UNIT 1: THERMOREGULATION AND RESPIRATION

CONTENT

1.1OBJECTIVES

Study of this unit will let the students to:

i. Explain Respiration

ii. Describe organs of respiratory system and respiratory pigments

iii. Understand the mechanism of Gaseous transport

iv. Explain the Gaseous exchange

v. Understand the Respiratory Pigment

1.2 INTRODUCTION

Respiration is essential for the survival of the organisms. It is an involuntary process that is common to almost all the organisms. Although the mode of the respiration can be different for different groups of organisms depending on their habitat and other factors, it remains the central process for sustaining the life. All life forms have optimized their way of respiration and have evolved as such. They have the specialized organs to achieve that. In mammals the inhaled oxygen helps in the oxidation of the digested food products and thus in turn helps in production of energy for the other metabolic processes. It is a co-ordinated effort of many organ systems of the body which work tirelessly to maintain the required level of the oxygen in the body. Our bodies have been evolved in such a way that they need oxygen (O2) for cellular oxidation and in turn release carbon dioxide (CO2). Any interference in this routine is not good for the body and may prove fatal.

1.3 CONCEPT OF POIKILOTHERMY AND HOMEOTHERMY

A **poikilotherm** is an animal whose internal temperature varies considerably. Poikilotherms have to survive and adapt to environmental stress. One of the most important stressors is temperature change, which can lead to alterations in membrane lipid order and can cause protein unfolding and denaturation at elevated temperatures. It is the opposite of a homeotherm, an animal which maintains thermal homeostasis. While the term in principle can apply to all organisms, it is generally only applied to animals, and mostly to vertebrates. Usually the fluctuations are consequence of variation in the ambient environmental temperature. Many

terrestrial ectotherms are poikilothermic. However some ectotherms remain in temperature-constant environments to the point that they are actually able to maintain a constant internal temperature (i.e.are homeothermic). It is this distinction that often makes the term "poikilotherm" more useful than the vernacular "cold-blooded", which is sometimes used to refer to ectotherms more generally.

Homeothermy is one of the three types of thermoregulation in warm-blooded animal species. **Homeothermy's** opposite is **poikilothermy**. A **poikilotherm** is an organism that does not maintain a fixed internal temperature but rather fluctuates based on their environment and physical behaviour.

Homeothermy, **homothermy** or **homoiothermy** is thermoregulation that maintains a stable internal body temperature regardless of external influence. This internal body temperature is often, though not necessarily, higher than the immediate environment (from Greek *homoios* "similar" and *thermē* "heat"). Homeothermy is one of the three types of thermoregulation in warm-blooded animal species. Homeothermy's opposite is poikilothermy. A poikilotherm is an organism that does not maintain a fixed internal temperature but rather fluctuates based on their environment and physical behaviour.

Homeotherms are *not* necessarily endothermic. Some homeotherms may maintain constant body temperatures through behavioral mechanisms alone, *i.e.*, behavioral thermoregulation. Many reptiles use this strategy. For example, desert lizards are remarkable in that they maintain near-constant activity temperatures that are often within a degree or two of their lethal critical temperatures.

1.4 SURVIVAL MECHANISM IN POIKILOTHERMS AND HOMEOTHERMS

Poikilothermic animals must be able to function over a wider range of temperatures than homeotherms. The speed of most chemical reactions vary with temperature, and in order to function poikilotherms may have four to ten enzyme systems that operate at different temperatures for an important chemical reaction. As a result, poikilotherms often have larger, more complex genomes than homeotherms in the same ecological niche. Frogs are a notable

example of this effect, though their complex development is also an important factor in their large genome.

Because their metabolism is variable and generally below that of homoeothermic animals, sustained high-energy activities like powered flight in large animals or maintaining a large brain is generally beyond poikilothermic animals. The metabolism of poikilotherms favors strategies such as sit-and-wait hunting over chasing prey for larger animals with high movement cost. As they do not use their metabolisms to heat or cool themselves, total energy requirement over time is low. For the same body weight, poikilotherms need only 5 to 10% of the energy of homeotherms.

Adaptation in Poikilotherms

- Some adaptations are behavioral. Lizards and snakes bask in the sun in the early morning and late evening, and seek shelter around noon.
- The eggs of the yellow-faced bumblebee are unable to regulate heat. A behavioral adaptation to combat this is incubation, where to maintain the internal temperatures of eggs, the queen and her workers will incubate the brood almost constantly, by warming their abdomens and touching them to the eggs. The bumblebee generates heat by shivering flight muscles even though they are not flying.
- Termite mounds are usually oriented in a north–south direction so that they absorb as much heat as possible around dawn and dusk and minimize heat absorption around noon.
- Tuna are able to warm their entire bodies through a heat exchange mechanism called the rete mirabile, which helps keep heat inside the body, and minimizes the loss of heat through the gills. They also have their swimming muscles near the center of their bodies instead of near the surface, which minimizes heat loss.
- Gigantothermy means growing to large size in order to reduce heat loss, such as in sea turtles and ice-age mega fauna. Body volume increases proportionally faster than does body surface, with increasing size; and less body surface area per unit body volume tends to minimise heat loss.
- Camels, although they are homeotherms, thermoregulate using a method termed "temperature cycling" to conserve energy. In hot deserts, they allow their body temperature

to rise during the day and fall during the night, adjusting their body temperature to cycle over approximately 6 °C.

- As ambient temperatures increase, **homeotherms** use evaporative cooling through sweating and/or panting to regulate body temperatures, and also vasodilate surface blood vessels to promote heat loss.

1.5 COLD RESISTANCE AND COLD DEATH, HEAT RESISTANCE AND HEAT DEATH

Hypothermia is defined as a body core temperature below 35.0 °C (95.0 °F) in humans. Symptoms depend on the temperature. In mild hypothermia, there is shivering and mental confusion. In moderate hypothermia, shivering stops and confusion increases in severe hypothermia, there may be paradoxical undressing, in which a person removes their clothing, as well as an increased risk of the heart stopping.

Hypothermia has two main types of causes. It classically occurs from exposure to extreme cold. It may also occur from any condition that decreases heat production or increases heat loss. Commonly this includes alcohol intoxication but may also include low blood sugar, anorexia, and advanced age. Body temperature is usually maintained near a constant level of 36.5–37.5 °C (97.7–99.5 °F) through thermoregulation. Efforts to increase body temperature involve shivering, increased voluntary activity, and putting on warmer clothing. Hypothermia may be diagnosed based on either a person's symptoms in the presence of risk factors or by measuring a person's core temperature.

The treatment of mild hypothermia involves warm drinks, warm clothing, and physical activity. In those with moderate hypothermia, heating blankets and warmed intravenous fluids are recommended. People with moderate or severe hypothermia should be moved gently. In severe hypothermia, extracorporeal membrane oxygenation (ECMO) or cardiopulmonary bypass may be useful. In those without a pulse, cardiopulmonary resuscitation (CPR) is indicated along with the above measures. Rewarming is typically continued until a person's temperature is greater than 32 °C (90 °F). Hypothermia is the cause of at least 1,500 deaths a year in the United States. It is more common in older people and males. One of the lowest documented body temperatures

from which someone with accidental hypothermia has survived is 13.0 °C (55.4 °F) in a near-drowning of a 7-year-old girl in Sweden. Survival after more than six hours of CPR has been described. In individuals for whom ECMO or bypass is used, survival is around 50%.Deaths due to hypothermia have played an important role in many wars. The term is from Greek*hupo*, meaning "under", and *thermia*, meaning "heat". The opposite of hypothermia is hyperthermia, an increased body temperature due to failed thermoregulation.

Hypothermia usually occurs from exposure to low temperatures, and is frequently complicated by alcohol consumption. Any condition that decreases heat production, increases heat loss, or impairs thermoregulation, however, may contribute. Thus, hypothermia risk factors include: substance use disorders (including alcohol use disorder), homelessness, any condition that affects judgment (such as hypoglycemia), the extremes of age, poor clothing, chronic medical conditions (such as hypothyroidism and sepsis), and living in a cold environment. Hypothermia occurs frequently in major trauma, and is also observed in severe cases of anorexia nervosa. Hypothermia is also associated with worse outcomes in people with sepsis. While most people with sepsis develop fevers (elevated body temperature), some develop hypothermia.

The **heat death of the universe** (also known as the **Big Chill** or **Big Freeze**) is a theory on the ultimate fate of the universe, which suggests the universe would evolve to a state of no thermodynamic free energy and would therefore be unable to sustain processes that increase entropy. Heat death does not imply any particular absolute temperature; it only requires that temperature differences or other processes may no longer be exploited to perform work. In the language of physics, this is when the universe reaches thermodynamic equilibrium (maximum entropy).

If the topology of the universe is open or flat, or if dark energy is a positive cosmological constant (both of which are consistent with current data), the universe will continue expanding forever, and a heat death is expected to occur, with the universe cooling to approach equilibrium at a very low temperature after a very long time period.

The hypothesis of heat death stems from the ideas of Lord Kelvin, who in the 1850s took the theory of heat as mechanical energy loss in nature (as embodied in the first two laws of thermodynamics) and extrapolated it to larger processes on a universal scale.

The idea of heat death stems from the second law of thermodynamics, of which one version states that entropy tends to increase in an isolated system. From this, the hypothesis implies that if the universe lasts for a sufficient time, it will asymptotically approach a state where all energy is evenly distributed. In other words, according to this hypothesis, there is a tendency in nature to the dissipation (energy transformation) of mechanical energy (motion) into thermal energy; hence, by extrapolation, there exists the view that, in time, the mechanical movement of the universe will run down as work is converted to heat because of the second law.

1.6 RESPIRATORY ORGANS IN DIFFERENT ANIMALS

Respiration is an oxidation process which involves degradation of a complex organic compound, hence carbon dioxide and water and energy are produced. Respiration process can be divided into two phases:

External Respiration or Breathing

In this process, animals intake oxygen and release carbon dioxide. It is also known as breathing. This is mainly two phases.

- Inspiration: It is the process by means of which oxygen is taken to the lungs.
- Expiration: During expiration, carbon dioxide is expelled out from the respiratory organs into the environment.

Internal Respiration or Cellular Respiration

In this process, oxygen is used in chemical reactions within the cells. These reactions release energy from food substances and produced carbon dioxide and water as waste products.

$$Sugar+O2 \longrightarrow CO2+H2O+Energy$$

Respiration in Animals

The mode of external respiration varies greatly from organism to organism. The basic process of respiration (cellular respiration) is similar in all living organisms. The process of exchange gases varies in different animals.

Through Plasma Membrane

In unicellular animals, such as amoeba, exchange of gases takes place through cell surface. They absorb oxygen from the surrounding air or water and give out carbon dioxide through plasma membrane by diffusion.

Through Body Wall or Skin

Tapeworms, earthworms, and leeches use their skin for the exchange of gases. The skin of Earthworms is very thin and moistened. Many blood cells are spread on this skin. These blood cells are known as capillaries. The exchange of gases occurs at capillaries. They die of suffocation if their skin is dried up.Amphibians such as frogs use more than one organ of respiration during their life. They breathe through gills while they are tadpoles. Mature frogs breathe mainly with lungs and also exchange gas with the environment through skin.

Through Tracheal System

In insects like cockroaches, grasshopper, transportation of gas or gaseous exchange take place by a special type of fine tubes is called tracheae. Air containing oxygen enters through spiracles into the tracheal tubes. It then diffuses into the body tissue and reaches every cell in the body. Carbon dioxide released from the cells goes into the tracheal tubes and comes out through spiracles.

Through Gills

A majority of aquatic animals like fish and prawns breathe through special organs called gills. Gills are projections of the skin that help in using oxygen dissolved in water. Gills contain blood vessels which help in exchange of gases.

Fish live in water. To get oxygen dissolved in water, fish gulp water through the mouth and pump it over the gills. Water passes into the gill chamber through gill slits. In each chamber, the water passes over the filaments. They absorb oxygen from the water and replace it with carbon dioxide formed. The water then passes out through the gill opening and this process is repeated again and again.

Through lungs

Amphibians, mammals, and birds exchange gases through special respiratory organs called lungs. Lungs are air-filled sac-like structures in the chest cavity. They are connected to the outside by a series of tubes and small opening.

Respiratory organs in Humans:

The respiratory system consists of **respiratory passage, lungs and associated organs**. The respiratory passage consists of **nostrils (external nares), nasal chambers, internal nares, pharynx, epiglottis, larynx (Voice box), trachea** or **wind pipe**, and two **bronchi**. Air enters through the external nares or nostrils and enters into pharynx through internal nares. Larynx is a cartilaginous tissue that is situated between pharynx and trachea. It is called sound box as it is associated with voice production. Epiglottis is part of larynx that serves as lid for closing of larynx during swallowing of food. Larynx is followed by the trachea which is a tubular structure about 4.5 inches long and a diameter of about 1 inch. It further extends through the neck region into the thorax where it divides into two branches called the right and the left bronchi. The trachea is provided with a series of 15-20 C-shaped cartilage rings which prevent the trachea from collapsing. The right and the left bronchi enter the respective lungs and further subdivide into smaller tubes. Right lung has three primary lobes while left has two, thus the right bronchus divides initially into three while left bronchus divides into two main bronchial branches. The bronchial tubes have the same cartilaginous rings as that of trachea. The bronchi further continue to divide smaller and smaller and are called bronchioles which have a diameter of 1mm or less. This branching is important to increase the available surface area for gaseous exchange.

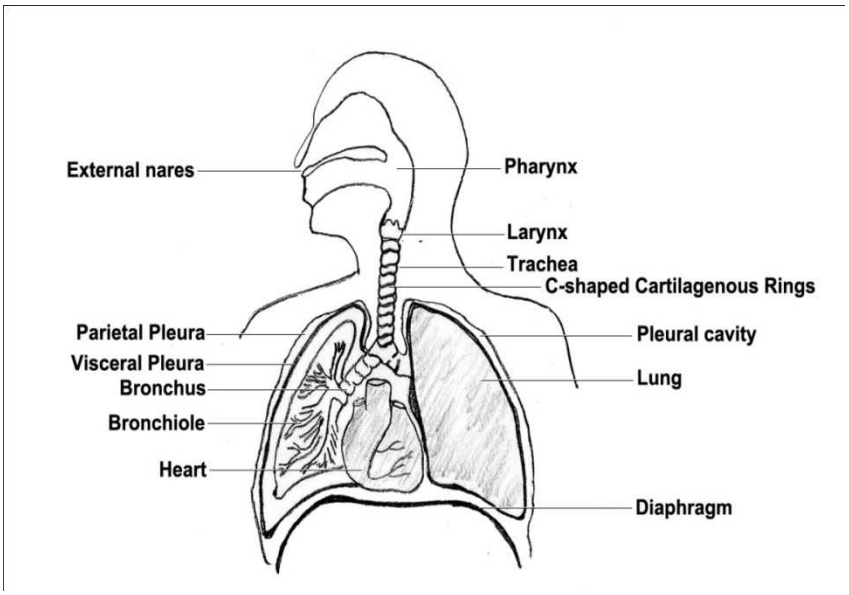


Fig 1.1 Respiratory System of Humans

Lungs: The bronchioles further divide and subdivide and terminate into a balloon like air sac called alveoli. Alveoli are the physiological unit of the lungs. There are numerous (about 7.5 x 10^8) alveoli in human lungs which makes the total surface area of about 100 square meters. The respiratory tract is lined by the ciliated columnar epithelial cells. The cilia beat synchronously propelling mucus and foreign bodies outwards for expulsion through trachea. The walls of the pulmonary or lung alveoli on the other hand are simply composed of a single layer of cuboidal non-ciliated cells. The alveoli are surrounded by an extensive network of capillaries. These capillaries are fed blood by pulmonary artery. The exchange of the gases takes place in the alveoli.

The alveolar wall is permeable only to gases and does not allow plasma to enter. The blood in the capillaries is only 10 mm Hg which is not enough for the diffusion of the plasma from the capillaries.

Each lung consists of its bronchial tree with many air sacs and alveoli unit together associated with blood vessels, nerves and pleura. All of these structures are associated supported and attached to each other by the connective tissue. They are covered externally by the visceral pleura and surrounded by the similar layer called parietal pleura forming a thin lining of the wall of the chest. Pleural cavity is filled with small amount of pleural fluid which prevents the friction of the lungs during breathing movements. The diaphragm is a dome shaped structure that forms the floor of the chest cavity and separates it from abdomen.

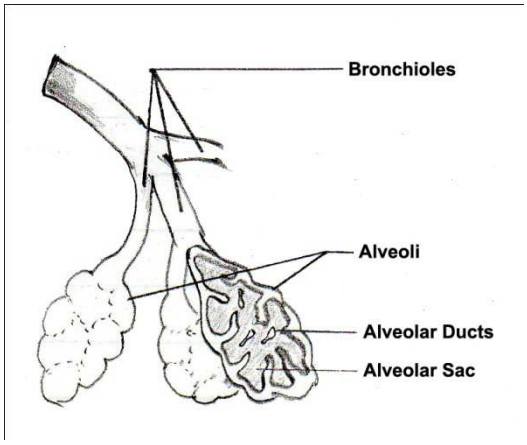


Fig1.2 Structural organization of Alveoli

1.7 TRANSPORT OF OXYGEN AND CARBON DIOXIDE

Oxygen has very low solubility in plasma (~0.3 ml/100ml). Most of the oxygen is carried by hemoglobin in the form of oxyhemoglobin. Most of the CO_2 on the other hand is transported by plasma in the form of soluble bicarbonates.

i) Transport of Oxygen: Oxygen is carried by hemoglobin which is found in red blood cells. The maximum amount of O_2 that normal human blood can absorb is 20 ml per 100 ml of blood. During the passage of oxygen from lung alveoli to lung capillaries, diffusion of oxygen occurs in to the blood and it is captured by the hemoglobin to form oxyhemoglobin.

$Hb_4 + 4O_2 \rightleftharpoons Hb_4(O_2)_4$

(Oxyhemoglobin)

Each molecule of hemoglobin has 4 iron atoms; therefore it can carry 4 molecules of oxygen. Normally, the arterial blood which has been exposed to the alveoli of the lungs is not completely oxidized. At the O_2 pressure of 100 mm Hg, blood is about 98 % saturated and therefore contain 19.6 ml of O_2 per 100 ml. About 0.2 -0.3 ml of O_2 is dissolved in plasma. The arterial blood and the alveoli have the same O_2 pressure (100 mm of Hg). But in the cells and tissues of the body the O_2 tension is quite low (1 to 40 mm of Hg). Now since the co-ordination of the oxygen with the hemoglobin is reversible, it dissociates from the oxyhemoglobin and diffuses into the cells. This phase is important to supply oxygen to cells as well as regenerate hemoglobin for further transport cycle.

$Hb_4(O_2)_4 \longrightarrow 4Hb + 4O_2$

(Oxyhemoglobin)

The reduced hemoglobin is transported back via blood to the lungs.

Oxygen hemoglobin dissociationcurve:

The binding of oxygen to hemoglobin is influences by four factors viz. partial pressure of oxygen and carbon–dioxide, temperature, H^+ concentration and 2,3-diphosphoglyceraldehyde (2,3-DPG). The quantity of oxygen that can be held by hemoglobin depends on the partial pressure of

oxygen (PO_2). The relationship between the two can be graphically represented by a curve called oxygen-hemoglobin dissociation curve. The curve is sigmoid (S-shaped) in nature.

The important feature of the oxygen-hemoglobin dissociation curve is that hemoglobin takes up oxygen when the partial pressure of the latter is high; oxyhemoglobin dissociates when the PO_2 is low. The hemoglobin is almost completely saturated at O_2 tension of 100 mm of Hg. But as the oxygen pressure drops below 60 mm of Hg, it dissociated rapidly thus forming the steep slope of the curve. When PO_2 is zero, all of the oxyhemoglobin is dissociates into hemoglobin. The actual relationship between the partial pressure of O_2 and the degree of saturation of the hemoglobin with O_2 is shown by Oxygen-hemoglobin dissociation curve (Fig. 1.3).

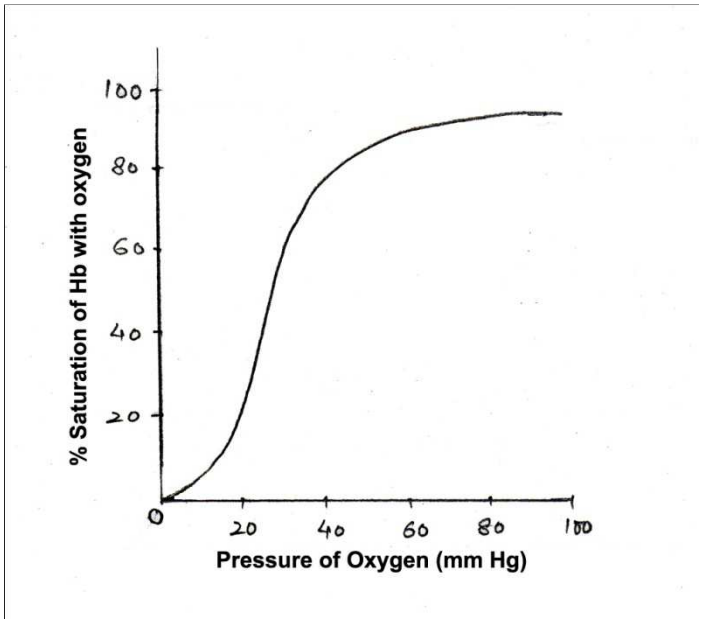


Fig 1.3 Oxygen-hemoglobin dissociation curve: shows the relationship between the partial pressure of the oxygen and the formation of oxyhemoglobin.

Hemoglobin gets saturated at about 100 mm Hg pressure and no more oxygen can be taken up even if the pressure is increased. Inside tissues where the partial pressure of oxygen is less the oxygen is rapidly dissociated from the oxyhemoglobin, thus yielding the larger quantities of the O_2 to the surrounding tissues and cells where it is needed most.

During exercise or hard physical work, the partial pressure of oxygen falls in tissues accompanied by the increase in pH, local temperature and increase in 2,3-DPG concentration. All these factors combined promote the dissociation of oxyhemoglobin to release more oxygen.

Factors that affect the oxygen hemoglobin binding

a) Effect of Partial pressure of CO_2: Partial pressure of CO_2 (PCO_2) also determines the equilibrium of Hb and O_2. An increase in the CO_2 shifts the curve to the right known as Bohr effect.A higher CO_2 concentration causes more oxygen to be dissociates at any given O_2 pressure. This phenomenon is important in tissues where the concentration of CO2 is relatively higher and they need oxygen. As soon as the oxygenated blood reached these cells the higher pressure of CO_2 from tissues forces the oxyhemoglobin to dissociate and thus supply the bound oxygen into the cell. Bohr Effect therefore results in delivery of additional oxygen into the tissues. Similarly when the blood is again oxygenated in the alveoli of the lungs, it reduces the CO_2 carrying capacity of the blood, thus facilitating the release of CO_2 to the alveoli.

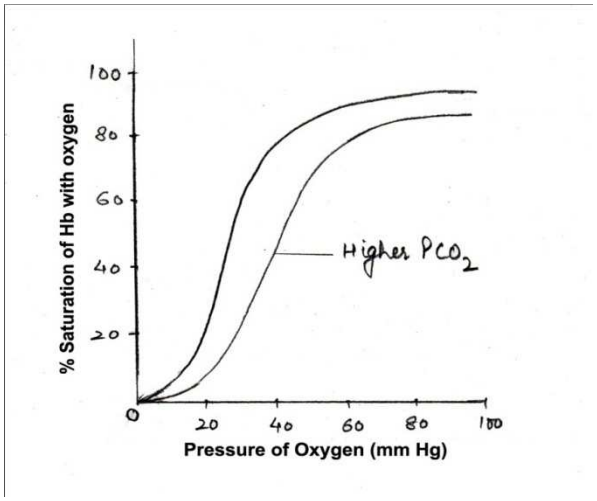


Fig 1.4 Oxygen-hemoglobin dissociation curve: Increase in concentration/ pressure of CO_2 shifts the curve to the right

b)Effect of temperature: A rise in temperature decreases the oxygen carrying capacity of lungs. When muscle activity is increased during exercise or physical work, the rise in local temperature results in splitting of oxyhemoglobin to hemoglobin and thus in turn releasing of higher amount

of oxygen in tissues. Therefore, temperature affects the dissociation curve of O_2 by affecting the partial pressure of oxygen.

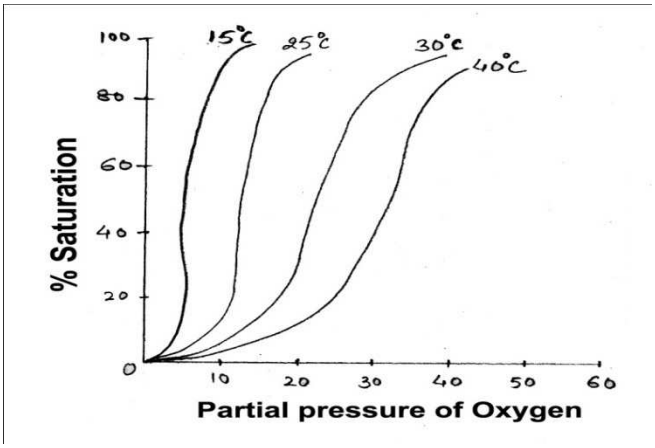


Fig 1.5 Effect of increasing temperature on the Oxygen-hemoglobin dissociation curve.

c) Effect of hemoglobin: Since the quantity of oxygen transported by blood is directly proportional to the amount of the hemoglobin present, it is obvious that the blood containing less hemoglobin will carry less oxygen.

d) Effect of pH: The pH of blood affects the degree of saturation of hemoglobin with oxygen. An increase in the metabolic rate in the issues increases the CO_2 and the acid metabolites. The partial pressure of oxygen is thus lowered and more oxygen is dissociated.

e) Effect of 2, 3 Diphosphoglycerate (DPG): DPG carries most of the phosphate in the erythrocytes and play an important role in the release of the oxygen to the tissues. An increase in the DPG concentration is associated with decrease in oxygen levels. This type of condition is found in persons suffering from anemia or cardiac inefficiency. DPG combines with hemoglobin and reduces its affinity for oxygen.

ii) Transport of Carbon dioxide:

CO_2 is formed in the body as a result of various metabolic activities of the cell and diffuse into the blood. CO_2 concentration in venous blood is about 60 ml/100 ml of blood while in arterial blood it is about 50 ml/100 ml of blood. CO_2 is transported in three ways which are as follows:

a) Transport as carbonic acid: From the body tissues as the CO_2 enters the blood; it reacts with water present in the plasma to form carbonic acid (H_2CO_3). About 5% of the total CO_2 dissolved in blood is carried as carbonic acid.

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

b) Transport as carbamino compounds: In Red Blood Cells (RBCs), CO_2 combines directly with the amino groups ($-NH_2$) of the hemoglobin to form the carbaminohemoglobin. About 10 % of the total CO_2 is transported as this complex.

$$CO_2 + Hb.NH2 \rightleftharpoons Hb.NH.COOH$$

(Carbaminohemoglobin)

c) Transport as bicarbonates: The remaining about 85 % of the CO_2 is carried in the form of bicarbonates both in plasma and RBCs. As CO_2 diffuses into the blood, it forms carbonic acid as discussed earlier which then dissociates to give bicarbonate ions (HCO_3^-) and hydrogen ion (H^+). The bicarbonate ion then combines with either sodium or potassium to form respective bicarbonates.

$Na^+ + HCO_3^-$ $\longrightarrow$ $NaHCO_3$

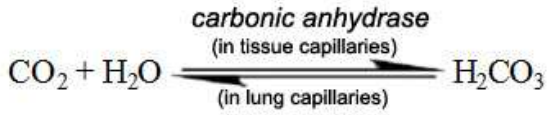
(Sodium bicarbonate)

$K^+ + HCO_3$ $\longrightarrow$ $KHCO_3$

(Potassium bicarbonate)

In normal conditions, most of the carbon-dioxide is present as bicarbonate ions. According to Henderson Hassel Bach equation, at pH of 7.4, the ratio of carbonic acid to bicarbonate ions is 1:20. The hydrogen ion formed as a result of dissociation of carbonic acid is neutralized by various buffering agents present in blood.

The RBCs contains an enzyme carbonic anhydrase which catalyzes the reversible reaction between CO_2 and H_2O resulting in the formation of carbonic acid (H_2CO_3) and subsequently bicarbonates.



The enzyme also facilitates the rapid release of CO_2 from the blood during its passage through the lungs. Thus despite the low concentration gradient (partial pressure of CO_2 in tissues is 45 mm of Hg while in arteriolar capillaries it is 40 mm of Hg) carbon dioxide diffuses rapidly from the tissues into the blood.

Isohydric Shift: This is an important phenomenon that occurs during the exchange of oxygen and CO_2 in tissues. During the gaseous exchange the carbonic acid formation tends to lower the pH of the blood while the dissociation of HbO_2 (oxyhemoglobin) to Hb (Hemoglobin) involves a change of pKa from 6.2 to 6.6 which raises the pH within the RBCs. Due to these opposing phenomena, the protons formed in the dissociation of H_2CO_3 are accepted by the groups in Hb. The net result is that the overall pH remains unchanged and K^+ ions previously neutralized by HBO_2 are now neutralized by bicarbonate ion. This set of transformation sis termed as *isohydric shift*.

Chloride shift: Chloride shift involves the passage of chloride ions from the plasma into the RBCs to balance the bicarbonate ions that have passedfrom the RBCs to plasma. This is important to maintain the acid base equilibrium for the blood and the electrical neutrality of the RBCs.

Release of CO_2 in the lungs: Carbonic acid, bicarbonates and carbamino compounds are the major species that carry CO_2 to the lungs via blood. Due to higher pressure of CO_2 in lung capillaries than in the lung alveoli, CO_2 is released from the blood. The reciprocal effect of the oxygenation on the acid strength of the hemoglobin also known as Haldane effect; accounts for the CO_2 exchange. In the lungs chloride ions move out of the RBCs and bicarbonate ions move

back in. Carbonic anhydrase rapidly generates the free CO_2 form the bicarbonates and the gas diffuses from blood into the lung alveoli.

Respiratory quotient.

The ratio of the CO_2 volume given off to the volume of O_2 consumed during same time is called respiratory quotient (R.Q.). The R.Q. can be calculated for the oxidation of various food materials. For example, in the following reaction:

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

R.Q. = 6 volumes of CO_2/6 volumes of O_2 = 1.0

It is different for different foods e.g. fats have a R.Q. of about 0.7, proteins have 0.8 and for the average mixed diet it is about 0.85.

1.8 RESPIRATORY PIGMENTS

A respiratory pigment is a molecule that increases the oxygen carrying capacity of the blood or in other words they are the substances which combine with oxygen reversibly and acts as the carrier or storage units for it. These pigments are generally carried by the blood. Their oxygen affinity determines the efficiency of these pigments and their use as the oxygen carrier. The oxygen affinity of these pigments is indicated by their *p*50 or partial pressure of oxygen at which they are half saturated with oxygen. The value of p50 is inversely proportional to the oxygen affinity of the pigment. Some of the common respiratory pigments are as follows:

i) Hemoglobin

Hemoglobin is the iron containing oxygen transport metalloprotein found in red blood cells (RBC) of all vertebrates as well as tissues of some invertebrates. With some very rare exception of leptocephalus (larvae of eel), all classes of vertebrates possess hemoglobin in their RBCs and their muscle contain myoglobin.

Structure: Hemoglobin is a conjugated protein made up of four subunits. Each subunit is made up of a protein part called globin and an iron containing protoporphyrin (heme) ring. Heme attaches to the polypeptide chain by a nitrogen atom to form one subunit of hemoglobin. Each of

the four heme portions of the hemoglobin molecule contains an atom of Iron (Fe) which binds oxygen. The iron in the heme is in ferrous state (Fe^{2+}). The protein moiety or globin varies considerably in size, amino acid composition, solubility and other physical properties from animal to animal. The iron content of mammalian hemoglobin is 0.336 % and the heme content is 4 %.

In each unit of heme, the iron atom is joined by four of its co-ordination bonds to the four nitrogen atoms of protoporphyrin and one of the remaining six co-ordination bond is joined to the molecule of globin.

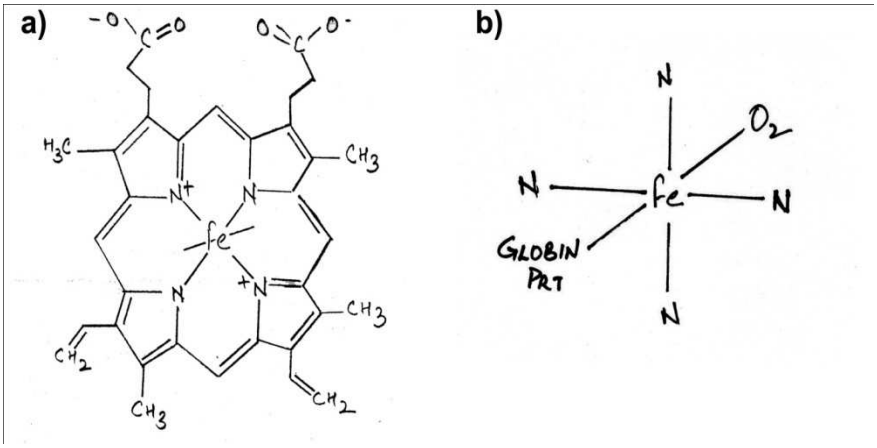


Fig. 1.6 a) Structure of protoporphyrin (Heme) ring; b) Schematic co-ordination of ferrous ion with oxygen and protein part of hemoglobin.

Hemoglobin devoid of oxygen is called **deoxyhemoglobin**. Adult blood contains two types of hemoglobin: 98 % **hemoglobin A** (HbA) and 20 % **hemoglobin A_2** (HbA_2). HbA contains two two α chains and two β chains ($\alpha_2\beta_2$) and HbA_2 contain a pair of α chain and a pair of δ chains ($\alpha_2\delta_2$). Each heme can combine with two atoms of oxygen to form **oxyhemoglobin** (HbO_2). Oxygen carrying capacity of the hemoglobin is the function of the iron atom. This co-ordination of heme iron with oxygen is reversible and it depends on the partial pressure of oxygen (PO_2). Oxyhemeoglobin is formed when PO_2 is high i.e. oxygen is present in excess and deoxyhemoglobin is formed when PO_2 is low i.e. oxygen concentration is low.

Since each hemoglobin molecule has four heme rings, it carries a total of 4 oxygen molecules. Hemoglobin is beautifully adapted to the task of oxygen carrier as it can pick up or release oxygen readily in response to the change in partial pressure of the oxygen in lungs, blood or tissues. Also, its affinity for oxygen changes with variations in pH and CO_2 concentrations. This is called **Bohr Effect**.

Hemoglobin can also combine with CO_2 or other gases. It can carry a small amount of the CO_2 out of tissues. Hemoglobin can combine with 4 molecules of carbon monoxide (CO) and form **carboxyhemoglobin**.The affinity of hemoglobin is about 200 times high for CO than oxygen. It can therefore cause CO poisoning if inhaled in even in small quantities and result in death by anorexia (lack of oxygen).

Fetal blood contains a distinct form of hemoglobin called **fetal hemoglobin**. Its structure is similar to hemoglobin A except that the β chains are replaced by γ chains making it $\alpha_2\gamma_2$.

ii) Myoglobin: Myoglobin (Mb) is found in vertebrate muscles and is an oxygen storage protein. It stores oxygen in resting skeletal muscles as oxymyoglobin (MbO_2). Myoglobin protein sequence has low similarity with the hemoglobin monomeric chains but it shares a striking similarity with the quaternary structure of Hemoglobin with the same kind of helical and other secondary structures.

In muscles, myoglobin binds O_2 reversibly. It does not exhibit Bohr effect and its oxygen dissociation curve is hyperbolic. During muscle contraction when the demand for the oxygen is highest, oxygen dissociates from the Myoglobin and is available for oxidation. Humans have a large quantity of myoglobin in cardiac muscles only. In birds the flight muscles are rich in myoglobin. Even at low partial pressure of oxygen, when the Hb is only partially saturated, myoglobin can be fully saturated. Myoglobin can even accept O_2 from hemoglobin and store it in muscle cells for later release.

iii) Haemerythrin: It is another respiratory pigment which is present in the blood of all sipunculid worms, a few polychaete forms and the branchiopod *Lingula*. It is a rare, reddish-violet, iron containing pigment. *Sipunculus*haemerythrin has a molecular weight of 105 KDa and contains 16 Fe^{2+} atoms. It binds one molecule of oxygen per iron atom.

iv) Haemocyanin: Haemocyanin or the blue pigment found mostly in mollusks and arthropods is a copper containing pigment. Squid haemocyanin is a decamer and each monomer contains two Cu^+ atoms and they bind one O_2 molecule per two Cu^+ ions.

5. Erythrocruorin: It is a large molecule consisting of multiple subunits and is found in many annelid worms and mollusks. *Limnodrillus*erythrocruorin consists of 108 subunits each having on heme group.

6. Chlorocruorin: It is green in color and is found in certain annelids like *Spirographis*. It is present in coelomic cavity and serves to store rather than transport oxygen.

1.9 TERMINAL QUESTIONS AND ANSWERS

1. In Respiration, the gas that is exhaled is:

a) Oxygen b) Carbon dioxide c) Nitrogen d) none of the above

2. The organ that is also known as sound box is:

a) Larynx b) Trachea c) Lungs d) Alveoli

3. Physiological unit of lungs is known as:

a) Trachea b) Bronchioles c) Alveoli d) None of the above

4. The volume of the air inspired or expired with each normal breath is called:

a) Tidal Volume b) Residual Volume c) Reservoir volume d) None of the above

5. The metal ion present in heme group of hemoglobin is:

a) Cu b) Zn c) Fe d) Mg

Answer: 1) b; 2) a; 3) c; 4) a; 5) c;

1. What is respiration? Differentiate between external and internal respiration?

2. What are respiratory pigments? Discuss various respiratory pigments?

3. Discuss the process of gaseous exchange in respiratory organs and tissues?

4. Discuss the structure of Hemoglobin? Explain oxygen transport by hemoglobin?

5. Discuss the transport of CO2 by blood?

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UNIT 2: CIRCULATION AND CARDIO VASCULAR SYSTEM

CONTENT

2.1. OBJECTIVES

Understanding the concepts presented in this chapter will enable the student to:

- Explain why circulation of fluids is required in organisms?
- Describe the different types of circulation in animals.
- Describe the types and number of chambers in hearts.
- Describe the neurogenic and myogenic hearts.
- Give a brief account of cardiac cycle, cardiac output, cardiac index.
- Explain the ECG and its role in diagnosis of cardiac disorders.
- Understand the hemostasis and mechanism of blood coagulation.
- Examples of natural and synthetic anticoagulants

2.2 INTRODUCTION

The most purposeful function of the circulation occurs in the microcirculation, which is transport of nutrients to the tissues and removal of cellular excreta. Animals possess body fluids for this purpose. These fluids circulate throughout the body in order to perform their function. So the circulatory system is a system of organs and structures which take part in flow of fluids for transport of materials inside an organism. The materials transported through circulatory system include water, oxygen, carbon dioxide, nutrients, vitamins, hormones and waste products. In higher animals nutrients are absorbed in intestine after digestion of food material but these must be transported to liver for assimilation before getting distributed throughout body via circulatory system. Similarly oxygen is absorbed in lungs or gills, from where it is taken up by the blood vascular system and carried to the tissues for oxidative processes. Waste products generated by the chemical processes and break down of tissues, being toxic, should be quickly excreted out of the body. Circulatory system removes these noxious substances to the ports of exit such as lungs, kidneys and intestine. Moreover, hormones produces by glands must use circulatory highways to reach their destinations. Hence, circulatory system is necessary to maintain connectivity among different parts of body.

In unicellular and very small multicellular animals, each cell is close to the surrounding medium so there is a direct exchange of materials between the cells and the external environment. Simple animals, like the sponges (Porifera) and rotifers (Rotifera), do not need a circulatory system because diffusion allows adequate exchange of water, nutrients, and waste, as well as dissolved gases. Organisms that are more complex, but still have only two layers of cells in their body plan, such as jelly fishes (Cnidaria) and comb jellies (Ctenophora), also use diffusion through their epidermis and internally through the gastro-vascular compartment. Both their internal and external tissues are bathed in an aqueous environment and exchange fluids by diffusion on both sides. Furthermore, in higher animals excess heat generated by muscles must be transported to the skin where it can be lost from the body surface to help maintain body temperature.

Types of circulation

There are two types of circulation in animals. 1. Intracellular and 2. Extracellular circulation

Intracellular circulation: Practically in all living cells and unicellular organisms the cytoplasm shows streaming movement called, *cyclosis*. Cyclosis helps in distribution of materials inside the cells uniformly. It also plays an important role in amoeboid locomotion found in *Amoeba* and WBCs.

Extracellular circulation: This type of circulation is common in multicellular and higher animals where fluid circulation occurs outside the cells or within the body cavity of animals. It is of many types.

(a) **Canal system-** It is a system of pores, canals, flagellated chambers, body cavity and exit pore, osculum to maintain constant water current through the body of sponges. Canal system helps in nutrition, respiration, excretion and exchange of gametes in sponges.

(b) **Gastro-vascular system-** This system occurs in coelenterates. Here these animals also circulate water in their body through mouth, gastro-vascular cavity and channels to distribute food and oxygen for different cells and elimination of carbon dioxide and wastes.

(c) **Parenchymal circulation**: This poorly developed circulation is found in flatworms and flukes. These animals are devoid of true body coelom. The body cavity is filled with a peculiar **parenchyma** tissue. The cells of this tissue are circulatory in function.

(d) **Blood vascular system**: Higher animals require greater and speedier supply of nutrients and oxygen to their tissues and also a rapid disposal of respiratory and nitrogenous wastes. So they have developed blood as a specialized circulatory fluid and the circulatory system consists of heart, blood and blood vessels for conducting and pumping blood to the tissues. The blood vascular system may be of two types-The open circulatory system and closed circulatory system.

Open circulatory system	**Closed circulatory system**
1. Blood flows through open spaces called lacunae and sinuses. 2. Capillaries are absent. 3. Blood flows at a very slow velocity. 4. Body cavity (haemocoel) is filled with blood (haemolymph). 5. Internal organs are bathed by blood. 6. Blood takes long time to complete circuit. 7. Supply and elimination of materials are very slow 8. Exchange of materials takes place between blood and sinuses. 9. Blood flow cannot be regulated. 10. It is found in arthropods (such as prawns, crabs, lobsters, insects and spiders) and most molluscs except cephalopods (such as snails, oysters and clams).	1. Blood flows through closed vessels. 2. Capillaries are present. 3. Blood flows at a very high velocity. 4. Haemocoel is absent. 5. Internal organs are not in direct contact with blood. 6. Blood takes short time to complete circuit. 7. Supply and elimination of materials are very rapid. 8. Exchange of materials occurs between blood and tissues. 9. Blood flow can be regulated. 10. It is found in most of the annelids (earthworms), cephalopods (squids, octopus) and vertebrates (fishes, amphibians, birds and mammals).

(e) **Lymphatic system**: This system occurs only in vertebrates and known as second circulatory system. It comprises lymph, lymphatic capillaries, lymphatic vessels and lymph nodes. Components of this system helps in immunity means fight to against disease and germs.

The circulatory system, which contributes to homeostasis by serving as the body's transport system, consists of the heart, blood and blood vessels.

2.3. HEART

Heart is a hollow, muscular, pumping organ that receives and pumps the blood through the circulatory system. It is pulsatile, which undergoes rhythmic contraction and relaxation (heart beat) but involuntary in function. Anatomically heart is a modified blood vessel. Depending on structure, function and regulation hearts are of various types.

1. **Pulsating heart**- In annelids and *Amphioxus* many vessels adopt a pulsating function by rhythmic peristalsis and the blood is propelled through various parts.
2. **Tubular heart**- This type of heart is found in arthropods where the heart assumes the shape of a contractile tube made of one or many chambers, each receiving blood from the haemocoel through paired opening called ostia. Cockroach heart is 13 chambered and supported by 13 pairs fan shaped *alary muscles*.
3. **Ampullar or accessory heart**- In cephalopods brachial heart is modified blood vessel which serves to pump the blood into the gills. Similarly some insects have ampullar hearts located at the base antennae, wings and legs. Lymph hearts of fishes, amphibians and reptiles are also regarded as accessary heart.
4. **Chambered heart**- Almost in all the vertebrates and few molluscs, the heart is made up of two or more chambers termed as atria and ventricles. Atria receive the blood and ventricles pump the blood to various body parts. To regulate the flow of blood , various types of valves are present between atria and ventricles and at the opening of various aortae, which prevent backward flow of blood.

Chambers in heart	**Examples**
1. Single-chambered heart	Protochordates (*Herdmania*, *Amphioxus*)
2. Two-chambered (one auricle and one ventricle) heart. Single circulation	Pisces (fishes). Heart of fish's also known as *venous heart* as it receives only deoxygenated blood.
3. Three-chambered heart (two atria and one ventricle). Double circulation	Amphibians (frogs and salamanders) Reptiles (except crocodiles) have three and

	half chambers in their heart. These have two atria and two incompletely partitioned ventricles.
4. Four-chambered heart (two atria and two ventricles). Double circulation	Crocodiles, Birds and mammals
5. 13 chambered heart (modified blood vessel) supported by 13 pairs fan shaped *Alary muscles.*	Cockroach

2.3.1. NEUROGENIC AND MYOGENIC HEARTS

Heart is a pulsatile muscular organ which spontaneously beat throughout life to pump and receive the blood. Rhythmic contraction of heart chambers is called *systole*, while relaxation of heart chambers is termed as *diastole*. On the basis of origin of cardiac impulses for heartbeat, hearts are of two types- neurogenic hearts and myogenic hearts.

Neurogenic hearts: In certain animals, the heart muscles are innervated by nerves. In such cases regulation of heart beats is dependent upon nervous regulation. Majority of arthropods and annelids in general possess neurogenic hearts. Among insects, especially the orthopteran species (cockroach, grasshopper) have neurogenic hearts. The nerve endings upon stimulation produce a chemical transmitter substance called acetylcholine which seems to accelerate the heart beats.

Myogenic hearts: The myogenic hearts show their rhythmic activity due to the muscles themselves. The vertebrate heart is myogenic type. The heart beat is initiated at the sinus venosus in case of fishes and amphibians. In birds and mammals, heart beat starts from the sinuauricular node (SA node). Some invertebrates also possess myogenic hearts in which the heart beats may originate from any point.

Characters	**Neurogenic heart**	**Myogenic heart**
Origin of heart beat	Nervous (by ganglion situated near the heart).	Nodal tissues (SA node) which modified cardiac

		muscles
Effect on removal of heart from the body	Heart normally stops beating	Heart continues to beat for some time
Transmission of cardiac impulse	Through nerve fibres	Through special nodal fibres, AV node, Bundle of HIS and Purkinje fibres.
Examples	Some annelids and most of the arthropods	Molluscs and vertebrates

2.4 CARDIAC CYCLE

The cardiac cycle includes all the events associated with the flow of blood through the heart during a single complete heartbeat. Cardiac cycle completes in three events.

(i) Auricular systole (0.1 sec)

(ii) Ventricular systole (0.3 sec)

(iii) Joint Diastole or complete cardiac diastole (0.4 sec)

(i) Auricular systole : The atria contract due to wave of contraction stimulated by S.A. node contraction of auricles drives most of their blood into respective ventricles as the A.V. valves are open. There is no backflow of blood into the large veins as the contraction begins at the upper end and passes towards ventricles and moreover, the valves present at the opening of these veins close. Also, blood is already present in large veins which offers resistance to the blood that may return from the atria. At the end of a atrial systole, there starts the relaxation of auricles (auricular diastole) and contraction of ventricles (ventricular systole) simultaneously. Atrial systole takes 0.1 second while atrial diastole is of about 0.7 seconds.

(ii) Ventricular systole : The ventricles begin to contract due to a wave of contraction stimulated by A.V. node. Due to ventricular systole, the pressure of blood in ventricles immediately rises above that in the auricles. With this pressure, the bicuspid and tricuspid valves close rapidly to prevent the backflow of blood. This closure of A.V. valves at the start of ventricular systole produces first heart sound called “Lubb” or Systolic sound. The semilunar

valves are also close at this time. When the pressure of blood in the ventricles exceeds that in the great arteries, the semilunar valves open and blood enters into the great arteries. This marks the end of ventricular systole which takes about 0.3 seconds. Now the ventricles start relaxing (ventricular diastole which lasts for about 0.5 sec.)

(iii) Joint diastole : The ventricles and auricles are in the diastolic phase simultaneously. As the ventricular diastole progresses, the pressure in the ventricles falls below that in the great arteries. So, to prevent backflow of blood from great arteries into ventricles, the semilunar valves close rapidly. This rapid closure of semilunar valves at the beginning of ventricular diastole produces second heart sound "Dup" or diastolic sound.

During joint diastole, blood from great veins and coronary sinus flows into the atria and some blood also passes from auricles into the respective relaxing ventricles due to less pressure in ventricles. This phase takes only 0.4 seconds and is also called as blood receiving period of heart. Thus a cardiac cycle is completed in 0.8 seconds.

2.4.1.CARDIAC OUTPUT (CO)

In a normal healthy person the volume of blood pumped by the heart per heart beat is called **stroke volume**. It is about 70 ml. Volume of blood pumped from heart (left ventricle) into the systemic aorta in one minute is called **cardiac output**. It is also called minute volume. It is calculated as the product of stroke volume (amount of blood pumped by left ventricle each time it contracts) and rate of heart beat.

i.e. Cardiac output = Stroke volume X Rate of heart beat

= 70 ml X 75 times/minute = 5040 ml/minute □ 5 litres/minute

Total amount of blood in human body is about 6.8 litres (7% of body weight). During mild exercise, the cardiac output rises to about 11 litres. Cardiac output is directly proportional to the size of the organism, metabolic rate etc. but is inversely proportional to age.

Fractions of cardiac output

- ✓ Cardiac fraction (to the heart) – 200 ml/min.
- ✓ Hepatic fraction (to the liver) – 1500 ml/min. (28% of blood as liver is the busiest organ of body and has maximum power of regeneration).
- ✓ Renal fraction (to the kidneys) – 1300 ml/min (25% of blood)
- ✓ Myofraction (to the muscles) – 600-900 ml/min.
- ✓ Cephalic organs (to the head/brain) – 700-800 ml/min.
- ✓ Remaining organs – Remaining blood.

2.4.2.CARDIAC INDEX (CI)

Cardiac output per square metre of body surface area per minute. As area of normal young adult is 1.7 metre square, so, cardiac index is 3 litres/min/square metre.

2.4.3. CARDIAC RESERVE (CR)

Maximum amount of blood that can be pumped by left ventricle under the conditions of maximum needs. In this condition, heart beat can go upto 250 and stroke volume can go upto 100 ml per systole. Cardiac reserve is 25-30 litres which is about 5-6 times of cardiac output.

2.4.4. ELECTROCARDIOGRAM (ECG)

A graphic record of electrical events occurring during a cardiac cycle is called *Electrocardiogram*. The instrument used for recording the heart's electrical variations is called *Electrocardiograph* in which the potential differences of heart muscles are recorded by a galvanometer.

History of ECG : The ECG was first recorded by Waller in frog. First human ECG was prepared by **Einthoven** who also discovered the electrocardiograph and discussed the principles of ECG. Hence, he is commonly called *"Father of Electrocardiography"*.

In ECG, there are 2 types of waves :

(i) Depolarisation waves : They represent the generation of the potential difference. These waves appear only when both electrodes of galvanometer are in different fields. When both the electrodes are in same field, there is no deflection and wave drops down to base line.

(ii) Repolarisation waves : They appear when depolarisation is over and the muscle fibre is returning to its original polarity. When both electrodes are in same polarity (means 100% repolarisation and 100% depolarisation), there is no deflection.

A normal ECG has 5 deflection waves – *P*, *Q*, *R*, *S* and *T*. Out of them – *P*, *R* and *T* waves are above the base line and are called positive waves (Figure 2). The *Q* and *S* waves are below base line and are called negative waves. The port of the base line between any 2 deflections is called interval.

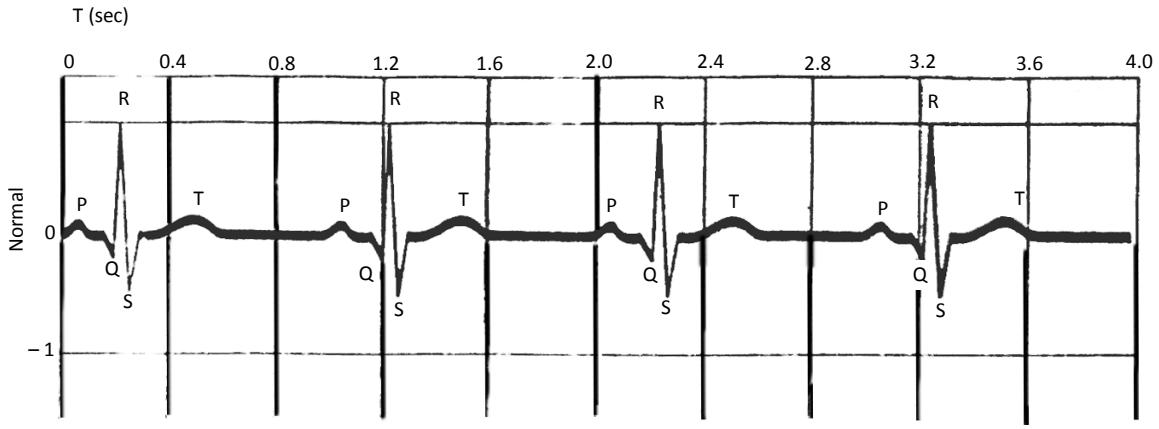

Figure 2. Pattern of waves of normal ECG

***P* wave :** Indicates impulse of contraction generated by S.A. node and its spread in atria causing atrial depolarisation. The interval *PQ* represents atrial contraction and takes 0.1 second.

QRS complex : Indicates spread of impulse of contraction from A.V node to the wall of ventricles through bundle of His and pukinje fibres causing ventricular depolarisation. This complex also represents repolarization of S.A. node.

The RS of QRS wave and ST interval show ventricular contraction (0.3 seconds). QRS is related to ventricular systole.

T wave : Indicates repolarisation during ventricular relaxation.

Any abnormality in the working of heart alters the wave pattern of ECG. Thus, ECG is of great diagnostic value in cardiac diseases. ECG also indicates the rate of heart beat.

If S.A. node is degenerated, the P wave disappears. This condition is called Heart fail. Atrial repolarisation wave is not seen in normal ECG because at this time, the depolarisation wave of ventricles is being recorded. When there is degeneration of bundle of His, the P to R interval increases. This is called Wenckebach phenomenon.

If bundle of His is completely cut, the P-R interval becomes infinite as the bundle of His is to transmit the cardiac impulses. It is called total heart fail or total heart block. In arborisation heart block, the defect lies in purkinje fibres. In heart attack, T waves become negative. When there is decrease in blood supply to a part of heart, there occurs death of myocardium. This condition is called Myocardial infarction (MI). It is acute heart attack. The ST part of ECG is depressed when heart muscles receive insufficient oxygen and is elevated in acute MI. When there is degeneration of myocardium and deposition of fibres, the condition is called fibrillation during which, ECG obtained is bizzare or non-decipherable.

2.5. HEMOSTASIS AND BLOOD CLOT FORMATION

2.5.1. HEMOSTASIS

Hemostasis means “stopping bleeding”. It involves responses that stop bleeding when a blood vessel is damages or punctured and so helps prevent the excessive loss of blood. The process of hemostasis occurs in three steps: vascular spasm, formation of a platelet plug, and formation of a blood clot, or thrombus.

Vascular Spasm: When a blood vessel is damaged, intrinsic mechanisms trigger a constriction called a vascular spasm, which increases resistance to blood flow. Damage also tends to activate the sympathetic nervous system, which causes further vaso-constriction. With less blood flowing to the area of damage, blood loss is minimized. Decreasing blood loss alone is not sufficient, however; blood loss must be stopped altogether.

Platelet Plug: Platelets, also called thrombocytes, possess granules containing a variety of substances that can be secreted into the plasma, including ADP, serotonin, epinephrine, and a

variety of chemicals that participate in the formation of a blood clot. Platelets also are "sticky" under certain circumstances, allowing them to adhere to surfaces, especially those of damaged blood vessels.

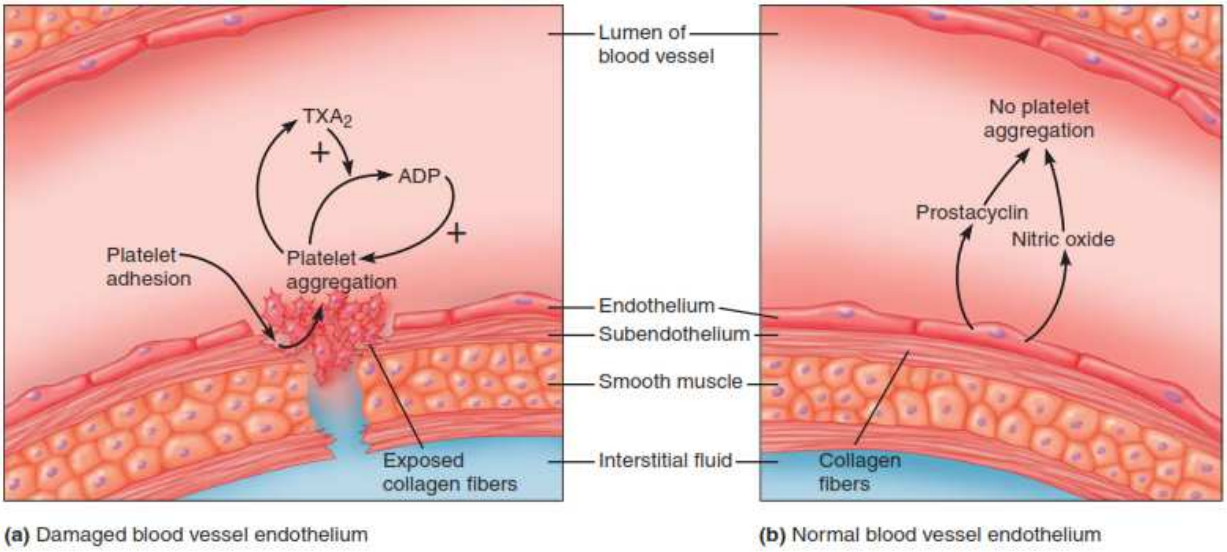

Figure 2.1. Mechanism of platelet plug formation (a) damaged blood vessel (b) normal blood vessel

Both the formation of platelet plugs and the subsequent blood clot require the presence of platelets and a fairly large set of specific plasma proteins. In platelet plug formation, the key protein is blood flow, might deprive tissue of its needed nutrients and allow waste products to accumulate. Platelet plugs do not form on normal endothelium because healthy endothelial cells continuously release prostacyclin and nitric oxide, both of which inhibit platelet aggregation (Figure 2.1). Whereas aggregated platelets convert arachidonic acid to TXA_2 to facilitate platelet plug formation, healthy endothelial cells convert arachidonic acid to prostacyclin to inhibit platelet plug formation. Platelets contain high concentrations of the contractile proteins actin and myosin. As platelets aggregate and form a plug, they contract to increase the "tightness" of the plug. Nevertheless, even a tight platelet plug cannot stop blood loss. The next step of hemostasis, forming the blood clot, is necessary.

2.5.2. FORMATION OF BLOOD CLOT

Blood coagulation is the conversion of liquid blood into semisolid jelly. It occurs at the place of injury to blood vessel from which blood begins to ooze out. Inside an intact blood vessel, blood does not coagulate due to presence of active anticoagulants, heparin and anti-thrombins. Blood clot mechanism completes in three steps

1. Development of Pro-thrombin Activator

Pro-thombin activator is a complex of several enzymes. It is formed by two pathways, extrinsic- in the walls of blood vessels and intrinsic- inside the blood. Stimulation is provided by vessel rupturing or trauma. In extrinsic development, tissue thromboplastin is secreted by damaged tissues. Thromboplastin is made of phospholipids, lipoproteins and it proteolytic enzyme. Tissue thromboplastin activates a number of factors which ultimately activate factor X (Stuart factor). In intrinsic development, trauma activates some blood factors and brings about release of platelet phospholipids (thromboplastin and platelet factor 3). This pathway also ultimately causes activation of factor X.

In the presence of calcium, factor V (in extrinsic pathway), or factor VIII (in intrinsic pathway), factor X gives rise to the development of prothrombin activator or prothrombinase (Figure 2.3).

2. Conversion of Prothrombin to Thrombin

Prothrombin is an α2 -globulin protein which is produced by liver in the presence of vitamin K. In the region of injury, prothrombin molecules get attached to receptors present over the surface of accumulated blood platelets. This ensures that prothrombin of only injured area is changed. In the presence of ionic calcium, prothrombin activator splits prothrombin and forms thrombin. Thrombin has proteolytic properties and is, therefore, acts as an enzyme.

3. Clot Formation

Clot formation completes in following three sub steps-

i. **Conversion of Fibrinogen to Fibrin:** Fibrinogen is a high molecular weight globulin protein originally produced by liver. It is acted upon by thrombin. The latter removes four low molecular weight peptides from fibrinogen and changes the same into fibrin monomers. Fibrin monomers have a tendency to undergo polymerisation, form long fibres which give rise to a reticulum. However, the monomer binding is non-covalent and therefore, weak. Strong covalent bonds are established with the help of fibrin stabilising factor, mainly released by aggregated platelets.

ii. **Blood Clot:** Fibrin stabilising factor produces a three dimensional meshwork of fibrin. The meshwork is attached to damaged wall of blood vessel. It entraps blood cells, more platelets and some plasma to form jelly like aggregate called blood clot. Blood clot covers the injured valve of blood vessels and stops blood loss.

iii. **Clot Retraction:** Within a few minutes of its formation, the blood clot contracts due to contraction of platelets attached to fibrin. Fibrin meshwork gets compressed. A liquid called serum is expend. As clot contracts broken edges of blood vessel come nearer and the spot gets healed up.

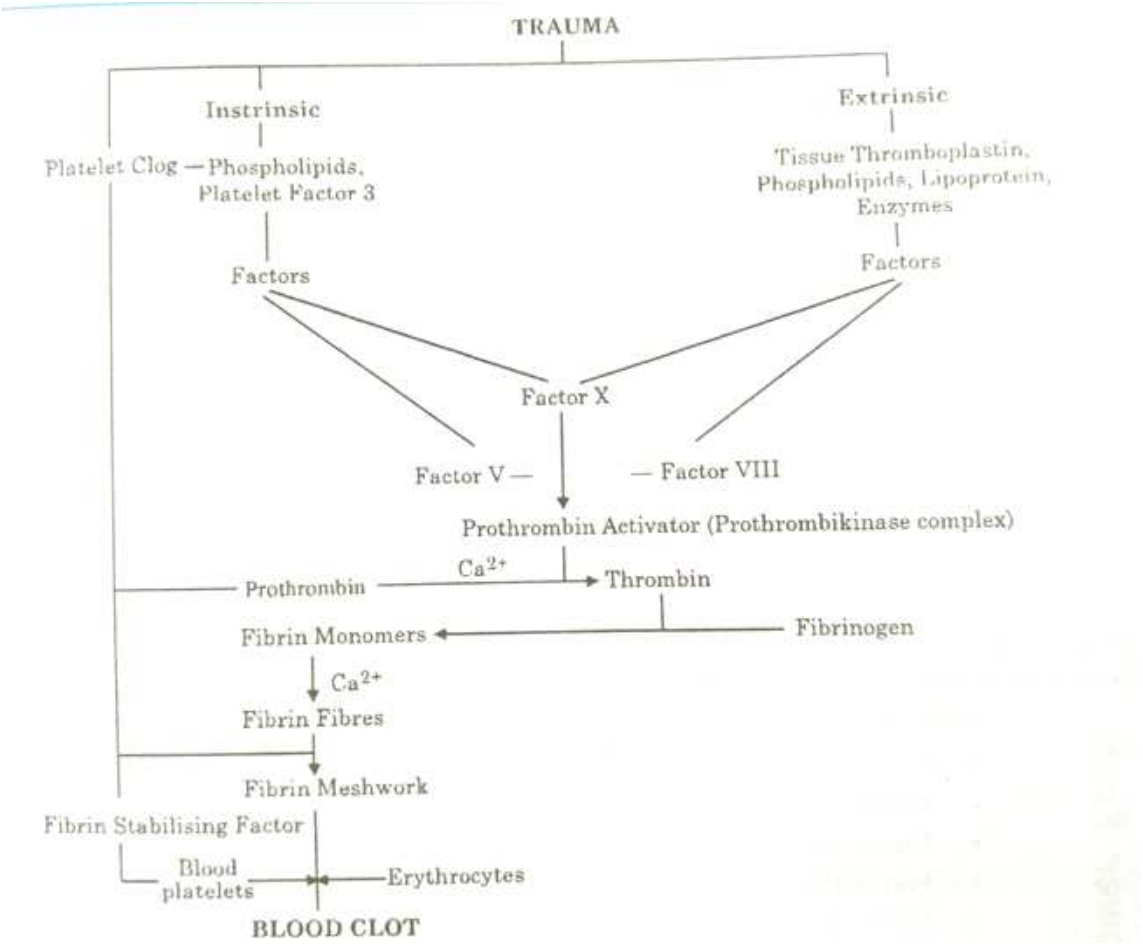

Figure 2.3. Showing mechanism of blood coagulation

Coagulation Time: It is period of time needed for exposed whole blood to get coagulated. The value is 4-10 minutes.

Bleeding Time: It is period of time needed for automatic stoppage of blood oozing from an injured area. Bleeding time is dependent upon the size of injury. For small cuts, it is 1-6 minutes.

According to cascade theory (proposed by Mac Ferlane) of blood clotting 13 factors are required for blood coagulation. These are written in roman numerals	
Factor I (Intrinsic and Extrinsic)	Fibrinogen
Factor II (Intrinsic and Extrinsic)	Prothrombin
Factor III (Extrinsic)	Tissue Thromboplastin (Tissue factor)
Factor IV (Intrinsic and Extrinsic)	Calcium ions
Factor V (Intrinsic and Extrinsic)	Proaccelerin (Labile factor), Ac-globulin
Factor VI	Accelerin (hypothetical activation product of factor V)
Factor VII (Extrinsic)	SPCA (Serum Prothrombin Conversion Accelerator), Proconvertin, Stable factor
Factor VIII (Intrinsic)	AHF (Anti Haemophilic Factor) A
Factor IX (Intrinsic)	AHF(Anti Haemophilic Factor) B, Christmas factor, PTC (Plasma Thromboplastin Component)
Factor X (Intrinsic and Extrinsic)	Stuart factor or Stuart- Prower Factor
Factor XI (Intrinsic)	PTA (Plasma Thromboplastin Antecedent)
Factor XII (Intrinsic)	Hagemann factor
Factor XIII (Intrinsic and Extrinsic)	FSF (Fibrin Stablising factor)

2.5.3. ANTICOAGULANTS

They are agents which prevent coagulation of blood. The important ones are as follows.

Heparin: It is the natural anticoagulant of human beings. It is formed by mast cells in connective tissue and basophils inside blood. Chemically it is a polysaccharide.

Anti-thrombins: They are alpha globulins that inactivate thrombin formed in intact blood. Anti-thrombin III is the most effective. Complex of heparin and anti-thrombin inactivates several coagulation factors.

Endothelial Lining: Endothelial lining of blood vessels is smooth. It prevents contact with intrinsic clotting factors. The cell coats of this layer also repel platelets and clotting factors. Thrombodulin is a protein attached to endothelial lining which binds any thrombin coming in its contact.

α2-Macroglobulin: It combines with coagulation factors and immobilise the same.

Hirudin: It is present in the saliva of leech. Leech pours saliva into wound of the victim. As a result, bleeding continues uninterrupted. Leech can, therefore, obtain the desired amount of blood.

Warfarin: It is a coumarin which blocks the activity of vitamin K in liver so that liver is unable to produce prothrombin and clotting factors.

Chilling: It reduces the activity of enzymes that produce clotting.

Synthetic anticoagulants: These are Oxalates, Citrates and EDTA. EDTA is ethylene diamine tetra-acetic acid. Common oxalates and citrates are those of sodium oxalate, potassium oxalate, sodium potassium or ammonium citrate. They precipitate or immobilize calcium of blood and therefore, prevent its coagulation.

2.6. SUMMARY

- Animals have a transport system to distribute substances uniformly in cytoplasm and throughout body called circulatory system. It is of two types- intracellular and extracellular circulation.
- Streaming movement of cytoplasm in unicellular animals (protozoans) is known as cyclosis. It is an example of intracellular circulation. Extracellular circulation includes canal system of sponges, gastro-vascular system in cnidarians, parenchymal circulation of helminthes, open blood vascular systemin arthropods, molluscs excepts cephalopods and closed blood vascular system of annelids, cephalopods and vertebrates. Lymphatic system is considered as second circulatory system of vertebrates.
- Blood vascular system of higher animals includes heart, blood and blood vessels.

- Heart is a hollow, muscular, pulsatile organ that receives and pumps the blood through the circulatory system. Protochordates like *Herdmania* and *Amphioxus* have single chambered heart. Heart has two chambers in fishes, three chambers in amphibians and four chambers in birds and mammals. Cockroach has 13 chambered tubular heart.

- On the basis of origin of cardiac impulses for heartbeat, hearts are of two types- neurogenic hearts and myogenic hearts. Lower animals like annelids, arthropods and molluscs have neurogenic hearts where cardiac impulses for heart beat are generated by neural tissues. Higher animals like vertebrates have myogenic hearts because cariac impulses for heart beat are generated by the muscles themselves.

- Cyclic events during heart beat constitute a cardiac cycle. In human being the duration os a cardiac cycle is 0.8 seconds. It completes in three events- auricular systole (0.1 sec), ventricular systole (0.3 sec) and joint diastole (0.4 sec).

- Cardiac Output (CO) is the volume of blood pumped from heart (left ventricle) into the systemic aorta in one minute. It is calculated as the product of stroke volume (amount of blood pumped by left ventricle each time it contracts) and rate of heart beat. In human beings the value of CO is about 5 litres.

- Cardiac Index (CI) is the cardiac output per square metre of body surface area per minute. It is about 3 litres/min/square metre for a normal healthy person.

- Cardiac Reserve (CR) means maximum amount of blood that can be pumped by left ventricle under the conditions of maximum needs. Cardiac reserve is 25-30 litres which is about 5-6 times of cardiac output.

- Electrocardiogram (ECG): A graphic record of electrical events occurring during a cardiac cycle is called *Electrocardiogram*. First human ECG was prepared by Einthoven (Father of Electrocardiography). A normal ECG has 5 deflection waves – *P*, *Q*, *R*, *S* and *T*.

- *P* wave indicates atrial depolarisation and takes 0.1 second. QRS complex indicates ventricular depolarisation. T wave represents repolarisation during ventricular relaxation. Any abnormality in the working of heart alters the wave pattern of ECG. Thus, ECG is of great diagnostic value in cardiac diseases. ECG also indicates the rate of heart beat.

- Maintaining the constant internal environment by living organisms is called *homeostasis*. Walter B. Cannon (1871-1945) coined the term *homeostasis* while he was elaborating on Claude Bernard's (1813-1878) concept of the *milieu intieur* (interior environment).
- Blood coagulation is the conversion of liquid blood into semisolid jelly. It occurs at the place of injury to blood vessel from which blood begins to ooze out. Blood clotting completes in three steps- Formation of prothrombinase, conversion of inactive prothrombin to thrombin and conversion of soluble fibrinogen into fibrin threads.
- Anticoagulants are the agents which prevent coagulation of blood. Heparin of human, hirudin of leech and anophilin of mosquitoes are some natural anticoagulants. Synthetic anticoagulants contain oxalates, citrates and EDTA.

2.7. SELF ASSESSMENT QUESTIONS AND POSSIBLE ANSWERS

2.7.1. MULTIPLE CHOICE QUESTIONS:

1. The most purposeful function of circulation in animals is:
   (a) Transport of nutrients (b) Removal of wastes
   (c) Transport of hormones (d) All the above
2. Intracellular circulation, cyclosis is found in:
   (a) Protozoans (b) Sponges
   (c) Cnidarian (d) Helminths
3. Which animal group has poorly developed circulation?
   (a) Earthworms (b) Flat worms
   (c) Round worms (d) Both b and c
4. Canal system for is found in
   (a) Star fishes (b) Sponges
   (c) Earthworm (d) Hydra
5. Gastro-vascular system occurs in:
   (a) Cnidaria (b) Annelida
   (c) Aschelminthes (d) Arthropoda
6. Open circulatory system is found in:

(a) Arthropoda (b) Mollusca

(c) Both a and b (d) Annelida

7. Closed circulatory system is found in:

(a) Annelida (b) Vertebrates

(c) Cephalopods (d) All the above

8. Which one of the following system found only in vertebrates?

(a) Lymphatic system (b) Blood vascular system

(c) Nervous system (d) Reproductive system

9. Thirteen chambered heart is found in

(a) Nereis (b) Earthworm

(c) Cockroach (d) Fishes

10. Fish heart is called as venous heart because?

(a) It receives only oxygenated blood

(b) It receives only deoxygenated blood

(c) It pumps oxygenated blood

(d) It is tubular and 3 chambered

11. Myogenic hearts are known for

(a) Generation of cardiac impulses by muscles

(b) Generation of cardiac impulses by nervous tissue

(c) Generation of cardiac impulses by hormones

(d) None of the above

12. In human beings a single cardiac cycle completes in

(a) 72 minutes (b) 88 seconds

(c) 8 seconds (d) 0.8 seconds

13. Cardiac Output (CO) can be defined as

(a) Volume of blood pumped from heart in one minute

(b) Volume of blood pumped from heart in one heart beat

(c) Volume of blood received from lungs in per minute

(d) Volume of blood received from lungs in per second

14. Total blood volume of a healthy person is

(a) 20-30 % of body weight (b) 7-8 % of body weight

(c) 40-50 % of body weight (d) 2-3 % of body weight

15. Who is considered is father of electrocardiography?

(a) Einthoven (b) Waller

(c) William Harvey (d) Jean Fernel

16. "T" wave in ECG indicates

(a) Atrial depolarisation (b) Ventricular repolarisation

(c) Atrial repolarisation (d) Ventricular depolarisation

17. Which component of formed element of blood plays important role in blood clotting?

(a) Erythrocytes (b) Leucocytes

(c) Thrombocytes (d) None of the above

18. Which vitamin is required for blood coagulation?

(a) Vitamin A (b) Vitamin E

(c) Vitamin D (d) Vitamin K

19. Which one of the following is not required in blood coagulation?

(a) Prothrombin (b) Fibronogen

(c) Calcium (d) Heparin

20. Conversion of inactive prothrombin into active thrombin is catalysed by

(a) Prothrombinase (b) Heparin

(c) Vitamin C (d) Thromboplastin

21. During blood clotting, enzyme prothrombinase is synthesized in the presence of

(a) Thromboplastin (b) Calcium

(c) Both a and b (d) None of the above

22. Synthetic anticoagulants contain

(a) Oxalates and citrates (b) Phosphates and carbonates

(c) Clorides and fluorides (d) Sulphates and phosphates

23. Which one of the following is NOT playing role as anti-coagulant?

(a) Heparin (b) Hirudin

(c) Warferin (d) Chitin

24. Hirudin is a natural anticoagulant of

(a) Leech (b) Bed bug

(c) Anopheles (d) Human

25. The complete process of blood coagulation is known as

(a) Homeostasis (b) Hemostasis

(c) Hematusis (d) Hemopoisis

26. Which one of the following statement is incorrect with respect to heparin

(a) It is secreted by mast cells of connective tissue

(b) It is secreted by basophil cells of blood

(c) Chemically it is a protein

(d) It is natural anticoagulant of human

2.7.2. VERY SHORT ANSWER TYPE QUESTIONS:

1. Which animal group has poorly developed circulation?
2. Which system of vertebrate is known as second circulatory system?
3. Which animal has alary muscles in their heart?
4. Name the two animals which have neurogenic heart?
5. Which reptile has four chambered heart?
6. Which animal group have heart beat initiation at the sinus venosus?
7. What is the normal duration of cardiac cycle in human being?
8. How much blood is pumped by heart per minute in human being?
9. Who discovered ECG?
10. Which complex in ECG represents ventricular systole?
11. What is the expanded form of ECG?
12. What is the normal coagulation time in human being?
13. Write the name of human anticoagulant.
14. Give the names of some synthetic anticoagulants.
15. Name the vitamin which is essential in blood coagulation?
16. Which ion is required during the mechanism of blood clotting?

2.7.3. SHORT ANSWER TYPE QUESTIONS:

1. Briefly describe the importance of circulation in animals.

2. Describe the different types of circulation in different animal groups.

3. Differentiate between intracellular and extracellular circulation.

4. Define cyclosis. Give the significance of this phenomenon in unicellular animals.

5. Differentiate between open and closed circulatory system.

6. Differentiate between neurogenic and myogenic hearts.

7. Briefly describe the cardiac cycle.

8. What is cardiac output? Write the value of cardiac output of a normal healthy person.

9. Define cardiac reserve.

10. Explain the normal ECG waves.

11. Draw the flowchart of mechanism of blood clotting.

12. Write the names of blood clotting factors.

13. Give the examples of natural anticoagulant.

14. Explain the role of oxalates and citrates in blood banks.

2.7.4. LONG ANSWER TYPE QUESTIONS:

1. Describe the significance of circulatory system in animals.

2. Differentiate between open and closed circulatory system of animals.Give examples.

3. Describe the various types of heart found in animals.

4. Describe the neurogenic and myogenic hearts with suitable examples.

5. Described the ECG in detail, how this machine play important role in diagnosis of cardiac disorders?

6. Describe the complete mechanism of blood coagulation.

ANSWERS:

MULTIPLE CHOICE QUESTIONS

1. D	2. A	3. D	4. B	5. A	6. C	7. D	8. A	9. C	10. B
11. A	12. D	13. A	14. B	15. A	16. B	17. C	18. D	19. D	20. A
21. C	22. A	23. D	24. A	25. B	26. C				

Very Short Answer Type Questions

1. Helminths 2. Lymphatic system 3. Cockroach 4. Crocodile 5. earthworm and cockroach 6. Fishes and amphibians 7. 0.8 seconds 8. About 5 litres 9. Einthoven 10.

QRS complex 11.Electrocardiogram 12. 4-10 minutes 13. Heparin 14. EDTA, Oxalates and Citrates 15. Vitamin K 16. Calcium

UNIT 3: PHYSIOLOGY OF DIGESTION AND EXERCTION

CONTENT

3.1 OBJECTIVES

Upon completion of this unit, you should be able to-

- State the the pattern of digestion and absorption in different types of animals .
- List the digestive enzymes, their source and function
- Describe the mechanism of digestion, absorption and utilization of various food components.
- Explain the function of kidneys on excretion and osmoregulation.
- Know the various types of nitrogenous wastes in different animals.
- Describe the various modes of excretion.
- Explain the mechanism of urea formation and sketch of Hans Krebs & Kurt Hensleit Cycle.
- Know the osmoregulation in reptiles, birds and mammals.

3.2 INTRODUCTION

All living organisms need organic raw materials to build up most of their own body molecules, and they require energy to operate the metabolic reactions that sustain life. The materials which provide the two primary requirements of life, namely , organic raw materials and energy, are called nutrients. A substance which taken to supply the necessary nutrients to the body is termed food, or diet. All organisms obtain their nutrients as food from their surrounding or habitat. The mode of obtaining of nutrients by the organisms is termed as nutrition.

Nutrition is the sum of all those activities which are concerned with ingestion, digestion, absorption of digested food into blood, lymph, cytoplasm, oxidation of simple food to produce energy for growth, repair, synthesis of biomolecules and egestion. Depending on the quantity and functions nutrients are classified as macronutrients and micronutrients. Macronutrients e.g. carbohydrates, proteins and lipids are taken in large amount and required to produce energy and for growth and repair. , Micronutrients e.g. vitamins and minerals do not provide energy and are required in very small amount but they are essential regulatory components of food, their deficiency can cause specific disease. The water we take in, plays an important role in metabolic processes and also prevents dehydration of the body. Biomacromolecules in food cannot be utilised by our body in their original form. They have to be broken down and converted into simple substances in the digestive system. This process of conversion of complex food substances to simple absorbable forms is called digestion and is carried out by our digestive system by mechanicaland biochemical methods.

3.3 PATTERNS OF DIGESTION AND ABSORPTION IN ANIMALS

Animals obtain their nutrients through a broad variety of feeding patterns. Sponges, for example, feed on small particles of food that enter their pores. Other aquatic organisms, such as sea cucumbers, wave their tentacles about and trap food on their sticky surfaces. Mollusks, such as clams and oysters, feed by filtering materials through a layer of mucus in their gills. Certain arthropods feed exclusively on fluids.

Some animals feed on food masses, and they usually have organs for seizing, chewing, and consuming food. Herbivores are animals that eat only plants, while carnivores are animals that

eat only other animals. Omnivores, which consume both plants and animals, are typified by humans.

3.3.1. DIGESTION IN HERBIVORES

Herbivores eat plant material. While no animal produces the digestive enzymes to break down the large cellulose molecules in the plant cell walls, micro-organisms' like bacteria, on the other hand, can break them down. Therefore herbivores employ micro-organisms to do the job for them.

There are two types of herbivore: ruminants and non-ruminants. The **ruminants** like cattle, sheep and goats, house these bacteria in a special compartment in the enlarged stomach called the rumen. The second group has an enlarged large intestine and caecum, called a functional caecum, occupied by cellulose digesting micro-organisms. These **non-ruminant** herbivores include the horse, rabbit and rat.

Plants are a primary pure and good source of nutrients, however they aren't digested very easily and therefore herbivores have to eat large quantities of food to obtain all they require. Herbivores like cows, horses and rabbits typically spend much of their day feeding. To give the micro-organisms access to the cellulose molecules, the plant cell walls need to be broken down. This is why herbivores have teeth that are adapted to crush and grind. Their guts also tend to be lengthy and the food takes a long time to pass through it. Eating plants have other advantages. Plants are immobile so herbivores normally have to spend little energy collecting them. This contrasts with another main group of animals - the carnivores that often have to chase their prey.

3.3.2. DIGESTION IN CARNIVORES

Carnivorous animals like those in the cat and dog families, polar bears, seals, crocodiles and birds of prey catch and eat other animals. They often have to use large amounts of energy finding, stalking, catching and killing their prey. However, they are rewarded by the fact that meat provides a very concentrated source of nutrients. Carnivores in the wild therefore tend to eat distinct meals often with long and irregular intervals between them. Time after feeding is spent digesting and absorbing the food.

The guts of carnivores are usually shorter and less complex than those of herbivores because meat is easier to digest than plant material. Carnivores usually have teeth that are specialised for dealing with flesh, gristle and bone. They have sleek bodies, strong, sharp claws and keen senses of smell, hearing and sight. They are also often cunning, alert and have an aggressive nature.

3.3.3. DIGESTION IN OMNIVORES

Many animals feed on both animal and vegetable material – they are **omnivorous**. There are currently two similar definitions of omnivorism:

1. Having the ability to derive energy from plant and animal material.

2. Having characteristics which are optimized for acquiring and eating both plants and animals.

Some animals fit both definitions of omnivorism, including bears, raccoons, dogs, and hedgehogs. Their food is diverse, ranging from plant material to animals they have either killed themselves or scavenged from other carnivores. They are well equipped to hunt and tear flesh (claws, sharp teeth, and a strong, non-rotational jaw hinge), but they also have slightly longer intestines than carnivores, which has been found to facilitate plant digestion. The examples also retain an ability to taste amino acids, making unseasoned flesh palatable to most members of the species.

Classically, humans and chimpanzees are classified as omnivores. However, further research has shown chimpanzees typically consume 95% plant matter (the remaining mass is largely termites), and their teeth, jaw hinge, stomach pH, and intestinal length closely matches herbivores, which many suggest classified them as herbivores. Humans, conversely, have chosen to eat meat for much of the archaeological record, although their teeth, jaw hinge, and stomach pH, and intestinal lengths also closely match other herbivores. Per the classical definition, omnivores lack the specialized teeth and guts of carnivores and herbivores but are often highly intelligent and adaptable reflecting their varied diet.

3.4 ROLE OF DIGESTIVE ENZYMES

Chemical processes are achieved by the different digestive enzymes (Table 3.1).

3.4.1. SALIVARY AMYLASES AND LYSOZYMES

These enzymes are produced by the salivary glands in oral cavity. The main function of these enzymes is to split the carbohydrates by the hydrolytic actions.The function of these enzymes are as follows:

Salivary amylases – 30% of starch molecules are converted into maltose by salivary amylases at the pH of 6.8.

Lysozymes – It acts against the bacterial infections. They are also called antibacterial agents.

3.4.2. GASTRIC GLAND ENZYMES

Gastric glands are present in the mucosa of the stomach. The following types of cell are present in the gastric gland.

Mucous neck cells – These cells secrete mucus, which is used to protect the mucosal epithelium from concentrated HCl. This concentrated HCl is secreted by the oxyntic cells.

Peptic or chief cells – These cells secrete the proenzyme pepsinogen. It is in an inactive form. This inactive proenzyme pepsinogen is activated by the chyme and converted into the active form of the enzyme which is called pepsin. Pepsin is used to convert the proteins into proteoses and peptones.

Parietal or oxyntic cells – These cells secrete concentrated HCl and intrinsic factor. Intrinsic factor plays an important role in the absorption of the vitamin B12.HCL is used to activate the proenzyme pepsinogen.

Finally, the following enzymes are secreted by gastric glands:

Pepsin – It is used to denature the proteins into peptones and proteases.

Rennin – It is a type of proteolytic enzyme which is present in the infant's gastric juice.

Gastric Lipase – Small amount of lipase enzyme is secreted by the gastric gland. It is used to convert the di and monoglycerides into fatty acids and glycerol.

Enzyme Category	Enzyme Name	Source	Substrate	Product
Salivary Enzymes	Lingual lipase	Lingual glands	Triglycerides	Free fatty acids, and mono- and diglycerides
Salivary Enzymes	Salivary amylase	Salivary glands	Polysaccharides	Disaccharides and trisaccharides
Gastric enzymes	Gastric lipase	Chief cells	Triglycerides	Fatty acids and monoacylglycerides
Gastric enzymes	Pepsin*	Chief cells	Proteins	Peptides
Brush border enzymes	α-Dextrinase	Small intestine	α-Dextrins	Glucose
Brush border enzymes	Enteropeptidase	Small intestine	Trypsinogen	Trypsin
Brush border enzymes	Lactase	Small intestine	Lactose	Glucose and galactose
Brush border enzymes	Maltase	Small intestine	Maltose	Glucose
Brush border enzymes	Nucleosidases and phosphatases	Small intestine	Nucleotides	Phosphates, nitrogenous bases, and pentoses
Brush border enzymes	Peptidases	Small intestine	Aminopeptidase: amino acids at the amino end of peptides Dipeptidase: dipeptides	Aminopeptidase: amino acids and peptides Dipeptidase: amino acids
Brush border enzymes	Sucrase	Small intestine	Sucrose	Glucose and fructose
Pancreatic enzymes	Carboxy-peptidase*	Pancreatic acinar cells	Amino acids at the carboxyl end of peptides	Amino acids and peptides
Pancreatic enzymes	Chymotrypsin*	Pancreatic acinar cells	Proteins	Peptides
Pancreatic enzymes	Elastase*	Pancreatic acinar cells	Proteins	Peptides
Pancreatic enzymes	Nucleases	Pancreatic acinar cells	Ribonuclease: ribonucleic acids Deoxyribonuclease: deoxyribonucleic acids	Nucleotides
Pancreatic enzymes	Pancreatic amylase	Pancreatic acinar cells	Polysaccharides (starches)	α-Dextrins, disaccharides (maltose), trisaccharides (maltotriose)
Pancreatic enzymes	Pancreatic lipase	Pancreatic acinar cells	Triglycerides that have been emulsified by bile salts	Fatty acids and monoacylglycerides
Pancreatic enzymes	Trypsin*	Pancreatic acinar cells	Proteins	Peptides

Table 3.1. Different digestive enzymes, their source and action

** These enzymes are activated by other substances*

3.4. 3. SMALL INTESTINE ENZYMES

In the small intestine, three major digestive juices are secreted. These are as follows: Bile juice, Pancreatic juice and Intestinal juice

Bile juice- Bile juice is secreted by the liver. It is a yellowish color fluid. The main function of bile juice is to digest the lipid molecules and to activate the lipase enzymes. Bile juice consists of the following components- bile pigments (Bilirubin and biliverdin), Bile salts (Sodium carbonates, bicarbonates, sodium glycolate and taurocholate), Cholesterol, Phospholipids but no digestive enzymes. Bile juice helps to break down the lipid molecules into di and monoglycerides by the lipase enzymes.

Pancreatic juice enzymes

The pancreatic juices are secreted by the pancreas. Pancreatic juice consists of the following inactive enzymes. These enzymes are activated by the intestinal mucosal secretions.

Trypsinogen – An inactive form of trypsinogen is converted into an active form, trypsin by enteropeptidase (one of the intestinal mucosa secretion). Trypsin is used to convert the protein molecules into dipeptides.

Chymotrypsinogen – An inactive form of chymotrypsinogen is converted into an active form, chymotrypsin. Proteins are denatured into dipeptides by chymotrypsin.

Procarboxypeptidases – An Inactive form of procarboxypeptidase is converted into an active form, carboxypeptidase. Carboxypeptidase is also used to denature the protein.

Amylases – Amylases are used to denature the polysaccharides into the disaccharides.

Lipases – Lipases are used to convert the fats into diglycerides and monoglycerides.

Nucleases – Nucleases are used to convert the nucleic acids into nucleotides and nucleosides.

Intestinal juice enzymes

The Intestinal mucous epithelium of the small intestine consists of brush border cells and goblet cells. The secretions of brush border cells and goblet cells from the intestinal juice in the small intestine. Intestinal juice consists of the following enzymes:

Disaccharidases – It is also called maltases. Maltases are used to convert the maltose into glucose.

Dipeptidases – These enzymes are used to convert the dipeptides into simple amino acids.

Lipases – Lipases are used to convert the diglycerides and monoglycerides into fatty acids and glycerols.

Nucleosidases – These enzymes are used to convert the nucleotides into nucleosides, sugars, and bases.

Lactases – Lactases are used to convert the lactose into simple glucose.

3.5 DIGESTION, ABSORPTION AND ASSIMILATION OF VARIOUS FOOD STUFFS

3.5.1 MECHANICAL DIGESTION OF FOOD

This process comprises mastication, swallowing and churing of food in stomach.

Mastication: It is the chewing of food by various types of teeth. The teeth are admirably designed for chewing. The anterior teeth (incisors) provide a strong cutting action, and the posterior teeth (molars) provide a grinding action. Chewing aids the digestion of food for further action of digestive enzymes act only on the surfaces of food particles; therefore, the rate of digestion is dependent on the total surface area exposed to the digestive secretions.

Swallowing (deglutition): Swallowing is a complicated mechanism, principally because the pharynx serves respiration and swallowing both.Tongue helps in mixing of saliva with the food.Saliva moistensand lubricates the food, which changes into semisolid form called bolus.

The bolus is then swallowed through Oesophagus to the stomach.Peristalsis movement of alimentary canal also helps in swallowing.

Churning in stomach: The wall of stomach undergoes periodic movement as well as contraction producing churning movement called peristalsis, which results in breakdown of complex food into simpler form.The bolus after mixing with gastric juice, turn into fine soluble form known as chyme.

3.5.2. CHEMICAL DIGESTION OF FOOD

It involves the breaking of covalent chemical bonds in organic molecules by digestiveenzymes.Carbohydrates are broken down into monosaccharides, proteins are broken down into amino acids, and fats are broken down into fatty acids and glycerol.

Digestion of Carbohydrates

Ingested carbohydrates consist primarily of polysaccharides, such as starches (rice, bread), disaccharides, such as sucrose (table sugar) and lactose (milk sugar); and monosaccharides, such as glucose and fructose (found in many fruits). During the process ofdigestion, polysaccharides are broken down into smaller chains and finally into disaccharides and monosaccharides. Disaccharides are broken down into monosaccharides.

a) digestion of carbohydrates in mouth- Carbohydrate digestion begins in the oral cavity with the partial digestion of starches bysalivary amylase.About 30 percent of starch is hydrolysed here by this enzyme amylase (optimum pH 6.8) into a disaccharide – maltose.Lysozyme present in saliva acts as an anti-bacterialagent that prevents infections.

b) digestion of carbohydrates in stomach and intestine- A minor amount of digestion occurs in the stomach through the action of gastric amylaseand gelatinase. Carbohydrate digestion is continued in the intestine by pancreatic amylase.A series of disaccharidases enzymes that are released by intestinal epithelium digest disaccharides into monosaccharides.

Digestion of Proteins

Proteins are taken into the body from a number of dietary sources.Pepsin secreted by the stomach catalyzes the cleavage of covalent bonds in proteins to produce smaller polypeptide chains.

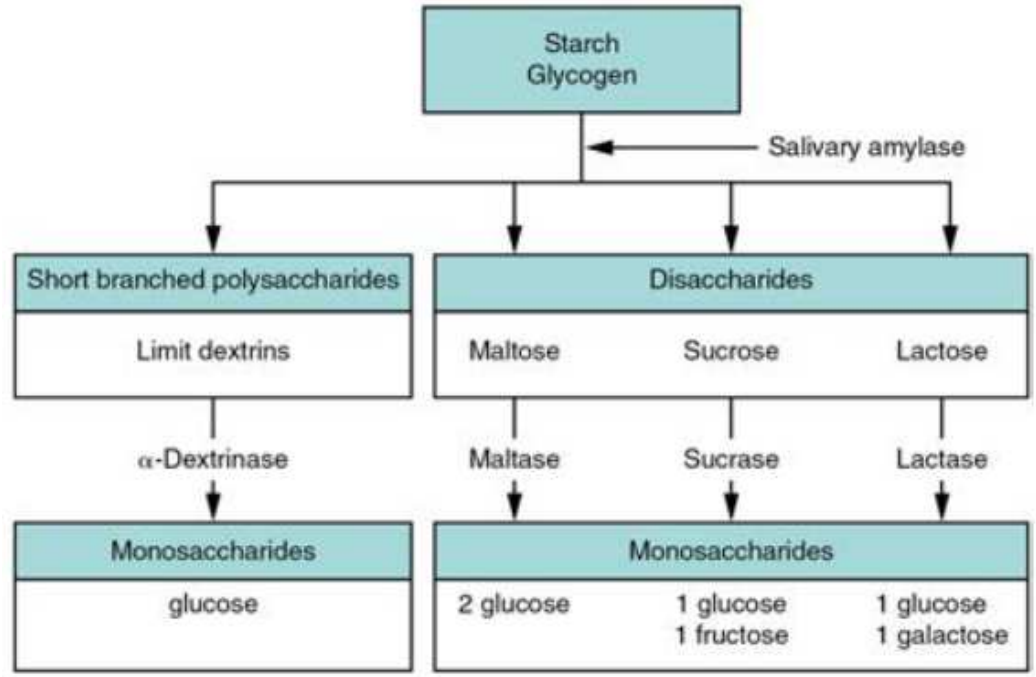

Figure. 3.1. Digestion of carbohydrates

a) digestion of protein in stomach and intestine- Gastric pepsin digests as much as 10%–20% of the total ingested protein.The mucosa of stomach has gastric glands.Gastric glands have three major types of cells namely –

(i) mucus cells: which secrete mucus;

(ii) peptic or chief cells; which secrete the proenzyme pepsinogen; and

(iii) parietal or oxyntic cells; which secrete HCl and intrinsic factor (factor essential for absorption of vitamin B12).

The stomach stores the food for 4-5 hours. The food mixes thoroughly with the acidic gastric juice of the stomach by the churning movements of its muscular wall and is called the chyme.

The proenzyme pepsinogen, on exposure to hydrochloric acid gets converted into pepsin.Pepsin then converts proteins into proteoses and peptones (peptides).The mucus and bicarbonates present in the gastric juice play an important role in lubrication and protection of the mucosal epithelium from excoriation by the highly concentrated hydrochloric acid. HCl provides the

acidic pH (pH 1.8) optimal for pepsin.Rennin is a proteolytic enzyme found in gastric juice of infants which helps in the digestion of milk proteins.

b) digestion of protein in intestine- The bile, pancreatic juice and the intestinal juice are the secretions released into the small intestine.Pancreatic juice and bile are released through the hepato-pancreatic duct.The pancreatic juice contains inactive enzymes – trypsinogen, chymotrypsinogen, procarboxypeptidases.Trypsinogen is activated by an enzyme, enterokinase, secreted by the intestinal mucosa into active trypsin, which in turn activates the other enzymes in the pancreatic juice.Pancreatic proteinases (all secreted in their inactive forms) digest peptides into amino acids. Trypsinogen is activated by enterokinase (secreted by duodenum) into trypsin, which in turn activates the other 3 enzymes –chymotrypsinogen becomes chymotrypisn, proaminopeptidase becomes aminopeptidase, and pro-carboxypeptidase becomescarboxypeptidase.

Digestion of Lipids

Lipids are molecules that are insoluble or only slightly soluble in water.Lipids include triglycerides, phospholipids, cholesterol, steroids, and fat-soluble vitamins.The first step in lipid digestion is emulsification, which is the transformation of large lipid droplets into much smaller droplets.The emulsification process increases the surface area of the lipid exposed to the digestive enzymes by decreasing the droplet size. Emulsification is accomplished by bile salts secreted by the liver and stored in thegallbladder.

Lipase digests lipid molecules. The vast majority of lipase is secreted by the pancreas. A minor amount of lingual lipase is secreted in the oral cavity, is swallowed with the food, and digests a small amount (<10%) of lipid in the stomach.The stomach also produces very small amounts of gastric lipase.The primary products of lipase digestion are free fatty acids and glycerol and few cholesterol and phospholipids.

3. 5.3. ABSORPTION

Absorption is the process by which the end products of digestion pass through the intestinal

mucosa into the blood or lymph (Table 3.2).It is carried out by passive, active or facilitated transport mechanisms.Water moves by osmosis; small fat soluble substances, e.g. fatty acids and

glycerol, are able to diffuse through cell membranes; while others are generally transported inside the villi by other mechanisms.

Source	Substance
Carbohydrates	Monosaccharides: glucose, galactose, and fructose
Proteins	Single amino acids, dipeptides, and tripeptides
Triglycerides	Monoacylglycerides, glycerol, and free fatty acids
Nucleic acids	Pentose sugars, phosphates, and nitrogenous bases

Table3.2. End products of digestion (absorbable food substances)

Passive transport:Small amounts of monosaccharides like glucose, amino acids and some electrolytes like chloride ions are generally absorbed by simple diffusion.The passage of these substances into the blood depends upon the concentration gradients.

Active transport: Active transport occurs against the concentration gradient and hence requires energy.Various nutrients like amino acids, monosaccharides like glucose, electrolytes like Na+ are absorbed into the blood by this mechanism.Some substances like glucose and amino acids are absorbed with the help of carrier proteins. This mechanism is called the facilitated transport (Table 3.3).

Fatty acids and glycerol being insoluble, cannot be absorbed into the blood. They are first

incorporated into small droplets called micelles which move into the intestinal mucosa. They are re-formed into very small protein coated fat globules called the *chylomicrons* which are transported into the lymph vessels (lacteals) in the villi. These lymph vesselsultimately release the absorbed substances into the blood stream.

Food	Breakdown products	Absorption mechanism	Entry to bloodstream	Destination
Carbohydrates	Glucose	Co-transport with sodium ions	Capillary blood in villi	Liver via hepatic portal vein
Carbohydrates	Galactose	Co-transport with sodium ions	Capillary blood in villi	Liver via hepatic portal vein
Carbohydrates	Fructose	Facilitated diffusion	Capillary blood in villi	Liver via hepatic portal vein
Protein	Amino acids	Co-transport with sodium ions	Capillary blood in villi	Liver via hepatic portal vein
Lipids	Long-chain fatty acids	Diffusion into intestinal cells, where they are combined with proteins to create chylomicrons	Lacteals of villi	Systemic circulation via lymph entering thoracic duct
Lipids	Monoacylglycerides	Diffusion into intestinal cells, where they are combined with proteins to create chylomicrons	Lacteals of villi	Systemic circulation via lymph entering thoracic duct
Lipids	Short-chain fatty acids	Simple diffusion	Capillary blood in villi	Liver via hepatic portal vein
Lipids	Glycerol	Simple diffusion	Capillary blood in villi	Liver via hepatic portal vein
Nucleic Acids	Nucleic acid digestion products	Active transport via membrane carriers	Capillary blood in villi	Liver via hepatic portal vein

Table 3.3 Absorption of food substances in different parts of alimentary canal

3.5.4. ASSIMILATION

The absorbed food materials are transported by blood and lymph. Lymph is finally transferred to the blood circulation. The blood transports absorbed food materials to different body cells where food materials become integral component of the living protoplasm and are used for energy, growth and repair. This is called assimilation of food.

Assimilation of proteins- Amino acids are not stored but are taken up by the cells in connection with the synthesis of proteins. Proteins are used for growth, repair, etc.Excess amino acids can be converted into glucose and then to fat and are thus stored. This is an irreversible reaction. Amino acids can also be converted to glucose and used as fuel for the cell. During their conversion to glucose the amino acids are deaminated (removal of amino groups NH2).The liver is chief site for deamination, i.e., a process by which the amino group is removed from the amino acids

resulting in the production of ammonia. The ammonia is soon converted into urea, which is filtered from the blood in the kidney.

Assimilation of carbohydrates- The excess of the monosaccharide's; the glucose, fructose and galactose are usually stored in the liver and muscle cells in the form of glycogen (glycogenesis). Whenever, there is a deficiency of glucose in the blood the glycogen is converted into glucose (glycogenolysis).Muscle glycogen is utilized during muscle contraction. Glucose is utilized in the production of energy for various body activities. A considerable amount of glucose is converted into fat and stored as such.

Assimilation of lipids- The fat is stored in the fat deposits of the body, such as subcutaneous layers, mesenteries, etc. The fat stored is a readily available source of fuel for the cells. Fat has important insulating properties in connection with the conservation of heat and maintenance of body temperature. Fat also plays a protective role as filling or around packing material and between organs. In the liver phospholipids are formed which are returned to the blood to be used by all the cells. In the liver cells the fats are converted into amino acids and carbohydrates. Vitamins, salts and water are also useful for various metabolic processes.

3.6 FUNCTIONS OF KIDNEY

We take in a lot of things in our body the whole day. They need to be simultaneously excreted out of the body to maintain the body's steady state. This process of removal of chemical wastes from our body is known as **excretion**. There are a number of substances that our body needs to get rid of. Some of them are carbon dioxide, nitrogenous wastes, excessive salts and vitamins, water and bile pigments. Excretion in humans occurs through the **kidney**, sweat glands, lungs etc.

Kidney

Kidneys are the chief excretory organs and are mainly concerned with the excretion of urea in the form of urine. The function of our kidney is monitored and regulated by the feedback mechanisms which involve hypothalamus, juxtaglomerular apparatus, and the heat.

Human Kidneysare located at about the T12 to L3 vertebrae, whereas the right is lower due to slight displacement by the liver.Each kidney weighsabout 125–175 g in males and 115–155 g in females. They are about 11–14 cm in length, 6 cm wide, and 4 cm thick, and

are directly covered by a fibrous capsule. A frontal section through the kidney reveals an outer region called the renal cortex and an inner region called the medulla. The renal columns are connective tissue extensions that radiate downward from the cortex through the medulla to separate the most characteristic features of the medulla, the renal pyramids and renal papillae (Figure 3.2). The papillae are bundles of collecting ducts that transport urine made by nephrons to the calyces of the kidney for excretion. The renal columns also serve to divide the kidney into 6–8 lobes and provide a supportive framework for vessels that enter and exit the cortex. The pyramids and renal columns taken together constitute the kidney lobes.

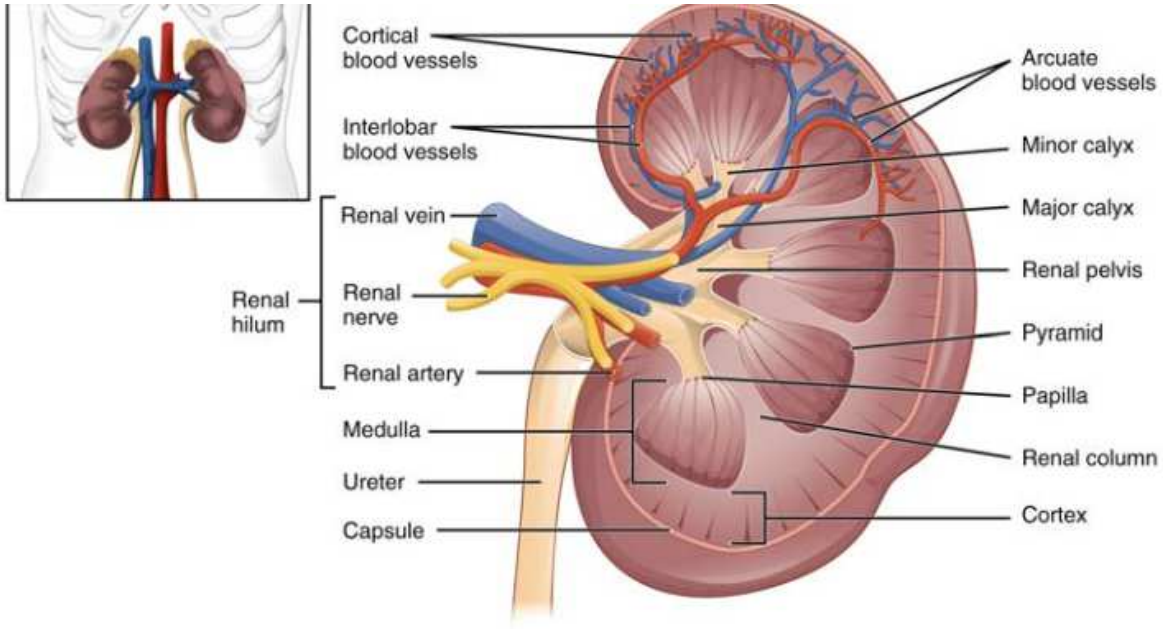

Figure3.2. Internal anatomy of human kidney

Regulation of Kidneys (RAAS: Renin Angiotensin Aldosterone System)

When there is excessive loss of fluid from the body, osmoreceptors are activated which stimulate the hypothalamus to release ADH – antidiuretic hormone from neurohypophysis. This hormone helps in reabsorption of water from the latter parts of the tubule and prevents the loss of water from the body. When the fluid volume of body increases, osmoreceptors are switched off and the release of ADH is suppressed. ADH may also increase the blood pressure thereby increasing the glomerular blood flow. When the glomerular blood flow decreases, juxtaglomerular cells release renin which converts angiotensin in blood to angiotensin I which is further converted to angiotensin II. This causes an increase in glomerular blood pressure. It converts angiotensin in blood to angiotensin I. It is further converted to angiotensin II. This causes an increase in glomerular blood pressure.

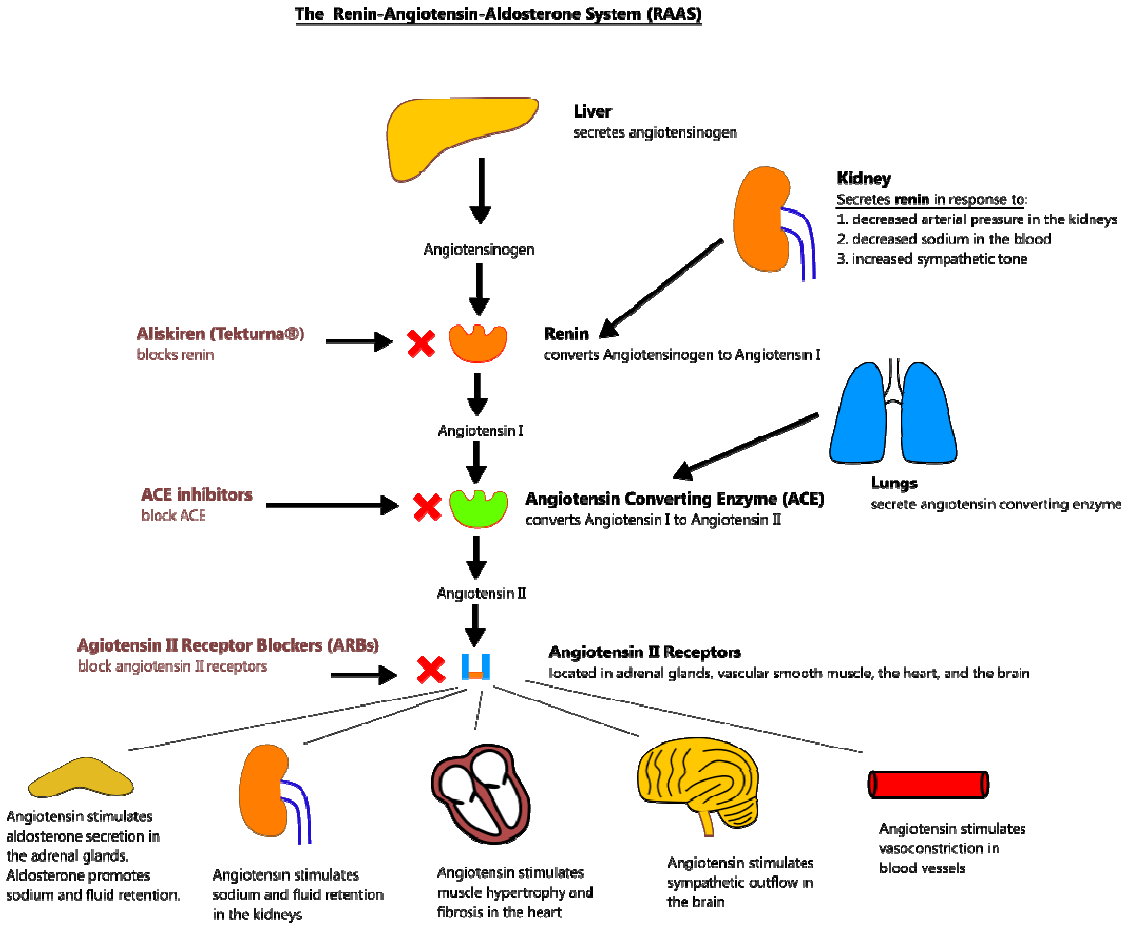

Figure 3.3.Renin-Angiotensin-Aldosterone System

Another function of angiotensin II is activation of the adrenal cortex to release aldosterone which causes reabsorption of sodium ion and water from the distal parts of the tubule. This also leads to

an increase in blood pressure and glomerular filtration rate. This entire mechanism is known as the renin-angiotensin mechanism (Figure 3.3). The Atrial Natriuretic Factor (ANF) is released when there is an increase in blood flow to the atria of the heart. It can cause a decrease in blood pressure by dilating blood vessels.

3.7 TYPES OF NITROGENOUS WASTES IN DIFFERENT ANIMAL GROUPS AND THEIR EXCRETION

Excretory products and their types

Metabolism of carbohydrates and fats produces $CO_2$and H_2O which are easy to remove. They are effectively removed through lungs (expired air), skin (sweat) or kidneys (urine).Other excretory products such as bile pigments (formed by the breakdown of RBCs), drugs etc. are removed in liver.Metabolism of proteins produces nitrogenous wastes such as ammonia, which is the basic nitrogenous catabolites of protein, formed by breakdown of amino acids is finally removed from Kidney.Depending upon the form in which nitrogenous waste is excreted from the body, the organisms are grouped as under into three categories:**Ammonotelic**, **Uricotelic** and **Ureotelic**.

3.7.1. AMMONOTELIC ORGANISM

Those animals which excrete their nitrogenous waste in the form of ammonia are known as **ammonotelic**. Ammonia is highly soluble in water with which it forms ammonium hydroxide (NH_4OH) which can damage cells directly by its alkaline caustic action. Excretion of ammonia requires large amounts of water, so that more water loss from the body. That is why such a mode is suitable for aquatic organisms which have a constant access to water. Ammonia is the first metabolic waste product of protein metabolism and no energy is required to produce ammonia. All aquatic invertebrates, bony fishes and aquatic amphibians are ammonotelic organisms.

3.7.2. URICOTELIC ORGANISM

Those animals which excrete their nitrogenous waste mainly in the form of uric acid and urates are known as **uricotelic**. The phenomenon is known as uricotelism. Elimination of uric acid requires lesser amount of water, comparatively less soluble in water and is less toxic as

compared to ammonia. All terrestrial animals like insects, reptiles, and birds excrete uric acid as nitrogenous wastes.

3.7.3. UREOTELIC ORGANISM

Those animals that excrete their nitrogenous waste mainly in the form of urea are known as **ureotelic** and the phenomenon is known as ureotelism. Ureotelic animals include *Ascaris*, earthworm (both are ammonotelic and ureotelic), cartilaginous fishes like sharks and sting rays, semi-aquatic amphibians such as frogs and toads, aquatic or semi aquatic reptiles like turtles, terrapins and alligators, and man and all other mammals.Urea is less toxic and less soluble in water than ammonia. Hence, it can stay for some time in the body. Sharks retain large quantity of urea in their blood, therefore, blood osmotic pressure approaches that of sea water, which minimizes water loss from their body.

3.7.4. OTHER EXCRETORY WASTES

Guanine- Spiders excrete guanine and are said to be guanotelic and their mode of excretion is called guanotelism.

Creatine and Creatinine- Muscle cells contain molecules of creatine phosphate, which are highly energy molecules and serve for storage of bioenergy like ATP. Excess amount of this phosphate is however, excreted out as such, or after being changed into creatinine. The latter is passed out through urine.

Tri-methylamine-oxide (TMO)- Marine teleost fishes excrete a large proportion of their nitrogen as trimethylamine oxide (TMO). Large amounts of this compound is also stored in their body for osmoregulation, (i.e., to minimize loss of water and entry of salts).

Ornithuric acid- It is excreted in small amount by birds and is formed by a combination of benzoic acid (formed during fat metabolism) with the amino acid ornithine.

Hippuric acid- It is formed when benzoic acid is combined with glycine. It is less toxic.

Bilirubin and Biliverdin- These are the bile pigments which are formed in the liver due to breakdown of haemoglobin of worn out RBCs. These are excreted through bile. In jaundice, level of bilirubin is high in the blood resulting yellow skin, white eyes, etc.

Allantoin- It is formed from uric acid as a result of an oxidation reaction catalyzed by the enzyme uricase. Higher primates including man do not have enzyme uricase. Allantoin is an excretory product of embryos of amniotes. In a very young embryo, the excretory matter is stored in allantois.

Bile Salts- Bile salts are the sodium and potassium salts of bile acids, which are conjugated with glycine or taurine. The bile acids (glycocholic acid and taurocholic acid) are derived from cholesterol.

Heavy metals- The liver also excretes heavy metals like lead, arsenic and bismuth. The other substances excreted in bile are heavy metals such as copper and iron, some toxins, some bacteria like typhoid bacteria, cholesterol, lecithin and alkaline phosphatase. Heavy metals and drugs are also excreted in the saliva.

Carbon Dioxide and Water- It is mainly expelled out by lungs. Some carbon dioxide is also excreted through sweat and defecation. Excess of water is a waste product and is eliminated in urine, faeces, sweat and expired air.

Drugs, Hormones and Other Substances- The liver is well known for its ability to detoxify or excrete into bile many drugs, including sulfonamides, penicillin, ampicillin and erythromycin. Several hormones secreted by the endocrine glands are either chemically altered or excreted by the liver, including thyroxine and essentially all the steroid hormones such as oestrogen, cortisol and aldosterone. The excess of water soluble vitamins like vitamin B complex and vitamin C is removed from the body in urine. Sebaceous glands (oil glands) secrete an oily secretion called sebum that contains some lipids such as sterols, other hydrocarbons and fatty acids. Sudoriferous glands (= sweat glands) in the skin and gastrointestinal tract also expel heat which is the result of various metabolic processes.

3.8 UREA PRODUCTION–HANS KREBS AND KURT HENSELEITCYCLE, URINEFORMATION

3.8.1. KREBS HENSLEITCYCLE (ORNITHINE CYCLE)

Liver converts toxic ammonia (NH3) into much less toxic urea which is excreted in urine. Urea is the end product of protein metabolism (amino acid metabolism).Urea is synthesized in liver and transported to kidneys for excretion in urine. Urea is produced through urea cycle which was discovered by Hans Krebs and Kurt Henseleit (1932), hence it is known as **Krebs-Henseleit cycle or Ornithine cycle**. The individual reactions, however, were described in more detail later on by Ratner and Cohen. Urea has two amino (-NH2) groups, one derived from NH3 and the other from aspartate. Carbon atom is supplied by CO2. Urea cycle includes five steps involving five distinct enzymes. The first two enzymes are present in mitochondria while the rest are localized in cytosol (the cytoplasm minus the mitochondria and endoplasmic reticulum).

(i) Synthesis of Carbamoyl Phosphate: Carbamoyl phosphate synthase 1 (CPS 1) of mitochondria catalyses the condensation of NH4+ ions with CO2 to form carbamoyl phosphate. This step consumes two ATPs.

(ii) Formation of Citrulline: Citrulline is synthesized from carbamoyl phosphate and ornithine by ornithine transcarbamoylase. Ornithine is regenerated and used in urea cycle. Ornithine and citrulline are basic amino acids.

(iii) Synthesis of arginosuccinate: Arginosuccinate synthase condenses citrulline with aspartate to produce arginosuccinate. This step requires ATP.

(iv) Cleavage of arginosuccinate: Arginosuccinate cleaves arginosuccinate to give arginine and fumarate. Fumarate liberated here provides a connecting link with Krebs cycle, gluconeogenesis, etc.

(v) Formation of Urea: Arginase is the fifth and final enzyme that cleaves arginine to form urea and ornithine. This ornithine enters mitochondria for its reuse in the urea cycle. The urea cycle (also called ornithine cycle) is irreversible.

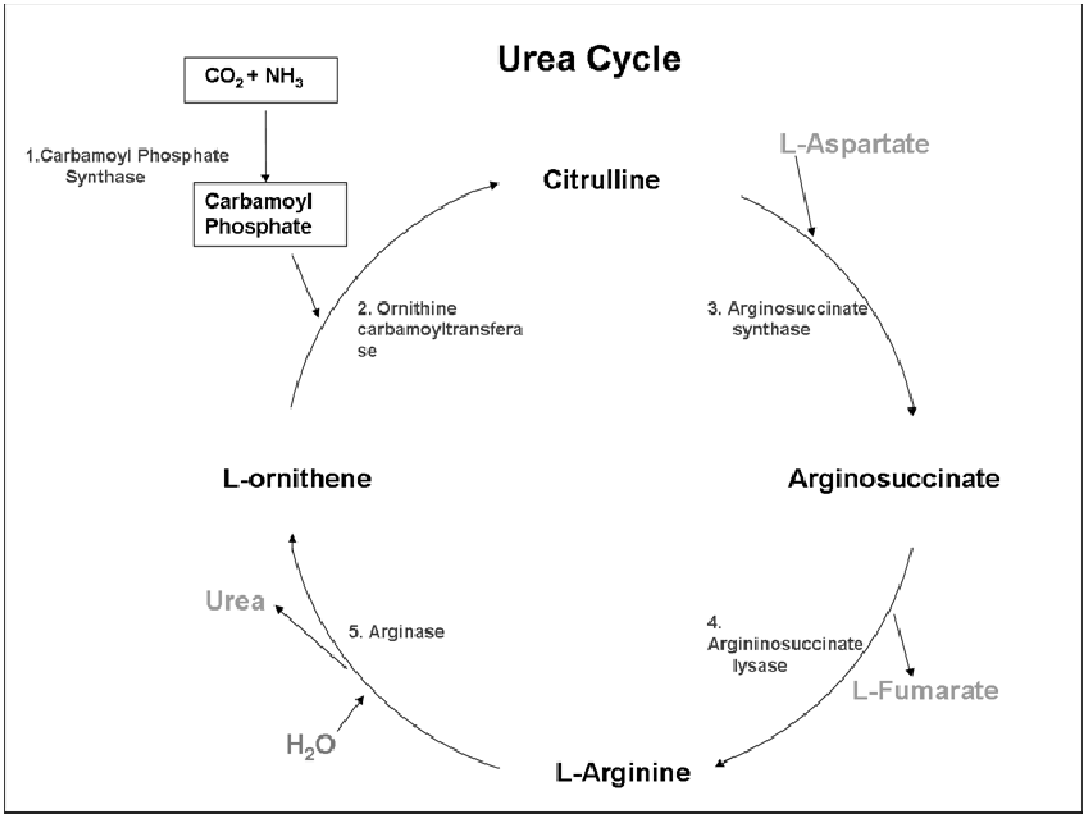

Figure 3.4 Mechanism of Urea formation (Krebs-Henseleit cycle)

3.8.2. MECHANISM OF URINE FORMATION

In Human beings urine is formed by kidneys. Each human kidney consists of about one millions of fine convoluted tubules called uriniferous tubules or nephrons. There are three major processes of urine formation in human body.

- Glomerular Filtration or Ultrafiltration
- Tubular Reabsorption or Selective reabsorption
- Tubular Secretion

1.Glomerular Filtration (= Ultrafiltration)

On an average 1100-1200 ml of blood is filtered by the kidneys per minute. The glomerular capillaries are narrower than the afferent renal arterioles. Therefore, the blood pressure in the glomerular capillaries becomes very high so that there is continuous process of ultrafiltration (filtration under pressure) through the semi-permeable glomerular capillaries. Thus water and many dissolved substances from the blood are filtered into the lumen of the Bowman's capsule through its walls. The glomerular filtrate contains a large amount of water and other dissolved sub-stances such as urea, uric acid, creatinine, amino-acids, glucose, sodium, potassium, vitamins, etc. Nephrons filter 125 ml of body fluid per minute; filtering the entire body fluid component 16 times each day. In a 24 hour period nephrons produce 180 liters of filtrate, of which 178.5 liters are reabsorbed. The remaining 1.5 liters forms urine.

Regulation of glomerular filtration- An increase in blood pressure, tends to stretch the afferent arteriole which increases the blood flow to the glomerulus. When the wall of the arteriole contracts, the diameter of the afferent arteriole is reduced that increases the flow of blood. Juxtaglomerular apparatus (JGA) cells secrete enzymes like renin that modulate blood pressure and thus renal blood flow. This regulates GFR. Blood vessels of the kidney are innervated by nerve fibres of the sympathetic neural system. When activated, the nerve fibres bring about constriction of renal arteries and cause decrease in renal flow and glomerular filtration rate.

2.Tubular Reabsorption

From the Bowman's capsule, the glomerular filtrate enters the proximal convoluted tubule. Absorption of selected materials takes place from the filtrate into the blood of the peritubular capillaries or vasa recta. It is termed the tubular reabsorption. Reabsorption involves both passive and active transport across the tubular epithelium. As already stated, the glomerular filtrate in the Bowman s capsule resembles blood plasma in composition except for plasma proteins and fats. Therefore, it is almost isotonic to the plasma.

Selective reabsorption at Proximal Convoluted Tubule (PCT): About 65 per cent of the glomerular filtrate is normally reabsorbed in the proximal convoluted tubule before reaching the loop of Henle. Glucose, amino acids, vitamins, hormones, sodium, potassium, chlorides, phosphates, bicarbonates, much of water and some urea from the filtrate are absorbed. Sulphates and creatinine are not reabsorbed. Sodium and potassium are reabsorbed by primary active

transport. Glucose and amino acids are reabsorbed by secondary active transport. Water is reabsorbed by osmosis. Chloride ions, urea and other solutes are reabsorbed by diffusion. The filtrate is isotonic to blood plasma.

Selective reabsorption at loop of Henle: It consists of descending limb and ascending limb.

(a) Descending limb of loop of Henle: As the filtrate flows in it, its water is reabsorbed due to increasing osmolality of interstitial fluid. Sodium and other solutes are not reabsorbed here. The filtrate becomes hypertonic to blood plasma.

(b) Ascending limb of loop of Henle: It is impermeable to water but permeable to K+, Cl– and Na+ and partially permeable to urea. Thus in the thick ascending limb of the loop of Henle sodium, potassium, calcium, magnesium, and chloride are reabsorbed. The filtrate becomes hypotonic to blood plasma.

Selective reabsorption at Distal convoluted tubules (DCT): There is active reabsorption of sodium ions from the filtrate under the influence of aldosterone (hormone secreted by the cortex of adrenal glands). Chloride ions are also reabsorbed in the distal convoluted tubules. Water is reabsorbed here under the influence of antidiuretic hormone (ADH) secreted by posterior lobe of pituitary gland. This makes the filtrate isotonic to blood plasma.

Selective reabsorption at Collecting duct: A considerable amount of water is reabsorbed in the collecting duct under the influence of ADH. Sodium is reabsorbed in the collecting duct under the influence of aldosterone. The filtrate is now called urine. Thus urine is hypertonic to blood and isotonic to medullary fluid.

3.Tubular Secretion

The cells of the renal tubule no. only remove substances from the filtrate by the process of reabsorption and send them to the blood capillaries (peritubular) but also excrete additional wastes from the blood stream into the filtrate by the process of secretion. Thus tubular secretion is the opposite of tubular reabsorption. It occurs as follows:

- Creatinine, hippuric acid, pigments, drugs including penicillin are actively secreted into the filtrate in the proximal convoluted tubule from the interstitial fluid. Hydrogen ions and ammonia are also secreted into the proximal convoluted tubule.
- Urea enters the filtrate by diffusion in the thin segment of the ascending limb of loop of Henle.
- Potassium, hydrogen ions, ammonia, HCO_3^- ions are secreted by active transport into the filtrate in the distal convoluted tubule.

Maximum hydrogen secretion occurs in the proximal convoluted tubule. Removal of hydrogen ions and ammonia from the blood in the proximal convoluted tubule and distal convoluted tubule helps to maintain the pH of the blood between 6 to 8 (pH of blood is usually 7.4).

Tubular secretion probably plays a minor role in the function of human kidneys but in animals like marine fishes and desert amphibians, whose nephrons do not possess developed glomeruli, their urine is formed mainly by the tubular secretion of urea, creatinine and mineral ions. Kidneys excrete about 1.5 litres of urine in a day.

3.9 OSMOREGULATION

Osmoregulation is the process by which an organism regulates the water balance in its body and maintains the homeostasis of the body. It includes controlling excess water loss or gain and maintaining the fluid balance and the osmotic concentration, that is, the concentration of electrolytes. It ensures that the fluids in the body do not get too diluted or concentrated.

There are two major types of Osmoregulation:

Osmoconformers- These organisms try to match the osmolality of their body with their surrounding, thus eliminating the need for spending energy on osmoregulation. Most invertebrate seawater organisms are osmoconformers.

Osmoregulators- These organisms maintain their internal osmolality, which can be extremely different from that of the surrounding environment, through physiological processes.

Osmoregulation of Fishes

Most Cartilaginous fishes such as sharks, Chimaeras, skates and ray are iso-osmotic to seawater. This is because of their plasma. The high osmotic level is retained by high concentration of urea in their blood.

Surplus inorganic electrolytes, (ex Na^+ and Cl^-) can drawn-out into the blood at the gills, and can be excreted through the kidneys. They also can be excreted out by a special organ called the rectal gland. This rectal gland t is located at the end of the alimentary canal. The kidneys of freshwater fishes remove water actively that was taken in inactively. These freshwater fishes lose salts to the dilute environment. The salt is replaced by vigorously absorbing ions from the nearby fluids into their bodies through their gills. The bodies of freshwater ray-finned fishes are hypertonic to their environment and water can diffuse easily into them, so therefore they maintain water balance by producing large volumes of dilute urine.

3.9.1 REPTILES, AVES AND MAMMALS

Osmoregulation of Reptiles

Marine reptiles are composed of different types of animals such as crocodiles, marine turtles, marine snakes, and even marine iguanas. They tend to be hyposmotic regulators. They don't have specialized kidneys that allow them to produce urine with a higher concentration than seawater. They differ from the other marine vertebrates in that they use their lungs which don't come in contact with the water. They have a respiratory epithelium, which is a protective layer that doesn't allow water to penetrate. However, it is not all the impermeable since reptiles tend to lose some water when in contact with the sea. They also have thinner epithelial tissue that covers their mouth, nasal passages as well as their eyes.Their skin is relatively impermeable as well. However, when a reptile feeds on a marine organism it increases the concentration of salt in its body to that of blood. Therefore, reptiles have developed ways to secrete this excess amount of solutes that comes through the consumption of food.Some reptiles excrete a high sodium chloride fluid into the water and out of their bodies. For instance, crocodiles act in a hyperosmotic way by decreasing the concentration of solutes through glands which are on their tongue that help them diffuse the excess salt. Sea turtles have lacrimal glands that aid them in the excretion of the fluid containing the high concentration of sodium chloride. Marine iguanas use

their nasal glands to excrete the excess salt from their bodies, which almost looks as if the iguana were sneezing.

Osmoregulation of Birds

Marine birds are categorized by their adaptation to marine settings. Many marine birds are able to dive into the water to capture prey and some birds, like penguins, are able to swim into deeper water, they also do not get wet when they enter the water. Birds have a preening gland that secretes waxes and fats. The bird spreads these wax and far throughout its feathers in order to make itself waterproof and insulated. Some bird feathers is made of keratin that aids in water proofing the birds. Salt glands in Marine birds allow them to drink salt water and expel the excess salt from their bodies. Salt glands concentrate salt from blood in an area close to the sinuses, the excess salt is excreted by the bird through sneezing. Some marine birds release the excess salt directly from salt glands.

Osmoregulation of Mammals

Mammals have relatively impermeable skin which is not able to be penetrated easily for processes like diffusion or osmosis to take place in the presence of a high/low concentration of solutes or water. When a mammal encounters high concentration of salt due to the swallowing of salt water when catching its prey, however, its kidneys react by increasing the urine flow as well as making the urine as salty as the blood. Marine mammals have a far more complex kidney than terrestrial because they are able to regulate water and electrolytes at a higher rate. Scientists have found that their kidneys have a more capability of producing highly concentrated urine which helps in the excretion of the excess solutes.

There seems to be some sort of mechanism by which these mammals are able to balance the levels of electrolytes in their body through the consumption of food. There have been strong suggestions implying that marine mammals do not rely on sea water in order to maintain water balance in their bodies. For instance, in a study done with marine mammals scientists have found that “drinking is not essential for maintaining water balance, but the incidental ingestion associated with feeding may be important for maintaining electrolyte homeostasis.

3.10 SUMMARY

- All living organisms need organic raw materials to build up most of their own body molecules, and they require energy to operate the metabolic reactions that sustain life.
- All organisms obtain their nutrients as food from their surrounding or habitat.
- Depending on the quantity and functions nutrients are classified as macronutrients and micronutrients. Macronutrients e.g. carbohydrates, proteins and lipids are taken in large amount and required to produce energy and for growth and repair. , Micronutrients e.g. vitamins and minerals do not provide energy and are required in very small amount but they are essential regulatory components of food, their deficiency can cause specific disease.
- Animals obtain their nutrients through a broad variety of feeding patterns.Herbivores eat plant material. Carnivorous animals like those in the cat and dog families, polar bears, seals, crocodiles and birds of prey catch and eat other animals. Many animals feed on both animal and vegetable material – they are omnivorous. There are currently two similar definitions of omnivorism
- The process of conversion of complex food substances to simple absorbable forms is called digestion.
- Digestion in animals is carried out by means of mechanical and chemical processes. Mechanical digestion comprises mastication, swallowing and churning of food in stomach.
- Chemical digestion of food is achieved by different types of hydrolytic digestive enzymes. These enzymes are secreted by salivary glands, gastric glands, pancreas and intestinal glands in their secretions.
- End products of digestion are absorbed through the intestinal mucosa into the blood or lymph. It is carried out by passive, active or facilitated transport mechanisms.
- The absorbed food materials are transported by blood and lymph. Lymph is finally transferred to the blood circulation. The blood transports absorbed food materials to different body cells where food materials become integral component of the living protoplasm and are used for energy, growth and repair.
- We take in a lot of things in our body the whole day. Metabolic reactions in body produces several byproducts which are unwanted, toxic and harmful on storage. They need to be

simultaneously excreted out of the body to maintain the body's steady state. This process of removal of chemical wastes from our body is known as excretion.

- Depending upon the form in which nitrogenous waste is excreted from the body, the organisms are grouped as under into three categories: Ammonotelic, Uricotelic and Ureotelic.
- All aquatic invertebrates, bony fishes and aquatic amphibians are ammonotelic organisms.
- All terrestrial animals like insects, reptiles, and birds excrete uric acid as nitrogenous wastes.
- Those animals that excrete their nitrogenous waste mainly in the form of urea are known as ureotelic and the phenomenon is known as ureotelism. Ureotelic animals include Ascaris, earthworm (both are ammonotelic and ureotelic), cartilaginous fishes like sharks and sting rays, semi-aquatic amphibians such as frogs and toads, aquatic or semi aquatic reptiles like turtles, terrapins and alligators, and man and all other mammals.
- Other excretory wastes include guanine, creatine, creatinine, TMO, Ornithuric acid, hippuric acid, bile pigments, hormones and drugs.
- Excretion in humans occurs through the kidney, sweat glands, lungs, liver, skin and alimentary canal.
- Kidneys are the chief excretory organs and are mainly concerned with the excretion of urea in the form of urine.
- Liver converts toxic ammonia (NH_3) into much less toxic urea which is excreted in urine. Urea is the end product of protein metabolism (amino acid metabolism). Urea is synthesized in liver and transported to kidneys for excretion in urine. Urea is produced through urea cycle or Krebs-Henseleit cycle or Ornithine cycle.
- In Human beings urine is formed by kidneys.There are three major processes of urine formation in human body.
  - ✓ Glomerular filtration
  - ✓ Tubular reabsorption
  - ✓ Tubular secretion
- Kidneys produce about 1.5 litres of urine in a day. Human is urine is slightly acidic (pH 6.8) and pale yellow in colour due to presence of urochrome (urobillins).
- Osmoregulation is the process by which an organism regulates the water balance in its body and maintains the homeostasis of the body.

- Osmoconformerorganisms try to match the osmolality of their body with their surrounding, thus eliminating the need for spending energy on osmoregulation. Most invertebrate seawater organisms are osmoconformers.
- Osmoregulatororganisms maintain their internal osmolality, which can be extremely different from that of the surrounding environment, through physiological processes. Higher animals like some fishes, reptiles, birds and mammals are good examples of osmoregulators.

3.11 TERMINAL QUESTIONS& ANSWERS

3.11.1. MULTIPLE CHOICE QUESTIONS

1. Which animal group has only intracellular digestion?
    a) Sponges
    b) Cnidarians
    c) Helminthes
    d) Arthropods
2. Saliva contains enzymes
    a) Trypsin
    b) Pepsin
    c) Ptyalin
    d) Nuclease
3. Enzyme secreting cells of gastric glands are
    a) Peptic cells
    b) Oxyntic cells
    c) Mucous cells
    d) G cells
4. Inactive trypsinogen is activated by
    a) HCl
    b) Enterokinase
    c) Calcium ions

d) Bile salts

5. Which one of the following enzyme acts in acidic medium?
   a) Pepsin
   b) Chymotrypsin
   c) Trypsin
   d) None of the above
6. Which one of them is not a ruminant?
   a) Cattle
   b) Sheep
   c) Goat
   d) Rabbit
7. Bacteriocidal enzymes are known as
   a) Amylases
   b) Lysosomes
   c) Lysozymes
   d) Liposomes
8. HCl (Hydrochloric acid) of gastric juice is secreted by
   a) Parietal cells
   b) Peptic cells
   c) Kupffer cells
   d) Dust cells
9. Milk protein ‘casein’ in infants is digested with help of
   a) Renin
   b) Rennin
   c) Lipase
   d) Nuclease
10. Bile juice is essential for
   a) Protein digestion
   b) Nucleic acid digestion
   c) Lipid digestion
   d) Carbohydrate digestion

11. Mechanical digestion of food to increase the surface area for enzyme action is carried out by
    a) Tongue
    b) Teeth
    c) Lips
    d) Oesophagus
12. Digestion of food in human beings starts in
    a) Mouth
    b) Oesophagus
    c) Stomach
    d) Intestine
13. In human beings protein digestion occurs in
    a) First in acidic then in alkaline medium
    b) Only in acidic medium
    c) Only in alkaline medium
    d) First in alkaline then in acidic medium
14. Castle's Intrinsic Factor (CIF) essential for absorption of vitamin B_{12} is secreted in
    a) Saliva
    b) Gastric juice
    c) Intestinal juice
    d) Bile juice
15. After digestion fat is absorbed in
    a) Blood capillaries
    b) Lymph capillaries
    c) Serum
    d) Tissue fluid
16. Glucose and fructose are absorbed respectively by means of
    a) Facilitated diffusion and co-transport
    b) Co-transport and Facilitated diffusion
    c) Only active transport
    d) Simple diffusion
17. Digested and absorbed food is used by body cells for

a) Energy
b) Growth
c) Repair
d) All the above

18. Structural and functional unit of kidneys are
a) Seminiferous tubules
b) Uriniferous tubules
c) Nephridia
d) Flame cells

19. Flame cells (solenocyte cells) are excretory structure of
a) Round worms
b) Flat worms
c) Earthworms
d) Rag worms

20. Match the columns A and B

Column A	**Column B**
(i) Ureotelic	(a) Grasshopper
(ii) Uricotelic	(b) Rabbit
(iii) Ammonotelic	(c) Tadpoles
(iv) Guanotelic	(d) Spiders

a) (i)- a (ii)- b (iii)- c (iv)- d
b) (i)- c (ii)- d (iii)- a (iv)- b
c) (i)- b (ii)- a (iii)- c (iv)- d
d) (i)- d (ii)- b (iii)- a (iv)- c

21. Atrial Natriuretic Factor (ANF) is secreted by heart to
a) Decrease blood pressure
b) Increase blood pressure
c) Increase protein synthesis
d) Promote enzyme action

22. Urea in mammals is synthesized in
    a) Kidneys
    b) Liver
    c) Muscles
    d) Under skin
23. Urea in synthesized by
    a) Krebs cycle
    b) Krebs- Henseleit cycle
    c) Glycolysis
    d) Cori cycle
24. Ultrafiltration of blood at glomerulus during urine formation is
    a) An active process
    b) A passive process
    c) Active and passive process both
    d) None of the above
25. Glomerular Filtration Rate (GFR) in human kidneys is
    a) 125 ml/minute
    b) 1100-1200 ml/ minute
    c) 1.5 litre/minute
    d) 180 litre/minute
26. On an average …… ml of blood is filtered by both kidneys per minute
    a) 120-125
    b) 1100-1200
    c) 178-180
    d) 1,5- 1.8
27. Most of the useful substances of nephric filtrate are absorbed by
    a) PCT
    b) DCT
    c) Descending loop of Henle
    d) Ascending limb of loop of Henle
28. Active reabsorption of sodium ions from the nephric filtrate at DCT is under the influence of

a) Anti Diuretic Hormone (ADH)
b) Oxytocin
c) Rennin
d) Aldosterone

29. Osmoregulation in crocodiles and marine turtles is carried out by
a) Kidneys
b) Skin
c) Tear glands
d) Lungs

30. Marine mammals like whale and dolphins maintains their osmotic balance in sea water by
a) Producing very dilute urine
b) By drinking more sea water
c) By producing concentrated urine
d) By retaining urea in their blood

3.11.2. VERY SHORT ANSWER TYPE QUESTIONS

1. Name the process of conversion of complex food into simple and absorbable form.
2. Name any two omnivorous animals.
3. Give the name of enzyme present in our saliva.
4. Which food component is partially digested in our oral cavity?
5. Name the excretory waste pigments of bile juice.
6. Food in stomach is digested in ……medium.
7. Inactive pepsinogen in stomach is activated by……..
8. Digested lipids are absorbed in lymph capillaries as ……..
9. What is the average weight of human kidney?
10. What is the main excretory waste of human beings?
11. Name the structural unit of kidneys.
12. Give the examples ammonotelic animals.
13. Name the excretory waste of spiders.

14. What is glomerulus?
15. How much nephric filtrate is produced per day by both of the human kidneys?
16. Name the cycle through which urea is synthesized in human liver.
17. Name the hormone which help in absorption of water reabsorption at DCT.
18. Write the names of two examples of osmoregulators.
19. Write the expanded form of RAAS.

ANSWER KEYS

3.11.1. MULTIPLE CHOICE QUESTIONS

1. A	2. C	3. A	4. A	5. A	6. D	7. C	8. A	9. B	10. C
11. B	12. A	13. A	14. B	15. B	16. B	17. D	18. B	19. B	20. C
21. A	22. B	23. B	24. B	25. A	26. B	27. A	28. D	29. C	30. C

3.11.2. VERY SHORT ANSWER TYPE QUESTIONS

1. digestion 2. human, crow 3. salivary amylase (ptyalin) 4. starch 5. bilirubin, biliverdin 6. acidic 7. HCl 8. chylomicron 9. 125-150 gm 10. urea 11. nephron 12. protozoans (amoeba, paramecium), sponges (sycon) 13. guanine 14. a bunch of capillaries 15. 180 litres 16. ornithine cycle or Krebs Henseleit cycle17. ADH 18. sharks and penguin 19. Renin Angiotensin Aldosterone System

3.11.3. SHORT ANSWER TYPE QUESTIONS

1. Define digestion and their role in animals life.
2. Define herbivorous, carnivorous and omnivorous feeding habitat.
3. Why digestion of food is essential for animals?
4. Write the composition of gastric juice.
5. Explain the role of bile juice in food digestion.
6. What are ruminants? Give some examples.
7. Name the substances of final digestion of carbohydrates, proteins and lipids.

8. What do you understand by assimilation of food? Give a brief account.
9. Describe the Renin Angiotensin Aldosterone system (RAAS) for kidney regulation.
10. Explain why most of the aquatic animals are ammonotelic?
11. Give a comparative account of ammonotelic, ureotelic and uricotelic animals.
12. Describe the Ornithine cycle for urea formation.
13. Why uricotelism is considered as mode of water conservation in animals?
14. Give a brief note on glomerular filtration of urine formation.
15. What do you understand by selective reabsorption? Mention its significance.
16. Explain the role of glomerulus in urine formation.
17. Write a short note on role of loop of Henle in making urine concentrate.
18. Define osmoregulation. Differentiate between osmoregulators and osmoconformers.
19. What are crocodile tears? Give the significance.
20. Explain how marine birds regulate their water and electrolyte balance?
21. Write a brief note osmoregulation in marine mammals.
22. Explain why nitrogenous wastes are harmful to store in body?

3.11.2. LONG ANSWER TYPE QUESTIONS

1. Describe the pattern of digestion and absorption in animals.
2. Write an essay on role of digestive enzymes in food digestion.
3. Describe the mechanism of digestion of food in small intestine.
4. Describe the role of different digestive juices, their composition in digestion.
5. Differentiate between mechanical and chemical digestion. Give a detailed account of chemical digestion of food in animals.
6. Describe the mechanism of protein digestion in different parts of alimentary canal.
7. Describe the mechanism of digestion and absorption of fat in mammals.
8. Explain how different components of food are absorbed in alimentary canal?
9. Describe the structure and function of human kidneys.
10. Give a detailed account of types of nitrogenous wastes and their elimination in different animals.
11. Describe the mechanism of urine formation in mammals.
12. Describe the role of different parts of nephron in urine formation.
13. Give a detailed account of osmoregulation in vertebrates.

14. Describe the role of different factors and components of kidney regulation.

3.12 REFERENCES

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UNIT 4: PHYSIOLOGY OF NERVOUS SYSTEM &MUSCLE STIMULATION

CONTENT

4.1 OBJECTIVES

Upon completion of this unit, you should be able to-

- Know the structure of neuron
- Know the generation and conduction of nerve impulse
- Get the concept of synaptic transmission of nerve impulse
- Learn the different types of neurotransmitters
- Know the different types of sensory receptors
- Learn about the senses of smell, taste and vision
- Learn about muscles, their structure, types and characteristics
- Know how muscles contract
- Know about neuro-muscular junction and their functioning

4.2 INTRODUCTION

The act of changing place or position by entire body or by one or more of its parts is called movement. Animals that can move are able to flee, hunt for prey, travel long distances or conquer new habitats. Movement may occur at cellular level, for instance cytoplasmic streaming or cyclosis in protozoans and swimming of gametes to achieve mother nature goal. Motion at organ level, such as heart beat and rotation of eyeball or at the organism level, for example swimming by fish, flying by a bird and walking by a man show the dynamics of life. With the evolution of neuromuscular systems, animals acquired the capacity for articulated movement, allowing them to develop complex patterns of behavior. Multicellular animals have structurally complex body organization. Due to this, there arises a need to have a system for coordinating various metabolic and homeostatic activities of different parts, organs, organ systems in the body. This is achieved by nervous and endocrine systems present in the body. Higher animals involve muscles, skeleton and joints for locomotion. Movement results from cooperation between muscles and skeletal elements. The muscles provide force and the skeleton offers hard

surface for the force to work against. The muscular system contains muscle tissues and interconnects with both the nervous system and skeletal system.

Nerves control the muscles and allow us to consciously direct movements. The nervous system allows for control and coordination of skeletal muscular movements that may be consciously predetermined, or may happen automatically, such as reflexes. Other parts of the nervous system control and coordinate subconscious body activities, including heart rate, gland secretions and smooth muscle movement in the digestive system. Some activities, such as breathing, can be controlled both subconsciously and consciously. The nervous system typically works quickly. It also allows us to integrate and store information, such as when you are learning.The nervous system transmits signals to different parts of the body to coordinate function. Electrochemical signals are processed in the brain and sent down the spinal cord, which runs the length of the back. From the spinal cord, peripheral nerves send signals out to the extremities. Return signals come in through sensory nerves and either return to the spinal cord for processing or back to the brain. The spinal cord processes reflexes and repeated patterns.

4.3 STRUCTURE OF A NEURON

The basic functional units of the nervous system that transmit messages are cells called neurons. Neurons are specialized cells of the nervous system that transmit signals throughout the body. Signals travel through a neuron as electrical impulses. Neurons release chemical substances, known as neurotransmitters, to transmit information to other neurons, to muscles, or to glands. The chemical messages of the nervous system are transmitted over short distances, and their effects are short-lived. You may already know that neurons can do many different things from sensing external and internal stimuli, to processing information and also directing muscle actions.

4.3.1 STRUCTURE OF A TYPICAL NEURON

The basic structure of a neuron is best studied in a spinal motor neuron. A neuron primarily consists of the cell body and processes called neurites, which are of two kinds, the dendrites and the axon (figure 4.1).

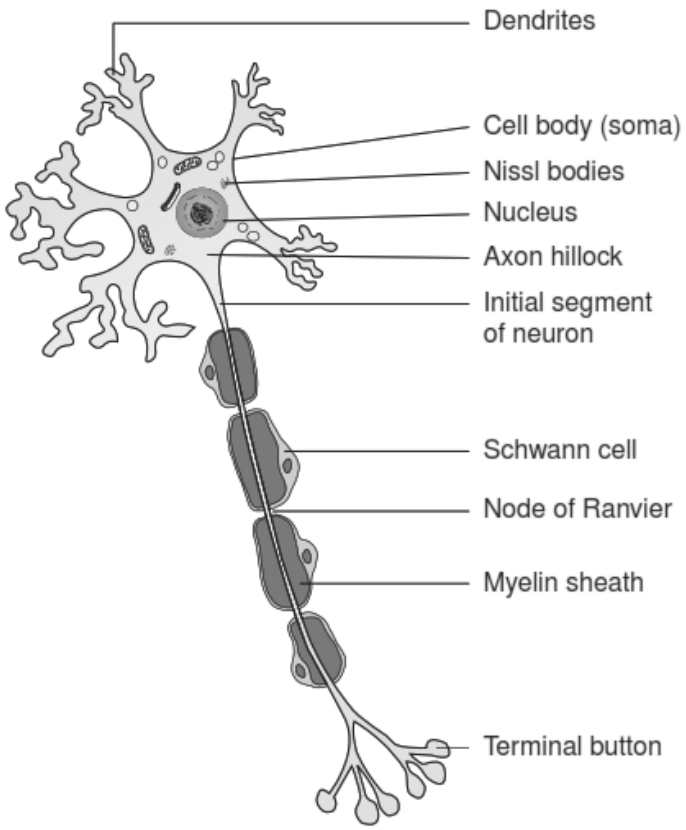

Figure 4.1 Structure of a typical Neuron

Cell Body

The cell body of a neuron is also called the soma or perikaryon and may be round, stellate, pyramidal or fusiform in shape. Like any other cell it consists of a mass of cytoplasm with all its principal constituents surrounded by a cell membrane. The cell body contains a large nucleus with one or two nucleoli but there is no centrosome. In addition to the general features of a typical cell, the cytoplasm of a neuron has following distinctive characteristics-

Nissl granules/bodies: These are basophilic granules, and composed of rough surfaced (with ribosomes) endoplasmic reticulum. These are concerned with protein synthesis in neurons. The proteins are needed for maintenance and repair, and for production of neurotransmitters and enzymes. The Nissl bodies are present in the dendrites as well but are usually absent from the axon hillock and the axon.

Neurofibrills- These consist of microfilaments and microtubules. These filaments provide a frame work of shape for cell body.

Dendrites

The dendrites are multiple small branched processes which contain Nissl bodies and neurofibres. Dendrites are the receptive processes of the neuron receiving signals from other neurons via their synapses with axon terminals.

Axon

The axon is the single longer process of the nerve cell. It varies in length from a few microns to one metre. It arises from the conical extension of the cell body called axon hillock, which is devoid of the Nissl bodies. The part of the axon between the axon hillock and the beginning of myelin sheath is called the initial segment. In the axon, the cell membrane continues as axolemma and the cytoplasm as axoplasm. The axon terminates by dividing into a number of branches, each ending in a number of synaptic knobs also known as terminal buttons or axon telodendria. Synaptic knobs contain microvesicles in which chemical neurotransmitters are stored. Myelin sheath is present around the axon in the so-called myelinated nerve fibres. Myelin sheath which consists of protein–lipid complex is produced by glial cells called Schwann cells which encircle the axon forming around it a thin sleeve. Each Schwann cell provides the myelin sheath for a short segment of the axon. At the junction of any two such segments, there is a short gap, i.e. periodic 1 μm constrictions at about 1 mm distance. These gaps are the nodes of Ranvier. There are some axons which are devoid of myelin sheath. Myelination of axons increases the speed of conduction, but greatly increases their diameter. Axons perform the specialized function of conducting impulses away from the cell body.

Note. The absence of centrosome indicates that the neuron has lost ability for division. Thus, neurons once destroyed are replaced by neuroglia only.

4.3.2 THE BASIC FUNCTIONS OF A NEURON

If you think about the roles of the three classes of neurons, you can make the generalization that all neurons have three basic functions. These are to:

1. Receive signals (or information).

2. Integrate incoming signals (to determine whether or not the information should be passed along).

3. Communicate signals to target cells (other neurons or muscles or glands).

4.3.3 Classes of neurons

Based on their roles, the neurons found in the human nervous system can be divided into three classes: sensory neurons, motor neurons, and interneurons.

Sensory neurons

Sensory neurons get information about what's going on inside and outside of the body and bring that information into the CNS so it can be processed. For instance, if you picked up a hot coal, sensory neurons with endings in your fingertips would convey the information to your CNS that it was really hot.

Motor neurons

Motor neurons get information from other neurons and convey commands to your muscles, organs and glands. For instance, if you picked up a hot coal, it motor neurons innervating the muscles in your fingers would cause your hand to let go.

Interneurons

Interneurons, which are found only in the CNS, connect one neuron to another. They receive information from other neurons (either sensory neurons or interneurons) and transmit information to other neurons (either motor neurons or interneurons).

Depending upon the number of poles from which processes arise, neurons are divided into four categories (figure 4.2).

1. **Unipolar** neurons have a single pole, from which both the processes—axon and dendrite arise. True unipolar cells are present only in embryonic stage in human being.

2. **Bipolar** neurons have two poles, one for axon and other for dendrite. Bipolar neurons are found in the vestibular and cochlear ganglia, in the nasal olfactory epithelium and as bipolar cells in the retina.

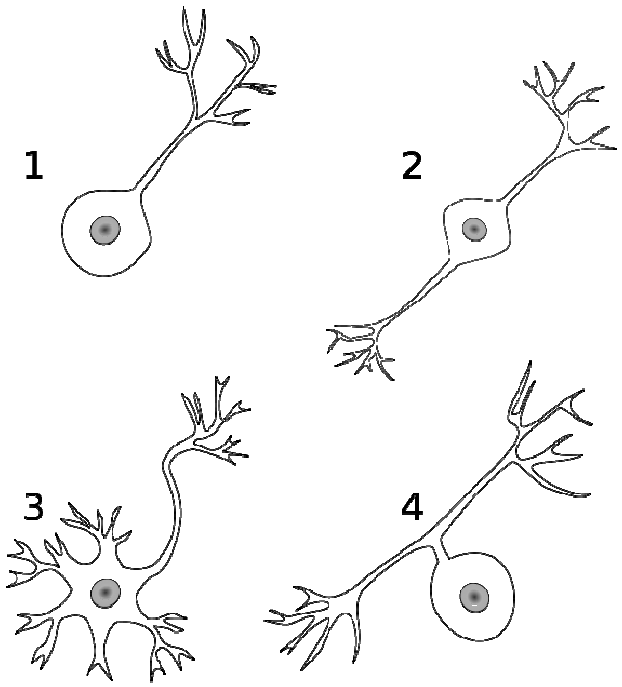

Figure 4.2.Different types of neurons. (1) Unipolar (2) Bipolar (3) Multipolar (4) Pseudounipolar

3. **Multipolar** neurons have many poles. One of the poles gives rise to axon and all others to dendrites. Most vertebrate neurons, especially in the central nervous system (CNS) are multipolar. The dendrites branch profusely to form the dendritic tree.

4. A**pseudounipolar**neuron (pseudo – false, uni – one) is a kind of sensory neuron in the peripheral nervous system. This neuron contains an axon that has split into two branches; one branch runs to the periphery and the other to the spinal cord. Pseudounipolar neurons are found in dorsal root ganglia of spinal nerves.

4.3.4 PROPERTIES OF NEURON OR NERVE CELL

Excitability : It is the ability of the nerve cells and fibres to enter into an active state called the state of excitation in response to a stimulus. Excitation arises at the receptors on account of various stimuli such as light, temperature, chemical, electrical or pressure which constantly act on the organisms.

Conductivity : The excitation does not remain at the site of its origin. It is transmitted along nerve fibres. The transmission of excitation in a particular direction is called conductivity.

4.3.5 Neuroglia or Glia Cells

Neuroglia, or glial cells, are part of the nervous system that support neurons by providing them nutrients, oxygen and insulation and by eliminating harmful pathogens. They comprise approximately half of the total cellular composition of the central nervous system, and are found in all regions of the spinal cord and brain. Glia were first described in 1856 by the pathologist **Rudolf Virchow**. There are six common types of glia cells in nervous system (figure 4.3).

(i) Microglia-clean up cellular debris via phagocytosis.

(ii) Astrocytes- support and repair neurons; form the brain-blood barrier within the central nervous system.

(iii) Satellite- form the brain-blood barrier within the central nervous system, function similarly to astrocytes.

(iv) Ependymal- form epithelial lining of the central nervous system. and produce cerebrospinal fluid.

(v) Oligodendrocytes-myelinates axons of the neurons in the central nervous system.

(vi) Schwann Cells-myelinates axons of the neurons in the peripheral nervous system.

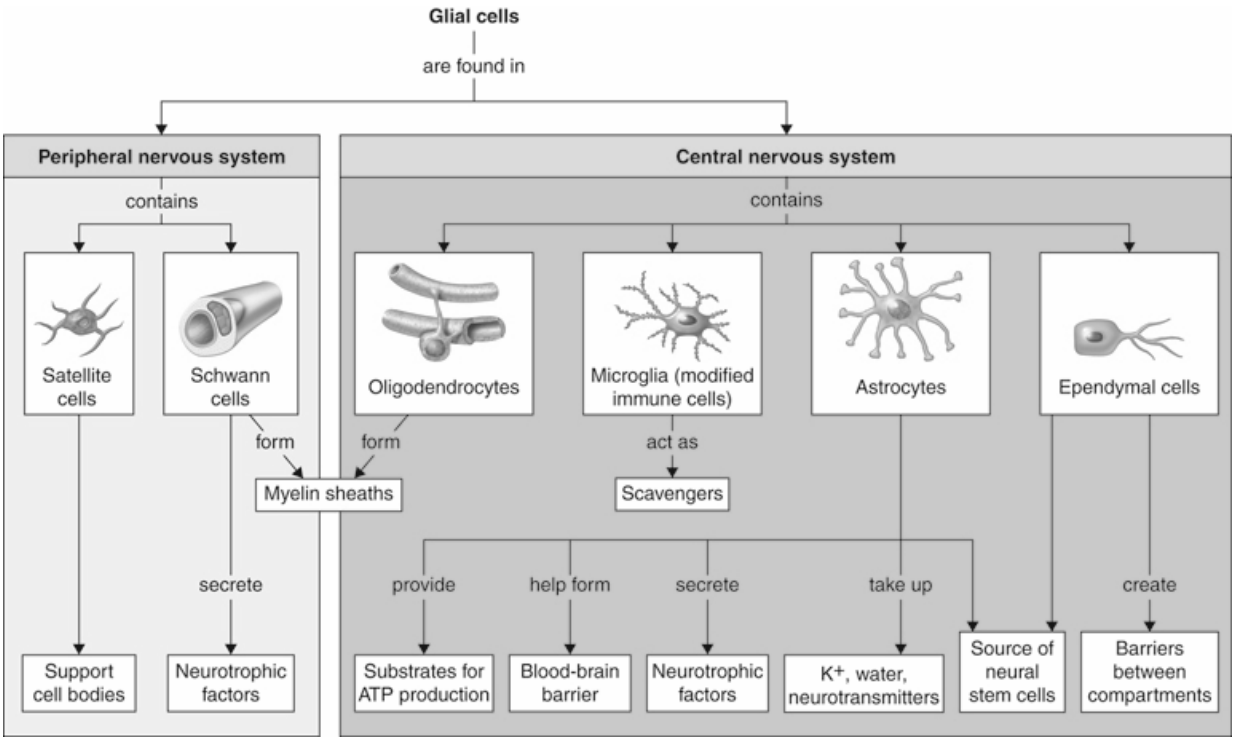

Figure 4.3.Types of glia cells and their function

4.4 GENERATION OF NERVE IMPULSE AND PROPAGATION

A wave of reversed polarity or depolarization (action potential) moving down an axon is called a ne**rve impulse**. The most accepted theory of nerve impulse conduction is **ionic theory** proposed by Hodgkin and Huxley (1952). This theory states that nerve impulse is an electro-chemical event governed by differential permeability of neurilemma to Na+ and K+ which in turn is regulated by the electric field. Generation and propagation of nerve impulse through nerve cell completes in three sequential events i.e. polarization, depolarization and repolarization (figure 4.4).

4.4.1 POLARIZATION (RESTING MEMBRANE POTENTIAL-RMP)

In a resting nerve fibre (a nerve fibre that is not conducting an impulse), sodium ions (Na+) predominate in the extracellular fluid, whereas potassium ions predominate in the intracellular fluid (within the fibre). Intracellular fluid also contains large number of negatively charged (anions) protein molecules. Na+ are 10 times more outside the neuron and K+ ions are 25 times more inside the cell. Thus it makes a considerable difference between the ion concentration outside and inside the plasma membrane. It also causes a difference in electrical charges on either side of the membrane. The plasma membrane is electrically positive outside and negative inside. This potential difference across the plasma membrane is known as **resting potential**. This potential averages – 70 mv (– 60 to – 90 mv) in inner side of membrane in respect to outer side.

Due to different concentrations of ions on the two sides of the membrane, sodium ions tend to diffuse into the nerve fibre and potassium ions tend to diffues out of the nerve fibre. The membrane of a resting nerve fibre is more permeable to potassium than to sodium. So potassium leaves the nerve fibre faster than sodium enters it.This results in a higher concentration of cations outside the membrane compared to the concentration of cations inside it. This state of the resting membrane is called polarised state and makes its inner side electronegative to its outerside.

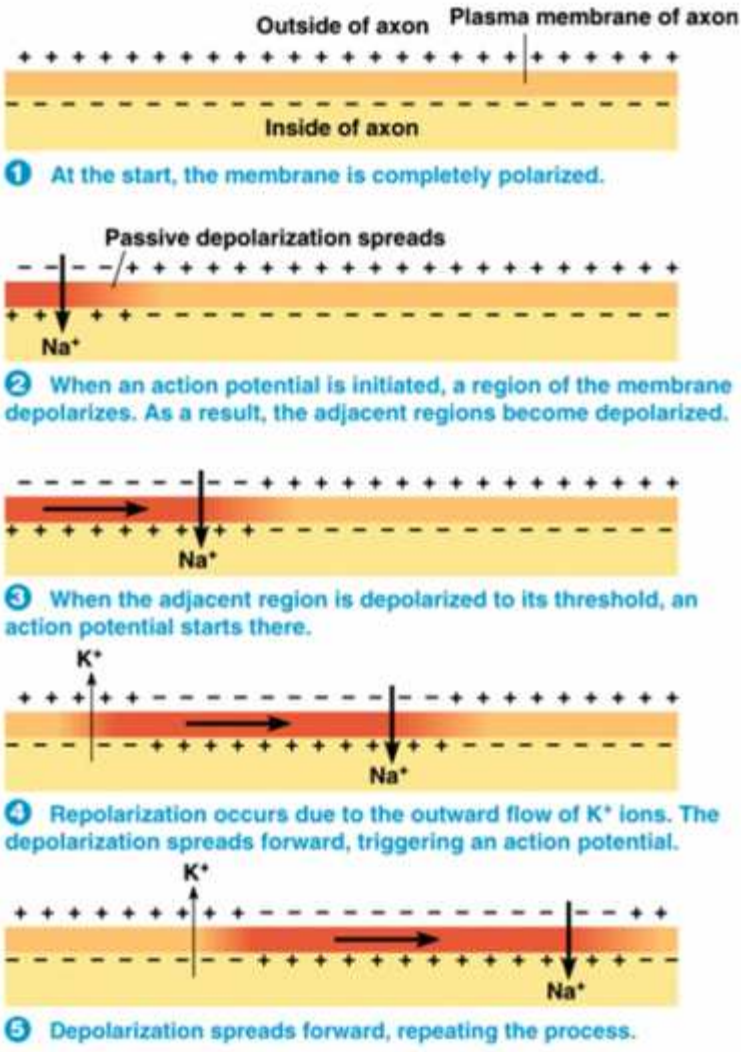

Figure 4.4 Generation and conduction of nerve impulse

4.4.2 DEPOLARIZATION (ACTION MEMBRANE POTENTIAL OR AMP)

When the nerve fibre is stimulated mechanically, electrically, thermally or chemically a disturbance is felt at the point of stimulation which gives rise to a local excitatory state. The membrane becomes permeable to sodium ions. Suddenly sodium ions rush inside the nerve fibre and potassium ions diffuse out of the axon membrane. Due to the diffusion of ions, more sodium ions enter the axon than potassium ions leave it, so that the positive and negative charges on the outside and inside of the axon membrane are reversed. The membrane is negatively charged on the outside and positively charged on the inside. The membrane with reversed polarity is said to

be **depolarized**. Thus the impulse is propagated as a wave of depolarization (reversed polarity). This wave of depolarization travelling down a nerve fibre is called action potential. Infact, the action potential "moves" in the manner of a spark moving along a fuse. This "moving" action potential constitutes the nerve impulse. The action potential (impulse) is the basic means of communication within the nervous system. The action potential of + 45 mv on inner side of axolemma in respect to its outer side is also called **spike potential**(figure 4.5).

4.4.3 REPOLARIZATION

With the increase of sodium ions inside the nerve cell, the mebrane becomes less permeable to sodium ions whereas the permeability membrane to potassium ions increases. The sodium ions are pumped out of the cell and potassium ions are pumped into the cell until the original resting state of ionic concentration is achieved. Thus this makes the membrane negative on inside and positive on outside. This process is called **repolarization**.

Sodium Potassium Pump and Refractory Period

The Na^+ and K^+ concentration gradients across the membrane of the cell are maintained by the activity of a protein called the **Na^+-K^+ ATPase**, often referred to as the sodium-potassium pump. The sodium-potassium pump is a process of expelling out sodium ions and drawing in potassium ions against concentration and electrocemical gradient. Each Na + K+ pump , for one ATP used, expels 3 Na + out for 2 K+ taken in. The entire process of repolarization requires some time during which the nerve cannot be stimulated again. This period is called **refractory period**. The refractory period is very short, being only about one millisecond (1/1000 of a second). Thus a nerve fibre can transmit about 1000 impulses per second. During repolarization, as the cell returns to its resting potential, the neuron is ready to receive another stimulus.

In non myelinated axons the impulse moves along the length of axon. Current generated in one channel acts as stimulus for next channel. This way every next channel is affected in succession moving the impulse ahead continuously towards the axon terminal. This is called **stepwise transmission**. It is comparatively a slower conduction and common in invertebrates.

In myelinated neurons the axon is insulated by myelin sheath which is impermeable for ion exchange. The impulse generated at axon hilock can affect the Na + channels only at the **Nodes of Ranvier** where axolemma is non myelinated. Thus generated impulse moves forward node to

node in jumping manner (figure 4.6). It is known as **saltatory conduction**. It is comparatively faster and found in vertebrates.

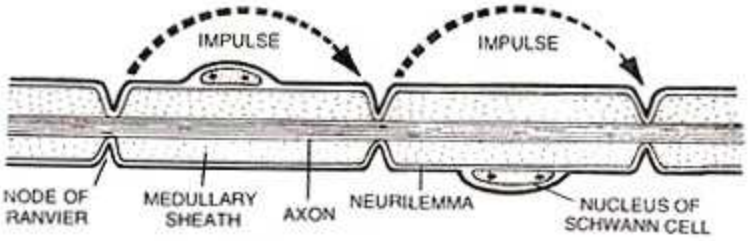

Figure4.5. Showing saltatory conduction in myelinated axon

4.5 SYNAPTIC TRANSMISSION AND NEUROTRANSMITTERS

Synapse

The synapse is an area of functional contact between one neuron and another for the purpose of transferring information. Synapses are usually found between he fine terminal branches of the axon of one neuron and the dendrites or cell body of another. This type of neuron is called axo-dendrite synapse. **Sir Charles Sherrington** (1861-1954) was the first person who used the term 'synapse' to the junctional points between two neurons.

A typical synapse consists of a bulbous expansion of a nerve terminal called a **pre-synaptic knob** lying close to the membrane of a dendrite. The synaptic knob contains numerous synaptic vesicles filled with chemical substances called neurotransmitters. The membrane of the dendrite is also thickened and is called the **post synaptic membrane**. These membranes are separated by a gap, the **synaptic cleft**. It is about 200 Å across. The post synaptic membrane contains large protein molecules which act as receptor sites for neurotransmitter and numerous channels and pores (figure 4.6).

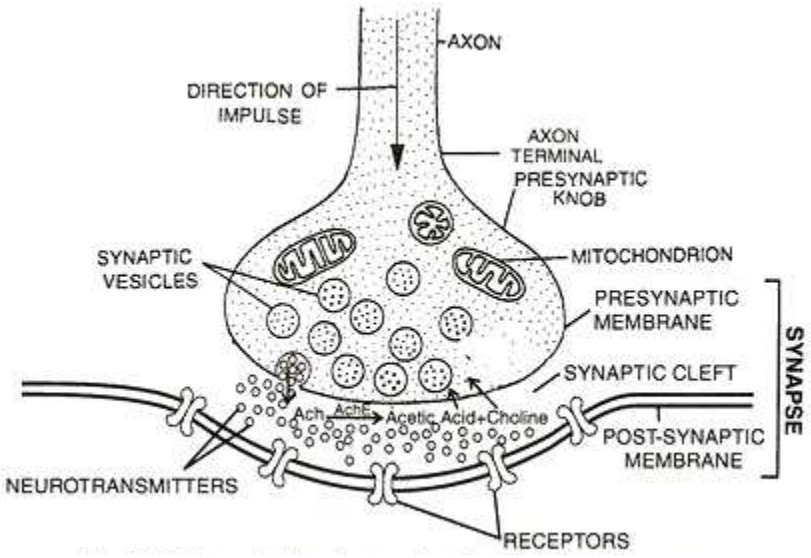

Figure 4.6. Structure of a synapse

The two main neurotransmitters in vertebrate nervous system are **acetylcholine (ACh)** and **noradrelaine**although other neurotransmitters also exist. Acetylcholine (ACh) was the first neurotransmitter to be isolated and obtained by Otto Loewi in 1920 from the endings of parasympathetic neurons of the vagus nerve in frog heart. Neurons releasing acetylcholine are described as **cholinergic** neurons and those releasing noradrenaline are described as **adrenergic** neurons.

Types of Synapses: There are two kinds of synapses that connect neurons. 1. chemical synapse and 2. electrical synapse.

Transmission of Nerve Impulse at a Chemical Synapse

The process of chemical transmission across synapses was discovered by **Henry Dale** (1936). The chemical transmission of impulse occurs in following steps.

(i) When an impulse arrives at a presynaptic knob, calcium ions from the synaptic cleft enter the cytoplasm of the presynaptic knob.

(ii) The calcium ions cause the movement of the synaptic vesicles to the surface of the knob. The synaptic vesicles are fused with the presynaptic membrane and get ruptured (exocytosis) to discharge their contents (neurotransmitter) into the synaptic cleft.

(iii) The synaptic vesicles then return to the cytoplasm of the synaptic knob where they are refilled with neurotransmitter.

(iv) The neurotransmitter of the synaptic cleft binds with protein receptor molecules on the post synaptic membrane. This binding action changes the membrane potential of the postsynaptic membrane, opening channels in the membrane and allowing sodium ions to enter the cell. his causes the depolarization and generation of action potential in the post-synaptic membrane. Thus the impulse is transferred to the next neuron (figure 4.7).

(v) Having produced a change in the permeability of the postsynaptic membrane the neurotransmitter is immediately lost from the synaptic cleft. In the case of cholinergic synapses, acetylcholine (ACh) is hydrolysed by an enzyme **acetylcholinesterase**(AChE) which is present in high concentration at the synapse.

(vi) The products of the hydrolysis are acetate and choline which are reabsorbed into the synaptic knob where they are resynthesized into acetylcholine, using energy from ATP.

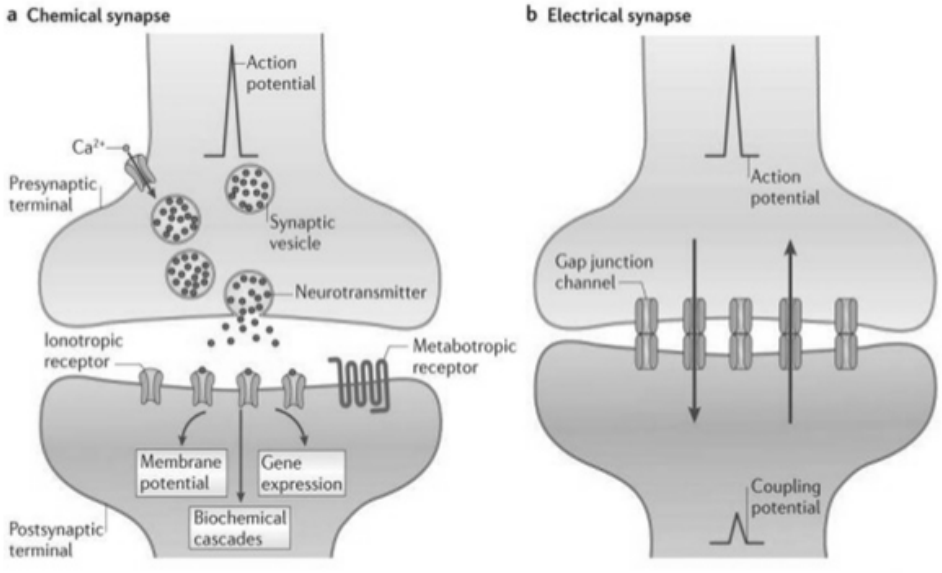

Figure 4.7 Transmission of impulse through (a) chemical synapse (b) electrical synapse

Transmission of Nerve Impulse at aElectrical Synapse

At electrical synapse there is continuity between the pre-synaptic and post-synaptic neurons. The continuity is provided by the gap junction between the two neurons. The gap junctions are small protein tubular structures that allow free movement of ions between the two neurons. Because of this, the action potential reaching the pre-synaptic terminal produces potential change in the post-synaptic neuron.In electrical synapse there is minimal synaptic delay because of the direct flow of electrical current from one neuron into the other through gap junction. Thus impulse transmission across an electrical synapse is always faster than that across a chemical synapse.Most impulse transmission across the synapse between neurons takes place at the chemical synapses. Electrical synapses are relatively rare. It is found in the cardiac muscle fibres, smooth muscle fibres of intestine and the epithelial cells of lens.

Neuromuscular junction : Impulses are conducted from a neuron to a muscle cell across an area of contact called neuromuscular junction. When a nerve fibre ends on a muscle fibre, it forms motor end plate. The motor end plates have vesicles and mitochondria. The vesicles secrete neurotransmitter (figure 4.8). When the motor impulse from the nerve is received on the motor end plates, a local depolarization occurs there resulting in the excitation of the muscle fibre.

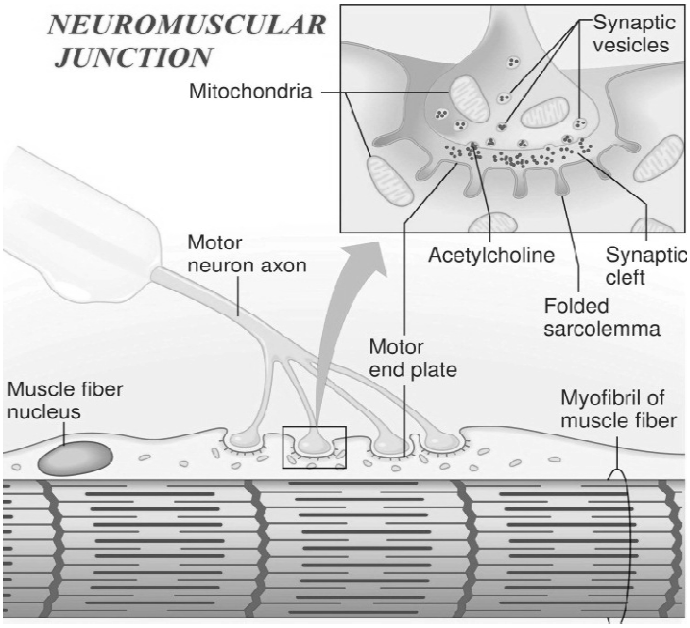

Figure 4.8. Neuromuscular junction

Neuroglandularjunction: It is an area of contact between a neuron and glandular cells. There is also a gap which is bridged at the time of the transmission of the impulse by a neurotransmitter.

Synaptic delay: Transmission of an impulse across a synapse is slower than its conduction along a neuron. This is because of the time needed for the release of a neurotransmitter, its diffusion through the synaptic cleft, and its action on the post-synaptic membrane. The difference in the rate is called synaptic delay. It amounts to about half a millisecond at body temperature (37^oC).

Synaptic fatigue: Repeated stimulation of the presynaptic knob may deplete the neurotransmitter, and this may fail to stimulate the post-synaptic membrane. This condition of the synapse is termed synaptic fatigue. It lasts for several seconds during which the neurotransmitter is re-synthesized. Synaptic fatigue is the only fatigue that affects the nervous tissue. Conduction of the nerve impulse along the neurons is not subject to fatigue.

Neurotransmitters

Neurotransmitters are the chemical substances which are responsible for transmission of an impulse through a synapse.

Characteristics of neurotransmitters

- A neurotransmitter should be synthesized by pre-synaptic neurons and stored in the vesicles, which are present in axon terminal. The synthesizing enzymes should be present in the nerve at storage site.
- A neurotransmitter should be released on stimulation of nerve.
- A neurotransmitter travels a very small distance between pre-synaptic membrane and post-synaptic membrane.
- A neurotransmitter is associated with an enzyme or enzyme system for its inactivation.
- A neurotransmitter when applied extrinsically should mimic the effects of the nerve stimulation.
- Drug which modifies the response to nerve stimulation should also modify the proposed transmitter action in a similar way.
- The most common neurotransmitter is **acetylcholine**, which is released at voluntary neural synapses, neuromuscular junctions, synapses of preganglionic nerve fibres, synapses of

postganglionic parasympathetic nerve fibres. The nerve fibres which release acetylcholine neurotransmitter are called **cholinergic**. In the synaptic cleft it is broken down by enzyme **cholinesterase** into choline and acetic acid. The latter two are reabsorbed by axon terminal for synthesis of acetylcholine. Acetylcholine has excitatory effect except at the ends of parasympathetic nerves. **Noradrenaline** (nor-epinephrine, similar to adrenal hormone) is formed at synapses and neuromuscular junctions of postganglionic sympathetic nerve fibres. The nerve fibres are called **andrenergic**. The transmitter is broken by enzyme **monoamine oxidase**. It excites some regions and inhibits a few others. Peripheral nervous system generally uses three neurotransmitters- acetylcholine, noradrenaline and adrenaline. Central nervous system uses these and some additional neurotransmitters like gamma amino butyric acid (GABA), glycine, glutamic acid, serotonin, endorphins and nitric oxide. Glycine, dopamine and gamma amino butyric acid (GABA) are **inhibitory** transmitters. Glutamate is **excitatory**. Serotonin is inhibitor of pain pathways of spinal cord. It may also control mood and induce sleep. Nitric oxide is formed at the site of transmission. It does not alter membrane potential but brings about changes in metabolic functions that modify neuronal excitability.

- Dopamine can play a lot of different roles in the brain, depending on the location. It also plays a role in attention, problem-solving, and memory.
- Serotonin is involved with mood, as well as your sleep cycle, pain control, and digestion. Serotonin can also help with forming blood clots and increasing sex drive.
- Acetylcholine (ACh) plays a major role in the formation of memories, verbal and logical reasoning, and concentration.
- GABA is also an inhibitory neurotransmitter that helps to balance any neurons that might be over-firing. GABA also plays a role in vision and motor control.
- Noradrenaline is an excitatory neurotransmitter that helps to activate the sympathetic nervous system, which is your “fight or flight” response to a stress. Norepinephrine also plays a role in attention, emotion, sleeping and dreaming, and learning.

Neurotransmitters and Disorders

1. **Depression-** decreases in the production of serotonin in the brain can lead to feelings of depression.

2. **Parkinson's Disease (PD)-** This is a neuro-degenerative disorder that affects the neurons responsible for movement in the body. Deficiency of dopamine is responsible for symptoms such as tremor, stiffness, or balance issues.

3. **Schizophrenia-** The "dopamine hypothesis" states that having excess amount of dopamine in the brain can cause schizophrenia. Schizophrenia is a disabling disorder that impacts how a person thinks, feels, and acts.

4.6CONCEPT OF SENSORY RECEPTORS (CHEMO AND PHOTO)

Sensation is the conscious or unconscious awareness of an external or internal stimulus with the help of sensory receptors. The conscious awareness and interpretation of sensation .is termed as perception. Sensory receptor is a specialised body structure having specialised cellswhich can pick up an external or internal stimulus and transmit the same to the central nervous system as nerve impulse. Only brain can perceive sensations. Sense organs are avenues for receiving stimuli.

Types of Receptors- According to type of stimuli receptors are classified into four categories (table 4.1).

1. Mechanoreceptors- sensitive to mechanical stimuli
2. Chemoreceptors- sensitive to chemical stimuli
3. Photoreceptors- sensitive to light wavelength
4. Thermoreceptors- sensitive to temperature
5. **Table 4.1. Sensory receptors and their examples**

Type of receptors	**Subcategory**	**Sensitive to**	**Location/ occurrence**	**Examples**
Mechanoreceptors	Tangoreceptor	Tactile, Touch	Skin	Meissner's corpuscle, Merkel's corpuscle, Free nerve endings
	Algesirereceptors	Pain	Skin	Free nerve endings
	Proprioreceptors	Internal	Deep in skin	Golgi- Mazzoni organs

		stimulus		Pacinian corpuscles
	Rheoreceptors	Water current	Skin	Lateral line organs of fishes and tadpoles
	Phonoreceptors	Sound	Ear	Organ of Corti
	Statoreceptors	Equilibrium	Ear	Cristae and maculae (vestibular apparatus)
	Baroreceptors	Pressure	Blood vessels, heart	Nerve endings
Chemoreceptors	Gustatoreceptors	Taste	Tongue	Taste buds
	Olfactoreceptors	Smell	Nose	Schneiderian membrane
Photoreceptors		Light	Head	Ocelli, Ommatidia, Rods and cone cells (Retina of eye)
Thermoreceptors	Caloreceptors	Heat	Skin	Ruffini's organ
	Frigidoreceptors	Cold	Skin	End bulbs of Krause

4.6.1. CHEMORECEPTORS

Chemoreceptors are sensitive to different chemicals like acids, alkali and gases. These receptors respond to change in concentration of chemical in surroundings. In higher animals tongue serves as gustatory organ sensitive to taste and nose acts as olfactory organ sensitive to smell.

Organ of Taste (The Tongue)

Sense of taste (gustation) is a chemical sense that is stimulated by food and drink. It contributes considerably to the quality of life and is important stimulant for digestion. **Tongue** is the main site of taste detection, contains numerous taste buds on its dorsal surface. In human beings tongue is found to attached with floor of pharynx by a membranous fold called ***frenulum lingulae***. The mucous membrane of the dorsal surface of tongue exhibits numerous papillae, which increase the surface area of the mucosa available for taste receptors. The taste buds are located in the walls of these papillae. Papillae, present on the tongue, are of four types (figure 4.9 a)-

1. **Circumvallate papillae.** These are large (2–4 mm in diameter) papillae, about 10–12 in numbers, forming a single row in basal side of tongue. About 200 taste buds are located along the sides of each circumvallate papilla.

2. **Fungiform papillae.** These are bright red, flat dot-like structures (each of about 1 mm in diameter) located in the anterior two-thirds of tongue along the edges, dorsum and tip. There are 8–10 taste buds on each papilla.

3. **Foliate papillae.** These are transverse mucosal folds, found on the posterolateral surfaces of the tongue anterior to the circumvallate papillae. Each foliate papilla has numerous taste buds. These papillae are absent in human beings but common in rabbit and other mammals.

4. **Filliform papillae.** These are small conical projections, covering the entire remaining surface of the dorsum of the anterior two-thirds of tongue, giving it a velvety appearance. They are arranged in rows parallel to the sulcus terminalis. They are not gustatory structures, i.e. do not contain taste buds.

Note*: Sulcus terminalis* is V-shaped groove (with apex posteriorly), which separates the anterior two-thirds of the dorsum of tongue from the posterior one-third.

Taste buds. Each taste bud is barrel shaped. Cluster of cells with a small opening (taste pore) in the surface that allows substances to reach the interior of the taste bud. Each taste bud measures about 50–70 μm in diameter, and consists of receptor cells, basal cells and supporting cells (figure 4.9b).

Taste areas on tongue. The taste buds for sweet taste are located at the tip and anterior surface of tongue, saltifshantero-laterally, sour on sides and bitter towards base (posterior side).

Functions of tongue. Tongue can distinguish the taste of the food, such as bitter, sour, sweet and salty. Tongue is responsible for speech. Tongue helps to keep the oral cavity clean. The food particles attached to the teeth are cleared by tongue.

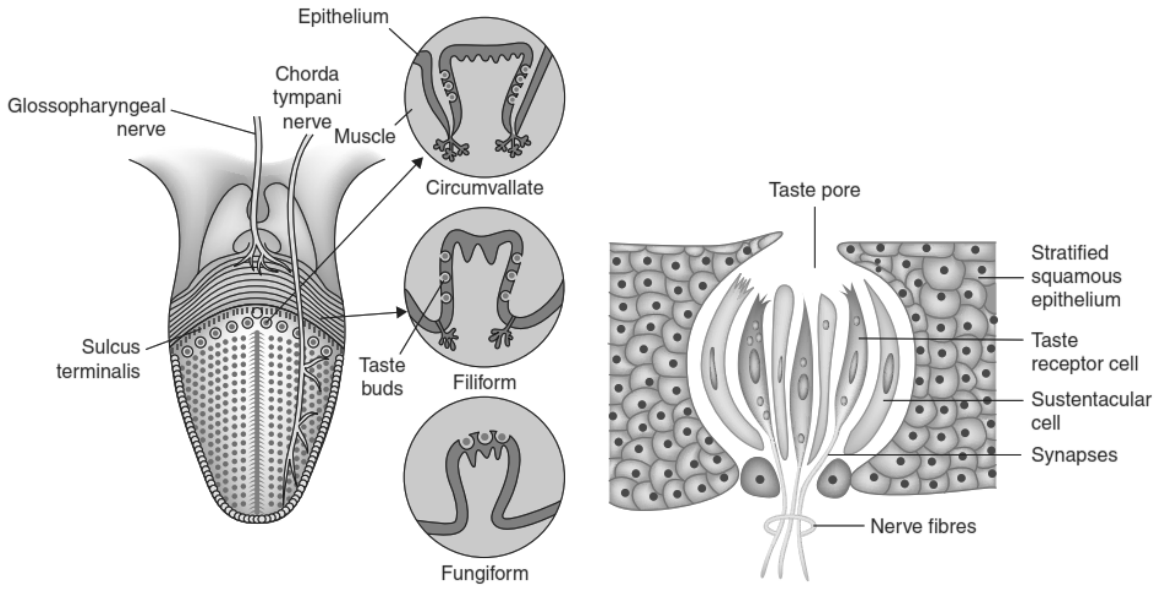

Figure 4.9. (a) Sensory papillae of tongue surface (b) structure of a taste bud

Organ of Smell (The Nose)

Approximately 80–90% of what we perceive as "taste" actually is due to the sense of smell. This accounts for how dull food tastes when we have a head cold or a stuffed-up nose. Our sense of smell depends on between 10 and 20 million olfactory cells located within olfactory epithelia high in the roof of the nasal cavity, called**Schneiderian membrane** (Figure 4.10). It is a modified mucous membrane which is lined by specialised Pseudo Stratified Columnar Ciliated Glandular Epithelium (PSCCGE). Olfactory cells are modified neurons. Each cell ends in a tuft of about five olfactory cilia, which bear receptor proteins for odor molecules.

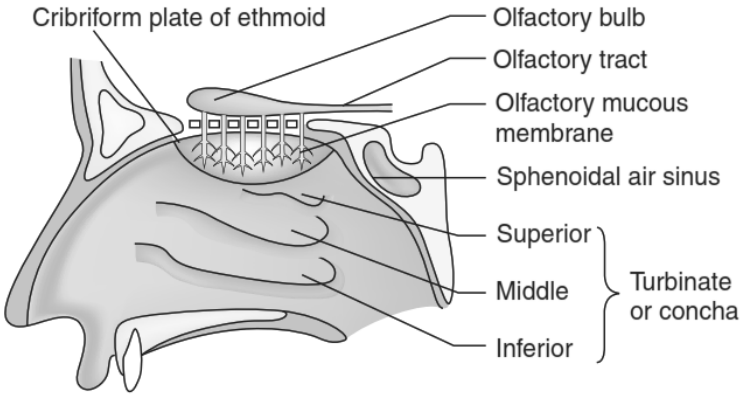

Figure 4.10. Olfactory epithelium in nasal cavity

Mechanism of sense of smell

Each olfactory cell has only one out of several hundred different types of receptor proteins. Nerve fibers from similar olfactory cells lead to the same neuron in the olfactory bulb (an extension of the brain). An odor contains many odor molecules, which activate a characteristic combination of receptor proteins. For example, a rose may stimulate olfactory cells. An odor's signature in the olfactory bulb is determined by which neurons are stimulated. When the neurons communicate this information via the olfactory tract to the olfactory areas of the cerebral cortex, we know we have smelled a rose or a carnation. The olfactory cortex is located in the temporal lobe. Some areas of the olfactory cortex receive smell sensations, and other areas contain olfactory memories.

4.6.2. PHOTORECEPTORS

The eye is the photo-receptor organ. Human eye is spherical about 2.5 cm in diameter. It is situated on an orbit of skull and is supplied by optic nerve. There are 6 sets of muscles attached to outer surface of eye ball which helps to rotate it in different direction. Four sets of these muscles are straight muscles; superior, inferior, medial and lateral rectal muscle and two sets are oblique muscles; superior and inferior oblique muscles.

Structurally two eyes are separated but some of their activities are coordinated so that they functions as a pair.

Structure Of Human Eye

Eye ball consists of three layers (figure 4.11)

1. Outer fibrous layer: Sclera, cornea and conjunctiva
2. Middle vascular layer: Ciliary body, choroid and iris
3. InnerNeuro-sensory layer: Retina

Sclera: It is outermost supporting layer consists of thick membrane of tough fibrous connective tissue.It covers 5/6 parts of eye ball.It maintains the shape of eye and provide attachment to the extrinsic muscle of eye.

Cornea: It is a thin transparent front part of sclera. It forms a slight bulge at the front and covers an anterior 1/6 part of sclera.Cornea is non-vascular and absorbs oxygen from air.It refracts light to focus on retina.

Conjunctiva:It is a thin transparent layer that covers the cornea.It is formed of single layer of stratified squamous epithelium. It protects the cornea. Any infection or inflammation in conjunctiva called *conjunctivitis*.

Choroid: It is thick vascular and pigmented layer situated below sclera. The pigmented cells absorb light and prevent it from being reflected. The function of choroid is to provide nutrition and to prevent reflection of light.

Ciliary body: These are attached to choroid and present at the junction of sclera and cornea. It consists of two sets of ciliary muscle and suspensory ligament. Ciliary body is attached to lens and holds it in position. Its function is to change the shape of lens by contraction or relaxation of muscle.

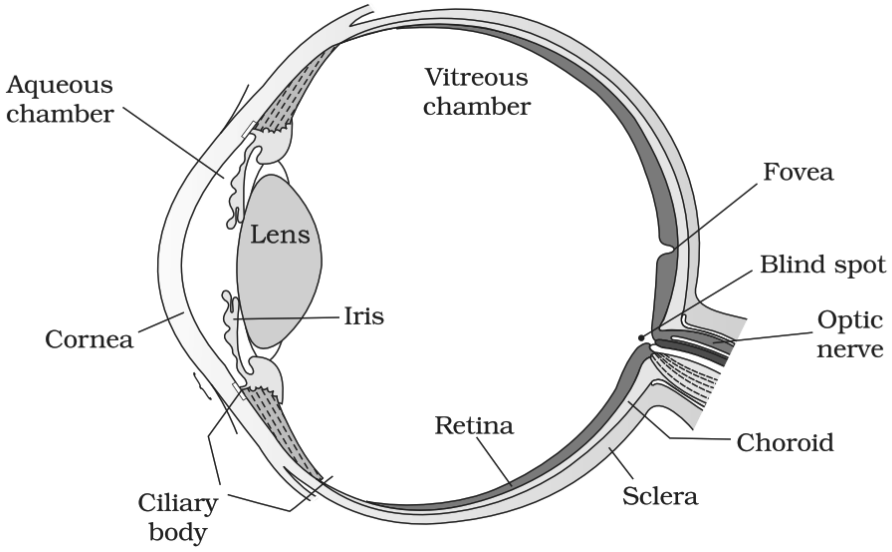

Figure 4.11. Structure of human eye

Iris: It is muscular, pigmented and opaque diaphragm which hangs in the eye ball in front of lens. It has small circular opening called pupil. It has two types of muscles; circular and radial

muscle. The movements of these muscles control the size of pupil. Pigment in iris gives color to eye. Iriscontrols the amount of light entering into eye by controlling the size of pupil.

Retina: Retina is innermost layer. Neuroretina contains highly specialized photoreceptor nerve cells; rods and cones. Each eye ball has 125 millions of rod cells and 7 millions of cone cells. Small depression in middle of retinal wall is called **macula lutea (yellow spot).** Its centre is known as *Fovea centralis*which contains only cone cells. **Fovea centralis** is highly sensitive to light and forms magnified image and give **sharp and acute** vision. The optic nerve enter retina at a point called **blind spot**. It does not contain any rods or cone cells. It is least sensitive to light and forms **no image** when light falls on blind spot.

Rod cells: Rods are sensors for perception of black to white shades. Night vision is almost rod vision. It function in dim light and contains a photosensitive pigment **rhodopsin** formed from vitamin A.

Cone cells: Cones are sensors for perception of colors. It functions in bright light and differentiate colors. Contains a photosensitive pigment **iodopsin**.

Ultra structure of retina : Retina consists of a photosensitive outer segment resting upon the pigmented epithelium and in inner segment between these two. The outer segment is conical in cone cells and cylindrical in rod cells. The rods and cones synapse with **bipolar neurons** which, in turn, synapse with **ganglion cells** (figure 4.12). Axons of ganglion cells converge to form the optic nerve. Certain horizontally extending cells connect the axon terminals of rods and cones, establishing an outer plexiform layer. Similarly, certain cells called **amacrine cells**, having no axons, connect ganglion cells with each other, establishing an inner plexiform layer. These also similarly connect the axons of bipolar cells together. All the above described neuronal elements of retina are bound together by supporting glial cells called **mullar cells**.

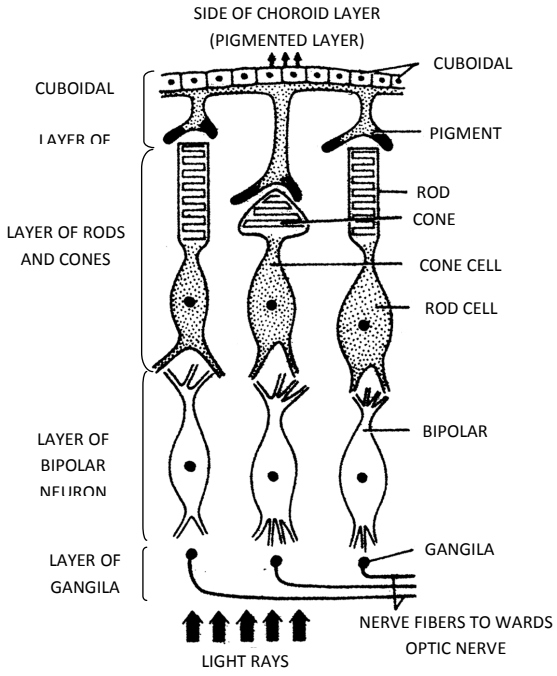

Figure 4.12. Detailed structure of retina

Eye Lens And Chambers

Eye Lens: It is a large, flexible, transparent biconvex and fibrous crystalline body situated behind iris. Lens is enclosed in a transparent elastic capsule. Ciliary muscles control the thickness of lens and its power of accommodation. It forms the image of the object on retina. Lens separates the eye ball into two chambers- anterior aqueous chamber and posterior vitreous chamber.

Aqueous chamber: It is a smaller fluid filled chamber between cornea and lens. It is filled with aqueous humour containing amino acids, glucose, ascorbic acid, hyaluronic acid and respiratory gases. The aqueous humour nourishes the lens and cornea and refracts light rays to focus on retina. Aqueous humor continually filters out of blood capillaries in the ciliary processes of the ciliary body and enters the posterior chamber. It then flows forward between the iris and the lens, through the pupil, and into the anterior chamber. From the anterior chamber, aqueous humor drains into the scleral venous sinus **(canal of Schlemm)** and then into the blood. Normally, aqueous humor is completely replaced about every 90 minutes.

Vitreous chamber: It is a larger fluid filled chamber between lens and retina, filled with gelatinous vitreous humour. It supports retina and refracts light to focus on retina. Unlike the aqueous humor, the vitreous humour does not undergo constant replacement. It is formed during embryonic life and consists of mostly water plus collagen fibers and hyaluronic acid.

The pressure in the eye, called ***intraocular pressure,*** is produced mainly by the aqueous humor and partly by the vitreous body; normally it is about 16 mm Hg. The intraocular pressure maintains the shape of the eyeball and prevents it from collapsing.

Accommodation: Accommodation is a reflex process to bring light rays from object into perfect focus on retina by adjusting the lens. When an object lying less than 6 meter away is viewed, image formed behind retina. But due to accommodation of lens image formed in retina and we can see the object. For accommodation to view closer object, ciliary muscle contract and lens become thick which causes focus on closer object (figure 4.13). Similarly, when distant object is viewed, ciliary muscles relaxes, so the tension of ligament become greater which pull lens and lens become thinner, due to which image forms on retina. The normal eye is able to accommodate light from object about 25 cm to infinity.

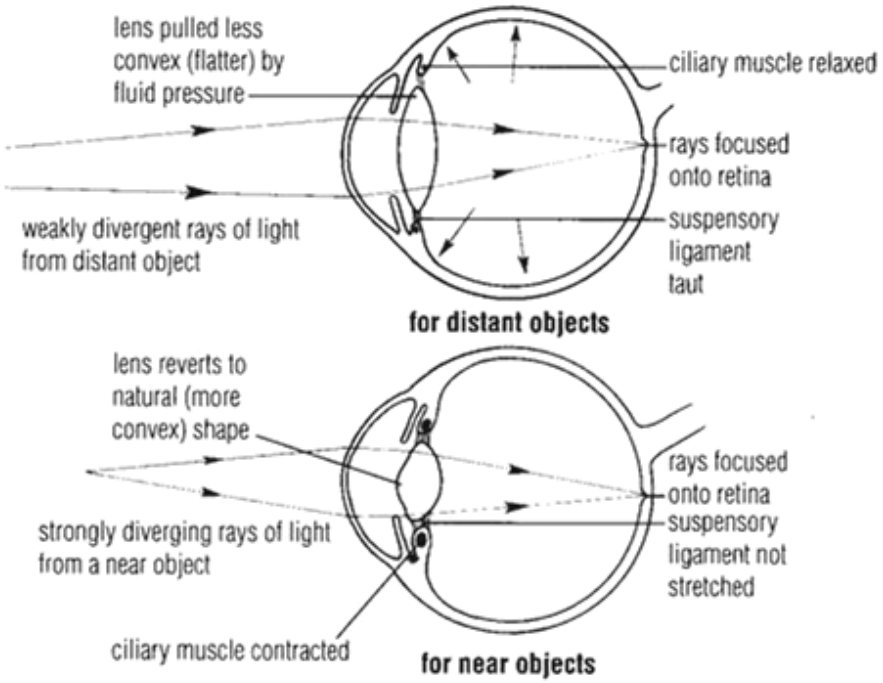

Figure 4.13Mechanism of accommodation in human eye

Mechanism of Vision

The light rays in visible wavelength focussed on the retina through the cornea and lens generate potentials (impulses) in rods and cones. The photosensitive compounds (photopigments) in the human eyes is composed of opsin (a protein) and retinal (an aldehyde of vitamin A). Light induces dissociation of the retinal from opsin resulting in changes in the structure of the opsin. This causes membrane permeability changes. As a result, potential differences are generated in the photoreceptor cells. This produces a signal that generates action potentials in the ganglion cells through the bipolar cells. These action potentials (impulses) are transmitted by the optic nerves to the visual cortex area of the brain, where the neural impulses are analysed and the image formed on the retina is recognized based on earlier memory and experience.

Common Eye Defects

1. **Myopia (Nearsightedness)**. In this eye defect, person has difficulty in seeing distant objects clearly. The person can see near object clearly. Hence it is also called short sight. In a near-sighted eye the eyeball is too long and the retina is too far from the lens. The light rays converge

at a point in front of the retina resulting in blurred image. Concave lens corrects this condition by bringing the light rays to a focus at a point farther back.

2. **Hypermetropia (Farsightedness).** In this eye defect the person has difficulty in seeing near objects. The person can see distant object clearly. Hence it is also called long sight. Hypermetropia is just the opposite of myopia. In a far-sighted eye, the eyeball is too short. Light rays converge at a point behind the retina resulting in a blurred image. Convex lenses correct the far-sighted condition by causing the light rays to converge farther forward.

3. **Astigmatism.** It is due to irregular cornea or lens, causing the image to be out of focus, producing faulty vision. It is corrected by cylindrical lens.

4. **Presbyopia (Old age farsightedness)**. It is a defect in accommodation occurring in advancing age. Lens becomes less elastic and is not able to focus the image of near object while the distant vision is not impaired. It is also called oldsightedness (farsightedness of old person). This defect is corrected by using convex lens.

5. **Strabismus(Squinting).** It is commonly known as *squint*. In this defect, the eye ball is somewhat bent on to a side in its orbit so that the optic axes cannot be directed to same object. Some extra-ocular muscle becomes longer or shorter than normal.

6. **Cataract (SAFAID MOTIA)**. In cataract, the lens loses its transparency and becomes opaque to light and hence vision is impaired. It is corrected by surgical removal of the opaque lens and using biconvex glasses. Intraocular lens implantation is also done. Cataract is more common in older people but it can occur at any age.

7. **Glaucoma (KALA MOTIA).** It is also more common in older people. If untreated, it leads to blindness. Worldwide, it is the major cause of blindness. In glaucoma the pressure in the anterior cavity of the eye increases to an abnormal level. It exerts pressure on the posterior cavity and greatly reduces the blood supply to the retina. Thus lack of nutrients ultimately damages the nerve cells of the retina. It can be corrected by surgery.

4.7STRUCTURE, KINDS AND CHARACTERISTICS OF MUSCLES

The muscle cell, like the neuron, is an excitable tissue,i.e. an action potential is generated when it is stimulatedeither chemically, electrically or mechanically. Further,the muscle is a contractile tissue with a chemicallystored energy which can be transformed into mechanicalenergy. Muscular tissues derive from embryonic mesoderm except for those of the iris and ciliary body

of eyes, which are ectodermal in origin. Muscles account 40-50 % of adults body weight. The scientific study of muscles is known as **myology**. There are three different types of muscles in the body- skeletal muscles, cardiac muscles and smooth muscles (table 4.2).

Table 4.2. Three different types of muscles and their properties

Properties	Striated or Striped or Skeletal or Voluntary muscle fibres	Non-striated or Unstriped or Smooth or Visceral or Involuntary muscle fibres	Cardiac muscle fibres
Shape	Long cylindrical	Fusiform (thick in middle tapering at ends) (0.02 nm to 0.2 nm long)	Network (branched) of fibres
Stripes	Dark A bands and light I bands present	Absent	Present
Nucleus	Many (syncytial) at periphery	Single at the centre of each cell	Many nuclei between successive end plates central position
Unit	Sarcomeres, cylindrical long myofibrils placed end to end forming cylindrical myofibrils	Fusiform cells with inconspicuous borders	Oblique cross-connecting fibres make this muscle an interconnected bundle of myofibrils
Attachment	To bones	To soft organs or viscera	Not attached to other organs except major blood vessels which are isolated and covered by pericardium
Sarcolemma	Distinct	Absent	Absent
Sarcoplasmic Reticulum	Well developed	Less extensive	Poorly formed
Blood supply	Rich	Poor	Rich
Contraction	Quick, fatigue fast	Slow, sustained contraction	Rhythmic, contractions originate in heart (pace maker immune to fatigue)
Location	Generally peripheral, tongue, proximal part of oesophagus	Central, in hollow visceral organs, iris of the eye, dermis of the skin	Only in heart

Intercalated discs	Absent	Absent	Present
T-tubule system	Well developed	Lacking	Well developed
Innervated nerves	Motor nerves from central nervous system (neurogenic)	Nerves from autonomic nervous system (neurogenic)	Nerves from central and autonomic nervous system (myogenic)
Fibres	Unbranched	Unbranched	Fibres join by short oblique bridges
Action	Voluntary	Involuntary	Involuntary

4.7.1. PROPERTIES OF MUSCULAR TISSUE

Muscular tissue has four special properties that enable it to functionand contributeto homeostasis:

1. **Electrical excitability.** It is theability to respond to certain stimuli by producing electricalsignals called action potentials (impulses).Formuscle cells, twomain types of stimuli triggeraction potentials. One is autorhythmicelectricalsignalsarisingin the muscular tissue itself, as in the heart'spacemaker.Theother is chemicalstimuli,such as neurotransmittersreleased by neurons, hormones distributedby the blood, orevenlocal changes in pH.

2. **Contractility.** It is the ability of musculartissue to contract forcefully when stimulated by an action potential.Whena skeletalmuscle contracts, it generates tension(forceof contraction) while pulling on its attachment points. Insomemuscle contractions, the muscle developstension (forceofcontraction) butdoes not shorten. Anexampleis holding abookin an outstretched hand. In other muscle contractions, thetensiongenerated is great enough to overcomethe load (resistance)of the object being movedso the muscle shortens andmovementoccurs. Anexampleis lifting a book offa table.

3. **Extensibility.**It is the ability of musculartissue to stretch, within limits, without being damaged. The connectivetissue within the muscle limits the range of extensibilityandkeepsit within the contractile range of the muscle cells.Normally,smooth muscle is subject to the greatest amount ofstretching.Forexample,each time your stomach fillswith food,thesmooth muscle in the wallis stretched. Cardiac muscle alsoisstretched each time the heart fillswith blood.

4. **Elasticity.** This ability of muscular tissue is to return to its original length and shape after contraction orextension.

4.7.2. STRUCTURE OF STRIATED MUSCLES

Each striated muscle consists of numerous muscle fibres segregated into several small and parallel bundles, called **Fasciculi**. Fibres of each fascicle are bound together by a connective tissue sheath, called **endomycium**. All fasciculi of a muscle are bound together by a connective tissue termed **perimycium**which also forms a sheath around each fascicle. Similarly, the whole muscle itself is covered by a connective tissue sheath, called **epimycium**. The latter extends as a tendons at each end of the muscle to insert it on to bones. Endomycium, perimycium and epimycium contain collagen and elastin fibres and also reticular fibres in some muscles.

Ultra Structure of Striated Muscle Fibres

Muscles are made up of highly specialized thin and elongated cells called **muscle fibres**. The muscle fibres contain specialized cytoplasm called **sarcoplasm** that contain network of the endoplasmic reticulum as**sarcoplasmic reticulum (SR)** numerous mitochondria as**sarcosome**.SR contains 'T' tubules, which are the depot of calcium ions. The muscle fibres may be bounded by the cell membrane called **sarcolemma**. Each muscle fibre may contain numerous longitudinal fibrils called **myofibrils**.

Striated muscle fibres shows transverse striation in the form of regular alternate dark **A** (anisotropic) and light **I** (isotropic) **bands**. The 'A' band contains thick **"myosin filaments"**. The I band contains thin, long **"actin filament"** which are twice as many as myosin filaments. Each I band is divided into two equal halves by a thin, fibrous and transverse zig-zag partition, called **'Z' band** ('Z' disc) or **Krause's membrane**. Each segment of a fibril between two adjacent 'z' bands is called a **sarcomere**. A slender transverse line, the **'M' or Hansen's line** is visible in middle of each 'A' band. The major, middle region of 'A' band is comparatively lighter, but its terminal parts appear darker. The middle lighter region is called **'H' zone** (figure 4.14). Geomatrically each myosin filament is encircled by six actin filaments (hexagon), while the of each actin filaments is encircled by three myosin filaments (trigon).

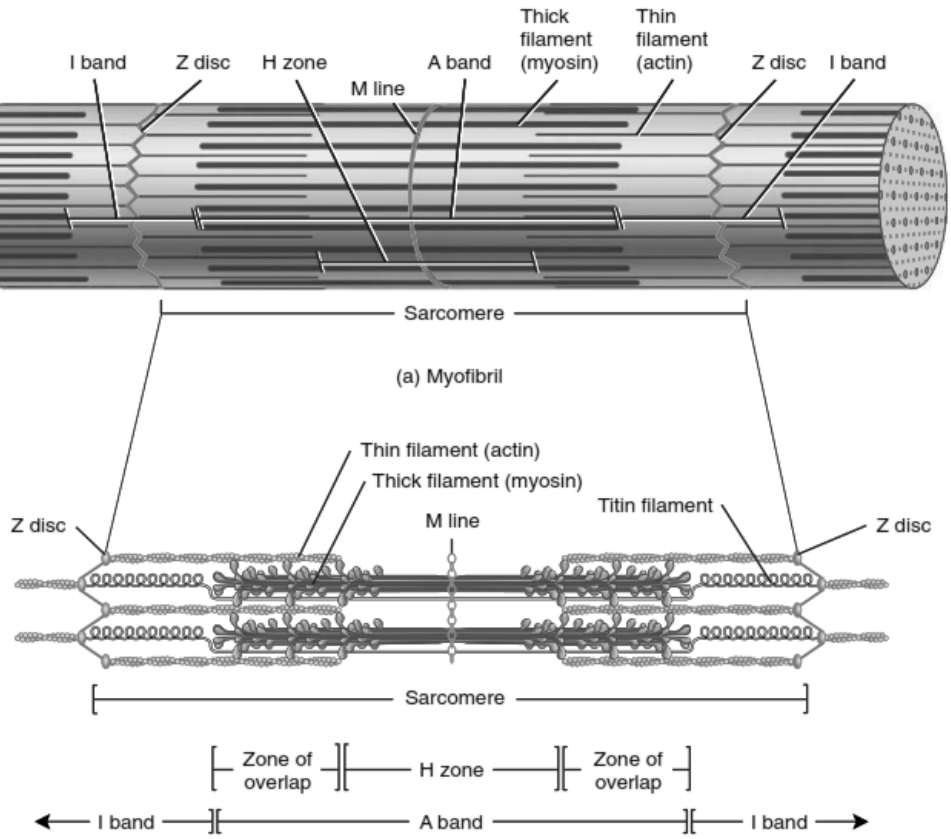

Figure 4.14. Structure of striated muscle fibre

Thick Myosin Filaments

Thick filaments are formed from a protein called **myosin** which has important properties of elasticity and contractibility.The shape of the myosin molecules has the appearance of two 'hockey sticks' or 'golf clubs' twisted together (figure 4.15 a). Each myosin molecule has a head formed of two light meromyosin (L_2) and tail made of two heavy meromyosin (H_2). Head has contractile and enzyme ATP-ase activity. Myosin heads form cross bridges with actin filament during muscle contraction.

ThinActin Filaments

The main component of thin filament is **actin**protein. Two actin polymers join to form an actin helix (Figure 4.15 b). On each actin molecule is a myosin-bindingsite,where a myosin head can attach. Smaller amounts of two regulatory proteins—**tropomyosin**and **troponin** are also part of

the thin filament. The tropomyosin strands in turn are held in place by troponin molecules. Troponin protein has strong affinity with calcium ions.

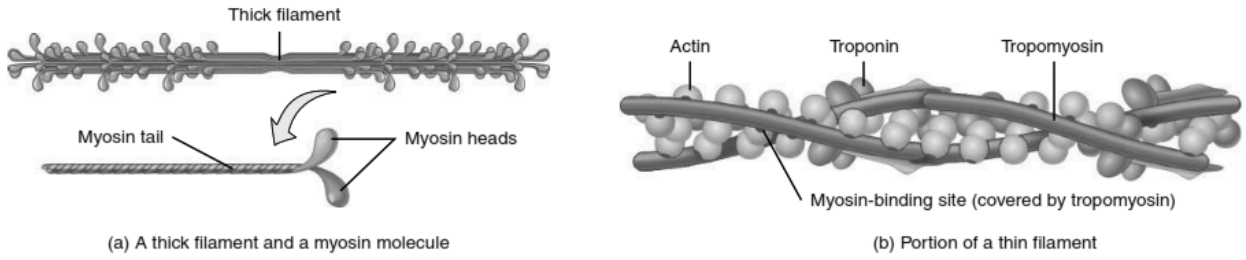

Figure 4.15. Ultrastructure of (a) thick myosin filament and (b) thin actin filament

4.8 MECHANISM OF MUSCLE STIMULATION AND CONTRACTION

The Sliding-Filament Theory

The sliding filament theory for muscle contraction was proposed by H.E. Huxley and A.F. Huxley in 1954. It was observed that when a fibril contracts, its 'A' bands remain intact, while the 'I' bands progressively shorten and eventually disappear when the fibril has shortened to about 65% of its resting length. At this stage 'H' zones also disappear because the actin filaments of both sides in each sarcomere reach, and may even overlap each other at the "M" line, and the 'Z' lines now touch the ends of myosin filaments. It was further observed that if a fibre is mechanically stretched, the zones of overlap between thick and thin filaments are shorter than in resting condition, resulting in wider 'H' zones. These observations led Huxley to propose that shortening of the fibrils in contraction is brought about by sliding movement of actin filaments over myosin filaments towards "M" line by means of rapidly forming and breaking cross bridges or rachets at the spurs of myosin filaments. Thus, thesarcomere were recognized as the 'ultimate units of contraction'.

It was also proved that the 'A' band occupies about 2/3 length of a sarcomere, so that as its maximum contraction, a muscle shortens by about 1/3 of its length. Actin has a strong affinity to myosin; if uninhibited, it readily combines with myosin to form a contractile complex called

actomyosin. Normally, tropomyosin and troponin of actin filaments inhibit formation of actomyosin. As a muscle fibre is stimulated by a motor nerve fibre, a large number of calcium ion (Ca^{++}) are released from the sarcoplasmic reticulum. Troponin has a strong affinity to (Ca^{++}). As these ions combine with troponin, the tropomyosin troponin complex is inactivated so that actin is now free to interact with the spurs of corresponding myosin filaments. Thus cross bridges of actomyosin are formed at the spurs (figure 4.16). The energy required for this interaction is provided by hydrolysis of ATP molecules in the heads of myosin which contain ATPase enzyme for this purpose. The energy is utilized in moving active sites of actin filaments over the thick myosin filaments. This act shortens the I band, disappearance of H zone and overall shortening of sarcomere. There is no change in the width of A band.

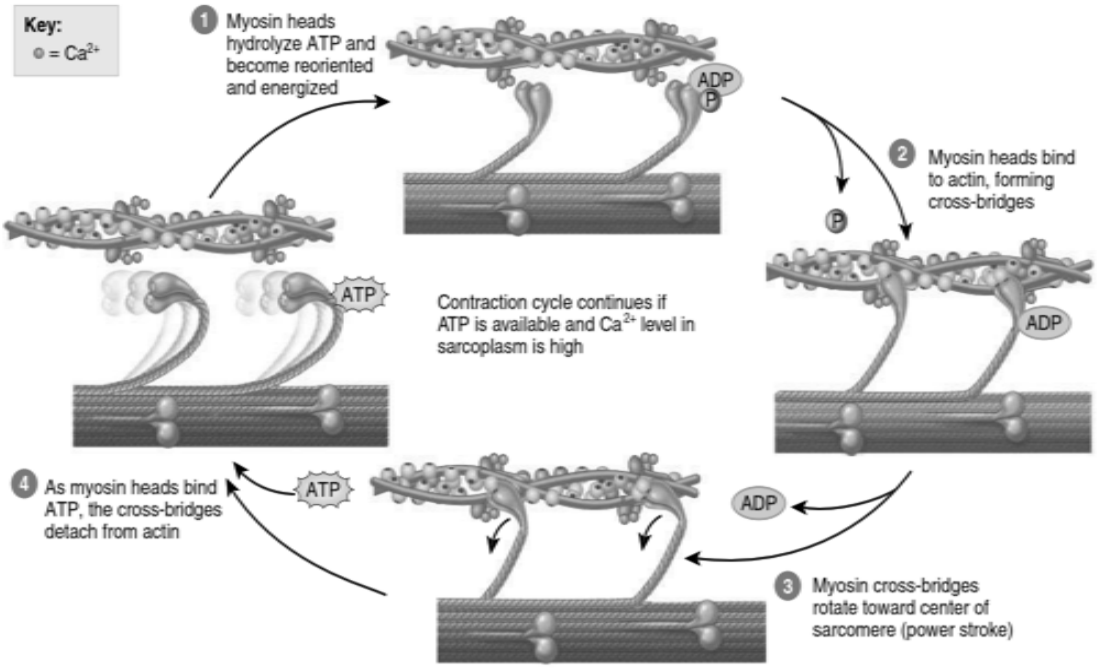

Figure 4.16 Mechanism of cross bridge formation and sliding of filaments

4.9 NEURO - MUSCULAR JUNCTION

Muscles (and other tissues) are controlled by the nervous system - which consists of nerve cells called neurons. Of the three types of neurons (motor neurons, sensory neurons and relay neurons), motor neurons instruct skeletal muscle cells to perform the series of actions that lead to sliding filaments and hence muscle contraction.A single motor neuron together with all of the

muscle fibers (muscle cells) to which it is attached, and therefore stimulates, is called a **motor unit**.

Neuromuscular junctions (NMJs) are the locations and means by which the motor neurons of the nervous system instruct the muscle cells of the muscular system to take actions - actions that, in turn, lead to the movement of muscles and the attached structures such tissues, bones, limbs etc.Each neuromuscular junction consists of the axon terminal of a motor neuron and the motor end plate of a muscle fibre. The axon terminals release **acetylcholine**at these junctions to transmit excitation impulses to the sarcolemma of the fibres. Acetylcholine depolarises the sarcolemma and thus triggers a self-propagating action potential spreading towards both ends of the fibres. The conduction of the impulse in the sarcolemma is electrochemically similar to that found in the neurons.

Muscle fatigue: A muscle that has contracted many times at short intervals, exhausts its store of ATP and glycogen and accumulates lactic acid. Hence its contractility gradually decreases and finally stops.

Oxygen debt: During active work or exercise, the rate of oxygen supply by the lungs falls short of the requirement of the muscles. Hence, lactic acid accumulates in the muscles and the breathing gradually becomes hard to enhance O2 intake by the lungs. This is called **oxygen debt**.

The Cori Cycle

The Cori cycle, or glucose-lactate cycle, was discovered by Carl Ferdinand Cori and Gerty Cori in 1929. In this cycle, lactate accumulated in the muscle cells due to anaerobic breakdown of glucose during strenuous exercise is taken up by the liver. The liver performs a chemical process known as gluconeogenesis, to convert lactate back to glucose.

4.10 SUMMARY

- Multicellular animals have various systems for coordinating various metabolic and homeostatic activities. Movement results from coordination between muscles, skeletal elements and nervous system.
- Neurons are the structural and functional unit of nervous system. Structurally neurons may be unipolar, pseudounipolar, bipolar and multipolar. Functionally neurons conduct impulses

towards CNC (sensory), conduct impulse away from CNS towards effectors (motor) or may function both (mixed).

- Excitability and conductivity are two defining properties of neurons. Central nervous system has non-nervous glia cells which account about 50% of total mass of CNS. Oligodendrocytes, Schwann cells, astrocytes, microglia, and ependymal cells are important components of glial network in CNS.
- During rest a normal nerve cell remain electro-positive outside and electro-negative inside with a potential difference of -70 mili volt (mV) as resting membrane potential. On stimulation neurilemma gets depolarized with + 35 mV potential difference. This small wave of depolarization is called nerve impulse.
- Nerve impulse is transmitted by along the length of axon and through synapse. Synapse is the functional gap between two neurons. Impulse through synapse is transmitted with the help of chemical called neurotransmitters. Acetylcholine, epinephrine, dopamine, serotonin are some common neurotransmitters.
- Sensory receptors are specialized cells (organs) which respond to different types of external and internal stimuli. In mammals nose, tongue, eye, ear and skin are different kind of receptors.
- Tongue perceives different types of tastes with the help of sensory papillae and taste buds located on upper surface.
- Nose perceive different kinds of chemicals of smell with their olfactory epithelium called Schneiderian membrane. It send sensory impulses to brain by first sensory cranial nerve called olfactory nerve.
- Human beings have one pair eyes as photoreceptors. Eye ball is lodged in eye orbit of skull. There are three layers in eye wall- outer sclera (the white of eye), middle choroid (the pigmented layer) and innermost retina (the neurosensory layer).
- Eye ball has a small aquous chamber and large vitrous chamber, between these two there is a crystelline lens. Outer a tranparent, convex cornea focus the light rays towards pupil. Lens focus these light rays on neurosensory retina. Image is formed on retina is transmitted to brain by second cranial nerve, the optic nerve.

- Retina is characterized by the presence of some special cells called rod cells (functional in dim light), cone cells (functional in bright light for coloured vision), amacrine cells and bipolar neurons.
- Muscles are mesodermal contractile tissues. These account 40-50% of body weight. There are three types of muscles- smooth muscles, cardiac muscles and skeletal muscles.
- Smooth muscles are spindle shaped,uninucleatefibres. These are unstriated, unbranched and functionally involuntary. These smooth muscles are found in in walls of visceral organs like alimentary canal, ducts, blood vessels and uterus.
- Cardiac muscles are highly specialized. These are cylindrical, branched and striated. Functionally these are involuntary and never get fatigue. Cardiac muscles have intercalated disc for rhythmicity.
- Skeletal muscles are most abundant and found to attached with bones and cartilage. These muscles are cylindrical, striated and arranged in bundles called fascicle. Muscle fibres show light light and dark striations represented as light I band and dark A bands.
- Anatomically each skeletal muscle fibre has thin and thick filaments of proteins. Thin filaments are made of actin, tropomysin and troponin proteins whereas thick filaments are made of only myosin proteins.
- Contractile property of skeletal muscles is due to sliding of thin filaments over the thick filament. During strenuous exercise in anaerobic conditions incomplete oxidation of glucose produce lactic in muscles. This causes muscle fatigue.

4.11 TERMINAL QUESTIONS & ANSWERS

4.11.1 MULTIPLE CHOICE QUESTIONS:

1. Which of the following system provides the fastest means of communication within the body ?

(a) Endocrine system

(b) Nervous system

(c) Circulatory system

(d) Digestive system

2. Which of the following are the properties of neural system ?

(a) Conductivity and elasticity

(b) Excitability and elasticity

(c) Flexibility and excitability

(d) Excitability and conductivity

3. Neuron never divides, because these lack
(a) Nucleus
(b) Centriole
(c) Mitochondria

(d) Golgi bodies

4. During rest neuron remain in state
(a) Depolarized

(b) Unpolarized

(c) Polarized

(d) Non responsive

5. During excitation a neuron has action potential of potential difference of
(a) +35 mV

(b) -70 mV

(c) +15 mV

(d) - 35 mV

6. Pseudounipolar neurons are found in
(a) ventral root of spinal nerve

(b) dorsal root of spinal nerves

(c) in retina of eye

(d) in embryonic stage only

7. Vascular pigmented layer of human eye wall is
(a) sclera

(b) choroid

(c) retina

(d) cornea

8. Area of most acute vision in human eye is
(a) blind spot

(b) foveacentralis

(c) at lens

(d) on complete retina

9. Largest sensory papillae on human tongue are
(a) Fungiform papillae

(b) filliform papillae

(c) circumfolliate papillae

(d) Circumvallate papillae

10. Olfactory Schneiderian membrane in dorsal surface of nose is lined by
(a) Pseudo stratified ciliated columnar glandular epithelium
(b) Pseudo stratified columnar glandular epithelium
(c) Pseudo unstratified cuboidal glandular epithelium

(d) Pseudo stratified ciliated cuboidal glandular epithelium

11. Which of the following statements are true about muscles?
(a) Muscle are contractile tissues

(b) Muscles are mesodermal in origin

(c) muscles account 40-50 % of body weight

(d) All the above are correct

12. Cardiac muscles are characterized by presence of
(a) branching pattern

(b) intercalated disc

(c) rhythmicity

(d) all the above

13. Which of them is the structural and functional unit of muscles?
(a) sarcosome

(b) sarcomere

(c) centromere

(d) fascicle

14. What is the correct reason of muscle fatigue?
(a) accumulation of citric acid
(b) accumulation of amino acid
(c) accumulation of lactic acid
(d) accumulation of acetic acid
15. Cori cycle is related with
(a) Amino acid metabolism
(b) Glycogen metabolism
(c) Urea metabolism
(d) Uric acid metabolism

Answer key MCQ

1. B	2. d	3. b	4. c	5. a
6. b	7. b	8. b	9. d	10. a
11. d	12. d	13. b	14. c	15. b

Very Short Answer type Question

1. Which system is responsible for coordination with external and internal stimuli?

2. Why neurons never divide?

3. How much will be the potential difference of action potential?

4. In which organ special bipolar neurons are found?

5. Which sensory papillae lack taste buds on tongue?

6. Which nerve send sensory impulses of image from eye to brain?

7. What is unit of skeletal muscles?

8. Which chemical accumulation causes muscle fatigue?

9. Name the type of muscles found in the wall of uterus.

10. Who proposed sliding filament theory of muscle contraction?

Short Answer type Question

1. Give a brief note on sensory, motor and mixed neurons.

2. Describes various types of neurons.

3. Describe the structure of a typical neuron.

4. Differentiate between aquous and vitrous chambers of eye.

5. Write a note on various types of sensory papillae on tongue.

6. What is saltatory conduction?

7. Describe the role of pupil and lens in eye.

8. Write a brief note on cardiac muscles.

9. Give a brief details and example of smooth muscles.

10. Differentiate between thin and thick filaments of muscle fibre.

11. Define muscle fatigue. How body manage this problem?

Long Answer type Question

1. Describe the generation and conduction of nerve impulse in a typical neuron.

2. Give the detail structure of a synapse and explain the mechanism of impulse conduction through synapne.

3. Describe the structure and mechanism of vision in human eye.

4. Describe the comparison details of smooth muscles, cardiac muscles and skeletal muscles.

5. Describe the ultrastructure of skeletal muscle in detail.

6. With the suitable diagram, explain the sliding filament theory of muscle contraction.

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Unit 5: HISTORY & SCOPE OF ENDOCRINOLOGY

5.1. OBJECTIVES

After reading this unit the readers will be able to:

- Define hormones
- Discuss the historical perspective of hormones
- Discuss the scope of endocrinology
- Explain the kinds of hormones
- Discuss the general characteristics of hormones
- Discuss the hormone versus enzyme
- Explain chemical nature of hormone
- Tell the general functions of hormones.

5.2. INTRODUCTION

In evolutionary history, Metazoa appeared as the earliest multicellular organisms. In these organisms different cell groups assumed specific functions.The emergence of these animals coincided with development of systems that allowed for communication and functional integration among the specialized groups. Two types of intercellular communication system evolved to assume important physiological roles-one **endocrine** and the other **nervous**. These both the systems acquired the same basic component- **sender cells** that produce and release chemical messengers and **target cells** that receive and respond to the chemical messengers.

In nervous system, the communication occurs between the neurons or from neurons to peripheral tissues. It is mediated by excitation of sender cell which release neurotransmitter into a synapse. The neurotransmitter diffuses across the synaptic cleft and binds to receptors of target cell, which inturn activate a cascade of signals to the interior of the target cell.

In endocrine system, the sender cell produces and secretes hormones into bloodstream. Once hormones enter the blood, they travel throughout the bodyand reach and bind to receptors of distantly placed target cell.Once a target site is bound by a particular hormone, a cascade of cellular events follows that culminates in the physiological response to a particular hormone.

Mainly hormones are produced by ductless or endocrine glands but certain cells of the brain, kidney, gonads, heart and other tissues also produces and secretes hormones with additional major non-endocrine functions.

Each specific hormone, together with its cells of origin and target tissues, constitutes a specific endocrine system. The endocrine system is the body's network of **nine** glands and over

100 hormones which maintain and regulate numerous events throughout the body. The glands of the endocrine system include the **pituitary**, **thyroid**,**parathyroids**, **thymus**, **pancreas**, **pineal**, adrenals, and **ovaries** or **testes.**The **hypothalamus**, in thebrain, regulates the release of pituitary hormones. The endocrine system is responsible for many critical life processes involving metabolism, **growth**, **reproduction**, **immunity**, and homeostasis. The branch of medicine that studies endocrine glands and the hormones which they secrete is called **endocrinology**. Endocrinology is concerned with the study of hormones, which are chemical messengers secreted by cells of endocrine glands and certain cells of organ and regulate the activity of other cells in the body.

5.3. BRIEF HISTORY AND SCOPE OF ENDOCRINOLOGY

5.3.1 HISTORICAL PERSPECTIVES OF ENDOCRINOLOGY

Endocrinology began with the first recorded endocrine experiment published by Berthold (1849). In 1849, Arnold Berthold, a French scientist, noted that castrated cockerels did not develop combs and wattles and they also failed to exhibit male behavior. He found that replacement of testes back into the abdominal cavity of the same bird or another castrated bird resulted in normal behavioral and morphological development.He concluded that the testes secreted a substance that "conditioned" the blood that, in turn, acted on the body of the cockerel to cause the development of male behavior. It was not proven that the testes released a substance that affects masculine features and behavior until it was shown that the extract of testes could replace their function in castrated animals.Finally testosterone, the hormone of testes, was isolated in pure and crystalline form in 1935 and shown to be the active substance.

The Graves' disease was named after Irish doctor, **Robert James Graves**, who described a case of goitre with exophthalmos in 1835. The German scientist, **Karl Adolph von Basedow**also reported the same constellation of symptoms in 1840, while earlier report of the disease was also published by the English physician Caleb Hillier Parry in the late 18th century.**Thomas Addison** was first to describe **Addison's disease** in 1855.

The British physiologists, **William Bayliss** and **Ernest Starling** (1902) performed an experiment in which they observed that acid of chyme, instilled into the duodenum, caused thepancreas to begin secretion, even after they had removed all nervous connections between the two. The acid instilled into denervated but vascularised section of jejunum caused a similar flow of pancreatic juice. Extract of jejunum mucosa produced similar effect on pancreatic secretion. Bayliss and Starling discovered that a substance was liberated by the mucosa of small intestine and stimulates the flow of pancreatic juice. They concluded that the control of pancreatic enzyme secretion was mediated by humoral rather than nervous stimulation.They named this substance

"secretin". In this way, the **first hormone** discovered was **secretin** by **Bayliss** and **Starling** in 1903. In 1905, **Starling**coined the term *hormone* for chemicals that act in this way.

Joseph von Mering and Oskar Minkowski made the observation in 1889 that removing the pancreas surgically led to an increase in blood sugar, followed by a coma and eventual death—symptoms of diabetes mellitus. In 1922, Banting and Best realized that homogenizing the pancreas and injecting the derived extract reversed this condition.

The neurons of brain that produces hormones are called neuroendocrine cells and the hormones released by neurons are accordingly called neurohormones. Neurohormones were first identified by **Otto Loewi** in 1921. He incubated a frog's heart with its attached vagus nerve in a saline solution, and left in the solution for some time. The solution was then used to bathe a non-innervated second heart. There was no effect of the solution on the inotropic (amplitude of beat) or chronotropic (rate of beat) characteristics of heart. If the vagus nerve innervating an incubated heart waselectrically stimulated and the saline solution then used to bathe another frog heart, a decrease inotropic and chronotropic activity was seen. This decreased myotropic response could be blocked using atropinewhich was known inhibitor to heart vagal nerve stimulation. So it was concluded from experiments that the vagus nerve released substances, which affect the relaxation and contraction of cardiac muscles. The "vagusstuff" was later identified to be acetylcholine and the accelerator substance as norepinephrine. **Loewi** received the **Nobel Prize** for his discovery.

Later on,the work in endocrinology was focused on the molecular mechanismsresponsible for triggering the effects of hormones. In 1962,**Earl Sutherland** investigated whether hormones enter cells to evoke action, or stayed outside of cells. He studied norepinephrine, which acts on the liver to convertglycogen into glucose via the activation of the phosphorylase enzyme. He homogenized the liver into a membrane fraction and soluble fraction. Phosphorylase was present in soluble fraction of tissue homogenate. When certain hormone(norepinephrine) was incubated with the membrane fraction of liver cell, a factor was produced that could, in turn, activate the phosphorylase enzyme present in soluble fraction.It indicated that norepinephrine's target receptor was on the cell membrane, not located intracellularly. He later identified the factor as cyclic AMP (cAMP) and with his discovery created the concept of second-messenger-mediated pathways. He received the Nobel Prize for his groundbreaking work in endocrinology.

Geoffrey Harris, an English endocrinologist, further suggested that the release of pituitary hormones was controlled by humoral factor of hypothalamic origin. Andrew Schally purified the hypothalamic extract of pig and provided the structure of throtropin releasing hormone (TRH). After this, several other hypothalamic factors were isolated that control the secretion of pituitary hormones.

Recently the endocrinology is progressing with the advent of recombinant DNA technology. Continued advances in molecular genetics will provide different in-vitro and in-vivo approaches to study molecular, cellular, physiological and behavioral aspects of hormone expression and actions.

5.3.2 SCOPE OF ENDOCRINOLOGY

Endocrine research has revealed a wealth of information about biology and physiology of endocrine system. The major advances of endocrinology involve the diagnostic evaluation of a wide variety of symptoms and variations due to disorders of one or more hormones. Mainly there are two categories of diseases: either oversecretion of hormones or undersecretion of hormones. The diagnosis and treatment of endocrine diseases are guided by laboratory tests. Many diseases are investigated through "excitation/stimulation" or "inhibition/suppression" testing. This might involve injection with a stimulating agent to test the function of an endocrine organ. Blood is then sampled to assess the changes of the relevant hormones or metabolites.Traditionally, endocrinology has all been about thoughtful science in which a gland's function may either be suppressed or supplemented. So, extensive knowledge of clinical chemistry and biochemistry is needed to understand the investigations.

Diagnostic imaging of endocrine organs may reveal incidental findings, which may or may not represent disease.Endocrinology involves caring for the person as well as the disease. Most endocrine disorders are chronic diseases that need life-long care.

So, the main scope of work of Endocrinologist is to diagnose and treat hormone imbalances and problems by helping to restore the normal balance of hormones in body. The interventions both therapeutic and diagnostic have been a tool to pave our way into the future. Diabetes, metabolic disorders, menopause, osteoporosis, infertility, hypertension, chronic diseases, lack of growth (short stature) and cancers of the endocrine glands are just a few of the major medical concerns that have a substantial endocrine basis.Care of diabetes, obesity and other chronic diseases necessitates understanding the patient at the personal and social level. The molecular and the physician–patient relationship can be an important therapeutic process.Apart from treating patients; many endocrinologists are involved in clinical science and medical research.

Diabetes remains the most common disorder in endocrine clinics. However, the endocrinologists have not been able to provide a cure, but in the near future it may be possible with stem cell transplantation. Islet cell transplantation is another rapidly developing technology.

On therapeutic front, brachytherapy is increasingly being used for pituitary, adrenal, and endocrine tumors with at least as good results as provided by external beam radiotherapy. More and more, nuclear medicine-based radiation therapies are expected in near future and these are expected to provide targeted therapy with minimal side effects. Some of these therapies are already available for tumors like metastatic medullary thyroid carcinoma and metastatic thyroid carcinoma.

Role of endocrine interventions in oncology is fast expanding. Rescuing ovarian reserve with

gonadotropin-releasing hormone (GnRH) agonists during cytotoxic chemotherapy is rapidly becoming a norm rather than being an exception. GnRH agonists are increasingly being used for medical gonadectomy in cases of prostate carcinomas.Replacement therapies for hormonal deficiencies in endocrinology have always resulted in miraculous results.So,no other medical or surgical field can have impact equivalent to endocrine interventions, especially the nonsurgical interventions.

5.4. CLASSIFICATION AND CHEMICAL NATURE OF HORMONES

Theterm hormone is derived from Greek word *Hormaein* means to excite or stir up, which gives the idea of a biologically highly active organic substance. Thus "hormone is such an active messenger compound which is secreted by endocrine cells of some part of body, circulates in blood, and its minute quantity affects the metabolism of specific target cells to alter the metabolism of other cells near or far, as a reaction to certain external or internal stimulus.

5.4.1 KINDS OF HORMONES

- Hormones can be classified into two main categories.

Circulating (Endocrine) hormones:

These hormones are diffused into blood, circulate throughout body and affect the metabolism of distant target cells. These are general hormones out of which few affect all or almost all the cells of the body eg. Growth hormone helps in growth of all or most parts of the body and thyroid hormone increases the rate of most chemical reaction in almost all the body's cell.

Local hormones:

These hormones are not diffused into blood and remains in ECF. These are short lived hormones which affect the metabolism of neighbouring cells or same cell from which they are secreted. So, the local hormones are categorized as follows.

i) Paracrine hormones affect the metabolism of neighbouring cells.Most of the local hormones are paracrine. These belong to the following categories.

a) Eicosanoids: These are lipids which are derived from fatty acid, arachidonic acid, synthesized in the plasma membrane of cells, and released in ECF. They include prostsglandins, prostocyclin, thromboxanes and leukotrienes.

b) Neuroregulators: These are protein in nature and synthesized in nerve cells. They include neurotransmitter and neuromodulators.

ii) Autocrine hormonesbinds to receptors on the same cell which secrete them, leading to changes in the cell. An example of an autocrine agent is the cytokine interleukin-1 in monocytes.

- Based on the mode of action hormones are classified into quick acting hormones and short acting hormones.

Quick acting hormones:

These hormones initiate immediate response from their target cells. These hormones are large sized.These hormones have outer plasma membrane receptors on the target cell. Example: Protein and amine hormones.

Short acting hormones:

These hormones initiate a delayed response. These hormones are small in size and they bind to the protein receptors present in the cytosol. Example: steroid hormones of reproductive organs and adrenal cortex.

5.4.2. GENERAL CHARACTERISTICS OF HORMONES

- Hormones are secreted by endocrine cells.
- Hormones are chemical messengers.
- They are chemical signals that circulate in the body fluids.
- The hormones regulate the behavior of the target cells.
- Hormones, unlike enzyme do not catalyze any reaction.
- They are secreted only when needed, they are not stored prior to requirement.
- Hormones may be proteinaceous or non-proteinaceous in nature (amino-acid or steroids)
- The secretion of hormones is regulated by the nervous system through the feedback effect.
- Hormones usually cause long term effects like change in behavior, growth etc.
- The hormones function is to stimulate or inhibit the target organs.

5.4.3. HORMONES AND ENZYMES

Like the hormones, the enzymes are also biological active compounds, which influences cell metabolism. In some properties, they resemble the hormones but in others both are different.

Similarities between Hormones and Enzyme

1) Both are synthesizedin cells.
2) Both are required in minute quantities.
3) Both are synthesized by cells, when required. These are not stored anywhere in the body.
4) Both performs cellular metabolism in specific manner, instead of being general.

Dissimilarities between Hormones and Enzyme

1) **Chemical Nature:** Enzymes are always proteinaceous, but hormones may be proteinaceous, amine or steroid in nature.
2) **Molecular weight:** Enzymes have high molecular weight, while hormones have low molecular weight.
3) **Diffusibility:** Enzymes are not able to diffuse through cell membrane, but hormones can diffuse through cell membrane.
4) **Site of action:** Enzymes are carried by duct to target organ or act intracellularly, but hormones are carried by blood to the target organ.
5) **Effect of concentration:** With increase in concentration, the enzyme increases the rate of reaction to certain limit. The deficiency or excess of hormone causes diseases and metabolic disorders.
6) **Reversibility:** The metabolic reactions catalyzed by enzymes are reversible, while the regulation of metabolic processes by hormones is irreversible.
7) **Consumption:** The enzymes remain unchanged i.e. even after participating in metabolic reactions, they are used again and again. Contrarily, after being used once, the hormones become inactivated and are degraded.

5.4.4. CHEMICAL NATURE OF HORMONES

Hormones secreted by different endocrine glands vary widely in chemical structure. All hormones, however, can be divided into a few chemical classes.

5.4.4.1. AMINO ACID DERIVED HORMONES

These are smallest hormones and derived from the amino acids tyrosine and tryptophan. They include the hormones secreted by the adrenal medulla, thyroid, and pineal glands. Tyrosine derived hormones are thyroxine and adrenaline, secreted from thyroid gland and adrenal medulla respectively. Tryptophan amino acid is the precursor of hormones like serotonin and melatonin. Serotonin regulates the movement of the intestine and is also associated with mood and low levels of this hormone often result in depression.

5.4.4.2. POLYPEPTIDES NATURED HORMONE

Polypeptide hormones are small peptides of few amino acids; generally contain less than 100 amino acids. ACTH, MSH, antidiuretic hormone, parathormone, glucogon and insulin etc. are polypeptide in nature. Out of these ACTH, parathormone, glucogon and insulinare long peptides hormones. MSH, antidiuretic hormone, and oxytocin are short peptides hormones.

5.4.4.3. PROTEIN NATURED HORMONES

Protein hormones are polypeptides with more than 100 amino acids. Growth hormone and lactogenic hormone (LTH) is protein natured hormone.

5.4.4.4. GLYCOPROTEIN NATURED HORMONES

These molecules consist of a long polypeptide (containing more than 100 amino acids) bound to one or more carbohydrate groups. Thyroid stimulating hormone, follicle-stimulating hormone (FSH) and luteinizing hormone (LH) are glycoprotein in nature.

5.4.4.5 STEROIDS NATURED HORMONES

Steroid hormones are derived from cholesterol and are soluble in lipids. These are synthesized in mitochondria and endoplasmic reticulum of endocrine cells. The steroid hormones include the sex hormones and the hormones produced by the adrenal gland. The sex hormone includes androgens, estrogens and progesterone. The adrenal hormones are mineralcorticosteroids and glucocorticosteroids. Steroids hormones are important as they take part in important functions including water balance, sexual development and stress response.

5.4.4.6 FATTY ACIDS DERIVED HORMONES

Hormones derived from the fatty acids are called eicosanoids. They are derived from arachidonic acid (Prostaglandins). These hormones are produced by every cell in the body. They have important roles in the body including inflammation, blood pressure and blood clotting.

5.4.5. GENERAL FUNCTIONS OF HORMONES

- They stimulate or inhibit growth.
- Hormones control the wake-up cycle and the circadian rhythms.
- Are responsible for mood swings.
- Induces or suppresses apoptosis.
- Activates or inhibits the immune system.
- Regulates metabolism.
- Prepares body for mating, fleeing, flighting and other activity.
- Also prepares body for new mode of life like puberty, parenting and menopause.
- It controls the activity of the reproductive cycle.
- Controls hunger.

5.5. SUMMARY

The nervous system and endocrine system are two integrating systems which were acquired by higher metazoans during the course of evolution. These systems co-ordinate functions of different parts of body in accordance with the changing demands of external and internal environmental conditions by transmitting informations from one to the other parts. The endocrine system achieves co-ordination and integration for persistent and slow responses of the body by transmitting the signals through chemical messengers. These chemical messengers are called hormones. These are released by endocrine gland into the blood, circulate in whole body and regulate persistent activities like metabolism, growth, homeostasis and reproduction etc.

Knowledge of hormones dates back to 1849 when Berthold first demonstrated that the secondary sexual characters are affected in roosters (cockerels) by removal of testes or by grafting testes in castrated roosters. In 1855, Thomas Addison demonstrated that symptoms of Addison's disease, caused by destruction of adrenal cortex and for his discoveries, he became"Father of Endocrinology".Bayliss and Starling extracted the first hormone from secretory cells of duodenal mucosa and named it secretin in 1903, because it was found to stimulate the pancreas for secretion.

Endocrinology is a branch of medicine that concerns thestudy of hormones and its disorders. The endocrine disorders are a varied group of diseases that usually occur due to hypofunctioning or hyperfunctioning of the endocrine glands.

Hormones can be categorized as circulating hormones and local hormones. The circulating hormones are diffused into blood, but instead of diffusing into blood, the local hormones remain in ECF. On the basis of mode of action, the hormones may be quick acting hormones or short acting hormones.

All hormones are relatively small molecules of low molecular weights. The hormones are chemically different. The chemical nature of hormones is summarized as follows.

A) Amino Acid Derivatives

(i) Derivatives of Tyrosine

Epinephrine and norepinephrine (Adrenal medulla)
Dopamine (Hypothalamus)
Thyroxine (Thyroid gland)

(ii)Derivative of Tryptophan

Melatonin (Pineal gland)

B) Peptide Hormones

(i)Short peptide and small proteins

ADH, oxytocin and regulatory hormones (Hypothalamus)
ACTH, GH, MSH and prolactin (Pituitary)
Insulin and glucagon (Pancreas)

Parathyroid hormone (Parathyroid gland)
Calcitonin (C-cells of thyroid)
Atrial natriuretic hormone (Heart)
Gastrointestinal hormones (GI Tract)

(ii)Glycoproteins

TSH, LH and FSH (Pituitary)
Erythropoietin (Kidney)

C) Lipid Derivatives

(i) Steroid hormones

Androgen, estrogen and progesterone (Gonads)
Mineralocorticoids and glucocorticoides (Adrenal cortex)

(ii)Eicosanoids

Prostaglandins

5.6. SELF ASSESSMENT QUESTIONS AND POSSIBLE ANSWERS

5.6.1. MULTIPLE CHOICE QUESTIONS

1. Who is known as Father of Endocrinology?

   (a) Starling (b) Addison

   (c) Sanger (d) Best

2. The term hormone was introduced by:

   (a) Karlson (b) Starling

   (c) Abel (d) Addison

3. The hormones oxytocin and ADH are secreted by

   (a) Hypothalamus (b) Adrenal Medulla

   (c) Neurohypophysis (d) Adenohypophysis

4. Which of the following is glycoprotein natured hormone?

   (a) FSH (b) ADH

   (c) ACTH (d) GH

5. Which of the following hormone is lipid derivative of arachidonicacid

   (a) Prostaglandin (b) Androgen

   (c) Corticoids (d) progestins

6. The hormones which affectthe metabolism of neighbouring cells are:

(a) Autocrine hormones (b) Pheromones

(c) Paracrine hormones (d) None of these

7. Endocrine glands and nervous Systems are

(a) Independent (b) Synchronous

(c) Antagonistic (d) Interdepedent

8. The target cells of a hormone always have

(a) Special channels through which hormones move

(b) Large amount of the hormone stored with in vesicles

(c) Special receptors to which hormones binds

(d) Undiffirentiated cytoplasm

9. Hormones may be:

(a) Steroid (b) Peptides

(c) Amino Acid derivatives (d) All of these

10. One similarity between enzymes and hormones is that both:

(a) are proteins (b) can be used again and again

(c) are used in minute amount (d) act at a particular pH

5.6.2. VERY SHORT QUESTIONS

1. Who introduce the term hormone?
2. Name two types hormones on the basis of mode of action.
3. Who is known as Father of Endocrinology?
4. Name two hormones which are derivatives of tyrosine?
5. Who discovered the first hormone?
6. What are the two integrating systems, found in our body?
7. Melatonin is derivative of which amino acid?
8. Define hormones?

ANSWERS

5.6.1. 1.(b); 2.(b); 3.(a); 4.(a); 5.(a); 6.(c); 7.(d); 8.(c); 9.(d); 10.(c).

5.6.2. 1.Starling; 2.Quick acting and short acting hormones; 3.Thomas Addison; 4.Epinephrine and thyroxine; 5.Bayliss and Starling;6.Nervous system and Endocrine system; 7.Tryptophan; 8.A hormone is a chemical messenger which is secreted by endocrine glands and carried to the other organs with the help of blood, where it influences the activity and metabolism of specific target cells.

5.7. TERMINAL AND MODEL QUESTIONS

1. Give an account of history and scope of endocrinology?
2. How do hormones resemble and differ from enzymes?
3. Describe the kinds of hormones?
4. Describe chemical nature of hormones?
5. What are the two interdependent systems found in our body? Explain the distinction between the two.
6. Give an account on chemical nature of hormones?

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UNIT6: PITUITARY AND THYROID GLANDS

CONTENTS

6.1. OBJECTIVES

After reading this unit the readers will be able to:

- Describe the location and structure of pituitary gland
- Discuss the hormones of pituitary gland
- Explain the functions of pituitary hormones
- Discuss the structure and functions of thyroid gland
- Discuss the irregularities of thyroid hormones
- Discuss the structure and functions of parathyroid gland
- Discuss the irregularities of parathormone

6.2. INTRODUCTION

The pituitary has often been referred to as master gland of vertebrates because it is located near the brain and controls such important endocrine glands as the adrenals, thyroid and the gonads. The pituitary gland is actually known to be subservient to hormonal stimuli derived from the glands and other endocrine glands.It can be regarded as relaying and amplifying signals obtaining from the hypothalamus. Early anatomists considered the pituitary as a part of brain and, in fact the gland does possess a neural component. The two different tissues, ectoderm from the oral cavity and neuroectoderm from the brain, have become integrated into one functional glandular component. So, the pituitary gland is a rich source of hormones that controls a variety of physiological functions.

The calcium ion is a key element in numerous physiological functions. This divalent cation is important in bone structure as well as remains available to serve in a variety of intracellular and extracellular roles. To control the calcium ion homeostasis, parathyroid hormone from parathyroid glands and calcitonin from parafollicular cells of thyroid gland play key role.

6.3. PITUITARY GLAND- STRUCTURAL ORGANIZATION

In vertebrate anatomy, the **pituitary gland**, or **hypophysis**, is an endocrine gland of about the size of a pea and weighing 0.5 to 1 gram in humans. The pituitary is recessed within the **sella turcica** or **Turkish saddle** of the **sphenoid bone**, beneath the hypothalamus near the optic

chiasma. Pituitary gland is connected to the ventral wall(hypothalamus) of diencephalon of the brain by a short infundibular stalk. That is why; it is also called **hypophysis cerebri**(Fig.6.1).

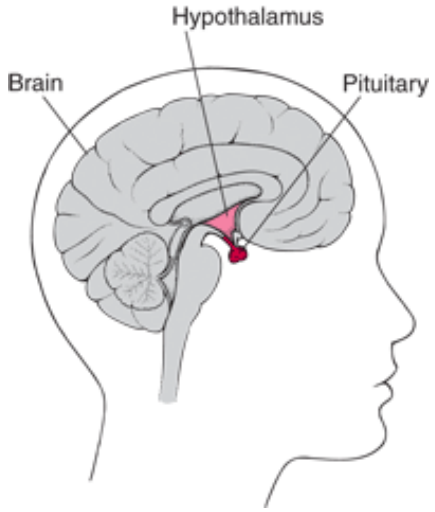


Fig. 6.1Pituitary gland of humans

The pituitary gland consists of tissues that are derived from two diverse origins. It is composed of adenohypophysis or anterior pituitary and neurohypophysis or posterior pituitary. The adenohypophysis is primarily glandular tissue. The neurohypophysis is composed of neuronal process that originates from neurons in the hypothalamus. A third narrow strip like part is formed from proliferation of cells adjacent to infundibulum. It is called pars intermedia or intermediate lobe. It is of considerable size in some species but in humans, the fetal pars intermedia regresses and is absent in the adult. In birds, the anterior pituitary is separated from the posterior pituitary by a layer of connective tissue and a pars intermedia does not develop.

6.3.1 ORIGIN OF ANTERIOR PITUITARY AND POSTERIOR PITUITARY

The anterior pituitary arises from an invagination of the oral ectoderm of the stomodeum and forms **Rathke's pouch**. Rathke's pouch elongates and constricted. This contrasts with the posterior pituitary, which originates from neuroectoderm of the floor of the forebrain. An infundibular process develops as a diverticulum from the floor of diencephalon. It increases in size and from the hypothalamic nuclei, nerve fibre grow into the infundibulum. The neuroepithelial cells differentiate into pituicytes. These pituicytes (neuroglial-like elements) are dispersed between the neuronal endings within infundibulum (Fig. 6.2).

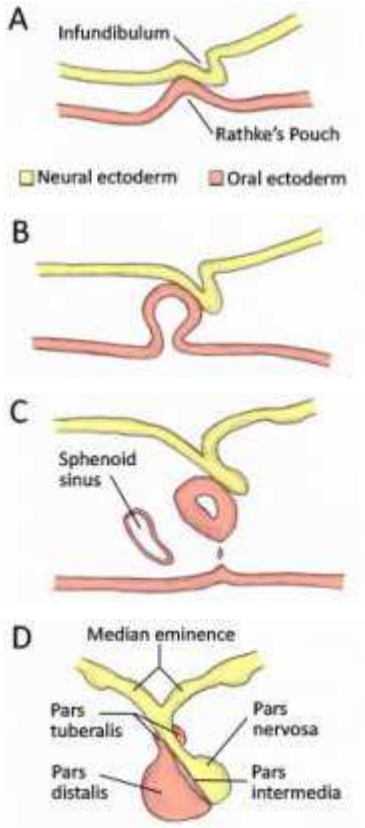


Fig.6.2. Developmental anatomy of pituitary gland

6.3.2 STRUCTURAL ORGANIZATION OF ANTERIOR PITUITARY

The anterior pituitary comprises about 75% part of the pituitary gland. The anterior pituitary consists of proximal **pars tuberalis** and a large **pars distalis**.

Cells of the anterior wall of rathke's pouch of anterior pituitary proliferate to give rise to the pars distalis. Dorsal extension of anterior pituitary surrounds the infundibular stalk to give rise to pars tuberalis. Pars tuberalis provides the anatomical link between the pars distalis and the hypothalamus.

Endocrine cells of the anterior pituitary are controlled by regulatory hormones released by parvocellular neurosecretory cells into the hypothalamic blood capillaries leading to infundibular blood vessels, which in turn lead to a second capillary bed in the anterior pituitary. This vascular relationship constitutes the **hypothalamo-hypophyseal portal system**. Diffusing out of the second capillary bed, the hypothalamic releasing hormones then bind to anterior pituitary endocrine cells and regulate their secretions.

Anterior pituitary containsfive types of cells, whichsynthesize and secrete hormones (Table 1).Depending on the affinity of cells for certain dyes used in histological strains, the individual cell types are also referred to acidophils, basophils or chromophobes.Somatotrophs and lactotrophs are acidophils, while the thyrotrophs and gonadotrophs are basophils. The corticotrophs are often referred to as chromophobes, however these are basophils.

Table 1. Histochemical classification of cells of anterior pituitary

S.No.	Type of cell	Hormone secreted	Percentage of type of cell	Staining characteristic
1.	Somatotrophs	human growth hormone (hGH)	30-40%	Acidophil
2.	Corticotrophs	adrenocorticotropin (ACTH)	20%	Basophil
3.	Thyrotrophs	thyroid stimulating hormone (TSH)	3-5%	Basophil
4.	Gonadotrophs	gonadotropic hormone i.e., both luteinizing hormone (LH) and follicle stimulating hormone (FSH)	3-5%	Basophil
5.	Lactotrophs	prolactin (PRL)	3-5%	Acidophil

6.3.3 STRUCTURAL ORGANIZATION OF POSTERIOR PITUITARY

The posterior pituitary is a compact lobe, comprising about 25% part of pituitary gland. It consists of three parts-

I) A **median eminence** at the base of hypothalamus
II) An **infundibular stalk** on ventral side of median eminence
III) A distal pars nervosa

The pars nervosa is like a nervous tissue and contains many axon terminals of neurosecretory cells of hypothalamus. The magnocellular neurosecretory cells of the supraoptic and paraventricular nuclei are located in the hypothalamus and project axons down the infundibulum and axon terminals reach to pars distalis. These axon terminals are embedded in pituicytes, which forms neuroglial tissue (Fig.6. 3).

The Posterior pituitary hormones are synthesized by cell bodies in the hypothalamic neurosecretory cells and remain stored in small vesicles in the axons and their terminals. These vesicles are called Hering bodies.

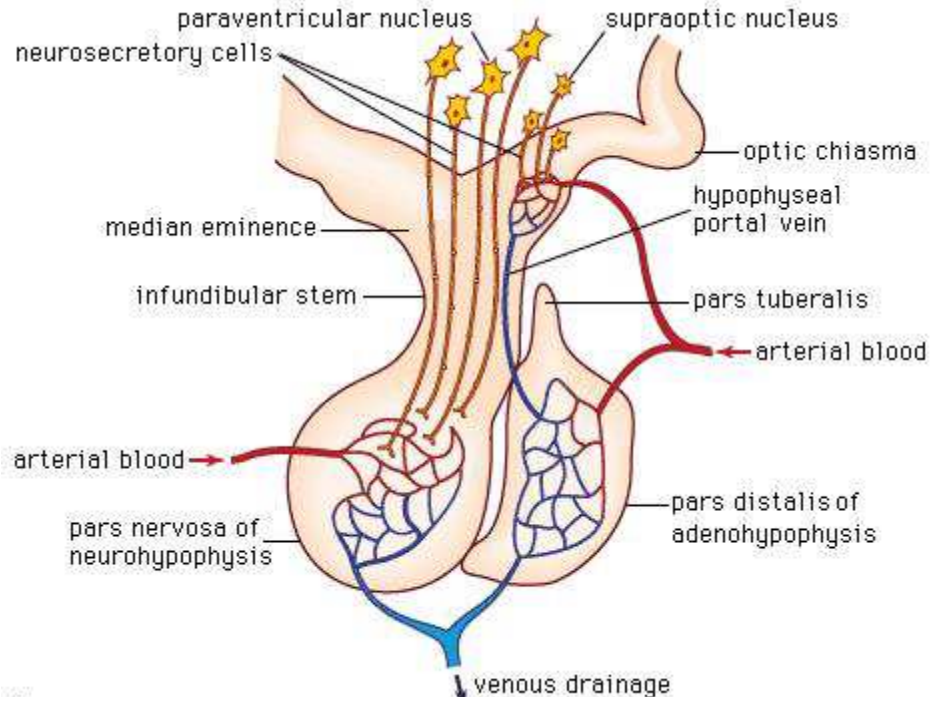


Fig.6.3. Vascular connection between the pituitary gland and hypothalamus

6.4. HORMONE SECRETION FROM PITUITARY AND THEIR HYPOTHALAMIC CONTROL

6.4.1 HYPOTHALAMUS AND PITUITARY GLAND

The hypothalamus monitors the body through the circulatory and nervous systems. When it detects that something is out of balance, it sends a message to the pituitary gland that a corrective

action is needed. When the pituitary gland gets this message from the hypothalamus, it releases specific hormones into the bloodstream that can stimulate other endocrine glands, organs or tissues, depending on what action is needed.

6.4.1.1 HYPOTHALAMIC CONTROL OF ANTERIOR PITUITARY:

The hypothalamus communicates with the anterior portion of the pituitary gland by way of hormonal messages. These messages come in the form of hypothalamic-releasing and hypothalamic-inhibiting hormones, which tell the anterior pituitary to start or stop an action.

The endocrine hypothalamus consists of neurosecretory neurons whose secretory activity provides the neurohormones that regulate adenohypophyseal function. The important **hypothalamic releasing** and **inhibitory hormones** are as follows.

Thyrotropin -releasing hormone (TRH): It stimulates release of TSH by thyrotroph cells of anterior pituitary.

Corticotropin- releasing hormone (CRH): It stimulates release of ACTH by corticotroph cells of anterior pituitary.

Growth hormone releasing hormone (GH-RH): It stimulates release of growth hormone by somatotroph cells of anterior pituitary.

Growth hormone inhibiting hormone (GH-IH): It inhibits the release of growth hormone by somatotroph cells of anterior pituitary.

Prolactin releasing hormone (PRH): It stimulates release of prolactin by lactotroph cells of anterior pituitary.

Prolactin inhibiting hormone (PIH): It inhibits release of prolactin by lactotroph cells of anterior pituitary.

Gonadotropin releasing hormone (Gn-RH): It stimulates release of gonadotropins by gonadotroph cells of anterior pituitary.

MSH releasing hormone (MSH-RH): It stimulates release of MSH by anterior pituitary.

MSH inhibiting hormone (MSH-IH): It inhibits release of MSH by anterior pituitary.

6.4.1.2 HYPOTHALAMIC CONTROL OF POSTERIOR PITUITARY

The posterior pituitary does not synthesize any hormone. **Magnocellular neurosecretory cells** are large neuroendocrine cells within the supraoptic nucleus and paraventricular nucleus of the hypothalamus. There are two types of magnocellular neurosecretory cells,**oxytocin-producing cells** and **vasopressin-producing cells**, but a small number can produce both hormones. These cells are electrically excitable, and generate action potentials in response to afferent stimulation. The synthesized hormones remain stored in Hering bodies and released from axon terminals by exocytosis and diffuse into adjacent blood capillaries, when needed.

6.4.2 HORMONES OF ANTERIOR PITUITARY

The anterior pituitary produces a number of peptide hormones. On the basis of functional significance these are grouped into **tropic hormones** and **gonadotropins**.

6.4.2.1 TROPIC HORMONES

These hormones activate other endocrine glands or target organs. Tropic hormones are as follows.

(i) Growth hormone (GH) or somatotropic hormone

Growth hormone is a polypeptide synthesized by somatotrophs of the pars distalis. The human hormone consists of 191 amino acids with two intramolecular disulphide bonds. It is the major hormone in the secretion of anterior pituitary.

Function of Growth Hormone: It is an anabolic hormone that enhances amino acid incorporation into muscle protein and stimulates extracellular collagen deposition. It is an important hormone for normal growth of body. It promotes biosynthesis of DNA, RNA and protein by all the body cells. It stimulates cellular growth and proliferation, growth and repair of bones, muscle and connective tissues. It promotes glycogenesis, deamination and gluconeogenesis in liver cells. It produces a positive nitrogen and phosphorus balancein body. Due to the increase uptake of sodium and potassium ion by growing tissues, the urinary excretion of these ions is decreased. These effects of growth hormone on protein metabolism and electrolyte balance are mediated by the action of **somatomedins**. The somatomedin is released from the liver in response to GH stimulation of hepatocytes. Somatomedin stimulates cellular growth in a variety of tissues and organs.

Effect of hyposecretion of growth hormone:

a. **Dwarfism**: The hyposecretion of GH during the growth years leads to short stature in the young child. Growth of all organs is retarded. Growth of bones stops at epiphyseal ends. Hence the bones do not grow in length, so that the body remains dwarf. The development of brain is normal in pituitary dwarfs. The circus dwarfs are pituitary dwarfs and also called **midgets**.

b. **Pituitary Myxoedema**: The hyposecretion of GH in the adult life (about age of 22 years) lead to the rare condition called Simmond's disease or pituitary myxoedema. The person becomes quite thin and shows sign of premature ageing. The symptoms are as follows.

- Reduced BMR and protein synthesis
- Graying and falling of hair
- Reduced blood pressure and low body temperature
- weakness of muscles and vision

- due to accumulation of mucus under the skin, the body becomes puffy

Effect of hypersecretion of growth hormone

a. **Gigantism**: Hypersecretion of growth hormone during childhood causes excessive growth of all body parts, which results into symmetrical giant body. It is called **proportionate gigantism**. The person may attain a height of 8 feet or even more.

b. **Acromegaly**: Hypersecretion of growth hormone after growth period also causes gigantism but the long bones do not grow in length due to closed hypophysis at their ends. The bones of hand, feet, lower jaw and rib cage become thick. The lips, eyelids, tongue, nose, chin etc also enlarge. The person has ugly face because of growth and thickness of facial bones, long jaws and protruding forehead. The body becomes gorilla like. This is called **disproportionate gigantism** or **acromegaly**. Sometimes a person develops hump due to bending of vertebral column. It is called **kyphosis**.

(ii) Thyroid stimulating hormone (TSH)

It is secreted by thyrotroph cells of anterior pituitary. In its molecule, the polypeptide has 201 amino acid residues.The secretion of TSH is controlled by a hypothalamic thyrotropin- releasing hormone (TRH). Under the negative feedback regulation, the secretion of TRH depends on blood level of TSH, thyroxine and glucose and on metabolic rates of body cells.

(iii) Adrenocorticotropic hormone (ACTH)

It is secreted by corticotroph cells of anterior pituitary. In its molecule, the polypeptide has 39 amino acid residues. The secretion of ACTH is controlled by a hypothalamic corticotropin-releasing hormone (TRH). The synthesis of hormones of adrenal cortex is intensified by ACTH. Under the negative feedback regulation, the concentration of glucocorticoids in blood affects the secretion of both ACTH and CRH.

(iv) Prolactin (PRL) or luteotropic hormone (LTH)

It is secreted by lactotroph cells of anterior pituitary. In its molecule, the polypeptide has 198 amino acid residues. The secretion of PRL by anterior pituitary is controlled by a hypothalamic prolactin- releasing hormone (PRH) and inhibited by prolactin-inhibiting hormone (PIH). The main physiological effect of PRL is to activate growth of breasts during pregnancy. It promotes secretion of milk by mammary glands after child birth that is why it is called as **mammotropic hormone (MTH)** or **lactogenic hormone**. The hypersecretion of PRL may hinder menstruation. In pigeon, PRL stimulates the epithelial cells of cropin both male and female to secrete **pigeon milk** for nutrition of newly hatched infants.

6.4.2.2 GONADOTROPINS

These are secreted by gonadotroph cells of anterior pituitary. The gonadotropins include FSH and LH. Both of these stimulate growth and activities of gonads. The secretion of gonadotropins begins 2-3 years before puberty. The secretion of gonadotropins is initiated by Genetic Biological Clock, located in hypothalamus. Under the regulation of clock, a hypothalamic gonadotropin-releasing hormone (Gn-RH) is secreted to regulate gonadotroph cells of anterior pituitary.

(i) Luteinizing hormone (LH) or interstitial cell stimulating hormone (ICSH)

It is glycoprotein in nature and its molecule has a polypeptide of 204 aminoacid residues. In males, it stimulates the interstitial cells of testes (Leydig cells) to secrete male hormone (testosterone), so also named as **ICSH**. The male hormone regulates the development of secondary sexual characters in male. In females, LH stimulates the last stages of oogenesis, ovulation, and development of corpus luteum and secretion of progesterone by corpus luteum.

(ii) Follicle stimulating hormone (FSH)

It is glycoprotein in nature and its molecule has a polypeptide of 204 aminoacid residues. In male, it stimulates growth of seminiferous tubules and spermatogenesis. In females, it stimulates growth of ovarian follicles and oogenesis.

6.4.3 HORMONES OF POSTERIOR PITUITARY

As discussed above, posterior pituitary do not synthesized any hormone. Two hormones are synthesized in the hypothalamic neurosecretory cells and remain stored in hering bodies. When required, these are released into adjacent blood capillaries.

(i) Vasopressin or Antidiuretic hormone (ADH)

This hormone promotes reabsorption of water from distal convoluted tubule of nephrons and collecting duct. So, it discourages water loss in urine, hence named as ADH. Its release into blood is controlled by an osmoregulatory centre, located in hypothalamus.

This hormone also increases blood pressure by contracting blood vessels in several tissues, hence named as **vasopressin**.

Hyposecretion of ADH causes diuresis, so urine becomes diluted and blood becomes concentrated resulting decreased blood pressure. This condition is called **polyurea** or **diabetes insipidus**. In acute condition, quantity of urine may increase to about 20 litres instead of 1-2 litres per day. Due to dehydration of body, the patient may die if water is not available. Pitressin (synthetic ADH) is used for antidiuresis.

Due to **hypersecretion of ADH**, the urine becomes concentrated and blood is diluted resulting increased blood pressure.

(ii) Oxytocin

This hormone stimulates uterine muscular contraction and induces labour pains during child birth. As signals from increasing labour pain reaches hypothalamus, more and more oxytocin is released from posterior pituitary under a positive feedback regulation. It dilates cervix at the time of child birth. After child birth, it stimulates mammary gland to facilitate release of milk during suckling. So, it is also called **milk ejecting hormone**. The milkmen inject synthetic oxytocin, called **pitocin**, into their cows and buffaloes to get more milk.

6.4.4 HORMONE OF INTERMEDIATE LOBE

(i) Melanocyte stimulating hormone (MSH)

It is secreted by intermediate lobe or pars intermedia, so also named as **intermedin**. Its molecule is a small peptide of 13 aminoacid residues. Its secretion is regulated by MSH-releasing hormone (MSH-RH) or MSH- inhibiting hormone (MSH-IH). In lower vertebrates, it acts on melanophores and increases pigmentation so, skin colour darkens. But in humans, it is vestigial hormone.

6.5. THYROID GLAND- STRUCTURAL ORGANIZATION

It is **largest** endocrine gland of our body.Thyroid gland is derived from endoderm of the cephalic portion of the embryo's alimentary canal. Firstly, a sac like diverticulum appears in the middle of the ventral surface of the pharynx and becomes bilobed glandular organ. It remains connected to the pharynx by a thyroglossal duct which becomes a solid stalk and usually atrophies. In humans, the two lateral lobes of thyroid become solid masses of tissue. These two lobes remain connected to each other by a narrow isthmus. A pyramidal lobe persists near the isthmus which is considered as a remnant of the thyroglossal stalk (Fig.6.4).

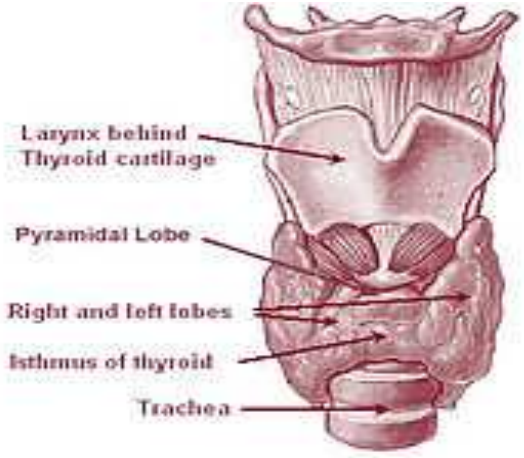


Fig.6. 4. Human thyroid gland

In human beings, thyroid gland measures about5 cm in length and 3cm in width. It weighs about 15 to 20 gms. Thyroid follicles are functional components of the thyroid gland, which consists of a cuboidal epithelium arranged as a single layer surrounding a lumen (Fig.6.5).Thyroid follicles contain a colloidal material, called thyroglobulin. Thyroglobulin is the substrate for tyrosine iodination and the subsequent synthesis of thyroid hormone.

C-cells are present within the follicular wall and in the extracellular space between the follicles. These cells are source of calcitonin hormone.

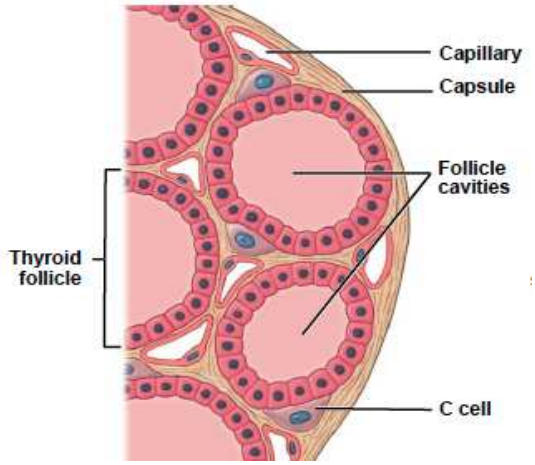


Fig.6.5 Histological representation of the human thyroid gland

6.5.1 HORMONES OF THYROID GLAND

Thyroid gland secretes two iodinated hormones- tetraiodothyronine and triiodothryonine and one noniodinated hormone- thyrocalcitonin.

(i) Iodinated hormones (tetraiodothyronine and triiodothryonine)

Thyroid gland is reservoir of iodine. Thyroid gland utilizes about 0.15 mg iodine per day to secrete iodinated hormones in normal amounts. So a person must daily obtain 150µg of iodine from food. Iodine of food is absorbed and circulated in blood in the form of iodide ions (I^-). Cells of thyroid follicles absorb iodide ion actively and in presence of **peroxidase enzyme**, iodide ions are converted into molecular iodine ($2I^- \rightarrow I_2$). Iodine is then, released by follicular cells into follicular cavity.

Thyroglobulin(TG) synthesis occurs continuously in the follicular cells under genic control. Thyroglobulin is released into the colloidal space by vesicular exocytosis.The molecule of thyroglobulin consists of 500 amino acid monomers, out of which 123 monomers are of tyrosine at fixed places. When thyroglobulin interacts with iodine, the oxidized iodine is incorporated with tyrosine monomers of thyroglobulin molecule. About 15 tyrosine monomers of each thyroglobulin molecule binds with single atom of iodine to produce monoiodotyrosine (T_1) and other tyrosine binds with two atoms of iodine, forming diiodotyrosine(T_2). This is called organification of thyroglobulin. Within thyroglobulin, diiodotyrosine residues undergo an oxidative coupling that results in the formation of tetraiodothryonines (T_4) or thyroxine. Similarly, coupling of monoiodotyrosine (T_1) and diiodotyrosine (T_2) results in the formation of small amount of triiodothyronines (T_3).

Iodination of tyrosine residues of TG and subsequent oxidative coupling to form iodothyronines may be facilitated by intraluminal ciliary action and subsequent movement of TG to reactive sites of apical surface of the follicular cells. The colloid is engulfed in follicular cells by the

process of pinocytosis and transported into the cells as colloid droplets. These colloid containing vesicles are fused with lysosomes, forming secondary lysosomes. Much of the TG is now degraded by lysosomal proteolytic enzymes.and thyroid hormones (T_3 and T_4) are then released into the cytoplasm. From cytoplasm, these hormones are diffused into the extracellular spaces and then into blood circulation.The daily output of thyroid gland is about 80μg ofT_4 and 4 μg of T_3.

The body has a complex mechanism for adjusting the level of thyroid hormones. It is provided by feedback control of the secretion of the thyroid hormone by thyroid gland. First, the hypothalamus, located just above the pituitary gland in the brain, secretes thyrotropin-releasing hormone, which causes the pituitary gland to produce thyroid-stimulating hormone (TSH). Just as the name suggests, TSH stimulates the thyroid gland to produce thyroid hormones. The pituitary gland slows or speeds the release of TSH, depending on whether the levels of thyroid hormones circulating in the blood are getting too high or too low.

Functions of thyroxine and T_3

The general effect of thyroid hormones is to cause nuclear transcription of large number of genes. Therefore, in cells of body, great number of protein enzymes, structural proteins, transport proteins and other substances increases and functional activities throughout the body increases. The thyroid hormones increase the metabolic activities of almost all the tissues of the body.

a) **Effect of thyroid hormone on growth:** Thyroid hormone has both general and specific effects on growth. In the human beings, the effect of thyroid hormone on growth is manifest mainly in growing child. This hormone promotes the growth and development of the brain during fetal life and for the first few years of postnatal life. Thyroxine is essential for the metamorphic changes of the tadpole into the adult frogs. Gudernatsch discovered that metamorphosis in frog's tadpole begins only when adequate amount of thyroxine is secreted by the thyroid of the tadpole.

b) **Effect of thyroid hormone on carbohydrate metabolism:** Thyroid hormones stimulate uptake of glucose by the interstitial cells. It enhances glycolysis and gluconeogenesis. All these effects probably results from overall increase in cellular metabolic enzyme, caused by thyroid hormones.

c) **Effect of thyroid hormone on fat metabolism:** These hormones enhance fat metabolism and accelerates the oxidation of free fatty acids by the cells.

d) **Effect of thyroid hormone on protein metabolism:** These hormones increase synthesis of proteins and RNA which precedes increased metabolism.

e) **Effect of thyroid hormone on basal metabolic rate:** These hormones increase metabolism in almost all cells of the body which results into increased basal metabolic rate.

f) **Effect of thyroid hormone on body weight:** Greatly increased thyroid hormones decrease the body weight and greatly decreased hormones increase the body weight.

g) **Effect of thyroid hormone on respiration:** The increased rate of metabolism increases the utilization of oxygen and the formation of CO_2. These effects activate all the mechanism which increases the rate and depth of respiration.

h) **Effect of thyroid hormone on heart rate:** The heart rate increases considerably more under the influences of thyroid hormones. It has direct effect on the excitability of the heart, which in turn increases the heart rate.

i) **Effect of thyroid hormone on other endocrine glands:** The increase in thyroid hormones enhances secretion of other endocrine glands. For example- Increase in thyroxine enhances the rate of glucose metabolism in the body which in turn increases insulin secretion by the pancreas.

Similarly, many metabolic activities related to bone formation also enhanced due to increase in thyroxine. It increases the need of parathyroid hormones.

(ii) Calcitonin or thyrocalcitonin

It is secreted by the parafollicular cells of thyroid gland and regulates metabolism of calcium and phosphorus ions. Calcitonin regulates upper limit of calcium level in blood. It promotes deposition of calcium in bones. It retards bone dissolution (osteoclastic action) and stimulates excretion of excess calcium in urine.

6.5.2 IRREGULARITIES OF THYROID SECRETIONS

Hyposecretion of thyroid hormones

Hyposecretion may be a hereditary defect, or it may be due to iodine deficiency in food, or overexcretion of iodine in urine. Due to hyposecretion of thyroid hormones following disorders occur.

a. Cretinism

It is caused by hypothyroidism during fetal life, infancy and childhood. It leads to failure of growth and mental retardation. In the sufferer, skeletal growth is more inhibited than soft tissue growth. The body becomes deformed with large head, short hand and feet, and enlarged belly. The skin becomes rough,thick and dry. These are called cretins because of poor mental development. Their reproductive organs also remain poorly developed.

b. **Myxoedema**

It is caused by hypothyroidism in adults. Mucus accumulates in the subcutaneous tissues, holding a lot of water which results puffiness to the skin. So body becomes swollen and heavy. It is characterized by low basal metabolic rate, low body temperature and low body pressure. Some other symptoms which may appear in patients are paleness and dryness of skin, loss of eyesight due to vitamin A deficiency, muscular weakness, cramps and stiffness, insomnia and degenerated sex organs and impotency.

c. Endemic goitre

The term ‘goitre’ means a greatly enlarged thyroid gland. It usually occurs due to iodine deficiency in food. Lack of iodine prevents production of both thyroxine and T_3 but does not stop

the formation of thyroglobulin. Hormone isnot available in blood to inhibit production of TSH, so large quantities of TSH are secreted and causes thyroid cell to secrete more thyroglobulin into the follicles. So, gland grows larger and larger. It may increase 10-20 times more than normal size.

d. Hashimoto's disease

Sometimes due to age, infection or other injury, thyroid secretion is reduced to the minimum. The thyroid hormone in traces or the drugs given for treatment of this condition, sometimes treated as antigen by the body. Now, the immune system of body starts forming antibodies. These antibodies invade and destroy the gland itself. So, this disease is also called as "autoimmune thyroiditis" or **"suicide of the thyroid"**.

Hypersecretion of thyroid hormones

Hyperactivity of thyroid leads to hypersecretion of thyroid hormone leading to high state of excitability, intolerance to heat, increased sweating, mild to extreme weight loss, muscular weakness, nervousness, mental restlessness and increased irritability.

Most people with hyperthyroidism develop some degree of protrusion of the eyeball. The condition is called **exopthalmic goitre**. The cause of the protruding eyes is edematous swelling of the retro-orbital tissues and degenerativechanges in the extraocular muscles. During hyperthyroidism, enlargement of gland occurs due to its diffused growth, which is called **Grave's** or **Basedow's diseases**. Sometimes, gland enlargement is due to formation of one or more hypersecretory nodules in the gland which is called **Plummer's disease**or **Toxic Adenoma.**

6.6. PARATHYROID GLANDS- STRUCTURAL ORGANIZATION

Two pairs of small, reddish or yellowish brown and ovoid glands are found in human beings. These are located separately on the posterior surface of the lobes of the thyroid gland (Fig.6.6). These glands are derived embryologically from **endoderm** of pharyngeal pouches.

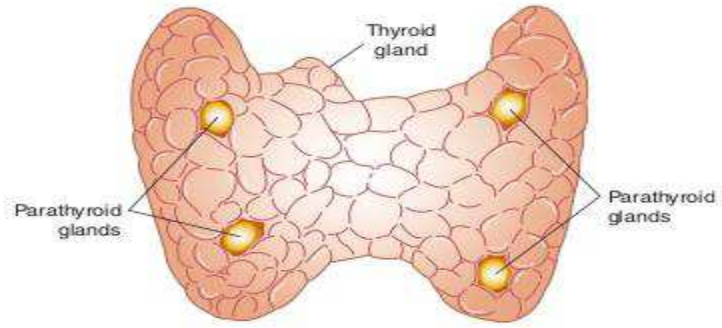


Fig.6. 6. Posterior view of thyroid gland showing parathyroid gland

The size of parathyroid gland is about 6 mm in length, 3 mm in width and 2 mm in thickness. Each parathyroid gland has a thin envelope of connective tissue and consists of a solid mass of

densely packed polygonal cells embedded in a highly vascular stroma. The cells are of two types- **Chief cells** and **Oxyphil cells** (Fig. 6.7). Chief cells are main hormone secreting cells and the function of oxyphil cells is not certain.

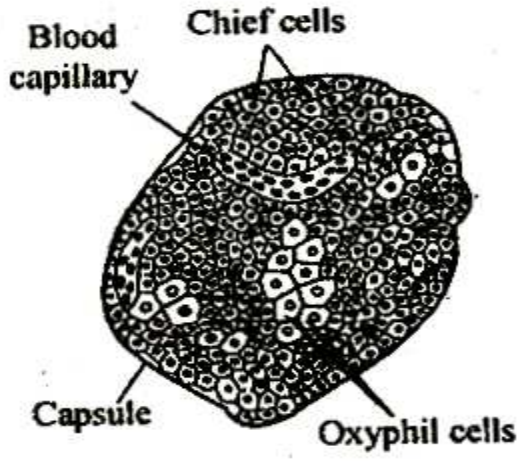


Fig.6.7. Ultrastructure of parathyroid gland

6.6.1 HORMONES OF PARATHYROID GLAND

The chief cells secrete a hormone called **parathormone** or **parathyroid hormone (PTH)** or **Collip hormone**. Parathormone is essential for survival, because it contributes to "homeostasis" by regulating the amount of calcium and phosphate ions in ECF. It promotes absorption of calcium from food in the intestine and its reabsorption from nephron in the kidneys. The calcium ion is, then, utilized by bone forming cells- osteoblasts, in bone formation under the influence of vitamin D_3. The unnecessary parts of newly formed asymmetrical bones are dissolved by osteoclasts under the influence of parathormone. It results in release of calcium and phosphate in blood.The parathormone accelerates elimination of phosphates in urine.

The process of bone-remodelling or reshaping and dissolution of asymmetrical parts of newly laid bones continue in the body throughout life under the influence of vitamin D_3 and parathormone. It serves as a mechanism of Ca^{2+} homeostasis.Vitamin D_3 also stimulates Ca^{2+} and Mg^{2+} absorption in intestine.

Vitamin D_3 is a steroid hormone and synthesized in skin from 7- dehydrocholesterol under the influence of UV rays of sunlight. Now, it is released in blood, from where liver cell take it and convert it into 25- hydroxycholecalciferol. It is released back into blood. In kidney the cells of PCT changes 25- hydroxycholecalciferol into 1-25- dihydroxycholecalciferol under the influence of parathormone. This last compound is released in blood as active vitamin D_3.

6.6.2 IRREGULARITIES OF PARATHYROID HORMONE

Hypoparathyroidism

Due to hyposecretion of parathormone, the level of calcium falls (hypocalcemia) and level of phosphates rises in the ECF. It increases neuromuscular hyper excitability, painful muscular spasms and convulsions. Sometimes the skeletal muscles of hand and feet fail to relax after contraction and remain in sustained contraction. This is called **tetany**. Titanic spasm of laryngeal and phernic muscle obstructs respiration which is the usual cause of death in tetany.

Hyperparathyroidism

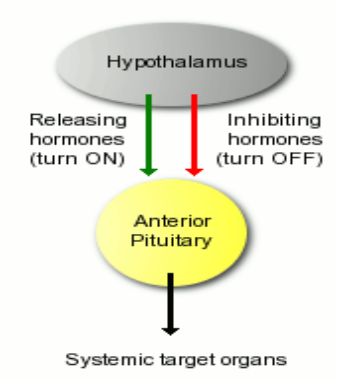
Oversecretion of parathormone causes demineralization of bones which, therefore, becomessoft weak and distorted. This is called **osteoporosis**. Some of the bone substances is replaced by cavities and are filled with fibrous tissues; this condition is called **osteitis fibrosa cystica**. This elevates the calcium concentration in blood and ECF(hypercalcemia) and reduces phosphate level because of increase renal secretion of phosphates.

Most patients with mild hyperparathyroidism show few signs of bone disease and few general abnormalities as a result of elevated calcium. But they do have extreme tendency to form kidney stones. The reason is that excess calcium and phosphate must be excreted in urine. As a result calciumphosphate tends to precipitate in the kidney which results calcium phosphate stone.

6.7. SUMMARY

The pituitary gland is often portrayed as the "master gland" of the body. Such praise is justified in the sense that the anterior and posterior pituitary secretes a battery of hormones that collectively influence all cells and affect virtually all physiologic processes.

The pituitary gland may be “The Leader of Endocrine Orchestra”, but the power behind the throne is clearly the hypothalamus. The hypothalamic hormones are referred to as **releasing hormones** and **inhibiting hormones**, reflecting their influence on anterior pituitary hormones.



The posterior lobe of the pituitary gland develops as an extension of the hypothalamus. As such, it is not capable of producing its own hormones; instead, it stores hypothalamic hormones for later release into the systemic circulation.

The thyroid gland secretes thyroid hormones, which control the speed at which the body’s chemical functions proceed (metabolic rate). Thyroid hormones affect many vital body

functions: the heart rate, the rate at which calories are burned, skin maintenance, growth, heat production, fertility, and digestion. To produce thyroid hormones, the thyroid gland needs iodine, an element contained in food and water. The thyroid gland traps iodine and processes it into thyroid hormones. As thyroid hormones are used, some of the iodine contained in the hormones is released, returns to the thyroid gland, and is recycled to produce more thyroid hormones. Oddly, the thyroid gland releases slightly less of the thyroid hormones if it is exposed to high levels of iodine transported to it in the blood. The thyroid gland also produces the hormone calcitonin, which may contribute to bone strength by helping calcium to be incorporated into bone.

The parathyroid glands are four small glands that have the sole purpose of secreting parathyroid hormone to regulate the calcium level in our bodies.The parathyroid essentially helps the nervous and muscular systems function properly. Calcium is the primary element that causes muscles to contract, and calcium levels are very important to the normal conduction of electrical currents along nerves.

6.8. SELF ASSESSMENT QUESTIONS AND POSSIBLE ANSWERS

6.8.1. MULTIPLE CHOICE QUESTIONS

1. Pituitary gland does not control the secretory activity of
   (a) Thyroid gland (b) Adrenal cortex
   (c) Adrenal medulla (d) Testes
2. Parathormone is secreted during
   (a) Increased blood calcium level (b) Decreased blood calcium level
   (c) Increased blood sugar level (d) Decreased blood sugar level
3. When subjected to thyroidectomy, a tadpole of frog will
   (a) Grow into a giant frog (b) Remain tadpole throughout life
   (c) Turn into a dwarf frog (d) Die immediately
4. Gonadotropic hormones are produced in
   (a) Posterior part of thyroid (b) Adrenal cortex
   (c) Adenohypophysis of pituitary (d) Neurohypophysis of pituitary
5. Thyroid gland of vertebrates is considered to be homologous to the following part of lower chordates
   (a) Nerve cord (b) Endostyle
   (c) Neural gland (d) Pharyngeal gill pouches

6. Regulator of basal metabolic rate in body cells is

(a) Pituitary (b) Heart

(c) Thyroid (d) Parathyroid

7. Addition of a trace of thyroid extract or even iodine to the water containing tadpoles of frog will

(a) Kill the tadpoles (b) Keep them in larval stage

(c) Slow down their metamorphosis (d) Hasten their metamorphosis

8. Which of the following gland is called "The Leader of Endocrine Orchestra"

(a) Pituitary gland (b) Thyroid gland

(c) Pancreas (d) Parathyroid

9. Iodine deficiency in man at any age may cause

(a) Acromegaly (b) Addison's disease

(c) Myxoedema (d) Goitre

10. Secretion of androgens by testes is regulated by

(a) Oxytocin (b) Follicle stimulating hormone

(c) Luteotropic hormone (d) Luteinizing Hormone

11. Vasopressin released by pituitary is

(a) Antidiuretic (b) Antisterility

(c) Anti-inflammatory (d) Anti-immune

12. Hypothyroidism in adulthood leads to

(a) Cretinism (b) Addison's disease

(c) Sterility (d) Myxoedema

13. Melanocyte-stimulating hormone is secreted by

(a) Parathyroid (b) Anterior pituitary

(c) Posterior pituitary (d) Pars intermedia of pituitary

14. Which gland is associated with consumption of iodized salt

(a) Pituitary (b) Thyroid

(c) Parathyroid (d) Thymus

15. Hormone which promotes Ca^{2+} absorption in intestine is

(a) Parathormone (b) Thyroxine

(c) Calcitonin (d) None

6.8.2. VERY SHORT QUESTIONS

1. Hypersecretion of growth hormone during childhood leads to which disorder?
2. Hypersecretion of growth hormone after growth period leads to which disorder?
3. Name five types of cells of anterior pituitary that synthesize and secrete hormones?
4. Name the hormone of pituitary which is vestigial in humans?
5. Name two types of cells of parathyroid which remainsembedded in its highly vascular stroma?
6. Name the condition in which bone substances is replaced by cavities and is filled with fibrous tissues?
7. What is exopthalmic goitre?
8. Name the cells of thyroid gland which secrete calcitonin?
9. Which iodinated hormone is known as thyroxine?
10. Name the largest endocrine gland of body?

ANSWERS

4.8.1. 1.(c); 2.(b); 3.(b); 4.(c); 5.(b); 6.(c); 7.(d); 8.(a); 9.(d); 10.(d); 11.(a); 12.(d); 13.(d); 14.(b); 15.(a)

4.8.2. 1.Gigantism; 2.Acromegaly; 3.Somatotrophs,Corticotrophs,Thyrotrophs,Gonadotrophs and Lactotrophs; 4. Melanocyte stimulating hormone; 5. Chief cells and oxyphil cells;6. Osteitis fibrosa cystica; 7. Hyperthyroidism develop some degree of protrusion of the eyeball, this condition is called exopthalmic goiter.; 8. Parafollicular cells; 9. tetraiodothyronine; 10. Thyroid gland.

6.9. TERMINAL AND MODEL QUESTIONS

1. Give an account of structure of pituitary gland.
2. Give an account of the hormones of neurohypophysis of pituitary. What is diabetes insipidus.
3. Give an account of the hormones of adenohypophysis of pituitary.
4. Describe causes of gigantism and acromegaly. How will you distinguish between two.
5. What are the hormones of thyroid gland. What are their functions.
6. Give an account of the origin, location and structure of parathyroid gland.
7. Briefly describe cretinism.

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UNIT 7: PANCREAS AND ADRENAL GLANDS

CONTENTS

7.1 OBJECTIVES

We study about the endocrine system and Basic introduction of pancreatic hormones and general study of Adrenal and function of cortical & medullary hormones in mammals.

7.2 INTRODUCTION

The various physiological activities of the body are controlled by different ductless gland known as endocrine gland in mammals & Humans. The endocrine system, along with the nervous system, functions in the regulation of body activities. The nervous system acts through electrical impulses and neurotransmitters to cause musclecontraction and glandular secretion. The effect is of short duration, measured in seconds, and localized. The endocrine system acts through chemical messengers called hormones that influence growth, development, and metabolic activities. The action of the endocrine system is measured in minutes, hours, or weeks and is more generalized than the action of the nervous system. The endocrine glands are located in particular parts of the body & they directly liberate secretion in the blood.

The pancreas is compound gland consisting of both the exocrine as well as the endocrine tissues. The exocrine part consists of tubuloacinous portion but the endocrine portion comprises islets of Langerhans embedded in the exocrine pancreas.

7.3 STRUCTURE OF PANCREAS

In ordinary haemotoxylin-eosin preparation the islets of Langerhans look like spheroidal bodies scattered in the pancreatic mass. These are aggressions of endodermal cells. Cells are arranged in the form of irregular anastomosing cords. The islets of Langerhans are richly supplied with blood capillaries. Some connective tissue fibres are present in the islets. These islets comprise about 1-2% of the total pancreatic mass. About 2 million islets are scattered in the human pancreas, however, the number varies in different individuals. There is greater number of islets in the tail area of the pancreas.

There are different types of cells in the islets of Langerhans. They are :-A or α-cells (alpha cells)B or β-cells (Beta cells) andD-cells.Another type of cells has also been described and they

are known as C-cells. There is abundance of A and B cells. The number of β-cells is greater than α-cells. These cells have been observed under the microscope when several staining techniques (Masson's trichrome, chrome haemotoxylin- phloxine, aldehyde fuchsin etc.) were employed.in α-cells, numerous red staining; fine granules are present (by chrome haemotoxylin-phloxine method).

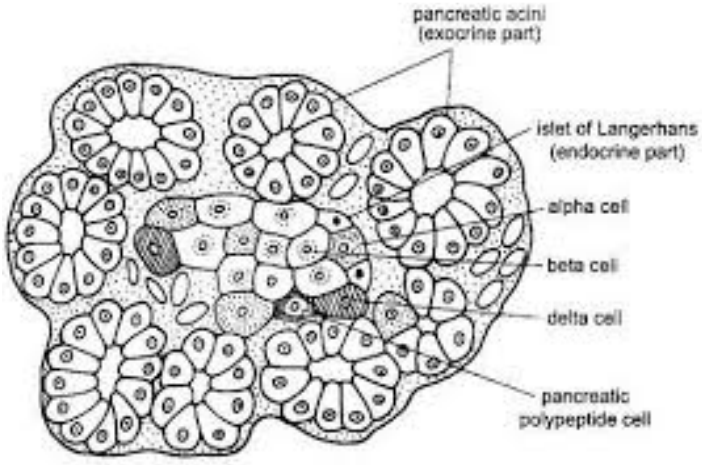


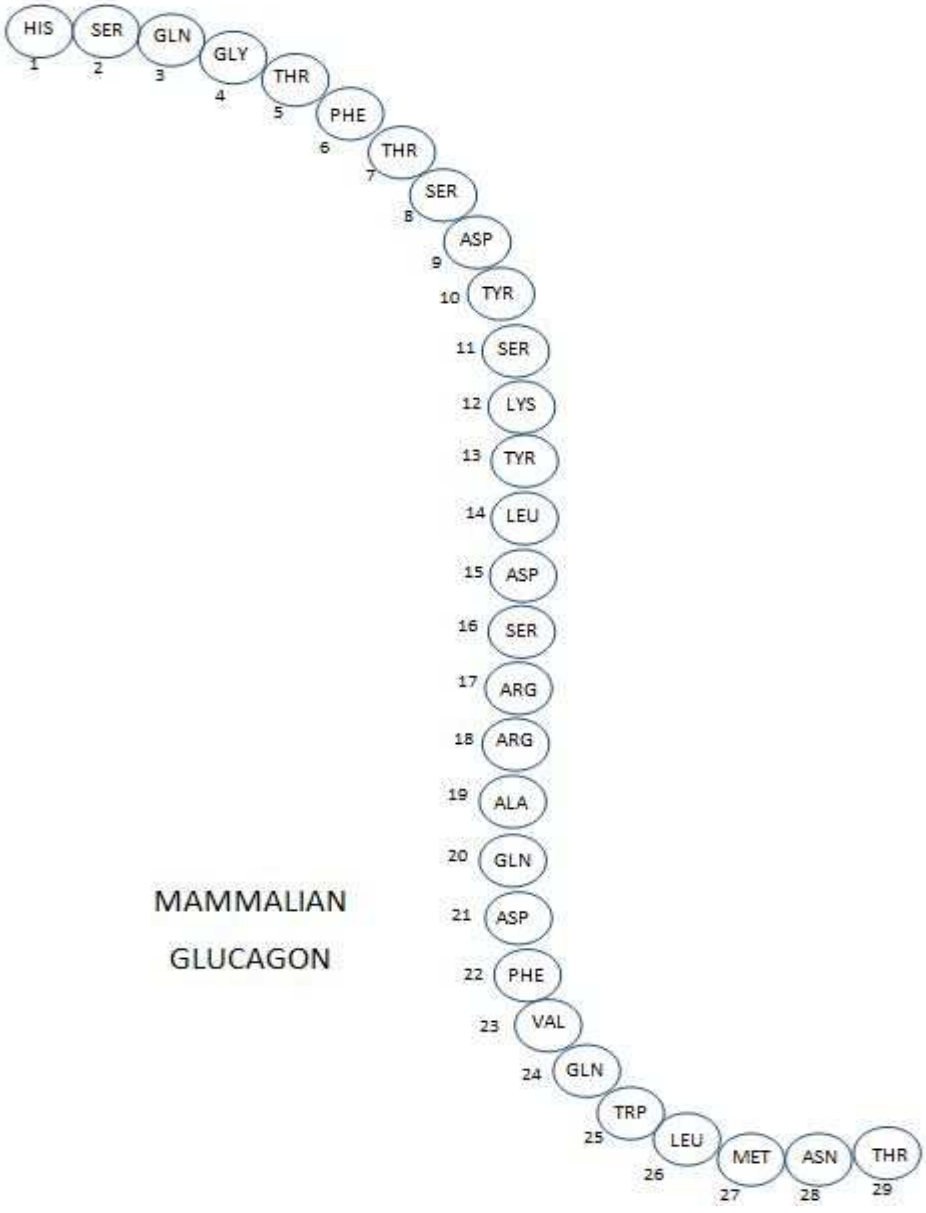
Fig.7.1A part of the T.S. of Pancreas showing alpha and beta cells of islet of Langerhans

The cell membranes in these cells are also distinct. The β-cells have comparatively coarse granules and they are stained dark blue by chrome-haematoxylin method. The cells membranes of these cells are not distinct. There are very few D-cells which can be differentiated by Masson's triple stain. C-cells have been described byBensley in the pancreas of guinea pig. These cells are devoid of granules. These cells are probably the progenitors of α-cells.

7.3.1 PANCREATIC HORMONES AND THEIR FUNCTIONS

Insulin and Glucagon are the main hormones of the islets of Langerhans. Insulin is secreted by the β –cells and glucagon is the product of α –cells. D –cells are said to secrete gastrin which affects the release of insulin in addition to activating gastric glands. Sanger et al. (1945-1955) determined the complete amino acid sequence of insulin in various mammalian species. Kotsoyannis and his colleagues (1963) synthesized sheep insulin. Human insulin was synthesized later on by separate contribution of Dixon, Du, kotsoyannis and others.

The ox insulin consists of two polypeptide chains, one chain is known as A-chain and another chain as B-chain. A-chain consists of 21 amino acids with glycine as the N-terminal residue. B-chain consist of 30 amino acid



Residues with phenylalanine as the N-terminal residue. The two chains (A and B) are linked by two Disulphide Bridge at positions 7 and 20 in the A-chain and 7 and 19 in the B-chain as shown in the figure. When they are joined by disulphide bridges it becomes physiologically active. In

addition to these, one intradisulphide bridge is also present in the A-chain which of insulin is 6000 (In man).

Glucagon is the product of α-cells. It is a straight chain polypeptide consisting of 29 amino acid residues. There is no disulphide bridge in this case. The glucagon molecule is devoid of cysteine. It is resistant to alkali. The molecular weight of glucagon is 3485.

PHYSIOLOGICAL ACTION OF INSULIN

The important physiological action of insulin have been summarised below:-

(1) Insulin in a hypoglycemic factor (decrease blood sugar level). It promotes conversion of glucose to glycogen. Insulin has some growth promoting effects.

(2) It facilitates the transport of a variety of substance e.g., glucose, monosaccharides, amino acids, Ions, nucleosides and several inorganic phosphates etc. Edelman et al. (1966) showed that insulin is rapidly concentrated in the sarcolemma and its tubular component is activated and thus selective transport occurs.

(3) It influences translation of mRNA.

(4) According to Bessman (1966), insulin acts to translocated hexokinase to a site at the mitochondrial level where the enzyme may serve to increase respiration by production ADP.

(5) It induces glycogen deposition, stimulates HMP (hexose mono-phosphate) shunt.

(6) It increases lipid synthesis by production CoA and NADPH, required for fatty acid synthesis.

(7) Insulin provides protection to the pancreatic cells against degeneration for any reason.

(8) Process of glycolysis is stimulated when insulin affect increase in the synthesis of enzymes like glucokinase, phosphofructokinase and pyruvate kinase.

(9) It represses the enzymes controlling gluconeogenesis mainly-pyruvate carboxylase, phosphoenol pyruvate carboxy-kinase, fructose 1, 6-phosphatase and glucose-6-phosphatase.

(10) It reduces tissue level of cyclic-AMP and there by depresses fatty acid release in the absence of glucose.

(11)It prevents ketonaemia, ketosis and ketonuria.

(12) Decreased glucose output, decreased urea production, decreased cyclic AMP, increased pot, and phos. Uptakes are some of the demonstrable actions on the isolated perfused liver.

(13) Weber and other (1966) suggested that insulin acts on a genetic locus in the nucleus.

(14) Insulin increases the electrical potential difference across cell membranes. A net movement of Pot. From extracellular to intracellular fluid has been suggested. There are evidences that insulin affects the Trans epithelial electrolyte transport of sodium, potassium, calcium and phosphate. Insulin facilitates renal sodium reabsorption.

(15)Insulin stimulates phosphate uptake by liver and muscle particularly

(16)Insulin has some osmoregulator role also.

PHYSIOLOGICAL ACTION OF GLUCAGON

There are certain physiological actions of glucagon which have been given below:

(1) It is hyperglaycemic factor (cause blood sugar elevation)
(2) The action of glucagon is glycogenolytic (Assan and Slusher, 1972). Glycogenolysis takes place in the liver.
(3) It increases cyclic-AMP level and hepatic phosphorylase activity.
(4) It stimulates the conversion of lactic acid and amino acid to glucose.
(5) It increases the breakdown of lipid to fatty acid and glycerol.
(6) It affects the release of insulin.
(7) Promotes urea and ketone bodies formation.
(8) An Osmoregulatory role glucagon may be mediated via stimulation of Prostaglandin synthesis.

7.3.2 DYSFUNCTION AND DISEASE OF PANCREATIC HORMONES

Glucose is an important source for brain energy metabolism and extensive regulatory mechanisms are in place to ensure protection from hypoglycemia. Glucose concentrations naturally reach a nadir a couple hours after birth and then begin to rise reaching normal values by day 3 of life. This is related to the abrupt cessation of placental glucose transfer at delivery causing a transient decrease in glucose levels with subsequent response of increased glucagon, decreased insulin levels, and an increase in catecholamine secretion to gradually normalize plasma glucose concentration. Regulatory mechanisms in older children are balanced by gluconeogenesis and glycogenolysis. Hypoglycemia definition varies based on the age group (40 mg/dL or below in neonates) and < 55-60 mg/dL in older children.

Hypoglycemia

Etiology: Hypoglycemia is due to defects of the hormones or enzymes of the glucose regulatory mechanisms that result in inadequate glucose or surplus of insulin.

Symptoms: An abrupt decrease in plasma glucose causes adrenergic symptoms (due to catecholamine release) such as pallor, sweating, tachycardia, tremor, and emesis. A slow decrease in plasma glucose causes neuroglycopenic symptoms such as confusion, diplopia, headache, dizziness, lethargy, seizure, and lack of coordination. Neonatal symptoms of hypoglycemia are more subtle, such as apnea, low temperature, poor tone, jitteriness, and poor feeding.

Diagnosis: Critical sample needs to be obtained when BG at or <40 mg/dL and includes serum free fatty acids, ketones, and insulin levels. Hormones to be also obtained include cortisol, ACTH, and growth hormone. Acylcarnitine and total carnitine, urine organic acids and serum amino acids to be considered based on the age group/ index of suspicion. If a child has hepatomegaly with hypoglycemia, suspect an enzyme deficiency. Males with a microphallus and hypoglycemia should be evaluated for hypopituitarism. Accidental ingestion of alcohol or salicylates can cause hypoglycemia so toxicology screen and history taking will help with diagnosis in this instance. Finally, if Munchausen by Proxy is suspected, then c-peptide along with insulin levels need to be obtained to investigate for exogenous insulin administration.

Treatment: Acute treatment includes early feeding (neonates), dextrose gel, or IV boluses of 2 mL/kg of 10% dextrose in water followed by continuous infusions of glucose. If hypoglycemia persists, it is then treated with continuous glucose infusion, diazoxide and/or somatostatin analogs. If hypoglycemia persists, pancreatectomy may be necessary.

Diabetes Mellitus

Diabetes mellitus (DM) is a common metabolic condition of hyperglycemia caused by complete or partial insulin deficiency and its actions.

Insulin physiology: Insulin is made on the ribosomes of pancreatic islet beta cells as a proinsulin precursor (single chain: chain A is connected to chain B by c-peptide) that is then cleaved into insulin and c-peptide molecule. It is then released into circulation as a double chain polypeptide linked by disulfide bridges.

7.4 STRUCTURAL ORGANIZATIONS OF ADRENALS

In the vertebrate series, several names have been used for the adrenal gland. It has been named according to its position with respect to kidneys. These names have thr prefixes ad(to or near), intra (within) and supra (above or over), so, this gland has been designated as adrenal, interrenal, intrarenal and suprarenal gland. But, now interrenal exclusively means the adrenal cortex (adrenocortical tissue).

The adrenal was first described in man by Eustachius (1563). Cuvier (1805) reveled that this gland consists of two parts; medulla and the cortex, Addison (1849) described some clinical aspects of this gland. Several important information have been contributed by a large number of researchers and some of them are : Deane and Greep (1946), Bush and Furguson (1953), Simpson (1953), Yates and Urquhart (1962), Edelman (1963), Greengard et al. (1963), Karlson (1964), Nandi et al.(1967) and others.

There is one pair of adrenal glands which lie above the kidney towards its cranial pole (one on each kidney). Each adrenal weighs 5-6 gm. only. The glands consist of two distinct portions:

the medulla and the cortex. The medulla is derived from the neuro-ectoderm but the cortex is mesodermal in origin.

The hormones of the adrenal cortex are known as corticoids, i.e.,

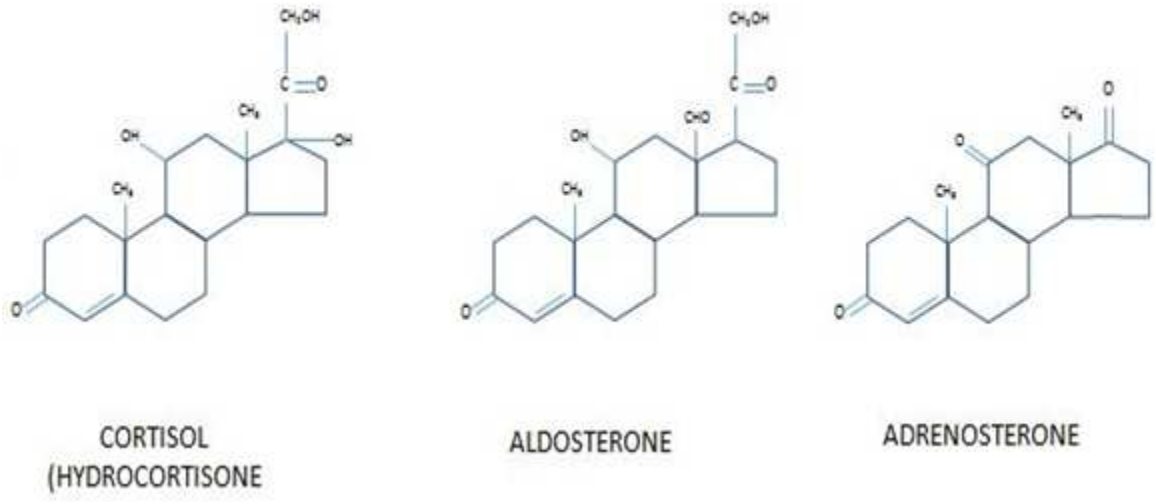
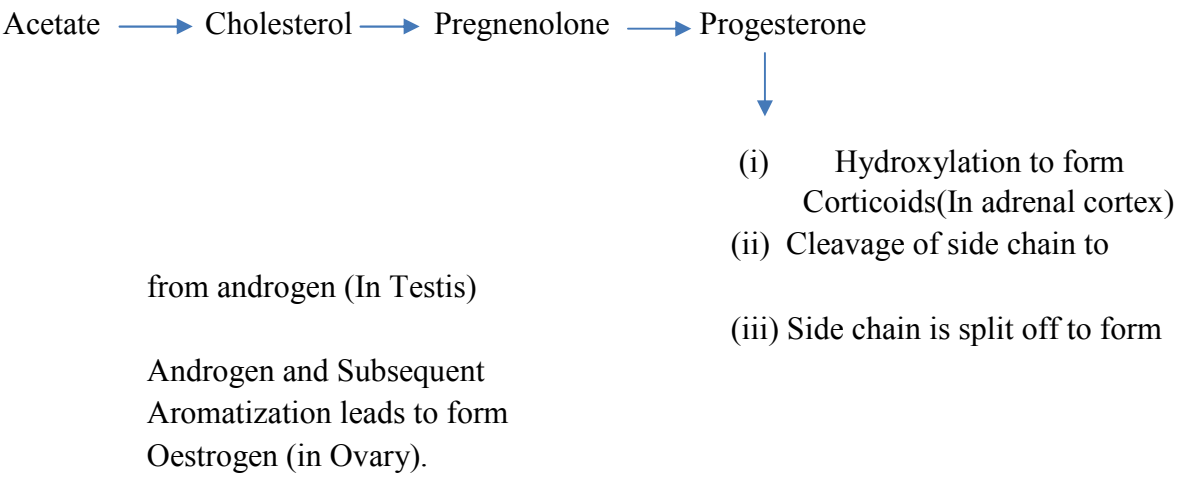


Fig.7.2 Some Adrenocortical Hormones

Glucocorticoids and Mineralocorticoids. Sex hormones are also se cortical cells and these hormones are the sex steroids. Glucocorticorticoids are steroids with =O or –OHat carbon position 11. The mineralocorticoids are also steroids, with or without =O or –OH at carbon position 11.cortisol and corticosterone are the important examples of glucocorticoids and aldosterone and deoxycorticosterone are the important examples of glucocorticoids aldosterone and deoxycorticosterone are the important examples of mineralocorticoids. The sex steroids have characteristically the side chain at carbon position 17 of –OH at 11 –C. Dehydroepiandrosterone (androgen).Oestradiol (estrogen) and progesterone (progestin) are the common sex hormones. Corticosterone binding protein carries the hormones to blood. There are evidences binding protein carries the evidences that glucocorticoids are secreted by zona fasciculate of the adrenal cortex. Mineralocorticoids are the product of zonaglomerulosa and the sex – hormones are secreted by zonareticularis the common biosynthetic pathway of theses steroid hormones according to many authors are as follows:-

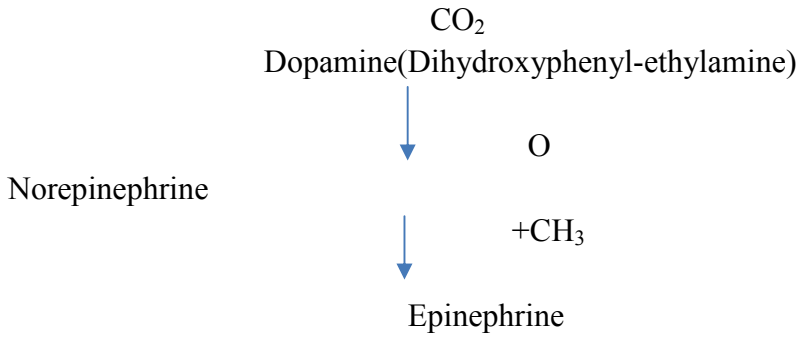


Some important enzymes are involved in the formation of the above hormens. In the conversion of pregnenolone from cholesterol Desmolase and NADPH are required. The reaction is said to be potentiated by cyclic AMP. Another enzymes is 3, β–hydroxydehydrogenase which require NAD. For each and every steroid hormone, a specific hydroqylating enzyme is required which is necessarily assisted by NADPH. These are present in mitochondria.

Medulla secretes two important hormones: Epinephrine (adrenalin) and Norepinephrine (Noradrenalin). They are respectively secondary and primary amines. Phenylalanine and tyrosine are regarded as the precursors of epinephrine.

The agreed biosynthetic pathway is:-

Phenlalanine Tyrosine Dopa (Dihydroxyphenylalanine)



Thus tyrosine is oxidized to dopa, this is decarboxylated to dopamine, which is oxidized to norepinephrine and finally, the norepinephrine is methylated to epinephrine. The process of

conversion of norepinephrine to epinephrine is catalysed by the enzyme Phenylethanolamine-N-Methyl transferase (PNMT).

REGULATION OF ADRENAL HORMONES

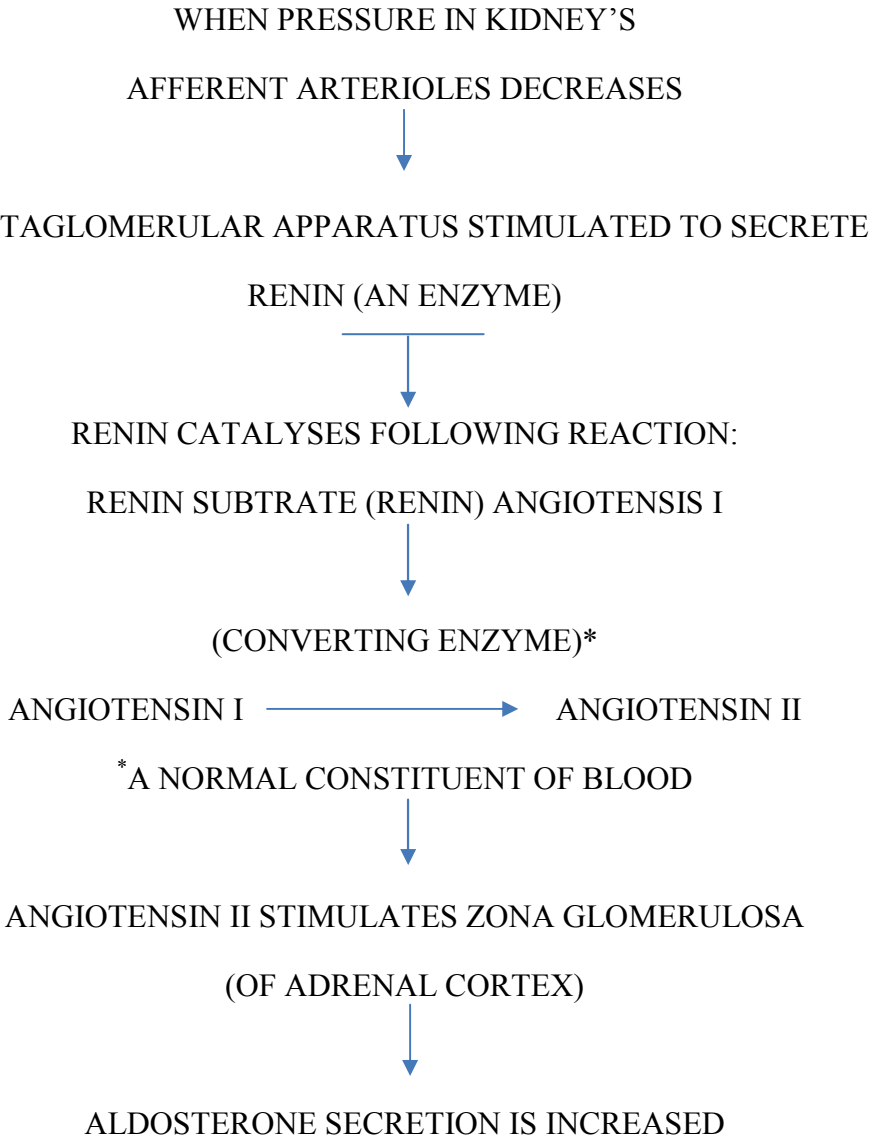


Fig. 7.3 Renin-angiotensin mechanism for regulation of aldosterone secretion

7.5 FUNCTIONS OF CORTICAL AND MEDULLARY HORMONES

CORTEX

The cortex has been classically divided into three distinct zones which from the outer toward the inner side are ;zonaglomerulosa, zona fasciculate and zonareticularis, Adrenal cortex is especially rich in cholesterol and ascorbic acid. Zonaglomerulosa is the outermost narrow zone which is formed by columnar cells. Ovoid groups Of cells are very prominent in this zone.

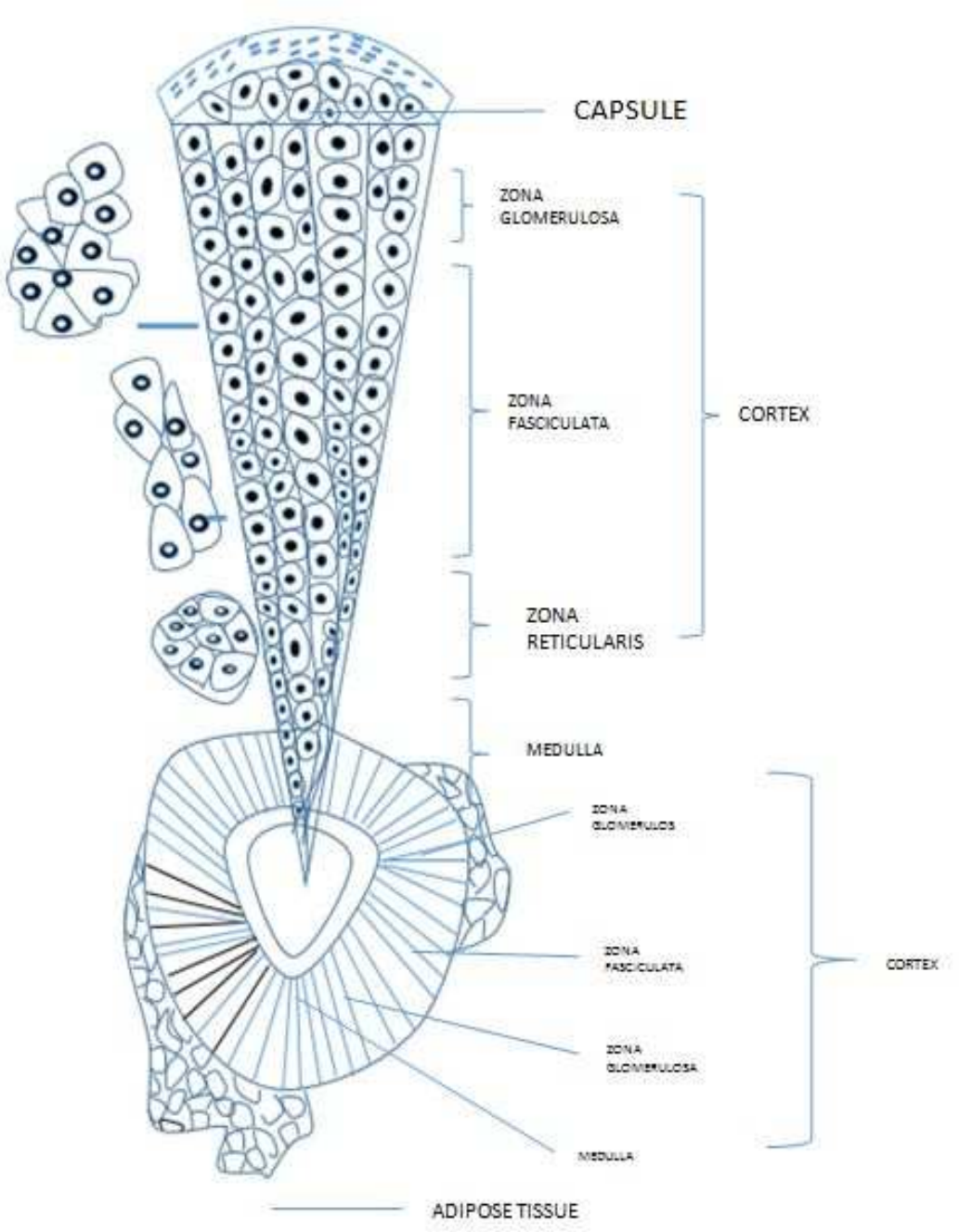


Fig. 7.3. Cross-section of Adrenal gland showing Zonation

There is no cavity within these groups of cells. The nuclei of these cells can be stained deeply with basics dyes. Very few lipid droplets can be observed in this zone. In cortical tissue the mitochondris and the Golgi body are very large structure.

Zonafasciculata is the middle zone. It is the widest zone. The cells in this zone are cuboidal or polyhedral in shape and are frequently binucleate, and nuclei are vesicular. The cords in this zone characteristically run parallel to each other and they are in straight line. The cords tend to be two cells in thickness. The cell are larger in size and they are filled with lipid droplets composed of fatty acid, cholesterol and neutral fats. These cells can be stained with osmic acid on account of their fat content. Some of the cells have spongy appearance because of the presence of dissolved lipids in them. They are called spongiocytes.

Zonareticularis is the innermost zone of the cortical tissue. Here the cords run obliquely and they are usually one cell in width. The cells of this zone contain many pigments. Some of the cells have deeply staining nuclei. The cords are branched and arranged in an anastomosing fashion. This zone touches the medullary area of the gland.

MEDULLA

Medulla is a neuroendocrine part of the adrenal gland. The medullary cells occur in groups. They are generally ovoid or polyhedral cells. They contain fine granules which can be stained brown with bichromate stain. They are called Chromaffin cells or pheochromes. The granules also become green when stained with ferric chloride, and yellow with Iodide. Cells in the medullar region are arranged haphazardly. Epinephrine and the Norepinephrine secreting cells are different and they cannot be distinguished by ordinary histological preparations. They require some special staining techniques. These two types of cells are collectively known as Catecholamine-containing cells. Under electron microscope the mitochondria show saccular or villous membrane instead of laminar arrangement.

7.6 TERMINAL QUESTIONS AND ANSWERS

1. The target cells of a hormone always have

    (a) Special channels through which hormones move

(b) Large amount of the hormone stored with in vesicles

(c) Special receptors to which hormones binds

(d) Undiffirentiated cytoplasm

2.. Hormones may be:

(a) Steroid (b) Peptides

(c) Amino Acid derivatives (d) All of these

3.. One similarity between enzymes and hormones is that both:

(a) are proteins (b) can be used again and again

(c) are used in minute amount (d) act at a particular pH

Answer:1. (c) 2. (d) 3. (c)

4. Write the Function of cortical Medullary Hormones?

5. Write the Physiological Action of Insulin?

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UNIT 8: VERTEBRATE REPRODUCTIVE ENDOCRINOLOGY

CONTENTS

8.1. OBJECTIVES

After reading this unit the readers will be able to:

- Describe the structure of mammalian primary sex organs
- Explain the structure of secondary sex accessory organs
- Discuss the hormonal control of male and female reproductive system
- Describeestrous and menstrual cycle
- Describe the role of placenta during pregnancy
- Describe hormonal control of child birth
- Discuss the role of hormones during lactation
- Discuss about pheromones

8.2. INTRODUCTION

The **reproductive system** or **genital system** is a system of sex organs within an organism which work together for the purpose of sexual reproduction. Many substances such as, hormones, and pheromones are also important accessories to the reproductive system. In both the males and females, the gonads develop within the **mesonephric ridge**and descend through the abdomen. However, unlike the testes, the ovaries stop in the pelvis.

The testes are the male gonads, that is; they are the primary male reproductive organs. They fulfil two key functions, the production of male gamete and the secretion of hormones, particularly the male hormone **testosterone**. Other structures in the male reproductive system, including the **male duct system** and **penis** are termed **accessory reproductive organs**, because rather than producing gametes, they play an accessory role in the reproductive cycle, by transporting **sperm**out of the testes.

The ovaries are the female gonads, that is; they are the primary female reproductive organs. These are paired, oval organs attached to the **posterior surface of the broad ligament** of the uterus by the **mesovarium** (a fold of peritoneum, continuous with the outer surface of the ovaries). They fulfil two key functions, the production of female gametes and the secretion of sex steroid hormones, **oestrogen** and **progesterone**, in response to pituitary gonadotropins (LH and FSH). Other structures in the female reproductive system including fallopian tube, uterus and vagina are termed accessory reproductive organs.

8.3. STRUCTURE OF MAMMALIAN TESTIS AND OVARY

8.3.1. STRUCTURE OF TESTES

The testes are located within the **scrotum** along with the epididymis situated on its posterolateral side. Commonly, the left testis lies lower than the right. The scrotum helps in maintaining the low temperature of the testes (2-2.5^{0}c lower than the normal internal body temperature). The testes are suspended from the abdomen by the **spermatic cord** i.e. collection of vessels, nerves and ducts that supply the testes.

Originally, the testes are located on the **posterior abdominal wall**. During embryonic development they descend down the abdomen, and through the inguinal canal to reach the scrotum. They carry their neurovascular and lymphatic supply with them. Arterial supply to the testes and epididymis is via the paired **testicular arteries,** which arise directly from the abdominal aorta. They descend down the abdomen, and pass into the scrotum via the **inguinal canal**, contained within the spermatic cord.Venous drainage is achieved via the paired **testicular veins.** In the abdomen, the left testicular vein drains into the left **renal vein**, while the right testicular vein drains directly into the **inferior vena cava**.

The multi-layered tunica covers the testes. It facilitates blood supply to the testes and creates a partition between sperm producing regions of the testes. There are three layers to the tunica, the tunica vasculosa, tunica albuginea and tunica vaginalis.

The tunica vasculosa is the inner layer of the tunica and consists of blood vessels and connective tissue. It is covered by the tunica albuginea and **facilitates blood supply to the testes.**

Tunica albuginea is a dense layer of tissue which encases the testes and connects to the layers of fibres which surround the epididymis.The tunica albuginea also extends into the testis, creating partitions between seminiferous tubules where sperms are produced. It has a bluish-white appearance and covers most of the inner layer of the tunica, the tunica vasculosa. Overlying this structure is the outer layer of the tunica, the tunica vaginalis.

The outermost layer is **tunica vaginalis**. There are two layers of the tunica vaginalis;**the visceral** and **the parietal**. The visceral layer overlies the tunica albuginea, while the parietal layer lines the scrotal cavity (Fig 8.1). A thin fluid layer separates the twolayers of the tunica vaginalis and reduces friction between the testes and the scrotum. An increased quantity of fluid between these layers can form a hydrocoel**e**.

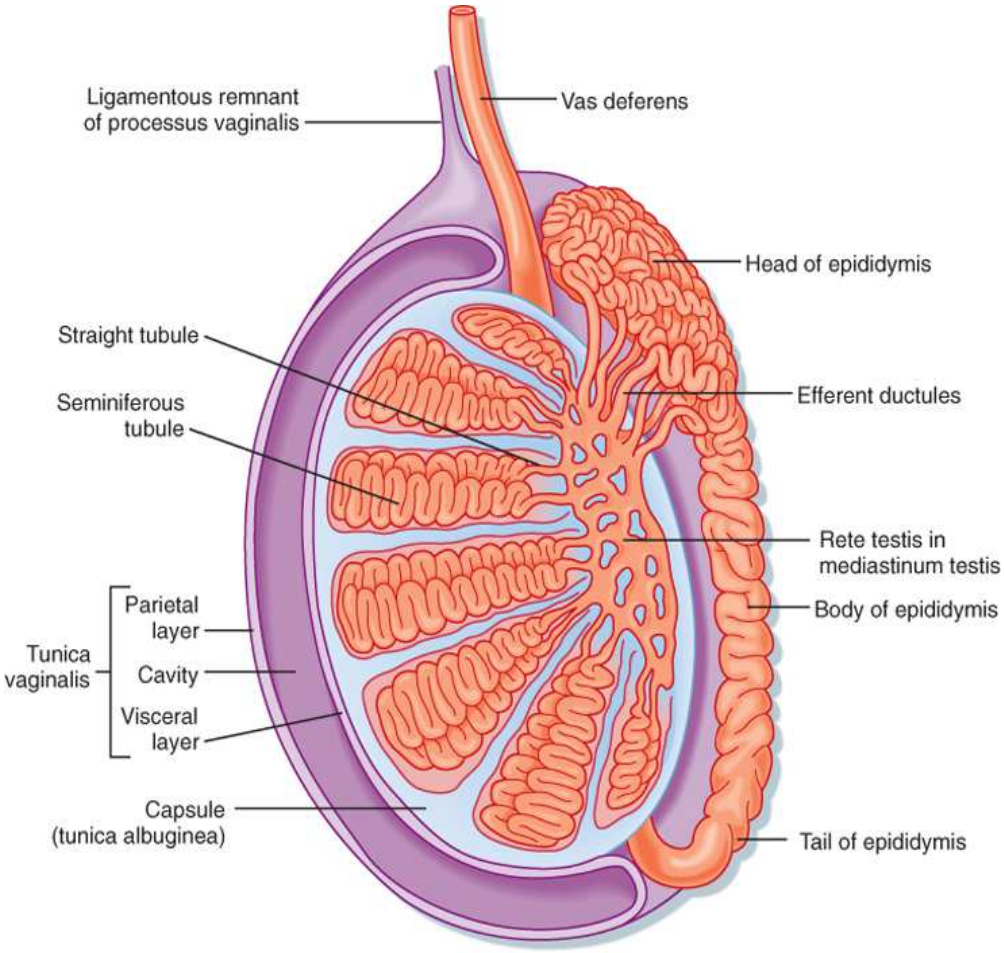

Figure 8.1. L.S. of testis

Seminiferous tubules lie within the testes and are separated by partitions, which are extensions of the tunica albuginea.Partitions divide the testes into **250 testicular lobules** which contain the seminiferous tubules. Each lobule contains 1–4 seminiferous tubules and each testis may contain up to 900 of these tubules. The tubules average 50 cm in length and are tightly coiled within the testis. Spermatozoa are produced in the seminiferous tubules. Each seminiferous tubule is lined on its inside by two types of cells called **male germ cells** and **sertoli cells(sustentacular cells).** The male germ cells undergo meiotic divisions finally leading to sperm formation. The primary function of sertoli cell in an adult is to provide nutrition to germ cells as they grow and develop into mature spermatozoa. The soft connective tissues surrounding the seminiferous tubules contain Leydig **cells**or **interstitial cells** (Fig. 8.2). The primary function of the Leydig cells is production and secretion of androgens particularly**testosterone** which is the key male hormone. The primary function of testosterone is to stimulate spermatogenesis (sperm production) and support the development of immature spermatozoa (sperm).

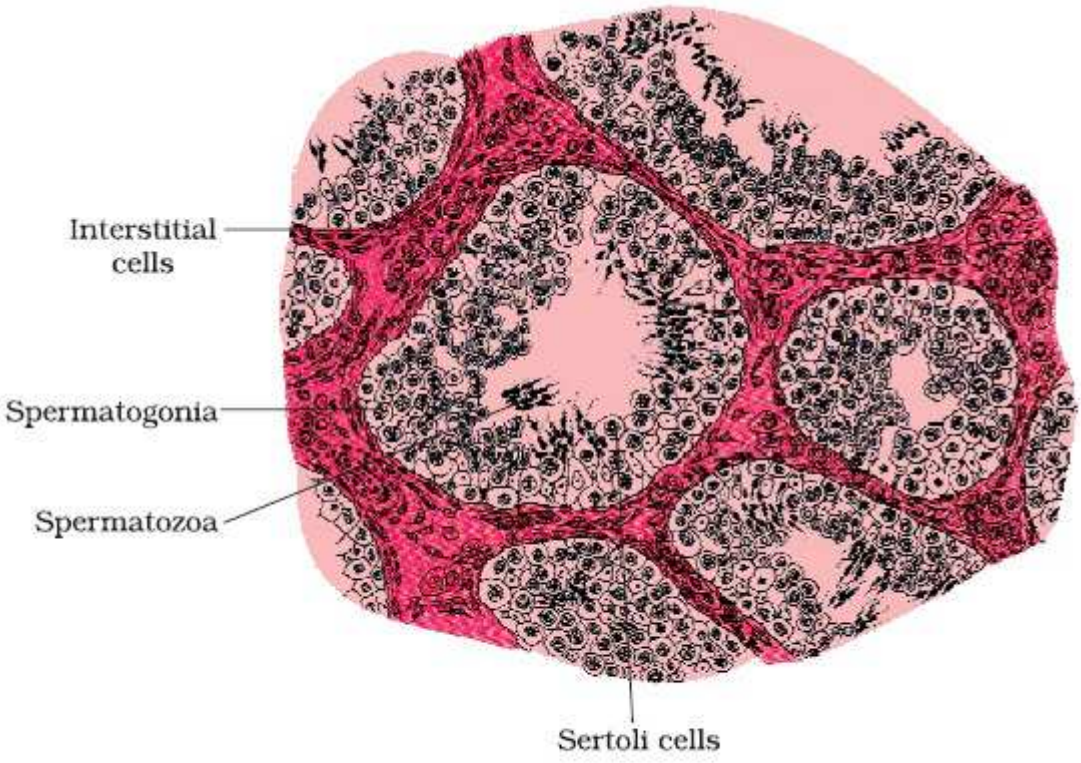

Fig.8.2. T.S. of testis showing semineferous tubule

8.3.2. STRUCTURE OF OVARY

The ovaries are the female pelvic reproductive organs that house the ova and are also responsible for the production of sex hormones. They are paired organs located on either side of the lower abdomen.Each ovary is about 2-4 cm in length and is connected to the pelvic wall and uterus by ligaments.Several paired ligaments support the ovaries. The ovarian ligament connects the uterus and ovary. The posterior portion of the broad ligament forms the mesovarium, which supports the ovary and houses its arterial and venous supply. The suspensory ligament of the ovary (infundibular pelvic ligament) attaches the ovary to the pelvic sidewall. This larger structure also contains the ovarian artery and vein, as well as nerve supply to the ovary.

Blood supply to the ovary is via the ovarian artery; both the right and left arteries originate directly from the descending aorta. The ovarian artery and vein enter and exit the ovary at the hilum. Nerve supply to the ovaries runs with the vascular supply via the suspensory ligament of the ovary, entering the ovary at the hilum.

The ovary has 3 components;

- **Surface**: The surface layer of the ovary is formed by simple cuboidal epithelium, known as germinal epithelium.

- **Cortex**: The cortex (outer part) of the ovary is largely comprised of a connective tissue stroma. It supports thousands of follicles. Each primordial follicle contains an oocyte surrounded by a single layer of follicular cells.
- **Medulla**: The medulla (inner part) is composed of highly vascular stroma and contains a rich neurovascular network which enters the hilum of ovary from the mesovarium. Follicles are usually not found in the medulla.

  At birth, a female has approximately 1-2 million eggs, but only 300 of these eggs will ever become mature and be released for the purpose of fertilization. A cross-section of the ovary reveals many cystic structures that vary in size. These structures represent ovarian follicles at different stages of development and degeneration (Fig. 8.3)

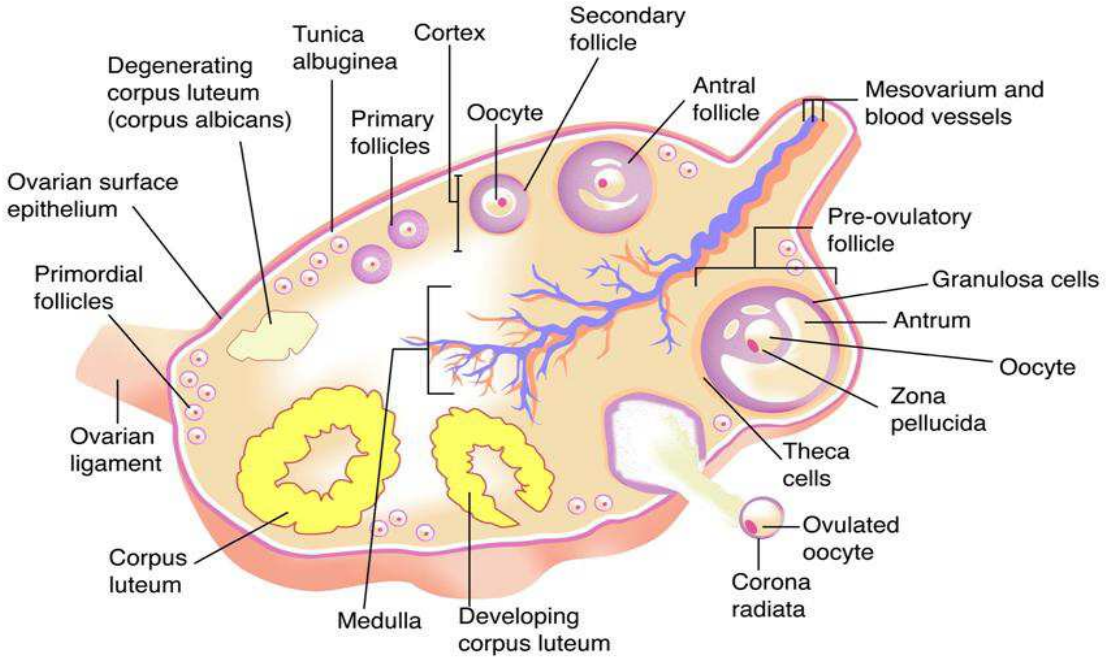

Fig. 8.3. Sectional view of ovary

8.4. MALE AND FEMALE SEX ACCESSORY ORGANS

8.4.1. MALE SEX ACCESSORY ORGANS

8.4.1.1 MALE SEX ACCESSORY DUCTS

The male sex accessory ducts include rete testis, vas efferentia, epididymis and vas deferens.

Straight tubules: Straight tubules, called **tubuli recti**, connect seminiferous tubules to the rete testis facilitating sperm transport.

Rete testes: The seminiferous tubules open into a series of channels called the rete testis.The rete testis facilitate the transport of sperm from the testes to the sperm transport ducts.

Vasa efferentia: The vasa efferentiaor efferent tubules are located between the rete testes and the epididymis. 15-20 fine ciliated vas efferentia connect the testes to the epididymis and facilitate the transport of sperm from the testes (Fig. 8.1).

Epididymis: The epididymis consists of about 6 metres long single heavily coiled **duct**. It can be divided into three parts; head, body and tail.

1. **Head** – It is the most proximal part of the epididymis, also called as **caput epididymis**. It is formed by the efferent tubules of the testes, which transport sperm from the testes to the epididymis.
2. **Body** – It is formed by the heavily coiled duct of the epididymis. This part is also called as **corpus epididymis**.
3. **Tail** – It is the most distal part of the epididymis, also called as **cauda epididymis**. It marks the origin of the vas deferens, which transports sperm to the urethra for ejaculation.

The epididymis stores the sperms prior to ejaculation. Storage in the epididymis makes the sperm motile and mature.

Vas deferens: From the tail of epididymis arises a duct,the vas deferens, which ascends to the abdomen and loops over the urinary bladder. It is about 40 cm long.

Ejaculatory duct:The vas deferens receives a duct from seminal vesicle and opens into urethra as ejaculatory duct. It is thin walled tube about 2 cm in length. The ejaculatory ducts of two sides, after passing through prostate gland open into urethra.

Urethra: It arises from urinary bladder and joins the ejaculatory duct to form urinogenital canal. It is about 30 cm long and passes through penis to its external opening called urethral meatus. Urethra is differentiated into three parts.

1. A short proximal **prostatic part** surrounded by prostrate gland.
2. A short middle **membranous urethra.**
3. **Penial urethra** which passes through the penis.

Penis: Penis is copulatory organ that lies in front of scrotum. It helps in transfer of sperm into female reproductive tract. It is made up of three columns of spongy erectile tissue with abundant

blood sinuses i.e. two dorsal **corpora cavernosa** and one ventral **corpus spongiosum**. When sinuses are filled with blood, it makes the penis rigid and erect.

The tip of penis is slightly enlarged into a highly sensitive **glans penis**. The glans is covered by a loose fold of skin called foreskin.

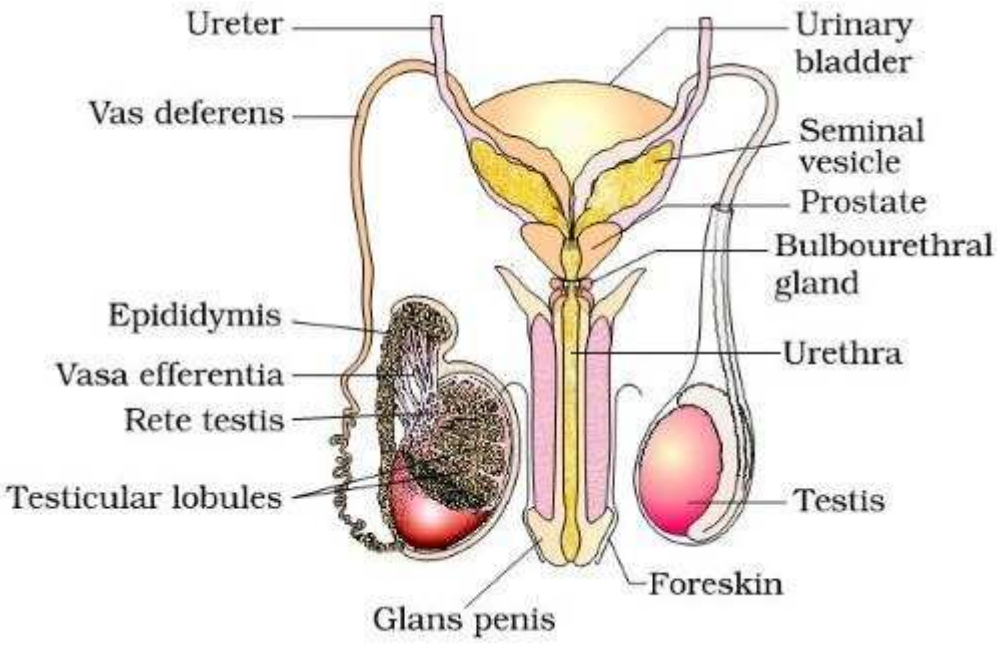

Fig. 8.4 Diagram showing male reproductive system

8.4.1.2 MALE SEX ACCESSORY GLANDS

It includes a pair of seminal vesicles, prostate gland and a pair of cowper's glands or bulbourethral glands (Fig. 8.4).

Seminal vesicle: The secretion of seminal vesicle forms 60% of semen plasma. It contains fructose, calcium and prostaglandins. **Fructose** acts as source of energy for the sperm and prostaglandin stimulate vaginal contractions to help in upward movement of sperm in female genital tract.

Prostate gland: The secretion of prostate gland forms 30% of semen plasma. It contains some lipids; small amount of citric acid and few enzymes.The secretion provides nutrition to sperm and increases their motility.

Cowper's gland: It secretes alkaline secretion before the release of sperms to neutralize acids of the urine. The mucus of the secretion lubricates the tip of penis.

8.4.2. FEMALE SEX ACCESSORY ORGANS

8.4.2.1. FEMALE SEX ACCESSORY DUCT

It consists of oviducts, uterus, cervix, vagina and external genitalia.

Fallopian tubes or oviducts: Fallopian tubes are about 10-12 cm long and extend from the periphery of each ovary to the uterus. It consists of following parts.

Infundibulum: It is funnel shaped proximal part close to the ovary. Its margin bears motile, finger- like processes called **fimbriae**, which helps in collection of the ovum after ovulation. Its opening into the body cavity is called **ostium**.

Ampulla: The infundibulum leads to a wider part of the oviduct called, **ampulla**.

Isthmus: The last part of fallopian tube is narrow and thick walled and called as isthmus. Fallopian tube joins uterus.

Uterus: It is a hollow and inverted pear shaped structure with thick muscular wall. It is also called **womb**. It lies in the pelvic cavity between the urinary bladder and rectum. It is attached to the pelvic wall by a fold of ligaments, the **mesometrium**. It comprises of four parts- **Fundus** is the upper wide, dome shaped part that receives fallopian tubes; **Cornua** is the upper corner where the oviducts enter the uterus; **Corpus** is the main body and**Cervix** is the lower narrow part. The uterus opens into vagina through a narrow cervix.The cavity of cervix is called **cervical canal**. The cervical canal along with vagina forms **birth canal.**

The wall of uterus has three layers. The external thin covering of peritoneum is called **perimetrium**, middle thick layer of smooth muscle fibres is called **myometrium** and inner glandular layer, that lines the uterine cavity, is called **endometrium**. The endometrium undergoes cyclic changes during menstrual cycle while the myometrium exhibits strong contraction during child birth.

Vagina: It is fibro-muscular tube of about 7-10 cm in length, extending from the cervix of uterus to the vestibule on the outer side. The opening of vagina is called **vaginal orifice**. It is often covered by a membrane called, **hymen** (Fig. 8.5).

External genitalia: It includes mons pubis, labia majora, labia minora, hymen and clitoris. **Mons pubis** is a cushion of fatty tissue covered by pubic hair and skin. The **labia majora** is pair of thick folds of skin which extend down from mons pubis and surround the vaginal opening. The **labia minora** are paired small folds lying on inner side of labia majora.

Clitoris is small erectile structure, located at the upper junction of the two labia majora. It is homologous to male penis.

The opening of urethra in the vestibule is called **urinary meatus**. It is situated below the clitoris and above the vaginal opening.

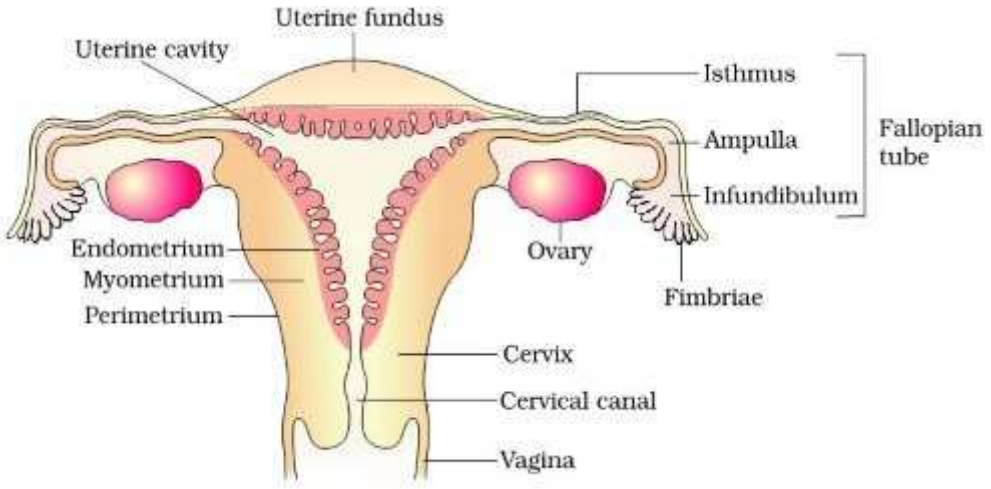

Fig.8.5. Diagram showing female reproductive system

8.4.2.2. FEMALE SEX ACCESSORY GLANDS

Bartholin glands: A pair of bean shaped glands, one on either side of vaginal orifice, opens into the vestibule. These glands secrete lubricating fluid.

Mammary glands: The mammary glands are modified **sweat gland**. These are paired structures, having glandular tissues and variable amount of fat. The glandular tissue of each mammary gland is divided into 15-20 mammary lobes. The lobes are separated by adipose tissue and dense connective tissue. Each mammary lobe consists of cluster of cells called **alveoli**, which secrete milk. Alveoli open into mammary tubules. The tubules of each lobe join to form **mammary ducts**. Several mammary ducts join to form a wide **ampulla**, which is connected to lactiferous duct. The **lactiferous duct** opens into nipple through which milk is sucked out.

8.5. HORMONES OF TESTIS AND OVARY- ESTROUS AND MENSTRUAL CYCLE

8.5.1. HORMONAL CONTROL OF MALE REPRODUCTIVE SYSTEM

The male reproductive system depends upon the action of many hormones. Leydig cells or interstitial cells of testes synthesize and secrete testicular or male hormone called **androgens** including **testosterone**, **dihydrotestosterone** and **androstenedione**. Testosterone is more abundant than the others thus, can be considered significant testicular hormone. Testosterone,

stimulate growth, maintenance and functions of secondary sex organs and accessory glands. Androgens produced by male embryos during the seventh week of development stimulate the embryo to develop into a male rather than a female. During puberty, high concentrations of androgens trigger the development of male characteristics as follows.

1. Testosterone causes the penis, scrotum and testes to enlarge about eightfold before the age of 20 years.
2. Testosterone causes growth of hair over the pubis, upward along the linea alba, on the face and usually on the chest. It decreases the growth of hair on the top of the head (baldness)
3. It causes low pitched voice.
4. It helps in increasing musculature after puberty.
5. After the great increase in circulating testosterone at puberty, the bones grow considerably in thickness and retain considerable additional calcium salts. Thus, it increases the total quantity of bone matrix and causes calcium retention.
6. The increased rate of metabolism is an indirect result of the effect of testosterone on protein metabolism.
7. Increased number of red blood cells in males is due to increased metabolic rate.
8. Increased body water is due to increased renal reabsorption of water and electrolytes.

Growth, maintenance and functions of seminiferous tubules and leydig's cells are regulated by follicle stimulating hormone (FSH) and luteinizing hormone (LH) or interstitial cells stimulating hormone (ICSH) of the anterior pituitary.

Release of FSH and ICSH, in turn, is regulated by the release of hypothalamic gonadotropin releasing hormone (GnRH).

8.5.1.1. HORMONAL CONTROL OF SPERMATOGENESIS

The formation of haploid sperm from diploid spermatogonia is called **spermatogenesis**. The spermatogonia near the wall of seminiferous tubule multiply constantly by mitosis. Some of them differentiate into **primary spermatocytes**, the cells that undergo meiosis. Meiosis- one of a primary spermatocyte produces two haploid **secondary spermatocytes**. Meiosis- two then forms four cells, called **spermatids**, each with the haploid number of chromosomes. The spermatids are transformed into sperms by the process called **spermiogenesis** (Fig 8.6). Sperms head become embedded in the sertoli cells, and finally released from the seminiferous tubules by the process of **spermiation.**

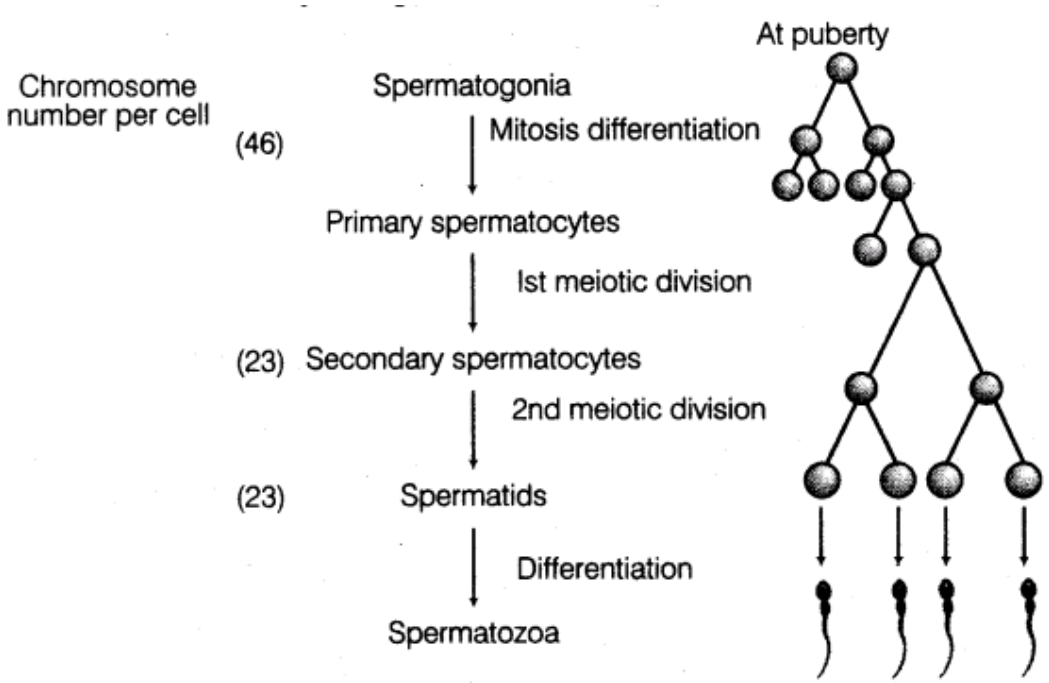

Fig. 8.6 Spermatogenesis in human male

Spermatogenesis starts at the age of puberty due to significant increase in **GnRH**. The increased level of GnRH then acts at anterior pituitary gland and stimulates secretion of **FSH** and **LH**. LH acts at the **Leydig cells** and stimulates synthesis and secretion of **androgens**, which in turn, stimulates the process of **spermatogenesis**. **FSH** acts on **sertoli cells** and stimulate them to secrete**androgen binding protein** (ABP) and **inhibin**. ABP concentrates testosterone in seminiferous tubule and helps in the process of **spermiogenesis**. When there is excess of FSH and GnRH, inhibin suppresses FSH synthesis by anterior pituitary and GnRH synthesis by hypothalamus.thus normal release of testosterone is under negative feed back control.

8.5.2. HORMONAL CONTROL OF FEMALE REPRODUCTIVE SYSTEM

FSH of anterior pituitary stimulates growth, development and hormone secretion**(estrogen)** of graafian follicle and maturation of ovum.

LH of anterior pituitary stimulates rupture of mature graafian follicle, ovulation and formation of corpus luteum which stimulates secretion of **progesterone**.

Estrogen and **progesterone**aresecreted by ovary which controls the growth and functions of female secondary sex organs.

Effect of estrogen on the primary and secondary female sex characteristics: The main function of the estrogen is to cause cellular proliferation and growth of the tissues of the sex organs and other related tissues. At puberty, the quantity of estrogen secreted under the influence of the gonadotropins increases 20-folds. So, the ovaries, fallopian tubes, uterus and vagina all increases in size. Estrogen causes development of stromal tissue as well as ductile system of the

breasts and deposition of fat in the breasts. Estrogen cause increased osteoblastic activity and has potent effect on skeletal growth. It increases metabolic rate slightly, but only about one-third as much as does the male sex hormone. Estrogen, like aldosterone, cause sodium and water retention by the kidney tubules.

Effect of progesterone on the primary and secondary female sex characteristics: The progesterone promotessecretary changes in the uterine endometrium during the latter half of the monthly female sexual cycle.It promotes secretary changes in the mucosal lining of the fallopian tube. It promotes development of the lobules and alveoli of the breast.Progesterone in large quantity,like estrogen, can enhance sodium, chloride and water reabsorption from the distal tubule of the kidney.

8.5.2.1.HORMONAL CONTROL OF OOGENESIS

The process of formation of a mature female gamete is called **oogenesis**. It is initiated during the embryonic development stage when a large number of oogonia are formed within each fetal ovary; no more oogonia are formed and added after birth. Each oogonium divides by mitosis and forms group of cells, out of which one cell enlarges and other forms follicular epithelium around it. This enlarged cell is known as primary **oocyte**. The primary oocyte alongwith follicular epithelium is known as **primary follicle**. At birth each ovary contains many thousands of follicle and each follicle contain one dormant **primary oocyte**, a diploid cell that has paused its cell cycle in **prophase** of meiosis I.

After puberty and until menopause, about every 28 days, FSH stimulates one of the dormant follicles to develop. The follicle enlarges, and the primary oocyte within it completes meiosis I, which is unequal. It results in the formation of a large haploid secondary oocyte and a small first polar body. The secondary oocyte has paused its cell cycle in **metaphase II** of meiosis II. Now follicle is ripened to form graafian follicle. About the time the secondary oocyte forms, the pituitary gland secretes LH, which causes **ovulation.** The graafian follicle bursts, releasing its secondary oocyte from the ovary. The ruptured follicle then develops into a corpus luteum. Cells of copus luteum secrete two hormones- **progesterone** which helps in maintaining pregnancy and **relaxin** toward the end of pregnancy.

The secondary oocyte enters the oviduct, and if sperm fuses with it, the secondary oocyte completes meiosis II, which is again unequal. It yields actual **ovum** and **second polar body** (Fig. 8.7). If fertilization does not occur, the secondary oocyte degenerates, and menstruation occurs.

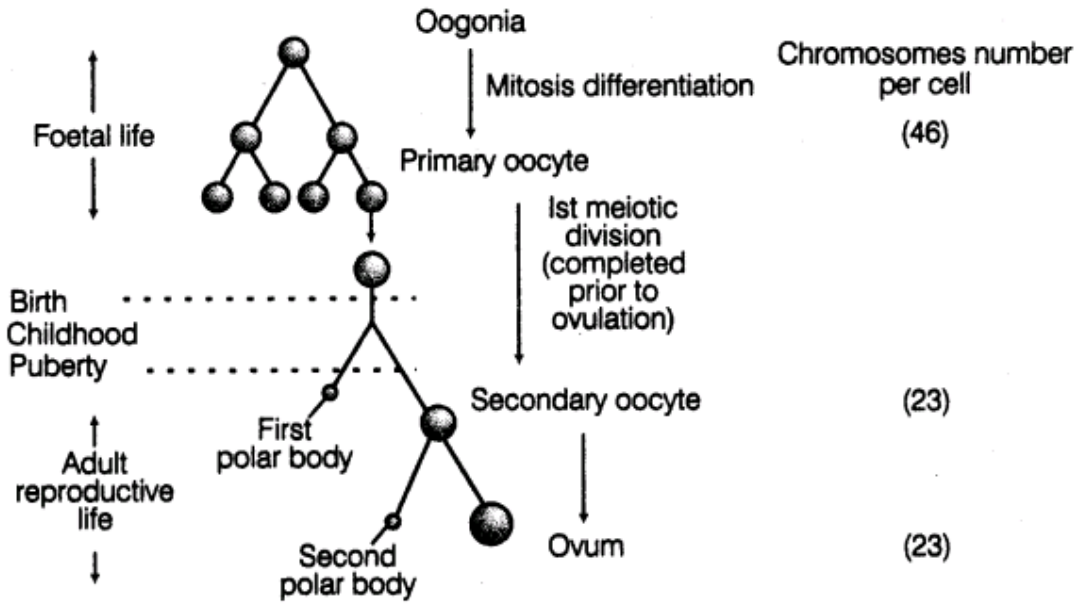

Fig. 8.7 Oogenesis in human female

8.5.2.2 HORMONAL CONTROL OF MENSTRUAL CYCLE

The females of placental mammals exhibit cyclic changes in the activities of ovaries and accessory ducts as well as hormones during the reproductive phase. Such cyclic changes in female primates is called **menstrual cycle**. Each month, the ovaries go through a series of stages, depending on stimulation by the anterior pituitary hormones, the **follicle stimulating hormone (FSH)** and the **luteinizing hormone (LH)**. In human females, sexual cycle begins when a girl attains puberty. The first menstruation is called **menarche**. In human female, reproductive cycle repeats itself once every28 days but cycles from 20-40 days are not uncommon. Thus, the cycle of events starting from one menstruation to the next is called **menstrual cycle**. In the middle of each cycle, one ovum is released from either of the two ovaries.It can be divided into four phases.

Menstrual phase: Menstrual phase marks the beginning of menstrual cycle. It is characterized by menstrual flow and lasts for 3-5 days. The menstrual flow results due to breakdown of endometrium, the blood rich inner lining of the uterus. Menstruation occurs only if the released ovum is not fertilized.

During menstrual phase, the level of **estrogen** and **progesterone** falls considerably. Thisinduces adenohypophysis to secrete **FSH** and **LH.**

Follicular phase or proliferative phase: Follicular phase extends from 6^{th} day to 13^{th} day of the menstrual cycle. During this phase, the primary follicle in the ovary grows to become fully mature graafian follicle and simultaneously the endometrium of uterus regenerates through proliferation.Hence this phase is also known as **proliferative phase**.

These changes in the ovary and the uterus are induced by changes in the level of **pituitary** and **ovarian hormones**. The secretion of FSH and LH increases gradually. Increased level of FSH stimulates one or more primary ovarian follicle to start growing. It also stimulates secretion of estrogen from growing follicle (Fig. 8.8).

Ovulatory Phase: After about 12 days, estrogen reaches at its peak, which causes a sudden surge of FSH and LH. The maximum level of LH during mid-cycle is called **LH surge**.LH causes ovulation and formation of corpus luteum. The developing follicle within the ovary bursts and releases its egg.

Luteal or secretory phase: The ovulatory phase is followed by the luteal phase during which the remaining parts of the graafian follicle transform as the **corpus luteum.** It grows for about 7 days and secretes progesterone. In case ovum is not fertilized, corpous luteum degenerates into a white mass, corpous albicans. This lowers the level of progesterone in blood.

In case, the egg is fertilized, progesterone further prepares the uterus for pregnancy. This phase is named as **secretory phase** because during this phase, uterine wall secretes some nutritious fluid in the uterus.

The permanent stoppage of the menstrual cycle in women is called **menopause**. The menopause normally occurs between the age of 45 and 50 years. During menopause, the primary follicle of the ovary fails to respond to the pituitary gonadotropins, so that graffian follicle does not develop.

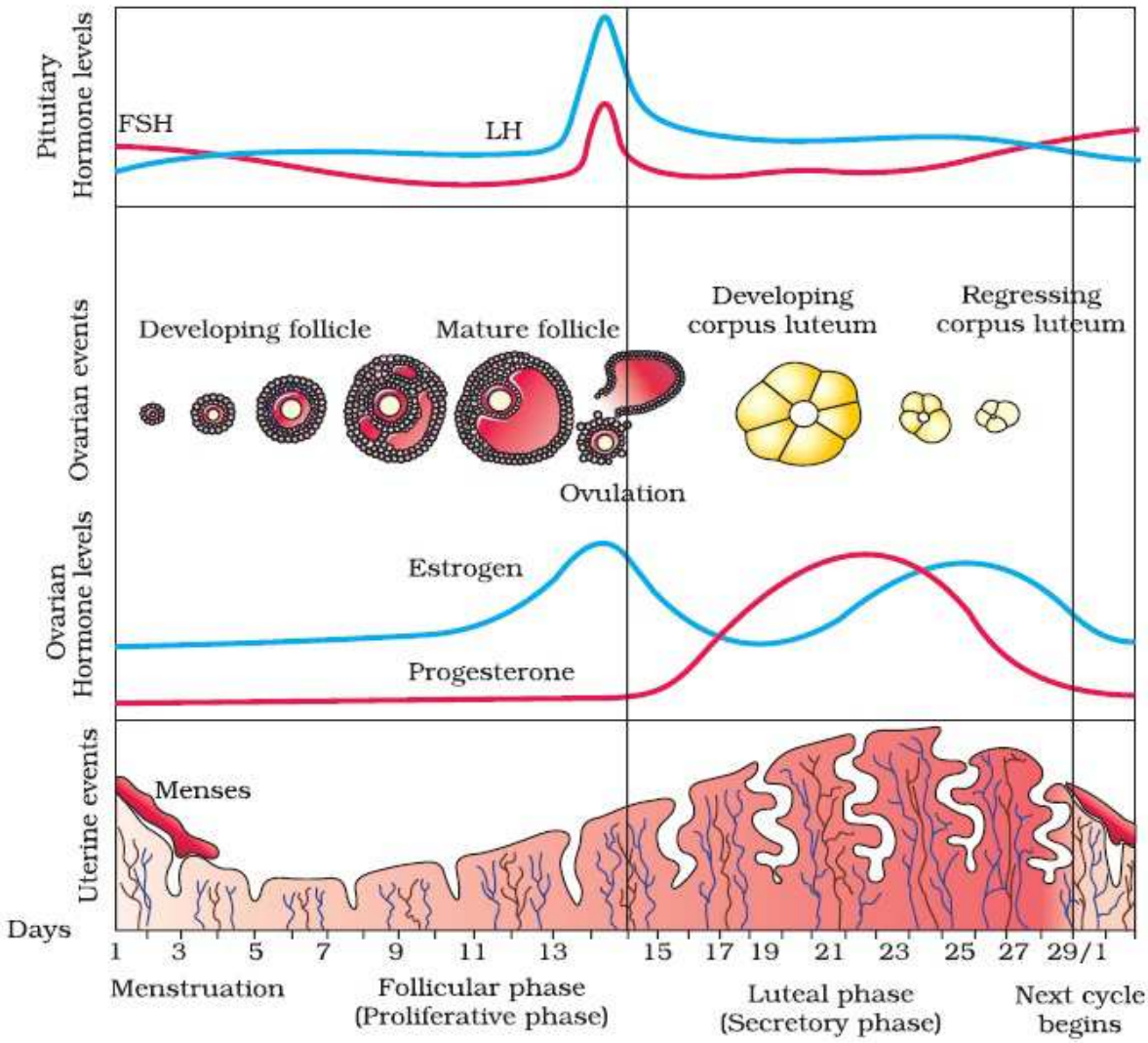

Fig.8.8. Diagrammatic presentation of different events and their hormonal control during menstrual cycle

8.5.2.3. HORMONAL CONTROL OF ESTROUS CYCLE

The cyclic changes during reproduction in nonprimates like cows, **sheep, rats,deers,dogs etc** is called **estrous cycle**. Puberty in female animals can be defined as the first estrus accompanied by ovulation. The endocrine basis for puberty in females is the development of the hypothalamic mechanisms responsible for **GnRH** release. The adenohypophysis is capable of releasing FSH and LH before GnRH becomes available to stimulate their release. Great variations in the timing of puberty can be found within a single species, depending on climate, level of nutrition, and heredity.

Estrous cycle is divided into following phases.

Proestrus: The first phase (proestrus) of the estrous cycle is the building-up phase. During this phase the ovarian follicle enlarges and begins to secrete estrogens under the influence of FSH and LH. One or several follicles of the ovary start to grow. Their number is species specific. Typically this phase can last as little as one day or as long as three weeks, dependingon the species. Under the influence of estrogen, the endometrium of uterus starts to develop.In polyestrous species, proestrus usually begins within a day or two of regression of the corpus luteum from the previous cycle.The female is not yet sexually receptive. The oldcorpus luteum gets degenerated. The uterus and the vagina get distended and filled with fluidand become contractile.The vaginal epithelium proliferatesand the vaginal smear shows a large number of noncornified nucleated epithelial cells.

Estrus: Estrus or **heat** is the period when female becomes sexual receptive. It is primarily initiated by the elevation in estrogens from mature follicles just prior to ovulation. The female then exhibitssexually receptive behavior, a situation that may be signaled by visible physiologic changes.In most domestic species, ovulation occurs within a day or two after the onset of behavioural estrus.Proestrus and estrus together comprise the follicular phase of the reproductive cycle.

Metestrus: The end of sexual receptivity marks the beginning of metestrus, the postovulatory phase dominated by corpus luteum function. During this period, **serum estrogens** decrease and **progesterone** increases. A fully developed corpus luteum has a notable effect on the uterus. The endometrial lining of the uterus thickens and uterine glands enlarge. The uterine muscles show increased development. The external genitalia return to their state before estrus as plasma estrogens decrease.In the absence of pregnancy the metestrus phase terminates with the regression of the corpus luteum. The lining in the uterus is not shed, but is reorganized for the next cycle.

Anestrus: Anestrus refers to the phase when the sexual cycle rests. This is typically a seasonal event and controlled by light exposure through the pineal gland that releases melatonin. Melatonin may repress stimulation of reproduction in long-day breeders and stimulate reproduction in shortday breeders. Melatonin is thought to act by regulating the hypothalamic pulse activity of the gonadotropin releasing hormone. During anestrus the uterine tubes and vagina shrink, and remain small until the next breeding season.

8.6. HORMONES OF PREGNANCY - PARTURITION

In humans, the embryonic development begins with fertilization. The process of fertilizing an egg,involving the fusion of male and female gametes to form a **zygote** is called **fertilization.** In a zygote, the chromosomes of the egg and sperm nuclei are eventually enclosed in a single diploid nucleus. As the zygote moves down through the isthmus of the oviduct, it undergoes mitotic division called **cleavage**. The embryo with 8-16 blastomeres is called a **morula**. The morula continues to divide to form **blastocyst**. The blastomere of blastocyst are arranged into an outer

layer called **trophoblast**. The inner group of cells attached to trophoblast called **inner cell mass.** Now the trophoblast layer gets attached to the endometrium and the inner cell mass gets differentiated as embryo. The blastocyst become embedded in the endometrium, this is called **implantation.** About 7 days after fertilization, implantation occurs and leads to pregnancy.

8.6.1. HORMONES DURING PREGNANCY

After implantation, the **trophoblast** becomes the part of **placenta**, the organ that provides nourishment and oxygen to embryo and helps dispose of its metabolic wastes. The finger-like projections appear on the trophoblast called **chorionic villi** which are surrounded by the uterine tissue and maternal blood. **The chorionic villi and uterine tissue jointly form a structural and functional unit between developing embryo and maternal body called placenta.Umbilical cord** is the lifeline between the embryo and the placenta (Fig 8.9). The chorionic villi absorb nutrients and oxygen from the mother's blood and pass these substances to the embryo. The villi also carry wastes from the embryo to the mother's blood. Placenta allows protective **antibodies (IgG)** to pass from the mother to the fetus, which induce passive immunity and insusceptibility to certain diseases like measles, diphtheria, small pox etc. to the fetus.Placenta also acts as an endocrine tissue and produces several hormones.

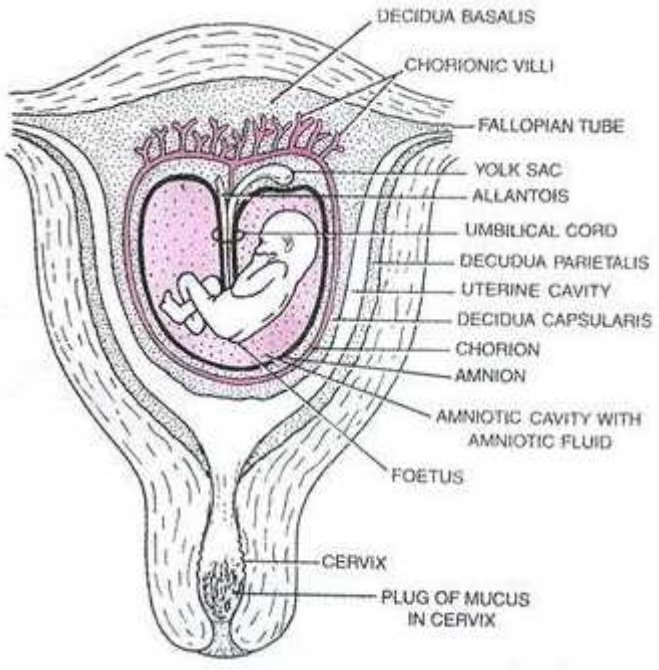

Fig.8.9. Human foetus within uterus showing placenta

8.6.1.1. ENDOCRINE FUNCTION OF PLACENTA

Human Chorionic Gonadotropin: It is secreted by chorionic cells of placenta soon after implantation of blastocyst. It maintains corpus luteum and stimulates it to secrete progesterone. Progesterone maintains endometrial lining throughout pregnancy so also named as **pregnancy hormone.**

Human Placental Lactogen: It stimulates growth and development of breasts during pregnancy and decreases insulin sensitivity of mother, so that mother is not able to utilize its own glucose. This makes more glucose available to the fetus.

Progesterone: Placental progesterone helps in maintaining pregnancy and encourages growth of endometrium.

Estrogen: Placenta converts adrenal androgen of mother and fetus into estrogen. This hormone helps in the enlargement of uterus, breast and external genitalia.

Relaxin: It is secreted by both corpus luteum and placenta. The hormone softens connective tissue of pubic symphysis for easy child birth.

Thus increased production of these hormones from placenta is essential for supporting fetal growth.

8.6. 2. HORMONAL CONTROL OF PARTURITION (CHILD BIRTH)

Immediately after implantation, the inner cell mass differentiates into an outer layer called **ectoderm** and an inner layer called **endoderm.** Soon, mesoderm appears between the ectoderm and the endoderm. These three layers give rise to all tissues and organs in the embryo. The average duration of human pregnancy is about 9 months which is called **gestation period**. **The act of expelling the full term fetus from mother uterus at the end of gestation is called parturition**. Parturition involvesvigorous muscular contractions of uterine wall which induces **labour**. Parturition is induced by a complex **neuroendocrine mechanism**. The signals for parturition originate from the fully developed fetus through secretion of certain hormones, which diffuse through placenta into mother's blood and cause secretion of oxytocin. It induces mild uterine contraction. These are called **fetal ejection reflexes**.**Oxytocin** acts on the uterine muscle and causes stronger uterine contractions, which in turn, stimulates further secretion of oxytocin. The stimulatory reflexes between the uterine contraction and oxytocin secretion continue. It results stronger and stronger uterine contraction, which leads to expulsion of baby out of the uterus through birth canal. Thus, oxytocin is named as **birth hormone**. **Relaxin**increases flexibility of pubic symphysis and dilates uterine cervix during parturition. **Corticotropin-releasing hormone (CRH)** is secreted by placenta towards the end of gestation to establish time of birth.

8.7. HORMONAL CONTROL OF LACTATION

The main function of mammary gland is to start producing milk towards end of pregnancy. The gland secretes and ejects milk. This is called **lactation**. Milk secretion and storage begins within 24 hours of child birth under the influence of hormone **prolactin**. The prolactin is secreted by anterior lobe of pituitary. After child birth, the ejection of milk is stimulated by oxytocin, which is released by posterior pituitary. The milk produced during the initial few days of lactation is called **colostrum**. The colostrum contains several antibodies, fat droplets, Casein (milk protein),

lactose (milk sugar), vitamins and water etc. The antibodies (IgA) of colostrum provide passive immunity to the newborn from certain infections.

8.8. PHEROMONES

The term pheromone was derived from Greek word *Pherein* means "to transfer excitement". This term was proposed by **Karlson** and **Luscher** in 1959.**Pheromones are the chemicals excreted or released by one animal to the exterior, but evoke a physiological or behavioral response in another animal of the same species.** Mostly pheromones are volatile and odorous fatty acids whose air-borne molecules are received by recipient animals through olfaction. According to **Karlson** (1960), **"pheromones are chemical signals exchanged between individuals of the same species, which cause a specific reaction either in the form of a behavioral response or in a particular developmental process"**. Pheromones are also called as **ectohormones** because they are released outside the body. Pheromone took important roles as messengers acting to attract, repel, and to identify the sex and status of individuals and also to control physiological processes of another individuals.The pheromones differ from hormones in several respects.

1. They are produced by the exocrine glands.
2. They are transmitted via the external environment.
3. They are more species- specific than the hormone.
4. They evoke specific behavioural, developmental or reproductive responses in the bodies of other individuals of the same species whereas the hormones regulate organism's own physiology.

A lot of work has been done in the field of insect pheromones. They perform various activities such as sex attractants, trail substances and alarm reaction.**Releaser** or **sex pheromones** are pheromones that cause an alteration in the behavior of the recipient. Some organisms use powerful attractant molecules to attract mates from a distance of two miles or more. This type of pheromone elicits a rapid response, but is quickly degraded. For example, female silkworm moth secretes**bombykol**and female gypsy moth secretes**gyplure** to attract their mating partner.

For guiding the food source and new nest site, **trail pheromones** are released. Social insects commonly use trail pheromones. For example, ants mark their paths with pheromones consisting of volatile hydrocarbons. Certain ants lay down an initial trail of pheromones as they return from the nest with food. This trail attracts other ants and serves as a guide. As long as the food source remains available, visiting ants will continuously renew the pheromone trail. The pheromone requires continuous renewal because it evaporates quickly. When the food supply begins to diminish, the trail-making ceases. Some insects release **geraniol** to transmit information of food source.

Aphids secrete **alarm pheromone** when they are attacked by lady birds. *Vespula squamosa* use alarm pheromones to alert others to a threat. In *Polistes exclamans*, alarm pheromones are also used as an alert to incoming predators.

Primer pheromones trigger a change of developmental events thus, they differ from all the other pheromones, which trigger a change in behavior.

Territorial pheromones mark the boundaries or territory, which is the sociographical area that an animal of a particular species consistently defends against animals of other species. In cats and dogs, these hormones are present in the urine, which they deposit on landmarks serving to mark the perimeter of the claimed territory.

8.9. SUMMARY

The male and female reproductive cycles are controlled by hormones released from the hypothalamus and anterior pituitary as well as hormones from reproductive organs. The hypothalamus monitors the need for the FSH and LH hormones that is released from the anterior pituitary. FSH and LH affect reproductive organs to cause the formation of sperm and the preparation of eggs for release and possible fertilization. In the male, FSH and LH stimulate sertoli cells and interstitial cells or Leydig cells in the testes to facilitate sperm production. The Leydig cells produce testosterone, which is responsible for the secondary sexual characteristics of males. In females, FSH and LH cause estrogen and progesterone to be produced. They regulate the female reproductive cyclewhich is completed in four phases. Menopause occurs when the ovaries lose their sensitivity to FSH and LH and the female reproductive cycles slowly stops. The hormonal control of oogenesis (Fig. 8.10) and spermatogenesis (fig. 8.11) is summarized by flowchart. After fusion of male and female gametes zygote is formed. In humans, developing organism from fertilization to the end of second month, until all the organs are differentiated, is called **embryo**. Human embryo from third month onward till birth is called **fetus**. The period of time from conception till birth is called gestation period or pregnancy. Placenta plays important role in pregnancy as it is intimate connection between fetus and uterine wall of the mother for exchange of materials. Placenta secretes many hormones to maintain the pregnancy. Parturition involves forceful muscular contraction under the influence of **oxytocin** thus, the full term fetus is expelled from the mother's uterus. Secretion of milk from mammary gland occurs within 24 hours of child birth under the influence of **prolactin**.

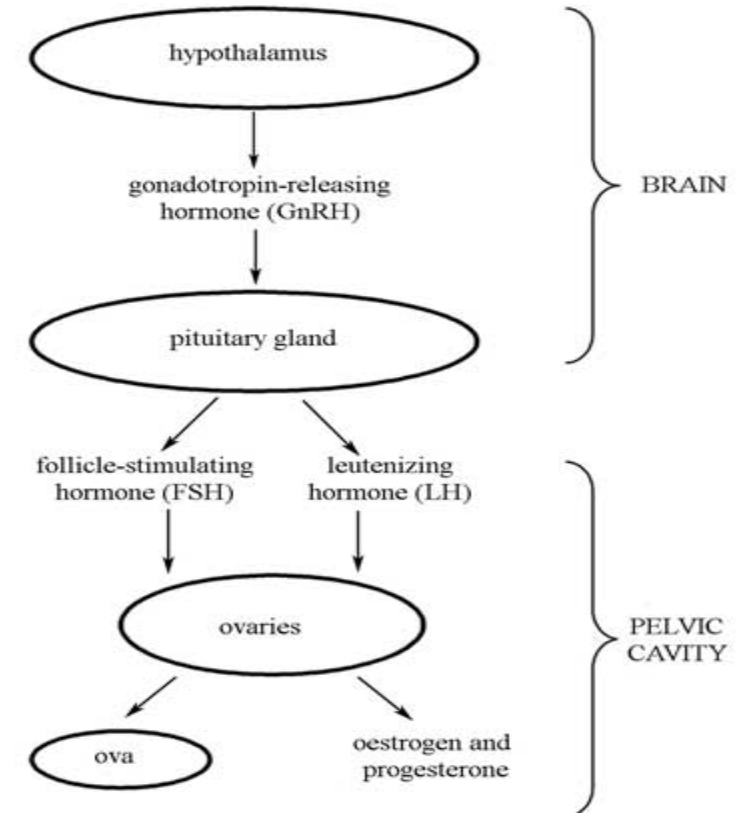

Fig. 8.10. Flow chart showing hormonal control of oogenesis

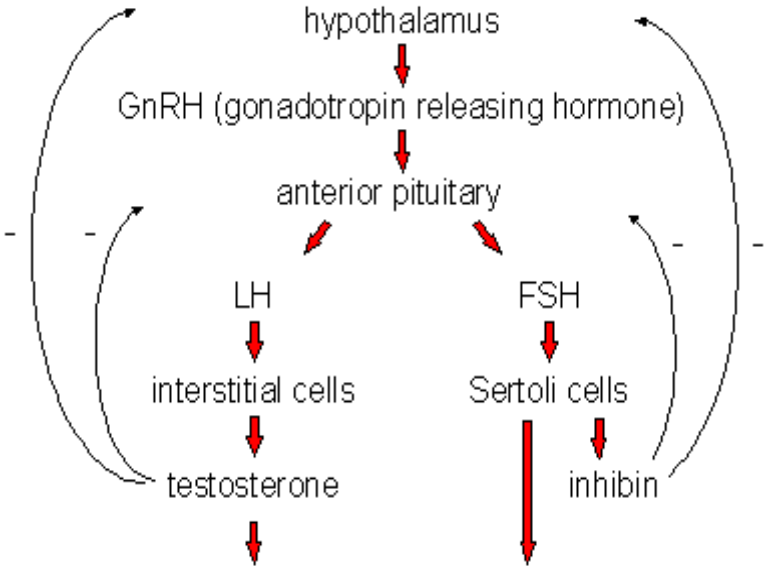

Fig.8.11. Flow chart showing hormonal control of spermatogenesis

8.10. SELF ASSESSMENT QUESTIONS AND POSSIBLE ANSWERS

8.10.1. MULTIPLE CHOICE QUESTIONS

1. Conversion of spermatid into spermatozoa is called

   (a) Spermatogenesis (b) Vitellogenesis

   (c) Spermiogenesis (d) Cytokinesis

2. Sertoli cells are found in

   (a) Seminiferous tubules (b) Ovarian follicles

   (c) Uriniferous tubules (d) In between seminiferous tubule

3. The embryo at 16-celled stage is known as

   (a) Morula (b) Gastrula

   (c) Blastula (d) Blastomere

4. The head of epididymis is called

   (a) Vas deferens (b) Cauda epididymis

   (c) Corpus epididymis (d) Caput epididymis

5. The foetal membranes of mammalian embryo are derived from

   (a) Trophoblast (b) Follicle cells

   (c) Inner cell mass (d) Formative cells

6. Corpus spongiosum is found in

   (a) Penis (b) Ovary

   (c) Testis (d) Uterine wall

7. Leydig cell secrete

   (a) Oestrogen (b) Progesterone

   (c) Testosterone (d) Corticosterone

8. Which of the following layer develops first during embryonic development?

   (a) Ectoderm (b) Endoderm

   (c) Mesoderm (d) Both B and C

9. Which of the following controlsthe function of sertoli cells?

   (a) FSH (b) Estrogen

(c) ACTH (d) Testosterone

10. Secretion of androgens by testes is regulated by

(a) Oxytocin (b) Follicle stimulating hormone

(c) Luteotropic hormone (d) Luteinizing Hormone

11. Which of the following hormone is responsible for milk ejection after child birth

(a) Oxytocin (b) Progesterone

(c) Prolactin (d) Estrogen

12. LH surge occurs during which phase of the menstrual cycle

(a) Menstrual phase

(b) At the beginning of proliferative phase

(c) At the middle of the cycle

(d) Luteal phase

13. Corpus luteum secrete

(a) Progesteron only (b) Progesterone and estrogen both

(c) Progesterone and LH (d) Estrogen only

14. Which of the following hormone is not a secretion product of human placenta

(a) Human chorionic gonadotropin (b) Prolactin

(c) Oestrogen (d) Progesteron

15. Secretion and storage of milk occurs under the influence of which hormone

(a) Prolactin (b) Oxytocin

(c) Human placental lactogen (d) None

8.10.2. VERY SHORT QUESTIONS

1. What is heat period?
2. What is significance of epididymis in male fertility?
3. Where are Leydig cells located? What do they secrete?
4. Mention the most significant function of oxytocin?
5. Give the site of secretion and function of relaxin?
6. Name the hormone that influences secretion of estrogen.
7. Name the layer of cells which forms the outer wall of blastocoels.

8. At what stage of life is oogenesis initiated in human female. When does the oocyte complete oogenesis.

ANSWERS

8.10.1. 1.(c); 2.(a); 3.(a); 4.(d); 5.(a); 6.(a); 7.(c); 8.(b); 9.(a); 10.(d); 11.(a); 12.(c); 13.(b); 14.(b); 15.(a)

8.10.2. 1.It is the period of sexual responsiveness of nonprimate females; 2.Physiological maturation of sperm occurs in epididymis; 3.Leydig cells are located in connective tissue between the seminiferous tubule. It secretes androgens; 4. It causes contraction of uterine muscle during child birth and ejection of milk during lactation; 5. Relaxin is secreted by placenta. It increases flexibility of pubic symphysis and dilates uterine cervix during labour; 6. FSH; 7.Trophoblast; 8. Oogenesis is initiated in fetal ovary. The oocyte complete oogenesis after the attainment of puberty during every menstrual cycle.

8.11. TERMINAL AND MODEL QUESTIONS

1. Briefly describe the events of menstrual cycle and their hormonal control.
2. Draw a neat labeled diagram of a transverse section of human ovary.
3. Briefly describe the events of estrus cycle and their hormonal control.
4. Describe the function of placenta.
5. Define spermatogenesis. Describe its process and hormonal control.
6. Name two types of cells found in seminiferous tubule. Draw a well labeled diagram of transverse section of testis.
7. Briefly describe zygotic development in human female and endocrine role of placenta in it.
8. Describe male and female accessory sex organs.
9. Describe role of testosterone on secondary sexual characteristics of male.
10. Describe role of estrogen and progesterone on secondary sexual characteristics of female.

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