

BIOLOGY HANDWRITTEN NOTES

Topics Covered :

- Biomolecules notes
- Cell division notes
- Excretory system
- Human health and disease notes
- Molecular Genetics notes
- Plant Anatomy notes
- Plant Embryology notes
- Skeletal system notes

Hope it Helps

Biomolecules

science world HSN

Date 20/08/2018
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- ① molecular biology is the study of molecular aspect of the cell.
- Biochemistry is the science in which we study the chemical and physicochemical aspect of life.
 - The chemicals or molecules, which are present in the living organisms are **biomolecules**.
- * The collection or sum total of different types of Biomolecules present in a cell is **cellular pool**.
- The organic biomolecules are Carbohydrate, Lipids, proteins, Nucleic acids, amino acids and many other diversified types.
 - A cell maintains its cellular pool by these processes as passive transport, Active transport and metabolic activities are involved.
 - Depending upon the m.wt., the biomolecules of cell are of two types:
 - ~~micro~~ **micromolecules** → m.wt. less than 1000 dalton.
 - ~~macro~~ **macromolecules** → m.wt more than 1000 dalton. Generally in a cell it is more than 1000 dalton.
- There is a wide diversity in living organisms in our biosphere; therefore all living organisms made of the same chemicals, i.e., elements & compounds.
- If we perform such an analysis on a plant tissue, animal tissue or a microbial paste, we obtain a list of elements like carbon, Hydrogen, oxygen and several others and their respective content per unit mass of a living tissue? If the same analysis is performed on a piece of earth's crust or an example of non-living matter; we obtain a similar list.

Elements	% wt.	
H	0.14	0.5
C	0.03	18.5
O	46.6	68.0
N	very little	3.3
S	0.03	0.3
Na	2.0	0.2

Ca	8.6	15
Mg	2.1	0.1
Si	21.7	Negligible

- what are the differences b/w the two lists?

In absolute terms, no such differences could be made out. ? All the elements present in a sample of earth's crust also present in a sample of living tissue? However, a closer examination reveals that the relative abundance of carbon and Hydrogen with respect to other elements is higher in any living organism than in earth's crust.

- How to analyse chemical composition?

- we can continue asking in the same way, what type of organic compound are found in living organisms?

- How does one go about finding the answer?

To get an answer, one has to perform a chemical analysis. ? we can take any living tissue [A vegetable or a piece of liver, etc] and grind it in (C₆H₅COOH) using a mortar and a pestle. ? we obtain a thick slurry?

If we were to strain this through a cheese cloth or cotton we would obtain two fractions? one is called the (filtrate or more technically, the acid-soluble, and the second, the (residue or acid insoluble fractions)?

- Scientists have found thousands of organic comp. in the acid soluble pool. ? All the carbon comp. that we get from living tissues can be called (Biomolecules):

- characteristic of Biomolecules: most of them organic comp. have specific shapes and dimensions? functional group determines their chemical properties? many of them are asymmetric? macromolecules are large molecules and are constructed from small building block molecules? Building block molecules have simple st?

- There are about 8000 chemicals in the living world comprising around 8000 types of Rn? In a cell 2000 enzymes may present to carry out

metabolism. These results due to relationship of molecules and not a property of any one molecule is statement given by Pauling.

Nobel prizes in the field of molecular biology: 2006 \rightarrow Andrew Fire and Craig Mello [for the discovery of RNA interference - gene silencing by ds RNA]; 2002 \rightarrow Sydney Brenner, Robert Horvitz and John Sulston [for programmed cell death (Apoptosis) and mechanism of genetic regulation of organ development]; 1999 \rightarrow Guenter Blobel [Discovery of intrinsic signals for proteins that govern their transport and localization in the cell]; 1994 \rightarrow Gilman and Rodbell [S^t and F^m of GTP binding proteins (G-protein coupled receptors)]; 1998 \rightarrow Sharp and Roberts [Discovery of split genes and RNA processing]; 1989 \rightarrow Thomas Lindahl and S. Altman [Discovery of non protein enzyme RNP Ribozyme (catalytic RNA)]; 1985 \rightarrow Brown and Goldstein [Regulation of cholesterol metabolism and Endocytosis]; 1982 \rightarrow A. Klug [S^t of Nucleic acid - protein complex]; 1980 \rightarrow Snell, Dausset and Donnall [Discovery of major Histocompatibility antigens]; 1980 \rightarrow Berg, Singer and Gilbert [Gene cloning technique]; 1978 \rightarrow Nathans, Smith and Arber [Discovery of Restriction enzyme]; 1975 \rightarrow Temin, Baltimore and Dulbecco [Relationship of primary and secondary S^t of proteins]; 1971 \rightarrow Sutherland [Role of cAMP in Hormone regulation]; 1968 \rightarrow Nirenberg, Khorana and Holley [Discovery of genetic code, Artificial gene synthesis, Base sequence of tRNA]; 1965 \rightarrow Jacob, Monod and Lwoff [Operon model and mRNA]; 1964 \rightarrow Hodgkin [S^t of complex organic molecules]; 1962 \rightarrow Kendrew and Perutz [3D S^t of myoglobin and Hemoglobin]; 1962 \rightarrow Watson, Crick and Wilkins [Double helix model of DNA]; 1959 \rightarrow Kornberg and Chock [In vitro synthesis of DNA and RNA respectively]; 1958 \rightarrow Beadle and Tatum [Gene expression]; 1958 \rightarrow Singer [1° S^t of protein]; 1957 \rightarrow Todd [Discovery of Nucleotides]; 1954 \rightarrow Linus Pauling [Studies of peptide bond of protein]; 1946 \rightarrow Sumner [Crystallization of Enzyme urease].

1943 \rightarrow George D. Haskay [Radioisotope tracer technique] { 1926 \rightarrow Svedberg [ultracentrifugation technique] } 1910 \rightarrow J. D. van der Waals [Physical properties of liquids] { 1910 \rightarrow Rössel [chemistry of Nucleus] } 1903 \rightarrow Buelchner [enzyme discovery] { 1902 \rightarrow Emil Fischer [studies of proteins] }

- ② Properties of water: Polar molecule, Cohesion, Adhesion, High specific heat, Heat & high heat of vaporization, less dense of a solid
- Hydrogen bonds: polar water molecules act like as magnets and attract each other; the attraction of the hydrogen end ($+$) of one molecule for the oxygen end ($-$) of another water molecule; they are the highest bonds that can form b/w molecules.
 - Atoms Special: chemical bonds of life; \rightarrow Covalent bonds - the binding force of living matter; Non covalent bonds \rightarrow essential in maintaining the three dimensional st^r of large molecules to bind specifically; Non covalent bonds are: Hydrogen bond, Ionic bond, Van der waals interactions, Hydrophobic interaction; Hydrogen bonds \rightarrow $\frac{1}{10}$ of the strength of covalent bond; Van der waals interactions \rightarrow weak force of attraction; water molecule also called (Golden molecule)
 - Cohesion: The attraction b/w molecules of the same substances (e.g. water); Allows some insects and spiders to walk on water; Results in; surface tension [a measure of the strength of water's surface]
 - Adhesion: Attraction b/w molecules of different substances [makes water stick to other substance]; Responsible for capillary forces in plants; Capillary action in water molecules will 'claw' each other along when in the thin glass tube. On another surface, happens in plants as well.
 - High specific heat: amount of heat needed to rise or lower 1 gm. of a substance 1°C; water resists temp. change, both for heating and cooling; water can absorb or release large amounts of heat energy with little change in actual temp.
 - Water vapour forms a kind of (global "blanket") which helps to keep

the earth warm. Heat radiated from the sun-warmed surface of the earth is absorbed and held by the vapour.

Homeostasis: Idea of Homeostasis \rightarrow Claude Bernard? Term w^r Walter Cannon
 Balanced internal environment \rightarrow same state. } Ability to maintain a steady state despite changing conditions. } water is imp. to this process because:
 ① make a good insulator ② Resists temp. change. ③ Universal solvent
 ④ Coolant ⑤ Ice protects against temp. extremes

However, living organisms have also got inorganic elements and comp. of them. How do we know this? A slightly different but destructive experiments has to be done; one wt. a small amount of living tissue (say a leaf or liver and this is called wet weight) and dry it. All the water, evaporates. The remaining material gives dry wt.; Now if the tissue is fully burnt, all the carbon comp. are oxidized to gaseous form (CO_2 , water vapour) and are removed. what is remaining is called ash? This ash contains inorganic elements like Ca, org. ate. } Inorganic comp. like SO_4^{2-} , PO_4^{2-} ate., are also seen in the acid-soluble fraction.

Therefore elemental analysis gives elemental composition of living tissues in the form of Hydrogen, oxygen, chlorine, Carbon. etc. while analysis for comp. gives an idea of the kind of organic and inorganic constituents present in living tissue; from a chemistry point of view, one can identify functional group like aldehyde, ketones, aromatic compounds. etc. But from a biological point of view, we shall classify them into amino acids, nucleotides, fatty acids etc.

Micromolecules of cell: These are small size simple chemicals having low molecular wt. and high solubility.

These are of following types: ① small carbohydrate the carbohydrate are poly hydroxy aldose / ketose or their derivatives } the aldose have terminal aldehyde group (-CHO) e.g. Glucose, Ribose, Xylose, Galactose, Glyceraldehyde; The ketose have internal keto group (-C=O) e.g. Fructose, Ribulose, Xylulose, Dihydroxy acetone

The carbohydrates are the hydrides of carbon ($C_n(H_2O)_n$) { $C:H:O = 1:2:1$ }

Carbohydrates are also called saccharides which means sugar? The

micromolecular carbohydrates are sweet in taste and are soluble in water.

Carbohydrate

Simple Carbohydrates

Monosaccharide
→ Glucose

fructose

Galactose

Disaccharide

→ lactose

→ sucrose

→ maltose

Oligosacchar.
(2-10 sugar unit)

→ Raffinose

→ Stachyose

Poly sacch.
(>10 sugar unit)

→ starch

→ Glycogen

→ Dietary fibers
[Cellulose]

Complex Carbohydrates

③ They are of as following :

- Monosaccharides : Triose [$C_3H_6O_3$] → Glyceraldehyde, Dihydroxy Acetone.
Tetrose [$C_4H_8O_4$] → Erythrose, Threose ? Pentose → Ribose, Ribulose,
Xylose, Arabinose, Lyxose. { Hexose → Glucose, Fructose, Galactose, Mannose
Altose, Sorbose, Idose } Heptose → Sedoheptose

- All monosacchar. have asymmetrical carbon hence these may be Dextro-rotatory or Laevorotatory. { most of the monosacchar. are D-isomers }

- Derivatives of monosaccharides :

- Deoxyribose : formed by the deoxygination of Ribose sugar.

Deoxyribose ; $C_5H_{10}O_4$ is an imp. component of DNA.

- Aminosugars : monosacchar. having amino group.

e.g. Glucosamine and Galactosamine

- Sugar acids : Ascorbic acid, Gluconic acid, and Galactonic acid

- Sugar alcohol : Glycerol, Mannitol.

- When two monosacchar. join together → Glycosidic bond (-C-O-C-) form.

- Pentose and Hexose are the most common sugars of the cell. { These may exist in both open chain as well as ring form. }

- Mutarotation is the change in the specific rotation of α - and β -

anomers in aqueous sol?

- Alpha glucose when the -OH group is on the opposite side of -CH₂OH group.
- Beta glucose when the -OH group is on the same side of the -CH₂OH group.
- In deoxyribose sugar one Oxygen is less in C-2, the ribose sugar.
- five-sided ring, like ribose, are called thymoses.
- Six-sided ring, like glucose, are called pyranoses.
- Disaccharides and oligosaccharides: Disacch. \rightarrow Two monosacch. join together. } Sucrose = Glucose + Fructose } maltose = Glucose + Glucose
Lactose = Glucose + Galactose.

- Triosecarides: Three monosacch. join together. } Raffinose = Glucose + Galactose + Fructose. } It is found in sugar beet.

- Sweetening index: maltose : 82 } lactose : 16 } Glucose : 70 } Fructose : 110 } Sucrose : 100 } Molulin is a protein, which is having sweetening index 2,00,000 } Chemical Saccharin - 40000

Special: Most of the oligosacch. in the cell are found on the cell memb? These are present at the outer side of the cell memb? These behaves like name tags } sucrose \rightarrow (Non reducing sugar) maltose and lactose \rightarrow (Reducing sugar). } Xylulose is a non nutritive sweet sugar, it is not having any calories. } Erythrose is a raw material for the synthesis of Lignin, Anthocyanin, Tyrosine Amino acid and Phenylalanine amino acids. } Ribose is a component of ATP, NADP, NAD, FAD & RNA. } Galactose is a component of Agar. Agar culture medium

④ Lipids: Term: Fats? Lipids are fatty acid esters of alcohols? Insoluble in water? But soluble in organic solvent? Made up of C, H and O but O content is much less in comparison to H & C? The basic component of lipid is fatty acid? Fatty acids are organic acids having hydrocarbon chains that end at a -COOH group? most of the fatty acids have 16-18 carbon.

The fatty acids are of two types:-

(Saturated) fatty acids: They do not possess any double bond in their carbon chain, they have High m.p. so they are solid or

Semisolid at room temp. } most of the animal fats are saturated }

$C_nH_{2n}O_2$ } General formula.

Ex. Palmitic acid $\rightarrow C_{16}H_{32}O_2$ } Stearic acid $\rightarrow C_{18}H_{36}O_2$

(Unsaturated) fatty acids: $C=C$ or $C\equiv C$ present? (low m.p.), so liquid at room temp. } most of the plant fats are unsaturated?

General formula $\rightarrow C_nH_{2n-2x}O_2$ } where x - No. of double bond.

Ex. Oleic acid $\rightarrow C_{18}H_{34}O_2$ } Linoleic acid $\rightarrow C_{18}H_{32}O_2$

Linolenic acid $\rightarrow C_{18}H_{30}O_2$ } Arachidonic acid $\rightarrow C_{20}H_{32}O_2$

Lipids are of three types:-

① Simple lipids: made up of fatty acid and Glycerol. e.g. Cutin, Suberin, wax.

② Compound or Conjugated lipids: These possess additional group besides fatty acids and Glycerol. e.g. phospholipid, Glycolipid, Lipoproteins.

③ Derivatives of lipids: Terpenes, steroids, prostaglandins.

- Special: In many animals, three types of fatty acids are not synthesized in the body. Linoleic acid, Linolenic acid & Arachidonic acid. These are called (essential fatty acid) [EFA]. These were identified by Evans and Byers. These must be present in our diet. Their source:

sunflower oil, ground nut oil, cotton seed oil and coconut oil. Due to deficiency of these fatty acids a disease may occur called (Phenodermia or follicular Hyper keratosis). Steroids are the crystalline lipids of high m.wt. which essentially possess 17 carbon nucleus which is made up of four fused hydrocarbon rings and having a long side chain.

The 17 carbon nucleus is C_6H_{12} (Cyclo pentane per hydro phenanthrene).

e.g. Cholesterol $\rightarrow C_{27}H_{48}O$ } Cholesterol is the most common steroid.

All this special: Butyric acid and caproic acid are present in butter; Caprylic acid and palmitic acid are present in coconut oil and palm oil.

Arachidic acid is present in ground nut oil. Palmitoleic acid is present in milk; oleic acid present in olive oil. Enueic acid present in mustard oil.

Prostaglandins are 20 C fatty acids having 8C ring. These are imp-

for hormone action. In soaps the soap action is due to the presence of

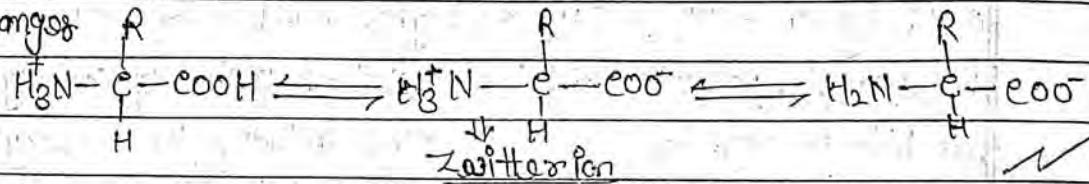
fatty acids. These reduces the surface tension of water which is the cleansing power of water.

Lipids are generally water insoluble. They could be simple fatty acids. A fatty acid has a carboxyl group attached to an 'R' group. The R-group could be a $-CH_3$, $-C_2H_5$ or higher number of $-CH_2$ groups [16 to 19c]. For example, palmitic acid has 16 carbons including carboxyl carbon. Arachidonic acid has 20 carbon atoms including the carboxyl carbon. Fatty acids could be saturated [without double bond] or unsaturated [with one or more $C=C$ double bond]. Another simple lipid is glycerol which is trihydroxy propane. Any lipid have both glycerol and fatty acids. Hence a fatty acids found esterified with glycerol. They can be then monoglycerides, diglycerides and triglycerides. These are also called fats and oils based on melting point. Oils have lower m.p. (e.g. ginkgo oil) and hence remain as oil in winters. Some lipids have phosphorous and phosphorylated organic comp. in them. These are phospholipids. They are found in cell membrane. (Leithin) is one example. Some tissues especially the neural tissues have lipids with more complex str.

(5) Amino Acids: Amino acids are organic comp. containing an amino group and an acidic group as substituents on the same carbon i.e., the α-carbon. Hence, they are called α-amino acids. They are substituted onethanes. Those are four substituent group occupying the four valency positions. These are hydrogen, carboxyl group, amino group and a variable group designated as 'R' group. Based on the nature of 'R' group there are many amino acids. However, those which occur in proteins are only of 20 types. The 'R' group in those proteinaceous amino acids could be a hydrogen [the amino acid is called glycine], a methyl group [alanine], a hydroxyl methyl [serine] etc. The chemical and physical property of amino acids are essentially of the amino, carboxyl and the 'R' functional group. Based on the number of amino and carboxyl groups, there are acidic (e.g. glutamic acid), basic

Lysine [and neutral (Valine), amino acids] similarly, the two aromatic amino acids [tyrosine, phenylalanine, tryptophan].

- A particular property of amino acids is the ionizable nature of $-\text{NH}_2$ and $-\text{COOH}$ groups? Hence in soln of different pHs, the st^r of amino acids changes.



The amino acids have acidic property due to $-\text{COOH}$ group? And have basic property due to $-\text{NH}_2$ group? The amino acids are basically substituted methanes? Based upon 'R' group there are many types of amino acids.

The property of amino acids depend upon the ionization of $-\text{NH}_2$ and $-\text{COOH}$ groups? In solution of different pH, the st^r of amino acid got changed? At a particular pH, the amino acid forms Zwitter Ion. This pH is pI (isoelectric pH)

Glycine is the simplest amino acids b/c it has only H in place of R' group so it is the only symmetrical amino acids.

In Proline and hydroxy proline amino acid in place of $-\text{NH}_2$ group the $-\text{NH}$ group is present so they are pI (amino acids).

All those amino acids which forms proteins are always L-isomers.

Only those amino acids are d-isomer which never forms proteins e.g. Ornithine, Citrulline, GABA.

In protein formation, only 20 types of amino acids are involved which are commonly called magic-20.

Types of Amino acids: (1) Neutral amino acid Glycine, Alanine, valine, Leucine, Isoleucine.

(2) Acidic amino acid: Aspartic acid, Asparagine, Glutamic acid, Glutamine.

(3) Basic amino acid: Arginine, Tyrosine.

~~Classification of amino acids.~~

① Sulphur containing amino acid : Cysteine, methionine

② Alcoholic amino acid : Serine, Threonine

③ Aromatic amino acid : Phenylalanine, Tyrosine, Tryptophan.

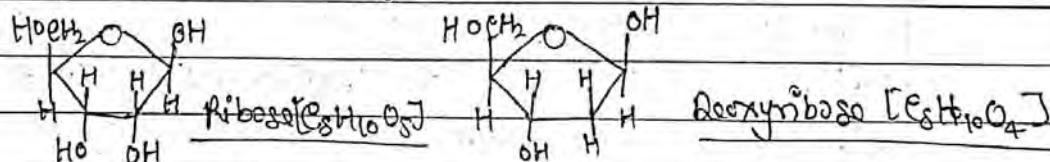
④ Heterocyclic amino acid : Proline, Histidine

- Amino acids special : Albert Hopkins, the animal can not synthesize amino acid out of 20 amino acids. These amino acids are known as Essential amino acids } Leucine, Isoleucine, Valine, Tryptophan, phenylalanine, tyrosine and methionine are essential amino acids } In adult human the amino acid threonine is also not synthesized so for human adults the essential amino acids are 8 in number. } In childrens amino acid Arginine and Histidine is also not synthesized so essential amino acids are 10 for childrens } Essential amino acids must be present in diet. } Arginine and Histidine are semi essential amino acids } Amino acids are the basic building blocks of proteins and enzymes } Aspartame is synthetic polypeptide, used as artificial sweetener } For the formation of protein chains, the amino acids are joined together by forming peptide bond C=O-NH_2 . } The chelating agents EDTA and nitriloacetic acid are α -amino acids that are industrially synthesized [non-natural]. } Proteins are defined by their unique sequence of amino acid residues; this sequence is the primary structure of the protein. } 20 amino acids are encoded by the standard genetic code and are called proteinogenic or standard amino acids. } Tryptophan is a precursor of the neurotransmitter serotonin. } Glycine is a precursor of porphyrin such as heme. } Branched-chain amino acids [BCAA] are those amino acids having aliphatic side chains that are non-linear; these are leucine, Isoleucine and Valine. } γ -Hydroxytryptophan [5HT] amino acid used in the treatment for depression and the neurological problems as medicine. } Amino acid γ -hydroxyphenylalanine is used in the treatment for Parkinsonism. } Monosodium glutamate amino acid used as food additive that enhances flavor.

② Nucleotide: Living organisms have a number of carbon compounds in which heterocyclic rings can be found. Some of these are Nitrogen bases. Adenine, guanine, cytosine, uracil and thymine. When found attached to a sugar, they are called Nucleosides. If a phosphate group is also found esterified to the sugar they are called Nucleotides.

Adenosine, guanosine, thymidine, Uridine and cytidine are nucleosides. Adenylic acid, thymidylic acid, guanylic acid, Uridylic acid and cytidylic acid are nucleotides. Nucleic acid like DNA and RNA consist of nucleotides only. DNA & RNA function as genetic material. Nucleotides: Nucleotides are the basic units of Nucleic acids. They also form energy carriers. So nucleotides work as coenzymes [NAD, NADP, FMN, FADJ].

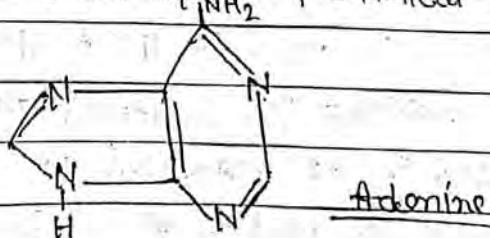
- A nucleotide is made up of 3 chemicals: ① Pentose sugar ② Nitrogen base ③ Phosphoric acid [Phosphate].
- Pentose sugar → Ribose ② Deoxyribose.



- Nitrogen Bases: The N.B. are Heterocyclic compounds. They are of two types:
① Purines ② Pyrimidines

① Purines: Large sized carbon-rich Nitrogen containing biomolecules. These are 9 membered double ring compounds. Those containing 4 Nitrogen in rings at 1, 3, 7 and 9 position. Purines are present in both DNA and RNA. Purines are of two types: → Adenine and Guanine.

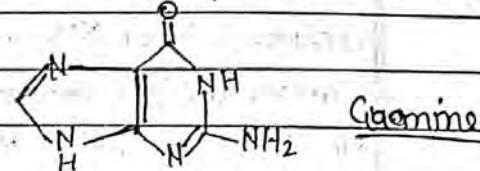
Adenine [AJ]: Present in both DNA and RNA. It is chemically 7H-purino-6-amine or 6-amino purine. Chemical formula → $\text{C}_5\text{H}_5\text{N}_5$?
mw. → 138.127.



- Q. In which of the following imp. component 5-methyl urea is present?
 ① DNA ② RNA ③ Both ④ None

Adenine is a purine with a variety of roles: in cellular respiration, in the form ATP; as cofactors nicotinamide adenine dinucleotide [NAD] and flavin adenine dinucleotide [FAD]; in protein synthesis, as a chemical component of DNA and RNA.

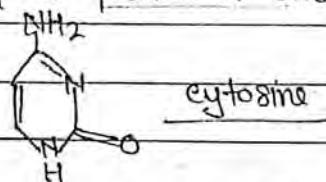
Guanine [G]: Present in both DNA and RNA; chemically 2-amino-6-oxo-purine; chemical formula $\text{C}_5\text{H}_5\text{N}_5\text{O}$; m.wt $\rightarrow 181 \cdot 1261$; it has two tautomeric forms, keto form and enol form.



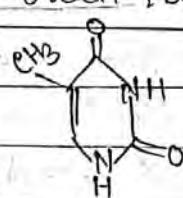
first isolation of guanine was reported in 1844 from the excreta of sea birds, kloz guano, which was generally used as a source of fertilizer.

② Pyrimidines: These are small sized heterocyclic N.B? These are 6 membered single ring compounds; those contains 2 N. in rings at 1 and 3 position.
 Three types: cytosine, Thymine and uracil.

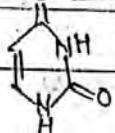
Cytosine [C]: Present in both DNA and RNA; chemically 4-amino-2H-pyrimidin-2-one; chemical formula $\text{C}_4\text{H}_5\text{N}_3\text{O}$; m.wt. $\rightarrow 111 \cdot 102$; it have an amino group at position 4 and a keto group at position 2.



Thymine [T]: Present only in DNA; chemically 5-methyl pyrimidine-2,4(1H,3H)-dione; chemical formula $\text{C}_5\text{H}_6\text{N}_2\text{O}_2$; m.wt. $\rightarrow 126 \cdot 11$.
 Also kloz 5-methyl Urea. It formed by methylation of urea at the 5th carbon.



Urea [U]: Present only in only RNA; chemically pyrimidine-2,4(1H,3H)-dione or 2-oxy-4-oxy-pyrimidine; chemical formula $\text{C}_4\text{H}_4\text{N}_2\text{O}_2$; m.wt $\rightarrow 112 \cdot 086$. Methylation of urea gives rise to thymine.



- Ureil shows tautomer shifts. { Take the keto tautomer is referred to as the tautom st}, while the enol tautomer is referred to as the tautom st. } These tautomeric forms are predominant at pH > 7. { The tautom st is the most common form of ureil. } (S-fluorouracil) is an antineoplastic drug. Allms special : (Xanthine) and (hypoxanthine) are the mutated forms of guanine and adenine, respectively. Due to mutagenic activity there is replacement of NH₂ group with -OH group.

- Nucleosides : A combination of nitrogen base and the pentose sugar is known as Nucleoside. } The N.B combine with the C-1 of pentose sugar by forming glycosidic bond (-C-N-C-) } Purine always join with their N-9 position while pyrimidine always join with their N-8 position.

- Ribonucleosides : Adenosine [A + Ribose], Guanosine [G + Ribose], Uridine [U + Ribose], cytidine [C + Ribose].

- Deoxyribonucleosides : Deoxyadenosine /dA/, Deoxyguanosine /dG/, Deoxythymidine /dT/, Deoxycytidine /dC/.

- Nucleotide : Nucleotides are phosphate acid esters of nucleosides } These are actually phosphorylated nucleosides } The PO₄²⁻ group join with the C-5 or C-3 of deoxyribose sugar [C5 and C3 are the only carbon atoms which has -OH group is present].

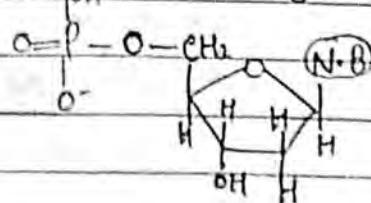
The PO₄²⁻ group join with the C-5, C-3 or C-2 of Ribose. } The PO₄²⁻ group join with that carbon of pentose which has -OH group.

- Ribonucleotides : Adenylic acid [AMP], Guanylic acid [GMP], Cytidylic acid [CMP], Uridylic acid [UMP].

- Deoxyribonucleotides : Deoxyadenylic acid [dAMP], Deoxyguanylic acid [dGMP], Deoxycytidylic acid [dCMP], Deoxythymidylic acid [dTTP].

- Ribonucleotide \hookrightarrow Building block of RNA

- Deoxyribonucleotide \hookrightarrow Building blocks of DNA.

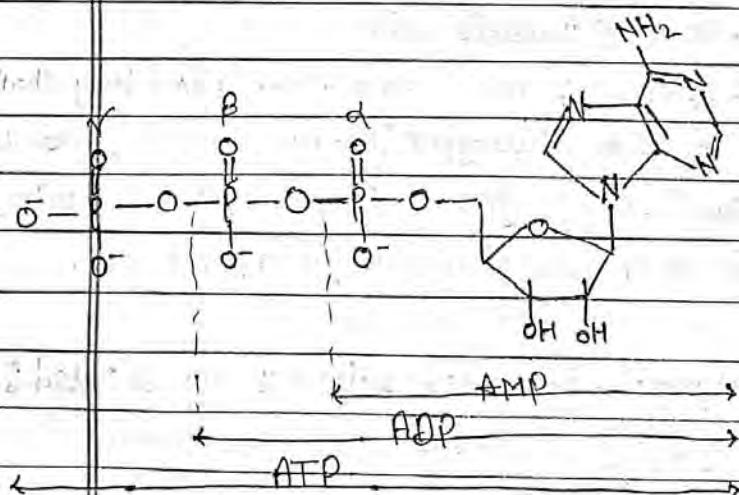


Q) Some special Nucleotides: Cyclic adenosine mono phosphate [cAMP]:
 Discovered by E.M.S. Sutherland [1986]. Got noble prize in 1971. It is formed by ATP. The enzyme adenylate cyclase is involved in its formation. This enzyme is present on the inner side of the cell membrane. The cAMP is 2nd messenger of cell. The cAMP is important for hormonal action. Hormones are primary messenger of the cell. Ca^{2+} ion also considered as secondary messenger of the cell.

Higher Nucleotides: These are those nucleotides which are having more than one phosphate group. All free higher nucleotides are \rightarrow Ribonucleotides. It never be deoxyribonucleotides. e.g. ATP, ADP, GTP, GDP, UTP, UDP, CTP, CDP.

Adenosine tri phosphate [ATP]: Discovered by German scientist K. Lohmann. Fippon \rightarrow father of ATP cycle. ATP is considered as energy currency of cell. It is present in all types of living cells. Chemical formula $\text{C}_{10}\text{H}_{16}\text{N}_5\text{O}_{18}\text{P}_3$.

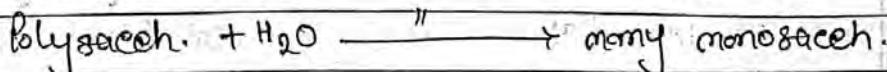
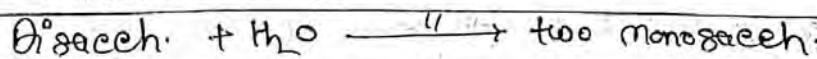
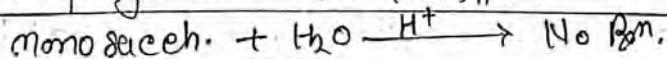
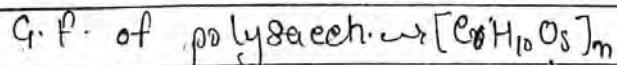
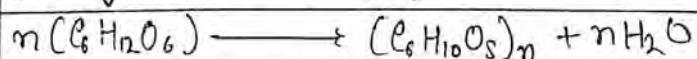
Chemical name of ATP: 5-(6-aminopurin-9-y1)-3, 4-dihydroxy-oxolan-2-y1 methoxy-hydroxy-phosphoryl oxy-hydroxy-phosphoryl oxy-phosphonic acid. Mol wt \rightarrow 307.181.



In ATP there are three phosphates; the first phosphate is $\text{Keto} \rightarrow \alpha$ phosphate. It is attached to the 5th carbon of ribose sugar by normal covalent bond. This bond has Bond energy 3.8 k.cal. [4.4 k.cal]

- The second phosphate is K_{α_2} β -phosphate. It is connected to the phosphate with high energy bond. {This bond has bond energy 6.5 k.cal. [7.3 kcal.]}
- The third phosphate is $\text{K}_{\alpha_3} \rightarrow \gamma$ -phosphate. It is connected to the β -phosphate by high energy bond. {The bond energy is 8.9 k.cal. [1.3 kcal.]}
- In general in a cell, there is conversion of $\text{ATP} \rightleftharpoons \text{ADP} + \text{P}_\gamma$
- The conversion of ADP into ATP \rightarrow (Endergonic reaction) in this process the energy is stored.
- The conversion of ATP into ADP \rightarrow (Exergonic Rxn) in this process the energy is released.
- Both these processes occur with the help of Enzyme ATPase. {ATP exists in the cell mostly in a complex with Mg^{2+} .} The total quantity of ATP in the human body is about 0.1 mole . At any given time, the total amount of ATP + ADP remains fairly constant.
- Macro molecules of cell. The macromolecules are large sized complex molecules having high m.wt. {These are generally insoluble.} Polymers of micromolecules. {In cell 3 types of macro molecules are present:}
 - ① polysaccharide ② protein ③ Nucleic acid
- Polysaccharides: made up of more than 9 monosacch. units. {long chain molecules and not sweet in taste.} Two types of homopolysacch: made up of single kind of monosaccharides e.g. starch, glycogen, cellulose, chitin, mucus.
- Heteropolysacch: made up of more than one type of monosacch. e.g. pectin, peptidoglycan, Agar-Agar.

- During formation of polysacch. the water molecules are released:



- Types of polysacchar.: 3 main types: ① food storage polysacchar. ② structural polysacchar. ③ mucopolysacchar.
- ① food storage polysacchar.: Two types: ① starch ② glycogen.
- ① Starch: Homopolysaccharide { Polymer of α -D glucose } End product of photosynthesis { consist of 2 components: ① Amylose ② amylopectin. }
- ① Amylose: (20-30%) of starch { unbranched } Helical structure { each turn of helix containing about 6 glucose } Having α -1,4-linkage { consists of 200-1000 glucose molecules } It gives blue black colour with Iodine soln.
- ② Amylopectin: (70-80%) of starch { branched } Having α -1,4-linkage and α -1,6-linkage { consists of 2000-20000 glucose molecules } Branching usually at the interval of about 25 glucose molecules { It gives red violet colour with I₂ soln. }
- ② Glycogen: Like animal starch { Reserved food in animal and fungi. } Store in liver and muscles { consists of 30000 glucose molecules } polymer of α -D-Glucose { Highly branched, branching at the interval of 6-14 glucose molecules } Having α -1,4-linkage and α -1,6-linkage { In a well-nourished adult there is about 250 gm. of glycogen divided equally by liver and muscles }
- Special: Inulin is a polymer of fructose; It is present in the roots of Dahlia plant. It is not metabolized in human body. It is filtered through the kidney so it is used to measure GFR.
- ② Structural polysacchar.: Two types - ① chitin ② cellulose
- ① Chitin: present in the cell wall of fungi. { Polymer of N-acetyl glucosamine [amino sugar] } Having β -1,4-linkage { 2nd most abundant biomolecules of the earth. }
- ② Cellulose: fibrous Homopolysacchar., has high tensile strength { component of plant cell wall } unbranched polysacchar. { polymer of β -D-Glucose, Having β -1,4-linkage } In a cellulose chain 2000-6000 glucose molecules may be present. It does not react with I₂ soln.
- ③ Mucopolysaccharide: It is a slimy substance commonly known as Mucilage.

most abundant component in a cell \rightarrow H₂O
organic component in a cell \rightarrow protein.

Date _____
Page _____

Made up of galactose, Mannose, Uronic acid, other sugar derivatives. e.g. chondroitin sulphate present in cartilage, Hyaluronic acid present in connective tissue, Husk of plantago ovata (Isabgol).

Special: (Bacterial cellulose) is a mixture of polysacch. of Xylose, Mannose, Galactose and Arabinoose? The enzyme cellulase can digest cellulose.

If it is present only in microbes. It acts upon cellulose and convert it into the cellulobiose. Cellulobiose is formed by partial degradation of cellulose.

Component	% of total cellular mass
water	70-90
Proteins	10-15
Carbohydrates	3
Lipids	2
Nucleic acid	8-7
Ions	1

Primary and secondary metabolites. The most exciting aspect of chemistry deals with isolating thousands of comp, small and big, from living organism, determining their st. and if possible synthesis them.

If one were to make a list of biomolecules, such a list would have thousands of organic comp. including amino acid, sugar, etc. We can call those biomolecules as metabolites. In animal tissues, one notices the presence of all such categories of comp. shown in fig 8.1. These are called primary metabolites.

However, when one analyses plant, fungal and microbial cells, one would see thousands of comp. other than those called primary metabolites. e.g. alkaloids, flavonoids, rubber, essential oils, antibiotics, coloured pigments, scents, gums, spices. These are called secondary metabolites.

Some secondary metabolites

Pigments

Carotenoids, anthocyanin, etc.

Alkaloids morphine , codeine.

Terpenoids monoterpenes , Diterpenes-

Essential oils lemon grass oil.

Toxins Abrin, Ricin

lectins Concanavalin A

Drugs Vinblastin, curcumin.

Polymeric substance Rubber, gum, cellulose

- while primary metabolites have identifiable function and play known roles in normal physiologic processes, we don't at the moment, understand the role or functions of all the 'secondary metabolites' in host organisms. However, many of them are useful to human welfare? (e.g. Rubber, drugs, spices, scents and pigments.) Some secondary metabolites have ecological importance.

Biomolecules: There is one feature common to all those comp. found in the acid soluble pool. They have m.wt. ranging from 10 to around 800 daltons (Da) approximately. {The acid insoluble fraction, has only 4 types of organic comp.- i.e., proteins, Nucleic acid, polysacch. and lipids} These classes of comp. with the exception of lipid, have m.wt. in the range of ten thousand Dalton & more; for this very reason, biomolecules, i.e. chemical comp. found in the living organisms are of two types. One, those which have m.wt. less than 1000 daltons and are usually referred to as micromolecules or simply biomolecules. While those which are found in the acid insoluble fraction are called macromolecules or biomolecules.

The molecule in the insoluble fraction with the exception of lipids are polymeric substances. Then why do lipids, whose m.wt. do not exceed 800 Da, come under acid insoluble fraction, i.e., macromolecular fraction? Lipids are indeed small molecular wt. comp. and are present not only as such but also arranged into structures like cell membrane and other membranes.

- when we grind a tissue, we are disrupting the cell & cell membr'n and other membr'n are broken into pieces, and form vesicles which are not water soluble. {Therefore, these membrane fragments in the form of vesicles got separated along with the acid insoluble pool and hence in the macromolecular fraction.

- Lipids are not strictly macromolecules

- The acid soluble pool represents roughly the cytoplasmic composition. {The macromolecules from cytoplasm and organelles become the acid insoluble fraction.} Together they represent the entire chemical composition of living tissue or organisms. {Water is the most abundant chemical in living organism.}

- Polysaccharides {The insoluble pellet also has polysacch. carbohydrate} as another class of macromolecules. {Polysacch. are long chain of sugars. They are thread (literally a cotton thread) containing different monosacch. as building blocks.} for example, cellulose is a polymeric polysacch. consisting of only one type of monosacch. i.e., glucose. {Cellulose is a homopolymer. Starch is a variant of this but present as a store house of energy in plant tissues. {Animals has another variant glycogen.} Mulin is a polymer of fructose.

- In polysacch. chain (say glycogen), the right end is called the reducing end and the left end is called the non-reducing end. {Starch has branches (starch forms helical secondary st.).} In fact, starch can hold I_2 molecules in the helical portion. {The starch- I_2 is blue in colour.} cellulose does not contain complex helices and hence can not hold I_2 .

- Plant cell walls made of cellulose. {paper made from plant pulp and cotton fibre is cellulose.} There are more complex polysacch. in nature. {They have as building blocks, amino-sugars and chemically modified sugars (e.g. Glucosamine, N-acetyl glucosamine, etc.).} Exo skeletons of arthropods, for example, have

a complex polysacchar. called chitin.) These complex polysacchar. are mostly ~~Heteropolysacchar.~~ Homopolymers.

⑨ Proteins: Proteins are polypeptide. They are linear chains of amino acids linked by peptide bond. Each protein is a polymer of amino acids. As there are 20 types of amino acids [e.g. alanine, cysteine, proline, tryptophan, lysine etc], a protein is a heteropolymer and not a homopolymer. A homopolymer has only one type of monomer repeating in number of times. Certain amino acids are essential for our health and they have to be supplied through our diet. Hence, dietary proteins are the source of essential amino acids. Therefore, amino acids can be essential or non-essential. The latter are those which our body can make, while we get essential amino acids through our diet [food].

- Proteins carry out many functions in living organisms; some transport nutrients across cell membrane, some fight infectious organisms, some are hormones, some are enzymes, etc.

<u>Protein</u>	<u>function</u>
Collagen	Intercellular ground substance
Trypsin	Enzyme
Insulin	Hormone
Antibody	Fights infectious agents.
Receptors	Sensory reception (smell, taste, hormone etc.)
* GLUT 4	Enables glucose transport into cells.

⑩ Collagen is the most abundant protein in animal world. Ribulose bisphosphate carboxylase - oxygenase [RuBisCO] is the most abundant protein in the whole of the biosphere.

- G.N. Ramachandran: Extensively worked in the field of protein structure. Founder of the 'Madras school' of conformational analysis of biopolymers. Discovery of the triple helical strⁿ of collagen. Analysis of the allowed conformations of proteins through the use of the 'Ramachandran Plot'. Outstanding contribution in structural biology. Ph.D from Cambridge.

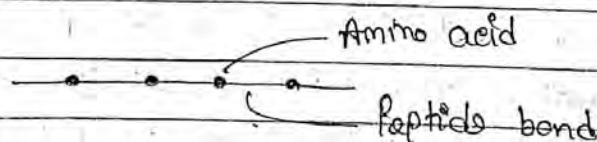
university.) At Cambridge, Ramachandran met Linus Pauling.

Protein? Term protein means \rightarrow to occupy first rank.) Protein term first time suggest by us Berzilius { protein term first time used by us G.J. Mulder } most abundant and variable macromolecules of the cells.) Constitute 80% of dry wt.) In a bacterial cell 1000-2000 types of proteins are present.) Each cell has unique kind of proteins. In closely related species \rightarrow most of the proteins are similar.) In distant species \rightarrow most of the proteins are dissimilar.) Thus we can say that proteins show evolutionary relationship.) Proteins are the building material of the organisms.) The min. mwt. of protein is 4800 Da. [ACTH - Adreno corticotropic hormone].

- mwt. of bovine insulin \rightarrow 5733 Da.) mwt of Bacterial ferridoxin \rightarrow 6000 Da.) mwt of human Hb \rightarrow 66500 Da.) mwt. of urease enzyme \rightarrow 483000 Da.) Proteins are the polymers of amino acid.
- Insulin \approx 51 amino acids.) Hb \rightarrow 574 amino acids.
- Proteins are forming colloidal complex in cell.) The amino acids join with the peptide bond and form peptide chain.
- The protein molecule which have only one poly peptide chain \rightarrow monomeric protein.) If protein contains more than one poly peptide chains \rightarrow oligomeric proteins.

The proteins have four levels of organisation: ① primary st^m ② secondary st^m. ③ Tertiary st^m ④ Quaternary st^m.

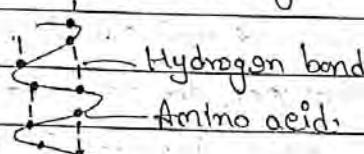
① Primary st^m of protein? Basic st^m of protein.) include arrangement of amino acids in a poly peptide chain.) The sequence of amino acid is determined by a message of DNA molecule [which are carried by the mRNA]. The dist. b/w two peptide bond is 0.38 nm.) First amino acid \rightarrow N terminal amino acid.) Last amino acid \rightarrow C terminal amino acid.



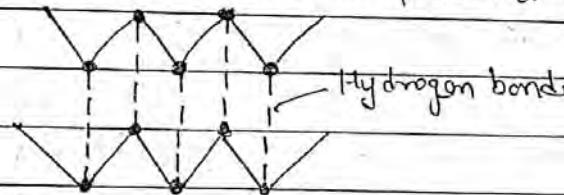
The first amino acid of every protein chain is always methionine.

② Secondary st^m of protein: When a polypeptide chain is coiled into a regular spiral st^m as α -Helix; it is stabilized by the Hydrogen bonds; These bonds are formed b/w -CO. and -NH group. Ex: of α -helix \rightarrow Keratin, myosin, epidermal proteins.

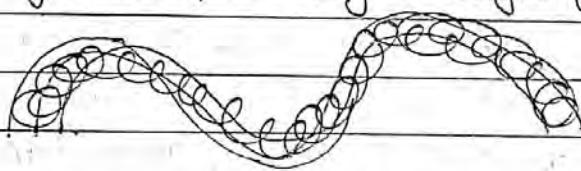
Pauling and Corey studied the secondary st^m of protein. They propose the α -helical model.



When two or more polypeptide chains get interconnected by hydrogen bonds and forming a sheet like st^m instead of helix as β -pleated sheet.
Ex. fibroin fibroin protein of silk.



When three polypeptide chains coiled around each other by hydrogen bonds \rightarrow Collagen Helix; seen only in Collagen protein.



③ Tertiary st^m of protein: The helical polypeptide molecule may fold in itself and assumes a complex but specific form. It may be rod shaped or spherical or any other form. These specific geometrical shapes are known as Tertiary st^m of protein. It is 3D st^m of protein. It is maintained by -H-bond, ionic bond, Disulphide bond, hydrophobic interaction, hydrophilic interaction, Vanderwall forces. The biological activity of protein depends upon its specific tertiary st^m.

Tertiary st^m is affected by:- PH, temp, chemicals. Changes in pH in these factors severely affect the tertiary st^m of the protein. So

protein activity greatly affected.) The tertiary st^m is mainly observed in Globular proteins.

④ Quaternary st^m of proteins; found in only oligomeric proteins.) In certain proteins several polypeptide chains are present.) Each chain has its own primary, secondary, and tertiary st^m.) These several chains together fit in a common st^m and form a quaternary st^m.) Ex. Human Hb. (2 α and 2 β chains), ~~enzymes~~.

⑩ Types of proteins on the basis of shape:- ① fibrous protein:-

Secondary st^m more important. Ex. Collagen, Actin, myosin, Keratin silk fibroin.

② Globular protein: Tertiary st^m more important? Ex. Histones, insulin, Albumin, haemoglobin, Globulin, myoglobin, Gluton of wheat.

③ On the basis of composition:- ① Simple protein: formed of amino acid only.

four types - ② Albumin: Neutral, soluble in water. Ex. Egg white, blood serum.

③ Globulins: Neutral, not soluble in water. Ex. Antibodies in blood.

④ Histones: Basic, soluble in water. Ex. Nucleosomal proteins. ④ Scleroproteins:

Not soluble in water, found only in animal Kingdom. Ex. Keratin, Elastin and collagen proteins.

⑤ Conjugated protein: Combination of globular protein and non protein substance? Non protein substance called prosthetic group.

Types of conjugated proteins: Glycoprotein, Nucleoprotein, Lipoprotein, Chromoprotein, Flavoprotein, phosphoprotein, metalloprotein.

⑥ On the basis of ionic nature: ① Acid proteins: most of the blood proteins. ② Basic proteins: Histone proteins.

⑦ On the basis of function: ① structural protein: Ex. collagen, Keratin, Actin, fibrin. ② functional protein: Ex. Enzyme. ③ transport protein: Ex. permease. ④ storage protein: Ex. ferritin, Casein, Gluton. ⑤ defence protein: Ex. fibrinogen, thrombin. ⑥ other protein: monelmin.

st^m of proteins: Biologists describe the protein st^m at four levels) the sequence of amino acids. i.e., the positional information in a

protein - which is the first amino acid, which is second and so on, is called the primary structure of a protein. { A protein is imagined as a line, the left end represented by the first amino acid and the right end represent by the last amino acid } The first amino acid is also called of N-terminal amino acid { The last amino acid is called the C-terminal amino acid }

- A protein thread does not exist throughout as an extended rigid rod. The thread is folded in the form of helix [similar to a revolving staircase]. Of course, only some portions of the protein thread are arranged in the form of a helix. }

* In proteins, only right handed helices are observed. { Other regions of the protein thread are folded into other forms in what is called the secondary structure }

- In addition, the long protein chain is also folded upon itself like a hollow woolen ball, giving rise to the Tertiary structure. { It gives us a 3-D view of a protein. } This tertiary structure is absolutely necessary for the many biological activities of protein.

- Some proteins are an assembly of more than one polypeptide or subunits

- The manner in which these individual folded polypeptides or subunits are arranged with respect to each other. (e.g. linear string of spheres, spheres arranged one upon each other in the form of a cube or plate etc) is the architecture of a protein otherwise called the Quaternary structure of a protein.

- Adult human haemoglobin consists of 4 subunits. { Two of these are identical to each other. Hence, two subunits of α -type and two subunits of β -type together constitute the human Haemoglobin [Hb]. }

- Nucleic acids : The other type of macromolecule that one could find in the acid insoluble fraction of any living tissue is the nucleic acid. { Those are polynucleotides } for nucleic acids, the building blocks is nucleotide. { It has three chemically distinct components. } One is a heterocyclic compound, the second is a monosaccharide, and the third a phosphoric acid or phosphate.

A nucleic acid containing deoxyribose is called deoxyribonucleic acid (DNA) while that which contains ribose is called Ribonucleic acid (RNA).

Nature of bond linking monomers in a polymers: In a polypeptide or a protein, amino acids are linked by a peptide bond which is formed when the carboxylic (-COOH) group of one amino acid reacts with the amino (-NH₂) group of the next amino acid with the elimination of a water moiety (the process is called dehydration).

In a polysacchar. the individual monosacchar. are linked by a glycosidic bond; this bond is also formed by dehydration. This bond is formed b/w two carbon atoms of two adjacent monosacchar.

In a nucleic acid a phosphate moiety links the 3'-carbon of one sugar of one nucleotide to the 5'-carbon of the sugar of the succeeding nucleotide. The bond b/w the phosphate and hydroxyl group of sugar is an ester bond. As there is one such ester bond on either side, it is called phosphodiester bond. Nucleic acid exhibit a wide variety of secondary ST. For example, one of the secondary ST exhibited by DNA is the famous Watson & Crick model.

(ii) This model says that DNA exists as a double helix. The two strands of polynucleotides are antiparallel i.e., run in opposite direction. The backbone is formed by the sugar-phosphate-sugar chain. The N.B. are projected more or less perpendicular to this backbone but face inside. A and G of one strand compulsorily base pairs with T and C, respectively, on the other strand. There are two hydrogen bonds b/w A and T and three hydrogen bonds b/w G and C. Each strand appears like a helical staircase. Each step of ascent is represented by a pair of bases. At each step of a ascent, the strand turns 36°. One full of the helical strand would involve ten steps or ten base pairs. The pitch would be 34 Å. The rise per B.P. would be 3.4 Å.

- This form of DNA with the above mentioned salient features is called B-DNA. In higher classes, you will be told that there are more than a dozen forms of DNA named after English alphabets with unique structural features.
- In 1869, Friedrich Miescher isolated DNA from the nucleus of pus cell and named it Nuclein. Altmann called it Nucleic acid. Zareckius proposed term DNA. Kossmel discovered purines and pyrimidines in DNA. He got Nobel prize in 1910. Hämmersten first time showed that DNA contains pentose sugar. Levone first time demonstrated that the pentose sugar of DNA is 2'-Deoxyribose. Fehling and Rosenthal discovered a specific staining technique for the staining of DNA in which basic fuchsin stain is used. This is called Fehling's test. Always use for DNA.
- Also Chargaff's rule: In double stranded DNA \rightarrow Amount of 'T' = Amount of 'A' and Amount of 'C' = Amount of 'G'.
- The ratio $A+T/G+C$ is variable but it is specific for a particular species.
For human beings $A+T/G+C = 1.52$.
For E. coli bacteria $A+T/G+C = 0.97$.
- This indicates that $G+C > A+T$ in lower organism while $G+C < A+T$ in higher organism.
- Double helical model of DNA: Watson and Crick in 1953 proposed the double helical model of DNA. They were awarded Nobel prize in 1962. Golden Jubilee year of double helical model \rightarrow 2003. Helical nature of DNA was first time demonstrated by Franklin.
- Arthur Kornberg discovered enzyme DNA polymerase from the E. coli bacteria. By the use of DNA polymerase Kornberg first time synthesized DNA in the laboratory. (*In vitro* DNA synthesis or DNA synthesis in cell free extract. For this he got Nobel prize in 1959.)
- *In vitro* DNA synthesis \rightarrow Kornberg. *In vitro* RNA synthesis \rightarrow Ochoa.
- Shapiro was the first scientist who obtained a photograph of gene. [Gene-gone]

- properties of DNA : A long chain polymer? dipoly nucleotide ? double helix. Both helices are antiparallel to each other, the antiparallelity is due to phosphodiester bond, it means that one strand begins from 3' end and terminates at 5' end; and its complementary strand begins at 5' end and terminated 3' end. Hence antiparallel to each other. In double helix of DNA, Adenine always pair with the thymine; B/w A' and T 2 H-bonds are present; In double helix DNA, Guanine always pair with cytosine; B/w G and C 3 H-bonds are present. Two helix of DNA are connected by the hydrogen bonds in one polynucleotide chain \leftrightarrow phosphodiester bonds. In double helix of DNA \rightarrow H-bonds { In b/w nucleotide of a polynucleotide chain \leftrightarrow PP bond; In b/w nucleotide of double helix \leftrightarrow H-bond; Ladder of DNA \leftrightarrow H-bond. Backbone of DNA \leftrightarrow PP bond.
- The Both helix of DNA are held together by hydrophobic interactions and H-bondings.
- When DNA strand is heated at the high temp. [100°C], then the H-bonds & b/w both strands are broken down \rightarrow both helix of DNA get separated from each other \rightarrow melting or Denaturation of DNA.
- The temp. at which DNA gets denatured \rightarrow Tm [Melting temp.]. It depends upon the GC content of DNA.
- When the denatured DNA cool down slowly \rightarrow the hydrogen bonds b/w two helix again formed \rightarrow Both helix reunite \rightarrow Annealing of DNA or Renaturation of DNA.
- Hyperchromism: By denatured DNA { more UV rays absorbed [40% more]}
- Hypochromism: By normal DNA { less UV rays absorbed}
- (12) By using the techniques of X-ray crystallography Wilkins, Stokes and Wilson discovered several intramolecular details of DNA.
- These intramolecular details are as following: DNA is having helical structure. The length of one pitch (one turn of DNA helix) \approx 34 Å. DNA helix have major groove \approx 22 Å and minor groove \approx 12 Å. Total length

of one turn $\rightarrow 34\text{ \AA}$. } 10 pairs of Nt are present in one turn of DNA double helix. } The distance b/w two base pair or nucleotide pair is 3.4 \AA . } This distance is ~~10~~ ~~less~~ axial rise. } In DNA double helix, two hydrogen bonds are present b/w A and T.

- first H-bond: - B/w the amino group of C₆ of adenine and keto group C₆ of thymine. } Length of bond: - 2.86 \AA .
- Second H-bond: - B/w the N₁ of adenine and N₁ of thymine. } Length of bond $\rightarrow 2.90\text{ \AA}$.
- Both A and T are also set at a particular angle with the pentose sugar.
- Angle b/w A and pentose sugar $\rightarrow 51^\circ$. } Angle b/w T and pentose sugar $\rightarrow 50^\circ$.
- In DNA double helix, three hydrogen bonds are present b/w G and C.
- first H-bond: B/w the keto group of C₆ of G and amino group C₄ of cytosine. } Length of bond: - 2.83 \AA .
- Second H-bond: B/w the amino group of C₂ of guanine and keto group C₂ of cytosine. } Length of Bond: - 2.84 \AA .
- Third H-bond: - B/w the N₁ of Guanine and N₁ of cytosine. } Length of Bond: - 2.90 \AA .
- Both G and C are also set at a particular angle with the pentose sugar.
- Angle b/w G and pentose sugar $\rightarrow 54^\circ$. } Angle b/w C and pentose sugar $\rightarrow 52^\circ$.
- In DNA double helix: The AT base pair occupy 11.1 \AA space and the GC base pair occupy 10.8 \AA space. } The diameter of DNA / first, b/w two strands of DNA / width of DNA $\rightarrow 20\text{ \AA}$. } Angular divergence of DNA $\rightarrow 36^\circ$. It represent the angle b/w two base pairs (rotational angle). } The tilt of DNA is 6° , it means that DNA forms an angle of 6° with its axis. } The DNA helix has Right handed coiling / Dextro coiling. } The absorption spectrum of DNA \rightarrow UV rays of 260 \AA .

Q How many Base pairs are present in $1\mu\text{m}$ long ds DNA?

- ① 1000 bp. ② 2000 bp. ③ 8000 bp. ④ 4000 bp.

Q A dsDNA has 40 nt: A, T, G and C all are 10 in number. what is the length of this dsDNA strand?

① 34 A ② 68 A ③ 102 A ④ 40 A

- Q If in a dsDNA, total 200 N⁺ are present. out of these 60 are having
 C. How many on those N⁺ have A.
 X ① 60 ② 40 ③ 80 ④ 120.

✓ ⑬ Concept of metabolism: All biomolecules have a turn over { This means that they are constantly being changed into some other biomolecules and also made from some other biomolecules } This breaking and making is through chemical Rn constantly occurring in living organisms. } Together all these chemical Rn are called metabolism. } Each of the metabolic Rn results in the transformation of biomolecules..

- A few examples for such metabolic transformation are: Removal of CO₂ from amino acids making an amino acid into an amino. } Removal of amino group in a nucleotide base. } Hydrolysis of a glycosidic bond in a disaccharide, etc.

* majority of these metabolic Rn do not occur in isolation but are always linked to some other Rn. } In other words, metabolites are converted into each other in a series of linked Rn called metabolic pathways. } These metabolic pathways are similar to the automobile traffic in a city. } These pathways are either linear or circular, these pathways cross-cross each other, i.e., there are traffic junctions.

- flow of metabolites through metabolic pathway has a definite rate and direction like automobile traffic. } This metabolite flow is called the dynamic state of body constituents.

- what is the most important is that this interlinked metabolic traffic is very smooth and without a single reported mishap for healthy conditions.

- Another feature of these metabolic Rn is that every chemical Rn is a catalyst Rn. } There is no uncatalyst Rn in metabolic conversion in living systems.

- Even CO₂ dissolving in water, a physical process, is a catalysed

Are in living system. { The catalyst which hasten the rate of a given metabolic conversation are also proteins. { These protein with catalytic power are named Enzymes.

- metabolic basis for living : metabolic pathways can lead to a more complex st. from a simpler st. [for ex., acetic acid becomes cholesterol] or lead to a simpler st. from a complex st. [for example, glucose becomes lactic acid in our skeletal muscles]
- the former cases are called biosynthetic pathway / anabolic pathway. { The latter constitute degradation and hence are called catabolic pathways
- Anabolic pathways, as expected, consume energy. { Assembly of a protein from amino acids requires energy input.
- on the other hand, catabolic pathways lead to the release of energy. { For example, when glucose is degraded to lactic acid in our skeletal muscles, energy is liberated; this metabolic pathway from glucose to lactic acid which occurs in 10 metabolic steps is called glycolysis.
- Living organisms have learnt to trap this energy liberated during degradation and store it in the form of chemical bond. { As and when needed, this bond energy is utilised by biosynthetic, osmotic and mechanical work that we perform.
- The most important form of energy currency in living systems is the bond energy in a chemical called ATP.
- The living state : Thousands of chemical compounds in a living organisms, otherwise called, metabolites, or biomolecules, are present at concentrations characteristic of each of them.
- The most important fact of biological systems is that all living organisms exist in a steady state characterised by concentrations of each of these biomolecules. { These biomolecules are in a metabolic flux.
- Any chemical or physical process moves spontaneously to equilibrium. This steady state is a non-equilibrium state. { one should remember from physics that systems at equilibrium can not perform work. }

As living organisms work continuously, they can not afford to reach equilibrium. Hence the living state is a non-equilibrium steady-state to be able perform work; living process is a constant effort to prevent falling into equilibrium. This is achieved by energy input metabolism provides a mechanism for the production of energy. Hence the living state and metabolism are synonymous. Without metabolism there cannot be a living state.

- (14) Enzymes: They are biocatalyst { mostly made up of proteins } without themselves being used up. [Not consumed in Rn]. Produced living cells only. They cannot move from cell to cell → having high mw.
- W. Kuhne [1878] → Term Enzyme { Edward Buchner [1897] → isolated Enzyme for the first time [Zymase complex] } * JB Sumner [1926] → pure crystalline form of urease enzyme from jack bean (*Canavalia ensiformis*). Nobel prize in 1946. Sumner defined enzyme as a protein with catalytic property. Northrop and Kunitz isolated pepsin, trypsin and chymotrypsin. Elsasser isolated rennet (Rennin). * Arber, Smith and Nathans → Nobel prize in 1978 for the discovery of restriction endonucleases. Inactive forms of enzyme → Zymogen, proenzymes.
 - Endoenzymes e.g. Hydrolyzing enzymes. Exoenzyme e.g. degrading enzymes.
 - Chemical nature of enzymes: mostly proteinaceous. All enzymes are proteins but all proteins are not enzymes. More than 100 amino acids linked to form an active enzyme. An enzyme shows tertiary st. { sequence of amino acid is specific in specific enzymatic proteins } Their tertiary st. is very specific and important for their biological activity. Loss of tertiary st. renders the enzyme activity. Ribozyme is a non proteinaceous enzyme. Like the catalyst enzymes regulate the speed and specificity of the reaction, but unlike the catalyst they are produced by living cells only.

Every cells produce its own enzymes & they can not move from cell to cell due to having high heat.

- On the basis of size of protein molecules, enzymes are divided into two types:-
- ① Simple enzymes: They are composed of only protein e.g. protease, Amylase, urease, lipase
- ② Complex or Conjugated proteins or Holoenzymes: A large number of enzymes require an additional non protein part. {The protein part of these enzymes is called apoenzyme.} Non protein part is called prosthetic group. {The complete enzyme [protein part + non protein] is called as holoenzyme.} Prosthetic group may be:- Activator and co-enzyme. {Activators → when metal acts as prosthetic group.} The separation of enzymes from its metal → complete loss of activity. {These enzymes are also called metalloenzymes.}
- metal ion for enzyme: Na^+ → ATPase. { Zn^{+2} → Carbonic anhydrase, dehydrogenase.} { Mn^{+2} → Peptidase, decarboxylase.} { Mg^{+2} → Nitrate reductase.} { Fe^{+2} → Catalases, aconitase.} { Cu^{+2} → Ascorbic acid oxydase.} { Mg^{+2} → Hexokinase, phosphatase.}
- Coenzyme → coenzyme substances act as prosthetic group. {These can be easily separated but this causes great reduction in enzyme activity.} Coenzyme is required for enzyme activity.
- Hydrogen transferring enzymes: NAD [Coenzyme I], NADP [Coenzyme II], FAD, FMN, Lipoic acid, Ubiquinone [Coenzyme Q].
- Group transferring coenzymes: Co enzyme A [CoA or CoA-SH] → acetyl group carrier. {Pyridoxal phosphate is amino group carrier. It is derivative of vit. B6 or pyridoxin.} Biotin [Coenzyme R] → Carboxyl group carrier. {Thiamine pyrophosphate [TPP] → Carboxyl group carrier.} Coenzyme F [Tetra hydrofolic acid] → Carrier of one carbon compound. {ATP → Acts as carrier of phosphate group.}
- ③ Characteristic of Enzymes: The effectiveness of an enzymatic reaction is expressed in terms of its turnover number or catalytic centre activity means number of substrate molecules in which one enzymes molecule acts in one minute. {Turn over number depends on the number of}

Properties of Enzymes

- active sites of an enzyme

- An active site is an area of enzyme which is capable of attracting and holding particular substance molecules by its specific charge, size and shape so as to allow the chemical change.

* Enzyme show 3-D structure R groups of amino acids which form active sites during folding of polypeptide chains.

* Usually 8-12 amino acids form an active sites; more the number of active sites, more is the turn over number of enzymes; Enzymes react with substrate only at the active sites.

* Highest turn over number \rightarrow Carbonic anhydrase [26 million/min.]

* Lowest turn over number \rightarrow Lysozyme [30 molecule/min.]

- Turn over number depends upon number of active sites, rapidity of reaction and separation of end product.

- Reversibility of action: \rightarrow An enzyme can speed up the reaction in both directions.

- Specificity of enzyme action: \rightarrow An enzyme is specific for both the kind of substrate and type of R.m.

- Sensitiveness to heat: \rightarrow Enzymes are thermolabile i.e., are denatured at high temp. in liquid medium. However, dried enzymes after extraction can endure high temp.

- Colloidal properties: \rightarrow Enzymes are colloidal in nature. They have high m.wt. usually ranging from 10,000 - 50,000.⁰

- Mode of Enzyme action: Enzymes lowers the activation energy of a reaction. The amount of energy required to raise or raise the energy of molecules to level at which chemical reaction can occur e.g., the activation energy of acid hydrolysis of sucrose at 28°C per molecule is 26,000 calories but in presence of enzymes sucrose it is reduced to 7,700 calories.

Two theories to explain the mode of enzyme action.

① Lock and key hypothesis ② Induced fit model.

lock and key theory: proposed by Fischer [1898] ? If it is also called as enzyme substrate complex theory. ? The enzyme molecule [E] combines with substrate molecule [S] to form an enzyme substrate complex. ? This combination takes place at a specific portion of enzymes called the active site. ? The active sites contain special group having $-NH_2$, $-COOH$, $-SH$ molecules. ? The contact is such that the substrate molecules or reactants come together causing the chemical changes ? for this reason the enzyme substrate complex is reformed as lock and key. ? Once a form has occurred, the complex breaks up into products and enzymes ? the free enzyme is able to bind more substrates. ? The best evidence for this lock and key of enzymes action comes from the observation that compounds similar in structure to substrate inhibit the reaction. ? This lock and key theory explains the specificity of enzymes action.

induced fit theory: proposed by Koshland. ? active site of the enzyme contains two groups \rightarrow buttressing and catalytic. ? The buttressing group is meant to be able to break the bonds of reactants by electrostatic and nucleophilic forces. ? Both buttressing and catalytic groups are normally at a distance. ? When substrate comes in contact with the buttressing group, the active site of an enzyme undergoes conformational changes to bring the catalytic group opposite the substrate bonds to be broken.

(1c) (16) **Isoenzymes:** Some times an enzymes exist in more than one form which slightly differ in their structure. ? These different forms of the same enzyme, perform same function, are called Isoenzymes. ? Those multiple molecular forms of an enzyme occurring in the same organism and having similar substrate activity are called Isoenzymes or Isozymes. Ex: Lactic dehydrogenase.

Lactate dehydrogenase: Exist in 5 forms ? LDH1 to LDH5.

α -amylase: found in wheat endosperm ? 16 Iso-enzymes

Alcohol dehydrogenase: found in maize ? 4 Iso-enzymes

Isoenzymes differ in activity optima and inhibition. So, they are useful to organism in adapting to varied environmental conditions.

Inducible enzyme: An enzyme which is synthesized only in the presence

of its substrate [Inducer] is called Inducible enzyme. e.g. β -Galactosidase

- Repressible enzyme: the presence of a specific substance may inhibit continued production of specific enzyme [Enzyme repression]. e.g. Tryptophan operon in E. coli.

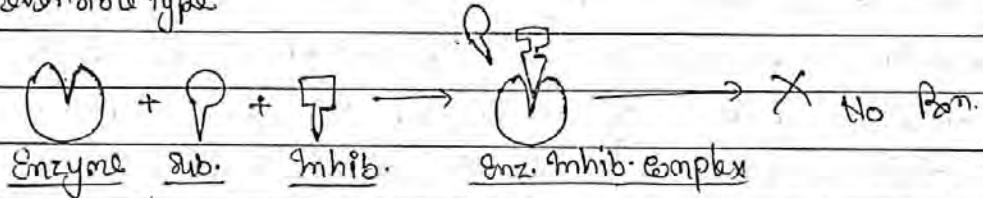
- Constitutive enzymes: The enzymes which are found in constant amounts under different growth conditions [regardless of its metabolic state] are called constitutive enzymes. e.g. Enzyme of respiratory cycle

- Hydrolysing enzymes: they catalyse the Rn in which complex organic compounds are broken into simpler compounds with the addition of water.

* In a cell digestive (hydrolytic) enzymes are mostly located in lysosome.

* Out of the total enzymes present in the cell, about 70% are located in mitochondria.

- Enzyme inhibition: ① Competitive inhibition: Some substances [inhibitors] have structural similarity with the substrate. So, both substrate and inhibitor compete for the active site of enzyme. This competitive inhibition is of reversible type.

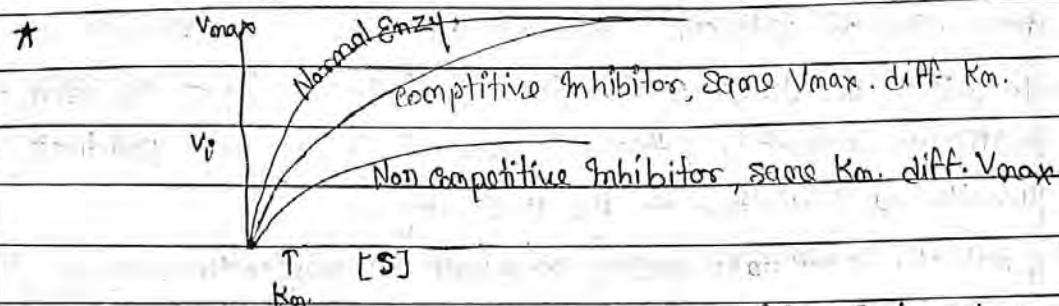


Example: Competitive inhibitor is malonic acid which inhibit the activity of enzyme succinic dehydrogenase [catalyse the conversion of succinic acid to fumaric acid]. Acetazolamide inhibit the activity of Carbonic anhydrase enzyme. Allopurinol inhibit the activity of Xanthine oxidase.

- Competitive inhibitor form enzyme inhibitor complex and inhibit the enzyme from acting on proper substrate.

- Competitive inhibition is important in that it provides evidence for lock and key hypothesis of enzyme action. Control of bacterial pathogens has been effected through competitive inhibition. Sulpha drugs inhibit the synthesis of folie acid in bacteria by competing with para-amino benzoic acid for the active site of enzyme. Substrate analogues

are not metabolized by enzymes. * Competitive inhibitor increases K_m but it has no effect on V_{max} .



① Non-Competitive Inhibition: Some inhibitors (Poisons) do not compete for active sites of enzyme but destroy the st^r of enzyme. As a result; the physical st^r of enzyme is altered. This fails to form enzyme substrate complex and Rxn fails to occur. This inhibition is irreversible type.

Example: Cyanide inhibits the activity of cytochrome oxidase (essential for all mammalian cells to perform respiration). It has no similarity with substrate or cytochrome but it acts at some other site of enzyme. DFP (Di-isopropyl fluorophosphate) inhibits the enzyme capable of catalysing hydrolysis of esters and peptide linkages (Acetylcholine, esterase, trypsin, chymotrypsin.) Na-acetamide inhibits the enzymes which have sulphhydryl or imidazol group. Non-Competitive inhibitors does the V_{max} of enzyme but they have no effect on K_m .

- feed back inhibition / Allosteric modulation: Accumulation of end product causes inhibition in the activity of the first enzyme of the series. This inhibition is due to final end product which is totally different in st^r from the substrate of the enzyme is called allosteric. ~~or~~ feedback inhibition, and such enzyme is called allosteric enzyme. The allosteric enzymes bears two types of sites active and allosteric. The end product combines with allosteric site of enzyme and checks its catalytic activity. (due to change in shape of enzyme so the active site of enzyme becomes unfit for making complex with its substrate). The inhibitor (end product) is also called modulator. The allosteric inhibition is reversible, when the concentration of the end product in the cell falls, it leaves the allosteric site and the

activity of allosteric enzyme is restored

e.g. This type of inhibition can be observed in E. coli at the time of formation of isoleucine amino acid.

Formation of isoleucine is stopped further when it has been formed in optimum quantity [threshold value]. So the end product isoleucine works as inhibitor at the first stage.

* Similarly hexokinase during glycolysis in respiration acts on glucose to form glucose 6- PO_4^{2-} and which inhibits the activity of Hexokinase.

- Classification of enzymes : Duclaux [1883] provided a system for naming enzymes by using the suffix -ase. At IUB [International Union of Biochemistry] the enzymes are classify into 6 groups on the basis of type of Rxn they catalyse

① Oxide-reductase : Transfer of H and O or electron from one substance to another. e.g. cytochrome oxidase and alcohol dehydrogenase

② Transferase : Transfer of specific group [methyl, acyl, amino or phosphate] from one substance to another. e.g. transaminase, kinase

③ Hydrolases : Hydrolysis Rxn. e.g. digestive enzymes

④ Lyases : Catalyse the cleavage of specific covalent-bonds. and removal of group without hydrolysis. They act on C-C, C-N, C-O or C-S bonds. e.g. decarboxylase, fumrase, aldolase.

⑤ Isomerase : catalyse the rearrangement of molecular st^r to form isomers. e.g. phosphogluco isomerase.

⑥ Ligases / Synthetases : Joining of two molecules by synthesis of new C-O, C-N, C-C bonds with breakdown of ATP. e.g. Acyl CoA, synthetase pyruvate decarboxylase.

* Ribozyme : Study of post transcriptional processing of RNA molecules has led to the most exciting discovery of the existence of some catalytic RNA molecules which have called as RNA enzymes. [Ribozymes]

All enzymes are not proteins as confirmed by Cech [1981] and Altman [1993].

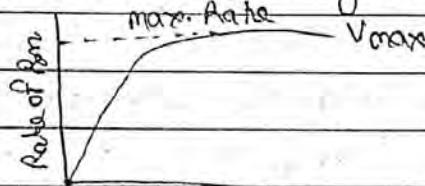
* Ribozyme and RNAase-P are non-protein enzymes where RNA acts as catalyst? Ribozyme was reported from Tetrahymena [a protozoan] by Cech 1981-1981.

- RNAase-P discovered Altman.

(17) Enzyme activity : Rate of R_{en} \Rightarrow Amount of substrate changed \Rightarrow amount product formed J in given period of time

- Enzyme activity affected by 4 factors : ① Temp. ② pH ③ Enzyme concentration ④ Substrate concentration.

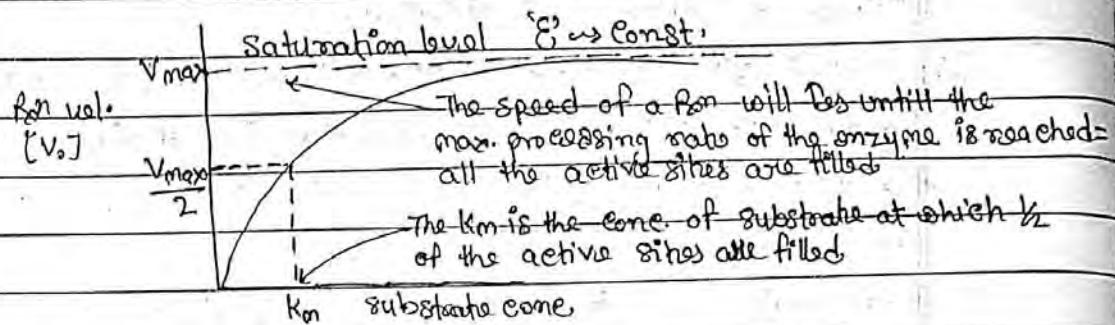
① Substrate concentration : Enzyme molecule is larger in size and bears several active sites over its surface. \Rightarrow If in substrate concentration enhances the rate of R_{en} due to occupation of more and active sites by the substrate molecule and higher number of collisions b/w substrate molecules. So, at constant enzyme concentration, If in substrate concentration \Rightarrow the rate of R_{en} . \Rightarrow further If in substrate concentration does not \Rightarrow the rate of R_{en} . \Rightarrow At this stage the enzyme molecules become fully saturated and no active site is left free to bind additional substrate molecules. This saturation effect is shown by all enzymes.



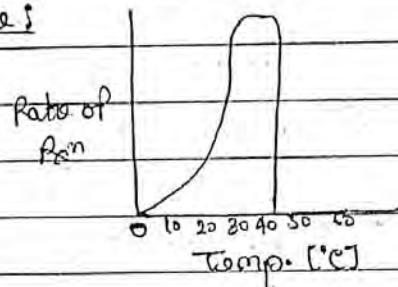
Substrate Concentration

Michaelis constant : Michaelis-Menten constant or K_m is a mathematical derivative or constant which indicates the substrate concentration at which the chemical R_{en} catalysed by an enzyme attains half its maximum velocity (V_{max}). \Rightarrow This constant (K_m) was given by L. Michaelis and M. Menten. \Rightarrow K_m indicates affinity of the enzyme for its substrate. \Rightarrow K_m value differs from substrate to substrate b/c enzymes differ in their affinity towards different substrates. A high K_m indicates low affinity while a low K_m shows strong affinity. \Rightarrow Proteases acts on different proteins. So it K_m value will differ from

protein to protein.) Allosteric enzymes do not show typical Michaelis-Menten Constant as allosteric enzymes do not obey Km Constant. K_m mostly lies b/w 10^1 to 10^6 M.

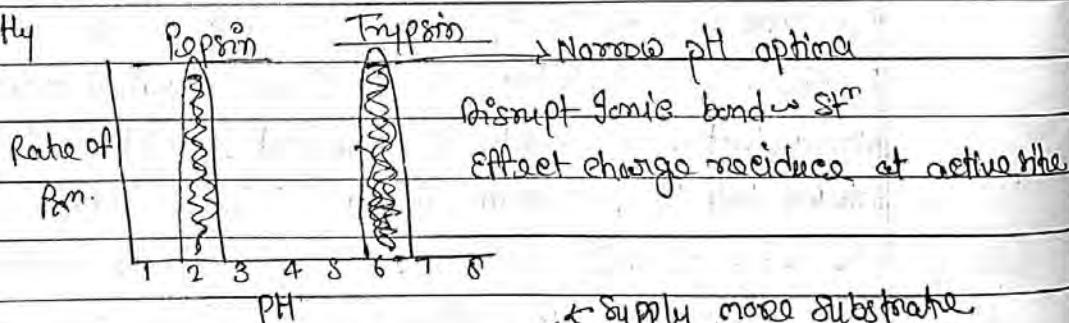


② Temperature:



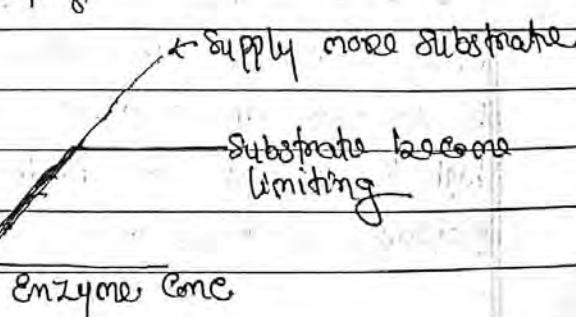
Each enzyme works best at a particular temp. \rightarrow optimum temp. When temp. is lower than optimum temp., activity of enzyme becomes lower. At low temp., enzymes become inactive. They become active again when the temp. is raised. Above the optimum temp., heat changes the shape of enzymes and their active sites, decrease their activities. When temp. is too high [Above 60°C], most enzymes are denatured and lose their catalytic property permanently.

③ pH:



④ Enzyme concentration:

Rate of Rxn



Cell cycle & cell division

science world H&B

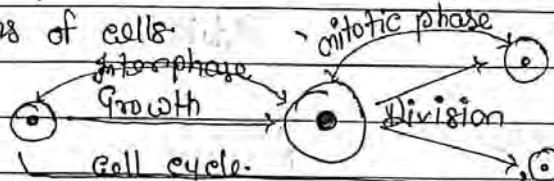
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NCERT

Growth and reproduction are characteristic of cells. All cell reproduce by dividing into two, with each parental cell giving rise to two daughter cells each time, they divide. These newly formed daughter cells can themselves grow and divide, giving rise to a new cell population that is formed by the growth and division of a single parental cell and its progeny. In other word such cycles of growth and division allow a single cell to form a st^r consisting of millions of cells.

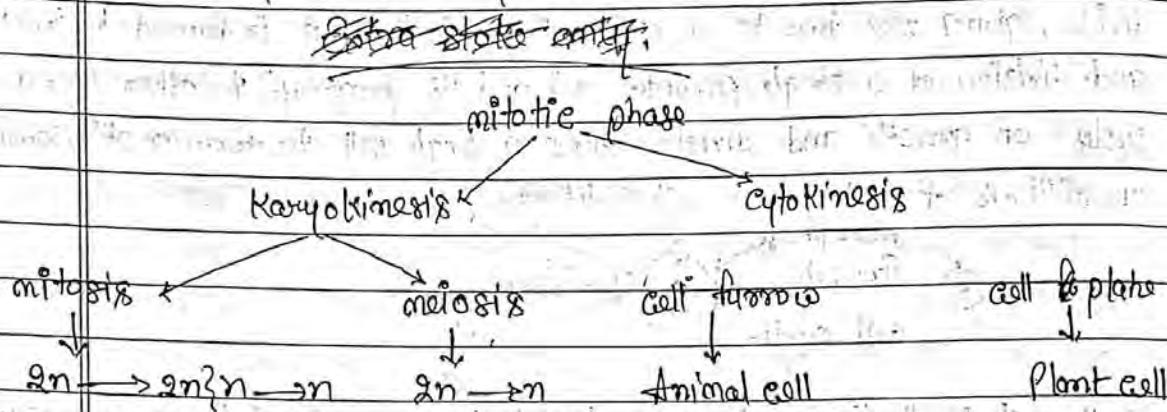


Cell cycle: cell division is a very important process in all living organism. During the division of a cell, DNA replication and cell growth also take place. All these processes, i.e., cell division, DNA replication, and cell growth, hence, have to take place in a coordinated way to ensure correct division and formation of progeny cells containing intact genomes. The sequence of events by which a cell duplicates its genome, synthesis of other constituents of the cell and eventually divides into two daughter cells is termed cell cycle. Although cell growth (in terms of cytoplasmic mass) is a continuous process, DNA synthesis occurs only during one specific stage in the cell cycle. The replicated chromosomes (DNA) are then distributed to daughter nuclei by a complex series of events during cell division. These events are themselves under genetic control.

Cell cycle: The sequence of events which occurs b/w the formation of a cell and its division into the daughter cells is called cell cycle. Before dividing a cell must double its mass and duplicate all its contents so that the new daughter cell contains all the components in the required amount which are needed to begin the life. In cell cycle, most of the time occupied for the preparation for division; this is kls Growth phase. Then the cell divides; this is kls division. Howard and pelc discovered four stages in a cell cycle: G₁ phase, S phase, G₂ phase & M phase.

Phases of cell cycle: A typical eukaryotic cell cycle is illustrated by human cells in culture. These cells divide once in approx. every 24 hours; However, this duration of cell cycle can vary from organism to organism and

also from cell type to cell types; Yeast for example, can progress through the cell cycle in only about 90 minutes; The cell cycle cycle is divided into two basic phases: Interphase and M phase (mitosis phase).



Special: Term mitosis and meiosis are concerned w/ Karyokinesis;
 Interphase → most active phase of cell cycle. Also k/a Energy phase;
 Best part, study of mitosis w/ Root tip cell of onion; Best part the
 study of meiosis w/ Anthers of the flower; Controls participation in
 mitosis than it is called w/ Centriole and Astral mitosis (e.g. Animal cell);
 Centriole does not participate in the mitosis than it is called w/
 Acentriole and Anastral mitosis (e.g. Plant cell).

The M phase represents the phase when the actual cell division or mitosis occurs and the interphase represents the phase b/w two successive M phases.
 It is significant to note that in the 24 hour average duration of cell cycle of a human cell, cell division proper lasts for only about one hour.

The Interphase lasts more than 98% of the duration of cell cycle.

The M phase starts with the nuclear division, corresponding to the separation of daughter chromosomes (Karyokinesis) and usually ends with division of cytoplasm (Cytokinesis). The Interphase, though called resting phase, is the time during which the cell is preparing for division by undergoing both cell growth and DNA replication in an orderly manner.

The Interphase is divided into three further phases:

① G₁ phase [Gap 1] ② S-phase [Synthesis] ③ G₂ phase [Gap 2]

= ② G₁ phase corresponds to the interval b/w mitosis and initiation of DNA replication; During G₁ phase the cell is metabolically active and

Continuously grows but does not replicate its DNA.

- G₁ phase: Intensive cellular synthesis. { Production of lysosome, G.B., vacuoles, ER, and other cell organelles. } Except mitochondria and chloroplast J. { Synthesis of mRNA, rRNA, and tRNA. } Production of ribosome. } sf and functional protein synthesis. } High metabolically active cell. { most of the cell growth take place. } The decision of cell division takes place in this phase. } In late G₁ phase, a restriction point occurs [R point]. } If cell cross this R-point \rightarrow It must divide. } If cell fail to cross this R-point \rightarrow It can not divide. } R-point is a critical level of specific protein molecules. } These protein molecules are Ras \rightarrow Trigger protein or Cdk-protein. } These protein help to cell to cross the R-point. Now these proteins are identified as cyclins, and CDK-Kinase [Cell cycle's Engine]. } If cell can not cross the R-point, it said G₀ phase. } It becomes a permanent cell and undergoes in differentiation. } Also known as G₁ phase / Gap I phase / Generation I phase / Pre-DNA synthesis phase.

- S-phase: synthetic phase marks the period during which DNA synthesis or replication takes place. } During this time the amount of DNA per cell doubles. } If the initial amount of DNA is denoted as 2C \rightarrow then it increases to 4C. } However, there is no change in the chromosome number; if the cell had diploid or 2n number of chromosomes at G₁, even after S-phase the number of chromosomes remain the same, i.e., 2n. } In animal cells, during the S-phase, DNA replication begins in the nucleus, and the centriole duplicates in the cytoplasm.

- S-phase: synthetic phase. { Cell doubles its DNA content. } DNA replication takes place. } Most active enzyme \rightarrow DNA polymerase. } DNA Histone proteins are synthesized in S phase. [G₁ & S]. } Once a cell doubles its DNA content \rightarrow It must divide to reduce its DNA content to normal. } During the G₂ phase, proteins are synthesized in preparation for mitosis while cell growth continues.

- G₂ phase: intensive cellular synthesis. } Use in energy store (ATP). } Division of mitochondria and chloroplast. } Spindle fibers are synthesized in this phase. } Rest of the cellular synthesis takes place.

- NCERT Ques. ? ① How do plants and animals continue to grow all their lives? ② Do all cells in plant divide all the time? ③ Do you think all cells continue

to divide in all plants and animals p④ Can you tell the name and the location of tissue having cells to divide all their life in higher plants?

⑤ Do animals have similar meristematic tissue?

Some ~~adult~~ cells in the adult animals do not appear to exhibit division [e.g. heart cells] and many other cells divide only occasionally, as needed to replace cells that have been lost b/c of injury or death of cell? These cells that do not divide further exit G₀ phase to enter an inactive stage called quiescent stage [G₀] of the cell cycle; cells in this stage remain metabolically active but no longer proliferate unless called on to do so depending on the requirement of the organism.

In animals, mitotic cell division is only seen in the diploid somatic cells. Against this, the plants can show mitotic divisions in both haploid and diploid cells.

M-phase: This is the most dramatic period of the cell cycle, involving a major reorganisation of virtually all components of the cell.

Molecular basis of cell cycle: The events that control different steps during mitosis and meiosis are genetically controlled; they are studied at molecular level. These studies were conducted on two varieties of yeast:

① Budding yeast [Saccharomyces cerevisiae] ② fission yeast [Schizosaccharomyces pombe].

The molecular events that control the cell cycle are ordered and directional; i.e., each process occurs in a sequential fashion and it is impossible to reverse the cycle. There are two key classes of regulatory molecules that determine a cell's progress through the cell cycle: cyclins and cyclin-dependent kinase.

Edmund H. Karschell, R. Timothy Hunt and Paul M. Nurse won the ~~2000~~ 2001 Nobel prize in physiology and medicine for their discovery of these control molecules (cyclins & CDK).

The cell cycle mutants of yeast varieties were used to discover these key regulators of cell cycle; mutant gene of fission yeast \rightarrow cdc gene; mutant gene of budding yeast \rightarrow cdk gene; In these cell cycle mutants, the cell cycle was arrested at specific points. These points were called as check points; Two main check points exist: the G₁/S check point and the G₂/M check points.

The machinery for cell cycle control is also identified in *Aspergillus*, frogs, *Drosophila* and mammals? Within the cells, there are devices ensures that the cell is not driven into the division before DNA synthesis is completed? Also control that the anaphase does not begin before the proper alignment of chromosomes? So we can say that in cells, there is a control system. In this control system, brakes and feed back signals can operate? Break can stop the cell cycle at check points? feed back signals can delay the events of cell cycle.

- * Cdk and cyclins are the molecules of cell cycle control.
- Cdk - cyclin complex perform a common biochemical reaction called phosphorylation that activates or inactivates target proteins to perform coordinated entry into the next phase of the cell cycle.
- Cyclin dependent kinase are of 7 types: Cdk 1 to Cdk 7. In yeast & Cdk 1 is very important? In majority of animals Cdk 1 and Cdk 2 are very important? In mammals Cdk 1, Cdk 2, Cdk 3, Cdk 4 and Cdk 6 are more important.
- Cyclins are of 3 types: mitotic cyclins are found in M phase? S cyclins are found in S phase? G1 cyclins are found in G1 phase.
- The S-phase is induced by Cdk and S-phase cyclins? The M-phase induced by Cdk 1 and mitotic cyclins? The Cdk 15 gene → stimulate the entry of cell into mitosis? The wee-1 gene → inhibit the entry of cell into mitosis.
- * The p53 gene is popularly known as Tumor suppressing gene? It produces p53 protein. This protein is like a watchman of genome b/c it respond to damaged DNA and abnormal DNA; and it arrests the cell cycle in case of any fault in DNA → inhibit carcinogenesis? In more than 80% genes of cancers → the p53 gene is mutated? Cancer is uncontrollable mitosis division. In cancer the cells are not controlled by the molecular mechanism; these cells are immortal.

- Affairs
- ③ Affair special: In S-phase there is no synthesis of DNA? The cell undergoes in division when karyoplasmic index is disturbed? In S-phase the DNA becomes 4C? Latest researches shows that due to hydration, the chromosomes become invisible in Interphase? Due to dehydration, the chromosomes becomes visible as in M-phase of cell cycle? The repair of damaged DNA takes place in the Interphase? Period b/w two successive cell division is

Generation time / Anaphase? Three major events of cell cycle are? DNA replication, Karyokinesis and cytokinesis. G_1 stage is absent in amoeba, fission yeast and some moulds. Tubulin proteins and kinase proteins are synthesized in G_2 phase. New centrole pair is formed in S-phase in animal cells. Centrioles initiate cell division in animal cells. mature neuron are unable to divide.

~ M-phase: This is the most dramatic period of the cell cycle, involving a major reorganisation of virtually all components of the cell. In mitosis, since the number of chromosomes in the parent and progeny cells is the same, it is also called as equational division. Through for convenience mitosis has been divided into four stages of nuclear division, it is very essential to understand that cell division is a progressive process and very clear-cut lines can't be drawn b/w various stages.

Mitosis: Also called somatic / equational cell division. In this type of division, the mature somatic cells divide in such a way that chromosome number is kept const. in the daughter cell. Mitosis discovered first in plant cell by German biologist Schleiden. Mitosis discovered in animal cell by Walther and Flemming. In salamander cell, J. Corn. mitosis. by Flemming. [mitos: thread; ois: state] Generally mitosis takes 30 minutes to 3 hours. The time of mitosis is species specific. It also depends upon temp. and type of tissue. Mitosis occurs in both diploid and haploid cells. It also occurs in polyploid cells. In plants, mitosis is commonly seen in apical meristem of root tip & shoot tip. [localized and unlimited growth]. Mitosis occurs during the embryonic development. It is the main division of growth.

- The mitosis consists of 4 phases: ① Prophase (longest phase) ② Metaphase

③ Anaphase (shortest phase) ④ Telophase

Mitosis is divided into the four stages: ① Prophase ② Metaphase ③ Anaphase ④ Telophase.

- Prophase: Longest phase. It takes 71 minute in onion root tip cell [2-3% time of cell cycle]. Prophase is differentiated into 3 sub-phases:

① Early prophase ② Middle prophase ③ Late prophase

- Early prophase: At the prophase begins, the viscosity and refractive index of cell increases. In early prophase, the chromatin threads separate from the chromatin nucleolus and undergoes spiralization. At this time, these chromatin threads look like a bunch of wool. So this is Ranvier stage. During spiralization, the chromatic thread shows pleiotropic coiling. In this type of coiling the chromatin threads coil in itself and with its paired thread. It results in condensation of chromosomes. The condensation of chromosome begins in early prophase. In animal cells, the centrosome of centrosome disappears [in cytoplasm]. The centrioles begin to move towards the opposite poles. The microtubule push them to the opposite pole.

- Middle prophase: It is characterized by more condensation of chromosomes. Hence they becomes shorter and thicker. The longitudinal splitting of chromosomes takes place except centromera. In other words the hidden [duplicated] thread of chromosome appears. So we can say that monad becomes dyad. In animal cells, the centriole moves away from each other.

- Late prophase: The nuclear membrane and nucleolus disappear. The nuclear membrane fragments are merge into ER. The nucleolus distributes its components in the form of RNA and proteins. This results the disappearance of nuclear membrane and nucleolus. Due to disappearance of nuclear membrane, the chromosomes are now exposed in cytoplasm. The chromosomes become more condensed. The late prophase is also called \rightarrow Prometaphase. Prometaphase is that time gap which is present b/w the disappearance of nuclear envelope and formation of nuclear spindle apparatus. At the time of formation of nuclear spindle apparatus, both centrioles becomes antipodal in position. It means that they are present opposite to each other. The microtubule are involved in the formation of nuclear spindle apparatus. Those microtubule which are involved in the formation of spindle fibers of nuclear spindle apparatus are charged. Their -ve end is towards the pole and +ve end is toward the equator.

- Anaphase: first stage of mitosis follows the S & G₂ phases of Interphase. In the S and G₂ phases the new DNA molecules formed are not distinct

but intertwined. Prophase is marked by the initiation of condensation of chromosomal material. The chromosomal material becomes untangled during the process of chromatin condensation. The centriole, which had undergone duplication during S-phase of interphase, now begins to move towards opposite poles of the cell. The completion of prophase can thus be marked by the following characteristic events: Chromosomal material condenses to form compact mitotic chromosomes. Chromosomes are seen to be composed of two chromatids attached together at the centromere. Initiation of the assembly of mitotic spindle, the microtubules, the proteinaceous components of the cell cytoplasm in the process. Cell at the end of prophase, when viewed under the microscope, do not show G.B., ER, Nucleolus and the nuclear envelope.

(A) Metaphase: It takes around 1% time of total cell cycle. It is characterised by the complete formation of the nuclear spindle apparatus. In metaphase stage, the chromosomes arrange themselves on the equator of the nuclear spindle apparatus. Equator is the broadest part of the nuclear spindle apparatus. The spindle fibres get attached to the centromere of the chromosomes. The spindle fibres from one pole of the nuclear spindle apparatus join at the one side of the centromere of the chromosomes (at the kinetochores plate). The centromere of chromosome is attracted with the spindle fibres of both the poles.

- At metaphase stage the chromosomes shows maximum condensation. So there is no genetic activity expressed in this phase. The metaphase gives the best count of chromosomes.

The complete disintegration of the nuclear envelope marks the start of the second phase of mitosis, hence the chromosome are spread through the cytoplasm of the cell. By this stage, condensation of chromosomes is completed and they can be observed clearly under the microscope. This then is the stage at which morphology of chromosomes is most easily studied. At this stage, metaphase chromosome is made up of two sister chromatids, which hold together by the centromere. Small disc-shaped spot at the surface of the centromeres are called kinetochores. These st. serve

as the site of attachment of spindle fibres [formed by the spindle fibres] to the chromosomes that are moved into position at the centre of the cell.] Hence, the metaphase is characterised by all the chromosomes coming to lie at the equator with one chromatid of each chromosome connected by its kinetochores to spindle fibres from one pole and its sister chromatid connected by its kinetochores to spindle fibres from the opposite pole; the plane of alignment of the chromosomes at the metaphase is referred to as the metaphase plate.

- The key features of metaphase are: spindle fibres attach to kinetochores of chromosomes; chromosomes are moved to spindle equator and get aligned along metaphase plate through spindle fibres to both poles.
- Anaphase: shortest phase of cell cycle; it takes less than 0.8% time of cell cycle; This phase is characterised by the splitting of centromeres; In anaphase stage the spindle fibres which are attached to the centromere undergoes in contraction; This results in the splitting of centromere and the chromatids now separate from each other; and they move towards opposite poles; In anaphase stage, 3 types of nuclear spindle fibres are observed: ① Continuous fiber ② chromosomal or discontinuous fibres ③ Interzonal fibres [seen in only anaphase]
- In anaphase, the chromosomal movement towards poles is observed; [shape of chromosomes is studied in anaphase. [shape and number both together in metaphase.] The NCERT
- At the onset of anaphase, each chromosome arranged at the metaphase plate is split simultaneously and the two daughter chromatids, now referred to as chromosomes of the future daughter nuclei, begin their migration towards the two opposite poles; As each chromosome moves away from the equatorial plate, the centromere of each chromosome is towards the pole and hence at the leading edge, with the arms of the chromosome trailing behind;
- Thus, anaphase stage is characterised by the following key events: Centromeres split and chromatids append separate; chromatids move to opposite poles.

- Telophase: It takes 1 to 1.8% time of total cell cycle. It begins when the chromosomes have reached the poles. This phase is characterised by the disappearance of the nuclear membrane and nucleolus. The nuclear membrane is organized by the ER. The nucleolus is organized by the NOR of SAT-chromosomes. At the end of telophase, the chromatid uncoil and expand; and these unites and form chromatin network. The microtubules of spindle nuclear apparatus get separated [disassembly] so these disappear.

- At the beginning of the final stage of mitosis, i.e., telophase, the chromosomes that have reached their respective poles decondense and lose their individuality. The individual chromosomes can no longer be seen and chromatin material tends to collect in a mass in the two poles. This is the stage which shows the following key events: chromosomes cluster at opposite spindle poles and their identity is lost as discrete elements. Nuclear envelope assembles around the chromosome clusters. Nucleolus, GB & ER re-form.

- Significance of mitosis: main division of growth produces genetically similar cells. main division of asexual reproduction. Embryogenesis. main division of repair [Healing].

- mitosis or the equational division is usually restricted to the diploid cells only. However, in some lower plants and in some social insects haploid cells also divide by mitosis. It is very essential to understand the significance of this division in the life of an organism. Mitosis usually results in the production of diploid daughter cells with identical genetic complement. The growth of multicellular organisms is due to mitosis. Cell growth results in distributing the ratio b/w the nucleus and the cytoplasm. If therefore becomes essential for the cell to divide to restore the nucleo cytoplasmic ratio. A very significant contribution of mitosis is cell repair. The cells of the upper layer of the epidermis, cells of the lining of the gut, and the blood cells are being constantly replaced. Mitotic divisions in the meristem tissue - the apical and the lateral cambium, result in a continuous growth of plants throughout their life.

⑥ Cytokinesis: It involves the division of cytoplasm.

- In Animal cells → By cell furrow method: {In general, the preparation of cytokinesis begins at metaphase during which the cell organelles arrange themselves equally on either side of equator [this distribution is not exact equal].} During anaphase in Karyokinesis, a dense body develops at the middle of equator. This is K/abs mid Body. Then, the cell membrane develops a constriction which deepens. {This constriction is K/abs cell furrow.} It develops contripetally. {At the end of telophase in Karyokinesis, finally cell divides into two.} The volume of daughter cell is half of the mother cell. This type of cytokinesis is K/abs cell furrowing.

- In plant cells → By cell plate method: {Golgi body is the cell organelle that actively participate in the cell wall formation.} It synthesizes and secretes all those chemicals that are required for cell wall formation. {These chemicals are released in vesicles b/w phragmoplast.} The plane and place of cell wall formation is determined by the microtubules. {At the decided plane, the phragmoplast arranges themselves and form the cell plate.} Phragmoplast are the precursors of cell plates. {The cell plate ultimately converts into the middle lamella. On both sides of middle lamella, cellulose get deposited.} This results in the formation of the primary wall. {Cell wall formation is centrifugally.}

mitosis accomplishes not only the segregation of duplicated chromosomes into daughter nuclei [Karyokinesis], but the cell itself is divided into two daughter cells by a separate process called cytokinesis at the end of which cell division is complete.

In animal cell, this is achieved by the appearance of a furrow in the plasma membrane. The furrow gradually deepens and ultimately joins in the centre dividing the cell cytoplasm into two. {Plant cells however, are enclosed by a relatively inextensible cell wall, therefore they undergo cytokinesis by a different mechanism.} In plant cells, wall formation starts in the centre of the cell and grows outward to meet the existing lateral walls. {The formation of the new cell wall begins with the formation of a simple precursor, called the cell plate that represent the middle lamella b/w the walls of two adjacent cells.} At the time of cytoplasmic division, organelles like mitochondria and plastids get distributed b/w the two daughter cells. {In some organism Karyokinesis is not followed by cytokinesis as a result of which multinucleate condition arises leading to the formation of ^{mistakenly NCERT} syncytium (e.g. Liquid endosperm in coconut).}

All this is special. The rate of mitosis vary with the age. {From prophase, meta-

phase, Anaphase and Telophase proposed by Strasburger; Interzonal spindle fibers pushes the chromosomes to the opposite poles so they are also kinesin pushing bodies? The chemicals which severely affect mitosis and stop it are kinesin inhibitors. These are following:

- ① Ribonucleases → inhibit prophase of mitosis.
- ② Mustard gas → It cause fragmentation of chromosomes.
- ③ Colchicine → It affect metaphase of mitosis. → Colchicine breaks the nuclear spindle apparatus so it prevents the chromosomal separation. This brings about duplication of chromosomal number. (Poly ploidy)
- ④ Colchicine obtained from the seed of beet colchicum luteum plant (Liliaceae). The mitosis affected by Colchicine is kinesin mitosis - C. Mitogens are those chemicals which induces mitosis; mitogens are: Growth hormones, insulin, Thyroxin, gibberellin, cytokinins, auxins, temp., steroids, lymphokines; epidermal growth factors (EGF), platelet derived growth factor (PDGF).
- Spindles can be observe with the help of polarizing microscope. In anaphase stage, the chromosome arranges themselves on the equatorial plate. For this purpose, they move towards equator; this movement is kinesin metakinesis/congression. In late prophase the nuclear membrane breaks up to fragments. This occurs due to activity of caspase.
- At anaphase the chromosomes move towards opposite poles at the speed of $\approx 1\mu\text{m}/\text{min}$. About 30 ATP are consumed to move a chromosome from equator to the pole. Due to endomitosis, the chromosomes become double but not separate from each other, they remain united by the centromere. This is kinesin SKI-configuration. The normal somatic cell does not lives forever. After undergoing a certain fixed number of divisions, they die. This limit is called Hayflick limit. In cancer cells, the Hayflick limit is not observed so these cells are naturally immortal.

Cancer: Abnormal cell growth; uncontrolled mitosis; may show metastasis; evantake healthy cells and destroy the organs involved.

Metastasis: cancerous cells break away from the primary tumor and spread to other organs.

Types of cancer: Carcinoma $\approx 85\%$ of cancerous organs; skin, nerves, membranes; Sarcomas $\approx 2\%$ of cancers: bone, blood, connective tissue; lymphomas \approx lymphatic cells; Hodgkin's disease; Leukemia; Blood and blood forming tissue; melanomas \approx skin cancer.

Sunshine [UV rays] is the single most important causative factor in all skin cancers.

These two categories of genes derive carcinogenesis: ① Onco genes → These are cancer genes responsible for the properties to cause cancer. ② Repressor genes/tumor suppression genes → Contain inhibition functions whose loss result in uncontrollable cell growth.

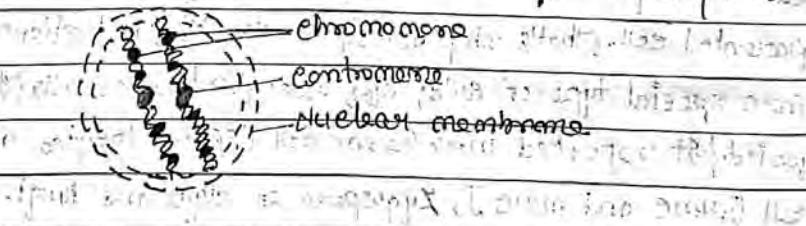
Onco genes: An onco gene is any gene that encodes a protein able to transform cells in culture or induce cancer in animals; most onco genes are derived from normal cellular genes [i.e. proto-onco genes] whose products participate in cellular growth controlling pathways; activation of a proto-onco genes generally involves mutation: [genetically point mutation or chromosomal translocation] that cause inappropriate expression of a growth-regulatory gene. {In 1991, Bishop and Varmus showed normal cells contain a gene c-sre [Proto-onco gene]; mutation of the proto-onco gene converted it into an onco gene. Proto-onco gene is an potential onco gene present in normal cells. After mutation the proto-onco gene may be altered into onco gene. The chromosomal translocation b/w chromosome 9 with chromosome 22 causes chronic myeloid leukemia [CML].}

Tumor/cancer suppressor gene: Rb gene and p53 gene
 Main oncogenic viruses: Herpes-related viruses → Leukemia, Hodgkin's disease, cervical cancer, and Burkitt's lymphoma; Epstein-Barr virus; Human papilloma virus → linked to cervical cancer; ~~Bacterium Helicobacter pylori~~ cause ulcers which are a major factor in the development of stomach cancer.
 Cancer's seven warning signals: changes in bowel or bladder habits; a sore that does not heal; unusual bleeding or discharge; thickening or lump in breast or elsewhere; indigestion or difficulty in swallowing; obvious change in a wart or mole; nagging cough or hoarseness.

⑥ Meiosis: Meiosis is a special type of division in which the chromosome duplicate once but the cell divides twice. So one parental cell produces 4 daughter cells each having half the chromosome number and DNA amount than the normal parental cell. That's why meiosis is also known as Reductive division. Meiosis is found in a special type of cells; karyocytes/mother cells. It is seen in special time periods. It is reported in → Germ cell (spermatocytes and oocytes), sporangium mother cell (MMC and MMC), Zygospore of algae and fungi.

Meiosis first time demonstrated by Von Borden; first time described by Winiwarter. Term meiosis → Farmer and Moore.

- meiosis is of 3 types : ① Zygotic meiosis ② Sporadic meiosis ③ Gametic meiosis.
- ① Zygotic meiosis / initial meiosis : observed in lower plant groups like algae { also seen in fungi } zygote undergoes in meiosis { so there is no embryo formation ? result plant body is Haploid }
- ② Sporadic meiosis / intermediate meiosis : seen in higher plants { take place in megasporangium cell and microsporangium cell during formation of megasporangium and microsporangium respectively. }
- ③ Gametic meiosis / terminal meiosis : seen in animals { take place in germ cells } As a result gamete are formed [egg and sperm]
- meiosis involves 2 divisions : ① meiosis I / Heterotypic division / Reductive division. ② meiosis II / Homotypic division / meiotic mitosis { between meiosis I ; it results in formation of two daughter cells which have chromosome number half to those in the parental cell so it is called Reductive division / Heterotypic division. }
- meiosis I involves following phases : ① Prophase I -> longest phase ② Metaphase I ③ Anaphase I ④ Telophase I
- ① Prophase I : longest phase of meiosis. { It compare to prophase of mitosis it is 100 to 200 times longer } Divided into 5 subphases : ① Leptonema ② Zygotene ③ Pachytene ④ Diplotene ⑤ Diakinesis.
- ① Leptonema : Also called thin thread stage { In leptotene, the chromosome appears like thin strands } In each chromosome, several ^{micro}chromosomes are observed which gives the chromosome a beaded appearance { the condensation and spiralization of chromosome begins } The chromosome show parameiotic coiling during spiralization { The longitudinal splitting of chromosome takes place except centromere but it is not visible under normal microscope } The telomere of chromosomes are attached to the nuclear envelope which gives it a bouquet arrangement.



- ② Zygotene : Also called paired, threaded stage { This subphase is characterized by the pairing of homologous chromosomes which is known as

Synapsis or synkinesis: first time reported by Montgomery.

The pairing of homologous chromosomes is of 3 types: ① Paracentric \leftrightarrow begins from the centromere. ② Procentric \leftrightarrow begins from the telomere. ③ Random \leftrightarrow begins from anywhere except centromere and telomere.

The pairing of homologous chromosome is in zip-like manner? It means tetrad axis of homologous chromosome is paired, the paired chromosomes are called bivalents.

Bivalent



* When the entire tetrad axis of homologous chromosome is paired, the st^{er} is called synaptonemal complex. It was first time reported by Moses in spermatocytes of ray fish.

Condensation of chromosome remain continues in this sub phase.

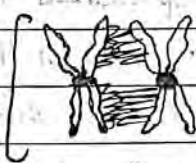
0.3-0.4% DNA replicates in Zygotene. This DNA is called Zyg-DNA? So to perform replication, the DNA strands are decondensed. perhaps this event results in pairing of chromosomes.

② Pachytene: also called thick-threaded stage? The chromosomes show further condensation?

The longitudinal splitting of chromosome now become visible [Except centromere]? Thus bivalents appear as Tetrad {Tetrad having 2 homologous chromosome each with two chromatids and one centromere? Tetrad \leftrightarrow 4 chromatid + 2 centromeres? This is called 4 strand stage? Crossing over takes place in 4 strand stage of pachytene of prophase I of meiosis.

This is called crossing over.

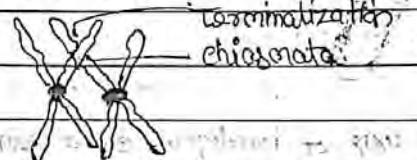
Tetrad.



- During crossing over, there is exchange of chromosomal segments b/w non-sister chromatid of homologous chromosomes.

- The most accepted mechanism of crossing over is breakage and reunion hypothesis, proposed by Darlington. Crossing over occurs randomly. It brings new recombinations of genes \leftrightarrow results in variations. Crossing over is an enzymatic activity [stem and blot].

④ **Diplotene:** Also called double-threaded stage. { longest of all subphases } It may takes few hours to several months { After the crossing over, now non-sister chromatids start separating from each other. } The separation begins from the centromere and it proceeds towards telomere. This kind of separation is **klug terminalization.** { This entire process is **Klug Desynapsis.** } As a result of terminalization, the non-sister chromatid separate from each other except at those points where already the crossing over has been taken place. { These contact points are X-shaped and are **Chiasmata.** } They were first time reported by Janssen.



- If chiasmata are present at the end of the chromosome \rightarrow Terminal chiasma.
- If they are present in the middle of the chromosome \rightarrow Interstitial chiasma.
- Chiasmata are the result of the crossing over; more the length of chromosome more will be the frequency of chiasma formation. { The telocentric chromosome forms more number of chiasmata. } max. 14 chiasmata are observed in Vicia faba plant chromosome.

⑤ **Diakinesis:** The Diplotene stage slowly changes into diakinesis. { In this phase terminalization is completed. } The nuclear membrane and nucleolus disappear; more condensation of chromosomes; the formation of nuclear spindle apparatus begins with the disappearance of nuclear membrane.

Mitosis: The production of offspring by sexual reproduction includes the fusion of two gametes, each with a complete haploid set of chromosomes. { Gametes are formed from specialized diploid cells. } This specialized kind of cell division that reduces the chromosome number by half results in the production of haploid daughter cells. This kind of cell division is called mitosis. { Mitosis ensures the production of haploid phase in the life cycle of sexually reproducing organisms whereas fertilization restores the diploid phase }

We come across mitosis during gametogenesis in plants and animals. This leads to the formation of haploid gametes.

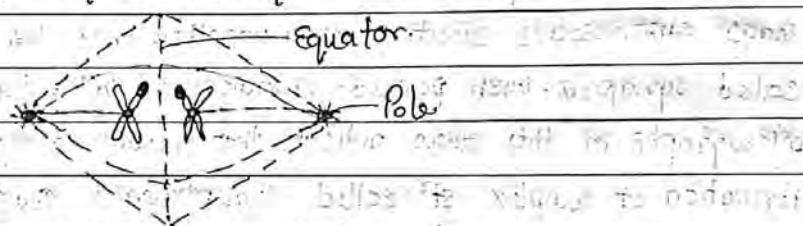
The key features of mitosis are as follows: mitosis involves two sequential cycles of nuclear and cell division called mitosis I and mitosis II but only

- a single cycle of DNA replication; meiosis I is initiated after the parental chromosomes have replicated to produce identical sister chromatids at the S-phase; meiosis involves pairing of homologous chromosomes and recombination b/w them. four haploid cells are formed at the end of meiosis II.
- meiotic events can be grouped under the following phases: meiosis I and meiosis II:
- meiosis I: Prophase I → prophase of the first meiotic division is typically longer and more complex when compared to prophase of mitosis. It has been further subdivided into the following five phases based on chromosomal behaviour, i.e., Leptonene, Zygotene, Pachytene, Diplotene and Diakinesis.
- During leptotene stage the chromosomes become gradually visible under the light microscope. The compaction of chromosomes continues throughout leptotene. This is followed by the second stage of prophase I called Zygotene. During this stage chromosomes start pairing together and this process is of association is called synapsis. Such paired chromosomes called homologous chromosomes. Electron micrographs of this stage indicate that chromosome synapsis is accompanied by the formation of complex structures called synaptonemal complex. This complex formed by a pair of synapsed homologous chromosomes is called bivalent or tetrad. However, those are more clearly visible at the next stage. The first two stages of prophase I are relatively short-lived compared to the next stage that is pachytene.
- During pachytene stage bivalent chromosomes now clearly appear as tetrads. This stage is characterized by the appearance of recombination nodules, the sites at which crossing over occurs b/w non-sister chromatids of the homologous chromosomes. Crossing over is the exchange of genetic material b/w two homologous chromosomes. Crossing over is also an enzyme mediated process and the enzyme involved is called recombinase. Crossing over leads to recombination of genetic material on the two chromosomes. Recombination b/w homologous chromosomes is completed by the end of pachytene, leaving the chromosomes linked at the sites of crossing over.
- The beginning of diplotene is recognized by the dissolution of the synaptonemal complex and the tendency of the recombined homologous chromosomes of the bivalents to separate from each other except at the sites of crossing over.

These X-shaped structures, are called chiasmata. In oocytes of some vertebrates, diplotene can last for months or years.

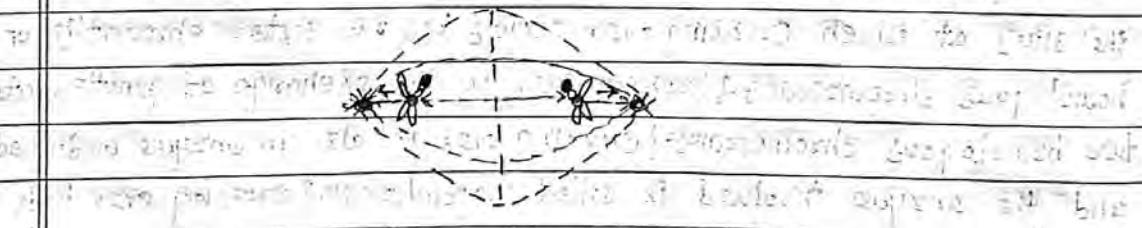
The final stage of prophase I is diakinesis. During this phase the chromosomes are fully condensed at the ends and the meiotic spindle is assembled to prepare the homologous chromosomes for separation. By the end of diakinesis, the nucleolus disappears and the nuclear envelope also breaks down. Diakinesis represents transition to metaphase.

Metaphase I: This phase is characterized by the complete formation of nuclear spindle apparatus. The chromosome arrange themselves on the equator of the nuclear spindle apparatus. At this time, the chromosome show congression movement by which two homologous chromosome arrange themselves equidistant from equator facing each other. The spindle fiber get attach to the centromere of chromosome.



Each chromosome is attached to the spindle fiber of only one side [The pole whose centromere is facing]. Some interzonal fiber develops b/w the centromere of homologous chromosomes.

Anaphase I: In anaphase I, separation of homologous chromosomes occurs. The homologous chromosomes move towards opposite poles; this is ~~is~~ ^{*} Disjunction. In anaphase I, the chromosome number becomes half at each pole.



In anaphase I, there is no splitting of centromeres. Disjunction is the normal process of meiosis → it results in half number of chromosome in the daughter nuclei. Mendelian character segregate in Anaphase I.

Telophase I: It begins when the chromosome have reached the pole. It is reverse process of prophase I. The nuclear membrane reappears; Decondensation of chromosomes but not completely. Spindle apparatus disappears; two nuclei

are formed which are having half number of chromosomes in comparison to the parental cell.

Interkinesis: It is the time gap b/w meiosis I and meiosis II; It involves only protein and RNA synthesis; consists of only G₁ and G₂ phase; S-phase absent.

Need of meiosis II: Disjunction is main feature of anaphase I which involves the separation of homologous chromosomes. So meiosis I is called reductional division; But after meiosis I, each chromosome is still a dyad [having two chromatids] so due to meiosis I, the chromosome number is halved but each chromosome still has double amount of DNA. Hence, so as to reduce this DNA content to normal in meiosis II is needed.

Meiosis II: Also called equational division / Homotypic division b/c chromosome number remains same as after meiosis I; meiosis II is just like simple mitosis.

Meiosis II involves following phases: ① prophase II ② metaphase II ③ Anaphase II ④ Telophase II.

① Prophase II: It is just like mitosis prophase; the nuclear spindle formation begins in the prophase II; The nuclear spindle apparatus organized perpendicular to that of meiosis I. The prophase II has 3 subphases which are exactly similar to the mitosis prophase sub phases.

② Metaphase II: It is just like mitosis metaphase; The chromosomes arrange themselves on the equator; Each centromere joined by the spindle fibers of both poles.

③ Anaphase II: It is just like mitosis anaphase; It is the only phase of meiosis II in which splitting of centromeres occurs; Dyad becomes monad in this phase; It normalize the amount of DNA in chromosome.

④ Telophase II: It is just like mitosis telophase; the nuclear membrane and nucleolus reappears; At the end of meiosis we get 4 type of genetically different nuclei.

Significance of meiosis: Meiosis is the division of sexual reproduction; It occurs at the time of gamete or spore formation; Meiosis and fertilization works together in coordination to maintain constant chromosome number generation after generation; Sexual reproduction without meiosis will result in tetraploidy; while sexual reproduction without fertilization will result in haploidy. So we can say that both meiosis and fertilization are responsible for maintaining constant

chromosome number generation after generation. } meiosis produce new combinations: Due to crossing over, segregation, independent assortment. } Crossing over brings variations; these variations are useful in biological evolution. } The variations which come through the sexual reproduction are ~~less~~ continuous variations. These are most important for evolution.

- Special: for the formation of n number of microspore, meiosis occurs $\rightarrow \frac{n}{4}$ times } for the formation of n number of megasporangium, meiosis occurs n times } for the formation of n . Number of Embryo or seeds, meiosis occurs $\rightarrow n + \frac{n}{4}$ times

- Metaphase I: The bivalent chromosomes align on the equatorial plate. The microtubules from the opposite poles of the spindle attach to the pair of homologous chromosomes.

- Anaphase I: The homologous chromosomes separate, while sister chromatids remain associated at their centromeres.

- Telophase I: The nuclear membrane and nucleolus reappear, cytokinesis follows and this is called as dyad of cells.

- Although in many cases the chromosomes do undergo some dispersion, they do not reach the extremely extended state of the interphase nucleus. } The stage b/w the two meiotic divisions is called interkinesis and is generally short lived. } Interkinesis is followed by prophase II, a much simpler prophase than prophase I.

- Meiosis II: Prophase II: \rightarrow Meiosis II is initiated immediately after cytokinesis, usually before the chromosomes have fully elongated. } In contrast to meiosis I, meiosis II resembles a normal mitosis. } The nuclear membrane disappears by the end of prophase II. } The chromosomes again become compact.

- Metaphase II: \rightarrow At this stage the chromosomes align at the equator and the microtubules from opposite poles of the spindle get attached to the kineto-chromes of sister chromatids.

- Anaphase II: \rightarrow It begins with the simultaneous splitting of the centromere of each chromosome (which was holding the sister chromatids together), allowing them to move toward opposite poles of the cell.

- Telophase II: \rightarrow Meiosis ends with telophase II, in which the two groups of

chromosomes once again get enclosed by a nuclear envelope; cytokinesis follows resulting in the formation of tetrad of cells; i.e. four haploid daughter cells.

significance of meiosis: meiosis is the mechanism by which conservation of specific number of each species is achieved across generations in sexually reproducing organisms, even though the process, per-se, paradoxically, result in reduction of chromosome number by half. It also \uparrow s the genetic variability in the population of organisms from one generation to the next. Variations are very important for the process of evolution.

Excretory system

Date 29/10/18.
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- ① Animals accumulate NH_3 , urea, uric acid, CO_2 , H_2O & ions like Na^+ , Cl^- , K^+ , PO_4^{3-} , SO_4^{2-} etc., either by metabolic activity or by other means like excess ingestion. These substances have to be removed totally or partially. { Ammonia, Urea, and Uric acid are the major forms of nitrogenous wastes excreted by the animals. }
- NH_3 is the most toxic form and requires large amount of water for its elimination, whereas uric acid, being the least toxic, can be removed with a minimum loss of water.
- The process of excreting ammonia is ammonotelism. { Many bony fish, aquatic amphibians and aquatic insects are ammonotelic in nature. }
- NH_3 , as it is readily soluble, is generally excreted by diffusion across body surfaces or through gill surfaces [In fish] as NH_4^+ ions. Kidney do not play any significant role in its removal.
- 78% of the NH_3 excreted by the fish through the gills.
- Terrestrial adaptation necessitated the production of less toxic nitrogenous wastes like urea and uric acid for conservation of water.
- Mammals, many terrestrial amphibians and marine fishes mainly excrete urea and are called ureotelic animals.
- Ammonia produced by metabolism is converted into urea in the liver of these animals and released into the blood which may be retained is filtered and excreted out by the kidney. { Some amount of urea may be retained in the kidney matrix of some of these animals to maintain a desired osmolarity. }
- Reptiles, birds, land snails, and insects excrete nitrogenous wastes as uric acid in the form of pellet or paste with a minimum loss of water and are called uricotelic animals.
- In animal kingdom a variety of excretory st^r are present. { In most of the invertebrates, the st^r are simple tubular forms whereas vertebrates have complex tubular organ called kidneys. }
- Protonephridia or flame cells are the excretory st^r in platyhelminthes.

Flatworms, e.g. *Platiria* J., rotifers, some annelids and the Cephalochordates - Amphioxus } protonephridia are primarily concerned with ionic and fluid volume regulation i.e., osmoregulation.

Nephridia are the tubular st^r of earthworms and other annelids } It helps to remove nitrogenous wastes and maintain a fluid and ionic balance.

Malpighian tubules are the excretory st^r of most of the insects including cockroaches } It helps in the removal of nitrogenous wastes and osmoregulation.

Antennal glands or green glands perform the excretory function in Crustaceans like prawns.

② Human Excretory system : In humans, the excretory system consists of a pair of kidneys, one pair of ureters, one urinary bladder and one urethra. } Kidneys are reddish brown, bean shaped st^r situated b/w the levels of last thoracic and third lumbar vertebra close to the dorso-lateral wall of the abdominal cavity.

Each kidney of an adult human measures 10-12 cm. length, 5-7 cm. in width, 2-3 cm. in thickness with an average wt. of 120-~~170~~ 170 gm.

Left kidney > Right kidney in size, male > female.

Towards the centre of the inner concave surface of the kidney is a notch called hilum through which ureter, blood vessels and nerves enter. } Inner to the hilum is a broad funnel shaped space called renal pelvis with projections called calyces.

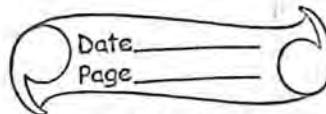
The outer layer of kidney is a tough capsule. Inside the kidney, there are two zones, an outer cortex and an inner medulla.

The medulla is divided into a few conical masses [medullary pyramids] projecting into the calyces [sing. Calyx]. } The cortex extends in b/w the medullary pyramids as renal columns called columns of Bertini.

Each kidney has nearly one million complex tubular st^r called nephrons, which are the functional units.

- Each nephron has two parts - the glomerulus and the renal tubule.
- Glomerulus is a tuft of capillaries formed by the afferent arterioles - a fine branch of renal artery. Blood from the glomerulus is carried away by an efferent arteriole.
- The renal tubule begins with a double walled cup like structure called Bowman's capsule, which encloses the glomerulus. Glomerulus along the Bowman capsule is called malpighian body or renal corpuscles.
- The tubule continues further to form a highly coiled network - proximal convoluted tubule. A hairpin shaped Henle's loop is the next part of the tubule which has a descending and an ascending limb. The ascending limb continues as another highly coiled tubular region called DCT.
- The DCTs of many nephrons open into a straight tube called collecting duct, many of which converge and open into the renal pelvis through medullary pyramids in the renal calyxes.
- The malpighian corpuscles, PCT & DCT of the nephron are situated in the cortical region of the kidney whereas the loop of Henle dips into the medulla. In majority of nephrons, the loop of Henle is short and extends only very little into the medulla. Such nephrons are called cortical nephrons. In some of the nephrons, the loop of Henle is very long and runs deep into the medulla. These nephrons are called juxta-medullary nephrons.
- The efferent arteriole emerging from the glomerulus forms a fine capillary network around the renal tubules called the peritubular capillaries. A minute vessel of this network runs parallel to the Henle's loop forming a 'U' shaped vasa recta. Vasa recta is absent or highly reduced in cortical nephrons.
- (8) Urine filtration: Urine filtration involves three main processes, that take place in different parts of the nephron: ① Glomerular filtration ② Reabsorption and ③ Secretion.
- The first step of urine formation is the filtration of blood, which is

macula densa cell + JG Cells \rightarrow JGA



Carried out by a glomerulus and is called glomerular filtration.

On an average, 100 - 1200 ml. of blood is filtered by the kidneys per minute which constitute roughly $1/5^{\text{th}}$ of the blood pumped out by each ventricle of the heart in a minute.

The "glomerular capillary" blood pressure causes filtration of blood through 3 layers; i.e., the endothelium of glomerular blood vessels, the epithelium of Bowman's capsule and a basement membrane between these two layers.

The epithelial cells of Bowman's capsule called podocytes are arranged in an intricate manner so as to leave some minute spaces called filtration slits or slit pores. Blood is filtered so finely through these membranes; that almost all the constituents of the plasma except the proteins pass onto the lumen of the Bowman's capsule. Therefore, it is considered as a process of ultrafiltration.

The amount of the filtrate formed by the kidney per minute is called glomerular filtration rate [GFR]. GFR in a healthy individual is approx 125 ml/min., i.e. 180 lit/day. The kidney have built-in mechanisms for regulation of GFR.

One such efficient mechanism is carried out by juxtaglomerular apparatus [JGA].

JGA is a special sensitive region formed by cellular modifications in the distal convoluted tubule and the afferent arteriole at the location of their contact.

A fall in GFR can activates the JG cells to release renin which can stimulate the glomerular blood flow and thereby the GFR back to normal.

RAAS : Hypertension process \rightarrow Stimulation of JGA \rightarrow JG cell

Inactive decapeptide
Angiotensin I formed

Renin cleaves the plasma protein angiotensinogen

Release renin

Angiotensin converting enzyme in lungs capillaries clips this to Angiotensin II

→ Angiotensin II stimulates the adrenals to secrete aldosterone.

(b) B.P. ← Aldosterone promotes Na^+ & H_2O reabsorption in the DCT

- A comparison of the volume of the filtrate formed per day [180 lit/day] with that of the urine released [1.5 lit.] suggests that nearly 99% of the filtrate has to be reabsorbed by the renal tubules. This is called reabsorption.
- The tubular epithelial cells in different segments of nephron perform this either by active or passive mechanism. For example, substances like glucose, amino acid, Na^+ etc., in the filtrate are reabsorbed actively whereas the nitrogenous wastes are reabsorbed by passive transport.
- Reabsorption of water also occurs passively in the initial segments of the nephrons. During urine formation, the tubular cells secrete substances like H^+ , K^+ and ammonia into the filtrate.
- Tubular secretion is also an important step in urine formation as it helps in the maintenance of ionic and acid-base balance of body fluid.
- ④ function of the tubules : (a) PCT :- PCT is lined by simple cuboidal brush border epithelium which is the surface area for reabsorption. Nearly all the essential nutrients, and 70-80% of electrolytes and water are reabsorbed by this segment. PCT also helps to maintain the ionic balance of the body fluids by selective secretion of H^+ , NH_3 & K^+ ion into the filtrate and by absorption of HCO_3^- from it.
- ⑤ Henle's loop : Reabsorption is minimum in its ascending limb. However, this region plays a significant role in the maintenance of high osmolarity of medullary interstitial fluid. The descending limb of loop of Henle is permeable to water but almost impermeable to electrolytes. This concentrates the filtrate as it moves down. The ascending limb is permeable to water but allows transport of electrolytes actively or passively. Therefore, as the concentrated filtrate passes upward, it gets diluted due to the passage of electrolytes to the medullary fluid.
- ⑥ DCT : Conditional reabsorption of Na^+ and H_2O takes place in the

segment.) DCT is also capable of reabsorption of HCO_3^- and selective secretion of H^+ , K^+ ions and NH_3 to maintain the pH and $\text{Na}^+ - \text{K}^+$ balance in blood.

(d) Collecting duct: This long duct extends from the cortex of the kidney to the inner parts of the medulla. Large amount of water could be reabsorbed from this region to produce a concentrated urine. This segment allows passage of small amounts of urea into the medullary interstitium to keep up the osmolarity. It also plays a role in maintenance of pH and ionic balance of blood by the selective secretion of H^+ & K^+ ions.

(5) Mechanism of concentration of the filtrate: mammals have the ability to produce concentrated urine. The Henle's loop and vasa recta play a significant role in this. The flow of filtrate in the two limbs of Henle's loop is in opposite directions and thus forms a counter current. The flow of blood through the two limbs of vasa recta is also in a counter current pattern.

The proximity b/w the Henle's loop and vasa recta, as well as the counter current in them help in maintaining an increasing osmolarity towards the inner medullary interstitium; i.e., from, 300 mOsmol/lit. in the cortex to about 1200 mOsmol/lit in the inner medulla. This gradient is mainly caused by NaCl and Urea.

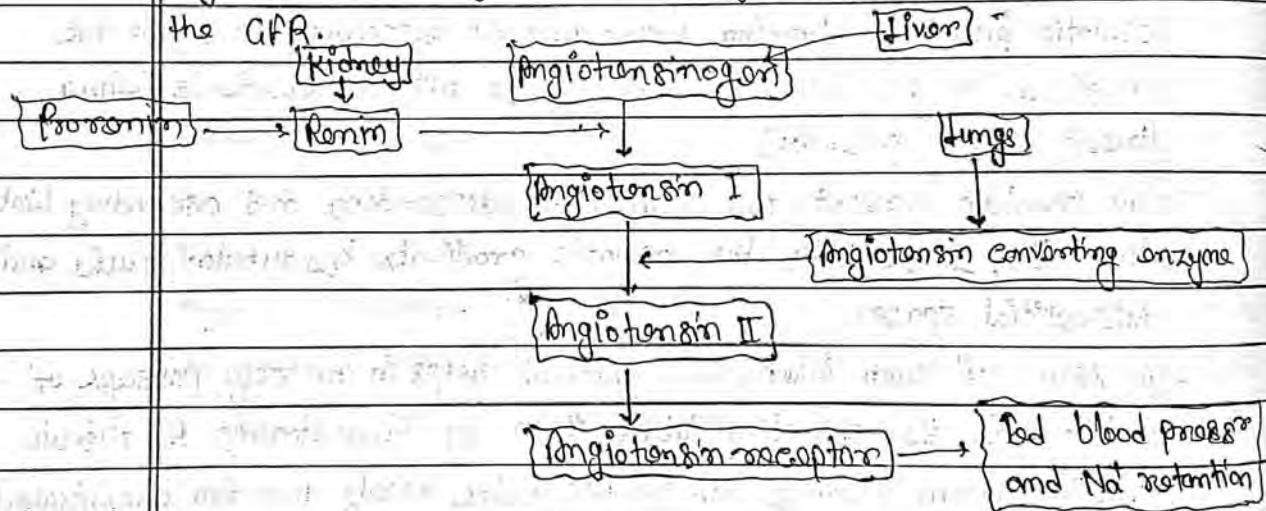
NaCl is transported by the ascending limb of Henle's loop which is exchanged with descending limb of vasa recta. NaCl is returned to the interstitium by the ascending portion of vasa recta. Similarly small amounts of enter the thin segment of the ascending limb of Henle's loop which is transported back to the interstitium by the collecting tubule.

Above the described transport of substance transport facilitated by the special arrangement of Henle's loop and vasa recta is called the counter current mechanism. This mechanism helps to maintain a concentration gradient in the medullary interstitium.

- The counter current term derives from the form and function of the loop of Henle, which consists of two parallel limbs of renal tubules running in opposite directions, separated by the interstitial space of the renal medulla? The descending limb of the loop of Henle is permeable to water but impermeable to solutes, due to presence of aquaporins in its tubular wall? Thus water moves across the tubular wall into the medullary space, making the filtrate hypertonic [with a lower water potential.] This is the filtrate that continues to the ascending limb.
 - The ascending limb is impermeable to water [b/c of a lack of aquaporins], but permeable to solutes, but here Na^+ , Cl^- & K^+ are actively transported into the medullary space, making the filtrate hypotonic [with a higher water potential.] The interstitium is now 'fatty' or hypertonic, and will attract water. This constitutes the single effect of the counter current multiplication process.
 - Active transport of these ions from the thick ascending limb creates an osmotic pressure drawing water from the descending limb into the hyperosmolar medullary space, making the filtrate hypertonic [with a lower water potential.]
 - The counter current flow within the descending and ascending limb thus ~~is~~, or multiplies the osmotic gradients b/w tubular fluid and interstitial space
 - pressure of such interstitial gradient helps in an easy passage of water from the collecting tube thereby concentrating the filtrate [urine]. Human kidneys can produce urine nearly four times concentrated than the initial filtrate formed
- (6) Regulation of Kidney function: The functioning of the kidney is efficiently monitored and regulation by :- Hormonal feedback mechanisms involving the hypothalamus, juxtaglomerular apparatus and to a certain extent, the heart.
- Osmoreceptors in the body are activated by → changes in blood volume,

body fluid volume and ionic concentration.

- An excessive loss of fluid from the body can activate these receptors which stimulates the hypothalamus to release antidiuretic hormone (ADH) or vasopressin from the neurohypophysis. { ADH facilitates water reabsorption from latter parts of the tubules, thereby preventing diuresis. [Ted or excessive production of urine.] }
- An increase in body fluid volume can switch off the osmoreceptors and suppress the ADH release to complete the feedback. { ADH can also affect the kidney function by its constrictor effects on blood vessels. This causes an increase in blood pressure. }
- An increase in blood pressure can increase the glomerular blood flow and thereby GFR. { The JGA ~~area~~ plays a complex regulatory role. }
- A fall in GFR can activate the JG cells to release renin which converts angiotensinogen in blood to angiotensin I and further to angiotensin II. { Angiotensin II, being a powerful vasoconstrictor, increases the GFR. }



- Angiotensin II activates the adrenal cortex to release Aldosterone. Aldosterone causes reabsorption of Na^+ and water from the distal parts of the tubule. { This also acts leads to an increase in blood pressure and GFR. } This complex mechanism is generally known as the Renin-Angiotensin mechanism.
- An increase in blood flow to the carotid of the heart can cause the

release of Atrial Natriuretic factor [ANF].} ANF can cause vaso-dilation [dilation of blood vessels] and thereby less the blood pressure} ANF mechanism, thereby, acts as a check on the renin-angiotensin mechanism.

⑦ micturition: urine formed by the nephrons is ultimately carried to the urinary bladder where it is stored till a voluntary signal is given by the CNS.} This signal is initiated by the stretching of the urinary bladder as it gets filled with urine.} In response, the stretch receptors on the walls of the bladder send signals to the CNS.

- The CNS passes on motor messages to initiate the contraction of smooth muscles of the bladder and stimulates simultaneous relaxation of the urethral sphincter causing the release of urine.} the process of release of urine is called micturition and the neural mechanisms causing it is called the micturition reflex.

- An adult human excretes, on an average, 1-1.5 lit. of urine per day.} The urine formed is a light yellow coloured watery fluid which is slightly ~~and~~ acidic [$\text{pH} - 6.0$] and has a characteristic odour.} On an average, 25 to 30 gm. of urea is excreted out per day.

- Various conditions can affect the characteristics of urine.} Analysis of urine helps in clinical diagnosis of many metabolic disorders as well as malfunctioning of the kidney.} For example, presence of glucose [Glycosuria] and ketone bodies [Ketonuria] in urine are indicative of diabetes mellitus.

- Albunuria \rightarrow albumin in urine.} Anuria \rightarrow absence of urine.} Glycosuria \rightarrow difficulty of painful urination.} Glycosuria \rightarrow sugar in the urine.} Haematuria \rightarrow blood in the urine.} Nocturia \rightarrow Night urination.} Oliguria \rightarrow scanty urination.} polyuria \rightarrow excessive urination.

⑧ Role of other organs in excretion: other than the kidneys, lungs, liver and skin also help in the elimination of excretory wastes.} Our lungs remove large amount of CO_2 [approx. 200 ml/minute] and

also significant quantities of water every day.

- Liver, is the largest gland in our body, secretes bile containing substances like bilirubin, biliverdin, cholesterol, degraded steroid hormones, vitamins and drugs; most of these substances ultimately pass out along with digestive wastes.

- The sweat and sebaceous glands in the skin can eliminate certain substances through their secretions; sweat produced by the sweat glands is a watery fluid containing NaCl, small amounts of urea, lactic acid etc; through the primary function of sweat is to facilitate a cool cooling effect on the body surface, it also helps in the removal of some of the wastes mentioned above.

- Our sebaceous glands eliminate certain substances like sterols, hydrocarbons and waxes through sebum. This secretion provides a protective oily covering for the skin. A small amount of nitrogenous wastes could be eliminated through saliva too.

- Disorders of the excretory system: malfunctioning of kidneys can lead to accumulation of urea in blood, a condition called uremia, which is highly harmful and may lead to kidney failure.

- In such patients, urea can be removed by a process called hemodialysis. Blood drained from a convenient artery is pumped into a dialysing unit after adding an anticoagulant like heparin. The unit contains a coiled cellophane tube surrounded by a fluid [dialysing fluid] having the same composition as that of plasma except the nitrogenous wastes.

The porous cellophane membrane of the tube allows the passage of molecules based on concentration gradient. As nitrogenous wastes are absent in the dialysing fluid, these substance freely moves out, thereby clearing the blood. The cleared blood is pumped back to the body through a vein after adding anti-heparin to it. This method is a boon for thousands of uremic patients.

- Kidney transplantation is the ultimate method in the correction of acute renal failures [Kidney failure]
- A functioning kidney is used in transplantation from a donor, preferably a close relative, to minimise its chances of rejection by the immune system of the host. Modern clinical procedures have test the success rate of such a complicated technique.
- Renal calculi: stone or insoluble mass of crystallised salts [oxalates etc] formed within the kidney.
- Glomerulonephritis: inflammation of glomeruli of kidney

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- ① Health, for a long time, was considered as a state of body and mind where there was a balance of certain humors.
Hippocrates as well as Indian Ayurveda system of medicine; the discovery of blood circulation by William Harvey disproved the 'good humor' hypothesis of health.
In later years, biology stated that mind influences, through neural system and endocrine system, our immune system and that our immune system maintains our health. Hence, mind and mental state can affect our health.
of course, health is affected by -
Genetic disorders - deficiencies with which a child is born and deficiencies / defects which the child inherits from parents from birth; } infections and } life style including food and water we take, rest and exercise we give to our bodies, habits that we have or lack etc.
- ② when the functioning of one or more organs or systems of the body is adversely affected, characterised by various signs and symptoms, we say that we are not healthy, i.e. we have a disease.
Disease can be broadly grouped into infectious and non-infectious; disease which are easily transmitted from one person to another, are called infectious disease; infectious diseases are very common and everyone of us suffers from these at sometime or other. Some of the infectious diseases like AIDS are fatal; Among non-infectious diseases, cancer is the major cause of death.
Drug and alcohol abuse also affect our health adversely.
Common diseases in humans; A wide range of organisms belonging to bacteria, viruses, fungi, protozoans, helminths etc, could cause disease in man. Such disease causing organisms are called pathogens; most of the parasites are therefore pathogens as they cause harm to the host by living in/on them.
The pathogens can enter our body by various means, multiply and interfere with normal vital activities, resulting in morphological and functional damage.
pathogens have to adapt to life within the environment of the host.

for example, the pathogens that enter the gut must know a way of surviving in the stomach at low pH and resisting the various digestive enzymes.

Disease: functioning of one or more organs or systems of the body is adversely affected {characterised by various signs and symptoms} may be infectious and non-infectious.

Cancer is major non-infectious disease {AIDS is a fatal infectious disease}

Terms: Pathology {Etiology} {Pathogenesis} {Epidemiology} {the incidence, distribution, and possible control of disease and other factors relating to health} {Diagnosis} {Incubation period} {Prognosis - outcome} {Recovery}

Special: Robert Koch co-founder of medical microbiology {Koch postulates not applicable on leprosy bacteria} Rudolf Virchow {father of modern pathology}

Hippocrates {father of medicine} Louis Pasteur {germ theory of disease}

parasites or pathogens:- Ectoparasites and Endoparasites {obligatory parasite e.g. Taenia and Trichomonas} {Temporary parasite e.g. fasciola / schistosomes} {facultative parasite e.g. candida fungi}

Disease {Endemic} {Epidemic} {Pandemic} {Quarantine} {Prophylaxis}

Typhoid fever:- *Salmonella typhi* is a pathogenic bacterium which causes typhoid fever in human beings {These pathogens generally enter the small intestine through food and water contaminated with them and migrate to other organs through blood} {Sustained high fever [39°-40°C], weakness, stomach pain, constipation, headache, and loss of appetite are some of the common symptoms of this disease} {Intestine perforation and death may occur in severe cases}

Typhoid fever could be confirmed by Widal test.

A classic case in medicine, that of Mary Mallon nicknamed ~~sex~~ Typhoid Mary, is worth mentioning here {she was a cook by profession and was a typhoid carrier who continued to spread typhoid for several years through the food she prepared}

Worldwide, typhoid fever affect roughly 17 million people annually.

causing nearly 600,000 deaths } The causative agent, *Salmonella enterica* typhi is an obligate parasite that has no known natural reservoir outside the humans.

- *S. typhi* originally isolated in 1880 by Karl J. Erberth. } *S. typhi* is a multi-organ pathogen that inhabits the lymphatic tissue of the small intestine, liver, spleen, and bloodstream of infected humans.
- It is not known to infect animals and is most common in developing countries with poor sanitary systems and lack of antibiotics, putting travelers to Asia, Latin America, and Africa in a high risk group.
- *S. typhi* is gram negative enteric bacillus [family Enterobacteriaceae]. It is a motile, facultative anaerobe that is susceptible to various antibiotics. Currently, 107 strains of this organisms have been isolated; Bacteria may have multi-drug resistance genes that complicates treatment.
- This disease is characterized by the
 - sudden onset of a sustained and systematic fever, several headache, nausea, and loss of appetite; other symptoms include constipation, Enlargement of spleen, possible development of meningitis, or general malaise, Rose spot on abdomen.
- Untreated typhoid fever cases result in mortality rates ranging from 12-30%. while treated cases allow for 99% survival.
- *S. typhi* virulence due to endotoxin and Vi antigen.
- produces and excretes a protein K1as invasin that allows non-phagocytic cells to take up the bacterium, where it is able to live intracellularly.
- The encounter of humans to *S. typhi* is made via fecal-oral route from infected individuals to healthy ones. The most common source of infection however, is drinking water, tainted by urine and feces of infected individuals. The estimated inoculum size necessary for infection is 100,000 bacteria.

- Once ingested, the organisms multiply in the small intestine over the period of 1-3 weeks, breach the intestinal wall, and spread to other organ systems and tissues; the innate host defences do little to prevent infection due to the inhibition of oxidative lysis and the ability to grow intracellularly after uptake.
- Transmission of *S. typhi* has only been shown to occur by faecal-oral route, often from asymptomatic individuals.
- 2-5% of previously infected individuals become chronic carriers who show no signs of disease, but actively shed viable organisms capable of infecting others.
- The damage caused by typhoid fever is reversible and limited if treatment is started early in the infection; this leads to a mortality rate of less than 1% among treated individuals who have an antibiotic-susceptible strain of *S. typhi*, making the outcome and prognosis for patients a positive one.
- Widal test: The Widal test, developed in 1896 and named after its inventors, Georges-Fernand Widal; it is a serological test for typhoid fever; bacterial suspension which carry antigen will agglutinate on exposure to antibodies to *Salmonella* organisms; the antigens used in the test are 'H' and 'O' antigens of *S. typhi* and 'H' antigen of *S. paratyphi*.
- Prevention: prevention of faecal contamination in drinking water and food supplies. [It is possible to control transmission by proper hygiene, waste management, water purification, and treatment of the sick.]; prevention can also be aided by TAB vaccination.
- Treatment: antibiotics → Ampicillin, chloramphenicol, ciprofloxacin, ofloxacin; cholecystectomy → in severe cases.
- ③ Pneumonia: Bacteria like *streptococcus pneumoniae* and *Haemophilus influenzae* are responsible for the disease pneumonia in humans which infects the alveoli of the lungs; as a result of the infection

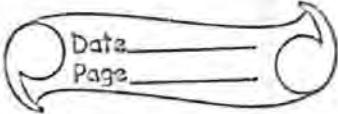
the alveoli got filled with fluid leading to severe problems in respiration.

- The symptoms of pneumonia include fever, chills, cough and headache? In severe cases, the lips and finger nails may turn grey to bluish in colour?
- A healthy person acquires the infection by inhaling the droplets/aerosols released by an infected person or even by sharing glasses and utensils with an infected person.
- characterized by accumulation of mucus or fluid in alveoli and bronchioles to that extent that breathing becomes difficult.
- Causative agent \rightarrow Streptococcus pneumoniae and Haemophilus influenzae
- Incubation period \approx 1-3 days
- Infected part \rightarrow Alveoli of lungs? Alveoli got filled with fluid leading to severe problems in respiration.
- Two types of pneumonia: lobar pneumonia [whole lung lobe affected] and lobular pneumonia or broncho-pneumonia [multiple areas in lungs affected-patches].
- Treatment of pneumonia \rightarrow antibiotics, oxygen support & antipyretics
- ✓ Dysentery, plague, diphtheria, etc., are some of the other bacterial diseases in man.
- Dysentery: It is an intestinal inflammation, primarily of the colon. It can lead to mild or severe stomach cramps and severe diarrhea with mucus or blood in the feces? without adequate hydration, it can be fatal. Infection with the shigella bacillus, or bacteria, is the most common cause.
- Bacillary dysentery, or shigellosis. This type produces the most severe symptoms. It is caused by the shigella bacillus. Poor hygiene is the main source. Shigellosis can also spread by of tainted food? Dysentery is an infection of the intestinal tract. Symptoms includes stomach cramps and diarrhea? Many people have mild symptoms, but dysentery can be fatal without adequate hydration.
- Complications of dysentery are few, but they can be severe.

Dehydration \rightarrow frequent diarrhea and vomiting can quickly lead to dehydration. In infants and young children, this can quickly become life threatening. Liver abscess \rightarrow if amoebae spread to the liver, an abscess can form there. postinfectious arthritis & joint pain may occur following the infection. Haemolytic uremic syndrome & shigella dysenteriae can cause the RBCs to block the ostium to the kidneys, leading to anemia, low platelets count, and kidney function failure.

④ **Plague**: The Black Death, also known as the Great plague, the black plague, or simply the plague, was one of the most devastating pandemics in human history, resulting in the death of an estimated 75 to 200 million people in Eurasia and peaking in Europe from 1347 to 1351.

- Plague disease is caused by a bacterial strain called *Yersinia pestis*. This bacterium is found in animals throughout the world and is usually transmitted to humans through rat fleas.
- *Yersinia pestis* [formerly *pasteurella pestis*] is a gram-negative, non-motile, rod-shaped coccobacillus, with no spore. It is a facultative anaerobe organism that can infect humans via the oriental rat flea. It causes the disease plague, which takes three forms: pneumonic, septicemic, and bubonic plagues.
- The oriental rat flea [*Xenopsylla cheopis*], also known as the tropical rat flea, is a parasite of rodents, primarily of the genus *Rattus*. It is a primary vector for bubonic plague. This occurs when the flea has fed on an infected rodent and bites a human, although this flea can live on any warm blooded mammal.
- The risk of plague is highest in areas that have poor sanitation, overcrowding, and a large population of rodents. Today, there are only few thousands cases reported worldwide each year, with the highest incidence in Africa.



- plague is a rapidly progressing disease that can lead to death if untreated? It needs immediate medical attention.
- people infected with *Y. pestis* often developed symptoms after an incubation period of 1-7 days } There are two main clinical forms of plague infection: bubonic and pneumonic. } Bubonic plague is the most common form and is characterized by painful swollen lymph nodes or 'bubbles'.
- plague can be a very severe disease in people, with a case-fatality ratio of 30% to 60% for the bubonic type, and is always fatal for the pneumonic kind when left untreated } Antibiotic treatment is effective against plague bacteria, so early diagnosis and early treatment can save lives } Conventional plague requires lab testing
- The best practice to identify *Y. pestis* from a sample of pus from a bubo, blood or sputum.
- Diphtheria: It is an infectious disease caused by the bacterium *Corynebacterium diphtheriae*, which primarily infects the throat and upper airways, and produces a toxin affecting other organs.
- The symptoms of diphtheria usually begin 2-7 days after infection. } Symptoms of diphtheria include fever of 38°C [100.4°F] or above, chills, fatigue, bluish skin coloration, sore throat, hoarseness of voice, cough, headache, difficulty swallowing, painful swallowing, difficulty in breathing, rapid breathing, foul smelling and blood stained nasal discharge, and lymphadenopathy.
- Within 2-3 days, diphtheria may destroy healthy tissue in the respiratory system. } The dead tissue forms a thick, grey coating that can build up in the throat or nose } This thick grey coating is called a 'pseudo-membrane'. It can cover tissues in the nose, tonsils, voice box, and throat, making it very hard to breathe and swallow.
- Human-to-human transmission of diphtheria typically occurs through the air when an infected individual coughs or sneezes } Breathing in particles released from the infected individual leads to infection.

- Quinvaxom is a widely administered pentavalent vaccine, which is a combination of ~~over~~ five vaccines in one that protects babies from diphtheria, among other common childhood disease } Diphtheria vaccine is usually combined in combination atleast with tetanus vaccine [Td] and often with pertussis [DTP, DTaP, TDaP] vaccines, as well.
- Many viruses also cause diseases in human beings } Rhino viruses represent one such group of virus which cause one of the most infectious human ailments - the common cold } They infect the nose and respiratory passage but not the lungs
- The common cold is characterized by nasal congestion and discharge, some throat, hoarseness, cough, headache, tiredness, etc, which usually last for 3-7 days } Droplets resulting from cough or sneezes of an infected person are either inhaled directly or transmitted through contaminated objects such as pens, books, cups, doorknobs, computer keyboard or mouse, etc, and cause infection in a healthy person.
- Flu and common cold are both respiratory illnesses but they are caused by different viruses } In general, flu is worse than the common cold, and symptoms are most common and intense } Colds are usually milder than flu. People with colds are more likely to have a runny or stuffy nose
- Swine flu: swine influenza is an infection caused by any one of several types of swine influenza viruses } Swine flu virus is swine influenza virus [SIV] or swine-origin influenza virus [S-OIV] is any strain strain of the influenza family of virus that is endemic in pigs
- SIV strains include H1N1, H1N2; H2N1, H3N2 and H2N3
- The swine flu was initially seen in humans in Mexico in 2009.
- Swine influenza virus is common throughout pig population worldwide } Transmission of the virus from pigs to humans is not common and does not always lead to human flu, often

resulting only in the production of antibodies in the blood; if transmission does cause human flu, is called zoonotic swine flu.

- people with regular exposure to pigs are at 1st risk of swine flu infection. Around the mid-20th century, identification of influenza subtypes became possible, allowing accurate diagnosis of transmission to humans.
- Symptoms of zoonotic swine flu in humans similar to those of influenza: chills, fever, sore throat, muscle pain, severe headache, coughing, weakness, shortness of breath, and general discomfort.
- In August 2010, the WHO declared the swine flu pandemic officially over.

⑤ two more bacterial disease: whooping cough [Pertussis]: primarily a disease of children. { affects the respiratory tract. It is caused by a bacteria *Bordetella pertussis*. } spreads by droplet infection and direct contact. { Incubation period is 10-16 days. } fever, severe coughing, vomiting and characteristic gasping 'whoop' [loud, crowing inspiration] are common symptoms. { Whooping cough vaccine [DPT] can minimize the infants }

Tuberculosis: commonly called T.B., is a very serious disease. { caused by rod shaped bacterium named *Mycobacterium tuberculosis*. } It affects the lungs, where small tubercles are formed but may attack any part of the body, including the brain. { The bacteria damage tissues and release a toxin named tuberculin which produce a disease. } Symptoms of pulmonary tuberculosis are fever, cough, blood containing sputum, pain in the chest and loss of weight. { Treatment in early stages of the disease yield best results. } BCG vaccine gives considerable protection against tuberculosis. { World tuberculosis day is celebrated on 24 march. }

- Tetanus [Lock jaw]: caused by an aerobic bacterium *Clostridium tetani*. { Bacteria enters the body through wounds. } Incubation period varies 4-8 weeks. { Tetanus results in painful muscular spasms and paralysis, which usually begins with jaw and neck muscles. These disease often

5

fatal } Tetanus organisms live in the intestine of horses and other animals without doing any harm. The spores are, therefore abundant in the soil manured with animal dung. They are also present in the road and street dust b/c the animals pass out dung as they move about. { Spores may survive for 60 or more years in the contaminated soil. } On entering the body by way of wounds, the spores release active bacteria. It is advisable to have tetanus toxoid injection in case of any injury in a road accident or a cut contaminated with street dust or animal dung. This will prevent tetanus. } All of us should have toxoid immunization as the safe preventive measure against this dangerous disease. } Tetanus toxoid gives active immunity. { Antitetanus serum [A.T.S.] produces passive immunity. } It is now a practice to immunize the infants against diphtheria, whooping cough [pertussis] and tetanus simultaneously by DPT or Triple vaccine.

~~Leprosy [Hansen's disease]~~: It is a chronic infectious disease, endemic in warmer climates; it is caused by a bacillus named *Mycobacterium leprae*, which is discovered by Hansen. } It primarily affects the skin, mucous membrane and peripheral nerves, but may affect internal organs also. } Its symptoms include, hypopigmented skin patches, partial or total loss of sensation in affected areas, lesions, ulcers, nodules, scales, deformity of fingers and toes, wasting of body parts, and thickened nerves. } Infection occurs by prolonged and close contact with leprosy patients. } Incubation period is not exactly known. It is commonly b/w 2-5 years, but may vary from a few months to 80-40 years. } It is curable disease.

- ~~few more viral disease~~: chickenpox : - It is a common, relatively mild, highly contagious disease of children, generally under 10 years of age. } Caused by chickenpox virus [Varicella zoster]. } Fever, rashes and general discomfort are the symptoms. } Blisters-like sores appear in successive crops, first on the trunk. } The sores open and a fluid

spreads out a short time later} The disease spread by direct contact with skin sores or with clothes and other articles soiled with discharges from sores} Incubation period is 2-5 weeks. The sores heal without leaving scars} Preventive measure is isolation of the patient till all crusts fall off. {one attack of chickenpox ordinarily gives permanent immunity to the disease} chickenpox is rarely fatal, but in adults attack could be severe.

- Small pox : It is an acute, highly communicable disease. {caused by variola virus} It starts as a sudden onset of high fever accompanied by headache, backache, and pain all over the body. {Rash appears on the 3rd to 4th day of illness} The rash gradually changes into pustules [pimples] containing clear fluid. {The pustules finally forms scabs which fall off by the third week} Incubation period is 12 days. {It is very serious, disfiguring and highly fatal disease} It has now been largely controlled through vaccination. {small pox vaccine was first prepared by Edward Jenner}

- Measles : most prevalent and serious disease of children, generally 3-8 years old {caused by rubella virus} It is characterized by fever, inflammation of nasal mucous membrane, red watery eyes sensitive to light, flushed face, loss of appetite, followed by a typical rash, i.e., eruption of small red spots [rubeola]. {Infection is spread by discharges from nose and throat [droplet infection]} Incubation period is 10 days. {one measles gives life-long immunity} Vaccine which produces active immunity is available. {Patients of measles are likely to catch secondary infection of pneumonia}

- Rabies [Hydrophobia] : 100% fatal disease. {caused by Rabies virus} The virus enters the human body with saliva of an infected [Rabid] animals generally by the bite of a dog. {virus induces biting behavior in its victim} fear of water is the main symptom, hence Hydrophobia. {Incubation period 1-3 months, but may vary from 10 days to one year} This long period of incubation makes it possible for a rabies vaccination after a bite to develop immunity and prevent the ~~infectivity~~ appearance of disease. {The pet should be watched for 10 days after it has bitten someone to make}

sure that it does not have rabies } symptoms of rabies in dogs are madness, changed voice and excessive salivation. } Rabid dogs should be immediately killed } Treatment of rabies discovered by Louis Pasteur. It involves a series of 14 injections given after the bite of a dog.

- Mumps [Infectious parotitis] : Acute communicable disease, generally in children. } caused by paramyxovirus, which has predilection for salivary glands } It is characterized by painful enlargement of one or both the parotid glands. } The patient has high fever and difficulty in opening mouth. } The virus is spread by discharges from the throat of an infected person [droplet infection] and by direct contact. } Incubation period varies from 12-26 days } In adults, testes and ovaries may also become inflamed. Infection of testes may cause sterility } one attack of mumps gives life long immunity.

- poliomyelitis or polio [Infantile paralysis] : - most prevalent in hot, dry weather } caused by polio virus. } This virus causes inflammation of nervous system and stiffness of the neck. } It is also destroys motor nerve cells in the spinal cord. } muscles fail to work and shrink due to the lack of nerves impulses. } This may cause paralysis of limbs in some cases. } The virus enters the digestive tract with contaminated food and water and multiplies in the intestine cells. It then passes into blood stream and lymphatic system, and finally reaches the spinal cord where it starts multiplication. } Incubation period ~ 7-14 days } A patient who recovers from polio has life-time immunity. } Now oral vaccine of polio is available. } oral vaccines are developed by Sabin in 1940. } public pulse polio immunization programme is organised in India for eradicating polio in 1996.

- Dengue fever [Back bone fever] : Tropical viral disease spread by the tiger mosquito ~~Aedes~~ Aedes aegypti. } Dengue fever / Dengue haemorrhagic fever, one of the dangerous diseases } symptoms of this disease include high fever, severe frontal headache, pain

behind eyes, muscles and joint pain, loss of appetite, measles-like rashes over chest and upper limbs, nausea and vomiting}

- "Yellow fever", caused by Arbovirus is a haemorrhagic disease transmitted by the infected Aedes aegypti. } Symptoms of yellow fever are headache, fever, vomiting, rupture of veins in kidneys, spleen, liver etc } In severe cases, the skin is suffused becomes from yellow from jaundice - hence the name yellow fever } Max Theiler in 1951 got noble prize for the development of vaccine for yellow fever

- Hepatitis : It is a liver inflammation caused by hepatitis virus { Highly infectious disease } may be following types :

① Hepatitis 'A' : - caused by Hepatitis A virus } transmitted through infected food, water, clothes and faeces } The virus does not damage liver cells

② Hepatitis 'B' : - caused by Hepatitis B virus } transmitted by blood products, such as plasma or by medical instruments contaminated with infected food } It results in the swelling of liver cells

③ cholera : Acute diarrhoeal disease. } caused by comma shaped, motile bacteria called Vibrio cholera. } The organisms live in the intestine. } Infection occurs with contaminated food and water. } Incubation period varies from few hours to 2-3 days. } The symptoms of the disease are sudden onset of severe diarrhoea and vomiting. } The stools are watery and give rice-water appearance. } If the disease is not checked early, it leads to dehydration, loss of minerals, muscular cramps, suppression of urine and death. } Rapid replacement of fluid and electrolytes is needed by oral rehydration therapy. } cholera epidemics are common in our country during fairs and floods and other natural calamities when water supplies and sanitation go out of gear. } preventive measures include proper community sanitation, functional cleanliness, and taking boiled water and heated food. } However, cholera vaccine is useful during epidemic and visit to a fair. } It, however, provides immunity for a short period, about 6 months. } visits to cholera

affected places and families should be avoided; *Vibrio cholerae* first isolated by R. Koch in 1883.

~~Sexually transmitted disease [STD]~~: also called venereal disease [VD].
spread by sexual intercourse with infected person. } major V.D. are
syphilis and gonorrhoea. } There are about 80 million cases of syphilis
and 180 million cases of gonorrhoea of the world. } However, the reported
cases are merely a fraction of the acute prevalence of these diseases.
The venereal diseases constitute a major medical problem in India.

① **Syphilis**: caused by *spirochaete bacterium*, *Treponema pallidum*. } It
affects the mucous membranes, in genital, rectal and oral regions,
and causes lesions. } Infection occurs by contact. } Incubation period
about 3 weeks. } The mothers may transmit the disease to their new-
born babies. } It is an easily curable disease. } Commonly known 'French
disease' or 'French pox'. } The patients of syphilis develop characteristic
'poxes' on teeth called 'Hutchinson teeth'. } Serological tests for early
diagnosis of syphilis are TPI [Treponema pallidum immobilization test],
VDRL [venereal disease research laboratory test], fAT-ABS
[Fluorescent treponemal antibody test] and Wassermann test.

② **Gonorrhoea**: caused by *diplococcus bacterium*, *Neisseria gonorrhoeae*.
The victim [patient] feels burning sensation during urination. } Incubation
period 2-5 days. } The disease affects the mucous membrane of the
urogenital tract, and spreads by sexual contact. } The infection may
spread to other parts of the body and cause arthritis and female
sterility. } The children born to afflicted mothers often suffer from eye
infection [gonococcal ophthalmia]. } Gonorrhoea is also easily curable.

Anthrax: common disease of domesticated animals; human may acquire
infection through contact with spore-containing animals. } Caused by
bacterium *Bacillus anthracis* which produces spores that can remain
dormant for many years in the soil. } The most common form of
anthrax in humans is cutaneous anthrax, others is pulmonary anthrax.

- Scarlet fever: caused by the infection of *streptococcus pyogenes* in upper respiratory tract or pharynx. } A toxin produced rash develops as small 'goose-pimples' on the skin within 12-24 hours. } The Wick test is performed to determine the presence of an immunity to scarlet fever.
 - Botulism [Food poisoning]: *Clostridium botulinum* is a gram negative anaerobic bacterium responsible for food poisoning known as botulism. } The bacilli release exotoxin to the environment, which is one of the most potent neurotoxic substances produced by microbes. } Main symptoms of botulism are swollen tongue, double vision, vomiting, diarrhoea, fatigue and respiratory failure.
- ⑦ Malaria: The attack of malaria is preceded by yawning, tiredness, headache and muscular pain. } During the fever, the patient feels chilly and shivers, and has acute headache, nausea and high temp. } After after a few hours, the body perspires freely and the temperature becomes normal. } The cycle is repeated if no medicine is taken. } Blood smear made during fever shows the malarial parasites. No parasites are seen at other times.
- In chronic cases, there is general weakness and anaemia [paleness] due to large-scale destruction of RBC. } This is also accompanied by enlargement of spleen and liver.
 - Malaria is caused by a toxin produced in the human body by the malarial parasites, *Plasmodium*. } The malarial parasites are carried from the infected to the healthy persons by the female Anopheles mosquito. } The mosquito picks up the parasites with the blood, when it bites an infected person. } When this infected mosquito bites a healthy person, parasites migrate into his blood with the saliva, which the mosquito injects before sucking blood to prevent its clotting.
 - Some of the human diseases are caused by protozoans too. } Malaria, a disease man has been fighting since many years. } Plasmodium, a tiny protozoan is responsible for this disease. } Different species of plasmodium [*P. vivax*, *P. malariae*, and *P. falciparum*] are responsible for different types of malaria. } Of these, malignant malaria caused by *P. falciparum* is the most serious.

one and can even be fatal.

- There are four species of plasmodium, which cause acute malaria -

① P. vivax: It causes Benign tertian malaria, which attacks every third day, i.e., after 48 hours. The fever is mild and seldom fatal. This species is wide spread in the tropical and temperate regions.

② P. ovale: It also causes Benign tertian malaria, which recurs every 48 hours. This species is found only in West Africa and South America.

③ P. malariae: It causes quartan malaria, which recurs every four day, i.e., after 72 hours. This species is found in both tropical and temperate regions, but it is not very common.

④ P. falciparum: It alone is capable of causing three types of malaria, viz., quotidian malaria, which attacks almost daily; malignant tertian malaria, which occurs every 48 hours, but is very severe and often fatal; and irregular malaria. This species is found only in tropical regions.

- Black water fever: massive intravascular haemolysis. } Due to Plasmodium falciparum. } Severe acute haemolytic anaemia. } Haemoglobinuria. } Total bilirubin. } Acute tubular necrosis and HB casts.

Plasmodium enters the human body as sporozoites [infectious form] through the bite of infected female Anopheles mosquito. } The parasites initially multiply within the liver cells and then attack the RBCs resulting in their rupture. } The rupture of RBCs is associated with release of a toxic substance, haemozoin, which is responsible for the chill and high fever recurring every three to four days. } When a female anopheles mosquito bites an infected person, these parasites enter the mosquito's body and undergo further development. } The parasites multiply within them to form sporozoites that are stored in their salivary glands. } When these mosquitoes bite a human, the sporozoites are introduced into his/her body, thereby initiating the events mentioned above. } It is interesting to know that the malarial parasite requires two hosts - human and mosquitoes.

- Treatment of the malaria depends on the following factors → Types of infection, status of the host and associated conditions or diseases.
- Drugs used in treatment of malaria :- Cineona alkaloids - quinine, quinidine }
4 aminoquinolines - chloroquine } Antibiotics - tetracycline, doxycycline,
clindamycin. } Biting mosquito compounds - artemesinato, artether, artether.
- Malaria vaccine is a vaccine that is used to prevent malaria. } The only approved vaccine is RTS,S. } It requires four injections, and has a relatively low efficacy. } Due to this low efficacy, WHO does not recommend the use of RTS,S vaccine in babies b/w 6 and 12 weeks of age.
- M② ENTAMOEBA HISTOLYTICA is a protozoan parasite in the large intestine of human which causes amoebiasis [Amoebic dysentery]. } Symptoms of this disease include constipation, abdominal pain and cramps, stools with excess mucus and blood clots. Clots } Houseflies act as mechanical carriers and flies serve to transmit the parasite from faeces of infected person to food and food products, thereby contaminating them. } Drinking water and food contaminated by the faecal matter are the main source of infection.
- Amoebiasis [Amoebic dysentery or Enteritis]. } It is widespread in India due to poor sanitary conditions and polluted drinking water. } The disease is caused by Entamoeba histolytica all over the world. } The parasites live in the large intestine and lower part of the small intestine of humans. } Infection occurs by ingesting cysts with food and drinks. } The parasite secrete a proteolytic enzyme, cytolysin, that erodes the mucous membrane of the intestine. } This may form bleeding ulcers that produce dysentery. } In this disease, the patient passes out blood and mucus with the stools. } He also experiences severe gripping pain in the abdomen, fever, nausea, exhaustion and nervousness. } In chronic cases, the intestinal wall is punctured. This may prove fatal. } The parasites that invade the intestinal mucous membrane may be carried by the blood.

to the liver, lungs and brain.} In these organs, the parasites, feed on cells and produce severe lesions and abscesses. The latter may cause death.

- Diarrhoea: Caused by flagellate protozoan named *Giardia intestinalis*.} *Giardia* was discovered by Leeuwenhook in his own stool in 1681.} It is the first human parasitic protozoan known.} It is found in all over the world.} It inhibits the upper parts [duodenum and jejunum] of human small intestine all over the world.} It lives firmly attached to the intestinal mucous membrane by adhesive disc, each perched on a separate cell.} Nutrition is saprozoic, i.e., fluid food is absorbed through the body surface.} Reproduction occurs by longitudinal binary fission.} At intervals the parasites change into cysts which escape with the host's faeces.} Infection occurs by taking cysts with food and drinks.} By covering the mucous membrane of the intestine, the parasites check or reduce the absorption of food, particularly fats. This causes diarrhoea or giardiasis [loose and frequent stools].} Preventive measures: Properly washing hand, fruits and vegetables before eating, and protecting the food articles from dust, flies, ants and cockroaches can check human infection.

- Ciliary dysentery: Caused by a ciliated protozoan named *Balantidium coli*.} The latter inhibits the human large intestine [colon] all over the world.} It feeds on tissue fragments, ABC, bacteria and faecal matter.} It reproduces asexually by transverse binary fission and sexually by conjugation. This latter is followed by cyst formation.} Cysts pass out in the host's faeces.} Infection occurs by ingesting cysts with food and drinks.} *Balantidium coli* causes ulcers in the colon and invades mucous membrane by secreting cytolysin. This generally results in diarrhoea, but may lead to severe or fatal dysentery.

- Trypanosomiasis: most serious protozoan disease caused by a flagellate protozoan.} Trypanosoma, found firstly in the blood, then in the lymph and finally in the cerebrospinal fluid of man. [pulmonary host].} Secondary host is a blood sucking insect *Glossina* [Tse-tse fly], so the life cycle

of trypanosoma is digenetic.

⑨ Taeniasis: Caused by pork tapeworm *Taenia solium*.} This tapeworm lives in the human intestine, firmly anchored by hooks and suckers.} It bites mouth and absorbs host's digested food through its skin [saprozoic nutrition].} It is hermaphrodite and undergoes self fertilization.} There is normally a single worm in one host.} This worm has enormous power of reproduction.

✓ Ascariasis, the common roundworm and *Wuchereria*, the filarial worm, are some of the helminths which are known to be pathogenic to man.} *Ascaris*, an intestinal parasite causes ascariasis.} Symptoms of these disease include intestinal bleeding, muscular pain, fever, anaemia and blockage of intestinal passage.} The eggs of the parasites are excreted along with the faeces of infected persons which contaminate soil, water, plants, etc.} A healthy person acquires this infection through contaminated water, vegetables, fruits, etc.

Ascariasis: Caused by roundworm *Ascaris lumbricoides*.} This roundworm lives in the human small intestine.} It lies free, having no organs for attachment.} It takes host's digested food by sucking through the mouth [holozoic nutrition].} It is more common in the children.} The food of the worm consists of semi-digested food of the host, the blood and the fluid of the alimentary canal of the host.} There is no secondary host in the life cycle of this parasite.} The disease can best be treated by administering anti-helminthic drugs such as oil of chenopodium, Albendazole, mebendazole etc.

✓ Wuchereria [*W. bancrofti* and *W. malayi*], the filarial worms cause a slowly developing chronic inflammation of the organs in which they live for many years, usually the lymphatic vessels of the lower limbs and the disease is called elephantiasis or filariasis.} The genital organs are also often affected, resulting in gross deformities.} The parasites are transmitted to a healthy person through the bite by the female mosquito vector.

- Filariasis [Elephantiasis]: Caused by filarial worms, *Wuchereria bancrofti*. This disease is characterised by the swelling of the legs, scrotum and of some other parts of the body. This disease is, therefore, commonly known as elephantiasis due to its resemblance to a leg of an elephant. The infestation is transmitted by *Culex* mosquitoes from one individual to the others. The worms live in the lymphatic system and produce young ones called 'microfilaria'. Once the swelling appears, there is no other treatment except surgical operation. A drug, Diethylcarbamazine has been shown to kill the microfilaria.

- Ancylostomiasis [hookworm disease]: Caused by hookworm, *Ancylostoma duodenale*. It lives in small intestine firmly attached to its wall. It feeds ~~from~~ on blood and bits of mucous membrane. Secretion from its pharyngeal gland prevent clotting of blood while the worm is feeding and causes considerable after the worm loss of blood after the worm has left the wound. Eggs laid by the female worm in the host's intestine escape with the faeces and hatch in the moist soil. The larvae feed on organic debris and get into the human body by boring through the skin of the foot, causing ground itch. They enter the veins, and passing through the heart, lungs, trachea, pharynx and oesophagus, reach the intestine. Hence, they mature. Adult worms live for about 5 years. Male worm is 8-11 mm. long, and female 10-13 mm.

Disease	Pathogen	Habitat	Mode of Infection
Taeniasis and cysticercosis	<i>Taenia solium</i>	Intestine	By taking raw or under-cooked pork.
Ascariasis	<i>Ascaris lumbricoides</i>	Small intestine	By taking eggs with food & water.
Filariasis	<i>Wuchereria</i>	Lymphatics and connective tissue	By bites of <i>Culex</i> mosquitoes
Elephantiasis	<i>Bancrofti</i>	Connective tissue	
Hookworm disease	<i>Ancylostoma duodenale</i>	Small intestine	By boring through the skin, usually of feet.

⑩ Many fungi belonging to the genera *Microsporum*, *Trichophyton* and

Epidemophyton are responsible for ringworms which is one of the most common infectious diseases in man. { appearance of dry, scaly lesions on various parts of the body such as skin, nails and scalp are the main symptoms of the disease } These lesions are accompanied by intense itching. Heat and moisture help these fungi to grow, which makes them thrive in skin folds such as those in the groin or b/w the toes } Ringworms are generally acquired from soil or by using towels, clothes or even the comb of infected individuals.

- Tinea pedis → Athlete's foot. { Tinea capitis → Ringworm of the scalp. } Tinea cruris → Ringworm of skin specially thigh of leg.

- They are all caused by dermatophytes - only the infected area differs.
- Dermatophytes like to grow on skin that's moist skin and warm and thrive in areas where skin comes into contact with other skin, such as the groin or b/w the toes } overweight men are more likely to develop jock itch if they sweat a lot or have folds of touching skin. { Tight clothing and hot, humid weather are other risk factors. }

- Tinea cruris is considered a mild condition and is usually treated with medications that often do not require a prescription. { It should easily clear up after 2-4 weeks with an antifungal cream, powder, or lotion applied to the affected area 2 or 3 times a day. } Antifungal creams and powders such as clotrimazole, or miconazole, available without prescription at the pharmacy, are effective against dermatophytes.

- It's important to continue use after the infection has disappeared for as long as the instructions recommend. { If the inflammation persists for much more than 2 or 3 weeks despite antifungal medication, see a doctor. }

✓ maintenance of personal and public hygiene is very important for prevention and control of many infectious diseases. { Measures for personal hygiene include keeping the body clean; consumption of

Clean drinking water, food, vegetables, fruits etc {Public hygiene includes proper disposal of waste and excreta; periodic cleaning and disinfection of water reservoirs, pools, eggpools and tanks and observing standardised practices of hygiene in public catering. } These measures are particularly essential where the infectious agents are transmitted through food and water such as typhoid, amoebiasis and ascariasis.

- In case of air-borne diseases such as pneumonia and common cold, in addition to the above measures, close contact with the infected persons or their belongings should be avoided } for diseases such as malacaria and filariasis that are transmitted through insect vectors, the most important measures is to control or eliminate the vectors and their breeding places } This can be achieved by after avoiding stagnation of water in and around residential areas, regular cleaning of household coolers, use of mosquito nets, introducing fishes like Gambusia in ponds that feed on mosquito larvae, spraying of insecticides in ditches, drainage areas and swamps, etc } In addition, doors and windows should be provided with wire mesh to preventing the entry of mosquitoes } Such precautions have become more important especially in the light of recent widespread incidences of the vector-borne [Aedes mosquitoes] diseases like dengue and chikungunya in many parts of India.

- The advancements made in biological sciences have armed us to effectively deal with many infectious diseases } The use of vaccines and immunization programmes have enabled us to completely eradicate a deadly disease like small-pox. } A large number of other infectious diseases like polio, diphtheria, pneumonia and tetanus have been controlled to a large extent by the use of vaccines } Discovery of antibiotics and various other drugs has also enabled us to effectively treat infectious diseases

(11) Immunity:

Adaptive immunity

Natural

Artificial

Innate immunity

Nature has provided certain ways in the body to defend ourselves from the invasion by pathogenic organisms and therefore, from the disease.

The ability of a host's body to prevent or overcome the effects caused due to the invasion by pathogenic organisms and its toxins is **resistance** and **immunity**.

Resistance is considered as an inherent factor and those acquired during life to overcome the disease, while the immunity that must be overcome by a pathogen before establishing an infection.

① External defense mechanism ② Internal defense mechanism.

External defense: It includes physical and chemical barrier.

① **Physical barriers**: Skin → its outer & tough layer, that stratum corneum prevents the entry of bacteria and virus. Mucous membranes → mucus secreted by mucus membrane traps the micro-organism and immobilises them. Micro-organism and dust particles can enter the respiratory tract with air during breathing which are trapped in the mucus. The cilia sweep the mucus loaded with micro-organisms and dust particles into the pharynx. From the pharynx it is thrown out or swallowed for elimination with the faeces.

② **Chemical barriers**: Oil secreted by the oil gland and sweat secreted by sweat gland make the surfaces of skin acidic. This does not allow the micro-organism to establish on the skin. Some friendly bacteria also occur on the skin which releases acid and other metabolic wastes that check the growth of pathogens. The sweat also contains an enzyme named lysozyme that destroys the cell wall of many bacteria. Certain bacteria normally live in vagina. These produce

bacteric acid, lactic acid kills the foreign bacteria.

- Thus physical and chemical barriers form the first line of defense.

④ internal defense: internal defense is carried on the WBC, macrophages, inflammatory reaction, fever and antitoxins.

⑤ WBC: The leucocytes in general and lymphocyte in particular are capable of squeezing out through the wall of blood capillaries into the extra vascular regions. This phenomena is called diapedesis. The leucocytes protect in different ways.

⑥ Lymphocytes: It can produce plasma cells which secrete antibodies to provide immunity.

⑦ Monocytes: They are phagocytic in action.

⑧ Eosinophils: They can attach themselves to parasitic forms and cause their destruction by liberating lysosomal enzymes on their surfaces.

⑨ Neutrophils: They eat harmful germs and are, therefore, phagocytic in nature.

⑩ macrophages: They are formed by enlargement of monocytes. They are large cells which are phagocytic in nature.

- Inflammatory Response: when the micro-organisms like bacteria, viruses, etc. enter the body tissue through some injury, these produce some toxic substances which kill more cells. These broken cells also release some material which attract the mast cells. The mast cells release Histamine. Histamine cause dilation of capillaries and small blood vessels surrounding the injury and increases the permeability of the capillary walls. The more blood flows to area making it red and warm. The fluid [plasma] leaks out into the tissue spaces, causing its swelling. This reaction of the body is local inflammatory response. The plasma that accumulates at the injured site dilutes the toxins secreted by bacteria & lessens their effect.

- Fever: The inflammatory response may be in the region of the wound [localized], or it may spread all over the body [Systemic]. In systemic inflammatory response, the number of WBC is generally, the fever is

caused by the toxins released by the pathogens or by compound called pyrogens [fever producing substance, Gr. pyro= fire]. } These comp. are released by body in order to regulate temp. of the body. } Moderate fever stimulates the phagocytes and inhibits growth of micro-organisms. However, a very high fever is dangerous.

Interferons: These are the low molecular weight glycoproteins released by the virus infected cells which they help to combat. } These interferons do not inactivate the virus, but they make the unattacked cells less susceptible so they are prevented from the attack of virus. } They also prevent the viruses from taking over the cellular machinery. } Interferons proteins have proved to be effective in treating influenza and Hepatitis, but their role in cancer treatment doubtful. } Thus the leucocytes, macrophages, inflammatory response, fever and interferons form second line of defense.

- ⑫ **Immunity:** Every day we are exposed to large numbers of infectious agents. } However, only a few of these exposures result of disease. } Why? - This is due to the fact that the body is able to defend itself from most of these foreign agents. } This overall ability of the host to fight the disease causing organisms, conferred by the immune system is called immunity. - Immunity is of two types: ① Innate immunity ② Acquired immunity
 ① **Innate immunity:** It is non-specific type of defense, that is present at the time of birth. } This is accomplished by providing different types of barriers to the entry of the foreign agents into our body. } Innate immunity consist of four types of barriers
 ② **Physical Barriers:** Skin on our body is the main barrier which prevents entry of the micro-organisms. } Mucous coating of the epithelium lining the respiratory, gastrointestinal, and urogenital tracts also help in trapping microbes entering our body.
 ③ **Physiological barriers:** Acid in the stomach. } Saliva in the mouth. } Tears from eyes → All prevent microbial growth.

- ① Cellular Barriers: contain types of WBC of our body like polymorpho-nuclear leucocytes [PMNL-neutrophils] and monocytes and natural killer type of lymphocytes] in the blood as well as macrophages in tissues can phagocytose and destroys microorganisms.
- ② Cytokine Barriers: virus infected cells secrete proteins called Interferons which protect non-infected cells from further viral infection.
- ③ Acquired Immunity: Acquired immunity, on the other hand is pathogen specific. It is characterized by memory. This means when our body encounters a pathogen for the first time produces a response called primary response which is of low intensity. Subsequent encounter with the same pathogen elicits a highly intensified secondary or anamnestic response. This is ascribed to the fact that our body appears to have memory of the first encounter.
- The primary and secondary immune responses are carried out with the help of two special types of lymphocytes present in our blood, B-lymphocytes and T-lymphocytes.
 - The B-lymphocytes produce an army of proteins in response to pathogen into our blood to fight with them. These proteins are called Antibodies. The T-cells themselves do not secrete antibodies but help B-cells to produce them.
 - Each antibody molecule has four peptide chains, two small called light chains and two longer called heavy chains. Hence, an antibody is represented as H_2L_2 .
 - Different types of antibodies are produced in our body. IgA, IgM, IgE, IgG are some of them. All these antibodies are found in the blood, the response is also called as humoral immune response. This is one of the two types of our acquired immune response - antibody mediated.

IgG { main antibody type in circulation, attack microorganism & their toxins

IgA { main antibody type in secretions, such as saliva and mucus, attack microorganism and their toxins

Ig E } Response for allergic reaction.

Ig M } Antibody type found in circulation; largest antibody, with 5 subunits

Ig G } Antibody type found primarily as a membrane bound immunoglobulin.

Antibodies

- These acts inside the cells

- They are slow acting

- They act against bacteria and viruses

- Their action is long lasting

Interfering

- These acts outside the cells

- They are quick acting

- They act only against viruses

- Their action is temporary

- Very often, when some human organs like heart, eye, liver, kidney fail to function satisfactorily, transplantation is the only remedy to enable the patient to live a normal life? Then a search begins - to find a suitable donor

- Why it is that the organs can not be taken from just anybody?

- What is it that the doctors check?

- Grafts from just any source - an animal, another primate, or any human beings can not be made since the grafts would be rejected sooner or later

- Tissue matching, blood group matching are essential before undertaking any graft/transplant and even after this the patient has to take immuno-suppressants all his/her life? The body is able to differentiate 'self' and 'non-self' and the cell mediated immune response is responsible for the graft rejection.

- Active and passive immunity: when a host is exposed to antigens, which may be in the form of living or dead microbes or other proteins, antibodies are produced in the host body. This type of immunity is called active immunity? Active immunity is slow and takes time to give its full effective response? Injecting the microbes deliberately during immunisation or infectious organisms gaining access into body during natural infection induce active immunity.

- When ready-made antibodies are directly given to protect the body against

foreign agents, it is called passive immunity.

- Do you know why mother's milk is considered very essential for the new-born infants?

- The yellowish fluid colostrum secreted by mother during the initial days of lactation has abundant antibodies [IgA] to protect the infant. } The foetus also receives some antibodies from their mother, through the placenta during pregnancy } These are some example of passive immunity.

- Vaccination and Immunisation: The principle of immunisation or vaccination is based on the property of memory of the immune system; In vaccination, a preparation of antigenic proteins of pathogens or inactivated or weakened pathogen [vaccine] are introduced into the body } The antibodies produced in the body against these antigens would neutralise the pathogenic agents during actual infection. } The vaccine also generates memory-B & T-cells that recognise the pathogen quickly on subsequent exposure and overwhelm the invaders with a massive production of antibodies.

- In a person is infected with some deadly microbes to which quick immune response is required as in tetanus, we need to directly inject the preformed antibodies, or antitoxin [a preparation containing antibodies to the toxin]. } Even in case of snakebites, the injection which is given to the patients, contains preformed antibodies against the snake venom. } This type of immunisation is called passive immunisation.

- mRNA technology has allowed the production of antigenic polypeptides of pathogen in bacteria or yeast. } Vaccine produced using this approach allows large scale production and hence greater availability for immunisation, i.e., hepatitis vaccine produced from yeast. ✓

✓ (13) When you have gone to a new place and suddenly you started sneezing, coughing for no explanation reason, and when you went away, your symptoms disappeared? Did this happen to you?

Some of us are sensitive to some particles in the environment. The above-mentioned reaction could be b/c of allergy to pollen, mites, etc., which are

in different places.

- **Allergist:** The exaggerated response of immune system to certain antigens present in the environment is called allergy. The substances to which such an immune response is produced are called allergens. The antibodies produced to these are of IgE type. Common example of allergens are mites in dust, pollens, animal dander, etc. Symptoms of allergic reactions include sneezing, watery eyes, running nose and difficulty in breathing.
- Allergy is due to the release of chemicals like histamine and serotonin from the mast cells. For determining the cause of allergy, the patient is exposed to or injected with very small doses of possible allergens, and the reaction studied.
- The use of drugs like antihistamines, Adrenalin and ~~steroids~~ steroids quickly reduce the symptoms of allergy.
- Somehow, modern day lifestyle has resulted in lowering of immunity and more sensitivity to allergens. More and more children in metro cities of India suffer from allergies and asthma due to sensitivity to the environment. This could be because of the protected environment provided early in life.
- **Autoimmunity:** memory based acquired immunity evolved in higher vertebrates based on the ability to differentiate foreign organisms (e.g. pathogens) from self cells. While we still do not understand the basis of this, two corollaries of this ability have to be understood. One, higher vertebrates can distinguish foreign molecules as well as foreign organism. Most of the experimental immunology deals with this aspect.
- Two, sometimes, due to genetic and other unknown reasons, the body attacks self-cells. This results in damage to the body and is called autoimmune disease. Rheumatoid arthritis which affects many people in our society is an autoimmune disease.
- Autoimmune diseases are of two types:-
 - ① **organ specific:** Are those whose antibodies and invasive destructive lesions are directed against one organ of the body. Target organs

core - Thyroid, adrenals, stomach and pancreas. } Ex: Hashimoto's, thyroiditis, Thyrotoxicosis, myasthenia gravis.

② Non-organ specific or systemic: are those where antibodies and lesions are directed to antigens which are widespread throughout the body. } Ex: Rheumatological disorders characteristically involve the skin, kidney, joints & muscles.

✓ (14) Immune system in the body: The human immune system consists of lymphoid organs, tissues, cells and soluble molecules (like antibodies). As you have seen, immune system is unique in the sense that it recognises foreign antigens, responds to those and remembers them. } The immune system also plays an important role in allergic reactions, autoimmune diseases and organ transplantation.

- Lymphoid organs: These are those organs whose origin and/or maturation and proliferation of lymphocytes occur. } The primary lymphoid organs are bone marrow and thymus where immature lymphocytes differentiate into antigen sensitive lymphocytes. } After maturation the lymphocytes migrate to secondary lymphoid organs like spleen, lymph nodes, tonsils, Peyer's patches of small intestine and appendix. } These secondary lymphoid organs provide the sites for interaction of lymphocytes with the antigen, which then proliferate to become effector cells. } The Bone marrow is the main lymphoid organ where all blood cells including lymphocytes are produced. } The Thymus is a lobed organ located near the heart and beneath the breastbone. } The thymus is quite large at the time of birth but keeps reducing in size with age and by the time puberty is attained it reduces to a very small size. } Both bone marrow and thymus provide micro-environment for the development and maturation of T-lymphocytes.

- Spleen is a large bean-shaped organ. } It mainly contains lymphocytes and phagocytes. } It acts as a filter of the blood by trapping blood-borne micro-organisms. } Spleen has also has a reservoir of erythrocytes.

- The lymph nodes are small solid ~~sp~~ located at different points along the lymphatic system. } Lymph nodes serve to trap the micro-organisms or other antigens, which happen to get into the lymph and tissue fluid. } Antigens trapped in the lymph nodes are responsible for the activation of lymphocytes present there and cause the immune response.
- The lymphoid tissue also located within the lining of the major tracts (respiratory, digestive and ~~urine~~ urogenital tracts) called mucosa-associated lymphoid tissue (MALT). } It constitutes about 50% of the lymphoid tissue in human body.
- The antigen are the foreign 'molecules' that invade the body of an organism. } The word 'antigen' is the shortened form of 'Antibody generating' b/c they stimulate the production of antibodies in response to infection. } Antigens are generally large molecules. The majority of them are made of proteins or polysacchar. found on the cell walls of bacteria and other cells ~~or~~ on the coats of virus. } All antigens are not the parts of micro-organisms. } Other sp^r like pollen grains, white of an egg, shell fish, certain fruits and vegetables, chicken, feathers of birds, blood cells from other persons or animals, drugs, chemicals, etc can also induce the immune system to produce antibodies.
- Cells of the immune system. } Lymphocytes are the main cells of immune system of the body. } Lymphocytes, meant for immune system, are of two types: T-cells and B-cells. } Both types of cells develop from the stem cells found in the liver of the fetus and in the bone marrow cells of the adult. } Those lymphocytes that migrate to the thymus and differentiate under its influence are called T-cells, while those cells that continue to be in the bone marrow ~~for~~ for differentiation are ~~as~~ B-cells.
- The final maturation of young lymphocytes occur in lymphoid tissues like lymph nodes, spleen & tonsils. } T-cells are responsible for cellular immunity, however, B-cells produce the antibodies - about 20 billions per day that take part in the humoral immunity. } Both T-cells & B-cells

require antigens to trigger them into action but they respond differently.)

B-lymphocytes are independent of the thymus and in fact probably complete their early maturation within the bone marrow. They are called B-cells b/c they mature within the Bursa of Fabricius in birds.

- Mode of action of B-cells to antigens: when antigens enter a tissue fluid, B-cells are stimulated to produce antibodies. The body has thousands of antigen-specific B-cells. The membrane of each B-cells type would have been sensitized by the various contact with the antigen. If this does not happen, the B-cells are destroyed. However, the new B-cells will keep on producing. Once an antigen-specific B-cell is activated by the antigen it multiplies very fast to form a clone of plasma cells. These plasma cells produce antibodies at a rate of about 2000 molecules per second. This capacity of the B-cells to produce specific antibodies is acquired during its process of development and maturation even before it was exposed to an antigen.

However, an antigen is necessary to stimulate the production of antibodies.

- Mode of action of T-cells to antigens: like B-cells, T-cells also respond to antigens by producing a clone of T-cells. T-cells live for 4-5 years or even longer. There are separate T-cells for each type of antigen that invades the body. T-cells of a clone that are produced in response to an antigen are similar morphologically but they perform different functions. As to their functions, they are mainly of three types:

① Cytotoxic killer T-cells: These cells attack directly and destroy antigens. In the process, these cells move to the site of invasion and produce chemicals that attack phagocytes and stimulate them so that they can feed mono-aggressively on antigens. They also produce substances that attract other T-cells.

② Helper T-cells: These cells stimulate B-cells to produce more of antibodies.

③ Suppressor T-cells: These cells suppress the entire immune system keeping it away from attacking the own body cells. Some of these cells also become memory cells.

- ✓ 15 AIDS. AIDS stands for 'Acquired immune deficiency syndrome' } This mean deficiency of immune system, acquired during the life time of an individual indicating that it is not a congenital disease } 'Syndrome' as group of symptoms } AIDS was first time reported in 1981 and in the last 25 years or so, it has spread all over the world killing more than 25 million persons.
- AIDS is caused by the ~~infective~~ Human immune deficiency virus [HIV]. } It is a member of group of viruses called retrovirus, which have an envelope enclosing the RNA genome.
 - Transmission of HIV infection generally occurs by - @ sexual contact with infected person. } ② by transfusion of contaminated blood and blood products } ③ by sharing infected needles [Intravenous drug abusers] } ④ from infected mother to her child through placenta.
 - So, people who are at high risk of getting this infection includes - individual who have multiple sexual partners, drug addicts who take drug intravenously, individuals who require repeated blood transfusion and children born to an HIV infected mother.
 - It is important to note that AIDS/HIV is not spread by mere touch or physical contact, it spreads only through body fluids } It is, hence, imperative, for the physical and physiological well being, that the HIV/AIDS infected persons are not isolated from family and society. } There is always a time-lag b/w the infection and appearance of AIDS symptoms. This period may vary from a few months to many years. [Usually 5-10 years].
 - After getting into the body of the person, the virus enters, into macrophages where RNA genome of the virus replicates to form viral DNA with the help of the enzyme reverse transcriptase } This viral DNA gets incorporated into host's cells DNA and directs the infected cells to produce virus particles.
 - The macrophages continue to produce virus and in this way acts like a HIV factory.

- Simultaneously, HIV enters into helper T-lymphocytes [TH], replicates and produce progeny viruses } The progeny viruses released in the blood attack other helper T-lymphocytes } This is repeated leading to a progressive decrease in number of helper T-lymphocytes in the body of the infected person } During this period, the person suffers from bouts of fever, diarrhoea and weight loss.
- Due to loss in the number of helper T-lymphocytes, the person starts suffering from infections that could have been otherwise overcome such as those due to bacteria especially, mycobacterium, viruses, fungi and even parasites like Toxoplasma. } The patient becomes so immune deficient that he/she is unable to protect himself/herself against these infections
- A widely used diagnostic test for AIDS is Enzyme linked immunosorbent assay [ELISA]. } Treatment of AIDS with antimicrobial drugs is only partially effective- } They can only prolong the life of the patient but can not prevent death, which is ~~inevitable~~ inevitable
- Prevention of AIDS : As AIDS has no cure, prevention is the best option. } Moreover, HIV infection, more often, spreads due to conscious behavioral patterns and is not something that happens inadvertently, like pneumonia or typhoid } Of course, infection in blood transfusion patients, new borns [from mother] etc., may take place due to poor monitoring ? The only excuse may be ignorance and it has been rightly said — 'don't die of ignorance'.
- In our country the National AIDS Control Organisation [NACO] and other non-governmental organisation [NGOs] are doing lot of educate people about AIDS } WHO has started a number of programmes to prevent the spreading of HIV infection. } Making blood bank [from blood bank] safe from HIV, ensuring the use of only disposable needles and syringes in public and private hospitals and clinics, free distribution of condoms, controlling drug abuse, advocating safe sex and promoting regular check-up for HIV in susceptible populations are some such steps taken up

- Infection of HIV or having AIDS is somethings that should not be hidden - since them, the infection may spread to many more people } HIV/AIDS infected people need help and sympathy instead of being shunned by society } Unless society recognises it as a problem to be dealt with in a collective manner - the chance of wider spread of the disease becomes manifold } It is malady that can only be tackled, by the society and medical fraternity acting together , to prevent the spread of the disease ✓
- HIV / AIDS virus : first indication of this syndrome came from new york and california [USA] in 1981. } AIDS is a acquired immunodeficiency syndrome } It is an infectious disease caused by a virus } In 1982, J. Montagnier first time isolated the causal organism of AIDS. He isolate a retrovirus from a west African patient and called it Lymphadenopathy Associated Virus [LAV]. } In 1984, R. Gallo also isolated a retrovirus from an AIDS patient and called it Human T-cell lymphotropic virus III [HTLV-III]
- In 1986 International committee on viral nomenclature proposed the name Human immunodeficiency virus [HIV]. } HIV produce infection in the peripheral blood } It attack on the T4-lymphocytes
- The main features of AIDS are as follows :- lymphopenia (low in lymphocyte count) } selective T-cell deficiency. } Helper Gammaglobulinemia [IgG, IgA less] } low cellular immunity } common infection become more severe
- HIV belongs to family Retroviridae } It is a spherical, enveloped virus } It is about 80-120nm in size } It is the only virus that has diploid genome } It has two identical ssRNA } Both RNA strands are exactly similar } The enzyme reverse transcriptase is present which is the characteristic feature of retroviruses } On the envelop of HIV, glycoproteinaceous spikes present.
- HIV can be isolated from :- Blood, spleen, semen, cervical fluid, cerebrospinal fluid, lungs
- for diagnosis of AIDS, serological tests are useful } following serological tests are useful :-

- Screening test : Enzyme linked immuno-sorbent assay (ELISA), fujirebio agglutination test, Karpo's test.

- If any of these tests positive then, we go to confirmatory test.

① Western blot test.

- If this test is positive then, the patient is 100% suffering from HIV.

- In India, first case of AIDS was seen in Chennai in 1986. { HIV does not gets transmitted by normal social domestic contact } presently, there is no treatment for AIDS. { AIDS patients die due to various kinds of infections } The survival of AIDS patient varies from person to person. { HIV is characterized by the presence of Glycoprotein 120 (Gp 120) on its surface }

✓ ⑯ Cancer : Cancer is one of the most dreaded diseases of human beings and is a major cause of death all over the globe. { more than 1 million Indian suffer from cancer and a large number of them die from it annually } The mechanisms that underline development of cancer or oncogenic transformation of cells, its treatment and control have been some of the most intense areas of research in biology and medicine.

- In our body, cell growth and differentiation is highly controlled and regulated.

- In cancer cells, there is breakdown of these regular mechanisms. Normal cells show a property called contact inhibition by virtue of which contact with other cells inhibits their uncontrolled growth. { ^{normal} cancer cells appear to have lost this property } As a result of this, cancerous cells just continue to divide giving rise to masses of cells called tumours.

- Tumours are of two types: Benign & malignant.

- Benign tumours normally remain confined to their original location and do not spread to other parts of the body and cause little damage. { The malignant tumours, on the other hand are a mass of proliferating cells called neoplastic or tumour cells. These cells grow very rapidly, invading and damaging the surrounding normal tissues } As these cells actively divide and grow they also starve the normal cells by competing for vital nutrients.

- Cells sloughed from such tumours reach distant sites through blood; and whenever they get lodged in the body, they start a new tumour there. } This property called metastasis is the most feared property of malignant tumours.
- Causes of cancer: Transformation of normal cells into cancerous neoplastic cells may be induced by physical, chemical or biological agents. These agents are called carcinogens. Ionising radiations like X-rays and γ -rays and non-ionising radiations like UV-rays cause DNA damage leading to neoplastic transformation. } The chemical carcinogens present in Tobacco smoke have been identified as a major cause of lung cancer.
- Cancer causing viruses called oncogenic viruses have genes called viral oncogenes; further more, several genes called cellular oncogenes [e-onc] or proto-oncogenes have been identified in normal cells which, when activated under certain conditions, could lead to oncogenic transformation of the cells.
- Cancer detection and diagnosis: Early detection of cancers is essential as it allows the disease to be treated successfully in many cases. } Cancer detection is based on biopsy and histological studies of the tissue and blood and bone marrow tests for red cell counts in the case of Leukemia.
 - In biopsy, a piece of suspected tissue cut into thin sections is stained and examined under microscope [histological studies] by a pathologist. } Techniques like radiography [use of X-rays], CT [computed tomography] and MRI [magnetic resonance imaging] are very useful to detect cancers of the internal organs. } Computed tomography uses X-rays to generate a three dimensional image of the internalities of an object. } MRI uses strong magnetic fields and non-ionising radiations to accurately detect pathological and physiological changes in the living tissue.
- Antibodies against cancer-specific antigens are also used to detection of certain cancers. } Techniques of molecular biology can be applied to detect genes in individuals with inherited susceptibility to certain cancers. } Identification of such genes, which predispose an individual to certain cancers, may be very helpful in prevention of cancers; such individual may be advised

Drug obtain from fungi \rightarrow LSD [Lysergic acid diimide]

\downarrow
Sporangia of clavicipitacean fungi.

Date _____

Page _____

to avoid exposure to particular carcinogens to which they are susceptible
(e.g., tobacco smoke in case of lung cancer).

- Treatment of Cancer: The common approaches for treatment of cancer are surgery, radiation therapy and immunotherapy. In radiography, tumour cells are irradiated lethally, taking proper care of the normal tissues surrounding the tumour mass. Several chemotherapeutic drugs are used to kill cancerous cells. Some of these are specific for particular tumours. Majority of drugs have side effects like hair loss, anaesthesia, etc. Most cancers are treated by combination of surgery, radiotherapy and chemotherapy. Tumour cells have been shown to avoid detection and destruction by immune system. Therefore, the patients are given substances called biological response modifiers such as α -interferon which activates their immune system and helps in destroying the tumour.

- ✓ (17) - Drugs and alcohol abuse: Surveys and statistics show that use of drugs and alcohols has been on the rise especially among the youth. This is really a cause of concern as it could result in many harmful effects. Proper education and guidance would enable youth to safeguard themselves against these dangerous behaviour patterns and follow healthy life styles.
- The drugs, which are commonly abused are opioids, cannabinoids and coca alkaloids. Majority of these are obtained from flowering plants. Some are obtained from fungi.
- Opioids are the drugs, which bind to specific opioid receptors present in our CNS and GIT.
- Heroin, commonly called smack is chemically diacetylmorphine, which is a white, odourless, bitter crystalline compound. This is obtained by acetylation of morphine, which is extracted from the latex of poppy plant *Papaver somniferum*. Generally taken by snorting and injection, heroin is a depressant and slows down body functions.
- Cannabinoids are a group of chemicals, which interact with cannabinoid receptors present principally in the brain. Natural cannabinoids are

obtained from the inflorescences of the plant *cannabis sativa* } this flower tops, leaves and the resin of *cannabis* plant are used in various combinations to produce marijuana, hashish, charas & Ganja } Generally taken by inhalation and oral ingestion, these are known for their effects on cardiovascular system of the body

- Coca alkaloid or cocaine is obtained from coca plant *Erythroxylum coca*, native to south America } It interferes with the transport of the neurotransmitter Dopamine } Cocaine, commonly called Coke or Crack coke is usually snorted } It has a potent stimulating action on CNS, producing a sense of Euphoria and Ted energy. } Excessive dosage of cocaine causes hallucinations } Other well-known plants with hallucinogenic properties are *Atropa belladonna* & *Datura*. } These days cannabinoids are also being abused by some sports persons
- Running Amok is an episode of sudden mass assault against people or objects usually by a single individual [psychopathological behaviour].
- Drugs like benzodiazepines, amphetamines, benzodiazepines, and other similar drugs, that are normally used in medicines to help patients cope with mental illnesses like depression and insomnia, are often abused
- Morphine is a very effective sedative and painkiller, and is very useful in patients who have undergone surgery
- Several plants, fruits and seeds having hallucinogenic properties have been used for hundreds of years in folk-medicine, religious ceremonies and rituals all over the globe } when these are taken for a purpose other than medicinal use or in amounts/frequency that impairs one's physical, physiological or psychological functions, it constitutes Drug abuse.
- Smoking also paves the way to hard drugs } Tobacco has been used by human beings for more than 400 years } It is smoked, chewed or used as a snuff. } Tobacco contains a large number of chemical substances including Nicotine, an alkaloid } Nicotine stimulates adrenal glands to release adrenaline and nor-adrenaline into blood circulation, both of which raise blood

prosthetic and the heart rate.

- Smoking is associated with the incidence of cancers of lungs, urinary bladder & throat, bronchitis, emphysema, coronary heart disease, gastric ulcers, etc. } Tobacco chewing is associated with the risk of cancer of the oral cavity. {smoking has CO content in blood and reduces the concentration of haem bound oxygen. This causes oxygen deficiency in the body}
- Adolescence & drug/alcohol abuse :- Adolescence means both a period and a process during which a child becomes mature in terms of his/her attitudes and beliefs for effective participation in society } The period b/w 12-18 years may be thought of as adolescence period } In other words, adolescence is a bridge linking childhood and adulthood
- Curiosity, need for adventure and excitement & experimentation, constitute common cause, which motivate youngsters towards drugs and alcohol use } Thus, the first use of drugs or alcohol may be out of curiosity or experiments, but later the child starts using these to escape facing problems } The perception among youth that it is 'cool' or progressive to smoke, use drugs or alcohol, is also in a way a major cause for youth to start these habits } Television, movies, newspapers, internet also help to promote this perception
- Addiction & Dependence :- Addiction is a psychological attachment to certain effects - such as euphoria and a temporary feeling of well-being - associated with drugs and alcohol.
- Consequently the receptors respond only to higher doses of drugs and alcohol leading to greater intake and addiction. } However, it should be clearly borne in mind that use of these drugs even once, can be a forerunner to addiction. } Thus, the addictive potential of drugs and alcohol, pull the user into a vicious circle leading to their regular use [abuse]. from which he/she may not be able to get out
- Dependence is the tendency of the body to manifest a characteristic