# APPLIED PHYSIOLOGY

## M.Sc. - 101

**Directorate of Distance Education**

**SWAMI VIVEKANAND SUBHARTI UNIVERSITY**

**MEERUT 250005**

**UTTAR PRADESH**

SIM MOUDLE DEVELOPED BY:

Reviewed by the study Material Assessment Committed Comprising:

1. Dr. N.K.Ahuja, Vice Chancellor
2.
3.
4.
5.



Published by: **Publishers Grid**

4857/24, Ansari Road, Darya ganj, New Delhi-110002.

Tel: 9899459633,7982859204

E-mail: publishersgrid@gmail.com, work.publishersgrid@gmail.com

***Printed by:*** A3 Digital Press

Edition : 2021

# CONTENTS

UNIT

# 1

# INTRODUCTION TO PHYSIOLOGY

**STRUCTURE**



## 1.1 LEARNING OBJECTIVE

After studying this unit, you will be able to:

- review the contributions by various scientists — historic view,
- describe the body systems,
- explain the role of metabolism, immunity etc., in contributing to growth and development,
- discuss the theories, which state why we age, and
- enumerate the role of various nutrients and their physiological contributions.

Now let us begin our discussion by going through the introduction to physiology and major historical developments of importance.

## 1.2 INTRODUCTION

In this unit, we will familiarize ourselves with the discipline called 'Physiology', what is it and its historical development. Then we will get to know about the physiology of growth and development, the process of ageing and the changes that occur in various body systems due to ageing, as well as, theories of ageing.

Finally, we will discuss what is nutrition, its significance and role of nutrients in maintaining body processes i.e., the interaction between nutrition and physiology.

In this unit, we will learn about concept of public nutrition, We would learn as to what public nutrition is all about and why do we want to study it? We will begin by explaining certain terms used in the area of public nutrition. We will also learn about the concept and essential component of health care and its delivery. This will help us to understand the role of public nutritionist in health care delivery.

## 1.3 PHYSIOLOGY AS A DISCIPLINE

The term physiology —physio meaning native and logos meaning discourse, is a Greek word, a synonym for natural philosophy.

Physiology is the study of processes in living tissue at the cellular, organ and whole-body organizational levels. Physiology, as a discipline, deals with the mechanisms by which the body functions in general. In unicellular organisms, a single cell carries out all major functions. The cell functions basically on the sol-gel theory. The medium, (plasma) which is 70% water, becomes a pool of molecules. These molecules interact with each other to produce complex molecules. These give rise to molecular basis of life. The major functional molecules are carbohydrates, proteins and lipids which contribute to the basic life functions.

As the evolutionary processes progressed, the need for a better functioning (viability) system became necessary. Thus, multicellularity evolved. These lead to the formation of group of cells performing function in a responsible manner. Similarity between cells helped them to group together. Thus, cells which are similar in structure and function formed a group called 'tissues'. The tissues further were responsible for the development of an organ. Various organs lead to the formation of organ systems. These organ systems contributed to an individual organism. This organism was able to function better because of division of labour.

Physiology, therefore, is the study of the physical and chemical processes that take place in living organisms during the performance of life functions. It is concerned with such basic activities as reproduction, growth, metabolism, excitation and contraction as they are carried out within the fine structure — the cells, tissues, organs and organ systems of the body.

Physiology is intimately linked with anatomy and was historically considered a part of medicine. Its emphasis on investigating biological mechanisms with the tools of physics and chemistry made physiology a distinct discipline in the 19th century. The tendency today, however, is toward a fragmentation and merging with the many specialized branches of the life sciences. Three broad divisions are recognized: general physiology, concerned with basic processes common to all life forms; the physiology and functional anatomy of humans and other animals, including pathology and comparative studies; and plant physiology, which include photosynthesis and other processes pertinent to plant life.

"Thales of Miletos" is known as the first physiologist, who lived around 600BC. The modern world calls "William Harvey" as the first physiologist (1578-1657). Herman Bochaave, a physician at Laden, described physiology as the science of body functions. Albrecht von Haller wrote the first textbook of physiology. Some

famous physiologists include Francois Magendie, Johannes Muller, Carl Ludwig, Claude Bernard, Walter Cannon, Hermann Helmholtz etc. H. Helmholtz also proposed law of conservation of energy, invented ophthalmoscope, proposed a theory of colour vision, physiology of hearing etc. Ludwig invented the Kymograph, which served as an important tool in understanding of various mechanical events during neuro-muscular transmission and muscle contraction.

Antony Van Leeuwenhoek's microscopes threw a lot of light in understanding the inner aspects of a cell. The observations made by Robert Hooke on a cork cell opened further avenues for exploring more about the cell. He also observed that the cells had different shapes and structures, which were observed in a leaf, as well as, in a liver cell. Though they differed in structural details, they could be viewed as a variation arising on a common theme. These variations were unique which attributed to a tissue. These observations culminated in formation of the cell theory - by Schwann and Schleiden (1939) – about which we shall learn in the next unit.

Among the most important advances of the 20th century are the discovery of new hormones, recognition of the role of vitamins, discovery of blood types, development of the electrocardiograph and electroencephalograph, to record the activity of the heart and brain, discovery of the cause and cure of pernicious anaemia by George Richards Minot, William Parry Murphy and George Hoyt Whipple and greater understanding of metabolism, the role of enzymes and the immune system.

The discussion above presented a brief insight into the contributions made by different scientists in the development of physiology as a discipline.

Next, let us get to know how cells joins together to form the different body systems. These organ systems, you would realize, contributed to an individual organism.

## 1.4 HOW CELLS JOIN TOGETHER

In a unicellular organism, the interior region of the organism is no longer in contact with the external environment. Thus simple processes of diffusion, phagocytosis, exocytosis and contact with sea water helped in exchanging the necessary molecules and nutrients. But a further increase in size and complexity of the organism lead to concentration of the pool of cytoplasm. The fluid in-between the cells were known as interstitial fluids. These fluids, due to constant exchange of molecules between the various cells lead to changes in the internal environment which influenced the functioning of the cell.

Physiology, we learnt earlier, is concerned with such basic activities as reproduction, growth, metabolism, excitation and contraction as they are carried out within the fine structure — the cells, tissues, organs and organ systems of the body. The various body systems of our body are enumerated next.

### 1.4.1 Body Systems

Based on the activities and functions, there are 9 major systems in human body.

Let us get to know about them.

The skeletal system provides a framework of support, protection and movement of the body. Body has 206 bones, connective tissues that hold them together, ligaments, tendons and various joints that allow free movement connecting the bones.

Bones can be pulled only when there is a need. This is done with the help of muscles. Man has over 600 muscles in the muscular system. The system not only helps in the movement of arms, legs, feet, hands, fingers, head and trunk but also helps in pushing food, making the blood circulate and removing waste products. Muscles do not move bones by chance, it is done when the signaling is done. This calls for a kind of networking system. The system has to be receptive and then react to the signals. This is co-ordinated through the nervous system. It involves the brain, spinal cord and the nerves along with it.

Any movement though co-ordinated activity requires energy to do so. This energy we get from food. The system, which would help in breaking and absorbing the food, is digestive system. Here, complex molecules of the food are broken into simpler ones and are absorbed by the body. Unit 6 presents a detailed discussion on this topic.

For release of energy from the absorbed food, $O_2$ is needed. Exchange of gases like $O_2$ and $CO_2$ occurs through respiratory system - consisting of nose, throat, trachea, bronchus, bronchioles and alveoli. This system helps in inspiration of $O_2$ and expiration of $CO_2$. When we work hard, we require more of $O_2$ and in exchange, we breathe out the $CO_2$ which is formed as end-product. We will learn about the respiratory system in Unit 5.

Energy-producing substances taken from food by digestive system and $O_2$ from air by the respiratory system has to be made available throughout the body. Circulatory system plays a major role here. The organ system is made of arteries, veins, capillaries and heart. Blood is the fluid that carries all the necessary' nutrients and gases to all parts of the body. The heart muscles help to pump the blood into the blood vessels. We shall learn about the cardiovascular system in Unit 4.

Though the blood vessels branch out to all parts of the body, food does not reach individual cells. A colourless fluid called 'lymph' squeezes the tiniest blood vessel, bathes the individual cells and supplies them with food. The lymphatic system consists of lymph fluid, which has WBCs, lymph vessels and lymph glands.

All these different systems require a coordination and control. This is brought out by nervous system and endocrine system together. Endocrine system produces hormones while nervous system produces neurotransmitters, which act as messengers. Together they are able to signal the body for various responses.

For maintenance of species and procreation, body has separate group of organs which brings this miraculous achievement of giving birth to new born, thereby, contributing to a new progeny. This is achieved through the reproductive system. Both male and female systems are separate. Male testicular duct joins with penis. Female system has a pair of ovaries, fallopian tubes, uterus, vagina

and mammary glands. We will learn about these organs later Unit 12.

All the systems about which we have discussed above, are completely covered and protected by the epidermis. It has several layers of cells stretched and flattened. These layers keep changing according to wear and tear. E.g. healing a cut/ wound is achieved very fast by body's own mechanism. Dermis plays a major role here, which also keeps the skin moist. Hair follicles are kept smooth and silky by the temperature by opening up the pores to remove the sweat. Skin uses the melanin, which is a pigment, which darkens according to sun's exposure. Skin cells are basically sensory in nature.

Having gone through the discussion above we now have a good understanding of the organ systems of our body, let us get to know about the physiology of growth and development, next.

## 1.5. PHYSIOLOGY OF GROWTH AND DEVELOPMENT

Growth refers to 'increase in size' and development refers to 'maturation of function'. They are generally associated with each other, but there can be exemptions, as in hypertrophy, where there is only increase in size.

Growth of various parts of the body does not follow a similar pattern, but there is a comparable relativity to size and shape, adaptability to various situations, responses to different stimuli etc. These would keep changing as the infant grows to adult stage. An adult differs from an infant with respect to the functional maturity. Secondly, the homeostatic mechanisms (the state of sustained equilibrium in which all cells, and all life forms, exists) are not as efficient as one observes in an adult. Certain components can be discussed where we can observe a change in-between infants and adults. These include:

i) **Metabolism:** Resting metabolic rate of a newborn is twice as that of an adult/unit body weight basis. Since only colostrums is available for 1st or 2nd day, infant depends on its reserve of fat and protein for energy. After this, carbohydrate is the preferred fuel. Since their liver functions are poor, there would be lot of fluctuations as far as glucose metabolism is concerned. The rate of protein synthesis is higher and a lot of amino acids are utilized for this.

ii) **Temperature regulation:** Surface area of the infant per unit weight is larger than the adult, hence infant loses/gains heat from the surroundings very easily. The temperature regulatory mechanisms are not so well developed as those of an adult. Due to this, the infant needs special care and protection from the extreme environmental conditions.

iii) **Immune mechanisms:** The immune system starts functioning in a baby through the inherited antibody (Ab) of the mother. But these antibodies keep breaking in the body. By another 1½ - 2 years, the normal level is attained. But there would be a lot of changes occurring till the thymus, an endocrine gland, becomes dysfunctional. This is attained only by the age of 8. Hence, we observe that babies are more prone to diseases like common cold, respiratory disorders, diarrhea etc. This is because of the poor development of immune

mechanisms. Further, the infant is more prone to allergic responses to its own Ab. This is known as autoimmunity. The second contribution to these allergies can be due to the high absorptive power of the gastrointestinal tract. Here, many major proteins are absorbed fully which possibly might be leading to allergic reactions.

iv) **Systemic physiology:** There is a change in the blood count and rate of hemoglobin (Hb) production during the early days. Cardiovascular and respiratory changes are observed, i.e. the Hb level after a few days fall down considerably. The first breath has a lot to do with $O_2$ accommodation and an adjustment between $pCO_2$ and p $O_2$ to have a good residual $O_2$ available for the body.

The components discussed above gives a good idea of the physiological changes typical in the infancy stage. The process of growth, development continues till the adult stage. What happens next? We shall get to know about the physiology of ageing in the next section.

## 1.6 PHYSIOLOGY OF AGEING

Ageing in simple terms refers to a physiological process that occurs in an organism as it gets older.

Ageing physiologically refers to the impaired ability to maintain homeostasis in the face of external or internal challenges or stresses. Hence, the individual becomes more vulnerable to those changes and stresses and thus succumbs to the end of life. The rate by which functional deterioration occurs in various parts of the body is neither simultaneous nor they are perpendicular in pattern. Hence, ageing process implies progressive deterioration of cells, tissues, organs and their functioning associated with increased age.

Let us look at the age related changes first.

### 1.6.1 Age Related Changes

Age related changes are mainly observed at a cellular level. The connective tissues throughout body show an increase in stiffness because of collagen (a fibrous protein which constitutes the connective tissue) fibers and hydrolysis of elastin which you might be aware is a protein similar to collagen. The changes observed in the different body systems and tissues are summarized next.

a) **Blood:** Here the haemopoiesis (the formation of blood cells) slows down. Fatty marrows replace the hematopoietic (red) marrow. Thus, the proliferation capacity gets reduced.

b) **Immune mechanisms:** The immune competence decreases with age. This affects the cell -mediated and humoral immunity. The thymus involutes (roll inwards), there is an increase in T cell auto reactivity and autoantibody titre. This makes the elderly more susceptible to infections. The severity of ageing can be reduced by good nutrition, regular physical exercises and mental tranquility.

c) **Respiratory system:** During ageing, alveoli (present in the lungs) become

flatter and shallower, alveolar ducts enlarge, walls become thinner, contains less capillaries, respiratory surface area decreases, elastic recoil response is lost, pulmonary diffusing capacity gets reduced. The respiratory response to hypoxia and hypercapnia is sluggish in the elderly. There is an overall impairment in ventilation, diffusion, regulation etc. that leads to slowing down of the respiratory responses.

**d) Cardiovascular system:** There is a decrease in elasticity of the aorta and other large arteries as age increases. Thickness of blood vessels increases leading to a rise in blood pressure. The myocardium (muscle wall of the heart) shows atrophy. There are structural changes in the valves. Number of pacemaker cells gets reduced, thereby a reduction in heart rate is observed.

**e) Alimentary canal:** Advancement in ageing leads to loss of teeth. In this process, first the enamel changes then dentine and cement. Thus their mastication (chewing) efficacy slows down. Frequent weakness of the pharyngeal musculatures leads to dysphagia (difficulty in swallowing), owing to decreased esophageal motility.

Mucosal atrophy occurs in gastrointestinal tract leading to reduced gastric and pancreatic secretions. The height of villi gets reduced as ageing progresses. Lactose activity gets reduced in brush border cells. Hence, the nutrient absorption is adversely affected. Liver function decreases due to decrease in hepatocytes.

**f) Excretory system:** There is a progressive decrease in the number and size of nephrons (basic unit of the kidney). There is a 10% decrease in renal plasma flow. Blood flow changes in glomeruli. Both secretory and reabsorptive function decreases. Glomerular filtration is hampered.

**g) Endocrine system:** There is a decrease in blood concentration of the hormone /binding protein transport. Sensitive hormone receptors diminish. Age-related decreases are seen in glucose response. As far as reproductive hormones are concerned — in females, there is a decrease in estrogen and progesterone after menopause. There is a negative feedback effect. In males, the testosterone levels go down tremendously. Though the leydig cells volume increases, it cannot achieve the normal testosterone level.

**h) Nervous system:** Varying degrees of atrophy in neuronal areas can be observed neurotransmitter functions are hampered. The cholinergic deficits seen in Alzheimer's disease, dopaminergic deficit in Parkinson's disease are examples. Senile dementia, hyperkinesias (tremors) etc. can be observed.

**i) Special senses:** Presbyopia (decline in the ability to focus near objects), senile cataract etc. can be observed as eye dysfunction. Ear shows diminished sensitivity (presbyeusis). Differentiating various sounds and speeches are hampered. Reduced mobility of transmission of sound in these areas in the ear can be observed. Sensation of smell also changes, but the tactile responses remain for a much longer time.

Having learnt about the age related changes, the next question that comes to mind is why does ageing occur? Various theories have been postulated. Let's get to know them.

NOTES

### 1.6.2 Theories of Ageing

Ageing is primarily a genetically determined process where natural factors have a potential effect. The various theories of ageing include:

a) **Error catastrophe theory:** As the cells age, there is a random increase in error in protein synthesis due to insertion of wrong amino acids. They become non - functional. Thus cell signaling goes wrong.

b) **The somatic mutation theory:** Random mutation makes the cells inefficient. An increase in the number of inefficient cells in an organ impairs their functioning. Random mutation can lead to the chromosomal aberration. This has an adverse effect.

c) **Free-radical theory:** The body is subjected to a dilemma. On one hand, $O_2$ is essential for life and on the other hand, oxidative reactions can set free a lot of impaired electrons which are highly reactive. These can possibly damage vital macromolecules like DNA, proteins etc. by the process of peroxidation.

d) **Genetic theory:** Rate of ageing varies between species. The difference is in the genetic changes in the species. Thus it can be said that gradual impairment of a function is genetically programmed. Progeria (ageing by 10 years of age) is due to a defect in genetic programming.

Well then ageing is a natural phenomenon. It is inevitable. One cannot stop it but certainly can modulate the process of ageing. How? Read and find out.

### 1.6.3 Modulating Process of Ageing

Despite various researches, ageing becomes an inevitable process. The only option is to have good control measures. These are highlighted herewith:

a) **Nutrition:** Caloric restriction retards ageing. Isn't that interesting? This is due to decrease in $O_2$ consumption, decrease in free radicals and a decrease in peroxidation.

b) **Exercise:** Regular exercises increase $O_2$ uptake capacity. It improves cardiac performance and reduces muscular-skeletal disabilities. Age-related 'Resting Metabolic Rate' (RMR) gets reduced in exercising individuals and helps to increase antioxidant reactions.

The only organism, which does not die, are the unicellular ones, they just divide as two cells. During meiosis (cell division process), recombination occurs. It replaces damaged DNA. Thus, the zygote has a perfect genome. Further life continues.

In the section above, we studied about the role of nutrition in modulating the process of ageing. What is the relation between nutrition and physiology as such?

## 1.7 NUTRITION AND PHYSIOLOGY

To common man, the word 'Nutrition' implies food. Food is essential for growth and development. Physiology becomes an interlink between nutrition and healthy human body. This includes processes like digestion, absorption and intermediary

metabolism of nutrients. The analysis of nutrients and its impact on daily life appropriates for the physiological disturbances caused. Any nutrient which is in excess or deficient can cause alterations in the general metabolism and the health of a person. The nutrients are classified into six major groups, as you already know: (l) Carbohydrates (2) Proteins (3) Fats (4) Vitamins (5) Minerals, and (6) Water. These entire components become a base for providing new life. They interact with each other and are capable of making new compounds which would provide energy for life.

The inter relationship of these components with physiology is enumerated next.

Nutritional components and their inter relationship with physiology

- **Carbohydrates:** Sugar, like a candle, can burn but burning requires oxygen. We eat to do work. To do their work, cells need an important group of food known as 'carbohydrates'. They are made up of C, H and O in a wide variety of combinations. Each combination is a different substance. The most important role of carbohydrates is to provide energy. The simplest form is glucose, one energy-packed molecule for muscular contractions, cell functions including brain cells. Carbohydrates are mainly stored in liver and muscles. Body converts all carbohydrates into simple sugars.

Energy from food is measured in units known as 'calories'. For example, a tablespoon of honey contains 100 calories. Scientists have figured out how much of food is to be consumed to do normal work; a one year old child needs 44 calories for every pound he/she weighs. As a general rule, a man of average weight of 70 kg with sedentary habits needs from 1800-2500 calories/day.

- **Fats:** Once the body stops eating, it begins to live on its fat. Fat storing depots 'adipocytes' are located in the different parts of the body. It gives twice the amount of energy than carbohydrates. It helps to remain as a blanket which keeps us warm during cold seasons. The storage under skin helps this process. It helps to anchor kidneys and other organs. The fat around joints, muscle fiber etc. acts as a cushion to prevent the injury.
- **Proteins:** These form building blocks through their 'amino acids'. They pass through blood stream and go to liver, where they are broken down further for repair mechanisms. Protein — rich foods are milk, cheese, meat, eggs, nuts etc.
- Vitamins and minerals: They play a major role in the body's functioning. Vitamin A is necessary for night vision in the eyes. Vitamin B complex - a collection of 12 components helps the functioning of the body in many ways (nerve transmission, RBC formation, skin texture). Vitamin C for small blood vessels and to work against scurvy. Vitamin D and E for bones and skin development and vitamin K for blood clotting. This comes from various food products. They are used by the body in different ways.

Thus, we can say that the food components play major role physiologically in maintaining a healthy status by their own interdependent mechanisms. Nutritional science, you would realize, is a highly interactive area. Though many complexities remained unanswered in the understanding of food molecules, development of physics, chemistry, biology, biotechnology, food technology etc. have contributed

to better solutions.

Our culture and civilization has influenced our beliefs on various food identities. The relation between food and temperament is highly emphasized in ancient Indian history. Upanishads says that purity of food leads to purity of thought. Geeta is suggestive in categorizing food as 'satwic', 'rajasic' and 'tamasic'.

Satwic are juicy fresh foods, are supposed to be favorites of the saintly and scholarly temperamented (the Rishi's). Rajasic are sour, salty, and pungent, preferred by those who are crazy for power and wealth. Tamasic foods are stale, rotten, and impure and are preferred by superstitious and ignorant. Charaka and Sushruta samhita (old Indian texts) emphasizes on foods and seasons, food and temperament, diseases, regional influences, various cooking practices and the impact on foods, usage of vegetarian and non-vegetarian foods, storage of food items etc.

Hippocrates, father of modern medicine considered food as a single entity. He provided valid advices on diet and diseases. If we pay attention to the quality and quantity of food consumed, a lot of diseases can be prevented. Celsus in the first century AD classified food into strong, medium, weak based on their energy contributions. Galen in second century wrote three books on: 1) Cereals and Pulses 2) Fruits and vegetables 3) Animal foods. He postulated that after digestion food is absorbed and incorporated by the body tissues.

The contribution of critical thinking, rational and experimental approach during 16th century developed remarkable areas of physics, chemistry and biology. This development, lead to advances in the area of nutrition science from $18^{th}$ century onwards. The experimental evidences and contributions in this area are discussed below.

## The Experimental Evidences and Contributions

James Lind in 1747 performed controlled experiments on people who were sailors and who developed scurvy. He divided these sailors into different groups. The group receiving 2 oranges and I lemon everyday showed dramatic improvements (in their health) over those who did not receive them. The group receiving cyder everyday showed some improvement, other groups did not show much improvement.

Lavosier's contributions were the ones which demonstrated more on combustion and biological oxidation which is very similar to utilizing $O_2$ and producing $CO_2$. He introduced the concept of 'Respiratory Quotient', effect of food and exercise on metabolism. The effects of fasting, a post prandial contribution etc. were performed by Seguin and Lavosier and was published in 1789. Unfortunately during the French Revolution, he was executed. Anyhow Lavosier is considered as father of modern Nutrition.

Another scientist, William Stark performed experiments with simple diets on himself. He used water and bread diet, found that it was not even providing enough energy. Addition of milk, sugar, olive oil etc. contributed to better health. Due to self experimentations he developed nutritional deficiencies and expired in 1770.

In the $19^{th}$ century the energy contributions by carbohydrates, proteins,

fats etc. were identified. A controversy developed whether the body can convert carbohydrates to fats. This was proposed by Dumas, a French chemist. Liebig, another equally reputed German chemist suggested that lean goose could be fatted on corn. Since corn is a rich carbohydrate based food, Liebig argued that, fat deposited by the goose had been derived by conversion of carbohydrate into fat. Dumas proved that corn contained 9% fat and proposed that 63% of fat must have come from corn. Liebig repeated the analysis of corn and found that corn had less fat. This led to further arguments and investigations.

In 1843 Milne Edwards experimented on bees. He fed them with honey. It was concluded that wax which was a fatty substance was manufactured by the bee, by converting the carbohydrates of the honey into fat. Another experiment by Boussingault was on pigs. The pigs were fed on potatoes. The pigs started drinking 9-10 liters of water per day. The conclusion was, a diet of carbohydrates when over fed led to fat conversion.

It was further established that carbohydrates and fat are preferred fuels, both at rest and during exercise. The body shifts from one fuel to the other depending upon the availability of nutrients. By 20th century the role of minerals and vitamins etc. were established by Lunin, Hopkins, and Eijkman & Funk. The term vitamin was coined by Funk by combining vital and amine.

The discussion above focused on experimental evidence and contributions at the international level. What about the Indian scenario? The next section highlights the contribution at the national level.

## The Indian Scenario

Nutrition research in India was pioneered by Dr. Robert Mc Carrison. His works on beriberi gained attention on interlinks between nutrition and health. Further, 'Nutrition Research Labs' (NRL) were developed in Coonoor in 1929. Dr. Wallace Akryod was the next director who contributed meaningful research for improving nutritional status of vulnerable groups in India. In the initial 10 years the major research contributions were from the British, but the successive years were more contributory from the Indian scenario. Dr. V.N. Patvardhan was the first Indian director who was succeeded by Dr. C. Gopalan, Dr. K Ramalingaswami and Dr. S.G Srikantia tobe named as a few. NRL was shifted to Hyderabad in 1966 and was renamed as 'National Institute of Nutrition', NIN for nutritional research in India.

Recent advances in cellular and molecular biology have opened new avenues for research in nutrition. Various interactive fields have been developed between nutrition and immunology, nutrition and neurosciences, nutrition and genetics etc. as major thrust areas.

Understanding the major nutritional problems of the country and contributing to the meaningful research, thereby developing proper solutions to combat the nutritional disorders lead to interactive areas of physiology of absorption / action of a particular nutrient Major contributions have been made in the area of iron deficiency anaemia, vitamin A control programme, fluorosis,

lathyrism, iodine deficiency disorders etc. To combat major deficiency disorders, fortification programmes are being developed. This has been achieved because of the major understanding about the physiological role of a nutrient and its metabolic influences on health.

## 1.8 LET US SUM UP

In the beginning of this unit, we learnt that in a single cell the interior regions were not able to maintain contact with external environment, hence multi cellularity evolved in the cells. Subsequently, we learnt that the various systems of the human body coordinate with each other to function better. Skeletal system has 206 bones and various muscles which help in movements. The energy for any system comes from food where digestive system plays a major role. Respiratory system helps in intake of $O_2$. $O_2$ is transported to all tissues along with other metabolites by circulatory system where blood acts as a main transporting system. Along with this system, runs the lymphatic system which contains WBCs, which help in maintaining immunity. All these systems require control and coordination. This is carried out by the nervous and endocrine systems. Propagation of species is achieved through reproductive organs.

The unit also focused on physiology of growth and development. The later part of the unit deals with ageing. Ageing, we learnt, is a natural process and refers to the impaired ability to maintain homeostasis. Age-related functional differences are seen in all the systems of the body. In general, the efficiency decreases. Good and healthy diet, ample amount of exercise can slow down the ageing process by consistently maintaining the functions but in a slow manner.

Finally the unit highlighted the contributions of many scientists towards the role of food and nutrients in maintaining a good physical and mental health.

## 1.9 GLOSSARY

**Adipocytes** : fat-storing cells/ depots.

**Ageing** : a physiological process which leads to a progressive deterioration of cells, tissues, organs and their functions associated with increased age.

**Alzheimer's disease** : a specific disease associated with the breakdown of nervous tissue in the brain, giving rise to dementia in the patient.

**Autoimmunity** : a condition in which the body's immune system fights and rejects itself.

**Haemopoiesis** : the formation of blood cells in the living body.

**Interstitial fluid** : the fluid in-between the cells.

**Kymograph** : an instrument for measuring and recording graphically the pressure of the blood in any of the

blood vessels of a living animal

**Lymph** : a colourless fluid which bathes individual cells and supplies them with food.

**Ophthalmoscope** : an instrument for viewing the interior of the eye, particularly the retina and optic nerve.

**Parkinson disease** : a disorder of the brain characterized of tremor and difficulty with walking, movement and coordination.

**Plasma** : colourless watery fluid of blood and lymph containing no cells and in which erythrocytes, leukocytes and platelets are suspended.

**Progeria** : a group of inherited conditions resembling accelerated ageing starting in childhood.

## 1.10 ANSWERS TO CHECK YOUR PROGRESS EXERCISES

UNIT

# 2

# CELL AND BLOOD

**STRUCTURE**



## 2.1 LEARNING OBJECTIVE

After studying this unit, you will be able to:

- discuss and understand cell cycle and cell division,
- explain the structure of the cell,
- describe the cell functions,
- explain the composition of blood and its role in our body,
- discuss about various blood groups,
- enlist the disorders of coagulation and haemostasis, and
- visualize the physiology of blood transfusion and blood flow dynamics.

## 2.2 INTRODUCTION

In this unit, we will study about the basic unit of life — the cell and the elixir of

life — the blood. The mysteries of a cell, its structure and working — organization, functions and divisions are the major aspects covered in this unit.

In this unit, we will also deal with the composition of blood, i.e. what makes it so unique, the different blood cells — their functions. Then the issues related to various blood groupings and incompatibility among blood groups will be dealt with.

NOTES

## 2.3 CELL: THE BASIC UNIT OF LIFE

You must be aware of the fact that the cell is the basic unit of life. What do you understand by the term 'cell'? What are the components of the cells, its structural features and functions that make it such an essential component of all the living beings? Well, here in this section, we shall study about all these aspects related to cell.

What would be the answer to the question what is a cell? Well, a cell is the smallest self-functioning unit found in all the living organisms. Cells may exist as independent units of life (as in monads) or may form colonies or tissues as in the higher plants and animals. Each cell is enclosed by an outer membrane or wall called as the cell membrane. A cell has receptors on its surface which have unique functions and identifying properties. Also, it contains genetic material (DNA) and other parts to carry out its life functions. Within the cell are the nucleus and the cytoplasm. The nucleus contains the genetic material-DNA. The cytoplasm contains organelles that carry out the cell's functions. We shall read about these components of the cell in a little while from now.

An aggregation of cells having a common origin and performing a similar but one or more specific functions in the body constitute a tissue (e.g. muscle). Several types of tissues may join collectively to form an organ that carries out one or more specific functions (e.g. kidney, liver, leaf and roots). In majority of animals, several organs are interrelated to perform a specific function within a multicellular organism and thus constitute an organ-system. We will learn about these organ systems i.e. gastrointestinal systems, renal system in the subsequent units. You would realize that several types of organ-systems in the body of an organism show unique example of division of labor.

It is important to note that the cells are not only the building blocks of the body, but are the functional unit of life too. Every cell arises from preexisting cells. The cells have the same genetic material. It is, therefore, capable of giving rise to a new individual. This potential of the cell to give rise to unlike cells and so to develop a new organism or a part is termed as totipotency.

Interestingly, all the activities of an organism are present in miniature form in each and every cell. Therefore, the cell can be called as a basic unit of life and the structural unit of an organism. 'All organisms are composed of cells'. 'All cells come from pre-existing cells'. These two statements constitute the cell theory. We will learn about how the cell was discovered and what the cell theory is, next.

NOTES

## 2.3.1 Discovery of Cell

Let us study here about the scientists who played a pioneer role in discovering the basic component of any living organism — the cell.

Robert Hooke (1665) is credited with the discovery of cell. Hooke observed a honeycomb-like pattern in a very thin slice of cork as shown in the Figure 2.1. As you can see, this honeycomb-like structure consists of a thick wall, enclosing box-like compartments for which he coined the term cellulae for the first time and this term is synonymous to what we call as cells. He regarded cellulae as passages for conducting fluids.

Antony Van Leeuwenhoek (1683), on the other hand, was the first to observe free cells, like bacteria, protozoa, red blood cells and sperm. You may already be aware that these are single organisms.

Let us now try and understand what the cell theory is.

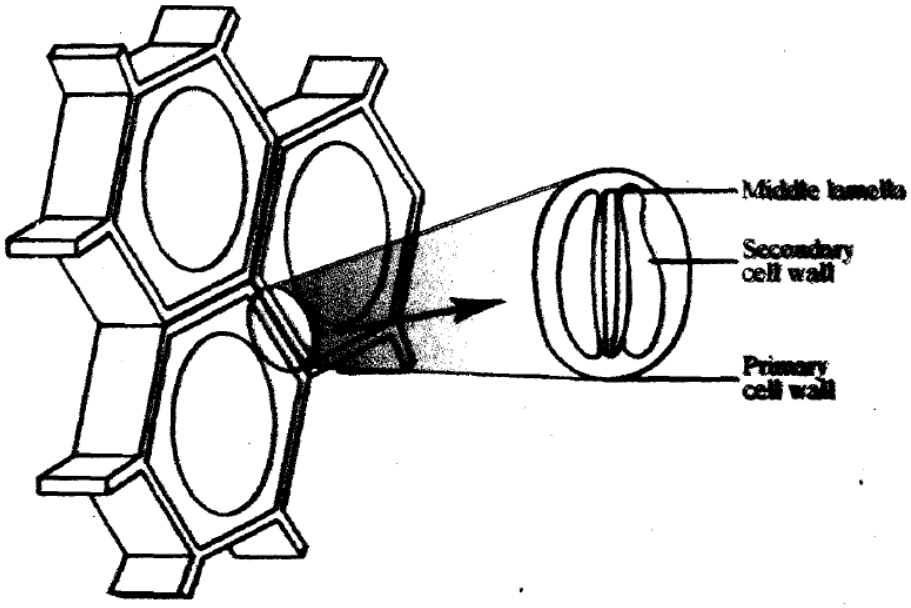



**Figure 2.1 : Microscopic structure of a cell**

## 2.3.2 Cell Theory

The cell theory, as we understand it today, is composed of following two tenets:

1) All living organisms are composed of cells and their products: The bodies of animals and plants are composed of the cells and products of cells. All plant tissues are made up of cells. These cells are having a thin outer layer, which we now know as plasma membrane.
2) All cells arise from pre-existing cells: Cells divide and new cells are formed from preexisting cells (Omnis cellulae-e cellulae). Louis Pasteur (1862), based on his experiment, successfully established that life originates from pre-existing life.

It is this basic understanding of the cell theory that leads to one of the fundamental requirements for life. The smallest living organisms are made of a single cell,

whether they are prokaryotes (e.g. bacteria) or single-celled eukaryotes (e.g. protista). What do we mean by prokaryotes and eukaryotes? We will get to know about prokaryotes and eukaryotes in section 2.3.

When we examine how multicellular organisms function, such as ourselves, we come back to how the muscle cells contract, nerve cells communicate, white blood cells detect and eliminate the infections. When we look at the structures of the bodies of organisms, we start at the building blocks, the cells. The shape of a bone starts with the shape of bone cells. The shape of our brain starts with how the brain's nerve cells connect with each other. Hence, we can say that the 'cell theory' is the most basic condition for determining if something is functional.

With our understanding of the cell theory, let us now study about the unicellular and multicellular organisms.

### 2.3.3 Unicellular and Multicellular Organisms

You may be aware that some organisms are made up of only one cell, while others have more than one cell. Well, the single-celled organisms are called as unicellular organisms, for example, bacteria and amoeba. These organisms are capable to breathe, divide and nourish. While, the organisms with more than one cell are termed as multicellular organisms, for example, humans, birds, reptiles and fish.

You might wonder what functions a single-celled organism is capable of performing. Surprisingly, a unicellular organism is able to perform a large number of functions such as respiration, absorption of nutrients, exchange of gases with the environment and metabolism. The volume of cell determines the amount of chemical activity of cells per unit of time, whereas, the surface area determines the amount of absorption and the amount of release of waste products by the cells. To maintain the surface area-to- volume ratio in a balanced state, some cells have acquired additional structures in the form of projections such as microvilli. These increase the absorptive surface area, for example, the cells-in the intestine have microvilli that help to increase the absorptive surface for absorption of essential nutrients for the body. We will read about this later in Unit 6, under gastrointestional system.

Multicellular organisms are specialized quite similar to a team that does a lot of work efficiently as compared to a single person who may only be able to perform only some of the functions. Most cells are tiny and their volume ranges between I to 1000μm3. Some of the benefits and constraints of multicellular organisms are as follows:

1) There is a unique co-ordination among the cells of multicellular organisms, like pumping of blood by the heart muscle and the transmission of information (nerve impulse) through the nerve cells. This co-ordination and specialization gives the organism a special edge in survival in the world and also helps us to understand the body's complex system and its wonders.
2) Living cells can multiply and replace the lost cell without loosing its own identity. This is a clear-cut benefit over unicellular organisms. Unicellular organisms

divide and the initial organism material is separated into two progeny cells.

3) Differentiation bestows tremendous benefits on the multicellular organisms. These are: a) increased survival b) increased specialization, and c) a proper balance between the cell surface and cell volume for receiving external stimuli, exchange of materials, transport, secretion etc. This is essential in interacting with its external environment and in communicating with the world.

Cells in an organism, you would realize, can be grouped under three major categories on the basis of the levels of differentiation:

1) **Undifferentiated cells:** These cells are capable of undergoing division and development, for example, the stem cells (animals) and meristematic cells (plants). These are the highly immature cells that can be molded like wet clay into cells that are called as differentiated cells.
2) **Differentiated cells:** These are the post-mitotic cells, which have undergone specialization and/or exhibit the division of labor. Therefore, these cells acquire distinct character and perform a definite function. For example, RBCs carry out the transportation of oxygen and carbon dioxide, the muscle cells perform kinetic functions or movement and the mesophyll cells carry out photosynthesis. These cells are the cells that help to perform the functions of our body.
3) **Dedifferentiated cells:** Some differentiated cells are capable of reverting back to the undifferentiated meristematic state as and when required. These cells are important for wound healing, regeneration and secondary growth. The process by which they lose their specialization is referred to as 'dedifferentiation'.

The cells that start or give rise to the new cells are called undifferentiated cells. Those that maintain body functions are the differentiated cells and those that have lost their specialized functions are called as the dedifferentiated cells.

Before we further move on to important cell constituents, let us take a break here and recapitulate what we have learnt so far.

## 2.4 STRUCTURE OF THE CELL

You have learnt about the diversity of the living world comprising of various organisms like microscopic bacteria to huge multicellular plants and animals. Let us now come to know the structure and ftlnctions carried out by various parts of the cell.

In general, the cells can be divided into two types:

a) **Eukaryotic cells:** These are the large multicellular cells that have a nucleus bounded by a double-layered membrane, for example, all plant and animal cells. They show a high degree of differentiation.
b) **Prokaryotic cells:** These are very small cells that multiply very' rapidly, for example, bacteria and blue green algae. These are unicellular and are believed to be evolutionary primitive.

Let us get to know them better.

## 2.4.1 Eukaryotic Cell and Organization

Eukaryotes (true nucleus) are organisms consisting of one or more eukaryotic cells, such cells contain membrane-bound nuclei, as well as organelles. Animals, plants, fungi, and various other groups collectively referred to as protista are all eukaryotes, varying from single-celled organisms to truly multicellular forms, in which different cells are specialized for different tasks and in general do not survive when isolated. Figures 2.2(a) and 2.2(b) illustrate the animal and plant cell respectively.

Now you must have a basic idea of what is a eukaryotic cell. You can see from Figures 2.2(a) and 2.2(b) that these cells have a highly complex organization consisting of the cytoplasmic matrix and several organelles such as mitochondria, endoplasmic reticulum, golgi apparatus, ribosomes, nucleus etc.

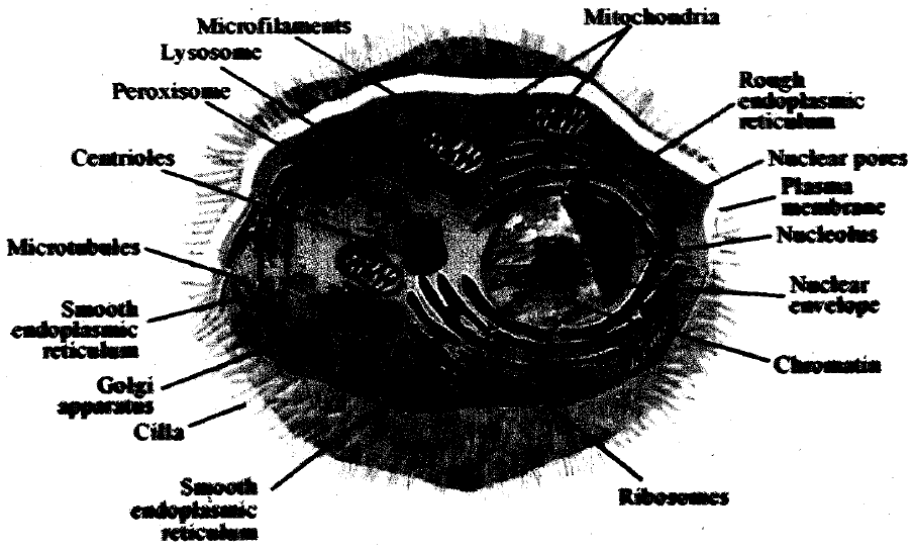



**Fig.2.2(a) : Animal Cell**

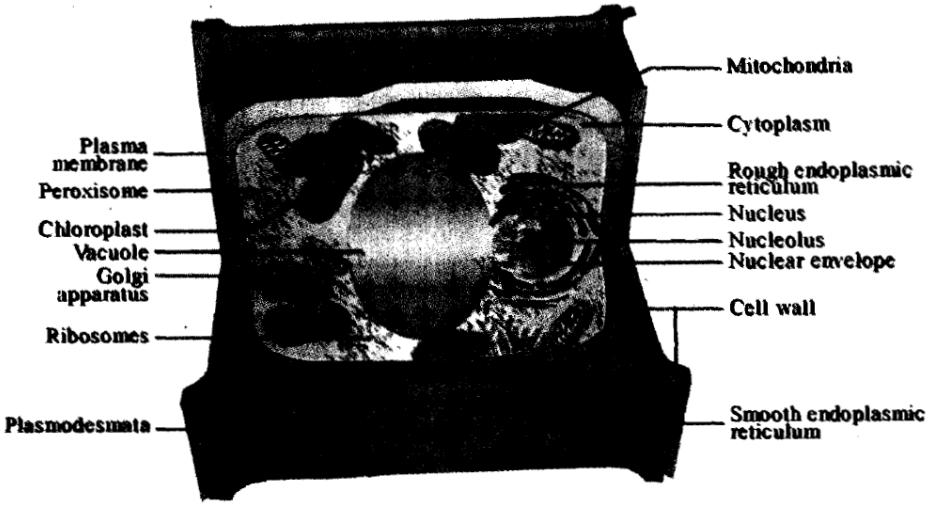



**Fig.2.2(b) : Plant Cell**

Let us now study the basic parts of the eukaryotic cell:

1) **Cell wall:** The plant cells have a definite cell wall, which the animal cells lack as can be seen in Figure 2.2(b). The plant cells have a fixed shape because of a cell wall. It is sufficiently strong, thick and rigid.
2) **Plasma Membrane:** Cells are guarded from the outside world by a membrane, called as the plasma membrane shown in Figure 2.2(a), (b). This membrane controls the flow of molecules to and fro the cell. This membrane is responsible for the communication of a cell the outside world.

The cell membrane is a dynamic structure undergoing a variety of changes. What makes the nature quasi-fluid? S. Jonathan Singer and Garth Nicholson (1972) proposed a Fluid mosaic model, as shown in the Figure 2.3.

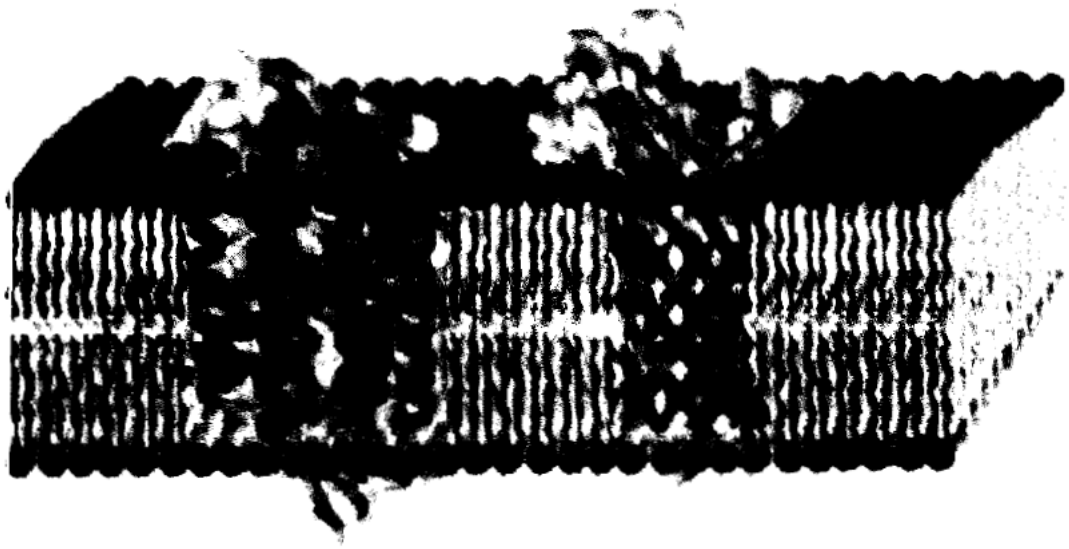


**Figure 2.3: Fluid mosaic model**

As you can observe from the Figure 2.3, the membrane is composed of a lipid bilayer and is studded with the structural proteins. It is a two-dimensional fluid or liquid crystal, in which the hydrophobic integral components such as lipids and membrane proteins are constrained within the plane of the membrane, but are free to diffuse laterally. In the Figure 2.3, you can see two integral membrane proteins are embedded in the membrane.

The membrane performs an incredible variety of roles. The proteins found freely on the surface act as the transporters and serve to carry molecules across the cell membrane. The cell membrane maintains the cell environment. It also has the enzymes essential for critical metabolic processes like respiration, photosynthesis of lipids and cell wall constituents. These membranes are selectively permeable and so they help in the transport of certain molecules.

1) **Cytoskeleton:** The ability of cells to change shape and carry well-directed movements depends on the skeleton of the cell, the cytoskeleton. The cytoskeleton is a network of fibers running throughout the matrix of living cells that provides a framework for organelles, anchors the cell membrane, facilitates cellular movement and provides a suitable surface for chemical reactions to take place.

These are of three types:

**i) Microfilaments:** These are a network of filaments within the cytoplasm as shown in Figure 2.4 which helps to play a major role in cell motion, allowing the cell to adapt to new shapes and maintaining the structural integrity of a cell. The microfilaments allow pigment granules to slide along them like a roller on a straw, they help plasma to stream and amoeba to move by pseudopodia or false feet. The microfilaments are solid tubes made up of actin-like protein.

**ii) Microtubules:** A network of proteinaceous cylindrical hollow tubes that are distributed throughout the cytoplasm of eukaryotic cells. It is made up of tubulin molecules, as shown in the Figure 2.4. The microtubules perform the following functions. These:

i) help in maintaining cell shape by providing support and anchoring the cell membrane,

ii) along with microfilaments, are involved in cell movement, and

iii) participate in intracellular transport, for example, movement of organelles and chromosomes at the time of cell multiplication.

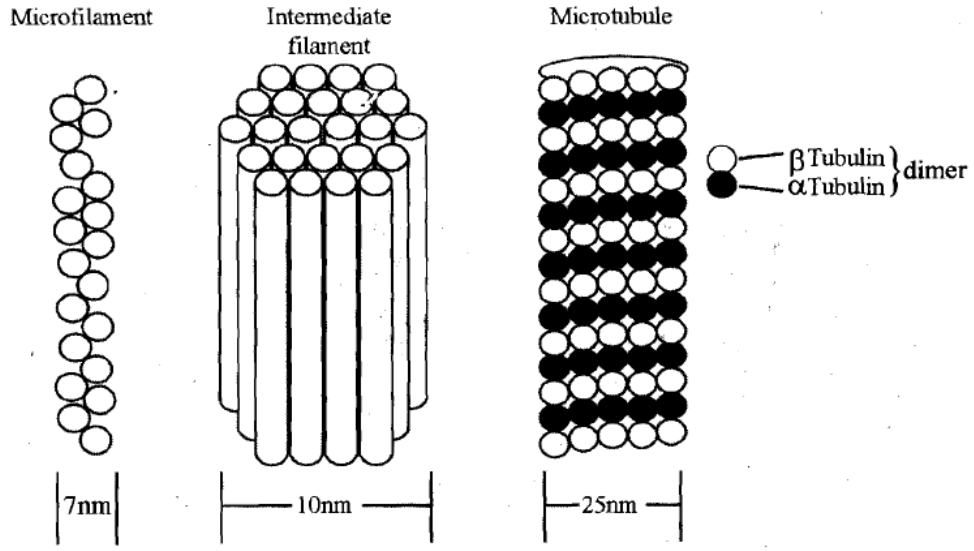



**Figure 2.4: Structure of microfilaments and microtubules**

**3) Intermediate filaments:** These are filaments of protein fibers in the cytoplasmic matrix. They bind cells together at cell-cell junctions and form a basket around the nucleus interweaving it in most of the animal cells. These provide the structure for the cell components. They are tough and durable.

**i) Endoplasmic Reticulum:** The endoplasmic reticulum (ER) is a fine reticulum or network in the plasma ofthe cell. The endoplasmic surface is studded on its outer surface with ribosomes as you can see in the Figure 2.5, and is termed as Rough Endoplasmic Reticulum (RER). These are present in abundance in the cells that are involved in active protein secretion, synthesis, modification and transport of cellular materials.

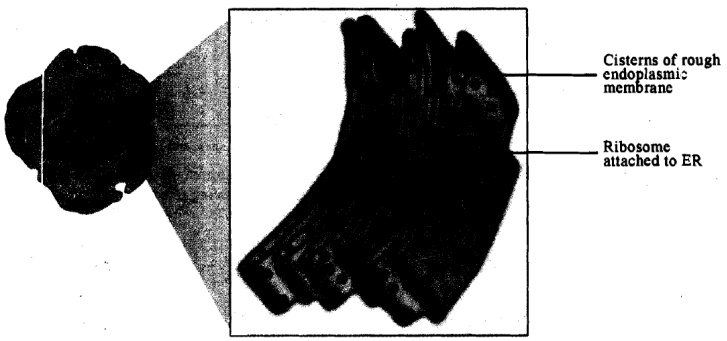



**Figure 2.5 : Structure of endoplasmic reticulum**

The cells which produce large quantities of lipid, have ER that is without the ribosomes. Such ER is known as Smooth ER (SER).

What are the functions of the ER? This remarkable network of membranous sheet of tubules performs a myriad of functions such as:

i) The RER synthesizes serum proteins, globulin, albumin, fibrinogen and membrane proteins of the lysosome and cell membrane.

ii) The SER synthesizes lipids.

iii) The ER detoxifies the impure food and drugs that we eat.

iv) The movement of muscles we flex is brought about by the calcium ions released.

**ii) Golgi apparatus:** As you can see in Figure 2.6, golgi apparatus consists of stacks of flat-membranous sacs. The golgi apparatus serves to package the material for export to- the other parts of the cell and prepare for secretions. The packaging industry of the cell moves material from the ER to the golgi apparatus. The proteins synthesized in the ER are modified by adding specific groups or folded and then bundled to their appropriate location in vesicles that bud from the golgi apparatus.

**iii) Lysosome:** Look at Figure 2.2(a) for the structure of lysosome. They are formed from the leftovers of the vesicles budded of the golgi apparatus. They are involved in intracellular digestion and are the scavengers of the cell. These release enzymes that digest the cell particles. If they are released in tissue, they may kill other cells and the cell in which they were stored. Thus, these are labeled as autophagic vacuoles or cell suicide causing particles.

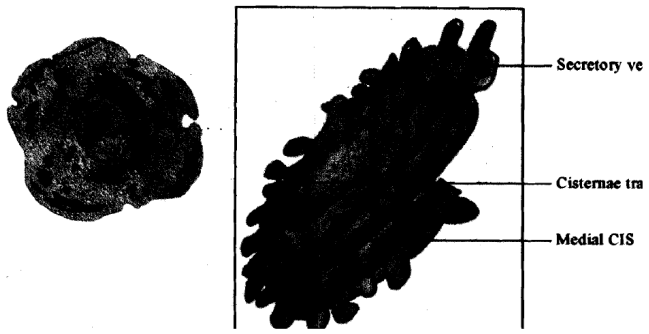



**Figure 2.6: Structure of golgi apparatus**

Cells take in material (Endocytosis) or give out or excrete (Exocytosis). Endocytosis is divided into cell drinking (Pinocytosis) and cell-eating (Phagocytosis). You can see the various steps of these processes in the Figure 2.7.

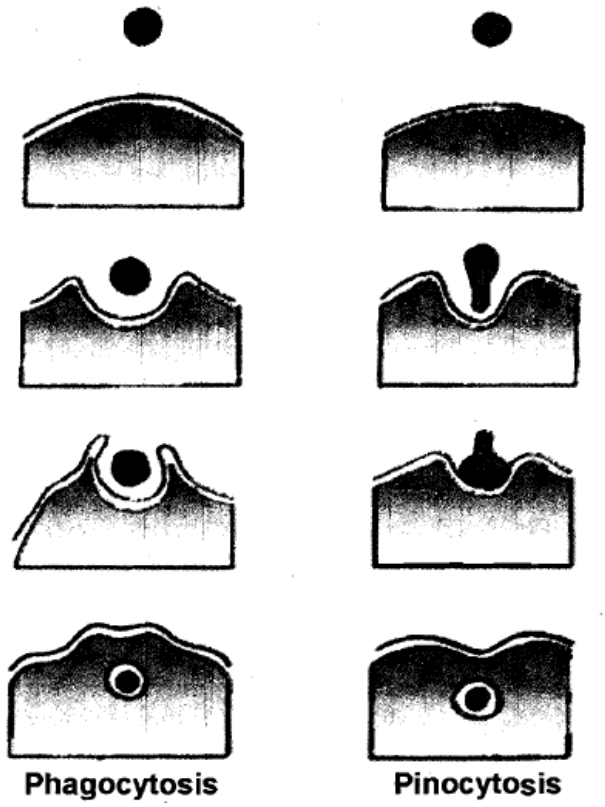



**Figure 2.7: Endocytosis in cells**

The cell membrane invaginates or encloses the fluid droplet or solid The cell membrane then completely engulfs the particle and a part of its membrane pinches off to encircle the particle within the cell. This ingested vacuole is termed as pinosome or phagosome. This is referred to as endocytosis.

Exocytosis involves expulsion of materials out of the cell. The unwanted materials are leftovers of digested particles found in vesicles called 'residual body'. The lysosomes are also important cellular organelles for nutrition.

**i) Cytoplasmic Vacuoles:** Figure 2.2(b) illustrates the structure of vacuoles. These are the voids in the cytoplasm which store small molecules such as water, ions, sucrose and amino acids. They appear as blobs and perform a variety of functions such as concentrating mineral salts in plant cells or excrete materials and digest food nutrients. Some primitive prokaryotes float in water because of air present in the vacuoles called as 'air vacuoles'.

**ii) Ribosomes:** Ribosomes are small, but complex structures, roughly 20 to 30 nm in diameter, consisting of two unequally sized subunits, referred to as large and small subunits which fit closely together as seen in Figure 2.8. These are the small cellular components composed of specialized ribosomal RNA and protein. We have just read that they are found studded like jewels on RERs. They are

NOTES

responsible for synthesizing proteins that form the membrane of secretory organelles and lysosome membranes.

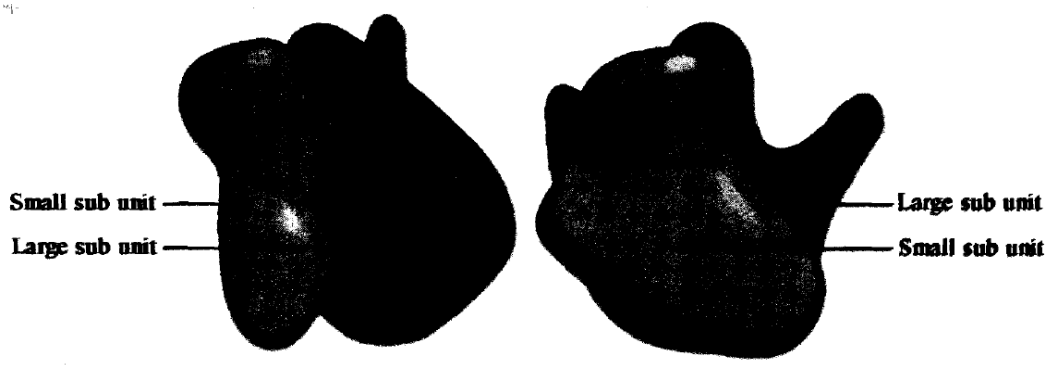



**Figure 2.8: Structure of a ribosome**

**iii) Mitochondria:** These are called as the 'powerhouse of the cell' , that contain their own DNA. They are associated with the generation of ATP, the energy currency of the cell. The longitudinal section of mitochondria in the Figure 2.9 (a) shows a double membrane, the outer membrane and the inner membrane bind the mitochondria. The inner membrane has many infoldings called as cristae as seen in the Figure 2.9 (b).

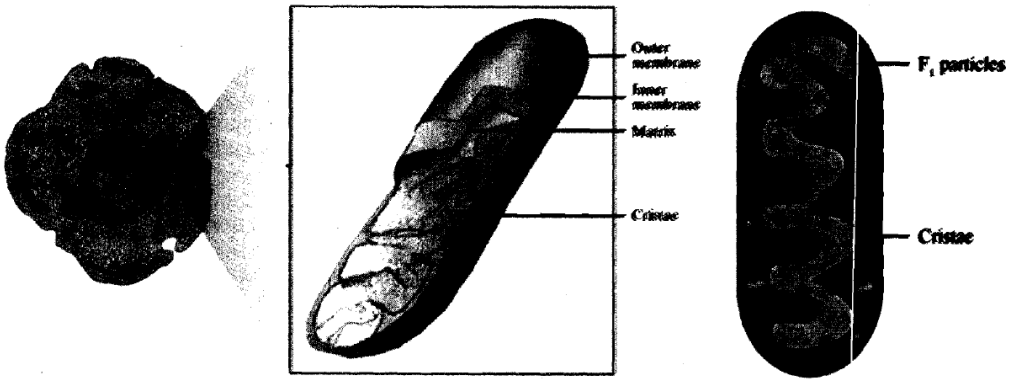



**Figure 2.9: Structure of the mitochondria**
**(a) Longitudinal section; (b) Sectional view**

The enzymes and electron carriers for the formation of the molecule ATP are located on cristae. The cristae enclose the matrix that contain enzymes for TCA (Tricarboxylic Acid) cycle that converts all food into $CO_2$, water and energy. You may recall reading about the TCA cycle in the Nutritional Biochemistry Course. Energy generated as electrons is transported down a waterfall-like gradient during breathing or cellular respiration. These organelles are the independent units, they produce their own proteins, multiply to pass on the information via DNA and provide energy to the entire cell.

**iv) Plastids:** Plastids are the self-replicating cytoplasmic organelles of plant an algal cells. See Figure 2.10, which illustrates the microscopic structure of a chloroplast. These contain pigments or starch or oil or protein. These are divided by their colors into three classes, namely, chloroplastids, chromoplastids and

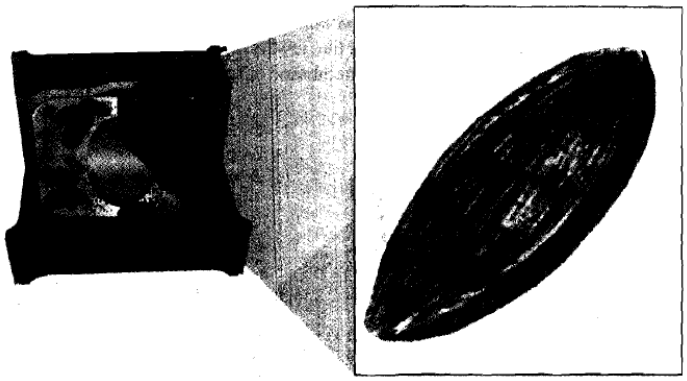


**Figure 2.10: Structure of a chloroplast**

Plastids are the organelles of plant cells that contain chlorophyll. Chlorophyll is the green colored pigment that traps light energy in leaves to make food. It is the "sunlight trap."

Yellow fruits and vegetables like mangoes, carrots, corn, papaya and pineapples are the rich sources of vitamin A. They have pigments called carotenoids in plastids called as chromophobes. These organelles are independent units like mitochondria, they produce their own proteins, multiply to pass on the information via DNA and trap energy for food production.

Nucleus: Nucleus is the core of the cell. It is a part of the cell that contains DNA and RNA and is responsible for growth and reproduction. It is a large organelle that controls all activities of the cell. The nucleus is the storehouse of hereditary information. Two membranes, the nuclear envelope, enclose it. This appears to modulate the exchange of nuclear fluid and cytoplasm. The envelope disappears during cell division and reappears in the daughter cell. The site for synthesis of ribosomes is the nucleolus. They control protein synthesis.

The molecule for heredity is the DNA. This is coiled like springs in threads called chromosomes, as seen in the Figure 2.11. Chromosomes have a short arm and a long arm and a central portion referred to as centromere.

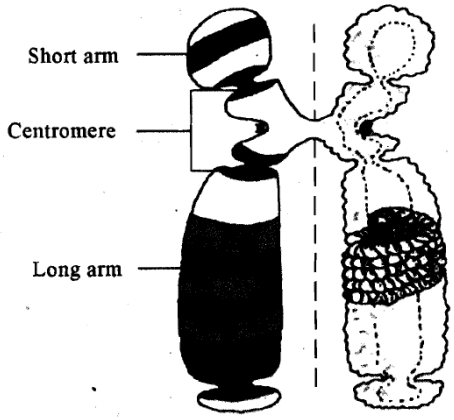



**Figure 2.11: Structure Of chromosomes**

Centrioles: These are the two small cylindrical cell organelles that are found near the nucleus. They are self-replicating, short, fibrous, rod-shaped organelles of animal cells. They are responsible for forming the cilia, flagella and astral spindle during cell division. Centrioles are composed of short microtubules arranged as a cylinder, as can be seen in Figure 2.12. They have a cartwheel — like organization having a whorl of nine protein molecules on the rim of the wheel connected by spokes to a center, (9 + 0) having 3 tubules, A, B and C, as shown in Figure 2.12. Centrioles come in pairs, each organized at right angle to the other.

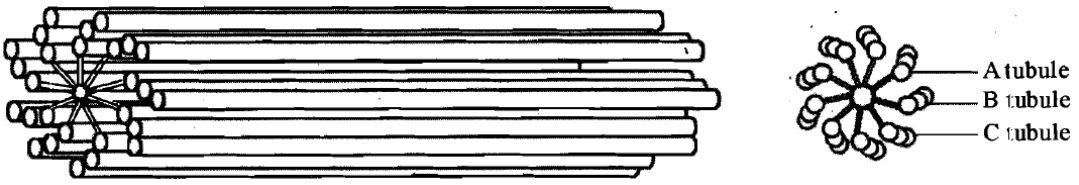



**Figure 2.12: Centriole in transverse section**

Cilia and Flagella: Look at Figure 2.2(a) and identify the cilia in the structure. Yes, cilia and flagella are projections from the cell. They are made up of microtubules, like the centrioles. They are motile and designed either to move the cell itself or to move substances over or around the cell. Cilia and flagella have the same basic structure but flagella are longer in proportion to the cell bearing them and present in much smaller numbers, as you can see from the Figure 2.13 and 2.14. Cilia and flagella beat at a rate of about 10-40 strokes or waves per second and propel microorganisms rapidly. The beating of cilia and flagella is termed as whip-like. See Figure 2.15 which illustrates the cilia movement. It has a power stroke in which the locomotion occurs in a direction opposite to the stroke and a passive recovery stroke in which the hair-like organelles come back and get ready for the power stroke. This is similar to the power stroke and recovery stroke of a flying bird.

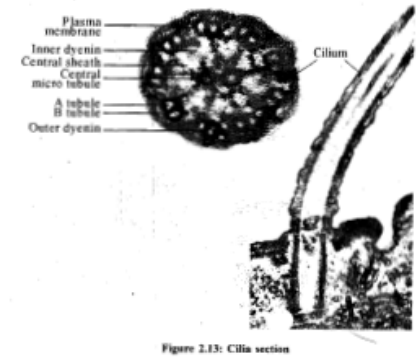



Figure 2.13: Cilia section

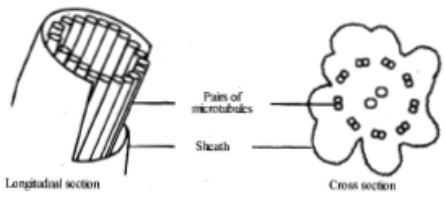



Figure 2.14: Structure of flagellum

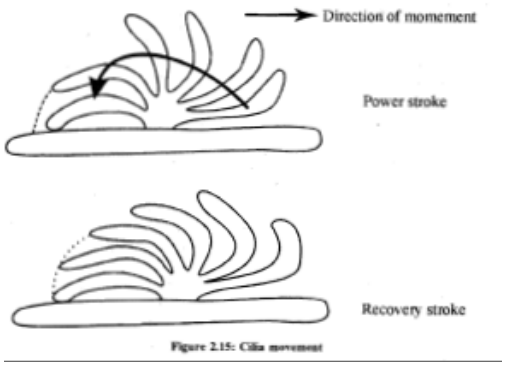



Figure 2.15: Cilia movement

The discussion above focused on the components of the eukaryotic cells. Next, let us see how the prokaryotic cell differs from the eukaryotic cell.

## 2.4.2 Prokaryotic Cell and Organization

Prokaryotic cells, you would realize, are the primitive cells lacking a nuclear membrane. These are very small cells that multiply very rapidly, for example, bacteria and blue green algae. Look at the Figure 2.16, which represents the structure of the prokaryotic cell.

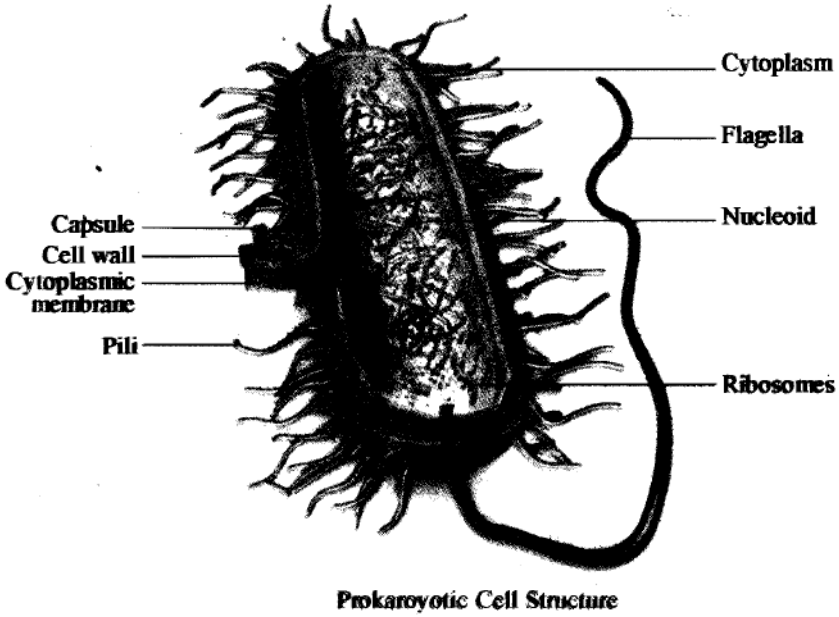



**Figure 2.16: A Bacterial cell**

Can you make out any differences between the eukaryotic and prokaryotic cell? Yes, in a prokaryotic cell:

- DNA is not coiled into springs but is arranged in a circular forms,
- Chromosomes and microtubules are absent, and
- membrane-bound organelles are absent, for example, mitochondria.

You would realize that prokaryotic cell may be divided into two types on presence

or absence of outer membrane — gram positive and gram negative. In gram-positive cell (bacteria), the stain is trapped by the layer of peptidoglycan, which forms the outer layer of the cell. In gram-negative bacteria, the outer membrane, present on the cell, prevents the stain from reaching the peptidoglycan layer in the periplasm.

## 2.5 CELL CYCLE

What do we mean by cell cycle? Let us first understand this concept. When a cell is to divide, the genetic material gets duplicated so that all the daughter cells get equal material. The orderly sequence of events by which the cell duplicates its contents and divides into two is termed a cell cycle. A typical cell cycle and its phases are shown in Figure 2.17. All cells divide except the nerve cells of mammals after birth. The division takes place either by mitosis or meiosis.

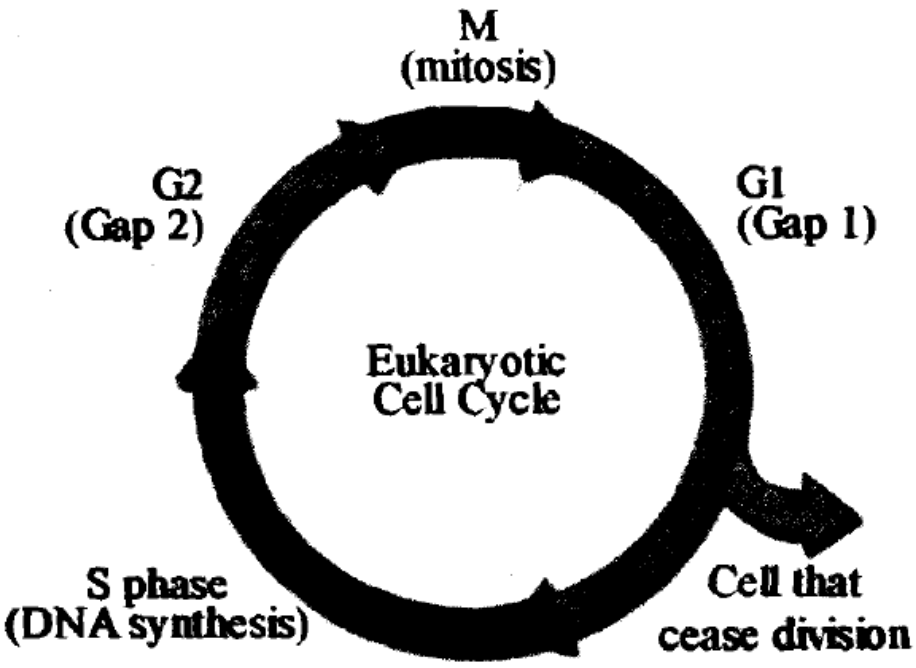



**Figure 2.17: Phases of cell cycle**

As you can see in Figure 2.17, the different phases are represented as GI, S, G2, M. What do these phases indicate? Let's find out. The cell cycle consists of four phases, which include:

GI = growth and preparation of the chromosomes for replication

S = synthesis of DNA (and centrosomes)

G2 = preparation for

M = mitosis, when nuclear (chromosomes separate) and cytoplasmic (cytokinesis division occur

Mitosis is further divided into four phases about which we shall read next. But,

## 2.5.1 Mitosis

NOTES

Mitosis is the process of nuclear division in cells that produces genetically identical daughter cells, which are identical to the parent cell. In this process of cell division, the chromosomes are duplicated and distributed equally to the daughter cells. It is also called as equational division. Figure 2.18 illustrates the various stages of mitosis in a typical plant cell. Interphase is often included in discussions of mitosis, but inter phase is technically not part of mitosis, but rather encompasses stages G l, S and G2 of the cell cycle we discussed above. The phases of mitosis include:

- Prophase: The chromatin, diffuse in interphase, condenses into chromosomes. Each chromosome has duplicated and now consists of two sister chromatids. Have a look at the Figure 2.18. At the end of prophase, the nuclear envelope breaks down into vesicles.
- Prometa phase: The nuclear membrane dissolves, marking the beginning of Prometa phase. Proteins attach to the centromeres creating the kinetochores. Microtubules attach at the kinetochores and the chromosomes begin moving.
- Metaphase: The chromosomes align at the equitorial plate as illustrated in the Figure 2.18 and are held in place by microtubules attached to the mitotic spindle and to part of the centromere.

Anaphase: The centromeres divide. Sister chromatids separate and move toward the corresponding poles as you can see in the Figure 2.18.

Telophase: Chromatids arrive at opposite poles of cell, and new membranes form around the daughter nuclei. The chromosomes disperse and are no longer visible under the light microscope. The spindle fibers disperse and cytokinesis or the partitioning of the cell may also begin during this stage.

## Cell and Blood

Cytokinesis results when a fiber ring composed of a protein called actin around the center of the cell contracts pinching the cell into two daughter cells, each with one nucleus. In plant cells, the rigid wall requires that a cell plate be synthesized between the two daughter cells.

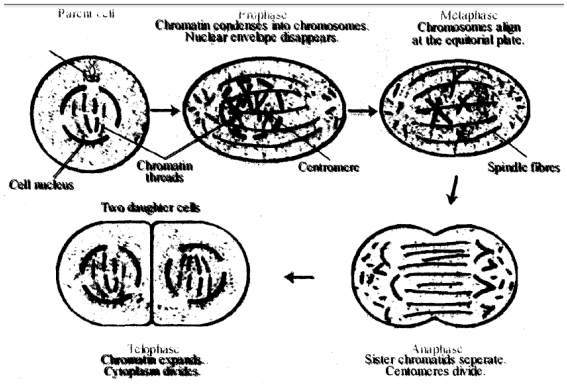



**Figure 2.18: Mitosis — cell division process**

Mitosis takes place in somatic cells or cells of the body. For example, cells of the skin are scraped off when you scratch it only to be replaced by underlying mitotically dividing cells. The cells divide only once and the chromosome number remains constant at the end of mitosis. What is the significance of mitosis?

Mitosis is significant for the following purposes:

i) Equal distribution of chromosomes. ensures same genetic constituents of al cells of the body.

ii) Mitosis restores the surface/volume ratio of the cell.

iii) Cells of the body are renewed and replaced through the process of mitosis. Fo example, the cells of the skin die and are replaced by underlying cells.

Next, let us learn about meiosis, the other cell division process.

## 2.5.2 Meiosis

A reproductive process that involves two successive divisions of a cell, results in four daughter cells, is called as meiosis. Unlike what occurs in mitosis, the daughter cells produced in meiosis are not identical to each other. Meiosis is the process by which sperm and egg cells are made. The division of germ cells to form gametes in sexually reproducing organisms occurs by a process of cell division termed as meiosis. In meiosis, the chromosomal number is reduced from double to half. See how this division takes place in the Figure 2.19. The different stages of meiosis are also highlighted in the figure. The genetic constituent of the daughter cell differs from the parent cell due to crossing over. Each chromosome of the daughter cells usually contains a mixture of mother and father genes.

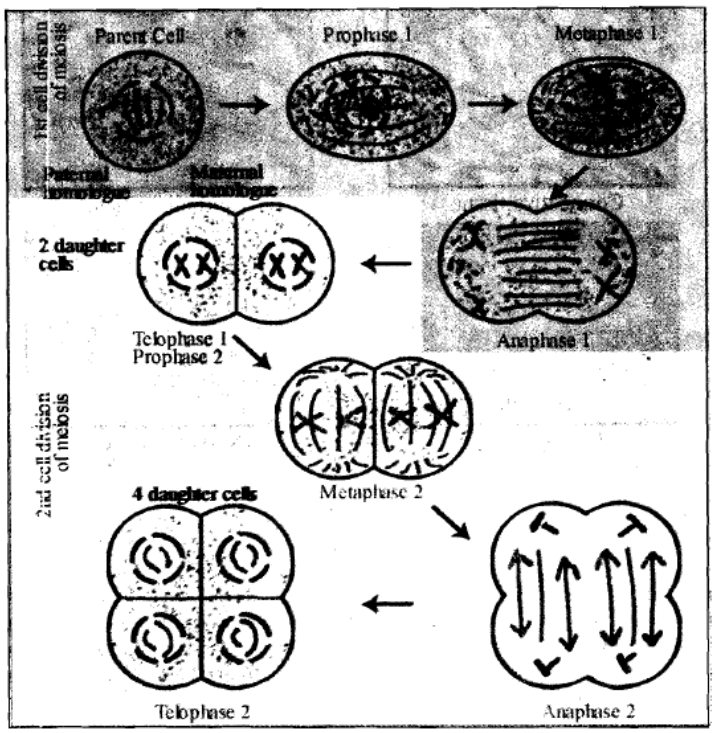



**Figure 2.19: Stages of meiosis**

What is the significance of meiosis?

Meiosis is important for the following purposes:

i) The meiosis maintains a definite and constant number of chromosome on organisms.

ii) By crossing over, the meiosis provides an opportunity of exchange of genes and thus, causes variation within species. This serves as the basis of evolution.

Having understood the structure, organization and function of the cells, we will move o to the study of tissues.

## 2.6 TISSUE AND THEIR FUNCTIONS

A tissue is a mass of similar cells usually continuous, held together in a supporting matrix, performing a common function usually forming a part of an organ. Animal tissues are usually classified as: Epithelial tissue, Connective tissue, Muscle tissue and Nervous tissue. Figure 2.20 illustrates these tissues. A detailed discussion on each of them follows.

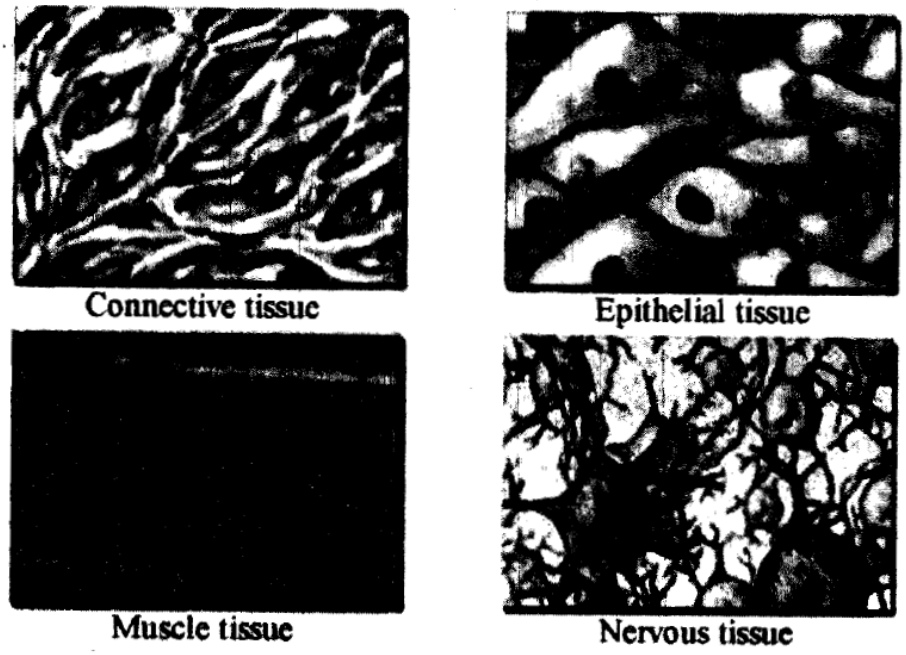



**Figure 2.20: The animal tissues**

### 2.6.1 Epithelial Tissue

Epithelial cells are generally closed packed cells, as can be seen in Figure 2.20, like a bricks in a pavement and form solid protective layers on the outside. You may remember having studied these cells under the microscope after taking scraping from the buccal (mouth) mucosa. The epithelial cells line external surfaces like skin, cavities like stomach, tubules like urethra and produce secretions and proliferate. Epithelial cells in glands exude secretions, for example, the earthworm

may secrete a cuticle or a crab may secrete a shell.

### 2.6.2 Connective Tissue

Connective tissues connect and bind different tissues and organs. They also provide a structural framework and mechanical support. They contain a lot of extra cellular material and very few cells, as shown in Figure 2.20. There are eight type of connective tissues: areolar, adipose, white fibrous tissue, tendon, ligament, cartilage, bone and blood. Let us get to know more about these connective tissues.

- **Areolar tissue**

This is a loose tissue beneath the scalp. They are made up of elastin and collagen fiber that provide support. They interweave a network of scar tissue during healing.

- **Adipose tissue**

This is the tissue that stores fat. It is very prominent in obese people, in animals living in Polar Regions. It prevents heat loss by forming a heat-insulating layer beneath the skin and also forms shock absorbers around the eyeballs and kidneys.

- **White fibrous tissue**

The tissue is made up of fibers that have great tensile strength. The many bones of the skull are made immovable by this tissue to render the skin as one protective unit.

- **Tendon**

Tendon joins muscle to bone. They are made of collagen fibers.

- Ligament

Ligament joins bones at the joints. They are made up of elastin fibers.

Cartilage

Cartilages are the flexible semi-rigid structures that are present in the pinna (part of the ear). Connect ribs to the sternum and between intervertebral discs.

- **Bone**

Bones have a cavity called marrow cavity. They are red and yellow marrows. Red marrow forms erythrocytes and leucocytes. Red marrows are found in ribs, vertebrae, skull bones and ends of the long bones. Yellow marrow is composed of fatty tissue. It stores fat and produces blood corpuscles only in emergency situations. It is found in the central parts of long bones, for example, femur.

### 2.6.3 Muscle Tissue

Muscle is a very specialized tissue that has both the ability to contract and to conduct electrical impulses. Muscle contractile proteins are actin and myosin, as shown in Figure 2.21.

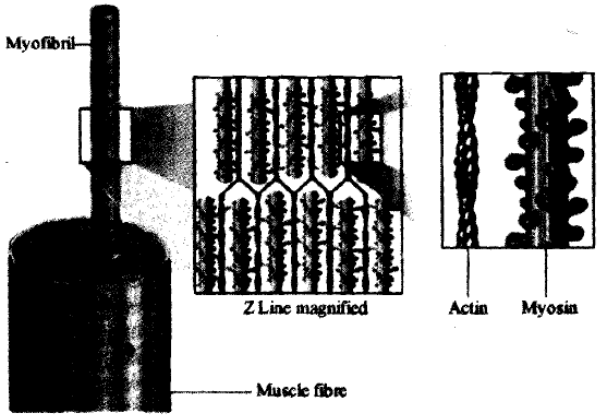
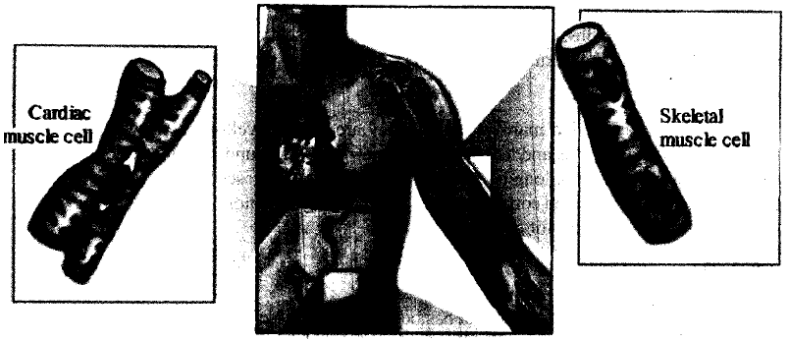



**Figure 2.21: The muscle proteins and myofibrils**

Muscles are classified both functionally as either voluntary or involuntary and structurally as either striated or smooth. The muscle fibers are striated, banded, unbranched and cylindrical and are termed as myofibrils as shown in Figure 2.21. During contraction, both the thick and thin filaments retain their original length, contraction results in an increase in overlap between the filaments. Plasma membrane called sarcolemma surrounds muscle cytoplasm or sarcoplasm. Basically, you would realize there are three types of muscles, as shown in Figure 2.22. A brief review on these muscle tissues follows:

- **Cardiac muscle —** striated involuntary muscle: The muscle proteins of cardiac muscle are identical to those of skeletal muscle. They are actin, tropomyosin and troponin. Under electron microscope, the cardiac muscle shows a striking resemblance to skeletal muscle, as you can observe in the Figure 2.22. We will learn more about the cardiac muscle in the next Imit.
- Skeletal muscle — striated voluntary muscle: Skeletal muscle is attached to the bones. One can contract them on desire and are thus termed as voluntary muscle.
- Smooth muscle — smooth involuntary muscle: Smooth muscle is known for its property of plasticity. The urinary bladder is a typical example. The urine fills without distending the pressure of the bladder till a point where the bladder contracts as one unit and expels the urine. Smooth muscle is not under voluntary control and is divided into type's — single unit or multi unit. Single unit act as a single unit and multiunits are present in the blood vessels.



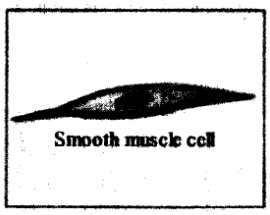



**Figure 2.22: The three types of muscle tissue**

### 2.6.4 Nervous Tissue

Nervous tissue comprises of two types of cells: nerve cells or neurons and glial cells. Neurons have numerous long processes and transmit nerve impulses. The glial cells have short processes and protect neurons. The largest neuronal process is termed as axon that transmits electrical signal away from the cell body. The remaining processes are small and radiate like branches of a tree and are called dendrites or dendrons. We will learn about these structures in greater details later in Unit 9. Nerve impulses or electrical signals cannot be transmitted at the same strength from head to toe. As a result, nature has designed a mannerism in which the impulses jump across clefts or synapses between the axon of a neuron and the cell body of another nerve cell. Nerve impulses jump from one node to the other by means Of saltatory conduction (jumping of a frog). A node is that bare part of the axon or nerve fibre that is not insulated by a lipid myelin sheath. Deficiency of Vitamin $B_{12}$ in the diet results in demyelinating diseases. This is quite common in strict vegetarians who don't even milk and milk products.

With nervous tissue, we end our discussion on tissues, their types and functions. Next, we shall focus on blood, the elixir of life. But before that, let us review what we have learnt so far.

## 2.7 BLOOD

"The ancients believed that blood was the seat of the emotions." Blood, a body fluid, has been rightly termed as an elixir of life. We all have blood flowing inside our bodies. Blood, as you already know, has several important roles to play. It carries oxygen and nutrients to the tissues and carries waste products away. Blood helps maintain body temperature and normal pH levels in body tissues. The protective functions of blood include clot formation and the prevention of infection.

Let us start our study on blood by first getting to know the historical development of the concept of blood.

### 2.7.1 History and Milestones

In this section, we will discuss about the historical development of the concept of blood and blood cells. This discussion is an overview of sequence of events that took place during different times in the past. Let us go through it.

- The ancients must have observed that if an animal or a man lost a considerable quantity of blood, it generally did not survive. This must have led them to

associate blood with life. Ebers Papyrus said that in ancient Egypt, it was believed that food in the stomach was turned into blood by heart.

- According to the ancient European doctrine of four humors, blood was one of the humors which makes the body. The other three humors were phlegm, black bile and blue bile. The blood is considered as one of the four humors.
- The Ayurvedic concept of three humors is very similar. The three humors are kapha (phlegm), pitta (bile) and vayu (air). Health is thought to be a state of balance of these humors. In this system, air comes closest to blood.
- In the recent history of growth of our knowledge about blood, the advent of microscopy in the seventeenth century was an important milestone. Antony Van Leeuwenhoek is considered a pioneer in microscopy. He examined blood under the microscope and could describe red blood cells and even measured their size.
- In the eighteenth century, extensive studies on blood and related structures such as lymphatics and thymus were undertaken by William Hewson. He described the leukocytes and demonstrated that coagulation was due to the changes in the plasma rather than the blood cells, and hence Hewson is called the 'father of hematology'.
- In the nineteenth century, Paul Ehrlich used dyes for staining cells, which helped him to distinguish different types of blood cells and red cell changes in diseases and also identified the different types of white blood cells.

In the twentieth century, George Whipple's studies on the relationship between diet and haemoglobin, George Minot 's discovery of the liver treatment for pernicious anaemia and William Castle's discovery of intrinsic and extrinsic factors were some of the milestones in hematology.

Having learnt about the historical development, let us next get to know about the constituents of blood.

## 2.8 BLOOD COMPOSITION

Blood, as you learnt earlier, is a fluid connective tissue. It is composed of 2 parts. The intercellular fluid is called plasma in which the blood cells or corpuscles float as shown in Figure 2.23 herewith. Thus, blood consists of a fluid (blood plasma) containing cells (erythrocytes and leucocytes) and platelets. Plasma forms about 55% of the blood volume, whereas, the cells occupy the remaining 45%.The composition of blood is as follows:

Water - 91.0 %

Protein - 08.0 % (Albumin, Globulin, Prothrombin, Fibrinogen)

Salts - 0.9 % (NaCI, NaHCOS, salts of calcium, phosphorus, magnesium, iron etc.)

The balance (0.1%) is made up of traces of a number of organic materials: glucose, fats, urea, uric acid, creatinine, cholesterol, amino acids, gases, internal secretions, enzymes and antigens.

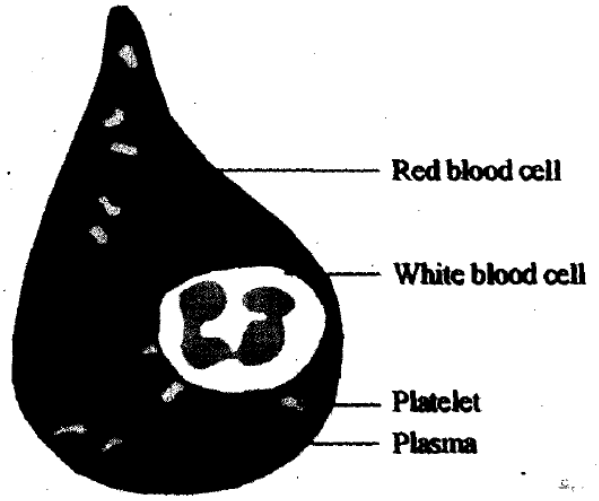



**Figure 2.23: Composition of blood**

Let us get to know more about the plasma and the cells next.

## 2.8.1 The Plasma

Plasma, as you already know, is the fluid in which the cellular elements of blood are suspended. Plasma is a faint yellow colour and has a Slightly alkaline PH. Plasma is 90% water and 10% solutes. in order to separate plasma from the blood cells, a substance which prevents the clotting of blood is added to the blood, after which the blood is left, for the cells to settle down. However, a speedy separation is achieved if blood containing the anticoagulant is centrifuged. The normal plasma volume of an adult is 3 liters. The composition of plasma resembles that of other extracellular fluids of the body except for the presence of a significant concentration of proteins.

Plasma contains different types of proteins, which perform a wide range of functions. Let us get to know about these proteins.

## Plasma proteins

Normal plasma has Proteins in a concentration of 6 to 8 g'/ 100 ml of plasma. The proteins present in the plasma act as enzymes, hormones and hormone-binding proteins. Some of these proteins perform specific functions in blood, like maintaining celloid osmotic pressure of blood, viscosity of blood and helps in the exchange of fluid across the capillary.

There are basically three types of plasma proteins, namely:

- Albumin (4-5 g/ 100 ml)
- Globulin (2-3 g/ 100 ml)
- Fibrinogen (0.3 g/ 100 ml)

Plasma albumin maintains plasma volume by holding water at the capillary level. Fibrinogen helps form a meshwork of solid fibrin that clots blood, preventing haemorrhage (excessive loss of blood). Plasma globulin is the body's defense against

invading pathogens. They constitute the immunoglobulins. Plasma proteins are synthesized in the liver. Immunoglobulins are formed in the plasma cells and B lymphocytes.

So we have seen that plasma is a pale yellow mixture of water, proteins and salts. One of the functions of plasma is to act as a carrier for blood cells, nutrients, enzymes and hormones. Let us learn about the functions of plasma proteins in greater details.

Functions of plasma protein the functions of plasma proteins are many and are listed as:

## Cell and Blood

1) **Osmotic Pressure:** Plasma proteins exert an osmotic pressure of 25 mm Hg, which helps in maintaining plasma volume. The osmotic pressure exerted by plasma proteins plays an essential part in the fluid balance. Having a small molecular size, albumin exerts the maximum colloid osmotic pressure.
2) **Viscosity:** Plasma proteins account for about half of the viscosity of blood, the other half being due to the blood cells. The contribution of each type of plasma protein to viscosity depends more on the molecular shape rather than the molecular size. That is why, a given concentration of fibrinogen, which has a long fibrillar molecule, contributes much more to viscosity than the same concentration of albumin, which has an elliptical molecule.
3) **Protein Reserve:** Plasma proteins provide a reserve, which can be drawn upon for vital functions in the situations of starvation and protein depletion/ malnutrition.
4) **Antibodies:** Plasma proteins belonging to the class of y-globulins act as antibodies, which protect us from infections and several other harmful substances.
5) **Clotting:** Several plasma proteins are involved in the cascade of chemical reactions, associated with the coagulation of blood.
6) **Transport:** Hormones and several other small molecules travelling in the plasma would themselves get filtered in the renal glomeruli and get excreted in the urine. This wastage is prevented during the journey of these substances from their origin to their destination by their getting bound to the Plasma proteins.

Next, let us study about the cells found in the blood.

## 2.8.2 Blood Cells

The cells found in blood are called corpuscles. These are also of three types as illustrated in Figure 2.24 and highlighted herewith:

l) Red Blood Cells (RBC) or Erythrocytes

2) White Blood Cells (WBC) or Leukocytes

3) Platelets or Thrombocytes

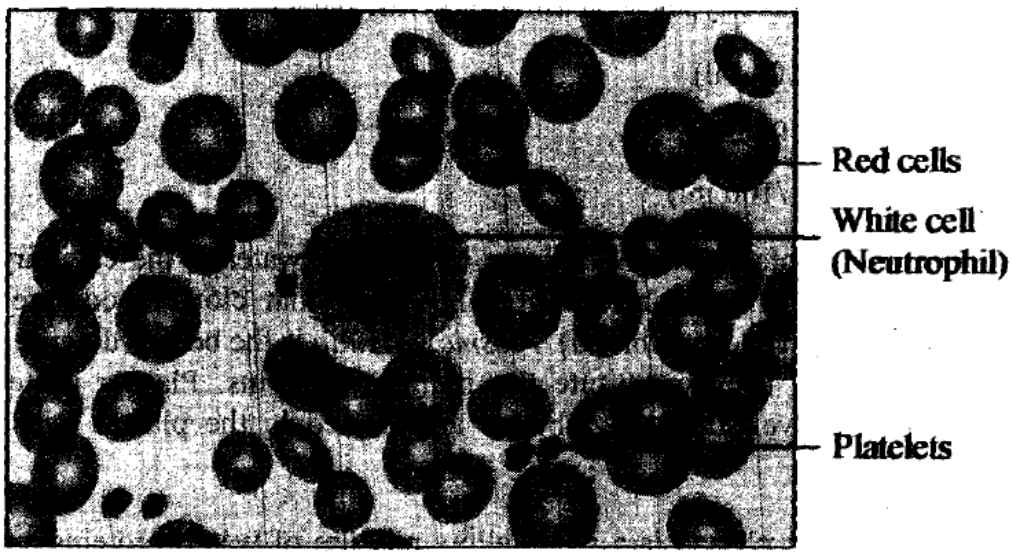



**Figure 2.24; The blood cells**

Let us get to know about them in more details.

## A) Red Blood Cells (RBCs)

RBCs are also called 'erythrocytes' (erythros, red; kytos, cell). They are biconcave in shape as can be seen in Figure 2.24, which has at least three major advantages, as highlighted here with:

- RBCs can swell quite bit before bursting in a hypotonic solution (a solution which contains less dissolved salts than cellular content).
- The biconcave shape (is best suited for) can squeeze through narrow spaces, by even bending along the middle, if necessary.
- The biconcave shape implies a large surface to volume ratio, which increases the efficiency of oxygen transfer across the RBC membrane.

Let us now further study about the dimensions of RBCs and the number of RBCs present in our body.

The mean diameter of RBC is 7.5 microns, maximum thickness at the edges is about 2.5 microns and minimum thickness in the center is about 0.8 microns.

The number of red cells in the blood is about 5 million per cubic mm of blood in normal healthy adults. It is about 0.5 million per cubic mm higher in men than women and higher in those living at high altitude than those living at sea level. RBCs occupy about 45% of the blood volume. This figure is referred to as 'packed cell volume' (PCV) or haematocrit. The concentration of haemoglobin in blood is about 15 g/ 100 ml of blood. The average volume of an RBC is called 'Mean Corpuscular Volume' (MCV). Mean Corpuscular Haemoglobin Concentration (MCHC) is the amount of haemoglobin per unit volume of red cell mass, expressed as a percentage.

Now, after having a basic understanding about how RBCs look like, let us move on to study its role in our body.

NOTES

## Function of Erythrocytes

The basic function of red cells is to transport oxygen, which is made possible by the high affinity, which the haemoglobin (Hb) has for oxygen. RBCs, contain haemoglobin, a protein that binds oxygen. You would be surprised to learn that one gram of Hb carries 1.34 cc of $O_2$. Further, have you ever wondered how much haemoglobin a RBC can carry/store? Well, the red blood cells (RBCs) have the ability to concentrate Hb in the cell fluid to upto about 34 g/dl of cells. This being the metabolic limit, the concentration never rises above. When the haematocrit (% age of blood cells) is 40-45%, the quantity of Hb is normal. Whole blood contains an average of 16 g/dl of Hb in men and 14 g,/dl of Hb in women, each gram of pure Hb is capable of combining with 1.34 millimeters of $O_2$.

Besides oxygen transport, haemoglobin also plays a role in carbon-dioxide transport and maintenance of pH of blood.

Next let us find out what is the life span of this cell.

## Erythrocytes — the dynamic blood cells

Blood cells, including erythrocytes, are a dynamic population. Old cells are destroyed and replaced by the new ones. The turnover is quite rapid, hence precursors of blood cells are among the most actively dividing cells of the body. What is the life span of erythrocytes? The life span of red cells in healthy individuals is about 120 days.

Let us now move on to the next cell that is WBC.

## B) White Blood cells (WBCs)

WBCs are also called leukocytes, as they are colourless. They are the army of the human body. Whenever a germ or infection enters our body, the WBCs snap to attention and destroy the culprit. Their primary function is to produce antibodies (humoral immunity) or kill the invading bacteria directly (cytotoxic immunity). We will learn more about this later in the next unit on the Immune System.

WBCs are divided into two types on basis of presence and absence of granules in the cytoplasm — granulocytes and agranulocytes. Under the light microscope as shown in Figure 2.25, they are classified into basophils, eosinophils, neutrophil (remember BEN is granulocytes) and monocytes and lymphocytes (are agranulocytes) on the basis of:

l) Size

2) Granules

3) Nucleus, and

4) Nucleus/ Cytoplasmic ratio

Each type of leukocyte is present in the blood in different proportions:

| | | |
|---|---|---|
| Neutrophil | : | 50 - 70% |
| Eosinophil | : | 2 - 4 % |

| | | |
|---|---|---|
| Basophil | : | 0.5 - 1% |
| Lymphocyte | : | 20 - 40% |
| Monocyte | : | 3 - 8% |

**NOTES**

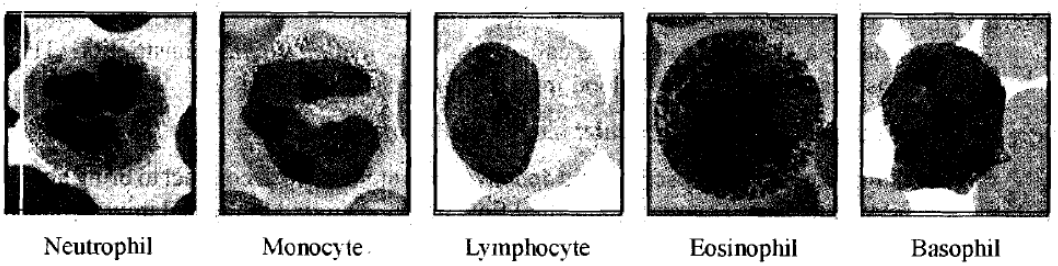



**Figure 2.25: Different types of WBCs**

The monocyte is the largest WBC measuring 2 to 3 times of the RBC. Monocytes leave the cells and become macrophages. Macrophages are large, phagocytic cells that engulf foreign material (antigens) that enter the body and dead and dying cells of the body. The nucleus of a monocyte is kidney-shaped (as can be seen in Figure 2.25), surrounded by an equal amount of cytoplasm and that of the lymphocyte occupies a major part of the cell. Lymphocytes are extraordinarily diverse in their functions. The most abundant lymphocytes are:

- B lymphocytes (often simply called B cells) and
- T lymphocytes (likewise called T cells).

Basophils have purple coarse granules. Basophils make up only a small portion of the number of white blood cells but are an important part of the body's immune response. They release histamine and other chemicals that act on the blood vessels when the immune response is triggered.

Neutrophils are the most abundant of WBCs. The neutrophil has pink fine powdery granules. The nucleus ofa neutrophil is multi-lobed (>2) as you can see in Figure 2.25. This is its distinguishing feature. Neutrophils squeeze through the capillary walls and into infected tissue where they kill the invaders (e.g., bacteria) and then engulf the remnants by phagocytosis.

The eosinophil is brick red coarse granules. Have a look at Figure 2.25. You would notice that it has a bi-lobed spectacle shaped nucleus. The number of eosinophils in the blood is normally quite low (2—4%). However, their numbers increase sharply in certain diseases, especially infestation by parasitic worms and allergies.

You might be wondering why does the body need so many types of WBC's? Basically, the neutrophils are the first line ofdefense that fights against the bacteria. The eosinophils have larger granules and fight larger parasites and are also active during skin infections and allergic condition such as asthma. The agranulocytes, such as monocytes and lymphocytes are active against bacteria present in the body for a long time such as tuberculosis and leprosy.

Next, w e shall look at the platelets.

### C) Platelets

Blood platelets, the third blood cells are the smallest (look at Figure 2.24) formed by the pinching Of a very large bone marrow cell called megakaryocyte. Platelets literally mean a small plate. The platelets form a plug to stop bleeding when an injury disrupts the lining of the blood vessel. Their diameter is about 2-3 gm, hence they are much smaller than erythrocytes. Their density in the blood is /mm3.

What-are the functions of platelets?

The main function of platelets, or thrombocytes, is to stop the loss of blood from wounds, i.e. haemostasis. Let us learn about this function. The platelets:

i) release a chemical substance called serotonin, that cause vasoconstriction. This ensures reduced flow of blood from the injured site,

ii) aggregate to plug the vascular plug at site of injury, and

iii) have like skeletal muscles, actin and myosin proteins, which contract to bring about clot retraction. This ensures normal flow of blood around the sealed injured blood vessel.

The plug formed by the platelet arrests bleeding. The time taken for the blood to cease flowing from an injured site is termed as bleeding time. The platelet plug that is formed is friable and cannot be relied to check bleeding for very long. The blood forms a fibrin meshwork of threads that forms a better plug. This may take a few minutes before such a first aid mechanism acts in the body. The time taken for a clot to form is termed as clotting time. Before a patient is taken to the operation theatre, the doctor assesses the bleeding and clotting time to prevent excessive loss of blood during time of operation. The patient whose bleeding time is less than 4 minutes and clotting time is less than 12 minutes may be taken up for surgery after the other investigations are normal.

So far, we have learnt about the constituents and functions of blood — the fluid connective tissue. Do you know how the blood formation takes place? In which part of the body the blood is formed? We will find the answers to all these querries in the next section, which deals with erythropoiesis.

## 2.9 ERYTHROPOIESIS

Erythropoiesis, derived from the word 'erythros' meaning red and 'poiesis' meaning making, is a part of a broader process, hemopoiesis, i.e., formation of blood cells in general. Let us get to know about it.

The precursor of all blood cells is a primitive stem cell, also called as a Totipotent Hematopoietic Stem Cell (THSC). THSC is a cell capable of rapid proliferation accompanied by differentiation. Differentiation of the THSC is associated with subtle biochemical changes, which eventually result in a cell committed to forming a specific variety of blood cell. The process of proliferation and differentiation continues till the mature blood cells, incapable of proliferation, are formed.

The general process of proliferation and progressive differentiation leads to

an important question. If the process of differentiation affects every daughter cell, why do we not finally reach a stage wherein all the cells are highly differentiated but are incapable of dividing? The answer to this question is that immature cell has a nucleus and as it matures, the nucleus disappears, and hence the cell is incapable of dividing but capable of differentiating.

You would realize that the site of erythropoies is varies somewhat with age. Let us go through the different stages and find out what these age-related differences are.

- During intrauterine life, in the early embryo, erythropoiesis occurs in the mesoderm (the middle of the three germ layers of an embryo) of yolk sac. In a few weeks, the process shifts to the mesoderm of the body. During these stages, erythropoiesis is intravascular. It takes place by some endothelial cells undergoing transformation into blood cells and detaching themselves from the vessel wall to enter the circulation.
- After the third intrauterine month, erythropoiesis takes place in the liver and spleen, in the mesenchymal tissue (embryonic connective tissue) between the blood vessels and tissue cells.
- After the fourth intrauterine month, the fetal bone marrow also starts manufacturing blood cells.
- By the time of birth, bone marrow takes over erythropoiesis completely. Thus, all extrauterine (occurring outside the uterus) erythropoiesis is medullary, i.e., in the bone marrow. Red cells, white cells and platelets are made in the marrow of bones,

But liver and spleen retain the potential for erythropoiesis throughout the life. Hence, in those situations where the demand for red cells exceeds the capacity of the bone marrow to manufacture them, extramedullary erythropoiesis is often seen. In a new born, all bones have a red bone marrow, i.e. the marrow which manufactures blood cells. But as the child grows, the bones also grow and so does the marrow. But the need for manufacturing blood cells does not grow proportionately. Hence, progressively larger parts of the bone marrow changes to yellow bone marrow, i.e., marrow which does not manufacture blood cells. The red marrow in the shafts of long bones is the first to be replaced by yellow marrow, followed b that at the ends of Ion bones.

Finally, in the adult, the red marrow exists only in the sternum, ribs, vertebrae, pelvis and skull. Therefore, if a sample of bone marrow is required for diagnostic purposes, it is usually obtained from either the sternum or the iliac crest (the hip bone in which a large quantity of bone marrow is concentrated). However, when the need for manufacturing blood cells is heavy, first the area occupied by the red marrow expands and then extramedullary haemopoiesis may also begin.

Let us now study about the regulation of the process of erythropoiesis in the following section.

## 2.8.1 Regulation of Erythropoiesis

Since the red cell mass of an individual is essentially stable in spite of constant formation and destruction of erythrocytes, the process must be finely regulated. The factors regulating erythropoiesis are as follows:

1) **Erythropoietin:** Erythropoietin is a glycoprotein, which is released predominantly from the kidneys in response to the tissue hypoxia. When the haemoglobin concentration of blood falls, oxygen tension in the tissues also falls at least slightly, the kidneys also share this fall in tissue oxygen tension and respond to it by secreting the hormone, erythropoietin into the blood stream. Hence low tension of02 in blood in the renal artery leads to the release of erythropoietin. Erythropoietin is also released by the isolated kidney if it is perfused with a hypoxic fluid. However, erythropoiesis continues fairly normally even after removal of both the kidneys.
2) **Androgens:** Since men have a higher red cell count than women, and the difference between sexes appears at puberty, androgens are likely to at least stimulate, if not regulate erythropoiesis.
3) **Oestrogen:** Oestrogen has an inhibitory effect on erythropoiesis.
4) **Thyroxine, Cortisol and Growth Hormone:** The deficiency of these hormones is generally associated with anaemia. These hormones stimulate erythropoiesis possibly by increasing the oxygen consumption of tissues and thereby promoting tissue hypoxia. Tissue hypoxia, in turn, stimulates erythropoietin production.
5) **Neural control:** Some controversial experimental evidence indicates that some hypothalamic cells may sense hypoxia and respond to it by stimulating erythropoiesis through a neurohumoral mechanism.
6) **Products of hemolysis:** It is controversial whether products released by red cells stimulate or inhibit erythropoiesis or do not affect the process at all. It is believed that some products of red cells may be exerting a feedback effect on erythropoiesis.
7) **Dietary factors:** Some dietary factors are essential for erythropoiesis. For example, amino acids are required for the synthesis of globin, iron for synthesis of heme, and Vitamin BE and folic acid for maturation of red cell precursors. Therefore, a deficiency of any of these factors reduces erythropoietic activity. And if the erythropoietic activity is low due to a dietary deficiency, the activity can be stimulated (or rather restored back to normal) by providing the deficient nutrient. This effect of nutrients cannot however, be termed as a regulatory effect.

The discussion above focused on erythropoiesis and the process of blood formation and regulation. With this discussion our understanding of blood is somewhat complete or is it. There is one more important aspect related to blood which can be of interest to us. What is it? You must have seen or heard about blood groups, such as B+ve, 0+ve, AB+ve and so on. What do we mean by these blood groups? Do all of us have similar blood groups? And if no, what parameters make it distinct from a person to person? We shall find the answers to all our queries in the next section.

We begin our discussion with an understanding about blood groups.

## 2.10 BLOOD GROUPS

NOTES

We start our discussion by answering the question — do all of us have the same blood group? No, each individual has a different blood group. The differences in human blood are due to the presence or absence of certain protein molecules called antigens and antibodies. The antigens are located on the surface of the red blood cells and the antibodies are in the blood plasma. Individuals have different types and combinations of these molecules. The blood group you belong to depends on what you have inherited from your parents.

Blood group, therefore, is based on the type of antigens present on the surface of RBCs. There are more than 30 antigens, but for the purpose of blood transfusion, very few of them are practically significant. For all practical purposes, the starting point in determining the suitability of a donor is to type the donors, as well as, recipients blood in terms of ABO and Rh grouping. Sometimes there can be a mismatch reaction. Hence, besides an ABO and Rh grouping, cross matching of the donors' and recipients' blood is important. What is the ABO and Rh grouping? Let's get to know about these grouping systems.

### 2.10.1 ABO Blood Grouping System

As the name suggest, this is based on the presence or absence of 9 antigens A and B, on the surface of RBC. If either of these antigens is present on the surface of RBC, it can react with the corresponding antibody. Reaction between a blood group antigen and its corresponding antibody leads to clumping (agglutination) of RBCs. Hence, blood group antigens are known as 'agglutinogens' and the corresponding antibodies are known as 'agglutinins'.

Landsteiner found that if RBC of an individual carries a particular group antigen, RBC can circulate safely only if corresponding antibody is not present in the plasma of same individual. Hence a law was formulated by him, which states that 'if an antigen is present on the surface of RBC, the corresponding antibody would be absent in plasma'. Conversely, if an antigen is absent, the corresponding antibody is present. This law is good for ABO and not for Rh system.

According to the ABO blood typing system, therefore, there are four different kinds of blood types: A, B, AB or O (null). What do they signify? Let's find out.

If you belong to the blood group A, it means you have A antigens on the surface of your red blood cells and B antibodies in your blood plasma, as shown in Figure 2.26. If you belong to the blood group B, you have B antigens on the surface of your red blood cells and A antibodies in your blood plasma. If you belong to the blood group AB, you have both A and B antigens on the surface of your red blood cells and no A or B antibodies at all in your blood plasma. If you belong to the blood group O (null), you have neither A or B antigens on the surface of your red blood cells, but you have both A and B antibodies in your blood plasma as you can see in the Figure 2.26.

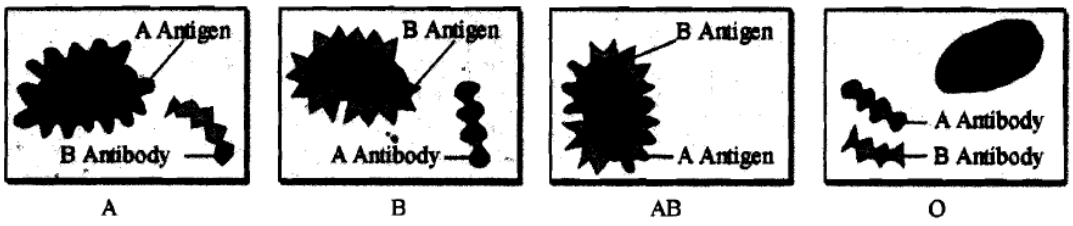



**Figure 2.26: The ABO blood grouping system**

The next question which might interest you is how do you find out which blood group one belongs to? The process is simple. First, the blood with three different reagents including either of the three different antibodies, A, B or Rh antibodies is mixed. Then one looks that in which mixtures agglutination has occurred? The agglutination indicates that the blood has reacted with a certain antibody and therefore is not compatible with blood containing that kind of antibody. If the blood does not agglutinate, it indicates that the blood does not have the antigens binding the special antibody in the reagent. If you know which antigens are in the person's blood, it's easy to figure out which blood group he or she belongs to.

Further, you may have come across the terms 'Universal Donor' and 'Recipients' in the context of blood transfusion. What do these terms mean? Let's find out.

## Universal Donor and Recipients

Based on the above mentioned concept, O group individuals are sometimes considered as 'universal donors since they have no antigens and the blood does not generate any antibody reaction. Group AB is called 'universal recipients' as their plasma has no antibody. They can receive blood from anybody as highlighted in Table 2.2 here with. The donor cells irrespective of whatever antigen they contain will not cause a reaction.

| Blood Group | Antigens | Antibodies | Can give blood to | Can receive blood from |
|---|---|---|---|---|
| AB | A and B | None | AB | AB, A, B, O |
| A | A | B | A and AB | A,O |
| B | B | A | B and AB | B, O |
| O | None | A and B | AB, A, B, O | O |

**Table 2.2: The blood groups and the universal recipient and donor concept**

Other than the A and B antigen, some other factor is also present on the surface of the RBCs. What is this factor and the corresponding blood grouping system? Let's find out.

## 2.10.2 Rh Blood Grouping System

Some individuals also have a so called Rh antigen on the surface of their RBCs.

Those who have it are called Rh (+) and those who do not have it are Rh (—). This is the basis of the Rh blood group system. In Caucasian (white) races, about 85% of human are Rh +ve, but among African blacks almost everyone is Rh —ve.

Rh stands for Rhesus monkey. RBC of Rhesus monkey when injected into rabbit develops antibodies to rhesus RBC. Later, it was discovered that rabbit serum containing anti- rhesus antibodies could agglutinate not only rhesus RBC, but also human RBC in about 85% cases, which was suggestive that these 85 % of human beings have on their RBC an antigen identical to or remarkably similar to Rhesus RBC. This antigen was named as 'Rh antigen'. Human beings having this antigen were labeled 'Rh positive'. Thus, in a Rh system, blood may be either positive or negative.

**A person with Rh —** ve blood does not have Rh antibodies naturally in the blood plasma (as one can have A or B antibodies, for instance). But a person with Rh —ve blood can develop Rh antibodies in the blood plasma if he or she receives blood from a person with Rh+ve blood, whose Rh antigens can trigger the production of Rh antibodies. A person with Rh+ve blood can receive blood from a person with Rh —ve blood without any problems. So it must be clear by now that Rh positive or negative individuals do not have anti Rh antibodies. But, ifan Rh —ve individual is given Rh +ve blood, he develops anti Rh—ve antibodies.

Rh incompatibility can therefore occur sometime. What are the consequences? Read and find out.

## Rh Incompatibility

Rh compatibility sometimes leads to complications which are generally not seen with other types of mismatched transfusions. If a Rh negative is given Rh positive blood, there is no immediate adverse reaction because Rh negative individuals do not normally have anti-Rh antibodies which may damage the donor red cells. The donor red cells induce immune response in the recipient, as a result of which anti-Rh antibodies are synthesized. It takes 2-4 months before a high tirtre of anti-Rh antibodies are achieved. By this time, most of the donor cells die a natural death. The anti-Rh antibodies can do no harm. Hence, first phase of transfusion passes silently. Ifthe second dose is given, the memory cells ensure anti-Rh antibodies are synthesized in proper amounts. Second transfusion acts as a booster dose. High dose of anti-Rh antibodies can be achieved.

By this time, most of donor cells are thus damaged. Since anyone may need a second blood transfusion later in life, Rh negative individuals should never be given Rh positive blood.

One of the critical manifestations of Rh-incompatibility is ' Erythroblastosis Foetalis '.

What is it? Let us study and find out.

Risking Girls: Erythroblastosis Foetalis

Besides the risk of a mismatch reaction during a second or during any subsequent blood transfusion, giving Rh-positive blood involves risk in case of young Rh-negative girls. This is because of the possibility of complication during pregnancy

if the girl happens to have a Rh-positive foetus in her uterus any time later in life. The chances of any abnormalities resulting from Rh incompatibility are negligible during first pregnancy, 3% during second and 10% during third. This is due to following reasons:

1) Red cells of the foetus are unable to cross normal placenta. There has to be some abnormality in the placenta before foetal red cells can enter the maternal circulation.
2) Foetal red cells may be destroyed by maternal plasma before they can induce an antibody response. E.g., if mother is O, Rh negative and the foetus is A, Rh positive, the foetal red cells would be haemolysed by the anti-A antibodies present in the maternal plasma.
3) If the foetus and mother happen to be of same group, i.e., A,B or AB but mother is Rh —ve and foetus Rh +ve, during 2nd and subsequent pregnancies, mother gets sensitize with Rh antigents of fetal blood, resulting in production of anti-Rh antibodies, which will destroy foetal RBC, causing 'erythoblastosis foetalis'.

Although erythroblastosis foetalis may be treated by exchange transfusion, the prevention is routinely attempted by desensitizing the mother for production of Rh antibodies during pregnancy. The desensitized mothers don't respond to foetal Rh+ve RBCs. Thus erythroblastosis foetalis is prevented.

Apart from the Rh incompatability as a complication leading to loss of blood, there is another condition wherein the RBCs are deficient. This is referred to as anaemia, a disorder related to deficiency of erythrocytes. As a student of dietetics, you must be familiar with anaemia and its consequences. Let us recharge our understanding on this topic.

## 2.11 ANAEMIA

Anaemia, as we already know, means 'deficiency of red blood cells, due to the rapid loss or slow production of RBCs '. Some types of anaemia and their physiological causes are summarized below:

1) Haemorrhagic or blood loss anaemia: The body replaces plasma within 1-3 days after a haemorrhage, but this leaves a low concentration of red blood cells. In chronic blood loss, a person frequently cannot absorb enough iron from the intestines to form Hb as rapidly as it is lost. Red cells are then produced with too little haemoglobin inside them giving rise to microcytic hypochromic anaemia. What is microcytic hypochromic anaemia? Read on and you will find out in a little while from now.
2) Aplastic anaemia: Bone marrow aplasia means 'lack of functioning of bone marrow'. This can occur due to excessive X-ray or radiation treatment, certain industrial chemicals, sensitive drugs, nuclear exposure etc.
3) Iron deficiency anaemia: This is due to inadequate dietary intake of iron, poor intestinal absorption of iron, abnormal loss of iron from the body. For example, menstruation or haemorrhage or heavy iron requirements such as pregnancy

or lactation. The RBCs in this condition are smaller than normal and have an increased zone ofcentral pallor. This is indicative of a hypochromic (less haemoglobin in each RBC) microcytic (smaller size of each RBC) anaemia. There is also increased anisocytosis (variation in size) and poikilocytosis (variation in shape),- as can be seen in Figure 2.27.

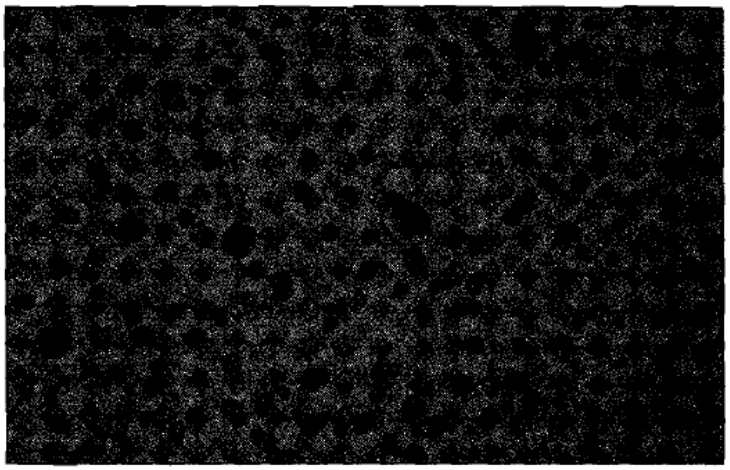


**Figure 2.27: Smaller than normal red blood cells with central pallor seen in iron deficiency anaemia**

**4) Megaloblastic anaemia:** The less availability of vitamin Be, folic acid, intrinsic factor of stomach mucosa etc. slows down the production of erythroblasts that occur in the bone marrow. Hence these cells grow too large with odd-shaped cells called as 'megaloblasts' as shown in Figure 2.28. The erythroblasts cannot proliferate rapidly to form enough RBCs. The cells which are formed are mostly oversized, bizarre shaped and have fragile membranes. They rupture easily, leaving the person for a need of an adequate number of cells.

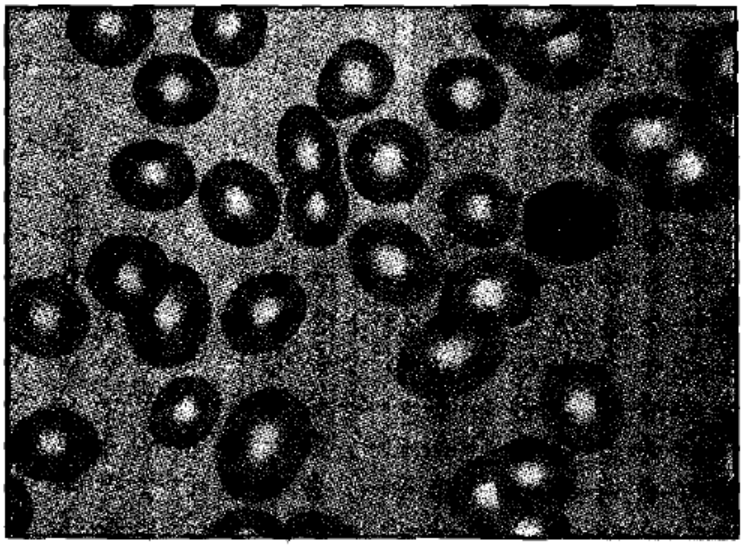


**Figure 2.28: Large, dense, oversized, red blood cells (RBCs) seen in megaloblastic anaemia**

**5) Hemolytic anaemia:** It can occur due to various reasons and situations. The general tendency is that the fragile cells rupture when they pass through the spleen.

In hereditary spherocytosis, red celleare spherical and small, they cannot be compressed on passing through spleen and are easily ruptured.

In sickle cell anaemia, the cells contain an abnormal type of Hb which is HbS because of abnormal B-chains. This when exposed to low 02, precipitated Hb damages the -cell membrane and cell becomes highly fragile, the patient suffers due to less 02 availability. The abnormal haemoglobin causes red blood cells to assume a sickle shape, like the ones seen in Figure 2.29.

**Figure 2.29: Blood smear of a sickel cell anaemic patient**

In erythroblastosisfoetalis, Rh—positive red blood cells, as you may recall reading earlier, are attacked by antibodies from a Rh—negative mother. These antibodies make the cells fragile, leading to rapid rupture causing the child to be born with serious anaemia.

The classification of anaemia presented above is based on etiology i.e. based on causes of anaemia. Anaemia, you would realize, can be further classified based on morphological classification i.e. based on the size of the RBC (Mean Corpuscular Volume or MCV) and the amount of haemoglobin in the RBC (MCH). Table 2.3 presents the morphological classification, also called the Wintrobes Classification.

| | **Normochromic** | **Hypochromic** |
|---|---|---|
| **Normocytic** | Acute Haemorrhage | Chronic Haemorrhage |
| **Macrocytic** | All megaloblastic anaemias e.g Vitamin $B_{12}$, Folic acid deficiency | Liver Disease |
| **Microcytic** | Chronic infections | Iron deficiency<br>Thalassemia |

**Table 2.3: Morphological classification Of anaemia**

What do these terms microcytic, macrocytic etc. mean? These terminologies are

explained herewith :

- hypochromic - less than normal color (decreased Hb content)
- hyperchromic - more than normal color (increased Hb content)
- macrocytic - larger than normal size
- microcytic - smaller than normal size
- normochromic - normal color (normal Hb content)

The disease conditions which present the following blood picture are summarized next:

- macrocytic normochromic : pernicious anaemia, folic acid deficiency and chronic liver disease
- normochromic normocytic : acute blood loss and hemolytic anaemias
- microcytic normochromic : neoplastic

microcytic hypochromic : Iron deficiency anaemia (look at the picture in Figure 2.27 above which is classical microcytic hypochromic picture), thalassemia, sideroblastic anaemias

We shall not go into any further details on this topic now, as it is not within the purview of this course. We hope that the information presented above, is sufficient for you to understand the anaemia types and their causes.

With this, we come to an end on our discussion on anaemia.

## 2.12 HAEMOSTASIS

Haemostasis (Haem: blood: Stasis: standing) ensures blood to coagulate into a solid gel during injury and also ensures free flow of blood in vessels under normal conditions. Haemostasis is a balance of the physiological processes, which on one hand prevent excessive bleeding after vessel injury, and on the other hand, maintain a viable circulation by keeping the blood in an uncoagulated state. Platelets are involved in almost all stages of haemostasis. What is the process of haemostasis? Primarily, haemostasis can be divided into the following four components:

- **Vessel constriction:** Vessel constriction occurs after vessel injury. This is the beginning of primary haemostasis which leads to protective vasoconstriction at the site of injury in order to arrest the bleeding. Time taken for this to occur is known as bleeding time.
- **Platelet function:** This process involves the formation of platelet plug at site of injury.
- **Coagulation :** This process include processes leading to the formation of a fibrin net which stabilizes the platelet plug in order to permanently stop bleeding.
- **Fibrinolysis:** This process involves the dissolution of blood clots. The fibrinolytic system is antagonist to the coagulation system, dissolving fibrin clots by the specific and powerful protease plasmin

The process above must have given you a fairly good idea about the mechanism

involved in the cessation of bleeding. This is a natural process which goes on in our body. But sometimes there can be a problem. There are a few disorders of haemostasis. Disorders of haemostasis can be roughly divided into platelet disorders (such as idiopathic thrombocytopenic purpura) and disorders ofcoagulation such as haemophilia. A brief knowledge ofthese disorder follows:

## Haemophilia

Haemophilia is a disease characterized by excessive bleeding due to deficiency of clotting factor VIII. The patient need repeated blood transfusion or may need a factor VIII concentrate.

## Idiopathic Thrombocytopenic Purpura (ITP)

"Thrombocytopenic" means the blood doesn't have enough platelets. "Purpura" means a person has excessive bruising. You may also hear IT P called "immune thrombocytopenic purpura".

We have seen that patients with haemophilia require repeated blood transfusion. What is blood transfusion? We shall look into this aspect before ending our study of blood the elixir of life.

## Transfusion of blood

Blood has been considered as the elixir of life. However, in ancient times, patients were bled to get rid of their foul fluid. Later, as blood was transfused after the discovery of circulation, patients died after receiving transfusion. The blood being transfused from one patient was not compatible with the recipient's. Why is this so? Certainly you would know why, especially now that you have studied about blood groups. Considerable advances in transfusion medicine took place during the two World Wars. During the first world war, the collection and storage of blood was perfected. During the second world war, individual components of blood were separated. In early 1980's, doctors started training in the specialty of blood transfusion and actively participating in patient care.

Blood transfusion, therefore, refers to the infusion of blood or blood components into an individual for the treatment of a medical condition (e.g., anaemia, loss of blood due to injury etc.). Transfused blood may be homologous (from a donor) or autologous (previously stored blood from the recipient).

It is important to note that blood transfusion is only to be given when there is no alternative. Though blood transfusion is safe, the main risk of transfusion is being given blood of the wrong group or a smaller risk of catching an infection. To ensure you receive the right blood, the clinical staff makes careful identification checks before any transfusion.

Finally, in what form is the blood given?

Blood is usually split up into four separate components:

Whole blood: This is rarely used these days, only really in instances of severe blood loss. Instead it's almost always separated into its individual components. Red cells:

These are used in the treatment of all kinds of anaemia which can't be medically corrected, such as when rheumatoid arthritis or cancer is involved, when red cells break down in the newborn, and for sickle cell disease. They're also essential to replace lost red cells after such things as accidents, surgery and after childbirth, not to mention pre-op 'top-ups' for existing anaemic patients and for burn victims.

**Platelets:** Bone marrow failure and post transplant and chemotherapy treatments and leukaemia. These are all instances when platelets can be of huge benefit to the recipient.

**Plasma:** Fresh frozen plasma is used after obstetric loss of blood (which is usually childbirth), during cardiac surgery and to reverse any anti-coagulant treatment. With this, we end our discussion on blood.

## 2.13 LET US SUM UP

In this unit we have studied about the cell structure, the basic unit of life and the elixir of life, the blood. The mysteries of our cell, its working, the cell as a factory and its organization functions and division are the major aspects that have been covered in the unit.

We also learnt about the structure and functions of blood and its components. The process of haemostasis was also discussed in this unit.

## 2.14 GLOSSARY

**Agglutinogens** : blood groups antigens.

**Aplastic Anaemia** : lack of functioning of bone marrow.

**Centriole** : twin bodies that are found near the nucleus. They are responsible for forming the cilia, flagella and astral spindle during cell division.

**Cisternae** : one of the sac-like vesicles that comprise the endoplasmic reticulum.

**Cytoskeleton** : the ability of cells to change shape and carry well- directed movements depending on the skeleton of the cell.

**Fibrinolysis** : a normal ongoing process that dissolves fibrin and results in the removal of small blood clots.

**Glial Cells** : cells having short processes that protect neurons

**Humors** : a body fluid.

**Hypotonic Solution** : a solution which contains less dissolved salt than cellular content.

**Mean Corpuscular Haemoglobin Concentration :** the amount of Hb per unit volume of red cell mass, expressed as a %.

**Mean Corpuscular Volume** : average volume of RBC.

**Microfilaments** : a network of filaments within the cytoplasm helps play a major role in cell motion and allowing the cell to adopt new shapes.

**Microtubules** : a network of hollow tubes that are made up of tubulin molecules.

**Microvilli** : some cells have acquired additional structures in the form of projections to maintain the surface area-to-volume ratio in a balanced state. These increase the absorptive surface area.

**Myofibrils** : the muscle fibers that are striated or banded unbranched cylindrical.

**Plasticity** : property of smooth muscle to maintain shape and size irrespective of force applied.

**Plastids** : organelles of the plant cells that contain chlorophyll.

**Tendon** : tendon joins muscle to bone. They are made of collagen fibers.

**Totipotent Hematopoietic Stem Cell :** a primitive stem cell; the precursor of all blood cells.

**Vasoconstriction** : the constriction or narrowing of blood vessels, so that the less blood is able to flow through at a time.

## 2.15 ANSWERS TO CHECK YOUR PROGRESS EXERCISES

**NOTES**

UNIT

# 3

# THE IMMUNE SYSTEM

**STRUCTURE**



## 3.1 LEARNING OBJECTIVE

After studying this unit, you will be able to:

- explain body's immune system,
- discuss the non-specific and specific defence mechanisms in the body,
- differentiate between the innate and specific acquired immunity,
- describe the development, regulation and functions of white blood cells in maintaining immunity in the body, and
- enumerate the methods of in-vitro detection of antigen-antibody interaction.

## 3.2 INTRODUCTION

Blood, a body fluid, has been rightly termed as an elixir of life. In the last unit we learnt that blood has several important roles to play. What makes it so unique? You would realize that the different blood cells — their functions and significance in maintaining immunity i.e., body's natural defence mechanism against foreign invaders, is what makes, blood so unique.

We are living on this globe with many organisms around us. Generally, human beings are scared ofsome insects or animals. Many are ignorant about the pathogenic organisms around us. Some of them are internal parasites, some are external. There are a number of bacteria, viruses etc. which are pathogenic to human system. We need to have resistance developed against these organisms. Our body is equipped with multiple defence mechanisms, generally known as immune mechanisms. In this unit, we will focus on the immune system. What are the components of the immune system? What are the defence mechanisms which protect our body? Why is it essential to have defence mechanisms in our body? These are a few issues discussed in this unit. Finally, we will discuss about the antigen-antibody relationship and the various methods of their in-vitro determination.

## 3.3 THE IMMUNE SYSTEM

The animals and the human beings are forced to encounter many dangerous microbes in their day-to-day life, through water, air and food. Inside our body there is an amazing protective mechanism called the immune system. It works silently inside our body for the entire life but we probably know almost nothing about it. What role does it play in our body? The immune system is designed to protect us from the millions of the microbes, toxins, parasites. The immune system protects us in three different ways:

1) It creates a barrier that prevents bacteria and viruses from entering our body.
2) If a bacterium or virus does get into the body, the immune system tries to detect and eliminate it before it can make itself at home and reproduce, and
3) If the virus or bacteria are able to reproduce and start causing problems, our immune system is in charge of eliminating it.

You certainly know about your heart, lungs and kidneys. But, do you know what are the organs working inside the body which protect us from germs, infections and other invading substances? Have you ever heard of the thymus? Yes, it is there in your chest, right next to your heart. Like thymus, there are other components of the immune system which include:

- Spleen
- Lymph system
- Bone marrow
- White blood cells
- Antibodies
- Complement system
- Horrnones

Figure 3.1 illustrates some of these organs. The thymus is responsible for producing cells (we will get to know about them in the next section on WBCs), and is especially important in newborn babies - without a thymus, a baby's immune system collapses the baby will die. Thymus is important, especially to T-cell maturation. The spleed filters the blood looking for foreign cells (the spleen is also looking for old red blood

cell in need of replacement). A person missing their spleen gets sick much more often someone with a spleen. Bone marrow produces new blood cells, both red and white. the case of red blood cells, the cells are fully formed in the marrow and then enter the bloodstream. In the case of some white blood cells, the cells mature elsewhere. marrow produces all blood cells from stem cells. They are called "stem cells" because. they can branch off and become many different types of cells — they are precursors different cell types. Stem cells change into actual, specific types of white blood cells We shall get to know about the other components as we go along reading the unit

It is amazing to know that the body develops different types of defence mechanis. The study of body's defence mechanisms against invading pathogens is call immunology. As per the different types of functioning, the defence mechanisms can of two types. They are:

1) non-specific defence mechanisms, and

2) specific defence mechanisms.

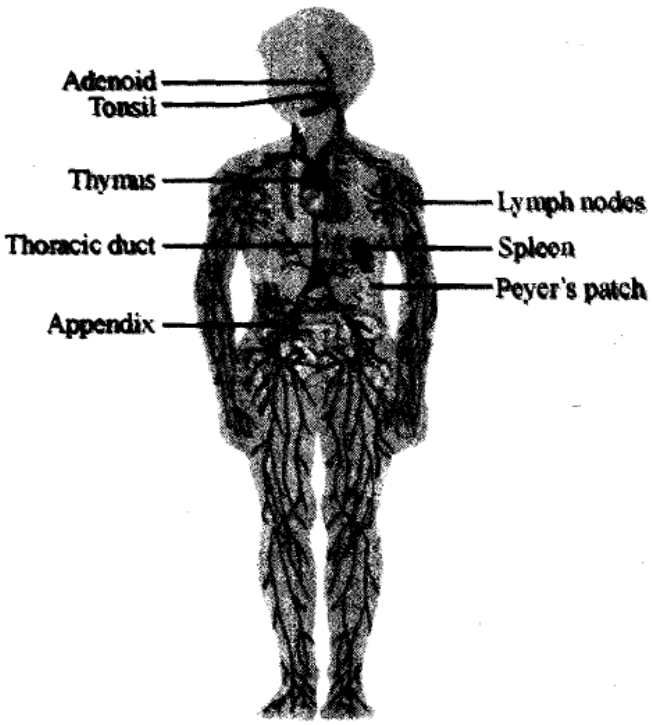



**Figure 3.1: Organs of the immune system**

One of the most obvious part of the immune system is what you can see i.e. the skin. This is indeed the first line of the defence mechanism the body has in place. The body has yet another second line of defence, about which we will read in a little while. The non-specific defence mechanisms are, therefore, sub divided into two:

a) first line of defence, and

b) second line of defence

Let us learn what these first and the second line of defence mechanisms are.

The first line of defence mechanism (external) includes:

a) skin's horny layer

b) mucous membranes

c) secretions of skin and mucous membranes, and

d) skin and gut bacteria

The second line defence (internal) includes:

a) phagocyte

b) inflammatory reactions

c) fever

d) interferons

e) complement system, and

f) natural killer cells

## 3.4 NON-SPECIFIC DEFENCE MECHANISM

The non-specific defence mechanism is implemented for different types of infections. It resists infection in two ways, firstly, by blocking the entry of pathogens into the body i.e. through external mechanism and secondly by destroying the microbes, if they enter the body through means other than the antibodies. Let us get to know about these external and internal defence mechanisms.

### 3.4.1 External Defence Mechanism

The external defence mechanism comprises of physical and chemical barriers to the entry of pathogens. What are the physical barriers? Let's find out first.

### 1) Physical barriers

The physical barriers are primarily of two types — skin and mucous.

**A) Skin:** It provides nice protective covering to the body. The outer layer- horny layer — contains dead keratinized cells. These cells have hard insoluble fibrous proteins called keratin, instead of soft protoplasm. This layer is water proof and germ proof. It can prevent entry of virus and bacteria.

**B) Mucous membranes:** The digestive, urinary, genital and respiratory tracts open out at one or both ends. They do not have a direct communication with other parts of the body. The parasites, microbes present are not in the physiological interior of the body. The mucous membranes in these tracts are treated as a part of external defence. These membranes can resist entry of parasites, microbes into tissues. Mucous traps the microorganisms and immobilizes them. How? Mucous, as you may know, is a clear, sticky substance and has glycoprotein and water. The microbes get trapped in this sticky fluid. Let us see what role the mucous has in the body systems and organs.

- **The gastrointestinal tract:** The microbes which enter through the mouth are caught in the mucous and eliminated with sputum. A coating of the mucous over the intestinal lining also traps the microbes for removal in the faeces.
- **Respiratory tract:** The microorganisms and dust particles often enter the respiratory tract with air during breathing. Many of these are caught in the hair mesh present in the nostrils. Those which are filtered are trapped in the mucous that covers the tract. The cilia sweeps the mucous loaded with pathogens and dust particles into the pharynx. Further it is thrown out, swallowed or eliminated through the faces.
- **Eyes:** The secretions from the tear glands, flickering movements of the eyelids flush out the microorganisms setting on the eyeballs from air.
- **Internal tracts:** Various tracts in the body are flushed with fluids such as saliva, digestive juices, bile and urine. All of these can sweep and trap the microbes away.

We have learnt about the physical barriers above. Next, let us get to know about the chemical barriers.

## 2) Chemical harriers

The skin and mucous membranes secrete certain chemicals which dispose the pathogen. These include:

**a) Skin secretions:** The oil and sweat secreted by sebaceous and soporiferous glands contains fatty and lactic acids, which makes the surface of the skin acidic (pH 3-5). These prevent the organisms from infecting the skin. Some friendly bacteria, which reside on the skin checks growth of microbes to a certain extent. Lysosomal enzymes of the skin have a bactericidal effect. Thus the skin becomes a self-disinfecting organ.

**b) Saliva:** Saliva contains microorganisms which are not the normal inhabitants. Dead microbes are passively flushed by the saliva and are swallowed.

**c) Gut secretions:** From the saliva and respiratory tract, bacteria reach the gut, here they are killed by the hydrochloric acid and proteolytic enzymes of the gastric juices. They are capable of killing the microbes. If they further escape and reach the large intestine, they are attacked by the gut microbes, which secrete antibiotics that kill many pathogenic bacteria. Note: Hepatitis A virus survives gastric juice.

**d) Bile:** It is an alkaline secretion of the liver, which checks the growth of foreign bacteria on the partially digested food.

**e) Tears:** Saline fluid secreted by lachrymal glands, has lysosomal activities, which prevents eye infection.

**f) Nasal secretions :** These can destroy harmful organisms due to lysosomal activities.

**g) Cerumen (wax of ear):** It traps and kills the bacteria. It contains an effective anti- bacterial component.

**h) Vaginal bacteria:** Certain bacteria normally live in the vagina. They produce

lactic acid, which kills the bacteria. Hence, these bacteria form a female's best natural defence against infections.

Skin and mucous membrane may sometimes fail to keep out the invaders. Some parasites make way through the skin e.g. hookworm. Others enter through wounds and openings of sweat glands and hair follicles. Since microorganisms may injure and pass through the thin, moist, relatively vulnerable mucous membranes of digestive, respiratory and urino-genital tracts and get into tissues or blood, it is now that the second line of defence acts for controlling further invasion. We shall learn about these internal defences next.

### 3.4.2 Internal Defence Mechanism

Body's internal defence mechanism is carried out by white blood corpuscles (WBCs), macrophages, inflammatory reactions, fever, interferons, complement system and natural killer cells, as you may recall reading earlier. All of them together check the damage caused by pathogens. The host usually recovers from such invasions. Let us learn about these internal defence mechanisms, in greater details starting with the WBCs.

### 1) The White Blood Corpuscles (Leukocytes)

The white blood cells are probably the most important part of our immune system. You may recall reading about the white blood cells in the last unit. We learnt that, whenever a germ or infection enters our body, the WBCs snap to attention and destroy the culprit. During an infection, the number of leukocytes increases. The total leukocyte count is about 4000-11000 per cubic mm of blood. Of these, 50 to 70 % are neutrophils, 20-40% are lymphocytes, 2-8% are monocytes, 1-4% eosinophils and 0-1% basophils.

WBCs creep out of the capillaries by amoeboid movement into the intercellular spaces if there is an infection. This process is called diapedesis (refer to Figure 3.2).

White blood cells are actually a whole collection of different cells that work together to destroy bacteria and viruses. You may recall studying earlier in Unit 2 that the white blood cells are primarily of two types:

**1) Granulocytes:** Their cytoplasm has granules. The nucleus is lobed and these include:

- Neutrophils: Generally three lobes, but may have 2-5 lobes
- Eosinophils: Generally bilobed
- Basophils: Generally bilobed

**2) Agranulocytes:** Their cytoplasm has no granules. These include:

- Monocytes: Nucleus — kidney shaped.
- Lymphocytes: Large nucleus.

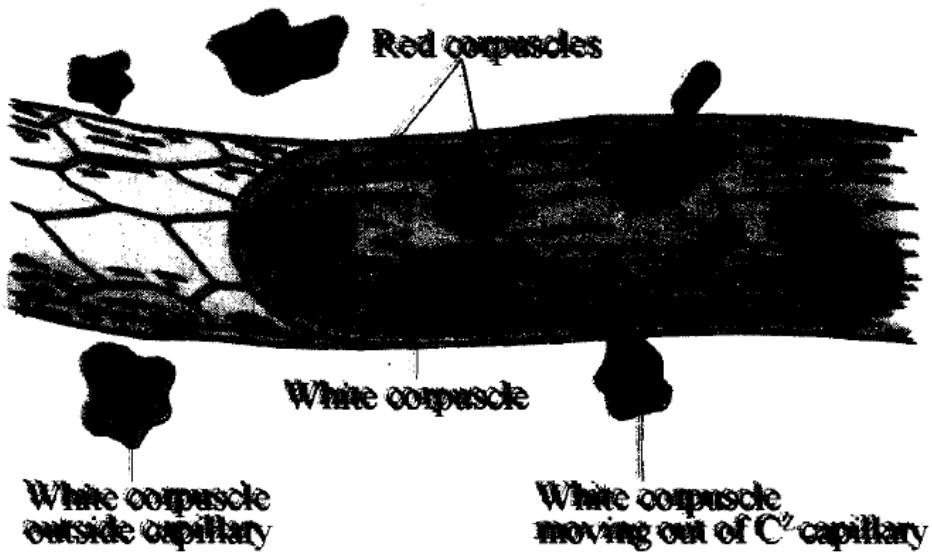



**Figure 3.2: Leukocytes moving out through capillary wall into tissue spaces (diapedesis)**

You would come across different types, names and classifications of white blood cells — Leukocytes, B-cells, Plasma cells, T-cells, Helper T-cells, Killer T-cells, Suppressor T-cells, Natural killer cells, Phagocytes, Macrophages — while studying about the immune system.

Let us briefly study about some of these different WBCs and their role as internal defence in the body. Later in this unit, in section 3.7, we shall also focus on how granulocytes are formed and what are the factors which influence granulopoiesis.

**Neutrophils:** They form about 50-70% cells. They have fine dust like particles in the cytoplasm which stain purplish. Tissues, cells damaged by the invading microbes release certain chemicals called chemokines, which attract neutrophils from blood. The neutrophils engulf and digest the microorganisms infecting the body tissues. They are called phagocytes and the process is known as phagocytosis. You may recall reading about this in Unit 2. To refresh your memory, in the phagocytosis process, the cell membrane of phagocyte invaginates and encloses a bacterium in a vacuole known as phagosome, the vacuole then fuses with lysosome to formphagolysosome. The bacteria are digested by the enzymes present in the lysosome. The doctrine of phagocytosis was advanced by a Russian physiologist, Elie Metchnikov in 1882. He got Nobel Prize for medicine and physiology in 1908. A neutrophil may engulf as many as twenty bacteria before it dies. If new entry of an organism is there, then it is trapped by another phagocytic cell known as the macrophage (big cells which can eat), about which we will learn in a little while from now.

**Basophils:** They form only 0.05% of the leukocytes. They release histamine that plays a major role in inflammatory reactions. Basophils also secrete heparin that prevents clotting of the blood in intact blood vessels. This can prevent clot setting in heart and thus prevent an attack. They help in expression of IgE (immunoglobulin

E) mediated allergies.

**Eosinophils:** They form only 1.5% of leukocytes. They defend against large parasites e.g. blood fluke. They position themselves on the surface of parasite and discharge destructive enzymes. They release histamine and inhibit mast cell degranulation, thus

**Monocytes:** They are motile and occasionally show phagocytic activity. They form only 5% of leukocytes, capable of providing more phagocytic defence. They circulate in the blood only for few hours and migrate into tissues change into macrophages. Note monocytes evolve into macrophages.

What are macrophages? Let us get to know about them.

**Macrophages:** They are large, long living effective phagocytes, which enlarge out of monocytes. It is an irregular cell about 25-50 mm in size. It has a large ovoid nucleus indented on one side. It has more mitochondria and lysosomes than a neutrophil. It engulfs more than 100 bacteria before it dies. Macrophages are of two types:

l) **Fixed types**, and

2) **Wandering types.**

The fixed types are located permanently in certain organs, which include:

Lungs - alveolar macrophages.

- Liver — kupffer cells.
- Renal glomeruli — mesangial cells.
- Brain — microglial cells
- Connective tissues histocytes.

They are also found in the spleen, lymph nodes and in the endothelium. They catch hold of the microbes and dead cells, that are carried along in the blood and lymph and are trapped in the spleen, lymph nodes etc. The wandering and fixed macrophages together form reticular endothelial system.

What are the functions of the macrophages?

The macrophages:

1) phagocytose microorganisms and inert particles

2) secrete IL-I (Interlukin 1), TNF (tumor necrosis factor), G-CSF ( granulocyte colony-stimulating factor) and M-CSF (macrophage colony-stimulating factor).

3) process and present the antigen to immuno competent cells.

4) destroy old RBC, initiates catabolism of Hb

Next, let us get to know about lymphocytes, one of the other agranulocytes. We have already studied about the other agranulocyte, i.e. the monocytes above.

Lymphocytes: They are agranulocytes. The nucleus occupies almost the entire cell, as you may recall seeing in Figure 2.25 in Unit 2. They vary in size from 6-18 mm diameter; sometimes divide into small and large lymphocytes. Lymphocytes make up 30% to 40% of all leukocytes. Lymphocytes come in two classes: B cells (those that mature in bone marrow) and T-cells (those that mature

in the thymus). Let us get to know them. B-cells, when stimulated, mature into plasma cells. These are the cells that produce antibodies. A specific B cell is tuned to a specific germ, and when the germ is Vesent in the body, the B-cell clones itself and produces millions of antibodies designed to eliminate the germ. T-cells, on the other hand, actually bump up against cells and kill them. T-cells known as Killer T-cells can detect cells in our body that are harboring viruses, and when it detects such a cell, it kills it. Two other types of T-cells, known as Helper and Suppressor T-cells, help sensitize killer T-cells and control the immune response.

What are the functions of lymphocytes? The lymphocytes handle most of the bacterial and viral infection that we get. In fact, lymphocytes are directly involved with specific acquired immunity. T-Lymphocytes for cell mediated and B-Lymphocytes for humoral immunity. We shall learn about these immunities later in sections 3.5 and 3.6.

With this, we come to an end of our discussion on white blood cells, one of the internal defence mechanisms of the body. Next, we shall study about the inflammatory responses, which you already know is yet another internal defence mechanism.

## 2) Inflammatory responses

Injury, cut, burn or bite (of an animal) brings foreign matter (bacteria, virus, and fungal spores) to enter the tissue. Certain substances released by damaged cells initiate formation of blood clot. Clotting checks the flow of blood.

From the immune system's standpoint, inflammation is a good thing. It brings in more blood and it dilates capillary walls so that more immune system cells can get to the site of infection. This is how it works. The invading microbes release their own toxic products. The mast cells and basophils release histamine, as you have already learnt earlier. Chemicals from microbes and histamine together cause dilation of capillaries and small blood vessels surrounding the injury and increase the permeability of the capillary wall. As a result, more blood flows to that area, making it red and warm, and fluid leaks out into tissue spaces, causing its swelling. This reaction of the body is called inflammatory response and is a part of internal defence. The events in the inflammatory reaction are illustrated in Figure 3.3.

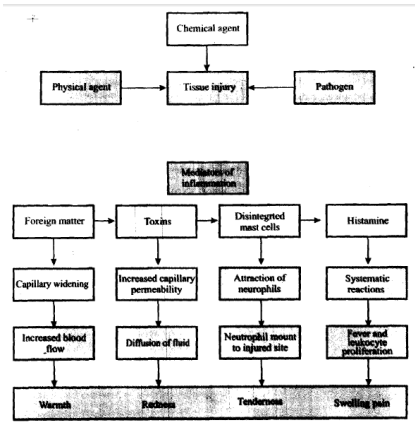



**Figure 3.3: Events in the inflammatory reaction**

The plasma that accumulates at the injured site dilutes the toxins secreted by bacteria and lessens their effect. Its fibrin forms a network which occludes the lymphatic channels, thus limits the spread of microorganisms. So now you can understand why the inflammatory response is so important.

The neutrophils are attracted to the site of injury or infection by chemicals, by injured cells elaborated by bacteria and histamine. Here they adhere to the lining of capillaries and push between its cells into the tissue spaces. Once the neutrophils reach the site, they move and eat up the microorganisms. By this time, the macrophages of the connective tissue begin their protective action. Monocytes also reach the site of the infection and develop into large macrophages for additional phagocytosis. They would further clean up the tissue and remains of neutrophils. Certain substances in the plasma strongly stimulate phagocytosis, they are called opsonins, which in a way make the bacteria 'tastier' to the phagocytes.

The other internal defence mechanism operational in our bodies is pus formation. Let us read about its role in the body, next.

## 3) Pus formation

Once a neutrophil finds a foreign particle or a bacterium, it will engulf it releasing enzymes, hydrogen peroxide and other chemicals from its granules to kill the bacteria. In a site of serious infection (where lots of bacteria have reproduced in the area), pus will form. Pus is simply dead neutrophils and other cellular debris. Many neutrophils and macrophages are killed by toxins released by highly virulent invaders. The dead phagocytes, microbes are trapped by still bigger phagocytes and they form a protective barrier. Dead phagocytes, enzymes, fluid, protein, damaged tissue cells etc. leak from capillaries and leave the body in the form of pus. This is a sure sign of infection.

Like pus, fever too is a defence mechanism. Let us find out how.

## 4) Fever

We have seen that due to injury, cut or bite, the inflammatory response develop and this is localized or systemic. The localized response is confined to the site of injury only. The systemic response affects the body in case of a severe infection or a serious injury. In this case, the WBC count increases. Body temperature rises causing fever. This may be brought about by toxins produced by pathogens and by a protein called endogenous pyrogen. When enough pyrogen reaches the brain, the body's thermostat is reset to higher temperature allowing the entire body temperature to rise.

Other components like interferons, complement system are discussed next.

## 5) Complement system

The complement system is a series of proteins. There are only a handful of proteins in the complement system and they are floating freely in our blood. The complement proteins are activated by and work with (complement) the antibodies, hence the name. They cause lysing (bursting) of cells and signal to phagocytes that

a cell needs to be removed.

### 6) Interferon

Interferon interferes with viruses (hence the name) and is produced by most cells in the body. Interferons, like antibodies and complements, are proteins, and their job is to let cells signal to one another. When a cell detects interferon from other cells, it produces proteins that help prevent viral replication in the cell.

The discussion so far focused on the non-specific defence mechanisms, which included the external and internal mechanisms. We shall next, study about the specific defence mechanisms.

NOTES

## 3.5 SPECIFIC DEFENCE MECHANISM

In the section on white blood cells, we learnt that whenever a germ or infection enters our body, the WBCs snap to attention and destroy the culprit. How does a white blood cell know what to attack and what to leave alone? Why doesn't a white blood cell attack every cell in the body? The answer to these questions lies in the discussion below.

The specific defence mechanism provides protection against specific foreign materials. The important characteristic is that its cells (lymphocytes) have an ability to recognize body's own cells and macro molecules (self) from those which are foreign invaders (non self It tolerates the 'self' but destroys the 'non self'. The lymphocytes bearing receptors specific for self i.e. molecules already present in the body, are either made non-functional or destroyed by programmed cell-death known as apoptosis. The lymphocytes that react to non self i.e. foreign molecules are left to function in immune responses.

So, you realize that there is a system built into all of the cells in our body that marks the cells in our body as "self'. Anything that the immune system finds that does not have these markings (or that has the wrong markings) is definitely "not self" and is therefore a fair game. This system is called the Major Histocompatibility Complex (MHC). Let us learn about this specific mechanism next.

### 3.5.1 Major Histocompatability Complex (MHC)

Major histocompatability complex is also known as the Human Leukocyte Antigen (HLA). MHC molecules are important components of the immune response. They allow cells that have been invaded by an infectious organism to be detected by the cells of the immune system called T-lymphocytes or T-cells. The MHC molecules do this by presenting fragments of proteins (peptides) belonging to the invader on the surface of the cell. The T-cell recognizes the foreign peptide attached to the MHC molecule and binds to it, an action that stimulates the T-cell to either destroy or cure the infected cell.

The 'MHC, therefore, is a set of genes that code for cell surface glycoproteins.

These glycoproteins mark the body cells as 'self' and are divided into two main classes — class I MHC molecules are found on the surface of almost every cell of the body. Class II MHC molecules are confined to a few specialized cell types, such as macrophages, B-cells and activated T-cells. Each MHC antigen combination forms a unique complex that is recognized by specific antigen receptors on T-cells as 'self'.

T-cell surface proteins CD4 and CD8 greatly enhance the interaction between an antigen presenting cell (APC) and killer T-cell and between APC and helper T-cell, respectively. The primary immunological function of MHC molecules, therefore, is to bind and antigenic peptides on the surfaces of cells for recognition (binding) by the antigen- specific T-cell receptors (TCRs) of lymphocytes.

The other specific defence mechanism in our body is the antibodies. Let us learn about their role in the immune system and their interaction with antigens.

## 3.5.2 Antibodies

Antibodies (also referred to as immunoglobulins and gammaglobulins) are produced by plasma cells. They are Y-shaped proteins (as illustrated in Figure 3.4) that each respond to a specific antigen. What is an antigen? The foreign matter (bacteria, virus or toxin) that enters the body and elicits a specific immune response by lymphocytes is called an antigen or immunogen. It stimulates the immune system to produce protective chemicals or special cells to destroy the antigens. These protective chemicals are called antibodies.

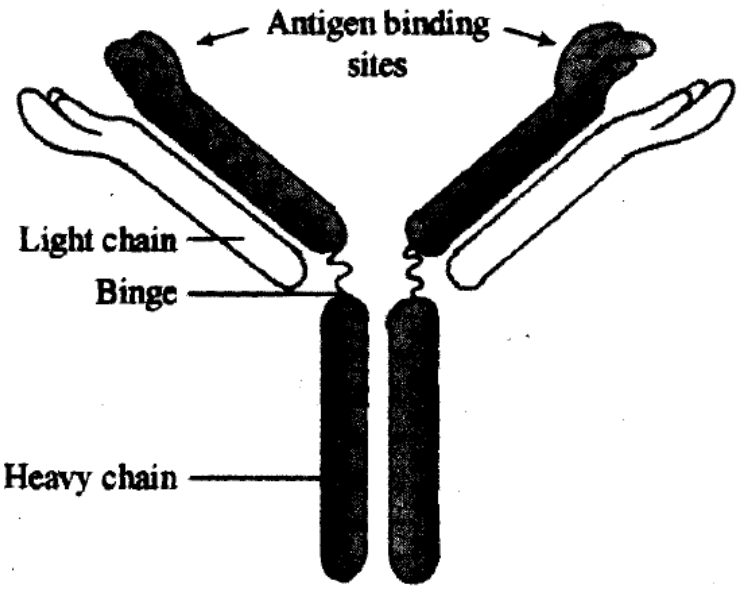



**Figure 3.4: Structure of antibody molecule**

The molecule of antibody has 2 pairs of peptide chains linked by disulphide bonds. The 2 longer chains are called as heavy chains and the 2 shorter chains are called light chains as shown in Figure 3.4. The 2 long and short chains are identical. The antigen (Ag) binding site is at the N-terminal end of the polypeptide chain. The site of complement fixation is towards C-terminal. The difference in structure

forms the basis of the antigen specificity of each antibody. The structure of the N-terminal varies from one antibody to another. Whereas long part of the peptide chain towards the C-terminal end are relatively constant. Within the variable region of the molecule, there are some selected amino acid sequences which are more variable than the rest, these are known as hyper variable regions. Splitting of the molecule is done by proteolytic enzyme.

The antigen entering the body may be molecules on the surface of viruses, bacteria, fungi, protozoan or worms. The protein molecule present on the surface of the foreign material act as antigens, but some carbohydrates and lipids also can act as antigens. Each antigen causes formation of a specific antibody. Antigens (Ag) and antibodies (Ab) have complementary reactive sites that fit together in a lock-and-key fashion, forming an antigen-antibody complex as shown in Figure 3.5.

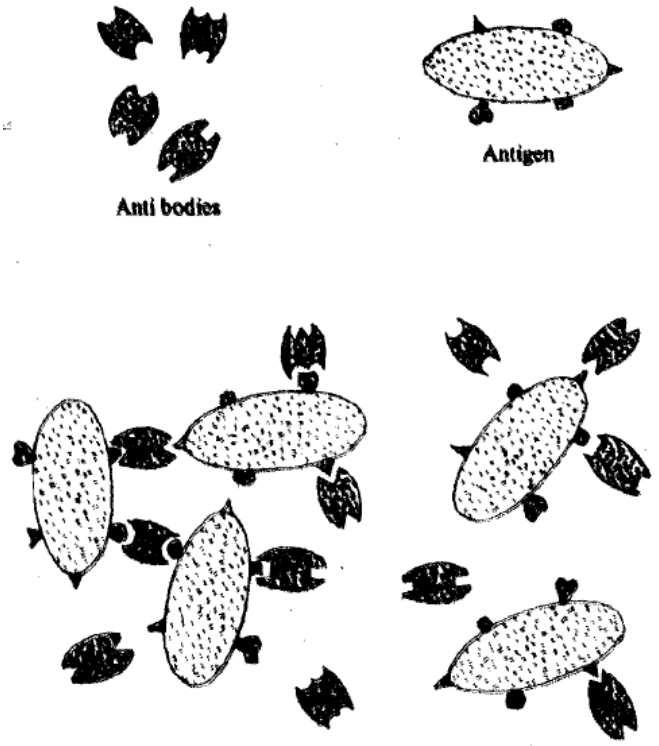



**Table 3.5 : Antigen-Antibody reaction**

Antibodies react with antigens and make them inactive or harmless. The differences between antigens and antibodies are highlighted in Table 3.3.

| Antigens (immunogens) | Antibodies (immunoglobulins) |
|---|---|
| 1. It is a foreign material, elicits antibody formation. | 1. It is a molecule synthesized by the organism to combat foreign material. |
| 2. It is a protein or polysaccharide molecule. | 2. Each antibody is a immunoglobulin |
| 3. It may occur on the surface of a microbe or as a free molecule. | 3. It occurs on the surface of a plasma cell and also in the body fluids. |

| | |
|---|---|
| 4. It binds to macrophages to reach a helper T cell to initiate immune response. | 4. It directly joins an antigen to destroy the latter. |

**NOTES**

**Table 3.3 : Differences between antigens and antibodies**

Other than bacteria, virus, the other antigens which enter the body include pollen, egg white, feathers, some fruits, vegetables, chicken, blood cells from other persons, transplanted tissues, organs, certain medicines, toxins such as snake poison.

Antibodies, on the other hand, are classified in five classes. These are:

- **Immunoglobulin A (IgA):** present in secretions, protects mucosal surfaces. It is found in tears, saliva, gastrointestinal secretion, respiratory and genitourinary tract. Secreted in combination with peptide — forms secretory piece is protected from proteolytic digestion.
- **Immunoglobulin D (IgD):** present on surface of B lymphocytes, along with IgM plays a role in Ag recognition.
- **Immunoglobulin E (IgE):** protects against organisms which escaped IgA, major deference against helminthes, mediates allergy. On coming in contact with specific Ag, it releases mast cell granules. These granules contain a chemical which leads to an inflammatory reaction and also chemotactic migration of granulocytes.
- **Immunoglobulin G (IgG):** major defence against bacteria and their toxins. It is the major Ig — 80% in the body, can cross the capillary wall very easily. It can cross placenta, secreted into milk, thus transfers immunity from mother to child.
- **Immunoglobulin M (IgM):** protects against bacteria, gives an early immune response, present on surface of lymphocytes. It stays confined to blood stream and is involved in Ag recognition.

The antigen-antibody reaction, about which you have studied above, is also useful in detecting infections. We will look at this aspect later in the unit.

In the sections above we have studied about the non-specific and the specific defence mechanisms in our body. It must be clear to you by now that our body is equipped with multiple defence mechanisms. These are generally known as immune mechanisms. Immunity, you would realize, is of 2 types — innate and acquired. In the next two sections, we shall get to know about the innate and acquired immunity.

## 3.6 INNATE IMMUNITY

The term 'innate immunity' refers to the basic resistance to disease that a species possesses the first line of defence against infection. In fact, innate immunity refers to antigen non-specific defence mechanisms that a host uses immediately or within several hours after exposure to almost any antigen. This is the immunity one is born with and is the initial response by the body to eliminate microbes and prevent infection.

In our discussion above we have seen that the best way to avoid pathogens/ infections is to create a barrier. This is a very sensible, desirable and effective way to protect the body from many infections. They are physical and chemical barriers, about which we learnt earlier. E.g. the skin is an impermeable covering. Here fatty acids and low pH sebaceous secretions prevent bacterial growth. On the other hand, the surface which cannot be covered by skin will have special barriers. E.g. eyes with tears, mouth with saliva, stomach with acids, air passage with mucous and cilia.

Potential pathogens are encountered routinely, but only rarely cause disease. The vast majority of microorganisms are destroyed within minutes or hours by innate defences. The acquired specific immune response comes into play only if these innate defences are breached. The efficacy of innate immunity improves in us after the pathogen enters in us and then we develop resistance. Unlike innate immunity, acquired immunity develops as a result of exposure to a pathogen which is very specific.

The characteristics of the innate immune response, therefore, include the following:

- Responses are broad-spectrum (non-specific)
- There is no memory or lasting protective immunity
- There is a limited repertoire (stock) of recognition molecules
- The responses are phylogenetically ancient

Pathogens have involved on earth before our studies on defence mechanism. The best way to drive them away is to have a need based defence mechanism and the system be activated by the invader itself. This can be achieved by initiating phagocytotic process.

In fact, the innate immune responses involve:

- phagocytic cells (neutrophils, monocytes and macrophages),
- cells that release inflammatory mediators (basophils, mast cells and eosinophils),
- natural killer cells (NK cells), and
- molecules such as complement proteins, acute phase proteins and cytokines.

Let us get to know about these innate responses next.

## 3.6.1 Phagocytosis

Phagocytosis involves the ingestion of particulate material including whole pathogenic microorganisms. The plasma membrane expands around the particulate material to form large vesicles called phagosomes. It is carried out either by neutrophils or macrophages. Neutrophils are highly effective against pus forming (pyogenic) bacteria. We already know that macrophages are tissue phagocytes and are derived from circulating monocytes. These monocytes and macrophages together contribute to the phagocytic system (reticulo endothelial system). Macrophages are most effective against those microorganisms which live within the cells.

## What is the mechanism of phagocytosis?

Figure 2.7 in Unit 2 illustrates phagocytosis. In phagocytosis, the organism is entrapped into vacuoles known as "Phagosome". The cytoplasmic granules, organelles or lysosomes fuse with the phagosome releasing powerful microbicidal substance. These substances are divided into:

a) those which are dependent on O2 mechanism, and

b) those which are O2 independent mechanisms

Example for O2 dependent mechanism is superoxide anion, singlet 02 hydroxyl free radicals. The 02 independent ones are lysosomes, proteolytic enzymes and several other hydrolytic enzymes.

The next innate response includes the complement system.

### 3.6.2 The Complement System

To remove a microorganism by phagocytosis requires phagocytes at the right place in the right time. The organism should adhere to the phagocyte. Many of these organisms may not be viable to this type of a situation. To deal with such a situation, therefore, one more non-specific defence mechanism is found in plasma. This is known as the complement system. You may recall reading about this earlier in section 3.3. Complement system contains about 20 proteins, when triggered can enter into cascade reaction (occurs one after the other sequentially, with a number of factors). The system helps to handle microbial invasion basically by 3 mechanisms.

### The Immune

1) Some components of a complement system coat microorganisms These organisms with such a coat can be easily phagocytosed because of the receptors, which are similar for the same complement components which coat the microorganisms.
2) Some component of the system stimulates the lethal mechanisms of phagocytes released earlier. They also release histamine and several other useful substances from mast cells and basophil granules. The major effects of granule release are vasodilatation and chemotactic migration of neutrophils and eosinophils to the site of infection.
3) The complement pathway leads to the formation of membrane attack complex which stabs a hole into the microbial cell wall which would lead to the entry of water and Na+ ions into microbial cells leading to its lysis.

### 3.6.3 Humoral Mechanisms

Besides the complement system, there are some other humoral mechanisms which help in innate immunity. These include:

**1) Acute phase proteins:** Following any infection, there is a rise in concentration of several plasma proteins. The best known amongst them are C— reactive proteins (CRP) which adheres to the surface of a number of microorganisms.

These CRP coated organisms can activate complement system. This, in turn, facilitates phagocytosis.

2) **Interferons:** Interferons are soluble proteins secreted naturally when cells become infected by foreign bodies. Infected lymphocytes release interferons alpha which is one out of the 14 sub types known. Other cell types when infected by some viruses release interferon beta. These interferons are released into extra cellular fluids, where they diffuse to form a protective ring of uninfectable cells, thereby limiting the spread of infection.

Besides this, they inhibit protein synthesis by interfering with the process of translation and promote degradation of mRNA.

Since viruses depend partly on nucleic acids of the host for protein synthesis, interferons have a marked inhibitory effect on the replication of viruses.

3) **Natural killer cells (NK cells):** They are large sized lymphocytes, specifically equipped to kill virally infected cells, some of the virally infected cells acquire a special glycoprotein on their surface which signals their neighbouring cells that they are in trouble and they need help.

The NK cells are especially receptive to this cry for help because they have surface proteins which are very similar to the ones which have glycoprotein coatings. When the 2 components come together in contact, the NK cells would release lethal substances which lead to the death of infected cell. The infected cell is killed and it has a chance to multiply. The major drawback of this process is that the host cell gets sacrificed.

4) **Contribution of eosinophils:** They are specifically equipped to deal with a lot of parasites (all helminth worms). The coating of helminthes and some complement components facilitates its adherence to the eosinophils. This releases several lethal particles from the eosinophil granules, which causes death.

Having studied about the innate immune response, we move on to specific acquired immunity.

## 3.7 SPECIFIC ACQUIRED IMMUNITY

Body in the long run develops specific immune mechanisms for each species. These mechanisms are not innate but are acquired after exposure to the specific organism. Acquired (adaptive) immunity, therefore, refers to antigen-specific defence mechanisms that take several days to become protective and are designed to react with and remove a specific antigen. This is the immunity one develops throughout life.

Adaptive immunity usually improves upon repeated exposure to a given infection and involves:

- antigen-presenting cells (APCs) such as macrophages
- the activation and proliferation of antigen-specific B-lymphocytes
- the activation and proliferation of antigen-specific T-lymphocytes, and

- the production of antibody molecules, cytotoxic T-lymphocytes (CTLs) and cytokines.

The human body can respond to antigens in many different ways. These fall into two major categories:

- **Antibody Mediated Immune System (AMIS) -** by circulating antibodies (Ab), also known as humoral immunity, about which you have learnt above, and
- **Cell Mediated Immune System (CMIS) -** by sensitized cells known as cell mediated immunity.

Both the systems need antigens to come into action and they respond in different ways. The B-cells and T-cells of the lymphocytes recognize the specific antigens by means of antigen receptors bound to their plasma membrane. Ag-receptors on a B-cell are simply antibody molecules that move from the cytoplasm onto the plasma membrane. These are called membrane antibodies. The T-cell receptors are structurally related to membrane antibodies.

## What is the scene of action?

Primary lymphoid organs, as you already know, are thymus and bone marrow. Secondary organs are lymph nodes, spleen and lymphoid tissue. When an Ag microorganisms enter the body, one of the secondary lymphoid organs traps it and mounts an immune response. An exact organ involved depends at the site of entry. Let us then get to know what are the sites of entry.

Sites of entry

- Tissue — traps in draining lymph node
- Blood stream — trapped in spleen
- Mucosal surface reponses in mucosal associated lymphoid tissue.

Irrespective of the above mentioned situation, the agent is trapped by phagocytic cells which degrade it, coat their surface with some chemical fragment derived from the agent. These fragments help in recognizing the phagocyte by immuno competent cells which finally leads to the production of effectors. Effectors in humoral immunity are specific Ab. In CMI, the effectors are lymphokinesis and cytotoxic lymphocytes.

Let us now get to know how the two acquired immunity system works. We start with AMTS.

## 3.7.1 Antibody Mediated Immune System (AMIS)

In antibody-mediated immunity, the antibodies dissolved in blood, lymph and other body fluids bind the antigen and trigger a response to it. AM IS, therefore, involves the production of antibody molecules in response to an antigen and is mediated by B-lymphocytes. This form of immunity is also called humoral immunity, as you may recall reading above.

## What is the specific role of AMIS?

The AMIS defends the body against free viruses, bacteria with polysaccharide capsules and toxins that enter the body fluids (blood and lymph).

## How are the antibodies formed?

NOTES

The process of antibody formation is illustrated in Figure 3.6. When membrane antibodies on B-cells surface bind antigens, the B-cell is activated and divides producing a clone of daughter B-cells. The daughter B-cells are of two types — Plasma B-cells and Memory B-cells.

Plasma B-cells are antibody factories. They secrete antibodies on stimulation of T- helper cells. The antibodies pass into and circulate in the lymph to dispose of the antigens. Each person makes about 107- 108 different kinds of Ab molecules so that there is an Ab on a B cell to fit any antigen. Thus, there are numerous antigen specific-B lymphocytes in the body. The plasma membrane of each B-cell should be sensitized by contact with a specific antigen for the release of antibodies. The plasma cells do not migrate to the site of infection and act through lymph. Hence, they are said to form humoral system (fluid mediated). The B-cells are short lived and are replaced every few days from bone marrow.

Memory B-cells live for a long time and serve to quickly dispose off the antigens, in case reinfection of the same virus or bacterium occurs.

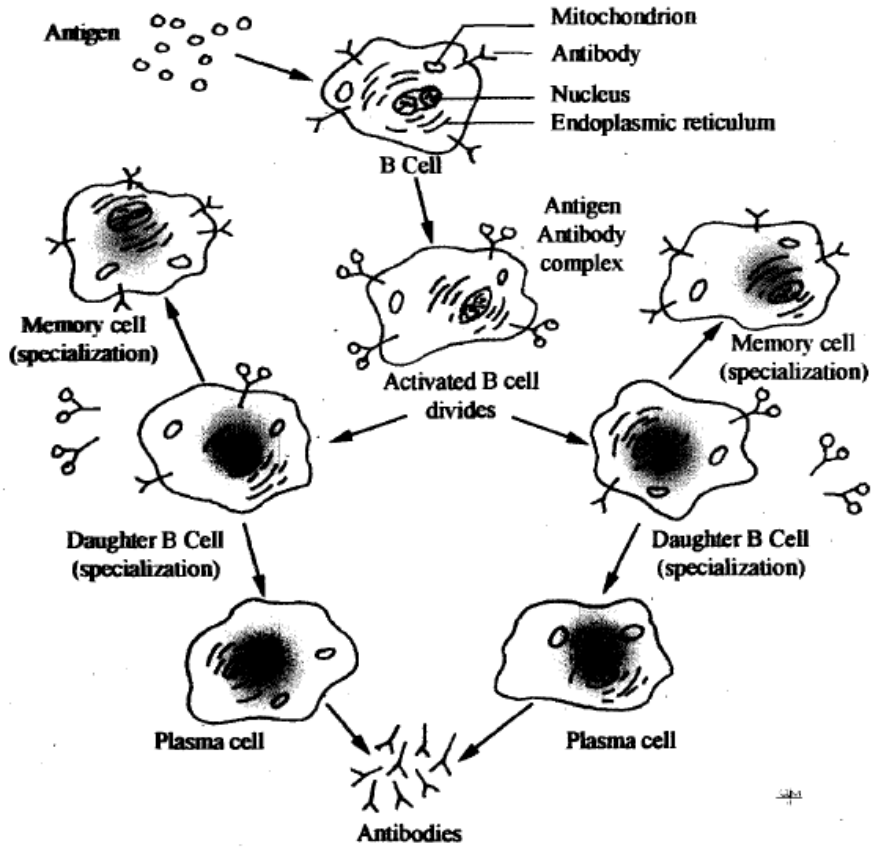



**Figure 3.6: Formation of plasma cells and memory cells from B-cells**

## How do antibodies act?

The antibodies bind to their specific antigens and inactivate the invading microorganisms or foreign molecules, so that these are conveniently disposed off by the phagocytes.

## How are the antigens disposed?

We have seen earlier that there are 5 types of antibodies — IgG, IgA, IgM, lgD, and lgE.

They fight the antigens in 5 different ways. These include:

**a) Neutralization:** Since antibodies neutralize the antigens (viral or bacterial toxins), make them ineffective, they are called as antitoxins. The phagocytes dispose off the antigen - antibody complexes.

**b) Agglutination:** Certain antibodies cause the particulate antigens (bacteria, red corpuscles) to stick together in clumps, thus immobilizing them for easy disposal by the phagocytes through ingestion. They are termed as agglutinins.

**c) Precipitation:** Other antibodies combine with the antigens to form precipitates that are easily ingested by phagocytes. They are known as precipitins.

**d) Opsonization:** Some antibodies coat the surface of the microbes and make them more susceptible to phagocytosis, such antibodies are known as opsonins.

**e) Complement activation:** Antibody-antigen complex activates complement proteins,

which may :

i) lyse walls of bacteria, causing their disintegration,

ii) initiate inflammatory response,

iii) ospomise antigens, and

iv) attract phagocytes to areas of infection.

Next, let us learn about the second arm of the immune response, referred to as cell mediated immune system.

## 3.7.2 Cell Mediated Immune System (CMIS)

Cell-mediated immunity is an immune response that does not involve antibodies, but rather involves the production of T-lymphocytes, activated macrophages, activated NK cells and cytokines in response to an antigen and is mediated by T-lymphocytes. Thus in CMIS, T-cells (lymphocytes) bind to the surface of other cells that display the antigen and trigger a response.

## What is the specific role of CMIS?

The CMIS defends the body against viruses and bacteria, which have entered the host cells, and also against protozoan, fungi and parasitic worms. Its defensive cells cannot deal with free antigens present in body fluids. It reacts with foreign tissue transplants and also against body's own cells which become cancerous. The

cancer cells are perceived as foreign cells.

Cellular Immunity, therefore, protects the body by:

1) activating antigen-specific cytotoxic T-lymphocytes (CTLs) that are able to lyse bodv cells displaying epitopes (sites on the surface of the antigen molecule to which a sir gle antibody molecule binds) of foreign anti gen on their surface, such as virus- infected cells, cells with intracellular bacteria, and cancer cells displaying tumor antigens
2) activating macrophages and NK-cells, enabling them to destroy intracellular path ogens, and
3) stimulating cells to secrete a variety of cytokines that influence the function of other cells involved in adaptive immune responses and innate immune responses.

## What is the mode of action?

The cellular immune response is given by T-cells, unlike the B-cells in AMIS. There are separate T-cells for each type of antigen that invades the body. T-cells have a life span of 4-5 years or even longer. They acquire the ability to recognize particular 'non self' cell surfaces and molecules in thymus.

On stimulation by contact with antigens, the T-lymphocytes produce a clone of T-cells by division -the lymphoblasts. The T-cells comprising the clone are committed T-cells having specific functions. They are of four types. They are morphologically similar but functionally different. These include:

a) Cytotoxic or killer T-cells (Tc)

b) Helper T-cells (Th)

c) Suppressor T-cells (Ts)

d) Memory T-cells (Tm)

Let us get to know them.

**a) Killer T-cells:** They migrate to the site of infection. They have a surface peptide that acts as receptors for foreign antigens. When a T-cell encounters 'non self" cell, its surface receptors draw the two cells into a physical contact. Killer T-cells secrete a protein called perform, which can puncture invader cell membrane. Take a look at Figure 3.7, here you can see how water and ions flow into the non- self cell, which swells up and finally lyses the infected cell. Death of infected cell helps the host in two ways: it deprives the pathogen of a place to multiply and expose the pathogen to circulating antibodies for disposal. Killer cell further proceeds to kill another non-self cell. Killer T-cells are guided by their receptors to the body cells covered with viruses. They destroy the body cells before the viruses can enter and multiply to spread infection. They can also destroy cancer cells. Since the killer cells must be present on the spot to play their role, they are said to form cell mediated immune system.

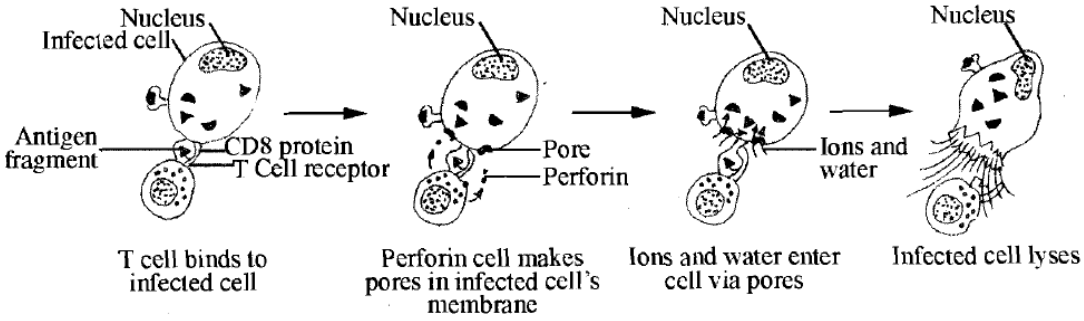



**Figure 3.7: Function of killer T-cells**

**b) Helper T-cells(Th):** These cells stimulate the B-cells to produce antibodies. They stimulate killer T-cells to destroy the non-self cells. Refer to Figure 3.8 for understanding the interaction of Helper T-cells with an infected cell (A) and macrophage (B).

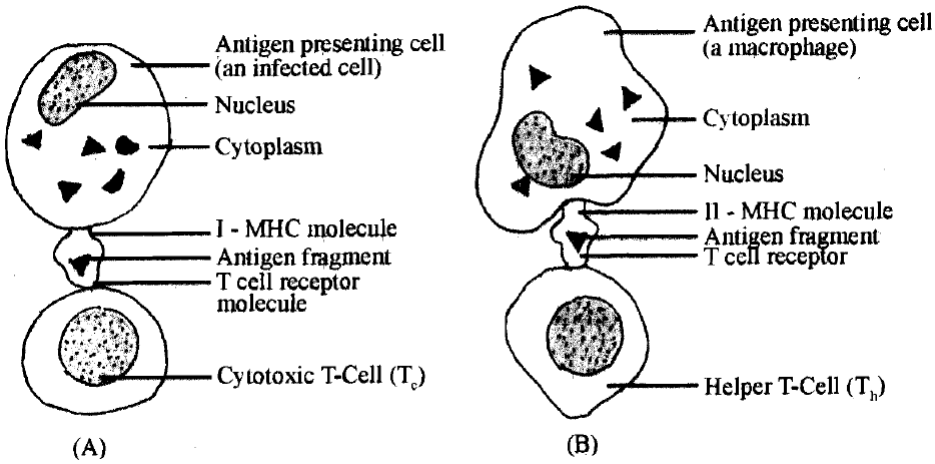



**Figure 3.8: Interaction of T-Cells with MI-IC molecules on an infected cell (A) and on a macrophage (B)**

**c) Suppressor T-cells (Ts):** These ceils inhibit the immune response of both T and B lymphocytes to foreign antigens when infections are controlled. They also inhibit the immune system from attacking the body's own cells.

**d) Memory T-cells:** These cells keep ready to mount a rapid and vigorous attack as soon as the same pathogens infect the body again.

In the discussion above, you may have realized that the helper T-cells (Th) and the suppressor T-cells (Ts) have a dual role to play. This role is highlighted next.

## Dual role of Th and Ts cells

The killer cells are the effector cells of the CMIS, whereas helper T- cells and suppressor T-cells are the regulatory cells of both AMIS and CMIS. Both Th and Ts cells secrete a protein known as interleukin-2, which stimulates proliferation of activated B-cells and T-cells.

The discussion above would have helped you to understand the innate and adaptive

immune response in our body. While talking about the immune mechanisms, we must re-emphasize the role of macrophages in the immune system. You may recall reading about the functions of macrophages earlier in section 3.3. Here we will focus on their role in the immune system, per se.

## Role of macrophages in immune system

Macrophages, you already know, are white blood cells that continually search for foreign (non-self ) antigenic molecules, viruses, or microbes. When found, the macrophages engulf and destroy them as shown in the Figure 3.9.

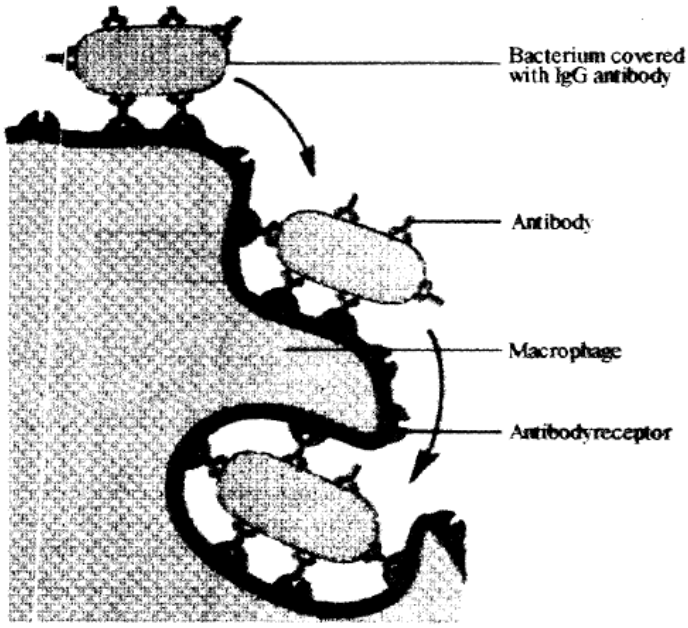



**Figure 3.9: Action of macrophages on foreign bodies**

The process involved includes:

1) Macrophages respond to infection.
2) They engulf microbes and display the antigen to alert the lymphocytes.
3) The antigen is held onto the surface of macrophage by a protein which marks the macrophage as 'self' (as own part).
4) With the antigen nagged on it, macrophage moves to nearest lymph node, meets various types of lymphocytes.
5) A helper T-cell recognizes the macrophages antigen flag and joins it. This initiates immune reaction.
6) Simultaneously macrophages secrete endogenous pyrogen, which:

a) activates T and B cells to grow and proliferate

b) causes fever, microbial action slows down.

All these steps are indicated in the flow chart given in Figure 3.10.

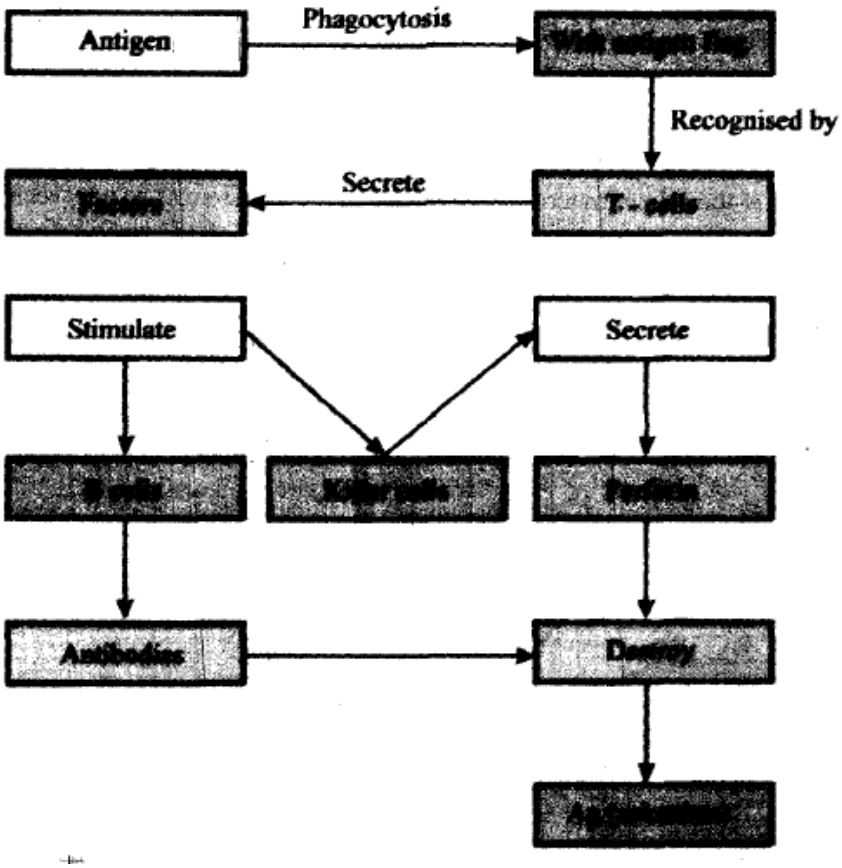



**Figure 3.10: Role of macrophages in immune system**

From the discussion above, it is clear that the macrophages, B-cells and T-cells interact to produce immune responses. What is the outcome?

- Infection disappears due to Ag-Ab interaction along with killer T-cells and non-self cells interaction.
- Some of the specific lymphocytes remain in the lymphatic tissue as "memory or primed cell". They produce killer cells if the same antigens reappear. Hence, a second attack of infections and disease elicits quick, abundant antibody formation.

Memory cells give rise to more effector cells and memory cells (effector cells have only a few days life-span). the memory cells live long, some even for whole life. Hence diseases which attack in childhood, do not attack again. Memory cells are stored in the spleen and lymph nodes.

## 3.8 THE LEUKOCYTES: DEVELOPMENT AND REGULATION

Since leukocytes play such a major role in the immune system, it is important that we learn about the development and regulation of leukocytes in our body.

In sub-section 3.3.2, we learnt that leukocytes or WBCs are classified as granulocytes and agranulocytes. Let us get to know how the granulocytes develop.

## 3.8.1 Development of Granulocytes

Granulocytes are formed in the bone marrow from the totipotent haemopoietic stem cell (myeloid series) (blood forming stem cells in the bone marrow). Following are the stages of granulocyte development:

1) **Myeloblast:** The first identifiable cell of the granulocyte series is the myeloblast. It has a large nucleus, 2-5 nucleoli, no granules in cytoplasm, capable of cell division and has poor motility.
2) **Promycelocyte:** Division and maturation of myeloblast yields promyelocyte (myelocyte A). This stage has primary granules in cytoplasm.
3) **Myelocytes (myelocyte B):** After promyelocyte division and maturation, the next stage is the myelocyte. In this stage, the nucleus is flattened on one side; primary and secondary granules in the cytoplasm are seen.
4) **Metamyelocyte (myelocyte C):** Metamyelocytes no longer divide or produce granules (capacity for mitosis is lost). Myelocytes are the last cells to undergo cell division. In this stage, the nucleus changes shape from round/oval to indented and nucleoli is absent. More secondary granules seen in the cytoplasm and fewer primary granules seen in the cytoplasm. Amoebid movements appear.
5) **Band cell (juvenile granulocyte):** Band cells are later stages of metamyelocyte. By this stage, the nucleus is deeply indented (sausage shaped) so that it resembles a hair band. The cytoplasm is filled with specific granules.
6) **Mature granulocyte:** Completely developed cells with a lobed nucleus. Neutrophils are abundant among granulocytes. Granulopoiesis, therefore, generally refers to the formation of neutrophils. Now that we know how the granulocytes are formed, let us briefly look at the factors which influence granulopoiesis.

A detailed discussion on these growth factors is present in sub-section 3.7.2. You will find this information a bit technical and advance. Do not panic. This is additional information for those of you who would like to know more on this topic. You will not be tested for this knowledge in the term end examination.

## 3.8.2 Growth Factors which Affect Granulopoiesis

The factors which influence granulopoiesis include:

1) **Interleukin-1:** Interleukin is a cytokine found in WBCs that stimulates to light infections. The structure of human IL-I is illustrated in Figure 3.12, Interleukin is a protein factor which is produced by T lymphocytes and macrophages (a type of white blood cell) in the presence of antigens. They cause the T lymphocytes to activate and proliferate . Interleukin acts on relatively early progenitor cells to stimulate their proliferation. It also enhances the effectors function of all types of leukocytes. Since macrophages are activated more during an injury, ILL seems to act as a general signal for intercellular dialogue which speaks in

NOTES

a language, which a wide variety of cells can understand.

**Figure 3.11: Structure of human Interleukin**

The cells that respond to IL-I produce growth factors which are specific in their action. It also directly releases mature neutrophils from bone narrow and stimulates cytotoxic effects of macrophages themselves.

2) **Tumour Necrosis Factor (TNF):** The name itself is because of its inhibitory effect on some of the tumors cells. It is produced by macrophages and its effects are known to be similar to that of IL-I. IL-I and TNF stimulate granulopoietic activity by involving a pathway through granulocyte macrophages colony stimulating factors (GM-CSF).

3) **Granulocyte macrophage colony stimulating factor (GM-CSF):** Stem cells obtained from the bone marrow are capable of giving rise to countable colonies of daughter ceils in spleen. The growth factors were identified on the basis of their ability for colonial proliferation. Thus the name was assigned.

GM-CSF stimulates the proliferation of committed cells to form granulocyte and macrophages. It also stimulates proliferation for precursors of eosinophils, megakaryocytes and erythrocytes. In addition, it acts on the mature neutrophils, eosinophils, macrophages to enhance their effector responses.

4) **Interleukin — 3 (IL — 3) or Multi CSF :** It is produced by T-lymphocytek and stimulates proliferation of precursors for neutrophils, eosinophils, basophils, and mast cells,

In addition, it also stimulates effectors responses of mature eosinophils and T-lymphocytes. It can activate many cells other than IL-I.

5) **Gametocyte colony stimulating factor ( G-CSF ):** It is produced by monocytes, fibroblasts and endothelial cells due to the stimulation of IL-I. It stimulates proliferation of processors which are very specific — granulocytes. It also enhances effector response of these cells. Further, it can specifically stimulate:

- neutrophil proliferation

- their phagocyoticability
- produces cytototic free radicals such as the super oxide components, thus activates the immune system.

6) **Macrophages — CSF (M-CSF):** It is produced by macrophages, fibroblasts and endothelial cells. They specifically stimulate precursors of macrophages. It also enhances effector response of mature macrophages.

7) **Inhibitory Factors:** Haemopoiesis may be inhibited by a decrease in the level of stimulatory growth factors. Generally there is a competition. No particular substance can actively inhibit this process. But now it is. known that tissue specific locally produced inhibitor of cell proliferation are chalones. A granulocytic chalone is produced by mature / immature granulocyte. It inhibits DNA synthesis granulocyte precursor cells, thereby, decreasing the number of mitosis and cell differentiation. They have specific factor to inhibit haemopoesis wherein neutrophil level increases. Some other inhibitory factors are small peptides "Fe" string proteins etc. They are not cytotoxic generally.

## The Immune System

The above regulation of haemopoesis generalizes to a statement that proliferation of stem cells and most immature committed cells is stimulated by one set of growth factors. These factors can stimulate specific factors which can act for both differentiated precursors and can promote production of one specific type of blood cell.

The discussion above focused on the formation and factors influencing the formation of granulocytes. How are agranulocytes formed? Let's get to know about this mechanism, next.

### 3.8.3 Development of Agranulocytes

Agranulocytes, we know, are the monocytes and lymphocytes. Agranålocytes develop in the bone marrow and thymus. They start as stem cells. They are primary lymphoid organs where pluripotent stem cells (cells which cannot grow into a whole organism) lörm lymphoblasts. They proliferate and differentiate into immature lymphocytes. The ones which mature in bone marrow are called B-lymphocytes. Another group which matures in the thymus is called T-lymphocytes. These lymphocytes travel to secondary lymphoid organs such as lymph nodes and spleen, where lymphopoiesis continues. They become unique among blood cells since their production is not limited to bone marrow alone.

With this, we end our discussion on development and regulation of leukocytes. We shall end our study of the immune system by presenting a review about the antigen-antibody relationship and the various methods of their in-vitro detection.

## 3.9 IN-VITRO DETECTION OF ANTIGEN-ANTIBODY INTERACTION

Any infection caused, requires a proper treatment. This can be achieved only if the correct organism is identified. Sometime organisms like viruses cannot be detected or an infection in the inaccessible part of the body can occur. During such situations it becomes necessary to depend on presence of specific antibodies in the blood as an indirect evidence of an infection. This is obtained by specific antigen-antibody interaction (Ag-Ab). They can be detected through various laboratory tests. Some common tests are as follows:

- **Precipitation:** If Ag-Ab are present in an appropriate ratio, they form a precipitate in blood. Turbidity is developed, this can be measured optically.
- **Agglutination:** If Ag is present on the surface of cells, or can be made to coat these surfaces of cells, these would form a clump in the presence of antibody. This process is known as agglutination. If no agglutination occurs that means Ab probably is absent.
- **Immunoassay:** This helps us to measure concentration of Ag derived from infectious organism or to measure specific Ab bound to it. Here specific antibodies are tagged. This can be further quantitatively estimated which gives a clue of the concentration of Ag-Ab complexes.
- **Immunoblotting (Western blots):** In this technique, different Ag (which may be viral proteins) are separated by electrophoresis in a solid phase. They are subjected to electrophoresis again on nitrocellulose sheets. This is known as blotting. The antigens are stained with radio labeled Ab. The technique is highly specific in detection of AIDS.
- **Immunohistochemistry:** Here the Ag is tagged with a fluorescent dye (e.g. rhodamine). Inspite of a tag, the Ab binds to the Ag. In the section of a tissue, the Ag with tag bounded to Ab can be detected in a fluorescence microscope. The location of the Ag gives the clue of the site of infection.

## 3.10 LET US SUM UP

In this unit, we learnt about the immune system. We were introduced to the various components of the immune system. We learnt about the defence mechanisms — non- specific and specific — functioning in our body.

Going through the unit we realized that our body is equipped with multiple defence rnechanisms. These are generally known as immune mechanisms. Immunity is of two types — innate and acquired. Innate immunity gets activated by invasion but is non- specific. Acquired immunity is the most highly evolved defence mechanism. The struggle for survival is never ending with us.

The unit also focused on the antigen - antibody interaction and how it helps in maintaining imlnunity. The different immunoglobulins and their functional role in the body was highlighted. Finally, we studied about different methods available to detect the presence of Ag-Ab complexes.

## 3.10 GLOSSARY

**Antigen** : a protein which is released as a specific immune response elicited on the entry of foreign matter in the body.

**Antibody** : protective chemicals or special cells produced by the immune system.

**Agglutinins** : the antibodies corresponding to the blood groups antigens.

**Antitoxins** : antigens that sense the antibodies, neutralize these and make them ineffective.

**Chalones** : a tissue-specific locally produced inhibitor of cell proliferation.

**Diapedesis** : the amoeboid movement of leukocytes into intercellular spaces in case of an infection.

**Endogenous Pyrogen** : a protein which is released in response to toxins produced by pathogens and causes the body temperature to rise.

**Fibrin** : a product of an activated coagulation system.

**Granulopoiesis** : process of formation of neutrophils.

**Hemopoiesis** : formation of blood cells.

**Immunology** : study of body's defence mechanisms against invading pathogens.

**Myeloblast** : a cell committed to differentiate into a granulocyte.

**Opsonins** : substances in the plasma which strongly stimulate phagocytosis.

**Perforin** : protein secreted by killer T-cells which can puncture the invader cell membrane.

**Phagosome** : a vacuole in which a bacterium is enclosed on account of invagination of the cell membrane of a phagocyte.

**Phagocytosis** : the process of engulfing the digesting the micro-organisms infecting the body tissues by neutrophils.

**Precipitins** : antibodies which combine with the antigens to form precipitates that are easily ingested by phagocytes.

## 3.10 ANSWERS TO CHECK YOUR PROGRESS EXERCISES

**NOTES**

UNIT

# 4

# CARDIOVASCULAR SYSTEM

**STRUCTURE**



## 4.1 LEARNING OBJECTIVE

After studying this unit, you will be able to:

- explain and illustrate the structure of the heart,
- describe the various functions of the heart,
- discuss the common terminologies of blood pressure and heart attack, and
- explain the role of exercise and diet in keeping the heart toned and body fit.

## 4.2 INTRODUCTION

In the first three units we have studied about the cell —the basic unit of life, blood — the elixir of life and about the immune system. In this unit, we shall unfold the mysteries of our heart and its connecting blood vessels. We shall learn about the structure and functioning of the heart and more about the commonly used terms -

blood pressure and heart attack.

## 4.3 DESIGN OF CARDIOVASCULAR SYSTEM

NOTES

The cardiovascular system consists of a pump - the heart - and a network of pipelines— the blood vessels. Let us begin our study of the cardiovascular system, with the pump.

### 4.3.1 Heart: the Pump

We all are familiar with the heart. The heart and its major components are shown in the Figure 4.1 . As you can see, the heart has four chambers. Can you list the names of the four chambers of the heart? Yes, the four chambers are the right atrium, right ventricle,

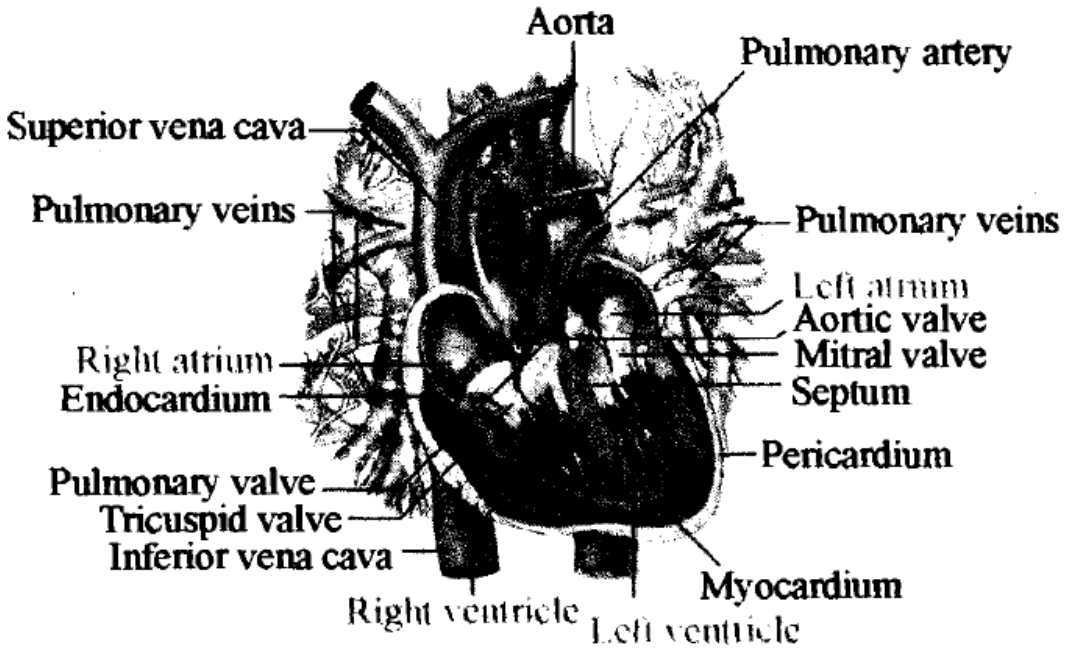



**Figure 4.1: Heart and its components**

Now how does the blood circulate in our body? This is explained diagrammatically in Figure 4.2, showing the major arteries and veins and the organs to which they supply blood. Let us now focus on the route, which the blood takes within the chambers of the heart. The right atrium receives blood from the body through two large veins — the superior and the inferior vena cava (as can be seen on the left hand side ofthe heart in Figure 4.1). It empties blood into another chamber of the heart, the right ventricle as shown in Figure 4.2. The right ventricle pumps the deoxygenated blood to the lungs, through the pulmonary artery.

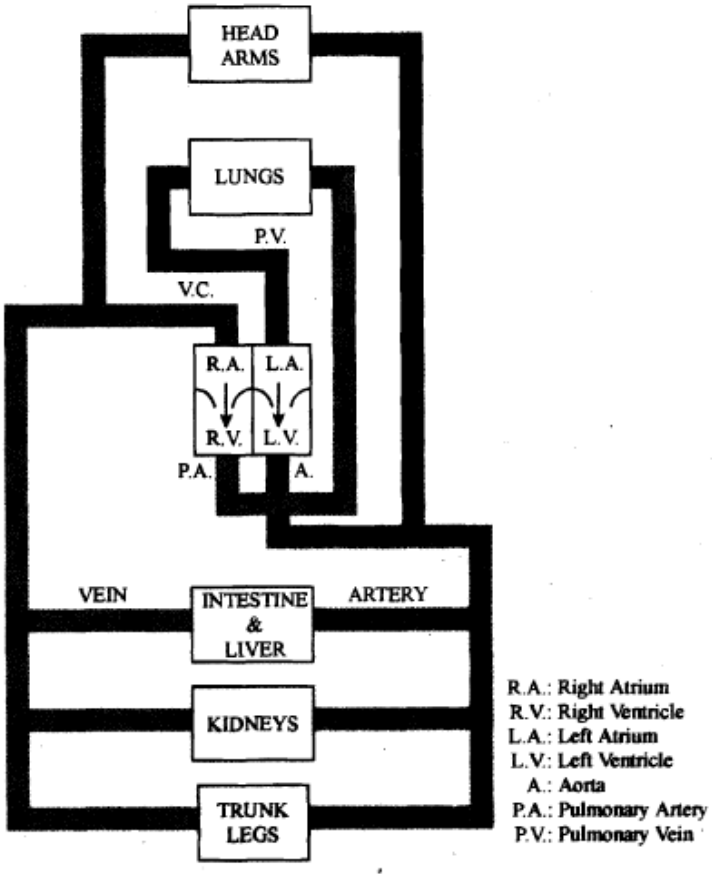



**Figure 4.2: Circulation of blood in our body**

Figure 4.3 (a) shows the inside of the right ventricle, which pumps blood into the pulmonary trunk and divides into right and left pulmonary arteries. A semi-lunar valve called the pulmonary valve, which prevents the flow of blood back into the right ventricle, guards the opening of the right ventricle into the pulmonary trunk.

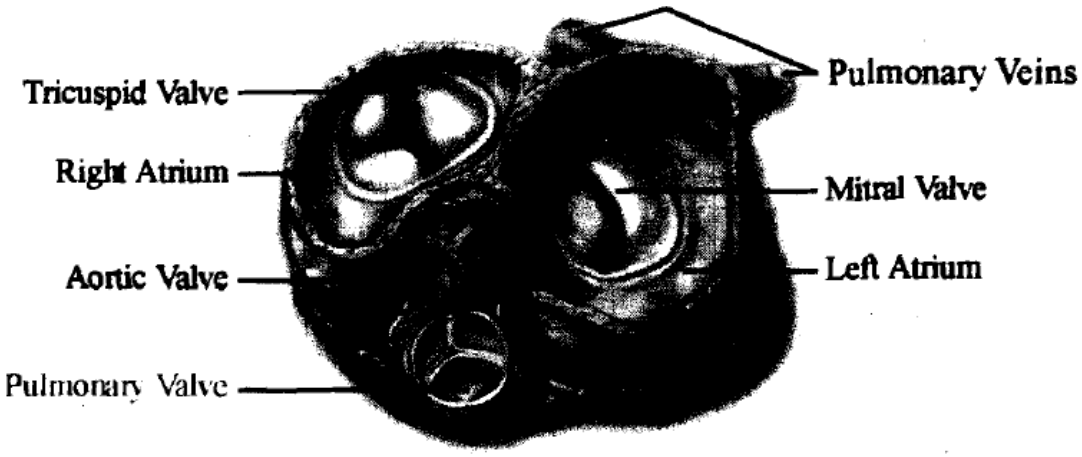



**Figure 4.3(a): Right ventricle**

Blood from the pulmonary trunk enters the pulmonary circulation and receives oxygen from the lungs as highlighted in Figure 4.2. This oxygenated blood flows

through pulmonary veins to the left atrium as can be seen in Figure 4.3(b). From the left atrium, the oxygenated blood enters the left ventricle. The left ventricle is the main pumping chamber sending the blood through the aorta to all of the body parts except lungs.

There is a valve at the junction of the right atrium and right ventricle. The tricuspid valve, as shown in Figure 4.3(a), ensures one-way flow i.e., it prevents the blood from flowing back from the right ventricle to the right atrium. Simi larly, there is a valve called bicuspid, mitral or left atrio-ventricular valve at the junction of the left atrium and left ventricle. Figure 4.3(a) highlights the valve. The mnemonic to remember the names of the valve is Banwari Lal Tota Ram i.e. Biscuspid Left heart Tricuspid Right.

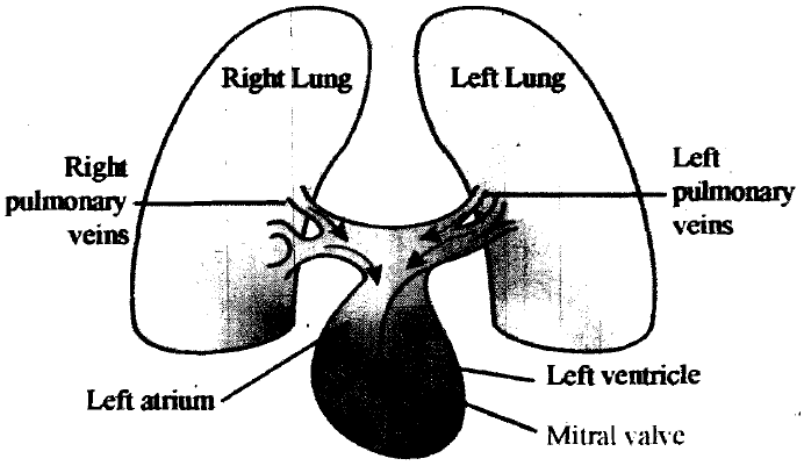



**Figure 4.3 (b): Left side**

Figure 4.3(c) summarizes the blood circulation within the chambers of the heart. The left ventricle pumps blood into the aorta as can be seen in Figure 4.3 (c). Here you would realize that the aorta supplies blood rich in oxygen and nutrients to the entire body system. The branches of the aorta are the arteries and are called systemic arteries. Since the systemic arterial network is much more extensive than the pulmonary arterial network, the left ventricle has to pump blood at a much higher pressure than the right ventricle — this is made possible by a much thicker wall (musculature) than that of the right ventricle.

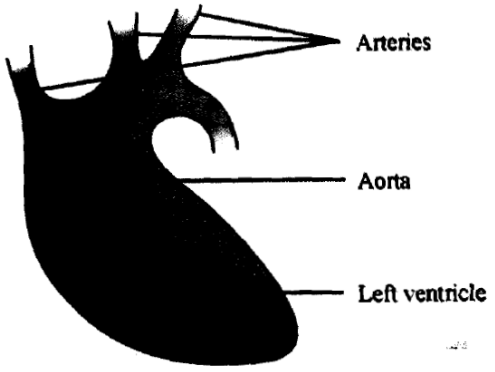



**Figure 4.3 (c): Blood distribution within the chambers of the heart**

In this section we studied the heart i.e. the pump. Next, let us learn about the blood vessels.

NOTES

## 4.3.2 Blood Vessels: the Pipelines

Blood vessels are the pipelines of the heart. Can you suggest which are the blood vessels of the heart? Yes, aorta, arteries, arterioles, capillaries and veins are the blood vessels of the cardiovascular system. The branches of the cardiovascular system may be likened to a tree, which divides itself into smaller thinner divisions. Aorta divides to arteries, arteries into arterioles and arterioles into capillaries and capillaries join to form veins. Let us now study about the functions of each of these. Starting with the aorta, the aorta we learnt above supplies oxygenated blood to the entire body. It is distensible. The elastic tissue present in the aortic wall absorbs the shocks of blood striking against it from the heart. This along with decrease in diameter of blood vessels away from aorta changes the spurty pulsatile blood flow into a continuous flow. This is termed as the windkessel effect, after the scientist who showed this effect.

Arterioles function as 'resistance vessels'. When their diameter is reduced, the blood flows with a much greater resistance and vice-versa. This is the manner in which the blood now is redistributed during aerobic exercise to other parts of the body. Arterioles ensure healthy blood supply to the vital organs of the body — the brain and the heart during exercise, decreasing blood supply to the intestines. That is why there is wisdom in the saying that one should not exercise after meals, as food may not be digested properly because of the decreased blood supply to the intestines after exercise. Continuous blood flow is essential for exchange of gases ($O_2$ and $CO_2$), food and water across vessels called capillaries. The capillaries are thin-walled narrow tubes without any muscular coat. The capillaries come in intimate contact with the cells while picking carbon dioxide and waste products from them. That is why they are termed as the exchange vessels.

Veins are the vessels that are extremely thin-walled. They lack the strength of the solid arterial wall but are extremely flexible. Their main function is to store blood in large capacities. They are called as capacitance vessels. The veins of the calf muscle in the lower leg are termed as peripheral hearts as they store a lot of blood that is pumped back by muscle action during running to the heart. Do you recall how the blood would flow from the legs to the heart? Yes, it is via the inferior vena cava to the right atrium.

Having understood the heart and its blood vessels, it is time for us to learn about the

## 4.3.3 Control of Our Heart Through Nerves

When we exercise in the mornings, the heart beats faster and when we sleep at night, it slows down. Have you ever wondered how does the heart tick? Our old Rishis and Saints have spent years answering this question. Some have managed to even stop their heart from beating while others have made it beat at will at a rate so fast that it would kill a normal human being. How do they manage to do

that? They, over the years, have simply gained control over their autonomic nerves that supply the heart and blood vessels. What are these nerves? Let us get to know them.

The nerves are divided into two systems: sympathetic and parasympathetic. They constitute the autonomic system (auto: independent from the rest, a system that is different and unique). How is this system unique? It's quite simple.

Sympathetic, as the word suggests, means to sympathize. The body sympathizes during fight, flight and fright reaction. For example, have you ever felt your heart beat faster when in the dark or when frightened? This increase in the heart rate is termed as 'positive chronotropic effect ' (Chrono: from chronological meaning related to time or rate). The heart also beats with an increased force as you may have experienced your heart pouncing against a heaving chest after a sprint. This is called as Positive inotropic effect', as the increase in force is brought about by the changes in ion concentration across the cell membrane. Calcium within the cell makes the heart beat stronger. (To remember, milk gives strength and milk has calcium). Have you ever wondered about the mechanism that makes the beat faster? Nature has designed a beautiful mechanism which symbioses the electrical impulse and the solid heart. A flame is ignited in the heart, which then travels to the cardiac muscle, imparting it energy to contract. The rate of transmission of this flame or electrical impulse increases during sympathetic situations and is termed as positive Oomotropic. An increase in the excitability of the cardiac tissue is termed as positive bathmotropic.

Another system that runs parallel to the sympathetic system is termed as the parasympathetic system. This system has an effect just opposite to the sympathetic system. It relaxes the heart, decreases the heart rate (negative chronotropic), the force of contraction (negative inotropic), the conduction rate (negative dromotropic) and the excitability of tissue (negative bathmotropic).

The nerves that supply the heart's atria are termed as vagi (singular vagus). As the name suggests, vagus is a vagabond, a wanderer charting an unfamiliar, vague course supplying the digestive tract, heart, the voice box etc. The heart is supplied by the right and left vagi. The peculiarity is that they do not supply the ventricles. The sympathetic system only supplies the ventricles.

Overall, we have seen that the heart hangs in a balance of positive and negative forces: the sympathetic and parasympathetic system. Now you know the mechanism that may be operating when our yogis increase their heart rate or stop it!

The sympathetic nerves have a chemical neurotransmitter called nor-adrenaline, whereas, the parasympathetic nerves release acetylcholine at the postganglionic nerve endings.

Next, like the heart, let us see how the nerves control the blood vessels.

## 4.3.4 Control of Our Blood Vessels Through Nerves

The sympathetic system supplying the blood vessels constricts the lumen, redistributing blood flow to the regions of the body. Parasympathetic nerves

usually do not supply blood vessels. If you recall, you have just read that these nerves do not supply even the ventricles. The exceptional blood vessels receiving parasympathetic innervation are those of the salivary glands, pancreas and genital organs. Stimulation of these nerves results in increasing the luminal diameter or vasodilatation (dilation of vessels). They play a role in increasing salivary and pancreatic secretion after meals and in erection of the penis (male sex organ). The neurotransmitter ofsympathetic nerves is nor-adrenaline.

There exists another specialized sympathetic nerve called sympathetic cholinergic nerves. Do you know how these neurons differ from sympathetic nerves? Just before the exercise, the very thought of exercise may increase the heart rate or some students may faint during the stress of an examination. These fibers produce vasodilatation of blood vessels of skeletal muscles, unlike the sympathetic nerves that cause vasoconstriction. How these fibers help the body to prepare for stressful situations is debatable. The neurotransmitter is acetylcholine, hence the name cholinergic.

## 4.4 WHAT IS THE HEART MADE UP OF?

Earlier in this unit, we have learnt about the design of our cardiovascular system. Here in this section, we shall study what the heart — as a pump, is made up of i.e. the tissues and the fibers and their functions.

### 4.4.1 Pacemaker and Conduction Tissues

Heart has a well-developed pacemaker tissue, which can generate rhythmic impulses. As the name suggests, the tissue sets the pace at which the heart beats. Figure 4.4 illustrates the heart and its tissues namely the sinoatrial (SA) node, atrioventricular(AV) node, atrioventricular bundle (Bundle of His). Pacemaker and conduction tissues are made up of modified cardiac muscles, which are not well striated. They conduct electrical impulses to the cardiac muscle. Let us get to know them.

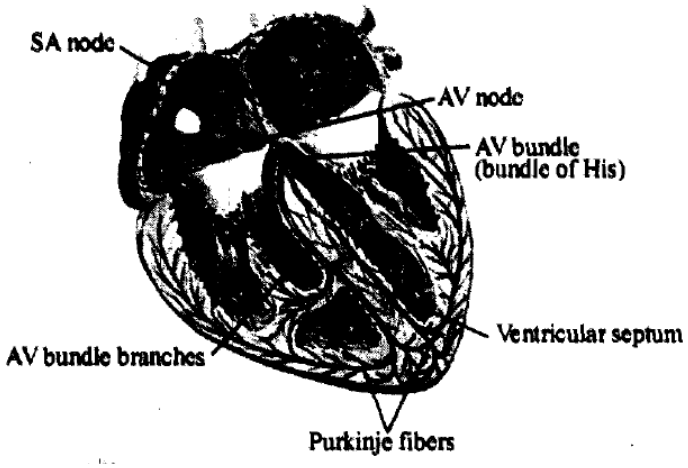



**Figure 4.4: Heart and major tissues**

The pacemaker of heart is the sinoatrial node (SA node), a section of the nodal tissue, that is situated in the right atrium near the opening of the superior vena cava as can be seen in Figure 4.4. This is the node from where the electrical impulses originate. Its functions are to set the rate of contraction for the heart and spontaneously generate nerve impulses that travel throughout the heart wall causing both atria to contract. The other pacemaker tissue is the atrioventricular node (AV' node). Notice in Figure 4.4 that this lies between the atrium and ventricle situated on right side of the inter- atrial septum (the wall between the two atria), near the opening of the coronary sinuses (the vessels that carry venous blood to the heart). The AV node controls the transmission of the electrical impulse from the atria to ventricles. Hence, its functions are to delay cardiac impulses from the sinoatrial node to allow the atria to contract and empty their contents first, and relay cardiac impulses to the atrioventricular bundle, as illustrated in Figure 4.4.

AV node is bulbous in appearance as can be seen in Figure 4.4 and gives rise to a bundle ofconduction tissues cal led as Bundle ofHis. It is a bundle of heart tissues that transmit the electrical impulses from the AV node to the ventricles causing cardiac muscles in the ventricles to contract. Next, the bundle passes along the posterior and inferior margin of the pars membranacea septi to reach its junction with the superior margin of the muscular interventricular septum. At this point, the main AV bundle divides into two bundle branches to the respective ventricles.

The Bundle of His divides into a network of purkinje fibers (refer to Figure 4.4) as they enter the ventricles. The microscopic structure of purkinje fibers reveals that these are not fibers but are actually modified strands of cardiac muscles as shown in Figure 4.5. These help to spread the impulses throughout the heart in a specific sequence at appropriate velocities to help make the heart contract and relax at the right time. The purkinje fibers are very large and conduct the action potential at about six times the velocity of ordinary cardiac muscle (i.e., 1.5 to 4.0 meters per second). Thus, the purkinje fibers permit a very rapid and simultaneous distribution of the impulse throughout the muscular walls of both ventricles. Did you also know that the cardiac muscle has a latent or sleeping pacemaker activity, which may be manifested if the normal pacemakers fail?

The cardiac impulse originates in the SA node, The impulse spreads to the atria like 'ripples in a pond'. Three specific conduction pathways have also been described which help spread through the atria faster. After spreading to the atria, the impulses reach the AV node. AV node has very slow conducting fibers. Therefore, the impulse is delayed by about 0.1 sec at the AV node, after which it spreads rapidly to the ventricles.

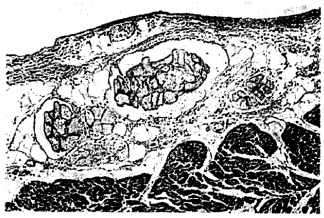


**Figure 4.5: Purkinje fibers**

After the cardiac tissue, it is the turn of cardiac muscle. Let's get to know it better.

### 4.4.2 The Cardiac Muscle

We have seen that our heart is an amazing structure. It pumps out blood about 70 times a minute for 70 years without a break. This herculean task is performed by unique musculature of the heart called cardiac muscle. What makes this muscle go on and on forever? Let's find out.

The cardiac muscle is not under voluntary control, unless you are a Rishi! This muscle is a branched one. Under the microscope, the muscle shows cross striations as shown in Figure 4.6.

Here, the longitudinal cardiac muscle can be identified by centrally placed round to oblong nuclei, striations, branching and intercalated discs. Each fiber is 100 microns long and about 15 microns wide. At the junction between two adjacent fibers are specialized areas called intercalated discs, which have a low electrical resistance. They enable faster transmission of impulse, Although the cardiac muscle fibers are separated from each other, they act as a functional syncitium or one unit because cells are electrically coupled. This means that an impulse generated anywhere in the cardiac muscle spreads throughout the musculature. The heart contracts as one system in a coordinated manner.

**Figure 4.6: Cardiac muscle**

So you can see our heart is unique. Let's see how unique our heart is, in the next section.

## 4.5 THE UNIQUENESS OF OUR HEART

Cardiac muscle has some unique properties that make it ideally suited for the function it performs. These properties can be easily understood in the light of the structural features as we have just read. These may be studied further as "Properties of a Beating Heart".

Let us have a look at what these properties are:

Properties of a Beating Heart

Let us study a few interesting properties of a beating heart which make it such a unique organ.

- **Automaticity**

Take out my heart from my body and it will still go on and on beating. How true! Even a completely denervated heart from the body continues to beat. The capability to contract even in the absence of neural control is called "automaticity".

- **Rhythmicity**

Not only does the denervated heart continues to beat, it does so remarkably rhythmically. What it means is that the heartbeats are extremely regular. It also means that the time interval between any two consecutive beats is exactly the same. Rhythmicity is conferred on the heart by the conduction system of the heart. The SA node discharges impulses at the fastest rate, the AV node next and the rest of the conduction system does so with the least frequency, This situation may be understood by imagining a train with more than one engine. If each of the engines is set for running at different speeds, the fastest engine will determine the speed of the train. fiat is why SA node is the pacemaker of the heart because it determines the pace of the heart. If the fastest engine fails, the second fastest engine will take over and will determine the speed of the train. In the same way, if the SA node fails, the AV node dictates the heartbeats at the slower rate. This orchestra goes on and on rhythmically and coordinated for life.

- **Long refractory period**

Refractory period is the period during which a stimulus fails to evoke a response. In a beating heart, if an external stimulus is applied during contraction, there is no response irrespective of how strong the stimulus is. This is because the cardiac muscle is refractory throughout the contraction. The reason why cardiac muscle has a long refractory period is tnat the duration of its action potential is almost as long as that of its mechanical activity. The fact that the heart sleeps and does not reacts when exposed to day-to-day exciting and stressful situations without missing a heartbeat every now and then ensures its smooth functioning hundred long years.

## Extrasystole and Compensatory Pause

During the relaxation period, cardiac muscle is in the relative refractory period i.e. sleeping but only just. If a sufficiently strong electrical stimulus is applied during this period, it leads to a contractile response. Since this contraction appears earlier than the normally expected contraction, it may be considered an ' extra' contraction. Hence, it is called extrasystole.

The next natural impulse then arrives during the refractory period corresponding to the extrasystole. Hence, the natural impulse is ineffective and a normally expected contraction is missed. As they say, "I missed a beat" The pause in cardiac activity is called compensatory pause.

In real life, if we drink too much coffee, the heart fires leading to premature

contraction of the ventricles and extrasystole may be produced.

Next let us look at the properties of a quiescent heart.

Length-Tension Relationship: The force of contraction of cardiac muscle is directly proportional to the initial length of the muscle fibers. This is known as the Starling's Law of the Heart after the scientist Frank Starling. In practice, the length of the - cardiac muscle increases when the venous return increases. Hence, an increase in venous return increases the force of contraction of the ventricle. This property has several implications for cardiovascular function and would be discussed in greater detail as we read along.

## 4.6 CARDIAC OUTPUT

Let us start by understanding what is meant by cardiac output. To put in the simple terms, cardiac output is the output of the heart per minute. We already know that the function of the heart is to pump blood. Hence, cardiac function is best expressed in quantitative terms as the amount of blood pumped by each ventricle per minute. The amount of blood pumped by either ventricle during every beat (called stroke volume) is about 70 ml at rest, and the heart beats about 70 times per minute at rest.

Hence, cardiac output is expressed as under:

Cardiac output = Stroke Volume x Heart Rate

= 70 ml x 70/min

= 4900 ml/min

= 5 L/ min (approx.)

The cardiac output per unit body surface areais relatively constant from one individual to another and is called cardiac index, which is expressed as under.

$$\text{Cardiac index} = \frac{\text{Cardiac output}}{\text{Body Surface Area}}$$

$$\text{Surface Area} = \frac{5 \text{ L/min}}{1.7 \text{m}^2}$$

$$= 3 \text{ L/min/ m}^2 \text{ (approx.)}$$

Body surface area (BSA) may be calculated from height and weight using dubois formula, which is as stated herewith:

$$\text{BSA (m}^2\text{)} = \text{Weight (kg)}^{0.425} \times \text{Height}^{0.725} \text{ (cm)} \times 0.007184$$

Alternatively, BSA may be read of from a nomogram.

Cardiac output varies in day-to-day situations. One everyday example of such a situation is exercise, which is associated with an increase in blood flow to the working muscles of the legs, hands and heart. During exercise, the cardiac output may increase up to about five-fold even in untrained persons and up to ten-folds in the trained athletes.

Having studied about the measure of heart functioning, next we shall get to know about the sequence of events that occur every time our heart beats, which is referred to as cardiac cycle.

NOTES

## 4.7 THE CARDIAC CYCLE

The cardiac cycle is the sequence of events that occur when the heart beats. You may have heard of the terms diastole and systole, particularly with reference to blood pressure. Well, these are the two phases of the cardiac cycle, as highlighted herewith:

l) Diastole - Ventricles are relaxed.

2) Systole - Ventricles contract.

A simplified representation of these phases is shown in Figure 4.7.

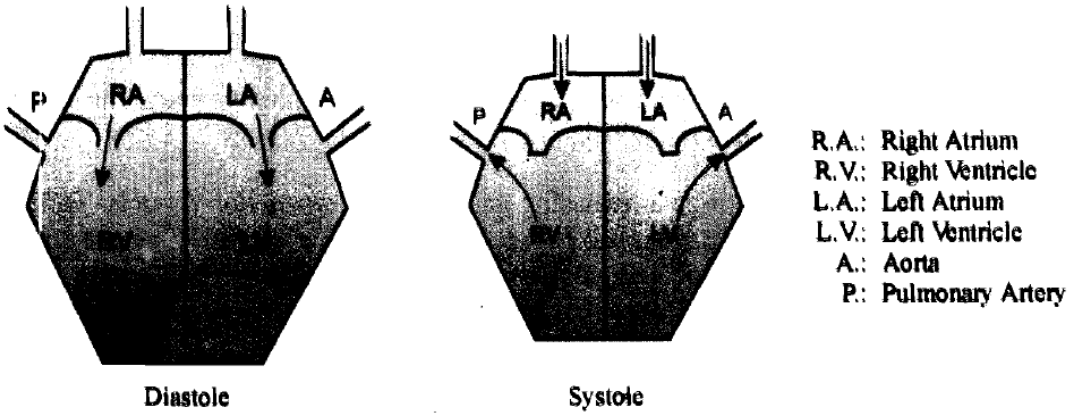



**Figure 4.7: Phases of cardiac cycle**

Let us now study about both of these phases in the right heart (right atrium and ventricle).

1) **The diastole phase -** During this phase, the atria and ventricles are relaxed and the atrioventricular valves are open. De-oxygenated blood from the superior and inferior vena cava flows into the right atrium. The open atrioventricular valves allow the blood to pass through to the ventricles, as you can see in the Figure 4.7. The SA node contracts, triggering the atria to contract. The right atrium empties its contents into the right ventricle. The tricuspid valve prevents the blood from flowing back into the right atrium.

2) **The systole phase -** During this phase, the right ventricle receives impulses from the purkinje fibers and contracts. The atrioventricular valves close and the semi- lunar valves open. The de-oxygenated blood is pumped into the pulmonary artery. The pulmonary valve prevents the blood from flowing back into the right ventricle. The pulmonary artery carries the blood to the lungs. There, the blood picks up oxygen and is returned to the left atrium of the heart by the pulmonary veins. This is more clearly depicted in the Figure 4.8.

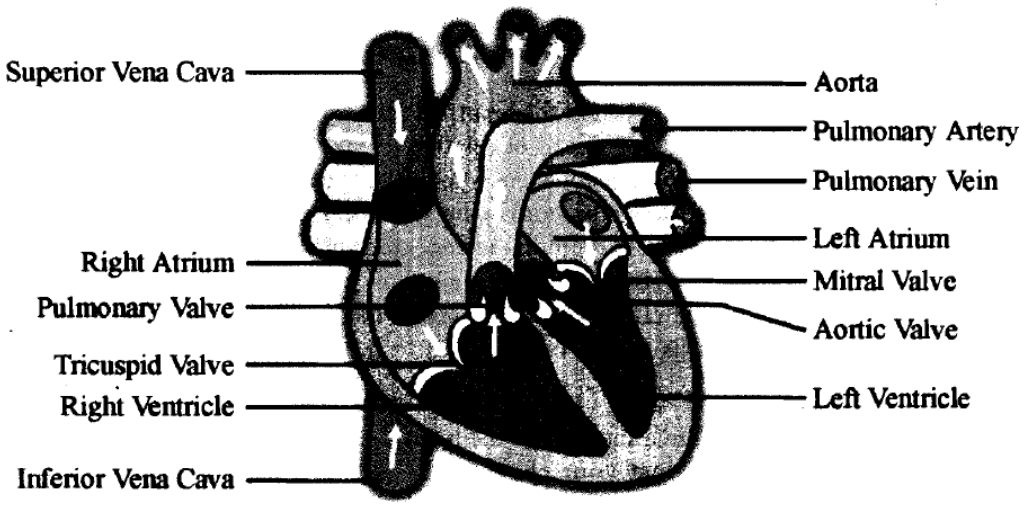



**Figure 4.8: The cardiac cycle**

Simultaneously in the left heart during diastole period, the semilunar valves close and the atrioventricular valves open. Blood from the pulmonary veins fills the left atrium. Blood from the vena cava is also filling the right atrium. The SA node contracts again, triggering the atria to contract. The left atrium empties its contents into the left ventricle. The mitral valve prevents the oxygenated blood from flowing back into the left atrium.

During the systole phase, the atrioventricular valves close and the semilunar valves open. The left ventricle receives impulses from the purkinje fibers and contracts. Oxygenated blood is pumped into the aorta. The aortic valve prevents the oxygenated blood from flowing back into the left ventricle.

The aorta branches out to provide oxygenated blood to all parts of the body. The oxygen- depleted blood is returned to the heart via the vena cava.

The heartbeat follows a regular recurring pattern. One contraction (systole) followed by relaxation (diastole) of the heart is known as cardiac cycle. There are several mechanical, physical and electrical events associated with the cardiac cycle. Understanding the time course of these events is interesting and also useful in management of cardiovascular diseases.

Suppose the heart rate is 75 per minute,

If 75 beat take I minute, then, 1 beat will take 1/75 min = lx 60 sec/ 75 = 0.8 sec

Thus the duration of the cardiac cycle is 0.8 sec. Out of this, ventricular systole (generally called "the systole") lasts 0.3 sec and ventricular diastole (generally called "the diastole") lasts 0.5 sec. When the heart rate increases, the duration of cardiac cycle decreases. In such a situation, the reduction in duration of diastole is greater than that of systole.

Next, let us learn about the heart sound.

### Heart Sounds

Have you ever heard your heart go lub...dub...? What are these sounds? "Lub" is the closing of the atrioventricular valves while "dub" is the closing of the pulmonary and aortic valves. Place a hand against your chest, preferably on the left side. Why left side? You know now that the heart is placed towards the left like a pyramid of Egypt only inverted with its apex placed on the left side.. .. What do you feel? Do you feel the heart beating? Yes, that is the thumping motion of the left ventricle against the chest. Then, why is there a gap in between the two thumps? It's simply because during this time, the heart is resting. Do you remember what this period is called? Yes, it is the diastole and the importance of this resting phase is that the heart receives its nutrition and air supply during this period. It's a well-deserved breather for an organ that goes on and on for a hundred odd years without stopping.

Now that you have palpated or felt the heart, let us hear or auscultate the chest. Place your ear on the chest of some friend or relative. What do you hear? Doctors use an instrument called as stethoscope to listen to your heart beat. It is an instrument used for examining the heart and lungs by conveying to the ear of the examiner, the sounds produced in the thorax. This is built on the very same principle of talking to someone 100 m away with a cord of string attached or a hollow bamboo conducting sound better when placed against the chest. The stethoscope has a bell and a conducting tube and earpieces. The bell is placed on the chest to hear the wonders the heart unveil before us.

The tap of the music is like the beat of the heart. Snap your fingers, tap your feet or make a baby sleep against your chest, what are the common factors? It's the synchronization with your heartbeat. The baby has a bonding and recognizes the mother from the heartbeat when placed on her chest from the womb memory. The song troupes synchronize their rhythmic dance routine by placing a hand on the heart. That's our fascinating four chambered heart beating as one, rhythmically that gets the coordination of the choreographic team right.

Thus we reach where we started from and the cardiac cycle starts all over again.

## 4.8 BLOOD PRESSURE

You may have seen someone record the blood pressure or someone may have taken your blood pressure.

Blood pressure is a very common term used casually in everyday conversation. People often advise others to check anger in order to prevent the blood pressure from going up, but forget it when they themselves are angry. Any declaration of high blood pressure by a physician immediately brings a lot of worries to the patient. However, blood pressure is most important for maintaining blood flow through tissues. Thus, blood pressure is a neeessary evil for survival. As long as it is within the normal limits, it does not bother us.

In fact, it keeps us alive. So then what is blood pressure?

## 4.8.1 What is Blood Pressure?

Blood pressure, without qualification, refers to the arterial blood pressure. Hence, it is the lateral pressure exerted by the column of blood on the walls of the arteries. The pressure is not steady, it fluctuates during the cardiac cycle. During ventricular systole, anerial blood pressure is higher than that during diastole. The normal range of systolic blood pressure is 100 to 140 mm Hg and that of diastolic pressure is 60 to 90 mm of Hg. Blood pressure is commonly measured using a mercury manometer and is commonly expressed in millimeters of mercury (mm Hg).

mood pressure may be measured fairly accurately by sphygmomanometer — this is a noninvasive method. The sphygmomanometer consists of an inelastic cuff, which contains an inflatable rubber bag. As you can see from the Figure 4.9, the rubber bag is connected to two tubes. One tube connects the bag to a manometer and the other tube is connected to a bulb fitted with a valve, which may be used for inflating air and deflating the rubber bag.

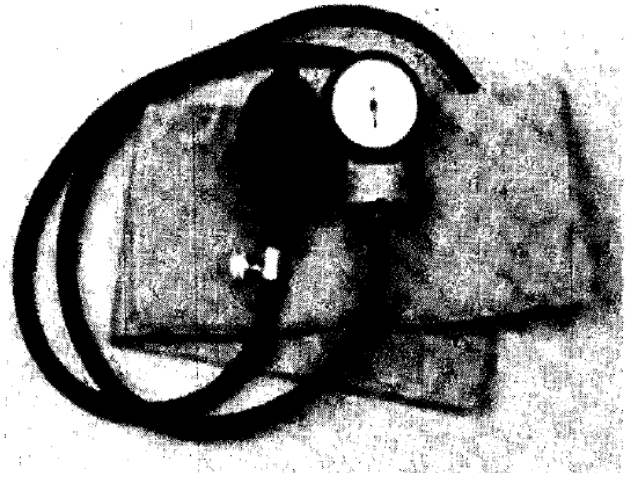


**Figure 4.9: Sphygmomanometer - BP apparatus**

The cuff is snugly placed around the arm, 3-4 cm above the elbow joint. It is inflated till the cuff pressure stops all the blood flow through the brachial artery. If kept for too long, the patients hand feels numb and may pain. The cuff pressure is gradually mm/sec) brought down. Then blood starts flowing into the brachial artery, as soon as the cuff pressure falls just below the systolic arterial pressure. As you are deflating cuff, place bell of stethoscope over brachial artery at the elbow and hear the loud tapping sounds getting muffled and finally disappear. The pressure at which the sounds just appear is known as systolic pressure. The pressure at which the sounds just disappear is taken as the diastolic pressure.

## Mean blood pressure

Mean blood pressure is not the arithmetic mean or average of the systolic and diastolic blood pressure. This is because systole is much shorter than diastole. Therefore, arterial pressure is near the diastolic pressure for a longer part of the cardiac cycle than it is nearer the systolic pressure. A mathematically pressure

method for finding the true mean pressure is when one-third of the pulse pressure is added to the diastolic pressure, we get a value which is very close to the mean pressure determined by the graphic method. That is, in the simpler terms, multiplying the diastolic pressure by two, adding the systolic pressure, and then dividing this sum by three estimates it. Therefore, if systolic pressure is 110 mm Hg and the diastolic pressure is 80 mm Hg, then

Mean blood pressure = 80 +1/3(110— 80) mm Hg or 80 x 2 +110/3 mm Hg

= 90 mm Hg

Mean blood pressure is the major determinant of blood flow through the tissues.

### How to record the blood pressure?

Blood pressure is recorded as two numbers— the systolic pressure (as the heart beats) over the diastolic pressure (as the heart relaxes between beats). The measurement is written one above or before the other, with the systolic number on top and the diastolic number on the bottom. For example, a blood pressure measurement of 120/80 mm Hg (millimeters of mercury) is expressed verbally as "120 over 80."

The difference between systolic and diastolic pressure is known as pulse pressure.

Therefore, the normal pulse pressure is approximately (120 — 80) = 40 mm Hg.

Let us now study about the factors affecting the blood pressure.

## 4.8.2 Factors Affecting Blood Pressure

From Ohm's Law, it is easy to deduce that the blood pressure would roughly equal to the product of cardiac output (CO) and peripheral resistance (PR).

Hence, BP = CO x PR

Hence, the factors which alter the cardiac output or peripheral resistance would also affect the arterial blood pressure.

Let us learn about these factors next.

### Factors Affecting Cardiac Output

Changes in the cardiac output affect mainly the systolic pressure while changes in the peripheral resistance affect mainly the diastolic pressure. Let us now study what are these changes. We shall first have a look at the consequences of increased cardiac output.

- **Increased Cardiac Output**

i) An increase in blood volume increases the venous return and leads to an increased stroke volume. The increase in the blood volume may be due to water retention, which may follow sodium retention, due to increased aldosterone secretion or some other factors.

ii) During exercise, the cardiac output increases due to an increase in both stroke volume and heart rate. Hence, systolic pressure generally increases during exercise.

iii) An increase in heart rate does not always alter the blood pressure because if stroke volume decreases simultaneously, cardiac output does not change significantly.

iv) Emotional excitement increases systolic, as well as, diastolic pressure because of increased sympathetic adrenal activity.

## Decreased Cardiac Output

- **Change of posture:** When a person stands up from lying down posture, there is an immediate but transient fall in systolic blood pressure. This is because, upon standing, there is a pooling of venous blood in the lower limbs due to gravity. This leads to a decreased venous return, which in turn decreases the stroke volume and cardiac output causing a fall in the systolic pressure. However, within fifteen seconds, the baroreceptor reflexes bring about a cardio acceleration and vasoconstriction. As a result, the blood pressure soon returns to normal or may rise above value due to overcompensation. You may work out the changes on standing.
- **Hypovolemia or reduction in blood volume:** Hypovolemia leads to a decrease in cardiac output, which causes a fall in the systemic blood pressure. Hypovolemia may be produced by hemorrhage. However, the baroreceptor reflex corrects the fall in blood pressure due to moderate hemorrhage. Ifthe loss of blood is less than 10% ofthe total blood volume, the compensatory mechanisms succeed in stabilizing the blood pressure at a level below the normal pressure. But if the loss is more than 30% of the blood volume, the compensatory mechanisms may fail leading to an irreversible and fatal fall in blood pressure.
- **Cardiac compression:** Rapid accumulation of fluid in the pericardial sac decreases ventricular distensibility leading to a decrease in cardiac output.
- **Myocardial ischemia and infarction:** Myocardial ischemia (insufficient blood flow) or myocardial infarction (death of heart cells) reduces myocardial contractile force and thereby reduces the cardiac output. Further, there is also a reflex fall in systemic blood pressure by liberation of certain metabolites which stimulate the ventricular unmyelinated afferent fibers.
- **Trauma:** Any injury which causes intense pain produces a fall in blood pressure.

Next, let us look at the factors affecting peripheral resistance which ultimately influences the blood pressure.

## Factors Affecting Peripheral Resistance

Resistance offered by arterioles or resistance vessels, as you have read above, is termed as peripheral resistance. Changes in peripheral resistance mainly affect diastolic pressure. The factors that affect peripheral resistance, include:

- If more than 30% of the blood volume of a person is lost through bleeding (haemorrhage), the compensatory mechanism may fail. In that case, there

may be a reduction in the vasomotor center activity and a fall in peripheral resistance, which may turn out to be irreversible. The perfusion to the tissues is decreased. This condition is known as shock.

- Some emotionally disturbing events, such as sight of blood or frightening objects may lead to fainting due to generalized vasodilation. Although this is called vaso- vagal attack, it seems to be mediated by sympathetic cholinergic vasodilatation fibers, which supply skeletal muscles. It is generally short-lasting. The treatment is to lie down so that the blood flow, especially to the brain, is maintained. If this treatment is not promptly instituted, the person may faint and fall due to a reduction in blood flow to the brain — a condition known as syncope. Syncope is actually a spontaneous loss-of consciousness caused by insufficient blood to the brain. It may be considered nature's way of instituting the treatment. Although rude and potentially traumatic, the fall can be life-saving.
- Anaphylactic shock, trauma, peritonitis (inflammation of the peritoneum), crush syndrome or an allergy following a bee bite. In all these conditions, there is production ofsome toxic substances, which lead to systemic vasodilation and increased capillary permeability. Increased vascular capacity due to vasodilation and reduced volume due to increased capillary permeability is a dangerous combination. It frequently leads to circulatory shock.
- Stimulation of myelinated pain fibers may produce generalized vasodilation.

Besides, the factors discussed above, there are a few other factors affecting the viscosity of b109d which also impacts on blood pressure. These are discussed next.

### Factors Affecting Viscosity of Blood

Viscosity of blood affects the systemic blood pressure in the same way as changes in the peripheral resistance. In anaemia, viscosity of blood is low and a fall in blood pressure may occur. In polycythemia (increase in the production of red blood cells or erythrocytes) viscosity is high and blood pressure may rise.

Next, we shall read about the factors regulating blood pressure.

### 4.8.3 Factors Regulating Blood Pressure

Blood pressure regulating mechanisms may be classified into two categories:

a) Short term regulating mechanisms, which regulate and maintain the normal blood pressure inspite of factors which tends to disturb it every minute. These regulators are mainly neural and includes baroreceptors, chemoreceptors etc.

b) Long term regulating mechanisms, which adjust the body fluid volume. These regulations are mainly through hormones. The hormonal mechanisms include the catecholamine release from adrenal medulla, renin-angiotensin mechanism of kidney etc.

## 4.9 PATHOPHYSIOLOGY OF HYPERTENSION

In spite of the regulatory mechanisms discussed above, they have their own limitations and the blood pressure frequently shows persistent elevation. Some rise in blood pressure with age is accepted as physiological. The rule of thumb is to consider the systolic blood pressure as normal if it is less than (100 + age in years) mm Hg. However, many specialists have an evidence to believe that a rise in blood pressure with age is a process we have to pay for our lifestyle, especially due to the high salt content of our diet and sedentary habits.

Some experts assert that if no additional salt is added to food throughout life, the blood pressure will stay Constant throughout life. Since this hypothesis cannot be widely tested on human beings at the present stage of our civilization, we have to accept some rise in blood pressure with age as a part of the aging process. Although the change is gradual, and there is not a sharp dividing line between normal and high blood pressure, an arbitrary upper limit is 140 and 90 mm Hg for systolic and diastolic blood pressure, respectively. Out of the two, the diastolic pressure is more reliable for determining whether a person is hypertensive because the systolic pressure shows wider fluctuations from time to time in the same individuals. In any case, a single casual reading is not enough to label a person hypertensive, especially in the borderline cases. But if the diastolic pressure is repeatedly found to be 90 mm Hg or above, on at least three occasions, the individual may be considered hypertensive, irrespective of age. The classification of hypertension is presented next.

## Classification of Hypertension

In most cases of hypertension, the cause is only vaguely known in terms of old age, familial tendency, emotional stress, sedentary life, overeating etc. In these cases, where the basic cause of hypertension cannot be pin-pointed, the hypertension is said to be primary or essential.

In the few cases where the underlying cause is known, the hypertension is said to be secondary. Another way to classify hypertension is in the terms of its prognosis. In cases where it progresses slowly, hypertension is called benign. In contrast, malignant hypertension progresses rapidly, is severe and often leads to death within two years if not treated. Some of the common causes of secondary hypertension are listed in Table 4.1.

| Cause | Mechanism |
|---|---|
| Renal disease | Excess renin production leading to high level of angiotensin II. |
| Hyperfunctioning of adrenal cortex | Excess aldosterone, a mineralocorticoid secretion leading to salt and water retention |
| a) Conn's disease | Excess glucocorticoid secretion. |
| b) Cushing's syndrome | Glucocorticoids also have weak minerolcorticoid activity (i.e. salt and water retention). |
| Long term oral contraceptive use | Mineralocorticoid activity of estrogen and progesterone. |
| Phaeochromocytoma | Tumor of adrenal medulla leading to excess secretion of adrenaline and nor-adrenaline. |
| Polycythemia | Increased viscosity of blood leading to higher peripheral resistance. |

**Table 4.1: Common causes of secondary hypertension**

The treatment of hypertension depends on its severity and cause. In essential hypertension, relaxation techniques, tranquilizers, vasodilators, diuretics, ß-blockers or some other drugs may be useful in different combinations. In case of secondary hypertension, it is best to treat the basic causes.

Other than hypertension, there are a few other conditions related to the heart functioning.

We shall get to know them next.

## 4.10 MYOCARDIAL ISCHEMIA AND INFARCTION

A patient experiencing a heart attack suffers from severe pain on the left side of chest that radiates to the left arm. He may sweat a lot, vomit and may not be able to even move because of the pain. The cause of heart attack is eating faulty diet. An old saying in the Gita goes: you* mind and body is what you eat.

A person over the years may eat fatty diet such as butter, meat and eggs rich in cholesterol. These may accumulate on the coronary vessels and obliterate it. When coronary blood flow decreases due to atherosclerosis, it leads to myocardial ischemia. If myocardial ischemia is very severe, or a coronary artery is blocked due to thrombosis, embolism or spasm, it causes death of the myocardium supplied by the blocked artery.

The condition is known as myocardial infarction, and is a serious condition, which may lead to death. The doctors dissolve the clot or remove the obstruction in the artery to restore blood supply to the cardiac muscle.

Earlier we referred to atherosclerosis. What is atherosclerosis? Atherosclerosis is the hardening of the walls of the arteries caused by fatty deposits that build on the inner walls of the arteries which interfere with blood flow as shown in Figure4.10-:

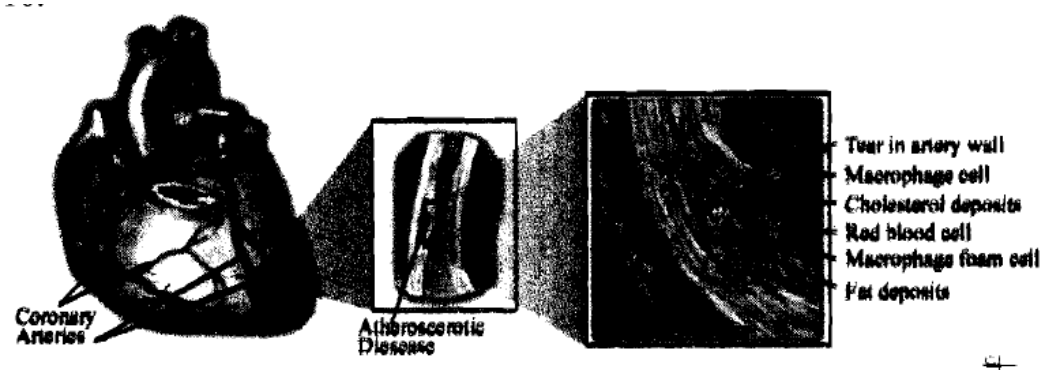



**Figure 4.10: Atherosclerosis**

Insufficient blood flow to the heart muscles from narrowing of coronary artery can cause chest pain referred to as angina pectoris.

So what do we do keep our heart healthy? Read the next section and find out. Do practise what you learn next.

## 4.11 AEROBICS EXERCISE AND DIET: HOW TO KEEP YOUR HEART HEALTHY

NOTES

Aerobics or exercise keeps the muscles of the body toned. The heart receives blood supply, rich in oxygen and nutrients. It pumps in more amount of blood over the years. Research has shown that the heart is larger in trained athletes. The person keeps happy because of the happy polypeptides, such as 'endorphins' , that are released. The exerciser delays retirement from the job as studies have shown. The morning is the best time to exercise when the sun rises and the air is fresh. The chirping of the birds has a positive therapeutic effect on the health.

Supplementing exercise with balanced diet is a must. Salt needs to be restricted in hypertensive as salt causes water retention and fluid overload, aggravating blood pressure. Less of fats and eating lots of fruits, green vegetables, and milk and cereals constitute a healthy nutritious diet.

We shall end our study of coronary vascular system with a discussion on ECG.

## 4.12 ECG — WHAT IT IS AND WHY DO WE NEED IT?

You may have seen a flat line on the monitor screen in the movies or in the hospital when the heart stops beating and the doctor declares that the patient is clinically dead. The flat line recording is an electrocardiogram or an ECG It is an electrical recording of the heart, made by electrodes, picking up cardiac activity from the human body surface.

The heart may be considered a small generator. This generator is situated in the human body, which is a good volume conductor. Thus, it is possible to record the electrical activity of the heart from the surface of the body even at a considerable distance from the heart. It is the insignia or language of the beating heart. It's a simple but commonly used procedure by the doctors to know about the patient's heart. It tells us about the heart rate, rhythm, regularity and state of every heart chamber.

Changes in hemodynamics, damage to the muscle fibers or a change in the ionic environment of the heart affects the ECG. The doctor knows if the heart is diseased or normal. It thus serves as an important diagnostic and prognostic tool for the assessment of cardiovascular function. It has to be combined, however, with clinical judgment and other laboratory investigation for greater reliability. The doctor decides on what medication or action he may have to prescribe by just looking at an ECG and by correlating with other findings. As a student ofdietetics we need not ponder much on this, however, we must learn about a few important diseased states diagnosed by an ECG. These are:

- **Sinus Bradycardia**

If the SA node discharge rate is slow, the heart rate is slow. ECG is normal in every respect except that the heart rate at rest is below 60 per minute. This is known as sinus bradycardia. It may be normally seen in athletes or abnormality

inpatients having an increased intracranial pressure or hypothyroidism.

- **Sinus Tachycardia**

When the only abnormality is that the heart rate at rest is more than 100 per minute, the condition is known as sinus tachycardia. It may be normally seen in emotional stress or exercise or abnormality in fever, hyperthyroidism or anaemia.

- **Sinus Arrhythmia**

In some adults and most children, there is an increase in heart rate during inspiration and a decrease during expiration. This rhythm is most commonly seen with breathing due to fluctuations in parasympathetic vagal tone. During inspiration, the chest expands creating a suction force that results in greater backflow of blood into the atria from the veins. Greater filling of right atrium results in higher heart rate, possibly by stretching the SA node.

- **Ventricular Fibrillation**

This is a fatal condition in which the heart beats like a bag of worms and the patient may die in a couple of hours, if the action is not taken immediately. You are already aware that the heart beats when electrical signals move through it. In case of ventricular fibrillation, the heart's electrical activity becomes disordered. When this happens, the heart's lower (pumping) chambers contract in a rapid, unsynchronized way. The ventricles "flutter" rather than beat. The heart does not pump sufficient blood to the entire body. The patient has no pulse and the heart is quivering. It may be necessary to give a high voltage DC shock to revive the patient. You may have seen this being done when the doctor places electrodes on the chest to provide electrical shock to jump-start the dying heart.

The action of the defibrillator is based on the principle that a high voltage current throws the entire ventricular musculature into contraction miraculously and simultaneously.

Ventricular fibrillation may be seen in the following two conditions:

l) when a person is electrocuted, and

2) as a consequence of heart attack, myocardial infarction.

There are certain abnormalities caused due to changes in serum electrolyte that influence ECG. We shall learn about these changes next.

Abnormalities due to Changes in Serum Electrolytes

The intracellular and extracellular electrolyte concentration difference is responsible for the resting membrane potential and the electrical activity of all excitable tissues of the body.

Since heart is a large organ made up of excitable tissues, serum electrolyte changes alter its electrical activity and hence the ECG. Serum electrolyte changes may affect life and can be suspected from ECG at an early stage so that the fatal impairment of cardiac function can be avoided. The serum electrolyte changes are discussed next.

## Sodium

A decrease in sodium ion concentration decreases the voltage in ECG. ECG changes are similar to pericarditis or inflammation of the pericardium.

- **Potassium**

An increase or a decrease in potassium ion concentration changes ECG considerably. It affects the depolarization or repolarization of the cardiac muscle. The heart becomes floppy in cases of hyperkalemia (increase in potassium ion concentration).

### Calcium

Hypercalcemia may lead to an increased force of contraction of the heart.

## 4.13 LET US SUM UP

In this unit, we have learnt about the heart and its connecting blood vessels, its structure and functioning of the heart. We have also studied about blood pressure and heart attack and understood the role of exercise and diet in keeping the heart toned and body fit.

## 4.14 GLOSSARY

| | |
|---|---|
| **Atherosclerosis** | : lipid and fat deposition in the walls of the arteries. |
| **Bathmotropic** | : excitability of the cardiac tissue. |
| **Cardiac index** | : the cardiac output per unit body surface area. |
| **Cardiac output** | : the amount of blood pumped by each ventricle per minute. Cardiac output = Stroke Volume x Heart Rate. |
| **Coronary sinuses** | : the vessels that carry venous blood to the heart from its own musculature |
| **Coronary arteries** | : two arteries arising from aorta and supplying nutrition and $O_2$ to heart. |
| **Dromotropic** | : rate of conduction. |
| **Embolism** | : undissolved matter in blood. |
| **Extrasystole** | : an 'extra' contraction due to stimulation of the heart during diastole relative refractory period. |
| **Inotropic** | : force of contraction. |
| **Myocardial ischemia** | : decreased blood supply to the heart. |
| **Parasympathetic** | : system of nerves that decreases the heart rate, rate of conduction and excitability of the heart tissue. |
| **Spasm** | : sudden contraction or narrowing. |

**Sympathetic** : system of nerves that increases the heart rate, force of contraction, rate of conduction and excitability of the heart tissue.

**Sympathetic cholinergic nerves** : these fibers produce vasodilation of blood vessels of skeletal muscles.

**Thrombosis** : Intravascular clotting

**Vagus Nerve** : the X cranial nerve.

## 4.14 CHECK YOUR PROGRESS EXERCISES

UNIT

# 5

# RESPIRATION

**STRUCTURE**



## 5.1 LEARNING OBJECTIVE

After studying this unit, you will be able to:

- illustrate the structure and functions of organs of respiratory system,
- describe the mechanics of respiration, and
- explain the regulation of breathing.

## 5.2 INTRODUCTION

Respiration is the process which deals with the act of respiring or breathing, the act of taking in and giving out air, the aggregate of those processes by which oxygen is introduced into the system and carbon dioxide is removed. This unit will deal with the mechanism of respiration, the respiratory organs and their functions in the body.

## 5.3 ORGANS OF THE RESPIRATORY SYSTEM

The respiratory system consists of various organs. They form a clear pathway for the air to enter and leave the lungs. The body needs a constant supply of oxygen from air and wants to dispose off carbon dioxide, produced as a waste product of cell metabolism. The blood transports oxygen from the lungs to the body cells and returns carbon dioxide from the cells to the lungs for excretion.

A number of organs are involved in the most crucial process of respiration. Can you

name them? Well, the organs of the respiratory system are:

- the nose and the nasal cavity
- the pharynx
- the larynx
- the trachea
- two bronchi
- the bronchioles and small air passages, and
- two lungs and the pleura.

Figure 5.1 illustrates the major respiratory organs. Please note that the mouth isn't considered a "respiratory organ" because it is also a "digestive organ". All of the respiratory organs can be considered to be either upper or lower respiratory tract organs. So. the nose and mouth fit into the upper respiratory tract category, while the larynx down upto lungs, fit into the lower respiratory tract category.

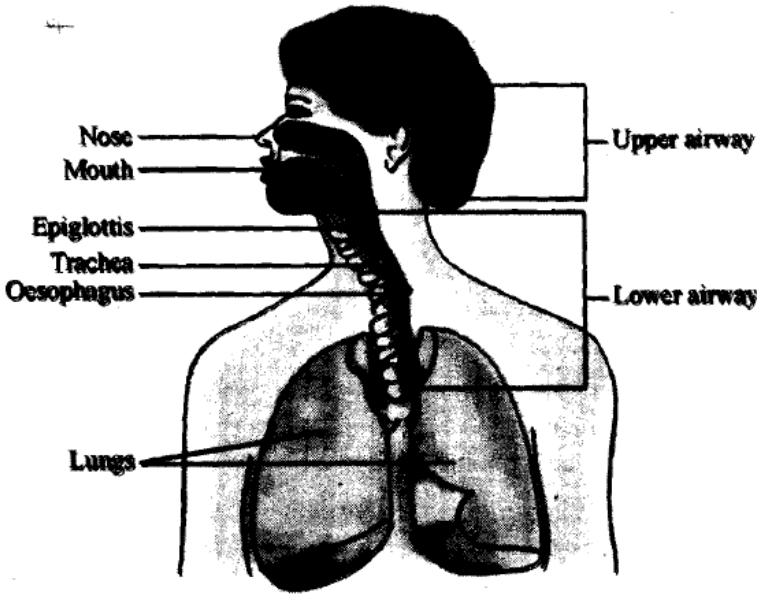



**Figure 5.1: Major respiratory organs**

Now, let us understand the structure and functions of each of these organs in the respiratory process. We shall begin with the nose and the nasal cavity.

## 5.3.1 The Nose and the Nasal Cavity

You would agree that one of the most prominent features of the face is the nose.

The nose is the first of the respiratory organs through which we respire, i.e. inhale oxygen and exhale carbon dioxide. What are the functions ofthe nose? We all are familiar with the functions of the nose. The nose:

- acts as a respiratory passage through which the incoming air passes, and
- warms, moistens and filters the air. The air becomes warm as it passes through the nose. It is moistened by contact with the moist mucous. The air gets filtered because the dust particles and other impurities (in form of particulate matter) stick to the mucous. Hence, nose acts as a filter. The cilia of the mucous membrane waft mucous and the dust particles from the nose towards the throat.

The nose has two nostrils, which serve as the first passageways. The nose is lined with a ciliated epithelium. The air that enters our nostrils runs into a larger opening, called the nasal cavity (posterior to the nose). To the front of the nasal cavity is the nose, while Respiration the back is continuous with the pharynx. The nasal cavity is important in warming and cleaning the air as it is inhaled. The olfactory epithelium lines this nasal cavity. The olfactory epithelium is a specialized epithelial tissue inside the nasal cavity that is involved in smell. The olfactory epithelium, in fact, is a mucous membrane, covered in mucus and ciliated at its apical edge. Any material in the air like dust and bacteiia, which is not useful for our respiratory system, tends to get stuck in the mucus. Therefore, by having mucus coating, our olfactory epithelium, we are able to filter our air before taking it into the lungs. However, once materials begin to accumulate in the mucus, we have to clean the mucus out. That's where the cilia come in. All of the cilia on our mucous membrane sweep mucus toward our pharynx (throat). The mucus is thus moved along into the pharynx (where we swallow it) and new mucus is secreted to cover the mucus membrane.

So briefly we have looked at the structure and functions of the nose and the nasal cavity. Next, we shall read about the pharynx.

## 5.3.2 The Pharynx

Pharynx or the airway of the respiratory system is at the back of the throat, as can be seen in Figure 5.2, through which air passes when one inhales. It acts as a passageway for air from the nasal cavity and/or the mouth to the lungs via the larynx and the trachea, for food and liquids from the mouth to the esophagus. Let us study about its structure and functions. Structure

The pharynx is a cone-shaped tubular section that extends from the mouth and the nasal cavities to the larynx, where it becomes continuous with the oesophagus. Hence, it is common to both respiratory system and digestive system. It is approximately 12 to 14 cm in length. The pharynx is divided into three parts as illustrated in Figure 5.2. These include:

- **The nasopharynx :** it is the part of the upper throat, which lies behind the nose. On its lateral wall are the two openings of the auditory tubes which lead from the nasopharynx to the middle ear. It is lined by a ciliated epithelium.
- **The oropharynx :** it is that part of the pharynx which lies above the oesophagus and is continuous with the mouth extending from below the level

of the soft palate to the level of second cervical vertebra.

- **The laryngopharynx :** it is the lower part of the pharynx which extends from the oro-pharynx above and continues as the oesophagus below, i.e. from the level of the second to the sixth cervical vertebra.

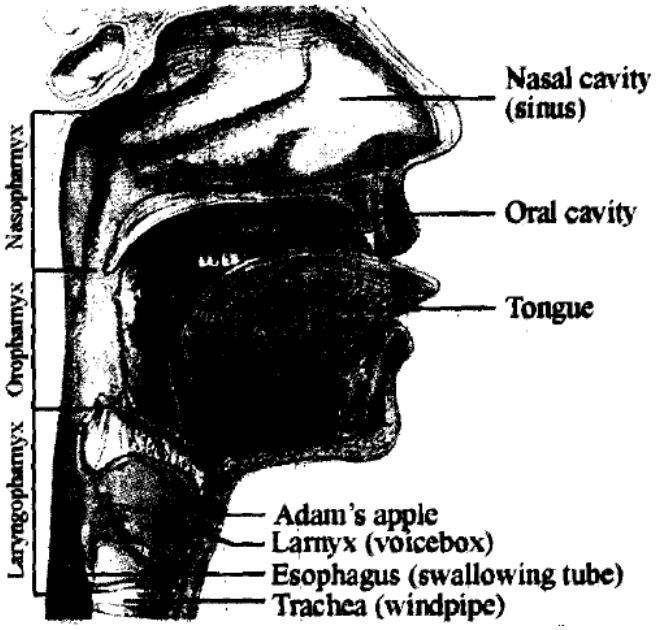



**Figure 5.2: The three parts of the pharynx**

Both oropharynx and laryngopharynx are lined by stratified squamous epithelium. The pharynx is composed of three layers of tissues. The mucous membrane lines the pharynx. The intermediate layer consists of fibrous tissue. The muscle layer is the outermost layer consisting of muscles known as the constrictor muscles of the pharynx. What is the role of the pharynx in our body? Let's find out. Functions

The functions are listed herewith:

- Both air and food pass through the pharynx.
- Air is further warmed up and moistened as it passes through the pharynx.
- As auditory tubes pass between the nasopharynx and middle ear, air passes through these tubes to the middle ear.

From the pharynx we move on to the larynx.

## 5.3.3 TheLarynx

The larynx or voice box is an organ in the neck that plays a crucial role in speech and breathing. The larynx is the portion of the trachea that contains the vocal cords i.e. the voice box. It is the primary organ of voice production. The vocal cords are the upper opening into the windpipe (trachea), the passageway to the lungs. This structure also separates the airway from the breathing tube while swallowing by closing.

Until puberty, there is a little difference in the size of the larynx in males and

females. But after puberty, there is a considerable enlargement in the males. What is the larynx made up of? Let's get to know its structure.

## Structure

NOTES

The larynx is a cylindrical grouping of cartilage, muscles and soft tissues attached to each other by ligaments and membranes which contains the vocal cords and the structures which help to produce sound. The framework of the larynx is made up of the thyroid cartilage as shown in Figure 5.3. The anterior portion of the thyroid cartilage can be easily felt in thin necks as the "Adam's apple". Try feeling this, in the neck.

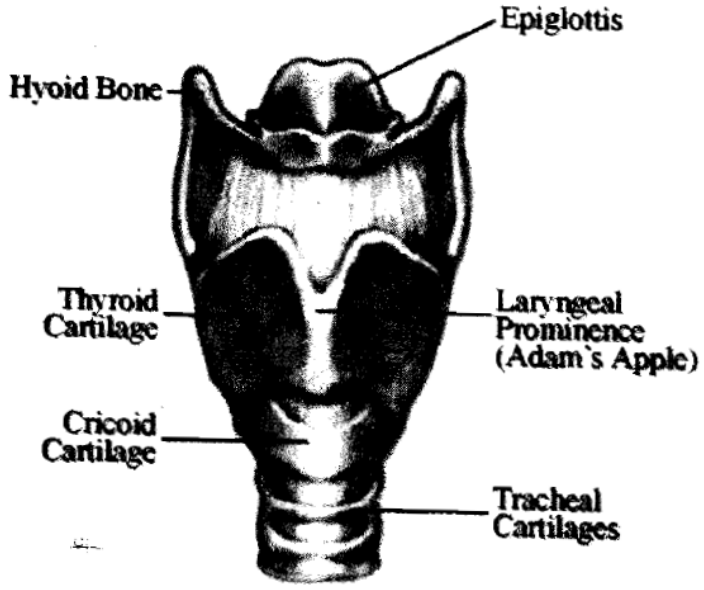



**Figure 5.3: Structure of larynx**

Coming to the vocal cords, these are the muscular bands covered by a thin layer called mucosa. There is a right and left cord, forming a "V" when viewed from above. The vocal cords extend from the root of the tongue to the trachea.

What is the role of larynx? Because of its location, the larynx has many functions to perform. These are listed next:

## Functions

The larynx perform the following functions:

- Control of the airflow during breathing. It ensures the passage of air from the pharynx to the trachea.
- Protection of the airway. Air is filtered, moistened and warmed here.
- Production of sound for speech. It ensures voice production due to the presence of vocal cords.
- It facilitates swallowing of food.

Above the larynx, if you look carefully at Figure 5.3, you will see a flexible

structure made up of cartilage called the epiglottis. When we swallow, the larynx, the epiglottis, and the vocal cords all close as much as possible to prevent food from getting into the lungs.

Next organ in the respiratory system is the trachea, about which we shall learn next.

### 5.3.4 The Trachea

The trachea better known as the windpipe, is a continuation of the larynx. It is in the front of your neck and is very hard with tough rings around it. Feel the front of your neck. Can you feel your trachea?

It is the tube that extends from the oral cavity into the chest (the fifth thoracic vertebra), where it branches into 2 major bronchial tubes (right and left bronchi) as can be seen in Figure 5.4. Let us now study about its structure and composition.

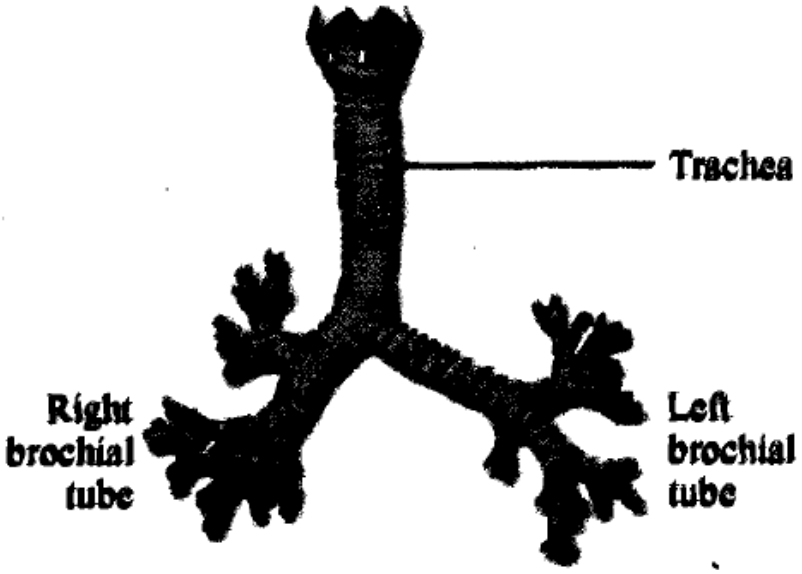



**Figure 5.4: The trachea**

### Structure

Trachea is composed of C-shaped hyaline cartilages (a type of connective tissue) joined together by the muscle tissues that conveys inhaled air from the larynx to the bronchi. The outer surface of the trachea is composed ofa fibrous tissue and an elastic tissue. They enclose the cartilages. The middle layer is again composed offibrous tissue lined with areolar tissue. It contains blood vessels, nerves and lymphatics. The inner lining is composed of ciliated epithelial cells and goblet cells. Goblet cells are the epithelial cells that secrete mucus.

Like the larynx, the trachea too performs the function ofpassage of air as highlighted in the functions herewith.

### Functions

The trachea:

- ensures the passage of air from the larynx to the bronchi, and
- warms, moistens and filters the air as it passes through the trachea.

We have seen above that the trachea branches into the right and the left bronchi. Let us learn about the bronchi next.

NOTES

## 5.3.5 The Bronchi

The trachea, as shown in Figure 5.4, is divided into left and right bronchi at about the level of 5th thoracic vertebra. Let us now study about the characteristic features and functions of the bronchi.

### Structure

The bronchi are composed of less well-defined cartilages. The bronchi are lined with a ciliated epithelium.

The right bronchus is a wider and shorter tube. It is approximately 2.5 cm in length. After entering the right lung, it divides into three branches, as illustrated in Figure 5.4, one of which passes to each lobe. Each branch is subdivided into numerous small branches. The left bronchus is narrower and longer than the right. It is about 5 cm in length. After entering the lung, the left bronchus divides into two branches, one of which goes to each lobe. Each branch is then subdivided into numerous small branches. The further subdivisions of the bronchi will be considered in the next section. We shall look at the function performed by these bronchi, next.

### Function

Air passes through the bronchi to reach the bronchioles. This is the main function of bronchi.

## 5.3.6 The Bronchioles and Smaller Air Passages

Bronchioles are the smaller branches or the sub-division of the bronchi, as illustrated in Figure 5.5, which connect to the alveoli or the air sacs. In simple terms, bronchiole is a tiny branch of air tubes in the lungs. Let us see now what is the structure and composition of these.

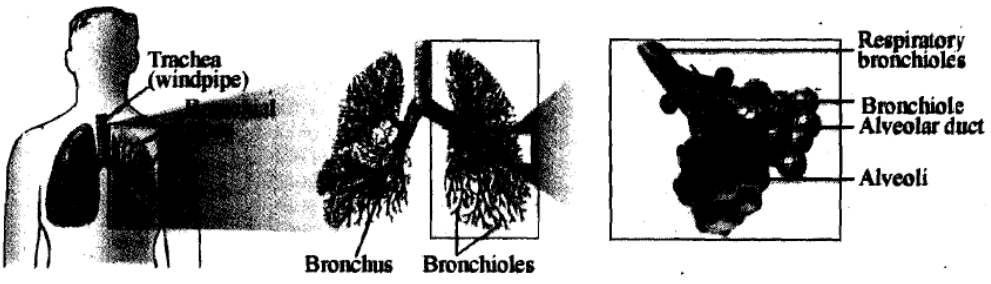



**Figure 5.5: The bronchioles and the alveoli**

## Structure

The bronchioles have a diameter of about 1 mm. The bronchioles contain no cartilage. They are composed of muscle tissue, fibrous tissue and elastic tissue with the innermost lining of ciliated columnar epithelium. As the tubes become smaller, the columnar epithelial cells are replaced by a single layer of flattened epithelial cells. Fibrous tissue and muscle tissue disappears.

The minute bronchioles, known as the terminal bronchioles divide to form respiratory bronchioles. These respiratory bronchioles again divide to form alveolar ducts. The alveolar ducts open into minute sac-like structure called as alveoli, as shown in Figure 5.5, in which the exchange of oxygen and carbon dioxide takes place. In the alveoli, interchange of gases takes place between the air in the alveoli and the blood in the capillaries.

Like the bronchi, the function of the bronchioles is also to aid in air passage.

Next, let us get to know about the lungs.

### 5.3.7 The Lungs and the Pleura

Lungs are a pair of two spongy organs, as can be seen in Figure 5.5, contained within the chest and are responsible for the respiration and the delivery of oxygen into the bloodstream.

Let us get to know the structure of this important organ.

### Structure of lungs

There are two lungs in our body. They are situated in the thoracic cavity separated from each other by the heart. They extend from the root of the neck above to the diaphragm below as can be seen in Figure 5.6. Diaphragm is a dome-shaped muscle that works with our lungs to allow us to inhale (breathe in) and exhale (breathe out) air. Lungs are roughly conical in shape, as can be seen in Figure 5.6.

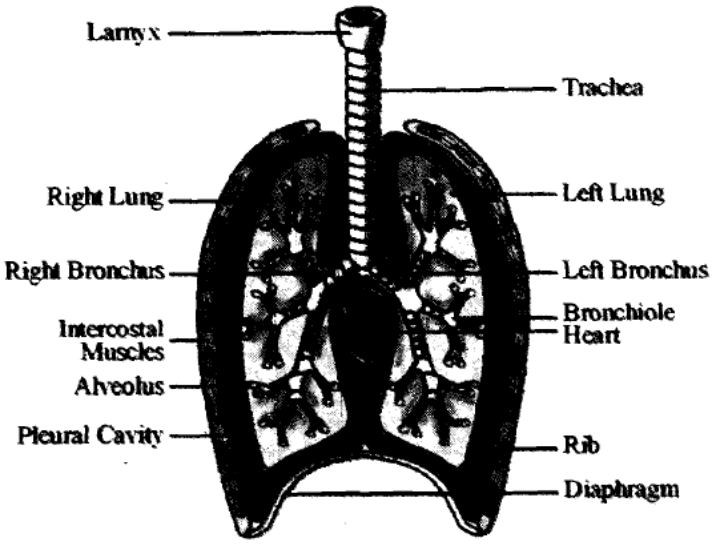



**Figure 5.6: The lungs and the pleura**

Look at Figure 5.7. You would have noticed that the right lung is divided into three distinct lobes: superior (upper), middle and inferior (lower). The left lung is divided into two lobes: superior (upper) and inferior (lower).

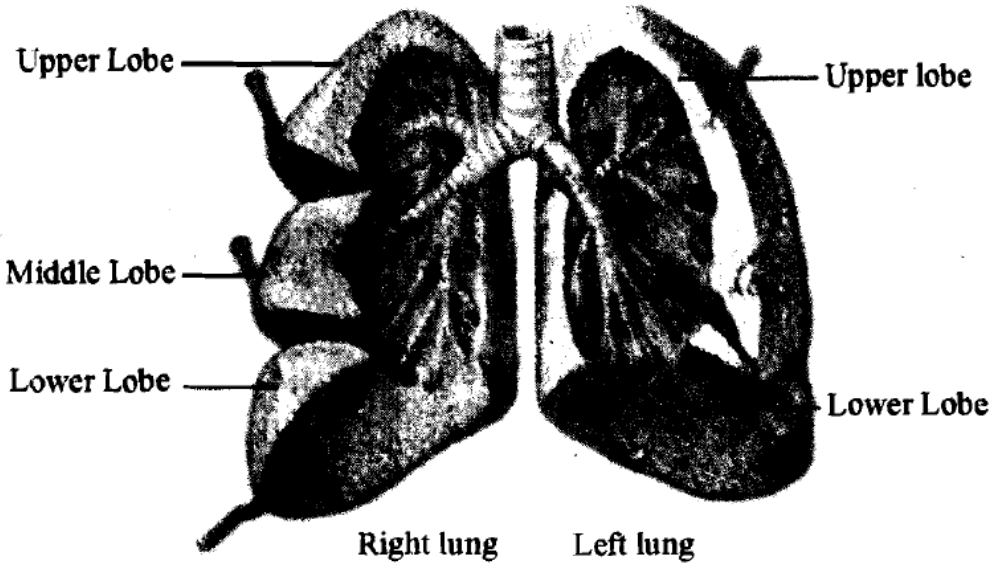



**Figure 5.7: Structure of the lungs**

The lungs are composed of the bronchi, bronchioles, alveolar ducts and alveoli as you have seen in Figure 5.6. We learnt that in chest cavity, the trachea splits into two small tubes called bronchi. Each bronchus then divides again into still smaller tubes called bronchioles, and finally end in the grapelike clusters of alveolar sacs. There are around 70 million alveoli in each lung. These are the tiny air sacs. It is here that oxygen enters the blood and carbon dioxide leaves it. The alveolar sacs are surrounded by a dense network of pulmonary capillaries, which are minute branches of the pulmonary artery transporting venous blood to the lungs.

The bronchioles, alveolar ducts and alveoli constitute the lobules of the lungs. These lobules are separated by areolar elastic tissue. Surrounding the lungs are two thin membranes known as the pleura, the space between the two layers is known as the pleural cavity as can be seen in Figure 5.6. We shall learn about the pleura in greater details in a little while from now.

In Unit 4, we learnt that the pulmonary artery, that is, a blood vessel delivering oxygen-poor blood from the right ventricle to the lungs, divides into left and right branch. The left branch supplies deoxygenated blood to the left lung and the right branch supplies deoxygenated blood to the right lung. The branches of pulmonary artery are again divided into many branches. They ultimately form a capillary network in the walls of the alveoli. The exchange of gases takes place between the air in the alveoli and blood in the capillaries. The pulmonary capillaries join up to form two main pulmonary veins which convey oxygenated blood to the left atrium of the heart. Having understood the structure of the lungs, it would not be difficult to visualize the functions of the lungs. The functions are

listed next.

### Functions of lungs

The main functions of lungs include:

- exchange of gases ($O_2$ and $CO_2$) between the alveoli of lungs and capillary network around them, and
- expand to take in air and then contract to expel it.

Now let us get a deeper insight into the structure and function of pleura. Pleura, as seen in Figure 5.6, is a membrane surrounding the outer surface of the lungs and the inner surface of the chest wall and the diaphragm. Let us see what it is composed of.

### Structure of Pleura

The serous membrane that covers the lung and the wall of the chest cavity to protect and cushion the lungs is called the pleura. The pleura are composed of flattened epithelial cells. Pleura are composed of two layers of membrane.

These are:

- **The parietal pleura:** It lines the walls of the chest cage and covers the upper surface of the diaphragm. It lines the ribs, sternum, costal cartilages and the internal intercostal muscles and covers the superior surface of the diaphragm.
- **The visceral pleura;** It is firmly attached to the lung itself, completely covering its surfaces and passing into the fissures which divides the lung into lobes.

In the normal condition, the parietal pleura and the visceral pleura are in close contact. There is a potential space between the two layers termed as pleural cavity shown in Figure 5.6. This space is filled with a serious fluid secreted from the epithelial cells of the membrane. This fluid prevents friction between these two layers. Interpleural pressure helps in the expansion of the lungs and is always negative.

With this, we come to an end of our study of the different organs of the respiratory system. Let us take a break here and recapitulate what we have learnt so far.

## 5.4 THE MECHANICS OF RESPIRATION

The process of respiration can be well understood by studying the mechanic of respiration. This can be explained through a respiratory cycle which consists of three phases:

**a) Inspiratory phase:** In inspiratory phase, there is an inhalation of air. It is an active process because it is the result of muscle contraction. It is partly voluntary and partly involuntary.

**b) Expiratory phase:** In expiratory phase, there is an exhalation of air. It is a passive process because in this phase, the diaphragm and the intercostal

muscles relax and the lungs recoil.

**c) Pause:** After expiration, there is a short pause.

Have you ever thought how the respiration cycle is performed? Well, it is performed with the help of the muscles. The muscles involved in respiration include intercostal muscles (external and internal intercostal muscles), the diaphragm and the abductor muscles in the larynx. Let us study how each of these muscles help in respiration. We shall begin with the intercostal muscles.

**A) The intercostal muscles:** Look at Figure 5.6. Can you spot the intercostal muscles? Yes, there are II pairs of intercostal muscles. The intercoastal muscles are the muscles between the ribs which contract during inspiration to increase the volume of the chest cavity. They are located in the spaces between the ribs. They are arranged in two layers called the external intercostal muscles and the internal intercostal muscles.

The external intercostal muscle fibres extend in a downward and forward direction from the lower border the rib above to the upper border of the rib below.

The internal intercostal muscle fibres extend in a downward and backward direction from the lower border of the rib above to the upper border of the rib below. They cross the external intercostal muscle fibres at right angles. The intercostal muscles are stimulated to contract by intercostal nerves.

During inspiration, the intercostal muscles contract. They move upwards and outwards causing enlargement of the thoracic cavity as shown in the Figure 5.8.

During expiration, the volume of thoracic cavity is decreased by relaxation of diaphragm and intercostal muscles which results in increase in thoracic pressure and pressure of lungs. As a result, air is expired from lungs to the atmosphere.

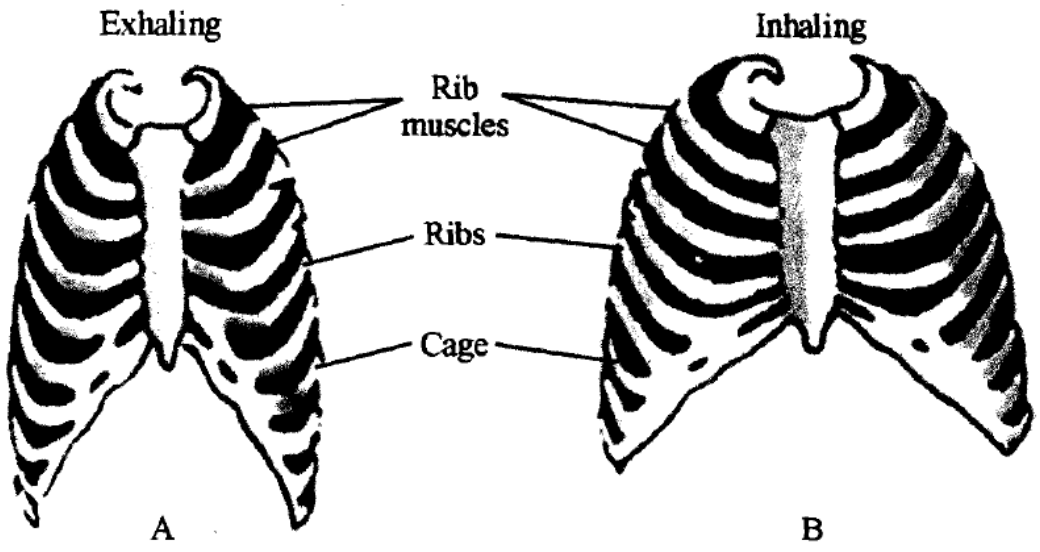



**Figure 5.8: The exhaling and inhaling process**

Next, let us see what the structure of diaphragm is and what is the role of, diaphragm muscles in the respiratory process.

**B) The diaphragm :** The diaphragm is a muscular membranous partition

separating the abdominal and thoracic cavities (refer to Figure 5.6) and functioning in respiration. It consists of a central tendon from which the muscle fibres radiate.

When the diaphragm contracts, its muscle fibres shorten and the central tendon is pulled downwards. Thus, the thoracic cavity is enlarged in length. The diaphragm is supplied by phrenic nerves. Phrenic nerves are a pair nerves that arises from cervical spinal roots and passes down the thorax to innervate the diaphragm and control breathing.

The muscles of the diaphragm and the intercostal muscles contract simultaneously.

Thus, the thoracic cavity is enlarged in all directions (antero-posterior and vertical).

Next, let us study about the third set of muscles involved in respiration, i.e., abductor muscles.

**C) Abductor muscles :** Abductor muscle is a muscle that serves to draw a part out, or from the median line (as the abductor oculi, which draws the eye outward). Abductor muscles in the larynx contract in the beginning of inspiration, pulling the vocal cords apart. The epiglottis is opened. Epiglottis, as you already know, is the vocal apparatus of the larynx, the true vocal folds and the space between them where the voice tone is generated. But during the stage of swallowing, contraction of the abductor muscles closes the epiglottis and prevents the aspiration of food into the lungs.

So you can visualize how important these three muscles, described above, are in the process of respiration. The three muscles, together, help in the respiration process.

Next, let us study what are the changes that take place in the lungs during the process of respiration.

Changes in lungs during respiration: In inspiration (when we breathe in air), the thoracic cavity (i.e. the cavity in the vertebrate body enclosed by the ribs between the diaphragm and the neck and containing the lungs and heart) is increased by the simultaneous contraction of intercostal muscles and the diaphragm.

The parietal pleura (the part of pleura attached to the inner wall of the thorax and to the diaphragm) moves with the walls of the thorax and the diaphragm. The visceral pleura (the part of pleura attached to the lungs) follows the parietal pleura. This reduces the pressure in the pleural cavity to a level considerably lower than the atmospheric pressure.

The lungs are stretched and pressure within the alveoli is reduced. This causes the air to come to the lungs in an attempt to equalize the atmospheric and alveolar air pressure.

During expiration (when we breathe out), when the diaphragm and the intercostal muscles relax, the thoracic cavity is reduced in size. The lungs recoil and expiration occurs.

The discussion above focussed on the mechanics of breathing. Do you know what is the normal rate of breathing in adults ? Read the next section and find out.

The rate and depth of breathing: Do you know what the normal rate of breathing in adults is and what are the factors on which it depends? Well, the normal rate of respiration in adults is 14-18 per minute. The rate and depth of breathing vary depending upon the health, physical activity and emotional state of the individual. The amount of air which enters or leaves the lungs varies in association with the changes in the depth of respiration. In normal breathing, the intercostal muscles and the diaphragm are involved, but in deep breathing, accessory muscles of respiration are involved. These muscles include sterno-mastoid, the pectoralis major (a skeletal muscle that adducts and rotates the arm) and the platysma (either of the two broad muscles located on the either side of the neck and innervated by the facial nerve, it extends from the lower jaw to clavicle and is involved in the movement of the mouth and jaw). Contraction of these muscles increases the capacity of the thoracic cavity.

In this section, we have learnt about the mechanics of respiration. We have seen how the air passes in and then exhaled out. During this process, there is volume of air in the lungs, what we call pulmonary volumes. Let us read more about this concept and the terminology used in this context.

## 5.5 PULMONARY VOLUMES

Pulmonary volumes are the volume of gases in lungs under different conditions of respiration. There are different terms associated with each of these conditions. Let us get to know them.

- **Tidal Volume (TV):** It is the volume of air that is taken in or given out during quiet breathing. The volume is about 500 ml.
- **Inspiratory Reserve Volume (IRV):** It is the volume of air that can be taken in by forceful inspiration over and above the tidal volume. It varies from 2000 to 3,300 mi.
- **Inspiratory Capacity (IC) :** It is the tidal volume and the volume of air taken during maximum inspiratory effort. It is about 3500 ml.
- **Expiratory Reserve Volume (ERV):** It is the volume of air that can be breathed out by forced expiration after normal expiration. It is about 1000 ml.
- **Residual Volume (RV) :** It is the volume of air that remains in the lungs after maximal expiration. The average volume is about 1200 ml.
- **Functional Residual Capacity (FRC):** It is the volume of air or gas remaining in the lungs after a normal expiration. It varies from 2500 ml to 3000 ml. It is the sum of the residual volume and expiratory reserve volume.
- **Total Lung Volume (TLV) or Total Lung Capacity (TLC) :** It is the volume of air remaining in the lungs after a maximal inspiration. It is the sum of the vital capacity and residual volume. It is about 5000 ml to 6000 ml
- **Vital Capacity (VC) :** It is the volume of air that can be breathed out by forced expiration, after taking forced inspiration. It is about 4800 ml in males and 3100 ml in females.

- **Dead Space:** It is the amount of air locked up in the respiratory passages, i.e. the pharynx, trachea and bronchi. The air in these spaces is not available for gaseous exchange. It is called as anatomical dead space or in other words, it is the volume of the conducting airways from the external environment (at the nose and mouth) down to the level at which the inspired gas exchanges oxygen and carbon dioxide with pulmonary capillary blood. The volume of the dead space amounts to about 150 ml.

The terms defined above are general terms and you would come across these terms during your study and practice of dietetics.

Next, after learning about the process of respiration, we shall move on to studying about the interchange of gases within the lungs.

## 5.6 INTERCHANGE OF GASES WITHIN THE LUNGS

The interchange of gases within the lungs takes place between the process of inspiration and expiration. You already know that the act of inhaling, the drawing in of air (or other gases) as in breathing is inspiration. On the other hand, the act or process of breathing out, or forcing air from the lungs through the nose or mouth is expiration.

This exchange of gases occurs between the blood in the capillary network which surrounds the alveoli and the air in the alveoli of lungs. Alveoli, you learnt earlier, are a small sac-like structural unit of the lung where oxygen is exchanged for carbon dioxide.

In physical chemistry, you have studied that gases always exert pressure upon the wall of their container and gases always tend to diffuse from a higher partial pressure to a lower partial pressure i.e. down the concentration gradient. Air, as you might already know, is a mixture of gases. Its approximate composition is given in Table 5.1.

| Constituents of Air | Percentage |
|---|---|
| Oxygen | 21 |
| Carbon dioxide | 0.04 |
| Nitrogen | 78 |
| Other gases | 1 |

**Table 5.1: Composition of air**

Each one of the above mentioned gases found in the air exerts a part of total pressure. This depends upon its concentration in the mixture. The proportion of total pressure provided by each gas is called its partial pressure. If the atmospheric pressure at sea level is 760 mm mercury (mm Hg) then,

$$\text{Partial pressure of oxygen } (pO_2) = \frac{21}{100} \times 760 = 160 \text{ mm Hg}$$

$$\text{Partial pressure of carbon dioxide } (pCO_2) = \frac{0.04}{100} \times 760 = 0.3 \text{ mm Hg}$$

and so on.

During inspiration and expiration, the lungs and respiratory passages are always filled up with air. The inspired air is mixed with the air in the lungs and the net result is that the p02 and pC02 remain fairly constant. Oxygen diffuses from the alveoli to the blood. Carbon dioxide diffuses from the blood to the alveoli. The blood in the capillaries flows slowly. Oxygen and carbon dioxide get sufficient time to interchange.

By this mechanism, oxygen is absorbed in blood and carbon dioxide is removed from the blood. The composition of expired and inspired air is therefore different as highlighted in Table 5.2.

| | Inspired air (%) | Expired air (%) |
|---|---|---|
| Oxygen | 21 | 17 |
| Carbon dioxide | 0.04 | 4.404 |
| Nitrogen | 78 | 78 |
| Inert gases | 1 | 1 |

**Table 5.2: Approximate composition of expired and inspired air**

Next, let us look at the various routes of oxygen and carbon dioxide transport. Let us start with transport of oxygen.

## 5.6.1 Transport of Oxygen

You may recall reading earlier that oxygen is carried in two ways by the blood — by the plasma and by the red blood cells. Let us learn how.

- **By Plasma:** At a tension of 100 mm Hg, 0.3 ml oxygen is dissolved in every 100 ml of blood. This small volume is negligible as far as the oxygen supply to the tissues is concerned, but is important in determining the oxygen tension gradient from the plasma to the tissues, upon which diffusion depends.
- **By Red Blood Cells:** Oxygen combines with haemoglobin, i.e., the red pigment in red blood cells. It combines with oxygen in the lungs, transports it around the body and releases the oxygen to cells that need it to form oxyhaemoglobin. Haemoglobin, you may already know, is a protein made up of 4 subunits, each of which contains a heme moiety attached to a polypeptide chain. Heme, is a complex made up ofa porphyrin and one atom of ferrous iron. Each of the 4 iron atoms can bind reversibly one oxygen molecule. The iron remains in the ferrous form and the resulting combination with oxygen is known as oxygenation. The entire process can be represented as:

$$Hb_4 + O_2 \text{—} Hb_4O_2$$

NOTES

$$Hb_4O_2 + O_2 - Hb_4O_4$$
$$Hb_4O_4 + O_2 - Hb_4O_6$$
$$Hb_4O_6 + 0_2 - Hb_4O_8$$

$Hb_4$ stands for haemoglobin and 02 stands for oxygen.

The tension of oxygen in the arterial blood is about 90 -100 mm Hg and oxygen tension in the tissues is less than 40 mm Hg. When the arterial blood passes through the tissues, it carries oxyhaemoglobin. As the oxygen tension in the tissues is much lower, oxygen tension in the arterial blood falls. The oxyhaemoglobin in the red blood cells is exposed to low tension of oxygen, it dissociates and oxygen leaves the blood stream and enters the tissue. The equilibrium of oxyhaemoglobin and nonbonded haemoglobin at various partial pressures can be best studied through a oxygen dissociation curve, discussed next.

Oxygen dissociation curve: When different partial pressures of oxygen are plotted against the amount of oxyhaemoglobin formed or dissociated, the sigmoid curve is obtained, as shown in Figure 5.9 which is called as oxygen dissociation curve.

The oxygen dissociation curve is a graph (Figure 5.9) that shows the percent saturation of haemoglobin at various partial pressures of oxygen. The purpose of an oxygen dissociation curve is to show the equilibrium of oxyhaemoglobin and nonbonded haemoglobin at various partial pressures. At high partial pressures ofoxygen, usually in the lungs, haemoglobin binds to oxygen to form oxyhaemoglobin. When the blood is fully saturated, all the erythrocytes are in the form of oxyhaemoglobin. As the erythrocytes travel to tissues deprived of oxygen, the partial pressure of oxygen will decrease. Consequently, the oxyhaemoglobin releases the oxygen to form haemoglobin.

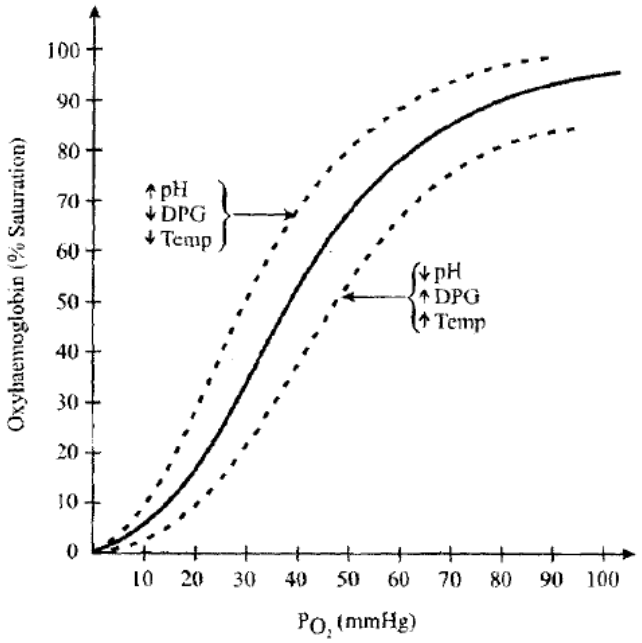



**Figure 5.9: Oxygen dissociation curve**

The degree of oxygen dissociation depends upon the oxygen tension, carbon dioxide tension, hydrogen ion concentration, strength of haemoglobin solution and temperature.

Oxygen dissociation curve is shifted towards the right during the rise of temperature or increase in the red cells of 2, 3 — diphosphoglycerate (DPG) or the fall of plasma pH, with the dicrease in pH showing decreased affinity of haemoglobin for oxygen as can be seen in Figure 5.9.

Foetal haemoglobin (haemoglobin in the foetus) has got a greater affinity for oxygen than the adult haemoglobin at low $pO_2$. So, the oxygen dissociation curve of foetal haemoglobin is shifted towards the left.

Now, let us look at the other aspect i.e. the transport of carbon dioxide.

## 5.6.2 Transport of Carbon Dioxide

Carbon dioxide is carried in the blood in three ways — in solution, in combination with protein, and as bicarbonate. We shall look at each of these mechanisms one by one. In solution: Carbon dioxide is a more soluble gas than oxygen. Its amount in solution is proportional to the tension. At a tension of 40 mm Hg, 3 ml carbon dioxide dissolves in every 100 ml blood. Carbon dioxide in solution forms carbonic acid, which ionizes at blood pH into hydrogen and bicarbonate ions as shown herewith.

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

- **In combination with protein:** Carbon dioxide forms a neutral carbamino compound with haemoglobin. It gombines with the haemoglobin in the red blood cell at a different site from that at which the oxygen combines. The oxygen combines with the iron haem radical, the carbon dioxide combines with the amine group of the protein forming carbamino groups with fully reduced haemoglobin. 8 ml ofcarbon dioxide is carried as carbamino by 100 ml of blood.
- **As bicarbonate :** The maximum portion of carbon dioxide in the blood is in the form of bicarbonate — sodium bicarbonate in the plasma and potassium bicarbonate in the red blood cells.

As the blood passes through the capillaries, bicarbonate (HCOA ) ions diffuse into the plasma. The protein anions cannot cross the cell membrane, sodium and potassium do not diffuse freely. Electrochemical neutrality is maintained by diffusion of chloride into the red cells. This phenomenon is known as chloride shift.

In the arterial blood, 3 ml carbon dioxide percent are in solution, 3 ml as carbamino and 42 ml as bicarbonate, making a total 48 mt carbon dioxide in blood. So the blood leaves the lungs and arrives at the tissues carrying 48 ml carbon dioxide per 100 ml of blood at a tension of 40 mm Hg. It leaves the tissue and arrives at the lungs carrying 52 ml carbon dioxide per 100 ml of blood at a tension of46 mm Hg. The three forms Of carbon dioxide are carried by the blood and they interact to form the total carbon dioxide ($CO_2$) dissociation curve as shown in Figure 5.10. The carbon dioxide dissociation curve is plotted as carbon dioxide absorbed in 100 ml of blood against the partial pressure of carbon dioxide.

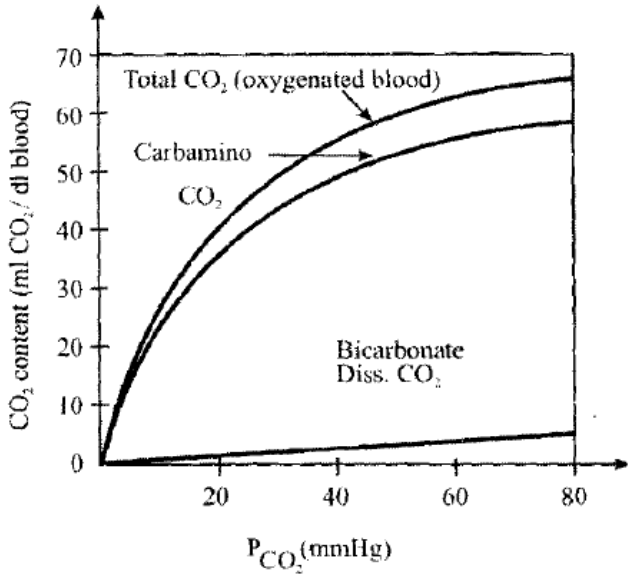



**Figure 5.10: Carbon dioxide dissociation curve**

As the carbon dioxide tension is increased, the total amount of carbon dioxide taken up by blood also rises. At any given carbon dioxide tension, the reduced blood takes up larger amount of carbon dioxide than oxygenated blood.

## 5.7 REGULATION OF RESPIRATION

We have studied the process of respiration above. You would have realized that it is a rhythmic process. The basic rhythm of breathing is controlled by respiratory centers located in the medulla and pons of the brainstem. Pons is a neural structure linking the medulla oblongata and the cerebellum with the mid brain as can be seen in Figure 5.11. Medulla is a white fatty substance that forms a medullary sheet around the axis cylinder of some nerve fibres. Within the medulla, a paired group of neurons known as the inspiratory center or the dorsal respiratory group, sets the basic rhythm by automatically initiating inspiratibn. The inspiratory center sends nerve impulses along the phrenic nerve to the diaphragm and along the intercostal nerves to the external intercostal muscles which continue for a period of about 2 seconds. This stimulates the inspiratory muscles to contract, initiating inspiration. The inspiratory center causes the phrenic nerve to stop firing for about 3 seconds, which allows the muscles of respiration to relax. The elastic recoil of the lungs and chest wall leads to expiration.

The rhythmic process of respiration is a well-coordinated and regulated activity. The control of respiration is partly neural and partly chemical. Neural and chemical controls are linked together. Let us study about each of these controls. We shall begin with the neural control or the nervous control over the respiratory process.

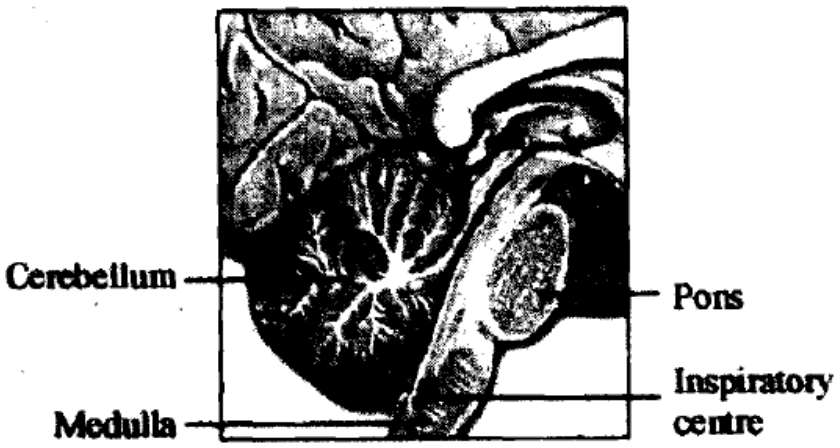



**Figure 5.11: Structures of pons and medulla**

## 5.7.1 Neural Control of Respiration

Neural control of respiration originates in the respiratory center, as you learnt above, and signals are transmitted through the phrenic nerves to excite the diaphragm. This excitation produces contraction of the diaphragm, expansion of the chest wall and lung, and an increase in airway pressure, flow and volume. Direct monitoring of the phrenic nerve is not possible, but the neural method monitors electrical signals to the diaphragm. These signals represent neural drive to the diaphragm and are a proxy for phrenic nerve activity.

There are two neural mechanisms which control respiration:

1) Voluntary system

2) Automatic system

What are these systems? Let's find out.

- **Voluntary system:** The centre for the voluntary system is located in the cerebral motor cortex, i.e., a part of the brain that is situated in frontal lobe. The cerebral motor cortex in the precentral gyrus consists of a collection of nerve cell bodies. We will learn about this region later in Unit 9. The cerebral motor cortex sends impulses to the respiratory motor neurons via the corticospinal tracts (CST). The CST is a direct link from cerebral cortex to the spinal cord and is involved with the precise and skilled movements of the extremities (hand and foot). It deals with the contraction of individual muscles and is the pathway for the selection of the prime movers for any muscular activity.
- **Automatic system:** The automatic centres are located in the medulla and the pons. The motor out flow from this system goes to the respiratory motor neurons located in the lateral and ventral portions of the spinal cord, which is a part of the central nervous system extending from the base of the skull through the vertebrae of the spinal column. It is continuous above with the brain stem and is involved in carrying the information from the body's nerves to the brain and signals from the brain to the body.

Now let us get to know more about the centres and their functions in regulating

the mechanism of respiration.

- **Medullary centre:** The respiratory centre is a collection of highly specialized cells situated in the medulla oblongata which are essential to normal respirations. There are two groups of neurons — the dorsal group and the ventral group as you can see in Figure 5.12. The dorsal respiratory group is the source of rhythmic drive to the phrenic neurons. The ventral group has two divisions — the cranial division and the caudal division. The cranial division is made up of neurons that innervate the accessory muscles of respiration. The caudal division is made up of neurons that provide the inspiratory and expiratory drive to the motor neurons supplying the intercostal muscles.

The respiratory centre consists of two main parts — inspiratory centre and the expiratory centre. The inspiratory centre is dominant. A reciprocal relationship exists between these two parts. When the inspiratory muscles are active, expiratory muscles are inhibited.

The respiratory centre initiates nerve impulses which pass out from the brain in the phrenic nerves to the diaphragm and intercostal nerves to the intercostal muscles. These impulses stimulate the muscles to contract. This increases the capacity of the thoracic cavity and inspiration occurs. A second group ofneurons in the medulla, the expiratory center appears to function mainly during forced expiration, stimulating the internal intercostal and abdominal muscles to contract.

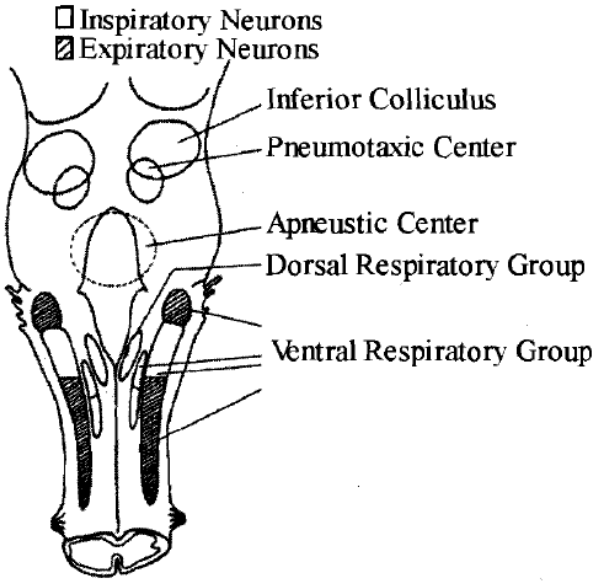



**Figure 5.12: The medullary centre**

- **Pontinecentre:** The rhythmic discharge of the neurons in the respiratory centre is modified by centers in the pons (apneustic and pneumotaxic centre) as seen in the Figure 5.11 Activity in these centers determines the depth of inspiration.

If the vagus nerves and the inferior portion of the pons (connection between these two pontine centers) are destroyed, the inspiratory neurons discharge continuously

and there is a sustained contraction ofthe inspiratory muscles. This arrest of respiration in inspiration is called apneusis. The area in the pons responsible for apneusis is called the apneustic centre. The area in the pons that prevents apneusis is called pneumotaric centre. This area is situated in the upper pons as you would have noticed in the Figure 5.12. It controls the exaggerated activity of the apneustic centre and produces a rhythmical respiratory activity.

The exact function of the pontine respiratory centre is not clear. But they determine the depth and make the rhythmic discharge of the medullary neurons smooth and regular.

There are certain other factors which are involved in the nervous regulation of respiration.

Let us have a look at each of these.

Role of other factors

- **The vagus nerve:** The rhythm and depth of respiration are controlled by the reflexes from the vagus nerve. When the lungs are inflated, there is an arrest of inspiration.

1) When lungs are deflated, the opposite effect is observed. This reflex is called 'Hering-Breuver reflex'. When both the vagus nerves are cut, respiration becomes slow. But if the central cut end of the vagus nerve is stimulated, then the respiration becomes more or less normal. From this experiment, it can be suggested that sensory impulses through the vagus nerve help to make the respiration normal.
2) It was also observed that if the vagus nerve were cooled to 0oc, inflation of lungs did not cause inhibition of respiration. But if vagus nerve was warmed, inflation of lungs did not inhibit the respiration. This later effect is called paradoxical reflex of head.
3) Vasomotor centre and cardio-inhibitory centre: The vasomotor centre (in the medulla ablongata) excites the respiratory centre. The pulmonary ventilation is increased. The factors which stimulate respiration may excite the vasomotor centre simultaneously. Cardio-inhibitory (which restrains the action of heart) centre inhibits the respiratory centers. Hence, during respiration, heart rate and BP may vary.

During inspiration, there is usually a rise in the heart rate and BP.

Reflex actions: Certain reflex actions are associated with the respiratory process. These are:

- **Cough reflex:** Cough reflex causes cough due to irritation of some receptors in u-acheo-bronchial tree. It is a protective reflex. The irritation may occur in the vagal sensory nerve endings of the larynx, trachea etc. Chemically induced coughing occurs due to inhalation of gas. Cough, either mechanically or chemically induced, is a sudden forcible expiratory' act.
- **Hiccup:** It is also a reflex associated with stimulation of sensory endings in the gastrointestinal tract or other tissue through irritation. It is a sharp sound of inhalation with spasm of the epiglottis and diaphragm.

- **Sneezing:** This reflex is an involuntary, sudden, violent and audible expulsion of air through the mouth and nose. Usually irritation of the nasal mucosa produces this reflex.
- **Yawning:** It is a deep inspiration drawn through open mouth. Low oxygen tension in the blood may be the cause of yawning.

From our discussion above, it must be clear that conveyor system (central vascular system) and ventilatory system (lungs) work in harmony to provide nutrients and gases ($O_2$ and $CO_2$ ) to tissues/cells for their metabolism and energy expenditure.

Next, let us learn about the chemical control of respiration.

## 5.7.2 Chemical Control of Respiration

Let us now focus on the chemical control of respiration. But before that, let's get to know which chemicals are involved in this process.

The main chemical factors which influence the respiratory centers are the tension of carbon dioxide and oxygen in blood. In the carotid body (a clump of large polyhedral cells richly supplied with the blood vessels and nerves situated near the carotid bifurcation on each side) and in the aortic bodies (cells in the walls of the arch of aorta), cells are sensitive to carbon dioxide excess (increased $pCO_2$) and oxygen lack (decreased $pO_2$ ). When carotid body and aortic body are stimulated, impulses pass to the respiratory centre in the medulla, through the branches of vagus and glossopharyngeal nerves and stimulate respiration. Figure 5.13 illustrates the carotid and aortic bodies and the nerves.

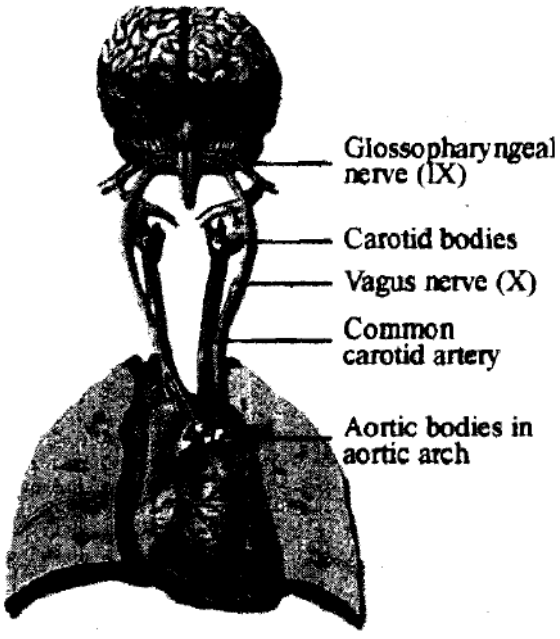



**Figure 5.13: The carotid and aortic bodies and the nerves**

Changes of carbon dioxide tension, oxygen tension and hydrogen ion concentration affect respiration. The effects of these changes are discussed below:

Effect of carbon dioxide tension: The accumulation of carbon dioxide in blood is the most important stimulus for respiration. A slight rise in carbon dioxide in the inspired air increases the rate and depth of respiration. How? increased carbon dioxide levels in the arterial blood result in decreased blood pH, which stimulates the peripheral sensory receptors (chemoreceptors). They respond by sending more nerve impulses to the respiratory centers, which stimulate the respiratory muscles, causing faster and deeper breathing. More carbon dioxide is exhaled, which drives the chemical reaction to the left and returns the $pCO_2$ and pH to normal levels. Thus, the total pulmonary ventilation is increased and adjusted and alveolar carbon dioxide remains constant. But if the percentage of carbon dioxide in the inspired air is above 5%, then the adjustment fails. Accumulation of carbon dioxide in the blood leads to acidosis (an excessive acidity of the body fluids due to either an accumulation of acids or a loss of bicarbonate i.e., the hydrogen ion concentration is increased and thus the pH is decreased).

Respiratory acidosis occurs when the lungs fail to eliminate sufficient amount of carbon dioxide. In this, the excess carbon dioxide combines with water to form carbonic acid, which increases the acidity of the blood. This may be due to the changes in lungs which prevent normal gas exchange, depression of the respiratory centre by drugs or respiratory obstruction.

Effect of hydrogen ion concentration: During acidosis when there is an excess retention of carbon dioxide in the body, the rate of respiration increases and the body tries to eliminate more carbon dioxide. As more carbon dioxide passes out of blood stream into the lungs, the hydrogen ion concentration of blood is lowered.

During alkalosis, rate of respiration decreases and the body tries to increase carbon dioxide tension. As more carbon dioxide is accumulated, hydrogen ion concentration of the blood is increased.

Effect of oxygen tension: The respiratory system is much more sensitive to carbon dioxide excess than to the oxygen deficiency. If oxygen tension in the inspired air can be reduced to 13%, there are no appreciable changes on respiration.

If it is less than 10%, then there is a feeling of discomfort and uneasiness.

Having gone through the discussion above, you would have got a clear idea about the neural and chemical control of respiration.

Next, we shall look at the internal respiration.

## 5.8 INTERNAL RESPIRATION

What do you understand by the term 'internal respiration'? Well, the interchange of gases between the blood and cells of the body is internal respiration.

The exchange of gases between the blood and tissues takes place between the arterial end of the capillaries and the tissue fluid. The process involved is termed as diffusion. Diffusion occurs from a higher concentration of oxygen in the blood to a lower concentration in the tissue fluid.

Oxygen is dissolved in the plasma and is carried from the lungs to the tissues.

Oxygen combines with haemoglobin to form oxyhaemoglobin. Oxyhaemoglobin breaks up easily to liberate oxygen. Tissue cells need a constant supply of oxygen. Hence, diffusion of oxygen from the blood to the tissue fluid and then to the cells is continuous.

The active cells receive more oxygen. When the cells become very active, there is a higher concentration of carbon dioxide. This helps in the release of oxygen from oxyhaemoglobin more rapidly.

Carbon dioxide is one of the waste products of carbohydrate and fat metabolism. The mechanism by which carbon dioxide is transferred from the cells into the blood is diffusion which occurs at the venous end of the capillaries.

Certain adjustments need to be made inside our body, to cope up with the varying environmental conditions. We shall learn about these adjustments next.

## 5.9 RESPIRATORY ADJUSTMENTS

Certain adjustments need to be made inside our body as well, to cope up with the varying environmental conditions, as well as, abnormal and normal conditions. Let us see what kind of respiratory adjustments are made in our body. Some of the common terms related to it are explained herewith.

- **Fatigue:** Fatigue means a state of decreased efficiency due to prolonged exertion. It may occur due to sustained muscle contraction. The muscles become ischemic. Fatigue may also occur due to acidosis on the brain.
- **Hypoxia:** Hypoxia is the oxygen deficiency at the tissue level below the physiological level. There are four types of hypoxia. Let's get to know them.
- **Hypoxic hypoxia:** It is a hypoxia resulting from defective oxygenation of the blood in the lungs. It is a problem in high altitudes where $pO_2$ of the arterial blood is reduced. It may also occur as a complication of pneumonia.
- **Anaemic hypoxia:** It is a type of hypoxia due to anaemia where the arterial $pO_2$ is normal but the amount of haemoglobin available to carry oxygen is reduced.
- **Stagnant or ischemic hypoxia:** It is a hypoxia resulting from slow peripheral circulation (such as follows congestive cardiac failure). In this, the blood flow to the tissues is so low that an adequate amount of oxygen is not delivered to it, inspite of having a normal $pO_2$ and haemoglobin concentration. The liver and the brain are damaged by stagnant hypoxia in congestive heart failure.

**d) Histotoxic hypoxia:** It is a type of hypoxia in which due to the action ofa toxic agent oxidative enzymes are poisoned hence the tissue cells cannot utilize oxygen supplied to them. Cyanide poisoning is one of the causes.

- **Dyspnoea:** Shortness of breath or dyspnoea is a feeling of difficult or labored breathing that is out of proportion to the patient's level of physical activity. In other words, the term also means distressed breathing and the subject is conscious of shortness of breath.
- **Hyperpnoea:** It is a term for an increase in the rate and depth of respiration.

The cause of hyperpnoea may be voluntary or due to impulses from the hypothalamus.

- **Orthopnoea:** Dyspnoea occurs even at rest in severe cardiac congestive failure.

This condition is called orthopnoea.

- **Tachypnoea:** It is a rapid, shallow breathing.
- **Apnoea:** Apnoea means cessation of breathing. Temporary apnoea may be seen in low carbon dioxide tension in blood. During swallowing, there is a temporary apnoea.
- **Cyanosis:** Cyanosis is a physical sign causing bluish discoloration of the skin and mucous membranes. Cyanosis is caused by a lack ofoxygen in the blood capillaries containing more than 5 g ofreduced haemoglobin in 100 ml of blood. Cyanosis is associated with the cold temperatures, heart failure, lung diseases and smothering. It is seen in infants at birth as a result of heart defects, respiratory distress syndrome, or lung and breathing problems. If the blood does not absorb enough oxygen during its passage through the lungs, then the arterial blood appears bluish in color. Acclimatization: A compensatory respiratory adjustment at moderately high altitudes is called acclimatization. Ifyou were to visit places like Leh (Ladakh) you would be told that you would need some time to acclimatize.

At very high altitudes, the alveolar $pO_2$ may fall to 40 millimeters of mercury and haemoglobin will be only 75% saturated. At this point, increased ventilation will make a dramatic difference in the amount of oxygen loaded into the blood. At high altitudes, there are not only changes in respiration but also changes in blood and circulation, in kidney.

- **Pneumothorax:** It is a collection of air or gas in the chest or pleural space that causes a part or all of a lung to collapse. Due to the rupture of chest wall, when air is admitted to the pleural space, the lining on the affected side is collapsed. Emphysema: Emphysema is a chronic respiratory disease where there is an over- inflation of the air sacs (alveoli) in the lungs, causing a decrease in the lung function, and often, breathlessness. In this, the lungs lose their elasticity in degenerative pulmonary disease. The walls between the alveoli breakdown so that the alveoli are replaced by large air sacs. Because ofuneven alveolar ventilation, severe hypoxia develops.
- **Asphyxia:** Improper aeration of blood produces a series of pathological manifestation and ultimately death. The symptoms are collectively called asphyxia. There is a pronounced stimulation of respiration with violent respiratory efforts. Blood pressure and heart rate rise.
- Hypercapnia: It is the retention of carbon dioxide in the body. There is a depression of the central nervous system.
- **Hypocapnia:** During hyperventilation, the arterial pCO2 falls. This condition is called hypocapnia.
- **Oxygen toxicity:** Exposure to oxygen at increased pressure can produce a marked increase in the dissolved oxygen in blood. It produces toxic effects on

NOTES

the respiratory system. The respiratory passages become irritated. There is nasal congestion, sore throat and coughing.

An exhaustive list of respiratory adjustments has been presented above. These respiratory adjustment terms you may have heard some time or the other. Now you know what they mean.

You may have also come across the term artificial respiration. What is it? The last section in this unit talks about artificial respiration.

## 5.10 ARTIFICIAL RESPIRATION

An artificial respiration needs to be given in the cases where the respiratory muscles are not able to provide an adequate ventilation of the lungs. The artificial respiration may be given either by equipment or manually.

Whatever be the technique of artificial respiration, the first essential step is to establish and maintain a clear airway from the nose or mouth to the lungs. Let us see how one can be given artificial means of respiration by the use of equipments.

Artificial respiration by an equipment

The equipments which aid in artificial respiration include:

a) **Cabinet respiration:** Such an apparatus is used when the respiratory muscles are paralyzed by an injury or an infection. A cabinet respirator consists of a box in which the patient is placed with his head outside and an air-tight seal around his neck. Respiratory movements are brought about by lowering and raising the pressure in the box.

b) **Intermittent positive pressure lung inflation:** When medulla is affected, the cough reflex may be lost. To prevent secretions entering the lungs, a tube is inserted into the trachea. This tube is connected to a positive pressure pump which inflates the lungs by blowing air into them. Alternatively, a negative pressure may be incorporated so that the expired air is sucked.

Next, we move on to the manual methods of respiration.

Artificial respiration by manual methods

The manual methods used for artificial respiration include:

a) **Mouth to mouth respiration:** If no instrument is available, one's own lung may be used as a positive pressure pump. Air may be blown into the lungs of the subject by way of his mouth or nose. This is known as mouth to mouth artificial respiration as shown in Figure 5.14. This is one of the most important and practical methods.

**b) External cardiac massage:** If respiration stops, then after a short time the heart will also stop beating due to oxygen lack. If the heart is still beating, external cardiac massage is not employed. If the heart stops beating, respiration will stop. In such cases, external cardiac massage is given to restore the circulation of blood.

## 5.11 LET US SUM UP

In this unit, we studied about the organs and the mechanism involved in the respiration process. The respiratory system consists of lungs and a series of air passages. They form a pathway for oxygen to enter and carbon dioxide to leave the lungs.

We learnt that respiration ensures an adequate intake of oxygen from the environment for the oxidative processes of the body. It also ensures the removal of carbon dioxide to maintain a constant hydrogen ion concentration in the blood.

Then we learnt about the cycle of respiration, which consists of inspiration, expiration and a pause. Inspiration, as you now know, means inhalation of air and expiration means exhalation of air. The main muscles involved in respiration are the diaphragm, intercostal muscles and abductor muscles.

Then, finally we saw that the regulation of respiration is partly chemical and partly nervous. These two systems, as you would have realized, are closely linked. Between the process of inspiration and expiration, interchange of gases takes place between the blood and the capillary network surrounding the alveoli and the air in the alveoli of the lungs.

Finally we had a look at the artificial methods of respiration using both equipments and manual methods.

## 5.12 GLOSSARY

**Acclimatization** : the process of becoming accustomed to a new environment.

**Apnoea** : cessation of breathing.

**Asphyxia** : it is produced by occlusion of the airway (strangulation, drowning) accute hypercapnia and hypoxia develop together.

**Cartilage** : a connective tissue that covers the ends of bones in a joint.

**Cyanosis** : a bluish coloration of skin and mucus membrane due to excessive reduced haemoglobin in blood.

**Diaphragm** : a thin dome-shaped skeletal muscle that separates the thoracic and abdominal cavities.

**Dyspnoea** : difficult breathing.

**Hypercapnia** : excessive carbon dioxide in blood.

**Hyperpnoea** : an abnormal increase in depth and rate or respiration.

**Hypocapnia** : the deficiency of carbon dioxide in blood.

**Hypoxia** : reduction of oxygen supply to a tissue.

**Pharvnx** : a cone-shaped tubular section of the alimentary canal that extends from the mouth and the nasal cavities to the larynx, where it becomes continuous with the oesophagus.

## 5.13 CHECK YOUR PROGRESS EXERCISES

UNIT

# 6

# PHYSIOLOGY OF GASTROINTESTINAL SYSTEM

## STRUCTURE



## 6.1 LEARNING OBJECTIVE

After studying this unit, you will be able to:

- illustrate the structure and describe the functions of different parts of the digestive system,
- discuss the secretory and digestive functions ofsalivary glands, stomach, pancreas, liver and intestine, and
- explain the mechanism of absorption of carbohydrates, proteins and fats.

## 6.2 INTRODUCTION

In this unit we shall focus on the gastrointestinal system. The gastrointestinal system, you would realize, is also referred to as the digestive system or the alimentary system, which deals with the food we eat.

Food, as we all know, is needed as the source of energy, for growth and repair of tissues. As the food passes through the gastrointestinal tract, it is broken down by some physical factors and enzymes until it is in a form suitable for absorption into the blood. After being absorbed, food is utilized in the body. There are some substances which are neither digested nor absorbed. These are excreted in the form of faeces.

What are the organs which form the gastrointestinal tract? What are their functions? What is the mechanism of absorption of the food we eat? These are a few issues discussed in this unit.

## 6.3 DESCRIPTION OF THE GASTROINTESTINAL TRACT

You may be familiar with the gastrointestinal tract in our body. The gastrointestinal tract is a long tube which starts at the mouth and ends at the anus. Can you list the organs which form the gastrointestinal tract? List them one by one and tally your responses with the list of organs presented herewith.

- Mouth
- Pharynx
- Oesophagus
- Stomach
- Small intestine
- Large intestine
- Rectum, and
- Anus

Figure 6.1 illustrates the structure of the gastrointestinal tract. Identify the different organs, as mentioned above, here in Figure 6.1.

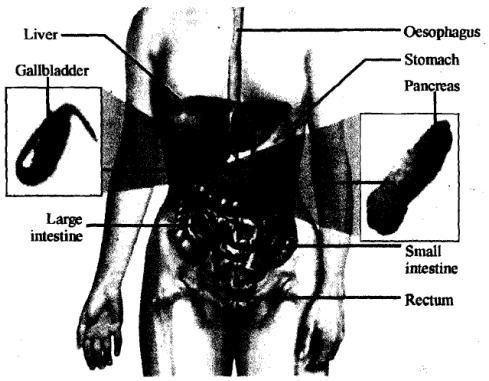



**Figure 6.1: Organs of the gastrointestinal tract**

As you read on, you will find that some of the functions are common to all parts e.g. the onward movement of the ingested food. But some of the functions of these organs are very specialized e.g. absorption of products of digestion by the small intestine. Similarly, there is a general structural plan throughout the length of the tract. But in some organs it is modified because of its specific function. Let us first learn about the general structural plan of the gastrointestinal tract. This will help us to understand their function better.

General Structural Plan of the Gastrointestinal Tract

The wall of the gastrointestinal tract consists of four layers 'of tissue. These are:

- adventitia or outer covering
- muscle layer
- submucous layer, and
- mucous membrane lining

Let us discuss each of these.

- **Adventitia or outer covering:** In the thorax, the outer covering is made up of loose fibrous tissue and in the abdomen, the organs are covered by a serous membrane called peritoneum. The peritoneum is the largest serous membrane of the body.
- **Muscle layer:** This layer consists of two layers of smooth muscle. The outer layer is a longitudinal muscle layer and the inner layer is a circular muscle layer. But there are some exceptions in some organs.

Between these two muscle layers, there is a network of nerves called the myenteric plexus. It contains both sympathetic and parasympathetic nerves.

The contraction of this smooth muscle layer is called peristalsis. You would realize that it is by peristalsis that the food contents of the gastrointestinal tract are pushed onwards.

- **Submucous layer:** This layer consists of loose areolar connective tissue. There are lymph vessels, plexuses of blood vessels and nerves. The nerve plexus is meissner 's plexus which contains both sympathetic and parasympathetic nerves.
- **Mucous membrane:** This layer is lined by the epithelial cells. Parts of the tract which are subject to mechanical injury, the layer consists of stratified squamous epithelium. Parts of the tract which secrete digestive juice and absorb food materials, the layer consists of columnar epithelium. This layer has three main functions — protective, secretory and absorptive.

Next, let us learn about the nerve supply of the gastrointestinal tract.

Nerve Supply of the Gastrointestinal Tract

The gastrointestinal tract is supplied by nerves from both sympathetic and parasympathetic nervous system. The parasympathetic supply is provided by cranial nerves, the vagus nerve. The sympathetic supply is provided by numerous nerves which emerge from the spinal cord in the thoracic and lumbar regions.

There are a few accessory organs which help in digestion. We shall get to know them now.

Accessory Organs which help in Digestion

The gastrointestinal tract receives various secretions. Some are secreted from the glands in the lining membrane of the organs, e.g. gastric juice by the glands of the stomach.

But some secretions are poured by glands located outside the tract. These are called accessory organs of digestion. Their secretions pass through ducts and reach the gastrointestinal tract. They Consist of:

- Three pairs of salivary glands
- Pancreas, and
- Liver, gall bladder and biliary tract.

We shall journey through these and the other organs of the gastrointestinal tract next. We shall start our journey from the mouth.

## 6.4 MOUTH

In this section we shall learn about the mouth and other organs present within, which help in digestion. We shall first look at the structure of the mouth.

### Structure

The mouth or oral cavity is a cavity bounded by muscles and bones. The mucous layer of the mouth consists of stratified squamous epithelium containing small mucus secreting glands. Superiorly (upper side), the mouth is bounded by a palate. Touch the upper portion of your mouth with your thumb. The hard part you feel is the palate. Actually, the palate is divided into the anterior part called the 'hard palate' and posterior part called the 'soft palate'. Figure 6.2 illustrates the structure of the mouth and the parts within. Now open your mouth wide. Can you see that little flap of skin visible at the back of your mouth? This is the uvula as you can also observe it in Figure 6.2. It is a curved fold of muscle covered with mucous membrane which hangs down from the soft palate.

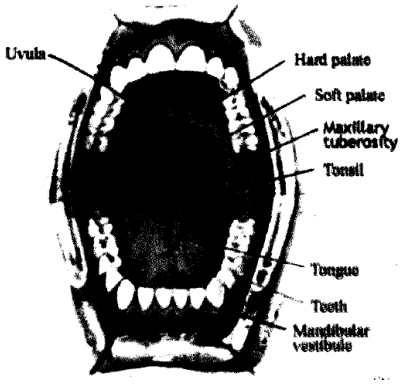



**Figure 6.2: Structure of the mouth**

In the structure above, you would have noticed that the mouth contains the teeth and the tongue. What is their role in the mouth? We are already aware of their functions. Let us get to know them a little better.

## Function

The mouth contains tongue and teeth which take part in mastication (chewing) and deglutition (swallowing) and thus help in digestion.

We shall get to know more about these two important parts next. We shall begin with the tongue.

### 6.4.1 Tongue

The tongue is an important organ. You will agree that the tongue accurately reflects the state of our digestive system. How? Well, you may have experienced that some times when we suffer from stomach upset or discomfort in the abdomen, our tongue too is soar, red or sometimes ulcerated. You may have found yourself looking at your tongue in the mirror, looking for the affected area. As a whole, the tongue has a high value as a diagnostic tool. What is the tongue made up of? Let's find out.

## Structure

The tongue is a muscular organ. It is covered with a mucous membrane. The tongue is attached by its base to the hyoid bone and by a fold of its mucous membrane covering called the frenulum. The superior surface of the tongue is covered by stratified squamous epithelium with little projections called papillae (small nodules of tissue). Papillae contain the taste buds (small and large) as shown in Figure 6.3 and the nerve endings of the sense of taste. There are three types of papillae. These are:

- **Circumvallate papillae:** These are the largest of the papillae, about 8 to 12 in number. These are arranged in a V-shape.
- **Fungiform papillae:** These area situated mainly at the tip and the edges of the tongue. They have a flat, rounded head like fungus. The fungiform papillae are rich in blood vessels and have a marked red colour.
- **Filiform papillae:** These are long and slender and are the smallest of the three types of papillae. They are found to be most numerous on the edges and anterior two thirds of the tongue

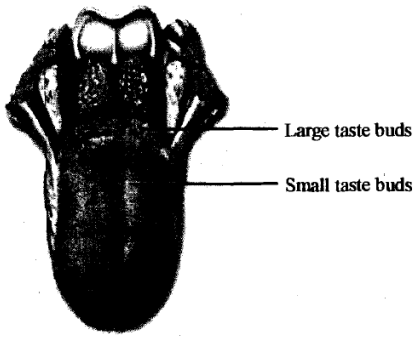



**Figure 6.3: Tongue**

Our tongue can sense different tastes. Do you know which are the basic tastes and the areas where these are sensed?

In humans, there are four basic tastes — sweet, sour, bitter and salt — as you may already know. Bitter substances are tasted on the back of the tongue, sour along the edges, sweet and salty tastes are appreciated mainly at the tip of the tongue. Sour and bitter substances are also tasted' on the palate along with some sensitivity to sweet and salt. All four modalities can also be sensed on the pharynx and epiglottis. Having studied about the structure, let us now look at the functions of the tongue.

## Functions

The tongue plays an important part in mastication or chewing, deglutition or swallowing and in speech. It is the organ of taste. Taste buds are found in the papillae of the tongue.

Now, we move on to the study of the teeth — where are these placed and what are the different types.

## 6.4.2 Teeth

The teeth are placed in the mandible (the lower jaw bone) and maxillae (the upper jaw bone) as shown in Figure 6.4. Each person has two sets of teeth, the temporary or deciduous or milk teeth and the permanent teeth.

At birth, teeth of both dentitions are present in immature form.

Temporary teeth are 20 in number, 10 in the upper jaw and 10 in the lower jaw. These teeth begin to erupt when the child is about 6 months old and usually are all present by the end of one year. After six years, they begin to fall. Their distribution in both jaws is given in Table 6.1.

| Jaw | Molars | Canine | Incisors | Incisors | Canine | Molars |
|---|---|---|---|---|---|---|
| Upper | 2 | 1 | 2 | 2 | 1 | 2 |
| Lower | 2 | 1 | 2 | 2 | 1 | 2 |

**Table 6.1: Temporary teeth**

The permanent teeth begin to replace the temporary teeth in the sixth year and the dentition is completed by twenty four years. Permanent teeth are 32 in number. Their distribution in upper and lower jaw is indicated in Table 6.2 and illustrated in Figure 6.4.

| Jaw | Molars | Pre-molars | Canine | Incisors | Incisors | Canine | Pre-molars | Molars |
|---|---|---|---|---|---|---|---|---|
| Upper | 3 | 2 | 1 | 2 | 2 | 1 | 2 | 3 |
| Lower | 3 | 2 | 1 | 2 | 2 | 1 | 2 | 3 |

**Table 6.2: Permanent teeth**

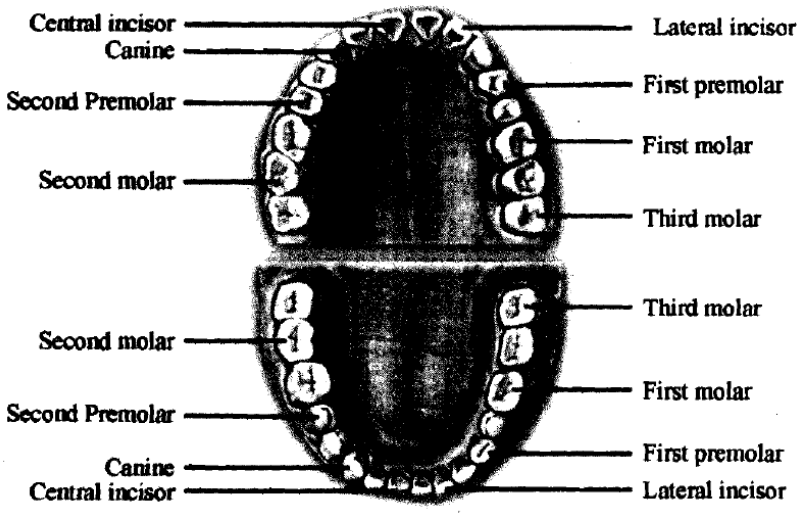



**Figure 6.4: Dental anatomy**

What is the tooth made up of ? Let's get to know.

## Structure of a tooth

The structure of a tooth includes dentin, pulp and other tissues, blood vessels and nerves embedded in the bony jaw as illustrated in Figure 6.5. Above the gum line, the tooth is protected by the hard enamel covering. As shown in Figure 6.5, the tooth consists of the following parts:

- the crown which protrudes from the gum,
- the root which is embedded in the bone,
- the neck which is the slightly constricted part where the crown merges with the root,
- the pulp cavity which contains blood vessels, lymph vessels and nerves in the centre of the tooth,
- the dentine, a hard substance, which forms the main body of the tooth,
- the enamel, which is a thin layer of hard substance outside the dentine of the crown, and
- the cement, which covers the root of the tooth and fixes it in its socket.

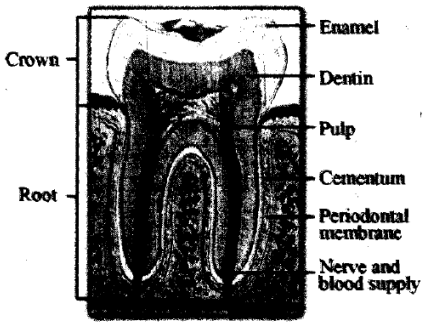



**Figure 6.5: Parts of a tooth**

### Functions

The incisors and canine teeth are the cutting teeth and are used for biting off pieces of food. Premolar and molar teeth are used for chewing the food.

Having studied the structure of the mouth and its parts, we shall move on to the salivary glands.

## 6.5 SALIVARY GLANDS

Salivary glands are the accessory glands of digestion. They lie outside the gastrointestinal tract. Their function is 'to secrete saliva, which is conveyed to the mouth by ducts.

There are three pairs of salivary glands. The salivary glands include the large parotid glands (one pair) as illustrated in Figure 6.6 and the smaller sub-mandibular glands (one pair) and sublingual glands (one pair). Let us get to know each of these structures.

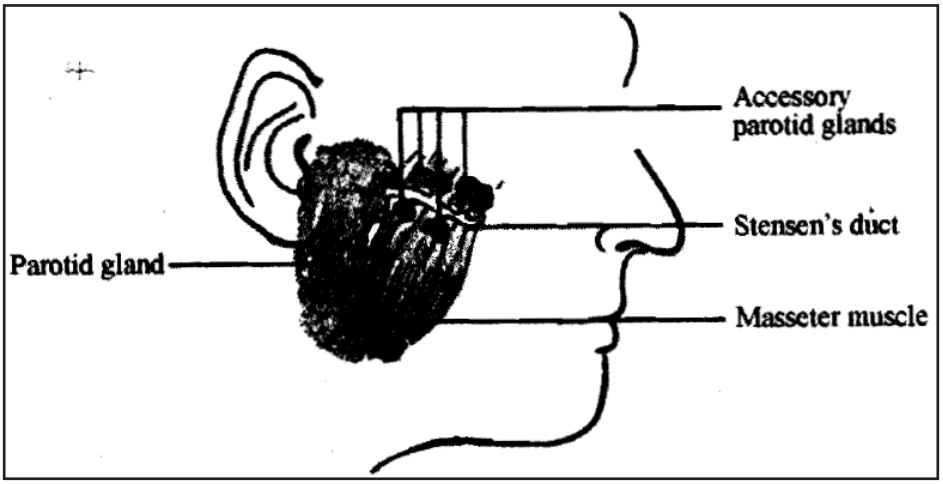



**Figure 6.6: Salivary gland**

**a) Parotid glands:** These are situated one on each side of the temporal region of face as shown in Figure 6.6. Each gland opens at the level of second upper molar tooth by a duct known as Duct of Stensen.

**b) Submandibular glands:** These lie on one on each side of the face under the angle of the jaw. The submandibular or submaxillary gland opens by Wharton 's duct.

**c) Sublingual glands:** They lie under the mucus membrane of the floor of the mouth in front of the submandibular glands. They have numerous small ducts which open in the mouth. They are called Ducts of Rivinus.

### Structure

Salivary glands are compound racemose (resembling a bunch of grapes as shown in Figure 6.6) glands. They consist of a number of lobules which are made up of small alveoli lined with the secretory cells.

The gland cells are of two types — serous and mucous. The parotid gland is composed entirely of serous cells. The sublingual gland is predominantly of mucous cells. The submandibular gland is a mixed type and contains serous and mucous both. The serous cells contain zymogen granules and mucous cells which contain mucinogen granules. The secretion of serous gland is watery, rich in enzyme (such as starch- splitting enzyme, amylase) and poor in solid. The secretion of mucous cells is thick and contains much mucus.

## Composition of Saliva

Saliva is a combined secretion from the salivary glands and the small mucus secreting glands of the lining of the oral cavity. It is slightly cloudy due to the presence of cells and mucin. Usually it is slightly acidic (pH 6.02—7.05). It consists of 99.5% of water and 0.5% of solid. Of the solids, 0.2% is inorganic salts and 0.3% is organic constituents. What are the inorganic and organic constituents present in saliva? Let's find out. Inorganic constituents: The inorganic salts such as sodium chloride, potassium chloride, sodium phosphate, potassium phosphate etc. are present.

Organic constituents: The organic constituents present in saliva include:

- enzymes (salivary amylase or ptyalin, lysozyme, carbonic anhydrase, phosphatase etc),
- mucus (added by the glands in mouth),
- cellular constituents (bacteria, desquamated epithelial cells etc), and
- small amount of urea and citrate.

## Functions of saliva

Saliva serves many roles, some of which are important to all species and others to only a few. Let us study about these functions which are significant to us.

Digestion of food: Salivary amylase or ptyalin acts on cooked starches (polysaccharides) and changes them into maltose as shown herewith.

Boiled starch ⟶ Soluble starch ⟶ Erythrodextrin and Maltose

Achrodextrins and Maltose ⟶ Isomaltose and Maltose.

The action of amylase is not complete in the mouth but it continues in the stomach until the reaction of the bolus has been made strongly acid by hydrochloric acid in the stomach. The pH of gastric juice is between 1.5 and 1.8. The pH of saliva is between 6.02 and 7.5.

- **Lubrication of food:** Dry food enters the mouth. It is moistened and lubricated by the saliva, before it can be made into a bolus ready for swallowing.
- **Cleansing:** Saliva is necessary to keep the mouth clean and to keep the structures within the mouth soft and pliable. In fever, when the salivary secretion is reduced, the food bolus is not properly washed away and bacteria multiply. This can cause tooth decay.
- **Taste:** Food substances, mixed with saliva stimulate the taste buds. Saliva

acts as a solvent and is essential for the sensation of taste.

- **Articulation:** Saliva helps in the smooth delivery of speech because it keeps the mouth moist. By facilitating movements of the tongue and lips, saliva makes rapid articulation possible. Decrease in salivary secretion in nervousness or fever may impair the speech.
- **Heat loss:** This is found in dog, sheep etc. who do not have sweat glands. In very hot climate, they secrete more saliva (panting) causing greater heat loss.
- **Bacteriolytic action:** Saliva contains lysozyme. It destroys cell walls of many bacteria.

Having looked at the functions of saliva, let us also get to know how the saliva secretion is controlled.

- **Control of salivary secretion:** The autonomic control of saliva secretion occurs in two ways, as unconditioned and conditioned reflex. What are these? Let's find out.
- **Unconditioned reflex:** This response occurs due to the presence of an object in the mouth.
- **Conditioned reflex:** This response occurs due to some previous experience. Sight, smell and even the thought of appetizing food results in salivation.

Parasympathetic stimulation of the glands causes copious salivary secretion. Atropine blocks the response and makes mouth dry. Many drugs / toxic substances can also be secreted in saliva.

## 6.6 THE PHARYNX

You may recall that we studied about the pharynx in the last unit on respiration. We learnt that it is divided into three parts — the nasopharynx, the oropharynx and the laryngopharynx. Well, the oropharynx and naso pharynx are related to the gastrointestinal tract, hence the discussion here. Food passes from the mouth to the oropharynx and then to the laryngopharynx before it enters the oesophagus. We shall get to know about the oesophagus next.

## 6.7 THE OESOPHAGUS

The oesophagus or the food pipe is the narrowest part of the gastrointestinal tract as can be seen in Figure 6.1. It lies in front of the vertebral column and behind the trachea and the heart. It is continuous with the pharynx above and the stomach below.

Let us look at the structure of the oesophagus.

### Structure of the Oesophagus

Histological study reveals that there are four layers of tissue in the oesophagus. The outer covering consists of elastic fibrous tissue, the muscle layer consists

of inner circular and outer longitudinal muscle fibres. In the upper portion, the muscles are voluntary, in the middle portion both voluntary and involuntary and in the lower portion only smooth muscles (involuntary) are found. The submucous layer consists of areolar tissue, blood vessels, lymph vessels, nerves etc. The inner lining consists of stratified squamous epithelium.

What is the role of oesophagus in our body? Read and find out next.

### Function of the Oesophagus

The oesophagus passes the food from the pharynx to the stomach by peristaltic movements (natural contractions of the muscular walls of the organ that moves the food contents forward) as illustrated in the Figure 6.7. This is the main function of the oesophagus.

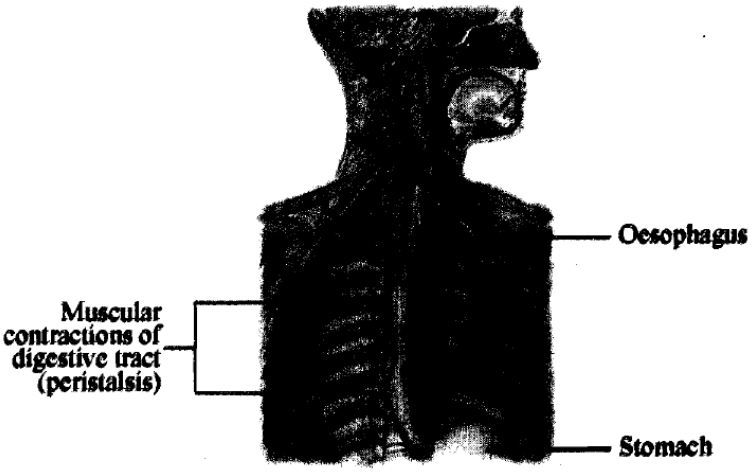



**Figure 6.7: Peristalsis**

## 6.8 THE STOMACH

The stomach is a J-shaped dilated portion of the gastrointestinal tract situated in the abdominal cavity between the oesophagus and the small intestine, as you may have noticed in Figure 6.1. The junction of the oesophageal mucosa with that of the stomach is abrupt. The opening by which the oesophagus communicates with the stomach is known as the cardiac orifice. The stomach opens into the duodenum through the pyloric orifice. The capacity of the average human stomach is about 1.12 - 1.70 litres.

### 6.8.1 Structure of the Stomach

The stomach is described as having two curvatures — lesser and greater curvature as can be seen in Figure 6.8. The lesser curvature is short and lies on the posterior surface of the stomach. As it can be observed from Figure 6.8, it is a continuation of the posterior part of the oesophagus. The greater curvature is on the anterior surface of the stomach.

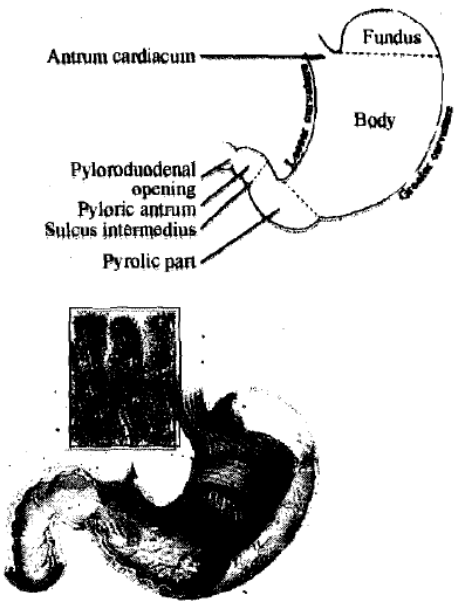



**Figure 6.8: Stomach**

The stomach is divided into 3 parts — the fundus, the body and the pylorus (pyloric part) as shown in Figure 6.8. The part of the stomach above and left of the cardiac orifice is called the fundus. The main part is the body of the stomach and the lower part which curves to the right is the pylorus. The pyloric orifice communicates with the duodenum, and its position is usually indicated on the surface of the stomach by a circular groove, the duodenopyloric constriction.

There are four layers of tissue which form the walls of the stomach. Figure 6.9 illustrates the layers of tissue which form the walls of the stomach. The outermost layer is a serous covering. The muscle layer (muscularis externa) consists of an outer longitudinal, middle circular and inner oblique layer. The submucous layer consists of areolar tissue, blood, lymph vessels and nerves. The innermost mucous layer consists of columnar epithelium and goblet cells.

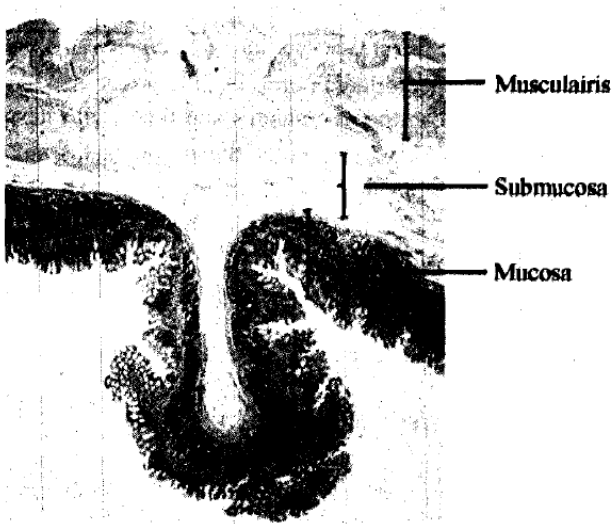



**Figure 6.9: Layers of tissue which form the walls of the stomach**

Within the mucous membrane, there are gastric glands. The gastric glands consist of mucous neck cells which secrete mucus, chief cells or peptic cells which secrete pepsinogen (the precursor of the enzyme pepsin), oxyntic cells or parietal cells which secrete hydrochloric acid. Enteroendocrine cells (G-cells) secrete the hormone gastrin. Figure 6.10 illustrates the gastric gland.

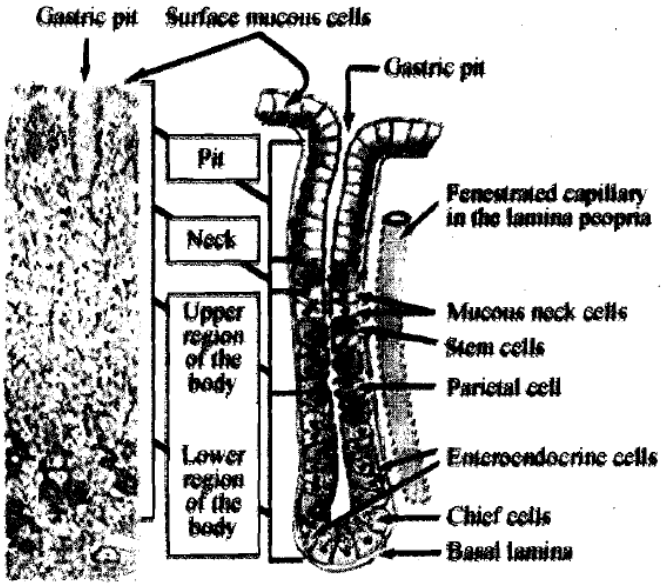



**Figure 6.10: Gastric gland**

The combined secretion of different types of cells of above glands forms the gastric juice.

In the fundus and the body of the stomach, the glands are straight and slender with a narrow lumen. In the pyloric region, the glands are fewer in number and shorter in length. Gastric glands in the pylorus do not contain oxyntic cells.

## 6.8.2 Functions of the Stomach

The functions of stomach are many. We shall get to know them one by one.

- **Reservoir function:** The stomach acts as a temporary reservoir for food. It allow the gastric juice to act on different food substances.
- **Mechanical function:** Muscular action of the stomach helps in the mixing of food with the digestive juices and also helps to propel the food into the duodenum.
- **Secretory function:** The stomach secretes gastric juice. Hydrochloric acid secreted from the stomach creates the acidic medium necessary for the digestion of protein. Also, hydrochloric acid acts as an antiseptic agent. Intrinsic factor secreted from the stomach is necessary for vitamin B12 absorption.
- **Digestive function:** Gastric juice begins the digestion of protein. Gastric rennin coagulates milk. Iron in the food is dissolved in the stomach in presence of hydrochloric acid.
- **Absorptive function:** Absorption takes place to a limited degree in the

stomach. Water, glucose, alcohol and some drugs are absorbed through the walls of the stomach into the venous circulation.

We have learnt above about the digestive function of the stomach and seen how the gastric juice is important for this function. Let us look at the composition of gastric juice next.

## 6.8.3 Composition and Functions of Gastric Juice

In resting condition, the secretion of gastric juice is little in amount and is about 10- 15 ml. After taking each meal, the amount of secretion begins to increase. The total secretion per day starts from 1500-2000 ml. Its pH is strongly acidic, i.e. 2.3. Its specific gravity is 1.002-1.004.

Gastric juice contains 99.45% of water and 0.55% solid. Of the solids, organic constituents are 0.4% and inorganic constituents are 0.15% of total gastric juice. Table 6.1 presents the composition of organic and the inorganic constituents present in gastric juice.

| Organic Constituents | Inorganic Constituents |
|---|---|
| Pepsin (the proteolytic enzyme), mucin, intrinsic factor (a mucoprotein, necessary for absorption of Vitamin $B_{12}$), gastric rennin (not present in human adults), and other gastric enzymes (lysozyme, carbonic anhydrase etc) | Free hydrochloric acid, lactic acid and other fermenting acid, sulphates, chlorides, phosphates of sodium, potassium, calcium and magnesium, and bicarbonates. |

**Table 6.1: Organic and the inorganic constituents present in gastric juice**

After understanding the composition, let us move on to the functions of gastric juice.

## Functions of Gastric Juice

Gastric juice performs many vital functions as discussed herewith:

- **Digestive function:** As the gastric juice contains water, it further liquefies the food swallowed. The hydrochloric acid acidifies the stomach contents and terminates the action of salivary amylase (ptyalin). Pepsinogen is converted to active pepsin by hydrochloric acid.
- **Enzyme action:** Pepsin begins the chemical digestion of proteins. It converts proteins to peptones. The enzyme rennin present in infants curdles the milk and changes the soluble caseinogen into insoluble casein. This casein is converted by pepsin into peptones.
- **Antiseptic action:** Hydrochloric acid in the gastric juice acts as a barrier to the passage of certain microorganisms harmful to the human system.
- **Haemopoietic function:** Gastric juice contains the intrinsic factor, which is necessary for the absorption of vitamin $B_{12}$. Vitamin $B_{12}$ present in food combines with intrinsic factor of the gastric juice. It is absorbed through the

walls of the small intestine and stored in the liver. It is required for red blood cell maturation in the bone marrow.

- **Protective function:** Large quantity of mucin is secreted by gastric glands. Mucin lubricates the food bolus (a mass of chewed food) and also gives a protective layer over the gastric mucosa.
- **Excretory function:** Certain toxins, heavy metals like lead and some alkaloids are excreted through the gastric juice.

## 6.7.4 Mechanism of Secretion of Gastric Juice

There is always a small quantity of gastric juice present in the stomach even when there is no food in the stomach. This is known as fasting juice. Secretion Of gastric juice is divided into three phases. These include:

- **Cephalic phase or neural phase:** 45% of the total gastric secretion is discharged in this Phase. The flow of juice occurs before food reaches the stomach. Sight of food, taste, smell and even the thought of an appetizing meal produces secretions by the reflex stimulation of vagus nerve. If vagus nerves are cut, this phase of gastric secretion stops. Through the vagus nerve, the parietal cells are stimulated.
- **Gastric phase:** Another 45% of the gastric secretion is discharged in this phase. The mechanical presence of food in the antrum of the stomach stimulates the production of a hormone, gastrin. Gastrin is secreted from the G cells of the antral mucosa and passes directly into the circulating blood. This hormone activates the parietal cells of the stomach to secrete more gastric juice. This gastric juice contains more acid, but little pepsin or mucus.
- Intestinal phase: Rest 10% of the total gastric secretion is discharged in this phase.

When partially digested contents of the stomach reach the duodenum, presence of certain food substances in the small intestine excites gastric secretion. These are meat extract, alcohol etc. Some substances inhibit gastric secretion. These are alkali and fat. If the intestinal food material contains a considerable amount of fat, a hormone enterogastrone is produced. It inhibits gastric secretion and gastric motility that is why after takins a fatty meal (paranthas) you don't feel hungry for about 3-4 hours again. By slowing down the emptying rate of the stomach the contents in the small intestine are thoroughly mixed with bile and pancreatic juice.

You must have read about the acid being one of the constituents of gastric juice.

How is the acid secreted in our body? Let's get to know, next.

Mechanism of secretion of hydrochloric acid

Sodium chloride (NaCl) solution is present in the extracellular fluid. It is ionized as

NaCl ($Na^+$ + $C1^-$).

Both at rest and during acid secretion, the mucosal surface of the body of the stomach is electronegative to serosal surface. Therefore secretion of chloride must

take place against an electrical gradient as well as a concentration gradient (from 107 mmol/l in the intracellular fluid to 170 mmol/l in the canaliculus). Movement of chloride ions across the membrane requires an active transport mechanism.

An unlimited supply of hydrogen is available from intracellular water ($H20 \longrightarrow H^+ + OH$). Accumulation of hydroxyl ions ($OH^-$) within the parietal cell results in the rise of intracellular pH sufficient to interfere with the cell metabolism. Hydroxyl ions are to be removed. Carbon dioxide is formed during metabolism of carbohydrate in the cells. It combines with water under the influence of carbonic anhydrase (present in the parietal cells) to form carbonic acid.

$$H_2O \xrightarrow{\text{Carbonic Anhydrase}} + CO_2\ H_2CO_3$$

$$H_2CO_3 + OH^- \longrightarrow H_2O + HCO_3$$

Accumulation of OH ions is thus prevented. Bicarbonates are transported into the blood. Chloride ions diffuse down against concentration gradient and enter the parietal cells. Its entry into the cell is facilitated by a carrier mechanism. In the same way, chloride ion is coupled with hydrogen ion to form hydrochloric acid.

$$H^+ + C1 \longrightarrow HC1$$

## 6.9 THE PANCREAS

From the stomach, the semi-liquid mass of partially digested food (called chyme) enters the small intestine. When the chyme enters the small intestine, it is mixed with the pancreatic juice and bile and then with the intestinal juice. Let us get to know our pancreas. We start with the structure.

### 6.9.1 Structure of the Pancreas

Pancreas lies outside the alimentary tract and is an accessory gland of digestion as you may recall reading earlier in this unit. It is a pale yellowish grey gland situated in the abdominal cavity. Figure 6.11 illustrates the pancreas. As you can see, it consists of a broad head. The head lies in the curve of the duodenum, a body which lies behind the body of the stomach and a narrow tail which lies left to the kidney.

The exocrine part of the pancreas is a compound tubular gland. The secretory portion consists of a number of lobules. Lobules are made up of alveoli lined with secretory cells. These alveoli are serous alveoli containing zymogen granules. Zymogen granules contain pro-enzymes. The pro-enzymes become activated to form enzymes. These enzymes are responsible for digestion of proteins, fats and carbohydrates.

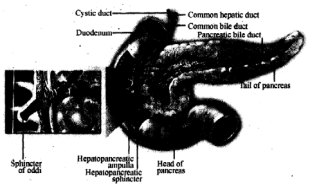



Figure 6.11: Pancreas

Each lobule has a small duct. This duct unites with other ducts and joins the main pancreatic duct which passes the whole length of the gland to open into the duodenum.

Just before entering the duodenum, the pancreatic duct joins the bile duct to form ampulla of the bile duct as shown in Figure 6.11. The duodenal opening is controlled by sphincter of oddi.

The endocrine part of the pancreas consists of collection of cells distributed throughout the substances of the pancreas. These collections of cells are called 'Islets of Langerhans '. The secretion produced by the islets of Langerhans is passed directly into the circulating blood and consists of hormones insulin and glucagon.

So the pancreas secretes the pancreatic juice and also secretions produced by the islets of Langerhans i.e. insulin and glucagon. What is the composition of the pancreatic juice? Let's find out.

## Composition of pancreatic juice

Pancreatic juice is the secretion of the exocrine part of the pancreas. It is alkaline in reaction. Its pH is 8.0 — 8.3. It consists of:

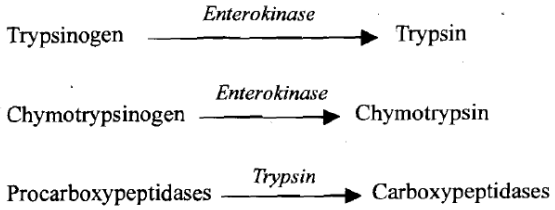
- water
- mineral salts (high bicarbonate, salts of sodium, potqssium, magnesium, calcium and zinc), and
- enzymes (trypsinogen, chymotrypsinogen, procarboxypeptidase, pancreatic lipase, pancreatic amylase etc).

## 6.9.2 Functions of the Pancreas

Pancreatic juice contains, as you have already learnt, many enzymes and so performs many vital jobs. The functions of pancreas are many-fold and include:

Neutralising action: Pancreatic juice is alkaline in nature and acid chyme is rendered alkaline by the strong alkalinity of the pancreatic juice. This alteration of reaction is important for an effective action of pancreatic secretion.

Digestive action: Trypsinogen and chymotrypsinogen are the inactive proteolytic enzymes of the pancreatic juice. When they come in contact with enterokinase of the intestinal juice, they are converted to trypsin and chymotrypsin, respectively as illustrated herewith. You may recall reading about this also in the Nutritional Biochemistry Course in Unit 5.




Trypsin and chymotrypsin, you know are the enzymes that act on partially digested proteins. This means that they convert peptones (formed in the

stomach) into peptides and polypeptides. Other enzymes called ribonuclease and deoxyribonuclease, act on two types of nucleic acids (ribonucleic acid and deoxyribonucleic acid).

Pancreatic amylase, the other enzyme of the pancreas, converts all polysaccharides (starches) to disaccharides. Starches, not affected by ptyalin, are digested here. Pancreatic lipase converts fats into fatty acid and glycerol. Bile salts emulsify the fats and breakdown fat into smaller globules and thus help the enzyme to act.

### 6.9.3 Mechanism of Pancreatic Secretion

The pancreatic secretion consists of two phases — nervous phase and hormonal phase.

a) **Nervous phase:** When stomach secretes gastric juice in cephalic phase and gastric phase, nerve impulses are simultaneously transmitted along the vagus nerves to the pancreas. This results in the secretion of moderate quantity of pancreatic enzymes.

b) **Hormonal phase:** After food enters from the stomach to the duodenum, pancreatic secretion starts increasing. Two hormones are responsible. One is secretin, another is cholecystokinin - pancreozymin (CCK-PZ).

Let us understand the role of these hormones in the digestive process.

- **Role of secretin:** Secretin is a polypeptide containing 27 amino acids. It is present in the mucosa of the upper small intestine in an inactive form prosecretin. When food mixed with hydrochloric acid enters the duodenum, secretin is released from prosecretin. Secfetin causes the pancreas to secrete large quantities of fluid containing a high concentration of bicarbonate ion. This copious flow of fluid is called hydrelatic secretion because it is mainly a thin watery solution containing almost no enzymes. Pancreatic juice containing large quantity of sodium bicarbonate is helpful to neutralize the acid content of substances emptied into the duodenum from the stomach. The reaction is as follows:

$$HCl + NaHCO_3 \longrightarrow NaCl + H_2CO_3$$

$$H_2CO_3 \longrightarrow H_2O + CO_2$$

(carbonic acid)

Carbonic acid dissociates into water and carbon dioxide. Carbon dioxide is absorbed into the body fluids. A neutral solution of sodium chloride is left.

Bicarbonate secretion also provides an appropriate pH for the action of pancreatic enzymes.

**Role of cholecystokinin :** pancreozymin (CCK-PZ): The presence of food in the upper small intestine also causes another hormone, CCK-PZ to be released. It is a polypeptide containing 33 amino acids, secreted from the intestinal mucosa.

Presence of peptones, fats and also acids in the small intestine are stimuli for cholecystokinin — pancreozymin secretion. Cholecystokinin-pancreozymin acts on pancreas via blood. It causes secretion of large quantity of digestive enzymes. This

type of secretion is called ecbolic secretion.

Having gone through the discussion above, you would have got a fairly good idea about the digestive function of pancreas and the mechanism of pancreatic secretions. Now, try answering the questions given next and check your understanding of the topic.

## 6.10 THE LIVER AND BILIARY SYSTEM

The liver is the largest gland in the body. It weighs about 1500 g. It is situated in the upper part of the abdominal cavity. The liver secretes bile. The biliary system comprises of the gall bladder and the bile ducts. Let's first learn about liver, its structure and functions.

### 6.10.1 Liver — Structure and Functions

The liver is enclosed in a thin capsule and is completely covered by a peritoneum. The liver is described as having four lobes. As you can see in Figure 6.12, only two lobes are visible - the left and the right lobe. The right lobe is the largest. The left lobe is smaller and wedge-shaped. The quadrate lobe is almost square in outline and the caudate lobe is tail-like in appearance. The latter two lobes can only be distinguished by viewing the liver from behind.

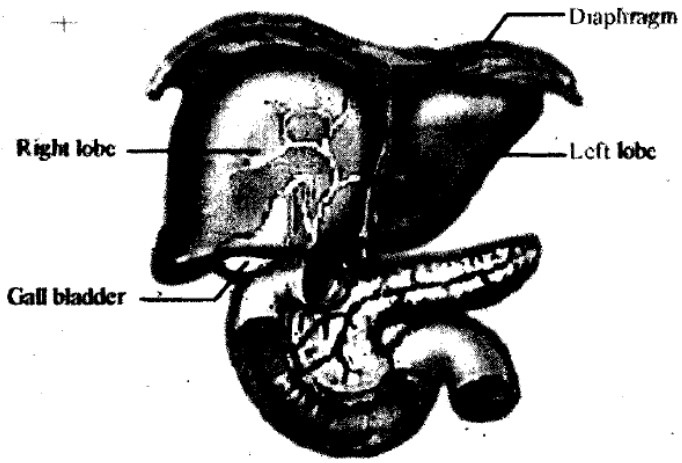



**Figure 6.12: Liver**

The lobes of the liver are made up of tiny lobules. These lobules are hexagonal in outline. They are formed by cubical shaped cells arranged in columns which radiate from a central vein. Between the columns of cells, there are sinusoids (blood vessels with incomplete walls) which contain a mixture of blood from the tiny branches of the portal vein and hepatic artery. Thus oxygenated blood and blood with a high concentration of nutritional materials come in direct contact with the cells of the liver. Blood drains into central vein. Central veins from all the lobules join up and unite to form hepatic veins which drain blood from the liver and empty into inferior vena cava. What are the functions of the liver? Certainly,

you may be aware of the important functions the liver performs in the body. Read the functions enumerated next and refresh your knowledge about the functions of the liver.

NOTES

## Functions of the liver

The liver has the following functions:

- **Secretion of bile:** The liver cells are able to synthesize bile. All constituents of bile are not present in the liver. Liver cells use different substances from mixed venous and arterial blood in the sinusoids.
- **Glycogenesis and glycogenolysis:** The liver converts glucose to glycogen in the presence of insulin and changes the liver glycogen back to glucose when required. You would recall reading about glycogenolysis and gluconeogenesis in the Nutritional Biochemistry Course. If not, we suggest you get back to this Course, look up Unit 6 and understand this concept.
- **Deamination of protein:** The nitrogenous portion of the amino acid is removed and urea is formed by the liver. Look up Unit 8 of the Nutritional Biochemistry Course for more details about the deamination reaction. Further, nucleoproteins are broken down to uric acid which is excreted in the urine. Liver also forms urea from the protoplasm of worn-out cells.
- **Storage of vitamin A, D, E, K and $B_{12}$ :** The liver stores vitamin A, D, E, K. It also stores vitamin $B_{12}$ until it is required by the bone marrow for the formation of red blood cells.
- **Formation of plasma proteins:** Serum albumin, serum globulin, prothrombin and fibrinogen and other coagulation factors are synthesized in the liver from the available amino acids.
- **Storage of iron:** The liver stores iron from the diet and from the breakdown of red blood cells in the spleen.

## 6.10.2 The Gall Bladder and the Bile Ducts

The gall bladder is a pear shaped sac attached to the liver by connective tissue. It is divided into three parts — fundus or expanded end, body or main part and a neck which is continuous with the cystic duct, as shown in Figure 6.13.

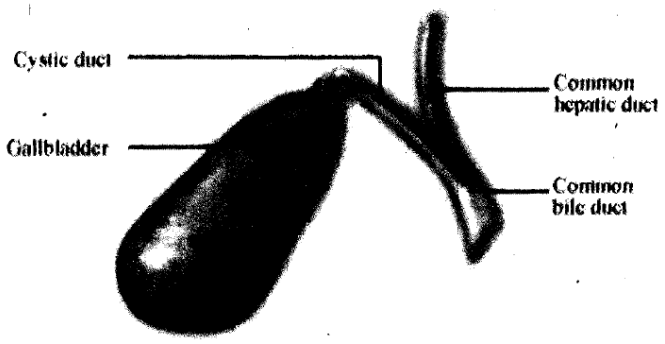



**Figure 6.13: Gall bladder and bile ducts**

There is a right and a left hepatic duct which join to form the common hepatic duct. As can be seen in the Figure 6.13, the common hepatic duct passes downwards and joins the cystic duct from the gall bladder at an acute angle. The cystic duct and common hepatic duct joins to form the bile duct. It passes downwards and joins the main pancreatic duct at the ampulla of the bile duct. The two together open into the duodenual papilla and its orifice is guarded by the sphincter of oddi.

Very briefly let us look at the tissues of the gall bladder. fie surface of the gall bladder, not attached to the liver, is covered by a peritoneum. The middle layer is a smooth muscle layer which contains longitudinal, circular and oblique fibres. The innermost lining is of mucous membrane. There are rugae in the gall bladder when it is empty. The rugae disappear when the organ is distended with bile.

## Functions of the gall bladder

Bile from the liver passes through the cystic duct to the gall bladder. The gall bladder acts as a reservoir of bile. By the absorption of water, the bile is concentrated in gall bladder. When a meal is taken, the gall bladder contracts. Then the bile passes through the cystic duct again and then down the bile duct and enters the duodenum. Bile enters the duodenum only when the sphincter of oddi is relaxed.

Next, the factors that influence the movement of gall bladder are enumerated.

## Factors Controlling Movements of Gall Bladder

Contraction of gall bladder can be controlled by reflex action, by the presence of foodstuff in the duodenum and by the hormone cholecystokinin. Let us discuss each of these control mechanisms.

- **Reflex control:** During digestion, reflex stimulation of gall bladder takes place. Entry of acid into the duodenum reflexly stimulates the gall bladder to contract and sphincter of oddi to relax. The stimulus may arise when the food is present in the mouth and stomach.
- **Presence of foodstuffs:** Fatty foods particularly cream, fatty acids and proteins to a less extent, stimulate the contraction of gall bladder. Bile is expelled from the gall bladder when these foodstuffs are eaten. Fatty meal is given to the patient to examine gall bladder movements during X-ray of gall bladder (referred to as cholecystography).
- **Cholecystokinin:** Active contraction of gall bladder during digestion is due to the hormone cholecystokinin. Acid extracts of the duodenal mucosa stimulate the secretion of cholecystokinin from the cells of the mucosa in the upper intestine.

## Composition of bile

Bile is a complex fluid. It is yellowish green in colour and bitter in taste. It contains:

- water
- mineral salts (chloride, carbonate and phosphate of sodium, potassium and

calcium)

- mucus
- bile salts (sodium taurocholate, sodium glycocholate)
- bile pigments (bilirubin and biliverdin)
- cholesterol, and
- traces of fatty acids

There is a slight difference between the composition of bile produced by the liver and bile stored in the gall bladder. Liver bile is alkaline (pH 7.7) and gall bladder bile is neutral or slightly alkaline (pH 7.0 - 7.6). The differences in the composition of bile produced by the liver and bile stored in the gall bladder are highlighted in Table 6.2.

| Constituents | Gall bladder bile % | Liver bile % |
|---|---|---|
| Water | 89.0 | 98.0 |
| Solids | 11.0 | 2.0 |
| Inorganic salts | 0.8 | 0.75 |
| Bile salts | 6.0 | 0.9 |
| Mucin and Pigments | 3.0 | 0.4 |
| Cholesterol | 0.38 | 0.06 |

**Table 6.2: Constituents of bile**

From Table 6.2 it must be evident that bile in the gall bladder is concentrated as compared to the bile produced in the liver. What functions does the bile perform in the body? Let's find out.

## Functions of Bile

The main function of the bile is digestive function. The digestive functions are many. These are:

- **Emulsification:** The bile salts, sodium taurocholate and sodium glycocholate are active in emulsifring fats in the duodenum. Bile salts break up the fat into tiny droplets. The fine globules of fat have a larger surface area for the enzyme to act. This is called emulsification. Due to this, digestion is quickened.
- **Activation of enzyme:** Bile salts activate pancreatic lipase. Lipase, as you already know, is a fat — splitting enzyme and splits fat into fatty acids and glycerol. Bile salts combine with fatty acids to make them soluble and enable them to be absorbed.
- **Cholagouge action:** Bile acts as its own stimulus. Bile salts are absorbed from the intestine, carried to the liver and stimulate further bile secretion.
- **Absorptive function:** Presence of bile in the small intestine is needed for the absorption of vitamin K and digested fat.
- **Laxative action:** Bile salts stimulate peristalsis and hence have a laxative

action.

- **Maintenance of pH:** Bile neutralises the hydrochloric acid and helps to maintain a suitable PH. This prevents the injurious effects of acids on gastric mucosa. Mucin of bile acts as a buffer and as a lubricant.
- **Excretory function:** Bile pigments (bilirubin and biliverdin) are the waste products of the breakdown of red blood cells and bile is their route of excretion. Also some metals (like copper, zinc) and toxins are excreted by bile.
- **Colouration of faeces:** The iron-free breakdown products of haemoglobin (i.e. bilirubin and biliverdin) oxidize to brown stereobilin. This stereobilin gives the faeces their characteristic brown-yellow colour. Thus bile colours the faeces. Dark coloured stools in jaundice patients indicate lot of RBC destruction and formation of more bile pigments.

What is the mechanism of bile secretion? The mechanism is discussed next.

## Mechanism of secretion of bile

Bile secretion is independent of neural influence. The normal stimuli for bile secretion are bile salt itself and some foodstuffs.

Substances which increase the output of bile from the liver are known as choleretic agents. Substances those which increase the volume of bile are called hydrocholeretic agents.

An excellent correlation exists between the bile flow and bile salt excretion. The secretion of bile salts into the biliary canaliculus is the most important factor promoting bile flow. This bile-salt dependent active secretion carries the bile pigments, organic anions and water with it. The passages of osmotically active bile salts generate water flow. The bile salts are present as micelles. A change in micellar size influences osmotic activity. This may be the regulatory mechanism for the flow of water into the bile.

There is also bile-salt independent flow. But it is only a small fraction of total bile flow. This fraction may be linked to active sodium transport. Substances like phenobarbitone or cortisol increase bile flow without enhancing bile salt secretion.

Fat and protein rich foods stimulate bile secretion. Carbohydrates exert no such effects. Bile secretion increases about one hour after meal.

Flow in the bile duct is controlled by the hormone 'secretin'. Ductular flow may serve to flush bile salts from the lower end of the common bile duct following gall-bladder contraction.

Earlier we looked at the constituents of bile. We learnt that bile is composed of cholesterol, bile salts, pigments etc. We shall now see how these individual constituents of bile are formed.

## Formation of individual constituents of bile

- **Cholesterol:** Cholesterol is an extremely important compound, a constituent of most cell membranes and the precursor of bile acids and steroid hormones.

Synthesis takes place mainly from acetate in microsome. The liver is particularly concerned with the production of cholesterol for export, largely as bile.

- **Bile salts:** The liver is the site for synthesis of bile salts. The amino acid glycine is synthesized in the body. Taurine is derived from the sulphur-containing amino acid cysteine. Glycocholic acid and taurocholic acid (i.e. bile salts) are formed by the combination of glycine and taurine with cholic acid respectively (cholic acid is a bile acid synthesized in the liver).
- **Bilg pigments:** The red blood cells are broken down when they are old (life span of red blood cell is 120 days). They are taken up by the reticuloendothelial system. Haemoglobin is released and by degradation, opening of the porphyrin ring system occurs. The degraded compound is known as 'verdohaemoglobin.' This is broken down to haem and globin. Globin is broken down to amino acids and enters the general amino acid pool of the body. Iron is stored in the body as apoferritin, haemosiderin which is re-utilized to form new haemoglobin. The rest of the haem is converted to yellow pigment called as bilirubin. Bilirubin is oxidised to green pigment biliverdin. The bilirubin then combines with plasma albumin. When it enters the liver cells, it is conjugated with glucuronic acid.

It is to be noted that bilirubin, present in blood (haemobilirubin) is not the same as the bilirubin present in bile (cholebilirubin). Haemobilirubin remains combined with serum albumin and cholebilirubin remains in combination with glucuronic acid.

Finally, before we end our discussion on bile, we must talk about the enterohepatic circulation of bile. What do we mean by the enterohepatic circulation of bile? Read the following section and find out.

## Enterohepatic Circulation of Bile

Any compound which is secreted in bile and subsequently reabsorbed from the small intestine, returns to the liver and is then resecreted in the bile. This is called enterohepatic circulation of bile. The enterohepatic circulation is a physiological conserving mechanism. The efficiency with which compounds recirculate may vary.

Bile salts are efficiently reabsorbed. Only a minute proportion escapes into the systemic circulation. Cholesterol and phospholipids are much less efficiently absorbed.

Let us study about the pathways of bile circulation. There is both a portal and extraportal pathway for the enterohepatic circulation. Bile acids undergo recirculation through the portal vein. Phosopholipids and cholesterol undergo an extraportal enterohepatic circulation. Various exogenous compounds such as antibiotics, barbiturates and digitalis undergo an enterohepatic circulation, which may be both portal and extraportal.

Compounds which undergo portal enterohepatic circulation are first secreted by the liver. Then they are passed into the intestine, then reabsorbed from the intestine and then transported back to the liver through the portal vein.

Compounds with an extraportal enterohepatic circulation are absorbed

from the small intestine into the lymphatics which then drain into superior vena cava. "These compounds then enter the systemic circulation and are transported throughout the body where they may be partially excreted e.g. by kidney or by skin. They then pass back to the liver where they are re-excreted in bile.

## 6.11 THE SMALL INTESTINE

The small intestine is continuous with the stomach at the pyloric sphincter and leads into the large intestine at the ileocolic valve. It is about 21 feet long. It lies in the abdominal cavity. It is surrounded by the large intestine.

The small intestine is divided into three parts — duodenum, jejunum and ileum as shown in Figure 6.14. Let us study about these parts:

- **Duodenum:** The first part of the small intestine is called the diodenum. It is about 10 inches in length. At the mid-point of the duodenum, there is a common opening of the pancreatic duct and the bile duct called papilla. It is guarded by the sphincter of oddi as you have seen earlier in Figure 6.11.
- **Jejunum:** The jejunum as illustrated in Figure 6.14, is the middle part of the small intestine and is about 8 feet in length.
- **Ileum:** The ileum is the last part of the small intestine. It is about 12 feet long. It terminates at the ileocolic valve. This controls the flow of material from the ileum to the large intestine and from the large intestine to the ileum.

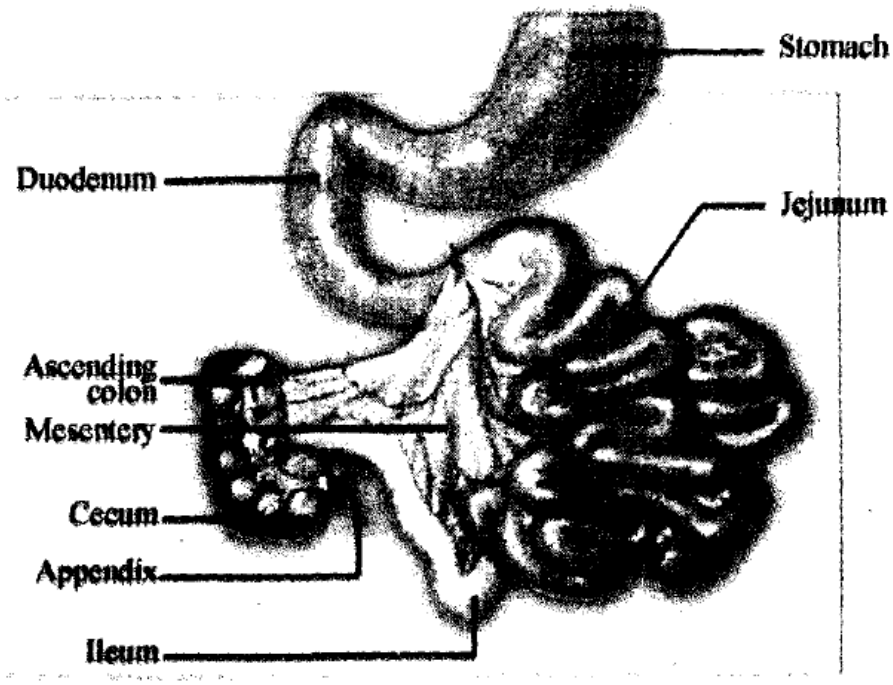



**Figure 6.14: Parts of the human intestines**

Let us also learn about the histological structure of the small intestine. There are four layers of tissue forming walls of the small intestine, same as you learnt earlier under the section on stomach. The outer covering of peritoneum is called as

'mesentery'. The next, muscle layer, consists of smooth muscle fibres — longitudinal and circular muscle fibres. The submucous layer consists of blood vessels, lymph vessels and nerves. The mucous membrane consists of circular folds and villi as you can see in the Figure .6.15.

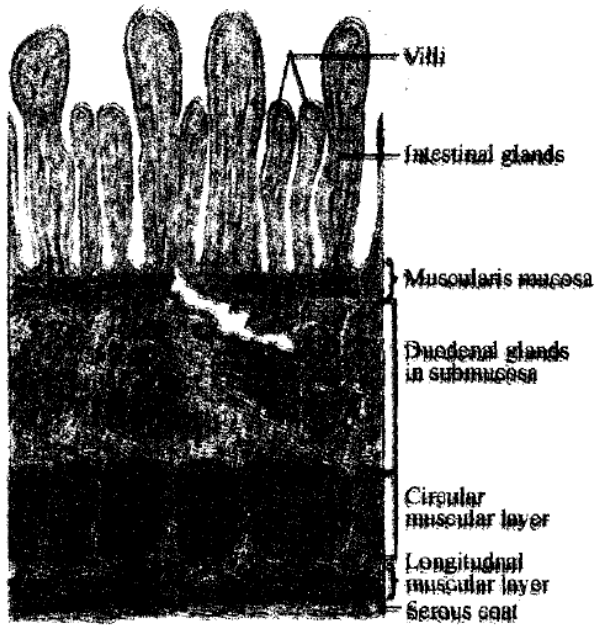



**Figure 6.15: Structure of small intestine**

Villi, as you may already know, are tiny finger-like projections into the lumen of the organ. The walls of the villi are composed of columnar epithelial cells which enclose a network of blood and lymph capillaries. The lymph capillaries are called lacteals. Nutrient materials are absorbed through the walls of villi. Fat is absorbed through lacteals.

There are intestinal glands between the villi. They secrete intestinal juice. Brunner's glands are present in the duodenum. There are numerous lymph nodes in the mucus membrane. The smaller ones are known as solitary lymphatic nodules. The larger ones are known as aggregated lymphatic nodules or Peyer's patches. They are situated towards the distal end of the ileum.

## Functions of small intestine

What functions does the small intestine perform? Can you list a few? Tally your responses with the functions enumerated herewith.

- The small intestine secretes intestinal juice.
- Intestinal juice containing enzymes completes the digestion of carbohydrates, proteins and fats.
- The small intestine protects the body against infection by bacteria with the help of solitary lymph nodes and aggregated glands.

The walls of villi of the small intestine are able to absorb glucose, amino acid, fatty acid, glycerol etc. These are the end-products of carbohydrate, protein and

fat metabolism, as you may have already studied in the Nutritional Biochemistry Course. Glucose and amino acids are absorbed through blood capillaries. Fatty acids and glycerol are absorbed into lacteals or lymph capillaries. The surface area for absorption of nutrients is vastly increased by the circular folds of the mucus membrane and by the large number of villi.

The main function of the small intestine, as you may have read above, is to secrete intestinal juices which help in digestion. What substances/constituents are present in the intestinal juice? Can you help How does it aid in digestion? These are a few aspects discussed next.

## What are the constituents of the intestinal juice?

Intestinal juice is also called succus entericus. The word succus means juice and entericus means intestinal. The digestive juice completes the digestion of carbohydrate, protein and fat. It is secreted by glands lying between intestinal villi.

The total quantity of intestinal juice per day is about 1-2 litres. It is alkaline in reaction (pH 8.0). The intestinal juice contains: water - 98.5% and solids - 1.5%. Of the solids, there are:

- **inorganic constituents** (salts of sodium, potassium, calcium, magnesium with chloride, bicarbonate and phosphate), and
- **organic constituents:** The organic constituents present in the juice include the proteolytic enzyme, carbohydrate-splitting and fat-splitting enzymes and some other enzymes. A brief review of these organic constituents present in the intestinal juice follows.
- **Proteolytic enzymes:** The proteolytic enzymes help in the digestion of proteins. These include: trypsin (a mixture of enzymes containing dipeptidases and amino peptidases) and nuclease (acts on different fractions of nucleic acid)
- Carbohydrate-splitting enzymes, namely amylase (acts on starch and dextrin), sucrase or invertase (acts on cane sugar), maltase (acts on maltose and isomaltase) and lactase (acts on lactose)
- Fat-splitting enzyme, the lipase
- Activating enzyme, the enteropeptidase or enterokinase (activates trypsinogen to trypsin)
- Other enzymes (alkaline phosphatase, cholesterol esterase etc), and
- Mucin

## What are the functions of the intestinal juice?

As already discussed, the main function of the intestinal juice is to aid in digestion. Other functions include protective, absorptive and regulatory functions. Let us learn about these exactions.

- **Digestive function:** Enzymes in succus entericus help in digestion of carbohydrates, proteins and fats present in our food. Let us get to know the enzymes involved.

NOTES

Enterokinase activates trypsinogen and chymotrypsinogen as highlighted herewith.

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

$$\text{Chymotrypsinogen} \xrightarrow{\textit{Enterokinase}} \text{Chymotrypsin}$$

Carbohydrate splitting enzymes act on disaccharide to form monosaccharides, as shown in the reaction herewith.

Sucrase acts on cane sugar, sucrose.

$$\text{Sucrose} \xrightarrow{\textit{Sucrase}} \text{Glucose + Fructose}$$

Maltase acts on beet sugar, maltose

$$\text{Maltose} \xrightarrow{\textit{Maltase}} \text{2 Glucose}$$

Lactase acts on milk sugar, lactose

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

Protein-splitting enzyme peptidase act on peptides (products of digested protein by trypsin of pancreatic juice) to form amino acids.

$$\text{Peptides} \xrightarrow{\textit{Peptidase}} \text{Amino Acids}$$

Fat-splitting enzyme lipase acts on fats to form fatty acid and glycerol.

$$\text{Fat} \xrightarrow{\textit{Lipase}} \text{Fatty Acid + Glycerol}$$

- **Protective function:** Succus entericus protects the intestinal epithelium from the corrosive action of bile, as well as, acid chyme.
- **Absorptive function:** Nutrient materials are absorbed by small intestine in the presence of succus entericus.
- **Regulation of water balance:** Secretion of intestingl juice regulates water balance in the body.

## Mechanism of secretion of succus entericus

The mechanism of secretion of succus entericus involves two factors. These include:

- **Local factors:** Presence of nutritional materials in the small intestine increases the flow of intestinal juice. Distention of the small intestine and the presence of chyme regulate intestinal secretion by various local reflexes.
- **Hormonal factors:** When chyme enters the small intestine, the hormone enterocrinin stimulates intestinal juice secretion.

## 6.12 THE LARGE INTES TINE

The large intestine or colon is about five feet long. It begins at the caecum as can be seen in Figure 6.16 and terminates at the rectum and anal canal.

It is divided into a number of parts — caecum, ascending colon, transverse colon, descending colon, pelvic colon, rectum and anal canal. Figure 6.16, illustrates these different parts of the large intestine. Now, let us study about these parts.

- **Caecum:** This is the first part of the colon. Ileocolic valve opens from the ileum on the medial aspect of the caecum. The vermiform appendix is a fine tube which leads from the caecum. It has the same structure as the walls of the colon but contains more lymphoid tissue.
- **Ascending colon:** The ascending colon passes upwards from the caecum to the level of the liver where it bends acutely to the left to become transverse colon. Transverse colon: This is a loop of colon which extends transversely across the abdominal cavity in front of the duodenum and the stomach.
- **Descending colon:** This part of the colon passes down the left side of the abdominal cavity.
- **Rectum:** This is a slightly dilated part of the colon. It leads from the pelvic colon.
- **Anal canal:** This is a short canal which leads from the rectum to the exterior. There are two sphincter muscles which control the anus. The internal sphincter consists of smooth muscle fibre and is under the control of autonomic nervous system. The external sphincter is formed by striated muscle. It is under voluntary nerve control.

Like other parts of the gastrointestinal tract, the large intestine also consists of four layers. Can you recall these four layers? Yes, the outermost covering is a peritoneum consisting of fibrous tissue. The next layer is a muscle layer. It consists of two layers of smooth muscle fibres. The Iongitudinal fibres are collected into three bands called taeriae coli. These bands of muscles tissue are slightly shorter than the total length They give puckered appearance-go the ocgan. The circular muscle fibres form a thin layer surrounding the colon; The sphincters are formed by thickening of these circular fibres. is the submucous layer which consists of areolar tissue, blood vessels, Iymphoid tissue and nerves. mucous membrane consists of columnar epithelium with numerous goblet cells.

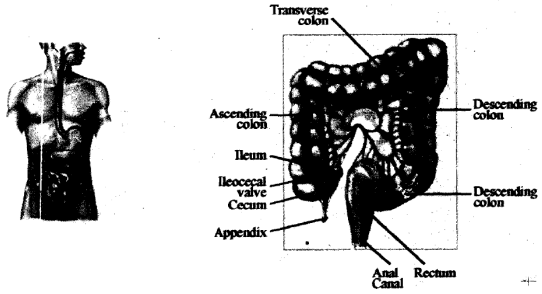



**Figure 6.16: Large intestine**

Next, let us get to know the functions of the large intestine. These functions are highlighted herewith.

## Functions of the large intestine

The multiple functions of large intestine include:

- **Absorption:** The large intestine helps in the absorption of saline, glucose, water, alcohol and drugs at a slow rate.
- **Secretion:** It secretes large quantity of mucin.
- **Bacterial action:** Coarse cellular material cannot be digested in the alimentary tract. In the large intestine, they are broken down by the bacterial action.
- **Synthesis:** A large number of bacteria in the large intestine possess the power to synthesize vitamin B complex and folic acid. It is, however, doubtful whether these vitamins are reabsorbed.
- **Defaecation:** The undigested and waste matter in the intestine is called faeces. The process of evacuation of faecal matter from the rectum is called defaecation.

Defaecation is one of the most important functions of the large intestine.

Let us learn about this function in greater details.

The rectum is normally empty. The faecal matter is stored in the pelvic colon. When there is a mass movement, it forces the contents of the pelvic colon into the rectum. As soon as the matter enters the rectum, there is a desire of defaecation. Nerve endings in the walls of the rectum are stimulated. Nerve impulses are conveyed to the brain and the brain can inhibit the reflex until a suitable time and place is available to defaecate. The colon contents pass into the anal canal and are finally removed from the body. Defaecation involves involuntary contraction of the muscle of the rectum and relaxation of internal anal sphincter and voluntary relaxation of external anal sphincter. Contraction of the abdominal muscles and lowering of diaphragm increases the intra-abdominal pressure. This helps in the process of defaecation. Remember, in infants, defaecation cannot be controlled and occurs by reflex action.

Do you know what the composition of faeces is? Faeces contain undigestible cellular material, such as:

- dead and living microorganisms
- epithehal cells from the intestinal wall
- some fatty acids, and
- mucus

Faeces are brow-n in colour due to the presence of bile pigments. With the discussion on the large intestine, we come to an end of our study on the different organs of the gastrointestinal tract. We shall now look at the movement of the gastrointestinal tract, which you would realize, is basic for performing the various functions of the organs of the gastrointestinal tract as discussed above.

## 6.13 MOVEMENTS OF THE GASTROINTESTINAL TRACT

Unless some kind of movement is present in the gastrointestinal tract, it will not be able to perform its digestive and absorptive functions. What do we mean by movement? You have studied about mastication, swallowing, peristalsis process earlier in the unit. These are the movements of the gastrointestinal tract. Movements are necessary to propel the food mass onwards, to bring the food in contact with different digestive juices and also for mixing and churning. Defaecation, the process of evacuation of the faecal matter, is also performed by contraction of muscle of the large intestine. When food is taken in the mouth, two types of movements — mastication and deglutition are important. What do you understand by these terms? Let's get to know about them.

- **Mastication:** Mastication or chewing means the grinding of food with the teeth. Teeth are designed for chewing. You learnt earlier in sub-section 6.3.1 that incisors and canine are cutting teeth. Premolar and molar are grinding teeth.

We know that chewing of food is important for digestion of all foods, but it is especially important for fruits and vegetables. Indigestible cellular membranes of fruits and vegetables must be broken before the food can be utilized. The total 'surface area of the foodstuff is increased during mastication. This enables the digestive enzymes to act faster on a large surface area.

Chewing is a reflex process. When the food bolus is present in the mouth, it first causes reflex inhibition of the muscles of mastication. This allows lower jaw to drop. The sudden drop, in turn, initiates a stretch reflex of the jaw muscles that leads to a rebound contraction. This automatically raises the jaw to cause closure of the teeth. But it also compresses the bolus against the lining of the mouth. The process is repeated again and again.

- **Deglutition:** Deglutition or swallowing is a complicated mechanism. In general, it is divided into three phases — the voluntary stage, the pharyngeal stage (involuntary) and the oesophageal stage (involuntary). Let us look at these processes.

During voluntary stage, the food bolus is thrown back to the pharynx by the upward elevation of the tongue.

In pharyngeal stage, when the food bolus is pushed backward in the mouth, it stimulates swallowing receptors around the opening of the pharynx. Impulses from these receptors reach the brain stem to initiate a series of automatic pharyngeal muscular contraction. The soft palate elevates, the nasal opening is closed and the larynx is pulled down. The food bolus reaches the pharyngeal cavity.

In oesophageal stage, the laryngeal opening is closed by a covering cartilage and the vocal cords are closed with each other. The food bolus is throw-n into the oesophagus.

Along with chewing and swallowing, there are two other basic types of movements in the gastrointestinal tract — mixing movement and propulsive movement. What

are these movements? Let's learn about these, next.

- **Mixing movement:** This movement helps the intestinal contents to be thoroughly mixed at all times. It is usually caused by the local contractions of small segments of the gut wall. Movements are modified in different parts of the gastrointestinal tract for performance of respective work. Let us understand the mixing movement now.

Gastric secretion comes into contact with the stored food in the stomach. When the stomach is filled, mixing waves move along the stomach wall approximately once in 20 seconds. Mixing movement by these waves tend to move the gastric secretions and the food gradually towards the antral part of the stomach. On entering the antrum, the waves become stronger. The food and gastric secretions become progressively mixed with a greater degree of fluidity.

In the small intestine, rhythmic contractions proceed at a rate of 11 to 12 per minute when the chyme enters the duodenum. In this way, there is a progressive mixing of solid food particles with the secretions from the small intestine.

Mixing movements also occur in the large intestine. Contractions are called haustral contractions. By this movement, the faecal material is gradually exposed to the surface of the large intestine and the fluid is progressively absorbed. These contractions also help to move the faecal contents of the cecum and. ascending colon into the transverse colon.

- **Propulsive movement:** The basic propulsive movement of the gastrointestinal tract is peristalsis. Peristalsis is the movement by which the gastrointestinal canal, having both longitudinal and circular muscle fibres, help propel the contents.

The usual stimulus for peristalsis is distention i.e. if a large amount of food collects at any point in the gut, the distention stimulates the gut wall 2 to 3 cm above this point. A contractile ring appears and a peristaltic movement starts.

Strong peristaltic waves occur about once every 20 seconds in the stomach. They become intense approximately at the incisura angularis, from which they spread through the antrum. The movement is necessary to propel the food mass onwards and to bring it in contact with the gastric juice.

Peristaltic movements take place in the large intestine also. It is called mass movement. Mass movement propels the faecal contents towards the anus. Let us take a break here before we move on to the gastrointestinal hormones and review what we have learnt so you.

## 6.14 GASTROINTESTINAL HORMONES

We have learnt earlier in the unit about the hormones present in the gastrointestinal tract which aid in digestion. Can you name these hormones? Yes, gastrin, secretin, CCK etc. What are hormones? Hormones, as we already know, are the secretions from the ductless glands in the body and have a particular target organ where they perform the functions. There are many types of hormones in our body. In this

unit, we shall study about gastrointestinal hormones.

The digestive functions of the gastrointestinal system are dependent on gastrointestinal hormones. Gastrointestinal hormones are the local hormones secreted by parts of gastrointestinal mucosa, transported in the blood circulation and influence the functions of the stomach, the intestine, the pancreas and the gall bladder. Some of these gastrointestinal hormones namely secretin, CCK have been discussed earlier in this unit.

### Gastrin

Gastrin is secreted from G-cells of the glands of the mucosa of the antral portion of stomach. A significant amount of gastrin is also secreted by the duodenal mucosa. Three types of gastrin have been isolated. The commonest form is called G17 containing 17 amino acids. Another form is G34, a big gastrin containing 34 amino acids. Gastrin containing 14 amino acids is called G14 or minigastrin.

The main functions of gastrin are stimulation of gastric acid and pepsin secretion. The substances that increase gastrin secretion include: peptides and amino acids, increased vagal discharge, calcium and epinephrine. The substances that inhibit gastrin secretion are: acid in the antrum, secretin, glucagon and calcitonin.

We have already studied about secretin and CCK in sub-section 6.8.3. Let us get to know about the other gastrointestinal hormones now.

- **Gastric inhibitory peptide (GIP):** It inhibits gastric secretion and motility.

Enterogastrone: It inhibits gastric acid secretion and motility.

- **Motilin:** It stimulates gastric acid secretion.
- **Vasoactive intestinal peptide (VIP):** It stimulates intestinal secretion of electrolytes and hence water.

Our understanding of gastrointestinal tract shall not be complete without a discussion pn the mechanism involved in the absortion and utilization of carbohydrates, proteins and fats in the GI tract. The next section summarizes the information.

## 6.15 ABSORPTION AND UTILIZATION OF CARBOHYDRATES, PROTEINS AND FATS

We have partly studied about the digestion of carbohydrates, proteins and fats earlier in section 6.10. Let us look at the digestion of these substances in greater details now.

We start with carbohydrates.

### 6.15.1 Absorption and Utilization of Carbohydrates

The digestion of carbohydrates in the body and the digestive juices involved in this process are summarized in Table 6.5.

| Organ | Digestive juice | Enzymes and their action |
|---|---|---|
| Mouth | Saliva | Ptyalin acts on cooked starches and converts starch to maltose. |
| Stomach | Gastric juice | Hydrochloric acid stops the action of salivary ptyalin. |
| Small intestine | Pancreatic juice | Pancreatic amylase converts all starches to disaccharides. |
| Small intestine | Intestinal juice | Sucrase, maltase and lactase convert all sugars to monosaccharides, mainly glucose. |

**Table 6.5: Digestion of carbohydrates**

You would have noticed that the end products of carbohydrate digestion are monosaccharides, namely glucose, fructose and galactose. Let us learn how these are absorbed and utilized.

- **Absorption of glucose:** Glucose is absorbed from the small intestine. The carrier for transport of glucose is present in the brush border of the epithelial cells. The carrier needs sodium-transport system for its action. Therefore, it is believed that the carrier has a receptor site for both glucose molecule and sodium ion. The energy to cause movement of the carrier from the exterior of the membrane to the interior is derived from the difference in sodium concentration between the outside and inside. As sodium diffuses to the inside of the cell, it drags the carrier and the glucose along with it. This is called sodium gradient theory for glucose transport. You can read more about the absorption of glucose in the Nutritional Biochemistry Course.
- **Transport of fructose:** Fructose is converted to glucose after it is being transported. This occurs before entering the portal blood. The conversion occurs inside the cell. Fructose first becomes phosphorylated, then converted to glucose and finally released from the epithelial cell into the blood.
- **Utilization of glucose :** A constant blood glucose level is maintained so that all body tissues have a constant supply. Excess glucose is converted to glycogen in the presence of insulin and stored in the liver and in the muscles. Remaining glucose is converted into fat and stored in the body. Glucose is used in the body to provide energy and heat. Oxygen helps in the process of breakdown of glucose. Waste products lea are carbon dioxide and water.

## 6.15.2 Absorption and Utilization of Proteins

The digestion of proteins is summarized in Table 6.6.

| Organ | Digestive juice | Enzymes and their action |
|---|---|---|
| Mouth | Saliva | No action. |
| Stomach | Gastric juice | Hydrochloric acid converts pepsinogen to pepsin. Pepsin converts all proteins to peptones. |

| | | |
|---|---|---|
| Small intestine | Pancreatic juice | Enterokinase of intestinal juice converts trypsinogen to trypsin and chymotrypsinogen to chymotrypsin. Trypsin and chymotrypsin convert peptones to peptides and polypeptides. |
| Small intestine | Intestinal juice | Peptidases convert [illegible] to amino acid. |

**Table 6.6: Digestion of proteins**

## Absorption of amino acid

Proteins are absorbed in the form of amino acids. Amino acid transport occurs only in the presence of simultaneous sodium transport. Carrier systems are present in the brush border of the epithelial cells. Amino acids are also transported by sodium gradient mechanism. ne carrier has a receptor site for both an amino acid molecule and a sodium ion. Only when both sites are filled, the carrier will move to the interior of the cell. The sodium diffusion to the cell interior pulls the carrier and its attached amino acids to the interior where amino acids are trapped. They diffuse through the sides or base of the cell into the portal blood. There are four different carrier systems — one transports neutral amino acid, second one transports basic amino acid, third transports acidic amino acids and the fourth transports proline and hydroxyproline.

## Utilization of amino acid

Amino acids are utilized in the liver to form plasma proteins like serum albumin, serum globulin, prothrombin and fibrinogen.

Amino acids, not required in the body, are deaminated in the liver. The nitrogenous part is converted into urea and excreted in the urine. The remaining part is used to provide energy and heat or deposited fat. To learn more about this process, look up Unit 8 in the Nutritional Biochemistry Course.

## 6.15.3 Absorption and Utilization of Fats

The digestion and absorption of fats in various orgasm of the body along with the enzymes involved is summarized in Table 6.7,

| Organ | Digestive juice | Enzymes and their action |
|---|---|---|
| Mouth | Saliva | No action. |
| Stomach | Gastric juice | No action. |
| Small intestine | Bile and pancreatic juice | Bile emulsifies fat. Lipase converts fats to fatty acids and glycerol. |
| Small intestine | Intestinal juice | Lipase completes the digestion of fats to fatty acids and glycerol. |

**Table 6.7 : Digestion of fat**

### Absorption of fatty acid and glycerol

Free fatty acid and glycerol dissolve in lipid portion of the bile micelles. They are soluble in chyme. In this form, they are transported to the epithelial cells. As they are lipid soluble, they become dissolved in the membrane and diffuse to the interior of cells. As they diffuse through the cell membrane, bile acid micelles are left in the chyme. They then absorb more fatty acids and transport them to the epithelial cells. Thus, the bile acids perform a ferrying function.

After entry into the epithelial cell, the fatty acids are reconstituted by the endoplasmic reticulum into triglycerides. Almost all of the glycerol that is utilized for this purpose is synthesized from glycerophosphate. Once formed, the triglycerides collect into globule, along with the absorbed cholesterol, absorbed phospholipids and newly synthesized phospholipids. Each of these is then encased in a protein coat. Such globules are called chylomicrons. Read Unit q of the Nutritional Biochemistry Course *for more this topic, Finally, globular mass along with the protein coat enters the intercellular spare from the sides of the epithelial cells. From here, it passes into central lacteal of the villi.

From the lacteals of villi, the chylomeroryxe propelled along the lymph through the Thoracic duct and is emptied into greatveins : superior vena cava and inferior vena cava. 80%-90% of fat gut and is transported to the blood in the form of chylomicrons.

Small quantities of short chain fatty acids from cow milk, butter etc. are absorbed directly into the portal blood. They are not converted into triglyceride and are not absorbed into the lymphatics. Actually, short chain fatty acids are more water soluble than long chain fatty acids. They are directly diffused from the epithelial cells into the capillary blood of the villus.

### Utilization of fatty acids

In the presence of oxygen, fatty acids are utilized to provide energy and heat. Waste products produced are carbon dioxide and water.

Fatty acids are stored as fat. When this stored fat is required in the body for oxidation, it must first be desaturated by the liver.

The discussion above presented a brief review on the digestion, absorption and utilization of nutrients in the GI tract. Finally, let us look at the disorders of the digestive tract. With this our study and understanding of the physiology of gastrointestinal tract will be completed.

## 6.16 SOME COMMON DISORDERS OF THE DIGESTIVE SYSTEM

Having understood the structure, functions of the various organs which constitute the gastrointestinal tract, you would now appreciate how important and crucial the functioning of this system is for good health. You may have sometimes experienced few common disorders related to the malfunctioning of the GI tract. What are

these disorders? Read and find out.

- **Constipation:** Constipation means infrequent or difficult evacuation of faeces. It is often associated with the large quantities of dry hard stool in the descending colon. One of the causes of constipation is irregular bowel habits, which may develop from the inhibition of the normal defecation reflex. Constipation can also result from spasm of a small segment of colon. Occasionally, a person develops constipation which is so severe that bowel movements occur only once in several weeks. This may be due to congenital lack of myenteric plexus. A large quantity of stool accumulates in the colon. The condition is called megacolon.

Intake of plenty of water, vegetable and roughage may relieve constipation.

Diarrhoea: Frequent evacuation of watery stool, you know, is called diarrhoea. There is a rapid movement of faecal matter from the large intestine. The major causes of diarrhoea may be infection or by parasympathetic stimulation of the large intestine.

Infection may be due to a bacteria or a virus. Usually the infection is extensive in the ileum and large intestine. Large quantity of fluid is lost in stool as it washes the infections agent toward the anus.

Psychogenic diarrhoea may occur due to nervous tension. There is excessive stimulation of the parasympathetic nervous system. It stimulates both motility and secretion of mucus in the distal colon resulting in diarrhoea.

There is excessive fluid and electrolyte loss. This loss can be compensated by taking fluid and salt. Infection should be treated.

- **Vomiting:** Vomiting is forcible ejection of contents of the stomach through the mouth. The stimuli that cause vomiting may occur in any part of the gastrointestinal tract.

When the vomiting centre is sufficiently stimulated, the effects are deep breath, closing of the epiglottis, and lifting of the soft palate followed by a strong downward contraction of the diaphragm along with contraction of abdominal muscles. The gastroesophageal sphincter relaxes and gastric contents come out.

Obstructive jaundice: When bile duct is obstructed due to presence of stones, growth, pressing bile duct, bile pigments don't reach small intestine and regurgitate back to blood, leading onto excess of these pigments in blood. These have an affinity for elastic tissue in sclera of eye, skin in mucosa of tongue, hence these organs become yellowish - hence jaundice.

With a brief study of disorder, we come to an end of our study of the physiology of the gastrointestinal system.

## 6.17 LET US SUM UP

In this unit, we studied about the digestive system and the organs involved. The digestive tract, as you know, is a long tube through which the food passes. It commences at the mouth and terminates at the anus.

We learnt in detail about the role of the different organs — mouth,

oesophagus, stomach, pancreas, liver, gall bladder, small intestine, large intestine etc.— involved in the process of digestion and how they function to ensure the proper functioning of the digestive system.

We also got to know four major functions performed by the digestive system — ingestion, digestion, absorption and elimination.

Finally, we saw how the major components of food that is, carbohydrates, proteins and fats are metabolized in our body and what are the various digestive enzymes involved in the process. We also had a brief review on some of the major gastro- intestinal disorders such as diarrhoea, constipation and jaundice.

## 6.18 GLOSSARY

**Antrum** : a dilated portion of the pyloric part of the stomach.

**Canaliculus** : an extremely narrow tubular passage or channel.

**Cephalic** : pertaining to the head.

**Cholagouge** : an agent that stimulates gall bladder contraction.

**Choleretic** : stimulating bile production by the liver.

**Chyme** : a semi-liquid mass of partially digested food.

**Deglutition** : swallowing.

**Haemopoietic** : pertaining to blood making.

**Hydrocholerectic** : stimulating bile production with increased water output.

**Ileocolic** : pertaining to ileum and colon.

**Myenteric Plexus** : a plexus of unmyelinated fibers and postganglionic autonomic cell bodies in the muscular coat of the esophagus and stomach and intestines.

**Peritoneum** : the serous membrane living the walls of the abdominal and pelvic cavities.

**Plexus** : network of vessels and nerves.

**Pylorus** : The distal aperture of the stomach opening into the duodenum.

**Sinusoids** : resembling a sinus (i.e. cavity or channel).

**Sphincter** : a ring like muscle which closes a natural orifice or passage.

## 6.19 CHECK YOUR PROGRESS EXERCISES

**NOTES**

UNIT

# 7

# PHYSIOLOGY OF RENAL SYSTEM

**STRUCTURE**



## 7.1 LEARNING OBJECTIVE

After studying this unit, you will be able to:

- illustrate the structure and describe the functions of the various organs of the stem,
- discuss the mechanism of urine formation,
- explain the non-excretory functions of the kidneys, and
- describe the medical aspects related to the abnormal or non-functioning of the
- kidneys, such as dialysis and renal transplant.

## 7.2 INTRODUCTION

In the last unit we learnt about the gastrointestinal tract. Now in this unit, we will deal with the physiology of the renal system including an in-depth study and

understanding of the key organs of the excretory system.

The body excretes substances which are unwanted and harmful to the body through urine, faeces, sweat etc. The excretory system consists of organs like kidneys, ureters, urinary bladder and urethra.

Kidneys are a pair of bean-shaped organs in the dorsal region of the vertebrate abdominal cavity, important to the health of an individual. Their function is to form urine and to pass urine to the ureters and bladder for excretion. In doing this function, several regulatory functions are carried out such as maintenance of water and electrolyte balance, regulation of acid-base concentration and filtration and disposal of metabolic waste materials (which are then excreted as urine). The discussion on kidneys, in this unit, will include mechanism of formation of urine and the regulation of volume of body fluids. It will also focus on structure, functions (both normal and abnormal) and certain medical aspects related to the abnormal functioning, such as dialysis and renal transplant.

Besides kidneys other excretory organs i.e. ureters, urinary bladder and urethra also have a specific role in storing and passage of urine outside the body. What are the functions of these organs? A detailed discussion is presented in this unit.

## 7.3 ORGANS OF THE URINARY SYSTEM

Look at Figure 7.1. It illustrates the organs of the urinary system. As is evident, the organs of the urinary system consist of 2 kidneys, 2 ureters, 1 urinary bladder and a urethra, through which the urine is discharged from the urinary bladder to the exterior.

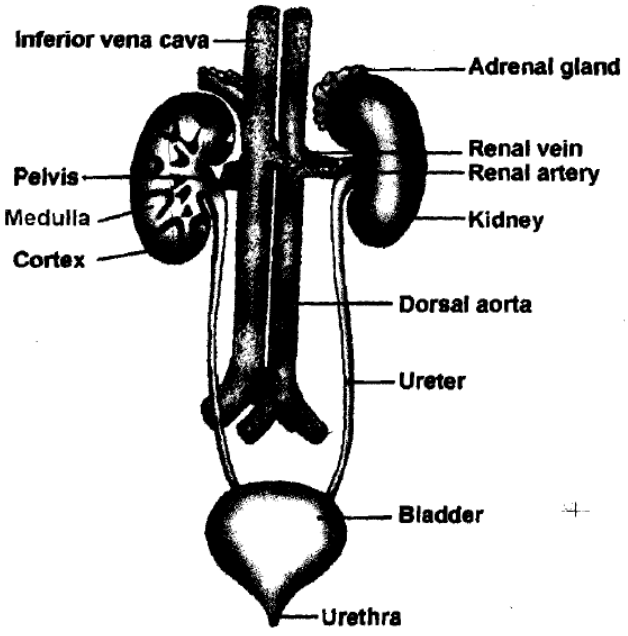



**Figure 7.1: Organs of the urinary system**

As you will read, you will learn that the kidneys form urine, the ureters thereby convey the urine from the kidneys to the urinary bladder, where the urine is temporarily stored. Finally, from the urethra the urine is discharged to the exterior. The complex function performed by each of these organs along with the structure is discussed in the subsequent sections. We shall start our study of the urinary system by getting to know the structure and functions of the kidney.

## 7.4 KIDNEY: STRUCTURE AND FUNCTIONS

Looking at Figure 7.1, you would have got a clear idea as to where the kidneys are situated. Yes, the kidneys are located in the posterior part of the abdomen, one on each side of the vertebral column. Vertebral column, as you may already know, is a column formed of a series of bones, called vertebrae forming the axis of the skeleton and protecting the spinal cord. The kidneys are described as the bean- shaped organs surrounded by the renal fat. Let us study about the structure of kidneys in detail.

### 7.4.1 Gross and Microscopic Structure of Kidney and Nephron

Our bean shaped kidneys are enclosed in capsule. If we were to cut a kidney in half, as shown in Figure 7.2, the internal structures of the kidney would be exposed. Underlying the capsule you will find the external part of the kidney known as cortex. The inner part is known as medulla. Medial to the medulla is a fissure, which is known as the hilum of the kidney. Hilum, in general, is that part of a kidney where the blood vessels and nerves enter. At the hilum, the renal artery and renal nerves enter the kidney and the renal vein leaves the kidney as can be seen in Figure 7.2.

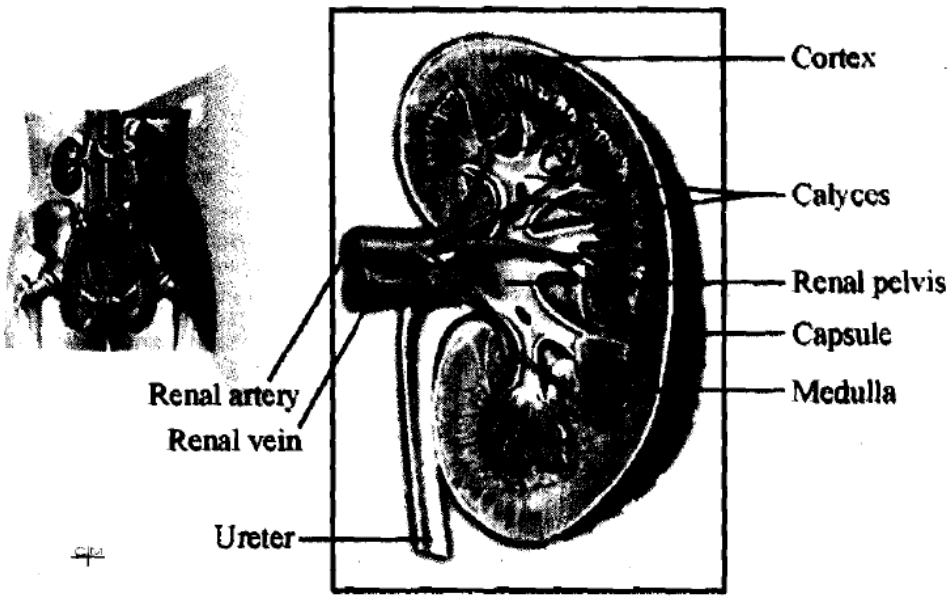



**Figure 7.2: Parts of the kidney**

To further understand how our kidneys work (to eliminate the waste materials), let us have a look at the microscopic structure of the kidneys. Here, we shall focus on the basic unit of kidney i.e. the nephron which is responsible for the kidney's functioning.

Look at the microscopic structure of kidneys in Figure 7.2. If you look closely at the cortex and medulla, many tiny tubular structures can be seen, that stretch across both regions perpendicular to the surface of the kidneys. In each kidney, there are one million of these structures, called nephrons. The nephron is described as the functional unit of kidney. It is a long thin tube, as can be seen in the Figure 7.3, packed between the cortex and medulla of the kidney. It is closed at one end and the other end opens at the collecting tubule and is surrounded by the capillaries i.e., tiny blood vessels that distribute oxygen-rich blood to the various parts of the body.

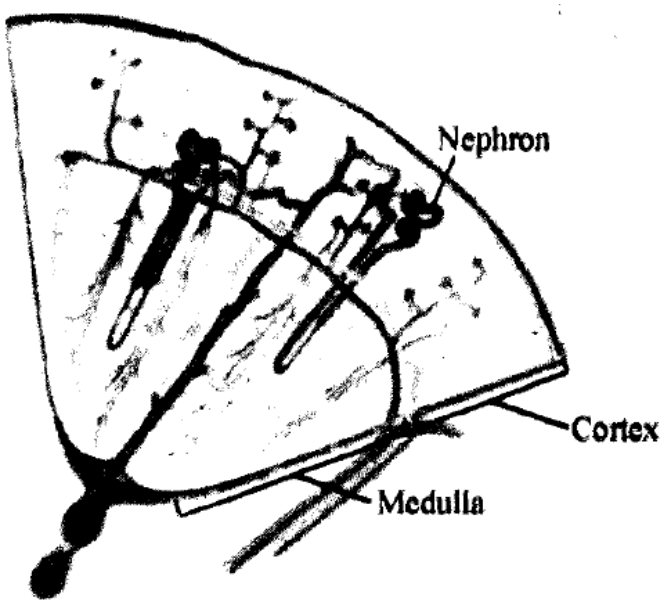



**Figure 7.3: Nephron the functional unit Of the kidney**

So we have seen that the basic structural and functional unit of the kidney is the nephron. Each kidney has about 1 million nephrons. What constitutes the nephron? Each nephron consists of a renal corpuscle and a renal tubule as illustrated in Figure 7.4. The renal corpuscle is composed of a glomerulus (a network of fine capillaries), associated with a surrounding, cup-shaped section of renal tubule called the glomerular (or Bowman's) capsule. The renal tubule is divided into three morphologically and functionally distinct regions, as illustrated in the Figure 7.4 which are:

1) the proximal convoluted tubule (PCT),
2) the loop of Henle (with its thin descending limb, thin ascending limb and thick ascending limb), and
3) the distal convoluted tubule (DCT).

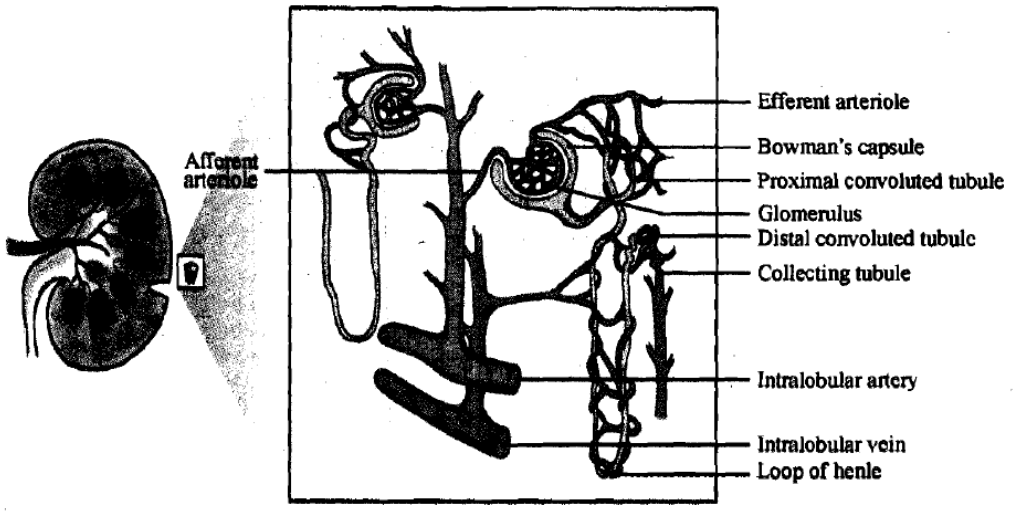



**Figure 7.4: Basie structure of a nephron**

Let us get to know a bit more about these structures of a nephron.

- **Glomerulus:** It is the main filter of the nephron and lies within the Bowman's capsule. It resembles a twisted mass of tiny tubes as can be seen in Figure 7.4, through which the blood passes. Being semi-permeable, it allows the passage of water and the soluble wastes. The glomerular capsule forms a cup-like structure and is a thin double membrane enclosing the glomerulus. The main function of glomerulus is to filter the waste products from the blood and thus, initiate urine formation.
- **Bowman's capsule:** It contains the primary filtering device of the nephron, that is, glomerulus. It is a double-walled, cup-shaped structure around the glomerulus of each nephron of the vertebrate kidney. It serves as a filter to remove organic wastes, excess inorganic salts and water. It is located in the cortex.
- **Proximal Convoluted Tubule or proximal tubule (PCT):** The proximal tubule is the most proximal part of the renal tubule which lies in the cortex. Once the glomerular filtrate passes through the opening in the Bowman's capsule, it goes through the PCT from where it passes through the Loop of Henle and the distal tubule (DCT), about which we shall learn next.
- **Loop of Henle:** The Loop of Venle is a long U-shaped part of the renal tubule, extending through the medulla from the end of the PCT to the beginning of the DC T. It begins with a descending limb having a thick-walled segment called the proximal straight tubule, followed by a thin-walled segment called the thin or attenuated tubule; this is followed by the ascending limb, which sometimes includes the distal end of the attenuated tubule and always ends with a long thick-walled segment called the distal straight tubule. The loops vary in the lengths of their segments according to their locations in the kidney. It is also called as ansa nephroni and is responsible for carrying urine out of the nephron.
- **Distal Convoluted Tubule or Distal Tubule (DCT):** A distal, rolled-together or coiled part of the ascending limb of the renal tubule. It lies in the cortex.

The urine from here passes into the collecting duct.

- **Collecting Duct/Tubules:** A long straight portion after the distal tubule is the open end of the nephron. It extends from the cortex down through the medulla.

These are responsible for collecting urine from DCT of the nephron and passing it to the renal pelvis. These are also of two types, proximal straight tubule and distal straight tubule.

Now that we have an understanding of the anatomy of the kidney and the nephron, let's have a look at how these parts allow the kidneys to do its jobs. But first let us check what we have learnt so far.

## 7.4.2 Functions of the Kidney

The functions of the kidneys, as you already know, are to form urine and to pass urine for excretion, maintain water and electrolyte balance. The bean-shaped kidneys, each about the size of a child's fist, performs several functions essential to health, the most important of which is to filter blood and produce urine. Without the kidneys, waste products and other toxins would soon build up in the blood to fatal levels. The kidneys also regulate blood pressure and the level of vital salts in the blood, as well as, secrete the hormone that controls the production of red blood cells. Hence, the physiological functions of the kidneys are many. These are enumerated herewith. The kidneys function to:

- keep the concentrations of various ions and other important substances constant. A number of chemicals are important to the blood chemistry, such as potassium, sodium, phosphorous, calcium, magnesium and chloride. The healthy kidneys ensure the right amounts of these in the blood.
- keep the volume of water in the body constant by removing excess fluid from the body. The kidneys regulate the volume of extra-cellular fluid by eliminating or retaining water. The re-absorption of water in the tubules is controlled by pituitary and hypothalamic actions. The pituitary is an endocrine gland found in the body about which we will learn later in Unit II. The posterior pituitary produces anti-diuretic hormone (ADH), which increases the amount of water reabsorbed, the adrenal cortex (another endocrine gland) produces the hormone aldosterone, which influences the re-absorption of sodium and water.
- regulate the osmolarity of extra-cellular fluid by regulating the amount of sodium chloride. and water excreted.
- remove the wastes from the body. Many metabolic waste products such as urea, uric acid, ammonia and creatinine need to be filtered, are removed from the body, by the kidneys.
- keep the acid/base concentration of the blood constant and regulate the blood pressure. Renin, an enzyme-- like substance of the kidney, helps in coverting angiotensinogen to angiotensin which is responsible for producing vascular constriction, thereby increasing the blood pressure. It also stimulates the secretion of aldosterone from the adrenal glands and causes sodium and water to be retained, increasing blood volume and blood pressure.

- stimulate the making of red blood cells. Erythropoietin is a hormone responsible for maintaining the right amount of RBC count in the body by stimulating the bone marrow to make more RBCs.
- maintain the body's calcium levels. Along with parathormone and calcitriol, kidney helps the body to absorb calcium.

Now we shall study in detail about a few major functions of the kidney, which we enumerated above and which makes it an important part of the excretory system. Let us get to know about the process of urine formation first, which as you know by now, is the main function of the kidney.

## 7.4.3 HOW THE KIDNEY WORKS

In the section above we learnt about the urine formation, water balance, maintenance of electrolyte and pH balance functions of the kidneys. Let us have a look at the urine formation function of the kidneys, first.

### A) Formation of Urine

The kidneys form urine in three phases: simple filtration, selective re-absorption and secretion. Let us begin with the process of filtration.

1) **Simple filtration:** The process of filtration takes place in the nephron where approximately 10% of the blood which the kidney receives gets filtered under pressure through the walls of the glomerular capillaries and Bowman's capsule. The filtrate is composed of water, ions (e.g., sodium, potassium and chloride), glucose and small proteins. The rate of filtration is approximately 125 mi/ minute or 180 L each day. Also, the amount of any substance that gets filtered is the product of the concentration of that substance in the blood and the rate of filtration. So, higher the concentration, greater the filtration rate, the more substance gets filtered.

A filter separates large and small particles by retaining the larger particles and allowing the smaller particles to pass through. The semi-permeable wall of the glomerulus acts as a filter. It allows the blood constituents having a molecular weight less than 68,000 (such as water, food substances like glucose and amino acids, inorganic salts, waste products like urea, uric acid and creatinine etc.) to pass through. It retains the larger molecules (red blood cells, white blood cells, platelets and plasma proteins etc.). These high molecular weight substances are unable to pass through the semi-permeable membrane of the glomerulus.

The volume of filtrate produced per minute is termed as the glomerular filtration rate. Let us get to know more about the GFR.

- **Glomerular Filtration Rate (GFR):** The kidneys receive a large amount of blood flow. The kidney blood flow is approximately 1200 ml per minute. One-tenth of this is filtered as the blood flows through the glomeruli i.e., about 120 ml. Filtration takes place through the semi-permeable walls of the glomerular capillaries, which are almost impermeable to proteins and large molecules.

The filtrate is thus virtually free of proteins and has no cellular elements. The glomerular filtrate is formed by squeezing the fluid through the glomerular capillary bed. The driving hydrostatic pressure (the pressure exerted by a liquid as a result of its potential energy) is controlled by the afferent and efferent arterioles (the muscular walled vessels leading to and from each glomerulus as shown in Figure 7.4), and is provided by the arterial pressure, that is, the pressure of the circulating blood on the arteries. The glomerular filtration rate decreases with age and disease.

In order to keep the renal blood flow and GFR relatively constant, the hydrostatic pressure in the glomerulus has to be kept fairly constant. When there is a change in the arterial blood pressure, there is a constriction or dilatation of the afferent and efferent arterioles. This process is called as autoregulation and can be more precisely defined as the tendency of the blood flow to organ to remain constant inspite of the pressure changes in the artery that delivers blood to that organ.

## Various factors influence GFR. These include:

l) **Renal blood flow:** A large proportion of blood flows into the glomerulus. The greater the rate of flow of blood into the glomerulus, the greater will be the GFR.

2) **Sympathetic stimulation:** If there is a mild or moderate sympathetic stimulation of the kidney, the GFR decreases. But if there is a strong sympathetic stimulation, glomerular pressure is reduced and the GFR falls to zero.

3) **Afferent arteriolar constriction:** Afferent arteriolar constriction decreases the rate of blood flow into the glomerulus, decreases the glomerular pressure and the GFR.

4) **Efferent arteriolar constriction:** Constriction of the efferent arteriole increases the glomerular and the GFR.

5) **Arterial pressure:** Though an increase in the arterial pressure causes an increase in GFR but the effect is minimized because of autoregulation of the kidney. Rise of arterial pressure increases constriction of afferent arteriole. This prevents a major rise in glomerular pressure causing the GFR to increase to only 15 to 20 percent.

Before we proceed to the second phase, i.e. selective reabsorption, let us get to know a few important terms associated with the mechanism of urine formation that might be of help to us to understand the process better. These are presented in Box 7.1.

**Box 7.1: Important terms associated with the mechanism of urine formation**

*Maximum Tubular Secretory Capacity:* The maximum rate at which tubules can transport a substance from the blood vessel to the lumen or from the lumen to the blood vessel is limited by the *carrier system*. The maximum rate is known as the *tubular maximum* and is usually expressed as milligram per minute.

**Active transport:** When the substances are transported through a cell membrane against a concentration gradient, that is, from a dilute solution to a concentrated solution, energy must be imported to the molecules. This process of transport is called as the active transport.

Active transport of sodium occurs from inside the epithelial cells into the spaces between the cells. This transport from the cell diminishes the sodium concentration inside the cell. Other substances, besides sodium, that are actively absorbed through the tubular epithelial cells include glucose, amino acids, phosphate ions and others.

Hydrogen ions and potassium ions are actively secreted into all or some portions of the tubules. Active secretion occurs in the same way as active absorption. Here, the cell membrane transports the secreted substances in the opposite direction i.e. from a low concentration to a high concentration, against a gradient.

Passive transport or diffusion: Diffusion means the random movement of particles in a fluid. The movement of particles from a high concentration area to a low concentration area takes place till the concentration is uniform. Although the particles move at random in all directions, a greater number of them move from a region of higher concentration to that of a lower concentration. When water is reabsorbed, the concentration of urea in the tubular fluid rises. This, in turn, causes urea to diffuse from the tubular fluid to the peritubular fluid (fluid surrounding the tubule). Chloride, phosphate and bicarbonate ions are attracted from the tubular fluid towards the peritubular fluid.

A few substances are secreted by diffusion in the same manner. For example, ammonium ions are synthesized inside the epithelial cells and diffuse into the tubular lumen. They help to control the degree of acidity of tubular fluid.

Now, let us get back to the second phase i.e. selective reabsorption and try to understand what role does this phase has in the formation of urine.

2) **Selective reabsorption:** The purpose of this process is to reabsorb those constituents of the filtrate which are essential to the body. By this reabsorption, the composition and volume of the filtrate is altered, fluid and electrolyte balance of the body is maintained.

The specialized cells of the tubules selectively reabsorb the constituents of the filtrate as they pass through the tubule. Plasma substances like glucose, amino acids and vitamin C are reabsorbed under normal circumstances. They have a high threshold value. But there is a limit to it. If the blood glucose is within 120 mg per 100 ml of blood then all the glucose in the filtrate is reabsorbed. If it exceeds 180 mg per 100 ml of blood, some glucose appears in the urine. This occurs in the case of diabetes mellitus. A major portion of the waste products like ammonia, creatinine and sulphates are not reabsorbed but excreted. These substances have low threshold values. In between these high threshold substances and low threshold substances, there are some substances which are reabsorbed according to the need of the body. For example, the reabsorption of inorganic salts-depends upon the plasma level of the substances.

Let us briefly look at the few important aspects that might help us in understanding

and remember the process of selective reabsorption. These are presented in Box 7.2.

**Box 7.2: Selective Reabsorption Process**

- Specialized proteins called 'transporters' are located on the membranes of the various cells of the nephron.
- These transporters grab the small molecules from the filtrate as it flows by them.
- Some transporters require energy, usually as ATP (active transport), while others don't (passive transport).
- Water gets reabsorbed passively by osmosis in response to the build up of reabsorbed Na in spaces between the cells that form the walls of the nephron.
- Other molecules get reabsorbed passively when they are caught up in the flow of water (solvent drag).
- Reabsorption of most substances is related to the reabsorption of Na, either directly, via sharing a transporter or indirectly through a solvent drag.

Both passive and active reabsorption of molecules from the nephron to the blood occurs at the PCT. Cells lining the PCT are anatomically adapted for active re-absorption. There are other features as well which play a role in the re-absorption.

These are:

**a) Microvilli:** Lots of microvilli, i.e. minute, hair-like projections of the cell membranes increase the surface area for reabsorption.

**b) Mitochondria:** Lots of mitochondria make ATP needed for active transport.

c) Active transport is selective re-absorption.

There are also two major factors that affect the reabsorption process. These include:

**1) Concentration of small molecules in the filtrate :** The higher the concentration, the more molecules can be reabsorbed.

**2) Rate of flow of the filtrate :** the flow rate affects the time available for the transporters to reabsorb molecules.

The useful products return to the blood and the water is passively reabsorbed. Sodium and chloride ions are actively reabsorbed, which encourages the water to follow. Amino acids and glucose are reabsorbed to blood. The reabsorption rate is 400 mg/100ml plasma. The rest of the glucose is in the urine. In diabetes mellitus, the excess glucose is present in the blood. A part in the filtrate is reabsorbed, part is not.

Next, we move on to the third and last phase in the process of urine formation, that is, secretion.

**3) Secretion:** In the process of filtration through the glomerulus, the non-threshold substances and drugs are not cleared from the blood because the blood does not

remain for a long time in the glomerulus. Such substances are secreted into the convoluted tubules and cleared from the blood. These substances include para-amino hippuric acid (PAH) and penicillin (a group of broad-spectrum antibiotic drugs obtained from penicillium molds or produced synthetically, used to treat various infections and diseases) etc. They pass from the blood into the urine.

Having learnt about the urine formation function, we move on to the water balance function of the kidney.

## B) Water Balance Function of the Kidney

Water is one of the most important constituent in the daily diet. You are already aware of the roles it plays in our body. Maintenance of water and electrolyte balance in the body is an equally important consideration. Let us see how kidneys help to regulate and maintain water balance. The body excretes excess water through the kidneys. The balance between intake and output is maintained by the posterior pituitary hormone ADH or anti-diuretic hormone or vasopressin. Substances that stimulate the formation of urine are termed as diuretics. The hormone ADH causes the suppression of urine. The minimum urinary output is about 500 ml per day average being 1500 ml.

There are cells in the hypothalamus (in the brain) which are sensitive to the changes in the osmotic pressure of the blood. These sensory receptors sensing the osmotic pressure are called as osmoreceptors.

When the concentration of sodium and other osmotically active substances in the extracellular fluid rises, there is an increased osmotic pressure in the fluid. Osmoreceptors (supraoptic nucleus) in the hypothalamus are stimulated. The hypothalamus sends message to the posterior pituitary gland and it secretes ADH. The ADH acts on the distal convoluted tubules and collecting ducts of the kidney to cause an increase in the penneability resulting in an increased reabsorption of water which reduces osmotic pressure of the blood. The pore size of the epithelial cell is increased. This is enough for the water molecules to diffuse through, but does not allow most other substances in the tubular fluid to pass through. Thus water is returned to the body fluids whereas the sodium and other solutes are lost in the urine. In this way, the osmotic and water balance is maintained.

If there is an increased concentration of dissolved substances in the blood, there is an increased ADH production. The water reabsorption under ADH influence in the DCT and collecting duct is known as facultative absorption. In deficiency of ADH, there is less facultative absorption, hence urine output is increased. This condition is called as diabetes insipidus. On the other hand, if the osmotic pressure of the blood is reduced due to increased plasma volume, the amount of ADH secretion is reduced and diuresis occurs. Two mechanisms that are involved in this process are:

- the structure and transport properties of the loop of Henle in the nephron, and
- the anti-diuretic hormone (ADH), also called as vasopressin, secreted by the pituitary gland.

Let us begin first by understanding the structure and transport properties of the

Loop of Henle.

Transport properties of Loop of Henle: The loop of Henle, as shown in Figure 7.5, has a descending limb and an ascending limb. As the filtrate moves down the loop of Henle, water is reabsorbed, but the ions (Na, C1) are not. The removal of water serves to concentrate the Na and C1 ions in the lumen. Now, as the filtrate moves up the other side (ascending limb), Na and C1 ions are reabsorbed but the water is not. What these two transport properties do is set up a concentration difference in NaC1 along the length of the loop with the highest concentration at the bottom and lowest concentration at the top. The loop of Henle can then concentrate NaC1 in the medulla. The longer the loop, the bigger the concentration gradient. This also means that the medulla tissue tends to be saltier than the cortex tissue. This property of loop of Henle to improve osmolarity of filtrate in a counter current flow - is known as Counter current Multiplier System — where Na is multiplied every time it passes through loop of Henle. That is the reason why filtrate is isotonic in PCT, becomes hypertonic as it passes through loop of Henle, hypo as it goes to DCT and finally hypertonic as it leaves collecting duct (Figure 7.5). So normally urine is highly concentrated and hypertonic as compared to blood.

Now, as the filtrate flows through the collecting ducts, which go back down through the medulla, water can be reabsorbed from the filtrate by osmosis. Have a look at the Figure 7.5. Here you will notice that water moves from an area of low Na concentration (high water concentration) in the collecting ducts to an area of high Na concentration (low water concentration) in the medullary tissue. If you remove water from the filtrate at this final stage, you can concentrate the urine.

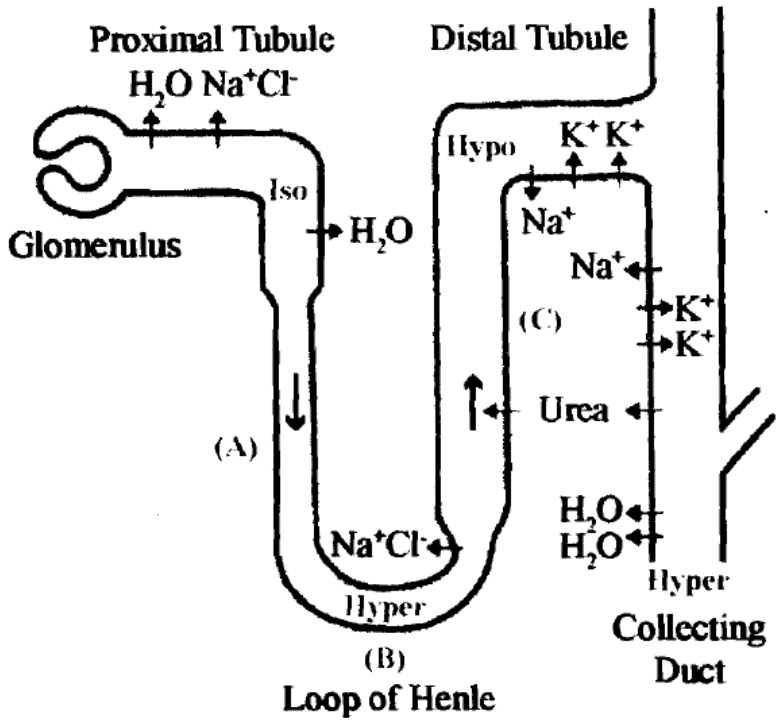



**Figure 7.5: Transport in loop of Henle**

Now let us study about the hormone ADH (anti-diuretic hormone) or vasopressin and its role in maintaining water balance.

**Anti-Diuretic Hormone (ADH):** It is secreted by the pituitary gland and controls the ability of water to pass through the cells in the walls of the collecting ducts. If ADH is not present, then water cannot pass through the walls of the ducts. The more the ADH present, the more water can pass through.

Just now we have studied about the specialized nerve cells called as osmoreceptors that are present in the hypothalamus of the brain. These cells, as you would recall, sense the Na concentration of the blood. The nerve endings of these osmoreceptors are located in the posterior pituitary gland and secrete ADH. If the Na concentration of the blood is high, the osmoreceptors secrete ADH. If the Na concentration of the blood is low, they do not secrete ADH. In reality, there is always some very low level of ADH secreted from the osmoreceptors. Thus we can see that the electrolyte balance is always maintained by the kidneys. This function is further elaborated next.

## C) Maintenance of Electrolyte Balance

In the process of formation of urine, the kidneys also maintain electrolyte balance. Sodium is the most important cation that exists in the extra-cellular fluid of the body. It comes from the diet and common salt. It is lost through the skin as a constituent of sweat and through kidneys as a constituent of urine. The kidneys maintain sodium balance by the help of adrenocortical hormone, aldosterone and also by the renin- angiotensin system. When there is a decreased concentration of sodium, aldosterone secretion increases. It increases the re-absorption of sodium from the glomerular filtrated and the level of sodium is increased in blood. A fall in the concentration of sodium stimulates renin secretion from the kidneys. Renin acts on the serum globulin to form angiotensin. Renin-angiotensin system stimulates aldosterone which helps in increasing sodium reabsorption from the tubules and maintain its concentration in the blood.

Levels of other ions like potassium, chloride, bicarbonate are also maintained along with sodium. When sodium ion reabsorption from the filtrate is increased, potassium ion excretion is increased. Along with potassium ions, hydrogen ions are also secreted into the tubules as illustrated in Figure 7.5. When hydrogen ions are secreted, the bicarbonate ions are accumulated in the blood and extra-cellular fluid, as hydrogen comes from carbonic acid (H2C03). Aldosterone causes an enhanced reabsorption of chloride ions.

Like maintaining the electrolyte balance, the kidneys also maintain the pH balance in the body. Let us learn how.

## D) Maintaining pH Balance

You must be aware of the term PH. pH we know provides a measure on a scale from () to 14 of the acidity or alkalinity of a solution (where 7 is neutral and greater than 7 is basic (alkaline) and less than 7 is acidic). It is essential that the body maintains an optimum pH of 7.4 and kidneys do play a major role in ensuring that.

Let us see how.

The kidneys can correct any imbalances by removing excess acid (hydrogen ion) or base (bicarbonate) in the urine and restoring the bicarbonate concentration in the blood to normal. The tubular cells produce a constant amount of hydrogen ions and bicarbonate ions because of their own cellular metabolism (production of carbon dioxide). Ihrough a carbonic anhydrase reaction similar to the red blood cells, hydrogen ions get produced and secreted into the lumen of the nephron. Also, bicarbonate ions get produced and secreted into the blood. In the lumen of the nephron, filtered bicarbonate combines with the secreted hydrogen ions to form carbon dioxide and water (carbonic anhydrase is also present on the luminal surface of the kidney cells). Whether the kidney removes hydrogen ions or bicarbonate ions in the urine depends upon the amount of bicarbonate filtered in the glomerulus from the blood relative to the amount of hydrogen ions secreted by the kidney cells. When the amount of filtered bicarbonate is greater than the amount of secreted hydrogen ions, then bicarbonate is lost in the urine. Likewise, if the amount of secreted hydrogen ion is greater than the amount of filtered bicarbonate, then hydrogen ions will be lost in the urine (i.e. acidic urine).

Now, this acid/base balance of our blood changes in response to many things. These include:

- **Diet:** the diets that are rich in meats provide acids to the blood when digested. In contrast, the diets rich in fruits and vegetables make our blood more alkaline because they are rich in bicarbonates.
- **Exercise:** exercising muscles produce lactic acid that must be eliminated from the body or metabolized.
- **Breathing:** a high altitude causes rapid breathing that makes our blood alkaline. In contrast, certain lung diseases that block the diffusion of oxygen can cause the blood to be acidic.

Let us further study the effect of diet on the acid/base balance by taking the example of acid diet and alkaline diet. We must, however, first understand what we mean by an acid diet and alkaline diet. A diet which is rich in proteins (meat, fish, eggs, cheese) and when catabolised leave an acidic residue to be excreted in the urine is referred to as acid diet. On the other hand, a diet consisting mainly of fruits, vegetables and milk, which when catabolised leave an alkaline residue to be excreted in the urine is alkaline diet.

Let us first see how the acid/base balance is maintained in a acid diet. The sequence of steps involved include:

1) Hydrogen ions added to the blood by breaking down a meat-rich diet combine with the bicarbonate ions in the blood and form carbon dioxide and water. This reaction reduces the bicarbonate concentration and the pH in the blood. The decreased bicarbonate concentration in the blood reduces the amount of bicarbonate filtered in the glomerulus.

All of the filtered bicarbonate combines with the hydrogen ion secreted by the kidney cells in the lumen to form carbon dioxide and water.

Because the filtered load of bicarbonate was less than the amount of hydrogen

ion secreted by the kidney cells, there is an excess of hydrogen ions in the urine. The amount of bicarbonate secreted from the kidney cells into the blood was equal to the hydrogen ion secreted into the lumen and greater than the filtered load of bicarbonate from the blood, therefore, the blood has a net gain of bicarbonate.

This process continues to lose hydrogen ions in the urine and gain bicarbonate in the blood until the concentration of hydrogen (pH) and bicarbonate ions in the blood are restored to normal.

Next we shall see how acid/base balance is maintained in case of an alkaline diet.

1) Bicarbonate ions added to the blood from the fruit or vegetable-rich diet combines with hydrogen ions to form carbon dioxide and water.
2) This reaction reduces the hydrogen ion concentration and increases the PH.
3) The increased bicarbonate concentration increases the amount of bicarbonate filtered in the glomerulus.
4) The filtered bicarbonate exceeds the amount of hydrogen ion secreted by the kidney cell, and excess bicarbonate is lost in the urine.
5) The amount of bicarbonate secreted from the kidney cells into the blood was equal to the hydrogen ions secreted into the lumen and less than the filtered load of bicarbonate from the blood, therefore, the blood has a net loss of bicarbonate.
6) This process continues to lose bicarbonate in the urine and reduce the bicarbonate in the blood until the concentrations of hydrogen (pH) and bicarbonate ions in the blood are restored to normal.

The discussion above must have given you a clear idea about the functions of kidney in maintaining the acid/base balance in the blood. Finally, let us get to know the regulatory function of the kidney.

## E) Regulation of Blood Composition

Each part of the nephron has different types of cells with different properties. An understanding of this is important to know how the kidneys regulate the composition of the blood. The nephron has a unique blood supply as compared to the other organs. Let us now study what is the unique blood supply of the nephrons and ultimately play a major role in regulating the blood composition:

- **Afferent arterioles:** Look at Figure 7.4 and identify the afferent arterioles. These connect the renal artery with the glomerular capillaries.
- **Glomerular capillaries:** There are the coiled capillaries that are inside the Bowman's capsule.
- **Efferent arterioles:** Identify the efferent arterioles in Figure 7.4. As you would have noticed, these connect the glomerular capillaries with the peritubular capillaries.
- **Peritubular capillaries:** These are located after the glomerular capillaries and surrounding the PCT, loop of Henle and the DCT.
- **Interlobular veins:** These are the veins that drain the peritubular capillaries into the renal vein.

The above mentioned blood vessels (forming portal circulation) help in the regulation of blood composition by the kidneys. Kidney is the only organ of the body in which the two capillary beds, in a series, connect arteries with the veins. This arrangement is important for maintaining a constant blood flow through and around the nephron despite fluctuations in the systemic blood pressure.

## 7.4.4 Counter Current Mechanism

What is counter current mechanism? Counter current mechanism is the mechanism by which the kidneys produce osmotically concentrated urine. Let us see how.

In the proximal convoluted tubule (PCT), the substances like glucose and amino acids are reabsorbed mainly as isotonic solution. Most of the reabsorption occurs here and this is the obligatory absorption. If more solute is to be absorbed, more water is reabsorbed and vice versa. This process mainly occurs in the PCT. When the filtrate reaches the loop of Henle, it is still isotonic (having the same or equal osmotic pressure) with the blood plasma.

According to Wirz, the filtrate becomes concentrated as it passes down the descending limb of the loop. This portion of the loop lies in the renal medulla and is hyperosmotic with respect to the plasma. Hence, water is lost from the descending limb to make the tubular fluid also hyperosmotic. In the ascending limb, a reverse set of actions occurs as you have already studied earlier under the water balance function of kidneys. The tubule passes from a hyperosmotic zone to a hypoosmotic zone. To maintain the balance, there is an active secretion of sodium chloride unaccompanied by water in the ascending limb, so that the tubular fluid becomes hypoosmotic with the plasma. This mechanism is known as the hair pin counter current multiplier mechanism. The filtrate as it passes down the descending limb of the loop of Henle, gets multiplied in its content of sodium which is through the interstitium and to descending limb through the secretion in the ascending limb. The vasa recta (arterial capillary) act as a counter current exchanger system, faithfully exchanging ions with the interstitium. Through this countercurrent mechanisms, kidney can maintain osmolarity between 300 mOsm/L to 1200 mOsm/L.

So far we studied about the contribution of the kidneys in urine formation and its role in maintaining the pH and performing other regulatory functions. Besides these, did you know that the kidneys also have non-excretory functions? The next sub-section focuses on these non-excretory functions of the kidney.

## 7.4.5 Non-Excretory Functions of Kidney

Though the major contribution of the kidneys, as you have learnt so far, is to form urine and to maintain the constancy of internal environment, certain functions are sub-served by the kidneys apart from excretion (non-excretory function). These are the non-excretory roles of kidney. The kindey serves:

- as an endocrine gland
- in metabolic activities, and
- in autoregulation.

Let us now discuss each of these roles of kidneys, in a greater detail.

**Kidney as an endocrine gland:** The kidney produces substances that can be described as hormones. Hormones are the chemicals produced by glands in the body and circulate in the bloodstream.

Erythropoietin, a glycoprotein, is released from the kidneys in response to the tissue hypoxia. It stimulates the production of red blood cells by the bone marrow. The cellular site of production of erythropoietin is not clearly known, but acts as a hormone.

The liver converts vitamin D (cholecalciferol) to 25-hydroxycholecalciferol. This 25- hydroxy compound is then converted into 1,25-dihydroxycholecalciferol by the kidney when the plasma calcium level is below normal. This di-hydroxy compound of vitamin D is much more active than the original vitamin in bringing about the absorption of calcium from the intestine and can be considered a hormone produced by the kidney.

An inadequate blood flow to the kidneys leds to the release of a protease enzyme called renin. Renin is secreted from juxtaglomerular apparatus (a group of cells located between afferent and efferent arterioles). It combines with angiotensinogen to form angiotensin I and angiotensin II, which is a powerful vasoconstrictor and increases the blood pressure. It also stimulates aldosterone (mineralocorticoid) secretion of the adrenal cortex.

Metabolic activities of the kidney: For synthesis of creatine, three amino acids glycine, arginine and methionine are involved directly. The first reaction is to form glycocyamine from arginine and glycine. This occurs in the kidneys. The synthesis is completed by methylation of glycocyamine in the liver. Creatinine is an anhydride of creatine.

The kidney is also involved in carbohydrate metabolism. Glucose-6-phosphate is present in the renal cortex. This enables the kidney to contribute some glucose to the blood of glycogenolysis (the breaking down or catabolism of the polysaccharide glycogen into molecules of the sugar glucose and molecules of glucose — 1 -phosphate within the body by enzymes). Kidneys also contribute glucose to the blood by gluconeogenesis (the production of glucose from non-carbohydrate precursors, such as amino acids, within the liver).

Autoregulation function of kidneys: The kidneys possess the property of autoregulation. This means that the blood flow in the kidneys remain constant. It is independent of the blood pressure changes, provided this pressure is within the range of 80-120 mm Hg. The glomerular blood flow and GFR are not affected by the small changes in blood pressure. But if after haemorrhage or due to any other reason, the blood pressure falls to a very low level, the autoregulation is lost. The glomerular filtration rate is reduced and may stop, resulting in anuria (no urine).

With this, we come to an end of our discussion on the organ responsible for urine formation i.e. the kidney and its functions, both excretory and non-excretory, in our body.

Let us now follow the path which the urine takes in the urinary system in its way out of the body. Once the urine is formed, it enters the ureters. Let us get to know

more about the ureters.

## 7.5 URETERS

NOTES

Ureters, as can be seen in Figure 7.1, are the two tubes which convey the urine from the kidneys to the urinary bladder. Each tube measures approximately 10 to 12 inches in length. They start from the pelvis of the kidney and pass downwards.

### What is the structure of the ureters?

The outer coat of the ureter consists of fibrous tissue. The middle layer is a muscle layer consisting of smooth muscle (outer longitudinal and inner circular). The inner lining is a mucous membrane consisting of transitional epithelium.

### What is the main function of the ureters?

The ureters propel the urine from the kidney into the bladder by contraction of the muscle layer. On the other hand, as the urinary bladder contracts, the walls of the ureters are pressed together. This prevents the urine to be forced back to the ureter. So by the simple contraction of the muscle, the urine is passed from the ureter to the urinary bladder. Let us get to know about the urinary bladder now.

## 7.6 THE URINARY BLADDER

The urinary bladder is a sac, which acts as a reservoir for urine. Look at Figure 7. for a view of the urinary bladder. You would realize that the size and position of the urinary bladder varies depending on the amount of urine content. It is roughly pear shaped, but becomes more oval in shape as it fills with urine. It lies in the pelvic cavity (a cavity extending from the lower end of abdominal cavity). But when the bladder is grossly distended, it rises to the abdominal cavity (largest cavity that is situated in the main part of the trunk below the diaphragm).

### What is the structure of the urinary bladder?

The bladder is composed of four layers of tissues. The outermost serous membrane is a thin membrane lining the closed cavities of the body and has two layers with a space in-between that is filled with the serous fluid which covers only the superior surface of the bladder. Next layer is a muscle layer composed of longitudinal and circular muscle fibre. The third layer is a sub-mucous layer containing blood vessels, lymphatics, sympathetic and parasympathetic nerves. The innermost layer is a mucous layer composed of transitional epithelium. There are three orifices in the bladder. The upper two orifices are the openings of the two ureters as illustrated in Figure 7.6. The inferior orifice is the point of origin of the urethra. These three orifices form a triangle described as the trigone of the bladder.

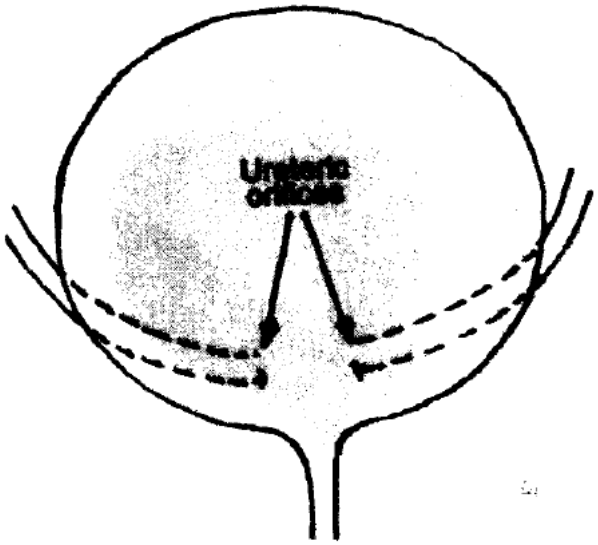



**Figure 7.6: Orifices of the bladder**

## What is the role of the urinary bladder?

As mentioned earlier, the urinary bladder acts as a reservoir for urine. When the urine gradually accumulates in the bladder, there is a change in the volume but there is a little change in pressure upto a certain limit. When the volume reaches upto 200 to 300 ml, the pressure stimulates the nerve endings in the bladder wall and initiates the process of micturition (to urinate) through spinal reflex in which the parasympathetic are the efferents to the bladder.

In simple terms, when the urinary bladder becomes filled with urine, it stretches out. When it stretches beyond a certain point, nerves in the wall of the bladder send a message 10 the spine. The spine sends a message to the brain, which is experienced by the body as discomfort. This signals to the person that it is time to urinate. Coinciding with the urge to urinate, the- nerve centers in the spinal cord cause the muscle around the urethra (the tube leaving from the bladder) to relax. This causes the main bladder muscle to shorten, which pushes urine outside of the body through the urethra.

You may have experienced that at times we can inhibit the urge to urinate until it is convenient to micturate. How is this possible? The brain can inhibit the spinal micturition reflex (the process of urination) for a limited period of time. Over-distension of the bladder causes an involuntary relaxation of the sphincters and a small amount of urine escapes. Micturition occurs when the muscular wall of the bladder contracts and the urethral sphincters relax.

In the infants, the nervous system is not fully developed. Micturition occurs simply by the reflex action and cannot be controlled voluntarily. In spinal cord injury, bladder disturbances are common.

Now we are familiar with the structure, role of urinary bladder. The last organ in the urinary system is the urethra. We shall now get to know the physiology of this organ.

## 7.7 THE URETHRA

The urethra is a canal which extends from the bladder to the exterior as illustrated in Figure 7.1. The length of the urethra varies between male and female. Where the urethra commences, there is a sphincter muscle i.e. a ring of muscle that contracts to close an opening, controls the passage of urine. The urethra opens at the external orifice guarded by a sphincter muscle, which is under the control of the will.

### What is the structure of the urethra?

The urethra is composed of three layers of tissue. The muscle coat consists of longitudinal and circular muscle. The second layer is a thin spongy coat containing large number of blood vessels and the innermost mucous membrane consists of stratified squamous epithelial cells.

### What is the function of urethra?

The urethra discharges urine from the urinary bladder to the exterior. We hope the discussion above must have given you a good insight into the structure and functioning of the urinary system. Starting with the kidney, we saw that the urinary system includes kidneys also the ureters, urinary bladder and the urethra. All these organs play a significant role either in urine formation or discharge of urine from the body. Do you know what are the constituents of urine? The next section focuses on this and on the examination of urine. Before we move on this topic let us recapitulate what we have learnt so far.

## 7.8 CONSTITUENTS AND EXAMINATION OF URINE

The quantity of urine in 24 hours in adult normal individual varies from 600 ml to 2500 ml. It is pale yellow in colour, hypertonic, acidic with a specific gravity of 1.007- 1.012. The urine comprises of various constituents. Let us get to know them.

### 7.8.1 Normal and Abnormal Constituents of Urine

The urine comprises of various constituents. These may be either normal or abnormal ones. Let us see what these are. We start with the normal constituents.

Normal constituents of urine: The normal constituents of urine are of two types. These are the organic substances and the inorganic substances as listed herewith.

- Organic substances: Urea, creatinine, ammonia, uric acid, hippuric acid, amino acid, urine pigments, vitamins, hormones and their degraded products, and enzymes.
- Inorganic substances: Chlorides, phosphates and sulphates of sodium, potassium, calcium, magnesium etc.

Sometimes, certain abnormal constituents are detected in urine. We call them abnormal because normally they are not present in the urine. What are these

constituents and under what conditions do they occur? Let's find out.

Abnormal constituents of urine: The detection of abnormal constituents in urine indicates the presence of certain metabolic disorders in the body. These abnormal constituents include:

1) **Glucose:** Presence of detectable amounts of glucose occurs in diabetes mellitus, Cushing syndrome, gigantism etc.
2) **Fructose:** Excretion of fructose in urine occurs as a metabolic defect in the liver.
3) **Galactose:** Galactose is present in the urine in the conditions of galactosemia, a metabolic defect caused due to the deficiency of the enzyme galactose-1-phosphate uridyl transferase.
4) **Proteins:** Abnormal amounts of proteins are excreted in certain inflammatory diseases like glomerulonephritis (inflammation of the glomerulus of the kidney, characterized by the decreased production of urine and by the presence of blood and protein in the urine and by edema) and nephrotic syndrome (a collection of symptoms that indicate kidney damage, such as high levels of protein in the urine, lack of protein in the blood and high blood cholesterol).
5) **Bence-Jones Protein:** Bence-Jones proteins are the small proteins (dimers of immunoglobulin light chains) normally produced by the plasma cells and are found in the urine. Bence-Jones proteins are sufficiently small to be excreted by the kidney. Persons suffering from multiple myeloma (a tumor of the bone marrow, usually malignant), leukemia (cancer of the blood) and Hodgkin disease (a cancer in the lymphatic system) excrete large amount of protein in urine called Bence-Jones protein.
6) **Ketone bodies:** Ketone body is an intermediate breakdown product of fats in the body. It can be any of three compounds (acetoacetic acid, acetone and/ or beta-hydroxybutyric acid) found in excess in blood and urine of persons with metabolic disorders. These three compounds may be excreted in the urine in severe diabetes mellitus or in prolonged starvation due to the impairment of the carbohydrate metabolism. You may also recall reading about ketone bodies in Nutritional Biochemistry Course, Unit 7.
7) **Bile pigments and bile salts:** These occur in urine in conditions of hepatic and obstructive jaundice i.e. obstruction to the flow of bile into the duodenum, whether intra or extra hepatic.
8) **Blood:** In acute inflammation and trauma, blood may be present in the urine. This condition is known as haematuria. Blood may be present in cancer, renal stone and tuberculosis, which you already know is an infectious disease caused by the bacteria — Mycobacterium tuberculosis — which may affect almost any tissue or organ of the body. The most common target of the disease, however, is the lungs.
9) **Calculi and casts:** An abnormal concretion in the body usually formed of mineral salts and found in the gall bladder, kidney or urinary bladder, for example, is referred to as calculi while casts refer to the small tubules. These may be present in urine due to the formation of renal stones in any part of the

urinary system.

10) **Pus:** Pus cells are found in the urine in infections of urinary tract. Pus is actually a viscous, yellowish-white fluid formed in infected tissue, consisting chiefly of leucocytes, cellular debris and liquefied tissue elements.

So that was an exhaustive list. Some normal and some abnormal constituents can be present in the urine. How can we detect these constituents? Well, simply by examination of the urine. Let us get to know about this process next.

## 7.8.2 Examination of Urine

Examination of urine is done to detect the presence of any abnormal constituent(s) and hence can be used as an important screening test for identifying metabolic disorders. Let us see what does the clinical examination involves and how does it help. We shall begin with general examination.

1) **General examination :** This includes general appearance, volume and specific gravity together with the simple chemical tests for reaction, albumin, sugar, ketones and blood. Let us learn about this examination in more details.
2) **General appearance:** Dilute urine is usually pale and straw-colored while the concentrated urine is dark and acid urine is darker. Blood may cause the urine to be red or brown. In obstructive jaundice, the presence of bile pigments in the urine causes it to be dark orange changing to green. Freshly passed normal urine is clear but may become cloudy due to the presence of phosphates. Hence depending on the general appearance of the urine, some judgment can be made.
3) **Volume:** Measurement of the volume of each urine specimen passed is necessary for the conditions in which the fluid balance is affected, for example, operation, oedema (swelling caused by an abnormal accumulation of fluid in the body tissues), dehydration (excessive loss of water from the body) and kidney failure (a chronic condition in which the body retains fluid and harmful wastes build up because the kidneys no longer work properly) etc.

Specific gravity and pH: Normally, the first morning urine has a specific gravity of 1.015 to 1.020. Normal urine is usually slightly acidic with a pH of about 6.0. Albumin: Albumin in the urine generally means leaking of the plasma albumin through the inflamed renal glomerulus (glomerulonephritis). It may also be present in violent exercise, during fever and in certain forms of chemical poisoning.

4) **Glucose:** Detectable amount of glucose is only found in the urine when the blood level exceeds a certain threshold value i.e., 180 mg/ 100 ml. In untreated diabetes mellitus, the blood level will exceed this value, especially after a carbohydrate meal. The result is that the glucose appears in the urine. This condition is called glycosuria. If the patient is treated with insulin, then also glucose may appear in the urine because some residual urine is left in the bladder. Higher the blood sugar level, greater the glycosuria.
5) **Ketones:** The ketone bodies accumulate in the blood in impaired glucose metabolism as in starvation and diabetes mellitus. The high levels of ketone bodies are excreted in the urine. Ketone bodies include acetone, acetoacetic acid and beta-hydroxybutyric acid.

After general examination, we move on to the microscopic and specific examination of urine. Let us see what is done in these examinations.

- **Microscopical examination:** By microscopical examination, the pus cells, RBC and cast cells are found if the infection is present. Microscopical examination also reveals the presence of crystals of chemical substances in the urine, for example, uric acid, urates, oxalates, phosphates etc.
- **Special examination:** The special examination requires the determination of various chemical substances in the urine including amino acids, bile pigments and salts, calcium, creatinine, drugs, electrolytes, hormones and porphyrin. Why are these chemicals examined in the urine? Let's find out.
- **Amino acids:** Normal urine contains only small amount of certain amino acids, for example, glycine and glutamine. Abnormal amounts and types of amino acids are found in liver failure and in a number of congenital disease i.e., a disease or disorder that is inherited genetically.
- **Bile pigments and salts:** The bile pigment, bilirubin (a pigment formed from the destruction of red blood cells), is altered in the intestine to urobilinogen, a coloured substance formed in the intestine from the breakdown of bilirubin. In the urine, the urobilinogen gradually changes to urobilin. In haemolytic jaundice (jaundice due to the breakdown of red blood cells), excretion of urobilin, a brown bile pigment, is increased upto 10 mg daily and in obstructive jaundice (jaundice caused by something blocking the bile duct, for example, gallstones and tumors), it is reduced usually to less than 0.3 mg daily.

Bilirubin appears in the urine when there is an appreciable amount of conjugated bilirubin present in the plasma.

- **Calcium:** Normally 100 to 300 mg of calcium is excreted in the urine daily. Urine calcium is low in intestinal malabsorption and rickets — a childhood disease caused by deficiency of vitamin D and sunlight, associated with impaired metabolism of calcium and phosphorus. It is high in hyperparathyroidism.
- **Creatine :** Normal urine contains little or no creatine. Some may be found during menstruation, pregnancy and childhood. Urine creatine is considerably increased in conditions involving muscular wasting.
- **Creatinine :** It is an end-product of protein metabolism, an anhydride of creatine, found in the blood and urine that can be used to help assess if the kidneys are working adequately. Normally 1.1 to 3.4 g of creatinine is excreted daily.
- **Drugs:** Levels of alcohol and barbiturates (a group of drugs derived from barbituric acid that is used to sedate, to control convulsions or to induce sleep) are estimated in the urine samples. In cases of suspected intoxication, they may provide valuable information, especially when the blood samples are not available.
- **Electrolytes:** Estimation of urine chloride, sodium, potassium is of significant importance when the electrolyte balance is disturbed.
- **Hormones :** Increased or decreased production of a hormone in the body

alters the amount of hormone or its degraded products excreted in the urine. For example, pregnancy tests are based on increased chorionic gonadotrophin present in the urine. Corticosteroid hormones are reduced in Addison's disease, which is due to a failure of the adrenal cortex.

- **Porphyrins :** Porphyrins (a group of compounds containing the porphin structure, four pyrrole rings connected by methine bridges in a cyclic configuration to which a variety of side chains are attached) are the intermediates in haemoglobin synthesis. In haemolytic anaemia, when the red blood cells are broken down excessively, the body tries to form more red blood cells and consequently the rate of haemoglobin synthesis increases. Excess porphyrins are produced and so are excreted in the urine.

In the section above, we have studied about the general, microscopic and specific examination of urine to detect abnormal constituents. In addition there are certain tests and procedures used to evaluate renal function. Let us learn about them.

## 7.9 RENAL FUNCTION TESTS

Renal function tests are the common tests and procedures used to evaluate renal function and for this, the analysis of blood and urine samples is essential. The purpose of these tests is to determine if the kidneys are performing their tasks adequately. These. tasks, as you are already aware of, involve many vital functions such as removing metabolic waste products from the bloodstream, regulating body's water balance and maintaining the PH. The following are some of the basic renal function tests:

1) **Blood urea nitrogen (BUN):** It is a test that measures the amount of urea nitrogen in the blood. Urea is formed in the liver as an end product of protein metabolism and is carried to the kidneys for excretion.

During digestion, protein is broken down to amino acids. Amino acids contain nitrogen, which is removed as NH4(ammonium ion), while the rest of the molecule is used to produce energy or other substances needed by the cell. The ammonia combines with other small molecules to produce urea. The urea makes its way into the blood and is ultimately eliminated in the urine by the kidneys. You may recall reading about this aspect in the Nutritional Biochemistry Course in Unit 8.

Nearly all kidney diseases cause an inadequate excretion of urea, elevating BUN levels in the blood. Other causes of high BUN levels include dehydration, gastrointestinal bleeding, steroid treatment and use of many other drugs compete with urea for elimination by the kidneys.

The normal values for the test are: 7 to 20 mg/dl and the abnormal results indicate many diseases.

2) **Serum creatinine test:** Creatinine is a breakdown product of creatine, an important component of muscle. A serum creatinine test measures the amount of creatinine in the blood. The production of creatinine depends on person's size and the muscle mass, which varies very little. Creatinine is excreted exclusively by the kidneys, and its level in the blood is proportional to the glomerular

filtration rate.

The serum creatinine level provides a more sensitive test of kidney function than BUN because kidney impairment is the most common cause of elevated creatinine.

The normal (usual) value for this test is 0.8 to 1.4 mg/dl. Females have a lower creatinine than males due to decreased muscle mass. The greater-than-normal and lower than normal values indicate various diseases.

3) **Urine creatinine test:** This test measures the amount of creatinine in urine. A measurement of the serum creatinine level is often used to evaluate kidney function. Urine creatinine levels can be used as a screening test to evaluate kidney function, or can be a part of the creatinine clearance test.

Creatinine, as you would know, is a breakdown product of creatine, which is an important constituent of muscle. By far, the most important source of energy inside cells are the high-energy phosphate bonds of the ATP molecule. When one of these bonds is broken, energy is released and ATP becomes ADP. Creatine phosphate represents a backup energy source for ATP because it can quickly re-convert ADP to ATP.

The creatine molecule gradually degrades to creatinine with time. Creatinine is a waste product, that is, it cannot be used by the cells for any constructive purpose. The daily production of creatine, and subsequently creatinine, depends on the muscle mass, which fluctuates little in most normal people over long ranges of time.

Creatinine is excreted from the body entirely by the kidneys. With normal kidney function, the serum (blood) creatinine level should remain constant and normal. In normal human adult, the value is relatively constant. The average value is 15 mV minute. Normal values are highly dependent on the age and lean body mass of the person from whom the urine is being collected from. Urine creatine (24 hour sample) values may, therefore, be quite variable and can range from 500 mg/ day to 2000 mg/ day.

The abnormal values of urine creatinine and creatinine clearance are often non-specific.

4) **Urine osmolality test:** Urine osmolality is a measurement of the number of dissolved particles in urine. It is a more precise measurement than specific gravity for evaluating the ability of the kidneys to concentrate or dilute the urine. Kidneys that are functioning normally will excrete more water into the urine as fluid intake is increased, diluting the urine. If the fluid intake is decreased, kidneys excrete less water and the urine becomes more concentrated.

The test may be done on a urine sample collected first in the morning, on multiple timed samples, or on a cumulative sample collected over a twenty-four hour period. The patient will typically be prescribed a high-protein diet for several days before the test and asked to drink no fluids the night before the test. The normal values for the test, in case of restricted fluid intake is 800 mOsm/Kg of water and with increased fluid intake, osmolality should be less than 100 mOsm/Kg.

5) **Urine protein test:** Healthy kidneys filter small molecules of proteins from the bloodslream and then reabsorb them, allowing no protein, or only slight

amounts of protein into the urine. The persistent presence of significant amounts of protein in the urine, then, is an important indicator of kidney disease. A positive screening test for protein (included in a routine urinalysis) on a random urine sample is usually followed- up with a test on a 24-hour urine sample that more precisely measures the quantity of protein. Such a sample should not contain more than 150 mg protein.

The best tests for assessing renal function are the renal clearance tests. The term 'plasma clearance' is used to express the ability of the kidneys to clean or clear the plasma of various substances. The following clearance tests are commonly used:

**i) Creatinine clearance test:** It determines how efficiently the kidneys are clearing creatinine from the blood and serves as an estimate of kidney function. It compares the level of creatinine in urine with the creatinine level in the blood. For this test, urine and serum levels of creatinine are measured, as well as the volume of urine excreted over a 24-hour period. The creatinine clearance rate is then calculated and expressed as the volume of blood, in milliliters, that can be cleared of creatinine in one minute. The normal results for the test are 90-139 ml/min for adult males less than 40 years old and 80-125 ml/min for adult females less than 40 years old. For people above 40, the values decrease by 6.5 ml/min for each decade of life. A low creatinine clearance value indicates abnormal kidney function.

Because creatinine is found in stable plasma concentrations, is freely filtered and not reabsorbed, and is minimally secreted by the kidneys, creatinine clearance is used to estimate the glomerular filtration rate (GFR). The GFR, in turn, is the standard by which kidney function is assessed.

**ii) Inulin clearance test:** Inulin is a complex polysaccharide found in certain plant roots. In the test, a known amount of inulin is infused into the blood at a constant rate. The inulin is filterable, that is, it passes freely through the glomerular membranes, so that its concentration in the glomerular filtrate equals that of the plasma. In the renal tubule, inulin is not reabsorbed to any significant degree nor is it secreted by the tubules. It does not alter the renal function and is easily estimable. Consequently, the rate at which it appears in the urine can be used to calculate the rate of glomerular filtration. Inulin clearance can be calculated from the following formula,

$$C_{In} = \frac{U_{In} \times V}{P_{In}} \text{ ml/minute}$$

where, $C_{In}$ = inulin clearance in ml/minute

$U_{In}$ = inulin concentration in mg per 1.0 ml of urine

$V$ = volume of urine in ml/minute

$P_{In}$ = inulin concentration in mg per 1.0 ml of plasma

The normal inulin clearance value is 125 ml per minute.

**iii) Urea clearance test:** A test of renal function based on urea clearance. Urea

is a waste product that is created by protein metabolism and excreted in the urine. The urea clearance test requires a blood sample to measure the amount of urea in the bloodstream and two urine specimens, collected one hour apart, to determine the amount of urea that is filtered, or cleared by the kidneys into the urine. The normal value of this test is 64-99 ml/min. The formula for urea clearance is given below:

$$Cu = \frac{Uu \times V}{Pu}$$

where, Cu = urea clearance in ml/minute
Uu = urine urea in mg/ml
V = volume of urine in ml
Pu = urea in mg per ml of plasma

iv) **Other blood tests:** Measurement of the blood levels of other elements regulated in part by the kidneys can also be useful in evaluating the kidney function. These include sodium, potassium, chloride, bicarbonate, calcium, magnesium, phosphorus, protein, uric acid and glucose. Apart from these, certain additional tests such as renal imaging (IVP, ultrasound, CT scan, MRI scan) and renal biopsy can be done to identify the cause of kidney problem.

You have been introduced to various tests, procedures used in the examination and assessment of renal functioning, in the discussion above. We hope this information will be of use to you in dietetic practice. Another aspect which we should know about is the consequences of abnormal kidney functioning. The next section focuses 01 this topic. But now let us take a break and recapitulate what we have learnt so far.

## 7.10 PATHOPHYSIOLOGY OF KIDNEY

Let us start by first understanding what we mean by pathophysiology of kidney. The junctional changes associated with or resulting from disease or injury of the kidneys is pathophysiology of kidney.

Now, let us study about the pathophysiology of kidney. The conditions associated with the abnormal kidney functioning include:

- **Acute glomerulonephritis:** Glomerulonephritis is a disease of the kidneys that results in the inflammation of the glomeruli of the nephrons. Acute glomerulonephritis is a common kidnéy disease, caused by toxins of certain streptococcal bacteria and occurs approximately 2 weeks after a severe streptococcal infection. It occurs mostly in children 3-10 years of age. The glomeruli becomes inflammed and swollen. Protein and red blood cells leak in larger quantities into the urine.
- **Chronic glomerulonephritis:** The repeated occurrence of acute glomerulonephritis, persisting proteinuria, hypertension and chronic renal failure may damage more and more nephrons, causing chronic glomerulonephritis. This may continue for a few too many years leading to

oedema and coma.

- **Nephrotic syndrome:** A type of nephritis (an inflammation of the kidneys) that is characterized by low serum albumin, proteinuria and swelling (oedema). Swelling, weight gain, high blood pressure and anorexia are the key features. Nephrotic syndrome can be seen with a number of illnesses that could cause damage to the kidney glomerulus. This may be due to the progressive glomerulonephritis, diabetes mellitus, malaria or certain drugs and toxic venom. It refers to the presence of proteinurea and oedema. We will learn about dietary management of nephrotic syndrome in the Therapeutic and Clinical Nutrition Course.
- **Renal failure :** It is the inability of the kidngys to manufacture and excrete urine causing the waste products to accumulate in the blood plasma. If the kidneys do not function, waste products like urea, uric acid, creatinine and sulphuric acid will accumulate in the blood. In kidney failure, the urea level rises from 30 mg/ 100 ml to 150 mg/ 100 ml or more. The GFR falls and the kidneys cannot maintain the electrolyte balance. Symptoms appear when the glomerular filtration rate has fallen from 12 ml/minute to 30 ml/minute. In this case, the water and electrolyte balance is maintained to some extent by a careful choice of diet. Protein is severely restricted to minimize the production of sulphuric acid. Your skills as a dietitian will be tested here for planning low protein diets. When the GFR is below 3 ml/minute, dialysis is needed to maintain life.

What is dialysis? The next section presents a review on dialysis.

## 7.11 DIALYSIS

By now, you must have well understood the functions of kidney and the implications of abnormal kidney functioning as well. Here in this section, we shall be focusing on a alternate strategy in case of kidney failure or improper kidney function. This process is referred to as dialysis. The word dialysis means a form of diffusion i.e., a form of filtration to separate the macromolecules from ions and low molecular weight compounds in a solution through a semi-permeable membrane. In simple terms, dialysis is a therapy which eliminates the toxic wastes from the body when the kidney fails, and cannot do its job of eliminating these toxic wastes.

An artificial kidney can be made by using a semi-permeable membrane between the blood and the dialyzing fluid. The artificial kidney uses the cellulose membranes in place of the phospholipid-bilayer membranes used by real kidneys to separate the components of blood. Parallel chains form linkages with one another by hydrogen bonding to make strong fibers. These fibers in turn, interact to form the strong, sheet- like structure of the membrane. It requires the cannulation (insertion of a tube) of an artery and a vein to enable the blood to be passed through the dialyzing apparatus.

When the kidneys do not function properly, dialysis must be performed artificially. Without this artificial kidney dialysis, toxic wastes build up in the

blood and tissues and cannot be filtered out by the ailing kidneys. This condition is known as uremia, which literally means urine in the blood. Eventually, this waste build-up leads to death.

The composition of a dialyzing fluid is adjusted so as to restore the blood to its correct composition. Such a technique, if carried out every few days, helps a patient with kidney failure to survive. The main functions of dialysis include clearing wastes from the blood, restoring proper balance of certain electrolytes in the blood and eliminating extra fluid from the body.

How is dialysis done? Let's find out.

Types of artificial kidney dialysis: Two types of artificial kidney dialysis are used clinically — hemodialysis and peritoneal dialysis. Let us briefly study about both of these processes.

- **Hemodialysis:** In hemodialysis, the process takes place inside a machine. Blood is taken from the body, pumped into the dialysis machine, cleaned and pumped back into the body. Hemodialysis uses a cellulose-membrane tube that is immersed in a large volume of fluid. The blood is pumped through this tubing and then back into the patient's vein as shown in the Figure 7.7. The membrane has a molecular weight cut-off that will allow most of the solutes in the blood to pass out of the tubing but retain the proteins and cells. The external solution in which the tubing is immersed is a salt solution with ionic concentrations near or slightly lower than the desired concentrations in the blood. Recall that if the external concentration of a particular species is lower than the internal concentration, then that species will pass through the cellulose membrane by diffusion into the external solution. In this manner, excess substances in the blood are removed from the body. To maintain the blood's concentration of a species, the external solution is made to have the same concentration of that species as the blood. In such a case, the two solutions are in dynamic equilibrium and so the blood's concentration does not change.

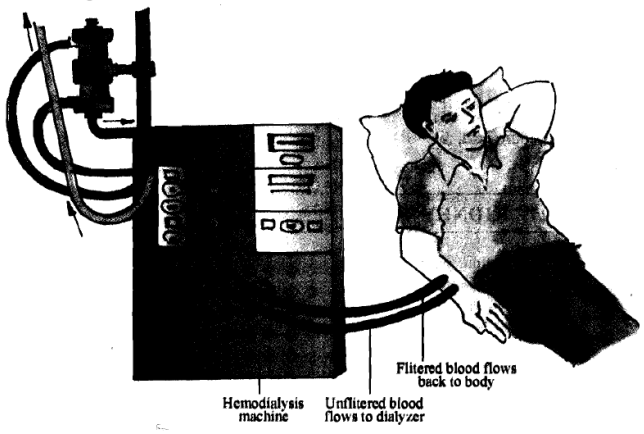



**Figure 7.7: Hemodialysis**

- **Peritoneal dialysis:** In peritoneal dialysis, the process of dialysis takes place inside the body. Peritoneal dialysis does not use an artificial membrane, but rather uses the lining of the patient's abdominal cavity, known as the

peritoneum, as a dialysis membrane. As illustrated in the Figure 7.8, a tube (catheter) is inserted into the abdomen during an operation. Special dialysis fluid is injected into the abdominal cavity and solutions diffuse from the blood into this fluid. Excess waste and water pass from the blood into the fluid. After several hours, the fluid is removed with a needle and replaced with a new fluid. The patient is free to normal activities between fluid change.

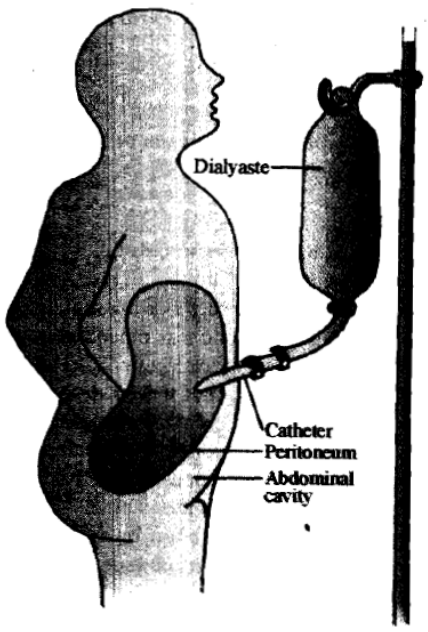



**Figure 7.8: Peritoneal dialysis**

Thus, artificial kidney dialysis uses the same chemical principles that are used naturally in the kidneys to maintain the chemical composition of the blood. Diffusion across semi-permeable membranes, polarity and concentration gradients are central to the dialysis process for both natural and artificial kidneys.

Other than renal dialysis, there is yet another alternative for patients with renal failure or end stage renal disease. This is kidney transplant. Let us learn about this procedure next. With this topic we shall end our study of the physiology of renal system.

## 7.12 KIDNEY TRANSPLANT

In this section, we will learn about what is kidney transplant and which are the conditions in which it becomes a necessity. So let us get started with what is kidney transplant.

### What is kidney transplant?

Kidney transplant is a surgical procedure to implant a healthy kidney into a patient with kidney disease or kidney failure. The kidney transplant may be taken from a living donor or from a recently deceased donor.

The kidney of a donor may be transplanted into the pelvis of the recipient (whose kidney has been damaged). A donated kidney may come from an anonymous donor who has recently died or from a living person, usually a relative. But there may be an immunological problem. So the kidney that is transplanted must be a good match for the recipient's body. The transplanted kidney tends to be rejected by the body of the recipient, if the body's immune system doesn't recognizes it as a normal body part. Red cell and white cell (HLA typing) and tissue matching are carried out between the recipient and possible donors before this procedure is carried out.

## Why is a renal transplant necessary?

A number of diseases can directly damage the kidney, which can seriously affect the removal of water and waste products, production of red blood cells, regulation of blood pressure and balance of electrolytes such as potassium, calcium and phosphorus. A kidney transplant may be recommended for patients with kidney failure caused by severe, uncontrollable high blood pressure, infections, diabetes, glomerulonephritis (a type of kidney disease caused by inflammation of the internal kidney structures, the glomeruli).

If the damage is severe enough, transplantation may be necessary. A transplant provides a patient with a kidney that can keep up with the demands of a full, active life.

You might think of a transplant as involving the removal of the old organ for replacement with the new, but' in a kidney transplant, the original kidneys are left in place. The new kidney is placed lower down as you can see in the Figure 7.9. The new kidney's blood vessels are joined to the blood vessels that supply the leg and its ureter is attached to the bladder. (A small plastic tube is often inserted into the ureter to prevent it from getting blocked).

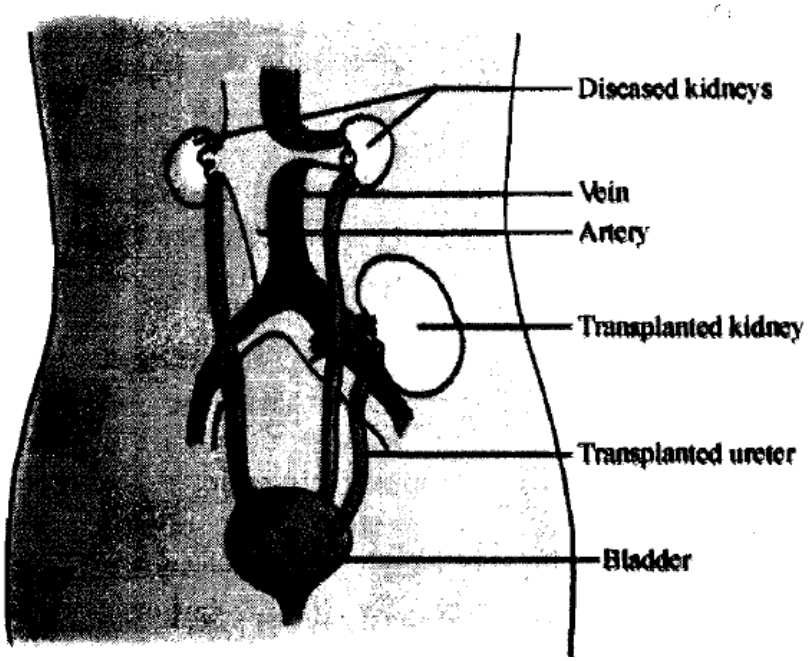



**Figure 7.9: Renal transplant**

## 7.13 LET US SUM UP

In this unit, we learnt about the renal system, the organs involved and their major roles. We saw that there are two kidneys in our bodies which act as excretory organs. Kidneys form urine by filtration, reabsorption and secretion. In forming the urine, the water and electrolyte balance is also maintained. We learnt about excretory functions of the kidneys besides other non-excretory functions. The kidney acts as an endocrine gland and sometimes involved in metabolism.

Next we studied about the other organs in the urinary system i.e. the ureters, urinary bladder and the urethera. We studied their structure and the functions. The unit also focused on the various diagnostic tests that are used to asses the functional status of kidneys. We studied about disorders that affect the kidney functioning. Finally, we studied about the preventive strategies which are being adopted for patients with renal failure. We learnt that the failure of kidney needs dialysis for maintaining life and in severe cases, kidney transplant is the only resort of saving one's life. The processes of dialysis and kidney transplant was discussed briefly.

## 7.14 GLOSSARY

**Acute Glomerulonephritis** : an inflammation of the glomerular nephrons caused by toxins of certain streptococcal bacteria.

**Auto regulation** : the intrinsic tendency of an organ or a tissue to maintain blood flow.

**Calculi** : an abnormal concretion in the body usually formed of mineral salts and found in the gall bladder, kidney, or urinary bladder.

**Casts** : the small tubules.

**Chronic Glomerulonephritis** : damage of a large number of nephrons caused by the repeated occurence of acuted glomerulonephritis persisting proteinuria, hypertension and chronic renal failure.

**Congenital disease** : a disease or disorder that is inherited genetically.

**Diuretics** : the substances that stimulate the formation of urine.

**Glomerulonephritis** : an inflammation of the glomerulus of the kidney, characterized by the decreased production of urine and by the presence of blood and protein in the urine and oedema.

**Hemolytic jaundice** : jaundice due to the excessive breakdown of red cells.

**Hodgkin's disease** : a type of lymphoma, a cancer of the lymphatic system. It causes the cells in the lymphatic system to abnormally reproduce, eventually making the body less able to fight infection along with the steady enlargement of lymph glands, spleen and other lymphatic tissue.

**Hyperosmotic** : describes a cell or other membrane-bound object which has a higher concentration of solutes than its surroundings. For example, a cell which has a higher salt concentration than the salt concentration of the surrounding medium is hyperosmotic. Water is more likely to move into the cell through osmosis as a result. This is the opposite of hypoosmotic.

**Hypoosmotic** : describes a cell or other membrane-bound object which has a lower concentration of solutes than its surroundings. For example, a cell in a high-salt concentration medium is hypoosmotic. Water is more likely to move out of the cell by osmosis as a result. This is the opposite of hyperosmotic.

**Juxtaglomerular cells** : a group of cells located between afferent and efferent arterioles.

**Myeloma** : a tumor of the bone marrow; usually malignant and composed of cells normally found in the bone marrow.

**Orifice** : an entrance or outlet of any body cavity.

**Osmolality** : a measurement of urine concentration that depends on the number of particles dissolved in it. Values are expressed as milliosmols per kilogram (mOsm/Kg).

**Porphyrins** : a group of compounds containing the porphin structure, four pyrrole rings connected by methane bridges in a cyclic configuration to which a variety of side chains are attached.

**Renal acidosis** : an abnormal excretion of acid from the distal tubule of each nephron.

**Renal failure** : the inability of the kidneys to manufacture and excrete urine causing the waste products to accumulate in the blood plasma.

**Transitional Epithelium** : an epithelium with large polyploid superficial cells, cuboidal in the relaxed state but broad and squamous in the distended state.

**Urobilinogen** : a coloured substance formed in the intestine from the breakdown of bilirubin.

## 7.15 CHECK YOUR PROGRESS EXERCISES

NOTES

UNIT

# 8

# MAINTENANCE OF BODY HOMEOSTASIS

**STRUCTURE**



## 8.1 LEARNING OBJECTIVE

After studying this unit, you will be able to:

- explain the concept of body homeostasis,
- enumerate the different body fluids essential to maintain body homeostasis,
- discuss various transport systems in the body, and
- describe body fluids and the methods of measuring and calculating these.
- Maintenance of Body

## 8.2 INTRODUCTION

In this unit, we will study about body homeostasis and different types of body fluids. Homeostasis, as you would realize, is a dynamic process that enables optimum conditions to be maintained for constituent cells. It involves all the systems of the human body, such as endocrine, nervous, respiratory and renal systems. The most common example is the regulation of salt and water balance. In the previous unit we got to know how the kidneys play an important role in maintaining water content of the body.

The advantage of homeostasis is that the organism can adjust to changes without

its component cells being adversely affected since their needs are met by the controlled internal environment. A possible disadvantage is that it requires the organism to invest effort into maintaining internal stability. For example, additional energy is required to maintain a warm body temperature in a cooler external environment. The concept of homeostasis is discussed in this unit.

Body fluids, on the other hand, are of different types and play a major role in maintaining homeostasis. In this unit we shall learn about the different body fluids and their role in homeostasis. Further, the methods used to measure and calculate these fluids will be discussed.

## 8.3 HOMEOSTASIS - AN INTRODUCTION HOMEOSTASIS

All the cells in our bodies are surrounded by a liquid called tissue fluid which has exactly the right conditions in which cells can work. Tissue fluid has the right temperature, the right amount of glucose and the right amounts of water and salt. How is this possible? Homeostasis is the important process that maintains these conditions at the right level.

Homeostasis is a term coined in 1959 to describe the physical and chemical parameters that an organism must maintain to allow proper functioning of its component cells, tissues, organs and organ systems. It is the maintenance of equilibrium or constant conditions in a biological system by means of automatic mechanisms that counteract influences tending toward disequilibrium. In simple terms, homeostasis is the state of sustained equilibrium in which all cells, and all life forms, exist.

An organism in homeostasis adapts to changed environmental conditions by adjusting its own internal state, for example, cold-blooded animals and warm-blooded animals that hibernate, adjust to colder temperatures by changing their own internal temperature, so that their entire system may remain in homeostasis. This ability to maintain a relatively constant internal environment is homeostasis.

## 8.4 BODY FLUIDS

From our discussion above, we realize that there are certain fluid compartments in our body. These include the intracellular fluid and the extracellular fluid compartment. Let us get to understand each of these.

### 8.4.1 Intracellular Fluid Compartment

About 25 to 40 litres of fluid in the body are inside 100 trillion cells of the body and are collectively called intracellular fluid. Figure 8.1 presents the distribution of the intracellular fluid in the body. The fluid of each cell contains its own individual mixture of different constituents, but the concentrations of these constituents are reasonably similar from one cell to another.

**Figure 8.1: Fluid compartments in the body**

## 8.4.2 Extracellular Fluid Compartment

All fluids outside the cells are called extracellular fluids and these fluids are constantly mixing. The total amount Of fluid in the extracellular compartment averages 15 litres in a 70 kg adult.

- The extracellular fluid can be divided into interstitial fluid, plasma, transcellular fluid which includes cerebrospinal fluid, fluids of the gastrointestinal tract and the potential spaces as highlighted in Figure 8.2. Let us learn about these, next.

**Figure 8.2: Distribution of total body water**

## a) Interstitial fluid

The interstitial fluid lies in the spaces between the cells. A small portion of it is free in the form of actual flowing fluid whereas the major portion is held tightly by hydrated substances in the interstitial spaces.

## b) Plasma

The plasma, as you may already know, is the non-cellular portion of blood. Yes, it is an extracellular fluid. It communicates continuously with the interstitial fluid through pores in the capillaries. The plasma volume averages 3 litres in the normal adult.

## c) Fluid in other extracellular spaces

The cerebrospinal fluid comprises all the fluid in the ventricles of the brain and in the subarachnoid spaces surrounding both — the brain and the spinal cord. Intraocu fluid is the fluid in the eyes and has properties similar to those of the cerebrospinal Maintenance of Bod fluid and this fluid is a product of diffusion and secretions. All these fluids get Homeostasis classified as transcellular fluid as highlighted in Figure 8.2, which is a subdivision of the extracellular compartment. Synovial fluid in the joints, glandular secretions and serous fluid within the body cavities are all transcellular compartments. Many spaces exist in the body that normally contain little fluid but under special conditions can become filled with large amounts. These are called potential spaces. An example of potential space is the space between visceral and parietal pleurae of the lungs. Normally, only 10 to 15 ml of fluid is present in the space, but under abnormal circumstances, the amount can become as great as several litres. A moderate amount of extracellular fluid is normally in the gastrointestinal tract. We have looked at the. extracellular and intracellular fluid compartments in our body. You would realize that there is a tight control of the distribution of total body water between body compartments. Interestingly, these compartments remain in equilibrium with one another so that any changes in the osmolality of a compartment will result in the movement of water to maintain equal osmolality.

Blood, you would realize, contains both extracellular fluid (fluid of the plasma) and intracellular fluid (the fluid in the blood cells). The average blood volume of a normal adult is almost exactly 5 litres. On an average, approximately 3 litres of this is plasma and the remaining 2 . litres is blood cells. However, these values vary greatly in different individuals and also depend on sex, weight and rhany other factors affecting the blood volume.

The percentage of red blood cell in the body is called the haematocrit. You may recall reading about this earlier in unit 2 as well. It is determined by centrifuging the blood in the 'haematocrit tubes' until the cells become packed tightly in the bottom of these tubes. The percentage of red blood cells in the blood can be determined roughly from the levels of the packed cells. Unfortunately, it is impossible for the red blood cells to be packed completely together, about 3 to 8% plasma remains entrapped among the cells. Therefore, the true cell percentage (H) averages about 96% of the measured haematocrit (Hct).

$$H = 0.96\ Hct$$

The normal hematocrit (H) is approximately 40 for a man and 36 for a woman. In severe anaemia, the haemaocrit may fall to as low as 10 but this small quantity of red blood cells is barely sufficient to sustain life. On the other hand, a few

conditions like polycythemia (haematocrit rises to 65 and occasionally to 80) causes an increase in haematocrit due to excessive production of red blood cells. However, excessive haematocrit causes the blood to become so viscous that death results because of multiple plugging of the peripheral vascular tree.

With the discussion above, we hope you have a clear idea about the body fluid compartments. We read earlier that the total body water in adults of average built is about 60% of body weight. Do you know how the body water is measured or for that matter, how the body fluid is measured? The next section focuses on this aspect. Let us get to know about this.

## 8.5 MEASUREMENT OF BODY FLUID VOLUMES

In this section, we shall learn about the principles and techniques involved in measuring body fluid volumes. We shall get to know how the total body water is measured. How do we calculate the interstitial fluid volume and extracellular fluid volume? Further, the determinants of blood volume would also be highlighted.

Before we move on to the techniques involved in blood fluid measurements, let us first review the principle involved in measuring fluid volumes.

### 8.5.1 The Dilution Principle for Measuring Fluid Volumes

For measuring fluid volumes, a dilution principle is used. In this, the volume of any fluid compartment of the body can be measured by placing a substance in the compartment, allowing it to disperse evenly throughout the fluid and then measuring the extent to which the substance becomes diluted.

The procedure involves that a small quantity of dye or any other foreign substance is placed in a fluid chamber and the substance is allowed to disperse throughout the chamber unti! it becomes mixed in equal concentrations in all areas as shown in Figure 8.3. Then a sample of dispersed fluid is removed and the concentration or the substance is analyzed chemically, photoelectrically or by any other means. Volume of the chamber can then be determined by the following formula:

**Figure 8.3: The dilution principle**

Having studied the dilution principle for measuring body fluids, let us now get to know how the body fluids are measured. Let us start with the measurement of blood volume.

NOTES

## 8.4.2 Determination of Blood Volume

The blood volume can be determined by use of certain substances. These substances are discussed in this section.

### What are the substances used in determining blood volume?

A substance used for measuring blood volume must be capable of dispersing throughout the blood with ease and it must remain in the circulatory system for long enough for the measurements to be made.

The two major groups of substances that satisfy these conditions for measurement of blood volume are the substances that combine with red blood cells or substances that combine with plasma proteins as both red blood cells and plasma proteins remain reasonably well in the circulatory system and any foreign substance that combines with either of them likewise remains in the blood stream.

Substances that combine with red blood cells and that are used for determining blood volume are radioactive iron, radioactive chromium and radioactive phosphate. Substances that combine with plasma proteins are vital dyes and radioactive iodine. Let us get to know more about them.

a) **Radioactive Red Blood Cells:** In order to make red blood cells radioactive, tagging of red blood cells with radioactive chromium ( 51Cr) is done A small quantity of 51Cr is mixed with a few milliliters of blood removed from the person and this is incubated at 360C for half an hour or more After this time, most of the 51Cr will have entered the red blood cells, but to remove the extra chromium from the mixture, the red blood cells are washed with saline

The total content of 51Cr is then determined with a Geiger or scintillation counter (apparatus for measuring the total number of radioactive disintegrations occurring in the sample per minute)

Then the radioactive cells are re-injected in the person. After mixing in the circulatory system for approximately 10 minutes, blood sample is taken from the circulatory system, and the radioactivity in this blood is determined, using dilution formula given above in dilution principle. Then actual volume is calculated i.e.

Actual blood volume = 1.1 x Measured blood volume

b) **Dyes for Measurement of Plasma Volume:** A number of dyes, generally known as 'vital dyes', have the ability to combine with proteins. When such a dye is injected into the blood, it immediately forms a slowly dissociable union with the plasma proteins. Thereafter, the dye travels wherever the proteins travel. The dye almost universally used for measuring plasma volume is T-1824, also called as evans blue.

In making determinations of plasma volume, a known quantity of the dye is injected and it immediately combines with the proteins and is dispersed throughout the

circulatory system within approximately 10 minutes. A sample of the blood is then taken and the red blood cells are removed from the plasma by centrifugation. Then by spectrophotometric analysis of the plasma, one can determine the exact quantity of dye in the sample of the plasma. From the determined quantity of dye in each millilitre of plasma and the known quantity of dye injected, the plasma volume is calculated.

To be even more exact in measuring the plasma volume, the rate of loss of dye from the circulatory system during the interval of mixing must also be considered. On an average, 5% of the dye is lost per hour, part of it is carried into the interstitial spaces by the leakage of plasma proteins through the capillary walls whereas a part of it is excreted out into the urine.

No vital dye enters the red blood cells. Therefore, this method does not measure the total blood volume. The blood volume can be calculated from the plasma volume, provided the haematocrit is determined, by using the following formula:

$$\text{Blood Volume} = \text{Plasma Volume} \times \frac{100}{100 - 0.87\ \text{Haematocrit}}$$

**c) Radioactive Proteins:** If a sample of plasma is allowed to incubate with the radioactive iodine (1311) for 30 minutes or more, some of the protein combines with iodine and the iodinated protein can be separated from the remaining iodine by dialysis. The radioactive protein is then injected into the subject, and the plasma and blood volumes are determined in the same manner as that for vital dyes.

## 8.4.3 Measurement of Extracellular Fluid Volume

This method involves the use of dilution principle. A substance that can readily diffuse through the entire extracellular fluid chamber, which passes easily through the capillary membranes but as little as possible, passes through the cell membranes into the cells, is injected. After half an hour or more of mixing, a sample of extracellular fluid is obtained by removing blood and separating the plasma from the cells by centrifugation. Plasma, which is actually a part of extracellular fluid, is then analyzed for injected substance.

What are the substances used in this measurement? These are highlighted next.

Substances used in measuring Extracellular Fluid Volume — The Concept of "Fluid Space "

Substances that have been used for measuring extracellular fluid volume are:

- Radioactive sodium
- Radioactive chloride
- Radioactive bromide
- Thiosulphate ion
- Thiocyanate ion
- Inulin, and
- Sucrose

Some of these, especially sucrose and inulin, do not diffuse readily into all out-of-the way places of the extracellular fluid compartment. Therefore, the volume of extracellular fluid measured with these is likely to be lower than the actual volume of the compartment.

On the other hand, other substances such as radioactive chloride, radioactive bromide, radioactive sodium and thiocyanate ion are likely to penetrate into the cells to a slight extent and therefore, are likely to measure a space somewhat excess of the extracellular fluid volume.

Because no single substance can measure the exact extracellular fluid volume, one usually speaks of the 'sodium space', 'thiocyanate space', 'inulin space' etc.

Let us understand this concept better, with the help of an example presented herewith.

Question: 150 mg of sucrose is injected into a 70 kg man. The plasma sucrose level after mixing becomes 0.01 mg per ml. 10 mg has been excreted or metabolized during the mixing. What is the volume of distribution of sucrose?

$$Answer = \frac{150\ mg - 10\ mg}{0.01\ mg/ml}$$

$$= \frac{140 \times 100}{1} = 14{,}000\ ml.$$

Hence, 14,000 ml is the space in which sucrose is distributed. Hence, it is known as 'sucrose space'.

While we are studying about the measurement of extracellular fluid, let us also look at the calculation of the interstitial fluid volume, which you learnt earlier is an extracellular fluid.

## How do we calculate the Interstitial Fluid Volume?

Since any substance that passes into the interstitial fluid also passes into almost all other portions of the extracellular fluid, there is no direct method for measuring interstitial fluid volume separately from the entire extracellular fluid volume. However, if the extracellular fluid volume and plasma volume have both been measured, the interstitial fluid volume can be approximated by subtracting the plasma volume from the total extracellular fluid volume. In a 70 kg adult, the normal interstitial fluid volume is 12 litres.

Constituents of the interstitial fluid are responsible for the regulation of:

- Temperature
- Osmolarity
- Ionic concentration
- Oxygen-Carbon dioxide tension, and
- Several other vital features.

### 8.4.4 Measurement of Total Body Water

Total body water is measured exactly the same way as extracellular fluid volume except that a substance must be used that will diffuse into the cells, as well as, throughout the extracellular fluid compartment.

The substance that gives best result is heavy water, which can be analyzed quantitatively either by accurate specific gravity measurements of water samples or by infrared spectrophotometry. Heavy water is water containing deuterium, a heavy isotope of hydrogen ($D_{20}$).

After administration of the heavy water, several hours are required for complete mixing with all the water of the body and appropriate corrections should be made for any fluid that is lost either into the urine or otherwise, during this period of mixing. The concentration of heavy water in the total body water can, at the end of the period of mixing is determined by simply measuring the heavy water concentration in plasma.

Another substance that has proved satisfactory for measuring the total body water is antipyrine, which diffuses almost uniformly into all cells of the body and which can be analyzed readily by chemical means. Antipyrine is a white powder formerly used to reduce fever and relieve pain.

## 8.6 TRANSPORT ACROSS CELL MEMBRANES

In section 8.2, we got to know that the total body water in an average built adult is about 60% of body weight. About 20% is extracellular and the remainder 40% is intracellular. A large number of molecules must constantly transit between the inside and outside of the cell, most frequently one-at-a-time, but also in large packages. The plasma membrane acts as a selectively permeable barrier between the cell and the extracellular environment. Cell membranes help organisms maintain homeostasis by controlling what substances may enter or leave the cells.

Some molecules, which are large in size, cannot pass through semi permeable walls of the capillaries. These substances, which remain in the blood are plasma proteins, erythrocytes, thrombocytes and leukocytes — except those, which are amoeboid. On the other hand, electrolytes, enzymes, hormones, antibodies, nutritional materials, oxygen, carbon dioxide, water etc. are small molecules, which can pass through the capillary walls as highlighted in Figure 8.4. Transport across cell membranes may be governed only by Dhysical processes.

**Figure 8.4: Transport across cell membrane**

The molecules move from where the substance is more concentrated to where it is less concentrated. Here, the membrane acts like any other non-living semi-permeable structure. In such cases, the transport is called passive transport. Water crosses the cell membranes by diffusion and osmosis and some other substances cross by active transfer involving energy expenditure.

You would realize that all transport across cell membranes takes place primarily by two fundamental processes. These include:

Passive transport: driven by the kinetic energy of the molecules being transported or by membrane transporters by facilitate crossing, and Active transport: depends upon the expenditure of cellular energy in the form of ATP hydrolysis.

For each of the two basic processes, several distinct types of transport — osmosis, simple diffusion, facilitated transport, couple transport, counter transport, dialysis etc. can be identified. In this section we shall learn about these mechanisms of transport across cell membranes. These transport systems help the cell to function properly. It helps to maintain homeostasis by transporting molecules.

Let us get to know about these important modes of transport. We shall start with the passive transport.

## 8.6.1 Passive Transport

Some substances such as water, oxygen and carbon dioxide, as illustrated in Figure 8.4, can cross the cell membrane without any input of energy by the cell. The movement of such substances across the membrane is known as passive transport.

A molecule or ion that crosses the membrane by moving down a concentration or electrochemical gradient and without expenditure of metabolic energy is said to be transported passively. Another name for this process is diffusion. All molecules and ions are in constant motion and it is the energy of motion — kinetic energy — that drives passive transport.

Transport of uncharged species across a membrane is dictated by differences in concentration of that species across the membrane — that is, by the prevailing concentration gradient. The difference in the concentration of molecules across a space is called a concentration gradient. If the molecules diffusing across the membrane from an area of high concentration to an area of low concentration were water molecules, the process would be called osmosis.

Glucose, sodium ions and choride ions are just a few examples of molecules and ions that must efficiently get across the plasma membrane but to which the lipid bilayer of the membrane is virtually impermeable. Their transport must therefore be "facilitated" by proteins that span the membrane and provide an alternative route or bypass. Facilitated diffusion is the name given to this process. It is similar to simple diffusion in the sense that it does not require expenditure of metabolic energy.

The three types of passive transport, we have discussed above are:' diffusion, osmosis, and facilitated diffusion. Ultrafilteration is yet another passive transport

system. Let us understand these processes in greater details now.

## A) Simple Diffusion

Diffusion, we learnt is a simple process of movement of individual molecules from one region to another. Figure 8.5 illustrates passive transport where molecules move from an area of high concentration to an area of low concentration without the use or input of energy by the cell. This process we know is diffusion. Diffusion is driven entirely by the kinetic energy the molecules possess.

**Figure 8.5: Process of diffusion**

Let us look at this process in the context of our body. All the molecules and ions in the body fluids, including both — water molecules and dissolved substances — are in constant motion, each particle having its own separate way. The greater the motion, the higher is the temperature and the motion never ceases, except at absolute zero temperature. All the molecules and ions, as a result of random molecular motion, strike the cell membrane. The frequency of collision depends on the concentration of the dissolved substance.

If the substance is present on both sides of the membrane, the frequency of collisions is higher on the side on which the substance is present in a higher concentration. Higher the frequency of collisions, greater is the probability of particles striking a pore through which they can pass to the other side of the membrane.

The fluids on each side of the membrane are believed to penetrate the protein portion of the membrane with ease so that any dissolved substances can diffuse into this portion of the cell membrane.

The lipid portion of the membrane is entirely a different type of fluid medium, acting as a limiting membrane between the extracellular and intracellular fluids. There are basically two different methods by which the substances diffuse through

the membranes:

- by becoming dissolved in lipid and diffusing through it, and
- by diffusing through minute pores that pass directly through the membrane at wide intervals over the surface.

If there is an electrical charge across the membrane, a charged particle will have a tendency to diffuse towards the oppositely charged side.

The influence of pressure gradient on the diffusion is somewhat non-specific. Pressure is the result of sum total of the collisions on a given side of the membrane. Pressure has a non-specific effect of driving the substances out. Hence, diffusion is increased from the side with the higher pressure to that with a lower pressure.

An example of application of diffusion process is dialysis. What is dialysis? Dialysis, you may recall reading in Unit 7, is a procedure for cleansing the blood, in which the principles of diffusion are applied for the treatment of renal failure. Kidney dialysis is used to substitute for the function of damaged/absent kidneys. In the patient's blood, nitrogenous waste products accumulate and electrolyte imbalance may occur due to renal failure. A solution is prepared in which the waste products are absent, electrolyte concentration is appropriately adjusted and nutrients are provided. The solution is separated from the patient's blood by a dialyzing membrane. The process of diffusion tends to normalize the composition in the patient's blood.

Having understood the diffusion process and its application, next, we move on to the other type of passive transport i.e. facilitated diffusion.

## B) Facilitated Diffusion

As we discussed earlier, in facilitated diffusion, the transport is carried out by the carrier present in the cell membrane. The carrier helps to incorporate even a water- soluble substance in the membrane. qince the carrier merely facilitates diffusion, the process is called facilitated diffusion. Figure 8.6 illustrates the facilitated diffusion process.

**Figure 8.6: Facilitated diffusion**

## Facilitated diffusion is influenced by the following factors:

Minor differences in the molecular structure may lead to a substantial difference in the rate of transport. Optimal transport depends on the precise fit between the molecule to be transported and the receptor site of the carrier.

Substances with a similar molecular structure compete with one another for transport.

Transport can be blocked by specific agents. If the blocking agent has a high affinity for the carrier, the blocking agent can also get transported and this block is known as competitive block (and can be overcome by high concentrations of substance whose transport has been blocked, hence is reversible). If the blocking agent binds to the carrier but does not get transported, it blocks the carrier irreversibly. Such a block is known as non-competitive block.

The relationship between the concentration of the substance and the rate at which it is transported is linear only up to a certain limit. After that, a further increase in the concentration does not increase the rate of transport. An example of facilitated diffusion is in small intestine where fructose is absorbed by facilitated transport.

Moving to the next process, i.e. osmosis.

## C) Osmosis

Osmosis, quite simply, is the physical process, wherein there is transfer of a liquid solvent (water) through a semi-permeable membrane that does not allow the dissolved solids (solutes) to pass. I.et us understand this process with the help of an example. Suppose a semi-permeable membrane separates two compartments. The membrane allows water to pass through but it does not allow the solute to pass through. On side A, there is water and on the other side B, there is solute dissolved in water. The membrane is permeable only to water, and the concentration of water is higher on side A. Hence, water diffuses from A to B, but in this type of solution, water is said to be transported by 'osmosis'.

Unlike simple diffusion, no matter how much water moves from A to B, the concentration of water will stay higher on side A because side B can have a more and more dilute solution of the solute. However, transport of water by osmosis does not occur indefinitely because osmosis of water increases the hydrostatic pressure of side B. Osmosis is said to stop when the excess hydrostatic pressure on side B equals the hydrostatic pressure exerted by the solute.

What do you mean by the term 'hydrostatic pressure'? Well to put in simple terms, hydrostatic pressure is a pushing pressure. Hence, the hydrostatic pressure on the side B tends to push the water from side B to A. While osmotic pressure is a pulling pressure, which in this case is exerted by the solute which pulls the water from A to B. When the pushing and pulling pressure become equal, there is no further movement of water. Finally, to summarize osmosis is the net movement of water from a region of high water concentration across a selectively permeable membrane to a region of low water concentration, driven by a difference in solute

concentrations on the two sides of the membrane. Figure 8.7 illustrates the osmosis process.

We have looked at diffusion, osmosis and the facilitative diffusion process so far. We shall also look at the processes of ultrafiltration which is included under the passive transport system.

**Figure 8.7: The osmosis process**

## D) Ultrafiltration

As the name suggests, ultrafiltration is a process of filtration. If we try to pass a solution through a filter, the solvent and other small molecules in the solution pass through while large molecules stay on the filter. Whether the given substance will pass through a filter or not, depends on the relative size of its molecules and on the process of the filter. The rate of filtration can be increased by applying pressure. For e.g. hydrostatic pressure in renal glomeruli is higher than any other capillaries of the body. As a result, water and small molecules filter through the glomeruli rapidly while proteins and blood cells do not.

## 8.6.2 Active Transport

Active transport is the mediated transport of biochemicals, and other molecular substances, across membranes. Unlike passive transport, this process requires chemical energy. In this form of transport, molecules move against either an electrical or concentration gradient (collectively termed as electrochemical gradient). This is achieved by either altering the affinity of the binding site or altering the rate at which the protein changes conformations.

Active transport, so we know now involves the utilization of energy. Depending on

NOTES

the source of energy, the active transport can be differentiated as:

- primary transport
- secondary transport

Primary transport uses energy directly, light or chemical energy is converted to electrochemical energy as electrochemical potential of the substances to be transported. This category comprises photosynthetic electron transport, light driven ion pumps, redox energy — dependent respiratory chains, transport ATPases and sodium pumps utilizing decarboxylation energy. Unlike primary transport, in secondary transport, the electrochemical energy originates from the electrochemical potential of another substance that is used up in symport (the transport of two different molecules or ions in the same direction through a membrane using a common carrier mechanism).

Active transport is required for maintaining the difference in the electrolyte composition between the intracellular and extracellular fluids. Inside the cell, the sodium ion concentration is much lower than outside, opposite is the situation in case of potassium ions. Active transport is also of special significance for the transport of several nutrients in the gastrointestinal tract. The absorption of nutrients should obviously continue until the luminal concentration has dropped to negligibly low levels even when the sizeable concentrations have built up in the enterocytes. This is possible only through active transport.

Since active transport needs metabolic energy, often a specific ATPase is present in the membrane of actively transporting cells. Active transport may be inhibited by the inhibitors of ATPase e.g. digitalis, which specifically inhibits the $Na^+$ — $K^+$ ATPase in cardiac muscle and omeprazole, which specifically inhibits the $H^+$— ATPase in the gastric parietal cells.

Active transport may also be non-specifically inhibited by dinitrophenol (DNP), which uncouples oxidation and phosphorylation in biological oxidation, by cyanide, which poisons the electron transport chain, and by fluoride or iodoacetate because these cells derive energy only from anaerobic glycolysis.

Having looked at the active transport, next we shall look at the secondary active transport operational in our body.

- **Secondary Active Transport:** In secondary active transport, there is no direct coupling of ATP, instead the electrochemical potential difference created by pumping ions out of the cells is used.

This is an ingenious device used by the cells to utilize the active transport of one substance to drive the uphill transport of one or more other substances as well. A few types of secondary active transport are as follows:

**a) Coupled transport:** The transport of two substances may be coupled to each other because they bind to the same carrier in the cell membrane.

**b) Co-transport:** If the two substances whose transport is coupled, move in the same direction, the phenomenon is called as co-transport or symport for e.g. in the small intestine, absorption of sodium ions is coupled with that of glucose, because they bind to the same carrier in the enterocyte membrane.

**c) Counter transport:** If the two substances whose transport is coupled, move in opposite directions, the phenomenon is called counter transport or antiport, e.g., in proximal convoluted tubules of kidneys, sodium is actively reabsorbed.

Simultaneously, for each sodium ion reabsorbed, one hydrogen ion is transported by the same carrier into the lumen of the tubule. Some examples of transport by solute-solvent interactions are secondary to the active transport of some substance. Let us get to know about solute-solvent interaction next.

## 8.7 SOLUTE-SOLVENT INTERACTION

A solution, as you may already know, is a mixture of solute (present in small amount) and solvent (present in large amount).

The interaction between solute-solvent inside the cell and outside the cell is governed by many physical factors like concentration gradient, electrical gradient, osmotic pressure difference and the characteristics of the membrane. Some molecules come out of the membrane through it gates and for others selective transport through these gates is pennissible. But for all living excitable cells, there is a potential difference during the resting state which is always negative towards inside the cell. When the cell becomes active, this potential difference is reversed and this is called action potential. So this interaction of solutes-solvent outside and inside maintain this important cell activity i.e., excitability. The main factors given below are responsible for this activity. Let us read about them.

### Osmosis

We have earlier studied about osmosis and the role of hydrostatic pressure in the osmotic process. Here, we shall see how osmosis acts as secondary phenomenon to the active transport. Entry of solute into a cell by active transport increases the osmotic pressure within the cell. Hence, water also enters the cell by osmosis. Reabsorption of water from the gut takes place by this mechanism.

### Solvent Drag

This is a process, which may be further secondary to the osmotic movement of water. Along with water, some substances dissolved in water may move in the same direction by bulk flow. This is known as solvent drag.

### Gibbs-Donnan Equilibrium

Let us consider a situation in which a semipermeable membrane separates two electrolyte solutions, only one ofwhich contains an ion to which the membrane is not permeable.

Let us imagine that the concentrations are as follows:

| A | B |
|---|---|
| $Na^+$ 30 | $Na^+$ 30 |
| $P^-$ 30 | $Cl^-$ 30 |

**NOTES**

where : $Na^+$ 30 is the concentration of Sodium ion 30

$C1^-$ 30 is the concentration of Chloride ion = 30

$p^-$ is Proteins which are negatively charged non-diffusable.

| A | B |
|---|---|
| ← | $Cl^-$ |
| ← | $Na^+$ |

The concentration gradient would lead to a diffusion of C1- from compartment B to A. However, that would create an electrical gradient, which would lead to a diffusion of Na also from B to A.

| A | B |
|---|---|
| $Na^+$45<br>$Cl^-$ 15<br>$P^-$ 30 | $Na^+$15<br>$Cl^-$ 15 |

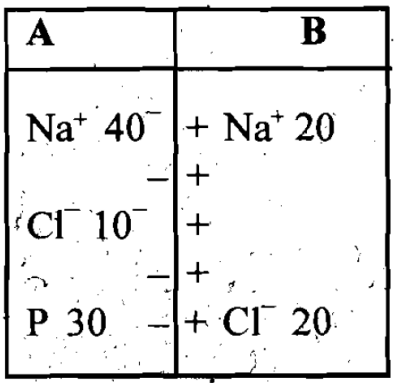
In effect, each $C1^-$ would be accompanied by Na+, leading to the situation as shown in the box alongside. This is also an unstable situation because the concentration of $Na^+$ is higher in A than and B

| A | B |
|---|---|
| $Na^+$ | → |
| $Cl^-$ | → |

Hence, $Na^+$ will diffuse from A to B and to maintain neutrality, $C1^-$ will accompany Na+. However, this does not go on indefinitely.

| A | B |
|---|---|
| ⇄ | |
| ⇄ | |

Diffusion of Na+ from A to B creates positivity on side B so that an equilibrium is reached when the concentration gradient from A to B exactly matches the electrical gradient




In the same way, for C1-, the concentration gradient from exactly balances the electrical gradient from A to B. As a result, the membrane will develop potential difference between its two surfaces, side B being positive as compared to A. The positivity on side B will prevent further diffusion of Na+ and the negativity on side A will prevent further diffusion' of' C1-

Thus the end result will be a higher concentration of $Na^+$ in A, a higher concentration of C1- in B and a membrane potential across the semipermeable membrane.

In a body, a situation like this develops across the capillaries. The capillary endothelium is permeable to electrolytes but not to proteins, and the capillaries contain plasma proteins which are negatively charged at a physiological PH. As a result, the sodiun concentration is higher in the plasma than the interstitial fluid. The chloride and bicarbonate coneentrations are the other way round, and there is a membrane potential (about 1 mV) across the capillary, the positivity being towards the interstitial fluid.

The concentration at which equilibrium is achieved in situations like this, are predictable and follow a mathematical relationship known as the Gibbs-Donnan equation. According to this equation,

$$[Na^+]_A \times [Cl^-]_A = [Na^+]_B \times [Cl^-]_B$$

OR

$$\frac{[Na^+]_A}{[Na^+]_B} = \frac{[Cl^-]_B}{[Cl^-]_A} = r$$

## 8.7 LET US SUM UP

In this unit, we studied about homeostasis. A variety of fluids such as intracellular, extracellular fluids as well as transport systems help in maintaining homeostasis. The unit focused on these fluids and the transport systems. A brief discussion on the body fluids and measurement techniques of various types of fluids was included. The transport systems, we learnt are of two types, passive and active. Passive transport involves simple diffusion, facilitated diffusion, osmosis, ultra filtration. The active transport can be primary or secondary transport. The secondary active transport, we learnt, includes solute-solvent interaction which further involves osmosis, solvent drag, etc. Gibbs-Donnan equilibrium, which helps to understand

the mechanisms involved in maintaining the concentration gradient.

## 8.9 GLOSSARY

NOTES

**Antiport** : the movement of two substances in opposite directions.

**Competitive block** : blockage of facilitated transport by a specific agent having a high affinity for the transport protein/ carrier.

**Hydrostatic pressure** : pressure which is exerted on a portion of a column of fluid as a result of the weight of the fluid above it.

**Mediated transport** : transport mediated by a transport protein.

**Non-competitive block** : blockage of facilitated transport — where in the blocking agent binds to the carrier but does not get transported and blocks the carrier reversibly.

**Osmolality** : a measure of moles of solute per kg of water. Osmolality basically measures the concentration of particles in a solution.

**Polycythemia** : an abnormally large number of red blood cells in the blood stream.

**Potential space** : a space in the body that normally contains little fluid but under special conditions can become filled with large amounts.

**Symport** : the movement of two substances in the same direction.

**Vital dye** : a dye which has the ability to combine with the proteins.

## 8.10 CHECK YOUR PROGRESS EXERCISES

UNIT

# 9

# NERVOUS SYSTEM

NOTES

## STRUCTURE



## 9.1 LEARNING OBJECTIVE

After studying this unit, you will be able to:

- discuss the morphology of neurons,
- understand the structural organization of the nervous system,
- enumerate the different systems operating within the nervous system,
- describe the functions of various parts of the brain, and
- explain the usefulness of electroencephalography (EEG) as a, diagnostic tool.

## 9.2 INTRODUCTION

In the previous units, we have studied about the different systems of our body. In this unit, we will study the sensory, motor and autonomic and control apparatus of our body, mostly constituted by nerve cells and fibre tracts — the nervous system. Along with the endocrine system, the nervous system regulates many internal functions and also co-ordinates the activities we know collectively as human behaviour, which include state .of consciousness, learning, memory and emotions. These phenomena which we attribute to 'mind' are believed to be related to the integrated activities of nerve cells of the brain. In vertebrates, as you would learn

in this unit, the nervous system is divided into three parts: the central, brain and spinal cord, the peripheral, cranial and spinal nerves; and the autonomic, sympathetic and parasympathetic. Finally, we will also learn the mechanism by which we can study brain electric potentials, which serve as an important diagnostic tool.

## 9.3 HOW DOES OUR BODY KNOW 'WHAT TO DO'?

Feeling, knowing, doing anything depends on special structures called nerves. Neuronal cells in the body act as various messengers according to the need involved. We are born with all the nerve cells we will ever have. There are about 100-billion nerve cells in our brain. If any nerve cell is somehow damaged, it will not be replaced by a new cell. Each nerve cell is known as a neuron. We will learn about the morphology of the nerve cell in the next section. The nervous system, as you may recall reading earlier, consists of 100-billion neurons and the glial cells. The whole brain is a collection of neuronal and glial cells. These cells are also responsible for higher functions of the brain like learning, memory, speech etc. This fascinating study of biological function of nervous system is called as neurobiology. So how does our body get to know, what to do? The terminal endings of the nerves are equipped with sensitive receptors. They generate the impulse in relation to any change in the environment i.e., temperature, pressure, touch and send them to main part of the nerve cell, to be transmitted to the brain. The brain receives such messages from various axonal tips. Further brain decides what information has to be processed. If actions are necessary, brain signals the muscles to carry out the work required. We will learn about this mechanism in greater details later here in this unit. A neuron releases its messages as chemicals. These are capable of changing polarity of cells. This is because of the ionic nature of the chemicals. Since it is achieved through movement of ions, we call them ionic channels. Their movement is termed as gait. The ions which play a major role are $Ca^{++}$ $Na^{++}$ $K^{+}$. They are able to create energy for nerve cells to function in a better manner. This creates some amount of electricity in the cell, which can be measured in volts. This principle was discovered by an Italian scientist Alessandre Volta during his experiment on frog leg muscle. We will understand the functioning of the nerve cell better by first getting to know the morphology of the nerve cell. The next section focuses on this aspect.

## 9.4 NERVE CELL

The basic unit of the nervous system as studied above, is the individual nerve cell — the neuron. The nerve cells operate by generating electrical signals and passing them from one part of the cell to another and by releasing chemical messengers to communicate with other nerve cells. Let us get to know about the nerve cell morphology first.

### 9.3.1 Nerve Cell Morphology

The neurons in the mammalian nervous system occur in a variety of shapes and sizes. A typical cell has a cell body, the dendrites, axon and its terminals. Look at Figure 9.1 which illustrates the structure of a nerve cell — the neuron. The cell body, which has a nucleus, arborizes to form dendrites which are the thin processes that extend out, as shown in Figure 9.1. From the thick concentrated region of the cell body arises a long extended fiber known as Each axon is covered by a myelin sheath. It is made up of a protein lipid complex. This is further surrounded by schwann cells (Glial cells).The axon is constricted at various positions, where it is denuded of myelin. This region is known as nodes of Ranvier.

**Figure 9.1: The structure of the nerve cell**

Let us look at each of these parts very closely: Cell Body: It is the portion of a neuron almost resembling with other cells. It contains a nucleus and cytoplasm, and receives impulses from dendrites. Axon: The long part of a neuron leading away from the cell body is the axon. It transmits impulses away from the cell body. Dendrites: These are the highly branched structures at one end of a neuron, which conducts impulses towards the cell body.

- **Schwann cells:** These aid in the nutrition and regeneration of axon and their myelination in the peripheral nerves. Having gone through the structure of the nerve cell, let us next learn how the neurons corrimunicate with each other. The neurons, you must realize, are important as they help to send and receive crucial messages to and from the brain. Let us read about this process next.

## 9.4.2 Communication between Neurons

Communication is possible only through chains of neurons. They should interconnect with parts of the neuronal terminals which brings the message and carries the message away. This communication can be from one neuron to the other or from one neuron to muscle. The anatomically specialized junction between two neurons, where one alters the activity of the other, through a chemical messenger is known as synapse. Figure 9.2 depicts a typical synapse. The term synapse was coined by Sir C. Sherington who was a famous neurophysiologist. The process of communication between two neurons across a synapse is called a synaptic transmission.

The synapse is a small gap separating neurons as can be seen in Figure 9.2. The synapse consists of:

- a presynaptic ending that contains neurotransmitters, mitochondria and other ceil organelles,
- a postsynaptic ending that contains receptor sites for neurotransmitters, and
- a synaptic cleft or space between the presynaptic and postsynaptic endings.

The neuron which sends a message is known as a presynaptic neuron and which receives a message is known as a postsynaptic neuron. A typical synapse junction is between the axon of presynaptic neuron and dendrites of a postsynaptic neuron.

**Figure 9.2: Synapse**

Communication among neurons typically occurs across microscopic gaps called synaptic clefts. Each neuron may communicate with hundreds of thousands of other neurons. A neuron sending a signal (i.e., a presynaptic neuron) releases a chemical called a neurotransmitter, which binds to a receptor on the surface of the receiving (i.e., postsynaptic) neuron. Neurotransmitters are released from presynaptic terminals, which may branch to communicate with several postsynaptic neurons. The receiving neuron then generates a nerve impulse in form of action potential to be transmitted across its axon to the next neuron

So it is clear to you that the neurons communicate through synapse. In the next section, we will further look into the mechanism of neural transmission of messages via the synapse

## 9.4.3 The Process of Synaptic Transmission

already studied, in this process, the message reaches in the form of action potentials propagated along the presynaptic axon as it reaches the presynaptic terminal to cross the synaptic cleft, the cell's electrical message must be converted into a chemical one. This conversion takes place when an action potential arrives at the axon tip, resulting in 'depolarization. The depolarization causes Ca2+ to enter -the cell. The increase in Nervous System intracellular Ca2+ concentration triggers the release of neurotransmitter molecules into the synaptic cleft. Once released from axon terminal, the neurotransmitter molecules diffuse along the cleft and fraction of them bind to the receptor sites of plasma membrane on postsynaptic cell. The

combination of transmitter with receptor triggers generation of postsynaptic excitatory or inhibitory action potential, which is further transmitted to the next neuron.

The excitatory potential opens sodium and potassium channels. This creates sodium influx and potassium efflux, further leading to depolarization. In an inhibitory type, it opens chloride and potassium channels. The net changes cause hyper polarization. Thus, you may have noted that when a neurotransmitter is received by a receptor (postsynap- tic), it either excites (depolarizes) or inhibits (hyperpolarizes) the postsynaptic neuron. When a neuron is depolarized, the membrane becomes more permeable to Na+ and is closer to firing (action potential). When a neuron is hyperpolarized, the membrane becomes impermeable to Na+ and will not fire. The neurotransmitter, thus crosses the synapye, binding to receptor molecules on the next neuron, prompting transmission of the message along the neuron's membrane.

In the discussion above we talked about neurotransmitters. What are neurotransmitters and what is their fate? Let's find out next

## 9.4.4 Neurotransmitter and Neuromodulators

Neurotransmitters are chemicals (small molecules or hormones), stored in small synaptic vesicles clustered at the tip of the axon (terminal buttons

A large number of substances have been identified which are very similar in neuronal transmission. Some of them have a long span of action. Under this influence, the postsynaptic neuronal sensitivity increases or decreases. Some of them are slow in action, hence they are called neuromodulators. A neurotransmitter has the following characters:

1) The synthesis should be from a neuron.
2) The stimulation of the cell should be releasing sufficient quantity of the neurotransmitters to affect the post synaptic membrane potentials.
3) The degradation-and uptake mechanism should exist at the concerned synapse.
4) Mimicking agents should release a similar effect like the neuronal cell.
5) Antagonist actions should be by specific neuronal inhibitors.

The most commonly discussed example of neurotransmitter is acetyl choline (ACh). It is synthesized from acetyl coenzyme A and choline. Choline is available in the diet (not synthesized in the body). The sources are vegetables and egg yolk, ACh acts at the neuromuscular junction, post ganglionic endings of parasympathetic nerves. In the central nervous system (CNS), ACh is employed as a neurotransmitter, which projects into hippocampus region. If the cholinergic neurons are less, it causes Alzheimer's disease.

Another neurotransmitter, nor-epinephrine (synthesis from phenylalanine or tyrosine), acts at post ganglionic endings of the sympathetic system. Decrease in levels of dopamine can cause Parkinson's disease.

5-Hydroxytryptamine (5 HT) is involved in sleep mechanisms. Gamma-amino butyric acid is a neurotransmitter which has powerful inhibitory actions. Some

of the neuromodulators are neuroactive peptides. They are generally polyproteins and act through secondary messengers like cyclic AMP (CAMP).

### 9.4.5 The Fate of the Neurotransmitter

Postsynaptic membranes bind the neurotransmitters by an active process. The chemicals keep moving in and out of the membrane. The synapse takes care not to have a continuous indefinite action. This is brought about by enzyme degradation, re- uptake mechanisms, recycling mechanisms etc. To illustrate, acetylcholine is removed by enzymatic hydrolysis from post synaptic membrane while nor-adrenaline is removed from the synaptic cleft by catechol-o-methyl transferase. It is further partly uptaken, partly recycled and inactivated by monoamine oxidase.

Neurotransmitters therefore, cross the synapse enabling impulse transmission to an adjacent neuron. Once in the synapse, they are active for only a short time — between 0.5 and 1 millisecond. Enzymes in the synapse inactivate neurotransmitters, which are either taken back into the axon (reuptake) and transported back to the neuron for re-usage or destroyed.

### 9.4.6 How do You Perceive and Respond to a Stimulus

In this world, our first perception is to see, then to hear, sense, smell or taste. The organs involved respectively are the eyes, ears, skin, nose and tongue. These organs have specific sensory cells which enable them to receive any change in the environment. These structures are generally known as receptors. They convey their messages to the brain. The brain translates the message into a state called perception (awareness). In addition to this, we have baroreceptors (senses pressure changes), chemoreceptors (senses chemical changes) and proprioreceptors (changes/ shifts in positions / posture). The basic mechanism is that all the sensory receptors are very similar. E.g. skin, it can feel pain, temperature, pricks and many more responses. Here, as soon as the receptor cell receives a stimulus, it brings a conformational change in the membrane so that Na+ ion channels become more penneable. This leads to depolarization and results in creation of a receptor potential. Further, it leads to generation of an action potential.

Action potential is brief, all or none depolarization occurs. The signal propagated slowly changes the frequency in the postsynaptic neuron. We generally get adapted to a prolonged stimulus. The degree and rate would vary e.g. though our touch receptors are fully functional, we are not aware of our clothes touching our body. This is because we are adapting ourselves to the stimulus. This occurs due to regular, continuous information which is persisting

Finally, in our study of the nerve cell, we will look at how the signals get conveyed to the central nervous system (CNS).

### 9.4.7 How the Signals are Conveyed to the CNS

Once the action potential is generated at the periphery receptors on the skin in relation to the specific stimulus such as pain, touch, temperature etc., as we have studied above, these action potentials go to the spinal cord through the dorsal root

ganglion cells can be seen from the Figure 9.3. In the spinal cord, the synapse occurs at the dorsal horn cell (which is first order sensory relay neurons). The information then passes along the spinothalmic tract system, as you may have noticed in Figure 9.3, to the specific sensory neurons ofthe thalamus (second order sensory relay neurons). From this thalamic area, the sensations project to the somato-sensory area of the cortex (third order neuron relay station). The sensations are processed and perceived in this area. Therefore, it must be clear to you that at least three neuron relay stations are required for processing 252 and perception of any sensation coming from the periphery. At each of these relay stations, the inter-neuronal transmission occurs through synaptic transmission. This system Nervous System involved in conveying the sensations from the periphery to the CNS is called the anterolateral (spinothalamic) system, which you have already studied in Figure 9.3

**Figure 9.3: Anterolateral system**

We have looked at the system involved in perceiving the signals coming from the periphery. What about the signals/sensations from the deep structures such as the joints, muscles etc.? How are these signals conveyed to the CNS? Let's find out. Sensations from the deep structures (proprioceptive i.e. from the joints, muscles, viscera etc.) after reaching the spinal cord column are relayed through the dorsal column and the lemniscal system to the higher centres, wherein, some of them are perceived and others are subconsciously processed. Figure 9.4 illustrates the dorsal column pathway which you now know are meant for deeper sensations

**Figure 9.4: Dorsal column system**

The processing and perception of this information is censored by the descending tracts at thalamus or spinal cord level (second order or first order relay station). This forms the descending fibres influencing the sensory system. The next sections focus on this aspect.

### 9.4.8 Descending Fibres of the Sensory System

The sensory cortex also sends descending fibers to the thalamic nuclei. They follow a similar route which is very close to that of ascending fibres at all levels. Thus, every region of nervous system has a control on the information that goes to it. A stimulus, perceived depends on the nature of the stimulus and descending influences. Descending fibre activity may be affected by accompanying sensory stimuli other than the one under consideration. The perception of a stimulus is affected by associated stimuli. E.g. intensity of a painful stimulus may be reduced by touch, specially a loving touch or needle movement/vibration as in acupuncture for treatment of pain.

## 9.5 STRUCTURAL ORGANIZATION OF NERVOUS SYSTEM

Nervous system has an axial organization. The central and peripheral nervous system make up the nervous system. The brain and spinal cord forms the central nervous system. It receives information through sensory neurons, passes the messages to carry out specific actions back by motor nerves. The peripheral nervous system has sensofy and motor nerves. The mixed nerves consist of sensory and motor fibers together. Together, the central and peripheral nervous system control every activity of our daily life, from breathing and blinking to helping us memorize facts for a test, Let us get to know the organs of the nervous system. We shall start with the central nervous system

## 9.6 THE CENTRAL NERVOUS SYSTEM

We have seen above that the brain and the spinal cord form the central nervous system. In this section we will study about the brain and understand how the spinal cord conducts sensory information from the peripheral nervous system (both somatic and autonomic) to the brain and conducts motor information from the brain to our various effectors — skeletal muscles, cardiac muscle, smooth muscle and glands. It also serves as a minor reflex center

The brain receives sensory input from the spinal cord, as well as, from cranial nerves (e.g., olfactory and optic nerves and others), and devotes most of its volume (and computational power) to processing its xarioii$ sensory inputs and initiating appropriate coordinated motor outputs

We shall learn the structure and functions. ofrthese organs in this section. We start with the brain.9.5.1 Organization of Brain

NOTES

**Figure 9.5: The brain**

The external covering, skull/cranium protects the brain. Brain being a soft tissue has a meningal membranes covering it. These membranes have spaces in between them which are filled with cerebrospinal fluid (CSF). In fact, the entire surface of the central nervous system is bathed by the clear, colourless cerebrospinal fluid. The CSF is contained within a system of fluid-filled cavities called ventricles. There are 4 ventricles as illustrated in Figure 9.6. Two are lateral, which communicate with the 3rd ventricle through independent openings, which are known as interventricular foramen (foramen of Monro). 3rd ventricle further communicates with narrow duct passing through mid brain called the aqueduct of Sylvius. This further leads through 4th ventricle as shown in Figure 9.6, which is enclosed by medulla oblongata and it continues through the spinal cord as central canal.

The 4th ventricle of the brain posses bunches of vascular tissue — choroid plexus. This is an arterial bunch which comes from main arterioles and supplies the brain. The major source of CSF is choroid plexus. The other sources of CSF are ependymal cells of the ventricles and the brain itself via the perivascular spaces. Total volume of CSF in an adult is about 100-125 ml. The rate of CSF formed per day averages to 500 ml per day.

**Figure 9.6: The ventricles**

So we have seen that the CSF flows through the ventricles. But what does the CSF do? What is its role in the brain? The CSF has many functions. These include the following:

1) It provides the optimum condition for a meaningful signal/stimulus. The neurons become very sensitive.
2) It helps in maintaining homeostasis. It can transmit neuronal messages to respond for chemo sensitivity which enhances the appropriate homeostatic signals.
3) It helps in removing the proteins which are leaked into the brain since no major lymphatic system prevails here. CSF further shunts these proteins to the blood stream
4) It protects the brain as a cushion by absorbing all the shocks/jerks etc. It also helps the brain to remain floating inside the skull-cavity.
5) It provides buoyancy to the brain. Because the brain is immersed in fluid, the net weight of the brain is reduced from 1400g to about 50 g only. Therefore, pressure at the base of the brain is reduced.
6) It helps in the excretion of waste materials. The one-way flow from the CSF to the blood takes potentially harmful metabolites, drugs and other substances away 256 from the brain.

We have seen how important CSF is. However, under certain pathological conditions Nervous System the CSF builds up within the ventricles. This condition is hydrocephalus

So when we look into the internal anatomy, the brain has hollow structures. These hollow spaces are known as ventricles. They are filled with Having got a general idea about the brain organization, next, let us look at each of the specific structures of the brain, starting with the cerebrum

### 9.6.1.1 The Cerebrum

The cerebrum is the largest part of the brain, consisting of two cerebral hemispheres. It is divided by a deep cleft, the longitudinal cerebral fissure, into right and left hemispheres, each contains one of the lateral ventricles. These hemispheres are connected by a mass of white matter — corpus callosum (refer to Figure 9.5). A thin layer of gray matter, the cerebral cortex, lies on the outside of the cerebrum and contains 75% of the cell bodies in the nervous system. Beneath the cortex lies a mass of white matter made up of myelinated nerve fibers connecting the cell bodies of the cortex with the rest of the nervous system

The superficial part of the cerebrum i.e. the cortex shows many infoldings or furrows of varying depths. These folds are known as gyri. They are separated by the fissures known as the sulci. These foldings increase the area of the cerebrum. The interior of the cerebrum, as learnt above, are connected by masses of nerve fibres, tracts which make up the white matter of the brain. The afferent or efferent fibres linking the different parts of the brain and spinal cord are:

- **Arcuate (association fibres):** connects different parts of the cerebral cortex

by extending from one gyrus to another, some are adjacent, some are distant.

- **Commissural fibres:** connects the two cerebral hemispheres (corpus callosum).
- **Projection fibres:** connects cerebral cortex gray matter with lower parts of the brain with the spinal cord.

The cerebral cortex is divided into four sections, called "lobes" - the frontal lobe, parietal lobe, occipital lobe and temporal lobe. Figure 9.7 presents the visual representation of the cortex, where you can locate these four lobes.

**Figure 9.7: The four lobes of the cerebral cortex**

What is each of these lobes associated with? Let us consider. Frontal Lobe: reasoning, planning, parts of speech, movement, emotions and problem solving.

- **Parietal Lobe:** niovement, orientation, recognition and perception of stimuli
- **Occipital Lobe:** visual processing.
- **Temporal Lobe:** perception and recognition of auditory stimuli, memory and

Looking at the functionality of each lobe, it must be evident to you that cerebrum has a major function in our body.

Let us get to know these functions.

## Functions of the cerebrum

The cerebrum is associated with higher brain functions such as thought and action. The three major varieties of activities involved are:

1) Mental activities involved in memory, intelligence, sense of responsibility, thinking, reasoning, moral sense and learning attributed to higher centres.
2) Sensory perception, including pain, touch, temperature, sight, hearing, taste and smell, and
3) Initiation and control of voluntary muscle contraction.

The main areas of the cerebrum are associated with sensory perception (sensory centre) and voluntary motor activity (motor activity). Both hemispheres are equally active unless mentioned specifically.

NOTES

**Figure 9.8 shows these cerebral functional areas**.

The motor area lies in the frontal lobe, immediately anterior to the central sulcus (a brain fissure extending upward on the lateral surface of both hemispheres, separates the frontal and parietal lobes). The nerve cells are pyramid shapes and imitate contraction of voluntary muscles. The nerve fibre from this cell passes downwards through internal capsule to the medulla and then crosses to the opposite side, descends in the spinal cord. In the spinal cord, the nerve synapse to stimulate a second neuron which terminates at the motor end-plate of a muscle fibre. This shows that the motor area of the right hemisphere of the cerebrum controls voluntary muscle movement on the left side of the body and vice-versa. The neuron which has its cell in the cerebrum is the upper motor neuron, while the one with the cell in spinal cord is the lower motor neuron. Damage to either of them causes paralysis.

In the motor area of the cerebrum, body is represented upside down, i.e. the cells nearest the cortex control the feet and those in the lowest part control the head, neck, face, fingers. In comparison with the trunk, the hand, tongue and lips are represented by large cortical areas.

The pre motor areas too lie in the frontal lobe immediately anterior to the motor area as highlighted in the Figure 9.8. The cells are thought to exert a controlling influence over the motor area, ensuring a series of movements, e.g. while writing or tying a shoe lace, many muscles contract but the movement must be carried out in a particular Nervous System sequence. This is described as manual dexterity. In the lower part of this area, just above the lateral sulcus is the broca's area which controls movement for speech. It is dominant in the left hemisphere in the right handed people and vice versa.

The frontal area or pole, as shown in the Figure 9.8, extends anteriorly from the pre motor area to include the remainder of the frontal lobe. This area is large and is highly developed in humans. Communications between this region and the other region and other areas are responsible for behaviour, character and emotional state of the individual, as mentioned above.

The post central area is behind the central sulcus. Here, the sensations of pain, temperature, pressure and touch, knowledge of muscular movements and position of joints are perceived. The sensory areas of the right hemisphere receive impulses from left side of the body and vice versa.

The parietal area, as you can see in the Figure 9.8, lies behind the post central area and includes greater part of parietal lobes of the cerebrum. It is functional in providing accufate knowledge ofobjects. The objects can be recognized by touch alone, because of the knowledge from past experience is retained in this area.

The sensory speech area is situated in the lower part of the parietal lobe and extends into temporal lobe as indicated in the Figure 9.8. This area perceives spoken word. Dominance is in left area if the individual is a right handed person and vice versa. The auditory area lies immediately below lateral sulcus within the temporal lobe as can be seen in Figure 9.8. Cells receive and interpret impulses transmitted from inner ear by vestibulocochlear nerve.

The olfactory area lies deep within the temporal lobe. Look at Figure 9.8 for its position. Cells receive and interpret impulses from nose which come through olfactory nerves. The taste area is above lateral sulcus, in deep layers of the sensory area. The visual area lies behind the parieto-occipital sulcus and includes greater part of occipital lobes. Optic nerve passes from eyes to this area which receives and interprets impulses as visual impressions.

Deep within the cerebral hemispheres are groups of nerve cells called nuclei or ganglia which act as relay stations, where impulses are passed from one neuron to next in a chain. The basal nuclei are, therefore, also called the basal ganglia. The term "basal" refers to the location of these collections of neurons (nuclei or ganglia) deep within the brain, seemingly at its very base. This region located at the base of the brain is composed of 4 clusters of neurons or nerve cells — sensory nuclei, association nuclei, non specific nuclei and motor nuclei. This area of the brain is responsible for body movements and coordination. The area influences skeletal muscle tone. If control is inadequate or absent, movements are jerky, clumsy and unco- ordinate.

The discussion above focused on the cerebrum. Next, let us look at the other structures of the forebrain i.e. the thalamus and hypothalamus (diencephalon), which you learnt earlier, are a part of the limbic system.

### 9.6.1.2 The Limbic System

The limbic system, as you would realize, is also referred to as the emotional brain. It is found buried within the cerebrum. This system contains the thalamus, hypothalamus and other related part like the amygdala and hippocampus. Let us get to know about the thalamus and the hypothalamus.

### Thalanaus

Thalamus is a large mass of gray matter deeply situated in the forebrain. Figure 9.9 illustrates the position of the thalamus.The structure has sensory and motor functions. Almost all sensory information enters this structure where neurons send Applied Physiology that information to-the overlying cortex. Axons from every sensory system (except olfaction) synapse here, as the last relay site before the information reaches the cerebral cortex.

Thalamus consists of two masses of nerve cells and fibres situated below corpus callosum, one on each side of the 3rd ventricle. Sensory inputs from skin, viscera and special sense organs are transmitted to the thalamus before re-distribution to the cerebrum. Thalamus is a collection of neurons which are organized into a number of nuclear masses, All sensory information reaches thalamus where it can be integrated. It also has non-sensory functions.

### Hypothalamus

The hypothalamus is composed of a number of groups of nerve cells. It is situated below and in front of thalamus, immediately above the pituitary gland. Refer to Figure 9.9 for identifying its location in the brain. Hypothalamus is linked to the posterior lobe Of pituitary gland by nerve fibres and to anterior lobe by a complex system of blood vessels. Through these connections, hypothalamus controls outpit of hormones from both lobes of the gland. The structure is involved in functions including homeostasis, emotion, thirst, hunger, body temperature, circadian rhythms, defensive reactions fear, anger, rage etc. and control of the autonomic nervous system. In addition, it controls the pituitary

### 9.6.1.3 Midbrain

The midbrain is the area of the brain situated around the cerebral aqueduct between the cerebrum above and the pons varolli below. Midbrain consists of a group of nerve cells and nerve fibers which connects the cerebrum with lower parts of the brain and spinal cord. These nerve cells act as relay stations for the ascending and descending nerve fibers.

The midbrain consists of the tectum and tegmentum. It is involved in functions such as vision, hearing, eye movement and body movement. The anterior part of the mid- brain has the cerebral peduncle, which is a huge bundle of axons travelling from the cerebral cortex through the brain stem and these fibers (along with other structures) are important for voluntary motor function. Often the midbrain, pons and medulla are referred together as the brain stem. Figure 9.9 illustrates the brain stem.

**Figure 9.9:' The brain stem**

The brain stem is the lowest part of the brain. It serves as the path for messages Nervous System travelling between the upper brain and spinal cord but is also the seat of basic and vital functions such as breathing, blood pressure and heart rate, as well as reflexes like eye movement and vomiting. A canal runs longitudinally through the brain stem structures i.e. medulla, pons and midbrain, carrying cerebrospinal fluid. Also distributed along its length is a network of cells, referred to as the reticular formation, which governs the state of alertness. We shall study about it later in section 9.5.1.7.

### 9.6.1.4 Pons Varolli

Look at Figure 9.9. Situated in front of the cerebellum below the midbrain and above the medulla oblongata, is the pons. It is involved in motor control and sensory analysis. For example, information from the ear first enters the brain in the pons. It has parts that are important for the level of consciousness and for sleep. Some structures within the pons are linked to the cerebellum, thus are involved in movement and posture

Pons consists mainly of nerve fibers which form a bridge between the two hemispheres of the cerebellum and fibers passing between higher levels of brain and spinal cord. There are groups of cells which act as relay stations and some of which are associated with the cranial nerves. The anatomical structure of pons varolli is different from that of cerebrum in the aspect that here the nerve cells lie deeply and nerve fibers are on the surface.

### 9.6.1.5 Medulla Oblongata

The medulla extends from the pons above and is continuous with the spinal cord below as can be seen in Figure 9.9. It is about 2.5 cm long shaped like a pyramid with a base upwards. It lies within the cranium just above foramen magnum. The anterior and posterior surfaces are marked by central fissures. The outer aspect is composed of white matter, which passes between the brain and spinal cord and gray matter lies centrally. Some cells constitute relay stations for sensory nerves passing from spinal cord to the cerebrum. The vital centers consisting of groups of cells associated with autonomic reflex activity lie in the deeper area. These are the cardiac, respiratory, vasomotor and reflex centers for vomiting, coughing, sneezing and swallowing' The medulla has several special features:

- **Pyramids:** Pyramids are the bulges of ventral surfaces, where most of the lateral corticospinal tracts originating from motor area of cerebrum decussate and cross over to opposite side. This means left hemisphere of cerebrum controls right half of the body and vice versa.
- **Sensory decussating:** Some of the sensory nerves ascending to the cerebrum from spinal cord, cross from pine side to the other in the medulla.
- **Cardiac centers:** These control rate and force of cardiac contraction. Sympathetic and parasympathetic fibers originating in the medulla pass to the heart. Sympathetic stimulation increases the rate and parasympathetic decreases. Respiratory center: The center for regulating rate and depth of

respiration is present in the medulla. Here, nerve impulses initiate respiratory mechanism. The center is stimulated by excess $CO_2$, to a lesser extent by deficiency of $O_2$ in blood.

- **Vasomotor center:** The vasomotor center is found in medulla. It controls diameter of the blood vessels especially the ones which have smooth muscle fibers in their walls. The impulse reaches the blood vessel through autonomic nervous system. Stimulation may either cause constriction or dilatation, depending on the site. It also controls vasomotor responses linked with body temperature, emotions, excitement, fall in blood pressure etc.
- **Reflex center:** This center present in the medulla is responsible for controlling Nervous System reflexes such as swallowing, vomiting, coughing and sneezing. When irritating substances are present in the stomach or respiratory tract, nerve impulses pass to medulla (which controls vomiting, coughing, sneezing and swallowing.) Cranial nerves: Four, cranial nerves (9-12) leave the medulla. So we have seen that the medulla oblongata is responsible for maintaining vital body functions, such as breathing, blood pressure and heart rate. Next, we shall review the third part of the hindbrain i.e. the cerebellum.

### 9.6.1.6 The Cerebellum

Cerebellum is situated behind pons and immediately below posterior region of the cerebrum occupying the posterior cranial fossae (as shown in Figure 9.9). It is ovoid in shape as can be seen in Figure 9.10 and is similar to the cerebrum in that it has two hemispheres and has a highly folded surface or cortex. Gray matter forms surface of the cerebellum and white matter lies deeply. This structure is associated with the regulation and coordination of movement, posture and balance. A number of fibers project to and from the cerebellum. They are mainly the cerebellar afferents and efferents. There are a number of nuclei in the center which connect through different pathways to the motor neurons.

**Figure 9.10: The cerebellum**

We shall look at the intra cerebellar organization next. This discussion will give you a good idea about the functioning of the cerebellum. You will find this section a bit technical. Do not get bog down by the information provided. Try to understand the organization and its function.

NOTES

The cortex of the cerebellum consists of 3 layers — molecular layer, purkinje cell layer and granular layer. The granular layer receives most of the inputs to the cerebellum and transmits them to molecular layer. The major cellular elements in the molecular layer are the stellate (star shaped), golgi and the basket cells and in the middle layer are present purkinje cells as illustrated in Figure 9.11. Inputs to cerebellum reach through mossy fibers from spinal cord and brainstem. The fiber makes a close synaptic contact with numerous granular cells and forms a glomerulus. The axons of these cells run perpendicular to the cerebellar cortical surface and on reaching the molecular layer, bifurcate into parallel fibers. They run parallel to each other and to the cortical surface. These fibers make axo-dendrite synapses with numerous purkinje cells and also with the 3 types of inter neurons i.e. golgi, stellate and basket cells.

Their axons further synapse with purkinje cells. Thus, purkinje cells receive direct and indirect inputs from parallel fibres

**Figure 9.11: A schematic representation showing intra cerebellar organization**

There is a single climbing fibre associated with single purkinje cell. This one to one contact of the fibre involves multiple synapses over the dendritic tree of each purkinje cell they activate. The purkinje cells in this way reflect a very powerful input.

A third input to cerebellar cortex is aminergic. It includes noradrenergic afferents. They regulate the excitability of the cortical neurons.

The parallel fibres through the 3 interneurons send inhibitory signalS to purkinje cells. Golgi cells send messages as feedback to inhibit granular cells thus shutting off the input via mossy fibre system. Basket and stellate cells also-inhibit purkinje cells. Thus, one can conclude that the function of this precise arrangement correlates to:

1) Mossy fibre activitation of granular cells can excite purkinje cells via parallel fibres.
2) Parallel fibres can excite basket and stellate cells which surrounds purkinje cells.

3) After a short delay, Golgi cell feedback inhibition shuts off the activating input from granular cells.

Thus, the regulatory action can govern the rate, range, direction and force of movements.

## What functions does the cerebellum perform?

The main functions of cerebellum include control of muscle tone and posture, equilibrium and coordination of movements. Let us see how these functions are performed.

Corticospinal tract informs the cerebellum about the output of motor cortex. The feedback is also received through spinocerebellar tract, which comes from muscles, tendons and joints. It can discriminate stages between actual movements and position.

Functional medial and lateral corticonuclear divisions of cerebellum (i.e. medial cortico fastigial or flocculonodular and lateral corticodentat) influence medial and lateral motor systems. Thus medial portion of cerebellum controls tone, postufe and equilibrium and lateral controls and coordinated fine and skilled movements at distal joints.

Having learnt about the functions, consider the situation when the cerebellum does Nervous System not functions properly. What are the disorders related to the non-functioning of the cerebellum? Let's find out.

## Some disorders of the cerebellum

Damage to cerebellum causes motor disorder. Synergy refers to smoothness and co-ordination of various movements. Disturbances can create asynergia or ataxia, a common form is dysmetria, in which the patient looses ability to bring his/her own muscles back to desired position. It produces an unsteady joint. It can also produce speech disorders. Cerebellar ataxia, tremors (trembling/shaking) and hypotonia (low muscle tone) are examples.

## 9.6.1.7 Reticular Formation

Reticular formation, as shown in Figure 9.9, is an apparently diffusely organized area that forms the central core of the brain stem. It is the collection of neurons and meshwork of fibres in the core of the brain stem. It has many synaptic links with other parts of the brain, hence constantly receiving information, being transmitted in specific ascending and descending tracts.

## What are the functions of the reticular formation?

The reticular formation is involved in four general types of functions: Motor control: Co-ordination of skeleton-muscular activity is associated with voluntary motor movements and the maintenance of balance.

Visceral control: It controls activities of autonomic nervous system e.g. cardio vascular, respiratory and gastrointestinal activity.

- **Sensory control:** Selective awareness through reticular activating system which selectively blocks or passes sensory information to the cerebral cortex. E.g. slight noise produced by an ill child's movement makes the mother awake but responses of regular trains passing may be suppressed.
- **Control of consciousness:** The activity of the cerebral cortex (arousal) depends upon ascending reticular activating system (ARAS). It also regulates cortical excitability hence electrical activity (EEG of the brain) With the functions of the reticular formation, we come to an end of our study of the brain.

## 9.6.2 The Spinal Cord

Spine is one of the most important parts of the body. Without it perhaps we would not keep ourselves upright or even stand up. In fact, it gives our body a structure and support. The spine is so designed so as to protect our spinal cord. The spinal cord is a column of neural tissue that connects our brain with the rest of our body, allowing us to control our movements. Figure 9.12 illustrates the spinal cord. Without a spinal cord, we would not be able to move any part of our body and our organs would not function.

**Figure 9.12: The spinal cord and the nerves supplying impulses to various organs**

The spinal cord is an elongated cylindrical part of the CNS. It is a column of millions of nerve fibers that run through our vertebral canal. The spinal cord is suspended in the vertebral canal surrounded by the meninges and cerebrospinal fluid. It extends from the brain to the area between the end of our first lumbar vertebra and top of the second lumbar vertebra. At the second lumbar vertebra, the spinal cord divides into several different groups of fibers that form the nerves that will go to the lower half of the body.

A protective membrane called the dura mater covers the spinal cord. The dura Nervous System mater forms a watertight sack around the spinal cord and the spinal nerves. Inside this sack, the spinal cord is surrounded by spinal fluid. The spinal cord is about 45 cm in length in Caucasian males. Nerves conveying

impulses from brain to various organs and tissues descend through the spinal cord. At appropriate levels, they leave the cord and pass to the structure they supply. This is why damage to the spinal cord can cause paralysis in certain areas and not others — it depends on which spinal nerves are affected. Figure 9.12 illustrates how the nerves supply impulses to various organs. The nerves of the cervical spine go to the upper chest and arms. The nerves in our thoracic spine go to our chest and abdomen. The nerves of the lumbar spine then reach to our legs, bowel and bladder. These nerves coordinate and control all the body's organs and parts, and let us control our muscles.

Similarly, sensory nerves from organs and tissues enter and pass upwards in the spinal cord to the brain. Spinal reflexes are independent of the brain. They are facilitated by extensive nervous connection between sensory and motor neurons at the same or different levels on the cord.

Spinal cord is incompletely divided into 2 equal parts by a shallow median fissure anteriorly and by a narrow posterior median septum at the posterior part. A cross section shows that it is composed of gray matter in the center and is surrounded by white matter supported by neuroglia as highlighted in Figure 9.13. Let us see what the gray and white matter is composed of.

**Figure 9.13: Cross-section of spinal cord**

## Gray matter

The gray maiter has two posterior, two anterior and two lateral columns. The area which lies transversely is known as transverse commissure. The nerve cells may be sensory cells receiving impulses from periphery of the body, it can transmit impulses to skeletal muscles through motor neurons.

A posterior column of gray matter contributes to the formation of white matter of the cord and transmits sensory impulses to the brain. Anterior columns promote onward movements of nerve impulses.

## White matter

The white matter of the spinal cord is arranged in three columns or tracts — anterior, posterior and lateral. These tracts are formed by the sensory nerve fibres

ascending towards brain and motor fibres descending from brain and fibres of connector.

Moving a muscle usually involes communication between the muscle and the brain through nerves. The impetus to move a muscle may originate with the senses. For example, the special nerve en4iqgé n (sensory receptors) may sense pain Applied Physiology when a person steps on a sharp rock or sense discomfort when a person picks up a very hot cup of coffee. This information is sent to the brain and the brain sends a message to the muscle about how to respond. This type of exchange, involves two complex nerve pathways: the sensory nerve pathway to the brain and the motor nerve pathway to the muscle. Figure 9.14 illustrates these pathways. Let's get to know about these ascending and descending nerve tracts next.

**Figure 9.14: Sensory and motor nerve pathways**

## A) Sensory Nerve tracts (Afferent/Ascending)

There are 2 main sources of sensation transmitted to the brain via spinal cord. These include:

1) **The nerve ending in the skin** — Cutaneous receptor is stimulated by three neurons to the sensory area in the opposite hemisphere of the cerebrums, Here it is perceived. Crossing to the other side or decussation occurs either at the level of entry into the scord or in the medulla.
2) **The tendons, muscles, joints** — Sensory nerve endings here are known as proprioceptors which are stimulated by .stretch. They are associated with balance, posture, perception of body position etc. with the inputs from eyes and ears. They specifically reach the areas by:

- 3 neuron system whereby the impulses reach sensory area of opposite hemisphere of cerebrum, and
- 2 neuron system, impulses reach cerebellar hemisphere of the same side.

**B) Motor Nerve tracts (Efferent/Descending):** Neurons, which transmit nerve impulses away from the brain, as you learnt earlier, are motor neurons. Their stimulation results in:

a) **Contraction of voluntary muscles (striated, skeletal):** Stimulations here were under our will, consciously controlled in the cerebrum. Some impulses are initiated in the midbrain, brainstem and cerebellum. This occurs below the level of consciousness. It is associated with co-ordination of muscular activity. e.g. fine movements required in posture and balance. The motor pathways from brain to muscle are made up of 2 neurons — upper motor. neuron and lower motor neuron.

b) **Contraction of the smooth (involuntary)** muscles and secretion by glands is controlled by nerves of the autonomic part of the system. Here, four neurons are involved:

1) **Upper motor neurons:** These have their cells in brain at a level below the Nervous System: cerebrum i.e. in midbrain, brain stem and spinal cord. They influence muscular movements with relation to posture balance, co-ordination and muscle tone.

2) **Spinal reflexes:** They have 3 elements — sensory neurons, connector neurons and lower motor neurons and simple reflex arc. A reflex action is an immediate motor response to a sensory stimulus. Impulses from skin are transmitted -to spinal cord by sensory nerves. These stimulate many connector and lower motor neurons in the cord which results in contraction of many skeletal muscles. Reflex action takes place quickly, the motor response may have occurred simultaneously with the perception itself. Reflexes of this type are invariably protective and occasionally can be inhibited e.g. a precious plate, which is very hot, when lifted every effort will be made to over come the pain to prevent dropping of the plate.

3) **Stretch reflexes:** Here only two neurons are involved. Cell of lower motor neuron is stimulated by sensory neuron. There are no connector neurons involved e.g. knee jerk reflex can be demonstrated here at any point, where a stretched tendon crosses a joint. Tap the tendon just below the knee when it is bent, sensory endings in the thigh muscle and tendons are stretched. This initiates an impulse to pass into spinal cord into the lower motor neuron in the anterior column of gray matter on the same side. As a result, thigh muscle suddenly contracts and the foot kicks forwards.

4) **Autonomic reflex:** We shall read about this subsequently in the section on autonomic nervous system.

Based on our discussion above, now can you highlight the functions of the spinal cord? Here, the functions have been presented for your perusal. The spinal cord carries out two main functions:

- It connects a large part of the peripheral nervous system to the brain. Information (nerve impulses) reaching the spinal cord through sensory neurons is transmitted up into the brain. Signals arising in the motor areas of the brain travel back down the cord and leave in the motor neurons.
- The spinal cord also acts as a minor coordinating center responsible for some simple reflexes like stretch reflex and the withdrawal reflex. With the study of the structure Of the spinal cord and the sensory and motor nerve impulses,

we end our discussion about the spinal cord.

We looked at the brain and the spinal cord which forms the central nervous system in this section. Next, let us focus on the peripheral nervous system.

NOTES

## 9.7 PERIPHERAL NERVOUS SYSTEM (PNS)

The peripheral nervous system or PNS, is a part of the nervous system and consists of the nerves and neurons that reside or extend outside the central nervous system- to serve the limbs and organs.

peripheral nervous system consists of:

- sensory neurons running from stimulus receptors that inform the central nervous system of the stimuli, and
- motor nerves running from the spinal motor neurons to the muscles and glands — called effectors — that take action. Figure 9.15 illustrates the systems within the PNS.

**Figure 9.15: The sensory and the motor neurons**

The peripheral nervous system, as can be seen in Figure 9.15, is subdivided into:

- Somatosensory nervous system, and
- Autonomic nervous system Let us now get to know these two systems within the PNS.

### 9.7.1 Somatosensory System

The somatosensory system consists of:

- 12 pairs of cranial nerves, and
- 31 pairs of spinal nerves.

All our conscious awareness of the external environment and all our motor activity to cope with it operate through the somatosensory division of the PNS. Each nerve has nerve bundles, each bundle has a covering of following protective connective Nervous System tissue:

**1) Endoneurium:** delicate tissue surrounding individual fibres 2) Perineurium: smooth tissue surrounding bundles of fibres. 3) Epineurium: surrounds and encloses members of bundles of nerve fibres. Let us get to know more about these nerves. We shall start with the spinal nerves.

## A) Spinal Nerves

As mentioned earlier, there are 31 pairs of spinal nerves that leave the vertebral canal by passing through the intervertebral foramina formed by adjacent vertebrae. All of the spinal nerves are "mixed", that is, they contain both sensory and motor neurons. A representation of these spinal nerves supplying to the specific organs, you may recall has already been presented, in Figure 9.12. Look up Figure 9.12 now. You will realize that these spinal nerves are named and grouped according to vertebrae to which they are associated.

8 — Cervical, 12 — Thoracic, 5 — Lumbar, 5 — Sacral, 1 — Coccygeal

Although there are only 7 cervical vertebrae, there are eight nerves because the first pair leaves the vertebral canal between the occipital bone and the atlas and eighth pair leaves below last cervical vertebrae.

Lumbar, sacral, coccygeal nerves leave spinal cord near its termination at the level of first lumbar vertebrae. They extend down inside the vertebral canal in the subarachnoid space, which forms a sheaf of nerves, which resembles a horse's tail — the cauda equina. They leave the vertebral canal at the appropriate lumbar, sacral or coccygeal level.

There are 12 pairs of thoracic nerve. Eleven of them are situated between the ribs, and are therefore termed intercostal; the twelfth lies below the last rib. They pass in-between the ribs supplying the intercostal muscles and overlying skin. The 12th pairs are the sub costal nerves. The 7th to 12th thoracic nerves also supply muscles of the skin of posterior and anterior abdominal walls.

The spinal nerve arises from both sides of spinal cord and emerges through intervertebral foramina. Each nerve is formed by the union of a motor and sensory nerve root and thus forms a mixed nerve, as mentioned above. Each spinal nerve has contributions from sympathetic part of autonomic nervous system in the form of a preganglionic fibre.

- **Nerve roots:** Each nerve is attached to the medulla spinalis by two roots, an anterior or ventral, and a posterior or dorsal (as you may have noticed in Figure 9.13). The anterior nerve root consists of motor nerve fibres which are the axons of nerve cells. The axons of nerve cells are in the anterior column of the gray matter in the spinal cord. In the thoracic and lumbar region, sympathetic nerve fibres which are axons of cells, is in the lateral columns of gray matter.

Posterior nerve root consists of sensory nerve fibres, having cell bodies in root ganglions and enter the spinal cord.

Immediately after emerging from the intervertebral foramen, each spinal nerve divides into ramus communicants. posterior and anterior ramus. The ramus communicants are part of pre ganglionic sympathetic neurons of the autonomic nervous system.

The posterior rami pass backwards and divide into medial and lateral branches to skin, muscles etc. The anterior rami supply anterior and lateral aspects of the trunk, upper and lower limbs.

In the cervical, lumbar and sacral regions, the anterior rami unite near the origins to form large masses of nerves or plexus. They divide and branch to proceed to sking muscles, jointy etc. There are 5 such large plexus. They are the cervical plexus, brachial plexus, lumbar plexus, sacral plexus and coccygeal plexus.

## B) Cranial Nerves

There are 12 pairs of cranial nerves originating from the brain. Some are sensory, some are motor and some mixed. Table 9.1 presents their type and functions. Look at Figure 9.16, which illustrates these nerves and their functions.

| Nerve | Type | Functions |
|---|---|---|
| I Olfactory | Sensory | Olfaction (smell) |
| II Optic | Sensory | Vision (contains 38% of all the axons connecting to the brain) |
| III Oculomotor | Motor | Eyelid and eyeball muscles |
| IV Trochlear | Motor | Eyeball muscle |
| V Trigeminal | Mixed | Sensory: facial and mouth sensation<br>Motor: chewing |
| VI Abducens | Motor | Eyeball movement |
| VII Facial | Mixed | Sensory:taste<br>Motor: facial muscles and salivary glands |
| VIII Auditory | Sensory | Hearing and balance |
| IX Glossopharyngeal | Mixed | Sensory:taste<br>Motor: swallowing |
| X Vagus | Mixed | Main nerve of the parasymethatic nervous system |
| XI Accessory | Motor | Swallowing; moving head and shoulder |
| XII Hypoglossal | Motor | Tongue muscle |

**Table 9.1: Cranial nerves — type and functions**

With the discussion on cranial nerves, we end our study of the somato- sensory system of the periphery nervous system. Next, we shall study about the autonomic nervous system, which you may recall reading earlier, is the other system of the PNS

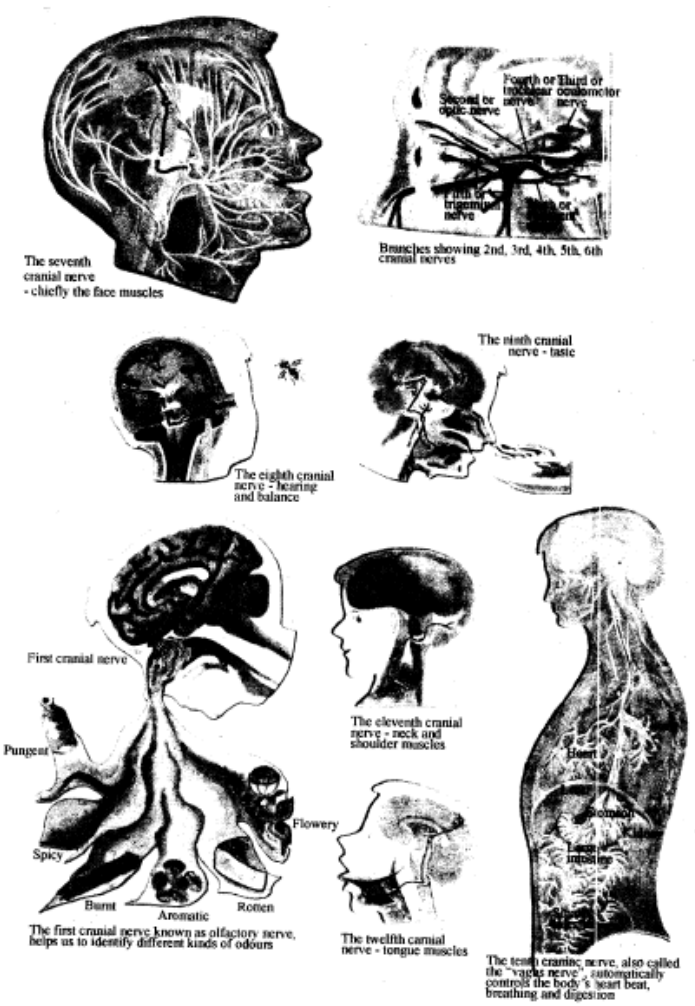



**Figure 9.16: The cranial nerves**

## 9.7.2 Autonomic Nervous System (ANS)

The autonomic or involuntary part of nervous system controls the functions of the body carried out automatically i.e. initiated in the brain below the level of cerebrum. Although stimulation may not occur voluntarily, the individual may be conscious of its effect, e.g. an increase in the heart rate. Some of the physiological activities controlled by the ANS are:

1) Rate and force of heart beat

2) Secretion of the glands of alimentary canal

3) Contractions of involuntary muscle

4) Size of pupil of the eyes

So it must be clear to you by now that the actions of the autonomic nervous system are largely involuntary (in contrast to those of the somatosensory system). The autonomic nervous system consists of sensory neurons and motor neurons that run between the central nervous system (especially the hypothalamus and medulla oblongata) and various internal organs such as the heart, lung, viscera and glands.

It is responsible for monitoring conditions in the internal environment and about appropriate changes in them. The contraction of both smooth muscle and cardiac muscle is controlled by motor neurons of the autonomic system.

We must also emphasize here that the autonomic nervous system also differs from the somatosensory system in using two groups of motor neurons — the preganglionic and postganglionic — to stimulate the effectors instead of one.

Autonomic nervous system is divided into 2 parts — sympathetic and parasympathetic. Sympathetic is a thoracolumbar outflow, parasympathetic craniosacral outflow. What do we mean by thoracolumbar and craniosacral outlfow? Let us get to know about these two systems.

## Sympathetic Nervous System

The sympathetic component of the autonomic nervous system is concerned with in- creasing the level of arousal and energy expenditure — primitive 'fight or flight' behaviour at times of stress.

Alike the parasympathetic nervous system, the central integrating center for sympathetic activity is within the hypothalamus. This may be influenced by higher cortical centre. Efferent fibres descend from the hypothalamus within the intermediolateral columns of the spinal cord. As sympathetic fibres emerge from the central nervous system at spinal segments T1 (thoracic) to L5 (lumbar), the sympathetic system is also known as the thoraco-lumbar outflow.

Here 3 neurons are involved in covering impulses from the hypothalamus and medulla oblongata to effectors organs and tissues.

Neuron — 1: has its cell in the brain and its fibre extends to the spinal cord.

Neuron — 2: has its cell in lateral column of gray matter in the spinal cord.

Neuron — 3: has its cell in a ganglion (small mass of nerve tissue containing the cell bodies of the neuron) and terminates in the organ or tissue supplied.

The preganglionic motor neurons of the sympathetic system arise in the spinal cord (lateral group column). They pass into sympathetic ganglia which are organized into two chains that run parallel to and on either side of the spinal cord.

The neurotransmitter of the preganglionic sympathetic neurons is acetylcholine (ACh). It stimulates action potentials in the postganglionic neurons. The neurotransmitter released by the postganglionic neurons is noradrenaline (also called norepinephrine). The action of noradrenaline on a particular gland or muscle is excitatory in some cases, inhibitory in others.

The main nerves of the parasympathetic system are the tenth cranial nerves, the vagus nerves. They originate in the medulla oblongata. Other preganglionic parasympathetic neurons also extend from the brain, as well as, from the lower tip of the spinal cord.

Two neurons are involved in .the transmission of impulses from their source to the effectors organ. Neuron T1 has its cell either. in the brain or spinal cord.

Neuron—2 has its cell either in a ganglion or in the wall' of the organ supplied. Having read about the sympathetic and parasympathetic system, now can you

explain what are the functions of the ANS? The functions are detailed next.

## What are the functions of ANS?

NOTES

Autonomic nervous system is involved in a complex of reflex activities, which also depend on sensory input and motor output to brain or spinal cord. The reflex actions are contractions of involuntary muscles or glandular secretion. The reflexes are co- ordinate in the brain below the level of consciousness below the cerebral level. The effects of autonomic stimulation on the body systems are summarized next in Table 9.2.

| Sympathetic | Parasympathetic |
|---|---|
| *On Cardiovascular System:* | |
| Increase rate and force of heart beat, causes dilatation of coronary arteries, increases blood supply to heart muscle. | Effects opposite to those of sympathetic stimulation on heart, spleen and blood vessels. |
| Causes dilations of blood vessels in skeletal muscles and thus increases the supply of $O_2$, nutritional materials thereby increasing capacity of muscles to do work. | |
| Causes sustained contraction of spleen, increases the volume of the circulating blood, can increase blood pressure of the skeletal muscles, can cause constriction of blood vessels and reduces flow of digestive juices. | |
| *On Respiratory System:* | |
| Causes dilatation of bronchi allowing greater amount of air to enter the lungs. $O_2$ intake and $CO_2$ output is increased. | Produces constriction of bronchi. |
| *Digestive System:* | |
| Liver converts increased amount of glycogen to glucose. | In stomach and intestine, rate of digestion and absorption of food is increased. |
| Adrenal glands are stimulated to release adrenaline and nor adrenaline. | There is an increase in the secretion of pancreatic juices and insulin release. |
| In stomach, intensive contraction and secretion of digestive juices are inhibited, micturation, defaecation | A urethral and anal sphincter relaxation of the sphincter are accompanied by contraction of muscles, micturation and defaecation occurs. |
| *On Eye:* | |
| Contracts muscle fibres of the iris, dilates the pupil, eyes open widely, alertness and excitement etc are maintained. | Circular muscle fibres contract, constricts the pupil, eyelids tends to close and sleepy appearance is met with. |
| *On Skin:* | |
| Increases sweat, increased heat loss occurs, can cause contraction of muscles in the skin, causes appearance of 'goose flesh'. | No parasympathetic supplies to the skin, hence a specific opposite reaction. |
| Causes constriction of blood vessels, prevents heat loss. Hence sympathetic has dual functions of facilitating heat loss and increases heat production. | |
| *On Genitalia:* | |
| Causes generalized vasoconstriction. | Generalized vasoconstriction. |

**Table 9.2: Effects of autonomic stimulation on the body systems**

Having gone through the effect of autonomic stimulation on the body, you would now know that, sympathetic stimulation has similar effects as produced by adrenaline and noradrenaline. It prepares the body to deal with excitement and stressful situation. It mobilizes the body for 'fight' or 'flight' responses. Parasympathetic stimulation, on the other hand, has a tendency to slow down body process except digestion and absorption of food and functions of genitourinary system. Its general effect is that of a peace maker allowing restoration process to occur quietly and peacefully. Normally the two systems function simultaneously maintaining a compatible environment.

In the discussion above, we looked at the functions of the ANS. The autonomic system also receives afferents that carry information about the internal organs. Let us get a brief insight into this aspect.

Afferent Impulses from Viscera

The sensory fibres from viscera, which travel along with autonomic nervous system, are called autonomic afferents. The impulses they transmit are associated with:

1) Visceral reflexes, usually at the unconscious level.

2) Sensation— hunger, thirst, nausea, sexual sensation, rectal bladder distension etc.

3) Visceral pain.

In visceral pain, the nerves are stretched, large number of fibres are stimulated, ischemia and accumulation of metabolites occurs. In referred pain, sensory fibres from viscus enter the same segment of the spinal cord as somatic nerves, they stimulate somatic nerves, transmits impulses to cerebral cortex, pain is perceived as originating in the area supplied by somatic nerve. For example, afferents from the heart enter the spinal cord at the same level as those from the shoulder region. This is why pain in the heart (a heart attack) is often referred to the shoulder. For other examples, look at the Table 9.3.

| Tissue of origin of pain | Site of referred pain |
|---|---|
| Heart | Shoulder |
| Biliary tract | Right shoulder |
| Kidney, urethra | Loin and grain |
| Uterus | Low back |
| Male genitalia | Low abdomen |
| Prolapsed disc | Leg |

**Table 9.3: Tissue of origin and site of referred pain**

## 9.7 ELECTROENCEPHALOGRAM (EEG)

EEG is short for electroencephalogram. An electroencephalography (EEG) is a painle.ss procedure used to measure the brain's electrical activity.

Oscillations in electrical potential occur almost continuously between any 2 electrodes placed on the surface of head or on cerebral cortex itself, the records are termed as Electroencephalogram (EEG) and Electrocorticogram (ECG) respectively. They persist in altered forms during excitement, drowsiness, sleep, coma, anesthesia, epileptic attacks etc. They serve as a direct and measurable indices of brain activity. The study of brain waves has become an important diagnostic tool in clinical medicine.

The spontaneous electrical activity of the brain was discovered by Caton in 1875. However, it was Hans Berger between 1929-1938 who showed that this could be recorded from the scalp surface of human beings and developed methods for making such recordings.The development of these techniques opened a faithful field of investigation for neurosurgery.

For those of you who are interested to know how EEG is recorded and analyzed, here is a simple description in Box 1.

**Box 1: All you wanted to know about EEG**

**Recording EEG**

To record an EEG, electrodes are placed in the frontal, parietal, temporal and occipital regions. These are called active electrodes. An indifferent electrode may be placed on the -tip of 7th cervical vertebrae, or may be attached to both ears and earthed. An EEG records potential difference between two active electrodes (bi-polar recording) or between an active and indifferent electrode (monopolar recording). EEG leads are named accordingly.

**Physiological basis of EEG**

An EEG samples the summated activity of a very large number of cortical neurons close to the active electrodes. Summation of excitatory and inhibitory, postsynpatic potentials is recorded. The amplitude of. EEG waves depends on how synchronous are the activities of the neurons. Synchronous activity gets summated to give large waves. Asynchronous activities lead to simultaneous deflection in opposite directions, which cancel each other out. A positive deflection may correspond to excitation very close to the surface or to inhibition at a slightly deeper level.

EEG Waveforms: There are normally four waves of EEG These include:

The alpha waves: They are recorded when a person is relaxed with their eyes closed. He is mentally relaxed and not distracted by sensory stimuli. Hence, it is best to record these waves in a quiet room with the subjects eyes closed. These waves have an average amplitude of about 50 micro volts in adults, at a frequency of 8-13/ second. The high amplitude is suggestive of synchronized activity. It is recorded in the best wave forms from parietal and occipital regions. The beta waves: These waves are recorded when a person is awake and alert or he is mentally busy or tense. Alpha is promptly replaced by beta rhythm by asking the person to open the eyes or by exposing the person to a sensory stimulus such as clap, bang or touch.

An EEG rhythm indistinguishable from beta rhythm is also recorded when a

person is in dream sleep. Beta waves have an average amplitude of 20 micro volts and a frequency of 13-30 per second. The brain is presumably highly active when beta waves are recorded, the amplitude is low due to desynchronized activity. It is recorded from frontal and parietal regions.

Theta waves: These can be recorded when a person is in light sleep, emotional stress and in normally awake children. Average amplitude is 10 micro volt and frequency 4-7/second.

Delta waves: These are recorded when a person is in deep sleep. They have an average amplitude of 100 micro volts and a frequency of 0.5-4/second. These waves represent a highly synchronous inherent activity of cortical neurons, when deprived of thalamic inputs.

Variation with age: Upto 2 years, they are in the delta range. The frequency of waves becomes lower during sleep. From 2 — 6 years of age, awake EEG activity is in theta range. Alpha rhythm appears at about 6 years of age. It is a characteristic of the awake inattentive state for the rest of the person's life. Analysis o/ EEG: The analysis of an EEG is known as power spectral analysis. The basic steps are: (l) the computer performs a Fourier analysis on 4 second . segment of the EEG, (2) the bar spectrum thus obtained is smooth, and (3) the graphs from 4 second segments are packed sequentially one upon another. Due to these operations, predominant frequency in EEG appears as a series of tall peaks. The frequency corresponding to the tallest peaks gives EEG rhythm during the recording.

## 9.9 LET US SUM UP

In this unit, we learnt about the neurons — the nerve cells. The nerve cell morphology gives us the structural details of a neuron. A neuron, as you would know, has a cell body, dendrites, nucleus and axon etc. Their main function is the transmission of signals. The nervous system, we learnt, is made up of the central and peripheral nervous system. The brain and the spinal cord form the central nervous system. We studied about the brain, the different organs/parts i.e. cerebellum, medulla, pons etc. and their functions. The spinal cord, we learnt, is a column of nerves that connect our brain with the rest of our body.

The peripheral nervous system, we learnt, is a part of the nervous system which consists of the nerves and neurons that reside outside the central nervous system. We studied the somatosensory and autonomic nervous system within the peripheral nervous system. The peripheral nervous system supplies nerves to all parts of the body. Spinal nerves are 31 pairs, spread throughout the body and reach all parts. There are 12 cranial nerves in our system. While the autonomic nervous system functions through sympathetic and parasympathetic fibers. They are antagonistic to each other and they can co-ordinate and control human systems.

Finally, we got to know about EEG which helps us to measure the firing and activity patterns of the brain during various physiological conditions.

## 9.10 GLOSSARY

**Autonomic afferents** : the sensory fibers from viscera which travel along with the autonomic nervous system.

**Electroencephalogram** : a record of electrical activity of the brain measured by electrodes placed on the surface of head or on cerebral cortex.

**Ganglia** : group of nerve cells which act as relay stations.

**Gyri** : folds of cerebral cortex.

**Manual dexterity** : cells of the pre-motor area having a controlling influence over motor area, ensuring a series to movements.

**Neurobiology** : a study of biological functions of nerves.

**Neuron** : nerve cell.

**Postsynaptic neuron** : neuron which receives message.

**Post Tetanic facilitation** : a higher frequency in the response of a fiber caused due to repeated stimulation of fiber.

**Presynaptic neuron** : neuron which sends a message.

**Receptors** : organs having specific sensory cells which enable them to receive a change in environment.

**Reflex action** : an immediate stereotyped involuntary motor response to a sensory stimulus.

**Sulci** : fissures separating the folds of cerebral cortex.

**Synapse** : the junction between two neurons or a neuron and muscle.

**Synaptic fatigue** : the reduction in the postsynaptic gradual response on repeated stimulation.

**Synaptic transmission** : process of communication between two neurons across a synapse.

**Synergy** : smoothness and coordination of various movement.

**Threshold** : the minimum magnitude by which a depolarized fiber triggers for an action potential.

**Vermis** : a narrow central 'C' shaped strip separating the 2 hemispheres of cerebellum.

## 9.10 CHECK YOUR PROGRESS EXERCISES

NOTES

UNIT

# 10

# SPECIAL SENSES

**STRUCTURE**



## 10.1 LEARNING OBJECTIVE

After going through this unit, you will be able to:

- describe the structure of eye and mechanism of vision,
- discuss the physiology and mechanism of taste perception,
- enumerate the factors affecting and inhibiting taste perception,
- explain how sound is transmitted and perceived, and discuss the mechanism of sense of smell.

Let us begin our discussion with the vision as a special sense, which helps us to see and perceive the world around us.

## 10.2 INTRODUCTION

We live in an information age. We are flooded with information, a lot of which is not relevant to our needs. There are a few organs in the body, which collect information of special significance to us from the external environment and are therefore called the 'organs of special senses'. Special senses include vision, hearing, taste and smell. The range of these sense organs is limited. For example, the eyes are sensitive to only a limited range of spectrum — the rainbow (VIBGYOR) and hearing to frequencies 20 Hz - 20 KHz and that too only if the intensity of the

sound is above a certain threshold. Thus the information perceived by our sense organs is only a fraction of what reality is.

Special senses include the senses for vision, hearing, smell and taste. Organs for special senses are the eyes, ears, nose and tongue. In this unit, we shall focus on the physiology and the mechanism of functioning of these organs.

NOTES

## 10.3 VISION

The eyes are the sense organs for vision. They contain receptors that are called photoreceptors e.g. cones and rods. These cells are responsible for converting the specific light energy into action potentials of nerve fibers. Thus, these act as solar cells converting light into electrical energy. The sun gives us light, the eye perceives this light and the brain interprets it. Let us now study the structure of the eye.

### 10.3.1 Structure of the Eye

The eyes are located in bony orbital cavities and are cushioned in a fatty connective tissue. The wall of each eyeball is made of three coverings. See Figure 10.1 and try to locate these. The first covering is the tough protective coat that is fibro-elastic in nature is the sclera (white of the eye). This layer is opaque and does not allow the light to pass through. It forms the posterior five-sixths of the eyeball. The thin transparent layer called cornea forms the anterior one-sixth of the outer layer of the eyeball. The middle layer, consists of the vascular choroid which forms ciliary body and iris anteriorly. The iris has a small adjustable circular gap in the front called pupil. The third, innermost layer is light-sensitive retina. Its central portion is maculalutea.

**Figure 10.1: The structure of the eye**

The eyeball is like a ball that has reins of muscles attached to it. These help move the eyes in all directions — up, below, left, right, clockwise and anticlockwise. These are supplied by the cranial nerves. That may be remembered by the chemical formulae of an imaginary compound LR6S04 REST3: Lateral Rectus: nerve,

Superior Oblique: 4d1 nerve and the 3rd nerve supply the rest of the muscles. The sclera provides a surface for attachment of these muscle strings. What will happen if these muscles become weak? In case of paralysis or weakness of these muscle strings, the condition which results is of squint. What is this condition and how does it occurs? The muscle of one eye pulls in one direction and that of the other in a different direction and this result in the squint. The person would see two instead of one object for example, two moons instead of one! This condition is termed as diplopia, meaning di or double vision.

The cornea acts as a convex lens, bending light reflected from the object. This helps in focusing an object on the 'innermost sensitive curtain of the eye called the retina. The retina is made up of cells and nerve fibers. See Figure 10.2 for the microscopic structure of retina.

**Figure 10.2: Structure of retina**

The retina nerve cells are the rods and cones as highlighted in Figure 10.2. The cones are not as sensitive to light as the rods. However, cones are most sensitive to one of three different colours — green, red or blue. Signals from the cones are sent to the brain which then translates these messages into the perception of colour. Cones, however, work only in bright light. That's why you cannot see colour very well in dark places. So, the cones are used for colour vision and are better suited for detecting fine details. There are about 3-6 million cones' in the human retina. Some people cannot tell some colours from others — these people are colour blind. Someone who is colour blind does not have a particular type of cone in the retina or one type of cone may be weak. We shall learn about colour blindness in a little while from now. The properties of rods and cones are highlighted in Table 10.1.

The rods are most sensitive to light and dark changes, shape and movement and contain only one type of light-sensitive pigment. Rods, therefore, are not good for colour vision. In a dim room, however, we use mainly our rods, but we are "colour blind." Rods are more numerous than cones in the periphery of the retina. Next time you want to see a dim star at night, try to look at it with your peripheral vision and use your rod vision to see the dim star. There are about 100 million rods in the human retina.

The cones are not as sensitive to light as the rods. However, cones are most sensitive to one of three different colours - green, red or blue. Signals from the cones are sent to the brain which then translates these messages into the perception of colour, Cones, however, work only in bright light. That's why you cannot see colour very well in dark places. So, the cones are used for colour vision and are better suited for detecting fine details. There are about 3-6 million cones' in the human retina. Some people cannot tell some colours from others -these people are colour blind. Someone who is colour blind does not have a particular type of cone in the retina or one type of cone may be weak. We shall learn about colour blindness in a little while from now. The properties of rods and cones are highlighted in Table 10.1.

| Rods | Cones |
|---|---|
| 100 million/retina | 3 million/retina |
| Vision in shades of grey | Colour vision |
| High sensitivity | Low sensitivity |
| Low activity | High activity |
| Night vision (Scotopic) | Day vision (Photopic) |
| More numerous in periphery | Concentrated in fovea |

**Table 10.1: Properties of Rods and Cones**

Rods have a pigrnent that is sensitive in even dim light. This pigment is purple coloured and is called rhodopsin. This pigment is formed by a series of reversible reactions as indicated in photochemical reactions shown in Figure 10.3.

**Figure 10.3: Photochemical reactions in light and dark**

Many nocturnal animals like the owls have only rods. This enables them to see even in the dark. A deficiency causes night blindness in man because rods cannot function if rhodopsin is not synthesized from vitamin A. The person cannot see in dim light and bumps into things in dim light. Vitamin A helps to restore the sight.

The blind spot (refer to Figure 10.1) is an area where there are no cones and rods. This area is devoid of the ability of vision. The blind spot marks the point of convergence of neurons that form the optic nerve.

Lateral to the blind spot, there is a depressed area of retina called fovea, which contains only cones and no rods. Ability for vision is highest in the fovea and the light falls directly on retina here. This may be responsible for love at first sight! Since the light is converted and transmitted at a faster rate here than other areas of the retina. The other peculiarity of the fovea is that it is backed by only four neurons with one to one representation from the cones. These are the bipolar cells, the amacrine cells, the horizontal cells and the ganglion cells, and the neuronal cells of the retina as shown in Figure 10.4. These neurons are responsible for appreciating the shape, contrast, directional orientation of light and Colour properties of the vision. The details on these topics are out of the scope of this unit, hence we shall not take this up any further.

**Figure 10.4: Retinal cells**

We shall move to the middle layer of the eye now. The middle layer consist; of the choroid, the ciliary body and the iris. The vascular structure the choroid is pigmented and separates two layers of the eye. Could you guess by seeing the diagram in Figure 10.1 what the two layers are? Yes, these are the outermost sclera and the innermost cornea.

The choroid is connected in front to a thick muscular structure — the ciliary body.

The muscles are smooth involuntary muscles and are called as the ciliary muscles. These suspend thread-like ligaments that attach to the edges of the lens. The lens is a transparent structure and has elongated cells. It is an elastic structure that can be bent like the contact lens in your fingers. This helps in accommodating near objects for example, during reading or inserting a thread in a needle. Have you ever seen some people have beautiful green eyes or blue eyes or even jet- black or

light brown? Ever wondered what gives this wonderful tinge to make each of us different? The answer lies in the genes that we inherit from our parents and which code for this wonderful pigment that gives us the colour. The coloured diaphragm in Figure 10.5 is the iris.

**Figure 10.5: The iris**

Take a torch and shine it in a dark room in the mirror. Observe the eye dilating and constricting. This is because of the sphincter and dilator papillae located in the iris, as shown in Figure 10.6. These radial and circular iris muscles allow the light to pass through the pupil to the lens. In Figures 10.5 and 10.6, you would notice a central black hole. This is called as the pupil of the eye. The lens then focuses the light to form a sharp image on the retina.

**Figure 10.6: Muscle of iris**

The cavity inside the eyeball is divided by the lens, ciliary body and suspensory ligaments into an anterior compartment and a posterior compartment. The anterior compartment is filled with a fluid called aqueous humor. Close your eyes. Remove

Special Senses your spectacles, if wearing. On the left eyeball, press the eyeball with your right index finger. Do you feel the eyeball displace? This may be better appreciated by feeling the eyeball with the left index finger. This displacement is of the aqueous humor. The aqueous humor is the fluid, which is responsible for providing nutrition to the lens and comea and by its pressure, it maintains shape of the eyeball and supports the lens. The posterior compartment is filled with a transparent gelatinous material called vitreous body that supports the lens and the retina

Glaucoma is a condition in which the eyeball bulges due to an increase in intraocular tension either due to an excessive production of aqueous humor because it cannot be drained through a narrow opening called the Canal of Schlemm. This fluid exerts a tension in the eyeball as does water when filled in a water balloon. The normal intraocular tension is 12 to 20 mm Hg. The intraocular pressure (IOP) is considered to be high if it is above 20 mm Hg (2.66 kPa) on repeated measurements. In an attack of acute glaucoma, it can exceed 60 mm Hg (8 kPa).

We have just read about the IOP. Have you wondered what makes us appreciate colour? Cones contain a violet-coloured photosensitive pigment called iodopsin. Sparrows that are active only during the daytime have only cones and are not active at night. Let us get to know about the mechanism of colour perception, next.

### 10.2.2 Mechanism of Colour Perception

How do we perceive colour? Let us, in this section try to understand the mechanism of colour perception and the factors that influence it. We start with the pre-requisites of colour perception.

### Pre-requisites of Colour Perception

To be able to perceive colour, there must be a light source, an object and of course, the organ of perception. The brain, which plays an important role, in colour perception, cannot be forgotten. Let us look at each of these pre-requisites.

l) **Light source:** No colour may be detected by the eyes or by an instrument in the dark i.e. in the absence of a light source emitting radiant energy in the visible range of the spectrum. Wrong results will be obtained if the light source is not emitting sufficient radiant energy at the critical wavelength. To avoid this, three standard illuminants i.e. light sources have been established by the International Commission of Illumination. These are:

- Illuminant A i.e. incandescent lamp (28440K)
- Illuminant B i.e. noon sunlight (40000K)
- Illuminant C i.e. cloudy daylight (68000K)

### 2) Object:

- **Metameric pair** — shows different colours at different wavelengths.

- **Non-Metameric pair** — shows same colour at all wavelengths

**3) Organ of perception:** These are the receptors. Receptors, as you may already know, are the rods and cones cells present in the retina of eyes. They are able fo receive the light and transmit the signal to the brain via .the nerve fibres.

**4) Brain or detector:** The fibre identification of colour takes place in the brain.

if any of these'four pre-requisites are not present, the perception will not take place. In case of colour perception, the reaction time is very fast. The perception is the resült of the interaction. of. light source, object, receiver and detector. The receiver is eye and the detector is brain. When light falls on an object, there is an imbalance of radiant energy and a number of phenomena may occur due to this imbalance, which include reflection, absorption and transmission. The colour perceived is dependent on the reflected light. Reflected ray is received by the retina of the eye, which gets stimulated, the impulse is transferred to the nerve fibres via optic nerve and finally, it goes to the brain. There are special centers in the brain where colour is identified.

To conclude, colour is the stimulus that results from the detection of light, after it has interacted with an object. Three factors are involved: a light source, an object and a receiver-detector. The light may be reflected, transmitted, absorbed or refracted by an illuminated object

Next, let us study the factors which influence colour perception.

Factors affecting colour perception

The two most important factors which influence colour perception include:

- Temperature, and
- Humidity

How do these factors influence colour perception? Both these factors affect the dullness or brightness of the colour. Colour appears to be brighter at a higher temperature, as the glossiness is increased at higher temperatures. Under humid conditions, reflected rays are more diffused so the object appears dull in colour. Earlier, we learnt that the cones are not as sensitive to light as the rods, but are most sensitive to one of three different colours — green, red or blue. So, the cones are used for colour vision. Some people cannot tell some colours from others — these people are "colour blind." Let us now try to understand what is meant by the term colour blindness and what its types are.

- **Colour Blindness:** Normal individuals possess three cone pigments viz. red, green and blue which are referred to as tri-chromates. Colour blindness refers to the partial i.e. reduced levels or complete absence of one or more of the cone pigments. Colour blindness can be classified into:
- **Dichromates or mild colour blindness:** A dichromate individual possesses only two cone pigments. Lack of the red pigment, called protanopia, makes distinguishing of the red and green colours impossible and the visual system is insensitive to deep red colours. Similarly, the lack of the green pigment, called deuteranopia also makes the differentiation of red and green colours impossible but the visual system is nevertheless sensitive to light in the range

normally served by green pigment because responsiveness of red and blue pigments overlaps into this range. Dalton was red green blind. Just imagine him driving a car at a traffic light signal! Lack of the blue pigment, called tritanopes makes the discrimination of blue and green colours impossible.

- **Monochromates or total colour blindness:** The monochromate individuals lack all cone pigments and cannot distinguish colours at all. They find bright light very unpleasant. They perforce have to use the scotopic system for seeing both in bright and dim light.

Colour blindness is Often assessed using Ishihara 's charts. If ever you visited an eye specialist, you too must have seen this chart. In this, the numbers are inscribed amongst different dotted coloured background. The degree of dotted coloured background is enhanced progressively thereby making it more and more difficult to discern numbers. Trichromates i.e. normal individuals can distinguish these numbers easily, while colour blind individuals cannot see or they recognize a wrong number

The next section focuses on the process of vision and disorders related to proper Special Senses image. But before we move to the section, tet us recaptitulate what we have learnt so far.

### 10.3.3 Optics of Vision

The overview of the vision process is presented first, in this section, followed by the vision process in the normal, disordered and corrected eye. For proper vision, light rays from a Visual object must be focused on the retina. In the resting state, the ciliary muscles remain relaxed, keeping the suspensory ligaments stoutly stretched. The stretch by the suspensory ligaments flattens the elastic lens to reduce its curvature. The lens in the resting state focuses parallel rays from distant objects, like the tree in the far end of the park, on the retina.

For viewing near objects, the lens curvature changes to accommodate the light rays on the retina. Figure 10.7 illustrates the relaxed and accommodated position of the lens. The 3rd nerve is activated from the cortex during reading to cause contraction of the suspensory ligaments and this reduces the stretching action of the lens.

The lens consequently increases its curvature due to its elasticity and its power is enhanced. It can now focus the divergent rays on the retina. This reflex is called as the accomodation reflex. The accommodation reflex is described as the constriction of the pupil as the eye fixates on near objects.

**Figure 10.7: Accomodation reflex**

NOTES

Having understood the vision process,, let us move on to study the disorders of the eye, and how it affects the vision process

An eye whose far and near points are normal is called emmetropic eye. However, it is a common knowledge that eyes cannot see objects at infinity or as near as 10 cm. Accordingly, three common errors have been defined — myopia, hypermetropia and presbyopia. Figure 10.8 explains the image formation in a normal eye, disordered eye and the corrected eye.

Disorders of image formation and its correction can be discussed as follows:

- **Myopia:** The lens and cornea of a normal eye will focus a distant object on the retina. However, in some individuals, the eyeball is too long or too short, relative to the power of the lens and cornea. If the eyeball is too long or the cornea and lens are too powerful, it causes the focal point to be too near to the lens. The image is formed in front of retina as you can see in the Figure 10.8b. This is called myopia or short-sightedness. In myopic condition, the individual cannot see the far objects distinctly. It is corrected by placing a divergent or concave lens in front of the myopic eye as illustrated in Figure 10.8d

**Figure 10.8: Disorders of image formation**

- **Hypermetropia:** On the other hand, if the cornea and lens are too weak or the eyeball is too short, it is called hypermetropia or far-sightedness. Have a look at the Figure 10.8c. In such condition, the image is formed behind the retina. It is corrected by placing a convex (convergent) lens in front of the hypermetropic eye as illustrated in Figure 10.8e
- **Presbyopia:** In older individuals, the lenses on the eyes loose some of the elasticity. Consequently, it becomes difficult to focus on the near objects. This condition is called presbyopia or restriction of accommodation.

- **The lens during aging:** The most apparent change that occurs as a consequence of aging is that the yellow tint or gloss of the lens gets intensified. In addition, as the years pass by, the lens becomes gradually more rigid, rendering it progressively harder for the ciliary muscles to change its shape i.e. to make it more spherical, as during accommodation. A person's ability to focus on close images deteriorates along With it. A young child can focus on the objects held within a distance of an inch from the eyeball, a young adult can only do that if the objects are placed at about S inches from the eyeball. By the time one reaches the age of 40 years, the lens has become stiffer and not able to focus objects placed nearby or two or three feet away. By the age of 40 years, the lens becomes as rigid, that it is almost impossible to adjust it very much either to distant or close objects. This condition is known as presbyopia. That is why bifocal or sometimes trifocal glasses are prescribed. Such lenses are designed to concede the inflexibility of the lens and to provide two or three other zones of 293 Applied Physiology focus artificially. The top of the bifocal length is usually slightly convex to concentrate on the things that are some distance away, while the semicircle along the bottom of the glasses is concave to permit focusing on the objects nearby.

The lens also looses its water with age. This results in an opaque lens called cataract. Modern treatment is replacing the lens with an artificial intraocular lens (IOL). With our discussion above, we end our study on the ONCS of vision. Next, what happens beyond the eye? How our eye focuses on a particular object and its image is perceived by us? Let's find out.

### 10.3.4 Beyond the Eye

Just now we have seen how our eye focuses on a particular object and its image is perceived by us. But how does this actually happeris? Well, the answer to this lie' in the 'columnar organization of the primary visual cortex', the details of which are shown in the Figure 10.9. See in Figure 10.9 how optic nerve transmits the signal to the visual cortex by means of optic tract and radiation.

**Figure 10.9: Principal visual pathway**

Vision is generated by photoreceptors in the retina, a layer of cells at the back of the eye. The information leaves the eye by the way of optic nerve, and there is a partial crossing of axons at the optic chiasma as can be seen in Figure 10.9. After the chiasma, the axons are called the optic tract. The optic tract wraps around the midbrain to get to the lateral geniculate nucleus (LGN), where all the axons must synapse. From there, the LGN axons fan out through the deep white matter of the brain as the optic radiations, which will ultimately travel to primary visual cortex in the occipital lobe at the back of the brain

Let us now understand what is this 'visual cortex' and its constituent cells, which have a major role to play in the mechanism of vision. This information is supplementary. Do not get bogged down by the details. It is only for your information.

The visual cortex consists of macro-columns, each macro-column measuring about 1 mm2 of the cortical surface. Cells in the various layers of a macro-column have receptive fields within the area of the visual fields. Macro-columns consist of 'orientation micro-columns', each of which contains simple, complex and hyper-complex cells. They all respond maximally to a single orientation. Each macro-column has a band of 'micro-columns', dominated by inputs from the left eye and a band dominated by inputs from the right eye. Each cortical macro-column seems to contain all of the circuitry needed to analyze the small portion of visual world. Details of Special Senses various cells playing their role in the primary visual cortex are as follows:

- **Simple cells:** They are most sensitive to lines oriented in a particular angle to the vertical. Simple cells probably receive a convergence of inputs from lateral geniculate cells whose receptive fields partly overlap.
- **Complex cells:** They are sensitive to both orientation and movement. For example, a line or edge with a particular tilt might stimulate a complex cell only if it was also moving in the right direction
- **Hyper complex cells:** They require not only the line or edge to be moving but it should also possess a certain length with a corner

With our discussion on visual cortex and its constituent cells, we come to an end of our study on how our eyes perceives an object.

## 10.4 HEARING

The ears, as we all know, are sense organs for hearing. The ear consists of an external ear, a middle ear and an internal ear. It houses receptors for both hearing and body equilibrium. The air conducts sound to the ear, which perceives it and the brain understands it. Let us get to know the physiology of the ear and the mechanism involved in the hearing process. But, first, we shall acquaint ourselves to the nature of sound.

## 10.4.1 The Nature of Sound

This section is a recapitulation of what you have learnt in school. You would recall that sound waves consist of the longitudinal waves of alternate compression and rarefaction. Areas of compression have a higher pressure and density of air molecules than the area of rarefaction. The waveform propagates itself for long distance because of the influence, which the areas of compression or rarefaction have on the neighbouring areas

Thus, it is only the waveform that is transmitted and not the air molecules. The velocity of sound depends on the medium through which it is transmitted. In air, the velocity is about 340 m/sec. The loudness of a sound is related to the amplitude of pressure waves and the pitch to their frequency: Let us understand what we mean by the term 'amplitude'

In simpler terms, amplitude is the amount or relative value of a signal. Amplitude is measured in units of pressure e.g. Newtons/sq. m. But what is physiologically more relevant is power, i.e. (amplitude) 2. The faintest whisper that the ear can hear is much weaker than the loudest sounds that the ear can tolerate without getting damaged. Therefore, if the entire range of intensity of audible sound were to be expressed directly, We would be dealing with very inconvenient figures. Hence, we use a logarithmic Scale to measure the intensity of sound. A logarithmic scale, as you know, is a highly condensed scale. The logarithm of I is 0, and log 1012 is 12, therefore the range from 1-1012 gets condensed to 0-12 on the logarithmic scale. Bel, the unit of measurement of sound, is named after Alexander Graham Bell. Bell was the inventor of the telephone, but for some curious reason, is spelt with a single 'l'. Bel is too large a unit. Hence a unit, one — tenth as high, called 'decibel' (dB) is more commonly used. Thus the range of human hearing extends from 0-120 dB. Besides intensity, the other important characteristic of sound is frequency, which is the major determinant of pitch. Pitch is expressed in cycles per sec or Hertz (Hz), named after an eminent German physicist of nineteenth century

What is the range of frequency of sound which we can hear comfortably? Well, the range is really long. The human ear can detect sounds between 20 and 20,000 Hz (20 kHz). But most of the common sounds fall between only 200 and 4,500 Hz. Frequencies above 16 KHz are called 'ultrasound' and those lower than 20 Hz 'infrasound'. The audible range of man thus extends from 20 Hz to 16 KHz and from 4 to 130 phon (dB). This is the audible area or range. In the middle of this are the frequencies and intensities produced in speaking. This area or range in which the speech falls, is called as the speech area (250 Hz to 4 KHz; 40 to 75 db). For speech to be adequately understandable, transmission systems (e.g. telephone) must transmit frequencies at least in the range 300 Hz - 3.5 KHz. In older people, sensitivity to high frequencies regularly declines, a phenomenon known as presbycusis

Let us now have a look at Table 10.2, where the various sources of sound, their level of loudness and its comparison to the faintest audible sound are given.

| S. No. | Sound source | Loudness (db) | Comparison to faintest audible sound (Threshold) |
|---|---|---|---|
| 1. | Rustle of leaves | 10 | 10 times more |
| 2. | Ticking of watch | 20 | 10 times more |
| 3. | Normal conversation | 60 | 1 million more |
| 4. | Shouting | 80 | 1 billion more |
| 4. | Loud rock concert | 120 | 1 billion |
| 6. | Take off Jet plane | 140 | 1 quadrillion |

**Table 10.2: Sources of sound and their level of loudness**

Having understood the nature of sound, let us get to know the structure which Special Senses enables us to hear these sounds i.e. our ears.

## 10.4.2 The Ear — The Organ of Hearing

The human ear consists of three sections: the outer ear, the middle ear, and the inner ear as illustrated in Figure 10.10. The outer ear includes the auricle (pinna), the visible part of the ear that is attached to the side of the head, and the waxy, dirt- trapping auditory canal. The tympanic membrane (eardrum) separates the external ear from the middle ear, an air-filled cavity.

The part of the ear, which we can see, is only a small and rather unimportant part of the ear, and is called the external ear or the pinna. The visible part, or the pinna, is a small appendage on our face, as can be seen in Figure 10.10. It is commonly thought to collect the sound waves and funnel them.

**Figure 10.10: The external, internal and middle ear**

But at least in human beings where the pinna is rather small, it is unlikely that this function is significant. Experiments have been conducted in which the various depressions of the external ear have been filled with a plasticine-like material to obliterate them. It has been found that doing so, makes no difference to the efficiency of hearing. Even in animals with large pinnae, a far more important

function of these structures is to help in the localization of sound. By moving the ears, such experiments can accentuate the difference in the intensity of the sound reaching the two ears, and thereby localize sound more accurately. Since human beings cannot move their ears, they cannot use the pinnae very efficiently for this purpose. For accentuating the difference in the intensity of sound reaching the two ears, they turn the whole head instead of turning just the ears. The direction from which a sound is coming is judged from the difference in the time at which the sound arrives at the two ears, and the difference in the intensity of the sound at the two ears.

The other part of the outer ear is the ear canal. The ear canal, which conveys the sound to the eardrum, is a rather tortuous canal. It is lined with skin, which secretes wax from ceruminous glands and oil from the sebaceous glands. The wax and oils help in keeping the ear canal clear by trapping cellular debris and dust particles. The ear canal is about 2.3 cm long in an adult, and is open at one end but closed at the other end.

Next let us explore the middle part of the ear.

The air-filled middle ear — a box-like structure — contains the tympanic membrane, the ossicles (malleus, incus, and stapes), their associated muscles and ligaments, and the opening of the auditory tube, which provides communication with the pharynx and equalizes pressure on both sides.

We have seen in Figure 10.10 that middle ear consists of three small bones or ossicles namely, the malleus, the incus, and the stapes. Let's get to know these and their functions. These bones mechanically relay vibrations from the tympanic membrane to the 3 mm2 membrane of the oval window. These bones also form a lever system, which produces a mechanical advantage and thus amplifies sounds by about a factor of two

There are certain factors which contribute to an approximately eighty-fold increase in sound wave pressure through middle ear. These are: Tympanic resonance (the tendency of the membrane to vibrate best over a particular range of frequencies Ossicle mechanical advantage, which amplifies sound twice.

Concentration of sound at small oval window. The difference in area between the tympanic membrane and the smaller oval window concentrates the sound energy by a factor of about 20

These factors constitute an impedence matching system that increases the wave pressure so that it is effectively transmitted from the low resistance medium of air into the higher resistance medium of the fluid in the inner ear.

One of the major functions of the middle ear is to protect the ear from loud sounds. Let us see how this is done.

## Protection from Loud Sounds

Sometimes, it might happen that we are accidentally or deliberately exposed to loud sounds. In such cases, how is our ear protected against the loud sounds? Well, the two muscles, the tensor tympani and stapedius, attached to the stapes, control the effectiveness of sound transmission through the ossicles. Loud sounds

initiate a reflex that activates these muscles, stiffening the chain of ossicles and decreasing sound transmission. Besides impedance matching, the middle ear also has some other functions. The tensor tympani and stapedius muscles possibly play a role in protecting the ear from the damaging effects of very loud sounds, and in protecting our mind from disturbing effects of our own voice. Stimulation of the ear by intense sounds produces contraction of the stapedius and tensor tympani muscles, this is known as the 'acoustic reflex's Stapedius pulls the stapes medially while the tensor tympani pull the malleus Special Senses anteriomedially. The overall effect of the actions of these muscles is to press the ossicles against one another, thereby increasing the rigidity of the ossicular lever system. This is the system which is more stable while at the same time, it reduces the efficiency with which the sound signal would be transmitted to the inner ear. In human beings, acoustic reflex is absent in diseases affecting the stapedius muscle but not when disease afflicts the tensor tympani.

This suggests that only contraction of the stapedius is of functional importance in the human acoustic reflex. The protective effect of the acoustic reflex is itself doubtful. The reflex is too slow to be useful in protecting the ear from damage due to loud sounds. Further, the ear is rarely exposed to sounds enough to evoke the reflex.

A more likely benefit of the reflexes is attenuation of internal sounds, and most of the internal sounds have low frequencies. Attenuation of internal sounds would reduce their masking effect, thereby improving the sensibility of the ear to external sounds, which needs to be heard.

Having learnt about the functions of the middle ear, we move on to the eustachian tube.

Look at Figure 10.10. Can you locate the eustachian tube in the ear? Eustachian tube joins the middle ear to the nasopharynx. It is about 4 cm long. Its diameter is three times larger at its middle ear opening than at its nasopharyngeal opening. In fact, the nasopharyngeal end of the tube is normally closed and opens only during swallowing, yawning, sneezing or shouting. The opening up of the tube, particularly during swallowing serves to keep the middle ear pressure equal to the pressure in the nasopharynx, which in turn, is equal to the atmospheric pressure.

The pressure in the external ear is also quite obviously equal to the atmospheric pressure. Thus, the eustachian tube keeps the pressure on the two sides of the tympanic membrane equal. This is important to prevent the tympanic membrane from bulging on either side. Bulging would impair its function, and bulging beyond a certain limit could damage the tympanic membrane.

Another function of the eustachian tube is to prevefit any fluid from collecting in the middle ear. It drains the fluid into the nasopharynx. If this drainage mechanism was absent, any fluid collecting as a result of inflammation or extravasations would tear through the tympanic membrane.

Every coin has two sides. The eustachian tube is not an unmixed blessing. In an upper respiratory infection, it may convey the infection from the nasopharynx

to the middle ear. While conveying the infection, the tube itself also gets inflamed.

Just now we saw how our ears are protected and which internal parts help us to do so. Let us now move on to the understanding of the structure and functions of the internal ear.

## 10.4.3 Structure and Function of the Internal Ear

We shall start with understanding the structure of the inner ear.

The inner ear, a labyrinth, consists of two parts — one concerned with equilibrium is referred to as the vestibule, and the one concerned with hearing is termed as the cochlea as can be seen in Figure 10.10. The cross section of the cochlea is shown here in Figure 10.11.

**Figure 10.11: The cochlea and the vestibular labyrinth**

Cochlea is the snail shaped structure you see in the inner ear which is the sensory organ of hearing. The cochlea, a coiled structure enclosing three fluid-filled chambers, is encased in the temporal bone with two membranous surfaces expösed at its base: the ovol window and the round window as can be seen in Figure 10.11. The foot plate of the stapes, the third middle ear bone, adheres to the oval window, transmitting sound vibrations into the cochlea.

The vestibular labyrinth comprises of the saccule and utricle (refer to Figure 10.11), the sense organs of balance which inform our brain about our linear position in space. They are stimulated by pull of gravity. The internal ear is made up of a bony labyrinth and membranous labyrinth. The bony labyrinth has three pairs of semicircular canals. The horizontal, anterior and posterior semicircular canals are also part of our vestibular labyrinth, and inform our brain about rotational movement in space i.e. angular acceleration and deceleration of rotational movements.

## What are the functions of the inner ear?

The inner ear plays an important function in the detection of sound.

In the last section, we left middle ear function at the point where the sound

stimulus results in movement of the stapes. The footplate of the stapes is adjacent to the oval window of the inner ear as you learnt above. The stapes footplate moves in and out like a piston in response to sound stimuli. Since the footplate is adjacent to the oval window of the inner -ear, its 'movements produce pressure variations in cochlear fluids. These variations result in movement of the basilar membrane (BM) found in the inner ear. Movements of the BM result in movements of hair cells. Hair cell movement displaces their steriocillia, which in turn, enhances or depresses hair cell excitability. Afferent nerve fibers to the centre nervous system convey altered excitability of hair cells. In short, the inner ear transducts vibratory stimulus to electrical signals to be transmitted to the central nervous system.

But the inner ear is more than a transducer. It also performs a preliminary analysis of the sound stimulus in terms of its frequency and amplitude characteristics. The BM plays an important role in this analysis.

With over a million essential moving parts, the auditory receptor organ or cochlea is the most complex mechanical apparatus in the human body. Surely you would agree, having looked at the Structure and the physiological role of this organ now. Next, let us see what happens beyond the ear. How does the central nervous system sense the sound?

### 10.4.4 Beyond the Ear

The ear is a wonderful and compact organ, which can receive, transduct and analyze an acoustic stimulus. But unless the electrical impulses that it generates in the auditory nerve are conducted to the central nervous' system,'it-would be impossible to hear 300 anything. Listening needs involvement of even high faculties of the central nervous system in auditory function, which is generally studied in terms of auditory pathway Special Senses from the cochlea to the cortex. Let us learn about this pathway.

There exists a fairly distinct chain of neurons from the hair cells of the cochlea to the cerebral cortex. The path taken by this chain is the ascending auditory pathway. The fact that the path exists, does not, however mean that the whole of it is actually used every time we receive a sound stimulus. The stimulus may merely evoke a reflex response involving only the brainstem.

There exists also a descending pathway through which the central nervous system can influence ear function. An ascending auditory pathway is represented in the Figure 10.12.

**Figure 10.12: Ascending auditory pathways**

You would realize that the auditory nerve fibers innervating the hair cells have their cell bodies located in the spinal ganglion. The axons of the neurons relay in the dorsal and ventral cochlear nuclei of the medulla oblongata. The fibers originating in the ventral cochlear nucleus project to the Olivary complexes. The Olivary complexes also project to the nuclei of the lateral lemniscus. From the nuclei of the lateral lemniscus, the auditory tract relays to the inferior colliculus, medial geniculate body of the thalamus and finally the auditory cortex. The primary auditory cortex is located in Brodmann's areas 41 and 42 in the superior temporal gyrus. Surrounding the primary auditory cortex are the auditory association areas, which receive inputs from the primary auditory cortex, as well as, the thalamus.

Information from either ear is projected to the auditory cortex on both sides but the projection is heavier on the contra lateral side. The main auditory pathway described above gives collaterals along its route by which it interacts with the pathways conveying other sensory inputs to the brain.

Let us now deal with the defects of hearing in the following section.

## 10.4.5 Applied Auditory Physiology

Many common disorders of hearing, their evaluation and treatment can be understood better in light of auditory physiology. These topics will receive only sketchy treatment here. Let us start by getting to know about the hearing defects.

Types of Hearing Defects: From a physiological point of view, impairment of hearing, or deafness, is of two types — conduction and sensorineural. See Figure 10.13. Let us discuss about them briefly and try to understand what is meant by these.

**Figure 10.13: Deafness**

### 1) Conduction deafness

In conduction deafness, sound cannot be conducted to the cochlear receptors (hair cells) efficiently. Although it could be due to a defect either in the external or the middle ear, conduction deafness is commonly understood to mean only middle

ear deafness. Common causes of conduction deafness are wax in the ear canal, perforation of the tympanic membrane, inflammatory disease of the middle ear (otitis media), or immobility of ossicles (otosclerosis).

NOTES

## 2) Sensorineural deafness or Nerve deafness

The auditory nerve pathways may get destroyed with age or with disease. As you can see in Figure 10.13, the defect lies in the inner ear.

These defects can be detected by conducting tests namely, Weber's test, Rinne's test and Schwabach's test. These are illustrated in the Figures 10.14, 10.15 and 10.16 respectively.

In Weber's test, the stem of a vibrating tuning fork is placed on the midline of the head, and the patient indicates in which ear the tone is heard louder. A patient with a unilateral conductive hearing loss (deafness) hears the tone louder in the ear with the conductive hearing loss. In contrast, a patient with a unilateral sensor neural hearing loss hears the tone Right ear Left ear louder in the normal ear because the tuning fork stimulates both inner ears equally and the patient perceives the stimulus with or longer the more sensitive, unaffected end organ and nerve.

**Figure 10.14: Weber's test**

Rinne's test compares the patient's Special Senses abilitv to hear a tone conducted via air and bone the mastoid process. A vibrating 512 Hz tuning fork is first placed on the mastoid process and then held in line with the external auditory meatus as shown in Figure 10.5.The patient is asked whether the sound is louder behind or in front — referring to bone and air conduction respectively. Normally air conduction of the sound of a tuning fork is longer than transmission of bone — if altered, there is an abnormality of conduction, not perception.

**Figure 10.15: Rinne's test**

Schwabach's test is a hearing test performed with the opposite ear masked, with tuning forks of 256, 512, 1024, and 2048 Hz, alternately placing the stem of the vibrating fork on the mastoid process of the patient and that of the control (whose hearing should be normal) until it is no longer heard by one of them. The result is expressed as "Schwabach prolonged" if heard longer by the patient (indicative of conduction deafness), as "Schwabach shortened or diminished" if heard longer by the examiner (indicative of sensorineural deafness), and as "Schwabach normal" if heard for the same time by both.

**Figure 10.16: Schwabach's test**

Besides these hearing tests, hearing in patients can also be assessed by:

- Puretone audiometry (subjective test to assess specific loss of frequency)
- Brain stem audiometry (to assess functional integrity of auditory pathways) very useful in newborn and children (objective testing).

Now, before moving on to the next section on taste, let us quickly review what we have learnt so far.

## 10.5 A SENSE OF TASTE - GUSTATION

Modem man/woman uses the sense of taste mainly to derive pleasure. He/she peruses food that tastes good, and often takes unwanted and even undesirable foods if they are tasty. Besides guiding us to pleasing foods and helping us avoid unpleasant foods, taste also helps us to recognize desired foods, accept and select the required foods. The fact that taste is an indicator of the needs of the body may not be completely true For example, there is no evidence to suggest that a liking for fried foods indicates a need for fats and calories, or that a craving for pickles during pregnancy is due to a need for any nutrient that only pickles can provide.

In course of evolution, the most useful role of taste possibly was to warn animals against poisonous foods. Poisonous plants are frequently bitter or unpleasant to taste, which would in turn help the animals to avoid the Same food later. Taste involves harmony, especially by fitness, critical capacity or quality in general. It has been noted many times that among human senses, taste might be

called the "poor relation" Perhaps it is because taste contributes so few important qualities to the sum of human experience when compared to vision or audition. What is taste, then? How is it sensed?

Well, taste is a combination of sensation conveyed by the tongue, and smell, temperature and even texture of the food. The sensation involves the detection of a stimuli dissolved in water, oil or saliva, by the taste buds which are located primarily on the mucosa of the palate and areas of the throat. The sensation is conveyed to the receptors present on the tongue and smell by the chemical molecules and thus is called chemical sense.

## 10.5.1 Organs Involved in Taste Perception

The tongue is a strong muscle in the mouth that is covered with papillae (small bumps on the. tongue) and taste buds (that sense bitter, salty, sweet and sour tastes) as illustrated in Figure 10.17. The taste buds are clustered along the sides of the tongue. Papillae are the visible specialized structures on the tongue and are called organs of taste.

**Figure 10.17: Taste buds**

Taste is initiated by contact of an aqueous solution of a chemical with the taste buds on the surface of the tongue and the adjacent region of the mouth and throat. In this, taste differs from smell, which reacts primarily to the chemicals in gases.

The receptors for taste are located on the surface of sensory cells, which are grouped into bud shaped clusters of about 40 each. Each of these clusters is called a taste bud as illustrated in Figure 10.17. They are grouped in structures called papillae (Papilla,nipple). The number of taste buds per papillae in the human varies from 33-508 and averaging about 250.The taste buds are also called "taste beakers" or "taste onions" — refers to the spindled shaped cells as shown in Figure 10.17, bulging out at the root and coming together at the taste pore, very much like the petals of a bud. Each bud contains a number of taste cells 5 to 18, together with the other cells which may be immature taste cells. Human taste buds are about 0.07 mm wide at their widest diameter.

Within the taste buds are the sustentacular cells and gustatory cells, arranged to enclose a small chamber i.e. grouped together into a bundle-like

structure. Each receptor cell contains numerous microvilli which extend into the' taste pore. These microvilli facilitate the rapid absorption of the taste substance.

In 1803, Charles Bell demonstrated that the tongue was insensitive to taste in regions where there were no papillae, gustatory sensibility was confined mainly to the tip and edges. Four kinds of papillae are found in the human tongue: fungiform, foliate, circumvallate and filiform as can be seen in Figure 10.18.

Let us get to know about these papillae:

a) Fungiform papillae, as the name suggests, resemble a fungus to be more specific, a mushroom. They are distributed almost the entire surface of the tongue.

b) Foliate papillae are So called because they are shape like foliage of a leaf, and are continued to the back of the tongue.

c) Circumvallate papillae or vallate papillae resemble a well or a moat and are present at the base of the tongue. Stick out your tongue in front of a mirror and the large papillae you see at the back are the circumvallate papillae.

d) Filiform (finger-shaped ) papillae but these have no taste buds. Their secretions possibly keep the surface of the tongue moist, wash away particulate matter from the tongue and also dilute the chemical substance which stimulates the taste receptors. The dilution may be of protective value in case of bitter and irritant substances.

**Figure 10.18: Types of papillae**

The sensitivity of the papillae to different stimuli varies. Have a look at the Figure 10.19. Here you would notice the different stimuli and the corresponding area of sensation on the tongue. For example, the tip of the tongue is most sensitive to sweet, edges to sour and the back is most sensitive to bitter. That is why when we have to swallow a bitter pill, we avoid letting it touch the back of the tongue. Salty and sour tastes are not clearly differentiated but that of sweet and bitter are differentiated not only from each other but also from saline and sour. This research proves that there are only four basic tastes, but these four appear to be different for each other. The number of distinct is very large but many believe that there are combinations of four basic tastes.

**Figure 10.19: Four taste reception**

Sweet taste is perceived more intensely on the tongue than on the hard palate. Bitter taste will be perceived on the palate, while the salty taste is sensed more intensely on the tip of the tongue. Sour taste is perceived more intensely on the hard palate. Similar to the sense of vision and hearing, the sense of gustation too declines with age. What happens in this case, let's read and find out.

With age, the number of papillae varies, becoming less in number and more restricted in distribution. In adults, the taste buds containing the receptors are located mainly in depressions or moats of the papillae, except for the fungi form type, but in children, they may also be found in the cheeks. A few are found on the larynx and pharynx. Besides the taste buds in the papillae, there are a few in the mucosa of the left palate, 306 and in children, on the sides and even on the roof of the mouth.

The taste stimulus is apparently carried down into the grooves by the convection Special Senses forces exerted by the contraction and expansion of the grooves due to dynamics of the musculature of the tongue. We shall learn about the mechanism of taste perception next.

## 10.5.2 Mechanism of Taste Perception

Salivary glands play a very important role in perceiving the taste. They are found in and around our mouth and throat. There are 3 pairs of salivary glands: parotid, sublingual and submaxillary, as can be seen in the Figure 10.20. They all secrete saliva into our mouth. The secretion of the parotid gland is watery and rich in enzymes mainly amylase. Sublingual and submaxillary secretion is viscous, having a protein mucin. These secretions are very important to have the dissociation of tasteful substances. Saliva also buffers acids and helps to control temperature by means of the relatively high specific heat content of the water component.

**Figure 10.20: Saliva glands**

Chewing stimulates salivary secretion, as do stimuli brought about by the thought, sight or odour of food. Let us next see how the four basic tastes are perceived. The mechanism of taste perception involves 4 steps:

Initiation — Perception — Transmission — Identification.

Let us get to know each of these.

1) **Initiation:** If food is a solid, it is first converted to semisolid form by the combined action of the chewing and secretion of salivary glands. If it is in liquid form, it directly enters into the taste buds and comes in contact with it.
2) **Perception:** It is due to the combination of saliva, taste buds and the tongue movements. Saliva contains various ions such as potassium (K) and thiocyanate. The concentration of these 2 ions differs among various individuals. Therefore, different individuals have got different sensitivity for various tastes. K influences the sensitivity for salty and bitter taste in the mouth. During the chewing action, food is uniformly distributed on the various parts of the tongue due to the tongue movement. As a result, there is a gradient created for different tastes or different taste components cannot perceive the taste. The muscular movements constantly disrupt the concentration.
3) **Transmission:** In this step, the taste is actually perceived by the taste cells. Through the taste cells, the signal is transmitted to the brain via the nerve cell.
4) **Identification:** In the final stage of identification, which takes place in the brain, special receptors present in the brain will identify different tastes.

A major taste pathway is indicated in the Figure 10.21. The pathway involves — taste buds* solitary tract nucleus— thalamus* cortex — as illustrated in Figure 10.21.

**Figure 10.21: Major taste pathway**

So we have seen that the perception of taste is a complex mechanism extending from the tongue to the brain. Have you heard of taste in mind? If not, then read the next section and find out.

## Taste in the Mind

In the brain, there is a pathway terminating in the cortex, and another in the limbic system. The former is possibly concerned with conscious perception while the

latter is responsible the emotional reaction to taste. When Mahatma Gandhi was in England, his commitment to vegetarianism and simplicity made him to turn to foods like boiled spinach (without condiments and spices). But his conviction was so strong that he relished even such insipid dishes. While quoting these details in his autobiography, he wrote, "Many such experiments taught me that the real seat of taste was not the tongue but the mind".

## What are the factors which affect taste perception?

The factors affecting taste perception include:

1) Effect of certain diseases: Temporary alterations in taste sensation take place due to certain metabolic disorders or it may be due to the consumption of various drugs or antibiotics. In jaundice, the bitter taste is perceived faster even after the convalescence period is over.
2) Defects in adrenal glands. Hormones of adrenals change the sensitivity of different taste receptors.
3) Irradiation of the tongue decreases the sensitivity for different taste except for sour and it takes two months to recover.
4) Taking too hot products causes injury to the taste buds and taste is not perceived for sometime.
5) Tobacco, pan parag or betel nut bring about certain changes in the taste receptors resulting in poor perception.
6) In case of diabetes, sensitivity for sweet taste increases because of certain physiological changes in the people suffering from the disease.
7) Consumption of lots of antibiotics cause the continuous perception of bitter taste.

In addition, there are certain other observations related to taste perception. These are Special Senses highlighted next.

## Certain other observations related to taste perception

A few interesting observations have been made with respect to taste perception. You might be aware of a few of these. What are these? Let us have a look.

1) Lack of sleep for 72 hours did not affect the threshold value for salty and sweet taste but lack of sleep for 48-72 hours decreases the sensitivity for sour taste.
2) Sensitivity for 4 basic tastes decreases during hunger. There is a slight decrease in sensitivity for about 1 hour after meal followed by increases in next 3-4 hours.
3) Depletion of body salts increases the sensitivity for salty taste.
4) Women have higher sensitivity for sweet and salty taste but less for sour and there is no difference for bitter taste.
5) New born has little differentiation for initial 4-40 days.
6) Smoking could also affect taste preferences.
7) Various vitamins are also known to affect sensitivity like vitamin A. For studying the effects, vitamin A deficiency experiment was done on rats. They were given the diet depleted in vitamin A and it was seen after a long time they

start rejecting bitter compounds which indicates greater sensitivity for bitter taste and sometimes after, salty substances were also rejected which indicates that even the vitamins have some role to play in the taste sensation.

Our study of the sense of taste shall not be complete without a look at the disorders linked with perception of taste. Lets us get to know them.

### Certain Disorders Linked with Perception of Taste

1) **Ageusia:** this is a permanent or a temporary loss of taste sensation. The person is not able to perceive the taste.
2) **Hypogeusia:** the taste sensation is reduced.
3) **Parageusia:** there is a wrong perception of taste which may be due to certain defects in the brain.

## 10.6 A SENSE OF SMELL - OLFACTION

The sense of smell is amazingly sharp in some animals. It is said that a dog can discriminate even the smells of individual human beings. Humans are not so gifted! They vary in their olfactory ability. At one extreme are the 'olfactory types', whose abilities are exceptional and may be made use of perfume industry. At the other extreme are those with partial or total anosmia (a, not; osme, smell). Humans can distinguish between 2000 and 4000 different odours.

Let us get to know about the primary odours.

### The Primary odours

The Primary odours, if any, are not known with certainty. One of the better-accepted schemes proposes seven primary odours: camphoraceous, musky, floral, peppermint, ethereal, pungent and putrid.

### Olfactory receptors

In the section on taste receptors earlier, we learnt that there is a regional distribution of taste buds for the primary taste sensations like sweet, salt, sour and bitter, whereas olfactory neurons are not specialized to detect single fundamental odours. Same receptors may respond vigorously to some stimulus molecules, weakly to several others and not at all to others.

Consequently, the olfactory system can mediate a large number of different odour sensations. For stimulation of olfactory receptors, molecules must dissolve in the mucus before causing stimulation, whereas, there is a direct interaction between taste receptors and molecules. Afferent information from the taste buds is relayed directly to specific location near the mouth region of somatosensory cortex by way of the brainstem and thalamus whereas the central afferents of olfaction split into two. The first one involves limbic system, which influences sex, emotion, feeding and visceral homeostasis. It is possible that olfactory signals process along this route, influence moods and behaviour without entering conscious awareness.

The second route leads to olfactory cortex. Connection between the olfactory cortex and other sensory regions ofthe cortex allow integration of olfactory sensations with those arising from other sensory modalities. Signals that are processed along this route are more likely to lead to conscious sensation.

The mechanism of smell perception is simple. Odourants are inhaled through the nose, where they contact the olfactory epithelium. Olfactory receptor neurons in the olfactory epithelium transduce molecular features of the odourant into electric signals Special Senses which then travel along the olfactory nerve into the olfactory bulb as can be seen in Figure 10.22. Axons from the olfactory sensory neurons converge in the olfactory bulb to form tangles called glomeruli. Inside the glomerulus, the axon contacts the dendrite (branched projection of the nerve cell) of mitral cells. Mitral cells send their axons to a number of brain area, including the piriform cortex. The function of piriform cortex relates to olfaction.

**Figure 10.22: Perception of smell**

With this, we come to an end on our discussion on special senses.

## 10.7 LET US SUM UP

In this unit, we have learnt about our special senses that include vision, hearing, taste and smell. The organs for special senses are the eyes, ears, nose and tongue. The information perceived by our sense organs provides us with knowledge of the outside world.

## 10.8 GLOSSARY

**Acoustic reflex** : contraction of the stapedius and tensor tympani muscles produced by the stimulation of the ear by intense sounds.

**Blind spot** : an area where there are no cones and rods. It marks the point of convergence of neurons that form the optic nerve.

**Cataract** : the loss of water with age resulting in an opaque lens.

**Choroid** : a highly vascular structure that is pigmented and separates other two layers of the eye.

**Ciliary body** : a thick muscular structure having smooth involuntary muscles to which the choroid is connected.

**Ciliary muscles** : smooth involuntary muscles of the choroid which suspend thread — like ligaments that attach to the edges of the lens.

**Complex cells** : cells that are sensitive to both orientation and movement.

**Fovea** : a depressed area of retina lateral to the blind spot, which contains only cones and no rods.

**Glaucoma** : a condition in which the eyeball bulges due to increase in intraocular tension either due to excessive production of aqueous humor because it cannot be drained through a narrow opening called the Canal of Schlemm.

**Hyper complex cells** : cells that require not only the line or edge to be moving but also possess a certain length with a comer.

**Iodopsin** : a violet-coloured photosensitive pigment, present in the cones.

**Neuronal cells of retina** : bipolar cells, the Amacrine cells, Horizontal cells and Ganglion cells. These neurons are responsible for appreciating the shape, contrast, directional orientation of light and colour properties of vision.

**Pupil** : the central black hole of the iris.

**Rhodopsin** : a purple coloured pigment that is sensitive in even dim light.

**Sclera** : an opaque layer which does not allow light to pass through. It forms the posterior five-sixths of the eyeball and provides surface for attachment of muscle strings.

**Squint** : in paralysis or weakness of ocular muscles, Special Senses the muscle of one eye pulls in one direction and that of the other in a different direction.

**Tympanic resonance** : the tendency of the membrane to vibrate best over a particular range of frequencies.

**Vitreous body** : the posterior compartment is filled with this transparent gelatinous material that supports the lens and the retina.

NOTES

## 10.9 CHECK YOUR PROGRESS EXERCISES

UNIT

# 11

# PHYSIOLOGY OF THE ENDOCRINE GLANDS

**STRUCTURE**



## 11.1 LEARNING OBJECTIVE

After studying this unit, you will be able to:

- illustrate the gross structure of endocrine glands,
- describe the role of various endocrine glands in the regulation of body functions, and
- discuss the effects of over secretion and under secretion of hormones.

## 11.2 INTRODUCTION

The first section in this unit will deal with the hormones and the mechanism of hormone action in the body. In the next section, we will study the endocrine glands and their functions.

You have already learnt about different systems of human body in the

previous units. It must be clear to you that each system has a distinct function. Functions of all the systems are coordinated by the endocrine system and the nervous system. We studied about the nervous system in Unit 9. Now let us get to know about the endocrine system.

The endocrine system consists of the glands that are widely distributed in the body having no connection with each other. These glands are the ductless glands. Secretions produced by these glands are called as hormones, which are directly secreted into the blood. Hormones are concerned with the long-term control of other systems and the metabolic functions of the body and the transport of substances through cell membrane or other aspects of cellular metabolism. The main abnormalities which occur in association with the endocrine glands are caused by either an oversecretion (hypersecretion) or an undersecretion (hyposecretion) of hormones.

What are these hormones? What is their classification and mechhnism of action? The first section in this unit focuses on these aspects. Next, you will find a detailed discussion on the different endocrine glands and their role in the body.

## 11.3 HORMONES

What is a hormone? A hormone, as you may already know, can be described as a chemical substance which having been formed in one particular organ or a gland is carried in the blood stream to another organ (target organ) where it has its effect, influencing its growth, nutrition and functions.

In general, hormones are of two types — local hormone and general hormone. Local hormones affect cells in the vicinity of the organ secreting the hormone, what we call as paracrine influence. Examples of local hormones are gastrin and secretin etc. (These are the gastrointestinal hormones). General hormones, on the other hand, are emptied into the blood by specific endocrine glands and then flow throughout the entire circulation to affect cells and organs in far distant part of the body referred to as endocrine influence. Examples of general hormones are thyroid hormone and adrenocortical hormone etc. Some general hormones affect all cells almost equally, others affect specific cells. For example, growth hormone secreted from anterior pituitary gland affects all cells of the body, whereas, gonadotrophic hormone from the anterior pituitary gland affects the sex organs much more than the other.

Further, hormones are of two different chemical types — protein hormone and steroid hormone. Most of the hormones belong to the category of small proteins or derivatives of proteins such as polypeptides, polypeptide amines or chemical compounds derived from one or more amino acids. The adrenocortical and sex hormones are steroid hormones. They have a chemical structure similar to that of cholesterol. Next, let us learn how do these hormones act or function i.e. the mechanism of hormone action.

- **Mechanism of hormone action:** Hormones affect cell function either by activating cyclic AMP (Adenosine monophosphate) mechanism or by

NOTES

activating genes. You may recall reading about the cyclic AMP mechanism in the Nutritional Biochemistry Course. If not, may we suggest you go back to Unit 6 and read it carefully. Here, you will find a brief explanation of the mechanism.

In the cyclic AMP mechanism, the activating hormone combines with a specific receptor substance on the surface of the cell membrane. This activates the enzyme adenyl cyclase in the membrane, which in turn converts some of the adenosine triphosphate (ATP) inside the cell into cyclic adenosine monophosphate (cyclic AMP). This substance has an activating effect on many intracellular reactions.

A second important way by which the hormone affects cell function is gene activation. This is the mechanism of hormonal control utilized by steroid hormones. In this case, the activating hormone reacts with a receptor substance in the cell cytoplasm and the combination of the hormone and the receptor then migrates into the nucleus where it activates one or more specific genes. These then promote specific functional effects within the cell. Thus, protein hormones (except thyroid hormones). act via cyclic AMP and steroid hormones including thyroid hormones act through cytoplasmic receptors before they migrate to nucleus. Through these two types of mode of action, the hormones can regulate growth, nutrition and metabolic activity of the cell. Hence, cellular nutrition and function are dependent on the hormonal action.

With this basic understanding of the mechanism of hormone action, we move on to learning about the different endocrine glands in our body.

## 11.4 ENDOCRINE GLANDS

What do you understand by the term endocrine glands and what is their role in our body? Well, those glands that manufacture one or more hormones and secrete them directly into the bloodstream are referred to as endocrine glands. These glands affect how the body uses food (i.e. metabolism). They also influence other body functions about which we shall learn in a little while from now.

First, let us get to know about the various endocrine glands. There are six very important endocrine glands in our body. These are:

1) The pituitary

2) The thyroid

3) The parathyroid

4) The pancreas

5) The adrenal, and

6) The gonads (ovary in female, testes in male)

Figure 11.1 gives a clear picture of these glands.

**Figure 11.1: Flow diagram for endocrine glands**

## 11.5 THE PITUITARY GLAND

The pituitary gland, also called as hypophysis, is a small gland that is attached to the underside or base of the brain, behind the nasal cavity as can be seen in Figure 11.2(a). It is approximately 1.5 cm long and 0.5 cm in diameter. In fact, it is no larger than the size of a pea. It lies in the saddle shaped boney depression at the base of skull, called Sella turcica (named after the turkish saddle) and is connected with the hypothalamus by the pituitary or hypophyseal stalk.

**Figure 11.2(a): The pituitary gland**

In man, the pituitary has two main compartments — anterior (adenohypophysis) and posterior (neurohypophysis) as illustrated in Figure 11.2 (b).

**Figure 11.2(b): The anterior and posterior lobe of pituitary**

Table 11.1 presents the major hormones synthesized and secreted by the two compart- ments of the pituitary gland, along with summary statements about their major target organs and physiological effects.

| | Hormone | Major target organ(s) | Major physiological effects |
|---|---|---|---|
| **Anterior Pituitary** | Growth hormone | Liver, adipose tissue | Promotes growth (indirectly), control of protein, lipid and carbohydrate metabolism |
| | Thyroid-stimulating hormone | Thyroid gland | Stimulates secretion of thyroid hormones |
| | Adrenocorticotropic hormone | Adrenal gland (cortex) | Stimulates secretion of glucocorticoids |
| | Prolactin | Mammary gland | Milk production |
| | Luteinizing hormone | Ovary and testis | Control of reproductive function |
| | Follicle-stimulating hormone | Ovary and testis | Control of reproductive function |
| **Posterior Pituitary** | Antidiuretic hormone | Kidney | Conservation of body water |
| | Oxytocin | Ovary and testis | Stimulates milk ejection and uterine contractions |

**Table 11.1 : Major hormones secreted by the pituitary gland**

## 11.5.1 Anterior Pituitary

The anterior pituitary gland or adenohypophysis consists of three types of cells — acidophils, basophils and chromophores according to their staining characteristics. The anterior pituitary, as already highlighted above, secretes six hormones: growth hormone, thyroid stimulating hormone, adrenocorticotropic hormone, follicle stimulating hormone, luteinizing hormone and prolactin. Since most of these are trophic hormones (controlling growth and nutrition of other glands), pituitary is also known as "master gland". Let us learn about these hormones secreted by anterior pituitary, one by one. We begin with growth hormone and its functions.

**A) Growth Hormone (GH):** It is a protein containing 191amino acids in a single chain. It is secreted by somatotrophs throughout life even though growth stops at adolescence. The main functions of GH are highlighted herewith. The growth hormone:

- promotes development and enlargement of all tissues during the growing phase of life,
- helps the bones to enlarge and lengthen and the skin thickens by the effect of growth hormone,
- increases transport of amino acids through cell membrane and protein synthesis.
- It promotes positive nitrogen balance and is a protein anabolic hormone, and
- increases blood glucose level by promoting hepatic output of glucose.

After adolescence, growth hormone secretion decreases. The growth of long bones stop by this time, short bones like lower jaw and nose continue to grow. Hence, before adolescence, growth of body depends on the proper action of growth hormone. Height of an individual depends on the proper action of this hormone.

Have you ever thought what would be the consequences of deficiency (hyposecretion) or on the other hand, an increased secretion (hypersecretion) of growth hormone during childhood and at adult stage? The discussion below describes both of these conditions.

- **Hyposecretion during childhood:** Due to deficiency of growth hormone or its receptors, stunted growth of the skeleton and organs occur with resultant dwarfism. Pituitary dwarfs are the individuals with stunted growth but normal physical and mental abilities. There is another type (Lorain type), where growth hormone level is normal but its receptors are deficient. Such dwarfs do not respond to growth hormone treatment.
- **Hyposecretion during adult life:** It is only currently becoming recognized, the usual feature being low blood glucose level (hypoglycemia). Extended deficiency leads to negative protein balance, physical decline and lot of weight gain due to fat accumulation.
- **Hypersecretion during childhood:** Due to an increased secretion of the growth hormone, gigantism occurs. There is an excessive skeletal growth and the individual may be more than 8 feet tall.
- **Hypersecretion during adult life:** This results in a condition known as

acromegaly.

There is an excessive growth of the bones of the face specially the frontal bone, nose, ears and the mandible. The hands and feet become large (acro means extremity, megaly means enlargement). Also, there is a thickening of the skin on the face and hands.

From our discussion above, you would have got a fairly good idea that the growth hormone is very important for regulating cellular nutrition, protein metabolism and somatic growth. This is why it is also known as Somatotrophic hormone.

Next. let us get to know about the other important hovmone i.e. thyroid stimulating hormone, secreted by the anterior pituitary.

**B) Thyroid Stimulating Hormone (TSH):** TSH, also known as thyrotropin is a glycoprotein and synthesized by thyrotroph cells of the anterior pituitary gland. Its functions are many and are listed as follows. The TSH:

stimulates the secretion of thyroxine (T4) and tri-iodothyronine (T3) from the thyroid gland,

- increases the number and size of thyroid cells, and controls general metabolism of the body through its activity on thyroid.

The thyroid gland becomes inactive and secretes almost no hormone when the anterior pituitary gland fails to secrete TSH. We shall learn about the thyroid gland in the next section.

**C) Adrenocorticotropic Hormone (ACTH):** ACTH, also known as corticotrophin, is a polypeptide and is synthesized by corticotroph cells of the anterior pituitary gland.

Its functions are to:

- increase both the number of cells in the adrenal cortex and their degree of activity, resulting in an increased output of adrenocortical hormones, and e regulate mineral and glucose metabolism of the cells.

**D) Gonadotropic Hormones (GTH):** There are two gonadotropic hormones which regulate gonadal functions. They are follicle stimulating hormone (FSH) and luteinizing hormone (LH). Both of the hormones are secreted from gonadotrops of anterior pituitary gland.

FSH contains 204 amino acids and is a glycoprotein. It has distinct functions in case of males and females. In males, FSH stimulates growth of the germinal epithelium in the testes, thus promoting the development of sperm. While in case of females, it initiates growth of the follicles in the ovaries. It also helps to cause the ovaries to secrete oestrogen, one of the female sex hormones.

LH in females joins with FSH to cause oestrogen and progesterone secretion. It also causes the follicle to rupture, allowing the ovum to pass into abdominal cavity and then through a fallopian tube. LH also helps in the formation of corpus luteum (hence the name luteinizing hormone) which secretes progesterone. In the males, LH causes the leydig cells of testes to secrete testosterone, the male sex hormone.

Hence, through its gonadotropic hormones, anterior pituitary controls the secretion of male and female sex hormones (gonadal hormones).

**E) Prolactin:** Prolactin is synthesized in lactotroph cells of anterior pituitary gland during pregnancy and during the entire period of milk production after the birth of the baby. Its role is to stimulate both breast growth and secretory functions of breasts.

With prolactin, we finish our discussion on the hormones secreted by the anterior pituitary. However, our discussion will be incomplete without a word about the hypothalamic control of anterior pituitary gland. How does the hypothalamus control the pituitary gland? Do you know? If not, read the following discussion and find out.

Hypothalamic control of anterior pituitary gland: The hypothalamus controls many of the automatic functions of the body. It secretes a series of different neurosecretory substances called hypothalamic releasing and inhibitory factors.

These factors are secreted into the blood vessels connecting hypothalamus and pituitary called the hypothalamic—hypophyseal portal system and then to the anterior pituitary gland, where they regulate secretion of the various anterior pituitary hormones. These factors include:

- Thyrotropin Releasing Factor (TRF) which causes release of TSH.
- Corticotropin Releasing Factor (CRF) which causes release of ACTH.
- Growth Hormone Releasing Factor (GRF) which causes release of GH.
- Gonadotrophin Releasing Hormone (GnRH) which causes release of both LH and FSH.
- Prolactin Release Inhibiting Factor (PIF) which inhibits the secretion and release of prolactin.
- Prolactin Releasing Factor (PRF) which causes releose of prolactin.
- Growth Hormone (GH) releases inhibiting hormone or somatostatin which inhibits the secretion and release of GH.

Now let's take a look at the posterior pituitary, its location, the hormones released from it and their functions in the body.

## 11.5.2 Posterior Pituitary

The posterior pituitary gland or neurohypophysis is located immediately behind the anterior pituitary gland, as you may have seen in Figure 11.2 (b). In a sense, the posterior pituitary is not a gland because hormones secreted from posterior pituitary are synthesized in the hypothalamus. Hormones from the posterior pituitary are oxytocin and antidiuretic hormone (ADH) or vasopressin. Let's get to know about them.

**a) Oxytocin:** Oxytocin is a polypeptide containing 9 amino acids. An 'oxytoxic' agent is a substance that causes the gravid uterus (uterus of a pregnant female) to contract and this is one of the primary effects of oxytocin. Oxytocin is secreted

in moderate quantities during the latter part of the pregnancy and at the time of parturition (delivery). It promotes contraction of the uterine muscles and aids in the expulsion of the body (process of parturition or labor). Oxytocin also causes myoepithelial cells of the mammary gland to contract, therefore, squeezing the milk from the alveoli into the ducts so that the baby can suck it during breastfeeding.

b) **Antidiuretic Hormone:** Antidiuretic hormone or ADH, also known as vasopressin, is another polypeptide containing 9 amino acids. As the name of the hormone suggests, its major action is to prevent diuresis i.e., it reduces the rate of urine formation. This hormone acts on the distal tubules of the kidney controlling the reabsorption of water. When the osmotic pressure is high, the osmoreceptors respond by stimulating the secretion of antidiuretic hormone which increases the reabsorption of water by the renal tubules. ADH is often called vasopressin because under the influence of this hormone, the smooth muscles of the intestine and blood vessels contract. Contraction of the muscle layer in the blood vessel wall increases the blood pressure. Hence the name 'vasopressin'. Hence, in dehydrated or malabsorptive diseases, these hormones try to regulate the water and mineral balance of the body by adjusting the quantity of urine formation in the kidney.

## 11.6 THE THYROID GLAND

The thyroid gland is situated in the neck in association with the larynx and trachea. It is of butterfly shape as can be seen in Figure 11.3. The gland is composed of acini having epithelial cells which vary from cubical to columnar, depending upon the activity of the gland. The cells are arranged in a single layer round a central space, the acinus. The space in the acinus contains a thick fluid known as colloid.

**Figure 113: The thyroid gland**

What is the role of thyroid and which are the hormones secreted by the thyroid? Let's learn. We shall start with the functions.

NOTES

## What are the functions of thyroid gland?

The thyroid gland:

increases the metabolic activities of most tissues of the body,

- controls the utilization of oxygen in the body and hence, the Basal MetaboliRate (BMR),
- controls the excitability of neurons and nerve fibres,
- stimulates the different aspects of carbohydrate and fat metabolism. Under the effects of these hormones, there is rapid uptake of glucose by the cells, enhanced glycolysis and gluconeogenesis and mobilization of lipid from adipose tissue, and makes the muscles react with vigor.

## What are the hormones secreted from the thyroid gland?

Thyroxine ($T_4$) and tri-iodothyroxine ($T_3$) are the two hormones of thyroid gland. Iodine, as you may already know, is an essential nutrient required by our body. Why? Well, iodine present in the blood is taken up by the thyroid gland and the hormones thyroxine ($T_4$) and tri-iodothyroxine ($T_3$) are formed. These hormones are stored in the gland in the form of thyroglobulin and are released into the blood when required. Iodine ingested by the body is mostly utilized in the formation oftri-iodothyroxine ($T_3$) and thyroxine ($T_4$). The uptake of iodine from the blood, formation of the hormone and their release are stimulated by thyroid stimulating hormone (TSH) which you may recall reading above is secreted from the anterior pituitary gland. You should also note that the thyroid gland secretes the hormone calcitonin as well, which is involved with calcium metabolism.

- **Regulation of thyroid hormone secretion:** TSH from the anterior pituitary gland controls the secretion of thyroid hormones. Thyrotropin Releasing Factor (TRF) from the hypothalamus stimulates TSH. When the level of thyroid hormones in the blood is increased, it inhibits the anterior pituitary secretion of TSH by a direct effect on the anterior pituitary itself (negative feedback) and by indirect effect acting throughout the hypothalamus. Of the various stimuli increasing TSH secretion, exposure to cold is one of them and is very important.

Do you know what the consequences of impaired regulatory mechanism are? What happens when there is either decreased secretion (hyposecretion) or increased secretion (hypersecretion) of the thyroid hormone ? Let's find out.

- **Hyposecretion (hypothyroidism) during infancy:** Decreased secretion of thyroid horrnone results in the development of the condition known as cretinism. There is a lack of skeletal development and stunted body growth. The child is mentally retarded due to lack of development of the nervous system. The skin is thick and dry, and the face is expressionless. Pulse and respiration rates are slow, there is a general sluggishness of all the body processes. Cretins are different from pituitary dwarfs as along with the stunted growth, they have mental retardation.
- **Hyposecretion (hypothyroidism) in adult life:** Decreased secretion of

thyroid hormone results in the development of myxoedema. There is a slowing of mental and physical activity. The basal metabolic rate is reduced and there is a considerable general oedema. The facial skin is coarse, thick and dry and there is a loss of hair especially from lateral regions of eyebrows.

- **Hypersecretion (hyperthyroidism) or thyrotoxicosis:** This condition generally occurs in adult life. This is commonly caused by hyperplasia of the gland and is called 'Grave's Disease'. Anti-thyroid antibodies (one such antibody is LATS or long acting thyroid substance) interact with thyroid follicular cells to cause an over secretion of thyroid gland. There is an increased mental and physical activity in the patient. The body temperature is above normal. There may or may not be exopthalmus, that is, the protrusion of the eyeball. The patient is nervous, restless, provocative and ready to pick up quarrel on trivial issues. His handshake is warm but wet. Due to increased BMR, heart rate and BP is high with lots of sweating.

Goitre or the enlargement of thyroid gland is one of the critical manifestations of iodine deficiency. Iodine, as you must have realized by now, is an important mictonutrient required by our body for the formation of thyroid hormone production. Only small amount, I mg per week is necessary for the formation of tri-iodothyroxine and thyroxine. If due to lack of iodine in water or soil or due to any reason, even this small amount of iodine is not supplied, enlargement of thyroid gland results. The actual swelling of the gland is due to the accumulation of colloid in the acini.

Sometimes, it could be possible that inspite of adequate iodine intake, there is a deficiency of iodine in our body. Now how does that happens? The answer to this is the presence of certain anti-thyroid substances in the body.

What are these 'anti-thyroid substances'? Well, anti-thyroid substances are those substances that suppress the thyroid activity. Thiocyanate and propylthiouracil are examples. Thiocyanate reduces the rate of uptake of iodine by thyroid cells. Propylthiouracil prevents the formation of thyroid hormones. These, along with other anti-thyroid drugs, can be used for the treatment of hyperthyroidism. Hence, by maintaining BMR, normal functioning of thyroid is essential to remain in a balanced state of metabolism.

Now let us move on to the next gland, i.e. the parathyroid gland.

## 11.7 THE PARATHYROID GLANDS

The parathyroid and thyroid glands are neighbours in the neck. You would realize that parathyroid glands are the small glands that lie behind the thyroid gland, arranged in two pairs — the superior and inferior parathyroids. In fact, there are four parathyroid glands, two behind each side of the thyroid, as can be seen in Figure 11.4. The glands are surrounded by the connective tissue capsules. The cells forming the glands are spherical in shape and are arranged in columns. These are known as the principal cells.

**Figure 11.4: The parathyroid gland**

## What is the hormone secreted from the parathyroid gland?

The parathyroid gland secretes parathormone. The amount secreted is strongly influenced by the level of calcium in the blood. Calcitonin from the thyroid gland antagonizes the action of parathormone.

Let us look at the functions of parathyroid next.

What are the functions of parathyroid gland?

The main function of the parathyroid gland is to regulate the calcium levels in our body so that the nervous and muscular functions (where calcium has an important role) can function properly. Parathyroid hormone is mainly responsible for:

- maintaining the constancy of plasma calcium (9 to 11 mg%). It has a direct effect on bone from which calcium resorption occurs.
- promoting absorption of calcium from the small intestine. But this is brought about mainly by controlling the production of , 25-dihydroxycholecalciferol in the renal tubules.

## How is the parathyroid hormone secretion regulated?

It is simple. An increase in parathyroid hormone causes an increase in calcium absorption from the intestine and renal tubules. When the bone is saturated with calcium salts, the slight excess of extracellular calcium ions reduces parathyroid hormone secretion.

But sometimes under certain conditions this regulation can become impaired. What are the consequences? These are enumerated next.

- **Hypoparathyroidism:** Hypoparathyroidism or a decrease in the secretion of

parathormone causes an upset in calcium metabolism. Hypocalcemia develops and the muscles go into a type of spasm known as tetany. Muscle spasms of the hands and feet are termed as carpopedal spasm. Also, there is twitching of the face and eye muscles. In infants and children, spasm of the muscles of the larynx (laryngismus strodulus) occurs accompanied by cyanosis. After . a pause, without breathing, a sharp inspiration occurs accompanied by a high-pitched crowing sound.

Hypoparathyroidism occurs very rarely and may be due to the removal of the parathyroid gland in error during the operation of thyroid gland or removal of the parathyroid gland when the thyroid gland is malignant or some defects in the gland for which it is unable to secrete parathormone.

- **Hyperparathyroidism:** Hyperparathyroidism may occur due to a tumour in one or more of the parathyroid glands. In this condition, the calcium level of the blood increases. There is an excessive demineralization of bones and non-utilization of calcium resulting in the softening of the bones. The bone becomes painful and fracture occurs frequently. Due to increased calcium in blood, there is a tendency of the formation of stones in the kidney. The disease is known as osteitis fibrosa cystica. Hence, parathormone along with thyroid calcitonin is essential for maintaining calcium balance in the body.

We move to the next gland i.e. the pancreas. You may be wondering why we are talking about pancreas here, when we have already studied about its structure and functions earlier in Unit 6 under the gastrointestinal and glucagon system. The reason being that pancreas is a gland which secretes the hormones insulin and glucagon.

Read and find more information on this aspect in the next section.

## 11.8 THE PANCREAS

The pancreas is a gland that lies immediately below the stomach, surrounded by the loop of duodenum. You can look up the structure of pancreas illustrated in Figure 6.10 in Unit 6 and refresh your memory.

The bulk of the pancreas is composed of pancreatic exocrine cells, whose ducts are arranged in clusters called acini (singular acinus). The cells are filled with secretory granules containing the digestive enzymes. Embedded throughout the exocrine tissue are small clusters of cells called the Islets of Langerhans, which are the endocrine cells of the pancreas and secrete insulin, glucagon and several other hormones.

Here we shall focus on the endocrine cells which secrete the hormones. Let us learn about the hormones secreted from the endocrine cells of pancreas.

### Hormones from the Islets of Langerhans

The cells which make up the Islets of Langerhans are found in clusters, distributed throughout the substance of the pancreas. There are many thousands of Islets of

Langerhans in the pancreas and contain (1 and ß types of cells. a-cells secrete glucagon whereas ß-cells secrete insulin. Both influence the level of glucose in the blood. Let us get to know about the two hormones in greater details.

NOTES

## A) Insulin

Insulin is a hormone synthesized from the precursor called preproinsulin. Preproinsulin has four peptides. Insulin circulates in the blood in a free state. Plasma levels of insulin are from 20 microunits per ml during fasting to about 150 microunits per ml after food. The functions of insulin are listed next.

### What are the functions of insulin?

The main function of insulin, as you may already know, is to maintain a steady level of blood sugar level in our body. Insulin, primarily:

- promotes glucose transport into all cells of the body except brain. Rapid transport of glucose into the cells decreases the blood glucose concentration. On the other hand, lack of insulin causes glucose to be accumulated in the blood.
- promotes glycogen storage in the liver and muscle. The glycogen concentration in liver cells sometimes increases to as high as 5 to 6 percent and in muscle cells to over 1 percent. After liver and muscle stores of glycogen have been filled, the rest of the glucose is stored in the fat tissue. Insulin helps in the transport of glucose in these cells.

Besides these functions, insulin also:

- helps in the transport of most of the amino acids through the cell membrane, and increases the formation of protein and RNA in cells.
- Having looked at the functions, let us next understand how insulin secretion is regulated.

### How is the insulin secretion regulated?

It is interesting to note that blood sugar level itself controls insulin secretion. How? When blood sugar level rises, insulin secretion automatically increases and it helps excess glucose to be transported into the cells, to be used for energy and to be stored as glycogen. A fall in the blood glucose concentration decreases insulin secretion. Next, we shall get to know the complications arising when the regulation of insulin secretion is effected.

- **Hyposecretion of insulin:** You may already be aware that an insufficiency of insulin in the body leads to the development of diabetes mellitus. It is caused by the degeneration of ß-cells of Langerhans, from where you learnt earlier that insulin is secreted. Inactivation of ß-cells may be inherited from the parents or sometimes antibodies may develop against ß-cells. Patients suffering from diabetes mellitus have a blood glucose level higher than normal. Sometimes it exceeds the renal threshold level and glucose is found in urine. If high concentration of glucose is present in urine, an excess amount of water is excreted leading to polyuria (excessive urination), polydipsia (excessive thirst),

polyphagia (excessive hunger) and dehydration (water loss). Also excess amount of fats are metabolized to the stage of ketoacids. Insulin is not stored in the body. So it has to be given daily to a young diabetes mellitus patient, if required. In adults, diabetes mellitus develops if there is a lack of insulin receptors. Insulin is normal or high, but non-reactive. In such patients, anti-diabetic drugs and strict dietary' regimen are essential to maintain blood glucose levels.

Next, let us see what happens when over secretion of insulin takes place.

Hyperinsulinism: Too much secretion of insulin or over treatment of a diabetic person with insulin may cause hyperinsulinism. In this condition, the blood glucose level is very low, resulting in reduced excitability of the brain and coma.

With this, we come to an end of our study on insulin. Next we shall learn about the other hormone produced by the pancreas i.e. glucagon.

### B) Glucagon

Glucagon is secreted by a-cells of Islets of Langerhans. It is a hormone containing amino acids. Its effects are opposite to that of insulin. Let us see how, by studying about its functions.

### What are the functions of glucagon?

As you have just studied that the functions of glucagon are opposite to that of insulin.

Hence glucagon:

- increases the breakdown of liver glycogen to glucose, thus making glucose available for transport into the blood, and
- increases gluconeogenesis (conversion of protein to glucose) by activating the liver cell enzymatic system.
- So it is clear that glucagon makes glucose available in the body. Let us see how the glucagon secretion is regulated.
- **Regulation of glucagon secretion:** It is simple, when the blood glucose concentration falls below normal, an increased quantity of glucagon is secreted. It helps to keep glucose concentration high enough in the blood and prevents hypoglycemic coma. Thus, in this section we learnt that the hormones of endocrine pancreas regulate the blood glucose level. You should know that the glucose levels can also be regulated by dietary control of carbohydrates, exercise and anti-diabetic agents.

## 11.9 THE ADRENAL GLANDS

Adrenal glands, also known as suprarenal glands are located on top of both kidneys as shown in Figure 11.5. Each gland is composed of two distinct parts — adrenal cortex (outer part) and adrenal medulla (inner part). These are shown in the Figure 11.6.

**Figure 11.5: Adrenal gland**

Let us get to know about the adrenal cortex and medulla in greater details.

## 11.9.1 Adrenal Cortex

The adrenal cortex is yellowish in colour and covered by a capsule. The cells are arranged in three layers as shown in Figure 11.6.

**Figure 11.6: Structure of adrenal cortex**

As you can see in Figure 11.6, the outer layer consists of groups of thickly set columnar cells called as zona glomerulosa. The middle layer consists of large polyhedral cells containing pigment called the zona fasciculata. The inner layer, where the cells become interlaced into a network is called the zona reticularis. The zona glomerulosa secretes predominantly mineralocorticoids. The zona fasciculata secretes predominately glucocorticoids and the zona reticularis secretes predominantly sex hormones. Thus, the hormones produced by the adrenal cortex include:

- Glucocorticoid hormone, which includes the cortisol and corticosterone hormone Mineralocorticoid i.e. aldosterone hormone, and

## Sex hormones

Let us learn about the functions of these hormones next. We start with the mineralocorticoids i.e. aldosterone hormone.

## a) Functions of mineralocorticoids

Aldosterone is the name given to the main physiological mineralocorticoid. As you go through the functions listed below, you will realize that aldosterone is associated with the maintenance of electrolyte balance in the body. Let us get to know about the functions of aldosterone.

Aldosterone increases sodium reabsorption in the renal tubules, especially from the ascending limb of loop of Henle and Distal Convoluted Tubule (DCT) and the collecting tubule. You may recall reading about this earlier in Unit 7 under renal system. When the amount of sodium reabsorbed is increased, the amount of potassium excreted is increased. Thus aldosterone helps in the uptake and retention of sodium in all cells and the extrusion of potassium from them.

Aldosterone tends to decrease the acidity of body fluids. Like potassium, the hydrogen ions are secreted into the tubules. Hydrogen ions originate from bicarbonic acid. When hydrogen ions are secreted, bicarbonate ions are left in the extra cellular fluid, resulting in alkalosis.

Aldosterone causes an enhanced absorption of chloride ions. Sodium, chloride and bicarbonate ions are accumulated in the extra cellular fluid. As a result, there is an increased water re-absorption.

Functions of aldosterone are, thus, associated with the maintenance of electrolyte balance in the body. How is the aldosterone secretion regulated? Let's find out. Regulation of aldosterone secretion: Increased potassium ion concentration and decreased sodium ion concentration increases the aldosterone secretion.

Renin-angiotensin system is also important for the regulation of aldosterone secretion. The juxtaglomerular cells of the kidney secrete renin. Once renin is released from the juxtaglomerular cells, it diffuses into the blood and circulates throughout the body. In the blood, it splits angiotensin I from renin substrate. Angiotensin J is further split to angiotensin II with the help of Angiotensin Converting Enzyme (ACE). Angiotensin 11 is a powerful vasoconstrictor and increases aldosterone secretion from zona glomerulosa. Hence, in hypertensive patients, advice of reduced salt intake is given along with anti-hypertensive drugs, including ACE inhibitors to reduce the aldosterone secretion.

- A minimal amount of ACTH is also needed for the secretion of aldosterone.
- The secretion of aldosterone is thus stimulated by: a drop in the level of sodium ions in the blood
- a rise in the level of potassium ions in the blood
- angiotensin II, and

- ACTH

## b) Functions of glucocorticoids

Cortisol, cortisone and hydrocortisone are the names given to the glucocorticoids. What is their function in our body? They play a major role in the body's response to stress. For example, under the influence of cortisol, the blood sugar level is maintained and even raised in the times of stress. In fact, these hormones are responsible for converting glycogen to glucose. They stimulate gluconeogenesis by liver. The blood sugar level may be raised during stress by the process of gluconeogenesis.

Further, these reduce protein stores in essentially all body cells except those of the liver. Catabolism of proteins in the cells release amino acids from the already existing proteins and it hastens the conversion of amino acid to glucose to replenish the glucose supply.

Finally, these promote mobilization of fatty acids from the adipose tissues.

Infection, trauma, intense heat or cold or any type of stress causes an increase in cortisol level in the blood. Let us now see how the glucocorticoid secretion is regulated.

Regulation of glucocorticoid secretion: Glucocorticoid secretion is mainly controlled by ACTH or adrenocorticotropic hormone from the anterior pituitary gland. In any stress, ACTH secretion increases. It stimulates glucocorticoids. ACTH secretion is controlled by CRF or Corticotropin Releasing Factor from the hypothalamus. When the concentration of glucocorticoids is very high, the feedback mechanism automatically reduces ACTH towards a normal level. Glucocorticoids also directly inhibit the formation of CRF. During extreme stressful states, increased production of glucocorticoids cope with the enhanced energy/nutrition requirements of the cells and tissues. Minute stress is essential for the normal gearing up of the body tissues. Too much of stress will exhaust the adrenals to cause crisis.

Finally, let us look at the functions of the adrenal sex hormones.

## c) Functions of adrenal sex hormones

Adrenal androgens have only weak effects in humans. Their functions are:

- It is possible that part of early development of the male sex organs results from childhood secretion of adrenal androgens.
- Most of the pubic and axillary hair in the female results from action of these hormones. Some amount of progesterone and oestrogens are also secreted by adrenals.
- How is the adrenal sex hormone secretion regulated?
- The secretion of adrenal androgens by the adrenal cortex is controlled by ACTH.

In the discussion above, we have seen how a fine tune mechanism works to regulate the hormone secretions of the adrenal cortex. An over secretion and under secretion

can lead to complications as described herewith.

- **Hyposecretion of adrenocortical hormones:** Hyposecretion of hormones from the adrenal cortex results in the development of the condition known as Addison's disease. There is muscular weakness, loss of weight due to loss of water, hypoglycemia, increased blood potassium and decreased blood sodium, pigmentation of the skin especially in the exposed parts of the body. There is a craving for salt. The first thing a patient picks up at the dining table is the salt. If not provided, due to some reason or the other (in diet or as table salt), craving is so great that the patient drinks his own urine.
- **Hypersecretion of adrenocortical hormones during childhood:** Children suffering from hypersecretion of adrenocortical activity are described as Infant Hercules. There is too early development of sexual organs and secondary sex characteristics, unusual muscular development and obesity.
- **Hypersecretion of adrenocortical hormones in adult:** This condition is known as Cushing's syndrome. It is characterized by virilism (hair growth above lips) in the females, that is, a tendency to develop male characteristics. In the males, feminism may develop, that is, a tendency to develop female sex characteristics. Besides this, there is wasting of muscles due to an excessive breakdown of proteins and hyperglycaemia develops due to an upset in carbohydrate metabolism.

Having studied about the adrenal cortex, next let us get to know about the medulla.

## 11.9.2 Adrenal Medulla

The adrenal medulla secretes epinephrine or adrenaline and norepinephrine or noradrenaline. The secretory cells of the medulla are modified postganglionic sympathetic neurons. Epinephrine and norepinephrine secreted from the adrenal medulla have similar stimulatory or inhibitory effects as the epinephrine and norepinephrine released from sympathetic nerves. Let us look at their functions next.

Functions of adrenomedullary hormones

The functions of the adrenal medulla hormones — adrenaline and noradrenaline — are to:

- prepare the body to deal with the abnormal conditions, so that it responds to fear and excitement,
- dilate coronary arteries and increase the blood supply to the heart muscles,
- dilate the pupil of the eye and allow increased quantity of light to enter,
- increase the activity of the sweat glands,
- dilate the bronchi and allow greater amount of air to enter the lungs at each inspiration,
- slow down peristalsis in the digestive tract and limit the flow of saliva,
- cause rapid breakdown of glycogen into glucose, thus ensuring sufficient glucose

- for sustained muscle contraction,
- cause intense vasoconstriction on the renal blood vessels and greatly decrease the output of urine, and contract the spleen thus increasing the volume of circulating blood.

Of all the endocrine glands, adrenals are essential for life. They prepare the individuals to cope up with the day-to-day stresses in life (General Adoption Syndrome) or make an individual to fight or flight from the enemy (3Fs — Fear, Fight and Flight).

With our understanding of the adrenal gland, we move on to study the pineal gland.

## 11.10 THE PINEAL GLAND

The pineal gland is a small body situated in the brain. It is reddish grey in colour as you can see in Figure 1 1.7. It is composed of epithelial cells arranged to form lobules, which are surrounded by a fine connective tissue. You would be interested to know that the pineal gland is about the size of a pea, and is in the center of the brain in a tiny cave behind and above the pituitary gland which lies a little behind the root of the nose. It is located directly behind the eyes.

**Figure 11.7; The pineal gland**

The pineal gland secretes the hormone, melatonin. Melatonin acts as a conveyor of photoperiodic information. It has an influence on other endocrine glands. It inhibits the secretion of gonadotrophins. In the jet age, when day and night rhythms are upset due to long flights, melatonin and its derivatives are given to the subjects to overcome jetlags and improve upon their biological rhythms.

## 11.11 THE THYMUS GLAND

The thymus gland lies in the thoracic cavity immediately behind the sternum as shown in Figure 11.8. The gland varies in size depending on the age of the individual. During childhood, it is fairly large in size and in adults it is quite small. The gland is composed of a cortex and a medulla. A substance called thymosin

has been isolated from the thymus which stimulates immunological activity in the lymphoid tissue, especially before puberty. In fact, of the two typo of immuno competent lymphocytes i.e., B and T, the latter are so named because they are processed in thymus. The thymus, therefore, is responsible for many immune system functions including the production of T lymphocytes, a type of white blood cell responsible for "cell-mediated immunity." It is in fact the master gland of the immune system.

**Figure 11.8: The thymus gland**

Finally we shall study about the kidneys as an endocrine gland. We have already Physiology of the studied about kidney as an organ responsible for formation and secretion of urine earlier in Unit 7. So you are familiar with its structure. Let us look at the hormones secreted by the kidney.

## 11.12 KIDNEY AS AN ENDOCRINE GLAND

Besides its excretory function, the kidney secretes some hormones and acts as an endocrine gland. In response to hypoxia, the kidney secretes the hormone erythropoietin, which stimulates erythrocyte production. In kidney diseases, there can be anaemia due to deranged erythropoietin production.

Cholecalciferol or vitamin D3 is taken in the diet from animal food sources. Cholecalciferol is converted into 25-hydroxycholecalciferol in the liver. This 25 hydroxycholecalciferol is transported in the blood stream to the kidneys as 1, 25 - dihydroxycholecalciferol, the active form of vitamin D.

Renin, secreted by the kidneys is responsible for the production of angiotensin in the plasma, which is essential for aldosterone production.

The discussion above highlighted the role of kidney as an endocrine gland.

With this, we come to an end of our study about endocrine glands. But we would

like to highlight that gonads (ovary and testes) are also endocrine glands, functions of which will be dealt in the physiology of reproduction, in the next Unit.

## 11.13. LET US SUM UP

NOTES

In this unit, we learnt about endocrine glands and their functions, including hypo and hyper activity of the glands.

We learnt that there are some endocrine glands in our body which secrete specific substances called hormones into the circulatory system. These hormones influence metabolism and other physiological processes.

Pituitary, thyroid, parathyroid, pancreas, adrenals and pineal gland are the major endocrine glands in our body. We learnt that thyroid hormones affect overall metabolism. Calcitonin from thyroid gland and parathormone from parathyroid gland controls calcium metabolism. Mineralocorticoids from the adrenal gland and vasopressin from the posterior pituitary gland regulate water and electrolyte balance. Glucocorticoids and adrenal medullary hormones are helpful in stressful conditions of life.

## 11.14 GLOSSARY

**Acromegaly** : a chronic metabolic disorder in adults caused by the presence of too much growth hormone. It results in gradual enlargement of body tissues including the bones of the face, jaw, hands, feet and skull.

**Addison's disease** : bronzed skin disease, caused by the hyposecretion of adrenal cortex particularly mineralocorticoids.

**Basal Metabolic Rate (BMR)** : the rate at which heat is produced by an individual in a resting state.

**Calcitonin** : a hormone produced by certain cells in the thyroid gland that lowers the levels of calcium and phosphate in the blood. It also inhibits the resorption of bone.

**Cretinism** : lack of thyroid secretion in childhood.

**Cushing's syndrome** : symptoms of excessive carbohydrate metabolism due to over activity of adrenal cortex.

**Cyanosis** : a bluish discolouration of skin and mucus membrane due to excessive reduction of haemoglobin in blood.

**Diuresis** : an increased output of urine by the kidneys.

**Dwarf** : a stunted individual due to the deficiency of

growth hormone during childhood.

**Exopthalamas** : abnormal protrusion of the eyeball.

**Gigantism** : an excessive secretion of growth hormone during childhood before the closure of the bone growth plates, which causes overgrowth of the long bones and very tall stature.

**Glycoprotein** : a protein which has carbohydrate groups attached to the polypeptide chain.

**Grave's disease** : hyperactivity of the thyroid gland.

**Hypophyseal stalk** : the funnel-shaped stalk connecting the pituitary gland to the hypothalamus.

**Melatonin** : a hormone produced by the brain's pineal gland that regulates circadian rhythms (sleep/ wakefulness cycle); helps induce sleep and acts as an antioxidant.

**Myxoedema** : accumulation of myxomatus fluid in the extra- cellular compartment due to lack of thyroid secretion in adults.

**Osteitis fibrosa cystica** : inflammation of the bones due to marked osteoclastic activity secondary to hyperparathyroidism.

**Spasm** : an involuntary and abnormal contraction of the muscles of hands, thumbs, feet, or toes that are sometimes seen with twitching and tetany. They can be severe and painful.

**Steroid hormone** : hormone derived from cholesterol, lipid soluble and not stored in the body (corticoids of adrenals)

**Tetany muscular spasms** : a sudden, violent, uncontrollable contraction of a group of muscles, caused by low Ca in blood.

**Thyrotoxicosis** : a condition due to over-activity of thyroid gland.

**Vasoconstrictor** : a substance that constricts or narrows the blood vessels.

## 11.7 CHECK YOUR PROGRESS EXERCISES

**NOTES**

UNIT

# 12

# THE REPRODUCTIVE SYSTEM

**STRUCTURE**



## 12.1 LEARNING OBJECTIVE

After studying this unit, you will be able to:

- Enumerate the various reproductive organs of the female and male along with their functions,
- Describe the role of different hormones involved,
- Highlight the physiological changes during pregnancy and lactation,
- Understand the disorders that affect the functioning of the reproductive system,
- Enlist the different methods of contraception and their benefits and limitations,
- Discuss the various pregnancy determination tests.

## 12.2 INTRODUCTION

In this Unit, We are going to deal with the reproductive system, both female and male reproductive organs along with their functions. The ability to reproduce,

as you already know, is one of the properties which distinguish living from the non-living matter. In human beings, this process is through sexual mode of reproduction. We will study about the role of different hormones that are involved in the growth and development of the sex organs. You would realize that like any other organ system, this system has also some disorders which could possibly affect the normal functioning of the reproductive system. What are these? What are their possible effects? In this unit, we would learn about these issues. Further in this unit, we shall look at the various physiological changes taking place in the body during the periods of pregnancy and lactation. Apart from these, we shall deal with contraception.

## 12.3 THE REPRODUCTIVE SYSTEM

The reproductive organs of the male and female differ anatomically and physiologically.Both the sexes produce specialized reproductive cells called gametes, containing genetic material, i.e. genes and chromosomes.

**Figure 12.1: Female and Male reproductive system**

Other body cells contain 46 chromosomes arranged in pairs. The gametes contain only one of each pair i.e. 23 chromosomes. When an ovum is fertilized by a spermatozoon (sperm), the resultant zygote contains the full complement of 23 pairs of chromosomes, half obtained from the mother and half from the father.

The zygote embeds in the wall of uterus where it grows and develops during the 40 week gestation period before birth. The function of the female reproductive system is, therefore, to form the ovum and if it is fertilized, to nurture it until it is born and feed it with breast milk until it is able to take a mixed diet. The function of the male reproductive system is to form the spermatozoa and transmit it to the female. Let us proceed first with the female reproductive system.

## 12.4 THE FEMALE REPRODUCTIVE SYSTEM

Female reproductive organs or genitalia are divided into external and internal organs. The external female genitalia performs two major functions, both allowing

the penis and thus the sperm to enter (in order to fertilize an ovum), as well as, protecting the more sensitive internal genital organs from pathogens, which can produce infection. The internal female genitals are: the vagina, the cervix, the uterus, the fallopian tubes and the ovaries

12.3.1 External Genitalia

The external genitalia are collectively known as vulva, which consists of:

1. Mons Pubis
2. Labia Majora
3. Labia Minora
4. Clitoris
5. Vestibule
6. Hymen
7. Greater Vestibular glands

**Figure 12.2: External genitalia**

- **Mons pubis:** The mons pubis is a pad of fatty tissue over the pubic bone. This structure, which becomes covered with hair during puberty, protects the internal sexual and reproductive organs.
- **Labia Majora:** The labia majora are two spongy folds of skin, one on either side of the vaginal opening, that cover and protect the genital structures. They form the boundary of vulva.It is composed of skin, fibrous tissue, fat and sebaceous glands. The fold joins anteriorly and posteriorly. At puberty, hairs grow on the mons pubis and lateral aspects of labia majora.
- **Labia Minora:** The labia minora are the two erectile folds of skin between the labia majora that extend from the clitoris on both sides of the urethral and vaginal openings. They have sebaceous gland and they posteriorly fuse. The cleft between labia minora is the vestibule. Here, vagina, urethra and ducts of greater vestibular glands open.

- **Clitoris:** It contains an erectile tissue. The clitoris, in fact, is an erectile, hooded organ at the upper joining of the labia that contains a high concentration of nerve endings and is very sensitive to stimulation. The clitoris is the only anatomical organ whose sole function is providing sexual pleasure. Vestibule: The vestibule is the space where the vagina opens.
- **Hymen:** It is the mucous membrane which partially occludes the vaginal membrane.
- **Greater Vestibular Glands:** They lie in labia majora near the vaginal opening. They have ducts opening into vestibule. They secrete mucous so that the vulva remains moist.

## 12.4.2 Internal Organ

The internal organs lie in the pelvic cavity and contain vagina, the cervix, uterus, fallopian tubes and the ovaries.

**Figure 12.3: The internal organs of the female reproductive system**

- **Vagina:** The vagina is a muscular, highly expandable, tubular cavity leading from the vestibule to the uterus. It is a fibro-muscular tube lined with stratified epithelium. It lies in front of anus and has rectum at the posterior part.
- **Uterus:** It is a hollow muscular pear-shaped organ, flattened antero-posteriorly, it lies in the pelvic cavity. When the body is in the upright position, it lies in almost horizontal position. Parts of the uterus are fundus, body and cervix.

The walls of the uterus has 3 layers of tissues perimetrium, myometrium and endometrium. The uterus is supported by surrounding organs, muscles of the pelvic floor, ligaments that suspend it from the walls of the pelvis.

**Figure 12.4: Location and parts of uterus**

The functions of the uterus have been considered at the different stages in the following discussion:

1. After puberty, uterus goes through a regular cyclic change, the menstrual cycle, which prepares it to receive, nourish and protect a fertilized ovum.
2. It helps the growth of foetus during the 40 week gestation period, at the end of which the baby is born. The cycle lasts between 26-30 days. If the ovum is not fertilized, the cycle ends with a short period of bleeding, referred to as menstruation.
3. If the ovum is fertilized, the zygote embeds in the uterine wall which relaxes to accommodate the growing foetus. It provides the right environment for the embryo and foetal growth. At the end of the gestation period, labour begins and is concluded when the baby is born, and the placenta is extruded.
4. During labour, the muscle of the fundus and body of the uterus contract intermittently, and the cervix relaxes and dilates. As labour progresses, the uterine contractions become stronger and more frequent. Thus the uterus muscles contract and expels the foetus and the placenta.

- **Uterine tubes (Fallopian tubes) :** The fallopian tubes are a pair of tubes that extend from the upper uterus, extending out toward the ovaries (but not touching them), through which ova (eggs) travel from the ovaries towards the uterus and in which fertilization of the ovum takes place. The end of each tube has finger — like projections called fimbrae.
- **Structure of fallopian tubes :** The tubes have an outer covering of peritoneum, middle layer of smooth muscle and are lined with ciliated epithelium.
- **Functions of fallopian tubes :** The fallopian tubes assist in transporting the ovary and spermatozoa. The mucous present in the fallopian tube helps in smooth movement of ova and spermatozoa. Fertilization takes place in the

uterine tubes, then the zygote moves into the uterus.

- **Ovaries :** They are female gonads or sex glands, lie shallow in the walls of pelvis. The ovaries are two organs located at the end of each fallopian tube, that produce ova (releasing one per month from puberty to menopause). The ovaries produce oestrogen and progesterone, the hormones responsible for the development of sex characteristics. Each ovary is attached to the upper part of uterus by the ligament of the ovary. Let us understand the structure and functions of ovaries.
- **Structure and functions of ovaries :** The ovaries have 2 layers of tissue. The medulla lies in the center and consists of fibrous tissue, blood and nerves. The cortex surrounds the medulla. It has a framework of connective tissue or stroma covered by germinal epithelium. It contains ovarian follicles, each of which contains an ovum. Before puberty, the ovaries are inactive but the stroma already contains immature (primordial) follicles as shown in Figure 12.5. During the child bearing years, one ovarian follicle matures, then ruptures and releases its ovum into the peritoneal cavity during each menstrual cycle. The process of ovum formation in females is called oogenesis.

Maturation of the follicle is stimulated by follicle stimulating hormone (FSH) from the anterior pituitary. While maturing, the follicle lining cells produce the hormone oestrogen. After ovulation, the follicle lining cells develop the corpus luteum (yellow body) under the influence of luteinizing hormone from the anterior pituitary. The corpus luteum, produces the hormone progesterone.

If the ovum is fertilized, it embeds in the wall of the uterus where it grows and develops and produces chorionic gonadotropin hormone which stimulates the corpus luteum to continue secreting progesterone for the first 3 months of the pregnancy.

**Figure 12.6: Female reproductive hormones and target tissues**

If the ovum is not fertilized, the corpus luteum degenerates, menstruation occurs and the next cycle begins, where all these steps have been indicated. Sometimes more than one follicle matures at a time, releasing 2 or more ova in the sarne cycle. When this happens and the ova are fertilized, the result is a multiple pregnancy

**Figure 12.7: A summary of stages- of development of the ovum and the associated hormones**

### 12.4.3 Menstrual Cycle

### What is menstrual cycle?

Menstrual cycle, is a series of events that occur regularly in females every 26-30 days. The cycle consists pf a series of changes that take place concurrently in the ovaries and uterine walls. Menstrual cycle, in fact is a recurring cycle (beginning at menarche and ending at menopause) in which the endometrial lining of the uterus prepares for pregnancy. Jf pregnancy does not occur, the lining is shed at menstruation. The average menstrual cycle is 28 days. Next, let us see how the cycle begins? The cycle begins with the hypothalamus. The hypothalamus, as you already know by now, is a structure in the brain responsible for regulating the body's thirst, hunger, sleep patterns, libido and endocrine functions. It releases the chemical messenger, follicle stimulating hormone releasing factor (FSH-RF) to tell the pituitary, another gland in the brain, to do its job. The anterior pituitary then secretes the following hormone.

1) **Follicle stimulating hormone:** promotes the maturation of ovarian follicles, secretion of oestrogen, leading to ovulation, and
2) **Luteinizing hormone:** stimulates corpus luteum and secretion of progesterone. The hypothalamus responds to changes in the blood of oestrogen and progesterone. It is depressed by high levels and stimulated when they are low.

The phases in the menstrual cycle are as follows:

1) **Proliferative phase (10. days):** An ovarian follicle stimulated by FSH, grows

towards maturity and produces oestrogen. Oestrogen stimulates proliferation' of endometrium, prepares for receiving the fertilized ovum. The endometrium lining becomes tall and thick by rapid cell multiplication. The phase ends when ovulation occurs and oestrogen production stops.

2) **Secretary phase (14 days):** After ovulation, the lining of ovarian follicle is stimulated by LH to develop corpus luteum which produces progesterone. The endometrium becomes oedematous, watery mucous increases. This is believed to assist the passage of spermatozoa through the uterus to uterine tubes where the ovum is usually fertilized. The ovum fertilizes by 8 hours. ne survival of the sperm is only for 24 hours. The date of ovulation however, cannot be predicted with certainty, even when the cycles are regular. If fertilization of ovum does not occur, cycle goes to a third phase — the menstrual phase.
3) **Menstrual Phase (4 days):** If the ovum is not fertilized, a high level of progesterone in the blood inhibits the activity of pituitary gland and the production of luteinizing hormone is reduced. The decrease in hormone causes degeneration of corpus luteum. Thus progesterone production is decreased. Around 14 days after ovulation, the lining of uterus degenerates and breaks down, menstruation begins. The flow consists of extra secretion of endometrial cells, blood from broken capillaries and the unfertilized ovum. When progesterone levels decreases considerably, another ovarian follicle is stimulated by FSH and the next cycle begins.

## What happens when the ovum is fertilized?

If the ovum is fertilized, there is no breakdown of endometrium and no menstrual flow. The fertilized ovum travels through uterine tube to the uterus where it becomes embedded in the wall and produces chorion gonadotrophins .This keeps corpus luteum intact enabling it to continue to secrete progesterone for the first 3-4 months of pregnancy, inhibiting the maturation of ovarian follicles. During that time, placenta develops and produces oestrogen, progesterone and gonadotrophins. The placenta provides an indirect link between the circulation of the mother and that of the foetus. Through the placenta, the foetus obtains maturational materials, $O_2$, antibodies and gets rid of $CO_2$ and other waste products.

## What is menopause?

The cessation of menstruation is menopause. Natural nienopause typically occurs between 45 and 55 years of age. It is caused by changes in concentration of the sex hormones. During menopause, the ovaries become less responsive to the FSH and LH and ovulation and menstrual cycle becomes irregular, eventually ceases. Other changes are vasodilatation, sweating palpitations, discomfort and disturbance in normal sleep and shrinking of breasts, atrophy of sex organs etc. The discussion above focused on menstruation and menopause. The two terms are used commonly with respect to female reproductive system. While studying about the female reproductive organs, you might also come across certain accessory glands such as the mammary glands.

### 12.4.4 Accessory Glands — Breasts or Mammary Glands

The breasts or mammary glands are accessory glands of the female reproductive system. They also exist in the male -but only in a rudimentary form.

**Figure 12.8: Structure of mammary gland or breast**

The breasts are small until puberty. They develop to their mature size under the influence of oestrogen and progesterone. During pregnancy, these hormones stimulate further growth. After the baby is born, protection from anterior pituitary stimulates the production of milk. The posterior pituitary stimulates release of milk in response to the stimulation of the nipple by the sucking baby. The mammary glands consist of a glandular tissue, fibrous tissue and a fatty tissue. In human females there are usually two mammary glands, one in each breast, although polythelia (accessory nipples) and polymastia (accessory glands) can occur anywhere from the knee to the neck. The mammary glands overlie the pectoral muscles and are attached to them via fascia (connective tissue). The glands are connected to the skin by the suspensory ligaments of the breast. These glands are modified sweat glands that produce and secrete milk during the lactation process to feed the newborn. During pregnancy, high blood oestrogen and progesterone levels stimulate lactation. The corpus luteum produces these hormones during early pregnancy, the placenta takes over later. The hormones stimulate the ducts and glands in the breasts, enlarging the breasts. So remember, the development of mammary glands is controlled by hormones. Oestrogen promotes formation of mammary glands, while testosterone inhibits it. Prolactin, which is stimulated by oestrogen, acts on the mammary glands to produce milk (lactation).

## 12.5 THE MALE REPRODUCTIVE SYSTEM

We have studied about the female reproductive system in the last section. We saw that most of the organs of the female reproductive system are located inside the pelvis. Unlike the female, the male have sex organs or genitals, both inside and outside the pelvis.

The male reproductive system includes:

1) The scrotum which contains -

a. two testes, and

b. two epididymis

2) A pair of vas deferens

3) A pair of spernhatic cords

4) A pair of seminal vesicles

5) A pair of ejaculatory ducts

6) Prostrate gland

7) Penis

Figure 12.9 illustrates these organs of the male reproductive system.

**Figure 12.9: Parts of the male reproductive system**

**1) Scrotum:** It is a pouch, divided into two compartments each of which contains a testis, an epididymis, testicular end of a spermatic cord. It lies in front of the upper part of the thighs and behind the penis. Let us get to know about these different parts within the scrotum.

**a) Testes:** They are male reproductive glands, suspended in the scrotum by spermatic cords. Testes produce and store millions of tiny sperm cells. Testes are surrounded by 3 layers of tissues.

- **Tunica vaginalis:** Outer covering which grows downward. In early foetal tife, they develop in lumbar region, just below the kidneys. They descend into the scrotum and peritoneum covers them. It also surrounds the testis. This is almost completed by 8th month of foetal life.
- **Tunica albugenia:** A fibrous cover surrounds the testes is situated under tunica vaginalis. It grows in depth, forms septa, and divides the glandular structure of testis into lobules.
- **Tunica vasculosa:** It consists of a network of capillaries supported by delicate connective tissue.

Testes are also a part of the endocrine system because they produce hormones, including testosterone. Along with the testes are the epididymis and vas deferens which make the duct system of the male reproductive system.

**b) Epididymis:** It is the tightly coiled, thin-walled tube that condåcts sperm from the testicles (testes) to the vas deferens. Figure 12.10 presents a schematic representation of the epididymis. The epididymis, as you can see, can be divided into a number of segments or regions: initial segment, caput (head), corpus (body), cauda (tail) and the vas deferens. The epididymis provides for the storage, transmission and maturation of sperm. Apart from this, it facilitates the transport of spermatozoa along the duct and protects spermatozoa from harmful substances.

**Figure 12.10: Schematic representation of an epididymis**

We have looked at the epididymis and the testicles in the discussion above. Note, the epididymis and the testicles hang in a pouch-like structure outside the pelvis in the scrotum. This bag of skin, called the scrotum helps to regulate the temperature of testicles, which need to be kept cooler than body temperature to produce sperm.

A pair of Vas Deferens: Its name is Latin, which literally means "carrying-away vessel". It is a long, muscular tube that passes upward alongside the testicles and carries spermatozoa from the epididymis to the ejaculatory duct , and transports the sperm-containing fluid called semen. During ejaculation, the wall of the vas deferens thickens and thins itself, thus propelling the sperm.

**Figure 12.11: Figure showing the location of vas deferens and testicles**

- **The Spermatic cords:** These are two, one leading from each testis, by suspending it in the scrotum. It is composed of fibrous tissue, smooth muscle, connective tissue, lymph and blood vessels, nerves and deferent duct.
- **Seminal vesicles :** These are two small fibro-muscular pouches lined with columnar cells. They are sac-like structures attached to the vas deferens to the side of the bladder. In fact, they lie on the posterior aspect of bladder. At its lower end, each vesicle opens into a short duct which joins the corresponding deferent duct to form an ejaculatory duct.
- **Ejaculatory ducts:** They are 2 tubes, 2 cm long, each formed by the union of the duct from a seminal vesicle and a deferent duct. They pass through prostrate gland and join the urethra. The tissue layers are parallel as in seminal vesicles.

**6) Prostrate glands:** It lies in the pelvic cavity. If you have a closer look at it, you will notice that the prostate gland, which produces some of the parts of semen, surrounds the ejaculatory ducts at the base of the urethra just below the bladder. The prostrate gland has an outer fibrous covering, layer of smooth muscles, glandular cells, columnar cells etc. It secretes a thin lubricating fluid, passes into urethra through numerous ducts.

**7) Urethra:** The urethra is the channel that carries the semen to the outside of the body through the penis. The urethra, about which you may recall reading earlier in Unit 7, is also part of the urinary system because it is also the channel through which urine passes as it leaves the bladder and exits the body. Hence, male urethra provides a common pathway for the flow of urine and semen. It is almost 18-20 cm long, originates at the. Urethral orifice in the bladder, where it is surrounded by prostate gland, passes through the perineum into the penis. There are 2 urethral sphincters, internal and external sphincter which consists of striated muscle fibres surrounding membranous part. Bladder

**Figure 12.12: Figure showing the location of urethra and prostrate glands**

**8) Penis:** The penis has a root and body. It is formed by 3 erectile masses of tissues and involuntary muscle. Erectile tissue is supported by fibrous tissue and covered with skin. It has a rich blood supply. The two lateral columns of tissues are known as corpora cavernosa and the median column is corpora spongiosa. At its tip, it is expanded into a triangular structure known as glans penis, above which is a flap of double layered movable skin referred to as prepuce. It is supplied with autonomic and somatic nerves. Parasympathetic stimulation leads to engorgement with blood and erection of penis.

## Sperm formation function

Sperm development, i.e. spermatogenesis takes place in the seminiferous tubules (ducts) of the testes. Cell division produces spermatozoa (mature sperm cells) that contain one-half of a man's genetic code. Each spermatogenesis cycle consists of six stages and takes about 16 days to complete. Approximately five cycles, or 2 h months are needed to produce one mature sperm. Mitochondria (energy-generating organelles) inside each sperm powers its tail (flagellum) so that it can swim to the female egg once inside the vagina. Sperm development is ultimately controlled by the endocrine (hormonal) system that comprises the hypothalamic-pituitary-gonadal axis.

**Figure 12.13: Structure of a spermatozoa**

The male reproductive organs are stimulated by gonadotrophic hormones from the anterior lobe of pituitary gland. The FSH stimulates the seminiferous tubules of testes to produce male germ cells, the spermatozoa. The spermatozoa passes through epididymis, deferent duct, seminal vesicle, ejaculatory duct and finally reach the urethra. Semen is the fluid ejaculated from urethra. It consists of

(a) spermatozoa

(b) viscid fluid, which nourishes the sperm

(c) thin lubricating fluid from prostrate glands, and

d) mucus by the glands of urethra.

In the epididymis and deferent duct, the spermatozoa become more mature and are capable of independent movement through a liquid medium. An ejaculation usually

consists of 2-5ml of semen containing 40-100 million spermatozoa/ml. If they are not ejaculated, they are reabsorbed by the tubules. Generally, spermatogenesis occurs at 3 degree Celsius less than the body temperature.



### Male Puberty

Puberty is the process that occurs when a child grows into a sexually mature individual. In fact, the reproductive system does not start functioning until puberty. The male maturation, i.e. puberty is from the age of 10-14 years. Puberty is caused by secretion of hormones. Luteinizing hormone from the anterior lobe of pituitary gland stimulates the interstitial cells of the testes to increase the production of testosterone. This hormone influences development of the body to sexual maturity.

The changes which occur at puberty. These include:

1) Growth of bones, muscles, increase in height and weight,

2) Enlargement of larynx and deepening of the voice — it 'breaks',

3) Growth of hair on the face,- maxillae, chest, abdomen and pubis,

4) Enlargement of penis, .scrotum and prostrate gland

5) Maturation Of seminiferous tubules and production of spermatozoa.

Though sexual ability in males declines with age, interestingly, there is no period in males comparable to menopause in the females..

Our study so far focused on understanding the Structure and the role of the different organs of the male and female reproductive system. We learnt that the female reproductive organs produce the eggs and the male organs produce the sperm. You may already know that the sperm and the egg unite in the mother's body to form a zygote which develops into the foetus. This period from conception to birth when a woman carries a developing foetus in her uterus is called pregnancy. Certain physiological changes take place in the mother's body to support the growth and development of the foetus. What are these physiological changes? In the next section we shall study about these aspects. We shall look at these changes during pregnancy and then during lactation.

## 12.6 GROWTH AND DEVELOPMENT DURING PREGNANCY

Pregnancy, as you may already know, is the period of time between fertilization of the ovum (conception) and birth, during Which-mammals carry their developing young in the 'uterus. The duration of pregnancy in humans is about 280 days, equal to 9 calendar months. After the fertilized ovum is implanted in the uterus, rapid changes occur in the reproductive organs of the mother. The uterus becomes larger and more flexible, the placenta develops, enlargement of the breasts begins, and alteration of renal function, blood volume and blood cell count occur. Growth and development during pregnancy largely reflects the growth and development of the foetus and the placenta.

### 12.5.1 The Placenta

The placenta is a transitory chorio-decidual structure developing during pregnancy and lies implanted on -the uterine wall. It is connected with the foetus through the umbilical cord. It is not a passive barrier between the mother and foetus but plays a very active role. For the developing foetus, it is the sole critical route for receiving nutrients from the mother and exchanging waste products. In the early days of pregnancy, the placenta and the two associated structures form from a tiny mass of cells.

**Figure 12.14: The placenta and associated structures**

The other two structures are:

i) The amniotic sac, which houses the developing foetus, and

ii) The umbilical cord, a rope-like structure which contains foetal blood vessels which extend through the foetus' umbilicus to the placenta. The placenta evolves during the 6th — 12th week of pregnancy from a small mass of cells into a complex spongy network of tissues and blood vessels. At 12 weeks of pregnancy, the placenta has attained its definite form.

| | Weeks of Pregnancy | | | |
|---|---|---|---|---|
| | 10 | 20 | 30 | 40 |
| Foetus (g) | 5 | 300 | 1500 | 3000-3300 |
| Placenta (g) | 20 | 170 | 430 | 650 |

**Table 12.1: Placenta size with progression of pregnancy**

After 12 weeks of pregnancy, the placenta has attained its definite form. The placenta has 2 principal parts: uterine and foetal. On the maternal side, the placenta is a part of the uterine mucosa. When the blastocyst (an early pre-implantation embryo) implants in the uterus at 6 — 7 days after fertilization, the uterine tissue and blood vessels breakdown to form small spaces (lacunae) that fill with maternal

blood. Blood begins to circulate in the spaces at about 12 day's gestation. On the foetal side, the trophoblast grows and sends out root-like villi into the pools of maternal blood. These villi contain capillaries, which will exchange nutrients and waste products between the mother and the foetus.

## What is the role of the placenta?

When you read through the functions of placenta, you will realize that it is a versatile, metabolically active organ.

| | |
|---|---|
| **Nourishes the foetus** | • facilitates transfer of oxygen and nutrients from mother to foetus. |
| **Removes wastes** | • picks up foetal waste products such as $CO_2$, urea, bilirubin. |
| **Foetal lung** | • performs the respiratory, absorptive and excretory functions that the foetus' lungs, digestive system and kidneys will provide after birth. |
| **Protective barrier** | • protects the foetus from harmful agents, which are of high molecular weight including proteins except maternal immuoglobulin G conferring immunity to the foetus.<br>• transports nutrients and in some cases can store them. |
| **Endocrine gland** | • produces several hormones that maintain pregnancy and prepare the mother's breasts for lactation. |

**Table 12.2: Functions of placenta**

One of the special functions of the placenta is to produce a variety of hormones. In chronological order, with progression of pregnancy, the hormones produced are:

- Human Chorionic Gonadotropin (HOG)
- Progesterone
- Human Placental Lactogen (HPL), and
- Chorionic Somatomammotropin

By means of these hormones, the placenta carries out the functions of the foetus's pituitary until the organ is ready to perform on its own. Since the placenta plays such a vital role, a healthy placenta is essential for foetal well-being. A well-developed healthy placenta is able to transfer nutrients efficiently. However, conditions such as reduced surface area of the villi, insufficient vascularisation, changes in the hydrostatic pressure in the intervillous space limit nutrient supply to the foetus and constrain growth. Maternal nutrition is important for ensuring placental development.

## 12.6.2 Foetal Growth and Development

Intrauterine life is one of the most critical periods. Foetal development begins with fertilization of an ovum by a sperm. Three stages follow: the zygote, embryo and foetus.

- **Zygote:** The newly fertilized ovum or zygote begins as a single cell. During the days after fertilization it divides. Within 2 weeks, the zygote embeds itself in

NOTES

the uterine wall (implantation). Cell division continues and as development proceeds, the zygote becomes an embryo. Embryo: The development in the embryonic period is amazing. Let us briefly list the accomplishments during this period (2 to 8 weeks of gestation).

- The number of cells at first doubles approximately every 24 hours.
- The size of the embryo changes very little. At 8 weeks, the 11/4 inch embryo has a complete central nervous system, a beating heart, a digestive system, well- defined fingers and toes, and the beginnings of facial features.
- **Foetus:** During the next 7 months, each organ grows to maturity on itsown schedule. Foetal growth is phenomenal, weight increases from < 1 gram to about3000 gms.

The developing foetus's vital statistics and main developmental features. What is of importance is that before the mother even knows she is pregnant, the embryo reaches a critical stage in its development. Therefore, it is vital to:

a) plan for pregnancy, and

b) ensure that the mother is well-nourished and cared for during pregnancy

**Table 12.3: Developing foetus's vital statistics and main developmental features**

Growth, as you know, consists of hyperplasia and hypertrophy — a combination of both enlargement and maturation of cells. What do we mean by hypertrophy and hyperplasia? The enlargement or overgrowth of an organ or tissue due to an increase in of its cells, rather than the number is hypertrophy.

On the other hand, enlargement of an organ or a tissue because of an increase in the number of cells in that organ or tissue is hyperplasia. You have seen that by 60 days of gestation all the major features of the human infant have been achieved. The foetal stage is a period of most rapid growth, from the 3td month to term, the weight increases nearly 500-fold. Figure 12.V5 depicts the average weight curve of foetal growth.

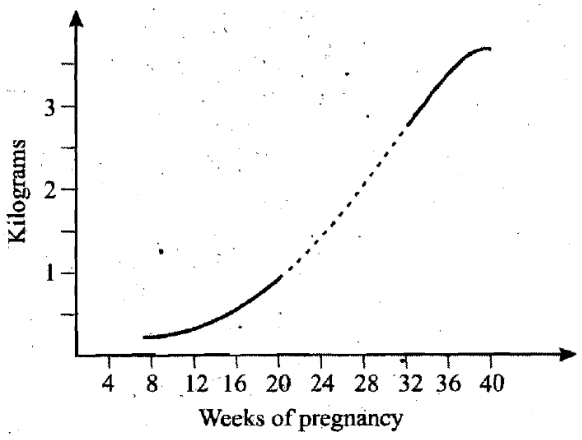



**Figure 12.15: Average curve of foetal growth**

## 12.7 PHYSIOLOGY OF LACTATION

Lactation is an ancient physiologic process. It is the period following pregnancy when a woman nourishes a fully developed and rapidly growing baby with breast. A lactating woman secretes about 500 ml milk/day in the first month which increases to about 1 L/day by the fifth month. On an average, a well-nourished lactating woman secretes about 850 ml milk/day. The process of breastfeeding is successfully initiated by at least 99% of women who try.

During pregnancy, a change occurs in the mother's breasts to prepare for milk production and as you have seen, body fat is deposited to ensure that energy is available for lactation. The establishment and maintenance of lactation are determined by several factors including the anatomical structure of the mammary gland and adequate development of the alveoli, ducts and nipples, initiation and maintenance of milk secretion and the ejection of milk from the alveoli to the nipple. Let us look at the anatomy of mammary glands, which you may recall reading earlier under the female reproductive system, are the accessory glands.

### 12.7.1 Anatomy of the Mammary Gland

The human mammary gland consists of milk-producing cells and a duct system embedded in connective tissue and fat

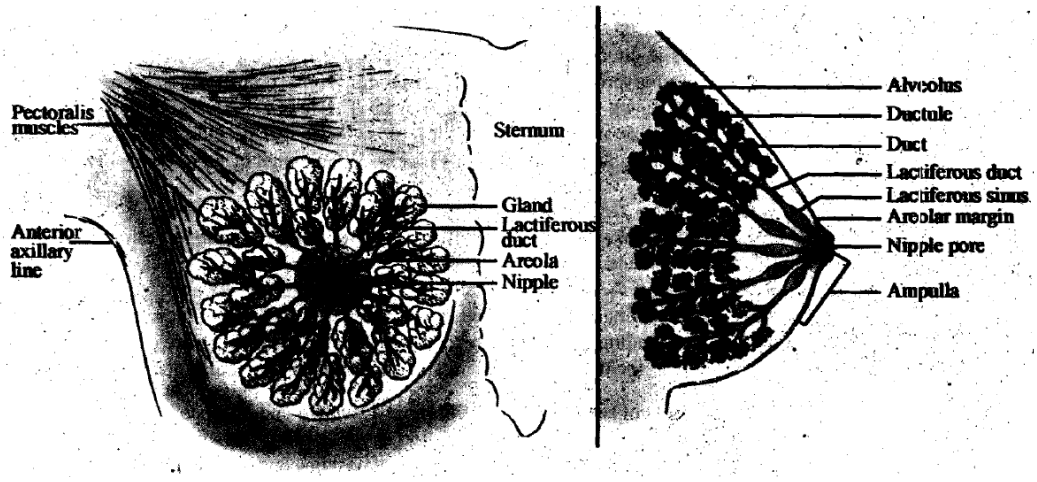



**Figure 12.16: General anatomical features of the human breast**

The basic components of the mammary. gland are the alveoli lined with-milk-secreting epithelial cells surrounded by myoepithelial cells and a rich capillary network. These alveoli join up to form lactiferous ducts that drain into openings in the areola.

Each breast consists of 15-20 lobes of glandular tissue, each lobe being made up of a number of lobules as can be seen in Figure 12.16. The lobules consist of a cluster of alveoli, which open into ducts and these unite to form large excretory ducts called lactiferous ducts. These ducts converge towards the center of the breast where they form dilatation or reservoirs for milk. Leading these dilatations, there are narrow ducts which open onto the surface at the nipple.

Fibrous tissue supports the glandular tissue and ducts, and covers the surface of the gland and is found between the lobes. The nipple is a small conical eminence at the center of the breast surrounded by a pigmented area, the areola. On the surface of areola, there are numerous sebaceous glands which lubricate the nipple in pregnancy. The function of this gland is to secrete milk. The nipple contains 15-20 lactiferous ducts surrounded by modified muscle cells. These ducts expand to form the short lactiferous sinuses in which milk may be stored. The sinuses are continuations of the mammary ducts, which extend outward from the nipple towards the chest wall with numerous secondary branches. The ducts end in epithelial masses, which form lobules (15-20 in number).

Generally, the terminal tubules and glandular structures are most numerous during the child-bearing period and reach their full physiological development only during pregnancy and lactation. There is proliferation of the terminal tubules, dilation of the tubular lamina and lining of the acinar structures by cuboidal epithelium. During the last trimester, the clumps of milk-producing cells progressively dilate in final preparation for the lactation process.

The breasts are capable of milk secretion sometime in the second trimester. The placenta plays an important role. The hormones secreted by the placenta human placental lactogen, prolactin and chorionic gonadotropin, contribute to mammary gland growth. Also placental estradiol and progesterone stimulate breast development. Shortly after parturition, proliferation of parenchymal cells occurs.

## 12.7.2 Physiology of Lactation

Lactogenesis is the onset of copious milk secretion around parturition, triggered by a fall in plasma progesterone levels. Although some colostrum is secreted after delivery (2-3 days), full lactation begins later. The first 2-3 days after delivery is a period of rapid lactation initiation, followed by the longer period of maintenance of lactation. This complex neuroendocrine process is facilitated by an interplay of various hormones.

Oxytocin and prolactin instigate the lactation process. Prolactin is responsible for milk production and oxytocin is involved in milk ejection from the breast. The basic secretory units of the mammary gland, as you may already know now, are the alveoli composed of a single layer of epithelial cells. The alveoli produce the secretory product. Surrounding the alveoli are the myoepithelial cells which are contractile and are responsible for the ejection of milk from alveoli and alveolar ducts. A cyclic process of secretory activity, luminal distention and expulsion of milk into the duct system continues throughout lactation as directed by the suckling of the infant and the letdown reflex.

Regular sucking stimulates the continuation of milk secretion. Milk removal from the breast is a product of coordinated interaction between suckling of the infant and letdown reflex of the mother. As the infant commences suckling, afferent impulses generated in the receptors in the areola travel to the brain where they stimulate the release of oxytocin from the posterior pituitary. Oxytocin travels

through the blood stream to the breast where it combines with specific receptors on the myoepithelial ceils, stimulating them to contract and force milk from the alveoli into the mammary ducts and sinuses.

NOTES

## 12.8 ROLE OF HORMONES IN REPRODUCTION

Throughout pregnancy, more than 30 different hormones are secreted in the mother's body, some being specially secreted in pregnancy. Others, which are normally secreted in the non-pregnant state, now have altered rates of secretion.

The mother's health and nutritional status influence their production. As you are aware, in any human being, complex feedback systems maintain homeostasis. During pregnancy, many of these mechanisms are "reset" in order to support retention, utilization or excretion of nutrients.

**Table 12.4: Hormonal effects on nutrient metabolism in pregnancy**

We can summarize the role of hormones as to: promote breast development,

- increase fat deposition to provide
- energy stores to be utilized during late pregnancy and lactation, promote uterine growth, and
- relax muscles and ligaments to accommodate the growing foetus and to allow for childbirth.

Among these hormones, progesterone and oestrogen have major effects on maternal physiology. Secretion of Oestrogen is lower than that of progesterone during the early months of pregnancy, but rises sharply near term. Thyroxine has a major role in metabolism and influences caloric requirements.

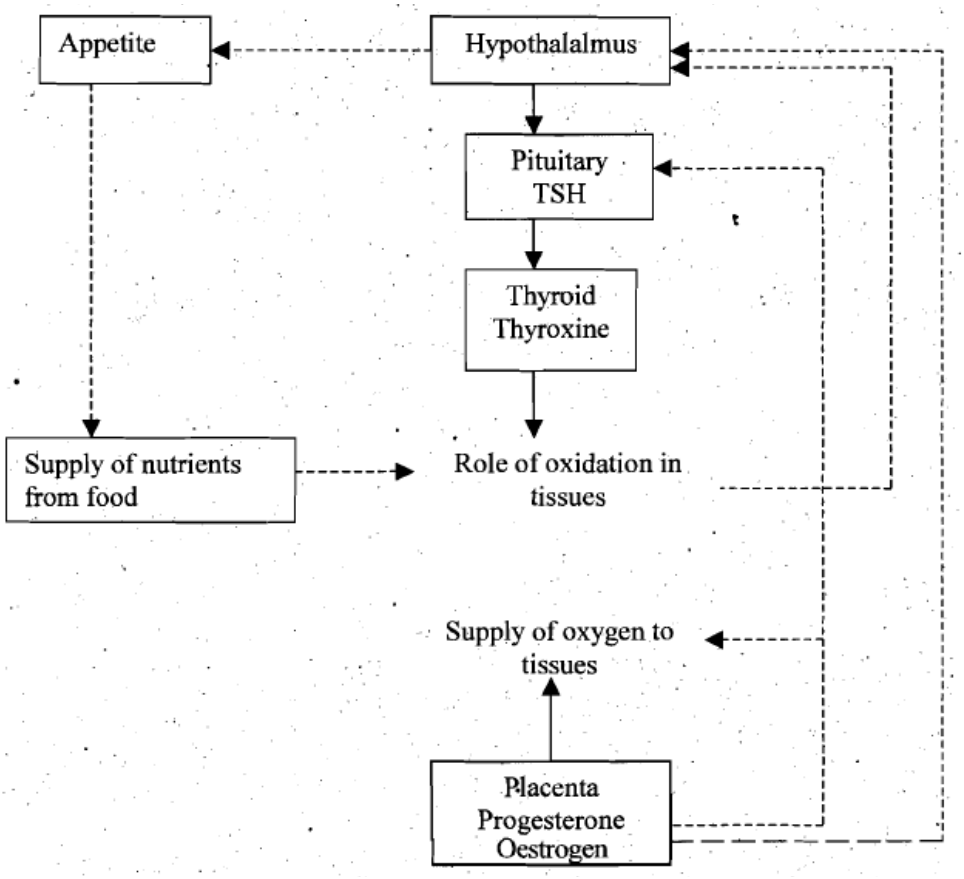



**Figure 12.17: Hormonal regulation of' energy metabolism in pregnancy**

## 12.9 DISORDERS OF THE REPRODUCTIVE SYSTEM

Disorders that may affect the proper functioning of the reproductive system include abnormal hormone secretion, sexually transmitted diseases and the presence of cancerous tissues in the region. Such problems frequently affect fertility and may complicate pregnancy. We shall look at the different disorders specific to the female and male reproductive system in this section. Let us start with the study of the disorders affecting female reproductive system.

### 12.9.1 Disorders of the Female Reproductive System

Over the last decade, there has been a growing concern regarding the prevalence and extent of reproductive tract infections (RTIs) and other gynaecological disorders in women in the developing countries. For a proper understanding of gynaecological disorders (including reproductive tract infections - RTIs), it is important to have a common conceptual framework for defining the different types of morbidity that can occur in women. Morbidity in women can be categorized as reproductive or non-reproductive morbidity. Reproductive morbidity refers to diseases that affect the reproductive system, although not necessarily as a consequence of reproduction. Reproductive morbidity can be subdivided into three broad categories:

1). Obstetric/maternal morbidity, which covers morbidity in a woman who is, or has been, pregnant from any cause related to or aggravated by the pregnancy or its management, but not from accidental or incidental causes. Genitourinary prolapse and vesico-vaginal fistula are classified as obstetric morbidities. Both conditions are usually the direct result of multiple pregnancies and prolonged or obstructed labour respectively. Vesico-vaginal fistula can also be caused by crude attempts at induced abortion, female genital cutting and accidental injury during obstetric Surgery and pelvic irradiation.

2). Gynaecological morbidity, which covers any condition, disease or dysfunction of the reproductive system that is not related to pregnancy, abortion or childbirth, but may be related to sexual behaviour.

3). Contraceptive morbidity, which covers any condition that result from efforts (other than abortion) to limit fertility, whether they are traditional or modern methods. There is a considerable overlap between these subcategories. Infertility, for example, can have an obstetric cause but can also be the result ofa gynaecological morbidity.

However, the focus here is on gynaecological morbidity. Gynaecological morbidity can further be divided into reproductive tract infections, endocrine disorders, infertility, gynaecological cancers, congenital malformations or birth defects, injuries, sexual dysfunction, menopausal symptoms and others.

i). Reproductive tract infections include three different types of infection that affect the reproductive tract. These are:

- **Sexually transmitted infections:** These include, for example, chlamydial infection, gonorrhoea; trichomniasis, syphilis, chancroid, genital herpes, genital warts (caused by the human papilloma virus) and HI V. They are caused by viruses, bacteria or other microorganisms that are transmitted through sexual activity with an infected partner.
- **Endogenous infections:** These include bacterial vaginosis and candidiasis, which result from an overgrowth of organisms normally present in the vagina.
- **Latrogenic infections :** These are caused by the introduction of microorganisms into the reproductive tract through a medical procedure. Iatrogenic infections are acquired through a number of routes, including unhygienic delivery conditions and other procedures such as pregnancy termination, menstrual

regulation, IUD insertion, sterilization procedures and circumcision carried out under unhygienic conditions.

Reproductive tract infections are often categorized by the site of infection. Infections that cause inflammation of the external genital area and lower reproductive tract in women are referred to as vulvovaginitis or vaginitis, inflammation of the cervix as cervicitis, and infection of the upper reproductive tract as pelvic inflammatory disease.

ii). Endocrine or hormonal disorders can affect several aspects of reproduction, from menstruation to fertility. Menstrual disorders are frequently reported in studies on gynaecological morbidity and include problems with the regularity, frequency, volume and duration of menstrual bleeding, as well as, painful menstruation and premenstrual syndrome.

iii). Infertility can be caused by endocrine disorders, long-term sequelae of sexually transmitted infections, puerperal sepsis, post-abortion sepsis and congenital malformations. In many societies, the social and psychological consequences of infertility are severe. Infertility is, therefore, a component of many population- based studies of gynaecological morbidity.

vi) Gynaecological cancers include cancers of the cervix, breast, endometrium, ovary, vagina, vulva and rarely, the fallopian tube. Cervical cancer is the most common cancer in women in the developing world and is often fatal if it is not diagnosed early.

v) Other gynaecological morbidities cover congenital malformations or birth defects of the genital organs. These occur in almost infinite variations and are often not apparent until an adolescent fails to menstruate or a sexually active woman fails to conceive.

vi) Injuries include those caused by traditional practices (such as female genital mutilation), sexual abuse or accidents. Recently, sexual abuse and violence against women have gained recognition as major causes of reproductive morbidity.

vii) Sexual dysfunction can be caused by a variety of factors, including infertility, childhood sexual abuse, rape, female genital mutilation, fistula, genito-urinary prolapse, vaginal infections, congenital malformations, adhesions from injuries or inconsiderate partners.

viii) Menopausal symptoms include: (i) hormone-related gynaecological problems that occur around the menopause, and (ii) post-menopausal uterine bleeding and atrophic vaginitis (inflammation of the vaginal mucosa secondary to thinning and decreased lubrication of the vaginal walls caused by a decrease in oestrogen).

ix) Other gynecological morbidity includes endometriosis, ovarian cysts, uterine fibroids and polyps, and non-inflammatory and inflammatory diseases of the pelvic organs not attributable to sexually transmitted infections (for example, female genital tuberculosis and genital tract schistosomiasis).

Gynecological morbidity and family planning are closely linked. Symptoms of reproductive tract infections may be attributed to contraceptive methods and might

thus change attitudes towards contraception. For example, the insertion of an IUD or tubal ligation may induce iatrogenic infections; the surgical instruments are not properly sterilized. Also, IUD insertion They induce pelvic inflammatory disease if lower reproductive tract infections are present at the time of the procedure. Hormonal contraceptives may disturb the balance of the vaginal environment and cause endogenous infections. On the other hand, they may decrease the risk of pelvic inflammatory disease. Unfortunately, the methods that best prevent pregnancy (hormonal methods, IUDs and sterilization) are not the same methods that best prevent transmission of Transmitted Infections (STIs) (male and female condoms Dual protection (protection from both unwanted pregnancy and STIS, including HIV) can be achieved, among other ways, through the use of another method in conjunction with male or female condoms. An alternative is the use of condoms as the principal method of contraception, with the use of emergency contraception in the event of condom slippage or breakage. Given the information gaps that exist, the interaction between gynecological morbidity and family planning methods, strategies for dual protection and the development of new methods (such as vaginal microbicides) to prevent STYs, including HIV will be the important areas of research in the next decade.

## 12.9.2 Disorders of the Male Reproductive System

Infertility is the. inability to conceive (reproduce) after at learnt one of unprotected intercourse. Since most people are able to conceive within this time, physicians recommend-that couples unable to do so be assessed for fertility problems. In men hormonal disorders, illness, reproductive anatomy trauma and obstruction, and sexual dysfunction can temporarily or permanently affect sperm and prevent conception. We have learnt earlier that sperm development takes over 2 months. SO any illness that was present during the first cycle may affect mature sperm, regardless of a man's health at-the time of examination. Some disorders become more difficult to treat the longer they persist without treatment.

The Primary causes of male infertility are problems with sperm production or delivery. Impaired production or delivery may result from hormonal dysfunction; trauma or a defect in the reproductive system and illness. Some of the causes include:

- Cryptorchidism (failure of testes to descend, can impair spermatogenesis)
- Cystic fibrosis (may cause absence of sperm, vas deferens or seminal vesicles)
- Ductal obstruction (Caused by repeated infection, inflammation or developmental defect)
- metabolic disorder, causes iron deposition in the testes)
- Hormone dysfunction (caused by a disorder in the hypothalamic-pituitary-gonadal axis)
- Drugs
- Retrograde ejaculation
- Sexually transmitted diseases (STDs, cause obstruction, infection and scarring)

- Sickle cell anaemia (can cause hypogonadism)
- Systemic disease (fever, infection, kidney disease, metabolic disorder; can impair
- spermatogenesis)
- Testicular cancer
- Testicular trauma (damage to testes)
- Varicocele (a varicose vein in the network of veins. that run from the testicles).

Apart from these, there are certain inflammatory infections of the reproductive organs which are either specific or non-specific.

- **Penis:** Inflammation of the glands and the prepuce (a fold of skin covering the tip of the clitoris) can be specific or non-specific. In the non-specific, it could be due to lack Of personal hygiene. In case of phimosis (an abnormal- tightness of the foreskin preventing retraction over the glands), the orifice in the prepuce is too small to allow for its normal retraction. If the infection becomes chronic, there may be fibrosis of prepuce which increases the phimosis.

Urethra Gonococcal urethritis is the most common specific type of infection. Non-specific infection may be spread from. bladder (cystitis) or can occur due to catheterization, cytoscopy or surgery. Both types may spread throughout the system to prostrate, -seminar vesicles, epididymis and testes. Due to chronic infection, fibrosis may lead to' urethral stricture or obstruction.

- **Epididymis and testes:** Non-specific epididymitis and orchitis are usually due to infection from the urethra, followed by prostratectomy. Microbes spread through vas deferens or via lymph. Specific epididymitis is caused by gonorrhoea from urethra. It is usually caused by an infection, such as the sexually transmitted disease chlamydia and results in pain and swelling next to one of the testicles. Orchitis is more commonly caused by mumps, viruses, blood-borne from parotid \ glands. Acute inflammation with oedema occurs about a week after appearance of parotid swelling. The infection is usually unilateral, causes damage to germinal epithelium, results in Sterility. Hydrocele occurs when fluid collects in the membranes surrounding the testes. Hydroceles may cause swelling of the testicle but are generally painless. In some cases, surgery may be needed to correct' the condition.
- **Prostate gland:** Non-specific infections from urethra, bladder, catheterization, cytoscopy, urethral dilatation, partial resection of glands etc. causes prostatitis i.e. inflammation of the prostrate gland. Fibrosis may occur during healing causing urethral .stricture or obstruction. Beningn prostrate enlargement is common in men above 50 years. Though the cause is not clear, it could be due to acceleration of aging and decline in androgen secretion.
- **Tumors:** Generally testicular tumors. are malignant. They occur in children and young adults in whom the affected testes have not descended. Tumor tends to remain in the upper half of the gland and further spreads via the lymphatic pathways to retroperitoneal glands around the aorta, and around the level of the kidney. It is asymptomatic and painless initially. Later, it causes pain,

nausea, vomiting etc.

NOTES

## 12.10 CONTRACEPTION

What is contraception? Birth control by the use of devices (diaphragm or intrauterine device or condom) or drugs or surgery is referred to as contraception. There are various contraceptive methods available today. The most common artificial methods are male/female condoms, spermicidal, sponge, diaphragm, cervical cap, oral contraceptives (birth control pills), injectable contraceptions (Depo-Provera), IUDs and surgical sterilization. The following discussion presents information on the traditional, modern, irreversible and the newest contraceptive options available t8day. Hope you find the discussion informative.

### A) "Folk" methods

People have been using birth control for thousands of years. Even quite early on, people had a pretty good idea of what they needed to do to prevent conception. Different folk methods have been used for ages. These included:

- **Coitus interruptus** — It refers to the withdrawal of the penis from the vagina prior to ejaculation. In theory, this method is probably as effective as some more conventional methods. However, in practice, some of the semen frequently escapes prior to full withdrawal. This may be sufficient to initiate a pregnancy. This is an unreliable method.
- Postcoital douche Douching i.e. cleaning shortly after intercourse. Because sperm can make their way beyond the cervix within 90 seconds after ejaculation, this method is ineffective and unreliable.
- **Breastfeeding** — It is not true that women cannot become pregnant while breastfeeding. In about 6% of women, ovulation returns with the first cycle after delivery. Women who are breastfeeding infants and do not desire another pregnancy at that time need to use a reliable form of contraception.

### B) "Traditional " methods

Certain methods have been used for long, which we have included here as traditional methods. These include:

- **Condoms** — Condom, you may already know, is a thin sheath (preferably latex to also protect from transmission of disease-causing organisms) placed on the penis or, in the case Of the female, within the Vagina prior to intercourse. Semen is collected inside the condom, which must be carefully maintained in place and then removed after intercourse. Effectiveness of condoms is increased when spermicidal is also used. Condoms are readily available at low cost in most drug arid grocery stores. Some family planning clinics may offer free condoms. About 14 pregnancies occur over 1 year out of 100 couples using male condoms, and about 21 pregnancies occur over 1 year out of 100 couples using female condoms.

- **Vaginal spermicidal —** These are the sperm-killing chemical jellies, foams, creams, or suppositories, inserted into the vagina prior to intercourse. This method is readily available. All forms can be purchased in most drug and grocery stores. However, this method used by itself is not very effective. About 26 pregnancies occur over I year out of 100 women using this method alone, so spermicidal are often combined with other methods (such as condoms).
- **Diaphragm —** Flexible rubber cup that is filled with spermicidal cream or jelly, and then placed into the vagina, over the cervix, before intercourse. It should be left in place for 6 to 8 hours after intercourse. Diaphragms must be prescribed by a woman's health care provider, who determines the correct type and size of diaphragm for each woman. About 20 pregnancies occur over 1 year in 100 women using this method.
- **Vaginal contraceptive sponge —** Soft synthetic sponge, saturated with a spermicidal, which is moistened and inserted into the vagina, over the cervix, before intercourse. It is quite similar to the diaphragm as a barrier mechanism. After intercourse, the sponge should be left in place for 6 to 8 hours. This method is available without a prescription in most drug and grocery stores. About 18 to 28 pregnancies occur over 1 year out of 100 women using this method. This method was removed from the market a few years ago, but plans are underway to re-introduce it in the near future.
- **Fertility awareness with abstinence (natural family planning) —** This method involves observing a variety of body changes in the woman (such as, Cervical mucus changes, basal body temperature changes) and recording them on the calendar in an attempt to determine when ovulation occurs. The couple abstains from unprotected intercourse for several days before and after the assumed day ovulation occurs. This method requires special education and training in recognizing the body's changes, as well as, a great deal of continuous and committed effort. About 15 to 20 pregnancies occur over 1 year out of 100 women using this method (for women who are properly trained).

## C) "Modern " methods

Few modem methods of contraception include:

- Oral contraceptives (the method utilizes a combination of estrogen and progestin medications in doses that prevent ovulation and regulate cycles. A health care provider must prescribe oral (by mouth) contraceptives. The method is highly effective if the woman remembers to take her pill consistently at the same time each day. Oral antibiotics may decrease the effectiveness of birth control pills. Therefore, a backup method of contraception should be used while taking antibiotics and until the next menstrual period after completion of the antibiotic. Because of the wide variety of oral contraceptives, women who experience unpleasant side effects on one type of pill are usually able to adjust to a different oral contraceptive. It is important for women who are just starting on 'the pill" to communicate with their health care provider for optimal "matching" of the type of oral contraceptive to each patient. About 2

to 3 pregnancies occur over 1 year out of 100 women using this method.

- **Progestin-only oral contraceptive (the "mini-pill")** — This type of birth control pill does not contain any oestrogen component. It is therefore an alternative for those women who desire a highly effective method of contraception in a "pill" form, but are sensitive to oestrogen or cannot take a contraceptive containing oestrogen for other reasons. The effectiveness of progestin-only oral contraceptives is slightly less than that of the combination type. About 3 pregnancies occur over a 1 year period in 100 women using this method.
- **Progestin implants (such as Norplant)** — Six small progestin-containing rods are implanted surgically beneath the skin, usually under the upper arm, by a woman's health care provider. The rods release a continuous dose of progestin that inhibits ovulation, changes the lining of the uterus and thickens cervical mucus, which may prevent sperm from entering the uterus. The implants provide contraceptive protection for a period of 5 years. The method is highly effective. Less than 1 pregnancy occurs over I year out of 100 women using this type of contraception.
- **Hormonal injections (such as Depo-Provera)** A progestin injection is ordered by a woman's health care provider and given into the muscular tissue of the upper arm or buttocks. This injection prevents ovulation. A single shot provides contraceptive protection for up to 90 days. This method is highly effective and does not depend on patient compliance. Less than I pregnancy occurs over 1 year in 190 women using this method.
- **Intrauterine contraceptive device (IUD)** — It is a small plastic or copper device, placed inside the woman's uterus by the health care provider, which changes the uterine environment to prevent pregnancy. IUDs may be left in place for up to ten years in some patients. The method should not be used by women who have a history of pelvic infection, ectopic pregnancy (a pregnancy in which a fertilized egg begin to develop outside the uterus i.e. in the fallopian tube) or who have more than one sexual partner (and are therefore at higher risk for acquiring sexually transmitted diseases). Depending on the IUD used, 1 to 3 pregnancies occur per year out of 100 wo men using this type .

## D) Permanent or irreversible methods

A number of permanent or irreversible methods of contraception are available. These include:

- **Tubal ligation** — this procedure is the most commonly used method of female sterilization. .Tubal ligations are usually done in an outpatient surgical center. During tubal ligation, a woman's fallopian tubes are cut, sealed or obstructed by a special clip, preventing eggs and sperm from entering the tubes, thus preventing conception. The operation can sometimes be reversed if a woman later chooses to become pregnant. Following tubal ligation reversal, about 60% to 80% of women eventually become pregnant. However, it is best to consider tubal ligation a perm-anent form of contraception.

- **Vasectomy -** A vasectomy is a simple, permanent sterilization procedure for men. The operation, usually done in a physician's office, requires cutting and sealing the vas deferens (tubes in the male reproductive system that carry sperm.) Like tubal ligations, vasectomies can sometimes be reversed through a vasovasectomy, an operation to reattach and open the vas deferens. Men who undergo vasovasectomies have a 30% to 40% chance of fathering children. However, it is best to consider vasectomy a permanent form of contraception. Other than the methods discussed above, few new contraceptive options have emerged.

## The newest contraceptive option

- **the Vaginal Ring -** If you want the newest, easy to use, once a month contraceptive method, ask your doctor about the vaginal ring. The vaginal ring is a new contraceptive method that offers protection against pregnancy without the inconvenience of barrier methods, spermicidal or remembering to take a daily pill.

## How does it work?

The ring is a unique "combined" hormonal contraceptive method which consists of a flexible, transparent, plastic ring of about 2 inches (5.4 cm) in diameter and about 1/8" (4 mm) thick. The ring contains hormones — oestrogen and a progestogen similar to the ones found in combined oral contraceptives (the pill). The ring is inserted into the vagina. The ring is left in place for 3 consecutive weeks, the same number of days that is in one cycle of oral contraceptive pills. During this period, it releases a steady low dose of hormones which prevent pregnancy by stopping the release of a mature egg (ovulation). After three weeks, the ring is removed to make way for a menstrual period, after a ring-free period of I week a new ring is inserted for another three weeks and so on.

## How effective is it?

When used as directed, the ring provides a reliable and high degree of protection against pregnancy. The reliability is comparable to that of the pill. The exact position of-the ring in the vagina is not critical for its action. As long as it feels comfortable, the ring is in the right position and will release the hormones necessary for contraception.

## The Male "Pill"

Male contraceptive research is beginning to yield a number of leads in the area of male contraception. Studies are now underway to test hormonal methods of birth control which will provide safe, reliable and reversible male contraception. One method currently under consideration is a combination of two hormones that stop the production of sperm. More studies are being done to determine whether an oral pill, an implant or injection, or a combination of these would be most effective. The promise of male contraception would means that men will also be able to

share the responsibility for birth control with their female partners. Emergency Contraception

What do you do if you've had unprotected sex or the birth control method you were using failed? Don't panic. Your next step may be the emergency contraceptive pill (ECP) one of the best-kept health secrets of modem contraception. ECP is available from your doctor, hospital or birth by prescription. ECP can*be useful for preventing pregnancy in many situations including:

- condom breaks
- a diaphragm moves out of position
- you forget your method of contraception and have unprotected sex
- you missed taking your oral contraceptive pills
- you are forced into having sex
- you miscalculate your most "fertile" days and have sex without birth control

### How does emergency contraception work?

There are basically two types of emergency contraception available:

- **The Emergency Contraceptive Pill (ECP) method -** The ECP method or ' 'morning after pill" uses a high dose of combined oral contraceptives (OCs) to prevent conception. The OC method is effective if used within 72 hours after unprotected intercourse.
- **The Intrauterine Device (IUD) method -**This method involves the insertion of an IUD into the uterus by your doctor. The IUD creates an unfriendly environment for egg and sperm. The IUD must be inserted within 7 days of unprotected sex. Emergency or the "morning after" pill consists of two doses of hormone pills taken as soon as possible within 72 hours after unprotected intercourse. The pill may prevent pregnancy by temporarily blocking eggs from being produced, by stopping fertilization or keeping a fertilized egg from becoming implanted in the uterus. The morning-after pill is reserved for emergency situations and not as a regular method of birth control. Emergencies include being raped, having a condom break or slip off during sex, missing two or more birth control pills during a monthly cycle, and haying unplanned sex. With emergency contraception, we end our study on contraception.

## 12.11 COMMON TESTS DURING PREGNANCY

Pregnancy, as you may have realized, is a period of physiological stress. To ensure a successful pregnancy, few common tests are recommended. The following are some of the more common tests performed during pregnancy:

- Alpha-fetoprotein screening (multiple marker screening)
- Arnniocentesis
- Chorionic villus sampling

- Foetal monitoring
- Glucose tolerance test
- Group B strep culture
- Ultrasound
- Genetic screening

## Alpha-fetoprotein screening (AFP)

This is a blood test that measures the level of alpha-fetoprotein in the mothers' blood during pregnancy. AFP is a protein normally produced by the foetal liver and is present in the fluid surrounding the foetus (amniotic fluid), and crosses the placenta into the mother's blood. The AFP blood test is also called MSAFP (maternal serum AFP).

Abnormal levels of AFP may signal the following:

- pen neural tube defects (ONTD) such as spina bifida
- Down syndrome
- other chromosomal abnormalities
- defects in the abdominal wall of the foetus
- twins - more than one foetus is making the protein
- a miscalculated due date, as the levels vary throughout pregnancy

AFP screening may be included as one part of a 2-, 3-, or 4-part screening, often called a multiple marker screen. The other parts are:

- **HCG -** human chorionic gonadotropin hormone (a hormone produced by the placenta).
- **Estriol —** a hormone produced by the placenta.
- **Inhibin —** a hormone produced by the placenta.

Abnormal test results of AFP and other markers may indicate the need for additional testing. Usually an ultrasound is performed to confirm the dates of the pregnancy and to look at the foetal spine and other body parts for defects. An amniocentesis may be needed for accurate diagnosis.

Multiple marker screening is not diagnostic. This means it is not 100 percent accurate, and is only a screening test to determine who in the population should be offered additional testing for their pregnancy. There can be false-positive results — indicating a problem when the foetus is actually healthy or false negative results — indicating a normal result when the foetus actually does have a health problem.

## How is an alpha-fetoprotein test performed?

Although the specific details of each procedure vary slightly, generally, an alpha-fetoprotein test follows this process:

- Blood is usually drawn from a vein between the 15th and 20th weeks of pregnancy (16th to 18th is ideal).
- The blood sample is then sent off for laboratory analysis.

NOTES

- Results are usually available within one to two weeks or less, depending on the laboratory.

## Amniocentesis

An amniocentesis is a procedure used to obtain a small sample of the amniotic fluid that surrounds the foetus to diagnose chromosomal disorders and open neural tube defects (ONTDs) such as spina bifida. Testing is available for other genetic defects and disorders depending on the family history and availability of laboratory testing at the time of the procedure. An amniocentesis is generally offered to women between the 15th and 20th weeks of pregnancy who are at increased risk for chromosome abnormalities, such as women who are over 35 years of age at delivery, or those who have had an abnormal maternal serum screening test, indicating an increased risk for a chromosomal abnormality or neural tube defect.

Chorionic villus sampling (CVS)

- **Chorionic villus sampling (CVS) is a prenatal test -** involves taking a sample of some of the placental tissue. This tissue contains the same genetic material as the foetus and can be tested for chromosomal abnormalities and some other genetic problems. Testing is available for other genetic defects and disorders depending on the family history and availability of laboratory testing at the time of the procedure. In comparison to amniocentesis, CVS does not provide information on neural tube defects such as spina bifida.

For this reason, women who undergo CVS also need a follow-up blood test between 16 to 18 weeks of their pregnancy, to screen for neural tube defects. Some women may not be candidates for CVS or may not obtain results that are 100 percent accurate, and may therefore, require a follow-up amniocentesis. In some cases:- there is an active vaginal infection such as herpes or gonorrhea, which will prohibit the procedure. Other times, the physician obtains a sample that does not have enough tissue to grow in the laboratory such that results are incomplete or inconclusive.

## Foetal monitoring

During late pregnancy and during labour, a physician may want to monitor the foetal heart rate and other functions. Foetal heart rate monitoring is a method of checking the rate and rhythm of the foetal heartbeat. The average foetal heart rate is between 110 and 160 beats per minute. The foetal heart rate may change as the foetus responds to conditions in the uterus. An abnormal foetal heart rate or pattern may mean that the foetus is not getting enough oxygen or there are other problems, An abnormal pattem may also mean that an emergency or cesarean delivery is needed.

## Glucose tolerance test

A glucose tolerance test, usually conducted in the 24 to 28 weeks of pregnancy, measures levels of sugar (glucose) in the mother's blood. Abnormal glucose levels may indicate gestational diabetes.

## How is a glucose tolerance test performed?

Although the specific details of each procedure vary slightly, generally, a glucose tolerance test follows this process:

The mother-to-be may be asked to only drink water on the day the glucose tolerance test is given. An initial fasting sample of blood is drawn from a vein. Then the subject is given a special glucose solution to drink. Blood will be drawn several times over the course of several hours to measure the glucose levels in the body.

## Group B strep culture

Group B Streptococcus (GBS) are bacteria found in the lower genital tract of 15 to 40 percent of all women. GBS infection usually causes no problems in women before pregnancy, but can cause illness in the mother during labour. GBS may cause chorioamnionitis (a severe infection of the placental tissues) and postpartum infection.

GBS is the most common cause of life-threatening infections in newborns, including pneumonia and meningitis. Newborn babies usually contract the infection from the mother's genital tract during labour and delivery. Treatment of mothers with certain risk factors or positive cultures may reduce the risk of transmission of GBS to the baby. However, no treatment has been shown to completely prevent early onset of GBS.

## ultrasound

An ultrasound scan is a diagnostic technique which uses high-frequency sound waves to create an image of the internal organs. A screening ultrasound is sometimes done during the course of a pregnancy to check normal foetal growth and verify the due date. Ultrasounds may be performed at various times throughout pregnancy for different reasons, which we shall not dwell upon in this unit. Ultrasound is a technique that is constantly being improved and refined. As with any test, results may not be completely accurate. However, ultrasound can provide valuable information for parents and health care providers to help manage and care for the pregnancy and foetus.

## What is genetic screening?

Many genetic abnormalities can be diagnosed before birth. A physician may recommend genetic testing during the pregnancy if you or your partner have a family history' of genetic disorders and/or you have had a baby with a genetic abnormality.

Exarnples of genetic disorders that can be diagnosed befote birth include the following:

- cystic fibrosis
- duchenne muscular dystrophy
- hemophilia A

- thalassemia
- sickle cell anaemia
- polycystic kidney disease, and
- Tay-Sachs disease

### What genetic Screening methods include?

Genetic screening methods include the following:

- ultrasound scan
- alpha-fetoprotein test (AFP) or multiple marker test
- chorionic villus sampling (CVS)
- amniocentesis, and
- percutaneous umbilical blood sampling (withdrawing a small sample of the foetal
- blood from the umbilical cord).

## 12.12 LET US SUM UP

In this unit, we learnt about physiology of reproductive system, where we got an in- depth knowledge about female and male reproductive organs. We saw the role of hormones involved in development and functioning of these organs.

Various physiological changes occurring during pregnancy and lactation were also emphasized. The various disorders of both female and male reproductive systems that could affect their normal functioning were also discussed in this unit.

Further, the unit focused on the issue of the different folk, traditional, modem and latest methods along with their drawbacks and benefits. Finally, in the last section, we learnt about various pregnancy determination tests.

## 12.13 GLOSSARY

**Amniotic fluid** : liquid that surrounds unborn child within the membranes inside the uterus.

**Benign-neoplasm** : a tumor-like overgrowth of tissue normally found in the area.

**Catheterization** : a procedure done to examine the structure and contents of chambers.

**Chancroid** : a disease known to be spread solely through sexual contact.

**Chlamydiasis** : sexually transmitted infection caused due to bacteria Chlamydia trachomatis.

**Chorion** : one of the membranes that encloses the foetus within the uterus.

**Down syndrome** : a combination of birth defects caused by the presence of an extra throm osome.

**Fibroids** : non-cancerous growth in or within the walls of the uterus.

**Gametes** : the reproductive cells in multicellular organisms that unite during sexual reproduction.

**Graanflan follicle** : a vascular body in a mammalian ovary enclosing a developing egg.

**Gynaecomastia** : an excessive development of the breasts in males, usually results from hormonal imbalance.

**Lactiferous ducts** : ducts of the mammary gland that carry milk to the nipple.

**Neural Tube Defect** : birth defects that occur very early in pregnancy leading to abnormalities in the development of spinal cord and brain.

**Polyp** : a structure consisting of a rounded head which grows outward from a broad base or stalk.

**Pyelonephritis** : the inflammation of the drainage system of the kidneys, one of the causes of kidney failure.

**Spina bifida** : a birth defect in which the neural tube fails to close during fetal development and a portion of the spinal cord and nerves fail to develop properly.

**Syphilis** : a disease usually transmitted by sexual contact that can cause malformation in unborn baby.

**Vestibule** : a body cavity leading to another cavity.

## 12.14 CHECK YOUR PROGRESS

**NOTES**