

SHREE VENKATESHWARA HITECH ENGINEERING COLLEGE, GOBICHETTIPALAYAM
(Autonomous)
DEPARTMENT OF SCIENCE & HUMANITIES
Ist BIO MEDICAL ENGINEERING



23BMT21 – BIOSCIENCES FOR MEDICAL ENGINEERING

SHORT NOTES

23BMT21

BIOSCIENCES FOR MEDICAL ENGINEERING

L	T	P	C
3	0	0	3

COURSE OBJECTIVES:

- 1. To study structural and functional properties of carbohydrates, proteins, lipids and amino acids.
- 2. To emphasize the role of these biomolecules by providing basic information on specific metabolic diseases and disorders of these biomolecules.
- 3. Gain knowledge on the structural and functional aspects of living organisms.

UNIT-I

CARBOHYDRATES, LIPIDS, PROTEIN

10

Classification of carbohydrates - mono, di, oligo and polysaccharides. Structure, physical and chemical properties of carbohydrates - Classification of lipids- simple, compound, and derived lipids. Nomenclature of fatty acid - Structure and properties of proteins, structural organization of proteins, classification and properties of amino acids. Nucleic acid: Structural aspects - Components of DNA and RNA, Nucleosides & Nucleotides (introduction, structure & bonding).

UNIT-II

VITAMINS AND MINERALS

8

Vitamins: classification (A, D, E, K, and B-complex members), basic structure, source, daily requirement, functions and deficiency symptoms- Minerals: classification- macro elements and microelements, specific function and deficiency disorders

UNIT-III

CELL DEGENERATION, REPAIR AND NEOPLASIA

10

Cell injury - Reversible cell injury and Irreversible cell injury and Necrosis, Apoptosis, Intracellular accumulations, Pathological calcification- Dystrophic and Metastatic. cellular adaptations of growth and differentiation, Inflammation and Repair including fracture healing, Neoplasia, Classification, Benign and Malignant tumours, carcinogenesis, spread of tumours Autopsy and biopsy.

UNIT-IV

HEMODYNAMIC DERANGEMENTS AND DISEASES

9

Edema, Hyperemia/Ischemia, normal hemostasis, thrombosis, disseminated intravascular coagulation, embolism, infarction, shock, Chronic venous congestion. Hematological disorders- Bleeding disorders, Leukaemias, Lymphomas Haemorrhage- Lifestyle diseases - diabetes, obesity, blood pressure.

UNIT-V

FUNDAMENTALS OF MICROBIOLOGY AND IMMUNOPATHOLOGY

8

Structure of Bacteria and Virus - List of common bacterial, fungal and viral diseases of human beings.- Basics of Microscopes : Light microscope, Electron microscope (TEM & SEM). - Natural and artificial immunity - Immunological techniques: immune diffusion, immuno electrophoresis, RIA and ELISA, monoclonal antibodies.

TOTAL: 45 PERIODS

COURSE OUTCOMES:

At the end of the course, the students will be able to

- CO1:** Acquire knowledge on structure, properties and biological functions of carbohydrates, lipids and proteins.
- CO2:** Assess the significance of vitamins and minerals
- CO3:** Comprehend genetics and the immune system
- CO4:** Outline cause, symptoms, diagnosis and treatment of common diseases.
- CO5:** Understand the basics of microbiology and pathology

TEXT BOOKS:

1. RAFI MD "Text book of biochemistry for Medical Student" Fourth Edition, Universities Press, Orient Blackswan Private Limited - New Delhi 2021.
2. Ramzi S Cotran, Vinay Kumar & Stanley L Robbins, "Pathologic Basis of Diseases", 10th edition: South Asia Edition Elsevier India, 2020.
3. Lehninger, A. L, Nelson D. L and Cox, M. M, "Principles of Biochemistry", Freeman Publishers, New York, Eighth edition, 2021.

REFERENCE BOOKS:

1. Dubey RC and Maheswari DK. "A Text Book of Microbiology" Chand & Company Ltd, 5th edition, 2022.
2. Diseases of the Human Body, Carol D. Tamparo and Marcia A. Lewis, F.A. Davis Company, 6th edition, 2016.
3. Ananthanarayanan & Panicker, "Microbiology" Orientblackswan, 10th edition 2017.
4. Prescott, Harley and Klein, "Microbiology", 10th edition, McGraw Hill, 2017.

E-RESOURCES:

1. NPTEL-Online Courses and Video lectures: <https://nptel.ac.in/>

CO's - PO's & PSO's MAPPING

CO/ PO/ PSO	PO1	PO2	PO3	PO4	PO5	PO6	PO7	PO8	PO9	PO10	PO11	PO12	PSO1	PSO2	PSO3
CO1	3	2	2	1	-	1	-	-	-	-	-	1	2	1	-
CO2	3	3	2	1	-	1	-	-	-	-	-	2	3	1	-
CO3	3	2	2	1	-	1	-	-	-	-	-	2	3	1	-
CO4	3	2	2	1	-	1	-	-	-	-	-	2	3	2	-
CO5	3	1	2	1	-	1	-	-	-	-	-	1	2	1	-
AVG	3	2	2	1	-	1	-	-	-	-	-	2	3	1	-

1 - low, 2 - medium, 3 - high, '-' - no correlation

23BML21

BIOSCIENCES LABORATORY

L	T	P	C
0	0	4	2

COURSE OBJECTIVES:

- 1. Estimation and quantification of biomolecules.
- 2. Separation of macromolecules.
- 3. Practice on chemical examinations, Histopathological examinations etc

LIST OF EXPERIMENTS

1. Preparation of solutions: 1) percentage solutions, 2) molar solutions, 3) normal solutions.
2. Standardization of pH meter, preparation of buffers, emulsions.
3. Spectroscopy: Determination of absorption maxima (λ_{max}) of a given solution.
4. General tests for carbohydrates, proteins and lipids.
5. Identification of Blood Collection Tubes and Phlebotomy equipment.
6. Preparation of serum and plasma from blood.
7. Estimation of Haemoglobin and blood glucose.
8. Estimation of creatinine, urea and Uric acid.
9. Separation of proteins by SDS electrophoresis (Demo) and amino acids by thin layer chromatography (Demo).
10. Urine physical and chemical examination (protein, reducing substances, ketones, bilirubin and blood).
11. Basic staining – Hematoxylin and eosin staining.
12. Special stains – cresyl fast Blue (CFV)- Trichrome – oil red O – PAS.

TOTAL: 60 PERIODS

COURSE OUTCOMES:

At the end of the course, the students will be able to

- CO1:** Understand the Biochemistry laboratory functional components
- CO2:** Have a sound knowledge of qualitative test of different biomolecules.
- CO3:** Understand the basics knowledge of Biochemical parameter and their interpretation in Blood sample.
- CO4:** Have a sound knowledge of separation technology of proteins and amino acids.
- CO5:** Student can perform practical experiments on staining Processes.

TEXT BOOKS:

1. Ramnik Sood, Modern Medical Laboratory Technology: methods and Interpretation, 7th Edition, Jaypee Brothers Medical Publishers, 2023.

REFERENCE BOOKS:

1. Manual prepared by the faculty of BME Department, SVHEC

E-RESOURCES:

1. NPTEL-Online Courses and Video lectures: <https://nptel.ac.in/>

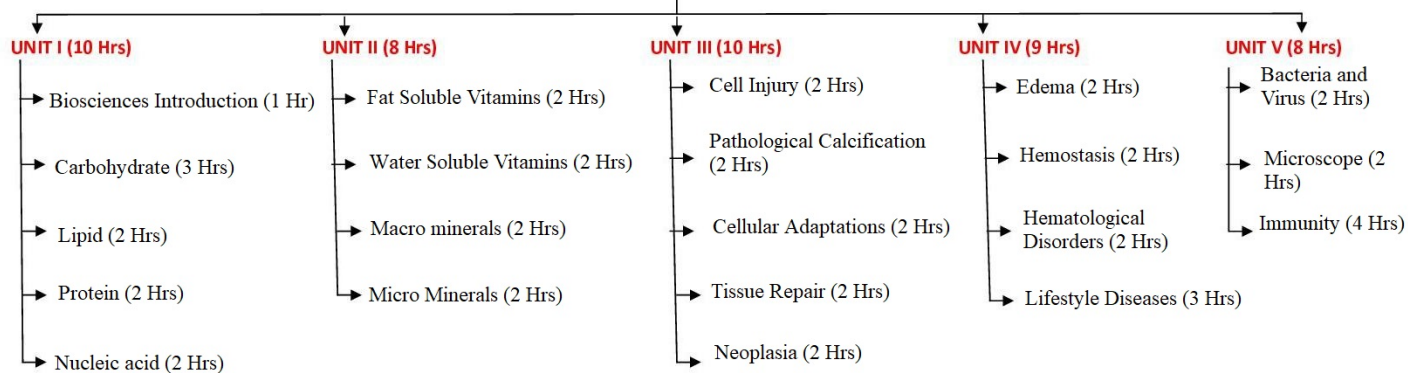
CO's – PO's & PSO's MAPPING

CO/ PO/ PSO	PO1	PO2	PO3	PO4	PO5	PO6	PO7	PO8	PO9	PO10	PO11	PO12	PSO1	PSO2	PSO3
CO1	3	2	1	1	1	1	-	-	-	-	-	1	1	-	-
CO2	3	3	1	1	2	2	-	-	-	-	-	2	1	-	-
CO3	3	3	2	1	2	2	-	-	-	-	-	2	1	-	-
CO4	3	3	2	1	1	2	-	-	-	-	-	2	1	-	-
CO5	3	2	2	1	1	1	-	-	-	-	-	1	1	-	-
AVG	3	3	2	1	1	2	-	-	-	-	-	2	1	-	-

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SHREE VENKATESHWARA HI-TECH ENGINEERING COLLEGE, GOBICHETTIPALAYAM
(Autonomous)
DEPARTMENT OF SCIENCE AND HUMANITIES
I YEAR BIO MEDICAL ENGINEERING
23BMT21 – BIOSCIENCES FOR MEDICAL ENGINEERING

LESSON PLAN (Total Hrs: 45 Hrs)



SHREE VENKATESHWARA HI-TECH ENGINEERING COLLEGE (Autonomous)
DEPARTMENT OF SCIENCE AND HUMANITIES
I YEAR / II SEMESTER – QUESTION BANK – IMPORTANT QUESTIONS

SUBJECT CODE : 23BMT21

SUBJECT NAME : BIOSCIENCES FOR MEDICAL ENGINEERING

Unit I – Carbohydrates, Lipids, Protein
Part A - 2 Marks

1. What is Carbohydrate?
2. If a carbohydrate molecule has 7 chiral carbons, possible isomers for the above molecule can be calculated as.
3. Define Protein.
4. Define Aminoacid.
5. What is zwitter ion?
6. Give examples for Disaccharides.
7. What is Lipid?
8. Differ Fat and Oil.
9. What is fatty acid?
10. Define triacylglycerol.
11. What is arachidonic acid?
12. What is Rancidity?
13. Define Mutarotation.
14. Define Isomerism.
15. Draw the Reference carbohydrate molecule.
16. What is Essential Aminoacid?
17. What is essential Fattyacid?
18. Define nucleic acid .
19. Short note on Types of RNA.
20. Write about denaturation?
21. Define Antibody and its type.
22. What is antigen?
23. What is the meaning of Amphipathic lipids?
24. What is sterol?
25. Explain about Trans fatty acid.
26. Short note on Eicosanoids.
27. Explain about Iodine number.
28. Explain about Saponification number.
29. Explain about RM Number.
30. What is Decarboxylation?
31. What is Deamination.
32. What is the meaning of Non standard aminoacid?
33. Explain about Peptide bond.
34. Short note on Purines and pyrimidines.

35. Write a short note on Nucleotide.
36. Explain about Transcription.
37. Explain about Transalation.
38. Short note on RDA.

Part B – 16 Marks

1. Classify the carbohydrate and explain its function.
2. Write an elaborate note on disaccharide.
3. Elaborate note on starch and glycogen .
6. Classify the lipids and explain its function.
7. Note on types of fatty acid.
8. Elaborate note on phospholipids.
9. Note on Steroids and sterols.
10. Write about lipoprotein.
11. Explain about the Nomenclature of fattyacid.
12. Write a note on Classification of protein.
13. Write a note on Classification of aminoacid.
14. List out 20 aminoacids with their structure.
15. Explain about Structural organization of protein.
16. Explain about the Structures of purine and pyrimidines.
17. Elaborate note on RNA and its types.

UNIT II – Vitamins and Minerals

PART A – 2 MARKS

1. Write about sources of Vitamin A.
2. What is sun shine vitamin?
3. Write about calcium.
4. What is the good sources of Iron?
5. Define Micromineral.
6. Define Macromineral.
7. Write about the functions of Zinc in human system.
8. List out B Complex vitamins.
9. Give the list of sources of vitamin C.

PART B – 16 MARKS

1. Elaborate note on Fat soluble vitamins.
2. Write an elaborate note on water soluble vitamins.
3. Write a note on macrominerals.
4. Write a note on microminerals.
5. Elaborate Note on Vitamin A.
6. Elaborate Note on Vitamin D.

7. Write a note on Calcium.
8. Write about Iron.

UNIT III – Cell Degeneration, Repair and Neoplasia

PART A – 2 Marks

1. Define cell.
2. What is the meaning of cell injury?
3. Difference between reversible and irreversible cell injury.
4. Define Necrosis.
5. Define Apoptosis.
6. What will happen if apoptosis not happen properly?
7. What is differentiation?
8. Differ Benign and Malignant tumors.
9. What is the difference between autopsy and biopsy?

PART B – 16 Marks

1. Write about cell injury.
2. Write about Cellular adaptation of growth and differentiation.
3. Discuss about carcinogenesis.
4. Discuss about fracture healing.

UNIT IV – Hemodynamic derangements and Diseases

PART A – 2 Marks

1. Define edema.
2. List out some bleeding disorders.
3. What are all the tests used for the diagnosis of bleeding disorders?
4. What is chronic venous congestion.
5. What will be the reason for diabetes mellitus.
6. List out the normal value of Fasting, Post prantial and Random blood sugar.
7. What is meant by Calorie surplus?
8. Consider a person who eat for 2500 calorie and work for 2000 calorie . What will happen to that person and why?
9. What is Blood pressure and mention the normal value of Blood pressure?

PART B – 16 Marks

1. Write about embolism.
2. Detail note on coagulation pathway.
3. Discuss about any two bleeding disorders.
4. Elaborate note on diabetes mellitus.
5. Discuss about obesity and Blood pressure.

UNIT V – Fundamentals of Microbiology and Immunopathology

PART A – 2 Marks

1. Differ gram positive and gram negative bacteria.
2. List out some viral diseases of human beings.
3. What is the use of microscopes?
4. What is meant by electrophoresis?
5. Define monoclonal antibodies.
6. What is Enzyme Linked Immunosorbent Assay?
7. What is antigen?

PART B – 16 Marks

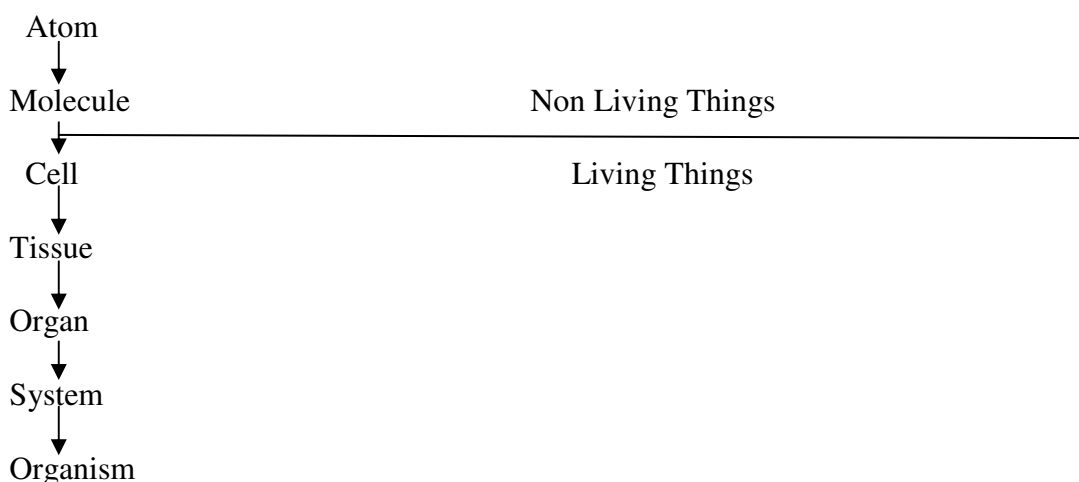
1. Elaborate note on types of immunity.
2. Write about Transmission Electron Microscope.
3. Write about Scanning Electron Microscope.
4. Write a detailed note on ELISA.
5. Elaborate note on Immunoelectrophoresis.
6. Write a note on HIV virus.

BIOCHEMISTRY
I Year BME
BSME
Short Notes

BASIC

1. LEVELS OF ORGANISATION

- ✚ The Earth has various things, they are mainly classified into two
 - I. Living
 - II. Non Living
- ✚ Everything present on the earth is made up of Atoms of 118 Elements.
- ✚ There is enormous number of nonliving and around 1.7 million types of documented living species exists in Earth.
- ✚ This diversity is possible by organization of atoms of elements in various patterns.
- ✚ Here is the organization of things in earth



2. LIVING

- ✚ Around 90% dry weight of human body is composed of 6 elements.
- ✚ They are Carbon, Hydrogen, Oxygen, Nitrogen, Sulfur and Phosphorous.
- ✚ Other atoms of elements also contribute to the living function in small quantities they are Ca, K, Na, Cl, Mg, Fe, Cu, Co, I, Zn, F, Mo, Se and some others.
- ✚ Among all the elements, carbon is special which leads to the formation of enormous number of compounds by C-C Chain of unlimited length.
- ✚ Nearly 90% of carbon compounds constitute living system.
- ✚ Biology is the study of life forms and living processes.

3. BIOCHEMISTRY

- ✚ Biochemistry is a study of structure, function, properties and chemical reactions of chemical substances that are available in living organism.
- ✚ It is a branch of Biology.
- ✚ Molecules in living things are called as Bio-molecules.
- ✚ Highly diverse bio-molecules are grouped into 6 groups based on their structural similarities. They are
 1. Carbohydrates
 2. Protein
 3. Lipids
 4. Vitamins
 5. Minerals
 6. Nucleic acid

LESSON STARTS

4. CARBOHYDRATE

- Carbohydrates may be defined as polyhydroxy aldehydes or ketones or compounds which produce them on hydrolysis.

Eg: Glucose, Lactose, Starch

- Aldehyde, Ketone, Hydroxyl are functional Groups of a molecule some of them are used in carbohydrate study they are listed below with formula

1. Aldehyde : - CHO
2. Ketone : - C=O
3. Hydroxyl : - OH
4. Carboxyl : - COOH

- Carbohydrates are type of bio-molecule composed of Carbon, Hydrogen and Oxygen in the ratio of 1:2:1. (eg: $C_6H_{12}O_6$) which has the empirical formula $(CH_2O)_n$

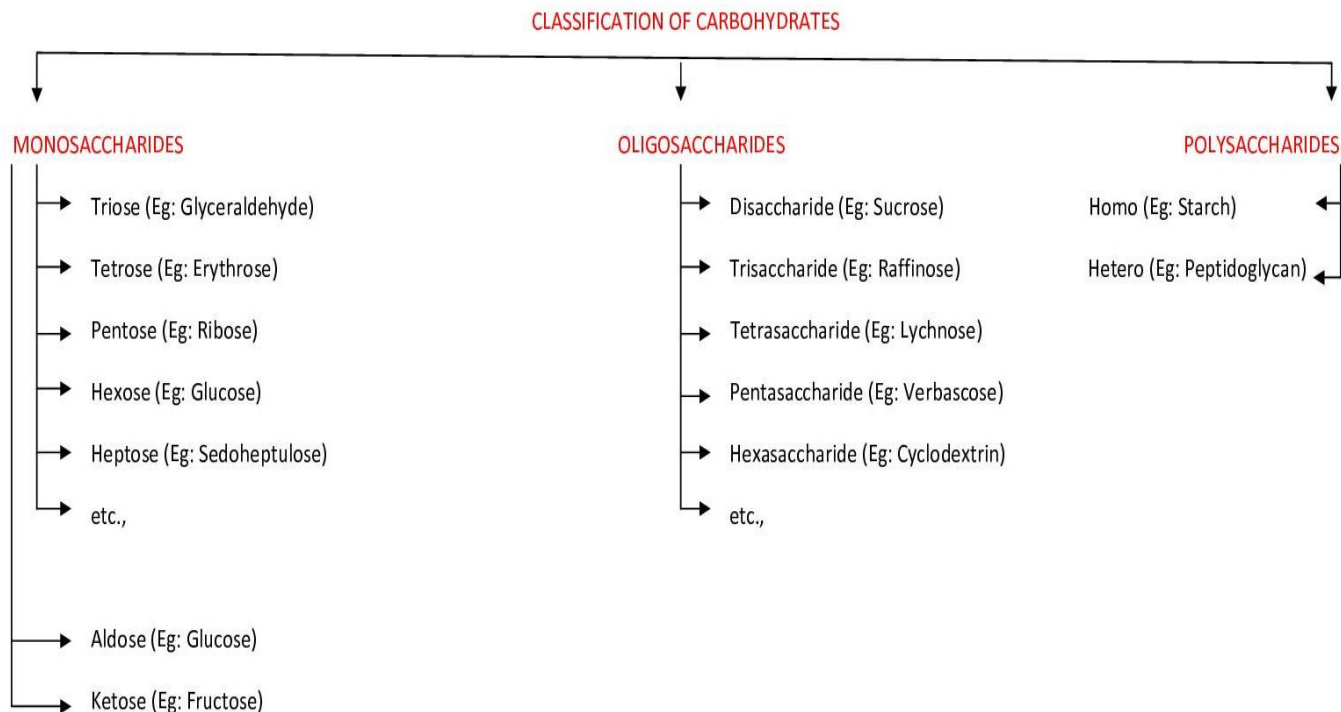
- n must be 3 or above to be called as carbohydrate.

- Ramhnohexose ($C_6H_{12}O_5$) and Deoxyribose ($C_5H_{10}O_4$) are some exceptions of carbohydrate empirical formula.

4.1 FUNCTION

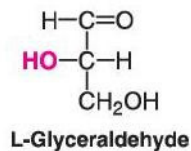
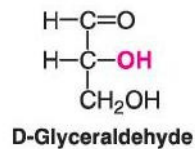
- Main function of carbohydrates is production of energy (4cal/gram).
- It also involved in structural construction in various organisms (eg: cellulose, Peptidoglycan and some others).
- Cellular function also needs the participation of some carbohydrates (eg: Glycoprotein, Glycolipid)

4.2 CLASSIFICATION



4.3 MONOSACCHARIDE

- Monosaccharides are simplest form of carbohydrates, they cannot be further hydrolysed.
- It can be classified as triose, tetrose, etc as mentioned above based on number of carbon.
- Glyceraldehyde (Triose) is a simplest form of monosaccharide (**Reference carbohydrate**).

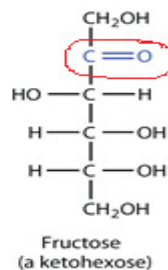
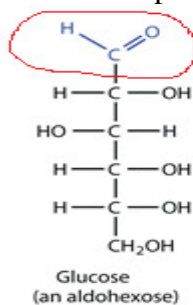


- Each division based on the number of carbon can be further classified into two based on their functional group.

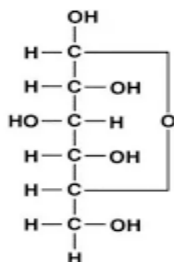
- For eg: Hexose

If the hexose contain Aldehyde Group that is called as aldose or Aldohexose

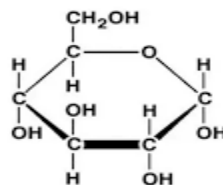
If the hexose contain Ketone Group that is called as Ketose or Ketohexose



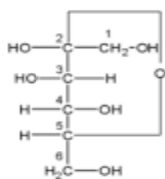
- Reaction between C1 - aldehyde and C5 - OH of leads to the formation of Hemiacetal (Ring Between C1 and C5)



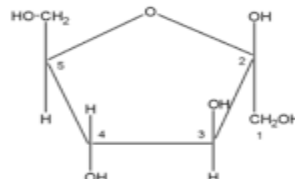
Glucose



- Likewise C2 – Ketone and C5 – OH forms ring in ketose, leads to Hemiketal.



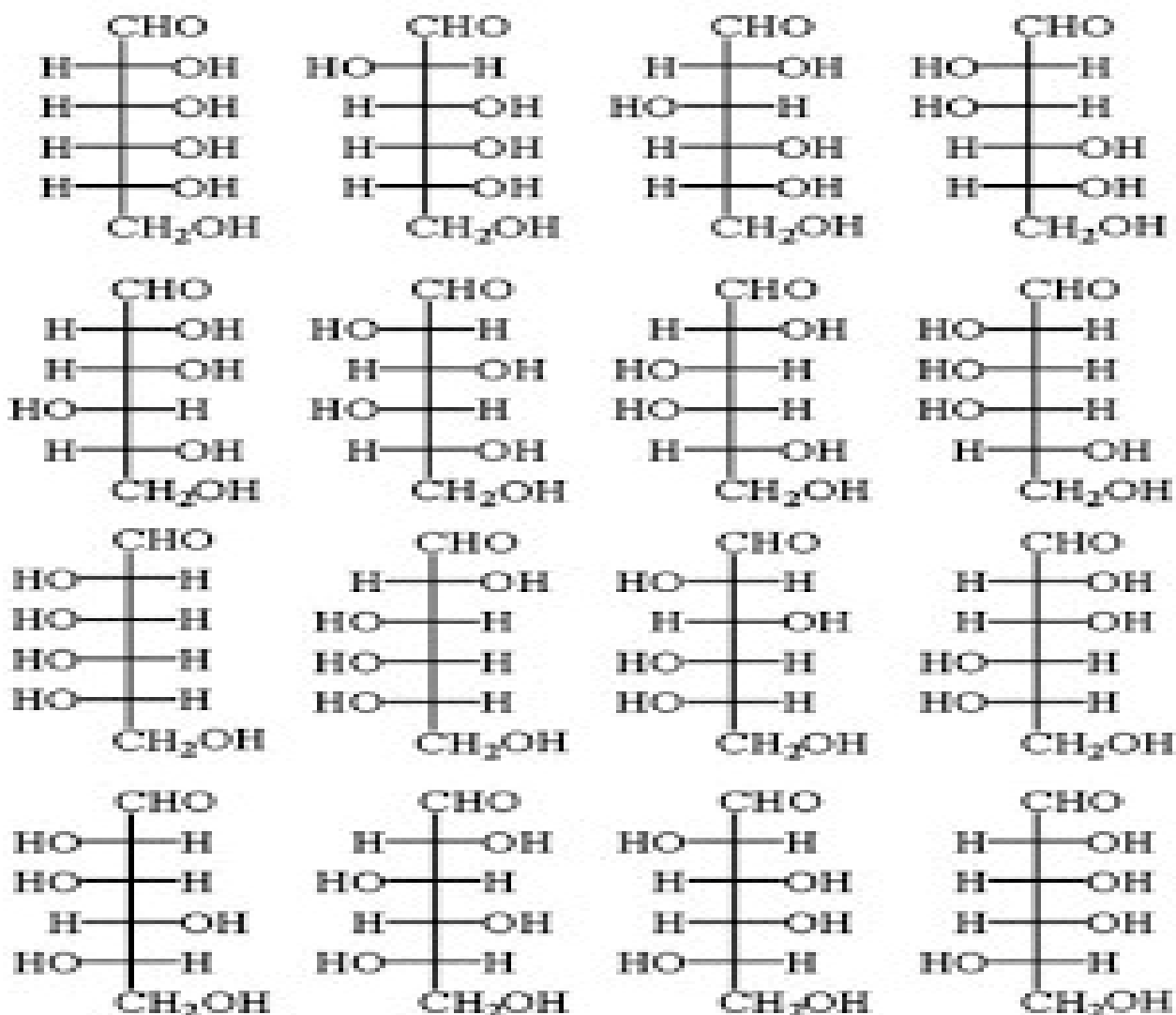
β -D-Fructose



4.3.1 ISOMERS

- Carbohydrates have a property called Isomerism as other carbon molecules.
- Stereoisomerism of carbohydrates makes more number of monosaccharide with same structural formula and different spatial arrangement.
- The number of isomers can be calculated using asymmetric carbon which is a carbon with four different groups attached to it. A formula for calculation is 2^n . Here the n Means the Asymmetric carbon atom
- For eg
Glucose has 4 asymmetric carbon atom so possible isomers will be $2^4 = 2 \times 2 \times 2 \times 2 = 16$

16 Aldohexoses



The names of the above aldohexoses are:

D-allose | D-altrose | D-glucose | D-mannose

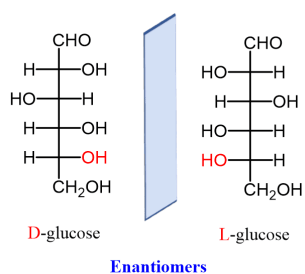
D-gulose | D-idose | D-galactose | D-talose

L-allose | L-altrose | L-glucose | L-mannose

L-gulose | L-idose | L-galactose | L-talose

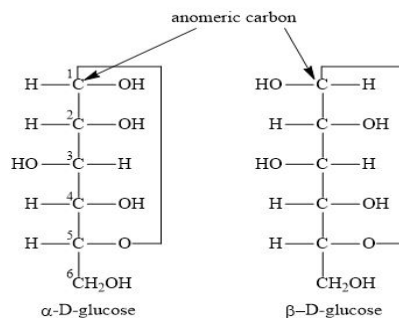
4.3.2 ENANTIOMERS (D & L ISOMERS)

- Enantiomers are type of isomer that can be mirror images for each other.
- D - Dextrorotatory and L - Levorotatory forms of carbohydrates are classified under Enantiomers.

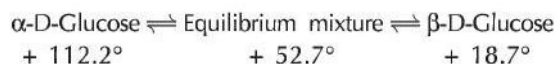


4.3.3 DIASTREOMERS (α and β ISOMERS)

- Diastereomers are non mirror images for each other.
- α and β forms are Diastereomers.
- interchange is happen in anomeric carbon so this is also under the category of **Anomers**.

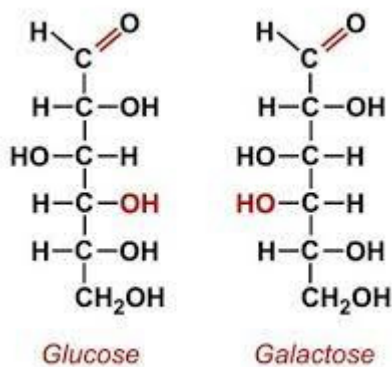


- Mutarotation** is defined as the change in the specific optical rotation representing the inter conversion of α and β forms of D Glucose to an equilibrium mixture.



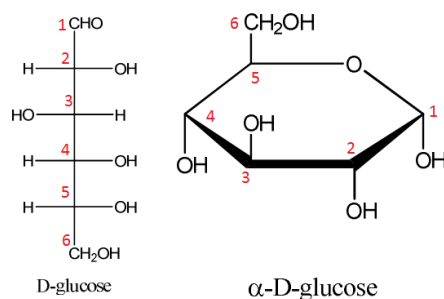
The equilibrium mixture contains 63% β anomers and 36% α anomer of Glucose with 1% open chain form.

- If the interchange is happen in non-anomeric single carbon that will be **Epimer** for each other. For eg: Glucose and Galactose.

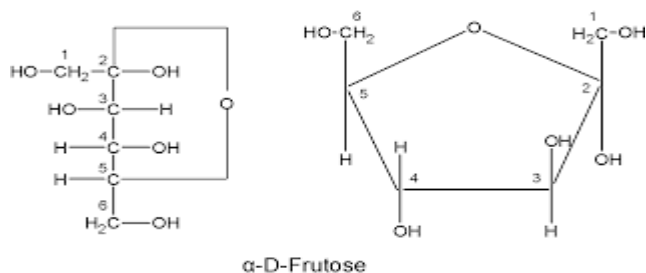


4.3.4 Fisher and Haworth structure and Numbering of carbons

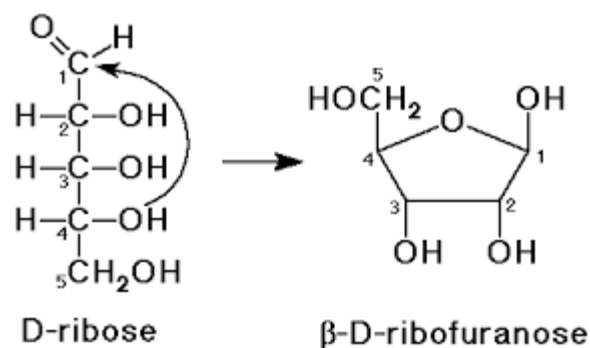
Fisher to Haworth (Pyranose (6C) Ring) for aldohexose



Fisher to Haworth (Furanose (5C) Ring) for ketohexose

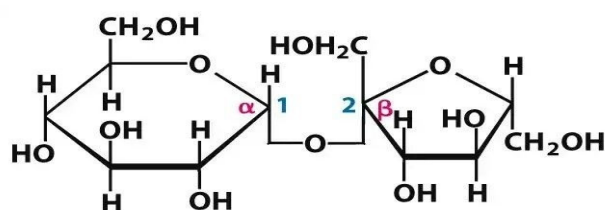


Fisher to Haworth (Furanose (5C) Ring) for Aldopentose



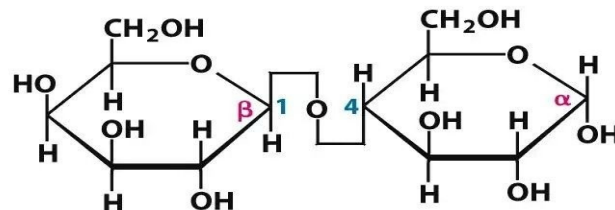
4.4 OLIGOSACCHARIDE

- ✚ Oligo means few, 2 to 9 units of monosaccharides joined together to form oligosaccharide.
- ✚ Oligosaccharide can be subdivided into more types. Among them Disaccharides are most important type.
- ✚ **Disaccharides** are type of oligosaccharide that is having two monosaccharide units. Examples are
 1. Sucrose
 2. Maltose
 3. Lactose



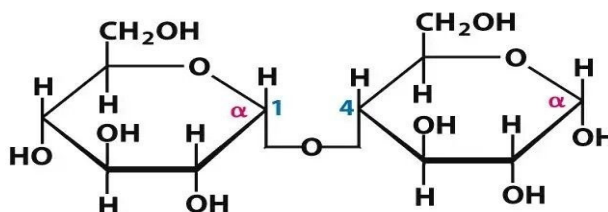
Sucrose

α D Glucose (1-2) β D Fructose



Lactose

β D Galactose (1-4) α D Glucose



Maltose

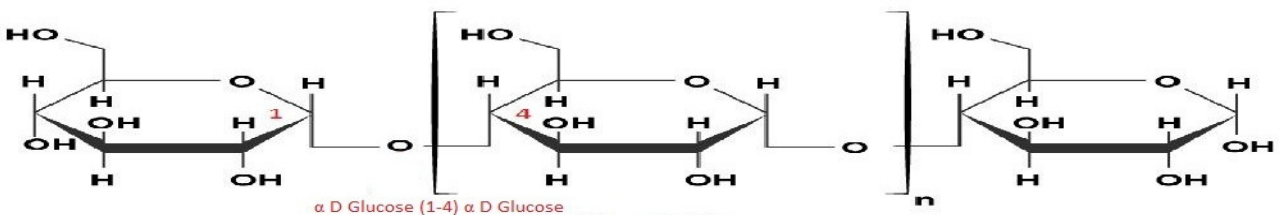
α D Glucose (1-4) α D Glucose

4.5 POLYSACCHARIDE

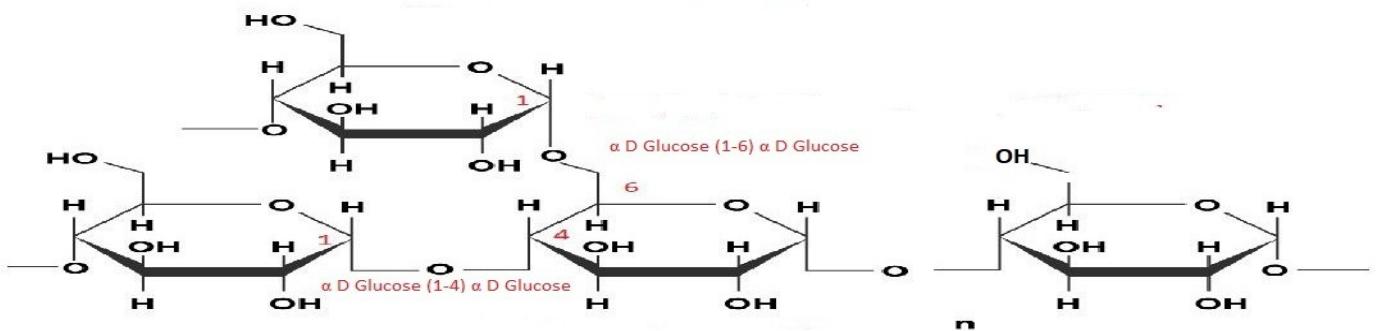
- Polysaccharides are carbohydrates that are made up of 10 or more than 10 Monosaccharide Units.
- Among more functions Storage (Starch) and structural (Cellulose) functions are most common.
- Units may be same type or different type based on this polysaccharides can be of two types
 - Homopolysaccharide
 - Heteropolysaccharide

4.5.1 HOMO POLYSACCHARIDE

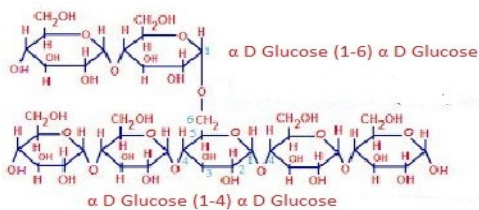
- It has 10 or more units of same type of monosaccharide.
- Starch** is a type of polysaccharide. It has two variants
 - Amylose (Water soluble)
 - Amylopectin (Water insoluble)
- Amylose is in unbranched form while the amylopectin have branches.
- It is used as a storage form of energy in plants
- Amylose is a polymer of frequent α D Glucose in (1-4) Linkage
- Amylopectin is polymer of frequent α D Glucose in (1-4) Linkage for Straight line and α D Glucose in (1-6) Linkage for branch opening
- Glycogen** is also called as animal starch hence it completely similar to that of amylopectin the only difference is more number of branches.
- It is the storage form of energy in animals. It is also present in plants that don't possess chlorophyll (eg : Yeast, Fungi)
- Cellulose** exclusively presents in Plants and it is the predominant constituent of plant cell wall.
- It is an un branched polymer of β D Glucose in (1-4) Linkage



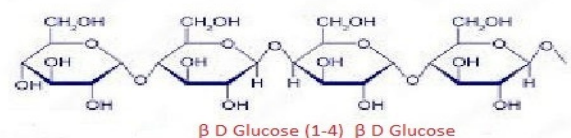
Amylose



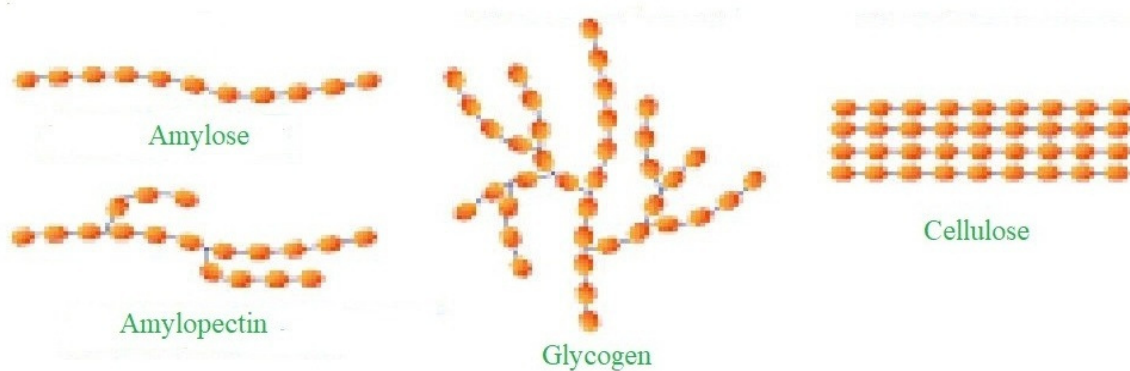
Amylopectin



Glycogen

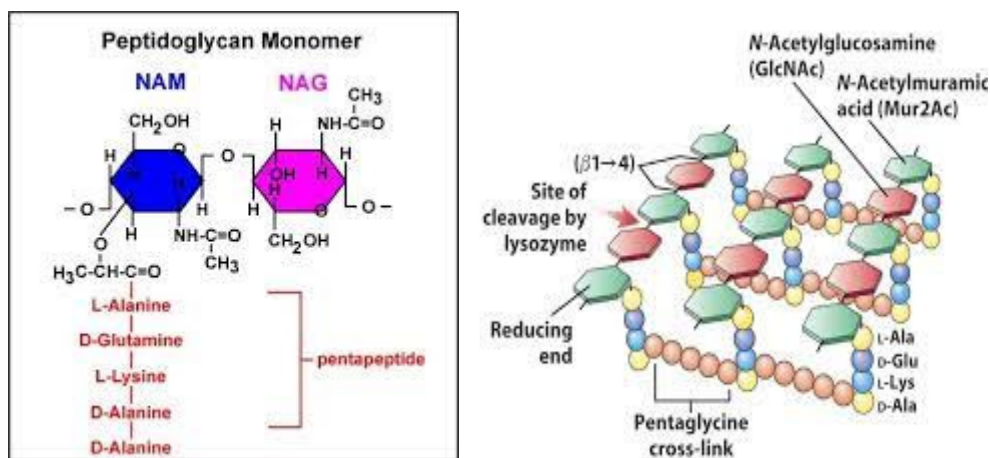


Cellulose



4.5.2 HETERO POLYACCHARIDES

- It has 10 or more units of different type of monosaccharide
- There are more numbers of hetero polysaccharides, Peptidoglycan is one of the example for hetero polysaccharide
- It is the polymer of repeating unit of NAM (N Acetyl Muramic acid) and NAG (N Acetyl Glucosamine) those are all derivatives of sugar molecule. It contain Acetyl and Penta peptide along with the sugar structure.



5. PROTEIN

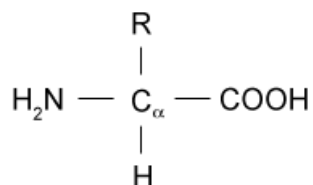
- Proteins** are defined as the biopolymer of α amino acid. It is also called as polypeptide. Aminoacids are joined by polypeptide bond.
Eg : Albumin, Globulin, Fibrinogen
- Proteins are the major constituents of all living organisms.
- They contain carbon (50 – 55%) , hydrogen (6 – 7.3 %) , Nitrogen (13 – 19) , oxygen (19 -24%) and sulphur (0-4%)
- Other elements also present in small proportions.
- Nitrogen present in the protein is used to find out the proteins present in the body fluids.

5.1 AMINOACID

- Aminoacids** are organic compound that has amino (NH_2) and carboxyl group(COOH).
- There are 300 aminoacids occurs in nature
- Among them 20 are standard aminoacids
- There is two more aminoacids present in some proteins
21st – Selenocysteine

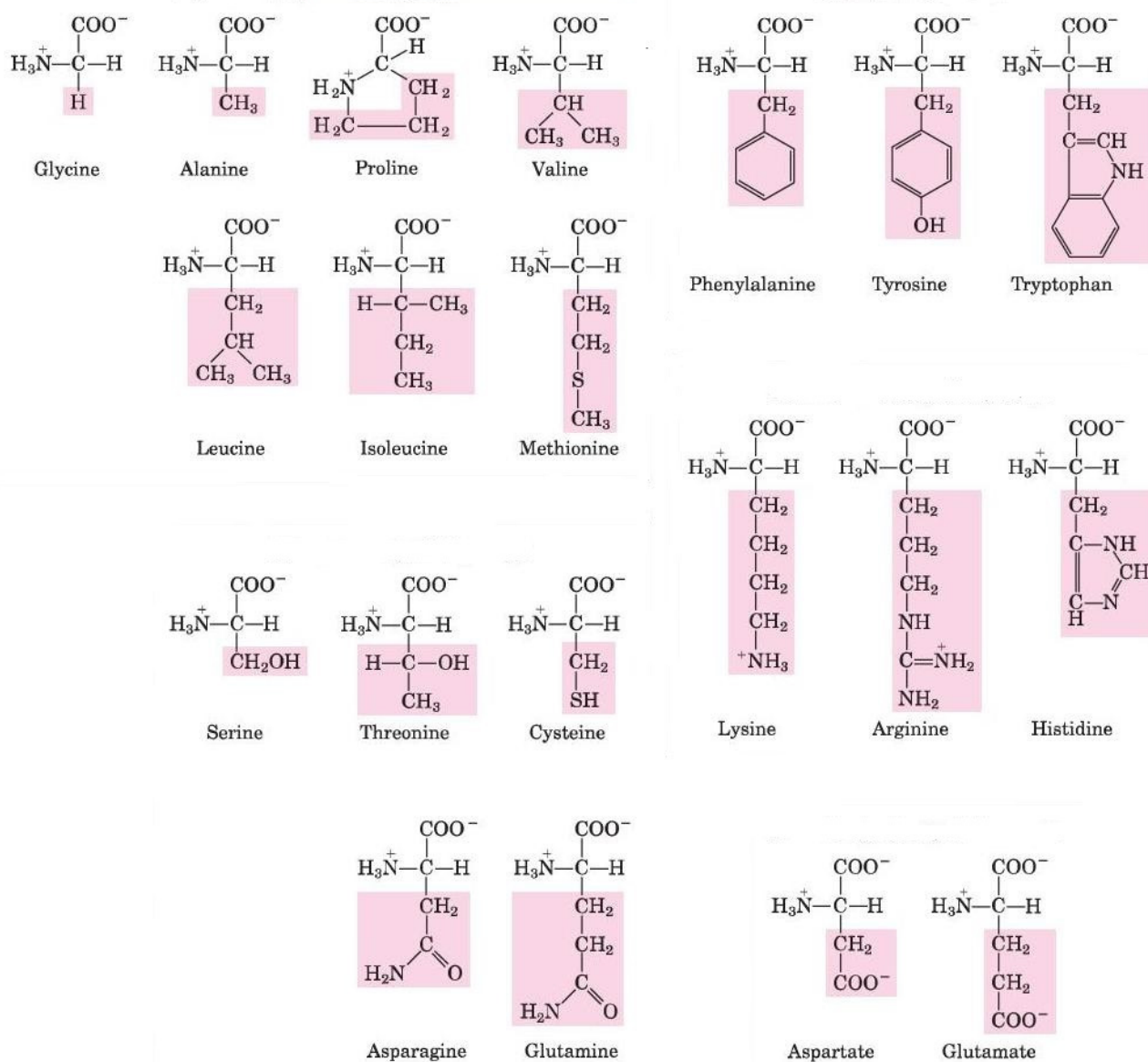
22nd - Pyrrolysine

- Proteins are synthesized by the use of amino acid controlled by genetic materials, after synthesis some amino acid form their derivatives.
- The general structure for amino acid is below



- If the amino and Carboxyl group attached in same carbon they are called as α amino acid.
- R group differs for 20 amino acids

List of 20 amino acid

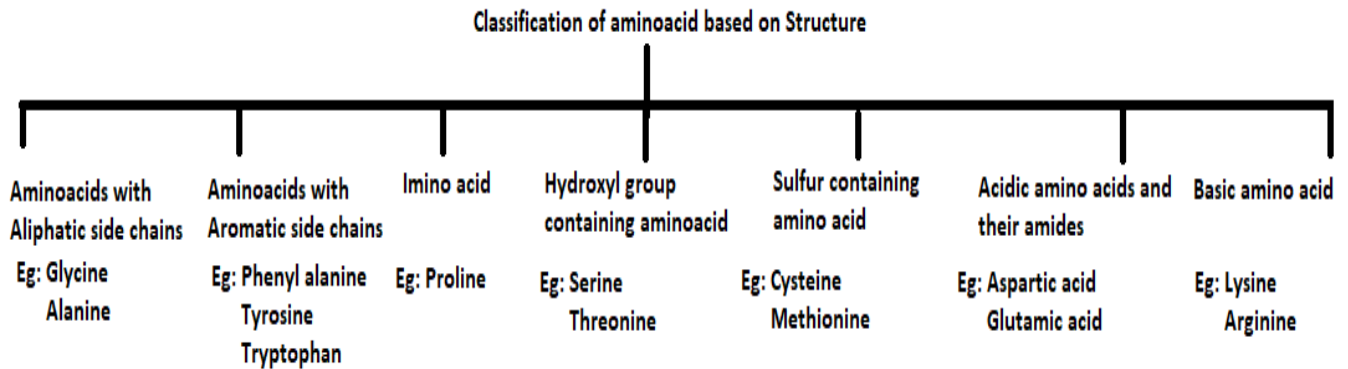


5.2 Classification of amino acid

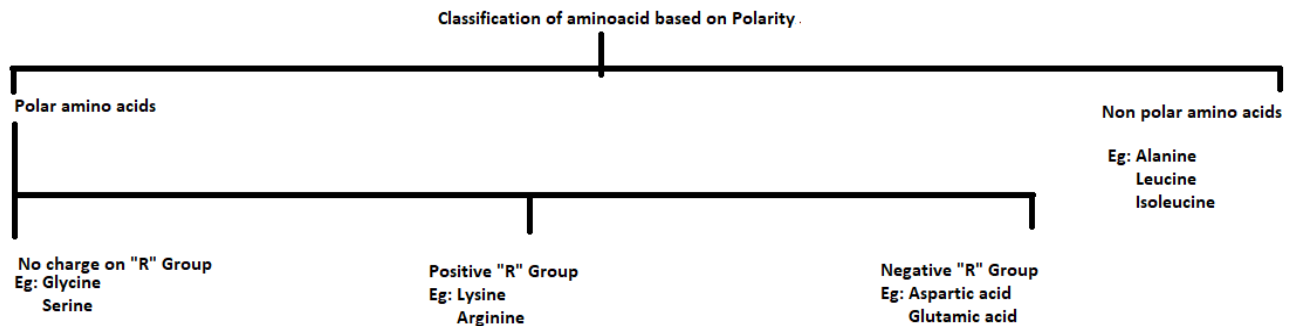
- Classification of amino acids commonly on four basis

1. Based on structure
2. Based on polarity
3. Based on metabolic fate
4. Based on nutritional importance

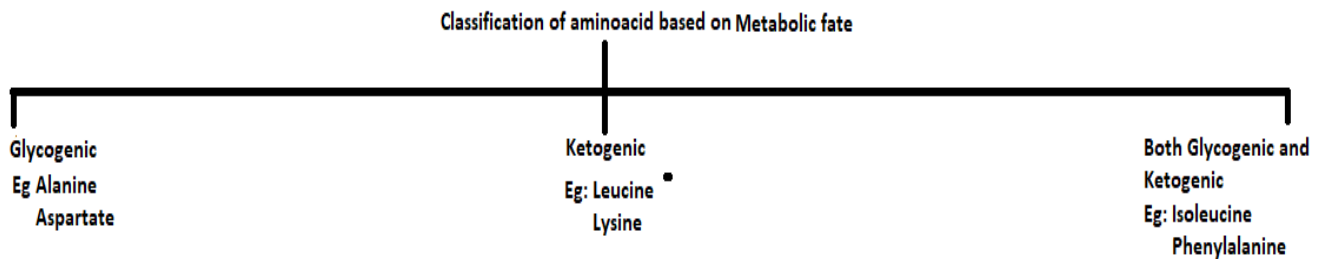
5.2.1 Classification of amino acid based on structure



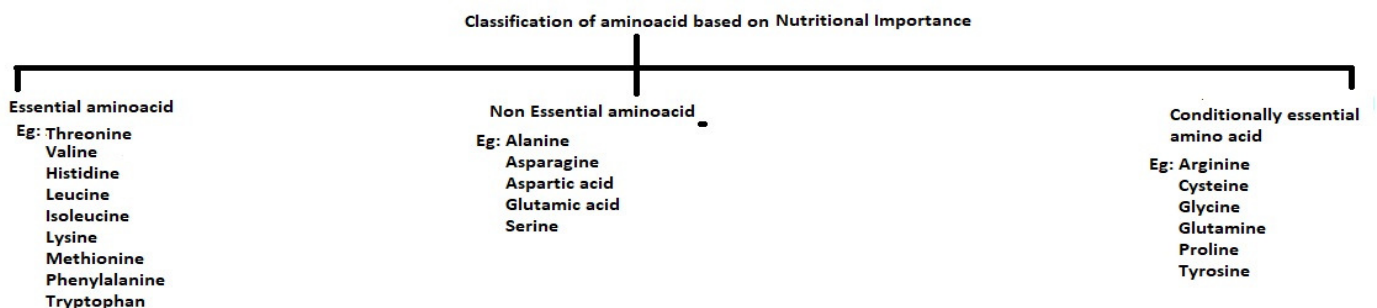
5.2.2 Classification of amino acid based on polarity



5.2.3 Classification of amino acid based on Metabolic fate

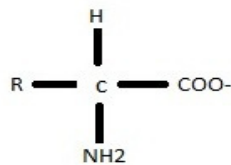


5.2.4 Classification of amino acid based on nutritional Importance

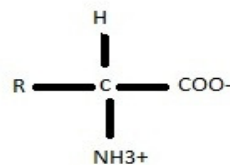


5.3 Zwitter Ion and Isoelectric Ph

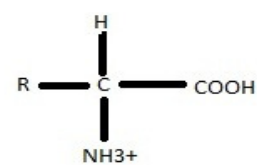
- Amino acids exist as ions according to the pH
- Zwitter ion or Dipolar ion** is a hybrid molecule containing positive and negative ionic groups.
- Isoelectric pH** is defined as the pH at which a molecule exists as a zwitter ion or dipolar ion and carries no net charge.
- Each amino acid has a specific pI value.



ANION
High pH



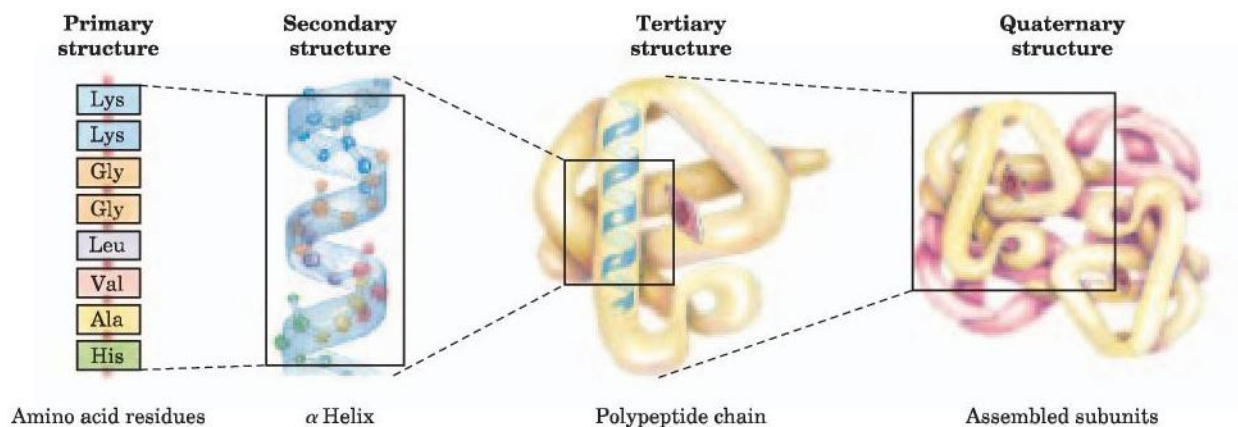
ZWITTER ION
Isoelectric pH



CATION
Low pH

5.4 Structural Organization of Protein and denaturation

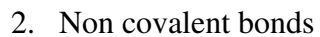
- Protein can be organized into four levels
 - Primary structure
 - Secondary structure (α helix and Beta sheet)
 - Tertiary structure
 - Quaternary structure



- The phenomenon of disorganization of native protein structure is known as **denaturation**.
- Denaturation results in the loss of secondary, Tertiary, Quaternary structure of protein.
- Physical agents responsible for denaturation include Heat, Violent shaking, X Rays, UV Radiation
- Responsible Chemical agents may be acids, alkalis, Organic solvents etc.,
- Denaturation results in the loss of both native structure and biological activity.

5.5 Bonds Responsible for protein structure

- Protein structure is stabilized by two types of bonds
 - Covalent bonds
 - 1.1 Peptide bond



2.1 Hydrogen bonds



-  Classification of protein is commonly on three basis

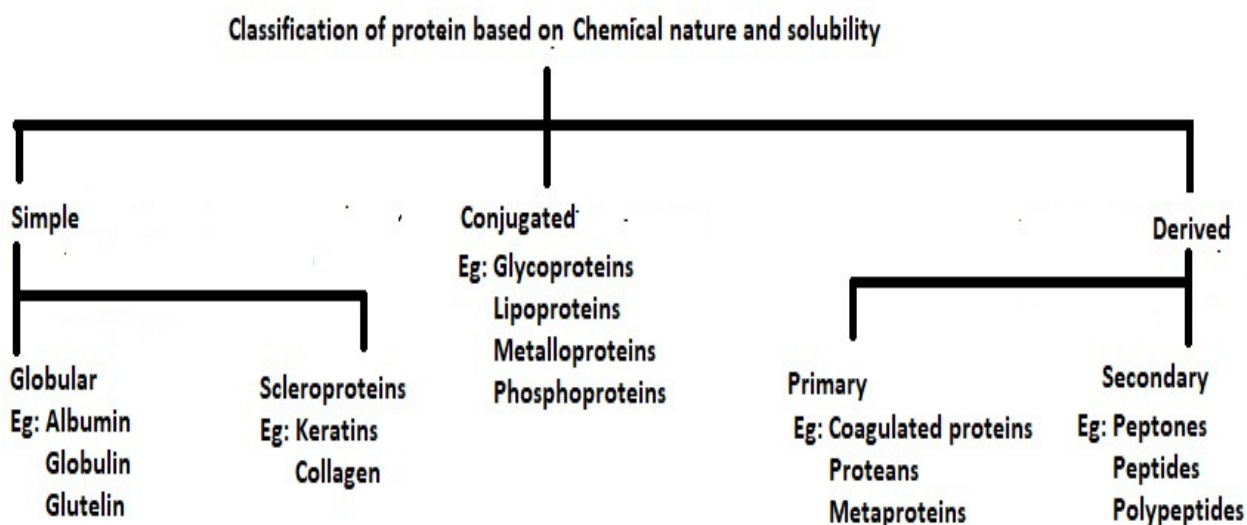
1. Classification based on function
2. Classification based on chemical nature and solubility
3. Classification based on nutritional importance

5.6.1 Classification based on function or functions of protein

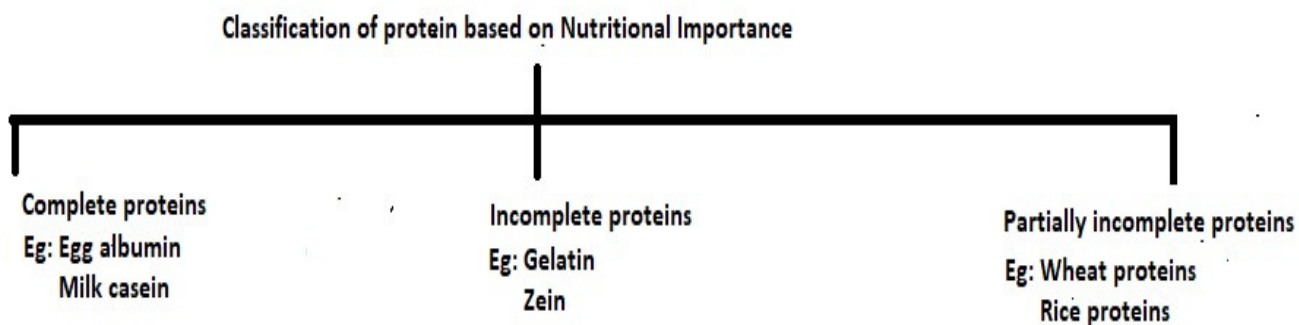
Classification of protein based on function (or) Functions of protein



5.6.2 Classification based on chemical nature and solubility



5.6.3 Classification based on nutritional importance



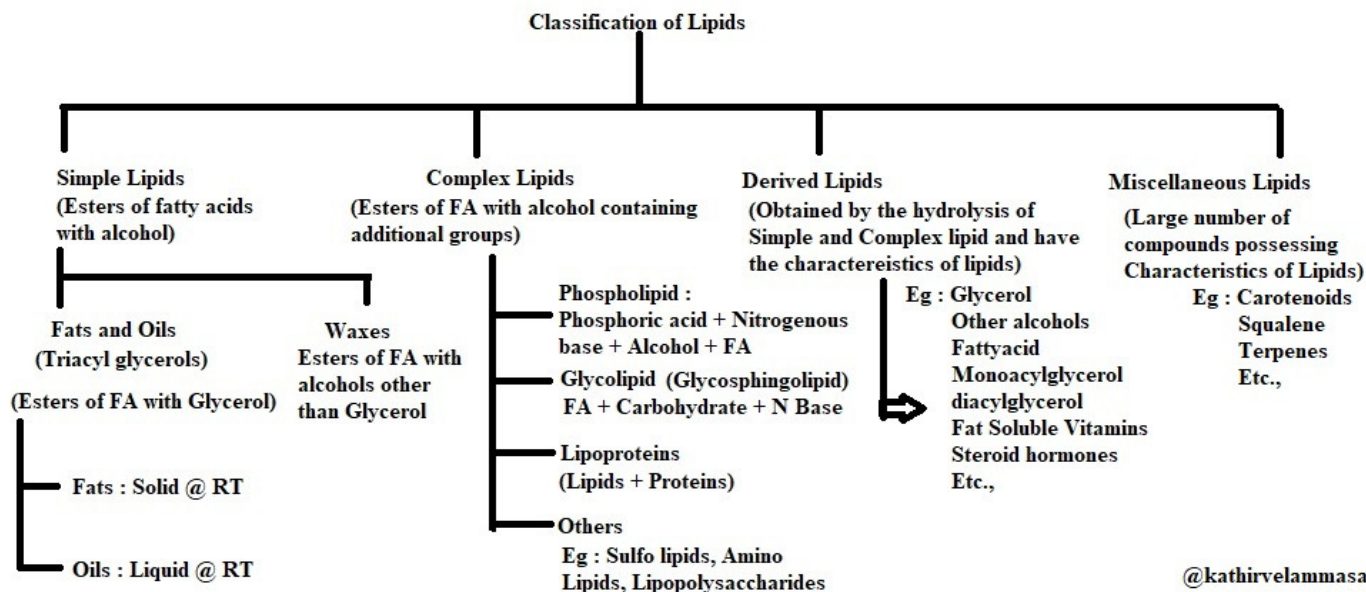
6. LIPIDS

- + Lipids are heterogenous group of compounds and therefore it is difficult to define them precisely.
- + Lipids may be regarded as organic substances relatively insoluble in water, soluble in organic solvents (alcohol, ether, etc.,) actually or potentially related to fatty acids and utilized by the living cells.
- + Unlike the polysaccharides, Protein and Nucleic acid lipids are not polymers (don't have the same repeating units/monomers).
- + Lipids are mostly small molecules.
- + Lipidomics is a study of lipids that include chemistry, Functions, Metabolism, pathology and various other aspects.

6.1 Functions of Lipid

- + They are the concentrated fuel reserve of the body (Triacylglycerol)
- + Lipids are the constituents of membrane structure and regulate the membrane permeability
- + They serve as a source of fat soluble vitamins
- + Lipids are important as cellular metabolic regulators (Steroid hormones and prostaglandins)
- + Lipid protect the internal organs, serve as insulating materials and give shape and smooth appearance to the body

6.2 Classification of Lipid



6.3 Fatty Acids

- ✚ Fatty acids are carboxylic acids with hydrocarbon side chain.
- ✚ It is mainly occur in the esterified form as major constituents of various lipids.
- ✚ They are also present as free (unesterified) fatty acid.
- ✚ Fatty acids of animal origin are much simpler than plant.
- ✚ Which often contain groups such as epoxy, keto, hydroxyl and cyclopentane ring.

6.3.1 Types of fatty acid

- ✚ **Saturated Fatty acid** doesn't contain double bonds while **unsaturated fatty acid** contains double bond.
- ✚ Fatty acids with one double bond are **monounsaturated fatty acid**.
- ✚ Fatty acids with two or more double bonds are called as **polyunsaturated fatty acids**.
- ✚ **Even carbon fatty acids** are fatty acids that has even number of carbon atoms (Usually 14 C to 20 C).
- ✚ Most fatty acid that occurs in nature is even chain fattyacid hence biosynthesis of fatty acid mainly occurs with sequential addition of 2 carbon atoms.
- ✚ Palmitic acid (16C) and Stearic acid are the most common even chain fattyacids.
- ✚ **Odd chain fatty acid** contains odd numbers of carbon.
- ✚ Propionic acid (3C) and Valeric acid ((5C) are well known odd chain fatty acid.

I. Saturated fatty acids

Acetic acid	Ethanoic acid	2 : 0	CH ₃ COOH
Propionic acid	n-Propanoic acid	3 : 0	CH ₃ CH ₂ COOH
Butyric acid	n-Butanoic acid	4 : 0	CH ₃ (CH ₂) ₂ COOH
Valeric acid	n-Pentanoic acid	5 : 0	CH ₃ (CH ₂) ₃ COOH
Caproic acid	n-Hexanoic acid	6 : 0	CH ₃ (CH ₂) ₄ COOH
Caprylic acid	n-Octanoic acid	8 : 0	CH ₃ (CH ₂) ₆ COOH
Capric acid	n-Decanoic acid	10 : 0	CH ₃ (CH ₂) ₈ COOH
Lauric acid	n-Dodecanoic acid	12 : 0	CH ₃ (CH ₂) ₁₀ COOH
Myristic acid	n-Tetradecanoic acid	14 : 0	CH ₃ (CH ₂) ₁₂ COOH
Palmitic acid	n-Hexadecanoic acid	16 : 0	CH ₃ (CH ₂) ₁₄ COOH
Stearic acid	n-Octadecanoic acid	18 : 0	CH ₃ (CH ₂) ₁₆ COOH
Arachidic acid	n-Eicosanoic acid	20 : 0	CH ₃ (CH ₂) ₁₈ COOH
Behenic acid	n-Docosanoic acid	22 : 0	CH ₃ (CH ₂) ₂₀ COOH
Lignoceric acid	n-Tetracosanoic acid	24 : 0	CH ₃ (CH ₂) ₂₂ COOH

II. Unsaturated fatty acids

Palmitoleic acid	<i>cis</i> -9-Hexadecenoic acid	16 : 1; 9	CH ₃ (CH ₂) ₅ CH = CH(CH ₂) ₇ COOH
Oleic acid	<i>cis</i> -9-Octadecenoic acid	18 : 1; 9	CH ₃ (CH ₂) ₇ CH = CH(CH ₂) ₇ COOH
Linoleic acid **	<i>cis</i> , <i>cis</i> -9,12-Octadeca-dienoic acid	18 : 2; 9, 12	CH ₃ (CH ₂) ₄ CH = CHCH ₂ CH = CH(CH ₂) ₇ COOH
Linolenic acid **	All <i>cis</i> -9,12,15-Octadecatrienoic acid	18 : 3; 9, 12, 15	CH ₃ CH ₂ CH = CHCH ₂ CH = CHCH ₂ CH = CH(CH ₂) ₇ COOH
Arachidonic acid	All <i>cis</i> -5,8,11,14-Eicosatetraenoic acid	20 : 4; 5, 8, 11, 14	CH ₃ (CH ₂) ₄ CH = CHCH ₂ CH = CHCH ₂ CH = CHCH ₂ CH = CH(CH ₂) ₃ COOH

* Total number of carbon atoms, followed by the number of double bonds and the first carbon position of the double bond(s).

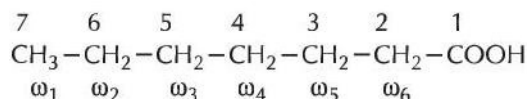
** Essential fatty acids.

- ✚ **Short chain fatty acid** represents the fatty acid with less than 6 carbon atom.
- ✚ **Medium chain fatty acid** represents 8 to 14 carbons.
- ✚ **Long chain fatty acid** represents 16 to 24 carbons.
- ✚ The fatty acid that cannot be synthesized by the body and therefore should be supplied in the diet are known as **Essential fatty acid**.
Eg : Linoleic acid,
Linolenic acid
- ✚ These are essential hence human lacks the enzyme that can introduce double bonds beyond 9 to 10.
- ✚ Certain fatty acids that become essential under some developmental or disease conditions are called as **conditionally essential fattyacid**.
Eg : Decosa hexaenoic acid (DHA)
- ✚ **Trans fatty acid** possess double bonds and are formed during hydrogenation (saturation) of natural oils.
- ✚ TFA are widely used in food industry (fast foods and packaged food) to increase the shelf life of the various food.
- ✚ It is highly detrimental to health, as their consumption is associated with increased risk of various disease including diabetes and cardio vascular disease.
- ✚ TFA have been implicated in systemic inflammation, Insulin resistance, Elevated LDL, Reduced HDL, etc. therefore TFA containing foods should be avoided in the diet.
- ✚ Margarine is the most commonly used TFA containing fat in food industry.
- ✚ **Eicosanoids** are related to eicosapolyenoic fatty acids.
- ✚ It includes Prostaglandins, Prostacyclins, Leukotrienes and Thromboxanes.
- ✚ Eicosanoids are considered as locally acting hormones with wide range of biochemical functions.

6.3.2 Nomenclature or Numbering of carbon

- ✚ Naming of fatty acid (Systematic name) is based on the hydrocarbon from which it is derived.

- ✚ Saturated fatty acid end with suffix “-anoic (eg: Octanoic acid)
- ✚ Unsaturated fatty acid end with a suffix “-enoic acid” (eg: Octadecenoic acid)
- ✚ Numbering of carbon atoms of fatty acid starts from carboxyl carbon which is taken as 1, adjacent carbon receive 2,3,4 and so on.
- ✚ Alternatively α , β , γ may be used.
- ✚ Omega numbers are numbering from methyl group of carbon atom.



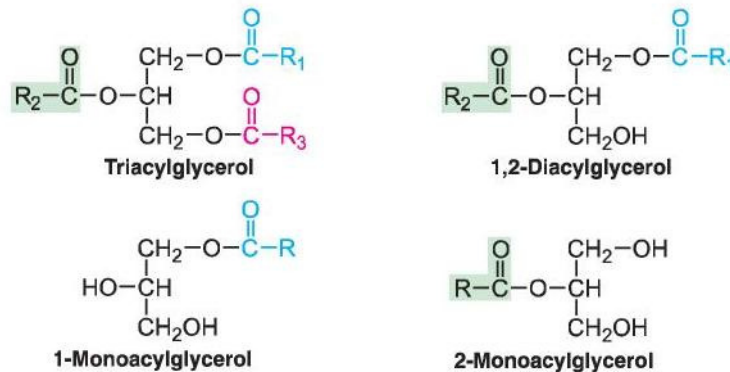
- ✚ Δ is used to represent the position of double bond from carboxyl end
- ✚ Δ^9 indicates that the double bond is between 9 and 10
- ✚ ω can be used to represent the position of double bond from methyl end
- ✚ ω^9 Indicates the double bond is between 9 and 10
- ✚ Naturally occurring fatty acid is belong to ω^9 , ω^6 , ω^3

6.3.3 Short hand representation of fatty acids

- ✚ Short hand notations are given to every fatty acid by number
- ✚ Numbers given to the fatty acid in the below order
 - Total number of carbon atom
 - Number of double bonds
 - Position of double bonds starting from carboxyl end
- ✚ Eg : Palmitic acid 16 : 0
 Oleic acid 18 : 1 ; 9
 Arachidonic acid 20 : 4 ; 5, 8, 11, 14

6.4 TRIACYL GLYCEROL

- ✚ **Triacylglycerols (or) Triglycerides (or) Neutral fats** are the esters of glycerol with fatty acid.
- ✚ **Fats and oils** that are widely distributed in both plants and animals are chemically triacylglycerol.
- ✚ They are insoluble in water.
- ✚ TGL are the most abundant group of lipids that primarily function as fuel reserves of animals.
- ✚ Adipocytes of adipose tissue, predominantly found in the subcutaneous layer and in the abdominal cavity are specialized for storage of TGL.
- ✚ Three molecules of fatty acids esterified with one molecule of glycerol is known as triacylglycerol while mono and di acyl glycerol has one and two fatty acids respectively.
- ✚ In general fatty acid attached to C1 is saturated, C2 is unsaturated and C3 can be either.
- ✚ **Simple TGL** has three same type of fatty acid
- ✚ **Mixed TGL** are more common they contain 2 or different types of fatty acids.
- ✚ TGL of plants, in general have higher content of unsaturated fatty acid compared to that of animals



6.5 PHOSPHOLIPIDS

6.5.1 Types of Phospholipids

- ✚ These are complex or compound lipids containing phosphoric acid in addition to fatty acids, Nitrogenous base and alcohol.
- ✚ There are two classes of phospholipids
 1. Glycerophospholipids (or) Phosphoglycerides – Glycerol as alcohol
 2. Sphingophospholipids (or) Sphingomyelin – Sphingosine as the alcohol
- ✚ **Glycerophospholipids** are the major phospholipids that occur in biological membranes
- ✚ There are different types of glycerophospholipids they are
 1. Phosphotidic acid
 2. Lecithin (Phosphotidyl choline)
 3. Cephaline (Phosphotidyl ethanolamine)
 4. Phosphotidyl inositol
 5. Phosphotidyl serine
 6. Plasmalogen
 7. Cardiolipin
- ✚ **Phosphotidic acid** is the simplest phospholipid.
- ✚ It doesn't occur in good concentration in the tissues.
- ✚ Basically phosphotidic acid is an intermediate in the synthesis of TGL and Phospholipids.
- ✚ The other glycerophospholipids containing different nitrogenous base or other groups may be regarded as the derivatives of phosphotidic acid.
- ✚ **Lecithins** are the most abundant group of phospholipids in the cell membranes.
- ✚ Chemically lecithin is a phosphotidic acid with choline as the base
- ✚ It represents the storage form of body's choline
- ✚ Dipalmitoyl lecithin is the important phosphotidylcholine present in the lungs that act as a lung surfactant
- ✚ Lysolecithin is formed by removal of the fatty acid either at C1 or C2 of lecithin.
- ✚ In **Cephalins** ethanolamine is the nitrogenous base
- ✚ **Phosphotidyl inositol** is the form of glycerophospholipid where myo-Inositol is attached to phosphotidic acid.
- ✚ This is an important component of the cell membranes.
- ✚ The action of certain hormones (Oxytocin and Vasopressin) is mediated through PI.
- ✚ The amino acid serine is present in the **Phosphotidyl serine**.
- ✚ It is also found in certain tissues and plays a major role in apoptosis.
- ✚ When a fatty acid is attached by an ether linkage at C1 of glycerol in the glycerophospholipid, the resultant compound is **plasmalogen**.
- ✚ Choline, Inositol and Serine may substitute ethanolamine to give other plasmalogens.
- ✚ **Cardiolipin** is named because it was first isolated from heart muscle. Structurally a cardiolipin consists of two molecules of phosphotidic acid held by an additional glycerol through phosphate group.

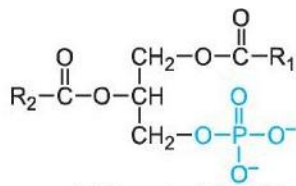
- ✚ It is an important component for inner mitochondrial membrane and essential for mitochondrial function.
- ✚ Decreased cardiolipin level may result in mitochondrial dysfunction, aging, hypothyroidism, Cardioskeletal myopathy (Barth syndrome). It is the only phosphoglyceride that possess antigenic property.
- ✚ In recent years detection of anti-cardiolipin antibodies is used as a diagnostic tool in the evaluation of embryo transfer and Organ transplantation.
- ✚ **Sphingomyelins** contain sphingosine as amino alcohol.
- ✚ Sphingosine is attached by an amide linkage to a fatty acid to produce ceramide.
- ✚ Sphingomyelins are important constituents of myelin and are found in good quantity in brain and nervous tissue.
- ✚ It is believed that sphingomyelins are involved in cell signaling and in apoptosis.

6.5.2 Functions of phospholipids

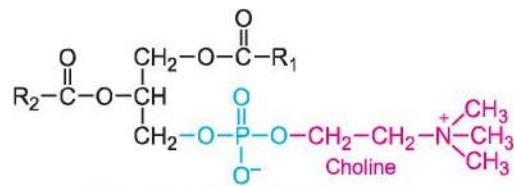
- ✚ In association with proteins, phospholipids form the structural components of membranes and regulate membrane permeability.
- ✚ Phospholipids in the mitochondria maintain the conformation of electron transport chain components and thus cellular respiration.
- ✚ Phospholipids participate in the absorption of fat from the intestine.
- ✚ Phospholipids are essential for the synthesis of different lipoproteins and thus participate in the transport of lipids.
- ✚ Accumulation of fat in liver (fatty liver) can be prevented by phospholipids, hence they are regarded as lipotropic factors.
- ✚ Arachidonic acid an unsaturated fatty acid liberated from phospholipid serves as a precursor for the synthesis of eicosanoids.
- ✚ It participate in the reverse cholesterol transport and thus help in the removal of cholesterol from the body.
- ✚ Phospholipids acts as surfactants for instance Dipalmitoyl phosphatidyl choline is an important lung surfactant.
- ✚ Cephalins an important group of phospholipids participate in the blood clotting.
- ✚ Phosphatidyl inositol is the source of second messengers – Inositol tri phosphate and diacyl glycerol that are involved in the action of some hormones.

6.6 Glycolipids

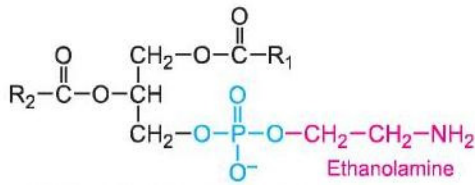
- ✚ Glycolipids (Glycosphingolipids) are important constituents of cell membrane and nervous tissues (Particularly the brain).
- ✚ They occur as cell surface carbohydrates to form glycocalyx in plasma membranes.
- ✚ **Cerebrosides** are the simplest form of glycolipids. They contain a ceramide (sphingosine attached to a fatty acid) and one or more sugars.
- ✚ Galactocerebroside (Galactosyl ceramide) and gluco cerebroside are the most important glycolipids.
- ✚ Sulfagalactosyl ceramide is the sulfatide derived from galactosylceramide.
- ✚ **Gangliosides** are predominantly found in ganglions and are the most complex form of glycosphingolipids.
- ✚ They are the derivatives of cerebrosides and contain one or more molecules of N Acetylneuraminic acid, the most important sialic acid.
- ✚ The most important gangliosides present in the brain are GM1, GM2, GD, GT.
- ✚ G Represents ganglioside while M, D, T indicate mono, di, tri sialic acid residues and the number denotes the carbohydrate sequence attached to the ceramide.
- ✚ **Globosides** are the type of glycolipid with two or more sugars linked to ceramide the sugars usually present are glucose and galactose.
- ✚ Lactosyl ceramide (Ceramide, Galactose, Glucose) is present in erythrocyte membrane.



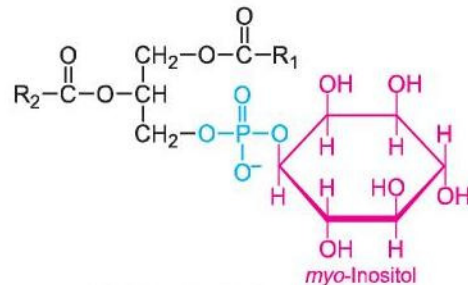
(1) **Phosphatidic acid**



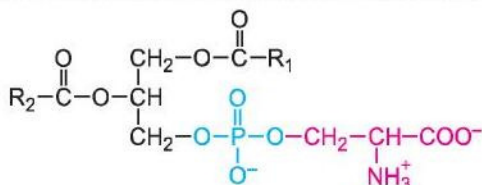
(2) **Lecithin** (phosphatidylcholine)



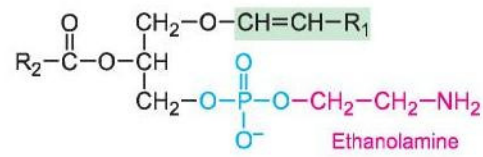
(3) **Cephalin** (phosphatidylethanolamine)



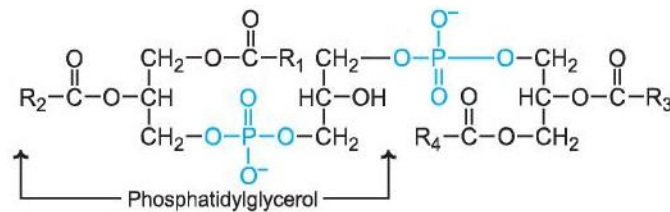
(4) **Phosphatidylinositol**



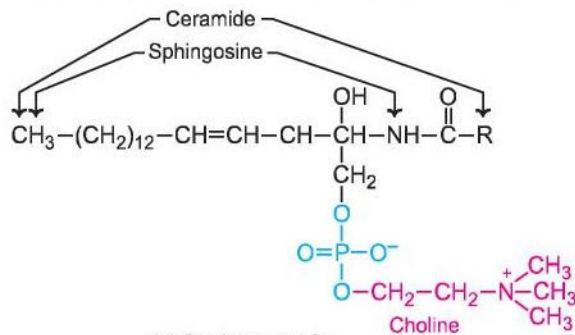
(5) **Phosphatidylserine**



(6) **Plasmalogen** (phosphatidylethanolamine)



(7) **Cardiolipin** (diphosphatidylglycerol)



(8) **Sphingomyelin**

6.7 Lipoproteins

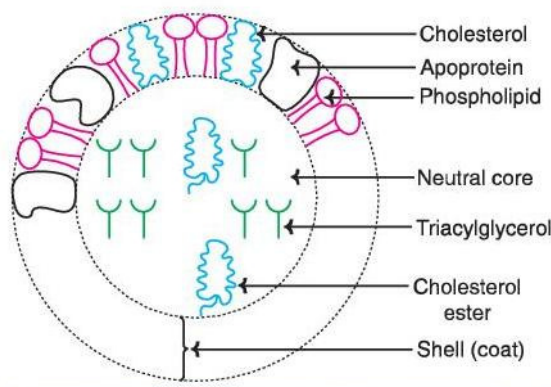
6.7.1 Types of Lipoproteins

- Lipoproteins are molecular complexes of lipids with proteins.
- They are the transport vehicles for lipids in the circulation.
- There are five types of lipoproteins
 1. Chylomicrons
 2. VLDL (Very low density lipoprotein)
 3. LDL (Low density lipoprotein)
 4. HDL (High density lipoprotein)
 5. Free fattyacid albumin complexes

- ✚ **Chylomicrons** are synthesized in the intestine and transport exogenous (dietary) triacyl glycerol to various tissues.
- ✚ They consist of highest lipid quantity (99%) and lowest concentration of protein (1%).
- ✚ The chylomicrons are least in density and large in size among the lipoproteins.
- ✚ **Very low density lipoprotein** is produced in the liver and intestine,
- ✚ It is responsible for the transport of endogenously synthesized TGL.
- ✚ **Low density lipoprotein** formed from the VLDL in the blood circulation.
- ✚ They transport cholesterol from liver to other tissues.
- ✚ **High density lipoprotein** are mostly synthesized in liver.
- ✚ HDL particles transport cholesterol from peripheral tissues to liver (Reverse cholesterol Transport)
- ✚ Free fatty acids in the in the circulation are in a bound form to albumin this is called as **free fatty acid – Albumin**
- ✚ Each molecule of albumin hold about 20 – 30 molecules of free fatty acid.
- ✚ This lipoprotein cannot be separated by electrophoresis.

6.7.2 Structure of Lipoprotein

- ✚ A lipoprotein basically consist of a neutral lipid core (With TGI or Cholesteryl esters) surrounded by a coat shell of phospholipids, Apoproteins and cholesterol
- ✚ The polar portions of phospholipids and cholesterol are exposed on the surface of lipoproteins so that lipoproteins are soluble in water.



6.8 Steroids

- ✚ Steroids are the compounds containing a cyclic steroid nucleus (or ring) namely cyclopentanoperhydrophenanthrene (CPPP).
- ✚ It consist of phenanthrene nucleus (rings A, B & C) to which a cyclopentane ring (D) is attached.
- ✚ The steroid nucleus represents saturated carbons, unless specifically shown as double bonds.
- ✚ The methyl side chains attached (18&19) to carbons 10 and 13 are shown as single bonds.
- ✚ At carbon 17, steroids usually contain a side chain.
- ✚ There are several steroids in the biological systems, these include
 1. Cholesterol
 2. Bile acids
 3. Vitamin D
 4. Sex hormones
 5. Adrenocortical hormones
 6. Sitosterols
 7. Cardiac glycosides
 8. Alkaloids
 9. Etc.,
- ✚ If the steroid contains one or more hydroxyl groups it is commonly known as sterol.

6.8.1 Cholesterol

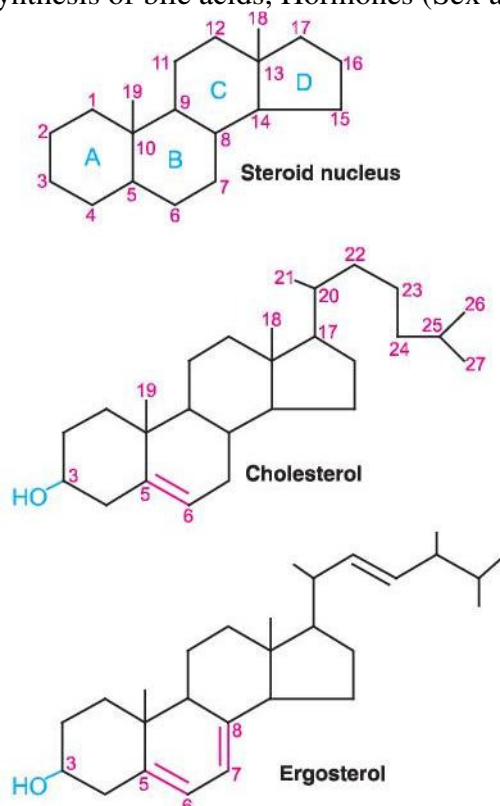
- ✚ Cholesterol exclusively found in animals is the most abundant animal sterol.
- ✚ It is widely distributed in all cells and is a major component of cell membranes and lipoproteins.
- ✚ Cholesterol was first isolated from bile. Cholesterol literally means the “Solid alcohol from bile”.

Structure of cholesterol

- ✚ The structure of cholesterol contain, one hydroxyl group at C3 and a double bond between C5 and C6.
- ✚ An 8 carbon aliphatic side chain is attached to C17.
- ✚ Cholesterol contains total of 5 methyl groups.
- ✚ Due to the presence of an –OH group cholesterol is weekly amphiphilic.
- ✚ As a structural component of plasma membranes, cholesterol is an important determinant of membrane permeability properties.
- ✚ The occurrence of cholesterol is much higher in the membranes of sub cellular organelles.
- ✚ Cholesterol is found in association with fatty acids to form cholesteryl esters. (Esterification occurs at the OH group of C3)

Functions of Cholesterol

- ✚ Cholesterol is a poor conductor of heat and electricity, since it has high dielectric constant, it is present in abundance in nervous tissues.
- ✚ Cholesterol functions as an insulating cover for the transmission of electrical impulses in the nervous tissue.
- ✚ Participate in the membrane structure and function.
- ✚ Helps in the synthesis of bile acids, Hormones (Sex and Cortical) and vitamin D.



6.8.2 Ergosterol

- ✚ Ergosterol occurs in plant.
- ✚ It is also found as a structural component of membranes in yeast and fungi.
- ✚ It is an important precursor for vitamin D.
- ✚ When exposed to light the ring B of ergosterol opens and it is converted to ergocalciferol, a compound containing vitamin D activity.

- The other sterols present in plant cells include Stigmasterol and β -sitosterol.

7. NUCLEIC ACID

7.1 Introduction

- Nucleic acids are the polymers of nucleotides or poly nucleotides.
- They are strongly acidic in nature and negatively charged at physiological pH.
- There are two types of Nucleic acid
 - DNA – Deoxyribonucleicacid
 - RNA - Rinonucleicacid

7.2 Functions of Nucleic acid

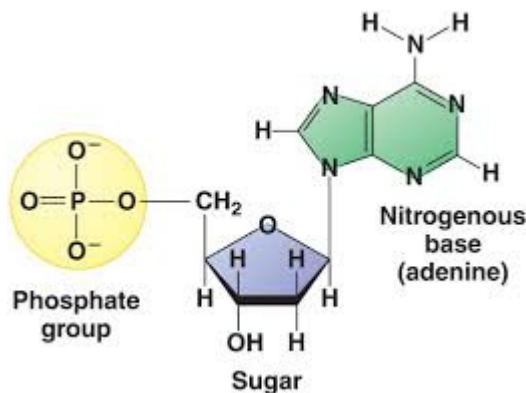
- One type of Nucleic acid called as DNA is a chemical basis of heredity and may be regarded as the reserve bank of genetic information.
- Every aspect of cellular function is under the control of DNA.
- DNA is organized into gene that is responsible for protein synthesis
- Ribosomal RNA, a type of nucleic acid responsible in the structure of Ribosome.
- mRNA and tRNA helps in the protein synthesis.
- The interrelationship of these three classes of biomolecules (DNA, RNA and Protein) constitutes the central dogma of molecular biology or more commonly the central dogma of life.

7.3 Nucleotides

- Nucleotides are building blocks of Nucleic acids.
- It is composed of
 - Nitrogenous base
 - Pentose sugar (Ribose or Deoxy Ribose)
 - Phosphate group
- There is an another term called as **Nucleoside** which include
 - Pentose sugar
 - Nitrogenous base
- So Nucleotide may a combination of Nucleoside + Phosphate group
- There are 8 type of nucleotide present based on nitrogenous base and pentose sugar

<i>Base</i>	<i>Ribonucleoside</i>	<i>Ribonucleotide (5'-monophosphate)</i>	<i>Abbreviation</i>
Adenine (A)	Adenosine	Adenosine 5'-monophosphate or adenylate	AMP
Guanine (G)	Guanosine	Guanosine 5'-monophosphate or guanylate	GMP
Cytosine (C)	Cytidine	Cytidine 5'-monophosphate or cytidylate	CMP
Uracil (U)	Uridine	Uridine 5'-monophosphate or uridylate	UMP
<i>Base</i>	<i>Deoxyribonucleoside</i>	<i>Deoxyribonucleotide (5'-monophosphate)</i>	<i>Abbreviation</i>
Adenine (A)	Deoxyadenosine	Deoxyadenosine 5'-monophosphate or deoxyadenylate	dAMP
Guanine (G)	Deoxyguanosine	Deoxyguanosine 5'-monophosphate or deoxyguanylate	dGMP
Cytosine (C)	Deoxycytidine	Deoxycytidine 5'-monophosphate or deoxycytidylate	dCMP
Thymine (T)	Deoxythymidine	Deoxythymidine 5'-monophosphate or deoxythymidylate	dTMP

- The structure of deoxyadenosine is given below.



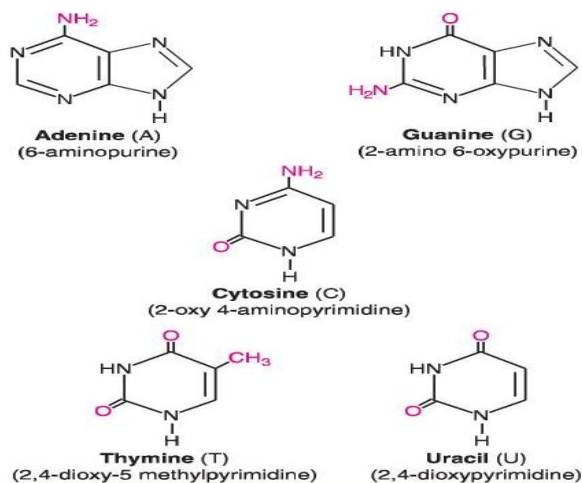
7.4 Functions of nucleotides

- ✚ It function as the monomeric unit for nucleic acid
- ✚ Involved in metabolic functions such as Energy metabolism, Protein Synthesis, etc.,
- ✚ Nucleotides are structural components of some coenzymes of B Complex vitamins eg: FAD and NAD.,
- ✚ Sugar Derivative of nucleotide namely UDP Glucose participate in the synthesis of glycogen.
- ✚ Lipid derivative of nucleotides namely CDP Acylglycerol is an intermediate in lipid biosynthesis.
- ✚ c AMP and and c GMP are second messengers for some hormonal action.
- ✚ GTP and GDP are involved in a cascade of event of signal transduction pathways.
- ✚ Synthetic analogs of nucleotides are employed in the treatment of cancer, AIDS, suppression of immune response during organ transplantation.

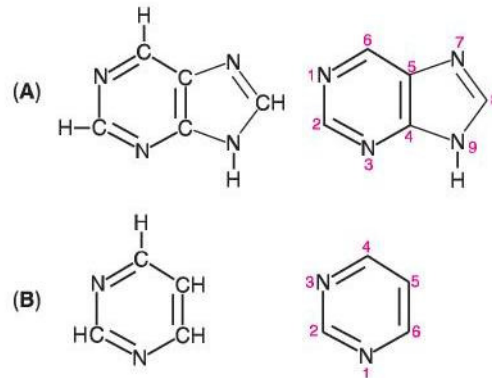
7.5 Nitrogenous base

- ✚ Nitrogenous base is one component of nucleotide
- ✚ It is subdivided into five different compounds
 1. Adenine (A) – 6 aminopurine
 2. Guanine (G) – 2 amino 6 oxypurine
 3. Cytosine (C) – 2 oxy 4 aminopyrimidine
 4. Thymine (T) – 2,4 dioxy 5 Methylpyrimidine
 5. Uracil (U) – 2,4 dioxy pyrimine
- ✚ Among them adenine and guanine are **Purine** category
- ✚ Cytosine, Thymine and Uracil (Present in RNA) are **Pyrimidine** category.
- ✚ Purine and Pyrimidine category is based on the rings present in the particular nitrogenous base.

7.5.1 Structure of Nitrogenous base

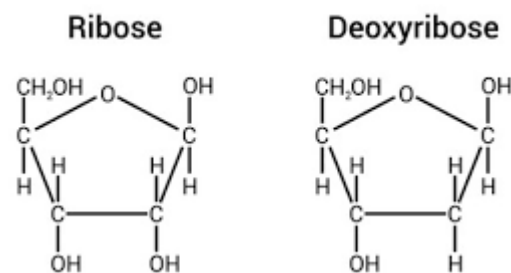


7.5.2 Numbering of Nitrogenous base

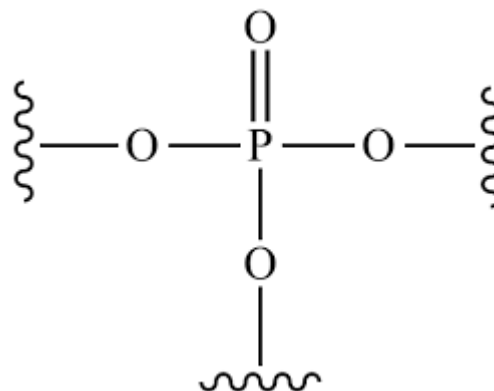


7.6 Pentose sugar and Phosphate group

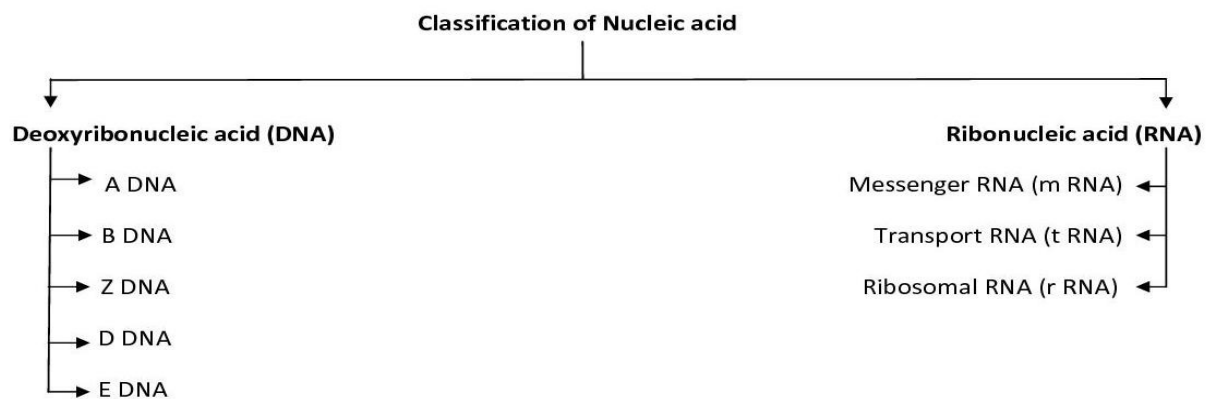
7.6.1 Pentose sugar



7.6.2 Phosphate Group



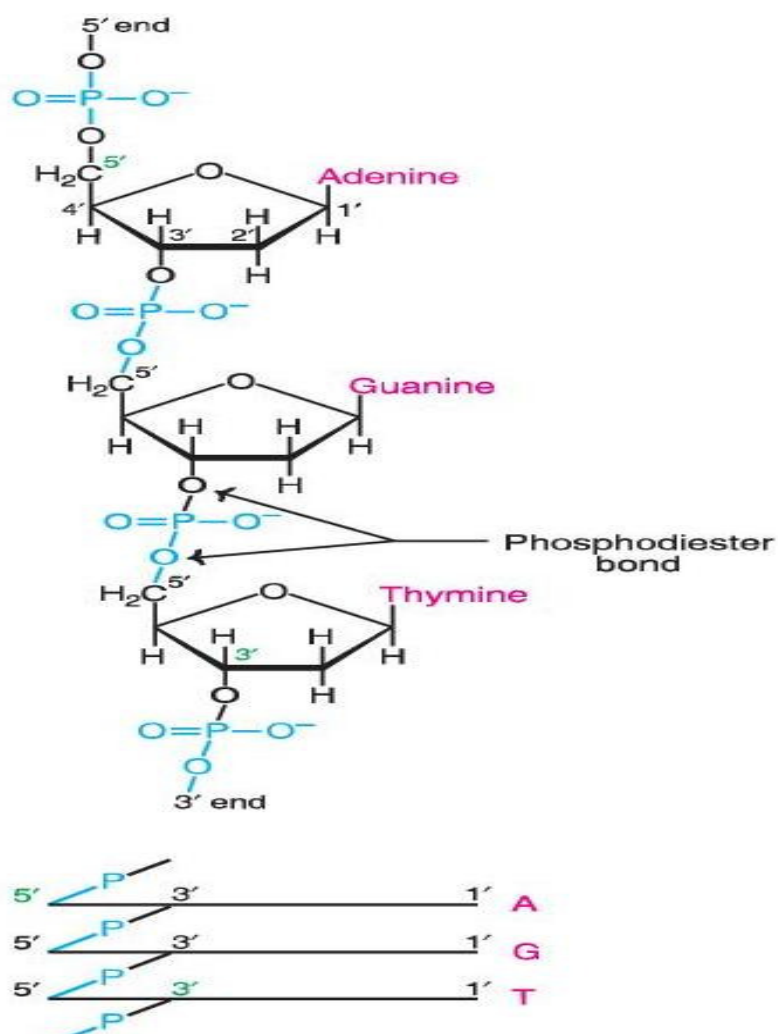
7.7 Classification of Nucleic acid



7.8 DNA

- ✚ DNA is a polymer of Dexoyribo nucleotides.
- ✚ It is composed of monomeric unit namely
 1. Deoxy adenylate (d AMP)
 2. Deoxy Guanylate (d GMP)
 3. Deoxy cytidylate (d CMP)
 4. Deoxy Thymidylate (d TMP)
- ✚ Nitrogenous bases present in DNAs are
 1. Adenine
 2. Guanine
 3. Thymine
 4. Cytocine
- ✚ DNA has the Deoxyribose sugar.

7.8.1 Structure of DNA



- ✚ The monomeric deoxyribonucleotides in DNA are held together by 3',5' phosphodiester bridges.
- ✚ Short hand notation for polynucleotide is also given above

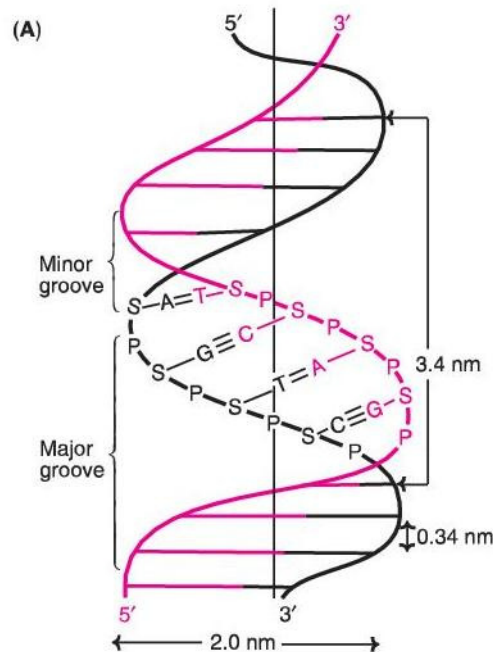
7.8.2 Chargaff's rule of DNA Composition

- ✚ Erwin chargaff in late 1940s quantitatively analysed the DNA hydrolysates from different species.
- ✚ He observed that in all the species he studied, DNA had equal number of adenine and thymine residues (A=T) and Guanine and Cytosine (G=C).

- ✚ This is known as Chargaff's rule of molar equivalence between the purines and pyrimidines in DNA structure.
- ✚ The double helical structure of DNA derives its strength from Chargaff's rule.
- ✚ Single stranded DNA and RNA won't obey this rule. But the double stranded RNA (present in some viruses) and DNA obeys the Chargaff's rule.

7.8.3 DNA double helix (Structure of DNA)

- ✚ The double helical structure of DNA was proposed by James Watson and Francis Crick in 1953.
- ✚ So this is also called as Watson and Crick model of DNA.
- ✚ The structure of DNA double helix is comparable to a twisted ladder.



- ✚ The DNA is a right-handed double helix.
- ✚ It consists of two polynucleotide chains twisted around each other on a common axis.
- ✚ The two strands are antiparallel. One strand runs in the 5' to 3' direction while the other strand runs in the 3' to 5' direction.
- ✚ The width of a double helix is $20 \text{ \AA}$ (2 nm).
- ✚ Each turn of the helix is $34 \text{ \AA}$ (3.4 nm) with 10 pairs of nucleotides, so each pair is placed at a distance of $3.4 \text{ \AA}$ (0.34 nm).
- ✚ Each strand of DNA has a hydrophilic deoxyribose phosphate backbone on the outside. And the hydrophobic nitrogenous bases are stacked inside.
- ✚ The two polynucleotide chains are not identical but complementary to each other due to base pairing.
- ✚ The two strands are held together by hydrogen bonds formed by complementary base pairs.
- ✚ The adenine and thymine pair has 2 hydrogen bonds, while guanine and cytosine have 3 hydrogen bonds.
- ✚ Base pairing will be specific; that is, adenine pairs with thymine itself and guanine pairs with cytosine itself.
- ✚ The genetic information resides on one strand that is called as template or sense strand. The opposite is the antisense strand.
- ✚ The double helix has major grooves and minor grooves along the phosphodiester backbone. Proteins interact with DNA at these grooves without disrupting the base pairs and double helix.

Conformations of DNA double helix

- ✚ Variation in the conformation of the nucleotides of DNA is associated with conformational variants of DNA.
- ✚ The structure has 6 variants
 1. A DNA
 2. B DNA
 3. C DNA
 4. D DNA
 5. E DNA
 6. Z DNA
- ✚ Among these 6 variants A, B, Z are very important.
- ✚ B DNA (Normal Double helix) is predominant under physiological conditions.

7.8.4 Comparison of Features of A, B, Z DNA

Feature	B-DNA	A-DNA	Z-DNA
Helix type	Right-handed	Right-handed	Left-handed
Helical diameter (nm)	2.37	2.55	1.84
Distance per each complete turn (nm)	3.4	3.2	4.5
Rise per base pair (nm)	0.34	0.29	0.37
Number of base pairs per complete turn	10	11	12
Base pair tilt	+19°	-1.2° (variable)	-9°

7.8.5 Denaturation of DNA Strands

- ✚ The two strands of DNA helix are held together by hydrogen bonds.
- ✚ Disruption of hydrogen bonds (by change in pH or increase in Temperature results in the the separation of polynucleotide strands.
- ✚ Phosphodiester bonds are not broken by denaturation.
- ✚ This phenomenon of loss of helical structure of DNA is known as **denaturation**.
- ✚ **Renaturation or reannealing** is the process in which the separated complementary DNA form a double helix.

7.9 RNA

- ✚ RNA is a polymer of Ribonucleotides held together by 3',5' phosphodiester bridges.
- ✚ Although RNA has certain similarities with DNA structure, they have specific differences.
 1. Pentose sugar – Ribose
 2. Pyrimidine – Uracil for Thymine
 3. Strand – Single strand
 4. Chargaff's rule – Not obeyed

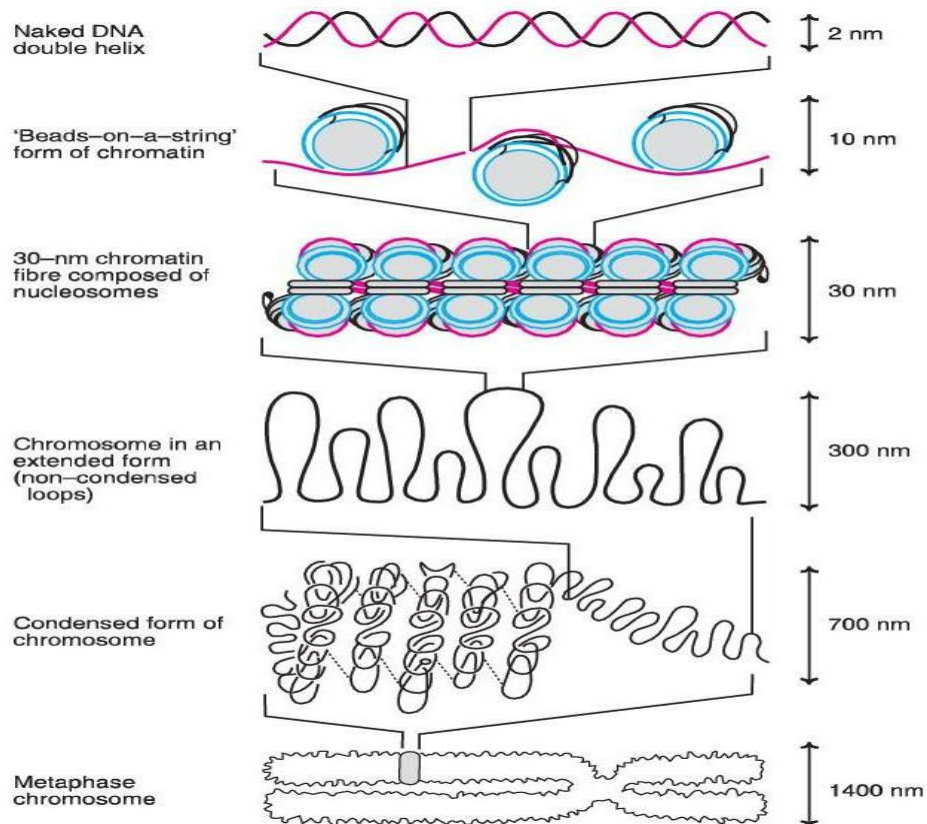
7.9.1 Types of RNA

- ✚ There are three major types of RNA by function
 1. Messenger RNA
 2. Transfer RNA
 3. Ribosomal RNA
- ✚ Besides these RNAs other types of RNA also present in the cells.
- ✚ Types of RNA with their function is tabled here

Type of RNA	Abbreviation	Function(s)
Messenger RNA	mRNA	Transfers genetic information from genes to ribosomes to synthesize proteins.
Heterogeneous nuclear RNA	hnRNA	Serves as precursor for mRNA and other RNAs
Transfer RNA	tRNA	Transfers amino acid to mRNA for protein biosynthesis.
Ribosomal RNA	rRNA	Provides structural framework for ribosomes.
Small nuclear RNA	snRNA	Involved in mRNA processing.
Small nucleolar RNA	snoRNA	Plays a key role in the processing of rRNA molecules.
Small cytoplasmic RNA	scRNA	Involved in the selection of proteins for export.
Transfer-messenger RNA	tmRNA	Mostly present in bacteria. Adds short peptide tags to proteins to facilitate the degradation of incorrectly synthesized proteins.

7.10 Chromosome

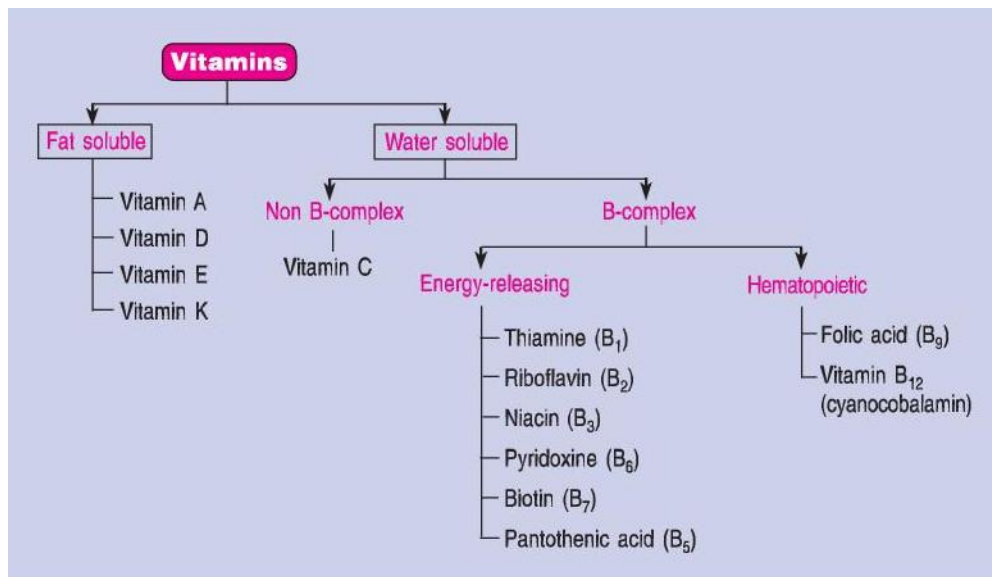
- In humans a 2 meter long DNA is packed in a nucleus of about 10 micrometer diameter.
- This is made possible by a compact and marvelous packaging and organization of DNA inside in cell called as **chromosome**.
- In prokaryotic cells, the DNA is organized as a single chromosome in the form of a double stranded circle.
- In the eukaryotic cell the DNA is associated with various proteins to form **chromatin**
- Which then gets organized into compact structures namely chromosomes.
- The DNA double helix is wrapped around the core proteins namely **Histones**.
- Each core with two turns of DNA around it is termed as a **Nucleosome**.



8. Vitamins

- ✚ Vitamins are low molecular weight organic compounds indispensable for the normal activity of the organism.
- ✚ Their absence causes deficiency symptoms.
- ✚ Most of the vitamins or their derivatives are coenzymes which are essential for many important enzymatic reactions in the cells.
- ✚ Vitamins are required in small quantities for a variety of biochemical functions in our body.
- ✚ Most of them cannot be synthesized by the body and must be supplied through the diet.
- ✚ Unlike carbohydrates and lipids, vitamins are not metabolized **for providing energy**.

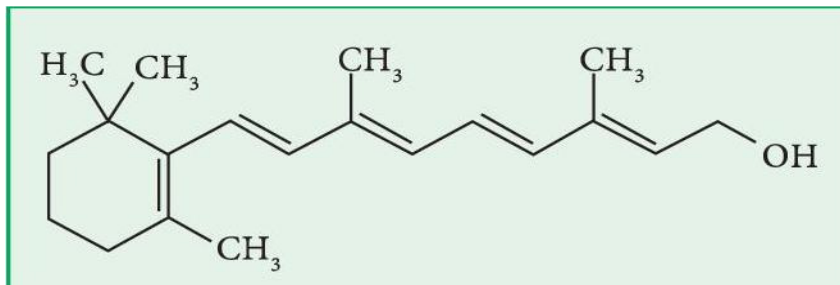
8.1 Classification



8.1.1 Fat soluble Vitamin

8.1.1.1 Vitamin A

- ✚ Vitamin A is available only in animal origin foods.
- ✚ There are three forms of vitamin A in animal
 1. Retinol
 2. Retinal
 3. Retinoic acid
- ✚ In plant exist in provitamin form (Carotenoids).
- ✚ Beta carotene is most active carotenoids.
- ✚ One molecule of carotene yields two molecule of vitamin A



Function of Vitamin A

- ✚ Vision – Synthesis of visual pigment Rhodopsin

- ✚ Bone Growth – Control Osteoplastic and Osteoclastic activity
- ✚ To maintain the integrity of epithelial cells
- ✚ In absence of vitamin A, keratinization occurs which causes reduce resistance for entry of infective organism. So it is called as anti infective vitamin.
- ✚ It promotes fertility
- ✚ Beta carotene acts as antioxidant.

Sources

- ✚ Animal source : Fish liver oils, Egg yolk, Milk fat
- ✚ Plant source : Carrot, all green leaves

RDA

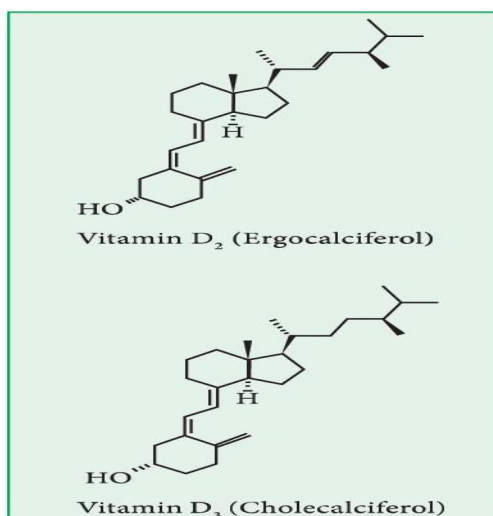
- ✚ 5000 IU

Deficiency

- ✚ Night Blindness
- ✚ Xerophthalmia
- ✚ Keratinization of epithelium
- ✚ Reduced Reproductive Performance
- ✚ Bone Deformities
- ✚ Nervous lesion
- ✚ Congenital Blindness

8.1.1.2 Vitamin D

- ✚ Vitamin D is a sterol compound.
- ✚ It is represented by a group of steroids occurring chiefly in animals, plants and yeast.
- ✚ There are two distinct forms of Vitamin D
 1. Vitamin D₂
 2. Vitamin D₃
- ✚ Vitamin D₃ is more active than Vitamin D₂
- ✚ Vitamin D₂ is also known as ergocalciferol.
- ✚ It is produced by the exposure of ergosterol to UV radiation.
- ✚ Ergosterol occurs in plants and yeast.
- ✚ Vitamin D₃ is also known as cholcalciferol, it is natural form of the vitamin ingested from food.
- ✚ It can also be formed by the exposure of 7 dehydrocholesterol present in the skin to sunlight.



Function of Vitamin D

- ✚ Vitamin D is required for normal growth in mammals.
- ✚ This is probably related to absorption and utilization of Calcium and Phosphorous.
- ✚ It helps in the normal development of bone and teeth.

Sources

- ✚ Cod liver oils (Rich source)
- ✚ Milk, Butter
- ✚ Egg yolk and Sun dried roughages/Grains

RDA

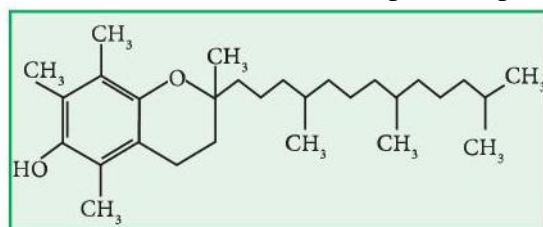
- ✚ 10 mg

Deficiency

- ✚ Rickets in young ones
- ✚ Osteomalacia in adult
- ✚ Retarded growth
- ✚ Increased loss of calcium and phosphorous in urine

8.1.1.3 Vitamin E

- ✚ Vitamin E comprises of a group of compounds called Tocopherols and Tocotrienols
- ✚ Out of eight natural forms of vitamin E, alpha tocopherol is more active



Functions of Vitamin E

- ✚ Antioxidant property
- ✚ It protects the red blood cells against hemolysis
- ✚ Vitamin E is essential for reproductive processes
- ✚ It plays an important protective role during ageing of cells
- ✚ Vitamin E is essential for biosynthesis of Coenzyme Q

Sources

- ✚ Cotton seed oil, Sunflower oil, Wheat germ oil and Leafy vegetables

RDA

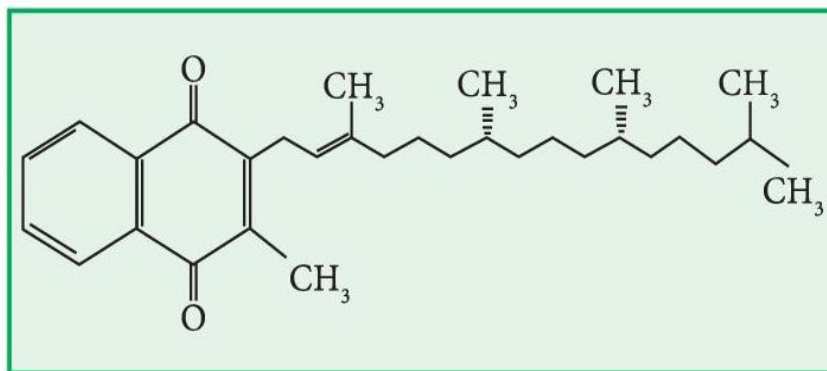
- ✚ 25 to 30 mg

Deficiency

- ✚ Reproductive failure
- ✚ Muscular dystrophy
- ✚ Combined deficiency of Vitamin E and selenium causes hepatic necrosis

8.1.1.4 Vitamin K

- ✚ Vitamins belonging to K group are poly isoprenoid substituted naphoquinones.
- ✚ It is also known as anti hemorrhagic vitamin.
- ✚ Three compounds which have the biological activity of Vitamin K are
 1. K1 – Phylloquinone – Green plants and Oil seeds
 2. K2 – Menaquinone – Intestinal bacteria
 3. K3 – Menadione – Synthetic product



Functions

- ✚ Essential for the synthesis of prothrombin and other clotting factors.
- ✚ It is also called as anti hemorrhagic vitamin
- ✚ Enhances the deposition of calcium in the tissues concerned.
- ✚ Involved in electron transport chain and oxidative phosphorylation.

Sources

- ✚ Green Vegetables, Soybean oils, Tomatoes, Spinach and cabbage

RDA

- ✚ 2 mg

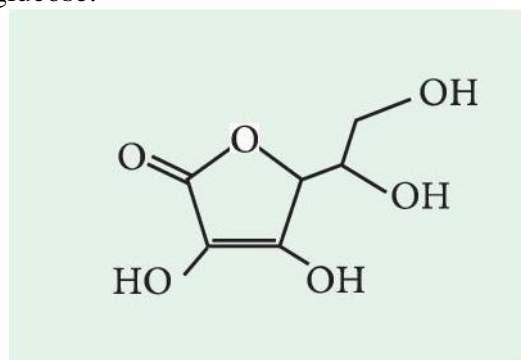
Deficiency

- ✚ Low prothrombin level in blood leads to hemorrhagic conditions.

8.1.2 Water Soluble Vitamin

8.1.2.1 Vitamin C

- ✚ Vitamin C is also called as ascorbic acid
- ✚ Ascorbic acid is an enediol-lactone of an acid with configuration similar to that of the sugar L-glucose.



Functions

- ✚ Involved in cellular oxidation-reduction reaction
- ✚ Vitamin C is essential for building collagen, the connective tissue protein which cements the cells and tissues together.
- ✚ It regulates carbohydrate metabolism
- ✚ Vitamin C is required as coenzyme for the enzyme dopamine hydroxylase which catalyzes the conversion of dopamine to nor-epinephrine.
- ✚ It is involved in the maturation of red blood cells.
- ✚ The absorption of iron is significantly enhanced by the presence of vitamin C.
- ✚ It has a general antioxidant role, especially in the regeneration of oxidized vitamin E in membranes.

Sources

- ✚ Citrus fruits like orange, lemon are especially rich in vitamin C. Water melons, tomatoes, grape and leafy vegetables are also good sources.

RDA

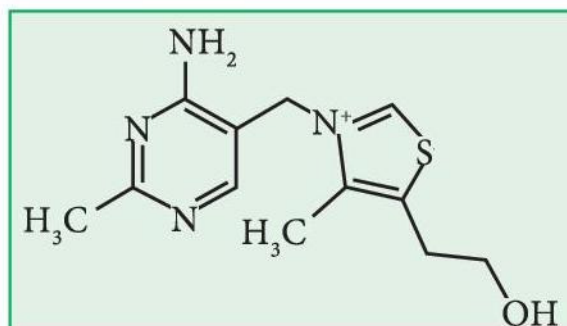
75 mg

Deficiency

- Scurvy is the classical syndrome of vitamin C deficiency. It is related to defective collagen synthesis which is indicated by fragile skin, muscle weakness, bleeding of the gums, loose teeth and delayed wound healing.

8.1.2.2 Vitamin B1 (Thiamine)

- Vitamin B1 which is also called as thiamine contains pyrimidine and thiazole ring.



Function

- Thiamine act as a coenzyme in the form of thiamine pyrophosphate (TPP) in many enzymatic reactions. These are involved mainly in the breakdown of glucose to yield energy.
- Thiamine pyrophosphate (TPP) also acts as a coenzyme for transketolase reactions in the phosphogluconate oxidative pathway of carbohydrate metabolism. This reaction is essential for ribose formation, a constituent of DNA and RNA.
- Vitamin B1 is also required in tryptophan metabolism for the activity of the enzyme tryptophan pyrolase.
- The adequate level of thiamine provides healthy nerves, a good mental outlook, a normal appetite and digestion.

Sources

- Liver, pork, meat, and rice are rich sources. Other good sources are beans and nuts.

RDA

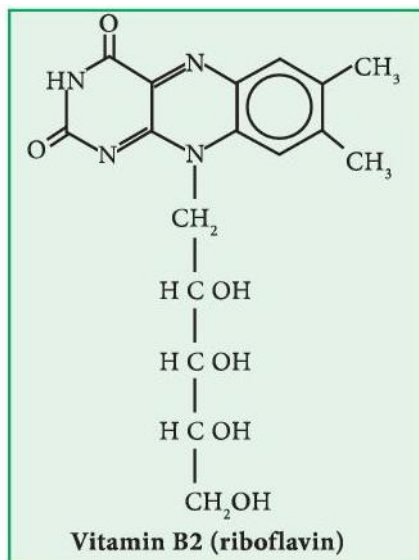
- 1.5 – 2.0 mg

Deficiency

- The symptoms of thiamine deficiency occur because the tissue cells are unable to receive sufficient energy from glucose. Therefore, they cannot carry out their normal functions.
- Early symptoms of thiamine deficiency include fatigue, irritability, depression and numbness of the leg and poor tone of the gastrointestinal tract together with constipation.
- Beriberi is the disease caused by thiamine deficiency. Beriberi is characterized by oedema in the legs. Usually, beriberi is caused by carbohydrate rich and low thiamine diets such as polished rice.

8.1.2.3 Vitamin B2

- Vitamin B2 consists of a heterocyclic isoalloxazine ring attached to ribitol (a pentose alcohol).
- It is an yellow coloured compound.



Functions

- ✚ Riboflavin is a component of two important coenzymes namely FMN (Flavin Mono Nucleotide) and FAD (Flavin adenine dinucleotide). They play key roles in various enzymatic reactions.
- ✚ Riboflavin is essential for a healthy skin and for good vision in bright light.

Sources

- ✚ Soy beans, green vegetables are good sources of this vitamin. High concentration occurs in yeasts, milk and egg

RDA

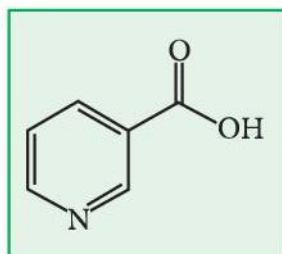
- ✚ 1.6 – 2.0 mg

Deficiency

- ✚ Riboflavin deficiency leads to cheilosis.
- ✚ It is characterized by the development of fissures in the lips and at the corners of the mouth.
- ✚ Riboflavin is extremely sensitive to string light.
- ✚ Due to sensitivity, riboflavin deficiency may occur in new born infants with hyper bilirubinemia who are treated by phototherapy.

8.1.2.4 Vitamin B3 (Niacin)

- ✚ Vitamin B3 which is also called as niacin or nicotinic acid pyridine 3-Carboxylic acid.
- ✚ It occurs in tissues as nicotinamide.



Functions

- ✚ Niacin is found in the form of its amide which is an important constituent of the coenzymes NAD⁺ and NADP⁺ and they take part in redox reactions which are associated with many dehydrogenases. For example NAD⁺ is the coenzyme for lactate dehydrogenase. NADP⁺ is the coenzyme for glutathione reductase.
- ✚ It promotes the formation of fat from carbohydrates.

- Niacin is essential for healthy skin, normal functions of the gastro intestinal tract and maintenance of the nervous system.

Sources

- Cereals, dark green leafy vegetables. Liver and kidney are rich sources of this vitamin.

RDA

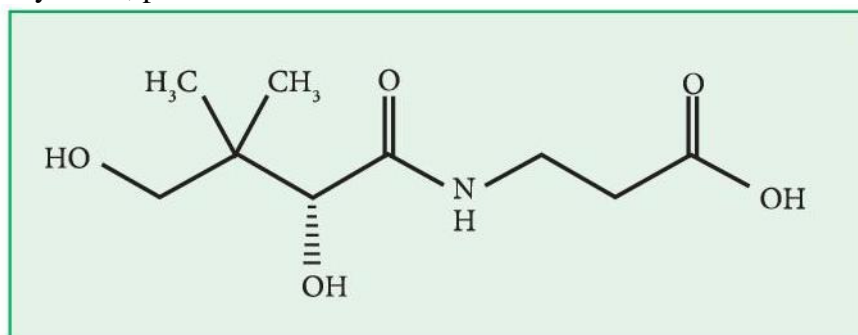
- 17 – 20 mg

Deficiency

- Nicotinic acid deficiency causes a disease called pellagra (Figure 8.20).
- Dermatitis-skin exposed to the sun, soreness of the mouth and swelling of the tongue.
- Diarrhoea.
- Dementia-mental changes including depression and confusion.

8.1.2.5 Vitamin B5 (Pantothenic acid)

- Pantothenic acid is found in every living cell including plant, animal and microbes.
- It is a part of coenzyme A which is an essential coenzyme involved in the catabolism of carbohydrates, proteins and fat.



Function

- Pantothenic acid forms a part of coenzyme A which is an essential coenzyme for metabolising carbohydrates, fat and proteins.
- It is necessary to synthesise vitamin D, steroid hormones and red blood cells
- It also helps to boost the immunity

Sources

- dried mushrooms, avocado, dried egg yolks and sunflower seeds in high amounts. Outer layer of whole grains contains the vitamin, but milling removes much of the pantothenic acid.

RDA

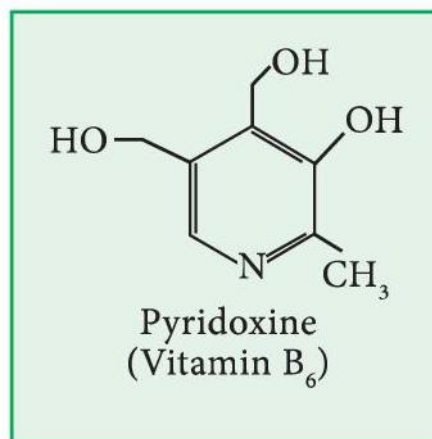
- 5 -12 mg

Deficiency

- Pantothenic acid deficiency is very rare and seen only in cases of severe malnutrition.
- Pantothenic acid is found in many common foods and average diets are thought to have an adequate amount of it.

8.1.2.6 Vitamin B6 (Pyridoxine)

- Vitamin B6 or Pyridoxine is also called as adermin.
- Vitamin B6 consists of three closely related pyridine derivatives.
 - Pyridoxine
 - Pyridoxal
 - Pyridoxal amine
- The metabolically active form of vitamin B6 is pyridoxal phosphate. It is formed from pyridoxal.



Function

- ✚ Pyridoxal phosphate acts as coenzyme for several enzymes of amino acid metabolism.
- ✚ Vitamin B6 is involved in the synthesis of coenzyme A from pantothenic acid.
- ✚ It is also involved in the production of antibodies.
- ✚ Pyridoxal phosphate plays a key role in glycogenolysis.

Sources

- ✚ Rich sources of this vitamin are yeast, whole grain, cereals and egg-yolk. Moderate amounts are present in organ meats like liver and kidney.

RDA

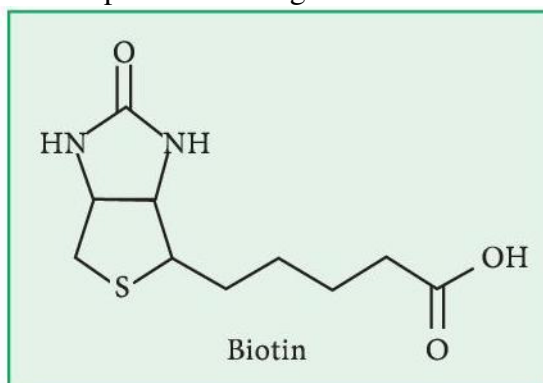
- ✚ 2 – 3 mg

Deficiency

- ✚ Deficiency of vitamin B6 is extremely rare.
- ✚ In infants its deficiency causes irritabilities, insomnia, muscular weakness and convulsion.
- ✚ The cause of the convulsions are severe impairment of the activity of the enzyme glutamate carboxylase, which is dependant on pyridoxal phosphate.
- ✚ The product of Glutamate decarboxylase is γ -aminobutyric acid (GABA), which is a regulatory neurotransmitter in the central nervous system.

8.1.2.7 Vitamin B7

- ✚ Biotin is a heterocyclic monocarboxylic acid
- ✚ It is a sulphur containing water soluble vitamin



Function

- ✚ It is essential for the synthesis of Lipids
- ✚ Acts as a coenzyme for the enzyme called carboxylases, which catalyzes the carboxylation reactions.
- ✚ It helps in the conversion of pyruvic acid to oxaloacetic acid.
- ✚ It helps to maintain the skin and nervous system in good condition.

- ✚ It involves in deamination of certain aminoacids like aspartate, serine and threonine

Source

- ✚ Foods rich in biotin are liver, kidney milk and egg-yolk. Vegetables, grains are good sources.

RDA

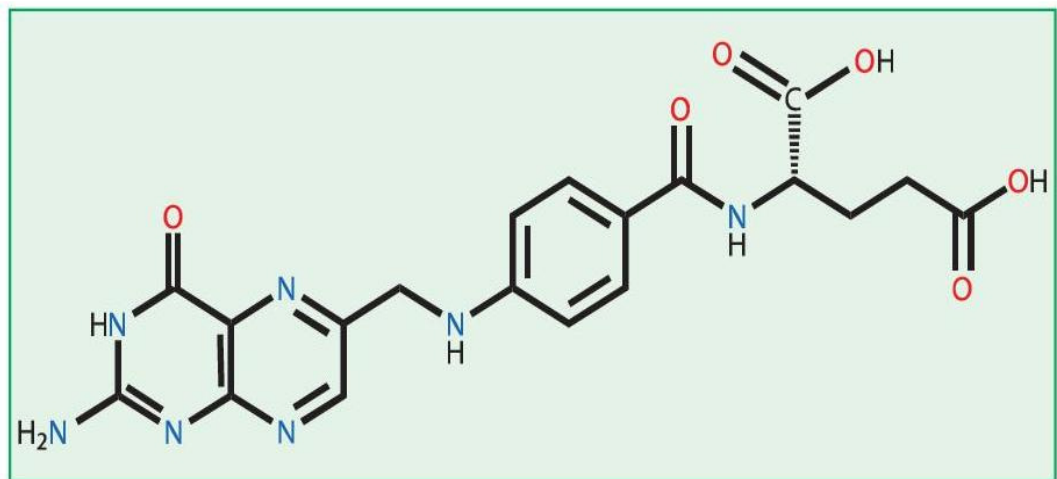
- ✚ 25 to 50 microgram

Deficiency

- ✚ Egg white contains a protein called avidin (egg white injury factor) which binds very tightly with biotin, preventing its absorption and thereby inducing biotin deficiency.
- ✚ The symptoms include depression, hair loss and muscle pain.

8.1.2.8 Vitamin B9 (Folic acid)

- ✚ Folic acid otherwise known as vitamin B9, Folavin or folate.
- ✚ The naturally occurring folate is susceptible to high heat and UV light and also be subject to oxidation.
- ✚ Active coenzyme is tetrahydrofolate.



Function

- ✚ Folic acid is essential for cell division and growth
- ✚ It is important for preventing birth defects.
- ✚ It is used in the synthesis of amino acid methionine.
- ✚ Tetrahydrofolate (THF) is needed to transfer one carbon units in the biosynthetic reactions.

Source

- ✚ Folate naturally occurs in a wide variety of foods, including dark green leaf vegetables, fruits, nuts, soybeans, chickpeas, dairy products, poultry and meat, eggs, seafood, grains. Vegetables such as avocado, beetroot, spinach, liver, yeast, asparagus, kale, and brussels and sprouts are among the foods with the highest levels of folate.

RDA

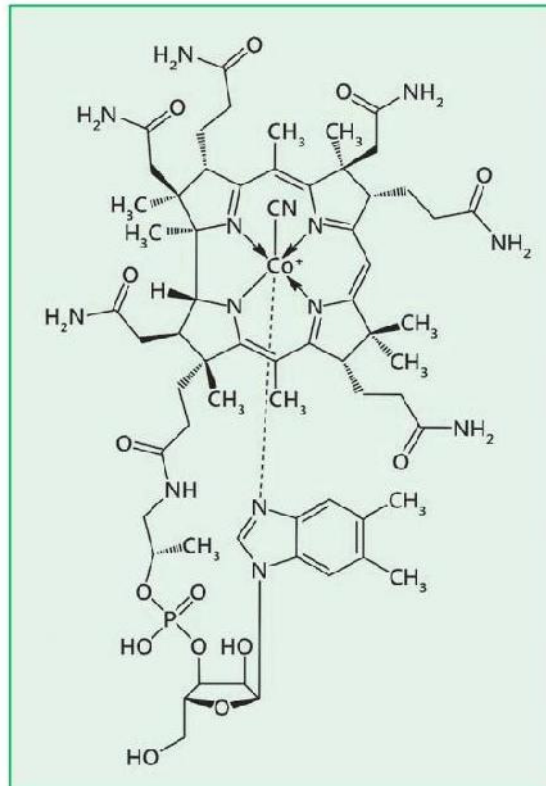
- ✚ 500 microgram

Deficiency

- ✚ Folate deficiency signs include anemia (megaloblastic anemia) and dysfunction of the gastrointestinal tract.
- ✚ The anemia is caused by the abnormal blood cell division resulting in fewer and larger red blood cells.
- ✚ Lack of folate in the diet can cause neural tube defects in an embryo of a pregnant woman. These can cause fatal birth defects.

8.1.2.9 Vitamin B12 (Cobalamin)

- Vitamin B12 has highly complex ring structure, similar to porphyrin ring which has a cobalt ion at its center.
- The active coenzyme forms of vitamin B12 are methylcobalamine and deoxyadenosyl cobalamine.



Function

- Many microorganisms require vitamin B12 for growth.
- Vitamin B12 is required as coenzyme for the conversion of L-methylmalonyl CoA to Succinyl CoA by the enzyme methylmalonyl CoA mutase. This reaction is essential for in the metabolism of some branched-chain amino acids and odd-chain fatty acids.
- Vitamin B12 is required for the maturation of red blood cells in the bone marrow and for the synthesis of proteins.

Sources

- Vitamin B12 is found in animal but not in vegetable foods and is unique in that it is the only known vitamin that holds an ion of metal (cobalt) in its molecule. Eggs and meat supply ample amounts of this vitamin.

RDA

- 3 microgram

Deficiency

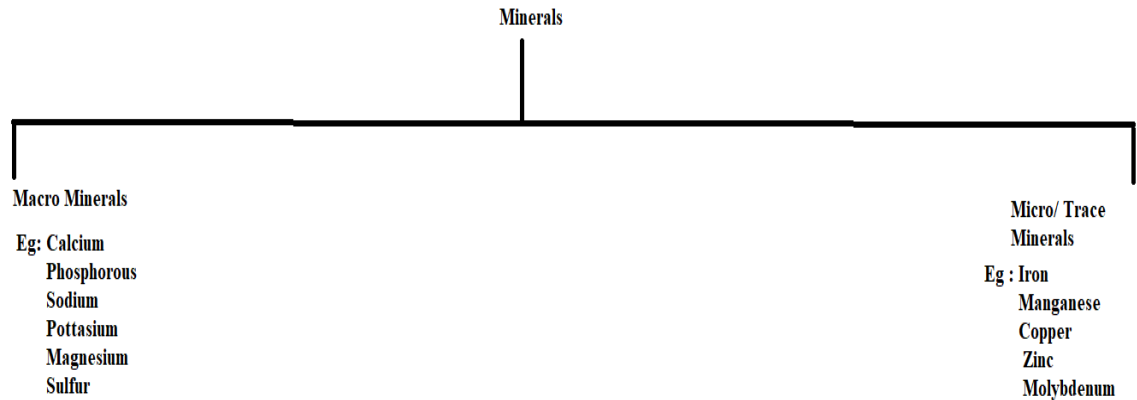
- When absorption is prevented by lack of intrinsic factor, it leads to the condition called pernicious anemia.
- It is characterized by a drastic decrease in red blood cell count and leads to formation of macrocytic red blood cells.
- Vitamin B12 deficiency causes an increased concentration of methyl malonic acid, which competes with malonyl CoA and impairs fatty acid synthesis.

9. Minerals

- Minerals are inorganic elements that are present in body fluids and tissues.
- They are supplied to the body through diet.
- For example sodium from table salt and sulfur from protein

- ✚ Each mineral is required in a specific amount ranging from microgram to grams per day.
- ✚ Minerals constitute about eight percent of total body mass of a human being.
- ✚ Unlike vitamins minerals are not destroyed during cooking process. However some loss may occur due to their solubility in water.

9.1 Classification of mineral



9.1.1 Macro Minerals

- ✚ Macro elements like sodium and potassium are required in large amount (>100mg/day) and present in large quantities in the body.

9.1.1.1 Calcium

- ✚ Calcium (Ca) is the most abundant inorganic mineral in the body.
- ✚ About 99% of it exists in the bone and teeth and 1% in soft tissues and extracellular fluid.

Function

- ✚ Bone and Teeth Development
- ✚ Essential for lactating animals
- ✚ Nerve and Muscle function
- ✚ Maintain acid base balance of bodily fluids
- ✚ Calcium plays an important role in blood coagulation
- ✚ Normal excitability of heart is calcium dependant
- ✚ Calcium is involved in the process of mitosis
- ✚ It also acts as cofactor for certain enzymes
- ✚ Calcium plays a major role as a secondary messenger in hormone action

Deficiency

- ✚ Rickets
- ✚ Osteophoresis
- ✚ Tetany

9.1.1.2 Phosphorous

- ✚ Phosphorus is the principal anion of the cell. It is widely present as phosphates in proteins, Nucleic acids and other various cellular components.
- ✚ Phosphorus and calcium are related in sources and metabolism.

Function

- ✚ Phosphorus is essential for formation of bones and teeth.
- ✚ High-energy phosphate compounds like ATP (Adenosine Tri Phosphate) and Creatine Phosphate play a role in storage and transport of energy.
- ✚ Phosphorylation and dephosphorylation reactions modify the activity of many enzymes.

- ✚ Phospholipids, the important constituent lipid of cell membranes and nervous tissue contain phosphorus.
- ✚ Acid-base balance is maintained by phosphate buffer in the kidneys.
- ✚ Several co-enzymes such as NADP⁺ and TPP involved in enzymatic reactions contain phosphate.

Deficiency

- ✚ Lameness
- ✚ Stiffness of joints
- ✚ Lowered appetite
- ✚ Reduced rate of gain
- ✚ Breeding problems

9.1.1.3 Sodium

- ✚ Sodium is the predominant cation of the extra cellular fluid.
- ✚ It is taken in the diet as sodium chloride.

Function

- ✚ Sodium ion is mainly associated with chloride and bicarbonate in the regulation of acid-base equilibrium.
- ✚ It maintains osmotic pressure of the body fluids and thus protects the body against excessive fluid loss.
- ✚ Sodium ions are involved in the transmission of nerve impulses.
- ✚ It plays an important role in the absorption of glucose and nutrients from small intestine by active transport.
- ✚ Sodium ions are also involved in heart function.

Deficiency

- ✚ Mineralocorticosteroids secreted by adrenal glands, regulate the metabolism of sodium.
- ✚ Decreased level of plasma sodium(hyponatremia) may be due to lack of aldosterone and loss from gastro- intestinal tract associated with conditions like diarrhoea.
- ✚ Maintain water balance

9.1.1.4 Pottssium

- ✚ Potassium is the main intracellular cation
- ✚ About 98% of potassium is present inside the cell.

Function

- ✚ Potassium maintains the intracellular osmotic pressure, water balance and acid-base balance.
- ✚ Potassium, along with sodium influences neuromuscular activity of cardiac and skeletal muscles.
- ✚ The glycolytic enzyme, pyruvate kinase requires potassium as cofactor.
- ✚ It maintains the alkalinity of the bile and blood.
- ✚ Protein synthesis is dependent on potassium levels inside the cells.

Deficiency

- ✚ Deficiency of potassium leads to depression in cardiac and nervous system.
- ✚ Severe vomiting, diarrhoea, loss of appetite, fasting or starvation over a long period of time may lead to deficiency
- ✚ It also occurs during renal failure and shock.
- ✚ Fatigue, growth retardation, muscular weakness, heart and respiratory dysfunction are common signs of potassium deficiency.

9.1.1.5 Chlorine

- ✚ Chlorine is taken in diet as sodium chloride.
- ✚ Chloride is the major anion in the extracellular fluid.

Function

- ✚ Chloride plays a vital role in acid-base balance by way of chloride shift and maintains blood pH.
- ✚ Chlorides also contribute to formation of gastric HCl.
- ✚ It also helps to maintain plasma osmotic pressure.
- ✚ Chloride ion is important as an activator of salivary amylase.
- ✚ Chloride mainly acts as a counter ion against cations in maintaining the electrical neutrality in body fluids

Deficiency

- ✚ Deficiency states of chloride are rare. Most often, sodium and chloride are associated with each other in their functions.
- ✚ Any clinical conditions like dehydration, affecting sodium concentration has an identical effect on chloride concentration.

9.1.1.6 Magnesium

- ✚ Magnesium is the second most abundant intracellular cation after potassium.
- ✚ Adult human body contains about 25g of magnesium.
- ✚ Bones contain nearly 70% of the body magnesium contributing as magnesium phosphate, which is about 1.5% of bone matter.

Function

- ✚ Magnesium, along with sodium, potassium and calcium controls the neuro muscular irritability.
- ✚ Magnesium is involved in the synthesis of proteins and nucleic acids.
- ✚ Magnesium is essential for the activity of peptidases and ribonucleases.
- ✚ It is an activator of many glycolytic enzymes, particularly in muscle.
Example : pyruvate kinase and enolase.
- ✚ It plays an important role in oxidative phosphorylation.

Deficiency

- ✚ The decreased level of serum magnesium causes depression, tetany and muscular weakness.

9.1.2 Micro Minerals

- ✚ Micro elements like iron and iodine are required in small quantities (<100mg/day) and are present in small amount in tissues and body fluids.

9.1.2.1 Iron

- ✚ Iron is one of the most essential micro elements in the body.
- ✚ It plays a vital role in many oxidation-reduction reactions.
- ✚ Hemoglobin and cytochromes contain Iron in them.

Function

- ✚ Iron is involved in the transport of oxygen by hemoglobin.
- ✚ Iron is essential for synthesis of cytochromes, a component of electron transport chain.
- ✚ Myoglobin is an iron containing protein similar to hemoglobin and is present in muscle tissue.
- ✚ Succinate dehydrogenase requires iron as a co-factor.
- ✚ Iron improves immune status.

Deficiency

- ✚ Deficiency of iron causes iron deficiency anemia.
- ✚ The deficiency may be due to dietary or lack of iron absorption

- ✚ due to gastro intestinal tract diseases like diarrhoea.

9.1.2.2 Iodine

- ✚ The adult human body contains about 50 mg of organically bound iodine.
- ✚ Nearly half of this is present in muscles. Most of the body iodine is present in the thyroid gland, but all cells contain traces of iodine.

Function

- ✚ The thyroid gland is chiefly concerned with the uptake of iodine for the synthesis of the thyroid hormones, tetra Iodothyronine(Thyroxine T₄) and tri Iodothyronine(T₃)
- ✚ which influence a large number of metabolic functions.
- ✚ These iodine containing hormones regulate energy metabolism, synthesis of proteins and cholesterol and also in the conversion of carotene to vitamin A.

Deficiency

- ✚ A deficiency of iodine leads to a decreased production of thyroxine, and in turn a lowered rate of energy metabolism.
- ✚ In an attempt to produce more thyroid hormones the thyroid gland enlarges. This condition is called simple or endemic goiter.

9.1.2.3 Zinc

- ✚ Adult human body contains approximately 1 to 2 grams of zinc.
- ✚ Like iron, zinc is absorbed according to the body needs.
- ✚ Prostate gland is very rich in zinc.

Function

- ✚ Zinc forms an integral part of several metallo- enzymes in the body.
- ✚ Zinc is essential for growth and reproduction.
- ✚ It has role in maintaining the plasma concentration of vitamin A.
- ✚ Zinc is essential for the storage of insulin in the β -islet cells.
- ✚ Zinc is necessary for wound healing.

Deficiency

- ✚ Zinc deficiency causes poor growth and hypogonadism during adolescence.
- ✚ In zinc deficiency, there is poor wound healing.
- ✚ Zinc deficiency may result in impairment of sensitivity to taste.
- ✚ Deficiency of zinc may interfere with storage and secretion of insulin.
- ✚ Zinc deficiency causes alopecia (Hair loss)

9.1.2.4 Copper

- ✚ Copper is an essential micro element.
- ✚ Copper content in an adult human is about 100 mg.
- ✚ Copper in whole blood is almost evenly distributed between cell and plasma.
- ✚ The highest concentrations are found in liver and kidney.

Function

- ✚ Copper forms integral part of certain enzymes like cytochrome oxidase and catalase.
- ✚ Ceruloplasmin a copper containing protein is required for iron absorption.
- ✚ Superoxide dismutase (SOD) contains copper ion, SOD converts super oxide radicals to hydrogen peroxide.
- ✚ It is also present in cytochrome C, which is involved in electron transport in mitochondria.
- ✚ Copper is also needed for bone formation as well as for the maintenance of myelin within the nervous system.
- ✚ Copper helps to form insoluble elastin fibres by cross-linking soluble pro-elastin.

Deficiency

- ✚ A diet deficient in copper causes loss of weight.
- ✚ Copper deficiency produces microcytic hypochromic anemia.
- ✚ Elastin formation is impaired in copper deficiency.

- ✚ Copper deficiency turns hair grey, which however, can be controlled by administration of copper.
- ✚ Deficiency of copper is sometimes associated with decrease in taste sensitivity, which is restored by oral administration of copper.

9.1.2.5 Cobalt

- ✚ Cobalt is a component of vitamin B12.
- ✚ Elemental cobalt of the diet can be converted to Cobalamine by the intestinal bacteria.
- ✚ Cobalt occurs in small amount in all tissues, higher concentrations occur in liver and kidneys.

Function

- ✚ Most of the cobalt is present in vitamin B12, which is necessary for maturation of red blood cells.
- ✚ Cobalt is an activator of the enzyme Phosphoglucomutase and glycyl - glycine peptidase.

Deficiency

- ✚ Cobalt deficiency is rare in human beings.
- ✚ Deficiency leads to anemia.

9.1.2.6 Manganese

- ✚ Manganese is an essential trace element.
- ✚ It is present as Mn^{2+} ion and found in high concentrations in the mitochondria.

Function

- ✚ Manganese acts as a cofactor for number of enzymes including arginase, hexokinase and isocitrate dehydrogenase.
- ✚ Manganese is essential for normal bone structure, reproduction and functioning of the central nervous system
- ✚ Manganese also functions with vitamin K in the formation of prothrombin
- ✚ It inhibits lipid peroxidation
- ✚ Manganese also participates in glycoprotein and proteoglycan synthesis.
- ✚ It helps in the porphyrin synthesis
- ✚ Manganese is involved in fattyacid and cholesterol synthesis.

Deficiency

- ✚ A deficiency of Mn reduces appreciably the synthesis of oligosaccharides.
- ✚ The deficiency of manganese leads to impaired growth and skeletal abnormalities.

9.1.2.7 Chromium

- ✚ Chromium is widely distributed throughout the body.
- ✚ The adult human body contains only 6 mg of chromium.

Function

- ✚ Chromium accelerates the utilization of glucose
- ✚ It reduces the serum cholesterol level
- ✚ Chromium is also said to be important in the metabolism of plasma lipoprotein.

Deficiency

- ✚ Chromium deficiency is characterized by impaired growth, weight loss and disturbances in glucose, lipid and protein metabolism.

PATHOLOGY
I Year BME
BSME
Short Notes

BASIC

1. INTRODUCTION

- ✚ The word 'Pathology' is derived from two Greek words—pathos meaning suffering, and logos meaning study.
- ✚ Pathology is, thus, scientific study of structure and function of the body in disease; or in other words, pathology consists of the abnormalities that occur in normal anatomy (including histology) and physiology owing to disease.
- ✚ Another commonly used term with reference to study of diseases is 'pathophysiology' comprised by two words:
patho=suffering; physiology=study of normal function.
- ✚ Pathophysiology, thus, includes study of disordered function or breakdown of homeostasis in diseases.
- ✚ Simply Pathology is the study of diseases, their causes, effects, and mechanisms within the human body.
- ✚ It includes branches like
 - a) anatomical pathology (examining tissues),
 - b) clinical pathology (analyzing bodily fluids), and
 - c) forensic pathology (investigating causes of death).
- ✚ Pathology is crucial for diagnosing diseases, understanding their underlying mechanisms, and guiding treatment decisions.

2. CELL

- ✚ A cell is the basic unit of life, enclosed by a membrane and containing genetic material.
- ✚ It performs essential functions necessary for the survival and functioning of organisms, such as metabolism, growth, and reproduction.
- ✚ Under normal conditions, cells are dynamic structures existing in fluid environment.
- ✚ A cell is enclosed by cell membrane that extends internally to enclose nucleus and various subcellular organelles suspended in cytosol

3. CELL INJURY

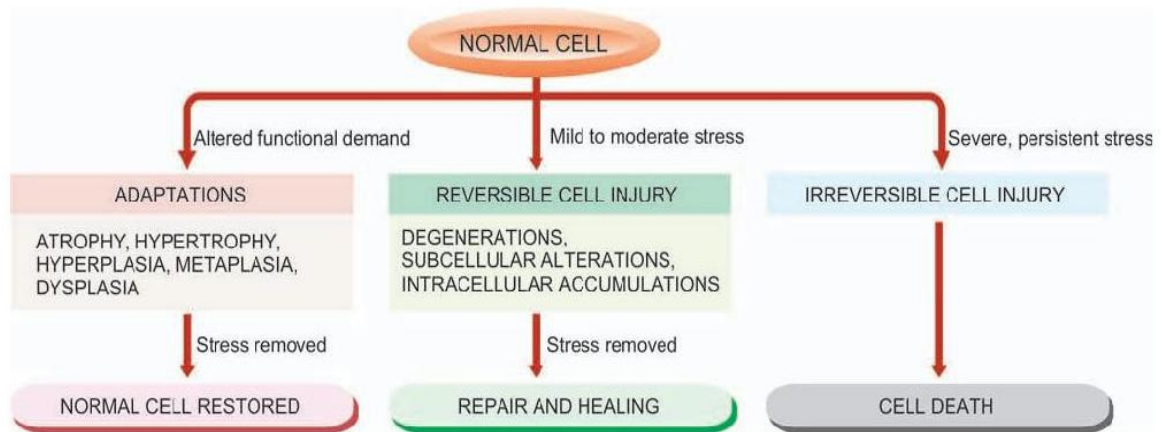
- ✚ The cells may be broadly injured by two major ways:
 - A. By genetic causes
 - B. By acquired causes
- ✚ Genetic causes include various genetic disorders resulted in abnormal cell injury.
- ✚ The acquired causes of disease comprise vast majority of common diseases afflicting mankind.
- ✚ Based on underlying agent, the acquired causes of cell injury can be further categorised as under:
 1. Hypoxia (Oxygen deficiency to cell) and ischaemia (Reduced Blood Supply)
 2. Physical agents
 - ✓ mechanical trauma (e.g. road accidents);
 - ✓ thermal trauma (e.g. by heat and cold);
 - ✓ electricity;
 - ✓ radiation (e.g. ultraviolet and ionising); and
 - ✓ rapid changes in atmospheric pressure.
 3. Chemical agents and drugs
 - ✓ chemical poisons such as cyanide, arsenic, mercury;
 - ✓ strong acids and alkalis;
 - ✓ environmental pollutants;
 - ✓ insecticides and pesticides;

- ✓ oxygen at high concentrations;
 - ✓ hypertonic glucose and salt;
 - ✓ social agents such as alcohol and narcotic drugs; and
 - ✓ therapeutic administration of drugs.
4. Microbial agents
 - ✓ Injuries by microbes include
 - ✓ infections caused by bacteria, rickettsiae, viruses, fungi,
 - ✓ protozoa, metazoa, and other parasites.
 5. Immunologic agents
 - ✓ hypersensitivity reactions;
 - ✓ anaphylactic reactions; and
 - ✓ autoimmune diseases.
 6. Nutritional derangements
 - ✓ Nutritional deficiency diseases may be due to overall deficiency of nutrients (e.g. starvation), of protein calorie (e.g. marasmus, kwashiorkor), of minerals (e.g. anaemia), or of trace elements.
 - ✓ Nutritional excess is a problem of affluent societies resulting in obesity, atherosclerosis, heart disease and hypertension.
 7. Aging
 - ✓ Cellular aging or senescence leads to impaired ability of the cells to undergo replication and repair, and ultimately lead to cell death culminating in death of the individual.
 8. Psychogenic diseases
 - ✓ There are no specific biochemical or morphologic changes in common acquired mental diseases due to mental stress, strain, anxiety, overwork and frustration e.g. depression, schizophrenia.
 9. Iatrogenic factors
 - ✓ occurrence of disease or death due to error in judgment by the physician and untoward effects of administered therapy
 10. Idiopathic diseases.
 - ✓ Idiopathic means “of unknown cause”.

Pathogenesis of Cell injury

- ✚ Injury to the normal cell by one or more of the above listed etiologic agents may result in a state of reversible or irreversible cell injury
- ✚ The following principles apply in pathogenesis of most forms of cell injury by various agents:
 1. Type, duration and severity of injurious agent: The extent of cellular injury depends upon type, duration and severity of the stimulus e.g. small dose of chemical toxin or short duration of ischaemia cause reversible cell injury while large dose of the same chemical agent or persistent ischaemia cause cell death.
 2. Type, status and adaptability of target cell: The type of cell as regards its susceptibility to injury, its nutritional and metabolic status, and adaptation of the cell to hostile environment determine the extent of cell injury e.g. skeletal muscle can withstand hypoxic injury for long-time while cardiac muscle suffers irreversible cell injury after 20-30 minutes of persistent ischaemia.
 3. Underlying intracellular phenomena: Irrespective of other factors, following essential biochemical phenomena underlie all forms of cell injury:
 - i) Mitochondrial damage causing ATP depletion.
 - ii) Cell membrane damage disturbing the metabolic and trans-membrane exchanges.
 - iii). Release of toxic free radicals.

4. Morphologic consequences: All forms of biochemical changes underlying cell injury are expressed in terms of morphologic changes. The ultrastructural changes become apparent earlier than the light microscopic alterations. The morphologic changes of reversible cell injury (e.g. hydropic swelling) appear earlier than morphologic alterations in cell death (e.g. in myocardial infarction).



Reversible Cell Injury

- ✚ Reversible cell injury is cellular damage that can be recovered if the damaging stimulus is removed promptly.
- ✚ It involves functional and structural changes in cells that are potentially reversible, allowing cells to return to their normal state once the injurious stimulus is eliminated.

Irreversible Cell Injury

- ✚ Irreversible cell injury refers to cellular damage that cannot be recovered, leading to cell death.
- ✚ This type of injury involves severe and irreversible structural and functional changes in cells, often caused by prolonged or severe insults such as extensive hypoxia, overwhelming toxins, or severe physical trauma.

4. Necrosis and Apoptosis

- ✚ **Necrosis** is a type of cell injury that results in the premature death of cells in living tissue. It can be caused by various factors such as infection, toxins, trauma, or lack of blood supply (ischemia).
- ✚ Unlike apoptosis, which is a programmed cell death that occurs naturally as part of tissue homeostasis, necrosis is a pathological process. There are different types of necrosis, including
 - Coagulative necrosis: This is the most common type and is characterized by the denaturation of proteins, leading to the formation of a firm, opaque mass. It often occurs in organs such as the heart, kidneys, and spleen.
 - Liquefactive necrosis: In this type, the affected tissue becomes liquefied due to the action of enzymes, resulting in the formation of a fluid-filled cavity. It's commonly seen in brain tissue following ischemic injury or infection.
 - Caseous necrosis: This type of necrosis is typically associated with tuberculosis and other granulomatous infections. It results in a soft, cheese-like appearance of the affected tissue.
 - Gangrenous necrosis: This term is used to describe necrosis that affects a considerable mass of tissue and often occurs in extremities like fingers, toes, or limbs due to impaired blood supply.

- **Fat necrosis:** This type occurs when adipose tissue is damaged, often as a result of trauma. It can lead to the formation of chalky white areas within the affected tissue.

✚ **Apoptosis**, often referred to as programmed cell death, is a highly regulated process of cell suicide that occurs in multicellular organisms.

✚ Unlike necrosis, which is usually a pathological process resulting from external factors, apoptosis is a normal and essential part of various biological processes, including embryonic development, tissue homeostasis, and immune system regulation. Key features of apoptosis include:

- ✓ **Cell Shrinkage:** During apoptosis, the cell undergoes shrinkage, becoming smaller and more compact.
- ✓ **Membrane Blebbing:** The cell membrane forms irregular bulges or blebs.
- ✓ **Nuclear Fragmentation:** The nucleus of the cell undergoes fragmentation into multiple smaller fragments, which are eventually engulfed by neighboring cells or phagocytes.
- ✓ **DNA Fragmentation:** The DNA within the nucleus undergoes cleavage into smaller fragments.
- ✓ **Formation of Apoptotic Bodies:** The cell breaks up into smaller membrane-bound vesicles called apoptotic bodies, which contain cellular debris and are subsequently engulfed and removed by phagocytes without triggering inflammation.
- ✓ Apoptosis serves several important functions in the body:
- ✓ **Embryonic Development:** Apoptosis helps shape and sculpt developing tissues and organs by eliminating excess or unwanted cells. For example, it plays a crucial role in the formation of fingers and toes during embryogenesis.
- ✓ **Tissue Homeostasis:** Throughout life, apoptosis helps maintain the balance between cell proliferation and cell death, ensuring the proper functioning of tissues and organs. It helps remove aged, damaged, or dysfunctional cells, preventing the accumulation of cellular debris and maintaining tissue integrity.
- ✓ **Immune System Regulation:** Apoptosis plays a role in immune system regulation by eliminating activated immune cells once they have completed their function. This helps prevent excessive immune responses and autoimmune reactions.
- ✓ **Tumor Suppression:** Apoptosis acts as a mechanism of tumor suppression by eliminating cells with damaged DNA or other abnormalities, thereby preventing the proliferation of potentially harmful cells.

5. Intracellular Accumulation

- ✚ Intracellular accumulation of cells occurs when various substances accumulate within the cytoplasm or organelles of cells, beyond what is considered normal or physiologically tolerable.
- ✚ This accumulation can have diverse causes and consequences, depending on the nature of the accumulating substance and the affected cell type.
- ✚ **Lipids:** Lipid accumulation within cells, often in the form of triglycerides, can occur due to conditions like fatty liver disease (hepatocytes), atherosclerosis (macrophages in arterial walls), or lipid storage diseases (various cell types).
- ✚ **Proteins:** Abnormal accumulation of proteins can occur due to defects in protein folding or degradation pathways. This can lead to the formation of protein aggregates within cells, as seen in neurodegenerative diseases like Alzheimer's (neurons) or inclusion body myositis (muscle cells).

- ✚ Glycogen: Glycogen accumulation can occur in conditions like glycogen storage diseases, where enzymes involved in glycogen metabolism are deficient. This leads to glycogen accumulation within affected cells, such as hepatocytes or muscle cells.
- ✚ Pigments: Certain pigments can accumulate within cells, causing characteristic discoloration. For example, melanin can accumulate in melanocytes or macrophages in conditions like melanoma or melanosis coli, respectively.
- ✚ Calcium: Calcium accumulation within cells can occur in various pathological conditions, leading to cellular dysfunction. For instance, calcium accumulation in mitochondria can disrupt cellular energy production and contribute to cell death.
- ✚ Exogenous substances: Cells can also accumulate exogenous substances, such as environmental toxins or drugs. For example, carbon particles accumulate in macrophages in the lungs of smokers, contributing to respiratory diseases like chronic obstructive pulmonary disease (COPD).

6. Pathological Calcification

- ✚ Pathological calcification is a process characterized by the abnormal deposition of calcium salts in soft tissues throughout the body.
- ✚ Unlike normal physiological calcification, which occurs as part of bone formation or in certain physiological processes like tooth enamel development, pathological calcification can occur in various organs and tissues where calcium salts are not normally found.
- ✚ This abnormal deposition can impair tissue function and lead to a range of clinical manifestations and complications. There are two main types of pathological calcification:

Dystrophic Calcification:

- ✚ Dystrophic calcification occurs in areas of damaged or necrotic tissue. It is not associated with abnormalities in systemic calcium metabolism; instead, it results from local factors that promote the precipitation of calcium salts in tissues.
- ✚ Dystrophic calcification is often seen in chronic inflammatory conditions or in tissues affected by trauma, infection, or ischemia. Common examples include calcific aortic valve stenosis, calcific tendinitis, and calcification in atherosclerotic plaques.
- ✚ In dystrophic calcification, the presence of tissue damage or necrosis provides sites for calcium salts to deposit. Even though the serum calcium and phosphate levels are typically normal, the local microenvironment within the affected tissues favors the precipitation of calcium salts.
- ✚ Over time, these deposits can lead to the hardening of tissues and impair their function. For example, in calcific aortic valve stenosis, calcium deposits accumulate on the aortic valve leaflets, causing them to become thickened and rigid, which can obstruct blood flow from the heart to the rest of the body.

Metastatic Calcification:

- ✚ Metastatic calcification occurs in otherwise normal tissues as a result of systemic factors that lead to elevated levels of calcium in the blood, known as hypercalcemia. Hypercalcemia can be caused by various underlying conditions, including hyperparathyroidism, vitamin D disorders, kidney failure, or certain cancers.
- ✚ When the serum calcium concentration exceeds the threshold for solubility, calcium salts precipitate and deposit in tissues throughout the body, particularly in the kidneys, lungs, blood vessels, and gastric mucosa.
- ✚ Metastatic calcification can have serious clinical implications depending on the affected organs and tissues. For example, calcification in blood vessels can increase the risk of cardiovascular diseases such as atherosclerosis and hypertension.

- ✚ In the kidneys, calcium deposits can contribute to renal dysfunction and the development of kidney stones. In the lungs, metastatic calcification can impair gas exchange and lead to respiratory symptoms.
- ✚ Management of pathological calcification depends on the underlying cause and the specific organs involved. Treatment may involve addressing the underlying disorder causing hypercalcemia, such as surgical removal of parathyroid gland tumors in hyperparathyroidism or treating vitamin D imbalances.
- ✚ In cases where tissue damage is the primary driver of calcification, management may focus on controlling inflammation, promoting tissue healing, and managing symptoms. In some instances, surgical interventions may be necessary to remove calcified tissues or repair damaged structures.

7. Cellular adaptations of growth and differentiation

- ✚ Cellular adaptations of growth and differentiation refer to the various ways cells respond to changes in their environment or stimuli, leading to alterations in their size, number, or functional capacity.
- ✚ These adaptations are crucial for maintaining tissue homeostasis, responding to physiological demands, and adapting to pathological conditions. Here's a detailed explanation:

Hypertrophy:

- ✚ Hypertrophy is an increase in the size of individual cells, leading to an overall enlargement of the affected tissue or organ.
- ✚ This adaptation typically occurs in response to increased functional demands or stimulation by growth factors or hormones.
- ✚ For example, skeletal muscle hypertrophy occurs in response to exercise, leading to an increase in muscle fiber size and strength.
- ✚ Cardiac hypertrophy can occur in response to conditions such as hypertension or valvular heart disease, resulting in the enlargement of the heart muscle (myocardium).

Hyperplasia:

- ✚ Hyperplasia refers to an increase in the number of cells in a tissue or organ due to enhanced cell division.
- ✚ It can be physiological, such as during tissue regeneration or hormonal stimulation (e.g., breast tissue during pregnancy and lactation).
- ✚ Pathological hyperplasia can occur in response to chronic irritation or hormonal imbalance, leading to abnormal tissue growth.
- ✚ For example, benign prostatic hyperplasia (BPH) involves the proliferation of prostatic glandular cells in response to hormonal changes in aging males.

Metaplasia:

- ✚ Metaplasia is the reversible change in which one differentiated cell type is replaced by another cell type.
- ✚ It often occurs in response to chronic irritation or inflammation, where the new cell type may better withstand the adverse environment.
- ✚ An example is the transformation of the normal columnar epithelium of the esophagus to a stratified squamous epithelium in response to chronic acid reflux (Barrett's esophagus).

Dysplasia:

- ✚ Dysplasia refers to the abnormal growth or development of cells within a tissue or organ.
- ✚ It is characterized by disordered cellular arrangement, increased nuclear size, altered nuclear-cytoplasmic ratio, and variations in cell size and shape.

- ✚ Dysplasia can be a preneoplastic change, indicating an increased risk of progressing to cancer if the underlying cause is not addressed.

Differentiation:

- ✚ Differentiation is the process by which cells become specialized in structure and function during development or in response to specific signals.
- ✚ It involves changes in gene expression and protein synthesis that lead to the acquisition of unique cellular characteristics.
- ✚ For example, stem cells differentiate into various cell types during embryonic development, giving rise to tissues and organs with distinct functions.
- ✚ In adult tissues, differentiation can occur in response to injury or regeneration, where progenitor cells differentiate into specific cell types to replace damaged or lost cells.
- ✚ Cellular adaptations of differentiation refer to the processes by which undifferentiated or less specialized cells acquire specific characteristics and functions.
- ✚ These adaptations are essential for the development, maintenance, and regeneration of tissues and organs in multicellular organisms. Here's a detailed overview:

Embryonic Development:

- ✚ During embryogenesis, undifferentiated stem cells undergo a series of differentiation steps to give rise to the diverse cell types and tissues of the developing organism.
- ✚ Differentiation is tightly regulated by signaling pathways and transcription factors that control gene expression and cellular fate decisions.
- ✚ The process involves sequential steps of cell fate specification, commitment, and terminal differentiation into specialized cell types, including ectoderm, mesoderm, and endoderm derivatives.

Tissue Homeostasis:

- ✚ In adult tissues, cellular differentiation is crucial for maintaining tissue integrity and function.
- ✚ Adult stem cells residing within various tissues can undergo differentiation in response to physiological cues or tissue damage.
- ✚ Differentiation pathways lead to the generation of mature cell types that replenish and replace old, damaged, or senescent cells, ensuring tissue homeostasis.
- ✚ Examples include the differentiation of hematopoietic stem cells into various blood cell lineages or the differentiation of epithelial stem cells in the skin or intestine to replace lost or damaged epithelial cells.

Regeneration and Repair:

- ✚ Following injury or tissue damage, cellular differentiation plays a critical role in tissue repair and regeneration.
- ✚ Progenitor cells or stem cells within the injured tissue undergo proliferation and differentiation to replace lost or damaged cells and restore tissue structure and function.
- ✚ This process involves coordinated interactions between various cell types, extracellular matrix components, and signaling molecules to promote tissue regeneration while minimizing scar formation.
- ✚ Examples include the differentiation of satellite cells into myoblasts for muscle repair or the differentiation of neural stem cells into neurons or glial cells in response to brain injury.

Plasticity and Reprogramming:

- ✚ Cellular differentiation is a dynamic process that can be influenced by external signals or environmental cues.

- ✚ In some cases, differentiated cells can exhibit plasticity, allowing them to change their phenotype or reprogram into different cell types.
- ✚ Induced pluripotent stem cells (iPSCs) represent a remarkable example of cellular reprogramming, where somatic cells can be reprogrammed into a pluripotent state resembling embryonic stem cells by the ectopic expression of specific transcription factors.
- ✚ This ability to reprogram differentiated cells holds promise for regenerative medicine, disease modeling, and drug discovery.

8. Inflammation and repair including fracture healing

- ✚ Inflammation and repair are intricate processes that are essential for the body's response to injury, including fracture healing. Fractures, or broken bones, can occur due to trauma, repetitive stress, or underlying medical conditions.
- ✚ Fracture healing involves a series of highly coordinated cellular and molecular events aimed at restoring the structural integrity and function of the injured bone. Here's a detailed explanation of inflammation, repair, and fracture healing:

Inflammation:

- ✚ Inflammation is the body's immediate response to tissue injury and serves to contain and eliminate pathogens, remove cellular debris, and initiate the repair process.
- ✚ When a bone fractures, disruption of blood vessels leads to bleeding and the formation of a hematoma at the fracture site.
- ✚ Inflammatory cells, primarily neutrophils and macrophages, are recruited to the site of injury to phagocytose debris and release cytokines and growth factors that modulate the repair process.
- ✚ Pro-inflammatory cytokines such as interleukin-1 (IL-1) and tumor necrosis factor-alpha (TNF- α) promote vasodilation, increase vascular permeability, and stimulate the migration of immune cells to the fracture site.

Repair Phase:

- ✚ The repair phase of fracture healing begins shortly after the inflammatory phase and involves the formation of a soft callus.
- ✚ Mesenchymal stem cells (MSCs), which reside in the bone marrow and periosteum, are activated and proliferate in response to injury.
- ✚ MSCs differentiate into chondrocytes, forming a cartilaginous callus that bridges the fracture gap. This process is known as endochondral ossification.
- ✚ Angiogenesis occurs concurrently, with new blood vessels infiltrating the fracture site to supply oxygen, nutrients, and precursor cells for bone formation.
- ✚ Subsequently, the cartilaginous callus is gradually replaced by woven bone, which is deposited by osteoblasts derived from MSCs and periosteal cells.

Remodeling Phase:

- ✚ The remodeling phase of fracture healing involves the gradual replacement of woven bone with lamellar bone, which restores the bone's strength and structure.
- ✚ Osteoclasts, which are derived from hematopoietic stem cells, resorb excess bone tissue, sculpting the bone into its proper shape and removing any bony projections formed during the repair phase.
- ✚ Osteoblasts deposit new bone matrix, which is subsequently mineralized to form mature, lamellar bone.
- ✚ The remodeling process is guided by mechanical stress and load-bearing activities, which stimulate bone formation and alignment along lines of mechanical stress.

9. Neoplasia

- ✚ Neoplasia refers to the abnormal growth of cells that results in the formation of a tumor.

- ✚ These tumors can be classified as either benign or malignant based on their behavior and characteristics.

Benign Tumors:

- ✚ Benign tumors are non-cancerous growths that typically grow slowly and do not invade nearby tissues or spread to other parts of the body (metastasize).
- ✚ They are usually well-defined, encapsulated masses of cells that resemble the tissue of origin.
- ✚ Benign tumors are often named based on the type of cells or tissues they arise from, such as adenoma (epithelial tissue), fibroma (fibrous tissue), or lipoma (adipose tissue).
- ✚ While benign tumors may cause symptoms depending on their size and location, they generally do not pose a significant threat to health unless they compress nearby structures or organs.

Malignant Tumors (Cancer):

- ✚ Malignant tumors are cancerous growths characterized by uncontrolled cell proliferation, invasion into surrounding tissues, and the potential to metastasize to distant sites.
- ✚ They lack the normal regulatory mechanisms that control cell growth and division, leading to unchecked proliferation and disruption of tissue architecture.
- ✚ Malignant tumors can arise from any type of tissue and are often named based on their tissue of origin, followed by the suffix "-carcinoma" (epithelial tissue) or "-sarcoma" (connective tissue).
- ✚ Malignant tumors exhibit a range of characteristics, including cellular atypia, increased mitotic activity, angiogenesis (formation of new blood vessels), and tissue invasion.
- ✚ Metastasis is a hallmark feature of malignancy, where cancer cells detach from the primary tumor, enter the bloodstream or lymphatic system, and establish secondary tumors in distant organs or tissues.
- ✚ Malignant tumors can cause a variety of symptoms, depending on their location and the organs they affect. These symptoms may include pain, changes in bowel or bladder habits, unexplained weight loss, and fatigue.
- ✚ Diagnosis of benign and malignant tumors typically involves a combination of imaging studies (such as X-rays, CT scans, or MRI scans), biopsy (sampling of tissue for microscopic examination), and laboratory tests (including tumor markers). Treatment options vary depending on the type, location, and stage of the tumor but may include surgery, radiation therapy, chemotherapy, targeted therapy, immunotherapy, or a combination of these modalities.

10. Carcinogenesis

- ✚ Carcinogenesis is the process by which normal cells undergo genetic and epigenetic changes that ultimately lead to the development of cancer.
- ✚ It is a multi-step process involving the accumulation of mutations in key regulatory genes, disruption of normal cellular functions, and dysregulation of signaling pathways controlling cell growth, proliferation, differentiation, and apoptosis. Here's a detailed explanation of carcinogenesis:

Initiation:

- ✚ Carcinogenesis often begins with the initiation stage, where exposure to carcinogens or genotoxic agents causes DNA damage in normal cells.
- ✚ Carcinogens can be physical agents (such as radiation), chemical agents (including tobacco smoke, asbestos, and certain industrial chemicals), biological agents (such as viruses), or environmental factors (such as ultraviolet radiation from the sun).

- ✚ DNA damage can take the form of single-strand breaks, double-strand breaks, base modifications, or cross-linking of DNA strands.
- ✚ If DNA damage is not repaired properly, it can result in mutations that alter the function of critical genes involved in cell cycle control, DNA repair, and cell signaling.

Promotion:

- ✚ Following initiation, the promotion stage involves the clonal expansion of initiated cells, leading to the formation of preneoplastic lesions or benign tumors.
- ✚ During promotion, initiated cells acquire additional genetic and epigenetic alterations that confer a selective growth advantage, allowing them to outcompete neighboring normal cells.
- ✚ Promoting factors include growth factors, hormones, chronic inflammation, and oxidative stress, which create a pro-proliferative microenvironment conducive to the survival and expansion of initiated cells.
- ✚ The promotion stage is reversible, and removal of promoting stimuli may halt or regress the progression of preneoplastic lesions.

Progression:

- ✚ The progression stage represents the transition from preneoplastic lesions to invasive cancer and is characterized by further genetic instability, clonal evolution, and acquisition of malignant phenotypes.
- ✚ Progression involves the accumulation of additional mutations and chromosomal abnormalities that promote uncontrolled cell proliferation, evasion of apoptosis, angiogenesis, tissue invasion, and metastasis.
- ✚ Key genetic alterations commonly observed in cancer cells include activation of oncogenes (e.g., mutations in RAS or MYC), inactivation of tumor suppressor genes (e.g., mutations in TP53 or PTEN), and genomic instability (e.g., chromosomal rearrangements or aneuploidy).

Metastasis:

- ✚ Metastasis is the spread of cancer cells from the primary tumor to distant sites in the body, leading to the formation of secondary tumors.
- ✚ Metastasis involves a series of sequential steps, including local invasion of surrounding tissues, intravasation into blood or lymphatic vessels, survival in the circulation, extravasation at distant sites, and colonization of secondary organs.
- ✚ The process of metastasis is highly inefficient, and only a small fraction of cancer cells successfully establish metastatic colonies. However, metastasis is responsible for the majority of cancer-related deaths and represents a significant challenge in cancer treatment.

Tumor Microenvironment:

- ✚ Throughout carcinogenesis, interactions between cancer cells and the surrounding tumor microenvironment play a critical role in tumor progression and metastasis.
- ✚ The tumor microenvironment consists of various cell types (including fibroblasts, immune cells, endothelial cells) and extracellular matrix components that provide structural support, signaling cues, and immune surveillance.
- ✚ Dysregulated communication between cancer cells and the tumor microenvironment promotes tumor growth, angiogenesis, immune evasion, and therapy resistance.

11. Spread of tumors

- ✚ The spread of tumors, known as metastasis, is a complex process that involves cancer cells detaching from the primary tumor, invading surrounding tissues, entering the bloodstream or lymphatic vessels, traveling to distant sites in the body, and establishing secondary tumors.

- ✚ Metastasis is a hallmark of malignant tumors and is responsible for the majority of cancer-related deaths. Here's a detailed explanation of the steps involved in the spread of tumors:

Local Invasion:

- ✚ The first step in metastasis is local invasion, where cancer cells within the primary tumor acquire the ability to invade surrounding tissues and extracellular matrix (ECM).
- ✚ Cancer cells undergo epithelial-to-mesenchymal transition (EMT), a process that enables them to lose cell-cell adhesion and gain increased motility and invasiveness.
- ✚ Proteolytic enzymes such as matrix metalloproteinases (MMPs) are secreted by cancer cells to degrade ECM components, allowing them to penetrate basement membranes and invade adjacent tissues.

Intravasation:

- ✚ Once cancer cells have invaded surrounding tissues, they can enter nearby blood vessels (intravasation) or lymphatic vessels.
- ✚ Cancer cells may directly breach the walls of blood vessels or lymphatic vessels, or they may be passively carried along by the flow of fluid within these vessels.
- ✚ Intravasated cancer cells are transported through the bloodstream or lymphatic system as circulating tumor cells (CTCs) or tumor emboli.

Survival in Circulation:

- ✚ Cancer cells face numerous challenges while circulating in the bloodstream or lymphatic system, including sheer stress, immune surveillance, and anoikis (apoptosis triggered by detachment from the extracellular matrix).
- ✚ Some cancer cells evade immune detection by downregulating cell surface antigens or expressing immune checkpoint proteins that inhibit immune responses.
- ✚ Cancer cells may also undergo phenotypic changes, such as increased expression of survival factors or enhanced resistance to apoptosis, to survive in circulation.

Extravasation:

- ✚ Upon reaching distant sites, cancer cells adhere to the endothelial lining of blood vessels or lymphatic vessels and extravasate into the surrounding tissues.
- ✚ Extravasation involves interactions between cancer cells and endothelial cells, as well as remodeling of the endothelial barrier.
- ✚ Cancer cells may secrete factors that disrupt the integrity of endothelial junctions or promote endothelial permeability, facilitating their migration into the tissue parenchyma.

Colonization and Secondary Tumor Formation:

- ✚ Once cancer cells have extravasated into distant tissues, they must adapt to the new microenvironment and establish secondary tumors (metastases).
- ✚ Cancer cells may undergo mesenchymal-to-epithelial transition (MET), reverting to a more epithelial phenotype conducive to forming solid tumors.
- ✚ Secondary tumors develop through a series of steps similar to those of primary tumor formation, including proliferation, angiogenesis, and evasion of immune surveillance.
- ✚ Metastases can develop in various organs and tissues, with the pattern of metastatic spread influenced by factors such as blood flow, lymphatic drainage, and tissue microenvironment.

12. Autopsy and Biopsy

- ✚ Autopsy and biopsy are both medical procedures used to examine tissues and organs for diagnostic or research purposes, but they differ in their scope, purpose, and methods. Here's an explanation of each:

Autopsy:

- ✚ An autopsy, also known as a postmortem examination, is a comprehensive medical procedure performed after death to determine the cause of death, understand the extent of disease, or investigate the effects of treatment.
- ✚ Autopsies are typically conducted by pathologists, medical examiners, or coroners in a specialized facility known as a morgue or autopsy suite.
- ✚ The procedure involves a systematic examination of the body, including external examination, internal examination (dissection of organs), and histological analysis (microscopic examination of tissue samples).
- ✚ Autopsies can provide valuable information about the presence and extent of disease, the effectiveness of medical treatments, the occurrence of complications, and the circumstances surrounding death.
- ✚ There are different types of autopsies, including forensic autopsies performed for legal or criminal investigations, hospital autopsies performed for quality assurance or research purposes, and clinical autopsies performed to determine the cause of death in medical cases.

Biopsy:

- ✚ A biopsy is a medical procedure in which a sample of tissue or cells is taken from a living patient for microscopic examination to diagnose or evaluate a suspected disease or abnormality.
- ✚ Biopsies can be performed on various tissues and organs, including skin, liver, lung, breast, prostate, and bone, using different techniques depending on the location and nature of the suspected abnormality.
- ✚ Common biopsy techniques include needle biopsy (using a thin needle to extract tissue samples), core biopsy (collecting a larger tissue core), incisional biopsy (removing a portion of tissue), and excisional biopsy (removing the entire lesion or tumor).
- ✚ Once the tissue sample is obtained, it is processed, fixed in formalin, embedded in paraffin, sliced into thin sections, stained with special dyes, and examined under a microscope by a pathologist.
- ✚ Biopsies are used to diagnose various conditions, including cancer, infections, inflammatory diseases, autoimmune disorders, and genetic abnormalities. They can also be used to monitor disease progression, assess treatment response, and guide treatment decisions.

13. Edema

- ✚ Edema is a condition characterized by the accumulation of excess fluid in the body's tissues, leading to swelling and puffiness. It can occur anywhere in the body but is most commonly noticed in the hands, arms, feet, ankles, and legs. Understanding the causes, symptoms, diagnosis, and treatment options for edema is crucial for managing the condition effectively.

Causes of Edema:

- ✚ **Fluid Retention:** This is one of the most common causes of edema. It can be due to several factors such as:
 - ✚ **Heart failure:** The heart's inability to pump blood effectively can lead to fluid buildup in the body, including the limbs and lungs.
 - ✚ **Kidney disease:** Impaired kidney function can result in fluid and electrolyte imbalances, leading to edema.

- ✚ **Liver disease:** Conditions like cirrhosis can cause fluid retention due to decreased protein production and increased pressure in the blood vessels.
- ✚ **Pregnancy:** Hormonal changes and increased blood volume during pregnancy can lead to edema, particularly in the legs and feet.
- ✚ **Inflammation and Injury:** Trauma or inflammation to a specific area of the body can cause localized edema. This can occur as a result of sprains, strains, or inflammatory conditions such as arthritis.
- ✚ **Medications:** Certain medications, including calcium channel blockers, corticosteroids, and nonsteroidal anti-inflammatory drugs (NSAIDs), can cause fluid retention and edema as side effects.
- ✚ **Venous Insufficiency:** When the veins in the legs have difficulty sending blood back to the heart, it can lead to fluid buildup and edema in the lower extremities. This condition is often seen in individuals with varicose veins or deep vein thrombosis (DVT).
- ✚ **Lymphatic Issues:** Lymphedema occurs when the lymphatic system is impaired, leading to fluid accumulation in the tissues. This can be congenital or acquired due to surgery, radiation therapy, or infection.
- ✚ **Infection:** Infections, particularly in the skin or underlying tissues, can cause localized swelling and edema as part of the body's immune response.

Symptoms of Edema:

- ✓ Swelling or puffiness in the affected area(s)
- ✓ Skin that appears stretched or shiny
- ✓ Increased size of the affected limb or body part
- ✓ Stiffness or limited range of motion in the affected joints
- ✓ Weight gain due to fluid retention

Diagnosis:

- ✚ Diagnosing edema typically involves a physical examination and medical history review. Your healthcare provider may also perform additional tests to identify the underlying cause, such as:
- ✚ Blood tests to check for kidney or liver function, electrolyte imbalances, or markers of inflammation
- ✚ Imaging tests such as ultrasound, CT scan, or MRI to evaluate the structure and function of organs and blood vessels
- ✚ Doppler ultrasound to assess blood flow and detect any vascular abnormalities

Treatment Options:

- ✚ Treatment for edema focuses on addressing the underlying cause and reducing fluid buildup. Depending on the severity and underlying condition, treatment options may include:
- ✚ **Medications:** Diuretics (water pills) may be prescribed to help the body eliminate excess fluid. However, these should be used cautiously under medical supervision to avoid electrolyte imbalances and other side effects.
- ✚ **Lifestyle Modifications:** Dietary changes, such as reducing salt intake, and elevating the affected limbs can help reduce fluid retention. Regular exercise and weight management may also be beneficial.
- ✚ **Compression Therapy:** Wearing compression stockings or sleeves can help improve circulation and reduce swelling in the legs and feet.
- ✚ **Surgical Interventions:** In cases of severe lymphedema or venous insufficiency, surgical procedures such as lymphatic drainage, vein stripping, or valve repair may be recommended.

- ✚ Management of Underlying Conditions: Treating the underlying medical conditions such as heart failure, kidney disease, or liver disease is essential for managing edema effectively.

14. Hyperemia

- ✚ Hyperemia is a physiological response in which there is an increase in blood flow to a specific area of the body.
- ✚ This increase in blood flow is often associated with a reddening or flushing of the affected tissue due to the higher concentration of oxygenated blood in the area.
- ✚ Hyperemia can occur for various reasons, including as a normal response to increased metabolic activity, such as during exercise or digestion, or as part of the body's response to injury or inflammation.

There are two main types of hyperemia: active hyperemia and passive hyperemia.

Active Hyperemia:

- ✚ This type of hyperemia occurs when there is an increase in blood flow to an organ or tissue in response to increased metabolic activity or demand.
- ✚ For example, during exercise, the muscles require more oxygen and nutrients to support increased activity. In response, the body dilates the blood vessels supplying the muscles, allowing more blood to flow into them.
- ✚ This increased blood flow helps deliver oxygen and nutrients to the muscles to meet the increased demand.

Passive Hyperemia:

- ✚ Passive hyperemia, also known as congestion, occurs when there is a buildup of blood in a tissue or organ due to impaired venous outflow.
- ✚ This can occur as a result of mechanical obstruction (such as compression of a vein) or functional impairment (such as venous insufficiency).
- ✚ For example, when a person sits or stands for a long time, gravity can impede the flow of blood back to the heart from the lower extremities, leading to passive hyperemia and causing the legs to become swollen and discolored.

Hyperemia can also be classified based on its duration:

Acute Hyperemia:

- ✚ This type of hyperemia is usually a short-term response to a specific stimulus, such as exercise or injury. It is characterized by a rapid increase in blood flow to the affected area, followed by a return to baseline once the stimulus is removed or resolved.

Chronic Hyperemia:

- ✚ Chronic hyperemia refers to a prolonged increase in blood flow to a tissue or organ. It can result from persistent metabolic demands, such as in tissues undergoing constant repair or growth, or it can be a consequence of underlying pathologies, such as chronic inflammation or heart failure.

15. Ischemia

- ✚ Ischemia refers to a condition characterized by an inadequate blood supply to a specific tissue or organ, resulting in a deficiency of oxygen and nutrients.
- ✚ This insufficient blood flow can lead to cellular damage and dysfunction if left untreated.
- ✚ Ischemia can occur in various parts of the body and can have numerous causes, ranging from arterial blockages to systemic diseases affecting blood flow regulation. Understanding ischemia is crucial as it underlies many common medical conditions, including myocardial infarction, stroke, and peripheral artery disease.

Causes of Ischemia:

Arterial Blockage:

- ✚ The most common cause of ischemia is the obstruction of arterial blood flow. This obstruction can result from atherosclerosis, a condition characterized by the buildup of plaque within the arteries, leading to narrowing and eventual blockage.

Embolism:

- ✚ Ischemia can also occur due to the occlusion of arteries by emboli, which are blood clots or other foreign materials that travel through the bloodstream and block smaller vessels.

Vasospasm:

- ✚ Spasms in the blood vessels, known as vasospasm, can also lead to ischemia by reducing blood flow to a particular area.
- ✚ Compression: External compression of blood vessels, such as that which occurs during compartment syndrome, can restrict blood flow and cause ischemia.
- ✚ Systemic Factors: Conditions affecting the overall blood flow regulation in the body, such as hypotension or shock, can also contribute to ischemia by reducing perfusion pressure to vital organs.

Types of Ischemia:

- ✚ **Acute Ischemia:** Acute ischemia refers to a sudden and severe decrease in blood flow to a tissue or organ. This can result from arterial blockage, embolism, or vasospasm and often requires urgent medical intervention to prevent irreversible damage.
- ✚ **Chronic Ischemia:** Chronic ischemia develops gradually over time due to progressive narrowing of arteries, commonly seen in conditions like peripheral artery disease (PAD). Symptoms may include intermittent claudication (pain with walking) and impaired wound healing.

Consequences of Ischemia:

Cellular Damage:

- ✚ Ischemia deprives cells of oxygen and nutrients, leading to cellular dysfunction and, ultimately, cell death if blood flow is not restored promptly. The extent of damage depends on the severity and duration of ischemia and the metabolic demands of the affected tissue.
- ✚ Organ Dysfunction: Ischemia can impair the function of affected organs, leading to a range of symptoms depending on the location and severity of the ischemic insult. For example, myocardial ischemia can cause chest pain (angina), while cerebral ischemia can result in stroke symptoms such as weakness, numbness, or difficulty speaking.

Management and Treatment:

- ✚ Revascularization: In cases of arterial blockage, restoring blood flow through revascularization procedures such as angioplasty or bypass surgery is often necessary to alleviate ischemia and prevent further damage.
- ✚ Medications: Medications such as antiplatelet agents, anticoagulants, and vasodilators may be prescribed to manage underlying conditions contributing to ischemia and prevent thrombotic events.
- ✚ Lifestyle Modifications: Lifestyle changes, including smoking cessation, regular exercise, and a healthy diet, can help reduce the risk factors associated with ischemic conditions such as atherosclerosis.

16. Normal Hemostasis

- ✚ Normal hemostasis is the complex physiological process by which the body maintains blood fluidity within vessels while simultaneously preventing excessive bleeding in response to injury.
- ✚ It involves a series of tightly regulated events, including vasoconstriction, platelet activation, coagulation, and fibrinolysis, working together to achieve hemostatic balance. Here's an overview of the key components of normal hemostasis:
- ✚ Vasoconstriction: When blood vessels are injured, they constrict to reduce blood flow to the site of injury. Vasoconstriction helps minimize blood loss and facilitates the formation of a temporary platelet plug.

Primary Hemostasis

Platelet Plug Formation:

- ✚ Platelet Adhesion: Platelets adhere to the exposed subendothelial collagen at the site of vascular injury. von Willebrand factor (vWF), released from endothelial cells, plays a crucial role in mediating platelet adhesion.
- ✚ Platelet Activation: Upon adhesion, platelets become activated, leading to changes in their shape and the release of granule contents, including adhesion molecules and platelet agonists such as thromboxane A₂. This activation further promotes platelet aggregation and the recruitment of additional platelets to the site of injury.
- ✚ Platelet Aggregation: Activated platelets aggregate and form a loose platelet plug, temporarily sealing the site of vascular injury.

Secondary Hemostasis - Coagulation Cascade:

- ✚ Intrinsic Pathway: Triggered by exposure of blood to subendothelial collagen, the intrinsic pathway involves a series of enzymatic reactions that culminate in the activation of factor X (Xa).
- ✚ Extrinsic Pathway: Simultaneously, tissue factor (TF) released from injured tissues initiates the extrinsic pathway by forming a complex with factor VII (VIIa), leading to the activation of factor X (Xa).
- ✚ Common Pathway: Activated factor X (Xa) converges with activated factor V (Va) to generate thrombin (IIa), the central enzyme in the coagulation cascade. Thrombin converts fibrinogen into fibrin, which forms a mesh-like network to stabilize the platelet plug and trap red blood cells, forming a stable blood clot.

Fibrinolysis:

- ✚ Once hemostasis is achieved and the vessel wall is repaired, the fibrin clot must be removed to restore blood flow and prevent thrombosis. Fibrinolysis involves the enzymatic degradation of fibrin by plasmin, which is generated from plasminogen by tissue plasminogen activator (tPA). Plasmin cleaves fibrin into soluble fibrin degradation products, leading to clot dissolution.

Regulation of Hemostasis:

- ✚ Anticoagulant Pathways: The body has several natural anticoagulant mechanisms, including antithrombin, protein C and S, and tissue factor pathway inhibitor (TFPI), which regulate coagulation and prevent excessive clot formation.
- ✚ Endothelial Function: Endothelial cells play a crucial role in maintaining hemostatic balance by releasing vasodilators (e.g., nitric oxide) and antithrombotic molecules (e.g., prostacyclin) while inhibiting platelet activation and coagulation factors.

17. Thrombosis

- ✚ Thrombosis is a pathological condition characterized by the formation of blood clots (thrombi) within the blood vessels.
- ✚ These clots can obstruct blood flow, leading to tissue ischemia or infarction, and can potentially result in severe medical complications such as stroke, heart attack, or pulmonary embolism.
- ✚ Understanding thrombosis is crucial as it underlies many cardiovascular diseases and other health conditions. Here's a comprehensive overview of thrombosis:

Types of Thrombosis:

- ✚ **Arterial Thrombosis:** Arterial thrombosis occurs when a blood clot forms within an artery. It often occurs in association with atherosclerosis, where plaque buildup on the arterial walls can rupture, exposing collagen and other prothrombotic substances, leading to platelet activation and thrombus formation. Arterial thrombosis can result in conditions such as myocardial infarction (heart attack) or ischemic stroke.
- ✚ **Venous Thrombosis:** Venous thrombosis involves the formation of blood clots within veins, most commonly in the deep veins of the legs (deep vein thrombosis, DVT) or the veins of the lungs (pulmonary embolism, PE). Venous thrombosis often occurs due to a combination of factors, including stasis of blood flow, endothelial injury, and hypercoagulability (Virchow's triad).

Pathophysiology of Thrombosis:

- ✚ **Virchow's Triad:** Thrombosis is classically described by Virchow's triad, which includes endothelial injury, abnormal blood flow (stasis or turbulence), and hypercoagulability. These factors contribute to the initiation and propagation of thrombus formation.
- ✚ **Platelet Activation:** Endothelial injury exposes subendothelial collagen, leading to platelet adhesion and activation. Activated platelets release granule contents, promoting further platelet aggregation and the formation of a platelet-rich thrombus.
- ✚ **Coagulation Cascade:** In addition to platelet activation, the coagulation cascade is triggered, leading to the generation of thrombin, which converts fibrinogen into fibrin. Fibrin forms a mesh-like network that stabilizes the platelet plug and reinforces the thrombus.

Risk Factors for Thrombosis:

- ✚ **Medical Conditions:** Certain medical conditions increase the risk of thrombosis, including atherosclerosis, atrial fibrillation, cancer, and inflammatory disorders such as vasculitis.
- ✚ **Genetic Factors:** Inherited thrombophilias, such as factor V Leiden mutation or deficiencies in antithrombin, protein C, or protein S, can predispose individuals to thrombotic events.
- ✚ **Lifestyle Factors:** Factors such as obesity, smoking, sedentary lifestyle, and hormone therapy (e.g., oral contraceptives) can increase the risk of thrombosis.
- ✚ **Surgery and Trauma:** Surgery, particularly orthopedic procedures, and trauma increase the risk of thrombosis due to endothelial injury, immobility, and other factors.

Clinical Presentation and Complications:

Symptoms:

- ✚ The clinical presentation of thrombosis varies depending on the location and severity of the clot. Common symptoms include pain, swelling, redness, and warmth in the affected area. Symptoms of arterial thrombosis may include chest pain, shortness of breath, or neurological deficits.

- ✚ Complications: Untreated thrombosis can lead to serious complications, such as tissue ischemia, infarction, or organ dysfunction. In cases of venous thrombosis, clot extension or embolization to vital organs such as the lungs (pulmonary embolism) can be life-threatening.

Prevention and Treatment:

- ✚ Anticoagulant Therapy: Anticoagulant medications, such as heparin and warfarin, are commonly used to prevent and treat thrombosis by inhibiting the coagulation cascade and preventing clot formation and propagation.
- ✚ Thrombolytic Therapy: Thrombolytic agents, such as tissue plasminogen activator (tPA), may be used to dissolve existing blood clots in certain clinical scenarios, such as acute myocardial infarction or ischemic stroke.
- ✚ Compression Therapy: Compression stockings or pneumatic compression devices may be used to prevent venous thrombosis in high-risk individuals, such as those undergoing surgery or hospitalized patients.
- ✚ Lifestyle Modifications: Lifestyle interventions, including smoking cessation, regular exercise, and maintaining a healthy weight, can help reduce the risk of thrombosis, particularly in individuals with modifiable risk factors.

18. Disseminated Intravascular Coagulation

- ✚ Disseminated Intravascular Coagulation (DIC) is a serious and complex disorder characterized by widespread activation of the coagulation cascade, leading to both thrombosis and simultaneous consumption of clotting factors and platelets.
- ✚ This dysregulated hemostatic response results in the formation of microthrombi throughout the vasculature, leading to tissue ischemia and organ dysfunction, while also predisposing patients to bleeding due to depletion of clotting factors.
- ✚ DIC can occur secondary to various underlying conditions, such as sepsis, trauma, malignancy, or obstetric complications, and it represents a medical emergency requiring prompt recognition and intervention.

Pathophysiology:

- ✚ Triggering Event: DIC typically occurs secondary to an underlying condition that triggers systemic activation of coagulation pathways. Common triggers include sepsis, severe trauma, major surgery, obstetric complications (such as placental abruption or amniotic fluid embolism), malignancy, and certain systemic diseases.
- ✚ Coagulation Activation: The triggering event leads to widespread activation of the coagulation cascade, resulting in the generation of thrombin and the formation of fibrin clots throughout the microvasculature.
- ✚ Consumption of Clotting Factors and Platelets: As clotting factors and platelets are consumed in the formation of microthrombi, the levels of these components in the bloodstream decrease, leading to a bleeding tendency.
- ✚ Endothelial Activation and Dysfunction: Concurrently, the endothelium becomes activated and dysfunctional, leading to increased expression of procoagulant molecules and decreased expression of anticoagulant and fibrinolytic molecules, further promoting thrombosis and exacerbating the consumption of clotting factors.

Clinical Presentation:

- ✚ Thrombotic Phase: Initially, patients may present with features of thrombosis, including microvascular occlusion, tissue ischemia, and organ dysfunction. Symptoms depend on the underlying trigger and the affected organs but may include skin changes (such as purpura or petechiae), neurologic deficits, respiratory distress, renal failure, or gastrointestinal bleeding.

- ✚ Hemorrhagic Phase: As the consumption of clotting factors progresses, patients may develop bleeding manifestations, such as mucosal bleeding (e.g., gingival bleeding, epistaxis), gastrointestinal bleeding, or hematuria. Severe cases may progress to life-threatening hemorrhage.

Laboratory Findings:

- ✚ Thrombocytopenia: Decreased platelet count due to consumption.
- ✚ Prolonged Clotting Times: Prolongation of prothrombin time (PT) and activated partial thromboplastin time (aPTT) due to depletion of clotting factors.
- ✚ Decreased Fibrinogen: Decreased levels of fibrinogen due to consumption in the formation of fibrin clots.
- ✚ Elevated D-dimer: Increased levels of D-dimer, a product of fibrin degradation, indicating ongoing fibrinolysis.

Treatment and Management:

- ✚ Addressing Underlying Cause: Treatment of the underlying trigger is paramount. This may involve antibiotics for sepsis, control of bleeding in trauma, or supportive measures for obstetric complications.
- ✚ Supportive Care: Supportive measures include hemodynamic support, respiratory support, renal replacement therapy for renal failure, and transfusion of blood products as needed (e.g., platelets, fresh frozen plasma, cryoprecipitate).
- ✚ Anticoagulant Therapy: Anticoagulants are generally contraindicated in DIC due to the risk of exacerbating bleeding. However, in select cases with predominant thrombosis and minimal bleeding, heparin may be considered under close monitoring.
- ✚ Monitoring and Serial Assessment: Close monitoring of laboratory parameters (platelet count, coagulation tests) and clinical status is essential for guiding treatment decisions and assessing response to therapy.

19. Embolism

- ✚ An embolism occurs when a mass, such as a blood clot, air bubble, fat droplet, or other foreign material, gets carried through the bloodstream and lodges in a blood vessel, obstructing blood flow.
- ✚ This obstruction can lead to serious health complications, depending on the size and location of the embolism.

Types of Embolism:

- ✚ Thromboembolism: This is the most common type and involves a blood clot that forms in one part of the body and travels to another. Deep vein thrombosis (DVT), where a clot forms in the deep veins of the legs, is a common precursor to thromboembolism.
- ✚ Air Embolism: This occurs when air bubbles enter the bloodstream. It can happen during medical procedures such as surgery, especially if the procedure involves the manipulation of blood vessels or when scuba diving.
- ✚ Fat Embolism: This typically occurs after a bone fracture or trauma, where fat tissue from the bone marrow enters the bloodstream and travels to the lungs or brain.
- ✚ Amniotic Fluid Embolism: This rare but serious condition happens when amniotic fluid enters the maternal bloodstream, usually during childbirth.

Risk Factors:

- ✚ Immobility: Prolonged periods of immobility, such as during long flights or bed rest, increase the risk of blood clots forming.
- ✚ Surgery: Certain surgical procedures, especially those involving the lower extremities, pelvis, or abdomen, increase the risk of thromboembolism.

- ✚ Obesity: Being overweight or obese can contribute to the formation of blood clots.
- ✚ Pregnancy: Pregnancy and childbirth increase the risk of amniotic fluid embolism.
- ✚ Smoking: Smoking damages blood vessels and increases the risk of clot formation.
- ✚ Inherited Conditions: Conditions such as factor V Leiden mutation or antiphospholipid syndrome increase the risk of blood clots.

Symptoms:

- ✚ Symptoms of an embolism vary depending on its location. Common symptoms include sudden shortness of breath, chest pain, rapid heartbeat, dizziness, confusion, and fainting.
- ✚ In the case of a stroke caused by an embolism, symptoms may include sudden weakness or numbness in the face, arm, or leg, especially on one side of the body, difficulty speaking or understanding speech, and trouble walking.

Treatment:

- ✚ Treatment for an embolism depends on its type and severity. In the case of a blood clot, anticoagulant medications such as heparin or warfarin may be prescribed to prevent further clot formation and to dissolve existing clots.
- ✚ In some cases, thrombolytic therapy may be used to dissolve a clot quickly.
- ✚ Surgical procedures, such as thrombectomy (removal of the clot) or embolectomy (removal of the embolus), may be necessary in severe cases.

Prevention:

- ✚ Prevention strategies include maintaining a healthy weight, staying physically active, avoiding prolonged periods of immobility, especially during long flights or car rides, quitting smoking, and managing underlying medical conditions such as high blood pressure, diabetes, and high cholesterol.
- ✚ For individuals at high risk of blood clots, especially after surgery or during pregnancy, prophylactic measures such as the use of compression stockings or anticoagulant medications may be recommended.

20. Infarction

- ✚ Infarction refers to tissue death (necrosis) caused by a lack of blood supply. This deprivation of blood flow typically occurs when a blood vessel supplying a particular area becomes blocked or obstructed, leading to ischemia (a lack of oxygen and nutrients) in that tissue.
- ✚ The severity and consequences of infarction depend on various factors, including the size of the affected area, the duration of the blockage, and the tissue's susceptibility to ischemia.

Types of Infarction:

- ✚ Ischemic Infarction: This type occurs when a blood clot or other material obstructs a blood vessel, cutting off blood supply to a specific area. Ischemic infarctions can occur in various organs, including the heart (resulting in a heart attack), brain (resulting in a stroke), lungs, kidneys, intestines, and limbs.
- ✚ Hemorrhagic Infarction: This occurs when there is bleeding into the infarcted tissue. It can happen when blood vessels rupture within the affected area or when blood leaks into the area from adjacent vessels.

Causes:

- ✚ Thrombosis: Formation of a blood clot (thrombus) within a blood vessel, often due to conditions like atherosclerosis (buildup of plaque in the arteries), which can narrow the vessel and promote clot formation.

- ✚ Embolism: The movement of a blood clot or other material from another part of the body to a blood vessel, leading to obstruction.
- ✚ Vasospasm: Sudden constriction of a blood vessel, reducing or stopping blood flow to an area. This can occur due to various factors, including trauma or certain medical conditions.
- ✚ Compression: External pressure on a blood vessel, restricting blood flow. This can happen in conditions such as compartment syndrome, where increased pressure within a muscle compartment limits blood supply.

Symptoms:

- ✚ Symptoms of infarction vary depending on the affected organ or tissue. Common symptoms may include pain, swelling, tenderness, discoloration, and loss of function in the affected area.
- ✚ In the case of a myocardial infarction (heart attack), symptoms may include chest pain or discomfort, shortness of breath, nausea, vomiting, and lightheadedness.
- ✚ In a cerebral infarction (stroke), symptoms may include sudden weakness or numbness in the face, arm, or leg (usually on one side of the body), difficulty speaking or understanding speech, confusion, dizziness, and sudden severe headache.

Diagnosis:

- ✚ Diagnosis of infarction typically involves a combination of medical history, physical examination, imaging studies (such as X-rays, CT scans, MRI, or ultrasound), and laboratory tests (including blood tests and cardiac enzyme tests).
- ✚ Electrocardiography (ECG or EKG) is often used to diagnose myocardial infarction by assessing changes in the heart's electrical activity.
- ✚ Imaging studies, such as CT angiography or magnetic resonance angiography, may be used to visualize blood vessels and assess blood flow to different organs.

Treatment:

- ✚ Treatment for infarction aims to restore blood flow to the affected area and minimize tissue damage.
- ✚ In the case of ischemic infarction, treatment may involve medications such as antiplatelet drugs (e.g., aspirin), anticoagulants, thrombolytic agents (to dissolve blood clots), and medications to manage symptoms such as pain and inflammation.
- ✚ Reperfusion therapy, including procedures such as percutaneous coronary intervention (PCI) or thrombectomy, may be necessary to restore blood flow in cases of myocardial or cerebral infarction.
- ✚ In some cases, surgery may be required to remove obstructions or repair damaged blood vessels.

Complications and Prognosis:

- ✚ Complications of infarction can vary depending on the affected organ and the extent of tissue damage. Common complications include tissue scarring, organ dysfunction, heart failure, stroke-related disabilities, and even death.
- ✚ The prognosis for individuals with infarction depends on factors such as the location and size of the infarct, the timeliness of treatment, the presence of underlying health conditions, and individual response to therapy.
- ✚ Prompt medical intervention and rehabilitation can improve outcomes and reduce the risk of long-term complications.

21. Shock

- ✚ Pathological shock is a medical emergency characterized by inadequate tissue perfusion, which leads to cellular and organ dysfunction.

- ✚ It's a critical condition where the body's organs and tissues do not receive enough oxygen and nutrients due to insufficient blood flow, leading to potentially life-threatening consequences if not promptly treated.
- ✚ There are several types of pathological shock, each with its underlying causes and mechanisms:

Hypovolemic Shock:

- ✚ This type of shock occurs due to a significant loss of blood or fluid volume, leading to a decrease in circulating blood volume.
- ✚ Causes include severe bleeding (hemorrhage), dehydration from vomiting, diarrhea, or inadequate fluid intake, burns, and fluid loss from major trauma or surgery.
- ✚ Reduced blood volume results in decreased cardiac output and inadequate tissue perfusion, leading to cellular hypoxia and organ dysfunction.

Cardiogenic Shock:

- ✚ Cardiogenic shock occurs when the heart fails to pump enough blood to meet the body's demands, leading to decreased cardiac output and systemic hypoperfusion.
- ✚ Causes include myocardial infarction (heart attack), severe heart failure, cardiomyopathy (disease of the heart muscle), severe arrhythmias, and cardiac tamponade (compression of the heart due to fluid accumulation around the heart).
- ✚ Impaired cardiac function leads to decreased tissue perfusion and oxygen delivery, resulting in organ dysfunction.

Distributive Shock:

- ✚ Distributive shock is characterized by widespread vasodilation and impaired vascular tone, leading to decreased systemic vascular resistance and blood pressure.

Types of distributive shock include

- Septic Shock: Caused by systemic bacterial or fungal infection leading to an exaggerated inflammatory response and widespread vasodilation.
- Anaphylactic Shock: Resulting from a severe allergic reaction causing systemic release of histamine and other mediators, leading to vasodilation and increased vascular permeability.
- Neurogenic Shock: Caused by disruption of sympathetic nervous system control over vascular tone, often due to spinal cord injury, anesthesia, or severe emotional stress.

Obstructive Shock:

- ✚ Obstructive shock occurs when there is physical obstruction to blood flow within the circulatory system.
- ✚ Causes include pulmonary embolism (blockage of pulmonary arteries), tension pneumothorax (buildup of air in the pleural space causing lung collapse and impaired venous return), cardiac tamponade, and severe aortic stenosis.
- ✚ Obstruction to blood flow leads to impaired cardiac output and inadequate tissue perfusion.

Mixed Shock:

- ✚ Mixed shock refers to a combination of different types of shock occurring simultaneously or sequentially, often seen in critically ill patients with multiple underlying conditions or injuries.

22. Chronic venous congestion

- ✚ Chronic venous congestion, also known as chronic venous insufficiency (CVI) or venous stasis, is a condition characterized by impaired venous blood flow in the lower extremities, leading to increased pressure within the veins and subsequent tissue damage.
- ✚ It typically occurs when the valves in the veins, which help maintain blood flow toward the heart, become damaged or incompetent, resulting in venous reflux (backward flow) and pooling of blood in the lower limbs.
- ✚ Chronic venous congestion can manifest with various signs and symptoms, and if left untreated, it can lead to complications such as venous ulcers and skin changes.

Causes:

- ✚ Chronic venous congestion can result from various factors, including:
- ✚ Damage to the venous valves due to aging, prolonged standing or sitting, obesity, or previous deep vein thrombosis (DVT).
- ✚ Chronic conditions that increase abdominal pressure, such as obesity, pregnancy, or tumors, leading to impaired venous return from the lower extremities.
- ✚ Congenital abnormalities of the venous system.
- ✚ Previous trauma or surgery affecting the veins.
- ✚ Inflammatory conditions affecting the veins, such as phlebitis or vasculitis.

Signs and Symptoms:

- ✚ Common signs and symptoms of chronic venous congestion include:
- ✚ Swelling (edema) in the lower legs and ankles, particularly worsening at the end of the day or after prolonged standing.
- ✚ Heaviness or aching sensation in the legs.
- ✚ Varicose veins, which are enlarged, twisted veins visible under the skin.
- ✚ Skin changes, including thickening, discoloration (such as brownish pigmentation), and inflammation (dermatitis).
- ✚ Venous ulcers, particularly around the ankles, which may be slow to heal and prone to recurrence.
- ✚ Itching or tingling sensation in the legs.
- ✚ Restless legs syndrome, characterized by an uncontrollable urge to move the legs, often worsened by rest or inactivity.

Diagnosis:

- ✚ Diagnosis of chronic venous congestion typically involves a combination of medical history, physical examination, and diagnostic tests.
- ✚ Physical examination may reveal characteristic signs such as varicose veins, edema, skin changes, and venous ulcers.
- ✚ Duplex ultrasound is a non-invasive imaging test commonly used to assess venous blood flow, identify venous reflux, and evaluate the integrity of venous valves.
- ✚ Other imaging modalities, such as venography or magnetic resonance venography, may be used in specific cases to provide detailed visualization of the venous anatomy.

Treatment:

- ✚ Treatment aims to alleviate symptoms, improve venous circulation, and prevent complications.

- ✚ Lifestyle modifications, such as elevating the legs, avoiding prolonged standing or sitting, regular exercise, weight management, and wearing compression stockings, can help improve venous return and reduce symptoms.
- ✚ Medical therapies may include medications to reduce swelling (diuretics), promote venous tone (phlebotonics), or control inflammation (topical corticosteroids).
- ✚ Interventional procedures, such as sclerotherapy or endovenous ablation, may be recommended to close off or remove damaged veins and redirect blood flow.
- ✚ In severe cases or those with complications such as venous ulcers, surgical procedures such as vein ligation, vein stripping, or venous bypass surgery may be necessary.

Complications:

- ✚ If left untreated, chronic venous congestion can lead to complications such as:
- ✚ Venous ulcers: Open sores that develop on the skin, particularly around the ankles, due to prolonged venous hypertension and tissue damage.
- ✚ Cellulitis: Bacterial infection of the skin and soft tissues, which can occur secondary to breaks in the skin caused by venous ulcers.
- ✚ Lipodermatosclerosis: Thickening and hardening of the skin and underlying tissues due to chronic inflammation and fibrosis.
- ✚ Venous thromboembolism (VTE): Increased risk of developing blood clots in the deep veins (DVT) due to venous stasis and endothelial damage.

23. Bleeding Disorders

- ✚ Bleeding disorders encompass a wide range of conditions characterized by abnormalities in the blood's ability to clot properly.
- ✚ Two common bleeding disorders are Hemophilia and von Willebrand Disease (VWD).

Hemophilia:

- ✚ Hemophilia is a genetic bleeding disorder characterized by deficiency or dysfunction of certain clotting factors, specifically factor VIII (hemophilia A) or factor IX (hemophilia B). These clotting factors are crucial for the formation of blood clots to stop bleeding.

Causes:

- ✚ Hemophilia is usually inherited as an X-linked recessive disorder, meaning it primarily affects males. Females are typically carriers of the defective gene but may experience mild symptoms. The genetic mutations lead to reduced or absent production of clotting factors, resulting in prolonged bleeding and poor clot formation.

Symptoms:

- ✚ Prolonged bleeding after minor injuries or trauma.
- ✚ Easy bruising.
- ✚ Excessive bleeding from cuts, dental procedures, or surgeries.
- ✚ Joint pain and swelling (hemarthrosis) due to bleeding into the joints, which can lead to chronic joint damage and disability.
- ✚ Bleeding into soft tissues and muscles, leading to swelling and pain.

Diagnosis:

- ✚ Diagnosis typically involves a combination of medical history, family history, physical examination, and laboratory tests.
- ✚ Blood tests can measure the levels of clotting factors, particularly factor VIII or IX, to confirm the diagnosis.

- ✚ Genetic testing may be performed to identify specific mutations associated with hemophilia.

Treatment:

- ✚ Management of hemophilia involves replacing the deficient clotting factor through intravenous infusion of clotting factor concentrates.
- ✚ Prophylactic (preventive) factor replacement therapy may be recommended to prevent bleeding episodes, particularly in severe cases.
- ✚ Desmopressin (DDAVP) may be used in some cases of mild hemophilia A to stimulate the release of stored factor VIII from endothelial cells.
- ✚ Additional treatments may include fibrinolytic inhibitors, such as tranexamic acid, to help stabilize blood clots and prevent excessive bleeding.
- ✚ Joint aspiration or drainage may be necessary to remove excess blood from affected joints during bleeding episodes.

Complications:

- ✚ Chronic joint damage and arthritis due to recurrent joint bleeding.
- ✚ Intracranial bleeding (hemorrhage) can occur, particularly after head injuries, posing a risk of life-threatening complications.
- ✚ Inhibitor development, where the body produces antibodies against infused clotting factor concentrates, can complicate treatment and increase the risk of bleeding.

von Willebrand Disease (VWD):

- ✚ Von Willebrand Disease is the most common inherited bleeding disorder, characterized by a deficiency or dysfunction of von Willebrand factor (vWF), a protein that plays a crucial role in blood clotting by facilitating platelet adhesion and stabilizing factor VIII.

Causes:

- ✚ VWD is typically inherited in an autosomal dominant pattern, meaning that an abnormal gene from one parent is sufficient to cause the disorder. However, some cases may result from autosomal recessive inheritance or occur sporadically due to new mutations. Defects in the vWF gene lead to reduced levels or impaired function of von Willebrand factor, resulting in defective platelet adhesion and clot formation.

Symptoms:

- ✚ Easy bruising and mucosal bleeding (e.g., nosebleeds, gum bleeding).
- ✚ Prolonged bleeding after minor injuries, surgeries, or dental procedures.
- ✚ Heavy or prolonged menstrual bleeding in females.
- ✚ Gastrointestinal bleeding, particularly in severe cases.

Diagnosis:

- ✚ Diagnosis involves a combination of medical history, family history, physical examination, and laboratory tests.
- ✚ Laboratory tests include measurement of vWF antigen levels, vWF activity (ristocetin cofactor activity), and factor VIII levels.
- ✚ Additional tests, such as platelet function assays and bleeding time tests, may be performed to assess platelet function and overall hemostasis.

Treatment:

- ✚ Treatment of VWD depends on the severity of the condition and the type of von Willebrand factor deficiency.
- ✚ Desmopressin (DDAVP) may be used to stimulate the release of stored vWF from endothelial cells in mild to moderate cases of VWD type 1 and some cases of type 2.

- ✚ Replacement therapy with plasma-derived von Willebrand factor concentrates or recombinant von Willebrand factor may be necessary for more severe cases or when desmopressin is ineffective.
- ✚ Antifibrinolytic medications, such as tranexamic acid, may be used to help stabilize blood clots and reduce bleeding in certain situations.

Complications:

- ✚ Iron deficiency anemia due to chronic blood loss, particularly in individuals with heavy menstrual bleeding or gastrointestinal bleeding.
- ✚ Increased risk of excessive bleeding during surgical procedures or childbirth.
- ✚ Intracranial bleeding can occur in severe cases, posing a risk of life-threatening complications.

24. Leukemia

- ✚ Leukemia is a type of cancer that affects the blood and bone marrow. It is characterized by the abnormal production of white blood cells, which are essential for the body's immune system.
- ✚ In leukemia, these white blood cells are produced in excessive amounts and are often immature or dysfunctional, leading to compromised immune function and other health problems.
- ✚ The disease originates in the bone marrow, where blood cells are formed. Normally, the bone marrow produces immature blood cells called blasts, which then mature into different types of blood cells, including white blood cells (leukocytes), red blood cells (erythrocytes), and platelets (thrombocytes).
- ✚ In leukemia, this process is disrupted, and abnormal blasts rapidly accumulate, crowding out healthy blood cells.
- ✚ There are several types of leukemia, classified based on the type of white blood cell affected and how quickly the disease progresses:
 - Acute Myeloid Leukemia (AML): AML affects myeloid cells, which give rise to red blood cells, platelets, and certain types of white blood cells. It is characterized by the rapid growth of abnormal myeloid blasts.
 - Acute Lymphoblastic Leukemia (ALL): ALL affects lymphoid cells, which give rise to lymphocytes, a type of white blood cell crucial for the immune system. It is characterized by the rapid growth of abnormal lymphoid blasts.
 - Chronic Myeloid Leukemia (CML): CML affects myeloid cells and typically progresses more slowly than acute leukemias. It is characterized by the overproduction of mature, but abnormal, myeloid cells.
 - Chronic Lymphocytic Leukemia (CLL): CLL affects lymphoid cells and is characterized by the gradual accumulation of abnormal mature lymphocytes.
- ✚ The exact cause of leukemia is not always clear, but several factors may contribute to its development, including genetic mutations, exposure to certain environmental toxins (such as benzene and certain chemotherapy drugs), radiation exposure, and certain viral infections (such as human T-cell leukemia virus).
- ✚ Symptoms of leukemia can vary depending on the type and stage of the disease but may include fatigue, weakness, fever, frequent infections, unexplained weight loss, easy bruising or bleeding, swollen lymph nodes, and bone pain.

- ✚ Diagnosis usually involves a combination of blood tests, bone marrow biopsy, and imaging studies to determine the type and extent of the disease.
- ✚ Treatment for leukemia depends on several factors, including the type of leukemia, its stage, and the patient's overall health. Common treatment options include chemotherapy, targeted therapy, radiation therapy, immunotherapy, and stem cell transplantation. Treatment goals may include achieving remission (where no evidence of the disease is present), managing symptoms, and prolonging survival.
- ✚ Prognosis for leukemia varies widely depending on factors such as the type of leukemia, its stage at diagnosis, the patient's age and overall health, and how well they respond to treatment.
- ✚ Advances in medical research and treatment have led to significant improvements in survival rates for many patients with leukemia, particularly in recent years. However, leukemia remains a serious condition that requires ongoing management and monitoring.

25. Lymphomas

- ✚ Lymphomas are a group of cancers that originate in the lymphatic system, which is part of the body's immune system.
- ✚ The lymphatic system includes lymph nodes, lymphatic vessels, spleen, thymus, and bone marrow. Lymphomas are characterized by the abnormal growth of lymphocytes, a type of white blood cell that helps the body fight infection. There are two main types of lymphoma:
- ✚ Hodgkin Lymphoma (HL): Hodgkin lymphoma is characterized by the presence of a specific type of abnormal cell called Reed-Sternberg cells within the lymph nodes. These cells are typically large, multinucleated cells that are derived from B lymphocytes. HL accounts for a smaller proportion of all lymphomas compared to NHL. It usually begins in a single lymph node or a group of lymph nodes and may spread to nearby lymph nodes as the disease progresses.
- ✚ Non-Hodgkin Lymphoma (NHL): Non-Hodgkin lymphoma is a diverse group of lymphomas that do not contain Reed-Sternberg cells. There are many subtypes of NHL, each with distinct characteristics and behaviors. NHL can originate from either B lymphocytes or T lymphocytes and may involve lymph nodes, other lymphoid tissues, or extranodal sites (organs outside the lymphatic system).

The exact cause of lymphoma is not fully understood, but several factors may increase the risk of developing the disease, including:

- ✚ Immunodeficiency: People with weakened immune systems, such as those with HIV/AIDS or those who have undergone organ transplantation and require immunosuppressive therapy, have an increased risk of developing lymphoma.
- ✚ Infections: Certain viral and bacterial infections, such as Epstein-Barr virus (EBV), human T-cell lymphotropic virus (HTLV-1), *Helicobacter pylori*, and certain types of human herpesvirus, are associated with an increased risk of lymphoma.
- ✚ Environmental factors: Exposure to certain chemicals, such as pesticides and herbicides, as well as other environmental toxins, may increase the risk of lymphoma.
- ✚ Genetic factors: Some genetic abnormalities and inherited conditions may predispose individuals to lymphoma.
- ✚ Symptoms of lymphoma can vary depending on the type and location of the disease but may include enlarged lymph nodes (swollen glands), fever, night

sweats, unexplained weight loss, fatigue, itching, and painless swelling of lymph nodes in the neck, armpits, or groin.

- ✚ Diagnosis of lymphoma usually involves a combination of physical examination, blood tests, imaging studies (such as CT or PET scans), and biopsy of an affected lymph node or other tissue. Additional tests, such as bone marrow biopsy and lumbar puncture, may be performed to determine the extent of the disease.
- ✚ Treatment for lymphoma depends on several factors, including the type, stage, and location of the disease, as well as the patient's overall health and preferences. Common treatment options may include chemotherapy, radiation therapy, immunotherapy, targeted therapy, and stem cell transplantation. Treatment goals may include achieving remission (where no evidence of the disease is present), managing symptoms, and improving quality of life.
- ✚ Prognosis for lymphoma varies widely depending on factors such as the type and stage of the disease, the patient's age and overall health, and how well they respond to treatment. Overall, many patients with lymphoma respond well to treatment, and survival rates have improved significantly in recent years due to advances in medical research and treatment. However, lymphoma remains a serious condition that requires ongoing management and monitoring.

26. Haemorrhage

- ✚ Hemorrhage, commonly referred to as bleeding, is the escape of blood from blood vessels due to injury, trauma, or an underlying medical condition. It can occur internally or externally and may range from minor to life-threatening, depending on the severity and location of the bleeding.

There are several types of hemorrhage:

- ✚ External Hemorrhage: This type of bleeding occurs when blood escapes from the body through an opening in the skin. Examples include cuts, wounds, abrasions, and surgical incisions.
- ✚ Internal Hemorrhage: Internal bleeding occurs inside the body and may not be immediately visible. It can result from trauma, such as a car accident or fall, or from medical conditions such as gastrointestinal bleeding, ruptured blood vessels, or bleeding into organs or body cavities.
- ✚ Arterial Hemorrhage: Arterial bleeding occurs when blood escapes from an artery, which carries oxygen-rich blood away from the heart to the body's tissues. Arterial bleeding is typically bright red and may spurt or pulsate in time with the heartbeat. It can be life-threatening due to the rapid loss of blood.
- ✚ Venous Hemorrhage: Venous bleeding occurs when blood escapes from a vein, which carries blood back to the heart from the body's tissues. Venous bleeding is usually darker in color and flows steadily rather than spurting.
- ✚ Capillary Hemorrhage: Capillary bleeding occurs when blood leaks from tiny blood vessels called capillaries. It is often minor and may result in oozing or slow bleeding.
- ✚ Hemorrhage can lead to symptoms such as bleeding from wounds or body orifices, bruising, swelling, lightheadedness, fainting, weakness, rapid heartbeat, low blood pressure, confusion, and shock.
- ✚ Treatment for hemorrhage depends on its severity and location. First aid measures for external bleeding may include applying direct pressure to the wound, elevating the injured limb, and applying a sterile dressing or bandage.

- ✚ In cases of severe bleeding, immediate medical attention is crucial to control the bleeding and stabilize the patient.
- ✚ Treatment for internal hemorrhage may involve surgery to repair damaged blood vessels or organs, blood transfusions to replace lost blood, medications to promote blood clotting, and interventions to address the underlying cause of the bleeding.
- ✚ Prompt recognition and appropriate management of hemorrhage are essential to prevent complications and improve outcomes. It's important to seek medical attention if you or someone else experiences significant bleeding or signs of internal bleeding, such as abdominal pain, dizziness, or fainting.

27. Diabetes

- ✚ Diabetes is a chronic metabolic disorder characterized by high levels of glucose (sugar) in the blood, either due to insufficient production of insulin by the pancreas or the body's inability to effectively use the insulin it produces. Insulin is a hormone produced by the pancreas that helps regulate blood sugar levels and allows cells to use glucose for energy.

There are several types of diabetes, each with its own causes, risk factors, and management approaches:

- ✚ **Type 1 Diabetes:** Type 1 diabetes, also known as insulin-dependent diabetes or juvenile diabetes, occurs when the immune system mistakenly attacks and destroys the insulin-producing beta cells in the pancreas. As a result, the pancreas produces little to no insulin. Type 1 diabetes typically develops in childhood or adolescence, although it can occur at any age. People with type 1 diabetes require lifelong insulin therapy to survive.
- ✚ **Type 2 Diabetes:** Type 2 diabetes, the most common form of diabetes, develops when the body becomes resistant to the effects of insulin and/or when the pancreas fails to produce enough insulin to maintain normal blood sugar levels. Type 2 diabetes is strongly associated with lifestyle factors such as obesity, physical inactivity, unhealthy diet, and genetics. It usually develops gradually and is often diagnosed in adulthood, although it is increasingly being diagnosed in children and adolescents due to rising rates of obesity. Type 2 diabetes can often be managed through lifestyle modifications, such as diet and exercise, and medications, including oral glucose-lowering drugs and insulin therapy if needed.
- ✚ **Gestational Diabetes:** Gestational diabetes occurs during pregnancy and is characterized by high blood sugar levels that develop for the first time during pregnancy. It occurs when the body is unable to produce enough insulin to meet the increased insulin demands of pregnancy. Gestational diabetes can increase the risk of complications during pregnancy and delivery and also increases the risk of developing type 2 diabetes later in life for both the mother and the child.
- ✚ **Other Types of Diabetes:** Other less common types of diabetes include monogenic diabetes (caused by mutations in a single gene), which includes maturity-onset diabetes of the young (MODY), and secondary diabetes, which can occur as a result of certain medical conditions, medications, or diseases of the pancreas.

Risk factors for developing type 2 diabetes include:

- ✓ Obesity or overweight, especially excess abdominal fat
- ✓ Sedentary lifestyle and lack of physical activity
- ✓ Unhealthy diet high in processed foods, sugar, and saturated fats
- ✓ Family history of diabetes
- ✓ Age (risk increases with age, especially after 45)
- ✓ Ethnicity (African American, Hispanic, Native American, and Asian American populations are at higher risk)
- ✓ Gestational diabetes or giving birth to a baby weighing over 9 pounds
- ✓ Polycystic ovary syndrome (PCOS)
- ✓ Hypertension (high blood pressure) and dyslipidemia (abnormal blood lipid levels)
- ✓ Complications of diabetes can affect various organs and systems in the body and can be acute or chronic. Acute complications include hypoglycemia (low blood sugar) and hyperglycemia (high blood sugar), which can lead to diabetic ketoacidosis (DKA) or hyperosmolar hyperglycemic state (HHS) if untreated, both of which are life-threatening emergencies.

Chronic complications of diabetes include:

- ✓ Cardiovascular disease: Diabetes significantly increases the risk of heart disease, stroke, and peripheral artery disease.
 - ✓ Nephropathy: Diabetes is a leading cause of kidney failure (end-stage renal disease) and may require dialysis or kidney transplantation.
 - ✓ Neuropathy: Diabetes can damage nerves throughout the body, leading to symptoms such as numbness, tingling, pain, and loss of sensation, particularly in the feet and hands.
 - ✓ Retinopathy: Diabetes can damage the blood vessels in the retina, leading to diabetic retinopathy, a leading cause of blindness in adults.
 - ✓ Foot complications: Diabetes increases the risk of foot ulcers, infections, and poor wound healing, which can lead to serious complications such as gangrene and lower limb amputation.
 - ✓ Skin conditions: People with diabetes are more prone to skin infections, including bacterial and fungal infections, and may also develop diabetic dermopathy, necrobiosis lipoidica diabetorum, and other skin disorders.
 - ✓ Complications of pregnancy: Gestational diabetes can increase the risk of preeclampsia, cesarean delivery, and birth complications for both the mother and the baby.
- 📌 Prevention and management of diabetes involve a combination of lifestyle modifications, medications, and regular medical care:
- ✓ Healthy Diet: Eating a balanced diet that is rich in fruits, vegetables, whole grains, lean proteins, and healthy fats can help regulate blood sugar levels, manage weight, and reduce the risk of complications. Monitoring carbohydrate intake and spacing meals evenly throughout the day can also help stabilize blood sugar levels.
 - ✓ Regular Physical Activity: Engaging in regular physical activity, such as walking, jogging, swimming, cycling, or strength training, can improve insulin sensitivity, lower blood sugar levels, and help manage weight. Aim for at least 150 minutes of moderate-intensity aerobic activity or 75 minutes of vigorous-

intensity aerobic activity per week, along with muscle-strengthening activities on two or more days per week.

- ✓ **Weight Management:** Maintaining a healthy weight through diet and exercise can help prevent type 2 diabetes and improve glycemic control in people with diabetes. Losing even a modest amount of weight (5-10% of body weight) can have significant health benefits.
- ✓ **Medications:** Depending on the type and severity of diabetes, medications may be prescribed to help lower blood sugar levels, improve insulin sensitivity, reduce glucose production by the liver, and manage other risk factors such as high blood pressure and high cholesterol. Medications may include oral glucose-lowering drugs, injectable medications (such as insulin and GLP-1 receptor agonists), and other medications to manage comorbid conditions.
- ✓ **Regular Monitoring:** Monitoring blood sugar levels regularly using a blood glucose meter or continuous glucose monitoring (CGM) system can help individuals with diabetes track their progress, make informed decisions about diet and medication adjustments, and identify patterns or trends in blood sugar control.
- ✓ **Regular Medical Care:** Regular medical check-ups with healthcare providers, including primary care physicians, endocrinologists, and diabetes educators, are essential for monitoring blood sugar levels, assessing diabetes-related complications, and adjusting treatment plans as needed. Health screenings for complications such as retinopathy, nephropathy, neuropathy, cardiovascular disease, and foot problems are also important for early detection and management.
- ✓ **Education and Support:** Diabetes self-management education (DSME) and support programs can provide individuals with the knowledge, skills, and resources needed to effectively manage their diabetes and reduce the risk of complications. These programs may cover topics such as nutrition, physical activity, medication management, blood sugar monitoring, stress management, coping strategies, and problem-solving skills.
- ✓ **Smoking Cessation:** Smoking increases the risk of cardiovascular disease, peripheral artery disease, neuropathy, and other complications of diabetes. Quitting smoking can significantly improve overall health and reduce the risk of complications.
- ✓ **Alcohol Moderation:** Alcohol consumption can affect blood sugar levels, increase the risk of hypoglycemia, and contribute to weight gain. Moderation is key, and individuals with diabetes should consult with their healthcare providers to determine safe limits for alcohol consumption.
- ✓ **Stress Management:** Chronic stress can affect blood sugar levels, increase the risk of emotional eating, and interfere with self-care behaviors. Stress-reduction techniques such as deep breathing, meditation, yoga, tai chi, progressive muscle relaxation, and mindfulness can help improve overall well-being and glycemic control.

28. Obesity

- 🚩 **Obesity** is a complex, chronic medical condition characterized by excessive accumulation of body fat that poses a risk to health. It is typically defined by a body mass index (BMI) of 30 or higher, although other factors such as waist circumference, body composition, and distribution of body fat also play a role in assessing obesity and associated health risks.

- ✚ Obesity has become a global epidemic, affecting people of all ages, genders, socioeconomic backgrounds, and ethnicities.

It is associated with a wide range of health problems and complications, including:

- ✚ Cardiovascular Disease (CVD): Obesity is a major risk factor for heart disease, hypertension (high blood pressure), stroke, coronary artery disease, heart failure, and other cardiovascular conditions. Excess body fat can lead to elevated levels of cholesterol and triglycerides, insulin resistance, inflammation, and endothelial dysfunction, all of which contribute to CVD.
- ✚ Type 2 Diabetes: Obesity is closely linked to the development of type 2 diabetes, a metabolic disorder characterized by high blood sugar levels resulting from insulin resistance and relative insulin deficiency. Excess body fat, particularly visceral fat around the abdomen, impairs insulin sensitivity and glucose metabolism, increasing the risk of diabetes.
- ✚ Hypertension: Obesity is a leading cause of hypertension, a condition characterized by elevated blood pressure levels. Excess body weight puts additional strain on the heart and blood vessels, leading to increased resistance to blood flow and higher blood pressure.
- ✚ Dyslipidemia: Obesity is associated with abnormalities in blood lipid levels, including high levels of LDL cholesterol (the "bad" cholesterol), triglycerides, and low levels of HDL cholesterol (the "good" cholesterol). Dyslipidemia increases the risk of atherosclerosis (hardening and narrowing of the arteries) and cardiovascular disease.
- ✚ Metabolic Syndrome: Obesity is a key component of metabolic syndrome, a cluster of metabolic abnormalities that increase the risk of cardiovascular disease, type 2 diabetes, and other health problems. Metabolic syndrome is characterized by central obesity (excess abdominal fat), insulin resistance, hypertension, dyslipidemia, and elevated blood sugar levels.
- ✚ Cancer: Obesity is associated with an increased risk of several types of cancer, including breast cancer, colorectal cancer, endometrial cancer, esophageal cancer, kidney cancer, liver cancer, pancreatic cancer, and prostate cancer. Excess body fat can promote inflammation, alter hormone levels, and affect cell growth and proliferation, contributing to carcinogenesis.
- ✚ Respiratory Problems: Obesity is a risk factor for respiratory problems such as obstructive sleep apnea, obesity hypoventilation syndrome, asthma, and chronic obstructive pulmonary disease (COPD). Excess body weight can lead to mechanical compression of the airways, reduced lung volume, and impaired lung function.
- ✚ Musculoskeletal Disorders: Obesity increases the risk of musculoskeletal disorders such as osteoarthritis, back pain, joint pain, and mobility limitations. Excess body weight places added stress on the joints, particularly weight-bearing joints such as the knees, hips, and spine, leading to cartilage degeneration, inflammation, and pain.

- ✚ Gastrointestinal Disorders: Obesity is associated with an increased risk of gastrointestinal disorders such as gastroesophageal reflux disease (GERD), gallbladder disease, fatty liver disease (nonalcoholic fatty liver disease or NAFLD), and pancreatitis. Excess body fat can disrupt normal digestive function, impair liver metabolism, and increase the risk of gallstones and pancreatic inflammation.
- ✚ Psychological and Social Consequences: Obesity can have significant psychological and social consequences, including depression, anxiety, low self-esteem, social stigma, discrimination, and impaired quality of life. Negative attitudes and stereotypes about obesity can contribute to weight bias and discrimination in healthcare, education, employment, and other settings.

The causes of obesity are multifactorial and involve a complex interplay of genetic, environmental, behavioral, socioeconomic, and cultural factors. Key contributors to the obesity epidemic include:

- ✚ Unhealthy Diet: Diets high in processed foods, refined carbohydrates, added sugars, unhealthy fats, and excessive calories contribute to weight gain and obesity. Poor dietary habits, such as excessive calorie intake, frequent consumption of fast food and sugary beverages, irregular meal patterns, and emotional eating, promote energy imbalance and weight gain.
- ✚ Sedentary Lifestyle: Physical inactivity and sedentary behaviors, such as prolonged sitting, screen time (television, computer, smartphone), and lack of regular exercise or recreational activity, contribute to energy imbalance and weight gain. Modern lifestyles characterized by increased mechanization, urbanization, transportation, and screen-based entertainment have reduced opportunities for physical activity and increased sedentary time.
- ✚ Environmental Factors: Environmental factors such as food availability, accessibility, affordability, portion sizes, food marketing, built environment (urban design, transportation infrastructure, parks, sidewalks), and neighborhood characteristics (safety, walkability) influence dietary choices, physical activity levels, and obesity prevalence. Socioeconomic disparities and food deserts (areas with limited access to healthy, affordable food) disproportionately affect low-income and marginalized communities, contributing to health inequities.
- ✚ Genetic Predisposition: Genetic factors play a role in susceptibility to obesity and influence individual differences in body weight, metabolism, appetite regulation, and fat storage. While genetic predisposition alone cannot explain the obesity epidemic, it interacts with environmental and behavioral factors to determine an individual's risk of obesity.
- ✚ Psychosocial Factors: Psychosocial factors such as stress, depression, anxiety, trauma, adverse childhood experiences (ACEs), emotional distress, and poor coping skills can contribute to overeating, binge eating, comfort eating, and other maladaptive eating behaviors that lead to weight gain and obesity. Food

may serve as a coping mechanism or source of pleasure and comfort in response to negative emotions or stressors.

- ✚ Preventing and managing obesity require a comprehensive, multidisciplinary approach that addresses the underlying causes and risk factors, promotes healthy behaviors, and supports individuals in achieving sustainable lifestyle changes. Key strategies for obesity prevention and management include:
- ✚ **Healthy Eating:** Adopting a balanced, nutritious diet that emphasizes whole, minimally processed foods such as fruits, vegetables, whole grains, lean proteins, and healthy fats can help control calorie intake, promote satiety, and support weight management. Portion control, mindful eating, and meal planning can also help prevent overeating and promote healthier food choices.
- ✚ **Regular Physical Activity:** Engaging in regular physical activity, including aerobic exercise, strength training, flexibility exercises, and recreational activities, can help burn calories, build muscle mass, improve metabolic health, and enhance overall well-being. Aim for at least 150 minutes of moderate-intensity aerobic activity or 75 minutes of vigorous-intensity aerobic activity per week, along with muscle-strengthening activities on two or more days per week.
- ✚ **Behavioral Changes:** Adopting healthy lifestyle behaviors such as setting realistic goals, self-monitoring (tracking food intake, physical activity, and weight), problem-solving, coping with stress, managing emotions, building social support networks, and seeking professional help (nutrition counseling, behavioral therapy, support groups) can help facilitate behavior change and long-term weight management.
- ✚ **Medical Management:** In some cases, medical management of obesity may be necessary, particularly for individuals with severe obesity or obesity-related complications. Medical treatments for obesity may include prescription medications (such as appetite suppressants, weight-loss medications, and anti-obesity drugs) and bariatric surgery (such as gastric bypass, gastric sleeve, and adjustable gastric banding) for individuals who have not achieved adequate weight loss with lifestyle interventions alone.
- ✚ **Public Health Interventions:** Population-based strategies and policy interventions aimed at creating supportive environments, promoting healthy behaviors, improving access to healthy food options, enhancing physical activity opportunities, regulating food advertising and marketing, implementing nutrition labeling, taxing sugar-sweetened beverages, and promoting urban planning and transportation policies that support active living can help prevent and reduce obesity on a societal level.
- ✚ **Health Equity:** Addressing social determinants of health, reducing health disparities, and promoting health equity are critical for addressing the obesity epidemic and improving population health outcomes. Efforts to address socioeconomic inequalities, promote food security, eliminate food deserts, improve access to healthcare, and create environments that support healthy

lifestyles for all individuals and communities are essential for reducing obesity prevalence and its associated health burden.

29. Blood Pressure

Definition:

- Blood pressure is the force exerted by circulating blood against the walls of the body's arteries, the major blood vessels. It is one of the principal vital signs and is crucial for ensuring that blood, oxygen, and nutrients are effectively delivered to organs and tissues throughout the body.

Components of Blood Pressure

1. Systolic Blood Pressure:

- The top number in a blood pressure reading.
- **Definition:** The pressure in the arteries when the heart beats (when the heart muscle contracts).
- **Normal Range:** Typically around 120 mmHg.

2. Diastolic Blood Pressure:

- The bottom number in a blood pressure reading.
- **Definition:** The pressure in the arteries when the heart is at rest between beats (when the heart muscle is relaxed).
- **Normal Range:** Typically around 80 mmHg.

Measurement of Blood Pressure

1. Instruments:

- **Sphygmomanometer:** A device consisting of an inflatable cuff to collapse and then release the artery under the cuff in a controlled manner, a measuring unit (mercury manometer or aneroid gauge) to measure the pressure, and a stethoscope to listen to arterial blood flow sounds (Korotkoff sounds).

2. Procedure:

- **Position:** The patient should be seated comfortably, with the arm supported at heart level.
- **Cuff Placement:** The cuff is wrapped snugly around the upper arm, just above the elbow.
- **Inflation:** The cuff is inflated until the brachial artery is occluded (usually around 180 mmHg).
- **Deflation and Measurement:** The cuff is slowly deflated while listening with a stethoscope for the Korotkoff sounds. The first appearance of these sounds is noted as the systolic pressure, and the point at which the sounds disappear is noted as the diastolic pressure.

Regulation of Blood Pressure

Blood pressure is regulated by various mechanisms involving the heart, blood vessels, kidneys, and endocrine system. These include:

1. Neural Regulation:

- **Baroreceptors:** Located in the carotid sinuses and aortic arch, baroreceptors sense changes in blood pressure and send signals to the brainstem to adjust heart rate, blood vessel diameter, and thus blood pressure.
- **Sympathetic and Parasympathetic Nervous System:** The sympathetic nervous system increases heart rate and constricts blood vessels, raising blood pressure, while the parasympathetic system reduces heart rate, lowering blood pressure.

2. Hormonal Regulation:

- **Renin-Angiotensin-Aldosterone System (RAAS):** Activated in response to low blood pressure, this system increases blood pressure by vasoconstriction and increasing blood volume through sodium and water retention.
- **Antidiuretic Hormone (ADH):** Promotes water retention by the kidneys, increasing blood volume and pressure.
- **Atrial Natriuretic Peptide (ANP):** Released by the heart in response to high blood pressure, ANP lowers blood pressure by promoting vasodilation and excretion of sodium and water.

3. Renal Regulation:

- The kidneys regulate blood pressure by controlling blood volume through the excretion or retention of water and electrolytes.

Clinical Significance

1. Hypertension:

- **Definition:** Chronic high blood pressure, typically defined as a reading of 140/90 mmHg or higher.
- **Causes:** Can be primary (essential hypertension with no identifiable cause) or secondary (due to underlying conditions such as kidney disease, endocrine disorders).
- **Consequences:** Increases the risk of heart disease, stroke, kidney disease, and other complications.
- **Management:** Lifestyle changes (diet, exercise, weight loss), medications (antihypertensives).

2. Hypotension:

- **Definition:** Abnormally low blood pressure, typically defined as a reading below 90/60 mmHg.
- **Causes:** Can result from dehydration, blood loss, severe infection (septicemia), heart problems, or endocrine disorders.
- **Consequences:** Can lead to dizziness, fainting, and shock in severe cases.
- **Management:** Addressing the underlying cause, increasing fluid and salt intake, medications to raise blood pressure if necessary.

Summary

Edema	– Fluid retention in the body tissues, swelling
Hyperemia	– Increased blood flow, redness of skin
Ischemia	– Restriction in blood supply to tissues
Normal Hemostasis	– Vaso constriction, Platelet plug, Clot formation
Thrombosis	- Formation of blood clot within a blood vessel
Disseminated Intravascular Coagulation	– Abnormal blood clotting and excessive bleeding throughout the
body	
Embolism	– When an embolus travels through the blood streams and becomes lodged in a blood vessel obstructing blood flow
Infarction	– Necrosis by sudden lack of blood supply
Shock	- Medical emergency characterized by inadequate blood flow to tissues
Chronic Venous Congestion	- Condition characterized by inadequate blood flow through the veins usually in the lower extremities
Bleeding Disorders	
Hemophilia	- Deficiency of VIII (Hemophilia A) and IX (Hemophilia B)
Van willerbrand Disease	- Deficiency of VWF factor
Leukemias	- Blood and Bone marrow cancer
Lymphomas	- Lymphatic system cancer
Hemorrhage	- Excessive bleeding Internally or Externally

MICROBIOLOGY AND IMMUNOPATHOLOGY

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Short Notes

BASIC

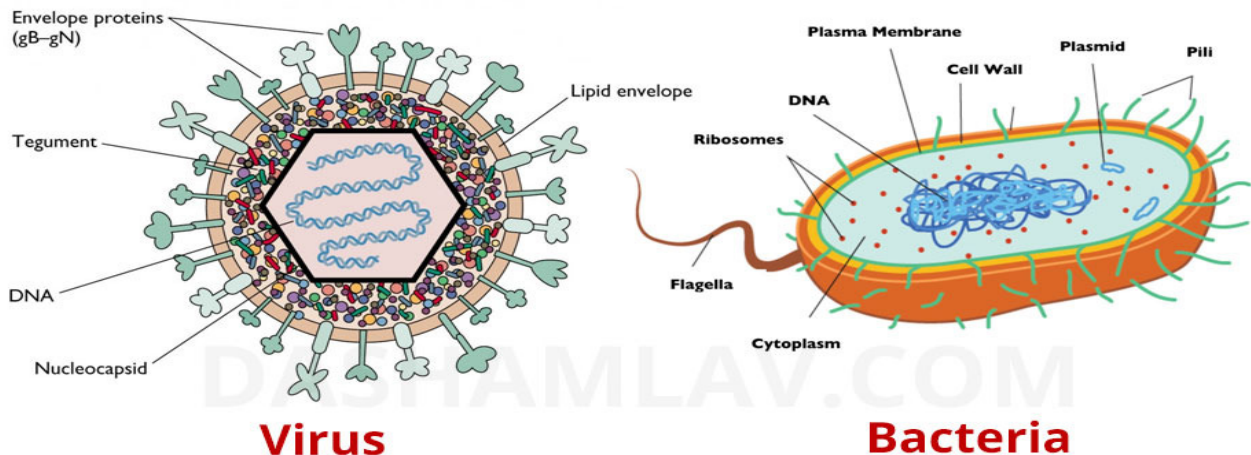
- ✚ Microbiology is the branch of science that focuses on the study of microorganisms, which are microscopic, unicellular, and cell-cluster organisms.
- ✚ This includes bacteria, viruses, fungi, protozoa, and algae. Microbiology encompasses various sub-disciplines such as bacteriology, virology, mycology, parasitology, and phycology.
- ✚ Immunopathology is a branch of medicine and biomedical science that studies diseases caused by dysfunctions of the immune system.
- ✚ This includes conditions resulting from an overactive immune response, an underactive immune response, or abnormal immune regulation. Immunopathology bridges the gap between immunology and pathology, focusing on how immune processes contribute to disease.

1. Bacteria, Virus and Fungi

- ✚ **Bacteria** are single-celled, prokaryotic microorganisms that are found in virtually every environment on Earth.
- ✚ They play essential roles in various biological processes, including nutrient cycling, decomposition, and even the functioning of human bodies.
- ✚ Bacteria are among the oldest forms of life, with a simple structure that allows them to thrive in diverse and often extreme conditions.
- ✚ **Viruses** are microscopic infectious agents that exist at the boundary between living and non-living entities.
- ✚ They cannot carry out metabolic processes or reproduce independently and must infect a host cell to replicate.
- ✚ Viruses infect all types of life forms, from animals and plants to microorganisms, including bacteria (bacteriophages).
- ✚ **Fungi** are a diverse group of eukaryotic organisms that include yeasts, molds, and mushrooms.
- ✚ They play crucial roles in ecosystems as decomposers, symbionts, and pathogens.
- ✚ Unlike plants, fungi do not perform photosynthesis; instead, they obtain nutrients through absorption after breaking down organic matter with enzymes.

2. Structure of Bacteria and Virus

Structural Differences Between Virus and Bacteria



3. List of Bacterial diseases

- ✚ Bacteria can cause a wide range of diseases in humans, animals, and plants.
- ✚ Here are some notable bacterial diseases:

- ✚ Tuberculosis (TB)

Causative Agent: *Mycobacterium tuberculosis*

Symptoms: Chronic cough, weight loss, fever, night sweats

Transmission: Airborne droplets

- ✚ Streptococcal Pharyngitis (Strep Throat)

Causative Agent: *Streptococcus pyogenes*

Symptoms: Sore throat, fever, swollen lymph nodes

Transmission: Respiratory droplets

- ✚ Pneumonia

Causative Agents: *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Mycoplasma pneumoniae*, and others

Symptoms: Cough, chest pain, fever, difficulty breathing

Transmission: Respiratory droplets

- ✚ Pertussis (Whooping Cough)

Causative Agent: *Bordetella pertussis*

Symptoms: Severe coughing fits, "whooping" sound, vomiting after coughing

Transmission: Respiratory droplets

- ✚ Lyme Disease

Causative Agent: *Borrelia burgdorferi*

Symptoms: Erythema migrans (bullseye rash), fever, fatigue, joint pain

Transmission: Tick bites

- ✚ Gonorrhea

Causative Agent: *Neisseria gonorrhoeae*

Symptoms: Painful urination, discharge, pelvic pain (women)

Transmission: Sexual contact

- ✚ Syphilis

Causative Agent: *Treponema pallidum*

Symptoms: Painless sores, rash, fever, swollen lymph nodes, potential organ damage if untreated

Transmission: Sexual contact

- ✚ Cholera

Causative Agent: *Vibrio cholerae*

Symptoms: Severe watery diarrhea, dehydration, electrolyte imbalance

Transmission: Contaminated water and food

4. List of Viral Diseases

- ✚ Viruses are responsible for a wide array of diseases in humans, animals, and plants.
- ✚ Here are some notable viral diseases:

✚ Influenza (Flu)

Causative Agents: Influenza A, B, and C viruses

Symptoms: Fever, chills, cough, sore throat, muscle aches, fatigue

Transmission: Respiratory droplets

✚ Common Cold

Causative Agents: Rhinoviruses, coronaviruses, adenoviruses

Symptoms: Runny nose, sore throat, cough, congestion, sneezing

Transmission: Respiratory droplets, direct contact

✚ HIV/AIDS

Causative Agent: Human Immunodeficiency Virus (HIV)

Symptoms: Weakening of the immune system, opportunistic infections, weight loss, fatigue

Transmission: Blood, sexual contact, mother-to-child during childbirth or breastfeeding

✚ COVID-19

Causative Agent: SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2)

Symptoms: Fever, cough, shortness of breath, loss of taste or smell, fatigue, complications like pneumonia

Transmission: Respiratory droplets, aerosols, contact with contaminated surfaces

✚ Hepatitis

Causative Agents: Hepatitis A, B, C, D, and E viruses

Symptoms: Jaundice, fatigue, abdominal pain, liver inflammation

Transmission: Varies by type (e.g., contaminated food and water for Hepatitis A and E, blood and bodily fluids for Hepatitis B, C, and D)

✚ Herpes Simplex Virus (HSV) Infections

Causative Agents: HSV-1 (oral herpes), HSV-2 (genital herpes)

Symptoms: Blisters and sores around the mouth or genitals, itching, pain

Transmission: Direct contact with infected skin or mucous membranes

5. List of Fungal Diseases

- ✚ Fungal diseases, or mycoses, affect humans, animals, and plants.
- ✚ Here are some notable fungal diseases across different categories:

✚ Human Fungal Diseases Athlete's Foot (Tinea Pedis)

Causative Agents: Trichophyton, Epidermophyton, and Microsporum species

Symptoms: Itching, scaling, and redness of the feet, especially between the toes

Transmission: Direct contact with infected skin or contaminated surfaces

✚ Ringworm (Tinea Corporis)

Causative Agents: Trichophyton, Epidermophyton, and Microsporum species

Symptoms: Red, circular, itchy rash with a clear center

Transmission: Direct contact with infected individuals or animals, contaminated objects

✚ Candidiasis

Causative Agent: *Candida* species (especially *Candida albicans*)

Symptoms: White patches in the mouth (oral thrush), itching and discharge in the genital area (vaginal yeast infection), skin infections, systemic infections in immunocompromised individuals

Transmission: Overgrowth of *Candida*, not typically person-to-person

✚ Histoplasmosis

Causative Agent: *Histoplasma capsulatum*

Symptoms: Fever, cough, fatigue, sometimes severe respiratory issues

Transmission: Inhalation of spores from contaminated soil, especially in areas with bird or bat droppings

✚ Aspergillosis

Causative Agent: *Aspergillus* species (especially *Aspergillus fumigatus*)

Symptoms: Respiratory issues, allergic reactions, invasive disease in immunocompromised individuals

Transmission: Inhalation of spores from the environment

✚ Cryptococcosis

Causative Agent: *Cryptococcus neoformans*

Symptoms: Lung infection, meningitis, especially in immunocompromised individuals

Transmission: Inhalation of spores from contaminated soil or bird droppings

✚ Blastomycosis

Causative Agent: *Blastomyces dermatitidis*

Symptoms: Fever, cough, muscle pain, sometimes severe lung and skin infections

Transmission: Inhalation of spores from contaminated soil or decaying organic matter

6. HIV/AIDS

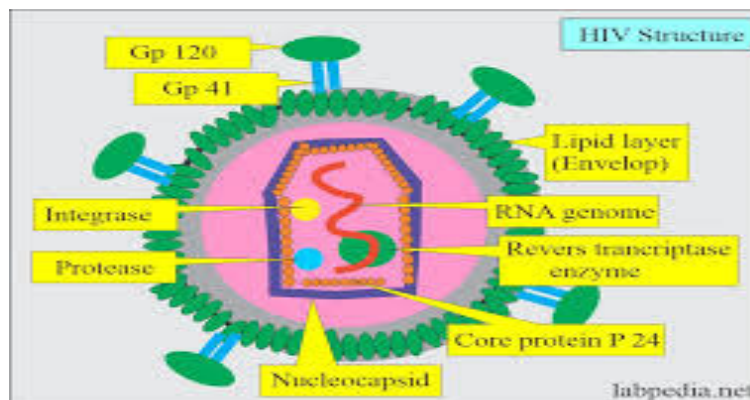
✚ Human Immunodeficiency Virus (HIV) and Acquired Immunodeficiency Syndrome (AIDS) represent one of the most complex and challenging public health issues of the modern era.

✚ Let's delve into these interconnected topics with a detailed overview:

HIV:

✚ HIV is a lentivirus, belonging to the retrovirus family. It primarily targets and infects CD4+ T cells, which play a central role in coordinating the immune response.

✚ The virus contains genetic material in the form of RNA, which it uses to hijack the host cell's machinery to replicate and produce more virus particles.



Transmission Routes:

- ✚ HIV is transmitted through specific bodily fluids, including blood, semen, vaginal secretions, rectal fluids, and breast milk.
- ✚ Common modes of transmission include unprotected sexual intercourse, sharing contaminated needles or syringes among injecting drug users, and transmission from mother to child during childbirth, breastfeeding, or pregnancy.

Stages of HIV Infection:

- ✚ Acute HIV Infection: Following exposure, the virus rapidly replicates in the body. Many individuals may experience flu-like symptoms during this phase, but others may remain asymptomatic.
- ✚ Chronic HIV Infection (Asymptomatic Stage): Without treatment, HIV infection progresses to a chronic stage characterized by ongoing viral replication but without significant symptoms.
- ✚ Advanced HIV Infection (AIDS): AIDS is diagnosed when the immune system becomes severely compromised, typically indicated by a low CD4 cell count or the occurrence of opportunistic infections or cancers.

AIDS:

Definition and Criteria:

- ✚ AIDS is the final stage of HIV infection, marked by a severely weakened immune system. It is defined by either a CD4 cell count below 200 cells/mm³ or the presence of specific opportunistic infections or cancers.
- ✚ Opportunistic infections are caused by organisms that take advantage of a weakened immune system, such as *Pneumocystis jirovecii* pneumonia (PCP), tuberculosis (TB), and certain fungal, viral, or bacterial infections.

Clinical Manifestations:

- ✚ AIDS-related symptoms can vary widely and may include persistent fever, night sweats, chronic diarrhea, unexplained weight loss, oral thrush, skin rashes, and neurological symptoms.
- ✚ Opportunistic infections and cancers associated with AIDS can affect various organ systems, leading to severe illness and, if untreated, death.

Prevention and Treatment:

Prevention Strategies:

- ✚ Safer Sex Practices: Consistent and correct use of condoms during sexual intercourse reduces the risk of HIV transmission.
- ✚ Harm Reduction Programs: Providing access to sterile needles and syringes for injecting drug users helps prevent HIV transmission through needle-sharing.
- ✚ Pre-Exposure Prophylaxis (PrEP): PrEP involves taking antiretroviral drugs before potential exposure to HIV to prevent infection.
- ✚ Post-Exposure Prophylaxis (PEP): PEP involves taking antiretroviral drugs after potential exposure to HIV to prevent infection.

Antiretroviral Therapy (ART):

- ✚ ART involves the use of combinations of antiretroviral drugs to suppress HIV replication, preserve immune function, and reduce the risk of HIV-related complications and transmission.

- ✚ When taken consistently and correctly, ART can allow people living with HIV to lead long and healthy lives while reducing their risk of transmitting the virus to others.

7. Basics of Microscope

- ✚ A microscope is an optical instrument that magnifies tiny objects or organisms to make them visible for detailed examination.
- ✚ It achieves this by using lenses and sometimes illumination techniques to enhance contrast and resolution.
- ✚ There are more types of microscopes available among them details of three microscopes given below

7.1 Light Microscope

- ✚ A light microscope, also known as an optical microscope, is a fundamental tool in scientific research, education, and medical diagnosis.
- ✚ It utilizes visible light and optical lenses to magnify and resolve the details of specimens. Here's a detailed overview of light microscopes:

Optical System:

Objective Lens:

- ✚ The primary lens closest to the specimen.
 - ✚ Determines the magnification and resolution of the microscope.
- Typically, light microscopes have multiple objective lenses with different magnification powers (e.g., 4x, 10x, 40x, 100x).

Eyepiece (Ocular):

- ✚ The lens through which the observer views the magnified image.
- ✚ Usually provides additional magnification (e.g., 10x or 15x).
- ✚ Together with the objective lens, it determines the total magnification of the microscope.

Condenser:

- ✚ Concentrates and focuses light onto the specimen.
- ✚ Located beneath the stage.
- ✚ Adjusting the condenser's aperture controls the amount and angle of light entering the specimen.

Illuminator:

- ✚ Provides the light source for illuminating the specimen.
- ✚ Can be a built-in light source (e.g., halogen bulb) or an external source.

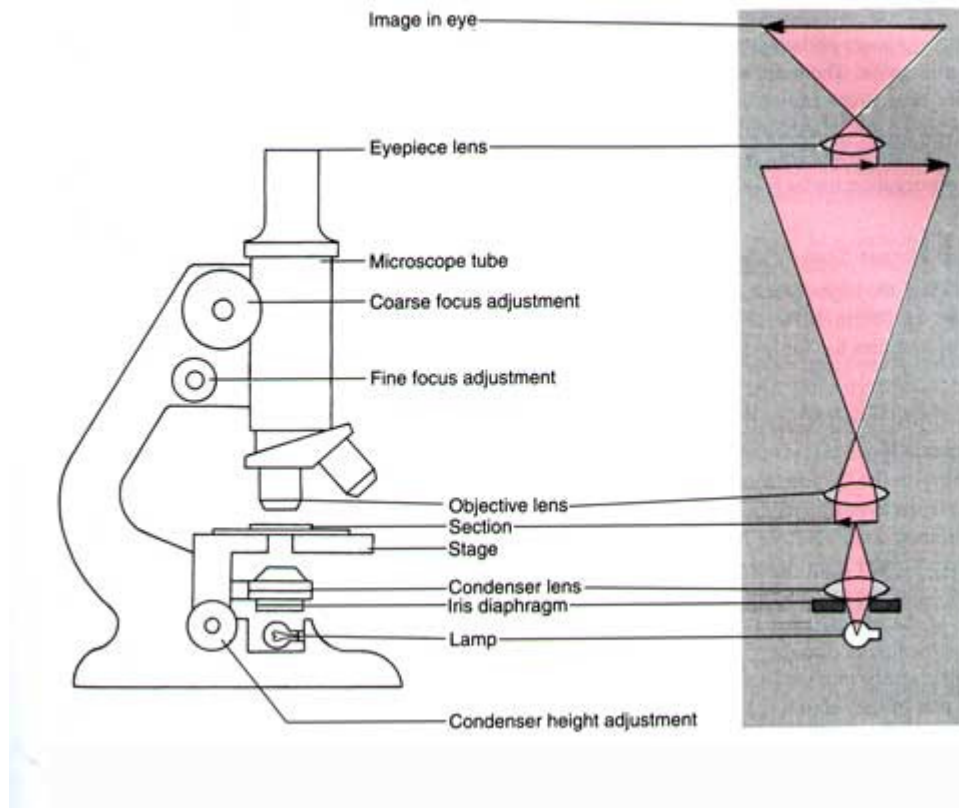
Specimen Stage and Focus:

Stage:

- ✚ Platform where the specimen is placed for observation.
- ✚ Typically includes clips or mechanical holders to secure the specimen in place.
- ✚ Some stages have mechanical controls for precise movement in X and Y directions.

Focus Adjustment:

- ✚ Allows for precise focusing of the specimen.
- ✚ Coarse adjustment knob: Used for initial focusing at low magnification.
- ✚ Fine adjustment knob: Allows for finer focusing, especially at higher magnifications.



Types of Light Microscopes:

Compound Microscope:

- ✚ Uses multiple lenses to achieve high magnification and resolution.
- ✚ Suitable for observing thin, transparent specimens, such as cells, tissues, and microorganisms.
- ✚ Commonly used in biological research, education, and clinical diagnosis.

Stereo Microscope (Dissecting Microscope):

- ✚ Provides a three-dimensional view of specimens.
- ✚ Suitable for observing larger, opaque objects, such as insects, plants, and electronic components.
- ✚ Used in fields like biology, geology, forensics, and manufacturing.

Applications:

Biological Research:

- ✚ Studying cellular structures, tissues, and microorganisms.
- ✚ Investigating biological processes, such as cell division and protein interactions.

Education:

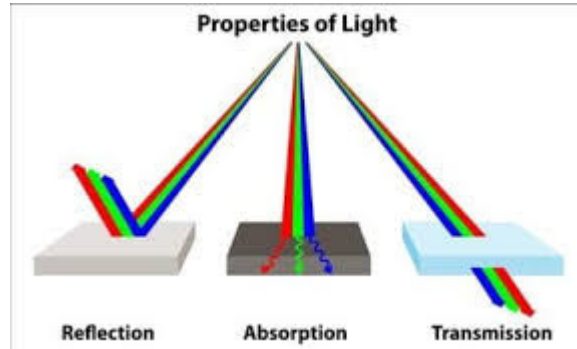
- ✚ Teaching fundamental concepts of biology, anatomy, and microscopy techniques.
- ✚ Allowing students to observe and explore microscopic worlds.

Clinical Diagnosis:

- ✚ Examining blood cells, tissue samples, and pathological specimens.
- ✚ Identifying microorganisms responsible for infectious diseases.

7.2 Transmission Electron Microscope

- ✚ The Transmission Electron Microscope (TEM) is a powerful microscopy technique that uses a beam of electrons to image the ultrastructure of specimens at incredibly high magnifications and resolutions.
- ✚ Here's an in-depth look at the Transmission Electron Microscope:



Principle of Operation:

Electron Beam Generation:

- ✚ Unlike light microscopes that use visible light, TEMs use a beam of electrons to illuminate specimens.
- ✚ Electrons are generated by an electron gun, typically from a heated tungsten filament or a field-emission source.
- ✚ The electron beam is accelerated to high energies (typically in the range of 50 to 400 kiloelectron volts, or keV) using electromagnetic fields.

Specimen Interaction:

- ✚ When the electron beam interacts with the specimen, it undergoes various interactions, including scattering, absorption, and diffraction.
- ✚ These interactions provide information about the specimen's composition, structure, and thickness.

Image Formation:

- ✚ Electrons that pass through the specimen are collected by a detector on the opposite side.
- ✚ The intensity and pattern of the transmitted electrons are used to create a highly detailed image of the specimen.

Components of a TEM:

Electron Gun:

- ✚ Generates the electron beam.
- ✚ Includes a cathode (electron source) and electromagnetic lenses to focus and shape the beam.

Vacuum System:

- ✚ Maintains a high vacuum environment inside the microscope to prevent electron scattering and absorption by air molecules

Specimen Holder:

- ✚ Holds the specimen in place and allows precise positioning for imaging.

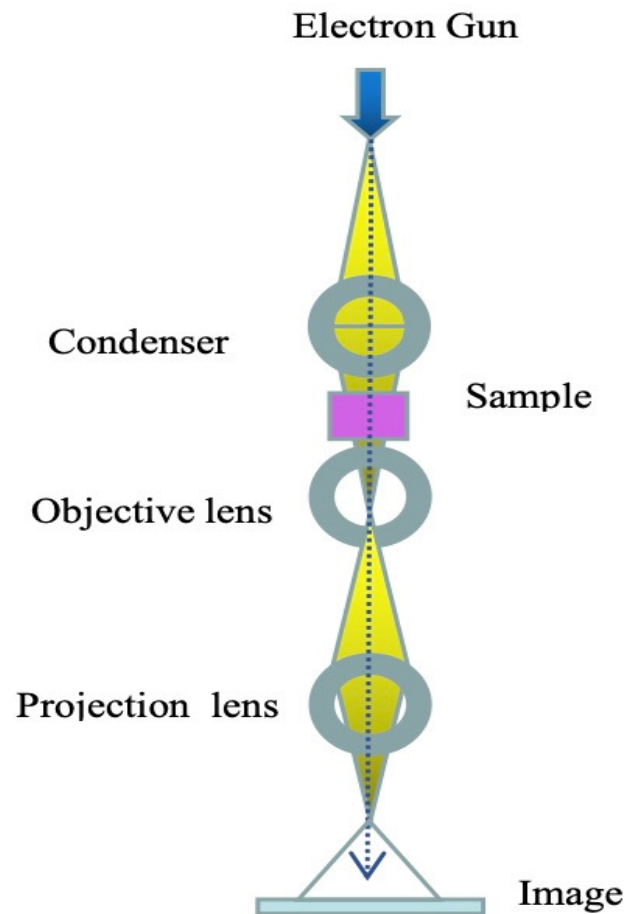
- Specimens are typically prepared as thin sections (less than 100 nanometers thick) to allow electron transmission.

Electromagnetic Lenses:

- Focus, condense, and deflect the electron beam to achieve high-resolution imaging.
- Consist of magnetic coils or electromagnetic lenses controlled by computer systems.

Detector System:

- Collects and records the transmitted electrons to generate the final image.
- Includes fluorescent screens, photographic films, or digital cameras for image capture.



Applications of TEM:

Cellular and Molecular Biology:

- Examining cellular organelles, protein structures, and macromolecular complexes.
- Investigating cellular processes such as mitosis, apoptosis, and membrane dynamics.

Material Science:

- Analyzing the structure and composition of materials at the atomic and nanometer scales.
- Studying defects, crystallography, and interfaces in materials such as metals, ceramics, polymers, and nanomaterials.

Nanotechnology:

- Characterizing nanoparticles, nanotubes, and nanomaterials for various applications in electronics, catalysis, and biomedical engineering.
- Investigating nanoscale phenomena such as quantum confinement and surface effects.

Medical Research:

- ✚ Visualizing viruses, bacteria, and other pathogens at the ultrastructural level.
- ✚ Studying the interactions between pathogens and host cells in infectious diseases.

7.3 Scanning Electron Microscope

- ✚ The Scanning Electron Microscope (SEM) is a powerful imaging technique that provides high-resolution three-dimensional images of the surface topography of specimens.
- ✚ Here's a comprehensive overview of the Scanning Electron Microscope:

Principle of Operation:

Electron Beam Scanning:

- ✚ Like the Transmission Electron Microscope (TEM), the SEM uses a beam of electrons for imaging.
- ✚ However, in SEM, the electron beam scans across the specimen's surface rather than transmitting through it.
- ✚ The electron beam interacts with the specimen, generating various signals that are used to create an image.

Signal Detection:

- ✚ When the electron beam strikes the specimen, it induces several interactions, including secondary electrons, backscattered electrons, and characteristic X-rays.
- ✚ These signals carry information about the specimen's topography, composition, and material contrast.

Image Formation:

- ✚ Signals emitted from the specimen are collected by detectors and processed to generate a grayscale image.
- ✚ Secondary electrons provide detailed topographical information, while backscattered electrons offer compositional contrast.

Components of an SEM:

Electron Source:

- ✚ Typically a tungsten filament or field-emission source that generates a beam of electrons.
- ✚ The electron beam is accelerated to high energies (ranging from a few kiloelectron volts to tens of kiloelectron volts).

Electromagnetic Lenses:

- ✚ Focus, scan, and deflect the electron beam to achieve high-resolution imaging.
- ✚ Consist of magnetic coils or electromagnetic lenses controlled by computer systems.

Specimen Stage:

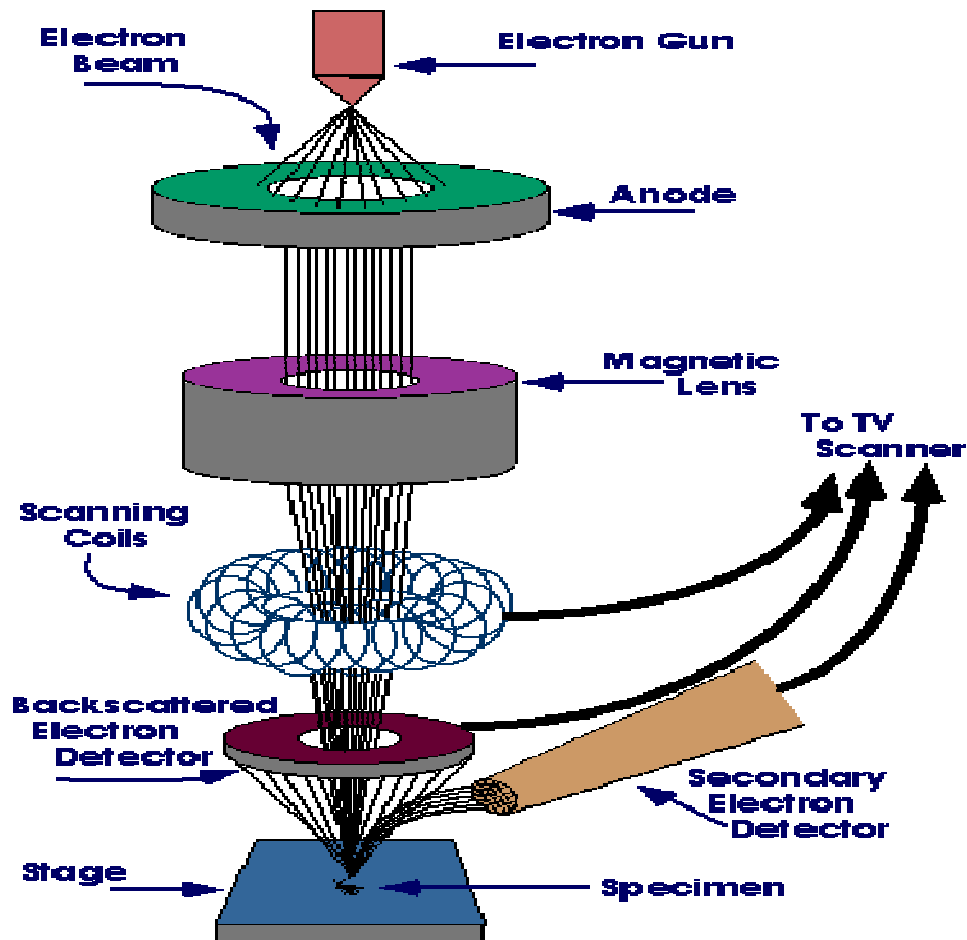
- ✚ Holds the specimen in place and allows precise positioning for imaging.
- ✚ May include heating or cooling capabilities for temperature control.

Detectors:

- ✚ Secondary Electron Detector: Collects secondary electrons emitted from the specimen's surface, providing detailed topographical information.
- ✚ Backscattered Electron Detector: Collects backscattered electrons, offering compositional contrast based on atomic number variations.
- ✚ X-ray Detector: Detects characteristic X-rays emitted from the specimen, enabling elemental analysis (Energy-Dispersive X-ray Spectroscopy, or EDS).

Vacuum System:

- ✚ Maintains a high vacuum environment inside the microscope to prevent electron scattering and absorption by air molecules.



Applications of SEM:

Material Science:

- ✚ Characterizing the surface morphology, texture, and composition of materials such as metals, ceramics, polymers, and composites.
- ✚ Analyzing surface defects, coatings, and adhesion properties in materials science and engineering.

Geology:

- ✚ Studying geological samples, including minerals, rocks, and fossils, to understand their formation processes and structural features.
- ✚ Investigating soil properties, particle size distribution, and mineral composition for environmental and geological studies.

Biology and Life Sciences:

- ✚ Imaging biological specimens, including cells, tissues, and microorganisms, to study surface structures and interactions.
- ✚ Visualizing biological samples with contrasting techniques such as gold coating, freeze-fracture, and critical point drying.

Nanotechnology:

- ✚ Characterizing nanomaterials, nanoparticles, and nanostructures for applications in electronics, catalysis, and biomedicine.
- ✚ Investigating nanoscale phenomena such as surface plasmon resonance, nanotube growth, and self-assembly processes.

8. Natural and Artificial Immunity

- ✚ Immunity refers to the body's ability to resist infections and diseases caused by pathogens such as bacteria, viruses, fungi, and parasites.
- ✚ It involves a complex network of cells, tissues, and organs working together to defend against harmful invaders while distinguishing them from the body's own healthy tissue.
- ✚ The immune system's primary goal is to detect, neutralize, and eliminate pathogens.
- ✚ There are two types of immunity
 1. Innate (Native) Immunity
 2. Acquired (Adaptive) Immunity
- ✚ Acquired immunity can be subdivided into two types
 1. Active Immunity
 2. Passive Immunity
- ✚ These two immunities have further subdivision of
 1. Active Natural Immunity
 2. Active Artificial Immunity
 3. Passive natural Immunity
 4. Passive Artificial Immunity

1. Active Natural Immunity

Description:

- ✚ Active natural immunity occurs when a person is exposed to a live pathogen, contracts the disease, and then recovers. During this process, the immune system responds to the infection, and memory cells are created.

Mechanism:

- ✚ When exposed to a pathogen, the body's immune system responds by recognizing the pathogen's antigens.
- ✚ B cells are activated to produce antibodies specific to the pathogen.
- ✚ T cells are also activated to help B cells and directly kill infected cells.
- ✚ Memory B and T cells are formed, which "remember" the pathogen for future encounters.

Characteristics:

- ✚ Long-lasting: Usually provides long-term immunity due to the formation of memory cells.
- ✚ Pathogen-specific: The immunity is specific to the pathogen that caused the infection.
- ✚ Natural Process: Occurs naturally without medical intervention.

Example:

- ✚ Recovery from Chickenpox: After recovering from chickenpox, a person usually has long-term immunity against the virus.

2. Active Artificial Immunity

Description:

- ✚ Active artificial immunity is acquired through deliberate exposure to a pathogen or its antigens via vaccination. Vaccines stimulate the immune system to produce a response without causing the disease.

Mechanism:

- ✚ A vaccine containing antigens (weakened, killed, or parts of the pathogen) is introduced into the body.
- ✚ The immune system recognizes these antigens as foreign and mounts a response.
- ✚ B cells produce antibodies, and T cells assist in the immune response.
- ✚ Memory B and T cells are generated, which provide long-term immunity.

Characteristics:

- ✚ Long-lasting: Provides long-term immunity through the formation of memory cells.
- ✚ Pathogen-specific: Immunity is specific to the pathogen included in the vaccine.
- ✚ Medical Intervention: Requires vaccination.

Example:

- ✚ MMR Vaccine: The measles, mumps, and rubella (MMR) vaccine stimulates immunity against these diseases without causing them.

3. Passive Natural Immunity

Description:

- ✚ Passive natural immunity is acquired naturally when antibodies are transferred from one individual to another without medical intervention.
- ✚ This often occurs from mother to child.

Mechanism:

- ✚ Antibodies are transferred from the mother to the baby across the placenta during pregnancy.
- ✚ After birth, antibodies are also passed through breast milk, especially colostrum, the first milk produced.

Characteristics:

- ✚ Immediate: Provides immediate protection to the newborn.
- ✚ Short-term: The immunity is temporary and lasts only a few months as the transferred antibodies eventually degrade.
- ✚ No Memory: The recipient's immune system does not produce memory cells.

Example:

- ✚ Maternal Antibodies: A newborn baby receives maternal antibodies against various diseases through the placenta and breast milk.

4. Passive Artificial Immunity

Description:

- ✚ Passive artificial immunity involves the transfer of antibodies from an immune individual to a non-immune individual through medical intervention.
- ✚ This provides immediate protection against specific pathogens.

Mechanism:

- ✚ Antibodies are collected from the blood of immune individuals or produced in the lab.
- ✚ These antibodies are then administered to the recipient through an injection or infusion.

Characteristics:

- ✚ Immediate: Provides immediate protection upon administration.
- ✚ Short-term: The immunity is temporary and lasts for weeks to months as the antibodies eventually degrade.
- ✚ No Memory: The recipient's immune system does not produce memory cells.

Example:

- ✚ Rabies Post-Exposure Prophylaxis: After potential exposure to rabies, rabies immunoglobulin (containing antibodies) is administered to provide immediate protection.

9. Immunological Techniques

- ✚ Immunological techniques are a vital toolkit for researchers and healthcare professionals engaged in studying the immune system, diagnosing diseases, and developing treatments.
- ✚ These techniques encompass a diverse array of laboratory methods designed to analyze various aspects of the immune response, including the detection and characterization of antigens, antibodies, immune cells, and cytokines.
- ✚ By leveraging the specificity and sensitivity of immune interactions, these techniques enable precise and detailed investigations into the complexities of immune function.
- ✚ Here we are going to see about 4 immunological techniques
 1. Immune diffusion
 2. Immuno electrophoresis
 3. Radio Immuno Assay
 4. Enzyme linked Immuno Sorbent Assay

9.1 Immuno diffusion

- ✚ Immunodiffusion, which is used to detect and quantify antigens or antibodies in a sample based on their diffusion through a gel matrix.
- ✚ Immunodiffusion assays are valuable tools in immunology research, clinical diagnostics, and vaccine development.

Principle of Immunodiffusion:

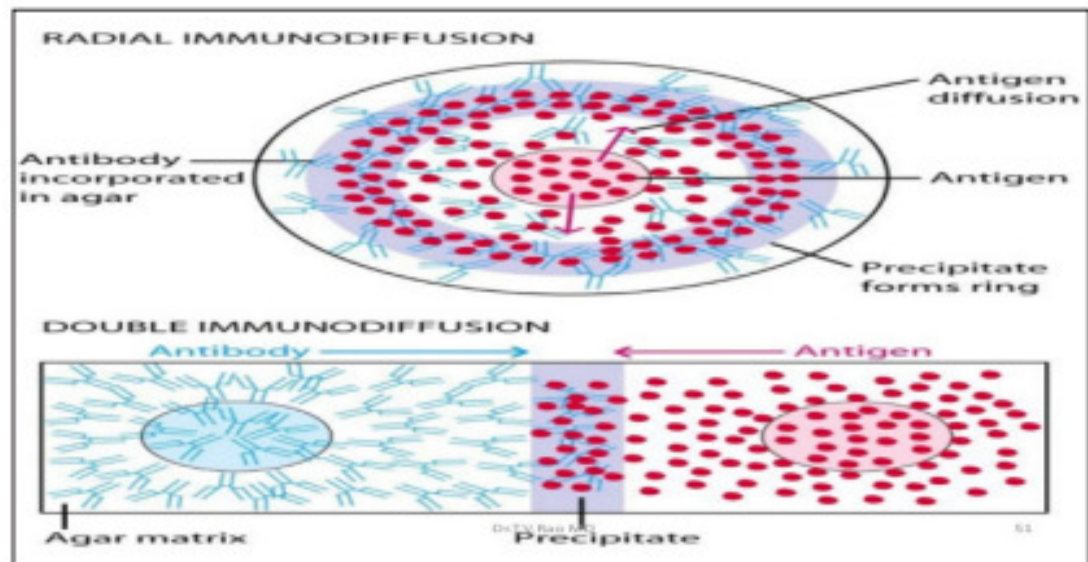
- ✚ In immunodiffusion, antigens and antibodies diffuse through a semi-solid medium, such as agarose or agar gel, forming visible precipitin lines where antigen-antibody complexes form.
- ✚ The formation of these lines is indicative of the presence and quantity of specific antigens or antibodies in the sample.

Types of Immunodiffusion:**Single Radial Immunodiffusion (SRID):**

- ✚ In SRID, a well is made in the agarose gel, and antigen-containing samples are added to the wells. As the antigen diffuses radially outward from the wells, it encounters antibodies incorporated into the gel. Precipitin lines form at the point where the antigen and antibody concentrations reach equivalence. The size of the precipitin ring is proportional to the antigen concentration.

Double Immunodiffusion (Ouchterlony Technique):

- ✚ In double Immunodiffusion, both antigen and antibody are allowed to diffuse through the gel from separate wells. If the antigen and antibody react, a visible line of precipitation forms where they meet. By observing the patterns of precipitation lines, the presence of specific antigens or antibodies and their relative concentrations can be determined.



Applications of Immunodiffusion:

- ✚ **Disease Diagnosis:** Immunodiffusion assays are used in clinical laboratories to diagnose infectious diseases, autoimmune disorders, and immunodeficiencies by detecting specific antigens or antibodies in patient samples.
- ✚ **Vaccine Development:** Immunodiffusion techniques are employed to quantify antigen content in vaccines, ensuring their potency and consistency. They are also used to assess the presence of antibodies in vaccinated individuals to determine immune responses.
- ✚ **Research:** Immunodiffusion is widely used in immunology research to study antigen-antibody interactions, antibody production, and immune system function. It allows researchers to characterize proteins, identify antigens, and investigate immune responses in various experimental settings.

9.2 Immuno-electrophoresis

- ✚ Immuno-electrophoresis is a laboratory technique used to analyze the presence and concentration of proteins in a sample, particularly serum or other body fluids.
- ✚ This technique combines the principles of electrophoresis and immunodiffusion to separate and identify proteins based on their size, charge, and antigenic properties.

Electrophoresis:

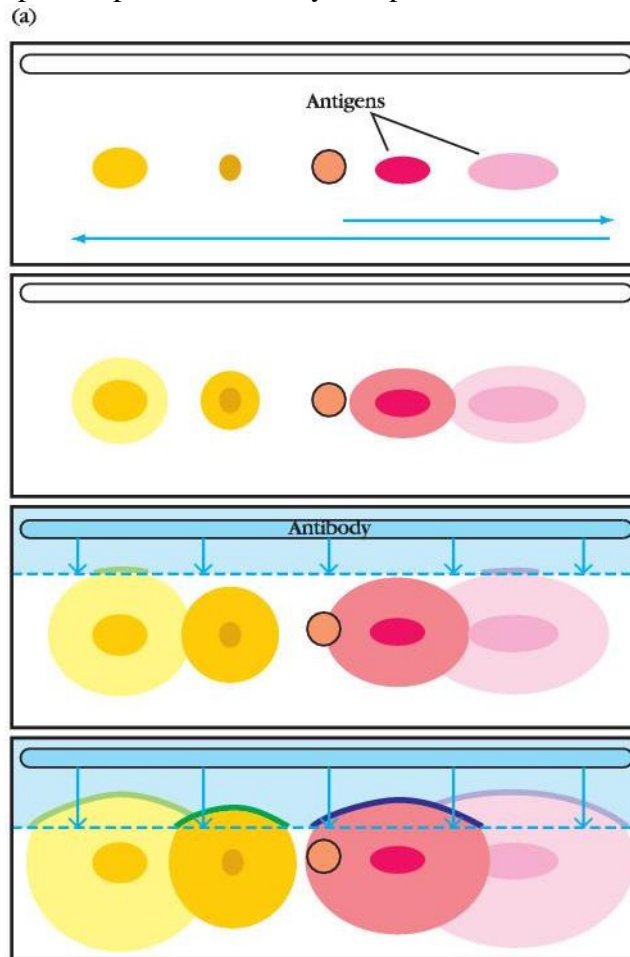
- The sample (e.g., serum) is first subjected to electrophoresis, a process that separates proteins based on their size and charge by applying an electric current. The proteins migrate through a gel, usually agarose, forming distinct bands.

Antiserum Application:

- After electrophoresis, a trough is cut parallel to the protein bands in the gel. Antisera containing antibodies specific to the proteins of interest are added to this trough.

Immunodiffusion:

- The antibodies and proteins diffuse towards each other in the gel. When they meet, they form precipitin lines (precipitation arcs) if there is an antigen-antibody reaction. Each arc corresponds to a specific protein-antibody complex.



Analysis:

- The resulting pattern of arcs is analyzed to determine the presence and quantity of specific proteins. Each arc's position and intensity provide information about the protein's characteristics and concentration.

Applications

- Diagnosis of Diseases:** Immunoelectrophoresis can help diagnose conditions characterized by abnormal protein levels, such as multiple myeloma, immunodeficiencies, and liver diseases.
- Protein Purity and Characterization:** It is used in research and biochemistry to assess protein purity and characterize complex protein mixtures.

- ✚ Quality Control in Biotechnology: Ensures the quality and consistency of protein products in pharmaceuticals and biotechnology industries.

Advantages

- ✚ Specificity: Combines the specificity of antibodies with the resolving power of electrophoresis.
- ✚ Visual Representation: Provides a clear visual representation of different proteins and their interactions with antibodies.

Limitations

- ✚ Complexity and Time: More complex and time-consuming than some other techniques like ELISA (Enzyme-Linked Immunosorbent Assay).
- ✚ Quantitative Precision: Less precise in quantifying proteins compared to some other modern techniques.

9.3 Radioimmunoassay

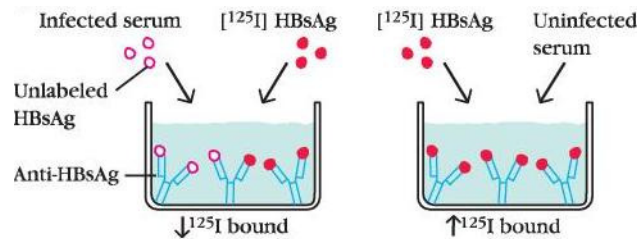
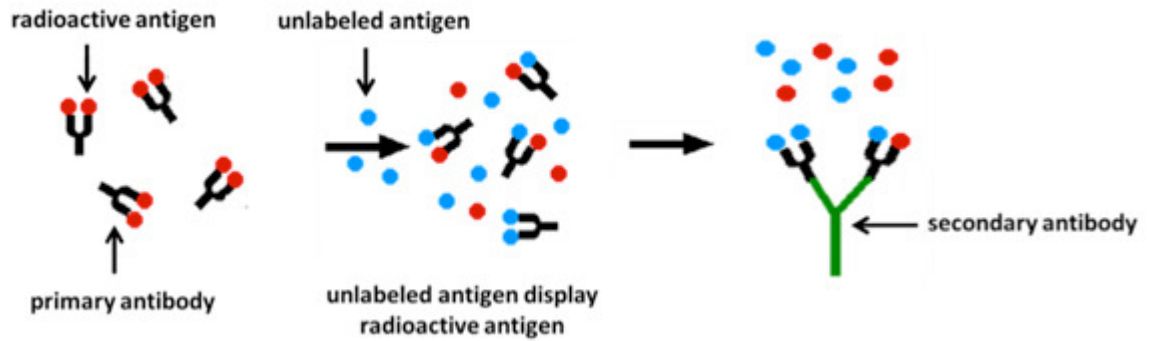
- ✚ Radioimmunoassay (RIA) is a sensitive and specific laboratory technique used to measure concentrations of antigens (such as hormones, drugs, or proteins) in various biological samples.
- ✚ It was first developed in the 1960s by Rosalyn Yalow and Solomon Berson, a breakthrough that earned Yalow the Nobel Prize in Physiology or Medicine in 1977.

Principles of Radioimmunoassay

- ✚ RIA is based on the competitive binding principle and involves the use of radioactively labeled substances.

Procedure

- ✚ Preparation of Radioactive Antigen: The antigen to be measured is labeled with a radioactive isotope, commonly iodine-125 (I-125).
- ✚ Competition Reaction: The test sample containing an unknown amount of the same antigen is mixed with a fixed amount of the radioactively labeled antigen and a specific antibody.
- ✚ Both the labeled and unlabeled antigens compete for binding sites on the antibody.
- ✚ Formation of Antigen-Antibody Complexes: The mixture is incubated to allow the formation of antigen-antibody complexes.
- ✚ Separation: The bound (antigen-antibody complex) and free (unbound) antigens are then separated.
- ✚ This can be done using various methods, such as precipitation, adsorption, or using a secondary antibody.
- ✚ Measurement: The radioactivity of either the bound or free antigen (depending on the method used) is measured using a gamma counter. The amount of radioactivity is inversely proportional to the concentration of the unlabeled antigen in the sample.
- ✚ Standard Curve and Quantification: A standard curve is generated by plotting the known concentrations of the unlabeled antigen against their corresponding radioactivity.
- ✚ The unknown concentration of the antigen in the test sample is then determined by comparing its radioactivity to the standard curve.



Applications

- ✚ Clinical Diagnostics: RIA is widely used to measure hormone levels (e.g., insulin, thyroxine, cortisol), detect drugs and their metabolites, and monitor therapeutic drug levels.
- ✚ Research: It is employed in research to study various physiological and pathological processes, including endocrinology, pharmacology, and immunology.
- ✚ Food and Environmental Testing: RIA is also used to detect contaminants and residues in food products and the environment.

Advantages

- ✚ High Sensitivity: RIA can detect very low concentrations of antigens, making it highly sensitive.
- ✚ Specificity: The use of specific antibodies ensures high specificity for the target antigen.
- ✚ Quantitative: Provides precise quantitative measurements.

Limitations

- ✚ Radioactive Hazards: The use of radioactive materials requires strict safety protocols and disposal procedures to protect laboratory personnel and the environment.
- ✚ Cost: The need for specialized equipment and reagents can make RIA relatively expensive.
- ✚ Regulatory Issues: Radioactive substances are subject to strict regulatory controls, which can limit the availability and use of RIA in some settings.

9.4 Enzyme Linked Immuno Sorbent Assay

- ✚ ELISA is a commonly used laboratory technique designed for detecting and quantifying soluble substances such as proteins, antibodies, hormones, and peptides.

- ✚ It is highly valued for its specificity, sensitivity, and versatility. The procedure relies on the specific interaction between an antigen and an antibody, combined with an enzyme-mediated color change, to indicate the presence and quantity of the substance of interest.

Types of ELISA

There are four main types of ELISA, each with distinct advantages and applications:

Direct ELISA

- ✚ Description: In this simplest form of ELISA, an antigen is directly immobilized on the assay plate, and a labeled antibody (conjugated with an enzyme) that is specific to the antigen is applied.
- ✚ Advantages: Fewer steps and reagents required, reducing the potential for error.
- ✚ Disadvantages: Less flexibility in signal amplification and often lower sensitivity.

Indirect ELISA:

- ✚ Description: The antigen is immobilized on the plate, followed by an unlabeled primary antibody specific to the antigen. A labeled secondary antibody, which binds to the primary antibody, is then used for detection.
- ✚ Advantages: Greater sensitivity due to signal amplification from multiple secondary antibodies binding to each primary antibody. Flexibility in using different secondary antibodies.
- ✚ Disadvantages: Requires additional steps and reagents, potentially increasing the complexity and time of the assay.

Sandwich ELISA:

- ✚ Description: This method involves a capture antibody that is immobilized on the plate, which captures the antigen from the sample. A second, labeled detection antibody, which binds to a different epitope on the antigen, is then applied.
- ✚ Advantages: High specificity and sensitivity since the antigen is bound by two different antibodies. Suitable for complex samples where the antigen might be present in low concentrations.
- ✚ Disadvantages: More complex and costly due to the need for two specific antibodies.

Competitive ELISA:

- ✚ Description: This format involves a competitive binding process between the sample antigen and a labeled antigen for a limited number of binding sites on a specific antibody. The signal inversely correlates with the concentration of the antigen in the sample.
- ✚ Advantages: Useful for small antigens that might not have multiple epitopes or for detecting antibodies.
- ✚ Disadvantages: Can be less straightforward to interpret and requires careful optimization.

ELISA Procedure Steps

Coating:

- ✚ The antigen or antibody is immobilized on a 96-well microtiter plate by overnight incubation.

Blocking:

- ✚ Non-specific binding sites on the plate are blocked using a blocking buffer (e.g., BSA, non-fat milk) to prevent non-specific interactions.

Incubation with Primary Antibody:

- ✚ If using an indirect or sandwich ELISA, the primary antibody is added and incubated to allow binding to the target antigen.

Incubation with Secondary Antibody:

- For indirect ELISA, a secondary antibody conjugated with an enzyme (e.g., HRP or alkaline phosphatase) is added, which binds to the primary antibody.

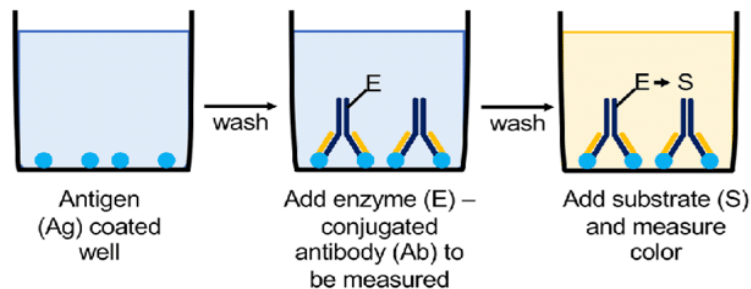
Substrate Addition:

- A substrate for the enzyme is added (e.g., TMB for HRP), which results in a color change due to the enzymatic reaction.

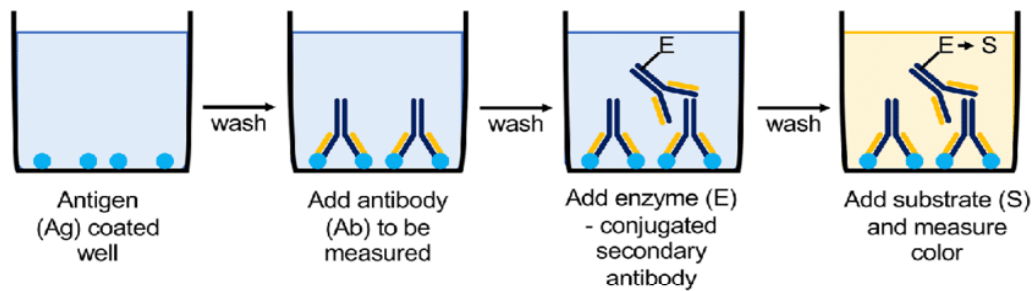
Signal Detection:

- The color change is measured using a spectrophotometer or ELISA reader at a specific wavelength. The intensity of the color correlates with the amount of antigen or antibody present in the sample.

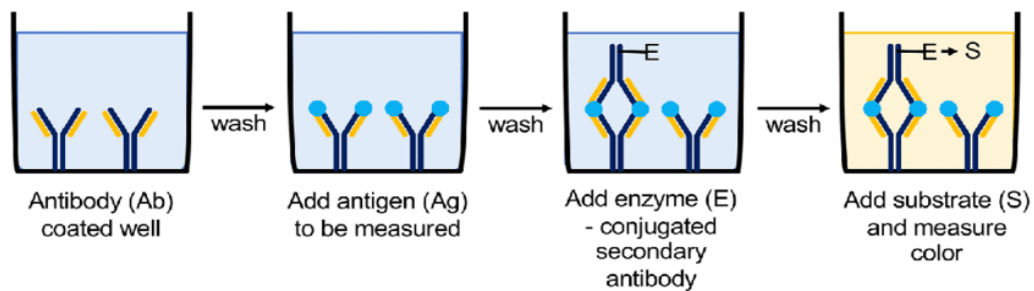
(a) Direct ELISA



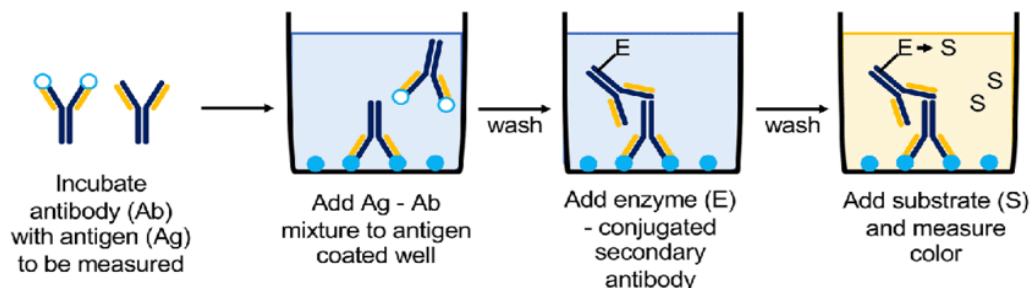
(b) Indirect ELISA



(c) Sandwich ELISA



(d) Competitive ELISA



Applications of ELISA

Medical Diagnostics:

- ✚ Detecting pathogens (e.g., viruses, bacteria) in patient samples.
- ✚ Measuring hormone levels (e.g., insulin, hCG).
- ✚ Detecting autoimmune diseases by identifying specific antibodies.

Research:

- ✚ Quantifying protein levels in biological samples.
- ✚ Investigating cell signaling pathways and protein interactions.

Food Industry:

- ✚ Detecting allergens or contaminants in food products.

Environmental Testing:

- ✚ Monitoring environmental pollutants and toxins.

Advantages of ELISA

- ✚ Sensitivity and Specificity: High sensitivity due to enzyme amplification and high specificity due to antigen-antibody interaction.
- ✚ Quantitative Results: Provides quantitative data that can be analyzed statistically.
- ✚ Versatility: Can be adapted to detect a wide range of substances.
- ✚ High Throughput: Suitable for screening large numbers of samples simultaneously

Limitations of ELISA

- ✚ Complexity and Cost: Some formats, like sandwich ELISA, require multiple antibodies and steps, increasing cost and complexity.
- ✚ Cross-reactivity: Potential for non-specific binding or cross-reactivity leading to false positives.
- ✚ Handling and Precision: Requires careful handling and precise pipetting to avoid variability and ensure accurate results.

10. Monoclonal Antibodies

- ✚ Monoclonal antibodies (mAbs) are antibodies that are made by identical immune cells, all of which are clones of a unique parent cell.
- ✚ They are designed to bind to a specific antigen with high specificity.
- ✚ Monoclonal antibodies have revolutionized many areas of medicine and research due to their ability to target specific molecules.

Discovery and Production

- ✚ The development of monoclonal antibodies began in the 1970s with the pioneering work of César Milstein and Georges Köhler, who introduced the hybridoma technology.
- ✚ This technique involves fusing an antibody-producing B cell with a myeloma (cancer) cell, creating a hybrid cell line known as a hybridoma.
- ✚ These hybridomas can be cultured indefinitely and produce large quantities of identical (monoclonal) antibodies.

Steps in Producing Monoclonal Antibodies

Antigen Preparation:

- ✚ An antigen, which is the target molecule for the antibody, is prepared and purified.

Immunization:

- ✚ An animal, often a mouse, is immunized with the antigen to stimulate the production of antibody-producing B cells.

Cell Fusion

- ✚ The spleen cells from the immunized animal, which contain B cells, are extracted and fused with myeloma cells using polyethylene glycol. This fusion creates hybridomas.

Selection:

- ✚ The hybridomas are cultured in a selective medium (HAT medium) that allows only the hybrid cells to survive.

Screening and Cloning:

- ✚ Hybridomas producing the desired antibody are identified through screening techniques (e.g., ELISA). These cells are then cloned to ensure monoclonality.

Antibody Production:

- ✚ The selected hybridomas are expanded in culture or injected into mice to produce ascites fluid, which is rich in monoclonal antibodies. Alternatively, they can be cultured in bioreactors for large-scale production.

Types of Monoclonal Antibodies

Murine Antibodies:

- ✚ Derived entirely from mice. These antibodies can be highly immunogenic when used in humans, potentially leading to human anti-mouse antibody (HAMA) responses.

Chimeric Antibodies:

- ✚ These antibodies are part mouse and part human. The variable regions are derived from mice, and the constant regions are human. This reduces immunogenicity compared to murine antibodies.

Humanized Antibodies:

- ✚ Mostly human, except for small mouse-derived sequences in the antigen-binding regions. They are less immunogenic than chimeric antibodies.

Fully Human Antibodies:

- ✚ Produced using genetically engineered mice or phage display libraries. These antibodies have minimal risk of immunogenicity and are well-tolerated in humans.

Mechanisms of Action

Neutralization:

- ✚ Directly binding to a pathogen or toxin, preventing it from interacting with its target.

Opsonization:

- ✚ Coating a pathogen to enhance its recognition and uptake by phagocytes.

Complement Activation:

- ✚ Triggering the complement cascade, leading to the lysis of the target cell.

Antibody-Dependent Cellular Cytotoxicity (ADCC):

- ✚ Binding to a target cell and marking it for destruction by natural killer (NK) cells.

Blocking Receptor-Ligand Interactions:

- ✚ Inhibiting interactions between cell surface receptors and their ligands, which can interfere with signaling pathways.

Modulating Immune Responses:

- ✚ Acting as immune checkpoint inhibitors to modulate the immune response against cancer cells.

Applications of Monoclonal Antibodies

Cancer Therapy:

- ✚ Targeting specific antigens on cancer cells to inhibit growth or induce cell death (e.g., Rituximab for non-Hodgkin's lymphoma, Trastuzumab for HER2-positive breast cancer).

Autoimmune Diseases:

- ✚ Modulating the immune response in diseases like rheumatoid arthritis (e.g., Adalimumab, Infliximab).

Infectious Diseases:

- ✚ Neutralizing pathogens or their toxins (e.g., Palivizumab for respiratory syncytial virus).

Diagnostic Tools:

- ✚ Used in diagnostic assays for detecting specific biomolecules (e.g., pregnancy tests, ELISA kits).

Targeted Drug Delivery:

- ✚ Conjugating antibodies with drugs, toxins, or radioactive substances to deliver them directly to target cells (e.g., Antibody-drug conjugates).

Advantages of Monoclonal Antibodies

Specificity:

- ✚ High specificity for their target antigen reduces off-target effects.

Versatility:

- ✚ Can be engineered for various applications, including therapeutic, diagnostic, and research uses.

Consistency:

- ✚ Batch-to-batch consistency due to the monoclonal nature ensures reliable performance.

Customizability:

- ✚ Can be modified to improve their efficacy, reduce immunogenicity, or alter their half-life.

Challenges and Limitations

Production Costs:

- ✚ High production costs and complex manufacturing processes can make monoclonal antibody therapies expensive.

Immunogenicity:

- ✚ Despite advancements, there is still a risk of immune responses against therapeutic antibodies, particularly non-human or chimeric antibodies.

Delivery and Stability:

- ✚ Some monoclonal antibodies may have stability issues or require specific delivery methods (e.g., intravenous infusion).

Resistance:

- ✚ Target cells, particularly in cancer, may develop resistance to monoclonal antibody therapy over time.