has small amounts of **intestinal lipase** and the enzyme **activator** ***enterokinase***. **Paneth cells** lining the bases of the intestinal glands secrete **lysozyme** which kills the bacteria that escape destruction in the stomach.

NOTE: The intestinal wall has some '**stem cells**' which play an important role in renewing the epithelial cells lost in the intestinal epithelium. The **Paneth cells** are believed to play an important role in the protection of those cells .

IV. Liver

Liver is the ***largest gland*** of the body weighing about 1.2 to 1.5 kg. in an adult human. It is situated in the abdominal cavity, just below the diaphragm towards the right side and has two lobes. Each liver lobe is formed of hexagonal hepatic lobules, surrounded by a thin connective tissue sheath called the **Glisson's capsule**. The hepatic lobules are the ***structural*** and the ***functional units*** of the liver, containing hepatic cells arranged in the form ***hepatic cords*** present around a central vein. The **bile** secreted by hepatic cells passes through the hepatic ducts and is stored and concentrated in a thin muscular sac called the **gall bladder**. The duct of the gall bladder (**cystic duct**) along with the common ***hepatic duct*** from the liver forms the ***common bile duct*** (CBD). The CBD is joined by the pancreatic duct to form the ***ampulla of Vater***. Its opening into the duodenum is guarded by the **sphincter of Oddi**.

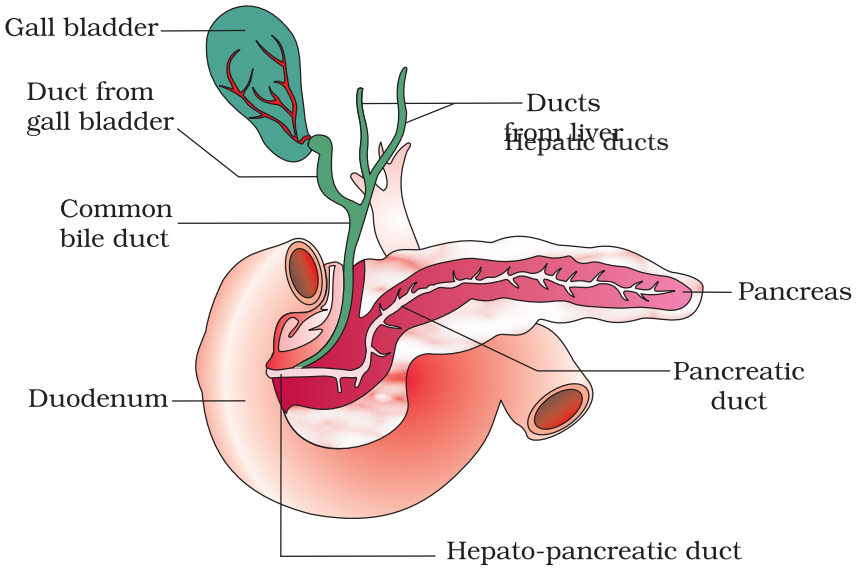


Figure 1.8 The duct system of liver, gall bladder and pancreas

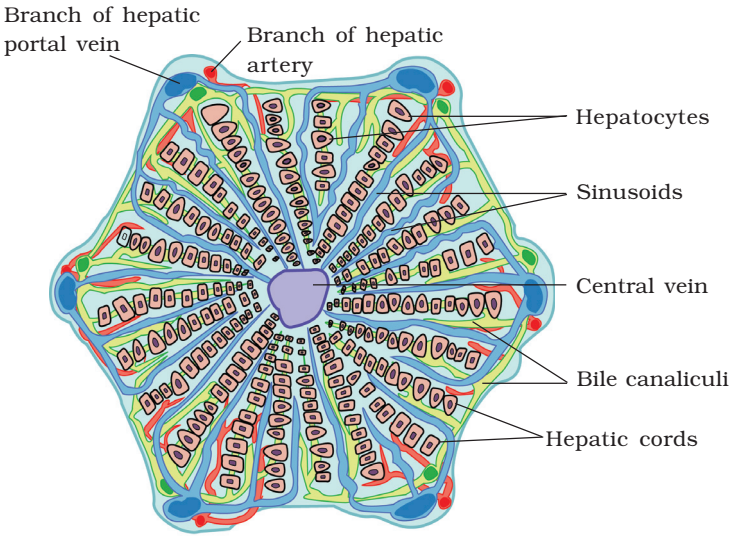


Figure 1.9 Components of a hepatic lobule

Do You Know: The pancreatic duct and the common bile duct unite to form the **ampulla of Vater/Hepatopancreatic ampulla.**

Functions of the liver

Liver performs a variety of functions such as synthesis, storage and secretion of various substances. There are as follows:

1. Liver secretes **bile juice** (yellowish-green in colour). It does not contain enzymes, but it contains bile salts such as **glycocholates** and **taurocholates** of **sodium** and **potassium** and **bile pigments** the **bilirubin** and **biliverdin** (formed by the breakdown of hemoglobin of the old RBC destroyed in the body).
2. Liver plays the 'key role' in carbohydrate metabolism (**glycogenesis**, **glycogenolysis**, **gluconeogenesis** and **lipogenesis**).
3. Liver also plays a role in lipid metabolism (synthesis of **cholesterol** and production of **triglycerides**).
4. **Deamination** of proteins (removal of NH_2 group from the amino acids) and conversion of ammonia into to urea (via the **ornithine cycle**).
5. The lactic acid formed during anaerobic muscle contraction is converted into glucose via pyruvates (**gluconeogenesis**) in the liver by **Cori cycle**.
6. Liver is the chief organ of **detoxification** of toxic substances that enter the gut along with food.

NOTE: Liver is the 'first check post' that bars entry of toxins into general circulation. Recall the role of the **smooth ER** in detoxification of toxins. The toxins that enter the body through food and water reach the liver via the hepatic portal vein, where they are detoxified. In the case of **alcoholics**, liver detoxifies alcohol to some extent before it is sent into general circulation. That is why liver is the first and most affected organ in chronic alcoholism (**cirrhosis**). This is the reason behind development of liver cancers by certain **fungal toxins**, produced by organisms such as ***Aspergillus flavus***. After entering the body, the '**aflatoxins**' are generally metabolized by the liver into some other non-toxic/ less toxic substances.

7. Liver acts as **thermoregulatory organ** *(like skeletal muscle, liver too takes part in* ***thermogenesis*** *as it has high glucose (in the form of glycogen) at its disposal).*
8. Liver acts as a **haemopoietic organ** in the foetus and **erythroclastic organ** in the adult (along with the spleen).

9. The liver synthesizes the plasma proteins such as **albumins, globulins**, blood clotting factors such as **fibrinogen**, **prothrombin**, etc. and the anticoagulant, called **heparin**.
10. **Kupffer cells** are the large phagocytic cells which remove unwanted substances and microbes that attack the liver by phagocytosis. They are present in the sinusoids that lie in between hepatic cords and they are also called **hepatic macrophages**.

V. Pancreas (Sweet gland / Mixed gland / Heterocrine gland)

The pancreas is the *second largest gland* in human body. It is a **mixed** (compound) gland situated between the limbs of 'U' shaped duodenum. Exocrine part of pancreas, the **pancreatic acini** secrete an alkaline ***pancreatic juice*** (pH **8.4**) containing enzymes and the endocrine part, the **islets of Langerhans** which secrete **insulin**, **glucagon** and other hormones. Pancreatic Juice contains **sodium bicarbonate**, **trypsinogen**, **chymotrypsinogen**, **carboxypeptidase**, **pancreatic lipase** (**steapsin**), **pancreatic amylase** and **nucleases** such as **DNAase** and **RNAase**.

1.1.3 Physiology of digestion

Digestion is the process of conversion of complex non--diffusible food substances into simple diffusible forms. The process of digestion is accomplished by mechanical (cutting and chewing of food by teeth and churning of food by peristalsis) and chemical (enzymatic reactions by hydrolysing enzymes)processes.

I. Digestion in the buccal cavity

Buccal cavity performs two major functions, **mastication** of food and facilitation of **swallowing** (***deglutition***). Teeth and tongue with the help of saliva masticate and mix up the food thoroughly. Mucus in saliva helps in lubricating and adhering the masticated food particles into a **bolus**. The saliva secreted into oral cavity contains electrolytes such as Na^+, K^+, Cl^-, HCO_3^- and enzymes, such as **salivary amylase** (**ptyalin**) and **lysozyme**. The chemical process of digestion is initiated in the oral cavity (buccal cavity) by the hydrolytic action of carbohydrate (starch) splitting enzyme, the salivary amylase. About 30% of starch is hydrolyzed here into a disaccharide called **maltose** by the enzyme *ptyalin*. **Lysozyme** present in the saliva acts as an *antibacterial agent* that prevents infections.

$$\text{Starch} \xrightarrow[\text{pH 6.8}]{\text{Salivary amylase}} \text{Maltose}$$

II. Digestion in the stomach

The stomach stores food for 4-5 hours. The food is mixed thoroughly with the acidic gastric juice of the stomach by the churning movements of its muscular wall and the product is called **chyme**. The mucus and bicarbonates present in the gastric juice play an important role in the *lubrication* and protection of the mucosal epithelium from 'excoriation' by the highly concentrated hydrochloric acid. **HCl** provides the acidic **pH (1.8)** which is optimal for the action of pepsin. It also kills the microorganisms ingested along with food. The proenzymes of gastric juice, the **pepsinogen** and **prorennin**, on exposure to hydrochloric acid are converted into the active enzymes, ***pepsin*** and ***rennin***, respectively. Pepsin can convert pepsinogen into pepsin (autocatalysis). Pepsin converts proteins into **proteoses** and **peptones**. **Rennin** is a proteolytic enzyme found in the gastric juice of infants. It acts on the milk protein, the **casein** in the presence of **calcium ions** and converts it into **calcium paracaseinate** (curdling of milk) and **proteoses**. Pepsin acts on calcium paracaseinate and converts it into **peptones**. **Proteoses** are a group of compounds formed during **protein digestion** and they are more complex than **peptones**. Certain other cells in the wall of the stomach produce **bicarbonate**, a base, to **buffer the acidic contents** of the stomach. They also prevent too much acidity in the stomach. The **mucus** produced by the wall of the stomach forms a **physical barrier** to prevent **HCl** from damaging the wall of the stomach.

$$\text{Prorennin (inactive)} \xrightarrow{\text{Hcl}} \text{Rennin (active)}$$

$$\text{Pepsinogen (inactive)} \xrightarrow{\text{Hcl}} \text{Pepsin (active)}$$

$$\text{Casein} \xrightarrow[Ca^{+2}]{\text{Rennin}} \text{Calciumparacaseinate}$$

$$\text{Calciumparacaseinate} \xrightarrow{\text{Pepsin}} \text{Peptones}$$

$$\text{Proteins} \xrightarrow{\text{Pepsin}} \text{Proteoses + Peptones}$$

III. Digestion in the small intestine

Various types of movements are generated by the **muscularis externa** layer of the small intestine. These movements help in thorough mixing up of the food with bile, pancreatic juice and intestinal juice in the intestine and thereby facilitate digestion. The mucus along with the bicarbonates from pancreas protects the intestinal mucosa from the acidic medium and provides an alkaline medium (**pH7.8**) for enzymatic activities. The duodenal cells of the proximal part also produce large amounts of **bicarbonate** to completely

neutralize any gastric acid that passes further down into the digestive tract. All the enzymes of the ***pancreatic juice*** and ***succus entericus*** (mentioned above) act only in **alkaline** medium.

i. Digestion of proteins

Trypsinogen, chymotrypsinogen and **procarboxy peptidases** are **inactive** enzymes. **Trypsinogen** is activated by the enzyme, **enterokinase**, secreted by the intestinal mucosa into active ***trypsin***, which in turn activates the other enzymes in the pancreatic juice. Trypsin itself can similarly activate trypsinogen into trypsin (**autocatalysis**).

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

Trypsinogen $\xrightarrow{\text{Trypsin}}$ Trypsin (Autocatalysis)

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

Proteins, proteoses and peptones (partly hydrolysed proteins) in the **chyme**, reaching the intestine are acted upon by the proteolytic enzymes of the pancreatic juice and intestinal juice as shown below:

Proteins, Proteoses, Peptones $\xrightarrow[\text{Carboxypeptidase, aminopeptidase}]{\text{Trypsin/Cymotrypsin}}$ Tripeptides + Dipeptides

Tripeptides $\xrightarrow[\text{Trypeptidase}]{\text{Tripeptidase}}$ Dipeptides + Amino acids

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

Thus the end products of digestion of proteins namely amino acids are formed in the small intestine.

ii. Digestion of fats

Bile salts of the bile help in the emulsification of fats i.e. break down of fats into very small **micelles**. Bile also activates lipases of pancreatic juice (**steapsin**) and intestinal lipases. These lipases act on emulsified fats and convert them into fatty acids and glycerols.

Fats $\xrightarrow{\text{Bile salts}}$ Emulsified fats

Emulsified fats $\xrightarrow{\text{Lipases}}$ Diglycerides $\xrightarrow{\text{Lipases}}$ Monoglycerides

Monoglycerides $\xrightarrow{\text{Lipases}}$ Fatty acids + Glycerol

iii. Digestion of Carbohydrates

Starch (Carbohydrates) in the chyme are hydrolysed by the pancreatic amylase into **disaccharides**. Intestinal **disaccharidases** act on the 'disaccharides' and convert them into **monosaccharides**.

Starch $\xrightarrow{\text{Amylase}}$ Maltose, Sucrose, lactose

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

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

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

iv. Digestion of nucleic acids

Nucleases (DNAase, RNAase) of the pancreatic juice act on the nucleic acids to form **nucleotides** and **nucleosides**. Nucleotidases and nucleosidases of the intestinal juice covert the nucleotides and nucleosides into pentose sugars and nitrogen bases.

Nucleic acids (DNA, RNA) $\xrightarrow[\text{DNAase,RNAase}]{\text{Nucleases}}$ Nucleotides

Nucleotides $\xrightarrow{\text{Nucleotidease}}$ Nucleosides + Phosphates

Nucleosides $\xrightarrow{\text{Nucleosidases}}$ Sugars + Bases

1.1.4 Peristalsis

It involves contraction and relaxation of smooth muscles of the wall of the gut, resulting in successive wave like movements throughout the gut. It causes propulsion of food through different parts of the gut and its exposure to efficient enzymatic action. The **bolus of food** formed in the buccal cavity is conveyed into pharynx and then into the oesophagus by swallowing or **deglutition**. The bolus further passes down through the oesophagus by successive waves of muscular contractions called **peristalsis**. Usually peristaltic movements are initiated from the oesophagus and are continued up to the rectum. However the sphincters associated with the gut regulate the passage of food through different parts of the gut. Peristaltic movements of the stomach (churning movements) are so powerful that they can cause ***mechanical digestion***. Peristaltic movements of the intestine are slow. Stimulation from the parasympathetic nervous system – increases the peristaltic movements of the gut and **relaxes** the **sphincters** (made of smooth muscles).

1.1.5 Absorption of digested food

Absorption is the process by which the end products of digestion pass through the intestinal mucosa into **blood** or **lymph**. It is carried out by **passive**, **active** or **facilitated transport** mechanisms. Monosaccharides such as **glucose** and **galactose** are transported into the cells of the villi via secondary active transport (SAT), coupled with Na^+ and from there into blood by Facilitated Diffusion. Substances such as fructose is absorbed by Facilitated Diffusion. From the intestinal epithelial cells, it is transported into blood by FD. Transport of water depends upon the **osmotic gradient**. Amino acids are actively transported or by Secondary Active Transport with Na^+ and from there they enter blood capillaries by FD. Short chain fatty acids 'diffuse' into the intestinal epithelial cells and blood capillaries.

Long chain fatty acids and glycerol, being insoluble in water cannot be absorbed into the blood directly. They are first modified into small droplets called **micelles**, which enter the intestinal mucosal cells by diffusion. In the intestinal epithelial cells they are formed into very small protein coated fat globules called **chylomicrons**. These chylomicrons are transported into the **lacteals** (lymph capillaries) in the villi by **exocytosis** (*they cannot enter the blood capillaries due to their large size*). The lymph vessels ultimately release the absorbed substances into the blood stream through the **left subclavian vein** via the **thoracic duct**. These chylomicrons (triglycerides) are broken down to fatty acids and glycerol by the action of the enzyme '***lipoprotein lipase***' present in the endothelial walls and they diffuse into the adipocytes of the adipose tissue, and liver for storage (as **neutral fat** / **tissue fat**). Vitamins are generally absorbed by simple diffusion. Vitamin B_{12} is actively reabsorbed in combination with Castle's Intrinsic Factor.

Absorption of substances takes place in different parts of the gut, like mouth, stomach, small intestine and large intestine. However maximum absorption of the end products of digestion occurs in the small intestine.

Summary of absorption of different parts of digestive system

Mouth	Stomach	Small intestine	Large Intestine
Certain drugs coming in contact with the mucosa of mouth and lower side of the tongue are absorbed in to the blood capillaries lining them.	Absorption of water, simple sugars, and alcohol, drugs etc., takes place.	Principal organ for the absorption of nutrients. The digestion is completed here and the final (end) products of digestion such as glucose, fructose, galactose, amino acids are absorbed into blood through mucosa whereas fatty acids and glycerol are absorbed through the mucosa into lymph of the lacteals.	Absorption of water, some minerals and drugs takes place.

Assimilation

The absorbed substances finally reach the tissues where food materials become integral components of the living protoplasm and are used for the production of energy, growth and repair. This process is called **assimilation**.

Defaecation

The undigested, unabsorbed substances are passed on to the large intestine. No significant digestive activity occurs in the large intestine. The functions of large intestine are 1. Absorption of some water, minerals and certain drugs. 2. Secretion of mucus which helps in holding the undigested particles together and lubricating it for easy passage. The undigested, unabsorbed substances which mostly include fibre of plant material generally called **roughage** enter the large intestine. Water and some useful substances are reabsorbed in it. It is temporarily stored in the rectum till it is expelled out through the anus (**defaecation**).

The undigested wastes, solidified into faeces in the rectum, initiate a **neural reflex** causing an urge for its removal. The egestion of faeces to the outside through the anal opening is a voluntary process and it is carried out by a '**mass peristaltic movement**' (forcible peristaltic movements that expel the contents of the large intestine).

1.1.6 Gastro Intestinal hormones

Activities of the gastrointestinal tract are under neural and hormonal control for proper coordination of different parts. The sight, smell and the presence of food in the oral cavity can stimulate the secretions of saliva. Gastric and intestinal secretions are also similarly stimulated by neural signals. The muscular activities of different parts of the alimentary canal are also moderated by neural mechanisms. Hormonal control of the secretions of digestive juices is carried out by the 'local hormones' by gastric and intestinal mucosa as given below.

Gastrin is secreted from the epithelium of the stomach; it stimulates the secretions of hydrochloric acid and pepsinogen.

Enterogastrone or **gastric inhibitory peptide** (**GIP**) is secreted by the epithelium of duodenum due to the effect of dietary lipids. It inhibits gastric acidity and gastro-intestinal motility.

Secretin is secreted by the epithelium of duodenum and acts on the pancreatic acini; stimulates the secretions of water and bicarbonates of the pancreatic juice.

Cholecystokinin (CCK)/Pancreozymin: It is secreted from the epithelium of the duodenum; acts on pancreas and gall bladder and stimulate the secretion of pancreatic enzymes and release of bile, respectively.

Enterocrinin secreted from the duodenal mucosa stimulates the secretions of succus entericus, **villikinin** secreted from intestinal villi, stimulates the movement of villi to increase absorption.

Calorific values of carbohydrates, proteins and fats

The oxidation of one gram of proteins and carbohydrates yield almost the same amount of energy i.e.**4.0 K cal**, whereas it is **9.0 K cal** in the case of fats.

1.1.7 Nutritional disorders

1. ***Protein energy Malnutrition (PEM) [Kwashiorkor] :*** Kwashiorkor is a disease caused due to deficiency of proteins in diet. The main symptom of this disease is the accumulation of fluid in intercullular spaces of tissues of body. As a result body shows oedema, hands, legs, face show swelling, skin becomes dry. The patient suffers from diarrhoea.
2. **Indigestion:** In this condition, the food is not properly digested leading to a feeling of 'fullness'. The causes of indigestion are mostly 'spicy foods', 'over eating' and 'anxiety'.
3. ***Vomiting:*** It is the 'throwing out' of the contents of the stomach through the mouth. This reflex action is controlled by the '**vomiting centre**' in the medulla oblongata. A feeling of nausea precedes vomiting.
4. ***Jaundice:*** The liver is affected (hepatitis); anorexia (lack of appetite) is a common symptom. Skin and the white part of the eye balls turn yellow due to deposition of bile pigments.
5. **Diarrhoea:** The abnormal frequency of bowl movement and increased liquidity of the faecal discharge is known as **diarrhoea**. It reduces the absorption of food and results in loss of water (**dehydration**).

   Constipation: In constipation, the faeces are retained within the rectum as it is hard due to low content of water and the movement of the bowel occurs irregularly.
6. **Marasmus:** This disease is caused due to deficiency of proteins and calories. It is observed in children born without sufficient interval. The child appears weak and surrers from swelling of joints, deficiency in development of muscles, dry skin, diarrhoea etc.

GLOSSARY

Adenoids: A mass of lymphoid tissue present in the nasopharynx, also called pharyngeal tonsil.

Ameloblasts: The epidermal cell that secrete the enamel of teeth.

Brunner's glands: Intestinal glands of the sub mucosa of the duodenum; secrete mucus.

Castle's intrinsic factor: It is secreted from the oxyntic cells of the stomach, and promotes the absorption of the vitamin B_{12} in the intestine.

Chyme: Partly digested acidic food formed in the stomach.

Crypts of Lieberkuhn: They are the 'tubular invaginations of the intestinal epithelium around the villi/ Intestinal glands of the mucosa of the ileum; secrete intestinal juice.

Cystic duct: Duct that arises from the gall bladder and joins the hepatic duct to form the common bile duct in liver.

Deamination: Removal of ammono group from amino acids during their metabolism (the amino group is used in the formation of ammonia) in liver.

Deciduous/milk teeth: A set of temporary teeth that are formed as the first set, they don't include premolar and last molars in man.

Glycogenesis: Conversion of excess glucose into glycogen in liver.

Glycogenolysis: Conversion of glycogen (animal starch) into glucose

Gluconeogensis: Synthesis of glucose from non-carbohydrates such as proteins and lipids.

Lacteals: Lymph capillaries of intestinal villi, help in the absorption of fats and fat soluble vitamins into lymph.

Lipogenesis: Conversion of excess carbohydrates and proteins into lipids and it occurs in liver.

Odontoblasts: Dentine producing cells of teeth.

Ornithine cycle: The synthesis of urea from ammonia and CO_2, which involves ornithine,citruline, arginine and the enzyme arginase.

Oxyntic cells: Cells of fundic glands of the stomach; secrete hydrochloric acid and Castle's intrinsic factor.

Parotid glands: The largest of the salivary glands of man, present below the pinnae on the inner surface of the cheeks.

Peptic ells: These are the chief cells; secrete pepsinogen and prorennin.

Periodontal membrane: It is a layer of dense irregular connective tissue that lines the sockets of the jaw bones ; fixes the root of a tooth in the alveolus of the jaw bone.

Sphincter of Oddi: A sphincter which guards the opening of the hepato-pancreatic duct into the duodenum.

Succus entericus: Intestinal juice secreted by both Brunner's glands and crypts of Lieberkuhn of the intestine.

Thecodont teeth: Teeth embedded in the sockets of jaw bone. e.g. mammals and crocodiles.

Vermiform appendix: A narrow finger like tubular projection, that arises from the caecum of man; it is a vestigial organ in man.

QUESTIONS

Very Short Answer Type Questions

1. Give the dental formula of adult human beings.
2. Bile juice contains no digestive enzymes, yet it is important for digestion. How?
3. Describe the role of chymotrypsin. Name two other digestive enzymes of the same category and secreted by the same gland.
4. What would happen if, *HCl* were not secreted in the stomach?
5. Explain the terms thecodont and diphyodont dentitions.
6. What is auto catalysis? Give two examples.
7. What is chyme?
8. Name the different types of salivary glands of man, and their locations in the human body.
9. Name different types of papillae present on the tongue of man.
10. What is the hardest substance in the human body? What is its origin?
11. Name the structure of gut which is vestigial in human beings, but well developed in the herbivores .And mention the type of tissue with which it is mostly formed.
12. Distinguish between deglutition and mastication
13. Distinguish between diarrhoea and constipation.
14. Name two hormones secreted by the duodenal mucosa.
15. Distinguish between absorption and assimilation

Short Answer Type Questions

1. Draw a neat labelled diagram of L.S. of a tooth.
2. Describe the process of digestion of proteins in the stomach.
3. Explain the role of pancreatic Juice in the digestion of proteins.
4. How are polysaccharides and disaccharides digested?
5. If, you take butter in your food, how does it get digested and absorbed in the body? Explain.
6. What are the functions of liver?

Long Answer Type Questions

1. Describe the physiology of digestion of various types of food in the human digestive system.
2. Explain the digestive system of man with neat labelled diagrams.

FOR IGNITED MINDS

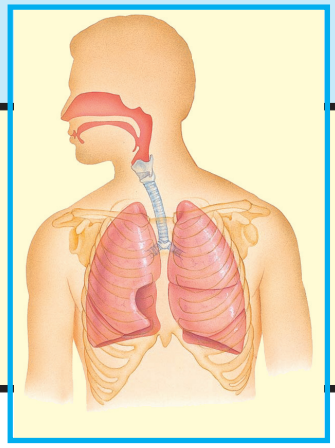
The 'Fuel Provider' and 'Life Sustainer'

Digestion and Absorption

1. Regarding the length of the alimentary canal in animals, in general-which type of animals possess a long alimentary canal and which possess a comparatively short alimentary canal? Can you give one example of a vertebrate which possesses a long alimentary canal in some stage of the life history and a relatively short alimentary canal in another stage. HINT: you probably heard of such animal in your school biology lessons.
2. Alcohol is harmful to the body. It gets directly absorbed into blood through the wall of the gut, as it does not require any digestion. In such a case will there be any difference between **drinking alcohol** (without diluting it with water) and injecting alcohol into blood directly through a vein? If you think there is a difference, what is it?.
3. Saliva is an important constituent of the human digestive process. Simultaneously, can your saliva be a part of any other important system in your body ? If so what is the system. HINT: Recall all the enzymes present in saliva.
4. If, 100 molecules each of glucose and fructose are required, hypothetically, from lactose and sucrose , how many molecules of 'invertase' and 'lactase' are required, respectively ? (CONDITION: You must use both the enzymes and hypothetically consider one molecule of enzyme working on one molecule of the substrate only).
5. We say that fats cannot be absorbed into blood directly, because of their larger molecular size and that they enter circulation through the lymph system. If so, when blood reaches tissues how do these fats pass into the tissues through the walls of the blood capillaries?
6. If you eat a piece of meat, it gets digested in the lumen of the gut, due to the activity of various enzymes. Can you guess why the same enzymes, do not digest the wall of your gut or the cells they are produced by , which are equivalent to the piece of meat eaten. HINT : You have a clue somewhere in this exercise / questionnaire .
7. Why are certain amino acids and fatty acids called 'essential amino acids' and 'essential fatty acids'?
8. Hypothetically, if more ammonia and CO_2 are injected into the blood in the HPV, what substance can be expected to be present in more quantity in the blood sample collected from the hepatic vein of the same person.
9. Presuming the microbial content of the blood sample from the HPV as 10,000 per cubic millimeter, what in your opinion will be the microbial content of blood sample taken from the hepatic vein? Will it be more/ less/ same ? Give reason(s).
10. The food we ingest contains potentially harmful toxins, which can cause serious consequences. One organ acts as a 'Guardian Angel' acting as a barrier and protecting other body parts from the ill effects to a lesser or greater extent. What is the name of the organ?

UNIT I B

Breathing and Exchange of Gases



1.2 Breathing and Exchange of Gases

Respiratory system - Your 'Calorie Burner' and 'Energy Provider'

*Respiration is a **catabolic process** of release of energy mostly by the oxidation of foods. Oxygen obtained from the surrouding medium is utilised in the production of '**metabolic water**', an end product of the 'burning of calories'. The direction of flow of blood in the gills and the direction of flow of water are in '**counter current flow**' mechanism, for efficient '**oxygenation**' of blood. Birds have developed a technique of continuous exchange of gases even during expiration, with the help of a unique feature - the presence of '**air sacs**' and '**parabronchi**'. Insects and some other arthropods supply oxygen directly to each cell via the tracheae and tracheoles. Thus every cell can virtually receive oxygen directly, making the '**tracheate animals**' very active.*

*At a height of about 6000 m the pO_2 becomes almost half of what it is at the mean sea level, hence the '**mountain sickness**' in people ascending mountains. The 'ribcage' and the 'diaphragm' help mammals breathe in air more effectively. Homeostasis of oxygen and carbon dioxide are under the control of the respiratory centre. Inhalation and exhalation are under the control of the **medulla oblongata**. There is a **pneumotaxic centre** in the **pons** and it controls the **rate** and **depth of breathing**. Man cannot hold his breath for long. He is forced to breathe in. **Elephant seal**, a mammal can remain under water for up to two hours. The muscles of the elephant seal and some other aquatic mammals, contains **myoglobin** (muscle haemoglobin) which has more affinity for oxygen.*

All living cells need constant supply of energy in order to carryout various metabolic activities. Energy is produced by the oxidation of micromolecules of digested food such as glucose, amino acids, and fatty acids. These are transported to the body cells through the circulatory system. Oxygen is utilized by organisms to breakdown stored food materials such as glucose, fatty acids etc. Carbon dioxide which is harmful (dissolves in water to form carbonic acid, which lowers the pH of blood threatening homeostasis) is also released during the above catabolic reactions. It is therefore, evident that O_2 has to be continuously provided to the body cells and CO_2 produced by the cells has to be sent out. *Respiration is a vital feature of life. The process of exchange of O_2 from the medium (air or water) with CO_2 produced by the cells at the same time is called '**breathing**' (Ref: NCERT Vol I, Page 268).* However, the process of respiration, during which air is inhaled into the lungs and exhaled out of the lungs is called 'breathing'. Many authors described the process of gaseous exchange as '**external respiration**' or '**ventilation**' because it emphasizes that the entry of oxygen and the exit of CO_2 happen at places other than the energy releasing sites. More accurately the *"**processes leading to, and including the chemical breakdown of food materials to provide energy for life is called respiration**."* As the chemical breakdown of the nutrients occurs inside the living cells of every organism, it is called ***internal respiration*** or ***cellular respiration***.

Anaerobic respiration is the incomplete break down of organic molecules with less yield of energy; it takes place in the absence of oxygen in organisms such as yeast and bacteria, muscles(under certain conditions) etc.

$$C_6H_{12}O_6 \rightarrow 2CO_2 + 2C_2H_5OH(\text{ethanol}) + 2ATP$$

$$C_6H_{12}O_6 \rightarrow 2C_3H_6O_3(\text{lactic acid}) + 2ATP$$

Aerobic (requiring oxygen) **respiration** yields more energy (gradually) due to complete breakdown of organic molecules, utilising oxygen.

$$C_6H_{12}O_6 + 6H_2O + 6O_2 \rightarrow 6CO_2 + 12H_2O + 36ATP$$

1.2.1 Respiratory organs in animals

Mechanisms of breathing vary among different groups of animals depending mainly on their habitats and levels of organisation. Protozoans and lower invertebrates such as the sponges, cnidarians, flatworms, etc., exchange with by **simple diffusion** over their entire **body surface**. Earthworms use their **moist body wall**; insects have a network of tubes (**tracheal system**) to transport atmospheric air with in the body. Spiders and scorpions have **book lungs** for aerial respiration. Special vascular structures called **gills**

are used by most of the aquatic arthropods and molluscs, whereas vascular bags called **lungs** are used by terrestrial forms for the exchange of gases. Among vertebrates' fishes, larvae of amphibians and some adult urodeles use gills, where as the reptiles, birds and mammals respire through lungs. Amphibians like frogs respire through their moist skin and lungs also. Mammals have a well developed respiratory system.

1.2.2 Human Respiratory System

Respiratory system of man includes the following:

I. External nostrils (External Nares)

A pair of external nostrils opens out above the upper lip. They lead into nasal chambers.

II. Nasal Chambers

They lie above the palate and are separated from each other by a **nasal septum**. Each nasal chamber can be differentiated into three parts namely; i. **vestibular part** (which has **hair** and **sebaceous glands** to prevent the entry of dust particles),ii. **respiratory part** (which is involved in the conditioning the temperature of inhaled air; it is supported by three thin, twisted bony plates called **turbinals /conchae**) and iii.**olfactory part** (which is lined by an olfactory epithelium to detect sense of smell).

III. Naso-pharynx

Nasal chambers lead into nasopharynx through a pair of **internal nostrils**, located above the soft palate. Nasopharynx is the upper portion of the pharynx.

IV. Larynx

Larynx is a cartilaginous box which helps in sound production, hence called the **voice box**. Wall of the larynx is supported by nine cartilages. **Thyroid**, **cricoid** and **epiglottis** are the unpaired cartilages, whereas **corniculate cartilages** (**cartilages of Santorini** - two small conical nodules of elastic cartilage articulating with the arytenoid cartilages), **arytenoids**, and **cuneiform cartilages** are the paired cartilages. **Epiglottis** is a thin leaf like elastic *cartilaginous flap* attached to the thyroid cartilage to prevent the entry of food into the larynx through the glottis. The *yellow elastic fibres* which connect the thyroid and arytenoid cartilages are called **vocal cords/vocal folds**. The opening between the ***true vocal cords*** and the ***arytenoid cartilages*** is called (some sources give a simple difinition- 'the narrow opening between the two vocal cords') **rima glottidis**.

- ❖ The mid ventral part of the thyroid cartilage forms the laryngeal prominence called **Adam's apple.**
- ❖ In males, the vocal cords are thicker, longer, and produce **low pitch voice**, where as in women and children the vocal cords are usually short and produce **high pitch voice.**

NOTE: Larynx contains two types of vocal cords: the 'false vocal cords' are the folds of mucous membrane, which do not have a role in sound production, and 'true vocal cords' which produce sound.

V. Trachea

Trachea, the wind pipe is a straight tube extending up to the mid-thoracic cavity. The wall of the trachea is supported by '**C**' shaped rings of hyaline cartilage. These rings are incomplete dorsally and keep the trachea always open preventing its collapse. Internally the trachea is lined by *pseudostratified ciliated epithelium*.

VI. Bronchi and Bronchioles

On entering the mid thoracic cavity, trachea divides at the level of the **fifth thoracic vertebra** into right and left **primary bronchi**. Each primary bronchus enters the corresponding lung and divides into **secondary bronchi** that further divide into **tertiary bronchi**. Each tertiary bronchus divides and re-divides to form primary, secondary, tertiary, terminal and respiratory bronchioles sequentially. Each respiratory bronchiole terminates in a cluster of **alveolar ducts** which end in **alveolar sacs**. Bronchi and initial bronchioles are supported by incomplete cartilaginous rings. The branching network of trachea, bronchi and bronchioles constitute the '**pulmonary tree**' (an upside down tree).

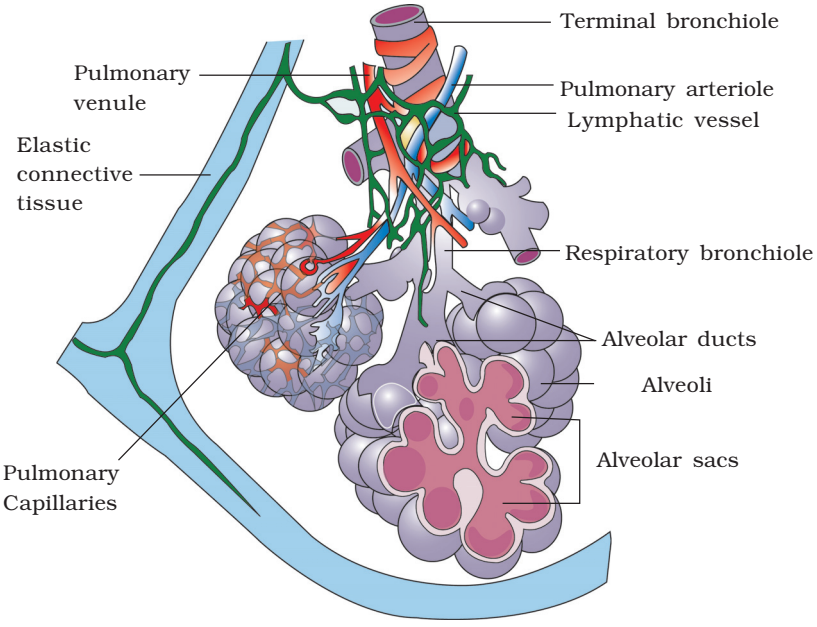


Figure 1.10 Structure of a part of a 'Pulmonary lobule'

VII. Lungs

Lungs occupy the greater part of the thoracic cavity. Lungs are covered by a double layered **pleura**, with **pleural fluid** between them. It reduces friction on the lung surface. The outer pleural membrane is in close contact with the thoracic lining whereas the inner pleural membrane is in contact with lung's surface. *The part starting with external nostrils up to the terminal bronchioles constitute the* ***conducting part****, whereas the alveoli and their ducts form the* ***respiratory*** *or* ***exchange part*** *of the respiratory system.* The conducting part transports the atmospheric air to the alveoli, clears it from foreign particles, humidifies and also brings the inhaled air to the body temperature. Exchange part is the site of actual diffusion of oxygen and carbon dioxide between blood and atmospheric air.

The lungs are situated in the thoracic chamber which is anatomically an **air-tight chamber**. It is formed dorsally by the vertebral column, ventrally the sternum, laterally by ribs and on the lower side by the dome-shaped diaphragm. The anatomical setup of lungs in the thorax is such that any change in the volume of thoracic cavity will be reflected in the lung cavity (pulmonary volume). Such an arrangement is essential for breathing, as the pulmonary volume cannot be directly altered.

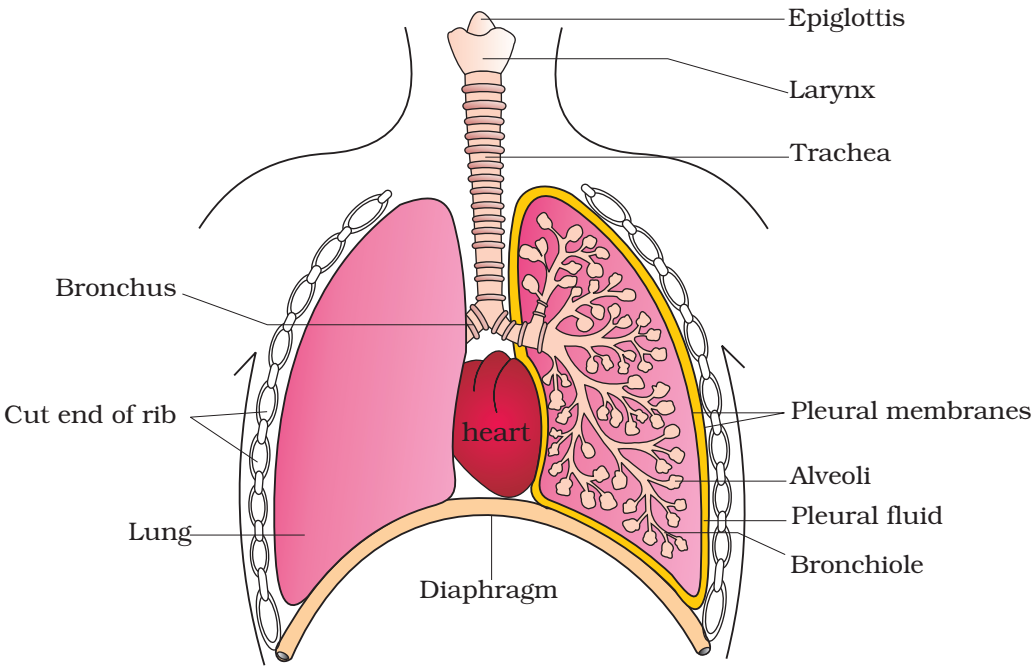


Figure 1.11 Diagrammatic view of human respiratory system (Sectional view of the left lung is also shown)

Respiration in humans involves the following steps:

i. **Breathing** or **pulmonary ventilation** by which atmospheric air with 21% of O_2 is drawn in and alveolar air rich in CO_2 is sent out.
ii. **Diffusion of gases** across the alveolar membrane
iii. **Transport of gases** by blood, between the lungs and tissues.
iv. **Diffusion of** O_2 and CO_2 between the blood in the systemic capillaries and the tissues.
v. **Utilization of** O_2 by the cells for catabolic reactions and resultant production of CO_2, H_2o, and ATP(**Cellular respiration**).

1.2.3 Mechanism of Breathing

Breathing is a means of maximising the process of gaseous exchange. The movement of air into and out of the lungs is carried out by creating a pressure gradient between the lungs and the atmosphere. Breathing involves two stages such as inspiration and expiration. Inspiration can occur if the pressure within the lungs (Intra-pulmonary pressure) is less than the atmospheric pressure, i.e., there is a negative pressure in the lungs with respect to atmospheric pressure. Similarly, expiration takes place when the intra-pulmonary pressure is higher than the atmospheric pressure. The muscular diaphragm and a specialized set of muscles, the external and internal inter-costal muscles help in generating such gradients.

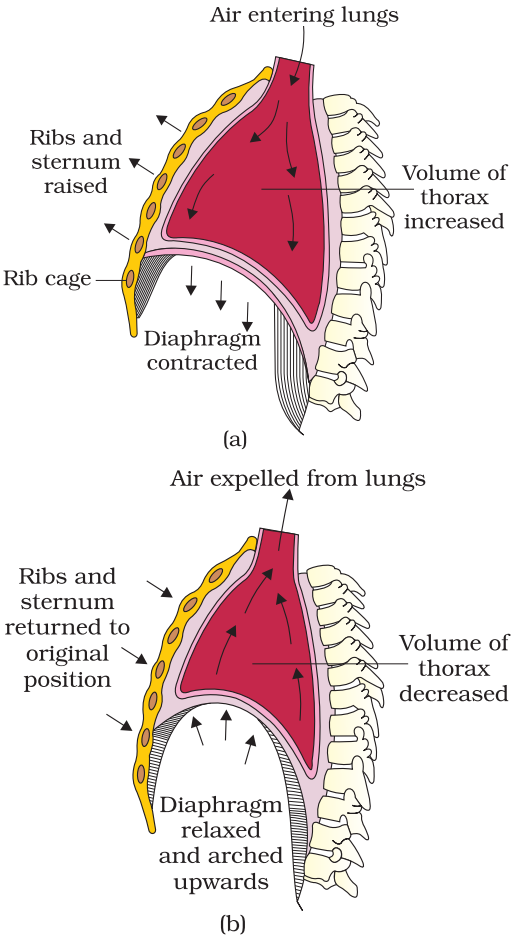


Figure 1.12 Mechanism of breathing showing: (a) inspiration (b) expiration

i. **Inspiration:** Intake of atmospheric air into the lungs is called inspiration. It is an **active process** , as it takes place by the contraction of the **muscles of the diaphragm** and the **external inter-costal muscles**, which extend in between the ribs. The contraction of the diaphragm (**phrenic muscles**) increases the volume of the thoracic chamber in the **antero-posterior axis.** The contraction of external inter-costal muscles lifts up the ribs and sternum causing an increase in the volume of the thoracic chamber in the **dorso-ventral axis**. The overall increase in the thoracic volume causes a similar increase in the 'pulmonary volume'. An increase in the pulmonary volume decreases the intra-pulmonary pressure to less than that of the atmosphere, which forces the air from the outside to move into the lungs, i.e. **inspiration**.

ii. **Expiration:** Release of alveolar air to the exterior is called expiration. It is a **passive process**. Relaxation of the diaphragm and the external inter-costal muscles returns the diaphragm and sternum to their normal positions, and reduces the thoracic volume and thereby the pulmonary volume. This leads to an increase in the intra-pulmonary pressure to slightly above that of the atmospheric pressure, causing the expulsion of air from the lungs, i.e. expiration.

NOTE : The contraction of the internal intercostal muscles and the lateral abdominal muscles help in 'forced expiration'.

We have the ability to increase the strength of inspiration and expiration with the help of additional muscles in the abdomen. On an average, a healthy human breaths **12-16** times/minute. The volume of the air involved in breathing movements, can be estimated by using a **spirometer**, which helps in clinical assessment of the pulmonary functions.

1.2.4 Exchange of gases

Alveoli are the primary sites of exchange of gases in the lungs. Exchange of gases also occurs between blood and tissues. O_2 and CO_2 are exchanged in these sites by **simple diffusion**. The exchange of gases is based on some important factors that can affect the rate of diffusion; these factors include (i) partial pressure / concentration gradient of gases, (ii) solubility of the gases, (iii) thickness of the respiratory membrane, (iv) surface area, (v) distance of diffusion.

The pressure contributed by an individual gas in a mixture of gases is called its **partial pressure** and is represented as pO_2 for oxygen and pCO_2 for carbon dioxide. The data given below in the table clearly indicates a concentration gradient for oxygen from the alveoli to the blood and from the blood to the tissues. Similarly, a gradient present for in the opposite direction i.e., from the tissues to the blood and from the blood to the alveoli.

Partial pressures (in mm Hg) of oxygen and carbon dioxide at different parts involved in diffusion in comparison to those in the atmospheric air

Respiratory Gas	Atmospheric Air	Alveoli	Blood (Deoxyge-nated)	Blood (Oxygenated)	Tissues
O_2	159	104	40	95	40
CO_2	0.3	40	45	40	45

As the solubility of CO_2 is 20-25 times higher than that of O_2 the amount of CO_2 that can diffuse through the diffusion membrane per unit difference in partial pressure is much higher compared to that of O_2. The **diffusion membrane** is made up of three major layers namely, the thin *squamous epithelium of the alveolar wall*, the *endothelium of the alveolar capillaries* and the *basement material in between them*. As it is a very thin border, it is favourable for diffusion of gases.

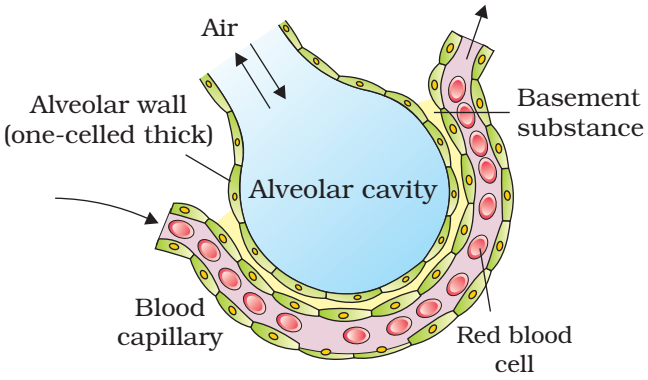


Figure 1.13 A section of an alveolus with a pulmonary capillary

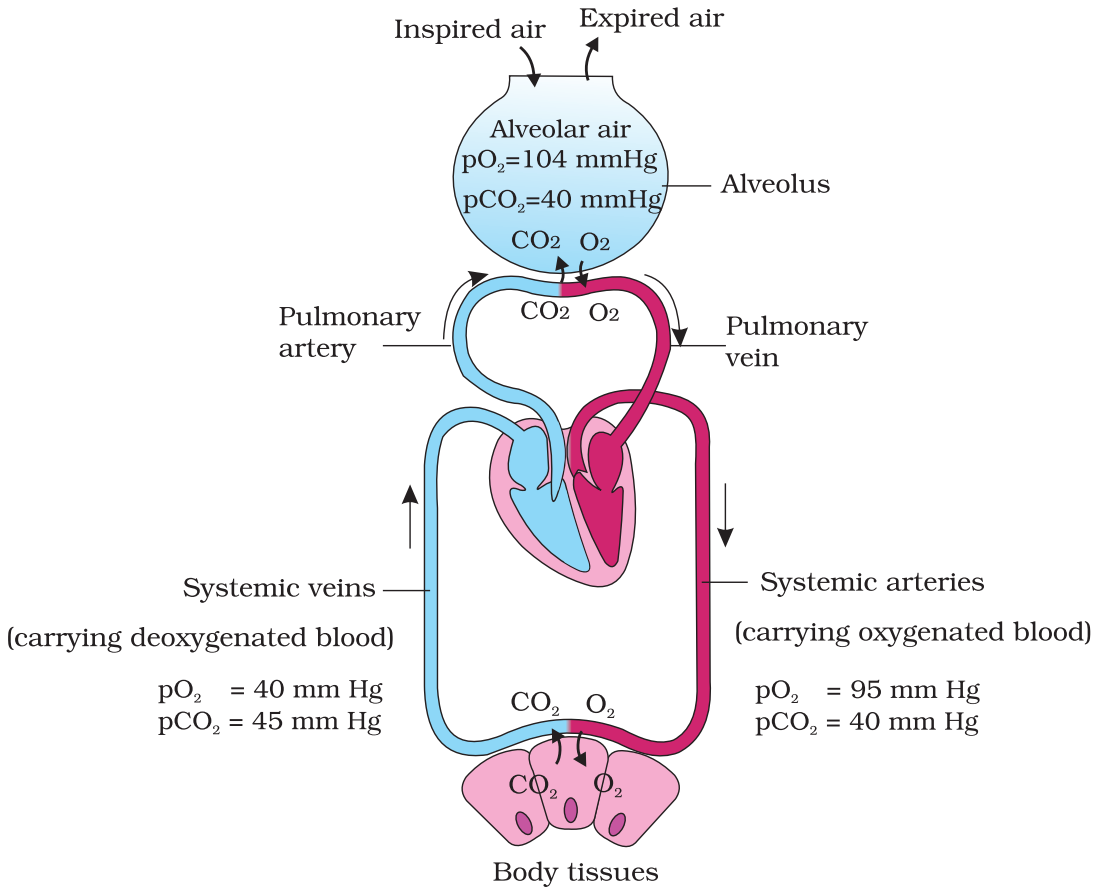


Figure 1.14 Diagrammatic represetnation of exchange of gases at the alveolus and the body tissues with blood and transport of O_2 and CO_2

I. Pulmonary gas exchange (External respiration)

Differences in pO_2 and pCO_2 of alveolar air and pulmonary capillaries favour the diffusion of O_2 from the alveolar air into the blood in the pulmonary capillaries and the diffusion of CO_2 in the opposite direction.

II. Systemic gas exchange (Internal respiration)

Difference in $pO_2$and pCO_2 of oxygenated blood in systemic capillaries and tissues favour the diffusion of O_2 from systemic capillaries into tissues and the diffusion of CO_2 in the opposite direction.

1.2.5 Transport of gases

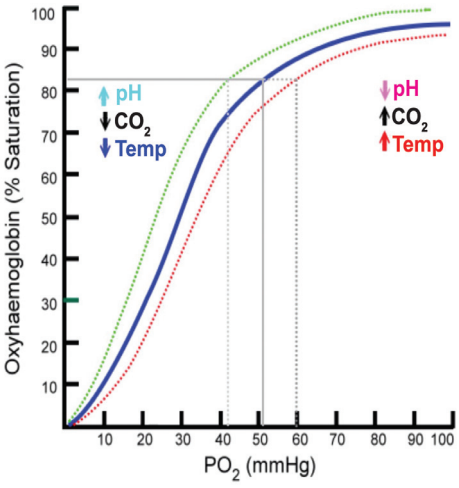
Blood is the medium of transport for O_2 and CO_2.

I. Transport of Oxygen

Oxygen is transported from the lungs to the tissues through the plasma and RBC of the blood.100ml of oxygenated blood can deliver 5 ml of O_2 to the tissues under normal conditions.

(i) **Transport of oxygen through plasma:** About **3%** of O_2 is carried through the blood plasma in a dissolved state.

(ii) **Transport of oxygen by RBC:** About **97%** of O_2 is transported by the RBCs in the blood. Haemoglobin is a red coloured iron containing pigment present in the RBCs. Each haemoglobin molecule can carry a maximum of **four molecules of oxygen**. Binding of oxygen with haemoglobin is primarily related to the partial pressure of O_2. At lungs, where the partial pressure of O_2 (oxygen tension) is high, oxygen binds to haemoglobin (purplish-bluish-red in colour) in a reversible manner to form oxyhaemoglobin (**bright red** in colour). This is called **oxygenation** of haemoglobin.



$$Hb + 4O_2 \rightleftharpoons Hb(O_2)_4$$

At the tissues, where the partial pressure of O_2 is low, oxyhaemoglobin dissociates into **haemoglobin** and **oxygen**. The other factors that influence binding of oxygen with haemoglobin are the partial pressure of CO_2, the hydrogen ion concentration (pH) and the temperature.

(iii) **Oxygen – haemoglobin dissociation curve:** It explains the relation between percentage saturation of haemoglobin and partial pressure of oxygen. A **sigmoid curve** is obtained when percentage saturation of haemoglobin with O_2 is plotted against the pO_2. This curve is called 'oxyhaemoglobin dissociation curve' and is highly useful in studying the effect of factors such as pCO_2, H^+ concentration, temperature, etc., on the binding of O_2 with haemoglobin. In the alveoli, where there is a high pO_2, low pCO_2, lesser H^+ concentration (high pH) and lower temperature, the factors are all favourable for the formation of **oxyhaemoglobin**. In the tissues where low pO_2, high pCO_2, high H^+ concentration (low pH) and higher temperature exist, the conditions are favourable for dissociation of oxygen from oxyhaemoglobin. Under these conditions, oxygen dissociation curve shifts away from the Y-axis (**to the right**). The effect of pCO_2 and H^+ concentration on the oxygen affinity of haemoglobin is called **Bohr Effect** (increase of carbon dioxide in the blood and decrease in pH results in the reduction of the affinity of hemoglobin for oxygen).

NOTE: A rise in pCO_2 and fall in pH decreases the affinity of haemoglobin for oxygen. On the other hand a fall in pCO_2 and rise in pH, increases affinity of haemoglobin for oxygen. *This clearly indicates that O_2 gets bound to haemoglobin at the lung surface and gets dissociated at the tissues.*

NOTE: At pO_2 of 100mmHg. typical in the lungs haemoglobin is saturated to about **97%**. At a **pO_2 of 40mm Hg** which is common in tissues during rest time, haemoglobin is about **75% saturated**. It means oxyhaemoglobin gives away about **22% oxygen** only to '**resting tissues**'. It also means, only about $1/5^{th}$ of the oxygen from blood is unloaded in the resting tissues. The remaining $4/5^{th}$ is in the form of 'Reserve' in the blood itself. If the tissues such as **skeletal muscles** are involved in vigorous exercise, there is more'**unloading tension**' in the oxyhaemoglobin and so more oxygen is given away rapidly (up to **62%** at 20mmHg.of **pO2** and the percent of saturation of haemoglobin is only **35%**). As mentioned above in a 'resting person', haemoglobin always carries about **70% oxygen** (which is still available to tissues, for the asking). Hence oxyhaemoglobin ensures supply of oxygen for survival for **4-5 minutes** after the stopping of heart or when breathing is interrupted.

II. Transport of Carbon Dioxide: CO_2 is transported in three ways.

(i) In dissolved state: 7 per cent of CO_2 is carried in a dissolved state (physical solution) through plasma.

$$CO_2 + H_2O \quad H_2CO_3$$

Do you know: Why is the P^H of deoxygenated (venous) blood less than that of oxygenated (arterial) blood.

(ii) As carbamino compounds: About 20-25 per cent of CO_2 combines directly with free amino group of the haemoglobin and forms **carbamino-haemoglobin** in a reversible manner.

$$\mathbf{Hb - NH_2 + CO_2 \quad Hb - NHCOO^- + H^+}$$

This binding of CO_2 is related to the partial pressure of CO_2. pO_2 is a major factor which could affect this binding. When pCO_2 is high and pO_2 is low as in the tissues, binding of more carbon dioxide occurs. When pCO_2 is low and pO_2 is high as in the alveoli, dissociation of CO_2 from carbamino – haemoglobin takes place, i.e., CO_2 which is bound to haemoglobin from the tissues is delivered at the alveoli. Carbamino compounds are also formed by the union of CO_2 with plasma proteins.

HCO_3^-

NOTE: Haemoglobin is an amphoteric compound (reacting chemically as either an acid or a base). It has the peculiar character of taking more oxygen in oxygen rich areas and release CO_2 and accepting more CO_2 in areas where the CO_2 is more and release oxygen.

(iii) As Bicarbonates: About 70 per cent of CO_2 is transported as ***bicarbonate***. RBCs contain a very high concentration of the enzyme, **carbonic anhydrase** and a minute quantity of the same is present in the plasma too. This enzyme facilitates the following reaction in both the directions.

$$CO_2 + H_2O \underset{\text{Carbonic anhydrase}}{\rightleftharpoons} H_2CO_3 \underset{\text{Carbonic anhydrase}}{\rightleftharpoons} \quad +H^+$$

At the tissue level, where partial pressure of CO_2 is high due to catabolism, CO_2 diffuses into the blood (RBC and Plasma) and forms carbonic acid which dissociates into HCO_3^- and H^+. At the alveolar site where pCO_2 is low, the reaction proceeds in the opposite direction leading to the formation of CO_2 and water. Thus CO_2 is mostly trapped as **bicarbonate** at the tissues and transported to the alveoli where it is released out as CO_2. Every **100 mL** of deoxygenated blood delivers approximately **4mL** of CO_2 to the alveolar air.

Chloride shift: Due to the permeability of plasma membrane of RBC to anions, HCO_3^- ions (formed due to dissociation of H_2CO_3) diffuse into the blood plasma from the RBC at the tissues. The **H^+** ions are 'buffered' (to curtail acidity) by haemoglobin which turns into **HHb** (acid haemoglobin). Haemoglobin can act as a buffer at physiological pH (7.4), because of its high content of ' histidine'.

$$H^+ + HCO_3 + Hb.4O_2 \rightarrow HHb + HCO_3 + 4O_2$$

As a result, the molecule loses its affinity for oxygen and so O_2 is released. It diffuses into the plasma and from there into the tissues (in the pulmonary capillaries of the lung, where the partial pressures and pH are reversed, all of these reactions run in the reverse way). To maintain electrolyte balance, Cl^- ions diffuse from plasma into RBC when the bicorbonate ions pass out of the RBC into plasma. This exchange of chloride and bicarbonate ions between RBC and plasma at the tissues is called **chloride shift** or **Hamburger's phenomenon/ Hamburger's shift**. Reverse chloride shift occurs when blood reaches the lungs.

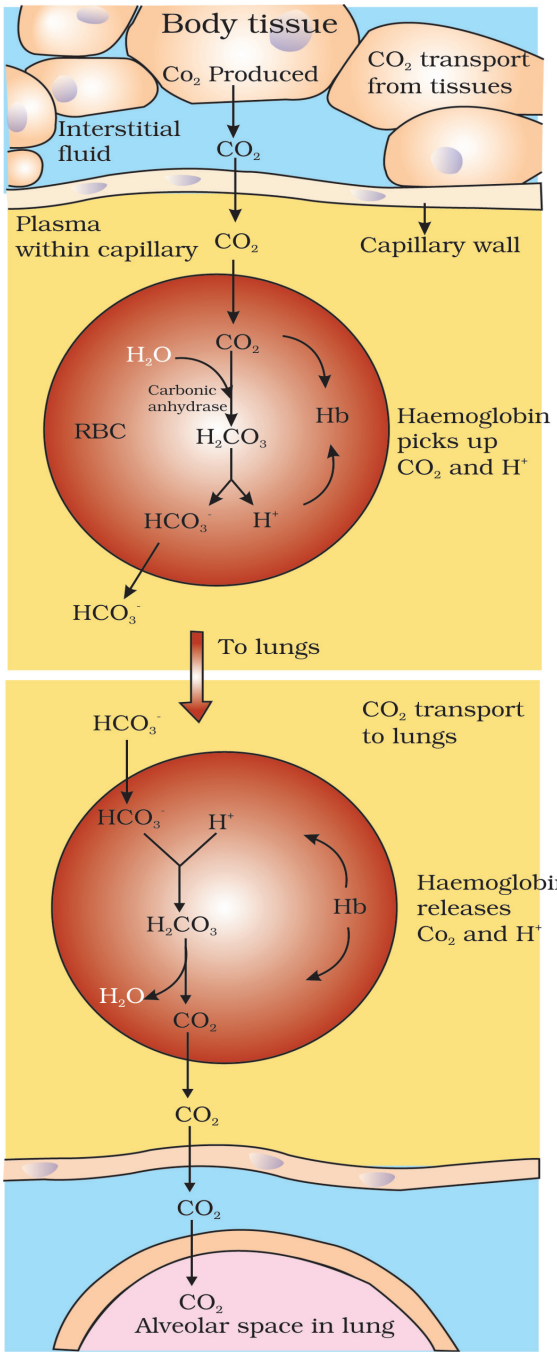


Figure 1.15 Carbon dioxide transport in the blood

1.2.6 Regulation of respiratory movements

Human beings have a significant ability to maintain and moderate the respiratory rhythm to suit the demands of the body tissues. This is done by the neural system.

1. A special centre present in the medulla region of brain, called '**Respiratory rhythm centre**' is primarily responsible for this regulation/respiratory rhythm.

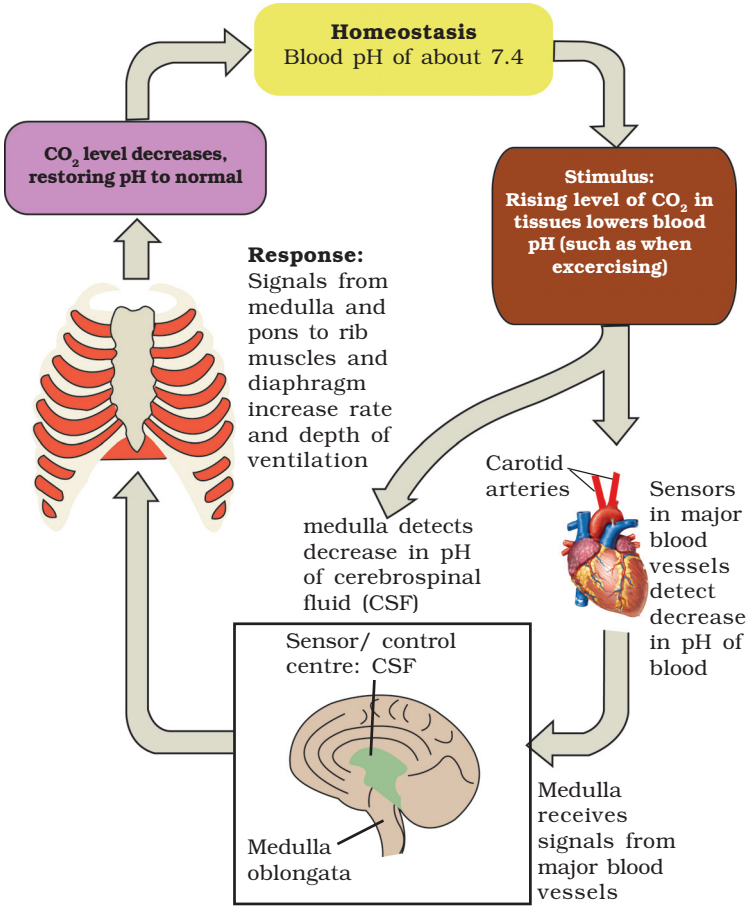


Figure 1.16 Homeostatic control of breathing

2. Another centre present in the ***pons*** of the brain stem called '***Pneumotaxic Centre***' can moderate the functions of the 'respiratory rhythm centre'. Neural signal from this centre can reduce the duration of inspiration and there by alter the respiratory rate.

3. A **chemo-sensitive area** is situated adjacent to the respiratory rhythm centre which is highly sensitive to CO_2 and hydrogen ions. Increase in these substances can activate this centre, which inturn can send signals to the respiratory rhythm centre to make necessary adjustments in the respiratory process by which these substances can be eliminated.

4. Receptors associated with **aortic arch** and **carotid artery** also recognize changes in CO_2 and H^+ concentration and send necessary signals to the respiratory rhythm centre and pneumo tactic centre for necessary actions (increase in the rate and depth of breathing when their concentration is high). The role of oxygen in the regulation of the respiratory rhythm is quite insignificant.

1.2.7 Respiratory volumes and Capacities

Tidal Volume (T.V.): Volume of air inspired or expired during normal inspiration or expiration. It is approximately 500 ml. i.e., a healthy man can inhale or exhale approximately 6000 to 8000 ml of air, per minute.

Inspiratory Reserve volume (IRV): The additional volume of air that can be inhaled during forced breathing, in addition to the 'tidal volume'. This is about 2500 ml to 3000 ml.

Expiratory reserve Volume (ERV): The additional volume of air that can be exhaled during forced expiration, in addition to the 'tidal volume'. This is about 1000ml to 1100ml.

Residual volume (R.V): The volume of air remaining in the lungs even after forcible expiration. This is about 1100 ml to 1200 ml.

By adding up a few 'respiratory volumes' described above, one can derive various pulmonary capacities, which are useful in clinical diagnosis of pulmonary disorders.

Inspiratory Capacity (IC): The total volume of air, a person can inhale after 'normal expiration'. This includes the 'tidal volume' and 'inspiratory reserve volume': IC = TV + IRV. It is about 3000 ml to 3500 ml.

Functional Residual Capacity (FRC): The volume of air that remains in the lungs after normal expiration: FRC=ERV + RV.

Vital Capacity (VC): The maximum volume of air a person can breathe in after 'forced expiration'. This includes ERV, TV and IRV or the maximum volume of air a person can breathe out after 'forced inspiration': **VC=TV+IRV+ERV**

Total Lung Capacity (TLC): The total volume of air accommodated in the lungs at the end of 'forced inspiration'. This includes RV, ERV, TV and IRV or vital capacity + residual volume: TLC=VC+RV or TLC= ERV+IRV+TV+RV

1.2.8 Disorders of the Respiratory System

1. **Asthma** is a disorder of difficulty in breathing caused due to inflammation of bronchi and bronchioles. It is characterized by the spasm of smooth muscles present in the walls of the bronchi and bronchioles. Symptoms include coughing, difficulty in breathing and wheezing .In the case of asthma, the allergen causes release of histamine and other inflammatory substances which cause constriction of the bronchi.
2. **Emphysema** is a chronic disorder in which alveolar walls are damaged and their walls coalesce due to which respiratory surface *area of exchange of gases is decreased*. The lung shows larger but fewer alveoli and more fibrous and less elastic. One of the major causes of this is 'smoking' of tobacco.

- **Bronchitis** is the inflammation of the bronchi, resulting in the swelling of mucous lining of bronchi, increased mucus production and decrease in the diameter of bronchi. Symptoms include chronic cough with thick mucus/ sputum (phlegm).
- **Pneumonia** is infection of lungs caused by bacteria such as *Streptococcus pneumoniae* and also by certain viruses, fungi, protozoans and mycoplasmas. Symptoms include inflammation of lungs, accumulation of mucus in alveoli, and impaired exchange of gases , leading to death if untreated .
- Emphysema, chronic bronchitis and asthma come under Chronic Obstructive Pulmonary diseases (**COPDs**).

3. Occupational Respiratory disorders: These are caused by exposure of the body to the harmful substances from certain industries, especially those involving grinding or stone breaking. Long term exposure of the body to such substances can give rise to inflammation of respiratory passage and lungs leading to several disorders.

i. **Asbestosis:** It occurs due to chronic exposure to asbestos dust in the people working in asbestos industry.

ii. **Silicosis:** It occurs because of long term exposure to 'silica dust' in the people working in mining industries, quarries etc.

iii. **Siderosis:** It occurs due to deposition of inhaled iron particles in tissues. It can cause different types of siderosis such as **pneumoconiosis, hyperferremia** and **hemosiderosis** (which causes recurrent alveolar hemorrhage).

iv. **Black-lung disease:** It is a lung disease that develops from inhalation of coal dust. It is common in long time coal mine workers.

GLOSSARY

Alveoli: Thin walled, irregular, highly vascularized bag like structures that form the sites of exchange of gases in the lungs.

Bohr Effect: Effect of CO_2 and H^+ on the oxygen-affinity of haemoglobin.

Carbonic anhydrase: (fastest known enzyme) An enzyme present in RBC, that catalyses the formation of carbonic acid from CO_2 and H_2O its dissociation into H^+ and HCO_3^-.

Chemo-sensitive area: It is an area situated adjacent to the respiratory rhythm centre; it is highly sensitive to CO_2 and H^+.

Chloride shift: Exchange of chloride and bicarbonate ions between erythrocytes and plasma. It is also called Hamburger's phenomenon.

Cricoid cartilage: Circular cartilage that forms the lower and posterior part of wall of larynx.

Glottis: It is an opening of the larynx into the pharynx.

Inter costal muscles: Muscles that extend in between ribs and help in bringing breathing movements.

Pneumotaxic centre: It is present in the pons region of brain and can moderate the functions of respiratory rhythm centre.

Pulmonary exchange: Exchange of O_2 and CO_2 between pulmonary capillaries and alveoli of lungs.

Respiratory rhythm centre: A specialized centre present in the medulla region, primarily responsible for regulation of respiration.

Systemic exchange: Exchange of O_2 and CO_2 between systemic capillaries and tissues.

Thyroid cartilage: The largest cartilage that supports the ventral and lateral walls of the larynx.

Vocal cords: A pair of thin strands of yellow elastic fibres that extend between thyroid and arytenoids cartilages. They help in the production of sound.

QUESTIONS

Very Short Answer Type Questions

1. Define vital capacity. What is its significance.
2. What is the volume of air remaining in lungs after a normal expiration?
3. Diffusion of oxygen occurs in the alveolar region only and not in the other parts of respiratory system. How do you justify the statement?
4. What is the effect of pCO_2 on oxygen transport?
5. What happens to the respiratory process in a man going up a hill?
6. What is Tidal volume? Find out the Tidal volume (approximate value) in a healthy human, in an hour.
7. Define oxyhaemoglobin dissociation curve. Can you suggest any reason for its sigmoidal pattern?
8. What are conchae?
9. What is meant by chloride shift?
10. Mention any two occupational respiratory disorders and their causes in human beings.
11. Name the muscles that help in normal breathing movements.
12. Draw a diagram of oxy-haemoglobin dissociation curve.

Short Answer Type Questions

1. Explain the process of inspiration and expiration under normal conditions.
2. What are the major transport mechanisms for CO_2? Explain.
3. How is respiratory movements regulated in man?
4. Distinguish between
   (a) IRV and ERV
   (b) Inspiratory capacity and expiratory capacity
   (c) Vital capacity and Total lung capacity.
5. Describe disorders of respiratory system.

Long Answer Type Questions

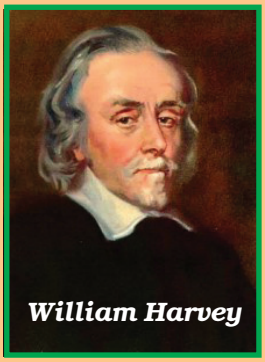
1. Describe the respiratory system in man.
2. Write an essay on the transport of oxygen and carbon dioxide by blood.

FOR IGNITED MINDS

Your 'Calorie Burner' and 'Energy Provider'

Breathing and Exchange of Gases

1. To maximise oxygen uptake fishes adopt a special technique with reference to flow of blood in their gills and direction of flow of water. What do we call it?
2. Why does a pregnant woman in advanced pregnancy gasp for breath, if she walks fast.
3. In some people, lungs have 'larger', but 'fewer alveoli' due to damage to alveolar partition tissue. What do you call such a disorder?
4. Do alpha and beta chains of haemoglobin carry the same amount of oxygen per chain?
5. What is the percentage of oxygen that is released from saturated RBC in a resting person and what is the percentage of saturation of haemoglobin of the blood that returns to the heart.
6. In two different studies it was found that the dissociation of oxyhaemoglobin is 60% and 40% at the same partial pressure of oxygen . Do you think it is possible? If so what could be the reason(s) for such a shift in the oxyhaemoglobin dissociation curve ?
7. Why do people who suffer from carbon monoxide poisoning tend to die?
8. What is the enzyme that plays an important role in the transport of CO_2 by blood?
9. Will the two oxyhaemoglobin dissociation curves of foetus and mother be similar or different? Can you give reasons for your opinion?
10. Evaluate the correctness of the following statement: If a person breathes in and out rapidly for some time (hyperventilation), his body allows him to hold his breath for a longer period than in the case of normal ventilation(for example when he is submerged in water). Is that due to (i) increase in O_2 levels in his body (ii) decreased level of CO_2 in his body at that time?


William Harvey

Unit-II

HUMAN ANATOMY AND PHYSIOLOGY - II

The third 'Integrating System' cum 'The Postman' cum 'The Policeman'

*Eucoelomate animals require a 'circulatory system' to carry **nutrients** and **oxygen** to the body parts, collect wastes including carbon dioxide from the tissues and carry them to the appropriate excretory organs. Blood and lymph are the only fluid tissues that collect various substances including respiratory gases, hormones etc., and deliver them to the appropriate organs/tissues, the '**Postman's job**'. Simultaneously the blood vascular system is involved in the defence system of the body as it contains various types of phagocytic cells including certain progenitors of '**macrophages**' (tissue fixed or otherwise), the '**Policeman's job**'. Blood contains several types of proteins such as **albumins**, **globulins** etc. The albumins provide '**capillary osmotic pressure**' to prevent excessive loss of fluids from blood and help maintain its normal consistency. **Fibrinogen** and **prothrombin** play a vital role in clotting of blood to prevent excessive bleeding. Blood carries various **hormones** to body parts from the organs of their secretion and help coordination of the body, hence deserves to be reckoned as the '**Third Integrating System**'. Circulatory system has a '**pumping station**', the **heart**. Blood pressure is monitored by 'pressure sensors' in the aorta and the volume of the blood is controlled by hormones such as **ADH** and **aldosterone**.*

UNIT II A

Body Fluids and Circulation

Different groups of animals have evolved various methods for transport of substances between body parts. Simple organisms such as sponges and cnidarians circulate water drawn from their surroundings through their body cavities facilitating exchange of these substances. More complex organisms use special 'circulatory' fluids within their bodies to transport such materials. Blood is the most commonly used circulatory fluid by most of the higher organisms, including the humans. In the higher animals, in addition to blood, another body fluid, the **lymph**, also helps in the transport of certain substances. Blood and lymph together constitute the **fluid tissues** in the human body. In this chapter, you will learn about lymph, clotting of blood, the structure and functioning of the heart, circulatory blood vessels along with certain disorders of the circulatory system.

NOTE: The composition of blood is not discussed here as it is already covered in the Junior Inter Text Book.

2.1 Lymphatic system

It is an extensive network of thin-walled vessels that arise as blind-ended lymph capillaries in most of the tissues of the body. The lymph capillaries unite to form a tree like structure of increasingly larger lymph vessels, which finally drain lymph into veins in the lower neck region. Lymphatic system is an **open circulatory system**.

- Lymph capillaries are microscopic, closed-ended tubes that form vast network in the intercellular spaces. The walls are composed of endothelial cells, with pores, through which interstitial fluid/extracellular fluid (**ECF**), proteins, microorganisms and absorbed fats can easily enter. Once the extra cellular fluid enters the lymphatic capillaries, it is referred to as **lymph**.
- The lymph capillaries merge and form large, lymphatic vessels which lead into larger **lymph ducts**. The walls of the lymph vessels and ducts are similar to those of veins and are provided with valves. The smooth muscles of their walls cause peristaltic waves of contraction pushing lymph towards the neck region.

All the lymph vessels from the lower part of the body eventually empty lymph into the thoracic duct. The **thoracic duct** of the lymphatic system is the **largest lymphatic vessel** (lymph duct) in the body. It is also known as the **left lymphatic duct, chyliferous duct** etc., and it empties the lymph into the venous system at the junction of the left internal jugular vein and **left subclavian vein**. Lymph collected from the left side of the head, the left arm, and the parts of the chest region also enters the thoracic duct before it empties into the venous system. Lymph from the right side of the neck, head, right arm, and the right part of the thorax is collected into the right lymphatic duct which empties it into venous system at the junction of the **right sub clavian vein** and right internal jugular vein. Thus, lymph ,which was once a part of the blood that came out of the blood vessels to supply oxygen and nutrients to tissues, as the ECF, is finally drained back into the left and right subclavian veins (venous system).

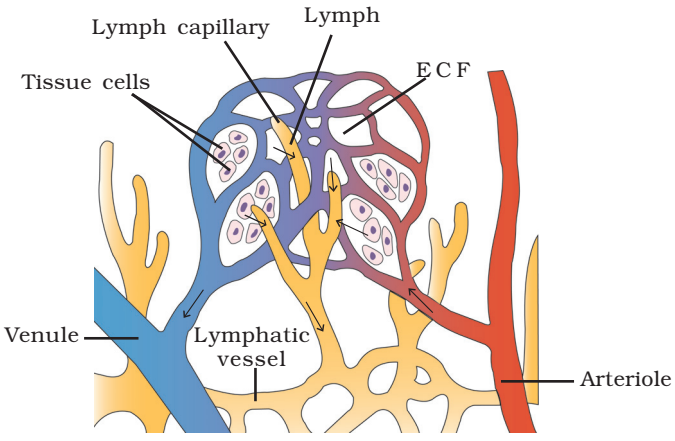


Figure 2.1 The relationship between blood capillaries and lymphatic capillaries and ECF

Before lymph is returned to the heart via the venous system, bacteria, viruses etc., are phagocytised by the WBC in the lymph nodes. The lymphatic system also consists of other organs such as spleen, thymus, tonsils etc. Mucosa associated lymphoid tissue (**MALT**) and appendix also constituting a part of the lymphatic system.

Do you know? **Spleen** is the largest lymphatic organ and is also the reservoir of red blood cells and lymphocytes .It acts as 'haemopoietic organ' until the fifth month of gestation.

Formation of lymph

When blood passes through the capillaries, due to high filtration pressure at the arteriolar ends of capillaries, along with plasma, many substances such as glucose, small sized organic molecules, inorganic salts etc. (except the large plasma proteins) are filtered into the extracellular spaces where it is called '**tissue fluid**'/'**ECF**'. This causes an increase in **colloidal osmotic pressure** of the plasma of the blood in the venular ends of the capillaries (due to **plasma proteins**). This pressure favours the movement of about 85 percent of the ECF into the capillaries at the venular ends after exchanging oxygen, CO_2, nutrients, other metabolites etc., with the tissues. The remaining 15% of ECF is collected into the lymphatic system through *lymph capillaries*. Henceforth it is called **lymph**.

DO YOU KNOW? In a pregnant woman when the enlarged uterus exerts pressure on the abdominal veins, it increases the capillary hydrostatic pressure, it leads to accumulation of fluids (**ECF**) in the legs, hence the swollen legs - '**edema**', in them.

Composition of lymph

Lymph is similar in its composition to the blood's plasma, except that it contains a much lower concentration of proteins and nutrients such as fatty acids and glycerol than those in the plasma. Erythrocytes are absent. Lymph contains water, some plasma proteins, electrolytes, leucocytes mostly **lymphocytes**, some coagulation factors, antibodies, enzymes, hormones, vitamins, nutrients etc. *An emulsion of lymph and triglyceride fat (chylomicrons), characteristically present in lacteals is called* ***chyle***.

Functions of lymphatic system

1. Lymph returns some ECF and wastes collected from the body parts to the blood.
2. It transports lymphocytes from the lymphatic glands to the blood.
3. It transports *digested fats* which are absorbed through lacteals, present in the intestinal villi, to the blood vascular system.
4. It destroys the invading microorganisms and foreign particles in the **lymph nodes**.

2.2 Clotting of blood

When a blood vessel is injured a number of physiological mechanisms are activated that promote **hemostasis** (hemo = blood; stasis = standing). Breakage of a blood vessel exposes collagen proteins to the blood. This initiates three separate, but overlapping hemostatic mechanisms - (1) vasoconstriction (2) the formation of a platelet plug, and (3) the production of a web of fibrin proteins (blood clot)

(1) **Vasoconstriction**: When a blood vessel is damaged, the smooth muscles in it's wall contract, which makes the lumen of the vessels narrow, sometimes so strongly that blood flow is completely stopped.

(2) **Platelet-plug formation**: When the endothelium is ruptured, platelets adhere to the collagen and release some secretions. These secretions aggregate other platelets and make them sticky, so that they adhere to those already stuck on the collagen and form a '**platelet- plug**'.

(3) **Production of web of fibrin protein**: The third mechanism for hemostasis is the formation of clot. The activator substances from the injured vascular wall, platelets and blood proteins adhering to the injured vascular wall, initiate the clotting process. Clot is a web of fibrin with blood cells trapped in it.

Mechanism of blood clotting

Clotting takes place in three essential steps.

i) **Step -1**: It involves the formation of a complex of activated substances collectively called, **prothrombin activator**. It is formed by a complex cascade of chemical reactions that occur in the blood by the involvement of clotting factors in two *pathways*.

   (a) Intrinsic pathway: It occurs when the blood is exposed to collagen of injured endothelium of blood vessel. This activates **Factor XII**, and in turn it activates another clotting factor, which activates yet another reaction (*cascade fashion*), which results in the formation of the **prothrombin activator**.

   (b) Extrinsic pathway: It occurs when the vascular wall is severely damaged and extra vascular tissue comes into contact with blood. This activates the release of tissue thromboplastin, from the damaged tissue. It activates the **Factor VII**. As a result of these cascade reactions, the final product formed is the **prothrombin activator**.

ii) **Step -2**: The prothrombin activator, in the presence of sufficient amounts of Ca^{++}, causes the conversion of inactive **prothrombin** to active **thrombin** *(activation of prothrombin)*.

iii) **Step -3:** Thrombin converts the soluble protein fibrinogen into soluble fibrin monomers, which are held together by weak hydrogen bonds. The fibrin stabilizing factor (Factor XIII, released from platelets) replaces hydrogen bonds with covalent bonds and cross links the fibres to form a 'mesh work'. The insoluble mesh work of fibrin fibers spreading in all directions adhere to the damaged surfaces and trap the blood cells and platelets.

Within a few minutes after the clot is formed. It begins to **contract** so that the fluid is expelled out. This is called **clot retraction** and the fluid thus formed is the **serum** (*plasma without fibrinogen*) and some other proteins.

Clotting factors

Factor	Name
I	Fibrinogen
II	Prothrombin
III	Thromboplastin
IV	Calcium ions (Ca^{++})
V	Proaccelerin (Labile factor)
VII	Proconvertin (Stable factor)
VIII	Antihemophilic Factor - A
IX	Plasmathromboplastin component (**PTC**) or Christmas Factor
X	Stuart-Prower Factor
XI	Plasmathromboplastin antecedent (**PTA**)
XII	Hageman's Factor
XIII	Fibrin Stabilizing Factor

*Factor VI is no longer referred as clotting factor.

Do You Know? Platelets are necessary for clot retraction. Failure of clot retraction is an indication that the number of platelets in the blood might be low. In the case of diseases such as '**dengue**' the platelet count falls low and the patient may require transfusion of blood platelets.

Anticoagulants

They are as follows:

- **Heparin** is an anticoagulant synthesized by mast cells and basophils. It activates antithrombin, a plasma protein, which combines with thrombin and inactivates it.
- Coumarins of plant origin are the precursors of anticoagulants such as **warfarin** (see glossary), which are antagonistic to Vit-K and thus prevent the synthesis of the blood clotting factors - **II**, **VII**, **IX** and **X**, formed in the **liver**.
- Clotting of blood in test tubes in clinical laboratories and 'Blood Banks' can be prevented by the addition of **citrates** or **oxalates** of sodium or Ethylene diamine tetra acetic acid (**EDTA**). They bind to calcium ions and thus make Ca^{++} unavailable for the action in clotting.

Circulating pathways

The circulatory patterns are of two types – **open** and **closed**.

a) Open type: In this type, blood (more appropriately - haemolymph) flows from the heart into the vessels. The vessels open into large spaces called sinuses. From the sinuses, the haemolymph is collected into the heart and distributed to body parts.

As the circulatory fluid comes out of the vessels and freely flows in the body spaces, this type of circulatory system is called **open type**. It is found in leeches, arthropods, molluscs, echinoderms and ascidians.

b) Closed type: In this type blood flows through blood vessels. The blood flows from the arteries to the veins through small blood vessels called capillaries. Closed type of blood vascular system is found in the **annelids**, **cephalopods** among the non-chordates, **cephalochordates** and all the **vertebrates** among chordates.

Plan of circulatory system in the vertebrates

In the vertebrates the principal differences in the blood-vascular system involve the gradual differentiation of the heart into two separate '**pumps**' as they evolved from the gill breathing aquatic life to the lung breathing, complete terrestrial life.

- **Fishes** have a 2-chambered heart with an **atrium** and a **ventricle.** It pumps out deoxygenated blood to gills for oxygenation, hence the name '**branchial heart**'. Blood passes through the heart only once in a complete circuit, hence called **single circulation**.
- **Amphibians** have a 3-chambered heart with two atria and one ventricle. Reptiles have two atria and an **incompletely divided ventricle** (*except in the crocodiles in which the ventricle is divided into two chambers*). The left atrium receives oxygenated blood from the gills/lungs/skin and the right atrium receives deoxygenated blood from the other parts of the body through the *venae cavae*. However, the two types of blood get mixed up in the single ventricle, which pumps out **mixed type of blood**. Thus these animals (amphibians and reptiles) show an **incomplete double circulation**.
- **Birds** and **mammals** possess a 4-chambered heart with two atria and two ventricles. In these animals the oxygenated and the deoxygenated types of blood received by the left and right atria, passes on to the left and right ventricles, respectively. The ventricles pump the blood out without any mixing of the oxygenated and deoxygenated types of blood i.e., there are two completely separate circulatory pathways namely **systemic** and **pulmonary** circulations. Hence, these animals are said to be showing '**double circulation**'.

2.3 Human cardio-vascular system

It consists of a four chambered muscular heart, a network of closed branching blood vessels and blood.

2.3.1 Structure of the heart

The heart is **mesodermal** in origin. It is a thick walled, muscular and pulsating organ, situated in the **mediastinum** (the region in the thorax between the two lungs), and with its apex slightly turned to the left. It is of the size of a clenched fist.

The heart is covered by a double walled pericardium which consists of the **outer fibrous pericardium** and the **inner serous pericardium**. The serous pericardium is double-layered, formed of an outer *parietal layer* and an inner *visceral layer*. The parietal layer is fused with the fibrous pericardium, whereas the visceral layer adheres to the surface of the heart and forms its outer layer, the **epicardium**. The two layers are separated by a narrow pericardial space, which is filled with the **pericardial fluid**. This fluid reduces friction between the two membranes and allows free movement of the heart.

The wall of the heart consists of three layers. They are the outer **epicardium**, the middle **myocardium** (a thick layer of cardiac muscles), and the inner most **endocardium** (a thin layer of endothelium). The endothelium covers the heart valves also and is continuous with the endothelial lining of the large blood vessels connected to the heart.

External structure

Human heart has four chambers, with two relatively smaller upper chambers, called **atria** and two larger lower chambers called **ventricles**. Atria and ventricles are separated by a deep transverse groove called **coronary sulcus** (atrio-ventricular groove). The muscular pouch like projection from each atrium is called **auricular appendix** (auricular appendage). The ventricles are separated by two inter ventricular grooves (anterior and posterior), in which the coronary arteries and their branches are lodged.

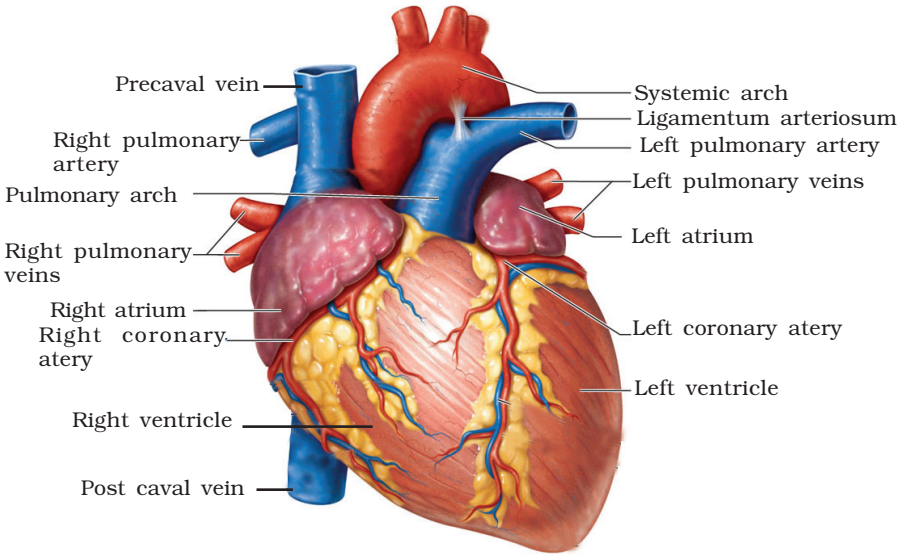


Figure 2.2 External structure of the heart.

Internal structure

i) **Atria**: Atria are thin walled 'receiving chambers' (upper chambers). The two atria are separated by thin inter-atrial septum. In the fetal heart, the atrial septum has a small pore called **foramen ovale**. Normally the foramen ovale closes at birth, when lungs become functional. It is represented by a depression in the septum between the right and left atria, called **fossa ovalis** (that marks the position of the foramen ovale in the fetus). If, the foramen ovale does not close properly, it is called a **patent foramen ovale.**

The right atrium receives deoxygenated blood from different parts of the body (except the lungs) through **two caval veins** viz. a precaval vein or superior vena cava (collecting blood from the the head, forelimbs and thoracic region) and a post caval vein (collecting blood from the hind limbs and abdominal organs). The heart also receives blood from the myocardium (wall of the

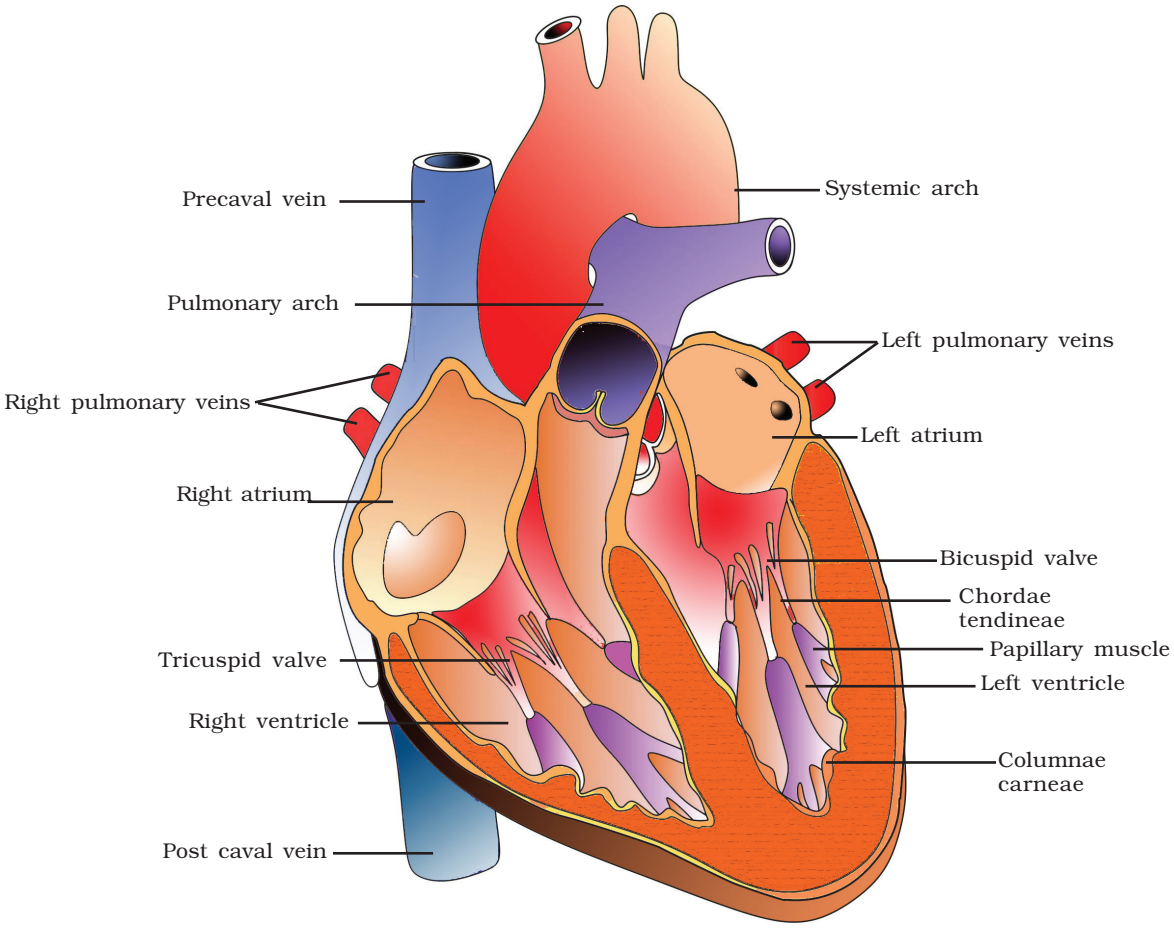


Figure 2.3 Internal structure of the Heart.

heart) through the coronary sinus, whose opening into the right atrium is guarded by the **valve of Thebesius**. Opening of the postcaval vein is guarded by the valve of the inferior vena cava or **Eustachian valve**. It directs the blood to the left atrium through the foramen ovale, in the foetal stage, but in the adult it becomes rudimentary and non-functional. The opening of the precaval vein into the right atrium has no valve. The left atrium receives blood from each lung through two pulmonary veins, which open into the left atrium.

Atria and ventricles are separated by a membranous **atrio-ventricular septum**, which possesses left and right atrioventricular apertures. The left and right apertures are guarded by **bicuspid** (**mitral valve**) and **tricuspid** valves respectively.

ii) **Ventricles**: These are the thick walled blood pumping chambers (lower chambers), separated by an interventricular septum. The wall of the left ventricle is thicker than that of the right ventricle. The inner surface

of the ventricles is raised into muscular ridges or columns called **columnae carneae**/ **trabeculae carneae** projecting from the inner walls of the ventricles. Some of these ridges are large and conical, and are called **papillary muscles**, whose apices are connected to the **chordae tendineae**, or '**heart strings**'. They are cord-like collagenous processes that connect the **papillary muscles** to the **tricuspid valve** and the **mitral valve** in the heart. They prevent the cusps of the atrioventricular valves from bulging too far into atria during ventricular systole.

Nodal tissue

A specialized cardiac musculature called the nodal tissue is also distributed in the heart. A patch of this tissue called the **sinoatrial node** (SAN) is present in the right upper corner of the right atrium near the opening of the superior vena cava. Another mass of this tissue, called the **atrioventricular node** (AVN), is seen in the lower left corner of the right atrium postero-inferior region of the inter atrial septum close to the opening of the coronary sinus. It electrially connects atrial and ventricular chambers. A bundle of nodal firbres, called **atrioventricular bundle** (AV bundle/'His' bundle) continues from the AVN into the inter-ventricular septum. It divides into right and left ***bundle branches***. These branches give rise to minute fibres called **Purkinje firbres** that extend throughout the ventricular musculature /walls of the respective sides.

SAN consists of specialized ***cardiomyocytes***. It has the ability to generate ***action potentials*** *without any external stimuli* (***myogenic***), ***hence called 'pace maker'***. **AV NODE** is a '**relay point**' that relays the action potentials received from the SA node to the ventricular musculature. SAN can generate action potentials every 0.6 sec. (which means it can initiate 100 beats per minute). Our heart normally beats 70-80 times per minute (on average 72 beats min^{-1}). Autonomous and hormonal coordination systems take charge of increasing or decreasing the rates, depending on the situation.

iii) Aortic arches: The **pulmonary arch** arises from the left anterior angle of the right ventricle. Its opening is guarded by the **pulmonary valve** and it carries deoxygenated blood to the lungs. The **systemic arch** (left) arises from the left ventricle and transports oxygenated blood to different parts of the body through its branches. Its opening is guarded by the '**aortic valve**'. The pulmonary and aortic velves are madeup of three semilunar flaps, each. A fibrous strand, known as **ligamentum arteriosum** is present at the point of contact of the systemic and

pulmonary arches. It is the remnant of the **ductus arteriosus**, which connects the systemic and pulmonary arches in the embryonic stage.

Do You Know? Human embryonic heart begins beating at around a month of embryonic development.

2.3.2 Cardiac cycle

The cardiac events that occur from the beginning of one heart beat to the beginning of the next constitute a cardiac cycle. This cardiac cycle consists of three phases, namely **atrial systole, ventricular systole** and **joint diastole**.

To begin with, all the four chambers of the heart are in a relaxed state/ **joint diastole stage**. Blood from the pulmonary veins and venae cavae flows into the respective atria. As the A-V valves are in open condition, blood flows into the left and right ventricles, through the left and right atrioventricular apertures. The semilunar valves of the pulmonary and aortic arches are closed at this stage.

Atrial systole (0.1 sec)

The SAN now generates an action potential which stimulates both the atria to contract simultaneously causing the '**atrial systole**'. This increases the flow of blood into the ventricles by about 30%. It means atrial systole accounts for about 30 % of the filling of the ventricles, the remaining blood flows into the ventricles before the atrial systole.

Ventricular systole (0.3 sec)

The action potentials from the SAN reach the AVN from where they are conducted through the bundle of His, its branches and the Purkinje fibres to the entire ventricular musculature. This causes the simultaneous *ventricular systole*. The atria undergo relaxation coinciding with the ventricular systole. Ventricular systole increases the pressure causing the closure of the **AV valves** preventing the '**backflow**' of blood. It results in the production of the first heart sound known as '**Lub**'. As the ventricular pressure increases further, the semilunar valves guarding the pulmonary artery and the aorta are forced open. This allows the blood in the ventricles to flow into the ***aortic arches*** and enter the circulatory pathway.

Joint diastole (0.4 sec)

The ventricles now relax and the ventricular pressure falls causing the closure of the semilunar valves which prevents the back flow of blood. This results in the production of the second heart sound known as '**Dup**'. As the ventricular pressure declines further, the AV valves are pushed open by the pressure in the atria exerted by the blood, which flowed into them through the larger

veins. The blood now once again flows freely into the ventricles. All the heart chambers are now again in a relaxed state (joint diastolic phase). Soon, another cardiac cycle sets in.

NOTE: The human heart beats **72** times per minute normally. Hence the duration of a cardiac cycle is about **0.8 sec**.

2.3.3 Cardiac output

The volume of blood pumped out by each ventricle, for each heart beat, is known as the ***stroke volume***. The volume of blood pumped out by the heart from each ventricle per minute is termed ***cardiac output***.

Cardiac output = **stroke volume** x **No. of beats per minute** = 70ml/ beat x 72 beats/minute = 5040 ml/min. or approximately **5 liters**

Do You Know? The body has the ability to alter the **stroke volume** (especially in athletes) as well as the **heart rate** and thereby the cardiac output. The cardiac output generally increases in the active state and decreases in resting condition.

2.3.4 Double circulation

The blood pumped by the right ventricle enters the **pulmonary artery**, whereas the left ventricle pumps blood into the **aorta**. The deoxygenated blood pumped into the **pulmonary arch** is passed on to the lungs from where the oxygenated blood is carried by the **pulmonary veins** into the **left atrium**. This pathway constitutes the **pulmonary circulation** (*lesser circulation*). The oxygenated blood entering the aorta is carried by a network of arteries, arterioles and capillaries to the tissues from where the deoxygenated blood is collected by a system of venules, veins and venae cavae and emptied into the right atrium. This is the **systemic circulation** (*greater circulation*). The systemic circulation provides nutrients, O_2 and other essential substances to the tissues and collects CO_2 and other harmful substances away, for their elimination.

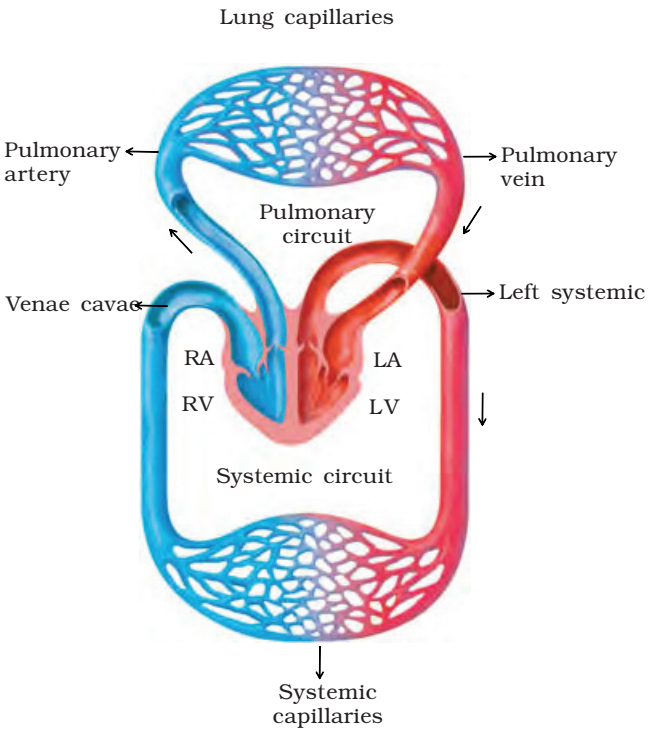


Figure 2.4 Double circulation.

Portal circulation and Coronary circulation

A blood vessel that starts in capillaries and ends in capillaries is called a 'portal vessel'. A system of portal vessel is named after the name of the organ in which it ends in capillaries. In man there is a portal system between the digestive tract and the liver. It is called **hepatic portal system**. The hepatic portal vein carries blood from the gut to the liver before it is delivered to the systemic circulation via the heart. The absorbed foods such as sugars, when present in excess, are converted into glycogen and stored in the liver cells (glycogenesis). A special coronary system of blood vessels is present in the human body exclusively for the circulation of blood to and from the heart/cardiac musculature. The coronary circulation in humans includes the right and left coronary arteries and four **cardiac veins/coronary veins**. The coronary veins open into the coronary sinus.

2.3.5 Regulation of cardiac activity

Normal activities of the heart are regulated intrinsically, i.e., auto regulated by specialized muscles (*nodal tissue*). A special neural centre in the medulla oblongata can moderate the cardiac function through the 'autonomic nervous system' (ANS). Neural signals through the sympathetic nerves (part of ANS) can increase the rate of heart beat, the strength of ventricular contraction and thereby the cardiac output. On the other hand, parasympathetic neural signals (another component of ANS) decrease the rate of heart beat and thereby the cardiac output. Adrenal medullary hormones, the **epinephrine** and **norepinephrine** can also increase the cardiac output. **Thyroxine** also increases the heart rate and cardiac output.

2.4 Blood vessels

Blood vessels form a tubular network through the body that permits blood to flow from the heart to all the living cells of the body and then back to the heart. Blood leaving the heart passes through vessels of progressively smaller diameter, referred to as arteries, arterioles, and capillaries. Capillaries are microscopic vessels that join the arterial flow to the venous flow. Blood returning to the heart from the capillaries passes through vessels of progressively larger diameters, called venules and veins.

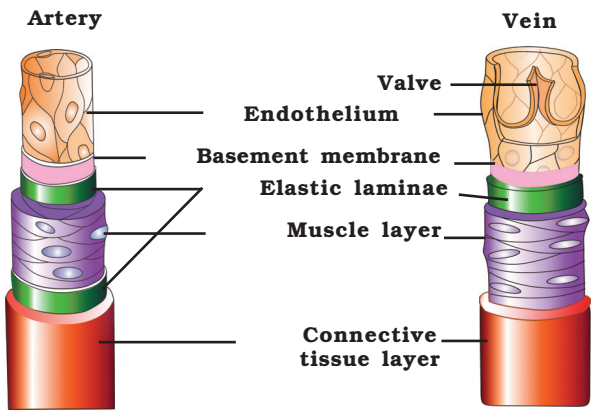


Figure 2.5 Blood vessels

Arteries and veins have essentially three layers in their walls. (1) **Tunica externa / tunica**

adventitia consists of fibrous connective tissue, (2) **tunica media** madeup of smooth muscles and (3) **tunica interna** made up of endothelium (and basement membrane).

In addition to the above layers arteries and arterioles have two elastic laminae one on either side of the muscle layer. Veins have one elastic lamina inner to the muscle layer. The muscle layer is much thicker in the arteries than in the veins. Endothelium of veins is double folded to form valves, which are directed towards the heart and they allow flow of blood towards the heart only.

Differences between arteries and veins

Arteries	Veins
Arteries carry oxygenated blood, away from the heart (except the pulmonary artery)	Veins carry deoxygenated blood, towards the heart (except the pulmonary veins)
These are bright red in colour	These are dark red in colour
These are mostly deep seated in the body	Veins are generally superficial
Arteries are thick-walled as the tunica media is relatively thick, with smooth muscles and two elastic laminae	Veins are thin walled (tunica media is relatively thin with one elastic lamina) and the walls are slightly muscular.
Lumen is narrow	Lumen is wide
Non-valvular	Valvular
Blood in the arteries flows with more pressure and by jerks	Blood in the veins flows steadily with relatively low pressure
Arteries end in capillaries	Veins start with capillaries

NOTE: The smallest vessels present in the walls of large blood vessels like aortic arches are called '**Vasa vasorum**' (the '**vessels of the vessels**').

Capillaries

These are the smallest blood vessels of the body, which connect arterioles and venules. Unlike the vessels of the arterial and venous systems, the walls of capillaries are composed of just one cell thick layer a **simple squamous epithelium**, or **endothelium**. The absence of smooth muscles and connective tissue layers permits rapid exchange of materials between the **blood** and the **tissues**.

2.5. Disorders of circulatory system

i) Hypertension (High blood pressure)

Hypertension is a chronic medical condition in which blood pressure in the arteries is elevated. The normal blood pressure at rest is **120**

mm.Hg. (Systolic)/**80 mm. Hg**. (diastolic) mmHg. on an average. High blood pressure leads to heart diseases and also affects other vital organs such as the *brain* and *kidneys*.

Blood pressure (BP): *It is the force exerted by the blood against the walls of the vessels. It is affected by age, sex and state of health. Blood pressure is measured in the brachial artery of the arm by using a* ***sphygmomanometer.*** *Pressure* ***120/80*** *mm.Hg is considered normal blood pressure in human beings. The upper reading pertains to systolic pressure and the lower one, the diastolic pressure. Blood pressure above* ***140/90*** *is considered* ***hypertension****. It is worth knowing that it is universally believed that excessive intake of* ***salt*** *causes hypertension (in addition to* ***genetic reasons****).*

ii) Coronary Artery Disease (CAD)

CAD often referred to as atherosclerotic heart disease. It is the result of the accumulation of calcium, fat, cholesterol and fibrous tissue along the wall of coronary arteries which makes their lumen narrow. This narrow blood vessel reduces the blood flow to the heart, causes **ischemia** (restriction of blood supply to muscle tissue, causing shortage of oxygen). Myocardial cells may die due to lack of oxygen and this is called a myocardial infarction. It leads to heart muscle damage. CAD is associated with smoking, diabetes and hypertension.

iii) Angina Pectoris

It is marked by '**chest pain**' caused by narrowing of blood vessels to the heart (**ischemia**). Angina pectoris is a '**warning signal**' of deprivation of blood supply to the heart muscles. However there is no necrosis (death) of the cardiac muscle tissue. It occurs in men and women of any age , but it is more common among the middle aged and the elderly people .

The major risk factors for angina include smoking , diabetes, high cholesterol, high blood pressure etc.

iv) Heart Failure

It is a condition in which the heart is unable to provide sufficient pumping action to distribute blood flow to meet the needs of the body. Common causes of heart failure include **myocardial infarction/heart attack** (localized death of heart tissue–*necrosis)* and other forms of ischemic heart diseases, hypertension etc. It is also called **congestive heart failure** because congestion of the lungs is one of the main symptoms of this disease. Heart failure is not the same as *cardiac arrest* or *heart attack* (see glossary).

GLOSSARY

Auricular appendix: A small conical ear-shaped pouch projecting from the upper anterior portion of each atrium of the heart, increasing slightly the atrial volume.

Bundle of His: It is a collection of heart muscle cells specialized for electrical conduction that transmits the electrical impulses from the AV node to the walls of the ventricles.

Cardiac arrest: It is also known as cardiopulmonary arrest or circulatory arrest. It is the cessation of normal circulation of the blood due to sudden stoppage of contraction of the heart (sudden cardiac arrest, which sometimes run in families).

Cascade reaction: A series of chemical or physiological processes that occur in successive stages, each of which is dependent of the preceding one, to produce a culminating effect. The steps involved in the clotting of blood occur as a cascade of reactions.

Colloid osmotic pressure: It is also referred to as *oncotic pressure and* is a measurement of pressure exerted within the blood vessels by *the proteins found in blood plasma*. The special nature of these proteins helps ensure passage of fluids in and out of the capillaries at the proper rate.

Lacteal: It is a lymphatic capillary in the villus of the small intestine that absorbs digested fats.

Mitral valve: Is a dual-flap (mitral-from the Latin, meaning *shaped like a mitre*) valve in the heart that lies between the left atrium and the left ventricle. Mitre is the cap/head gear with two flaps worn by bishops.

Myocardial infarction (MI): It is commonly known as a heart attack, and it results from the lack of blood supplyto a part of the heart, causing heart cells to die. This is most commonly due to blockage of a coronary artery following the rupture of a vulnerable atherosclerotic plaque. The heart tissue deprived of oxygen becomes a *necrotic spot* (an area of localized death of an organ)

Myocardial ischemia: It is a disease/or condition characterised by reduced blood supply to the heart muscle, (coronary artery disease- atherosclerosis of the coronary arteries), which results in narrowing of the parts of arteries that supply blood to the muscles of the heart. 'Ischemia' is common in aged people and people who consume 'fat rich food'.

Portal venous system: It is a system of a blood vessel starting in capillaries in one organ and ending in capillaries in another organ.

Purkinje fibers: These are located in the inner ventricular walls of the heart, just beneath the endocardium. These fibers consist of specialized *cardio myocytes* that are able to conduct *cardiac action potentials* more quickly and efficiently than any other cells in the heart.

Tricuspid valve: It is a valve between the right atrium and the right ventricle of the mammalian heart, usually has three leaflets connected to three papillary muscles by chordae tendineae.

Warfarin: It is also known under the brand names *Coumadin*, *Jantoven* etc. It is an anticoagulant, normally used in the prevention of thrombosis and thromboembolism (the formation of blood clots in the blood vessels and their migration elsewhere in the body)

QUESTIONS

Very Short Answer Type Questions

1) Write the differences between 'open' and 'closed' systems of circulation.
2) Sino-atrial node is called the pacemaker of our heart. Why?
3) What is the significance of artrio-ventricular node and antrio-ventricualr bundle in the functioning of the heart?
4) Name the valves that guard the left and right atrioventricualr apertures in man.
5) Where is the valve of Thebesius in the heart of man?
6) Name the aortic arches arising from the ventricles of the heart of man.
7) Name the heart sounds. When are they produced.
8) Define cardiac cycle and cardiac output.
9) What is meant by double circulation? What is its significance?
10) Why the arteries are more elastic than the veins?

Short Answer Type Questions

1) Describe the evolutionary change in the structural pattern of the heart among the vertebrates.
2) Describe atria of the heart of man.
3) Describe the ventricles of the heart of man.
4) Draw a labeled diagram of the L.S of the heart of man.
5) Describe the events in a cardiac cycle, briefly.
6) Explain the mechanism of clotting of blood.
7) Distinguish between SAN and AVN.
8) Distinguish between arteries and veins.

Long Answer Type Questions

1) Describe the structure of the heart of man with the help of neat labelled diagram.
2) Write notes on the working of the heart of man.

FOR IGNITED MINDS

'Third Intergrating System' cum
'The postman' cum 'The Policeman

Body Fluids and Circulation

1. In what type of animals blood from the respiratory organs does not return to the heart directly and goes to the tissues instead.
2. Veins generally carry blood towards the heart (except the portal veins), whether it is oxygenated or deoxygenated blood. Can you give an example of a vein that does not carry blood to the heart directly, but carries away from it.
3. What is the purpose of the presence of the sheet of connective tissue separating the atria from the ventricles.
   HINT: It has something to do with the conduction of impulses in the chambers of the heart.
4. Why do doctors suggest people with angina pectoris to carry/to keep with them nitroglycerine tablets and asprin tablets with them always.
5. What is the difference between a 'heart attack' and 'angina pectoris'.
6. When a person is running a long race (such as marathon) and is closing on the finish line, he makes the maximum effort to win the race. Do you think there will be 'more cardiac output' or 'more stroke volume' or 'both' in him at that time?
7. Which period of interval is shorter comparatively, with reference to the heart sounds popularly called 'lub' and 'dup'. Is it '1ub' to 'dup' or 'dup' to 'lub'?
8. It is scientifically true that S.A. node can generate an action potential every 0.6 sec. which by logical inference means the heart beats 100 times/min. In a normal healthy person, it is however 70-80 times (on average 72 times). What system in the human body slows it down to the normal/average level?
9. If somebody says-"The left atrial systole is completely responsible for the left ventricular filling, in a cardiac cycle" -do you agree with the statement? If you do not agree, why?
10. If your neighbor has angina pectoris and if you have immediate access to a medical shop, what type of tablets would you bring and administer to him (provided you are permitted to take a chance).
    Hint: You can go for two types of drugs - a vasodilator and a blood thinner.

UNIT II B

Excretory Products and their Elimination

Excretion- Good Riddance, And Homeostasis

*Excretion is the elimination of nitrogenous and other waste materials from the body. Kidneys are the chief excretory organs. Nitrogenous wastes are sent out along with some water. Water is the most important constituent of protoplasm, the living substance. Dehydration kills a person much faster than lack of food. Metabolism of proteins and nucleic acids produces ammonia, a toxic waste (no energy is spent for the production of ammonia). Aquatic animals excrete ammonia (**ammonotelic**) through body surface, gill surface etc. by diffusion. They can send ammonia through dilute urine as they can afford to lose much water. In others, ammonia is converted into **urea** (along with carbon dioxide), which is less toxic, via the '**ornithine cycle**' in the liver (**ureotelic**). In insects, reptiles birds and land snails the end product of nitrogen metabolism is **uric acid** (**uricotelic**), to conserve water (uric acid is almost insoluble in water and production of uric acid involves expenditure of more energy). Uric acid is produced by mammals too by **purine metabolism**. Many mammals except apes, man etc., produce the enzyme '**uricase**' by which they can convert uric acid into a more soluble "**allantoin**". Some animals excrete the excess amino acids also (**aminotelic**).*

*Kidneys also maintain acid-base balance by excreting H^+ ions. The regulation of internal fluids (water balance) is an example of '**homeostasis**'. Kidneys are involved in the homeostasis of the body fluids and their concentration (**the salt balance**). The tissues of cartilaginous fishes are well adapted to tolerate/survive high urea concentrations. These fishes (and many other salt water fishes and molluscs also) have large quantities of **trimethyl amine oxide** (TMAO), an organic molecule that protects body proteins from the damaging effect of urea.*

2.6 Modes of excretion

Animals cannot eliminate free nitrogen, but can eliminate it in the form of nitrogenous end products. The metabolism of excess amino acids, and the nitrogen bases of nucleic acids produce ammonia from which urea or uric acid is formed depending upon the need.

I. **Ammonotelism:** The elimination of ammonia as the chief nitrogenous waste material is termed **ammonotelism**. Ammonia is formed by the oxidative deamination of amino acids. **Deamination** chiefly occurs in the liver of the vertebrate body. The amino group, separated from the amino acid, combines with hydrogen and becomes ammonia (NH_3). Ammonia is highly toxic and readily soluble in water, hence it should be eliminated from the body quickly and in the form of a very dilute solution. Therefore excretion of ammonia is most common in aquatic species. Many lower invertebrates expel ammonia through the whole body surface by simple **diffusion.** In bony fishes, most of the ammonia is lost as ammonium ions (NH_4) across the epithelium of the gills, with kidneys excreting only minor amounts of nitrogenous wastes. The animals which excrete ammonia are called **ammonotelic animals**.

II. **Ureotelism:** Terrestrial adaptation necessitated the production of lesser toxic nitrogenous wastes such as urea and uric acid for the conservation of water. The elimination of urea as the principal nitrogenous waste material is termed **ureotelism**. It is produced in the vertebrate liver by a metabolic cycle (ornithine cycle) that combines ammonia with carbon dioxide. The circulatory system transports urea to the kidneys for filtration and elimination. Urea is 100,000 times less toxic than ammonia. This permits some animals to transport and store urea safely at higher concentrations (Physiological uremia as seen in cartilaginous fishies). Thus 'urea-excreting' animals require much less water than the ammonotelic animals. Some amount of urea may be retained in the medullary fluid of kidneys to maintain the desired osmolarity. Earthworms, cartilaginous fishes, most of the amphibians (which spend most of the time on land) and mammals excrete urea as their chief nitrogenous waste and are called **ureotelic animals**.

III. **Uricotelism:** The elimination of uric acid as the chief nitrogenous waste material is called uricotelism. Uric acid is mainly formed from ammonia mostly in the liver of sauropsids and in the Malpighian tubules of tracheate arthropods. Uric acid is less toxic than urea and being insoluble in water can be excreted as semisolid paste or pellets with very little water loss. This is a great advantage for animals with little

access to water. Tracheate arthropods, land snails, many reptiles and birds excrete uric acid as their major nitrogenous waste, hence they are called **uricotelic animals**.

Excretory organs

The organs responsible for the elimination of metabolic waste products are called excretory organs. They help in the elimination of nitrogenous wastes, water balance and maintains constant ionic composition of the extracellular fluids in the body. A variety of excretory organs are present in the animal kingdom. In most invertebrates, these structures are simple tubular forms. However, in man and other vertebrates they are complex tubular structures called kidneys. Some of the excretory structures in invertebrates are mentioned here.

- **Protonephridium** is a network of dead-end tubules with cellular units called flame bulbs. Each flame bulb has a tuft of cilia projecting into the tubule. Protonephridia are found in platyhelminths, rotifers, larvae of annelids and molluscs and lancelets (with solenocytes). Protonephridia are primarily concerned with ionic and fluid volume regulation i.e **osmoregulation**.
- **Metanephridia** are tubular excretory structures which are immersed in the coelomic fluid and enveloped by a capillary network. They are found in most annelids such as the earthworms. They help to remove nitrogenous wastes and maintain fluid and ionic balance.
- **Malpighian tubules** are 'blind' tubular structures floating in the haemolymph and opening into the digestive tract. They are found in insects and other terrestrial arthropods. Besides excretion, they have a role in conserving water and salts effectively, as they send wastes into the gut where water is reabsorbed.
- **Antennary glands** or **green glands** are paired structures which lie at the bases of the antennae and open to the exterior. These structures draw waste materials from the haemolymph. They are found in crustaceans.
- **Coxal glands** are the excretory structures in the arachnids.
- **Kidneys** (metanephridia/renal organs) and **pericardial glands** are the excretory structures found in the adult molluscs.

2.7 Human Excretory System

In humans, the excretory system consists of a pair of kidneys, a pair of ureters, a urinary bladder and urethra.

Kidneys

Kidneys are reddish brown, bean shaped structures, situated on either side of the vertebral column between the levels of the last thoracic and third **lumbar vertebrae**, in a '**retroperitoneal position**'**.** The right kidney is slightly lower than the left one due to the presence of large liver.

Do you Know? The average weight of kidney is 120 – 170 gms in man.

The outer surface of the kidney is convex and the inner surface has a deep notch called **hilum**, the point at which the renal artery and nerves enter and the renal vein and ureter leave. Each kidney is surrounded by a tough, fibrous **capsule** that protects its delicate inner surface.

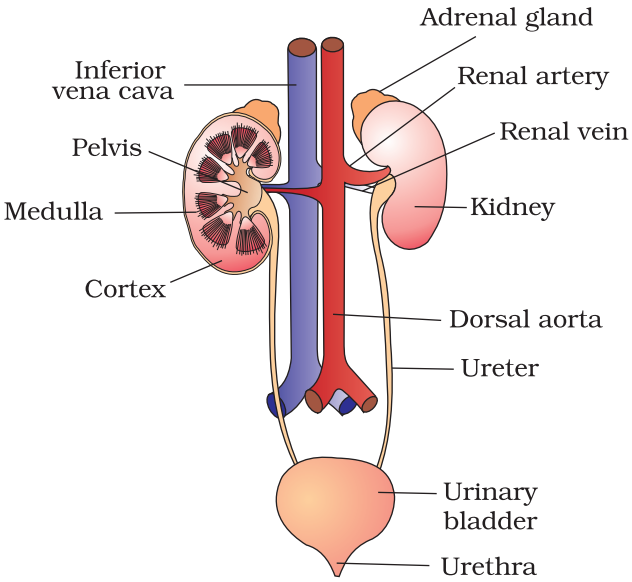


Figure 2.6 Human urinary system

Internal structure

A longitudinal section of the human kidney shows two distinct regions, the outer **cortex** and the inner **medulla**. The medulla is divided into multiple cone shaped masses of tissue called **renal pyramids**. The renal pyramids are separated by the projections of the cortex called **columns of Bertin** **(renal columns)**. The base of each pyramid originates at the border between the cortex and the medulla and terminates in the renal papilla. Renal papillae project into cup like **calyces**, formed by the extensions of funnel shaped **pelvis,** which continues out as the ureter.

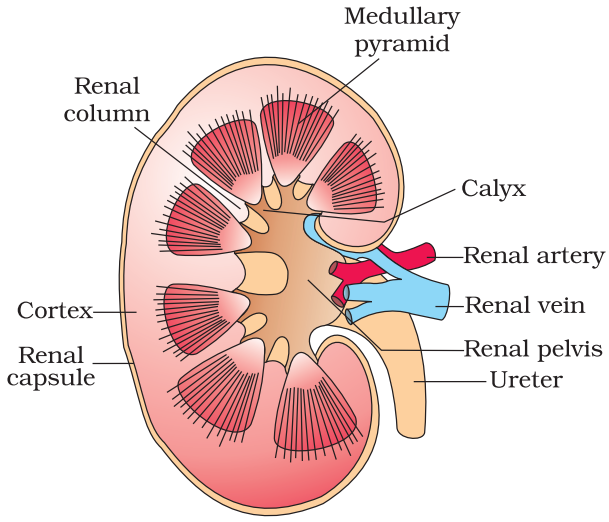


Figure 2.7 L.S of Kidney

Ureters

These are slender whitish tubes which emerge from the pelvis of the kidneys. Their walls are lined by 'transitional epithelium'. The ureters run downwards and open into the urinary bladder.

Urinary bladder

It is a median storage sac, situated in the lower abdominal cavity. It has thick, muscular, distensible wall lined by 'transitional epithelium'. The neck of the bladder leads into the urethra, which has an **internal urethral sphincter** (made of smooth muscles) and **external urethral sphincter** (made of striped muscles). Urethra opens near the vaginal orifice in the females and through penis in the males.

> **Do you know?** Infection of the urinary tract is more common in women than in men, due to her short urethra **(more close to the anal aperture on par with its surface)**and the greater possibility of 'germs' passing in the ***anal-urinary tract*** route.

Structure of a Nephron

Each kidney has nearly **one million** nephrons or uriniferous tubulus which are the 'structural' and 'functional' units. Each nephron has two parts – the 'renal corpuscle' or malpighian corpuscle and the 'renal tubule'. Renal corpuscle is composed of a network of blood capillaries called glomerulus and a double walled cup called Bowman's capsule. The **glomerulus** is formed by the **afferent renal arteriole** – a fine branch of the renal artery. Blood from the glomerulus is carried away by an **efferent renal arteriole** of a lesser diameter. The inner wall of the Bowman's capsule has certain unique cells called **podocytes** which wrap around each capillary of the glomerulus. The podocytes are arranged in an intricate manner so as to leave some minute spaces called '***filtration slits***' or '***slit pores***'. The endothelial cells of the capillaries have numerous pores or '***fenestrations***'. The glomerulus along with the Bowman's capsule constitutes the **Malpighian body** or **renal corpuscle**.

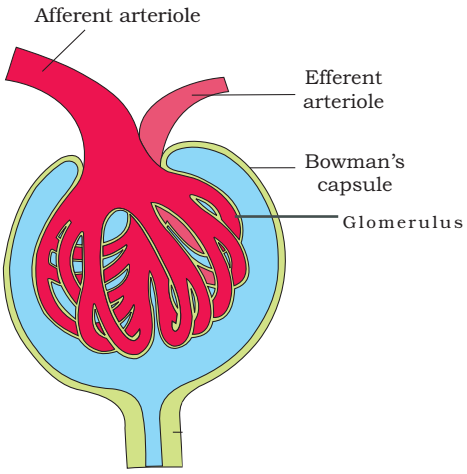


Figure 2.8 Malpighian body (renal corpuscle)

The renal tubule continues further and forms a highly coiled **proximal convoluted tubule** (PCT). A hairpin shaped **Henle's loop**, which has descending and ascending limbs, is the next part of the tubule. The proximal part of the ascending limb is thin and the distal part is thick. The thick ascending limb continues into the **distal convoluted tubule** (DCT). The DCT continues as the '***initial collecting duct***' in the cortex. Some initial collecting ducts unite to form a **straight collecting duct**, which passes through the medullary pyramid. In the medulla, the collecting ducts

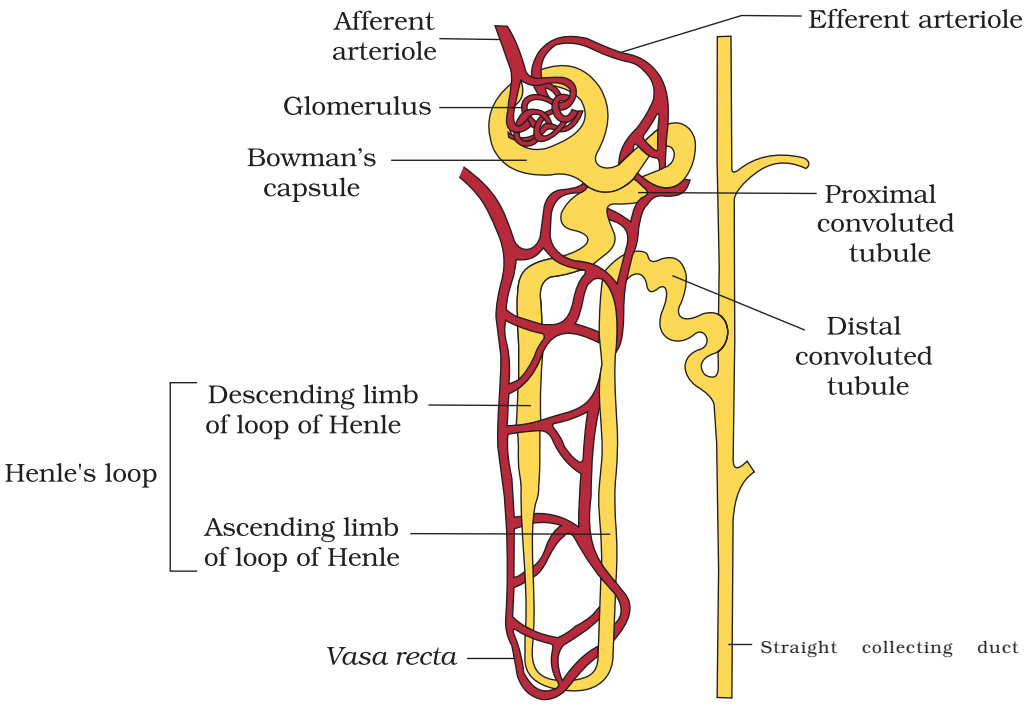


Figure 2.9 A diagrammatic representation of a nephron showing blood vessels, collecting duct and tubule

of each pyramid join and form the central large **duct of Bellini**, which finally opens on the tip of the renal papilla. The contents of the duct of Bellini are discharged into the ***renal pelvis*** through the renal ***calyx*.**

The Malpighian corpuscle, PCT and DCT of a nephron are situated in the cortical region of the kidney, whereas the loop of Henle is in the medulla. In a majority of nephrons, the loop of Henle is too short and extends only very little into the medulla. Such nephrons are called **cortical nephrons**. In some of the nephrons, the loops of Henle are very long and run deep into the medulla. These nephrons are called **juxtamedullary nephrons** (as their renal corpuscles are located close to the medulla in the inner cortex).

The efferent arteriole emerging from the glomerulus forms a fine capillary network called the **peritubular capillaries**, around the renal tubule. The portion of the peritubular capillaries that surrounds the loop of Henle is called the **vasa recta.** The vasa recta is absent or highly reduced in the cortical nephrons. The **juxtamedullary nephrons** possess well developed **vasa recta**.

Do you know? After the age of 40 years, the number of functioning nephrons usually decreases, by about 10 percent, every 10 years.

2.8 Urine Formation

The formation of urine involves three main processes namely, **glomerular filtration, selective reabsorption** and **tubular secretion.**

a) **Glomerular filtration:** The first step in the formation of urine is the 'filtration' of the blood from the glomerulus into the lumen of the Bowman's capsule and this 'passive' (non-energy consuming process) process is called **glomerular filtration**. The hydrostatic pressure of the blood while flowing in the glomerulus is 60 mmHg. It is opposed by '**glomerular colloidal osmotic pressure**' of 32 mmHg (which is exerted by the non-filtered plasma proteins of the blood in the glomerular capillaries) and Bowman's capsular hydrostatic pressure of 18mmHg. The net filtration pressure (NFP) is 10mm Hg {60–(32+18) =10}. This causes the filtration of blood through the 3 layered *filtrate membrane* formed by the endothelial cells of glomerular capillary together with the basement membrane and podocytes of the Bowman's cup. Blood is filtered through the fine slit pores and fenestrations due to the NFP. Therefore, this process is called '**ultrafiltration**'. The filtrate contains almost all the constituents of the plasma, except the proteins. The filtrate thus formed is called ultra-filtrate or 'glomerular filtrate' or '*primary urine*', which is **hypotonic** to the cortical fluid. It passes into the next part of the renal tubule.

Do you know? On an average 1100 – 1200 ml of blood is subjected to filtration by the kidneys per minute which constitute roughly 1/5th of the blood pumped out by each ventricle of the heart in a minute.

NOTE: The amount of filtrate formed by both the kidneys, per minute, is called **Glomerular Filtration Rate**. The GFR in a healthy individual is approximately 125ml/minute, i.e., 180L per day. Although about 180L of glomerular ultra-filtrate is produced each day, the kidneys normally excrete only 1 to 1.5 L of urine in a 24 hour period. A comparison of these two volumes suggests that nearly 99% of the filtrate is reabsorbed by the renal tubules. This process is called **reabsorption/ selective reabsorption**.

b) **Selective reabsorption and secretion:** The tubular epithelial cells in different segments of a nephron reabsorb certain substances of the glomerular filtrate either by active or passive mechanisms. About 85% of the filtrate formed is reabsorbed in a constant, unregulated fashion by the PCT and descending limb of Henle's loop (obligatory or mandatory reabsorption) and the reabsorption of the rest of the fluid is 'regulated'.

Based on the necessity of re-absorption, the substances of glomerular filtrate can be categorized into '**high threshold substances**' (essential and are efficiently reabsorbed e.g. glucose, amino acids, vitamins, some salts etc.), '**low threshold substances**' (absorbed in very little amounts e.g. urea, uric acid etc.) or '**athreshold substances**' (actual excretory products and are not reabsorbed at all e.g. creatinine).

During the formation of urine, the tubular cells secrete substances such as H^+, K^+ and NH_3 into the filtrate. Tubular secretion is also an important step in the formation of urine as it helps in the maintenance of ionic and acid-base balance of the body fluids. Mechanism of selective reabsorption and secretion in different parts of a nephron takes place as follows:

i) **In the proximal convoluted tubule:** PCT is lined by simple cuboidal epithelium with 'brush border', which increases the surface area of absorption. Nearly all the essential nutrients and 70-80% of electrolytes and water are reabsorbed by this segment. Na^+ is actively transported into the cortical interstitial fluid. This transfer of positive charge drives the passive transport of Cl^-. Glucose, amino acids, and other essential substances are also '**actively**' transported. Movement of water occurs by '**osmosis**'.

PCT also helps to maintain the pH and ionic balance of the body fluids by selective secretion of **hydrogen ions**, and **ammonia** into the filtrate and by the reabsorption of K^+ and HCO_3^- from it.

ii) **In the Henle's loop:** Reabsorption in this segment is minimum. However, this region plays a significant role in the maintenance of high osmolarity of the medullary interstitial fluid.

The descending limb of loop of Henle is permeable to water and almost impermeable to electrolytes, hence reabsorption of water continues as the filtrate moves along the descending limb (passive transport). As a result, the filtrate concentration gradually increases as it moves towards the inner medulla. The ascending limb has two specialized regions, a proximal **thin segment**, in which NaCl diffuses out into the interstitial fluid ***passively***, and a distal **thick segment**, in which NaCl is ***actively*** pumped out. The ascending limb is impermeable to water. Thus the filtrate becomes progressively more dilute as it moves up to the cortex (towards the DCT).

iii) **In the distal convoluted tubule (DCT)**

The cells here are shorter than those in the proximal tubule and lack 'microvilli', indicating that they are not involved much in reabsorption.

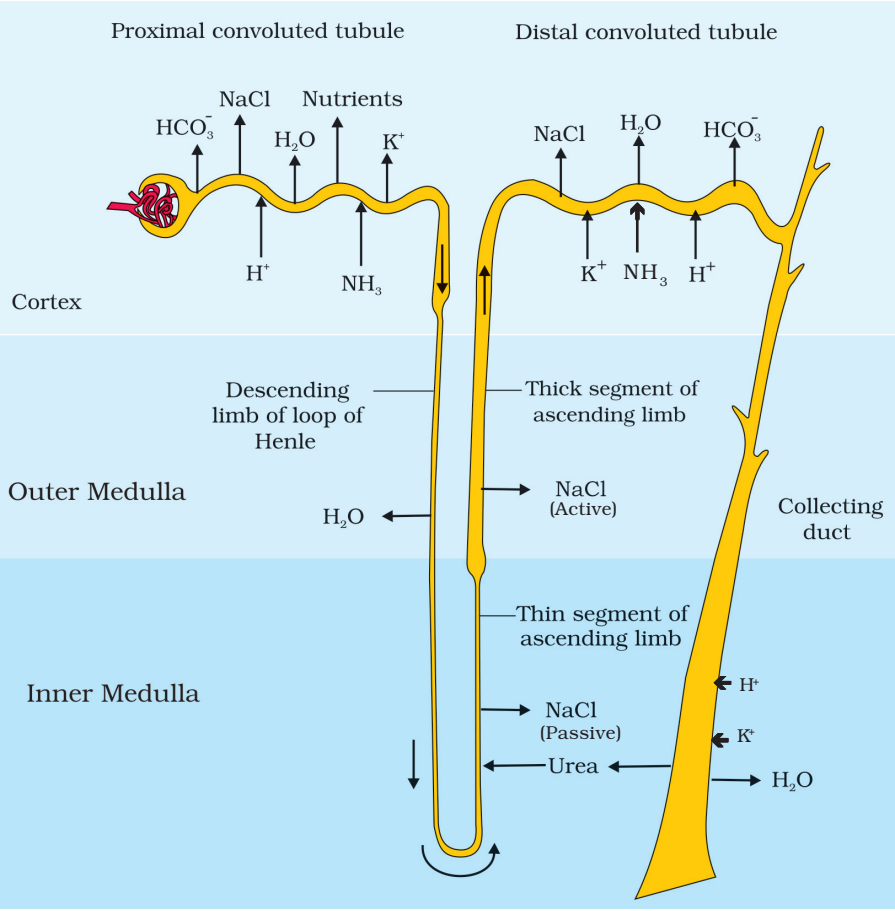


Figure 2.10 Reabsorption and secretion of major substances at different parts of the nephron (arrows indicate direction of movement of materials.)

'***Conditional reabsorption***'/'***facultative reabsorption***' of Na^+ and water takes place in this segment. The reabsorption of water is *variable* depending on several conditions and is regulated by ADH. DCT is also capable of reabsorption of HCO_3^- and selective secretion of H^+ and K^+ ions and NH_3 into the DCT from the peritubular network via the cortical interstitium to maintain the pH and sodium–potassium balance in the blood.

iv) In the collecting duct (CD)

This long duct carries the filtrate through the medulla to the renal pelvis. Considerable amount of water could be reabsorbed from this region to produce concentrated urine. This segment allows passage of small amount of urea to the medullary interstitum to keep up its **osmolarity**. It also plays a role in the maintenance of pH and ionic balance of blood by the selective secretion of H^+ and K^+ ions. The renal fluid after the process of facultative reabsorption in the CD, influenced

by ADH, constitutes the 'urine', that is sent out .Urine in the CD is ***hypertonic*** to the plasma of blood.

Urinary excretion = glomerular filtration – tubular reabsorption + tubular secretion

2.8.1 Mechanism of concentration of the filtrate

Mammals have the ability to produce concentrated urine. The Henle's loop and vasa recta play a significant role in this. The flow of the renal filtrate in the two limbs of Henle's loop is in **opposite directions** and thus forms a **counter current**. The flow of blood through the two limbs of **vasa recta** is also in a counter current pattern. The proximity between the Henle's loop and vasa recta, as well as the counter currents of renal fluid and blood in them help in maintaining an increasing osmolarity towards the inner medullary interstitium. i.e., from 300 mOsml/L in the cortex to about 1200 mOsml/L in the inner medulla. This gradient is mainly caused by NaCl and

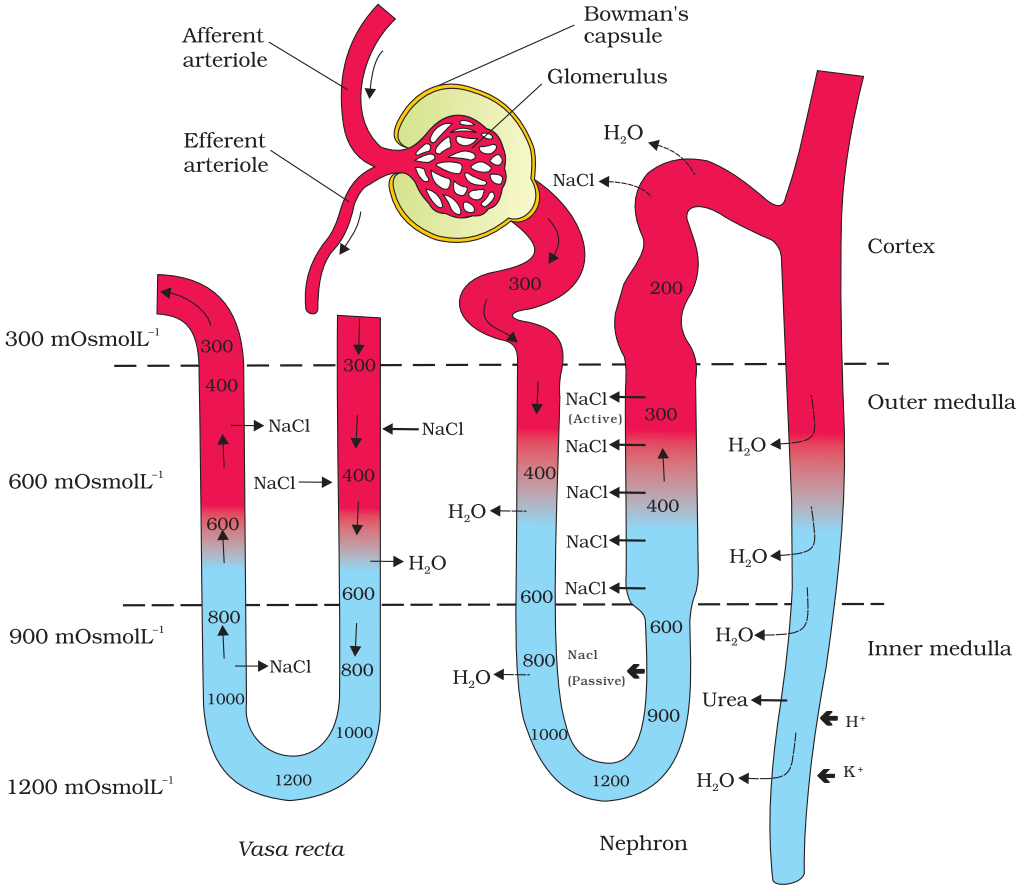


Figure 2.11 Diagrammatic representation of a nephron and *vasa recta* showing counter current mechanisms

urea. NaCl passes out of the ascending limb of Henle's loop, and it enters the blood of the descending limb of vasa recta. NaCl is returned to the interstitium from the ascending portion of the vasa recta. Similarly, small amounts of urea enter the thin segment of the ascending limb of Henle's loop which is transported back to the interstitium, from the collecting duct.

The above described transport of substances facilitated by the special arrangement of Henle's loop and vasa recta is called the **counter current mechanism** (the two limbs of the loop of Henle constitute a *counter current multiplier system*). This mechanism helps to maintain a concentration gradient in the medullary interstitium. Presence of such interstitial gradient helps easy passage of water from the collecting duct, thereby concentrating the filtrate (urine). Human kidneys can produce urine nearly four times concentrated than the initial filtrate formed.

2.8.2 Osmoregulation

The process of maintaining the quantity of water and dissolved solutes in balance is referred to as **osmoregulation** (the main concern in this lesson is to deal with the maintainance of the homeostatis of the organism's water content). This can be achieved by excretion through organs, such as the skin and the kidneys. Regulation of the amount of water and salts in urine generally takes place with the help of hormones such as **ADH, aldosterone** and **angiotensin II.**

2.8.3 Regulation of kidney function

The functioning of the kidneys is efficiently monitored and regulated by hormonal feedback control mechanism involving the ***hypothalamus***, ***Juxta Glomerular apparatus*** (JGA) and to a certain extent, the ***heart***.

Osmoreceptors in the hypothalamus monitor the solute concentrations in the blood. Excessive loss of fluid from the body can activate these receptors which stimulate the hypothalamus to release **antidiuretic hormone** (ADH)/ **vasopressin** via the neurohypophysis. ADH facilitates reabsorption of water from the DCT and the collecting duct, thereby preventing **diuresis**. An increase in the volume of the body fluid can switch off the osmoreceptors and suppress the release of ADH (negative feedback control). Defects in ADH receptors or inability to secrete ADH leads to **diabetes insipidus** (characterized by excessive thirst and excretion of large quantities of dilute urine) resulting in ***dehydration*** and ***fall in BP***.

The **Juxta Glomerular Apparatus** plays a complex regulating role. The JGA is the region in each nephron where the afferent arteriole comes into contact with the DCT. A group of modified epithelial cells of the DCT are crowded in

this region, constituting the **macula densa**. The wall of the afferent renal arteriole has **JG cells** (they are modified smooth muscle cells of the afferent arteriole). Macula densa together with **JG cells** form the JGA.

A fall in glomerular blood flow/glomerular blood pressure/GFR can activate the JG cells to release an enzyme called ***renin*** (angiotensinogenase) into the blood. This enzyme catalyses the conversion of **angiotensinogen** (a protein produced by the liver) into angiotensin I, which is converted into angiotensin II, by **angiotensin converting enzyme** (ACE). This conversion occurs primarily as blood passes through the capillaries of the lungs, where most of the converting enzyme is present. Angiotensin II stimulates the adrenal cortex to secrete ***aldosterone***. Aldosterone causes reabsorption of Na^+ (and water indirectly) from the DCT and CD to reduce loss through urine, and also promotes secretion of K^+ ions into the DCT and CD. It leads to an increase in the blood pressure and GFR. This complex mechanism is generally known as **renin - angiotensin – aldosterone system** (***RAAS***).

An increase in the flow of blood to the right atrium of the heart stretches its wall. It causes the release of atrial natriuretic factor (ANF)/atrial natriuretic peptide (ANP). ANP can cause vasodilation (dilation of blood vessels) and there by decrease the blood pressure by relaxing vascular smooth muscles and inhibiting RAAS. 'ANP' mechanism therefore, acts as a counter check on the '**RAAS**'.

Micturition

Urine formed by the nephrons is ultimately carried to the urinary bladder where it is stored till a voluntary signal is given by the central nervous system (CNS). This signal is initiated by the stretching of the urinary bladder as it gets filled with urine. In response, the stretch receptors on the walls of the bladder send signals to the CNS. The CNS passes on motor messages to initiate the contraction of smooth muscles of the bladder and simultaneous relaxation of the **urethral sphincters**, causing the release of urine. The process of passing out urine is called ***micturition*** and the neural mechanism involved is called '***micturition reflex***'.

Urine

An adult human excretes, on an average 1 to 1.5 litres of urine per day. The urine formed is a light yellow coloured watery fluid which is slightly acidic (**pH–6.0**) and has a characteristic odour. Urine of a healthy individual contains 96% of water, 2% of urea, 2% of other dissolved substances. On an average 25-30 gms. of urea is excreted per day. Various conditions can affect the quantity and composition of urine. Analysis of urine helps in the clinical diagnosis of many metabolic disorders as well as malfunctioning

of the kidney. For example, presence of glucose (**glycosuria**) and **ketone bodies** (**ketonuria**) in urine are indicative of ***diabetes mellitus*.**

2.9 Role of other organs in excretion

In addition to the kidneys, lungs, liver and skin also help in the elimination of excretory wastes.

(a) Lungs: Lungs regularly eliminate about 18L of CO_2 and also significant amount of water in the form of water vapor in normal resting condition per day. The quantity of water loss increases in dry climates. Various volatile materials are also eliminated through the lungs.

(b) Liver: Liver is the largest gland in our body. It changes the decomposed haemoglobin of the worn-out RBCs into bile pigments, namely, bilirubin and biliverdin. These pigments pass into the alimentary canal along with the bile for elimination. The liver also excretes cholesterol, degraded products of steroid hormones, certain vitamins and drugs via bile.

(c) Skin: Human skin possesses two types of glands for the elimination of certain substances through their secretion.

i) **Sweat glands** secrete a watery fluid called sweat. Primary function of sweat is to facilitate a cooling effect on the body surface. It also helps in the removal of some of the wastes like NaCl, small amounts of urea, lactic acid etc.

ii) **Sebaceous glands** eliminate certain substances like sterols, hydrocarbons, waxes through **sebum**. This secretion provides a protective 'oily covering' to the skin.

Do you know? Small amounts of nitrogenous wastes are also eliminated through saliva.

2.10 Disorders of the excretory system

(a) Uremia: The presence of excessive amounts of urea in the blood is known as uremia. The chief cause of uremia is damage to the kidneys, It occurs due to glomerulonephritis or hypertension or diabetes mellitus or some other disorders that impair the functioning of the kidney. It is usually treated by ***hemodialysis*** *(a procedure used to remove wastes from blood using a dialyser, a mechanical device to clean the patient's blood).*

(b) Renal calculi: Renal calculi or kidney stones are hard crystalline structures formed in the urinary tract when the concentration of certain constituents, such as uric acid, oxalates etc., in the urine becomes too high. Dehydration is the major risk factor/cause for kidney stone formation.

(c) **Glomerulonephritis (GN):** It is a renal disease characterized by inflammation of glomeruli or small blood vessels of the kidneys. It occurs due to certain infections (bacterial, viral or parasitic pathogens), drugs or diabetes.

(d) **Renal failure (RF):** Renal failure or kidney failure (formerly called renal insufficiency) is a situation in which kidneys fail to function adequately. A number of other diseases or health problems may cause renal failure. Renal failure is typically detected by an elevated serum creatinine level.

2.10 Artificial kidney/Dialysis

Artificial kidney/dialyser, is a machine that is used to filter the blood of a person whose kidneys are damaged. The process is called **hemodialysis**. In this process blood is taken out from the main artery, mixed with an anticoagulant, such as ***heparin***, and then pumped into the apparatus called **dialyser**. In this apparatus blood flows through channels, or tubes made of **cellophane**. The membrane is **impermeable** to macromolecules, such as plasma proteins, but permeable to small solutes such as urea, uric acid, creatinine and mineral ions. The membrane separates the blood flowing inside the tube and the dialyzing fluid (dialysate), which has the same composition as that of plasma, except the nitrogenous wastes. The cellophane membrane allows the passage of molecules based on concentration gradient. As nitrogenous wastes are absent in the dialyzing fluid, these substances from the blood freely move out, there by clearing the blood of its wastes. This process is called ***dialysis***. The cleared blood is pumped back to the body through a vein after adding anti-heparin to it. Each dialysis session lasts 2 to 6 hours. This method is a boon for thousands of **uremic/kidney failure patients** all over the world.

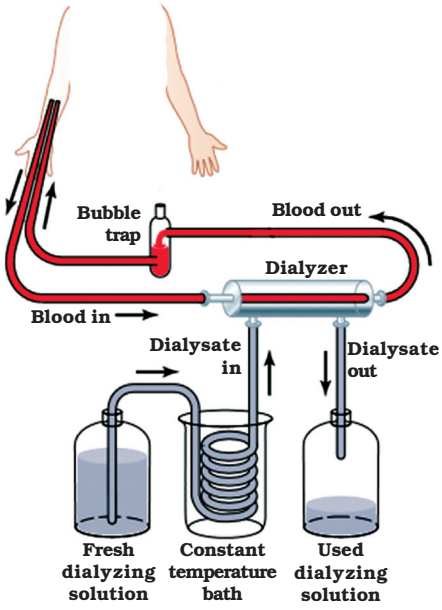


Figure 2.12 Haemodialysis

Kidney transplantation

Kidney transplantation is the ultimate solution for acute renal failure (kidney failure). A functioning kidney is used in transplantation from a donor, preferably a close relative, to minimize its chances of rejection by the immune system of the host. Modern clinical procedures have increased the success rate of such a complicated technique.

GLOSSARY

Atrial natriuretic peptide (ANP): It is a peptide hormone secreted by the wall of the right atrium, when the blood pressure increases (wall of the right atrium is stretched). It is a vasodilator and thus lowers the blood pressure. It is involved in the homeostatic control of fluids in the body countering the effect of aldosterone.

Cellophane: It is a thin, transparent sheet made of cellulose and is used in a dialyser , which removes wastes from blood in patients suffering from renal failure.

Counter current exchange: This is accomplished by the vasa recta which run parallel to the loop of Henle of Juxta meduallary nephrons. It maintains hypertonicity of the renal medulla by exchanging the ions and collecting water from the limbs of the loop of Henle.

Countercurrent multiplier system: It is a system involving the two limbs of the loop of Henle, which play an important role in maintaining the concentration gradient in the medulla, which is vital for the formation of concentrated urine.

Deamination: It is the removal of an amine group from a molecule. Enzymes which catalyse this reaction are called **deaminases**. It is the first step in the production of major nitrogenous wastes.

Duct of Bellini: Any of the large excretory ducts of the uriniferous tubules of the kidney that open at the tip of the renal papilla into a calyx and thus into the renal pelvis; also called 'papillary duct'.

Glomerular filtration rate (GFR): It is the volume of fluid filtered from the renal glomerular capillaries into the Bowman's capsule, per unit time. GFR is an important clinical indicator of the functioning of the kidney.

Osmolarity: Is the measure of solute concentration, defined as the number of osmoles (Osm) of solute per litre (L) of solution (osmol/L or OsmL).

Renal column (column of Bertin): It is a medullary extension of the renal cortex in between the renal pyramids. It allows the cortex to be better anchored in the medullary tissue.

Renal pelvis: It is the funnel-like dilated proximal part of the ureter in the kidney.

Renal threshold of a substance: A substance is excreted in the urine only when its concentration in the plasma exceeds a certain 'threshold value'. For example glucose has high threshold, urea has low threshold and creatinine has no threshold (athreshold substance). High threshold substances are reabsorbed even though they are filtered in the Bowman's capsule.

Renin: It is an enzyme secreted by JG cells (also called 'angiotensinogenase'). This enzyme catalyzes the conversion of **angiotensinogen** into angiotensin I, which is converted into angiotensin II by angiotensin converting enzyme (ACE).

QUESTIONS

Very Short Answer Type Questions

1) Name the blood vessels that enter and exit the kidney.
2) What are renal pyramids and renal papillae?
3) What are the columns of Bertin?
4) Name the structural and functional units of kidney. What are the two main types of structural units in it.
5) Distinguish between cortical and juxta medullary nephrons.
6) Define glomerular filtration.
7) Define Glomerular Filtration Rate (GFR).
8) What is meant by mandatory reabsorption? In which parts of nephron does it occur?
9) Distinguish between juxtaglomerular cells and macula densa.
10) What is juxtaglomerular apparatus?
11) Distinguish between the enzymes renin and rennin.
12) What is meant by the term osmoregulation?
13) What is the role of atrial natriuretic peptide in the regulation of urine formation?

Short Answer Type Questions

1) Terrestrial animals are generally either ureotelic or uricotelic and not ammonotelic. Why?
2) Differentiate vertebrates on the basis of the nitrogenous waste products they excrete, giving examples.
3) Draw a labeled diagram of the V.S. of kidney.
4) Describe the internal structure of kidney of man.
5) Explain micturition
6) What is the significance of juxta glomerular apparatus (JGA) in kidney function?
7) Give a brief account of the counter current mechanism.
8) Explain the autoregulatory mechanism of GFR.
9) Describe the role of liver, lungs and skin in excretion.
10) Name the following
    a) A chordate animal having protonephridial type excretory structures.
    b) Cortical portions projecting between the medullary pyramids in the human kidney.
    c) Capillary network paralleling the loop of Henle
    d) A non chordate animal having green lands as excretory structures

Long Answer Type Questions

1) Describe the excretory system of man, giving the structure of a nephron.
2) Explain the physiology of urine formation.

FOR IGNITED MINDS

Excretion-Good Riddance and Homeostasis

Excretory Products and their Elimination

1. Do you think, human being can excrete **allantoin**. Give your reasons for how or why not?
2. What type of nitrogenous waste do organisms who have access to plenty of water supply, tend to excrete.
3. If an organism is able to live in isotonic, hypotonic and hypertonic surrounding water, what technical name do you offer it?
4. If a patient is prescribed to take diuretic tablets (tablets which help in passing more urine), what type of cardio vascular condition he might be suffering from?
5. Why do people who drink alcohol feel 'dehydrated' the next morning? Can you give specific reason for this 'effect'?

   Hint: The answer lies in your brain.
6. If there is excessive production of aldosterone in a person, he is likely to be affected by a cardiovascular problem.

   Hint: The answer can be one among the following: **Hypothermia, Hypochondria, Hypertension, Hypotension.**
7. "**Biological economics**" refers to how a cell conserves or spends energy. Biological economics wise, among the aminotelic, ammonotelic, ureotelic and uricotelic animals, which are more liberal in spending energy to produce the nitrogenous waste, they excrete.
8. If the following animals which has the probability of sending out 'isotonic urine' - **snake, bird, spider, ant, shark** ?
9. If you are asked to conduct an experiment on a uricotelic organism, which animal among the following would you select as your experimental animal - **King crab, Jelly fish, silver fish, cuttle fish**.
10. Of all the veins you have studied, which veins are likely to possess blood highest urea content and least urea content, respectively.

Unit-III

Human Anatomy and Physiology - III

The Body Movement and Posture

The human body has two important systems to give it the right posture and movement of body parts. Movement is the property of the muscular system. Providing support to the body parts is the function of the skeletal system. These two systems are closely integrated to provide posture and movement to the various body parts. The human body has hundreds of muscles, about 640 in total.

We deal with the mechanism of contraction of the skeletal muscles as they constitute the bulk of our body. There are myosin 'motors' effecting change in the length of a muscle by pulling actin molecules amidst them. You will be exposed to all the biochemical events involved in effecting the contraction and relaxation of these muscles. The skeletal muscles are controlled by the 'somatic nervous system' and the cardiac and visceral muscles are controlled by the 'autonomous system' (Sympathetic and parasympathetic systems).

The skeletal system provides support to body parts, protects inner delicate organs, gives posture to the body and it offers space for the attachment of various muscles, without which the muscles cannot work. It is the skeletal system that transforms muscle contraction into locomotion. The skeletal system has two major components–the 'axial skeleton' (skull, vertebral column, ribs and sternum) and 'appendicular skeleton' (the limb skeletons, girdles etc.). The muscular and skeletal systems are so interdependent that they are treated under one unit – the ***musculo-skeletal system****.*

UNIT III A

Musculo-Skeletal System

Movement is one of the significant features of living beings. Animals and plants exhibit a wide range of movements. Change in the position of body parts is called movement. For example human beings can move limbs, jaws, eyelids, tongue, etc. Streaming of protoplasm in the acellular organisms like *Amoeba* is a simple form of movement. Movement of cilia, flagella and tentacles are shown by many organisms.

Some of the movements result in a change of place or location. Such voluntary movements are called **locomotor** movements. Walking, running, climbing, flying, swimming etc., are some forms of locomotor movements. Locomotor structures may perform other functions also in some organisms. For example, in *Paramecium*, cilia help in the movement of food through cytopharynx and in locomotion, as well. *Hydra* can use its tentacles for capturing its prey and also use them for locomotion. We use limbs for changing body postures and locomotion too.

The above observations suggest that movements and locomotion cannot be studied separately. In animals locomotion is performed generally to search for food, shelter, mate, suitable breeding grounds, and favourable climatic conditions or to escape from enemies/predators.

TYPES OF MOVEMENT

The cells of the human body exhibit three main types of movements, namely, amoeboid, ciliary and muscular.

i. Some specialized cells in our body such as the macrophages and leucocytes in blood exhibit **amoeboid movement**. It is effected by pseudopodia formed by the streaming of protoplasm in certain cells (as in *Amoeba*). Cyto-skeletal elements such as **microfilaments** are also involved in amoeboid movement. Dynein arms act as motors utilising ATP.

ii. Ciliary movement occurs in most of our internal tubular organs such as the respiratory passages, genital ducts and ventricles of the brain which are lined by ciliated epithelium.

iii. Movement of our limbs, jaws, tongue, etc., requires muscular movement. The contractile property of muscles is effectively used for locomotion and other movements by human beings and majority of multicellular organisms. Locomotion requires a perfect coordinated activity of muscular, skeletal and neural systems. In this chapter, you will learn about the ultrastructure of muscle cell , and mechanism of its contraction and important aspects of the human skeletal system.

3.1 The Muscle

Muscle is a specialized tissue of mesodermal origin. About 40-50 percent of the body weight of a human adult is contributed by the muscles. They have special properties such as *excitability*, *contractility*, and *relaxation*. The skeletal muscles are primarily involved in locomotor actions and bringing in changes in body postures.

3.1.1 Structure of a Skeletal Muscle

Let us examine a skeletal muscle in detail to understand the structure and mechanism of contraction. Each organised skeletal muscle in our body is made of a number of **muscle bundles** or **fascicles.** Each fascicle contains a number of cylindrical muscle fibers. The fascicles are held together by a common collagenous connective tissue layer called **fascia.**

NOTE: Collagen is a fibrous protein constituent of bone, cartilage, tendon, and other connective tissue. It is the chief protein in the human body.

A) Ultra structure of a Skeletal Muscle Fibre

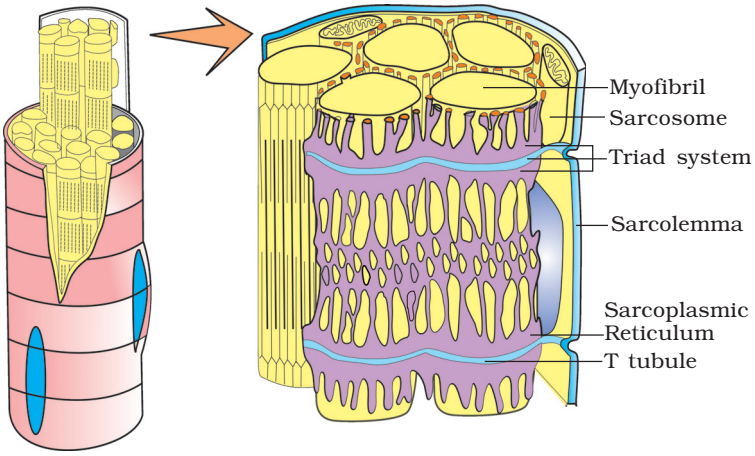


Figure 3.1 Skeletal Muscle Fibre

Each muscle fibre is lined by the plasma membrane called sarcolemma enclosing the sarcoplasm. Skeletal muscle fibre is a '**syncytium**', as each fiber is formed by fusion of embryonic, mononucleate '**myoblasts**'. Hence, the skeletal muscle cells are multinucleate, with characteristically **peripheral nuclei** (just below the sarcolemma). The endoplasmic reticulum, also called **sarcoplasmic reticulum** of the muscle fibers is the store house of **calcium ions**. A characteristic feature of the muscle fiber is the presence of a large number of parallel filaments called **myofilaments** or **myofibrils,** in the sarcoplasm.

i) Structure of Myofibril

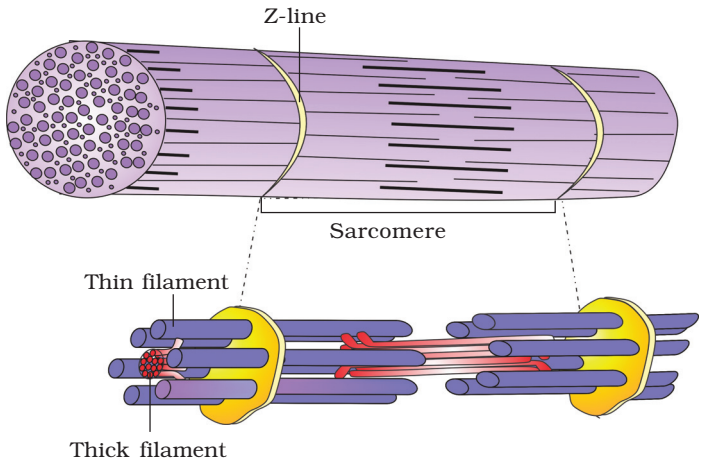


Figure 3.2 Sarcomere

Each myofibril has alternate dark and light bands in it. A detailed study of the myofibril has established that the striated appearance is due to the distribution pattern of two important proteins – **actin** and **myosin**. The light band contains ***actin*** and two regulatory proteins called ***troponin*** and ***tropomyosin***. The light band is called **I-band** or Isotropic band. The dark band called **A –band** or Anisotropic band contains ***myosin***. Both the proteins, actin and myosin, are arranged as rod-like structures, parallel to each other and also to the longitudinal axis of the myofibrils. Actin filaments are thinner compared to the myosin filaments, hence actin and myosin filaments are commonly called ***thin*** and ***thick*** filaments, respectively.In the centre of each 'I' band is an

elastic fiber called **'Z'** line (*called Z line because of its 'Z' like appearance in electron micrographs*) which bisects it. The thin filaments are firmly attached to the '**Z**' line (also called **Krause's membrane** or **Dobie's line**). The thick filaments are also held together in the middle of the 'A' band by a thin fibrous membrane called '**M**' line. All the thick filaments are arranged at the same level in a muscle fibre, thus giving the characteristic striated/striped appearance. The 'A' and 'I' bands are arranged alternately throughout the length of the myofibrils.

ii) Sarcomere

The portion of the myofibril between two successive '**Z' lines** is called '***sarcomere***'. It is the functional unit of contraction. In the resting /relaxed state, the edges of the thin filaments encroach into the A –band on either side and partially overlap the free ends of the thick filaments. The central part of the A –band/dark band without the thin filaments is called the 'H' zone / 'H' band / **Hensen's disc**. It is relatively less dark than the edges of the A-band as there are no 'thin filaments' in it.

iii) Structure of Contractile Proteins

Each actin (thin) filament is made of two 'F' (filamentous) actin molecules helically wound around each other. Each **'F'** actin is a polymer of monomeric '**G**' (globular) actin molecules. Two filaments of another protein, called **tropomyosin** also run close to the 'F' actin molecules, throughout their length. A complex protein called '**troponin**' is distributed at regular intervals on the tropomyosin.

Troponin is made of three polypeptide units named **Tn-T**, **Tn-I**, and **Tn-C**. Tn-T binds to tropomyosin. **Troponin-I** (Tn-I), inhibits the myosin binding site on the actin. Tn-C can bind to Ca^{2+}. When calcium ions are not bound to troponin (Tn-C), it stabilizes tropomyosin in its **blocking position** over the **active sites of actin**. When Calcium ions attach to the Tn-C of the troponin, the tropomyosin moves away/is pulled away from the 'active sites' allowing the myosin heads to bind to the active sites of actin (conformational change). ***Troponin*** and ***tropomyosin*** *are* often called '**regulatory proteins**', because of their role in masking and unmasking the active sites.

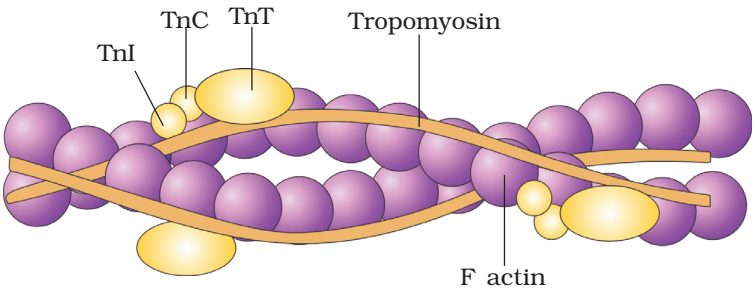


Figure 3.3 Thin filament

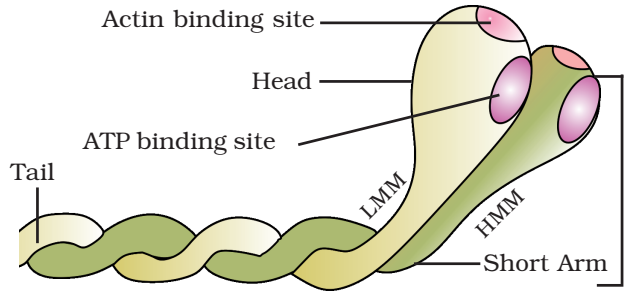


Figure 3.4 Myosin

Myosin is a '**motor protein**' that is able to convert '***chemical energy***' in the ATP molecules into '***mechanical energy***'. Each myosin (thick) filament is a polymerized protein. Each myosin molecule consists of two polypeptide chains wrapped around each other. Many monomeric proteins called ***meromyosins*** constitute one thick filament. Each meromyosin has two important parts, a globular ***head*** with a short ***arm*** (***neck***) and a ***tail***. The globular head with short arm is composed of *heavy meromyosin* (HMM) and the tail is made of *light meromyosin* (LMM). The short arm /neck serves as a '*flexible link*' between the head and tail regions. Half of the myosin molecules have their 'heads' oriented towards one 'Z' membrane and the other half towards the other 'Z' membrane of the same sarcomere, so as to pull actin molecules/ thin filaments from either side. It means the 'tails' of all myosin molecules in an 'A' band are directed towards the 'M' line. The head and short arm project outwards at regular distances and angles from each other from the surface of a polymerized myosin filament and is known as ***cross arm.*** Each head has two binding sites, one for ATP and the other for an active site on the actin molecule. The heads on the two ends of the thick filaments are oriented in opposite directions to pull in actin filaments of both the sides towards the M-line.

iv) Triad System

Sarcolemma, in many types of muscles, invaginates into the sarcoplasm and forms transverse tubules (**T-tubules**) at the level of Z line in the non-mammalian vertebrates. *In the mammals, they penetrate into the junction between the **A** and **I** bands.* Each T tubule is flanked on either side by several terminal cisternae of the sarcoplasmic reticulum. T tubule and the two terminal cisternae at its sides form the ***triad system***. Most of the stored **calcium** of the sarcocyte is located in the terminal cisternae.

B) Motor Unit

A motor neuron and the set of muscle fibres innervated by all the telodendrites constitute a ***motor unit***. The junction between a motor neuron and the sarcolemma of a muscle fibre is called the ***neuromuscular junction*** or ***motor-end plate***. Sarcomere of a striated muscle can be considered a '***functional unit***' of contraction.

3.1.2 Mechanism of Muscle Contraction

Mechanism of muscle contraction is best explained by the '***Sliding Filament Theory***'. It states that contraction of a muscle fibre takes place by the sliding of the thin filaments **over / in between** the thick filaments. It was proposed by **Jean Hanson** and **Hugh Huxley**. The process of muscle contraction can be studied under the following heads:

i) **Excitation of muscle:** Muscle contraction is initiated by a signal sent by the central nervous system (CNS) via a motor neuron. A neural signal reaching the neuromuscular junction releases a neurotransmitter (**acetylcholine**) which generates an '**action potential**' in the sarcolemma. When the action potential spreads to the triad system through the T tubules, the cisternae of the sarcoplasmic reticulum release ***calcium ions*** into the sarcoplasm.

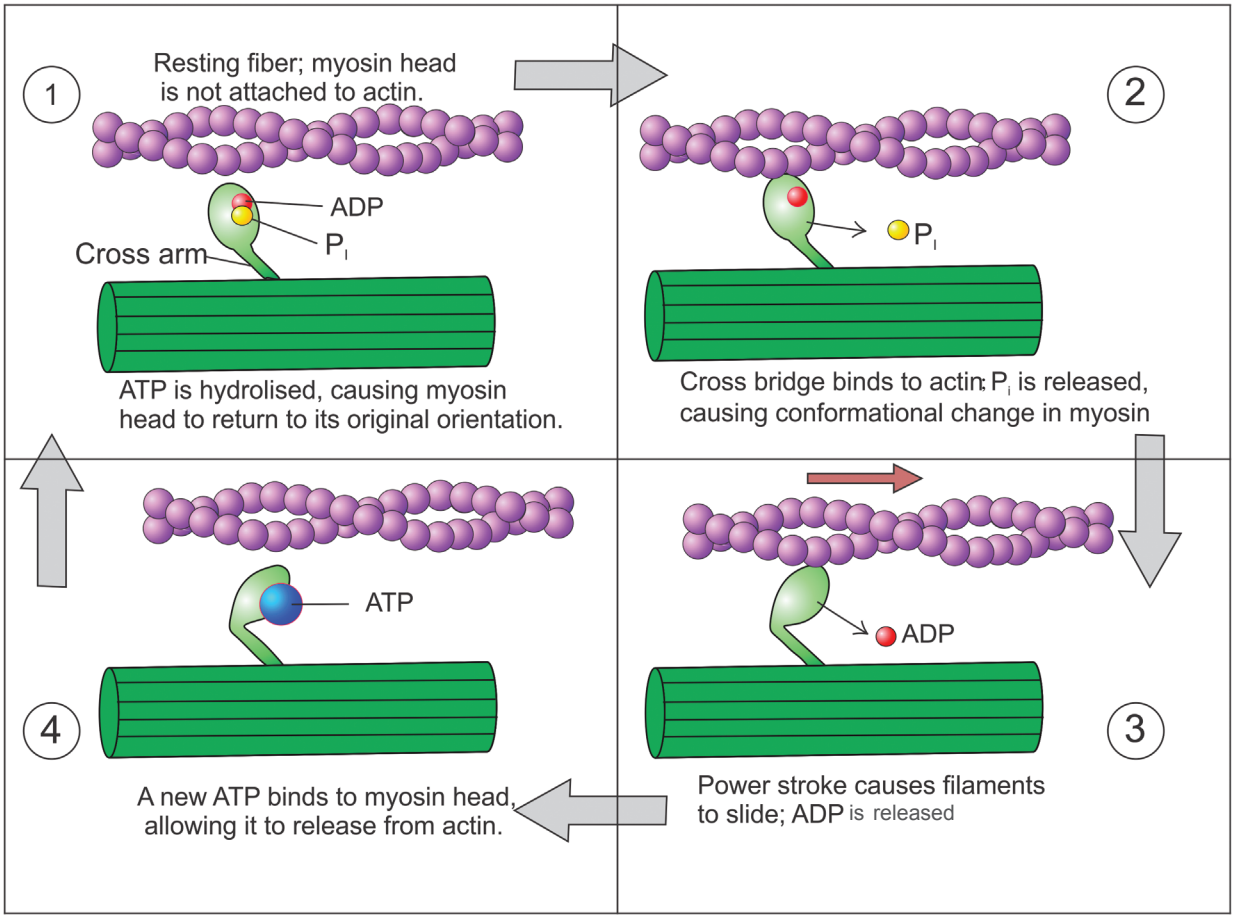


Figure 3.5 Mechanism of Muscle Contraction

ii) **Formation of Cross bridges:** Increase in the Ca^{2+} level leads to the binding of calcium ions to the subunit Tn-C of the troponin of the thin filaments. This makes troponin and tropomyosin complex to move away from the active sites of actin molecules. Now, the active sites are exposed to the heads of the myosin. Utilizing the energy released from hydrolysis of ATP, the myosin head now binds to the exposed 'active sites' on the actin molecules to form a *cross bridge* and $\mathbf{P_i}$ is released

iii) **Power Stroke:** The cross bridge pulls the attached actin filaments towards the centre of the 'A' band. The 'Z' lines attached to these actin filaments are also pulled inwards from both the sides, thereby causing shortening of the sarcomere, i.e., **contraction**. During the shortening of the muscle, the 'I' bands get reduced in size/length (**Z membranes of the sarcomere are brought closer**), whereas the 'A' bands retain their size / length. It is important to note that myofilaments do not actually shorten. As the thin filaments are pulled deep in to the A bands making the H bands narrow, the muscle shows the effect- **contraction**.

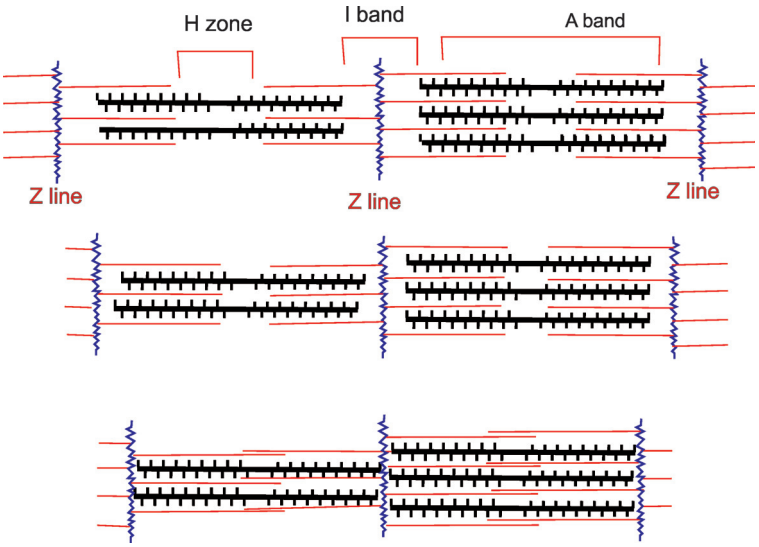


Figure 3.6 Sliding Filaments

Cross bridge cycle: When myosin heads hydrolyse *ATP* into *ADP* and P_i, the conformation of the myosin is changed to an active state so that it can perform the 'power stroke'. When myosin head binds to actin (formation of 'crosss bridge'), it releases P_i and undergoes another conformational change, pulling the thin filaments towards the centre of the 'A' band / sarcomere. Thus the 'power stroke' is completed and the myosin head releases the *ADP*. At the end of the power stroke, the myosin head binds to a new molecule of ATP, which displaces/releases it from actin. This entire process is called '**cross bridge cycle**'. The combined power of several cross bridge cycles causes the muscle to contract. These cycles continue as long as the muscle receives stimuli.

iv) **Recovery Stroke:** The myosin head goes back to its relaxed state and releases ADP. A new ATP molecule binds to the head of myosin and the cross-bridge is broken. Now the new ATP is hydrolysed by the ATPase of the myosin head and the cycle of conformational change in myosin leads to cross bridge formation, and pulling of thin filaments is repeated causing further sliding.

v) **Relaxation of Muscle:** When motor impulses stop the Ca^{2+} ions are pumped back into the sarcoplasmic cisternae. It results in the masking of the active sites of the actin filaments. The myosin heads fail to bind with the active sites of actin. These changes cause the return of 'Z' lines back to their original position, i.e., ***relaxation***.

3.1.3 Muscle Fatigue

Repeated activation of the skeletal muscles can lead to the accumulation of lactic acid due to anaerobic breakdown of glucose in them, causing fatigue. At this state the skeletal muscle fails to contract temporarily.

Cori Cycle

The lactic acid produced during rapid contractions of skeletal muscles under low availability of oxygen is partly oxidized and a major part of it is carried to the liver by the blood, where it is converted into pyruvic acid (pyruvate) and then to glucose through ***gluconeogenesis***. The glucose can enter the blood and be carried to muscles and immediately used. In case glucose is not immediately required, it can be used to rebuild reserve of glycogen through glycogenesis. This two way traffic between skeletal muscle and liver is called the **Cori cycle.**

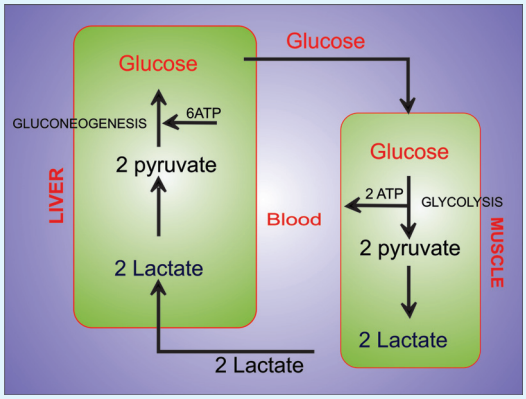


Figure 3.7 Cori cycle

Types of Muscle Fibers

Muscle contains a red coloured oxygen storing pigment called '***myoglobin***' (muscle haemoglobin). Myoglobin content is high in some of the muscles which give a reddish appearance. Such muscle fibers are called the **red fibers**. These muscles with red fibers also contain plenty of mitochondria which can utilise the large amount of oxygen stored in them for the production of ATP. These muscles, therefore, can also be called ***aerobic muscles***.

On the other hand, some of the muscles possess very less quantity of myoglobin in their muscle fibers and therefore, appear pale or whitish. These muscle fibers are **white fibers**. Mitochondria are also few in them, but the amount of sarcoplasmic reticulum is more. They depend on ***anaerobic*** process for the release of energy. White fibres show short term, high intensity contractions.

3.2 The Skeleton

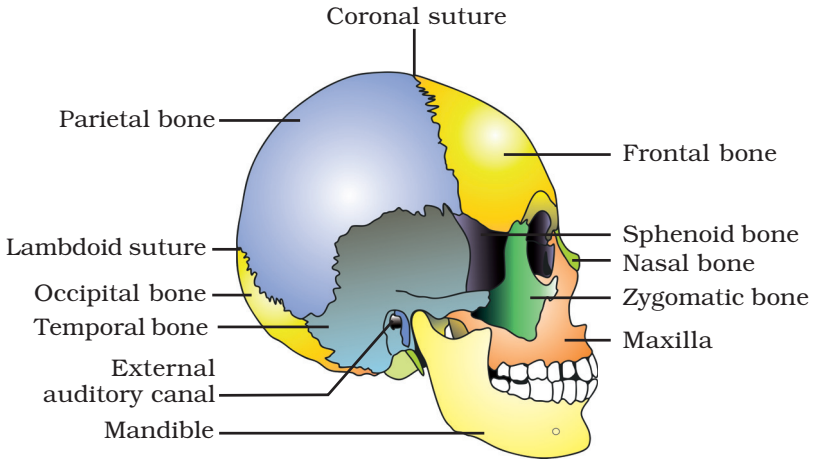


Figure 3.8 The Skull

Skeletal system consists of a framework of bones and a few cartilages. This system has a significant role in maintaining the posture and the movement of body parts. In adult human beings, skeletal system is made up of 206 bones and a few cartilages. It is grouped into two principal divisions – the ***axial skeleton*** and the ***appendicular skeleton***.

3.2.1 Axial skeleton

It comprises 80 bones distributed along the main axis of the body. The skull, vertebral column, sternum and ribs constitute the axial skeleton.

I. The skull

It is composed of two sets of bones –cranial and facial bones (22 bones in all).

Cranium, the brain box, is formed by eight flattened bones. They are a) *frontal bone* (1), b) *Parietals* (2), c) *Temporal bones* (2), d) *Occipital bone* (1),e) *Sphenoid bone* (1) and f) *Ethmoid bone*(1).

i) **Frontal bone**: It forms the forehead, anterior part of the cranial floor, and the roof of the orbits.

ii) **Parietal bones:** They form the major portion of the sides and roof of the cranial cavity. They are joined to the frontal bone by a ***coronal suture*** and posteriorly to the occiput by **lambdoid suture**.

iv) **Temporal bones**: They form the lateral parts and the floor of the cranium.

iii) **Occipital bone:** It forms the posterior part and most of the base of the cranium. It has a large opening, the foramen magnum. Medulla oblongata passes out through this foramen and joins the spinal cord. Two occipital condyles are present one on each side of the foramen magnum (**dicondylic skull**).

iv) **Sphenoid bone:** It is present at the middle part of the base of the skull. It is the **keystone bone** of the cranium because it articulates with most of the other cranial bones.

v) **Ethmoid bone:** It is present on the midline of the anterior part of the cranial floor.

A) The facial region is made up of 14 skeletal elements which form the front part of the skull. The bones of the facial skeleton are the *nasals (2), the maxillae (2), the zygomatic bones (2), the mandible (1), the lacrimal bones (2), the palatine bones (2), inferior nasal conchae (2),* and *the vomer (1)*

i) **Nasal bones:** These are paired bones that form the bridge of the nose.

ii) **Maxillae:** Two maxillae join together and form the upper jaw. The maxilla bears sockets (alveoli) for lodging the maxillary teeth. The palatine processes are involved in the formation of the anterior part of the ***hard palate.***

iii) **Zygomatic bones:** These are known as cheek bones.

iv) **Lacrimal bones:** These are the smallest bones of the face

v) **Palatine bones:** They form the posterior portion of the hard palate.

vi) **Inferior nasal conchae:** These are scroll like bones that form a part of lateral wall of the nasal cavity.

vii) **Vomer:** It is a triangular bone present on the floor of the nasal cavity.

viii) **Mandible (Lower jaw):** It is '**U**' shaped and is the longest and strongest of all the facial bones. It is the only movable skull bone (except the ear ossicles).

B) Skeletal structures associated with sense organs

i) The ***nasal cavity*** is divided into left and right cavities by a vertical partition called the nasal septum.

ii) ***Orbits***: Orbits are bony depressions which accommodate the eyeballs and associated structures.

iii) ***Ear Ossicles***: Each middle ear contains three tiny bones – ***Malleus*** (modification of articular), ***Incus*** (modified quadrate) and ***Stapes*** (modified hyomandibula), collectively called **ear ossicles**.

C) Hyoid Bone

It is a single U shaped bone present at the base of the buccal cavity between the larynx and the mandible. The hyoid bone keeps the larynx open.

II. Vertebral Column

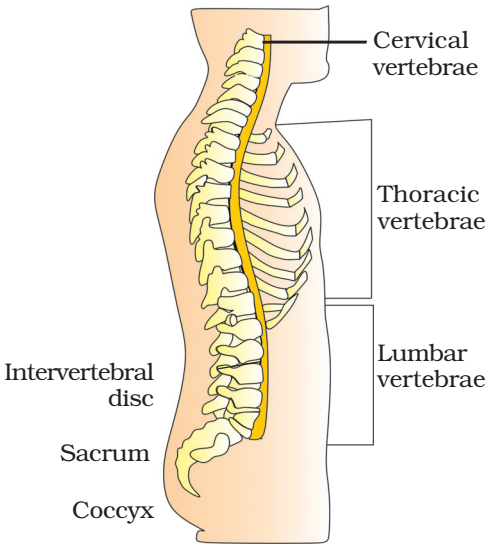


Figure 3.9 Vertebral column

Our **vertebral column** is formed by 26 serially arranged units called vertebrae.

Structure of Vertebra

Each vertebra has a central hollow portion (neural canal) through which the spinal cord passes. A typical vertebra consists of the body (centrum), vertebral (neural) arch, and many processes for articulation or attachment of muscles. Articulatory skeletal structures between the bodies of successive vertebrae are called ***intervertebral discs***.

The vertebral column is differentiated into cervical (7), thoracic (12), lumbar (5), sacral (1-fused) and coccygeal (1-fused) regions starting from the skull.

a) **Cervical vertebrae:** The first vertebra is called the **atlas** and the second the **axis**. Atlas is articulated with the occipital condyles, and has an odontoid canal. Axis has a strong odontoid process that fits in to odontoid canal of the atlas to facilitate rotation of head.

b) **Thoracic vertebrae:** Thoracic region consists of twelve vertebrae. The heads of ribs namely capitulum and tuberculum articulate with the 'articular facets' of the thoracic vertebrae.

c) **Lumbar vertebrae**: These are the largest and strongest free vertebrae. They provide surface for the attachment of the large back muscles.

d) **Sacrum:** It is a triangular bone formed by the fusion of five sacral vertebrae.

e) **Coccyx:** It is a triangular bone formed by the fusion of four coccygeal vertebrae.

Functions

i) Vertebral column protects the spinal cord in its neural canal

ii) It supports the skull

iii) It serves as the point of attachment for the ribs and musculature of the back.

III. Sternum (breast bone)

It is a flat bone on the mid ventral line of the thorax. It consists of three parts. The superior (anterior) part is the manubrium, the middle part is the body, and the inferior (posterior) smallest xiphoid process. The sternum provides space for the attachment of the thoracic ribs and abdominal muscles too.

IV. Ribs

Twelve pairs of **ribs** are present in the human chest**.** Each rib is a thin flat bone connected dorsally to the vertebral column and ventrally to the sternum. It has two articulation surfaces on its dorsal end, hence called **bicephalic.** The first seven pairs of ribs are called **true ribs** (vertebro-sternal ribs). Dorsally, they are attached to the thoracic vertebrae and ventrally connected to the sternum with the help of hyaline cartilages. The remaining ribs are called 'false ribs'. The 8th, 9thand 10thpairs of ribs do not articulate directly with the sternum but join the cartilaginous (hyaline cartilage) parts of the seventh rib. These are called **vertebro-chondral ribs**. Last 2 pairs (11thand 12th) of ribs are not connected ventrally either to the sternum or the anterior ribs, hence called **floating ribs**. The last five pairs of ribs which are not attached to the sternum directly are called '**false ribs**'. The thoracic vertebrae, ribs and sternum together form the ***rib cage***.

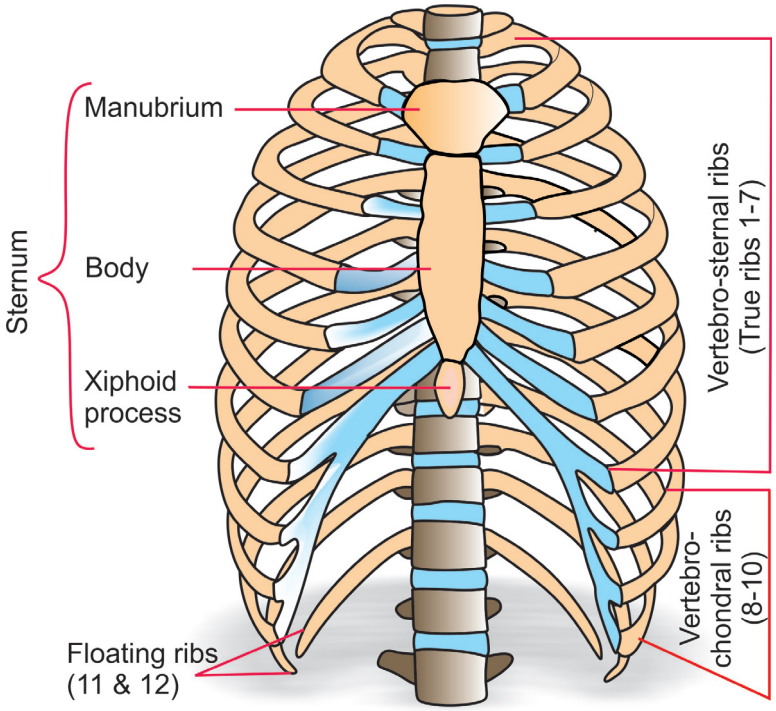


Figure 3.10 Rib cage

3.2.2 Appendicular Skeleton

The bones of the limbs along with their girdles constitute the **appendicular skeleton.** The appendicular skeleton is composed of 126 bones.

i) Bones of the Forelimb

Each **limb** is made of 30 bones. The bones of the hand (forelimb) are humerus, radius and ulna, carpals (wrist bones – 8), metacarpals (palm bones – 5) and phalanges (digital bones – 14).

ii) Bones of the Hind limb

The bones of the leg are *Femur (1)* (thigh bone – the longest bone), *tibia (1)* and *fibula* (1), *tarsals* (ankle bones – 7), *metatarsals* (5) and phalanges (digital bones– 14) are the bones of the legs (hind limbs). A cup shaped bone called patella (***knee cap***) (1) covers the knee joint ventrally.

RECALL: Bones such as the knee cap are formed in tendons and are called 'sesamoid bones'.

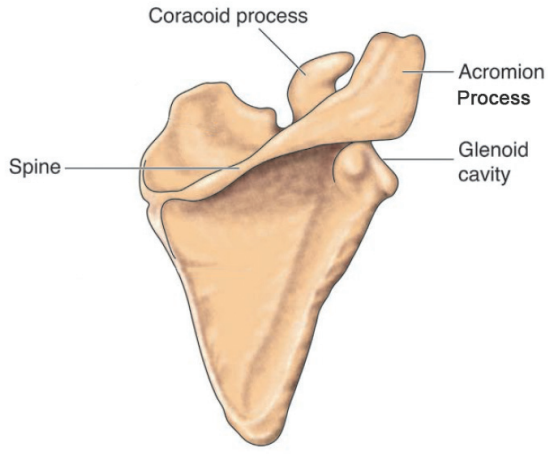


Figure 3.11 Scapula

iii) Pectoral Girdle

Pectoral girdle consists of two halves and helps in the articulation of the upper limbs with the axial skeleton. Each half of pectoral girdle consists of a ***clavicle*** (collar bone) and a ***scapula***. The scapula is a large triangular, flat bone situated in the dorsal part of the thorax between the second and the seventh ribs. The dorsal, flat, triangular body of the scapula has a slightly elevated ridge called the ***spine*** which projects as a flat, expanded process called the **acromion process**. The clavicle articulates with it. The acromion process articulates with the clavicle and provides space for attachment of the muscles of the upper limb and chest. Below the acromion process is a depression called the ***glenoid cavity,*** which articulates with the head of the humerus to form the shoulder joint.

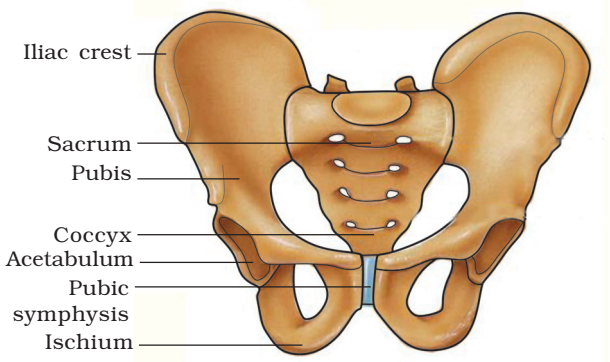


Figure 3.12 Pelvic Girdle with a part of the vertebral column

iv) Pelvic Girdle

Pelvic girdle consists of two identical halves called **coxal bones**/hip bones. Each coxal bone is formed by the fusion of three bones – ***ilium***, ***ischium*** and ***pubis***. At the point of fusion of the above bones is a cavity called ***acetabulum*** which the thighbone articulates. The two halves of the pelvic girdle meet ventrally to form the ***pubic symphysis*** containing ***fibrous cartilage***.

3.3 JOINTS

Joints are essential for all types of movements involving the bony parts of the body. Locomotor movements are no exception to this. *Joints are points of*

contact between bones, or between bones and cartilages. Force generated by the muscles is used to carry out movement through joints, where the joint acts as a ***fulcrum***. The movability at these joints varies depending on different factors.

3.3.1 Types of Joints

Joints are classified into three major structural forms, namely **fibrous joints**, **cartilaginous joints** and **synovial joints**.

A. Fibrous joints: The fibrous joints do not allow any movement (synarthroses). These are composed of dense irregular connective tissue. These are three types- sutures, syndesmoses and gomphoses. a) **Sutures** are present between cranial bones, e.g., **coronal suture** present between frontal and parietal bones. b) **Syndesmoses** e.g., Interosseous membrane between tibia and fibula. c) **Gomphoses** e.g., Dento-alveolar joint. Sutures and gomphoses are immovable joints (synarthroses). Syndesmosis is slightly movable (amphiarthrosis).

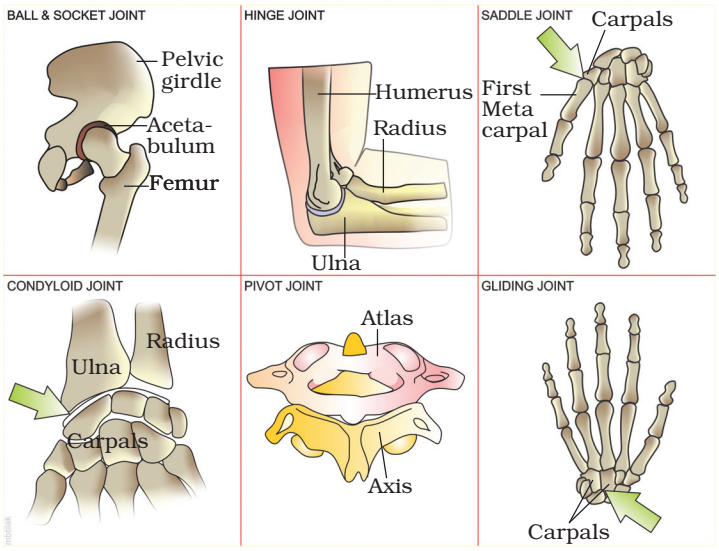


Figure 3.13 Joints

B. Cartilaginous joints: The bones involved are joined together with the help of cartilages. These are two types- a) **Synchondrosis** e.g., epiphyseal plate present between epiphysis and diaphysis. (b) **Symphysis** e.g., pubic symphysis of pelvic girdle and the joint between two adjacent vertebrae of a mammal. It is an amphiarthrosis. Synchondrosis is a synarthrosis and symphysis is an amphiarthrosis.

C. Synovial joints: These are characterized by the presence of a fluid filled *synovial cavity* between the articulating surfaces of the two bones. The articular surfaces of the bones are covered by hyaline cartilage. All synovial joints are **diarthroses** (freely movable joints).

3.3.2 Structure of synovial joint

Synovial joint is covered by a double layered synovial capsule. The outer layer consists of dense fibrous irregular connective tissue with more collagen fibres. This layer is continuous with the periosteum and resists stretching and prevents the dislocation of joints. Some fibres of these membranes are arranged in bundles called ligaments. The inner layer of synovial capsule is

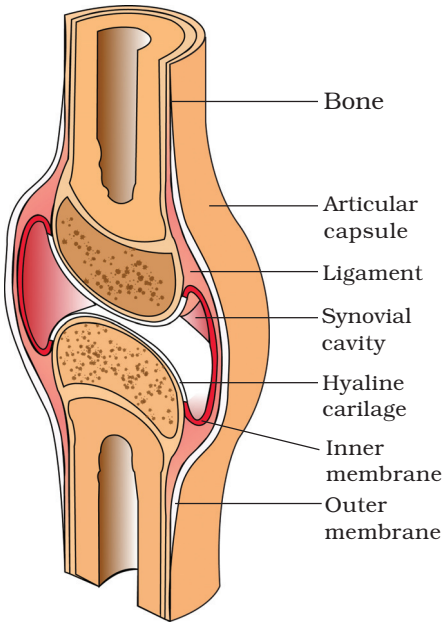


Figure 3.14 Synovial joint

formed of areolar tissue and elastic fibers. It secretes a viscous *synovial fluid* which contains hyaluronic acid , phagocytes etc. and acts as a 'lubricant' for the free movement of the joints .

3.3.3 Types of synovial joints

Synovial joints include *Ball and socket joint, Hinge joint, Pivot joint, Gliding joint, Condyloid joint, Saddle joint*

a) **Ball and socket joint:** e.g. hip joint (between femur and pelvic girdle), shoulder joint (between humerus and pectoral girdle).

b) **Hinge joint:** e.g. elbow joint, knee joint etc

c) **Pivot joint:** e.g. atlanto-axial joint and the joint between ulna and radius. The pivot joint allows rotation of our fore arm at the elbow and to move our hand side to side.

d) **Gliding joint:** e.g. inter-carpal joints, inter-tarsal joints.

e) **Condyloid joint:** e.g. the joints between the carpals and metacarpals, joint between occipital condyles and atlas.

f) **Saddle joint:** e.g. joint between the carpal and metacarpal of the thumb.

3.4 Disorders of Muscular and Skeletal Systems

a) **Myasthenia gravis:** An autoimmune disorder affecting the neuromuscular junctions leading to fatigue, weakening and paralysis of skeletal muscles. Acetylecholine receptors on the sarcolemma are blocked by antibodies/auto-immune bodies, leading to weakness of muscles.

b) **Muscular dystrophy:** Progressive degeneration/wasting of skeletal muscle due to certain genetic disorders such as **Duchenne Muscular Dystrophy (DMD)** or nutritional disorders.

c) **Tetany:** Muscle spasms in muscles a state of prolonged contraction of muscles, caused by low blood calcium level, arising from vitamin D deficiency or underactive parathyroid glands (hypoparathyroidism), resulting in tetany.

d) **Arthritis:** Inflammation of joints.

e) **Osteoporosis:** Age-related disorder characterized by decreased bone mass (loss of calcium due to reabsorption) whereby chances of fractures increase. A decreased level of estrogen is a common cause, especially in post menopause women.

f) **Gout:** Inflammation of joints due to accumulation of ***uric acid*** crystals.

g) **Rigor mortis:** Stiffening of the body after death. In a dead person cells do not produce ATP and so cross bridges cannot be broken and the muscles become 'stiff'.

GLOSSARY

Acetabulum Cup: like hollow on each side of pelvic girdle into which head of femur fits.

Acromion process: Point of attachment of clavicle to scapula in the pectoral girdle of mammals.

Amphiarthroses: Slightly movable joints of vertebrates

Clavicle: Membrane bone of the ventral side of the pectoral girdle of many vertebrates; also called collar bone of man

Coccyx: Fused tail vertebrae. In man it comprises four coccygeal vertebrae

Cori cycle: The lactic acid produced in a fast working muscle, in low oxygen conditions, to release energy for the contraction of muscles is mostly converted into glucose in the liver cells (gluconeogenesis) by Cori cycle.

Coxal bones: Each half of the pelvic girdle. It is made of ilium, ischium and pubis.

Diarthroses: Freely movable joints of vertebrates. E.g. Most of these are synovial joints.

Fascia: Sheet of connective tissue enclosing muscles

Fascicles: Bundle of muscle fibers. These are covered by a connective tissue sheath, the perimysium.

Fatigue: The inability of a muscle to contract after repeated muscle contractions due to lack of ATP and accumulation of lactic acid.

Foramen magnum: Opening at the back of the vertebrate skull; the medulla oblongata passes out through this foramen and joins the spinal cord

Glenoid cavity: Cup-like hollow space on each side of the pectoral girdle into which head of the humerus fits.

Hyoid bone: Ventral element of the second visceral arch of the early vertebrates. It supports the tongue.

Hyomandibula: Dorsal element of the second visceral arch (hyoid arch). It becomes the ear ossicle called stapes, in mammals; it is the smallest bone of the human skeletal system.

Ligaments: Connective tissue joining one bone to another bone. Elastic ligaments consist primarily of elastic fibers and collagenous ligaments consist of parallel bundles of collagen.

Lumbar vertebrae: Bones of the lower back region, lacking rib attachments and situated between the thoracic and sacral vertebrae

Manubrium: The first upper(anterior most) bone of the sternum.

Motor end plate: Depression of sarcolemma on which the tips of the motor axon terminals end.

Myoglobin: Myoglobin is an iron containing and oxygen-binding protein found in the muscle tissue of almost all mammals.

Rigor mortis: Stiffening of the body after death. In a dead person cells do not produce ATP and so cross bridges cannot be broken and the muscles become 'stiff'.

Sarcomere: Structural and functional contraction unit of a myofibril Synarthroses. Immovable joints of vertebrates

Tonus: A state of partial contraction of a muscle

QUESTIONS

The Muscle

Very Short Answer Type Questions

1. What is a 'motor unit' with reference to muscle and nerve ?
2. What is triad system?
3. Write the difference between actin and myosin

Short Answer Type Questions

1. Describe the important steps in muscle contraction.
2. Describe the structure of a skeletal muscle.
3. Write short notes on contractile proteins
4. Draw a neat labeled diagram of the ultrastructure of muscle fiber
5. Draw the diagram of a sarcomere of skeletal muscle showing different regions.
6. What is Cori's cycle – explain the process.

Long Answer Type Questions

1. Explain the mechanism of muscle contraction.

The Skeleton

Very Short Answer Type Questions

1. Name two cranial sutures and their locations
2. Name the keystone bone of the cranium. Where is it located?
3. Human skull is described as dicondylic skull. Give the reason
4. Name the ear ossicles and their evolutionary origin in human beings.
5. Name the type of joint between a) atlas/axis b) carpal/metacarpal of the human thumb
6. Name the type of joint between Femur and hip bone.
7. Name the type of joint between a) cranial bones b) Inter-tarsal joint

Short Answer Type Questions

1. List out the bones of the human cranium.
2. Write short notes on the ribs of human being .
3. List the bones of human fore limb
4. List the bones of the human leg
5. Draw a neat labeled diagram of pelvic girdle.
6. Describe the structure of synovial joint with the help of a neat labeled diagram

Long Answer Type Questions

7. Describe the structure of human skull

FOR IGNITED MINDS

The Body Movement and Posture

The Musculo Skeletal System

1. In which type of muscles do we find 'multiple nuclear', 'structural units'?
2. What is the tiniest bone that plays an important role in a certain sensory perception?
3. Which muscles do you think are the most powerful muscles in the body of a tiger or a shark ?
4. Do muscles have any role in the homeostasis of temperature in our body? How do they help?
5. If you are asked to identify a single inorganic element that actually facilitates initiation of the contraction process in a muscle, what would you choose / what strikes your mind first? And do you think it has another important role in the proper functioning of one our circulatory fluids? what is it?
6. Does nodding the head 'yes' involve movement at the same joint as shaking the head 'no'?

   Clue: Condylid joint and Pivot joint
7. Which joint allows you to twist your forearm almost 180^0 (rotate the fore arm elbow)?

   Clue: Pivot joint.
8. Unlike arms (shoulder joints) we cannot move or rotate our legs (hip joints) freely. Why?
9. In the human limb skeleton can you identify a bone which is rather feeble and does not have much role in supporting body weight or maintaining posture, and doctors use pieces of it to transplant to other broken bones, where necessary?
10. The sternum's main purpose is to protect the inner delicate organs such as the heart. Why should majority of the ribs be attached to the sternum. What is the significance of such attachment?
11. Long duration low intensity exercises mostly use red fibers of muscles and high intensity actions lasting a few seconds use predominantly white fibers. Of the above two types, what type of muscles help a high jumper most?

UNIT III B

Neural Control and Co-ordination

The integrating net work of the 'Ultimate Biocomputer'

*Nervous system evolved from the basic non-polarised nerve cells forming a diffuse 'nerve net' as seen in the diploblastic organisms to a highly organized 'integrating system' with the '**Think Tank**", the '**Brain**' (containing 100 billion neurons), controlling it. Man has come to know more about this 'Head Quarters' of the nervous system, with the help of 'Functional Magnetic Resonance Imaging' (FMRI) technique. A three dimensional map of brain's functioning can be obtained with FMRI and a computer. These studies could pinpoint the various physiological regions of the brain and correlate them with specific tasks we perform in our daily life. Nervous tissue has connecting cells called '**neurons**' and '**supporting cells**' called '**glial cells**'. The system mainly controls the body activities by receiving stimuli (**sensory stimuli**), processing them and reacting to them by sending '**motor**' signals. Among the vertebrates, the nervous system reached the peak of evolution in man ,especially with the development of the '**neopallium**' (cerebral cortex,the '**grey matter**' with 10% of the total neurons of the brain in it), and the '**corpus callosum**' (nervous connection between the right and left halves of the cerebrum). Although both are structurally similar, the two cerebral hemispheres are responsible for different activities. For example, most neuronal processing related to language is performed in the left hemisphere of the '**right handed people**' and about 65% in the '**left handed people**'. **Hippocampus** of the brain is responsible for the formation and recall of **memory**. Our brain has developed two types of memory – the **long term memory** and **short term memory**. The '**limbic system**' of the brain formed by hippocampus and amygdale along with the hypothalamus is responsible for the **emotional response**. Research work is going on why people develop **dementia**, involving memory loss as seen in **Alzheimer's**. The human brain remains an ultra-computer, the working mechanism of whose processor has not yet been deciphered or may be it can never be deciphered at all.*

Introduction

As you know, the functions of the organs/organ systems in our body must be coordinated to maintain **homeostasis**. **Coordination** is the process through which two or more organs interact and complement the functions of one another. For example, when we do physical exercise, the energy demand is increased for maintaining increased muscular activity. The increased demand of oxygen necessitates an increase in the rate of respiration, heart beat and increased blood flow via the blood vessels. When physical exercise is stopped, the activities of nerves, lungs, heart and kidneys gradually return to their normal conditions. Thus, the functions of muscles, lungs, heart, blood vessels, kidney and other organs are coordinated while performing physical exercise. In our body the neural system and the endocrine system jointly coordinate and integrate all the activities of the organs so that they function in a synchronized fashion.

The neural system provides an organized network of point-to-point connections for a quick coordination. You will learn about the neural system of human beings, mechanisms of neural coordination like transmission of nerve impulse, its conduction across a synapse, the physiology of reflex action and also sensory perception, along with the structure of the most important sense organs in the human body, the eye and ear, in this chapter.

3.5 Human Neural System

It is divided into two parts: (I) The Central Neural System (**CNS**) and (II) The Peripheral Neural System (**PNS**)

3.5.1 The Central Neural System (CNS)

The CNS includes the brain and the spinal cord. It develops from **neurectoderm**.

BRAIN ('the living super computer')

It is the site of information processing and control. It is protected in the cranial cavity and covered by three connective tissue membranes called '***cranial meninges***' namely**, dura mater**, **arachnoid mater** and **pia mater**. **Dura mater** is the outer most, thick, *double layered* membrane which lines the inner surface of the cranial cavity. **Arachnoid mater** is a thin, webby middle membrane covering the brain. **Pia mater** is the thin, innermost meninx which closely adheres to the brain. Pia mater is separated from the arachnoid membrane by the **subarachnoid space**. The brain can be divided into three major parts called **i**. **Forebrain, ii. Midbrain** and **iii. Hindbrain.**

I. *Forebrain (Prosencephalon)*

The forebrain consists of **i. Olfactory bulb, ii. Cerebrum** and **iii. Diencephalon**.

i. **Olfactory Bulb:** Olfactory bulbs receive impulses pertaining to smell from the olfactory epithelium.

ii. **Cerebrum :** Cerebrum forms the major part of the brain and is longitudinally divided into the left and the right *cerebral hemispheres* by a deep cleft called '**longitudinal fissure**'. The two hemispheres are internally connected by a transverse, wide and flat bundle of myelinated fibres beneath the cortex, called '**corpus callosum**' (**colossal commissure**). It brings 'coordination' between the right and left sides of the cerebral hemispheres. The surface of the cerebrum is composed of grey matter and is called the '**cerebral cortex**'. The neuronal cell bodies are concentrated in the **cerebral cortex.**

The surface of the cerebral cortex shows many convolutions or folds and grooves. The folds are called **gyri** (singular: gyrus), the deepest and shallower grooves between the folds are called **fissures** and **sulci**, respectively. Gyri and sulci increase the surface area of the cerebral cortex (which is an indication of the higher level of evolution of the human being).

Cerebral cortex has three functional areas called **a)sensory areas**, that receive and interpret the sensory impulses **b) motor areas**, which control voluntary muscular movements **c) association areas**, which are neither clearly sensory nor motor in function and they deal with more complex 'integrative functions' such as *memory* and *communications*. The **cerebral medulla** consists of mostly myelinated axons (white matter). Each cerebral hemisphere of the cerebrum is divided into four lobes namely **frontal**, **parietal**, **temporal** and **occipital** lobes.

iii. ***Diencephalon (Thalamencephalon):*** The main parts of the diencephalon are the epithalamus, thalamus and hypothalamus.

i) **Epithalamus**: It is the roof of the diencephalon. It is a non-nervous part which is fused with the pia mater to form the **anterior choroid plexus**. Just behind the anterior choroid plexus, the epithelium of the epithalamus forms a pineal stalk, which ends in a rounded structure called **pineal body**.

ii) **Thalamus**: It lies superior to the mid brain. It is the major coordinating centre for sensory and motor signalling.

iii)**Hypothalamus (the thermostat of the body):** It lies at the base of the thalamus. The hypothalamus forms a funnel-shaped downward extension called '**infundibulum**', connecting the hypothalamus with

the pituitary gland. It also contains several groups of neurosecretory cells, which secrete hormones called **hypothalamic hormones**. Hypothalamus controls and integrates the activities of the autonomous nervous system (ANS) and it has osmoregulatory, thermoregulatory, thirst, feeding (hunger) and satiety centres.

Limbic system

The inner parts of the cerebral hemispheres and a group of associated deep structures like **amygdala** or **amygdale**, **hippocampus** etc. form the **limbic system**. The limbic system is involved in the regulation of *sexual behaviour* and *expression of emotional reactions/ responses*.

II. Midbrain (Mesencephalon)

The midbrain is located between the thalamus/ hypothalamus of the forebrain and the pons Varolii of the hindbrain. The ventral portion of the midbrain consists of a pair of longitudinal bands of nervous tissue called **cerebral peduncles** or **crura cerebri** (sing: **crus cerebrum**) *which connect the cerebral hemispheres with the pons*. The dorsal portion of the midbrain consists of four rounded lobes called **corpora quadrigemina** (Four optic lobes). The two larger anterior optic lobes are called superior colliculi and the smaller posterior lobes are called inferior colliculi. The superior colliculi and the inferior colliculi are concerned with visual and auditory functions, respectively.

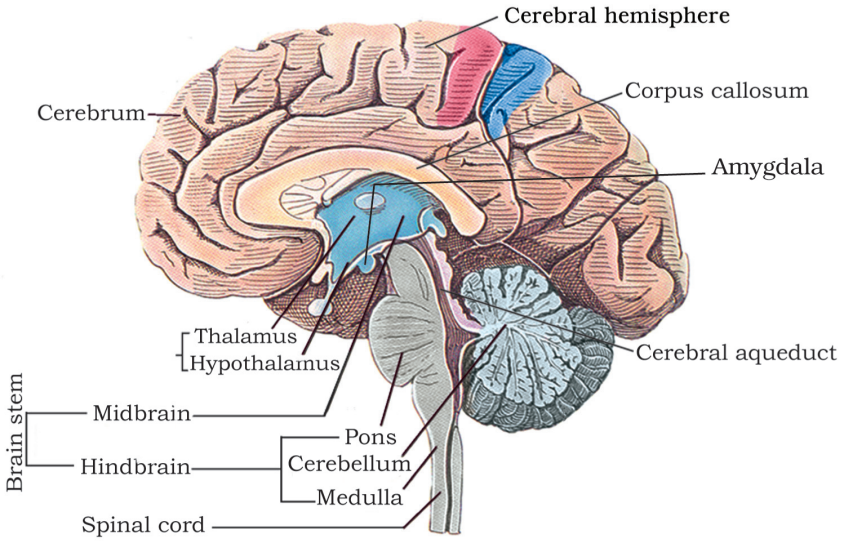


Figure 3.15 Sagittal section of human brain

III. Hindbrain (Rhombencephalon)

The hind brain comprises cerebellum, pons Varolii and medulla oblongata.

Cerebellum ('the little brain'): It is the second largest part of the brain. It consists of two cerebellar hemispheres and a central **vermis**. Each cerebellar hemisphere consists of three lobes namely anterior, posterior and floccular lobes. It has a branching tree - like core of white mater called **arbor vitae** (**the *tree of life***) surrounded by a sheath of grey matter (**cerebellar cortex**).

NOTE: Cerebellum is responsible for the control and coordination of locomotor movements. The cerebellum is called the 'gyroscope of the body' because it maintains equilibrium. Damage to cerebellum often results in *ataxia* (uncoordinated voluntary muscle movements).

Pons Varolii

It lies in front of the cerebellum below the mid brain and above the medulla oblongata. It consists of nerve fibres which form a bridge between the two cerebellar hemispheres. It is a ***relay station*** between the cerebellum, spinal cord and the rest of the brain. Pons has the **pneumotaxic centre** (**involved in the control of the respiratory muscles** as it regulates the amount of air a person can take in (rate of breathing and depth of respiration).

Medulla oblongata

It is the posterior most part of the brain. It extends from the pons Varolii above and continuous with the spinal cord below. It has a very thin, vascular folded structure called **posterior choroid plexus**. Medulla includes cardiovascular and respiratory centers, the centers for swallowing, vomiting, coughing, sneezing and hiccupping. The midbrain, pons and the medulla oblongata are together referred to as the '**brain stem**'.The medulla oblongata passes out of the cranium through the foramen magnum and joins the spinal cord.

Ventricles of the human brain

Human brain consists of four ventricles. The first and second ventricles (lateral ventricles or paracoels) are present in the right and left cerebral hemispheres respectively. The third ventricle (diocoel) occurs in the diencephalon. The two paracoels are connected to the median diocoel individually by the two '**foramina of Monro**' (interventricular foramina). The fourth ventricle (**myelocoel**) is present in the medulla. The myelocoel and the diocoel are connected by a narrow canal called **iter** or **aqueduct of Sylvius/cerebral aqueduct**. The myelocoel is continuous with the central canal of the spinal cord.

The ventricles of the brain, and the subarachnoid space are filled with **Cerebro-spinal fluid** (**CSF**). CSF is an alkaline, colourless fluid which is filtered from the choroid plexuses into the ventricles of the brain.

NOTE: **CSF** serves as shock absorbing medium. CSF is recycled (flushed) 4 times per day in order to clear out metabolites and toxins.

3.5.2 Spinal Cord

The spinal cord is located in the vertebral canal (neural canal) of the vertebral column. It is protected by the bony arch of each vertebra and the three ***spinal meninges*** called dura mater, arachnoid mater and pia mater.

In the adult, it extends from the medulla oblongata to the superior border of the second lumbar vertebra. It has two conspicuous enlargements, the superior enlargement called ***'cervical enlargement'*** and the inferior enlargement called ***'lumbar enlargement'.*** The spinal cord is divided into right and left halves by two grooves namely, the anterior (ventral) **median fissure** and the posterior (dorsal) **median sulcus**. Inferior to the lumbar enlargement, the spinal cord tapers to a conical portion known as the ***conus medullaris***, which ends at the level of the intervertebral disc between the first and second lumbar vertebrae in the adult. The extension of the conus medullaris as the non-nervous fibrous tissue to the coccyx is called *'**filum terminale**'.*

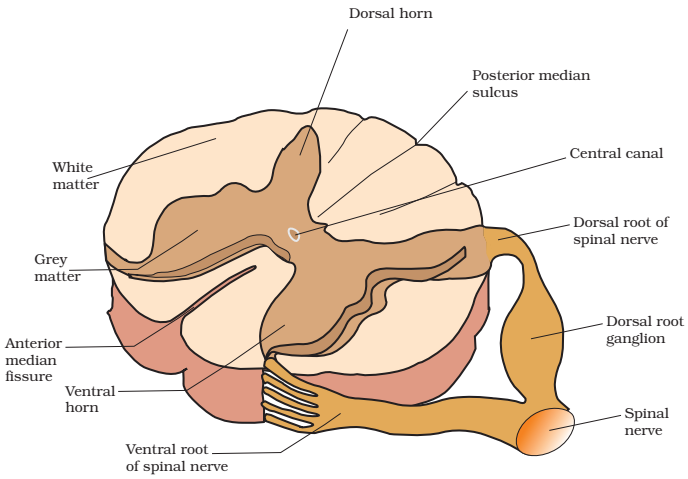


Figure 3.16 T.S of spinal cord

The internal anatomy of the spinal cord shows **H- shaped** or **butterfly shaped** central area of grey matter surrounded by the outer white matter. The grey matter is composed of cell bodies, neuroglia, dendrites and unmyelinated axons and it surrounds a narrow longitudinal cavity called '**central canal**' or '**spinal neurocoel**' which is the continuation of the fourth ventricle of the brain and is lined by the **ependymal epithelium**. The grey matter is subdivided into regions called '**anterior and posterior horns**' on each side.

The white matter consists of bundles of myelinated axons and it is organized into the regions called **anterior (ventral) funiculus, posterior (dorsal) funiculus and lateral funiculi**, one on each side. *The spinal cord acts as a coordinating centre for simple spinal reflexes. It also acts as the '**middle man**' between the receptors and the effectors, as it conducts sensory and motor impulses to and from the brain.*

3.5.3 The Peripheral Neural System (PNS)

The **PNS** is formed by the nerves that are associated with brain (**cranial nerves**) and spinal cord (**spinal nerves**).

3.5.3.1 The Cranial Nerves

The nerves that are associated with the brain are called **cranial nerves**. They enter or emerge out of the cranium through different foramina. They are **12 pairs** in man. Functionally they are of three types, namely, **sensory, motor** and **mixed** nerves.

I) **Olfactory nerve (sensory):** It arises from the olfactory epithelium of the nasal chamber, and extends to the 'temporal lobe' of cerebral hemisphere via the olfactory bulb.

II) **Optic nerve (sensory):** It arises from the retina of the eye. The two optic nerves cross each other on the floor of the diencephalon in front of the infundibulum. This crossing is called **optic chiasma**. Finally the impulses reach the visual cortex in the occipital lobe of the brain.

III) **Oculomotor nerve (motor):** It arises from the floor of the mid brain and innervates the inferior oblique, superior, inferior and medial rectus muscles, ciliary and iris muscles of the eye ball.

IV) **Pathetic or Trochlear nerve (motor):** It arises from the floor of the mid brain and innervates superior oblique muscles of the eye ball.

V) **Trigeminal nerve (mixed):** It is associated with the pons Varolii and joins the Gasserian ganglion. It has three branches. They are ophthalmic (sensory), maxillary (sensory) and mandibular (mixed) branches. The trigeminal nerve receives the sensory impulses from the conjunctiva, lacrimal glands, eye lids, palate, teeth, lips, nose, tongue, cheek and it sends motor impulses to the lacrimal glands, muscles of the lower jaw, sublingual and sub maxillary salivary glands.

VI) **Abducens nerve (motor):** It arises from the **pons** and ends in the **lateral rectus** muscle of the eye ball.

VII) **Facial nerve (mixed):** Its motor fibres arise from the pons and end in facial parts, palate, hyoid, sublingual and submaxillary salivary glands. Its sensory fibres extend from the taste buds of the anterior two-thirds of the tongue to the pons through the **gasserian ganglion**.

VIII) **Vestibulo-cochlear nerve / Acoustic** or **Auditory nerve (sensory):** It has two branches called '**cochlear**' and '**vestibular**' branches. Cochlear branch arises from the organ of Corti of the cochlea and terminates in a sensory nucleus called the cochlear nucleus which is located at the junction of the pons and medulla. The vestibular branch arises from the semicircular canals, sacculus and utriculus of the internal ear and ends in the vestibular nuclear complex located in the floor of the fourth ventricle.

IX) **Glossopharyngeal nerve (mixed):** Its motor fibres arise from the medulla and end in the muscles of the pharynx and the parotid, sublingual and

sub maxillary salivary glands. Its sensory fibres conduct impulses to the medulla from the taste buds of the 'posterior third' of the tongue and pharynx.

X) **Vagus nerve (mixed):** The motor fibres of the vagus nerve arise from the medulla and terminate in the muscles of organs such as the lungs, heart, oesophagus, stomach, and intestine, from which sensory fibres arise and terminate in the medulla.

XI) **Spinal accessory or accessory nerve (motor):** It arises from the medulla and terminates in the muscles of the pharynx, larynx, neck and shoulder.

XII) **Hypoglossal (motor):** It arises from the medulla and terminates in the muscles of the tongue, which control the tongue movements pertaining to speech, food manipulation, and swallowing.

3.5.3.2 The Spinal Nerves

The spinal nerves are formed by the union of dorsal and ventral roots soon after they leave the spinal cord. The first pair of cervical spinal nerves emerges between the atlas and occipital bone of the cranium. All other spinal nerves emerge from the vertebral column through the **intervertebral foramina** between the adjoining vertebrae. There are **31 pairs** of spinal nerves in man which are classified into five groups based on their location, they are: **i**. **Cervical** (**8** pairs) **ii**. **Thoracic** (**12** pairs) **iii**. **Lumbar** (**5** pairs) **iv**. **Sacral** (**5** pairs) **v**. **Coccygeal**/ caudal (**1** pair). Before emerging out from the intervertebral foramina, the lumbar, the sacral and the caudal nerves extend back along with the filum terminale forming a thick bundle of nerves called **cauda equina**.

Certain spinal nerves are joined to form networks called plexuses on either side. They are: **1)cervical plexus**(**1**st to **4**th cervical nerves), **2) brachial plexus** (**5**th to **8**th cervical and **1**st thoracic nerves), **3) lumbar plexus** L_1, L_2, L_3 and L_4 lumbar nerves, **4) sacral plexus** (Branches of L_4, L_5 and S_1, S_2 and S_3 nerves) and **5) coccygeal plexus** (parts of **4**th and **5**th sacral and coccygeal nerve). Functionally, the **PNS** is divided into two divisions called ***Somatic*** and ***Autonomic neural systems***.

3.5.4 Somatic neural system (SNS)

The somatic neural system includes both **sensory** and **motor** neurons. The sensory neurons conduct sensory impulses from the different somatic receptors to the CNS. All these sensations normally are consciously perceived. Somatic motor neurons innervate the skeletal muscles and produce voluntary movements. The axon of a single myelinated somatic motor neuron extends from the **CNS** all the way to the skeletal muscle fibres. In the **SNS**, the effect of a somatic motor neuron always is ***excitation***.

3.5.5 Autonomic Neural System (ANS)

The ANS usually operates without conscious control. The autonomic neurons are associated with **interoceptors** (located in the viscera and sense internal stimuli), such as chemoreceptors. These sensory signals are generally not consciously perceived. Autonomic motor neurons regulate the involuntary activities of the cardiac muscles, smooth muscle and glands. The ANS has two divisions: 1. **Sympathetic** and 2. **Parasympathetic divisions**.

1. **Sympathetic division**: In the sympathetic division, the preganglionic neurons arise from the thoracic and lumbar regions of the spinal cord, hence called '**Thoracolumbar division**'. The sympathetic nervous system is said to exhibit '**Thoracolumbar outflow**' (outflow of information, which refers to its 'motor' signals). The sympathetic system consists of two sympathetic chains, pre-ganglionic sympathetic fibres, post-ganglionic sympathetic fibres and collateral ganglia.
   A pair of sympathetic chains / trunks of ganglia extend from the base of the skull to the pelvis of the body along the sides of the dorsal aorta. The 'chain ganglia' contain cell bodies of many neurons and are connected serially by nerve fibres extending between them in the trunk. The preganglionic sympathetic fibres may synapse directly with the post ganglionic neurons in the chain ganglia or may synapse directly with the **collateral ganglia**. There are three collateral ganglia located in the abdominal cavity close to the origins of arteries with the same names on each side. They are **coeliac**, **superior mesenteric** and **inferior mesenteric ganglia**. It means the postganglionic sympathetic neurons may have their cell bodies, either in one of the **chain ganglia** or in the **collateral ganglia**. As the sympathetic trunk ganglia are closer to the spinal cord, most sympathetic preganglionic axons are shorter and the postganglionic axons are longer. In general, postganglionic axons from the sympathetic trunk mostly innervate organs anterior to the diaphragm, whereas, post ganglionic axons from the collateral ganglia innervate organs posterior to the diaphragm.
2. **Parasympathetic division**: The cell bodies of the preganglionic neurons of the parasympathetic division are located in the brain and in the sacral region of the spinal cord. Hence, the parasympathetic division is also known as the ***cranio sacral division***. The axons of the parasympathetic neurons that emerge from the brain occur in the ***III, VII, IX*** *and* ***X*** cranial nerves. The axons of the parasympathetic preganglionic neurons that emerge from the spinal cord occur in the **II, III** and ***IV*** sacral spinal nerves. The parasympathetic neural system is said to exhibit '**cranio-sacral outflow**' (out flow of information / 'motor' signals) as the '*efferent impulses of these nerves*' originate in the cranial and sacral regions of the CNS.

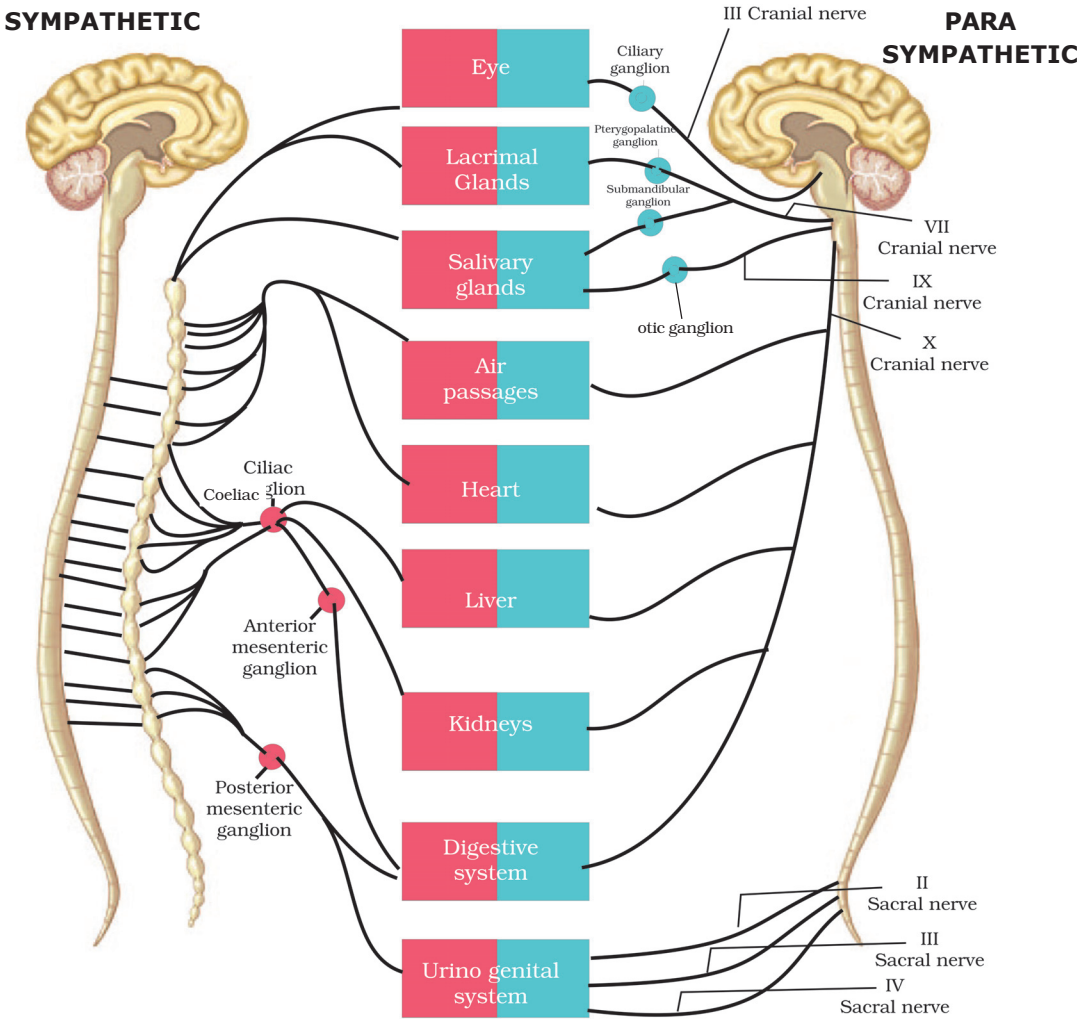


Figure 3.17 Autonomic Neural System (ANS)

The 'cranial out flow' of the parasymapathetic unit includes ***the ciliary, pterygopalatine, submandibular*** *and* ***Otic ganglia*** which receive preganglionic fibres from the cranial nerves ***III,VII and IX*** and send post-ganglionic fibres to smooth muscles of **the eye ball**, **nasal mucosa, palate, pharynx, lacrimal glands and salivary glands** in the head.

The preganglionic fibres that leave the brain as part of the **vagus** nerve are the last components of the cranial out flow which extend to many terminal ganglia in the thorax and abdomen. It sends fibres to the **heart, lungs** and to the **components of the digestive system**. Sacral out flow includes the pelvic plexus which receives preganglionic fibres from the **2nd** to **4th** sacral spinal nerves and supplies nerves mainly to the urinary and genital systems. As the parasympathetic ganglia are nearer to the organs they innervate, most parasympathetic preganglionic axons are longer and the postganglionic axons are shorter.

Differences between sympathetic and parasympathetic neural systems

Sympathetic neural system	Parasympathetic neural system
1. SNS originates in the thoracic and lumbar regions of the spinal cord	PNS originates in the cranial region of the brain and the sacral region of the spinal cord
2. Its ganglia are linked up to form a chain (one chain on each side of the vertebral column)	Its ganglia remain isolated
3. Preganglionic fibres are short and the postganglionic fibres are long	Preganglionic fibres are long and the postganglionic fibres are short
4. Norepinephrine is produced at the terminal ends of the post-ganglionic fibres at the synapses on the effectors organ. Hence the system is called 'adrenergic' usually.	Acetylcholine is produced at the terminal ends of the postganglionic fibres at the effector organ. Hence the system is called 'cholinergic' usually.
5. Active during stressful conditions, preparing the body to face them.	Active during relaxing times, restoring normal activity after stress.
6. The overall effect is excitatory and stimulating.	The overall effect is inhibitory.

Comparison of effects of sympathetic and parasympathetic systems on some organs

ORGAN	SYMPATHETIC (Fight or Flight response)	PARASYMPATHETIC (Rest and digest response)
Eye	Dilates pupil of the eye	Constricts pupil of the eye
Heart	Increases rate and force of contraction	Slows down the rate and force of contraction
Blood Vessels	Constricts	Dilates
Digestive tract	Inhibits peristalsis	Increases peristalsis
Salivary glands	Inhibits salivary secretion	Stimulates salivary secretion
Pancreas	Inhibits activity of pancreas	Stimulates activity of pancreas
Lungs	Relaxes bronchi	Constricts bronchi
Kidney	Increases secretion of renin	Decreases the secretion of renin
Urinary bladder	Inhibits emptying bladder	Promotes emptying the bladder

3.6 Generation and Conduction of Nerve Impulse

Nerve cells exhibit a special property called electrical excitability. The signal that travels along the length of a nerve fiber and ends in the release of neurotransmitters is called a *nerve impulse*. Neurons can respond to external and internal stimuli and conduct nerve impulses (*action potentials*) because in a neuron a membrane potential is established across the neuronal membrane. It means there is an 'unequal distribution of ions' (charged atoms) on the two sides of a nerve cell membrane with the cell's interior more negative with respect to that of the exterior. Ions keep moving in and out of an axon through several '*ion channels*'. The neuronal membrane of a neuron has the following three different types of ion channels.

1) **Leakage channels**: They are k^+ and Na^+ leakage channels. K^+ leakage channels are more than those of Na^+ leakage channels. Hence axolemma has greater permeability to K^+ ions than Na^+ ions.
2) **Ligand-gated channels:** They are located in the post synaptic membrane (dendrites and cell bodies) and ***open*** or ***close*** in response to ***chemical stimuli***.
3) **Voltage gated channels**: These channels open in response to a change in membrane potential. There are **sodium voltage gated** and **potassium voltage gated channels** across the axolemma. Sodium voltage gated channels have two types of gates. They are **sodium activation and inactivation voltage gates**. Each potassium **voltage gated channel** has only one activation gate.

Resting membrane potential

The resting membrane potential exists because of a small buildup of negative ions in the axoplasm along the inside of the membrane, and an equal buildup of positive ions in the extra cellular fluid along the outer surface of the membrane. Such a separation of positive and negative electrical charges is a form of **potential energy**. In neurons, the resting membrane potential ranges from **-40** to **-90** mV. A typical value of resting membrane potential is **-70 mV**. The minus sign indicates that the inside of the cell is negative relative to the outside.

At **resting phase**, the axolemma is polarized. The membrane potential can change from its resting value when the membrane's permeability to particular ions changes. If the inner side becomes less negative, it is said to be **depolarized**. If the inner side becomes more negative, it is said to be **hyperpolarized**. *During the resting phase the activation gates of sodium are closed, the inactivation gates of sodium are open and the activation gates of potassium are closed.*

Sodium - potassium pump

Sodium and potassium ions diffuse inwards and outwards , respectively, down their concentration gradients through leakage channels. Such a movement of ions, if unchecked, would eventually disturb the resting membrane potential. These flows of ions are offset by ***sodium - potassium pumps*** (**Na^+ / K^+ ATPases**) present in the axonal walls. These pumps expel **three Na^+ ions** for each **two K^+ ions** imported. As these pumps remove more positive charges from the axoplasm than they bring into it, they contribute to the negativity of the resting membrane potential **i.e., -70mV**.

Depolarization (Rising phase)

When a nerve fibre is stimulated, the plasma membrane first becomes more permeable to Na^+ ions than to K^+ ions as the activation and inactivation state voltage gates of sodium open and activation voltage gates of potassium are in closed. As a result the rate of flow of Na^+ into the axoplasm exceeds the rate of flow of K^+ in to the **ECF**. Hence, the axolemma is positively charged inside and negatively charged outside. This reversal of electrical charge is called **"depolarization"**

Outer face of the point which is adjacent to the site of depolarization remains positively charged. The electrical potential difference between these two areas is called **"action potential".** An action potential occurs in the membrane of the axon of a neuron when depolarization reaches a certain level called '**threshold potential**' **(-55 mV).** The particular stimulus which is able to bring the membrane potential to threshold is called **'threshold stimulus'**. The action potential occurs in response to a threshold stimulus or supra threshold stimulus but does not occur at subthreshold stimuli. It means the nerve impulse is either conducted totally or not conducted at all and this is called **'all- or - none principle'.** Due to the rapid influx of **Na+ ions**, the membrane potential shoots rapidly up to **+45 mV** (**spike potential**).

> **NOTE:** The initial entry of sodium ions causes charge reversal from negative to positive inside. It results in the opening of more and more sodium channels leading to a larger **influx of sodium ions** (called **POSITIVE FEED BACK REGULATION**).

Repolarization (Falling phase)

As the wave of depolarization passes away from its site of origin to the adjacent point, the activation gates of sodium remain open, inactivation gates of sodium close and activation gates of potassium open at the site of origin of depolarization. As a result the influx of **Na^+ ions** into the axoplasm from the

ECF is checked and '**efflux**' of **K^+ions** occurs, which leads to the returning of axolemma to the resting state (***exit of potassium ions causes a reversal of membrane potential to negative inside***). This is called **'repolarization'.**

Hyperpolarization (Undershoot)

The repolarization typically goes more negative than the resting potential to about **-90 mV**. This is called **'hyperpolarization'.** This occurs because of the increased K^+ permeability that exists while voltage-gated K^+ channels are open **(K voltage gates** close rather slowly and are said to be '**lazy**' **gates**), activation and inactivation gates of Na^+ channels remain **closed**. The membrane potential returns to its original resting state as the K^+ channels close completely. As the voltage falls below the **-70mV** level of the resting state, it is called '**undershoot**'

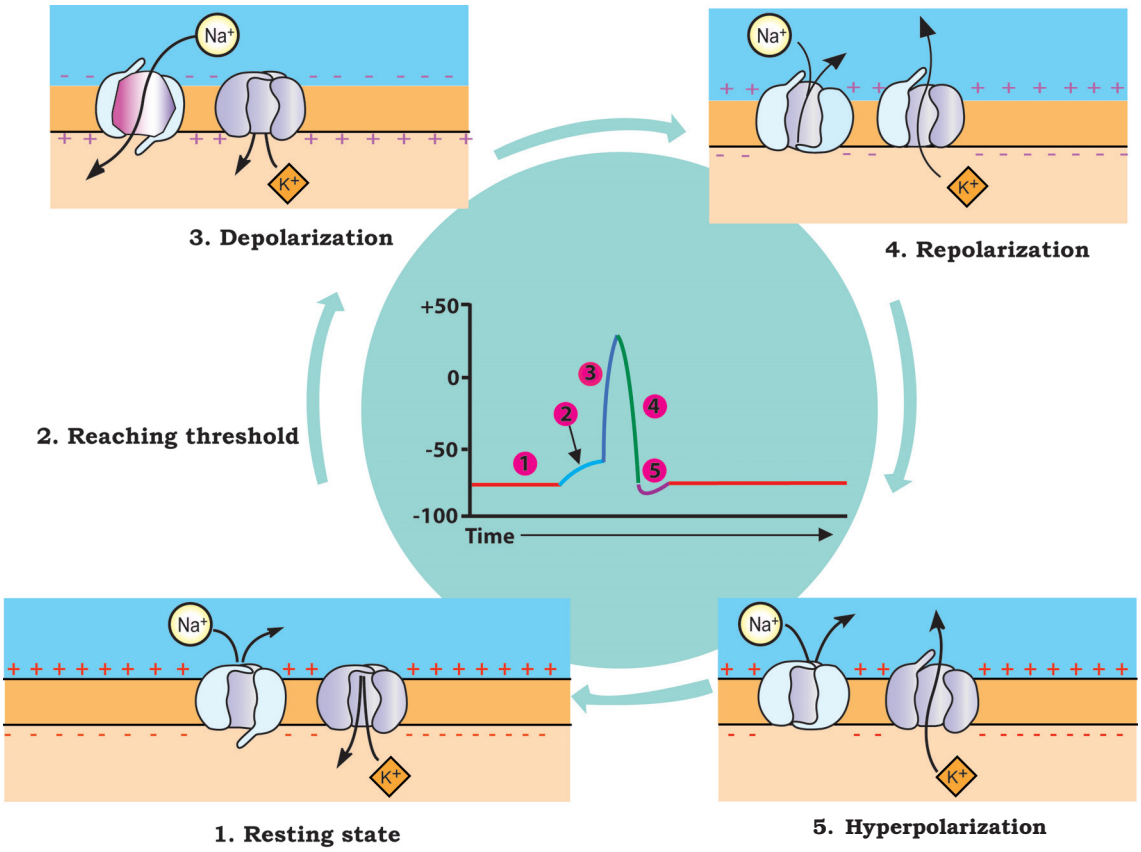


Figure 3.18 Nerve Impulse

The various types of responses of voltage gated sodium and potassium channels to depolarization.

Channel	*type of gate*	*resting state*	*depolarisation*	*repolarisation*	*hyperpol-arisation*	*speed of response*
SODIUM	ACTIVATION	CLOSED	OPENS	OPENS	CLOSES	*FAST*
SODIUM	INACTIVATION	OPENS	OPENS	CLOSES	CLOSES	*SLOW*
POTASSIUM	ACTIVATION	CLOSED	CLOSED	OPENS	OPENS	*SLOW*

The Refractory Periods

The period of time after an action potential begins during which the neuron cannot generate another action potential in response to a normal threshold stimulus is called the '**refractory period**'. There are two kinds of refractory periods, namely **absolute refractory period** and **relative refractory period**. During the absolute refractory period, even a very strong stimulus cannot initiate a second action potential. This period coincides with the periods of **depolarization** and **repolarization**. The relative refractory period is the time during which a second action potential can be initiated by a larger- than -normal stimulus. It *coincides* with the period of **hyperpolarization**.

Conduction speed

The conduction speed of a nerve impulse depends on the diameter of the axon: the greater the axon's diameter, the faster is the conduction. In a myelinated axon, the voltage-gated Na^+ and K^+ channels are concentrated at the **nodes of Ranvier**. As a result the impulse 'jumps' from one Ranvier's node to the next, rather than traveling the entire length of the nerve fibre. This mechanism of conduction is called **Saltatory conduction**. Saltatory conduction is faster (in myelinated fibres) than the continuous conduction (in nonmyelinated fibres).

3.6.1 Synaptic Transmission

A nerve impulse is transmitted from one neuron to another through junctions called **synapses**. A synapse is formed by the membranes of a pre-synaptic neuron and a post-synaptic neuron, which may or may not be separated by a gap called **synaptic cleft**. There are two types of synapses, namely, *electrical synapses* and *chemical synapses*. At electrical synapses, the membranes of pre- and post -synaptic neurons are in very close proximity compared to chemical synapses. These electrical synapses are electrically conductive links between two neurons and are also called '**gap junctions**'. Impulse transmission across an electrical synapse is always faster than that across a chemical synapse and they are in some cases bidirectional conductions.

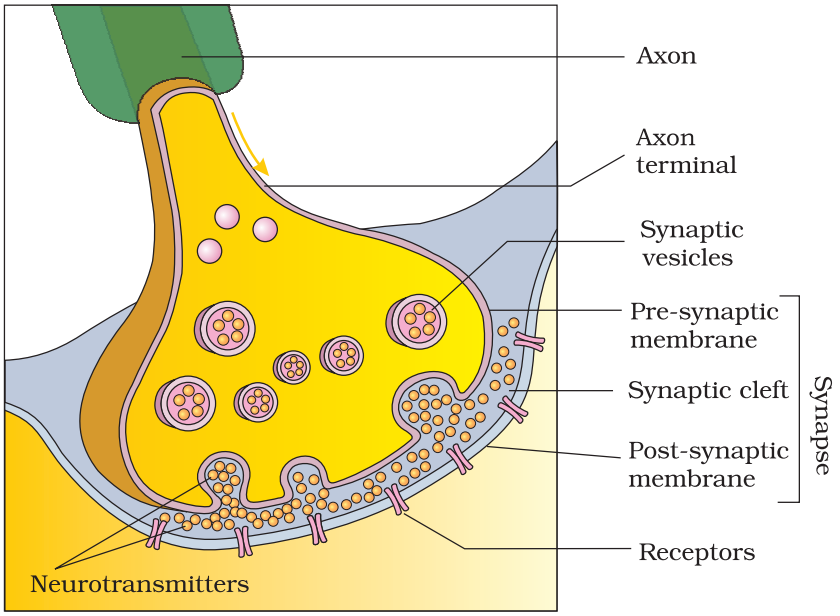


Figure 3.19 Synaptic Transmission

At a chemical synapse, the membranes of the pre- and post-synaptic neurons are separated by a fluid-filled space called synaptic cleft (**a structural gap** and **a functional bridge**). Chemicals called *neurotransmitters* are involved in the transmission of impulses at these synapses. The axon terminals (**boutons**) contain vesicles filled with these neurotransmitters. When an impulse (**action potential**) arrives at the axon terminal, it depolarizes the membrane opening voltage gated calcium channels. Calcium ions stimulate the movement of the synaptic vesicles towards the membrane where they fuse with the plasma membrane and release their ***neurotransmitters*** in the synaptic cleft by exocytosis. The released neurotransmitters bind to their ***specific receptors***, present on the post-synaptic membrane. **Acetyl choline** is the most common neurotransmitter. **Epinephrine**, **norepinephrine**, **dopamine**, **serotonin** etc. are either excitatory or inhibitory neurotransmitters. Glycine, GABA (Gamma Amino Butyric Acid) are inhibitory neurotransmitters. The post synaptic membrane has ***ligand gated channels***. They are **ion channels** which respond to chemical signals (**ligands**), rather than to changes in the membrane potential). The entry of ions can generate a new potential in the post-synaptic neuron. The new potential developed may be either ***excitatory*** or ***inhibitory***. Excitatory post synaptic potentials (**EPSPs**) cause depolarization, whereas inhibitory post synaptic potentials (**IPSPs**) cause hyperpolarisation of post synaptic membrane. Post synaptic potentials are **graded potentials** and '**summation**' of these potentials occurs at the '**axon hillocks**'. Summation of inputs from many presynaptic membranes is called '**spatial summation**', whereas summation of successive inputs from a single presynaptic membrane is called '**temporal summation**'. Development of an action potential depends on **which ever is more**? - ***The sum of excitatory post synaptic potentials*** *or* ***the sum of inhibitory postsynaptic potentials***.

3.7 Reflex Action and Reflex Arc

An automatic, involuntary, instantaneous and unconscious action brought about by the involvement of the central nervous system is called a reflex action. The reflex action is mediated by the 'neuronal components', which constitute the '**reflex arc**'. A reflex arc is the 'route' followed by a nerve impulse in the production of a reflex action (the neural pathway involved in a reflex action). The neural (reflex) pathway comprises at least one *afferent neuron* (receptor), one *internuncial neuron* and one *efferent* (***effector*** *or* ***excitor***) *neuron* arranged in series. The afferent neuron receives signal from a sense organ and transmits the impulse via the dorsal root of a spinal nerve to the CNS (at the level of the spinal cord). The efferent neuron then carries signals from the CNS to the effector through the ventral root of the spinal nerve. The stimulus and response thus forms a reflex action as shown in the diagram showing ***knee jerk reflex***.

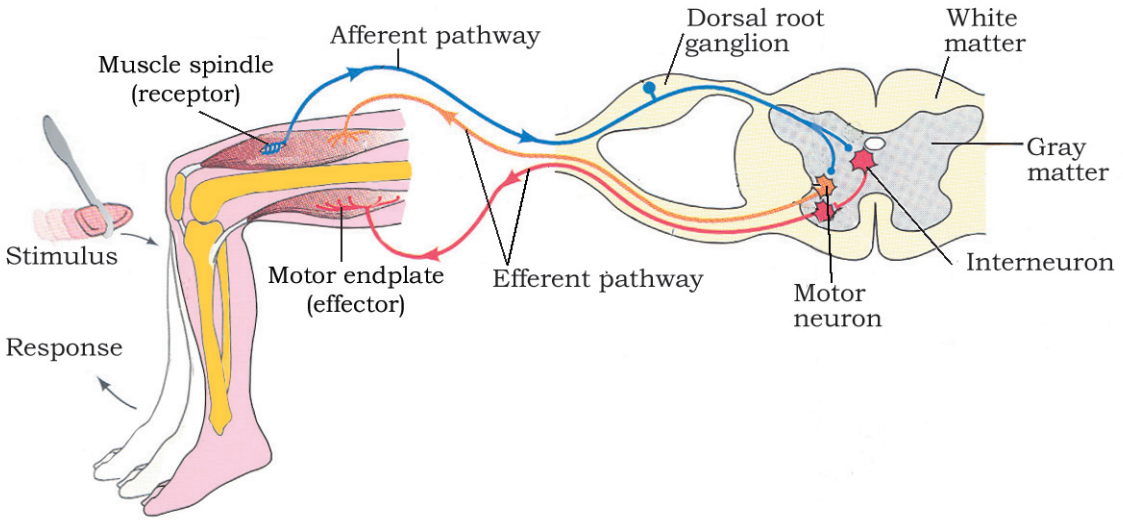


Figure 3.20 Reflex arc

3.8 Sensory Reception and Processing

In the human body the different types of receptors detect all types of changes in the environment and send appropriate signals to the CNS, where all the inputs are processed and analysed. Then the different controlling centres of the brain send 'motor impulses' to the 'effectors' through motor nerves. This is how you can sense changes in the environment. In the following sections, you will be introduced to some of the important receptors of human body.

1) **Exteroceptors**: They are located at or near the surface of the body, and sensitive to external stimuli like hearing, vision, touch, taste and pain etc.
2) **Interoceptors (visceroceptors)**: They are located in the visceral organs and blood vessels and sensitive to internal stimuli.
3) **Proprioceptors**: They are also a kind of interoceptors and they provide information about body position and movement and are located in muscles, tendons, joints and the internal ear.
4) **Thermoreceptors**: They respond to heat (**caloreceptors**) and cold (**frigidoreceptors**).

3.8.1 The Eye

The eye is the organ of vision which is located in the orbit of the skull. Eye consists of **accessory structures** and the **eye ball**.

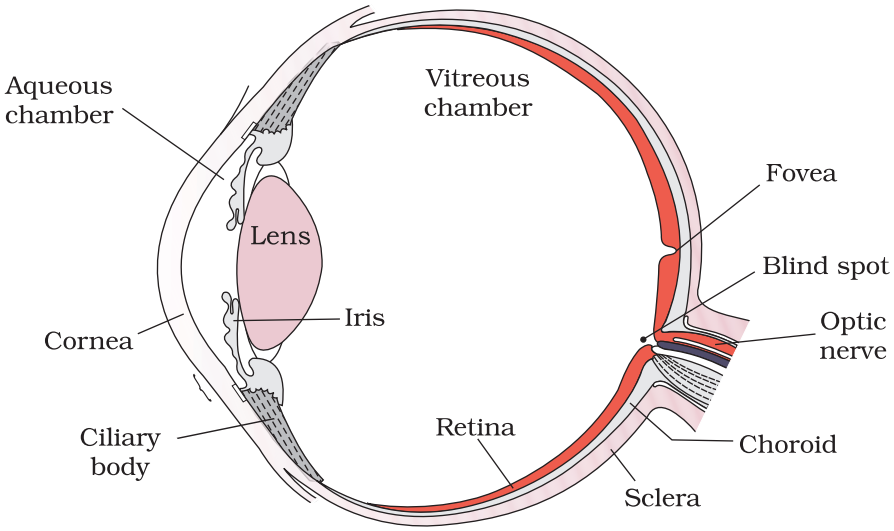


Figure 3.21 Diagram showing parts of eye

Accessory structures of eye

Eye lids, eye lashes, eye brows, lacrimal appartus and extrinsic eye muscles are the accessory structures of eye. The eye lids, the eye lashes and the eye brows are useful for the protection of the eye. The lacrimal apparatus is a group of structures that produce and drain lacrimal fluid or ***tears*** which contains salts, mucus and bactericidal enzyme called **lysozyme**. There are six extrinsic (extra ocular) eye muscles present attached to the human eye, namely **superior**, **inferior**, **lateral, medial rectus muscles,** and **superior oblique** and **inferior oblique muscles**. These muscles aid in the movement of the eye and they receive their innervations from the **III**, **IV** and **VI** cranial nerves.

The eye ball

Anatomically, the wall of the eye ball can be divided into three layers: fibrous tunic, vascular tunic , nervous tunic (retina). It also has a lens which is held in position by suspensory ligaments.

Fibrous tunic

It is the outer coat of the eye ball consisting of the anterior cornea (acts as a sort of ***'fixed lens'***) and the posterior sclera. The cornea is a non-vascular, transparent coat that covers the coloured iris. Cornea is covered by a thin layer called **conjunctiva**. The **sclera**, '**white**' of the eye, is a coat that covers the entire eye ball. The sclera gives shape to the eye ball, makes it more rigid, and protects its inner parts. At the junction of the sclera and cornea is a channel known as the **scleral venous sinus** or **canal of Schlemm.**

Vascular tunic

The vascular tunic or ***uvea*** is the middle layer of the eye ball. It has three portions: ***choroid, ciliary body*** and ***iris.*** The choroid is highly vascularised and looks bluish in colour. It is thick in the anterior part to form the **ciliary body**. The ciliary body is a pigmented and vascularized part that consists of the **ciliary processes**. The muscle associated with the ciliary body is a circular band of smooth muscle that holds and alters the shape of the lens for **near** or **far vision** (eye accommodation power- the process by which the eye changes optical power to focus on an object as its distance varies).

The ***iris*** is the coloured portion of the eyeball. It is suspended between the cornea and the lens and is attached at its outer margin to the ciliary processes. The aperture in the centre of the iris is called **pupil**. The principal function of the iris is to regulate the amount of light entering the **vitreous chamber** of the eye ball through the pupil. The diameter of the pupil is regulated by the muscles of the iris.

Retina (Nervous tunic)

This is the third and inner coat of the eye. It consists of a **pigmented epithelium** (**non-visual portion**) and a **neural portion** (**visual portion**). The pigmented epithelium is a sheet of melanin - containing epithelial cells that lie between the choroid and the neural portion of the retina. The neural portion of the retina has three layers of retinal neurons namely: **photoreceptor layer** (the layer closest to the choroid coat), **bipolar cell layer** and **ganglion cell layer**.

> **NOTE:** *Light must pass through ganglion layer, bipolar cells to reach the photo receptor cones and rods. Ganglion cells are the only cells of the retina capable of sending 'action potentials ' to the brain .*

Photoreceptor layer consists of two types of photoreceptor cells called **rods** and **cones**. Rods contain a purplish-red protein called the **rhodopsin** or **visual purple**, which is formed by the reversible combination of the protein opsin and a light absorbing molecule called 'retinal' derivation from

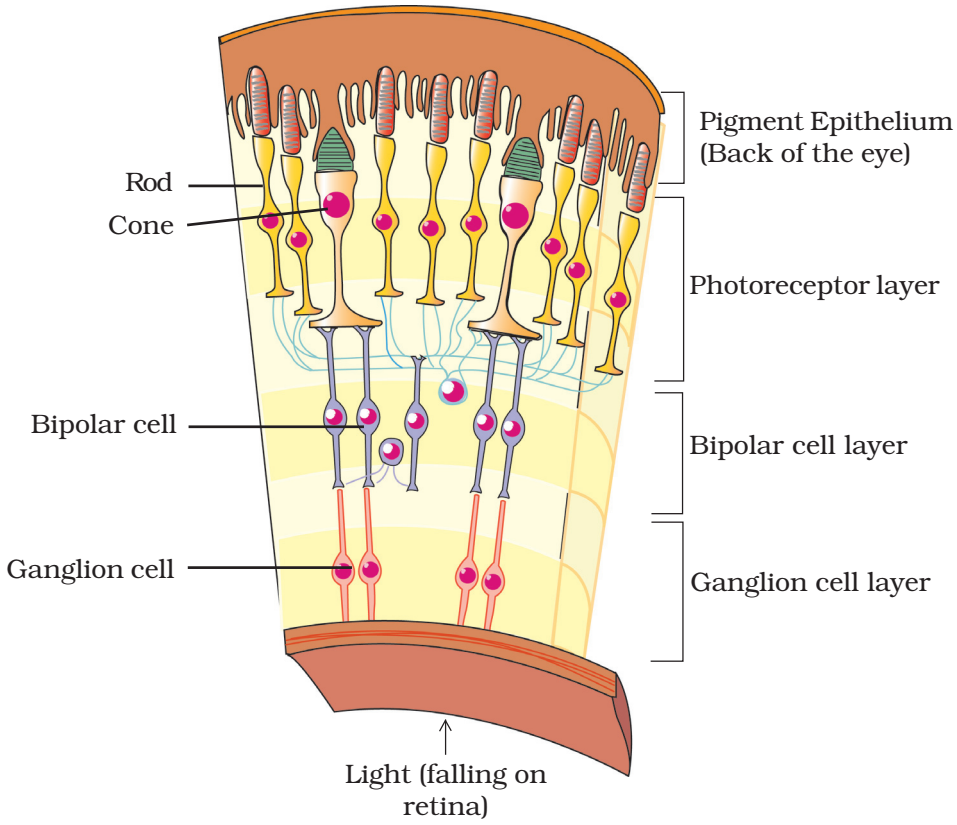


Figure 3.22 Microscopic structure of the retina

Vitamin A. Rods are important in twilight (***scotopic vision****- the vision of the eye under low light conditions*). Cones contain a visual pigment called **iodopsin** and they are important in daylight (**photopic**) vision and **colour vision**. There are three types of cones, each having different sensitivity (difference in light absorption pattern) and they provide '*optimal response*' to **red**, **green** and **blue** colours. Equal stimulation of all the cones produces a sensation of white colour (trichromacy theory).

The centre of the posterior portion of the retina is called the **macula lutea** or **yellow spot**. A small depression present in the centre of the yellow spot is called **fovea centralis,** and it contains only cones. Fovea is responsible for sharp, central vision, which is useful while walking, reading, driving etc. The axons of the ganglion cells extend posteriorly and exit the eye ball as the optic nerve. The site of the retina where the optic nerve exits the eye ball is called **optic disc** or **blind spot** which is devoid of photoreceptor cells (no image is formed at that spot).

Why *does the sales person in a cloth store switch on all the lights, when we go in, to purchase clothes?*

Lens

A non-vascular and transparent **lens** is present within the cavity of the eye ball just posterior to the pupil and iris. The lens is held in position by encircling **suspensory ligaments**. Ciliary muscles control the shape of the lens helping focusing light on the retina.

Chambers of the eye's interior

The interior space of the eye ball is divided by the lens into anterior and posterior chambers**.** The anterior chamber is filled with **aqueous humor (secreted by ciliary processes)**, which helps in nourishing the lens and the cornea. The posterior cavity lies between the lens and the retina and contains a jelly like substance called **vitreous body / vitreous humor.** The vitreous body contributes to the **intraocular pressure** along with aqueous humor and helps to protect the shape of the eye ball.

Mechanism of Vision

The light rays of visible wave length focused on the retina through the cornea and lens generate potentials (impulses) in rods and cones. As mentioned earlier, the photosensitive compounds (photo pigments) in the human eyes are composed of **opsin** (a protein) and **retinal**. Light induces dissociation of the retinal from opsin resulting in changes in the structure of the opsin. This causes changes in membrane permeability. As a result action potentials develop. These action potentials (impulses) are transmitted by the optic nerve to the visual cortex area of the brain (occipital lobes of the cerebrum), where the neural impulses are analyzed.

3.8.2 The Ear (The stato - acoustic receptor)

The ear is the site of reception of two senses, namely **hearing** and **equilibrium**. Anatomically, the ear is divided into three principal regions: the **external ear**, the **middle ear** and the **internal ear**.

External ear (outer ear)

The outer ear consists of the **pinna**(auricle), **external auditory meatus**(external auditory canal) and **ear drum**. The auricle is a flap of elastic cartilage covered by skin. It collects vibrations in the air that produce sound. The external auditory meatus is a curved tube that leads inwards and extends upto the **tympanic membrane** (the ear drum), which is a thin, semi transparent partition between the external auditory canal and middle ear. The tympanic membrane is composed of connective tissues covered with skin outside and with mucus membrane inside. There are very fine hairs and ear's wax secreting 'sebaceous glands' called **ceruminous glands** in the

skin of the pinna and the meatus. The combination of hair and **cerumen** (**ear's wax**) helps to prevent dust and foreign particles from entering the ear.

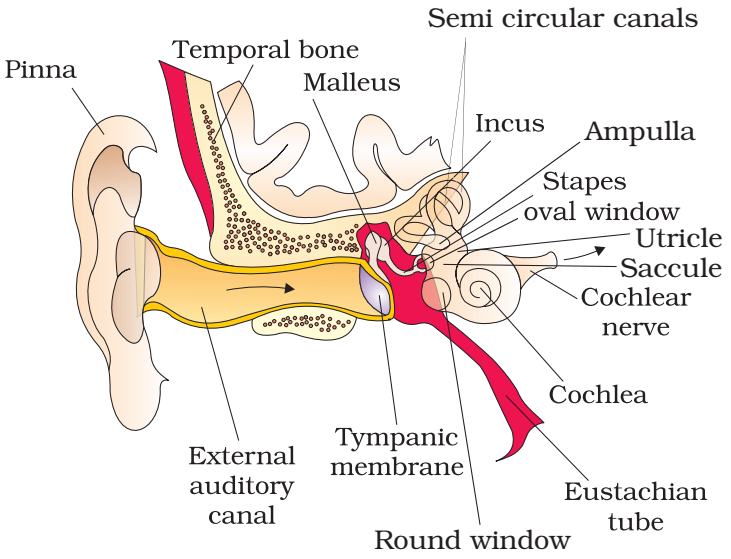


Figure 3.23 Diagram showing parts of ear

The middle ear

The middle ear (**tympanic cavity**) is a small, air - filled cavity in the temporal bone. It is separated from the external ear by the eardrum and from the internal ear by a thin bony partition that contains two small membrane - covered openings called the **oval window** (fenestra ovalis) and the **round window** (fenestra rotunda). The middle ear contains three ossicles called **malleus** (hammer bone), **incus** (anvil bone) and **stapes** (stirrup bone) which are attached to one another in a chain-like fashion. The malleus is attached to the tympanic membrane and its head articulates with the incus. The **incus** is the intermediate bone in the series of 'ear ossicles' and articulates with the head of the stapes. The stapes is attached to the oval window in the thin bony partition between the middle and inner ear. The ear ossicles transmit sound waves to the inner ear. A **Eustachian tube** connects the middle ear cavity with the pharynx. The Eustachian tube helps in equalising the pressures of air on either sides of the ear drum.

Inner ear

The fluid-filled inner ear called **labyrinth** consists of two parts, the **bony** and the **membranous labyrinths**. The *bony labyrinth* is a series of channels which can be divided into three areas: **1**) **cochlea**, **2**) **vestibule,** and **3**) **semicircular canals**. The *cochlea* is a coiled (watch spring like) portion of the labyrinth. Infact the cochlea is '**three tubes in one**'. The three tubes are namely **scala vestibuli**, **scala media** (**cochlear duct**) and **scala tympani**. The scala vestibuli and scala media are separated by a membrane called **Reissner's membrane**, the scala media and scala tympani are separated by another membrane called **basilar membrane**. Scala vestibuli and scala tympani are filled with **perilymph**. However the scala media is filled with **endolymph**. At the base of the cochlea, the scala vestibuli ends at the '*oval window*', while the scala tympani terminates at the '*round window*' which leads to the middle ear. The cochlear epithelium forms a sensory ridge called

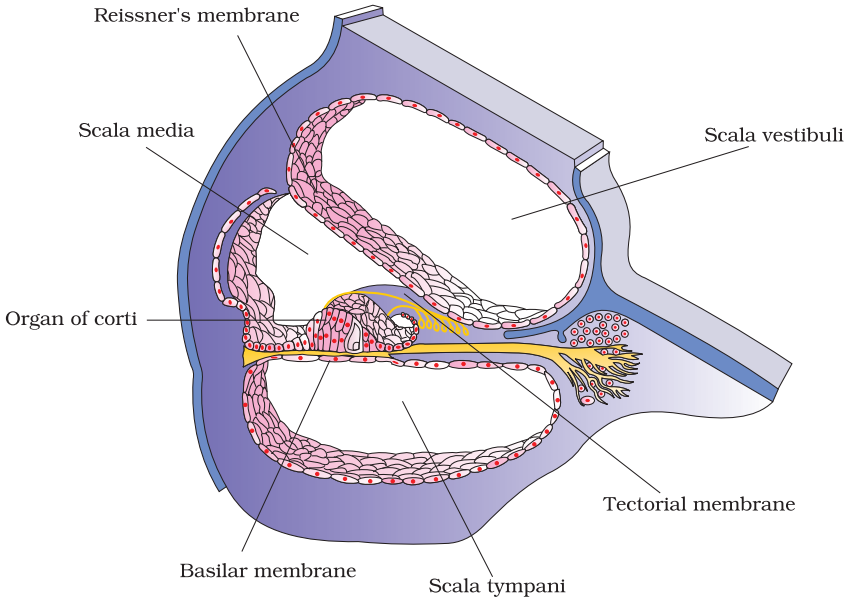


Figure 3.24 Section of Cochlea

"**organ of Corti**" on basilar membrane. The organ of Corti contains '**hair cells**' that act as 'auditory receptors'. The hair cells are present in rows on the internal side of the organ of Corti. These cells are innervated by the nerve fibres of the **cochlear branch** of the **VIII** cranial nerve. The basal end of the hair cell is in close contact with the auditory nerve fibres. A large number of processes called **stereocilia** are projected from the apical part of each hair cell. Above the rows of the hair cells is a thin elastic membrane called **tectorial membrane**.

There are three semicircular canals, each one lies approximately at right angles to the other two. The base of each canal is swollen and is called **ampulla**, which contains a *projecting ridge* called **crista** (which has '**hair cells**'). The semicircular canals provide a sense of '***angular acceleration***' perceiving '***rotation***' of the body (direction of body movement or turning of head to sides). The vestibule is the oval central part of the bony labyrinth located between the cochlea and the semicircular canals. The membranous labyrinth in the vestibule consists of two sacs called the **saccule** and the **utricle** (collectively called the **otolith organ**). The saccule and the utricle contain a projecting ridge called **macula**. It has receptors for ***gravity*** .Saccule and utricle provide a sense of '***linear acceleration***'. The saccule perceives ***vertical movement*** (as when you are going in a lift –moving upwards or downwards). The utricle perceives ***horizontal movement*** (as when you are going in a car – moving forwards or backwards).

The semi-circular canals and the otolith organ together constitute the "**vestibular apparatus**". The semi-circular canals, the saccule and the utricle are innervated by the **vestibular branch** of **VIII** cranial nerve. This vestibular apparatus is concerned with **equilibrium** (*maintenance of balance of the body and posture*).Vestibular branch of the auditory nerve carries these impulses to the brain.

Mechanism of Hearing

The external ear receives sound waves and directs them to the ear drum. The ear drum vibrates in response to the sound waves and these vibrations are transmitted through the ear ossicles to the oval window. The vibrations are passed through the oval window on to the fluid of the cochlea, where they generate waves in the peri and endolymphs. These waves induce a ripple in the **basilar membrane**. These movements of the basilar membrane press the hair like process of the hair cells against the **tectorial membrane**. As a result, nerve impulses are generated in the associated afferent neurons. These impulses are transmitted by the afferent fibres via the auditory nerves to the auditory cortex of the brain, where the impulses are analyzed and the sound is recognized.

Disorders of Human Neural system

1. Alzheimer's disease (AD): It is the most common form of **dementia** (Senile Dementia of the Alzheimer Type) in people above 65 years of age. It is a progressive neurologic disease of the brain, leading to the loss of neurons and the loss of intellectual abilities, including memory. It worsens with age and eventually it leads to death.

2.Meningitis: It is the inflammation of the protective membranes (meninges) covering the brain and the spinal cord. The inflammation may be caused by infection with viruses, bacteria and rarely by certain drugs.

3.Parkinson's disease: It is a progressive disorder of a certain region in the brain. It affects movements producing motor symptoms, which include autonomic dysfunction, neuropsychiatric problems, and sleep difficulties, and uncontrolled movements of other body parts.

4.Stroke or Cerebro-Vascular Accident (CVA): It is the rapid loss of brain functions due to disturbance in the blood supply to the brain. This can be due to **ischemia** (reduced blood flow) caused by partial blockage, or hemorrhage. As a result, the affected area of the brain cannot function, and it might cause inability to move one or more limbs on one side of the body, and the inability to understand or speak.

GLOSSARY

Adrenergic nerve fibres : Nerve fibres that release adrenaline at their terminal ends.

Amygdala: The part of the telencephalon, located in the temporal lobe. It is involved in memory, emotion, and fear, essentially acting as the **'brain's warning center'.** This is a component of the limbic system.

Brain stem: The region of the brain that consists of the midbrain, pons and medulla; responsible for the functions such as breathing, heart beat and blood pressure.

Blind spot: The place of retina which has no photoreceptors.

Cochlea: A spirally coiled part of the internal ear in which the organ of Corti is present.

Corpus callosum: The large bundle of axons which connects the two cerebral hemispheres. It disseminates the information from the cerebral cortex on one side of the brain to the same region on the other side; it is the system that helps communication between the right and left cerebral cortices.

Gyrus: The elevated portion of the cerebral surface.

Hippocampus: It is a part of the cerebral hemisphere in the basal medial part of the temporal lobe. This part of the brain is important for learning and for converting short term memory to permanent (long-term) memory.

Iris: It is a shelf-like diaphragm of choroid of the eye. It works-like a diaphragm of a photographic camera.

Limbic system: A group of structures including the amygdala and hippocampus (and others); important for controlling emotions and memory.

Neurotransmitter: A chemical substance which is released by the presynaptic neurons at synapses that transmits information to the next neurons.

Organ of Corti: The hearing apparatus that is present in the 'middle canal' of the cochlea.

Sulcus: The depression between gyri of the cerebrum.

QUESTIONS

Very Short Answer Type Questions

1. Name the cranial meninges covering the brain of man
2. What is corpus callosum?
3. What do you know about arbor vitae?
4. Why the sympathetic division is called thoraco-lumbar division?
5. Why the parasympathetic division is called cranio-sacral division?
6. Distinguish between the absolute and relative refractory periods.
7. How do rods and cones of human eye differ from each other chemically and functionally?
8. Distinguish between the blind spot and the yellow spot.
9. What is organ of Corti?

Short Answer Type Questions

1. Draw a labelled diagram of the T.S of the spinal cord of man.
2. Describe sympathetic nervous system.
3. Give an account of the retina of the human eye.
4. Give an account of synaptic transmission.
5. List out the differences between sympathetic and parasympathetic neural systems in man.

Long Answer Type Questions

1. Give a brief account of the structure and functions of the brain of man.
2. Explain the transmission of nerve impulse through a nerve fibre with the help of suitable diagrams.

FOR IGNITED MINDS

The integrating network of the 'Ultimate Biocomputer'

Neural control and Coordination

1. Why does a person who gets a hard hit on the back of the upper neck region die almost instantaneously ?
2. What happens if the corpus callosum of the cerebrum is severed/cut ?
3. Which component of the nervous system brings a 'Fight or Flight Response' in human body ?
4. If you are reading your news paper,sipping your coffee, quietly, what part of your nervous system is perhaps actively working /dominating?
5. If you think of a lemon, most probably you will notice salivation in your oral cavity. What do you call this type of response in your body with reference to your nervous system's functioning, if you are asked to give your answer in just 'two words'?
6. When a clinical investigator pricks your finger for a sample of a drop of blood, if the prick continues to give you pain for some time, it is due to successive 'action potentials' from the same region, causing you the pain. What do you call this in terms of development and conduction of action potentials?
7. If a person suffers from 'hyperacidity', do you think cutting the branch of the pneumogastric nerve to the stomach will help him reduce hyperacidity? If so what is the reason you can offer?
8. If you, hypothetically, introduce some gamma amino butyric acid in a synapse, what will happen in the succeeding neuron's membrane potential, if it is already in a normal, polarized state by that time.
9. If the room in which you are sitting is relatively hot and humid, which part of your CNS will show a neural response to take care of your problem to the extent possible to it?
10. If the 'inactivation gates of sodium' are closed and 'potassium voltage gated channels' are open, in what phase is the 'action potential' in your body? – Rising, Falling or Undershoot?

Arnold Adolph Berthold

Unit-IV

HUMAN ANATOMY AND PHYSIOLOGY - IV

Hormones - The Biochemical 'Integrators'

*Hormones are mostly the body's **long distance signaling** substances. They are released by the endocrine glands (ductless glands with the exception of **pancreas** which is a '**dual gland**'). Endocrine secretions are released into circulating fluids and they have a role in the body's '**homeostasis**'. In higher animals we come across various types of cytokines which are also 'local regulators' (dealt with in the lesson on immunity). Hormones such as vasopressin, oxytocin are secreted by parts of the central nervous system and reach target cells via the circulatory fluids. Many animals (e.g. insects) are known to produce regulatory molecules called **pheromones** which are released to the exterior. They help in chemo-communication. Some hormones in our body are produced from cholesterol (by some enzymatic modifications). Water soluble hormones cannot pass through plasma membrane. They show their action by stimulating certain **cell surface receptors**. The lipid soluble hormones can pass through the plasma membrane and bind to some **receptors in the cytoplasm**. These complexes can pass into the nucleus of the cell and cause their effect on the DNA.*

Certain hormones which stimulate the production of other hormones in other parts of the body are called "Tropic hormones", e.g. Adrenocorticotropic hormone (ACTH) stimulates some of the cells of the adrenal cortex.

UNIT IV A

Endocrine System and Chemical Co-ordination

INTRODUCTION

All functions in the human body are coordinated and regulated in order to maintain homeostatic state in the body. You have already learnt that the neural system provides a point-to-point rapid coordination among organs, which is rather short lived compared to the 'chemical coordinating' system. As the nerve fibers do not innervate all the cells of the body and the cellular functions need to be continuously regulated, a special kind of coordination and integration has to be provided. This function is performed by the endocrine glands through their secretions called '**hormones**'. The endocrine system regulates the functions that do not require instantaneous response and the effects persist for a relatively longer period. It is believed that the neural and endocrine systems originated and developed side by side, as the needs of communication became more complex due to the increased complexity in body organization, particularly in mammals. The principal role of both the systems is the coordination and control of many of the major physiological activities.

Endocrine (Greek: endo = inner; crine = away) system consists of discrete tissues or organs called endocrine glands and their secretions. These glands do not possess ducts to carry their secretions out, hence called **ductless glands**. The secretions of these glands namely **hormones**, released directly

into the blood stream or lymph, are circulated in the body to reach their target cells / tissues / organs.

As per one of the current scientific definitions, '***hormones are non-nutrient chemicals which act as intercellular messengers and are produced in trace amounts***'. The new definition covers a number of new molecules in addition to the hormones secreted by the organised endocrine glands.

Hormones

The term hormone (hormone = to excite) was coined by **Starling**. **Secretin** was the first hormone to be detected. Usually, hormones function on targets away from their production sites except some local hormones such as gastrin, somatostatin etc. Hormones coordinate, accelerate or inhibit one or more physiological activities. They are biomolecules of small size and are effective in very low concentrations. Most of the hormones are highly specific regarding their 'targets' (e.g. TSH, ACTH), but some hormones such as thyroxine and STH act on nearly all somatic cells. Hyper or hypo secretion of any hormone produces certain disorders. Hormones are short lived and they are degraded by tissues and excreted through **bile** (by the liver) and **urine** (by the kidneys).

Chemically hormones fall into three classes

They are as follows:

1. **Amine hormones** which are derivatives of a single amino acid. The examples for this class are : a) catecholamines (epinephrine and nor-epinephrine) and thyroxine, as derivatives of 'tyrosine' and b) melatonin, a derivative of 'tryptophan'.
2. **Peptide** and **protein hormones** are polymers of amino acids. Small peptide hormones (3 to 49 amino acids) include **ADH**, **oxytocin** etc. The peptides that are formed by numerous amino acids (50 to 200) are referred to as **protein hormones** and the examples include the hormones of the anterior pituitary, pancreas, parathyroids etc. The more complex protein hormones, with carbohydrate side chains, namely glyco-proteins include FSH, TSH, LH etc.
3. **Steroid hormones**, the derivatives of cholesterol, include hormones such as aldosterone, testosterone, estrogens and progesterone. The widely studied **prostaglandins** are derivatives of **eicosanoids** (a large group of molecules derived from the 'essential fatty acids' such as the omega-3 and omega-6 fatty acids).

Some higher invertebrates possess very simple endocrine system that produces a few hormones, whereas a well developed endocrine system that produces a large number of hormones occurs in the vertebrates. The human endocrine system is described here.

4.1 Human Endocrine System

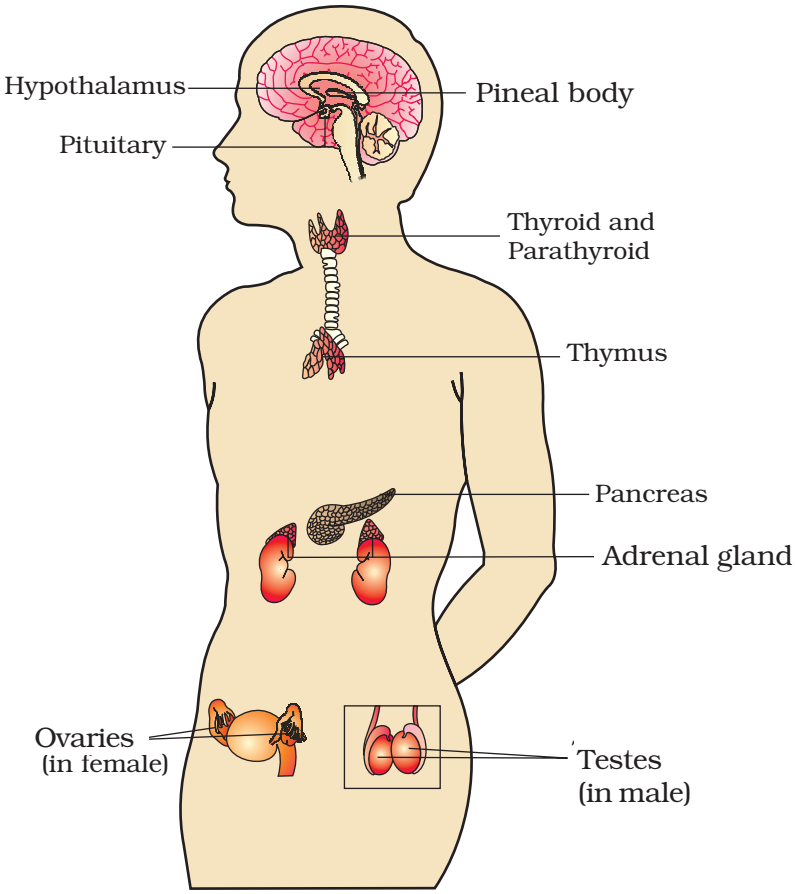


Figure 4.1 Location of endocrine glands

The endocrine glands of human beings are well studied than those of any other animal because of their role in the maintenance of human health. The endocrine glands and the hormone producing diffused tissues / cells located in different parts of the human body constitute the ***endocrine system***. The organized endocrine tissues / organs in the human body include **pituitary, pineal, thyroid, parathyroid, adrenal, pancreas, thymus and gonads** (**testes** and **ovaries**). Besides these, some other non-endocrine organs such as gastrointestinal tract, liver, kidney, and heart also produce hormones. A brief account of the structure and functions of all the major endocrine glands and hypothalamus is given below.

4.1.1 Hypothalamus

(Greek: Hypo = under; Thalamus = chamber)

The hypothalamus is located below the thalamus, constituting the floor of the diencephalon, a part of the fore brain. It connects the neural and endocrine systems as it is closely tied to the pituitary gland. It responds to the sensory impulses received from different receptors by sending out appropriate neural or endocrine signals.

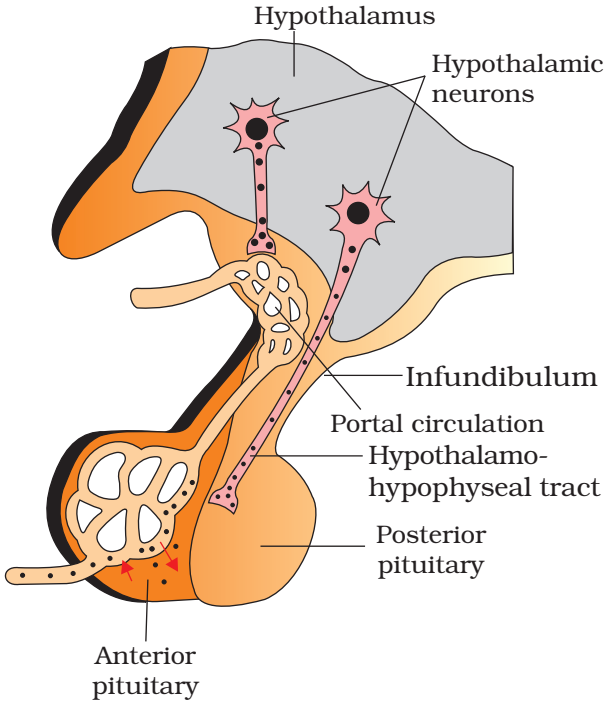


Figure 4.2 Pituitary gland and hypothalamus

It regulates a wide range of body functions. It contains several groups of **neurosecretory cells** called '***nuclei***' which produce hormones called neuro-hormones. They are transported to the neurohypophysis through the axons of the **hypothalamo-hypophysial tract**. The two other types of hormones produced by the hypothalamus are 1) the **releasing hormones** (which stimulate secretion of pituitary hormones), and 2) the **inhibiting hormones** (which inhibit secretions of pituitary hormones).

NOTE: The hypothalamus is the '**Master Control Centre**' of the endocrine system, as its secretions directly control the pituitary gland which in turn secretes hormones that regulate the growth and functioning of other endocrine glands.

For example, a hypothalamic hormone called **growth hormone releasing hormone** (**GHRH/Somatocrinin**) stimulates the synthesis and release of **Somatotropin (growth hormone)** by the **pituitary**. On the contrary the **growth hormone-inhibiting hormone** (**GHIH**) or **somatostatin** from the hypothalamus inhibits the release of growth hormone from the pituitary. These hormones originating in the hypothalamic neurons pass through axons and are released from their nerve endings. They reach the anterior pituitary through a portal circulatory system called **hypophysial portal system** and regulate the functions of the anterior pituitary. The posterior pituitary is under the direct neural regulation of the hypothalamus.

4.1.2 Pituitary Gland

The pituitary gland, also called 'hypophysis', is a small unpaired round body. It is located immediately beneath the hypothalamus, attached to it by a stalk, called the infundibulum. It lies in a bony depression called **sella turcica** of the sphenoid bone. It is divided anatomically into **anterior pituitary** (parsdistalis) or **adenohypophysis** and **posterior pituitary** or **neurohypophysis**. Between these two is a small zone called the ***pars intermedia***, which is considered a part of the anterior pituitary in man, as it is almost fused with the anterior lobe.

Origin of the pituitary

Embryologically the two portions of the pituitary have their origins from two different sources (**dual origin**). The anterior pituitary (**adenohypophysis**) develops from the **Rathke's pouch** which is an embryonic outgrowth from the roof of the oral region. It is the major secretory part of the pituitary. An outgrowth from the floor of the hypothalamus gives rise to the infundibular process which becomes the **neurohypophysis**.

Anterior pituitary / Adenohypophysis

The anterior pituitary produces six important protein hormones. The hormones of the anterior pituitary play major roles in the control of metabolic functions throughout the body.

1. **Growth Hormone** (**GH**)**:** It is also called **somatotropin**. It stimulates mostly the cells of the liver to produce insulin-like growth factors (IGFs).They stimulate cell division in the epiphyseal plates leading to '***elongation of bones***'. They also promote growth of the entire body by accelerating protein synthesis, cell division and cell differentiation. They also decrease the catabolism of proteins.
2. **Prolactin:** It is also called lactogenic hormone / luteotropic hormone (**LTH**): It causes enlargement of the **mammary glands** of the breasts and prepare them for the production of milk. In women the major action of prolactin is to initiate and sustain lactation. Prolactin also helps in maintaining the **corpus luteum** of the **ovary**, which is the source of a natural female sex hormone **progesterone**, and thus it helps to sustain pregnancy.
3. **Thyroid Stimulating Hormone** (**TSH**) / (**Thyrotropin**): It stimulates the synthesis and secretions of thyroid hormones from the thyroid gland.
4. **Adrenocorticotropic Hormone** / **Corticotropin** (**ACTH**): Controls the synthesis and secretion of steroid hormones called glucocorticoids, mineralocorticoids and sex corticoids by the adrenal cortex.

5. **Follicle Stimulating Hormone** (**FSH**): It stimulates growth and development of the ovarian follicles in females. In males FSH, along with the androgens, regulates **spermatogenesis.**
6. **Luteinizing hormone** (**LH**): In males it stimulates the interstitial cells of Leydig of the testes for the synthesis and secretion of hormones called androgens ('testosterone' is the chief androgen). In females, this hormone stimulates 'ovulation' from the fully mature Graafian follicles. Besides this, it stimulates the ovaries to produce '**estrogens**' and **progesterone.** It maintains the corpus luteum formed from the remnants of the Graafian follicles, after ovulation.

> ***NOTE**: The two hormones of the anterior pituitary, namely FSH and LH are called 'gonadotropins' because they stimulate the gonads to produce other hormones.*

Pars intermedia secretes only one hormone called melanocyte stimulating hormone (MSH). In human beings, pars intermedia is almost merged with pars distalis and the role of MSH is not significant, excepting that it can darken the hair by increasing deposition of melanin in the developing hair shaft. MSH regulates pigmentation in the melanocytes of the lower vertebrates and its role in man is not significant.

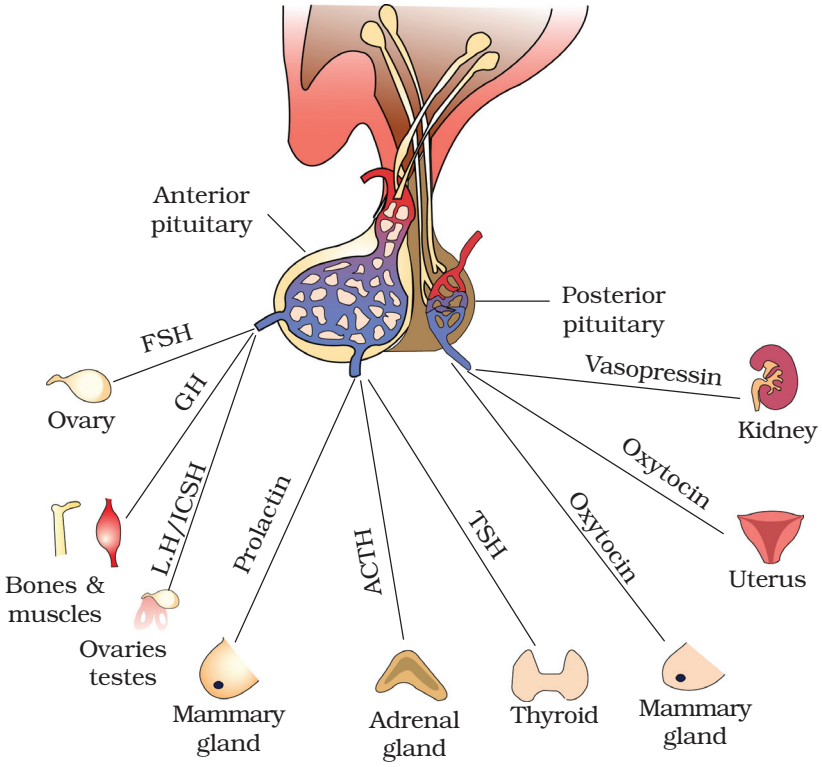


Figure 4.3 Hormones secreted by pituitary gland and their target organs

Posterior pituitary / Neurohypophysis: It stores and releases two hormones called ***oxytocin*** and ***vasopressin*** /ADH, which are actually synthesized by the hypothalamus and are called neuro-secretions. They are small chain peptides. **Oxytocin** works on the smooth muscles of the body and induces their contraction. In a female it stimulates powerful contractions of the uterus during child birth and ejection of milk from the mammary glands.
Vasopressin affects the kidney and stimulates reabsorption of water and electrolytes by the DCT and the collecting duct from the nephric filtrate. Thus urine becomes more concentrated and **diuresis** (increased excretion of the urine) is prevented. Hence, it is also called 'anti-diuretic hormone' (**ADH**).

4.1.3 Pineal Gland

The pineal gland or ***epiphysis cerebri*** is located on the dorsal surface of the diencephalon. The pineal gland secretes a hormone called **melatonin**. It plays a very important role in the regulation of 24 hour (diurnal / circadian) rhythms of our body. For instance, it helps in maintaining the normal rhythms of the **sleep-wake cycle**, body temperature etc. Besides this, melatonin influences metabolism, pigmentation, menstrual cycle and defence capability of our body. In some animals it stimulates gonads while in others it inhibits the gonads.

> ***NOTE:*** *Secretion of melatonin is more in darkness (night time). Recent studies indicate that the main target of melatonin is the suprachiasmatic nucleus (SCN) of the hypothalamus which acts as the "Biological clock" in humans.*

4.1.4 Thyroid Gland

It is the largest endocrine gland and is endodermal in origin. It lies close to the body surface, in the neck near the junction of larynx and the trachea. The thyroid consists of two lobes connected by a thin flap of connective tissue called **isthmus**. The lobes lie on either side of the trachea and extend upwards along the sides of the larynx. The complete thyroid gland somewhat resembles a butterfly with its wings spread (H shaped).

4.1.4.1 Thyroxine

The thyroid gland is composed of **follicles** and **stromal tissues**. Each thyroid follicle is composed of follicular cells, enclosing a cavity. These follicular cells produce two major hormones, namely tetra-iodothyronine or **thyroxine** (T_4) and tri-iodothyronine (T_3). Iodine is necessary for the normal rate of hormone synthesis in the thyroid. Thyroxine (T4) and Triiodothyronine have the same endocrine functions.

Thyroid hormones (calorigenic hormones) play an important role in the regulation of the **basal metabolic rate (BMR),** the rate of consumption of oxygen per unit weight of the body, at rest. Thyroid hormones increase the basal metabolic rate by stimulating the use of cellular oxygen to produce ATP. As cells produce and use more ATP, more heat is given off and the temperature of the body rises. In this way, they maintain normal body temperature of a homeotherm. These hormones stimulate the process of erythropoiesis. Thyroid hormones control the metabolism of carbohydrates, proteins and fats. Maintenance of water and electrolyte balance is also influenced by thyroid hormones.

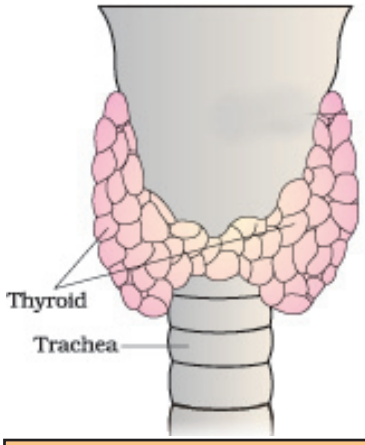


Figure 4.4 Thyroid gland

4.1.4.2 Calcitonin

The parafollicular cells also called **'C'** cells of the thyroid produce a polypeptide hormone called Thyrocalcitonin (**TCT**). It plays an important role in maintaining proper levels of calcium (Ca^{2+}) and phosphates in the blood. It decreases blood calcium by promoting deposition of calcium in bones and thus it counters the effect of parathormone. Higher calcium content in the plasma stimulates the secretion of calcitonin (negative feedback control mechanism).

4.1.5 Parathyroid Glands

In humans there are four parathyroid glands, located on the back side of the thyroid gland. Each lobe of thyroid has one pair of parathyroids, of endodermal origin. The parathyroid glands secrete a hormone called **parathyroid hormone** (PTH) / ***parathormone***. The secretion of PTH is controlled by the levels of Ca^{2+} in the circulatory fluids. This hormone augments the Ca^{2+} levels in the blood. Thus it is a **hypercalcemic hormone**. It stimulates the process of bone resorption (dissolution/demineralization of the bone) by stimulating the osteoclasts to dissolve calcium phosphate of the matrix of bones releasing calcium into blood. PTH also stimulates reabsorption of calcium ions by renal tubules and increases the absorption of Ca^{2+} from the gut. Together with thyrocalcitonin (TCT), it plays a significant role in calcium

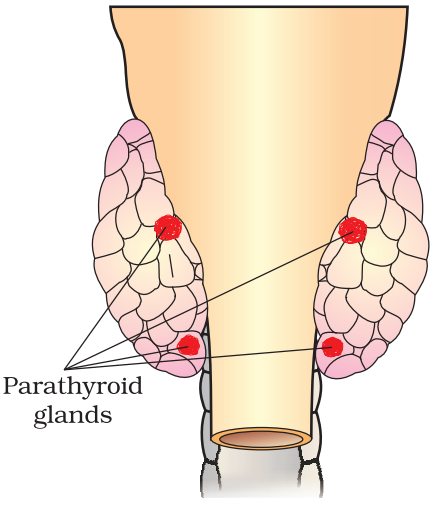


Figure 4.5 Parathyroid glands

balance in the body. It promotes the activation of vitamin D into its active form, the 'hormone' called 'calcitriol'.

NOTE: *Vitamin D (calciferol) is actually an inactive form of a hormone, the calcitriol. Parathyroid hormone is indirectly involved in the absorption of calcium from the intestine by promoting formation of Calcitriol / 1,25-dihydroxy vitamin D. Calcitriol increases blood calcium levels (Ca^{2+}) by promoting absorption of calcium from the gastrointestinal tract.*

Thymus Gland

The thymus gland is a lobular structure located just above the heart and the aorta, underneath the '***breast bone***'. This gland plays a significant role in strengthening the immune system. It secretes peptide hormones called **thymosins**. Thymosins play a major role in the differentiation of T-lymphocytes, which provide **cell-mediated immunity**. In addition, thymosins also promote the production of antibodies to provide **humoral immunity**.

NOTE: *Thymus is small at birth. It increases in size during childhood and reaches its maximum size at the age of 'puberty'. During adulthood, it shrinks to its size at birth. In old persons, thymus gland is degenerated, resulting in a decreased production of thymosin. Thus immune response of old people becomes weak, which is often said to be the cause of the process of ageing.*

4.1.6 Adrenal Glands

One pair of adrenal glands is present in the body of a human being, located one at the anterior part of each kidney. It is also called **suprarenal gland.** Adrenal gland is composed of two types of tissues. The peripheral tissue is the **adrenal cortex** (mesodermal in origin) and the centrally located tissue is called **adrenal medulla** (ectodermal in origin).

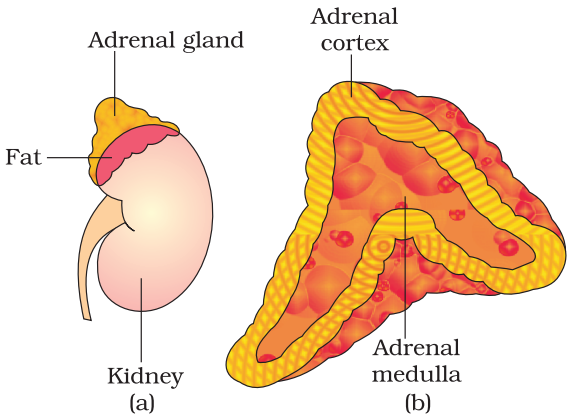


Figure 4.6 (a) Adrenal gland at the superior border of the kidney (b) Section showing two parts of the adrenal gland

a. Adrenal Cortex: Adrenal cortex is the peripheral tissue of the adrenal gland. It is differentiated into three zones. The outer zone is called **zona glomerulosa**, the middle one is known as **zona fasciculata** and the inner one, the **zona reticularis**. The adrenal cortex secretes many hormones commonly called **corticoids** (steroid hormones).

Zona glomerulosa secretes mineralo-corticoids (aldosterone is the chief mineralo-corticoid). Aldosterone regulates the balance of water and electrolytes in the body. Aldosterone, whose secretion is stimulated by 'angiotensin II' when the blood pressure falls , acts mainly on the renal tubules and stimulates the reabsorption of Na^+ and water from renal tubules and excretion of K^+ and phosphate ions. Thus aldosterone helps in the maintenance of electrolytes, body fluid volume, osmotic pressure and blood pressure.

NOTE: Aldosterone not only retains Na but also promotes excretion of K, which, if accumulated, is harmful. Removal of the adrenal cortex or diseases that prevent secretion of aldosterone can kill a person.

Zona fasciculata secretes glucocorticoids. They are concerned with the carbohydrate metabolism. In the body of humans **cortisol** is the chief glucocorticoid. The glucocorticoids are 'life saving' hormones.

Glucocorticoids stimulate gluconeogenesis, lipolysis and proteolysis. These corticoids inhibit cellular uptake and utilization of amino acids. Cortisol (also called hydrocortisone) regulates the cardio-vascular system and the kidney functions.Glucocorticoids, specially **cortisol**, generates ***anti-inflammatory reactions*** and *suppresses immune* responses in the case of tissue and organ transplants. Cortisol stimulates RBC production. Cortisol is a "stress combat" hormone.

Zona reticularis synthesize sex hormones. **Androgens** are the male sex hormones and testosterone is the chief androgen. It is concerned with the development of growth of axial, pubic and facial hair during puberty.

b. Adrenal medulla: It secretes two hormones called ***adrenaline*** or ***epinephrine*** and ***noradrenaline*** or ***norepinephrine***. These are commonly called **catecholamines**. These hormones are secreted in response to **stress** of any kind and during emergency situations, hence are called **emergency hormones** or **hormones of fight** or **flight**. These hormones enhance alertness, dilation of pupils, piloerection (involuntary erection of hair on skin), sweating, dilation of the bronchioles etc. These hormones increase the rate of heartbeat, the strength of the contraction of heart and also increases the rate of respiration. Catecholamines also stimulate the breakdown of glycogen, lipids and proteins (Glycogenolysis, gluconeogenesis). Thus the concentration of glucose in the blood increases.

4.1.7 Pancreas

Pancreas is both exocrine and endocrine in function. It is an elongated organ located posterior to the stomach. The exocrine portions of pancreas are known as ***acini***. The endocrine portion of the pancreas is just 1 to 2% and consists of 1 to 2 million ***Islets of Langerhans***. The two main types of cells in the Islets of Langerhans are the ***α-cells*** and ***β-cells***. The α-cells produce the hormone, **glucagon**, whereas the β-cells produce **insulin**. Glucagon is secreted in response to hypoglycemia. Its action is mainly on the liver cells (hepatocytes) and it stimulates **glycogenolysis**. This increases the sugar level in the blood (**hyperglycemia**). It also converts amino acids and fatty acids into glucose (**gluconeogenesis**) which also increases the level of glucose in the blood. This hormone decreases the uptake of glucose and its utilization by the cells. Therefore glucagon is a **hyperglycemic hormone**.Insulin regulates the normal glucose level in the blood. It mainly acts on the liver cells and adipocytes and increases the uptake and utilization of glucose by the body cells. Glucose is taken up by the hepatocytes, skeletal muscles and adipocytes, thus reducing the level of glucose in the blood (**hypoglycemia**). Insulin promotes conversion of glucose into glycogen (**glycogenesis**) in the target cells (***hypoglycemic hormone***). Both glucagon and insulin maintain the homeostasis of glucose in the blood. Persistent **hyperglycemia** leads to a complex disorder called **diabetes mellitus**.

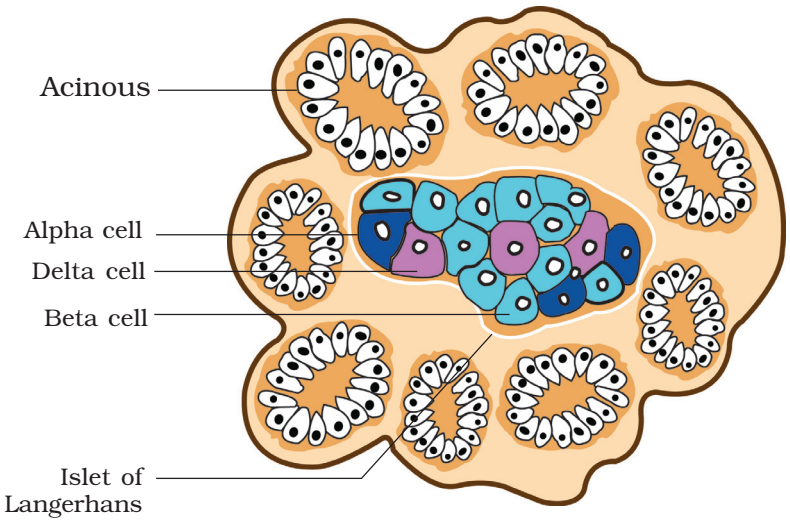


Figure 4.7 A section of pancreas showing islets of Langerhans and acini

4.1.8 Testes

(Male Gonadal Glands)

Testes are the male gonads. Each testis is enclosed in a scrotal sac outside the abdomen. Testis is a cytogenic organ (an organ which produces cells), and it produces both sperms and sex hormones. The **Leydig cells** or **interstitial cells of Leydig** , lie in the 'inter-seminiferous tubule spaces', they produce **androgens**, chiefly the **testosterone**. Male sex hormones are

required for the development, maturation and functioning of the male accessory sex organs such as epididymis, vas deferens, seminal vesicles, prostate gland, urethra etc. These hormones control muscular growth, growth of facial and **axillary hair**, aggressiveness, low pitch voice (masculine voice) etc. Androgens stimulate the process of spermatogenesis. Androgens affect the central neural system, controlling the male sexual behaviour (**libido / sex drive /sexual urge**) and also have an effect on ***protein*** and ***carbohydrate anabolism***. Androgens are also called **anabolic steroids**.

4.1.9 Ovaries

(Female Gonadal Gland)

Ovaries are the female gonadal organs present in the abdominal cavity. These are cytogenic organs and produce one ovum during each menstrual cycle. Besides this, ovaries act as endocrine glands too producing the female hormones chiefly: ***estrogen*** and ***progesterone***. Ovarian follicles and stromal tissues are present in the ovary. The hormone **estrogen** is produced by the growing follicles of the ovary. After ovulation, the ruptured follicle becomes a **'yellow body'** called ***corpus luteum*** (*which acts as a* ***temporary endocrine gland***) and secretes **progesterone**. After a few days, in the absence of pregnancy, the corpus luteum stops functioning and becomes the '**corpus albicans**'.

Estrogen is responsible for the development and the activity of the female secondary sex organs, development of the ovarian follicles, high pitch of voice etc. and the development of the mammary glands. Estrogen also controls the female sexual behaviour.

Progesterone has an important role in preparing the uterus for the implantation of the blastocyst in the wall of the uterus. It inhibits contraction of the uterus. Thus it supports pregnancy. In case of deficiency of this hormone, pregnancy fails to maintain. It stimulates the formation of alveoli (sac like structures which store milk) in the mammary glands and secretion of milk.

Hormones of Kidney, Heart, Gastro-intestinal Tract and Liver

In addition to the endocrine glands, some tissues which are not fundamentally endocrinous in nature also secrete certain hormones that perform important functions. Among such non-endocrine tissues /organs, the kidney, heart and gastrointestinal tract are important

The muscle cells in the atria (**atrial myocytes**) of the human heart secrete a peptide hormone of vital importance when the pressure of blood increases. It is called ***atrial natriuretic factor / atrial natriuretic peptide*** (**ANF/**

ANP). This hormone dilates the blood vessels, and lowers the blood pressure when the blood pressure increases. It decreases renal reabsorption of sodium which also helps in lowering the blood pressure.

Kidney also produces a hormone called **erythropoietin**. The juxtaglomerular cells of the kidneys secrete this hormone, which stimulates ***erythropoiesis*** (formation of RBC). The role of **erythropoietin** is to control the formation of red blood cells by regulating the ***proliferation*** and ***differentiation*** of ***erythroid progenitor cells*** (Proerythorblasts) in the bone marrow.

The mucosa of the gastrointestinal tract has some kinds of cells which produce five major peptide hormones, helping in the digestion of food. These hormones include ***gastrin***, ***secretin***, **cholecystokinin** (**CCK**), **enterocrinin, gastric inhibitory peptide** (**GIP**) etc.

Gastrin acts on gastric glands and stimulates the secretion of hydrochloric acid and pepsinogen. **Secretin** is produced by the duodenal mucosa. It acts on the exocrine part of the pancreas and stimulate secretion of water and bicarbonate ions. **Cholecystokinin** is a 'polypeptide hormone' produced in the duodenum, in response to the presence of fats in the chyme. It causes contraction of the gallbladder, release of bile, and secretion of pancreatic digestive enzymes. It relaxes the *sphincter of Oddi*. It is also called *pancreozymin*. **Gastric inhibitory peptide** inhibits gastric secretion and motility (inhibits emptying of the stomach).

Many other non-endocrine tissues secrete hormones called '**growth factors**'. These factors are necessary for the normal growth of tissues and their repair/ regeneration.

4.2 Mechanism of Hormonal Action

Hormones stimulate or inhibit the target cells' activities. Hence they are called **regulators**. Hormones play a vital role in regulating the functions of the body.

Hormones produce their effects on target tissue by binding to specific proteins called **hormone receptors** located in the target tissues only. Hormone receptors present on the cell membranes of the target cells are called **membrane bound- receptors** and the hormone receptors present inside the target cells are called **intracellular receptors.** Hormone receptors are specific, as each receptor is specific to a certain hormone only. A hormone and its receptor protein together form a **hormone-receptor complex.** This hormone-receptor complex generates biochemical changes in the target cells.

Hormones interacting with membrane bound receptors (fixed receptors) do not enter the target cell, but they generate 'second messengers' (e.g. **Cyclic AMP** produced from ATP by the action of the enzyme adenylate cyclase/ Adenylyl cyclase). These ***second messengers*** regulate cellular metabolism in the target cells in a cascading action amplifying the final effect. In this way even a very small quantity of the hormone can cause a series of enzymatic actions, each step having a multiplicating effect, bringing a powerful cascading effect.

We can take an example to understand the action of **hydrophilic** hormone, such as **Epinephrine**, which cannot enter a cell. In the ***liver cells*** **1)** Epinephrine attaches to cell membrane **receptor 2) G protein** of cell membrane binds to **GTP** and activates **adenylate cyclase**, a membrane enzyme **3)** Activated Adenylate cyclase forms **cAMP** from **ATP 4)** cAMP activates **Protein Kinase–A**, which activates the enzyme '**phosphorylase**' **5)** Phosphorylase 'phosphorylates' **Glycogen** to **Glucose-6 -phosphate** and it, in turn produces **glucose**. Thus the liver cell is able to produce several molecules of glucose needed to the cell under the action of **epinephrine** (***one of the fight and flight responses of the body***).

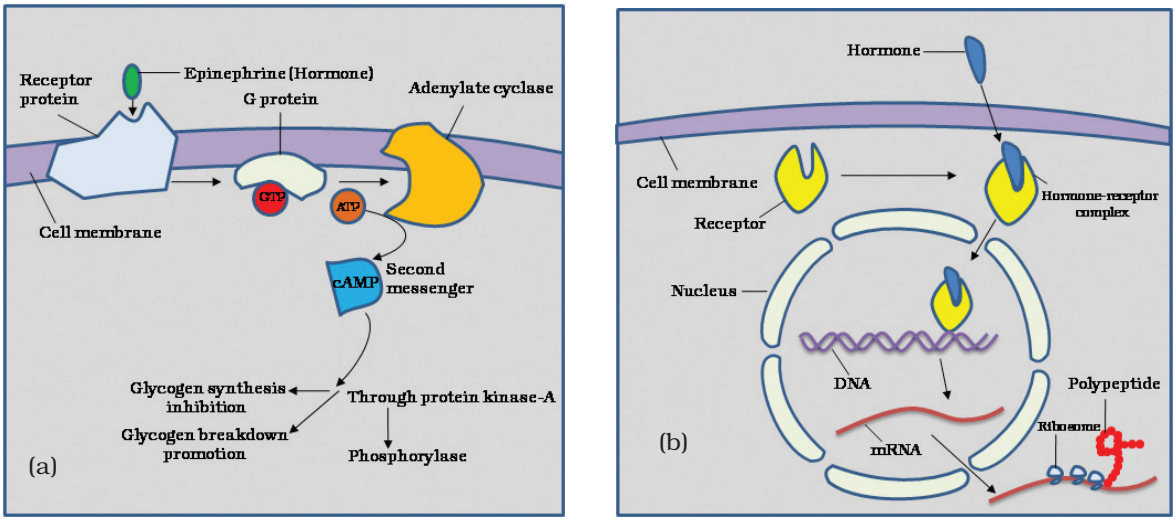


Figure 4.8 Mechanism of hormonal action (a) Membrane bound - receptor mechanism (b) Intracellular receptor mechanism

NOTE: *The cyclic-AMP (cAMP) is a 'signalling molecule'. A single hormone molecule activates hundreds of phosphorylations by causing a series of 'cascading actions' initiating with cAMP.*

Hormones which interact with *intracellular receptors* (e.g. steroid hormones, iodothyronines, etc.) are lipid soluble and they diffuse through the plasma membrane into the cytoplasm. They bind to certain **internal receptors** and the complex enters the nucleus and ***regulates gene expression***. The hormonal

mechanism of steroid hormones is called mobile-receptor mechanism (as the receptors are not fixed in the cell membrane).

***Mechanism of action of lipid soluble hormone**: Aldosterone is a lipid soluble hormone which can easily diffuse through the cell membrane. It binds to a specific receptor in the cytoplasm forming an aldosterone –receptor complex molecule .This complex molecule enters the nucleus and binds to the DNA and stimulates the production of a specific mRNA molecule. The mRNA passes into the cytoplasm and attaches to ribosomes making them produce the specific protein. These proteins are produced by the cell as a response to aldosterone.*

Thus, hormones play a major role in maintaining homeostasis by their integrated actions and feedback control mechanisms.

4.3. Human hormonal disorders due to hypo and hyper secretions

When hormones are secreted in normal quantities, a dynamic effect is exerted in the maintenance of 'homeostasis and regulation of biological processes'. If the production of the hormones is imbalanced by over production or under production, the biological processes are disturbed, and abnormalities occur. Some important disorders caused by hypo or hyper secretion of hormones include dwarfism, gigantism, acromegaly, cretinism, simple goiter, exophthalamic goiter, diabetes (mellitus and insipidus), *Addison's disease*, *Cushing syndrome* etc.

Hypersecretion of growth stimulating hormone (somatotropin), before puberty and completion of ossification, leads to an abnormality called **gigantism**. This is 'over growth' of the skeleton resulting in abnormal height of the person affected. Hypersecretion of this hormone in adults results in an abnormality called **acromegaly.** This disease is characterized by enlargement of the bones of the jaw, hands and feet, thickened nose, lips, eyelids and wide finger tips and 'gorilla like appearance' of the person affected.

Hyposecretion of GH during childhood retards growth, resulting in a '**pituitary dwarf**' / '**midget**'. The pituitary dwarf is sexually and intellectually a normal individual.

Over activity of the thyroid, cancer of the gland or development of nodules of thyroid lead to hyperthyroidism. In adults abnormal growth causes a disease called ***exophthalmic goiter***, with characteristically protruded eyeballs. Hyperthyroidism also affects the physiology of the body (increased metabolic rate). Inadequate supply of iodine in the diet results in hypothyroidism and enlargement of the thyroid gland. This condition is called ***simple goiter.***

During pregnancy, due to hypothyroidism, defective development of the growing baby leads to a disorder called **cretinism**. Physical and mental growth gets severely stunted (***thyroid dwarf***) due to untreated '***congenital hypothyroidism'*** (deficiency of thyroid hormones *by birth).* Stunted growth, mental retardation, low intelligence quotient, deafness and mutism are some of the characteristic features of this disease. In adult women, hypothyroidism may cause irregular menstrual cycles. In adults the hypothyroidism results in a condition called **myxedema**. Lethargy, mental impairment, intolerance to cold, puffiness of face and **dry skin** are some of the symptoms of myxedema.

Over activity of parathyroid gland (***hyper parathyroidism***) causes excess decalcification by promoting the action of osteoclasts leading to bone deformities and fractures. Besides this, calcification (stone formation) in the kidneys takes place. Underactivity of parathyroid gland (hypo-parathyroidism) leads to **tetany** (prolonged contraction of muscles) and the calcium ion levels in the blood decrease (hypocalcemia).

Under secretion of insulin by the pancreatic gland (hypo-secretion) increases the level of glucose in blood (hyperglycemia). Prolonged hyperglycemia leads to a disease called **diabetes mellitus**, associated with loss of glucose through urine (glycosuria) and formation of harmful compounds called 'ketone bodies'. Insulin therapy is used to treat diabetic patients.

Hyper secretion of insulin leads to decreased level of glucose in the blood (hypoglycemia) resulting in **insulin shock**.

Deficiency of **vasopressin** causes a disease called **diabetes insipidus**. It does not involve loss of sugar in urine (a difference from diabetes mellitus) .

Addison's disease is caused due to hyposecretion of glucocorticoids by the adrenal cortex. This disease is characterised by loss of weight, muscle weakness, fatigue and reduced blood pressure. Sometimes darkening of the skin in both exposed and nonexposed parts of the body occurs in this disorder. This disorder does not allow an individual to respond to stress.

Cushing's syndrome: It results due to over production of glucocorticoids. This condition is characterized by breakdown of muscle proteins and redistribution of body fat resulting in spindly arms and legs accompanied by a round **moon face**, **buffalo hump** on the back and **pendulous abdomen**. Wound healing is poor. The elevated level of cortisols causes hyperglycemia, over deposition of glycogen in liver and rapid gain of weight.

GLOSSARY

Acromegaly: An abnormal growth, especially of the bones of the face and extremities associated with the over secretion of the pituitary growth hormone after reaching adulthood. It is also called disproportionate gigantism. It gives a gorilla like appearance to the affected person.

CAMP : Cyclic Adenosine Mono Phosphate. Acts as a second messenger (intracellular messenger) in the case of water soluble hormones.

Catecholamines: A common name given to the hormones namely adrenaline, noradrenaline and dopamine.

Cytogenic organ: An organ which produces cells (gametes).

Diabetes Insipidus: Excessive urination and extreme thirst as a result of inadequate output of the pituitary hormone ADH (anti-diuretic hormone).

Diabetes Mellitus: A condition resulting from lack of insulin as a result of which, the body cannot store or oxidise sugar efficiently (and sugar is lost through urine).

Diuresis: Diuresis is an increase in the production of urine by the kidneys

Erythropoietin: A hormone produced in the kidneys which induces production of RBC (erythrocytes).

Growth Factors: Hormones secreted by non-endocrine tissue, which are essential for normal growth of tissues and their repair.

Hepatocytes: Liver cells.

Infundibulum: A stalk like structure that connects pituitary gland with the hypothalamus.

Melanocytes: Melanin containing cells.

Midget: Pituitary dwarf, a condition caused by hyposecretion of growth hormone in children.

Piloerection: Raising of hair, caused by the secretion of emergency hormones during emergency situations.

Puberty: The age at which the secondary sexual characters appear.

Sella turcica: A cavity of the sphenoid bone in the skull in which the pituitary gland is lodged.

Simple Goiter: A condition in which enlargement of the thyroid gland due to iodine deficiency occurs.

Somatotropic Hormone: The growth hormone secreted by the anterior lobe of the pituitary gland that regulates the growth of the skeleton.

QUESTIONS

Very Short Answer Type Questions

1. What is acromegaly? Name the hormone responsible for this disorder.
2. Which hormone is called anti-diuretic hormone? Write the name of the gland that secretes it.
3. Name the gland that increases in size during childhood and decreases in size during adulthood. What important role does it play in case of infection?
4. Distinguish between diabetes insipidus and diabetes mellitus.
5. What are Islets of Langerhans?
6. What is 'insulin shock'?
7. Which hormone is commonly known as fight and flight hormone?
8. What are androgens? Which cells secrete them?
9. What is erythropoietin? What is its function?

Short Answer Type Questions

1. List out the names of endocrine glands present in human beings and mention the hormones they secrete.
2. Describe the role of hypothalamus as a neuro-endocrine organ.
3. Give an account of the secretions of pituitary gland.
4. Compare a 'pituitary dwarf' and a 'thyroid dwarf' in respect of similarities and dissimilarities they possess.
5. Explain how hypothyroidism and hyperthyroidism can affect the body.
6. Write a note on Addison's disease and Cushing's syndrome.
7. Why does sugar appear in the urine of a diabetic?
8. Describe the male and female sex hormones and their actions.
9. Write a note on the mechanism of action of hormones.

FOR IGNITED MINDS

Hormones - The Biochemical 'Integrators

Endocrine System and Chemical Coordination

1. What is the indirect effect of alcohol on the functioning of the kidneys in man.
2. Why do women after menopause tend to develop osteoporosis.
3. Nerve cells secrete neurotransmitters that act locally stimulating the next neuron's dendrites. However there are certain hormones secreted by neural tissue and act on receptors in certain distant parts in the body. Can you name one such hormone?
4. What is the difference between 'tropic' and 'non-tropic' hormones.
5. Can you name a hormone whose main job is controlling biorhythms.
6. Excepting some parts of the pituitary, is there any other endocrine gland derived from the 'neural tissue' during development?
7. Did you ever observe 'milking' a cow. Why does not milk start flowing out immediately even though the udder is full of milk. What happens most initially when the teats are squeezed?
8. In the good old days physicians (doctors) used to prescribe calcium tablets to people affected by osteoporosis. Nowadays they are prescribing combinations of calcuim and Vit. D or Calcium and calcitriol. Can you explain the reason behind this change.
9. Does increased production of ACTH help a person whose Na, K balance in the body is out of order?

UNIT IV B

Immune System

Edward Jenner

IMMUNE SYSTEM - The "Body Guard" with Powerful "Arsenal"

*Immune system is the **24 hr/7day 'bodyguard' system**. The human body defends itself offering a "**Three Line**" defence. The pattern of defence is either, '**innate**' (present by birth / congenital) or '**acquired**' (after birth). The most external '**First Line of Defence**' of the body is provided by the skin, the largest organ in the body. It chiefly acts as the '**Physical Barrier**' for the invading germs. In addition, it can mount an attack on the germs with the **lysozyme** present in the sweat. The sebum with its low pH also helps in the process of defence. The mucus secreted by the wall of the gut, saliva and tears containing '**lysozyme**' too offer the first line of defence. Epithelial layers in different parts of the body are known to produce **antimicrobial proteins**. Microbes entering the body through inhaled air are caught in the '**mucus**' of the bronchioles and bronchi and the mucus along with the killed microbes is 'swept' out by the ciliature of the lining epithelium. The **phagocytes** (both tissue fixed and the wandering types), NK cells, high temperature, inflammatory response etc., provide the **Second Line of Defence**. High temperature (fever) is body's natural defence to **inhibit rapid multiplication** of the microbes. Phagocytes such as the **macrophages** '**phagocytise**' microbes and digest them. The most, powerful defence is the one provided by the **'T' cells**, **'B' cells** and the **antibodies**. They constitute the **Third Line of Defence.** Thus the immune system is the '**GUARDIAN ANGEL**' acting as the '**BODY GUARD SYSTEM**'.*

Introduction

Every day we are exposed to a large number of infectious agents. However, only a few of them result in diseases- why? It is due to the fact that the body is able to defend itself from most of them. This overall ability of an individual to fight against the disease causing organisms is called immunity. The network of organs, cells and proteins that protect the body from harmful, infectious agents such as bacteria, viruses, animal parasites, fungi etc., is called the **Immune System**. The basic requirement of the immune system is to differentiate between **self** and **non-self** and to protect the body from harmful foreign substances, micro-organisms, toxins and malignant cells etc. The branch of biology that deals with immunity or the study of immune system is called **Immunology**. **Edward Jenner** is acknowledged as the **Father of Immunology**.

4.4 Basic concepts of Immunology

To understand immunology better, we have to know certain basic concepts such as *lines of defence*, *cells*, *organs* and *soluble mediators* of the immune system, *antigens*, *types of immunity*, *mechanism of immunity* and *immunological disorders.*

4.4.1 Lines of Immunity or Lines of defence in the body

Whenever bacteria, viruses, fungi and parasites try to enter the body of an organism, skin, mucous membranes and the enzyme **lysozyme** of saliva, tears, etc., prevent their entry. This is called the **First line of defence**. If the microorganisms cross this line and enter the body, the phagocytes, natural killer cells, antimicrobial substances, inflammation, fever, etc., destroy them. This is called the **Second line of defence**. These two lines of defence are very fast reacting responses but they are not **specific**. If the microbes cross even this line, then the lymphocytes and antibodies fight against them. It is called the **Third line of defence.** It is highly specific but takes several days to become fully functional. If all the three lines of defence fail, it results in diseases.

4.4.2 Cells of the immune system

These are mainly of three types, namely (i) **Lymphocytes**, (ii) **Phagocytes** and (iii) **Auxiliary cells**

4.4.2.1 Lymphocytes

These are the *chief cells* of the *immune system* which are again of three types namely (a) **B-cells**, (b) **T-cells** and (c) **Large granular lymphocytes** (**LGL**s).

Note: Based on the size, lymphocytes can be divided into small lymphocytes and large lymphocytes. Small lymphocytes include B-cells and T-cells, wheres the large lymphocytes include large granular lymphocytes that consist of Natural killer cells (NK-cells)

(a) B-cells (B-Lymphocytes): The lymphocytes capable of producing antibodies and can capture circulating antigens are called **B-cells**. They are produced from the 'stem cells' in the bone marrow of adult mammals, liver of foetus and *bursa of Fabricius* in birds. Mature B-cells synthesize various types of antibodies which are displayed on their membrane surfaces. The **mature B-cells** are also called ***immuno-competent B-cells***. These mature immuno-competent B-cells reach the secondary lymphoid organs and develop into **functional immune cells** which later differentiate into '**long lived**' memory cells and '**effector**' plasma cells. The plasma cells produce antibodies specific to the antigen to which they are exposed. Memory cells store information about the specific antigens and show quick response, when the same type of antigen invades the body later.

(b) T-cells (T-Lymphocytes): The lymphocytes that are not capable of producing antibodies and cannot recognize the free or circulating antigens are known as **T-cells.** They are produced in the bone marrow, reach the **thymus gland** and differentiate into **mature T-cells** or **immuno-competent T-cells**. In the secondary lymphoid organs, they transform into functional T-cells. On exposure to antigens both T_H and T_c cells produce memory cells and effector cells.

Do you know? Though T-cells cannot recognize the free or circulating antigens, they can recognize antigens, if presented by **antigen presenting cells** (**APCs**) or **altered self cells** by MHC molecules. APCs include dendritic cells, macrophages and B lymphocytes.

Types of T cells

On the surface of T-cells, certain glycoprotein molecules called '*cluster of differentiation molecules*' (**CD markers**) are present**.** Based on these glycoprotein molecules, the T-cells are of two types, namely **CD4+ cells** or **T_4** cells and **CD8+ cells** or **T_8** cells. Based on their function, the T cells are of two types, namely *T helper cells* and *T cytotoxic cells.* Monocytes, macrophages and dendritic cells also bear CD4 markers.

i. T helper cells or T_H cells

These are CD4+ cells. They can *recognise* the exogenous **antigens** presented by the **APCs** through MHC class-II proteins. They help the B-cells in producing antibodies, help mononuclear phagocytes (MNPs) in stimulating phagocytosis

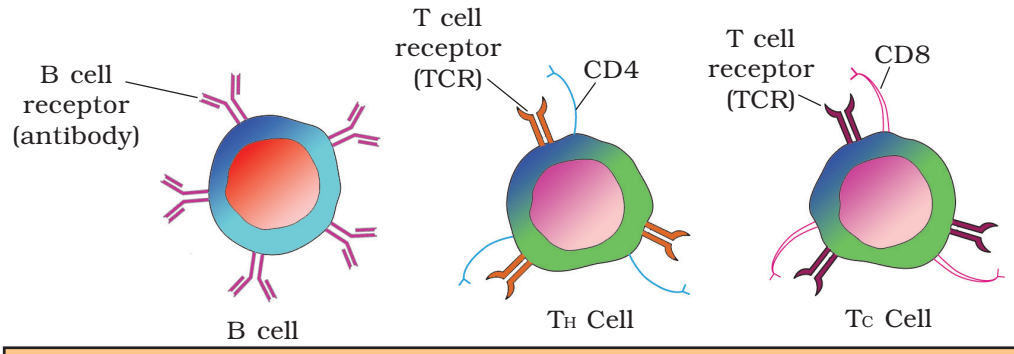


Figure 4.9 Types of Lymphocytes

and also activate T_C cells to initiate 'cell mediated immunity'. Hence they are involved in both humoral immunity and cell mediated immunity. T cells are also involved in the rejection of 'transplanted tissues /organs. T_H cells secrete gamma interferons which stimulate cells such as macrophages. The macrophages, inturn secrete cytokines such as interleukins that stimulate T_H cells. T_H cells are activated only when they are needed. This is ensured by a protein called CD28, which can bind to a protein called B7 present on the APCs.

ii. T_C cells or Killer T cells

These are **$CD8^+$ cells**. They can *recognise* the **antigens** presented by **ASCs** (altered self cells) through MHC class-I protein. As soon as they receive the antigens and stimulation from interleukins, they are differentiated into Cytotoxic T Lymphocytes (**CTLs**) or effector T cells which kill the virus-infected host cells as well as the tumour cells and APCs. Thus, these cells are involved only in cell mediated immunity.

(c) Large Granular Lymphocytes (LGLs) : *Natural killer cells form the body's most important cells of defence and they destroy the infected cells or altered self cells (such as cancer cells) in an* antibody independent manner (non-specific). *The reaction time of NK cells is fast as they are always in an active form to identify and destroy even small cancer cells well before they form a tumour.* (you will learn more in the 'mechanism of cell mediated immunity').

Note: NK cells are a part of the innate immune system and play a major role in defending the host from VIRUS infected cells and tumours (cancer cells).

4.4.2.2 Phagocytes

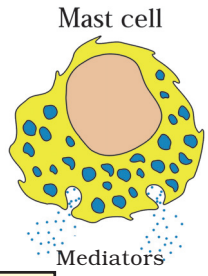
Based on the types of nuclei present, they are of two types, namely (a) Mononuclear phagocytes (**MNPs**) and (b) Polymorphonuclear phagocytes (**PMNs**).

(a) **Mononuclear phagocytes (MNPs):** The monocytes of the blood enter the extra-capillary spaces and transform into **histiocytes** in the **connective tissue**, **Kupffer cells** in the **liver**, **microglia** in the **brain**, **osteoclasts** in the **bone** and **synovial cells** in the **synovial fluid**, etc.

(b) **Polymorphonuclear phagocytes:** *They are the 'granulocytes' of the blood including* ***neutrophils***, ***basophils*** *and* ***eosinophils****. However, in common usage this term is mostly used for neutrophils as they constitute the majority.*

4.4.2.3 Auxiliary cells

The cells that *help lymphocytes* in immune responses are called ***auxiliary cells***. These cells include basophils, mast cells, platelets and antigen presenting cells (APCs). Basophils, mast cells and platelets secrete *inflammatory mediators* which cause inflammation in the surrounding tissues. Antigen presenting cells include macrophages, B-cells and dendritic cells which present the antigens to T_H cells.



Do you know? The cells of the host with the processed antigenic polypeptides on the class-I MHCs are called **altered self-cells.**

4.4.3 Organs of immune system

The organs involved in the origin, maturation and proliferation of lymphocytes are called lymphoid organs. Based on their function, they are of two types, namely (i) Primary lymphoid organs and (ii) Secondary lymphoid organs

(i) **Primary lymphoid organs:** The organs where the lymphoid stem cells become mature lymphocytes *(which are antigen-sensitive)* are called *primary lymphoid organs,* e.g. **Bursa of Fabricius** of birds, bone marrow and thymus gland of mammals

(ii) **Secondary lymphoid organs:** The organs where the mature lymphocytes transform into functional lymphocytes are called the *secondary lymphoid organs*. They provide the sites for interaction of lymphocytes with the antigens, which then proliferate to become effector cells, e.g. spleen, lymph nodes, tonsils, **Peyer's patches** of small intestine, **appendix**, etc.

Spleen: It is a large bean-shaped organ located at the upper-left part of the abdomen under the diaphragm. It mainly contains lymphocytes and phagocytes. It acts as a ***filter of the blood*** by trapping blood-borne micro-organisms. It acts as a large **reservoir** of erythrocytes as well as the **burial ground** or **grave yard** of the old and worn out RBC.

Lymph nodes: These are small solid structures located at different points along the lymphatic system. They trap micro-organisms or other antigens

which are responsible for the activation of lymphocytes present there and cause the immune response.

Do you know? There is a lymphoid tissue located within the lining of the major tracts like respiratory, gastrointestinal and urinogenital tracts, called **mucosa-associated lymphoid tissue** (**MALT**). It constitutes about 50 per cent of the lymphoid tissue in the human body.

4.4.4 Soluble mediators of immunity

They are of three types namely (i) Complement proteins, (ii) Cytokines and (iii) Antibodies

1. **Complement proteins:** These are a group of inactive **plasma proteins** and **cell surface proteins**. When activated, they form a ***membrane attack complex*** (**MAC**) that forms pores in the plasma membrane of the affected cells allowing ECF to enter the cells and make them swell and burst. Some of them form a coat on the surface of the pathogens and attract neutrophils and macrophages to phagocytose and destroy them (**opsonisation**). Complement proteins and their activities are together called **complement system**.
2. **Cytokines:** They are small, soluble molecules secreted mostly by the T_H cells or infected cells. They bind to cell surface receptors and initiate activation or differentiation of the cells of the immune system to stimulate phagocytosis and cytolysis of the infected cells. They are mainly of two types namely **Interleukins** and **Interferons.**

(i) Interleukins (ILs): They are produced by leucocytes and are primarily involved in the differentiation of the cells of the immune system. IL-I reaches the brain (hypothalamus) and causes fever response.

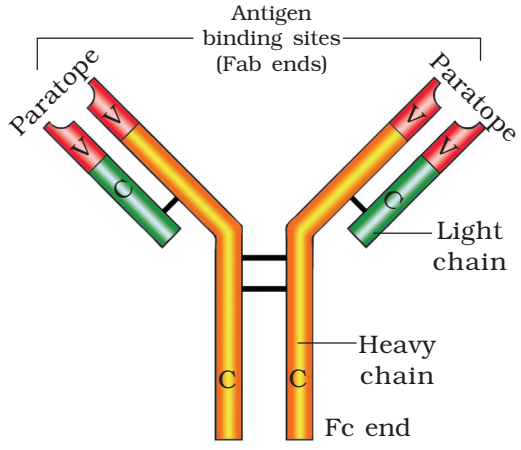


Figure 4.10 Structure of Antibody

(ii) Interferons (IFNs): They are antiviral proteins *produced by virus infected cells* and are involved in protecting the neighbouring cells from the viruses of infected cells. There are of three types, namely **alpha**, **beta** and **gamma** interferons.

3. **Antibodies (Immunoglobulins):** Whenever pathogens enter our body, the B-lymphocytes produce an army of proteins called antibodies to 'fight' with them. They are highly specialized for binding with specific antigens. The part of an antibody that recognizes an antigen is called the **paratope** (antigen binding site). Based on

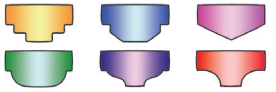
their mobility, antibodies are of two types, namely *circulating* or *free antibodies* and *surface antibodies*. The circulating or free antibodies are present in the body fluids whereas the surface antibodies are present on the surface of the mature B-cells as well as the memory cells.

Structure: The basic structure of an antibody was proposedby **Rodney Porter.** It is a **Y** shaped molecule with four polypeptide chains of which two are long, identical **heavy chains (H)** and two are small, identical light chains **(L)**. Hence, an antibody is represented as $H_2 L_2$. The two chains are linked by disulphide bonds. One end of the antibody molecule is called F_{ab} **end** (***F****ragment-****a****ntigen* ***b****inding*) and the other end is called F_c **end** (***F****ragment-****c****rystallizable or* ***F****ragment-****c****ell binding*). Based on the structure, the antibodies are of five types, namely IgD, IgE, IgG, IgA and IgM.

Do you know? **IgD**, **IgE** and **IgG** are monomeric units, whereas **IgA** is **dimeric** and **IgM** is a pentameric form of antibody.

4.4.5 Antigens

The molecular substances such as *polysaccharides, proteins, lipoproteins, nucleoproteins, nucleic acids, etc.*, that can **induce a detectable immune response** are called antigens. They can be recognized by B-cells or T-cells (if presented by APCs or ASCs). The antigenic site that binds to a paratope of antibody is called the **epitope**. Based on their existence, they are of various types like free or circulatory antigens that freely circulate in the body fluids, intra cellular antigens which are present inside the infected cells and cell surface antigens such as the blood group deciding antigens.



Epitopes of Antigens

Processing and presentation of antigens

Whenever a pathogen is taken in by cells such as macrophages, it gets broken-down by the action of enzymes released from lysosomes. These broken pieces are called **antigenic determinants (epitopes)**. This is called the **processing of antigens**. These antigenic determinants are presented by specialized group of molecules called Major Histocompatibility Complex (**MHC**) molecules (*called human leukocyte antigen system /**HLA system** in human-beings*) which are of two types namely Class-I and Class-II MHCs.

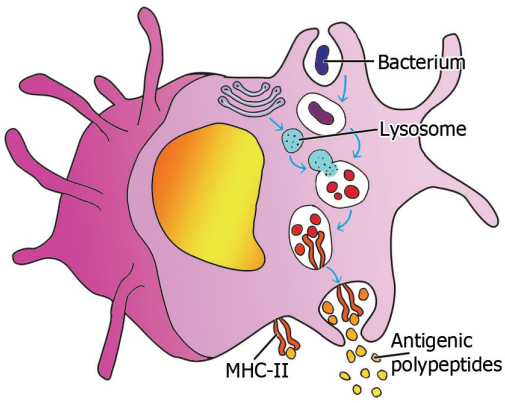


Figure 4.11 Processing of Antigen

Class–I MHC molecules: They are found on the surface of almost all nucleated cells of the body. They present the antigens to **Tc cells** for cell mediated immunity.

Class–II MHC molecules: They are found only on the surface of APCs **(*in addition to Class-I MHC molecules*)**. They present the antigens to T_H cells for cell mediated or humoral immunity.

Do you know? To recognize antigenic polypeptides, T-cells have some receptors called **antigen specific receptors** **(ASR)** on their surface and can recognize the antigenic polypeptides, only if bound to the MHC molecules.

4.5 Types of immunity

4.5.1 Based on the nature of response, immunity is mainly of two types, namely (i) Innate immunity and (ii) Acquired immunity.

1. **Innate Immunity (*Innate – inborn or present at the time of birth*):** The inborn resistance to diseases, possessed by all the living organisms is called **innate immunity**. It is a **non-specific type of defence** and does not depend on prior contact with the micro-organisms. This is executed by providing different types of barriers like:
   - **(a) Physical barriers:** Skin and mucous membranes are the main physical barriers. Skin prevents the entry of micro-organisms whereas the mucus membranes help in trapping and killing the microbes entering our body.
   - **(b) Physiological barriers:** Secretions of the body such as HCl in the stomach, saliva in the mouth, tears from the eyes are the main physiological barriers against microbes.

NOTE: Saliva, tears, sweat contain '**lysozyme**' which can 'digest' the bacterial cell walls. Oil (**sebum**) and sweat of skin have a pH range of 3-5, making the skin (*the largest organ in the body*) an effective inhibitor of microbial growth.

   - **(c) Cellular barriers:** Certain types of cells like polymorpho-nuclear leukocytes (**PMN** - neutrophils), monocytes and natural killer cells in the blood as well as macrophages in the tissues are the main cellular barriers. They phagocytose and/ or destroy the microbes.
   - **(d) Cytokine barriers:** The cytokines such as interferons protect the non-infected cells from infection.
2. **Acquired Immunity** or **Adaptive immunity**

   The immunological resistance developed by an individual throughout the life after the birth is known as **acquired immunity** or **adaptive immunity.** It is pathogen **specific** and depends on prior contact with the infectious micro-organisms. Hence it is characterised by **immunological memory.** It varies from person to person. It is again of two types namely (A) Active acquired immunity and (B) Passive acquired immunity.

(A) Active acquired immunity

The immunological resistance developed by the organisms through the production of antibodies in their body, is called active immunity. It is a lifetime-immunity or long lasting immunity. But it is slow and takes time to show its fully effective response. It is again of two types, namely (a) Natural active acquired immunity and (b) Artificial active acquired immunity

(a) **Natural active immunity:** The resistance developed by an individual in response to natural infection, from which a person recovers is called **natural active acquired immunity**, e.g. the lifetime immunity acquired by an individual after recovering from infections such as smallpox, chickenpox, etc.

(b) **Artificial active immunity:** The immunity developed by an individual due to the inoculation of weakened (attenuated) antigens into the body is called **artificial active acquired immunity**, e.g. immunity that develops due to vaccination e.g., injection of 'tetanus toxoid' to generate immunity aganist tetanus.

(B) Passive acquired immunity

The immunological resistance developed by an organism due to the transfer of ready-made (preformed) antibodies is called **passive acquired immunity**. It is again of two types, namely (a) Natural passive immunity and (b) Artificial passive immunity.

(i) Natural passive immunity: If the preformed antibodies are transferred from mother to child, it is called **natural passive acquired immunity**, e.g. Transfer of antibodies from mother to foetus across the placenta or from mother to child through ***colostrum***.

> **Do you know?** Why is mother's milk considered very essential for the new-born infant? The **colostrum** secreted by the mother during the initial days of lactation has abundant **IgA** antibodies, to protect the infant.

(ii) Artificial passive immunity: If the pre-formed antibodies are transferred from an immunised donor to a non-immunised individual, it is called **artificial passive acquired immunity**, e.g. Injection of anti-tetanus serum (ATS), anti-rabies serum and serum containing antivenin against the venom of a snake, etc. These antibodies are generally produced in the body of an immunised horse or sheep.

4.5.2 Based on the **types of responses evoked**, immunity is of two types, namely (i) Humoral immunity and (ii) Cell mediated immunity

(i) Humoral Immunity (HI): The immunity mediated by the antibodies that are released into the fluids of the body (humors) such as plasma, lymph, etc. is called **humoral immunity.** It is generated due to the interaction of B-cells with free antigens.

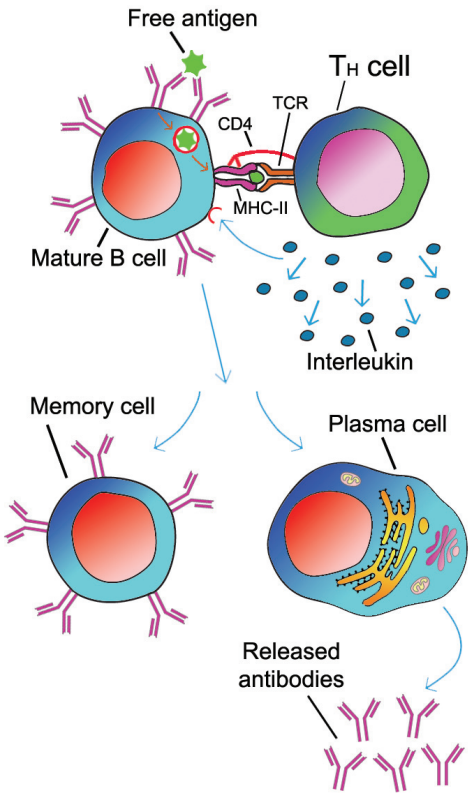


Figure 4.12 Mechanism of humoral immunity

Mechanism of Humoral immunity (HI)

In the secondary lymphoid organs, the free antigens bind to the **F_{ab} end** of the antibodies that are present on the surface of mature B-cells. They engulf and process the antigens. Then they display the antigenic fragments on their membrane with the help of **Class-II MHC** molecules. T_H cells recognise them and interact with the **antigen-MHC-II complex** and release a type of **interleukin,** which stimulates the B-cells to proliferate and differentiate into **memory cells** and **plasma cells**. The **plasma cells** release specific antibodies into the plasma or extra cellular fluids. These antibodies help in **opsonising** and **immobolising** the bacteria, **neutralising** and **cross linking** of antigens leading to **agglutination** of *insoluble* antigens and **precipitation** of *soluble* antigens. They also activate the **phagocytes** and **complement system**.

Do you know? The products of antigen, antibody reactions are called 'antigen- antibody complexes' or immunocomplexes, which are removed by eosinophils and monocytes.

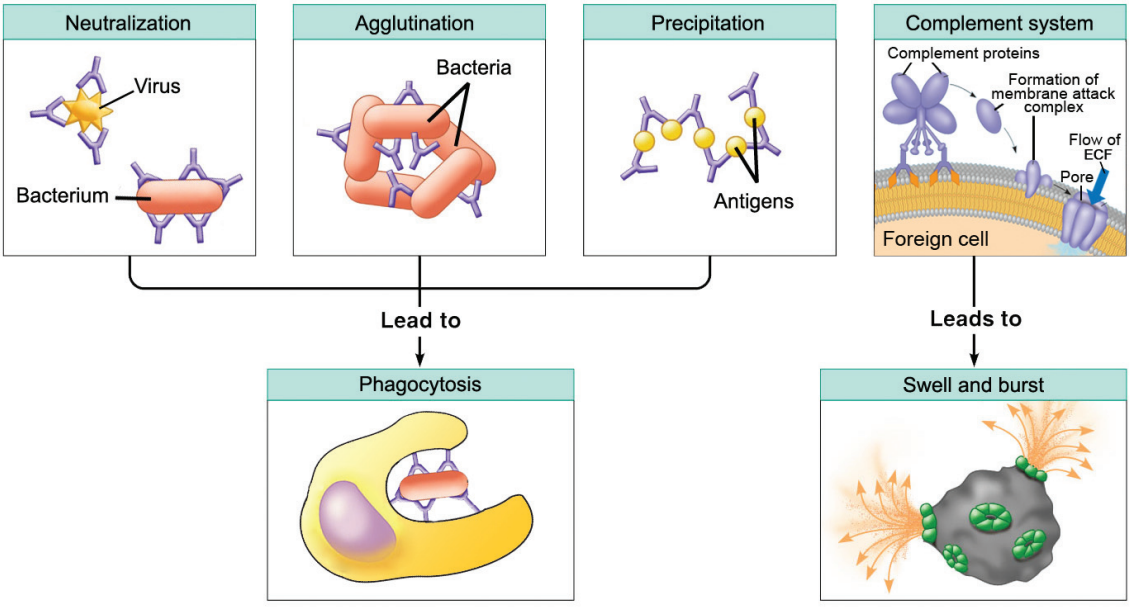


Figure 4.13 Function of Antibodies

(ii) Cell Mediated Immunity (CMI): The immunity mediated by the activated T-cells, natural killer cells, etc., is known as **cell mediated immunity.** It is effective against both exogenous and endogenous antigens. It does not involve production of antibodies.

Mechanism of Cell mediated immunity (CMI)

Antigen presenting cells process the exogenous antigens whereas the altered self-cells process endogenous antigens. Then, the processed antigenic fragments are displayed on their (APCs or ASCs) membranes. They are recognised by T-cells. Binding of T-cells to the APCs or ASCs causes the production of activated T cells and memory T cells. The activated T_H cells secrete various types of interleukins which transform activated Tc cells into effector **Cytotoxic T-Lymphocytes** (CTLs / Killer cells). CTLs attach to the infected cells and release certain enzymes called **perforins** and **granzymes**. Perforins form pores in the cell membrane of the infected cells. Then granzymes enter the infected cells through these perforations and activate certain proteins (e.g. **caspases**) which help in the **destruction of the infected cell (apoptosis)**. The NK cells are similar in their action to CTLs. However NK cells distroy the infected cells in an antibody independent manner where as the CTLs destroy the infected cells in an antibody dependent manner.

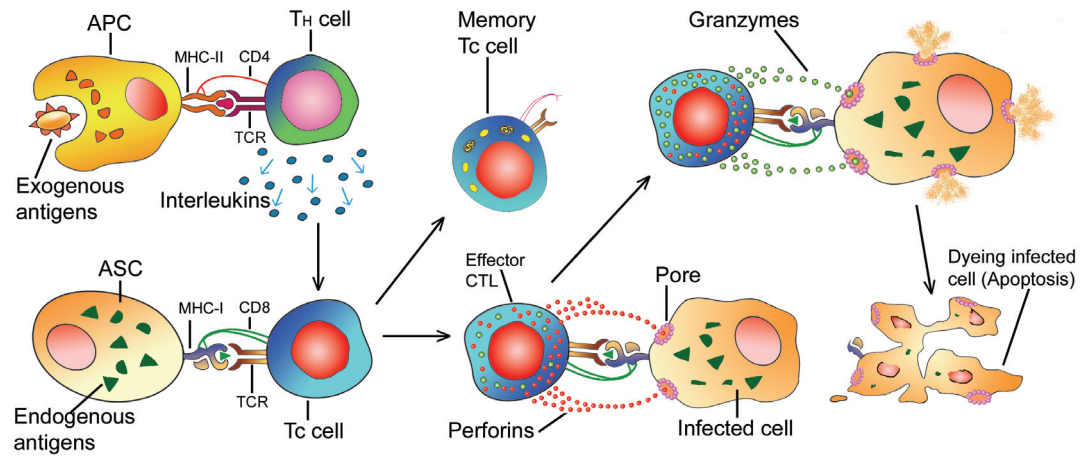


Figure 4.14 Mechanism of cell mediated immunity

Vaccination or Immunization

The principle of vaccination or immunization is based on the property of the **immunological memory** of the immune system. During the process of vaccination, inactivated (killed) or weakened (attenuated) pathogens (vaccines) or antigenic proteins of the pathogen are introduced into the body of the host. They initiate the production of appropriate antibodies in the host and also generate memory–B cells and memory T cells. On subsequent exposures, the memory cells recognise that pathogen quickly and overcome the invader with a rapid and massive production of antibodies.

Do you know? Recombinant DNA Technology has allowed the production of antigenic polypeptides of pathogens in bacteria or yeast. Vaccines can be produced on a large scale using this method, e.g. **Hepatitis-B** vaccine is produced by using genetically modified (recombinant) **yeast**.

Immunological Disorders

Any situation that results in the impairment of immune system is referred to as **immunological disorder.** These are of various types like (a) immunodeficiency disorders, (b) hypersensitivity disorders, (c) auto-immune disorders, (d) graft rejections, etc.

Immunodeficiency disorders

They occur when the immune response of the body is reduced or absent. These are again of two types, namely primary and secondary immunodeficiency disorders. Primary immunodeficiency disorders are caused by the defective genes, e.g. Severe combined immunodeficiency (**SCID**). The secondary immunodeficiency disorders are caused by various factors like infections, ageing, etc., e.g. HIV/AIDS

Do you know? A person positive to HIV is not called AIDS patient until the virus completely destroys the immune system and makes the person susceptible to certain 'opportunistic diseases'.

4.6 Acquired Immuno Deficiency Syndrome (AIDS)

It is a transmissible (mostly sexually transmitted) lethal disease, caused by Human Immunodeficiency Virus **(HIV).** It was first reported in 1981 by CDC (*Centre for Disease Control*), USA and in the last thirty years, it has spread all over the world, killing more than 25 million people.

1. Mode of infection

It generally occurs by sexual contact with an infected person, by transfusion of the virus contaminated blood, by sharing the infected needles and from an infected mother to her child through placenta. It is important to note that HIV/AIDS is not spread by mere touch (physical contact).

2. Structure of HIV

It is a **retrovirus** which has an envelope enclosing two **ssRNA** (single stranded RNA) molecules **as the genetic material** and two molecules of the enzyme **reverse transcriptase**. The ssRNA is surrounded by a protein coat, followed by a layer of proteins which is again surrounded by an **outer lipid layer** that contains a number of **glycoproteins** such as **gp41 and gp120.** These proteins bind to host cell's surface receptors during infection.

3. Mechanism

After getting into the body of a person, the HIV enters the T_H cells, macrophages or dendritic cells. In these cells the ssRNA of HIV synthesizes a DNA strand 'complementary' to the viral RNA, using the enzyme reverse transcriptase. The **reverse transcriptase** also catalyses the formation of the second DNA strand 'complementary' to the first strand forming the **double stranded viral DNA**. This viral DNA gets incorporated into the host cell's DNA by a viral enzyme (**integrase**) and it is now in the form of a '**provirus**'. Transcription of the DNA results in the production of RNA, which can act as the 'genome' for the new viruses or it can be translated into viral proteins. The various components of the viral particles are 'assembled' and the HIV are produced. The infected human cells continue to produce **virus particles** and in this way they act like **HIV generating factories**. New viruses '**bud off**' from the host cell. This leads to a progressive decrease in the number of T_H cells in the body of an infected person leading to the immunodeficiency in him. Even though HIV attacks any cells with CD4 marker, for reasons not known, only **T_H cells** are destroyed and not the 'macrophages'. The gp120 molecules on the surface of HIV attach to CD4 receptors of human cells, mostly the T_H cells (**gp120 fits the CD4 marker**). Attack on certain types of cells/ tissues only by viruses such as HIV is referred to as '**tissue tropism**'.

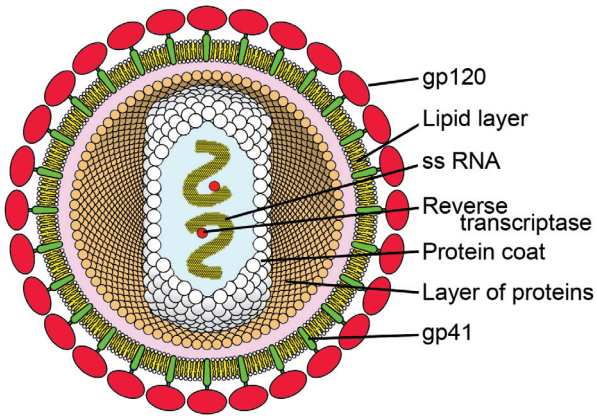


Figure 4.15 Structure of HIV

4. Symptoms

There is always a time-lag between the first infection and appearance of symptoms. This period may vary from a few months to many years (usually 5-10 years) to develop into full blown AIDS. During this period, the person suffers from bouts of fever, diarrhoea and loss of weight. Due to decrease in the number of T_H cells, the person starts suffering from infections due to bacteria (especially *Mycobacterium),* viruses, fungi and other parasites such as *Toxoplasma.* The patients become so immuno-deficient that they are unable to protect themselves against these minor infections, which normal healthy people can easily overcome.

NOTE: The time between the first exposure to HIV and the production of antibodies by the immune system in response to HIV infection is called "**window period**" during which time the presence of virus cannot be detected.

5. Diagnosis

A widely used diagnostic test for detecing HIV infection is the Enzyme Linked Immuno-Sorbent Assay (**ELISA**) test. This can be detected within **15 days** to **4 months** after the exposure to virus. ELISA is only a '***screening test'***. **Western blot** is used as a more reliable confirmation test for HIV infection.

6. Treatment of HIV infection and prophylaxis

Treatment of AIDS with 'anti-retroviral drugs' can only prolong the life of the patient but cannot prevent death. Hence, it is better to follow prophylactic methods to avoid HIV infection.

7. Prophylaxis

Safe sex, proper sterilization of hospital syringes and needles and screening the blood for HIV before transfusion, are some of the important prophylactic methods. In our country the *National AIDS Control Organization* (**NACO**) and other non-governmental organization (NGOs) are doing a lot to educate people about AIDS.

Hypersensitivity disorders (Allergies)

Did this happen to you? You went to a new place and soon you started sneezing, wheezing for no explained reason. When you returned from that place, your symptoms disappeared. What could be the reason?
Reason: Some people are highly sensitive to dust particles, pollen etc., present in the environment. If they avoid allergens, the symptoms subside. The above mentioned reactions could be due to allergic response by the body.

The exaggerated response of the immune system to certain antigens present in the environment is called hypersensitivity. There are different types of hypersensitivity reactions of which Type-I hypersensitivity is referred to as **allergy.** It is due to the release of chemicals such as **histamine** and **serotonin** from the mast cells. The antibodies responsible for allergies are of the group **IgE**. The substances to which allergy is produced are called **allergens**. Common examples of allergens are dust mites, pollen, animal dander, etc. Symptoms include sneezing, watery eyes, running nose and difficulty in breathing.

For determining the cause of allergy, the patient is exposed to or injected with very small doses of possible allergens, and the reactions are studied. The use of drugs like anti-histamine, adrenalin and steroids quickly control the symptoms of allergy.

Did You Notice? More and more children in metro cities of India suffer from allergies leading to **asthmatic attacks** due to environmental pollutants. This could be mostly due exposure to various types of pollutants in the urban atmosphere.

HAVE YOU EVER HEARD OF ANAPHYLAXIS /ANAPHYLACTIC SHOCK: Sometimes hypersensitivity reaction occurs within seconds and **blood pressure falls** to critical low levels, which may even cause death.

Auto-immune disorders

Generally our immune system can recognise our own proteins and does not attack our own tissues. Unfortunately, in some cases our immune system fails to recognise some of our own body proteins and treats them as foreign antigens that results in attacks on our own tissues. This leads to some very serious diseases collectively known as **auto-immune diseases**, e.g. **Graves' disease**, **Rheumatoid arthritis**, myasthenia gravis, Addison's disease etc., which are treated with **immuno suppressants**.

Graft rejections

When some human organs like cornea, heart, liver, kidney, etc., fail to function satisfactorily, transplantation is the only remedy to enable the patient to lead a normal life. Whenever such organs are transplanted, the host body identifies them as foreign and initiates the graft rejection sooner or later. Hence **tissue matching** and **blood group matching** are essential before undertaking any graft or transplant. Even after this, the patient has to take immuno–suppressant drugs throughout their life.

GLOSSARY

Barrier: Anything that obstructs free movement

Bursa of Fabricius: A lymphoid organ in birds that is connected to the cloaca and is the site of B cell maturation

Colostrum: It is the first milk containing **IgA** antibodies, produced by mother after child birth

Congenital disease: A disease or disorder that is inherited genetically (by birth)

Cytolysis: Destruction of cell

Dander: Small scales from animal skins, hair or feathers of a bird, that can cause allergic reactions in some people

Dendritic cells: Immune cells forming a part of the mammalian immune system. Their main function is to process an antigen /pathogen and present it to the T_H cells. They show branched-extensions which look like the dendrites of neurons. They are present in tissues in contact with the external environment, such as the skin, inner lining of the nose, lungs, stomach and intestines.

Immunological memory: When our body encounters a pathogen for the first time it produces a response called primary response which is of low intensity. Subsequent encounter with the same pathogen causes a highly intensified secondary or anamnestic (renewed) response. This is due to the fact that our body appears to have memory of the first encounter.

Immunosuppressants: Medication which decreases the immune response especially in the case of tissue transplants.

Inflammation: A protective response brought about by the mast cells and other immunological cells, in an organism to initiate the healing process. It is characterised by pain, burning sensation, redness and swelling

Inoculation: Introduction of attenuated pathogens (vaccine) to develop immunity, as a precaution against contacting a disease

Lymphoid stem cells: The undifferentiated cells which give rise to lymphocytes

Malignant cells: Tumour-cells capable of invading and growing in other tissues and organs of the body and cause secondaries of cancer (metastasis)

Opsonisation: The process by which bacteria and other cells are altered so as to be more efficiently engulfed by phagocytes; a process whereby opsonins make an invading microorganism more susceptible to phagocytosis.

Peyer's patches: Oval elevated patches of closely packed lymphoid follicles in mucous and sub-mucous layers of the small intestine.

Phagocytose: The action of engulfing by phagocytes

Provirus: A virus genome that is integrated into the DNA of a host cell

Syndrome: A group of symptoms

Tonsils: The masses of lymphatic tissue present one on either side of the oropharynx

Wheezing: A whistling sound during breathing due to a respiratory disorder

QUESTIONS

Very Short Answer Type Questions

1) Define the terms immunity and immune system.
2) Define the non-specific lines of defence in the body.
3) Differentiate between mature B-cells and functional B-cells.
4) Write the names of any four mononuclear phagocytes.
5) What are complement proteins?
6) "Colostrum is very much essential for the new born infants". Justify.
7) Differentiate between perforins and granzymes.
8) What are interferons?
9) What is meant by paratope?
10) Which substances form membrane attack complex?

Short Answer Type Questions

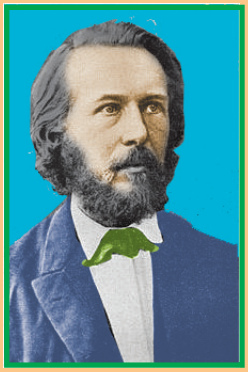
1) Write short notes on B-cells.
2) Write short notes on immunoglobulins.
3) Describe various types of barriers of innate immunity.
4) Explain the mechanism by which HIV multiplies and leads to AIDS.
5) What are various types of immunity?

FOR IGNITED MINDS

The 'Body Guard' with Powerful 'Arsenal'

Immune System

1. HIV infection cannot be controlled by vaccinations as they are yet to be developed. In the case of poliomyelitis, another viral disease, vaccinations or oral drops of polio vaccine are successful. What is the reason for such a difference?
2. With reference to infection to attack by germs - is skin a physical barrier or physiological barrier or both. How do you justify your opinion?
3. In the history of evolution of the medical science, who first observed that pre exposure to a disease/ disease causing organism, prevented subsequent infections (atleast in the near future)?
4. Certain T cells directly attack 'non-self cells' or 'altered self cells'. What type of immunity is it called? What is the name of such cells?
5. All nucleated cells possess MHC Class-I proteins. In what type of cells do you find MHC class- II proteins?
6. Which two types of 'cells' in our body exhibit almost the same immune mechanism, with reference to destruction of altered/foreign cells.
7. In case of rejection of a transplant (cell/tissue), what are the cells that are primarily involved in the mediation of 'transplant rejection'?
8. Of the activated B cells, T_H cells and T_C Cells, which cells produce, memory cells.
9. With reference to showing immune response to a certain pathogen, it is 15 days in a certain case (hypothetically). However a person showed immune response on exposure to the said pathogen in one week or even less time. What could be the reason?
10. Why do almost all infections result in 'fever'? What is the reason/significance people 'sneeze', 'cough' and have a 'running nose' when infected by certain pathogens or allergens?



Ernst Haeckel

Unit-V

HUMAN REPRODUCTION

Asexual reproduction is the process adopted by many lower organisms, which have a high degree of regenerative capacity, sometimes helping in that process. Sexual reproduction creates another organism(s) showing variation from the parent. ***Variations*** *are raw materials for evolution, and* ***Natural Selection*** *operates on them. Formation of gametes taking part in sexual reproduction involves* ***meiosis****, the reduction division, making them haploid. During meiosis there is some degree of exchange of chromatids between the chromosomes of the paternal set and maternal set. This phenomenon is called* ***cross over*** *and it leads to novelty in the DNA which is important for evolution to occur. Among the sexually reproducing organisms* ***viviparity*** *is of a higher degree of evolution, where the mother supplies nourishment and oxygen through placenta. Sexual cycles in animals are controlled by hormones whose production is sometimes linked to favourable season, for the young ones to survive, grow and reproduce (****genetic continuity****). The wealth of a Nation is the health of its people. As many people are under educated, at least regarding* ***reproductive health****, it is necessary to educate adolescents on reproductive health, sexually transmitted diseases, necessity of a planned family, misconceptions regarding sex etc. You will discover more on human reproductive system, puberty, secondary sexual features, gametogenisis, fertilisation, implantation of embryo, gestation and post natal care along with reproductive health etc. in this chapter.*

UNIT V A

Human Reproductive System

Human reproduction is a form of sexual reproduction resulting in the conception of a child, typically involving sexual intercourse between a man and a woman. The reproductive events in humans include formation of gametes (**gametogenesis**), i.e. sperms in males and ova in females, transfer of sperms into the female genital tract (**insemination**) and fusion of male and female gametes (**fertilisation**) leading to the formation of zygote. This is followed by the formation and development of blastocyst and its attachment to the uterine wall (**implantation**), embryonic development (**gestation**) and delivery of the baby (**parturition**). All these reproductive events occur after puberty (sexual maturity; the first occurrence of maturation in girls). There are remarkable differences between the reproductive events in a male and a female. Let us examine the male and female reproductive systems in humans.

5.1 The Male Reproductive System

The **male reproductive system** (male genital system) consists of a number of sex organs that are a part of the human reproductive process. The sex organs which are located in the pelvic region include a pair of **testes** (sing: *testis*) along with accessory ducts, glands and the external genitalia.

1. Testes

The testes (**testicles**) are a pair of oval pinkish male primary sex organs suspended outside the abdominal cavity within a pouch called **scrotum**. The scrotum helps in maintaining the low temperature of the testes (2-2.5^0 C lower than the normal internal body temperature) necessary for spermatogenesis. The cavity of the scrotal sac is connected to the abdominal cavity through the **inguinal canal**. Testis is held in position in the scrotum by the **gubernaculum**, a fibrous cord that connects the testis with the bottom of the scrotum. A **spermatic cord**, formed by the vas deferens, nerves, blood vessels and other tissues runs from the abdominal wall, down to each testicle, through the inguinal canal. Each testis is enclosed in a fibrous envelope, the **tunica albuginea**, which extends inward to form septa that partition the testis into lobules. There are about 250 testicular lobules in each testis. Each lobule contains 1 to 3 highly coiled

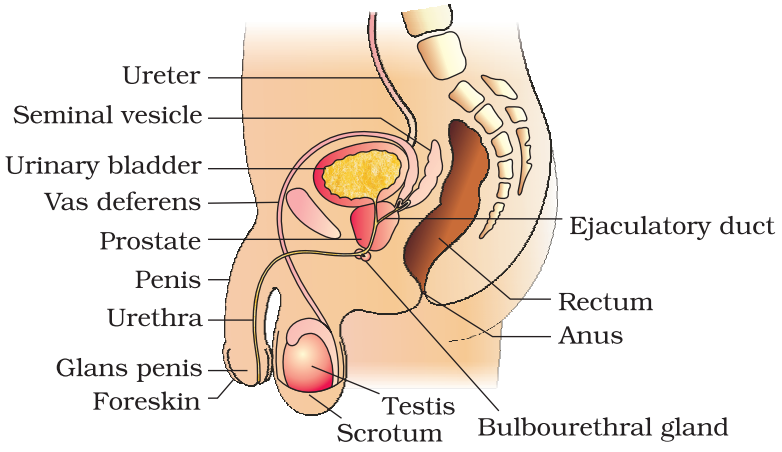


Figure 5.1(a) Diagrammatic sectional view of male pelvis showing reproductive system

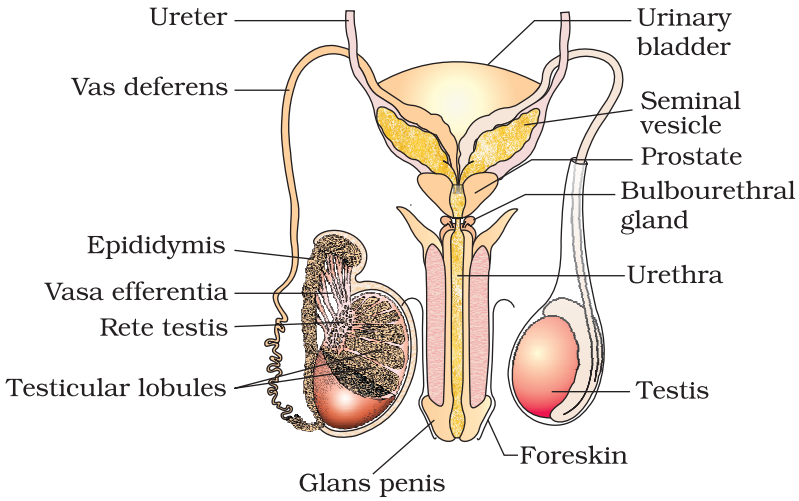


Figure 5.1(b) Diagrammatic view of male reproductive system

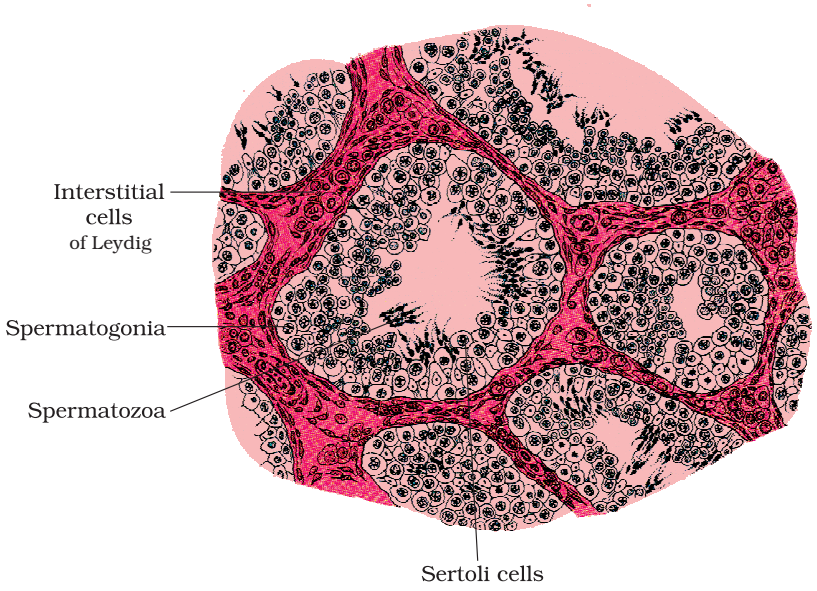


Figure 5.2 Diagrammatic sectional view of seminiferous tubule

seminiferous tubules. A pouch of serous membrane (peritoneal layer) called **tunica vaginalis** covers the testis.

Each seminiferous tubule is lined by the **germinal epithelium** which consists of undifferentiated male germ cells called **spermatogonial mother cells** and it also bears 'nourishing cells' called **Sertoli cells**. The spermatogonia produce the **primary spermatocytes** which undergo meiotic division, leading to the formation of spermatids which form spermatozoa or sperms (spermatogenesis). Sertoli cells provide nutrition to the spermatozoa and also produce a hormone called inhibin, which inhibits the secretion of FSH. The regions outside the seminiferous tubules, called interstitial spaces, contain **interstitial cells of Leydig** or **Leydig cells**. Leydig cells produce androgens, the most important of which is **testosterone.** Testosterone controls the development of secondary sexual characters and spermatogenesis. Other immunologically competent cells are also present. The seminiferous tubules open into the **vasa efferentia** through the **rete testis** (a network of tubules in the testis, carrying spermatozoa from the seminiferous tubules to the vasa efferentia).

NOTE: *The testes descend into the scrotum just before birth. The condition in which the testes do not descend into the scrotum is called cryptorchidism*

2. Epididymis

The vasa efferentia leave the testis and open into a narrow, tightly coiled tube called epididymis located along the posterior surface of each testis. The epididymis provides a storage space for the sperms and gives the sperms time to mature. It is differentiated into three regions – **caput epididymis**, **corpus epididymis** and **cauda epididymis**. The caput epididymis receives spermatozoa via the vasa efferentia of the **mediastinum testis** (a mass of connective tissue at the back of the testis that encloses the rete testis).

3. Vasa deferentia

The **vas deferens** or **ductus deferens** is a long, narrow, muscular tube. The mucosa of the ductus deferens consists of pseudostratified columnar epithelium and lamina propria (areolar connective tissue). It starts from the tail of the epididymis, passes through the inguinal canal into the abdomen and loops over the urinary bladder. It receives a duct from the seminal vesicle. The vas deferens and the duct of the seminal vesicle unite to form a short **ejaculatory duct/ductus ejaculatorius**. The two ejaculatory ducts, carrying spermatozoa and the fluid secreted by the seminal vesicles, converge in the centre of the prostate and open into the **urethra**, which transports the sperms to outside.

Passage Of Spermatozoa:
Seminiferous tubules → Rete testis → Vasa efferentia → Epididymis → Vas deferens → Ejaculatory duct → Urethra → Vagina of the female

4. Urethra

In males, the **urethra** is the shared (common) terminal duct of the reproductive and urinary systems. The urethra originates from the neck of the urinary bladder and extends through the penis to its external opening called **urethral meatus**. The urethra provides an exit for urine and semen during ejaculation, in males

5. Penis

The penis and the scrotum constitute the male external genitalia. The penis serves as a urinal duct and also intromittent organ that transfers spermatozoa to the vagina of a female. The human penis is made up of three columns of tissue; two upper **corpora cavernosa** on the dorsal aspect and one **corpus spongiosum** on the ventral side. Skin and a subcutaneous layer enclose all three columns. The corpora cavernosa consist of special tissue with spaces that are filled with blood. They help in erection of the penis to facilitate insemination. The enlarged and bulbous end of penis called **glans penis** is covered by a loose fold of skin (**foreskin**) called **prepuce**. The urethra traverses the corpus spongiosum, and its opening called urethral meatus lies at the tip of the glans penis.

6. Male accessory genital glands

The male accessory glands include paired **seminal vesicles, a prostate gland** and **bulbourethral glands**.

i. Seminal vesicles

The seminal vesicles are a pair of simple tubular glands present postero-inferior to the urinary bladder in the pelvis. Each seminal vesicle opens into the corresponding vas deferens, where the vas deferens enters the prostate gland. The secretion of the seminal vesicles constitute about 60 percent of the volume of **seminal fluid**. It is an alkaline, viscous fluid that contains fructose, proteins, citric acid, inorganic phosphorus, potassium, and prostaglandins. Once this fluid joins the sperm in the ejaculatory duct, fructose acts as the main energy source for the sperm outside the body. **Prostaglandins** are believed to aid fertilization by causing the mucous lining of the cervix to be more receptive to sperm as well as by aiding the movement of the sperm towards the ovum with peristaltic contractions of the uterus and fallopian tubes, after coitus.

ii. Prostate gland

Prostate gland is located directly beneath the urinary bladder. The gland surrounds the **prostatic urethra**, and sends its secretions through several prostatic ducts. In man, the prostate contributes 15–30 percent of the semen. The fluid from the prostate is clear and slightly acidic. The prostatic secretion 'activates' the spermatozoa and provides nutrition.

iii. Bulbourethral Glands

Bulbourethral glands, also called **Cowper's glands**, are located beneath the prostate gland at the beginning of the internal portion of the penis. They add an alkaline fluid to semen during the process of ejaculation. The fluid secreted by these glands lubricates the urethra. It is also thought to function as a 'flushing agent' that washes out the acidic urinary residues that may remain in the urethra, before the semen is ejaculated.

5.2 The Female Reproductive System

The female reproductive system consists of a pair of **ovaries** along with a pair of **oviducts, uterus, vagina** and the **external genitalia** located in the pelvic region. These parts of the system along with a pair of the **mammary glands** are integrated structurally and functionally to support the processes of ovulation, fertilization, pregnancy, birth and child care.

1. Ovaries

Ovaries are the primary female sex organs that produce the female gametes (**ova**) and several steroid hormones (ovarian hormones). A pair of ovaries is located one on each side of the lower abdomen. The double layered fold of peritoneum connecting the ovary with the wall of the abdominal cavity is known as the **mesovarium**.

The ovaries are covered on the outside by a layer of simple cuboidal epithelium called **germinal (ovarian) epithelium**. This is actually the visceral peritoneum that envelops the ovaries. Underneath this layer there is a dense connective tissue capsule, the **tunica albuginea**. The ovarian **stroma** is distinctly divided into an outer **cortex** and an inner **medulla**. The cortex appears more dense and granular due to the presence of numerous **ovarian follicles** in various stages of development. The medulla is a loose connective tissue with abundant blood vessels, lymphatic vessels, and nerve fibers. Each follicle is formed by the infolding of the germinal epithelium.

2. Fallopian tubes (Oviducts)

Each fallopian tube extends from the periphery of each ovary to the uterus, and it bears a funnel shaped **infundibulum**. The edges of the infundibulum possess finger like projections called **fimbriae**, which help in collection of the ovum after 'ovulation'. The infundibulum leads to a wider part of the oviduct called **ampulla**. The last part of the oviduct, **isthmus** has a narrow lumen and it joins the uterus. Fallopian tube (Ampulla-isthmus junction) is the site of fertilization. It conducts the ovum or zygote towards the uterus by peristalsis. The fallopian tube is attached to the abdominal wall by a peritoneal fold called **mesosalpinx**.

3. Uterus

The uterus is single and it is also called **womb**. It is a large, muscular, highly vascular and inverted pear shaped structure present in the pelvis between the bladder and the rectum. The uterus is connected to the abdominal wall by the peritoneal fold called **mesometrium**.

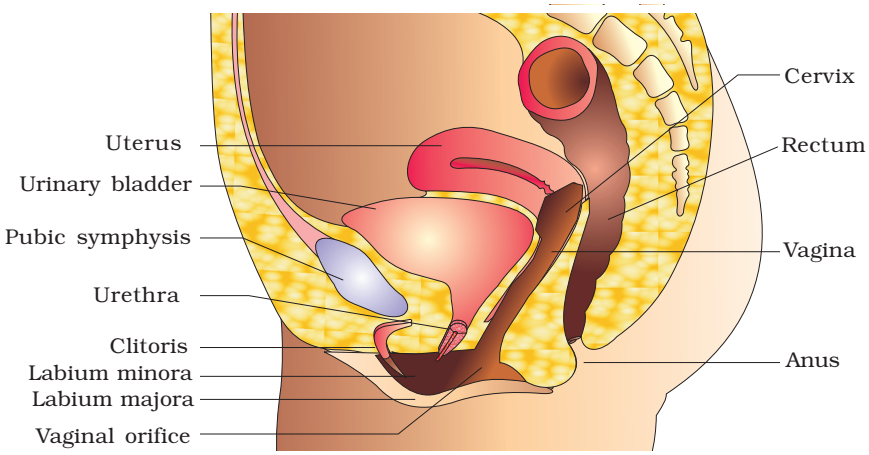


Figure 5.3(a) Diagrammatic sectional view of female pelvis showing reproductive system

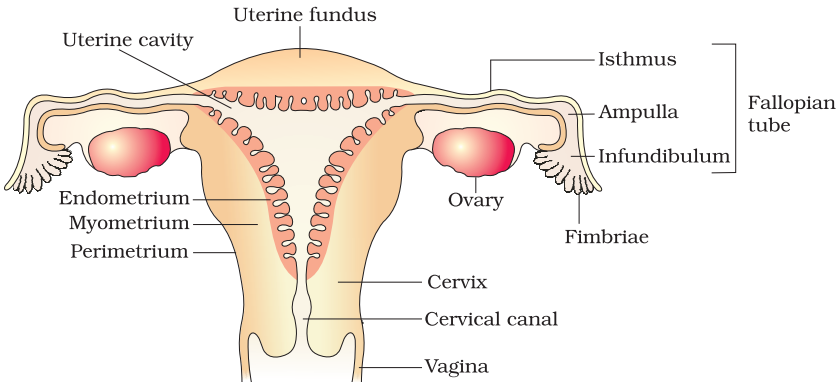


Figure 5.3(b) Diagrammatic sectional view of the female reproductive system

The lower, narrow part through which the uterus opens into the vagina is called the **cervix**. The cavity of the cervix is called **cervical canal** which along with vagina forms the **birth canal**.

The wall of the uterus has three layers of tissue. The external thin membranous **perimetrium**, the middle thick layer of smooth muscle called **myometrium** and inner glandular lining layer called **endometrium**. The endometrium undergoes cyclic changes during menstrual cycle while the myometrium exhibits strong contractions during parturition.

4. Vagina

The vagina is a large, median, fibro-muscular tube that extends from the cervix to the **vestibule** (the space between the labia minora). It is lined by non-keratinised stratified squamous epithelium. It is highly vascular, and opens into the vestibule by the **vaginal orifice**.

5. Vulva

The term vulva (vulva=to wrap around) or **pudendum** refers to the external genitals of the female. The vestibule has two apertures- the upper external **urethral orifice** of the urethra and the lower **vaginal orifice** of vagina. Vaginal orifice is often covered partially by a membrane called hymen which is a mucous membrane. Vestibule is bound by two pairs of fleshy folds of tissue called **labia minora** (inner) and larger pair called **labia majora** (outer). **Clitoris** is a sensitive, erectile structure, which lies at the upper junction of the two labia minora above the urethral opening. The clitoris is homologous to the penis of a male as both are supported by **corpora cavernosa** internally. There is a cushion of fatty tissue covered by skin and pubic hair present above the labia majora. It is known as **mons pubis**.

NOTE: *The hymen is often torn during the first coitus (intercourse). However, it can also be broken by a sudden fall or jolt, insertion of a vaginal tampon, active participation in some sports like horseback riding, cycling, etc.*

6. Accessory reproductive glands of female

These glands include **Bartholin's glands**, **Skene's glands** and **mammary glands**.

i. Bartholin's glands

The Bartholin's glands (**Greater vestibular glands**) are two glands located slightly posterior and to the left and right of the opening of the vagina. They secrete mucus to lubricate the vagina and are homologous to the bulbourethral glands of the male reproductive system.

ii. Skene's glands

The Skene's glands (**Lesser vestibular glands**) are located on the anterior wall of the vagina, around the lower end of the urethra. They secrete a lubricating fluid when stimulated. The Skene's glands are homologous to the prostate gland, of the male reproductive system.

iii. Mammary glands

A functional mammary gland is characteristic of all female mammals. The mammary glands are paired structures (**breasts**) that contain glandular tissue and variable amount of fat. The glandular tissue of each breast is divided into 15-20 **mammary lobes** containing clusters of cells called **alveoli**. The cells of the alveoli secrete milk, which is stored in the cavities (lumens) of the alveoli. The alveoli open into mammary tubules. The tubules of each lobe join to form a **mammary duct**. Several mammary ducts join to form a wider **mammary ampulla** which is connected to **lactiferous duct** in the 'nipple' through which milk is sucked out by the baby.

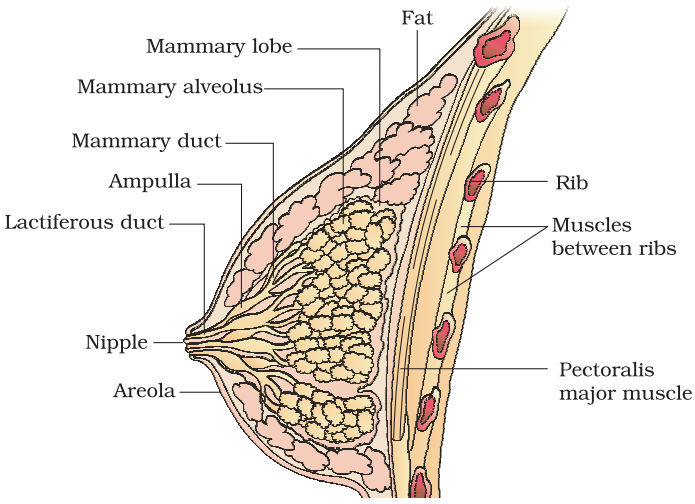


Figure 5.4 A diagrammatic sectional view of Mammary gland

5.3 Gametogenesis

Gametogenesis is the process of formation of gametes i.e. sperms and ova from the primary sex organs – the testes and ovaries respectively. Gametogenesis in a male is called **spermatogenesis** and that in a female is called **oogenesis**.

5.3.1 Spermatogenesis

In the testis, the immature male germ cells, **spermatogonia** produce sperms by **spermatogenesis** that begins at puberty. The **spermatogonial stem cells** (present in the seminiferous tubules) multiply by mitotic divisions and increase in numbers. Each spermatogonial stem cell is diploid and contains 46 chromosomes. Some of the spermatogonial stem cells develop into **primary spermatocytes** which undergo meiosis periodically. A primary spermatocyte completes the first meiotic division (Meiosis-I) leading to formation of two equal sized, haploid cells called **secondary spermatocytes**, which have only 23 chromosomes each. The secondary spermatocytes undergo the second meiotic division (Meiosis-II) to produce four equal sized haploid **spermatids**. The spermatids are transformed into **spermatozoa** (sperms) by the process called **spermiogenesis**. After spermiogenesis, sperm heads become embedded in the Sertoli cells, and are finally released from the seminiferous tubules by the process called **spermiation**.

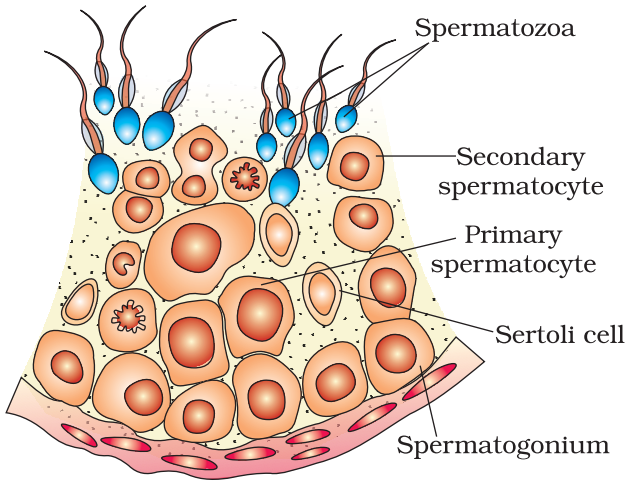


Figure 5.5 Diagrammatic sectional view of a seminiferous tubule (enlarged)

Spermatogenesis starts at the age of puberty due to significant increase in the secretion of **gonadotropin releasing hormone** (GnRH) which is a hypothalamic hormone. The increased levels of GnRH then acts on the adenohypophysis of pituitary gland and stimulates secretion of two types of gonadotropins – **luteinising hormone** (LH) and **follicle stimulating hormone** (FSH). LH acts on the Leydig cells and stimulates secretion of androgens. Androgens, in turn, stimulate the process of spermatogenesis. FSH acts on the Sertoli cells and stimulates secretion of some factors which help in the process of spermiogenesis.

5.3.1.1 Structure of a mature spermatozoon

The spermatozoon is a microscopic structure composed of **head, neck, middle piece** and a **tail**. A plasma membrane envelops the whole body of spermatozoon. The head of a spermatozoon contains an elongated haploid nucleus. The head is covered by a cap-like structure, the **acrosome**. The acrosome contains numerous enzymes (proteases, acid phosphatase, hyaluronidase etc.) that help fertilisation of the ovum (penetration into the

ovum). The middle piece possesses numerous **mitochondria** which produce energy for the movement of the tail. Sperm motility is essential for fertilization. A human male ejaculates about 200 to 300 million sperms during coitus. At least 60 percent sperms must have normal shape and size and at least 40 percent of them must show vigorous motility, for normal fertility.

Sperms released from the seminiferous tubules, are transported by the accessory ducts. Secretions of epididymis, vas deferens, seminal vesicle and prostate are essential for maturation and motility of sperms. The **seminal plasma** along with the **sperms** constitutes the **semen**. The functions of male sex accessory ducts and glands are maintained by the testicular hormones (androgens).

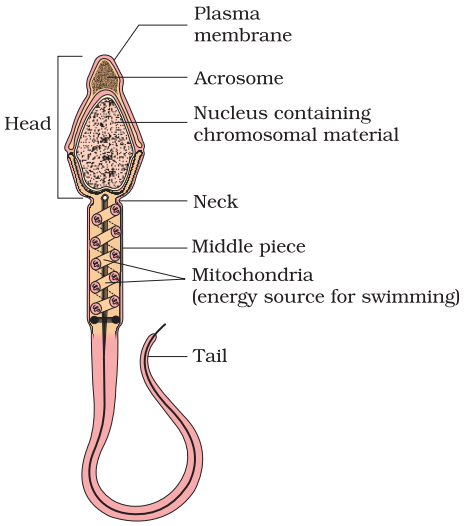


Figure 5.6 Structure of a sperm

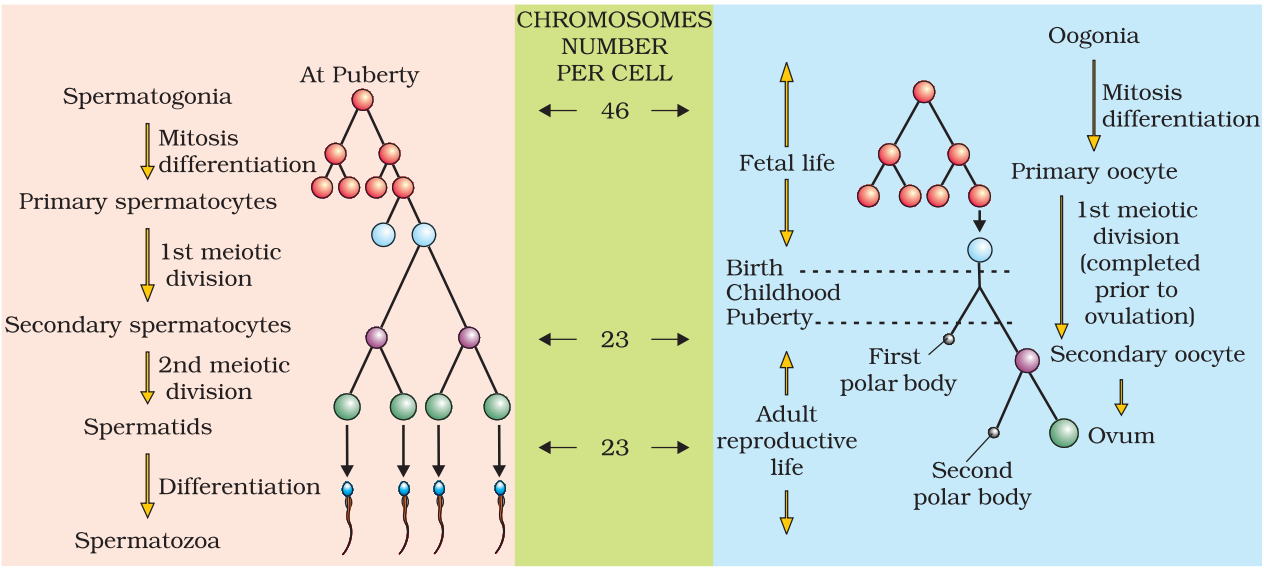


Figure 5.8 Schematic representation of (a) Spermatogenesis; (b) Oogenesis

5.3.2 Oogenesis

The process of formation of a mature female gamete is called **oogenesis**. Oogenesis is initiated during the embryonic development stage when a couple of million **gamete mother cells (oogonia)** are formed within each foetal ovary and do not multiply thereafter. These cells start division and stop the process at **prophase-I** of the **meiosis-I**. At this stage these are called **primary oocytes**.

5.3.2.1 Formation of ovarian follicles

Each primary oocyte then gets surrounded by flattened layer of follicular (squamous) cells. It is called the **primordial follicle**. A large number of these follicles degenerate during the period from birth to puberty. Therefore, at puberty only 60,000-80,000 follicles are left in each ovary. Later the flattened follicular cells become cuboidal and proliferate to produce a stratified epithelium which constitutes the **membrana granulosa**. The cells are called **granulosa cells**. Follicles at this stage of development are called **primary follicles**. A homogenous membrane, the **zona pellucida**, appears between the primary oocyte and granulosa cells. Zona pellucida is a membrane derived from the ovum. The innermost layer of granulosa cells are firmly attached to zona pellucida forming the **corona radiata**.

A cavity (**antrum**) appears within the membrana granulosa. The follicular cavity increases in size. As a result, the wall of the follicle becomes relatively thin. The oocyte now lies eccentrically in the follicle surrounded by some granulosa cells. It is called **cumulus oophorus**. As the follicle expands the stromal cells surrounding the membrana granulosa become condensed to form a covering called the **theca interna**. Outside the theca interna some fibrous tissue becomes condensed to form another covering called **theca externa**. Now these follicles are called **secondary follicles**. The cells of theca interna later secrete a hormone called **oestrogen**. At this stage, the primary oocyte within the secondary follicle grows in size and completes **Meiosis I**. It is an unequal division resulting in the formation of a large haploid **secondary oocyte** and a tiny **first polar body** (haploid).The secondary oocyte retains bulk of the cytoplasm (nutrient rich) of the primary oocyte. Then the second meiotic division begins, but stops at the metaphase-II. The secondary follicle further changes into the mature follicle called **Tertiary follicle** or **Graafian follicle**.

5.3.2.2 Ovulation

The release of ovum (**secondary oocyte**) from the ovary is called **ovulation**. The Graafian follicle is at first very small compared to the thickness of the cortex of the ovary. As it enlarges, it becomes so big that it reaches the surface of the ovary, and forms a bulging. Ultimately, the follicle ruptures releasing the ovum.

5.3.2.3 Structure of ovum

The ovum that is shed from the ovary is not fully mature (it is arrested in the metaphase-II of the maturation division-Meiosis-II). It is surrounded by the **zona pellucida**. Between the cell membrane (**vitelline membrane**) and the

zona pellucida, a distinct space called **perivitelline space** is seen. In it lies the first polar body, which separates from the ovum during the first meiotic division.

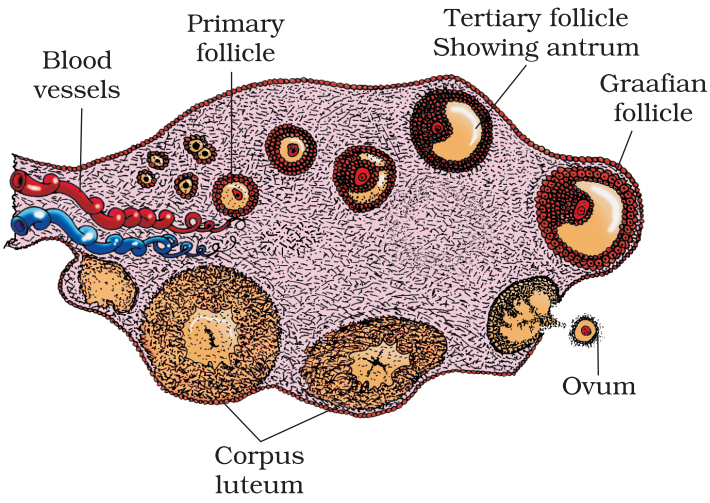


Figure 5.7 Diagrammatic Sectional view of ovary

5.3.2.4 *Corpus luteum*

After ovulation the granulosa cells in the follicle proliferate and are transformed into a yellowish glandular mass called **corpus luteum** (yellow body). If the ovum is not fertilised, the corpus luteum persists for about 14 days. During this period it secretes **progesterone** and at the end of its functional life, it degenerates and forms a mass of fibrous tissue called the **corpus albicans** (white body).

If the ovum is fertilized leading to pregnancy, the corpus luteum persists for three to four months. Now it is called **corpus luteum of pregnancy**. The progesterone secreted by it is essential for the maintenance of pregnancy in the first few months. After the fourth month, the corpus luteum is no longer needed, as the placenta begins to secrete progesterone. The series of changes that begin with the formation of an ovarian follicle and end with the degeneration of the corpus luteum constitute what is called an **ovarian cycle**.

5.3.2.5 *Reproductive period*

In an individual the formation of gametes takes place only during the reproductive period which begins at the age of puberty (10 to 14 years). In women it ends between 45 and 50 years with the onset of menopause and in men it extends much longer.

5.4 Menstrual Cycle

The reproductive cycle in the female primates (e.g. monkeys, apes and human beings) is called **menstrual cycle**. The term menstrual cycle is applied to cyclical changes that occur in the endometrium every month (mensem: month). The first menstruation begins at puberty and is called **menarche**. In human females, menstruation is repeated at an average interval of about 28/29 days. One ovum is released (**ovulation**) during the middle of each menstrual

cycle. The major events of the menstrual cycle are Menstrual phase, Follicular phase, Ovulatory phase and Luteal phase.

Menstrual phase

The cycle starts with the menstrual phase (**menstruation** or **menses**), when menstrual flow occurs and it lasts for 3-5 days. The **menstrual flow** results due to breakdown of endometrial lining of the uterus and its blood vessels which forms a fluid that comes out through the vagina. Menstruation occurs only if the released ovum is not fertilised. Absence of menstruation may be indicative of pregnancy. However, it may also be caused due to some other underlying causes like stress, poor health etc.

Follicular phase

During this phase, the primary follicles in the ovary grow to become a fully mature Graafian follicles and simultaneously the endometrium of the uterus regenerates through proliferation. These changes in the ovary and the uterus are induced by changes in the levels of pituitary and ovarian hormones. The secretion of **gonadotropins (LH** and **FSH)** increases towards the end of the follicular phase, and stimulates follicular development as well as secretion of estrogens by the growing follicles.

Ovulatory phase

Both LH and FSH attain a peak level in the middle of cycle (about 14th day). Rapid secretion of LH leading to its maximum level during the mid-cycle is called **LH surge**. It induces rupture of Graafian follicle and thereby the release of ovum, the secondary oocyte (**ovulation**).

Luteal phase

During luteal phase the remaining parts of the Graafian follicle transform into the corpus luteum. The corpus luteum secretes large amounts of **progesterone** which is essential for maintenance of the uterine endometrium. Such an endometrium is necessary for **implantation** of the 'blastocyst' stage and other events of pregnancy. During pregnancy all events of the menstrual cycle stop and there is no menstruation. In the absence of fertilization, the corpus luteum degenerates into a whitish body called **corpus albicans**. This causes disintegration of the endometrium leading to menstruation.

In human beings, menstrual cycles cease around 50 years of age and it is referred to as **menopause (natural cessation of menstrual cycles)**. Cyclic

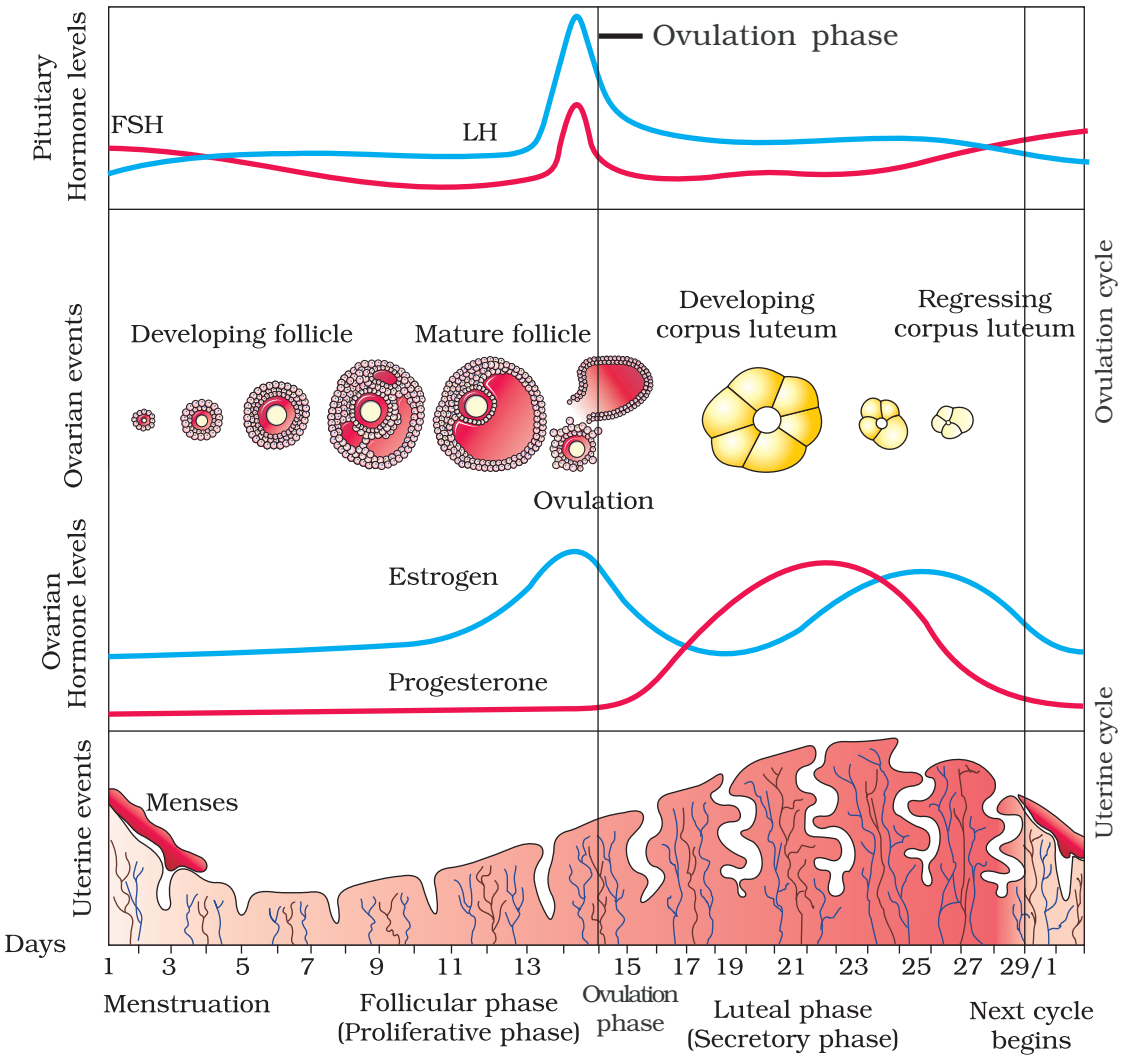


Figure 5.9 Diagrammatic presentation of various events during a menstrual cycle

menstruation is an indicator of normal reproductive phase and extends between the menarche and the menopause.

Copulation

During **copulation** (coitus) semen is ejaculated through the penis into the vagina (**insemination**). Spermatozoa acquire the ability to fertilize the ovum only after they undergo some changes in the female genital tract. These changes are called **capacitation**. The changes in the properties of the zona pellucida after the entry of a sperm constitute the **zona reaction**.

NOTE: *Sperm capacitation refers to the physiological changes that the spermatozoa must undergo in order to be able to penetrate and fertilize an egg. Changes take place in the membranes over the acrosome and enable release of lysosomal enzymes. This is called acrosome reaction. The acrosomal vesicle at the tip of the head fuses with the plasma membrane of the egg, releasing enzymes from the tip of the sperm.*

5.5 Fertilisation and Development

The motile sperms swim rapidly, pass through the cervix, enter the uterus and finally reach **ampullary-isthmic junction** of the fallopian tube. The ovum released by the ovary is also transported to the fallopian tube where fertilisation (also called **conception** in humans) takes place.

The oocyte-cumulus complex of the female is surrounded by a zona pellucida, corona radiata, and cumulus layer. When a motile sperm reaches the ovum, it makes its way through the corona radiata and zona pellucida. In this process, the enzyme **hyaluronidase** released by the acrosome of a sperm (it is a corona penetrating enzyme) plays an important role in dissolving the **hyaluronic acid** in the ground substance of the follicle cells. The enzyme **acrosin** released from the acrosome as an effect of **acrosome reaction**, dissolves/digests the zona pellucida (lysis of the zona pellucida to facilitate penetration of the sperm). Though several sperms penetrate through the zona pellucida into the perivitelline space, only one sperm enters the ovum (**monospermy**). This induces the completion of the **meiosis-II** of the secondary oocyte (ovum). The second meiotic division is also unequal and results in the formation of a **second polar body** and an **ovum** (**ootid**). The fusion of gametes is called **syngamy** or **amphimixis**. The nuclear union results in the formation of **synkaryon (zygotic nucleus)**. Corona radiata disappears after fertilisation. The entry of sperm causes release of calcium which blocks the entry of other sperms. A parallel reaction is the 'zonal reaction'.

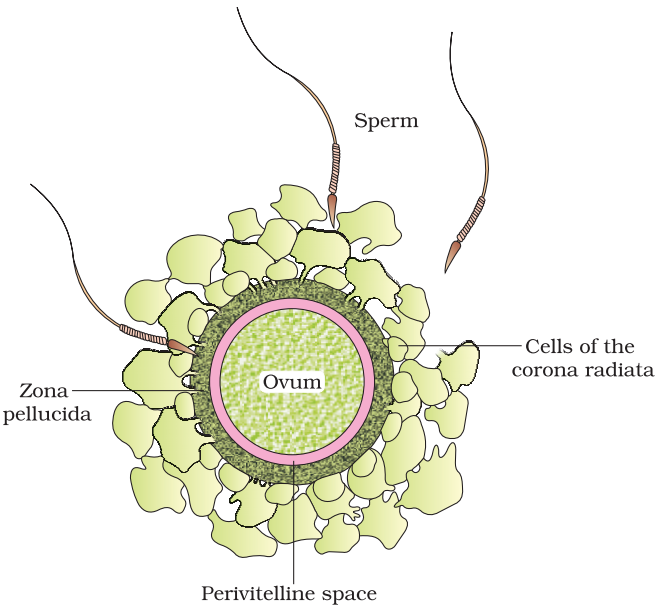


Figure 5.10 Ovum surrounded by some sperms

NOTE: *One has to remember that the sex of the baby has been decided at the time of fertilization itself. Let us see how? As you know the chromosome pattern in the human female is XX and that in the male is XY. Therefore, all the haploid gametes produced by the female (ova) have the sex chromosome X, whereas the male gametes (sperms) have either X chromosome or Y chromosome (**50 percent of sperms carry the X chromosome while the other 50 percent carry the Y chromosome**). After fusion of the male and female gametes the zygote would carry either XX or XY depending on what type of sperm fertilised the ovum. The zygote carrying 'XX' would develop into a female child and that with 'XY' would form a male child. So, the sex of a child depends on the male parent (heterogametic parent).*

5.6 Develpment

5.6.1 Cleavage

Human embryology is the study of human development during the first eight weeks after fertilization. From the beginning of the 9th week, the developing young one is called ***foetus***. The type of cleavage is **holoblastic**, because of the ***microlecithal*** condition of egg, and **indeterminate**. The first division(cleavage) occurs at about **36** hours after fertilization. The blastomeres are equal in size.

5.6.2 Morula

When the number of daughter cells is 16-32, the ***solid ball of cells*** is called ***morula*** as it looks like a 'mulberry'. At this stage the cells start to bind firmly together and this process is called ***compaction*** (the cells of the morula become bound tightly together and the outer surface of blastomeres 'flatten' against each other). This tightly packed arrangement is stabilized by '***tight junctions***' that form between the outer cells of the morula. The cells within the sphere form '***gap junctions***', which help in better passage of substances between them. The tiny embryo is still surrounded by the glyco-proteinous layer of the egg, the ***zona pellucida***. At the completion of ***cleavage/ blastulation***, the embryo has a central cavity called 'blastocoel'. Now the embryo has a superficial flat cell layer and an '**inner cell mass**'. *The cells on the exterior of this early embryo develop into the **trophoblast*** or ***trophectoderm*** (the outer epithelium of the blastocyst). The ***blastocyst*** is formed while the early embryo passes through the fallopian tube.

5.6.3 Blastocyst

Some fluid is secreted into this cavity. As the quantity of the fluid increases, the embryo acquires the shape of a 'cyst', hence the name 'blastocyst'. The process of formation of a space around the formative cells is called '**cavitation**'.

The 'inner cell mass / '**formative cells**', which give rise to the 'embryo proper' and some fetal membranes and so these cells constitute the '**embryoblast**'. They are the source of all the *pluripotent* '***embryonic stem cell lines***' . In addition to the embryo proper the inner cell mass gives rise to the ***extra-embryonic membranes*** also.

5.6.4 Implantation

The blastocyst 'hatches' out/comes out of the envelope, the zona pellucida, by lysing its wall with the help of the enzyme called ***strypsin.*** Later the cells of the zona pellucida gradually disappear. The cells of the trophoblast stick to the uterine *endometrium* and form a part of the '***foetal part***' of the '***placenta***' later. The trophoblast invades the endometrium of the uterus. In humans, the process of implantation begins on the 6th day after fertilisation. The process of implantation is aided by ***proteolytic enzymes*** produced by the cells of the trophoblast.The trophoblast thickens through cell division and the wall of the trophoblast develops villi ('***trophoblastic villi***') that branch and project into the highly vascular uterine endometrium, to draw 'nourishment' for the embryo. The trophoblast differentiates into an *inner cellular layer* called '***cyto-trophoblast***' (*cellular trophoblast*) or '***layer of Langhans'*** consisting of *cuboidal epithelial cells* , and *outer* '***syncytio-trophoblast***' (a layer of *fused cells).* The embryo along with its membranes is called ***conceptus.***

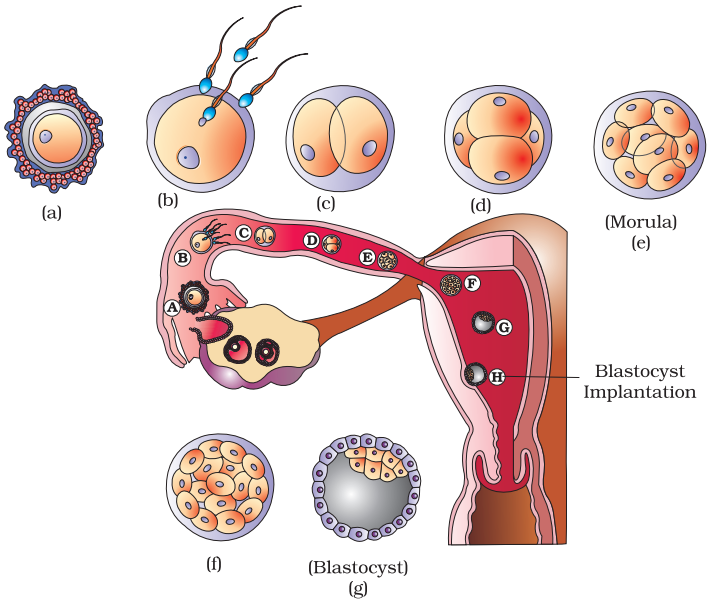


Figure 5.11 Transport of ovum, fertilization and passage of growing embryo through fallopian tube

Formation of Bilaminar Embryonic Disc

Implantation of the blastocyst is completed by the end of the *second week*. The inner cell mass forms into a 'disc' called **embryonic disc** or **germinal disc**. The embryonic disc has an outer group of cells called the '**EPIBLAST**' (primitive ectoderm) and inner layer of cells ,the '**HYPOBLAST**' (primitive endoderm *made up of cuboidal cells*).The hypoblast lines surface

facing the blastocyst cavity. It is the **future extra embryonic endoderm**.The hypoblast is pushed down(*delamination*) and it forms the lining of the 'yolk sac'(exocoelomic cavity). The remaining part of the embryonic disc is called the **epiblast** (*primitive ectoderm made up of columnar cells*). Now the embryonic disc is called **bilaminar embryonic disc**. Further development involves 'gastrulation'.

Gastrulation

Gastrulation is an important 'dynamic process' in the development of the early embryo, which involves movement of cell masses to their definitive positions in the embryo and form their three primary germinal layers. These movements are called ***morphogenetic movements***.

Along the longitudinal axis of the embryonic disc, a **primitive streak** is formed. Formation of the primitive streak marks the beginning of gastrulation. A longitudinal furrow known as **primitive groove** forms along the middle of the primitive streak. On either side of it are the **primitive folds**. Anteriorly the primitive streak has a shallow ***primitive pit***. The region in front of the primitive streak becomes thickened. This thickened part of the streak is called the **primitive knot** or **primitive node** or ***Hensen's node.*** The primitive streak and Hensen's node provide places / avenues for the migration / ingression of the future mesodermal and chorda-mesodermal cells to their respective places for further differentiation. This process of migration of cells is called 'gastrulation'. The process of gastrulation transforms the two-layered embryo into a three-layered embryo.

Trilaminar Embryo - Formation of Primary Germ Layers

Ingression of the future endodermal cells from the epiblast, replaces the hypoblast and forms the **endoderm** of the embryo. The future mesodermal cells converge towards the primitive folds, move through the primitive groove and reach between epiblast and endoderm. The remaining epiblast now constitutes the **ectoderm**. Thus the three germinal layers namely ***ectoderm, mesoderm*** and ***endoderm*** are all derived from the undifferentiated cells of the **epiblast**.Thus the **bilaminar embryonic disc** is transformed into a **trilaminar embryonic disc**.

5.6.2 Formation of the Notochord and Neural Tube

The chorda mesodermal cells present in the epiblast of the embryo converge and involute through the Hensen's node and extend 'forwards' as **notochordal process / notochordal rudiment**. This is later transformed

into a solid rod – the **notochord**, the ***embryonic axial skeleton*** which is replaced by the 'vertebral column'. The notochordal mesoderm induces the '*overlying ectodermal cells*' to form the **neural plate**. This is a good example of **induction** where one tissue induces the formation of another. The neural plate *invaginates* towards the notochord to form a **neural groove**, which deepens progressively to form a tube by the fusion of the lateral neural folds. The process of formation of **neural tube** is referred to as '**neurulation**' .

Differentiation of Mesoderm and Formation of Coelom

The **intra embryonic mesoderm** spreads in all directions between the outer ectoderm and inner endoderm. The longitudinal column of mesoderm adjacent to the notochord and neural tube on either side is called **epimere** (paraxial mesoderm). The mesoderm around the gut is the **hypomere** (lateral plate mesoderm). The mesoderm in between these two is the **mesomere** (intermediate mesoderm). The epimere become s segmented into cubical blocks called **somites** or **metameres**. Each somite differentiates into **sclerotome, myotome,** and **dermatome**. The sclerotome forms the vertebral column. The myotome forms the voluntary muscles of the body. The dermatome forms the dermis of the skin and other connective tissues. The mesomere forms the urinogenital organs and their ducts. The hypomere splits into outer **somatic** and inner **splanchnic mesodermal layers**. **Intra embryonic coelom** is formed between these two layers. It gives rise to pericardial, pleural, peritoneal cavities etc.

Extraembryonic Membranes

Development of the foetal /extra-embryonic membranes helps protect the embryo from desiccation, mechanical shock, absorption of nutrients, exchange of gases etc. The epiblast adjacent to the trophoblast 'migrates' away from the 'trophoblast' forming the amniotic cavity. (NOTE: The formation of amnion and chorion in human embryos is different from that in the other amniotes). The lining of the amniotic cavity is made up of cells called '***amnioblasts***', derived from the 'epiblast'. The amnion is filled with 'water' (amniotic fluid). The ***hypoblast*** is pushed 'down' forming the lining of a cavity called ***yolk sac***. The chorion consists of an outer layer formed by the primitive ectoderm or *trophoblast*, and an inner by the *somatic mesoderm* / *extraembryonic mesoderm* from which the chorionic cavity is formed. The chorion undergoes rapid proliferation of cells and forms *chorionic villi*. The chorionic villi invade the endometrium and help in the transfer of nutrients and oxygen from maternal blood to fetal blood. The chorion surrounds the embryo and other membranes. Soon, a *fourth* membrane called ***allantois*** develops as an outgrowth from the 'embryonic hindgut'

(***splanchnopleure*** consisting of outer mesodermal layer and inner endoderm). The membrane of the allantois meets the inner surface of the chorion and forms a highly vascularised region called ***allanto-chorion***.The allanto–chorion contributes the 'foetal part' of the placenta.The placenta facilitates a more effective and efficient part for exchange / passage of nutrients , respiratory gases ,hormones ,antibodies etc. between the foetus and mother by the 12th week of pregnancy.

Organogenesis: During organogenesis, regions of the three embryonic germ layers develop into the rudiments of organs.

5.7 Formation of Placenta

The ***placenta*** consists of two essential portions: a **maternal part of the placenta** derived from the endometrium of the uterus, and **foetal membranes of the foetal part** of the placenta. The maternal components of the placenta are : Uterine epithelium, Uterine connective tissue and Uterine capillary endothelium. The foetal components of the placenta are foetal capillary endothelium, foetal connective tissue and foetal chorionic epithelium. The inner region of the chorionic villi develops a network of capillaries of the umbilical artery and umbilical vein. These vessels run in the tough *umbilical cord* .The placenta of humans is called **chorioallantoic placenta** as allantois also fuses with the chorion in the process of vascularisation. Placenta is described as **haemochorial** as the maternal blood comes into direct contact with the membrane of the foetal chorionic villi.

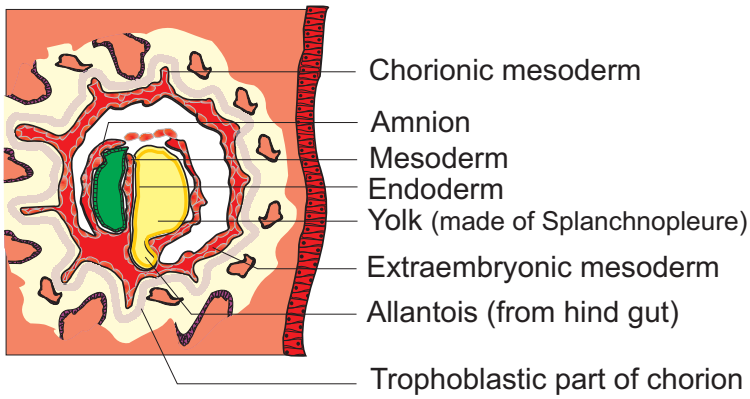


Figure 5.12 Formation of Placenta

Functions of Placenta

The placenta facilitates the supply of oxygen and nutrients to the embryo and also removal of carbon dioxide and excretory/waste materials produced by the embryo. The placenta is connected to the embryo through an **umbilical cord** which helps in the transport of substances to and from the embryo.

Progesterone secreted by the placenta is essential for the maintenance of pregnancy after the 4th month (when the corpus luteum degenerates).

Oestrogens (mainly estradiol) produced by the placenta reach maternal blood and promote uterine growth and development of the mammary glands. **Human chorionic gonadotropin** (**hCG**) produced by the placenta is similar in its actions to luteinizing hormone.Human chorionic gonadotropin sends the ***message of pregnancy*** to the Master Endocrine System so that **LH** is secreted to maintain corpus luteum and prevent menstruation and further ovulation. Gonadotropins are excreted through maternal urine where their presence in urine is used as a test to ***detect pregnancy*** in its early stages. **Somatomammotropin,** also called '***placental lactogen***' has an 'anti-insulin effect' on the mother leading to increased plasma levels of glucose and amino acids in the maternal circulation. In this way it increases the availability of these materials to the foetus. The placenta protects the foetus from the relatively high blood pressure of the maternal circulation .The foetal tissue having paternal chromosomal effect, acts as foreign structure(***antigenic allograft***) to the mother who produces antibodies. The foetus sustains such a rejection for about 38-40 weeks by producing certain ***immunosuppressant*** substances .

5.8 Pregnancy

Pregnancy is the intra uterine development of the embryo or foetus (also called **gestation period**), in a woman's uterus. Human pregnancy averages 266 days (38 weeks) from fertilization of the egg, or 40 weeks from the start of the last menstrual cycle.

Timetable of some events during pregnancy

Human gestation can be divided for convenience into **three trimesters** of about three months each. The first trimester is the main period of **organogenesis**, the development of the body organs. In human beings, after one month of pregnancy, the embryo's heart is formed. The first sign of growing foetus may be noticed by listening to the heart sounds carefully using a stethoscope. By the end of the second month of pregnancy, the foetus develops limbs and digits. By the end of 12 weeks (**first trimester**), most of the major organ systems are formed, for example, the limbs and external genital organs are well-developed. The first movements of the foetus and appearance of hair on the head are usually observed during the fifth

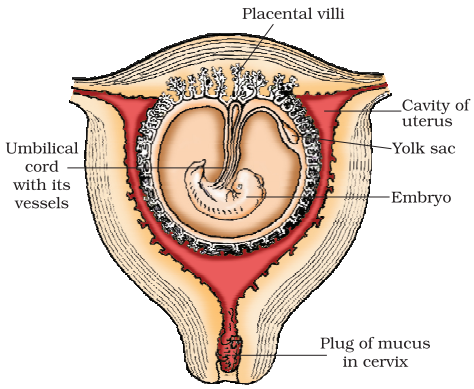


Figure 5.13 The human foetus within the uterus

month. By the end of 24 weeks (**second trimester**), the body is covered with fine hair, eye-lids separate, and eyelashes are formed. By the end of nine months of pregnancy (**third trimester**), the foetus is fully developed and is ready for delivery.

5.9 Parturition

Childbirth begins with **labor**, a series of strong, rhythmic uterine contractions that push the fetus and placenta out of the body. This process of delivery of the foetus (childbirth) is called **parturition**. Parturition is induced by a complex ***neuroendocrine mechanism***. The signals for parturition originate from the 'fully developed foetus' and the 'placenta', which induce mild uterine contractions called **foetal ejection reflex.** This triggers release of **oxytocin** from the maternal pituitary. Oxytocin acts on the uterine muscle and causes stronger uterine contractions, which in turn stimulate further secretion of oxytocin. The stimulatory reflex between the uterine contractions and oxytocin secretion continues resulting in increasingly stronger contractions. This leads to expulsion of the baby out of the uterus through the birth canal. Soon after the infant is delivered, the placenta along with decidua is also expelled out of the uterus.

5.10 Lactation

One aspect of post-natal care unique to mammals is **lactation**, the production of mother's milk. In response to suckling by the newborn, as well as changes in estradiol levels after birth, the hypothalamus signals the anterior pituitary to secrete prolactin, which stimulates the mammary glands to produce milk. The **mammary glands** of the female undergo differentiation during pregnancy and starts producing milk towards the end of pregnancy (**lactation**). This helps the mother in feeding the newborn. The milk produced during the initial few days of lactation is called **colostrum**, which contains several antibodies (***especially Ig-A)*** absolutely essential to protect the new-born babies from initial sources of infections. **Breast-feeding** during the initial period of infant growth is recommended by doctors for bringing up a healthy baby.

GLOSSARY

Androgens: Androgens are the generic term for any natural or synthetic compound, usually a steroid hormone, that stimulates or controls the development and maintenance of male characteristics in vertebrates.

Decidua: After the implantation of the embryo, the uterine endometrium is differentiated into a spongy, vascular layer called **decidua**. The portion of the decidua where the placenta is to be formed (i.e. inner to the developing blastocyst lying between the *blastocycst* and uterine *myometrium*) is called the **decidua basalis.** The part of the decidua that separates the embryo from the uterine lumen is called the **decidua capsularis**. The part lining the rest of the uterine cavity is called the **decidua parietalis /deciduas vera**. At the end of pregnancy the decidua is shed off, along with the placenta and membranes.

Foetus: It is a developing mammal or other viviparous vertebrate after the embryonic stage and before birth.

Formative cells : the embryonic cells which are capable of producing new cells or tissue.

Intromittent organ: An intromittent organ is a general term for an external organ of a male organism that is specialized to deliver sperm during copulation (the male copulatory organ of an animal).

Involution: The inward growth and curling inward of a group of cells (prospective mesodermal cells), as in the formation of a gastrula from a blastula.

Oogonium: A primordial oocyte during fetal development; it is derived from a primordial germ cell and before birth becomes a primary oocyte; The primitive egg mother cell from which the oocytes develop.

Polar body: One of the small cells produced during the two meiotic divisions in the maturation of a female gamete, or ovum. Polar bodies are nonfunctional and incapable of being fertilized.

Somatopleure: A complex sheet of embryonic cells formed by association of part of the mesoderm with the ectoderm. It continues as the amnion and chorion external to the embryo.

Splanchnopleure: Greek *splanchno* = the viscera; *pleur* = the side, a layer of tissue in the early developing embryo, formed by the union of extra embryonic endoderm and splanchnic mesoderm. It gives rise to the embryonic gut and the visceral organs and continues externally to the embryo as the yolk sac and allantois.

Umbilical cord: In placental mammals, the umbilical cord (birth cord or funiculus umbilicalis) is the connecting cord from the developing embryo or foetus to the placenta.

QUESTIONS

Very Short Answer Type Questions

1. Where are the testes located in man? Name the protective coverings of each testis.
2. Name the canals that connect the cavities of scrotal sac and abdominal cavity. Name the structures that keep the testes in their position.
3. What are the functions of Sertoli cells of the seminiferous tubules and the Leydig cells in man?
4. Name the copulatory structure of man. What are the three columns of tissues in it?
5. Define spermiogenesis and spermiation.
6. Name the yellow mass of cells accumulated in the empty follicle after ovulation. Name the hormone secreted by it and what is its function?
7. Define gestation period. What is the duration of gestation period in the human beings?
8. What is implantation, with reference to embryo?
9. Distinguish between epiblast and hypoblast.
10. Write two major functions, each of testis and ovary.
11. Draw a labelled diagram of a sperm.
12. What are the major components of the seminal fluid?
13. What is menstrual cycle? Which hormones regulate menstrual cycle?
14. What is parturition? Which homones are involved in inducing parturition?
15. What is capacitation of sperms?
16. Distinguish between involution and ingression in the human development.

Short Answer Type Questions

1. Describe microscopic structure of testis of man.
2. Describe the microscopic structure of ovary of woman.
3. Describe the Graaian follicle in woman.
4. Draw a labelled diagram of the male reproductive system.
5. Draw a labelled diagram of the female reproductive system.
6. Describe the structure of seminiferous tubule.
7. What is spermatogenesis? Briefly describe the process of spermatogenesis in man.
8. What is oogenesis? Give a brief account of oogenesis in a woman.
9. Draw a labelled diagram of a Graafian follicle.
10. In our society women are often blamed for giving birth to daughters. Can you explain why this is not correct?
11. Describe the accessory glands associated with male reproductive system of man.
12. Describe the placenta in a woman.

Long Answer Type Questions

1. Describe female reproductive system of a woman with the help of a labelled diagram.
2. Describe male reproductive system of a man. Draw a labelled diagram of it.
3. Write an essay on different events that occur during development of a human.

UNIT V B

Reproductive Health

In simple terms, the term 'reproductive health' refers to having healthy reproductive organs with normal functioning. However in a broader point of view, it includes the ***emotional*** *and* ***social aspects*** *of reproduction also. According to the* ***World Health Organization (WHO)****, 'reproductive health' is a state of complete well being of individuals in physical, functional, emotional, behavioral and social aspects of reproductive system. A society will be considered 'reproductively healthy' when the people have physically and functionally normal reproductive processes and normal emotional and behavioral interactions among themselves, in all sex related aspects.*

5.11 Need for Reproductive Health and Prevention of Sexually Transmitted Diseases

Reproductive health problems remain the leading cause of death and disease in the people of reproductive age, worldwide. In India **maternal mortality rate** and **infant mortality rate** are high. Spread of Sexually transmitted diseases (**STDs**) is still a major problem. Approximately 2 million people in India live with **HIV/AIDS**.

Everyone has the right to enjoy reproductive health and healthy children. India is among the first countries in the world to initiate action plans and programmes at the national level to attain total reproductive health as a social goal. These programmes called **Family Planning Programmes** were initiated as far back as in 1951. Improved programmes covering wider reproduction-related areas are currently in operation under the popular name **Reproductive and Child Healthcare (RCH) Programmes**. Programmes such as massive child immunization, supply of nutritional food to the pregnant women, **Janani Suraksha Yojana** (for promoting institutionalized deliveries) etc. are some important healthcare programmes taken up at national level by the Government. Creating awareness among the people on various reproduction-related aspects and providing facilities and support for building up a reproductively healthy society are the major tasks under these programmes.

Governmental and non-governmental agencies have taken various steps to educate people on reproduction-related issues using audio-visual and print media. Introduction of **sex education** in schools will provide right information to the young on sex and other related issues. Proper information about the reproductive organs, adolescence and related changes, safe and hygienic sexual practices, sexually transmitted diseases such as HIV/AIDS, etc. would help people, especially those in the adolescent age group to lead a reproductively healthy life. People, especially fertile couples and those in marriageable age group, should be well informed about available birth control options, care of pregnant mothers, post natal (after birth) care of the mother and new born child, importance of breast feeding, giving equal preference for male and female child etc. This will help in bringing up healthy families of desired size. Awareness should be created in the society on problems caused by uncontrolled population growth and social evils like **sex abuse** and **sex related crimes** etc.

Female Foeticide – A Burning Problem In India: *Female foeticide* (the act of aborting a female foetus) is a major social problem in India. Sex determination of the foetus first became possible in India with the advent of ***amniocentesis*** in 1970s. This technology intended to detect genetic abnormalities in foetuses, was often used to determine the sex of the foetus. As early as in 1976 the Government banned the use of these tests for the purpose of sex determination of the foetus. Later in 1987 **3D ultra sound scanning technique** was invented for detecting developmental abnormalities in foetuses. Misuse of ultrasound scanning for the sex determination of foetus became very common which significantly increased the number of female foeticides in the country. As a measure to legally check increasing female foeticides, the Government of India enacted the **Pre-natal Diagnostic Techniques (Regulation and prevention of misuse) Act, 1994** with stringent punishment rules.

ACTION PLANS: Successful implementation of various *action plans* to attain reproductive health requires strong infrastructural facilities, professional expertise and material support. These are essential to provide medical assistance and care to people in reproduction-related problems namely pregnancy, delivery, STDs, abortions, contraception, menstrual problems, infertility, etc.

Sexually Transmitted Diseases (STDs)

Diseases or infections which are transmitted through sexual contact (intercourse) are collectively called sexually transmitted diseases (**STDs**) or venereal diseases (**VDs**) or reproductive tract infections (**RTI**). Most common STDs and their causative organisms are shown in the table below.

S.No	Name of the Disease	Causative organism
1	Gonorrhea	*Neisseria gonorrhoeae* (bacteria)
2	Syphilis	*Treponema pallidum* (spirochete bacterium)
3	Genital herpes	Herpes simplex virus (HSV)
4	Genital warts, cervical cancer	Human papilloma virus (HPV)
5	Trichomoniasis	*Trichomonas vaginalis* (a protozoan parasite)
6	Chlamydiasis	*Chlamydia trachomatis* (bacteria)
7	Hepatitis – B	HBV
8	HIV infection/AIDS	HIV (Human immunodeficiency virus)

General Information About STDs

Except for hepatitis-B, genital herpes and HIV infection, all the above diseases are completely curable if they are detected early and treated properly. Sharing injection needles, surgical instruments etc. with infected persons, transfusion of contaminated blood, or from infected mother to the foetus are the other possible ways of transmission of Hepatitis-B, HIV infections etc. Early symptoms of most of the above mentioned diseases are minor and include itching, fluid discharge, slight pain, swellings etc. in the genital region. Infected females may often be asymptomatic and hence may remain undetected for long. Untreated STDs in women may lead to complications such as pelvic inflammatory diseases (**PID**), abortions, still births, ectopic pregnancies (ectopic pregnancy is an abnormal pregnancy that occurs outside the uterus and the foetus generally cannot survive), infertility or even cancer of the reproductive tract. STDs are a major threat to a healthy society. Therefore prevention or early detection and cure of these diseases are given prime consideration under the reproductive healthcare programmes. Persons in the age group of 15-24 years are more vulnerable to contract STDs. But there is no need to panic as the prevention is right in the hands of youngsters themselves if they follow the simple principles mentioned below.

i) Avoiding sex with unknown partners/multiple partners,
ii) Using condoms compulsorily during coitus
iii) Consulting qualified doctor for early detection of STDs and getting complete treatment in case of infections.

5.12 Birth Control – Need And Methods

In the last century an all-round development in various fields significantly improved the quality of life of the people. However, the increased healthcare facilities along with better living conditions had an explosive impact on the population growth. Probable reasons for this growth rate are decline in death rate, **maternal mortality rate** (**MMR**) and **infant mortality rate (IMR)**. According to the 2011 census the population growth rate (annual %) is still around 1.64 percent. Such a high growth rate could lead to an absolute scarcity of even the basic requirements i.e. food, shelter and clothing, in spite of significant progress made in those areas.

To overcome the problem of population explosion, **birth control** is the only available solution. People should be motivated to have smaller families by using various contraceptive methods. Statutory raise of marriageable age of the females to 18 and that of males to 21 years, and providing incentives to couples with smaller families are two of the other measures taken by the Government to tackle this problem.

5.12.1 Contraception

The intentional prevention of **conception** (fertilization of an egg by a sperm at the beginning of pregnancy) by natural or artificial means is called **contraception**. **Contraceptives** prevent pregnancy by interfering with the normal process of ovulation, fertilization, and implantation. There are different kinds of contraceptives that act at different points of the process of conception. An ideal contraceptive should have the following qualities. i) user- friendly, ii) easily available, iii) effective and reversible with no or less side effects and iv) does not affect the sexual life of the user.

A wide range of **contraceptive methods** are presently available which could be broadly classified as follows. 1. Natural/Traditional methods, 2. Barriers, 3. Intrauterine devices (IUDs), 4. Oral contraceptive pills, 5. Injectables, Implants, Vaginal rings and Skin patches, and 6. Surgical methods

1. Natural methods

These methods depend on the principle of avoiding chances of sperms meeting the ovum. These are of three types.

i) **Periodic abstinence:** In this method couples avoid or abstain from coitus from the **10th to the 17th day** of the menstrual cycle (the **fertile period**), when ovulation generally occurs.

ii) **Withdrawal** or **Coitus interruptus:** In this method, the male partner withdraws his penis from the vagina, just before 'ejaculation', so as to avoid insemination.

iii) **Lactational amenorrhea method:** Amenorrhoea means absence of menstruation (missing of menstrual period). Ovulation generally will not occur during the period of intense lactation by the mother following parturition (delivery). This is known as **Lactational amenorrhea**. Some couples utilize the contraceptive benefit of this method.

NOTE: As long as the mother fully breast feeds her child, chances of conception are almost zero. In addition breast feeding offers many benefits to the infant such as enhanced immunity, protection against allergies etc. However, this method has been reported to be effective only up to a maximum of six months following parturition

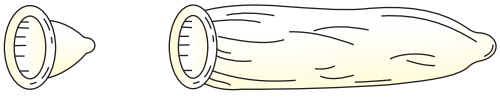


Figure 5.13 Condom for male

2. Barrier methods

In barrier methods, sperms are prevented from physically meeting with the ovum by barriers. **Condoms** (male and female condoms) are popular barriers in use. They are made of thin rubber/

latex sheath. Condoms are used to cover the penis in the male and *cervix* (neck of the uterus) or vagina in the female to prevent ejaculated semen from entering into the uterus of the female. **Nirodh** is an easily wearable popular brand of condoms for males, widely used in India. Using condom will give an additional benefit of protection from contracting (getting infected by) STDs. Other types of 'reusable' 'female barriers' called **diaphragms**, **cervical caps** and **vaults** (made of rubber) are available. **Spermicidal creams, jellies** and **foams** are also useful.

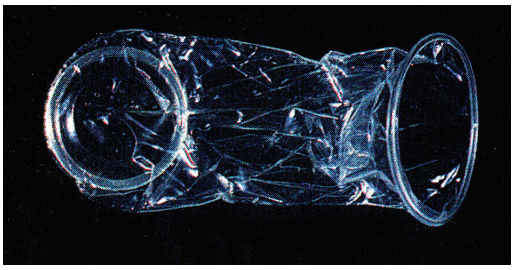


Fig 5.14 Female condom

3. Intra Uterine Devices (IUDs)

These devices are inserted into the uterus by doctors or trained nurses through vagina. Different types of **IUDs** such as **Non-medicated IUDs** (e.g. **Lippes loop**), **Copper releasing IUDs** (**Cu T, Cu 7, Multiload 375**) and **hormone releasing IUDs** (**Progestasert, LNG-20**) are available for contraception. IUDs promote 'phagocytosis' of sperms by white blood corpuscles within the uterus and the copper ions released suppress the motility, viability and fertilizing capacity of the spermatozoa. The hormone releasing IUDs, in addition, make the uterus unsuitable for implantation and the cervix hostile/antagonistic to the sperms. IUDs are ideal contraceptives to females who want to delay and/or have space between children. This is a widely accepted method of contraception in India.

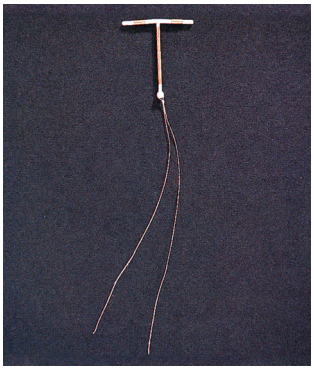


Fig 5.15 Copper T

4. Oral contraceptive pills (OCPs)

Oral administration of small doses of **progestogens** or **progestogen-estrogen combinations** in the form of tablets or pills is another popular contraceptive method used by females. Pills have to be taken daily for a period of 21 days starting preferably within the first five days of the menstrual cycle. After a gap of 7 days (during which menstruation occurs) the same course in the same pattern has to be repeated as long as the female desires to prevent conception. The **pill** inhibits ovulation, implantation and also alters the quality of cervical mucous and retards entry of sperms. A **once a week pill** by name **Saheli** developed by **CDRI, Lucknow** is a non-steroidal oral contraceptive preparation with very few side effects and high contraceptive value.

5. Contraceptive Injections, Drug releasing Implants, Vaginal rings and Skin patches

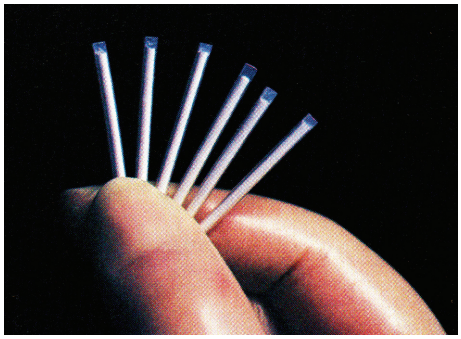


Fig 5.16 Implants

Progestogens alone or in combination with estrogen can also be used by females in the form of injections, implants, vaginal rings and skin patches. An injection of **depot medroxyprogesterone acetate (DMPA)** provides protection against pregnancy for three months. A contraceptive **implant** is a single rod about the size of a match stick. A health care provider inserts the implant under the skin with a special applicator. It prevents pregnancy for a period of three years. **Vaginal ring** is a flexible, plastic ring to be inserted into vagina. It releases small doses of estrogen and progestogen which prevent conception. Small **skin patches** loaded with contraceptive hormones are worn on the skin. These patches slowly release **estrogen** and **progestogen** into blood stream to prevent pregnancy.

> **NOTE**: Administration of progestogens or progestogen-estrogen combinations or copper-bearing IUDs within 72 hours of coitus have been found to be very effective ***emergency contraceptives*** as they could be used to avoid possible pregnancy due to rape or casual unprotected intercourse.

6. Surgical methods :

Surgical procedure to prevent pregnancy is also known as **sterilization**. Sterilization procedure in the male is called **vasectomy** and that in the female, **tubectomy**.

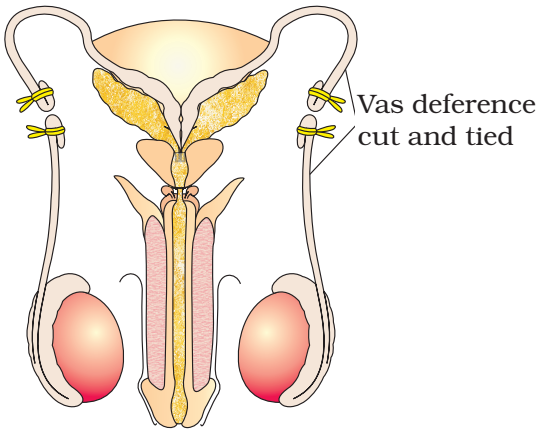


Fig 5.17 Vasectomy

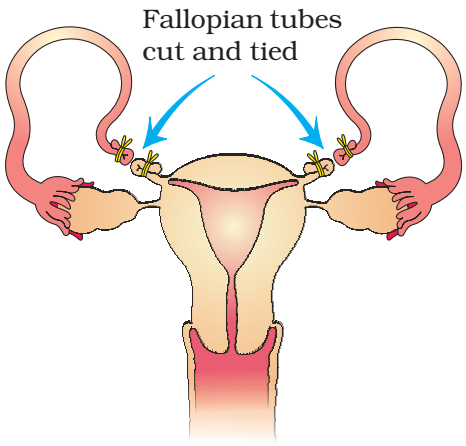


Fig 5.18 Tubectomy

i. **Vasectomy :** A small part of the **vas deferens** on either side is removed or tied up through a small incision on the scrotum. Thus the sperms are prevented from reaching seminal vesicle and so the 'semen' in 'vasectomised' males do not contain sperms.

ii. **Tubectomy:** A small part of the **fallopian tube** on both sides is removed or tied up through a small incision made in the abdomen or through vagina. This will block the entry of ova into the fallopian tubes and thus pregnancy is prevented.

5.12.2 Medical Termination of Pregnancy (MTP)

Intentional or voluntary termination of pregnancy before the full term of gestation is called **Medical termination of pregnancy (MTP)** or **induced abortion**. In this procedure pregnancy is terminated with the help of medications. Government of India made an act in 1971 legalizing MTP with certain restrictions and conditions to avoid its misuse. These restrictions are more important that the administrative machinery can keep a check on indiscriminate and illegal female foeticides. Legalizing MTP is still an issue of serious debate in many countries because of ethical, religious and social issues involved.

Medical Terminaiton of Pregnancy (MTP)

It is considered to be the only available choice to get rid of unwanted pregnancies resulted due to casual unprotected intercourse, failure of the contraceptive used during coitus or in case of rapes or in the case of confirmed incurable genetic disorders in the foetus. In cases where continuation of pregnancy could be harmful or even fatal either to the mother, or to the foetus or for both, MTP is the inevitable solution.

5.13 Amniocentesis, Infertility and Assisted Reproductive Technology (ART)

5.13.1 Amniocentesis

Amniocentesis is a diagnostic procedure to detect genetic defects in the unborn baby. In this procedure, usually a needle is inserted through the mother's abdominal wall into the amniotic sac. The physician carefully punctures the sac and extracts some **amniotic fluid**. For prenatal diagnosis of suspected genetic disorders, the foetal cells are separated from the extracted sample. The chromosomes of the stained foetal cells are examined under a microscope for abnormalities. The most common abnormalities that can be detected by amniocentesis are Down syndrome, Edwards syndrome and Turner's syndrome.

The purpose of **amniocentesis**, **ultrasound scanning** etc. is often defeated because such tests mostly end up in illegal female foeticide, at least in certain parts of India.

5.13.2 Infertility

Another important sub-topic to be discussed under the heading **Reproductive Health** is **Infertility**. Infertility is biological inability of a person to contribute to conception. A large number of couples in the conceivable age all over the world are childless. The reasons could be many - physical, genetic, certain diseases, drugs, immunological or even psychological. In India female partners are often blamed for not conceiving, in childless couple. But in many cases, the problem lies with male partner. Infertility clinics and specialized health care units could help in diagnosis and corrective treatment of some of these disorders and enable the couples to have children in natural way.

5.13.3 Assisted Reproductive Technology (ART)

In the cases where such corrections are not possible, the couple could be assisted to have children through certain special techniques known as **Assisted Reproductive Technology (ART)**. The following are some important techniques employed in ART.

1. ***In Vitro Fertilization and Embryo Transfer (IVF-ET)***

   Fertilization of ovum by sperm done outside the body of a woman is called **in vitro fertilization**. The resultant early embryonic stage (with generally 8 blastomeres) is transferred into the mother's uterus for further development (**Embryo Transfer or Intra Uterine Transfer - IUT**). In this method, which is popularly known as **Test Tube Baby Procedure**, ova from the wife/female donor and sperms from the husband/male donor are collected, mixed and induced to form zygote under simulated conditions (almost similar conditions as that in the female body) in the laboratory. If the mother's uterus is not medically fit to receive the embryo produced in vitro, it can be implanted in the uterus of another woman (**surrogate mother**) willing to carry this embryo.

2. ***Zygote Intrafallopian Transfer (ZIFT)***

   This is another technique used to overcome infertility. The ovum is extracted and fertilized in vitro (outside the body) and the **zygote** is transferred to the woman's **fallopian tube** to complete its further course of development ("intrafallopian" means "inside the fallopian tubes").

3. *Gamete Intrafallopian Transfer (GIFT)*

Some women cannot produce ova either due to defects or diseases in the ovaries, but still can provide suitable environment for fertilization and further development of the embryo in their uteri. In such cases an ovum collected from a donor is transferred to the fallopian tube of the recipient woman for fertilization. This method is known as ***GIFT***.

4. *Intracytoplasmic Sperm Injection (ICSI)*

This is another specialized procedure in which a sperm is directly injected into the ovum with the help of a microscopic needle to form an embryo in the laboratory. Later the embryo is transferred to the uterus or fallopian tube for further development. This method is employed to assist the couple where there are problems with the sperms such as decrease in sperm count.

5. *Artificial Insemination (AI)*

In cases of infertility either due to inability of the male partner to inseminate the female or due to very low sperm count in the ejaculate, artificial insemination technique is suggested. In this technique, semen is collected from the husband/healthy donor and is introduced into the uterus (**Intrauterine insemination- IUI**) for achieving fertilization.

Surrogacy

In the instances where the women have problems with conceiving or providing suitable environment for the development of the embryo in her uterus, **surrogacy** is suggested. The ovum of the wife/donor and the sperm of the husband/male donor are fertilized and the zygote is transferred into the womb of a **surrogate mother** (a woman who provides her uterus for the development of some other person's embryo and carries the baby until delivery).

NOTE: *Though there are many options to tackle infertility problems, all those techniques require professionals and use of expensive instrumentation. Religious and social factors may discourage the adoption of some of the procedures. There is one good way out – the adoption of a child .Indian law permits legal adoption and it is the best choice for the childless couples looking for parenthood.*

GLOSSARY

Amenorrhea: Absence of menstrual period / menstruation in women of reproducible age.

Amniotic sac: The amniotic sac is the extra-embryonic sac filled with amniotic fluid (liquor amnii). Amnion surrounds and protects the embryo from shock /injury, and also provides a watery bag in which free movements of the fetus during the later stages of pregnancy are facilitated.

Blastomere: Any of the cells resulting from the cleavage of a fertilized ovum/zygote during the early embryonic development.

Coitus: Sexual union between a male and a female involving insertion of the penis into the vagina.

Coitus interruptus: Deliberate interruption of Sexual intercourse by withdrawal of the penis from the vagina prior to ejaculation of semen (fluid containing sperms and other secretions).

Contraception: Also known as Birth control and Fertility control. , It refers to methods or devices used to prevent pregnancy.

Foeticide: The destruction of a foetus in the uterus.

Implantation: It is the process of the early embryo (blastocyst) becoming fixed or embedded in the wall of the uterus / lining of the womb to receive nourishment from the mother, for development, in the 'placental mammals'.

Insemination: 'Insemination' is the introduction of sperm into the uterus for impregnating a female. Insemination normally takes place during coitus. When semen is introduced by a medical procedure to facilitate conception, it is called 'artificial insemination'.

In vitro: In an artificial environment (for example in a test tube in a laboratory) outside the living organism's body.

In vivo: Within the living organism or within the body of an animal or human being.

Intra Uterine Device (IUD): A small T – shaped device inserted into the uterus to prevent pregnancy.

Maternal mortality: Death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the duration and site of the pregnancy, from any cause related to pregnancy or its management (WHO definition).

Phagocytosis: Cellular process of engulfing solid particles by the cell membrane to form an internal phagosome by phagocytes and protists.

QUESTIONS

Very Short Answer Type Questions

1. What are the measures one has to take to prevent contracting STDs?
2. What in your view are the reasons for population explosion, especially in India?
3. It is true that 'MTP is not meant for population control'. Then why did the Government of India legalize MTP?
4. What is 'amniocentesis'? Name any two disorders that can be detected by amniocentesis.
5. Mention the advantages of 'lactational amenorrhea method'.

Very Short Answer Type Questions

1. Briefly describe the common sexually transmitted diseases in human beings.
2. Describe the surgical methods of contraception.
3. Write short notes on any two of the following.
   a) IVF b) ICSI c) IUDs
4. Suggest some methods to assist infertile couples to have children.
5. Is sex education necessary in schools? Why?

FOR IGNITED MINDS

Human Reproduction and Reproductive Health

1. Why do fish, frogs etc., show **external fertilisation** and reptiles, aves and mammals show **internal fertilisation**?
2. Why do children of the same family/parentage show difference in morphological, physiological and psychological differences?
3. A frog has no tail. Why does its **tadpole larva** possess a tail?
4. Why don't young children show **secondary sexual features** such as beard, and breast development until they reach a certain age?
5. How does fertilisation occur in animals which lay **shelled eggs**?
6. The developing embryo of fish or frog does not run the risk of **drying up** generally. How do embryos of terrestrial vertebrates protect themselves from drying up?
7. We say that nervous system is ectodermal in origin. How can nervous system, which is enclosed in the mesodermal bony skeletal structures, arise from the outermost germinal layer, the ectoderm?
8. How many times does a normal woman get a chance to become pregnant in her life time, assuming that she lives into her sixties?
9. Placing an **IUD**, can lead to **phagocytosis** of spermatozoa. How?
10. How do you differentiate between **GIFT** and **ZIFT** with reference to assisting childless couples?

T.H. Morgan

Unit-VI

GENETICS

Genetics - Mendel's 'Breakfast', Morgan's 'Dinner' and a Versatile Teacher's 'Cup of Tea'

Life is diverse, encased in the shell of 'conservatism of Nature' - Well that is Genetics, though not literally. Genetics, the enigma of heredity,has its roots lying in the Mendelian experiments on ***heredity*** *and* ***variations****.*

LIKE FATHER LIKE SON *- yet different in phenotype/ appearance and attitudes. How does it occur in its manifold patterns? Is only the genetic material passed on from the parent to the child responsible for this? It is true, with certain limitations, that* ***GENES LOAD THE GUN BUT THE ENVIRONMENT TRIGGERS IT.*** *Genes (****cistrons****) control '****traits****'. However a single gene may have two or more allelic forms each allele controlling a contrasting feature of a specific trait.* ***T.H. Morgan****, a Nobel laureate, contributed to the glory of the science of 'Genetics' with his experiments on* ***Drosophila melanogaster****, the '****fruit fly****'. Morgan's work laid a firm foundation to the genetical theory of inheritance in animals and today man has come to know of the* ***genetical roots*** *of various diseases which are evading cure. The working out of the* ***HUMAN GENOME*** *and identification of the individual chromosomal and '****genic errors****' and their patterns of inheritance and of course the fruitful research going in the field of* ***Gene Therapy*** *are steps to making human life better. This unit mainly deals with topics such as-* ***Multiple alleles*** *and* ***Human blood groups****,* ***Sex determination****,* ***Sex – linked Inheritance****,* ***Genetic disorders****,* ***Human genome project****,* ***DNA Fingerprinting*** *etc., to help you get a grasp on the different dimensions of Mendelian and Non-Mendelian Gentics.*

Genetics

Genetics, a discipline of biology, is the science of heredity and hereditary variations in living organisms. The word 'genetics' is derived from the Greek word **genesis**, which means "origin of anything" or "a beginning". The term genetics was coined by **W. Bateson**. Genetics deals with the patterns of inheritance from the parent to the offspring, gene distribution, variation and change in populations.

6.1 Heredity and variations

Heredity is the study of transmission of characters from one generation to the next. The characters that are passed from one generation to the other are called hereditary characters. Variations on the other hand may be defined as the differences in characteristics shown by the individuals of a species and also by the progeny of the same parents. Humans knew from as early as 8000-1000 B.C. that one of the causes of variations was hidden in sexual reproduction. They exploited the variations that were naturally present in the wild populations of plants and animals to selectively breed and select organisms that possessed desirable characters. For example, through artificial selection and domestication from ancestral wild cows, we developed well known Indian breeds, such as **Sahiwal cows** of Punjab.

However, the modern science of genetics, which seeks to understand the process of inheritance, only began with the work of **Gregor Mendel** in the mid-19th century. Although he did not know the physical basis for heredity, Mendel observed that organisms inherit traits via distinct units of inheritance, which are now called 'genes'/'cistrons'. After the rediscovery of Mendel's work by **de Vries**, **Correns** and **Tschermak**, scientists tried to determine which molecules in the cell were responsible for inheritance. **Chromosome Theory of Inheritance** or the **Sutton – Boveri Theory** is a fundamental unifying theory of genetics which identifies chromosomes as the carriers of genetic material. It states simply those chromosomes, which are seen in all dividing cells and pass from one generation to the next, are the basis for all genetic inheritance.

Experimental verification of the "Chromosomal theory of inheritance" by **Thomas Hunt Morgan** and his colleagues, led to discovering the basis for the variation that sexual reproduction produced. For his work, Morgan selected a species of fruit fly, ***Drosophila melanogaster***, which can be grown on simple synthetic medium in the laboratory. It completes its life cycle in about two weeks, and a single mating could produce a large number of progeny. Further, it has many types of morphological, hereditary variations that can be seen under a low power microscope. Another advantage of the fruit fly is that it has only four pairs of chromosomes, which are easily distinguishable under a light microscope. There are three pairs of autosomes and one pair of sex chromosomes. Female fruit flies have a pair of homologous X-chromosomes, and males have one X- chromosome and one Y-chromosome.

6.2 Mendel's laws of inheritance in *Drosophila*

Gregor Mendel performed hydridisation experiments on ***Pisum sativum*** (garden pea plant) in the middle of 19th century (1856-1863) and proposed laws of inheritance, which become very popular as **Law of segregation** and **Law of independent assortment**, Which you have studied in detail in Botany. We may discuss these laws in animals also. T.H.Morgan explained them in ***Drosophila melanogaster*** (fruit fly).

1. **Law of segregation:** It states that -

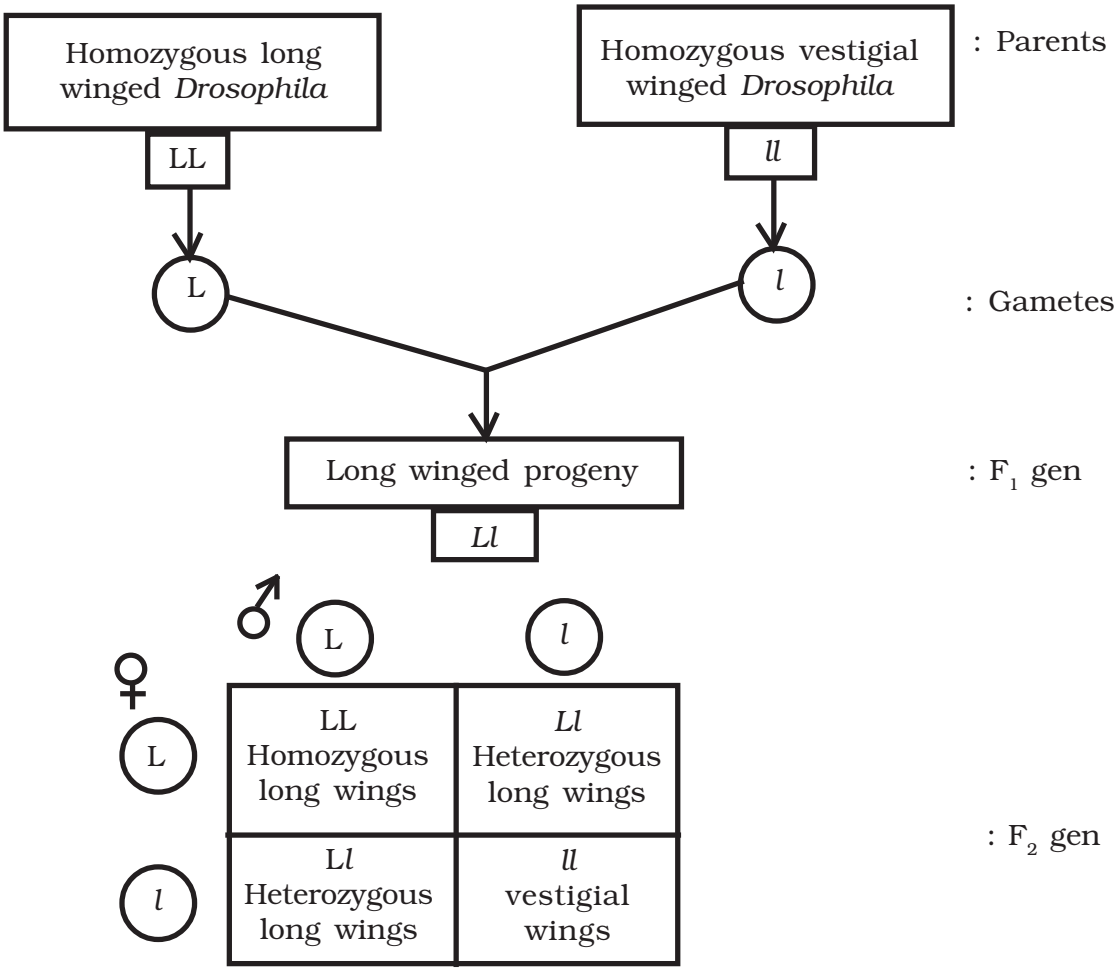
   i. The alleles in parents did not mix with each other.

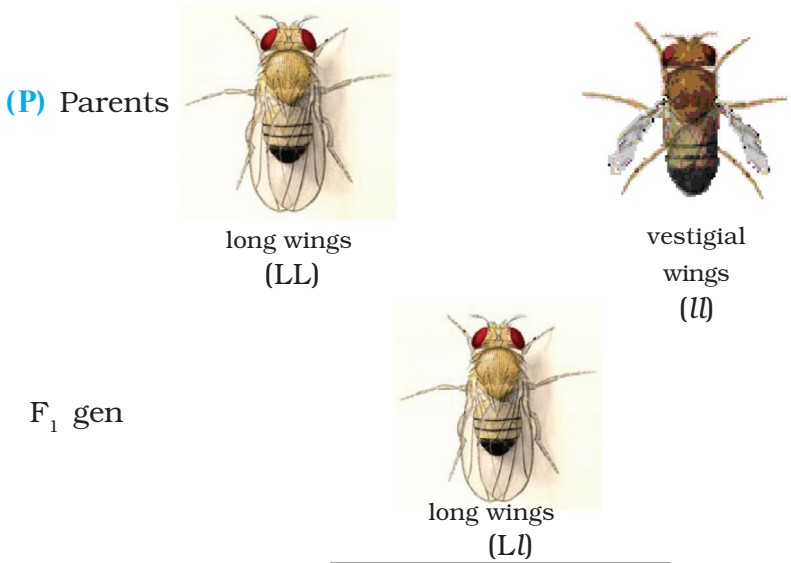
   ii. During gametogenesis, paternal and maternal alleles separate. Hence, each gamete receives one allele only of that particular trait.

   iii. Homozygous parents produce similar types of gametes (e.g., T or t). Heterozygous parents produce two types of gametes (e.g., T and t).

iv. During fertilisation, as per their union, homozygous progeny (TT or tt) or heterozygous progeny (Tt) are produced. Hence, the traits which are not expressed in first filial generation (F_1 generation) are expressed in second filial generation (F_2 generation).

Let us explain law of segregation based on the size of wings of ***Drosophila***. In this insect long wing trait is dominant and vestigial wing trait is recessive. If a homozygous long winged (LL) ***Drosophila*** is crossed with a homozygous vestigial winged (ll) ***Drosophila*** (Monohybrid cross), in F_1 generation, all insects have long wings. When they are interbred, in F_2 generation, long winged and vestigial winged flies are formed in 3 :1 ratio. Observe the illustration given below.





LL = Long winged ***Drosophila*** - Homozygous (1)

Ll = Long winged ***Drosophila*** - Heterozygous (2)

ll = Vestigial winged ***Drosophila*** - Homozygous (1)

Phenotypic ratio of Monohybrid cross - 3 : 1

Genotypic ratio of Monohybrid cross- 1 : 2 : 1

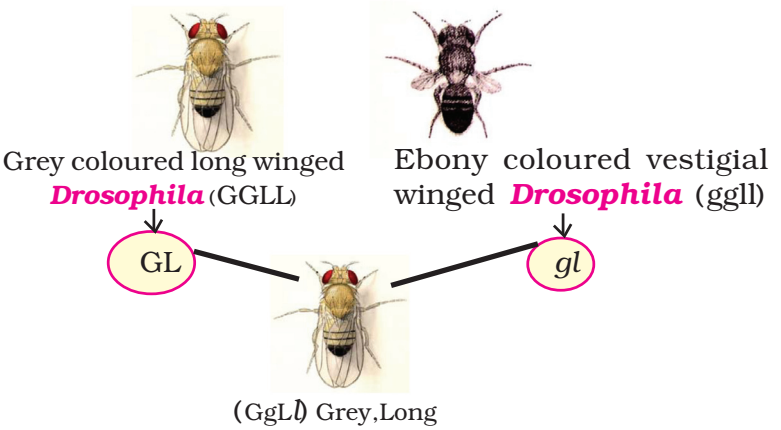
As shown in the illustration, the progeny formed in F_1 generation is heterozygous (L*l*). The dominant (L) and recessive (*l*) alleles segregate in it. Hence, in F_2 generation, long winged and vestigial winged ***Drosophila*** are produced. Their phenotypic ratio is 3:1 and genotypic ratio is 1:2:1.

2. Law of independent assortment: As per this law proposed by Mendel, if in a hybrid two pairs of different alleles are considered, one pair independently segregate from the other and inherited to next generation. Through dihybrid cross in ***Drosophila***, law of independent assortment can be prooved.

In ***Drosophila***, the genes that influence body colour (grey or ebony), wing size (long or vestigial) follow the independent assortment. In these, the

genes for the traits grey colour and long wings are dominant (GGLL) and that of ebony (black) and vestigial wings are recessive (*ggll*).

When a grey coloured long winged male ***Drosophila*** and a ebony coloured, vestigial winged female ***Drosophilia*** are crossed, in F_1 generation, heterozygous grey colured long winged (G*gLl*) progeny are formed. When they are interbred, in F_2 generation, grey, long; gery, vestigial; ebony, long and ebony, vestigial flies are formed in 9:3:3:1 ratio. Here, in addition to parental types, two new varieties are formed.



P- gen

: F_1 gen

♀ \ ♂	*GL*	G*l*	*g*L	*gl*
GL	GGLL grey long	GGL*l* grey long	GgLL grey long	G*g*L*l* grey long
G*l*	GGL*l* grey long	GG*ll* grey veste	G*g*L*l* grey long	G*gll* grey veste
*g*L	G*g*LL grey long	G*g*L*l* grey long	*gg*LL Ebony long	*gg*L*l* Ebony long
gl	G*g*L*l* grey long	G*gll* grey veste	*gg*L*l* Ebony long	*ggll* Ebony veste

: F_2 gen

Drosophilia

Grey colured, long winged ***Drosophila*** = 9(9/16)

Grey colured, vestigial winged ***Drosophila*** = 3(3/16)

Ebony colured, long winged ***Drosophila*** = 3(3/16)

Ebony colured, vestigial winged ***Drosophila*** = 1(1/16)

Phenotypic ratio of dihybrid cross = 9 : 3 : 3 : 1

Mendel's dihybrid phenotypic ratio = 9 : 3 : 3 : 1

Genotypic ratio = 1 : 2 : 2 : 4 : 1 : 2 : 1 : 2 : 1

Generally genes for grey colour and long wings occur in pairs. Similarly genes for ebony colour and vestigial wings occur in pairs. But in F_1 dihybrid, during gamete formation, due to segregation of genes, four types of gametes are formed. But at the time of fertilisation, they unite randomly and bring about all possible combinatons of different traits. This is called independent assortment of genes. Hence, four types of ***Drosophila*** are formed in 9:3:3:1 ratio.

Along with the above experiment, T.H. Morgan performed test cross by crossing the dihybrid (GgLl) ***Drosophila*** with recessive one (*ggll*). As a result, majority of the progeny resemble the parents, Morgan concluded that the genes for body colour and size of wings in ***Drosophila*** are to linked in same ***chromosome***.

6.3 Pleiotropy

It is an established fact that a specific gene controls a specific phenotypic trait. This finding is not always true. Studies on 'gene expression' have revealed that a single gene often influences more than one phenotypic trait. This phenomenon of multiple effects of a single gene is called **pleiotropy.** The usual underlying mechanism is that, the same gene is activated in several different tissues producing different phenotypic effects. One of the most widely cited examples of pleiotropy in humans is the genetic disorder **Phenylketonuria** (PKU). This disorder is caused by the deficiency of the enzyme **phenylalanine hydroxylase**. If this enzyme is not produced because of a mutated gene, the amino acid **phenylalanine** cannot be converted to **tyrosine** and is converted into **phenylpyruvic acid**, which accumulates in body fluids. The buildup of phenylpyruvic acid causes multiple phenotypes associated with PKU, including mental retardation, reduced hair and skin pigmentation. Pleiotropic alleles are responsible for the multiple symptoms associated with certain other diseases, such as **Cystic fibrosis** and **Sickle-cell disease**.

6.4 Multiple alleles and human blood groups

Generally a gene has two alternative forms/versions called **alleles**. They are present at the same locus in a pair of homologous chromosomes. Two alleles of a gene can form three genotypes in a diploid organism. Sometimes a gene may have more than two alleles. When more than two allelic forms occur at the same locus on the homologous chromosomes of an organism, they are called **multiple alleles**. When more than two alleles exist in a population of a specific organism, the phenomenon is called **multiple allelism.** As mentioned above 'multiple alleles' cannot be observed in the genotype of a diploid individual, but can be observed in a population. The number of kinds of genotypes that can occur for multiple alleles is given by the expression **n(n+1)/2**, where, n = number of alleles. A well known example of multiple allelism in man is the expression of **ABO blood types** by three alleles of a single gene which can produce six genotypes.

6.4.1 ABO Blood Types

The ABO blood group system was proposed by **Karl Landsteiner.** He was awarded the Nobel Prize in Physiology or Medicine in 1930 for his work. The phenotypes (blood types) **A, B, AB** and **O types** are characterized by the presence or absence of 'antigens' on the plasma membrane of the RBCs. The A and B antigens are actually carbohydrate groups (**sugar polymers**) that are bound to lipid molecules (fatty acids) and they protrude from the membrane of the red blood cell. They are also called **isoagglutinogens** because they cause blood cell agglutination in the case of incompatible blood transfusions. 'Blood type A' persons have **antigen A** on their RBCs and **anti-B** antibodies in the plasma. 'Blood type B' persons have **antigen B** on their RBCs and **anti-A** antibodies in the plasma. 'Blood type AB' persons have antigens 'A' and 'B' on the RBCs and no antibodies in the plasma. 'Blood type O' persons have no antigens on their RBCs and both 'anti-A' and 'anti-B' antibodies are present in the plasma.

Bernstein discovered that these phenotypes were inherited by the interaction of three 'autosomal alleles' of the gene named **I**, located on **chromosome 9**. I^A, I^B and **i** (or I^O) are the three alleles of the gene **I**. The antibodies 'anti-A' and 'anti-B' are called **isoagglutinins** (also called **isohaemagglutinins**) which are usually **IgM** type. The isoagglutinins of an individual cause agglutination reactions with the antigens of another individual. The alleles I^A and I^B are responsible for the production of the respective antigens 'A' and 'B'. The allele **i** does not produce any antigen. The alleles I^A and I^B are dominant to the allele **i**, but **co-dominant** to each other **($I^A = I^B > i$)**. A child receives one of

Table 1 : Genetic control of the human ABO blood groups

Genotype	Antigens present on red blood cells	ABO blood group phenotype	Antibodies present in blood plasma	Blood types that can be tolerated	Blood types that can accept blood for transfusion
I^AI^A	*A*	*Type A*	*Anti-B*	*A & O*	*A & AB*
I^Ai	*A*	*Type A*	*Anti-B*	*A & O*	*A & AB*
I^BI^B	*B*	*Type B*	*Anti-A*	*B & O*	*B & AB*
I^Bi	*B*	*Type B*	*Anti-A*	*B & O*	*B & AB*
I^AI^B	*A & B*	*Type AB*	*Neither anti-A nor anti-B*	*A,B, AB & O*	*AB only*
ii/I^OI^O	*Neither A nor B*	*Type O*	*Anti-A & anti-B*	*O only*	*A,B, AB & O*

the three alleles from each parent, giving rise to six possible genotypes and four possible blood types (phenotypes). The genotypes are **I^AI^A, I^Ai, I^BI^B, I^Bi, I^AI^B** and **ii**. The phenotypic expressions of **I^AI^A** and **I^Ai** are 'A' – type blood, the phenotypic expressions of **I^BI^B** and **I^Bi** are 'B'–type blood, and that of **I^AI^B** is 'AB'–type blood. The phenotype of **ii** (**I^OI^O**)is 'O'–type blood.

Blood Typing

The ABO phenotype of any individual is ascertained by mixing a blood sample with an **antiserum** containing 'anti-A' or 'anti-B' antibodies. If a clump is formed with 'anti-A' serum, the type of blood can be 'A' or 'AB'. If a clump is formed with 'anti-B' serum, the type of blood can be 'B' or 'AB'. If a clump is formed with both 'anti-A' and 'anti-B' antibodies, the type of blood is 'AB' and if no clump is produced with either of the antibodies, the type of blood is 'O'.

Importance of ABO groups in blood transfusion

While transfusing blood, the type/types of antigens of the donor and the type/types of antibodies of the recipient are to be taken into consideration. The antibodies of the donor and the antigens of the recipient are relatively of less importance. The RBCs of an 'O group' have no antigens and so agglutination does not occur with any other group of blood. So, persons with 'O group blood' are called **universal donors**. The plasma of persons with 'AB group' blood has no antagonistic antibodies. This does not cause agglutination of RBC received from persons of other groups of blood. So people with 'AB group' blood are called **Universal recipients**. Can you think of how an AB group person can be considered a 'universal donor' with reference to transfusion of plasma?

NOTE : Type AB^+ is the **universal recipient**. Although those with AB blood type may be referred to as universal recipients, in actuality, type **AB^+** blood is that of the universal recipient, whereas type **AB^-** is not. This is an important distinction to make. Because **A^-**, **A^+**, **B^-**, **B^+**, **AB^-**, **AB^+**, **O^-** and **O^+** individuals can all receive blood from donors of type **O^-** blood. An individual with **type O^-** blood is deemed a **universal donor**.

6.4.2 Rh Blood Types

Karl Landsteiner and **Alexander S. Wiener** discovered another antigen called **Rh-antigen** or **Rh factor** on the surface of RBCs of **Rhesus monkeys** (***Macaca mulatta***) and later in human beings. But the term 'Rh factor' strictly refers only to the most immunogenic **D antigen** of the Rh-blood group system. The persons having D antigen are called 'Rh D positive (Rh^+)' and those without D antigen are called Rh D negative (Rh^-). Rhesus factor in the blood is an inherited dominant trait. **Anti-D** antibodies are absent in the plasma of any person normally (naturally). However, if an 'Rh negative' person is exposed to Rh positive blood cells (erythrocytes) for the first time, 'anti-D antibodies' are formed in that person's blood. On the other hand, an Rh positive person can receive Rh negative blood without any consequent effects/complications.

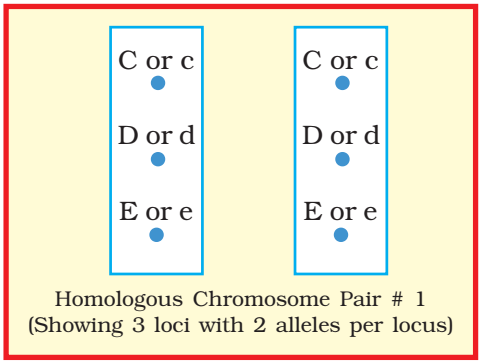


Figure 6.1 Fisher And Race Hypothesis - Rh Blood Type

6.4.3 Genetic control of Rh system

Fisher and Race hypothesis

Unlike the A-B-O blood types where all the alleles occur on one pair of loci on chromosome pair 9, the Rh factor involves three different pairs of alleles located on three different closley linked loci on the **chromosome pair 1**. The Fisher-Race system, which is more commonly in use today, uses the **CDE nomenclature**.

In the above figure, 3 pairs of Rh alleles (Cc, Dd and Ee) occur at 3 different loci on homologous chromosome pair-1. The possible genotypes will have one C or c, one D or d, and one E or e from each chromosome. For example: **CDE/cde; CdE/cDe; cde/cde; CDe/CdE**, etc. All genotypes carrying a dominant 'D allele' will produce 'Rh-positive' phenotype and double recessive genotype 'dd' will give rise to 'Rh-negative' phenotype.

Wiener hypothesis

Wiener proposed the existence of eight alleles (**R^1**, **R^2**, **R^o**, **R^z**, **r**, **r'**, **r''**, **r^y**) at a single Rh locus. All genotypes carrying a dominant 'R allele' (**R^1**, **R^2**, **R^o**, **R^z**)

will produce 'Rh-positive' phenotype and double recessive genotypes **rr** (or **rr'**, **rr''**, **rr^{y}**) will give rise to 'Rh-negative' phenotype.

6.4.4 Erythroblastosis foetalis

Erythroblastosis foetalis/**Haemolytic Disease of the Newborn**/**Haemolytic disease of the foetus and newborn** (**HDN/HDFN**) is an alloimmune condition that develops in an Rh positive foetus whose father is Rh positive and mother is Rh negative. The genetic consequence in this marriage is the **Rh incompatibility** between the mother (Rh^-) and the growing foetus (Rh^+). The foetal blood cells may pass through the ruptured placenta at birth into the Rh nagative meternal blood. The mother's immune system recognizes the Rh antigens and gets sensitized. The sensitized immune system in the mother produces Rh antibodies. The Rh antibodies are of the **IgG** type which are small in size. So, they can pass through the placental barrier and enter the foetal blood circulation. Generally the first child of this 'genetically incompatible marriage' is unaffected because foetus is delivered by the time the mother gets sensitized and produces anti '**D**' antibodies.

During the second pregnancy,if the second child is Rh positive, these antibodies cross the placental border and enter the foetal blood circulation. The blood cells of the Rh positive foetus are destroyed, causing HDN.

Haemolytic anaemia and **jaundice** are the symptoms of this disorder in the affected neonatal babies. To compensate the haemolysis of more and more number of RBCs, there is a rapid production of RBCs, not only from the bone marrow, but also from spleen and liver. Now, many large and immature cells in **erythroblast stage** are released into circulation. Because of this, the disease is called **erythroblastosis foetalis**.

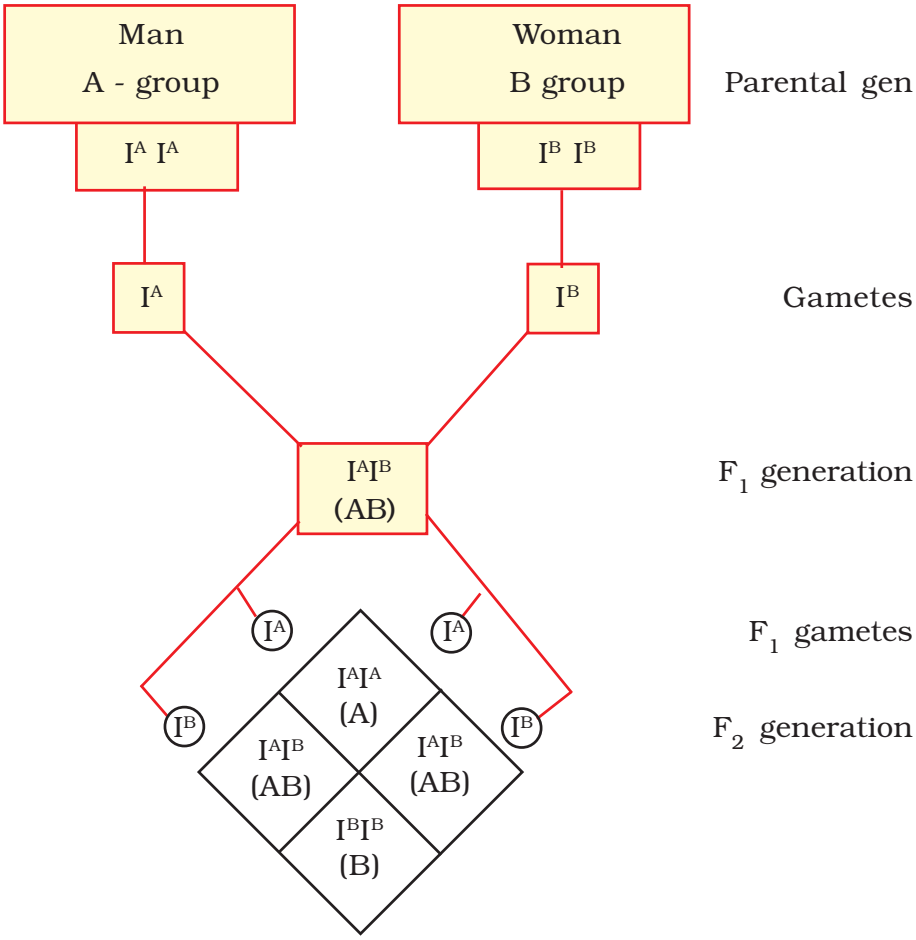
Prevention of Erythroblastosis Foetalis

*If the mother is found to be 'Rh negative' and the foetus is 'Rh positive', **IgG anti-D antibodies (Rho (D) Immuno Globulin)** should be administered to the mother at 28th and 34th weeks of gestation as a prophylactic measure. If the 'Rh negative' mother delivers 'Rh-positive' baby, then anti-D antibodies should be administered to the mother soon after delivery. This develops **passive immunity** and prevents the formation of 'anti-D antibodies' in the mother's blood, by destroying the Rh positive foetal erythrocytes, before the mother's immune system is 'sensitized'. This has to be done every time the lady is pregnant.*

6.5 Codominance

The expression of paternal and maternal traits equally in the heterozygotes of F_1 generation is known as **codominance**. In this phenomenon there is no recessive trait. Hence the alleles of the two phenotypes are visible in the

indeviduals of F_1 generation. It means, the substances (e.g. proteins, glycoproteins, glycolipids) formed expression of both alleles are present in equal amounts in F_1 individuals. Hence codominance is also called eqal dominance.



Explanation

genotype	phenotype	Ratio
I^AI^A	A blood group	1
I^AI^B	AB blood group	2
I^BI^B	B blood group	1

Codominance in AB blood group in human beings

For example, the alleles responsible for human blood groups - I^A and I^B are codominant. Due to their expression, A and B antigens are formed on

RBC in equal numbers. Due to I^AI^A homozygous condition A group and due to I^BI^B homozygous condition B-group are formed. But in I^AI^B heterozygote the antigens A and B are formed in equal numbers and hence AB-group is produced. When a man with A-blood group marries a woman with B-blood group, in their children AB-blood group is expressed. If two F_1 heterozygotes marry, in F_2 generation in their children the three blood groups, namely, A, AB and B are expressed in 1:2:1 ratio. See the illustration above.

6.6 Polygenic Inheritance

Mendel studied characters that could be classified on an either-or basis, such as purple versus white flower color. But for many characters, such as human skin color and height, an either-or classification is impossible because the characters vary in the population in gradations along a continuum. These are called **quantitative characters**. Quantitative variation usually indicates **polygenic inheritance**, an additive/cumulative effect of two or more genes on a single phenotypic character (the converse of pleiotropy, where a single gene affects several phenotypic characters).

Skin colour in man

For example human skin colour varies in the population in gradations. It is called a quantitative character. There is evidence, for instance, that skin pigmentation in humans is controlled by at least three separately inherited genes (probably more, but we will simplify). Let us assume that three genes namely A,B,C control skin colour in human with the dominant alleles A, B and C responsible for dark skin colour and the recessive alleles a, b and c for light skin colour. An **AABBCC** person would be very dark, while an **aabbcc** individual would be very light/fair in complexion. An **AaBbCc** person would have skin of an **intermediate shade**. The genotypes AaBbCc and AABbcc would make the same genetic contribution (three major units) to skin's darkness. There are **different skin-color phenotypes** that could result from a mating between AaBbCc heterozygous organisms. In this manner the number of each type of alleles in the genotype would determine the degree of darkness or lightness of the skin in an individual. Environmental factors, such as exposure to the sun, also affect the skin-color.

6.7 Sex Determination

The mechanism of sex determination has always been a puzzle to geneticists. In fact, the cytological observations made in a number of insects led to the development of the concept of genetic/chromosomal basis of sex determination.

6.7.1 Sex Chromosomes

In most of the animals a pair of chromosomes is responsible for the determination of sex. These two chromosomes are called **sex chromosomes** or **allosomes.** The chromosomes other than the sex chromosomes are called **autosomes**. The first indication that sex chromosomes were distinct from the other chromosomes came from the experiments conducted by **Henking.** He could trace a specific nuclear structure all through spermatogenesis in wasps, and it was also observed by him that 50 percent of the spermatozoa received this structure after spermatogenesis, whereas the other 50 percent did not receive it. Henking gave the name **X–body** to this structure, but he could not explain its significance. Further investigations by other scientists led to the conclusion that the X–body of Henking was in fact a chromosome and that is why it was given the name **X–chromosome**. **Stevens** and **Wilson** first identified **Y–chromosome** as a sex-determining chromosome in the **mealworm, *Tenebrio molitor***. They revealed that the chromosomal basis of sex depended on the presence or absence of the Y–chromosome.

NOTE : If the two sex chromosomes are similar (**XX**), the individual is described as **homogametic**. Gametes produced from it are similar. If the two sex chromosomes are different (**XY**) or it contains only one sex chromosome (**XO**), the individual is described as **heterogametic**. Gametes formed in a heterogametic individual are dissimilar. The reproductive organs that produce gametes form the 'primary sexual characters'. The various explanations given for sex determination are chiefly - **i**. **Chromosomal theory** of sex determination, **ii**. **Genic balance theory** of sex determination and **iii**. **Haplodipoidy method**

6.7.2 Heterogametic Sex Determination

Heterogametic sex refers to the sex of a species in which the sex chromosomes are not similar. The process of sex determination by allosomes is called **genetic** or **chromosomal sex determination**. In the heterogametic sex determination, one of the sexes produces 'similar' gametes and the other sex (heterogametic sex) produces dissimilar/unlike gametes. The sex of the young one is determined at the time of **syngamy** (**fertilization**). It depends on which gamete of the two dissimilar gametes unites with the other gamete produced by the 'homogametic parent'.

1. Male Heterogamety

In this method of sex determination, the males (heterogametic) produce dissimilar gametes while females (homogametic) produce similar gametes.

Male heterogamety is of two kinds, **XX – XO type** and **XX – XY type** (XX refer to female).

A. XX – XO type

In some insects such as bugs, grasshoppers and cockroaches, females are with two X-chromosomes and males are with one X-chromosome in each somatic cell. **McClung** discovered this type in grasshoppers. The unpaired X-chromosome determines the male sex. The karyotype of the female (homogametic) is **AAXX** and that of the male (heterogametic) is **AAXO**. All the ova contain 'AX' complement of chromosomes and the sperms are of two types. One half of the sperms have 'AX' complement and the other half have 'A' complement of chromosomes. The sex of the offspring depends on the type of sperm that fertilizes the ovum.

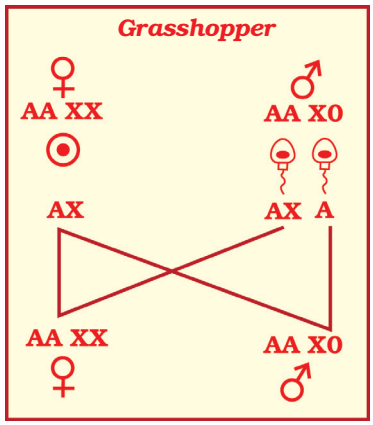


Figure 6.2 Sex determination in grasshopper

B. XX – XY type

In human beings and some insects such as *Drosophila*, both females and males have the same number of chromosomes. The karyotype of the female is **AAXX** and that of the male is **AAXY**. Females are 'homogametic' with 'XX' chromosomes. They produce similar ova having one X-chromosome each. Males are 'heterogametic' with X and Y-chromosomes. They produce two kinds of sperms; one half of them with X-chromosome and the other half with Y-chromosome. The sex of the offspring depends on the fertilizing sperm. The XX - XY type is also found in most other mammals.

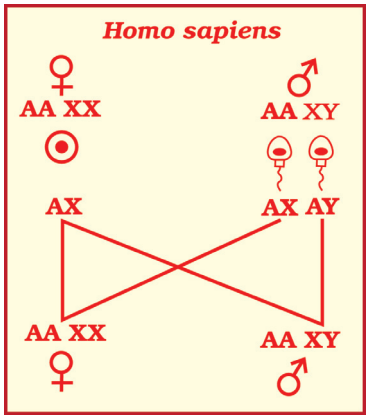


Figure 6.3 Sex determination in human being

2. *Female Heterogamety*

In this method of sex determination, the males produce 'similar gametes' while females produce 'dissimilar gametes'. Female heterogamety is of two kinds, **ZO – ZZ type** and **ZW – ZZ type**.

A. ZO - ZZ type

In moths (e.g., Fumea) and some butterflies, female is heterogametic with one Z-chromosome (ZO) and male is homogametic with two Z-chromosomes (ZZ). The karyotype of female is **AAZO** and male is **AAZZ**. Females

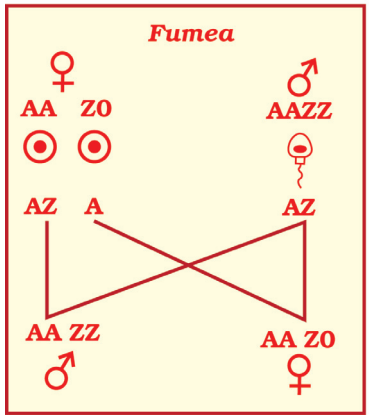


Figure 6.4 Sex determination in Fumea

produce two kinds of ova, half of them with a Z-chromosome and the other half with no sex chromosome. Males produce similar type of sperms. The sex of the offspring depends on the type of ovum that is fertilized.

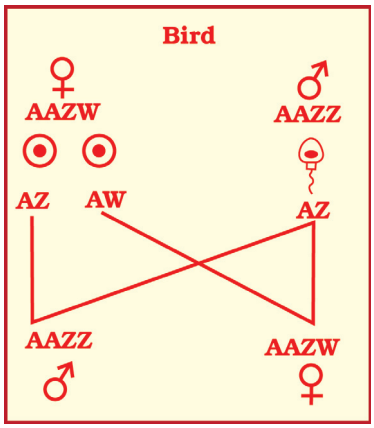


Figure 6.5 Sex determination in fowl

B. ZW – ZZ type

In birds, reptiles, some fishes, etc., the females are heterogametic with **ZW**- allosomes and males are homogametic with **ZZ** – allosomes. The karyotype of the female is **AAZW** and that of the male is **AAZZ.** All sperms are similar with the **allosome- Z**. Ova are of two different kinds; one half of the ova are with the **allosome- Z** and the other half with the **allosome-W**. The sex of the offspring depends on the type of ovum that is fertilized.

6.7.3 Sex Determination in Humans

It has already been mentioned that the sex determining mechanism in case of humans is **XX - XY type**. Out of 23 pairs of chromosomes present, 22 pairs are exactly same in both males and females; these are the autosomes. A pair of X-chromosomes is present in the female, whereas the presence of an X and Y-chromosome are determinant of the male characteristic. During spermatogenesis among males, two types of gametes are produced. 50 percent of the total sperm produced carry the X-chromosome and the rest 50 percent has Y-chromosome besides the autosomes. Females, however, produce only one type of ovum with an X-chromosome. There is an equal probability of fertilisation of the ovum by the sperm carrying either X or Y-chromosome. In case the ovum is fertilised by a sperm carrying X-chromosome, the zygote develops into a female and the fertilisation of ovum with Y-chromosome carrying sperm results into a male offspring. Thus, it is evident that it is the genetic makeup of the sperm that determines the sex of the child. It is also evident that in each pregnancy there is always 50 per cent probability of either a male or a female child.

NOTE: *It is unfortunate that in our society women are blamed for producing female children and have been ostracised (to exclude from the society) and ill-treated because of this false notion.*

6.7.4 Genic Balance Theory

By studying the Chromosomal theory of sex determination, it may appear at first glance that some genes carried on the sex chromosomes, for example, X

and Y are entirely responsible for determining the sex of the offspring. But this is not always true.

The **Genic Balance Theory** of determination of sex was proposed by **Bridges** while working on *Drosophila*. This theory explains the mechanics of sex determination in *Drosophila melanogaster*. According to his concept, the sex of an individual is determined by the 'balance' between the genes for femaleness located on the X-chromosome and those for maleness located on the 'autosomes'. Hence, the sex of an individual is determined by the ratio of number of its X chromosomes and that of its autosomal sets, the 'Y' chromosome taking no part in the determination of the sex. The ratio is termed **sex index** and is expressed as follows.

Sex index = Number of X chromosomes / Number of sets of autosomes (X/A)

Bridges studied the offspring resulting from the non-disjunction of X-chromosomes during meiosis in females. **Non-disjunction** (not coming apart) is the failure of paired chromosomes to segregate or separate during the anaphase stage of the first or second meiotic divisions. The result is the production of gametes with abnormal numbers of chromosomes. There were various types of gametes such as the ones which contained one extra X-chromosome (**AXX**) and some others contained one chromosome less (**AO**). Syngamy of such gametes and normal gametes produces zygotes with **aneuploid** karyotypes such as **2n+1**, **2n-1** etc. AAXO male is produced when an unusual ovum (AO) in the female is fertilised by a sperm with AX chromosome complement. An 'AAXXY female' is produced when an unusual ovum with AXX and a sperm with AY fuse. Bridges found that the 'AAXXY flies' were 'fertile females' and 'AAXO flies' were 'sterile males'. It is important to note that the presence of Y-chromosome in the 'AAXXY flies' did not cause maleness, and its absence in the 'AAXO flies' did not produce femaleness.

When Bridges crossed triploid females (**AAAXXX**) with normal diploid males (**AAXY**), he obtained normal diploid females, males, triploid females,

Table 2 Chromosome complements and Sexual phenotypes in Drosophila

Sex Chromosome Complement	Haploid Sets of Autosomes	X : A Ratio	Sexual Phenotype
XX	AA	1.0	Female
XY	AA	0.5	Male
XO	AA	0.5	Male
XXY	AA	1.0	Female
XXX	AA	1.5	Metafemale
XXXY	AA	1.5	Metafemale
XX	AAA	0.67	Intersex
XO	AAA	0.33	Metamale
XXXX	AAA	1.33	Metafemale

intersexes, super males and super females. The occurrence of triploid intersexes from such a cross clearly established that autosomes have a role with determination of sex.

Bridges realized that the critical factor in determining sex is the ratio of X chromosomes to the number of haploid sets of autosomes (A) present. He concluded that Y-chromosome in *Drosophila* lacks male determining factor, **TDF** (encoded by the **SRY gene - Sex-determining Region Y**). However, the Y-chromosome of *Drosophila* is required for **male fertility**. In 'XO males', sperms develop but are non-motile.

NOTE : Females have a ratio equal to **1.0**. If the ratio is **>1.0**, such females are called **super females/metafemales**, and they are 'infertile'. Normal males have a ratio of X-chromosomes to sets of autosomes of **0.5**. When the ratio is **< 0.5** the males are called **super males/ metamales**, and they are infertile. If the ratio is **between 0.5 and 1.0**, the flies are called **intersexes**, which are larger, with morphological abnormalities and rudimentary bisexual gonads. The investigations on *Drosophila* by **Bridges** showed that female determiners are located on the **X**-chromosomes and the male determiners are on the **autosomes.**

6.7.5 Haplodiploidy in honeybees

Haplodiploidy is a mechanism of sex determination that is common in the hymenopteran insects such as honey bees, ants, and wasps. In this system, the sex of the offspring is determined by the number of sets of chromosomes, it receives. Fertilized eggs develop into females, and unfertilized eggs develop (**parthenogenesis**) into males (drones). This means that the males have half the number of chromosomes (haploid) and the females have 'double' the number (diploid), hence the name 'haplodiploidy' for this system of sex determination.

In ***Apis mellifera***, drones are haploid with 16 chromosomes, queen and worker bees are diploid with 32 chromosomes in each somatic cell. Males produce sperms by mitosis. As per this type, males have no father and they cannot have sons, but they do have grandfathers and grandsons. Female that feeds on royal jelly becomes the fertile queen. Other females that feed on honey and pollen become sterile females called worker bees. If a queen bee mates with one drone, her daughters share ¾ of their genes with each other and not ½ as in the XY and ZW systems.

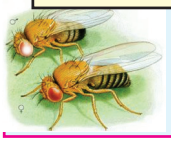
Barr Bodies

In mammals, males are heterogametic (XY) and females, homogametic (XX). As the female has two copies of the X chromosome, **Dosage Compensation** is achieved by the random inactivation of one of the two 'X' chromosomes. The extra X-chromosome undergoes **heterochromatinisation** and becomes inactive during early embryonic development. The descendant cells inherit the same inactivated X chromosome. The heterochromatinized X-chromosome appears as a darkly-staining body attached to the nuclear membrane. This phenomenon was first described by **Murray L. Barr** and the **heterochromatinised X chromosomes** are now called **Barr Bodies**.

Barr and **Bertram** observed chromatin bodies in the nerve cells of female cats that were not present in the cells of the male. In humans, this body can be easily demonstrated in the female cells derived from the buccal mucosa (cheek cells) or in fibroblasts (undifferentiated connective tissue cells), but not in similar male cells. A Barr body appears as a small drumstick-like projection (drumstick appendage) on one of the lobes of some neutrophils in females . With this technique, the sex of human embryos can be distinguished at early stages of development. This cellular characteristic generally seems to apply to all mammals.

X-inactivation (also called **Lyonisation,** proposed by **Mary Lyon** and **Liane Russell**) is a process by which one of the two copies of the X-chromosome present in the body cells of female mammals is inactivated. The inactive X-chromosome is 'silenced' by making it a **transcriptionally inactive** structure called **heterochromatic body**. As female mammals have two X-chromosomes in each cell, X-inactivation in their cells causes them not to have twice as many products of the X-chromosomal genes as those of the males which possess a single copy of the X-chromosome in each cell (**Dosage Compensation**).

NOTE : Regardless of how many X-chromosomes a somatic cell possesses, all but one of them appears to be inactivated and can be seen as **Barr bodies**. For example, no Barr body is seen in the somatic cells of Turner females 45, XO; one is seen in Klinefelter males 47,XXY; two in 47,XXX females; three in 48,XXXX females; and so on. Therefore, the number of Barr bodies follows an **N-1 rule (N minus one rule)**, where **N** is the total number of X-chromosomes present.



NOTE : *The female progeny share between them 50% of the mother's genes (16 out of 32) and 100% of the male parent's genes (entire male genome of 16 chromosomes). It accounts for 50+100=150 out of a possible 200 (considering the male genome of 16 chromosomes as 100% of male genes). It amounts to saying that the female progeny share between them 150 out of a possible 200 parental units (genes), which is equal to* ¾ *or* **75%** *and not 50% as seen in human beings.*

6.8 Sex – Linked Inheritance

The inheritance of a trait that is determined by a gene located on one of the sex chromosomes is called **sex-linked inheritance**. This mode of inheritance is in contrast to the inheritance of traits controlled by the autosomes, where both the sexes have the same probability of inheritance. Sex linked inheritance depends on how the chromosomes (allosomes) determine the sex.

Sex Linkage in *Drosophila*

Thomas H. Morgan (Father of Modern Genetics) discovered **sex linkage** in *Drosophila melanogaster*. Morgan wanted to analyze the behavior of the two alleles of a fruit fly's eye-colour gene. When he crossed a white eyed (mutant) male to a normal (wild) red eyed female, in the F_1 generation all the males and females were red eyed. When the F_1 generation 'red eyed female' was crossed to a 'red eyed male', in the F_2 generation all the females were red eyed and 50 percent of the males were 'white eyed'. The white eyed trait from the male is

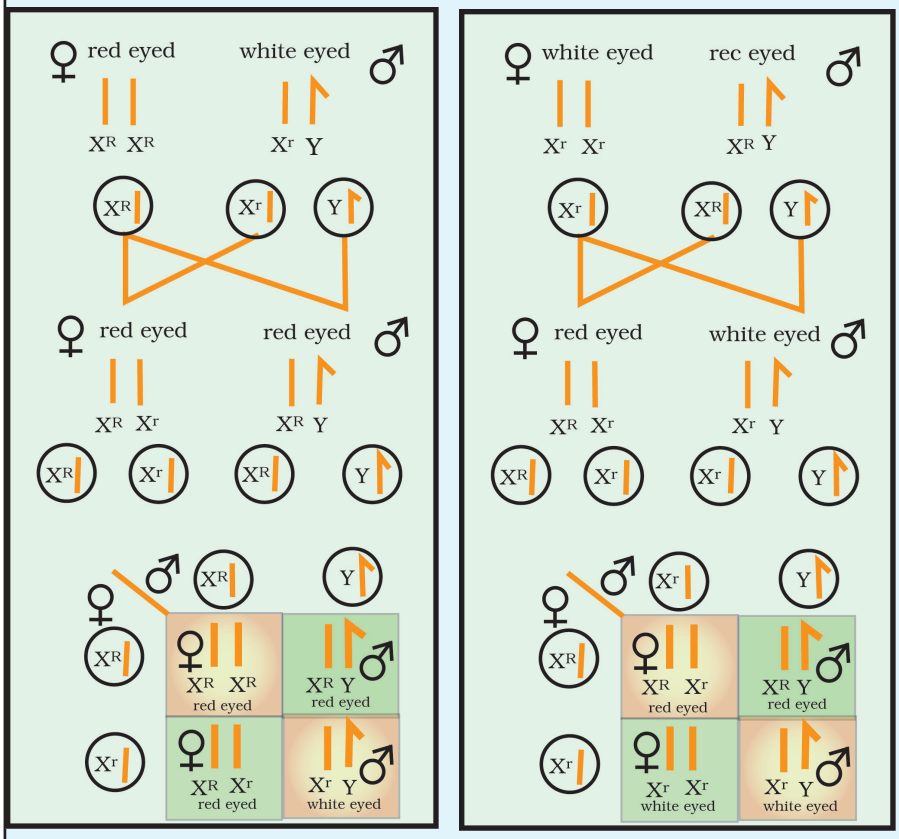


Figure 6.6 Sex linkage in *Drosophila melanogaster*

inherited to the male of the F_2 generation through the 'carrier daughter' of the F_1 generation. This pattern of inheritance is called **crisscross pattern of inheritance (skip gene-ration inheritance)** in which a gene responsible for the white eyes is transmitted from a male parent to a male grandchild through carrier female of the first generation.

In a **reciprocal cross** (to test the role of parental sex on inheritance pattern), in which a white eyed female was crossed to a red eyed male, the results were different. The first generation male offspring had white eyes while the female offspring had red eyes. The reason was that the allele responsible for the white eye is **sex-linked** (more specifically X-linked, as it occurs on the X-chromosome) and **recessive**. Males always inherit the X-linked recessive traits from the female parents.

Morgan's discovery that transmission of the X-chromosome in *Drosophila* correlates with the inheritance of an eye-color trait was the first solid evidence indicating that a specific gene is associated with a specific chromosome.

6.8.1 Sex-linked Genes

Genes that are present on the X or Y-chromosome are called **sex-linked genes**. The genes located on the X-chromosome, whose alleles are absent on the Y-chromosome are called **X-linked genes**. Male human beings are **hemizygous** and females are **homozygous** or **heterozygous** for these alleles. The genes located on the Y-chromosome, whose alleles are absent on the X-chromosome are called **Y-linked genes** or **holandric genes**. Males are hemizygous for these alleles also. X-linked and Y-linked genes (on their non-homologous parts) do not undergo pairing or crossing over during meiosis. The genes which are located on the **homologous segments** (**pseudoautosomal regions**) of the X and Y-chromosomes are called **XY-linked genes**. These are also called **incompletely sex-linked genes** as these regions undergo pairing and crossing–over.

6.8.2 Sex-linked inheritance in Human beings

Characters in individuals may be classified into two categories – those which do not show any difference in the pattern of inheritance in reciprocal crosses and those which are inherited differently in reciprocal crosses. The characters of the first category occur on the **autosomes**, while those of the second category are on the **sex chromosomes**. The sex chromosomes carry **sex-linked genes** for some traits that are unrelated to sex characteristics and the inheritance is called **sex linked inheritance**. While most Y-linked genes help determine sex, the X chromosomes have genes for many characters unrelated to sex.

1. X-Linked inheritance

Genetic diseases caused by mutations of genes on the X-chromosome have specific characteristics. X-linked diseases are mostly recessive and restricted to the males who carry the mutant allele. This is because males have only one X-chromosome, whereas females have two. Thus, females who carry a single mutant allele are generally unaffected.

2. X-Linked Recessive Inheritance

X-linked recessive inheritance is the of inheritance in which a mutation in a gene on the X-chromosome causes the phenotype to be expressed in males (who are necessarily hemizygous for the 'recessive allele' and they have only one X chromosome) and in the females who are homozygous for the allele (i.e., they have a copy of the allele on each of their two X chromosomes). Affected males get the allele from their mothers. If a female is homozygous affected, all her sons are affected. All affected females have an affected father and a carrier or affected mother. X-linked recessive traits are typically passed on from an affected father to 50 percent of his grandsons through carrier daughter. The most common X-linked recessive disorders are Haemophilia, Colour blindness (protanopia and deuteranopia), Duchenne muscular dystrophy etc.

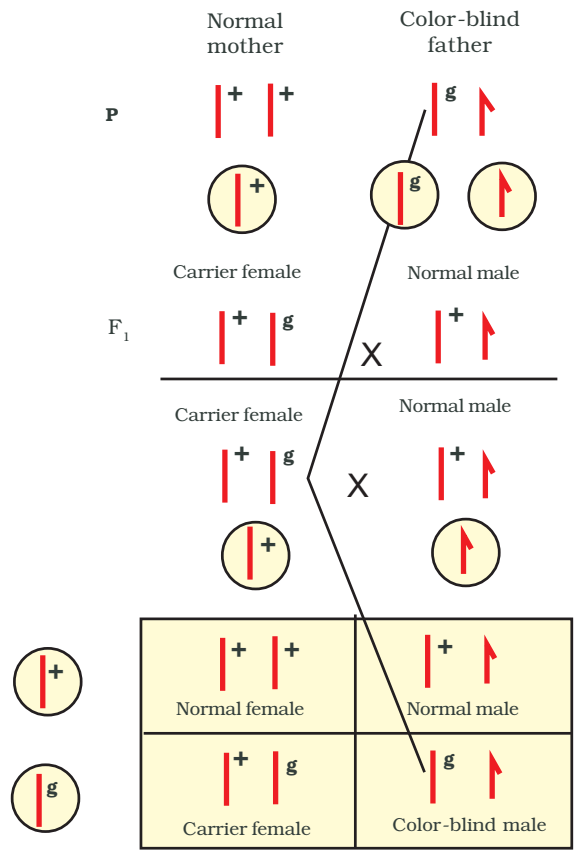


Figure 6.7 : X-linked recessive inheritance - Colour blindness

A. Colour blindness

Two types of colour blindness are sex-linked recessive disorders. Retina of the eye in man contains the cells sensitive to red and green colours. This phenotypic trait is genetically controlled. Its alleles are located on the X-chromosome. When a woman with normal vision (homozygous) marries a colour-blind man, all the sons and daughters are normal, but daughters are '**carriers**' (heterozygous). If a carrier woman marries a man with normal vision,

* Dystrophin is a protein that connects cytoskeleton of a muscle fiber to the surrounding extra cellular matrix through the cell membrane. These links help to dissipate the contractile force of the muscular cytoskeleton to the extracellular matrix.

all the daughters and half of the sons have normal vision and the other half of the sons are colour-blind. Colour-blind trait is inherited from a male parent to his grand sons through carrier daughter, which is an example of crisscross pattern of inheritance.

B. Haemophilia

Haemophilia A is a recessive X-linked genetic disorder involving lack of the functional clotting **Factor- VIII** and accounts for about 80% of haemophilia cases. **Haemophilia B** is also a recessive X-linked genetic disorder involving lack of the functional clotting **Factor IX**. When a person with hemophilia is injured, bleeding is prolonged because a firm clot is slow to form. Haemophilia follows the characteristic crisscross pattern of inheritance like that of colour-blindness.

Duchenne muscular dystrophy

Duchenne muscular dystrophy (DMD) is a recessive X-linked form of muscular dystrophy, affecting around 1 in 3,600 boys. The disease is characterized by a progressive weakening of the muscles and loss of coordination. Affected individuals rarely live past their early 20s as they do not posses the protein dystrophin. The disorder is caused by a mutation in the **dystrophin gene** (the largest known gene in humans) located on the X-chromosome, which codes for the protein **dystrophin***, an important structural component within muscle tissue (connects sarcolemma and the outer muscle filaments and supports muscle fiber strength). If the mother is known to be a carrier of this gene, one half of her male children are expected to be affected. All female children born to a carrier mother do not suffer from DMD, are expected to be normal, since the possibility of their being homozygous for this sex-linked recessive gene is virtually non-existent.

X-Linked Dominant Inheritance

X-linked dominant inheritance is a mode of genetic inheritance transmitted by a dominant allele carried on the X chromosome with reference to inheritance pattern, it is less common than the X-linked recessive type. X-linked dominant inheritance indicates that the allele responsible for a genetic disorder is located on the X chromosome, and only one copy of the allele is sufficient to cause the disorder when inherited from a parent who has the disorder. The exact pattern of inheritance varies, depending on whether the father or the mother has the trait of interest. All daughters of an affected father will be affected but none of his sons will be affected if mother doesnot suffer from the disorder. If mother is homozygous affected, all her children are affected. Males are more severely affected than the heterozygous females, because males do not have a normal copy of the gene to balance the effects of the mutation on their single X-chromosome.

Presently, there are only a few known human X-linked dominant traits. They include: Follicular Hyperkeratosis, Incontinentia Pigmenti etc.

Follicular hyperkeratosis

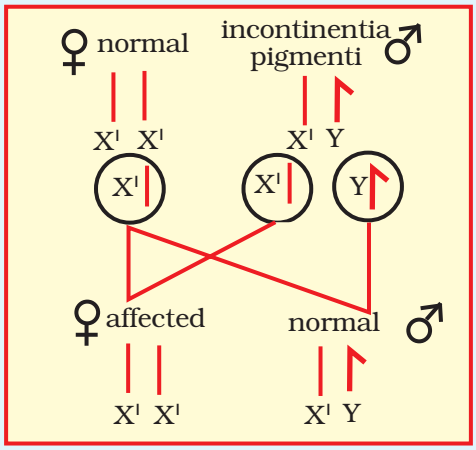


Figure 6.8 X-linked dominant inheritance

Follicular hyperkeratosis (also called **Phrynoderma**) is a skin condition characterized by excessive development of keratin in hair follicles, resulting in rough, cone-shaped, elevated papules. The openings are often closed with a white plug of encrusted sebum.

Incontinentia Pigmenti

Incontinentia pigmenti is an uncommon disorder. IP is inherited in an X-linked dominant manner. IP is lethal in most, but not all, males. A random loss of melanin from skin leads to mosaic appearance of skin. A female with IP may have inherited the mutant allele from either of parents or she might have had a new gene mutation in the very early development. Homozygous IP in female is lethal.

Y-Linked Inheritance

Y-linked inheritance is also called **holandric inheritance**. The genes controlling Y-linked characters, also called **holandric genes**, are located on the non-homologous part of Y-chromosome. Y-linked disorders are caused by mutations on the Y-chromosome. Because males inherit a Y-chromosome from their fathers, every son of an affected father will be affected. Because females only inherit the X chromosome from their fathers and they do not show the 'Y' linked disorder. Males are hemizygous for these genes. The **SRY gene** is on the **Y chromosome** and causes the development of male characteristics in humans. Y-linked characters in human being are hypertrichosis (excessive growth of hair on the pinna of the ear), webbing of toes, porcupine man (straight and stiff hair on the body).

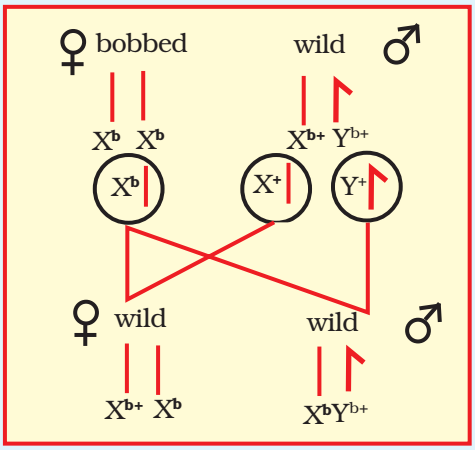


Figure 6.9 XY-linked inheritance in *Drosophila*

XY - Linked Inheritance

The probability of inheritance of traits by **XY-linked genes** (incompletely sex linked genes present on the pseudoautosomal regions of X and Y chromosomes) is similar in both sexes because they are homozygous or heterozygous for these traits. Unlike the autosomal genes of male, the genes on X-chromosome can be inherited only to females, whereas genes on Y-chromosome can be inherited only to males.

In *Drosophila*, XY-linked alleles for bobbed bristles occur on same loci of X-chromosomes in females. In males, these alleles are present on the X-chromosome and Y-chromosome (in the homologous regions). e.g. Bobbed condition in *Drosophila* is due to a recessive (mutant) allele (b). The normal allele is wild type (b^+).

Sex-Limited Inheritance

In contrast to X-linked inheritance, patterns of gene expression may be affected by the sex of an individual even when the genes are not on the X chromosome. **Sex-limited genes** are autosomal genes present in both males and females. Their phenotypic expression is limited to only one sex due to internal hormonal environment, e.g. beard in man, development of breast and secretion of milk in woman etc. are sex limited traits.

Sex-Influenced Inheritance

Sex-influenced genes are the autosomal genes present in both males and females. In sex-influenced inheritance, the genes behave differently in the two sexes, probably because the sex hormones provide different cellular environments in males and females. Thus, the heterozygous genotype may exhibit one phenotype in males and the contrasting one in females. Cases of sex-influenced inheritance include pattern baldness in humans, horn formation in certain breeds of sheep (e.g. Dorset Horn sheep).

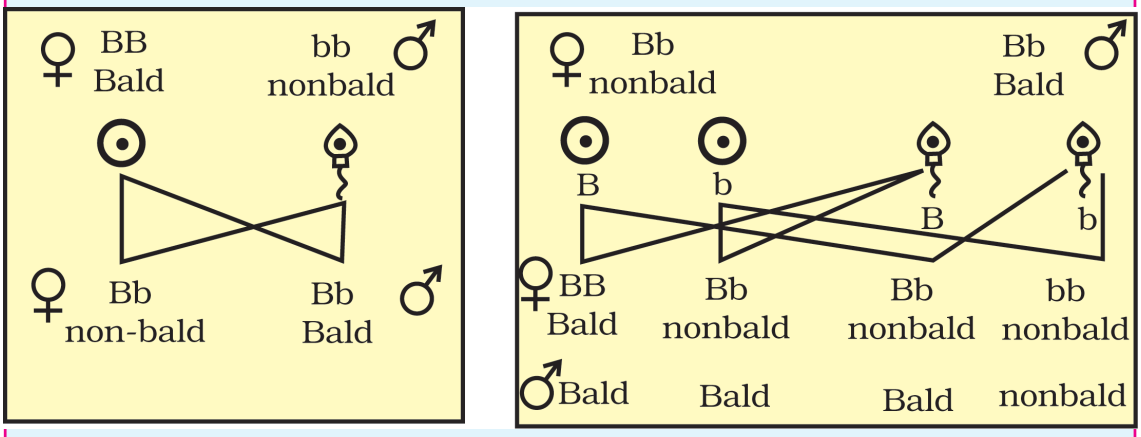


Figure 6.10 Inheritance of pattern baldness in human being

Pattern-baldness

The allele for baldness behaves dominant (B) in males but recessive (b) in females. The amount of thinning of the hair or balding that is observed depends both on genotype and the amount of testosterone exposure.

A male who is 'BB' will show severe balding. A female who is 'BB' will also be affected, and usually less severely, with thinning of the hair, rather than total loss. A male who is heterozygous (Bb) will also become bald, whereas a female who is heterozygous (Bb) will not be affected. Individuals of either sex who are fully recessive (bb) will not be affected. If a heterozygous non-bald woman (Bb) marries a heterozygous bald man (Bb), in the offspring the **ratio of bald to non-bald** in the male progeny is **3 : 1**, while in females it is **1: 3.**

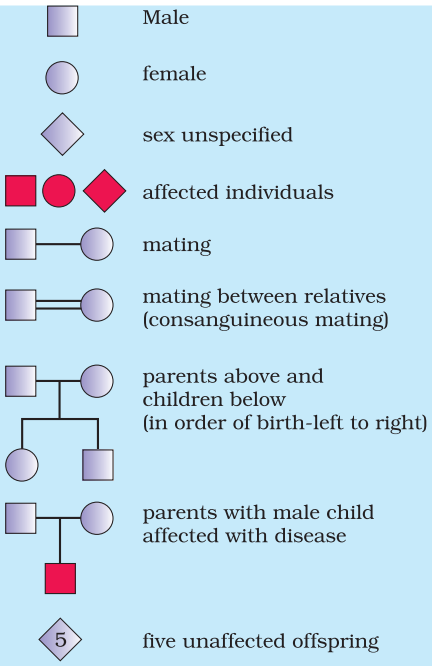


Figure 6.11 Symbols used in the human pedigree chart

Pedigree Analysis

Scientists have devised an approach called **pedigree analysis**, to study the inheritance of a specific trait, abnormality or disease. Pedigree is a chart showing the record of inheritance of certain traits over two or more ancestral generations of a person in the form of a diagram of **family tree** (**pedigree chart**). Pedigree analysis is useful in many ways like it helps to work out the possible genotypes from the knowledge of the respective phenotypes. It helps to study the pattern of inheritance of a dominant or a recessive trait. The possible genetic makeup of a person for a trait can also be known with the help of the pedigree chart. Some of the important standard symbols used in the pedigree analysis are shown in the figure.

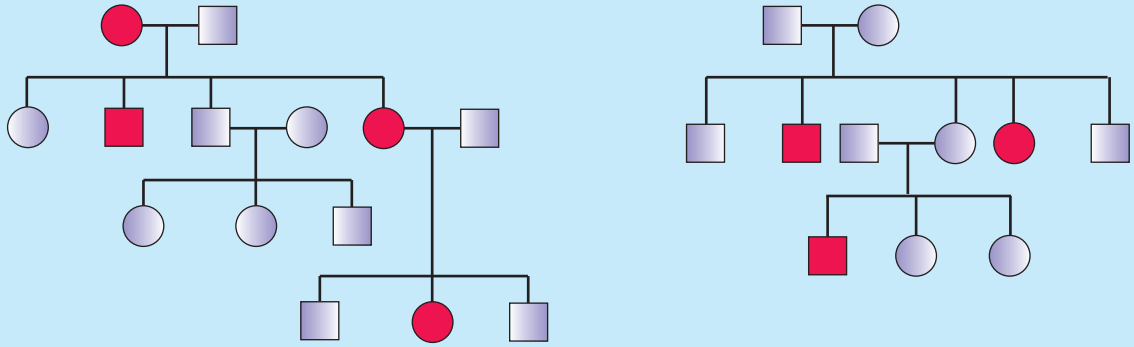


Figure 6.12 Representative pedigree chart for the analytsis of (a) Autosomal dominant trait (for example: Myotonic dystrophy) (b) Autosomal recessive trait (for example: Sickle-cell anaemia)

6.9 Genetic Disorders

A genetic disorder is a disease or syndrome that is caused by an abnormality in an individual's DNA. Abnormalities can range from a small mutation in a single gene to the addition or subtraction of an entire chromosome or even a set of chromosomes. The occurrence of genetic disorders is based on the heritability of certain characteristic features in families. After the rediscovery of Mendel's work, the practice of analyzing the pattern of inheritance of traits in human beings began. As controlled crosses can be performed in pea

plants and some other organisms and not possible in human beings, alternative studies were made to study the family history about the inheritance of a particular trait.

A number of disorders in human beings have been found to be associated with the inheritance of changed or altered genes or chromosomes. Genetic disorders may broadly be grouped into two categories – **Mendelian disorders** and **Chromosomal disorders**.

6.9.1 Mendelian disorders

Mendelian disorders are genetic diseases showing **Mendelian pattern of inheritance**, caused by a single mutation in the structure of DNA, which causes a single basic defect with pathologic consequences, in some cases. Mendelian disorders are also called **monogenic diseases.** Monogenic diseases run in families and can be dominant or recessive and autosomal or sex-linked (allosomic). The pattern of inheritance of Mendelian disorders can be traced in a family with the help of pedigree charts and their analyses.

The most common and prevalent Mendelian disorders are Haemophilia, Cystic fibrosis, Sickle-cell anaemia, Colour blindness, Phenylketonuria, Thalassemia, DMD, Albinism, etc.

1. Haemophilia

Haemophilia A (caused by deficiency of clotting factor VIII) and **Haemophilia B** (caused by deficiency of clotting factor IX) are X-linked recessive disorders that impair the body's ability to control clotting or coagulation of blood. **Haemophilia C** is an autosomal recessive disorder involving lack of the functional clotting 'factor XI'. Haemophilia is also called **bleeder's disease**. Haemophilia A and B follow the characteristic **crisscross pattern of inheritance** like that of colour-blindness. In this disease, a single protein that is a part of the cascade of reactions involved in the clotting of blood is affected.

Haemophilia is more likely to occur in males than in females. This is because females have two X-chromosomes while males have only one, and so the defective gene on the X will certainly express in the male who carries it. As it is caused by a recessive allele on the X chromosome, a female human being has to be 'double recessive' to express haemophilia. Because the chance of a female having two defective copies of the gene (alleles) is very remote, the females are mostly **asymptomatic carriers** of the disorder. The 'allele' is typically passed on from an affected father to 50% of his grandsons through his 'carrier daughters'. The family pedigree of **Queen Victoria** shows a number of haemophilic descendents, as she was a carrier for the disease.

2. Sickle-cell anaemia

Sickle-cell anaemia is an autosomal recessive genetic blood disorder characterized by red blood cells that assume an abnormal, rigid, sickle shape in hypoxia conditions (at high altitudes or under physical stress, for instance). Sickled cells may clump and clog small blood vessels, often leading to other symptoms throughout the body, including physical weakness, pain, organ damage, and even paralysis.

This disease is controlled by a single pair of alleles, Hb^A and Hb^S found on the chromosome 11. The homozygous individuals for sickle-cell anaemia **(Hb^S Hb^S)** express the diseased phenotype. Heterozygous individuals **(Hb^A Hb^S)** appear 'unaffected' but they are still, carriers of the disease. Even though two sickle cell alleles are necessary to cause sickle cell anaemia, one dose can affect the phenotype. Persons 'heterozygous' to sickle cell trait can usually lead a healthy life but in prolonged periods of reduced oxygen content in the blood may suffer from symptoms of SCD as both normal and sickle cell haemoglobin are formed in them.

Sickle cell anaemia is caused by a **point mutation** in the DNA that codes for the beta globin polypeptide chains of the haemoglobin molecule, causing the replacement of the **glutamic acid** in the sixth position by **valine.** The

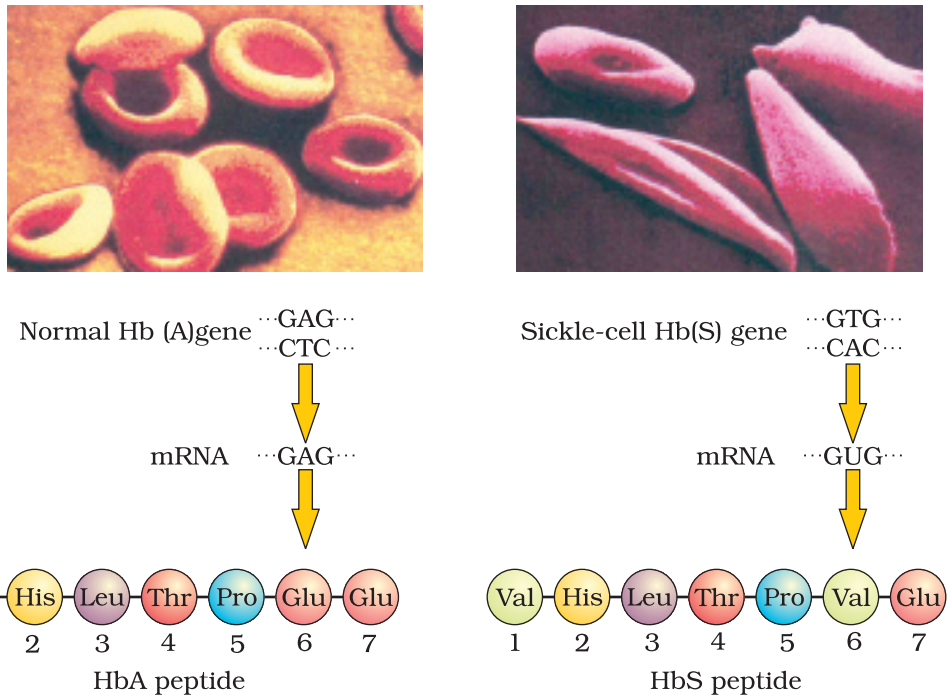


Figure 6.13 Micrograph of the red blood cells and the amino acid composition of the relevant portion of β-chain of haemoglobin: (a) From a normal individual; (b) From an individual with sickle-cell anaemia

heterozygous individuals are relatively resistant to the most severe effects of malaria such as those of 'falciparum malaria' also (although they are not resistant to malaria infection) – an effect called **heterozygote advantage**. The heterozygous individuals carry the deleterious alleles in their genomes (**genetic load**).

3. Phenylketonuria [PKU]

Phenylketonuria was discovered by **A. Folling**. This is an autosomal recessive, metabolic genetic disorder caused by a mutation in the gene (**PAH-Phenylalanine hydroxylase gene**) located on the chromosome 12 for the hepatic enzyme 'phenylalanine hydroxylase'. The affected individual lacks the above mentioned enzyme that converts the amino acid **phenylalanine** into **tyrosine**. When phenylalanine hydroxylase's is absent, phenylalanine accumulates and is converted into **phenylpyruvate** (also known as phenylketone) and other derivatives. Accumulation of these substances in the brain causes mental retardation. Adherence to a low phenylalanine diet prevents major mental retardation.

Colour blindness

Colour blindness (**colour vision deficiency**) is a sex-linked recessive disorder. It is the inability or decreased ability to see certain colours or perceive differences between some colours. This phenotypic trait is due to mutation in certain genes located on X-chromosome. The most common inherited forms of colour blindness are **Protanopia** (red colour blindness), **Deuteranopia** (green colour blindness) and **Tritanopia** (blue colour blindness which is autosomal).

The son of a woman who carries one allele has a 50 percent chance of being colour-blind. The mother herself is not colour-blind because the allele is recessive. That means its effect is suppressed by her matching dominant normal allele. A daughter will not normally be colour blind, unless her mother is 'colour-blind' or a 'carrier' and her father is colour-blind. The **Ishihara colour test**, which consists of a series of pictures of coloured spots, is most often used to diagnose red-green colour blindness.

4. Thalassemia

Thalassemia is an autosome linked recessive blood disorder. This disease is caused by the excessive destruction or degradation of red blood cells due to formation of abnormal haemoglobin molecules, because of defects caused by genetic mutations. Normally, haemoglobin is composed of four polypeptide chains, two **alpha** and two **beta globin chains** arranged into a heterotetramer. In the case of thalassemia, patients have defects in either the alpha or beta

globin chain (unlike sickle-cell anaemia, which is caused due to a specific change in the beta chain), causing production of abnormal haemoglobin molecules resulting in anaemia which is characteristic of the disease.

Thalassemias are classified based on which chain of haemoglobin molecule is affected. In **Alpha thalassemia**, the production of alpha globin chain is affected. Alpha thalassemia is controlled by two closely linked genes **HBA1** and **HBA2** on chromosome 16 of each parent and it is caused due to mutation or deletion of one or more of the four alpha gene "alleles". The more genes affected, the less alpha globin molecules are produced and more severe in the disease. In **Beta thalassemia (Cooley's Anaemia)** production of beta globin chain is affected. The Beta thalassemia is controlled by a single gene **HBB** on the chromosome 11. It is the most common type of thalassemia. In this disorder the alpha chains wihch are relatively more in number bind to the RBCs and damage the membranes of RBC.

5. Cystic fibrosis

Cystic fibrosis is an autosomal recessive genetic disorder. CF is the result of mutations affecting a gene on the long arm of chromosome 7 that influences salt and water movement across epithelial cell membranes. The genetic defect causes increased sodium and chloride content in sweat and increased resorption of sodium and water from respiratory epithelium. The extracellular chloride causes the mucus that coats the cells to become more viscous and sticky. The mucus clog builds up in organs such as lungs, pancreas, GI tract etc. and leads to further complications and may lead to death by the age five, if untreated.

6. Alkaptonuria

Alkaptonuria is a rare genetic disorder due to recessive gene in autosomes. In this disorder the urine of affected persons becomes black when it is exposed to air. (Gk. Alkapton - black). When our body is unable to utilise the aminoacids phenyl aniline and tyrosine properly, homogentisic acid or alkapton is accumulated in the tissues of skin and catilages. When it is eliminated through urine, on exposure to air, it becomes black. Alkaptonuria is resulted when homogentisate 1, 2 dioxugemase (enzyme) is not produced in sufficient amounts. This condition is due to a mutation in the HGD gene (homogentisate dioxygenase gene). The affected persons suffer from joint pains (especialy in vertebral column), blackening of cartilages, formation of black spots in retina and sclera of eye. The pinnae, tip of nose become black due to accumulation of alkaptone.

6.9.2 Chromosomal disorders

Chromosomal disorders are caused by errors in the 'number' or 'structure' of chromosomes. Chromosomal anomalies usually occur when there is an error

in cell division. **Aneuploidy** is a chromosomal aberration where there is a gain or loss of one or more chromosomes in a 'set'. It is caused by **non-disjunction of chromosomes**. The result of this error is origin of cells with a deviation from the normal number of chromosomes – aneuploidy.

NOTE : Monosomy (**2n-1**) is a chromosomal aberration where one chromosome is lost from a pair. Monosomy 23 (loss of an X chromosome) causes a syndrome called **Turner's syndrome** in human females. **Trisomy** (**2n+1**) is a chromosomal aberration where one chromosome is added to the already existing homologous pair. When a chromosome is added to the 21st pair of autosomes, it is called **trisomy 21**. Trisomy 21 in man causes a syndrome called **Down syndrome**. Trisomy of sex chromosomes is due to the addition of one sex chromosome. It causes a syndrome called **Klinefelter's syndrome**.

A. Allosomal disorders

i. Klinefelter's syndrome

This genetic disorder is caused by **trisomy 23rd pair in males**. The karyotype is **47, XXY**. A **Klinefelter male** possesses an additional X-Chromosome along with the normal XY. The principal effects include hypogonadism and reduced fertility. At the same time, feminine sexual development is not entirely suppressed. Slight enlargement of the breasts (**gynecomastia**) is common. The somatic cells of a Klinefelter male exhibit Barr bodies in their nuclei.

NOTE : ***Karyotype 47, XXY****. Note the convention used in designating these chromosome compositions: the number states the total number of chromosomes present, and the symbols after the comma indicate the deviation from the normal diploid number.*

ii. Turner's syndrome

The Karyotype is **45, X**. It is due to **monosomy 23rd pair,** where one X-chromosome is lost. A **Turner female** does not show Barr bodies in her somatic cells. The symptoms are short stature, gonadal dysgenesis, webbed neck and broad shield like chest with widely spaced nipples.

B. Autosomal disorders

Most of the following disorders are common in children born to women who conceive babies rather late in their reproductive phase.

Down syndrome (Trisomy 21)

Down syndrome is a genetic condition that causes delays in physical and intellectual development. The cause of this genetic disorder is the presence of an additional copy of the chromosome numbered 21 (**trisomy of 21st set**).

The karyotype is designated as **Trisomy 21** (**47,+21**). The affected individual is short statured with small round head, furrowed tongue and partially open mouth. Physical, psychomotor and mental development is retarded.

Edwards syndrome (Trisomy 18)

Edwards syndrome (**47,+18**) is a chromosomal abnormality characterized by the presence of an extra copy of the genetic material of the 18th chromosome, either in whole (**trisomy 18**) or in part (such as due to translocations). Edwards syndrome occurs in both males and female but is more common in the female offspring. The majority of people with the syndrome die during the foetal stage; infants who survive experience serious defects (cardiac abnormalities and kidney malfunction) and commonly live for short periods of time.

Patau syndrome (Trisomy 13)

Patau syndrome, is a chromosomal condition associated with severe intellectual disability and physical abnormalities in many parts of the body. Most cases of **trisomy 13 (47,+13)** result from having three copies of chromosome 13 in each cell in the body instead of the usual two copies. Individuals with trisomy 13 often have heart and kidney defects, brain or spinal cord abnormalities, very small or poorly developed eyes (microphthalmia), cleft palate etc. Due to the presence of several life-threatening medical problems, many infants with trisomy 13 die within their first days or weeks of life.

Cri-du-Chat syndrome (5p minus syndrome)

Cri-du-chat syndrome (cat-cry) is due to a partial deletion of the short arm of chromosome 5, (also called **5p monosomy)**. It might be considered a case of partial monosomy, but since the region that is missing is so small, it is better referred to as 5p segmental deletion. The karyotype is **46,5p$^-$**. It is a French term referring to the characteristic cat-like cry of the affected children due to problems with the larynx and nervous system. Such infants are mentally retarded, have a small head with unusual facial features. They die in infancy or early childhood.

Chronic Myelogenous (Myeloid) Leukemia (CML)

In certain cancers such as **Chronic myelogenous leukemia** (also called **Chronic granulocytic leukemia**), a piece of the chromosome 9 and a piece of the chromosome 22 break off and 'switch places' (exchange places) with each other (**reciprocal translocation**). This results in the formation of an abnormally **short chromosome 22** and abnormally **long chromosome 9**. The short 22nd chromosome is called **Philadelphia chromosome** produced by translocation which is also called **Philadelphia translocation**. The karyotype is **46, t(9 ; 22)**. The Philadelphia chromosome results in the production of an abnormal enzyme called a **tyrosine kinase**. Along with other abnormalities, this enzyme causes uncontrolled cell cycle progression leading to the cancer called chronic myelogenous leukemia.

6.10 Human Genome Project

6.10.1 What is a chromosome/DNA?

Chromosome is a chain of DNA wrapped in a proteinous pellicle (eukaryotic chromosome). DNA consists of a linear series of **nucleosomes**. A nucleosome consists of a group of protein molecules (8 molecules of histone protein) wrapped around twice by DNA. The dense mass of loops and coils inside the nucleus constitute the **chromatin**. Chromatin occurs in two forms - the deeply staining **heterochromatin** and the light staining **euchromatin**. Some DNA codes for specific proteins which control the structure and functioning of the body of the organism – in this case, man. Some DNA is involved in regulating the expression of the genes that code for specific proteins (e.g. repressor protein). The remaining nonfunctional DNA is called **Junk DNA**.

A **genome** (whole hereditary information encoded in DNA/a set of DNA instructions in a cell) is an organism's complete set of deoxyribonucleic acid (DNA) molecules. DNA is a chemical compound that contains the genetic instructions needed to develop and direct the activities of every organism (in the form of a set of chromosomes). The genetic make-up of an organism or an individual lies in the DNA sequences. If two individuals differ, then their DNA sequences should also be different, at least at some places. These assumptions led to the quest of finding out the complete DNA sequence of human genome.

6.10.2 What is Human Genome Project?

Human Genome Project (HGP) was a mega project. It was an International efforts formally begun in October 1990. The HGP was a 13-year project coordinated by the **U.S. Department of Energy** and the **National Institute of Health**. During the early years of the HGP, the **Wellcome Trust (U.K.)** became a major partner, and additional contributions came from Japan, France, Germany, China and others. The project was almost completed by 2003. Knowledge about the effects of DNA variations among individuals can lead to revolutionary new ways to diagnose, treat and someday hopefully prevent thousands of disorders that affect human beings. HGP was closely associated with the rapid development of a new area in biology called **Bioinformatics**.

Besides providing clues to understanding human biology, learning about non-human organisms' DNA sequences can lead to an understanding of their natural capabilities that can be applied towards solving challenges in health

care, agriculture, energy production, environmental remediation. Genomes of many non-human model organisms, such as bacteria, yeast, *Caenorhabditis elegans* (a free living non-pathogenic nematode), *Drosophila*, plants (rice and *Arabidopsis*), etc. have also been sequenced. In a way they helped the progress of HGP.

6.10.3 Goals of HGP

Some of the important goals of HGP were as follows:

i) Identify all the approximately 30,000 genes in human DNA.
ii) Determine the sequences of the 3 billion chemical base pairs that make up human DNA.
iii) Improve tools for data analysis.
iv) Address the ethical, legal, and social issues (**ELSI**) that may arise from the project.

6.10.4 Methodologies

The methods involved two major approaches. One approach focused on identifying all the genes that expressed as RNA (referred to as **Expressed Sequence Tags (ESTs)**. The other took the blind approach of simply sequencing the whole set of genome that contained all the coding and non-coding sequence, and later assigning different regions in the sequence with functions (a term referred to as **Sequence Annotation**).

What is DNA sequencing?

DNA sequencing, the process of determining the exact order of the 3 billion paired chemical building blocks (called 'bases' - **A**, **T**, **C**, and **G**) that make up the DNA of the 24 different human chromosomes (23 + Y in a male), was the greatest technical challenge in the Human Genome Project.

For sequencing, the total DNA from a cell is isolated and converted into random fragments of relatively smaller size and cloned in a suitable host using specialized vectors. The cloning results in the amplification of DNA fragments which are used for sequencing the bases. The commonly used hosts are bacteria and yeast, and the vectors are called **BAC** (bacterial artificial chromosomes), and **YAC** (yeast artificial chromosomes). The fragments were sequenced using automated **DNA sequencers** that work on the principle of a method developed by **Frederick Sanger**. Alignment of these sequences was humanly not possible. Therefore, specialized computer based programs were developed. These sequences were subsequently annotated and were assigned to each chromosome. The latest method of sequencing even longer fragments, by a method called **Shotgun sequencing** using super computers, replaced the traditional sequencing methods.

6.10.5 Salient Features of Human Genome

Some of the salient observations drawn from human genome project are as follows:

i) The human genome consists of chromosoms made up of nucleotide base pairs.

ii) The average gene consists of 3000 bases, but sizes vary greatly, with the largest known human gene being the one that codes for the protein called **dystrophin**.

iii) The total number of genes is estimated at 30,000. Almost all (99.9 %) nucleotide bases are exactly the same in all people.

iv) The functions are unknown for over 50 % of the genes discovered.

v) Less than 2 per cent of the genome codes for proteins.

vi) Repeated sequences make up very large portion of the human genome.

vii) Repetitive sequences are stretches of DNA sequences that are repeated many times. They are thought to have no direct coding functions, but they shed light on chromosome structure, dynamics and evolution.

viii) **Chromosome 1** has the highest number of genes (**2,968**), and the **Y-chromosome** has the fewest genes (**231**).

ix) Scientists have identified about 1.4 million locations where single base DNA differences (**SNPs – single nucleotide polymorphism**, pronounced as **snips**) occur in humans. This information promises to revolutionise the processes of finding chromosomal locations for disease-associated sequences and tracing human history.

6.10.6 Advantages of HGP

1. In the area of health care, identification and mapping of the genes responsible for genetic diseases helps in diagnosis, treatment and prevention of these diseases.

2. Detailed knowledge of the genomes of humans and other species will give a clearer picture of Gene expression, Cellular growth and differentiation and evolutionary biology.

3. Earlier detection of genetic predispositions to disease, rational drug design, Gene therapy is going to be easy with more knowledge on human genome.

4. A new era of **Molecular Medicine**, characterized by looking into the most fundamental causes of disease than treating the symptoms will be an important advantage.

6.11 DNA Finger Printing

Introduction

Over 99.9% of the 3 billion nucleotide pairs in human DNA are identical among all individuals. No two people (other than identical twins) have exactly the same sequence of bases in their DNA. **Restriction Fragment Length Polymorphisms** (RFLPs -pronounced '**riflips**') are characteristic to every person's DNA. They are called **Variable Number Tandem Repeats** (VNTRs) and are useful as **Genetic markers**. The VNTRs of two persons generally show variations. DNA fingerprinting involves identifying differences in some specific regions in DNA sequence called **repetitive DNA**, because in these sequences, a small stretch of DNA is repeated many times. These sequences show high degree of polymorphism and form the basis of DNA fingerprinting. They are bits of chromosomes that can be cut by **restriction endonucleases**. The 'fundamental technique' involved in DNA Finger Printing was pioneered and perfected by **Jeffrys** of Great Britain. He observed that the gene pertaining to **myoglobin** of muscles contains many segments that vary in size and composition, from one person to another. For example in the following hypothetical example **nucleotide base sequence**, there are 6 Tandem Repeats of 16 bases each (count the first 16 and note how they are repeated)

5' GACTGCCTGCTAAGATGACTGCCTGCTAAGATGACTGCCTGCTAAGAT

GACTGCCTGCTAAGATGACTGCCTGCTAAGATGACTGCCTGCTAAGAT 3'

Such clusters of 10 -100 nucleotides are called **mini satellites**. Such tandem repeats are characteristic of every person's DNA. The VNTRs of two persons differ in the number of tandem repeats or the sequence of bases. Such changes are caused due to mutations and gene recombinations. For example a child might inherit a chromosome with 6 tandem repeats from the mother and the same tandem repeated 4 times from the father in homologous chromosomes. It means some of the VNTR segments of the child resemble those of the mother and the others, those of the father. This is a 'heterozygous condition with reference to VNTR segments'. These tandem repeats serve as basis of a technique called **DNA fingerprinting**.

NOTE : DNA fingerprinting, also known as **DNA Typing** or **Genetic Fingerprinting**, is a method for identifying individuals by the particular structure of their DNA. DNA fingerprinting is used for many purposes, particularly paternity/maternity testing and for forensic work. DNA can be obtained from blood, semen, vaginal fluid, hair roots, almost any tissue, and even from bones that have been buried for a long time, for fingerprinting. DNA fingerprinting is a technique by which the DNA of an individual can be compared with that found in a sample or another individual (a suspect in a crime).

6.11.1 DNA Fingerprinting-Protocol

1. **Obtaining DNA** (Isolation/Extraction) : The first step is to obtain a sample of DNA from blood, saliva, hair roots, semen etc. If needed many copies of the DNA can be produced by PCR (cloning/DNA amplification)
2. **Fragmenting DNA** (Restriction Digestion) : Treating DNA with Restriction Enzymes (Restriction endonucleases) which cut the DNA into smaller fragments by cutting it at specific sites.
3. **Separation of DNA fragments by electrophoresis** : DNA fragments are applied at one end of **agarose gel** plate. When an electric current is applied to the gel, the DNA fragments (which are slightly negatively charged) travel across the gel (smaller and more mobile pieces travel farther). This technique of separation of DNA fragments into individual bands is called **Gel Electrophoresis.**
4. **Denaturing DNA** : The DNA on the gel is 'denatured' using alkaline chemicals or by heating. (denaturing means separation/splitting of the double helix into 'single strands' by breaking hydrogen bonds between the two strands).
5. **Blotting** : A thin **nylon membrane** is placed over the 'size fractionated DNA strands' and covered by paper towels. As the towels draw moisture the DNA strands are transferred on to the nylon membrane by capillary action. This process is called 'Blotting' – more precisely **Southern blotting,** after the name of its inventor **E.M. Southern**.
6. **Using probes to identify specific DNA:** A **radioactive probe** (DNA labeled with a radioactive substance) is added to the DNA bands. The Probe is a single stranded DNA molecule that is 'complementary' to the gene of interest in the sample under study. The probe attaches by base pairing to those restriction fragments that are complementary to its sequence. The probes can be also prepared by using either 'fluorescent substances' or 'radioactive isotopes'.
7. **Hybridisation with probe**: After the probe hybridises and the excess probe washed off, a photographic film is placed on the membrane containing 'DNA hybrids'.
8. **Exposure on film to make a Genetic/DNA Finger Print**: The radioactive label exposes the film to form an image (image of bands) corresponding to specific DNA bands. The thick and thin dark bands form a pattern of **bars** which constitute a Genetic fingerprint.

A given person can never have a VNTR which his parents do not have. Obtaining hybrid with radioactive probe and matching DNAs of different

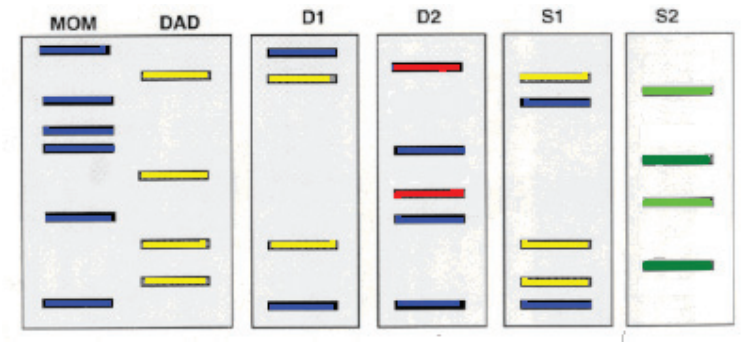
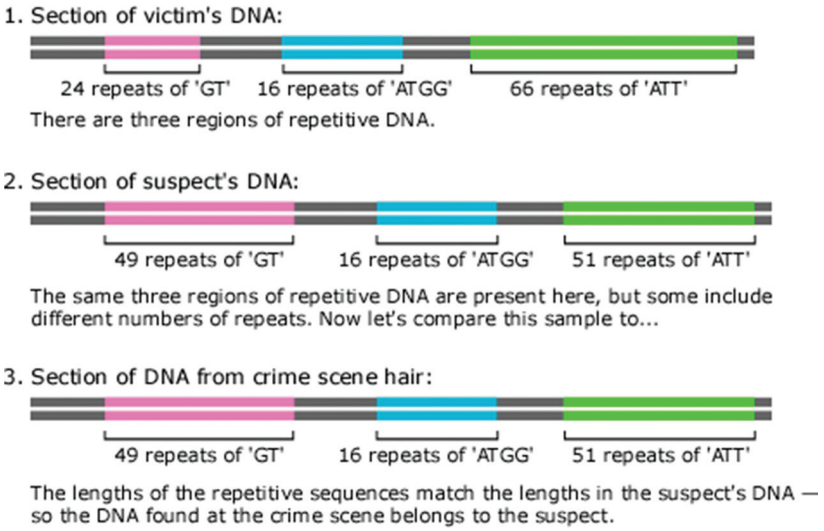


Figure 6.13 Forensic application of DNA fingerprinting

members of a family with biological children and adopted children, gives us an idea of how DNA Finger Prints help identification of paternity/maternity, by studying the 'DNA Finger Prints' of members of a Family – **Biological and non-biological relationships**.

The illustrations given below are the VNTR patterns for, **Mrs. Rose** [blue], **Mr. Rao** [yellow], and their **four children** : **D1** (Mr. Rao's biological daughter), **D2** (Mr. Rao's step-daughter, child of Mrs. Rose and her former husband [red], **S1** (Mr. Rao's biological son), and **S2** (Mr. Rao's adopted son - not biologically related, his parents' DNA marked in light and dark green bands).



6.11.2 Applications of DNA Finger Printing

1. **Conservation of wild life** – protection of endangered species. By maintaining their DNA records for identification of tissues of the dead endangered organisms
2. **Taxonomical applications** – study of phylogeny.
3. **Pedigree analysis** – inheritance pattern of gene through generations.
4. **Anthropological studies** –charting of origin and migration of human population.
5. **Medico-legal cases** – establishing paternity and/or maternity more accurately.
6. **Forensic analysis** – positive identification of a suspect in a crime.

GLOSSARY

Agglutinogens: An antigen that stimulates the production of a particular agglutinin, such as an antibody.

Aneuploid: Having a chromosome number that is not an exact multiple of the haploid number of the species.

Antiserum: Antiserum is the blood serum containing antibodies against a specific antigen, used to treat or provide immunity to a disease. It is extracted from an animal that was artificially made to develop antibodies and thus a specific immunity to a particular disease.

Erythroblast: An immature form(developmental immature stage) of a red blood cell. It is normally found only in bone marrow and contains haemoglobin.

Genetic markers: A genetic marker is a gene or DNA sequence with a known location on a chromosome that can be used to identify individuals or species.

Haemolytic anaemia: It is a form of anemia due to haemolysis, the abnormal breakdown of red blood cells, either in the blood vessels (intravascular haemolysis) or elsewhere in the human body (extravascular).

Heterochromatin: The part of a chromosome that is inactive in gene expression but may function in controlling metabolic activities, transcription, and cell division. It stains most intensely during interphase and usually remains in a condensed state throughout the cell cycle.

Ig G antibody: IgG is the main antibody found in the blood and extracellular fluid, allowing it to control infection of body tissues by binding many kinds of pathogens, such as viruses, bacteria, and fungi—IgG protects the body from infection. They are simple antibodies that cross the placental border and cause HDNB in the case of Rh incompatibility.

Ig M antibody: It is a basic antibody that is produced by B cells. IgM is physically the largest antibody in the human circulatory system. It is the first antibody to appear in response to initial exposure to antigen. The spleen is the major site of specific IgM production.

Isoagglutinin: An isoantibody normally present in the serum of an individual that causes the agglutination of the red blood cells of another individual of the same species.

PCR: The polymerase chain reaction (PCR) is a biochemical technology to amplify a single or a few copies of a piece of DNA into thousands to millions of copies ; it is a process of 'cloning' DNA.

Point mutation: A point mutation, or single base substitution, is a type of mutation that causes the replacement of a single base nucleotide with another nucleotide of the genetic material, DNA or RNA. The term point mutation also includes insertions or deletions of a single base pair.

Pseudoautosomal regions: These are sequences of nucleotides on the homologous regions of the X and Y

chromosomes. The pseudoautosomal regions get their name because any genes located within them are inherited just like any autosomal genes and they show genetic recombination by cross over as in autosomal pairs.

Restriction endonucleases : Restriction enzymes are 'DNA-cutting enzymes' They cut within the molecule, and so they are called restriction endonucleases. A restriction enzyme recognizes and cuts DNA only at a particular unique sequence of nucleotides, allowing for restriction sites to be mapped.

Satellite DNA : Short, highly repeated eukaryotic DNA sequences, usually clustered in heterochromatin and generally not transcribed.

QUESTIONS

Very Short Answer Type Questions

1. What is pleiotropy?
2. What are the antigens causing 'ABO' blood grouping? Where are they present?
3. What are the antibodies of 'ABO' blood grouping? Where are they present?
4. What are multiple alleles?
5. What is erythroblastosis foetalis?
6. A child has blood group 'O'. If the father has blood group 'A' and mother blood group 'B', work out the genotypes of the parents and the possible genotypes of the other off spring.
7. What is the genetic basis of blood types in ABO system in man?
8. What is polygenic inheritance?
9. Compare the importance of Y-chromosome in human being and Drosophila.
10. Distinguish between heterogametic and homogametic sex determination systems.
11. What is haplo-diploidy?
12. What is Klinefelter's syndrome?
13. What is Turner's syndrome?
14. What is Down syndrome?
15. What is sex-linked inheritance?
16. Define hemizygous condition?
17. What is crisscross inheritance?
18. Why are sex-linked recessive characters more common in the male human beings?
19. How many base pairs are observed in human genome? What is the average number of base pairs in a human gene?
20. What is 'junk DNA'?
21. What are VNTRs?
22. List out any two applications of DNA fingerprinting technology.

Short Answer Type Questions

1. How is sex determined in human beings?
2. Describe erythroblastosis foetalis.
3. Mention any two allosomal genetic disorders with their symptoms.
4. Describe the genetic basis of ABO blood grouping.
5. Describe male heterogamety.
6. Describe female heterogamety.
7. Describe the Genic Balance Theory of sex determination.
8. Explain the inheritance of sex linked recessive character in human being.
9. A man and woman of normal vision have one son and one daughter. Son is colour-blind and his son is with normal vision. Daughter is with normal vision, but one of her sons is colour-blind and the other is normal. What are the genotypes of the father, mother, son and daughter?
10. A colour-blind man married a woman who is the daughter of a colour-blind father and mother homozygous normal vision. What is the probability of their daughters being colour-blind?
11. Write the salient features of 'HGP'.
12. Describe the steps involved in DNA fingerprinting technology.

Long Answer Type Questions

1. What are multiple alleles? Describe multiple alleles with the help of ABO blood groups in man.
2. Describe chromosomal theory of sex determination.
3. What is crisscross inheritance? Explain the inheritance of one sex linked recessive character in human beings.
4. Write an essay on common genetic disorders.
5. Why is the Human Genome project called a mega project?
6. What is DNA fingerprinting? Mention its applications.

FOR IGNITED MINDS

Genetics

1. Can a human being with relatively more dark pigment in the skin, give birth to a fair complexioned child? If so, how? (Do not consider gametic donors, in vitro fertilisation etc.).
2. Is it scientifically possible for the first Rh positive child of a Rh negative mother, with no transplacental 'sensitisation' during the gestation period, die of HDNB, for whatever possibility? **Hint** : The mother need not necessarily be sensitised by the Rh positive foetus only.
3. What is the statistical possibility of the birth of four consecutive homogametic human offspring in a family with normal healthy husband and wife?
4. The Guinness Book of Records says that there is a family with five Rh positive children born to an Rh negative mother. The children do not have large 'age gaps' between them. How was that possible?
5. If the mother is Rh negative, all her Rh positive children will suffer from HDNB (assuming the normal sensitisation of mother during parturition)? Do you endorse this statement or challenge the validity of the statement?
6. The word 'UNIVERSAL DONOR' can never be used for, with reference to transfusion of fluid tissues or components of it? Comment.
7. All 'gene based disorders'/'genetic disorders' are congenital (expression by birth), for the simple reason they are 'gene based'. Do you agree with the statement?
8. How many genes control the ABO system of blood groups in man? **HINT**: It is the question of application of a little 'genetical sense'.
9. When the blood of an 'A' group person is transfused to a 'B' blood group person, the B group person (recipient) dies predominantly due to 'clumping' of his RBCs due to the anti B anti bodies of the donor's blood. Can you defend the statement or can you prove it wrong?
10. If your class mate says "the first child in a family, who receives Rh antigen from the paternal source and Rh antibodies from his Rh negative mother, suffers from HDNB" - do you agree with him? If not why don't you agree?
11. If an animal cell has 'XO' allosomic condition, what are the possible influences you can draw regarding that person and condition.
12. Failure of a process during cell divisions causes most of the common syndromes in human beings. What do you call that process?
13. Mostly allosomes and sometimes autosomes too take part in the determination of the sex of the embryo. Can you give an example where neither allosomes, nor autosomes or their ratios do not decide the sex of the young one?

A.R. Wallace

Unit-VII

ORGANIC EVOLUTION

Organic Evolution – 'Darwin's Play Field' and the 'Mystery of Mysteries'

Gone are the days when people believed that some supernatural force created this world and that the Earth had all the current ***fauna*** *and* ***flora*** *right from the beginning. The term '****Organic Evolution****' was coined by* ***Herbert Spencer****. The core of the evolution spins around 'alleles' and changes in their frequencies, with several natural phenomena governing them.* ***Lamarck*** *is recognized to be the first person to have proposed an organized theory to explain evolutionary process,which was based on '****inheritance of acquired characters****'. Darwin,with his historical book '****On The Origin of Species****" revolutionized the human approach to this 'mystery of mysteries' –the evolution, better called '****organic evolution****'. Natural Selection according to Darwin is the 'force' that 'selects the fittest' and the one which is selected has obviously better features to adapt to the environment. It passes its special features of survival and over a long time the 'slow and gradual accumulation of beneficial variations caused 'speciation' (****Descent with Modification****) according to Darwin (****microevolution****). Hugo de Vries laid more stress on the role of 'mutations' in evolution - ****macroevolution****. It is clear that individual organisms do not evolve. The present day concept of evolution is – it is the gradual change in the allelic frequencies in a population. It lays more stress on occurrence of variations through* ***mutations****,* ***gene recombinations****,* ***genetic drift****,* ***gene flow*** *etc., and the selection of the 'heritable' beneficial variations through* ***positive selection pressure****, reproductive isolation. Mutation is the ultimate source of genetic variation and thus it makes evolution possible, as considered by NeoDarwinists. Beneficial mutations tend to accumulate and are considered the 'driving force' of evolution. A non-evolving population is in a state of equilibrium called '****HARDY-WEINBERG EQUILIBRIUM****'. You are going to learn in depth, the efforts humans are making to make us understand this '****mystery****'.*

Organic Evolution

Introduction

Evolution is the branch of biology that deals with the origin of life and the diversity of organisms on the earth through ages. The literal meaning of evolution is **unfolding** or **rolling out**. The word '**organic evolution**' was coined by **Herbert Spencer.** Evolution is a continuous process of development of more complex organization from simple level. "Nothing in Biology makes sense except in the light of Evolution" according to Dobzhansky.

7.1 Origin of life

Life had a beginning. When did life begin on the earth? What is the mechanism involved in the origin of the life? Since the origin of living organisms, did they change through time? - are some of the important questions that confront our minds. Many theories have been proposed to explain the origin of life. But most of them are of only historical importance. Some of them are discussed here.

I. **Theory of Special creation:** It is purely a mythological belief. This theory states that living organisms on the earth were created by a **Divine Power**.

II. **Cosmozoic theory** or **Panspermia:** According to this theory, life might have existed else where in the universe (*cosmos*) and it might have reached the Earth in the form of resistant spores called **cosmozoa** or **panspermia**.

III. **Theory of Spontaneous generation** or **Abiogenesis:** According to this theory, life originated from non-living or decaying and rotting substances like manure, dew, etc. **Aristotle**, **Thales**, **Plato** and **Von Helmont** believed in this idea of abiogenesis.

IV. **Theory of Catastrophism:** This theory was proposed by **Georges Cuvier**. According to this theory, earth was subjected to periodic catastrophes. It essentially states that all the existing organisms would die and new organisms would be created after every catastrophe that occurred in the history of the Earth.

V. **Theory of Biogenesis:** According to this theory, living organisms originate from pre-existing organisms. **Louis Pasteur** expiremental proved that 'life' cannot arise from non-living substances by his swan-neck flask experiment.

VI. **Theory of Chemical and Biological Origin of life** or **Coacervate theory:** This theory was proposed by **A.I. Oparin** of Russia and supported by **J.B.S. Haldane** of England. According to this theory, primitive organisms evolved spontaneously from the inorganic substances as a result of physical forces such as lightning, ultraviolet radiation, volcanic activities, etc. in the Primordial environment of the Earth. Thus origin of life was primarily a phenomenon of 'chemical evolution' that later led to 'biological evolution'.

1. Chemical evolution: This includes the origin of the earth and the primitive atmosphere, formation of early simple organic molecules which later formed the complex organic molecules. The earth originated approximately 4.5 to 5 billion years ago. At that time, the temperature of the earth was estimated to be around 5000^{o}C to 6000^{o}C and it slowly cooled down over millions of years. During this process, lighter elements such as helium, hydrogen, nitrogen, carbon, etc., flowed to the surface and formed the primitive atmosphere. This was hot with **abundant hydrogen** and **absence of free oxygen**. Thus, it was a **reducing atmosphere**. The elements combined and formed compounds such as ammonia, methane, etc. The water vapour in the atmosphere condensed into droplets of rain, which ran over the land as streams, rivers and finally collected to form oceans. Ammonia, methane, etc., were washed down along with the rain water. Mineral-rocks were also dissolved leading to the accumulation of minerals in the water. Highly reactive radicals such as CH^- and CH_2^- are condensed to form a variety of hydrocarbons. They reacted with ammonia and water to produce various

simple organic molecules like sugars, amino acids, fatty acids, purines and pyrimidines which later formed nucleosides and nucleotides. All these reactions occurred in the pools of boiling water on the Earth, which was described as the **hot dilute soup** or **prebiotic soup** by **J.B.S. Haldane**. In the prebiotic soup, these simple organic molecules produced complex polymers like **polysaccharides**, **proteins**, **fats** and **nucleic acids**. Nucleic acids and proteins combined to form **nucleoproteins.**

2. Biological evolution : This includes (i) the formation of protobionts, (ii) the origin of living organisms from them and their diversification.

(i) The formation of Protobionts: From the complex organic molecules, large colloidal aggregates called **coacervates** (*bubble like droplets*) were synthesized due to intermolecular attractions. Some type of chemical organisers (*considered **free genes***) developed to give these droplets 'the ability to take-in molecules from the surroundings'. Later they acquired lipid membranes. Some of the proteins inside them acquired the property of enzymes resulting in the fast multiplication of molecules.

(ii) The origin of living organisms: The 'Free Genes' started absorbing organic molecules from the prebiotic soup and evolved into **anaerobic heterotrophs** approximately three to four billion years ago. They obtained their **energy by the fermentation** of some organic molecules. The earliest living organisms had clumps of nucleoproteins containing one or two DNA molecules and were similar to the present day **prokaryotes**. During the course of evolution these early prokaryotes acquired the **carbohydrate-synthesis catalysing enzymes**. Thus early **chemo-autotrophic organisms (*e.g. iron and sulphur bacteria*)** which can thrive at high temperatures evolved. These organisms could take carbon dioxide into their bodies and used the chemical energy to create carbohydrates and sugars. Meanwhile some bacteria synthesised **bacterial chlorophyll (*e.g. purple and green sulphur bacteria*)** from the **magnesium porphyrin** of ocean waters. This pigment trapped the solar energy and fixed the CO_2. These were the **anoxygenic photo-autotrophic organisms.** Later the bacterial chlorophyll evolved into **true chlorophyll** as in cyanobacteria and plants. As a result, **oxygenic photo-autotrophic organisms** (***like blue green algae***) evolved. It resulted in the increase of large quantity of oxygen in the atmosphere about two billion years ago. These events transformed the reducing atmosphere into the modern oxidising atmosphere. With the availability

of free oxygen, finally aerobic mode of respiration evolved. Later, the eukaryotes evolved probably by two processes. a) Some prokaryotes entered the bodies of the ancestral eukaryotes and lived symbiotically. They evolved into organelles such as **mitochondria** and **plastids**. b) The endomembrane system of eukaryotes might have evolved by the infoldings of plasma membrane of the ancestral prokaryotes.

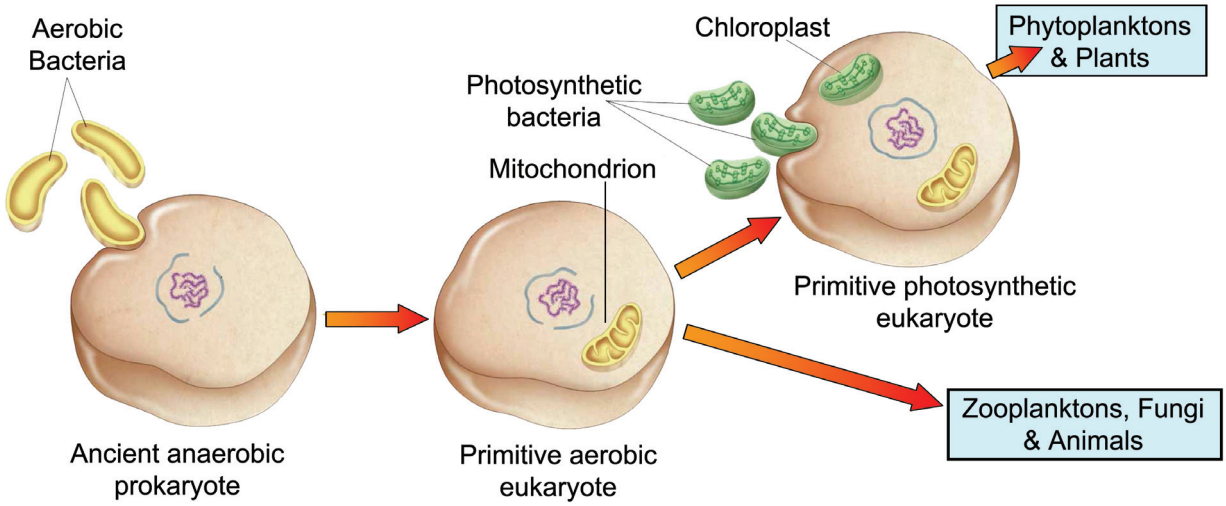


Figure 7.1 Formation of Eukaryotes

Experimental verification of chemical origin of life

Harold Urey and **Stanley Miller** successfully proved the chemical origin of life that was explained by Oparin, with their **simulation experiment**. They tried to create the primordial conditions in the laboratory. They sealed a mixture of **water vapour, methane, ammonia** and **hydrogen** (***simulation of primordial atmosphere***) in a spark chamber which was provided with electrodes for electric discharge (***simulation of lightning energy***). It was connected to another flask with the provision for boiling. The spark chamber was connected on the other end to a condenser tube (***simulation of rain and Cooling***). After some days, they noticed

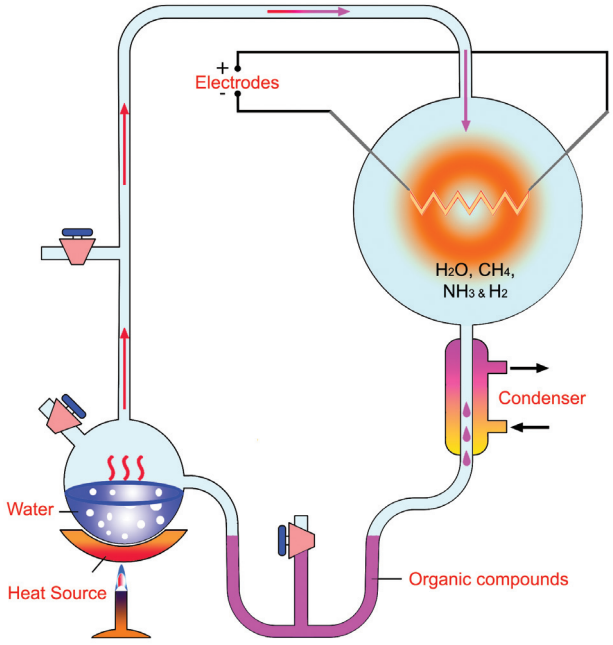


Figure 7.2 Urey & Miller Experiment

simple amino acids such as **glycine**, **alanine** and **aspartic acid** in the aqueous solution. Later in similar experiments, formation of all types of amino acids, and also formation of adenine and other nitrogen bases were noticed.

7.2 Evidences for Biological Evolution

The theories that explain the evolution are hypothetical. There is no practical proof for them. In fact, it is not possible for anybody to observe even a single change in favour of evolution that occurs in the body of organisms as our life span is too short to notice such slow changes. Hence scientists collected evidences from different branches of biology. Some of them are

a. Evidences from palaeontology,
b. Evidences from embryology,
c. Evidences from comparative anatomy
d. Evidences from cell and molecular biology

1. **Evidences from Palaeontology:** Palaeontology (*Gr. Palaios - old, on-existing, logos - to study*) is the study of prehistoric life through fossils. Fossils are the **remnants** of plants or animals that were preserved in the layers of the earth and have been excavated from the soil. They are of various types like **moulds**, **casts**, **petrifications**, **coprolites** (fossilized faecal matter), **actual remains** of animals preserved in ice, etc. They support the idea that life has gradually evolved on the earth. The biologists and palaeontologists have found the fossils of many transitional forms (**connecting links**) which link all the major groups of vertebrates e.g. ***Eusthenopteron*** between fishes and amphibians, ***Seymouria*** between amphibians and reptiles, ***Archaeopteryx*** between reptiles and birds, ***Cynognathus*** between reptiles and mammals, etc.

Do you know? The age of a fossil is calculated by using **Carbon^{14}**, **Uranium^{238}** and **Potassium^{40}**. Of these, as **C^{14}** is **commonly** used to determine the age of comparatively recent and this method is called **Radio Carbon Dating method**.

A complete fossil record of the various stages in the evolution of horse is available. It indicates that evolution is a gradual process and not a sudden creation of a species.

Geological Time Scale: The earth contains different layers of sediments of which, the bottom layer is the oldest layer and the upper layer is the most recent layer. Based on the age of rocks, a time scale was prepared and it is called the **geological time scale**, it depicts the different stages of the evolution

of life on the earth over the past millions of years. It consists of Eras which are divided into Periods that may be further subdivided into Epochs (in the coenozoic Era). These Eras, Periods and Epochs depict the time of origin and dominance of certain groups of animals during certain Eras or Periods. It **provides the most direct evidences for the concept of evolution.**

Table 1 Geological Time Scale

Era	Period	Epoch	Significance
Coenozoic Era (Age of mammals)	Quaternary	Holocene	Civilization of human beings
		Pleistocene	Origin of human beings
	Tertiary	Pliocene	Origin of many mammals
		Miocene	
		Oligocene	
		Eocene	
		Palaeocene	
Mesozoic Era Golden age of reptiles)	Cretaceous	No Epochs	Extinction of dinosaurs by the end
	Jurassic		Origin of birds
	Triassic		Origin of dinosaurs and mammals
Palaeozoic Era	Permian	No Epochs	Extinction of trilobites and many other marine animals
	Carboniferous		Golden age of amphibians, Origin of cotylosaurs (first reptiles)
	Devonian		Golden age of fishes, Origin of amphibians
	Silurian		Origin of fishes
	Ordovician		Origin of ostracoderms
	Cambrian		Origin of trilobites
Precambrian Era Comprises 88% of the geologic time			

Do you know? If the entire earth is considered a book, then the layers are the pages and the fossils are letters with which the history of the earth was written. Hence the fossils are considered the **documentary evidences** in support of evolution (meaning that fossils are some kind of written proofs for evolution)

2. Evidences from embryology: The study of the formation and early development of an organism is called embryology. **Ernst Haeckel** is considered the '**Father of Embryology**' and **Von Baer** is considered the **Father of Modern Embryology**. When the embryos of different animals are observed, we find a fundamental similarity which tells us that there is a relationship among the animals. Embryology provides evidences from i) the observations of Von Baer, ii) sequence of the developmental stages of some animals, and iii) recapitulation of certain ancestral features during embryonic development.

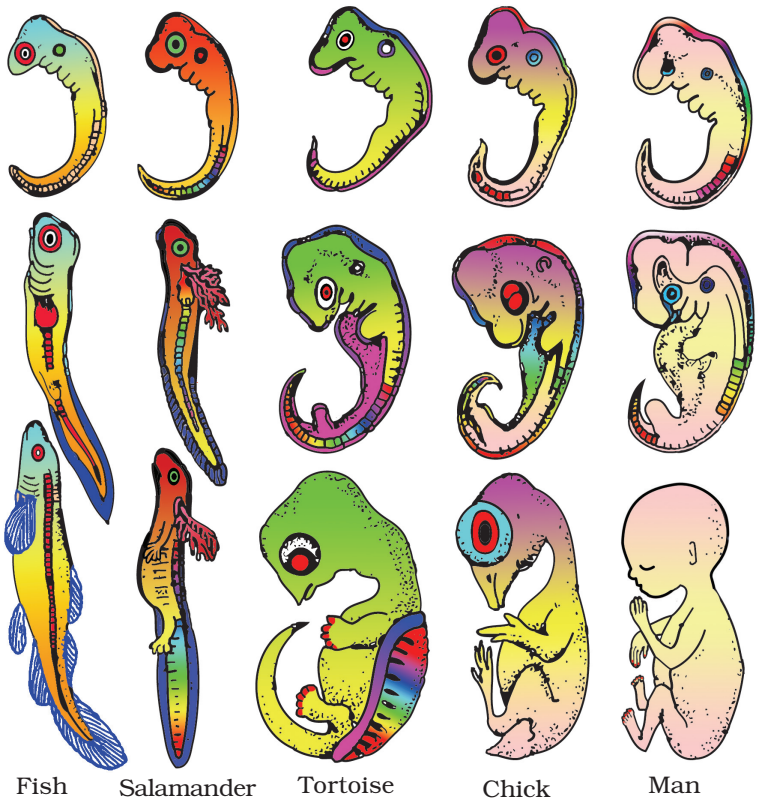


Figure 7.3 Embryological Evidences

i) **The observations of Von Baer:** Von Baer studied the embryology of fish, salamander, tortoise, chick and man. He observed that the early embryos of the above animals resemble each other closely in some basic/ fundamental features. However these embryos differ in the final stages due to the formation of specialized characters. It indicates that the above animals have a common ancestor.

ii) **Sequence of the developmental stages:** The life of all the multicellular organisms begins with a single celled stage, the zygote. It undergoes cleavages to produce the first stage embryo, the **morula**, which develops into a single layered second stage embryo, the **blastula**. It develops into the third stage embryo, the **gastrula**, which finally develops into adult. During this process, the zygote represents the unicellular stage, morula and blastula stages represent the colonial protozoan stages, whereas the gastrula stage represents the cnidarian stage. The development of the embryos of different organisms differs after the gastrula stage. This sequence of embryos shows that every multicellular organism passes through the above stages representing their common ancestry.

iii) **Biogenetic Law** or **Theory of recapitulation:** It was proposed by **Ernst Haeckel**. It states that **ontogeny repeats phylogeny** which means the developmental history of an organism repeats the evolutionary history of its ancestor, e.g. 1) Tadpole larva of frog resembles fish both externally and internally. It possesses a tail, gills and two chambered heart like that of a fish. Later it metamorphoses into adult frog 2) Caterpillar larva of butter fly recapitulates its closest ancestor, the annelid in body form 3) In the embryos of birds and mammals, the heart is initially two chambered as in fish, then three chambered as in amphibians, and after that an incompletely divided four chambered heart as in reptiles and finally four chambered (as seen in birds and mammals).

3. **Evidences from comparative anatomy:** When we compare the anatomy of different animals, we find some similarities among them. For example, the fore limbs of different vertebrates are similar in origin and internal structure. All these indicate that there is a relationship among the organisms. These relationships can be studied under i) Homologous organs, ii) Analogous organs, iii) Vestigial organs, iv) Atavistic organs and v) Connecting links

i) **Homologous organs:** The organs which have similar structure and origin but not necessarily the same function are called homologous organs. The evolutionary pattern that describes the occurrence of similarity in origin and internal structure is called homology. Such organs show adaptive radiation, hence 'divergent evolution', e.g. the appendages of vertebrates such as the flippers of whale, wings

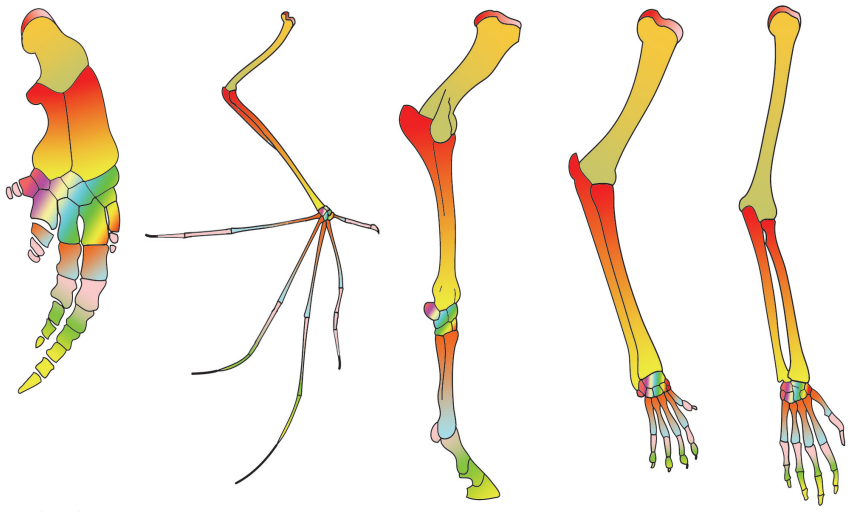


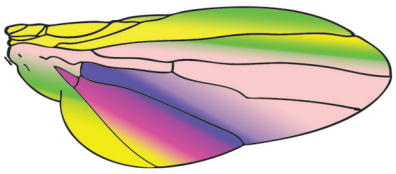
Figure 7.4 Homologous Organs

of bat, forelimbs of horse, paw of cat and hand of man, have a common pattern in the arrangement of bones even though their external form and functions may vary to suit their mode of life. It explains that all the vertebrates might have had a common ancestor.

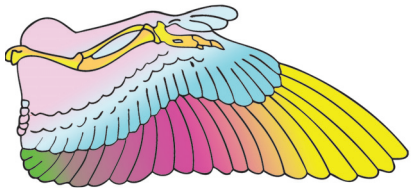
Do you know? When the animals (*of a species*) of a certain habitat enter into different habitats, they evolve into different forms. This phenomenon is called adaptive radiation and it indicates **divergent evolution**, e.g. In **Darwin's finches** of **Galapagos islands**, many forms with variations in beak pattern were formed from the original seed-eating birds believed to have come from the main land, the South America.

ii) **Analogous organs:** The organs which have dissimilar structure and origin but perform the same function are called the analogous organs. Analogous organs suggest 'convergent evolution', e.g. wings of a butterfly and wings of a bird.

Do you know? When different animals live in the same habitat, they tend to show similarity in body form, e.g. shark and whale have the same body form as both live in aquatic environment. Earthworm and snake have the same body form as both live in burrows. This type of evolution is called **convergent evolution**.



Wing of an insect



Wing of a bird

Figure 7.5 Analogous organs

iii) **Vestigial organs:** The organs which were functional in the ancestors but **non-functional** and **reduced** in the **descendants** are called vestigial organs. Presence of vestigial organs is the most convincing evidence in favour of organic evolution and also supports the concept of disuse proposed by Lamarck, e.g. Hind limbs in python, hind limbs and pelvic girdle in whale, wings of flightless birds, vermiform appendix, coccyx, plica semilunaris (vestigial *nictitating membrane*), auricular muscles that move the pinna, hair on the body, mammary glands in males, etc., in human beings.

Do you know? In man there are nearly 180 different types of vestigial organs. Hence Weidersheim described human being a '**Moving Museum of Antiquities**'.

iv) **Atavistic organs:** **Sudden appearance** of some vestigial organs in a better developed condition as in the case of the tailed human baby is called **atavism**. Such organs are called atavistic organs they strongly support the concept of organic evolution.

v) **Connecting links:** The organisms which possess the characters of two different groups between which they are transitional are called **connecting links**. They clearly explain the path of evolution, e.g. *Peripatus* between annelida and arthropoda, prototherians between reptilia and mammalia, etc.

Figure 7.6 Atavism

4. **Evidences from cell and molecular biology:** The field of cell and molecular biology provides the most detailed and convincing evidence in favour of biological evolution. They are studied under three headings, namely i) Fundamental unity of life, ii) Blood precipitation (serological) tests and iii) Biochemical recapitulations

Do you know? The nature of DNA, the functioning of enzymes and other protein molecules in all the living organisms from bacteria to humans suggest that all organisms evolved from a common ancestor.

i) **Fundamental unity of life:** In all the living organisms, the structural and functional units are the cells. Every eukaryotic cell contains all the kinds of cell organelles such as Golgi complex, mitochondria, E.R., ribosomes, lysosomes, nucleus, chromosomes, D.N.A. and R.N.A. In all the living organisms, mitochondria help in energy production and storage, ribosomes help in protein synthesis; DNA has the same four types of nucleotides; all the proteins are synthesized from different combinations of the same 20 types of amino acids, the genetic code is virtually the same everywhere; different types of biochemical substances such as enzymes, hormones, respiratory pigments, etc., and different types of biochemical reactions that occur in all the living organisms are the same, indicating some relationship among all the organisms on the earth.

Do you know?In frog, the hormone thyroxine is essential for metamorphosis. If human thyroxine is injected to a tadpole, whose thyroid is removed, it undergoes metamorphosis. This indicates that the function of thyroxine is the same in all animals.

ii) **Blood precipitation tests:** They are also called **serological tests** and were first conducted by **H.F. Nuttal.** He first injected a small amount of human serum into a rabbit. As our serum proteins are foreign to rabbit, antihuman antibodies are produced in that rabbit. The serum of the rabbit was collected, and it is called **anti human serum.** When it is mixed with the serums of an anthropoid ape, a monkey and a dog in separate test tubes, within a short time, a

thick precipitate is formed with the serum of the anthropoid ape, moderate precipitate with that of the monkey and no precipitate with that of the dog. It indicates that the anthropoid ape is more closely related to man than to monkey and dog. These tests also proved that whale is closely related to pig and the south American Llamas are closely related to the camels of Eurasia. Is it not interesting to see that evolutionary relationships can be proved by such simple tests?

iii) **Biochemical recapitulations:** Animals recapitulate the biochemical aspects of their ancestors, e.g. a) An adult frog excretes urea but its tadpole excretes ammonia as the fishes do. b) The embryo of a bird excretes ammonia during the first four days of development as the fishes do, then urea in the next nine days as the amphibians do and finally uric acid as the reptiles and birds do. c) Even the mammalian embryo first excretes ammonia then uric acid and finally urea.

7.3 Theories of evolution

Various theories have been proposed to explain the process of evolution, but the theories that explain the scientific basis of organic evolution are Lamarckism, Mutation theory of de Vries, Darwinism and Modern synthetic theory (Neo-Darwinism).

7.3.1 Lamarckism

Figure 7.7 Lamarck

It was explained by **Jean Baptiste de Lamarck** (1774-1829), a French Biologist in his book **Philosophie Zoologique**. It deals with the influence of environment on organisms, use or disuse of organs and the inheritance of acquired characters. According to him, whenever the environment of certain organisms undergoes some changes, it forces the organisms to **use** certain organs more and put certain other organs to **disuse**. The organs that are used more will increase in size and those not used continuously will degenerate. Such characters that are developed during the life time of an organism are called **acquired characters**. They are passed on to the next generation (Inheritance of acquired characters).

Examples: Elongation of neck and forelimbs in giraffe **(use)**, absence of limbs in snakes **(disuse)**.

Objections: The main objection for Lamarckism came from **Augustus Weismann**. He conducted **decaudalisation** experiments on mice and proposed that the bodies of all the living organisms possess somatoplasm and germplasm. If any change occurs in the somatoplasm, it will not be transferred to the next generation but if any change occurs in the germplasm, it will be inherited to the next generation, e.g. 1) Well-developed muscles of athletes are not inherited to their children. 2) Making perforations to pinna for wearing ornaments has been in practice in India for the past several centuries. However no girl child is born with ready-made perforations in their pinna.

Neo-Lamarckism: The contributions of Lamarck paved the way for the gradual acceptance of the concept of biological evolution (*not creation*) and stimulated many further studies in this field later, it was modified to make it more acceptable. The followers of Lamarck (*Neo-Lamarckists*) like **Cope, Osborn, Packard, Spencer,** etc., tried to explain the Lamarck's theory on a more scientific basis. They considered that **adaptations are universal**. Organisms acquire new structures due to their adaptations to the changed environmental conditions. They argue that external conditions stimulate the somatic cells to produce certain 'secretions' which reach the sex cells through the blood. Such variations can be inherited by the offspring. **Paul Kammarer** observed the development of normal eyes and skin colour in the cave dwelling salamander, ***Proteus anguinus,*** when exposed to daylight. This somatic character was passed on to the next generation.

7.3.2 Darwinism

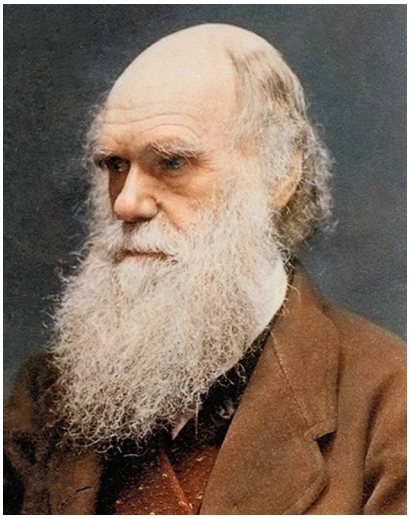


Figure 7.8 Darwin

It is an evolutionary theory proposed by **Charles Robert Darwin** (1809-1882), an English Naturalist. He went on a voyage for five years on a world survey-ship of the British Government, **H.M.S. Beagle** and explored the fauna and flora of a number of continents and islands. He was much influenced by three publications namely '**An Essay on the Principles of Populations'** of **Thomas Malthus,** which states that animals increase in geometric progression, whereas their food sources increase in arithmetic progression, the book written by **Sir Charles Lyell** entitled **'Principles of Geology'** that explains the phenomenon of **gradualism** (*earth has changed slowly and gradually through ages*) and **uniformitarianism** (*the fundamental laws that operate today on the earth are in the same way as they did in the past*) and the paper titled **'On the tendency of**

varieties to depart from original types' of **Alfred Russell Wallace.** He published his theory in his book titled **'The Origin of Species** by means of **Natural Selection'.**

Theory of Natural Selection: Darwin's theory of Natural Selection does not explain what exactly evolution is, but explains how evolution might have occurred in nature. He believed that evolution is a gradual, rather than a sudden biological event. His theory was based on several facts, observations and inferences. They are

i. **Prodigality of production** or **over production:** Every organism tends to increase its population in large proportions. For example, *Paramecium* divides by binary fission at the rate of three to four times a day. At this rate, the volume of all the Paramecia equals to 10,000 times that of the earth at the end of the 9000th generation. **Salmon** fish produces 28 million eggs and **starfish** one million eggs in a season. If all of them hatch and the larvae grow to reproductive age, all the seas will be filled with them in a few generations. Even the slowest breeder, the elephant can produce 19 million descendants at the end of the 800th generation in the absence of any check.

ii. **Constancy in population:** However, such an abnormal increase is not noticed in the population of any species in nature as the offspring die in large numbers before reaching the reproductive age. It is true that the food and the other sources do not increase in the same proportion as that of the population.

iii. **Struggle for existence:** As the food sources are limited, severe competition exists among the members of a population. Darwin called it **struggle for existence** which is of three types as:

1. **Intraspecific struggle:** The competition found among the individuals of the same species is called intraspecific struggle. It is for food, shelter and mate. It is the **most severe check** on the rate of reproduction.

2. **Interspecific struggle:** The competition found among the animals of different species is called interspecific struggle. Most of the species have the same type of food habits. Hence, competition exists among them chiefly for food and shelter.

3. **Struggle with the environment:** All living organisms struggle with the adverse environmental conditions such as cyclones, floods, earthquakes, tsunamis, volcanic eruptions, etc.

iv. **Universal occurrence of variations:** No two organisms are exactly similar. They show variations. Even the offspring of the same parents are different. These variations may be harmful or useful or neutral. The useful variations help an organism to overcome struggle. Such variations are passed on to the next generation.

v. **Natural selection:** According to Darwin, the individuals possessing harmful variations are reproductively less successful. The organisms with beneficial variations would increase the ability to reproduce and leave more fertile offspring. They are said to be the 'fittest organisms' and they only can survive. The organisms with less reproductive success are not represented in future generations, however fit they may be in the struggle for existence. This is called the **Natural Selection**. **Herbert Spencer** called this phenomenon '**survival of the fittest'.**

vi. **Origin of species:** Darwin concluded that 'the struggle for existence resulting in the survival of the fittest' allows successive generations to become better adapted to the environment. All the variations selected by Nature accumulate from generation to generation. Such an accumulation over a long period of time brings so many changes in an organism that it does not interbreed any more with the original parental species. Such a reproductively isolated organism is considered a 'new species'.

Do you know? Darwin considered that formation of a new species is due to the cumulative effect of 'fluctuating variations'.

II. **Objections to Darwinism:** Though Darwinism is considered the best explanation for the organic evolution; some objections were raised against it. Some of them are

i) It failed to explain the mechanism by which variations occur. Thus Darwin faced the criticism 'DARWINISM EXPLAINS THE SURVIVAL OF THE FITTEST BUT NOT THE ARRIVAL OF THE FITTEST'.

ii) It could not explain the occurrence of vestigial organs, over specialisation of some organs like large tusks in extinct mammoths, oversized antlers in the extinct Irish deer, etc.

iii) It focused on small, fluctuating variations which are mostly non-heritable.

iv) It did not distinguish between somatic and germinal variations.

v) Darwin did not consider the importance of macro-variations and considered them '**sports of nature**'.

Do you know? **Alfred Russell Wallace**, a British naturalist who worked in Malayan Archipelago had also come to conclusions similar to those of Darwin, around the same time.

Experimental verification of Natural Selection – Industrial melanism

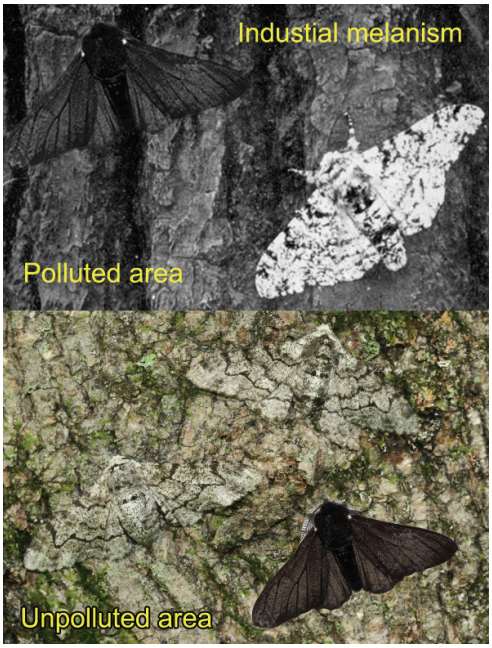


Figure 7.9 Industrial melanism

An important practical proof for the operation of Natural Selection is the classical case of industrial melanism, exhibited by peppered moth – *Biston betularia.* These moths were available in two colours, **grey** and **black**. Prior to industrial revolution, the grey moths were abundant. During the industrial revolution, the black forms were more and the grey forms were less in the industrial cities like Birmingham. Biologists proposed that with the industrial revolution, more soot was released due to the burning of coal, which resulted in the darkening of the barks of trees. Grey moths on the dark bark were easily identified and predated more by birds. Hence the number of grey moths decreased and that of the black moths increased in the population. It means Nature offered '**positive selection**' pressure to the black (melanic) forms. **Bernard Kettlewell**, a British ecologist, tested this hypothesis experimentally. He collected both the grey and the black forms of *Biston betularia* for his experiment. He released them in two sets of equal numbers; one set in Birmingham, a polluted urban area, and the other set in Dorset, an unpolluted rural area. After a few days he recaptured them. Of those moths recaptured from Birmingham, there were more black forms. Among those recaptured from Dorset there were more grey forms. The reason for such a difference is: the melanic forms could not be easily spotted by predator birds as their body colour merged with the dark colour of the bark of trees in Birmingham area. In the rural areas (Dorset) the grey forms had better survival chance as their body colour merged with the light coloured surroundings. This explains the differential survival of the moths due to Natural Selection. It will be interesting to know that there was a reversal in the selection process after the introduction of pollution check laws in the urban areas.

7.3.3 Mutation Theory

It was proposed by **Hugo de Vries**, a Dutch botanist who coined the term 'mutation'. Mutations are **sudden, random inheritable changes** that occur in organisms. He found four different forms in ***Oenothera lamarckiana*** (commonly called 'evening primrose') such as *O. brevistylis*-small style, *O. levifolia*-smooth leaves, *O. gigas*-the giant form, *O. nanella*-the dwarf form (mutant varieties). **T. H. Morgan** studied the inheritance pattern of mutations in ***Drosophila melanogaster***. **Darwin** called mutations (*large variations*) **sports of nature** or **saltations**, whereas **Bateson** called them **discontinuous variations**.

Salient Features of Mutation theory

1) Mutations occur from **time to time** in naturally breeding populations.
2) They are **discontinuous** and are not accumulated over generations.
3) They are **full-fledged**, and so there are no 'intermediate forms'.
4) They are **subjected** to Natural Selection.

7.4 Modern synthetic theory of Evolution or Neo-Darwinism

Weismann's germplasm theory, de Vries' mutation theory and Mendel's laws of inheritance helped a lot in understanding the origin and inheritance of variations. The scientists such as **Huxley, Haeckel, Simpson,** etc., supported Darwinism. Later Fisher, Sewall Wright, Mayr explained Natural Selection in the light of post-Darwinian discoveries **(Synthetic theory/Genetical theory/Neo-Darwinism)**. According to this theory, five basic factors are involved in the process of organic evolution. They are (i) Gene mutations, (ii) Chromosomal mutations, (iii) Genetic recombinations, (iv) Natural Selection and (v) Reproductive isolation.

i) **Gene mutations:** Changes in the structure of a gene (DNA molecule) are called gene mutations or point mutations. They alter the phenotypic characters of the individuals. Thus, gene mutations tend to produce 'variations' in the offspring.

ii) **Chromosomal mutations:** Changes in the structure of chromosomes (*due to deletion, addition, duplication, inversion or translocation*) are called chromosomal mutations. They also bring about variations in the phenotype of organisms which lead to the occurrence of variations in the offspring.

iii) **Genetic recombinations:** Recombinations of genes due to crossing over during meiosis are also responsible for bringing about genetic variability among the individuals of the same species, thus, contributing to the occurrence of heritable variations.

iv) **Natural Selection:** Natural selection does not produce any genetic changes but once genetic changes occurred, it favours some genetic changes while rejecting others. Hence it is considered the ***driving force of evolution*.**

v) **Reproductive isolation:** The absence of gene exchange between populations is called the reproductive isolation. It plays a great role in giving rise to new species and preserving the species integrity.

7.5 Mechanism of evolution

The process by which variations appear and new species are formed is called the mechanism of evolution. Some of these mechanisms include deviations from Hardy-Weinberg equilibrium, different types of evolutionary forces leading to speciation.

I. Hardy-Weinberg equilibrium

The Hardy-Weinberg equilibrium was explained independently by **Hardy** of U.K. and **Weinberg** of Germany. It is a principle stating that the allelic frequencies in a population will **remain constant** from generation to generation under certain conditions. They are;

1) Size of the population should be large.
2) Mating should be random (panmictic).
3) There should be no evolutionary forces like Natural Selection or mutations or large scale migrations.
4) There should be no differential reproductive success, among the organisms of a population.
5) All the members of a population should be homogenous in age.

Significance of Hardy-Weinberg equilibrium

Any deviation from one or more of these conditions will disturb the equilibrium by changing allelic frequency or genotypic frequency or both. These changes in frequencies are significant in producing variations, which are the **raw materials** for evolution.

Hardy-Weinberg Equation

It is a mathematical model which explains the **genetic equilibrium** in a population. In a stable population, for a gene with two alleles '**A**' (dominant) and '**a**' (recessive), three genotypes, namely '**AA**' (*homozygous dominant*), '**Aa**' (*heterozygous*) and '**aa**' (*recessive*)' are possible. If the frequency of 'A' is '**p**' and that of 'a' is '**q**', then the genotypic frequencies of 'AA, Aa and aa' can be expressed by the equation $p^2 + 2pq + q^2 = 1$ or $(p+q)^2 = 1$.

In mathematical terms, if $(p+q)^2 = 1$, then $(p+q) = 1$. Where,

p = frequency of dominant allele, q = frequency of the recessive allele,

p^2 = frequency of the homozygous dominant genotype,

2pq = frequency of the heterozygous dominant genotype and

q^2 = frequency of the recessive genotype

Example I: Assume in a population of 1600 individuals, 256 individuals are with a recessive trait. Find out the homozygous dominant and heterozygous dominant individuals in that population.

Solution: *To work out this problem, first we have to find out the recessive genotypic frequency (q^2), then recessive allelic frequency (q) and finally substitute the values.*

- Frequency of recessive genotype (q^2)

$$= \frac{\text{number of recessive individuals}}{\text{total number of individuals in a population}} = \frac{256}{1600} = 0.16$$

then the allelic frequency $q = \sqrt{0.16} = 0.4$

- As we have come to know the value of 'q', now we have to find out the value of 'p' by using the equation $(p + q) = 1$, where $q = 0.4$, then $p = (1 - q) = (1 - 0.4) = 0.6$.
- So the dominant allelic frequency 'p' = 0.6, then the homozygous dominant genotypic frequency (p^2) = 0.6X0.6 = 0.36.
- Now we can find out the number of homozygous dominant individuals by using the formula: $\text{frequency} = \frac{\text{number}}{\text{total number of population}}$

where frequency of p^2 is 0.36, and the total number of population is 1600, then

- The number of homozygous dominant individuals = frequency x total number of the population = 0.36 X 1600 = 576
- The heterozygous genotypic frequency = 2pq = 2 X 0.6 X 0.4 = 0.48, then the number of heterozygous dominant individuals = 0.48 x 1600 = 768.

Example II : Assume, in a population of 200 individuals, the homozygous dominant are 114, the heterozygous dominants are 76 and the recessive are 10. Find out the dominant and recessive allelic frequencies.

Solution : Dominant allelic frequency = p

$$= \frac{2 \text{ (no. of homozygous dominant individuals)} + \text{no. of heterozygous individuals}}{2(\text{total no. of individuals in the population})}$$

$$= \frac{2(114) + 76}{2(200)} = \frac{304}{400} = 0.76,$$

Recessive allelic frequency = q

$$= \frac{2 \text{ (no. of recessive individuals)} + \text{no. of heterozygous individuals}}{2(\text{total no. of individuals in the population})}$$

$$= \frac{2(10) + 76}{2(200)} = \frac{96}{400} = 0.24$$

II. Evolutionary forces

The forces that bring changes in the gene pool of populations are called evolutionary forces. They include Natural Selection, gene flow, genetic load, genetic drift, etc.

i) **Natural Selection:** It is mainly of three types, namely a) stabilising selection, b) directional selection and c) disruptive selection

a) **Stabilising Selection (centripetal selection):** This selection operates in a stable environment. In this process, the organisms with average phenotype are preserved whereas the extreme individuals from both the ends are eliminated. Hence this does not promote any evolutionary change that leads to speciation, but maintains the phenotypic stability within the population over generations. For example, in England, weights of new born babies were studied in a large sample. Greater mortality was found in the babies whose weight was greater or lesser than the average weight of 8 lbs.

b) **Directional Selection:** This selection operates in an environment which gradually undergoes changes. It works by constantly removing the individuals from one end and constantly shifting the average value of fitness towards the other end of the phenotypic distribution. For example, in the case of giraffes the average value of the length

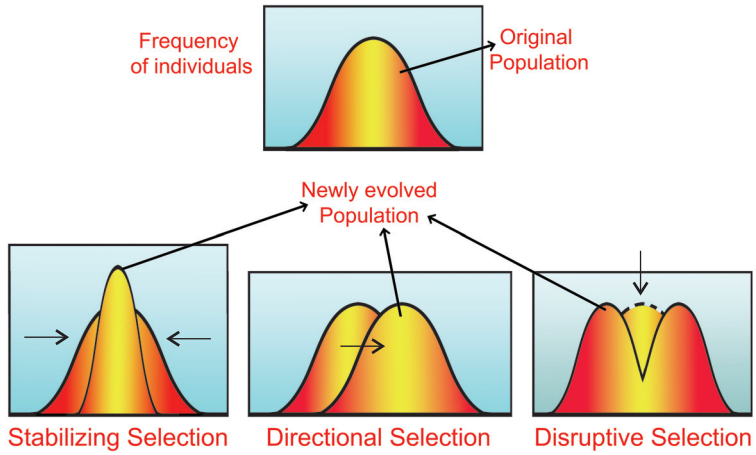


Figure 7.10 Types of Phenotypic Distribution

of the neck shifted towards the long-neck. Stabilising selection takes over the directional selection once the average value of the phenotype coincides with the new optimum environmental conditions. The development of resistance to DDT by mosquitoes is another example for directional selection.

c) **Disruptive Selection (centrifugal selection):** This type of selection operates when homogenous environment changes into a heterogenous type. In this process, the organisms of both the extreme phenotypes are selected while the individuals with average phenotype are eliminated. This can split the population into two or more subpopulations/species populations. Though it is a rare form of selection, it can lead to the formation of two or more different species. It is also called adaptive radiation, e.g. Dark and light coloured species in ***Biston betularia***, **Darwin's finches** with different shapes of beaks, sunflower populations in California which split into two subpopulations of which one was adapted to dry area and the other was adapted to wet area. If the two sub populations do not inter breed (sexually isolated) they develop in to new species.

ii) **Gene Flow:** The movement of alleles from one population to another is called gene flow. The random introduction of alleles into the recipient population (immigration) and their removal from donor population (emigration) affect the allelic frequencies of both the populations.

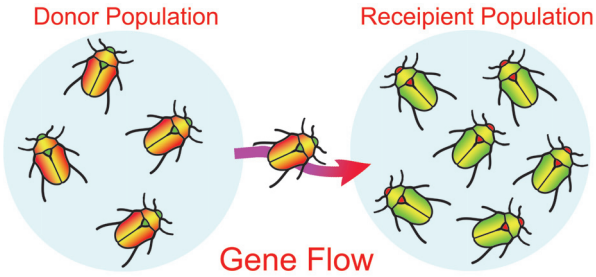


Figure 7.11 Gene Flow

iii) **Genetic Load:** The existence of deleterious genes within the populations is called **genetic load**, e.g. Gene for **sickle cell anaemia**. The individuals homozygous for sickle cell gene (Hb^S Hb^S) usually die early due to anaemia. Those heterozygous (Hb^A Hb^S) can live reasonably healthy and exhibit resistance to malaria. So this disadvantageous gene is carried in heterozygous condition.

iv) **Genetic Drift:** The change in the frequency of a gene that occurs merely by **chance** and not by selection, in small populations, is called **genetic drift** or **Sewall Wright effect**. Suppose, for a gene with two alleles, the frequency of a particular allele is 1% (q = 0.01), the probability of losing that allele by chance from the small population is more. The end result is either **Fixation** (p or q = 1)or **Loss** (p or q = 0) of that allele. The probability of reaching the end point depends on the size of the population. Genetic drift tends to reduce the amount of genetic variation within the population mainly by removing the alleles with low frequencies. It can be exemplified by the **Founder Effect** and **Bottleneck Effect**.

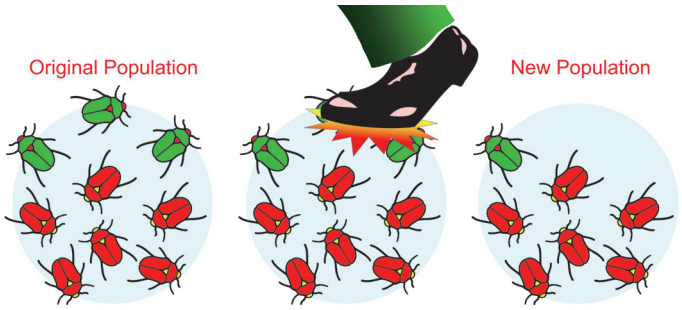


Figure 7.12 Genetic drift by Chance

Founder effect: If a small group of individuals from a population start a new colony in an isolated region, those individuals are called the **founders** of the new population. The allelic frequencies of their descendants are similar to those of the founders rather than to their ancestral parent population, e.g. presence of O^{+ve} blood group in nearly 100% of the Red-Indians. It means

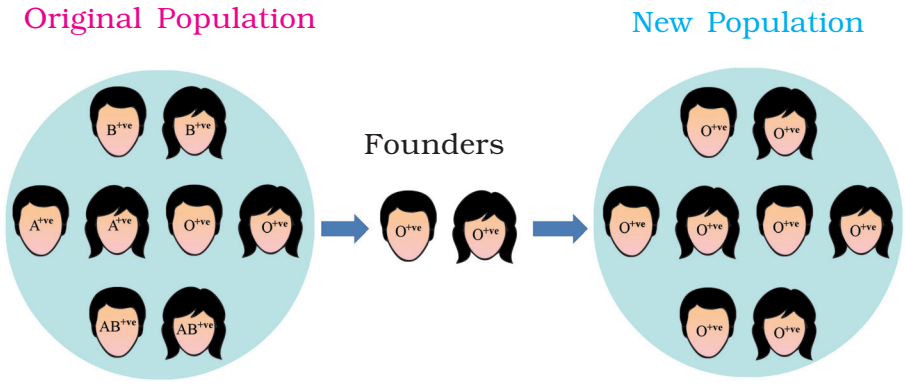


Figure 7.13 Founder Effect

the forefathers of the Red Indian tribe were predominantly O^{+ve} and they isolated themselves reproductively from other populations.

Bottleneck effect: Natural calamities such as earthquakes, volcanic eruptions, floods etc., reduce the size of a population drastically. After these calamities, the lucky survivors may be genetically different from the original population in their genetic makeup. This condition is known as the Bottleneck Effect, e.g. Polydactylic dwarf individuals in the Old Order Amish population of Lancaster in USA

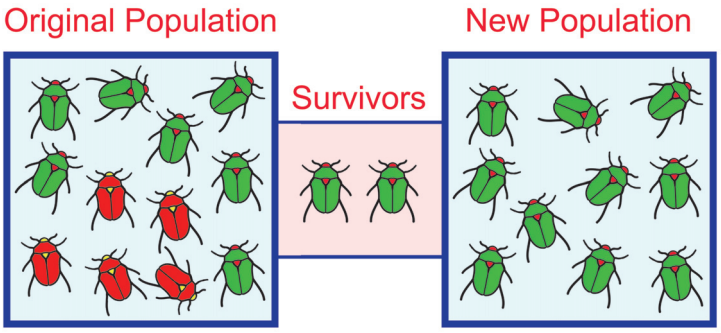


Figure 7.14 Bottleneck effect (Hypothetical)

III. Speciation

The process by which one species evolves into one or more different species is called speciation. Evolution of new species in a single lineage is called **anagenesis** or **phyletic evolution**. On the other hand, if one species diverges to become two or more species, it is called **cladogenesis** or **divergent evolution**. If speciation takes place due to geographical isolation, it is called **allopatric speciation**. If speciation takes place in the organisms which live in the **same habitat**, capable of interbreeding, but do not interbreed due to some isolation mechanisms is called **sympatric speciation**.

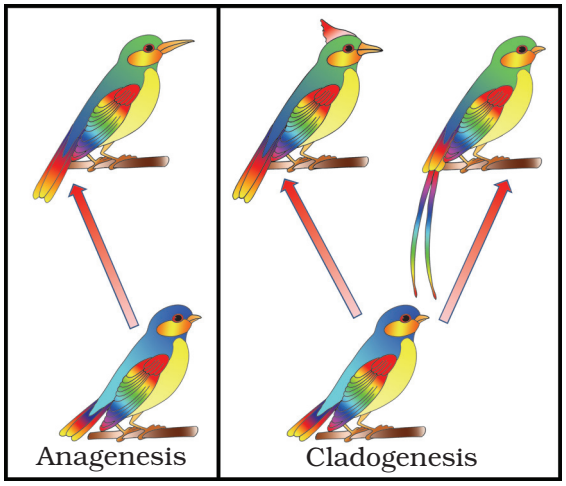


Figure 7.15 Speciation

Do you know? The evolutionary changes that cause differences in populations of a species are referred to as **microevolution** whereas the evolution of taxa higher than the level of species is referred to as **macroevolution**.

A brief account of evolution

The first non-cellular forms of life might have originated approximately 3000 million years ago. The first cellular forms of life appeared about 2000 mya. Invertebrates originated about 500 mya. Jawless fishes evolved during the ordovician period. Fish with stout and lobe like fins could move on to land and evolved into the amphibians. Later amphibians evolved into reptiles which dominated the terrestrial habitat, e.g. Dinosaurs. The biggest of them was ***Tyrannosaurus rex***, which was about 20 feet in height and had dagger like teeth. Some of the land reptiles went back into water and evolved into fish like reptiles such as ***Ichthyosaurus***. The dinosaurs became extinct by the end of the cretaceous period. Some of the reptiles evolved into mammals and later some others into birds. The most successful episode in the history of evolution is the '**origin of man**' with language skills, intelligence and self-consciousness.

7.6 Origin and evolution of man

The origin and evolution of human beings did not occur in a linear manner (straight line). However, we can get a general idea by looking back at the evolution of the primates which includes the animals distantly related (**hominoids**), less closely related (**hominids**) and more closely related (**Homo**) to the humans. About 15 million years ago, there used to live certain hominoids called ***Dryopithecus*** and ***Ramapithecus*** which were hairy and walked like gorillas and chimpanzees. ***Dryopithecus*** was more ape-like while ***Ramapithecus*** was more man-like. A few fossils of bones similar to those of man were discovered in Ethiopia and Tanzania leading to the belief that about 3 to 4 million years ago, man-like primates (***hominids***) walked in the eastern Africa. They were probably 4 feet in height but walked up right. About 2 million years ago, ***Australopithecus*** lived in East African grasslands. The first human-like being was ***Homo habilis*** *(also around* ***2 mya****)*. Evidences show that they hunted with sharp stone tools, but essentially ate fruit. Their cranial capacities* were between ***650-800cc***. They probably did not eat meat. Fossils discovered in **Java** in **1891** revealed the next stage i.e. ***Homo erectus*** (about **1.5 mya**). *Homo erectus* had a comparatively larger cranial capacity of ***around 900 cc***, and probably ate meat. *Homo erectus* and *Homo ergaster* spread through Africa and were the first to leave Africa.

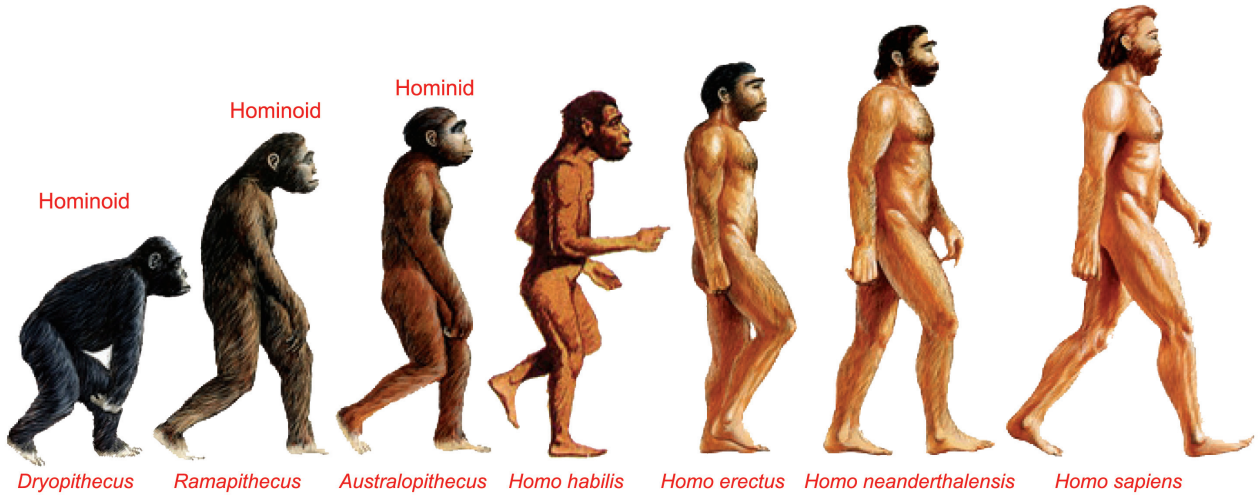


Figure 7.16 Evolution of man

The next important form was ***Homo neanderthalensis***, with a cranial capacity of around **1400cc**, who lived in East and Central Asia between **1,00,000** to **40,000 ya**. They used hides to protect their body and buried their dead. Later during the **ice age** between **75,000-10,000 ya**., **modern *Homo sapiens*** arose in Africa and moved across the continents (first to Asia and later to Europe) and developed into distinct ***races***. *Early modern humans* of the European region is informally called **Cro-Magnon man.** He is known for his cave paintings about **18,000 ya** and agriculture came around **10,000 ya** and then human settlements started.

GLOSSARY

Actual remains (unaltered fossils): Fossils of the actual animal or animal parts trapped in amber, ice, etc., like woolly mammoth in ice in the Siberian snow lands, insects in amber (a plant resin) etc.

Archipelago: A group of many islands in a large body of water

Cast: When empty space of a mould is filled with mud with dissolved minerals and sediment, slowly the water in the mud evaporates forming a rock-like fossil. It gives the form of the organism that was fossilized.

Catastrophe: A sudden violent natural calamity like an earthquake, tsunami, volcanic eruption etc.

Coprolites: Fossilized faecal matter of organisms

Deleterious genes: The genes which are harmful to the organisms possessing them.

Gene pool: The sum total of all the genes present in a sexually reproducing population during a given period of time.

Hides: The skin of an animal, to be used as leather.

Lineage: The descendants of an individual

Mould: Fossilized impression made in the sediment or a 'negative image' of the organism. When an organism is buried in sediment, such as sand, silt or clay, the organic matter completely decomposes over a period of time, leaving behind a hollow area with the organism's shape.

Ontogeny: Developmental history of an individual.

Petrification: The process of replacement of hard parts of an organism with minerals, making it a fossil.

Phylogeny: Ancestral history of an individual.

Protobionts: Molecules with limited metabolic activity, believed to be formed during the early part of evolution of life.

Reproductive success: The proportion of fertile offspring produced by a genotype relative to the other genotypes is called reproductive success.

Simulation: The act of creating conditions similar to those believed to be present actually.

Traces: Fossilized nests, burrows, footprints (tracks), etc.

QUESTIONS

Very Short Answer Type Questions

1. What are panspermia?
2. Define prebiotic soup. Who coined this term?
3. How did eukaryotes evolve?
4. What are the components of the mixture used by Urey & Miller in their experiments to simulate the primitive atmosphere?
5. Mention the names of any four connecting links that you have studied.
6. Define Biogenetic Law, giving an example.
7. Define atavism with an example.
8. Cite two examples to disprove Lamarck's inheritance of acquired characters.
9. Who influenced Darwin most, in formulating the idea of Natural Selection?
10. What is common between Darwinism and Lamarckism?
11. What is meant by genetic load? Give an example.
12. Distinguish between allopatric and sympatric speciations.
13. Mention the scientific names of ape like and man like earlier primates. Which man like primate first used hides to cover the bodies?

Short Answer Type Questions

1. Distinguish between homologous and analogous organs.
2. Write a short note on the theory of mutations.
3. Explain Darwin's theory of Natural Selection with industrial melanism as an experimental proof.
4. Discuss the role of different patterns of selections in evolution.
5. Write a short note on Neo-Darwinism.
6. In a population of 100 rabbits which is in Hardy-Weinberg equilibrium, 24 are homozygous long-eared. Short ears are recessive to long ears. There are only two alleles for this gene. Find out the frequency of recessive allele in the population.
7. What is meant by genetic drift? Explain genetic drift citing the example of Founder Effect.

FOR IGNITED MINDS

'Darwin's Play Field' and the 'Mystery of Mysteries

Organic Evolution

1. If in a H.W population of fruit flies, the frequency of the red eyed (dominant) individuals in 96%, what is the frequency of the dominant allele in that population?
2. In the experiments conducted on *Biston betularia* in England, the frequency of melanic forms was 93% in 1959. If has dropped to 15% in 1995. Can you explain the reason for this drop in the melanic forms?
3. We know that birth records showed that the babies born underweight or overweight showed a higher mortality as Natural Selection operates in normalising / stabilising manner. With the advent of medical facilities mortality in the over weight babies has considerably decreased. What do you think, will happen over the coming decades with perhaps still better medicare is available to the overweight born children. Will the birth weight increase or decrease with the Natural Selection process in operation.
4. Will Genetic Drift bring changes in genotypic frequencies or allelic frequencies or both?
5. When organisms from the extremes of a population mean are removed what type of selection is it called?
6. What type of selection does not occur singly but is followed by another type at some point?
7. What are popularly the 'Documentary evidences' of evolution?
8. Would you support Biogenetic law? Can you think of one example so familiar to you and most probably you read about it in your school curriculum?
9. **DATA**: The embryo of a chick excretes nitrogenous wastes in the form of ammonia in the early part. Later it excretes urea for some days. Finally before hatching out, it starts excreting uric acid.

   Question: Do you think this data is scientifically correct? What is the 'principle' behind such a phenomenon, if you believe in it?
10. If in a population, the rate of change of allelic frequencies is zero, what type of population is it, in the light of the phenomenon of evolution?

Dr. Kurian

Unit-VIII

APPLIED BIOLOGY

Biology And Its 'Multifaceted Glory'

Many years of research have gone into the study of biology as a pure science. Nowadays more stress is laid on application of biology to human utility, health and welfare. Biology has applications in ***Animal husbandry***, ***Agriculture***, ***Aquaculture***, ***Pollution Management***, ***Synthetic preparation of Hormonal analogues***, ***Manufacture of Vaccines***, ***Molecular Diagnosis of various human ailments*** *etc., are a few that come to our mind first. Production of* ***Transgenic Animals*** *and obtaining products of commercial utility at the industrial level is going on at a rapid pace, with the sole objective of making human life better and comfortable.*

This unit also deals with ***Medical Biotechnology Tools*** *and* ***Testing Methodologies***. *The Green Revolution, Blue Revolution and White Revolution (production of more milk from domestic cattle) etc., are applied branches of biology. Naturally, Breeding Technologies in domesticated animals to produce high milk, egg and meat yielding animals improved with the acquisition of in depth knowledge in the fields of* ***Genetics***. ***Molecular Biology*** *and related sciences such as* ***Biochemistry*** *paved the way to developing Biomedical technology 'kits' in the field of testing certain human body functions,in easy and quick ways. Providing certain scientific inputs into rearing fish, poultry birds, honeybees, silk worm moths proved very useful. This unit also gives you an insight into* ***Cancer biology***, ***Gene Therapy*** *and* ***Bio-safety issues***.

The present day Biology student should know at least the basics involved in ***X - ray radiography***, ***CT scan***, ***MRI***, ***ECG***, ***EEG***, ***ELISA*** *etc. So, this chapter gives an over view of all the above.*

Applied Biology

8.1 Animal Husbandry

The strategies adopted for enhancing food production are bound to play a major role in meeting the requirement of food for the ever increasing world's population in the near future. The biological principles that are applied to animal husbandry will become crucial in our efforts to increase the food production.

Animal husbandry is the agricultural practice of breeding and raising livestock (all domesticated animals reared for the benefit of man). It includes buffaloes, cows, pigs, horses, cattle, sheep, camels, goats etc. However the term livestock is often used for farm animals. If extended, it also includes poultry farming and fisheries. Since time immemorial, animals like bees, silk-worm, prawns, crabs, fishes, birds, pigs, cattle, sheep, goats and camels have been used by humans for products such as honey, silk, meat, pork, milk, hydes, wool, etc. Dairy farms, Dairy industry, Poultry and Aquaculture have been providing employment and additional source of income, mainly in rural areas.

The average annual milk yield is about 170 liters per cow in India. Contrary to it, the average annual milk yield is about 4,100 liters per cow in Netherlands. Because of its low productivity the Indian cow is known as **'teacup cow'**. So, newer technologies have to be applied to achieve improvement in quality and productivity. Modern methods of breeding, MOET (multiple ovulation and embryo transfer) and production of transgenic animals must be taken up on a large scale in addition to conventional practices and care.

Cattle population in India consists of three groups of breeds. They are:

1. Milch breeds which yield higher quantity of milk and the bullocks are not useful in farms or transport. The superior milch buffalo breed is the MURRAH breed.
2. Draught breeds: Bullocks are excellent draught animals (useful in agricultural practices).
3. Dual purpose (general utility)

Do You Know? **1**. The **ONGOLE** breed bull is the costliest of all the types of bulls in India. **2**. Anand dairy (in Gujarat), the most popular dairy in India sells its milk products under the brand name '**AMUL**' - Anand Milk Union Limited.

A. Management of Farm and Farm Animals

A professional approach to farm management gives the much needed boost to our food production and it certainly has an edge on traditional practices. The farm management ensures optimum quality feed, breeding and caring. It provides good infrastructure and takes care of sick animals.

B. Dairy Farm Management

Breeding, feeding and management of milch animals, production, processing and marketing of their milk and milk products on economic basis constitute dairying. Commercial dairy systems house five to hundreds of hybrid cows or **Murrah** hybrid buffaloes. The different kinds of products that can be made with milk from a dairy farm are butter, ghee, curds, butter milk, cheese, paneer, etc.

Dairying provides an occupation and income in all seasons to the farmers. Milk is considered an indispensable food for $1/4^{th}$ of the population which includes infants and children. In recent years dairying has assumed new dimensions with emphasis on increased production of quality milk through technical innovation and modern management methods. Indian dairy industry had witnessed fantastic growth, since the inception of the programme/ project '**Operation Flood**' by NATIONAL DAIRY DEVELOPMENT BOARD (**NDDB**).

Do You Know? The father of 'white revolution' in INDIA, the founder of ANAND DAIRY and the founder chairman of NDDB was Dr. Kurian.

In dairy farm management, we deal with processes and systems that increase yield and improve quality of milk. The following are essential components.

Figure 8.1 Holstein-Friesian cow

1. Selection of good breeds having high yielding potential, combined with disease resistance is important as milk yield primarily depends on the quality of breeds in the farm. Examples include high yielding hybrid cows of the exotic breeds like Holstein-Friesian, Jersey, Ayrshire and Brown Swiss. Holstein-Friesian cow yields up to 30 litres of milk/day.
2. Proper housing with adequate water, ventilation, suitable temperature, etc., is needed to enhance the yield potential.
3. Feeding of cattle with special emphasis on quality and quantity of fodder should be done in a scientific manner.
4. While milking, storage and transport, cleanliness and hygiene are of paramount importance. As these processes are mechanised, direct contact of the produce with the handler is reduced.
5. A regular visit by a veterinary doctor is necessary.
6. Proper record keeping and inspections would help to identify and rectify the problems at the earliest.

Do You Know? In India, at present buffaloes' milk accounts for about 54% and the rest for cow's milk. Uttar Pradesh occupies the first place followed by Punjab and Haryana, in milk production.

Animal Breeding

Animal breeding is an important aspect of animal husbandry which aims at increasing the yield of animals and improving the desirable qualities of the produce. ***A breed is a group of animals related by descent and similar in most characters like appearance, features, size, configuration, etc.*** The following are the desirable qualities for which we breed animals:

1. Disease resistance,
2. Increase in the quality and quantity of milk, meat, wool, etc.
3. Fast growth rate,

4. Enhanced productive life by improving the genetic merit of livestock,
5. Early maturity and
6. Economy of feed.

Methods of animal breeding are broadly two types. They are 1) INBREEDING 2) OUTBREEDING.

1. Inbreeding

When crossing is done between animals of the same breed it is called inbreeding. It refers to mating of more closely related individuals within the same breed of individuals in a lineage. The breeding strategy is the identification and mating of superior males and superior females of the same breed. A superior female, in the case of cattle, is the cow (*Bos indicus*) or buffalo (***Bubalus bubalis***) that produces more milk per lactation. On the other hand a superior male is the bull which gives rise to a superior progeny as compared to those of other males. The progeny obtained from such matings are evaluated and the superior ones among them are used for mating purpose.
Inbreeding is of two types 1.Close breeding, 2. Line breeding.

Close breeding is mating between male parent (sire) and female offspring and/or female (dam) with male offspring. **Line breeding** (cousin mating) is the selective breeding of animals for a desired feature by mating them within a closely related line (but not as close as close breeding). It leads to upgrading (to improve the quality of livestock by selective breeding for desired characteristics) of a desired commercial character.

Advantages of Inbreeding

1. Inbreeding increases **homozygosity.** Thus, inbreeding is necessary if we want to evolve a pure line animal.
2. It helps in the accumulation of superior genes and elimination of less desirable genes.
3. This approach, where there is selection at each step, increases productivity of inbred population.

Disadvantages of Inbreeding

1. Inbreeding may express harmful recessive alleles and the phenotypes (that are generally eliminated by Natural Selection) concerned.
2. Continued inbreeding, especially close breeding, usually reduces fertility and even productivity. This is called INBREEDING DEPRESSION.

Note: Whenever inbreeding depression becomes a problem, selected animals of the breeding population should be mated with unrelated superior animals of the same breed. This usually helps restore fertility and yield.

2. Out Breeding

Out-breeding is the breeding of the unrelated animals. Out-breeding is of three types 1.Out-crossing 2. Cross-breeding 3. Interspecific hybridisation.

A. Out-crossing

It is the practice of mating of animals within the same breed, but having no common ancestors on either side of the pedigree for 4-6 generations. The offspring of such a mating is known as an **out-cross**. It is the best breeding method for animals that are below average in milk production, growth rate (in beef cattle) etc. At times a single out-cross often helps to overcome inbreeding depression.

B. Cross-breeding

In this method, superior males of one breed are mated with superior females of another breed. The offspring of such a mating is said to be a **cross-breed.** Cross-breeding allows the desirable qualities of two different breeds to be combined. The progeny (cross breeds) are not only used for commercial production but also inbreeding and selection to develop stable breeds which may be superior to existing breeds. For example **Hisardale** is a new breed of sheep developed in Punjab by crossing '**Bikaneri ewes**' and '**Marino rams**'.

C. Interspecific hybridisation

In this method, male and female animals of two different related species are mated. The progeny may combine desirable features of both the parents and is different from both the parents. For example when a male donkey (jackass) is crossed with a female horse (mare), it leads to the production of a mule (sterile). Similarly when a male horse (stallion) is crossed with a female donkey (jennet), hinny (sterile) is produced. Mules have considerable economic value.

Jackass X mare = mule; Stallion X jennet = hinny

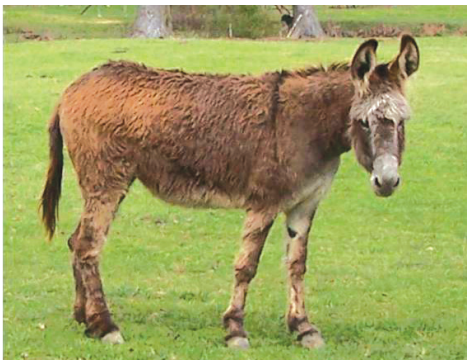


Figure 8.2 Mule

Controlled Breeding Experiments

They are carried out using artificial insemination and multiple ovulation and embryo transfer technology (MOET).

Artificial insemination (AI) is the technique in which semen is collected from superior bulls and introduced into the female reproductive tract when the female is in 'heat'. This semen can be used immediately or can be frozen and used at a later period. It can be transported in a frozen form to the place where a female is housed. In this way desirable crosses can be made. The major advantage of AI over natural mating is that it permits the dairy farmer to use top proven sires (males) for genetic improvement of his herd and control of venereal diseases. AI is also of tremendous value in making optimal use of different sires and enables dairy farmer to breed individual cows to selected sires according to their breeding goals.

The breeding centre at SALON in Rae Bareli is at present the breeder and producer of top quality frozen semen of pure exotic breeds.

Multiple Ovulation and Embryo Transfer (MOET)

The following are the steps involved in MOET.

1. A cow is administered hormones, with FSH-like activity.
2. This induces **follicular maturation** and **super ovulation** (In super ovulation- instead of one egg, which they normally produce per cycle, they produce 6-8 eggs).
3. The animal (cow) is either mated with an elite bull or artificially inseminated.
4. The embryos are at **8-32 celled stages** are recovered non-surgically and transferred to **surrogate** mother (an animal that develops the offspring of another animal in its womb).

Now the genetic mother is ready for another round of super ovulation. This technology is in use for cattle, sheep, rabbits, buffaloes, mares etc. High milk-yielding breeds of females and high quality (lean meat with less lipid) meat-yielding bulls have been bred successfully to increase the herd size in a short period of time.

8.2 Poultry Farm Management

Poultry

It is a class of domesticated fowls (birds) reared for the production of eggs or meat or both. It includes chicken, peafowls, ducks, turkeys, geese, pigeons, pheasants and emus. The birds which are raised exclusively for the production of eggs are called **LAYERS**. The birds which are raised only for their meat are called **BROILERS**. They are of either sex under the age of 8—10 weeks, weighing 1.5 kg and with a smooth textured breast.

Figure 8.3
White leg horn

Scientific poultry management aims at maximising returns with minimum investment. Poultry farming is spread all over India both as cottage and large scale industry in India. At present India ranks third in egg production and fifth in chicken meat production in the world. Andhra Pradesh is the largest egg producer in India.

Do You Know? Padmasri **Dr. B.V. Rao** is the **FATHER OF MODERN POULTRY IN INDIA**. He was the founder chairman of **National Egg Coordination Committee** (NECC) which monitors marketing of eggs in India and their exports.

The central poultry breeding farms established at Mumbai, Bhubaneswar and Hesserghatta develop hybrid strains of layers. Indian Veterinary Research Institute (IVRI) at Izatnagar produces quality broiler strains and poultry vaccines.

Important Components of Poultry Management

1. **Selection of disease free and suitable breeds**: The selected breed should get acclimatised to a wide range of climatic conditions. Hybrid layers used in India are BV-300, Hyline, Poona pearls, etc. Commercial broiler strains used in India include Hubbard, Vencobb, etc.,
2. **Feed management (proper feed and water):** Balanced diet is a must to maximise the yield. Brooder/chick mash, grower mash, pre-layer mash and layer mash are fed to layers at different ages. Likewise pre-starter mash, starter mash and finish mash are the types of feeds given to broilers. 'Safe water' should be supplied through waterers at all times.
3. **Health care:** Vaccination against viral diseases (Ranikhet, Marek's, and Gumboro) and using antibiotics to treat bacterial diseases {Fowl cholera, Infectious coryza, Chronic Respiratory Disease (CRD)} make the poultry birds disease free. Fungal diseases affecting poultry are Brooder's pneumonia, Aflatoxicosis and Thrush.
4. In addition to the above, hygiene, proper and safe farm conditions ensure better produce.

   Nutritional value of chicken meat and egg (only proteins, lipids and calorific value) are given below.

WEIGHT %	PROTEIN %	FATS%	ENERGY IN K CAL
100g of egg	13.3	11.5	173
100g of Chicken meat	20	2.5	109

Egg is a highly nutritious food item for humans because of its high Biological value (96%) and PER (4.5).

AVIAN FLU (BIRD FLU) is an important disease affecting poultry birds and man has to be very watchful about this disease as it is very dangerous to him too.

Causative organism: Bird flu is caused by an 'avian flu virus', the **H5N1**. The virus that causes the bird infection infects humans too. It can start a **worldwide epidemic** (**Pandemic disease**).

Mode of infection: Infection may be spread simply by touching contaminated surfaces. Birds infected by this type of influenza, continue to release the virus as in their faeces and saliva for as long as **10 days**.

Symptoms: Infection by the avian influenza virus H5N1 in humans causes typical flu-like symptoms, which might include: cough (dry or with phlegm), diarrhoea, difficulty in breathing, fever, headache, malaise, muscle aches and sore throat.

Prevention

1. Avoiding consumption of undercooked chicken meat reduces the risk of exposure to avian flu.
2. People who work with birds should use protective clothing and special breathing masks.
3. Complete culling of infected flock by burying or burning them.

8.3 Bee-Keeping/Apiculture

In the insect world, the economically important honeybees exemplify colonial living, reciprocal communication, division of labour and polymorphism (caste differentiation). Bee-keeping or apiculture is the maintenance of hives of honey bees for the production of honey and wax. Bee-keeping is an age-old cottage industry.

The two **species** of **honey bees** widely used in bee keeping in India are:

1. ***Apis mellifera*** (European bee): A favourite for apiculture; yields large quantities of quality honey.

2. ***Apis cerana indica*** (Indian or Asian hive bee): It is wild and is also domesticated.

A BEE COLONY: Queen (fertile female), drones (haploid males) and workers (sterile females) are the three castes in a beehive.

i. QUEEN: It is the largest individual in the colony; It is a fertile, diploid female, one per bee hive and the egg layer of the colony. She lives for about five years and her only function is to lay eggs. The queen bee during its nuptial flight receives sperms from a drone and stores in the spermathecae and lays two types of eggs, the fertilised and unfertilised. All fertilised eggs develop into females. All the larvae are fed with the royal jelly (vitamin and nutrient rich secretion from the glands in the hypopharynx of the nurse workers) for the first 3 days only. Afterwards royal jelly is fed only to the bee that is bound to develop into next queen, whereas the other larvae fed on bee bread (honey and pollen) become workers (sterile females) and drones.

ii. DRONES (haploid, fertile males)

These are robust, large winged, small numbered, short lived and are fed with bee bread by nurse workers. They are developed from the unfertilized ova by *arrhenotoky* (**male parthenogenesis**).

iii. Worker Bees

They are multifaceted sterile females which develop from the fertilised eggs and perform diverse functions. They live for two or three months. They are the smallest in size among the 3 castes. Worker bees secrete wax, build hexagonal cells of the honey-comb, gather nectar from flowers, manufacture and store honey, gather pollen, make **propolis** (bee glue-used to seal the cracks in the combs). The scout bees (worker bees) perform a 'waggle dance' after returning to the hive, to inform other bees about source of nectar. Waggle dance informs the other worker bees the direction with reference to sun's position and distance of availability of food (discovered by **Nobel Laureate Karl von Frisch**). They also guard the hive for which purpose they possess a poisonous sting. They have chewing and lapping type of mouth parts.

> **Do you know**? Worker bees have pollen brushes on the tarsi of the legs and pollen baskets on the tibia of the metathoracic legs.

Beehive

It is an enclosed structure in which honey bees live and raise their young. Domesticated honeybees live in man-made beehives (boxes) in 'apiaries'. Bee wax is produced from their abdominal glands (present on 2nd to 5th abdominal

segments). Bees use the storage cells to store food (honey and pollen) and brood cells to house the "brood" (eggs, larvae, and pupae).

Economic importance of Honey bees

The bee products like Honey, wax, propolis and bee venom are used in various ways.

1. **Honey** is a rich source of fructose, water, glucose, minerals and vitamins.
2. **Bee's wax** is used in the preparation of cosmetics, polishes of various kinds and candles.
3. **Propolis** is used in the treatment of inflammation and superficial burns.
4. **Bee's venom**, which is extracted from the sting of worker bees, is used in the treatment of arthritis.
5. **Pollination**: Bees are the pollinators of our crop plants such as sunflower, Brassica, apple and pear.

Factors /requirements for successful Bee-keeping:

1. Knowledge of nature and habits of honey bees.
2. Selection of suitable location (termed Apiary or Bee yard) for keeping the beehives.
3. Raising a hive with the help of a queen and small group of worker bees.
4. Management of beehives during different seasons
5. Handling and collection of honey and bee wax.

8.4 Fishery Management/Pisciculture

Fishery is an industry or occupation devoted to the catching, processing for storage in freezers and selling of fish, shellfish or any other aquatic animals for human consumption.

Types of Fisheries

Based on how the fishery resource is obtained, fishery can be categorised broadly into two types 1. Capture and 2. Culture fisheries.

1. **Capture fishery:** In capture fishery the resource is obtained from the natural body of water. Capture fishery is either marine or inland. If the capture is from the sea, it is called marine fishery. In the sea, if the resource is captured from open waters, it is called **offshore fishery**. If the resource is captured from coastal waters, it is called **inshore fishery**. If the capture is from estuaries or fresh water it is called **inland fishery**.

2. **Culture fishery (aquaculture):** It involves rearing and management of selected aquatic organisms under regulated conditions and their subsequent harvesting after the stipulated time.

Aqua culture can be categorised into certain types based on the medium used in culturing (fresh water, brackish water and mariculture), organisms selected for culturing (prawn, crab, oyster and pisciculture) and the presence or absence of fins in those organisms (fin fish fishery/shell fish fishery). ***AQUACULTURE*** (culture fishery) not only includes the culturing of fish, but also culturing of other aquatic organisms under regulated conditions to achieve better production. The term ***PISCICULTURE*** is used when the organisms cultured are exclusively fin fishes.

The organisms selected for culture practices must obviously possess certain features to make their culture profitable. They show fast rate of growth, economy of feed, early maturity, disease resistance, high nutritious value, high consumer demand and export value. Indian carps namely ***Catla catla*** (catla), ***Cirrhinus mrigala*** (mrigal), ***Labeo rohita*** (rohu) are extensively used in fresh water pisciculture in INDIA. The common carp, grass carp and silver carp (**exotic-Chinese carps**) are also used in pisciculture in recent years in India, as growth rate and reproductive potential are high in them. The Indian carps are also harvested from natural fresh water bodies (capture fishery).

Figure 8.4 *Catla Catla*

Marine water fishes include **Hilsa**, **Sardine**, **Bombayduck**, **Mackerel** and **Silver pomfret. Oil sardine** fishery along the Kerala coast is the largest fishery in India.

Hypophysation or induced breeding is followed in artificial breeding. Pituitary extracts containing gonadotropins (FSH and LH) or ***ovaprim*** *(a synthetic analogue of gonadotropin releasing agent and Dopamine inhibitor) are injected into brood fish to induce release of spawn for seed production.*

Economic Importance of Fishery

1. As Food

Fish meat, in general, is a good source of proteins, vitamins (A and D), minerals and rich in iodine. Tunas, shrimps and crabs are not only edible but have export value also.

2. By-products

A. Shark and cod liver oils are good sources of vitamins A and D. Oil from Sardine and Salmon are good sources of **omega 3 fatty acids**, which have multiple functions (reduce cholesterol, help prevent cancer cell growth etc.,).

B. Fish guano: Fertilizer prepared from 'scrap fish'.

C. Other fish by-products are shagreen (dried skin of fish such as sharks), Isinglass (substance obtained from dried swim bladders of mostly cat fish, used in clarification of wines) etc.

Fisheries have carved a niche in the Indian economy. We now talk about '**Blue Revolution**' as being implemented on lines similar to '**Green Revolution**'.

In addition to pisciculture, the culture of prawns, crabs and pearl oysters enable us earn foreign exchange worth millions of dollars from their exports.

8.5 Biotechnological Applications in Medicine

Recombinant DNA technology involves manipulation of genes or microorganisms to produce certain products useful to mankind. These recombinant DNA technological processes have made an immense impact in the area of human health care. They are used in the production of hormones, synthetic vaccines, effective therapeutic products etc. These products like the recombinant therapeutics do not induce unwanted immunological responses. At present about 30 recombinant therapeutics have been approved for human use, the world over.

Genetically Engineered Insulin

You have already learnt that **INSULIN** is a protein hormone produced from the beta cells of islets of Langerhans of the pancreas and is required to accelerate the uptake of glucose into the body cells and to promote glycogenesis, lipogenesis, protein synthesis, etc. Insulin must be injected or given via an insulin pump. It cannot be administered orally, because it is a protein and is broken down in the stomach before it can be absorbed. Attempts are underway to develop orally administerable insulin.

Prior to the development of humulin, diabetic patients used to be dependent upon animal insulin extracted from the pancreatic islet tissue of slaughtered cattle and pigs. The animal insulin is more expensive, less accessible and causes allergies. They also cause several side effects, due to certain non-self proteins in them, which act as antigens. Currently, genetically engineered ***E.coli*** which can be grown in large quantities to produce human (humulin) insulin is available and from which we can make as much insulin as we need.

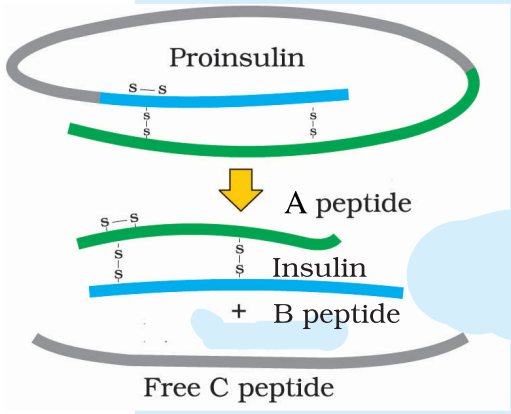


Figure 8.5 Maturation of pro-insulin into insulin

Structure of insulin: Human insulin is made up of **51** amino acids arranged in two polypeptide chains -**chain A** (21 amino acids) and **chain B** (30 amino acids), which are linked together by **disulphide linkages**. In mammals, including humans, insulin is synthesised as a **pro-hormone** (like a pro-enzyme, which needs to be processed before it becomes fully mature and functional hormone) which contains an extra stretch called the **c peptide**. This c peptide is not present in the mature insulin and is removed during maturation into insulin.

The main challenge for the production of insulin in the laboratory using rDNA technique was getting insulin assembled into its mature form. In 1983, **Eli Lilly**, an **American company**, prepared two DNA sequences coding for A and B chains of human insulin and introduced them into plasmids of *E.coli* to produce insulin chains. The chains A and B were produced separately and combined by creating disulphide bonds to form 'humulin' which is the brand name for a group of biosynthetic human insulin products.

8.6 Vaccines

The term 'vaccine' was coined by **Edward Jenner**. He immunised a boy against small pox by inoculating him with a relatively less dangerous cow pox virus. The technique of attenuating or weakening of a microbe was developed by Pasteur.

A vaccine is a biological preparation that improves immunity to a particular disease. A vaccine typically contains the disease-causing microorganism, and is often made from weakened or killed forms of the microbe. The toxins or one of the surface proteins of the microorganisms are also used in preparing vaccines.

Vaccines are generally used as prophylactic measures. Moreover, they may not guarantee total protection from a disease. It may be due to inadequate immune response of the host's immune system. Even if the host develops antibodies, the human immune system may not effectively defend the body from the pathogen immediately. Therefore certain adjuvants are used to enhance the immune response stimulated by the antigens . Most often aluminium adjuvants are used.

Use of vaccines in the Afro-Asian countries has reduced the mortality rate. For example smallpox could be eradicated completely in India/World by intensive vaccination programme in an organised manner, by governmental agencies,as it is being done in the case of polio, nowadays. Though there are vaccines available against several pathogens, vaccines against dreaded diseases such as AIDS and Malaria are yet to be developed.

The following are some important Biotechnologically produced vaccines.

1. **Attenuated Whole Agent Vaccines**
   They contain disabled (made less virulent) live microorganisms. Mostly they are antiviral. Examples: vaccines against yellow fever, measles, rubella and mumps and the bacterial disease such as typhoid.
2. **Inactivated Whole Agent Vaccines**
   They contain '**killed microbes**' (virulent before killing). Examples: vaccines against influenza, cholera, bubonic plague, polio, hepatitis A, rabies and **Salk's polio vaccine**.
3. **Toxoids**
   They contain '**toxoids**' which are inactivated '**exotoxins**' of certain microbes. Examples: the vaccines against **Diphtheria** and **Tetanus**.

Thus, vaccines are used in the prevention of diseases as they induce artificially acquired active immunity.

> **Do you know?** Jonas Salk produced polio vaccine (inactivated polio visus) which became popular as Salk's vaccine. Later SABIN'S oral polio vaccine (attenuated poliomyelitin virus) produced by ALBERT SABIN became much more popular as its effect lasts longer and is easy to administer.

8.7 Molecular Diagnosis

We know that for effective treatment of a disease, early diagnosis and understanding its pathophysiology is very important. Using conventional methods of diagnosis (serum, urine analysis, etc.) early detection is not possible. Recombinant DNA Technology, Polymerase Chain Reaction (PCR) are some of the techniques that help early diagnosis.

Presence of a pathogen (bacteria, viruses, etc.) is normally suspected only when the pathogen has produced a disease symptom. By this time the concentration of pathogen is already very high in the body. However, very low concentration of bacteria or viruses (at a time when the symptoms of the disease are not yet visible) can be detected by amplification of their nucleic acid by PCR. PCR helps to detect very low amounts of DNA by amplification of the small DNA fragment. PCR is now routinely used to detect HIV in suspected cases. It is being used to detect mutations in suspected cancer patients too. It is a powerful technique to identify many other genetic disorders such as haemophilia, phenylketonuria, etc.

A single stranded DNA or RNA, tagged with a radioactive molecule (probe) is allowed to hybridize with its complementary DNA in a clone of cells followed by its detection using autoradiography. The '**clone**' having the mutated gene will not appear on the photographic film, because the probe does not show complementarity with the mutated gene.

Molecular Diagnostics is constantly translating new discoveries and novel technologies into useful clinical tests that detect 'molecular fingerprints' of diseases.

8.8 Gene Therapy

Gene therapy is the insertion of genes into an individual's cells and tissues to treat a disease, such as a hereditary disease in which a deleterious mutant allele is replaced with a functional one. The biology of human gene therapy

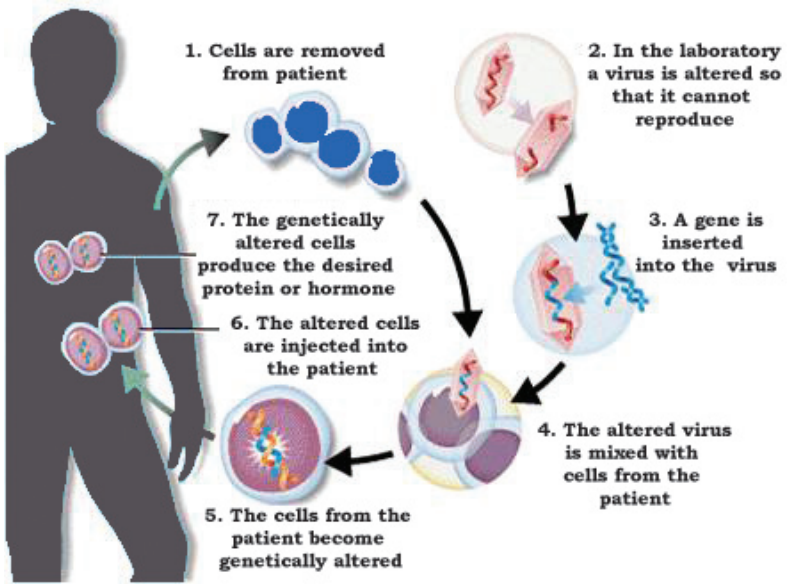


Figure 8.6 Important steps in the process of Gene Therapy

is a collection of methods/techniques that allows correction of a gene defect that has been diagnosed in a child/embryo.

Basic Technique: A normal gene is inserted into the genome to supplement an abnormal gene (mutated gene), which is disease causing. To deliver the normal gene (therapeutic gene) a vector must be used. The vector unloads its genetic material containing the '**therapeutic human gene**' into the target cell. The generation of a functional protein product from the therapeutic gene restores the cell to its normal state.

Types of Gene Therapy: Two basic types of gene therapy can be applied to humans, germ line and somatic line.

a. **Germ line gene therapy**: In this type of therapy, functional genes (normal genes) are introduced into sperms or ova and are thus integrated in to their genomes. Therefore the change or modification becomes heritable. Due to various technical and ethical reasons, the germ line gene therapy remained at the '**infant stage**' for the time being.

b. **Somatic line therapy**: In this type of therapy, functional genes are introduced into somatic cells of a patient. The approach is to correct a disease phenotype by treating some somatic cells in the affected person. The changes effected in this type of GT are non-heritable.

Somatic line therapy can be either ex-vivo or in vivo. In **ex-vivo**, cells are modified outside the body and then transplanted back. In **in-vivo**, genes are changed in cells, while they are still inside the body.

First Clinical Gene Therapy

The first clinical gene therapy was given in 1990 to a four year old girl with **adenosine deaminase** (**ADA**) deficiency. This enzyme is crucial for the immune system to function. ADA deficiency causes severe combined immunodeficiency (SCID). It is caused by the deletion or dysfunction of the gene encoding for the enzyme ADA. In some children ADA deficiency can be cured by bone marrow transplantation, in others it can be treated by an enzyme replacement therapy, but both these approaches are not completely curative.

As a first step towards gene therapy, lymphocytes from the blood of the patient are kept in a nutrient medium outside the body. A functional ADA cDNA (using a retroviral vector) is then introduced into these lymphocytes, which are subsequently returned to the patient. However, as these cells are not immortal the patients require periodic infusion of such genetically engineered lymphocytes. Permanent cure is possible when the gene isolated

from marrow cells producing ADA is introduced into the cells at early embryonic stages.

Diseases and Gene Therapy: Scientists are focusing on diseases caused by single-gene defects, such as cystic fibrosis, haemophilia, muscular dystrophy and sickle cell anaemia, wherein scientists are trying to introduce genes directly into human cells. Currently, most gene therapy studies are aimed at cancer and hereditary diseases linked to a genetic defect. In spite of so many efforts, the biology of GT remains complex and many techniques need improvement and perfection. The genetic link of many diseases is to be understood more fully before GT can be used appropriately.

Transfer of Genetic Material: Genetically modified DNA can be introduced into a eukaryotic cell by a process called '**Transfection**'. It can also be introduced by *Gene guns* or through '**electroporation**' of the cells. **Viral vectors** are used to send the genetic material into cells, a process similar to **bacterial transduction**. In methods in which DNA is directly sent, the DNA to be delivered is protected from damage during transfer /entry into recipient cell by enveloping it in lipid coats (**Lipoplexes**) or enveloping in complexes of polymers (**Polyplexes**). Synthetic oligodeoxy nucleosides are used to inactivate genes (**Silencing the genes**) involved in causing disease.

8.9 Transgenic Animals

Animals that have their own genome and had their DNA manipulated to possess and express an extra (foreign) gene are known as transgenic animals. Transgenic rats, rabbits, pigs, sheep, cows and fish have been produced, although over 95 percent of all existing transgenic animals are mice. Transgenic animals are produced for many reasons aiming at benefitting human beings. Let us try and explore some of the common reasons:

i) **Normal physiology and development**: Transgenic animals can be specifically designed to allow the study of how genes are regulated, and how they affect the normal functions of the body and its development, e.g. study of complex factors involved in growth such as insulin-like growth factor. By introducing genes from other species that alter the formation of this factor and studying the biological effects that result, information is obtained about the biological role of the factor in the body.

ii) **Study of disease**: Many transgenic animals are designed to increase our understanding of how genes contribute to the development of disease. These are specially made to serve as models for human diseases so that investigation of new treatments for diseases is made possible. Today

transgenic models exist for many human diseases such as cancer, cystic fibrosis, rheumatoid arthritis and Alzheimer's (Discussed in unit iii).

iii) **Biological products**: Medicines required to treat certain human diseases can contain biological products, but such products are often expensive to produce. Transgenic animals that produce useful biological products can be created by the introduction of the portion of DNA (or genes) which codes for a particular product such as human protein (**α-1 antitrypsin**) used to treat emphysema. Similar attempts were made for treatment of phenylketonuria (PKU) and cystic fibrosis. In 1997, the first transgenic cow, **Rosie**, produced human protein-enriched milk (2.4 grams per litre). The milk contained the human **alpha–lactalbumin** and was nutritionally a more balanced product for human babies than what is available in normal milk from untreated cows.

> **NOTE**: *Alpha-lactalbumin* is rich in *essential amino acids* and is the dominant protein in human milk.

iv) **Vaccine safety**: Transgenic mice are being developed for use in testing the safety of vaccines before they are used on humans. Transgenic mice are being used to test the safety of the polio vaccine. If successful and found to be reliable, they could replace the use of monkeys to test the safety of batches of the vaccine.

v) **Chemical safety testing**: This is known as toxicity/safety testing. The procedure is the same as that used for testing toxicity of drugs. Transgenic animals, that carry genes which make them more sensitive to toxic substances than non-transgenic animals are produced. They are then exposed to the toxic substances and the effects studied. Toxicity testing in such animals will allow us to obtain results in less time. Indian government has setup GEAC (Genetic Engineering Approval Committee) to look into misuse of DNA manipulation and safety of introducing GM-organisms for public services.

8.10 Cancer Biology

Cancer is a leading killer disease in the world. It is basically a condition of failure of cell division control. Unchecked division of cells leads to the formation of 'neoplasm' (tumor) and such an abnormal proliferation of cells is called 'neoplasia' (formation of a tumor). Neoplasm may be (1) **Benign** (harmless e.g. uterine fibroids in a female human being) (2) **Pre-malignant** (also called 'carcinoma in situ'– in which cells transform into cancerous cells in due course of time) (3) **Malignant** (cancer, in which cells invade and destroy surrounding cells forming 'metastasis'). Some neoplasms, however

do not form tumor e.g. **Leukemia**. ***Oncology*** is the branch of medicine that deals with tumors, including study of their development, diagnosis, treatment, and prevention. Cancers are caused chiefly due to '*failure of cell cycle regulation*' which is not yet clearly understood.

Normal cells show a phenomenon called '**contact inhibition**' (which means cessation of cell division and cell mobility, when they are in close (physical) contact with each other. Cancer cells (**neoplastic cells** or **tumor cells**) lose this property and keep on dividing.

GUESS: Cancer cells lack 'anchorage dependence'. Normal cells attach/ anchor to the surface of the dish in which they grow when the medium is sterile and supply of nutrients is enough. Now the question is – I. What happens when 'normal cells' are grown in a dish containing all the requirements necessary? II. What happens when 'cancer cells' are grown in a dish containing all the requirements necessary?

As cancer cells actively divide and grow, they starve the normal cells by competing for 'vital nutrients'. Normal cells are joined by '*intercellular adherens junctions*' called '***cadherins***' (***calcium dependent trans membrane proteins***) and they are missing in cancer cells (hence their ability to detach and cause metastasis). Cancer is a disease in which damaged cells do not undergo '***programmed cell death***' (**apoptosis**). Cancer cells have abnormal changes on their cell surface /unusual profile of surface antigens,which can be recognized and destroyed by **NK cells** and Tc cells of the immune system. Another important aspect of tumors is – there is **increased growth of blood vessels** towards the tumors. When tumors grow in size, diffusion of oxygen and nutrients becomes restricted and so tumors resort to attracting more blood vessels from their surrounding matrix (***angiogenesis***). If extension of blood vessels can be inhibited, the cancer cells starve and die.

Proto-oncogenes, oncogenes, tumor suppressor genes

Human genome has some '***proto-oncogenes'*** which are normal cellular genes. Due to the effect of certain mutagens,proto-oncogenes mutate into cellular '***oncogenes'*** which cause cancers. There are some ***tumor suppressor genes*** also in the genome. For example the ***gene p53*** is a gene that codes for a 'protein' (***p53 protein***) that inhibits the development and growth of tumors. Mutations of proto-oncogenes are dominant (a single copy of the oncogene can lead to cancer). Interestingly, in the case of tumor suppressor genes such as the p53 gene, both copies of the gene in the homologous pair of chromosomes must undergo mutation to allow cancer to develop. The **protein**

p53 plays an important role with reference to the **'*G1 check point*'** in the regulation of cell division cycle. It guards the 'integrity of the DNA' (it is often called the GUARDIAN ANGEL OF **CELL'S GENOME**). It stops cell division and helps repair the damaged DNA. If the damage is repaired, the p53 protein allows the cell to enter the 'S' phase. If it is irreparable,it directs the cell to undergo 'apoptosis'. Hence the gene p 53 is called '***tumor suppressing gene'***. The **retinoblastoma protein** (pRB) is also a '**tumor suppressor protein**' that is dysfunctional in several major **cancers**. Its function is similar to that of p53 protein.

Carcinogens: A **carcinogen** is a substance that causes **cancer**. Carcinogens damage the DNA. Several radioactive substances e.g. ***gamma rays***, some ***U-V rays***, ***X rays*** etc. and '**inhaled asbestos**', certain '**Dioxins**', **tobacco** smoke (which contains many types of carcinogens such as **benzopyrene, nitrosamines** and inorganic compounds such as **chromium**, **cadmium, arsenic, polonium-210**) etc. are **carcinogenic**. If the DNA damage is too severe to repair, the cells undergo **apoptosis**, but if the programmed cell death pathway is damaged, ***the cell becomes a cancer cell.***

Do You Know? If,for example,cancer cells from the liver move to brain and cause a tumor there,it is not called 'brain cancer'. It is rather called 'Secondaries' (metastasis) of liver cancer in the brain.

Types of cancers

There are different types of cancers such as **carcinomas** (cancers of **epithelial tissues/cells** which are **most common** as epithelial cells divide more often), **sarcomas** (cancers of connective tissues), **leukemias** (cancers of bone marrow cells resulting in unrestrained production of WBC – a **liquid tumor**), **lymphomas** (cancers of the **lymphatic system**). Certain types of cancers are called '**familial cancers'** (cancer that occurs in families; genetic based) and others **'sporadic cancers'** (non-hereditary cancers occurring without any family history). Some types of cancers are caused by 'tumor forming RNA viruses' (**oncoviruses**), e.g. ***Rous sarcoma virus*** which causes 'avian sarcoma'.

Do You Know? When a retro virus enters a host cell, it ***reverse transcribes*** into **cDNA**, which 'integrates' with the host cell's DNA and starts producing more viruses.

Did You Come to Know? A recent advance in science is the recognition that cervical cancer (cancer of the neck of the uterus) in women is caused by a VIRUS called Human Papillomavirus (HPV) and an effective vaccine against cervical cancer is available as a prophylactic against cervical cancer. Women are 'screened' to detect potentially pre-cancerous condition by the test called *Pap test / Pap smear test.*

Detection of cancer

Cancer detection is based on**'biopsy' (**removal and microscopic examination of a sample of body tissue from a living organism for diagnostic purposes**)**. It is essentially a '**histopathological**' study to detect abnormalities such as cancer. Blood test is performed to detect '**leukemia**' (increased leucocyte count, commonly referred to as '**blood cancer**'). The **PSA** (Prostate Specific Antigen) test is used to screen for early **prostate cancer**. A ***mammogram*** is a low-energy x-ray exam of the breasts to detect breast cancer. X ray, CT scan (**Computed Tomography**), MRI (**Magnetic Resonance Imaging**) etc., are used for **diagnostic imaging** of body parts to detect cancer. **PET scan** detects cancer, and help physicians diagnose breast cancer, lung cancer, colo-rectal cancer, cervical cancer etc.

Treatment of cancer: Treatment of cancer generally involves

1. **Surgical removal** of the malignant tumor.
2. **Radiation treatment** to destroy cancer cells in the tissues adjoining the tumor (to destroy any more cancer cells that may be remaining).
3. **Chemotherapy** and **immunotherapy** to destroy cancer cells that might have moved to other parts of the body. Chemotherapy has **side effects** such as loss of hair due to destruction of 'hair follicle cells' (alopecia),anaemia (due to inhibition of division/destruction of the 'normal' cells of the bone marrow). **Anti-cancer drugs such as 'taxol'** can stop active division of cells. Usually cancer cells avoid detection and destruction by the immune system. Hence cancer patients are given substances known as 'BIOLOGICAL RESPONSE MODIFIERS' such as **alpha interferons** which activates the immune system of the patient and help in destroying tumors. Monoclonal antibody–based biologic drugs are also useful in treating certain cancers (**Biotherapy**)..

8.11 Stem Cells

Stem cells are undifferentiated cells found in most, if not all multicellular animals. They are characterised by the ability to go through numerous mitotic cycles while maintaining the undifferentiated state. The normal cells produced by mitosis differentiate into diverse specialized cell types. Stem cells are responsible for development, repair of adult tissues and cancer, when the control over their division is lost. Stem cell research has the potential to revolutionize the future of medicine with the ability to regenerate damaged and diseased organs. In addition to self-renewal, stem cells also exhibit 'cellular potency'.

Potency specifies the differentiation potential of the stem cells. **Totipotent** (Latin, 'totus'means entire)/ **omnipotent**: These stem cells can construct a complete, viable organism. Cells produced by the first few divisions of the zygote and those from the morula are also totipotent. **Pluripotent** (Latin,plures means several or many) stem cells are the descendants of totipotent cells and can differentiate into nearly all types of cells, i.e. cells derived from any of the three germ layers, ectoderm, endoderm and mesoderm, e.g.embryonic stem cells. **Multipotent** stem cells can differentiate into a number of types of cells, but only those of a closely related family of cells,e.g.haemopoietic stem cells. **Unipotent** (Latin, 'unus' means one) cells can produce only one cell type, their own.

In mammals, there are two broad types of stem cells: embryonic stem cells and adult stem cells.

Embryonic Stem Cells (ES CELLS)

They are isolated from the epiblast tissue of the inner cell mass of a blastocyst. ES cells are pluripotent and can give rise to the three primary germ layers-ectoderm, endoderm and mesoderm. When given the necessary stimulation, they can develop into more than 200 cell types of the adult body. **ES cells** are immortal cells i.e. they can proliferate in a sterile culture medium perennially and they are a source of a large number of cells in the **undifferentiated** state.

Adult stem cells

They are found in various tissues of children as well as adults. Any cell which is found in the body of a developed animal that has the ability to divide and create another cell like it is called an adult stem cell or somatic stem cell. These cells act as a repair system for the body, replenishing adult tissues. Most of the adult stem cells are **multipotent**.

The red bone marrow is a rich source of adult stem cells. The other examples include mesenchymal stem cells, adipocyte stem cells, endothelial stem cells, etc.

Do you know? Pluripotent adult stem cells are rare and generally in small number; occur in umbilical cord.

Haemopoietic stem cells (HSCs) of red bone marrow are multipotent stem cells. HSCs are of two types namely **myeloid stem cells** and **lymphoid stem cells** that give rise to all the blood cell types.

Myeloid stem cells and lymphoid stem cells are together called secondary stem cells or common progenitors.

Myeloid stem cells: These are non-renewing cells and give rise to erythroid committed progenitor, basophil committed progenitor, eosinophil committed progenitor, granulocyte-monocyte progenitor and Megakaryoblast. Each of these cells give rise to different but specific cell(s).

1. **Erythroid committed progenitor** (proerythroblast): Erythrocyte is formed through stages like proerythroblast, erythroblast and reticulocyte.
2. **Basophil committed progenitor**: Gives rise to basophils which give rise to 'Mastcells'.
3. **Eosinophil committed progenitor**: Gives rise to eosinophil.
4. **Granulocyte-monocyte progenitor**: It gives rise to myeloblast and monocyte committed progenitors. Neutrophil is formed from myeloblast committed progenitor and monocyte is formed from monocyte committed progenitor Monocytes give rise to macrophages in tissues.
5. **Megakaryoblast**: It forms megakaryocyte which by fragmentation gives blood platelets.

Lymphoid stem cells: It gives rise to T-cell committed progenitor and B-cell committed progenitor. T-cell committed progenitor differentiates into T-lymphocyte in Thymus. T-cells may be T-helper or T-cytotoxic cell. B-cell committed progenitor produces B-lymphocyte in the bone marrow.

Note: Natural killer cells originate directly from lymphoid stem cells whereas dendritic cells originate from both myeloid stem cells and lymphoid stem cells directly.

Applications Of Stem Cell Therapy

Stem cells, taken from umbilical cord, can be transform into specialized cells to replace myocytes or neurons or perhaps the entire organism through cell culture. A number of adult stem cell therapies already exist.

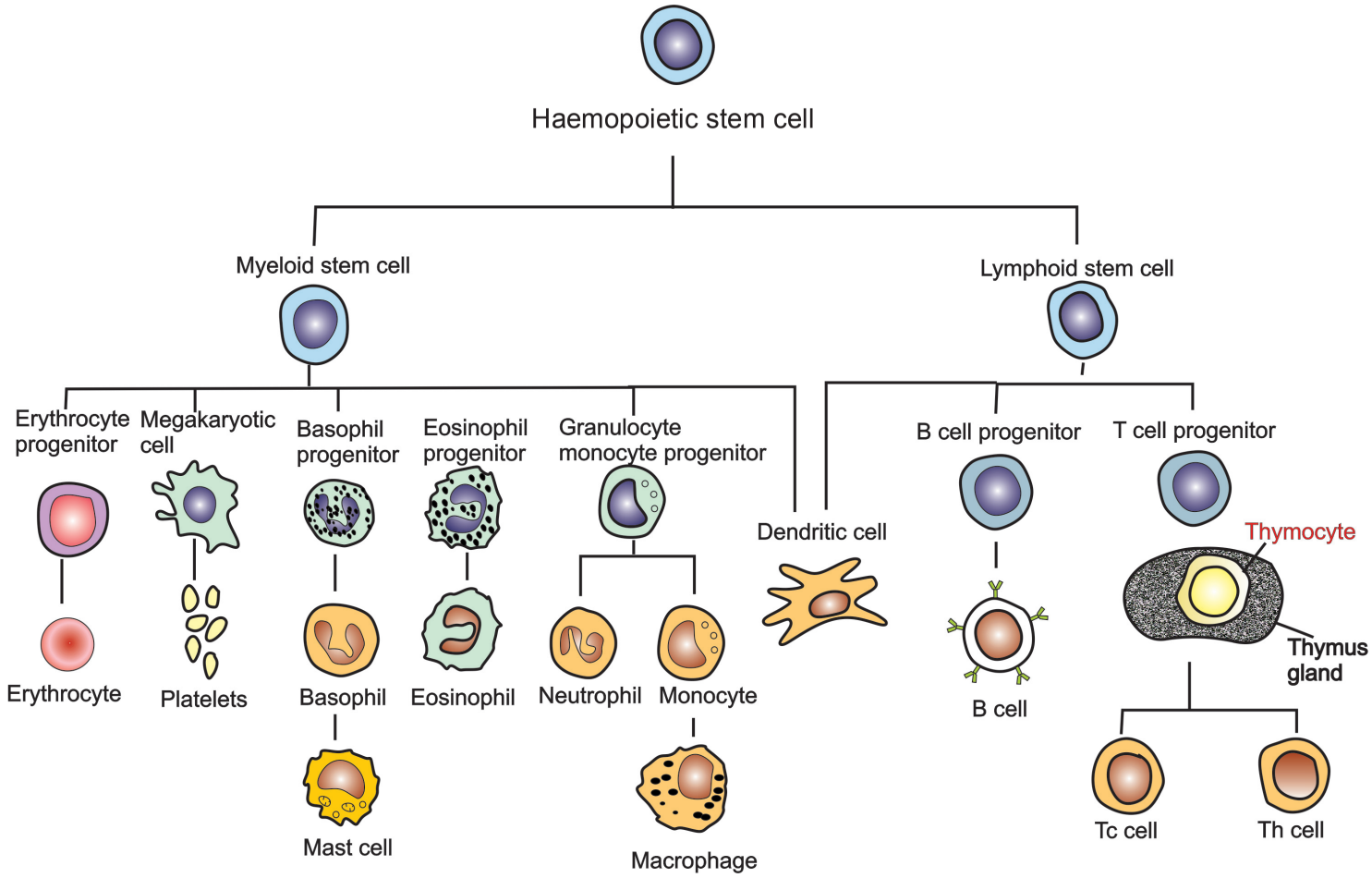


Figure 8.7 Haemopoietic stem cells

8.12 Biomedical Technology

Biomedical technology is the application of principles of biophysics and biochemistry for studying certain biological aspects. It involves-

1. Diagnostic imaging: X- ray imaging , Computed Axial Tomography (CAT scan) or Computed tomography (CT scan), Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET scan), Sonography etc.
2. Biomedical procedures to study body's vital functions and their disorders (ECG, EEG)
3. Biochemical procedures to estimate various biochemical components in body fluids (ELISA,Western Blot/Protein immunoblot etc.).

8.12.1 X ray Radiography

X-Rays, discovered by **Rontgen,** are useful in diagnostic radiography. It is a simple radiological technique to observe the human body parts and diagnose any physical (anatomical) variations. X-Ray images show areas of different densities and composition in different identifiable/diagnosable forms.

A beam of X-rays is produced by an X-ray generator and is projected on the body parts. X –rays that pass through the body parts are recorded on a photographic film or observed on a fluorescent screen. Photographs developed using X-rays are known as radiographs or skiagraphs. Dense bones absorb much of the X- radiation and soft tissues allow more X-rays to pass through. So, bones appear more white and soft tissues look greyish. Calcifications in tissues too appear whitish. Air in the lungs appears blackish as it does not blcok X-rays. The X- ray film provides a 2D representation of all the structures of the body part superimposed on each other (***X-ray radiograph***) or it can be stored as a digital image. It is used to diagnose or treat patients by assessing the presence or absence of disease, foreign objects, and structural damage or other anomalies. ***Angiography*** involves taking a series of X-rays as blood flows through blood vessels such as the coronary or carotid arteries,to study 'blocks' in them. This procedure involves injecting dyes into blood to get ***contrast images*** and nowadays ***Digital Subtraction Angiography*** is used to get a better resolution images.

Portable X-ray machines are also available, nowadays. X-rays help to detect skeletal fractures, pneumonia, tuberculosis, cancers etc. Every precaution should be taken to avoid exposure of gonads and foetus of a pregnant woman, as X-rays may prove to be more dangerous to them.

8.12.2 Computed Axial Tomography (CAT)

Computed Tomography (**CT**) or Computerized Axial Tomography (CAT) scan is a medical imaging method that employs Tomography (a process of producing

a two dimensional slice through a 3 dimensional object). A large donut shaped X-ray machine takes **X-ray images** at many different angles around the body. The X-ray detector of the CT-scanner can detect hundreds of different levels of density of tissues in body organs. The data is transmitted to a computer which builds up **3-D cross sectional picture** of the part of the body and displays the picture on the screen. This recorded image is called '**tomogram**'. The body can be seen on CAT scan as slices from the skin to the central part.

A CAT scanner emits a series of narrow beams of X-rays through the human body as it moves through an arc, unlike an X-ray machine which sends just one radiation beam. The final 3-D picture of a CAT scan is far more superior and detailed than an ordinary X-ray picture. Sometimes, patients may be given a contrast dye for better resolution.

CAT scans are useful to measure accurately the density of bones in evaluating **osteoporosis**. CAT scans are performed to analyse the head injuries (blood clots and skull fractures) to know the anatomy of various visceral organs.

8.12.3 MRI (Magnetic Resonance Imaging)

What is an MRI scan?

An **MRI** (**Magnetic Resonance Imaging**) scan is a '***Diagnostic Radiology Technique***' that uses magnetism, radio waves and a computer to produce '**images of body components**'. It is important to note that MRI ***does not use ionizing radiation***, as involved in ***X-rays***, and is generally a very safe procedure. MRI is a ***non-invasive*** medical '**imaging technique**' that helps physicians diagnose certain **anatomical abnormalities** or **pathological conditions**. This technique uses nuclear magnetic resonance of protons to generate '***proton density images of body parts***'. Magnetic Resonance Imaging uses a powerful ***magnetic field***, ***radio frequency pulses*** and a ***computer*** to produce detailed pictures of organs, soft tissues, bones and virtually all other internal body structures.

NOTE: MRI provides good contrast between the different soft tissues of the body, which makes it especially useful in imaging the brain, muscles, the heart, and cancerous tissues compared to other medical imaging techniques such as Computed Tomography (CT) or X-rays.

MRI scanner and procedure

MRI scanner is a giant circular ***magnetic tube***. The patient is placed on a movable bed that is inserted into the magnet. Human body is mainly composed of water molecules which contain two ***hydrogen nuclei / protons***, each. The magnet creates a strong 'magnetic field' that makes these protons *align with the direction of the magnetic field* (protons are not aligned under normal conditions). A second radiofrequency electromagnetic field is then turned on for a 'brief period'. The 'protons' absorb some energy from these 'radio waves'. When this 'second radio frequency emitting field' is turned off, *the protons release energy* at a radiofrequency which can be detected by the MRI *scanner* (the protons return to their '*equilibrium state*' from the '*energized state*' at different 'relaxation' rates).

Different types of tissues emit different 'quanta' of energy (in the form of different wave lengths and at different rates). Abnormal tissues, such as tumors, can be detected because the *protons in different types of tissues return to their equilibrium state at different rates.* Tissues such as bones with less water content (*hence, less number of protons*) look different in an MRI image. Accordingly there is a contrast between the 'images' of 'different tissues' based on their water content. Even in the case of the same tissue, 'normal healthy cells' and 'pathological cells' emit different energy waves – hence the difference in the images of the different types of cells.

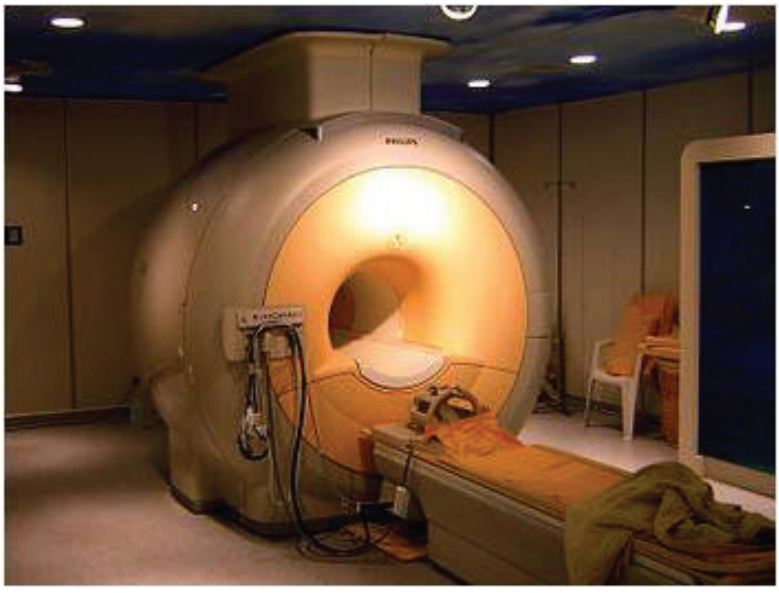


Figure 8.8 MRI Scanner

The information received is processed by a computer, and an image is generated. The image and resolution produced by MRI is quite detailed and can detect tiny changes of structures within the body. For some procedures, ***radiocontrast agents***, such as ***gadolinium***, are used to increase the **accuracy /resolution** of the images. After scanning is completed, the computer generated images (***tomographs–images of thin slices of body parts***) can be transferred to a **film** (***hard copy***). A radiologist interprets the images of the body parts and gives his diagnostic opinion.

> ***NOTE:*** MRI is used to distinguish pathologic tissue (such as *brain tumors*) from *normal tissue*. MRI can show even *hairline fractures* of the pelvis and hip that may not be detected by the traditional X ray or CT Scan. Balooning of blood vessels called **aneurysms** can be detected using MRI (aneurysms may occur when a tear begins in the layers of the walls of aorta, arteries, veins or parts of heart. More over MRI is preferred to CT scans, as CT scan involves 'effects' of '*ionising radiation*' whereas MRI does not have ionising radiation .

8.12.4 ECG

What is ECG?

The word ECG may mean electrocardiogram/electrocardiograph, but it is most commonly used for **electrocardiogram.** Electrocardiography is a commonly used, non-invasive **procedure for recording electrical changes in the heart.** The graphic record, which is called an ***electrocardiogram*** (**ECG** or **EKG**), shows the series of **waves** that relate to the **electrical impulses** which occur during each cardiac cycle. An electrocardiograph is a device which records the **electrical** activity of the **heart** muscle (**depolarisations** and **repolarisations**).

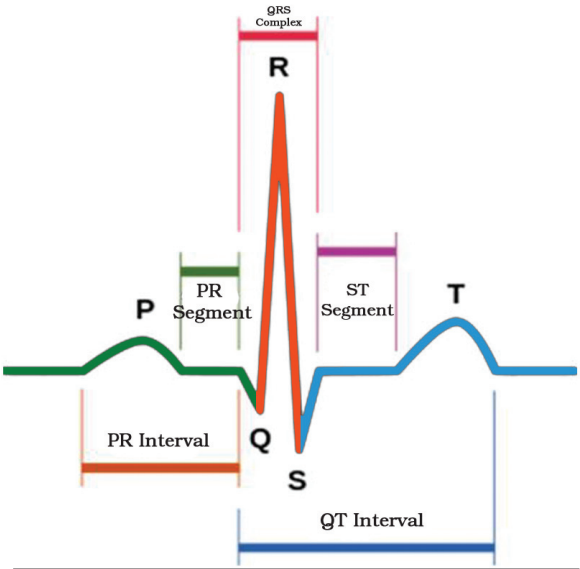


Figure 8.9 Electrocardiogram

What is electrocardiography?

Electrocardiography is the technique by which the electrical activities of the heart are recorded for study. Sensors (electrodes) are placed at specific parts of the body and linked to the ECG machine. ECG is recorded using 12 'LEADS' (sensors from limbs and chest).

Obtaining an **electrocardiogram** typically takes a few minutes, after which the electrodes are removed.

The essential components of an ECG

A normal ECG consists of **i**. **Waves ii**. **Intervals iii**. **Segments** and **iv**. **Complexes.**

WAVES: *The waves in a normal record are named P, Q, R, S, and T, in that order.*

A typical ECG tracing of a normal heartbeat (or cardiac cycle) consists of **I**. a 'P' wave, **II**. a 'QRS complex' of 'waves', **III**. a 'T' wave.

P wave: It represents the 'atrial depolarization or atrial systole'**. P wave** shows that the impulse is passing through the ***atria.*** The normal duration of a P wave is – **0.1 sec**.

QRS complex of 'waves': (Ventricular depolarization/ventricular systole) i. **Q** wave is a small negative wave **ii**. **R** wave is a tall positive wave **iii**. **S** wave is a negative wave. The normal duration of QRS complex of waves is about **0.08- 0.1 sec.**

T wave is a positive wave. It represents the **ventricular repolarisation**. Its duration is **0.2** sec.

Intervals

i. **P-R interval** is the interval between the onset of P wave and the onset of Q wave. **P-R interval** is normally **0.12 – 0.2** sec.

ii. **Q-T interval** is the interval between the onset of Q wave and the end of the T wave. It represents the **electrical activity in the muscle of the ventricles** (ventricular depolarisation). '**QT Interval** ' is dependent on the 'heart **rate**' **(the 'faster' the 'heart rate' – the 'shorter' the interval)**. It lasts for about **0.4 sec.**

iii. **R-R interval** signifies the duration of one 'cardiac cycle' and it lasts for about 0.8 sec. (60/75= 0.8 sec.).

Segments: S-T segment is the time period between the end of the S wave and the onset of the T wave. It is an 'isoelectric/zero voltage' period.

Clinical Inferences from ECG

1. ***Enlarged P wave***, indicates enlarged atria.
2. Variations in the duration, amplitude and morphology of the ***QRS complex*** indicate disorders such as bundle branch block (block of conduction of impulses through the branches of the bundle of His).

3. If the duration of the ***P-R interval*** is prolonged, it indicates delay in conduction of impulses from S-A node (pace maker) to the A-V node. P-R interval is prolonged in '**bradycardia**' (slow beating of the heart) and shortened in '**tachycardia**' (fast beating of the heart).
4. ***Prolonged Q-T interval*** indicates **myocardial infarction (MI)** and hypothyroidism. Shortened Q-T interval indicates '**hypercalcemia**'
5. ***Elevated S-T segment*** indicates **myocardial* infarction**.
6. ***Tall T wave*** indicates ***hyperkalemia***; **small, flat or inverted T wave** indicates **hypokalemia.**

8.12.5 EEG

Electroencephalography is the process of recording the electrical activity of the brain (graphical recording called electroencephalogram) with the help of an EEG machine and some 'electrodes' placed all over the scalp. Electroencephalograph is a very useful tool in diagnosing neurological and sleep disorders. The changed EEG patterns in the case of 'epilepsy' are conveniently studied with the help of an EEG. Brain shows continuous electrical activity of innumerable neurons. The intensity and pattern of electrical activity depends on wakefulness, sleep, coma, certain pathological and psychological conditions. The main **diagnostic** application of EEG in neurological studies is the diagnosis of **epilepsy** (***seizures***). EEG shows distinct abnormal pattern in the case of epilepsy. EEG is also useful in the diagnosis of 'coma' and 'brain death'. EEG studies are useful in analyzing sleep disorders (such as **insomnia**).

Waves of EEG: The waves recorded by an EEG consist of

i. Synchronized waves which are common in normal healthy people and
ii. In certain neurological conditions the waves are desynchronized (irregular wave pattern). The wave pattern can be broadly classified into ALPHA, BETA, THETA and DELTA wave patterns. The nature of the waves depends on the intensity of activity of the different parts of the cerebral cortex.

Alpha waves: They are rhythmical 8-13 cycles per second. This type of wave pattern is seen in persons who are drowsy/sleepy with closed eyes.

Beta waves: These waves occur at a high frequency of **13-40 cycles** per second. Their amplitude is low. These are 'desynchronised waves' recorded in persons who are mentally very active and tense.

* Myocardial infarction involves necrosis (death of tissue) of heart muscle and is generally refered to as 'heart attack'.

Delta waves: Their frequency is quite low (**less than 3** cycles per sec.). However they have high amplitude. They are common in early childhood in awaken condition. In adults they occur in deep sleep. In the case of brain tumors, epilepsy, mental depression etc. these waves occur in awake adults too.

Theta waves: Their frequency is between **4** and **7 cycles** per second. These waves are common in children of less than 5 years of age. They are also recorded during **emotional stress** in adults.

8.12.6 ELISA (*Enzyme Linked Immunosorbent Assay*)

What is ELISA?

ELISA is the acronym (short form) of **Enzyme-Linked Immunosorbent Assay**. It is a biochemical procedure to detect '**antigens**' or '**antibodies**' in a given sample. All microbes have at least an antigen that is unique. This antigen can be purified and used to generate specific '**monoclonal antibodies**'. Thus MABs are made available for this procedure. Both the antibodies and the purified antigens provide effective diagnostic tools. It is a method used mainly to detect the presence of specific **antibodies** or **antigens** in a sample of serum, urine etc. It is the first and most basic 'tool' to determine if an individual is *positive* or *negative* for a particular pathogen such as **HIV.** It is a useful tool both for determining serum antibody concentrations (such as the antibodies produced in a person infected by pathogens such as HIV) and also for detecting the presence of ***specific antigens*** and hormones such as human ***chorionic gonadotropins*** (hCGs).

Requirements for ELISA

i. a ***microtitre plate***
ii. a **purified antibody** (for detecting a specific ***antigen***)
iii. a **purified antigen** (for detecting a specific ***antibody***)
iv. an enzyme that catalyses the production of colour from a chromagenic substance (mostly ***peroxidase*** or ***alkaline phosphatase*** or ***beta galactosidase).***
v. a **buffer** (wash) fluid to remove unbound substances in the well.
vi. a substrate **(chromogenic substance)**
vii. **a spectrophotometer** to measure the intensity of the colour of the substrate.

NOTE: Monoclonal antibodies are used as :**1. Primary** antibodies (which react with the antigens of interest) **2. Secondary** antibodies (which react with the primary antibodies).

ELISA is a fundamental tool of ***clinical immunology***, and the purpose of an ELISA is to determine if a particular protein is present in a sample, such as serum of a person affected by a pathogen and if so, how much.

ELISA is of two types

I. **Direct ELISA** - ELISA used to detect ***antigens***

II. **Indirect ELISA** - ELISA done to detect ***antibodies***

Direct ELISA:

Direct ELISA is performed by using 'primary antibodies' (antibodies against the 'antigen' of interest) attached/adsorbed on the solid surface of the 'well' on the titre plate. This antibody has affinity for the **antigen of interest** (antigen for whose detection this test is being conducted). It is of two types.

I) **Sandwich Assay**: In this type, '*Enzyme coupled antibodies*' are used. It measures the amount of antigen '***sandwiched***' between two layers of antibodies (**primary antibodies**).

The antigen to be measured should contain at least 2 antigenic sites (multivalent antigen-having several attachment sites for an antibody). Sandwich assays are used to quantify multivalent antigens such as proteins or polysaccharides.

In the illustration given you can notice how an antigen is sandwiched between two antibodies (primary antibodies) The second antibody which is tagged with the enzyme attaches to the primary antibody. When a substrate is added the enzyme acts on it and changes the colour. It happens only if the antigen is present in the sample given for testing. Otherwise there will be no change in colour.

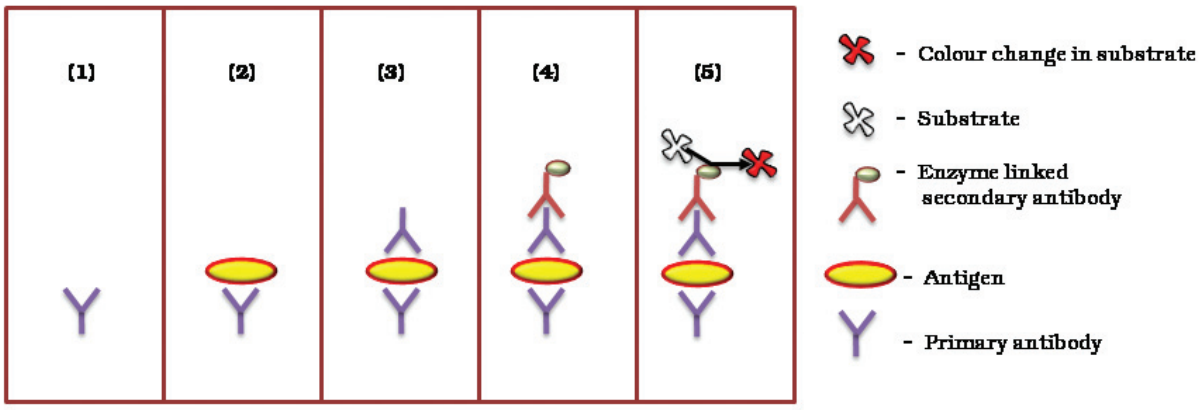


Figure 8.10 Sandwich Elisa

II) **Competitive Assay:** The common '**pregnancy test**' using *Human Chorionic Gonadotropin* (hCG), as an indicator of pregnancy is an example for which '**Competitive ELISA**' is conducted.

Protocol (plan of the experiment/assay)

1. Adsorption (the process by which molecules of a substance, collect on the surface of another substance) of the primary antibodies.
2. Adding the 'test sample' (blood, urine) to the TEST SYSTEM
3. If there are hCG molecules in the sample they attach to the adsorbed antibodies.
4. Now purified hCG molecules linked to an enzyme are added to the TEST SYSTEM.

NOTE-I: If there is no hCG in the test sample, only hCG with linked enzyme will bind to the adsorbed antibodies.NOTE-II-The more hCG in the test sample, the less enzyme linked hCG will bind to the antibodies.

5. Then the ***substrate*** (chromogenic substance) is added.
6. The intensity of change in the colour of the solution is measured, if there is any change.

NOTE-1: If the colour changes it means more molecules of the hCG linked to an enzyme are attached to the primary antibodies .It thus means that less or no molecules of the specific antigen in the 'test sample' are attached to the primary antibodies.If the colour is intense, it indicates – **NO PREGNANCY**.

NOTE -2: If there is no colour change, it means no enzyme linked hCGs are attached to the antibodies (as they were already occupied by the hCG molecules of the test sample)–it indicates **PREGNANCY**.

NOTE-3: As the two types of hCGs are competing for the space on the antibodies,this is called '**COMPETITIVE ELISA**'.

Indirect ELISA

It is used to detect ***antibodies***. The blood of the person undergoing the 'assay' (for example the HIV test) is allowed to clot and the clear ***serum*** with antibodies (called ***primary antibodies***) is obtained.

Protocol

1. It is used to detect 'antibodies'.
2. A known 'antigen' (HIV antigen in this case) is added to the 'well' (adsorbed)
3. Patient's antiserum (serum with specific antibodies) is added

4. The 'antibodies' in the patient's 'antiserum' (primary/ complementary antibodies) bind to the antigens coated on the surface of the 'well'.
5. Enzyme linked antihuman immune serum globulins (**anti HISGs**) are added. They bind to the specific antibodies which are already bound to the antigens.
6. Enzyme's substrate is added and the reaction produces a visible colour change which can be measured by a **spectrophotometer.**

NOTE-A: Certain 'Human serum proteins' (Human immune serum globulins- HISGs) are injected into experimental animals such as rabbit, goat etc. B. In the blood of rabbit, '*antibodies to HISGs*' are produced. They are called "*Antihuman immune serum globulins*". C. These s*econdary antibodies* are conjugated to a '*substrate-specific enzyme*' before they are added to the contents of the '*well*'.

If there are no "anti HIV antibodies" in the serum sample, there is no binding of primary antibodies to the antigens and so 'enzyme linked secondary antibodies' do not bind to the primary antibodies. There cannot be any enzymatic action and so no colour change is observed. The test is said to be 'Negative' and the person is described 'HIV negative'. However ELISA can be "False positive "under certain circumstances and so it cannot be used as a confirmation test for the presence of HIV antibodies. Similarly False negatives also can occur during the "window period" between infection and development of antibodies against the virus.

GLOSSARY

Adjuvant: An immunologic adjuvant is an substance that acts to accelerate, prolong or enhance antigen specific immune responses when used in combination with specific vaccine agents.

Aneurysm: Balooning of an artery/vein or a part of heart due to weakening of their walls.

Apoptosis: A form of cell death in which a programmed sequence of events leads to the elimination of cells without releasing harmful substances into the surrounding area.

Assay: It means to assess; chemical testing done to determine the composition of a substance or the concentration of its components.

Attenuation: The process by which a virus, bacterium, etc., changes under laboratory conditions to become harmless or less virulent.

Conventional practices: Practices which are in accordance with established norms and conventions and requirements.

Epidemic: A disease affecting many persons at the same time, and spreading from person to person in a locality where the disease is not permanently prevalent.

Hyperkalemia: It refers to the condition in which the concentration of the electrolyte potassium (K+) in the blood is elevated.

Hypokalemia: It refers to the condition in which the concentration of potassium (K+) in the blood is low.

Insulin pump: It is a medical device used for the administration of insulin in the treatment of diabetes mellitus and is an alternative to multiple daily injections of insulin.

Malaise: It is a feeling of general discomfort or uneasiness, often the first indication of an infection or other disease.

Milch animal: Domestic animal suitable for milk production.

p53protein: It is a tumour suppressor protein which is crucial in multicellular organisms, where it regulates the cell cycle and, thus, functions as a tumour suppressor and is involved in preventing cancer. As such, p53 has been described as "the guardian of the genome" because of its role in conserving stability by preventing genome mutation.

Pathophysiology: The study of the biological and physical manifestations of disease as they correlate with the underlying abnormalities and physiological disturbances.

Rheumatoid arthritis: Rheumatoid arthritis (RA) is a chronic, systemic inflammatory disorder that may affect many tissues and organs, but principally attacks flexible (synovial joints). RA is considered a systemic autoimmune disease.

Serum: It is the clear liquid that separates from blood when it is allowed to clot completely, and is therefore blood's plasma from which fibrinogen has been removed during clotting.

Small pox: A highly infectious and often fatal disease caused by the ***Variola*** virus of the genus Orthopoxvirus and characterized by fever, headache, and severely inflamed skin sores that result in extensive scarring.

Transfection: It is the direct uptake/ introduction of foreign material into eukaryotic cells.

QUESTIONS

Very Short Answer Type Questions

1. What factors constitute dairying?
2. Mention any two advantages of inbreeding.
3. Distinguish between out-cross and cross-breed.
4. Define the terms layer and broiler.
5. What is apiculture?
6. Distinguish between a drone and worker in a honey bee colony.
7. Define the term Fishery.
8. Differentiate aquaculture and pisciculture.
9. Explain the term hypophysation.
10. List out any two Indian carps and two exotic carps.
11. Mention any four fish by-products
12. How many amino acids and polypeptide chains are present in insulin?
13. Define the term 'vaccine'.
14. Mention any two features of PCR.
15. What does ADA stand for?Deficiency of ADA causes which disease?
16. Define the term transgenic animal.
17. What is popularly called 'Guardian Angel of Cell's Genome'?
18. List out any four features of cancer cells.
19. How do we obtain radiographs?
20. What is tomogram?
21. MRI scan is harmless –justify.
22. What is electrocardiography and what are the normal components of ECG?
23. What does prolonged P-R interval indicate?
24. Differentiate between primary and secondary antibodies.
25. Which substances in a sample are detected by direct and indirect ELISA respectively?

Short Answer Type Questions

1. What are the various methods employed in animal breeding to improve livestock?
2. Define the term 'breed'. What are the objectives of animal breeding?
3. Explain the role of animal husbandry in human welfare.
4. List out the various steps involved in MOET.
5. Write short notes on controlled breeding experiments.
6. Explain the important components of poultry management.
7. Discuss in brief about 'Avian Flu'.
8. Explain in brief about queen bee.
9. Honey bees are economically important-justify.
10. What are the various factors required for bee keeping.
11. Fisheries have carved a niche in Indian economy-explain
12. Explain in brief structure of Insulin.
13. Define vaccine and discuss about types of vaccines.
14. Write in brief the types of gene therapy.
15. List out any four salient features of cancer cells.
16. Explain the different types of cancers.
17. Write about the procedure involved in MRI.
18. Write briefly about different waves and intervals in an ECG.
19. Discuss briefly the process of indirect ELISA.
20. Write short note on EEG.

Long Answer Type Questions

1. Write in detail about outbreeding.
2. Explain in detail clinical inferences from ECG.

FOR IGNITED MINDS

Biology and it's multifaceted Glory

Applied Biology

1. What do you call 'programmed cell death'?
2. If a person thinks he is affected by HIV due to unprotected sex, and goes for a blood check, the next day –do you think some test such as an ELISA or WESTERN BLOT will help? If so how? If not why?
3. If there is a flat or inverted T wave in a person's ECG, what additives do you suggest in that person's diet?
4. If in a victim of 'dengue' the platelet count falls to a critical low, one of the methods of treatment is transfusion of platelets. Under such condition improvement in the production of what type of heamopoeitic stem cells will help.
5. If a doctor suggests a person to get his PSA test report from a Biochemist. Probably what ailment is the doctor suspecting?
6. Of the two – Attenuated whole agent vaccine and Inactivated whole agent vaccine – which do you think is more risk free?
7. Why is invitro modification of T cells used in Gene Therapy not a permanent, one time cure?
8. What is the chief difference between insulin obtained from animals and the one obtained biotechnologically?
9. Why is cross breeding preferable over inbreeding?
10. India is a big country and Biodiversity is reasonably good .Why did we have to introduce some exotic carps into the country from other countries?

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Intermediate II Year Syllabus

Subject: ZOOLOGY-II (W.E.F 2013-14)

Unit I : Human Anatomy and Physiology-I

22 Periods

Unit I A: Digestion and absorption

Alimentary canal and digestive glands; Role of digestive enzymes and gastrointestinal hormones; Peristalsis, digestion, absorption and assimilation of proteins, carbohydrates and fats, egestion, Calorific value of proteins, carbohydrates and fats (for box item- not to be evaluated); Nutritional disorders: Protein Energy Malnutrion (PEM), indigestion, constipation, vomiting, jaundice, diarrhea, Kwashiorkor.

Unit I B: Breathing and Respiration

Respiratory organs in animals; Respiratory system in humans; Mechanism of breathing and its regulation in humans - Exchange of gases, transport of gases and regulation of respiration; Respiratory volumes; Respiratory disorders: Asthma, Emphysema, Occupational respiratory disorders – Asbestosis, Silicosis, Siderosis, Black Lung Disease in coal miners.

Unit II : Human Anatomy and Physiology-II

22 Periods

Unit IIA Body Fluids and Circulation

Covered in I year composition of lymph and functions; Clotting of blood; Human circulatory system – structure of human heart and blood vessels; Cardiac cycle, cardiac output, double circulation; regulation of cardiac activity; Disorders of circulatory system: Hypertension, coronary artery disease, angina pectoris, heart failure.

Unit IIB Excretory products and their elimination

Modes of excretion – Ammonotelism, Ureotelism, Uricotelism; Human excretory system – structure of kidney and nephron; Urine formation, osmoregulation; Regulation of kidney function –Renin-Angiotensin – Aldosterone system, Atrial Natriuretic Factor, ADH and diabetes insipidus; Role of other organs in excretion; Disorders: Uraemia, renal failure, renal calculi, nephritis, dialysis using artificial kidney.

Unit III : Human Anatomy and Physiology-III

20 Periods

Unit IIIA: Muscular and Skeletal system

Skeletal muscle – ultra structure; Contractile proteins & muscle contraction; Skeletal system and its functions; Joints. **(to be dealt with relevance to practical syllabus)**; Disorders of the muscular and skeletal system: myasthenia gravis, tetany, muscular dystrophy, arthritis, osteoporosis, gout, regormortis.

Unit III B: Neural control and co-ordination

Nervous system in human beings – Central nervous system, Peripheral nervous system and Visceral nervous system; Generation and conduction of nerve impulse; Reflex action; Sensory perception; Sense organs; Brief description of other receptors; Elementary structure and functioning of eye and ear.

Unit IV : Human Anatomy and Physiology-IV

15 Periods

Unit IVA: Endocrine system and chemical co-ordination

Endocrine glands and hormones; Human endocrine system – Hypothalamus, Pituitary, Pineal, Thyroid, Parathyroid, Adrenal, Pancreas, Gonads; Mechanism of hormone action **(Elementary idea only);** Role of hormones as messengers and regulators; **Hypo and Hyper activity and related disorders:** Common disorders –Dwarfism, acromegaly, cretinism, goiter, exophthalmic goiter, diabetes, Addison's disease, Cushing's syndrome.(Diseases & disorders to be dealt in brief).

Unit IVB: Immune system

Basic concepts of Immunology - Types of Immunity - Innate Immunity, Acquired Immunity, Active and Passive Immunity, Cell mediated Immunity and Humoral Immunity, Interferon, HIV and AIDS.

Unit V: Human Reproduction

22 Periods

Unit VA: Human Reproductive System

Male and female reproductive systems; Microscopic anatomy of testis & ovary; Gametogenesis " Spermatogenesis & Oogenesis; Menstrual cycle; Fertilization, Embryo development up to blastocyst formation, Implantation; Pregnancy, placenta formation, Parturition, Lactation **(elementary idea).**

Unit VB: Reproductive Health

Need for reproductive health and prevention of sexually transmitted diseases (STD); Birth control – Need and methods, contraception and medical termination of pregnancy (MTP); Amniocentesis; infertility and assisted reproductive technologies – IVF-ET, ZIFT, GIFT **(elementary idea for general awareness).**

Unit VI: Genetics

20 Periods

Heredity and variation: Mendel's laws of inheritance with reference to ***Drosophila***. (*Drosophila melanogaster* Grey, Black body colour; Long, Vestigial wings), Pleiotropy; Multiple alleles: Inheritance of blood groups and Rh-factor; Co-dominance (Blood groups as example); Elementary idea of polygenic inheritance; Skin colour in humans (refer Sinnott, Dunn and Dobzhansky); Sex determination – in humans, birds, Fumea moth, genic balance theory of sex determination in *Drosophila melanogaster* and honey bees; **Sex linked inheritance** – **Haemophilia**, **Colour blindness**; Mendelian disorders in humans: **Thalassemia**, **Haemophilia**, **Sickle celled anaemia**, **cystiefibrosis PKU**, Alkaptonuria; Chromosomal disorders –**Down's syndrome**, **Turner's syndrome** and **Klinefelter syndrome**; Genome, Human Genome Project and DNA Finger Printing,

Unit VII: Organic Evolution

15 Periods

Origin of Life, Biological evolution and Evidences for biological evolution (palaeontological, comparative anatomical, embryological and molecular evidences); Theories of evolution: Lamarckism (in brief), Darwin's theory of Evolution -Natural Selection with example (Kettlewell's experiments on *Biston bitularia*), Mutation Theory of Hugo De Vries; Modern synthetic theory of Evolution - Hardy-Weinberg law ; Types of Natural Selection; Gene flow and genetic drift; **Variations** (**mutations** and **genetic recombination**); **Adaptive radiation** – viz., **Darwin's finches and adaptive radiation in marsupials**; Human evolution; Speciation – Allopatric, sympatric; Reproductive isolation**.**

Unit VIII: Applied Biology

15 Periods

Apiculture; Animal Husbandry**:** Pisciculture, Poultry management, Dairy management; Animal breeding**;** Bio-medical Technology : Diagnostic Imaging (X-ray, CTscan, MRI), ECG, EEG; Application of Biotechnology in health: Human insulin and vaccine production ; Gene Therapy; Transgenic animals; ELISA; Vaccines, MABs, Cancer biology, stem cells.

BOARD OF INTERMEDIATE EDUCATION

A.P., HYDERABAD

MODEL QUESTION PAPER ZOOLOGY-II (W.E.F 2013-14)

SECTION-A **10 X 2 =20**

Answer all the questions (Very short answer type)

1. Define chyme and chyle ?
2. Name the muscles that help in breathing movement of man ?
3. How many pace makers are present in the human heart ? What are they ?
4. What is a sarcomere ?
5. Name the meninges of the mammalian nervous system from the outer most to the inner most ?
6. Write the functions of Leydig cells and Sertoli cells ?
7. Distinguish between 'Humoral immunity' and 'Cell mediated immunity'.
8. How is acromegaly caused ?
9. Write any four important advantages of poultry farming ?
10. What is the principle involved in X ray radiography.

SECTION-B **6 X 4 =24**

Answer any Six Questions (Short Answer Type)

11. Explain the process of digestion in the stomach.
12. What are the bio-chemical changes that occur in a muscle during contraction.
13. Write a brief note on Morphological Evidences in favour of organic evolution?
14. Draw a diagram of internal structure of testis.
15. Write a brief note on different types of immunities ?
16. Explain the following phenomena.
    a) Turners Syndrome.
    b) Down Syndrome.
17. How does Hardy Weinberg principle explain equilibrium of allelic frequency ?
18. What is the importance of MRI in diagnostic imaging ?

SECTION-C **2 X 8 =16**

Answer any Two Questions (Long Answer Type)

19. How does human heart function to pump blood to the body parts ?
20. Describe the female reproductive system with the help of a labelled diagram ?
21. Describe the determination of sex by Genetic Balance theory of Bridges in Drosophila.