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PROPOSED SYLLABUS

B. Sc. (Part III) Zoology

PAPER – I : BIOCHEMISTRY AND PHYSIOLOGY

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UNIT

1

STRUCTURE AND PROPERTIES OF AMINO ACIDS

STRUCTURE

- Introduction
- Structure of Amino Acids
- Properties of Amino Acids
- Summary
- Student Activity
- Test yourself

LEARNING OBJECTIVES

After going through this unit you will learn:

What are amino acids

What is the basic structure of amino acids

What are basic properties of amino acids

1.1. INTRODUCTION

Amino acids play central role both as building blocks of proteins and as intermediates in metabolism. The 20 amino acids that are found within proteins convey a vast array of chemical versatility. The precise amino acid content, and the sequence of those amino acids, of a specific protein, is determined by the sequence of the bases in the gene that encodes that protein. The chemical properties of the amino acids of proteins determine the biological activity of the protein. Proteins not only catalyze all (or most) of the reactions in living cells, they also control virtually all-cellular process. In addition, proteins contain within their amino acid sequences the necessary information to determine how that protein will fold into a three dimensional structure, and the stability of the resulting structure. Thus by understanding amino acid structure and properties we will be able to understand protein structure and properties. Humans can produce 10 of the 20 amino acids because they do not have all the enzymes required for the biosynthesis of all of the amino acids. The others must be supplied in the food.

The 10 amino acids that we can produce are alanine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, proline, serine and tyrosine. Tyrosine is produced from phenylalanine, so if the diet is deficient in phenylalanine, tyrosine will be required as well. The essential amino acids are arginine (required for the young, but not for adults), histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, and valine. These amino acids are required in the diet. Plants are able to make all the amino acids.

Amino acids are molecules containing an amine group, a carboxylic acid group, and a side-chain that is specific to each amino acid. The key elements of an amino acid are carbon, hydrogen, oxygen, and nitrogen. They are particularly important in biochemistry, where the term usually refers to alpha-amino acids. The various alpha-

amino acids differ in their side-chain (R-group) attached to alpha carbon, and can vary in size from just one hydrogen atom to a large heterocyclic group.

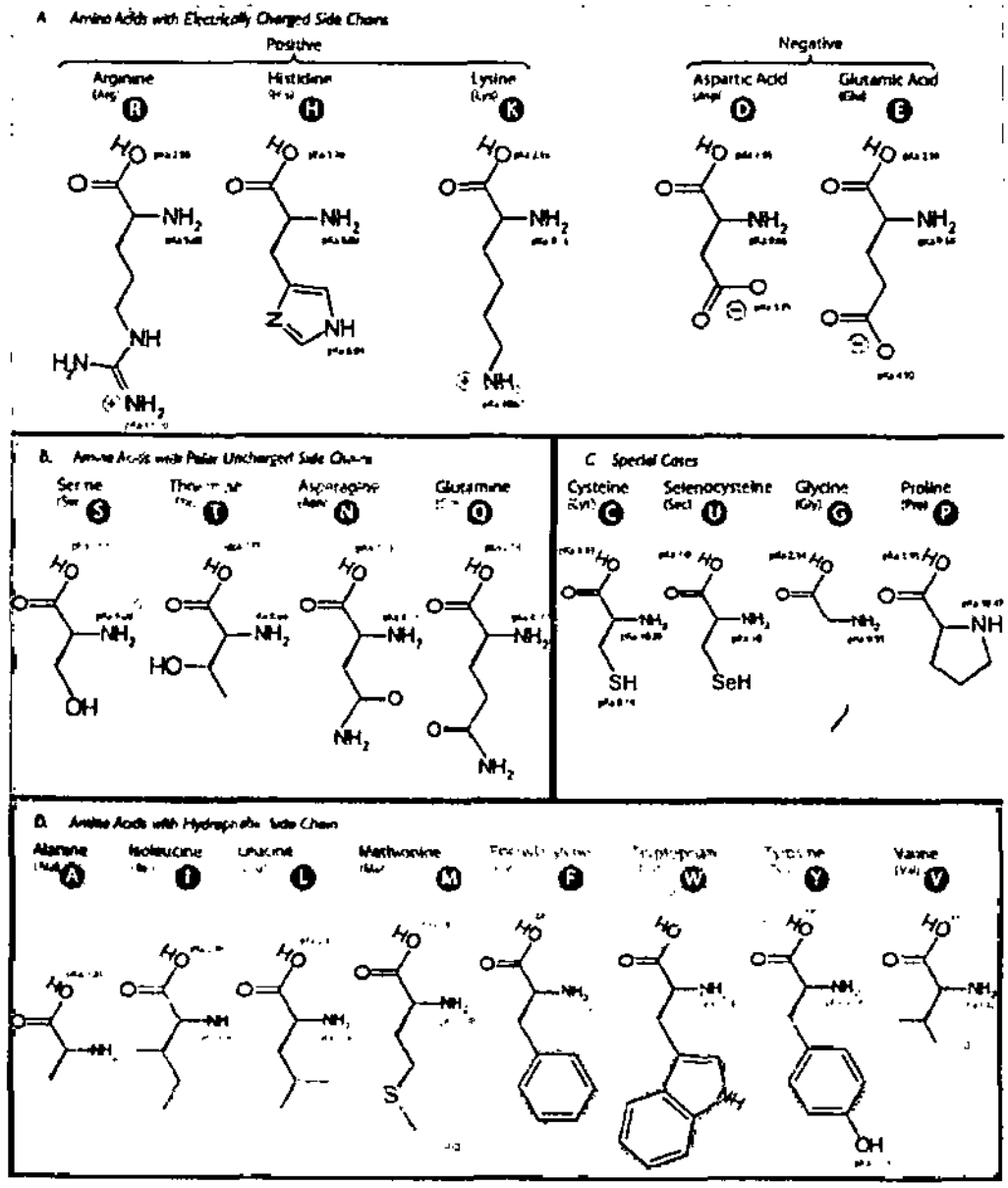


Fig 1: twenty-one Amino Acids found in eukaryotes.

1.2. STRUCTURE OF AMINO ACIDS

Amino acids are the compounds containing an amino group, $-NH_2$, and a carboxylic acid group, –COOH.

The biologically important amino acids have the amino group attached to the carbon atom next to the -COOH group. They are known as ***2-amino acids*** or ***alpha-amino acids***.

The general formula for a 2-amino acid is:

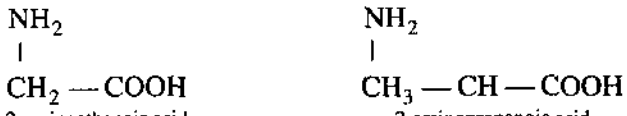
$$\begin{array}{l} NH_2 \\ | \\ R\text{-}CH\text{-}COOH \end{array}$$

where "R" can be quite a complicated group containing other active groups like -OH, -SH, other amine or carboxylic acid groups, and so on. Other types of amino acids form when the amino group is attached to a different carbon atom. For example; in gamma

AMSWGR-5

amino acid, the carbon atom with amino group is separated from the carboxylate group by two other carbon atoms.

Because of the biological importance of molecules like these, they are normally known by their traditional biochemical names. The two simplest of these amino acids are 2-aminoethanoic acid (glycine) and 2-aminopropanoic acid (alanine).



2-aminoethanoic acid
glycine

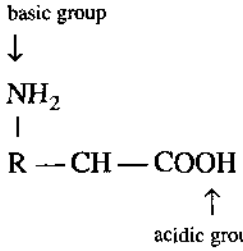
2-aminopropanoic acid
alanine

1.3 PROPERTIES OF AMINO ACIDS

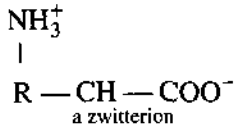
1. Melting points :

The amino acids are crystalline solids with surprisingly high melting points. It is difficult to bring their melting points down because the amino acids tend to decompose before they melt. Decomposition and melting tend to be in the 200 - 300°C range.

This is because the general structure of an amino acid has both a basic amine group and an acidic carboxylic acid group.



There is an internal transfer of a hydrogen ion from the -COOH group to the $-NH_2$ group to leave an ion with both a negative charge and a positive charge. This is called ***zwitter ion***.



a zwitterion

A zwitter ion is a compound with no overall electrical charge, but which contains separate parts which are positively and negatively charged. This is the form that amino acids exist in even in the solid state. These ions have much stronger ionic attractions between each other. These ionic attractions are so strong that it takes more energy to break and so the amino acids have high melting points.

2. Solubility :

Amino acids are generally soluble in water but are insoluble in non-polar organic solvents such as hydrocarbons.

This is again due to the presence of the zwitterions. In water, the ionic attractions between the ions in the solid amino acid are replaced by strong attractions between polar water molecules and the zwitterions. It is almost the same as any other ionic substance dissolving in water.

The extent of the solubility in water varies depending on the size and nature of the "R" group.

The lack of solubility in non-polar organic solvents such as hydrocarbons is due to the lack of attraction between the solvent molecules and the zwitterions because

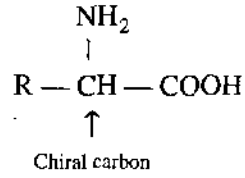
without strong attractions between solvent and amino acid, there would not be enough release of energy to pull the ionic lattice apart.

4. Isoelectric point :

At pH values between the two pKa values, the zwitterion predominates, but coexists in dynamic equilibrium with small amounts of net negative and net positive ions. At the exact midpoint between the two pKa values, the trace amount of net negative and trace of net positive ions exactly balance, so that average net charge of all forms present is zero. This pH is known as the isoelectric point pI, so pI = 1/2 (pKa_1 + pKa_2). All amino acids have slightly different pKa values, so have different isoelectric points. For amino acids with charged side-chains, the pKa of the side-chain is involved. Amino acids have zero mobility in electrophoresis at their isoelectric point. Zwitterions have minimum solubility at their isolectric point and some amino acids can be isolated by precipitation from water by adjusting the pH to the required isoelectric point.

5. Optical activity :

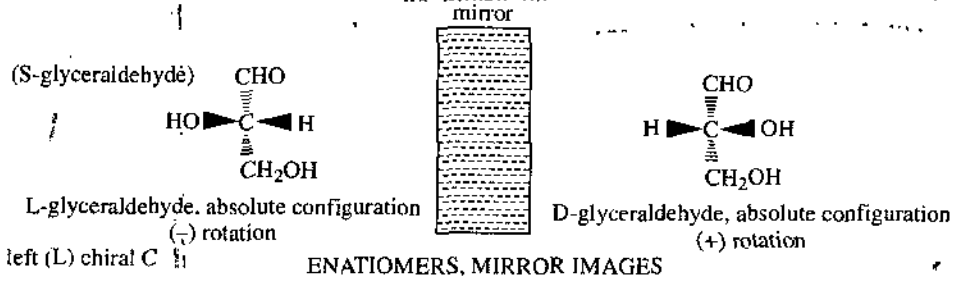
We have studied in the general formula for an amino acid, that (apart from glycine, 2-aminoethanoic acid) the carbon at the centre of the structure has four different groups attached i.e. amino acids (apart from glycine) are **chiral.**



This is equally true for the structure of the zwitter ion instead of this simpler structure.

Furthermore, the lack of a plane of symmetry means that there will be two stereoisomers of an amino acid (apart from glycine) - one the non-superimposable mirror image of the other.

The isomers of a general amino acid can be shown as



All the naturally occurring amino acids have the "L-" configuration. The other structure is known as the "D-" configuration.

In alternative fashion, the (*S*) and (*R*) designators are also used to indicate the absolute stereochemistry.

6. Spectral properties :

Amino acids (Trp, Tyr, and Phe) contain conjugated aromatic rings. Consequently, they absorb light in the ultraviolet range (UV). The extinction coefficients (or molar absorption coefficients) of these three amino acids are:

Amino acid	Extinction Coefficient ε (λ_{max})
Trp	5,050 $M^{-1} cm^{-1}$ (280 nm)
Tyr	1,440 $M^{-1} cm^{-1}$ (274 nm)
Phe	220 $M^{-1} cm^{-1}$ (257 nm)

The amount of light absorbed by a solution of concentration [X] is given by the Beer-Lambert Law :

$$A = \log \frac{I_0}{I} = \varepsilon [X] 1$$

where, A is termed the "absorbance" of the sample;

I_0 is the intensity of the incident light;

I is the intensity of the light that leaves the sample;

ε is the molar extinction coefficient at a specific wavelength, *e.g.* at λ_{max};

[X] is the concentration of the absorbing species; and

l is the path length (usually 1 cm).

A solution that does not absorb any light ($I = I_0$) has an absorbance of 0. A solution that absorbs most of the light that passes through it, has a large absorbance. For example, if 90% of the light was absorbed, $I_0 / I = 10$, and $A = 1.0$.

The above table shows that Trp absorbs than the strongest UV light. Furthermore, since both Trp and Tyr show the maximum light absorbance at approximately 280 nm the absorption maximum of most proteins is around 280 nm. In contrast, the absorption maximum for nucleic acids is approximately 260 nm.

Charge

Monomeric amino acids have an alpha amino group and a carboxyl group, both of which may be protonated or deprotonated, and *a R* group, some of which may be protonated or deprotonated. When the amino group is protonated it has *a* + 1 charge, and the carboxyl group as *a*0 charge while when the amino group is deprotonated it has no charge and the carboxyl group has *a* – 1 charge. The *Henderson Hasselbach* equation gives us a way to determine the charge state of any ionizable group knowing the pKa of the group. Each functional group on being protonated forms HA, and on deprotonated form A. The charge of HA and A will be determined by the functional group. The Ka for the reaction is :

$$Ka = [H_3O^+] [A] / [HA].$$

or $$[H_3O^+] = Ka[HA] / [A].$$

$$- \log [H_3O^+] = - \log Ka + \log [A] / [HA]$$

or $$pH = pKa + \log [A] / [HA]$$

This is the famous Henderson-Hasselbach (HH) equation.

The properties of a protein will be determined partly by whether the side chain functional groups, the N terminal, and the C terminal are charged or not. The HH equation tells us that this will depend on the pH and the pKa of the functional group.

- If the pH is 2 units below the pKa, the HH equation becomes, – 2 = log A/HA, or .01 = A/HA. This means that the functional group will be about 99% protonated (with either 0 or +1 charge, depending on the functional group).
- If the pH is 2 units above the pKa, the HH equation becomes 2 = log A/HA, or 100 = A/HA. Therefore the functional group will be 99% deprotonated.
- If the pH = pka, the HH equation becomes 0 = log A/HA, or 1 = A/HA. Therefore the functional group will be 50% deprotonated

From these simple examples, a simple ± 2 is derived. This rule is used to quickly determine protonation, and hence charge state.

1.4. SUMMARY

Amino acids are the building blocks of proteins. The 20 amino acids that are found within proteins convey a vast array of chemical versatility. Humans can produce 10 of the 20 amino acids because they do not have all the enzymes required for the biosynthesis of all of the amino acids. The 10 amino acids that humans can produce are alanine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, proline, serine and tyrosine. The other 10 amino acids are arginine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, and valine. These amino acids are required in the diet.

1.5. STUDENT ACTIVITY

1. What are amino acids?

   _____

   _____

   _____

2. Name 2 ways your body uses amino acids.

   _____

   _____

   _____

3. Give the general structure of an amino acid and discuss the R group.

   _____

   _____

   _____

1.6. TEST YOURSELF

1. Amino acids linked together to make proteins by removing a molecule of _____ in a process called _____.
2. Chains of amino acids make _____ which can join together to make a _____.
3. _____ bonds form when water is removed to hold _____ acids together.

ANSWERS

1. Water, condensation
2. Polymers, protein
3. Peptid, amino.

❑❑❑

UNIT

2

CARBOHYDRATES AND LIPIDS

STRUCTURE

- Classification of carbohydrates
- Functions of carbohydrates
- Structure and functions of lipids
- Summary
- Student Activity
- Test yourself

LEARNING OBJECTIVES

After going through this unit you will learn:

What are carbohydrates ?

What are the functions of carbohydrates ?

What are basic properties of lipids ?

Carbohydrates are the main energy source for the body. This is because they can be converted more readily into glucose, the form of sugar that is transported and used by the body.

2.1. CLASSIFICATION OF CARBOHYDRATES

The carbohydrates are divided into three major classes on the basis of whether or not they undergo hydrolysis, and if they do, on the number of products formed.

(i) Monosaccharides : The monosaccharides are polyhydroxy aldehydes or polyhydroxy ketones which cannot be decomposed by hydrolysis to give simpler carbohydrates. Examples are glucose and fructose.

$$\underset{\substack{\text{glucose or}\\ \text{fructose}}}{C_6H_{12}O_6} + H_2O \xrightarrow{H^+} \text{No reaction}$$

Monosaccharides are further classified according to three different characteristics:

(a) The placement of its carbonyl group: If the carbonyl group is an aldehyde, the monosaccharide is an aldose; if the carbonyl group is a ketone, the monosaccharide is a ketose.

(b) The number of carbon atoms it contains: Monosaccharides with three carbon atoms are called trioses, those with four are called tetroses, five are called pentoses, six are hexoses, and so on.

Table 1: Classifications of Monosaccharide on the basis of number of carbons

Number of Carbons	Category Name	Examples
4	Tetrose	Erythrose, Threose
5	Pentose	Arabinose, Ribose, Ribulose, Xylose, Xylulose, Lyxose
6	Hexose	Allose, Altrose, Fructose, Galactose, Glucose, Gulose, Idose, Mannose, Sorbose, Talose, Tagatose
7	Heptose	Sedoheptulose, Mannoheptulose

(c) **Chiral handedness:** Each carbon atom bearing a hydroxyl group (–OH), with the exception of the first and last carbons, are asymmetric, making them stereo centers with two possible configurations (R or S). Because of this asymmetry, a number of isomers may exist for any given monosaccharide formula. The aldohexose *D*-glucose, for example, has the formula $(CH_2O)_6$, of which all but two of its six carbon atoms are stereogenic, making D-glucose one of $2^4 = 16$ possible stereoisomers.

(ii) Oligosaccharides: The oligosaccharides are carbohydrates, which yield a definite number (2-9) of monosaccharide molecules on hydrolysis. They include,

(*a*) *Disaccharides :* These are the compounds, which yield two monosaccharide molecules on hydrolysis. Examples are sucrose and maltose.

$$\underset{\text{sucrose}}{C_{12}H_{22}O_{11}} + H_2O \xrightarrow{H^+} \underset{\text{glucose}}{C_6H_{12}O_6} + \underset{\text{fructose}}{C_6H_{12}O_6}$$

$$\underset{\text{Maltose}}{C_{12}H_{22}O_{11}} + H_2O \xrightarrow{H^+} 2\underset{\text{glucose}}{C_6H_{12}O_6}$$

(*b*) *Trisaccharides:* Trisaccharides are the carbohydrates which yield three monosaccharide molecules on hydrolysis. Example is raffinose, which has molecular formula, $C_{18}H_{32}O_{16}$.

$$\underset{\text{raffinose}}{C_{18}H_{32}O_{16}} + 2H_2O \xrightarrow{H^+} \underset{\text{glucose}}{C_6H_{12}O_6} + \underset{\text{fructose}}{C_6H_{12}O_6} + \underset{\text{galactose}}{C_6H_{22}O_6}$$

(*c*) *Tetrasaccharides, etc.*

(iii) Polysaccharides: The polysaccahrides are carbohydrates of high molecular weight which yield many monosaccharide molecules on hydrolysis. Examples are starch and cellulose.

$$\underset{\text{starch}}{(C_6H_{10}O_5)_n} + nH_2O \xrightarrow{H^+} \underset{\text{glucose}}{nC_6H_{12}O_6}$$

In general, the monosaccharides and oligosaccharides are crystalline solids, soluble in water and sweet to taste. They are collectively known as sugars. The polysaccharides, on the other hand, are amorphous, insoluble in water and tasteless. They are called non-sugars. The carbohydrates may also be classified as either reducing or non-reducing sugars. All those carbohydrates which have the ability to reduce Fehling's solution and Tollen's reagent are referred to as reducing sugars, while others are non-reducing sugars. All monosaccharides and the disaccharides other than sucrose are reducing sugars.

2.2. STRUCTURE OF CARBOHYDRATES

Carbohydrates consist of the elements carbon (C), hydrogen (H) and oxygen (O) with a ratio of hydrogen twice that of carbon and oxygen. Carbohydrates include sugars, starches, cellulose and many other compounds found in living organisms. In their basic form, carbohydrates are simple sugars or monosaccharides. These simple sugars can combine with each other to form more complex carbohydrates.

Starch and cellulose are two common carbohydrates. Both are macromolecules with molecular weights in the hundreds of thousands. Both are "**polysaccharides**" that is, each is built from repeating units of monomers.

(I) Monosaccharides

Three common sugars, glucose, galactose and fructose, have the same molecular formula: $C_6H_{12}O_6$. Because of their six carbon atoms, each is a **hexose**.

Although all three share the same molecular formula ($C_6H_{12}O_6$), the arrangement of atoms differs in each case. Substances such as these three, which have identical molecular formulas but different structural formulas, are known as **structural isomers**.

Glucose, galactose, and fructose are "single" sugars or **monosaccharides**. Two *monosaccharides can be linked together to form a* "double" sugar or **disaccharide**.

(II) Disaccharides

Disaccharides are the carbohydrates with two monomer units. Although the process of linking the two monomers is rather complex, the end result in each case is the loss of a hydrogen atom (H) from one of the monosaccharides and a hydroxyl group (OH) from the other. The resulting linkage between the sugars is called a **glycosidic bond**.

(III) Polysaccharides

Starches : *Starches are polymers of glucose. Two types of starches are found:*

- **amylose** consists of linear, unbranched chains of several hundred glucose residues (units). The glucose residues are linked by a glycosidic bond between their 1st and 4th carbon atoms.
- **amylopectin** differs from amylose in being highly branched. At approximately every thirtieth residue along the chain, a short side chain is attached by a glycosidic bond to the 6th carbon atom (the carbon above the ring). The total number of glucose residues in a molecule of amylopectin *is several thousand.*

Glycogen : The structure of glycogen is similar to that of amylopectin, although the branches in glycogen tend to be shorter and more frequent.

2.3. FUNCTIONS OF CARBOHYDRATES

All animals derive the major portion of their food calories from the different types of Carbohydrates in their diets. Most of the energy for the metabolic activities of the cell in all organisms is derived from the oxidation of Carbohydrate. Important functions *of Carbohydrate are listed below.*

1. **Carbohydrate functions as Bio Fuel:** Carbohydrate functions as an energy source of the body and acts as Bio fuel. Step wise details for the process of production of energy are discussed below.
   (a) Polysaccharides such as starch and glycogen are first hydrolyzed by enzymes to Glucose.
   (b) Glucose is the transported from one cell to another by blood in case of animals and cell sap in case of plants.

(c) Glucose is then oxidized to produce carbon dioxide and water.

(d) Energy is released in this process which is used for functioning of the cells.

2. **Carbohydrate as protector:** Fats, proteins and carbohydrates all provide energy but **carbohydrate functions as primary source of energy**. Fats are only burned if there is non availability of carbohydrates. When fat is burned in absence of carbohydrates, toxic compounds like **ketone bodies** are produced. Accumulation of these ketone bodies over long period causes **ketosis** in which blood becomes unable to carry oxygen properly and results in death of organism. Thus, one of the important function of carbohydrate is to burn fat and to protect organism.

3. **Carbohydrate as stored food:** Different forms of Carbohydrate are stored in living organism as storage food.

(a) Polysaccharide (starch) acts as storage food for plants.

(b) Glycogen stored in liver and muscles acts as storage food for animals.

(c) Inulin acts as storage food of dahlias, onion and garlic.

Thus carbohydrate performs the function of storing food.

4. **Carbohydrate as framework in body:** Different Carbohydrates especially Polysaccharides act as framework in living organism.

(a) Cellulose forms cell wall of plant cell along with hemicelluloses and Pectin.

(b) Chitin forms cell wall of fungal cell and exoskeleton of arthropods.

(c) Peptidoglycan forms cell wall of bacteria and cyanobacteria.

Thus carbohydrates function as contributing material to the cellular structure.

5. **Carbohydrate as Anticoagulant:** Heparin is a polysaccharide (carbohydrate) which acts as anticoagulant and prevents intravascular clotting.

6. **Carbohydrate as Antigen:** Many antigens are glycoprotein (which contains oligosaccharide) in nature and give immunological properties to the blood.

7. **Carbohydrate as Hormone:** Many Hormones like FSH (Follicular Stimulating Hormone) and LH (Leutinizing Hormone) are glycoprotein and help in reproductive processes.

8. **Carbohydrate provide raw material for industry:** Carbohydrates are an important component of many industries like textile, paper, laequers and breweries.

9. **Other Functions**

(a) **Agar** is polysaccharide used in culture media, laxative and food.

(b) **Cellulose** acts as roughage of food. It stimulates peristalsis movement and secretion of digestive enzymes.

(c) **Hyaluronic acid** found in between joints acts as synovial fluid and provides frictionless movement.

2.4. LIPIDS

Lipids are organic substances present in all living organisms. They include fats, oils, waxes and other related compounds. The term lipid describes a group of biological compounds that are insoluble in water but are relatively soluble in many organic solvents. Thus, unlike the other major groups of biological molecules—(proteins,

carbohydrates, and nucleic acids) lipids are categorized by a physical property rather than by structural features. They are esters of long chain fatty acids and alcohols.

2.5. CLASSIFICATION OF LIPIDS

They are broadly classified into simple lipids, complex lipids, derived lipids and miscellaneous lipids based on their chemical composition.

1. **Simple Lipids:** These lipids are the esters of fatty acids with alcohols. They are of two types; triglycerols, fatty acids, sterols and waxes.

   (a) Triglycerols (fats and Oils): They are esters of fatty acids with glycerol. They are insoluble in water, non-polar in character, and are commonly called neutral fats.

   (b) Fatty acids: A fatty acid is a long-chain monocarboxylic acid.

   (c) Sterols: Sterols are a special class of alcohols, containing a fused four-ring structure, or steroid nucleus. Sterols may combine with a fatty acid to form sterol esters.

   (d) *Waxes: They are the esters of fatty acids long chain monohydroxy* alcohols other than glycerol. They have higher melting points then neutral fats.

2. **Complex Lipids or Compound Lipids (heterolipids) :** Complex lipids with additional groups are called compound lipids. These lipids are esters of fatty acids with alcohols and other groups such as phosphate, nitrogenous base, etc. They are again divided into 3 types.

   (a) Phospholipids (phosphatids): These lipids contain phosphoric acid, fatty acid, nitrogenous base and alcohol. They are again sub-divided into

   - Glycero Phosphlipids: These contain glycerol as alcohol. They are also called phosphoglycerides.
   - Sphingophospholipids:These contain sphingosine as alcohol. They are also called as *sphingomyelins.*

   *(b) Glycolipids:*They contain a fatty acid, carbohydrate and nitrogenous base but no phosphorus. They are also called as glycosphingo lipids. They have sphingosine as alcohol.

   (c) ***Lipo Proteins:* These are the macromolecular complexes of lipids with proteins.**

3. **Derived Lipids:** These lipids are obtained on hydrolysis of simple and complex lipids. These lipids contain glycerol and other alcohols. This class of lipids includes steroid hormones, ketone bodies, hydrocarbons, fatty acids, fatty alcohols, mono and diglycerides, terpenes and carotenoids. These are sometimes present as waste products of metabolism.

4. **Miscellaneous Lipids:** These include compounds, which contain characteristics of lipids. They include squalene, terpenes, hydrocarbons, carotenoids, etc.

2.6. STRUCTURE OF LIPIDS

1. Simple Lipids :

(a) *Triglycerides:* These are esters of glycerol with long chain fatty acids. Fatty acids always have an even number of carbons and may be saturated or unsaturated.

(b) *Waxes:* They are esters of long chain saturated and unsaturated fatty acids with long chain monohydroxy alcohols. The fatty acids range between C_{14} and C_{36} and the alcohols range from C_{16} to C_{36}. Most of the waxes are mixtures.

2. Complex Lipids: Among the complex lipids important structural types are phosphoglycerides, phosphosphingo lipids and glycolipids. The parent phosphoglyceride, phosphatidic acid, is similar in structure to a triglyceride except that the 3-hydroxyl group of the glycerol component is esterified to phosphoric acid rather than to fatty acid.

Further esterification of the phosphoric acid of , phosphatidic acid with a variety of small, hydroxyl-containing molecules leads to a series of derived phosphoglycerides, including phosphatidyl choline, commonly known as lecithin, phosphatidyl ethanolamine, and phosphatidyl serine.

The sphingophospholipids are derived from sphingosine, a long-chain dialcohol with an amino group. The formation of an amide with an fatty acid at one point along this chain yields ceramide. Esterification of a ceramide derivative with phosphorylcholine yields sphingomyelin, which is the major phospho-sphingolipid.

2.7. FUNCTIONS OF LIPIDS

Lipids perform several important functions in biosystems.

- Phospholipids are the constituents of cell mebrane and regulate membrane permeability.
- Phospholipids are also used as detergents to emulsify fat for transport within the body.
- They act as cellular metabolic regulators.
- They protect internal organs, serve as insulating materials and give shape and smoothness to the body.
- They serve as a source of fat-soluble vitamins.
- Essential fatty acids are useful for transport of cholesterol, formation of lipoproteins, etc.
- Triacyl glycerols are the concentrated fuel reserves of the body.
- Phospholipids in mitochondria are responsible for confirmation of electron transport chain components.
- Accumulation of fat in liver is prevented by phospholipids.
- Phospholipids help in removal of cholesterol from the body by participating in reverse cholesterol transport.
- Cholesterol is a constituent of membrane structure and it synthesizes bile acids, hormones and vitamin D. It is the principal sterol of higher animals.

2.8. SUMMARY

Carbohydrates are an ideal source of energy for the body. These can be classified into three main classes called the monosaccarides, disaccharides and polysaccharides. Mono saccarides are again divided on the basis of number of carbon it has.

Lipids are organic substances present in all living organisms. They include fats, oils, waxes and other related compounds.

2.9. STUDENT ACTIVITY

1. Which elements do carbohydrates contain, and in what ratio?

2. What are disaccharides ? Give an example.

3. In how many classes lipids can be classified ? Give the name of those classes.

2.10. TEST YOURSELF

1. Based on their molecular formulas, which of the following are NOT carbohydrates?
   (a) $C_3H_8O_3$
   (b) $C_{10}H_{18}O_9$
   (c) $C_{18}H_{32}O_{16}$
   (d) $C_4H_8O_2$
   (e) $C_{16}H_{32}O_2$
   (f) $C_6H_{12}O_6$
2. For each molecule below, determine if it is a monosaccharide, a disaccharide, or a polysaccharide:
   (a) Fructose
   (b) Ribose
   (c) Cellulose
   (d) Glucose
   (e) Sucrose
   (f) Glycogen
   (g) Starch
   (h) Maltose
3. Name a disaccharide.
4. Most lipids are made of _____ acids.

5. Hydophilic means water _____.
6. The nonpolar end of a fatty acid is said to be _____ or "water fearing".
7. Plant pigments like _____ are also _____.

ANSWERS

1. a, b, c, f, 2. Monosaccarides-a, b, d, Disaccarides-e, h Polysaccarides-c, f, g,
3. Sucrose, 4. Amino, 5. oving, 6. Hydrophobic, 7. Chlorophyll, lipids.

❑❑❑

UNIT

3

VITAMINS

STRUCTURE

- Introduction
- History of Vitamins
- Structure of Vitamins
- Functions of Vitamins
- Summary
- Student Activity
- Test yourself

LEARNING OBJECTIVES

After going through this unit you will learn:

What are vitamins ?

What are the structures of different vitamins ?

Why vitamins are important in our life ?

3.1. INTRODUCTION OF VITAMINS

A **vitamin** is an organic compound required as a vital nutrient in tiny amounts by an organism. When it cannot be synthesized in sufficient quantities by an organism, must be obtained from the diet. Thus, the term is conditional both on the circumstances and on the particular organism. For example, ascorbic acid (vitamin C) is a vitamin for humans, but not for most other animals, and biotin and vitamin D are required in the human diet only in certain circumstances. Thirteen vitamins are universally recognized at present.

Vitamins are classified by their biological and chemical activity and not by their chemical structure. Thus, each "vitamin" refers to a number of *vitamer* compounds that all show the biological activity associated with a particular vitamin. Such a set of chemicals is grouped under an alphabetized vitamin "generic descriptor" title, for example "vitamin A", which includes the compounds retinal, retinol as vitamer. Vitamers by definition are convertible to the active form of the vitamin in the body, and are sometimes inter-convertible as well.

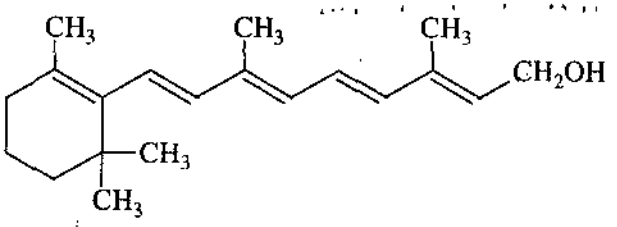
3.2. HISTORY OF VITAMINS

In 1905, an Englishmen, William Fletcher determine that if special factors (vitamins) were removed from food disease occurred. Doctor Fletcher was researching the causes of the disease Beriberi when he discovered that eating unpolished rice prevented Beriberi.

In 1906, English biochemist Sir Frederick Gowland Hopkins also discovered that certain food factors were important to health. The name *vitamin* is derived from the Latin words *vita* (meaning life) and *amine* (an organic chemical nitrogen containing molecule). This name was used for the first time by Kasimir Funk in 1910.

3.3. STRUCTURE OF VITAMINS

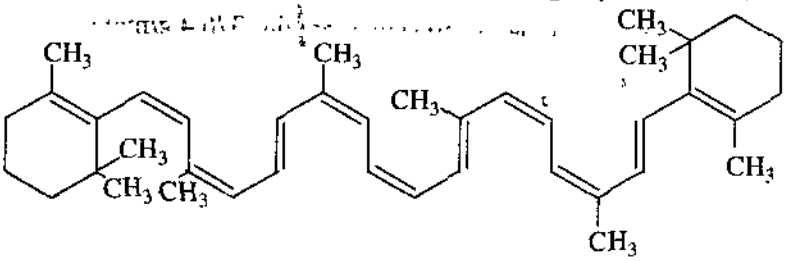
Vitamin A



Chemical name: Retinol or All-Trans-Retinol

Molecular formula: $C_{20}H_{30}O$; Molecular weight: 286.46 g/mole

The pro-vitamin of vitamin A is Beta-carotene (orange dye of carrots).



Chemical name: Beta-Carotene

Molecular formula: $C_{40}H_{56}$; Molecular weight: 536.90 g/mole

Vitamin A is a fat-soluble vitamin.

Retinol is probably formed by an oxidative splitting of the beta-carotene in the small intestine. That is why beta-carotene is also called pro-vitamin A.

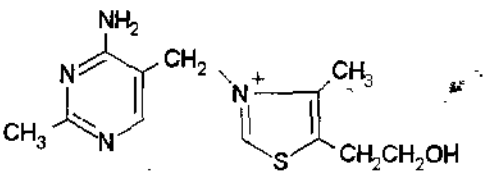
Vitamin B-complex

Vitamin B consisted out of more than one vitamin. To distinguish the different vitamins they were numbered 1 to 13. Later on, some vitamins were removed from the B-complex because they were found not to be real vitamins. Finality, 8 vitamins were left, namly :

1. B1 / Thiamine,
2. B2 / Riboflavin,
3. B3 / Nicotinic acid,
4. B5 / Pantothenic acid,
5. B6 / Pyridoxine,
6. B8 / Biotin,
7. B11 / Folic acid,
8. B12 / Cobalamin.

These vitamins from the B-complex are all active in the metabolism of the body. They are all water-soluble and are all precursors of coenzymes.

Vitamin B1

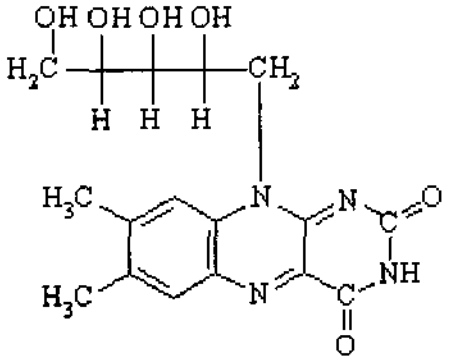


Chemical name: Thiamine

Molecular formula: $C_{12}H_{17}N_4OS$; Molecular weight: 265.36 g/mole

Vitamin B1 is a water-soluble and sulphur containing vitamin.

Vitamin B2

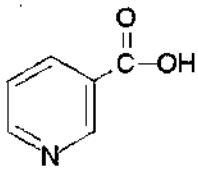


Chemical name: Riboflavin or Lactoflavin

Molecular formula: $C_{17}H_{20}O_6N_4$; Molecular weight: 376.4 g/mole.

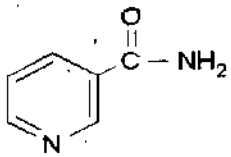
Vitamin B3

There are two forms of vitamin B3 nicotinic acid and nicotinamide.



Chemical name: Niacin or Nicotinic acid

Molecular formula: $C_6H_5NO_2$; Molecular weight: 123.11 g/mole

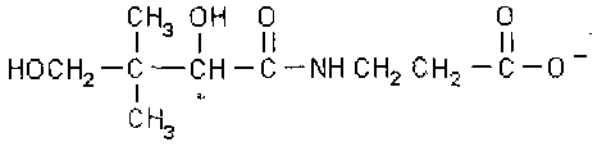


Chemical name: Niacin or Nicotinamide

Molecular formula: $C_6H_6N_2O$; Molecular weight: 122.13 g/mole

Vitamin B3 is a water-soluble vitamin.

Vitamin B5

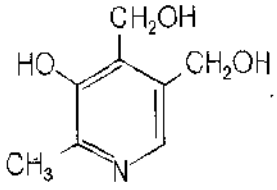


Chemical name: Pantathenic acid

Molecular formula: $C_9H_{16}O_5N$; Molecular weight: 218.23 g/mole

Vitamin B5 is water-soluble.

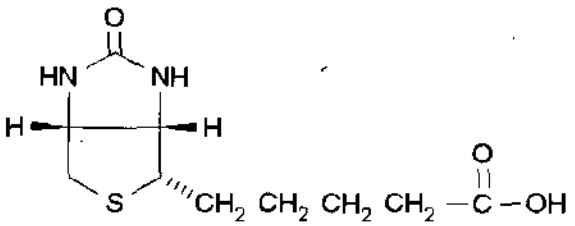
Vitamin B6



Chemical name: Pyridoxine

Molecular formula: $C_8H_{11}NO_3$; Molecular weight: 169.18 g/mole.

Vitamin B8

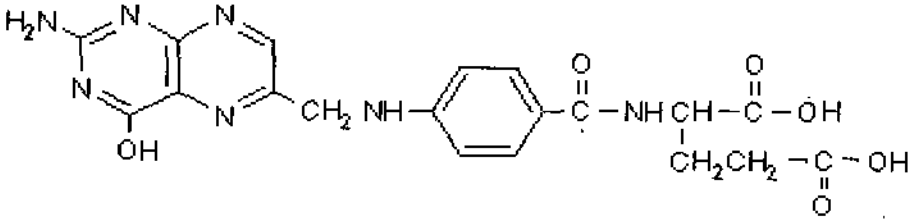


Chemical name: D-Biotin

Molecular formula: $C_{10}H_{16}N_2O_3S$; Molecular weight: 244.3 g/mole

Although biotin is also called vitamin H, it is part of the B-family and is also called vitamin B8. Biotin is a water-soluble vitamin. It can be converted in the body into the coenzyme biocytin (Molecular formula: $C_{16}H_{28}N_4O_4S$; Molecular weight: 372.5 g/mole).

Vitamin B9

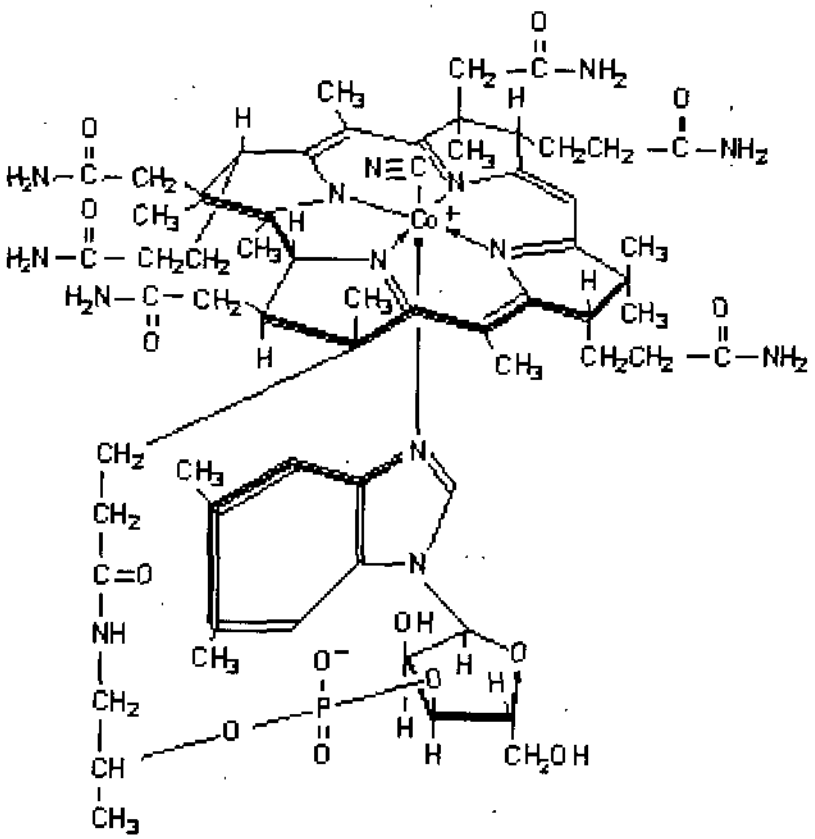


Chemical name: Folic acid

Molecular formula: $C_{19}H_{19}N_7O_6$; Molecular weight: 441.40 g/mole

Folic acid is just as all vitamin from the vitamin B family water-soluble.

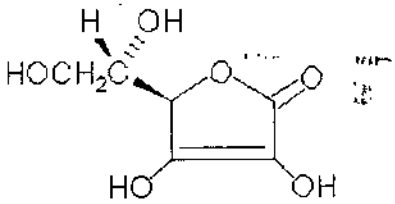
Vitamin B12



Chemical name: Cobalamin

Molecular formula: $C_{63}H_{88}CoN_{14}O_{14}P$; Molecular weight: 1355.4 g/mole

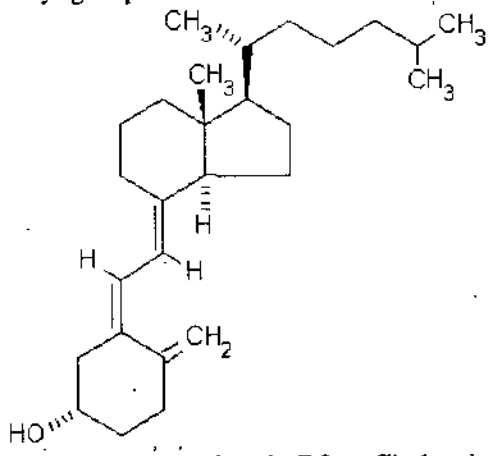
Vitamin C



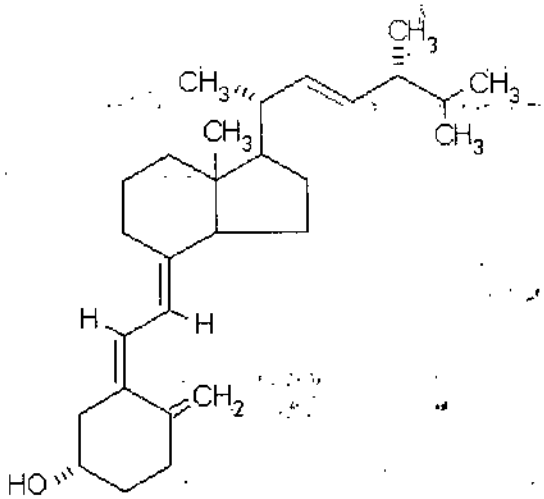
Chemical name: L-Ascorbic Acid, L-ascorbate, or E300
Molecular formula: $C_6H_8O_6$; Molecular weight: 176.12 g/mole
Vitamin C is a water-soluble vitamin.

Vitamin D

There are two forms of vitamin D – D3 and D2. Vitamin D2 differs only with one, double bond and one methyl group from vitamin D3.



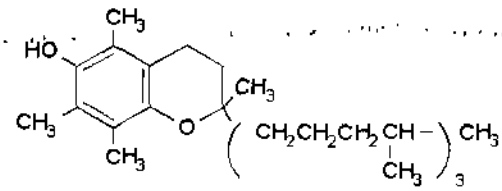
Chemical name: vitamin D3 or Cholecalciferol
Molecular formula: $C_{27}H_{44}O$; Molecular weight: 384.6 g/mole



Chemical name: vitamin D2, Calciferol or Ergosterol
Molecular formula: $C_{28}H_{44}O$; Molecular weight: 396.7 g/mole

Vitamin D is an fat-soluble vitamin. Vitamin D3 is formed in our body from cholesterol under influence of ultraviolet light. The antirachitic properties of UV-light rest on the formation of vitamin D3. Vitamin D2 is also formed from cholesterol, but via another pathway. Vitamin D2 and D3 have biologically the same function. Therefore vitamin D2 is also used as a food supplement.

Vitamin E

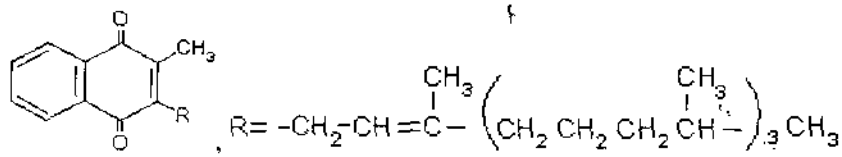


Chemical name: D-Alpha-Tocopherol
Molecular formula: $C_{29}H_{50}O_2$; Molecular weight: 430.7 g/mole
Vitamin E is an fat-soluble vitamin.

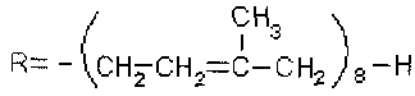
Vitamin K

There are three forms of vitamin K – K1, K2 and K3.

All three forms have the same basic structure as indicated below. The rest group (R) is different in the three forms.



Chemical name: Vitamin K1 or Phylloquinone
Molecular formula: $C_{31}H_{46}O_2$; Molecular weight: 450.68 g/mole



Chemical name: vitamin K2 or Menaquinine

R= -H

Chemical name: vitamin K3 or Menadione
Vitamin K is a fat-soluble vitamin.

3.4. FUNCTIONS OF VITAMINS

Vitamins have diverse biochemical functions. Either they work as regulators of metabolism cell and tissue growth or function as antioxidants. The largest numbers of vitamins (*e.g.,* B complex vitamins) functions as precursors for enzyme cofactors, which help enzymes in their work as catalysts in metabolism. In this role, vitamins may be tightly bound to enzymes as part of prosthetic groups: For example, biotin is part of enzymes involved in making fatty acids. Vitamins may also be less tightly bound to enzyme catalysts as coenzymes, detachable molecules that function to carry chemical groups or electrons between molecules.

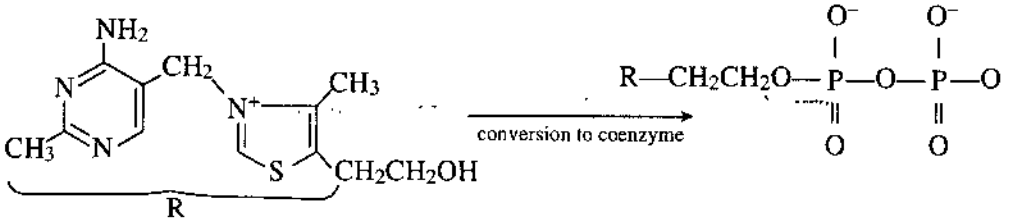
Vitamin A: It is used for growing healthy new cells like skin, bones, and hair. Also is used for surface lining upkeep of the eyes, urinary tract, intestinal tract, and respiratory system. Night vision is also assisted by Vitamin A. Vitamin A also performs other major functions in the body. It is required for reproductive functions such as normal growth and development of sperm and ovaries. Vitamin A also helps vision by keeping cells which are used for transduction of light into nerve signals healthy. Vitamin can be found from certain foods such as egg yolk, whole milk, and butter.

Vitamin B: are essential for creating dopamine, epinephrine, serotonin, and myelin. They also help the mind to focus, help hemoglobin to hold oxygen and lower cholesterol. Vitamin B is essential to good health. It is also used for energy production in the human cells. These vitamins help to convert food often consumed as

carbohydrates into ATPs. They also help the nervous system to function properly. Good sources of Vitamin B are bananas, potatoes, whole grains, and chilli peppers.

Vitamin B1: Thiamin is another name for vitamin B1. It helps to convert blood sugar into energy for your body. It also helps the mucous membranes of the muscular, cardiovascular, and nervous systems in good shape.

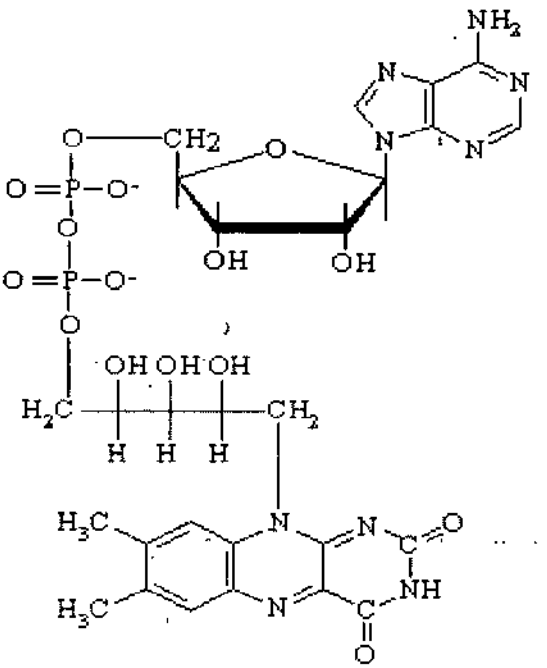
Vitamin B1 is necessary in the metabolism. It is active in the body as a coenzyme that is called thiamine di-phosphate or thiamine pyrophosphate. It is almost the same molecule as thiamine. The only difference is that there are two phosphate groups attached instead of a hydrogen atom.



Vitamin B1

This coenzyme prepares pyruvate for the further breakdown in the citric acid cycle. This coenzyme helps to decarboxylate (= to split off a carbon atom) pyruvate as part of the enzyme pyruvate dehydrogenase complex. It is also a part of the enzyme alpha-ketoglutarate dehydrogenase complex that is also active in the citric acid cycle. In that way it regulates especially the carbohydrate breakdown in which energies are obtained.

Vitamin B2: Riboflavin is another name for vitamin B2. It works with the other B vitamin complexes to process the carbohydrates, proteins, and fats into calories for energy in body.



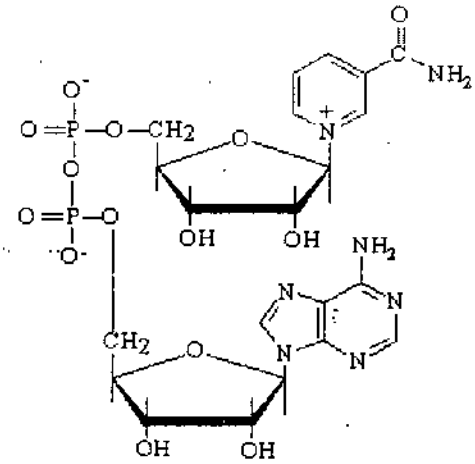
The body also needs this for healthy skin, good vision, growth, and red blood cell creation. In the body riboflavin is transformed into the coenzyme that is called Flavin Adenine Dinucleotid, FAD.

This coenzyme is active as a redox potential. This means that in this molecule energy can be stored. It is active in the citric acid cycle.

Vitamin B3: Niacin is another name for vitamin B3. It also works with other B vitamin complexes to process the carbohydrates, proteins, and fats into calories for energy in the body. The difference is that it helps the digestive system functions along

with promoting a healthy appetite and healthy nerves. Large doses of niacin could lower LDL cholesterol but large doses is recommended to be taken under physician supervision.

In the body niacin is converted into a coenzyme, which is called nicotinamine adenine dinucleotide, NAD.



This coenzyme is active as a redox potential, this means that in this molecule energy can be stored and subsequently be taken. The energy is in the form of hydrogen atoms. Because NAD is always recycled by "recharging" (in the catabolism) and using (in the anabolism), only little (18 mg) of this vitamin is necessary in our daily diet. The coenzyme is active in the citric acid cycle and in the glycolysis.

Vitamin B5: Pantathenic Acid is another name for vitamin B5. Like B3 and B2 it helps to break down carbohydrates, proteins, and fats for energy. Some good sources of Vitamin B5 are meat, pea, and whole grain cereals

Vitamin B6: Pyridoxine is another name for Vitamin B6. Vitamin B6 working along with B12 and B9 helps prevent heart attacks. Just like B2, B3 and B5 this vitamin helps the body to process proteins, carbohydrates, and fats into energy. Some good sources of B6 is from meats, eggs, soybeans, whole grains, and nuts.

Vitamin B7: Vitamin H or Biotin are other names for Vitamin B7. Vitamin B7 helps in the formation of fatty acids and glucose to be used as fuel for the body. Some good sources of B7 is from bananas, yeast, cereal, and liver.

Vitamin B9: Folic Acid is another name for vitamin B9. It is very important during pregnancy since it is used for making and maintaining new cells. B9 prevents anemia by keeping up the production of red blood cells and prevent low birth weight and prematurity in births. Some good sources of B9 is from mushrooms, leafy greens, vegetables, peas, and broccoli.

Vitamin B12: Cobalamin is another name for vitamin B12. It works with B9 in keeping red blood cells healthy and also helps to keep the central nervous system healthy. Some good sources of B12 are meat, eggs, and dairy. The two organizations that create guidlines for vitamin intake are by the Food and Nutrition Board of the National Academy of Sciences and the Food and Drug Administration(FDA). In the body vitamin B12 can be converted into a coenzyme (coenzyme B12) by a addition of a ribose- and an adenine molecule as a rest group.

This coenzyme is necessary for the function of two enzymes. Firstly for an enzyme which functions in the fatty acid metabolism, namely *methylmalonyl-CoA mutase*. This enzyme is one of the enzymes that is responsible for the breakdown of fatty acids with an odd number of carbon atoms.

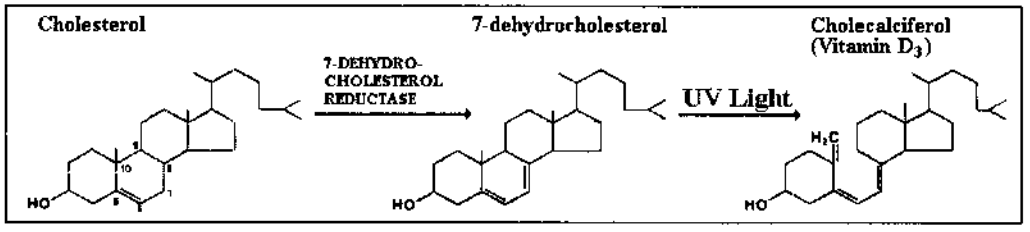
Vitamin C: It helps to regulate the immune system and relieve pain caused by tired muscles. It is also needed in the manufacture of collagen and norepinephrine. Vitamin C is also an antioxidant which can enhance the immune system by stimulating white blood cells in the body. Vitamin C also helps to benefit the skin, teeth and bones. Vitamin C is often found in citrus fruits such as papayas, oranges, and lemons.

Vitamin D: is needed for the body to properly use calcium and phosphorous. It is also used in the formation of some RNA to maintain a normal heart beat, keep a stable nervous system and blood clotting. Along with absorbing calcium, Vitamin D can also help to regulate the amount of calcium and phosphorus that is present in the blood. Vitamin D can be found in dairy products, fish, and oysters. Deficiency of Vitamin D causes severe growth retardation. The lack of calcium in the bones results in deformities of the skeleton, characterized by a widening at the ends of the long bones because of disorganization in the hypertrophy and maturation of chondrocytes in the epiphyseal plates. Vitamin D deficiency is also associated with a low-normal blood calcium, low or low-normal fasting blood phosphorus, and elevated parathyroid hormone (PTH) levels that cause a mineralization defect in the skeleton.

Specific biochemical functions of Vitamin D

1. The formation of vitamin D from cholesterol under influence of ultraviolet-light.

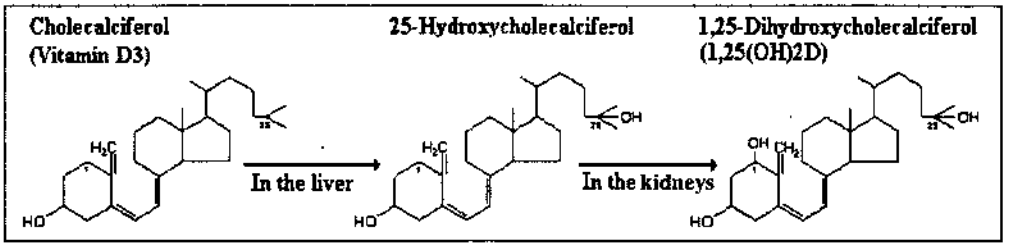
Vitamin D3 is formed in the body from cholesterol under influence of ultraviolet light. The antirachitic properties of UV light rests on the formation of vitamin D3. From cholesterol, 7-dehydrocholesterol is produced by removing a hydrogen atom from place 7 and 8. This reaction is catalysed by 7-dehydrocholesterol reductase. From this 7-dehydrocholesterol, vitamin D3 (cholecalciferol) is produced under the influence of UV light.



Vitamin D2 is also formed from cholesterol, but is vegetable and via another pathway. Vegetable ergosterol is made from cholesterol and this ergosterol is subsequently converted in ergocalciferol (vitamin D2). Under influence of UV-light Vitamin D2 and D3 have biologically the same function. Therefore vitamin D2 is also used as a food supplement.

2. Vitamin D activates a hormone in the calcium and hosphatemetabolism.

Vitamin D is actually a hormone. As vitamin D it is not active yet. It is made active in subsequent metabolic processes, firstly in the liver and after that in the kidneys. In the liver, an OH group is placed on carbon atom number 25 and in the kidneys also an OH group is placed but now on carbon atom number 1. The synthesised hormone is called 1, 25-dihydroxycholecalciferol or 1,25(OH)2D.



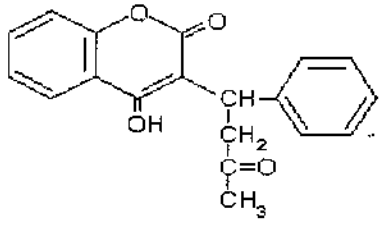
This hormone stimulates the production of Ca^{2+}-binding protein and is in this way responsible for the increased uptake of calcium (Ca) and phosphate ($P(PO_4^{2-})$ in the blood. Ca2+-binding protein transports calcium ions and phosphate ions from outside of the cell to the inside of the cell.

Vitamin E: is an antioxidant that helps the body get rid of free radicals to keep tissues healthy. It is also used in the creation of red blood cells. The use of vitamin A,C and K are assisted by Vitamin E. Although the role of Vitamin E is not completely understood but it is clear that it presents antioxidant properties in the body. They get rid of the free radicals in the body by preventing the oxidation of lipid-based cell membranes. Free radicals are very reactive and can steal electrons from membranes which could ultimately damage DNA. Good sources of Vitamin E are almonds, spinach, wheat, and asparagus. Of the many such dietary components, vitamin E has commanded most interest because of its availability, strong marketing potential, overall health impact, and central role in preventing oxidation at the cellular level.

Vitamin K:

1. It assists in creating proteins in the body like those that create blood clots. Vitamin K is indispensable for the formation of thrombin or prothrombin (thrombinogen) and other coagulation factors in the liver. Vitamin K's ability to help the clotting of blood is important for healing. The clotting ability could help in slowing or stopping bleeding in injured patients. During surgery, Vitamin K is often given to patients to reduce bleeding.

When vitamin K is missing or when a competitive inhibitor is present (like warfarin, a poison for rats), then abnormal thrombine is formed, that only shows 1% to 2% of the normal activity.



Normal active thrombine contains ten amino acids gamma- carboxyglutamate (gla). Abnormally, hardly active thombine on the other hand contains instead of gamma-carboxyglutamate (gla), glutamic acid (glu). From this it became clear that vitamin K functions as cofactor in the post translational processes in the formation of thrombine.

2. It also allows for calcium regulation within the body.

3. Vitamin K functions in the conversion of glutamic acid (glu) in gamma-carboxyglutamate (gla).

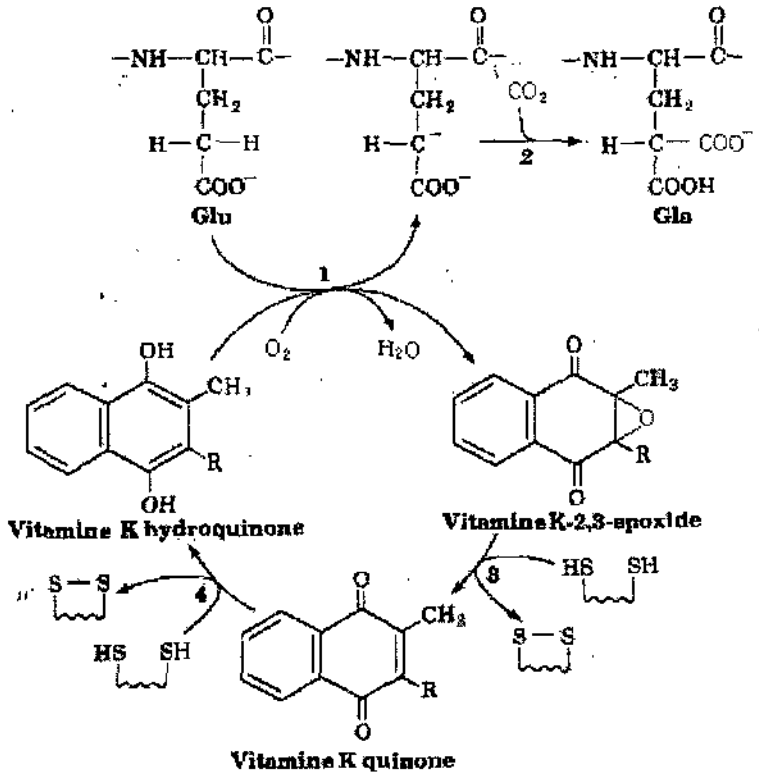
This image shows conversion of group "glu" into "gla".

Step 1: Vitamin K is in its active hydroquinone form and a H^+ ion (a proton) is removed from the "glu" in an oxygen (O_2) consuming reaction. Because of this reaction a carbon ion arises on the "glu" molecule.

Step 2: The "glu" carbon ion reacts with CO_2 so that "gla" arises.

Step 3 and 4: Active vitamin K in the hydroquinone form is regenerated in two reactions. These reactions are catalysed by the same enzyme that use thiols (like lipoic acid). The rat poison warfarin and also dicoumarol block these regeneration reactions.

It is shown below that how vitamin K is re-used. This explains why we only need a little (80 micro grams) of this vitamin in our daily diet.



3.5. SUMMARY

Vitamins are the organic compounds required as a vital nutrient in tiny amount by an organism. Vitamin were discovered in 1905 by an English men, Williom Fletcher, who determine that if special factors (vitamins) were removed from food disease occurred. Mainly vitamins could be A, B, C, D, E and K. All these vitamins play different roles in our body.

3.6. STUDENTS ACTIVITY

1. Explain the role of vitamin K in blood clotting reaction.

3.7. TEST YOURSELF

1. Which statement is true about a vitamin?
   (a) It cannot be synthesized by the body.
   (b) It is a macronutrient.
   (c) It supplies energy to the body.
   (d) It requires energy to be formed.
2. An important function of vitamin A is to:
   (a) help with blood clotting.
   (b) act as an anticoagulant.
   (c) helps to maintain eyesight.
   (d) prevent osteoporosis.
3. A deficiency of vitamin A in the body may result in :
   (a) bile obstruction.

(b) rapid breakdown of cell membranes.
(c) color blindness.
(d) night blindness.

4. The function of folic acid is to prevent:
   (a) neural tube defects.
   (b) visual disturbances.
   (c) pellagra.
   (d) dry, cracked lips.
5. Vitamin D is sometimes called the sunshine vitamin because:
   (a) the initial stage of synthesis occurs in the skin when exposed to sunlight.
   (b) the sunlight stimulates synthesis of vitamin D in foods.
   (c) the vitamin is degraded when exposed to sunlight.
   (d) in its natural form the vitamin has a bright yellow appearance.
6. A deficiency of vitamin D in growing children will result in the malformation of skeletal tissues called:
   (a) muscular dystrophy.
   (b) osteoporosis.
   (c) arthritis.
   (d) rickets.
7. The fat-soluble vitamin that is responsible for the synthesis of blood-clotting factors by the liver is:
   (a) A
   (b) D
   (c) E
   (d) K
8. In third world countries there is a high incidence of blindness in children due to a deficiency of vitamin ____.
   (a) A
   (b) D
   (c) E
   (d) K
9. A vitamin C deficiency is associated with the disease known as:
   (a) scurvy
   (b) pernicious anemia
   (c) rickets
   (d) beriberi
10. Vitamin C helps to maintain the integrity of tissues because it:
    (a) is incorporated into the cell membrane
    (b) creates a physical barrier
    (c) can recognize foreign substances
    (d) forms collagen to bind cells together

ANSWERS

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

❑❑❑

UNIT

4

STRUCTURE AND BIOLOGICAL SIGNIFICANCE OF PROTEINS

STRUCTURE

- Structure of Proteins
- Properties of Proteins
- Functions of Proteins
- *Summary*
- Student Activity
- Test yourself

LEARNING OBJECTIVES

After going through this unit you will learn:

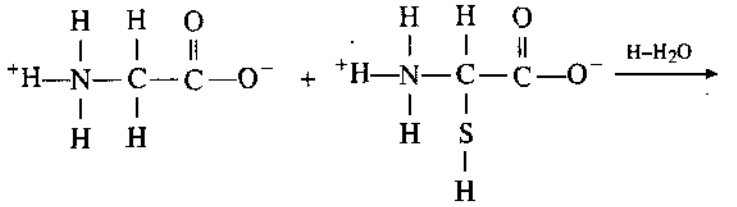
What are proteins ?

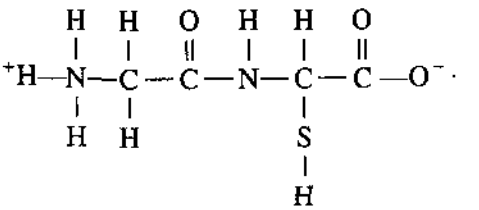
What is the basic structure of proteins ?

How proteins are beneficial for us ?

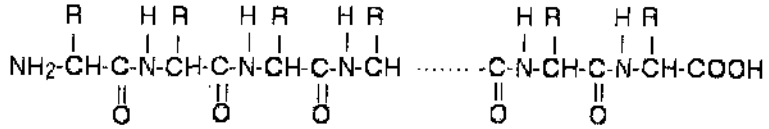
4.1. THE STRUCTURE OF PROTEINS

Proteins are polymers of amino acids joined together by peptide bonds into a chain. There are 20 different amino acids that make up essentially all proteins on earth. Amino acids are covalently bonded together in chains by peptide bonds. Peptide bonds are formed between the carboxyl group of one amino acid and the amino group of the next amino acid. Peptide bond formation occurs in a condensation reaction involving loss of a molecule of water. If the chain length is short (< 30 amino acids) it is called a peptide; longer chains are called polypeptides or proteins.





The head-to-tail arrangment of amino acids in a protein means that there is a amino group on one end (called the *amino-terminus* or *N-terminus*) and a carboxyl group on the other end (*carboxyl-terminus* or *C-terminus*). A protein chain (with the N-terminal on the left) will therefore look like this :



The "R" groups come from the 20 amino acids, which occur in proteins. The peptide chain is known as the ***backbone***, and the "R" groups are known as ***side chains***.

Structural features of proteins are usually described at four levels of complexity:

The primary structure of proteins: The term "primary structure" is used in two different ways.

At its simplest, the term is used to describe the order of the amino acids joined together to make the protein. In other words, if the "R" groups of the above structure is replaced by real groups we would have the primary structure of a particular protein.

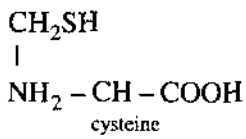
This primary structure is usually shown using abbreviations for the amino acid residues. These abbreviations commonly consist of three letters or one letter.

For example by using three letter abbreviations a bit of a protein chain might be represented as :

... Try.Gly.Lys.Pro.Val.Gly.Lys.Lys.Arg.Arg.Pro.Val.Lys.Val.Tyr.Pro.Ala.Gly.Gul...

If we follow the protein chain all the way to its left-hand end, we will find an amino acid residue with an unattached $-NH_2$ group. The N-terminal is always written on the left of a diagram for a protein's primary structure - whether we draw it in full or use these abbreviations.

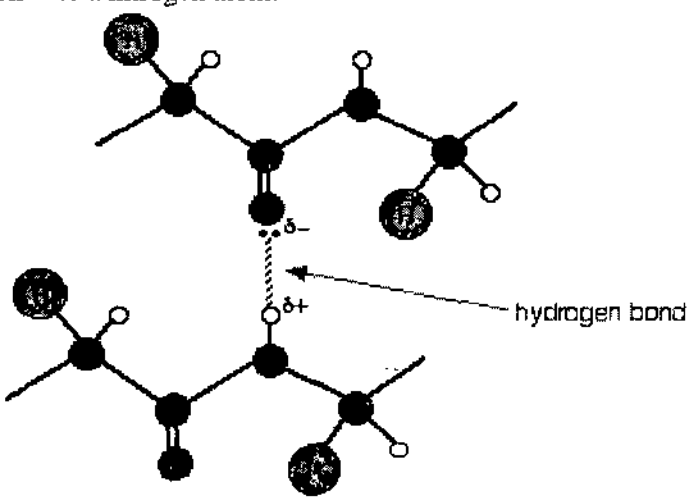
The wider definition of primary structure includes all the features of a protein which are a result of covalent bonds. There is an additional feature in proteins which is also covalently bound. It involves the amino acid cysteine.



The secondary structure of proteins

Within the long protein chains there are regions in which the chains are organised into regular structures known as alpha-helices (alpha-helixes) and beta-pleated sheets. These are the secondary structures in proteins.

These secondary structures are held together by hydrogen bonds. These form as shown in the diagram between one of the lone pairs on an oxygen atom and the hydrogen attached to a nitrogen atom:

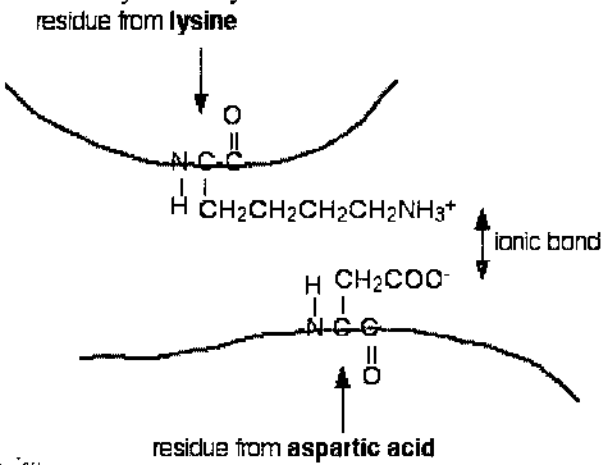


The tertiary structure of proteins

The tertiary structure of a protein is a description of the way the whole chain (including the secondary structures) folds itself into its final 3-dimensional shape. The tertiary structure of a protein is held together by interactions between the side chains and the "R" groups. There are several ways this can happen.

(a) Ionic interactions: Some amino acids (such as aspartic acid and glutamic acid) contain an extra –COOH group. Some amino acids (such as lysine) contain an extra – NH_2 group. The two groups can be interacted by

- The transfer of a hydrogen ion from the –COOH to the $-NH_2$ group to form zwitterions just like simple amino acids.
- An ionic bond between the negative and the positive group of the chains folded in such a way that they were close to each other.



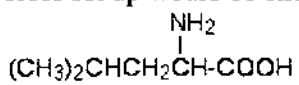
(b) Hydrogen bonds: The bond that joins the two chains are hydrogen bonds between side groups and not between groups actually in the backbone of the chain.

Lots of amino acids contain groups in the side chains which have a hydrogen atom attached to either an oxygen or a nitrogen atom. This is a classic situation where hydrogen bonding can occur.

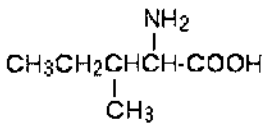
For example, the amino acid serine contains an –OH group in the side chain. A hydrogen bond could be formed between two serine residues in different parts of a folded chain.

(c) van der Waals forces: Several amino acids have quite large hydrocarbon groups in their side chains. A few examples are shown below. Temporary fluctuating dipoles in one of these groups could induce opposite dipoles in another group on a nearby folded chain.

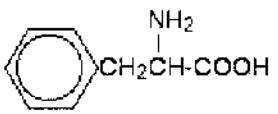
The dispersion forces set up would be enough to hold the folded structure together.



leucine



isoleucine



phenylalanine

The primary structure of a protein can readily be deduced from the nucleotide sequence of the corresponding messenger RNA. Based on primary structure, many features of secondary structure can be predicted with the aid of computer programs. However, predicting protein tertiary structure remains a very tough problem, although some progress has been made in this important area.

4.2. PROPERTIES OF PROTEINS

Solubility in water: In an aqueous solution protein molecules tend to seek their native structure and it is the water molecules that determine the structure of protein molecules. Water molecules form hydrogen bonds within protein molecules (with peptide and charged groups of amino acids), which determine the structure of protein molecules in solution.

Effect of acid and base: When protein solutions are acidified the net positive charge on the protein molecules increase, increasing the similar charge repulsion. The structural disturbance created within the protein molecules due to the similar charge repulsion leads to increase in the protein-to-protein interaction and consequently proteins precipitate.

When alkali is added to the protein solution it will increase the net negative charge on the protein molecule and a similar structural disturbance will lead to protein precipitation.

Effect of Heat: When a protein solution is heated, the thermal energy increases the rotation within the peptide bond leading to unfolding of the protein molecules followed by increase in the protein-to-protein interaction and protein precipitation.

Effect of salts: Salts, such as ammonium sulfate, compete for the protein bond water molecules (*i.e.* structured water) depriving the proteins of water molecules, which increases the protein-to-protein interaction and results in protein aggregation and precipitation. The concentration of salt that triggers protein precipitation is dependent on the primary structure of the proteins.

Effect of electricity: Protein molecules migrate depending on native net charge, a protein molecule with a net positive charge will migrate towards the anode and a protein molecule with net negative charge will migrate towards the cathode.

Effect of detergents: When a protein is treated with a non-ionic detergent it will have no effect on protein migration. On the other hand when a protein is treated with an anionic detergent it will render the protein negatively charged forcing the protein molecules to migrate towards the cathode. An anionic detergent will have the opposite effects.

Optical activity: As all the amino acids, with the exception of glycine, exhibit optical activity therefore, proteins also are optically active. They are usually levorotatory (*i.e.,* they rotate the plane of polarization to the left) when polarized light of wavelengths in the visible range is used.

Association of protein subunits: Many proteins with molecular weights of more than 50,000 occur in aqueous solutions as complexes: dimers, tetramers, and higher polymers—*i.e.,* as chains of two, four, or more repeating basic structural units. The subunits, which are called monomers or protomers, usually are present as an even number. Less than 10 percent of the polymers have been found to have an odd number of monomers. The arrangement of the subunits is thought to be regular and may be cyclic, cubic, or tetrahedral. Some of the small proteins also contain subunits. Insulin, for example, with a molecular weight of about 6,000, consists of two peptide chains linked to each other by disulfide bridges (–S–S–).

Protein denaturation: When a solution of a protein is boiled, the protein frequently becomes insoluble—*i.e.*, it is denatured—and remains insoluble even when the solution is cooled. Denaturation can be brought about in various ways. Proteins are denatured by treatment with alkaline or acid, oxidizing or reducing agents, and certain organic solvents.

4.3. FUNCTIONS OF PROTEINS IN THE BODY

Protein is the fundamental life force. Proteins are necessary in initiating every biochemical process in the body as well as in providing us an invaluable source of energy. In the absence of protein, the body would simply shut down. The main functions of proteins are :

1. **Proteins as Hormons** – These are messenger proteins, which help to coordinate certain bodily activities. Examples include insulin, oxytocin, and somatotropin. Insulin regulates glucose metabolism by controlling the blood-sugar concentration. Oxytocin stimulates contractions in females during childbirth. Somatotropin is a growth hormone that stimulates protein production in muscle cells.
2. **Proteins as enzymes**-Proteins are responsible for almost every biochemical reaction that takes place in the body. These reactions are catalized by enzymes, which are actually proteins. The amount of enzymes present in the body determines the rate at which a chemical event can occur. Thus if there is deficiency of enzymes, there will be a slower reaction.Several thousand enzymes have been discovered till date and virtually every one is a protein.
3. **Transportation and storage**-Proteins have a unique ability to transport substances across cell membranes that other molecules can't penetrate. Hemoglobin is a type of protein that is responsible for carrying oxygen in red blood cell. Myoglobin responsible for carrying oxygen is also a protein. Ferritin is a protein that assists in the storage of iron and stores blood in the liver. Without protein for transportation and storage, we would not have blood to nourish our bodies.
4. **Cell and tissue growth**-The body needs continues supply of amino acids in order to build the protein that creates tissue. Throughout our everyday lives, we constantly manufacture new tissues such as hair, teeth, skin and nails. The blood cells and skin cells last about a month while the cells situated in our digestive system lining last only two weeks. When the cells die and slough off, our bodies need new healthy tissue to replace them. So, it is only through the regeneration of new tissue that we can become healthy again.
5. **Mechanical support**-Collagen, the most abundant protein found in the human body is a type of structural protein that is fibrous in nature. Collagen is responsible for giving strength and support to tissues that undergo continual wear and tear for example skin and bones.
6. **Coordination and motion**-Proteins are a major component in muscle contraction. Muscle contraction occurs when two fibrous protein filament glide across each other. Sperms move by their flagella, which are made up of contractile units made of protein.
7. **Immune protection**-Immunity is the natural power of the body to fight against disease. Antibodies are highly specific proteins that are responsible for detecting a foreign substance known as "antigen". The body produces a specific antibody to respond to an antigen and inactivate it.

8. **Nerve generation and impules**-The nervous system is responsible for keeping the body in balance. When a certain stimulus triggers the nervous system, it responds with an appropriate reaction. This cannot occur without a receptor site. These receptor sites are made of protein complexes and are responsible for transmitting nerve messages from cell to cell.
9. **Fluid balance**-Protein have the unique ability to regulate the amount of fluid within a cell. The amount of protein within a cell will determine the cell's water content, as water is attracted to protein. When protein levels are low, fluid imbalances result. This type of system is important to prevent dehydration, as well as to enhance muscle and nerve cell function.

to quickly determine protonation, and hence charge state.

4.4. SUMMARY

Proteins are polymers of amino acids joined together by peptide bonds into a chain. There are 20 different amino acids that make up essentially all proteins on earth.

Protein is the fundamental life force. Proteins are necessary in initiating every biochemical process in the body as well as in providing us an invaluable source of energy. In the absence of protein, the body would simply shut down.

4.5. STUDENTS ACTIVITY

1. What is the tertiary structure of proteins?

2. Why proteins are important for us?

4.6. TEST YOURSELF

1. Using diagrams &/or description, describe the following:
   Primary structure
   Secondary structure
   Tertiary structure
2. What are the building blocks for making proteins?
3. How many of these building blocks are involved in making proteins ?

ANSWERS

2. Amino acids 3. 20

□□□

UNIT

5

ENZYMES AND COENZYMES

STRUCTURE

- Enzymes
- Properties of enzymes
- Factor affecting enzymes activity
- Structure of enzymes
- Activity of enzymes
- Function of enzymes
- Types of enzymatic reactions
- Coenzymes
- Some important coenzymes and their function
- Summary
- Student Activity
- Test yourself

LEARNING OBJECTIVES

After going through this unit you will learn:

What are enzymes and their significance in body ?

What are the factors affecting enzymes activity and rate of reaction ?

What are basic properties of amino acids ?

What are coenzymes ?

5.1. ENZYMES

Enzymes are very special types of proteins that catalyse chemical reactions inside body of all living organisms and so are also called **organic catalysts**. A catalyst is any substance that speeds up the rate of a chemical reaction but is itself not affected once the reaction is completed. Enzymes are used in organisms to increase the rate of the chemical reactions that are necessary for life.

An enzyme can catalyze a reaction by joining it with one or more of the molecules in the reaction. The molecules that attaches to an enzyme are called substrates, and when they join they form an enzyme-substrate complex.

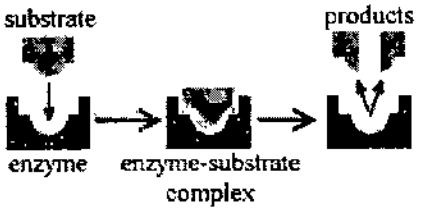


Fig 1: Process of enzyme action.

However, enzymes are able to attach only to certain substrates because they are specific in structure. Almost all chemical reactions in a biological cell need enzymes in order to occur at rates sufficient for life. Since enzymes are selective for their substrates and speed up only a few reactions from among many possibilities, the set of enzymes

made in a cell determines which metabolic pathways occur in that cell. Each enzyme has an area called the active site where the substrate will join. These active sites are specific in nature and only certain substrates will fit into the active site.

Some enzymes have special areas other than the active site. These special areas are sometimes called regulatory sites. Any molecule that attaches to the regulatory site is called an allosteric factor.

5.2. PROPERTIES OF ENZYMES

Like all catalysts, enzymes work by lowering the activation energy ($E_a^{\ddagger}$) for a reaction, thus increasing the rate of the reaction. As a result, products are formed faster. Most enzyme reaction rates are millions of times faster than those of comparable uncatalyzed reactions.

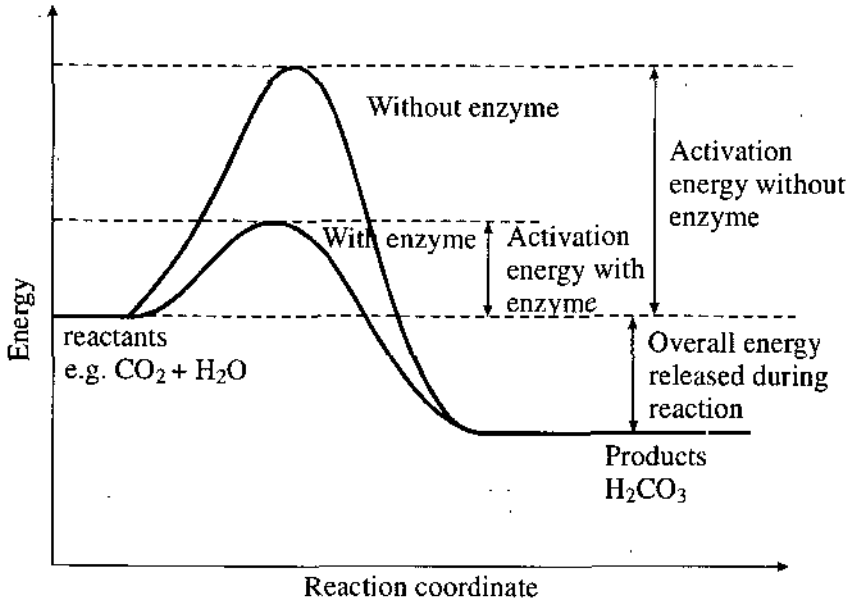


Fig 2: Effect of enzyme on rate of reaction.

Enzymes are known to catalyze about 4,000 biochemical reactions. A few RNA molecules called ribozymes also catalyze reactions, with an important example being some parts of the ribosome. Synthetic molecules called artificial enzymes also display enzyme-like catalysis.

1. As all catalysts, enzymes do not alter the position of the chemical equilibrium of the reaction. Usually, in the presence of an enzyme, the reaction runs in the same direction as it would without the enzyme, just more quickly. However, in the absence of the enzyme, other possible uncatalyzed, "spontaneous" reactions might lead to different products, because in those conditions this different product is formed faster.
2. An enzyme can couple two or more reactions, so that a thermodynamically favorable reaction can be used to "drive" a thermodynamically unfavorable one. For example, the hydrolysis of ATP is often used to drive other chemical reactions.
3. Enzymes catalyze the forward and backward reactions equally. They do not alter the equilibrium itself, but only the speed at which it is reached. For example, carbonic anhydrase catalyzes its reaction in either direction depending on the concentration of its reactants.

$$CO_2 + H_2O \xrightarrow{\text{Carbonic anhydrase}} H_2CO_3 \text{ (in tissues; high } CO_2 \text{ concentration)}$$

$$H_2CO_3 \xrightarrow{\text{Carbonic anhydrase}} CO_2 + H_2O \text{ (in lungs; low } CO_2 \text{ concentration)}$$

Nevertheless, if the equilibrium is greatly displaced in one direction, that is, in a very exergonic reaction, the reaction is in effect irreversible. Under these conditions, the enzyme will, in fact, catalyze only thermodynamically allowed reactions.

5.3. FACTORS ACTIVITY ENZYMES ACTIVITY

Enzyme activity can be affected by other molecules. Inhibitors are molecules that decrease enzyme activity; activators are molecules that increase activity. Many drugs and poisons are enzyme inhibitors. Activity is also affected by temperature, chemical environment (*e.g.*, pH), and the concentration of substrate.

1. Temperature

As the temperature rises kinetic energy of reacting molecules increases. This increases the chances of a successful collision and so the rate increases. There is a certain temperature at which an enzyme's catalytic activity is at greatest this temperature is called optimal temperature. This optimal temperature is usually around human body temperature (37.5 °C) for the enzymes in human cells.

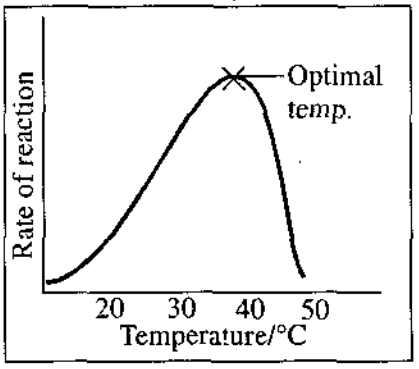


Fig 3: Effect of change of temperature on enzyme catalyzed rate of reaction

Above this temperature the enzyme structure begins to break down (**denature**) since at higher temperatures intra- and intermolecular bonds are broken as the enzyme molecules gain even more kinetic energy.

2. pH

Each enzyme works within a quite small pH range. There is a pH at which its activity is greatest (the optimal pH). This is because changes in pH can make and break intra- and intermolecular bonds, changing the shape of the enzyme and, therefore, its effectiveness.

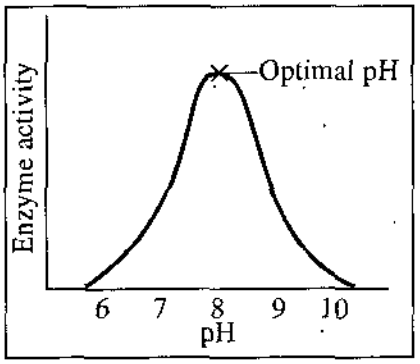


Fig. 4: Effect of change of pH on enzyme catalyzed rate of reaction

4. Enzyme Concentration

In order to study the effect of increasing the enzyme concentration upon the reaction rate, the substrate must be present in an excess amount; i.e., the reaction must be independent of the substrate concentration. Any change in the amount of product

formed over a specified period of time.will be dependent upon the level of enzyme present. Graphically this can be represented as:

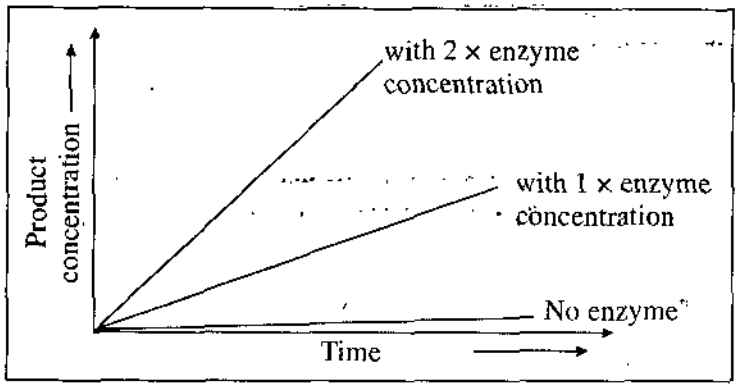


Fig. 5 : Effect of enzyme concentration on rate of reaction.

These reactions are said to be "zero order" because the rates are independent of substrate concentration, and are equal to some constant k.

1. Substrate Concentration

It has been shown experimentally that if the amount of the enzyme is kept constant and the substrate concentration is then gradually increased, the reaction velocity will increase until it reaches a maximum. After this point, increase in substrate concentration will not increase the velocity ($\Delta A/\Delta T$). This is represented graphically in Figure .

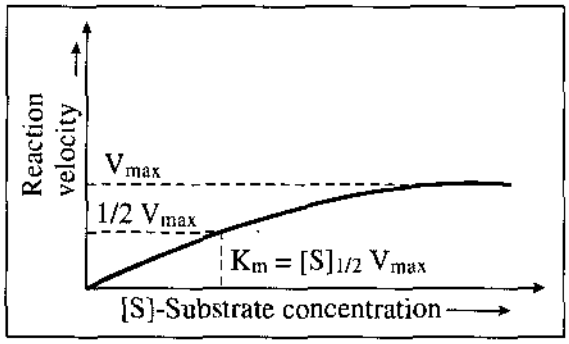


Fig 6: Effect of substrate conc. on enzyme catalyse reaction rate.

It is theorized that when this maximum velocity had been reached, all of the available enzyme has been converted to ES (the enzyme substrate complex). This point on the graph is designated Vmax. Using this maximum velocity and equation (1), Michaelis developed a set of mathematical expressions to calculate enzyme activity in terms of reaction speed from measurable laboratory data.

$$E + S \underset{K-1}{\overset{K+1}{\rightleftharpoons}} ES \underset{K-2}{\overset{K+2}{\rightleftharpoons}} P + E \quad [1]$$

The Michaelis constant Km is defined as the substrate concentration at 1/2 the maximum velocity. This is shown in Figure 1. Using this constant and the fact that Km can also be defined as :

$$K_m = K_{-1} + K_2 / K_{+1}$$

K^{+1}, K^{-1} and K^{+2} being the rate constants from equation (1). Michaelis developed the following

$$V_i = \frac{V_{max}\,[S]}{K_m + [S]}$$

where

V_1 = velocity at any time

[S] = substrate concentration at this time

V_{max} = the highest velocity under this set of experimental condition (pH, temperature, etc.)

K_m = the Michaelis constant for the particular enzyme being investigated.

Michaelis constants have been determined for many of the commonly used enzymes. The size of Km tells us several things about a particular enzyme.

- A small Km indicates that the enzyme requires only a small amount of substrate to become saturated. Hence, the maximum velocity is reached at relatively low substrate concentrations.
- A large Km indicates the need for high substrate concentrations to achieve maximum reaction velocity.

5.4. STRUCTURE OF ENZYMES

Enzymes are in general globular proteins and range from just 62 amino acids to over 2,500. A small number of RNA-based biological catalysts exist, with the most common being the ribosome; these are referred to as either RNA-enzymes or ribozymes. The activities of enzymes are determined by their three-dimensional structure.

5.5. ACTIVITY OF ENZYMES

There are two proposed theories for the description of how enzymes work in a biological reaction:

1. "Lock and key" Model

Enzymes are very specific in their function. It was first suggested by the organic chemist Emil Fischer in 1894 that both the enzyme and the substrate possess specific complementary geometric shapes that fit exactly into one another. This is often referred to as "the lock and key" model. In this analogy, the lock is the enzyme and the key is the substrate. Only the correctly sized **key (substrate) fits** into the **key hole (active site)** of the **lock (enzyme)**.

Smaller keys, larger keys, or incorrectly positioned teeth on keys (incorrectly shaped or sized substrate molecules) do not fit into the lock (enzyme). Only the correctly shaped key opens a particular lock.

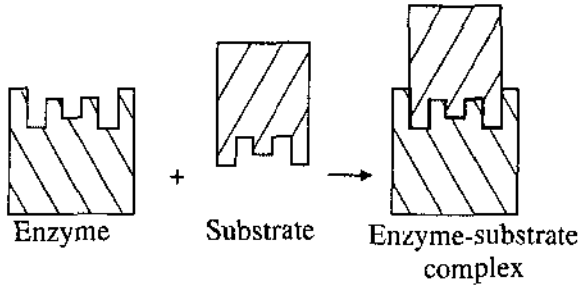


Fig. 7. Lock and key hypothesis

1. Induced fit hypothesis

Not all experimental evidence can be adequately explained by using the so-called rigid enzyme model assumed by the lock and key theory. For this reason, in 1958, Daniel Koshland suggested a modification to the lock and key model: since enzymes are rather flexible structures, the active site is continuously reshaped by interactions with the substrate as the substrate interacts with the enzyme. As a result, the substrate

does not simply bind to a rigid active site; the amino acid side-chains that make up the active site are molded into the precise positions that enable the enzyme to perform its catalytic function. In some cases, such as glycosidases, the substrate molecule also changes shape slightly as it enters the active site. The active site continues to change until the substrate is completely bound, at which point the final shape and charge is determined.

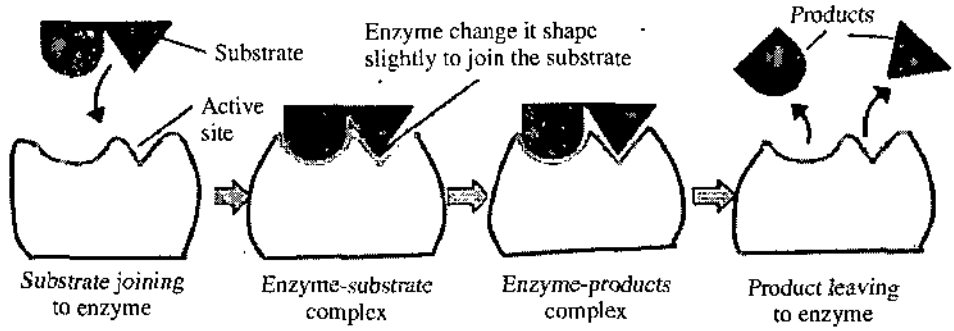


Fig. 8. Induced fit hypothesis.

5.6. BIOLOGICAL FUNCTION

Enzymes perform wide variety of functions inside living organisms.

1. They work in for signal transduction and cell regulation.
2. They also generate movement by hydrolyzing ATP to generate muscle contraction.
3. Other ATPases in the cell membrane are ion pumps involved in active transport.
4. Enzymes are also involved in more exotic functions, such as luciferase generate light in fireflies.
5. Enzymes in virus can also cause disease by infecting cells, such as the HIV integrase and reverse transcriptase.
6. A major function of enzymes is in the digestion of food different enzymes digest different food. Enzymes such as amylases and proteases break down large molecules into smaller ones, so they can be absorbed by the intestines. Starch molecules, for example, are too large to be absorbed from the intestine, but enzymes hydrolyze the starch chains into smaller molecules such as maltose and eventually glucose, which can then be absorbed.
7. Several enzymes can work together in a specific order, creating metabolic pathways. In a metabolic pathway, one enzyme takes the product of another enzyme as a substrate. After the catalytic reaction, the product is then passed on to another enzyme.
8. Sometimes more than one enzyme can catalyze the same reaction in parallel; this can allow more complex regulation.

5.7. TYPES OF ENZYME REACTIONS

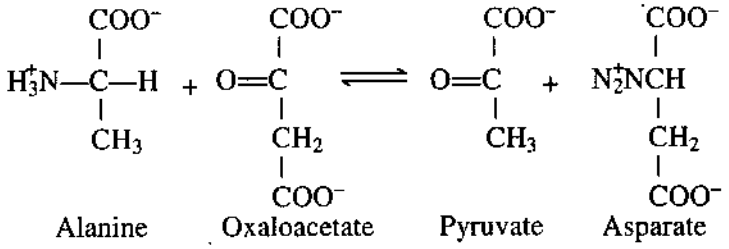
Although a huge number of reactions occur in living systems, these reactions fall into only six types. The reactions are :

1. Oxidation and reduction: In this type of reactions one molecule is oxidized while other is reduced. The enzymes that carry out these reactions are called **oxidoreductases.** For example, alcohol dehydrogenase converts primary alcohols to aldehydes.

$$H_3CCH_2OH + NADH_3CCHO + NADH + H^+$$

In this reaction, ethanol is converted to acetaldehyde and the *cofactor* NAD is converted to NADH. In other words, ethanol is oxidized, and NAD is reduced. The charge on the reaction is not balance, because NAD has some other charged groups).

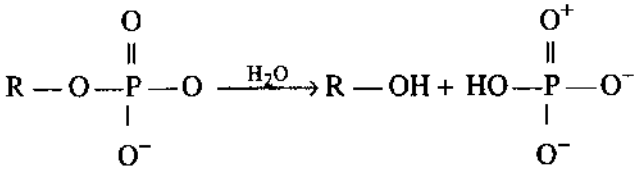
2. Group transfer reactions: In these reactions enzymes, called **transferases,** move functional groups from one molecule to another. For example, alanine aminotransferase shuffles the alpha-amino group between alanine and aspartate:



Alanine Oxaloacetate Pyruvate Asparate

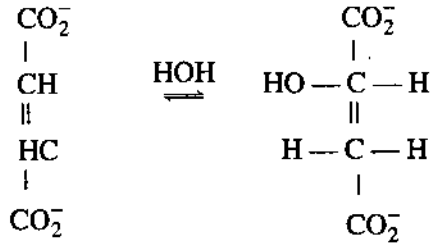
Other transferases move phosphate groups between ATP and other compounds, sugar residues to form disaccharides and so on.

3. Hydrolysis: These enzymes, termed **hydrolases,** break single bonds by adding the elements of water. For example, phosphatases break the oxygen-phosphorus bond of phosphate esters :

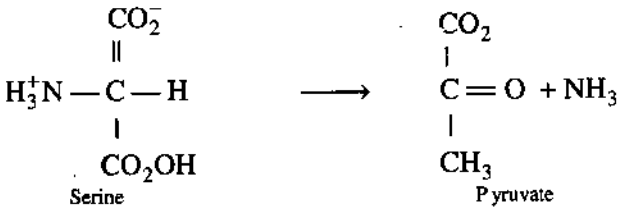


Other hydrolases function as digestive enzymes, for example, by breaking the peptide bonds in proteins.

4. Formation or removal of a double bond with group transfer: The functional groups transferred by these **lyase** enzymes include amino groups, water and ammonia. For example, decarboxylases remove CO_2 from alpha- or beta-keto acids, Dehydratases remove water, as in fumarase (fumarate hydratase):



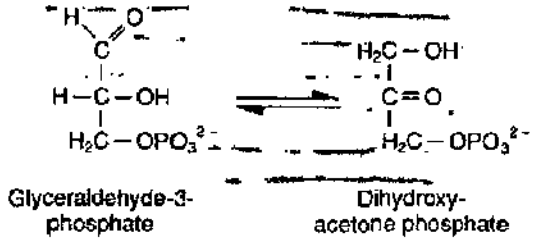
Deaminases remove ammonia, for example, in the removal of amino groups from amino acids:



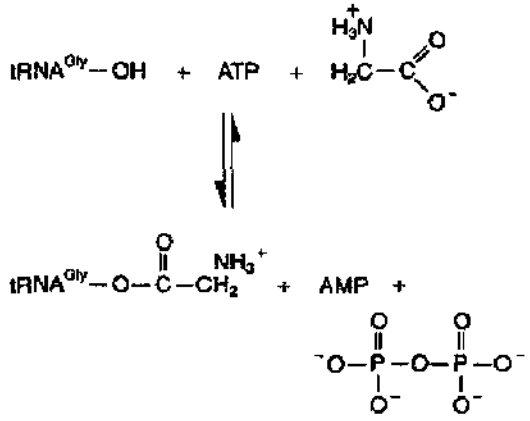
Serine Pyruvate

5. Isomerization of functional groups: In many biochemical reactions, the position of a functional group is changed within a molecule, but the molecule itself contains the same number and kind of atoms that it did in the beginning. In other

words, the substrate and product of the reaction are *isomers*. The **isomerases** (for example, triose phosphate isomerase, shown following), carry out these rearrangements.



6. Single bond formation by eliminating the elements of water: Hydrolases break bonds by adding the elements of water; **ligases** carry out the converse reaction, removing the elements of water from two functional groups to form a single bond. Synthetases are a subclass of ligases that use the hydrolysis of ATP to drive this formation. For example, *aminoacyl-transfer RNA synthetases* join amino acids to their respective transfer RNAs in preparation for protein synthesis; the action of glycyl-tRNA synthetase is illustrated in this figure:



5.8. COENZYMES

Coenzymes are organic chemicals that assist enzymes during the catalysis of reactions. Coenzymes are non-protein organic molecules that are mostly derivatives of vitamins soluble in water by phosphorylation.

Enzymes without their necessary cofactors are called apoenzymes, which are the inactive form of an enzyme. Coenzymes bind an apoenzyme to produce an active holoenzyme, which is the active form.

A coenzyme is a small, organic, non-protein molecule that carries chemical groups between enzymes. It is the cofactor for the enzyme and does not form a permanent part in the enzyme's structure. Sometimes, they are called cosubstrates and are considered substrates that are loosely bound to the enzyme. In metabolism, coenzymes play a role in group-transfer reactions, such as ATP and coenzyme A, and oxidation-reduction reactions, such as NAD+ and coenzyme Q10. Coenzymes are frequently consumed and recycled. Chemical groups are added and detached continuously by an enzyme. ATP synthatase enzyme phosphorylates and converts the ADP to ATP, while Kinase dephosphorylates the ATP back to ADP at continuous rates as well. Coenzyme molecules are mostly derived from vitamins. They are also commonly made from nucleotides such as adenosine triphosphate and coenzyme A.

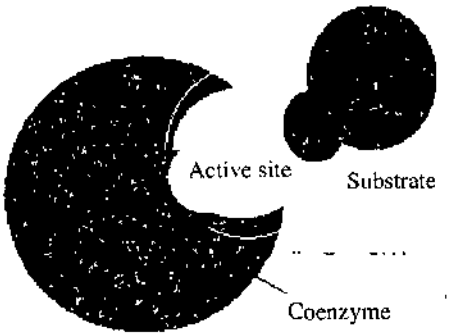


Fig. 9 : Position of co-enzyme in enzymes

5.9. SOME IMPORTANT Co-Enzymes AND THEIR FUNCTIONS

1. NADH

Nicotinamide Adenine Dinucleotide (NAD) is a coenzyme derived from vitamin B3. NAD+ is capable of carrying and transferring electrons and functions as oxidizing agent in redox reactions. It also works as a substrate for DNA ligases in post translational modification, where the reaction removes acetyl groups from proteins. In glycolysis and the citric acid cycle, NAD+ oxidizes glucose and releases energy, which is then transferred to NAD+ by reduction to NADH. NADH later on releases the extra electron through oxidative phosphorylation to generate ATP, which is the only energy source in humans. In addition to catabolic reactions, NADH is also involved in anabolic reactions such as gluconeogenesis, and it also aids in the production of neurotransmitters in the brain.

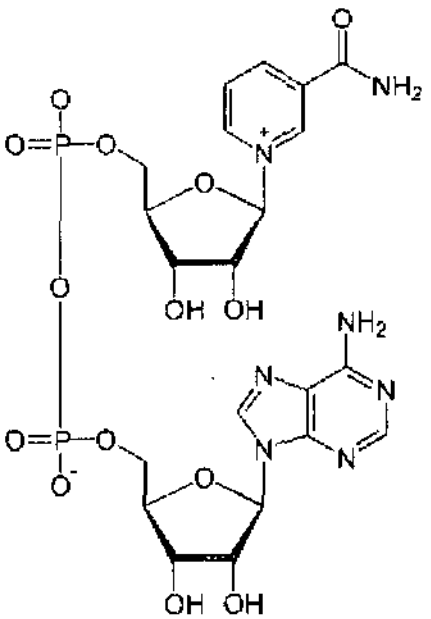


Fig. 10 : Structure of NAD^+

2. FADH

Flavin Adenine Dinucleotide (FAD) is a prosthetic group that, like NADH, functions as a reducing agent in cellular respiration and donates electrons to the electron transport chain.

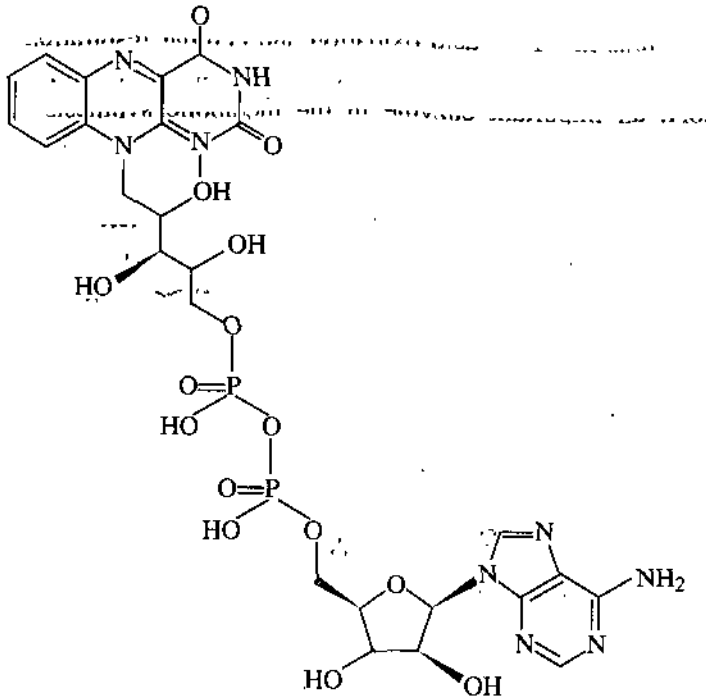
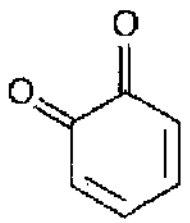
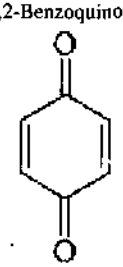


Fig. 11 : Structure of FAD

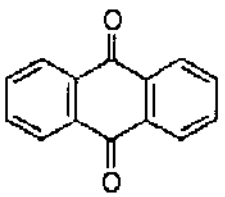
3. Quinone



1,2-Benzoquinone



1,4-Benzoquinone



Anthraquinone

Fig. 12 : Structure of various quinones

Quinone's structure gives them the ability to form substances with colours. They exist as pigments in bacteria, fungi, and certain plants, and give them their characteristic colors. In biological systems, they serve as electron acceptors in electron transport chains such as those in photosynthesis and aerobic respiration.

4. Co-A

Coenzyme-A, synthesized from pantothenic acid ATP, functions as acyl group carriers to transport functional groups such as acetyl by forming acetyl-CoA in

metabolic reactions like fatty acid oxidation and cellular respiration. It is also used in transfer of fatty acids from cytoplasm to mitochondria. CoA is an important precursor to HMG-CoA, an important enzyme in the metabolic synthesis of cholesterol and ketones.

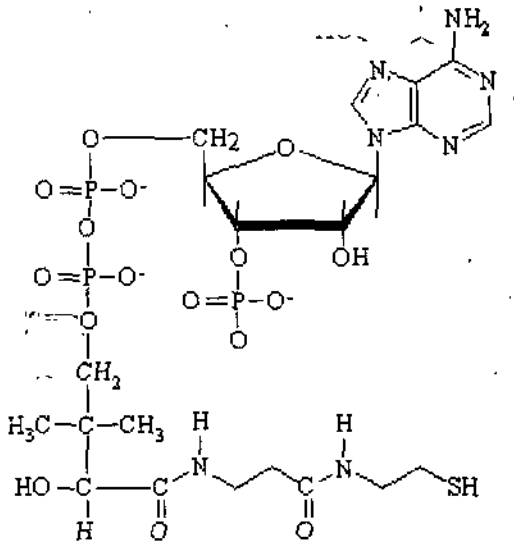


Fig. 13 : Structure of CoA

to quickly determine protonation, and hence charge state.

5.10. SUMMARY

Enzymes are very special types of proteins that catalyse chemical reactions inside body of all living organisms and so are also called **organic catalysts**. The main factors that affects enzyme activity are

- Temperature
- pH
- Enzyme Concentration
- Substrate Concentration

5.11. STUDENTS ACTIVITY

1. How does the "**Lock and Key**" theory of enzyme action differ from the "Induced Fit" theory?

2. Why enzymes are important for us?

3. What are co-enzymes?

5.12. TEST YOURSELF

1. In the equation S + E → SE → P + E, what do the letters S, P, SE and E stand for?
2. Name two environmental factors that can change the shape of an enzyme.
3. Name two factors that can speed up enzymatic reactions
4. -Enzymes have helpers called _____. What is the function of NAD in cells?
5. What is the effect of lowering the temperature on enzyme activity?

ANSWERS

1. S: substrate, P: product, SE: substrate-enzyme complex, E: enzyme,
2. (i) temperature, (ii) Ph
3. (i) increase temp (ii) increase in the conc. of substrate or enzyme
4. coenzymes, Carries H atoms in oxidation reduction reactions.
5. activity of the enzymes increases

❑❑❑

UNIT

6

DIGESTION AND ABSORPTION OF FOOD

STRUCTURE

- Digestive System
- Physiology of alimentary Canal
- Digestive Glands
- Digestion of Food
- Absorption of food
- Summary
- Student Activity
- Test yourself

LEARNING OBJECTIVES

After going through this unit you will learn :

How is our digested system ?

How food is digested there ?

What is absorption of food ?

How food is absorbed in alimentary canal ?

6.1. DIGESTIVE SYSTEM

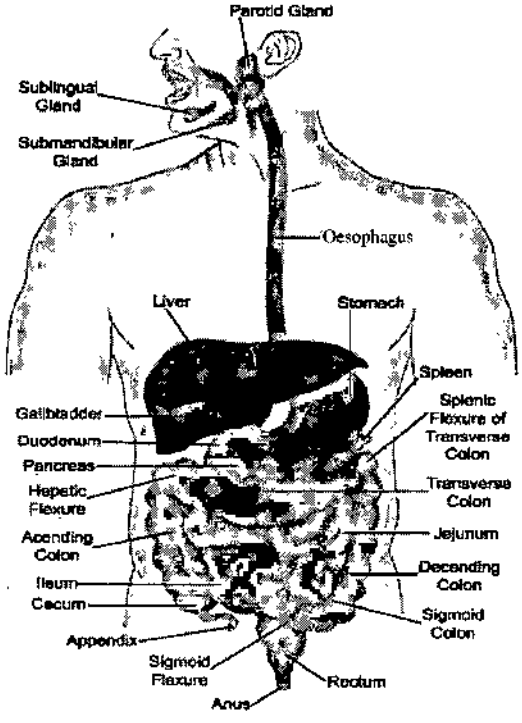


Fig. 1. The human digestive system.

Food is one of the basic requirements of all living organisms. The food that we eat has major components of carbohydrates, proteins, fats and small quantities of vitamins and minerals. Food provides energy and organic materials for growth and repair of tissues. The water plays an important role in metabolic processes. Bio-macromolecules in food are not utilised by our body in their original form. They are 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 mechanical and biochemical methods.

The human digestive system consists of the alimentary canal and the associated glands. Major parts of the digestive system are shown in the fig.1.

1. Mouth

The alimentary canal begins with the mouth, and it ends posteriorly through the anus. The mouth leads to the buccal cavity or the oral cavity. The oral cavity has 28-32 teeth and a muscular tongue. Each tooth is embedded in a socket of jaw bone (Figure 2). This type of attachment is called thecodont. Majority of mammals including human being forms two sets of teeth during their life, a set of temporary milk or deciduous teeth replaced by a set of permanent or adult teeth. This type of dentition is called diphyodont. The hard chewing surface of the teeth, made up of enamel, helps in the mastication of food. An adult human has four types of teeth i.e. they have Heterodont dentition

(i) Incisors (I): These are front teeth. The Incisors are used for cutting food into small chewable pieces

(ii) Canine (C): The Canines have a sharp, pointed biting surface and has grip to tear food.

(iii) Premolars (PM): The Premolars have a flat biting surface, they tear and crush food molars (M). The Molars are used for chewing and grinding food. Third molars are commonly called "wisdom teeth" and may never erupt into the mouth or form at all. If any additional teeth form, for example, fourth and fifth molars, which are rare, they are referred to as supernumerary teeth.

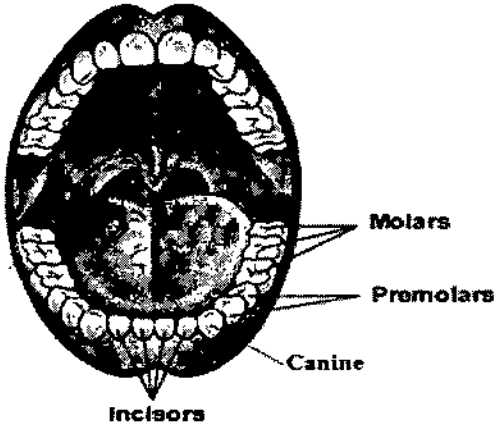


Fig. 2. Arrangement of teeth in the jaw.

Arrangement of teeth in each half of the upper and lower jaw in the order I, C, PM, M is represented by a dental formula. In human among 32 permanent teeth, 16 are found in the upper jaw and 16 in the lower jaw, so the dental formula is

$$\frac{\text{Upper half jaw}}{\text{Lower half jaw}} = \frac{2.1.2.3}{2.1.2.3} \times 2$$

The tongue is a freely movable muscular organ attached to the floor of the oral cavity by the frenulum. The upper surface of the tongue has small projections called papillae, some of which bear taste buds. The uvula (Latin for "little grape") is a fleshy

piece of muscle, tissue and mucous membrane that hangs down from the palate. It is the part that flips up and helps to close off the nasal passages when we swallow.

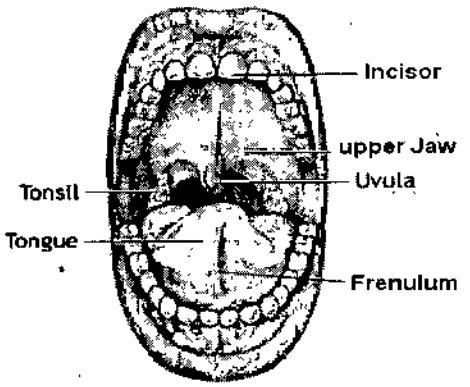


Fig. 3. Anatomy of Mouth.

2. Oesophagus

The oral cavity leads into a short pharynx which serves as a common passage for food (oesophagus) and air (trachea). The oesophagus or food pipe is part of the digestive system. It is also sometimes called the gullet. It is the tube that carries food from mouth to stomach. The oesophagus is about 26cm (10.5 inches) long in adults. It lies between the windpipe (trachea) and spinal cord. The oesophagus is a thin, long tube. It extends posteriorly passing through the neck, thorax and diaphragm and leads to a 'J' shaped bag like structure called stomach. Glands in the wall of the oesophagus produce mucous to help food to slide down more easily when swallowed. It is the cells of these glands that become cancerous in adenocarcinoma of the oesophagus.A cartilaginous flap called epiglottis prevents the entry of food into the glottis.

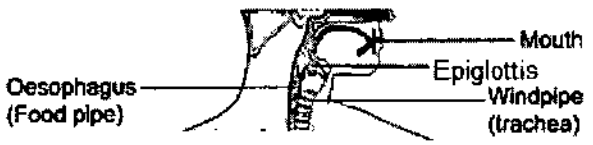


Fig. 4. Position of food and wind pipe

4. Stomach

A muscular **sphincter** (gastro-oesophageal) regulates the opening of oesophagus into the stomach. The stomach, located in the upper left portion of the abdominal cavity, has three major parts – a cardiac portion into which the oesophagus opens, a fundic region and a pyloric portion which opens into the duodenum (first part of small intestine) (Figure 5).

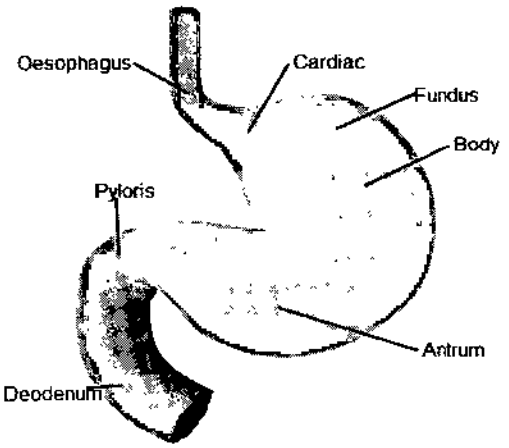


Fig. 5. Parts of stomach

5. Small Intestine

The small intestine is the longest section of the digestive tube and consists of three segments forming a passage from the pylorus to the large intestine:

- ***Duodenum:*** It is a 'U' shaped short section that receives secretions from the pancreas and liver via the pancreatic and common bile ducts. The opening of the stomach into the duodenum is guarded by the pyloric **sphincter**. The duodenum is almost 100% involved in digestion but not in absorption.
- ***Jejunum:*** It is a long coiled portion considered to be roughly 40% of the small gut in man, but closer to 90% in animals.
- ***Ileum:*** It empties into the large intestine. It is highly coiled part and considered to be about 60% of the intestine in man.

In most animals, the length of the small intestine is roughly 3.5 times to the body length.

6. Large Intestine

The large intestine forms an upside down U over the coiled small intestine. It begins at the lower right-hand side of the body and ends on the lower left-hand side. The large intestine is about 5-6 feet long. It has 3 parts: the cecum, the colon, and the rectum. The cecum is a pouch at the beginning of the large intestine. This area allows food to pass from the small intestine to the large intestine. A narrow finger -like tubular projection, the vermiform appendix which is a vestigial organ, arises from the caecum. The colon is where fluids and salts are absorbed and extends from the cecum to the rectum. The last part of the large intestine is the rectum, which is where feces (waste material)is stored before leaving the body through the anus.

The small intestine is so called because it is smaller in diameter than large intestine.

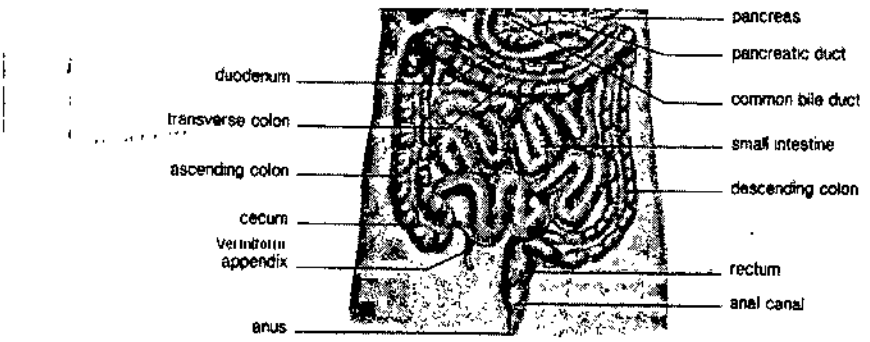


Fig. 6. Small and large intestine

6.2. PHYSIOLOGY OF ALIMENTARY CANAL

The wall of alimentary canal from oesophagus to rectum possesses four layers (Figure 8) namely serosa, muscularis, sub-mucosa and mucosa. Serosa is the outermost layer and is made up of a thin mesothelium (epithelium of visceral organs) with some connective tissues. Muscularis is formed by smooth muscles usually arranged into an inner circular and an outer longitudinal layer. An oblique muscle layer may be present in some regions. The submucosal layer is formed of loose connective tissues containing nerves, blood and lymph vessels. In duodenum, glands are also present in sub-mucosa. The innermost layer lining the lumen of the alimentary canal is the mucosa. This layer forms irregular folds (rugae) in the stomach and small finger-like foldings called villi in the small intestine. The cells lining the villi produce numerous microscopic projections called microvilli giving a brush border appearance. These modifications increase the surface area enormously. Villi are supplied with a network of capillaries and a large

lymph vessel called the lacteal. Mucosal epithelium has goblet cells which secrete mucus that help in lubrication. Mucosa also forms glands in the stomach (gastric glands) and crypts in between the bases of villi in the intestine (crypts of Lieberkuhn). All the four layers show modifications in different parts of the alimentary canal.

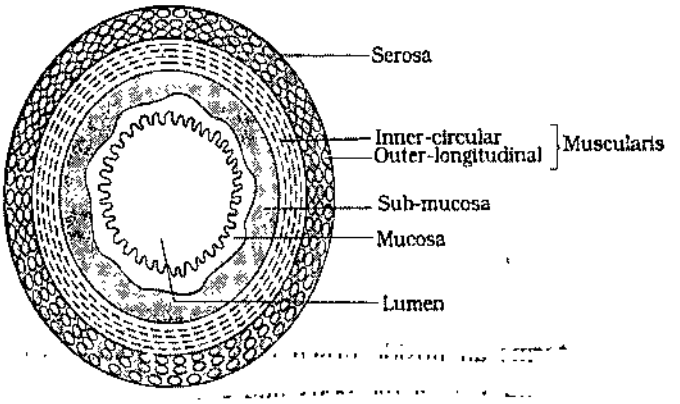


Fig. 7. Diagrammatic representation of transverse section of gut.

6.3. DIGESTIVE GLANDS

The digestive glands associated with the alimentary canal include the salivary glands, the liver and the pancreas. Saliva is mainly produced by three pairs of salivary glands, the parotids (cheek), the sub-maxillary/sub-mandibular (lower jaw) and the ublinguals (below the tongue). These glands situated just outside the buccal cavity secrete salivary juice into the buccal cavity.

1. Liver

Liver is the largest gland of the body weighing about 1.2 to 1.5 kg in an adult human. It is situated in the abdominal cavity, just below the diaphragm and has two lobes. The hepatic lobules are the structural and functional units of liver containing hepatic cells arranged in the form of cords. Each lobule is covered by a thin connective tissue sheath called the Glisson's capsule. The bile secreted by the hepatic cells passes through the hepatic ducts and is stored and concentrated in a thin muscular sac called the gall bladder. The duct of gall bladder (cystic duct) along with the hepatic duct from the liver forms the common bile duct (Figure 8).

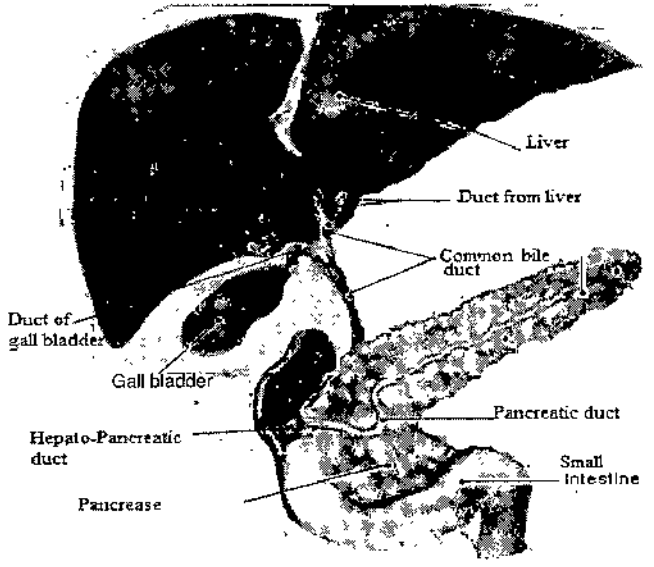


Fig. 8. The duct systems of liver, gall bladder and pancreas.

The bile duct and the pancreatic duct open together into the duodenum as the common hepato-pancreatic duct which is guarded by a sphincter called the sphincter of Oddi.

2. Pancreas

The pancreas is a compound (both exocrine and endocrine) elongated organ situated between the limbs of the 'U' shaped duodenum. The exocrine portion secretes an alkaline pancreatic juice containing enzymes and the endocrine portion secretes hormones, insulin and glucagon.

6.4. DIGESTION OF FOOD

The process of digestion is completed by mechanical and chemical processes. The digestion of food starts from mouth and completed in large intestine. The whole process of digestion is as follows :

(i) Digestion in mouth: The oral cavity performs two major functions, mastication of food and facilitation of swallowing. The teeth and the tongue masticate and mix up the saliva into the food thoroughly. The saliva secreted into the oral cavity contains electrolytes Na^+, K^+, Cl^+, HCO_3^- and enzymes, salivary amylase and lysozyme which maintain the pH of mouth to 6.8. The chemical process of digestion is initiated in the oral cavity by the hydrolytic action of the carbohydrate splitting enzyme, the salivary amylase. About 30 per cent of starch is hydrolysed here by this enzyme into a disaccharide – maltose. Lysozyme present in saliva acts as an antibacterial agent that prevents infections. Mucus in saliva helps in lubricating and adhering the masticated food particles into a bolus. The bolus is then conveyed into the pharynx and then into the oesophagus by swallowing or deglutition. The bolus further passes down through the oesophagus by successive waves of muscular contractions called peristalsis. The gastro-oesophageal sphincter controls the passage of food into the stomach.

(ii) Digestion in stomach: The mucosa of stomach has gastric glands. Gastric glands have three major types of cells namely

- mucus neck cells which secrete mucus;
- peptic or chief cells which secrete the proenzyme pepsinogen; and
- 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 the active enzyme pepsin, the proteolytic enzyme of the stomach. Pepsin 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 pepsins. Rennin is a proteolytic enzyme found in gastric juice of infants which helps in the digestion of milk proteins. Small amounts of lipases are also secreted by gastric glands. This partially digested food is then passed to small intestine.

(iii) Digestion in small intestine: Almost complete digestion takes place here. The muscular layer of the small intestine generates various types of movements. These movements help in a thorough mixing up of the food with various secretions in the intestine and thereby facilitate digestion. 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, amylases, lipases and nucleases. 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. The bile released into the duodenum contains bile pigments-bilirubin and bili-verdin, bile salts, cholesterol and phospholipids but no enzymes. This bile helps in emulsification of fats, *i.e.,* breaking down of the fats into very small micelles. Bile also activates lipases.

The intestinal mucosal epithelium has goblet cells, which secrete mucus. The secretions of the brush border cells of the mucosa alongwith the secretions of the goblet cells constitute the intestinal juice or succus entericus. This juice contains a variety of enzymes like disaccharidases (such as maltase), dipeptidases, lipases, nucleosidases, etc. The mucus alongwith the bicarbonates from the pancreas protects the intestinal mucosa from acid as well as provide an alkaline medium (pH 7.8) for enzymatic activities. Brunner's glands (Sub-mucosal glands) also help in this.

Digestion of various food products by these enzymes are as follows :

$$\text{Carbohydrates (starch)} \xrightarrow{\text{Amylase}} \text{Disaccharides}$$

$$\text{Fats} \xrightarrow[\text{Bile}]{\text{Lipases}} \text{Diglycerides} \xrightarrow[\text{Bile}]{\text{Lipases}} \text{Monoglycerides}$$

$$\text{Nucleic acids} \xrightarrow{\text{Nucleases}} \text{Nucleotides} \xrightarrow{\text{Nucleases}} \text{Nucleosides}$$

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

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

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

$$\text{Sucrose} \xrightarrow{\text{Sucrase}} \text{Glucose} + \text{Fructose}$$

$$\text{Nucleotides} \xrightarrow{\text{Nucleotidases}} \text{Nucleosides} \xrightarrow{\text{Nucleotidases}} \text{Sugars} + \text{Bases}$$

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

$$\left.\begin{matrix}\text{Proteins}\\ \text{Peptones}\\ \text{Proteoses}\end{matrix}\right\} \xrightarrow[\text{Carboxypeptidase}]{\text{Trypsian/Chymotrypsin}} \text{Dipeptides}$$

The simple substances thus formed are absorbed in the jejunum and ileum regions of the small intestine. The undigested and unabsorbed substances are passed in to the large intestine.

(iv) Large Intestine: No significant digestive activity occurs in the large intestine. It only takes part in absorption of some water, minerals and certain drugs, secretion of mucus and storage of undigested food. The mucus helps in adhering the waste particles together and lubricating it for an easy passage.

The undigested, unabsorbed substances are called faeces. These enter into the caecum of the large intestine through ileo-caecal valve, which prevents the back flow of the faecal matter. It is temporarily stored in the rectum till defaecation.

6.5. ABSORPTION OF DIGESTED FOOD

Absorption is the process by which the smallest products of digestion pass through the wall of alimentary canal into the blood or lymph. Absorption of various substances of digested food takes place in different parts of the alimentary canal, like mouth, stomach, small intestine and large intestine. However, maximum absorption occurs in the small intestine. It is carried out by passive, active or facilitated transport

mechanisms. Monosacharides like glucose, amino acids and some of electrolytes like chloride ions are generally absorbed in the small intestine by simple diffusion. The absorption of these substances into the blood depends upon the concentration gradients while some of the substances like fructose and some amino acids are absorbed with the help of the carrier ions like Na^+. This mechanism is called the facilitated transport.

Transport of water depends upon the osmotic gradient. Active transport occurs against the concentration gradient and hence requires energy. Various nutrients like amino acids, monosacharides like glucose, electrolytes like Na^+ are absorbed into the blood by this mechanism.

Fatty acids and glycerol cannot be absorbed because they are insoluble. 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 vessels ultimately release the absorbed substances into the blood stream.

The various substances absorbed in different parts of digested system are:

- **MOUTH:** Certain drugs coming in contact with the mucosa of mouth and lower side of the tongue are absorbed into the blood capillaries lining them.
- **STOMACH:** Absorption of water, simple sugars, and alcohol etc. takes place.
- **SMALL INTESTINE:** Principal organ for absorption of nutrients. The digestion is completed here and the final products of digestion such as glucose, fructose, fatty acids, glycerol and amino acids fructose, fatty acids, glycerol and amino acids are absorbed through the mucosa into the blood stream and lymph.
- **LARGE INTESTINE:** Absorption of water, some minerals and drugs takes place.

The absorbed substances finally reach the tissues, which utilise them for their activities. This process is called assimilation. The digestive wastes, solidified into coherent faeces in the rectum initiate a neural reflex causing an urge or desire for its removal. The egestion of faeces to the outside through the anal opening is called defaecation is a voluntary process which is carried out by a mass peristaltic movement.

6.6. SUMMARY

The food that we eat is not used as such in our body. For is use in body it is divided into small particles called digestion. Absorption is the process by which the smallest products of digestion pass through the wall of alimentary canal into the blood or lymph.

6.7. STUDENTS ACTIVITY

1. Why is it preferable to break food items into smaller pieces?

2. What is the difference between a Gastrovascular Cavity and a Complete Digestive Tract?

3. Name the main segments of the human digestive tract.

6.8. TEST YOURSELF

1. Fill in the blanks
   a. In digestion, Polysaccharides are digested into _____.
   b. Fats are digested to _____.
   c. Proteins are digested to _____.
   d. Nucleic acids are digested to _____.
   e. The enzymatic process for digestion is termed_____.
2. What enzyme is released into the oral cavity?
3. What is the function of the Oesophagus?
4. What substances are present in Gastric Juice?
5. What are the functions of the acid in Gastric Juice?
6. What is Pepsin?
7. What is the substrate for Pepsin and what are the products of its action?
8. What is the Pyloric Sphincter and what does it do?
9. The first part of the small intestine, the duodenum, receives secretions via ducts from two other glands/organs. Name these structures.
10. What substances come from the Pancreas?
11. What substances come from the Liver?
12. What enzymes are involved in the digestion of carbohydrates?
13. What enzymes are involved in the digestion of proteins?
14. What are the main functions of the Large Intestine?
15. What is the uvula and what is it's purpose?
16. What is peristalsis?
17. We _____our food to break it down into small bits.
18. We produce _____ to help us swallow our food.

ANSWERS

1. (a) (b) monoglycerids (c) Dipeptids
   (d) Nucleosides (e) digestion
2. amylase and lysozyme 3. to conduct food from mouth of to stomach
4. HCl and pepsinogen and
5. Convert pepsinogen to pepsin
6. an active enzyme in stomach
7. proteins, proteases and peptones
8. Valve in stomach
9. Pancreases and liver
10. Bile
11. Pancreatic juice
12. Amylase
13. Pepsin, Trypsian, Chymotrypsin
14. Absorption of water and minerals
15. It is a fleshy piece of muscular tissue which close off the nasal passage when food is swallowed.
16. Unvoluntary movements in digestive system
17. digest
18. Saliva

❑❑❑

UNIT

7

RESPIRATION

STRUCTURE

- Introduction
- Respiratory System
- Mechanism of Breathing
- Gas Exchange Between Lungs and Blood
- Respiratory Values
- Role of Hemoglobin in respiration
- Summary
- Student Activity
- Test yourself

LEARNING OBJECTIVES

After going through this unit you will learn :

What is respiratory system

How respiration occurs

What is the role of hemoglobin in respiration

7.1. INTRODUCTION

The main respiratory organs are lungs. Lungs provide continuous gas exchange between inspired air and the blood in the pulmonary circulation. They supply oxygen during inspiration and remove carbon dioxide during expiration.

7.2. RESPIRATORY SYSTEM

The respiratory tract extends from the mouth and nose to the alveoli of lungs. The parts of respiratory system and their function are as follows :

1. **Nose or Nostrils:** These serves to filter airborne particles, humidify and warm the inspired gases. The patency of the airway in the nose and oral cavity is largely maintained by the bony skeleton, but in the pharynx is dependent upon the tone in the muscles of the tongue, soft palate and pharyngeal walls.
2. **Larynx:** The larynx lies at the level of upper cervical vertebrae between C4-C6, and its main structural components are the thyroid and cricoid cartilages, along with the smaller arytenoid cartilages and the epiglottis, which sit over the laryngeal inlet. The thyroid and cricoid cartilages are linked anteriorly by the cricothyroid membrane, through which access to the airway can be gained in an emergency.
3. **Trachea and bronchi:** The trachea extends from below the cricoid cartilage to the carina, the point where the trachea divides into the left and right main bronchus, with a length of 12-15cm in an adult and an internal diameter of 1.5-2.0cm. The carina lies at the level of 5th thoracic vertebra (T5) at

expiration and 6th thoracic vertebra (T6) during inspiration. Its circumference is made up of a series of C-shaped cartilages. The right main bronchus is less sharply angled from the trachea than the left, making aspirated material more likely to enter the right lung. In addition, the right upper lobe bronchus arises only about 2.5cm from the carina.

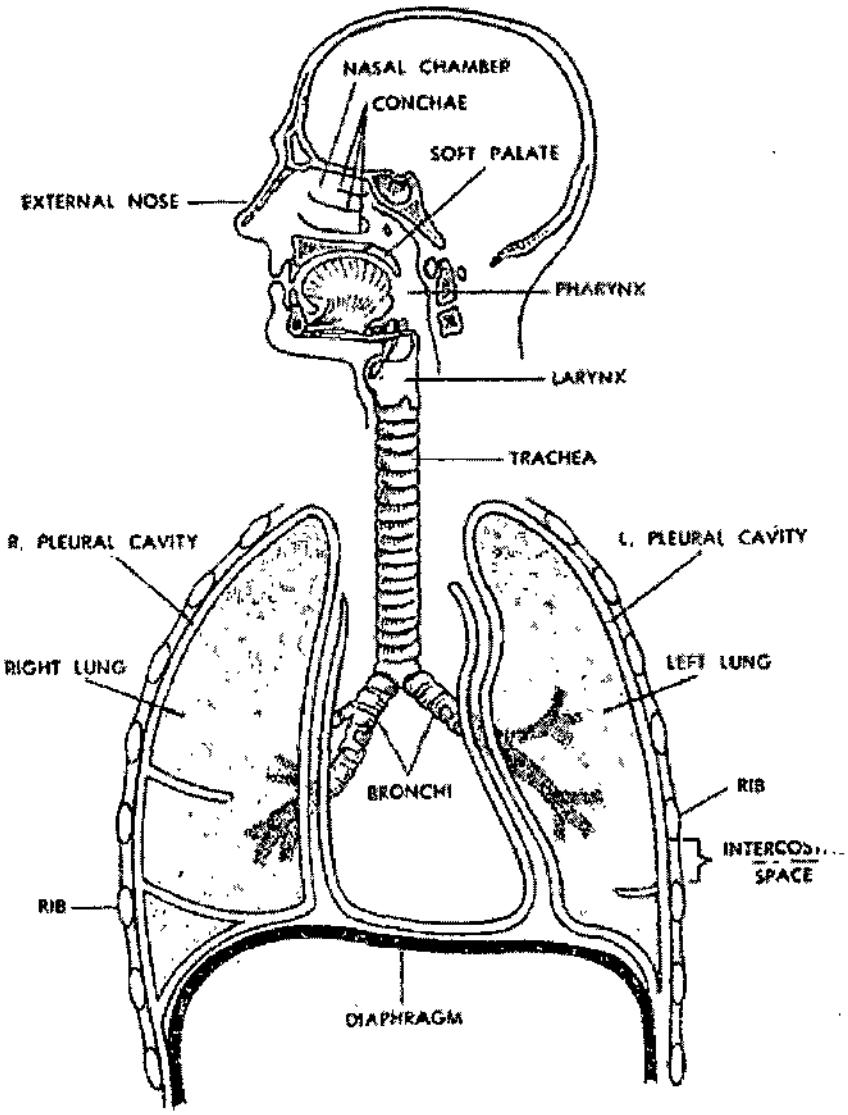


Fig. 7.1.

4. **Lungs and pleura:** The right lung is divided into 3 lobes (upper, middle and lower) whereas the left lung has only 2 (upper and lower), with further division into the broncho-pulmonary segments (10 right, 9 left). In total there are up to 23 airway divisions between trachea and alveoli. The bronchial walls contain smooth muscle and elastic tissue as well as cartilage in the larger airways. In the large airways the Gas movement occurs by tidal flow. In the small airways it results from diffusion only. The lungs are not directly attached to the chest wall but they change their volume and shape according to the changes in shape and volume of the thoracic cavity. Pleura is a double layer covering the surfaces of the lungs or the thoracic cavity together with a thin (20 μm) layer of liquid between them create a liquid coupling. The visceral pleura envelop the lung and the parietal pleura line the thoracic cavity. The pleura and lungs extend from just above the clavicle down to the

8th rib anteriorly, the 10th rib laterally and the level of 12th thoracic vertebra *T12 posteriorly*.

5. **Diaphragm:** The main muscle generating the negative intrathoracic pressure that produces inspiration is the *diaphragm*, a sheet separating the thorax from the abdomen. Its muscular part is peripheral, attached to the ribs and lumbar vertebrae, with a central tendon. Innervation is from the *phrenic nerves* (C3-C5) with contraction moving the diaphragm downwards forcing the abdominal contents down and out.

7.3. MECHANISM OF BREATHING

The complete mechanism of breathing is as follows :

INSPIRATION: Inspiration is the active part of the breathing process, which is initiated by the respiratory control centre in medulla oblongata (Brain stem). Activation of medulla causes a contraction of the diaphragm and intercostal muscles leading to an expansion of thoracic cavity and a decrease in the pleural space pressure. The diaphragm is a dome-shaped structure that separates the thoracic and abdominal cavities and is the most important muscle of inspiration. When it contracts, it moves downward and because it is attached to the lower ribs it also rotates the ribs toward the horizontal plane, and thereby further expands the chest cavity. In normal quite breathing the diaphragm moves downward about 1 cm but on forced inspiration/expiration total movement could be up to 10 cm. The external intercostal muscles connect adjacent ribs. When they contract the ribs are pulled upward and forward causing further increase in the volume of the thoracic cavity. As a result fresh air flows along the branching airways into the alveoli until the alveolar pressure equals to the pressure at the airway opening.

EXPIRATION: Expiration is a passive event due to elastic recoil of the lungs. However, when a great deal of air has to be removed quickly, as in exercise, or when the airways narrow excessively during expiration, as in asthma, the internal intercostal muscles and the anterior abdominal muscles contract and accelerate expiration by raising pleural pressure.

VENTILATION: Inhaled air passes through the *conducting airways* and eventually reaches the respiratory epithelium of the lungs. The conducting airways consist of a series of branching tubes which become narrower, shorter and more numerous as they penetrate deeper into the lung. The *trachea* divides into right and left *main bronchi*, which in turn divide into *lobar*, then *segmental* 12 *bronchi*. This process continues down to the *terminal bronchioles*, which are the smallest airways without alveoli. Since the conducting airways have no alveoli they do not take part in gas exchange but constitute the *anatomical dead space*. Its volume is about 150 ml but it varies because airways are not rigid; during inspiration, respiratory tubes are lengthened and dilated, especially in deep breathing. Since the airways serve as a barrier as well, harmful foreign material including most micro-organisms can not easily enter the lower respiratory passages. The very first barrier starts at the vestibules of the nose, which contain hairs, and healthy, sticky mucus intercepting air-borne particles. Caught particles are then ejected by ciliated epithelium, which covers the entire upper respiratory tract. The alveolated region of the lung includes *respiratory bronchioles* and *alveolar ducts* (completely lined with alveoli). This zone is called *respiratory zone* and the gas exchange occurs here. The distance from the terminal bronchiole to the distal

alveous is only a few mm, but the respiratory zone makes up most of the lung, its volume being about 2.5 to 3 L. Blood is brought to the other side of the blood-gas barrier from the right heart by pulmonary arteries, which also form a series of branching tubes leading to the pulmonary capillaries and back to the pulmonary veins. The capillaries lie in the walls of the alveoli and form a dense network that the blood continuously runs in the alveolar wall. At resting not all the capillaries are open but when the pressure rises (e.g. running) recruitment of the close capillaries occurs. The pulmonary artery receives the whole output of the right heart, but resistance of pulmonary circuit is very low. This enables the high blood flow to the circuit.

7.4. GAS EXCHANGE BETWEEN LUNGS AND BLOOD

Oxygen and carbon dioxide move between air and blood by simple diffusion. It is a passive process which means requires no energy. ***Fick's law of diffusion*** determines the amount of gas moves across the tissue is proportional to the area of the tissue but inversely proportional to its thickness.

Because the blood-gas barrier in the lung is extremely thin and has a very large area (50-100 m^2), it is well suited to its function.

The lung achieve such a large surface area of blood-gas barrier inside the limited thoracic cavity by wrapping the pulmonary capillaries around an enormous number of small air sacs, alveoli, and each about 1/3 mm in diameter. There are about 300 million alveoli in the human lung, creating 85 m^2 surface area but having a volume of only 4 L.

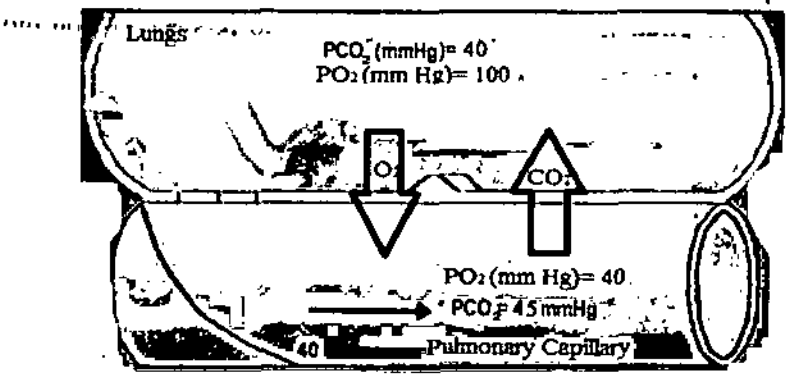


Fig. 7.2. Exchange of gases between lungs and blood.

Amount of Oxygen and Carbon Dioxide Partial Pressures:

Total pressure of a gas mixture is equal to the sum of the pressures that each gas in the mixture would have independently (**Partial Pressure** of each gas).

$$P_{dry\ atmosphere} = PN_2 + PO_2 + PCO_2 = 760 \text{ mm Hg}$$

Since O_2 constitutes 21 % of the atmosphere, $PO_2 = 159$ mm Hg.

Nitrogen 78%, $PN_2 = 593$ mmHg.

Inspired air also contains moisture and its amount may vary with temperature etc. However, when the inspired air arrived the alveoli it is normally saturated with water vapour. Because the temperature in the lungs does not change significantly water vapour of the alveolar air could be considered constant (47 mm Hg)

$$P_{wet\ atmosphere} = PN_2 + PO_2 + PCO_2 + PH_2O = 760 \text{ mm Hg}$$

$PO_2 = 0.21\ (760 - 47) = 150$ mm Hg (oxygen partial pressure of the inspired air when it arrives alveoli, before the gas exchange).

7.5. CELLULAR RESPIRATION

Respiration is the process by which organisms burn food to produce energy. The starting material of cellular respiration is me sugar **glucose**, which has energy stored in its chemical bonds. Just as burning coal produces heat and energy in the form of electricity, the chemical processes of respiration convert the energy of glucose into usable form.

Adenosine triphossphate (ATP) is the usable form of energy produced by respiration.

Respiration is the process of making ATP rather than breaking it down. To make ATP, the cell burns glucose and adds new phosphate groups to AMP or ADP, creating new power molecules.

There are actually two general types of respiration, aerobic and anaerobic. Acrobic respiration occurs in the presence of oxygen, while anaerobic respiration does not use oxygen. Both types of cell respiration begin with the process of glycolysis, after which the two diverge.

7.5.1. Aerobic Cell Respiration

Aerobic respiration is more efficient and more complicated than anaerobic respiration. Aerobic respiration uses oxygen and glucose to produce carbon dioxide, water, and ATP. More precisely, this process involves six oxygen molecules for every sugar molecule :

$$O_2 + C_6H_{12}O_6 \longrightarrow 6CO_2 + 6H_2O + \text{ATP energy}$$

This general equation for aerobic respiration is actually the product of three separate stages : glycolysis, the Krebs cycle, and the electron transport chain.

(a) Glycolysis : Glycosis is the first stage of aerobic (and anaerobic) respiration. It takes place in the cytoplasm of the cell. In glycolysis ("glucose breaking"). ATP is used to split glucose molecu9les into a three-carbon compound called **pyruvate.** This splitting produces energy that is stored in ATP and a molecule called **NADH.** The chemical formula for glycolysis is :

$$C_6H_{12}O_6 + 2ATP + 2NAD^+ \longrightarrow 2\ \text{pyruvate} + 4ATP + 2NADH$$

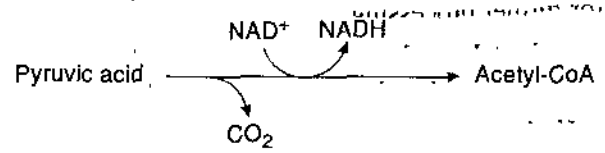
As the formula indicates, the cell must invest 2 ATP molecules in order to get glycolysis going. But by the time glycolysis is complete, the cell has produced 4 new ATP, creating a net gain of 2 ATP. The 2 NADH molecules travel to the mitochondria, where, in the next two stages of aerobic respiration, the energy stored in them is converted to ATP.

The most important things to remember about glycolysis are :

- Glycolysis is part of both aerobic and anaerobic respiration.
- Glycolysis splits glucose, a six-carbon compound, into two pyruvate molecules, each of which has three carbons.

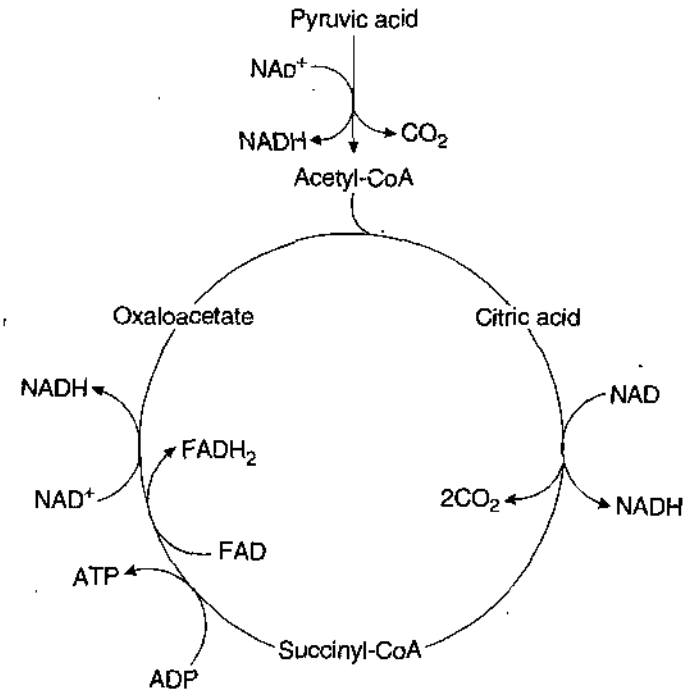
- In glycolysis, a 2 ATP investment result in 4 ATP payoff.
- Unlike the rest of aerobic respiration, which takes place in the mitochondria, glycolysis takes place in the crytoplasm of the cell.
- Unlike the rest of aerobic respiration, glycolysis does not require oxygen.

(b) The Krebs Cycle : After glycolysis, the pyruvate sugars are transported to the mitochondria. During this transport, the three-carbon pyruvate is converted into the two-carbon molecule called **acetate.** The extra carbon from the pyruvate is released as carbon dioxide, producing another NADH molecule that heads off to the electron transport chain to help create more ATP. The acetate attaches to a coenzyme called coenzyme A to form the compound **acetyl CoA.**



Acetyl-CoA enters the first major cycle for aerobic respiration, the **Krebs Cycle.** The Krebs cycle begins when acetyl-CoA and oxaloacetate interact to form the six-carbon compound eitric acid. (The Krebs cycle is also sometimes called the **citric acid cycle**). This citric acid molecule then undergoes a series of eight chemical reactions that strip carbons to produce a new oxaloacetate molecule. The extra carbon atoms are expelled as CO_2 (the Krebs cycle is the source of the carbon dioxide we exhale). In the process of breaking up citric acid, energy is produced. It is stored in ATP, NADH, and $FADH_2$. The NADH and $FADH_2$ proceed on to the electron transport chain.

The **Krebs cycle** is summarized below.



It is also important to remember that each glucose molecule that enters glycolysis is split into two pyruvate molecules, which are then converted into the acetyl-CoA that moves through the Krebs cycle. This means that for every glucose molecule that enters

glycolysis, the Krebs cycle runs twice. Therefore, for one glucose molecule running through aerobic cell respiration, the equation for the Krebs cycle is :

$$2 \text{ actyl-CoA} + 2 \text{ oxaloacetate} \longrightarrow 4CO_2 + 6NADH + 2FADH_2 + 2ATP + 2 \text{ oxaloacetate}$$

The most important things to remember about the Krebs cycle are :

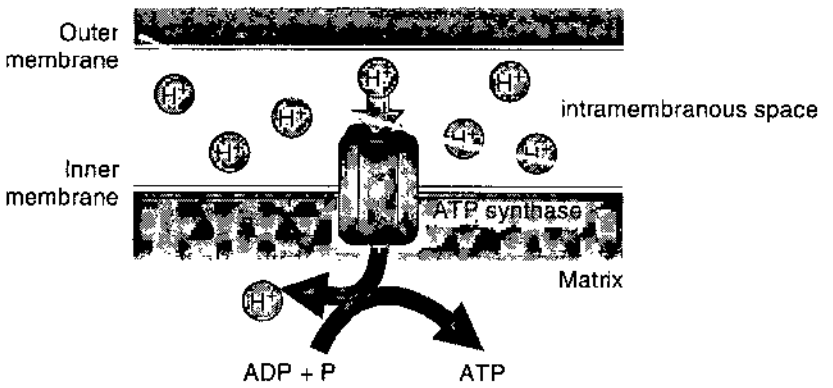
- The Krebs cycle results in 2 ATP molecules for each glucose molecule run through glycolysis.
- The Krebs cycle sends energy-laden NADH and $FADH_2$ molecules on to the next step in respiration, the electron transport chain. It does not export carbon molecules for further processing.
- The Krebs cycle takes place in the mitochondrial matrix, the innermost compartment of the mitochondria.
- Though the Krebs cycle does not directly require oxygen, it can only take place when oxygen is present because it relies on by-products from the electron transport chain, which requires oxygen. The Krebs cycle is therefore an aerobic process.

(c) The electron Transport Chain : A great deal of energy is stored in the NADH and FADH2 molecules formed in glycolysis and the Kerbs cycle. This energy is converted to ATP in the final phase of respiration, the electron transport chain :

$$10 \text{ NADH} + 2 \text{ FADH}_2 \longrightarrow 34ATP$$

The electron transport chain consists of a set of three protein pumps embedded in the inner membrane of the mitochondria. $FADH_2$ and NADH are used to power these pumps. Using the energy in NADH and $FADH_2$, these pumps move positive hydrogen ions (H^+) from the mitochondrial matrix to the intermembrane space. This creates a concentration gradient over the membrane.

In a process called **oxidative phosphorylation.** H^+ ions flow back into the matrix through a membrane protein called at ATP synthase. This channel is the opposite of the standard membrane pumps that burns ATP to transport molecules against their concentration gradient : ATP synthase uses the natural movement of ions along their concentration gradient to make ATP. All told, the flow of ions through this channel produces 34 ATP molecules. The waste products from the powering of the electron transport chain protein pumps combine with oxygen to produce water molecules. By accepting these waste products, oxygen frees NAD^+ and FAD to play their roles in the Krebs cycle and the electron transport chain. Without oxygen these vital energy carrier molecules would not perform their roles and the processes of aerobic respiration could not occur.



The most important points to remember about the electron transport chain and oxidative phosphorylation are :

- Four ATP molecules are produced by glycolysis and the Krebs cycle combined. The electron transport chain produces 34 ATP.
- The electron transport chain occur across the inner membrane of the mitochondria.
- The electron transport chain requires oxygen.

7.6. RESPIRATORY VALUES

The various terms used to describe lung excursion (movement) during quiet and maximal respiration are shown in figure 1.

The tidal volume (500ml) multiplied by the respiratory rate (14 breaths/min) is the minute volume (7,000ml/min). Not all of the tidal volume takes part in respiratory exchange, as this process does not start until the air or gas reaches the respiratory bronchioles (division 17 of the respiratory tree). Above this level the airways are solely for conducting, their volume being known as the anatomical dead-space. The volume of the anatomical dead-space is approximately 2ml/kg or 150ml in an adult, roughly a third of the tidal volume. The part of the tidal volume which does take part in respiratory exchange multiplied by the respiratory rate is known as the alveolar ventilation which is approximately 5,000ml/min.

Functional residual capacity (FRC) is the volume of air in the lungs at the end of a normal expiration approximately 2,500 ml. FRC value is determined by a balance between the inward elastic forces of the lung and the outward forces of the respiratory cage (mostly due to muscle tone). FRC falls with lying supine, obesity, pregnancy and anaesthesia.

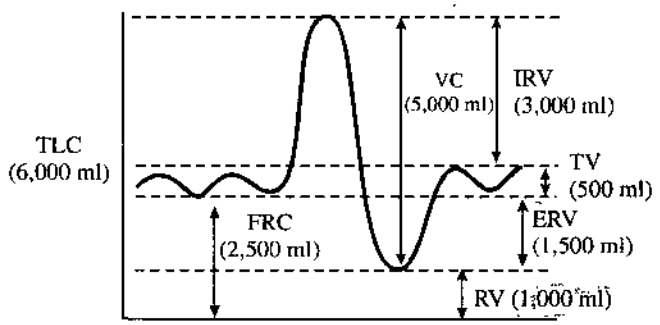


Fig. 7.3. Respiratory values.

In the absence of respiratory effort, the lung will come to lie at the point of the FRC.

7.7. ROLE OF HAEMOGLOBIN

Haemoglobin (Hb) = Heme (iron-porphyrin) + globin (protein)

Globin has 4 protein polypeptide chains: 2 alpha (each has 141 amino acid) and 2 beta (each has 146 amino acid).

Differences in the amino acid sequence of these chains give rise to various types of Hb.

Hb-A: Normal adult Hb

Hb-F: Foetal Hb, which makes part of the total Hb at birth and is gradually, replaced by Hb-A.

Hb-S: S stands for sickle. This Hb has valine in the beta chain instead of glutamic acid. Deoxygenated form of this Hb is poorly soluble and crystallises in the erythrocytes which results in changes in red cell shape. The fragility of the red cells is increased and there is a tendency to thrombus formation. Each polypeptide chain is combined with one heme group. In the centre of each heme group there is one atom of iron, which can combine with one oxygen molecule. Thus one Hb molecule can bind 4 oxygen molecules. Heme contains iron in the reduced form (Fe^{++}, ferrous iron). In this form the iron can share electrons and bond with oxygen. Oxygen forms a *reversible* combination with Hb.

$$O_2 + Hb \leftrightarrow HbO_2 \text{ (oxyhemoglobin)}$$

When oxyhaemoglobin dissociates to release oxygen to the tissues (the heme iron is still in ferrous form), and the Hb is called **deoxyhaemoglobin** (reduced Hb). Essentially, haemoglobin is an allosetric protein that has more than one shape and can undergo conformational changes in its structure based on environment conditions. There are two alternative structures of haemoglobin; the relaxed structure (R) which has a greater oxygen affinity, and the tense structure (T) which has lower affinity for oxygen. The change between the T and R structures is the result of a rotation of 15 degrees between the two alpha-beta dimers. This rotation changes the bonds between the side chains of the alpha-beta dimers in the F helix and therefore causes the heme molecule to change positions. In the T structure, the iron ion is pulled out of the plane of the porphyrin ring and becomes less accessible for oxygen to bind to it, thus reducing its affinity to oxygen. In the R structure the iron atom is in the plane of the porphyrin ring and is accessible to bind oxygen, thus increasing its oxygen affinity. The transformation from the T to R structure occurs when oxygen binds to the T structure under the high oxygen pressure environment in the lungs, which causes the rotation of the two dimers and shifts the remaining iron atoms so that they become more accessible to oxygen. Likewise, the transformation from the R to T structure occurs when oxygen is released under the low oxygen pressure environment of the tissues which causes the dimers to rotate back and shifts the iron atoms so that they become less accessible to oxygen. Thus, the cooperatively of the hemoglobin molecule can be explained by its unique structure which allows it to shift between the T and R structures in the presence or absence of oxygen.

The oxygen affinity of haemoglobin can also be regulated by external chemical factors including pH, carbon dioxide, and DPG (2, 3-diphosphoglycerate). In general any chemical agents that strengthen the bonds between the alpha subunits and prevent the rotation to the R structure decrease the oxygen affinity of the haemoglobin. When CO_2 is released into the blood from the tissues it acidifies the blood by increasing the concentration of hydrogen ions. This lowering in pH causes the oxygen affinity of the haemoglobin to decrease, which is known as the Bohr effect. The molecular basis behind the Bohr effect is that the T structure of haemoglobin binds hydrogen more readily than the R structure, so under a condition of low pH (high hydrogen ion concentration) the T structure, which has a decreased oxygen affinity, dominates. CO_2 has a similar effect on the haemoglobin, but instead of binding to the h ame molecule like oxygen, CO_2 binds to the N-terminus of the alpha globin molecule. The CO_2 binds

better to the globin in the T structure, so the release of oxygen in the tissues by the T structure of haemoglobin facilitates the uptake of CO_2. Then in the lungs, the uptake of oxygen causes the haemoglobin to change to the R structure, which causes the release of the CO_2 into the lungs, because CO_2 does not bind as well to the R structure. Finally, DPG is an allosteric effector that changes the oxygen affinity of haemoglobin by binding to the haemoglobin itself. DPG can bind to the T structure of haemoglobin, because of the change in structural conformation which allows it to fit, but can't bind to hemoglobin in the R structure. Therefore, the presence of DPG lowers the oxygen affinity by keeping the hemoglobin in the T structure.

The oxygen carrying capacity of the blood is determined by the Hb concentration. If it is below normal, **anaemia**, the oxygen concentration of the blood is reduced. When the Hb concentration is high, **polycythemia**, the oxygen carrying capacity of the blood is increased. The Hb and red blood cell production in the body is under control of erythropoietin, which is produced by the kidneys. Its production is stimulated when the amount of oxygen delivered to the kidneys is lower than normal. Normally Hb concentration in men is higher than women, because the red cell production is also stimulated by androgen.

One gram of Hb can combine with 1.39 ml oxygen and because normal blood has 15 mg of Hb/100 ml and the oxygen capacity of the 100 ml blood is 20.8 ml.

Oxygen saturation of the arterial blood (PO_2 = 100 mm Hg) is 97.5 % while oxygen saturation of the venous blood (PO_2 = 40 mm Hg) is 75 % to quickly determine protonation, and hence charge state.

7.8. SUMMARY

Respiration is the process of exchange of gases between lungs and blood. During inspiration O_2 from outside air enters into blood while during expiration CO_2 from blood goes to outside. The whole phenomena of exchange of gases occurs due to partial pressure difference.

7.9. STUDENTS ACTIVITY

1. Describe the Mechanism of Breathing.

2. How many O_2 molecules are carried by Hb ?

3. What is ventilation ?

4. During expiration CO_2 from ..... goes to ..... .

ANSWERS

2. 4. 4. Lungs, outside.

UNIT

8

BLOOD VASCULAR SYSTEM

STRUCTURE

LEARNING OBJECTIVES

After going through this unit you will learn

What is blood ?

What is blood vascular system ?

How blood is circulated in the body ?

What are functions of blood ?

8.1. INTRODUCTION

Blood is a red fluid that oozes out when we have got injured. It is the medium to transport dissolved gases, nutrients, hormones and waste products. Blood along with the heart and the blood vessels (*e.g.* veins and arteries) comprises the circulatory system of the body. A human being has an average 5 liters of blood in his body. It occupies 8% of total body weight and has an average density of about 1060 kg/m^3. The intricate network of veins and arteries, distributes blood throughout the body. The pumping action of the heart helps in circulation of blood.

8.2. STRUCTURE OF HUMAN HEART

The adult human heart has a mass of between 250 and 350 grams and is about the size of a first. It is located anterior to the vertebral column and posterior to the sternum.

It is enclosed in a double-walled sac called the **pericardium.** The superficial part of this sac is called the fibrous pericardium. This sac protects the heart, anchors its surrounding structures, and prevents overfilling of the heart with blood.

The outer wall of the human heart is composed of three layers. The outer layer is called the **epicardium,** or visceral pericardium since it is also the inner wall of the pericardium. The middle layer is called the **myocardium** and is composed of cardiac muscle which contracts. The inner layer is called the **endocardium** and is in contact with the blood and the heart pump. Also, it merges with the inner lining (**endothelium**) of blood vessels and covers heart valves.

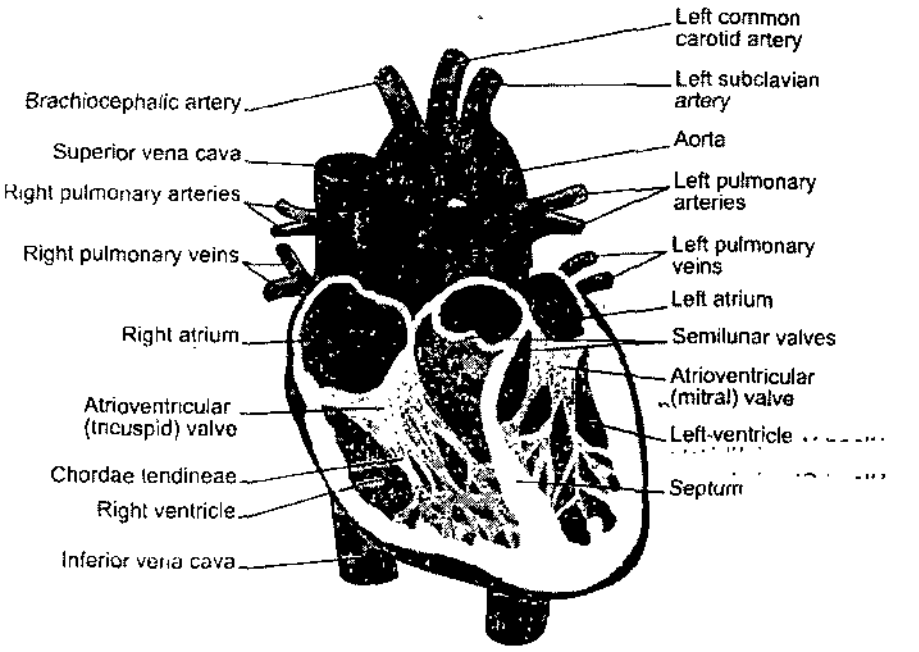


Fig. 1. Structure of the human heart

The human heart has four chambers, two superior atria (sigular called atrium) and two inferior ventricles. The atria are the receiving chambers and the ventricles are the discharging chambers. The pathway of blood through the human heart consists of a pulmonary circuit and a systemic circuit. Deoxygenated blood flows through the heart in one direction, entering through the **superior vena cava** into the **right atrium** and is pumped through the **tricuspid valve** into the **right ventricle** before being pumped out through the **pulmonary valve** to the **pulmonary arteries** into the **lungs.** It returns from the **lungs** through the **pulmonary veins** to the **left atrium** where it is pumped through the **mitral valve** into the **left ventricle** before leaving through the **aortic valve** to the **aorta.**

8.3. COMPOSITION OF BLOOD

Blood is composed of a red coloured liquid called plasma and cellular part. The cellular part contains three types of cell: Red Blood Cell (RBC), White Blood Cell (WBC) and Platelets. All the parts of blood are described below:

(i) Blood Plasma: Blood Plasma is the straw colored liquid portion of the blood. 92% is composed of water and the rest 8% is made up of plasma proteins. It is mostly composed of dissolved proteins, mineral ions, glucose, clotting factors and carbon dioxide. It circulates dissolved nutrients (amino acids, fatty acids and glucose) and removes waste products (carbon dioxide, lactic acid and urea) from the body. Other components of blood plasma are serum, albumin, lipoprotein, immunoglobulins, electrolytes, etc.

(ii) Red blood cells: RBCs are also called erythrocytes. These are *disc* shaped cells which make up 99% of blood. They constitute 45% of blood by volume. Mature RBCs are biconcave and flexible, lacking cell nucleus and organelles. They are the principal carriers of the red colored molecules **haemoglobin**. Haemoglobin is an iron containing protein that binds about 97% of all oxygen in the body. Each hemoglobin molecule binds four oxygen molecules to itself- consequently hemoglobin permits human blood to carry more than 70 times the amount of oxygen that it could have carried otherwise. The surface shape of red blood cells is so that oxygen get maximum surface area to facilitate absorbtion and release.

The cell membrane of red blood cells contains different proteins, which are responsible for different types of blood. There are primarily two types of proteins found in the cell membrane of red blood cells- protein A and B. Different combinations of these proteins and their antibodies results in four types of blood

- type A : have protein A and antibodies of b protein
- type B : have protein B and antibodies of a protein
- type AB : have both protein A and B but neither of the antibodies
- type O : have neither proteins but have both the antibodies

Type AB is called 'universal acceptor' and type O is called 'universal donor'.

(iii) White blood cells: These are also called as leukocytes. They make for 1% by volume of total blood. The white blood cells have a vital role of defense against external organisms. White blood cells also serve as 'sanitary engineers' cleaning up dead cells and tissue debris that would otherwise accumulate to and lead to problems. Leukocytes are classified as granulocytes and agranulocytes. Granulocytes cells include neutrophils, basophils and eosinophils, whereas agranulocytes cells are lymphocytes, monocytes and macrophages.

Many infections stimulate the body to release into the bloodstream large number of protective leukocytes that are normally held in reserve, causing the white cell number to rise. Some white blood cells may die in the process of fighting against an infection and their dead bodies accumulate and contribute to the white substance that is commonly seen at the sight of infections, usually called 'pus'. Not all infections lead to an increase in the white blood count- the virus that is responsible for AIDS results in a reduced white blood count and hence reduced ability to fight other infections.

(iv) Platelets : Platelets are also known as thrombocytes. They are derived from precursor cells known as megakaryocytes and are devoid of nucleus. The lifespan of platelets is 5-9 days. The most important function of platelets is blood coagulation or blood clotting. If damage occurs to a blood vessel, circulating platelets immediately get trapped at the injury site. On accumulating the platelets 'plug' the leak in the vessel providing a first step in damage control. This mechanism is supplemented by 'blood coagulation', or clotting, which is the most important means of defense against bleeding. As mentioned plasma contains several dissolved proteins. **Fibrinogen** is a rod shaped *soluble* protein which in the presence of a catalyst **thrombin** gets converted to an *insoluble* protein **fibrin** . Fibrin molecules make a tangled net of fibers by adhering end-to-end and side-to-side which immobilizes the fluid portion of blood (causing it to solidify) and also traps the red blood cells. The combined action of the platelets and 'fibrin web' is sufficient to prevent a dangerous loss of blood. In cases where the formation of fibrin and hence formation of a clot is impaired due to some reason a person is at great risk of bleeding to death.

8.4. BLOOD VASCULAR SYSTEM

The blood vascular systems are classified as specialized connective tissue. The blood vascular system consists of the :

- Heart
- Pulmonary circulation: It is system of blood vessels to and from the lungs.
- Systemic circulation: The system of blood vessels bringing blood to and from all the other organs of the body.

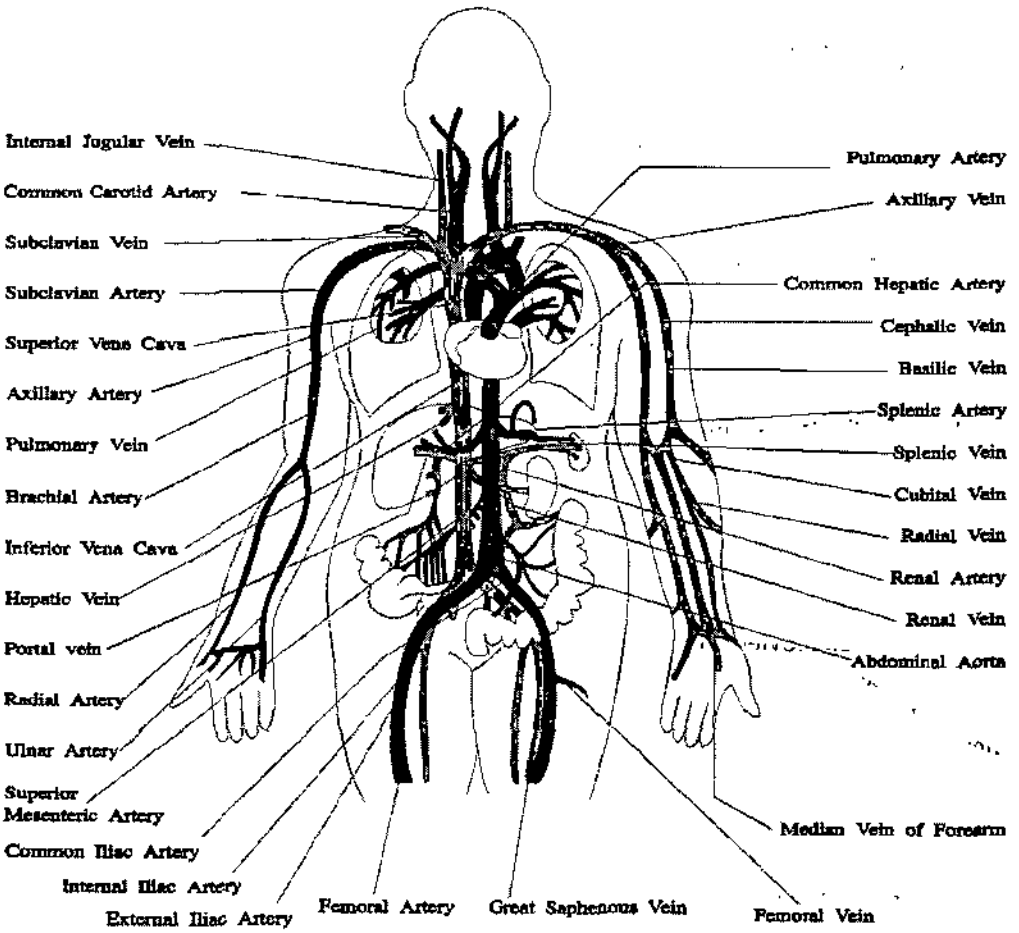


Fig. 8.1. Blood vascular system

Complete blood vascular system has following types of blood vessels :

- Arteries
- Veins, and
- Capillaries

(I) Arteries: These vessels bring blood from the heart to the tissues in a high-pressure, fast-flow, system and consequently the arterial wall needs to be able to withstand the biomechanical stresses. The arterial wall is composed of three main layers or tunics.

- ***Tunica intima*** (internal tunic) consisting of :
  - **(a) endothelium** (single lining layer of endothelial cells)
  - **(b) sub-endothelial layer**
  - **(c) inner elastic limiting membrane** (elastic lamina, which after fixation appears undulating).
- ***Tunica media*** (middle tunic) consisting of :
  - (a) circular smooth muscle (or spiral)
  - (b) concentric elastic lamina (formed by the smooth muscle cells).
- ***Adventitia*** (outer layer) composed of :
  - **(a) connective tissue** surrounding the vessel
  - **(b) outer elastic limiting membrane** (on the border between the *Tunica media* and the *Adventitia*

(a) Vasa vasorum. These are small blood vessels supplying oxygen and nutrients to the wall of the artery. The blood flow in the arterial lumen is too great for exchange of oxygen or nutrients.

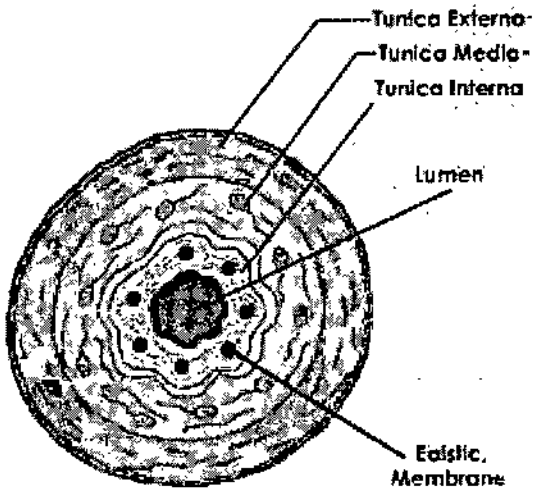


Fig. 8.2. Layers of arteries

Arteries are classified into two main groups:

(i) Conducting (Elastic Arteries): These are large arteries closest to the heart such as aorta, renal artery. They have very high blood pressure and flow and need to withstand stresses of extremely high blood flow. Their structure is best seen in the aorta. They are called elastic arteries as their Tunica media possesses 50-75 well-developed elastic lamina in between the thick smooth muscle bands. These have a similar appearance to the inner elastic limiting membrane. The elastic lamina prevents the excessive expansion of the vessel diameter and when they spring back they push the blood onwards. The smooth muscle in arteries is important in maintaining the vessel diameter during blood flow and also plays a role in blood pressure levels. The vascular smooth muscle is in a state of **tonus** (partial contraction). The degree of tonus of the smooth muscle cells in the wall of arteries and arterioles is controlled by the autonomic nervous system and also by endocrine secretions. In **hypertension** (high blood pressure), often associated with stress or aging, the peripheral arterial vessels show increased tonus.

(ii) Distributing (Muscular Arteries): These are smaller in diameter with a slower blood flow. The arteries lead to smaller vessels, the **arterioles**, which lead to the **capillaries**. Arterioles are small vessels with a diameter of 0.5mm or less. They consist of three basic layers:

(a) ***Tunica intima*** with endothelium alone (no subendothelial layer) and a very thin inner elastic limiting membrane

(b) ***Tunica media*** with only 4-5 layers of smooth muscle

(c) ***Adventitia*** that is fairly thin

The capillaries are present in the form of microcirculation networks (**capillary beds**) in the organs and tissues. Exchange of metabolites and transport through the vessel wall is only possible in the capillaries, as only here the blood flow is sufficiently low and the vessel walls are sufficiently thin. Metarterioles are small vessels that are on the border between arterioles and the capillary bed. They can act as sphincters and cut off the flow of blood into the capillary bed.

Arterial blood in the systemic circulation is richly oxygenated, whereas the venous blood has little oxygen. In the Pulmonary Circulation the arterial blood is poorly

oxygenated, whereas the venous blood, are highly oxygenated as they replenished its oxygen supplies in the lungs.

(II) Veins : The veins constitute a **low-pressure system** of vessels. The return of blood to the heart from the capillary beds of the tissues follows a route of **small venules → small veins →large veins**. The route of the veins is in parallel to that of the arteries.

Characteristics of veins:

- more numerous than arteries
- diameter of vessels is larger than that of adjacent arteries
- walls of veins are thinner and less elastic or distensible than arteries. (As a result in histological preparations the lumen often appears collapsed or irregular)
- the relative numbers of *vasa vasorum* are greater in the veins (necessary as the vessels have much less oxygenated blood)
- valves are found in veins.

Veins are classified as large, medium or small veins.

Veins have three layers;

(a) ***Tunica intima:*** The *T. intima* is composed only of endothelium. The smooth muscles of the *T. media* are all **circular muscles**; grouped in bundles,

(b) ***Tunica media:*** The *T. media* is composed of two muscle layers- an inner longitudinal layer and an outer circular layer. Elastic fibers are present throughout the media.

(c) ***Adventitia:*** The muscles present in the adventitia are **longitudinal**.

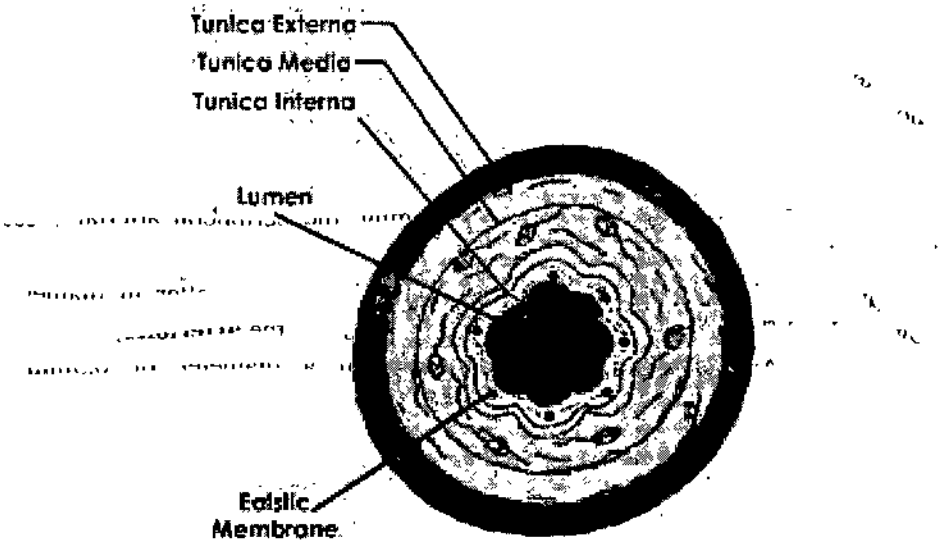


Fig. 8.3. Layers of vein

The movement of blood in veins is passive. The muscles play a role in tonus. Most of the muscles in veins are present in the adventitia and are longitudinal. **Valves** are present in veins, especially in those that transport blood against the force of gravity, such as in the legs. The valves are composed of folds of the *Tunica intima* (endothelium and connective tissue). The valves prevent the backflow of blood. Weakness in the walls of veins can result in **varicose veins** and improper closure of the valves.

Venules :

These have a very small diameter (20-50 μm). In total preparations such as from the mesentery, the venule wall is so thin that the erythrocytes are visible, whereas they are not seen in the adjacent and parallel arterioles.

(III) Capillaries : They have a diameter of about 7-9 μm, which is almost equal to the dimensions of erythrocytes (about 7.2 μm). The diameter of the capillaries varies according to the functional status of the tissue or organ. When functional demands rise the diameter of the capillaries enlarges, allowing increased exchange of oxygen and metabolites.

There are three different types of capillaries:

- **Continuous capillaries**: These have continuous endothelial cells located on a continuous basal lamina. In cross sections they are seen to be composed of 2-3 endothelial cells, connected by tight junctions. In the region of the contact between the ends of two endothelial cells there is a small area in which the edge of one of the cells protrudes into the lumen called marginal fold. Continuous capillaries are characterized by abundant small invaginations of the cells called caveolae and numerous micropinocytotic vesicles in the cytoplasm. All the materials crossing the cell (transcellular transport), in both directions do so via these micropinocytotic vesicles.

Continuous capillaries are found in those organs that need strict control on access of the substances from the blood. These include all the organs with a "blood-barrier".

- **Fenestrated capillaries:** These possess endothelial cells with groups of very small **pores** or **fenestrae** of about 80-100nm diameter. These are seen in transmission electron micrographs and in particular after freeze-etching techniques. One prominent site for fenestrated capillaries is in the renal glomeruli. Fenestrated capillaries are also common in most of the endocrine glands.
- **Sinusoids:** Sinusoids are irregular vessels with large diameters of about 30-40nm. In most cases the sinusoids are not cylindrical. Sinusoids are found in the liver, endocrine glands and in the hematopoietic organs (bone marrow, spleen). In many cases the sinusoids are also fenestrated. This is the case in those organs which need a very rich blood supply including most of the endocrine glands.

The exchange of materials through capillary walls can be:

(a) transcellular: when material is passed through

- micropinocytotic vesicles in the endothelium (as in continuous capillaries)
- fenestrations (as in fenestrated endothelium or sinusoids)
- **intercellular**: when material is passed through
- gap junctions
- spaces between endothelial cells (as in sinusoids of spleen, liver).

Endothelial cells are known to produce a variety of local factors that are important in the functioning of the cardiovascular system. These include nitric oxide.

Endothelial cells

The endothelial cells are derived from embryonic mesenchyme and should not be regarded as epithelial, but as connective tissue cells. Endothelial cells line the lumina of all the vessels of the blood vascular and lymphatic vascular systems. Endothelial cells lining the blood vessels are very flattened, elongated cells, with elongated nuclei that protrude into the lumina. The total number of endothelial cells in the body is

approximately 6×10^{23} and covers about 700–1000m^2 area and in total weigh about 1.5 kg.

8.5. BLOOD CIRCULATION

The oxygenated and deoxygenated blood flow in a cycle as follows:

Oxygenated Blood

- Oxygenated blood leaves the lungs and enters the Left Atrium (LA) of the heart via the pulmonary veins.
- This oxygenated blood is then pumped from the Left Atrium (LA) of the heart to the Left Ventricle (LV) of the heart, and then out of the heart to the body tissues via the aorta, which is the major artery leaving the heart.
- The aorta divides into other arteries that serve different parts of the body (as mentioned on the page about the structure of the heart). These can be separated into two categories: blood supply to the upper-body, and blood supply to the lower-body.
- Blood Supply to the Upper-Body: The aorta leads to the subclavian arteries that take blood to the arms (some of which eventually reaches the hands), and also to the carotid artery that carries blood to the head.
- Blood Supply to the Lower-Body: The aorta also leads to the hepatic artery that carries blood to the liver, the mesenteric artery that carries blood to the small intestines, the renal arteries that carry blood to the kidneys, and the iliac arteries that carry blood to the legs (some of which eventually reaches the feet.).

Deoxygenated Blood

- Blood is deoxygenated when it leaves the tissues and organs it has supplied with oxygen and other nutrients, to return back to the pulmonary circulatory system. This can also be summarised for the upper-body and lower-body separately:
- Return of Blood from the Upper-Body: Blood returns from the head via the jugular veins, and from the arms via the subclavian veins. All of the blood in the major veins of the upper body flows into the superior vena cava, which returns the blood to the right ventricle of the heart.
- Return of Blood from the Lower-Body: Blood returns from the small intestines by passing through the hepatic portal vein to the liver. Blood returns from the liver via the hepatic vein, from the kidneys via the renal veins, and from the legs via the iliac veins. All of the blood in the major veins of the lower body flows into the inferior vena cava, which returns the blood to the right ventricle of the heart.
- After re-entering the right atrium of the heart via the superior vena cava and the inferior vena cava, deoxygenated blood is pumped into the right ventricle of the heart and then out of the heart to the lungs via the pulmonary artery.
- Deoxygenated blood enters the lungs and is oxygenated before leaving the lungs (as oxygenated blood), and so the cycle begins again.

The complete cycle of blood flow can be shown as (dark area represents deoxygenated blood flow and light area shows oxygenated blood flow):

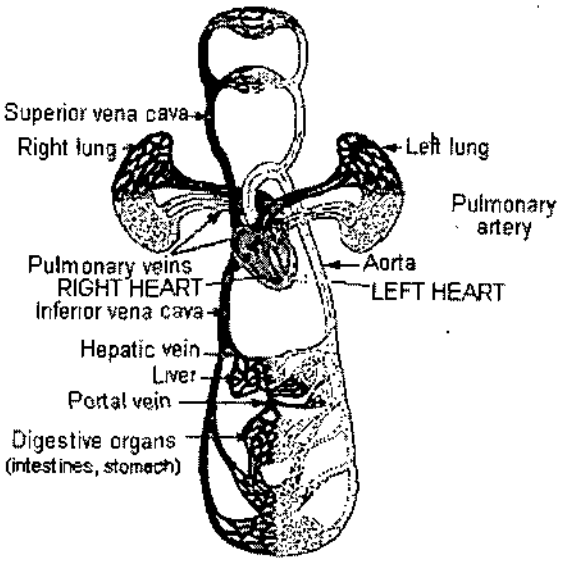


Fig. 8.4. Blood circulation in body.

8.6. FUNCTIONS OF BLOOD

Blood has three main functions: transport, protection and regulation.

(i) **Transport:** Blood transports the following substances:

- Gases, namely oxygen (O_2) and carbon dioxide (CO_2), between the lungs and rest of the body
- Nutrients from the digestive tract and storage sites to the rest of the body
- Waste products to be detoxified or removed by the liver and kidneys
- Hormones from the glands in which they are produced to their target cells
- Heat to the skin so as to help regulate body temperature.

(ii) **Protection**: Blood has several roles in inflammation:

- Leukocytes, or white blood cells, destroy invading microorganisms and cancer cells
- Antibodies and other proteins destroy pathogenic substances
- Platelet factors initiate blood clotting and help minimise blood loss

(iii) **Regulation**: Blood helps to regulate:

- pH by interacting with acids and bases
- Water balance by transferring water to and from tissues

to quickly determine protonation, and hence charge state.

8.7. SUMMARY

Blood is a red fluid that transport dissolved gases, nutrients, hormones and waste products. Blood along with the heart and the blood vessels (e.g. veins and arteries) comprises the circulatory system of the body. Blood is mainly composed of

(i) Blood Plasma
(ii) Red blood cells
(iii) White blood cells
(iv) Platelets.

8.8. STUDENTS ACTIVITY

1. What are the four main functions of the blood in body?

2. What are the four components of the blood?

3. What is the major function of platelets?

8.9. TEST YOURSLEF

1. Fill in the blanks
   (a) Look like red discs .....
   (b) Small granular fragments; no nucleus; vary in size.....
   (c) Straw-colored fluid .....
   (d) Red blood cells (RBC's) made in .....
   (e) Hemoglobin gives RBC's the ability to .....
   (f) The key raw material for RBC's is.....
   (g) The RBC's job in transportation is .....
   (h) The function of white blood cell is .....
2. Match the white blood cells with their function (draw lines connecting the word and function) :

(a) Neutrophil	(i) Produce humoral defenses
(b) Macrophage	(ii) Fight bacteria and eat them
(c) Lymphocyte	(iii) Eat dead cells and other debris
(d) Plasma	(iv) Produce antibodies

3. What do platelets do in the body? .....
4. Blood is composed of ....., ... and ..... .
5. Arteries carry ..... blood

6. Veins carry ..... Blood.
7. Capillaries are sites of .....
8. Which white blood cells are phagocytes?

ANSWERS

1. (a) R.B.C. (b) W.B.C.
   (c) Plasma (d) bone marrow
   (e) join oxygen (f) proteins
   (g) to carry oxygen (h) destroy invading micro organism
3. inhibits blood clothing 4. RBCs, WBCs, Platelets
5. Pure 6. impure
7. exchange of gas and metabolites.
8. Leukocytes.

❑❑❑

UNIT

9

HEART BEAT, CARDIAC CYCLE AND E.C.G.

STRUCTURE

- Cardiac Cycle
- Events of cardiac cycle
- Origin and conduction of heart beat
- Control of heart beat
- Electro Cardio Gram (ECG or EKG)
- Summary
- Student Activity
- Test yourself

LEARNING OBJECTIVES

After going through this unit you will learn :

How cardiac cycle occurs ?

What is the path of cardiac cycle ?

How an ECG can be drown and read ?

9.1. INTRODUCTION

Cardiac cycle refers to the cardiac events that occur from the beginning of one heart beat by spontaneous generation of action potential in SA node to the beginning of the next. When the heart rate is 75/min, the period of one cardiac cycle is 0.8 sec. One cardiac cycle completes with

1. Diastole: a period of relaxation during which heart fills with blood
2. Systole: a period of contraction during which the blood is ejected from the heart.
3. Isovolumetric: a phase when all valves are closed and ventricle behaves as a closed chamber and volume within ventricle remains constant

Time period of various events of cardiac cycle:

A) Atrial Cycle: 0.8 sec
   1. Systole: 0.1 sec
   2. Diastole: 0.7 sec

B) Ventricular Cycle: 0.8 sec
   1. Systole: 0.3 sec
      - Isovolumetric contraction: 0.05 sec
      - Rapid ejection phase: 0.1 sec
      - Reduced ejection phase: 0.15 sec
   2. Diastole: 0.5 sec
      - Isovolumetric relaxation: 0.1 sec
      - Rapid filling phase: 0.1 sec

- Reduced filling phase (Diastasis): 0.2 sec
- Last Rapid filling phase (Atrial systole): 0.1 sec

Normally, atrial and ventricular systoles never coincide. Ventricular systole occurs during atrial diastole and atrial systole occurs during ventricular diastole. For a period of about 0.4 sec (Isovolumetric ventricular relaxation, Rapid ventricular filling phase and Reduced ventricular filling phase), both the ventricles and atria relax.

9.2. EVENTS OF CARDIAC CYCLE:

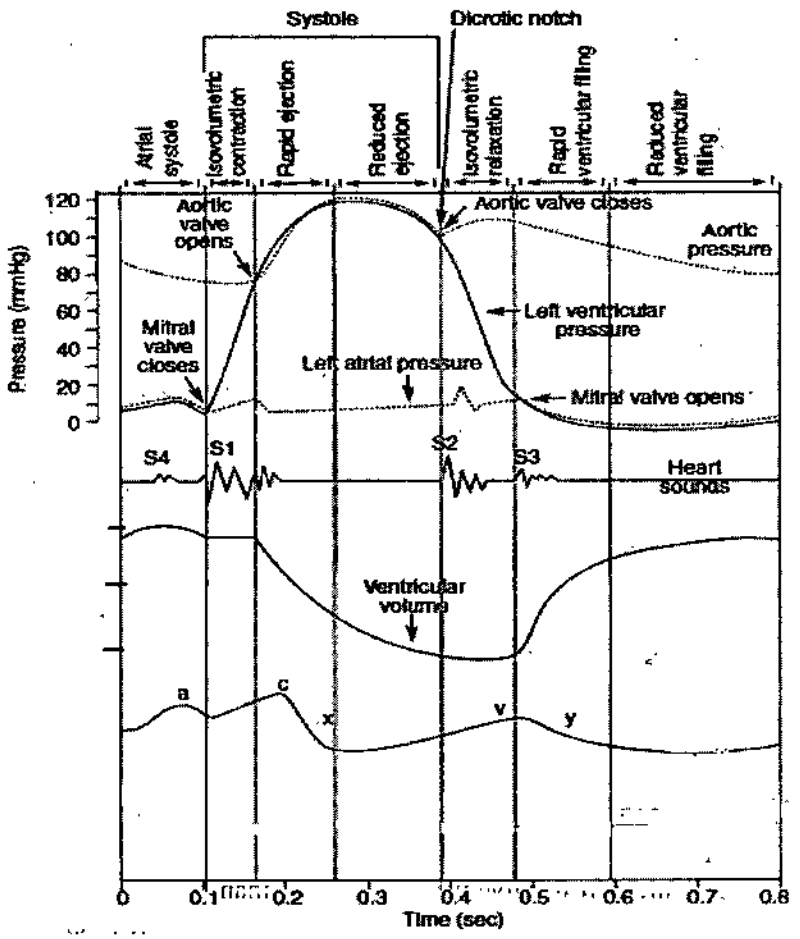


Fig. 1. Events during one cardiac cycle.

1. **Atrial Systole :**
   - It begins due to spontaneous generation of action potential in SA node.
   - Contributes to last rapid phase of **ventricular filling (20% filling)** but is not essential for ventricular filling.
   - Filling of ventricle by atrial systole gives rise to **4th Heart sound (S4)**, which is not audible in normal adults.
   - **"a" wave** appears on atrial pressure curve due to increase in atrial pressure (4 to 6 mmHg in right atrium and 7 to 8 mmHg in left atrium).
2. **Isovolumetric ventricular contraction :**
   - Ventricles are filled with blood: 80% filling occurred before atrial systole and 20% filling occurred during atrial systole.
   - Immediately after beginning of ventricular contraction begins, pressure rises abruptly.

- When Ventricular pressure is more than Atrial pressure, **Atrioventricular (AV) valve closes** giving rise to **2nd heart sound** (S2). As mitral valve closes before tricuspid valve, 1st heart sound may split.
- Since AV valves and semilunar valves (aortic and pulmonary valves) are both closed, isovolumetric contraction occurs and there is **rapid rise in ventricular pressure**.

3. Rapid Ventricular Ejection :

- When the left ventricular pressure rises above the aortic pressure (~80 mm Hg), **aortic valve opens** and there is **rapid ejection (70% ejection)** of blood into the aorta.
- When the right ventricular pressure rises above the pulmonary pressure (~8 mm Hg), **pulmonary valve opens** and there is rapid ejection (70% ejection) of blood into the pulmonary trunk.
- **"c" wave** appears on atrial pressure curve due to bulging AV valve on atria due to increasing ventricular pressure.
- Pressure rise in the ventricles is slower because the blood flows into the arteries. The entry of blood into the arteries causes arteries to stretch and pressure increases. During this period, the pressure in the left ventricle and aorta reaches a **maximum** of 120 mmHg (systolic pressure) and that in right ventricle and pulmonary trunk reaches a maximum of 24 mm Hg.
- Atrial filling begins .

4. Reduced Ventricular Ejection :

- Ejection of **blood (30% ejection)** from the ventricles continues, but is slower.
- Ventricular **pressure begins to decrease**.
- Aortic and Pulmonary pressure also decreases because of runoff of blood from larger arteries into smaller arteries.
- Atrial filling continues.

5. Isovolumetric ventricular relaxation :

- Repolarization of Ventricles is now complete.
- Ventricular pressure begins to fall.
- When the pressure in respective ventricles is less than the pressure in aorta and pulmonary trunk, the **semilunar valves close** (closure of aortic valve followed by pulmonary valve) giving rise to **2nd heart sound (S2)**. Inspiration causes splitting of 2nd heart sound.
- **Dicrotic notch or incisura** appears on aortic pressure curve as a "blip" after closure of aortic valve due to short period of backward flow of blood immediately before closure of the valve, followed by sudden cessation of the backflow.
- Since, AV valves and semilunar valves are both closed; isovolumetric relaxation.
- Ventricular how falls rapidly but the elastic walls of the arteries maintain a high pressure in the arteries, even during diastole although there is a fall in arterial pressure.
- **"v" wave** appears on atrial pressure curve due to accumulation of blood in atria against closed AV valves.
- When ventricular pressure is less than the atrial pressure, **AV valves (Mitral and Tricuspid) open**.

6. **Rapid Ventricular Filling :**
   - Rapid flow of blood, long accumulated in the atria to the ventricles gives rise to the **3rd heart sound**, which is normal in children but pathologic in adults.
7. **Reduced ventricular filling (Diastasis) :**
   - **Longest phase** of cardiac cycle.
   - Only a small amount of blood flows into the ventricles at a slower rate from the great veins via atria.
   - During this period, the blood in both atrium and ventricle becomes continuous as if a single cavity.
   - **Time required for diastasis and ventricular filling depends on the heart rate.** Increase in heart rate decreases the time available for ventricular filling.
8. **Last rapid filling phase :**
   - Coincides with the atrial systole.

9.3. ORIGIN AND CONDUCTION OF HEART BEAT

The heart is consists of cardiac muscles. These muscles have the property of excitability and conductivity. So, when the cardiac muscles are stimulated by a specific stimulus, these got excited and initiate the waves (depolarization) of electric potential called cardiac impulses which are conducted along the special cardiac muscle fibers on the wall of the heart chambers.

Initiation of heartbeat is under three special bundles of cardiac muscles called nodal tissues:

1. Sinu-auricular or sino-atrial node (S.A. node). It lies in the right wall of right auricle, below the opening of superior vena cava. It is also called pacemaker as it is first to originate the cardiac impulses and determines the rate of heart beat. It has the highest degree of autorhythmicity (70-80 times/ minute) but least conductivity. It maintains the basic rhythm of heartbeat. These cardiac impulses are conducted along the tracts of special cardiac muscle fibers (called internal pathways) over both the auricles at the rate of 1 meter/second. These impulses reach the A.V. node about 0.03 second after their origin from S.A. node. These impulses cannot be passed to the wall of ventricles as the cardiac muscle fibers of auricles and ventricles are separated by a thin layer of fats, annular pad. It has a rest potential of only -55 to -60 mV

2. Atrio-ventricular node (A.V. node). It lies in the right atrium near the junction of interauricular and interventricular septum close to opening of coronary sinus. It is stimulated by the waves of contraction initiated by S.A. node. It generates the cardiac impulses, which are conducted to the muscles of the ventricles through bundle of Hiss and Purkinje fibers at the rate of 1.5 to 4 meters/second.

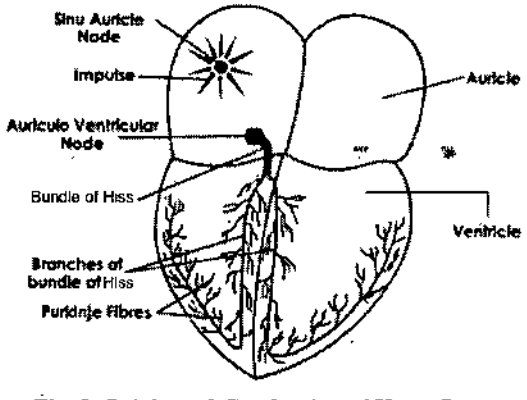


Fig. 2. Origin and Conduction of Heart Beat.

3. Bundle of His. It is also called A.V. bundle. The bundle of Hiss originates from the AV node as a bundle of tissue. Immediately after its origin it divides into 2 branches. These branches run along the inner border of each ventricle and reach to the tip of the ventricle and then run upwards along the outer margin of the ventricle. These bring about synchronous contraction of the ventricles from the apex of heart, which forces the blood into the pulmonary arch and aortic arch.

4. Purkinje fiber: The bundle of Hiss and its branches produce minute branches called Purkinje fibers on the wall of the ventricles.

S.A. node, A.V. node, Bundle of Hiss (A.V. bundle) and Purkinje fibers collectively form the conducting system of the heart and is responsible for autorhythmicity of heart. During a heart beat, the auricles contract first and the ventricles contract later. This is because there is no muscular continuity between the auricles and the ventricles. The auricles receive the impulses directly from the SA node. The impulses reach the AV node about 0.03 seconds after their origin from the SA node. So the ventricles always contract after the auricles. When S.A. node is damaged, then it is not able to generate the cardiac impulses, then the heart beat becomes irregular called arrhythmia. It is corrected by an artificial pacemaker. It is set in the chest of the patient, by surgical grafting, to pump the required amount of blood. It stimulates the heart electrically at regular intervals to beat at normal rate. So human heart is called myogenic or autorhythmic heart.

9.4. CONTROL AND REGULATION OF HEART BEAT

Apart from the myogenic control, the heart beat is also regulated by two controls viz. nervous and hormonal controls. Only because of these controls the rate of heart beat can be adjusted according to the needs of body *e.g.* it increases during exercise, *fear, anger etc. while decreases during the rest.*

Nervous control. The rate of heart beat as well as the strength of the beat is controlled by two cardiovascular centers of the autonomic nervous system, these centers are located in the upper part of the ventral wall of the medulla oblongata.

- One sends nerve impulses down **accelerans nerves**. The accelerans nerve is part of the sympathetic branch of the **autonomic nervous system**, and like all post-ganglionic sympathetic neurons releases **noradrenaline** at its endings on the heart.
- The other sends nerve impulses down a pair of **vagus nerves**. The vagus nerves are part of the parasympathetic branch of the **autonomic nervous system**. They, too, run from the brain (medulla oblongata) to the heart. Their activity **slows** the heartbeat.

(a) Cardiac acceleratory center. It is associated with the sympathetic nerve fibers, which, in turn, are associated with the S.A. node. These nerve fibers stimulate and increase the rate and depth of the contraction of S.A. node through a neurotransmitter chemical called adrenalin or epinephrine. It increases the rate of heart beat (about 200 to 250 times/minutes) as well as strength of heart beat (two-fold). Cardiac acceleratory center works during exercise.

(b) Cardiac inhibitory center. It is associated with the vagal or parasympathetic nerve fibers, which, in turn, are associated with the S.A. node. These nerve fibers are responsible for the inhibition and decrease in the rate and depth of contraction of S.A. *node through a neurotransmitter chemical called acetylcholine. It decreases the rate of* heart beat (about 20 to 30 times/ minute) as well as strength of heart beat (by 20 to 30 per cent). Cardiac inhibitory center dominates during the rest.

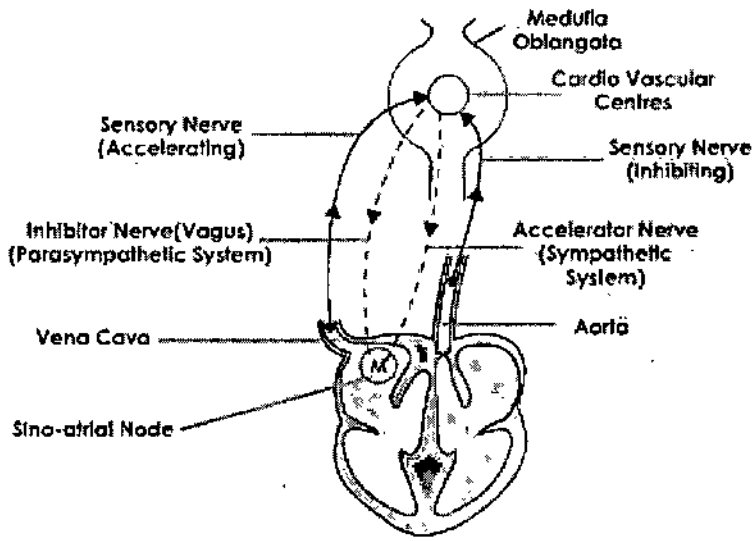


Fig. 3. Neurons connecting the heart to the cardiovascular system.

2. Hormonal control. It consists of two amine hormones–epinephrine (adrenalin) and norepinephrine (noradrenalin) which are secreted by adrenal medulla of adrenal gland. Both hormones accelerate the rate of heart beat but operate in different conditions. Epinephrine increases the heart beat during emergency conditions, while norepinephrine increases heart beat during normal conditions.

9.5. ELECTRO CARDIO GRAM (EKG OR ECG)

The heart contains special tissue that produces and sends electrical impulses to the heart muscle. It is these impulses that trigger the heart to contract. Each time the heart beats, it sends out an electric-like signal. The heart's electrical signals can be measured with a special machine called an electrocardiogram (EKG or ECG).

To record the ECG, small patches or stickers called electrodes are placed on different parts of the body. One is put on each arm and leg and six across the chest. Each of these leads monitors distinct areas of the heart. Using combinations of these electrodes, different tracings of the heart's electrical activity can be made and permanently recorded on paper or in a computer. The graph can show the heart's rate and rhythm, it can detect enlargement of the heart, decreased blood flow, or the presence of current or past heart attacks. ECG's are inexpensive, Non-invasive, quick, and painless. Electro Cardio Gram using electrodes that are swallowed or inserted through the mouth into the esophagus are called transesophageal ECG's. This technique may be useful in more difficult cases to diagnose atrial arrhythmias, because the oesophagus lies directly behind the atria.

Four major waves of electric signals appear on the ECG. Each one shows a different part of the heartbeat.

P wave: It is the first wave Shown in ECG. It records the electrical activity of the heart's upper two chambers (atria).

QRS wave: The second and largest wave is the QRS wave. It records the electrical activity of the heart's two lower chambers (ventricles).

T wave: The third wave is the T wave. It records the heart's return to the resting state.

U wave: the fourth wave of the ECG is U wave. It is rarely seen, and thought to possibly be the repolarization of the papillary muscles.

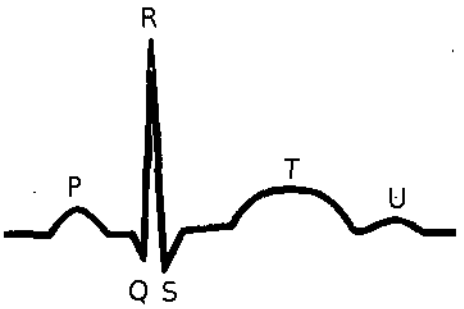


Fig. 4: Wave form of ECG.

By studying the shape and size of the waves, the time between waves, and the rate and regularity of beating, a doctor can learn a lot about the heart and its rhythm.

9.6. SUMMARY

Cardiac cycle refers to the cardiac events that occur from the beginning of one heart beat to the beginning of the next. One cardiac cycle completes with

- Diastole
- Systole
- Isovolumetric

Each time the heart beats, it sends out an electric-like signal. The heart's electrical signals can be measured with a special machine called an electrocardiogram (EKG or ECG.

9.7. STUDENTS ACTIVITY

1. What is a cardiac cycle?

2. What is cardiac systole?

3. *What is cardiac diastole and what is the time of ventricle diastole?*

9.8. TEST YOURSELF

1. Write the functions for the following parts of the heart :
   (a) SA node .....
   (b) AV node .....
   (c) AV bundle (bundle of His) .....

(d) Purkinje fibers .....

2. On an ECG, what do the following wave forms reflect?
   (a) P wave .....
   (b) QRS complex .....
   (c) T wave .....
3. The pacemaker is another name for .....
4. Match the stages of the cardiac cycle to their description.

1a. Ventricular Filling: Passive	v. Ventricles contract and intraventricular pressure rises, closing the AV valves.
1b. Ventricular Filling: Atrial Contraction	w. Ventricles relax and ventricular pressure drops. Blood backflows, closing semilunar valves.
2a. Ventricular Systole: Isovolumetric Contraction	x. Blood flows passively into the atria, through open AV valves, and into the ventricles.
2b. Ventricular Systole: Ejection	y. Rising ventricular pressure forces semilunar valves open. Blood is ejected from the heart.
3. Isovolumetric Relaxation	z. Atria contract, forcing the remaining blood into the ventricles.

5. What causes heart valves to open and close ?

ANSWERS

2. (a) activity of atria (b) activity of vensides
   (c) resting position of heart
3. S. A. node
5. Blood pressure.

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UNIT

10

MUSCLE CONTRACTION

STRUCTURE

LEARNING OBJECTIVES

After going through this unit you will learn :

What are muscles ?

How skeletal muscles contract ?

How smooth muscle contract ?

10.1. INTRODUCTION

The movement of body is impossible without muscle. There are three general types of muscular tissues :

- Skeletal muscle responsible for movement
- Cardiac muscle responsible for pumping blood
- Smooth muscle responsible for sustained contractions in the blood vessels, gastrointestinal tract, and other areas in the body

Skeletal and cardiac muscles are called striated muscle. In fact, in man about 40% of the body mass is striated muscle, making it the most abundant tissue. **Striated muscle** is so named because of its characteristic cross-striped appearance. Most striated muscle is skeletal muscle, involved in rotation of bones around joints and therefore responsible for most of the movements of body. Other striated muscles move the eyes and serve as valves to check the flow of blood or other fluids. **Cardiac muscle** is also striated in appearance, but it differs significantly from other striated muscle in both its structure and its behavior. **Smooth muscles are** not concluded in straight muscles because they lack the characteristic cross-striations, but contain the same contractile proteins. The smooth muscles are found in the linings of the gastrointestinal tract, as linings of blood vessels and as valves.

Out of the these three types of muscle, skeletal and cardiac muscle have been studied most thoroughly. It is presumed that the mechanism of contraction is the same for both types and only the details of initiating and controlling the contraction differ. However all striated muscles do not behaves in the same way. For example, skeletal muscles of vertebrates all appear to initiate contractions with sodium spikes, whereas striated muscles of some invertebrates initiate contractions with calcium spikes.

10.2. TYPES OF CONTRACTION

1. Concentric contraction

A **concentric contraction** is a type of muscle contraction in which the muscles shorten while generating force. For example in relation to the elbow, a concentric contraction of the biceps would cause the arm to bend at the elbow as the hand moved from near to the leg to close to the shoulder.

2. Ecentric contraction

During an **ecentric contraction**, the muscle elongates because an opposing force being greater than the force generated by the muscle. For example during an ecentric contraction of the biceps muscle, the elbow starts the movement while bent and then straightens as the hand moves away from the shoulder. During an ecentric contraction of the triceps muscle, the elbow starts the movement straight and then bends as the hand moves towards the shoulder. Desmin, titin, and other z-line proteins are involved in eccentric contractions.

3. Isometric contraction

An **isometric contraction** of a muscle generates force without changing length. An example can be found when the muscles of the hand and forearm grip an object; the joints of the hand do not move, but muscles generate sufficient force to prevent the object from being dropped.

10.3. SKELETAL MUSCLE CONTRACTION

Mechanisms of skeletal muscular contraction is described as follows

1. An action potential originating in the CNS reaches an alpha motor neuron, which then transmits an action potential down its own axon.
2. The action potential propagates by activating voltage-gated sodium channels along the axon toward the neuromuscular junction. When it reaches the junction, it causes a calcium ion influx through voltage-gated calcium channels.
3. The Ca^{2+} influx causes vesicles containing the neurotransmitter acetylcholine to fuse with the plasma membrane, releasing acetylcholine out into the extracellular space between the motor neuron terminal and the neuromuscular junction of the skeletal muscle fiber.
4. The acetylcholine diffuses across the synapse and binds to and activates nicotinic acetylcholine receptors on the neuromuscular junction. Activation of the nicotinic receptor opens its intrinsic sodium/potassium channel, causing sodium to rush in and potassium to trickle out. Because the channel is more permeable to sodium, the muscle fiber membrane becomes more positively charged, triggering an action potential.
5. The action potential spreads through the muscle fiber's network of T-tubules, depolarizing the inner portion of the muscle fiber.
6. The depolarization activates L-type voltage-dependent calcium channels (dihydropyridine receptors) in the T tubule membrane, which are in close proximity to calcium-release channels (ryanodine receptors) in the adjacent sarcoplasmic reticulum.

7. Activated voltage-gated calcium channels physically interact with calcium-release channels to activate them, causing the sarcoplasmic reticulum to release calcium.
8. The calcium binds to the troponin C present on the actin-containing thin filaments of the myofibrils. The troponin then allosterically modulates the tropomyosin. Under normal circumstances, the tropomyosin sterically obstructs binding sites for myosin on the thin filament; once calcium binds to the troponin C and causes an allosteric change in the troponin protein, troponin T allows tropomyosin to move, unblocking the binding sites.
9. Myosin (which has ADP and inorganic phosphate bound to its nucleotide binding pocket and is in a ready state) binds to the newly uncovered binding sites on the thin filament (binding to the thin filament is very tightly coupled to the release of inorganic phosphate). Myosin is now bound to actin in the strong binding state. The release of ADP and inorganic phosphate are tightly coupled to the power stroke (actin acts as a cofactor in the release of inorganic phosphate, expediting the release). This will pull the Z-bands towards each other, thus shortening the sarcomere and the I-band.
10. ATP binds myosin, allowing it to release actin and be in the weak binding state (a lack of ATP makes this step impossible, resulting in the rigor state characteristic of rigor mortis). The myosin then hydrolyzes the ATP and uses the energy to move into the "cocked back" conformation. In general, evidence (predicted and *in vivo*) indicates that each skeletal muscle myosin head moves 10–12 nm each power stroke, however there is also evidence (*in vitro*) of variations (smaller and larger) that appear specific to the myosin isoform.
11. Steps 9 and 10 repeat as long as ATP is available and calcium is present on thin filament.
12. While the above steps are occurring, calcium is actively pumped back into the sarcoplasmic reticulum. When calcium is no longer present on the thin filament, the tropomyosin changes conformation back to its previous state so as to block the binding sites again. The myosin ceases binding to the thin filament, and the contractions cease.
13. The calcium ions leave the troponin molecule in order to maintain the calcium ion concentration in the sarcoplasm. The active pumping of calcium ions into the sarcoplasmic reticulum creates a deficiency in the fluid around the myofibrils. This causes the removal of calcium ions from the troponin. Thus, the tropomyosin-troponin complex again covers the binding sites on the actin filaments and contraction ceases.

Types of skeletal muscle contractions :

Skeletal muscle contractions can be divided into two parts- twitch and tetanic contractions. When a brief stimulus is applied to the muscle or a single

stimulus is applied to the nerve, a single action potential will be elicited in the muscle and, after an activation delay of about 5 msec, the muscle will contract. The time-course of this contraction, called a **twitch contraction.**

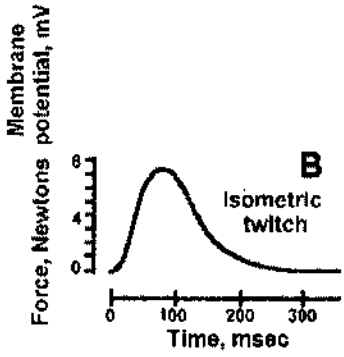

Fig.1. Twitch contraction.

If the stimulation is long enough, the muscle reaches peak force and plateaus at this level, resulting in a tetanic contraction. If the stimulation is not intense enough, force will oscilate during the plateau and be submaximal, but with sufficient stimulation, there will be a constant force level until stimulation stops.

10.4 SMOOTH MUSCLE CONTRACTION

The interaction of sliding actin and myosin filaments is similar to smooth muscle. There are differences in the proteins involved in contraction in vertebrate smooth muscle compared to cardiac and skeletal muscle. Smooth muscle does not contain troponin, but does contain the thin filament protein tropomyosin and other notable proteins – caldesmon and calponin. Contractions are initiated by the calcium-activated phosphorylation of myosin rather than calcium binding to troponin. Contractions in vertebrate smooth muscle are initiated by agents that increase intracellular calcium. This is a process of depolarizing the sarcolemma and extracellular calcium entering through L-type calcium channels, and intracellular calcium release predominately from the sarcoplasmic reticulum. Calcium release from the sarcoplasmic reticulum is from Ryanodine receptor channels (calcium sparks) by a redox process and Inositol triphosphate receptor channels by the second messenger inositol triphosphate. The intracellular calcium binds with calmodulin, which then binds and activates myosin light-chain kinase. The calcium-calmodulin-myosin light-chain kinase complex phosphorylates myosin on the 20 kilodalton (kDa) myosin light chains on amino acid residue-serine 19. initiating contraction and activating the myosin ATPase. The phosphorylation of caldesmon and calponin by various kinases is suspected to play a role in smooth muscle contraction.

Phosphorylation of the 20 kDa myosin light chains correlates well with the shortening velocity of smooth muscle. During this period, there is a rapid burst of energy utilization as measured by oxygen consumption. Within a few minutes of initiation, the calcium level markedly decreases, the 20 kDa myosin light chains' phosphorylation decreases, and energy utilization decreases; however, force in tonic smooth muscle is maintained. During contraction of muscle, rapidly cycling crossbridges form between activated actin and phosphorylated myosin, generating force. It is hypothesized that the maintenance of force results from dephosphorylated "latch-bridges" that slowly cycle and maintain force. A number of kinases such as Rho

kinase, Zip kinase, and Protein Kinase C are believed to participate in the sustained phase of contraction, and calcium flux may be significant.

10.5 SUMMARY

The movement of body is impossible without muscle. There are three general types of muscular tissues

- Skeletal muscle responsible for movement
- Cardiac muscle responsible for pumping blood
- Smooth muscle responsible for sustained contractions in the blood vessels, gastrointestinal tract, and other areas in the body

There are three types of muscle contractions

(i) Concentric contraction

(ii) Ecentric contraction

(iii) Isometric contraction

An **isometric contraction** of a muscle generates force without changing length.

During an **ecentric contraction**, the muscle elongates because an opposing force being greater than the force generated by the muscle.

A **concentric contraction** is a type of muscle contraction in which the muscles shorten while generating force.

10.6 STUDENTS ACTIVITY

1. What are the three types of muscle tissue :
   (a) .....
   (b) .....
   (c) .....

10.7 TEST YOURSELF

1. Fill in the blanks
   (a) Muscles that move bones are called ..... because they are under conscious control; all other muscle tissue is called ..... because it cannot be consciously controlled.
   (b) Ca^{2+} binds to ..... in the thin filaments, exposing the myosin binding sites on actin.
   (c) The movement where the myosin head pulls the thin filaments inward is called the ..... .
2. Place the following events in order by placing a number (1-6) :
   (a) ..... Power stroke (ADP and P dissociate from myosin).
   (b) ..... Thin filament returns to relaxed state.
   (c) ..... Ca^{2+} binds troponin causing a conformational change of the thin filament
   (d) .....Myosin heads bind to actin
   (e) ..... Electrochemical signal causes release of Ca^{2+} from sarcoplasmic reticulum
   (f) ..... ATP binds myosin head

ANSWERS

2. (a) 5 (b) 6
   (c) 2 (d) 1
   (d) 3 (f) 4

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UNIT

11

NERVE CELL AND NERVE CONDUCTION

STRUCTURE

LEARNING OBJECTIVES

After going through this unit you will learn :

What are nerve Cells ?

What is the basic structure of Nerve cell ?

How nerve impulse is conducted ?

11.1. INTRODUCTION

The basic unit of living tissue is the cell. Cells are specialized in their anatomy and physiology to perform different tasks. All cells exhibit a voltage difference across the cell membrane. Nerve cells and muscle cells are excitable. Their cell membrane can produce electrochemical impulses and conduct them along the membrane.

11.2. STRUCTURE OF NERVE CELL

The nerve cell may be divided into three main parts :

(1) The Cell B*ody:* It is also called the soma. The body of a nerve cell is similar to that of all other cells. It includes the nucleus, mitochondria, endoplasmic reticulum, ribosomes, and other organelles. Nerve cells have about 70 - 80% water; the dry material is about 80% protein and 20% lipid. The cell volume varies between 600 and 70,000 μm^3.

(2) D*endrites*: These are short processes of the cell body which receive impulses from other cells and transfer them to the cell body (*afferent signals*). The effect of these impulses may be *excitatory* or *inhibitory*. A *cortical neuron* may receive impulses from tens or even hundreds of thousands of neurons.

(3) A*xon*: The axon is the long nerve fiber which transfers the signal from the cell body to another nerve or to a muscle cell. Mammalian axons are usually about 1 - 20 µm in diameter. Some axons in larger animals may be several meters in length. The axon may be covered with an insulating layer called the *myelin sheath*, which is formed by *Schwann cells*. The myelin sheath is not continuous but divided into sections, separated at regular intervals by the *nodes of Ranvier*.

These are described in Figure 1.

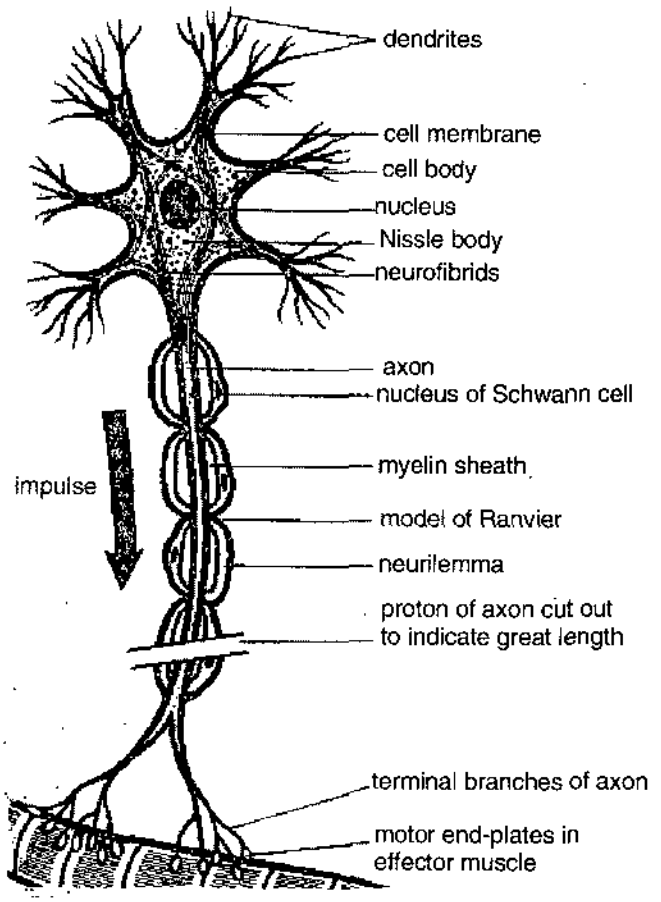

Fig. 1. The major components of a neuron.

11.3. THE CELL MEMBRANE

The cell is enclosed by a cell membrane whose thickness is about 7.5 - 10.0 nm. Its structure and composition resemble a soap-bubble film, since one of its major constituents, fatty acids, has that appearance. The fatty acids that constitute most of the cell membrane are called *phosphoglycerides*. A phosphoglyceride consists of phosphoric acid and fatty acids called *glycerides*. The head of this phosphoglyceride, is *hydrophilic* i.e. attracted to water. The fatty acids have tails consisting of hydrocarbon chains which are *hydrophobic* i.e. repelled by water.

If fatty acid molecules are placed in water, they form little clumps, with the acid heads that are attracted to water on the outside, and the hydrocarbon tails that are repelled by water on the inside. If these molecules are very carefully placed on a water surface, they orient themselves so that all acid heads are in the water and all hydrocarbon tails protrude from it. If another layer of molecules were added and more water put on top, the hydrocarbon tails would line up with those from the first layer, to form a double layer. The acid heads would protrude into the water on each side and the hydrocarbons would fill the space between. This bilayer is the basic structure of the cell membrane.

From the bioelectric viewpoint, the *ionic channels* constitute an important part of the cell membrane. These are macromolecular pores through which sodium, potassium, and chloride ions flow through the membrane. The flow of these ions forms the basis of bioelectric phenomena.

11.4. THE SYNAPSE

The junction between an axon and the next cell with which it communicates is called the *synapse*. Information proceeds from the cell body unidirectionally over the synapse, first along the axon and then across the synapse to the next nerve or muscle cell. The part of the synapse that is on the side of the axon is called the *presynaptic terminal* and the part on the side of the adjacent cell is called the *postsynaptic terminal*. Between these terminals, there exists a gap, the synaptic cleft, with a thickness of 10 - 50 nm. The fact that the impulse transfers across the synapse only in one direction, from the presynaptic terminal to the postsynaptic terminal, is due to the release of a chemical transmitter by the presynaptic cell. When this transmitter is released, it activates the postsynaptic terminal (Figure 2). The synapse between a motor nerve and the muscle it innervates is called the *neuromuscular junction*.

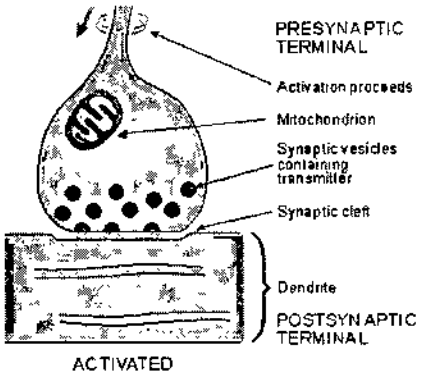

Fig. 2. The anatomy of the synapse.

11.5. TRANSMISSION OF NERVE IMPULSE

Nerve impulses have a domino effect. Each neuron receives an impulse and must pass it on to the next neuron and make sure the correct impulse continues on its path. Through a chain of chemical events, the dendrites (part of a neuron) pick up an impulse that's shuttled through the axon and transmitted to the next neuron. The entire impulse passes through a neuron in about seven milliseconds — faster than a lightning strike. Complete process of nerve conduction is as follows :

1. Polarization of the neuron's membrane: Cell membranes surround neurons just as any other cell in the body has a membrane. When a neuron is not stimulated its membrane is polarized. Not paralyzed, Polarized, Being polarized means that the electrical charge on the outside of the membrane is positive while the electrical charge on the inside of the membrane is negative. The outside of the cell contains excess sodium ions (Na^+); the inside of the cell contains excess potassium ions (K^+).

The charge inside the cell would be negative while the cell contains positive ions because in addition to the K^+, negatively charged protein and nucleic acid molecules also inhabit the cell; therefore, the inside is negative as compared to the outside.

The Na^+ and K^+ do, in fact, move back and forth across the membrane. There are Na^+/K^+ pumps on the membrane that pump the Na^+ back outside and the K^+ back inside. The charge of an ion inhibits membrane permeability.

2. Resting potential: When the neuron is inactive and polarized, it's said to be at its resting potential. It remains this way until a stimulus comes along.

3. Action potential: When a stimulus reaches a resting neuron, the gated ion channels on the resting neuron's membrane open suddenly and allow the Na^+ that was on the outside of the membrane to go rushing into the cell. As this happens, the neuron goes from being polarized to being depolarized.

When the neuron was polarized, the outside of the membrane was positive, and the inside of the membrane was negative. After more positive ions go charging inside the membrane, the inside becomes positive, as well; polarization is removed and the threshold is reached.

Each neuron has a threshold level. This is the point at which there's no holding back. After the stimulus goes above the threshold level, more gated ion channels open and allow more Na^+ inside the cell. This causes complete depolarization of the neuron and an action potential is created. In this state, the neuron continues to open Na^+ channels all along the membrane. When this occurs, it's an all-or-none phenomenon. "All-or-none" means that if a stimulus doesn't exceed the threshold level and cause all the gates to open, no action potential results; however, after the threshold is crossed, there's no turning back: Complete depolarization occurs and the stimulus will be transmitted.

When an impulse travels down an axon covered by a myelin sheath, the impulse must move between the nodes of Ranvier.

4. Repolarization: After the inside of the cell becomes flooded with Na^+, the gated ion channels on the inside of the membrane open to allow the K^+ to move to the outside of the membrane. With K^+ moving to the outside, the membrane's repolarization restores electrical balance, although it's opposite of the initial polarized membrane that had Na^+ on the outside and K^+ on the inside. Just after the K^+ gates open, the Na+ gates close to repolarise the membrane.

5. Hyperpolarization: When the K^+ gates finally close, the neuron has slightly more K^+ on the outside than it has Na^+ on the inside. This causes the membrane potential to drop slightly lower than the resting potential, and the membrane is said to be hyperpolarized because it has a greater potential. This period doesn't last long, though. After the impulse has traveled through the neuron, the action potential is over, and the cell membrane returns to normal that is to the resting potential.

6. Refractory period: The refractory period is when the Na^+ and K^+ are returned to their original sides: Na^+ on the outside and K^+ on the inside. While the neuron is busy returning everything to normal, it doesn't respond to any incoming stimuli. After the Na^+/K^+ pumps return the ions to their rightful side of the neuron's cell membrane, the neuron is back to its normal polarized state and stays in the resting potential until another impulse comes along.

The following figure shows transmission of an impulse.

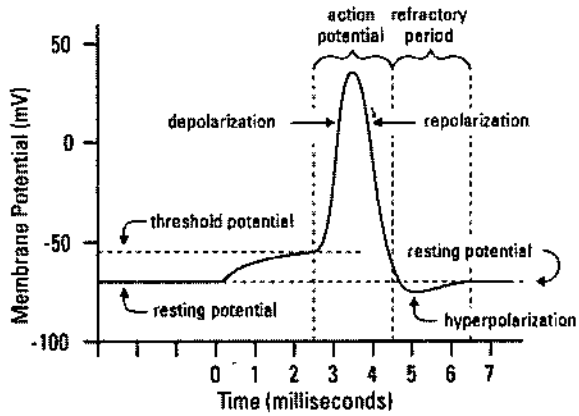

Fig. 3.Transmission of a nerve impulse.

The signal must traverse the synapse to continue on its path through the nervous system. Electrical conduction carries an impulse across synapses in the brain, but in

other parts of the body, impulses are carried across synapses as the following chemical changes occur :

1. Calcium gates open.

At the end of the axon from which the impulse is coming, the membrane depolarizes, gated ion channels open, and calcium ions (Ca^{2+}) are allowed to enter the cell.

2. Releasing a neurotransmitter.

When the calcium ions rush in, a chemical called a neurotransmitter is released into the synapse.

3. The neurotransmitter binds with receptors on the neuron.

The chemical that serves as the neurotransmitter moves across the synapse and binds to proteins on the neuron membrane that's about to receive the impulse. The proteins serve as the receptors. Different proteins serve as receptors for different neurotransmitters — that is, neurotransmitters have specific receptors.

5. Excitation or inhibition of the membrane occurs.

Whether excitation or inhibition occurs depends on what chemical served as the neurotransmitter. The impulse is stopped dead if an action potential cannot be generated.

After the neurotransmitter produces its effect, whether it's excitation or inhibition, the receptor releases it and the neurotransmitter goes back into the synapse. In the synapse, the cell "recycles" the degraded neurotransmitter. The chemicals go back into the membrane so that during the next impulse, when the synaptic vesicles bind to the membrane, the complete neurotransmitter can again be released.

11.6 SUMMARY

Name cells found in brain.

Nerve cell or neuron composed of three basic parts (1) cell body (2) Dendrites and (3) Axon.

11.7 STUDENTS ACTIVITY

1. What are the three main parts of a neuron?
   (a) _____
   (b) _____
   (c) _____
2. What is a synapse?

_____

_____

_____

_____

11.8 TEST YOURSELF

1. Fill in the blanks
   (a) Signals are conducted by ..... which are bundles of .... wrapped in connective tissue.
   (b) Sensory and motor neurons are collectively called the .....
   (c) The structural and functional unit of the nervous system is the ....

(d) The site of contact between a synaptic terminal of a neuron and a target, such as another neuron, a muscle cell, or a gland, is called a ....

(e) The simplest type of nerve circuit is termed as ....

(f) All cells have an electrical charge difference across their plasma membrane called the ....

(g) The membrane potential of an unstimulated neuron is called the ....

(h) If a sufficiently strong stimulus causes depolarization to reach "threshold potential" it triggers a different type of response called an ....

2. What is the minimum number of neuros that can make up a "reflex arc", and what would these neurons be?
3. What cells form the insulating sheaths around axons?
4. What is the principal charged ion outside of a cell?
5. What is the principal charged ion inside of a cell?
6. How do these ions move across the cell membrane?
7. In a neuron, an action potential can only be generated in the ....

ANSWERS

1. (a) nerves, neurons (b) peripheral nervous system
   (c) neuron (d) synapse
   (e) reflex arc (f) membrane potential
   (g) resting membrane potential
   (h) action potential
2. There must be at least one sensory neuron and at least one motor neuron.
3. Schwann cells
4. Na+
5. K+
6. Due to potentional difference
7. axon

❑❑❑

UNIT

12

STRUCTURE AND FUNCTIONS OF KIDNEYS

STRUCTURE

- The Kidneys
- Structure of Kidneys
- Functions of Kidneys
- Summary
- Student Activity
- Test yourself

LEARNING OBJECTIVES

After going through this unit you will learn:

What is the structure of kidneys ?

How urine forms ?

What are nephrons ?

12.1. INTRODUCTION

There are only two major sets of **paired organs** in the body, the kidneys and the lungs. The kidneys are large, bean shaped organs which lie on the dorsal side of the visceral cavity, roughly level with the waistline.

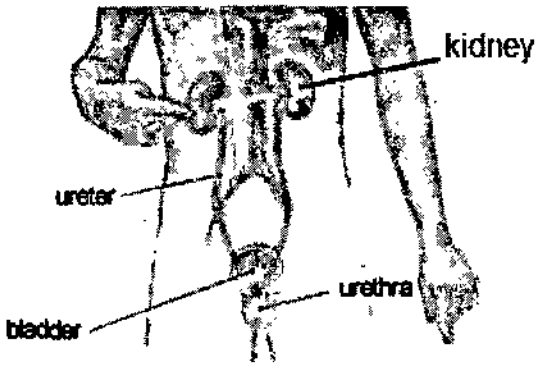

Fig 1: Position of kidney

Blood is supplied to the kidneys by the renal arteries which branch off the aorta. The kidneys are drained by the the renal veins into the inferior vena cava. From the kidneys, urine passes to the urinary bladder via the ureters. Urine is passed to the outside environment via the urethra (this is routed differently in males and females). Under normal conditions, the body will utilize both organs, but if one of the organs is damaged in some way, the other organ can take over the entire function and operate as if **both** organs were present.

12.2. STRUCTURE OF THE KIDNEYS

1. Macrostructure of the Kidney

The outer skin of the kidney is called the **renal capsule** (renal refers to the kidney). The kidney is divided into two main parts, a central part and an outer,

peripheral part (Figure 2). The peripheral part consists of the **cortex** and the **medulla**, with the medulla consisting of **medullary pyramids**; the inner, central part consists of a group of tubes (the **calyx** and the **pelvis**) that lead out of each pyramid and into the **ureter** (the tube that drains urine into the bladder).

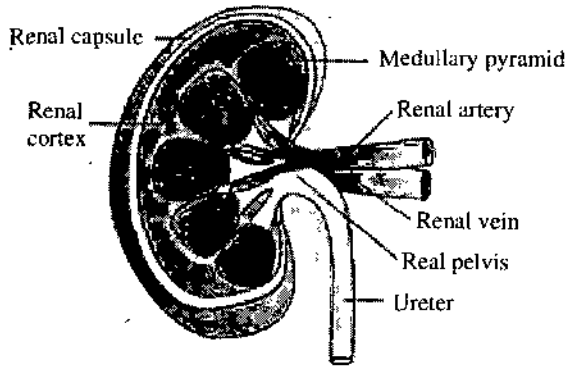

Fig. 2: internal structure of kidney

2. Microstructure of the Kidney

Within the cortex and the medullary pyramids are found millions of tiny structures called **nephrons** (Figure 3). The nephrons are responsible for filtering out of the bloodstream an estimated 43 gallons of water a day- about twice the body's entire weight in fluid - through an intricate network of **tubules**.

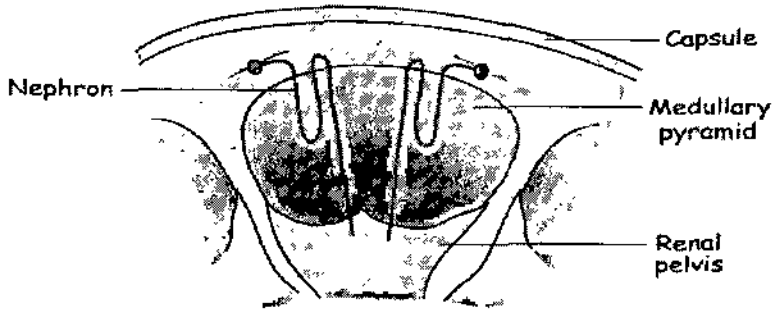

Fig 3: Position of nephrons

The shape of a nephron is unique, unmistakable, and admirably suited to its function of producing urine (Figure 4).It looks a little like a big "mouth" hooked to a really long and winding neck. The "mouth" is filled with what looks like a round lawbreaker that is so big that the "mouth" cannot close! In reality, the nephron is composed of two main parts: the **renal corpuscle** (the mouth and the jawbreaker) and the **renal tubule** (the long and winding neck). The "mouth" of the renal corpuscle is actually called **Bowman's capsule** and the " jawbreaker" is actually called the **glomerulus** from the Latin word for "small ball" (the plural form is glomeruli). The glomerulus is a network of blood capillaries that is surrounded, first, by a double membrane (the **glomerular capsular membrane**) and then is surrounded by Bowman's capsule. The renal tubule (the long and winding neck) consists of the **proximal tubule** (the thick, winding part of the neck that extends just up to where it begins to make a U-turn); the **loop of Henle** (the thinner part of the neck that actually makes the U-turn); and the **distal tubule** (the last, thicker part of the neck that travels away from the U-turn, winds all around, and eventually leads into **collecting tubules**).

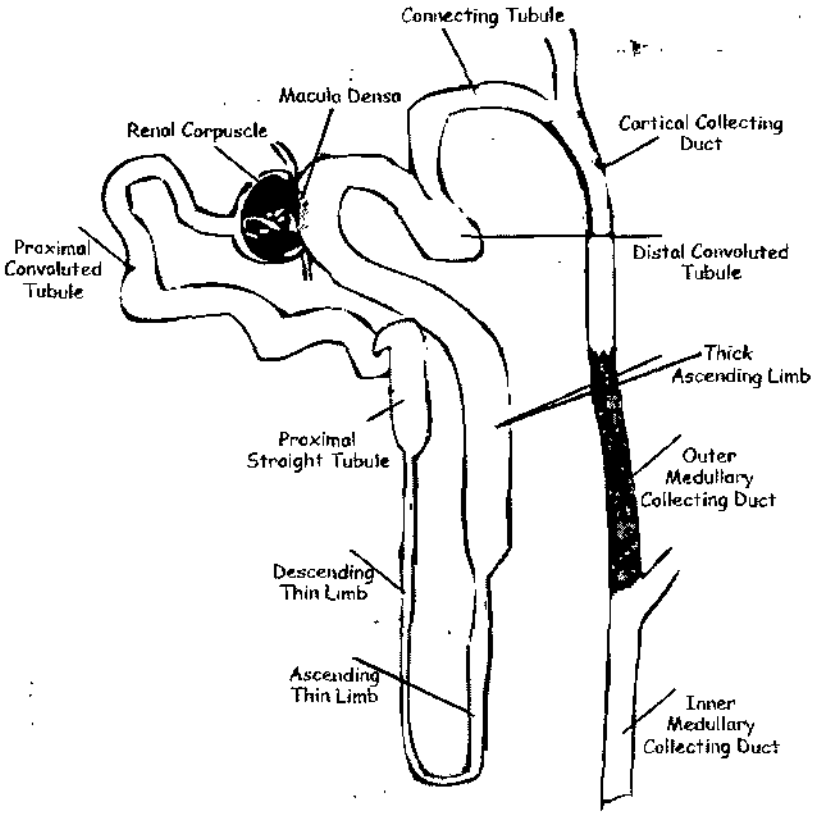

Fig 4: Structure of the nephron.

12.3. FUNCTIONS OF KIDNEY

The primary roles of the kidney are:

1. Control of the body's water balance. The amount of water in the body must be balanced against the amount of water which we drink and the amount we lose in urine and sweat etc.

2. Regulation of blood pressure via the renin-angiotensin-aldosterone system

3. Regulation of blood electrolyte balance - Na^+, Ca^{2+}, K^+ etc.

4. Excretion of metabolic wastes such as urea, creatinine and foreign substances such as drugs and the chemicals we ingest with our food

5. Help in the regulation of the body's acid base balance

6. Regulation of red blood cell production via the hormone erythropoietin

7. Help in the production of vitamin D

1. Water regulation by kidneys

Most of the control of water conservation takes place in the distal and collecting tubules of the nephrons under control of anti-diuretic hormone, (ADH), sometimes called vasopressin. This hormone is released by the posterior pituitary under control of the hypothalamus in the mid-brain area. The hypothalamus monitors the water content of the blood. If the blood contains too little water (indicating dehydration) then more ADH is released. If the blood contains too much water (indicating over-hydration) then less ADH is released into the blood stream.

ADH released from the pituitary travels in the blood stream to the peritubular capillaries of the nephron. ADH binds to receptors on the distal and collecting tubules of the nephrons which cause water channels to open in the tubule walls. This allows water to diffuse through the tubule walls into the interstitial fluid where it is collected

by the peritubular capillaries. The more ADH present, the more water channels are open and the more water is reabsorbed.

Over 99% of the filtrate produced each day can be reabsorbed. The amount of water reabsorbed from the filtrate back into the blood depends on the water situation in the body. When the body is dehydrated, most of the filtrate is reabsorbed but note that even in cases of extreme of water shortage, the kidneys will continue to produce around 500 ml of urine each day in order to perform their excretory function.

2. The micturition reflex

Micturition is another word for urination and in most animals it happens automatically. As the bladder fills with urine, stretch receptors in the wall of the bladder send signals to the parasympathetic nerves to relax the band of smooth muscle that forms the internal urethral sphincter. As the muscle relaxes, the urethra opens and urine is voided to the outside environment.

A second sphincter, the external urethral sphincter is skeletal muscle controlled by motor neurons. These neurons are under conscious control and this means we are able to exercise control over when and where we urinate. This control is a learned response that is absent in the new-born infant.

3. Renin-Angiotensin-Aldosterone (RAA) System.

The long-term control of blood pressure is via the renin-angiotensin-aldosterone (RAA) system. This system is also one of the body's compensatory mechanisms to a fall in blood pressure. The kidneys release renin into the bloodstream and this converts angiotensinogen to angiotensin I which in turn is converted to angiotensin II by angiotensin converting enzyme in the capillaries of the lungs. Under the influence of Angiotensin II, aldosterone levels increase. This increases blood sodium levels by decreasing the amount of salt excreted by the kidneys. Retaining salt instead of excreting it into urine increases the osmolarity of the blood and so the blood volume. As the volume increases, so does the blood pressure. Angiotensin II is also a potent vasoconstrictor which raises blood pressure by increasing vascular resistance.

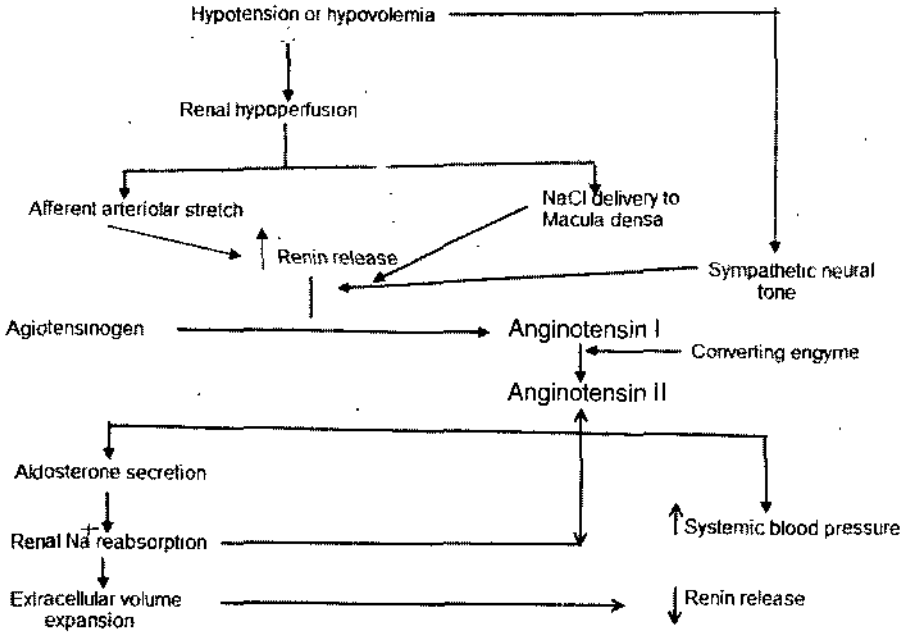

Fig 5: Renin-angiotensin-aldosterone (RAA) system.

4. Formation of urine

Our body releases certain waste products by the process of urination. The production of urine is vital to the health of the body. We could not survive if we did not produce and eliminate it. As the blood flows through the body, wastes resulting from the metabolism of foodstuffs in the body cells are deposited into the bloodstream. These deposites are removed by urine. A major part of this "cleaning" of the blood takes place in the kidneys and, in particular, in the nephrons, where the blood is filtered to produce the urine. Urine is composed of water, certain electrolytes, and various waste products that are filtered out of the blood system. Normally, about 20% of the total blood pumped by the heart each minute will enter the kidneys to undergo filtration. This is called the **filtration fraction**. The rest of the blood (about 80%) does not go through the filtering portion of the kidney, but flows through the rest of the body to service the various nutritional, respiratory, and other needs that are always present.

The kidneys do not simply pick waste products out of the bloodstream. About 2 million or more nephrons in kidneys (about a million in each kidney) form urine by three precisely regulated processes: filtration, reabsorption, and secretion.

(a) Filtration :

It is the first step of urine formation, which goes on continually in the renal corpuscles (Figure 6). As blood passes through the glomeruli, much of its fluid, containing both useful chemicals and dissolved waste materials, soaks out of the blood through the membranes (by osmosis and diffusion). Here it is filtered and then flows into the Bowman's capsule. This process is called **glomerular filtration**. The water, waste products, salt, glucose, and other chemicals that have been filtered out of the blood are known collectively as glomerular filtrate. The glomerular filtrate consists primarily of water, excess salts (primarily Na^+ and K^+), glucose, and a waste product of the body called **urea**. Urea is formed in the body to eliminate the very toxic ammonia products that are formed in the liver from amino acids. Since humans cannot excrete ammonia, it is converted to the less dangerous urea and then filtered out of the blood. Urea is excreted in largest amount by the kidneys.

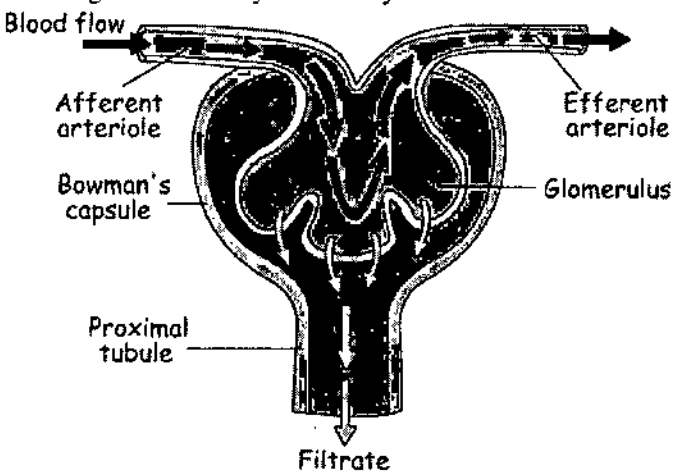

Fig. 6 : Eiltration by nephron.

The total rate of glomerular filtration (**glomerular filtration rate** or **GFR**) for the whole body is normally about 125 ml per minute. That is, about 125 ml of water and dissolved substances are filtered out of the blood per minute. The GFR per hour is :

125 ml/min X 60min/hr= 7500 ml/hr.

The GFR per day is: 7500 ml/hr X 24 hr/day = 180,000 ml/day or 180 liters/day.

This is the amount of water that is released from kidney in a day.Actually it also includes other chemicals, but the vast majority of this glomerular filtrate is water.

(b) Reabsorption

Reabsorption is the movement of substances out of the renal tubules back into the blood capillaries called the **peritubular capillaries** and located around the tubules . Substances reabsorbed are water, glucose and other nutrients, and sodium (Na^+) and other ions. Reabsorption begins in the proximal convoluted tubules and continues in the loop of Henle, distal convoluted tubules, and collecting tubules.

(i) Reabsorption of water : About 99% of the 180 liters of water that leave the blood each day by glomerular filtration returns to the blood from the proximal tubule through the process of **passive reabsorption**. It is because the physical forces acting on the water in these tubules actually push most of the water back into the blood capillaries.

(ii) Reabsorption of blood sugar : All the glucose that seeps out through the glomeruli into the tubules is reabsorbed into the blood from the proximal tubules. In fact, it is **actively transported** out of the tubules and into the peritubular capillary blood. None of this valuable nutrient is wasted by being lost in the urine. However, even when the kidneys are operating at peak efficiency, the nephrons can reabsorb only so much sugar and water. But if too much sugar is present in blood, the tubules reach the limit of their ability to pass the sugar back into the bloodstream, and the tubules retain some of it. It is then carried along in the urine, often providing a doctor with her first clue that a patient has diabetes mellitus.

(iii) Reabsorption of Sodium ions : Sodium ions (Na^+) and other ions are only partially reabsorbed from the renal tubules back into the blood. For the most part, however, sodium ions are **actively transported** back into blood from the tubular fluid. The amount of sodium reabsorbed varies from time to time; it depends largely on how much salt we take in from the foods that we eat. If a person takes high amount of salt into the food, that person's kidneys decrease the amount of sodium reabsorption back into the blood. That is, more sodium is retained in the tubules. Therefore, the amount of salt excreted in the urine increases. Similarly if less amount of salt is intake, the amount of sodium reabsorption back into the blood increase, and thus the amount of salt excreted in the urine decreases.

(c) Secretion

The third important process in the formation of urine is **secretion.** It is the process by which substances move into the distal and collecting tubules from blood in the capillaries around these tubules. In reabsorption substances moves out of the tubules and into the blood while in secretion moves substances out of the blood and into the tubules thus secretion is reverse of reabsorption. After secretion they mix with the water and other wastes and are converted into urine. These substances are secreted through either an **active transport** mechanism or as a result of **diffusion** across the membrane. Substances secreted are hydrogen ions (H^+), potassium ions (K^+), ammonia (NH_3), and certain drugs.

5. Acid base balance or pH control

The body controls the acidity of the blood very carefully because any deviation from the normal pH of around 7.4 can cause problems - especially with the nervous system. Deviations in pH can occur due to trauma or diseases such as diabetes, pneumonia and acute asthma. The mechanisms that resist and redress pH change are

1. Minor changes in pH are resisted by plasma proteins acting as buffers in the blood.

2. Adjustment to the rate and depth of breathing. An increase in acidity (decrease in pH) increases the rate and depth of breathing which gets rid of carbon dioxide from the blood and so reduces acidity.

3. The kidneys respond to changes in blood pH by altering the excretion of acidic or basic ions in the urine. If the body becomes more acidic, the kidneys excrete acidic hydrogen ions (H^+) and conserve basic bicarbonate ions (HCO^{-3}). If the body becomes more basic, the kidneys excrete basic bicarbonate ions and conserve acidic hydrogen ions.

Together, these three mechanisms maintain tight control over the pH of the body.

6. Formation of Vitamin D
   (a) Hydroxylation by the kidney converts 25-hydroxycholecalciferol (25-Vitamin D) to 1,25-dihydroxycholecalciferol (1,25-Vitamin D) in response to parathyroid hormone (PTH) and hypophosphatemia
   (b) 1,25-Vitamin D results in:
      (i) Decreased calcium and phosphate excretion by the kidney
      (ii) Calcium and phosphate absorption from the small intestine
      (iii) Increased osteoclast activity and bone turnover (via PTH)

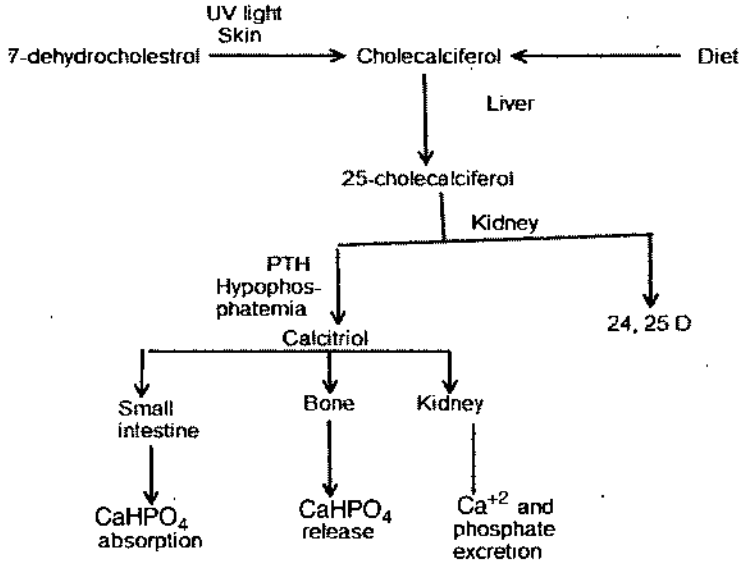

Fig 7: Formation of Vitamin-D.

12.4 SUMMARY

Kidneys are large, bean shaped, paired organ.

Internal kidneys are divided into two major parts :

(1) Medulla and (2) cortex. All the associated parts viz. artery etc. are added with prefix renal for renal artery.

They are mainly associated with water regulation.

12.5 STUDENTS ACTIVITY

1. What is filtration and where does it occur?

2. Describe the internal structure of kidneys.

_____

_____

_____

12.6 TEST YOURSELF

1. 45 liters is about 12 gallons. Can you figure out how many gallons of blood the kidneys process in a day? In one year? 100 years?

   _____ x _____ = _____ liters of blood in one day

   _____ x _____ = _____ liters of blood in one year

   _____ x _____ = _____ liters of blood in 100 years

2. Fill in the blanks in the following statements.

   (a) Blood enters the kidney via the ..... artery.

   (b) The kidney is consists of two regions, the outer..... and the inner.....

   (c) Another word for the kidney tubule is the.....

   (d) Filtration of the blood occurs in the.....

   (e) The hormone..... is responsible for controlling water reabsorption in the collecting tube.

ANSWERS

2. (a) renal artery (b) medulla, cortex,
   (c) nephron (d) kidney
   (e) ADH

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UNIT

13

HORMONES

STRUCTURE

- Endocrine glands and their hormones
- Summary
- Student Activity
- Test yourself

LEARNING OBJECTIVES

After going through this unit you will learn :

What are endocrine glands ?

How each endocrine gland is useful for us ?

Why hormones are important for us ?

13.1. ENDOCRINE GLANDS AND THEIR HORMONES

The endocrine system is made up of the endocrine glands that secrete hormones. Some glands also have non-endocrine regions that have functions other than hormone secretion. For example, ovaries and testes secrete hormones and also produce the ova and sperm. There are ten major endocrine glands.

1. Pituitary Gland
2. Hypothalamus
3. Thymus
4. Pineal Gland
5. Testes
6. Ovaries
7. Thyroid
8. Adrenal Glands
9. Parathyroid
10. Pancreas

1. Pituitary Gland

The pituitary gland or hypophysis is about 1 centimeter in diameter. It rests in a depression in the sphenoid bone. This depression is called sella turcica. The gland is connected to the hypothalamus of the brain by a slender stalk called the infundibulum.

The pituitary gland is also called as "master gland" because it influence a number of other body organs by releasing a large number of hormones.

The pituitary gland is divided into two parts, front (anterior) and back (posterior).

The **anterior pituitary** produces several types of hormones :

- **Prolactin or PRL** - PRL stimulates milk production from a woman's breasts after childbirth and can affect sex hormone levels from the ovaries in women and the testes in men.

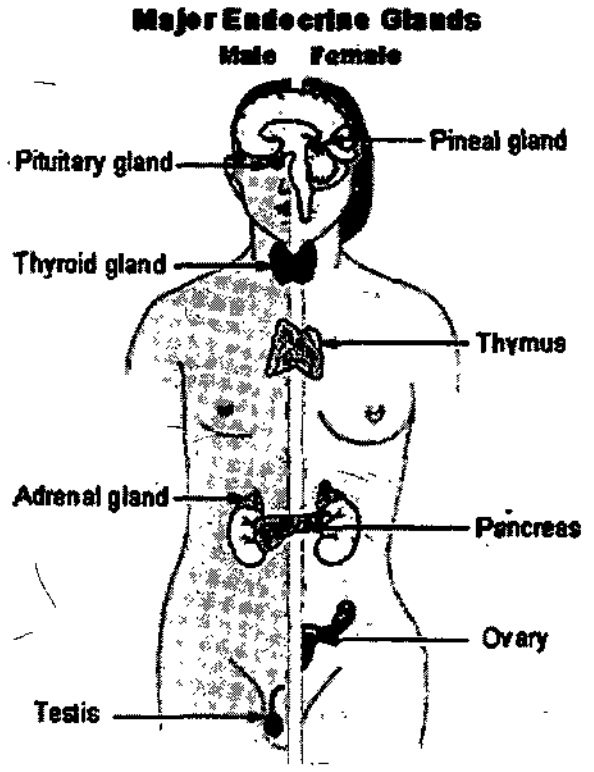

Fig.. 1. Position of different endocrine glands in body

- **Growth hormone or GH** - GH stimulates growth in child. In adults it is also important as it maintains muscle mass and bone mass. It can affect fat distribution in the body.
- **Adrenocorticotropin or ACTH**-ACTH stimulates production of cortisol by the adrenal glands. Cortisol is also called stress hormone and is vital to survival. It helps to maintain blood pressure and blood glucose levels.
- **Thyroid-stimulating hormone or TSH**-TSH stimulates the thyroid gland to produce thyroid hormones, which, in turn, control and regulate the body's metabolism, energy, growth and development, and nervous system activity.
- **Luteinizing hormone or LH**-LH regulates testosterone in men and estrogen in women, which are sex hormone.
- **Follicle-stimulating hormone or FSH** - FSH promotes sperm production in men and stimulates the ovaries to release ovum in women. LH and FSH work together for the normal functioning of ovaries or testes.

The **posterior pituitary** produces two hormones :

- **Oxytocin** - Oxytocin causes milk let down in mothers and contractions during childbirth.
- **Antidiuretic hormone or ADH**–ADH is also called vasopressin. It is stored in the posterior part of the pituitary gland and regulates water balance.
- **Over-** or underproduction of these hormones leads to hormonal imbalance. For example, too much release of growth hormone can cause gigantism (excessive growth), while too little GH may cause dwarfism.

2. Hypothalamus

The hypothalamus is part of the brain that lies just above the pituitary gland. Hypothalamus releases following hormones-growth hormone-releasing hormone or GHRH; thyrotropin-releasing hormone, or TRH; and corticoptropin-releasing hormone, or CRH;and Gonadotropin-releasing hormone (GRH). It tells the pituitary gland to make luteinizing hormone (LH) and follicle-stimulating hormone (FSH), which are important for normal puberty.

The harmones of hypothalamus are called "releasing" hormones because they control release of pituitary hormones.

3. *Thymus*

The thymus gland starts functioning in early life. Its main function is to control normal immune function. The thymus gland secretes hormones called humoral factors. These hormones help to develop the lymphoid system, which helps to reach a mature immune response in cells to protect them from invading bodies, like bacteria.

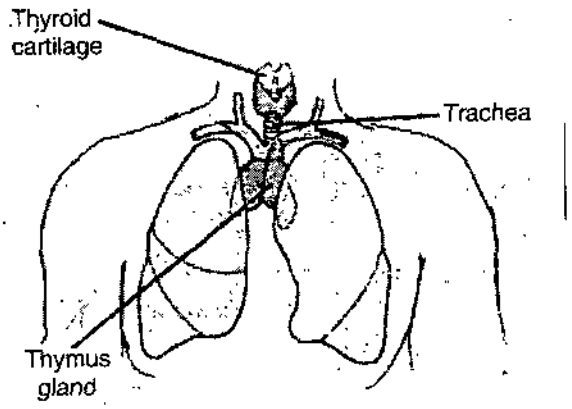

Fig. 2. Position of thymus gland

4. Pineal Gland

It produces melatonin hormone. Melatonin may inhibit the action of gonadotropin harmones, which causes the ovaries and testes to develop and function. It may also help to control sleep patterns.

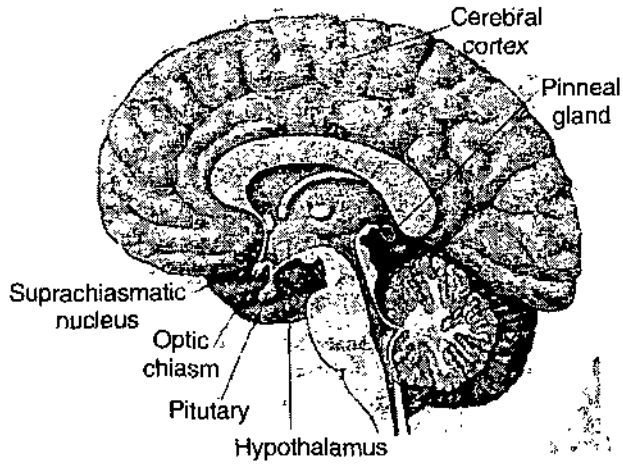

Fig. 3. Position of pineal gland

5. Testes

Testes are male reproductive glands that produce the hormone testosterone. Testosterone develops and maintains sexual traits in boys. During puberty, testosterone bring physical changes, such as growth of the penis and testes, growth of facial and

pubic hair, deepening of the voice, increase in muscle mass and strength and increase in height.

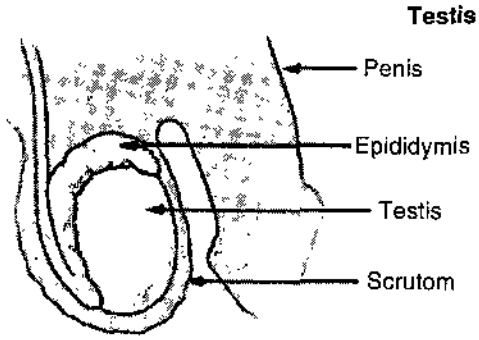

Fig. 4. Position of testis.

6. Ovaries

The two most important hormones estrogen and progesterone of a woman are produced by ovaries. These hormones are responsible for developing and maintaining female sexual traits, as well as maintaining a pregnancy. Along with the pituitary gonadotropins (LH and FSH), they also control the menstrual cycle. The ovaries also produce inhibin, a protein that inhibits the release of follicle-stimulating hormone from the anterior pituitary and also controls egg development.

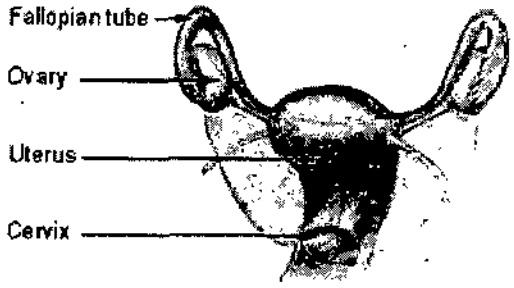

Fig. 5. Position of ovaries.

A condition called polycystic ovary syndrome (PCOS) is caused by overproduction of male hormones in females. PCOS can affect menstrual cycles, fertility, and hormone levels, as well as cause acne, facial hair growth and male pattern balding.

7. Thyroid

It is a small gland inside the neck, located in front of trachea just below Adam's apple. The thyroid produces two hormones, T3 called tri-iodothyronine and T4 called thyroxine. The thyroid hormones controls metabolism, which is the body's ability to break down food and store it as energy and the ability to break down food into waste products with a release of energy in the process.

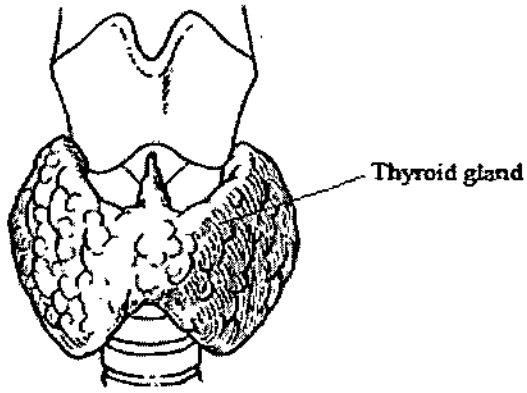

Fig. 6. Position of thyroid gland

If too little or too much thyroid hormones are secreted they cause disorders. Too little release of thyroid hormone causes hypothyroidism. Symptoms of hypothyroidism (too little hormone) include decreased energy, slow heart rate, dry skin, constipation, and feeling cold all the time. In children, hypothyroidism most commonly leads to slowed growth. Infants born with hypothyroidism can have delayed development and mental retardation if not treated. In adults, this disorder often causes weight gain. An enlarged thyroid, or goiter, may develop.

But if too much harmones are secreted by thyroid they cause hyperthyroidism. Hyperthyroidism may impact normal thyroid size and result in exophthalmic goiter, or Grave's disease. Symptoms of this thyroid disease include anxiety, fast heart rate, diarrhea, and weight loss. An enlarged thyroid gland (goiter) and swelling behind the eyes that causes the eyes to push forward or bulge out, are common.

8. Adrenal Glands

The adrenal or suprarenal gland is paired with one gland located near the upper portion of each kidney. Each gland is divided into two parts. The outer portion is called the adrenal cortex. The inner portion is called the adrenal medulla. The cortex and medulla of the adrenal gland are like the anterior and posterior lobes of the pituitary that develop from different embryonic tissues and secrete different hormones. The adrenal cortex is essential to life, but the medulla may be removed with no life-threatening effects.

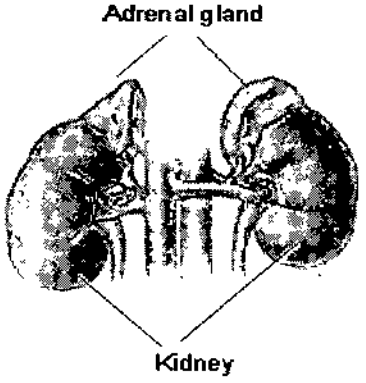

Fig. 7. Position of adrenal glands.

9. Hormones of the Adrenal Cortex

The adrenal cortex consists of three different regions, with each region producing different types of hormones. Chemically, all the cortical hormones are steroid. Mineralocorticoids are secreted by the outermost region of the adrenal cortex. The principal mineralocorticoid is aldosterone. Glucocorticoids are secreted by the middle region of the adrenal cortex. The principal glucocorticoid is cortisol.The third group of hormones secreted by the adrenal cortex is the gonadocorticoids, or sex hormones. These are secreted by the innermost region. Male hormones, androgens, and female hormones, estrogens, are secreted in minimal amounts in both sexes by the adrenal cortex, but their effect is usually masked by the hormones from the testes and ovaries. In females, the masculinization effect of androgen secretion may become evident after menopause, when estrogen levels from the ovaries decrease.

Glucocorticoids that helps the body to control blood sugar, increase the burning of protein and fat, and respond to stressors like fever, major illness, and injury. The mineralcorticoids control blood volume and help to regulate blood pressure by acting on the kidneys to help them hold onto enough sodium and water.

Two important disorders caused due to abnormal functioning of adrenal cortex are Cushing's syndrome and Addison's disease. Cushing's syndrome is caused due to too much cortisol and Addison's disease occurs when there is too little cortisol.

The adrenal medulla produces epinephrine (adrenaline) and norepinephrine. Epinephrine increases the heart beating rate, opens airways to improve oxygen intake, and increases blood flow to muscles, usually when a person is scared, excited, or under stress.

Norepinephrine is more related to maintaining normal activities as opposed to emergency reactions. Too much norepinephrine can cause high blood pressure.

9. Parathyroid

Four small masses of epithelial tissue are embedded in the connective tissue capsule on the posterior surface of the thyroid glands. These are parathyroid glands, and they secrete parathyroid hormone or parathormone. This hormone helps to control calcium and phosphorous levels in the body. The parathyroid glands are necessary for proper bone development. In response to too little calcium in the diet, the parathyroid glands make parathyroid hormone (PTH) that takes calcium from bones so that it will be available in the blood for nerve conduction and muscle contraction.

If the parathyroids are removed during a thyroid operation, low blood calcium will result in symptoms such as irregular heartbeat, muscle spasms, tingling in the hands and feet, and possibly difficulty breathing. A tumor or chronic illness can cause too much secretion of PTH and lead to bone pain, kidney stones, increased urination, muscle weakness, and fatigue.

10. Pancreas

The pancreas is a long, soft organ that lies transversely along the posterior abdominal wall, posterior to the stomach, and extends from the region of the duodenum to the spleen. This gland has an exocrine portion that secretes digestive enzymes that are carried through a duct to the duodenum. The endocrine portion consists of the pancreatic islets, which secrete glucagons and insulin.

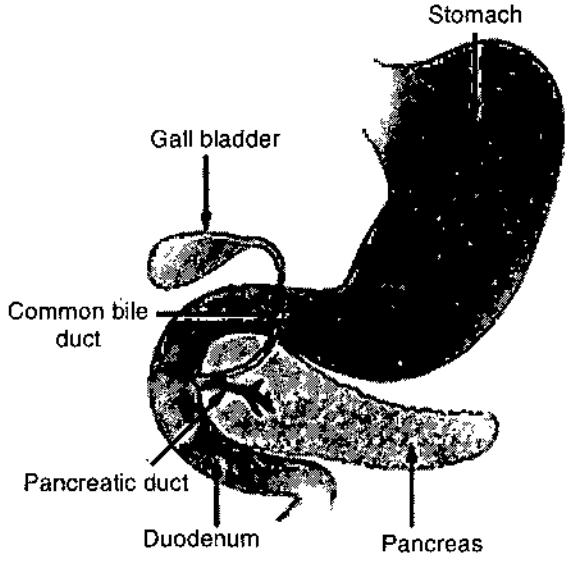

Fig. 8. Position of pancreas

Insulin helps to remove glucose from the blood into the cells where it is used for energy. The pancreas secretes glucagon when the blood sugar is low. Glucagon tells the liver to release glucose, stored in the liver as glycogen, into the bloodstream.

13.2 SUMMARY

Hormone secreting glands are called endocrine gland. These are autonomous i.e., function by their own. There are mainly 10 endocrine glands in human body which secrets various kinds of hormones. Pituitary glands is also called as master gland.

13.3 STUDENTS ACTIVITY

1. What gland produces the hormone thyroxin? What is the function of thyroxin in metabolism?

2. What are the two parts of the Adrenal Gland, what hormones are secreted by each part, and what do these hormones do in the body?

3. Where is the pineal gland located? What hormone does it produce?

13.4 TEST YOURSELF

1. What is an Endocrine Gland?
2. Endocrine glands are also called _____ because they secrete their chemical messengers into _____.
3. The chemical messenger secreted by an endocrine gland is called a _____
4. Name 9 endocrine glands in a human body.
5. What hormones are released by the hypothalamus to control the anterior pituitary gland?
6. What hormones are released from the posterior pituitary?
7. What hormones are released from the anterior pituitary?
8. What hormones are secreted by the Thyroid gland?
9. What hormone is secreted by the Parathyroid Gland?
10. Name the endocrine glands located in the following areas of the body
    (a) Above each kidney
    (b) On each side of the uterus in the female
    (c) Master gland located just under the brain (sella turnica)
    (d) In front of the upper part of the trachea

(e) Behind an attached to the thyroid

(f) Glandular organ behind the stomach

ANSWERS

2. ductless glands, blood
3. harmone
5. Releasing

❑❑❑